Identification of a covalent importin-5 inhibitor, goyazensolide from a collective synthesis of furanoheliangolides

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a) General information (Chemistry)

NMR spectra were recorded on AMX-300, AMX-400 and AMX-500 Bruker Avance spectrometers at 298 K with CDCl₃ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million, relative to chloroform (¹H, δ 7.26; ¹³C, δ 77.16) unless otherwise stated. Data for ¹H NMR are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuple, sept. = septuple, m = multiplet) and coupling constants. Infrared spectra (IR) were recorded on a Perkin-Elmer 1650 FT-IR spectrometer using neat samples on a diamond ATR Golden Gate sampler. High-resolution mass spectra (HRMS) were obtained on a Xevo G2 Tof spectrometer (Ionization mode: ESI positive polarity; Mobile phase: MeOH 100 µl/min). Optical rotations were recorded on OMNI Lab JASCO P-1030 polarimeter at 589 nm and are recorded as [α]₀° (concentration in grams/100 mL solvent). Analytical thin layer chromatography (TLC) was performed using 0.25 mm silica gel 60-F254 plates from Merck, using 250nm UV light as the visualizing agent and a solution of phosphomolybdic acid or KMnO₄ and heat as developing agents. Flash chromatography was performed using 200-400 mesh silica gel. Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated. Reverse phase column chromatography was performed using Isolera Biotage using SNAP Cartridge KP-C18-HS of 60 g or 12 g. The X-ray diffraction data was collected on an Agilent Supernova diffractometer equipped with an ATLAS CCD detector using Cu radiation. The enantiomeric excess (ee) was determined by HPLC analysis. Chiral HPLC analysis was performed on Waters Acquity UPC2 with column OJ-H. All reagents were used as supplied by Aldrich, Fluka, Acros or Strem and used without purification unless otherwise noted. All reactions were carried out in oven-dried glassware under nitrogen atmosphere unless otherwise noted.

Safety Statement

No unexpected or unusually high safety hazards were encountered.
b) Summary of synthesized natural products (Figure S1) and other structurally similar natural products (Figure S2)

**Figure S1.** Isolation, structure and activity of compounds 1-17.
**Atriplacilide-tiglate (5)**

**Isolation**
Eremotherus australis

$^1$H NMR, reassignment as C$_2$ lactone
Phytochemistry, 1980, 18, 2665-2668

**Atriplacilide-tiglate (6)**

**Isolation**
Eremotherus crotonoides

$^1$H NMR, reassignment as C$_2$ lactone
Phytochemistry, 1982, 21, 1669-1673

**Mannose alcohols**
J. Braz. Chem. Soc. 2005, 16, 677-680

**Whole assignment by us**
(9C, 11C, 14$^1$H COSY, HSQC, HMBC, NOESY)

**Activity**

Cytostatic
IC$_{50}$ 0.58 µM

**Isolation**

Calaxin (8) - continued

Calea pilosa
Phytochemistry, 1981, 20, 743-749

Calea species

Phytochemistry, 1981, 20, 1643-1647

Saccharum aestivum

Biochem. Syst. Ecol. 1991, 19, 523

Heliconia obacra
Phytochemistry, 1982, 21, 1669-1673

**8-epi-Atriplacilide-tiglate (10)**

**Isolation**

Isocarpa arypepsiloxalis $^1$H NMR
Phytochemistry, 1978, 17, 471-474

Calea pilosa

Calea moric

Phytochemistry, 1981, 20, 743-749

**Bacopa monnieri**

Phytochemistry, 1981, 20, 1633-1642

**Cucurbitaceae**

Phytochemistry, 1982, 21, 2117-2118

**Heliconia species**

Biochem. Syst. Ecol. 1989, 17, 519-528

**Heliconia sanganetusa**

Phytochemistry, 1991, 30, 1861-1867

Vigorea species

Flora, 1998, 69, 80-87

**Whole assignment by us**
(9C, 11C, 14$^1$H COSY, HSQC, HMBC, NOESY)

**Activity**

Antibacterial activity

Fitoterapia, 1998, 69, 80-87

NF-kB p65 inhibition

QSAR, IC$_{50}$ 0.5 µM

J. Med. Chem. 2004, 47, 9042-9054

J. Med. Chem. 2006, 49, 2241-2252

Antileishmanial

IC$_{50}$ 872 µM, related Mck, DODEN

Eur. J. Med. Chem. 2018, 127, 852-866

**Isolation**

**8-epi-Lychonilopide (15-deoxysudinol A, 9)**

**Isolation**

Calea pilosa $^1$H NMR
Phytochemistry, 1981, 20, 743-749

Dipteryx helminthica
Phytochemistry, 1981, 20, 1077-1080

Calea convallaria
Phytochemistry, 1982, 21, 2593-2596

Calea villosa
Phytochemistry, 1982, 21, 2117-2121

Heliconia obacra
Phytochemistry, 1982, 21, 2035-2040

Calea hymenocalyx
Phytochemistry, 1982, 21, 2045-2048

Calea involucrata $^1$H NMR

Calea involucrata $^1$H NMR
Phytochemistry, 1982, 21, 464-465

Heliconia obtusiloba
J. Nat. Prod. 1984, 47, 1021-1023

Calea diverrucata
J. Nat. Prod. 1985, 48, 302-306

Heliconia obacra
Phytochemistry, 1985, 24, 1108-1110

Vigorea sylvestris
Phytochemistry, 1985, 24, 2737-2740

Heliconia species (Xathanthae)
Biochim. Syst. Ecol. 1987, 17, 519-528

Heliconia strobilacea
Phytochemistry, 1981, 20, 1661-1673

Saccharum aestivum $^1$H NMR
Biochim. Syst. Ecol. 1991, 19, 523

Heliconia obtusiloba
Phytochemistry, 1987, 49, 909-917

**8-epi-Atriplacilide-isouleyraltar (12)**

**Isolation**

Isocarpa arypepsiloxalis $^1$H NMR
Phytochemistry, 1978, 17, 471-474

Calea pilosa

Calea moric

Phytochemistry, 1981, 20, 743-749

**Cucurbitaceae**

Phytochemistry, 1981, 20, 1633-1642

**Cucurbitaceae**

Phytochemistry, 1982, 21, 2117-2118

Heliconia species

Biochem. Syst. Ecol. 1989, 17, 519-528

Heliconia sanganetusa

Phytochemistry, 1991, 30, 1861-1867

Vigorea species

Flora, 1998, 69, 80-87

**Whole assignment by us**
(9C, 11C, 14$^1$H COSY, HSQC, HMBC, NOESY)

**Activity**

Antibacterial activity

Fitoterapia, 1998, 69, 80-87

NF-kB p65 inhibition

QSAR, IC$_{50}$ 0.5 µM

J. Med. Chem. 2004, 47, 9042-9054

J. Med. Chem. 2006, 49, 2241-2252

Antileishmanial

IC$_{50}$ 872 µM, related Mck, DODEN

Eur. J. Med. Chem. 2018, 127, 852-866
Isolation
Helianthus tuberosus \( ^{1} \text{H} \) NMR

Physicochemistry, 1978, 18, 676

Calix arundin

Physicochemistry, 1962, 21, 2171-2178

Calix nigricans

Physicochemistry, 1986, 29, 1753-1754

Helenium cespitum

Biochim. Biophys. Acta, 1989, 97, 519-528

Helianthus atropurpureus

Physicochemistry, 1991, 30, 1815-1817

Structure elucidation of 8-epi-MeBu

Whole assignment by us
\( ^{1} \text{H}, ^{13} \text{C}, ^{2} \text{H}, ^{13} \text{COSY}, \text{HSQC, HMBC, NOESY} \)

Eremantholide C (14)

Isolation
Eremanthus aequilaterale (Schuit. -top) \( ^{1} \text{H} \) NMR

J. Chem. Soc., Perkin Trans. 1, 1978, 1572-1580

Eremanthus bimucronatus

Physicochemistry, 1980, 70, 265-2668

Lychnophora uniflora

Physicochemistry, 1981, 20, 1149-1151

Lychnophora affinis Gardn.

J. Org. Chem. 1982, 47, 1519-1521

Piptopappus leptosporophyllus

Physicochemistry, 1982, 21, 1439-1441

Eremanthus croceolus

Physicochemistry, 1982, 21, 1669-1673

Eremanthus gossypii

Planta Med 1986, 51, 36-39

Eremanthus gusseyanus

Physicochemistry, 1989, 29, 1441-1451

Lychnophora rupestris

Physicochemistry, 1995, 39, 367-369

Lychnophora amoena

Physiol. Res. 1994, 10, 292-295

Cunninghamella echinulata

Fisetosapine, 2000, 77, 60-64

Mimosa elaeophylla

J. Braz. Chem. Soc. 2005, 16, 577-580

\( ^{13} \text{C} \) NMR

J. Org. Chem. 2012, 77, 9374-9378

NMR assignment

Magn. Reson. Chem. 2008, 46, 576-581

Activity
Anti-inflammatory

J. Ethnopharmacol. 2012, 142, 845-850

Phytother. Res. 2013, 27, 394-399

Planta Med. 2015, 81, 1296-1307

J. Pharm. Pharmacol. 2019, 71, 910-919

Trypanocidal

Phytother. Res. 1996, 10, 292-295

Molecules, 2013, 18, 7761-7767

Antibacterial

Fisetosapine, 2000, 77, 60-64

Anti-hypertensive

J. Ethnopharmacol. 2012, 142, 845-850

Rev. Bras. Farmacogn. 2019, 29, 241-246

Cytotoxicity

J. Am. Soc. Perkin Trans. 1, 1978, 1572-1580

Molluscidal

Planta Med. 1985, 57, 38-39

8-epi-Abreusitolide-2'-(S)-MeBu (13)

5-epi-Isogoyazenisolide (15)

Tagitinin C (17)

Isolation
Tithonia tagitina (Non NMR)

J. Pharm. Sci. 1976, 65, 918-920

Tithonia diversifolia

Cytotoxicity \( ^{13} \text{C} \) NMR

J. Org. Chem. 1979, 44, 1835-1835

Chromenone reductase

Physicochemistry, 1987, 28, 1999-2006

\( ^{13} \text{C} \) NMR

Photochem. Photobiol. 2006, 92, 14-20

Activity
Feeding deterrents/antifeedant

Physicochemistry, 1986, 14, 77-80

Phytochemistry, 2008, 69, 2552-2556

Chemistry & industry, 1985, 5, 167-168

Arab. J. Chem. 2020, 13, 5922-5928

Germination and growth inhibitory

Physicochemistry, 1994, 36, 29-36

Phytochemistry, Acta, Biol. Hung. 2017, 68, 187-195

Activity
Plants Med. 2002, 68, 543-545

anti-tumorantitumorantioxidant

W.O 2000051955 A1 20000609

Chem. Pharm. Bull. 2007, 55, 1240-1244

FR 2941967 A1 20100806

Fisetosapine, 2011, 82, 331-341

J. Nat. Med. 2013, 67, 989-106

Eur. J. Med. Chem. 2013, 63, 313-320

J. Nat. Prod. 2002, 65, 532-536

J. Agric. Food Chem. 2011, 59, 2547-2535

Curr. Top. Med. Chem. 2017, 17, 3256-3268

Anti-inflammatory

Metabolites, 2015, 5, 404-430

Rev. Bras. Farmacogn. 2015, 25, 111-116

Planta Med. 2015, 81, 1296-1307

Anti-Tobacco mosaic virus

Pestic. Biochem. Phys. 2017, 140, 24-29

Anti-cancer

Molecules, 2011, 16, 665-674

Antihypertensive/antihyperlipidemic/atacayacoid

Molecules, 2014, 19, 5070-5079

Fisetosapine, 2018, 124, 145-151

Eur. J. Med. Chem. 2018, 157, 852-866

Int. Immunopharmacol. 2019, 77, 105861

Antimicrobial

Bioorg. Med. Chem. 2008, 17, 3229-3256

Hap60 inhibitors

Biology, 2013, 3, 101-138

S5
Figure S2. Other structurally similar natural products.
c) Structure revision of atripliciolide (2)

The name atripliciolide was initially used for the proposed structure of a parent compound of an 8β-OH derivative by King and Robison in 1978 (Phytochemistry, 1978, 17, 471-474). Its isolation was reported by the same group in 1982 (Phytochemistry, 1982, 21, 1669-1673).

The structure was confirmed by $^1$H NMR comparison with other known 8β-OH furanoheliangolides (structure of 19 followed from its molecular formula and the $^1$H NMR spectrum (Table 2). The presence of a 6, 12-lactone was deduced from the characteristic signals of H-5 through H-8, which were similar to those of 20. The 8β-hydroxyl group was assigned from the couplings observed and from the chemical shifts of H-13, which were at lower fields due to the free hydroxyl at C-8. --original sentences from Phytochemistry, 1982, 21, 1669-1673).

However, the proposed 8β-OH compound was isolated along with other 8α-esters instead of 8β-esters. For example, Phytochemistry, 1982, 21, 1669-1673 and J. Braz. Chem. Soc., 2005, 16, 677-680, indicating that atripliciolide might be 8α-OH.

Both 8α-OH and 8β-OH compounds were synthesized and the spectral data was compared with the data obtained from the natural product (based on 2D NMR spectroscopic analyses as well). The structure of atripliciolide was finally revised to have an 8α-OH (2). The absolute configuration of 2 was also determined by X-ray diffraction.
Table S1. Comparison of natural and synthetic proposed/revised atripliciolide (2) (CDCl3)\(^1\)

|                  | \(^1\)H NMR | \(^13\)C NMR |
|------------------|-------------|-------------|
|                  | Natural (400 MHz) | 8\(\alpha\)-OH 2 (Revised) (500 MHz) | 8\(\beta\)-OH 7 (Proposed) (500 MHz) | Natural 2 (125 MHz) | 7 (125 MHz) |
| 1                | -           | -           | - | - | 206.0 | 206.0 |
| 2                | 5.60, s     | 5.60, s     | 5.59, s | - | 103.2 | 103.2 |
| 3                | -           | -           | - | - | 186.4 | 186.4 |
| 4                | -           | -           | - | - | 131.4 | 131.4 |
| 5                | 5.90, dq (3.5, 1.5) | 5.91, dq (3.6, 1.7) | 5.95, dq (4.4, 1.8) | - | 134.6 | 134.6 |
| 6                | 4.86, ddq (4.3, 1.5) | 4.86, tq (4.0, 1.9) | 5.63, tq (4.5, 2.0) | - | 81.0 | 81.0 |
| 7                | 3.68, dddd (4, 2.5, 2) | 3.66, tt (5.2, 2.7) | 3.44, dtd (4.5, 2.9, 1.5) | - | 52.3 | 52.3 |
| 8                | 3.82, m     | 3.82, m     | 4.21, qd (3.3, 1.6) | - | 71.8 | 71.8 |
| 9\(\alpha\)     | 2.31, dd (14.5, 2.5) | 2.31, dd (14.7, 2.5) | 2.44, dd (14.7, 2.5) | - | 44.9 | 44.9 |
| 9\(\beta\)      | 2.17, dd (14.5, 8.3) | 2.18, dd (14.6, 8.6) | 2.30, dd (14.6, 8.6) | - | - | - |
| 10               | -           | -           | - | - | 89.9 | 87.7 |
| 11               | -           | -           | - | - | 134.1 | 140.6 |
| 12               | -           | -           | - | - | 169.7 | 169.7 |
| 13a              | 6.45, dd (3, 0.7) | 6.43, dd (3.0, 0.7) | 6.35, d (3.1) | - | 127.4 | 123.6 |
| 13b              | 5.86, dd (2.5, 0.7) | 5.84, dd (2.6, 0.7) | 5.61, d (2.7) | - | - | - |
| 14               | 1.44, s     | 1.56, s     | 1.45, s | - | 20.7 | 21.8 |
| 15               | 2.07, dd (1.5, 1.5) | 2.07, t (1.9) | 2.06, t (1.9) | - | 19.9 | 19.6 |
| OH               | -           | 2.32        | 2.32 | - | - | - |

\(2\)D NMR correlations

|                  | \(^1\)H-\(^1\)H COSY | HMBC | NOESY | X-Ray |
|------------------|----------------------|------|-------|-------|
| 2                | ![Diagram 2](image2.png) | ![Diagram HMBC 2](image3.png) | ![Diagram NOESY 2](image4.png) | ![Diagram X-Ray 2](image5.png) |
| 7                | ![Diagram 7](image6.png) | ![Diagram HMBC 7](image7.png) | ![Diagram NOESY 7](image8.png) | ![Diagram X-Ray 7](image9.png) |

\(^1\) Only the \(^1\)H NMR data was available in the literature (Phytochemistry, 1982, 21, 1669-1673). The solvent peak was set to be 7.27 ppm instead of 7.26 ppm. The chemical shift of 14-Me was erroneous, and has been correct by our full assignment. To the best of our knowledge no carbon NMR had been previously reported.
d) Structure elucidation of 13

8-epi-Atripliciolide-2’-methyl butylate was first reported by Bohlmann and Dutta in 1979 (Phytochemistry, 1979, 18, 676). The configuration of the side chain was not assigned.

In this work 2’-(S)-MeBu-13 was prepared from commercially available (S)-(+) -2-methyl butyric anhydride and 2’-(R,S)-MeBu-13 from (+)-2-methyl butyric anhydride. The diastereomers are inseparable. The structures were fully elucidated based on 2D NMR spectroscopic analyses.

Based on ¹H NMR comparison (Figure S3), the structure of natural product was finally elucidated as 8-epi-atripsiliolide-2’-(S)-MeBu (13).

**Figure S3.** ¹H NMR comparison of 8-epi-atripsiliolide-2’-(S)-MeBu (13) and 8-epi-atripsiliolide-2’-(R,S)-MeBu.
**Table S2.** Comparison of 2\(^\prime\)-(S)-MeBu-13, 2\(^\prime\)-(R)-MeBu-13 and natural 13 (\(^1\)H NMR)\(^2\)

![Structural diagram of 2\(^\prime\)-MeBu-13]

|          | 1\(^\prime\) | 2\(^\prime\) | 3\(^\prime\) | 4\(^\prime\) | 5\(^\prime\) |
|----------|-------------|-------------|-------------|-------------|-------------|
| **1\(^\prime\)H NMR** |             |             |             |             |             |
| Natural (270 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(S)-MeBu-13 (400 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(R)-MeBu-13 (400 MHz) | 5.60, s     | 5.60, s     | 5.60, s     | -           | -           |
| Natural (100 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(S)-MeBu-13 (100 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(R)-MeBu-13 (100 MHz) | -           | -           | -           | -           | -           |
| **1\(^3\)C NMR** |             |             |             |             |             |
| 2\(^\prime\)-(S)-MeBu-13 (400 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(R)-MeBu-13 (400 MHz) | 105.44      | 105.50      | -           | -           | -           |
| Natural (100 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(S)-MeBu-13 (100 MHz) | -           | -           | -           | -           | -           |
| 2\(^\prime\)-(R)-MeBu-13 (100 MHz) | -           | -           | -           | -           | -           |

**2D NMR correlations**

|          | \(^1\)H-\(^1\)H COSY | HMBC | NOESY |
|----------|-----------------------|------|-------|
| 13       | ![Diagram of 2D NMR correlations](image) |

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\(^2\) Previous report (*Phytochemistry, 1979, 18, 676-676*) provided \(^1\)H NMR data without showing the spectra and did not assign the side chain configuration. To the best of our knowledge no carbon NMR had been previously reported.
e) Data comparison and full analyses of 1, 3-6, 8-12, 14-17

Table S3. Comparison of natural and synthetic goyazensolide (1) (CDCl₃)

|        | Natural (270 MHz) | Synthetic (500 MHz) | Natural (68 MHz) | Synthetic (126 MHz) |
|--------|------------------|---------------------|-----------------|---------------------|
| 1      | -                | -                   | 204.6           | 204.6               |
| 2      | 5.83, s          | 5.82, s             | 106.4           | 106.6               |
| 3      | -                | -                   | 184.6           | 184.2               |
| 4      | -                | -                   | 135.6           | 135.5               |
| 5      | 6.27, dt (1.5, 1.5) | 6.30, dt (1.5)     | 134.6           | 134.2               |
| 6      | 5.33, dt (1.3, 2.5) | 5.36, dd (4.9, 2.6) | 81.7            | 81.5                |
| 7      | 3.80, m (2.5, 2.5, 3.3, 3.0) | 3.82, t (5.3)     | 51.0            | 50.9                |
| 8      | 4.53, dt (2.5, 13) | 4.57, dt (2.2, 11.7) | 73.5            | 73.2                |
| 9α     | 2.50, dd (13, 15) | 2.56-2.48, m       | 43.3            | 43.9                |
| 9β     | -                | -                   | -               | -                   |
| 10     | -                | -                   | 89.7            | 89.8                |
| 11     | -                | -                   | 135.6           | 135.3               |
| 12     | -                | -                   | 166.8           | 166.8               |
| 13a    | 6.22, d (3.3)    | 6.25, d (3.1)      | 126.2           | 126.6               |
| 13b    | 5.49, d (3.0)    | 5.49, d (2.7)      | -               | -                   |
| 14     | 1.52, s          | 1.56, s             | 20.6            | 20.7                |
| 15     | 4.38, s (1.5, 1.3) | 4.42, dt (3.1, 1.7) | 62.9            | 63.2                |
| 1'     | -                | -                   | 168.7           | 168.7               |
| 2'     | -                | -                   | 133.6           | 133.1               |
| 3'a    | 6.02, s (1)      | 6.03, s             | 124.5           | 124.6               |
| 3'b    | 5.56, m (1.5)    | 5.59-5.54, m       | -               | -                   |
| 4'     | 1.83, m          | 1.85, s             | 17.8            | 18.0                |

³ For NMR, see: Phytochemistry, 1976, 15, 191-193, structure misassignment as C-8 lactone. For structure revision, see: J. Org. Chem. 1982, 47, 2798-2800. For detailed full spectral assignments, see: Magn. Reson. Chem. 2001, 39, 3219-221.
Table S4. Comparison of natural and synthetic 15-deoxygozyazensolide (3) (CDCl₃)⁴

|                  | **¹H NMR**                  |                  | **¹³C NMR**                  |
|------------------|-----------------------------|------------------|-----------------------------|
|                  | Natural (500 MHz)           | Synthetic (400 MHz) | Natural (125 MHz)           | Synthetic (100 MHz) |
| 1                | -                           | -                | 204.8                       | 204.8               |
| 2                | 5.71, s                      | 5.71, s          | 104.7                       | 104.7               |
| 3                | -                           | -                | 186.8                       | 186.9               |
| 4                | -                           | -                | 130.4                       | 130.3               |
| 5                | 6.00, m                      | 6.00, m          | 135.0                       | 135.0               |
| 6                | 5.26, m                      | 5.26, m          | 81.5                        | 81.5                |
| 7                | 3.72, m                      | 3.73, dq (5.7, 2.9) | 51.1                        | 51.1                |
| 8                | 4.55, dt (11.5, 2.9)         | 4.54, dt, (11.6, 2.5) | 73.4                        | 73.3                |
| 9α               | 2.48, dd (13.8, 11.5)        | 2.48, dd (13.9, 11.6) | 43.8                        | 43.8                |
| 9β               | 2.31, dd (13.8, 2.0)         | 2.31, dd (13.9, 2.1) | -                           | -                   |
| 10               | -                           | -                | 89.6                        | 89.6                |
| 11               | -                           | -                | 133.5                       | 133.4               |
| 12               | -                           | -                | 168.8                       | 168.8               |
| 13a              | 6.22, d (3.1)                | 6.21, d (3.1)    | 124.4                       | 124.5               |
| 13b              | 5.46, d (2.8)                | 5.45, d (2.7)    | -                           | -                   |
| 14               | 1.53, s                      | 1.53, s          | 20.6                        | 20.6                |
| 15               | 2.08, t (2.2)                | 2.07, t (2.0)    | 20.3                        | 20.4                |
| 1’                | -                           | -                | 166.7                       | 166.7               |
| 2’                | -                           | -                | 135.5                       | 135.4               |
| 3’a              | 6.01, dq (1.6, 1.0)          | 6.01, m          | 126.4                       | 126.5               |
| 3’b              | 5.54, quint (1.6)            | 5.54, m          | -                           | -                   |
| 4’                | 1.83, dd (1.6, 1.0)          | 1.83, dd (1.6, 1.0) | 18.0                        | 18.0                |

⁴Previous report (Magn. Reson. Chem. 2004, 42, 364–367) provides detailed full spectral assignments; for first isolation, see Phytochemistry, 1976, 15, 1775-1776; for structure revision, see J. Org. Chem. 1982, 47, 2798-2800. ¹³C chemical shifts are reported relative to chloroform δ 77.00 ppm instead of 77.16 ppm.
Table S5. Comparison of natural and synthetic lychnopholide (4) (CDCl$_3$)$^5$

|                  | Natural (270 MHz) | Synthetic (400 MHz) | Natural (68 MHz) | Synthetic (100 MHz) |
|------------------|------------------|---------------------|------------------|---------------------|
| 1                | -                | -                   | 204.71           | 204.85              |
| 2                | 5.72, s          | 5.72, s             | 104.69           | 104.75              |
| 3                | -                | -                   | 186.83           | 186.91              |
| 4                | -                | -                   | 130.44           | 130.31              |
| 5                | 6.02, dq (3, 1.7)| 6.02, dt (3.2, 1.7)| 135.12           | 135.06              |
| 6                | 5.30, ddq (5, 3.2, 2.7)| 5.31, dt (5.1, 2.6)| 81.61            | 81.69               |
| 7                | 3.72, dddd (5, 3.5, 2.8, 2.5)| 3.72, dq (5.5, 2.8)| 51.23            | 51.17               |
| 8                | 4.54, ddd, (12, 2.5, 2) | 4.54, dt (11.8, 2.4)| 73.00            | 72.97               |
| 9α               | 2.49, dd (14, 12)| 2.48, dd (13.8, 11.7)| 44.04            | 44.04               |
| 9β               | 2.32, dd (14, 2) | 2.31, dd (13.9, 2.1)| -                | -                   |
| 10               | -                | -                   | 89.64            | 89.70               |
| 11               | -                | -                   | 133.84           | 133.72              |
| 12               | -                | -                   | 168.02           | 168.91              |
| 13a              | 6.23, d (3.2)    | 6.23, d (3.1)       | 124.10           | 124.27              |
| 13b              | 5.44, d (2.8)    | 5.44, d (2.7)       | -                | -                   |
| 14               | 1.54, s          | 1.54, s             | 20.65            | 20.70               |
| 15               | 2.09, dd (2.7, 1.7)| 2.09, t (2.0)       | 20.22            | 20.35               |
| 1’               | -                | -                   | 167.00           | 167.06              |
| 2’               | -                | -                   | 126.51           | 126.38              |
| 3’               | 6.09, qq (7, 1.5)| 6.09, qq (7.3, 1.4) | 140.54           | 140.80              |
| 4’               | 1.90, dq (7, 1.5)| 1.89, dq (7.3, 1.5) | 15.64            | 15.71               |
| 5’               | 1.80, dq (1.5, 1.5)| 1.79, p (1.6)       | 19.93            | 20.03               |

2D NMR correlations

|                  | 1H-1H COSY | HMBC | NOESY |
|------------------|-----------|------|-------|
|                  |           |      |       |

$^5$ Previous report (phytochemistry, 1980, 19, 2381-2385) provides the $^1$H NMR. Solvent peak was set up at 7.27 ppm instead of 7.26 ppm. And the $^{13}$C NMR was provided in a later publication (phytochemistry, 1989, 28, 1441-1451) with the solvent peak set up at 77 ppm instead of 77.16 ppm.
Table S6. Comparison of natural and synthetic atripliciolide-tiglate (5) (CDCl₃)\(^6\)

|                  | \(^1^H\) NMR Natural (270 MHz) | \(^1^H\) NMR Synthetic (400 MHz) | \(^1^3^C\) NMR Natural (100 MHz) | \(^1^3^C\) NMR Synthetic (100 MHz) |
|------------------|-------------------------------|----------------------------------|---------------------------------|-----------------------------------|
| 1                |                               |                                  |                                 |                                   |
| 2                | 5.71, s                       | 5.70, s                          | -                               | 104.8                             |
| 3                | -                             | -                                | -                               | 187.0                             |
| 4                | -                             | -                                | -                               | 130.4                             |
| 5                | 6.00, dq (3, 1.7)             | 6.01, dq (3.4, 1.7)              | -                               | 135.2                             |
| 6                | 5.28, ddq (5, 3, 2.5)         | 5.28, dt (5.2, 2.7)              | -                               | 81.7                              |
| 7                | 3.73, dddd (5, 3.2, 2.8, 2.5) | 3.72, dq (5.6, 2.9)              | -                               | 51.3                              |
| 8                | 4.54, ddd, (12, 2.5, 2)       | 4.54, dt (11.6, 2.5)             | -                               | 73.3                              |
| 9α               | 2.47, dd (14, 12)             | 2.47, dd (13.9, 11.6)            | -                               | 44.1                              |
| 9β               | 2.30, dd (14, 2)              | 2.31, dd (14.0, 2.1)             | -                               | -                                 |
| 10               | -                             | -                                | -                               | 89.8                              |
| 11               | -                             | -                                | -                               | 133.7                             |
| 12               | -                             | -                                | -                               | 169.1                             |
| 13a              | 6.20, d (3.2)                 | 6.20, d (3.1)                    | -                               | 124.4                             |
| 13b              | 5.44, d (2.8)                 | 5.44, d (2.6)                    | -                               | -                                 |
| 14               | 1.53, s                       | 1.53, s                          | -                               | 20.8                              |
| 15               | 2.08, dd (2.5, 1.7)           | 2.08, t (2.0)                    | -                               | 20.5                              |
| 1’               | -                             | -                                | -                               | 167.5                             |
| 2’               | -                             | -                                | -                               | 127.9                             |
| 3’               | 6.77, qq (7, 1.5)             | 6.77, qq (7.1, 1.4)              | -                               | 138.8                             |
| 4’               | 1.77, dq (7, 1.5)             | 1.76, dd (7.1, 1.2)              | -                               | 14.6                              |
| 5’               | 1.73, dq (1.5, 1.5)           | 1.73, t (1.3)                    | -                               | 11.9                              |

2D NMR correlations

|                  | \(^1^H-^1^H\) COSY | HMBC | NOESY |
|------------------|--------------------|------|-------|
| 5 | ![Diagram](attachment:image) | ![Diagram](attachment:image) | ![Diagram](attachment:image) |

\(^6\) Solvent peak was set up at 7.27 ppm instead of 7.26 ppm. \(^1^H\) NMR had been previously reported (Phytochemistry, 1980, 19, 2663-2668). To the best of our knowledge no carbon NMR had been previously reported.
Table S7. Comparison of natural and synthetic atripliciolide-isobutyrate (6) (CDCl₃)⁷

|                  | Natural (270 MHz) | Synthetic (500 MHz) | Natural (125 MHz) | Synthetic (125 MHz) |
|------------------|-------------------|---------------------|-------------------|---------------------|
| **1H NMR**       |                   |                     |                   |                     |
| 1                 | -                 | -                   | -                 | 205.0               |
| 2                 | 5.70, s           | 5.70, s             | -                 | 104.7               |
| 3                 | -                 | -                   | -                 | 187.1               |
| 4                 | -                 | -                   | -                 | 130.4               |
| 5                 | 5.90, dq, (3, 1.5)| 5.99, dt (3.1, 1.8)| -                 | 135.2               |
| 6                 | 5.23, ddq (5, 3, 1.5) | 5.23, dp, (4.9, 2.3)| -                 | 81.8                |
| 7                 | 3.72, dddd (5, 3, 2.5, 2.5) | 3.71, dq (5.6, 2.8)| -                 | 51.3                |
| 8                 | 4.42, ddd (11.5, 2.5, 2) | 4.42, dt, (11.8, 2.4)| -                 | 72.8                |
| 9α               | 2.40, dd (14, 2)  | 2.42, dd (13.9, 11.6) | -         | 44.1                |
| 9β               | 2.25, dd (14, 11.5) | 2.25, dd (13.9, 2.0) | -                 | -                   |
| 10                | -                 | -                   | -                 | 105.0               |
| 11                | -                 | -                   | -                 | 133.3               |
| 12                | -                 | -                   | -                 | 168.9               |
| 13α              | 6.26, d (3)       | 6.26, d (3.1)      | -                 | 124.4               |
| 13β              | 5.47, d (2.5)     | 5.46, d (2.6)      | -                 | -                   |
| 14                | 1.52, s           | 1.52, s            | -                 | 20.8                |
| 15                | 2.08, dd (1.5, 1.5) | 2.07, t (2.0)     | -                 | 20.5                |
| 1’                | -                 | -                   | -                 | 176.7               |
| 2’                | 2.39, qq (7, 7)   | 2.39, sept, (7)    | -                 | 33.8                |
| 3’/4’             | 1.40, d (7)       | 1.04, d (7)        | -                 | 18.9                |
| 3’/4’             | 1.08, d (7)       | 1.08, d (7)        | -                 | 18.7                |

|                  | ²H-²H COSY       | HMBC                | NOESY               |
|------------------|------------------|---------------------|---------------------|
| **2D NMR correlations** |                  |                     |                     |
| 7                 |                  |                     |                     |

⁷ ¹H NMR had been previously reported (phytochemistry, 1982, 21, 1669-1673) with different chemical shifts for H₅ and H₃, and J coupling constants of 9α and 9β swapped. To the best of our knowledge no carbon NMR had been previously reported.
Table S8. Comparison of natural and synthetic calaxin (8) (CDCl₃)

|                | Natural (270 MHz) | Synthetic (500 MHz) | Natural (125 MHz) | Synthetic (125 MHz) |
|----------------|-------------------|---------------------|-------------------|---------------------|
| 1              | -                 | -                   | -                 | 205.4               |
| 2              | 5.59, s           | 5.60, s             | -                 | 103.3               |
| 3              | -                 | -                   | -                 | -                   |
| 4              | -                 | -                   | 185.2             | -                   |
| 5              | 5.94, dq (2.5, 1.5) | 5.95, dq (3.6, 1.8) | -                 | 134.2               |
| 6              | 5.28, dq (2, 1.5) | 5.28, tq (4.0, 1.9) | -                 | 75.3                |
| 7              | 3.70, m           | 3.69, dd (4.6, 2.7, 1.9) | -                 | 48.5                |
| 8              | 5.18, ddd (5, 3, 3) | 5.19, ddd (5.4, 3.4, 1.9) | -                 | 75.1                |
| 9α             | 2.55, dd (15, 5)  | 2.55, dd (15.2, 5.4) | -                 | 42.6                |
| 9β             | 2.31, dd (15, 3)  | 2.31, dd (15.1, 3.4) | -                 | -                   |
| 10             | -                 | -                   | -                 | 87.8                |
| 11             | -                 | -                   | -                 | 139.0               |
| 12             | -                 | -                   | -                 | 168.9               |
| 13a            | 6.35, d (3)       | 6.35, d (2.9)       | -                 | 123.6               |
| 13b            | 5.67, d (2.5)     | 5.67, d (2.6)       | -                 | -                   |
| 14             | 1.48, s           | 1.49, s             | -                 | 21.5                |
| 15             | 2.07, dd (1, 1.5) | 2.07, t (1.9)       | -                 | 19.7                |
| 1’             | -                 | -                   | -                 | 165.9               |
| 2’             | -                 | -                   | -                 | 135.2               |
| 3’a            | 6.02, br s        | 6.02, p (1.0)       | -                 | 127.6               |
| 3'b            | 5.60, dq (7, 1)   | 5.61, dq (7.1, 1.1) | -                 | 18.3                |
| 4’             | 1.86, br s        | 1.86, dd (1.6, 0.9) | -                 | 21.5                |

2D NMR correlations

| 8              | ¹H-¹H COSY | HMBC | NOESY |
|----------------|------------|------|-------|

For ¹H NMR, see: *Phytochemistry*, 1978, 17, 471-474. To the best of our knowledge no carbon NMR had been previously reported.
Table S9. Comparison of natural and synthetic 8-epi-lychnopholide (9) (CDCl₃)

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Table S10. Comparison of natural and synthetic 8-epi-atriplicilolide-tiglate (10) (CDCl₃)\textsuperscript{10}

|         | \( ^1H \) NMR (270 MHz) | \( ^1H \) NMR (400 MHz) | \( ^13C \) NMR (100 MHz) | \( ^13C \) NMR (100 MHz) |
|---------|--------------------------|--------------------------|--------------------------|--------------------------|
| 1       | -                        | -                        | 205.4                    | -                        |
| 2       | 5.59, s                  | 5.59, s                  | 103.3                    | -                        |
| 3       | -                        | -                        | 185.1                    | -                        |
| 4       | -                        | -                        | 131.8                    | -                        |
| 5       | 5.94, dq (2.5, 1.5)      | 5.94, dq (3.6, 1.8)      | -                        | 134.3                    |
| 6       | 5.28, dq (2, 1.5)        | 5.28, m                  | -                        | 75.4                     |
| 7       | 3.70, m                  | 3.69, m                  | -                        | 48.6                     |
| 8       | 5.18, ddd (5, 3, 3)      | 5.19, ddd, (5, 4, 3, 1.9)| -                        | 74.8                     |
| 9α      | 2.52, dd (15, 5)         | 2.52, dd (15, 1, 5.4)    | -                        | 42.7                     |
| 9β      | 2.30, dd (15, 3)         | 2.30, dd (15, 1, 3.4)    | -                        | -                        |
| 10      | -                        | -                        | -                        | 87.8                     |
| 11      | -                        | -                        | -                        | 139.1                    |
| 12      | -                        | -                        | -                        | 169.0                    |
| 13a     | 6.33, d (3)              | 6.33, d (2.9)            | -                        | 123.5                    |
| 13b     | 5.65, d (2.5)            | 5.66, d (2.5)            | -                        | -                        |
| 14      | 1.48, s                  | 1.48, s                  | -                        | 21.5                     |
| 15      | 2.07, dd (1.5, 1.5)      | 2.07, t (1.9)            | -                        | 14.8                     |
| 1'      | -                        | -                        | -                        | 166.6                    |
| 2'      | -                        | -                        | -                        | 127.6                    |
| 3'      | 6.76, qq (7, 1)          | 6.76, qq (7, 1.4)        | -                        | 139.7                    |
| 4'      | 1.78, dq (7, 1)          | 1.78, dq (7, 1.1)        | -                        | 19.7                     |
| 5'      | 1.74, br s               | 1.74, p (1.1)            | -                        | 12.0                     |

2D NMR correlations

|         | \(^1H^1H\) COSY | HMBC | NOESY |
|---------|----------------|------|-------|
| 10      |                 |      |       |

\textsuperscript{10}For \(^1H\) NMR, see: Phytochemistry, 1978, 17, 471-474. To the best of our knowledge no carbon NMR had been previously reported.
Table S11. Comparison of natural and synthetic ciliarin (11) (CDCl₃)\(^{11}\)

|       | Natural (270 MHz) | Synthetic (400 MHz) | Natural (100 MHz) | Synthetic (100 MHz) |
|-------|-------------------|---------------------|-------------------|---------------------|
| 1     | -                 | -                   | 205.5             |                     |
| 2     | 5.59, s           | 5.60, s             | -                 | 103.1               |
| 3     | -                 | -                   | 185.1             |                     |
| 4     | -                 | -                   | -                 | 132.0               |
| 5     | 5.94, dq (2.5, 1.5) | 5.93, dq (3.6, 1.8) | -                 | 134.2               |
| 6     | 5.34, dq (2, 1.5) | 5.34, tq (3.9, 1.9) | -                 | 75.4                |
| 7     | 3.67, m           | 3.67, dq (4.8, 2.6) | -                 | 48.6                |
| 8     | 5.21, ddd (5, 3, 3) | 5.21, ddd, (5.7, 3.6, 2.1) | -                 | 74.0                |
| 9α    | 2.48, dd (15, 5)  | 2.48, dd (15.1, 5.4)| -                 | 42.0                |
| 9β    | 2.24, dd (15, 3)  | 2.24, dd (15.1, 3.6)| -                 | -                   |
| 10    | -                 | -                   | -                 | 87.5                |
| 11    | -                 | -                   | -                 | 138.5               |
| 12    | -                 | -                   | -                 | 168.9               |
| 13a   | 6.35, d (3)       | 6.35, d (2.9)       | -                 | 124.1               |
| 13b   | 5.67, d (2.5)     | 5.67, d (2.5)       | -                 | -                   |
| 14    | 1.48, s           | 1.47, s             | -                 | 21.3                |
| 15    | 2.07, dd (1.5, 1.5)| 2.07, t (1.8)       | -                 | 19.7                |
| 1’    | -                 | -                   | -                 | 175.6               |
| 2’    | 2.46, qq          | 2.46, m             | -                 | 34.1                |
| 3’/4’ | 1.08, d           | 1.10, d (2.5)       | -                 | 19.0                |
| 3’/4’ | 1.07, d           | 1.08, d (2.6)       | -                 | 18.6                |

2D NMR correlations

|      | 1H-1H COSY | HMBC | NOESY |
|------|------------|------|-------|
| 11   | ![Diagram](1H-1H COSY) | ![Diagram](HMBC) | ![Diagram](NOESY) |

\(^{11}\)For \(^1\)H NMR, see: Phytochemistry, 1978, 17, 471-474. To the best of our knowledge no carbon NMR had been previously reported.
Table S12. Comparison of natural and synthetic 8-epi-atripsiliolide-isovalerate (12) (CDCl₃)\textsuperscript{12}

|                  | \(\text{\textsuperscript{1}H NMR}\) | \(\text{\textsuperscript{13}C NMR}\) |
|------------------|--------------------------------------|-------------------------------------|
|                  | Natural (270 MHz) | Synthetic (400 MHz) | Natural (100 MHz) | Synthetic |
|                  |                      |                                      |                          | (100 MHz) |
| 1                | -                     | -                                   | -                       | 205.6     |
| 2                | 5.59, s               | 5.60, s                             | -                       | 103.2     |
| 3                | -                     | -                                   | -                       | 185.1     |
| 4                | -                     | -                                   | -                       | 132.0     |
| 5                | 5.93, dq (2.5, 1.5)   | 5.93, dq (4.4, 1.7)                 | -                       | 134.2     |
| 6                | 5.34, dq (2.1.5)      | 5.34, td (4.4, 2.1)                 | -                       | 75.5      |
| 7                | 3.65, m               | 3.64, dq (4.9, 2.5)                 | -                       | 48.5      |
| 8                | 5.23, ddd (5, 3, 3)   | 5.24, ddd, (5.8, 3.6, 2.1)          | -                       | 74.0      |
| 9α               | 2.48, dd (15.5)       | 2.48, dd (15.2, 6)                  | -                       | 42.0      |
| 9β               | 2.22, dd (15, 3)      | 2.23, dd (15.1, 3.6)                | -                       | -         |
| 10               | -                     | -                                   | -                       | 87.5      |
| 11               | -                     | -                                   | -                       | 138.5     |
| 12               | -                     | -                                   | -                       | 168.9     |
| 13a              | 6.36, d (3)           | 6.36, d (2.9)                       | -                       | 124.1     |
| 13b              | 5.68, d (2.5)         | 5.68, d (2.6)                       | -                       | -         |
| 14               | 1.48, s               | 1.47, s                             | -                       | 21.2      |
| 15               | 2.07, dd (1.5, 1.5)   | 2.07, t (1.8)                       | -                       | 19.7      |
| 1'               | -                     | -                                   | -                       | 171.6     |
| 2'               | 2.09, dd              | 2.10, m                             | -                       | 42.9      |
| 3'               | 1.98, m               | 1.97, ddd (12.9, 7.5, 6.4)          | -                       | 25.5      |
| 4'/5'            | 0.90                  | 0.89, d (4.8)                       | -                       | 22.5      |
| 4'/5'            | 0.87                  | 0.88, d (4.8)                       | -                       | 22.4      |

|                  | \(\text{\textsuperscript{1}H-\textsuperscript{1}H COSY}\) | \(\text{HMBC}\) | \(\text{NOESY}\) |
|------------------|----------------------------------------------------------|-----------------|-----------------|
| 12               | ![Diagram](image1.png)                                   | ![Diagram](image2.png) | ![Diagram](image3.png) |

\textsuperscript{12}For \(\text{\textsuperscript{1}H NMR}\), see: Phytochemistry, 1978, 17, 471-474. In this report the chemical shift of 0.87 ppm was wrongly moved to another column on the results table. To the best of our knowledge no carbon NMR had been previously reported.
Table S13. Comparison of natural and synthetic eremantholide C (14) (CDCl₃)

|     | ¹H NMR       | ¹³C NMR       |
|-----|--------------|--------------|
|     | Natural      | Natural      | Synthetic    | Natural      | Natural      | Synthetic    |
|     | (500 MHz)    | (500 MHz)    | (500 MHz)    | (125 MHz)   | (125 MHz)   | (125 MHz)   |
| 1   | -            | -            | -            | 205.2       | 205.8       | 205.3       |
| 2   | 5.62, s      | 5.63, s      | 5.61, s      | 104.5       | 104.5       | 104.7       |
| 3   | -            | -            | -            | 186.8       | 187.2       | 186.9       |
| 4   | -            | -            | -            | 130.2       | 130.0       | 130.3       |
| 5   | 6.03, dq (2.7, 1.6) | 6.03, dq (2.7, 1.6) | 6.03, dq (3.6, 1.8) | 134.6       | 134.7       | 134.7       |
| 6   | 4.98, dddq (7, 2.7, 2.4, 0.6) | 5.00, dddq (7.1, 2.7, 2.2, 0.6) | 4.98, dp (7.2, 2.4) | 81.5        | 81.4        | 81.6        |
| 7   | 2.85, dd (7, 4.2) | 2.82, dd (7.1, 4.2) | 2.86, dd (7.2, 4.3) | 62.5        | 62.5        | 62.5        |
| 8   | 4.14, dddd (11.9, 4.2, 2.6, 0.6) | 4.10, dddd (11.9, 4.2, 2.6, 0.6) | 4.15, dddd (11.8, 4.3, 2.8) | 78.5        | 78.3        | 78.6        |
| 9α  | 2.06, dd (13.6, 11.9) | 2.01, dd (13.6, 11.9) | 2.05, m      | 43.7        | 43.5        | 43.9        |
| 9β  | 2.41, dd (13.6, 2.6) | 2.47, dd (13.6, 2.6) | 2.39, dd (13.6, 2.6) | -           | -           | -           |
| 10  | -            | -            | -            | 89.9        | 90.2        | 90.1        |
| 11  | -            | -            | -            | 59.8        | 59.8        | 59.9        |
| 12  | -            | -            | -            | 175.4       | 175.7       | 175.6       |
| 13  | 1.19, s      | 1.18, s      | 1.20, s      | 21.9        | 21.9        | 22.0        |
| 14  | 1.49, s      | 1.46, s      | 1.50, s      | 20.6        | 20.5        | 20.7        |
| 15  | 2.06, dd (2.4, 1.6) | 2.05, dd (2.2, 1.6) | 2.06, m      | 20.3        | 20.3        | 20.5        |
| 1'  | -            | -            | -            | 106.2       | 106.1       | 106.3       |
| 2'  | -            | -            | -            | 142.0       | 142.1       | 142.1       |
| 3'a | 5.08, dq (2.0, 1.8) | 5.07, dq (2.0, 1.8) | 5.08, p (1.6) | 116.1       | 115.8       | 116.4       |
| 3'b | 5.33, dd (2.0, 0.9) | 5.30, dq (2.0, 1.1) | 5.33, dq (1.8, 0.8) | -           | -           | -           |
| 4'  | 1.90, dd (1.5, 0.9) | 1.90, dd (1.8, 1.1) | 1.89, dd (1.6, 0.9) | 18.9        | 18.9        | 19.1        |
| -OH | -            | 3.62, br 's  | -            | -           | -           | -           |

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¹³Sass, D. C., Heleno, V. C. G., Cavalcante, S., da Silva Barbosa, J., Soares, A. C. F., Constantino, M. G. *J. Org. Chem.* **2012**, *77*, 9374–9378.

¹⁴Heleno, V. C. G., de Oliveira, K. T., Lopes, J. L. C., Lopes, N. P., Ferreira, A. G. *Magn. Reson. Chem.* **2008**, *46*, 576-581.
Table S14. Comparison of natural and synthetic 5-epi-isogoyazensolide (15) (CDCl₃)

|        | ¹H NMR Natural (270 MHz) | ¹H NMR Synthetic (400 MHz) | ¹³C NMR Natural (100 MHz) | ¹³C NMR Synthetic (100 MHz) |
|--------|------------------------|-----------------------------|--------------------------|-----------------------------|
| 1      | -                      | -                           | 203.7                    | 203.8                       |
| 2      | 5.97, s                | 5.96, s                     | 106.5                    | 106.5                       |
| 3      | -                      | -                           | 185.2                    | 185.2                       |
| 4      | -                      | -                           | 137.3                    | 137.1                       |
| 5      | 4.69, ddd (9.5, 2, 2)  | 4.67, dt (9.6, 2.2)         | 74.0                     | 73.9                        |
| 6      | 4.60, dd (9.5, 5)      | 4.60, dd (9.6, 6)           | 85.0                     | 85.0                        |
| 7      | 3.66, dddd (5, 2, 3.5, 3) | 3.66, m                    | 51.2                     | 51.1                        |
| 8      | 4.39, ddd (2, 11.5, 2) | 4.37, dt (12, 1.8)         | 70.6                     | 70.5                        |
| 9α     | 2.50, dd (13, 11.5)    | 2.50, dd (13.7, 11.9)      | 45.2                     | 45.2                        |
| 9β     | 2.37, dd (13, 2)       | 2.37, dd (13.9, 1.7)       | -                        | -                           |
| 10     | -                      | -                           | 90.2                     | 90.2                        |
| 11     | -                      | -                           | 133.0                    | 132.8                       |
| 12     | -                      | -                           | 167.6                    | 167.6                       |
| 13a    | 6.28, d (3.5)          | 6.28, d (3.5)               | 124.7                    | 124.9                       |
| 13b    | 5.57, d (3)            | 5.56, d (3.1)               | -                        | -                           |
| 14     | 1.53 s                 | 1.54, s                     | 21.2                     | 21.2                        |
| 15a    | 6.25, dd (2, 1)        | 6.25, dd (2.3, 0.9)        | 123.1                    | 123.3                       |
| 15b    | 6.01, m                | 6.01, m                     | -                        | -                           |
| 1'     | -                      | -                           | 166.8                    | 166.8                       |
| 2'     | -                      | -                           | 135.4                    | 135.3                       |
| 3'a    | 6.01, m                | 6.01, m                     | 126.6                    | 126.7                       |
| 3'b    | 5.56, br s             | 5.55, m                     | -                        | -                           |
| 4'     | 1.83, br s             | 1.83, dd (1.6, 1)          | 17.9                     | 18.0                        |

2D NMR correlations

|        | ¹H-¹H COSY | HMBC |
|--------|------------|------|
| 15     | ![Diagram](image1) | ![Diagram](image2) |

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15 Bohlmann, F., Zdero, C., Robinson, H., King, R. M. Phytochemistry, 1981, 20, 731-734.

16 Lopes, J. L. C. J. Braz. Chem. Soc. 1995, 6, 307-311. In this manuscript the chemical shift for protons 11 and 2' were wrongly assigned and they should have been swapped.
Table S15. Comparison of natural and synthetic tagitin F (16) (CDCl$_3$)$^{17}$

![Image of tagitin F (16)]

|       | Natural (300 MHz) | Synthetic (400 MHz) | Authentic sample (100 MHz) | Synthetic (100 MHz) |
|-------|------------------|---------------------|----------------------------|---------------------|
| 1     | 5.81, d (6)      | 5.81, (d, 5.5)      | 127.9                      | 127.9               |
| 2     | 6.31, d (6)      | 6.33, (d, 5.7)      | 139.6                      | 139.6               |
| 3     | -                | -                   | 108.5                      | 108.5               |
| 4     | -                | -                   | 139.5                      | 139.5               |
| 5     | 5.69, m          | 5.68, m             | 131.3                      | 131.3               |
| 6     | 5.90, dd (5, 3)  | 5.91, dh (6.1, 1.3) | 74.7                       | 74.7                |
| 7     | 3.42, ddd (2.5, 2.1) | 3.42, m          | 48.0                       | 48.0                |
| 8     | 5.08, t (5.4)    | 5.08, td (3.6, 0.9) | 76.6                       | 76.6                |
| 9α    | 2.36, dd (15.4)  | 2.36, dd (16.2, 3.9) | 43.9                       | 43.9                |
| 9β    | 2.28, dd (15.5)  | 2.28, dd (16.2, 3.3) | -                          | -                   |
| 10    | -                | -                   | 87.2                       | 87.2                |
| 11    | -                | -                   | 139.0                      | 139.0               |
| 12    | -                | -                   | 169.7                      | 169.7               |
| 13a   | 6.30, d (2.5)    | 6.35, d (2.9)       | 124.3                      | 124.3               |
| 13b   | 5.69, d (2)      | 5.67, d (2.5)       | -                          | -                   |
| 14    | 1.41, s          | 1.40, s             | 31.8                       | 31.8                |
| 15    | 1.93, t (1.5)    | 1.93, t (1.5)       | 20.8                       | 20.8                |
| 1'    | -                | -                   | 175.9                      | 175.9               |
| 2'    | 2.49, hept (7.2) | 2.50, hept (7)      | 34.4                       | 34.4                |
| 3'    | 1.11, d (7.2)    | 1.11, d (7)         | 19.1                       | 19.1                |
| 4'    | 1.13, d (7.2)    | 1.13, d (7)         | 18.9                       | 18.9                |

2D NMR correlations

|       | $^1$H-$^1$H COSY | HMBC | NOESY |
|-------|----------------|------|-------|
| 16    | ![Image of HMBC](image1.png) | ![Image of NOESY](image2.png) | ![Image of NOESY](image3.png) |

$^{17}$Fernandes, V. H. C. Viera, N. B. Zanini, L. B. L. Silva, A. F. Salem, P. P. O. Soares, M. G. Nicacio, K. J. de Paula, A. C. C. Virtuoso, L. S. Oliveira, T. B. Silva, E. O. Dias, D. F. Chagas-Paula, D. A. *Photochem. Photobiol.* **2020**, *96*, 14-20.
### Table S16. Comparison of natural and synthetic tagitinin C (17) (CDCl₃)

![Chemical Structure of Tagitinin C (17)]

|                  | **1H NMR** |                  |                  | **13C NMR** |                  |
|------------------|------------|------------------|------------------|------------|------------------|
|                  | Natural¹⁷ | Natural¹⁸        | Synthetic       | Natural¹⁸  | Synthetic       |
|                  | (500 MHz) | (270 MHz)        | (500 MHz)       | (68 MHz)   | (125 MHz)       |
| 1                | 6.94, (d, 17.1) | 6.94, (d, 17)   | 6.91, (d, 17.1) | 160.49     | 159.88          |
| 2                | 6.26, (d, 17.1) | 6.26, (d, 17)   | 6.24, (d, 17.1) | 129.57     | 129.72          |
| 3                | -          | -                | -                | -          | -                |
| 4                | -          | -                | -                | -          | -                |
| 5                | 5.87, like d (9) | 5.88, br d (10) | 5.87, br d (9.5) | 137.14     | 137.15          |
| 6                | 5.41, like d (9) | 5.42, br d (10) | 5.39, br d (9.1) | 76.05      | 75.93           |
| 7                | 3.54, m    | 3.55, m          | 3.53, m          | 47.05      | 47.06           |
| 8                | 5.37, m    | 5.33, m          | 5.36, m          | 74.11      | 73.73           |
| 9α               | 2.49       | ~2.4             | 2.46             | 48.37      | 48.47           |
| 9β               | 2.02       | ~2               | 2.01, dd (14.4, 4.5) | -          | -                |
| 10               | -          | -                | -                | 71.91      | 72.18           |
| 11               | -          | -                | -                | 136.11     | 136.00          |
| 12               | -          | -                | -                | 169.75     | 169.58          |
| 13a              | 6.34, d (1.5) | 6.36, d (2)     | 6.36, d (1.8)   | 124.43     | 124.49          |
| 13b              | 5.81, d (1.5) | 5.81, d (2)     | 5.80, d (1.7)   | -          | -                |
| 14               | 1.53, s    | 1.56             | 1.54, s          | 28.88      | 29.16           |
| 15               | 1.95, like s | 1.97, br        | 1.96, br s      | 19.65      | 19.69           |
| 1'               | -          | -                | -                | 176.18     | 176.06          |
| 2'               | 2.42, m    | 2.44, m          | 2.43, m          | 34.06      | 34.03           |
| 3'               | 1.07, d (4.5) | 1.10, d (7.1)   | 1.08, d (7)     | 18.80      | 18.81           |
| 4'               | 1.05, d (4.5) | 1.08, d (7.1)   | 1.06, d (7)     | 18.64      | 18.62           |

#### 2D NMR correlations

|                  | **1H-1H COSY** | **HMBC** | **NOESY** |
|------------------|----------------|----------|-----------|
| 17               | ![1H-1H COSY](image1) | ![HMBC](image2) | ![NOESY](image3) |

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¹⁸ Baruah, N. C., Sharma, R. P., Madhusudanan, K. P., Thyagarajan, G., Herz, W., Murari, R. *J. Org. Chem.*, 1979, **44**, 1831-1835.
f) Experimental procedures for Scheme 1

Figure S4. Synthesis of 20a from commercially available 3-butyn-1-ol (S4-1).

Vinyl iodide 24 was prepared from commercially available 3-butyn-1-ol using a carboalumination /iodination process.19 The reaction can be ran in a decagram scale and the product can be used in the next step without further purification.

To a 0 °C solution of alcohol 24 (~132 mmol) in CH₂Cl₂ (250 mL) Dess–Martin periodinane (DMP, 56 g, 132 mmol) was slowly added in portions. The mixture was stirred at room temperature for 3 hours, till TLC analysis showed disappearance of starting material (aldehyde, Rf = 0.60, Pentane/Ethyl acetate = 5/1). Then, the mixture was cooled down again to 0 °C and a catalytic amount of p-TsOH+H₂O (1.0 g) was added, followed by addition of CH(OMe)₃ (21.6 mL, 198 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 30 minutes. The mixture was then quenched with saturated aqueous NH₄Cl and Na₂SO₃ (v/v = 1:1, 500 mL) and extracted with CH₂Cl₂ (3 × 500 mL). The combined organic layers were washed with brine (500 mL), dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 30/1) to provide the S4-3 as yellow oil (26.4 g, 78%).

Data of vinyl iodide S4-3: yellow oil;
¹H NMR (400 MHz, CDCl₃) δ 6.02 (m, 1H, H₁), 4.47 (t, J = 5.7 Hz, 1H, H₄), 3.32 (s, 6H, -OMe), 2.50 (dd, J = 5.7, 1.0 Hz, 2H, H₃), 1.88 (d, J = 1.1 Hz, 3H, H₅) ppm;
¹³C NMR (100 MHz, CDCl₃) δ 143.4 (C₂), 102.9 (C₄), 77.8 (C₅H), 53.1 (-OMe), 42.5 (C₃H₂), 24.6 (C₃H₃) ppm;
IR (film, cm⁻¹) 2931, 1729, 1118, 1072; TLC: Rf = 0.40, Pentane/Ethyl acetate = 25/1).

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19 Prasad, K. R., Pawar, A. B. Org Lett., 2011, 13, 4252-4255.
To a stirred solution of vinyl iodide S4-3 (20.8 g, 81 mmol) in THF/i-Pr2NH (150 mL/50 mL) was added trimethylsilyl acetylene (13.5 mL, 97.5 mmol) at 0 °C. Then Pd(PPh3)2Cl2 (2.8 g, 4.05 mmol) and CuI (1.54 g, 8.1 mmol) were added at the same temperature. The reaction mixture was allowed to reach room temperature and stirred for 1 hour till TLC analysis showed disappearance of starting material. Then pentane (800 mL) was added to the reaction mixture, stirred for 30 minutes, the mixture was filtered and the solution washed with saturated aqueous NH4Cl (200 mL). The aqueous phase was extracted with CH2Cl2 (2 × 100 mL). The combined organic layers were dried over Na2SO4, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 50/1 ~ 25/1) to provide the 25 as light-yellow oil (13.3 g, 72%).

Data of vinyl iodide 25: light-yellow oil;
1H NMR (400 MHz, CDCl3) δ 5.38 (m, 1H, H3), 4.47 (t, J = 5.7 Hz, 1H, H6), 3.30 (s, 6H, -OMe), 2.37 (d, J = 5.8 Hz, 2H, H5), 1.94 (d, J = 0.8 Hz, 3H, H7), 0.18 (s, 9H, -TMS) ppm;
13C NMR (100 MHz, CDCl3) δ 148.9 (C4), 107.9 (C6H), 103.2 (C2), 103.1 (C3H), 97.6 (Ci), 52.9 (-OMe), 41.8 (C5H2), 20.2 (C7H3), 0.2 (-TMS) ppm;
IR (film, cm⁻¹) 2957, 2135, 1249, 1120, 1064, 838, 509;
HRMS(ESI) [M + H]+ calculated for C12H23O2Si: 227.1467, found: 227.1250;
TLC: Rf = 0.30 (Pentane/Ethyl acetate = 25/1).

A 500 mL round bottom flask equipped with a magnetic stir bar was charged with K2OsO2(OH)2•2H2O (320 mg, 0.9 mmol), (DHQD)2Pyr (1.2 g, 1.36 mmol), K3Fe(CN)6 (44.6 g, 136 mmol), K2CO3 (18.8 g, 136 mmol) and t-BuOH/H2O (100 mL/100 mL). The biphasic mixture was stirred at room temperature for 30 minutes, then MeSO2NH2 (4.8 g, 50.5 mmol) was added and the mixture was stirred for another 30 minutes. Enyne 25 (10.2 g, 45 mmol) was added to the AD-mix-β mixture and stirred at room temperature for 8 hours. The reaction was followed by NMR analysis till disappearance of the starting material. The reaction slurry was filtered and the filtrate was extracted with CH2Cl2 (2 × 100 mL). The combined organic layers were dried over Na2SO4, filtered, concentrated in vacuo and then used directly for silyl protection without further purification. The crude product was dissolved in CH2Cl2 (300 mL) and imidazole (7.7 g, 113 mmol) was added. Then TBDPSCI (21 mL, 81 mmol) was added dropwise together with a catalytic amount of DMAP (100 mg). The reaction mixture was then stirred at room temperature for 8 hours or till the TLC analysis showed disappearance of starting material. Then, the mixture was quenched with water (100 mL) and extracted with CH2Cl2 (2 × 200 mL). The combined organic layers were washed with brine (500 mL), dried over Na2SO4, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 15/1 ~ 5/1) to provide the 26 as a colorless oil (18 g, 80%).
The enantiomers were found not to be separated by chiral HPLC using various columns under different conditions. The ee value was confirmed after TMS deprotection.

Data of alcohol 26: Colorless oil; 
[α]_D^20 -53.0 (c 1.0, CHCl_3);

^1^H NMR (400 MHz, CDCl₃) δ 7.74-7.68 (m, 4H, -TBDPS), 7.45-7.32 (m, 6H, -TBDPS), 4.69 (t, J = 5.6 Hz, 1H, H_6), 4.18 (s, 1H, H_5), 3.29 (s, 3H, -OMe), 3.28 (s, 3H, -OMe), 2.05 (dd, J = 14.4, 5.2 Hz, 1H, H_3), 1.88 (dd, J = 14.8, 6 Hz, 1H, H_3), 1.31 (s, 3H, H_7), 1.07 (s, 9H, -TBDPS), -0.01 (s, 9H, -TMS) ppm;

^1^3^C NMR (100 MHz, CDCl₃) δ 136.4 (TBDDS), 136.3 (TBDDS), 133.7 (TBDDS), 133.0 (TBDDS), 130.0 (TBDDS), 129.7 (TBDDS), 127.7 (TBDDS), 127.4 (TBDDS), 104.4 (C_2), 102.4 (C_3H), 92.1 (C_4), 73.8 (C_4), 71.7 (C_3H), 53.1 (-OMe), 53.0 (-OMe), 39.5 (C_3H_2), 27.2 (TBDDS), 23.6 (C_3H), 19.6 (TBDDS), -0.3 (TMS) ppm;

IR (film, cm⁻¹) 2957, 1719, 1428, 1250, 1111, 843, 701;

HRMS(ESI) [M + Na]⁺ calculated for [C₂₈H₂₇NaO₄Si₂]⁺: 521.2514, found: 521.2520;

TLC: Rf = 0.50 (Pentane/Ethyl acetate = 10/1).

To a stirred solution of TMS alkyne 26 (18 g, 36 mmol) in MeCN/H₂O (90 mL/5 mL) was added DBU (8.1 mL, 54 mmol) at room temperature. The reaction mixture was stirred at for 4 hours or till the TLC analysis showed disappearance of starting material. The reaction mixture was concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 20/1 ~ 3/1) to provide the alkyne 20a as colorless oil (13.3 g, 87%).

Chiral HPLC analysis of 20a: chiral stationary column: AD-H, mobile phase: n-hexane/i-PrOH = 99:1, 1.0 mL/min, 210 nm, 30 °C, tₚ (major) = 12.80 min, tₚ (minor) = 11.05 minutes. The result indicated 91% ee. See Supplementary Section k for details.

Data of alkyne 20a: colorless oil;

[α]_D^20 -39.8 (c 0.19, CHCl₃);

^1^H NMR (400 MHz, CDCl₃) δ 7.79-7.67 (m, 4H, -TBDPS), 7.46-7.33 (m, 6H, -TBDPS), 4.66 (t, J = 5.7 Hz, 1H, H_6), 4.22 (d, J = 2.2 Hz, 1H, H_3), 3.28 (s, 3H, -OMe), 3.27 (s, 3H, -OMe), 3.07 (s, 1H, -OH), 2.26 (d, J = 2.2 Hz, 1H, H_3), 2.06 (dd, J = 14.4, 6 Hz, 1H, H_3), 1.89 (dd, J = 14.5, 5.5 Hz, 1H, H_3), 1.31 (s, 3H, H_7), 1.10 (d, J = 2.9 Hz, 9H, -TBDPS) ppm;

^1^3^C NMR (100 MHz, CDCl₃) δ 136.4 (TBDDS), 136.3 (TBDDS), 133.7 (TBDDS), 133.0 (TBDDS), 130.0 (TBDDS), 129.7 (TBDDS), 127.7 (TBDDS), 127.4 (TBDDS), 102.3 (C_4H), 82.6 (C_3H), 75.1 (C_4), 73.8 (C_4), 71.0 (C_3H), 53.2 (-OMe), 52.9 (-OMe), 39.3 (C_3H_2), 27.2 (TBDDS), 23.6 (C_3H) ppm;

IR (film, cm⁻¹) 3501, 2933, 1427, 1107, 1092, 700;

HRMS(ESI) [M + Na]⁺ calculated for [C₂₈H₃₄NaO₄Si₂]⁺: 449.2119, found: 449.2124;

TLC: Rf = 0.50 (Pentane/Ethyl acetate = 7/1).
Figure S5. Synthesis of 27 from 2-butyn-1-ol (S5-1)

Aldehyde 27 was prepared from commercially available 2-butyn-1-ol (S5-1) in 2 steps using a carboalumination / iodonation then modified DMP oxidation process. All spectroscopic and spectrometric analyses were in agreements with the literature accordingly for allylic alcohol (Z)-3-iodobut-2-en-1-ol (S5-2)\textsuperscript{20} and aldehyde 27.\textsuperscript{21}

Modified DMP oxidation: To a stirred solution of crude allylic alcohol S5-2 (~ 42 g, 212 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (400 mL) was added DMP (90 g, 212 mmol) in portions at 0 °C. The reaction was monitored by TLC until no starting material remained (2 hours). Then pentane (1.2 L) was added to the reaction and stirred at room temperature for 30 minutes. The white precipitate was filtered off and the resulting colorless solution was concentrated \textit{in vacuo} to give a yellow to brown oil 27 (~ 42 g) which was used directly for Barbier reaction without any further purification.

Figure S6. Synthesis of 28

Allylic bromide 28 is known compound and was prepared in 2 steps including Baylis–Hillman reaction\textsuperscript{22} and bromination\textsuperscript{23} from triethyl phosphonoacetate (S6-1). All spectroscopic and spectrometric analyses were in agreements with the literature accordingly.

A 2.5 L round bottom flask equipped with a magnetic stir bar was charged with aldehyde 27 (82 g, 418 mmol), allylic bromide 28 (121 g, 627 mmol), THF (800 mL) and NH\textsubscript{4}Cl saturated solution (160 mL). The yellow bi-phasic mixture turned colorless and was cooled down to 0 °C. Then Zn (54 g, 836 mmol) was added in small portions within 30 minutes (caution the reaction is very exothermic). The reaction mixture was stirred at 0 °C for 20 minutes or till the TLC analysis showed disappearance of the starting material. The reaction mixture was filtered, the filtrate was concentrated \textit{in vacuo} and redissolved

\textsuperscript{20} Dakoji, S.; Li, D.; Agnihotri, G.; Zhou, H.; Liu, H. \textit{J. Am. Chem. Soc.} 2001, 123, 9749-9759.

\textsuperscript{21} Meyer, C., Marek, I., Normant, J. F. \textit{Synlett}. 1993, 6, 386-388.

\textsuperscript{22} Patil, S., Chen, L., Tanko, J. M. \textit{Eur. J. Org. Chem.} 2014, 3, 502-505.

\textsuperscript{23} Li, Y., Zhang, J., Li, D., Chen, Y. \textit{Org. Lett.} 2018, 20, 3296-3299.
in CH₂Cl₂ (800 mL). The organic layer was washed with water (200 mL) and brine (200 mL), dried over Na₂SO₄, filtered, concentrated in vacuo and used directly for cyclization without further purification. The crude product was dissolved in CH₂Cl₂ (500 mL) and a catalytic amount p-TsOH•H₂O (1.0 g) was added. The reaction mixture was stirred at room temperature for 12 hours or till the TLC analysis showed disappearance of starting material. Then the mixture was washed with sat. aq. NaHCO₃ (100 mL), brine (100 mL), dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 20/1 ~ 5/1) to provide the 29 as light-yellow oil (70.6 g, 64%).

Data of lactone 29: light-yellow oil;

1H NMR (400 MHz, CDCl₃) δ 6.25-6.20 (m, 1H, H₈), 5.71 (dt, J = 7.6, 1.8 Hz, 1H, H₅), 5.65 (q, J = 2.2 Hz, 1H, H₆), 5.04 (dt, J = 9.8, 6.8 Hz, 1H, H₄), 3.25 (ddt, J = 17.1, 7.7, 2.3 Hz, 1H, H₃), 2.64 (dddt, J = 17.2, 6.2, 3.0, 1.3 Hz, 1H, H₂), 2.54 (d, J = 1.7 Hz, 3H, H₇) ppm;

13C NMR (100 MHz, CDCl₃) δ 171.0 (C₁), 133.8 (C₄), 126.6 (C₈), 122.6 (C₉H₂), 104.3 (C₆), 81.3 (C₄H), 33.8 (C₃H₃), 33.6(C₃H₂) ppm; ¹³C NMR of C₂ overlaps with C₅;

IR (film, cm⁻¹) 1765, 1242, 1116, 1016;

HRMS(ESI) [M + H]+ calculated for [C₈H₁₀O₂]+: 264.9725, found: 264.9709; TLC: Rf = 0.60 (Pentane/Ethyl acetate = 5/1).

To a stirred solution of lactone 29 (22 g, 83 mmol) in dioxane (500 mL) was added SeO₂ (50 g, 450 mmol) in 3 portions at 95 °C within 2 h. The reaction mixture was stirred at the same temperature for another hour and cooled down to room temperature. Then dioxane was evaporated and Et₂O (800 mL) was added, stirred for 30 min, filtered and the solution was washed with saturated aqueous NaHCO₃ (100 mL), diluted Na₂S (50 mL) and brine (100 mL). The organic phase was dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 1/1) to provide the 21 as light-yellow oil (9.8 g, 42%).

Lactone 21 was obtained as a mixture of inseparable 1.8/1 diastereomers (determined by ¹H NMR). The structures were fully elucidated based on 2D NMR spectroscopic analyses, which indicated trans as the major product.

Data of lactone 21: Light yellow oil;

IR (film, cm⁻¹) 3420, 1753, 1250, 1129, 973;

HRMS(ESI) [M + H]+ calculated for [C₈H₁₀O₃]+: 280.9669, found: 280.9675;

TLC: Rf = 0.50 (Pentane/Ethyl acetate = 1/1);

Major-trans: ¹H NMR (400 MHz, CDCl₃) δ 6.44 (d, J = 2.3 Hz, 1H, H₈), 6.00 (d, J = 2.1 Hz, 1H, H₆), 5.65 (dq, J = 8.0, 1.5 Hz, 1H, H₅), 4.89 (dd, J = 8.1, 4.5, 0.7 Hz, 1H, H₄), 4.67 (ddt, J = 6.5, 4.4, 2.2 Hz, 1H), 2.89 (d, J = 6.1 Hz, 1H, -OH), 2.59 (dd, J = 1.6, 0.6 Hz, 3H, H₇) ppm;

¹³C NMR (100 MHz, CDCl₃) δ168.5 (C₁), 137.7 (C₂), 131.3 (C₄H), 126.6 (C₉H₂), 106.9 (C₆), 88.7 (C₄H), 73.7 (C₃H), 34.2 (C₃H₂) ppm; ¹³C NMR of C₂ of cis and trans are overlaped;
**Minor-cis:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.45 (d, $J = 1.7$ Hz, 1H, $H_8$), 6.04 (d, $J = 1.5$ Hz, 1H, $H_8$), 5.81 (dq, $J = 7.5, 1.5$ Hz, 1H, $H_5$), 5.06 (ddd, $J = 7.5, 5.7, 0.8$ Hz, 1H, $H_4$), 5.03-4.97 (m, 1H, $H_3$), 2.63 (dd, $J = 1.6, 0.6$ Hz, 3H, $H_7$), 2.50 (d, $J = 4.8$ Hz, 1H, -OH). ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.9 (C$_1$), 137.7 (C$_2$), 128.8 (C$_8$H$_2$), 127.5 (C$_8$H$_2$), 107.2 (C$_6$), 86.4 (C$_4$H), 69.1 (C$_3$H), 34.3 (C$_7$H$_3$) ppm; $^{13}$C NMR of C$_2$ of cis and trans are overlaped.

To a stirred solution at room temperature and under inert atmosphere of N$_2$ of alkyne 20a (8.0 g, 18.8 mmol) and vinyl iodide 21 (8.0 g, 28.6 mmol) in DMF/NEt$_3$ (60 mL/10 mL) was added PPh$_3$ (1.1 g, 4.2 mmol) followed by Pd$_2$dba$_3$ (3.6 g, mmol) and CuI (0.6 g, mmol). The resulted mixture was stirred for 3 hours or till the TLC analysis showed disappearance of starting material. The reaction was then quenched by addition of sat. aq. NH$_4$Cl (100 mL) and extracted with ethyl acetate (3 × 200 mL). The combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 1/2) to provide enyne 21-1 as yellow oil (4.3 g, 40%). The reaction can be run from milligrams to a eight grams scale with yields varyling from 40% ~ 84% depending on the scale.

Enyne 21-1 was obtained as a complicated mixture of diastereomers and that could not be seperated by convencional chromatographic techniques.

Data of enyne 21-1: yellow oil;
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.75-7.69 (m, 4H), 7.50-7.31 (m, 6H), 6.39-6.37 (m, 1H), 6.02-5.80 (m, 1H), 5.59-5.54 (m, 0.88H), 5.26 (t, $J = 9.3$ Hz, 0.13H), 5.08-4.77 (m, 1H), 4.75 – 4.61 (m, 1.27H), 4.56 (dd, $J = 6.2, 4.5$ Hz, 0.23H), 4.48-4.46 (m, 0.56H), 4.37 (dd, $J = 16.1, 4.2$ Hz, 1H), 4.00 (dd, $J = 20.7, 6.8$ Hz, 0.44H), 3.32-3.26 (m, 6H), 2.45 (d, $J = 4.9$ Hz, 0.24H), 2.31 (d, $J = 4.8$ Hz, 0.27H), 2.22-1.85 (m, 2.5H), 1.73-1.62 (m, 2.5H), 1.39-1.29 (m, 3H), 1.14-1.05 (m, 9H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 175.2, 168.7, 136.2, 136.2, 136.1, 133.4, 132.6, 130.3, 129.9, 129.7, 129.6, 127.9, 127.6, 126.1, 102.8, 102.3, 94.6, 80.9, 80.5, 74.4, 74.2, 71.6, 53.7, 53.5, 53.1, 52.8, 39.4, 27.1, 27.0, 24.1, 22.9, 22.3, 19.6 ppm; IR (film, cm$^{-1}$) 3414, 2929, 2213, 1969, 1769, 1428, 1113, 704; HRMS(ESI) [M + Na]$^+$ calculated for C$_{33}$H$_{42}$NaO$_7$Si: 601.2596, found: 601.2598; TLC: Rf = 0.30 (Pentane/Ethyl acetate = 1/1).

A 100 mL round bottom flask equipped with a magnetic stir bar was charged with enyne 21-1 (1.7 g, 2.9 mmol) and Et$_2$O (30 mL). The reaction mixture was cooled down to -78 °C and PBr$_3$ (0.7 mL, 7.35 mmol) was added. The temperature was allowed to rise to -20.
°C and stirred for 3 hours or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with water (5.0 mL) and extracted with Et2O (3 × 50 mL). The combined organic layers were dried over Na2SO4, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1 ~ 3/1) to provide bromolactone 19a as colorless oil (0.98 g, 56%) as a 1:1 mixture of inseparable diastereomers.

Data of bromolactone 19a: colorless oil;
IR (film, cm\(^{-1}\)) 3482, 2933, 1764, 1428, 1110, 1040, 703; HRMS(ESI) \([M + H]^+\) calculated for C\(_{31}\)H\(_{36}\)BrO\(_5\)Si: 595.1510, found: 595.1516; TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 2/1);

**Diastereomer I:**
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.90 (m, 1H, \(H_9\)), 7.75-7.67 (m, 4H, TBDP), 7.49-7.35 (m, 6H, TBDP), 7.00 (q, \(J = 1.4\) Hz, 1H, \(H_6\)), 5.24-5.16 (m, 2H, \(H_5 + H_9\)), 4.47 (s, 1H, \(H_1\)), 4.02-4.05 (m, 2H, \(H_{13}\)), 2.77 (dd, \(J = 15.8, 2\) Hz, 1H, \(H_8\)), 2.69 (dd, \(J = 15.7, 2.8\) Hz, 1H, \(H_9\)), 1.67 (d, \(J = 0.8\) Hz, 3H, \(H_{14}\)), 1.47 (s, 3H, \(H_{15}\)), 1.06 (s, 9H, TBDP) ppm;
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 201.81 (C\(_3\)), 170.97 (C\(_{12}\)), 151.03 (C\(_H\)), 136.13 (TBDP), 135.98 (TBDP), 133.12 (TBDP), 131.65 (TBDP), 130.75 (C\(_{11}\)), 130.62 (TBDP), 130.11 (TBDP), 129.48 (C\(_{15}\)), 128.19 (TBDP), 127.73 (TBDP), 124.56 (C\(_4\)), 94.20 (C\(_2\)), 85.16 (C\(_3\)), 79.64 (C\(_{10}\)), 74.71 (C\(_{10}\)), 71.43 (C\(_{11}\)), 50.80 (C\(_{9}\)), 26.94 (TBDP), 23.66 (C\(_{14}\)), 22.77 (C\(_{1}\)), 20.83 (C\(_{13}\)), 19.66 (TBDP) ppm;

**Diastereomer II:**
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.88 (m, 1H, \(H_9\)), 7.75-7.67 (m, 4H, TBDP), 7.49-7.35 (m, 6H, TBDP), 6.65 (d, \(J = 1.3\) Hz, 1H, \(H_6\)), 5.24-5.16 (m, 2H, \(H_5 + H_9\)), 4.47 (s, 1H, \(H_1\)), 4.02-4.05 (m, 2H, \(H_{13}\)), 2.76 (dd, \(J = 15.7, 2\) Hz, 1H, \(H_8\)), 2.66 (dd, \(J = 15.7, 2.8\) Hz, 1H, \(H_9\)), 1.65 (d, \(J = 1.4\) Hz, 3H, \(H_{14}\)), 1.46 (s, 3H, \(H_{15}\)), 1.07 (s, 9H, TBDP) ppm;
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 201.8 (C\(_3\)), 170.95 (C\(_{12}\)), 150.84 (C\(_H\)), 136.03 (TBDP), 135.91 (TBDP), 132.91 (TBDP), 132.05 (TBDP), 130.87 (C\(_{11}\)), 130.50 (TBDP), 130.22 (TBDP), 129.54 (C\(_{15}\)), 128.11 (TBDP), 127.74 (TBDP), 124.31 (C\(_4\)), 94.36 (C\(_2\)), 85.07 (C\(_3\)), 79.64 (C\(_{10}\)), 74.80 (C\(_{10}\)), 71.44 (C\(_{11}\)), 50.78 (C\(_{9}\)), 27.00 (TBDP), 23.71 (C\(_{14}\)), 22.81 (C\(_{1}\)), 20.97 (C\(_{13}\)), 19.61 (TBDP) ppm;

A 50 mL round bottom flask equipped with a magnetic stir bar was charged with bromolactone 19a (1.03 g, 1.73 mmol) and DMF (10 mL). The reaction mixture was cooled down to 0 °C and CrCl\(_2\) (532 mg, 4.3 mmol) was added. The temperature was allowed to rise to room temperature and stirred for 1 hour or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NH\(_4\)Cl (20 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\), then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 3/1 ~ 1/3) to provide 18a as a waxy solid (272 mg, 30%) and 30 as a light yellow solid (270 mg, 30%).
The structures of 18a and 30 were fully elucidated based on 2D NMR spectroscopic analyses. The absolute configuration of 30 was determined by X-ray diffraction. Single crystals of 30 suitable for X-ray crystallographic analysis were obtained by a single recrystallization at room temperature by slow evaporation using n-hexanes/CH2Cl2 as solvent mixture. See Supplementary Section m for detail.

Data of 18a: waxy solid; [α]D 20 -130.2 (c 0.2, CHCl3);
$^1$H NMR (400 MHz, CDCl3) δ 87.69 (ddd, J = 10.3, 8.1, 1.5 Hz, 4H, -OTBDPS), 7.47-7.31 (m, 6H, -OTBDPS), 6.36 (br s, 1H, H13), 5.86 (m, 1H, H3), 5.73 (br s, 1H, H13), 5.02 (dt, J = 3.7, 1.9 Hz, 1H, H6), 4.15 (s, 1H, H3), 3.92 (br s, 1H, H2), 3.88 (m, 1H, H6), 2.72 (br d, J = 15.3 Hz, 1H, H2), 2.07 (dd, J = 15.2, 6.1 Hz, 1H, H9), 1.61 (t, J = 1.8 Hz, 3H, H13), 1.41 (s, 3H, H14), 1.11 (s, 9H, -OTBDPS) ppm;
$^{13}$C NMR (100 MHz, CDCl3) δ 170.3 (C12), 139.6 (C3H), 136.4 (TBDDS), 136.1 (TBDDS), 135.8 (C11), 133.2 (TBDDS), 133.0 (TBDDS), 130.13 (TBDDS), 130.05 (TBDDS), 127.8 (TBDDS), 127.5 (TBDDS), 125.7 (C1H2), 120.3 (C4), 99.4 (C2), 84.7 (C3), 79.5 (C4H), 77.5 (C10), 71.9 (C1H), 71.1 (C3H), 50.7 (C4H), 31.7 (C14H3), 27.2 (TBDDS), 20.9 (C3H3), 19.5 (TBDDS) ppm; Signal of C2/C3/C9 could not be detected on $^{13}$C NMR because of the conformational changes, the chemical shift of C2 and C3 were confirmed by HMBC, but the chemical shift of C8 could not be confirmed by any 2D NMR. $^{13}$C NMR of C10 overlaps with the solvent peak, the chemical shift was confirmed by HMBC;
IR (film, cm⁻¹) 3475, 2963, 1765, 1429, 1269, 1112, 823, 743, 703, 547; HRMS(ESI) [M + H]⁺ calculated for C31H37O5Si: 517.2417, found: 517.2410;
TLC: Rf = 0.40 (Pentane/Ethyl acetate = 2/1).

Data of 30: light yellow solid, m.p. = 124.4 - 125.8 °C;
[α]D 20 -86.6 (c 1.0, CHCl3);
$^1$H NMR (400 MHz, CDCl3) δ 7.69-7.65 (m, 4H, -OTBDPS), 7.34-7.45 (m, 6H, -OTBDPS), 6.44 (d, J = 3.3 Hz, 1H, H13), 5.94 (dt, J = 2.6, 1.6 Hz, 1H, H3), 5.76 (d, J = 2.8 Hz, 1H, H13), 4.91 (dt, J = 6.8, 2.3 Hz, 1H, H6), 4.61-4.42 (m, 1H, H8), 4.23 (s, 1H, H1), 3.96-3.76 (m, 1H, H2), 2.54 (dd, J = 15.0, 7.6 Hz, 1H, H9), 1.91 (dd, J = 15.0, 3.0 Hz, 1H, H9), 1.58 (t, J = 1.8 Hz, 3H, H13), 1.44 (s, 3H, H14), 1.09 (s, 9H, -OTBDPS) ppm;
$^{13}$C NMR (100 MHz, CDCl3) δ 169.5 (C12), 136.5 (C3H), 136.2 (TBDDS), 136.1 (TBDDS), 134.9 (C11), 133.2 (TBDDS), 132.6 (TBDDS), 130.3 (TBDDS), 130.1 (TBDDS), 128.0 (TBDDS), 127.6 (TBDDS), 123.3 (C3H2), 118.7 (C4), 95.9 (C2), 87.1 (C3), 80.3 (C4H), 75.8 (C10), 70.3 (C1H), 67.9 (C3H), 49.0 (C2H), 46.0 (C3H2), 27.2 (C14H3), 27.2 (TBDDS), 22.2 (C15H3), 19.6 (TBDDS) ppm; $^{13}$C NMR of C14 is overlap with TBDDS, the chemical shift is confirmed by HMBC;
IR (film, cm⁻¹) 3475, 2963, 1765, 1429, 1269, 1112, 823, 743, 703, 547; HRMS(ESI) [M + Na]⁺ calculated for C31H36NaO6Si: 539.2236, found: 539.2230;
TLC: Rf = 0.05 (Pentane/Ethyl acetate = 2/1).
To a solution of TBDPS-protected alcohol 30 (50 mg, 0.097 mmol) in an Eppendorf safe-lock tube 1 drop of THF followed by hydrogen fluoride pyridine (hydrogen fluoride ~70%, 0.2 mL) were added. The reaction mixture was left on a shaker at room temperature for 40 minutes. Then, CH₂Cl₂ (2.0 mL) was added and the reaction was quenched carefully with sat. aq. NaHCO₃ (caution: the mixture bubbles out while quenching) until the evolution of gas stopped. The mixture was extracted with ethyl acetate (5 × 10 mL), the combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 1/1 ~ 1/3) to provide 30-1 as a white powder (18.7 mg, 69%).

Data of 30-1: white powder, m.p. = 64 - 66 °C;
[α]ᵡ²⁰ +58.9 (c 1.0, CHCl₃);
¹H NMR (400 MHz, methanol-d₄) δ 6.30 (d, J = 3.3 Hz, 1H, H₁₃), 6.08 (dq, J = 3.1, 1.6 Hz, 1H, H₃), 5.79 (d, J = 2.8 Hz, 1H, H₁₃), 5.04 (dp, J = 6.9, 2.2 Hz, 1H, H₆), 4.73 (ddd, J = 7.0, 2.5, 1.2 Hz, 1H, H₈), 4.11 (ddd, J = 7.1, 3.6, 1.2 Hz, 1H, H₇), 4.07 (s, 1H, H₁), 2.55 (dd, J = 15.2, 6.9 Hz, 1H, H₉), 1.89 (t, J = 1.8 Hz, 3H, H₁₅), 1.82 (ddd, J = 15.2, 2.6, 1.0 Hz, 1H, H₁₀), 1.34 (s, 3H, H₁₄) ppm;
¹³C NMR (100 MHz, methanol-d₄) δ 172.1 (C₁₂), 137.1 (C₉H), 136.1 (C₁₁), 124.1 (C₁₃H₂), 120.1 (C₆), 98.5 (C₁₅), 85.8 (C₃), 82.2 (C₂H), 75.7 (C₁₀), 69.5 (C₁₁H), 68.3 (C₁₃H), 50.6 (C₁₄H), 46.7 (C₁₅H), 27.7 (C₁₅H₃), 23.0 (C₁₅H₃) ppm;
IR (film, cm⁻¹) 3391, 2928, 1743, 1277, 140, 1022;
HRMS(ESI) [M + Na]⁺ calculated for C₁₅H₁₈NaO₅: 301.1068, found: 301.1052;
TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 1/2).
To a stirred solution of triol 30-1 (15 mg, 0.054 mmol) in CH₂Cl₂ (5.0 mL) was added MnO₂ (47 mg, 0.79 mmol). The reaction mixture was stirred at room temperature for 3 hours or till TLC analysis showed disappearance of starting material. Then, MnO₂ was filtered off and washed with CH₂Cl₂ (1.0 mL). Bu₃AuNTf₂ (2.2 mg, 0.003 mmol) was added to the CH₂Cl₂ solution and the mixture was stirred for 10 minutes or till the TLC analysis showed disappearance of starting material. The resulting solution was concentrated in vacuo and the residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1~1/1) to provide the 30-3 as waxy solid (5.6 mg, 38%).

Data of 30-2: waxy solid;
[α]°D +345.3 (c 0.2, CHCl₃);
1H NMR (400 MHz, CDCl₃) δ 6.50 (d, J = 3.0 Hz, 1H, H₁₃), 6.38 (dq, J = 4.6, 1.6 Hz, 1H, H₅), 5.94 (dd, J = 2.6, 0.5 Hz, 1H, H₁₃), 5.05 (ddt, J = 6.0, 3.6, 1.8 Hz, 1H, H₆), 4.24 (p, J = 4.9 Hz, 1H, H₈), 3.54 (d, J = 1.4 Hz, 1H, -OH), 3.49 (ddt, J = 5.8, 4.9, 2.9 Hz, 1H, H₇), 2.51 (dd, J = 15.6, 4.8, 1.4 Hz, 1H, H₉), 2.29 (dd, J = 15.5, 5.1 Hz, 1H, H₉), 2.23 (d, J = 4.9 Hz, 1H, -OH), 1.99 (t, J = 1.7 Hz, 3H, H₁₃), 1.50 (s, 3H, H₁₄) ppm;
13C NMR (100 MHz, CDCl₃) δ 13C NMR (101 MHz, CDCl₃) δ 190.5 (C₁₇), 169.2 (C₁₁), 144.9 (C₇), 133.2 (C₁₂), 127.1 (C₁₃), 118.1 (C₆), 102.2 (br, C₃), 93.8 (C₂), 81.2 (C₁₉), 80.5 (C₉), 70.5 (C₈), 50.0 (C₄), 48.1 (br, C₂), 26.7 (C₁₄), 20.8 (C₁₃) ppm;
IR (film, cm⁻¹) 3450, 2925, 2184, 1763, 1671, 1326, 1278, 1135, 1077, 1010, 817;
HRMS(ESI) [M + Na]⁺ calculated for C₁₅H₁₆NaO₅: 299.0905, found: 299.0895;
TLC: Rf = 0.40 (Petroleum ether/Ethyl acetate = 1/2).

Data of 30-3: waxy solid;
[α]°D +249.9 (c 0.2, CHCl₃);
1H NMR (400 MHz, CDCl₃) δ 6.52 (d, J = 2.7 Hz, 1H, H₁₃), 6.09-5.98 (m, 1H, H₅), 5.80 (d, J = 2.4 Hz, 1H, H₁₃), 5.63 (m, 2H, H₆ + H₂), 4.06 (td, J = 7.1, 3.5 Hz, 1H, H₈), 2.85 (dq, J = 6.1, 2.8 Hz, 1H, H₇), 2.29 (dd, J = 14.5, 2.4 Hz, 1H, H₉), 2.17 (dd, J = 14.5, 9.7 Hz, 1H, H₉), 2.04 (possible d, 1H, -OH), 2.03 (d, J = 2.0 Hz, 3H, H₁₃), 1.56 (s, 3H, H₁₄) ppm;
13C NMR (100 MHz, CDCl₃) δ 206.7 (C₁), 183.5 (C₃), 169.8 (C₁₂), 140.0 (C₇), 133.4 (C₁₁), 129.5 (C₁₂), 127.6 (C₁), 102.0 (C₂), 86.3 (C₁₀), 82.4 (C₁₉), 71.1 (C₈), 55.4 (C₁₉), 45.0 (C₁₄), 21.0 (C₁₄), 18.2 (C₁₃) ppm;
IR (film, cm⁻¹) 3522, 1760, 1567, 1276, 1120, 995, 546;
HRMS(ESI) [M + Na]⁺ calculated for C₁₅H₁₆NaO₅: 299.0905, found: 299.0895;
TLC: Rf = 0.35 (Petroleum ether/Ethyl acetate = 1/2).

To a stirred solution of alcohol 30-3 (5.6 mg, 0.02 mmol) in THF (1.0 mL) was added NEt₃ (50 μL, 0.36 mmol) and methacrylic anhydride (25 μL, 0.17 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for approximately 3 hours or till the TLC analysis showed disappearance of the starting material. Then, the reaction was quenched with sat. aq. NaHCO₃ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na₂SO₄, filtered and
concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 4/1 ~ 5/2) to provide the 32 as a waxy solid (2.5 mg, 36%).

Data of 32: waxy solid;
[α]_D
^20
+327.9 (c 0.2, CHCl_3);

1H NMR (500 MHz, CDCl_3) δ 6.25 (d, J = 2.6 Hz, 1H, H13), 6.05 (dt, J = 2.6, 1.4 Hz, 2H, H5 + H3), 5.73 (dp, J = 4.6, 2.2 Hz, 1H, H6), 5.64 (s, 1H, H2), 5.57 (m, 1H, H3), 5.47 (d, J = 2.3 Hz, 1H, H13), 5.03 (d, J = 11.3, 4.8, 2.3 Hz, 1H, H8), 2.89 (dq, J = 6.5, 2.5 Hz, 1H, H7), 2.38 (dd, J = 14.0, 11.3 Hz, 1H, H9), 2.25 (dd, J = 14.1, 2.3 Hz, 1H, H9), 2.04 (t, J = 1.9 Hz, 3H, H15), 1.87 (dd, J = 1.6, 1.0 Hz, 3H, H4), 1.58 (s, 3H, H14) ppm;

13C NMR (126 MHz, CDCl_3) δ 206.3 (C1), 183.6 (C3), 169.1 (C12), 166.9 (C11), 140.0 (C3H), 135.9 (C2), 133.9 (C11), 127.3 (C4), 126.6 (C2H2), 126.3 (C13H2), 102.1 (C2), 85.6 (C10), 82.8 (C6H1), 73.8 (C5H1), 54.0 (C1H1), 41.6 (C14H2), 21.3 (C13H3), 18.6 (C15H3), 18.2 (C8H3) ppm;

IR (film, cm\(^{-1}\)) 3400, 2958, 2350, 1746, 1277, 1153, 1019, 818, 533;

HRMS(ESI) [M + Na]^+ calculated for C_{19}H_{26}NaO_{6}: 367.1151, found: 367.1158;

TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 1/2).

To a solution of TBDPS-protected alcohol 18a (130 mg, 0.25 mmol) in an Eppendorf safe-lock tube was added 1 drop of THF followed by hydrogen fluoride pyridine (hydrogen fluoride ~70%, 0.3 mL). The reaction mixture was left on a shaker at room temperature for 40 minutes. Then CHCl_2 (2.0 mL) was added and the reaction was quenched carefully with sat. aq. NaHCO_3 (caution the mixture bubbles out while quenching) until the evolution of gas stopped. The mixture was extracted with ethyl acetate (5 × 10 mL), the combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1 ~ 1/2) to provide the 31 as a waxy solid (25 mg, 36%).

Data of 31: waxy solid;
[α]_D
^20
-183.3 (c 1.0, CHCl_3);

1H NMR (400 MHz, CDCl_3) δ 6.40 (d, J = 1.8 Hz, 1H, H13), 5.97 (dt, J = 3.6, 1.8 Hz, 1H, H3), 5.78 (dd, J = 1.6, 0.7 Hz, 1H, H13), 5.12 (dt, J = 3.8, 2.0 Hz, 1H, H8), 4.21 (d, J = 4.1 Hz, 1H, H1), 4.02 (br, d, J = 9.1 Hz, 1H, H7), 3.86 (br s, 1H, H8), 3.23 (br s, 1H, -OH), 2.60 (br d, J = 15.7 Hz, 1H, H9), 2.12 (d, J = 4.4 Hz, 1H, C1-OH), 2.06 (dd, J = 15.5, 6.5 Hz, 1H, H9), 1.83 (t, J = 1.8 Hz, 3H, H13), 1.49 (s, 3H, H14) ppm;

13C NMR (100 MHz, CDCl_3) δ 170.2 (C12), 140.5 (C5H), 135.8 (C11), 126.0 (C13H2), 120.2 (C4), 99.3 (C2), 84.4 (C3), 79.3 (C6H), 76.9 (C10), 71.0 (C3H), 50.7 (br, C8H), 31.3 (br, C14H2), 21.0 (C15H3) ppm; Signal of C2/C3 could not be detected on 13C NMR because of the conformational changes; the chemical shift of C2 and C3 were confirmed by HMBC;

IR (film, cm\(^{-1}\)) 3403, 2958, 2350, 1746, 1277, 1153, 1019, 818, 533;

HRMS(ESI) [M + Na]^+ calculated for C_{15}H_{18}NaO_{5}: 301.1068, found: 301.1052;

TLC: Rf = 0.30 (Petroleum ether/Ethyl acetate = 1/2).
To a stirred solution of triol 31 (22 mg, 0.079 mmol) in CH₂Cl₂ (1.0 mL) was added MnO₂ (69 mg, 0.79 mmol). The reaction mixture was stirred at room temperature for 2 hours or till TLC analysis showed disappearance of starting material. Then, MnO₂ was filtered off and washed with CH₂Cl₂ (1.0 mL). tBu₃AuNTf₂ (3.3 mg, 0.004 mmol) was added to the CH₂Cl₂ solution and stirred for 10 minutes or till the TLC analysis showed disappearance of starting material. The resulted solution was concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1) to provide the 2 as white solid (17.6 mg, 81%).

The absolute configuration of 2 was determined by X-ray diffraction measurements. Single crystals of 2 suitable for X-ray crystallographic analysis were obtained by a single recrystallization by slow evaporation at room temperature using n-hexanes/CH₂Cl₂ as a solvent mixture. See Supplementary Section m for detail.

Data of 31-1: waxy solid;
[α]°D -376.9 (c 0.1, CHCl₃);
¹H NMR (400 MHz, CDCl₃) δ 6.45 (d, J = 2.5 Hz, 1H, H₁₃), 6.37 (dt, J = 3.0, 1.5 Hz, 1H, H₅), 5.85 (d, J = 2.2 Hz, 1H, H₁₃), 5.15 (dp, J = 4.6, 2.3 Hz, 1H, H₆), 4.22 (br s, 1H, H₈), 4.00 (br s, 1H, H₇), 3.61 (br s, 1H, -OH), 2.45-2.43 (m, 2H, H₉), 1.97 (like t, J = 1.9 Hz, 3H, H₁₅), 1.51 (s, 3H, H₁₄) ppm;
¹³C NMR (100 MHz, CDCl₃) δ 189.1 (C₁), 169.1 (C₁₂), 145.8 (br, C₃H), 134.3 (C₁₁), 125.7 (br, C₁₃H₂), 117.6 (C₄), 98.5 (C₅), 93.7 (br, C₂), 80.6 (C₁₀), 78.9 (br, C₆H), 70.5 (C₅H), 50.2 (C₇H), 42.1 (C₈H₂), 27.4 (br, C₁₄H₃), 21.10 (br, C₁₃H₃) ppm; Signal of C₉ could not be detected on ¹³C NMR because of the conformational changes, the chemical shift was confirmed by HMBC;
IR (film, cm⁻¹) 3443, 2927, 2183, 1751, 1675, 1278, 1136, 1014;
HRMS(ESI) [M + H]+ calculated for C₁₅H₁₇O₅: 277.1068, found: 277.1076;
TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 3/1).

Data of 2: white solid; m.p. = 210 - 211 °C;
[α]°D -50.4 (c 0.25, CHCl₃);
¹H NMR and ¹³C NMR data, see Table S1;
IR (film, cm⁻¹) 3454, 1765, 1701, 1577, 1289, 1135, 1001, 815;
HRMS(ESI) [M + H]+ calculated for C₁₅H₁₇O₅: 277.1068, found: 277.1076;
TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 1/1).
To a stirred solution of alcohol 2 (4.0 mg, 0.014 mmol) in THF (1.0 mL) was added NEt3 (50 μL, 0.36 mmol) and methacrylic anhydride (25 μL, 0.17 mmol) followed by a trace of DMAP. The reaction mixture was then stirred at room temperature for 30 minutes or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO3 (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na2SO4, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 5/1) to provide the 5 as a waxy solid (3.9 mg, 93%).

Data of 3: waxy solid; 
[α]20D -38.5 (c 0.20, CHCl3); lit. [α]24D -38 (c 0.76, CHCl3) (Phytochemistry, 1976, 15, 1775-1776);
1H NMR and 13C NMR data, see Table S4;
IR (film, cm⁻¹) 2925, 2854, 1769, 1707, 1588, 1292, 1138, 1027, 520;
HRMS(ESI) [M + Na]+ calculated for C19H20NaO6: 367.1151, found: 367.1158;
TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 3/1).

To a stirred solution of alcohol 2 (2.0 mg, 0.007 mmol) in THF (1.0 mL) was added NEt3 (50 μL, 0.36 mmol) and angelic anhydride (25 μL, 0.14 mmol) followed by a trace of DMAP. The reaction mixture was then stirred at room temperature for 30 hours or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO3 (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na2SO4, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 5/1) to provide the 4 as a waxy solid (1.1 mg, 45%).

We observed partial isomerization from angelate to tiglate (angelate/tiglate = 11/1 as determined by crude 1H NMR) and a little amount of 5 was isolated from this reaction.

Data of 4: waxy solid; 
[α]20D -50.0 (c 0.035, CHCl3); lit. [α]24D -56.9 (c 0.26, CHCl3) (Phytochemistry, 1980, 19, 2381-2385);
1H NMR and 13C NMR data see Table S5;
IR (film, cm⁻¹) 1769, 1709, 1589, 1291, 1234, 1138, 1030, 527;
HRMS(ESI) [M + H]+ calculated for C20H23O6: 359.1495, found: 359.1517;
TLC: Rf = 0.55 (Petroleum ether/Ethyl acetate = 3/1).
To a stirred solution of alcohol 2 (2 mg, 0.007 mmol) in THF (1 mL) was added NEt₃ (50 μL, 0.36 mmol) and tiglic anhydride (25 μL, 0.14 mmol). Then trace DMAP was added. The reaction mixture was stirred at room temperature for 90 min or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO₃ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 5/1) to provide the 5 as a waxy solid (1.5 mg, 60%).

Data of 5: waxy solid; 
[α]$_D^{20}$ -49.5 (c 0.020, CHCl₃); lit. [α]$_D^{24}$ -54.3 (c 2.0, CHCl₃) (Phytochemistry, 1980, 19, 2663-2668);

$^1$H NMR and $^{13}$C NMR data see Table S6;
IR (film, cm$^{-1}$) 1769, 1706, 1589, 1291, 1274, 1137, 1029;
HRMS(ESI) [M + H]$^+$ calculated for C$_{20}$H$_{23}$O$_6$: 359.1495, found: 359.1478;
TLC: Rf = 0.50 (Pentane/Ethyl acetate = 3/1).

To a stirred solution of alcohol 2 (2 mg, 0.007 mmol) in THF (1 mL) was added NEt₃ (50 μL, 0.36 mmol) and isobutyric anhydride (25 μL, 0.15 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 90 minutes or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO₃ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 5/1) to provide the 6 as a waxy solid (1.6 mg, 64%).

Data of 6: waxy solid;
[α]$_D^{20}$ -88.0 (c 0.025, CHCl₃); lit. [α]$_D^{24}$ -158 (c 0.54, CHCl₃) (Phytochemistry, 1982, 21, 1669-1673);

$^1$H NMR and $^{13}$C NMR data see Table S7;
IR (film, cm$^{-1}$) 1770, 1709, 1588, 1291, 1139, 1029;
HRMS(ESI) [M + H]$^+$ calculated for C$_{19}$H$_{23}$O$_6$: 347.1495, found: 347.1512;
TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 3/1).
The reaction was conducted following a previously reported procedure.\textsuperscript{24}

A solution of 15-deoxygoyazensolide (3) (1.0 mg, 0.0029 mmol) in THF (0.2 mL) and commercially available Stryker's reagent (3.0 mg, 0.0015 mmol), were mixed together forming a homogeneous solution that was stirred at room temperature for 2 hours in a glove box under an inert N\textsubscript{2} atmosphere. The reaction was then quenched with sat. aq. NH\textsubscript{4}Cl (1.0 mL), extracted with ethyl acetate (3 × 5.0 mL), dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated \textit{in vacuo}. The residue was purified by preparative TLC (Pentane/Ethyl acetate = 3/1) to provide 14 as a waxy solid (0.4 mg, 40%).

Data of 14: waxy solid;
\textsuperscript{1}H NMR and \textsuperscript{13}C NMR data see Table S13; HRMS(ESI) [M + Na]\textsuperscript{+} calculated for C\textsubscript{19}H\textsubscript{22}NaO\textsubscript{6}: 369.1314, found: 369.1323; TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 1/1).

A 10 mL round bottom flask equipped with a magnetic stir bar was charged with alcohol 18a (40 mg, 0.078 mmol) and CH\textsubscript{2}Cl\textsubscript{2} (2.0 mL), followed by addition of DMP (50 mg, 0.12 mmol). The reaction was stirred for 30 minutes or till the TLC analysis showed disappearance of starting material. The reaction was then quenched with diluted Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} solution (2.0 mL) and extracted with CH\textsubscript{2}Cl\textsubscript{2} (3 × 10 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, then filtered and concentrated \textit{in vacuo} to provide 18a-1 as a waxy solid. The crude product was used directly as starting material for the Evans–Saksena reduction without further purification.

A 10 mL round bottom flask equipped with a magnetic stir bar was charged with 18a-1, MeCN (2.0 mL) and AcOH (2.0 mL). Then, the mixture was cooled down to 0 °C, Me\textsubscript{4}NBH(OAc)\textsubscript{3} (102 mg, 0.39 mmol) was added in portions and the reaction was stirred for 3 hours or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO\textsubscript{3} (15 mL, caution the mixture bubbles out while quenching) until the evolution of gas stopped and extracted with CH\textsubscript{2}Cl\textsubscript{2} (3 × 10 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, then filtered and concentrated \textit{in vacuo}. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1) to give alcohol 33 as a waxy solid (27 mg, 30%).

Data of 18a-1: yellow oil;
[α]\textsubscript{D}\textsuperscript{20} -120.9 (c 1.0, CHCl\textsubscript{3});
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \textsuperscript{d} 7.70-7.67 (m, 4H, -OTBDPS), 7.45-7.36 (m, 6H, -OTBDPS), 6.28 (d, J = 3.5 Hz, 1H, H\textsubscript{13}), 5.97 (dq, J = 3.3, 1.6 Hz, 1H, H\textsubscript{5}), 5.57 (d, J = 3.1 Hz, 1H, H\textsubscript{13}), 5.55-5.50 (m, 1H, H\textsubscript{6}), 4.42-4.39 (m, 1H, H\textsubscript{7}), 4.40 (s, 1H, H\textsubscript{1}), 2.93 (d, J = 13.7 Hz, 1H, H\textsubscript{9}), 2.68 (d, J = 13.7 Hz, 1H, H\textsubscript{9}), 1.58 (t, J = 1.8 Hz, 3H, H\textsubscript{15}), 1.51 (s, 3H, H\textsubscript{14}), 1.10 (s, 9H, -OTBDPS) ppm;

\textsuperscript{24} Sass, D. C., Heleno, V. C. G., Cavalcante, S., da Silva Barbosa, J., Soares, A. C. F., Constantino, M. G. \textit{J. Org. Chem.} \textbf{2012}, \textit{77}, 9374–9378.
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 203.1 (C\(_9\)), 167.37 (C\(_{12}\)), 136.3 (TBDPS), 136.1 (TBDPS), 134.9 (C\(_{11}\)), 134.7 (C\(_3\)H), 132.8 (TBDPS), 132.5 (TBDPS), 130.3 (TBDPS), 130.1 (TBDPS), 128.0 (TBDPS), 127.6 (TBDPS), 122.8 (C\(_{13}\)H), 119.5 (C\(_1\)), 97.0 (C\(_2\)), 86.9 (C\(_2\)), 79.6 (C\(_{10}\)), 77.8 (C\(_{\text{OTBDPS}}\)), 71.8 (C\(_{15}\)H), 59.0 (C\(_{2}\)H), 48.2 (C\(_9\)H), 27.1 (TBDPS), 24.3 (C\(_{14}\)H), 21.6 (C\(_{15}\)H), 19.5 (TBDPS) ppm; IR (film, cm\(^{-1}\)) 1767, 1703, 1288, 1110, 1041, 703; HMRMS (ESI) [M + Na]\(^+\) calculated for C\(_{31}\)H\(_{36}\)NaO\(_3\)Si: 537.2067, found: 537.2073; TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 5/1).

Data of 33: waxy solid; 
[\(\alpha\)]\(_D\) \(^{13}\)c 0.53 (CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.65-7.68 (m, 4H, OTBDPS), 7.33-7.45 (m, 6H, OTBDPS), 6.31 (d, \(J = 2.9\) Hz, 1H, H\(_{13}\)), 5.96 (m, 1H, H\(_{13}\)), 5.95 (m, 1H, H\(_5\)), 5.14 (br t, \(J = 7\) Hz, 1H, H\(_6\)), 4.63 (br s, 1H, H\(_8\)), 4.01 (s, 1H, H\(_1\)), 3.32 (br s, 1H, H\(_7\)), 2.61 (br d, \(J = 15.6\) Hz, 1H, H\(_9\)), 2.13 (br s, 1H, H\(_{\text{OH}}\)), 1.75 (br s, 1H, H\(_{\text{OH}}\)), 1.73 (dd, \(J = 15.6, 6.3\) Hz, H\(_9\)), 1.64 (t, \(J = 1.5\) Hz, 3H, H\(_{15}\)), 1.39 (s, 3H, H\(_{14}\)), 1.08 (s, 9H, OTBDPS) ppm;

\(^1\)H NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.6 (C\(_{15}\)H), 123.4 (C\(_{3}\)H), 119.5 (C\(_1\)), 97.0 (C\(_2\)), 86.9 (C\(_2\)), 79.6 (C\(_{10}\)), 77.8 (C\(_{\text{OTBDPS}}\)), 71.8 (C\(_{15}\)H), 59.0 (C\(_{2}\)H), 48.2 (C\(_9\)H), 27.1 (TBDPS), 24.3 (C\(_{14}\)H), 21.6 (C\(_{15}\)H), 19.5 (TBDPS) ppm;

IR (film, cm\(^{-1}\)) 1767, 1703, 1288, 1110, 1041, 703; HMRMS (ESI) [M + Na]\(^+\) calculated for C\(_{31}\)H\(_{36}\)NaO\(_3\)Si: 537.2067, found: 537.2073; TLC: Rf = 0.30 (Petroleum ether/Ethyl acetate = 2/1).

To a solution of TBDPS-protected alcohol 33 (27.6 mg, 0.1 mmol) in an Eppendorf safe-lock tube was added 1 drop of THF followed by hydrogen fluoride pyridine (hydrogen fluoride \(\sim 70\%), 0.1\) mL). The mixture was left on shaker at room temperature for 40 minutes. Then CH\(_2\)Cl\(_2\) (2.0 mL) was added to the reaction followed by addition of \(\text{sat. aq. NaHCO}_3\) for quenching (caution the mixture bubbles out while quenching) until the evolution of gas stopped. The mixture was extracted with ethyl acetate (5 \(\times\) 10 mL), the combined organic layers were dried over Na\(_2\)SO\(_4\), filtered and concentrated \(\text{in vacuo}\). The residue was purified on silica gel chromatography (Petroleum/Ethyl acetate = 2/1 \(\sim\) 1/2) to provide the 33-1 as waxy solid (12.8 mg, 86%).

Data of 33-1: waxy solid; 
[\(\alpha\)]\(_D\) \(^{13}\)c 0.53 (CHCl\(_3\)).

\(^1\)H NMR (400 MHz, acetone-\(d^6\)) \(\delta\) 6.07 (dd, \(J = 2.5, 1.1\) Hz, 1H, H\(_{13}\)), 5.99 (br s, 1H, H\(_5\)), 5.74 (br s, 1H, H\(_{13}\)), 5.35 (br s, 1H, H\(_6\)), 4.71 (d, \(J = 6.2\) Hz, 1H, H\(_9\)), 4.49 (br s, 1H, H\(_{\text{OH}}\)), 4.02 (t, \(J = 3.1\) Hz, 2H, H\(_{15}+\)H\(_{15}\)), 3.74 (br d, \(J = 4.5\) Hz, 1H, H\(_7\)), 3.70 (br s, H\(_{\text{OH}}\)), 2.69 (br s, H\(_9\)), 1.80 (t, \(J = 1.6\) Hz, 3H, H\(_{15}\)), 1.63 (dd, \(J = 15.1, 4.7\) Hz, 1H, H\(_9\)), 1.41 (s, 3H, H\(_{14}\)) ppm;
To a stirred solution of triol 33-1 (11.2 mg, 0.04 mmol) in CH$_2$Cl$_2$ (1.0 mL) was added MnO$_2$ (35 mg, 0.4 mmol). The reaction mixture was stirred at room temperature for 2 hours or till the TLC analysis showed disappearance of starting material. Then MnO$_2$ was filtered off and washed with CH$_2$Cl$_2$ (1.0 mL). tBu$_3$AuNTf$_2$ (1.7 mg, 0.002 mmol) was added to the CH$_2$Cl$_2$ solution and stirred for 10 minutes till the TLC analysis showed disappearance of starting material. The resulted solution was concentrated in vacuo and the residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 1/1) to provide the 7 as waxy solid (9.8 mg, 79%).

Data of 33-2: waxy solid;
[α]$^{$D}$_{D}$$=$-215.6 (c 0.2, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) δ 6.47 (dq, J = 6.1, 1.6 Hz, 1H, H$_3$), 6.37 (dd, J = 3.3, 1.0 Hz, 1H, H$_{13}$), 6.23 (dd, J = 2.9, 1.0 Hz, 1H, H$_{13}$), 5.27 (ddq, J = 8.8, 6.0, 1.3 Hz, 1H, H$_{9}$), 4.71 (ddd, J = 7.0, 4.4, 2.3 Hz, 1H, H$_8$), 3.47 (ddt, J = 9.1, 4.4, 3.1 Hz, 1H, H$_7$), 3.12 (br s, 1H, -OH), 2.58 (dd, J = 15.9, 2.2 Hz, 1H, H$_9$), 2.10 (dd, J = 15.8, 7.3 Hz, 1H, H$_9$), 1.98 (t, J = 1.5 Hz, 3H, H$_{13}$), 1.40 (s, 3H, H$_3$) ppm;
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 190.5 (C$_1$), 169.5 (C$_{12}$), 146.5 (C$_5$H), 134.6 (C$_{11}$), 125.4 (C$_{13}$H$_2$), 120.4 (C$_4$), 102.0 (C$_3$), 95.4 (C$_2$), 79.7 (C$_{10}$), 78.1 (C$_{6}$H), 69.1 (C$_8$H), 50.6 (C$_{7}$H), 40.6 (C$_9$H$_2$), 28.2 (C$_{14}$H$_3$), 20.5 (C$_{15}$H$_3$) ppm;
IR (film, cm$^{-1}$) 3480, 2179, 1765, 1671, 1323, 1274, 1239, 1127, 1026, 986, 555;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{15}$H$_{18}$NaOs: 301.1068, found: 301.1052; TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 1/2).

Data of 7: waxy solid;
[α]$^{$D}$_{D}$$=$-142.7 (c 0.15, CHCl$_3$);
$^1$H NMR and $^{13}$C NMR data see Table S1;
IR (film, cm$^{-1}$) 3430, 2924, 1761, 1704, 1589, 1280, 1143, 611;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{15}$H$_{16}$NaOs: 299.0905, found: 299.0895; TLC: Rf = 0.40 (Petroleum ether/Ethyl acetate = 3/1).
To a stirred solution of alcohol 7 (1.5 mg, 0.005 mmol) in THF (1.0 mL) was added NEt₃ (25 μL, 0.18 mmol) and methacrylic anhydride (13 μL, 0.09 mmol) followed by a trace of DMAP. The reaction mixture was then stirred at room temperature for 3 hours or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NaHCO₃ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 3/1) to provide the calaxin 8 as a waxy solid (1.1 mg, 59%).

Data of calaxin 8: waxy solid; [α]D₂₀ -63.2 (c 0.05, CHCl₃);
¹H NMR and ¹³C NMR data see Table S8;
IR (film, cm⁻¹) 2362, 2343, 1771, 1707, 1593, 1291, 1151, 617;
HRMS(ESI) [M + Na]+ calculated for C₁₉H₂₀NaO₆: 367.1151, found: 367.1158;
TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 2/1).

To a stirred solution of alcohol 7 (1.5 mg, 0.005 mmol) in PhMe (1.0 mL) was added angelic 2,4,6-trichlorobenzoic anhydride (Ang-TCB, 4.6 mg, 0.015 mmol) and DMAP (1.8 mg, 0.016 mmol). The reaction mixture was stirred at room temperature for 6 hours or till the TLC analysis showed disappearance of starting material. Then, the reaction was filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 3/1) to provide compound 9 as a waxy solid (<0.1 mg, ~5%) together with 8-epi-atripliciolidel-tiglate 10 (0.8 mg, 40%).

We observed major isomerization from angelate to tiglate (angelate/tiglate = 1/8 as determined by crude ¹H NMR). Unfortunately, the material obtained was not enough for full characterization, but ¹H NMR data comparison showed unequivocally the compound to be natural product 9. See Table S9 for detail.

Data of 9: waxy solid;
HRMS(ESI) [M + H]+ calculated for C₂₀H₂₃O₆: 359.1495, found: 359.1517;
TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 2/1).
To a stirred solution of alcohol 7 (1.5 mg, 0.005 mmol) in PhMe (1.0 mL) was added tiglic 2,4,6-trichlorobenzoic anhydride (Tig-TCB, 4.6 mg, 0.015 mmol) and DMAP (1.8 mg, 0.016 mmol). The reaction mixture was stirred at room temperature for 24 hours till the TLC analysis showed disappearance of the starting material. Then the reaction was filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 3/1) to provide 8-epi-attriplicirole-tiglate 10 (0.5 mg, 31%) as a waxy solid.

Data of 8-epi-attriplicirole-tiglate 10: waxy solid; 
[α]$_D^{20}$ -204.4 (c 0.025, CHCl$_3$); 
$^1$H NMR and $^{13}$C NMR data, see Table S10; 
IR (film, cm$^{-1}$) 1767, 1710, 1594, 1291, 1127, 1080, 593; 
HRMS(ESI) [M + H]+ calculated for C$_{20}$H$_{23}$O$_6$: 359.1495, found: 359.1478; 
TLC: Rf = 0.55 (Petroleum ether/Ethyl acetate = 2/1).

To a stirred solution of alcohol 7 (1.5 mg, 0.005 mmol) in THF (1.0 mL) was added NEt$_3$ (25 μL, 0.18 mmol) and isobutyric anhydride (13 μL, 0.08 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 6 hours till the TLC analysis showed disappearance of the starting material. The reaction was then quenched with sat. aq. NaHCO$_3$ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 3/1) to provide the 11 as a waxy solid (1.6 mg, 89%).

Data of 11: waxy solid; 
[α]$_D^{20}$ -132.1 (c 0.10, CHCl$_3$); 
$^1$H NMR and $^{13}$C NMR data see Table S11; 
IR (film, cm$^{-1}$) 1770, 1706, 1592, 1290, 1144; 
HRMS(ESI) [M + Na]$^+$ calculated for C$_{19}$H$_{22}$NaO$_6$: 369.1323, found: 369.1314; 
TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 2/1).
To a stirred solution of alcohol 7 (1.0 mg, 0.0036 mmol) in THF (0.5 mL) was added NEt$_3$ (15 μL, 0.11 mmol) and isovaleric anhydride (10 μL, 0.05 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 4 hours till the TLC analysis showed disappearance of the starting material. The reaction was then quenched with sat. aq. NaHCO$_3$ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 2/1) to provide the 12 as a waxy solid (0.9 mg, 69%).

Data of 12: waxy solid;
[α]$^20$D -51.8 (c 0.045, CHCl$_3$); lit. [α]$^24$D -41 (c 0.8, CHCl$_3$) (Phytochemistry, 1978, 17, 471-474);
$^1$H NMR and $^{13}$C NMR data, see Table S12;
IR (film, cm$^{-1}$) 2960, 1770, 1739, 1709, 1595, 1291, 1162, 1130, 1005, 815;
HRMS(ESI) [M + H]$^+$ calculated for C$_{20}$H$_{25}$O$_6$: 361.1651, found: 361.1625;
TLC: Rf = 0.60 (Petroleum ether/Ethyl acetate = 2/1).

To a stirred solution of alcohol 7 (1.4 mg, 0.0051 mmol) in THF (0.5 mL) was added NEt$_3$ (15 μL, 0.11 mmol) and (±)-2-methylbutyric anhydride (10 μL, 0.05 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 12 hours till the TLC analysis showed disappearance of the starting material. The reaction was then quenched with sat. aq. NaHCO$_3$ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 2/1) to provide the (±)-13 as a waxy solid and a mixture 1:1 of inseparable diastereomers (1.4 mg, 78%).

Data of (±)-13: waxy solid;
$^1$H NMR and $^{13}$C NMR data, see Supplementary Section d;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{20}$H$_{24}$NaO$_6$: 383.1471, found: 383.1475;
TLC: Rf = 0.70 (Petroleum ether/Ethyl acetate = 2/1).
The same procedure for synthesis of \((R+S)-13\) was used and 1.2 mg of \(8\)-\textit{epi}-atripliciolid-\(2'-\)(S)-MeBu \((13)\) were obtained from 1.0 mg of \(7\), representing a yield of 92%.

Data of \(8\)-\textit{epi}-atripliciolid-\(2'-\)(S)-MeBu \((13)\): waxy solid;
\([\alpha]_D^{20} -47.3 (c 0.06, \text{CHCl}_3)\);
\(^1\)H NMR and \(^{13}\)C NMR data, see \textbf{Supplementary Section d};
IR (film, cm\(^{-1}\)) 2912, 2193, 1982, 1595, 1263, 1132, 1023, 800;
TLC: \(R_f = 0.70\) (Petroleum ether/Ethyl acetate = 2/1).

To a stirred solution of alcohol \((11 \text{ mg}, 0.021 \text{ mmol})\) in THF (2.0 mL) was added NEt\(_3\) (18 \(\mu\)L, 0.13 mmol) and isobutyric anhydride (11 \(\mu\)L, 0.06 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 2 hours till the TLC analysis showed disappearance of the starting material. The reaction was then quenched with \textit{sat. aq.} \(\text{NaHCO}_3\) (2.0 mL), the mixture was extracted with ethyl acetate (3 \(\times\) 10 mL), the combined organic layers were dried over \(\text{Na}_2\text{SO}_4\), then filtered and concentrated \textit{in vacuo}. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1 ~ 2/1) to provide \((34)\) as a white solid (12 mg, 96%).

The absolute configuration of \((34)\) was determined by X-ray diffraction measurements. Single crystals of \((34)\) suitable for X-ray crystallographic analysis were obtained by a single recrystallization by slow evaporation at room temperature using \(n\)-hexanes/\(\text{CH}_2\text{Cl}_2\) as a solvent mixture. See \textbf{Supplementary Section m} for detail.

Data of \((53)\): white solid, m.p. 154-156 °C;
\([\alpha]_D^{20} -669.7 (c 0.2, \text{CHCl}_3)\);
\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.73-7.57 (m, 4H, -OTBDPS), 7.53-7.32 (m, 6H, -OTBDPS), 6.25 (d, \(J = 2.2 \text{ Hz}, 1\text{H}, H_{13}\)) 5.88 (dq, \(J = 3.3, 1.6 \text{ Hz}, 1\text{H}, H_5\)), 5.72 (br s, 1H, \(H_{13}\)), 5.39 (br s, 2H, \(H_6 + H_8\)), 4.01 (s, 1H, \(H_1\)), 3.68 (br s, 1H, \(H_7\)), 2.81 (dd, \(J = 15.0, 9.7 \text{ Hz}, 1\text{H}, H_9\)), 2.49 (hept, \(J = 7.0 \text{ Hz}, 1\text{H}, H_2\)), 1.72 (dd, \(J = 15.1, 3.9 \text{ Hz}, 1\text{H}, H_2\)), 1.63 (t, \(J = 1.7 \text{ Hz}, 3\text{H}, H_{15}\)), 1.42 (s, 3H, \(H_{13}\)), 1.13 (d, \(J = 7.0 \text{ Hz}, 3\text{H}, H_{3/4}\)), 1.11 (d, \(J = 7.0 \text{ Hz}, 3\text{H}, H_{3/4}\)), 1.09 (s, 9H, -OTBDPS) ppm;
\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 176.5 (\(C_1\)), 170.5 (\(C_{12}\)), 140.4 (br, \(C_6\)), 137.2 (br \(C_{11}\)), 136.4 (\(TBDBPS\)), 136.1 (\(TBDBPS\)), 133.2 (\(TBDBPS\)), 132.9 (\(TBDBPS\)), 130.2 (\(TBDBPS\)), 130.1 (\(TBDBPS\)), 127.9 (\(TBDBPS\)), 127.5 (\(TBDBPS\)), 123.4 (\(C_{13}H_2\)), 120.4 (br, \(C_4\)), 98.8 (\(C_2\)), 85.2 (br, \(C_3\)), 77.0 (\(C_3H\)), 75.4 (\(C_{10}\)), 75.4 (\(C_8\)), 72.6 (\(C_7\)), 49.3 (br, \(C_5\)), 36.0 (\(C_9H_2\)), 34.3 (\(C_2H\)), 30.2 (\(C_{14}H_3\)), 27.2 (\(TBDBPS\)), 20.9 (\(C_{15}H_3\)), 19.5 (\(TBDBPS\)), 18.9 (\(C_3H_3\)), 18.8 (\(C_4H_3\)) ppm; \(^{13}\)C NMR
signal of $C_3$ $C_4$ $C_5$ $C_7$ $C_{11}$ are broad because of the conformational changes. $^{13}$C NMR of $C_8$ and $C_{10}$ overlap, and $C_8$ most likely has very weak signal. $^1$H NMR of H-6 and H-8 overlap and makes the NOESY hard to detect. There is a correlation between H-5 and H-7; IR (film, cm$^{-1}$) 3475, 2933, 1753, 1428, 1111, 703; HRMS(ESI) [M + Na]$^+$ calculated for $C_{35}H_{42}NaO_6Si$: 609.2661, found: 609.2648; TLC: Rf = 0.85 (Petroleum ether/Ethyl acetate = 1/1).

To a solution of TBDPS-protected alcohol 34 (13.6 mg, 0.023 mmol) in an Eppendorf safe-lock tube was added hydrogen fluoride pyridine (hydrogen fluoride ~70%, 0.1 mL). The reaction mixture was left on a shaker at room temperature for 40 minutes. Then CH$_2$Cl$_2$ (2.0 mL) was added to the reaction mixture and followed by addition of sat. aq. NaHCO$_3$ for quenching (caution the mixture bubbles out while quenching) until the evolution of gas stopped. The mixture was extracted with ethyl acetate (3 × 10 mL), the combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was used for acetylation without further purification. To a solution of crude propargyl alcohol 34-1 in CH$_2$Cl$_2$ (1.0 mL) was added NEt$_3$ (16 μL, 0.12 mmol) and acetic anhydride (4.3 μL, 0.046 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 5 hours or till the TLC analysis showed disappearance of starting material. The reaction was then quenched with sat. aq. NaHCO$_3$ (2.0 mL), the mixture was extracted with CH$_2$Cl$_2$ (3 × 10 mL), the combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 4/1) to provide 35 as waxy solid (7.7 mg, 75%).

Data of propargyl alcohol 34-1: waxy solid;
$[\alpha]_D^{20}$ -301.2 (c 0.06, CHCl$_3$);
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.28 (d, J = 2.3 Hz, 1H, $H_{13}$), 6.02 (dq, J = 4.7, 1.6 Hz, 1H, $H_5$), 5.77 (d, J = 2.1 Hz, 1H, $H_{13}$), 5.48 (br s, 2H, $H_6 + H_8$), 4.09 (d, J = 4.1 Hz, 1H, $H_4$), 3.73 (br s, 1H, $H_7$), 2.65 (dd, J = 15.2, 8.9 Hz, 1H, $H_9$), 2.49 (hept, J = 7.0 Hz, 1H, $H_2$), 2.00 (d, J = 4.2 Hz, 1H, -OH), 1.85 (t, J = 1.7 Hz, 3H, $H_{15}$), 1.73 (dd, J = 15.1, 4.2 Hz, 1H, $H_9$), 1.49 (s, 3H, $H_{14}$), 1.12 (d, J = 6.1 Hz, 3H, $H_{3/4}$), 1.11 (d, J = 6.2 Hz, 3H, $H_{3/4}$) ppm;
$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 176.5 ($C_1$), 170.3 ($C_{12}$), 141.0 (br, $C_3$H), 136.9 (br, $C_{11}$), 123.5 ($C_{13}$H$_2$), 120.4 (br, $C_4$), 98.4 ($C_2$), 85.1 (br, $C_3$), 77.1 ($C_6$H), 74.8 ($C_{10}$), 74.8 ($C_6$H), 71.0 ($C_7$H), 49.4 ($C_8$), 35.8 ($C_9$H$_2$), 34.3 ($C_2$H), 29.6 ($C_{14}$H$_3$), 21.0 ($C_{13}$H$_3$), 18.9 ($C_7$H$_3$), 18.8 ($C_4$H$_3$) ppm; $^{13}$C NMR signal of $C_3$ $C_4$ $C_5$ $C_{11}$ are broad because of the conformational changes. $^{13}$C NMR of $C_8$ and $C_{10}$ overlap, and $C_8$ most likely has very weak signal. $^1$H NMR of H-6 and H-8 overlap and makes the NOESY hard to be detected; IR (film, cm$^{-1}$) 3441, 2977, 1752, 1270, 1200, 1147, 1008; HRMS(ESI) [M + Na]$^+$ calculated for $C_{19}H_{24}NaO_6$: 371.1472, found: 371.1471; TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 3/1).

Data of 35: waxy solid;
[\alpha]_D^{20} = -219.7 (c 0.2, CHCl_3);

\(^1\)H NMR (500 MHz, CDCl_3) \( \delta \) 6.28 (d, \( J = 2.3 \) Hz, 1H, \( H_{13} \)), 5.85 (d, \( J = 1.4 \) Hz, 1H, \( H_1 \)), 5.73 (dq, \( J = 3.6, 1.7 \) Hz, 1H, \( H_3 \)), 5.62 (d, \( J = 2.3 \) Hz, 1H, \( H_{13} \)), 5.56 (dt, \( J = 11.5, 4.5 \) Hz, 1H, \( H_6 \)), 5.37 (dq, \( J = 4.0, 2.0 \) Hz, 1H, \( H_6 \)), 4.99 (d, \( J = 1.4 \) Hz, 1H, \( H_2 \)), 3.94 (tt, \( J = 4.1, 2.4 \) Hz, 1H, \( H_7 \)), 2.84 (dd, \( J = 14.6, 11.5 \) Hz, 1H, \( H_9 \)), 2.44 (hept, \( J = 7.0 \) Hz, 1H, \( H_7 \)), 2.08 (s, 3H, -OAc), 1.88 (t, \( J = 1.8 \) Hz, 3H, \( H_{14} \)), 1.65 (s, 3H, \( H_{14} \)), 1.62 (dd, \( J = 14.6, 4.7 \) Hz, 1H, \( H_9 \)), 1.07 (d, \( J = 6.9 \) Hz, 3H, \( H_3 \)), 1.05 (d, \( J = 7.0 \) Hz, 3H, \( H_4 \)) ppm;

\(^{13}\)C NMR (126 MHz, CDCl_3) \( \delta \) 176.3 (\( C_1 \)), 170.7 (OAc), 169.9 (\( C_{12} \)), 157.7 (\( C_3 \)), 136.0 (\( C_{11} \)), 133.1 (\( C_6 \)), 123.3 (\( C_{13} \)), 120.8 (\( C_2 \)), 87.9 (\( C_{10} \)), 84.9 (\( C_9 \)), 75.6 (\( C_4 \)), 71.6 (\( C_8 \)), 50.0 (\( C_7 \)), 34.2 (\( C_2 \)), 32.1 (\( C_8 \)), 22.8 (\( C_{14} \)), 21.5 (\( C_{15} \)), 21.1 (OAc), 19.2 (\( C_3 \)), 18.8 (\( C_5 \)) ppm;

IR (film, cm\(^{-1}\)) 2924, 1768, 1738, 1462, 1375, 1281, 1230, 1135, 1034, 1004; HRMS(ESI) [M + H]\(^+\) calculated for \( C_{21}H_{27}O_7 \): 391.1729, found: 391.1757;

TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 5/1).

To a solution of 35 (3.0 mg, 0.0077 mmol) in \( CH_2Cl_2 \) (1.0 mL) was added \( tBu_3AuNTf_2 \) (0.3 mg, 0.0004 mmol) and stirred for 24 hours or till the TLC analysis showed disappearance of the starting material. The resulted solution was concentrated \textit{in vacuo}. The residue was purified on \( \text{NEt}_3 \) pre-treated silica gel chromatography (Pentane/ Ethyl acetate = 5/1~3/1) to provide the 36 as a waxy solid (1.9 mg, 63%).

The low isolated yield of 36 may result from the instability under acidic conditions.

Data of 36: waxy solid;

[\alpha]_D^{20} = -333.8 (c 0.1, CHCl_3);

\(^1\)H NMR (500 MHz, CDCl_3) \( \delta \) 6.28 (d, \( J = 2.6 \) Hz, 1H, \( H_{13} \)), 6.04 (dq, \( J = 4.7, 1.6 \) Hz, 1H, \( H_5 \)), 5.78 (d, \( J = 2.1 \) Hz, 1H, \( H_{13} \)), 5.48 (br s, 2H, \( H_6 + H_8 \)), 5.08 (s, 1H, \( H_1 \)), 3.74 (br s, 1H, \( H_7 \)), 2.67 (dd, \( J = 15.1, 8.9 \) Hz, 1H, \( H_9 \)), 2.49 (hept, \( J = 7.0 \) Hz, 1H, \( H_7 \)), 2.12 (s, 3H, -OAc), 1.84 (t, \( J = 1.7 \) Hz, 3H, \( H_{13} \)), 1.79 (dd, \( J = 15.1, 4.2 \) Hz, 1H, \( H_9 \)), 1.42 (s, 3H, \( H_{14} \)), 1.12 (like t, \( J = 7.0 \), 6H, \( H_5 + H_4 \)) ppm;

\(^{13}\)C NMR (126 MHz, CDCl_3) \( \delta \) 176.5 (\( C_1 \)), 170.3 (\( C_{12} \)), 169.6 (OAc), 141.5 (br, \( C_6 \)), 136.9 (br, \( C_{11} \)), 123.6 (\( C_{13} \)), 120.4 (br, \( C_8 \)), 95.3 (\( C_2 \)), 85.0 (br, \( C_3 \)), 77.0 (\( C_9 \)), 74.5 (\( C_8 \)), 74.0 (\( C_{10} \)), 49.4 (\( C_7 \)), 36.8 (\( C_6 \)), 34.3 (\( C_2 \)), 29.6 (\( C_{14} \)), 21.0 (OAc), 20.9 (\( C_{15} \)), 18.9 (\( C_3 \)), 18.8 (\( C_5 \)) ppm; \(^{13}\)C NMR signal of \( C_8 \) and \( C_9 \) overlap and what makes the NOESY correlation hard to be detected; HRMS(ESI) [M + Na]\(^+\) calculated for \( C_{21}H_{26}NaO_7 \): 413.1579, found: 413.1576; TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 3/1).
To a solution of 35 (1.9 mg, 0.0049 mmol) in CH₂Cl₂ (0.5 mL) was added tBu₃AuNTf₂ (0.2 mg, 0.00024 mmol) and stirred for 2 hours till the TLC analysis showed disappearance of the starting material. Then silica gel (cat. 2.0 mg) was added to the solution and stirred at same temperature for 5 hours. The residue was directly purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1) to provide the tagitinine F (16) as a waxy solid (1.7 mg, quant.).

Data of tagitinine F 16: waxy solid; [α]_D^-117.8 (c 0.075, MeOH); lit. [α]_D^-12.5 (c 0.1, MeOH) (Photochem. Photobiol., 2020, 96, 14-20.);

¹H NMR and ¹³C NMR data, see Table S15; IR (film, cm⁻¹) 3453, 2972, 2927, 1759, 1736, 1280, 1148, 1099, 1063, 1021, 982; HRMS(ESI) [M + Na]⁺ calculated for C₁₉H₂₄NaO₆: 371.1472, found: 371.1471;

TLC: Rf = 0.55 (Petroleum ether/Ethyl acetate = 1/1).

To a solution of 35 (2.0 mg, 0.0051 mmol) in CDCl₃ (0.5 mL) in NMR tube was added tBu₃AuNTf₂ (0.2 mg, 0.00024 mmol) and left on a shaker for 2 hours till the crude ¹H NMR analysis showed disappearance of the starting material and formation of 36. Then TFA (1 μL, 0.013 mmol) was added to the solution and the tube was left on shaker at same temperature for 3 hours. Crude ¹H NMR showed formation tagitinine F 16. The residue was treated with silica (cat. 2.0 mg) and left of shaker for another 12 hours. The crude ¹H NMR showed disappearance of tagitinine F. The resulted mixture was directly purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1~2/1) to provide the tagitinine C 17 as a waxy solid (0.3 mg, 17%) together with other compounds. Similar reaction with CH₂Cl₂ as solvent was repeated and same result was obtained.
When 35 (wll-ug13-81) is treated with tBu3AuNTf2, cyclization happens fast to give 36 (wll-ug13-84-30min). This reaction is accomplished within 2 hours depending on the amount of the catalyst. When the cyclized product 36 is treated with TFA and the transformation to tagitinine F 16 happens gradually (wll-ug13-84-+TFA/wll-ug13-84-+TFA-360min), which indicating that TFA plays a similar function as silica gel. Addition of silica gel induces yet a different reaction. Directing monitoring by 1H NMR gives no signals because all the compounds are adsorbed by the silica gel. A Simple filtration followed by a wash with ethyl acetate followed by concentration shows the unequivocal formation of tagitinine C 17 together with two other compounds (wll-ug13-84-CR), in a ratio of 20: compound 1 : compound 2 = 1:2:1.
Figure S8. Proposed mechanism.

When 35 is treated with the gold catalyst, the alkyne could be activated inducing the cyclization between C10-OH and alkyne-C3 giving 36. Then reaction would be slower than when C1 is a ketone. Compound 36 is not stable and a [3,3]-Sigmatropic oxo-rearrangement/Hemiacetal ester/H2O exchange could give rise to tagitinine F 16. Tautomerization then could generate the enone ring opened 16. Tagitinine C 17 could derive from a Z/E isomerization of the 1,2-double bond. The cocktail of TFA and silica would be necessary for this reaction. A control experiment was also conducted where TFA itself lead to no transformation without silica gel under various conditions (heat, light, etc).

Data of tagitinine C 17: waxy solid; 
[α]20D -268.8 (c 0.07, MeOH); lit. [α]24D -23.5 (c 0.1, MeOH) (Photochem. Photobiol., 2020, 96, 14-20.);

1H NMR and 13C NMR data see Table S16;

IR (film, cm⁻¹) 3480, 2974, 2927, 1768, 1736, 1656, 1121, 993;

HRMS (ESI) [M + Na]^+ calculated for C19H24NaO6: 371.1472, found: 371.1471;

TLC: Rf = 0.50 (Petroleum ether/Ethyl acetate = 1/1).
g) Experimental procedures for Scheme 2

Figure S9. Synthesis of 5-epi-isogoyazensolide (15) from 37 and 20a.

Lactone S9-6 is a known compound and was prepared in 5 steps from 37 as previously reported.

To a stirred solution of lactone S9-6 (1.7 g, 4.8 mmol), NaH₂PO₄ (2.5 g, 20.8 mmol) and silica (5.0 g) in dioxane (50 mL) was added SeO₂ (2.5 g, 22.5 mmol) in 3 portions at 95 ºC within 2 hours. The reaction mixture was stirred for 1 more hour and then cooled down to room temperature. Then dioxane was evaporated and Et₂O (200 mL) was added, the mixture was stirred for 30 minutes, filtered and the solution was washed with saturated aqueous NaHCO₃ (100 mL), diluted Na₂S (10 mL) and brine (50 mL). The organic layer was dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified.

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on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 1/1) to provide 22 as light-yellow oil (1.36 g, 77%), which gradually became solid in the fridge.

The structure of lactone 22 was fully elucidated based on 2D NMR spectroscopic analyses, indicating a trans product. See Supplementary Section I for detail information.

Data of lactone 22: yellow oil to waxy solid;
[a]$_D$:$^2$ +43.3 (c 0.2, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.21 (m, 2H, H$_{t1}$), 6.89 (m, 2H, H$_{t2}$), 6.41 (d, $J = 2.3$ Hz, 1H, H$_o$), 6.12 (dd, $J = 2.1$, 1.0 Hz, 1H, H$_r$), 5.93 (d, $J = 1.9$ Hz, 1H, H$_o$), 5.90 (dd, $J = 2.0$, 0.6 Hz, 1H, H$_r$), 4.68 (d, $J = 11.7$ Hz, 1H, H$_o$), 4.60 (ddt, $J = 5.8$, 4.1, 2.1 Hz, 1H, H$_3$), 4.53 (t, $J = 3.7$ Hz, 1H, H$_a$), 4.30 (d, $J = 11.7$ Hz, 1H, H$_o$), 4.04 (ddd, $J = 3.7$, 1.1, 0.5 Hz, 1H, H$_3$), 3.82 (s, 3H, H$_{t4}$), 2.09 (d, $J = 6.1$ Hz, 1H, -OH) ppm;
$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.2 (C$_1$), 159.8 (C$_{2}$), 138.4 (C$_3$), 130.1 (C$_{11}$H), 128.6 (C$_{10}$), 127.3 (C$_6$), 125.9 (C$_4$H$_2$), 121.4 (C$_2$H), 114.2 (C$_{22}$H), 83.5 (C$_3$H), 80.8 (C$_3$H), 71.0 (C$_3$H), 55.5 (C$_{12}$H$_3$) ppm;
IR (film, cm$^{-1}$) 3434, 2935, 2860, 1768, 1613, 1514, 1450, 1112, 821, 705;
TLC: Rf = 0.40 (Petroleum ether/Ethyl acetate = 2/1).

To a stirred solution of alkyne 20a (51 mg, 0.12 mmol) and vinyl bromide 22 (40 mg, 0.11 mmol) in DMF/N$_2$Et$_3$ (3.0 mL/1 mL) was added Pd$_2$dba$_3$ (20 mg, 0.022 mmol) and CuI (2 mg, 0.011 mmol). The mixture was then stirred for 2 hours or till TLC analysis showed disappearance of the starting material. The reaction was quenched by addition of sat. aq. NH$_4$Cl (10 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1 ~ 1/1) to provide enyne S9-7 as a yellow oil (39 mg, 50%).

Data of enyne S9-7: yellow oil;
[a]$_D$:$^2$ -40.2 (c 0.5, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.75-7.73 (m, 4H, TBDPS), 7.44-7.33 (m, 6H, TBDPS), 7.19 (like d, $J = 8.6$ Hz, 2H, PMB), 6.87 (like d, $J = 8.7$ Hz, 2H, PMB), 6.32 (d, $J = 2.6$ Hz, 1H, H$_r$), 5.81 (d, $J = 2.1$ Hz, 1H, H$_r$), 5.53 (br t, $J = 1.3$ Hz, 1H, H$_{i3}$), 5.40 (br s, 1H, H$_{i5}$), 4.65 (dd, $J = 6.5$, 4.6 Hz, 1H, H$_o$), 4.53 (d, $J = 11.6$ Hz, 1H, PMB), 4.49 (br s, 1H, H$_o$), 4.35 (s, 1H, H$_i$), 4.25-4.14 (m, 2H, PMB + H$_o$), 3.81 (s, 3H, PMB), 3.71 (br d, $J = 5.4$ Hz, 1H, H$_3$), 3.26 (s, 3H, C$_8$-OMe), 3.25 (s, 3H, C$_8$-OMe), 2.11 (dd, $J = 14.6$, 6.6 Hz, 1H, H$_o$), 1.91 (dd, $J = 14.6$, 4.6 Hz, 1H, H$_r$), 1.34 (s, 3H, H$_{t4}$), 1.09 (s, 9H, TBDPS) ppm;
$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.2 (C$_1$), 159.6 (PMB-C), 138.6 (C$_{12}$), 136.3 (TBDPS), 136.2 (TBDPS), 133.5 (TBDPS), 132.6 (TBDPS), 130.2 (TBDPS), 129.9 (TBDPS), 129.7 (PMB-CH$_2$), 129.3 (PMB-C), 127.9 (TBDPS), 127.6 (TBDPS), 126.0 (C$_{13}$H$_2$), 125.8 (C$_3$), 125.0 (C$_{13}$H$_2$), 114.0 (PMB-CH$_2$), 102.4 (C$_{11}$H), 90.9 (C$_2$), 85.0 (C$_3$H), 84.7 (C$_3$), 79.5 (C$_{11}$H), 74.3 (C$_{10}$), 71.4 (C$_9$H), 70.6 (PMB-CH$_2$), 69.5 (C$_9$H), 55.5 (PMB-CH$_3$), 53.6 (C$_8$-OMe), 52.8 (C$_8$-OMe), 39.4 (C$_{12}$H$_2$), 27.1 (TBDPS), 24.0 (C$_9$H$_3$), 19.6 (TBDPS) ppm;
IR (film, cm$^{-1}$) 3434, 2935, 2860, 1768, 1613, 1514, 1450, 1112, 821, 705;

S52
A 10 mL round bottom flask equipped with a magnetic stir bar was charged with enyne S9-7 (30 mg, 0.042 mmol) and Et\textsubscript{2}O (3.0 mL). The reaction was cooled down to -30 °C and PBr\textsubscript{3} (7 µL, 0.084 mmol) was added. The mixture was stirred for 5 hours or till the LC-MS analysis showed disappearance of the starting material. Then the reaction was quenched with water (5.0 mL) and extracted with Et\textsubscript{2}O (3 × 10 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 3/1 ~ 1/1) to provide bromolactone S9-8 as a colorless oil (15 mg, 49%).

Data of bromolactone S9-8: colorless oil;
[\(\alpha\)]\textsubscript{D}\textsuperscript{20} = -59.2 (c 0.1, CHCl\textsubscript{3});
\(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 9.85 (t, \(J = 2.5\) Hz, 1H, H\textsubscript{s}), 7.78 – 7.66 (m, 4H, TBDPS), 7.45 – 7.35 (m, 6H, TBDPS), 7.18 (like d, \(J = 8.6\) Hz, 2H, PMB), 6.98 (m, 1H, H\textsubscript{7}), 6.87 (like d, \(J = 8.5\) Hz, 2H, PMB), 5.42 (br s, 1H, H\textsubscript{i}), 5.30 (br s, 1H, H\textsubscript{i}), 4.72 (dd, \(J = 5.8\), 1.6 Hz, 1H, H\textsubscript{6}), 4.50 (d, \(J = 11.5\) Hz, 1H, PMB), 4.38 (s, 1H, H\textsubscript{1}), 4.21 (d, \(J = 11.5\) Hz, 1H, PMB), 3.93 (dt, \(J = 6.8\), 1.4 Hz, 2H, H\textsubscript{10}), 3.81 (s, 3H, PMB), 3.73 (d, \(J = 5.7\) Hz, 1H, H\textsubscript{9}), 2.78 – 2.70 (m, 1H, H\textsubscript{9}), 2.66 (dd, \(J = 15.6\), 2.9 Hz, 1H, H\textsubscript{9}), 1.44 (s, 3H, H\textsubscript{13}), 1.07 (s, 9H, TBDPS) ppm;
\(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 202.1 (C\textsubscript{8}H), 170.6 (C\textsubscript{12}), 159.7 (PMB-C), 149.7 (C\textsubscript{4}H), 136.2 (TBDPS), 136.0 (TBDPS), 133.3 (TBDPS), 132.0 (TBDPS + C\textsubscript{11}), 130.5 (TBDPS), 130.0 (TBDPS), 129.8 (PMB-CH), 128.9 (PMB-C), 128.1 (TBDPS), 127.6 (TBDPS), 127.0 (C\textsubscript{13}H\textsubscript{2}), 125.8 (C\textsubscript{4}), 114.1 (PMB-CH), 90.4 (C\textsubscript{2}), 85.2 (C\textsubscript{3}), 81.5 (C\textsubscript{10}H), 80.0 (C\textsubscript{5}H), 74.8 (C\textsubscript{10}), 71.6 (C\textsubscript{1}H), 70.8 (PMB-CH\textsubscript{2}), 55.5 (PMB-CH\textsubscript{3}), 50.7 (C\textsubscript{7}H\textsubscript{2}), 27.0 (TBDPS), 23.7 (C\textsubscript{14}H\textsubscript{3}), 20.9 (C\textsubscript{15}H\textsubscript{2}), 19.6 (TBDPS) ppm;
IR (film, cm\textsuperscript{-1}) 3457, 2942, 2314, 1977, 1768, 1513, 1248, 1108, 823, 705;
HRMS(ESI) [M + Na]\textsuperscript{+} calculated for C\textsubscript{39}H\textsubscript{43}BrNaO\textsubscript{7}Si: 753.1859, found: 753.1861;
TLC: Rf = 0.50 (Pentane/Ethyl acetate = 2/1).

A 10 mL round bottom flask equipped with a magnetic stir bar was charged with bromolactone S9-8 (15 mg, 0.02 mmol) and DMF (1.0 mL). The reaction mixture was cooled down to -30 °C and CrCl\textsubscript{2} (6.2 mg, 0.5 mmol) was added. The temperature was allowed to rise to room temperature and stirred for 30 minutes or till the TLC analysis showed disappearance of starting material. Then, the reaction was quenched with sat. aq. NH\textsubscript{4}Cl (5.0 mL) and extracted with ethyl acetate (3 × 5.0 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, then filtered and concentrated in vacuo. The residue was...
purified on silica gel chromatography (Pentane/Ethyl acetate = 2/1) to provide S9-9 as a waxy solid (6.7 mg, 50%).

Data of S9-9: waxy solid; 
\([\alpha]^{20}_{D} = 93.2\) (c 0.04, CHCl₃);

\(^1\)H NMR (500 MHz, CDCl₃) δ 7.72 – 7.68 (m, 4H, TBDPS), 7.43 – 7.34 (m, 6H, TBDPS), 7.29 (likd d, J = 8.6 Hz, 2H, PMB), 6.87 (d, J = 8.7 Hz, 2H, PMB), 6.40 (d, J = 2.6 Hz, 1H, H₁₃), 5.78 (d, J = 2.3 Hz, 1H, H₃), 5.75 (d, J = 1.8 Hz, 1H, H₁₅), 5.32 (t, J = 1.8 Hz, 1H, H₁₅), 4.58 (d, J = 11.2 Hz, 1H, PMB), 4.52 (d, J = 11.1 Hz, 1H, PMB), 4.40 – 4.36 (m, 2H, H₆ + H₈), 4.11 (s, 1H, H₁), 4.05 (br s, 1H, H₁₂), 3.82 – 3.81 (m, 1H, H₅), 3.80 (s, 3H, PMB), 2.38 (dd, J = 14.8, 3.4 Hz, 1H, H₉), 1.97 (dd, J = 14.9, 9.2 Hz, 1H, H₉), 1.38 (s, 3H, H₁₄), 1.10 (s, 9H, TBDPS) ppm;

\(^{13}\)C NMR (125 MHz, CDCl₃) δ 169.9 (C₁₂), 159.5 (PMB-C), 136.4 (TBDPS), 136.2 (TBDPS), 135.0 (C₁₁), 133.0 (TBDPS), 132.6 (TBDPS), 130.3 (TBDPS), 130.1 (TBDPS), 129.8 (PMB-CH), 129.7 (PMB-C), 128.0 (TBDPS), 127.7 (TBDPS), 125.9 (C₅), 125.2 (C₁₃H₂), 124.5 (C₁₃H₃), 114.0 (PMB-CH), 94.1 (C₂), 85.9 (C₃), 84.1 (C₆H), 81.7 (C₆H), 76.6 (C₁₀), 73.0 (PMB-CH₂), 71.2 (C₆H), 70.3 (C₆H), 55.4 (PMB-CH₃), 47.8 (C₇H), 42.5 (C₈H₂, br), 29.2 (C₉H₃, br), 27.2 (TBDPS), 19.5 (TBDPS) ppm; the signal of C₉/C₁₄ are broad on \(^{13}\)C NMR because of the conformational changes, the chemical shift were confirmed by HMBC;

IR (film, cm\(^{-1}\)) 3429, 2944, 1984, 1900, 1108, 826, 706; HRMS(ESI) [M + H]⁺ calculated for C₃₉H₄₅O₄Si: 653.2935, found: 653.2936; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

To a stirred solution of alcohol S9-9 (2.5 mg, 0.004 mmol) in THF (1.0 mL) was added NEt₃ (50 µL, 0.36 mmol) and methacrylic anhydride (25 µL, 0.17 mmol) followed by a trace of DMAP. The reaction mixture was stirred at room temperature for 24 minutes or till the TLC analysis showed disappearance of starting material. The reaction was then quenched with sat. aq. NaHCO₃ (2.0 mL), the mixture was extracted with ethyl acetate (2 × 5.0 mL), the combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 5/1) to provide the S9-10 as a waxy solid (1.7 mg, 59%).

Data of S9-10: waxy solid; 
\([\alpha]^{20}_{D} = -95.8\) (c 0.10, CHCl₃);

\(^1\)H NMR (500 MHz, CDCl₃) δ 7.80 – 7.74 (m, 4H, TBDPS), 7.48 – 7.34 (m, 6H, TBDPS), 7.28 (like d, J = 8.7 Hz, 2H, PMB), 6.85 (d, J = 8.7 Hz, 2H, PMB), 6.40 (d, J = 3.0 Hz, 1H, H₁₃), 5.99 (m, 1H, H₅), 5.93 (dd, J = 10.3, 3.9 Hz, 1H, H₆), 5.86 (d, J = 2.5 Hz, 1H, H₁₃), 5.83 (t, J = 1.9 Hz, 1H, H₁₅), 5.52 (t, J = 1.6 Hz, 1H, H₂), 5.23 (t, J = 1.9 Hz, 1H, H₁₅), 4.62 (d, J = 11.0 Hz, 1H, PMB), 4.50 (d, J = 11.1 Hz, 1H, PMB), 4.41 – 4.35 (m, 1H, H₉), 4.21 (dd, J = 9.3, 5.5 Hz, 1H, H₉), 4.09 (s, 1H, H₁), 3.85 – 3.80 (m, 1H, H₅), 3.79 (s, 3H, PMB), 2.36 (dd, J = 14.6, 4.0 Hz, 1H, H₉), 2.02 – 1.98 (m, 1H, H₉), 1.87 (t, J = 0.9 Hz, 3H, H₄), 1.36 (s, 3H, H₁₄), 1.12 (s, 9H, TBDPS) ppm;

\(^{13}\)C NMR (125 MHz, CDCl₃) δ 169.9 (C₁₂), 166.2 (C₇), 159.5 (PMB-C), 136.5 (TBDPS), 136.3 (TBDPS), 136.2 (C₂), 134.6 (C₁₁), 132.9 (TBDPS), 132.5 (TBDPS), 130.3 (TBDPS), 130.0
AcOH (1.4 μL, 0.024 mmol) and TBAF (1M solution in THF, 24 μL, 0.024 mmol) were mixed and stirred in THF (0.1 mL) at room temperature for 30 minutes and the resulting mixture was added to a stirred solution of S9-10 (1.7 mg, 0.0024 mmol) in THF (0.5 mL). The reaction was then stirred at room temperature for further 48 hours, until the TLC analysis showed disappearance of the starting material. The reaction was diluted with ethyl acetate (25 mL) and washed with brine (5.0 mL), dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on preparative TLC (Pentane/Ethyl acetate = 1/1) to provide the S9-11 as a waxy solid (1.0 mg, 86%).

Data of lactone S9-11: waxy solid;
[α]$_D^{20}$ -35.4° (c 0.1, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.30 (like d, J = 8.7 Hz, 2H, PMB), 6.87 (d, J = 8.7 Hz, 2H, PMB), 6.44 (d, J = 2.9 Hz, 1H, H3), 6.00 - 5.98 (m, 2H, H8 + H15), 5.91 (d, J = 2.5 Hz, 1H, H13), 5.78 (dd, J = 10.7, 3.5 Hz, 1H, H6), 5.70 (t, J = 1.8 Hz, 1H, H15), 5.55 (p, J = 1.6 Hz, 1H, H5), 4.68 (d, J = 11.1 Hz, 1H, PMB), 4.57 (d, J = 11.1 Hz, 1H, PMB), 4.40 (dt, J = 5.8, 2.8 Hz, 1H, H7), 4.24 (br s, 1H, H1), 4.19 (dd, J = 9.1, 5.4 Hz, 1H, H5), 3.97 (dt, J = 9.3, 1.9 Hz, 1H, H3), 3.80 (s, 3H, PMB), 2.26 - 2.20 (m, 1H, H9), 2.12 - 2.06 (m, 1H, H9), 1.85 (t, J = 1.6, 1.0 Hz, 3H, H4), 1.46 (s, 3H, H4) ppm;
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 169.7 (C13), 166.9 (C7), 159.6 (PMB-C), 135.8 (C2), 134.4 (C11), 129.8 (PMB-CH), 129.6 (PMB-C), 126.9 (C3), 125.7 (C4), 125.6 (C13H2), 124.1 (C13H2), 114.0 (PMB-CH), 93.7 (C2), 86.7 (C1), 84.1 (C8H), 81.6 (C3H), 75.6 (C10), 73.8 (PMB-CH2), 72.6 (C9H), 69.6 (C1H), 55.4 (PMB-CH3), 45.9 (C7H), 40.3 (C9H2), 28.1 (C13H3, br), 18.2 (C4) ppm;
IR (film, cm$^{-1}$) 3497, 2934, 2455, 1744, 1513, 1254, 1113, 1045, 826;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{27}$H$_{30}$O$_8$Na: 505.1838, found: 505.1802;
TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

To a stirred solution of S9-11 (1.0 mg, 0.0021 mmol) in CH$_2$Cl$_2$ (1.0 mL) was added MnO$_2$ (2.7 mg, 0.031 mmol) and the solution was stirred at room temperature for 2 hours, or till the TLC analysis showed disappearance of the starting material. The reaction was...
filtered and a trace of tBu3PAuNTf2 was added to the solution and stirred for 10 minutes till the the TLC analysis showed disappearance of the starting material. The resulted solution was concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1) to provide S9-12 as a white solid (0.9 mg, 90%).

Data of lactone S9-12: waxy solid; 
$[\alpha]^{20}_D$ +5.05 (c 0.04, CHCl3);
$^1$H NMR (400 MHz, CDCl3) δ 7.34 (like d, J = 8.6 Hz, 2H, PMB), 6.89 (like d, J = 8.6 Hz, 2H, PMB), 6.27 (d, J = 3.4 Hz, 1H, H13), 6.20 (dd, J = 2.1, 1.0 Hz, 1H, H1), 5.99 (p, J = 1.2 Hz, 1H, H3), 5.97 (dd, J = 2.1, 1.0 Hz, 1H, H15), 5.95 (s, 1H, H2), 5.53 (p, J = 1.5 Hz, 1H, H3), 5.52 (d, J = 3.0 Hz, 1H, H13), 4.85 (d, J = 11.1 Hz, 1H, PMB), 4.67 (dd, J = 9.4, 5.8 Hz, 1H, H6), 4.59 (d, J = 11.1 Hz, 1H, PMB), 4.40 – 4.35 (m, 2H, H6 + H5), 3.81 (s, 3H, PMB), 3.62 (dt, J = 6.3, 3.0 Hz, 1H, H3), 2.52 – 2.47 (m, 1H, H9), 2.35 (dd, J = 13.8, 1.8 Hz, 1H, H9), 1.82 (dd, J = 1.6, 1.0 Hz, 3H, H4'), 1.52 (s, 3H, H14) ppm;
$^{13}$C NMR (100 MHz, CDCl3) δ 204.1 (C1), 185.1 (C3), 168.7 (C12), 166.7 (C1), 159.6 (PMB-C), 137.4 (C4), 135.5 (C2'), 133.1 (C11), 129.9 (PMB-CH), 129.6 (PMB-C), 126.7 (C5'), 123.9 (C15H2), 114.1 (PMB-CH), 106.9 (C6H), 90.5 (C10), 85.6 (C3H), 80.8 (C6H), 74.8 (PMB-CH2), 70.8 (C5H), 55.5 (PMB-CH3), 51.9 (C4H), 45.5 (C9H2), 21.2 (C14H3), 18.1 (C4H3) ppm;
IR (film, cm$^{-1}$) 3498, 2170, 1769, 1713, 1250, 1159, 1040, 813;
HRMS(ESI) [M + Na]$^+$ calculated for C27H28O8Na: 503.1682, found: 503.1685;
TLC: Rf = 0.5 (Pentane/Ethyl acetate = 2.5/1).

To a stirred solution of S9-12 (0.9 mg, 0.0019 mmol) in CH2Cl2/H2O (1.0 mL/ 4 drops) was added DDQ (1.3 mg, 0.0057 mmol) and the mixture was stirred at room temperature for 24 hours till the TLC analysis showed disappearance of the starting material. The reaction mixture was then quenched by saturated aqueous NaHCO3 (1.0 mL) and extracted with CH2Cl2 (2 × 10 mL). The combined organic layers were dried over Na2SO4, filtered, concentrated in vacuo and purified on silica gel chromatography (Pentane/Ethyl acetate = 5/1 ~ 2/1) to provide 15 as a waxy solid(0.5 mg, 74%).

Data of 15: waxy solid; 
$[\alpha]^{20}_D$ -18 (c 0.04, CHCl3);
$^1$H NMR and $^{13}$C NMR data, see Table S14; 
IR (film, cm$^{-1}$) 3678, 2921, 1988, 1711, 1261, 1144, 819;
HRMS(ESI) [M + Na]$^+$ calculated for C19H20NaO7: 383.1107, found: 383.1115;
TLC: Rf = 0.20 (Petroleum ether/Ethyl acetate = 3/1).
Figure S10. Synthesis of 20b from 25-1.

Compound 25-1 can also be obtained after SAD from 25. To a mixture of compound 25-1 (13.4 g, 51.5 mmol), acetic anhydride (5.84 mL, 61.85 mmol) and DMAP (628 mg, 5.15 mmol) in CH$_2$Cl$_2$ (200 mL) was added dropwise Et$_3$N (17.8 mL, 129 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred 1 hour. After the reaction was diluted with CH$_2$Cl$_2$ (200 mL) and washed with HCl 0.1 M (100 mL), followed by H$_2$O (100 mL) and Brine (100 mL). The organic layer was then dried over sodium sulfate, the solvent was removed and a pale-yellow oil was obtained S10-1 (15.5 g, yield 99%).

Data of S10-1: pale-yellow oil;
[α]$^0_{D}$ -34 (c 0.3, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) δ 5.42 (s, 1H), 4.73 (dd, $J = 6.4, 5.3$ Hz, 1H), 3.40 (d, $J = 9.9$ Hz, 6H), 2.15 (s, 3H), 2.09 (dd, $J = 14.6, 5.3$ Hz, 1H), 1.91 (dd, $J = 14.6, 6.5$ Hz, 1H), 0.19 (s, 9H) ppm;
$^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.9, 102.3, 100.4, 92.0, 72.7, 69.7, 53.5, 53.2, 39.8, 23.0, 21.0, -0.2 ppm;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{14}$H$_{26}$O$_5$Si: 325.1550, found: 325.1437;
TLC: Rf = 0.35 (Pentane/Ethyl acetate = 2/1).

To a solution of S10-1 (15.5 g, 51.5 mmol) in THF (170 mL) was added dropwise TBAF (51.5 mL, 1M in THF, 51.5 mmol) at 0 °C. The reaction mixture was then stirred for 15 minutes and quenched with saturated NH$_4$Cl (50 mL), then diluted with Et$_2$O (200 mL) and washed with HCl 0.1M (100 mL) H$_2$O (100 mL) and Brine (100 mL). The organic layer was then dried over Na$_2$SO$_4$. The solvent was removed and the residue was purified by chromatography on silica gel (pentane/ethyl acetate 7/3) to give a pale-yellow oil 20b (9.75 g, yield 82%).

Data of 20b: pale-yellow oil;
[α]$^0_{D}$ -19.4 (c 0.1, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) δ 5.38 (d, $J = 2.2$ Hz, 1H), 4.74 (t, $J = 5.8$ Hz, 1H), 3.40 (d, $J = 4.4$ Hz, 6H), 2.50 (d, $J = 2.2$ Hz, 1H), 2.15 (s, 3H), 2.11 (dd, $J = 14.6, 5.6$ Hz, 1H), 1.93 (dd, $J = 14.6, 6.0$ Hz, 1H) ppm;
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.8, 102.2, 79.0, 74.8, 72.5, 69.3, 53.4, 53.2, 39.5, 23.2, 20.9 ppm; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

Figure S11. Synthesis of Goyazensolide (1) and GOYA-1 from 38 and 20b.

38 was prepared from S11-1 according to the reported procedure.$^{26}$

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$^{26}$Koura, M., Yamaguchi, Y., Kurobuchi, S., Sumida, H., Watanabe, Y., Enomoto, T., Matsuda, T., Koshizawa, T., Matsumoto, Y., Shibuya, K. *Bioorg. Med. Chem.* 2016, 24, 3436-3446.
To a solution of **38** (38 g, 104 mmol) in THF (400 mL), was added vitride (53 mL, 3.5 M in toluene, 185 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 minutes, and then Br₂ (6.96 mL, 135 mmol) was added over 5 minutes. After 15 minutes, saturated aqueous Na₂S₂O₃ (100 mL) and saturated aqueous Rochelle’s salt (100 mL) were added at room temperature, and the mixture was stirred for 30 minutes. The mixture was then extracted with ethyl acetate (100 mL × 3), and the combined organic layers were washed with brine (200 mL), dried over MgSO₄, and concentrated to give the crude alcohol as a colorless oil (28 g, 67%).

Data of **S11-2**: colorless oil;

⁴H NMR (400 MHz, CDCl₃) δ 7.69 (dd, J = 7.9, 1.5 Hz, 4H), 7.44 (ddd, J = 18.9, 7.6, 6.1 Hz, 6H), 6.39 (tt, J = 6.1, 1.6 Hz, 1H), 4.34 (d, J = 6.1 Hz, 2H), 4.30 (d, J = 1.5 Hz, 2H), 1.11 (s, 9H) ppm;

¹³C NMR (101 MHz, CDCl₃) δ 135.5, 132.9, 129.9, 127.8, 126.8, 126.6, 68.0, 61.8, 26.7, 19.2 ppm;

TLC: Rf = 0.4 (Pentane/Ethyl acetate = 3/1).

To a solution of **S11-2** (25 g, 61.7 mmol) in CH₂Cl₂ (300 mL) was added DMP (31.3 g, 74 mmol) in portions at 0 °C. The mixture was stirred at 0 °C for 15 minutes, and mixture allowed to warm to room temperature. After 30 minutes, saturated aqueous Na₂S₂O₃ (50 mL) and saturated aqueous NaHCO₃ (50 mL) were added at room temperature, and the mixture was stirred for 10 more minutes. The whole was extracted with Et₂O (150 mL × 3), and the combined organic layers were washed with brine (200 mL) dried over MgSO₄, and concentrated to give crude aldehyde as a paled yellow oil (20.3 g, yield 82%).

Data of **S11-3**: paled yellow oil;

⁴H NMR (400 MHz, CDCl₃) δ 10.00 (d, J = 6.9 Hz, 1H), 7.67 (d, J = 8.0 Hz, 4H), 7.47 (dd, J = 15.8, 6.0 Hz, 6H), 6.93 (d, J = 6.9 Hz, 1H), 4.43 (s, 2H), 1.11 (s, 9H) ppm;

¹³C NMR (101 MHz, CDCl₃) δ 192.5, 147.3, 135.1, 131.8, 129.9, 127.7, 125.2, 68.1, 26.4, 18.9 ppm;

TLC: Rf = 0.6 (Pentane/Ethyl acetate = 4/1).

To a mixture of **S11-3** (8.5 g, 21.2 mmol), allylic bromide **28** (6.13 g, 31.8 mmol) in THF/water (6/1, 140 mL) at 0 °C under a vigorous stirring was added Zn (2.48 g, 38.2 mmol) in portions. The mixture was allowed to warm to room temperature for 1 hour. The reaction mixture was then diluted with Et₂O (200 mL) and water (150 mL). The organic phase was washed with Brine (100 mL), dried over Na₂SO₄ and volatiles were evaporated in vacuo. The crude was diluted in CH₂Cl₂ (150 mL) and to the solution was added PTSA (0.86 g, 5.0 mmol). Then the mixture was stirred for 4 hours at room temperature. The reaction was then diluted with HCl (0.1M, 100 mL), the organic phase was then washed with H₂O (100 mL) and Brine (100 mL), dried over Na₂SO₄ and the
solvent was removed in vacuo. Chromatography on silica gel (pentane/ethyl acetate 8/2) gave a pale-yellow oil (8.1 g, yield 81%).

Data of S11-4: pale-yellow oil;
$^1H$ NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (dd, $J$ = 8.7, 3.8 Hz, 4H), 7.50–7.39 (m, 6H), 6.36 (dt, $J$ = 7.6, 1.7 Hz, 1H), 6.30 (t, $J$ = 2.8 Hz, 1H), 5.70 (t, $J$ = 2.5 Hz, 1H), 5.37 (dd, $J$ = 14.6, 7.6 Hz, 1H), 4.36–4.24 (m, 2H), 3.30 (dd, $J$ = 17.1, 7.9 Hz, 1H), 2.66 (dd, $J$ = 17.1, 6.7 Hz, 1H), 1.10 (s, 9H) ppm;
$^{13}C$ NMR (101 MHz, CDCl$_3$) $\delta$ 170.0, 135.4, 135.4, 133.7, 132.7, 132.5, 130.0, 130.0, 128.9, 127.9, 127.8, 126.1, 122.5, 76.0, 67.8, 33.8, 26.7, 19.2;
HRMS(ESI) [M + H]$^+$ calculated for C$_{24}$H$_{27}$BrO$_3$Si: 471.0913, found 471.1007;
TLC: $R_f$ = 0.5 (Pentane/Ethyl acetate = 4/1) ppm.

To a stirred solution of lactone S11-4 (2.0 g, 4.2 mmol) in dioxane (20 mL) was added SeO$_2$ (2.8 g, 25.2 mmol) in 3 portions at 95 °C within 1.5 hours. After the addition, the reaction mixture was stirred at the same temperature for another 30 minutes and then cooled down to room temperature. Then dioxane was evaporated and Et$_2$O (80 mL) was added, stirred for 30 minutes, filtered and the solution was washed with saturated aqueous NaHCO$_3$ (20 mL), diluted Na$_2$S (10 mL) and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 10/1 ~ 1/1) to provide 23 as a light yellow oil (860 mg, 42%).

Data of 23: light yellow oil;
Obtained as a mixture of diastereomers (dr = 2:1 as determined by $^1H$ NMR);
$^1H$ NMR (400 MHz, CDCl$_3$) $\delta$ 7.66 (td, $J$ = 7.2, 1.5 Hz, 4H), 7.48–7.39 (m, 6H), 6.51 (d, $J$ = 1.7 Hz, 0.33H), 6.49 (d, $J$ = 2.4 Hz, 0.66H), 6.40 (dt, $J$ = 7.6, 1.7 Hz, 0.33H), 6.26 (dt, $J$ = 8.0, 1.7 Hz, 0.66H), 6.06 (d, $J$ = 1.5 Hz, 0.33H), 6.02 (d, $J$ = 2.1 Hz, 0.66H), 5.35 (dd, $J$ = 7.5, 5.6 Hz, 0.33H), 5.14 (dd, $J$ = 8.0, 4.7 Hz, 0.66H), 5.01 (dt, $J$ = 5.6, 1.6 Hz, 0.33H), 4.63 (dt, $J$ = 4.6, 2.3 Hz, 0.66H), 4.36 (d, $J$ = 5.0 Hz, 0.66H), 4.34 (s, 1.32H), 1.10 (s, 9H) ppm;
$^{13}C$ NMR (101 MHz, CDCl$_3$) $\delta$ 167.9, 137.4, 135.5, 132.7, 132.4, 131.0, 130.1, 129.8, 126.1, 123.5, 121.1, 83.4, 81.0, 73.8, 69.1, 67.9, 26.7, 26.7, 19.2 ppm;
HRMS(ESI) [M + Na]$^+$ calculated for C$_{24}$H$_{27}$BrO$_4$Si: 509.0862, found 509.0772;
TLC: $R_f$ = 0.25 (Pentane/Ethyl acetate = 4/1).

To a stirred solution of alkyne 20b (269 mg, 1.17 mmol) and vinyl bromide 23 (860 mg, 1.76 mmol) in DMF/Et$_3$N (6.0 mL/2.0 mL) was added PPh$_3$ (60 mg, 0.23 mmol) at room temperature. under N$_2$. Then Pd$_2$dba$_3$ (109 mg, 0.12 mmol) and Cul (11 mg, 0.06 mmol)
were added to the reaction. The resulted mixture was stirred at the same temperature for 3 hours or till the TLC analysis showed disappearance of starting material. The reaction was quenched by sat. aq. NH₄Cl (5.0 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (CH₂Cl₂/ethyl acetate = 1/1) to provide enyne S11-5 as mixture of diastereomers as a yellow oil (402 mg, 54%).

Data of S11-5: yellow oil;

1H NMR (400 MHz, CDCl₃) δ 7.66 (m, 4H), 7.42 (m, 6H), 6.47 (m, 1H), 6.22 (m, 1H), 6.01 (m, 1H), 5.51–5.33 (m, 1H), 5.30–4.97 (m, 1H), 4.77–4.55 (m, 2H), 4.23 (m, 2H), 3.45–3.24 (m, 6H), 2.18–1.98 (m, 4H), 1.96–1.79 (m, 1H), 1.33 (t, 3H), 1.08 (s, 9H) ppm; 13C NMR (101 MHz, CDCl₃) δ 170.2, 168.4, 137.9, 137.6, 135.5, 133.4, 133.0, 132.8, 132.7, 132.7, 129.9, 129.8, 128.0, 127.8, 126.3, 126.1, 126.0, 126.0, 102.3, 102.1, 102.0, 92.4, 92.4, 84.0, 83.9, 81.6, 80.1, 74.1, 74.1, 72.8, 72.7, 72.7, 70.5, 70.4, 70.2, 69.8, 65.0, 64.7, 64.7, 53.6, 53.5, 53.4, 53.3, 53.2, 39.4, 39.4, 39.3, 26.7, 26.7, 23.9, 23.8, 23.7, 20.9, 20.9, 19.2 ppm; HRMS(ESI) [M + Na]+ calculated for C₃₅H₄₄O₉Si: 659.2755, found 659.2652; TLC: Rf = 0.3 (DCM/Ethyl acetate = 1/1).

To a solution of S11-5 (402 mg, 0.63 mmol) in Et₂O (20 mL) at -25 °C, was added dropwise a solution of PBr₃ (1.2 mL, 1M in Et₂O). After 30 minutes, the mixture was quenched with cold H₂O (1 mL) and allowed to warm to room temperature. Then the reaction was extracted with CH₂Cl₂ (50 mL), and the organic layer was dried over Na₂SO₄ and concentrated. The residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 7/3 ~ 3/7) to give a yellow solid corresponding to S11-6 as a mixture of inseparable 1:1 diastereoisomers (213 mg, yield 52%).

Data of S11-6: yellow solid;

1H NMR (400 MHz, CDCl₃) δ 9.85 (t, J = 3.8 Hz, 1H), 7.71–7.60 (m, 4H), 7.52–7.37 (m, 7H), 7.35 (d, J = 1.2 Hz, 1H), 5.96–5.81 (m, 2H), 5.48 (d, J = 2.6 Hz, 1H), 4.21 (d, J = 0.7 Hz, 2H), 4.14 (d, J = 0.8 Hz, 2H), 2.70 (ddd, J = 29.0, 15.2, 9.3 Hz, 2H), 2.13 (s, 3H), 1.41 (s, 3H), 1.07 (s, 9H) ppm; 13C NMR (101 MHz, CDCl₃) δ 201.30, 201.28, 170.98, 170.95, 169.66, 169.64, 150.55, 135.68, 135.66, 135.63, 135.61, 132.85, 132.74, 131.53, 131.51, 130.18, 129.33, 129.32, 128.04, 127.88, 92.58, 92.52, 81.81, 81.79, 79.31, 79.28, 77.41, 77.16, 76.91, 73.45, 70.19, 70.17, 65.17, 50.65, 50.60, 26.91, 24.18, 24.16, 20.98, 20.96, 19.38 ppm; HRMS(ESI) [M + Na]+ calculated for C₃₃H₃₇BrO₇Si: 675.1492, found 675.1390; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).
A 10 mL round bottom flask equipped with a magnetic stir bar was charged with bromolactone S11-6 (213 mg, 0.33 mmol) and DMF (10 mL). The reaction mixture was cooled down to -30 °C and CrCl₂ (405 mg, 3.3 mmol) was added. The temperature was allowed to rise to room temperature and stirred for 30 minutes till the TLC analysis showed disappearance of the starting material. Then the reaction was quenched with sat. aq. NH₄Cl (50 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic layers were dried over Na₂SO₄, then filtered and concentrated in vacuo. The residue was purified on silica gel chromatography (CH₂Cl₂/Ethyl acetate = 1/1) to provide S11-7 as a yellow solid (72 mg, 38%).

Data of S11-7: yellow solid;
[α]D -108 (c 0.25, CHCl₃);
¹H NMR (500 MHz, CDCl₃) δ 7.64 (dd, J = 6.5, 5.0 Hz, 4H), 7.48–7.36 (m, 6H), 6.46 (s, 1H), 6.41 (s, 1H), 5.81 (s, 1H), 5.20 (s, 1H), 5.16 (s, 1H), 4.15 (s, 2H), 4.10 (s, 1H), 3.98 (s, 1H), 2.63 (d, J = 14.0 Hz, 1H), 2.16–2.09 (m, 4H), 1.42 (s, 3H), 1.07 (s, 9H) ppm;
¹³C NMR (126 MHz, CDCl₃) δ 169.7, 169.3, 139.2, 135.5, 135.5, 132.8, 132.8, 129.9, 129.9, 127.8, 125.7, 70.4, 63.9, 29.7, 26.8, 20.8, 19.2 ppm;
HRMS(ESI) [M + Na]+ calculated for C₃₃H₃₈O₇Si: 597.2387, found 597.2284; TLC: Rf = 0.35 (DCM/Ethyl acetate = 1/1).

To a solution of S11-7 (50 mg, 0.087 mmol), methacrylic anhydride (20 µL, 0.13 mmol) and DMAP (1.0 mg, 9.0 µmol) in CH₂Cl₂ (1.0 mL) at 0 °C, was added dropwise a solution of Et₃N (30 µL, 0.22 mmol) in CH₂Cl₂ (0.5 mL). Mixture allowed to warm at room temperature and after 4 hours, HCl 0.1M (1.0 mL) was added. The whole was extracted with CH₂Cl₂ (2.0 mL × 2), and the combined organic layers were washed with brine (1.0 mL), dried over MgSO₄, and purified by silica gel chromatography (pentane/Ethyl acetate = 6/4) to give a yellow oil (27.5 mg, yield 49%).

Data of S11-8: yellow oil;
[α]D -61 (c 0.15, CHCl₃);
¹H NMR (400 MHz, CDCl₃) δ 7.67–7.64 (m, 4H), 7.45–7.38 (m, 6H), 6.50 (d, J = 2.4 Hz, 1H), 6.43 (d, J = 2.8 Hz, 1H), 6.04 (s, 1H), 5.86 (s, 1H), 5.84 (d, J = 2.3 Hz, 1H), 5.59 (s, 1H), 5.02 (dd, J = 5.1, 2.6 Hz, 1H), 4.53 (dd, J = 5.1, 2.5 Hz, 1H), 4.20–4.12 (m, 2H), 2.39 (dd, J = 14.8, 3.6 Hz, 1H), 2.20 (t, J = 8.3 Hz, 4H), 1.91 (s, 3H), 1.39 (s, 3H), 1.09 (s, 9H) ppm;
¹³C NMR (101 MHz, CDCl₃) δ 169.7, 166.2, 138.5, 135.8, 135.5, 134.8, 132.8, 129.9, 127.8, 126.4, 124.0, 122.7, 95.9, 80.4, 74.7, 72.6, 69.4, 64.2, 46.2, 29.6, 26.8, 20.8, 19.2, 18.2 ppm; Traces of DCM (integration = 0.9), water (integration = 9.51) and grease (integration = 4.28), purity of the compound is 80.7%.
HRMS(ESI) [M + H]^+ calculated for C_{37}H_{42}O_{8}Si: 643.2649, found 643.2888; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

To a solution of S11-8 (27.5 mg, 0.043 mmol) in MeOH (2.0 mL) at 0 °C, was added dropwise a solution of K$_2$CO$_3$ (27 µL, 1M in H$_2$O). The mixture was stirred 20 minutes at 0 °C and quenched with a cold mixture of CH$_2$Cl$_2$/H$_2$O (10mL). The reaction was then extracted with CH$_2$Cl$_2$ (5.0 mL), and the combined organic layers were washed with brine (5.0 mL), dried over MgSO$_4$, concentrated and purified by PTLC (pentane/ethyl acetate = 1/1) to give propargyl alcohol S11-9 as a yellow oil (24 mg, yield 92%).

Data of S11-9: yellow oil; [α]$_D$$^2$ -48 (c 0.12, CHCl$_3$);
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.66 (dd, $J$ = 7.9, 1.5 Hz, 4H), 7.47–7.37 (m, 6H), 6.46 (dd, $J$ = 6.5, 2.6 Hz, 2H), 6.06 (s, 1H), 5.92 (d, $J$ = 9.4 Hz, 1H), 5.86 (d, $J$ = 2.5 Hz, 1H), 5.63–5.58 (m, 1H), 4.95 (dd, $J$ = 5.6, 2.6 Hz, 1H), 4.43 (td, $J$ = 4.6, 2.5 Hz, 1H), 4.26 (s, 1H), 4.23–4.16 (m, 2H), 4.14 (d, $J$ = 7.1 Hz, 1H), 2.29 (dd, $J$ = 15.0, 3.3 Hz, 1H), 1.90 (s, 3H), 1.45 (s, 3H), 1.09 (s, 9H) ppm; $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.4, 166.9, 137.7, 135.6, 135.5, 134.6, 132.8, 129.9, 127.8, 126.9, 123.8, 122.6, 98.7, 84.5, 80.3, 75.7, 72.5, 69.6, 64.4, 60.4, 53.4, 46.0, 39.8, 29.0, 26.8, 21.0, 19.2, 18.0, 14.2 ppm; HRMS(ESI) [M + H]^+ calculated for C$_{35}$H$_{40}$O$_7$Si: 601.2543, found 601.2622; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

To a stirred solution of S11-9 (24 mg, 40 µmol) in CH$_2$Cl$_2$ (5.0 mL) was added MnO$_2$ (35 mg, 0.4 mmol) and the solution was stirred at room temperature for 2 hours, till the TLC analysis showed disappearance of the starting material. The reaction was filtered and a trace of tBu$_3$PAuNTf$_2$ was added and the solution was stirred for 10 more minutes till the TLC analysis showed disappearance of the starting material. The resulted solution was concentrated in vacuo and the residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 3/1) to provide the S11-10 as a white solid (19 mg, 82%).

Data of S11-10: white solid; [α]$_D$$^2$ -36 (c 0.12, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70–7.62 (m, 4H), 7.51–7.39 (m, 6H), 6.80 (q, $J$ = 2.0 Hz, 1H), 6.49 (d, $J$ = 3.3 Hz, 1H), 6.09 (s, 1H), 5.84 (t, $J$ = 4.5 Hz, 1H), 5.81 (d, $J$ = 2.9 Hz, 1H), 5.66–5.59 (m, 1H), 5.28 (dq, $J$ = 7.3, 2.5 Hz, 1H), 4.32–4.25 (m, 2H), 4.01 (dt, $J$ = 6.0, 2.8 Hz, 1H), 3.78 (s, 3H), 2.29 (dd, $J$ = 15.0, 3.3 Hz, 1H), 1.45 (s, 3H), 1.10 (s, 9H) ppm; $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.4, 166.9, 137.7, 135.6, 135.5, 134.6, 132.8, 129.9, 127.8, 126.9, 123.8, 122.6, 98.7, 84.5, 80.3, 75.7, 72.5, 69.6, 64.4, 60.4, 53.4, 46.0, 39.8, 29.0, 26.8, 21.0, 19.2, 18.0, 14.2 ppm; HRMS(ESI) [M + H]^+ calculated for C$_{35}$H$_{40}$O$_7$Si: 601.2543, found 601.2622; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).

To a stirred solution of S11-9 (24 mg, 40 µmol) in CH$_2$Cl$_2$ (5.0 mL) was added MnO$_2$ (35 mg, 0.4 mmol) and the solution was stirred at room temperature for 2 hours, till the TLC analysis showed disappearance of the starting material. The reaction was filtered and a trace of tBu$_3$PAuNTf$_2$ was added and the solution was stirred for 10 more minutes till the TLC analysis showed disappearance of the starting material. The resulted solution was concentrated in vacuo and the residue was purified on silica gel chromatography (Pentane/Ethyl acetate = 3/1) to provide the S11-10 as a white solid (19 mg, 82%).

Data of S11-10: white solid; [α]$_D$$^2$ -36 (c 0.12, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70–7.62 (m, 4H), 7.51–7.39 (m, 6H), 6.80 (q, $J$ = 2.0 Hz, 1H), 6.49 (d, $J$ = 3.3 Hz, 1H), 6.09 (s, 1H), 5.84 (t, $J$ = 4.5 Hz, 1H), 5.81 (d, $J$ = 2.9 Hz, 1H), 5.66–5.59 (m, 1H), 5.28 (dq, $J$ = 7.3, 2.5 Hz, 1H), 4.32–4.25 (m, 2H), 4.01 (dt, $J$ = 6.0, 2.8 Hz, 1H), 3.78 (s, 3H), 2.29 (dd, $J$ = 15.0, 3.3 Hz, 1H), 1.45 (s, 3H), 1.10 (s, 9H) ppm; $^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.4, 166.9, 137.7, 135.6, 135.5, 134.6, 132.8, 129.9, 127.8, 126.9, 123.8, 122.6, 98.7, 84.5, 80.3, 75.7, 72.5, 69.6, 64.4, 60.4, 53.4, 46.0, 39.8, 29.0, 26.8, 21.0, 19.2, 18.0, 14.2 ppm; HRMS(ESI) [M + H]^+ calculated for C$_{35}$H$_{40}$O$_7$Si: 601.2543, found 601.2622; TLC: Rf = 0.25 (Pentane/Ethyl acetate = 2/1).
2.51 (dd, $J = 15.5, 5.7$ Hz, 1H), 2.36 (dt, $J = 6.4, 2.9$ Hz, 1H), 1.92 (s, 3H), 1.47 (s, 3H), 1.10 (d, $J = 6.4$ Hz, 9H) ppm;

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 190.0, 169.0, 167.0, 143.8, 136.1, 135.9, 133.5, 133.0, 130.7, 128.5, 127.7, 125.1, 121.4, 96.0, 94.4, 80.3, 80.2, 71.2, 64.8, 50.9, 44.4, 27.3, 25.6, 19.8, 18.7 ppm;

HRMS (ESI) [M + H]$^+$ calculated for C$_{35}$H$_{38}$O$_7$Si: 599.2387, found 599.2465;

TLC: $R_f = 0.3$ (Pentane/Ethyl acetate = 2/1).

Data of S11-10: white solid;

$[\alpha]_{20}^20^{-2}$ (c 0.1, CHCl$_3$);

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.69–7.65 (m, 4H), 7.50–7.38 (m, 6H), 6.26 (d, $J = 3.2$ Hz, 1H), 6.14 (d, $J = 2.9$ Hz, 1H), 6.03 (s, 1H), 5.68 (s, 1H), 5.58–5.54 (m, 1H), 5.48 (d, $J = 2.7$ Hz, 1H), 5.30 (dd, $J = 5.0, 2.3$ Hz, 1H), 4.53 (d, $J = 11.8$ Hz, 1H), 4.40 (dd, $J = 34.3, 13.9$ Hz, 2H), 3.77–3.72 (m, 1H), 2.49 (dd, $J = 13.8, 11.8$ Hz, 1H), 2.32 (d, $J = 11.9$ Hz, 1H), 1.85 (s, 3H), 1.51 (s, 3H), 1.09 (s, 9H) ppm;

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 204.6, 184.7, 166.8, 166.7, 135.6, 135.5, 135.4, 134.3, 133.9, 133.3, 132.6, 130.1, 127.8, 127.8, 126.4, 124.3, 106.4, 89.6, 81.5, 73.1, 64.1, 50.8, 43.9, 29.6, 26.7, 20.6, 19.2, 17.9 ppm;

HRMS (ESI) [M + H]$^+$ calculated for C$_{35}$H$_{38}$O$_7$Si: 599.2387, found 599.2450;

TLC: $R_f = 0.25$ (Pentane/Ethyl acetate = 2/1).

To a solution of S11-10 (17 mg, 0.029 mmol) in THF (2.0 mL) at 0 °C, was added dropwise a solution of HF-pyridine 70% (85 µL) in THF (1.0 mL). The mixture was stirred 4 hours at 0 °C and quenched with saturated NaHCO$_3$ (2.0 mL). The quenched mixture was then extracted with Et$_2$O (5.0 mL × 2), and the combined organic layers were washed with brine (5.0 mL), dried over MgSO$_4$, and purified by PTLC (Pentane/Ethyl acetate = 2/8) to give (−)-Goyazensolide (8.5 mg, yield 82%).

Data of 1: waxy solid;

$[\alpha]_{20}^20^{-19}$ (c 0.1, CHCl$_3$);

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.30 (dt, $J = 3.0, 1.5$ Hz, 1H), 6.25 (d, $J = 3.1$ Hz, 1H), 6.03 (s, 1H), 5.82 (s, 1H), 5.59–5.54 (m, 1H), 5.49 (d, $J = 2.7$ Hz, 1H), 5.36 (dd, $J = 4.9, 2.7$ Hz, 1H), 4.57 (dt, $J = 11.7, 2.2$ Hz, 1H), 4.42 (dt, $J = 3.1, 1.7$ Hz, 2H), 3.82 (t, $J = 5.3$ Hz, 1H), 2.56–2.48 (m, 1H), 1.85 (s, 3H), 1.56 (s, 3H) ppm;

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 204.6, 184.2, 166.8, 135.5, 135.3, 134.2, 133.1, 126.6, 124.6, 106.6, 89.8, 81.5, 73.2, 63.2, 50.9, 43.9, 20.7, 18.0 ppm;

HRMS (ESI) [M + H]$^+$ calculated for C$_{19}$H$_{20}$O$_7$: 361.1209, found 361.1392;

TLC: $R_f = 0.2$ (DCM/Ethyl acetate = 1/2).
To a solution of 1 (5.0 mg, 14 µmol), pent-4-ynoyl chloride (2.4 mg, 21 µmol) and DMAP (0.17 mg, 0.0014 mmol) in CH₂Cl₂ (0.3 mL) at 0 °C, was added dropwise a solution of Et₃N (6.0 µL, 42 µmol) in CH₂Cl₂ (0.1 mL). The mixture was allowed to warm to room temperature and after 4 hours, HCl (0.1M, 0.2 mL) was added. The solution was then extracted with CH₂Cl₂ (1.0 mL × 2), and the combined organic layers were washed with brine (1.0 mL), dried over MgSO₄, and purified by PTLC (Pentane/Ethyl acetate = 1/1) to give a white solid (2.5 mg, yield 41%).

Data of GOYA-1: white solid; 
[α]D 20 -13 (c 0.1, CHCl₃);
¹H NMR (400 MHz, CDCl₃) δ 6.39–6.34 (m, 1H), 6.26 (d, J = 3.1 Hz, 1H), 6.03 (s, 1H), 5.83 (s, 1H), 5.57 (s, 1H), 5.49 (d, J = 2.7 Hz, 1H), 5.35 (d, J = 1.9 Hz, 1H), 4.86 (s, 2H), 4.60–4.51 (m, 1H), 3.80 (d, J = 2.5 Hz, 1H), 2.63 (t, J = 6.8 Hz, 2H), 2.59–2.49 (m, 3H), 2.34 (dd, J = 13.9, 1.9 Hz, 1H), 2.02 (t, J = 2.6 Hz, 1H), 1.85 (s, 3H), 1.57 (d, J = 7.8 Hz, 3H) ppm;
¹³C NMR (101 MHz, CDCl₃) δ 204.4, 183.0, 170.9, 168.4, 166.8, 138.7, 135.3, 132.9, 129.5, 126.6, 124.7, 106.8, 89.8, 82.0, 81.2, 73.2, 69.5, 63.6, 50.8, 43.9, 33.1, 20.6, 17.9, 14.3 ppm; HRMS(ESI) [M + H]⁺ calculated for C₂₄H₂₄O₈: 441.1471, found 441.1394; TLC: Rf = 0.2 (Pentane/Ethyl acetate = 1/1).

Figure S12. Synthesis of GOYA-2.
A sealed solution of propargyl alcohol (1.2 g, 21.4 mmol), ethyl 2-(bromomethyl) acrylate 28 (5.8 g, 30 mmol), NaI (320 mg, 2.1 mmol) and Et$_3$N (12 mL, 85.6 mmol) in CH$_2$Cl$_2$ (80 mL) was heated overnight at 50 °C. The mixture was then diluted with CH$_2$Cl$_2$ (50 mL) and HCl (0.1M, 100 mL). The aqueous phase was extracted with CH$_2$Cl$_2$ (100 mL), and the combined organic layers were washed with brine (200 mL), dried over MgSO$_4$, concentrated and purified by silica gel chromatography (Pentane/Ethyl acetate = 8/2) to give a pale yellow oil (2.8 g, yield 78%).

Data of S12-1: pale yellow oil;
$^1$H NMR (400 MHz, CDCl$_3$) δ 6.34 (s, 1H), 5.89 (s, 1H), 4.30 (s, 2H), 4.27 – 4.20 (m, 4H), 2.46 (t, $J = 2.4$ Hz, 1H), 1.31 (d, $J = 7.1$ Hz, 3H) ppm;
$^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.7, 136.7, 126.2, 79.3, 74.7, 67.9, 60.7, 57.8, 14.1 ppm;
TLC: Rf = 0.4 (Pentane/Ethyl acetate = 4/1).

A solution of S12-1 (500 mg, 2.98 mmol) in 6N HCl (5.0 mL) was heated at 65 °C overnight. The mixture was then diluted with H$_2$O (20 mL) and CH$_2$Cl$_2$ (20 mL). The solution was then extracted with CH$_2$Cl$_2$ (10 mL × 2), and the combined organic layers were washed with brine (10 mL), dried over MgSO$_4$, and concentrated to give crude acid S12-2 as a brownish solid (308 mg, yield 74%).

Data of S12-2: brownish solid;
$^1$H NMR (400 MHz, CDCl$_3$) δ 6.49 (s, 1H), 6.04 (s, 1H), 4.31 (s, 2H), 4.24 (s, 2H), 2.48 (s, 1H) ppm;
$^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.9, 135.9, 129.0, 79.2, 74.9, 67.4, 57.9 ppm;
TLC: Rf = 0.3 (Pentane/Ethyl acetate/AcOH = 1/1/0.01).

To a solution of S12-2 (308 mg, 2.2 mmol) and Et$_3$N (608 µL, 4.4 mmol) in CH$_2$Cl$_2$ (6.0 mL) at 0 °C, was added dropwise a solution of acyl chloride S12-3 (644 mg, 2.64 mmol) in CH$_2$Cl$_2$ (2.0 mL). The mixture was then allowed to warm to room temperature and after 30 minutes, HCl (0.1M, 5.0 mL) was added. The solution was then extracted with CH$_2$Cl$_2$ (5.0 mL × 2) and the combined organic layers were washed with brine (5.0 mL), dried
over MgSO₄, and purified by Isolera Biotage using SNAP Cartridge KP-C18-HS 12 g column (Water/acetonitrile 9/1 to 1/1) to give a yellow oil (153 mg, yield 53%).

Data of 39: yellow oil, compound unstable on silica gel;
¹H NMR (400 MHz, CDCl₃) δ 6.50 (s, 1H), 6.19 (s, 1H), 4.35 (s, 2H), 4.26 (s, 2H), 2.48 (s, 1H) ppm;
¹³C NMR (101 MHz, CDCl₃) δ 161.0, 136.0, 130.3, 75.1, 67.2, 65.8, 58.0 ppm;
HRMS(ESI) [M + Na]^+ calculated for C₁₄H₁₄O₅: 285.0841, found 285.0836.

To a solution of S11-7 (50 mg, 0.087 mmol), 39 (103 mg, 0.39 mmol) in DCE (1.0 mL) at 50 °C, was added dropwise a solution of DMAP (46 mg, 0.38 mmol) in CH₂Cl₂ (0.3 mL). The mixture was stirred 2 hours and then allowed to cool at room temperature. HCl (0.1M, 1.0 mL) was added and the mixture was extracted with CH₂Cl₂ (5.0 mL × 2), the combined organic layers were washed with brine (5.0 mL), dried over MgSO₄, the solvent was evaporated in vacuo and the resulting residue was purified by silica gel chromatography (Pentane/Ethyl acetate = 7/3) to give S12-4 as a yellow oil (16 mg, yield 26%).

Data of S12-4: yellow oil;
[α]°D -57 (c 0.1, CHCl₃);
¹H NMR (400 MHz, CDCl₃) δ 7.66–7.62 (m, 4H), 7.46–7.38 (m, 6H), 6.47 (dd, J = 3.3, 2.0 Hz, 2H), 6.42 (d, J = 2.3 Hz, 1H), 6.04 (d, J = 1.4 Hz, 1H), 5.90 (d, J = 1.2 Hz, 1H), 5.64 (s, 1H), 5.19 (s, 1H), 5.09 (s, 1H), 4.49 (d, J = 2.1 Hz, 1H), 4.36–4.30 (m, 2H), 4.25 (d, J = 2.4 Hz, 2H), 4.21 (dd, J = 5.0, 2.4 Hz, 2H), 2.49 (m, J = 3.5 Hz, 2H), 2.17 (m, 4H), 1.36 (s, 3H), 1.08 (s, 9H) ppm;
¹³C NMR (101 MHz, CDCl₃) δ 169.5, 168.4, 164.3, 138.7, 135.9, 135.5, 134.8, 132.8, 129.9, 128.8, 127.8, 127.7, 79.1, 78.9, 75.2, 74.9, 74.7, 72.8, 69.8, 68.2, 67.6, 64.0, 57.9, 57.7, 30.0, 29.7, 20.8, 19.2 ppm;
HRMS(ESI) [M + Na]^+ calculated for C₄₀H₄₄O₉Si: 719.2755, found 719.2653;
TLC: Rf = 0.3 (Pentane/Ethyl acetate = 2/1).

To a solution of S12-4 (8.0 mg, 11 µmol) in MeOH (1.0 mL) at 0 °C, was added dropwise a solution of K₂CO₃ (0.6 µL, 1M in H₂O). The reaction was stirred for 20 minutes at 0 °C...
and quenched with a cold mixture of CH$_2$Cl$_2$/H$_2$O (1 mL/1mL). The solution was then extracted with CH$_2$Cl$_2$ (2.0 mL) and the combined organic layers were washed with brine (1.0 mL) dried over MgSO$_4$, concentrated and purified by PTLC (Pentane/Ethyl acetate = 1/1) to give propargyl alcohol S12-5 as a pale-yellow oil (4.1 mg, yield 54%).

Data of S12-5: pale-yellow oil; 
[α]$^D$ -51 (c 0.2, CHCl$_3$);

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.66 (dd, J = 6.6, 1.3 Hz, 4H), 7.48–7.39 (m, 6H), 6.43 (d, J = 2.5 Hz, 2H), 6.33 (s, 1H), 5.92 (d, J = 1.1 Hz, 1H), 5.84 (d, J = 2.1 Hz, 1H), 5.77 (s, 1H), 5.02 (d, J = 2.1 Hz, 1H), 4.42 (s, 1H), 4.28 (s, 1H), 4.24 (s, 1H), 4.22–4.20 (m, 2H), 4.19 (d, J = 1.8 Hz, 1H), 4.17 (d, J = 2.3 Hz, 1H), 4.14 (d, J = 7.1 Hz, 1H), 2.49 (t, J = 2.3 Hz, 1H), 2.40 (d, J = 13.1 Hz, 1H), 2.15 (dd, J = 14.5, 10.5 Hz, 1H), 1.43 (s, 3H), 1.08 (s, 9H) ppm;

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 171.1, 170.9, 169.4, 165.0, 137.9, 135.8, 134.7, 132.8, 129.9, 129.3, 127.8, 124.4, 123.1, 79.8, 78.9, 75.7, 75.2, 69.8, 68.0, 64.3, 60.4, 57.77, 53.4, 46.4, 31.9, 29.7, 26.8, 22.7, 21.0, 19.2, 14.2, 14.1 ppm;

HRMS(ESI) [M + Na]$^+$ calculated for C$_{38}$H$_{42}$O$_8$Si: 677.2649, found 677.2546;

TLC: Rf = 0.3 (Pentane/Ethyl acetate = 1/1).

To a stirred solution of S12-5 (4.1 mg, 6.26 µmol) in CH$_2$Cl$_2$ (1.0 mL) was added MnO$_2$ (5.0 mg, 63 µmol) and the solution was stirred at room temperature for 2 h, till the TLC analysis showed disappearance of the starting material. The reaction was filtered and a trace of tBu$_3$PAuNTf$_2$ was added to the CH$_2$Cl$_2$ solution and the mixture stirred for 10 more minutes till the TLC analysis showed disappearance of the starting material. The resulted reaction was then concentrated in vacuo, and the residue obtained was purified on a PTLC (Pentane/Ethyl acetate = 3/1) to provide S12-6 as a white solid (2.7 mg, 66%).

Data of S12-7: white solid; 
[α]$^D$ -56 (c 0.1, CHCl$_3$);

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.66 (ddd, J = 8.0, 2.5, 1.4 Hz, 4H), 7.50–7.39 (m, 6H), 6.78 (d, J = 2.3 Hz, 1H), 6.49 (d, J = 3.2 Hz, 1H), 6.32 (d, J = 0.9 Hz, 1H), 5.96 (d, J = 1.3 Hz, 1H), 5.82 (d, J = 2.8 Hz, 2H), 5.27 (dd, J = 6.6, 2.6 Hz, 1H), 4.28 (dd, J = 4.0, 2.1 Hz, 2H), 4.24 (d, J = 1.0 Hz, 2H), 4.23–4.19 (m, 2H), 4.03 (d, J = 5.1 Hz, 1H), 2.50 (dt, J = 4.7, 4.1 Hz, 2H), 2.42–2.37 (m, 1H), 1.47 (s, 3H), 1.10 (s, 9H) ppm;

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 189.2, 168.3, 164.8, 143.2, 135.8, 135.5, 132.9, 132.4, 130.1, 128.7, 127.9, 124.7, 120.9, 95.3, 94.0, 79.0, 75.1, 70.9, 67.7, 64.1, 60.4, 57.8, 53.4, 50.1, 31.9, 29.7, 26.8, 25.2, 22.7, 21.0, 19.2, 14.1 ppm;

HRMS(ESI) [M + Na]$^+$ calculated for C$_{38}$H$_{44}$O$_8$Si: 675.2492, found 675.2390;

TLC: Rf= 0.35 (Pentane/Ethyl acetate = 2/1).
Data of S12-6: white solid; 
\[[\alpha]_{D}^{20} -11 \text{ (c 0.1, CHCl}_3\text{);}
\]
\(^1\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 7.68-7.65 \text{ (m, 4H), 7.44-7.39} \text{ (m, 6H), 6.26 (dd, } J = 3.7, 2.2 \text{ Hz, 2H), 6.15-6.12} \text{ (m, 1H), 5.91 (d, } J = 1.3 \text{ Hz, 1H), 5.68 (s, 1H), 5.50 (d, } J = 2.7 \text{ Hz, 1H), 5.28 (d, } J = 2.3 \text{ Hz, 1H), 4.56 (d, } J = 11.9 \text{ Hz, 1H), 4.46-4.33} \text{ (m, 2H), 4.18 (d, } J = 2.6 \text{ Hz, 2H), 4.14 (d, } J = 7.2 \text{ Hz, 2H), 3.75 (d, } J = 2.6 \text{ Hz, 1H), 2.54-2.46} \text{ (m, 2H), 2.36-2.31} \text{ (m, 1H), 1.52 (s, 3H), 1.09 (s, 9H) ppm;}
\]
\(^{13}\text{C NMR (126 MHz, CDCl}_3\text{) } \delta 204.5, 168.6, 135.7, 135.6, 135.5, 134.3, 133.9, 132.6, 130.1, 127.9, 127.8, 124.7, 106.4, 89.5, 81.5, 74.9, 73.5, 67.4, 64.1, 60.4, 57.8, 50.8, 43.9, 31.9, 29.7, 29.3, 26.8, 22.7, 20.6, 19.2, 14.1 \text{ ppm;}
\]
HRMS(ESI) \([M + H]^+\) calculated for C\(_{38}\)H\(_{40}\)O\(_8\)Si: 653.2492, found 653.2570; TLC: \(R_f = 0.3\) \(\text{(Pentane/Ethyl acetate = 2/1).}\)

To a solution of S12-6 \((2.3 \text{ mg, 3.5 } \mu\text{mol})\) in THF \((1.0 \text{ mL})\) at 0 °C, was added dropwise a solution of hydrogen fluoride pyridine \((\text{hydrogen fluoride } \sim 70\%, 10 \mu\text{L})\) in THF \((0.2 \text{ mL})\). The mixture was stirred 4 hours at 0 °C and quenched with saturated NaHCO\(_3\) \((0.5 \text{ mL})\). The mixture was then extracted with Et\(_2\)O \((2.0 \text{ mL } \times 2)\), and the combined organic layers were washed with brine \((1.0 \text{ mL})\), dried over MgSO\(_4\), and purified by PTLC \((\text{Pentane/Ethyl acetate } = 2/8)\) to give GOYA-2 \((0.21 \text{ mg, yield 14.5%})\) as a waxy solid.

Data of GOYA-2: waxy solid; 
\[[\alpha]_{D}^{20} -14 \text{ (c 0.1, CHCl}_3\text{);}
\]
\(^1\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 6.30 \text{ (s, 1H), 6.23 (s, 2H), 5.91 (s, 1H), 5.82 (s, 1H), 5.51 (s, 1H), 5.35 (s, 1H), 4.63-4.40} \text{ (m, 3H), 4.24-4.12} \text{ (m, 4H), 3.83 (d, } J = 2.4 \text{ Hz, 1H), 2.58-2.48} \text{ (m, 1H), 2.47 (t, } J = 2.3 \text{ Hz, 1H), 2.37 (dd, } J = 15.7, 8.7 \text{ Hz, 1H), 1.32 (s, 9H) ppm;}
\]
\(^{13}\text{C NMR (126 MHz, CDCl}_3\text{) } \delta 196.2, 184.1, 135.6, 132.8, 127.9, 124.9, 106.6, 89.6, 81.0, 75.0, 73.4, 63.1, 57.6, 50.8, 43.2, 31.8, 29.3, 22.7, 20.6, 13.9 \text{ ppm; Traces of water (integration } = 135.65\text{) and grease (integration } = 75.65\text{). Purity 19\%. DMSO stock solutions have been prepared by weighting residues after high vacuum evaporation. HRMS(ESI) \([M + H]^+\) calculated for C\(_{22}\)H\(_{32}\)O\(_8\): 414.1315, found 415.1394; TLC: \(R_f = 0.25\) \(\text{(CH}_2\text{Cl}_2/\text{Ethyl acetate } = 1/1).}\)
h) Experimental procedures for Figure 2

**General information**

**Biological materials.** All materials were purchased from Sigma Aldrich unless otherwise stated. DMEM/High glucose medium, F12-K media, phosphate buffered saline (PBS), MEM Non-Essential Amino Acids, Penicillin-Streptomycin (Pen/Strep) and Trypsin-EDTA were obtained from Life Technologies. Protein concentration was determined using a Q-Bit assay. HeLa cell line (Adenocarcinoma), PC3 cell line (Prostate; derived from metastatic site: bone), HT29 cell line (Colorectal adenocarcinoma), U2OS cell line (Metastatic: lung, other bones), SW620 cell line (Colorectal adenocarcinoma) obtained from ATCC. IPO5 (Sigma-Aldrich, HPA056548) antibody was purchased from Sigma Aldrich. Phospho-AKT (Ser 473) antibody was purchased from Cell signaling. Karyopherin β1, Karyopherin β2, IPO7, IPO8 and IPO12 antibodies were purchased from Santa Cruz biotechnology. UBA1, ACLY, RASAL2, β-actin, anti-rabbit and anti-rabbit Alexa Fluor 488 antibodies were purchased from ABCAM. Images were obtained by image stacking (Confocal microscope Zeiss LSM800). Fluorescence measured with ImageJ software.

**Cell culture and preparation of lysates.** HeLa, PC3, HT29, U2OS and SW620 cells were maintained in their corresponding media supplemented with 10% (v/v) fetal calf serum (FCS) and Penicillin-Streptomycin 1% (v/v). Cells were grown at 37 °C under 5% CO₂ atmosphere in a humidified incubator. Cells were allowed to grow to confluence and harvested by scraping, centrifuged at 4 °C and resuspended in PBS. Cells were then lysed by sonication in lysis buffer and protein concentration was determined using a Q-Bit assay.

**Pull-down experiments.** PC3 cells were seeded (350,000 cells/mL) on 10 cm dishes and grown to confluence for 2 days. The cells were harvested and lysates (3 mg/mL, 100 µL each) were prepared as described above. Lysates were treated with DMSO (1 µL) or goyazensolide 10 µM (1 mM, 1 µL) for 30 minutes and then incubated with GOYA-2 10 µM (1 mM, 1 µL) for 30 minutes. Click reaction was achieved by addition of desthiobiotinylated Cy3-N₃ (20 µM, 50X stock in DMSO, Figure S13 for synthesis), TCEP (1 mM, 50X fresh stock in H₂O), TBTA (100 µM, 16X stock in DMSO: tButanol = 1:4), copper (II) sulfate (1 mM, 100 µM stock in H₂O) and incubated for 1 hour at room temperature in the dark. Proteins were precipitated by adding 450 µL of cold MeOH, 117 µL of cold CHCl₃ and 350 µL of cold H₂O, vortexed and centrifuged for 5 minutes at 14000 g (4 °C). The protein layer was isolated, dried and solubilized in 100 µL of 0.2% SDS in PBS via sonication. Tubes were centrifuged at 4,700 g for 5 minutes, and soluble fractions were transferred to new tubes. Streptavidin agarose beads (25 µL) were added and incubated for 2 hours. Supernatant was discarded and the beads were washed three times with PBS (100 µL). Then 10 µL of 2% SDS and 5 µL of Laemmli buffer were added to the beads and heated 5 minutes at 95°C. Proteins were separated using a 10% SDS-PAGE gel. Gels were visualized at 625 nm using a fluorescence scanner.

**In-Gel tryptic digestion.** The bands cutted from the SDS-PAGE were cut in smaller pieces and washed twice with a mixture of 50% NH₄HCO₃ 50 mM in CH₃CN, twice with 200 µL CH₃CN, then twice again with 200 µL NH₄HCO₃ 100 mM and finally twice with 200 µL
CH$_3$CN. The gel fragments were incubated then for 30 minutes at 37 °C with 30 µL of DTT 10 mM in H$_2$O, followed by 30 minutes with 30 µL iodoacetamide 30 mM in H$_2$O. Gel pieces were washed again twice with CH$_3$CN, followed by NH$_4$HCO$_3$ 100 mM and finally twice with CH$_3$CN. Then, the in-gel digestion started with 30 µL of a mixture of Trypsin + Glu-C + Chymotrypsin (1.0 µg each in 500 µL of NH$_4$HCO$_3$ 50 mM) at 37 °C for 18 hours. 50 µL of NH$_4$HCO$_3$ 50 mM were added to the digested mixture and incubate for 10 minutes at room temperature. The supernatant was removed and place into a microtube and the remaining gel fragments were incubated for 10 minutes with 50 µL of extraction buffer 1 (20% CH$_3$CN, 80% H$_2$O, 1% formic acid). The supernatant was then collected and the fragments incubate for another 10 minutes with 50 µL of extraction buffer 2 (95% CH$_3$CN, 5% H$_2$O, 1% formic acid). The combined supernatants were lyophilized and submitted to MS/MS analysis.

**LC-MS/MS analysis.** Peptides were resuspended in water with 2% MeCN, 0.1% formic acid (FA) and analyzed using an EASY-nLC 1000 nano-UHPLC coupled to an Orbitrap Fusion mass spectrometer (Thermo Scientific). Chromatography was performed on a 50 cm EASY-spray column (75µm i.d.), LC solvents were 0.1% formic acid in H$_2$O (Buffer A) and 0.1% FA in MeCN (Buffer B), peptides were eluted into the mass spectrometer at a flow rate of 300 nL/min over a 30 minutes linear gradient (5-35% Buffer B) at 45 °C, data was acquired in a data-dependent mode, MS scans were acquired at 120000 resolution with an AGC-target of 20000 and 118 ms fill-time, and MS/MS-scans using HCD, CID and EThcD fragmentation were acquired in the Orbitrap on each selected precursor using an AGC-target of 20000 and a fill time of 200 ms.

**Mass spectrometry analysis.** MS data were analyzed using ProteomeDiscoverer 2.0 software (Thermo Scientific) and MSMS-spectra were grouped according by fragmentation technique and searched against the homo sapiens Uniprot database using the Sequest and MS-Amanda algorithms. Search against b- and y-ions was specified for HCD and CID spectra and against c- and z-ions for EThcD spectra. A search tolerance of 10 ppm was applied for the precursor and 0.05 Da for fragment ions. Oxidation of methionine and modification of cysteines by carbamidomethylation or by Goyazensolide or thiolated Goyazensolide were allowed as variable modifications.

**Safety Statement**

No unexpected or unusually high safety hazards were encountered.
To a solution of desthiobiotin S13-1 (100 mg, 0.46 mmol), N-Boc-ethylenediamine S13-2 (90 mg, 0.56 mmol), HATU (213 mg, 0.56 mmol) in DMF (4.0 mL) was added Et3N (190 μL, 1.38 mmol) at 0 °C. The mixture was allowed to warm to room temperature stirred 10 more minutes, and then diluted with ethyl acetate (20 mL) and HCl 0.1N (10 mL). The solutions was extracted with ethyl acetate (10 mL × 3) and the combined organic layers were washed with brine (20 mL) dried over MgSO4, concentrated and purified by silica-gel chromatography (CH2Cl2/ethyl acetate = 8/2) to give the amide as a pale-yellow oil. The crude product was dissolved in dichloromethane (3.0 mL) and cooled down to 0 °C. Trifluoro acetic acid (0.3 mL) was added to the solution and the reaction was carried out for 2 hours at 0 °C. The solvents were evaporated to give S13-3 as a yellow oil (137 mg, yield 81%).

To a solution of deprotected amine S13-3 (137 mg, 0.37 mmol), (S)-6-azido-2-(tert-butoxycarbonylamino) hexanoic acid S13-4 (121 mg, 0.44 mmol), HATU (167 mg, 0.44 mmol) in DMF (4.0 mL) was added Et3N (153 μL, 1.11 mmol) at 0 °C. The mixture was allowed to warm to room temperature, stirred for 10 more minutes, and then was diluted with ethyl acetate (20 mL) and HCl 0.1N (10 mL). The solution was extracted with ethyl acetate (10 mL × 3), and the combined organic layers were washed with brine (20 mL), dried over MgSO4, concentrated and purified by silica-gel chromatography (CH2Cl2/ethyl acetate = 7/3) to give the amide S13-5 as a pale-yellow oil (188 mg, yield 71%).

HRMS(ESI) [M + Na]+ calculated for C23H42O8N5: 511.3278, found 511.3366.

S13-5 (188 mg, 0.37 mmol) was dissolved in dichloromethane (3.0 mL) and cooled down to 0 °C. Trifluoro acetic acid (0.3 mL) was added to the solution and the reaction was carried out for 2 hours at 0 °C. The solvents were evaporated to give a yellow oil S13-6 (178 mg, yield 92%).
To a solution of **S13-6** (178 mg, 0.34 mmol), Cy3 **S13-7** (194 mg, 0.34 mmol), HATU (155 mg, 0.41 mmol) in DMF (5.0 mL) was added Et3N (141 µL, 1.02 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred 10 minutes. The mixture directly purified by reverse chromatography (H2O/acetonitrile 8/2) followed by lyophilization to give **Desthiobiotinylated Cy3-N3** as a pink powder (135 mg, yield 42%).

HRMS(ESI) [M + H]+ calculated for C47H67N10O4: 835.5341, found 835.5364.

**Figure S14.** Competition experiment with **GOYA-2** with different incubation time.

SW620 cell lysate was labeled with 10 µM of **GOYA-2** in different incubation time followed by CuAAC reaction with **Cy3-N3**. The labeling experiment shows optimal conditions with 30 min of incubation.

**Figure S15.** Competition experiments with **GOYA-2** with different cell lines.

The cell lysates were preincubate for 30 min with the indicated concentration of goyazensolide and then labelled with 10 µM of **GOYA-2** followed by CuAAC reaction with **Cy3-N3**. The labelling/competition experiment showed the target is not cell-line specific. **Cy3-N3** = Cyanine3-azide.
Table S17. Full protein list.

|   | Description                                                                 | Coverage | Unique Peptides | MW [kDa]   |
|---|-----------------------------------------------------------------------------|----------|-----------------|------------|
| 1 | Importin-5 OS=Homo sapiens GN=IPO5 PE=1 SV=4                               | 40.65634 | 63              | 123.55     |
| 2 | Pyruvate carboxylase, mitochondrial OS=Homo sapiens GN=PC PE=1 SV=2         | 32.85229 | 52              | 129.55     |
| 3 | Heterogeneous nuclear ribonucleoprotein U OS=Homo sapiens GN=HNRNUPE=1 SV=6 | 28.84848 | 33              | 90.528     |
| 4 | Acetyl-CoA carboxylase 1 OS=Homo sapiens GN=ACACA PE=1 SV=2                | 10.99744 | 27              | 265.39     |
| 5 | Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6           | 36.3354  | 26              | 65.999     |
| 6 | Ubiquitin-like modifier-activating enzyme 1 OS=Homo sapiens GN=UBA1 PE=1 SV=3 | 17.76938 | 19              | 117.77     |
| 7 | Alanine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=AARS PE=1 SV=2         | 17.56198 | 19              | 106.74     |
| 8 | ATP-citrate synthase OS=Homo sapiens GN=ACLY PE=1 SV=3                     | 13.44233 | 18              | 120.76     |
| 9 | Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6          | 28.42466 | 16              | 58.792     |
| 10| Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3           | 28.73194 | 15              | 62.027     |
| 11| Importin-7 OS=Homo sapiens GN=IPO7 PE=1 SV=1                               | 11.75337 | 11              | 119.44     |
| 12| iRT Kit Fusion                                                             | 89.55224 | 10              | 14.157     |
| 13| Ran-binding protein 6 OS=Homo sapiens GN=RANBP6 PE=1 SV=2                  | 6.244344 | 10              | 124.63     |
| 14| Matrin-3 OS=Homo sapiens GN=MATR3 PE=1 SV=2                                | 10.27155 | 9               | 94.565     |
| 15| Heterogeneous nuclear ribonucleoprotein U-like protein 2 OS=Homo sapiens GN=HNRNPU2 PE=1 SV=1 | 9.638554 | 9               | 85.052     |
| 16| Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2 | 19.40532 | 8               | 65.393     |
| 17| Heat shock protein 105 kDa OS=Homo sapiens GN=HSPH1 PE=1 SV=1              | 9.440559 | 8               | 96.804     |
| 18| Keratin, type II cytoskeletal 5 OS=Homo sapiens GN=KRT5 PE=1 SV=3          | 18.30508 | 8               | 62.34      |
| 19| Transcription intermediary factor 1-beta OS=Homo sapiens GN=TRIM28 PE=1 SV=5 | 8.263473 | 8               | 88.493     |
| 20| Fatty acid synthase OS=Homo sapiens GN=FASN PE=1 SV=3                      | 3.345281 | 8               | 273.25     |
| 21| Heat shock 70 kDa protein 4 OS=Homo sapiens GN=HSPA4 PE=1 SV=4              | 8.452381 | 8               | 94.271     |
| 22| Trifunctional purine biosynthetic protein adenosine-3 OS=Homo sapiens GN=GART PE=1 SV=1 | 7.425743 | 8               | 107.7      |
| 23| Putative elongation factor 1-alpha-like 3 OS=Homo sapiens GN=EEF1A1P5 PE=5 SV=1 | 17.74892 | 8               | 50.153     |
| 24| Elongation factor 1-alpha 1 OS=Homo sapiens GN=EEF1A1 PE=1 SV=1            | 17.74892 | 8               | 50.109     |
| 25| Acetyl-CoA carboxylase 2 OS=Homo sapiens GN=ACACB PE=1 SV=3                | 3.091945 | 7               | 276.37     |
| 26| Protein transport protein Sec24C OS=Homo sapiens GN=SEC24C PE=1 SV=3       | 5.758684 | 6               | 118.25     |
| 27| Eukaryotic translation initiation factor 3 subunit C-like protein OS=Homo sapiens GN=ELF3CL PE=3 SV=1 | 5.36105 | 6               | 105.41     |
| 28| Eukaryotic translation initiation factor 3 subunit C OS=Homo sapiens GN=ELF3C PE=1 SV=1 | 5.366922 | 6               | 105.28     |
|   | Gene Name                                                                 | Species   | protein Name | protein Start | protein End |   |
|---|---------------------------------------------------------------------------|-----------|--------------|---------------|-------------|---|
|29 | Keratin, type II cytoskeletal 6B OS=Homo sapiens GN=KRT6B PE=1 SV=5       |           |              | 13.65248      | 5           | 60.03 |
|30 | Keratin, type II cytoskeletal 6C OS=Homo sapiens GN=KRT6C PE=1 SV=3       |           |              | 13.47518      | 5           | 59.988 |
|31 | Keratin, type II cytoskeletal 6A OS=Homo sapiens GN=KRT6A PE=1 SV=3       |           |              | 13.47518      | 5           | 60.008 |
|32 | Unconventional myosin-Ib OS=Homo sapiens GN=MYO1B PE=1 SV=3              |           |              | 3.961268      | 5           | 131.9 |
|33 | Elongation factor 1-alpha 2 OS=Homo sapiens GN=EEF1A2 PE=1 SV=1           |           |              | 9.50324       | 5           | 50.438 |
|34 | Chymotrypsinogen B2 OS=Homo sapiens GN=CTRBB2 PE=2 SV=2                  |           |              | 10.64639      | 4           | 27.905 |
|35 | Chymotrypsinogen B OS=Homo sapiens GN=CTRBB1 PE=2 SV=1                   |           |              | 10.64639      | 4           | 27.852 |
|36 | 116 kDa U5 small nuclear ribonucleoprotein component OS=Homo sapiens GN=EFTUD2 PE=1 SV=1 |           |              | 4.835391      | 4           | 109.37 |
|37 | Heat shock protein HSP 90-beta OS=Homo sapiens GN=HSP90AB1 PE=1 SV=4     |           |              | 5.662983      | 4           | 83.212 |
|38 | Staphylococcal nuclease domain-containing protein 1 OS=Homo sapiens GN=SND1 PE=1 SV=1 |           |              | 4.395604      | 4           | 101.93 |
|39 | Phosphorylase b kinase regulatory subunit beta OS=Homo sapiens GN=PHKB PE=1 SV=3 |           |              | 3.85178       | 4           | 124.81 |
|40 | Tubulin alpha-1C chain OS=Homo sapiens GN=TUBA1C PE=1 SV=1               |           |              | 9.35142       | 4           | 49.863 |
|41 | Tubulin alpha-1B chain OS=Homo sapiens GN=TUBA1B PE=1 SV=1               |           |              | 9.312639      | 4           | 50.12  |
|42 | Tubulin alpha-1A chain OS=Homo sapiens GN=TUBA1A PE=1 SV=1               |           |              | 9.312639      | 4           | 50.104 |
|43 | Keratin, type I cytoskeletal 14 OS=Homo sapiens GN=KRT14 PE=1 SV=4        |           |              | 15.55932      | 3           | 51.529 |
|44 | Keratin, type I cytoskeletal 2 oral OS=Homo sapiens GN=KRT76 PE=1 SV=2    |           |              | 6.269592      | 3           | 65.8   |
|45 | Heat shock protein HSP 90-alpha A2 OS=Homo sapiens GN=HSP90AA2P PE=1 SV=2|           |              | 8.746356      | 3           | 39.34  |
|46 | Heat shock protein HSP 90-alpha OS=Homo sapiens GN=HSP90AA1 PE=1 SV=5    |           |              | 4.098361      | 3           | 84.607 |
|47 | Ubiquitin-like modifier-activating enzyme 6 OS=Homo sapiens GN=UBA6 PE=1 SV=1|           |              | 2.471483      | 3           | 117.9  |
|48 | Trypsin-3 OS=Homo sapiens GN=PRSS3 PE=1 SV=2                             |           |              | 8.552632      | 3           | 32.508 |
|49 | Tubulin alpha-3E chain OS=Homo sapiens GN=TUBA3E PE=1 SV=2               |           |              | 5.777778      | 3           | 49.827 |
|50 | Tubulin alpha-3C/D chain OS=Homo sapiens GN=TUBA3C PE=1 SV=3             |           |              | 5.777778      | 3           | 49.928 |
|51 | Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1                  |           |              | 8.266667      | 3           | 41.766 |
|52 | Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1                   |           |              | 8.266667      | 3           | 41.71  |
|53 | Asparagine synthetase [glutamine-hydrolyzing] OS=Homo sapiens GN=ASNS PE=1 SV=4 |           |              | 5.525847      | 3           | 64.329 |
|54 | Drebrin OS=Homo sapiens GN=DBN1 PE=1 SV=4                                |           |              | 5.701079      | 3           | 71.385 |
|55 | Filamin-A OS=Homo sapiens GN=FLNA PE=1 SV=4                             |           |              | 1.511145      | 3           | 280.56 |
Figure S16. Pyruvate carboxylase as non-competed target.

Treatment of PC3 cell lysate with DMSO or 10 µM goyazensolide for 30 min followed by treatment with **GOYA-2** (10 µM, 30 min). CuAAC reaction with the biotinylated fluorophore and streptavidin enrichment, SDS-PAGE followed by silver staining, gave a band that was not eliminated upon competition with 10 µM goyazensolide. MS analysis from tryptic in-gel digests of these bands yielded Pyruvate Carboxylase (red rectangle).

**Full gel of Figure 2d.** Immunoblot of IPO5, ACLY and UBA1 (Full gels and western blots).
Western blots of α-IPO5, α-UBA1 and α-ACLY. SDS-PAGE/Immunoblot of goyazensolide upon treatment of SW620 lysate with DMSO or 10 µM goyazensolide for 30 min followed by treatment with GOYA-2 (10 µM, 30 min). CuAAC reaction with the desthiobiotinylated fluorophore, streptavidin enrichment and SDS-PAGE.

**Figure S17.** Goyazensolide is a selective binder for IPO5 compared to other importins.

Western blots of α-IPO5, α-KPNB1, α-Karyopherin β1, α-Karyopherin β2, α-IPO7, α-IPO8, α-IPL12. SDS-PAGE/Immunoblot of goyazensolide upon treatment of SW620 lysate with DMSO or 10 µM goyazensolide for 30 min followed by treatment with GOYA-2 (10 µM, 30 min). CuAAC reaction with the desthiobiotinylated fluorophore, streptavidin enrichment and SDS-PAGE.
i) Experimental procedures for Figure 3

**Figure S18.** Competition experiment with 50 µM of 1-17 and 32.

Goyazensolide and atripliciolide selectively bind IPO5 versus other members of the same family of heliangolides. Competition experiment. A SW620 Lysate was incubated for 30 minutes with DMSO or one of the natural products (50 µM) for 30 min, and then labeled with 10 µM of GOYA-2 followed by CuAAC reaction with Cy3-N3. The labelling/competition experiment shows selective binding of goyazensolide (1) and atripliciolide (2) to IPO5 protein.

**Quantification (Image) software**

**Figure S19.** Competition experiment with 10 µM of analogs 1-17 and 32.

PC3 cell lysate were preincubate for 30 min with 10 µM of DMSO or analogs and then labeled with 10 µM of GOYA-2 followed by CuAAC reaction with Cy3-N3. Proteins were separated using a 10% SDS-PAGE gel. Gels were visualized at 625 nm using a fluorescence scanner and then stained with Coomassie brilliant blue.
Quantification

The binding efficiency was calculated by density of the fluorescent band. We used Coomassie as reference.

1) Grey intensity determination for fluorescence

![Image 1](image1.png)

2) Grey intensity determination for Coomassie

![Image 2](image2.png)
3) Calculation

**Table S18.** Quantification for competition.

| Analogs | Gel1 Fluorescence density | Gel1 Coomassie density (dye) | F/C | Fraction |
|---------|---------------------------|------------------------------|-----|---------|
| 1       | 9938.844                  | 5119.347                     | 1.941428 | 1       |
| 2       | 3166.782                  | 5275.811                     | 0.600246 | 0.309177 |
| 3       | 2863.225                  | 5417.861                     | 0.528479 | 0.272211 |
| 4       | 5077.43                   | 5651.154                     | 1.505432 | 0.775425 |
| 5       | 7714.823                  | 5615.276                     | 1.373899 | 0.707675 |
| 6       | 6462.045                  | 5792.276                     | 1.115631 | 0.574645 |
| 7       | 9108.43                   | 5645.276                     | 0.600246 | 0.309177 |
| 8       | 10058.309                 | 5812.811                     | 1.730369 | 0.891287 |
| 9       | 9769.966                  | 5093.296                     | 1.918201 | 0.988036 |
| 10      | 11011.693                 | 5687.468                     | 1.936133 | 0.997272 |

| Analogs | Gel2 Fluorescence density | Gel2 Coomassie density (dye) | F/C | Fraction |
|---------|---------------------------|------------------------------|-----|---------|
| 11      | 11349.67                  | 4811.569                     | 2.35883 | 1       |
| 12      | 3077.953                  | 4637.569                     | 0.6637 | 0.281368 |
| 13      | 11662.79                  | 4956.861                     | 2.352859 | 0.997469 |
| 14      | 10525.38                  | 4756.154                     | 2.213002 | 0.938178 |
| 15      | 10426.62                  | 4422.326                     | 2.357724 | 0.999531 |
| 16      | 10538.92                  | 4654.569                     | 2.264209 | 0.959886 |
| 17      | 8101.48                   | 4933.326                     | 1.642194 | 0.69619 |
| 18      | 10379.97                  | 4987.983                     | 2.080995 | 0.882215 |
| 19      | 9482.602                  | 4648.619                     | 2.039875 | 0.864783 |
| 20      | 11447.21                  | 4881.447                     | 2.345044 | 0.994156 |

Binding efficiency representation. We observed a difference of binding efficiency by comparison of compounds 1-6 versus 7-13. The C8 stereochemistry plays an important role in the binding efficiency.
**Pulldown experiment with viruses NLS.** 10µL of 100µM solutions of the corresponding NLS (0.2% SDS in PBS) were added to 30 µL of magnetic streptavidin beads and the suspension was shaken for 1 hour. The supernatant was discarded and the beads were washed 5× with a solution of 0.2% SDS in PBS. The pre-treated lysates (30 µL of treated lysate (3 mg/mL) with DMSO or goyazensolide 10 µM for 30 min) were added to the beads and shaken 3 hours. The supernatants were discarded and the beads were washed 2× times (20 µL) with 0.2% SDS in PBS. 15 µL of Laemli buffer were added to the beads and the mixtures were shaken and heated at 95°C for 3 minutes followed by SDS-PAGE and western blot. Incubation with IPO5 antibody (1 : 1000) followed by rabbit secondary antibody (1 : 10000). Chemoluminescence was used for detection.

**Full gel of Figure 3b.** Immunoblot of competitive interaction between NLS and IPO5. Magnetic streptavidin beads were saturated with corresponding NLS and then incubated for 2 hours with HT29 lysate treated with DMSO or goyazensolide (10 µM, 30 min).

![Image of gel](image)

**Preparation of NLS-1 and NLS-2**

NLS-1 and NLS-2 were synthesized using solid-phase synthesis. General procedure described in PLoS One *2020, 15, e0238089.*
Figure S20. Chemical structures of NLS-1 and NLS-2.
Data of **NLS-1:**

$(C_{110}H_{194}N_{56}O_{26}S), [M+H]^+ \text{ isotopic peaks with relative distribution: } 2748.53 (100.0\%), 2747.53 (84.1\%), 2749.54 (35.9\%)$

![Data of NLS-1](image)

Data of **NLS-2:**

$(C_{167}H_{299}N_{65}O_{42}S_3), [M+H]^+ \text{ isotopic peaks with relative distribution: } 3984.24 (100.0\%), 3985.25 (66.1\%), 3983.24 (55.4\%), 3986.25 (46.9\%), 3985.24 (24.0\%)$

![Data of NLS-2](image)
j) Experimental procedures for Figure 4

**Microscopy.** Cells (50000/well) were seeded on coverslips in a 12 well plate. After 24 hours, cells were treated with goyazensolide (1) or DMSO for 3 hours. Cells were fixed with PFA 4% for 25 minutes at room temperature. After a wash 3× with PBS, cells were blocked using 5% BSA + 0.1% saponin in PBS for 2 hours. Then they were incubate with anti IPO5 antibody (1 : 100) in 1% BSA in PBS (30 µL/well) for 3 hours at room temperature.

For the incubation, the coverslips were taken out of the plate, and place on a drop of antibody solution on parafilm in a humidity chamber, then they were washed 3× with PBS, incubate with anti-rabbit AlexaFluor488 (1 : 400), washed 3× with PBS, incubate with Hoescht diluted 2000× in PBS for 10min, washed 3× with PBS, then water and finally the edges were dried. The coverslips were then mounted on a clean slide treated with 5 µL ProlongDiamond per coverslip for 24 hours at room temperature and finally sealed with nail polish.

**Ratio (cytosol/nucleus) caculation of RASAL2.**

**Figure S21. Confocal microscopy images of SW620 cells after treatment with DMSO or goyazensolide.** Ratio of RASAL2 levels in the cytosol and nucleus was calculated applying a threshold mask to quantify fluorescence intensity in the cytosol and in the nucleus.

**Calculation of fluorescence intensity in the cytosol/nucleus.**

Threshold masks were generated in ImageJ software to calculate the integrated density of the signal in the green channel (Alexa488, RASAL2) and blue channel (Hoecht, nuclei).

Step 1 : Cell surface and green density determination.
Step 2: Determination of the surface and green density within the nucleus

Step 3: Determination of the surface and green density within the cytosol by difference

Step 4: Ratio calculation to all pictures
### Table S19. Ratio calculation.

|                | Area  | Integrated density | Int/Area | Ratio     |
|----------------|-------|--------------------|----------|-----------|
| **DMSO No Treatment** |       |                    |          |           |
| Whole cells A | 999.836 | 79215.392          | 79.22839 |           |
| Nucleus       | 524.499 | 35443.651          | 67.5762  |           |
| Cytosol       | 475.337 | 43771.741          | 92.0857  | 1.362694  |
| Whole cells B | 1326.899 | 122651.425         | 92.43464 |           |
| Nucleus       | 726.149 | 64428.407          | 88.72615 |           |
| Cytosol       | 600.75  | 58223.018          | 96.9172  | 1.092318  |
| Whole cells C | 1143.299 | 47116.191          | 41.21073 |           |
| Nucleus       | 559.298 | 20005.295          | 35.76858 |           |
| Cytosol       | 584.001 | 27110.896          | 46.42269 | 1.297862  |
| Whole cells D | 2663.854 | 264164.23          | 99.16618 |           |
| Nucleus       | 1405.78 | 131809.013         | 93.76219 |           |
| Cytosol       | 1258.074 | 132355.217         | 105.2046 | 1.122037  |
| **Average Ratio DMSO** |       |                    | 1.218728 |           |
| **Goyazensolide** |       |                    |          |           |
| Whole cells 1A | 1036.597 | 70567.839          | 68.07645 |           |
| Nucleus       | 383.935 | 17332.133          | 45.1434  |           |
| Cytosol       | 652.662 | 53235.706          | 81.56704 | 1.806843  |
| Whole cells 1B | 2079.43 | 142805.488         | 68.6753  |           |
| Nucleus       | 1030.202 | 52726.816          | 51.18105 |           |
| Cytosol       | 1049.228 | 90078.672          | 85.85233 | 1.677424  |
| Whole cells 25A | 1452.821 | 70476.786          | 48.5103  |           |
| Nucleus       | 618.297 | 18677.594          | 30.20813 |           |
| Cytosol       | 834.524 | 51799.192          | 62.07034 | 2.054756  |
| Whole cells 25B | 890.415 | 42677.438          | 47.92983 |           |
| Nucleus       | 405.471 | 12686.904          | 31.2893  |           |
| Cytosol       | 484.944 | 29990.534          | 61.84329 | 1.9765    |
| **Average Ratio 1 µM** | 1.742134 |                    | |           |
| **Average Ratio 2.5 µM** | 2.015628 |                    | |           |
| **Ratio increasing (%)** | 65.38786 |                    | |           |
Table S20. Raw data

| RAW DATA | ImageJ Software | 1 : Whole cells | 2 : Nucleus |
|----------|-----------------|----------------|------------|
|          |                 | Area           | Mean       | Min       | Max       | IntDen    | RawIntDen |
| PICTURE A| Area            | 999.836        | 79.228     | 11        | 255       | 79215.392 | 15905174  |
| 1        | Area            | 524.499        | 67.576     | 0         | 255       | 35443.651 | 7116514   |
| PICTURE B| Area            | 1326.899       | 92.435     | 19        | 255       | 122651.425| 24626430  |
| 2        | Area            | 726.149        | 88.726     | 0         | 255       | 64428.407 | 12936186  |
| PICTURE C| Area            | 1143.299       | 41.211     | 5         | 255       | 47116.191 | 9460172   |
| 2        | Area            | 559.298        | 35.769     | 0         | 225       | 20005.295 | 4016741   |
| PICTURE D| Area            | 2663.854       | 99.166     | 6         | 255       | 264164.23 | 53039921  |
| 2        | Area            | 1405.78        | 93.762     | 0         | 255       | 131809.013| 26465126  |
| PICTURE 1A| Area          | 1036.597       | 68.076     | 12        | 255       | 70567.839 | 14168885  |
| 2        | Area          | 383.935        | 45.143     | 0         | 255       | 17332.133 | 3480013   |
| PICTURE 1B| Area          | 2079.43        | 68.675     | 6         | 255       | 142805.488| 28673041  |
| 2        | Area          | 1030.202       | 51.181     | 0         | 255       | 52726.816 | 10586965  |
| PICTURE 25A| Area       | 1452.821       | 48.51      | 5         | 255       | 70476.786 | 14150603  |
| 2        | Area       | 618.297        | 30.208     | 0         | 227       | 18677.594 | 3750160   |
| PICTURE 25B| Area       | 890.415        | 47.93      | 6         | 255       | 42677.438 | 8568942   |
| 2        | Area       | 405.471        | 31.289     | 1         | 255       | 12686.904 | 2547326   |

Figure S22. Plot profile determination (Image J software).
**Figure S23.** DMSO treatment.

**Figure S24.** Goyazensolide 1 µM treatment.
**Figure S25.** Goyazensolide 2.5 µM treatment.

![Figure showing RASAL2 and Hoechst staining with intensity graph](image)

**Table S21.** Standard deviation (STDEV) and Standard error of mean (SEM)

| Ratio     | Goyazensolide 1 µM | Goyazensolide 2.5 µM | Standard deviation | Standard error of mean |
|-----------|--------------------|----------------------|--------------------|------------------------|
| DMSO      | 1.362694           | 2.054756             | 0.132056852        | 0.066028426            |
| 1.092318  | 1.677424           | 1.9765               | 0.091513053        | 0.0647095              |
| 1.297862  |                    | 0.055335348          | 2                  | 0.039128               |
| 1.122037  |                    |                      |                    |                        |

**pAKT assay.**

SW620 Cells were seeded (350,000 cells/mL) in a 6 well plate and left two days to attach and grow. Cells were incubated with DMSO or goyazensolide (5 µM) in a time dependant manner. Cells were lysed and scrapped in the presence of phosphatase inhibitors at 4 °C. Lysates were centrifuge at 14000g for 15 minutes at 4 °C. SDS-PAGE followed by western blot treated with respective antibodies (pAKT and actin).
**Full gel of Figure 4d.** Immunoblot of p-AKT (p-AKT Ser473 antibody) expression upon treatment of SW620 cells with DMSO or goyazensolide (5 µM, 4 h).

![Immunoblot of p-AKT (p-AKT Ser473 antibody) expression upon treatment of SW620 cells with DMSO or goyazensolide (5 µM, 4 h).](image1)

**Figure S26.** Time-/Dose-dependent manner of pAKT assay.

| Goyazensolide (5µM) | - | + | + | + | + | - | + | + | + | + | + |
|---------------------|---|---|---|---|---|---|---|---|---|---|---|---|
| Time (min)          | 30| 30| 60| 90| 150| 210| 30| 30| 60| 90| 150| 210|

![Immunoblot of p-AKT (p-AKT Ser473 antibody) expression upon treatment of SW620 cells with DMSO or goyazensolide (5 µM, 4 h).](image2)

Immunoblot of p-AKT (p-AKT Ser473 antibody) expression upon treatment of SW620 cells with DMSO or goyazensolide (5 µM, 4 h).
k) Chiral-HPLC spectra of 20a

|      |      |          |
|------|------|----------|
| Major|      | 12.797 min |
| Minor|      | 11.048 min |

14/02/2020 18:46:56

**Analysis Report**

*Sample Information*
- Sample Name: wi-uq-13-54-rac
- Sample ID: ...
- Data Filename: wi-uq-13-54-rac-AD-9901.lic
- Method Filename: Aqui Coll 99-1 1 mL 40 MIN.lic
- Batch Filename: new template.lic
- Vial #: 1-91
- Injection Volume: 10 uL
- Date Acquired: 14/02/2020 15:43:44
- Date Processed: 14/02/2020 16:23:46
- Sample Type: Unknown
- Acquired by: System Administrator
- Processed by: System Administrator

*Chromatogram*
- mAU
- PDA Multi 1 210nm,4nm

*Peak Table*

| Peak# | Ret Time | Area%   |
|-------|----------|---------|
| 1     | 11.048   | 50.182  |
| 2     | 12.797   | 49.818  |
| Total |          | 100.000 |

S91
Analysis Report

Sample Information:
- Sample Name: wil-ug-13-54-chiral
- Data Filename: wil-ug-13-54-chiral-AD-9901.lcd
- Method Filename: Aqu CoLi 99-1 1mL 40 MIN lcm
- Batch Filename: new template.lcb
- Vial #: 1-92
- Injection Volume: 10 µL
- Date Acquired: 14/02/2020 16:24:16
- Date Processed: 14/02/2020 17:04:17
- Sample Type: Unknown
- Acquired by: System Administrator
- Processed by: System Administrator

Chromatogram:

Peak Table:

| Peak | Ret. Time | Area% |
|------|-----------|-------|
| 1    | 11.010    | 4.429 |
| 2    | 12.768    | 95.571|
| Total|           | 100.000|
I) $^1$H and $^{13}$C NMR spectra
15-Deoxygoyazensolide
diastereoisomer 32

grease

2.0  11.5  11.0  10.5  10.0  9.5  9.0  8.5  8.0  7.5  7.0  6.5  6.0  5.5  5.0  4.5  4.0  3.5  3.0  2.5  2.0  1.5  1.0  0.5  0.0  -0.5

260  250  240  230  220  210  200  190  180  170  160  150  140  130  120  110  100  90  80  70  60  50  40  30  20  10  0

5120
| Parameter | Value |
|-----------|-------|
| Title     | mH5013-59-k.16.1.2Hy | 15-Deoxygoyazenolide (diastereomer 32) |
| Comment   | NMR 1H, 13C CDCl3 / cpe | |
| Temperature | 298.0 | |
| Acquisition Date | 2020-02-14T05:29:33 | |
| Spectrometer Frequency | 500.13, 125.78 | |

**Parameter**
- Title: mH5013-59-k.16.1.2Hy
- Comment: NMR 1H, 13C CDCl3 / cpe/ tripple 3.55Hz/ data/ winsolper nr n+ 4
- Temperature: 298.0
- Acquisition Date: 2020-02-14T05:29:33
- Spectrometer Frequency: 500.13, 125.78

**Diagram**
- 15-Deoxygoyazenolide (diastereomer 32)
Parameter Value
1 Title WLI-NG13-15-11-54
2 Comment MP_nmr CDCl3 / sps_tosphp3𝚝پپШ data/ wischenberg nr: 2
3 Temperature 298.1
4 Acquisition Date 2020-01-06T19:15:38
5 Spectrometer Frequency 125.77

Parameter Value
1 Title WLI-NG13-15-11-54
2 Comment MP_nmr CDCl3 / sps_tosphp3𝚝پپШ data/ wischenberg nr: 2
3 Temperature 298.1
4 Acquisition Date 2020-01-06T19:15:38
5 Spectrometer Frequency 125.77

Me Arlepicide (2, revised structure)
10 steps (L15)

Me Arlepicide (2, revised structure)
10 steps (L15)
| Parameter | Value |
|-----------|-------|
| Title     | mHup1:35.19 A4 |
| Comment   | PROTON (DMSO) / spt topolin:3.2 datal wrexcker lido 41 |
| Temperature | 298.0 |
| Acquisition Date | 2019-01-31/12:09:39 |
| Spectrometer Frequency | 400.13 |

**15-Decafoyazensolde (3)**

![Chemical Structure](image1)

**15-Decafoyazensolde (3)**

![Chemical Structure](image2)

S132
Attilipicicidice-lactate (5)

grease

Amiplicicidice-lactate (5)
Atrolicilide-tiglate (S)
Calaxin (B)

n-pentane, grease
| Parameter   | Value |
|-------------|-------|
| Title       | weh-ug13(15:1.1-2 | |
| Compound    | 1H-NMR (CDCl$_3$) 500 MHz, DMSO-d$_6$ 800 MHz, pmr | |
| Temperature | 296.0 K | |
| Acquisition Date | 2023-05-27T09:47:49 | |
| Spectrometer Frequency | (500.1, 1000.1) | |

**Diagram 1:**

8-epi-Arhiplicolide-2'(R+S)-MeBu
(R+S)-13

**Diagram 2:**

8-epi-Arhiplicolide-2'(R+S)-MeBu
(R+S)-13
| Parameter       | Value          |
|-----------------|----------------|
| Title           | (+)-22         |
| Comment         |                |
| Temperature     | 256.0          |
| Acquisition Date | 2023-02-11T19:43:05 |
| Spectrometer Frequency | 400.13, 400.13  |

**Diagram 1:***

**Diagram 2:**
m) X-Ray data of 2, 30 and 34

Table 1 Crystal data and structure refinement for WL2.

| Property                                      | Value                      |
|----------------------------------------------|----------------------------|
| Identification code                          | WL2                        |
| Empirical formula                           | C_{15}H_{16}O_{5}          |
| Formula weight                               | 276.28                     |
| Temperature/K                                | 149.99(10)                 |
| Crystal system                               | orthorhombic               |
| Space group                                  | P2_12_1_2_1                |
| a/Å                                         | 8.11197(3)                 |
| b/Å                                         | 9.30326(4)                 |
| c/Å                                         | 17.61440(7)                |
| α/°                                         | 90                         |
| β/°                                         | 90                         |
| γ/°                                         | 90                         |
| Volume/Å^3                                   | 1329.320(9)                |
| Z                                            | 4                          |
| ρ_cal/cm^3                                   | 1.380                      |
| μ/mm^2                                       | 0.866                      |
| F(000)                                       | 584.0                      |
| Crystal size/mm^3                           | 0.214 × 0.169 × 0.102      |
| Radiation                                    | Cu Kα (λ = 1.54184)        |
| 2θ range for data collection/°              | 10.044 to 147.598          |
| Index ranges                                 | -10 ≤ h ≤ 9, -11 ≤ k ≤ 11, -21 ≤ l ≤ 21 |
| Reflections collected                        | 61110                      |
| Independent reflections                     | 2690 [R_int = 0.0304, Rsigma = 0.0071] |
| Data/restraints/parameters                   | 2690/0/189                 |
| Goodness-of-fit on F^2                       | 1.043                      |
| Final R indexes [I>=2σ(I)]                  | R_1 = 0.0233, wR_2 = 0.0605 |
| Final R indexes [all data]                  | R_1 = 0.0235, wR_2 = 0.0606 |
| Largest diff. peak/hole / e Å^-3             | 0.18/-0.12                 |
| Flack parameter                              | -0.01(17)                  |

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for WL2. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

| Atom | x     | y     | z     | U(eq) |
|------|-------|-------|-------|-------|
| O1   | 5570.9(15) | 8694.9(15) | 7454.2(7) | 40.0(3) |
| O7   | 6273.6(13)  | 5594.8(12)  | 5471.0(7)  | 28.7(3) |
| O12  | 2119.0(17)   | 2290.0(12)   | 4442.5(7)   | 39.2(3) |
| O13  | 1707.8(15)    | 3217.2(12)   | 5595.5(6)   | 33.1(3) |
Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for WL2. The Anisotropic displacement factor exponent takes the form: -2π^2[h^2a^*2U_{11}+2hka^*b^*U_{12}+...].

| Atom | U_{11} | U_{22} | U_{33} | U_{12} | U_{13} | U_{23} |
|------|--------|--------|--------|--------|--------|--------|
| O1   | 29.3(6) | 54.5(8) | 36.2(6) | -14.2(6) | -6.2(5) | -2.3(6) |
| O7   | 18.9(5) | 25.9(5) | 41.5(6) | -8.5(5) | 0.7(5) | 2.9(4) |
| O12  | 48.4(7) | 27.2(6) | 42.1(7) | -5.8(5) | -3.4(6) | -11.7(5) |
| O13  | 39.2(7) | 25.2(5) | 34.9(6) | 2.1(4) | 0.8(5) | -11.1(5) |
| C1   | 32.4(8) | 22.6(7) | 46.5(9) | -4.0(7) | 4.3(7) | 1.3(6) |
| C5   | 20.1(7) | 21.6(7) | 26.2(7) | -1.7(6) | 1.0(6) | -1.8(5) |
| C6   | 18.1(6) | 20.7(7) | 24.0(7) | -1.0(5) | -1.3(5) | 1.2(5) |
| C8   | 18.0(7) | 21.2(6) | 24.0(6) | 2.4(5) | -1.2(5) | -0.3(5) |
| C9   | 21.3(7) | 21.9(7) | 27.4(7) | -2.0(6) | -4.9(5) | -1.1(5) |
| C10  | 33.1(9) | 36.1(9) | 30.0(8) | -6.9(7) | 1.7(7) | -9.0(7) |
| C11  | 28.4(8) | 24.1(7) | 31.4(7) | 1.6(6) | -5.2(6) | -2.4(6) |
| C14  | 24.6(7) | 25.8(7) | 26.7(7) | 2.4(6) | -2.3(6) | -5.5(6) |
| C15  | 22.2(7) | 38.9(9) | 30.4(7) | 6.7(7) | 0.5(6) | -7.7(7) |
| C16  | 20.1(7) | 40.9(9) | 27.2(7) | 8.5(7) | 2.8(6) | -0.6(6) |
| C17  | 23.7(8) | 54.7(11) | 43.4(9) | 1.6(9) | 8.2(7) | 0.1(8) |
| C18  | 22.0(7) | 31.6(7) | 24.7(6) | 0.7(6) | 4.3(6) | 4.5(6) |
| C20  | 28.7(8) | 49.2(10) | 23.1(7) | 2.3(7) | 1.3(6) | 1.8(7) |

Table 4 Bond Lengths for WL2.

| Atom Atom | Length/Å | Atom Atom | Length/Å |
|-----------|----------|-----------|----------|
| C2 C1    | 1.219(2) | C5 C6   | 1.533(18) |
| C7 C6   | 1.418(17) | C8 C9   | 1.575(18) |
| C11 C10 | 1.211(19) | C8 C9   | 1.504(2)  |
| C11 C14 | 1.337(2)  | C8 C14  | 1.562(19) |
| C14 C10 | 1.470(18) | C9 C10  | 1.321(2)  |
| C19 C11 | 1.459(17) | C9 C11  | 1.476(2)  |
| C18 C14 | 1.361(18) | C14 C15 | 1.510(2)  |
| C2 C3   | 1.532(2)  | C15 C16 | 1.331(2)  |
| C2 C20  | 1.443(2)  | C16 C17 | 1.508(2)  |
Table 5 Bond Angles for WL2.

| Atom  | Atom  | Angle/°  | Atom  | Atom  | Angle/°  |
|-------|-------|----------|-------|-------|----------|
| C11   | O13   | 111.86(11)| C10   | C9    | 130.40(14)|
| C18   | O19   | 107.48(11)| C10   | C9    | 120.80(14)|
| O1    | C2    | 123.40(15)| C11   | C9    | 108.78(12)|
| O1    | C2    | 130.63(16)| O12   | C11   | 122.12(14)|
| C20   | C2    | 105.89(12)| O12   | C11   | 127.86(15)|
| O19   | C3    | 103.38(11)| O13   | C11   | 110.02(13)|
| O19   | C4    | 109.76(12)| O13   | C14   | 106.22(11)|
| O19   | C5    | 106.84(11)| O13   | C14   | 105.75(12)|
| C4    | C3    | 113.19(13)| C15   | C14   | 118.61(13)|
| C4    | C3    | 112.13(13)| C16   | C15   | 126.94(14)|
| C5    | C3    | 110.98(12)| C15   | C16   | 124.01(15)|
| C3    | C5    | 116.30(12)| C15   | C16   | 118.68(14)|
| O7    | C6    | 103.98(12)| C18   | C16   | 117.26(15)|
| O7    | C6    | 113.85(11)| O19   | C18   | 112.86(13)|
| C5    | C6    | 112.63(11)| C20   | C18   | 114.33(14)|
| C9    | C8    | 116.03(11)| C20   | C18   | 132.65(15)|
| C9    | C8    | 102.42(11)| C18   | C20   | 107.49(14)|
| C14   | C8    | 113.99(11)|       |       |          |
Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for WL2.

| Atom | x     | y     | z     | U(eq) |
|------|-------|-------|-------|-------|
| H7   | 6290(30) | 4680(20) | 5494(12) | 45(6) |
| H4A  | 3497.02 | 10315.37 | 5613.29 | 51    |
| H4B  | 4948.34 | 10574.92 | 6213.23 | 51    |
| H4C  | 3065.47 | 10677.44 | 6478.95 | 51    |
| H5A  | 6105.62 | 8013.21  | 5873.34 | 27    |
| H5B  | 4659.92 | 8013.13  | 5258.35 | 27    |
| H6   | 4884.8  | 5807.29  | 6389    | 25    |
| H8   | 2462.37 | 6311.53  | 5356.35 | 25    |
| H10A | 4173.87 | 4076.8   | 3770.46 | 40    |
| H10B | 4847.59 | 5617.07  | 4108.93 | 40    |
| H14  | 2944.46 | 4162.26  | 4640.27 | 31    |
| H15  | -346.59 | 4494.77  | 6309.98 | 37    |
| H17A | -1002.74| 6813.04  | 7708.6  | 61    |
| H17B | -2005.57| 5987.95  | 7058.8  | 61    |
| H17C | -1492.36| 7634.32  | 6942.81 | 61    |
| H20  | 2941.55 | 6972.47  | 7943    | 40    |

Experimental

Single crystals of C_{15}H_{16}O_{5}[WL2] were [2]. A suitable crystal was selected and [2] on a XtaLAB Synergy, Dualflex, HyPix-Arc diffractometer. The crystal was kept at 149.99(10) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of [WL2]

Crystal Data for C_{15}H_{16}O_{5} (M = 276.28 g/mol): orthorhombic, space group P2_12_2_1 (no. 19), a = 8.11197(3) Å, b = 9.30326(4) Å, c = 17.61440(7) Å, V = 1329.320(9) Å^3, Z = 4, T = 149.99(10) K, μ(Cu Kα) = 0.866 mm^-1, Dcalc = 1.380 g/cm^3, 61110 reflections measured (10.044° ≤ 2θ ≤ 147.598°), 2690 unique (Rint = 0.0304, Rsigma = 0.0071) which were used in all calculations. The final R1 was 0.0233 (I > 2σ(I)) and wR2 was 0.0606 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:
1. Twinned data refinement
   Scales: 1.01(17)
   -0.01(17)
2. Fixed Uiso
   At 1.2 times of:
   All C(H) groups, All C(H,H) groups
   At 1.5 times of:
   All C(H,H,H) groups
3.a Ternary CH refined with riding coordinates:
   C6(H6), C8(H8), C14(H14)
3.b Secondary CH2 refined with riding coordinates:
   C5(H5A,H5B)
3.c Aromatic/amide H refined with riding coordinates:
   C15(H15), C20(H20)
3.d X=CH2 refined with riding coordinates:
   C10(H10A,H10B)
3.e Idealised Me refined as rotating group:
   C4(H4A,H4B,H4C), C17(H17A,H17B,H17C)

This report has been created with Olex2, compiled on Nov 21 2019 18:26:39 for OlexSys.
Table 1 Crystal data and structure refinement for exp_2516.
Identification code exp_2516
Empirical formula C_{31}H_{36}O_{5}Si
Formula weight 516.69
Temperature/K 180.01(10)
Crystal system orthorhombic
Space group P2_{1}2_{1}2_{1}
a/Å 9.52826(14)
b/Å 11.72660(18)
c/Å 25.7421(4)
α/° 90
β/° 90
γ/° 90
Volume/Å³ 2876.27(8)
Z 4
ρ_{calcd}/g/cm³ 1.193
μ/mm⁻¹ 1.015
F(000) 1104.0
Crystal size/mm 0.312 × 0.144 × 0.039
Radiation CuKα (λ = 1.54184)
2θ range for data collection/° 6.868 to 141.618
Index ranges -11 ≤ h ≤ 10, -10 ≤ k ≤ 14, -31 ≤ l ≤ 28
Reflections collected 22000
Independent reflections 5480 [R_{int} = 0.0418, R_{sigma} = 0.0306]
Data/restraints/parameters 5480/0/346
Goodness-of-fit on F² 1.069
Final R indexes [I>=2σ (I)] R_{1} = 0.0473, wR_{2} = 0.1186
Final R indexes [all data] R_{1} = 0.0524, wR_{2} = 0.1215
Largest diff. peak/hole / e Å⁻³ 0.69/-0.36
Flack parameter 0.02(4)

Table 2 Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for exp_2516. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

| Atom | x   | y   | z   | U(eq) |
|------|-----|-----|-----|-------|
| Si1  | 4040.7(9) | 4210.0(7) | 4263.6(3) | 28.0(2) |
| O5   | 850(3) | 10947.3(18) | 3223.4(9) | 40.7(6) |
| O6   | 2309(2) | 9819.9(18) | 2780.1(9) | 34.6(5) |
| O14  | 2806(2) | 4793.0(18) | 3898.9(8) | 28.8(5) |
| O16  | 994(3) | 4625.2(18) | 2652.2(8) | 30.5(5) |
| O19  | -287(2) | 7368.9(18) | 2618.4(9) | 29.8(5) |
| C1   | 1698(3) | 7967.2(2) | 3118.4(11) | 25.9(6) |
| C2   | 778(4) | 8894(2) | 3335.9(11) | 30.0(6) |
| C3   | -349(5) | 8840(3) | 3638.2(16) | 49.3(10) |
| C4   | 1260(3) | 9997(3) | 3122.9(13) | 32.3(7) |
Table 3 Anisotropic Displacement Parameters (Å\(^2\)×10\(^3\)) for exp_2516. The Anisotropic displacement factor exponent takes the form: 
\[ -2\pi^2 [h^2a^2U_{11} + 2hkabU_{12} + ...]. \]

| Atom | \(U_{11}\) | \(U_{22}\) | \(U_{33}\) | \(U_{12}\) | \(U_{13}\) | \(U_{23}\) |
|------|-----------|-----------|-----------|-----------|-----------|-----------|
| Si1  | 29.9(4)   | 23.6(4)   | 30.6(4)   | 1.0(3)    | -2.9(3)   | 0.0(3)    |
| O5   | 52.0(14)  | 18.0(10)  | 52.2(13)  | -4.9(9)   | -12.1(12) | 7.5(11)   |
| O6   | 32.8(11)  | 18.6(10)  | 52.3(13)  | 7.0(9)    | -3.7(10)  | -2.6(9)   |
| O14  | 32.2(11)  | 25.2(10)  | 28.8(10)  | 0.3(8)    | -3.1(8)   | 2.8(9)    |
| O16  | 38.4(11)  | 19.2(9)   | 33.8(10)  | -1.1(8)   | -6.3(9)   | -1.1(9)   |
| O19  | 23.3(10)  | 20.5(10)  | 45.7(13)  | -0.8(9)   | -9.2(9)   | 2.8(8)    |
| C1   | 25.5(14)  | 19.0(13)  | 33.1(14)  | 0.0(11)   | -1.3(11)  | -1.3(11)  |
| C2   | 35.6(16)  | 21.4(14)  | 32.9(14)  | -3.3(10)  | -0.5(13)  | 1.2(12)   |
| C3   | 61(2)     | 32.2(18)  | 55(2)     | -1.5(15)  | 22.5(19)  | 10.6(17)  |
| C4   | 35.6(17)  | 23.4(15)  | 37.9(15)  | -1.1(12)  | -9.7(12)  | 1.2(13)   |
| C7   | 26.6(14)  | 20.6(13)  | 35.8(14)  | 1.6(11)   | -1.4(12)  | -3.9(12)  |
| C8   | 28.3(14)  | 25.5(14)  | 38.4(15)  | 1.0(11)   | 2.9(13)   | -10.3(13) |
| C9   | 20.6(14)  | 33.0(16)  | 38.4(16)  | 0.7(13)   | 1.2(11)   | -2.4(13)  |
| C10  | 21.3(15)  | 43(2)     | 68(2)     | 3.7(17)   | 6.4(14)   | -0.7(14)  |
| C11  | 21.2(13)  | 26.2(14)  | 37.9(14)  | 1.4(12)   | -1.7(12)  | 5.5(12)   |
| C12  | 22(13)    | 24.8(15)  | 33.4(14)  | 0.5(11)   | -1.6(11)  | 5.8(12)   |
| C13  | 29.2(14)  | 18.2(13)  | 29.2(13)  | 0.6(10)   | -4.1(11)  | 6.0(12)   |
| C14  | 26.3(14)  | 19.7(13)  | 31.1(13)  | 0.4(10)   | -4.0(11)  | -2.4(12)  |
| C15  | 24.8(13)  | 20.3(14)  | 37.4(15)  | 1.8(11)   | 1.8(11)   | -0.5(11)  |
| C17  | 36.3(17)  | 20.9(14)  | 42.4(17)  | 3.5(12)   | -2.3(13)  | -4.7(13)  |
| C18  | 20.3(12)  | 15.8(12)  | 34.6(13)  | 1.0(10)   | -1.5(11)  | 3.0(11)   |
Table 4 Bond Lengths for exp_2516.

| Atom | Atom | Length/Å |
|------|------|----------|
| Si1  | O14  | 1.653(2) |
| Si1  | C20  | 1.874(3) |
| Si1  | C26  | 1.882(4) |
| Si1  | C32  | 1.899(3) |
| O5   | C4   | 1.209(4) |
| O6   | C4   | 1.350(4) |
| O6   | C7   | 1.464(3) |
| O14  | C13  | 1.432(3) |
| O16  | C14  | 1.428(3) |
| O19  | C18  | 1.440(3) |
| C1   | C2   | 1.505(4) |
| C1   | C7   | 1.546(4) |
| C1   | C18  | 1.535(4) |
| C2   | C3   | 1.327(5) |
| C2   | C4   | 1.478(4) |
| C7   | C8   | 1.504(4) |
| C8   | C9   | 1.332(5) |
| C9   | C10  | 1.514(4) |
| C9   | C11  | 1.441(4) |
| C11  | C12  | 1.205(4) |

Table 5 Bond Angles for exp_2516.

| Atom Atom Atom | Angle/° |
|----------------|--------|
| O14 Si1 C20    | 111.62(14) |
| O14 Si1 C26    | 110.37(13) |
| O14 Si1 C32    | 102.85(13) |
| C20 Si1 C26    | 108.90(17) |
| C20 Si1 C32    | 106.98(16) |
| C26 Si1 C32    | 116.02(17) |
| C4 O6 C7       | 111.3(2) |
| C13 O14 Si1    | 126.99(19) |
| C2 C1 C7       | 102.7(2) |
| C2 C1 C18      | 115.5(3) |
Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for exp_2516.

| Atom | x     | y     | z     | U(eq) |
|------|-------|-------|-------|-------|
| H16  | 820(50)| 3960(40)| 2618(17)| 46    |
| H19  | -470(50)| 6940(40)| 2407(18)| 45    |
| H1   | 2349.84| 7696.53| 3396.82| 31    |
| H3A  | -853.87| 9515.38| 3719.8 | 59    |
| H3B  | -649.54| 8126.97| 3773.05| 59    |
| H7   | 2184.75| 8385  | 2349.17| 33    |
| H8   | 4670.46| 9028.85| 2618.02| 37    |
| H10A | 6804.41| 7105.76| 3081.19| 66    |
| H10B | 6792.75| 8184.19| 2700.24| 66    |
| H10C | 6674.11| 6922.84| 2467.01| 66    |
| H13  | 3013.07| 3946.21| 3232.1 | 31    |
| H15A | 849.83 | 6287.31| 3642.44| 33    |
| H15B | -522.46| 5983.48| 3314.59| 33    |
| H17A | -724.92| 3939.66| 3368.98| 50    |
| H17B | 221.14 | 4176.68| 3871.17| 50    |
| H17C | 663.81 | 3203.18| 3467.47| 50    |
| H18  | 1552.91| 6565.36| 2629.67| 28    |
| H21  | 4672.63| 6629.79| 4071.67| 59    |
| H22  | 6561.62| 7854.18| 4259.09| 86    |
| H23  | 8603.75| 7133.74| 4631.92| 87    |
| H24  | 8771.12| 5210.54| 4829.72| 78    |
| H25  | 6938.86| 3985.89| 4625.83| 59    |
| H27  | 2976.78| 1829.49| 4182.69| 72    |
| H28  | 3815.08| 122.23 | 3843.38| 96    |
| H29  | 5977.06| 60.34  | 3415.32| 96    |
| H30  | 7273.79| 1729.2 | 3319.42| 87    |
| H31  | 6464.22| 3434.6 | 3671.19| 66    |
Experimental

Single crystals of C$_{31}$H$_{36}$O$_{5}$Si [exp_2516] were [30]. A suitable crystal was selected and [30] on a SuperNova, Dual, Cu at home/near, Atlas diffractometer. The crystal was kept at 180.01(10) K during data collection. Using Olex2 [1], the structure was solved with the olex2.solve [2] structure solution program using Charge Flipping and refined with the ShelXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). Acta Cryst. A71, 59-75.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of [exp_2516]

Crystal Data for C$_{31}$H$_{36}$O$_{5}$Si ($M$ = 516.69 g/mol): orthorhombic, space group P2$_1$2$_1$2$_1$ (no. 19), $a$ = 9.52826(14) Å, $b$ = 11.72660(18) Å, $c$ = 25.7421(4) Å, $V$ = 2876.27(8) Å$^3$, $Z$ = 4, $T$ = 180.01(10) K, $\mu$(CuKα) = 1.015 mm$^{-1}$, $D_{calc}$ = 1.193 g/cm$^3$, 22000 reflections measured (6.868° ≤ 2θ ≤ 141.618°), 5480 unique ($R_{int}$ = 0.0418, $R_{sigma}$ = 0.0306) which were used in all calculations. The final $R_1$ was 0.0473 (I > 2σ(I)) and $wR_2$ was 0.1215 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:
1. Twinned data refinement
   Scales: 0.98(4)
   0.02(4)
2. Fixed Uiso
   At 1.2 times of:
   All C(H) groups, All C(H,H) groups
   At 1.5 times of:
   All C(H,H,H) groups, All O(H) groups
3.a Ternary CH refined with riding coordinates:
   C1(H1), C7(H7), C13(H13), C18(H18)
3.b Secondary CH2 refined with riding coordinates:
   C15(H15A,H15B)
3.c Aromatic/amide H refined with riding coordinates:
   C8(H8), C21(H21), C22(H22), C23(H23), C24(H24), C25(H25), C27(H27), C28(H28),
   C29(H29), C30(H30), C31(H31)
3.d X=CH2 refined with riding coordinates:
   C3(H3A,H3B)
3.e Idealised Me refined as rotating group:
   C10(H10A,H10B,H10C), C17(H17A,H17B,H17C), C33(H33A,H33B,H33C), C34(H34A,H34B,
   H34C), C35(H35A,H35B,H35C)

This report has been created with Olex2, compiled on 2018.05.29 svn.r3508 for OlexSys.
Table 1 Crystal data and structure refinement for WL3c.

| Parameter                  | Value                                    |
|----------------------------|------------------------------------------|
| Identification code        | WL3c                                     |
| Empirical formula          | C35H42O6Si                               |
| Formula weight             | 586.77                                   |
| Temperature/K              | 150.00(10)                               |
| Crystal system             | orthorhombic                             |
| Space group                | P2_12_1                                  |
| a/Å                        | 9.10599(3)                               |
| b/Å                        | 15.40214(5)                              |
| c/Å                        | 23.08098(7)                              |
| α/°                        | 90                                       |
| β/°                        | 90                                       |
| γ/°                        | 90                                       |
| Volume/Å³                  | 3237.148(18)                             |
| Z                          | 4                                        |
| ρcalc/g/cm³                | 1.204                                    |
| μ/mm⁻¹                     | 0.985                                    |
| F(000)                     | 1256.0                                   |
| Crystal size/mm³           | 0.376 × 0.195 × 0.097                    |
| Radiation                  | Cu Kα (λ = 1.54184)                      |
| 2θ range for data collection/° | 6.9 to 148.85                           |
| Index ranges               | -11 ≤ h ≤ 10, -19 ≤ k ≤ 19, -28 ≤ l ≤ 28 |
| Reflections collected      | 144009                                   |
| Independent reflections    | 6598 [Rint = 0.0487, Rsigma = 0.0108]    |
| Data/restraints/parameters | 6598/0/390                               |
| Goodness-of-fit on F²      | 1.039                                    |
| Final R indexes [I>2σ(I)]  | R₁ = 0.0250, wR₂ = 0.0665                |
| Final R indexes [all data]| R₁ = 0.0252, wR₂ = 0.0666                |
| Largest diff. peak/hole / e Å⁻³ | 0.16/-0.23                             |
| Flack parameter            | 0.00(2)                                  |

Table 2 Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for WL3c. Ueq is defined as 1/3 of the trace of the orthogonalised Uij tensor.

| Atom | x      | y      | z      | U(eq)   |
|------|--------|--------|--------|---------|
| Si1  | 5657.2(4) | 4971.8(3) | 8198.2(2) | 22.72(9) |
| O8   | 12510.2(12) | 3724.5(8) | 6543.6(5) | 29.2(2)  |
| O10  | 13658.7(13) | 3370.7(9) | 5723.0(5) | 36.7(3)  |
| O15  | 10518.9(11) | 5071.3(7) | 6018.1(4) | 25.8(2)  |
| O17  | 9170.8(13)  | 5934.8(8) | 5436.8(5) | 35.4(3)  |
| O23  | 6620.0(12)  | 3719.5(7) | 6160.3(5) | 27.5(2)  |
| O25  | 6173.2(12)  | 4904.2(7) | 7512.8(4) | 26.7(2)  |
| C1   | 6264.9(17)  | 4155.7(9) | 7152.0(6) | 23.8(3)  |
| C2   | 7420.3(17)  | 3558.4(10) | 7350.6(6) | 25.8(3)  |
| C3   | 8492.8(17)  | 3132.7(10) | 7452.5(6) | 25.9(3)  |
Table 3 Anisotropic Displacement Parameters (Å\(^2\)×10\(^3\)) for WL3c. The Anisotropic displacement factor exponent takes the form: \(-2\pi^2[h^2a^*U_{11}+2hka^*b^*U_{12}+...]\).

| Atom | \(U_{11}\) | \(U_{22}\) | \(U_{33}\) | \(U_{23}\) | \(U_{13}\) | \(U_{12}\) |
|------|-------------|-------------|-------------|--------------|--------------|--------------|
| Si1  | 19.6(18)    | 24.0(18)    | 24.5(18)    | 1.06(15)     | 1.26(14)     | 0.39(16)     |
| O8   | 19.6(5)     | 39.2(6)     | 28.8(5)     | -0.6(5)      | -0.6(4)      | -1.4(5)      |
| O10  | 23.0(6)     | 47.7(7)     | 39.4(6)     | -3.9(5)      | 5.1(5)       | 1.1(5)       |
| O15  | 21.0(5)     | 29.3(6)     | 27.2(5)     | 4.3(4)       | 0.0(4)       | -2.4(5)      |
| O17  | 32.0(6)     | 38.4(6)     | 36.0(6)     | 7.9(5)       | -5.6(5)      | -0.2(5)      |
| O23  | 21.4(5)     | 29.4(6)     | 31.8(5)     | -8.4(4)      | -2.0(4)      | -0.4(4)      |
| O25  | 31.3(5)     | 23.1(5)     | 25.8(5)     | -0.4(4)      | 3.6(4)       | 0.6(4)       |
| C1   | 21.4(7)     | 22.6(6)     | 27.5(7)     | -0.6(6)      | 1.2(5)       | 0.1(6)       |
| C2   | 25.2(7)     | 24.4(7)     | 27.7(7)     | 0.7(5)       | 2.2(6)       | -2.0(6)      |
| C3   | 26.8(8)     | 25.4(7)     | 25.5(7)     | 1.9(6)       | 1.3(6)       | -2.2(6)      |
| C4   | 26.6(8)     | 27.4(7)     | 26.7(7)     | -0.9(6)      | -4.1(6)      | 2.3(6)       |
| C5   | 32.4(9)     | 32.6(8)     | 35.0(8)     | 7.1(7)       | -6.0(7)      | 0.6(7)       |
| C6   | 23.7(8)     | 32.2(8)     | 29.4(8)     | 0.7(6)       | -3.9(6)      | 6.6(6)       |
| C7   | 19.4(7)     | 31.9(7)     | 26.4(7)     | -1.0(6)      | 0.1(6)       | 0.7(6)       |
| C9   | 23.8(7)     | 30.3(8)     | 31.7(8)     | -0.4(6)      | -0.6(6)      | 1.5(6)       |
| C11  | 23.1(7)     | 27.1(7)     | 29.0(7)     | 0.2(6)       | 0.3(6)       | 0.8(6)       |
Table 4 Bond Lengths for WL3c.

| Atom | Atom | Length/Å | Atom | Atom | Length/Å |
|------|------|----------|------|------|----------|
| C12  | O25  | 1.6537(11)| C12 | C14 | 1.534(2) |
| C13  | C26  | 1.8904(16)| C14 | C21 | 1.5289(19) |
| C14  | C30  | 1.8755(16)| C16 | C18 | 1.515(2) |
| C16  | C36  | 1.8663(16)| C18 | C19 | 1.523(3) |
| O8   | C7   | 1.4662(18)| C18 | C20 | 1.529(3) |
| O8   | C9   | 1.3469(19)| C21 | C22 | 1.5547(19) |
| O10  | C9   | 1.212(2)  | C22 | C24 | 1.521(2) |
| O15  | C14  | 1.4643(17)| C26 | C27 | 1.541(2) |
| O15  | C16  | 1.3528(19)| C26 | C28 | 1.534(2) |
| O17  | C16  | 1.204(2)  | C26 | C29 | 1.537(2) |
| O23  | C22  | 1.4341(18)| C30 | C31 | 1.399(2) |
| O25  | C1   | 1.4246(17)| C30 | C35 | 1.398(2) |
| C1   | C2   | 1.471(2)  | C31 | C32 | 1.384(3) |
| C1   | C22  | 1.552(2)  | C32 | C33 | 1.380(3) |
| C2   | C3   | 1.200(2)  | C33 | C34 | 1.381(3) |
| C3   | C4   | 1.434(2)  | C34 | C35 | 1.387(3) |
| C4   | C5   | 1.504(2)  | C36 | C37 | 1.397(2) |
| C4   | C6   | 1.340(2)  | C36 | C41 | 1.402(2) |
| C6   | C7   | 1.502(2)  | C37 | C38 | 1.388(3) |
| C7   | C12  | 1.555(2)  | C38 | C39 | 1.383(3) |
| C9   | C11  | 1.484(2)  | C39 | C40 | 1.384(3) |
| C11  | C12  | 1.509(2)  | C40 | C41 | 1.385(3) |
| C11  | C13  | 1.321(2)  |      |     |           |
Table 5 Bond Angles for WL3c.

| Atom | Atom | Atom | Angle/° | Atom | Atom | Angle/° |
|------|------|------|---------|------|------|---------|
| O25  | Si1  | C26  | 103.78(7)| O17  | C16  | O15     | 123.42(14) |
| O25  | Si1  | C30  | 112.11(6)| O17  | C16  | C18     | 125.73(15) |
| O25  | Si1  | C36  | 108.16(7)| C16  | C18  | C19     | 111.10(15) |
| C30  | Si1  | C26  | 114.32(7)| C16  | C18  | C20     | 108.06(15) |
| C36  | Si1  | C26  | 108.60(7)| C19  | C18  | C20     | 111.90(15) |
| C9   | O8   | C7   | 110.99(12)| O23  | C22  | C1      | 107.39(12) |
| C16  | O15  | C14  | 117.06(11)| O23  | C22  | C21     | 108.67(11) |
| C1   | O25  | Si1  | 128.82(9)| O23  | C22  | C24     | 110.72(12) |
| O25  | C1   | C2   | 111.46(12)| C1   | C22  | C21     | 110.31(12) |
| O25  | C1   | C22  | 107.64(11)| C24  | C22  | C1      | 109.49(12) |
| C2   | C1   | C22  | 109.05(12)| C24  | C22  | C21     | 110.22(12) |
| C3   | C2   | C1   | 170.17(16)| C27  | C26  | Si1     | 111.54(11) |
| C2   | C3   | C4   | 173.33(16)| C28  | C26  | Si1     | 111.34(12) |
| C3   | C4   | C5   | 119.18(14)| C28  | C26  | C27     | 110.49(14) |
| C6   | C4   | C3   | 118.47(14)| C28  | C26  | C29     | 108.24(15) |
| C6   | C4   | C5   | 122.35(14)| C29  | C26  | Si1     | 108.00(11) |
| C4   | C6   | C7   | 125.42(14)| C29  | C26  | C27     | 107.05(15) |
| O8   | C7   | C6   | 106.93(12)| C31  | C30  | Si1     | 123.50(13) |
| O8   | C7   | C12  | 105.67(11)| C35  | C30  | Si1     | 119.38(13) |
| C6   | C7   | C12  | 115.88(13)| C35  | C30  | C31     | 117.10(16) |
| O8   | C9   | C11  | 109.52(13)| C32  | C31  | C30     | 121.26(18) |
| O10  | C9   | O8   | 121.29(15)| C33  | C32  | C31     | 120.60(18) |
| O10  | C9   | C11  | 129.19(15)| C32  | C33  | C34     | 119.35(18) |
| C9   | C11  | C12  | 107.73(13)| C33  | C34  | C35     | 120.18(19) |
| C13  | C11  | C9   | 122.40(15)| C34  | C35  | C30     | 121.51(17) |
| C13  | C11  | C12  | 129.86(15)| C37  | C36  | Si1     | 121.68(13) |
| C11  | C12  | C7   | 101.45(12)| C37  | C36  | C41     | 117.42(15) |
| C11  | C12  | C14  | 111.10(12)| C41  | C36  | Si1     | 120.37(12) |
| C14  | C12  | C7   | 113.78(12)| C38  | C37  | C36     | 121.02(18) |
| C14  | C12  | C12  | 104.81(11)| C39  | C38  | C37     | 120.51(18) |
| O15  | C14  | C21  | 108.01(11)| C38  | C39  | C40     | 119.51(18) |
| C21  | O14  | C12  | 116.22(12)| C39  | C40  | C41     | 120.00(18) |
| O15  | C16  | C18  | 110.81(13)| C40  | C41  | C36     | 121.52(16) |

Table 6 Torsion Angles for WL3c.

| A    | B    | C    | D    | Angle/° | A    | B    | C    | D    | Angle/° |
|------|------|------|------|---------|------|------|------|------|---------|
| Si1  | O25  | C1   | C2   | -66.87(16)| C9   | C11  | C12  | C14  | 103.15(14) |
| Si1  | O25  | C1   | C22  | 173.60(10)| C11  | C12  | C14  | O15  | -61.81(14) |
| Si1  | C30  | C31  | C32  | -177.44(13)| C11  | C12  | C14  | C21  | 179.07(12) |
| Si1  | C30  | C35  | C34  | 178.22(14)| C12  | C14  | C21  | C22  | -77.34(16) |
| Si1  | C36  | C37  | C38  | -170.22(18)| C13  | C11  | C12  | C7   | 161.06(18) |
| Si1  | C36  | C41  | C40  | 170.09(15)| C13  | C11  | C12  | C14  | -77.7(2)  |
| O8   | C7   | C12  | C11  | 21.17(15)| C14  | O15  | C16  | O17  | 3.6(2)   |
| O8   | C7   | C12  | C14  | -98.21(14)| C14  | O15  | C16  | C18  | -174.44(12) |
| O8   | C9   | C11  | C12  | 8.68(17)| C14  | C21  | C22  | O23  | 5.93(17) |
| O8   | C9   | C11  | C13  | -170.58(16)| C14  | C21  | C22  | C1   | 123.40(13) |
| O10  | C9   | C11  | C12  | -170.77(17)| C14  | C21  | C22  | C24  | -115.56(14) |
| O10  | C9   | C11  | C13  | 10.0(3)| C16  | O15  | C14  | C12  | 156.38(12) |

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| Atom  | x       | y       | z       | U(eq)  |
|-------|---------|---------|---------|--------|
| H23   | 5680(30)| 3606(14)| 6043(9) | 41     |
| H1    | 5298    | 3847.9  | 7150.01 | 29     |
| H5A   | 9299.83 | 1441.39 | 7782.5  | 50     |
| H5B   | 9575.3  | 2095.79 | 8309.98 | 50     |
| H5C   | 10939.24| 1709.76 | 7956.67 | 50     |
| H6    | 11896.82| 2609.36 | 7247.9  | 34     |
| H7    | 10815.03| 4228.66 | 7005.58 | 31     |
| H12   | 9186.88 | 3170.16 | 6343.12 | 29     |
| H13A  | 11465.25| 2699.95 | 5055.49 | 44     |
| H13B  | 9698.38 | 2783.69 | 5194.05 | 44     |
| H14   | 8780.38 | 4402.9  | 5699.41 | 29     |
| H18   | 12258.13| 6281.7  | 5981.34 | 38     |
| H19A  | 10874.71| 7201.83 | 5051.7  | 67     |
| H19B  | 12373   | 7505.3  | 5352.24 | 67     |
| H19C  | 10876.52| 7500.55 | 5715.79 | 67     |
| H20A  | 12890.31| 5199.28 | 5301.95 | 65     |
| H20B  | 13634.95| 6098.4  | 5116.34 | 65     |

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for WL3c.
Experimental

Single crystals of C_{35}H_{42}O_{6}Si [WL3c] were [34]. A suitable crystal was selected and [34] on a XtaLAB Synergy, Dualflex, HyPix-Arc diffractometer. The crystal was kept at 150.00(10) K during data collection. Using Olex2 [1], the structure was solved with the olex2.solve [2] structure solution program using Charge Flipping and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). Acta Cryst. A71, 59-75.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of [WL3c]

Crystal Data for C_{35}H_{42}O_{6}Si (M=586.77 g/mol): orthorhombic, space group P2_{1}2_{1}2_{1} (no. 19), a = 9.10599(3) Å, b = 15.40214(5) Å, c = 23.08098(7) Å, V = 3237.148(18) Å³, Z = 4, T = 150.00(10) K, μ(Cu Kα) = 0.985 mm⁻¹, Dcalc = 1.204 g/cm³, 144009 reflections measured (6.9° ≤ 2θ ≤ 148.85°), 6598 unique (Rint = 0.0487, Rsigma = 0.0108) which were used in all calculations. The final R₁ was 0.0250 (I > 2σ(I)) and wR₂ was 0.0666 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:
1. Twinned data refinement
   Scales: 1.00(2)
   0.00(2)
2. Fixed Uiso
   At 1.2 times of:
   All C(H) groups, All C(H,H) groups
   At 1.5 times of:
   All C(H,H,H) groups, All O(H) groups
3a. Ternary CH refined with riding coordinates:
   C1(H1), C7(H7), C12(H12), C14(H14), C18(H18)
3.b Secondary CH2 refined with riding coordinates:
   C21(H21A,H21B)
3.c Aromatic/amide H refined with riding coordinates:
   C6(H6), C31(H31), C32(H32), C33(H33), C34(H34), C35(H35), C37(H37), C38(H38),
   C39(H39), C40(H40), C41(H41)
3.d X=CH2 refined with riding coordinates:
   C13(H13A,H13B)
3.e Idealised Me refined as rotating group:
   C5(H5A,H5B,H5C), C19(H19A,H19B,H19C), C20(H20A,H20B,H20C), C24(H24A,H24B,
   H24C), C27(H27A,H27B,H27C), C28(H28A,H28B,H28C), C29(H29A,H29B,H29C)
This report has been created with Olex2, compiled on Nov 21 2019 18:26:39 for OlexSys.
### n) Abbreviation

| Abbreviation | Description |
|--------------|-------------|
| Ac           | acetyl      |
| ACLY         | ATP-citrate synthase |
| AD-mix-α     | a mixture of (DHQ)2PHAL, potassium osmate dihydrate, potassium carbonate, and potassium ferricyanide |
| AKT          | protein kinase B |
| Boc          | tert-butyloxycarbonyl |
| tBu          | tert-butyl |
| CID          | collision-induced dissociation |
| mCPBA        | meta-chloroperoxybenzoic acid |
| CSA          | camphorsulfonic acid |
| CuAAC        | Cu¹-catalyzed azide/alkyne cycloaddition |
| Cy3          | Cyanine 3 |
| dba          | dibenzylideneacetone |
| DBU          | 1,8-diazabicyclo[5.4.0]undec-7-ene |
| DCE          | 1,2-dichloroethane |
| DCM          | CH₂Cl₂, dichloromethane |
| DDQ          | 2,3-dichloro-5,6-dicyano-1,4-benzoquinone |
| (DHQD)₂Pyr   | hydroquinidine-2,5-diphenyl-4,6-pyrimidinediyl diether |
| DIPEA        | N,N-diisopropylethylamine |
| DMAP         | 4-dimethylaminopyridine |
| DMEM         | Dulbecco's modified eagle medium |
| DMF          | dimethylformamide |
| DMSO         | dimethyl sulfoxide |
| dr           | diastereomeric ratio |
| DTT          | dithiothreitol |
| DMP          | Dess–Martin periodinane |
| EDTA         | ethylenediaminetetraacetic acid |
| ee           | enantiomeric excess |
| Et           | ethyl |
| FCS          | fetal calf serum |
| HATU         | 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate |
| HCD          | higher-energy C-trap dissociation |
| HF           | hydrofluoric acid |
| HPLC         | high-performance liquid chromatography |
| HRMS         | high resolution mass spectrometry |
| Imid.        | imidazole |
| IPO5         | importin-5 |
| IR           | infrared spectra |
| Abbreviation | Full Form |
|--------------|-----------|
| KPNB1        | karyopherin subunit beta 1 |
| LC-MS        | liquid chromatography–mass spectrometry |
| Me           | methyl |
| m.p.         | melting point |
| NLS          | nuclear localization sequence |
| NOE          | nuclear overhauser effect |
| PBS          | phosphate-buffered saline |
| PFA          | paraformaldehyde |
| PhMe         | toluene |
| PMB          | p-methoxybenzyl |
| PPh₃         | triphenylphosphine |
| PTLC         | preparative thin-layer chromatography |
| PTSA         | p-TsOH, p-toluenesulfonic acid |
| Py           | pyridine |
| RASAL2       | RAS protein activator like 2 |
| Red-Al       | vitride, sodium bis(2-methoxyethoxy)aluminium hydride |
| r.t.         | room temperature |
| SAD          | Sharpless asymmetric dihydroxylation |
| Sat. aq.     | saturated aqueous solution |
| SDS          | sodium dodecyl sulphate |
| SDS-PAGE     | sodium dodecyl sulphate–polyacrylamide gel electrophoresis |
| SEM          | standard error of mean |
| STDEV        | standard deviation |
| TBAF         | tetra-n-butylammonium fluoride |
| TBDPSCI      | tert-Butyl(chloro)diphenylsilane |
| TBTA         | tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine |
| TCEP         | tris(2-carboxyethyl)phosphine hydrochloride |
| Tf           | triflate |
| TFA          | trifluoroacetic acid |
| THF          | tetrahydrofuran |
| TLC          | thin-layer chromatography |
| TMS          | trimethylsilyl |
| TMSOTf       | trimethylsilyl trifluoromethanesulfonate |
| UBA1         | ubiquitin-like modifier-activating enzyme 1 |