Supporting Information

An Unexpected Transannular [4+2] Cycloaddition during the Total Synthesis of (+)-Norcembrene 5

Michael Breunig*, Po Yuan*, and Tanja Gaich*

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All reactions were carried out in oven- or flame-dried glassware. Anhydrous solvents were used for all reactions besides solvent mixtures with water unless stated otherwise. All anhydrous solvents (THF, CH₂Cl₂, Et₂O, PhH, DMF, MeCN, PhMe, MeOH, EtOH, pyridine) were purchased from Acros Organics or Sigma-Aldrich and used as received. Solvents used for flash column chromatography were distilled prior to use. Commercially available reagents were used as supplied unless stated otherwise. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with silica gel 60-F254 aluminum plates from Merck. TLC plates were visualized by exposure to ultraviolet light (UV, 254 nm) and/or exposure to an aqueous solution of potassium permanganate (KMnO₄), an aqueous solution of ceric ammonium molybdate (CAM), an ethanolic solution of vanillin or an ethanolic solution of 4-anisaldehyde followed by heating with a heat gun. Flash column chromatography was performed with silica gel 60 M (40–63 μm) from Macherey-Nagel. Preparative thin layer chromatography was performed with silica gel 60-F254 aluminum plates from Merck. Yields refer to chromatographically and spectroscopically pure compounds unless stated otherwise. NMR spectra were recorded on a 400 MHz spectrometer (Avance III 400), a 600 MHz spectrometer (Avance III 600) with and without cryoplatform or an 800 MHz spectrometer (Avance NEO) with cryoplatform from Bruker. All NMR spectra were measured in CDCl₃ solution and referenced to the residual CHCl₃ signal (¹H, δ = 7.26 ppm, ¹³C, δ = 77.16 ppm). All ¹H and ¹³C shifts are given in ppm (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal). Assignments of proton resonance were confirmed, when possible, by correlated spectroscopy. High resolution mass spectra were measured on an LTQ Orbitrap Velos spectrometer from Thermo Fisher Scientific (Velos Pro) with or without loop-mode injection from a Waters (RP18) HPLC system or a Micromass LCT spectrometer via loop-mode injection from a Waters (Alliance 2695) HPLC system. Ionization was achieved by ESI, modes of ionization, calculated and found mass are given. IR spectra were measured on a PerkinElmer Spectrum 100 FT-IR spectrometer. Optical rotation values were measured on a Jasco P-2000 Digital Polarimeter using the sodium D line (589 nm). X-ray diffraction analysis of single crystals was performed at 100 K on a STOE IPDS-II diffractometer equipped with a graphite-monochromated radiation source (λ = 0.71073 Å) and an image plate detection system. A crystal mounted on a fine glass fiber with silicon grease was employed.
2. Experimental Procedures and Characterization Data

2-allylfuran (14)

![2-allylfuran](image)

To a solution of furan (9.87 g, 145 mmol, 1.2 equiv) in THF (53 mL) was added *n*-butyllithium (2.5 M in hexanes, 53.2 mL, 133 mmol, 1.1 equiv) dropwise at –78 °C. The reaction mixture was allowed to warm to 0 °C and stirred for 2.5 h. Then, the reaction mixture was cooled to –78 °C and a solution of allyl bromide (14.6 g, 121 mmol, 1 equiv) in THF (12 mL) was added dropwise. The reaction mixture was allowed to warm to 0 °C and stirred for 1 h. The reaction was quenched by the addition of brine (4 mL) and diluted with water (70 mL). The aqueous layer was extracted with Et₂O (2 × 100 mL). The combined organic layers were washed with water (70 mL) and brine (70 mL), dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by fractional distillation at atmospheric pressure (b.p. 112 °C) under nitrogen to obtain 2-allylfuran (14, 8.82 g, 81.6 mmol, 67%) as colorless liquid. Analytical data for 14 were in full agreement with previously reported values.[1]

1H NMR (400 MHz, CDCl₃): δ = 7.32 (dd, J = 1.9, 0.8 Hz, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.03–6.01 (m, 1H), 5.94 (ddt, J = 16.7, 10.1, 6.6 Hz, 1H), 5.18–5.10 (m, 2H), 3.42–3.38 (m, 2H) ppm.

(E)-4-(furan-2-yl)but-2-enoic acid (15)

![E-4-(furan-2-yl)but-2-enoic acid](image)

Acrylic acid (2.40 g, 33.2 mmol, 1 equiv) was dissolved in CH₂Cl₂ (165 mL). 2-Allylfuran (14, 7.19 g, 66.5 mmol, 2.0 equiv) and Hoveyda–Grubbs II catalyst (208 mg, 0.332 mmol, 0.01 equiv) were sequentially added and the reaction mixture was heated to reflux for 14 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 4:1 to 3:1) to yield (E)-4-(furan-2-yl)but-2-enoic acid (15, 4.52 g, 29.7 mmol, 89%) as dark yellow oil and dimer (E)-1,4-di(furan-2-yl)but-2-ene (A, 3.04 g, 16.2 mmol) as yellow oil. Dimer A could be used in a further reaction cycle.
(E)-4-(furan-2-yl)but-2-enoic acid (15):

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta = 7.35$ (d, $J = 1.8$ Hz, 1H), 7.14 (dt, $J = 15.6$, 6.5 Hz, 1H), 6.32 (dd, $J = 3.2$, 1.9 Hz, 1H), 6.10 (d, $J = 3.0$ Hz, 1H), 5.88 (dt, $J = 15.6$, 1.7 Hz, 1H), 3.58 (d, $J = 6.5$ Hz, 2H) ppm.

$^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 171.1, 151.0, 146.7, 142.1, 122.5, 110.6, 106.9, 31.1$ ppm.

IR (neat sample): 3012, 1694, 1653, 1506, 1420, 1285, 1209, 1011, 984, 928, 807, 733 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_8$H$_9$O$_3$ [M+H]$^+$: 153.0552, found: 153.0544.

$R_f$: 0.25 (PE/EtOAc, 4:1).

(E)-1,4-di(furan-2-yl)but-2-ene (A):

$^{1}H$ NMR (400 MHz, CDCl$_3$): $\delta = 7.32$ (dd, $J = 1.9$, 0.9 Hz, 1H), 6.29 (dd, $J = 3.2$, 1.9 Hz, 1H), 6.04–5.98 (m, 1H), 5.70–5.67 (m, 1H), 3.39 (d, $J = 4.4$ Hz, 2H) ppm.

$^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta = 154.4, 141.4, 128.1, 110.4, 105.5, 31.4$ ppm.

IR (neat sample): 1596, 1506, 1424, 1174, 1146, 1075, 1008, 968, 935, 884, 798, 724 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{12}$H$_{13}$O$_2$ [M+H]$^+$: 189.0916, found: 189.0909.

$R_f$: 0.94 (PE/EtOAc, 4:1).

(E)-4-(furan-2-yl)but-2-enoic acid (15) from (E)-1,4-di(furan-2-yl)but-2-ene (A)

(15)

(E)-1,4-di(furan-2-yl)but-2-ene (A, 6.34 g, 33.7 mmol, 1 equiv) was dissolved in CH$_2$Cl$_2$ (170 mL). Acrylic acid (2.43 g, 33.7 mmol, 1 equiv) and Hoveyda–Grubbs II catalyst (211 mg, 0.337 mmol, 0.01 equiv) were sequentially added and the reaction mixture was heated to reflux for 15 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 9:1 to 3:1) to afford (E)-4-(furan-2-yl)but-2-enoic acid (15, 4.43 g, 29.1 mmol, 86%) as dark yellow oil and starting material (E)-1,4-di(furan-2-yl)but-2-ene (A, 3.12 g, 16.6 mmol) as yellow oil. The starting material could be used in a further reaction cycle.
To a solution of carboxylic acid 15 (2.57 g, 16.9 mmol, 1 equiv) in CH₂Cl₂ (170 mL) were sequentially added oxalyl chloride (2.57 g, 20.3 mmol, 1.2 equiv) and catalytic amounts of DMF (30 drops) at 0 °C. After 15 min, the strong gas evolution ceased and the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. The reaction mixture was concentrated under reduced pressure and the crude acid chloride was used without further purification.

(S)-4-phenyloxazolidin-2-one (3.17 g, 19.4 mmol, 1.15 equiv) was dissolved in THF (190 mL) and the mixture was cooled to −78 °C. n-Butyllithium (2.5 M in hexanes, 7.43 mL, 18.6 mmol, 1.1 equiv) was added dropwise and the reaction mixture was stirred at −78 °C for 2 h. The crude acid chloride was dissolved in THF (170 mL), the mixture was cooled to −78 °C and the first reaction mixture with the lithiated oxazolidinone was added dropwise via cannula. After complete addition, the mixture was stirred for further 30 min. Then, aqueous KHSO₄ solution (0.5 M, 600 mL) was added and the mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et₂O (3 × 400 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 4:1) to yield (S,E)-3-(4-(furan-2-yl)but-2-enoyl)-4-phenyloxazolidin-2-one (13, 4.07 g, 13.7 mmol, 81%) as dark yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.41–7.29 (m, 7H), 7.13 (dt, J = 15.3, 6.8 Hz, 1H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.07 (d, J = 3.2 Hz, 1H), 5.48 (dd, J = 8.7, 3.9 Hz, 1H), 4.70 (dd, J = 8.8, 8.8 Hz, 1H), 4.29 (dd, J = 8.9, 3.9 Hz, 1H), 3.60 (d, J = 6.7 Hz, 2H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 164.4, 153.8, 151.3, 146.1, 141.9, 139.1, 129.3, 128.9, 126.1, 122.2, 110.6, 106.7, 70.1, 57.9, 31.4 ppm.

IR (neat sample): 1775, 1686, 1637, 1384, 1353, 1384, 1353, 1322, 1281, 1198, 1110, 1061, 1010, 935, 736, 710 cm⁻¹.

HRMS (ESI): m/z calcd for C₁₇H₁₆NO₄ [M+H]⁺: 298.1079, found: 298.1071.

[α]D²: +103.8 (c 0.24, CHCl₃).

Rf: 0.33 (PE/EtOAc, 4:1).
Freshly recrystallized copper(I) bromide dimethyl sulfide complex (7.67 g, 37.3 mmol, 1.3 equiv) was dispersed in THF (150 mL) and the mixture was cooled to –78 °C. Isopropenylmagnesium bromide (0.5 M in THF, 74.6 mL, 37.3 mmol, 1.3 equiv) was added dropwise and the dark red solution was stirred at –78 °C for 70 min. Then, compound 13 (8.53 g, 28.7 mmol, 1 equiv) dissolved in THF (95 mL) was added dropwise and the reaction mixture was stirred for 1 h. Saturated aqueous NH₄Cl solution (400 mL) was added and the mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et₂O (3 × 550 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure to obtain 16 (9.69 g, 28.6 mmol, quant.) as ocher solid, which was used in the next step without further purification. An analytical sample was purified by flash column chromatography on silica gel (PE/EtOAc = 7:1).

**1H NMR** (400 MHz, CDCl₃): δ = 7.38–7.23 (m, 6H), 6.25 (dd, J = 3.0, 1.8 Hz, 1H), 6.00 (d, J = 3.2 Hz, 1H), 5.36 (dd, J = 8.7, 3.7 Hz, 1H), 4.70–4.61 (m, 3H), 4.23 (dd, J = 8.9, 3.7 Hz, 1H), 3.21–3.11 (m, 1H), 3.08–2.98 (m, 2H), 2.80–2.65 (m, 2H), 1.67 (s, 3H) ppm.

**13C NMR** (100 MHz, CDCl₃): δ = 171.4, 153.8, 153.8, 146.3, 141.3, 139.1, 129.2, 128.7, 126.0, 111.9, 110.1, 106.5, 70.0, 57.7, 42.0, 38.8, 32.2, 20.1 ppm.

**IR** (neat sample): 2921, 1775, 1702, 1457, 1382, 1320, 1194, 1107, 1044, 1007, 896, 732, 699 cm⁻¹.

**HRMS** (ESI): m/z calcd for C₂₀H₂₁NNaO₄ [M+Na]⁺: 362.1368, found: 362.1367.

[α]D⁺: +71.6 (c 0.23, CHCl₃).

**m.p.:** 113 °C.

**Rf:** 0.43 (PE/EtOAc, 4:1).
To a solution of oxazolidinone 16 (3.00 g, 8.84 mmol, 1 equiv) in CH$_2$Cl$_2$ (88 mL) was added DIBAL-H (1.0 M in hexane, 17.7 mL, 17.7 mmol, 2.0 equiv) dropwise at −78 °C. After complete addition, the reaction mixture was stirred for 20 min. Saturated aqueous Na/K-tartrate solution (340 mL) was added, the mixture was diluted with CH$_2$Cl$_2$ (250 mL) and allowed to warm to room temperature. After stirring vigorously for 2 h, the layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 300 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 7:1) to obtain aldehyde 11 (1.22 g, 6.85 mmol, 77%) as bright yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$): δ = 9.59 (t, J = 2.3 Hz, 1H), 7.33–7.28 (m, 1H), 6.27 (dd, J = 3.2, 1.9 Hz, 1H), 6.04–6.02 (m, 1H), 4.83–4.75 (m, 2H), 3.10–3.01 (m, 1H), 2.82 (dd, J = 14.9, 6.5 Hz, 1H), 2.68 (dd, J = 14.9, 8.2 Hz, 1H), 2.51–2.45 (m, 2H), 1.73 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 201.8, 153.4, 145.9, 141.5, 112.4, 110.3, 106.9, 46.7, 40.8, 32.5, 19.9 ppm.

IR (neat sample): 2918, 2727, 1722, 1646, 1596, 1507, 1436, 1377, 1146, 1009, 897, 804, 732 cm$^{-1}$.

HRMS (ESI): m/z calcd for C$_{11}$H$_{15}$O$_2$ [M+H]$^+$: 179.1072, found: 179.1067.

[$\alpha$]$_D^{24}$: +24.8 (c 0.24, CHCl$_3$).

$R_f$: 0.73 (PE/EtOAc, 3:1).

(R)-oxiran-2-ylmethyl 4-methylbenzenesulphonate (B)

To a solution of (S)-(−)-glycidol (4.93 g, 66.6 mmol, 1.05 equiv) in CH$_2$Cl$_2$ (60 mL) were sequentially added triethylamine (13.47 g, 133 mmol, 2.1 equiv) and DMAP (407 mg, 3.33 mmol, 0.05 equiv). The reaction mixture was cooled to 0 °C and a solution of tosyl chloride (12.1 g, 63.2 mmol, 1 equiv) in CH$_2$Cl$_2$
(60 mL) was added dropwise. After stirring at 0 °C for 50 min, aqueous NaHSO₄ solution (0.5 M, 130 mL) was added. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 130 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 4:1 to 3:1) to afford tosylate B (13.5 g, 59.0 mmol, 93%) as colorless oil. Analytical data for B were in full agreement with previously reported values.[3]

^1^H NMR (400 MHz, CDCl₃): δ = 7.83–7.79 (m, 2H), 7.36 (d, J = 8.1 Hz, 2H), 4.25 (dd, J = 11.4, 3.5 Hz, 1H), 3.96 (dd, J = 11.4, 6.0 Hz, 1H), 3.21–3.16 (m, 1H), 2.83–2.80 (m, 1H), 2.59 (dd, J = 4.8, 2.5 Hz, 1H), 2.45 (s, 3H) ppm.

(R)-2-hydroxy-4-methylpent-4-en-1-yl 4-methylbenzenesulfonate (C)

Copper(I) iodide (2.25 g, 11.8 mmol, 0.20 equiv) was dispersed in THF (36 mL) and the suspension was cooled to −78 °C. Isopropenylmagnesium bromide (0.5 M in THF, 248 mL, 124 mmol, 2.1 equiv) was added dropwise. After complete addition, the clear yellow solution was stirred at −78 °C for 1 h. Then, a solution of tosylate B (13.5 g, 59.0 mmol, 1 equiv) in THF (55 mL) was added dropwise. The reaction mixture was stirred for 30 min before it was allowed to warm to −45 °C within 1.5 h. Saturated aqueous NH₄Cl solution (380 mL) was added and the mixture was allowed to warm to room temperature. Et₂O (570 mL) and aqueous NH₃ solution (25%, 200 mL) were added and the layers were separated. The organic layer was washed with a mixture of aqueous NH₄Cl/NH₃ solution (3:1, 2 × 280 mL). The combined aqueous layers were extracted with Et₂O (300 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 4:1 to 3:1) to obtain alcohol C (15.3 g, 56.4 mmol, 96%) as colorless oil.

^1^H NMR (400 MHz, CDCl₃): δ = 7.81–7.76 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 4.85–4.82 (m, 1H), 4.75–4.72 (m, 1H), 4.04 (dd, J = 9.4, 3.1 Hz, 1H), 4.01–3.95 (m, 1H), 3.92 (dd, J = 9.4, 6.2 Hz, 1H), 2.43 (s, 3H), 2.22 (s, 1H), 2.16 (d, J = 6.7 Hz, 2H), 1.70 (s, 3H) ppm.

^13^C NMR (100 MHz, CDCl₃): δ = 145.1, 141.0, 132.8, 130.0, 128.0, 114.2, 73.4, 67.2, 41.5, 22.4, 21.7 ppm.
(5R)-5-(2-methylallyl)-3-(phenylselanyl)dihydrofuran-2(3H)-one (12)

To a solution of diisopropylamine (18.0 g, 178 mmol, 3.15 equiv) in THF (120 mL) was added n-butyllithium (2.5 M in hexanes, 70.0 mL, 175 mmol, 3.1 equiv) dropwise at −10 °C and the reaction mixture was stirred for 30 min. 2-(Phenylselanyl)acetic acid[4] (18.2 g, 84.6 mmol, 1.5 equiv) was dissolved in THF (95 mL) and added dropwise. The reaction mixture was stirred at −10 °C for 15 min, allowed to warm to room temperature and stirred for further 2 h.

Meanwhile, HMDS (10.0 g, 62.1 mmol, 1.1 equiv) was dissolved in THF (87 mL) and cooled to −78 °C. n-Butyllithium (2.5 M in hexanes, 23.7 mL, 59.2 mmol, 1.05 equiv) was added dropwise, the reaction mixture was warmed to 0 °C and stirred for 15 min. Alcohol C (15.3 g, 56.4 mmol, 1 equiv) was dissolved in THF (120 mL), added dropwise at 0 °C and the mixture was stirred for 1 h.

The first reaction mixture with the formed dianion was cooled to −78 °C and the second reaction mixture with the in situ formed epoxide was added dropwise via cannula over 1 h. The reaction mixture was allowed to warm to room temperature slowly overnight. Aqueous HCl solution (1 M, 800 mL) was added and the aqueous layer was extracted with Et₂O (3 × 600 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure.

The crude product was dissolved in CH₂Cl₂ (860 mL) and DMAP (689 mg, 5.64 mmol, 0.1 equiv) was added. The reaction mixture was cooled to 0 °C and DIC (7.83 g, 62.1 mmol, 1.1 equiv) was added. After stirring at 0 °C for 1.5 h, the reaction mixture was concentrated under reduced pressure. The crude mixture was dissolved in CH₂Cl₂, filtered over Celite and concentrated. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 19:1 to 9:1) to afford selenolactone 12 (16.1 g, 54.5 mmol, 97%) as dark brown oil as inconsequential mixture of diastereomers.
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**$^1$H NMR** (400 MHz, CDCl$_3$, two diastereomers): $\delta = 7.70$–7.64 (m, 2H), 7.41–7.30 (m, 3H), 4.85–4.80 (m, 1H), 4.72 (s, 0.8H), 4.69 (s, 0.2H), 4.60–4.51 (m, 0.2H), 4.45–4.36 (m, 0.8H), 4.04–3.98 (m, 0.8H), 3.94–3.91 (m, 0.8H), 2.72 (ddd, $J = 13.7, 9.5, 6.7$ Hz, 0.2H), 2.44 (dd, $J = 14.5, 6.9$ Hz, 0.8H), 2.37–2.31 (m, 1.8H), 2.22 (dd, $J = 14.4, 6.3$ Hz, 0.8H), 2.10 (dd, $J = 14.4, 6.6$ Hz, 0.2H), 2.03–1.94 (m, 0.2H), 1.70 (s, 3H) ppm.

**$^{13}$C NMR** (100 MHz, CDCl$_3$, two diastereomers): $\delta = 175.8, 175.7, 140.2, 140.2, 136.0, 135.9, 129.6, 129.5, 129.3, 129.0, 126.9, 114.0, 77.8, 43.6, 43.3, 37.4, 37.0, 36.6, 22.9 ppm.

**IR** (neat sample): 3074, 2972, 2936, 1769, 1651, 1578, 1478, 1438, 1350, 1175, 1051, 1022, 925, 897, 739, 692 cm$^{-1}$.

**HRMS** (ESI): $m/z$ calcd for C$_{14}$H$_{17}$O$_2$Se [M+H]$^+$: 297.0394, found: 297.0388.

$R_f$: 0.33/0.26 (PE/EtOAc, 9:1).

(5$R$)-3-((3S)-3-(furan-2-ylmethyl)-1-hydroxy-4-methylpent-4-en-1-yl)-5-(2-methylallyl)furan-2(5$H$)-one (17a/b)

Diisopropylamine (2.58 g, 25.5 mmol, 1.2 equiv) was dissolved in THF (60 mL) and the solution was cooled to $-10$ °C. n-Butyllithium (2.5 M in hexanes, 9.76 mL, 24.4 mmol, 1.15 equiv) was added dropwise, the reaction mixture was stirred for 25 min and then cooled to $-78$ °C. A solution of selenolactone 12 (6.89 g, 23.3 mmol, 1.1 equiv) in THF (60 mL) was added dropwise and the mixture was stirred for 30 min. Then, a solution of aldehyde 11 (3.78 g, 21.2 mmol, 1 equiv) in THF (60 mL) was added dropwise. After 10 min, saturated aqueous NH$_4$Cl solution (600 mL) was added and the reaction mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et$_2$O (3 $\times$ 700 mL). The combined organic layers were washed with water (500 mL), dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was used without further purification.

The crude product was dissolved in CH$_2$Cl$_2$ (1.0 L). Saturated aqueous NH$_4$Cl solution (200 mL) was added and the biphasic mixture was cooled to 0 °C. Aqueous H$_2$O$_2$ (30%, 19.5 mL, 191 mmol, 9.0 equiv) was added and the reaction mixture was stirred vigorously at 0 °C. After 2.5 h and 3 h, additional H$_2$O$_2$ (30%, 9.75 mL, 95.5 mmol, 4.5 equiv) was added each. After 3 h 50 min, TLC showed full consumption
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of starting material and the layers were separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 500 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude product mixture was purified by flash column chromatography on silica gel (PE/EtOAc = 7:1 to 5:1 to 3:1) to obtain alcohols 17a (3.68 g, 11.6 mmol, 55%) and 17b (1.11 g, 3.51 mmol, 17%) as dark yellow oils.

(R)-3-((1S,3S)-3-(furan-2-ylmethyl)-1-hydroxy-4-methylpent-4-en-1-yl)-5-(2-methylallyl)-furan-2(5H)-one (17a, OH-down):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.29–7.26 (m, 1H), 7.22–7.20 (m, 1H), 6.24 (dd, $J$ = 3.1, 1.9 Hz, 1H), 6.02–5.99 (m, 1H), 5.08–5.02 (m, 1H), 4.93–4.88 (m, 1H), 4.85–4.78 (m, 3H), 4.45–4.39 (m, 1H), 2.90–2.80 (m, 1H), 2.74 (dd, $J$ = 14.9, 7.5 Hz, 1H), 2.66 (dd, $J$ = 14.9, 7.5 Hz, 1H), 2.42 (dd, $J$ = 14.4, 7.3 Hz, 1H), 2.32 (dd, $J$ = 14.4, 6.5 Hz, 1H), 1.90 (ddd, $J$ = 14.0, 11.2, 2.8 Hz, 1H), 1.78 (s, 3H), 1.71 (s, 3H), 1.61 (ddd, $J$ = 14.0, 10.2, 3.7 Hz, 1H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 172.3, 154.2, 148.0, 146.0, 141.1, 139.8, 137.3, 114.4, 113.4, 110.2, 106.2, 80.2, 65.2, 42.7, 41.4, 38.0, 33.0, 23.0, 18.2 ppm.

IR (neat sample): 3452, 2923, 1751, 1646, 1438, 1379, 1336, 1059, 1008, 897, 729 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{19}$H$_{24}$NaO$_4$ [M+Na]$^+$: 339.1572, found: 339.1562.

$[\alpha]_D^{2}$: $-78.8$ (c 0.26, CHCl$_3$).

$R_f$: 0.34 (PE/EtOAc, 3:1).

(R)-3-((1R,3S)-3-(furan-2-ylmethyl)-1-hydroxy-4-methylpent-4-en-1-yl)-5-(2-methylallyl)-furan-2(5H)-one (17b, OH-up):

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.29–7.27 (m, 1H), 7.16–7.13 (m, 1H), 6.26 (dd, $J$ = 3.2, 1.8 Hz, 1H), 6.03–5.99 (m, 1H), 5.10–5.04 (m, 1H), 4.95–4.91 (m, 1H), 4.85–4.81 (m, 1H), 4.81–4.78 (m, 1H), 4.77–4.73 (m, 1H), 4.50–4.44 (m, 1H), 2.75–2.71 (m, 2H), 2.65–2.56 (m, 1H), 2.45 (dd, $J$ = 14.3, 7.2 Hz, 1H), 2.35 (dd, $J$ = 14.4, 6.6 Hz, 1H), 1.98–1.90 (m, 1H), 1.86–1.77 (m, 4H), 1.72 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 172.4, 154.0, 148.5, 147.5, 141.1, 139.7, 136.1, 114.6, 112.8, 110.3, 106.4, 80.3, 66.3, 43.8, 41.4, 38.5, 32.6, 23.1, 18.8 ppm.

IR (neat sample): 3470, 2928, 2188, 1751, 1647, 1439, 1341, 1203, 1062, 896, 730, 661 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{19}$H$_{24}$NaO$_4$ [M+Na]$^+$: 339.1572, found: 339.1569.

$[\alpha]_D^{2}$: $-35.6$ (c 0.38, CHCl$_3$).

$R_f$: 0.21 (PE/EtOAc, 3:1).
To a solution of alcohol 17a (849 mg, 2.68 mmol, 1 equiv) in CH₂Cl₂ (40 mL) were sequentially added pyridine (637 mg, 8.05 mmol, 3.0 equiv) and DMAP (32.8 mg, 0.268 mmol, 0.1 equiv) and the reaction mixture was cooled to 0 °C. Acetic anhydride (548 mg, 5.37 mmol, 2.0 equiv) was added and the reaction mixture was stirred at 0 °C for 50 min. Saturated aqueous NH₄Cl solution (140 mL) was added and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 140 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 7:1) to afford acetate 18a (844 mg, 2.35 mmol, 88%) as yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.27 (dd, J = 1.8, 0.9 Hz, 1H), 7.10–7.08 (m, 1H), 6.24 (dd, J = 3.2, 1.8 Hz, 1H), 5.99 (d, J = 2.8 Hz, 1H), 5.46–5.40 (m, 1H), 5.06–4.99 (m, 1H), 4.92–4.87 (m, 1H), 4.82–4.79 (m, 1H), 4.79–4.76 (m, 1H), 4.70–4.66 (m, 1H), 2.76–2.59 (m, 1H), 2.40 (dd, J = 14.4, 7.3 Hz, 1H), 2.30 (dd, J = 14.4, 6.5 Hz, 1H), 2.07 (s, 3H), 2.05–1.94 (m, 1H), 1.84–1.77 (m, 1H), 1.75 (s, 3H), 1.68 (s, 3H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 170.8, 169.8, 154.0, 149.0, 145.1, 141.1, 139.7, 134.1, 114.4, 113.6, 110.2, 106.2, 79.8, 67.5, 42.8, 41.3, 35.4, 32.8, 23.0, 20.8, 18.1 ppm.

IR (neat sample): 2954, 2343, 1754, 1649, 1374, 1230, 1062, 1033, 899, 741 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₁H₂₆NaO₅ [M+Na]⁺: 381.1678, found: 381.1673.

[α]D²: –50.9 (c 0.38, CHCl₃).

Rf: 0.40 (PE/EtOAc, 4:1).
(1R,3S)-3-(furan-2-ylmethyl)-4-methyl-1-[(R)-5-(2-methylallyl)-2-oxo-2,5-dihydrofuran-3-yl]-pent-4-en-1-yl acetate (18b)

To a solution of alcohol 17b (1.11 g, 3.51 mmol, 1 equiv) in CH₂Cl₂ (52 mL) were sequentially added pyridine (833 mg, 10.5 mmol, 3.0 equiv) and DMAP (42.9 mg, 0.351 mmol, 0.1 equiv) and the reaction mixture was cooled to 0 °C. Acetic anhydride (716 mg, 7.02 mmol, 2.0 equiv) was added and the reaction mixture was stirred at 0 °C for 45 min. Saturated aqueous NH₄Cl solution (90 mL) was added and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 90 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 9:1 to 7:1 to 4:1) to afford acetate 18b (1.08 g, 3.01 mmol, 86%) as light yellow oil.

1H NMR (400 MHz, CDCl₃): δ = 7.29–7.27 (m, 1H), 7.18–7.16 (m, 1H), 6.26 (dd, J = 3.2, 1.8 Hz, 1H), 6.00 (d, J = 3.1 Hz, 1H), 5.56–5.50 (m, 1H), 5.09–5.02 (m, 1H), 4.95–4.91 (m, 1H), 4.84–4.80 (m, 1H), 4.77–4.72 (m, 1H), 4.68–4.64 (m, 1H), 2.73–2.69 (m, 2H), 2.43 (d, J = 7.1 Hz, 2H), 2.34 (dd, J = 14.4, 6.6 Hz, 1H), 2.05 (s, 3H), 2.04–1.91 (m, 2H), 1.80 (s, 3H), 1.70 (s, 3H) ppm.

13C NMR (100 MHz, CDCl₃): δ = 170.9, 170.0, 153.9, 150.7, 146.0, 141.2, 139.7, 133.2, 114.7, 112.8, 110.3, 106.5, 79.9, 67.7, 43.5, 41.3, 35.0, 32.8, 23.2, 21.1, 18.6 ppm.

IR (neat sample): 2968, 2343, 1756, 1648, 1506, 1440, 1373, 1232, 1064, 1026, 895, 736 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₁H₂₇O₅ [M+H]⁺: 359.1858, found: 359.1855.

[α]D²: +24.3 (c 0.41, CHCl₃).

Rf: 0.31 (PE/EtOAc, 4:1).
(1S,3S)-3-((5-formylfuran-2-yl)methyl)-4-methyl-1-((R)-5-(2-methylallyl)-2-oxo-2,5-dihydro-furan-3-yl)-pent-4-en-1-yl acetate (19a)

Acetate 18a (842 mg, 2.35 mmol, 1 equiv) was dissolved in DMF (0.20 mL, 2.58 mmol, 1.1 equiv). Phosphoryl chloride (396 mg, 2.58 mmol, 1.1 equiv) was added and the reaction mixture was stirred vigorously at room temperature in a water bath. After 10 min, the dark red and viscous mixture was diluted with EtOAc (100 mL) and poured onto ice-cold water (150 mL). The layers were separated and the aqueous layer was adjusted to pH 7 with aqueous NaOH solution (1 M). The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 3:1 to 2:1) to afford aldehyde 19a (856 mg, 2.22 mmol, 94%) as yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 9.51 (s, 1H), 7.15 (d, J = 3.5 Hz, 1H), 7.13–7.10 (m, 1H), 6.25 (d, J = 3.5 Hz, 1H), 5.46–5.40 (m, 1H), 5.08–5.02 (m, 1H), 4.93–4.89 (m, 1H), 4.85–4.82 (m, 1H), 4.81–4.77 (m, 1H), 4.72–4.68 (m, 1H), 2.87–2.71 (m, 3H), 2.42 (dd, J = 14.4, 7.3 Hz, 1H), 2.31 (dd, J = 14.4, 6.5 Hz, 1H), 2.11–2.01 (m, 4H), 1.85–1.75 (m, 4H), 1.71 (s, 3H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 177.1, 170.8, 170.0, 161.2, 152.1, 150.9, 145.1, 139.6, 132.8, 123.5, 114.7, 113.5, 110.3, 80.0, 67.5, 43.0, 41.2, 35.0, 32.9, 23.1, 21.1, 18.5 ppm.

IR (neat sample): 3080, 2922, 1750, 1675, 1518, 1438, 1373, 1230, 1062, 1024, 961, 897, 792 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₂H₂₇O₆ [M+H]⁺: 387.1808, found: 387.1805.

[α]ᵢ²: −13.9 (c 0.41, CHCl₃).

Rₛ: 0.15 (PE/EtOAc, 3:1).
Acetate 18b (521 mg, 1.45 mmol, 1 equiv) was dissolved in DMF (0.125 mL, 1.60 mmol, 1.1 equiv). Phosphoryl chloride (245 mg, 1.60 mmol, 1.1 equiv) was added and the reaction mixture was stirred vigorously at room temperature in a water bath. After 10 min, the dark red and viscous mixture was diluted with EtOAc (65 mL) and poured onto ice-cold water (100 mL). The layers were separated and the aqueous layer was adjusted to pH 7 with aqueous NaOH solution (1 M). The aqueous layer was extracted with EtOAc (2 × 65 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 3:1) to afford aldehyde 19b (483 mg, 1.25 mmol, 86%) as yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.51$ (s, 1H), 7.23–7.21 (m, 1H), 7.14 (d, $J = 3.5$ Hz, 1H), 6.26 (d, $J = 3.5$ Hz, 1H), 5.55–5.49 (m, 1H), 5.11–5.05 (m, 1H), 4.94–4.90 (m, 1H), 4.84–4.81 (m, 1H), 4.78–4.74 (m, 1H), 4.69–4.65 (m, 1H), 2.88–2.77 (m, 2H), 2.65–2.56 (m, 1H), 2.44 (dd, $J = 14.4$, 7.1 Hz, 1H), 2.36 (dd, $J = 14.4$, 6.5 Hz, 1H), 2.11–1.93 (m, 5H), 1.79 (s, 3H), 1.70 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 177.1$, 170.8, 169.8, 161.5, 152.2, 149.2, 144.1, 139.7, 133.9, 123.7, 114.6, 114.6, 110.2, 80.0, 67.4, 42.6, 41.4, 35.4, 33.1, 23.1, 20.9, 18.0 ppm.

IR (neat sample): 2967, 2298, 2012, 1913, 1756, 1675, 1518, 1236, 1029, 898, 771 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{22}$H$_{27}$O$_6$ [M+H]$^+$: 387.1808, found: 387.1798.

$[\alpha]_2^\infty$: +43.8 (c 0.67, CHCl$_3$).

$R$$_f$: 0.12 (PE/EtOAc, 3:1).
Methyltriphenylphosphonium bromide (240 mg, 0.673 mmol, 1.3 equiv) was dispersed in THF (6.8 mL). The suspension was submitted to ultrasonic for 5 min and was then cooled to –78 °C. KHMDS solution (0.7 M in toluene, 0.961 mL, 0.673 mmol, 1.3 equiv) was added dropwise. The reaction mixture was warmed to 0 °C and stirred for 30 min, before it was recooled to –78 °C. Meanwhile, aldehyde 19a (200 mg, 0.518 mmol, 1 equiv) was dissolved in THF (5.2 mL) and cooled to –78 °C. Then, the freshly prepared ylide solution was added dropwise to the aldehyde solution via cannula. After complete addition, the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. Saturated aqueous NH₄Cl solution (70 mL) was added and the aqueous layer was extracted with Et₂O (3 × 70 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 9:1 to 7:1) to yield triene 10a (143 mg, 0.372 mmol, 72%) as pale yellow oil.

$^1$H NMR (400 MHz, CDCl₃): δ = 7.13–7.07 (m, 1H), 6.43 (dd, J = 17.5, 11.2 Hz, 1H), 6.13 (d, J = 3.2 Hz, 1H), 5.99 (d, J = 3.2 Hz, 1H), 5.56 (dd, J = 17.5, 1.5 Hz, 1H), 5.50–5.41 (m, 1H), 5.11–5.01 (m, 2H), 4.94–4.88 (m, 1H), 4.85–4.82 (m, 1H), 4.81–4.78 (m, 1H), 4.74–4.69 (m, 1H), 2.78–2.59 (m, 3H), 2.42 (dd, J = 14.4, 7.3 Hz, 1H), 2.31 (dd, J = 14.4, 6.5 Hz, 1H), 2.08 (s, 3H), 2.02 (ddd, J = 14.7, 10.0, 3.1 Hz, 1H), 1.84 (ddd, J = 14.2, 10.4, 3.4 Hz, 1H), 1.77 (s, 3H), 1.71 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl₃): δ = 170.8, 169.9, 153.9, 152.0, 149.1, 145.1, 139.7, 134.1, 125.3, 114.5, 113.8, 110.9, 109.0, 108.1, 79.9, 67.6, 42.9, 41.4, 35.4, 33.0, 23.1, 20.9, 18.2 ppm.

IR (neat sample): 2920, 1751, 1646, 1439, 1372, 1230, 1095, 1032, 958, 895, 789 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₃H₂₉O₅ [M+H]⁺: 385.2015, found: 385.2007.

$[\alpha]_D^2$: –35.0 (c 0.32, CHCl₃).

$R_f$: 0.51 (PE/EtOAc, 3:1).
HMDS (112 mg, 0.696 mmol, 1.15 equiv) was dissolved in THF (0.70 mL) and the solution was cooled to −78 °C. n-Butyllithium (2.5 M in hexanes, 0.266 mL, 0.666 mmol, 1.1 equiv) was added dropwise, the reaction mixture was warmed to 0 °C and stirred for 10 min. Methyltriphenylphosphonium bromide (238 mg, 0.666 mmol, 1.1 equiv) was dispersed in THF (6.8 mL). The suspension was submitted to ultrasonic for 5 min and was then cooled to −78 °C. The freshly prepared LiHMDS solution was added dropwise. The reaction mixture was warmed to 0 °C and stirred for 30 min, before it was recooled to −78 °C. Meanwhile, aldehyde 19b (234 mg, 0.606 mmol, 1 equiv) was dissolved in THF (6.1 mL) and cooled to −78 °C. Then, the freshly prepared ylide solution was added dropwise to the aldehyde solution via cannula. After complete addition, the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. Saturated aqueous NH₄Cl solution (90 mL) was added and the aqueous layer was extracted with Et₂O (3 × 90 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 9:1 to 7:1) to yield triene 10b (150 mg, 0.390 mmol, 64%) as yellow oil.

^1H NMR (400 MHz, CDCl₃): δ = 7.18–7.16 (m, 1H), 6.41 (dd, J = 17.5, 11.3 Hz, 1H), 6.12 (d, J = 3.2 Hz, 1H), 5.98 (d, J = 3.2 Hz, 1H), 5.57–5.50 (m, 2H), 5.09–5.02 (m, 2H), 4.93–4.90 (m, 1H), 4.83–4.80 (m, 1H), 4.77–4.74 (m, 1H), 4.68–4.65 (m, 1H), 2.70 (d, J = 7.3 Hz, 2H), 2.55–2.46 (m, 1H), 2.42 (dd, J = 14.4, 7.1 Hz, 1H), 2.33 (dd, J = 14.3, 6.5 Hz, 1H), 2.10–1.92 (m, 5H), 1.78 (s, 3H), 1.71 (s, 3H) ppm.

^13C NMR (100 MHz, CDCl₃): δ = 170.9, 169.9, 153.7, 152.0, 150.6, 145.8, 139.6, 133.2, 125.3, 114.7, 112.8, 111.0, 109.0, 108.3, 79.9, 67.6, 43.5, 41.2, 35.0, 32.8, 23.1, 21.0, 18.6 ppm.

IR (neat sample): 2967, 2297, 1760, 1678, 1646, 1440, 1375, 1232, 1094, 1031, 895, 790 cm⁻¹.

HRMS (ESI): m/z calcd for C23H28NaO5 [M+Na]^+: 407.1834, found: 407.1823.

[α]D²: +26.2 (c 0.33, CHCl₃).

Rf: 0.44 (PE/EtOAc, 3:1).
Triene 10a (137 mg, 0.356 mmol) was distributed in three equal portions. Each portion (45.7 mg, 0.119 mmol, 1 equiv) was dissolved in degassed benzene (119 mL each; three cycles of freeze, pump, thaw) in a three-necked flask with reflux condenser and nitrogen T-tube on top. 1,4-Benzquinone (2.57 mg, 23.8 μmol, 0.2 equiv each) was added and the reaction mixtures were heated to 90 °C. Grubbs II catalyst (5.04 mg, 5.94 μmol, 0.05 equiv each) dissolved in degassed benzene (2.0 mL each) was added and the reaction mixtures were stirred under reflux. After 2 h, additional Grubbs II catalyst (5.04 mg, 5.94 μmol, 0.05 equiv each) dissolved in degassed benzene (2.0 mL each) was added to the reaction mixtures. This process was repeated after 4 h and 6 h, so that in total 0.2 equiv of Grubbs II catalyst had been added to each portion. After 8 h, the reaction mixtures were allowed to cool to room temperature, combined and concentrated. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 19:1 to 9:1) to afford macrocycle 20a (74 mg, 0.208 mmol, 58%) as light brown solid.

\[^{1}H\text{NMR}\ (600\text{ MHz}, \text{CDCl}_3): \delta = 6.88–6.80 (m, 1H), 6.16 (s, 1H), 6.11 (d, J = 3.2 Hz, 1H), 6.08 (dd, J = 3.2, 1.3 Hz, 1H), 5.54 (dd, J = 8.1, 4.9 Hz, 1H), 4.94 (ddd, J = 11.6, 5.1, 1.1 Hz, 1H), 4.80–4.78 (m, 2H), 3.14–3.09 (m, 1H), 2.76–2.72 (m, 2H), 2.66 (dd, J = 15.6, 10.4 Hz, 1H), 2.46–2.37 (m, 2H), 2.04 (s, 3H), 1.98 (s, 3H), 1.79 (s, 3H), 1.68 (ddd, J = 13.3, 7.2, 4.9 Hz, 1H) ppm.\]

\[^{13}C\text{NMR}\ (150\text{ MHz}, \text{CDCl}_3): \delta = 171.0, 170.6, 155.8, 154.0, 151.0, 148.8, 128.9, 128.7, 118.0, 111.3, 110.7, 108.7, 78.5, 68.3, 42.0, 40.2, 37.0, 33.9, 26.1, 21.1, 20.8\text{ ppm}.\]

\[\text{IR\ (neat\ sample): 2972, 2930, 1759, 1646, 1445, 1374, 1239, 1092, 1050, 1022, 955, 894, 791, 734\text{ cm}^{-1}.}\]

\[\text{HRMS\ (ESI): } m/z\ \text{calcd for } C_{21}H_{25}O_5\ [M+H]^+: 357.1702, \text{ found: 357.1700.}\]

\[\left[\alpha\right]_D^{25} = -82.6\ \text{(c 0.37, CHCl}_3).\]

\[\text{m.p.:} \ 140^\circ\text{C.}\]

\[R_f: 0.23\ (\text{PE/EtOAc, 4:1}).\]
Triene 10b (117 mg, 0.304 mmol) was distributed in three equal portions. Each portion (39.0 mg, 0.101 mmol, 1 equiv) was dissolved in degassed benzene (101 mL each; three cycles of freeze, pump, thaw) in a three-necked flask with reflux condenser and nitrogen T-tube on top. 1,4-Benzquinone (2.19 mg, 20.3 μmol, 0.2 equiv each) was added and the reaction mixtures were heated to 90 °C. Grubbs II catalyst (4.31 mg, 5.07 μmol, 0.05 equiv each) dissolved in degassed benzene (2.0 mL each) was added and the reaction mixtures were stirred under reflux. After 2 h, additional Grubbs II catalyst (4.31 mg, 5.07 μmol, 0.05 equiv each) dissolved in degassed benzene (2.0 mL each) was added to the reaction mixtures. This process was repeated after 4 h, so that in total 0.15 equiv of Grubbs II catalyst had been added to each portion. After 6 h, the reaction mixtures were allowed to cool to room temperature, combined and concentrated. The crude material was purified by flash column chromatography on silica gel (PE/EtOAc = 19:1 to 9:1) to afford macrocycle 20b (75 mg, 0.210 mmol, 69%) as light brown oil. An analytical sample for X-ray diffraction was crystallized from Et₂O/pentane.

\(^1\)H NMR (600 MHz, CDCl₃): \(\delta = 7.15\) (d, \(J = 1.5\) Hz, 1H), 6.14 (s, 1H), 6.13 (d, \(J = 3.2\) Hz, 1H), 6.07 (dd, \(J = 3.2, 1.5\) Hz, 1H), 5.39 (dd, \(J = 12.2, 4.0\) Hz, 1H), 5.05 (ddd, \(J = 11.9, 4.7, 1.5\) Hz, 1H), 4.98–4.96 (m, 1H), 4.75–4.93 (m, 1H), 3.25–3.20 (m, 1H), 2.77 (dd, \(J = 11.9, 4.7\) Hz, 1H), 2.70 (dd, \(J = 15.5, 4.5\) Hz, 1H), 2.61 (dd, \(J = 15.4, 12.7\) Hz, 1H), 2.28–2.22 (m, 1H), 2.06–2.01 (m, 1H), 2.00 (s, 3H), 1.94 (s, 3H), 1.77 (s, 3H), 1.30–1.26 (m, 1H) ppm.

\(^{13}\)C NMR (150 MHz, CDCl₃): \(\delta = 172.1, 169.6, 154.4, 153.8, 151.4, 144.7, 133.4, 127.3, 117.8, 113.7, 111.6, 109.4, 79.1, 65.6, 41.9, 39.5, 36.9, 33.1, 25.8, 21.1, 19.4\) ppm.

IR (neat sample): 2933, 1762, 1646, 1446, 1371, 1235, 1201, 1056, 1025, 964, 907, 783 cm⁻¹.

HRMS (ESI): \(m/z\) calcd for \(C_{21}H_{25}O_5\) [M+H]⁺: 357.1702, found: 357.1700.

\([\alpha]_D^2\): +24.7 (c 0.56, CHCl₃).

Rₚ: 0.25 (PE/EtOAc, 4:1).
To a solution of macrocycle 20a (46.5 mg, 0.130 mmol, 1 equiv) in a mixture of acetone/THF/H$_2$O (1:1:1, 2.6 mL) was added NMO (50% in H$_2$O, 0.03 mL, 0.124 mmol, 0.95 equiv) and the reaction mixture was cooled to 0 °C. Osmium tetroxide (4% in H$_2$O, 0.085 mL, 0.013 mmol, 0.1 equiv) was added and the reaction mixture was stirred at 0 °C for 2 h. Brine (10 mL) was added and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated under reduced pressure (water bath 20 °C!). The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 1:1 to 1:2) to yield diol 21a (23.5 mg, 0.060 mmol, 46%) as dark brown oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.24 (d, $J$ = 3.2 Hz, 1H), 6.17 (d, $J$ = 3.1 Hz, 1H), 6.00 (s, 1H), 5.66 (dd, $J$ = 11.3, 5.1 Hz, 1H), 4.93 (dd, $J$ = 11.4, 5.9 Hz, 1H), 4.79–4.75 (m, 2H), 4.43 (s, 1H), 2.84 (d, $J$ = 15.3 Hz, 1H), 2.73–2.57 (m, 2H), 2.38–2.22 (m, 3H), 1.99 (s, 3H), 1.89–1.83 (m, 1H), 1.78 (s, 3H), 1.36 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 170.7, 170.1, 155.1, 155.0, 149.4, 149.0, 129.5, 110.4, 110.1, 108.0, 78.5, 75.5, 72.9, 67.1, 41.1, 40.1, 36.6, 33.6, 23.0, 21.2, 21.0 ppm.

IR (neat sample): 3492, 3468, 2972, 1755, 1675, 1447, 1375, 1234, 1163, 1090, 1028, 958, 911, 787, 731 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{21}$H$_{27}$O$_7$[M+H]$^+$: 391.1757, found: 391.1753.

$[\alpha]_D^{25}$: +83.2 (c 0.40, CHCl$_3$).

$R_f$: 0.19 (PE/EtOAc, 1:2).
Diol 21a (23.5 mg, 60.2 μmol) was dissolved in benzene (1.2 mL) and heated to reflux. After 80 min, the reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure. An analytical sample was purified by flash column chromatography on silica gel (PE/EtOAc = 1:2) to afford pentacyclic compound 22 as colorless crystals.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.65$ (d, $J = 5.7$ Hz, 1H), 6.49 (d, $J = 5.7$ Hz, 1H), 5.08 (s, 1H), 5.01 (s, 1H), 4.78 (dd, $J = 11.6, 5.1$ Hz, 1H), 4.52 (ddd, $J = 6.3, 3.9, 2.3$ Hz, 1H), 3.84 (d, $J = 10.8$ Hz, 1H), 2.95–2.88 (m, 1H), 2.85–2.73 (m, 2H), 2.66–2.58 (m, 2H), 2.56 (s, 1H), 2.41 (d, $J = 6.2$ Hz, 1H), 2.35–2.26 (m, 2H), 2.03 (s, 3H), 1.87 (s, 3H), 1.82 (dd, $J = 16.1, 3.9$ Hz, 1H), 1.34 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.6, 170.4, 147.4, 142.9, 137.7, 111.9, 91.3, 90.5, 74.2, 73.6, 72.3, 71.2, 62.9, 49.6, 39.2, 38.8, 27.9, 26.2, 24.3, 22.9, 21.2$ ppm.

IR (neat sample): 3531, 3504, 2972, 2936, 2367, 2306, 1755, 1455, 1378, 1232, 1164, 1031, 957, 906, 736 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{21}$H$_{27}$O$_7$ [M+H]$^+$: 391.1757, found: 391.1753.

[$\alpha$]$_D$:$^2$: $+48.7$ (c 0.30, CHCl$_3$).

$R_f$: 0.14 (PE/EtOAc, 1:2).
(12R,3S,7S,9S,2Z)-3-hydroxy-3-methyl-15-oxo-7-(prop-1-en-2-yl)-12,15-dihydro-1(2,4),5(2,5)-difurancyclononaphane-9-yl acetate (9a)

To a solution of diol 21a (15.5 mg, 39.7 μmol, 1 equiv) in CH₂Cl₂ (2.65 mL) were sequentially added triethylsilane (27.7 mg, 238 μmol, 6.0 equiv) and BF₃·Et₂O (16.9 mg, 119 μmol, 3.0 equiv) at −35 °C. The reaction mixture was stirred between −35 and −25 °C for 70 min. Saturated aqueous NH₄Cl solution (10 mL) was added and the reaction mixture was allowed to warm to room temperature. The aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure (water bath 20 °C). The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 3:1 to 2:1 to 1:1) to afford tertiary alcohol 9a (7.00 mg, 18.7 μmol, 47%) as colorless oil.

¹H NMR (400 MHz, CDCl₃): δ = 6.22 (s, 1H), 6.11–6.08 (m, 2H), 5.72 (dd, J = 11.0, 4.8 Hz, 1H), 4.89 (dd, J = 11.1, 5.3 Hz, 1H), 4.78–4.75 (m, 2H), 2.92–2.79 (m, 2H), 2.78 (d, J = 15.0 Hz, 1H), 2.67–2.55 (m, 2H), 2.50 (dd, J = 14.0, 5.4 Hz, 1H), 2.33–2.25 (m, 1H), 2.02–1.97 (m, 4H), 1.87 (ddd, J = 13.4, 10.6, 4.8 Hz, 1H), 1.78 (s, 3H), 1.43 (s, 3H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 170.7, 170.3, 155.1, 154.4, 149.8, 149.1, 129.2, 110.3, 109.4, 107.9, 78.6, 71.3, 67.2, 45.6, 44.0, 41.5, 36.1, 33.5, 26.4, 21.2, 20.9 ppm.

IR (neat sample): 3508, 2968, 2926, 2189, 1751, 1647, 1445, 1374, 1234, 1162, 1031, 959, 916, 794, 731 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₁H₂₇O₆ [M+H]⁺: 375.1808, found: 375.1803.

[α]D²: −22.1 (c 0.30, CHCl₃).

Rf: 0.38 (PE/EtOAc, 1:2).
Tertiary alcohol 9a (6.00 mg, 16.0 μmol) was dissolved in benzene (0.64 mL) and heated to reflux. After 80 min, the reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure to afford pentacyclic compound 23 as light brown oil.

**1H NMR** (800 MHz, CDCl₃): δ = 6.47 (d, J = 5.7 Hz, 1H), 6.42 (d, J = 5.8 Hz, 1H), 5.10–5.07 (m, 1H), 5.02–5.00 (m, 1H), 4.80 (dd, J = 11.7, 5.1 Hz, 1H), 4.65 (ddd, J = 6.3, 4.0, 2.2 Hz, 1H), 2.93–2.89 (m, 1H), 2.48–2.42 (m, 2H), 2.30–2.26 (m, 2H), 2.20 (d, J = 6.2 Hz, 1H), 2.05–2.01 (m, 4H), 1.87 (s, 3H). 1.66 (dd, J = 15.6, 4.0 Hz, 1H), 1.29 (s, 3H) ppm.

**13C NMR** (200 MHz, CDCl₃): δ = 173.8, 170.5, 147.6, 143.7, 137.8, 111.9, 90.7, 87.6, 74.5, 74.5, 67.5, 62.3, 47.0, 39.1, 38.8, 38.6, 30.4, 27.9, 24.3, 23.0, 21.2 ppm.

**IR** (neat sample): 3553, 2966, 2935, 1751, 1443, 1375, 1232, 1163, 1133, 1085, 959, 909, 816, 733 cm⁻¹.

**HRMS** (ESI): m/z calcd for C₂₁H₂₇O₆ [M+H]⁺: 375.1808, found: 375.1804.

**[α]D²**: +10.7 (c 0.30, CHCl₃).
To a solution of macrocycle 20b (54.0 mg, 0.152 mmol, 1 equiv) in a mixture of acetone/THF/H₂O (1:1:1, 0.96 mL) was added NMO (50% in H₂O, 0.034 mL, 0.144 mmol, 0.95 equiv) and the reaction mixture was cooled to 0 °C. Osmium tetroxide (4% in H₂O, 0.10 mL, 0.015 mmol, 0.1 equiv) was added and the reaction mixture was stirred at 0 °C for 3 h. Brine (10 mL) was added and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure (water bath 20 °C). The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 1:1 to 1:2) to yield diol 21b (14.0 mg, 0.036 mmol, 24%) as colorless oil.

¹H NMR (400 MHz, CDCl₃): δ = 6.36 (s, 1H), 6.26 (d, J = 3.1 Hz, 1H), 6.11 (d, J = 3.1 Hz, 1H), 5.37 (dd, J = 11.9, 2.8 Hz, 1H), 5.08–5.01 (m, 1H), 4.90–4.86 (m, 2H), 4.55 (s, 1H), 2.91 (s, 1H), 2.77 (s, 1H), 2.70 (d, J = 14.7 Hz, 1H), 2.57–2.48 (m, 1H), 2.38 (dd, J = 14.6, 4.4 Hz, 1H), 2.25–2.16 (m, 1H), 1.98 (s, 3H), 1.92 (d, J = 11.4 Hz, 1H), 1.77 (s, 3H), 1.69 (d, J = 10.3 Hz, 1H), 1.41 (s, 3H) ppm.

To a solution of diol 21b (14.5 mg, 37.1 µmol, 1 equiv) in CH₂Cl₂ (2.4 mL) were sequentially added triethylsilane (25.9 mg, 223 µmol, 6.0 equiv) and BF₃·Et₂O (15.8 mg, 111 µmol, 3.0 equiv) at −40 °C. The
reaction mixture was stirred at –40 °C for 40 min. Saturated aqueous Na/K-tartrate solution (5 mL) was added and the reaction mixture was allowed to warm to room temperature. The aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc = 2:1 to 1:1) to afford tertiary alcohol 9b (5.00 mg, 13.4 μmol, 36%) as light yellow oil and diol 21b (6.00 mg, 15.4 μmol, 42%).

^1H NMR (400 MHz, CDCl₃): δ = 6.81 (s, 1H), 6.10 (d, J = 3.0 Hz, 1H), 6.01 (d, J = 3.0 Hz, 1H), 5.42–5.35 (m, 1H), 4.99 (dd, J = 11.1, 4.5 Hz, 1H), 4.90–4.86 (m, 2H), 2.93 (d, J = 14.9 Hz, 1H), 2.85 (d, J = 14.9 Hz, 1H), 2.65 (d, J = 15.0 Hz, 1H), 2.57–2.52 (m, 1H), 2.39 (dd, J = 13.9, 4.6 Hz, 1H), 2.11–2.05 (m, 3H), 2.00 (s, 3H), 1.78–1.75 (m, 4H), 1.44 (s, 3H) ppm.

^13C NMR (100 MHz, CDCl₃): δ = 171.5, 169.6, 153.9, 153.3, 149.7, 145.7, 132.6, 113.0, 109.3, 108.4, 79.1, 71.2, 65.5, 45.4, 42.8, 42.1, 35.7, 33.0, 27.1, 21.2, 19.1 ppm.

IR (neat sample): 3475, 2968, 2929, 1755, 1646, 1444, 1373, 1235, 1207, 1116, 1023, 966, 912, 792, 732 cm⁻¹.

HRMS (ESI): m/z calcd for C₂₁H₂₅O₆[M+H]⁺: 375.1808, found: 375.1805.

[α]D²: +14.5 (c 0.28, CHCl₃).

Rf: 0.42 (PE/EtOAc, 1:2).

(3R,7R,9S,Z)-1-methyl-5,11,14-trioxo-9-(prop-1-en-2-yl)-4,16-dioxatricyclo[11.2.1.13,6]-heptadec-6(17)-en-7-yl acetate (24)

To a solution of tertiary alcohol 9b (7.00 mg, 18.7 μmol, 1 equiv) in acetone (0.94 mL) was added Jones reagent⁵ (2.67 M, 7.7 μL, 20.6 μmol, 1.1 equiv) and the reaction mixture was stirred at room temperature. After 35 min, saturated aqueous NaHCO₃ solution (5 mL) was added and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure to obtain norcembrenolide 24 (5.80 mg, 14.9 μmol, 80%) as
colorless oil. An analytical sample was purified by preparative thin layer chromatography with silica gel on aluminum (PE/EtOAc = 1:2).

$^1$H NMR (800 MHz, CDCl$_3$): $\delta$ = 7.56 (s, 1H), 5.40 (dd, $J$ = 11.6, 3.4 Hz, 1H), 5.24 (ddd, $J$ = 5.8, 3.9, 1.6 Hz, 1H), 4.88–4.85 (m, 1H), 4.74 (s, 1H), 4.23 (dd, $J$ = 10.1, 3.3 Hz, 1H), 2.92 (dd, $J$ = 14.9, 3.4 Hz, 1H), 2.59 (dd, $J$ = 11.1, 3.1 Hz, 1H), 2.54 (dd, $J$ = 15.1, 5.9 Hz, 1H), 2.52–2.47 (m, 2H), 2.45 (d, $J$ = 17.6 Hz, 1H), 2.40 (d, $J$ = 17.7 Hz, 1H), 2.33 (dd, $J$ = 15.2, 4.0 Hz, 1H), 2.25 (t, $J$ = 11.3 Hz, 1H), 2.14 (dd, $J$ = 11.4, 2.3 Hz, 1H), 2.07 (ddd, $J$ = 14.0, 11.2, 3.5 Hz, 1H), 2.01 (s, 3H), 1.73 (s, 3H), 1.35 (s, 3H) ppm.

$^{13}$C NMR (200 MHz, CDCl$_3$): $\delta$ = 212.3, 207.4, 172.0, 169.8, 155.5, 145.3, 130.2, 113.6, 79.1, 78.7, 74.7, 64.8, 49.4, 46.6, 42.8, 39.8, 33.9, 25.0, 21.2, 18.1 ppm.

IR (neat sample): 2964, 2934, 1758, 1713, 1374, 1237, 1108, 1089, 1027, 957, 906, 789 cm$^{-1}$.

HRMS (ESI): $m/z$ calcd for C$_{21}$H$_{27}$O$_7$ [M+H]$^+$: 391.1757, found: 391.1751.

[$\alpha$]$_D^2$: +62.2 (c 0.06, CHCl$_3$).

$R_f$: 0.39 (PE/EtOAc, 1:2).

(+)-norcembrene 5 (1)

Norcembrenolide 24 (1.20 mg, 3.07 μmol, 1 equiv) was dissolved in MeOH (0.10 mL). K$_2$CO$_3$ (0.637 mg, 4.61 μmol, 1.5 equiv) was added and the reaction mixture was stirred at room temperature for 15 min. Then, the reaction mixture was acidified to pH1 with aqueous HCl solution (1 M). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 5 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude product was purified by preparative thin layer chromatography with silica gel on aluminum (PE/EtOAc = 1:2) to yield (+)-norcembrene 5 (1, 0.70 mg, 1.93 μmol, 63%) as colorless solid.

$^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 6.76 (t, $J$ = 7.7 Hz, 1H), 4.95 (s, 1H), 4.72 (s, 1H), 4.41 (dd, $J$ = 9.7, 3.3 Hz, 1H), 3.73 (s, 3H), 3.64 (d, $J$ = 18.7 Hz, 1H), 3.52 (d, $J$ = 18.7 Hz, 1H), 3.45 (d, $J$ = 17.9 Hz, 1H), 3.02 (d, $J$ = 13.1 Hz, 1H), 2.87–2.82 (m, 1H), 2.68 (dd, $J$ = 17.0, 3.3 Hz, 1H), 2.60 (dd, $J$ = 17.2, 10.2 Hz,
SUPPORTING INFORMATION

1H), 2.60–2.55 (m, 1H), 2.53 (d, J = 13.1 Hz, 1H), 2.38 (dd, J = 15.4, 2.9 Hz, 1H), 2.32 (dd, J = 7.8, 4.8 Hz, 2H), 2.28 (d, J = 17.8 Hz, 1H), 1.79 (s, 3H), 1.38 (s, 3H) ppm.

13C NMR (150 MHz, CDCl3): δ = 215.1, 206.9, 206.4, 167.6, 144.9, 140.3, 128.2, 112.2, 80.5, 75.9, 52.1, 49.5, 45.8, 45.8, 44.9, 43.6, 29.1, 29.0, 22.0 ppm.

IR (neat sample): 2960, 2924, 2849, 1759, 1714, 1647, 1437, 1378, 1291, 1200, 1093, 904, 759 cm⁻¹.

HRMS (ESI): m/z calcd for C20H27O6 [M+H]+: 363.1808, found: 363.1801.

[a]D²: +51.4 (c 0.04, CHCl3).

m.p.: 179.3 °C.

Rf: 0.68 (PE/EtOAc, 1:2).

Table 1: Comparison of 1H and 13C NMR data of naturally isolated (−)-norcembrene 5 and synthetic (+)-norcembrene 5 (1).

| C# | 1H NMR Isolated[6] (−)-norcembrene 5 (360 MHz, CDCl3) [ppm] | 1H NMR Synthetic (+)-norcembrene 5 (600 MHz, CDCl3) [ppm] | 13C NMR Isolated[6] (−)-norcembrene 5 (50 MHz, CDCl3) [ppm] | 13C NMR Synthetic (+)-norcembrene 5 (150 MHz, CDCl3) [ppm] |
|----|-------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|
| 1  | 2.85 (ddddd, J = 12.0, 4.8, 4.8, 3.0 Hz, 1H)               | 2.87–2.82 (m, 1H)                                          | 39.6                                                        | 39.6                                                        |
| 2a | 2.58 (dd, J = 15.4, 12.0 Hz, 1H)                           | 2.60–2.55 (m, 1H)                                          |                                                             |                                                             |
| 2b | 2.38 (dd, J = 15.4, 3.0 Hz, 1H)                            | 2.38 (dd, J = 15.4, 2.9 Hz, 1H)                            |                                                             |                                                             |
| 3  | ---                                                         | ---                                                         | 214.8                                                       | 206.9                                                       |
| 4a | 2.69 (dd, J = 17.0, 3.5 Hz, 1H)                            | 2.68 (dd, J = 17.0, 3.3 Hz, 1H)                            |                                                             |                                                             |
| 4b | 2.60 (dd, J = 17.0, 9.3 Hz, 1H)                            | 2.60 (dd, J = 17.2, 10.2 Hz, 1H)                           |                                                             |                                                             |

214.8 206.9
|    | Chemical Shift 1 | Chemical Shift 2                  | Chemical Shift 3 | Chemical Shift 4                  |
|----|------------------|----------------------------------|------------------|----------------------------------|
| 5  | 4.42 (dd, J = 9.3, 3.5 Hz, 1H) | 4.41 (dd, J = 9.7, 3.3 Hz, 1H) | 75.8             | 75.9                             |
| 6  | ---               | ---                              | 206.6            | 215.1                            |
| 7a | 3.45 (d, J = 18.0 Hz, 1H)  | 3.45 (d, J = 17.9 Hz, 1H)        | 49.4             | 45.6                             |
| 7b | 2.28 (d, J = 18.0 Hz, 1H)  | 2.28 (d, J = 17.8 Hz, 1H)        | 49.5             | 49.5                             |
| 8  | ---               | ---                              | 80.3             | 80.5                             |
| 9a | 3.02 (d, J = 13.0 Hz, 1H)  | 3.02 (d, J = 13.1 Hz, 1H)        | 45.5             | 49.5                             |
| 9b | 2.50 (d, J = 13.0 Hz, 1H)  | 2.53 (d, J = 13.1 Hz, 1H)        | 206.6            | 206.4                            |
| 10 | ---               | ---                              | 206.1            | 206.4                            |
| 11a| 3.64 (d, J = 18.6 Hz, 1H)  | 3.64 (d, J = 18.7 Hz, 1H)        | 44.7             | 44.9                             |
| 11b| 3.52 (d, J = 18.6 Hz, 1H)  | 3.52 (d, J = 18.7 Hz, 1H)        | 128.1            | 128.2                            |
| 12 | ---               | ---                              | 128.1            | 128.2                            |
| 13 | 6.76 (dd, J = 7.8, 7.8 Hz, 1H) | 6.76 (dd, J = 7.7, 7.7 Hz, 1H)  | 140.2            | 140.3                            |
| 14 | 2.32 (dd, J = 7.8, 4.8 Hz, 2H) | 2.32 (dd, J = 7.8, 4.8 Hz, 2H)  | 29.6             | 29.1                             |
| 15 | ---               | ---                              | 144.9            | 144.9                            |
| 16a| 4.96 (s, 1H)      | 4.95 (s, 1H)                     | 112.0            | 112.2                            |
| 16b| 4.72 (s, 1H)      | 4.72 (s, 1H)                     | 112.0            | 112.2                            |
| 17 | 1.80 (s, 3H)      | 1.79 (s, 3H)                     | 28.7             | 22.0                             |
| 18 | 1.38 (s, 3H)      | 1.38 (s, 3H)                     | 21.8             | 29.0                             |
| 19 | ---               | ---                              | 167.4            | 167.6                            |
| 20 | 3.72 (s, 3H)      | 3.73 (s, 3H)                     | 51.9             | 52.1                             |
3. Single Crystal X-ray Diffraction Analysis

Compound 20b

CCDC number 1941507

**Figure 1**: Asymmetric unit of a single crystal of 20b consisting of four independent molecules; all molecules showing the same stereochemistry (1S/10R/13R) at the three stereogenic centers.

**Figure 2**: ORTEP representation of 20b (left) and 2D representation of 20b (right) with defined stereocenters.
The asymmetric unit of $20\text{b}$ (Figure 1) with the orthorhombic space group $P\ 2_1\ 2_1\ 2_1$ consists of four independent molecules each showing a different conformation of the 14-membered macrocycle. For simplification, the ORTEP representation in Figure 2 (left) shows a single molecule of $20\text{b}$ from its crystal structure at the 25% probability level. The protons have been omitted for clarity in both the asymmetric unit and the ORTEP representation.

Computing details

Data collection: STOE X-AREA; cell refinement: STOE X-AREA; data reduction: STOE X-RED; structure solution: SHELXS-2013 (Sheldrick, 2013); structure refinement: SHELXL-2016/6 (Sheldrick, 2016).

Crystal data and structure refinement

| Property                        | Value                          |
|--------------------------------|--------------------------------|
| Identification code            | shelx                          |
| Empirical formula              | C21 H24 O5                     |
| Formula weight                 | 356.40                         |
| Temperature                    | 100(2) K                       |
| Wavelength                     | 0.71073 Å                      |
| Crystal system                 | Orthorhombic                   |
| Space group                    | $P\ 2_1\ 2_1\ 2_1$            |
| Unit cell dimensions           | $a = 9.89630(10)$ Å, $a = 90^\circ$; $b = 18.6122(3)$ Å, $b = 90^\circ$; $c = 41.0547(6)$ Å, $g = 90^\circ$. |
| Volume                         | 7561.95(18) Å³                 |
| Z                              | 16                             |
| Density (calculated)           | 1.252 Mg/m³                    |
| Absorption coefficient         | 0.089 mm⁻¹                     |
| $F(000)$                       | 3040                           |
| Crystal size                   | 0.500 x 0.250 x 0.050 mm³      |
| Theta range for data collection| 1.201 to 25.301°.              |
| Index ranges                   | -11<=h<=11, -22<=k<=22, -49<=l<=49 |
| Reflections collected          | 93541                          |
| Independent reflections        | 13762 [R(int) = 0.0983]         |
| Completeness to theta = 25.242° | 100.0 %                        |
| Absorption correction          | Integration                    |
### SUPPORTING INFORMATION

| Max. and min. transmission | 0.9842 and 0.9579 |
|----------------------------|--------------------|
| Refinement method          | Full-matrix least-squares on F² |
| Data / restraints / parameters | 13762 / 0 / 949 |
| Goodness-of-fit on F²      | 1.149              |
| Final R indices [I>2sigma(I)] | R1 = 0.0418, wR2 = 0.1014 |
| R indices (all data)       | R1 = 0.0452, wR2 = 0.1048 |
| Absolute structure parameter | -0.1(2)           |
| Extinction coefficient     | n/a                |
| Largest diff. peak and hole | 0.673 and -0.778 e.Å³ |

**Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³).**

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

|   | x         | y         | z         | U(eq)     |
|---|-----------|-----------|-----------|-----------|
| C(1) | 5562(2)  | 9781(1)  | 6714(1)  | 31(1)    |
| C(2) | 5363(3)  | 10358(1) | 6446(1)  | 35(1)    |
| C(3) | 5518(3)  | 11105(1) | 6568(1)  | 34(1)    |
| C(4) | 6254(3)  | 11678(2) | 6470(1)  | 41(1)    |
| C(5) | 6051(3)  | 12227(2) | 6706(1)  | 42(1)    |
| C(6) | 5214(3)  | 11960(1) | 6939(1)  | 33(1)    |
| C(7) | 4755(3)  | 12278(1) | 7240(1)  | 34(1)    |
| C(8) | 3962(3)  | 12021(1) | 7479(1)  | 33(1)    |
| C(9) | 3334(2)  | 11281(1) | 7481(1)  | 31(1)    |
| C(10)| 4176(2)  | 10749(1) | 7680(1)  | 30(1)    |
| C(11)| 5530(2)  | 10615(1) | 7535(1)  | 29(1)    |
| C(12)| 5645(2)  | 9932(1)  | 7444(1)  | 28(1)    |
| C(13)| 6754(2)  | 9578(1)  | 7253(1)  | 28(1)    |
| C(14)| 6865(2)  | 9900(1)  | 6912(1)  | 31(1)    |
| C(15)| 5465(3)  | 9025(1)  | 6573(1)  | 34(1)    |
| C(16)| 6536(3)  | 8790(2)  | 6338(1)  | 52(1)    |
| C(17)| 4465(3)  | 8594(2)  | 6657(1)  | 42(1)    |
| C(18)| 3647(3)  | 12477(1) | 7771(1)  | 39(1)    |
| C(19)| 4379(3)  | 9562(1)  | 7536(1)  | 30(1)    |
| C(20)| 9032(3)  | 9254(1)  | 7381(1)  | 31(1)    |
| C(21)| 10222(3) | 9461(2)  | 7586(1)  | 39(1)    |
| C(22)| 1084(2)  | 6858(1)  | 6812(1)  | 29(1)    |
| C(23) | -255(3) | 7241(1) | 6728(1) | 34(1) |
|-------|---------|---------|---------|-------|
| C(24) | -662(3) | 7165(1) | 6382(1) | 34(1) |
| C(25) | -1842(3) | 7006(1) | 6253(1) | 39(1) |
| C(26) | -1589(3) | 7006(1) | 5892(1) | 40(1) |
| C(27) | -253(3) | 7151(1) | 5847(1) | 35(1) |
| C(28) | 533(3) | 7172(1) | 5551(1) | 38(1) |
| C(29) | 1863(3) | 7006(1) | 5498(1) | 37(1) |
| C(30) | 2926(3) | 7275(1) | 5759(1) | 35(1) |
| C(31) | 3508(3) | 6540(1) | 5861(1) | 35(1) |
| C(32) | 2569(3) | 6118(1) | 6070(1) | 31(1) |
| C(33) | 1028(2) | 6056(1) | 6723(1) | 31(1) |
| C(34) | 1477(2) | 7007(1) | 7163(1) | 30(1) |
| C(35) | 2062(3) | 7736(2) | 7228(1) | 40(1) |
| C(36) | 1346(3) | 6539(2) | 7406(1) | 38(1) |
| C(37) | 2407(3) | 5753(1) | 6674(1) | 29(1) |
| C(38) | 3435(3) | 4590(1) | 6679(1) | 32(1) |
| C(39) | 3166(3) | 3806(1) | 6718(1) | 40(1) |
| C(40) | 441(3) | 1643(1) | 6580(1) | 32(1) |
| C(41) | 380(3) | 1008(1) | 6822(1) | 35(1) |
| C(42) | 598(3) | 294(1) | 6670(1) | 33(1) |
| C(43) | 1396(3) | -272(2) | 6745(1) | 40(1) |
| C(44) | 1165(3) | -806(2) | 6499(1) | 33(1) |
| C(45) | 241(3) | -529(1) | 6287(1) | 33(1) |
| C(46) | -290(3) | -829(1) | 5990(1) | 34(1) |
| C(47) | -1107(3) | -546(1) | 5764(1) | 32(1) |
| C(48) | -1709(2) | 199(1) | 5779(1) | 32(1) |
| C(49) | -875(2) | 760(1) | 5595(1) | 31(1) |
| C(50) | 457(2) | 915(1) | 5752(1) | 30(1) |
| C(51) | 505(2) | 1595(1) | 5848(1) | 29(1) |
| C(52) | 1578(3) | 1976(1) | 6043(1) | 31(1) |
| C(53) | 1765(3) | 1641(1) | 6380(1) | 32(1) |
| C(54) | 221(3) | 2360(1) | 6751(1) | 34(1) |
| C(55) | 998(3) | 2498(2) | 7057(1) | 39(1) |
| C(56) | -608(3) | 2846(2) | 6627(1) | 44(1) |
| C(57) | -1493(3) | -981(1) | 5468(1) | 37(1) |
### SUPPORTING INFORMATION

|   |   |   |   |   |
|---|---|---|---|---|
| C(61) | -785(3) | 1942(1) | 5756(1) | 33(1) |
| C(62) | 3761(3) | 2421(1) | 5882(1) | 35(1) |
| C(63) | 4977(3) | 2249(2) | 5682(1) | 42(1) |
| C(64) | 3874(3) | -157(1) | 5025(1) | 32(1) |
| C(65) | 5308(3) | -403(1) | 4926(1) | 35(1) |
| C(66) | 5741(3) | 2421(1) | 5882(1) | 37(1) |
| C(67) | 6823(3) | 550(2) | 4193(1) | 36(1) |
| C(68) | 5323(2) | 294(1) | 4107(1) | 34(1) |
| C(69) | 4577(3) | 356(1) | 3806(1) | 32(1) |
| C(70) | 3308(3) | 174(1) | 3730(1) | 34(1) |
| C(71) | 2275(3) | -120(1) | 3965(1) | 33(1) |
| C(72) | 1450(2) | 478(1) | 4130(1) | 31(1) |
| C(73) | 2251(2) | 895(1) | 4373(1) | 31(1) |
| C(74) | 1801(2) | 763(1) | 4671(1) | 30(1) |
| C(75) | 2387(2) | 965(1) | 4997(1) | 30(1) |
| C(76) | 3808(3) | 666(1) | 5042(1) | 32(1) |
| C(77) | 3382(3) | -514(1) | 5335(1) | 37(1) |
| C(78) | 4216(4) | -422(2) | 5638(1) | 63(1) |
| C(79) | 2259(3) | -896(2) | 5342(1) | 46(1) |
| C(80) | 2807(3) | 255(2) | 3386(1) | 45(1) |
| C(81) | 625(2) | 279(1) | 4645(1) | 32(1) |
| C(82) | 1422(3) | 2127(1) | 5061(1) | 34(1) |
| C(83) | 1731(3) | 2903(2) | 5119(1) | 42(1) |
| C(84) | 4857(2) | 11263(1) | 6855(1) | 32(1) |
| O(1) | 3522(2) | 10050(1) | 7669(1) | 31(1) |
| O(2) | 4067(2) | 8938(1) | 7503(1) | 39(1) |
| O(3) | 8002(2) | 9719(1) | 7432(1) | 31(1) |
| O(4) | 8961(2) | 8747(1) | 7201(1) | 38(1) |
| O(5) | 340(2) | 7261(1) | 6150(1) | 32(1) |
| O(6) | 4666(2) | 6673(1) | 6069(1) | 37(1) |
| O(7) | 5181(2) | 6506(1) | 6595(1) | 39(1) |
| O(8) | 2279(2) | 4976(1) | 6665(1) | 30(1) |
| O(9) | 4536(2) | 4863(1) | 6667(1) | 46(1) |
| O(10) | -130(2) | 149(1) | 6392(1) | 32(1) |
| O(11) | -1586(2) | 1441(1) | 5613(1) | 33(1) |
| O(12) | -1157(2) | 2553(1) | 5800(1) | 42(1) |
| O(13) | 2844(2) | 1885(1) | 5861(1) | 33(1) |
### SUPPORTING INFORMATION

|    | 3576(2)  | 2965(1)  | 6036(1)  | 46(1)    |
|----|----------|----------|----------|----------|
| O(15) | 4801(2)  | -101(1)  | 4363(1)  | 32(1)    |
| O(16) | 403(2)   | 136(1)   | 4324(1)  | 34(1)    |
| O(17) | -70(2)   | 20(1)    | 4856(1)  | 38(1)    |
| O(18) | 2562(2)  | 1736(1)  | 5031(1)  | 34(1)    |
| O(19) | 311(2)   | 1861(1)  | 5046(1)  | 39(1)    |
| O(20) |          |          |          |          |

### Bond lengths [Å] and angles [°]

| Bond | Length [Å] | Bond | Length [Å] | Bond | Length [Å] |
|------|------------|------|------------|------|------------|
| C(1)-C(15) | 1.525(3) | C(29)-C(30) | 1.506(4) | C(55)-C(56) | 1.527(3) |
| C(1)-C(14) | 1.541(3) | C(29)-C(39) | 1.509(4) | C(57)-C(59) | 1.323(4) |
| C(1)-C(2) | 1.548(3) | C(30)-C(31) | 1.540(4) | C(57)-C(58) | 1.498(4) |
| C(2)-C(3) | 1.487(4) | C(31)-O(7) | 1.451(3) | C(61)-O(13) | 1.207(3) |
| C(3)-C(4) | 1.351(4) | C(31)-C(32) | 1.490(4) | C(61)-O(12) | 1.357(3) |
| C(3)-O(1) | 1.379(3) | C(32)-C(33) | 1.334(4) | C(62)-O(15) | 1.208(3) |
| C(4)-C(5) | 1.422(4) | C(33)-C(40) | 1.482(3) | C(62)-O(14) | 1.351(3) |
| C(5)-C(6) | 1.358(4) | C(33)-C(34) | 1.501(3) | C(62)-C(63) | 1.491(4) |
| C(6)-O(1) | 1.387(3) | C(34)-O(9) | 1.455(3) | C(64)-C(78) | 1.516(4) |
| C(6)-C(7) | 1.445(4) | C(34)-C(35) | 1.520(3) | C(64)-C(77) | 1.536(3) |
| C(7)-C(8) | 1.344(4) | C(36)-C(38) | 1.331(4) | C(64)-C(65) | 1.546(4) |
| C(8)-C(18) | 1.501(4) | C(36)-C(37) | 1.498(4) | C(65)-C(66) | 1.487(4) |
| C(8)-C(9) | 1.511(3) | C(40)-O(8) | 1.204(3) | C(66)-C(67) | 1.347(4) |
| C(9)-C(10) | 1.531(3) | C(40)-O(7) | 1.364(3) | C(66)-O(16) | 1.387(3) |
| C(10)-O(2) | 1.453(3) | C(41)-O(10) | 1.203(3) | C(67)-C(68) | 1.426(4) |
| C(10)-C(11) | 1.486(3) | C(41)-O(9) | 1.352(3) | C(68)-C(69) | 1.363(4) |
| C(11)-C(12) | 1.329(3) | C(41)-C(42) | 1.492(4) | C(69)-O(16) | 1.384(3) |
| C(12)-C(19) | 1.479(3) | C(43)-C(57) | 1.522(4) | C(69)-C(70) | 1.443(4) |
| C(12)-C(13) | 1.502(3) | C(43)-C(44) | 1.545(4) | C(70)-C(71) | 1.338(4) |
| C(13)-O(4) | 1.460(3) | C(43)-C(56) | 1.547(3) | C(71)-C(81) | 1.501(4) |
| C(13)-C(14) | 1.528(3) | C(44)-C(45) | 1.483(4) | C(71)-C(72) | 1.510(3) |
| C(15)-C(17) | 1.319(4) | C(45)-C(46) | 1.352(4) | C(72)-C(73) | 1.537(4) |
| C(15)-C(16) | 1.498(4) | C(45)-O(11) | 1.380(3) | C(73)-O(17) | 1.454(3) |
| C(19)-O(3) | 1.209(3) | C(46)-C(47) | 1.433(4) | C(73)-C(74) | 1.494(3) |
| C(19)-O(2) | 1.357(3) | C(47)-C(48) | 1.365(4) | C(74)-C(75) | 1.326(4) |
| C(20)-O(5) | 1.201(3) | C(48)-O(11) | 1.382(3) | C(75)-C(82) | 1.476(3) |
| C(20)-O(4) | 1.354(3) | C(48)-C(49) | 1.439(4) | C(75)-C(76) | 1.507(3) |
| C(20)-C(21) | 1.496(4) | C(49)-C(50) | 1.340(4) | C(76)-O(19) | 1.452(3) |
|   |   |   |   |
|---|---|---|---|
| C(22)-C(36) | 1.518(3) | C(50)-C(60) | 1.506(3) | C(76)-C(77) | 1.523(3) |
| C(22)-C(35) | 1.538(3) | C(50)-C(51) | 1.511(4) | C(78)-C(80) | 1.320(4) |
| C(22)-C(23) | 1.544(3) | C(51)-C(52) | 1.531(3) | C(78)-C(79) | 1.503(4) |
| C(23)-C(24) | 1.485(4) | C(52)-O(12) | 1.451(3) | C(82)-O(18) | 1.207(3) |
| C(24)-C(25) | 1.347(4) | C(52)-C(53) | 1.494(3) | C(82)-O(17) | 1.362(3) |
| C(24)-O(6)  | 1.387(3) | C(53)-C(54) | 1.328(4) | C(83)-O(20) | 1.207(3) |
| C(25)-C(26) | 1.429(4) | C(54)-C(61) | 1.480(4) | C(83)-O(19) | 1.348(3) |
| C(26)-C(27) | 1.362(4) | C(54)-C(55) | 1.507(3) | C(83)-C(84) | 1.496(4) |
| C(27)-O(6)  | 1.387(3) | C(55)-O(14) | 1.467(3) |   |   |
| C(27)-C(28) | 1.443(4) |   |   |   |   |
| C(28)-C(29) | 1.337(4) |   |   |   |   |
| C(15)-C(1)-C(14) | 112.6(2) | C(36)-C(22)-C(23) | 110.32(19) | C(45)-C(44)-C(43) | 114.2(2) |
| C(15)-C(1)-C(2)  | 111.3(2) | C(35)-C(22)-C(23) | 111.3(2) | C(46)-C(45)-O(11) | 109.8(2) |
| C(14)-C(1)-C(2)  | 112.4(2) | C(24)-C(23)-C(22) | 113.7(2) | C(46)-C(45)-C(44) | 133.6(2) |
| C(3)-C(2)-C(1)   | 113.4(2) | C(25)-C(24)-O(6)  | 109.9(2) | O(11)-C(45)-C(44) | 116.6(2) |
| C(4)-C(3)-O(1)   | 109.9(2) | C(25)-C(24)-C(23) | 133.2(2) | C(45)-C(46)-C(47) | 106.8(2) |
| C(4)-C(3)-C(2)   | 133.9(2) | O(6)-C(24)-C(23)  | 116.9(2) | C(48)-C(47)-C(46) | 107.1(2) |
| O(1)-C(3)-C(2)   | 116.0(2) | C(24)-C(25)-C(26) | 106.8(2) | C(47)-C(48)-O(11) | 108.9(2) |
| C(3)-C(4)-C(5)   | 106.8(2) | C(27)-C(26)-C(25) | 107.6(2) | C(47)-C(48)-C(49) | 129.7(3) |
| C(6)-C(5)-C(4)   | 107.5(3) | C(26)-C(27)-O(6)  | 108.6(2) | O(11)-C(48)-C(49) | 121.3(2) |
| C(5)-C(6)-O(1)   | 108.9(2) | C(26)-C(27)-C(28) | 129.9(3) | C(50)-C(49)-C(48) | 131.0(2) |
| C(5)-C(6)-C(7)   | 130.1(2) | O(6)-C(27)-C(28)  | 121.4(2) | C(49)-C(50)-C(60) | 120.0(2) |
| O(1)-C(6)-C(7)   | 121.0(2) | C(29)-C(28)-C(27) | 132.0(3) | C(49)-C(50)-C(51) | 124.6(2) |
| C(8)-C(7)-C(6)   | 131.5(2) | C(28)-C(29)-C(30) | 125.1(2) | C(60)-C(50)-C(51) | 115.3(2) |
| C(7)-C(8)-C(18)  | 120.1(2) | C(28)-C(29)-C(39) | 120.2(3) | C(50)-C(51)-C(52) | 113.1(2) |
| C(7)-C(8)-C(9)   | 124.7(2) | C(30)-C(29)-C(39) | 114.6(2) | O(12)-C(52)-C(53) | 103.76(19) |
| C(18)-C(8)-C(9)  | 115.2(2) | C(29)-C(30)-C(31) | 112.8(2) | O(12)-C(52)-C(51) | 108.07(19) |
| Bond          | Dist (Å) | Bond          | Dist (Å) | Bond          | Dist (Å) |
|--------------|----------|--------------|----------|--------------|----------|
| C(8)-C(9)-C(10) | 111.6(2) | O(7)-C(31)-C(32) | 104.1(2) | C(53)-C(52)-C(51) | 113.3(2) |
| O(2)-C(10)-C(11) | 103.86(19) | O(7)-C(31)-C(30) | 107.6(2) | C(54)-C(53)-C(52) | 110.1(2) |
| O(2)-C(10)-C(9) | 108.74(19) | C(32)-C(31)-C(30) | 113.0(2) | C(53)-C(54)-C(61) | 108.0(2) |
| C(11)-C(10)-C(9) | 112.8(2) | C(33)-C(32)-C(31) | 110.4(2) | C(53)-C(54)-C(55) | 129.2(2) |
| C(12)-C(11)-C(10) | 110.5(2) | C(32)-C(33)-C(40) | 107.3(2) | C(61)-C(54)-C(55) | 122.6(2) |
| C(11)-C(12)-C(19) | 107.5(2) | C(32)-C(33)-C(34) | 130.1(2) | O(14)-C(55)-C(54) | 106.13(18) |
| C(11)-C(12)-C(13) | 129.0(2) | C(40)-C(33)-C(34) | 122.2(2) | O(14)-C(55)-C(56) | 108.1(2) |
| C(19)-C(12)-C(13) | 123.2(2) | O(9)-C(34)-C(33) | 113.05(19) | C(54)-C(55)-C(56) | 111.9(2) |
| O(4)-C(13)-C(12) | 106.03(18) | O(9)-C(34)-C(35) | 105.70(19) | C(55)-C(56)-C(43) | 112.2(2) |
| O(4)-C(13)-C(14) | 109.31(19) | C(33)-C(34)-C(35) | 111.1(2) | C(59)-C(57)-C(58) | 121.4(2) |
| C(12)-C(13)-C(14) | 111.06(19) | C(34)-C(35)-C(22) | 111.0(2) | C(59)-C(57)-C(43) | 120.8(2) |
| C(13)-C(14)-C(1) | 111.6(2) | C(38)-C(36)-C(37) | 119.9(2) | C(58)-C(57)-C(43) | 117.7(2) |
| C(17)-C(15)-C(16) | 121.5(3) | C(38)-C(36)-C(22) | 124.5(2) | O(13)-C(61)-O(12) | 122.2(2) |
| C(17)-C(15)-C(1) | 120.6(2) | C(37)-C(36)-C(22) | 115.7(2) | O(13)-C(61)-C(54) | 129.5(2) |
| C(16)-C(15)-C(1) | 117.9(2) | O(8)-C(40)-O(7) | 121.5(2) | O(12)-C(61)-C(54) | 108.3(2) |
| O(3)-C(19)-O(2) | 121.9(2) | O(8)-C(40)-C(33) | 129.7(2) | O(15)-C(62)-O(14) | 123.3(2) |
| O(3)-C(19)-C(12) | 129.4(2) | O(7)-C(40)-C(33) | 108.8(2) | O(15)-C(62)-C(63) | 126.1(3) |
| O(2)-C(19)-C(12) | 108.66(19) | O(10)-C(41)-O(9) | 122.6(2) | O(14)-C(62)-C(63) | 110.5(2) |
| O(5)-C(20)-O(4) | 123.6(2) | O(10)-C(41)-C(42) | 125.4(2) | C(78)-C(64)-C(77) | 112.6(2) |
| O(5)-C(20)-C(21) | 126.4(2) | O(9)-C(41)-C(42) | 111.9(2) | C(78)-C(64)-C(65) | 112.7(2) |
| O(4)-C(20)-C(21) | 110.0(2) | C(57)-C(43)-C(44) | 111.6(2) | C(77)-C(64)-C(65) | 110.3(2) |
| C(36)-C(22)-C(35) | 114.4(2) | C(57)-C(43)-C(56) | 111.6(2) | C(66)-C(65)-C(64) | 111.7(2) |
|               |          | C(44)-C(43)-C(56) | 111.9(2) | C(67)-C(66)-O(16) | 109.7(2) |
| Bond Lengths | Bond Angles |
|--------------|-------------|
| C(67)-C(66)-C(65) | 134.6(2) |
| O(16)-C(66)-C(65) | 115.5(2) |
| C(66)-C(67)-C(68) | 107.1(2) |
| O(17)-C(67)-C(68) | 108.5(2) |
| C(69)-C(68)-C(66) | 107.3(2) |
| O(20)-C(68)-C(66) | 122.4(2) |
| C(68)-C(69)-O(16) | 108.9(2) |
| O(20)-C(69)-O(16) | 120.2(2) |
| C(68)-C(69)-C(70) | 130.9(2) |
| O(19)-C(69)-C(70) | 111.4(2) |
| O(16)-C(69)-C(70) | 120.2(2) |
| C(3)-O(1)-C(6) | 106.86(19) |
| C(71)-C(70)-C(69) | 131.3(2) |
| C(19)-O(2)-C(10) | 109.44(18) |
| C(70)-C(71)-C(81) | 120.3(2) |
| C(20)-O(4)-C(13) | 116.41(18) |
| C(70)-C(71)-C(72) | 125.3(2) |
| C(24)-O(6)-C(27) | 107.1(2) |
| C(81)-C(71)-C(72) | 114.4(2) |
| C(40)-O(7)-C(31) | 109.26(19) |
| C(71)-C(72)-C(73) | 112.2(2) |
| C(41)-O(9)-C(34) | 115.79(19) |
| O(17)-C(73)-C(74) | 103.83(18) |
| C(45)-O(11)-C(48) | 107.35(19) |
| O(17)-C(73)-C(72) | 107.6(2) |
| C(61)-O(12)-C(52) | 109.83(18) |
| C(74)-C(73)-C(72) | 112.9(2) |
| C(62)-O(14)-C(55) | 117.24(19) |
| C(75)-C(74)-C(73) | 110.0(2) |
| C(69)-O(16)-C(66) | 107.02(19) |
| C(74)-C(75)-C(82) | 108.1(2) |
| C(82)-O(17)-C(73) | 109.31(18) |
| C(74)-C(75)-C(76) | 130.1(2) |
| C(83)-O(19)-C(76) | 116.3(2) |
| C(82)-C(75)-C(76) | 121.4(2) |
| O(19)-C(76)-C(75) | 112.2(2) |
| O(19)-C(76)-C(77) | 103.89(19) |
| C(75)-C(76)-C(77) | 111.8(2) |
| C(76)-C(77)-C(64) | 113.5(2) |
| C(80)-C(78)-C(79) | 120.4(3) |
| C(80)-C(78)-C(64) | 121.6(3) |
| C(79)-C(78)-C(64) | 117.9(2) |
Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for gs18 006b. The anisotropic displacement factor exponent takes the form: $-2\pi^2 \left[ h^2 a^* a^*_1 + \ldots + 2hk a^* b^* U^{12} \right]$

|     | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|-----|----------|----------|----------|----------|----------|----------|
| C(1)| 28(1)    | 37(1)    | 26(1)    | 1(1)     | 0(1)     | 1(1)     |
| C(2)| 37(1)    | 42(1)    | 26(1)    | -1(1)    | 1(1)     | 4(1)     |
| C(3)| 34(1)    | 40(1)    | 28(1)    | 5(1)     | 2(1)     | 5(1)     |
| C(4)| 42(2)    | 43(1)    | 36(1)    | 10(1)    | 7(1)     | 3(1)     |
| C(5)| 40(2)    | 38(1)    | 49(2)    | 8(1)     | 5(1)     | -1(1)    |
| C(6)| 33(1)    | 28(1)    | 37(1)    | 3(1)     | -1(1)    | 0(1)     |
| C(7)| 35(1)    | 28(1)    | 40(1)    | 0(1)     | -3(1)    | 1(1)     |
| C(8)| 31(1)    | 29(1)    | 38(1)    | 0(1)     | -2(1)    | 3(1)     |
| C(9)| 28(1)    | 31(1)    | 34(1)    | -1(1)    | 1(1)     | 1(1)     |
| C(10)| 33(1)  | 28(1)   | 30(1)   | -2(1)   | 1(1)    | -4(1)   |
| C(11)| 29(1) | 29(1)  | 29(1)  | 1(1)   | -3(1)  | -2(1)  |
| C(12)| 31(1) | 29(1)  | 24(1)  | 1(1)   | -3(1)  | -1(1)  |
| C(13)| 26(1) | 30(1)  | 29(1)  | 1(1)   | -4(1)  | 0(1)   |
| C(14)| 29(1) | 35(1)  | 29(1)  | 2(1)   | 0(1)   | -1(1)  |
| C(15)| 34(1) | 39(1)  | 28(1)  | -1(1)  | -1(1)  | 5(1)   |
| C(16)| 50(2) | 47(2)  | 60(2)  | -17(1) | 15(2)  | 3(1)   |
| C(17)| 44(2) | 39(1)  | 43(2)  | -2(1)  | -2(1)  | 0(1)   |
| C(18)| 45(2) | 31(1)  | 42(1)  | -1(1)  | 0(1)   | 4(1)   |
| C(19)| 34(1) | 28(1)  | 26(1)  | 1(1)   | 1(1)   | 1(1)   |
| C(20)| 32(1) | 32(1)  | 30(1)  | 1(1)   | -2(1)  | 1(1)   |
| C(21)| 34(1) | 43(1)  | 40(1)  | -5(1)  | -8(1)  | 5(1)   |
| C(22)| 27(1) | 28(1)  | 32(1)  | 0(1)   | 4(1)   | 2(1)   |
| C(23)| 30(1) | 33(1)  | 38(1)  | -2(1)  | 3(1)   | 5(1)   |
| C(24)| 32(1) | 30(1)  | 39(1)  | 2(1)   | 3(1)   | 4(1)   |
| C(25)| 31(1) | 38(1)  | 48(2)  | 2(1)   | -2(1)  | 3(1)   |
| C(26)| 37(1) | 37(1)  | 46(2)  | -1(1)  | -10(1) | 0(1)   |
| C(27)| 40(1) | 30(1)  | 35(1)  | -2(1)  | -8(1)  | 4(1)   |
| C(28)| 49(2) | 31(1)  | 32(1)  | -1(1)  | -8(1)  | 3(1)   |
| C(29)| 50(2) | 31(1)  | 29(1)  | 1(1)   | 0(1)   | 2(1)   |
| C(30)| 40(1) | 33(1)  | 32(1)  | 1(1)   | 3(1)   | -2(1)  |
| C(31)| 37(1) | 37(1)  | 30(1)  | -3(1)  | 1(1)   | 1(1)   |
| C(32)| 32(1) | 28(1)  | 33(1)  | -2(1)  | 0(1)   | 1(1)   |
| C(33) | 30(1) | 27(1) | 30(1) | -1(1) | 1(1) | 1(1) |
|-------|-------|-------|-------|-------|------|------|
| C(34) | 30(1) | 25(1) | 32(1) | -1(1) | -1(1) | -2(1) |
| C(35) | 28(1) | 29(1) | 35(1) | 0(1) | 3(1) | -2(1) |
| C(36) | 26(1) | 32(1) | 32(1) | 0(1) | 5(1) | 4(1) |
| C(37) | 45(2) | 37(1) | 37(1) | -1(1) | -3(1) | -4(1) |
| C(38) | 42(2) | 37(1) | 34(1) | 3(1) | 5(1) | 1(1) |
| C(39) | 62(2) | 50(2) | 32(1) | -2(1) | 3(1) | 2(1) |
| C(40) | 30(1) | 30(1) | 35(1) | 2(1) | 4(1) | 2(1) |
| C(41) | 30(1) | 34(1) | 33(1) | -3(1) | -2(1) | 5(1) |
| C(42) | 43(2) | 31(1) | 47(2) | 1(1) | -2(1) | 5(1) |
| C(43) | 29(1) | 39(1) | 28(1) | -1(1) | 2(1) | -3(1) |
| C(44) | 38(1) | 41(1) | 25(1) | -1(1) | 1(1) | -7(1) |
| C(45) | 36(1) | 40(1) | 23(1) | 1(1) | 1(1) | -8(1) |
| C(46) | 44(2) | 45(2) | 33(1) | 4(1) | -9(1) | -3(1) |
| C(47) | 44(2) | 38(1) | 37(1) | 1(1) | -6(1) | 2(1) |
| C(48) | 37(1) | 33(1) | 30(1) | 2(1) | 1(1) | -1(1) |
| C(49) | 38(1) | 32(1) | 33(1) | 0(1) | 3(1) | -2(1) |
| C(50) | 34(1) | 34(1) | 28(1) | -2(1) | 3(1) | -4(1) |
| C(51) | 28(1) | 39(1) | 28(1) | 0(1) | 1(1) | -2(1) |
| C(52) | 32(1) | 32(1) | 29(1) | 0(1) | 0(1) | 3(1) |
| C(53) | 27(1) | 35(1) | 26(1) | 3(1) | 3(1) | 0(1) |
| C(54) | 31(1) | 35(1) | 23(1) | 3(1) | 2(1) | 1(1) |
| C(55) | 30(1) | 35(1) | 29(1) | 1(1) | 5(1) | -1(1) |
| C(56) | 31(1) | 38(1) | 27(1) | 0(1) | 3(1) | -2(1) |
| C(57) | 31(1) | 41(1) | 31(1) | -3(1) | 5(1) | -4(1) |
| C(58) | 45(2) | 40(1) | 31(1) | -3(1) | 0(1) | -8(1) |
| C(59) | 40(2) | 47(2) | 44(2) | -11(1) | -1(1) | 3(1) |
| C(60) | 42(1) | 37(1) | 32(1) | -1(1) | -4(1) | -4(1) |
| C(61) | 35(1) | 37(1) | 28(1) | 1(1) | 1(1) | 0(1) |
| C(62) | 34(1) | 40(1) | 31(1) | 5(1) | -3(1) | -7(1) |
| C(63) | 36(1) | 55(2) | 36(1) | 2(1) | 3(1) | -8(1) |
| C(64) | 31(1) | 33(1) | 32(1) | -4(1) | -3(1) | -1(1) |
| C(65) | 34(1) | 36(1) | 34(1) | -2(1) | -5(1) | 5(1) |
| C(66) | 28(1) | 39(1) | 34(1) | -7(1) | -5(1) | 6(1) |
| C(67) | 26(1) | 44(1) | 41(1) | -9(1) | -4(1) | 2(1) |
| C(68) | 28(1) | 40(1) | 41(1) | -7(1) | 4(1) | -3(1) |
| C(69) | 28(1) | 34(1) | 33(1) | -5(1) | 5(1) | 0(1) |
| C(70) | 31(1) | 39(1) | 32(1) | -5(1) | 5(1) | -1(1) |
| C(71) | 32(1) | 43(1) | 28(1) | -6(1) | 3(1) | -5(1) |
|-------|-------|-------|-------|-------|------|-------|
| C(72) | 30(1) | 39(1) | 31(1) | -6(1) | 1(1) | -6(1) |
| C(73) | 27(1) | 42(1) | 26(1) | 2(1)  | 2(1) | -3(1) |
| C(74) | 27(1) | 33(1) | 32(1) | -1(1) | 3(1) | 0(1)  |
| C(75) | 26(1) | 32(1) | 30(1) | 0(1)  | 1(1) | 1(1)  |
| C(76) | 31(1) | 30(1) | 29(1) | -3(1) | 1(1) | 1(1)  |
| C(77) | 29(1) | 34(1) | 32(1) | -6(1) | -2(1)| 0(1)  |
| C(78) | 38(1) | 38(1) | 36(1) | 2(1)  | 0(1) | 2(1)  |
| C(79) | 67(2) | 86(3) | 36(2) | 9(2)  | -9(2)| -22(2)|
| C(80) | 44(2) | 41(2) | 53(2) | 9(1)  | -2(1)| 0(1)  |
| C(81) | 38(2) | 70(2) | 28(1) | -3(1) | 1(1) | -10(1)|
| C(82) | 24(1) | 42(1) | 29(1) | -2(1) | 1(1) | 1(1)  |
| C(83) | 37(2) | 41(1) | 24(1) | 2(1)  | 1(1) | 9(1)  |
| C(84) | 51(2) | 37(1) | 39(1) | -3(1) | -2(1)| 12(1) |
| O(1)  | 34(1) | 32(1) | 29(1) | 2(1)  | 2(1) | 1(1)  |
| O(2)  | 33(1) | 27(1) | 33(1) | -2(1) | 4(1) | -3(1) |
| O(3)  | 43(1) | 28(1) | 45(1) | -2(1) | 6(1) | -5(1) |
| O(4)  | 30(1) | 32(1) | 33(1) | -5(1) | -5(1)| 3(1)  |
| O(5)  | 34(1) | 36(1) | 44(1) | -8(1) | -2(1)| 4(1)  |
| O(6)  | 32(1) | 33(1) | 32(1) | 0(1)  | -1(1)| 1(1)  |
| O(7)  | 32(1) | 42(1) | 36(1) | 4(1)  | 4(1) | -1(1) |
| O(8)  | 34(1) | 43(1) | 40(1) | 4(1)  | -4(1)| -7(1) |
| O(9)  | 29(1) | 24(1) | 35(1) | 1(1)  | -2(1)| 1(1)  |
| O(10) | 32(1) | 37(1) | 70(1) | -1(1) | -1(1)| 3(1)  |
| O(11) | 34(1) | 35(1) | 26(1) | -2(1) | -1(1)| -3(1) |
| O(12) | 32(1) | 35(1) | 33(1) | 1(1)  | -1(1)| 4(1)  |
| O(13) | 44(1) | 37(1) | 44(1) | -1(1) | -4(1)| 9(1)  |
| O(14) | 32(1) | 37(1) | 31(1) | -3(1) | 7(1) | -4(1) |
| O(15) | 44(1) | 40(1) | 56(1) | -8(1) | 1(1) | -6(1) |
| O(16) | 29(1) | 35(1) | 31(1) | -4(1) | -1(1)| 0(1)  |
| O(17) | 25(1) | 51(1) | 27(1) | -1(1) | 1(1) | -7(1) |
| O(18) | 29(1) | 54(1) | 31(1) | 4(1)  | 3(1) | -6(1) |
| O(19) | 34(1) | 32(1) | 34(1) | -4(1) | 1(1) | 4(1)  |
| O(20) | 35(1) | 48(1) | 35(1) | 5(1)  | 4(1) | 9(1)  |
4. DFT Calculations

Computational details

The ground state electronic structures of the full models of compounds 21a, 21b, 22, 22b and the corresponding transition state structures 21a‡ and 21b‡ were calculated by density functional theory (DFT) methods using the Gaussian 16 program packages.[7] Open shell systems were calculated by the unrestricted Kohn–Sham approach (UKS). Geometry optimization followed by vibrational analysis was performed in solvent media. Solvent effects were described by the polarizable continuum model (PCM) with standard parameters for benzene.[8] The 6-31G(d) polarized double-ζ basis sets[9] were employed together with the Becke Three-Parameter Hybrid Functionals (B3LYP).[10] Gibbs free energies (G) and energy differences (ΔG) are listed in Tables 2/3 and atomic coordinates of the calculated structures are listed in Tables 4–9.

Table 2: Gibbs free energies (G) of compounds 21a/b, 21a/b‡ and 22/22b.

| compound | Gibbs free energy (G) [hartree] |
|----------|---------------------------------|
| 21a      | −1342.011862                    |
| 21b      | −1342.030828                    |
| 21a‡     | −1341.975546                    |
| 21b‡     | −1341.968419                    |
| 22       | −1342.009209                    |
| 22b      | −1342.004552                    |

Table 3: Gibbs free energy differences (ΔG).

| compounds       | Gibbs free energy difference (ΔG) [hartree] | Gibbs free energy difference (ΔG) [kcal/mol] |
|-----------------|---------------------------------------------|---------------------------------------------|
| 21a – 21b       | 0.018966                                     | 11.901                                      |
| 21a‡ – 21b‡     | 0.007127                                     | 4.4723                                      |
| 21a – 21a‡      | 0.036316                                     | 22.789                                      |
| 21b – 21b‡      | 0.062409                                     | 39.162                                      |
| 22 – 22b        | 0.004657                                     | 2.9223                                      |
Figure 3: Calculated structures of compounds 21a/b, 21a/b‡ and 22/22b.
Table 4: Atomic coordinates of structure 21a.

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | 2.33118 | 1.60194 | 0.42496 |
| C    | 2.6372  | 2.85776 | -0.0177 |
| C    | 1.47487 | 3.35107 | -0.70644 |
| C    | 0.5277  | 2.36681 | -0.63949 |
| O    | 1.04438 | 1.31883 | 0.0687 |
| H    | 3.57603 | 3.37631 | 0.12236 |
| H    | 1.37218 | 4.30554 | -1.20437 |
| C    | -0.79421 | 2.09063 | -1.2907 |
| H    | -0.6147 | 1.34595 | -2.07825 |
| H    | -1.12768 | 2.99778 | -1.80415 |
| C    | -1.94948 | 1.55042 | -0.3611 |
| H    | -1.47813 | 1.13826 | 0.53671 |
| C    | -2.75827 | 0.39607 | -1.02816 |
| H    | -2.65935 | 0.42351 | -2.12017 |
| H    | -3.82228 | 0.51921 | -0.80871 |
| C    | -2.40563 | -1.03631 | -0.56088 |
| H    | -3.04118 | -1.74989 | -1.09119 |
| C    | -0.96424 | -1.40584 | -0.76449 |
| C    | 0.08829  | -1.07311 | -0.01242 |
| C    | 1.35062  | -1.3508 | -0.7766 |
| H    | 0.08977  | -0.59923 | 0.95696 |
| C    | 2.56092  | -1.83769 | 0.01766 |
| H    | 2.24232  | -2.32305 | 0.94466 |
| H    | 3.09222  | -2.59399 | -0.56874 |
| C    | 3.60529  | -0.73725 | 0.36899 |
| C    | 3.09333  | 0.53617 | 1.15504 |
| H    | 4.02593  | 1.03088 | 1.47853 |

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | -0.45447 | -2.16136 | -1.93905 |
| O    | 0.91693 | -2.2437 | -1.83589 |
| O    | -1.0674 | -2.6678 | -2.85061 |
| C    | -2.80686 | 2.72878 | 0.10266 |
| C    | -2.2399  | 3.51081 | 1.26316 |
| H    | -1.2305 | 3.88081 | 1.03953 |
| H    | -2.86923 | 4.36889 | 1.51859 |
| H    | -2.14565 | 2.87517 | 2.15416 |
| C    | -3.9479  | 3.09464 | -0.49155 |
| H    | -4.37187 | 2.55771 | -1.3355 |
| H    | -4.50468 | 3.96381 | -0.1503 |
| O    | -2.73886 | -1.08039 | 0.85278 |
| C    | -3.01686 | -2.30002 | 1.38051 |
| O    | -3.00233 | -3.32854 | 0.74087 |
| C    | -3.34019 | -2.18126 | 2.85052 |
| H    | -4.16574 | -1.4786 | 3.0014 |
| H    | -3.60786 | -3.16194 | 3.24493 |
| H    | -2.47322 | -1.78917 | 3.39284 |
| H    | 1.63087  | -0.4299 | -1.29703 |
| C    | 4.4304  | -0.32765 | -0.85258 |
| H    | 5.17913 | 0.4292 | -0.58525 |
| H    | 4.95147  | -1.20042 | -1.25821 |
| H    | 3.80599  | 0.10105 | -1.64245 |
| O    | 4.44217  | -1.42724 | 1.32618 |
| H    | 5.26838  | -0.92341 | 1.42013 |
| O    | 2.34083  | 0.11763 | 2.28888 |
| H    | 2.86156  | -0.61223 | 2.67228 |
Table 5: Atomic coordinates of structure 21b.

| atom | X      | Y      | Z      |
|------|--------|--------|--------|
| C    | 2.63742| 1.19574| -0.97335|
| C    | 2.401  | 1.46989| -2.28951|
| C    | 1.13715| 2.14454| -2.34727|
| C    | 0.69035| 2.25372| -1.06174|
| O    | 1.59846| 1.66754| -0.21389|
| H    | 3.05644| 1.23818| -3.11825|
| H    | 0.6366 | 2.5216 | -3.22868|
| C    | -0.51926| 2.85862| -0.42865|
| H    | -1.11728| 3.33939| -1.21144|
| H    | -0.19843| 3.64954| 0.25823 |
| C    | -1.3919 | 1.82038| 0.34297 |
| H    | -0.68817| 1.29038| 1.0012  |
| C    | -1.98767| 0.79644| -0.64721|
| H    | -1.32154| 0.69553| -1.51111|
| H    | -2.94448| 1.15394| -1.0363 |
| C    | -2.18493| -0.59573| -0.0396 |
| C    | -0.88919| -1.26718| 0.3224  |
| C    | 0.29645 | -1.24742| -0.29846|
| C    | 1.29231 | -2.06819| 0.46812 |
| H    | 0.55004 | -0.72797| -1.215  |
| C    | 2.53168 | -1.34061| 1.02058 |
| H    | 2.21462 | -0.43909| 1.55292 |
| H    | 2.96251 | -2.01732| 1.76397 |
| C    | 3.68033 | -0.99269| 0.03531 |
| C    | 3.789   | 0.54425 | -0.27399|
| H    | 4.64737 | 0.63318 | -0.96564|
| C    | -0.75385| -2.11468| 1.53503 |
### Table 6: Atomic coordinates of structure 21a.

| atom | X   | Y   | Z    |
|------|-----|-----|------|
| C    | -1.67941 | -0.97604 | -0.68871 |
| C    | -0.94188  | 0.88881  | -0.30023 |
| C    | 0.25349   | 0.61304  | 0.42577  |
| C    | 0.23619   | -1.57339 | 0.16523  |
| C    | 0.38885   | -1.64413 | -1.25447 |
| C    | -0.8186   | -1.29427 | -1.78976 |
| C    | 1.67825   | 0.79431  | -0.03102 |
| C    | 2.72159   | 0.05893  | 0.83661  |
| C    | 2.65805   | -1.48964 | 0.9032   |
| C    | 1.21835   | -2.02192 | 1.2009   |
| C    | -3.20409  | -1.02716 | -0.77479 |
| C    | -3.91808  | 0.33579  | -0.51789 |
| C    | -3.36829  | 0.96603  | 0.76516  |
| C    | -1.93349  | 1.52025  | 0.67529  |
| O    | -1.3374   | 1.38849  | 1.97572  |
| C    | -0.06657  | 0.8516   | 1.86203  |
| O    | 0.60854   | 0.6876   | 2.85963  |
| C    | 3.3705    | -2.22729 | -0.23381 |
| C    | 3.44257   | -3.73265 | -0.09337 |
| C    | 3.965     | -1.61634 | -1.26718 |
| O    | -1.10616  | -1.55196 | 0.44097  |
| O    | -3.65788  | -1.99389 | 0.15175  |
| O    | -5.28893  | -0.06339 | -0.30031 |
| C    | -3.88531  | 1.2576   | -1.74057 |
| H    | -0.89394  | 1.3229   | -1.29213 |
| H    | -1.96297  | 2.60041  | 0.48241  |
| O    | 1.97975   | 2.23665  | 0.0624   |
Table 7: Atomic coordinates of structure 21b\textsuperscript{1}.

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | -1.33595 | -0.63783 | -1.03674 |
| C    | -0.96339 | 0.83773  | 0.38802 |
| C    | 0.23342  | 0.36846  | 0.99914 |
| C    | 0.61615  | -1.29628 | -0.32992 |
| C    | 0.84515  | -0.59959 | -1.55627 |
| C    | -0.38301 | -0.20742 | -2.01147 |
| C    | 1.62112  | 1.0506  | 1.03189 |
| C    | 2.76187  | 0.02859  | 1.38916 |
| C    | 2.95287  | -1.32191 | 0.64249 |
| C    | 1.61406  | -2.10146 | 0.44039 |
| C    | -2.81933 | -0.83308 | -1.33249 |
| C    | -3.77547 | 0.07271  | -0.49766 |
| C    | -3.40449 | -0.02189 | 0.98555 |
| C    | -2.09645 | 0.68138  | 1.39841 |
| O    | -1.52771 | -0.1015  | 2.4701  |
| C    | -0.18607 | -0.2458  | 2.29621 |
| O    | 0.48469  | -0.79161 | 3.15198 |
| C    | 3.85683  | -1.30768 | -0.59311 |
| C    | 4.17345  | -2.66715 | -1.18021 |
| C    | 4.42513  | -0.2094  | -1.1054 |
| O    | -0.71771 | -1.62401 | -0.27979 |
| O    | -3.13094 | -2.1957  | -1.11496 |
| O    | -5.06135 | -0.55333 | -0.70277 |
| C    | -3.85617 | 1.50182  | -1.04182 |
| H    | -0.9662  | 1.74068  | -0.20778 |
| H    | -2.32366 | 1.67143  | 1.81431 |
| O    | 1.93173  | 1.67706  | -0.21729 |

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| O    | 0.96234 | 3.60195 | 0.49677 |
| C    | 1.57572 | 2.97737 | -0.34371 |
| C    | 2.05349 | 3.53314 | -1.66447 |
| H    | 1.81609 | -0.35476 | -1.9568 |
| H    | -0.61081 | 0.41831 | -2.86581 |
| H    | 1.62239 | 1.7846  | 1.80178 |
| H    | 2.57957 | -0.22372 | 2.43575 |
| H    | 3.69992 | 0.59249  | 1.36309 |
| H    | 3.50859 | -1.94929 | 1.35705 |
| H    | 1.80908 | -3.05396 | -0.067 |
| H    | 1.2007  | -2.3453  | 1.42187 |
| H    | -2.97741 | -0.57071 | -2.39201 |
| H    | -4.22527 | 0.37809  | 1.59514 |
| H    | -3.30774 | -1.08417 | 1.22864 |
| H    | 4.46432 | -3.38332 | -0.4 |
| H    | 3.308   | -3.10075 | -1.69802 |
| H    | 4.99045 | -2.60268 | -1.90483 |
| H    | 5.11867 | -0.28033 | -1.94025 |
| H    | 4.21756 | 0.78712  | -0.73433 |
| H    | -4.10235 | -2.20745 | -1.02118 |
| H    | -5.66655 | -0.24431 | -0.01039 |
| H    | -2.89038 | 2.01387  | -1.04389 |
| H    | -4.23643 | 1.48163  | -2.06809 |
| H    | -4.54812 | 2.09918  | -0.43622 |
| H    | 3.14828 | 3.5294   | -1.69626 |
| H    | 1.70109 | 2.90706  | -2.49008 |
| H    | 1.6882  | 4.5535   | -1.78496 |
Table 8: Atomic coordinates of structure 22.

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | -1.57379 | -0.90291 | -0.65263 |
| C    | -1.02712 | 0.56519 | -0.38584 |
| C    | 0.29223 | 0.2602 | 0.36885 |
| C    | 0.35492 | -1.3161 | 0.2473 |
| C    | 0.48357 | -1.67577 | -1.23813 |
| C    | -0.71073 | -1.44667 | -1.77832 |
| C    | 1.6434 | 0.80452 | -0.09476 |
| C    | 0.35492 | 0.29223 | 0.36885 |
| C    | 0.48357 | -1.3161 | 0.2473 |
| C    | -0.71073 | -1.67577 | -1.23813 |
| C    | 1.6434 | 0.80452 | -0.09476 |
| C    | 2.78364 | 0.21198 | 0.75776 |
| C    | 2.80951 | -1.3388 | 0.86467 |
| C    | 1.3866 | -1.93009 | 1.17263 |
| C    | -3.1045 | -1.07715 | -0.80775 |
| C    | -3.9118 | 0.19839 | -0.40759 |
| C    | -3.29085 | 0.79253 | 0.86104 |
| C    | -1.89527 | 1.37626 | 0.60295 |
| O    | -1.18792 | 1.3912 | 1.86179 |
| C    | 0.64338 | 0.71652 | 1.80973 |
| O    | 3.55203 | -2.05105 | -0.26909 |
| C    | 3.75645 | -3.53908 | -0.08249 |
| C    | 4.06721 | -1.42877 | -1.33761 |
| O    | -1.03594 | -1.61086 | 0.49705 |
| O    | -3.50476 | -2.18433 | -0.02945 |
| O    | -5.23395 | -0.30073 | -0.12937 |
| C    | -4.01563 | 1.20092 | -1.56329 |
| H    | -0.88115 | 1.11436 | -1.31731 |
| H    | -1.96593 | 2.41786 | 0.27629 |
| O    | 1.62644 | 2.25105 | 0.0424 |

| atom | X     | Y     | Z     |
|------|-------|-------|-------|
| H    | 1.39797 | -1.99472 | -1.71886 |
| H    | -1.0195 | -1.52461 | -2.8148 |
| H    | 1.77785 | 0.57545 | -1.15409 |
| H    | 3.73836 | 0.57159 | 0.36612 |
| H    | 2.6703 | 0.61738 | 1.76432 |
| H    | 3.4039 | -1.56244 | 1.76281 |
| H    | 1.38564 | -3.01842 | 1.06706 |
| H    | 1.12859 | -1.699 | 2.20796 |
| H    | -3.31044 | -1.27159 | -1.8739 |
| H    | -3.94003 | 1.56895 | 1.286 |
| H    | -3.20123 | -0.01056 | 1.59956 |
| H    | 4.14974 | -3.76296 | 0.91822 |
| H    | 2.81812 | -4.09969 | -0.182 |
| H    | 4.4576 | -3.9372 | -0.82182 |
| H    | 4.63506 | -1.9826 | -2.08161 |
| H    | 3.95543 | -0.36476 | -1.52258 |
| H    | -4.4551 | -2.03661 | 0.13417 |
| H    | -5.69986 | 0.34602 | 0.42312 |
| H    | -3.03831 | 1.53476 | -1.92708 |
| H    | -4.55059 | 0.74052 | -2.39965 |
| H    | -4.57571 | 2.08987 | -1.24891 |
| O    | 3.17689 | 2.44602 | -1.59971 |
| C    | 2.453 | 2.9548 | -0.76858 |
| C    | 2.34823 | 4.43391 | -0.48856 |
| H    | 2.94429 | 4.98654 | -1.21536 |
| H    | 1.30414 | 4.7586 | -0.53151 |
| H    | 2.71405 | 4.64373 | 0.52233 |
Table 9: Atomic coordinates of structure 22b.

| atom | X       | Y       | Z       |
|------|---------|---------|---------|
| C    | -1.31363| -0.46047| -0.9402 |
| C    | -1.03417| 0.60392 | 0.20646 |
| C    | 0.29722 | 0.06372 | 0.79691 |
| C    | 0.62746 | -1.09715| -0.21941|
| C    | 0.86116 | -0.48474| -1.60414|
| C    | -0.33804| -0.12553| -2.05561|
| C    | 1.54546 | 0.94255 | 1.04436 |
| C    | 2.76358 | 0.05978 | 1.39502 |
| C    | 3.02249 | -1.25208| 0.59279 |
| C    | 1.69824 | -2.03822| 0.28826 |
| C    | -2.78784| -0.68328| -1.35947|
| C    | -3.81124| 0.00665 | -0.40451|
| C    | -3.35426| -0.21275| 1.04125 |
| C    | -2.05909| 0.54492 | 1.36195 |
| O    | -1.41123| -0.14222| 2.45663 |
| C    | -0.14307| -0.49435| 2.16972 |
| O    | 0.51561 | -1.12312| 2.96749 |
| C    | 3.96501 | -1.14142| -0.60806|
| C    | 4.46591 | -2.46208| -1.15386|
| C    | 4.41171 | 0.00975 | -1.12486|
| O    | -0.70172| -1.64556| -0.36534|
| O    | -3.02464| -2.07365| -1.42021|
| O    | -5.04326| -0.69958| -0.64751|
| C    | -4.03178| 1.48189 | -0.75928|
| H    | -0.96404| 1.6154  | -0.18882|
| H    | -2.27769| 1.55469 | 1.72073 |
| O    | 1.86355 | 1.74749 | -0.11963|

| atom | X       | Y       | Z       |
|------|---------|---------|---------|
| O    | 0.6275  | 3.48413 | 0.65819 |
| C    | 1.36943 | 3.0079  | -0.17645|
| C    | 1.86972 | 3.71991 | -1.4093 |
| H    | 1.83326 | -0.34904| -2.05665|
| H    | -0.59717| 0.38665 | -2.97495|
| H    | 1.36271 | 1.63883 | 1.86642 |
| H    | 2.60749 | -0.23748| 2.43359 |
| H    | 3.65796 | 0.68994 | 1.37941 |
| H    | 3.56877 | -1.90104| 1.293   |
| H    | 1.87607 | -2.83004| -0.44459|
| H    | 1.35183 | -2.51483| 1.20738 |
| H    | -2.92131| -0.23479| -2.3584 |
| H    | -4.14045| 0.08632 | 1.74637 |
| H    | -3.1731 | -1.28388| 1.17595 |
| H    | 4.87685 | -3.09156| -0.35293|
| H    | 3.66528 | -3.04111| -1.62751|
| H    | 5.24857 | -2.30902| -1.90271|
| H    | 5.13039 | 0.01095 | -1.94121|
| H    | 4.07674 | 0.9789  | -0.77468|
| H    | -3.99231| -2.16015| -1.33262|
| H    | -5.6369 | -0.55108| 0.10506 |
| H    | -3.11215| 2.07426 | -0.71735 |
| H    | -4.44029| 1.55743 | -1.77185 |
| H    | -4.75115| 1.93624 | -0.06739 |
| H    | 1.41346 | 4.70833 | -1.47129 |
| H    | 2.95953 | 3.81903 | -1.36792 |
| H    | 1.62809 | 3.13644 | -2.30325 |
5. \(^1\)H- and \(^{13}\)C-NMR Spectra
SUPPORTING INFORMATION
(+)-norcembrenine 5 (1)
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