1. Synthesis of the C1–C7 fragment:

**(5S,6R) Methyl 5,6,7-trihydroxyheptanoate 2**

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\begin{align*}
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**Supporting Information:**

**General Remarks:** Reaction solvents were dried by standard procedures prior to use when necessary. All reactions including moisture- or air-sensitive reagents were carried out under an argon atmosphere. \(^1\)H NMR, \(^13\)C NMR and 2D Spectra (COSY, HSQC, HMBC, NOESY) spectra were recorded at room temperature with a Bruker ARX400 or AV400 or AC300 spectrometer in CDCl\(_3\) using the signal of residual CHCl\(_3\) (7.26 ppm), and CD-Cl\(_2\) (5.32 ppm) as internal standards. Deuterated solvents were purchased from Deutero GmbH. IR spectra were recorded with a Jasco FT/IR-400 plus spectrometer with single reflection horizontale ATR (ZnSe window). FD Mass spectra were obtained using a Finnigan MAT 95, the high-resolution mass spectra (HRMS) were recorded with a Waters Q Tof Ultima 3 Micromasses spectrometer. Optical rotation were recorded with Perkin-Elmer’s P 241 polarimeter. C, H, N, S analyses were conducted with a varioEL (Foss-Heracuts). Column chromatography was performed on MN silica gel 60M from Macherey-Nagel (grain size: 0.040-0.063 mm).

Analytical HPLC Systems were used to analyse the products: Knauer HPLC Pump 64 connected to a Phenomenex Gemini-NX C18 (110-5 4.6x250mm) column, a Knauer Variable Wavelength Monitor at \(\lambda=254\) nm or 220 nm and Knauer Differential Refractometer. Standard column (4x250 mm) Nucleosil 50-5 (5 µm). The remaining chromatographic conditions: flow rate and mobile phase are noted in analytical data.

**Preparative HPLC:** Knauer WellChrom Preparative Pump K-1800 (5S,6R)

Methyl 5,6,7-trihydroxy-2-heptenoate \(I\) \(\text{(5S,6R)}\)

1. Under Ar, methyl triphenylphosphoranylidenacetate (25 g, 75 mmol) in dry THF (350 mL), was treated with 2-deoxy-D-ribose \(I\) (6.47 g, 48 mmol). The resulting mixture was refluxed for 5 h, then, the mixture was stirred at 23 °C for 24 h. After completion of the reaction (TLC, \(^1\)H-NMR spectrum), the solvent was removed in vacuum to give the crude 43,5R-methyl 5,6,7-trihydroxy-2-heptenoate \(I\) (28.94 g including triphenylphosphine oxide), which was subjected to the proceeding hydrogenation without further purification.

**(5S,6R) Methyl 5,6,7-trihydroxy-2-heptenoate 2**

Under Ar, methyl heptenoate \(I\) (28.94 g, crude material) was dissolved in MeOH (400 mL). After addition of 10% Pd/C catalyst (1.6 g) and exchanging the Ar atmosphere against H\(_2\), the mixture was stirred for 2 d at 23 °C. After completion of the hydrogenation (TLC, \(^1\)H-NMR spectrum), the catalyst was filtered off and the solvent was removed via vacuum distillation to give a white solid. After purification via column chromatography (silica gel, EtOAc/MeOH 20:1), the methyl heptanoate \(2\) (7.68 g, 40 mmol, 83.3 %) was obtained as a colourless solid. \(R_e\) (EtOAc/MeOH 20:1): 0.19, mp: 35 - 36 °C (lit. 61 – 62 °C). [\(\alpha\)]\(D\) = -14.65⁰ (c = 1.03, 23°C, EtOH), [\(\alpha\)]\(D\) = -4.86⁰ (c = 1.04, 23°C, CH\(_2\)Cl\(_2\)). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta = 4.35\) (d, br, \(\deltaJHH = 5.6\) Hz, 1H, HO), 4.15 (s, br, 1H, OH), 4.00 (d, br, \(\deltaJHH = 5.6\) Hz 1H, OH), 3.69-3.64 (m, 2H, H-6, H-5), 3.64-3.58 (m, 1H, H-7), 3.62 (s, 3H, H-8), 3.55-3.50 (m, 1H, H-7'), 2.32 (t, \(\deltaJHH = 7.3\) Hz, 2H, H-2), 1.87-1.74 (m, 1H, H-4), 1.68-1.54 (m, 1H, H-4'), 1.54-1.36 (m, 2H, H-3). \(^13\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta = 174.53\) (C-1), 154.13 (C-2), 148.53 (C-3), 132.13 (C-4), 121.13 (C-5), 112.13 (C-6), 106.13 (C-7), 80.13 (C-8). IR (ATR): \(\nu = 3303\) (m), 2954 (m), 2905 (m), 1732 (s), 1461 (w), 1436 (m), 1236 (m), 1195 (m), 1175 (m), 1060 (m), 1017 (m), 921 (w), 869 (m), 668 (m) cm\(^{-1}\). MS [EI, 70 eV, 80 °C]: m/z (%): 192 [M\(^+\), < 1%], 160 [M-CH\(_2\)OH\(^+\), 3%], 132 [M-CH\(_2\)COOH\(^+\), < 1%], 129, [M-C\(_2\)H\(_5\)OH\(^+\), 2%], 128 [M-C\(_3\)H\(_4\)OH\(^+\), 22%], 99 [C\(_2\)H\(_3\)O\(_2\)\(^+\), 100%]. Analysis (C\(_3\)H\(_6\)O\(_3\)): calcd.: C = 49.99 %, H = 8.39 %, found: C = 49.88 %, H = 8.53 %.
Tritylether protection of (5S,6R) Methyl 5,6,7-trihydroxy-heptanoate 2

![Chemical structure of 2](image)

Methyl 5,6,7-trihydroxy-heptanoate 2 (6.92 g, 36 mmol) in pyridine (120 mL) was treated with chloro triphenylmethane (11.15 g, 40 mmol) and a catalytic amount of dimethylaminopyridine (DMAP) and the dark yellow solution was stirred for 24 h at 23 °C. Then, the mixture was heated to 60 °C for 6 h. After completion of the reaction (TLC) the mixture was cooled to 23 °C (red-brown colour) and poured into a mixture of ice and conc. Aq. HCl (1:1). The resulting mixture was extracted with EtOAc (3x 200 mL), the organic layer was washed with brine (1x 100 mL) and dried (MgSO4). After removal of the solvent, the residue was purified by column chromatography (silica gel, CH2Cl2/acetone 15:1). Yield: 5,6-dihydroxy-7-triphenylmethyloxephanolic acid methyl ester III (5 g, 11.5 mmol, 32 %) as a viscous oil and 6-(1-hydroxy-2-triphenylmethoxy)-tetrahydropyran-2-one II (8.45 g, 21 mmol, 52 %) as a colourless solid.

(6S)-6-[(1R)-1-Hydroxy-2-triphenylmethyloxypentanoic acid methyl ester III: Rf = 0.22 (CH2Cl2/acetone 9:1), mp: 56 – 57 °C, [α]D= -10.85° (c = 1.0, 23°C, CH2Cl2). 1H-NMR (400 MHz, CDCl3): δ = 7.42 (d, br, JHH = 7.43 Hz, 6H, H-10), 7.30 (dd, br, JHH = 6.5 Hz, JHH = 8.4 Hz, 6H, H-11), 7.24 (t, br, JHH = 7.44, 3H, H-12), 4.35 (ddd, JHH = 3.2 Hz, JHH = 5.4 Hz, JHH = 10.6 Hz, 1H, H-5), 3.92 – 3.85 (m, 1H, H-6), 3.38 (dd, JHH = 6.1, JHH = 9.7, 1H, H-7), 3.26 (dd, JHH = 5.4, JHH = 9.7, 1H, H-7'), 2.68 – 2.63 (m, br, 1H, OH), 2.58 – 2.48 (m, 1H, H-2), 2.43 – 2.33 (m, 1H, H-2'), 1.91 – 1.69 (m, 3H, H-3, H-4), 1.68 – 1.53 (m, 1H, H-4'). 13C-NMR (100 MHz, CDCl3): δ = 171.2 (C-1), 143.56 (C-9), 128.55 (C-11), 127.87 (C-10), 127.13 (C-12), 86.99 (C-8), 80.73 (C-5), 71.56 (C-6), 63.55 (C-7), 29.69 (C-4), 22.26 (C-2), 18.15 (C-3). IR (ATR); ν = 3447 (m), 2948 (m), 1730 (s), 1448 (m), 1217 (s), 1066 (s), 832 (s), 774 (s), 632 (m) cm⁻¹.


(5S,6R)-5,6-Dihydroxy-7-triphenylmethyloxephanolic acid methyl ester III: Rf = 0.44 (CH2Cl2/acetone 9:1), [α]D= -7.14° (c = 1.1, 23°C, CH2Cl2). 1H-NMR (400 MHz, CDCl3): δ = 7.51 – 7.43 (m, 6H, H-11), 7.38 – 7.31 (m, 6H, H-12), 7.31 – 7.24 (m, 3H, H-13), 3.69 – 3.58 (m, 2H, H-6, H-5), 3.62 (s, 3H, H-8), 3.35 (dd, JHH = 3.0 Hz, JHH = 9.6 Hz, 1H, H-7), 3.22 (dd, JHH = 6.0, JHH = 9.6 Hz, 1H, H-7'), 2.70 (s, br, OH), 2.31 (s, br, OH), 2.29 (t, JHH = 9.1 Hz, 2H, H-2), 1.83 – 1.70 (m, 1H, H-4'), 1.65 – 1.52 (m, 1H, H-4'), 1.44 – 1.33 (m, 1H, H-3), 1.33 – 2.12 (m, 1H, H-3'). 13C-NMR (100 MHz, CDCl3): δ = 175.66 (C-1), 145.64 (C-10), 130.21 (C-12), 129.78 (C-11), 128.94 (C-13), 88.81 (C-9), 74.80 (C-6), 74.37 (C-5), 66.37 (C-8), 53.20 (C-8), 35.50 (C-2), 33.50 (C-4), 22.92 (C-3). IR (ATR); ν = 3431 (m), 2934 (m), 1724 (s), 1489 (w), 1447 (m), 1241 (m), 1051 (s), 745 (s), 698 (s), 632 (m) cm⁻¹.


(6S)-6-[(1S)-1-tert.-Butyldimethylsilyloxy-2-oxo]-tetrahydropyran-2-one 5: Under Ar, trityl-protected valerolactone II (2.0 g, 5 mmol), imidazole (0.82 g, 12 mmol) in dry DMF (20 mL) were treated with tert.-butyldimethylsilyl chloride (0.9 g, 6 mmol) at 23 °C with stirring. After 78 h of stirring, work-up started by...
dilution with Et₂O (20 mL). The organic phase was washed with H₂O (3x 30 mL) and dried (MgSO₄). After removal of the solvent, the residue was purified via column chromatography (silica gel, gradient EtOAc/petroleum ether 1:10 - 1:5) to give fully protected valerolactone 3 (2.03 g, 3.9 mmol, 78 %) as a colorless solid. Rᵣ = 0.29 (EtOAc/petroleum ether 1:5), mp: 86 - 88 °C. [α]D₂⁺ = -19.9° (c = 1.03, 22°C, CH₂Cl₂). ¹H-NMR (400 MHz, CDCl₃): δ = 7.42 - 7.35 (m, 6H, H-10), 7.32 - 7.25 (m, 6H, H-11), 7.25 - 7.20 (m, 3H, H-12), 4.56 (dd, 1JHH = 2.6 Hz, 2JHH = 4.0 Hz, 1JHH = 10.6 Hz, 1H, H-5), 4.00 (dd, 2JHH = 2.6 Hz, 3JHH = 5.0 Hz, 1H, H-5). 13C-NMR (100 MHz, CDCl₃): δ = 176.7 (1H, H-2), 2.30 (dd, 1JHH = 6.8 Hz, 1JHH = 10.2 Hz, 1H, H-2'), 1.92 - 1.80 (m, 1H, H-4), 1.78 - 1.59 (m, 2H, H-3'), 1.59 - 1.46 (m, 1H, H-4'), 0.78 (s, 3H, H-9), 0.01 - 0.08 (2x s, 2x 3H, H-15). IR (ATR): ν = 2927 (m), 2852 (m), 1736 (s), 1447 (m), 1250 (s), 1057 (s), 827 (s), 778 (s), 700 (s), 632 (m) cm⁻¹. MS [EI, 70 eV, 180 °C]: m/z (%): 517 [M⁺, 5%], 259 [(C₃H₇O₅)⁺, 6%], 257 [(C₃H₅O₇Si⁺, 6%], 243 [(C₃H₅O₇Si⁺, 75%], 165 [(C₃H₆O⁺, 12%], 73 [(C₃H₇O₇Si⁺, 100%]. HRMS (220 °C, 80 eV): [C₉H₁₅O⁺]: calcd.: 257.11229, found: 257.11207, [C₁₃H₁₅O₂⁺]: calcd.: 257.15730, found: 257.15710. Analysis (C₉H₁₅O): calcd. C = 74.38 %, H = 7.80 %, found: C = 74.28 %, H = 7.84 %.

(6S) 6-[(IR) 1-tert-Butyl(dimethyl)silyloxy-2-hydroxy)-tetrahydropyran-2-one IV: Under Ar, to a solution of trityl protected valerolactone 3 (1.8 g, 3.48 mmol) in dry CH₂Cl₂ (20 mL) was added ZnBr₂ (1.83 g, 8.1 mmol). The mixture was stirred at 23 °C for 3.5 d (TLC). The reaction was quenched with sat. aq. NaHPO₄ (25 mL) and diluted with CH₂Cl₂ (20 mL). After stirring at 23 °C for 2 h, MgSO₄ was added until the aq. layer solidified. The organic layer was decanted and the solid residue was washed with CH₂Cl₂ (5x 30 mL). The combined organic phases were dried (MgSO₄) and the solvent was removed in vacuum. The residue was purified via column chromatography (silica gel, gradient EtOAc/petroleum ether 1:3 - 1:1) to give hydroxy valerolactone IV (0.64 g, 2.3 mmol, 66 %) as a colorless solid. Rᵣ = 0.24 (EtOAc/petroleum ether 1:1), mp: 81 - 83 °C. [α]D₂⁺ = -0.47° (c = 10, 22°C, CH₂Cl₂). ¹H-NMR (400 MHz, CDCl₃): δ = 4.38 (dd, 2JHH = 3.4 Hz, 1JHH = 5.2 Hz, 1JHH = 11.1 Hz, 1H, H-5), 3.82 (dd, 1JHH = 4.1 Hz, 1JHH = 5.1 Hz, 1H, H-6), 3.67 (dd, br, 1JHH = 4.1 Hz, 1JHH = 11.4 Hz, 1H, H-7), 3.59 (dd, 1JHH = 5.1 Hz, 1JHH = 11.4 Hz, 1H, H-7), 2.55 (dd, 2JHH = 1.5 Hz, 3JHH = 4.6 Hz, 1JHH = 6.6 Hz, 1JHH = 17.7 Hz, 1H, H-2), 2.36 (dd, 1JHH = 6.9 Hz, 1JHH = 9.7 Hz, 1JHH = 17.7 Hz, 1H, H-2'), 2.15 (br, s, 1H, OH), 2.01 - 1.87 (m, 2H, H-3, H-4), 1.86 - 1.73 (m, 1H, H-3'), 1.72 - 1.60 (m, 1H, H-4'), 0.90 (s, 9H, H-9), 0.12, 0.10 (2x s, 2x 3H, H-10). ¹³C-NMR (100 MHz, CDCl₃): δ = 171.18 (C-1), 80.55 (C-5), 74.42 (C-6), 63.40 (C-7), 30.29 (C-4), 25.94 (C-9), 23.20 (C-2), 18.68 (C-3), 18.20 (C-8), -4.61 (C-10). IR (ATR): ν = 3448 (m), 2954 (m), 2856 (m), 1731 (s), 1471 (m), 1360 (s), 1248 (m), 1053 (s), 834 (s), 776 (s), 632 (m) cm⁻¹. MS [EI, 70 eV, 180 °C]: m/z (%): [M⁺, 1%, 257 (M-OH)⁺, 4%, 243 [(CH₃OH)⁺], 11%, 217 [(CH₃₂O₅Si⁻, 19%), 199 [(CH₃₂O₅Si⁺), 62%], 171 [(CH₃₂O₅Si⁻, 30 %], 125 [(CH₂OH)⁺, 74%], 75 [(CH₃OH⁻, 100%]. HRMS (100 °C, 80 eV): [C₁₉H₂₀O₃Si⁺]: calcd.: 257.15729, found: 257.15633, [C₁₉H₂₀O₃Si⁻]: calcd.: 243.14165, found: 243.14255. Analysis (C₁₉H₂₀O₃Si): calcd. C = 56.89 %, H = 9.55 %, found: C = 56.82 %, H = 9.62 %.

(6S) 6-[(IS) 1-tert-Butyl(dimethyl)silyloxy-2-oxo]-tetrahydropyran-2-one 5: Under Ar, DMSO (26.7 mg, 0.34 mmol) in dry CH₂Cl₂ (2.5 mL) was treated dropwise with oxalyl chloride (36.3 mg, 0.29 mmol) in dry CH₂Cl₂ (0.7 mL) at -78 °C with stirring. After about 20 min hydroxyvalerolactone IV (52.2 mg, 0.19 mmol) in dry CH₂Cl₂ (2.0 mL) was slowly added via syringe and stirring at -78 °C was continued for another 1 h. A cloudy liquid was formed. 
Et₃N (100 mg, 0.14 mL, 1 mmol) was added dropwise and the mixture was warmed-up to 23 °C over a period of 2 h. Work-up started by dilution with Et₂O (50 mL) and hydrolysis with H₂O (25 mL). The organic layer was washed with H₂O (25 mL) and brine (30 mL) and dried (MgSO₄). The solvent was removed in vacuum to give the crude aldehyde 5 (48.7 mg, 0.179 mmol, 94%), which was used for the Julia Kocienski olefination without further purification. Selected data: Rᵣ = 0.46 (EtOAc/petroleum ether 1:1). ¹H-NMR (400 MHz, CDCl₃): δ = 9.66 (s, br, 1H, H-7), 4.66 - 4.59 (m, 1H, H-5), 4.27 (d, 2JHH = 3.4 Hz, 1H, H-6), 2.68 - 2.56 (m, 1H, H-2'), 2.48 - 2.35 (m, 1H, H-2'), 2.03 - 1.89 (m, 1H, H-4), 1.86 - 1.68 (m, 3H, H-4', H-3), 0.93 (s, 9H, H-9), 0.14, 0.12 (2x s, 2x 3H, H-10). ¹³C-NMR (100 MHz, CDCl₃): δ = 201.86 (C-7), 170.38 (C-1), 80.28 (C-5), 79.04 (C-6), 29.84 (C-4), 25.67 (C-9), 22.02 (C-2), 18.33 (C-3), 18.16 (C-8), -4.84, -4.84 (C-10).
(55,6S) 5,6-Di-tert.-butyldimethylsilyloxy-7-oxo-heptanoic acid methyl ester 6:

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\begin{align*}
\text{(III)} & \xrightarrow{\text{OTBS}} \text{(IV)} \\
\text{(IV)} & \xrightarrow{\text{OTBS}} \text{(V)} \\
\text{(V)} & \xrightarrow{\text{OTBS}} \text{(VI)}
\end{align*}
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(55,6R) 5,6-Di-tert.-butyldimethylsilyloxy-7-triphenylmethylxyo-heptanoic acid methyl ester 4: Under Ar, triyl-protected heptanoic ester III (5.72 g, 13 mmol), imidazole (7.95 g, 117 mmol) in dry DMF (60 mL) were treated with tert.-butyldimethylsilyl chloride (17.8 mL, 15.5 g, 50% in PhMe) at 23 °C with stirring. After 78 h of stirring, work-up started by dilution with EtO (30 mL). The organic phase was washed with H2O (3x 50 mL) and dried (MgSO4). After column filtration (silica gel, Et2O), the residue (5.08 g) was purified via preparative HPLC (nucleosil 50-5, 5 μm, 32x250 mm, MeOH/CH2Cl2, ρ = 1.31, flow 10 mL/min, 44 bar, Rf = 17.36 min) to give fully protected heptanoic ester 4 (4.74 g, 7.15 mmol, 55 %) as a colorless oil. Rf = 0.48 (EtOAc/petroleum ether 1:10), [α]D = -4.95° (c = 1.02, 23°C, CH2Cl2). 1H-NMR (400 MHz, CDCl3): δ = 7.46 – 7.42 (m, 6H, H-11), 7.32 – 7.25 (m, 6H, H-12), 7.25 – 7.19 (m, 3H, H-13), 3.86 (dd, JH-HH = 5.8 Hz, JHH = 6.1 Hz, H-6), 3.75 (dd, JHH = 1.8 Hz, JHH = 3.9 Hz, JHH = 7.7 Hz, H-5), 3.65 (s, 3H, H-8), 3.16 (dd, JHH = 6.1 Hz, JHH = 9.7 Hz, H-7), 3.00 (dd, JHH = 5.8 Hz, JHH = 9.7 Hz, H-7), 2.26 (t, JHH = 7.53 Hz, 2H, H-2), 1.81 – 1.69 (m, 1H, H-14), 1.62 – 1.43 (m, 2H, H-3), 1.39 – 1.29 (m, 1H, H-4), 0.84, 0.83 (2x s, 2x 9H, H-15), -0.02, 0.06, 0.04, 0.00, -0.02 (4 s, 4x 3H, H-16). 13C-NMR (100 MHz, CDCl3): δ = 174.00 (C-1), 144.12 (C-10), 128.76 (C-12), 127.70 (C-11), 126.89 (C-13), 86.96 (C-9), 74.91 (C-6), 74.82 (C-5), 65.31 (C-7), 51.43 (C-8), 34.32 (C-2), 32.03 (C-4), 25.92 (C-15), 21.63 (C-3), 18.14 (C-14), -4.85, -3.95 (C-16). IR (ATR): ν = 2928 (m), 2856 (m), 1740 (s), 1448 (w), 1360 (m), 1250 (m), 1073 (s), 832 (s), 772 (s), 757 (s), 703 (s) cm⁻¹. MS [El, 70 eV, 140 °C]: m/z (%): 662 [(M+) + 1%, 661 [(M-C2H5O)⁺, 1%, 257 (1%) 243 [(C15H17)⁺, 100%], 165 [(C13H11)⁺, 9%], 73 [(C6H5Si)⁺, 7%]. Analysis of C29H35O4S2I2: calcd. C = 70.65 %, H = 8.82 %, %, found: C = 70.57 %, H = 8.81 %.

(55,6R) 5,6-Di-tert.-butyldimethylsilyloxy-7-hydroxy-heptanoic acid methyl ester V: Under Ar, to a solution of trityl-protected heptanoic ester 4 (464 mg, 0.70 mmol) in dry CH2Cl2 (5 mL) was cooled to -30 °C with stirring. A solution of BCl3 (0.35 mL, 0.35 mmol, 1 M in hexanes) was added and the mixture was stirred at -30 °C for 30 min (TLC), a yellow color occurred. The reaction was quenched with dry MeOH (0.3 mL → colorless solution) at -30 °C and stirring continued for 10 min. Then, the solution was poured into sat. aq. NaHCO3 (5 mL) with vigorous stirring. The aqueous layer was extracted with CH2Cl2 (4x 5 mL). The combined organic phases were washed with brine (2x 5 mL) and dried (MgSO4) and the solvent was removed in vacuum. The residual crude carbinal (460 mg) was purified via preparative HPLC (16x250 mm, Nucleosil 50-5, 1.5 % EtOAc in hexanes, 20 mL/min, 100 bar) to give 7-hydroxy heptanoic ester V (223.7 mg, 0.53 mmol, 76 %) as a colorless oil and remaining ester 4 (28 mg, 0.042 mmol, 6 %). Rf = 0.22 (EtOAc/petroleum ether 1:10), [α]D = 3.02° (c = 1.08, 22°C, CH2Cl2). 1H-NMR (400 MHz, CDCl3): δ = 3.76 - 3.60 (m, 1H, H-6), 3.70 - 3.63 (m, 1H, H-5), 3.66 (s, 3H, H-8), 3.61 - 3.57 (m, 2H, H-7), 2.28 (t, JHH = 7.3 Hz, 2H, H-2), 2.06 - 2.00 (m, br, 1H, OH), 1.72 - 1.60 (m, 2H, H-3), 1.59 - 1.47 (m, 2H, H-4), 0.88, 0.87 (8x s, 2x 9H, H-10), 0.09, 0.08, 0.06 (4x s, 4x 3H, H-11). 13C-NMR (100 MHz, CDCl3): δ = 173.70 (C-1), 76.47 (C-6), 73.67 (C-5), 63.75 (C-7), 51.26 (C-8), 34.11 (C-2), 33.16 (C-4), 25.69 (C-10), 20.19 (C-3), 18.04 (C-9), -4.60 (C-11). IR (ATR): ν = 3512 (m), 2929 (m), 2857 (m), 1741 (s), 1472 (w), 1360 (m), 1251 (m), 1096 (s), 832 (s), 774 (s), 669 (m) cm⁻¹. MS [El, 70 eV, 80 °C]: m/z (%): 420 [(M+) + 1%, 405 [(M-C2H5O)⁻, 10%], 389 [(M-C2H5O)⁻, 15%, 331 (28%), 271 (77%), 245 [(C15H17)⁺, 90%, 231 [(C13H11)⁺, 100%], 73 [(C6H5Si)⁺, 96%]. HRMS [(M-C2H5O)⁺, C15H17O2Si3]: calcd.: 389.25333, found: 389.25433. Analysis of C29H35O4S2I2: calcd. C = 57.09 %, H = 10.54 %, found: C = 57.15 %, H = 10.54 %.

(55,6S) 5,6-Di-tert.-butyldimethylsilyloxy-7-oxo-heptanoic acid methyl ester 6: Under Ar, DMSO (26.7 mg, 0.34 mmol) in dry CH2Cl2 (2.5 mL) was treated dropwise with oxalyl chloride (36.3 mg, 0.29 mmol) in dry CH2Cl2 (0.7 mL) at -78 °C with stirring. After about 20 min hydroxyester V (80 mg, 0.19 mmol) in dry CH2Cl2 (2.0 mL) was slowly added via syringe and stirring at -78 °C was continued for another 1 h. A cloudy liquid was formed. Et3N (100 mg, 0.14 mL, 1 mmol) was added dropwise and the mixture was warmed-up to 23 °C over a period of 2 h. Work-up started by dilution with EtO (50 mL) and hydrolysis with H2O (25 mL). The organic layer was washed with H2O (25 mL) and brine (30 mL) and dried (MgSO4). The solvent was removed in vacuum to give the crude aldehyde (80 mg, 0.19 mmol, 100%), which was used for the Julia Kociensky olefination without further purification. Selected data: Rf = 0.5 (EtOAc/petroleum ether 1:10). 1H-NMR (400 MHz, CDCl3): δ = 9.57 (d, br.
2. Synthesis of the C8 – C21 Fragment: Assembly of the Carbon Framework

Methyl cycloheptatrienyl 1-carboxylate 8

1-Acetyl-1,3,5-cycloheptatriene VI.\(^5\) Under Ar, in a three-necked flask equipped with a KPG stirrer ZnCl\(_2\) (156.73 g, 1.15 mol, 1.2 eq.) was suspended in dry HOAc (110 mL) and gently cooled. Acetyl chloride (90.43 g, 83.0 mL, 1.15 mol, 1.2 eq.) in dry CH\(_2\)Cl\(_2\) (250 mL) was added dropwise and the mixture was stirred for 30 min. After cooling to -40 °C, 1,3,5-cycloheptatriene (88 g, 0.96 mmol, 1 eq.) was added dropwise and the mixture was stirred for 5 h at -40 °C (color: dark brown). Work-up started by hydrolysis with ice water (300 mL) and the temperature was raised to 23 °C upon continuing stirring. Then, the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3x 150 mL)9 the combined organic layers were washed with 2.5 % aq. NH\(_4\)\(_2\)SO\(_4\) (5x). The resulting dark brown residue was purified via vacuum distillation (47 °C, 1.1 mbar) to give 1-acetylcycloheptatriene VI (51.25 g, 0.38 mol, 40 %) as a yellow liquid.

\(\text{H-NMR (EtOAc/petroleum ether 1:3): } \delta = 7.10 \text{ (d, } ^3J_{HH} = 5.9 \text{ Hz, 1H, H-2), 6.87 \text{ (dd, } ^3J_{HH} = 5.7, 11.2 \text{ Hz, 1H, H-4), 6.68 \text{ (dd, } ^3J_{HH} = 5.9 \text{ Hz, } ^3J_{HH} = 11.2 \text{ Hz, 1H, H-3), 6.28 \text{ (dd, } ^3J_{HH} = 5.7, 9.3 \text{ Hz, 1H, H-5), 5.63 - 5.54 \text{ (m, 1H, H-6), 2.66 (d, } ^3J_{HH} = 7.0 \text{ Hz, 2H, H-7), 2.39 (s, 3H, H8).}\)

\(\text{C-NMR (75 MHz, CDCl}_3\): } \delta = 197.5 \text{ (C-8), 135.9 \text{ (C-4), 133.0 \text{ (C-2), 131.7 \text{ (C-1), 129.1 \text{ (C-3), 127.1 \text{ (C-5), 125.8 \text{ (C-6), 26.1 \text{ (C-9), 25.2 \text{ (C-7). IR (neat): } } v = 3026 \text{ (w), 2887 \text{ (w), 1659 \text{ (s), 1604 \text{ (m), 1526 \text{ (m), 1429 \text{ (m), 1384 \text{ (m), 1362 \text{ (m), 1267 \text{ (m), 1210 (m), 1182 (m), 975 (m), 788 (m), 758 (m), 702 (s) cm}^{-1}.}\) MS [FD, 5kV/10mA/min]: m/z (\%): 134.14 (100 [M], 135.16 (11) [M]\(^+\]). MS-ESI C\(_9\)H\(_7\)O\(_2\): calcld.: 135.0810, found: 135.0815.\

1,3,5-Cycloheptatriene 1-carboxylic acid VII.\(^6\) In a three-necked flask equipped with a KPG stirrer a solution of NaOH (152 g, 3.8 mol, 1 eq.) in H\(_2\)O (307 mL) was treated with Br\(_2\) (62.5 mL, 194.97 g, 1.22 mol, 3.2 eq.) with stirring at 0 °C. 1-Acetylcycloheptatriene VI (51.05 g, 0.38 mol) in dioxane (50 mL) was slowly added at -10 to 0°C. After stirring for 1 h at 0°C, the reaction temperature was allowed to reach 23 °C over a period of 2.5 h. After stirring at 23 °C for another 30 min, the layers were separated and the aqueous phase was extracted with Et\(_2\)O (5x). Excess of Br\(_2\) was reduced upon adding conc. aq. NaHSO\(_3\). The pH of the aqueous layer was adjusted to about 1 by adding conc. aq. HCl (37%). The resulting turbid solution was extracted with CH\(_2\)Cl\(_2\) (4x), the solvent of the organic phases was removed to give 1,3,5-cycloheptatriene 1-carboxylic acid VII (49.2, 0.361 mol, 95 %) as yellow needles. \(R_t \text{(EtOAc/petroleum ether 1:3): } 0.33, \text{ mp: 61 °C (lit. 61 – 62 °C).}\)

\(\text{H-NMR (300 MHz, CDCl}_3\): } \delta = 12.09 \text{ (s, br, 1H, OH), 7.35 \text{ (d, br, } ^3J_{HH} = 6.0 \text{ Hz, 1H, H-2), 6.87 \text{ (dd, } ^3J_{HH} = 5.7, 11.2 \text{ Hz, 1H, H-4), 6.68 \text{ (dd, } ^3J_{HH} = 0.9, 6.0 \text{ Hz, } ^3J_{HH} = 11.2 \text{ Hz, 1H, H-3), 6.27 \text{ (dd, } ^3J_{HH} = 5.7, 9.4 \text{ Hz, 1H, H-5), 5.60 (br, } ^3J_{HH} = 7.0, 9.4 \text{ Hz, 1H, H-6), 2.63 (d, } ^3J_{HH} = 7.0 \text{ Hz, 2H, H-7).}\)

\(\text{C-NMR (75 MHz, CDCl}_3\): } \delta = 171.9 \text{ (C-8), 136.07 \text{ (C-4), 134.70 \text{ (C-2), 129.00 \text{ (C-3), 127.2 \text{ (C-5), 124.6 (C-6), 121.1 (C-1), 26.27 (C-7). IR (ATR): } } v = 3026 \text{ (br), 1673 (s), 1612 (m), 1527 (m), 1416 (m), 1279 (m), 1232 (m), 1217 (m), 927 (m), 780 (m), 714 (s) cm}^{-1}.\) MS [FD, 5kV/10mA/min]: m/z (\%): 136.1 (100 [M]\(^+\)). HRMS-ESI C\(_9\)H\(_7\)O\(_2\): calcld.: 156.73 (M\(^+\)), found: 156.73.

1,3,5-Cycloheptatriene 1-carboxylic acid methyl ester 8.\(^5\) 1,3,5-Cycloheptatriene 1-carboxylic acid VII (13.0 g, 95.5 mmol) and acetyl chloride (1.7 mL, 1.87 g, 24 mmol, 0.25 eq.) in dry MeOH (600 mL) were refluxed for 24 h. After completion of the conversion (TLC) the solvent was removed under reduced pressure. The residue was dissolved in Et\(_2\)O, washed with H\(_2\)O and brine and dried (MgSO\(_4\)). After removal of the solvent, the methyl ester 8 (13.69 g, 91.2 mmol, 95.5 %) was obtained as a yellow liquid pure enough for further transformations.

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(EtOAc/petroleum ether 1:10): 0.52. 'H-NMR (300 MHz, CDCl3): δ = 7.21 (dd, 3JHH = 0.9 Hz, 3JHH = 6.0 Hz, 1H, H-2), 6.78 (ddd, 3JHH = 0.9 Hz, 3JHH = 11.2 Hz, 1H, H-4), 6.63 (ddd, 3JHH = 0.9 Hz, 3JHH = 6.0 Hz, 3JHH = 11.2 Hz, 1H, H-3), 6.23 (ddd, 3JHH = 0.9 Hz, 3JHH = 5.8 Hz, 3JHH = 9.4 Hz, 1H, H-5), 5.54 (td, 3JHH = 7.0 Hz, 3JHH = 9.4 Hz, 1H, H-6), 3.75 (s, 3H, H-9), 2.61 (d, 3JHH = 7.0 Hz, 2H, H-7). \text{13C-NMR (75 MHz, CDCl3)}: δ = 166.6 (C-8), 135.3 (C-4), 132.7 (C-2), 129.1 (C-3), 127.1 (C-5), 124.2 (C-6), 121.8 (C-1), 51.9 (C-9), 26.7 (C-7). IR (neat): ν = 3491 (br), 3026 (w), 2987 (w), 1708 (s), 1613 (m), 1529 (m), 1346 (m), 1382 (w), 1350 (w), 1274 (s), 1229 (m), 1210 (s), 1184 (m), 1090 (s), 876 (w), 826 (w), 788 (w), 758 (m), 726 (m), 688 (m) cm⁻¹. MS [FD, SkV/10mA/min]: m/z (%): 150.1 (100) [M]⁺, 321.9 (12) [M₂+MeOH]⁺. HRMS-ESI C₉H₁₀O₂: calcd.: 151.0759, found: 151.0762.

6-(1-Oxohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester 10

6-Chloro-6-(1-oxohexyl)-1,3-cycloheptadiene 1-carboxylic acid methyl ester 10 (two-step-procedure):

5-Chloro-6-(1-oxohexyl)-1,3-cycloheptadiene 1-carboxylic acid methyl ester 9: Under Ar, to a mixture of AlCl₃ (12.34 g, 92.53 mmol 3 eq.) in dry CH₂Cl₂ (60 mL) was added hexanoyl chloride (10.37 g, 10.92 ml, 77.11 mmol, 2.5 eq) at 0 °C with stirring. Then, the cooling bath was removed and the mixture was heated to reflux. Cycloheptatriene carboxonate 8 (4.63 g, 30.84 mmol) in dry CH₂Cl₂ (20 mL) was added dropwise. After stirring at 40 °C for 4 h (TLC), the reaction mixture was cooled to 22 °C and then to -15 °C. Glacial acetic acid (18.3 mL) were added dropwise and the mixture was heated to reflux. Cycloheptatriene chloroketone 5-Chloro-6-(1-oxohexyl)-1,3-cycloheptadiene 1-carboxylic acid methyl ester 9

6-(1-Oxohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester 10: Under Ar, to a solution of NaOMe (0.81 g, 14.93 mmol, 2 eq.) in MeOH (30 mL) chloroacetone 9 (2.12 g, 7.44 mmol) in MeOH (20 mL) was added dropwise with stirring at 22 °C. The color of the reaction mixture changed from yellow to red-brown. After completion of the reaction (TLC), the mixture was diluted with H₂O (30 mL). The aqueous layer was extracted with Et₂O (4x 30 mL), the combined organic phases were washed withaq. 2 N HCl (2x) and sat. aq. K₂CO₃ (2x) and dried (MgSO₄). The solvent was removed under vacuum to give a oily residue. Purification via column chromatography (silica gel, EtOAc/petroleum ether 1:10) afforded cycloheptatriene chloroketone 9 (7.81 g, 27.44 mmol, 88.9 %) as a mixture of diastereomers. Rf = 0.45 (EtOAc/petroleum ether 1:5). 'H-NMR (300 MHz, CDCl₃): δ = 7.02 (d, 3JHH = 7.4 Hz, 1H, H-10), 6.21 (dd, 3JHH = 4.4 Hz, 3JHH = 12.2 Hz, 1H, H-12), 5.99 (ddd, 3JHH = 1.5 Hz, 3JHH = 7.4 Hz, 3JHH = 12.2 Hz, 1H, H-11), 5.06 (dd, br, 3JHH = 4.4 Hz, 3JHH = 6.5 Hz, 1H, H-13), 3.75 (s, 3H, H-22), 3.17 (ddd, 3JHH = 3.9 Hz, 3JHH = 6.5 Hz, 3JHH = 6.5 Hz, 1H, H-14), 2.89 (d, br, 3JHH = 3.9 Hz, 1H, H-21), 2.88 (d, br, 3JHH = 6.5 Hz, 6.5 Hz, 1H, H-21'), 2.46 (m, 2H, H-16), 1.16 – 1.43 (m, 2H, H-17), 1.34 – 1.15 (m, 4H, H-18, H-19), 0.85 (t, 3JHH = 6.9 Hz, 3JHH = 6.9 Hz, 3H, H-20).

6-(1-Oxohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester 10: Under Ar, to a solution of NaOMe (0.81 g, 14.93 mmol, 2 eq.) in MeOH (30 mL) chloroacetone 9 (2.12 g, 7.44 mmol) in MeOH (20 mL) was added dropwise with stirring at 22 °C. The color of the reaction mixture changed from yellow to red-brown. After completion of the reaction (TLC), the mixture was diluted with H₂O (30 mL). The aqueous layer was extracted with Et₂O (4x 30 mL), the combined organic phases were washed withaq. 2 N HCl (2x) and sat. aq. K₂CO₃ (2x) and dried (MgSO₄). The solvent was removed under vacuum and the residue was purified via column chromatography (silica gel, petroleum ether/EtOAc 5:1) to give ketoester 10 (1.69 g, 6.79 mmol, 91.2 %) as a yellow oil. Rf = 0.34 (petroleum ether/EtOAc 5:1). For data see below.

6-(1-Oxohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester 10 (one-step-procedure): Under Ar, to a mixture of AlCl₃ (19.7 g, 148 mmol) in dry CH₂Cl₂ (88 mL) was added hexanoyl chloride (14.9 g, 111 mmol) at 0 °C with stirring. Then, the cooling bath was removed and the mixture was heated to reflux. Cycloheptatriene carboxonate 8 (7.3 g, 48.6 mmol) in dry CH₂Cl₂ (10 mL) was added dropwise. After stirring at 40 °C for 2 h (TLC), the reaction mixture was cooled to 22 °C and then to -15 °C, glacial acetic acid (18.3 mL) were added dropwise and stirring was continued for 30 min. H₂O (58.4 mL) was added and the mixture was stirred for another 1 h at -15 °C.
After warming to 22 °C, the aqueous layer was extracted with CH₂Cl₂ (4x 150 mL), the combined organic phases were washed with sat. aq. NaHCO₃ (4x 150 mL) and H₂O (150 mL) and dried (MgSO₄). The solvent was removed under vacuum to give a light brown residue (11.5 g). After column filtration (silica gel, EtOAc/hexanes 1:10), the residue was purified via preparative HPLC (nucleosil 50-5, 5 µm, 32x250 mm, 10% EtOAc in hexanes, flow 21 mL/min, 36 bar, Rf = 4.7 min) to give cycloheptatriene ketoester 10 (3.55 g, 14.3 mmol, 29.4 %) as a light yellow oil. Rf = 0.5 (EtOAc/hexanes 1:2).

1H-NMR (400 MHz, CDCl₃): δ = 7.25 (d, 3J_HHH = 4.7 Hz, 1H, H-10), 7.09 (d, 3J_HHH = 4.7 Hz, 1H, H-13), 6.91 – 6.82 (m, 2H, H-11, H-12), 3.77 (s, 3H, H-22), 2.98 (s, 2H, H-21), 2.70 (t, 3J_HHH = 7.6 Hz, 2H, H-16), 1.64 – 1.55 (m, 2H, H-17), 1.33 – 1.20 (m, 4H, H-19, H-18), 0.85 (t, 3J_HHH = 7.6 Hz, 3H, H-20). 13C-NMR (100 MHz, CDCl₃): δ = 199.30 (C-15), 166.00 (C-8), 133.81 (C-14), 133.68 (C-12), 133.48 (C-11), 131.32 (C-10), 131.55 (C-9), 125.57 (C-9), 128.29 (C-11), 121.54 (C-9), 75.30 (C-13), 38.45 (C-16), 31.46 (C-18), 24.77 (C-21), 24.19 (C-19), 18.06 (C-17), 22.48 (C-19), 13.83 (C-20). IR (KBr): ν = 2954 (s), 2930 (s), 2858 (s), 1714 (s), 1610, 1534, 1436 (w), 1275, 1436 (m), 1275, 1097 (s), 739 (m) cm⁻¹. MS [EI, 80 eV, 100 °C]: [M+H]⁺: calcd.: 248.14431, found: 248.14325.

Selected data of aromatic side products VIII (mixture, crude): Methyl o, m, p (2-oxoheptyl) benzoate:

1H-NMR (400 MHz, CDCl₃): δ = 8.04 – 7.98 (m, aryl-H adjacent to CO₂Me), 7.87 – 7.81 (m, br, aryl-H adjacent to CO₂Me), 7.56 – 7.50 (triplets, ar-H between 2x ArH, o-product), 7.49 – 7.39 (m, aryl-H adjacent to CO₂Me), 7.36 – 7.32 (d, br, ar-H adjacent to CO₂Me) (all ar-CH=CH: 4H), 3.91 – 3.89 (several s, CO₂Me and Ar-CH₂ of o-product), 3.76 – 3.75 (2x s, Ar-CH₃ of m-, p-products) (all CO₂Me and Ar-CH₂: 5H). 2.45 – 2.39 an 2.06 – 2.00 (triplets, H-8), 1.70 – 1.58 and 1.56 – 1.44 (2x m, H-9, H-10), 1.36 – 1.08 (m, H10, H-11), 0.91 – 0.76 (m and t, H-12). Compared to the cycloheptatriene fragment, the sp²-CH-protons suffered from a significant downfield shift (ar-CH). Because of additional impurities, the integration of the H-8 – H-12 protons did not display the correct integrals.


Reduction of Ketoester 10

6-[(R/S)-1-Hydroxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R/S-11 (racemic): Ketoester 10 (2 g, 8 mmol) in MeOH (30 mL) was treated portion-wise with NaBH₄ (0.61 g, 16 mmol) over a period of 5 min while stirring at 0 °C. After 2 h at 0 °C (TLC), the mixture was warmed to 22 °C and the solvent was removed in vacuum. The residue was dissolved in H₂O (8 mL), the aqueous layer was extracted with Et₂O (3x 30 mL), the combined organic phases were washed with brine (30 mL) and dried (MgSO₄). The solvent was removed in vacuum affording a yellow oil (1.9 g). After purification by column chromatography (silica gel, hexanes/EtOAc 5:1), racemic hydroxyester R/S-11 (1.73 g, 6.9 mmol, 86 %) was isolated as a light yellow oil. Rf = 0.5 (EtOAc/hexanes 1:2).

1H-NMR (400 MHz, CDCl₃): δ = 7.20 (d, 3J_HHH = 6.0 Hz, 1H, H-10), 6.77 (dd, br, 3J_HHH = 6.0 Hz, 3J_HHH = 11.2 Hz, 1H, H-12), 6.59 (dd, br, 3J_HHH = 6.0 Hz, 3J_HHH = 11.2 Hz, 1H, H-11), 6.13 (dd, br, 3J_HHH = 6.0 Hz, 1H, H-13), 4.23 (m, br, 1H, H-15), 3.77 (s, 3H, H-22), 2.92 (d, 3J_HHH = 13.1 Hz, 1H, H-21), 2.44 (d, 3J_HHH = 13.1 Hz, 1H, H-21'), 2.33 (m, br, 1H, OH), 1.75 – 1.58 (m, 2H, H-16), 1.39 – 1.16 (m, 6H, H-17, H-18, H-19), 0.86 (t, 3J_HHH = 6.8 Hz, 3H, H-20). 13C-NMR (100 MHz, CDCl₃): δ = 166.89 (C-8), 142.25 (C-14), 134.77 (C-12), 133.17 (C-10), 128.29 (C-11), 122.66 (C-13), 121.54 (C-9), 75.30 (C-15), 51.99 (C-22), 35.68 (C-16), 31.65 (C-18), 26.92 (C-21), 25.33 (C-17), 22.41 (C-19), 13.91 (C-20). IR (KBr): ν = 3452 (m), 2952, 2930 (s), 2858 (s), 1711 (s), 1614, 1534, 1436 (w), 1275, 1093 (s), 739 (s) cm⁻¹. MS [EI, 80 eV, 100 °C]: [M+H]⁺: calcd.: 248.14431, found: 250.15690, found: 250.15888. Analysis (C₁₃H₂₀O₃): calced. C = 71.97 %, H = 8.86 %, found: C = 71.72 %, H = 8.97 %.

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Chiral HPLC of racemic carbinol rac-11: Chirobiotic T, 4x250 mm, eluent 2 % \(i\)-PrOH in hexanes, flow: 1 mL/min, \(R_s\): S-11: 18.98 min, R-11: 19.86 min.

6-[(IR)-1-Hydroxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R-11 (CBS reduction): Under Ar, (S)-tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]-oxazaborol (0.45 g, 1.55 mmol) in dry THF (15 mL) was treated with borane dimethylsulfide (0.378 mL, 3.78 mmol, 10 M). After stirring an -15 °C for 30 min, ketoester 10 (940 mg, 3.78 mmol) in dry THF (10 mL) was added dropwise and the mixture was stirred for 2 h at -15 °C and another 2 h at 22 °C (TLC). Work-up started by quenching with MeOH (80 mL) and stirring for 30 min. Then, the solvent was removed in vacuum and the residue was purified via column chromatography (silica gel, petroleum ether/EtOAc 5:1) affording hydroxyester R-11 (0.8 g, 3.2 mmol, 84%) as bright yellow oil. \(R_f\) = 0.23 (EtOAc/petroleum ether 1:5). \([\alpha]_D\) = -15.72° (\(c = 1.08, 20\)°C, CH\(_2\)Cl\(_2\), 70 % ee). For further data see above R/S-11.

Reaction with S-oxazaborolidine complex (0.117 g, 0.403 mmol), borane methylsulfide complex (0.041 mL, 0.403 mmol) and ketoester 10 (100 mg, 0.403 mmol) in THF at -78°C, 1 h, quenching with MeOH at -20 °C, evaporation of the solvent in vacuum, dissolving the residue in Et\(_2\)O (5 mL). Then, diethanolamin (0.093 mL, 0.886 mmol, 2.2 eq) was added, a white precipitate occurred. After stirring at 22 °C for 30 min, the solids were filtered off (careful washing with pentane). The solvents were distilled off in vacuum and the \(\alpha\)-pinene could be removed in high vacuum (8x10\(^{-3}\) mbar, 12 h). The residual crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 10:1) affording hydroxyester S-11 (76.4 mg, 0.305 mmol, 75.8 %) as bright yellow oil. \(R_f\) = 0.25 (EtOAc/petroleum ether 1:5). \([\alpha]_D\) = -21.38° (\(c = 1.04, 23\)°C, CH\(_2\)Cl\(_2\), 95.2 % ee). For further data see above R/S-11.

Analytical HPLC: column Chirobiotic T, 4x250 mm, eluent 0.7 % \(i\)-PrOH/cyclohexane, 0.3 mL/min, 39 bar: \(R_t\) (S-11): 111.25 min, \(R_t\) (R-11): 115.15 min

6-[(IS)-1-Hydroxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester S-11 (Brown reduction): Under Ar, to a solution of (-)-disopinocampheylchloroborane (0.194 g, 0.604 mmol, 1.5 eq) in dry TFH (2 mL) was added ketoester 10 (100 mg, 0.403 mmol) in dry THF (2 mL) at 0 °C with stirring. After a reaction time of 3 d (TLC) at 0 °C, the solvent was removed in vacuum and the residue was dissolved in Et\(_2\)O (5 mL). Then, diethanolamin (0.093 mL, 0.886 mmol, 2.2 eq) was added, a white precipitate occurred. After stirring at 22 °C for 30 min, the solids were filtered off (careful washing with pentane). The solvents were distilled off in vacuum and the \(\alpha\)-pinene could be removed in high vacuum (8x10\(^{-3}\) mbar, 12 h). The residual crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 10:1) affording hydroxyester S-11 (31.9 mg, 0.127 mmol, 31.6 %) as bright yellow oil. \(R_f\) = 0.25 (EtOAc/petroleum ether 1:5). \([\alpha]_D\) = 21.51° (\(c = 1.015, 22\)°C, CH\(_2\)Cl\(_2\), 95.8 % ee). For further data see above R/S-11.
Analytical HPLC: column Chirobiotic T, 4x250 mm, eluent 0.7 % i-PrOH/cyclohexane, flow 0.3 mL/min, 39 bar: Rᵣ (S-11): 108.88 min, Rᵣ (R-11): 116.57 min.

6-[(S)-1-Hydroxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester S-11 via Mitsunobu inversion and ester cleavage from hydroxyester R-11:

6-[(S)-1-Benzoxoxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester S-12 (Mitsunobu inversion): Under Ar, hydroxyester R-11 (100 mg, 0.399 mmol, 70 % ee) in CH₂Cl₂ (1 mL) and pyridine (5 mL) was added benzoyl chloride (0.05 mL, 0.4 mmol, 1 eq.) at 0°C with stirring. The reaction mixture was stirred at 22 °C for 14 h. Then, the solvent was removed in vacuum and the residue was purified via column chromatography (silica gel, petroleum ether/EtOAc 10:1) to give benzoate S-12 (131.4 mg, 0.371 mmol, 92.8 %). Rᵣ = 0.55 (EtOAc/petroleum ether 1:5). [α]D= -21.25° (c = 0.985, 23°C, CH₂Cl₂). ¹H-NMR (300 MHz, CDCl₃): δ = 8.07 (d, J₃HH = 7 Hz, 2H, H-25), 7.53 (m, 1H, H-27), 7.43 (t, J₂HH = 7.7 Hz, 2H, H-26), 7.22 (dd, J₁HH = 6 Hz, 1H, H-10), 6.73 (dd, J₁HH = 6 Hz, J₃HH = 6 Hz, 1H, H-12), 6.59 (dd, J₁HH = 6 Hz, J₃HH = 6 Hz, 1H, H-11), 6.28 (d, J₁HH = 6 Hz, 1H, H-13), 5.56 (t, J₃HH = 6.9 Hz, 1H, H-15), 3.72 (s, 3H, H-22), 3.23 (d, J₁HH = 5.9 Hz, J₁HH = 11.2 Hz, 1H, H-12), 6.58 (dd, J₁HH = 5.9 Hz, J₁HH = 11.2 Hz, 1H, H-11), 6.28 (d, J₁HH = 5.9 Hz, 1H, H-13), 5.56 (t, J₃HH = 6 Hz, 1H, H-12). MS [EI, 80 eV, 70 °C]: m/z (%): 354 (1, [M]+), 222 (24, [M-CO₂CH₃]+), 175 (19, [M-C₂H₄O₂-C₃H₅]+), 162 (5, [M-C₃H₅O₂-C₃H₇O]+), 105 (100, [C₂H₅O₂]+), 96 (5, [C₃H₇O₂]+), 77 (18, [C₃H₇]+), 51 (16, [C₃H₇]+). Analysis (C₂H₂N₂O₂): calcd. C = 74.55 %, H = 7.39 %, found: C = 74.87 %, H = 7.28 %.
Swern oxidation of hydroxyester 11:

Under Ag, to a solution of oxalyl chloride (0.06 mL, 0.66 mmol, 1.65 eq.) in dry CH₂Cl₂ (2 mL) was injected dropwise dry DMSO (0.2 mL, 0.88 mmol, 2.2 eq.) at -65 °C with stirring. After 15 min, hydroxyester 11 (100 mg, 0.4 mmol) in dry CH₂Cl₂ (0.5 mL) was added and stirring was continued for 30 min at -65 °C. Triethylamine (0.27 mL, 1.997 mmol, 5 eq.) was added at -65 °C, then, the mixture was allowed to warm up to 22 °C. A white precipitate of triethylammonium chloride occurred. Work-up started by quenching with H₂O (5 mL). After removal of the solvent in vacuum, the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 5:1) affording alkenoic ester 10 (52.2 mg, 0.21 mmol, 52.6 %), chloroester IX (13.4 mg, 0.05 mmol, 12.5 %) and alkenylester X (traces).

6-(1-Oxohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester 10: R₁ = 0.48 (Petroleum ether/ EtOAc 5:1).

For further data see above.

6-(1-chlorohexyl)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester IX: R₁ = 0.7 (Petroleum ether/EtOAc 5:1). ¹H-NMR (300 MHz, CDCl₃): δ = 7.22 (d, br, J HH = 5.8 Hz, 1H, H-10), 6.70 (dd, br, J HH = 5.8 Hz, J IH = 11.3 Hz, 1H, H-12), 6.62 (ddd, J HH = 0.9 Hz, J IH = 5.8 Hz, J IH = 11.3 Hz, 1H, H-11), 6.21 (d, J HH = 5.8 Hz, 1H, H-13), 4.50 (t, J HH = 7.4 Hz, 1H, H-15), 3.77 (s, 3H, H-22), 3.32 (d, J HH = 13.5 Hz, 1H, H-21), 2.32 (d, J HH = 13.5 Hz, 1H, H-20), 2.28 (d, J HH = 13.5 Hz, 1H, H-21), 1.98 – 1.85 (m, 2H, H-16), 1.33 – 1.10 (m, 6H, H-17, H-18, H-19), 0.82 (t, J HH = 6.8 Hz, 3H, H-20). ¹³C-NMR (75 MHz, CDCl₃): C = 132.1 (C-12), 133.7 (C-10), 129.5 (C-11), 123.9 (C-13), 123.5 (C-9), 66.9 (C-15), 52.0 (C-22), 36.9 (C-16), 31.1 (C-18), 26.9 (C-21), 26.8 (C-17), 22.4 (C-19), 13.9 (C-20). IR (KBr): v = 2927 (s, CH₃), 1753 (s), 1710 (s), 1616, 1536, 1434 (m), 1274, 1092 (s), 736 (w), 713 (s) cm⁻¹. MS (EI, 50 °C, 80 eV): m/z (%) = 268 (19, [M]+), 253 (55, [M-CH₃]+), 175 (45, [M-C₃H₇Cl]+), 162 (25, [M-C₆H₅Cl]+), 149 (52, [M-C₃H₇Cl]+), 137 (25, [C₆H₅Cl]⁺), 131 (50, [M-C₆H₅ Cl]+), 118 (12, [C₆H₅Cl]+), 116 (23, [C₆H₅Cl]+), 115 (70, [C₆H₅Cl]+), 105 (36, [C₆H₅Cl]+), 104 (15, [C₆H₅Cl]+), 103 (28, [C₆H₅Cl]+), 96 (100, [C₆H₅O₂]+), 91 (81, [C₇H₇]+), 77 (28, [C₆H₅]+), 59 (29, [C₆H₅Cl]+); 41 (28, [C₆H₅]+). Analysis (C₁₅H₁₂ClO₂): calcd. C = 67.03 %, H = 7.88 %, found: C = 66.97 %, H = 7.74 %.

Structure elucidation - Mandelic esters:

Acidic conditions:

6-(E,1-hexeny)-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester X: In a flask equipped with a Soxhlet extractor (Molecular sieves 4Å) and a reflux condenser under Ar, mandelic acid (88 mg, 0.58 mmol, 1.1 eq.), p-TsOH (7 mg, 0.04 mmol, 0.075 eq.) and hydroxyester RS-11 (132 mg, 0.527 mmol) in dry toluene (100 mL) were heated to reflux for 18 h. Then, the solvent was removed in vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 5:1) affording alkenoi ester X 51.3 mg, 0.222 mmol, 42.1 % as pale green oil. R₁ = 0.58 (Petroleum ether/EtOAc 5:1). ¹H-NMR (300 MHz, CDCl₃): δ = 7.24 (d, J HH = 6 Hz, 1H, H-10), (6.79 (dd, J HH = 6 Hz, J IH = 6 Hz, 1H, H-12), 6.53 (dd, J HH = 6.0 Hz, J IH = 11.1 Hz, 1H, H-11), 6.39 (dd, J HH = 6.9 Hz, J IH = 15.4 Hz, 1H, H-16), 6.14 (2x d, J HH = 6.0 Hz, 1H, H-13, J HH = 15.4 Hz, 1H, H-15), 3.75 (s, 3H, H-22), 2.80 (s, 2H, H-21), 2.21 – 2.10 (m, 2H, H-17), 1.48 – 1.22 (m, 4H, H-18, H-19), 0.89 (t, J HH = 7.1 Hz, 3H, H-22).
6-[(IS)-{2R)-2-Pivaloyloxy-2-phenyloxy]-hexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester S,R-XI:

HPLC: $R_t = 52.2$ min. Yield: 16.2 mg, 0.035 mmol, 8.7 %; $R_t = 0.51$ (EtOAc/petroleum ether 1:5); $[\alpha]_D = 13.33^\circ$ ($c = 1.12, 24^\circC, \text{CH}_2\text{Cl}_2$).

1C-NMR (300 MHz, CDCl$_3$): $\delta = 7.44$ (m, 2H, H-29), 7.33 (m, 3H, H-30, H-31), 7.14 (d, $^3J_{HH} = 6$ Hz, 1H, H-10), 6.52 (m, 2H, H-11, H-12), 5.88 (d, $^3J_{HH} = 6$ Hz, 1H, H-13), 5.89 (s, 1H, H-24), 5.28 (t, br, $^3J_{HH} = 7$ Hz, 1H, H-15), 3.73 (s, 3H, H-22), 3.00 (d, $^3J_{HH} = 4$ Hz, 1H, H-21), 1.71 (d, $^3J_{HH} = 4$ Hz, 1H, H-21'), 1.28 (s, 9H, H-27), 1.24 (m, 2H, H-16), 1.18 (m, 6H, H-17, H-18, H-19), 0.80 (m, 3H, H-20).

IR (KBr): $\nu = 2955$, 2925 (s), 2855 (m), 1735, 1710 (s), 1499, 1411, 1374 (m), 1335, 1267 (s), 1222 (s), 1154 (s), 1095 (s), 734 (w) cm$^{-1}$. MS (FD, RT, 80eV): m/z (%) = 468 (100, [M$^+$]).

Basic conditions
Under Ar, R-mandelic acid (67 mg, 0.439 mmol, 1 eq.) in dry pyridine (4 mL) was activated by dropwise addition of pivaloyl chloride (0.108 mL, 0.879 mmol, 2.2 eq.) at 0 °C with stirring. A white precipitate of pyridinium chloride was formed. Then, hydroxyster $R\text{-11}$ (100 mg, 0.3995 mmol, 70 % ee) in dry CH$_2$Cl$_2$ (1 mL) was added at 0 °C and the reaction mixture was stirred at 22 °C for 4 d. Then, the solvent was removed in vacuum and the residue was pre-purified by column filtration. The crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 30:1) affording a mixture of mandelic esters XI and XII (86.3 mg, 0.184 mmol, 46.2 %) and neat hydroxyster $R\text{-11}$ (36.5 mg, 0.0146 mmol, 36.5 %). The mandelic ester mixture XI and XII was separated by preparative HPLC (nucleosil 50-5, 5 µm, 16x250 mm, 1 % EtOAc in hexanes, flow 10 mL/min, 32 bar) affording neat diastereomers and a remaining sample of the mixture of XI and XII (3.9 mg).

6-[(IR)-{2R)-2-Pivaloyloxy-2-phenyloxy]-hexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R,R-XII:

HPLC: $R_t = 58.0$ min. Yield: 37.2 mg, 0.08 mmol, 19.9 %. $R_t = 0.51$ (EtOAc/petroleum ether 1:5). 1H-NMR (300 MHz, CDCl$_3$): $\delta = 7.47$ (m, 2H, H-29), 7.37 (m, 3H, H-30, H-31), 7.20 (d, $^3J_{HH} = 6$ Hz, 1H, H-10), 6.70 (dd, $^3J_{HH} = 6$ Hz, $^3J_{HH} = 6$ Hz, 1H, H-11), 6.57 (dd, $^3J_{HH} = 6$ Hz, 1H, H-13), 5.90 (s, 1H, H-4), 5.30 (t, br, $^3J_{HH} = 7$ Hz, 1H, H-15), 3.75 (m, 3H, H-22), 3.13 (d, $^3J_{HH} = 13$ Hz, 1H, H-21), 2.22 (d, $^3J_{HH} = 13$ Hz, 1H, H-21'), 1.54 (m, 2H, H-16), 1.28 (s, 9H, H-27), 1.05 (m, 4H, H-17, H-18), 0.86 (m, 2H, H-19), 0.74 (t, $^3J_{HH} = 7$ Hz, 3H, H-20). 13C-NMR (75 MHz, CDCl$_3$): $\delta = 177.6$ (C-24), 168.1 (C-23), 166.2 (C-8), 136.4 (C-12), 134.6 (C-28), 134.3 (C-10), 133.5 (C-11), 128.6 (C-30), 128.6 (C-31), 127.4 (C-14), 127.3 (C-29), 123.6 (C-13), 122.2 (C-9), 78.7 (C-24), 74.3 (C-15), 52.0 (C-22), 42.9 (C-26), 38.7 (C-16), 33.0 (C-18), 31.2 (C-21), 27.1 (C-27), 24.7 (C-17), 22.3 (C-19), 13.9 (C-20). IR (KBr): $\nu = 2955$, 2927 (s), 2871 (s), 1735, 1710 (s), 1616, 1538, 1479 (w), 1273, 11209, 1140 (s), 736 (w), 696 (s) cm$^{-1}$. MS (FD, RT, 80eV): m/z (%) = 468 (100, [M$^+$]).

6-[(IR)-1-Hydroxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R-11: $R_t = 116.57$ min, $[\alpha]_D = -22.45^\circ$ ($c = 0.875, 22^\circC, \text{CH}_2\text{Cl}_2$, ee = 100 %). For further data see above.
Structure elucidation - Mosher esters 13:

\[
\begin{align*}
\text{R/S-11} & \quad \text{or} \quad \text{R-11} \\
\text{OH} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CO}_2\text{Me} & \quad \overset{\text{O}}{\longrightarrow} \\
\text{O} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CF}_3 & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{Ph} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CO}_2\text{Me} & \quad \overset{\text{O}}{\longrightarrow} \\
\text{O} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CF}_3 & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{Ph} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CO}_2\text{Me} & \quad \overset{\text{O}}{\longrightarrow} \\
\text{O} & \quad \overset{\text{OMe}}{\longrightarrow} \\
\text{CF}_3 & \quad \overset{\text{OMe}}{\longrightarrow}
\end{align*}
\]

Under Ar, S-(−)-α-methoxy-α-trifluoromethyl phenyl acetic acid (70 mg, 0.3 mmol) and N,N-dimethylformamide (DMF, 22 mg, 0.3 mmol) in n-hexane (10 mL) were treated dropwise with oxalyl chloride (190 mg, 1.5 mmol) at 22 °C with stirring. A colorless precipitate occurred, which dissolved upon continued stirring after about 1 h. Now, an oily layer occurred. The hexane layer was decanted and the hexane was distilled off in vacuum. The residual R-(−)-Mosher acid chloride was dissolved in CHCl\(_3\) (2 mL).

To a solution of hydroxyester 11 (50 mg, 0.2 mmol), dimethylaminopyridine (DMAP, 12.6 mg, 0.1 mmol) and Et\(_3\)N (61 mg, 0.6 mmol) in CHCl\(_3\) (4 mL) was injected dropwise the freshly prepared Mosher acid chloride solution (2 mL) and the mixture was stirred at 22 °C for 2 h. Then, CH\(_2\)Cl\(_2\) (10 mL) was added and the so obtained organic layer was washed with sat. aq. NaHCO\(_3\) (10 mL) and brine (10 mL) and dried (MgSO\(_4\)). The solvent was removed in vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 10:1) affording a pale yellow oil of Mosher esters 13 (60 mg, 0.129 mmol, 80%).

Starting from racemic hydroxyester R/S-11 and S-Mosher acid, two diastereomers R,S-13 and S,S-13 were obtained in a 1:1 ratio.

Analytical HPLC: column Nucleosil 50-5, 4x250 mm, eluent 1.5 % EtOAc/hexane, flow 1.0 mL/min, 39 bar: Rs (R,S-13): 12.57 min, Rs (S,S-13): 13.29 min.

6-[(IR/S)-(2S)-2-Methoxy-2-phenyl-3,3,3-trifluoropropionyl]-oxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R,S-13 (mixture of diastereomers): (Yield: 74.6 mg, 0.16 mmol, 80%). R\(_f\) = 0.51 (EtOAc/petroleum ether 1:5). \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.58 - 7.26\) (m, 5H, H-28, H-29, H-30), 6.79 - 6.54 (m, 2H, H-11, H-12), 6.35, 6.15 (2x d, \(^{3}J_{HH} = 5.5\) Hz, \(^{3}J_{HH} = 5.9\) Hz, 1H, 2x H-13), 5.50 (2x dd, \(^{3}J_{HH} = 6.6\) Hz, \(^{3}J_{HH} = 7.4\) Hz, 1H, 2x H-15), 3.73 (s, 3H, H-22), 3.55, 3.49 (2x s, 3H, H-26), 3.33, 3.19 (2x d, \(^{2}J_{HH} = 13.2\) Hz, \(^{2}J_{HH} = 13.3\) Hz, 1H, 2x H-21), 2.05, 1.86 (2x d, \(^{3}J_{HH} = 13.2\), \(^{3}J_{HH} = 13.3\) Hz, 1H, 2x H-21'), 1.94 - 1.52 (m, 2H, H-16), 1.35 - 0.93 (m, 6H, H-19, H-18, H-17), 0.90 - 0.68 (m, br, 3H, H-20). \(^1\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta = 166.02, 166.06\) (C-8), 165.74, 165.89 (C-23), 135.23, 135.31 (C-14), 134.18, 134.24 (C-12), 133.30, 133.42 (C-10), 132.00, 132.42 (C-27) 129.46, 129.51 (C-28), 129.25, 129.39 (C-30), 128.27, 128.31 (C-29), 127.26, 127.38 (C-11), 124.75, 124.98 (C-13), 122.40, 122.51 (C-9), 117.59 - 128.68 (2x q, \(^{1}J_{CF} = 288.22\) Hz, \(^{1}J_{CF} = 258.83\) Hz, 2x C-25), 84.40 - 84.56 (2x q, \(^{2}J_{CF} = 12.42\) Hz, \(^{2}J_{CF} = 9.04\) Hz, 2x C-24), 80.29, 80.46 (C-15), 55.34, 55.52 (C-26), 51.97 (C-22), 32.80 (C-16), 31.16, 31.20 (C-18), 26.51, 26.64 (C-21), 24.82, 25.14 (C-17), 22.33 (C-19), 13.87 (C20). IR (KBr): \(\tilde{\nu} = 2952\) (m), 1745, 1709 (s), 1435 (m), 1247 (s), 1172 (s), 1164 (s), 1121 (m), 1014,
989 (m), 737, 718, 697 (s) cm$^{-1}$. MS [FD]: m/z = 466.4. Analysis (C$_{25}$H$_{29}$F$_{3}$O$_{5}$): calcd. C = 64.37 %, H = 6.27 %, found: C = 64.38 %, H = 6.33 %.

Starting from scalemic $R$-11 (~70 % ee) and $S$-Mosher acid, two diastereomers $R,S$-13 and $S,S$-13 were obtained in a 85:15 ratio. Data of the major diastereomer 6-[(1$R$)-{(2$S$)-2-Methoxy-2-phenyl-3,3,3-trifluoropropionyloxy}hexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester $R,S$-13: (Yield: 75 mg, 0.16 mmol, 80 %). $R_f$ = 0.53 (EtOAc/petroleum ether 1:5).

$^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 7.47 – 7.41 (m, 2H, H-28) 7.37 – 7.29 (m, 3H, H-29, H-30), 7.19 (d, br, $^3$J$_{HH}$ = 5.9 Hz, 1H, H-10), 6.69 (dd, $^3$J$_{HH}$ = 5.9 Hz, $^3$J$_{HH}$ = 11.2 Hz, 1H, H-11), 6.59 (dd, $^3$J$_{HH}$ = 5.8 Hz, $^3$J$_{HH}$ = 11.2 Hz, 1H, H-12), 6.16 (d, $^3$J$_{HH}$ = 5.8 Hz, 1H, H-13), 5.49 (t, br, $^3$J$_{HH}$ = 7.1 Hz, 1H, H-15), 3.73 (s, 3H, H-22), 3.55 (s, 3H, H-26), 3.19 (d, $^2$J$_{HH}$ = 13.5 Hz, 1H, H-21), 1.87 (d, $^2$J$_{HH}$ = 13.5 Hz, 1H, H-21'), 1.89 – 1.64 (m, 2H, H-16), 1.30 – 1.10 (m, 6H, H-17, H-18, H-19), 0.82 (t, $^3$J$_{HH}$ = 6.9 Hz, 3H, H-20).

$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ = 166.05 (C-8), 165.73 (C-23), 135.20 (C-14), 134.18 (C-12), 133.30 (C-10), 132.20 (C-27), 129.46 (C-28), 129.25 (C-30), 128.26 (C-29), 127.62 (C-21), 124.74 (C-13), 122.38 (q, $^1$J$_{CF}$ = 288 Hz, C-25), 84.45 (q, $^2$J$_{CF}$ = 28.3 Hz, C-24), 80.45 (C-15), 55.33 (C-26), 51.98 (C-22), 32.80 (C-16), 31.21 (C-18), 26.51 (C-21), 25.13 (C-17), 22.34 (C-19), 13.87 (C-20). IR (KBr): $\tilde{\nu}$ = 2952 (m), 1745, 1708 (s), 1435 (m), 1272 (s), 1212 (s), 1163 (s), 1121 (m), 1014, 989 (m), 736, 718, 696 (s) cm$^{-1}$. MS [FD]: m/z = 466.4. Analysis (C$_{25}$H$_{29}$F$_{3}$O$_{5}$): calcd. C = 64.37 %, H = 6.27 %, found: C = 64.28 %, H = 6.27 %.

Analytical HPLC: column Nucleosil 50-5, 4x250 mm, eluent 1.5 % EtOAc/hexane, flow 1.0 mL/min, 39 bar: $R_t$ ($R,S$-13): 12.57 min, $R_t$ ($S,S$-13): 13.29 min.

Starting from hydroxyester $R$-11 (~95 % ee) and $S$-Mosher acid, diastereomer $R,S$-13 was obtained. Filtration via a short silia gel column delivered pure product (nearly 100 %).

Starting from hydroxyester $R$-11 (~95 % ee) and $R$-Mosher acid, diastereomer $R,R$-13 was obtained. Filtration via a short silia gel column delivered pure product (nearly 100 %).

4. Synthesis of the C8 – C21 Fragment: Completion of the C8-C20 Building block 16 (70 % ee):

6-[(1$R$)-1-tert.-Butyldimethylsilyloxyhexyl]-1,3,5-cycloheptatriene 1-carboxylic acid methyl ester R-14 (TBS protection): Under Ar, hydroxyester R-11 (2.2 g, 8.79 mmol) and Et$_3$N (6.13 mL, 43.95 mmol) in dry CH$_2$Cl$_2$ (60 mL) were cooled to 0 °C. Under stirring, tert.-butyldimethylsilyl chloride (6.62 g, 43.95 mmol) was added. After about 30 min, the reaction mixture was warmed to 22 °C and then heated to reflux for 72 h. After cooling to 22 °C...
and quenching with MeOH (10 mL - stirring for 30 min), sat. aq. NaHCO₃ (30 ml) was added. The aqueous phase was extracted with Et₂O (3x 20 mL), the combined organic layers were dried (MgSO₄) and the solvent was removed in vacuum. The crude silyl ether was purified via column chromatography (silica gel, petroleum ether/EtOAc 20:1) affording TBS protected ester R-14 (2.53 g, 6.94 mmol, 79 %) as bright yellow oil. Rt = 0.48 (EtOAc/petroleum ether 1:20).

6-Hydroxymethyl-1-[[(R)-1-tert-butylidimethylsilyloxyethyl]-1,3,5-cycloheptatriene R-15 (DIBAL-H reduction): Under Ar, to a solution of TBS protected ester R-14 (2.45 g, 6.72 mmol, 70 % ee) in dry toluene (40 mL) was added dropwise diisobutylaluminium hydride (DIBAL-H, 26.5 mL, 39.75 mmol, 1.5 M in toluene) at 0 °C with stirring. After about 30 min, the reaction mixture was warmed to 22 °C and stirring was continued for 2 h (TLC). The reaction was stopped by subsequent quenching with MeOH (20 mL, 10 min of stirring) and sat. aq. potassium sodium tartrate (15 mL, 30 min of stirring). The organic layer was diluted with Et₂O (30 mL), the aqueous phase was solidified by addition of MgSO₄. The organic layer was decanted and the solid residue was thoroughly washed with Et₂O (5x 40 mL). The combined organic layers were dried (MgSO₄) and the solvent was removed in vacuum. The residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 10:1) affording carbinal R-15 (2.12 g, 6.31 mmol, 94 %) as colorless oil. Rt = 0.41 (EtOAc/petroleum ether 1:5). [α]D = 14.42º (c = 1.0, 20°C, CH₂Cl₂, ~70 % ee). 1H-NMR (400 MHz, CDCl₃): δ = 6.47 - 6.64 (m, 2H, H-12, H-11), 6.14 - 6.10 (m, 1H, H-10), 6.02 - 5.99 (m, 1H, H-13), 4.27 (dd, JHH = 5.5 Hz, JHH = 14.2 Hz, 1H, H-8), 4.20 (dd, JHH = 4.1 Hz, JHH = 14.2 Hz, 1H, H-8'), 4.13 (dd, JHH = 6.0 Hz, JHH = 7.0 Hz, 1H, H-15), 2.70 (d, JHH = 13.1 Hz, 1H, H-21), 2.14 (d, JHH = 13.1 Hz, 1H, H-21'), 1.84 - 1.79 (m, br, 1H, OH), 1.63 - 1.44 (m, 2H, H-16), 1.34 - 1.10 (m, 6H, H-19, H-18, H-17), 0.87 (s, 9H, H-23), 0.86 (t, JHH = 6.8 Hz, 3H, H-20), -0.04, -0.05 (2x s, 2x 3H, H-22). 1C-NMR (100 MHz, CDCl₃): δ = 139.03 (C-14), 135.76 (C-9), 129.39 (C-12), 129.04 (C-11), 121.89 (C-13), 121.44 (C-10), 76.94 (C-15), 66.38 (C-8), 36.62 (C-16), 31.72 (C-18), 28.27 (C-21), 25.90 (C-23), 25.47 (C-17), 22.63 (C-19), 18.35 (C-22), 14.07 (C-20), -4.61, -4.95 (C-24). IR (FT-IR, neat): ʋ = 3313 (cm), 2958, 2928 (s), 2856 (s), 1462 (w), 1252, 1060 (s), 834 (w), 773 (s), 739 (st) cm⁻¹. MS [FD]: m/z = 363.6. Analysis (C₂₅H₃₆O₃Si): calcd: C = 71.37 %, H = 10.78 %, found: C = 71.30 %, H = 10.73 %.

1-[(R)-1-tert-Butyldimethylsilyloxyethyl]-6-(1-phenyl-1H-1,2,3,4-tetrazol-5-yl)-(thiomethyl)-1,3,5-cycloheptatriene XIII (Mitsunobu reaction): Under Ar, to a solution of carbinal R-15 (2.02 g, 6.0 mmol, 70 % ee), triphenylphosphine (1.97 g, 7.5 mmol) and 1-phenyl-1-

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1-[(IR)-1-tert.-Butyldimethylsilyloxyhexyl]-6-(1-phenyl-1H-1,2,3,4-tetrazol-5-yl)-sulfonymethyl]-1,3,5-cycloheptatriene R-16 (sulfide oxidation): Under Ar, to a solution of mercaptotetrazole XIII (1.1 g, 2.21 mmol, 70 % ee) in EtOH was slowly added ammonium molybdate (NH₄)₂MoO₇·2x 4 H₂O (0.75 g, 0.61 mmol) in 30% eq. H₂O₂ (1.19 mL, 10.5 mmol). After 1h at 0 °C the reaction mixture was stirred at 22 °C for 96 h (TLC). Work-up started by dilution with Et₂O (10 mL). The organic layer was extracted with H₂O (10 mL) and brine (10 mL). The aqueous layer was extracted with Et₂O (3x 10 mL), the combined organic phases were dried (MgSO₄), the solvent was removed in vacuum and the crude sulfone was purified by column chromatography (silica gel, petroleum ether/EtOAc 10:1) affording sulfone R-16 (0.972 g, 1.18 mmol, 83 %) as pale yellow oil. R₂ = 0.27 (EtOAc/petroleum ether 1:10). [α]D = 3.33° (c = 1.0, 20°C, CH₂Cl₂, -70 °C ee).

1H-NMR (400 MHz, CDCl₃): δ = 7.66 – 7.55 (m, 5H, H-27, H-28, H-29), 6.55 (dd, JHH = 5.8 Hz, JHH = 11.2 Hz, 1H, H-12), 6.39 (dd, JHH = 5.8 Hz, JHH = 11.2 Hz, 1H, H-11), 6.22 (d, JHH = 5.8 Hz, 1H, H-10), 6.04 (d, JHH = 5.8 Hz, 1H, H-13), 4.57 (d, JHH = 13.9 Hz, 1H, H-8), 4.46 (d, JHH = 13.9 Hz, 1H, H-8), 4.25 (d, JHH = 13.9 Hz, 1H, H-8), 4.12 (t, JHH = 6.5 Hz, 1H, H-15), 2.61 (d, JHH = 6.5 Hz, 1H, H-21), 2.31 (d, JHH = 6.5 Hz, 1H, H-21), 1.58 – 1.41 (m, 2H, H-16), 1.35 – 1.12 (m, 6H, H-17, H-18, H-19), 0.87 - 0.84 (m, 3H, H-20), 0.85 (s, 9H, H-23), 0.01, -0.09 (2x s, 6H, H-24). 13C-NMR (100 MHz, CDCl₃): δ = 153.43 (C-25), 139.81 (C-14), 132.98 (C-26), 132.58 (C-10), 131.41 (C-12), 129.54 (C-29), 128.19 (C-11), 125.31 (C-27), 121.87 (C-13), 117.72 (C-9), 76.08 (C-15), 63.55 (C-8), 37.01 (C-16), 31.62 (C-18), 31.34 (C-21), 25.84 (C-23), 25.25 (C-17), 18.29 (C-24), 13.99 (C-20), -5.04, -4.62 (C-22). IR (FT-IR): v = 2958, 2928 (s), 2856 (s), 1737 (w), 1497 (w), 1461 (w), 1345 (w), 1249 (w), 1155 (s), 1072 (s), 835 (s), 759 (s), 686 (s) cm⁻¹. MS [FD]: m/z = 638.6 (100%), 528.3 (28.56%), 527.3 (39.59%), 471.3 (37.54%), 319.3 (45.05%). Analysis (C₂₂H₆₄N₂O₁₃S): calcd. C = 61.33 %, H = 7.62 % N = 10.60 %, S = 6.06 %, found: C = 61.23 %, H = 7.57 % N = 10.65 %, S = 6.05 %.

5. Synthesis of 15R-LXA₄ methyl ester 19

Synthesis of from lactone 5 and sulfone R-16:

![Chemical structure image]

(6S)-6-[3-[(IR)-1-tert.-Butyldimethylsilyloxyhexyl]-1,3,5-cycloheptatrienyl]-1R)-tert.-butyldimethylsilyloxy-2E-propenyl]-tetrahydropyran-2-one 17 (Julia-Kocienski Olefination): Under Ar, to a solution of sulfone R-16 (270 mg, 0.51 mmol, 70 % ee) in dry DMF (10 mL, mp -61°C) was cooled to about -70 °C with stirring. Lithium bis-(trimethylsilyl)-amide (0.51 mL, 0.51 mmol, 1 M in THF) was added dropwise via syringe over a period of 10 min. A dark red colored solution occurred. For completion of deprotonation, the reaction was stirred at -70 to -78 °C for 3 – 4 h.

Freshly prepared crude lactone aldehyde 5 (140 mg, 0.51 mmol) in dry DMF (5 mL) were stirred in the presence of some beads of molecular sieves (4 Å) for 3 – 4 h at -60 to -70 °C. The so prepared solution of aldehyde 5 was transferred into the sulfone solution and the mixture was stirred for 4 – 5 h at -70 - -78 °C (TLC) and for further 24 h at 22 °C. Then, the reaction was stopped by quenching with H₂O (5 mL, stirring for 30 min). After dilution with Et₂O (20 mL), the mixture was extracted with 5 % eq. NaHCO₃ (40 mL). The aqueous phase was extracted with Et₂O (3x 20 mL), the combined organic phases were washed with H₂O (2x 15 mL) and brine (15 mL) and dried (MgSO₄). After removal of the solvent in vacuum and pre-purification by column chromatography (silica gel, petroleum ether/EtOAc 10:1, 1% Et₄N), preparative HPLC (dilnucleosil 50-5, 5 µm, 32x250 mm, 0.5 % iso-ProH in hexanes + 0.5 % Et₃N, flow 28 mL/min, Rₚ = 12.73 min) afforded cycloheptatrienyl valerolactone 17 (93.9 mg, 0.163 mmol, 32 %) as colorless oil. R₂ = 0.21 (EtOAc/petroleum ether 1:10). [α]D = -32.15° (c = 1.0, 20°C, CH₂Cl₂).

1H-NMR (400 MHz, CDCl₃): δ = 6.50 – 6.45 (m, 2H, H-11, H-12), 6.36 (d, JHH = 15.8 Hz, 1H, H-8), 6.14 – 6.09 (m, 1H, H-13), 6.06 – 6.01 (m, 1H, H-13), 5.88 (dd, JHH = 5.70 Hz, JHH = 15.8 Hz, 1H, H-7), 4.57 – 4.49 (m, 1H, H-6), 4.23 (dd, JHH = 3.9 Hz, JHH = 6.8 Hz, 1H, H-5), 4.06 (dd, JHH = 5.1 Hz, JHH = 7.5 Hz, 1H, H-15), 3.32 and 3.17 (2x d, JHH = 13.1 Hz, 1H, H-21), 2.55 (dd, JHH = 5.05, JHH = 17.7 Hz, 1H, H-2), 2.42 – 2.31 (m, 1H, H-2), 2.00 – 1.91 (m, 1H, H-4), 1.91 – 1.80 (m, 2H, H-3), 1.78 – 1.67 (m, 1H, H-4'), 1.72 (d, JHH = 13.0 Hz, 1H, H-21'), 1.52 – 1.41 (m, 1H, H-16), 1.41 – 1.31 (m, 1H, H-16'), 1.29 –
1.11 (m, 6H, H-17, H-18, H-19), 0.89, 0.88 (2x s, 2x 9H, 2x H-23), 0.83 (t, J_HH = 7.0 Hz, 1H, H-20), 0.08, 0.03, 0.00, -0.07 (4 s, 4x 3H, H-24). 1^1C-NMR (100 MHz, CDCl3): δ = 171.08 (C-1), 139.33 (C-9), 132.89 (C-8), 130.85 (C-14), 130.21 (C-7), 129.12 (C-12), 128.22 (C-11), 127.10 (C-10), 121.26 (C-13), 83.29 (C-6), 76.55 (C-5), 74.36 (C-15), 36.69 (C-16), 31.67 (C-18), 30.14 (C-21), 27.02 (C-23), 25.83 (C-23), 25.53 (C-17), 22.60 (C-2), 21.09 (C-19), 18.47 (C-3), 18.22, 18.15 (C-22), 14.01 (C-24), -4.63, -4.75, -4.81, -5.13 (C-24). IR (FT-IR): ν = 2954, 2928 (s), 2856 (s), 1741 (w), 1666, 1049 (s), 834 (s), 774, 738, 669 (w) cm\(^{-1}\). MS [FD]: m/z = 574.4. MS [ESI] (M+Na\(^+\)): 597.4601. Analysis (C\(_{33}\)H\(_{38}\)O\(_{5}\)S\(_{2}\)): calcd. C = 68.93 %, H = 10.17 %, found: C = 68.97 %, H = 10.22 %.

Side product XIV of the Julia-Kocienski olefination
Yield: 0.16 g, 0.34 mmol, 43 %, R\(_f\) = 0.18 (petroleum ether/EtOAc 10:1), [α]_D = 68.25° (c = 1.15, 20°C, CH\(_2\)Cl\(_2\)).

1H-NMR (400 MHz, CDCl3): δ = 7.34 (m, 5H, H-27, H-28, H-29), 6.40 (dd, J = 5.52, J = 8.88, H-12), 6.19 (d, J = 11.03 Hz, H-11), 6.00 (d, J = 5.51 Hz, 1H, H-13), 4.11 (t, J = 6.25, J = 5.51 Hz, 1H, H-15), 2.82 (d, J = 12.50 Hz, 1H, H-21), 2.20 (d, J = 12.87 Hz, 1H, H-21′), 1.81 (s, 3H, H-8), 1.43 (m, 2H, H-16), 1.20 (m, 6H, H-19, H-18, H-17), 0.84 (m, 12H, H-23, H-20), -0.05, 0.03 (2 s, 6H, H-24). 13C-NMR (100 MHz, CDCl3): δ = 153.38 (C-25), 141.11 (C-14), 138.67 (C-10), 134.27 (C-26), 130.75 (C-11), 129.31 (C-28, C-29), 128.79 (C-12), 123.52 (C-27), 122.13 (C-23), 117.92 (C-9), 76.36 (C-15), 36.59 (C-16), 34.60 (C-18), 31.65 (C-21), 25.84 (C-23), 25.27 (C-17), 22.54 (C-19), 22.11 (C-8), 18.25, (C-22), 14.02 (C-24), -5.01, -4.64 (C-24). IR (FT-IR): ν = 2953, 2928 (s), 2856 (s), 1741 (w), 1666, 1049 (s), 834 (s), 774, 738, 669 (w) cm\(^{-1}\). MS [ESI] (M+Na\(^+\)): 464.4. Analysis (C\(_{27}\)H\(_{30}\)N\(_2\)O\(_5\)S\(_2\)): calcd. C = 69.78 %, H = 8.68 %, N = 12.06 %, found: C = 69.90 %, H = 8.90 %, N = 11.86 %.

(6S)-6-[6-[(IR)-1-Hydroxyhexyl]-1,3,5-cycloheptatrienyl]-(1R)-hydroxy-2E-propenyl]tetrahydropyran-2-one XV (silyl ether cleavage): Under Ar, cycloheptatrienyvalerolactone XV (45 mg, 0.078 mmol in THF (3 mL) was treated dropwise with tetrabutylammonium fluoride (0.63 mL, 0.63 mmol, 1 M in THF). The color of the solution turns to dark red/purple. The mixture was stirred at 22 °C for 24 h (TLC). For quenching sat. aq. NH\(_3\) (M)

J = 5.50 Hz, 2H, H-12′), 6.19 (d, J = 11.03 Hz, H-11′), 6.00 (d, J = 5.51 Hz, 1H, H-13′), 4.11 (t, J = 6.25, J = 5.51 Hz, 1H, H-15′), 2.82 (d, J = 12.50 Hz, 1H, H-21′), 2.20 (d, J = 12.87 Hz, 1H, H-21″), 1.81 (s, 3H, H-8′), 1.43 (m, 2H, H-16′), 1.20 (m, 6H, H-19′, H-18′, H-17′), 0.84 (m, 12H, H-23′, H-20′), -0.05, 0.03 (2 s, 6H, H-24). 13C-NMR (100 MHz, CDCl3): δ = 153.38 (C-25′), 141.11 (C-14′), 138.67 (C-10′), 134.27 (C-26′), 130.75 (C-11′), 129.31 (C-28′, C-29′), 128.79 (C-12′), 123.52 (C-27′), 122.13 (C-23′), 117.92 (C-9′), 76.36 (C-15′), 36.59 (C-16′), 34.60 (C-18′), 31.65 (C-21′), 25.84 (C-23′), 25.27 (C-17′), 22.54 (C-19′), 22.11 (C-8′), 18.25, (C-22′), 14.02 (C-24′), -5.01, -4.64 (C-24′). IR (FT-IR): ν = 2953, 2928 (s), 2856 (s), 1741 (w), 1666, 1049 (s), 834 (s), 774, 738, 669 (w) cm\(^{-1}\). MS [ESI] (M+Na\(^+\)): 369.2540. Analysis (C\(_{27}\)H\(_{30}\)N\(_2\)O\(_5\)S\(_2\)): calcd. C = 69.78 %, H = 8.68 %, N = 12.06 %, found: C = 69.90 %, H = 8.90 %, N = 11.86 %.

8-[6-[(IR)-1-Hydroxyhexyl]-1,3,5-cycloheptatrienyl]-(5S,6R)-dihydroxy]-7E-octenoic acid methyl ester 19
(Zemplén reaction): Under Ar, to a solution of cycloheptatrienyl dihydroxyvalerolactone XV (19.5 mg, 0.056 mmol) in dry MeOH (5 mL) were injected several drops of Et\(_3\)N. The solution was stirred at 22 °C for 2 h, then, the solvent was removed under reduced pressure and the residue was purified via column chromatography (silica gel, EtOAc) to give cycloheptatrienyl methyl ester 19 (15.7 mg, 0.0416 mmol, 74 %) as oil. R\(_f\) = 0.11 (EtOAc). For data see below.

Synthesis of LXA\(_4\) methylester 19 from ester 6 and sulfone R-16:
Freshly prepared crude ester aldehyde 6 (71 mg, 0.17 mmol) in dry DMF (3 mL) were stirred in the presence of some beads of molecular sieves (4 Å) for 3 – 4 h at -60 to -70 °C. The so prepared solution of aldehyde 6 was transferred into the sulfone solution and the mixture was stirred for 4 – 5 h at -70 to -78 °C (TLC) and for further 24 h at 22 °C. Then, the reaction was stopped by quenching with \( \text{H}_2\text{O} \) (3 mL, stirring for 30 min). After dilution with \( \text{Et}_2\text{O} \) (10 mL), the mixture was extracted with 5% aq. \( \text{NaHCO}_3 \) (20 mL). The aqueous phase was extracted with \( \text{Et}_2\text{O} \) (3x 10 mL), the combined organic phases were washed with \( \text{H}_2\text{O} \) (2x 8 mL) and brine (8 mL) and dried (\( \text{MgSO}_4 \)). After removal of the solvent in vacuum and purification by column chromatography (silica gel, petroleum ether/EtOAc 10:1, 1% \( \text{Et}_2\text{N} \) protected cyclohexenyl ester 18 (28.4 mg, 0.039 mmol, 26%) was isolated as colorless oil. \( \text{Rf} = 0.36 \) (EtOAc/petroleum ether 1:20), \( \left[a\right]_{D} = 25.84^{\circ} \) (c = 1.19, 20 °C, \( \text{CH}_2\text{Cl}_2 \)).

\[ \text{IR (FT-IR)}: \nu = 2952, 2928 \text{ (s), 2856 (s), 1742 (w), 1471 (w), 1360 (w), 1250 (s), 1069(s), 833 (s), 773, (s), 739 (w), 668 (w) cm}^{-1}. \text{MS [FD]}: m/z = 720.5. \text{MS [ESI]} (\text{M+Na}): 733.5 \text{Da}. \]

8-[6-[(IR)-1-tert.-Butylidimethylsilyloxyhexyl]-1,3,5-cycloheptatrienyl]-(5S,6R)-dihydroxy-7E-octenoic acid methyl ester 19 (silyl ether cleavage): Under Ar, protected cyclohexenyl ester 18 (20 mg, 0.028 mmol) in THF (1 mL) was treated dropwise with tetrabutylammonium fluoride (0.42 mL, 0.42 mmol, 1 M in THF, < 5% \( \text{H}_2\text{O} \)). The color of the solution turns to dark red/purple. The mixture was stirred at 22 °C for 24 h (TLC). For quenching sat. aq. \( \text{NH}_4\text{Cl} \) (1 mL) was added. The aqueous layer was extracted with \( \text{CH}_2\text{Cl}_2 \) (3x 5 mL), the combined organic phases were dried (\( \text{MgSO}_4 \)) and the solvent was removed in vacuum. The crude product was purified via column chromatography (silica gel, EtOAc) to give cyclohexenyl methyl ester 19 (7.5 mg, 0.02 mmol, 71%) as a colorless oil. \( \text{Rf} = 0.11 \) (EtOAc), \( \left[a\right]_{D} = -9.48^{\circ} \) (c = 0.7, 20 °C, \( \text{CH}_2\text{Cl}_2 \)).

\[ \text{IR (FT-IR)}: \nu = 2952, 2928 \text{ (s), 2856 (s), 1742 (w), 1471 (w), 1360 (w), 1250 (s), 1069(s), 833 (s), 773, (s), 739 (w), 668 (w) cm}^{-1}. \text{MS [FD]}: m/z = 757.6 (58.75% - 2 M), 378.3 (42.50% - M), 360.4 (68.75%), 346.3 (58.75%), 254.3 (100%), 115.2 (75.63%). \text{MS [ESI]} (\text{M+Na}): 401.2756. \text{Analysis (C}_{22}\text{H}_{23}\text{O}_{3}): \text{calc. C} = 69.81 \%, \text{H} = 9.05 \%. \text{found: C} = 69.77 \%, \text{H} = 9.05 \%. \]


For a preparation procedure see Ref. 3


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4 For a preparation procedure see Ref. 3


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Spectra of new compounds:

1. Synthesis of the C1 – C7 fragment
2. Synthesis of the C8 – C21 Fragment: Assembly of the Carbon Framework
R,S-

R,R-

O

O

39
$R,S\text{-13}$: blue (minor $S,S\text{-13}$), $R,R\text{-13}$: red

$R,S\text{-13}$: blue (minor $S,S\text{-13}$), $R,R\text{-13}$: red
4. Synthesis of the C8 – C21 Fragment: Completion of the C8-C20 Building block 16 (70 % ee)
5. Synthesis of 15R-LXA₄ methylester 19