Concise Total Synthesis of Agarozizanol B via a Strained Photocascade Intermediate

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1. **General Methods**

1.1. **Experimental Techniques**

The synthesized molecules are named according to IUPAC. The numbering in the carbon chain is based on the position of the carbon atom.

All reactions involving air-sensitive or moisture-sensitive reagents are performed under argon atmosphere. The used glass devices were heated under vacuum with a heat gun (650 °C). Solid reagents were added under argon counter flow and liquid reagents via disposable syringes and needles.

Percentages (%) refer to mass percentages. The ratios of solvent mixtures are given in volume units. Solutions refer to solutions in water.

The calculated yields refer to the limiting reagent component.

Paraffin oil baths are used as heat baths. The temperature is set and controlled via an adjustable contact thermometer. Depending on the temperature, mixtures of ice/water (0 °C), acetone/dry ice (−78 °C) were used for ice baths. If applicable, the aimed temperature is set via a HAAKE EK90 cooling device (−78 °C - 0 °C) in Dewar flasks.

High pressure reactions (10 bar/ 30 bar) were carried out in ROTH high-pressure laboratory autoclaves Model II.

**Reagents**

All commercially available reagents are used without purification.

CAUTION! An urgent safety warning must be issued regarding reagents 1-(2-methoxyethoxy)-3-methylbut-2-ene and 1-(chloromethoxy)-3-methylbut-2-ene, which are highly cancerogenic. They are always handled with Campapren®-gloves. All contaminated cannulas, syringes and glass devices are always rinsed with an ammonia solution (25%) to destroy remaining residues.

**Solvents**

Dried solvents for moisture-sensitive reactions were taken from a MB-SPS-800 device by M. Braun GmbH. The solvents ran through the following columns:

- **Dichloromethane**: *Merck Emsure®, p.a., 99.8%, <0.03% H₂O*,
  Column: 2×MB-KOL-A.

- **Diethyl ether**: *Merck Emsure®, p.a., 99.7%, <0.03% H₂O*,
  Column: 1×MB-KOL-A, 1×MB-KOL-M Typ 2.

- **Tetrahydrofurane (THF)**: *Merck Emsure®, p.a., 99.8%, <0.03% H₂O*,
  Column: 2×MB-KOL-M Typ 2.
Dried solvents from the given companies were used with the corresponding quality grades. The solvents were stored above molecular sieve and used without further purification:

- Dioxane: *Acros Organics*, Extra Dry, 99.8%, <0.005% H₂O
- N,N-Dimethylformamide (DMF): *Acros Organics*, Extra Dry, 99.8%, <0.005% H₂O
- Ethanol: *Acros Organics*, Extra Dry, 99.8%, <0.005% H₂O
- Methanol: *Acros Organics*, Extra Dry, 99.8%, <0.005% H₂O
- Toluene: *Acros Organics*, Extra Dry, 99.8%, <0.005% H₂O

For thin layer chromatography (TLC) and column chromatography the following solvents were distilled before use: acetone, dichloromethane, diethyl ether, ethyl acetate, methanol.

The used sodium chloride-, ammonium chloride-, sodium hydrogen carbonate- and sodium thiosulfate-solutions were saturated aqueous solutions.

Solvents used in the photochemical reactions were degassed under a continuous argon flow in an ultrasonication bath for 15 minutes.
# Datasheet FLT021

## Basic Information

| Type             | Fluorescent light tube |
|------------------|------------------------|
| Description      | Luzchem LZC-UVA         |
| Manufacturer / Supplier | Hitachi / Luzchem     |
| Order number / Date of purch. | LZC-UVA / 09/2015 |
| Internal lot / serial number | 2015-09 / FLT021 |

## Specification Manufacturer

| Type / size      | T5 tube, G5 socket |
|------------------|--------------------|
| Mechanical specification | 16 mm diameter, 288 mm length |
| Electrical specification | 8 W |
| Wavelength (range, typ.) | 300 - 400 nm, 350m nm, UV-A |
| Spectral width (FWHM) | ~ 40 nm |

## Characterization

Description of measurement: Measured with Ocean-optics USB4000 spectrometer using a calibrated setup (cosine corrector/fibre). The cosine corrector was placed at 20 mm distance from a single fluorescent tube at half height.

| Measured dominant wavelength / Int. | 350 nm     | 115 μW/mm²nm |
|-------------------------------------|------------|--------------|
| Measured spectral width (FWHM)    | 40 nm      |              |
| Integral Reference intensity / range | 5017 μW/cm² | 300-425 nm  |

![Spectrum Diagram](image-url)
1.2. Analytics

Irradiation Equipment

Photochemical experiments at 350 nm were carried out in flame-dried Duran tubes in a positive geometry setup (cylindrical array of 16 lamps, 350 nm: Luzchem LZC-UVA, \( \lambda_{\text{max}} = 350 \text{ nm} \)) with the sample placed in the center of the illumination chamber.

Column Chromatography and Thin Layer Chromatography

For the column chromatography silica gel Si 60 (230-400 mesh, ASTM) with a particle size of 40-63 \( \mu \text{m} \) by the company Merck was used. The corresponding eluent ratios are found in the individual experimental procedures.

Thin layer chromatography silica gel 600G F254 glass plates by Merck were used as the stationary phase. The substances were verified via fluorescence detection. Therefore, the TLC-plates were analyzed under UV-light (\( \lambda = 254 \text{ nm} \)) and, if necessary, evaluated by the following solution heat treatment included (250 °C):

Potassium permanganate-solution [KMnO₄]: KMnO₄ (2.25 g), K₂CO₃ (15.0 g) and NaOH (250 mg) in water (250 mL).

NMR Spectroscopy

Nuclear magnetic resonance spectra were recorded with the devices AVHD300, AVHD400 and AVHD500 by the company Bruker at 300 K or a Bruker AV-II-500 equipped with a cryo probe head. The chemical shifts are given in \( \delta \)-values (ppm). Deuterated chloroform CDCl₃ (Deutero GmbH, 99.8%) or Methanol-d₄ (Deutero GmbH, 99.8%) were used as the solvent. When chloroform was used, the signals of residual protons of the solvent were used in the \(^1\)H-NMR-spectra (\( \delta = 7.26 \text{ ppm} \)) and \(^{13}\)C-NMR-spectra (\( \delta = 77.16 \text{ ppm} \)) as internal standard for calibration.

When methanol was used, the signals of residual protons of the solvent were used in the \(^1\)H-NMR-spectra (\( \delta = 4.87 \text{ ppm} \)) and \(^{13}\)C-NMR-spectra (\( \delta = 49.00 \text{ ppm} \)) as internal standard for calibration.

The spectra were viewed via MestReNova 10.0 of the company Mestrelab Research. The chemical shifts \( \delta \) are given in [ppm] (parts per million). For a clear assignment of the signals the following abbreviations were used for the spin multiplicities: s – singlet, d – doublet, t – triplet, q – quartet, p – quintet, h – sextet, hept – septet, m – multiplet, br. – broad. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of magnetically non-equivalent protons are marked as virt. – virtual. To fully characterize compounds, standard-NMR-measurements like DEPT-, HSQC-, HMBC-, and \(^1\)H-\(^1\)H- COSY-experiments were carried out.
Infrared Spectroscopy

IR spectra were recorded using a *Perkin-Elmer* 1600 FT-IR (KBr pellet, film). The intensities were designated with the following abbreviations: w (weak), m (medium), s (strong), vs (very strong), b (broad).

Mass Spectrometry

EI-MS: Mass spectrometry (MS) and high-resolution mass spectrometry (HRMS) were performed on a DFS double-focusing (BE geometry) magnetic sector mass spectrometer DFS (*ThermoFisher Scientific*, Bremen, Germany). Mass spectra were measured with electron ionization (EI) at 70 eV.

ESI-MS: Mass spectrometry (MS) and high-resolution mass spectrometry (HRMS) were performed on a LTQ FT Ultra (*Thermo*), a linear ion trap with a Fourier Transform Ion Cyclotron Resonance (FT-ICR) MS detector. The instrument is coupled online to an analytical HPLC (UltiMate 3000 HPLC system Dionex). Mass spectra were measured with electrospray ionization (ESI).

Melting Points

Melting points of solids were measured using a *Kofler* apparatus (“Thermopan”, *Reichert*, Vienna) or an IA9100 melting point measuring device from *Electrothermal* and are not corrected.

UV-Vis-Spectroscopy

UV-Vis spectra were measured with a Lambda 35 UV-Vis spectrometer from *Perkin-Elmer*.

HPLC was performed (Dionex Ultimate 3000 pump, Dionex Ultimate 3000 Autosampler, Dionex Ultimate 3000 photodiode array detector) using different chiral stationary phases (Daicel ChiralCel, *Chemical Industries*) and UV detection (\(\lambda = 215\) and 254 nm) at 20 °C or 25 °C.

Specific Rotation

was determined using an ADP440+ polarimeter (Fa *Bellingham+Stanley*) and is reported as follows: \([\alpha]_D^\lambda\) (c in g per 100 mL solvent).
2. Synthetic Procedures and Analytical Data

Agarozizanol B was synthesized in its racemic form and its (+)-enantiomeric form.

Scheme SI-1. Structure of Agarozizanol B (+)-4.

The reaction sequence to obtain photocascade product rac-11 is the same for both synthetic routes. The precursor rac-7 for the photochemical reaction cascade was synthesized according to the scheme shown below, starting from γ-butyrolactone A, phenol B and prenol C. (Scheme SI-2).

Scheme SI-2. General synthetic sequence for the preparation of photocascade product rac-11.

For the route to rac-4, the photocascade product rac-11 was reduced to compound rac-14 with sodium borohydride and subsequently transformed to the desired natural product (4% yield) over eleven steps (Scheme SI-3).

Scheme SI-3. General synthetic sequence for the preparation of racemic Agarozizanol B rac-4.
(+)-Agarozizanol B (+)-4 was synthesized in accordance with the synthetic routes shown in Schemes SI-2 and SI-3 over eleven steps in 2% yield. The sequence only differs in the transformation of the photocascade product rac-11 via a Corey-Bakshi-Shibata-reduction[1] to compound 14 with 96% ee (Scheme SI-4).

Scheme SI-4. General synthetic sequence for the preparation of Agarozizanol B (+)-4.

For simplification, the experimental procedures, which both routes have in common, are described in detail only for the racemic form of the respective compound.
7-Hydroxy-3-methyl-2,3-dihydro-1H-inden-1-one (rac-5)

In a flame-dried flask, a mixture of aluminium(III)chloride (20.2 g, 151 mmol, 4.00 eq.) and sodium chloride (4.00 g, 68.4 mmol, 1.81 eq.) was heated to 140 °C. At this temperature, a solution consisting of phenol (B) (3.56 g, 37.8 mmol, 1.00 eq.) dissolved in γ-butyrolactone (A) (2.94 mL, 38.6 mmol, 1.02 eq.) was added dropwise. After successful addition, the reaction mixture was heated to 180 °C and was stirred for 2 h. After allowing the mixture to cool to r.t., it was slowly quenched with sat. K/Na-tartrate solution (10.0 mL) until no further gas formation was visible. After the mixture had cooled to r.t. again, dichloromethane (30.0 mL) was added, and the resulting mixture was stirred overnight. The layers were separated, and the aqueous layer was extracted with dichloromethane (8 × 20.0 mL). The combined organic layers were dried over Na$_2$SO$_4$, the volatiles were removed in vacuo and the crude product was purified by flash chromatography (P/EtOAc = 50/1) yielding the desired product rac-5 (1.64 g, 10.1 mmol, 27%) as a yellow oil.

**TLC:** $R_f = 0.48$ (P/EtOAc = 9/1) [UV/ KMnO$_4$].

**$^1$H-NMR:** (400 MHz, CDCl$_3$): δ [ppm] = 9.05 (s, 1 H, OH), 7.49 (t, $^3$J = 7.8 Hz, 1 H, C$_8$H), 6.95 (d, $^3$J = 7.8 Hz, 1 H, C$_9$H), 6.76 (d, $^3$J = 7.8 Hz, 1 H, C$_6$H), 3.43 (pd, $^3$J = 7.2 Hz, $^3$J = 3.3 Hz, 1 H, C$_3$H), 2.95 (dd, $^3$J = 19.2, $^3$J = 7.2 Hz, 1 H, C$_2$H), 2.31 (dd, $^3$J = 19.2, $^3$J = 3.3 Hz, 1 H, C$_2$H), 1.39 (d, $^3$J = 7.2 Hz, 3 H, C$_{10}$H$_3$).

The observed analytical data was in perfect accordance with literature.$^{[2]}$
1-((2-Methoxyethoxy)methoxy)-3-methylbut-2-ene (D)

In a flame-dried Schlenk flask, prenol (C) (8.61 g, 100 mmol, 1.00 eq.) was dissolved in dry THF (100 mL) and treated portionwise with sodium hydride (60% in oil, 4.40 g, 110 mmol, 1.10 eq.), until hydrogen evolution had ceased. The mixture was cooled to 0 °C and treated dropwise with methoxyethoxymethyl chloride (12.5 g, 11.4 mL, 100 mmol, 1.00 eq.). After allowing the mixture to warm to r.t., it was stirred for 16 h. The volatiles were removed in vacuo and the crude product was obtained by vacuum distillation. Purification was achieved by flash chromatography (two runs, P/EtOAc = 15/1) to obtain compound D in form of a colorless liquid (13.4 g, 77.0 mmol, 77%).

**TLC:** $R_f = 0.29$ (P/EtOAc = 9/1) [UV/ KMnO$_4$].

**IR** (ATR): $\bar{\nu}$ (cm$^{-1}$) = 2901 (w, C−H), 1451 (w), 1381 (w), 1102 (s), 1049 (s), 1021 (s), 980 (m), 939 (w), 848 (w), 781 (w).

**$^1$H-NMR:** (500 MHz, CDCl$_3$): $\delta$ [ppm] = 5.35 (ddhept, $^3J = 7.1$ Hz, $^2J = 5.9$ Hz, $^4J = 1.4$ Hz, 1 H, C$_2$H), 4.72 (s, 2 H, OC$_5$H$_4$O), 4.07 (d, $^3J = 7.1$ Hz, 2 H, C$_1$H$_2$), 3.74−3.68 (m, 2 H, C$_7$H$_2^+$), 3.60−3.54 (m, 2 H, C$_6$H$_2^+$), 3.40 (s, 3 H, OC$_8$H$_3$), 1.75 (d, $^4J = 1.4$ Hz, 3 H, C$_4$H$_3$), 1.69 (d, $^4J = 1.4$ Hz, 3 H, C$_4$H$_3^+$).

**$^{13}$C-NMR:** (101 MHz, CDCl$_3$) $\delta$ [ppm] = 137.8 (C$_3$), 120.6 (C$_2$), 94.8 (C$_5$), 72.0 (2 C, C$_6$, C$_7$), 64.0 (C$_1$), 59.2 (C$_8$), 25.9 (C$_4$), 18.1 (C$_4^+$).

*Signals exchangeable.

**HRMS** (ESI): [M+Na]$^+$ calculated: 197.1148 found: 197.1149.
1-(chloromethoxy)-3-methylbut-2-ene (6)

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
5 & \quad 1 \\
2 & \quad 3 \\
\end{align*}
\]

16, 41%
C₆H₁₁ClO
134.60 g/mol

In a flame-dried flask, 1-((2-methoxyethoxy)methoxy)-3-methylbut-2-ene (D) (15.5 g, 89.0 mmol, 1.00 eq.) was dissolved in dry pentane (25.0 mL) and cooled to 0 °C. After treatment with dropwise boron trichloride solution (1 M in hexanes, 29.4 mL, 29.4 mmol, 0.33 eq.), the mixture was allowed to warm to r.t. and stirred for 16 h. The volatiles were removed in vacuo. Purification was achieved by vacuum distillation to obtain compound 6 in form of a colourless liquid (5.03 g, 37.4 mmol, 42%).

**B.p.:** 66-67 °C (45 mbar).

**TLC:** \( R_f = 0.16 \) (P/EtOAc = 9/1) [UV/ KMnO₄].

**\( ^1H-NMR: \)** (500 MHz, CDCl₃): \( \delta \text{[ppm]} = 5.51 \) (s, 2 H, C⁵H₂), 5.32 (tqq, \( ^3J = 7.2 \) Hz, \( ^4J = 2.1 \) Hz, \( ^4J = 1.4 \) Hz, 1 H, C³H) (d, \( ^3J = 7.2 \) Hz, 2 H, C¹H₂), 1.78 (d, \( ^4J = 2.1 \) Hz, 3 H, C⁴H₃), 1.73 (d, \( ^4J = 1.4 \) Hz, 3 H, C⁴H₃).

The observed analytical data was in perfect accordance with literature.\[^{[3]}\]
(3RS)-methyl-7-(((3-methylbut-2-en-1-yl)oxy)methoxy)-2,3-dihydro-1H-inden-1-one (rac-7)

In a flame-dried round bottom Schlenk flask, indanone rac-5 (1.44 g, 8.87 mmol, 1.00 eq.) was dissolved in dry DMF (15.0 mL). Linker 6 (2.39 g, 17.7 mmol, 2.00 eq.) and sodium carbonate (1.13 g, 10.7 mmol, 1.20 eq.) were added subsequently and the resulting mixture was stirred for 17.5 h at r.t. Afterwards, the reaction was quenched with sat. NH₄Cl-solution (15 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 15 mL) and the organic layer was washed with deionized water (15 mL). The combined organic layers were dried over Na₂SO₄ and the volatiles were removed in vacuo. The crude product was then purified by flash chromatography (P/EtOAc = 10/1) to obtain starting material rac-7 in form of a yellow liquid (1.65 g, 6.32 mmol, 71%).

**TLC:** R<sub>f</sub> = 0.16 (P/EtOAc = 9/1) [UV/KMnO₄].

**IR** (ATR): \( \tilde{\nu} \) (cm<sup>-1</sup>) = 2918 (w, C-H), 1708 (s, C=O), 1593 (s, C=C), 1476 (m), 1233 (m), 1080 (m), 1007 (s), 992 (s), 925 (m), 797 (w), 745 (w).

**<sup>1</sup>H-NMR:** (400 MHz, CDCl₃): \( \delta \) [ppm] = 7.51 (t, \( ^3J = 7.9 \) Hz, 1 H, C<sup>5</sup>H), 7.08 (dd, \( ^3J = 7.9 \) Hz, \( ^4J = 3.2 \) Hz, 2 H, C<sup>4</sup>H, C<sup>7</sup>H), 5.39 (s, 2 H, C<sup>12</sup>H₂), 5.33 (tqq, \( ^3J = 7.1 \) Hz, \( ^4J = 3.6 \) Hz, \( ^4J = 2.2 \) Hz, 1 H, C<sup>13</sup>H), 4.23 (d, \( ^3J = 7.1 \) Hz, 2 H, C<sup>12</sup>H₂), 3.36 (pd, \( ^3J = 7.4 \) Hz, \( ^3J = 3.7 \) Hz, 1 H, C<sup>3</sup>H), 2.91 (dd, \( ^2J = 18.7, ^3J = 7.4 \) Hz, 1 H, C<sup>2</sup>H<sup>2</sup>H<sup>2</sup>), 2.27 (dd, \( ^2J = 18.7 \) Hz, \( ^3J = 3.7 \) Hz, 1 H, C<sup>2</sup>H<sup>2</sup>H<sup>2</sup>), 1.73 (s, 3 H, C<sup>15</sup>H<sub>3</sub>), 1.66 (s, 3 H, C<sup>15</sup>H<sub>3</sub>), 1.38 (d, \( ^3J = 7.4 \) Hz, 3 H, C<sup>10</sup>H₃).

**<sup>13</sup>C-NMR:** (101 MHz, CDCl₃): \( \delta \) [ppm]: 204.0 (C<sup>1</sup>O), 162.6 (C<sup>7</sup>O), 155.5 (C<sup>9</sup>), 138.9 (C<sup>14</sup>), 136.4 (C<sup>5</sup>), 125.4 (C<sup>9</sup>), 119.9 (C<sup>13</sup>), 118.2 (C<sup>4</sup>), 113.2 (C<sup>6</sup>), 92.5 (C<sup>11</sup>), 65.1 (C<sup>12</sup>), 46.1 (C<sup>2</sup>), 32.4 (C<sup>3</sup>), 25.9 (C<sup>15</sup>), 21.6 (C<sup>10</sup>), 18.1 (C<sup>15</sup>).

**HRMS (ESI):** [M+Na]<sup>+</sup> calculated: 283.1305 found: 283.1305.
(1R/S,3a1R/S,4aR/S,8aS/R,10aS/R)-1,4,4-trimethyl-1,2,4a,5-tetrahydro-3H,3a1H,4H-cyclopenta[1′,2′]cy-clopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-one (rac-11)

(1S/R,3a1R/S,4aR/S,8aS/R,10aS/R)-1,4,4-trimethyl-1,2,4a,5-tetrahydro-3H,3a1H,4H-cyclopenta[1′,2′]cyclopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-one (rac-11′)

\[ \text{C}_{16}H_{20}O_3 \]
\[ 260.3330 \text{ g/mol} \]

Compound rac-7 (150 mg, 576 µmol, 1.00 eq.) was added to a flame-dried Duran phototube (diameter 2 cm, volume 60 mL) and dissolved in dry MeOH (60.0 mL). The reaction mixture was purged with argon (ultrasound, 20 min). The phototube was equipped with a balloon and subjected to irradiation (\( \lambda_{\text{max}} = 350 \text{ nm} \)) for 24 h. At this point, the solvent was removed in vacuo and the crude residue was purified by flash chromatography (P/EtOAc = 10/1 \( \rightarrow \) 8/1) to give the desired photocascade adduct rac-11 (63.1 mg, 242 µmol, 42%) in form of a colorless solid and minor diastereoisomer rac-11′ as a colorless oil (30.0 mg, 115 µmol, 20%) with a d.r. = 67/33 (via \( \text{1H-NMR} \)).

**Compound rac-11:**

**TLC:** \( R_f = 0.59 \) (P/EtOAc = 9/1) [UV/ KMnO₄].

**M.p.:** 153 °C.

**IR (ATR):** \( \delta \) (cm\(^{-1}\)) = 2957 (w, C-H), 2868 (w, C-H), 1697 (vs, C=O), 1462 (w), 1369 (w), 1304 (m), 1228 (m), 1190 (m), 1058 (m), 967 (vs), 900 (s), 842 (m), 771 (s), 654 (w).

**\( \text{1H-NMR} \):** (400 MHz, CDCl₃): \( \delta \) [ppm] = 6.28 (d, \( 3^J = 5.9 \text{ Hz} \), 1 H, C\(^3\)H), 6.24 (d, \( 3^J = 5.9 \text{ Hz} \), 1 H, C\(^2\)H), 5.03 (d, \( 2^J = 6.8 \text{ Hz} \), 1 H, C\(^{16}\)H), 5.00 (d, \( 2^J = 6.8 \text{ Hz} \), 1 H, C\(^{16}\)H\(\text{H} \)), 3.91 (dd, \( 2^J = 10.6 \text{ Hz} \), \( 3^J = 4.1 \text{ Hz} \), 1 H, C\(^{13}\)H\(\text{H} \)), 3.58 (dd, \( 3^J = 11.9 \text{ Hz} \), \( 2^J = 10.6 \text{ Hz} \), 1 H, C\(^{13}\)H\(\text{H} \)), 3.28 (s, 1 H, C\(^{11}\)H), 2.62 (dd, \( 3^J = 11.9 \text{ Hz} \), \( 3^J = 4.1 \text{ Hz} \), 1 H, C\(^{10}\)H), 2.47 (virt. p, \( 3^J \approx 3^J = 6.9 \text{ Hz} \), 1 H, C\(^{10}\)H), 2.28 (dd, \( 2^J = 16.9 \text{ Hz} \), \( 3^J = 7.2 \text{ Hz} \), 1 H, C\(^9\)H\(\text{H} \)), 1.72 (d, \( 2^J = 16.9 \text{ Hz} \), 1 H C\(^9\)H\(\text{H} \)), 1.55 (s, 3 H, C\(^{15}\)H\(\text{H} \)), 1.15 (d, \( 2^J = 6.9 \text{ Hz} \), 3 H, C\(^{12}\)H\(\text{H} \)), 0.92 (s, 3 H, C\(^{14}\)H\(\text{H} \)).

**\( \text{13C-NMR} \):** (101 MHz, CDCl₃): \( \delta \) [ppm] = 207.9 (C\(^8\)O), 133.0 (C\(^2\)), 128.9 (C\(^3\)), 91.2 (C\(^4\)), 90.3 (C\(^{16}\)), 65.6 (C\(^{13}\)), 62.6 (C\(^5\)), 59.7 (C\(^1\)), 57.6 (C\(^7\)), 57.1 (C\(^{11}\)), 43.6 (C\(^9\)), 38.9 (C\(^6\)), 30.6 (C\(^{15}\)), 29.4 (C\(^{10}\)), 21.4 (C\(^{14}\)), 20.0 (C\(^{12}\)).
The relative configuration and constitution of the compound were secured by single crystal X-ray crystallographic analysis (figure 1, for details see 7. X-ray Crystallographic Details).

**Figure 1.** Crystal structure of compound rac-11.

**Compound rac-11**:  

**TLC:** $R_f = 0.62$ (P/EtOAc = 9/1) [UV/ KMnO₄].

**IR** (ATR): $\tilde{\nu}$ (cm⁻¹) = 2957 (w, C-H), 2868 (w, C-H), 1697 (vs, C=O), 1462 (w), 1369 (w), 1304 (m), 1228 (m), 1190 (m), 1058 (m), 967 (vs), 900 (s), 842 (m), 771 (s), 654 (w).

**1H-NMR** (400 MHz, CDCl₃): $\delta$ [ppm] = 6.28 (d, $^3J = 6.3$ Hz, 1 H, C₃H), 6.10 (d, $^3J = 6.3$ Hz, 1 H, C₂H), 5.04 (d, $^2J = 6.8$ Hz, 1 H, C₁₆HH), 5.01 (d, $^2J = 6.8$ Hz, 1 H, C₁₆HH), 3.91 (dd, $^2J = 10.6$ Hz, $^3J = 4.0$ Hz, 1 H, C₁₃HH), 3.57 (dd, $^3J = 11.9$ Hz, $^2J = 10.6$ Hz, 1 H, C₁₃HH), 3.25 (s, 1 H, C₁₁H), 2.68-2.56 (m 1 H, C₁₀H), 2.60 (dd, $^3J = 11.9$ Hz, $^3J = 4.0$ Hz, C₅H), 2.20 (dd, $^2J = 16.9$ Hz, $^3J = 8.1$ Hz, 1 H, C₉HH), 1.67 (dd, $^2J = 16.9$ Hz, $^3J = 10.0$ Hz, 1 H, C₉HH), 1.54 (s, 3 H, C₁₅H₃), 1.10 (d, $^3J = 6.6$ Hz, 3 H, C₁₂H₃), 0.92 (s, 3 H, C₁₄H₃).

**13C-NMR** (101 MHz, CDCl₃) $\delta$ [ppm] = 207.4 (C₈O), 134.6 (C²), 129.4 (C³), 91.2 (C⁴), 90.3 (C¹₆), 65.7 (C¹₃), 62.3 (C⁵), 59.9 (C¹), 59.0 (C⁷), 53.4 (C¹¹), 43.3 (C⁹), 39.4 (C⁶), 30.8 (C¹₅), 29.9 (C¹₀), 21.3 (C¹₄), 16.9 (C¹₂).

**HRMS** (EI, 70 eV): [M⁺] calculated: 260.1407 found: 260.1407.
(4aR/S,5aS/R,5a1R/S,8R/S,8aR/S,10aS/R)-5,5,8-trimethyldecahydro-6H-cycloenta[7,1]indeno[1,2-d][1,3]dioxin-6-one (rac-12)

\[
\text{C}_{16}H_{24}O_3 \\
264.3650 \text{ g/mol}
\]

In a flame-dried flask PtO$_2$ (9.16 mg, 40 µmol, 0.70 eq.) was suspended in dry EtOAc (2.00 mL). An H$_2$-balloon was added, and the atmosphere was change via vacuum/flushing with H$_2$. The suspension was stirred for 20 min, before photoproduct rac-11 (15.0 mg, 58.0 µmol, 1.00 eq.) was added as a solution in dry EtOAc (1.00 mL). The mixture was stirred for 24 h and subsequently filtered over Celite. Removal of the volatiles in vacuo yielded product rac-12 (15.1 mg, 58.0 µmol, quant.) as a colourless oil.

**TLC:** $R_f = 0.56$ (P/EtOAc = 7/3) [UV/ KMnO$_4$].

**IR** (ATR): $\tilde{\nu}$ (cm$^{-1}$) = 2926 (m, C-H), 2868 (m, C-H), 1706 (w, C=O), 1461 (w), 1364 (w), 1186 (m), 1136 (m), 1056 (m), 985 (s), 901 (m), 867 (m), 782 (w), 737 (w), 671 (w).

**$^1$H-NMR** (400 MHz, CDCl$_3$) $\delta$ [ppm] = 4.89 (d, $^2J = 6.8$ Hz, 1 H, C$^{16}$H), 4.81 (d, $^2J = 6.8$ Hz, 1 H, C$^{16}$H), 4.00 (dd, $^2J = 10.4$ Hz, $^3J = 3.4$ Hz, 1 H, C$^{13}$H), 3.77 (t, $^2J = 10.9$ Hz, 1 H, C$^{13}$H), 2.70 (dd, $^3J = 12.1$ Hz, $^3J = 7.3$ Hz, 1 H, C$^{11}$H), 2.51 (d, $^3J = 12.1$ Hz, 1 H, C$^7$H), 2.49–2.43 (m, 1 H, C$^1$H), 2.40–2.25 (m, 2 H, C$^3$H, C$^9$H), 2.24-2.13 (m, 2 H, C$^5$H, C$^{10}$H), 2.00–1.82 (m, 3 H, C$^2$H, C$^3$H, C$^9$H), 1.45 (dd, $^2J = 12.2$ Hz, $^3J = 9.5$ Hz, $^3J = 2.5$ Hz, 1 H, C$^2$H), 1.28 (s, 3 H, C$^{15}$H$_3$), 0.96 (d, $^3J = 6.5$ Hz, 3 H, C$^{16}$H$_3$), 0.69 (s, 3 H, C$^{14}$H$_3$).

**$^{13}$C-NMR** (101 MHz, CDCl$_3$) $\delta$ [ppm] = 212.9 (C$^8$O), 92.9 (C$^4$), 89.4 (C$^{16}$), 65.8 (C$^{13}$), 56.8 (C$^5$), 56.7 (C$^7$), 53.5 (C$^{11}$), 43.7 (C$^9$), 42.9 (C$^6$), 41.2 (C$^1$), 32.7 (C$^3$), 32.5 (C$^{15}$), 29.7 (C$^{10}$), 23.7 (C$^2$), 20.4 (C$^{12}$), 17.2 (C$^{14}$).

**HRMS** (EI, 70 eV): [M$^+$] calculated: 264.1720 found: 264.1721.
(1R/S,3aR/S,4aR/S,8aS/R,10aS/R)-1,4,4-trimethyl-2,3,4a,5-tetrahydro-1H,3aH,4H-cyclopenta[1′,2′]cyclopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-ol (rac-14, rac-14′)

In a flame-dried Schlenk flask, compound rac-11 (400 mg, 1.54 mmol, 1.00 eq.) was dissolved in dry MeOH (20.0 mL). The solution was cooled to 0 °C and NaBH₄ (424 mg, 11.2 mmol, 7.30 eq.) was added portionwise under counterflow of Argon. The mixture was then stirred for 4 h. After quenching with sat. NH₄Cl-solution (20 mL), the organic layer was washed with deionized water (20 mL) and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over Na₂SO₄ and the volatiles were removed in vacuo. The crude product was then purified by flash chromatography (P/EtOAc = 3/1). The major diastereoisomer rac-14 was obtained in form of a yellow liquid (322 mg, 1.23 mmol, 80%) and the minor diastereoisomer rac-14′ (63.8 mg, 24.4 mmol, 16%) was obtained in form of a colorless solid (d.r. = 5/1, via ¹H-NMR).

**Compound rac-14:**

**TLC:** Rₚ = 0.85 (P/EtOAc = 3/1) [UV/ KMnO₄].

**IR (ATR):**  ν (cm⁻¹) = 3492 (br, O−H), 2956 (m, C–H), 2876 (m, C–H), 1463 (w), 1377 (w), 1235 (w), 1183 (s), 1104 (m), 1056 (m), 973 (m), 879 (w), 757 (w), 741 (w).

**¹H-NMR:** (400 MHz, CDCl₃): δ [ppm] = 6.25 (d, ³J = 5.8 Hz, 1 H, C³H), 6.14 (d, ³J = 5.8 Hz, 1 H, C²H), 5.03 (d, ³J = 6.7 Hz, 1 H, C¹⁶H/H), 4.96 (d, ²J = 6.8 Hz, 1 H, C¹⁶HH), 4.38 (d, ³J = 4.6 Hz, 1 H, C⁹OH), 3.89 (dd, ²J = 10.5 Hz, ³J = 3.9 Hz, 1 H, C¹³H/H), 3.61 (dd, ³J = 11.9 Hz, ²J = 10.5 Hz, 1 H, C¹³HH), 2.52 (dd, ³J = 11.9 Hz, ³J = 3.9 Hz, 1 H, C⁵H), 2.41 (s, 1 H, C¹¹H), 2.18 (p, ²J = 7.3 Hz, 1 H, C¹⁰H), 1.59–1.50 (m, 1 H, C⁹HH), 1.40 (s, 3 H, C¹⁵H₃), 1.36 (d, ²J = 14.6 Hz, 1 H, C⁹HH), 1.26 (d, ³J = 7.3 Hz, 3 H, C¹²H₃), 1.02 (s, 3 H, C¹⁴H₃).

**¹³C-NMR** (101 MHz, CDCl₃): δ [ppm] = 135.4 (C³), 126.4 (C²), 91.3 (C⁴), 90.1 (C¹⁶), 74.8 (C⁸), 66.2 (C¹³), 63.3 (C⁵), 59.7 (C¹), 52.5 (C⁷), 51.2 (C¹¹), 40.3 (C⁹), 38.7 (C⁶), 33.8 (C¹⁰), 30.1 (C¹⁵), 22.4 (C¹⁴), 21.0 (C¹²).

**HRMS** (EI, 70 eV): [M⁺] calculated: 262.1563 found: 262.1557.
Compound rac-14':

**TLC:** $R_f = 0.40$ (P/EtOAc = 3/1) [UV/ KMnO₄].

**M.p.:** 137 °C.

**IR (ATR):** $\tilde{\nu}$ (cm⁻¹) = 3492 (br, O-H), 2956 (m, C-H), 2876 (m, C-H), 1463 (w), 1377 (w), 1235 (w), 1183 (s), 1104 (m), 1056 (m), 973 (m), 901 (w), 879 (w), 757 (w), 741 (w).

**¹H-NMR:** (400 MHz, CDCl₃): $\delta$ [ppm] = 6.14 (d, $^3J$ = 5.9 Hz, 1 H, C³H), 6.15 (d, $^3J$ = 5.9 Hz, 1 H, C²H), 5.04 (d, $^3J$ = 6.8 Hz, 1 H, C¹⁶H), 4.98 (d, $^2J$ = 6.8 Hz, 1 H, C¹⁶H), 4.53-4.48 (m, 1 H, C⁸H), 3.90 (dd, $^2J$ = 10.5 Hz, $^3J$ = 3.9 Hz, 1 H, C¹³H), 3.60 (dd, $^3J$ = 11.9 Hz, $^2J$ = 10.5 Hz, 1 H, C¹³H), 2.96 (s, 1 H, C¹¹H), 2.54 (dd, $^3J$ = 11.9 Hz, $^2J$ = 3.9 Hz, 1 H, C⁶H), 2.19 (p, $^3J$ = 7.3 Hz, 1 H, C¹⁰H), 1.75 (dd, $^2J$ = 13.2 Hz, $^3J$ = 7.3 Hz, 1 H, C⁹H), 1.34 (s, 3 H, C¹⁵H), 1.33-1.28 (m, 1 H, C⁹H), 1.03 (d, $^3J$ = 7.3 Hz, 3 H, C¹⁶H), 0.91 (s, 3 H, C¹⁴H).

**¹³C-NMR** (101 MHz, CDCl₃): $\delta$ [ppm] = 135.2 (C³), 126.9 (C²), 91.5 (C⁴), 90.1 (C¹⁶), 71.2 (C⁸), 66.0 (C¹³), 63.5 (C⁵), 58.3 (C¹), 52.9 (C⁷), 49.0 (C¹¹), 39.7 (C⁹), 38.2 (C⁶), 32.5 (C¹⁰), 30.7 (C¹⁵), 21.3 (C¹⁴), 20.3 (C¹²).

**HRMS** (El, 70 eV): [M⁺] calculated: 262.1563 found: 262.1557.
In an Argon filled glovebox, a 25 mL Schlenk tube was charged with \((R)-(-)-2\)-methyl-CBS-oxazaborolidine (13) (556 mg, 2.01 mmol, 1.00 equiv.). The tube was sealed and brought out of the glovebox under inert atmosphere. Subsequently, ketone rac-11 (522 mg, 2.01 mmol, 1.00 equiv.) was added, the mixture was purged with Argon three times and dissolved in 5.00 mL anhydrous THF. The mixture was cooled to 0 °C over 30 minutes and BH₃(SMe₂) complex (2.0 M in THF, 602 µL, 1.20 mmol, 0.60 equiv.) was added slowly in drops over 5 minutes. The mixture was stirred at 0 °C for 2 h. Methanol (1.00 mL) was added at 0 °C to quench the reaction. The mixture was warmed to room temperature and the solvent was removed in vacuo. Purification was achieved by flash chromatography (P/EtOAc = 6/1→ 3/1) to yield diastereomers 14 (230 mg, 883 µmol, 44%, 96% ee) as a white solid and 14’ (225 mg, 864 µmol, 43%, 96% ee) as a white solid.

**Compound 14:**

The analytic data for TLC, IR, ¹H NMR, ¹³C NMR and HRMS of diastereomer 14 agree with the data of compound rac-14.

M.p.: 104 °C.

Specific rotation: \([\alpha]_D^{20} = +24 \ (c = 0.3, \text{MeOH})\).

**Compound 14’:**

The analytic data for TLC, M.p., IR, ¹H NMR, ¹³C NMR and HRMS of diastereomer 14’ agree with the data of compound rac-14’.

Specific rotation: \([\alpha]_D^{20} = -20 \ (c = 0.3, \text{MeOH})\).
(1R/S,3a1R/S,4aR/S,8aS/R,10aR/S)-1,4,4-trimethylhexahydro-3H,3a1H,4H-cyclopenta[1',2']cyclopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-one (rac-15)

In a flame-dried flask, a suspension of platinum(IV)-oxide (179 mg, 788 µmol, 0.30 eq.) and alcohol rac-14 (689 mg, 2.63 mmol, 1.00 eq.) was stirred in freshly distilled EtOAc (10.0 mL) under hydrogen atmosphere (1 atm) for 1 h at r.t., before it was filtered over Celite and rinsed with EtOAc. The volatiles were removed in vacuo, giving the hydrogenated product (694 mg, 2.63 mmol, quant.) in form of a yellow oil.

**Oxidation, Method 1**

In a flame-dried Schlenk flask, a solution of hydrogenated compound (282 mg, 1.07 mmol, 1.00 eq.) in dry CH2Cl2 (10.0 mL) was cooled to 0 ºC. Subsequently, solid NaHCO3 (215 mg, 2.56 mmol, 2.40 eq.) and portionwise Dess-Martin periodinan (633 mg, 1.49 mmol, 1.46 eq.) were added. The mixture was allowed to warm to r.t. and stirred for 15 h. The reaction was quenched slowly with a 1:1 mixture of sat. Na2S2O3- and NaHCO3-solution (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over Na2SO4 and the volatiles were removed in vacuo. Purification was achieved by flash chromatography (P/EtOAc = 9/1). Product rac-15 (235 mg, 897 µmol, 84%) was obtained in form of a colorless crystalline solid.

**Oxidation, Method 2**

In a flame-dried Schlenk tube, to a solution of hydrogenated compound (181 mg, 685 µmol, 1.00 eq.) in dry CH2Cl2 (12.0 mL), pyridinium chlorochromate (369 mg, 1.71 mmol, 2.50 eq.) was added. The mixture was stirred at r.t. for 2 h, before the reaction mixture was filtered and the volatiles were removed in vacuo. Purification was achieved by flash chromatography (P/EtOAc = 4/1). Product 15 (145 mg, 162 µmol, 81%) was obtained in form of a colorless crystalline solid.

**TLC:** Rf = 0.54 (P/EtOAc = 7/3) [KMnO4].

**M.p.:** 120 ºC.

**IR (ATR):** ð (cm⁻¹) = 2959 (m, C-H), 2925 (m, C-H), 2888 (m, C-H), 1713 (s, C=O), 1461 (w), 1374 (w), 1190 (w), 1147 (m), 1001 (w), 983 (m), 903 (s).
\textbf{\(^1\text{H-NMR:}\) (400 MHz, CDCl\textsubscript{3}): }\delta \text{ [ppm] } = 4.89 \text{ (d, } ^2J = 6.6 \text{ Hz, } 1 \text{ H, } \text{C}^{16}H/\text{H}), 4.66 \text{ (d, } ^2J = 6.6 \text{ Hz, } 1 \text{ H, } \text{C}^{16}H/\text{H}), 3.92 \text{ (dd, } ^2J = 11.1 \text{ Hz, } ^3J = 3.7 \text{ Hz, } 1 \text{ H, } \text{C}^{13}H/\text{H}), 3.70 \text{ (virt. } t, ^2J \cong ^3J = 11.1 \text{ Hz 1 H, } \text{C}^{13}H/\text{H}), 2.64 \text{ (s, 1 H, C}^6\text{H}), 2.52 \text{ (ddd, } ^2J = 11.1 \text{ Hz, } ^3J = 3.7 \text{ Hz, } ^4J = 1.5 \text{ Hz, 1 H, } \text{C}^5\text{H}), 2.43 \text{ (ddd, } ^2J = 13.4 \text{ Hz, } ^3J = 8.0 \text{ Hz, } ^3J = 4.3 \text{ Hz, 1 H, } \text{C}^9\text{H/}\text{H}), 2.32 \text{ (virt. } p, ^3J \cong ^3J = 6.8 \text{ Hz, 1 H, } \text{C}^{10}\text{H}), 2.28-2.15 \text{ (m, 3 H, } \text{C}^2\text{H/}\text{H, C}^9\text{H/}\text{H}), 2.03 \text{ (ddd, } ^2J = 13.4 \text{ Hz, } ^3J = 12.1 \text{ Hz, } ^3J = 6.4 \text{ Hz, } 1 \text{ H, } \text{C}^3\text{H/}\text{H}), 1.61 \text{ (d, } ^2J = 15.6 \text{ Hz, 1 H, } \text{C}^9\text{H/}\text{H}), 1.58 \text{ (s, 3 H, } \text{C}^{15}\text{H}_3), 1.00 \text{ (d, } ^3J = 6.8 \text{ Hz, 3 H, } \text{C}^{16}\text{H}_3), 0.87 \text{ (s, 3 H, } \text{C}^{14}\text{H}_3).

\textbf{\(^{13}\text{C-NMR:}\) (101 MHz, CDCl\textsubscript{3}): }\delta \text{ [ppm] } = 209.6 \text{ (C}^8\text{O), 90.1 \text{ (C}^{16}), 88.5 \text{ (C}^4), 65.1 \text{ (C}^{13}), 61.9 \text{ (C}^5), 59.2 \text{ (C}^1), 51.7 \text{ (C}^7), 50.1 \text{ (C}^{11}), 43.3 \text{ (C}^9), 39.2 \text{ (C}^6), 31.4 \text{ (C}^{19}), 31.1 \text{ (C}^3), 29.8 \text{ (C}^{15}), 27.0 \text{ (C}^2), 21.1 \text{ (C}^{14}), 19.6 \text{ (C}^{12}).

\textbf{HRMS (EI, 70 eV): }[M^+ ] \text{ calculated: 262.1563 found: 262.1563.}

The relative configuration and constitution of the compound were secured by single crystal X-ray crystallographic analysis (figure 2, for details see 7. X-ray Crystallographic Details).

![Figure 2. Crystal structure of compound rac-15.](image-url)
(1R,3a1R,4aR,8aS)-1,4,4-trimethylhexahydro-3H,3a1H,4H-cyclopenta[1',2']cyclopropa
[3,4]pentaleno[6a,1-d][1,3]dioxin-3-one (15)

Compound 15 was synthesized according to the procedure for the synthesis of compound rac-
15, using oxidation method 1. Starting with compound 14 (181 mg, 685 µmol, 1.00 eq.) in dry
CH2Cl2 (10.0 mL), with NaHCO3 (138 mg, 1.64 mmol, 2.40 eq.) and Dess-Martin periodinane
(407 mg, 959 mmol, 1.46 eq.) compound 15 (151 mg, 575 µmol, 84%) was obtained in form of
a colorless powder.
The analytic data for TLC, IR, 1H NMR, 13C NMR and HRMS of compound 15 agree with the
data of compound rac-15.
M.p.: 120 °C.
Specific rotation: [α]D20 = +25 (c = 0.3, MeOH).
Compound 15 (102 mg, 389 µmol, 1.00 eq.) was dissolved in dichloromethane (7.00 mL). Trimethylsilyl chloride (78.1 µL, 66.8 mg, 615 µmol, 1.58 eq.) and sodium iodide (106 mg, 707 µmol, 1.82 eq.) were added. The mixture was stirred for 96 h at room temperature. After filtration, water (10 mL) was added, and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. At this point, the solvent was removed in vacuo and the crude residue was purified by flash chromatography (P/EtOAc = 10/1 → 5/1) to give the desired product rac-16 as an orange powder (122 mg, 313 µmol, 80%) and to reisolate compound rac-15 (7.40 mg, 28.2 µmol, 7%).

**TLC:** Rf = 0.10 (P/EtOAc = 6/1) [KMnO₄].

**M.p.:** 135 °C.

**IR (ATR):** ν (cm⁻¹) = 2957 (m, C-H), 2925 (m, C-H), 2870 (m, C-H), 1735 (s, C=O), 1458 (m), 1165 (vs), 1063 (vs), 694 (m).

**¹H-NMR:** (300 MHz, CDCl₃): δ [ppm] = 4.96 (d, ²J = 7.0 Hz, 1 H, C¹⁶/H¹), 4.66 (d, ²J = 7.0 Hz, 1 H, C¹⁶/H¹), 4.20 (s, 1 H, C¹¹/H¹), 3.98 (dd, ²J = 11.7 Hz, ³J = 3.6 Hz, 1 H, C¹³/H¹), 3.72 (vıırt. t, ²J = 11.8 Hz, 1 H, C¹³/H¹), 2.51 (dd, ²J = 19.0 Hz, ³J = 8.3 Hz, 1 H, C³/H¹), 2.42-2.29 (m, 2 H, C²/H¹, C⁷/H¹), 2.29-2.16 (m, 1 H, C¹⁰/H¹), 2.23 (s, 1 H, C³/H¹), 2.04-1.89 (m, 2 H, C³/H¹, C⁹/H¹), 1.78 (dd, ²J = 19.0 Hz, ³J = 11.3 Hz, 1 H, C¹³/H¹), 1.48-1.41 (m, 1 H, C¹⁰/H¹), 1.36 (d, ³J = 6.5 Hz, 3 H, C¹²/H₁), 1.27 (s, 3 H, C¹⁵/H₁), 1.01 (s, 3 H, C¹⁴/H₁).

**¹³C-NMR:** (75 MHz, CDCl₃): δ [ppm] = 212.2 (C⁴O), 91.1 (C¹⁶), 82.4 (C⁸), 71.4 (C⁵), 64.3 (C¹⁳), 53.8 (C¹), 53.3 (C⁷), 52.9 (C¹¹), 46.5 (C³), 36.0 (C²), 33.6 (C⁹), 32.0 (C¹⁵), 25.9 (C⁹), 21.4 (C¹⁰), 16.5 (C¹⁴), 15.5 (C¹²).

**HRMS (ESI):** [M−I]⁺ calculated: 263.1642. found: 263.1652.

\[(4aR/S,5aR/S,8R/S,8aS/R,10aR/S,11R/S)-11\text{-}\text{iodo}-5,5,8\text{-}\text{trimethyloctahydro-6H-8a,10a-methanoazu-}6,5\text{-}d\text{][1,3]}\text{dioxin-6-one (rac-16)}\]
The relative configuration and constitution of the compound were secured by single crystal X-ray crystallographic analysis (figure 3, for details see 7. X-ray Crystallographic details).

**Figure 3.** Crystal structure of compoundrac-16.

\[
\text{(4aR,5aR,8R,8aS,10aR,11R)-11-iodo-5,5,8-trimethyloctahydro-6H-8a,10a-methanoazulenol[6,5-d][1,3]dioxin-6-one (16)}
\]

Compound 16 was synthesized according to the procedure for the synthesis of compoundrac-16. Starting with compound 15 (145 mg, 552 µmol, 1.00 eq.), using trimethylsilyl chloride (111 µL, 94.8 mg, 872 µmol, 1.58 eq.) and sodium iodide (106 mg, 707 µmol, 1.82 eq.) in dichloromethane (10.0 mL), compound 16 (160 mg, 409 µmol, 74%) was obtained as a brown, crystalline solid.

The analytic data for TLC, IR, \(^1\)H NMR, \(^{13}\)C NMR and HRMS of compound 16 agree with the data of compound rac-16.

**M.p.:** 127 °C.

**Specific rotation:** \([\alpha]_D^{20} = +14\) (c = 0.3, MeOH).
(4aR/S,5aR/S,8R/S,8aS/R,10aS/R)-5,5,8-trimethyloctahydro-6H-8a,10a-methanoazu-leno[6,5-d][1,3]-dioxin-6-one (rac-17)

Compound rac-16 (230 mg, 589 µmol, 1.00 eq.) was dissolved in dry toluene (10.0 mL) and tributyltin hydride (318 µL, 343 mg, 1.18 mmol, 2.00 eq.) was added dropwise. AIBN (2.75 mg, 16.7 µmol, 0.03 eq.) was added afterwards as a solution in toluene (200 µL) and the reaction mixture was heated to 50 °C and stirred for 1 h. After cooling down to room temperature, the volatiles were removed in vacuo and the crude residue was purified by flash chromatography (P/EtOAc = 6/1) to give the desired product rac-17 as colorless oil (156 mg, 589 µmol, quant.).

**TLC:** $R_f = 0.31$ (P/EtOAc = 6/1) [KMnO₄].

**IR (ATR):** $\tilde{\nu}$ (cm⁻¹) = 2957 (s, C-H), 2925 (s, C-H), 2873 (s, C-H), 1735 (vs, C=O), 1454 (w), 1157 (vs), 1025 (s), 931 (w).

**1H-NMR:** (400 MHz, CDCl₃): $\delta$ [ppm] = 4.88 (d, $^3J = 6.3$ Hz, 1 H, C¹⁶H), 4.69 (d, $^3J = 6.3$ Hz, 1 H, C¹⁶H), 4.03 (dd, $^2J = 11.4$ Hz, $^3J = 4.2$ Hz, 1 H, C¹³H), 3.75 (t, $^2J = 11.4$ Hz, 1 H, C¹³H), 2.45–2.33 (m, 2 H, C³H, C⁹H), 2.15–2.11 (m, 1 H, C²H), 2.08 (d, $^2J = 10.2$ Hz, 1 H, C¹¹H), 1.99–1.93 (m, 1 H, C⁷H), 1.96 (s, 1 H, C⁵H), 1.83 (td, $^2J = 13.4$ Hz, $^3J = 5.5$ Hz, 1 H, C¹⁰H), 1.72 (dd, $^2J = 18.7$ Hz, $^3J = 12.0$ Hz, 1 H, C³H), 1.60 (dt, $^2J = 13.4$ Hz, $^3J = 5.5$ Hz, 1 H, C⁹H), 1.33 (d, $^3J = 10.2$ Hz, 1 H, C¹¹H), 1.31–1.28 (m, 1 H, C¹⁰H), 1.25 (s, 3 H, C¹⁵H), 1.04 (d, $^3J = 6.7$ Hz, 3 H, C¹²H), 0.97 (s, 3 H, C¹⁴H).

**13C-NMR:** (101 MHz, CDCl₃): $\delta$ [ppm] = 215.1 (C⁴O), 90.4 (C¹⁶), 82.3 (C⁸), 69.4 (C⁵), 64.7 (C¹³), 52.3 (C⁷), 49.9 (C¹), 48.5 (C¹¹), 45.4 (C³), 33.8 (C⁶), 35.0 (C²), 32.5 (C¹⁵), 27.1 (C⁹), 22.1 (C¹⁰), 16.6 (C¹⁴), 13.3 (C¹²).

**HRMS (ESI):** [M+H]^⁺ calculated: 265.1798 found: 265.1791.
Compound 17 was synthesized according to the procedure for the synthesis of compound rac-17. Starting with compound 16 (145 mg, 372 µmol, 1.00 eq.) in dry toluene (11.0 mL), with tributyltin hydride (200 µL, 216 mg, 1.18 mmol, 2.00 eq.), AIBN (2.75 µg, 16.7 µmol, 0.03 eq.) compound 17 (98.1 mg, 371 µmol, quant.) was obtained as a colorless oil. The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 17 agree with the data of compound rac-17.

Specific rotation: $[\alpha]_D^{20} = –12$ (c = 0.3, MeOH).
In a flame-dried Schlenk flask, a suspension of LiAlH₄ (91.6 mg, 2.29 mmol, 4.00 eq.) in dry THF (5.00 mL) was cooled to 0 °C. Compound rac-17 (152 mg, 573 µmol, 1.00 eq.) was added dropwise as a solution in dry THF (7.00 mL). The reaction mixture was stirred for 4 h at room temperature and subsequently quenched at 0 °C by addition of a mixture of H₂O/THF (1:1, 10.0 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (6 × 10 mL) and dried over Na₂SO₄. The volatiles were removed in vacuo and the crude residue was purified by flash chromatography (P/EtOAc = 6/1 – 4/1) to give the desired product rac-18 as a mixture (d.r. = 3/2, via ¹H-NMR) of major diastereoisomer rac-18a (93.3 mg, 350 µmol, 61%) in form of a yellow oil and diastereoisomer rac-18b (46.7 mg, 31%) in form of a yellow oil.

**Compound rac-18a:**

![Compound rac-18a](image)

**TLC:** Rₙ = 0.58 (P/EtOAc = 2/1) [KMnO₄].

**IR (ATR):** ν (cm⁻¹) = 3477 (br, O-H), 2953 (m, C-H), 2927 (m, C-H), 2870 (m, C-H), 1453 (w), 1158 (vs), 1082 (vs), 1033 (s), 931 (m).

**¹H-NMR:** (300 MHz, CDCl₃): δ [ppm] = 4.87 (d, 2J = 6.1 Hz, 1 H, C¹⁶HH), 4.68 (d, 3J = 6.2 Hz, 1 H, C¹⁶HH), 4.47 (ddd, 3J = 7.2 Hz, 3J = 5.2 Hz, 3J = 2.4 Hz, 1 H, C⁴HOH), 4.02 (dd, 2J = 11.3 Hz, 3J = 4.2 Hz, 1 H, C¹³HH), 3.79 (t, 2J = 11.3 Hz, 1 H, C¹³HH), 2.46–2.35 (m, 2 H, C⁴HH, C⁹HH), 1.98 (d, 2J = 10.0 Hz, 1 H, C¹¹HH), 1.96–1.88 (m, 2 H, C⁴H, C¹⁰HH), 1.83–1.73 (m, 2 H, C⁴H, C¹⁰HH), 1.55 (ddd, 2J = 13.1 Hz, 3J = 4.7 Hz, 4J = 2.0 Hz, 1 H, C⁹HH), 1.22 (d, 3J = 5.3 Hz, 1 H, C⁵H), 1.17 (s, 3 H, C¹⁵H₃), 1.15–1.10 (m, 1 H, C³HH), 1.12 (s, 3 H, C¹⁴H₃), 1.07 (dt, 2J = 10.0 Hz, 4J = 2.0 Hz, 1 H, C¹¹HH) 0.97 (d, 3J = 7.0 Hz, 3 H, C¹²H₃).

**¹³C-NMR:** (75 MHz, CDCl₃): δ [ppm] = 90.9 (C¹⁶), 82.0 (C⁸), 73.5 (C⁴), 65.9 (C¹³), 63.6 (C⁵), 53.0 (C⁷), 52.1 (C¹¹), 50.8 (C¹), 45.9 (C³), 37.8 (C²), 36.0 (C⁶), 33.8 (C¹⁵), 28.2 (C⁹), 24.0 (C¹⁰), 20.8 (C¹⁴), 16.1 (C¹²).

**HRMS (ESI):** [M+K]⁺ calculated: 305.1514 found: 305.1512.
Compound rac-18b:

TLC: \( R_f = 0.33 \) (P/EtOAc = 2/1) [KMnO₄].

IR (ATR): \( \tilde{\nu} \) (cm\(^{-1}\)) = 3477 (br, O-H), 2953 (m, C-H), 2870 (m, C-H), 1453 (w), 1158 (vs), 1082 (vs), 1033 (s), 931 (m).

\(^1\)H-NMR: (300 MHz, CDCl₃): \( \delta \) [ppm] = 4.88 (dd, \( ^2J = 6.3 \) Hz, \( ^4J = 1.1 \) Hz, 1 H, C\(^{16}\)H), 4.68 (d, \( ^3J = 6.3 \) Hz, 1 H, C\(^{16}\)H), 4.28 (td, \( ^3J = 8.7 \) Hz, \( ^2J = 3.7 \) Hz, 1 H, C\(^{4}\)OH), 4.06 (dd, \( ^2J = 11.5 \) Hz, \( ^3J = 4.6 \) Hz, 1 H, C\(^{13}\)H), 3.74 (t, \( ^2J = 11.5 \) Hz, 1 H, C\(^{13}\)H), 2.90 (ddt, \( ^2J = 12.6 \) Hz, \( ^3J = 9.1 \) Hz, \( ^3J = 3.7 \) Hz, 1 H, C\(^{13}\)H), 2.80-2.70 (m, 1 H, C\(^{2}\)H), 2.17-2.07 (m, 1 H, C\(^{7}\)H), 1.82 (d, \( ^2J = 10.2 \) Hz, 1 H, C\(^{11}\)H), 1.78-1.62 (m, 2 H, C\(^{2}\)H), 1.59-1.57 (m, 1 H, C\(^{10}\)H), 1.54 (dd, \( ^2J = 8.7 \) Hz, \( ^3J = 1.4 \) Hz, 1 H, C\(^{5}\)H), 1.51-1.43 (m, 1 H, C\(^{9}\)H), 1.25-1.20 (m, 1 H, C\(^{11}\)H), 1.21-1.19 (m, 1 H, C\(^{10}\)H), 1.17 (s, 3 H, C\(^{15}\)H), 0.86 (d, \( ^3J = 6.8 \) Hz, 3 H, C\(^{12}\)H).

\(^{13}\)C-NMR: (101 MHz, CDCl₃): \( \delta \) [ppm] = 90.4 (C\(^{16}\)), 82.6 (C\(^{8}\)), 71.5 (C\(^{4}\)), 66.7 (C\(^{5}\)), 65.2 (C\(^{13}\)), 52.0 (C\(^{7}\)), 51.4 (C\(^{1}\)), 48.8 (C\(^{11}\)), 42.7 (C\(^{3}\)), 36.7 (C\(^{2}\)), 33.9 (C\(^{6}\)), 33.7 (C\(^{15}\)), 26.9 (C\(^{9}\)), 22.1 (C\(^{10}\)), 18.0 (C\(^{14}\)), 13.8 (C\(^{12}\)).

HRMS (ESI): [M+K]^+ calculated: 305.1514 found: 305.1512.

(4aR,5aR,6S,8R,8aS,10aS)-5,5,8-trimethyloctahydro-4H-8a,10a-methanoazuleno[6,5-d][1,3]dioxin-6-ol (18)

Compound 18 was synthesized according to the procedure for the synthesis of compound rac-18. Starting with compound 17 (90.0 mg, 340 \( \mu \)mol, 1.00 eq.) lithium aluminum hydride (54.4 mg, 1.36 mmol, 4.00 eq.) in THF (4.50 mL), compound 18 (75.1 mg, 282 mmol, 83%) was obtained as a yellow oil (d.r. = 3/2, via \(^1\)H-NMR).

Compound 18a:

The analytic data for TLC, IR, \(^1\)H NMR, \(^{13}\)C NMR and HRMS of compound 18a agree with the data of compound rac-18a.

Specific rotation [\( \alpha \)]\(_D^{20}\) = +10 (c = 0.3, MeOH).
Compound 18b:

The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 18b agree with the data of compound rac-18b.

Specific rotation $[\alpha]_{D}^{20} = -12$ (c = 0.3, MeOH).
In a flame-dried Schlenk flask, n-BuLi (420 µL, 1.05 mmol, 2.00 eq., as a 2.5 M solution in hexanes) was added dropwise to a solution of alcohol rac-18 (140 mg, 526 µmol, 1.00 eq.) in dry THF (10.0 mL) at 0 °C. The mixture was stirred for 45 min at this temperature, before adding dropwise carbon disulfide (431 µL, 543 mg, 7.13 mmol, 13.6 eq.) and stirring for 3 h at r.t. At this point, iodomethane (861 µL, 1.96 g, 13.8 mmol, 26.3 eq.) was added dropwise at 0 °C, and the mixture was stirred for another 2 h. After quenching with H2O (12 mL), the layers were separated, and the aq. layer was extracted with diethyl ether (6 × 12 mL). The combined org. layers were dried over Na2SO4 and the volatiles removed in vacuo. Purification was obtained by flash chromatography (P/EtOAc = 6/1) to yield product rac-19 as a mixture of diastereomers in form of a yellow-brown oil (187 mg, 526 µmol, quant.).

**Compound 19a:**

\[
\text{TLC: } R_f = 0.41 \text{ (P/EtOAc = 6/1) [KMnO}_4\text{].}
\]

**IR (ATR):** \(\tilde{\nu} \text{ (cm}^{-1}) = 2956 \text{ (m, C-H), 2926 (m, C-H), 2870 (m, C-H), 1453 (w), 1230 (s), 1206 (s), 1158 (vs), 1059 (vs), 1080 (s), 938 (m).}

**\(^1\text{H-NMR} \text{ (500 MHz, CDCl}_3\):}** \(\delta = 6.12 \text{ (ddd, }^3J = 7.1 \text{ Hz, }^3J = 5.1 \text{ Hz, }^3J = 2.0 \text{ Hz, 1 H, C}\text{^4}H\text{OH}, 4.88 \text{ (d, }^3J = 6.2 \text{ Hz, 1 H, C}\text{^16}H\text{H), 4.68 \text{ (d, }^3J = 6.2 \text{ Hz, 1 H, C}\text{^16}H\text{H), 4.01 \text{ (dd, }^2J = 11.4 \text{ Hz, }^3J = 4.2 \text{ Hz, 1 H, C}\text{^11}H\text{H), 3.77 \text{ (virt. t, }^2J \cong ^3J = 11.4 \text{ Hz, 1 H, C}\text{^13}H\text{H), 2.59–2.49 \text{ (m, 1 H, C}\text{^3}H\text{H), 2.55 \text{ (s, 3 H, -SC}\text{^18}H\text{H), 2.41 \text{ (dddd, }^2J = 12.0 \text{ Hz, }^3J = 9.2 \text{ Hz, }^3J = 4.6 \text{ Hz, }^4J = 2.2 \text{ Hz, 1 H, C}\text{^9}H\text{H), 2.04 \text{ (d, }^2J = 10.2 \text{ Hz, 1 H, C}\text{^11}H\text{H), 1.98 \text{ (ddd, }^3J = 11.4 \text{ Hz, }^3J = 4.2 \text{ Hz, }^4J = 1.6 \text{ Hz, 1 H, C}\text{^7}H\text{), 1.93–1.84 \text{ (m, 2 H, C}\text{^2}H\text{, C}\text{^10}H\text{H), 1.78 \text{ (tdd, }^2J = 13.1 \text{ Hz, }^3J = 4.7 \text{ Hz, }^4J = 1.4 \text{ Hz, 1 H, C}\text{^10}H\text{H), 1.64–1.55 \text{ (m, 1 H, C}\text{^9}H\text{H), 1.55 \text{ (dd, }^3J = 5.1 \text{ Hz, }^4J = 1.3 \text{ Hz, 1 H, C}\text{^5}H\text{), 1.30–1.23 \text{ (m, 1 H, C}\text{^5}H\text{H), 1.17–1.14 \text{ (m, 1 H, C}\text{^11}H\text{H), 1.14 \text{ (s, 3 H, C}\text{^13}H\text{H), 0.96 \text{ (d, }^3J = 7.0 \text{ Hz, 3 H, C}\text{^12}H\text{H), 0.93 \text{ (s, 3 H, C}\text{^14}H\text{H).}
\]
\(^{13}\text{C-NMR}\) (126 MHz, CDCl\(_3\)): \(\delta = 214.9\) (C\(^{17}\)), 90.5 (C\(^{16}\)), 85.1 (C\(^4\)), 81.9 (C\(^8\)), 65.4 (C\(^{13}\)), 62.9 (C\(^5\)), 52.4 (C\(^7\)), 51.5 (C\(^{11}\)), 51.0 (C\(^1\)), 41.4 (C\(^3\)), 37.4 (C\(^2\)), 35.2 (C\(^6\)), 33.4 (C\(^{15}\)), 27.6 (C\(^9\)), 23.1 (C\(^{10}\)), 20.0 (C\(^{14}\)), 19.3 (C\(^{18}\)), 15.3 (C\(^{12}\)).

**HRMS** (ESI): [M+NH\(_4\)]\(^+\) calculated: 374.1818 found: 374.1808.

**Compound 19b:**

TLC: \(R_t = 0.41\) (P/EtOAc = 6/1) [KMnO\(_4\)].

**IR** (ATR): \(\bar{\nu}\) (cm\(^{-1}\)) = 2956 (m, C-H), 2926 (m, C-H), 2870 (m, C-H), 1453 (w), 1230 (s), 1206 (s), 1158 (vs), 1059 (vs), 1080 (s), 938 (m).

\(^1\text{H-NMR}\) (500 MHz, CDCl\(_3\)): \(\delta = 5.93–5.83\) (m, 1 H, C\(^4\)H), 4.88 (d, \(3J = 6.2\) Hz, 1 H, C\(^{16}\)HH), 4.68 (d, \(3J = 6.2\) Hz, 1 H, C\(^{16}\)HH), 4.01 (dd, \(2J = 11.3\) Hz, \(3J = 4.2\) Hz, 1 H, C\(^{13}\)HH), 3.77 (\textit{v}irt. t, \(2J \cong 3J = 11.3\) Hz, 1 H, C\(^{13}\)HH), 2.59–2.49 (m, 1 H, C\(^3\)HH), 2.54 (s, 3 H, -SC\(^{18}\)H\(_3\)), 2.33 (dddd, \(2J = 12.0\) Hz, \(3J = 9.2\) Hz, \(4J = 4.6\) Hz, \(4J = 2.2\) Hz, 1 H, C\(^9\)H/H), 2.07 (dddd, \(3J = 11.4\) Hz, \(3J = 4.2\) Hz, \(4J = 1.6\) Hz, 1 H, C\(^3\)H), 1.95 (d, \(2J = 10.2\) Hz, 1 H, C\(^{11}\)HH), 1.93–1.86 (m, 1 H, C\(^9\)HH), 1.78 (ttdd, \(2J = 13.1\) Hz, \(3J = 4.7\) Hz, \(4J = 1.4\) Hz, 1 H, C\(^{10}\)HH), 1.64–1.55 (m, 1 H, C\(^9\)HH), 1.54–1.49 (m, 1 H, C\(^5\)H), 1.30–1.23 (m, 1 H, C\(^3\)HH), 1.17–1.14 (m, 1 H, C\(^{11}\)HH), 1.06 (s, 3 H, C\(^{15}\)H\(_3\)), 0.89 (d, \(3J = 7.0\) Hz, 3 H, C\(^{12}\)H\(_3\)), 0.88 (s, 3 H, C\(^{14}\)H\(_3\)).

\(^{13}\text{C-NMR}\) (126 MHz, CDCl\(_3\)): 215.4 (C\(^{17}\)), 90.5 (C\(^{16}\)), 84.0 (C\(^4\)), 82.3 (C\(^8\)), 65.2 (C\(^{13}\)), 63.0 (C\(^5\)), 51.9 (C\(^7\)), 50.9 (C\(^{11}\)), 48.6 (C\(^1\)), 38.9 (C\(^3\)), 37.1 (C\(^2\)), 33.8 (C\(^6\)), 33.2 (C\(^{15}\)), 26.8 (C\(^9\)), 22.0 (C\(^{10}\)), 19.2 (C\(^{14}\)), 18.5 (C\(^{18}\)), 14.3 (C\(^{12}\)).

**HRMS** (ESI): [M+NH\(_4\)]\(^+\) calculated: 374.1818 found: 374.1808.

\(S\)-methyl\(O\-(\(4\text{aR,5aR,6S,8R,8aS,10aS}\)-5,5,8-trimethylectahydro-\(4\text{H}-8\text{a,10a-methanooazuleno}[6,5-\text{d}][1,3]\text{dioxin-6-y}]\)carbonodithioate (19)

\[\text{C}_{18}\text{H}_{38}\text{O}_3\text{S}_2\] 356.5390 g/mol

Compound 19 was synthesized according to the procedure for the synthesis of compound \textit{rac-19}. Starting with compound 18 (70.0 mg, 263 \(\mu\)mol, 1.00 eq.) in THF (6.00 mL), using \(n\)-BuLi (210 \(\mu\)L, 526 \(\mu\)mol, 2.00 eq., as a 2.5 M solution in hexanes), carbon disulfide (215 \(\mu\)L,
271 mg, 3.56 mmol, 13.6 eq.) and iodomethane (431 µL, 982 mg, 6.92 mmol, 26.3 eq.), compound 19 (93.7 mg, 263 µmol, quant.) was obtained as a brown-yellow oil.

**Compound 19a:**

The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 19a agree with the data of compound rac-19a.

**Compound 19b:**

The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 19b agree with the data of compound rac-19b.
Xanthongenate ester rac-19 (187 mg, 524 μmol, 1.00 eq.) was dissolved in dry dioxane (22.0 mL) in a flame-dried Schlenk flask. Hypophosphoric acid (115 mg, 1.75 mmol, 3.33 eq., 231 μL as a 50% aqueous solution) and triethylamine (458 μL, 3.30 mmol, 6.30 eq.) were added dropwise. After addition of AIBN (47.4 mg, 288 μmol, 0.55 eq.), the mixture was heated up to 120 °C and stirred for 4 h. The reaction mixture was cooled to r.t. and slowly quenched with water (25 mL). After phase separation, the aq. layer was extracted with ether (4 × 25 mL). The combined organic layers were washed with brine (25 mL) and dried over Na2SO4. The volatiles were removed in vacuo and the crude product was purified by flash chromatography (P/EtOAc = 10/1) to obtain the desired product rac-20 as colorless crystals (124 mg, 496 μmol, 93%).

**TLC:** \( R_f = 0.36 \) (P/EtOAc = 12/1) [KMnO4].

**M.p.:** 65 °C.

**IR** (ATR): \( \bar{\nu} (\text{cm}^{-1}) = 2951 \) (s, C-H), 2862 (m, C-H), 2838 (m, C-H), 1450 (m), 1230 (s), 1159 (vs), 1081 (s), 1029 (vs), 1080 (s), 929 (s), 673 (w).

**1H-NMR** (500 MHz, CDCl3): \( \delta = 4.87 \) (d, \( ^2J = 6.2 \) Hz, 1 H, C16H), 4.69 (d, \( ^2J = 6.2 \) Hz, 1 H, C16H), 4.02 (dd, \( ^2J = 11.4 \) Hz, \( ^3J = 4.2 \) Hz, 1 H, C13H), 3.74 (virt. t, \( ^2J = 11.4 \) Hz, 1 H, C13H), 2.32–2.24 (m, 1 H, C9H), 1.99 (ddd, \( ^2J = 11.4 \) Hz, \( ^3J = 4.2 \) Hz, \( ^4J = 1.9 \) Hz, 1 H, C7H), 1.91 (d, \( ^2J = 10.0 \) Hz, 1 H, C11H), 1.86–1.72 (m, 2 H, CH2C), 1.60–1.43 (m, 5 H, CH2C, C5H, C9H, C10H), 1.28–1.21 (CH1H), 1.12 (dt, \( ^2J = 10.0 \) Hz, \( ^4J = 1.9 \) Hz, 1 H, C11H), 1.11–1.07 (m, 1 H, C3H), 0.99 (s, 3 H, C15H), 0.86 (d, \( ^3J = 6.6 \) Hz, 3 H, C12H), 0.77 (s, 3 H, C14H).

**13C-NMR** (75 MHz, CDCl3): \( \delta = 90.5 \) (C16), 82.7 (C8), 65.6 (C13), 59.3 (C5), 52.1 (C7), 50.8 (C1), 49.1 (C11), 39.0 (C2), 34.0 (C6), 33.2 (C15), 30.2 (C3), 27.0 (C9), 20.8 (2 C, C4, C10), 17.8 (C14), 14.3 (C12H).

**HRMS** (EI, 70 eV): [M+] calculated: 250.1927 found: 250.1928.
Compound 20 was synthesized according to the procedure for the synthesis of compound rac-20. Compound 19 (93.0 mg, 261 μmol, 1.00 eq.) in 1,4-dioxane (11.0 mL) was transformed via hypophosphoric acid (57.3, 869 μmol, 3.33 eq., 115 μL as a 50% aqueous solution), triethylamine (228 μL, 1.64 mmol, 6.30 eq.) and AIBN (23.6 mg, 143 μmol, 0.55 eq.) to the desired compound 20 (63.0 mg, 252 μmol, 96%) as colorless crystals.

The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 4 agree with the data of compound rac-4.

The analytic data for TLC, IR, $^1$H NMR, $^{13}$C NMR and HRMS of compound 20 agree with the data of compound rac-20.

M.p.: 37 °C.

Specific rotation: $[\alpha]_D^{20} = +13$ (c = 0.3, MeOH).
The observed analytical data was in perfect accordance with literature.\textsuperscript{[4]}
The relative configuration and constitution of the final product were secured by single crystal X-ray crystallographic analysis (figure 4, for details see 7. X-ray Crystallographic Details).

**Figure 4.** Crystal structure of racemic Agarozizanol B (rac-4).

(+)-Agarozizanol B (4)

(+)-Agarozizanol B (4) was synthesized according to the procedure for the synthesis of compound rac-4. Starting with compound 20 (59.0 mg, 221 µmol, 1.00 eq.), transformation via glacial acetic acid (66.5 mg, 63.3 µL, 1.11 µmol, 5.00 eq.) and trifluoroacetic anhydride (233 mg, 154 µL, 1.11 µmol, 5.00 eq.) gave the corresponding intermediate. Subsequent saponification with 1 N solution of NaOH (MeOH/ H₂O = 9:1, 826 µL) yielded desired product 4 as a colorless solid (51.1 mg, 214 µmol, 92%).

The analytic data for TLC, IR, ¹H NMR, ¹³C NMR and HRMS of compound 4 agree with the data of compound rac-4.

**M.p.:** 77 °C.

**Specific rotation:** [α]ᵣᵅ = +15 (c = 0.30, MeOH).
### 3. NMR comparison table for (+)-agarozizanol B

![Chemical structure of (+)-agarozizanol B](image)

| Position | δ_H (natural) | δ_H (synthetic) | Δ δ_H [ppm] | δ_C (natural) | δ_C (synthetic) | Δ δ_C [ppm] |
|----------|---------------|-----------------|-------------|---------------|----------------|-------------|
| 1        | 53.0          | 53.1            | 0.1         |               |                |             |
| 2        | 1.76          | 1.77-1.72       | -           | 40.2          | 40.2           | 0.0         |
| 3a       | 1.85          | 1.89-1.85       | -           | 31.5          | 31.6           | 0.1         |
| 3b       | 1.14          | 1.20-1.11       | -           |               |                |             |
| 4a       | 1.53          | 1.53            | -           | 21.9          | 22.0           | 0.1         |
| 4b       | 1.53          | 1.53            | -           | 21.9          | 22.0           | 0.1         |
| 5        | 1.54          | 1.54            | -           | 60.4          | 60.4           | 0.0         |
| 6        |               | 35.8            | 0.0         |               |                |             |
| 7        | 1.80          | 1.87-1.82       | -           | 58.1          | 58.1           | 0.0         |
| 8        |               | 83.6            | 0.0         |               |                |             |
| 9a       | 2.00          | 2.03-1.97       | -           | 32.2          | 32.2           | 0.0         |
| 9b       | 1.56          | 1.56            | -           | 32.2          | 32.2           | 0.0         |
| 10a      | 1.55          | 1.55            | -           |               |                |             |
| 10b      | 1.26          | 1.28-1.23       | -           | 21.8          | 21.8           | 0.0         |
| 11a      | 1.89          | 1.89            | 0.0         | 52.2          | 52.3           | 0.1         |
| 11b      | 1.09          | 1.09            | 0.0         |               |                |             |
| 12a      | 0.87          | 0.87            | 0.0         | 14.4          | 14.4           | 0.0         |
| 12b      | 0.87          | 0.87            | 0.0         | 14.4          | 14.4           | 0.0         |
| 13a      | 3.89          | 3.89            | 0.0         | 62.4          | 62.4           | 0.0         |
| 13b      | 3.77          | 3.80            | 0.0         | 62.4          | 62.4           | 0.0         |
| 14       | 0.79          | 0.79            | 0.0         | 17.8          | 17.9           | 0.1         |
| 15       | 1.06          | 1.06            | 0.0         | 33.9          | 34.0           | 0.1         |
4. Determination of the absolute configuration

After the synthesis of racemic Agarozizanol B (\textit{rac-4}), the (+)-enantiomer was selectively synthesized. The synthesis of the required ketone 15 was accomplished by a sequence of reduction-hydrogenation-oxidation. While reduction could be performed with NaBH$_4$ in MeOH to generate alcohol \textit{rac-14}, it was found that the reduction step can also be combined with a resolution step employing chiral oxazaborolidine 13 in a \textit{Corey-Bakshi-Shibata} (CBS) reduction.\textsuperscript{[1]} Under the given conditions the reduction is known to occur from the \textit{Re} face,\textsuperscript{[5]} illustrated in the scheme below in accordance to the initially proposed mechanism by \textit{Corey}, \textit{Bakshi} and \textit{Shibata}.\textsuperscript{[1]}

\begin{center}
\textbf{Scheme SI- 5.} Proposed \textit{Corey-Bakshi-Shibata} reduction delivering compound 14.
\end{center}
Lebsack et al. implemented a resolution step employing \((R)\)-oxazaborolidine 13 for the total synthesis of Shahamin K, using a similar ketone. The studies by Watanabe et al. also stabilize the proposed outcome (Scheme SI-6).\(^5\)

**Scheme SI-6.** CBS-studies by Lebsack et al. and Nakada with comparable ketone moieties.

HPLC-traces in comparison show the successful resolution (Scheme SI-7, racemic compound \textit{rac}-14 left, enantiomerically enriched compound 14 right).

**Scheme SI-7.** HPLC traces of compound \textit{rac}-14 (left) and compound 14 (right).

To confirm the absolute conformation, compound 16 was analysed by single crystal X-ray crystallography. A crystal structure was obtained of epimer \textit{epi}-16, due to epimerization in \(\alpha\)-position to the carbonyl moiety (figure 5). In the racemic series, iodide \textit{rac}-16 crystallized readily while crystallization of enantiopure compound 16 was not observed.
Figure 5. Crystal structure illustrating the absolute configuration of compound \textit{epi-16}.

Since \textit{epi-16} displays the same absolute configuration as \textbf{16}, except for the single stereogenic center in \(\alpha\)-position to the carbonyl group, the anomalous X-ray diffraction data for \textit{epi-16} confirm the absolute configuration of \textbf{16}. (For data see 7. X-ray Crystallographic Details).
5. Stereochemical assignment of rac-12

A direct conversion of photocascade product rac-11 to compound rac-15 with the prezizane skeleton was initially attempted. Unfortunately, hydrogenation conditions led to opening of the cyclopropane ring in a wrong fashion, obtaining compound rac-12. The stereochemical assignment of compound rac-12 as pictured below could be accomplished thanks to the identification of critical nOes. To assign all the hydrogen and carbon atoms of the compound, a set of 1D- and 2D-NMR experiments (\(^1\)H, \(^{13}\)C, COSY, HSQC, HMBC) were conducted.

Figure 6. Proton assignment by \(^1\)H NMR of the compound rac-12.
Figure 7. $^{13}$C NMR spectrum of compound \textit{rac}-12.

Figure 8. COSY experiment of compound \textit{rac}-12.
Figure 9. HSQC experiment of compound rac-12.

Figure 10. HMBC experiment for compound rac-12.
Once all the hydrogens were assigned, a NOESY experiment was conducted with the objective of the identification of critical nOes. In this regard, critical nOes were observed between H and one of the H in the dioxane ring (contact a), between H of the methyl group and H (contact b)), and between H and H (contact c)). What unambiguously establishes the relative configuration of the protons of the cyclohexanone moiety are the nOes between between H and one H of the methyl group in the cyclopentyl moiety (contact d)) and between H and H (contact e)). A $^3J$ coupling constant of 12.1 Hz was observed between H and H, which indicates a low dihedral angle between the two protons and supports the proposed structure. However, this relative configuration may be caused by epimerization of H. The nOes between H and H are observed (contact f) and the signal of H is observed as dd. Additionally to the nOe contacts listed above, the nOe contact between H and H (contact g)) was observed. Due to coupling of the respective protons and no further meaningful nOe contacts, the relative configuration of H cannot be fully confirmed, and the respective C-H bond is drawn as a wavy bond in the illustration pictured below.

Figure 11. NOESY experiment of compound rac-12.
6. **Stereochemical assignment of compound 14**

The stereochemical assignment of compound 14 could be accomplished thanks to the identification of critical nOes, as explained below. To assign all the hydrogen and carbon atoms of the compound, a set of 1D- and 2D-NMR experiments ($^1$H, $^{13}$C, COSY, HSQC, HMBC) were conducted.

![Proton assignment by $^1$H NMR of compound 14.](image)

**Figure 12.** Proton assignment by $^1$H NMR of compound 14.
Figure 13. $^{13}$C NMR spectrum of compound 14.

Figure 14. COSY experiment of compound 14.
Figure 15. HSQC experiment of compound 14.

Figure 16. HMBC experiment of compound 14.
Once all the hydrogens were assigned, a NOESY experiment was conducted with the objective of the identification of critical nOes. In this regard, a critical nOe was observed between H and the CH$_3$ in the cyclopentane ring (contact a)), what unambiguously establishes the relative configuration of the hydroxy group in the desired compound 14. In addition, a critical nOe was observed between CH$_3$ and the olefinic H (contact b)) which clarifies the relative configuration of the methyl group in the cyclopentanol-ring.

![Figure 17. NOESY experiment of compound 14.](image-url)
7. X-ray Crystallographic Details

Data were collected on a single crystal X-ray diffractometer equipped with a CMOS detector (Bruker Photon-100), a TXS rotating anode with MoKα radiation (λ = 0.71073 Å) and a Helios optic (compound epi-16) or a CPAD detector (Bruker Photon II), IMS microsources with MoKα radiation (λ = 0.71073 Å) (compounds rac-11, rac-15, rac-16) and CuKα radiation (λ = 1.54178 Å) (compound rac-4) and a Helios optic using APEX3 software package.[6] The measurement was performed on a single crystal coated with perfluorinated ether. The crystals were fixed on top of a kapton micro sampler and frozen under a stream of cold nitrogen. A matrix scan was used to determine the initial lattice parameters. Reflections were corrected for Lorentz and polarisation effects, scan speed, and background using SAINT.[7] Absorption correction, including odd and even ordered spherical harmonics was performed using SADABS.[7] Space group assignment was based upon systematic absences, E statistics, and successful refinement of the structure. The structures were solved using SHELXT with the aid of successive difference Fourier maps, and were refined against all data using SHELXL in conjunction with SHELXLE.[8,9,10] Hydrogen atoms were calculated in ideal positions as follows: Methyl hydrogen atoms were refined as part of rigid rotating groups, with a C–H distance of 0.98 Å and U_{iso}(H) = 1.5\cdot U_{eq}(C). Non-methyl H atoms were placed in calculated positions and refined using a riding model with methylene, aromatic, and other C–H distances of 0.99 Å, 0.95 Å and 1.00 Å, respectively, and U_{iso}(H) = 1.2\cdot U_{eq}(C). Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bound to heteroatoms were refined freely, if possible. A split-layer refinement was used for disordered groups or molecules and similarity and rigid-body restraints were employed to stabilise the refinement of the layers, if necessary. Full-matrix least-squares refinements were carried out by minimizing Σw(F_o^2 - F_c^2)^2 with the SHELXL weighting scheme.[8] Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from International Tables for Crystallography.[11] Images of the crystal structure were generated with Mercury and PLATON.[12,13] CCDC 2095909-2095913 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.
Compound *rac*-4 (CCDC 2095912)

Diffractometer operator C. Jandl
scanspeed 3-30 s per frame
dx 37 mm
2938 frames measured in 9 data sets
phi-scans with delta phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

\[ \text{C}_{15}\text{H}_{26}\text{O}_{2} \]

\[ M_r = 238.36 \]

Triclinic, \( \overline{P1} \)

Hall symbol: -\( P \)

Melting point: \(? \) K

\( a = 9.6620 (4) \) Å

\( b = 9.7612 (5) \) Å

\( c = 14.9153 (7) \) Å

\( \alpha = 83.239 (2)^\circ \)

\( \beta = 80.006 (2)^\circ \)

\( \gamma = 87.825 (2)^\circ \)

\( V = 1375.50 (11) \) Å\(^3\)

\( Z = 4 \)

\[ F(000) = 528 \]

\[ D_x = 1.151 \) Mg m\(^{-3}\)

Mo \( K\alpha \) radiation, \( \lambda = 0.71073 \) Å

Cell parameters from 9909 reflections

\( \theta = 2.4-25.7^\circ \)

\( \mu = 0.07 \) mm\(^{-1}\)

\( T = 100 \) K

Fragment, colourless

\( 0.28 \times 0.26 \times 0.11 \) mm
Data collection

Bruker D8 Venture diffractometer 5035 independent reflections
Radiation source: IMS microsource 4549 reflections with $I > 2\sigma(I)$
Helios optic monochromator $R_{int} = 0.037$
Detector resolution: 7.5 pixels mm$^{-1}$ $\theta_{max} = 25.4^\circ$, $\theta_{min} = 2.1^\circ$
phi– and $\omega$–rotation scans $h = -11$ 11
Absorption correction: multi-scan SADABS 2016/2, Bruker $k = -11$ 11
$T_{\min} = 0.716$, $T_{\max} = 0.745$ $l = -17$ 17
60441 measured reflections

Refinement

Refinement on $F^2$ Secondary atom site location: difference Fourier map
Least-squares matrix: full Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)] = 0.044$ H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.116$ $W = 1/[\Sigma(FO^2) + (0.0508P)^2 + 0.6184P]$
$S = 1.08$ WHERE $P = (FO^2 + 2FC^2)/3$
5035 reflections $(\Delta/\sigma)_{\text{max}} \leq 0.001$
482 parameters $\Delta\rho_{\text{max}} = 0.23$ e Å$^{-3}$
732 restraints $\Delta\rho_{\text{min}} = -0.30$ e Å$^{-3}$
0 constraints Extinction correction: none
Primary atom site location: iterative Extinction coefficient: -
**Compound rac-11 (CCDC 2095909)**

Diffractometer operator C. Jandl
scanspeed 1-5 s per frame
dx 37 mm
2402 frames measured in 18 data sets
phi-scans with delta_phi = 1.0
omega-scans with delta_omega = 1.0
shutterless mode

**Crystal data**

\[
C_{16}H_{20}O_3
\]

\[M_r = 260.32\]

Orthorhombic, \(P2_12_12_1\)

Hall symbol: \(P 2ac 2ab\)

\[\alpha = 6.0253 \text{ (6) \AA}\]

\[b = 12.9827 \text{ (12) \AA}\]

\[c = 16.8046 \text{ (16) \AA}\]

\[V = 1314.5 \text{ (2) \AA}^3\]

\[Z = 4\]

\[F(000) = 560\]

\[D_x = 1.315 \text{ Mg m}^{-3}\]

Melting point: 2 K

Cu \(K\alpha\) radiation, \(\lambda = 1.54178 \text{ \AA}\)

Cell parameters from 9812 reflections

\[\theta = 6.3 - 72.1^\circ\]

\[\mu = 0.72 \text{ mm}^{-1}\]

\[T = 100 \text{ K}\]

Fragment, colourless

\[0.37 \times 0.28 \times 0.25 \text{ mm}\]
**Data collection**

| Details | Values |
|---------|--------|
| Bruker D8 Venture diffractometer | 2479 independent reflections |
| Radiation source: IMS microsource | 2469 reflections with $I > 2\sigma(I)$ |
| Helios optic monochromator | $R_{\text{int}} = 0.041$ |
| Detector resolution: 7.5 pixels mm$^{-1}$ | $\theta_{\text{max}} = 70.0^\circ$, $\theta_{\text{min}} = 6.3^\circ$ |
| phi- and o-rotation scans | $h = -7$ 7 |
| Absorption correction: multi-scan | $k = -15$ 15 |
| SADABS 2016/2, Bruker | $l = -20$ 20 |
| $T_{\text{min}} = 0.613$, $T_{\text{max}} = 0.754$ | 21803 measured reflections |

**Refinement**

Refinement on $F^2$

| Least-squares matrix: | full |
|-----------------------|------|
| $R[F^2 > 2\sigma(F^2)] = 0.029$ | Hydrogen site location: inferred from neighbouring sites |
| $wR(F^2) = 0.074$ | H-atom parameters constrained |
| $S = 1.08$ | $W = 1/\sum^2(FO^2) + (0.0409P)^2 + 0.3022P$ |
| 2479 reflections | WHERE $P = (FO^2 + 2FC^2)/3$ |
| 175 parameters | $(\Delta/\sigma)_{\text{max}} < 0.001$ |
| 0 restraints | $\Delta\rho_{\text{max}} = 0.28$ e Å$^{-3}$ |
| 0 constraints | $\Delta\rho_{\text{min}} = -0.17$ e Å$^{-3}$ |
| Primary atom site location: iterative | Extinction correction: none |
| Secondary atom site location: difference Fourier map | Extinction coefficient: $z$ |
| Absolute structure: Flack, Parsons$^{[14,15]}$ | Absolute structure parameter: 0.01 (4) |
Compound *rac*-15 (CCDC 2095911)

Diffractometer operator C. Jandl
scanspeed 1-5 s per frame
dx 40 mm
2945 frames measured in 15 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

*Crystal data*

\[ \text{C}_{16}\text{H}_{22}\text{O}_3 \] \hspace{1cm} F(000) = 284 

\[ M_r = 262.34 \]

Triclinic, \( P\bar{1} \)

Hall symbol: \(-P\bar{1}\)

Melting point: ? K

\( a = 8.2480 (8) \) Å \hspace{1cm} \text{Mo K}\alpha\text{ radiation, } \lambda = 0.71073 \) Å

\( b = 8.8290 (8) \) Å \hspace{1cm} \text{Cell parameters from 9814 reflections}

\( c = 9.8685 (10) \) Å \hspace{1cm} \theta = 2.2 - 25.7°

\( \alpha = 100.088 (3)° \) \hspace{1cm} \mu = 0.09 \text{ mm}^{-1}

\( \beta = 100.702 (3)° \) \hspace{1cm} T = 100 K

\( \gamma = 102.998 (3)° \)

\( V = 670.15 (11) \text{ Å}^3 \) \hspace{1cm} Fragment, colourless

\( 0.45 \times 0.30 \times 0.20 \text{ mm} \)

\( Z = 2 \)
Data collection

Bruker D8 Venture diffractometer

2532 independent reflections

Radiation source: IMS microsource

2437 reflections with $I > 2\sigma(I)$

Helios optic monochromator

$R_{int} = 0.027$

Detector resolution: 7.5 pixels mm$^{-1}$

$\theta_{\text{max}} = 25.7^\circ$, $\theta_{\text{min}} = 2.4^\circ$

phi– and o–rotation scans

$h = -10 \text{ to } 10$

$k = -10 \text{ to } 10$

Absorption correction: multi-scan

$SADABS 2016/2$, Bruker

$T_{\text{min}} = 0.717$, $T_{\text{max}} = 0.745$

$l = -12 \text{ to } 12$

29709 measured reflections

Refinement

Refinement on $F^2$

Secondary atom site location: difference Fourier map

Least-squares matrix: full

Hydrogen site location: inferred from neighbouring sites

$R[F^2 > 2\sigma(F^2)] = 0.036$

H-atom parameters constrained

$wR(F^2) = 0.090$

$W = 1/[\Sigma^2(FO^2) + (0.042P)^2 + 0.3685P]\$

WHERE $P = (FO^2 + 2FC^2)/3$

$(\Delta/\sigma)_{\text{max}} \leq 0.001$

2532 reflections

$\Delta\rho_{\text{max}} = 0.34 \text{ e Å}^{-3}$

175 parameters

$\Delta\rho_{\text{min}} = -0.21 \text{ e Å}^{-3}$

0 restraints

Extinction correction: none

0 constraints

Extinction coefficient: -

Primary atom site location: iterative
Compound rac-16 (CCDC 2095910)

Diffractometer operator C. Jandl
scanspeed 1-5 s per frame
dx 40 mm
1895 frames measured in 9 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

\(\text{C}_{16}\text{H}_{23}\text{IO}_3\)

\(M_r = 390.24\)

Monoclinic, \(P2_1/c\)

Hall symbol: -\(P\ 2ybc\)

\(a = 9.9676 (11) \text{ Å}\)

\(b = 11.9343 (14) \text{ Å}\)

\(c = 13.7168 (16) \text{ Å}\)

\(\beta = 110.874 (3)^\circ\)

\(V = 1524.6 (3) \text{ Å}^3\)

\(Z = 4\)

\(F(000) = 784\)

\(D_x = 1.700 \text{ Mg m}^{-3}\)

Melting point: ? K

\(\text{Mo }K\alpha \text{ radiation}, \lambda = 0.71073 \text{ Å}\)

Cell parameters from 9926 reflections

\(\theta = 2.3-26.7^\circ\)

\(\mu = 2.11 \text{ mm}^{-1}\)

\(T = 100 \text{ K}\)

Fragment, colourless

\(0.49 \times 0.32 \times 0.16 \text{ mm}\)
Data collection

Bruker D8 Venture
diffractometer
3114 independent reflections

Radiation source: IMS microsource
3100 reflections with \( I > 2\sigma(I) \)

Helios optic monochromator
\( R_{int} = 0.029 \)

Detector resolution: 7.5 pixels mm\(^{-1}\)
\( \theta_{\text{max}} = 26.4^\circ, \theta_{\text{min}} = 2.3^\circ \)

phi– and o–rotation scans
\( h = -12 \quad 12 \)

Absorption correction: multi-scan
SADABS 2016/2, Bruker
\( k = -14 \quad 14 \)

\( T_{\min} = 0.584, T_{\max} = 0.745 \)
\( l = -17 \quad 17 \)

41334 measured reflections

Refinement

Refinement on \( F^2 \)

Secondary atom site location: difference
Fourier map

Least-squares matrix: full

Hydrogen site location: inferred from neighbouring sites

\( R[F^2 > 2\sigma(F^2)] = 0.020 \)

H-atom parameters constrained

\( wR(F^2) = 0.045 \)

\( W = 1/[\Sigma(FO^2) + 2.0338P] \) WHERE \( P = (FO^2 + 2FC^2)/3 \)

\( S = 1.28 \)

\( (\Delta\sigma)_{\text{max}} = 0.001 \)

3114 reflections
\( \Delta\rho_{\text{max}} = 0.46 \) e Å\(^{-3}\)

194 parameters
\( \Delta\rho_{\text{min}} = -0.61 \) e Å\(^{-3}\)

0 restraints

Extinction correction: none

0 constraints

Extinction coefficient: –

Primary atom site location: iterative
Compound epi-16 (CCDC 2095913)

Diffractometer operator C. Jandl
scanspeed 1-10 s per frame
dx 50 mm
4771 frames measured in 18 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

C\textsubscript{16}H\textsubscript{23}IO\textsubscript{3}

\(M_r = 390.24\) \hspace{1cm} \(D_x = 1.740 \text{ Mg m}^{-3}\)

Orthorhombic, \(P2_12_12_1\)

Hall symbol: \(P 2\ac 2\ab\)

Melting point: \(\text{?} \text{ K}\)

Mo K\(\alpha\) radiation, \(\lambda = 0.71073 \text{ Å}\)

Cell parameters from 9556 reflections

\(a = 8.6775 (10) \text{ Å}\)
\(b = 10.6368 (12) \text{ Å}\)
\(c = 16.1426 (18) \text{ Å}\)

\(\theta = 2.3–28.3°\)
\(\mu = 2.15 \text{ mm}^{-1}\)

\(V = 1490.0 (3) \text{ Å}^3\)

\(T = 100 \text{ K}\)

\(Z = 4\)

Fragment, colourless

\(F(000) = 784\)

0.27 × 0.17 × 0.05 mm
Data collection

Bruker D8 Venture diffractometer
3540 independent reflections

Radiation source: TXS rotating anode
3512 reflections with $I > 2\sigma(I)$

Helios optic monochromator
$R_{int} = 0.042$

Detector resolution: 16 pixels mm$^{-1}$
$\theta_{\text{max}} = 27.9^\circ$, $\theta_{\text{min}} = 2.3^\circ$

phi– and $\omega$–rotation scans
$h = -11$ 11

Absorption correction: multi-scan
SADABS 2016/2, Bruker
$k = -13$ 13

$T_{\text{min}} = 0.638$, $T_{\text{max}} = 0.746$
$l = -21$ 21

89553 measured reflections

Refinement

Refinement on $F^2$
Hydrogen site location: inferred from neighbouring sites

Least-squares matrix: full
H-atom parameters constrained

$R[F^2 > 2\sigma(F^2)] = 0.017$

$wR(F^2) = 0.045$

$S = 1.06$

3540 reflections

184 parameters

0 restraints

0 constraints

Primary atom site location: iterative

Secondary atom site location: difference Fourier map

8. NMR spectra

The $^1$H NMR and $^{13}$C NMR spectra of unknown compound are shown below.
**Compound D:** $^1$H NMR (300 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)*

*The $^{13}$C NMR spectrum of compound D shows traces of MEMCl that could not be removed.*
Compound rac-7: $^1$H NMR (400 MHz, CDCl₃, 298 K)

$^{13}$C NMR (101 MHz, CDCl₃, 298 K)
**Compound rac-11**: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

![NMR spectrum of compound rac-11](image1)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)

![NMR spectrum of compound rac-11](image2)
Compound rac-11*: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)
Compound *rac*-12: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)
**Compound 14**: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

[Chemical structure image]

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)

[Chemical structure image]
**Compound 14**: \(^1\)H NMR (400 MHz, CDCl\(_3\), 298 K)

\[^{13}\text{C}\] NMR (101 MHz, CDCl\(_3\), 298 K)
Compound 15: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)
**Compound 16**: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

![NMR spectrum of Compound 16](image)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)

![NMR spectrum of Compound 16](image)
Compound 17: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$ 298 K)
Compound 18a: $^1$H NMR (500 MHz, CDCl$_3$ 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$ 298 K)
Compound 18b: $^1$H NMR (500 MHz, CDCl$_3$, 298 K)*

*The $^1$H NMR-spectrum of compound 18b still shows the signals of ethylacetate and acetone, which were not possible to be removed due to the viscosity of the compound.

$^{13}$C NMR (75 MHz, CDCl$_3$, 298 K)
**Compound 19:** $^1$H NMR (500 MHz, CDCl$_3$, 298 K)

![NMR Spectrum](image)

$^{13}$C NMR (126 MHz, CDCl$_3$ 298 K)

![NMR Spectrum](image)
Compound 20: $^1$H NMR (400 MHz, CDCl$_3$, 298 K)

$^{13}$C NMR (101 MHz, CDCl$_3$, 298 K)
(+)-Agarozizanol B: $^1$H NMR (500 MHz, MeOD, 298 K)

$^{13}$C NMR (101 MHz, MeOD 298 K)
9. **HPLC Traces**

(1R,3S,3a1R,4aR,8aS,10aS)-1,4,4-trimethyl-2,3,4a,5-tetrahydro-1H,3a1H,4H-cyclopenta[1',2']cyclopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-ol (14)

![Chemical Structure](image)

**Table 1: HPLC Data for Compound 14**

| No. | Ret. Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel. Area (%) | Amount (%) | Type |
|-----|-----------------|-----------|--------------|----------------|---------------|------------|------|
| 1   | 10.99           | n.a.      | 100,003      | 24,346         | 50.66         | n.a.       | BMB  |
| 2   | 13.30           | n.a.      | 91,213       | 23,715         | 49.34         | n.a.       | BMB  |
| Total |                 |           | 191,217      | 48,051         | 100.00        | 0.000      |      |

**Table 2: HPLC Data for Compound 14 (modified by COMPUTER)**

| No. | Ret. Time (min) | Peak Name | Height (mAU) | Area (mAU*min) | Rel. Area (%) | Amount (%) | Type |
|-----|-----------------|-----------|--------------|----------------|---------------|------------|------|
| 1   | 10.98           | n.a.      | 262,275      | 70,798         | 98.01         | n.a.       | BMB  |
| 2   | 12.90           | n.a.      | 6,989        | 1,437          | 1.99          | n.a.       | BMB  |
| Total |                 |           | 269,234      | 72,235         | 100.00        | 0.000      |      |
(1S,3S,3a1S,4aS,8aR)-1,4,4-trimethyl-2,3,4a,5-tetrahydro-1H,3a1H,4H-cyclopenta-
[1',2']cyclopropa[3,4]pentaleno[6a,1-d][1,3]dioxin-3-ol (14')

14' (96% ee)
(1R,3a1R,4aR,8aS,10aS)-1,4,4-trimethyl-1,2,4a,5-tetrahydro-3H,3a1H,4H-cyclopenta-[1',2']cyclopropa[3,4]pentalen[6a,1-d][1,3]dioxin-3-one. (15)

15 (96% ee)
10. References

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