# SUPPORTING INFORMATION

## PORPHYRIN- AND BODIPY-HELICENE CONJUGATES: SYNTHESES, SEPARATION OF ENANTIOMERS AND CHIROPTICAL PROPERTIES

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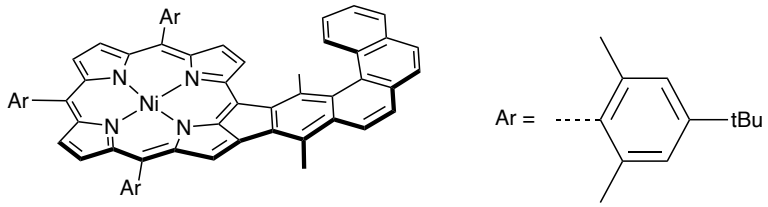
## NMR and MS data of compound 8




Chemical Formula: $C_{76}H_{72}N_4Ni$
Molecular Weight: 1100.1334

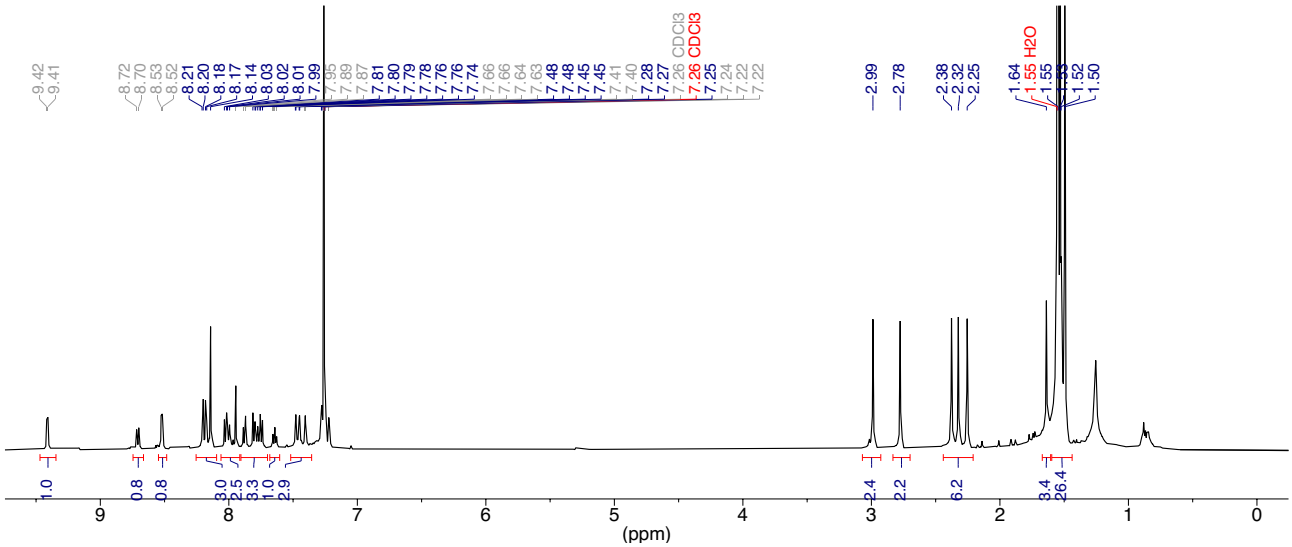



**Figure S01:** $^1$H NMR spectrum of compound **8** in $CDCl_3$ at 298 K (500 MHz).

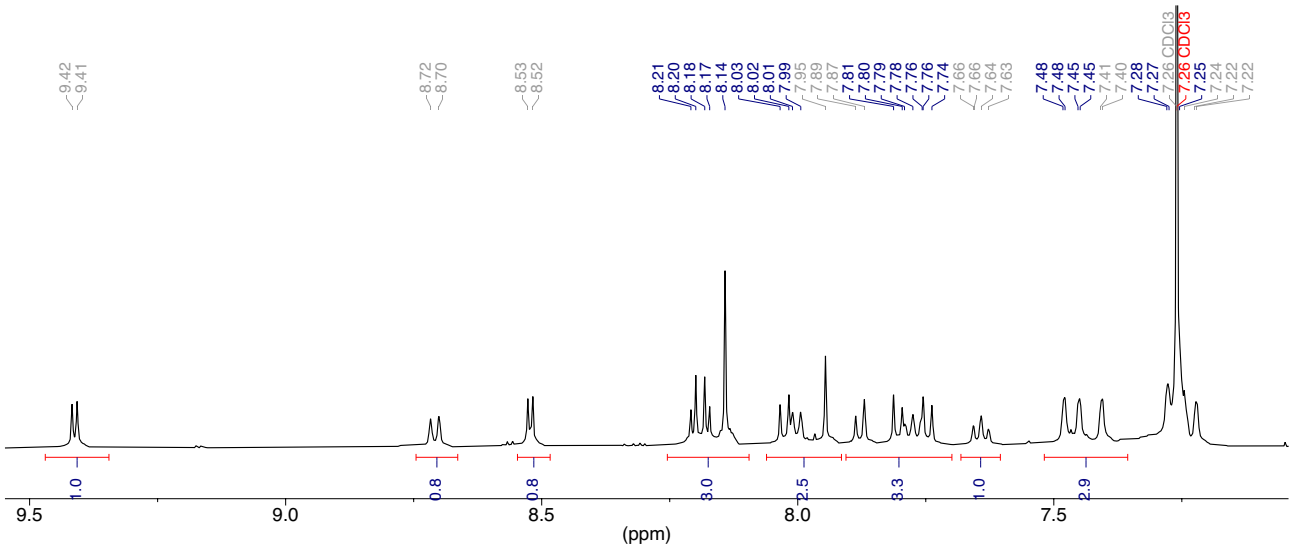



**Figure S02:** $^1$H NMR spectrum (aromatic area) of compound **8** in $CDCl_3$ at 298 K (500 MHz).

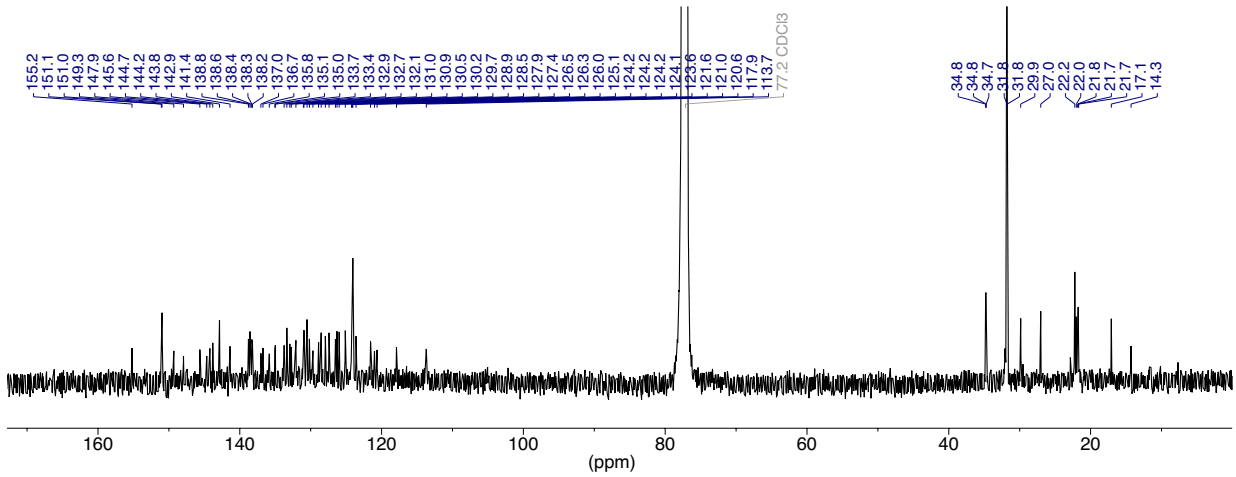



**Figure S03:** $^{13}C$ NMR spectrum of compound **8** in $CDCl_3$ at 298 K (126 MHz).

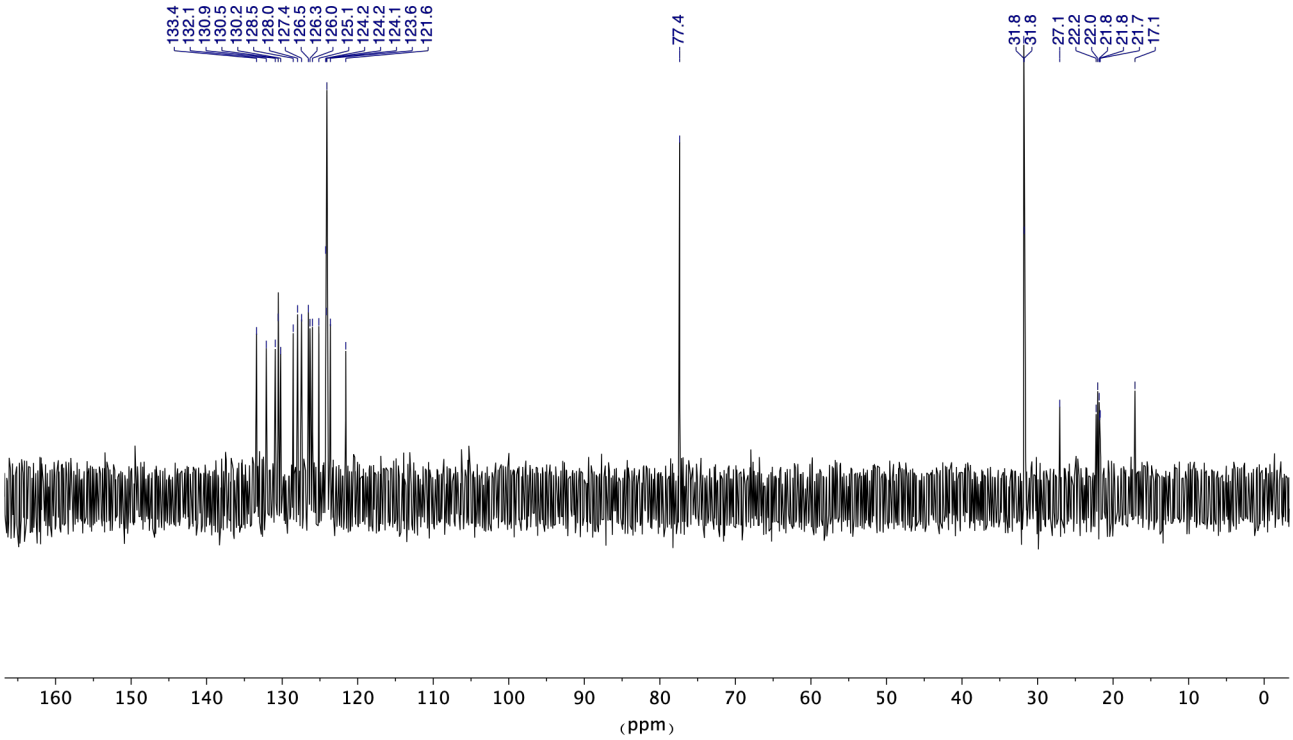



**Figure S04:** $^{13}C$ NMR DEPT spectrum of compound **8** in $CDCl_3$ at 298 K (126 MHz).

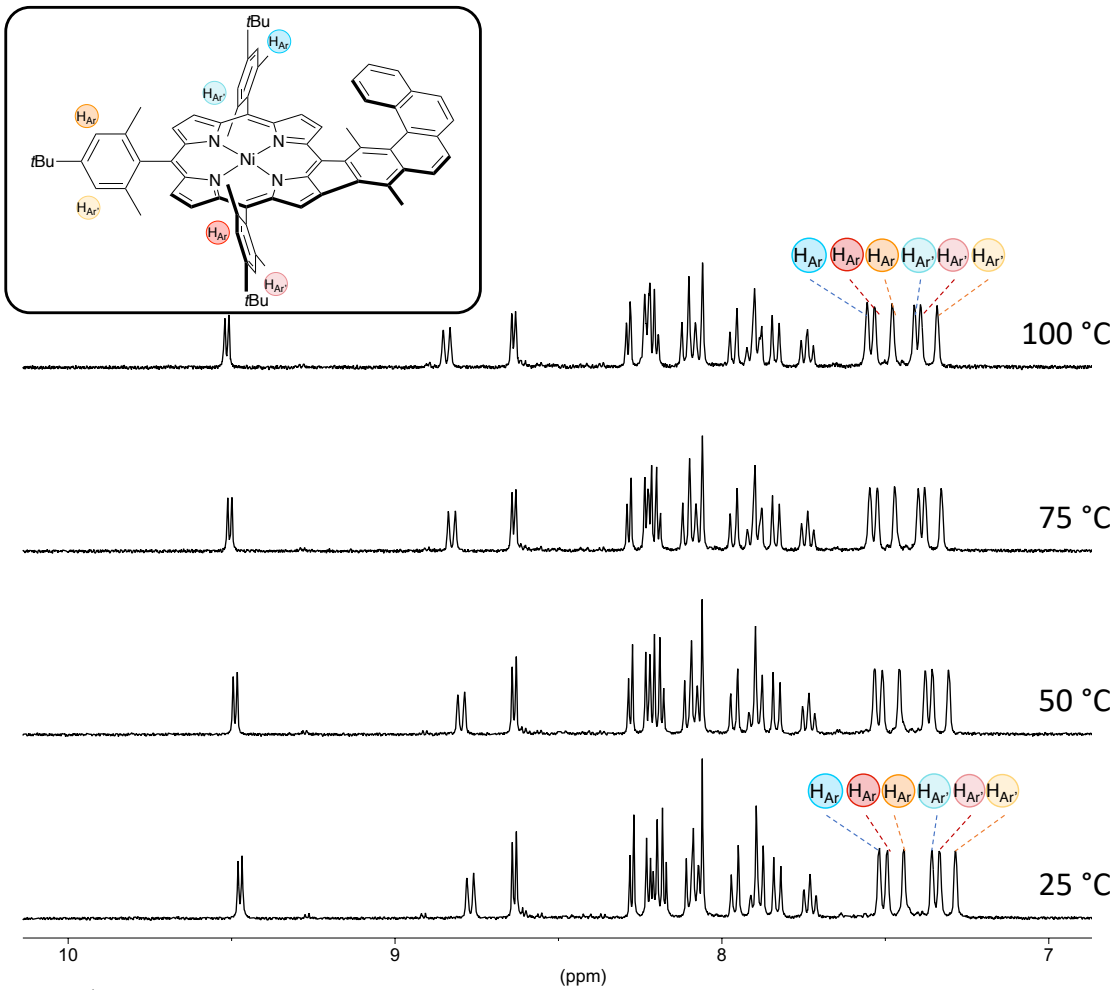



**Figure S05:** $^{1}$H NMR spectrum (aromatic area) of compound **8** in $C_2D_2Cl_4$ at different temperatures.

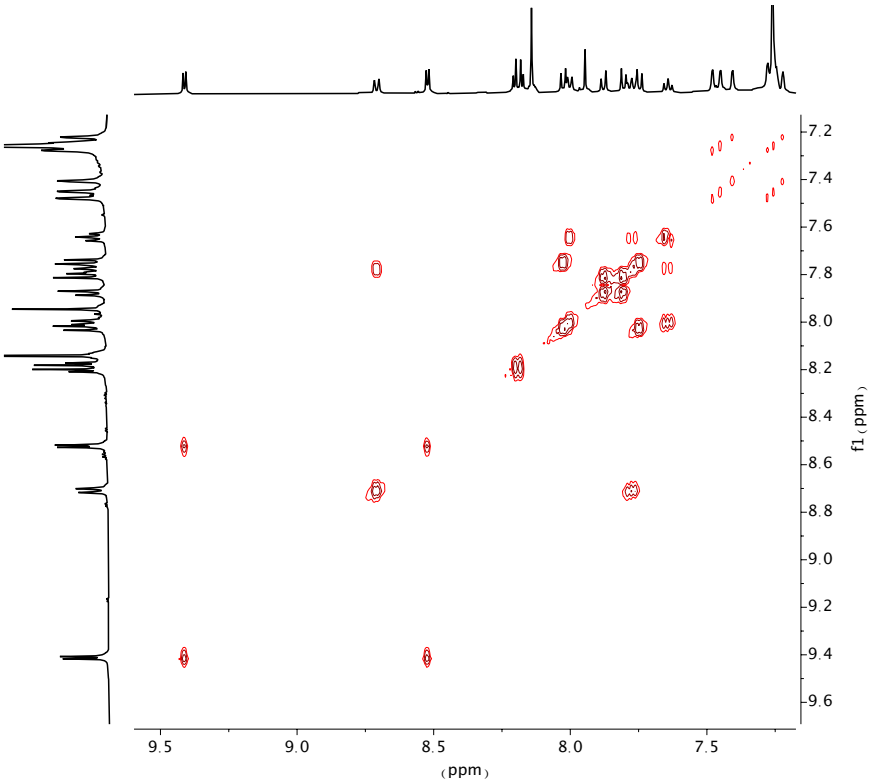



**Figure S06:** $^{1}$H-$^{1}$H COSY NMR spectrum (aromatic area) of compound **8** in $CDCl_3$.

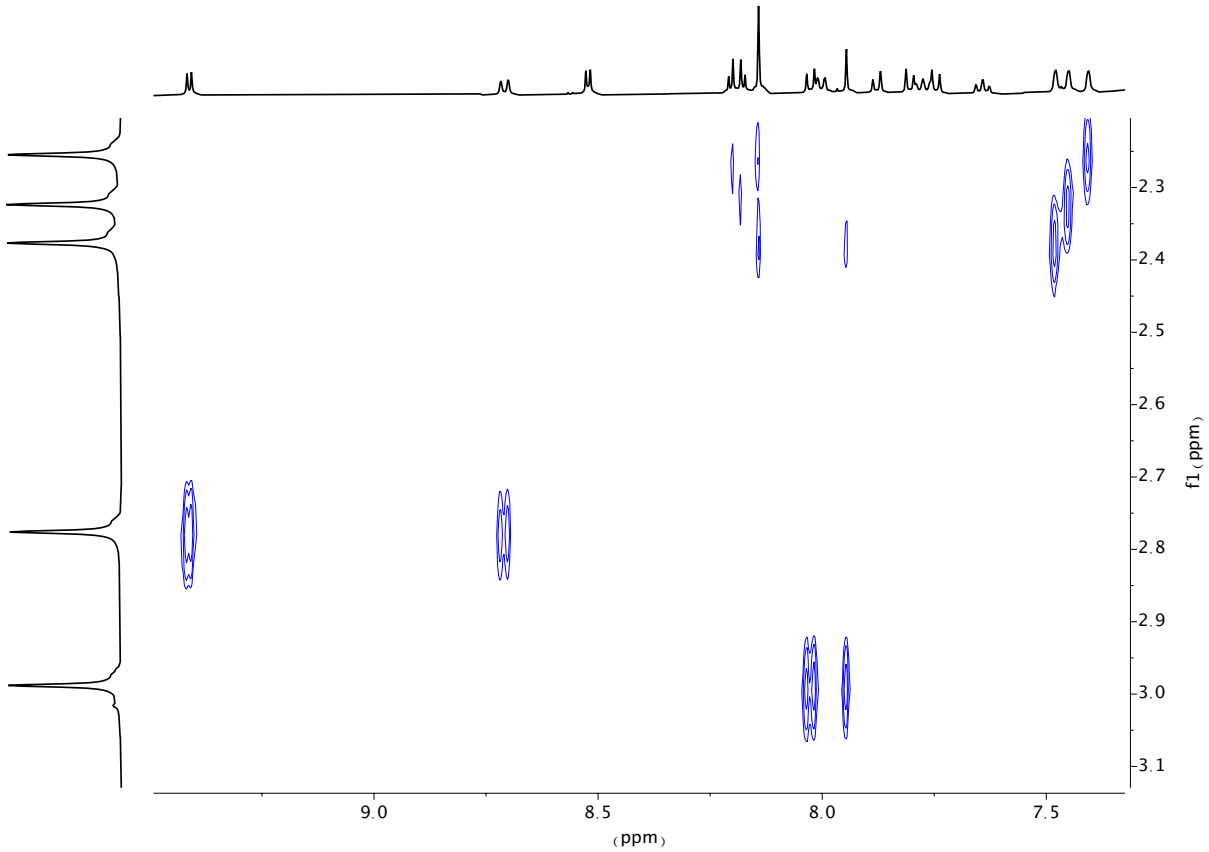



**Figure S07:** NOESY $^{1}H$ NMR spectrum (useful area for assignement) of compound **8** in $CDCl_3$.

In compound **8**, all aromatic protons of the three *meso*-aryl groups are well separated and the three pairs of $^{4}J$ coupled protons were found at 7.51-7.31, 7.48-7.29 and 7.44-7.25 ppm (see Figure S06, top right corner). In addition all methyl groups are also well separated. All beta-pyrrolic protons are well separated: three AB systems (at 9.44-8.55, 8.23-8.21 and 8.19-8.16 ppm) and one singlet at 7.98 ppm. These beta-pyrrolic protons are close to methyl groups of the meso-aromatic substituents. From the NOESY spectrum (Figure S07), it can be deduced that the pyrrolic proton at 7.98 ppm is close to the methyl group at 2.41 ppm and the aromatic proton at 7.51 ppm. The pyrrolic protons at 8.16-8.19 ppm are also close to the methyl groups at 2.41 ppm and 2.28 ppm (corresponding to the aromatic proton at 7.44 ppm).

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | F10334SK.d | Acquisition Date | 17/09/2021 11:28:07 |
| Method | Tune_pos_Mid.m | Operator | BDAL@DE |
| Sample Name | VS443 | Instrument | micrOTOF II |
| Comment | | | |

**Acquisition Parameter**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Source Type | ESI | Capillary | 4500 V | Nebulizer | 0.3 Bar | Corona | 0 nA |
| Ion Polarity | Positive | n/a | n/a | Dry Gas | 3.0 l/min | n/a | n/a |
| n/a | n/a | n/a | n/a | Dry Heater | 200 °C | APCI Heater | 0 °C |

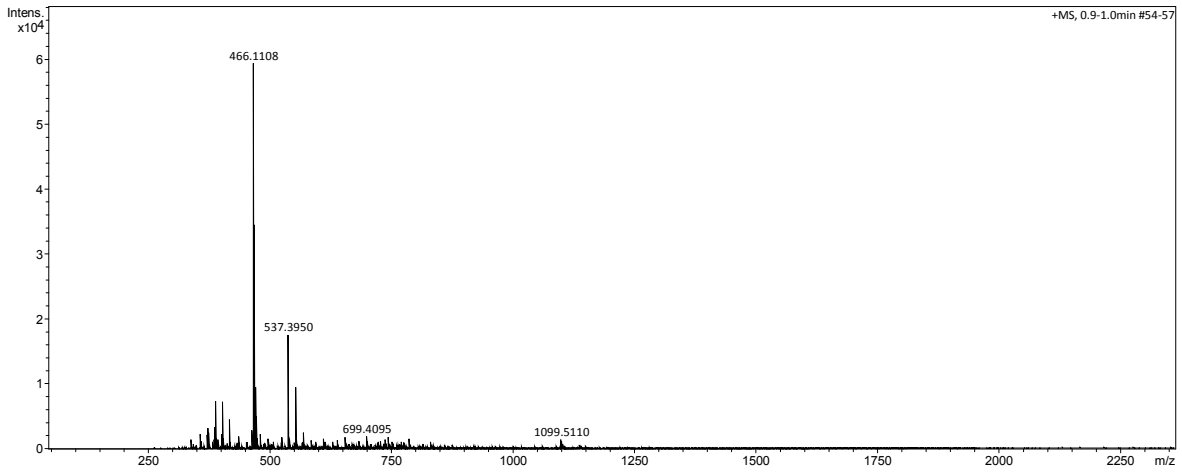



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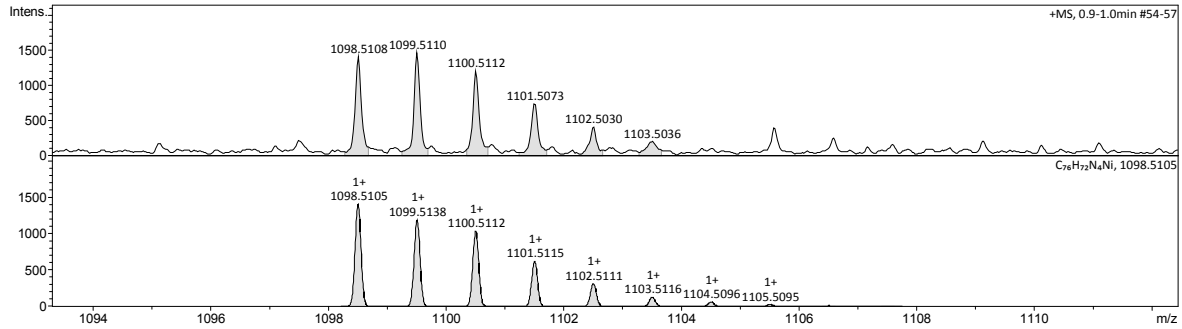
**Figure S08**. HRMS of compound **8**.

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Corrector Fill | 50.9 V |
| n/a | n/a | n/a | n/a | n/a | n/a |
| Scan Begin | 50 m/z | n/a | n/a | Set Reflector | 1800.0 V |
| Scan End | 3000 m/z | n/a | n/a | Set Flight Tube | 8600.0 V |
| | | n/a | n/a | Set Detector TOF | 2008.9 V |



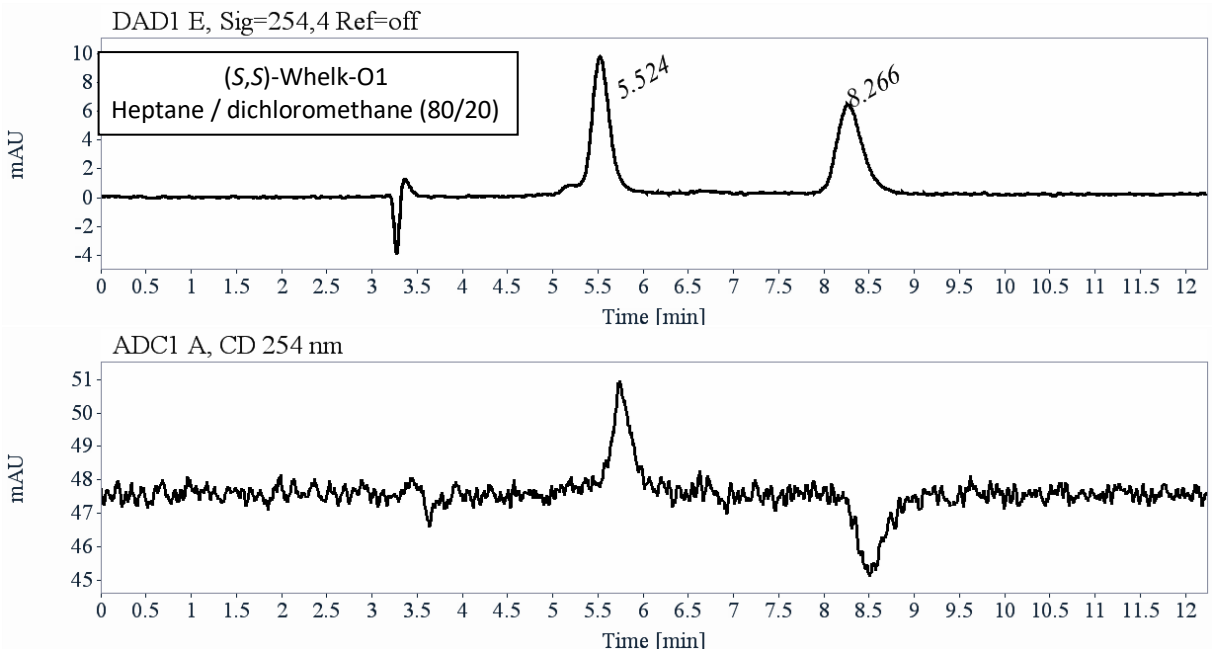

| Meas. m/z | # | Ion Formula | m/z | err [ppm] | Mean err [ppm] | rdb | N-Rule | e¯ Conf | mSigma | Std I | Std Mean m/z | Std I VarNorm | Std m/z Diff | Std Comb Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1098.510785 | 1 | C76H72N4Ni | 1098.510493 | -0.3 | 932.8 | 43.0 | ok | odd | 74.3 | 46.9 | n.a. | n.a. | n.a. | n.a. |

**Figure S09**. HRMS of compound **8** (top: experimental MS, bottom: simulation)

**Analytical chiral HPLC separation for compound 8**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **(*S*,*S*)-Whelk-O1** | Heptane / dichloromethane (80/20) | 5.52 (+) | 0.87 | 8.27 (-) | 1.80 | 2.06 | 6.34 |



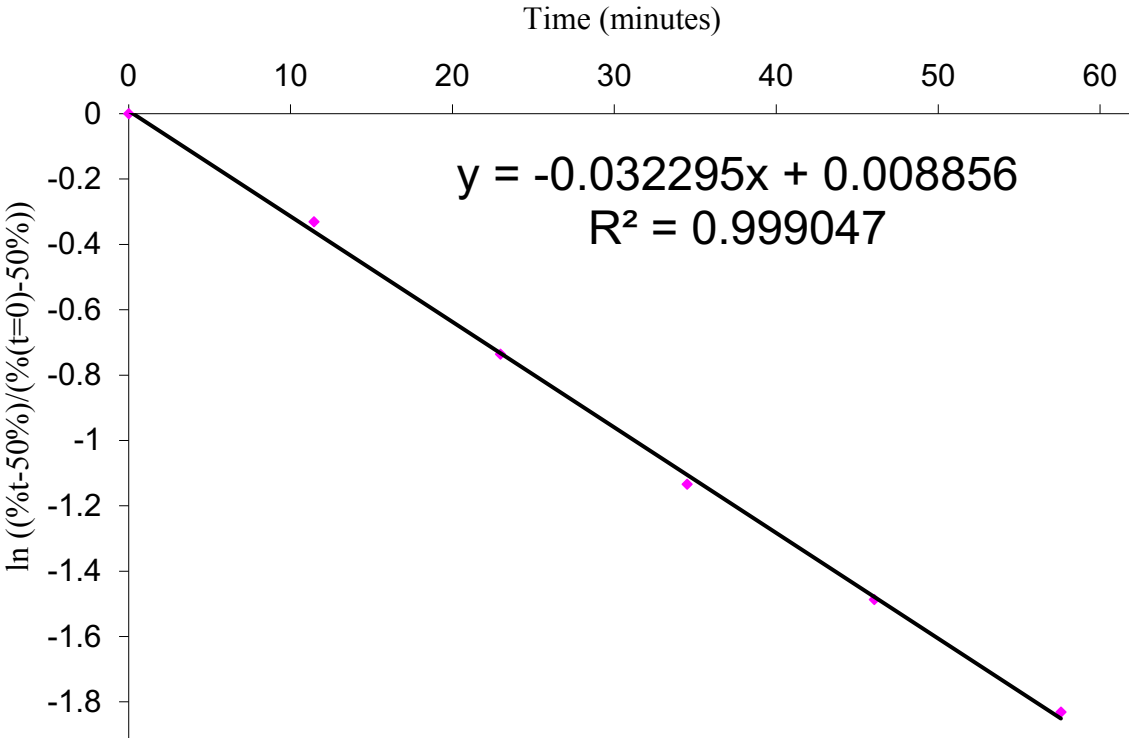

| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 5.52 | 147 | 53.22 | 0.87 | | |
| 8.27 | 129 | 46.78 | 1.80 | 2.06 | 6.34 |
| Sum | 276 | 100.00 | | | |

One injection was done on (*S*,*S*)-Whelk-O1 (250 x 10 mm), with hexane / dichloromethane (80/20) as mobile phase, flow-rate = 5 mL/min and UV detection at 254 nm, to obtain an enantio-enriched solution of the second eluted enantiomer in the mobile phase.

**Kinetic of enantiomerisation of compound 8**

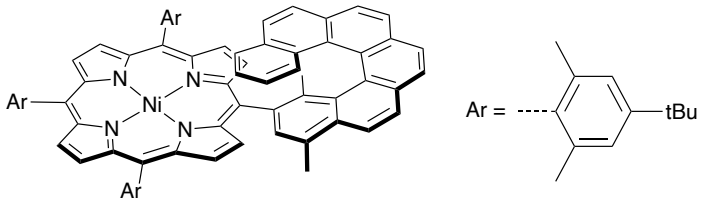
An enantio-enriched solution in the second eluted enantiomer of compound **8** is thermostated at 25°C in the mixture heptane / dichloromethane (80/20). 10 µL are taken and then injected on (*S*,*S*)-Whelk-O1 (80:20 heptane / dichloromethane, 1 mL/min, UV 254 nm). The percentage decrease of the second eluted enantiomer is monitored.

| Time (min) | % second eluted enantiomer | ln ((%t-50%)/(%(t=0)-50%)) |
|---|---|---|
| 0.00 | 89.953 | 0.00000 |
| 11.45 | 78.705 | -0.33063 |
| 22.97 | 69.134 | -0.73624 |
| 34.50 | 62.851 | -1.13428 |
| 46.05 | 59.031 | -1.48704 |
| 57.58 | 56.402 | -1.83109 |




$k_{enantiomerisation} = 2.69.10^{-4}\ s^{-1}$ (25°C, heptane / dichloromethane 80:20)
$\Delta G^{\neq} = 93.4\ kJ.mol^{-1}$ (25°C, heptane / dichloromethane 80:20)
$t_{1/2} = 21$ minutes (25°C, heptane / dichloromethane 80:20)

## NMR data of compound 11




Chemical Formula: $C_{84}H_{78}N_4Ni$
Molecular Weight: 1202.2694

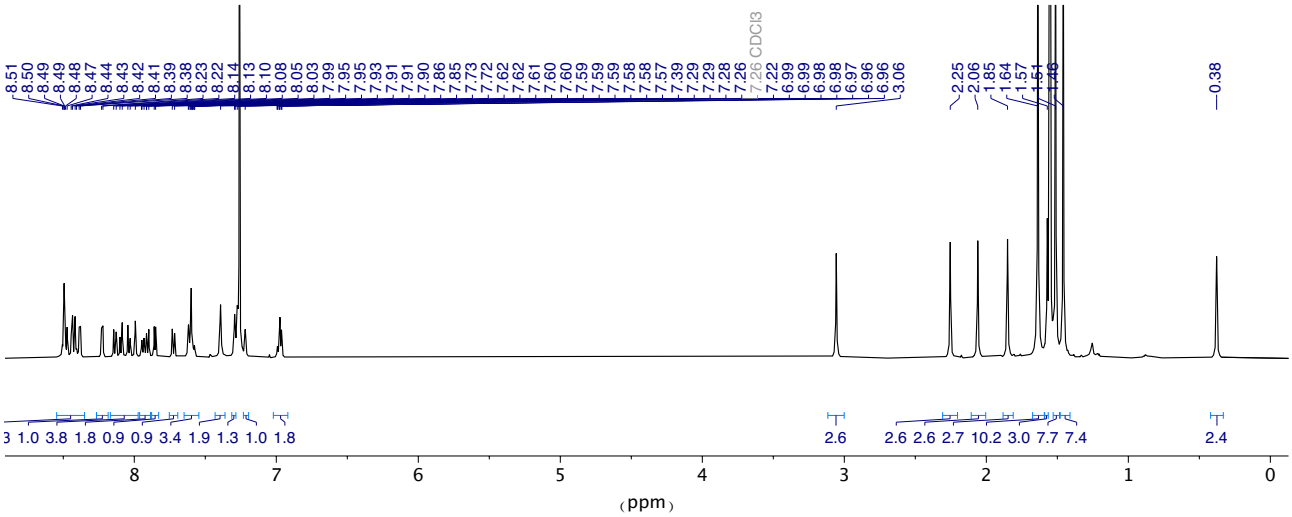



**Figure S10:** $^1$H NMR spectrum of compound **11** in $CDCl_3$ at 298 K (500 MHz).

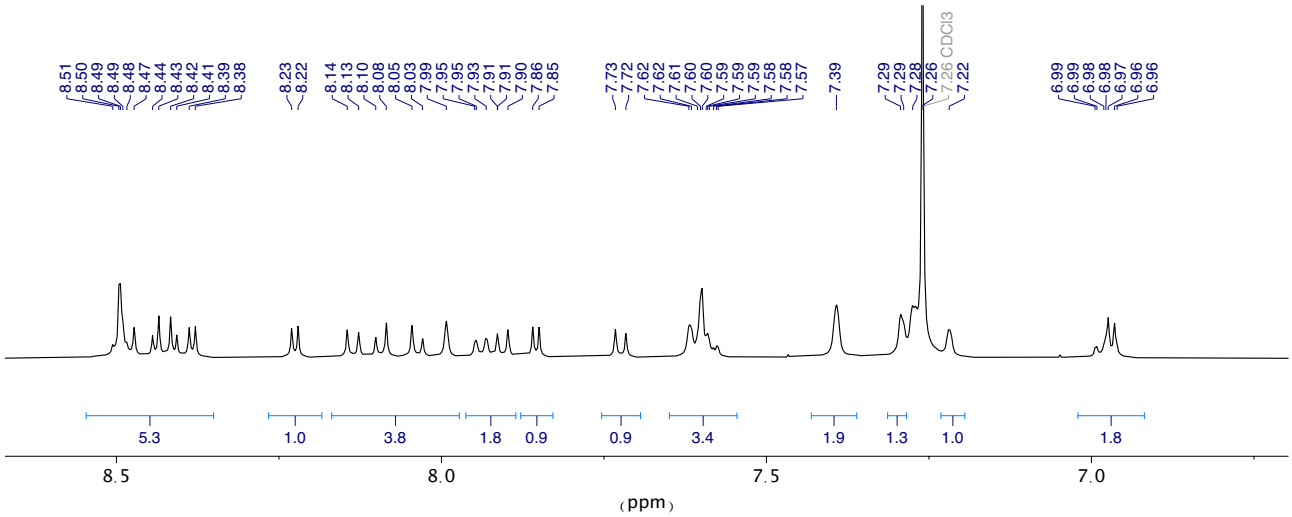



**Figure S11:** $^1$H NMR spectrum (aromatic area) of compound **11** in $CDCl_3$ at 298 K (500 MHz).

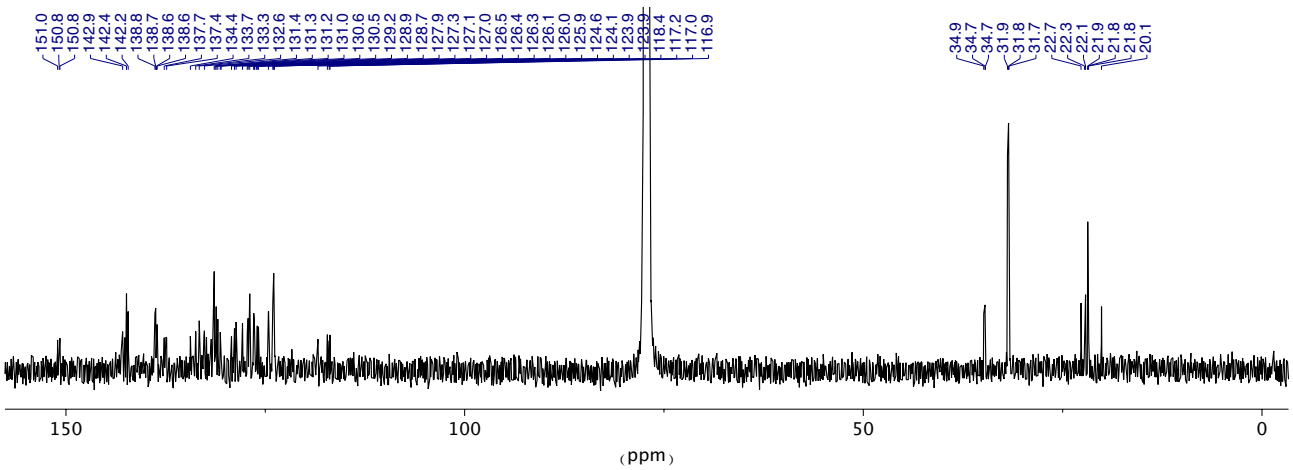



**Figure S12:** $^{13}C$ NMR spectrum of compound **11** in $CDCl_3$ at 298 K (126 MHz).

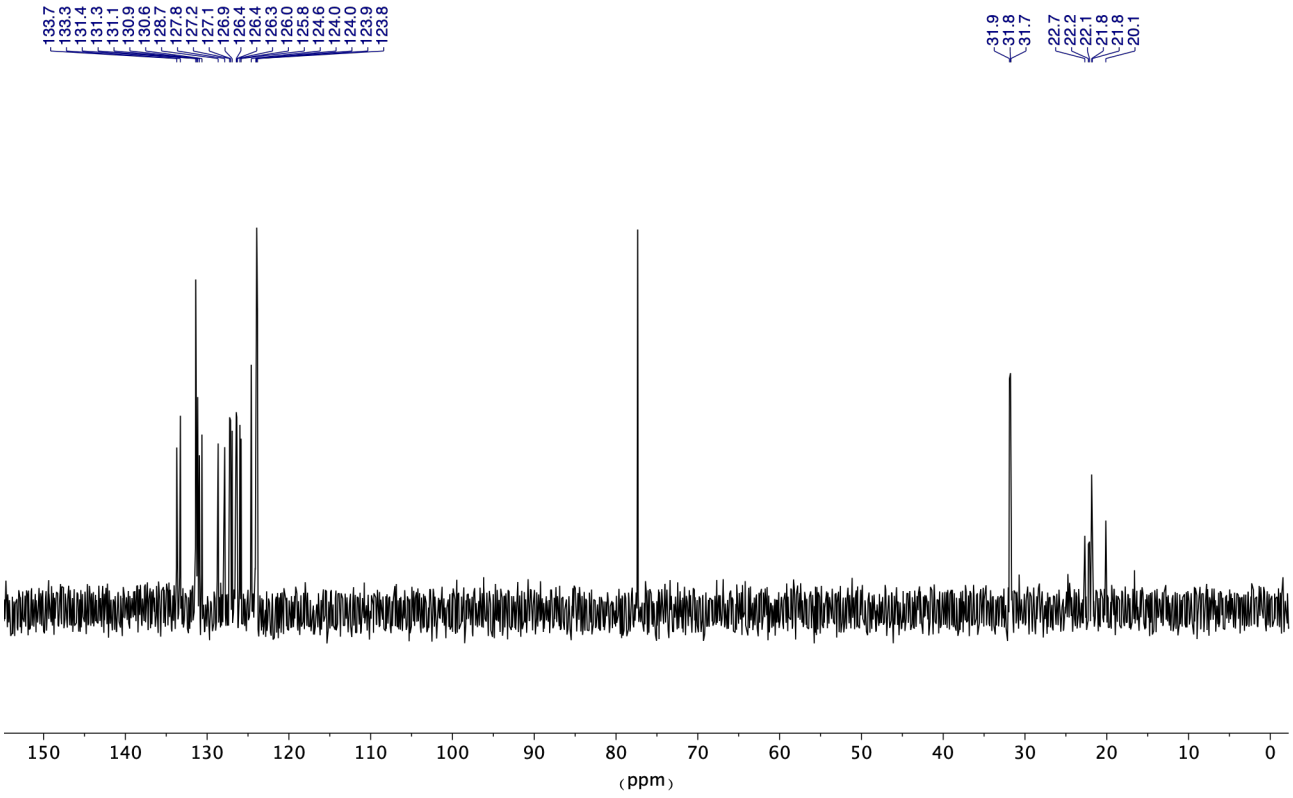



**Figure S13:** $^{13}C$ NMR DEPT spectrum of compound **11** in $CDCl_3$ at 298 K (126 MHz).

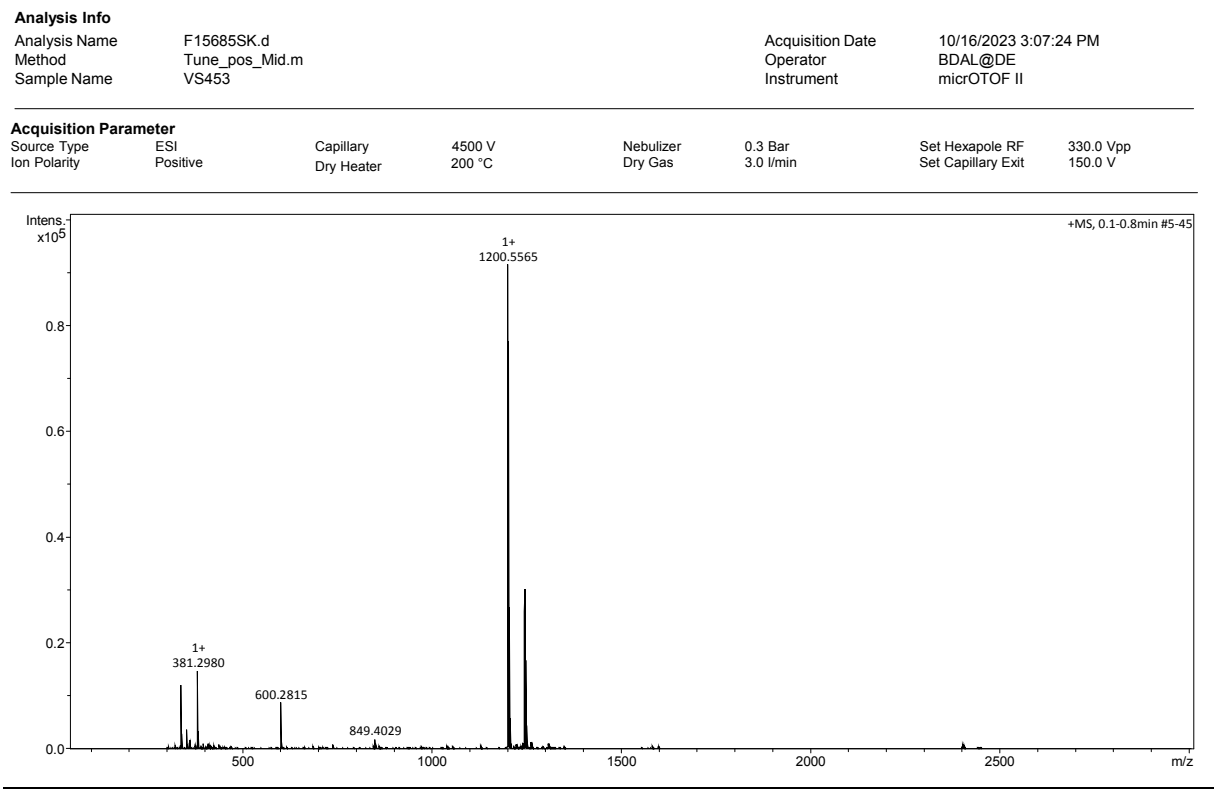



**Figure S14**. HRMS of compound **11** (the peak at 2400 corresponds to the assembly of a neutral molecule with the cationic molecule, at 600 the doubly charged molecule and at 1245 the addition of formate).

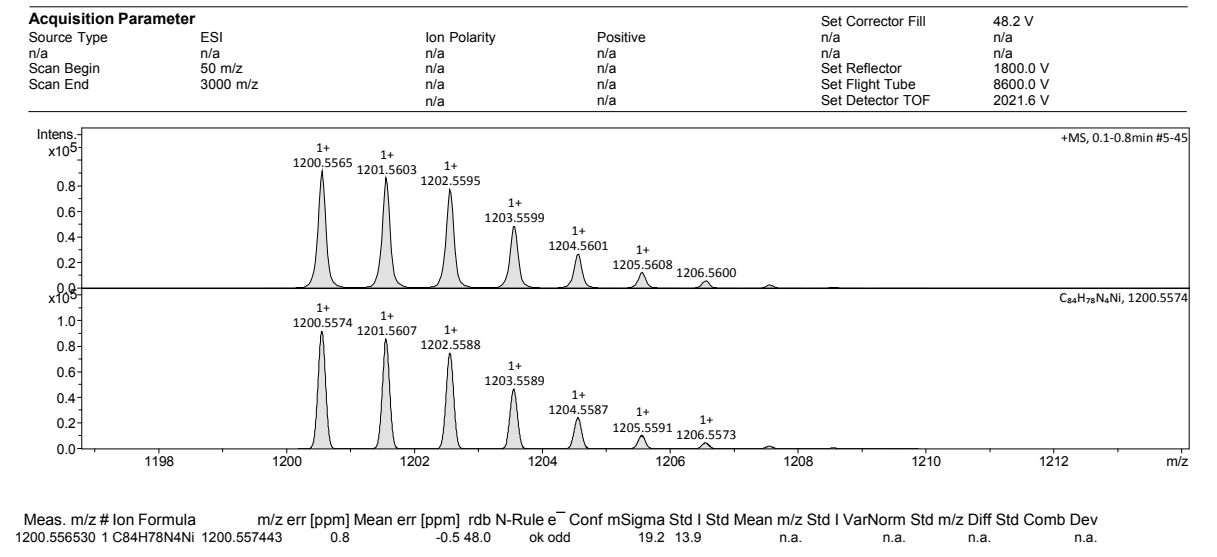
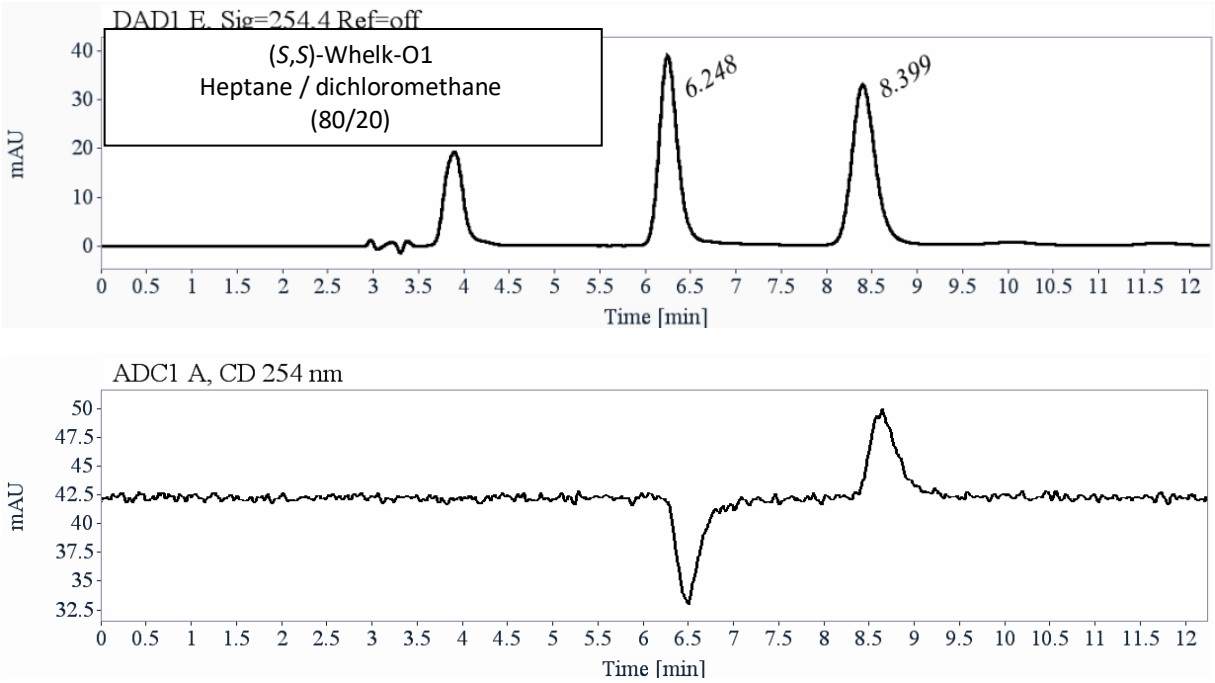



**Figure S15**. HRMS of compound **11** (top: experimental MS, bottom: simulation)

**Analytical chiral HPLC separation for compound 11**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **(*S*,*S*)-Whelk-O1** | Heptane / dichloromethane (80/20) | 6.25 (-) | 1.12 | 8.40 (+) | 1.85 | 1.65 | 5.15 |

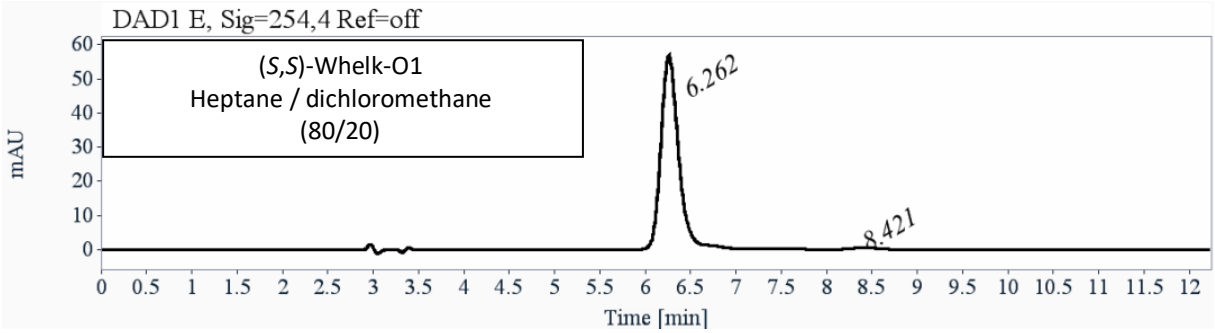



| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 6.25 | 575 | 49.14 | 1.12 | | |
| 8.40 | 595 | 50.86 | 1.85 | 1.65 | 5.15 |
| Sum | 1170 | 100.00 | | | |

**Preparative separation for compound 11**

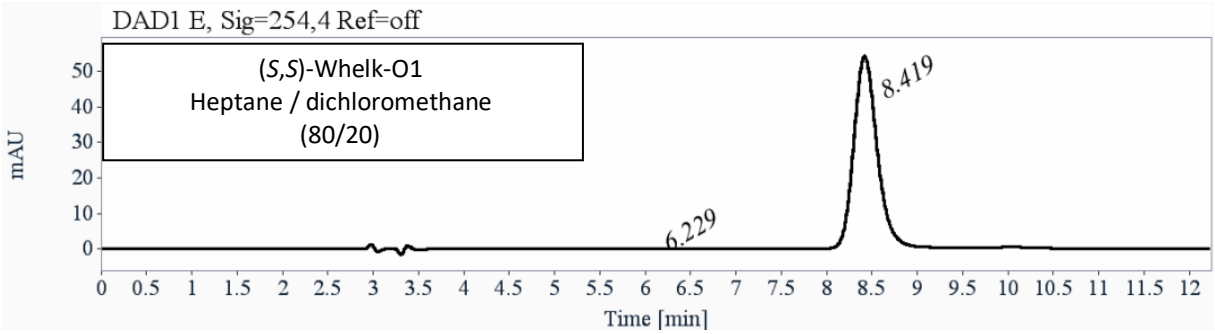
• Sample preparation: About 7.2 mg of compound **11** are dissolved in 1.8 mL of a mixture of dichloromethane and hexane (50/50).
• Chromatographic conditions: (*S*,*S*)-Whelk-O1 (250 x 10 mm), hexane / dichloromethane (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.
• Injections (stacked): 18 times 100 µL, every 9 minutes.

• First fraction: 1.6 mg of the first eluted enantiomer with ee > 97.5 %



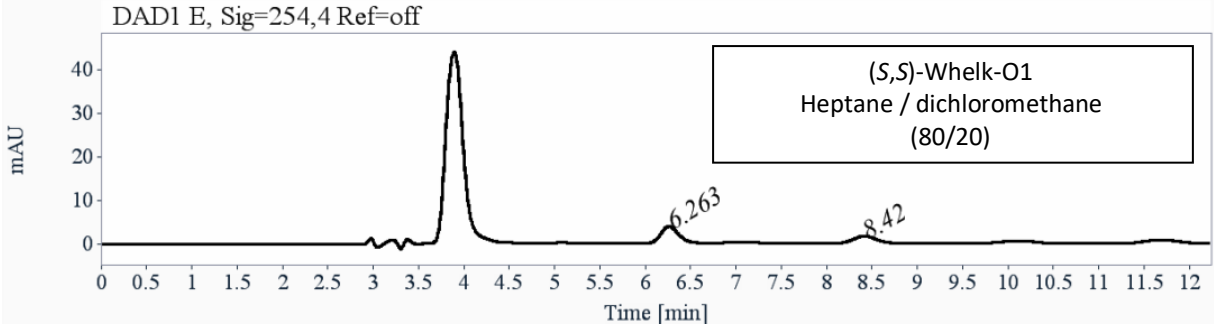

| RT [min] | Area | Area% |
|---|---|---|
| 6.26 | 792 | 98.95 |
| 8.42 | 8 | 1.05 |
| Sum | 800 | 100.00 |

• Second fraction: 1.7 mg of the second eluted enantiomer with ee > 99.5 %




| RT [min] | Area | Area% |
|---|---|---|
| 6.23 | 1 | 0.06 |
| 8.42 | 979 | 99.94 |
| Sum | 979 | 100.00 |

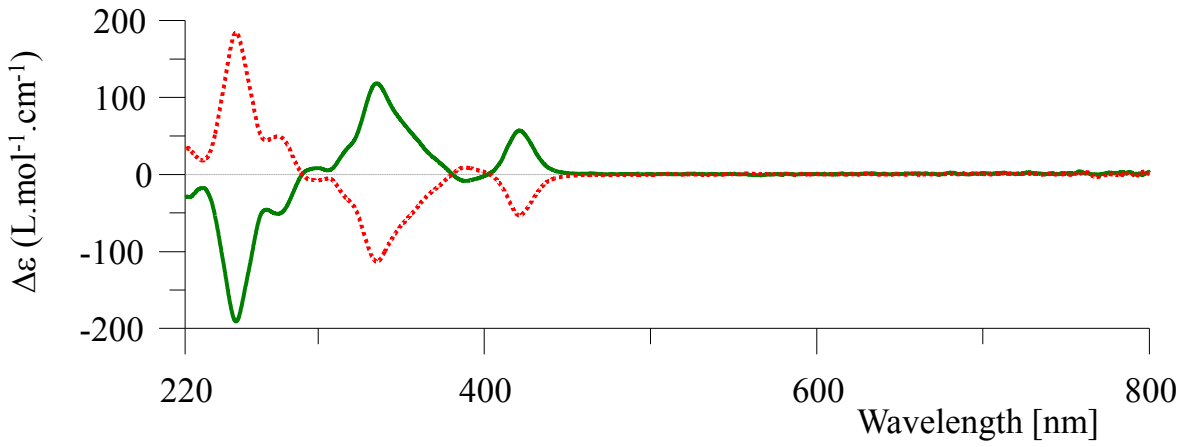
Intermediate: 3.9 mg

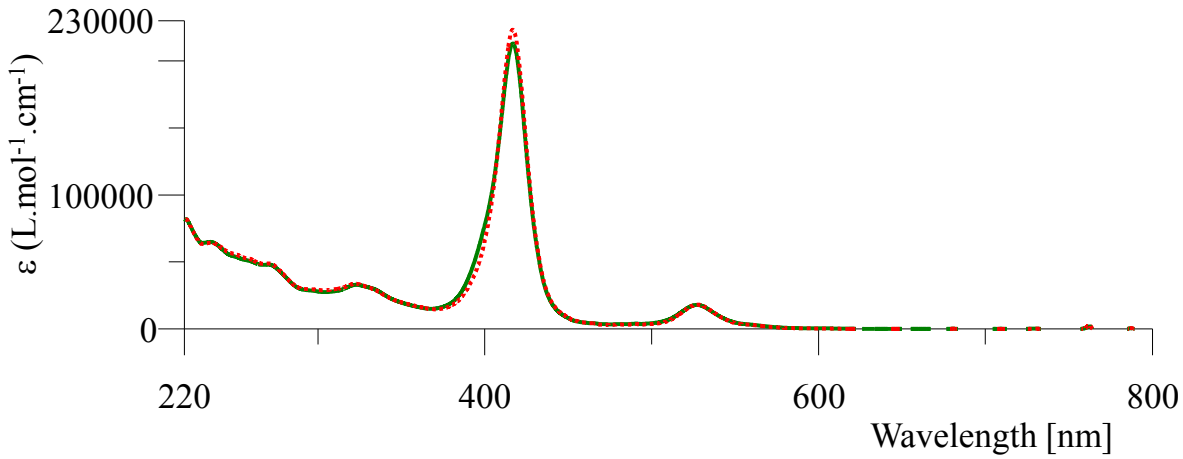


**Electronic Circular Dichroism - compound 11**

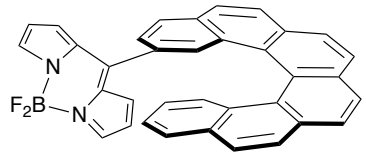
ECD and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at 25.0 ± 0.2°C. A CD quartz cell of 1 mm of optical pathlength was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted.
The baseline was always measured for the same solvent and in the same cell as the samples.
The spectra are presented without smoothing and further data processing.

Compound **11**, first eluted on (*S*,*S*)-Whelk-O1: green solid line, concentration = 0.073 mmol.L$^{-1}$ in dichloromethane.
Compound **11**, second eluted on (*S*,*S*)-Whelk-O1: red dotted line, concentration = 0.076 mmol.L$^{-1}$ in dichloromethane.
Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.



**NMR and MS data of compound 12**




Chemical Formula: $C_{35}H_{21}BF_2N_2$
Molecular Weight: 518,37

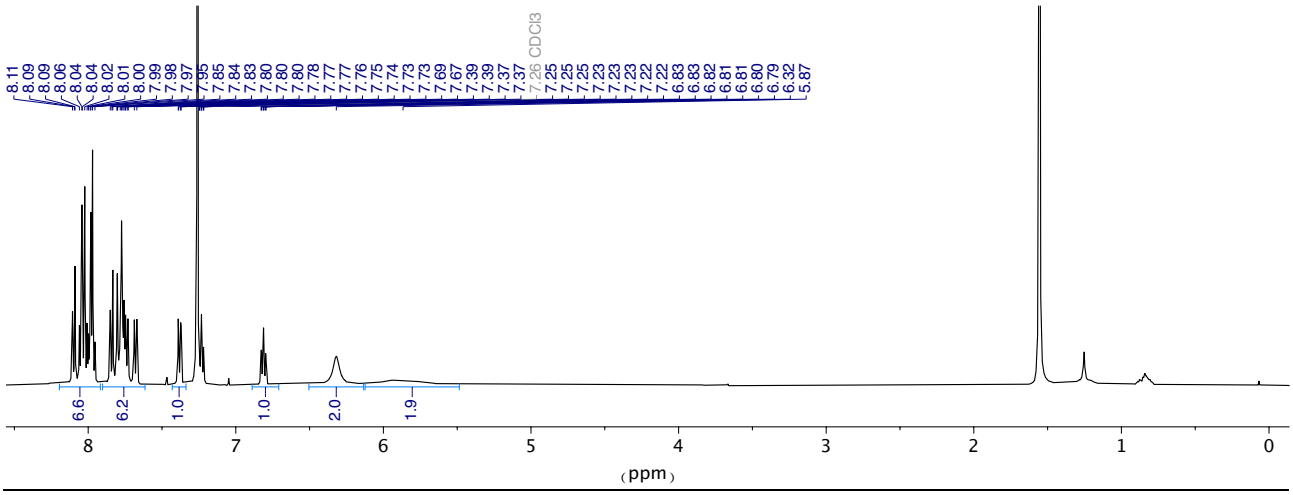



**Figure S16:** $^1$H NMR spectrum of compound **12** in $CDCl_3$ at 298 K (500 MHz).

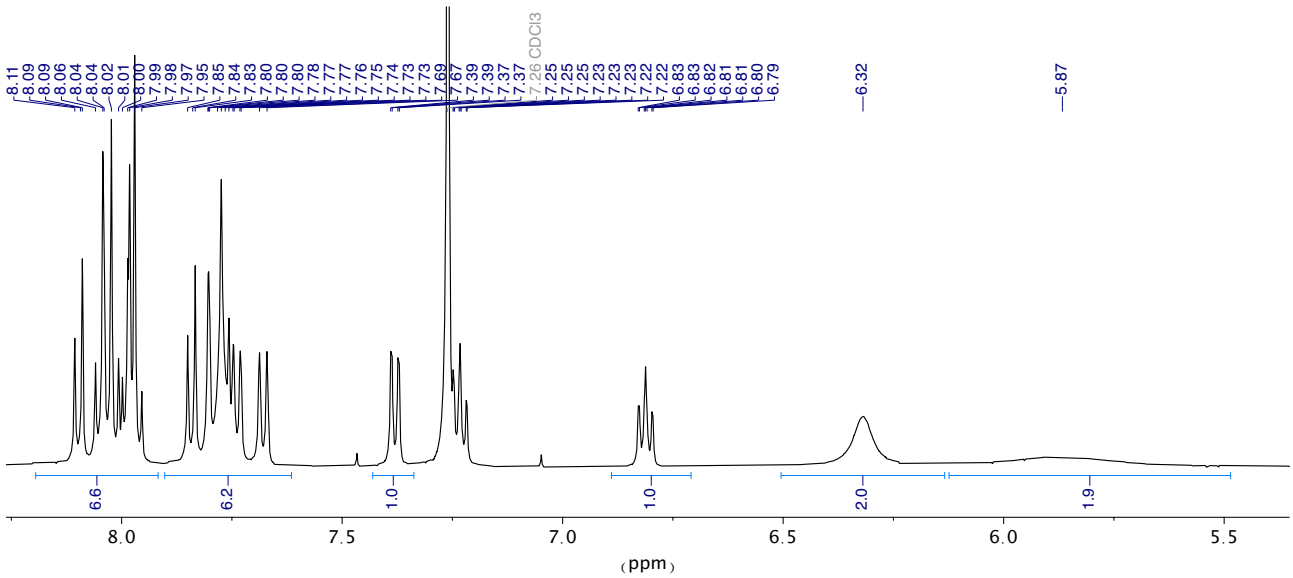



**Figure S17:** $^1$H NMR spectrum (aromatic area) of compound **12** in $CDCl_3$ at 298 K (500 MHz).

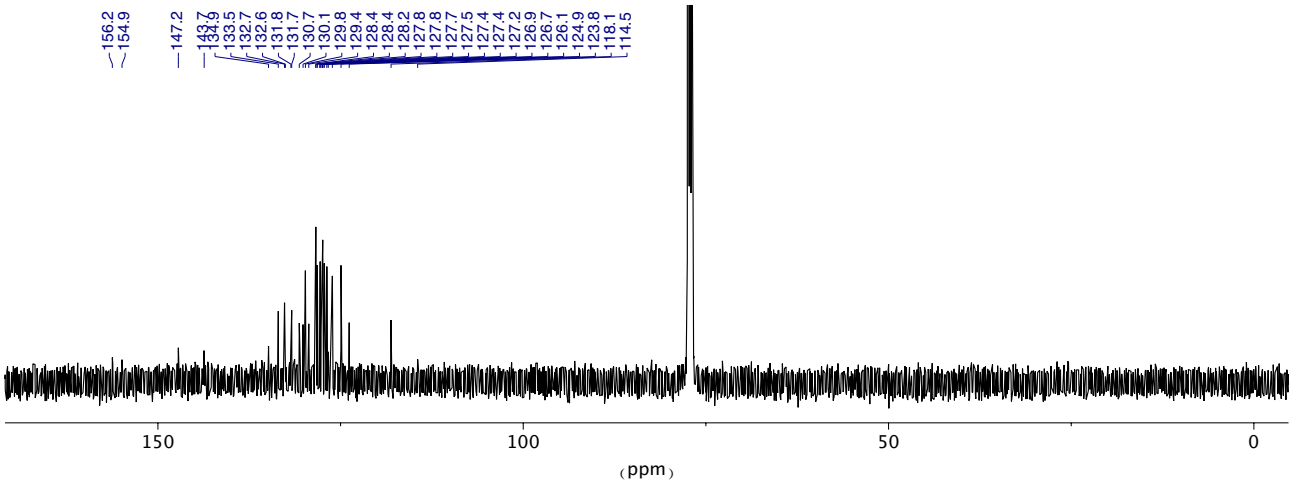



**Figure S18:** $^{13}C$ NMR spectrum of compound **12** in $CDCl_3$ at 298 K (126 MHz).

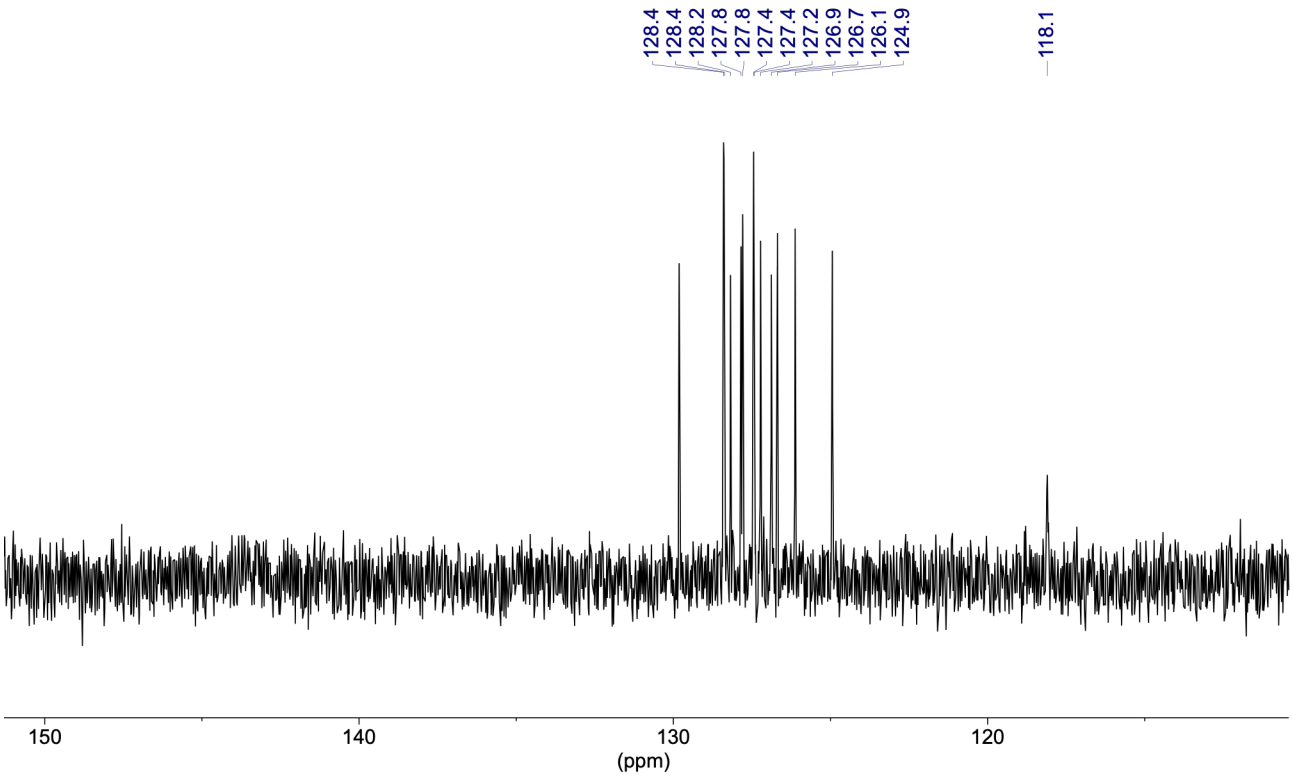



**Figure S19:** $^{13}C$ NMR DEPT spectrum of compound **12** in $CDCl_3$ at 298 K (126 MHz).

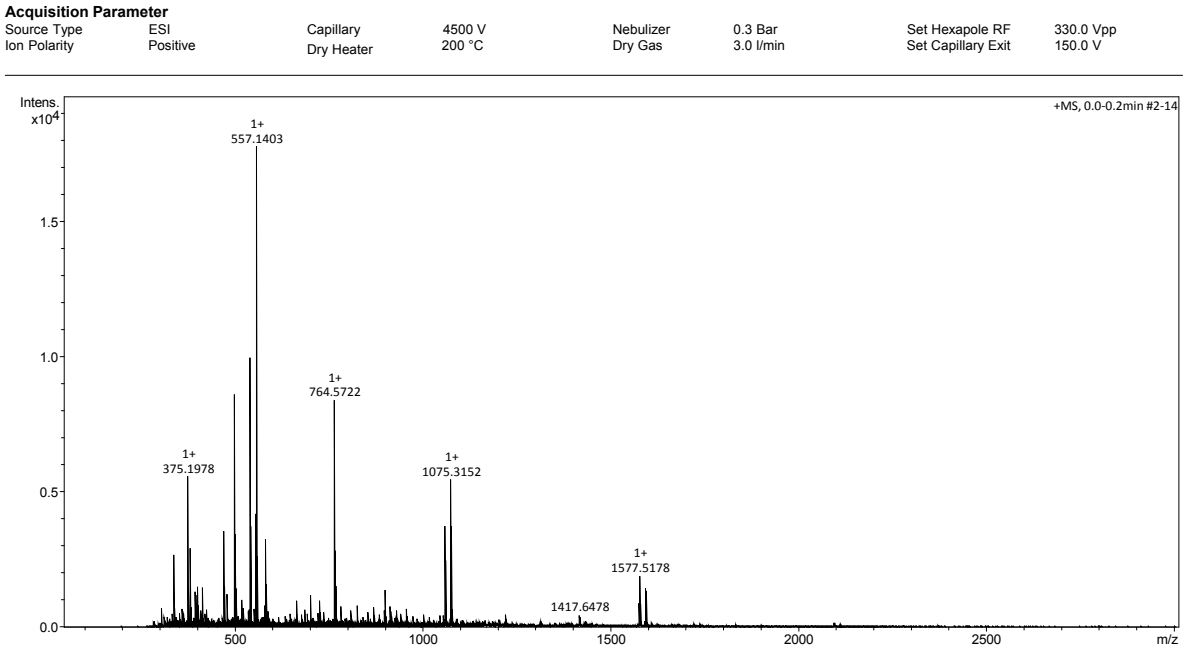



**Figure S20:** HRMS (ESI positive) of compound **12**. (The "molecular peak" at 557.14 correspond to Compound **12** + $K^+$).

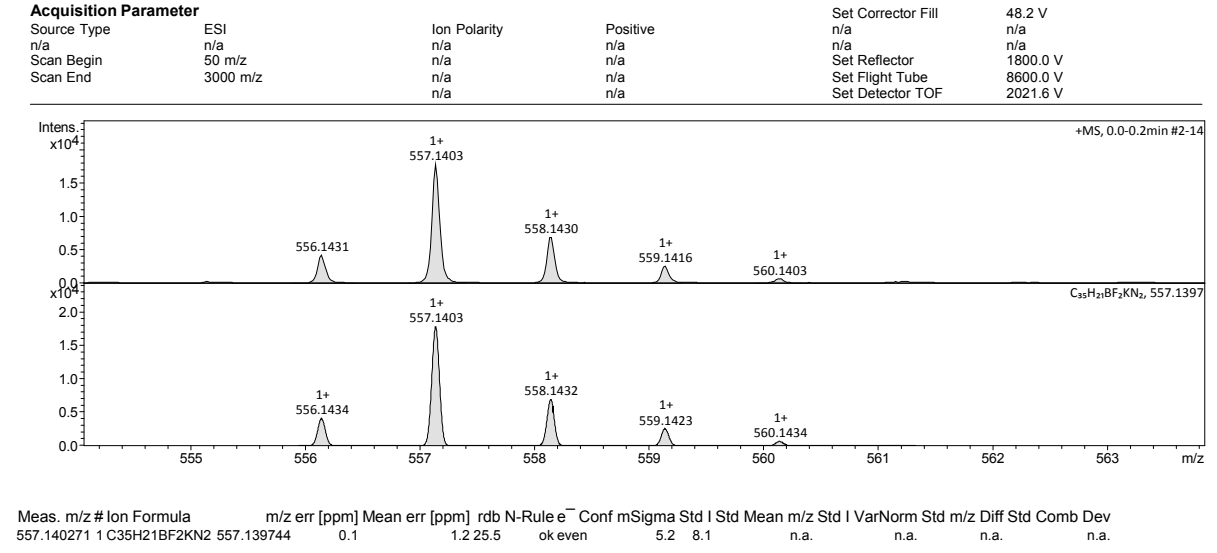
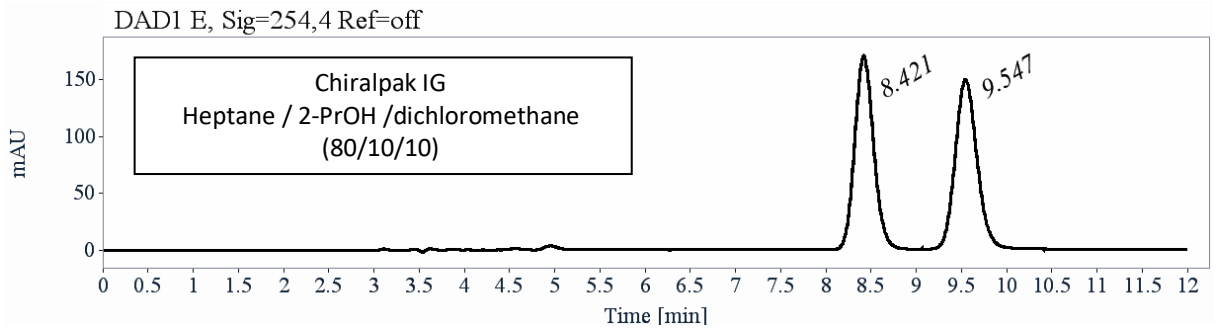


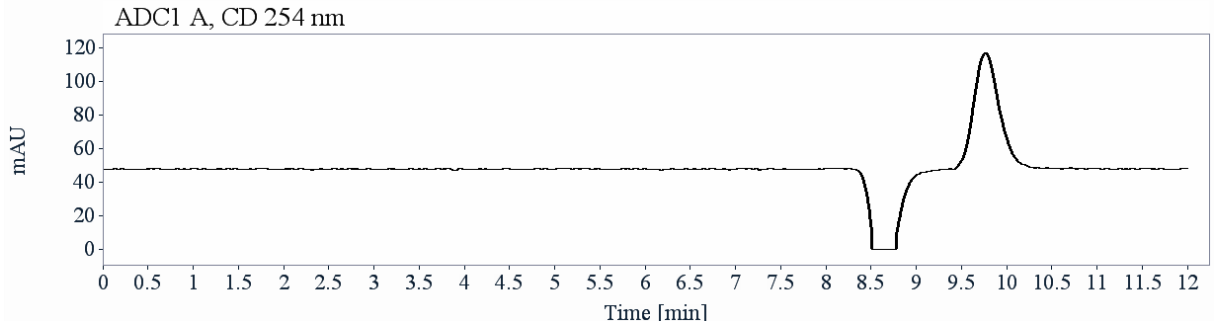

**Figure S21**. HRMS of compound **12** (top: experimental MS, bottom: simulation)

**Analytical chiral HPLC separation for compound 12**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **Chiralpak IG** | Heptane / 2-PrOH / dichloromethane (80/10/10) | 8.42 (-) | 1.85 | 9.55 (+) | 2.24 | 1.21 | 2.74 |




| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 8.42 | 2481 | 49.71 | 1.85 | | |
| 9.55 | 2510 | 50.29 | 2.24 | 1.21 | 2.74 |
| Sum | 4991 | 100.00 | | | |

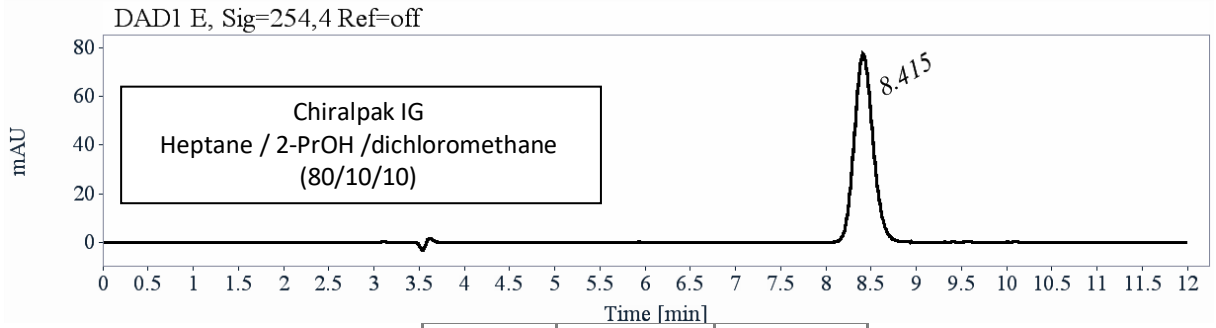
**Preparative separation for compound 12**

• Sample preparation: About 4.9 mg of compound **VS458** are dissolved in 3.5 mL of a mixture of dichloromethane and hexane (70/30).

• Chromatographic conditions: Chiralpak IG (250 x 10 mm), hexane / 2-PrOH / dichloromethane (80/10/10) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.

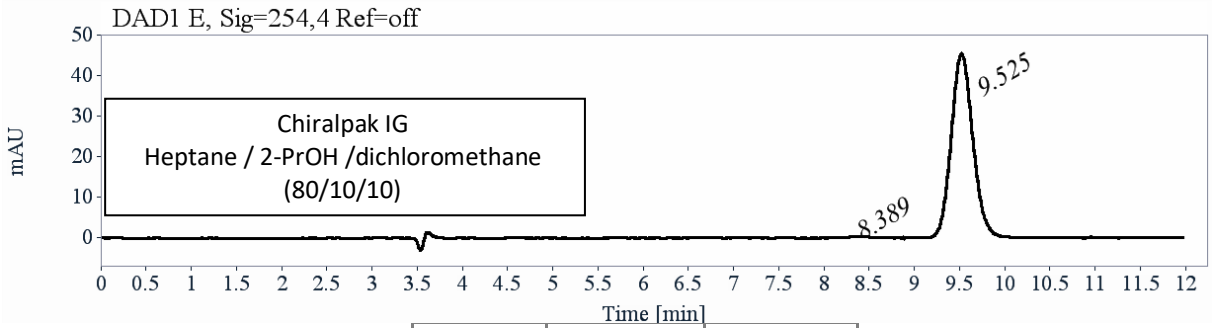
• Injections (stacked): 43 times 80 µL, every 3 minutes.

• First fraction: 1.5 mg of the first eluted enantiomer with ee > 99.5 %



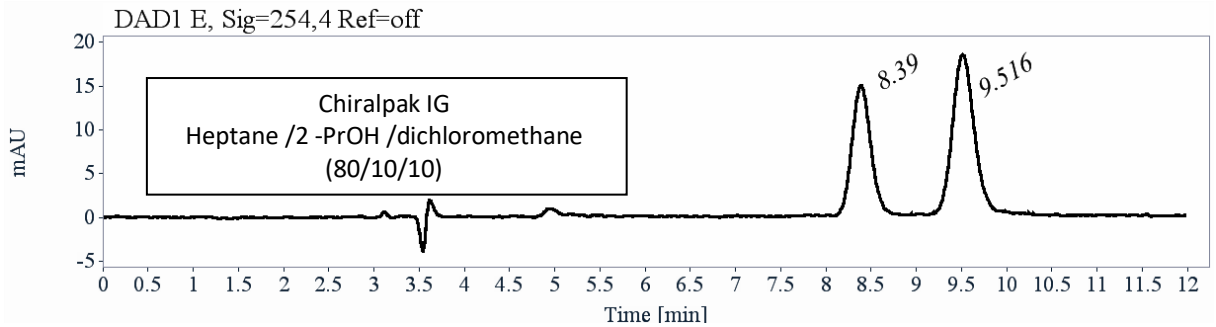

| RT [min] | Area | Area% |
|---|---|---|
| 8.41 | 1123 | 100.00 |
| Sum | 1123 | 100.00 |

• Second fraction: 1.7 mg of the second eluted enantiomer with ee > 99.5 %




| RT [min] | Area | Area% |
|---|---|---|
| 8.39 | 1 | 0.15 |
| 9.53 | 765 | 99.85 |
| Sum | 766 | 100.00 |

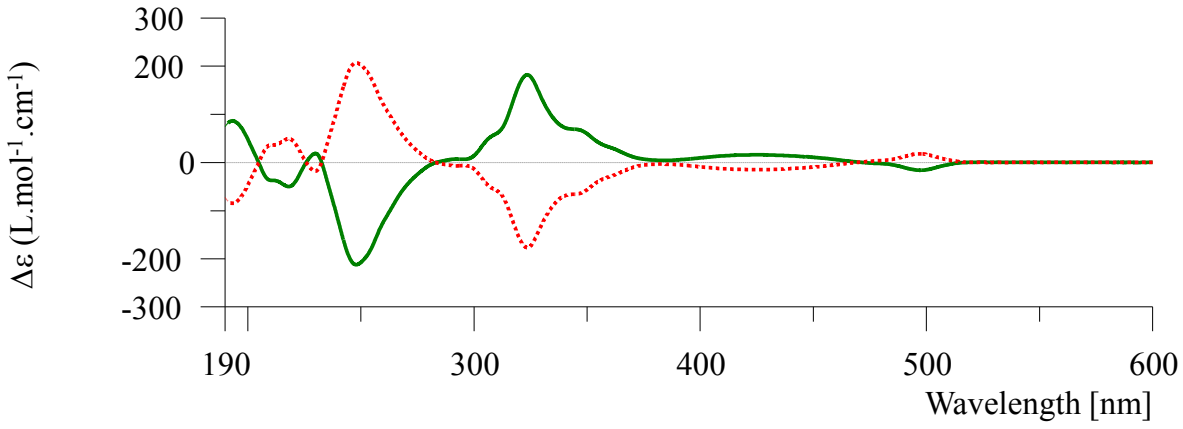
Intermediate: 1.2 mg

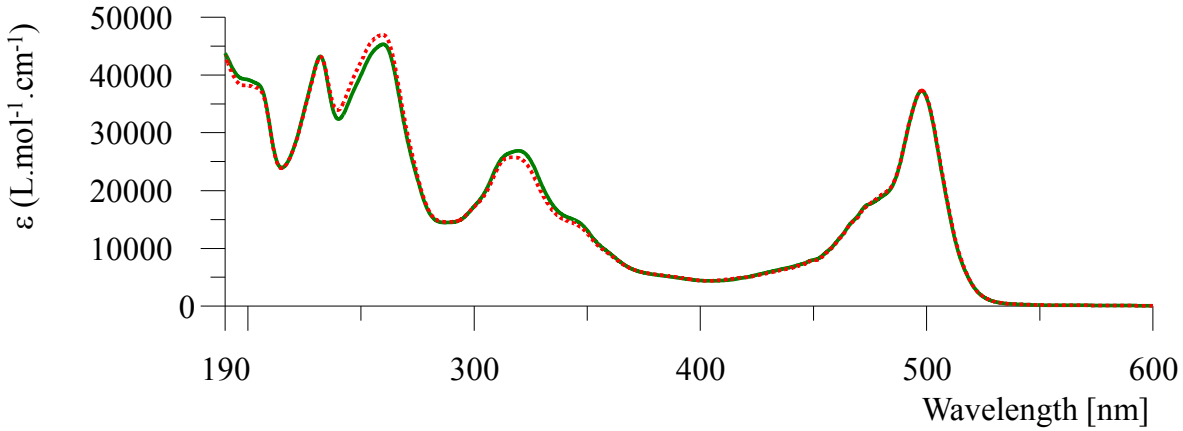


**Electronic Circular Dichroism - compound 12**

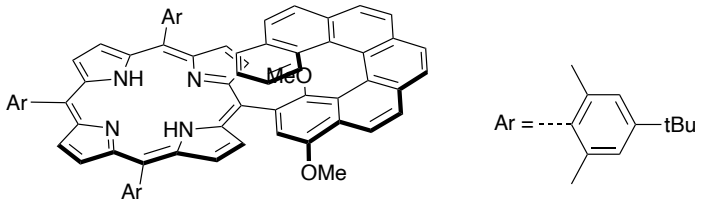
ECD and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at 25.0 ± 0.2°C. A CD quartz cell of 1 mm of optical pathlength was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted.
The baseline was always measured for the same solvent and in the same cell as the samples.
The spectra are presented without smoothing and further data processing.

Compound **12**, first eluted on Chiralpak IG: green solid line, concentration = 0.210 mmol.L$^{-1}$ in acetonitrile.
Compound **12**, second eluted on Chiralpak IG: red dotted line, concentration = 0.175 mmol.L$^{-1}$ in acetonitrile.
Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.



**NMR and MS data of compound 13**




Chemical Formula: $C_{84}H_{80}N_4O_2$
Molecular Weight: 1177.5900

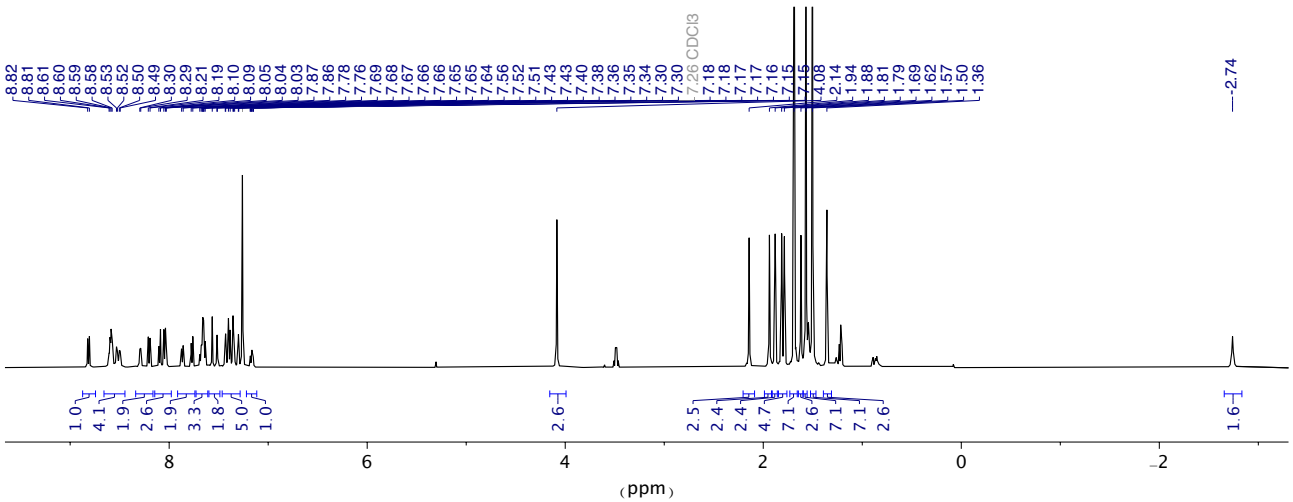



**Figure S22:** $^1$H NMR spectrum of compound **13** in $CDCl_3$ at 298 K, residual ether present (500 MHz).

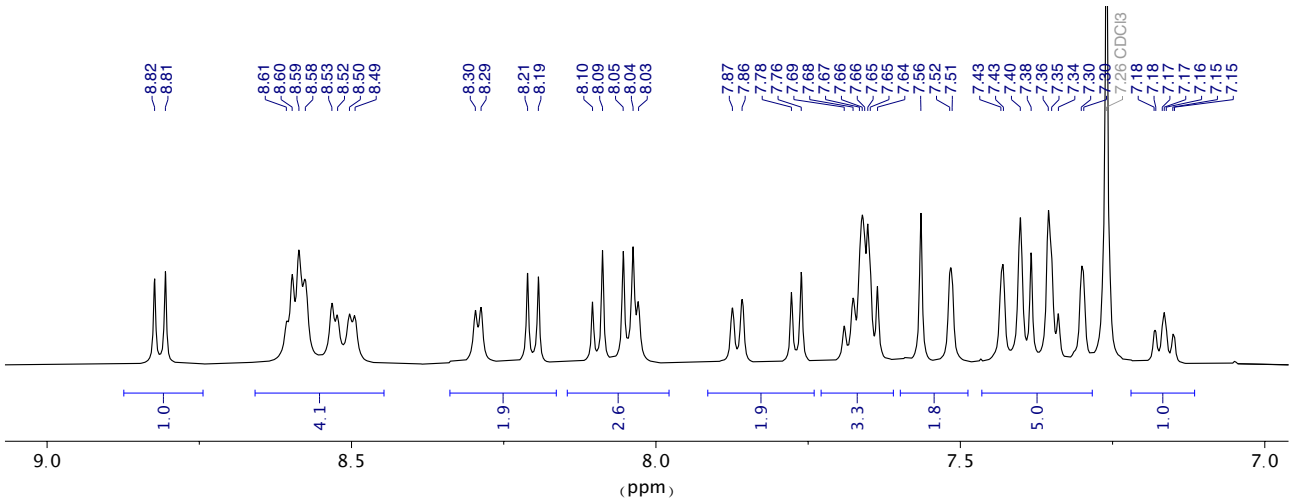



**Figure S23:** $^1$H NMR spectrum (aromatic area) of compound **13** in $CDCl_3$ at 298 K (500 MHz).

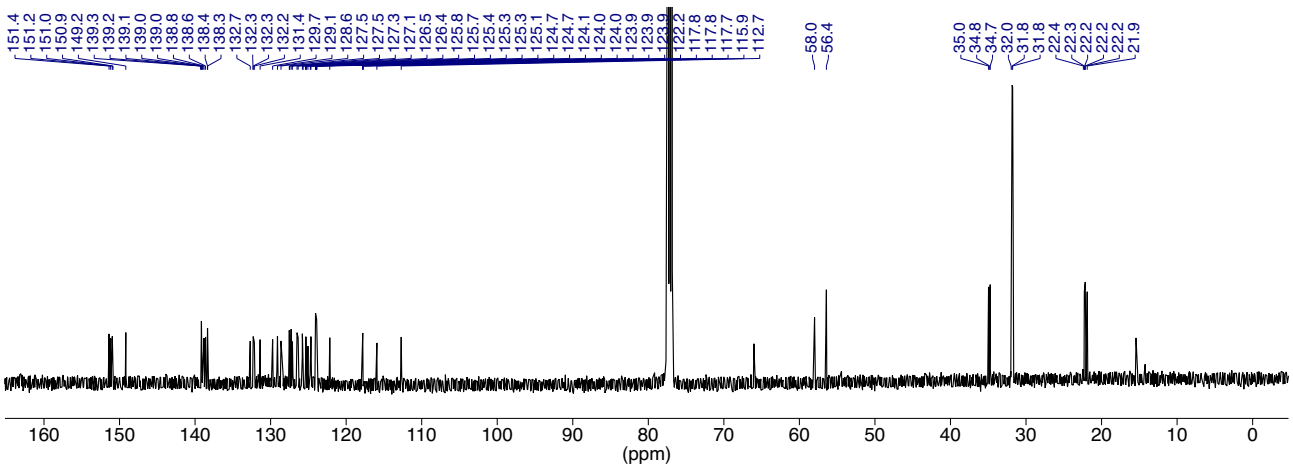



**Figure S24:** $^{13}C$ NMR spectrum of compound **13** in $CDCl_3$ at 298 K (126 MHz), residual ether present.

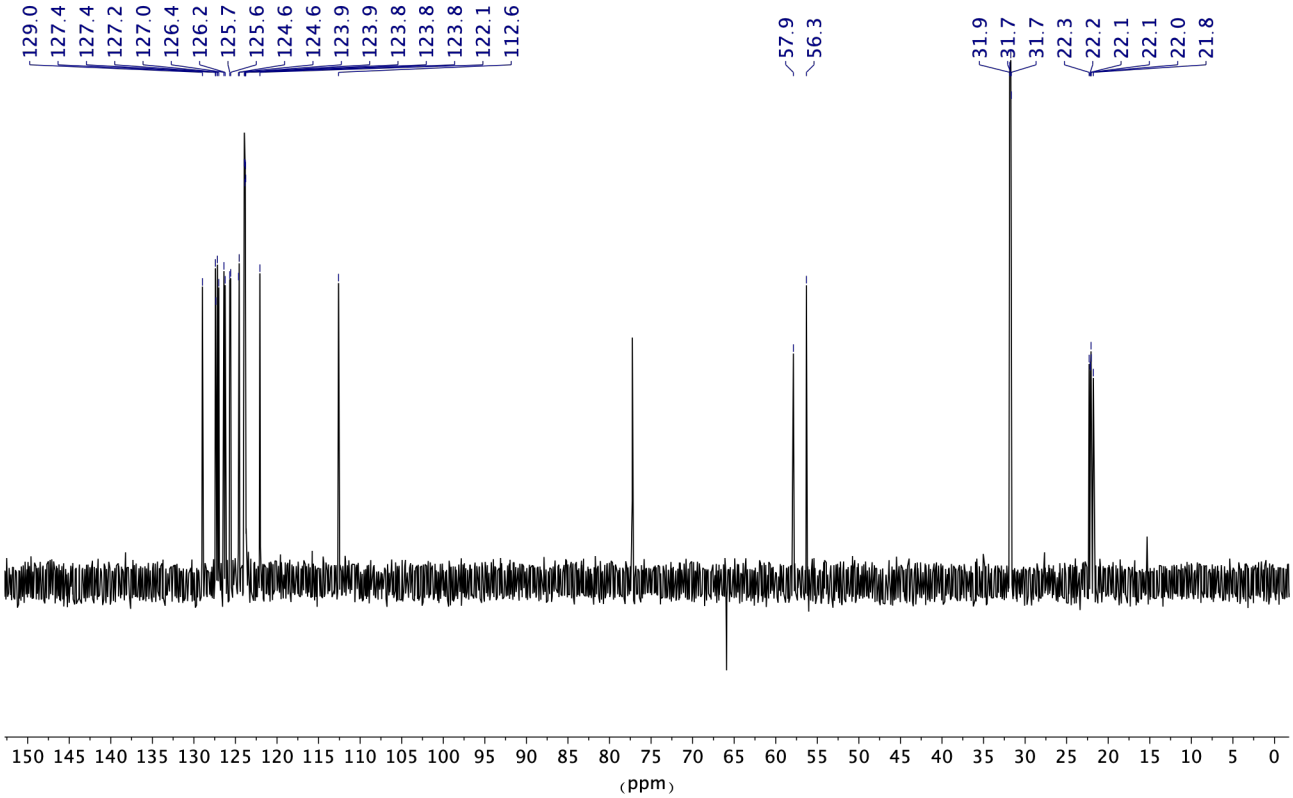



**Figure S25:** $^{13}C$ NMR DEPT spectrum of compound **13** in $CDCl_3$ at 298 K (126 MHz), residual ether present.

**Acquisition Parameter**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Source Type | ESI | Capillary | 4500 V | Nebulizer | 0.3 Bar | Set Hexapole RF | 330.0 Vpp |
| Ion Polarity | Positive | Dry Heater | 200 °C | Dry Gas | 3.0 l/min | Set Capillary Exit | 250.0 V |

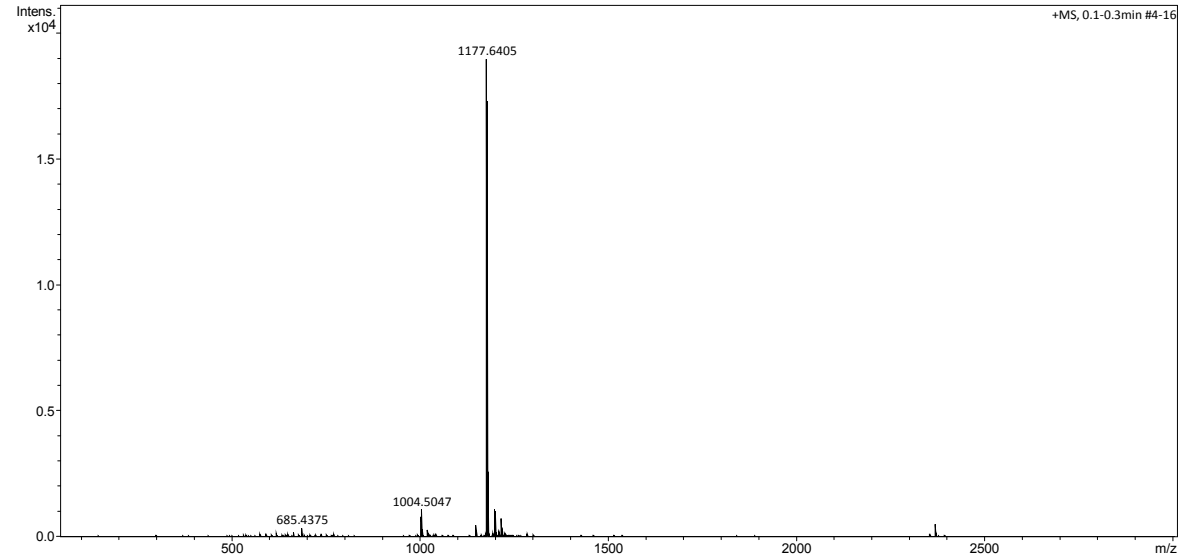
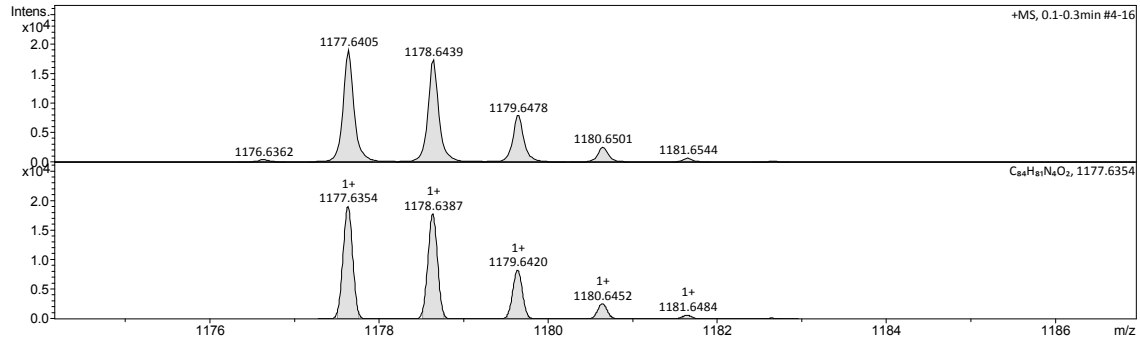



**Figure S26.** HRMS of compound **13**.

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Corrector Fill | 52.4 V |
| n/a | n/a | n/a | n/a | n/a | n/a |
| Scan Begin | 50 m/z | n/a | n/a | Set Reflector | 1800.0 V |
| Scan End | 3000 m/z | n/a | n/a | Set Flight Tube | 8600.0 V |
| | | n/a | n/a | Set Detector TOF | 1985.0 V |



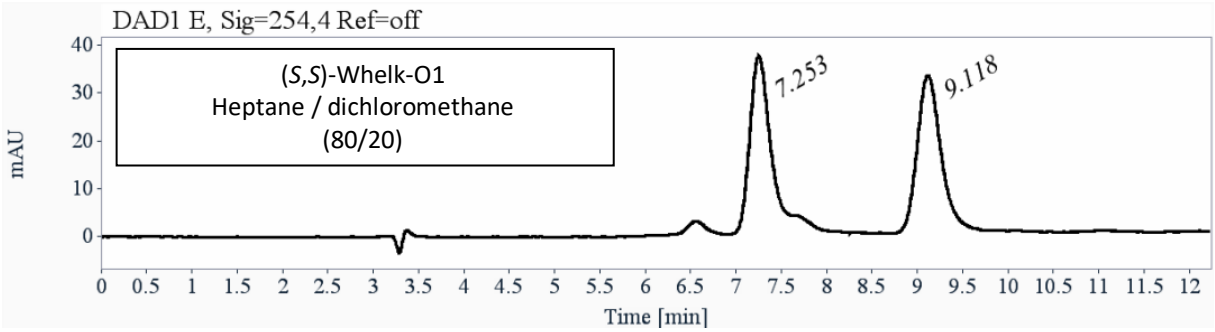

| Meas. m/z | # | Ion Formula | m/z err [ppm] | Mean err [ppm] | rdb | N-Rule | e⁻ Conf | mSigma | Std I | Std Mean m/z | Std I | VarNorm Std m/z | Diff Std Comb | Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1177.640480 | 1 | C84H81N4O2 | 1177.635404 | -4.3 | -4.5 | 46.5 | ok | even | 13.4 | 9.0 | n.a. | n.a. | n.a. | n.a. |

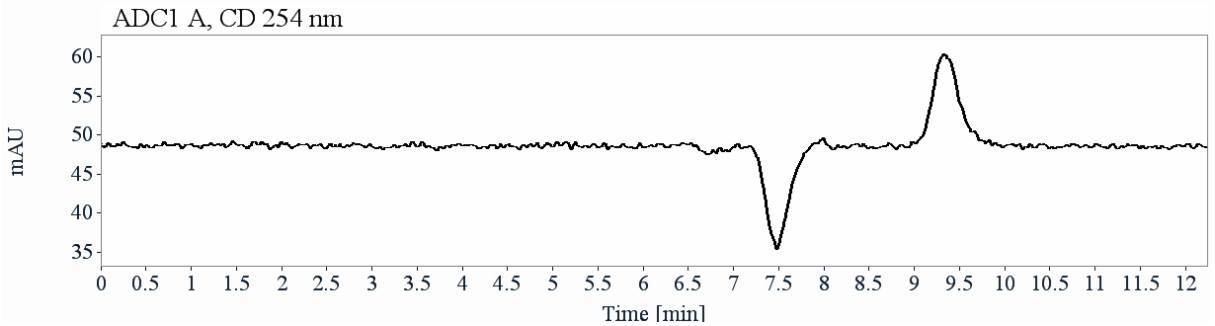
**Figure S27.** HRMS of compound **13** (top: experimental MS, bottom: simulation)

**Analytical chiral HPLC separation for compound 13**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **(*S*,*S*)-Whelk-O1** | Heptane / dichloromethane (80/20) | 7.25 (-) | 1.46 | 9.12 (+) | 2.09 | 1.43 | 4.27 |




| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 7.25 | 653 | 51.93 | 1.46 | | |
| 9.12 | 605 | 48.07 | 2.09 | 1.43 | 4.27 |
| Sum | 1258 | 100.00 | | | |

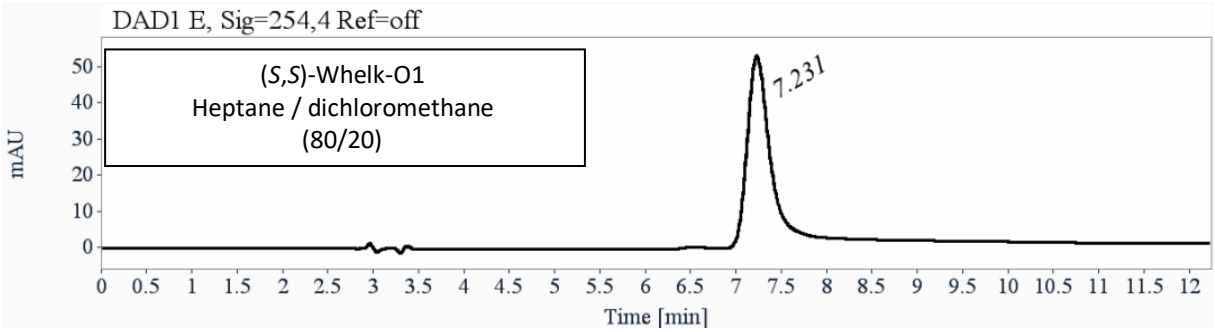
**Preparative separation for compound 13**

• Sample preparation: About 2.65 mg of compound **13** are dissolved in 1.8 mL of a mixture of dichloromethane and hexane (50/50).

• Chromatographic conditions: (*S*,*S*)-Whelk-O1 (250 x 10 mm), hexane / dichloromethane (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.

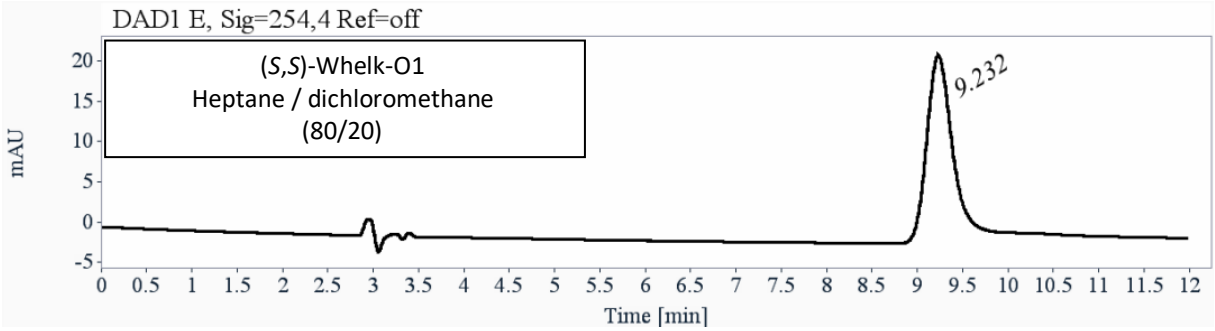
• Injections (stacked): 18 times 100 µL, every 10.2 minutes.

• First fraction: 0.8 mg of the first eluted enantiomer with ee > 99.5 %



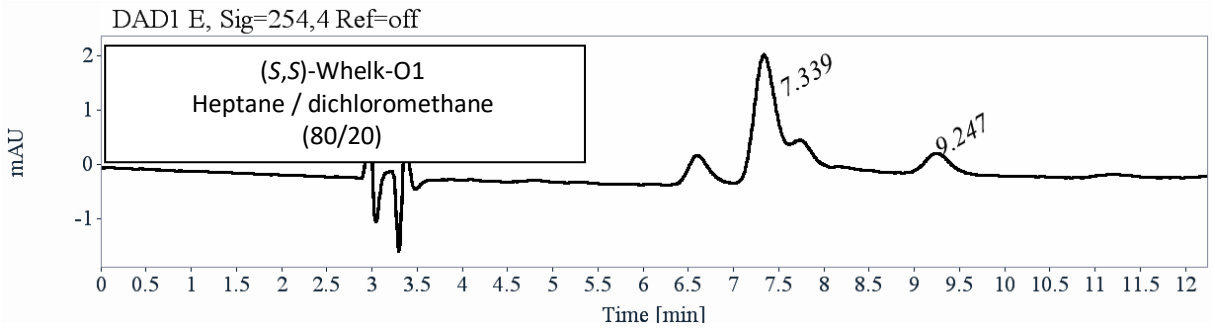

| RT [min] | Area | Area% |
|---|---|---|
| 7.23 | 1258 | 100.00 |
| Sum | 1258 | 100.00 |

• Second fraction: 0.9 mg of the second eluted enantiomer with ee > 99.5 %




| RT [min] | Area | Area% |
|---|---|---|
| 9.23 | 544 | 100.00 |
| Sum | 544 | 100.00 |

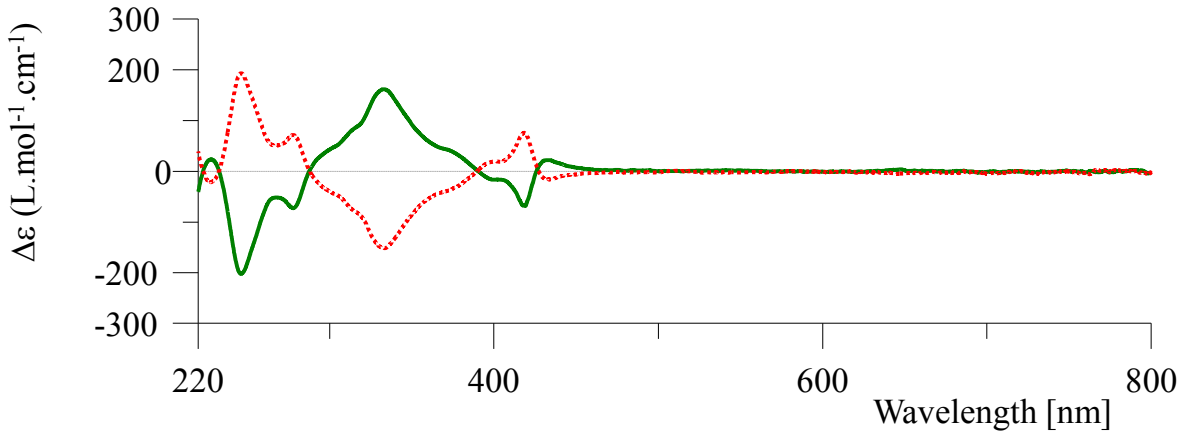
Intermediate: 0.3 mg

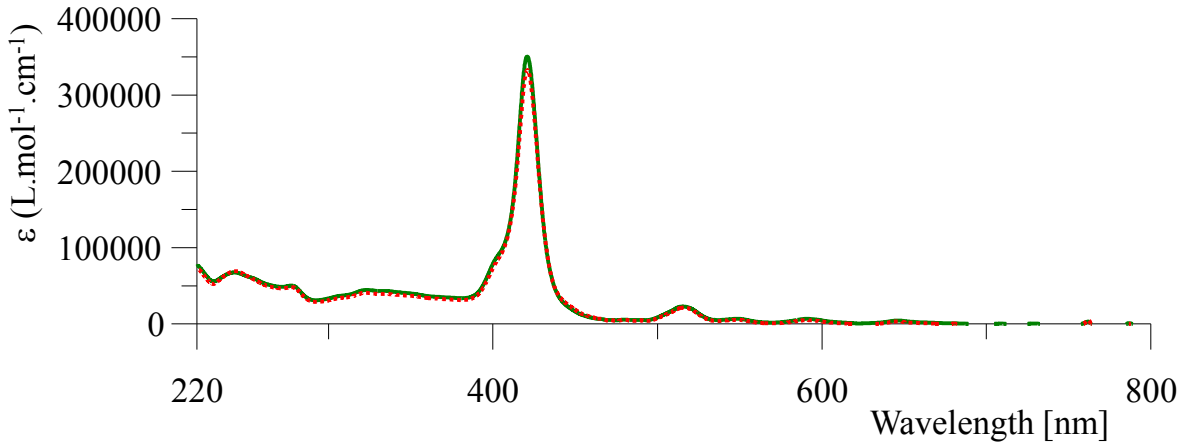


**Electronic Circular Dichroism - compound 13**

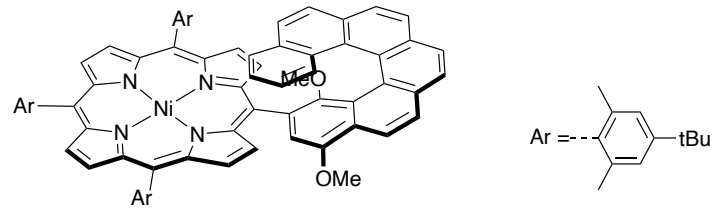
ECD and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at 25.0 ± 0.2°C. A CD quartz cell of 1 mm of optical pathlength was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted.
The baseline was always measured for the same solvent and in the same cell as the samples.
The spectra are presented without smoothing and further data processing.

Compound **13**, first eluted on (*S*,*S*)-Whelk-O1: green solid line, concentration = 0.057 mmol.L$^{-1}$ in dichloromethane.
Compound **13**, second eluted on (*S*,*S*)-Whelk-O1: red dotted line, concentration = 0.039 mmol.L$^{-1}$ in dichloromethane.
Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.



## NMR and MS data of compound 14




Chemical Formula: $C_{84}H_{78}N_4NiO_2$
Molecular Weight: 1234.2674

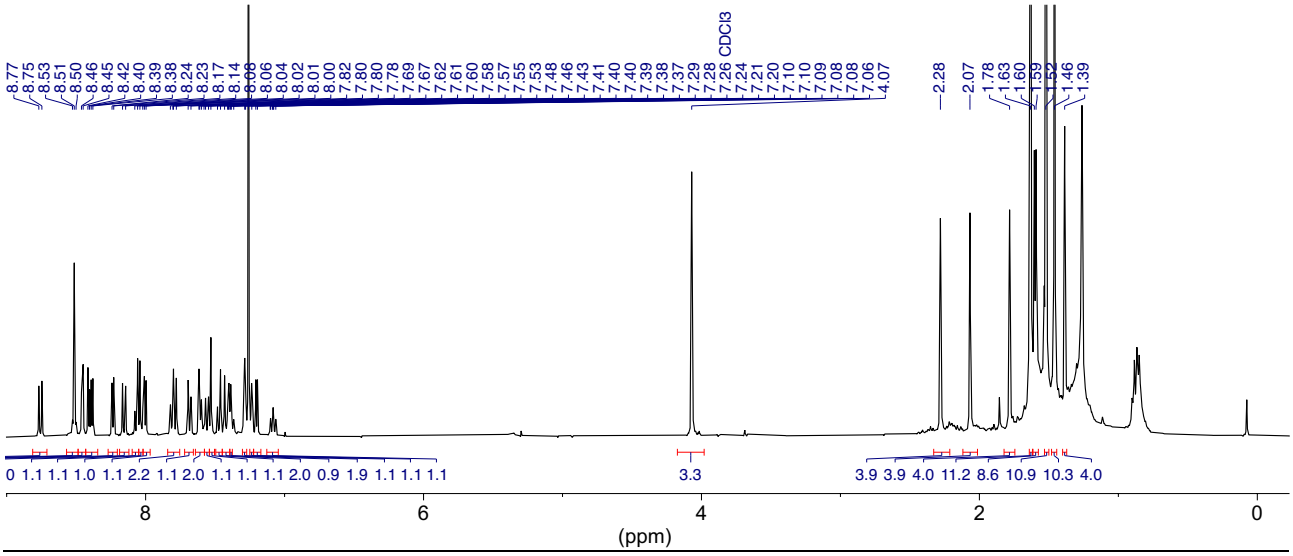



**Figure S28:** $^1$H NMR spectrum of compound **14** in $CDCl_3$ at 298 K (500 MHz).

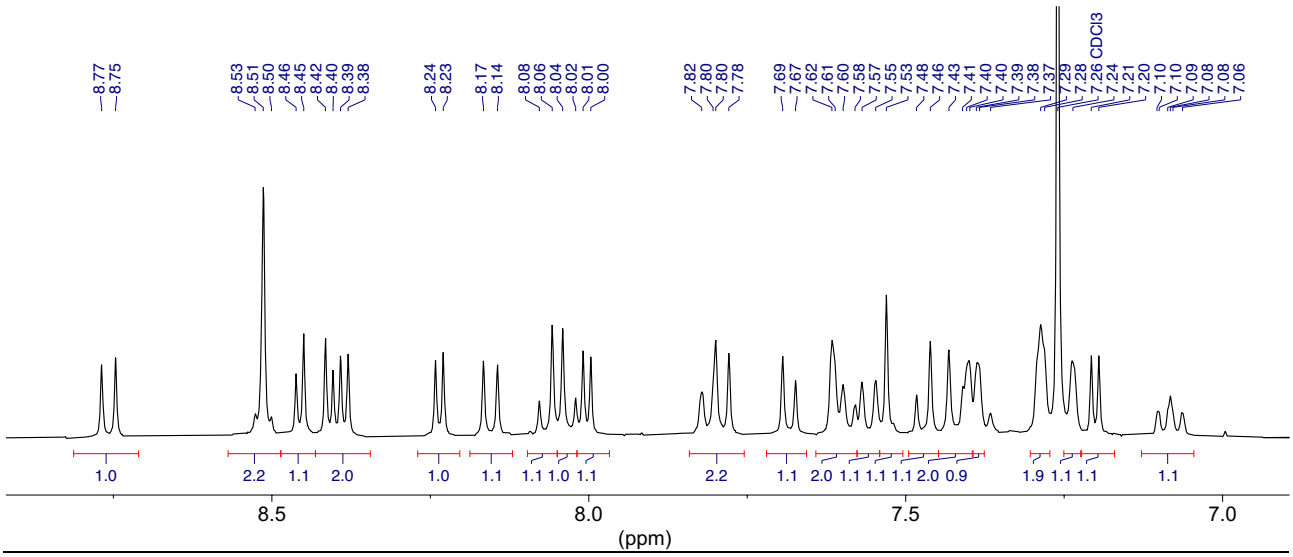



**Figure S29:** $^1$H NMR spectrum (aromatic area) of compound **14** in $CDCl_3$ at 298 K (500 MHz).

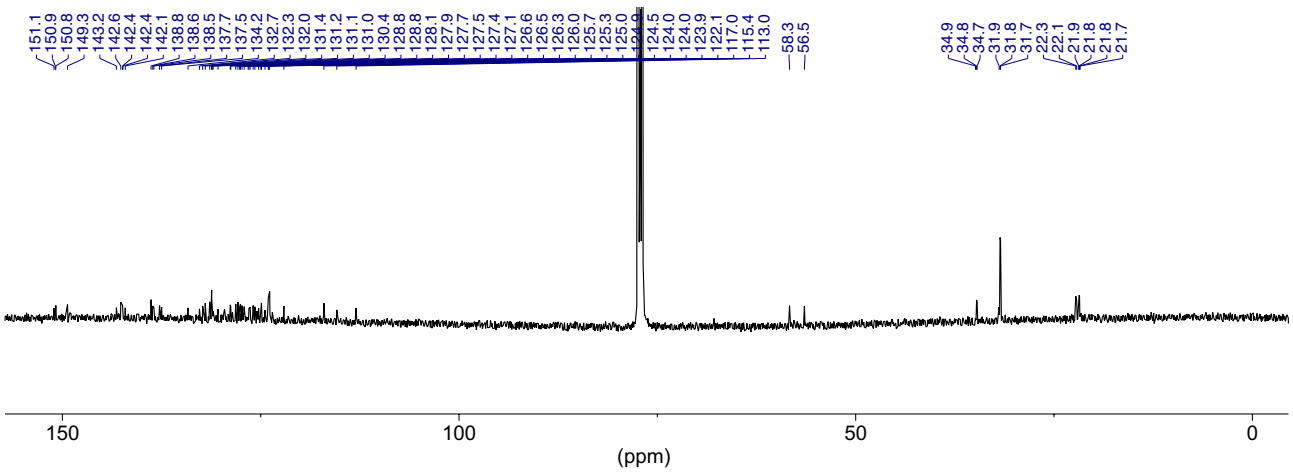



**Figure S30:** $^{13}C$ NMR spectrum of compound **14** in $CDCl_3$ at 298 K (126 MHz).

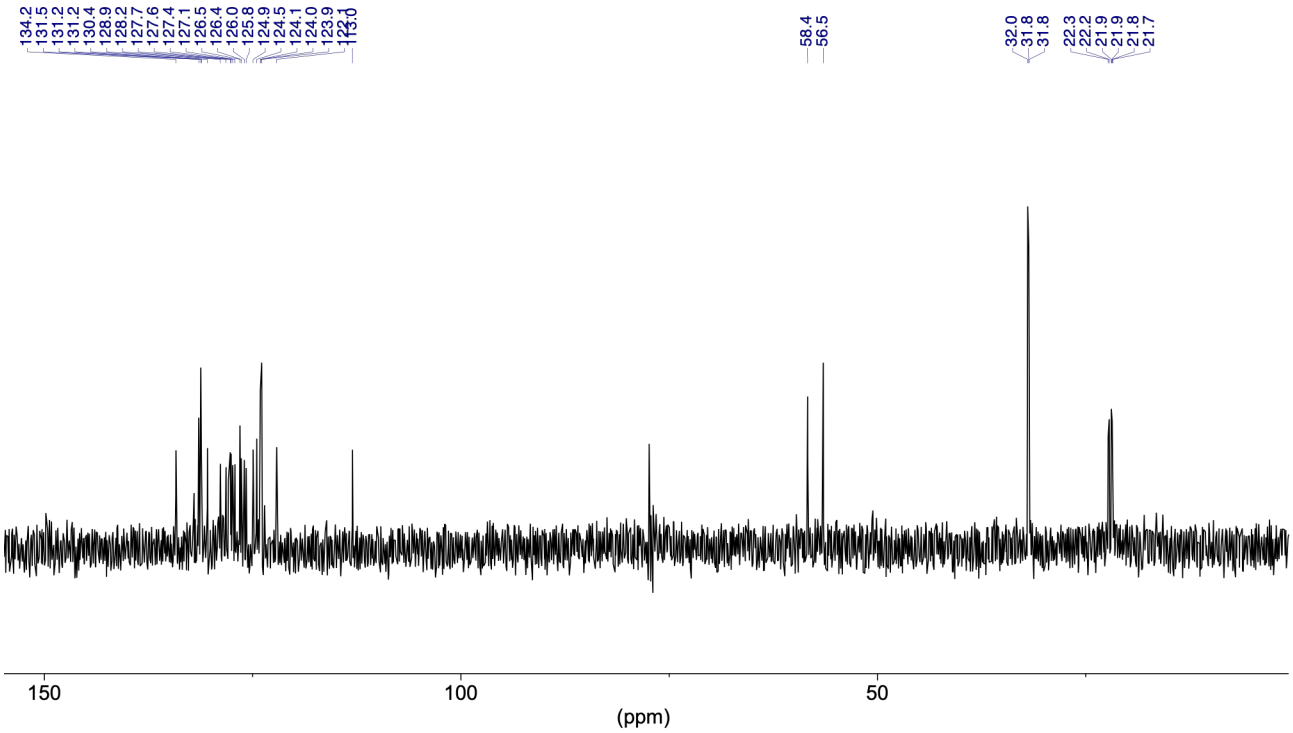



**Figure S31:** $^{13}C$ NMR DEPT spectrum of compound **14** in $CDCl_3$ at 298 K (126 MHz).

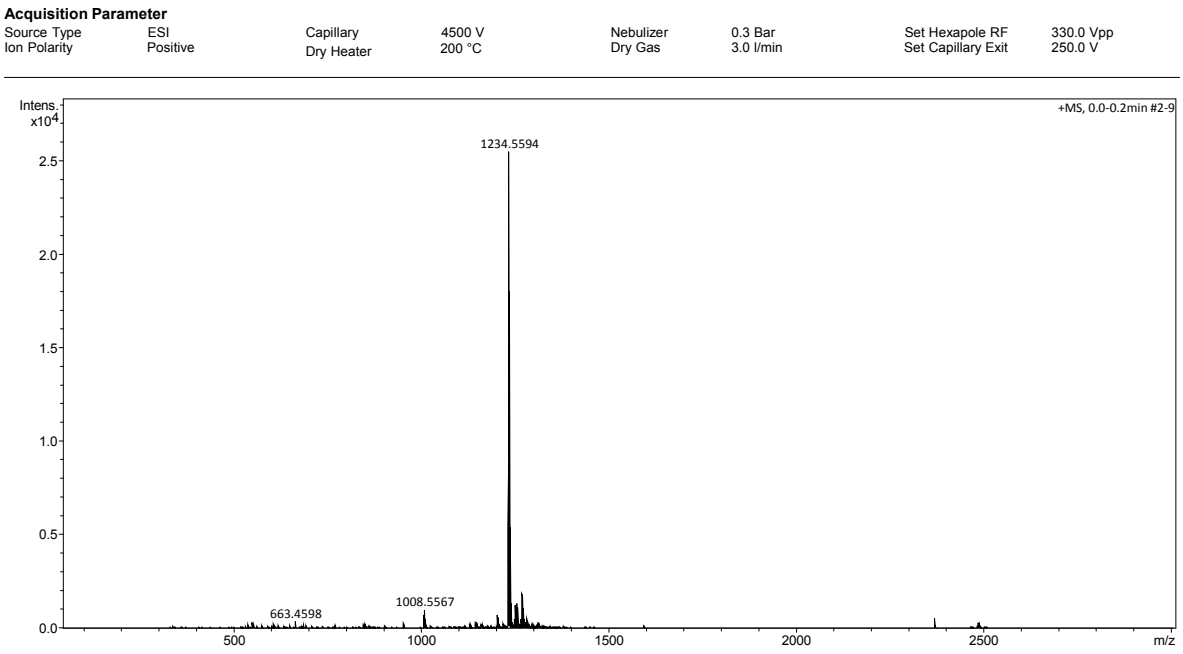
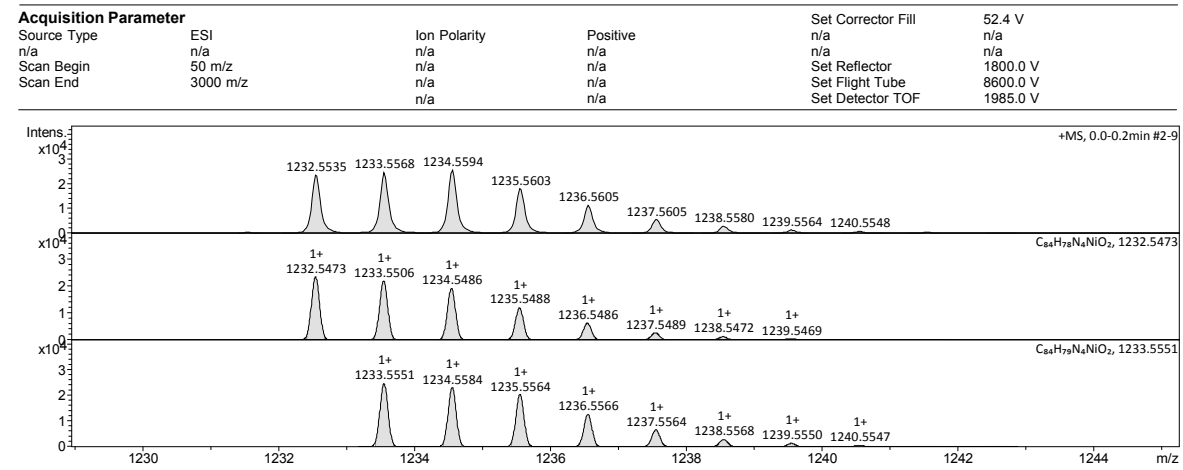



**Figure S32.** HRMS of compound **14**.



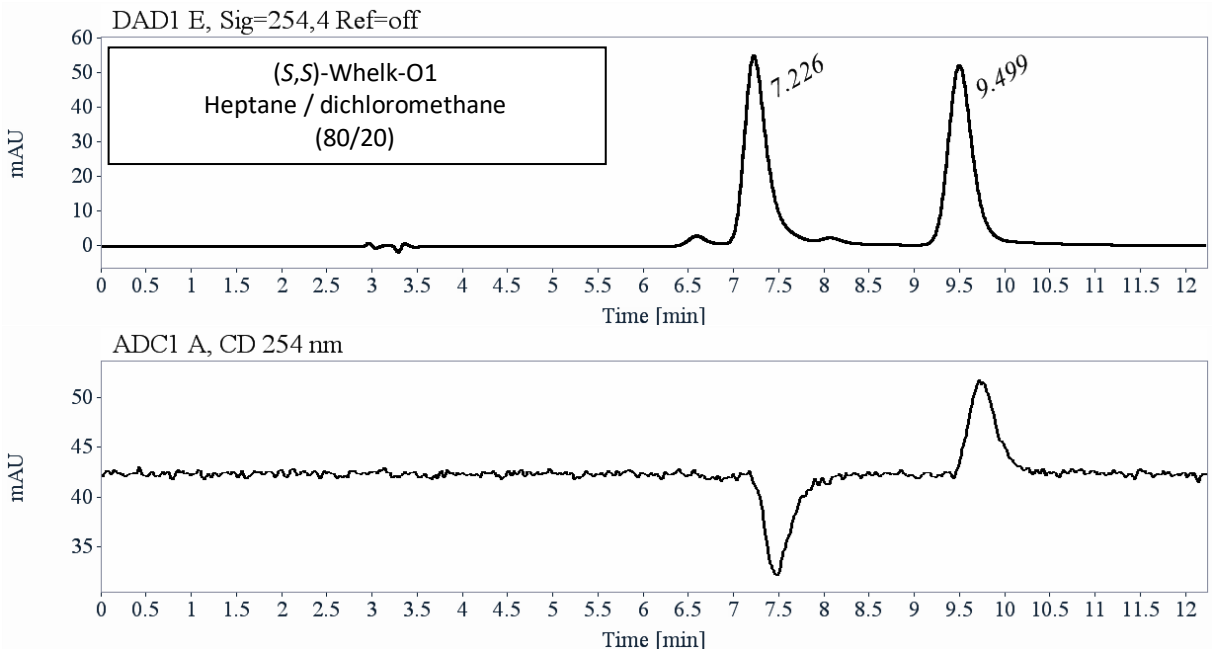

| Meas. m/z | # | Ion Formula | m/z | err [ppm] | Mean err [ppm] | rdb | N-Rule | e⁻ Conf | mSigma | Std I | Std Mean m/z | Std I | VarNorm | Std m/z | Diff Std Comb | Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1232.553509 | 1 | C84H78N4NiO2 | 1232.547272 | -5.1 | -7.4 | 48.0 | ok | odd | 124.3 | 81.3 | n.a. | | n.a. | | n.a. | |
| 1233.556760 | 1 | C84H79N4NiO2 | 1233.555097 | -1.3 | -1.8 | 47.5 | ok | even | 57.4 | 42.4 | n.a. | | n.a. | | n.a. | |

**Figure S33.** HRMS of compond **14** (top: experimental MS, middle and bottom: simulation).

**Analytical chiral HPLC separation for compound 14**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **(*S*,*S*)-Whelk-O1** | Heptane / dichloromethane (80/20) | 7.23 (-) | 1.45 | 9.50 (+) | 2.22 | 1.53 | 4.89 |




| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 7.23 | 986 | 51.05 | 1.45 | | |
| 9.50 | 945 | 48.95 | 2.22 | 1.53 | 4.89 |
| Sum | 1931 | 100.00 | | | |

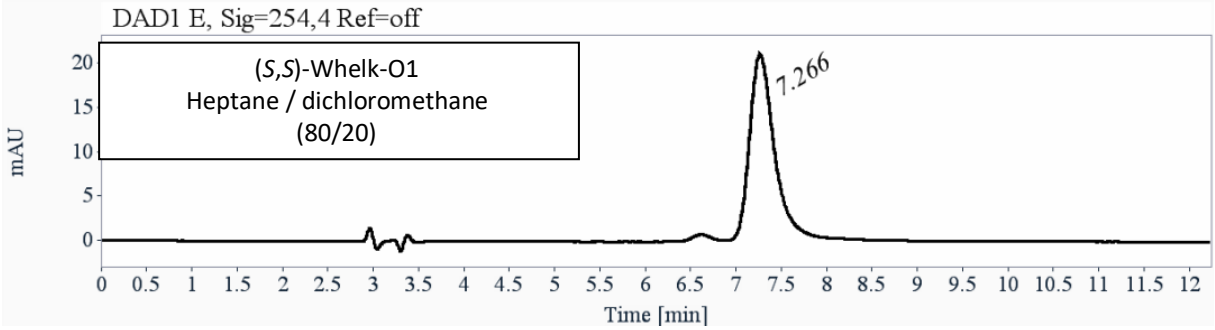
**Preparative separation for compound 14**

• Sample preparation: About 2.0 mg of compound **14** are dissolved in 1.8 mL of a mixture of dichloromethane and hexane (50/50).

• Chromatographic conditions: (*S*,*S*)-Whelk-O1 (250 x 10 mm), hexane / dichloromethane (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.

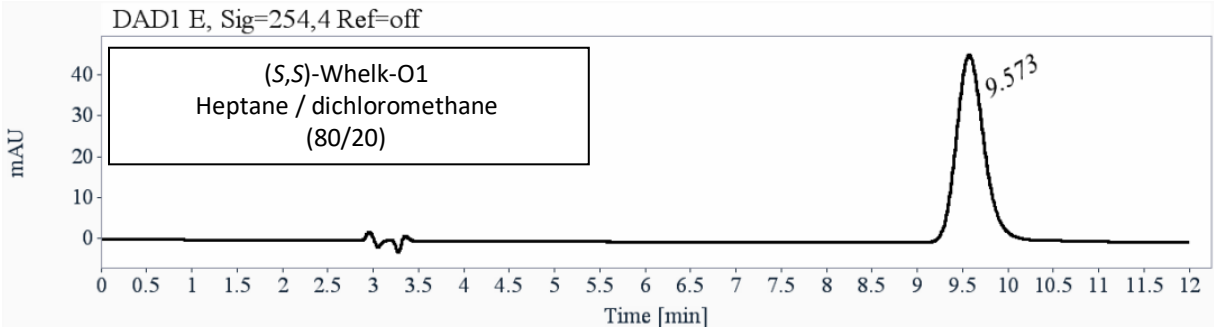
• Injections (stacked): 12 times 160 µL, every 10.8 minutes.

• First fraction: 0.8 mg of the first eluted enantiomer with ee > 99.5 %



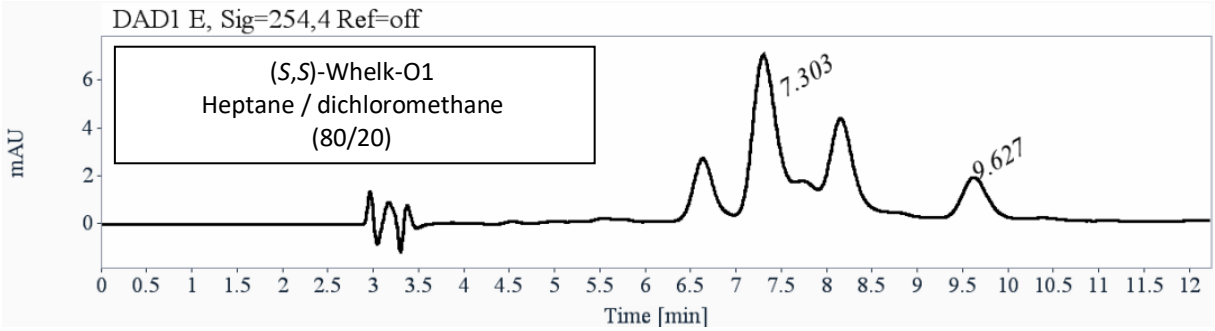

| RT [min] | Area | Area% |
|---|---|---|
| 7.27 | 420 | 100.00 |
| Sum | 420 | 100.00 |

• Second fraction: 0.9 mg of the second eluted enantiomer with ee > 99.5 %




| RT [min] | Area | Area% |
|---|---|---|
| 9.57 | 1010 | 100.00 |
| Sum | 1010 | 100.00 |

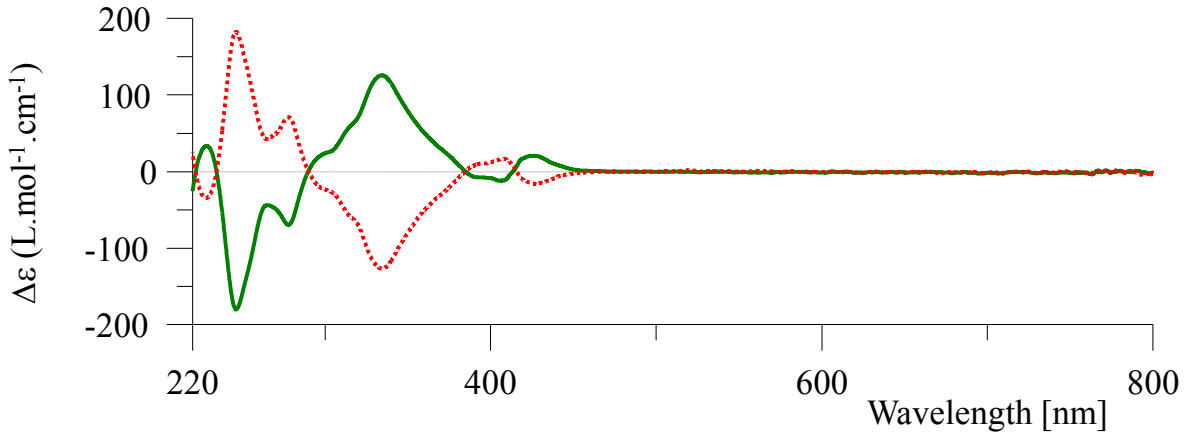
Intermediate: 0.2 mg

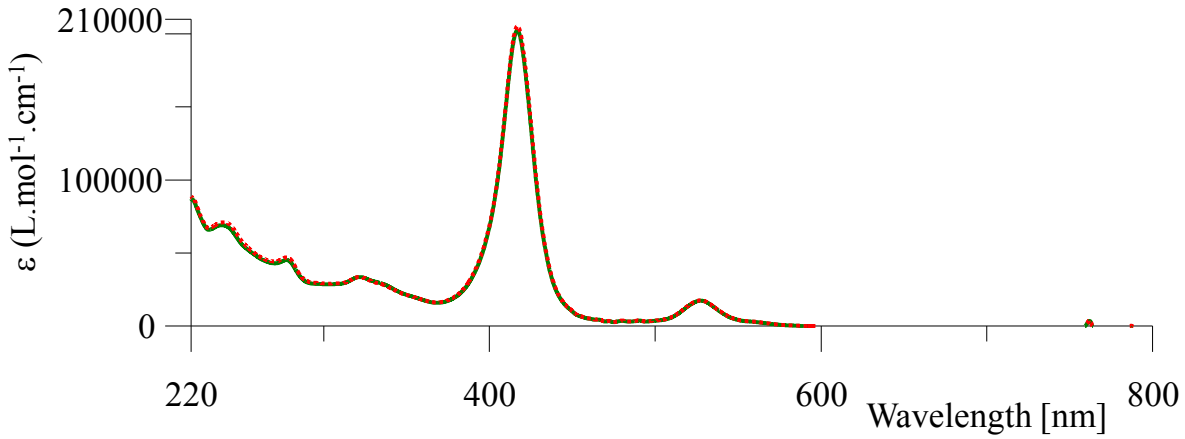


**Electronic Circular Dichroism**

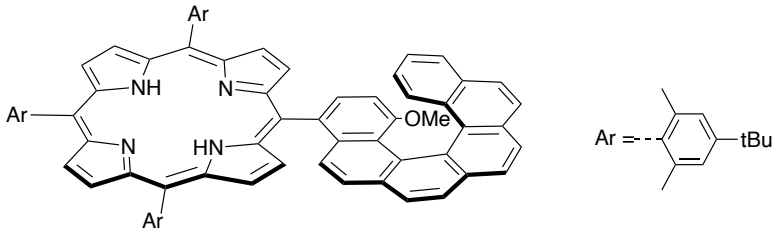
ECD and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at 25.0 ± 0.2°C. A CD quartz cell of 1 mm of optical pathlength was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted.
The baseline was always measured for the same solvent and in the same cell as the samples.
The spectra are presented without smoothing and further data processing.

Compound **14**, first eluted on (*S*,*S*)-Whelk-O1: green solid line, concentration = 0.074 mmol.L$^{-1}$ in dichloromethane.
Compound **14**, second eluted on (*S*,*S*)-Whelk-O1: red dotted line, concentration = 0.077 mmol.L$^{-1}$ in dichloromethane.
Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.



## NMR and MS data of compound 15




Chemical Formula: $C_{83}H_{78}N_4O$
Molecular Weight: 1147.5640

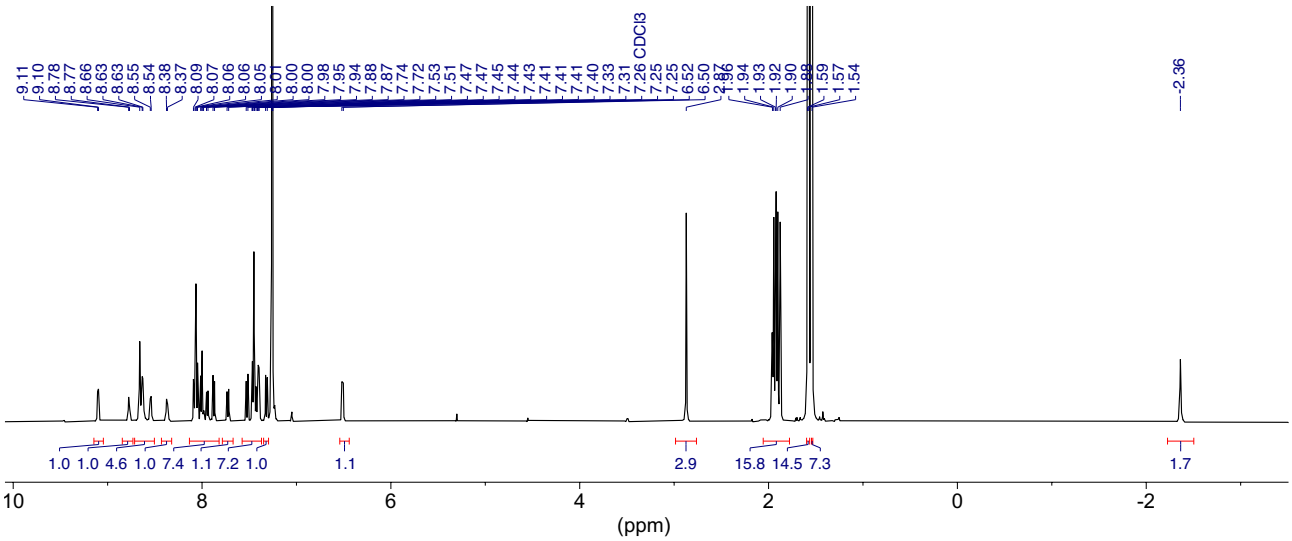



**Figure S34:** $^1$H NMR spectrum of compound **15** in $CDCl_3$ at 298 K (500 MHz).

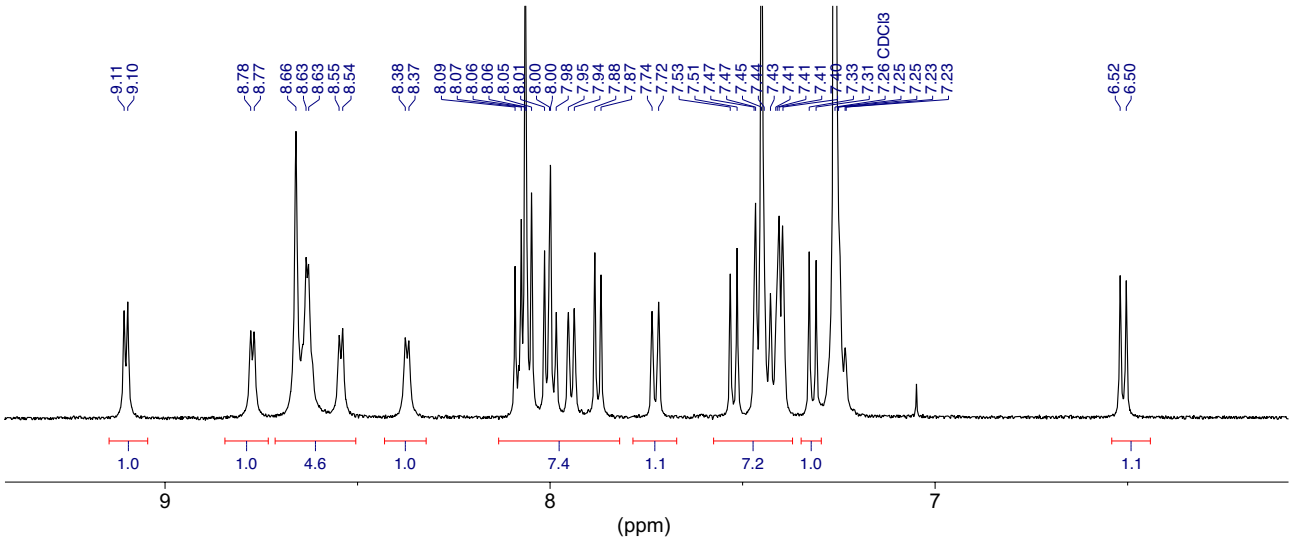



**Figure S35:** $^1$H NMR spectrum (aromatic area) of compound **15** in $CDCl_3$ at 298 K (500 MHz).

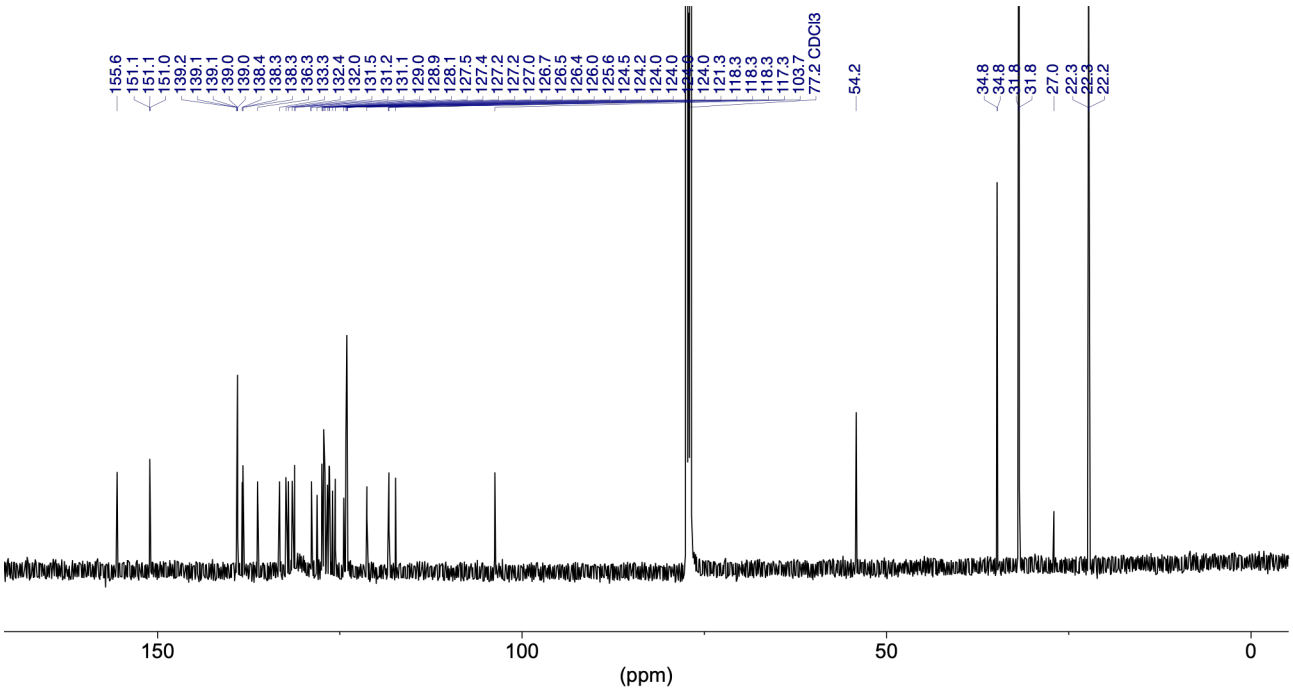



**Figure S36:** $^{13}C$ NMR spectrum of compound **15** in $CDCl_3$ at 298 K (126 MHz).

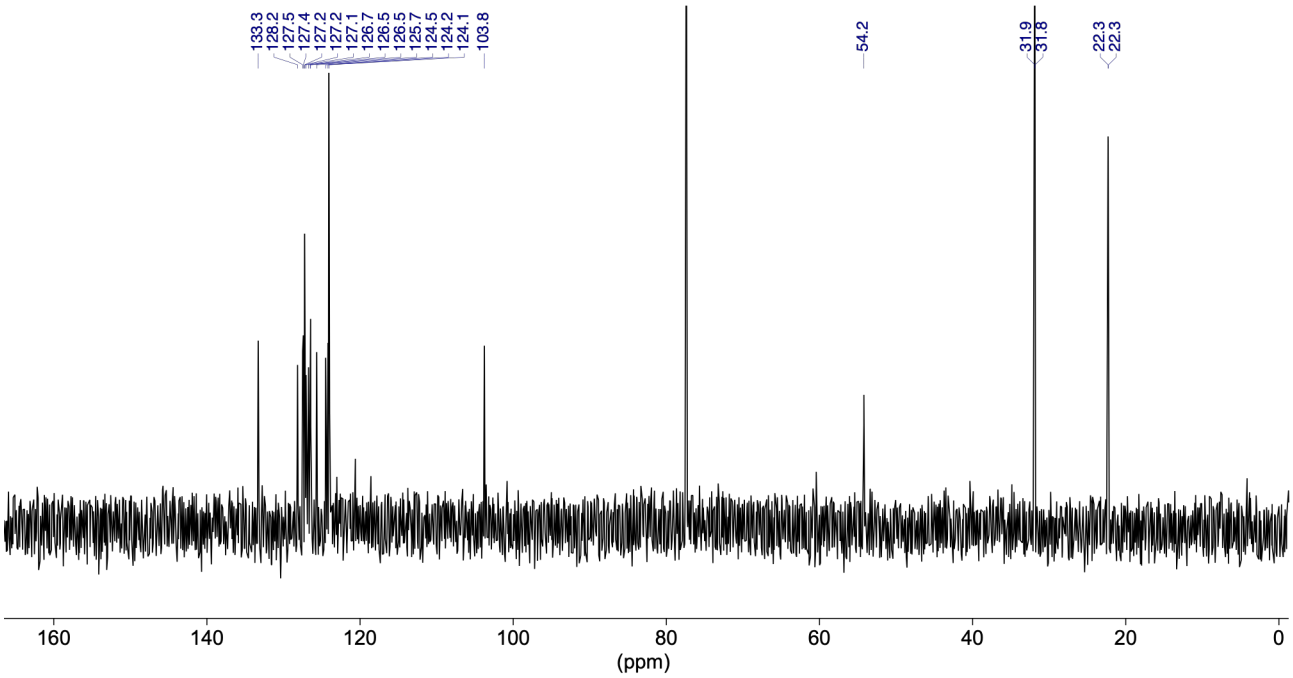



**Figure S37:** $^{13}C$ NMR DEPT spectrum of compound **15** in $CDCl_3$ at 298 K (126 MHz).

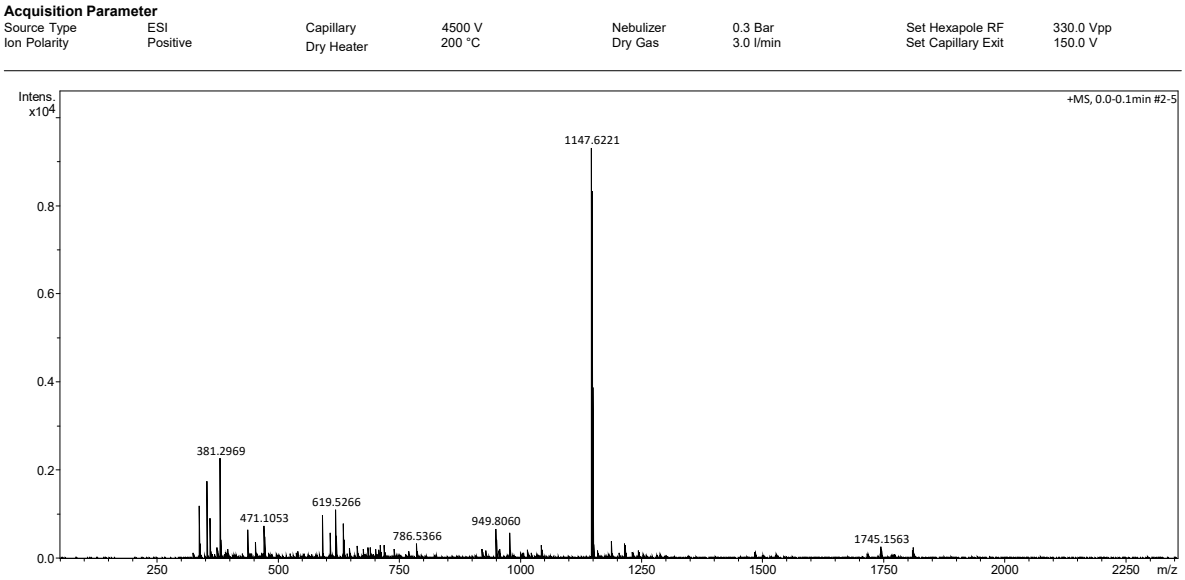
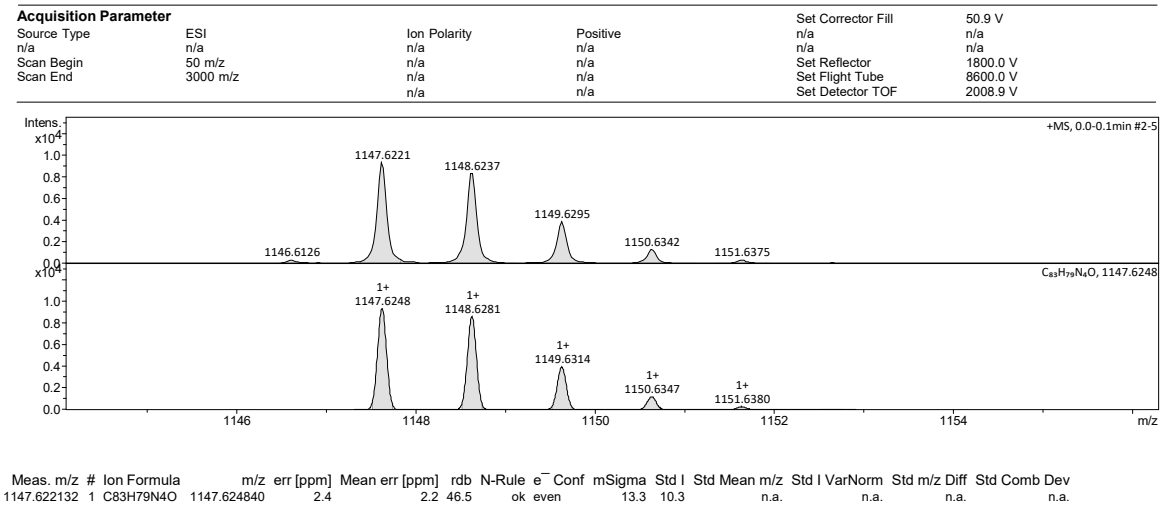



**Figure S38.** HRMS of compound **15**.



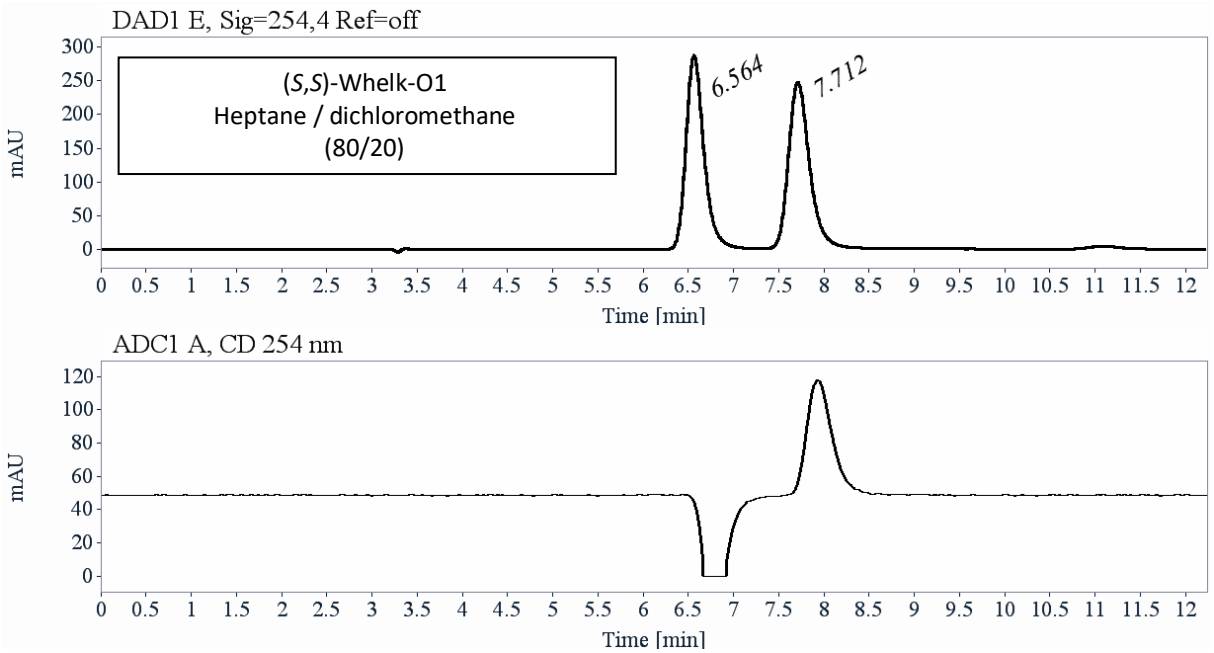

| Meas. m/z | # | Ion Formula | m/z | err [ppm] | Mean err [ppm] | rdb | N-Rule | e¯ Conf | mSigma | Std I | Std Mean m/z | Std I VarNorm | Std m/z Diff | Std Comb Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1147.622132 | 1 | C83H79N4O | 1147.624840 | 2.4 | 2.2 | 46.5 | ok | even | 13.3 | 10.3 | n.a. | n.a. | n.a. | n.a. |

**Figure S39.** HRMS of compound **15** (top: experimental MS, bottom: simulation).

**Analytical chiral HPLC separation for compound 15**

• The sample is dissolved in dichloromethane, injected on the chiral column, and detected with a UV detector at 254 nm and a circular dichroism detector at 254 nm. The flow-rate is 1 mL/min.

| Column | Mobile Phase | t1 | k1 | t2 | k2 | α | Rs |
|---|---|---|---|---|---|---|---|
| **(*S*,*S*)-Whelk-O1** | Heptane / dichloromethane (80/20) | 6.56 (-) | 1.22 | 7.71 (+) | 1.61 | 1.32 | 2.99 |

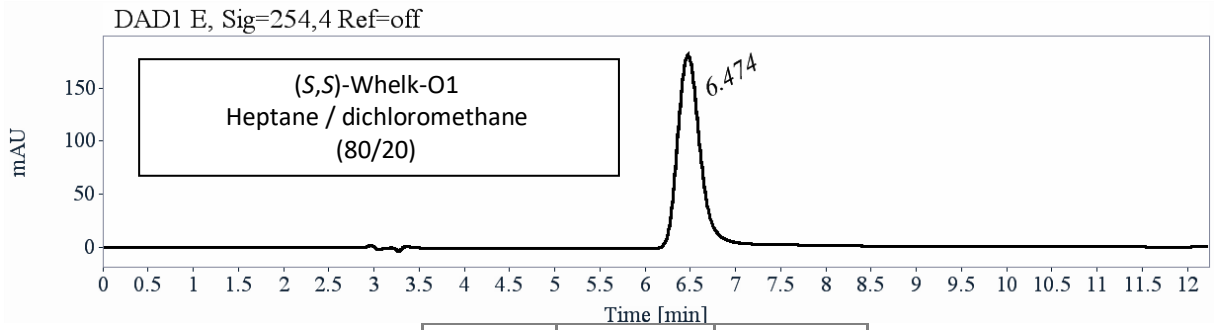



| RT [min] | Area | Area% | Capacity Factor | Enantioselectivity | Resolution (USP) |
|---|---|---|---|---|---|
| 6.56 | 4002 | 49.73 | 1.22 | | |
| 7.71 | 4046 | 50.27 | 1.61 | 1.32 | 2.99 |
| Sum | 8047 | 100.00 | | | |

**Preparative separation for compound 15**

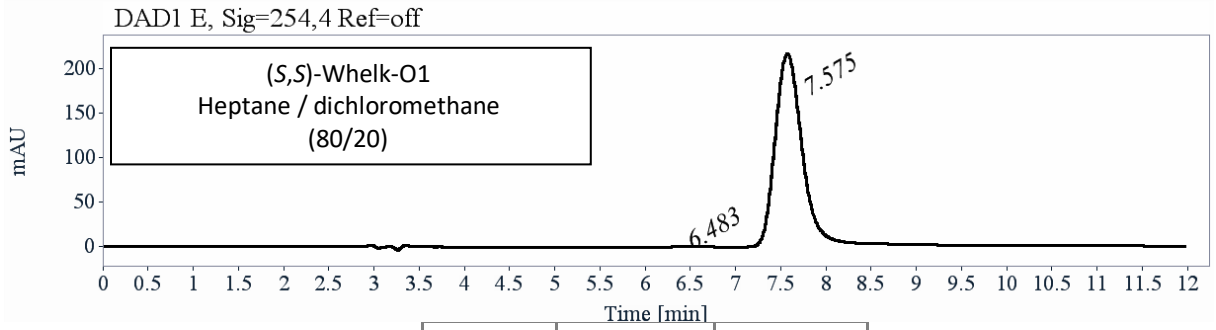
• Sample preparation: About 10.5 mg of compound **15** are dissolved in 1.8 mL of a mixture of dichloromethane and hexane (56/44).
• Chromatographic conditions: (*S*,*S*)-Whelk-O1 (250 x 10 mm), hexane / dichloromethane (80/20) as mobile phase, flow-rate = 5 mL/min, UV detection at 310 nm.
• Injections (stacked): 36 times 50 µL, every 8 minutes.

• First fraction: 4.5 mg of the first eluted enantiomer with ee > 99.5 %



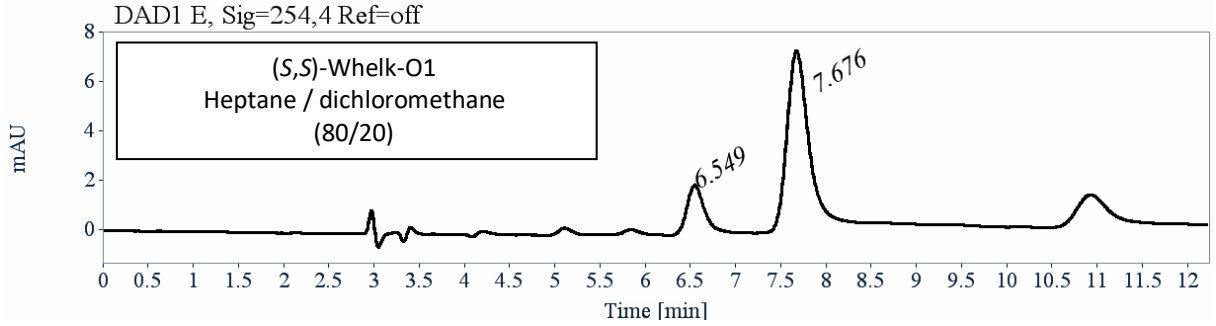

| RT [min] | Area | Area% |
|---|---|---|
| 6.47 | 3332 | 100.00 |
| Sum | 3332 | 100.00 |

• Second fraction: 4.5 mg of the second eluted enantiomer with ee > 99 %




| RT [min] | Area | Area% |
|---|---|---|
| 6.48 | 17 | 0.37 |
| 7.57 | 4541 | 99.63 |
| Sum | 4558 | 100.00 |

Intermediate: 1.5 mg



**Electronic Circular Dichroism - compound 15**

ECD and UV spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at 25.0 ± 0.2°C. A CD quartz cell of 1 mm of optical pathlength was used. The CD spectrometer was purged with nitrogen before recording each spectrum, which was baseline subtracted.
The baseline was always measured for the same solvent and in the same cell as the samples.
The spectra are presented without smoothing and further data processing.

Compound **15**, first eluted on (*S*,*S*)-Whelk-O1: green solid line, concentration = 0.047 mmol.L$^{-1}$ in dichloromethane.
Compound **15**, second eluted on (*S*,*S*)-Whelk-O1: red dotted line, concentration = 0.045 mmol.L$^{-1}$ in dichloromethane.
Acquisition parameters: 0.1 nm as intervals, scanning speed 50 nm/min, band width 2 nm, and 3 accumulations per sample.