

Electronic Supplementary Information

**Enantioselective deprotometalation of alkyl
ferrocenecarboxylates using bimetallic bases**

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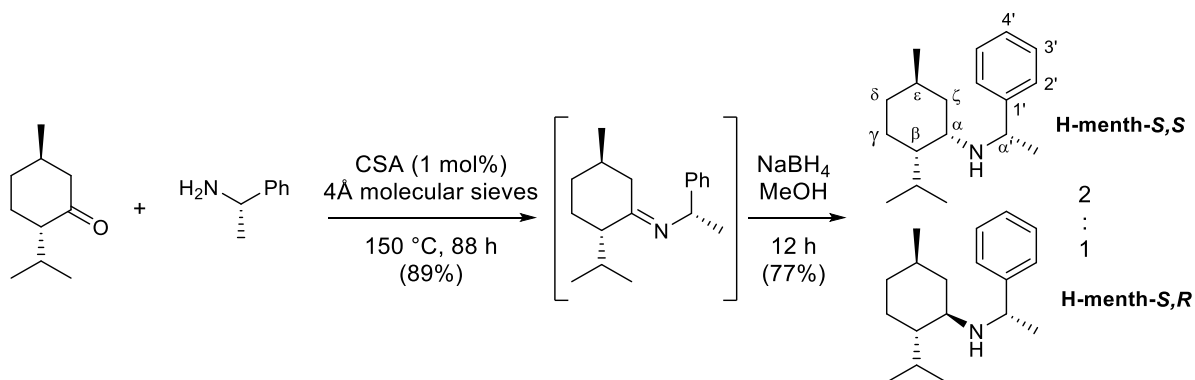
Synthesis of the secondary amines

General crystallographic details

The X-ray diffraction data of **H-menth-*S,S*·HCl**, **H-pino-*R,R*·HCl**, **4-O₂NC₆H₄CO-pino-*S,S***, **H-pino-*S,R*·HCl** and **4-O₂NC₆H₄CO-isopino-*S,R*** were collected at $T = 150(2)$ K on an APEXII Bruker AXS diffractometer by using monochromatized Mo-K α radiation ($\lambda = 0.71073$ Å; graphite monochromator). The structure was solved by direct methods using the SIR97 program,¹ and then refined with full-matrix least-square methods based on F^2 (SHELXL program).² All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. The molecular diagrams were generated by ORTEP-3 (version 2.02).³

(*αS*)-*α*-Methyl-*N*-[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-*S,S*)

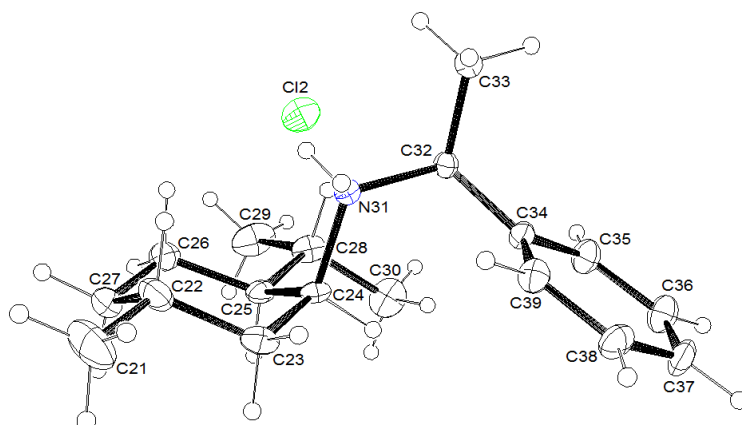
and **(*αS*)-*α*-methyl-*N*-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-*S,R*)**



They were prepared by adapting a procedure described.⁴ A mixture of (*S*)-*α*-methylbenzylamine (5.1 mL, 40 mmol), L- or (–)-menthone (3.1 g, 20 mmol), and camphorsulfonic acid (46 mg, 0.20 mmol) was heated under stirring in the presence of 4Å molecular sieves (7 g) at 150 °C for 4 days. The mixture was cooled and filtered through celite (washing using 80 mL Et₂O). The organic solution was washed with saturated aqueous NaHCO₃ (2 x 10 mL), saturated aqueous NaHSO₃ (3 x 10 mL), and brine (10 mL). It was then dried (Na₂SO₄) and evaporated. The imine,⁵ obtained in 89% yield, was directly used in the reduction step. A solution of the imine (4.65 g, 18 mmol) in MeOH (25 mL)

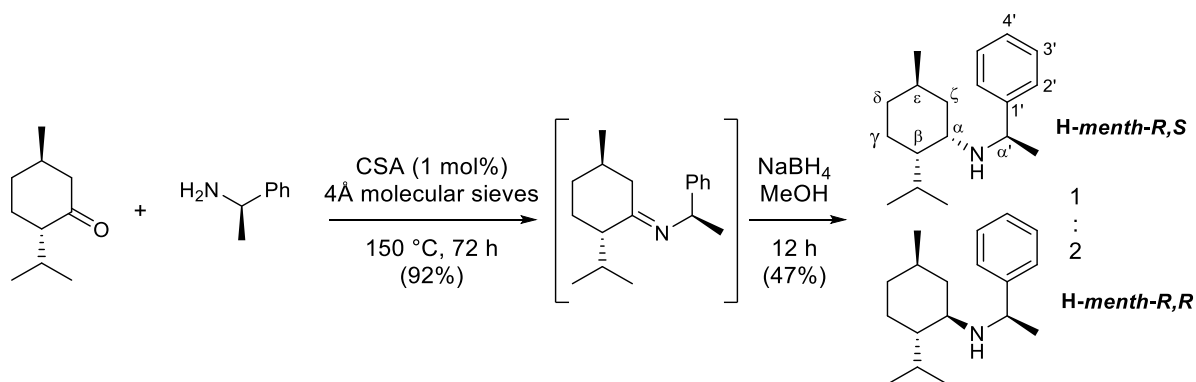
was progressively treated by NaBH₄ (1.4 g, 36 mmol) at 0 °C over a period of 2-3 h. The mixture was then stirred at room temperature for 3 h. MeOH was removed under reduced pressure and water (20 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 20 mL). The organic solution was washed with 20% FeSO₄ (2 x 20 mL) and brine (20 mL). It was then dried (Na₂SO₄) and evaporated before separation of the 2:1 stereoisomeric mixture by column chromatography over silica gel (eluent: heptane-Et₃N 99:1 for silica wash then heptane-Et₂O 98:2). **(*αS*)-*α*-Methyl-*N*-[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (*H*-menth-*S,S*)**⁵ was first isolated in 50% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 80:20) 0.6; [α]_D -8.0 (c 1.25); ¹H NMR (300 MHz, CDCl₃) δ 0.73 (d, 3H, *J* = 6.5 Hz, *Me*-Cε), 0.66-0.94 (m, 3H, Hβ, Hδ and Hζ), 0.91 (d, 3H, *J* = 6.6 Hz, *Me*₂CH), 0.97 (d, 3H, *J* = 6.6 Hz, *Me*₂CH), 1.01-1.24 (m, 2H, Hγ and NH), 1.29 (d, 3H, *J* = 6.5 Hz, *Me*-Cα'), 1.49-1.68 (m, 5H, Hζ, Hδ, Hγ, Hε and CHMe₂), 3.05 (q, 1H, *J* = 2.9 Hz, Hα), 3.80 (q, 1H, *J* = 6.5 Hz, Hα'), 7.18-7.24 (m, 1H, H4'), 7.27-7.33 (m, 2H, H3' and H5'), 7.36-7.40 (m, 2H, H2' and H6'); ¹³C NMR (75 MHz, CDCl₃) δ 21.1 (CH₃, *Me*₂CH), 21.6 (CH₃, *Me*₂CH), 22.6 (CH₃, *Me*-Cε), 23.7 (CH₃, *Me*-Cα'), 25.0 (CH₂, Cγ), 25.8 (CH, Cε), 29.1 (CH, CHMe₂), 35.6 (CH₂, Cδ), 38.9 (CH₂, Cζ), 48.8 (CH, Cβ), 52.1 (CH, Cα), 56.3 (CH, Cα'), 126.7 (CH, C4'), 126.8 (2CH, C2' and C6'), 128.3 (2CH, C3' and C5'), 148.2 (C, C1'); HRMS (ESI; MeOH), *m/z* 260.2378 (0 ppm) found (calcd for C₁₈H₃₀N, [M+H]⁺, requires 260.23783). The structure of ***H*-menth-*S,S*** was confirmed unambiguously by X-ray diffraction of the corresponding hydrochloride ***H*-menth-*S,S*·HCl** [mp 191 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.68-0.82 (m, 5H), 0.89-0.96 (m, 7H), 1.65-1.77 (m, 3H), 1.94-2.27 (m, 6H), 3.20 (q, 1H, *J* = 3.3 Hz), 4.27 (q, 1H, *J* = 6.8 Hz), 7.28-7.41 (m, 3H), 7.79-7.82 (m, 2H), 8.70 (br s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 20.8 (CH₃), 21.3 (CH₃), 21.6 (CH₃), 21.8 (CH₃), 23.8 (CH₂), 26.0 (CH), 27.4 (CH), 34.5 (CH₂), 38.6 (CH₂), 47.7 (CH), 55.8 (CH), 61.6 (CH), 128.0 (2CH, Ph), 128.6 (CH, Ph), 128.9 (2CH, Ph), 137.6 (C, Ph)]. *Crystal data for H-menth-*S,S*·HCl*: C₁₈H₃₀ClN, *M* = 295.88, 150(2)K, monoclinic, *P* 2₁, *a* = 11.4383(9), *b* = 10.9604(14), *c* = 14.2059(13) Å, β = 98.636(4)°, *V* = 1760.8(3) Å³, *Z* = 4, *d* = 1.116 g cm⁻³, μ = 0.210 mm⁻¹. A final refinement on *F*² with 7320 unique intensities and 369 parameters converged at ω*R*(*F*²) = 0.0962 (*R*(*F*) = 0.0533) for 5011 observed

reflections with $I > 2\sigma(I)$. CCDC 2110270. (***αS***)-***α***-Methyl-*N*-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (**H-menth-*S,R***) was next isolated in 27% yield as a colorless syrupy liquid: *R*_f (heptane-Et₂O 80:20) 0.5; [*α*]_D -54.0 (c 2.1); ¹H NMR (300 MHz, CDCl₃) δ 0.87 (d, 3H, *J* = 6.6 Hz, Me-C_ε), 0.89 (d, 3H, *J* = 6.7 Hz, Me₂CH), 1.03 (d, 3H, *J* = 6.7 Hz, Me₂CH), 1.12-1.38 (m, 4H), 1.30 (d, 3H, *J* = 6.6 Hz, Me-C_{α'}), 1.38-1.69 (m, 5H), 1.77 (ddt, 1H, *J* = 13.3, 8.3 and 6.7 Hz), 2.55 (dt, 1H, *J* = 7.6 and 3.9 Hz, H_α), 3.90 (q, 1H, *J* = 6.6 Hz, H_{α'}), 7.18-7.25 (m, 1H), 7.30-7.31 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 22.0 (CH₃), 22.1 (CH₃), 22.9 (CH₃), 24.6 (CH₂, C_γ), 24.9 (CH₃), 26.7 (CH), 30.2 (CH), 31.5 (CH₂), 35.6 (CH₂), 45.9 (CH), 54.9 (CH, C_α), 55.0 (CH, C_{α'}), 126.7 (CH, C_{4'}), 126.8 (2CH, C_{2'} and C_{6'}), 128.3 (2CH, C_{3'} and C_{5'}), 146.6 (C, C_{1'}); HRMS (ESI; MeOH), *m/z* 260.2379 (0 ppm) found (calcd for C₁₈H₃₀N, [M+H]⁺, requires 260.23783).



(***αR***)-***α***-Methyl-*N*-[(1*S*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (**H-menth-*R,S***)

and (***αR***)-***α***-methyl-*N*-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl]benzylamine (**H-menth-*R,R***)

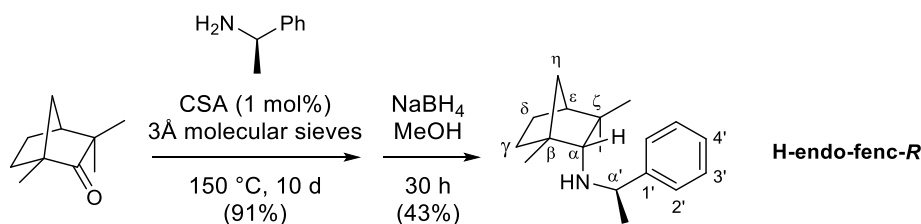


They were prepared by adapting a procedure described:⁴ A mixture of L- or (–)-menthone (3.1 g, 20 mmol), (*R*)-*α*-methylbenzylamine (5.1 mL, 40 mmol), and camphorsulfonic acid (46 mg, 0.20

mmol) was heated under stirring in the presence of 4Å molecular sieves (7 g) at 150 °C for 3 days. The mixture was cooled and filtered through celite (washing using 80 mL Et₂O). The organic solution was washed with saturated aqueous NaHCO₃ (2 x 10 mL), saturated aqueous NaHSO₃ (3 x 10 mL), and brine (10 mL). It was then dried (Na₂SO₄) and evaporated. The imine,⁵ obtained in 92% yield, was directly used in the reduction step. A solution of the imine (4.65 g, 18 mmol) in MeOH (25 mL) was progressively treated by NaBH₄ (1.4 g, 36 mmol) at 0 °C over a period of 2-3 h. The mixture was then stirred at room temperature for 3 h. MeOH was removed under reduced pressure and water (20 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 20 mL). The organic solution was washed with 20% FeSO₄ (2 x 20 mL) and brine (20 mL). It was then dried (Na₂SO₄) and evaporated before separation of the 2:1 stereoisomeric mixture by column chromatography over silica gel (eluent: heptane-Et₃N 99:1 for silica wash then heptane-Et₂O 98:2). **(αR)-α-Methyl-N-[(1S,2S,5R)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-R,S)**⁵ was first isolated in 17% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 80:20) 0.7; [α]_D +78.5 (c 1.0); ¹H NMR (300 MHz, CDCl₃) δ 0.59 (d, 3H, *J* = 6.6 Hz, Me), 0.65-0.81 (m, 2H, H_β and H_ζ), 0.84 (d, 3H, *J* = 6.6 Hz, Me), 0.89 (d, 3H, *J* = 6.5 Hz, Me₂CH), 0.92-1.28 (m, 3H, H_γ, H_δ and NH), 1.32 (d, 3H, *J* = 6.6 Hz, Me-Cα'), 1.55-1.77 (m, 4H, H_γ, H_δ, H_ε and CHMe₂), 2.00 (ddd, 1H, *J* = 13.6, 5.7 and 3.1 Hz, H_ζ), 2.63 (q, 1H, *J* = 2.8 Hz, H_α), 3.83 (q, 1H, *J* = 6.6 Hz, H_α'), 7.18-7.25 (m, 1H, H₄'), 7.27-7.40 (m, 4H, H₂', H₃', H₅' and H₆'); ¹³C NMR (75 MHz, CDCl₃) δ 21.1 (CH₃, Me-C_ε), 21.4 (CH₃), 22.8 (CH₃), 24.7 (CH₂), 25.7 (CH₃, Me-Cα'), 25.8 (CH), 28.5 (CH), 35.7 (CH₂), 37.8 (CH₂, C_ζ), 48.6 (CH), 50.1 (CH), 54.2 (CH), 126.8 (CH, C₄'), 127.1 (2CH, C₂' and C₆'), 128.2 (2CH, C₃' and C₅'), 146.3 (C, C₁'); HRMS (ESI; MeOH), *m/z* 260.2380 (1 ppm) found (calcd for C₁₈H₃₀N, [M+H]⁺, requires 260.23783). **(αR)-α-Methyl-N-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-R,R)** was next isolated in 30% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 80:20) 0.6; [α]_D +34.7 (c 0.95); ¹H NMR (300 MHz, CDCl₃) δ 0.87 (d, 3H, *J* = 6.3 Hz, Me-C_ε), 0.93 (d, 3H, *J* = 6.7 Hz, Me₂CH), 0.96-1.12 (m, 2H), 1.14 (d, 3H, *J* = 6.6 Hz, Me₂CH), 1.16-1.26 (m, 2H), 1.27 (d, 3H, *J* = 6.6 Hz, Me-Cα'), 1.31-1.42 (m, 3H), 1.51 (td, 1H, *J* = 8.2 and 4.1 Hz), 1.76-1.76 (m, 1H), 1.79-1.93 (m, 1H),

2.55 (dt, 1H, $J = 10.6$ and 3.7 Hz), 3.87 (q, 1H, $J = 6.6$ Hz), 7.19-7.25 (m, 1H, H4'), 7.27-7.35 (m, H2', H3', H5' and H6'); ^{13}C NMR (75 MHz, CDCl_3) δ 22.3 (CH_3), 22.4 (CH_3), 23.9 (CH_3), 24.6 (CH_3), 25.7 (CH), 26.7 (CH_2 , C γ), 30.9 (CH_2), 31.8 (CH), 38.2 (CH_2), 41.9 (CH), 54.8 (CH, C α), 56.9 (CH, C α'), 126.6 (CH, C4'), 126.7 (2CH, C2' and C6'), 128.4 (2CH, C3' and C5'), 146.8 (C, C1'); HRMS (ESI; MeOH), m/z 260.2376 (1 ppm) found (calcd for $\text{C}_{18}\text{H}_{30}\text{N}$, $[\text{M}+\text{H}]^+$, requires 260.23783). The corresponding carboxamide [mp ~ 55 °C (gum); $[\alpha]_{\text{D}} +119.2$ (c 0.65); HRMS (ESI; MeOH), m/z 431.2308 (1 ppm) found (calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_3\text{Na}$, $[\text{M}+\text{Na}]^+$, requires 431.23106)] was prepared by reaction of **H-menth-*R,R*** with 4-nitrobenzoyl chloride, but did not afford suitable crystals for X-ray diffraction.

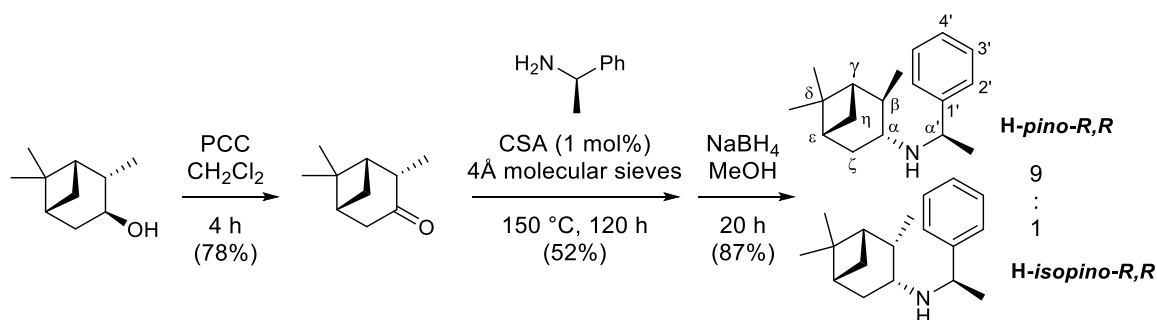
Endo-(+)-(α*R*)-N-(α-phenylethyl)fenchylamine (H-endo-fenc-*R*)



Note that this reaction does not work by using (*S*)- α -methylbenzylamine instead of the (*R*).

A mixture of (-)-fenchone (3.2 mL, 20 mmol), (*R*)- α -methylbenzylamine (5.1 mL, 40 mmol), and camphorsulfonic acid (47 mg, 0.20 mmol) was heated under stirring in the presence of 3 Å molecular sieves (7 g) at 150 °C for 10 days. The mixture was cooled and filtered through celite (washing using 80 mL Et_2O). The organic solution was washed with saturated aqueous NaHCO_3 (2 x 10 mL), saturated aqueous NaHSO_3 (3 x 10 mL), and brine (10 mL). It was then dried (Na_2SO_4) and evaporated. The imine, obtained in 91% yield as a yellow syrupy liquid, was directly used in the reduction step. A solution of the imine (4.65 g, 18 mmol) in MeOH (45 mL) was progressively treated by NaBH_4 (1.4 g, 36 mmol) at 0 °C over a period of 2-3 h. The mixture was then stirred at room temperature for 30 h. MeOH was removed under reduced pressure and water (30 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 30 mL). The organic solution was washed with 20% FeSO_4 (2 x 30 mL) and brine

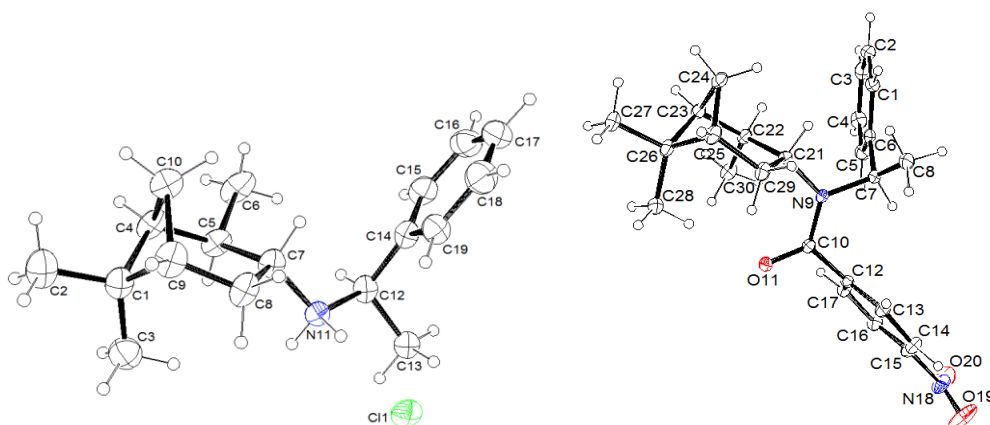
(30 mL). It was then dried (Na₂SO₄) and evaporated before separation of the 85:15 stereoisomeric mixture by column chromatography over silica gel (eluent: heptane-Et₃N 99:1 for silica wash then heptane-Et₂O 99:1). **Endo-(+)-(αR)-N-(α-phenylethyl)fenchylamine (H-endo-fenc-R)** was the only pure amine obtained, isolated in 43% yield as a colorless syrupy liquid: [α]_D +91.4 (c 1.0); ¹H NMR (300 MHz, CDCl₃) δ 0.81-1.04 (m, 1H), 0.93 (s, 3H, Me), 0.99 (s, 3H, Me), 0.99 (s, 3H, Me), 1.07-1.19 (m, 1H), 1.29 (d, 3H, *J* = 6.6 Hz, *Me-Cα'*), 1.23-1.51 (m, 4H), 1.58-1.70 (m, 2H), 1.81-2.21 (m, 1H), 3.79 (q, 1H, *J* = 6.6 Hz, Hα'), 7.19-7.25 (m, 1H, H4'), 7.26-7.36 (m, 4H, H2', H3', H5' and H6'); ¹³C NMR (75 MHz, CDCl₃) δ 20.2 (CH₃), 20.8 (CH₃), 25.6 (CH₃), 26.3 (CH₂), 26.6 (CH₂), 32.6 (CH₃), 39.1 (C), 42.7 (CH₂), 48.8 (C), 49.2 (CH), 57.5 (CH), 69.3 (CH), 126.7 (CH, C4'), 127.2 (2CH, C2' and C6'), 128.1 (2CH, C3' and C5'), 146.6 (C, C1'); HRMS (ESI; MeOH), *m/z* 258.2222 (0 ppm) found (calcd for C₁₈H₂₈N, [M+H]⁺, requires 258.22218). An attempt to obtain suitable crystals of the corresponding hydrochloride [white solid; mp 105-120 °C (gummy); ¹H NMR (300 MHz, CDCl₃) δ 1.01 (s, 3H), 1.11-1.24 (m, 2H), 1.29 (s, 3H), 1.36-1.57 (m, 2H), 1.53 (s, 3H), 1.67 (s, 2H), 1.99 (t, 1H, *J* = 9.6 Hz), 2.15 (d, 3H, *J* = 6.8 Hz), 2.43-2.46 (m, 1H), 4.20-4.24 (m, 1H), 7.34-7.46 (m, 3H), 7.84-7.87 (m, 2H), 8.96 (br s, 1H), 9.14 (br s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 19.7 (CH₃), 21.6 (CH₃), 21.8 (CH₃), 25.7 (CH₂), 27.5 (CH₂), 32.0 (CH₃), 39.8 (C), 43.4 (CH₂), 48.7 (C), 49.2 (CH), 61.6 (CH), 71.7 (CH), 128.5 (2CH, Ph), 129.0 (CH, Ph), 129.3 (2CH, Ph), 137.4 (C, Ph); HRMS (ESI; MeOH), *m/z* 258.2221 (0 ppm) found (calcd for C₁₈H₂₈N, C⁺, requires 258.22218)] failed. This, its structure was assigned by comparison of the NMR spectra with similar derivatives.⁶



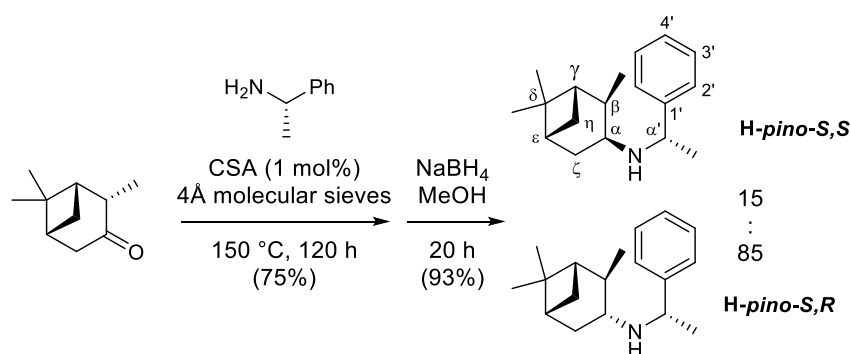
(-)-Isopinocampheone⁷ was first prepared from (+)-isopinocampheol as follows. To a stirred mixture of pyridinium chlorochromate (PCC; 12.9 g, 60 mmol), powdered 4Å molecular sieves (14 g) and magnesium sulfate (3 spatulas) in dichloromethane (60 mL) was added (+)-isopinocampheol (6.2 g, 40 mmol). The reaction mixture was stirred at rt for 4 h and filtrated through celite. The filtrate was concentrated under reduced pressure and the crude was purified by column chromatography over silica gel (eluent: heptane-Et₂O 94:6) to afford (-)-isopinocampheone in 78% yield as a colorless liquid: R_f (heptane-Et₂O 80:20) 0.8; ¹H NMR (300 MHz, CDCl₃) δ 0.87 (s, 3H, Me₂C), 1.19 (d, 1H, *J* = 10.2 Hz), 1.21 (d, 3H, *J* = 7.4 Hz, MeCH), 1.31 (s, 3H, Me₂C), 2.05 (td, 1H, *J* = 6.2 and 1.9 Hz), 2.09-2.15 (m, 1H), 2.42-2.69 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 16.6 (CH₃), 21.7 (CH₃), 26.8 (CH₃), 34.2, 38.8, 39.0 (C), 44.5, 44.8, 51.1, 214.6 (C, C=O); HRMS (ESI; MeOH), *m/z* 175.1099 (0 ppm) found (calcd for C₁₀H₁₆ONa, [M+Na]⁺, requires 175.10988). A mixture of (-)-isopinocampheone (3.7 g, 24.5 mmol), (*R*)-α-methylbenzylamine (6.3 mL, 49 mmol), and camphorsulfonic acid (57 mg, 0.245 mmol) was heated under stirring in the presence of 4Å molecular sieves (8.5 g) at 150 °C for 5 days. The mixture was cooled and filtered through celite (washing using 100 mL Et₂O). The organic solution was washed with saturated aqueous NaHCO₃ (2 x 10 mL), saturated aqueous NaHSO₃ (3 x 10 mL), and brine (10 mL). It was then dried (Na₂SO₄) and evaporated. The imine,⁸ obtained in 52% yield, was directly used in the reduction step. A solution of the imine (3.2 g, 12.5 mmol) in MeOH (20 mL) was progressively treated by NaBH₄ (0.95 g, 25 mmol) at 0 °C over a period of 2-3 h. The mixture was then stirred at room temperature for 20 h. MeOH was removed under reduced pressure and water (20 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 20 mL). The organic solution was washed with 20% FeSO₄ (2 x 20 mL) and brine (20 mL). It was then dried (Na₂SO₄) and evaporated before separation of the 9:1 stereoisomeric mixture by column chromatography over silica gel (eluent: heptane-Et₃N 99:1 for silica wash then heptane-Et₂O 99:1). **(1*S*,2*R*,3*R*,5*R*)-2,6,6-Trimethyl-*N*-[(*αR*)-*α*-phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*R,R*)** formed in 78% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 90:10) 0.6; [*α*]_D -39.6 (c 1.4); ¹H NMR (500 MHz, CDCl₃) δ 0.92 (s, 3H, Me, Me₂C), 1.10 (d, 3H, *J* = 6.6 Hz, Me-Cβ), 1.25-1.28 (m, 1H, NH), 1.26 (s, 3H,

Me_2C), 1.34-1.36 (m, 1H, H_η), 1.42 (d, 3H, $J = 6.5$ Hz, $Me-C\alpha'$), 1.48-1.54 (m, 1H, H_ζ), 1.71 (td, 1H, $J = 5.8$ and 1.3 Hz, H_γ), 1.86 (p, 1H, $J = 6.8$ Hz, H_β), 1.92 (qd, 1H, $J = 5.7$ and 1.1 Hz, H_ϵ), 2.03-2.13 (m, 2H, H_ζ and H_η), 2.66 (q, 1H, $J = 7.9$ Hz, H_α), 4.00 (q, 1H, $J = 6.5$ Hz, $H_{\alpha'}$), 7.28-7.31 (m, 1H, $H_{4'}$), 7.37-7.40 (m, 2H, $H_{3'}$ and $H_{5'}$), 7.45-7.47 (m, 2H, $H_{2'}$ and $H_{6'}$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.0 (CH_3 , $Me-C\beta$), 20.1 (CH_3 , Me_2C), 23.8 (CH_3 , $Me-C\alpha'$), 23.9 (CH_2 , C_η), 26.6 (CH_3 , Me_2C), 34.5 (CH_2 , C_ζ), 38.7 (CH , C_β), 39.6 (C , C_δ , CMe_2), 40.7 (CH , C_ϵ), 47.6 (CH , C_γ), 54.2 (CH , C_α), 56.6 (CH , $C_{\alpha'}$), 126.7 (CH , $C_{4'}$), 126.8 (2CH, $C_{2'}$ and $C_{6'}$), 128.3 (2CH, $C_{3'}$ and $C_{5'}$), 147.4 (C , $C_{1'}$); HRMS (ESI; MeOH), m/z 258.2220 (1 ppm) found (calcd for $C_{18}H_{28}N$, $[M+H]^+$, requires 258.22218). The corresponding carboxamide [HRMS (ESI; MeOH), m/z 407.2339 (1 ppm) found (calcd for $C_{25}H_{31}N_2O_3$, $[M+H]^+$, requires 407.23347)] was prepared by reaction of **H-pino-*R,R*** with 4-nitrobenzoyl chloride, but did not afford suitable crystals for X-ray diffraction. However, the structure of **H-pino-*R,R*** was confirmed unambiguously by X-ray diffraction of the corresponding hydrochloride **H-pino-*R,R*·HCl** (white solid; mp 229 °C; 1H NMR (300 MHz, $CDCl_3$) δ 0.95-1.20 (m, 10H), 1.47-1.61 (m, 2H), 1.74 (q, 1H, $J = 5.5$ Hz), 1.88-1.96 (m, 1H), 2.00-2.05 (m, 3H), 2.24 (dd, 1H, $J = 6.7$ Hz), 2.35-2.76 (m, 2H), 4.35 (q, 1H, $J = 5.9$ Hz), 7.32-7.43 (m, 3H), 7.74-7.79 (m, 2H), 9.88 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0 (CH_3), 20.6 (CH_3), 21.0 (CH_3), 22.9 (CH_2), 26.2 (CH_3), 30.7 (CH_2), 34.3 (CH), 40.0 (C), 40.1 (CH), 47.6 (CH), 57.5 (CH), 61.4 (CH), 128.6 (2CH, Ph), 129.2 (2CH, Ph), 129.3 (CH , Ph), 136.8 (C , Ph)). *Crystal data for H-pino-*R,R*·HCl*: $C_{18}H_{28}ClN$, $M = 293.86$, 150(2)K, monoclinic, $P 2_1$, $a = 11.0788(17)$, $b = 7.5785(11)$, $c = 11.6867(18)$ Å, $\beta = 118.618(5)^\circ$, $V = 861.3(2)$ Å³, $Z = 2$, $d = 1.133$ g cm⁻³, $\mu = 0.214$ mm⁻¹. A final refinement on F^2 with 3503 unique intensities and 173 parameters converged at $\omega R(F^2) = 0.1915$ ($R(F) = 0.0835$) for 2299 observed reflections with $I > 2\sigma(I)$. CCDC 2110271. **(1*S*,2*S*,3*R*,5*R*)-2,6,6-Trimethyl-N-[(α *R*)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-isopino-*R,R*)** was also formed in about 9% yield, but could not be separated. Its structure was assigned by X-ray diffraction of the corresponding carboxamide **4-O₂NC₆H₄CO-isopino-*R,R*** [white solid; mp 61-63 °C; Rf (heptane-AcOEt 90:10) 0.3; 1H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, 3H, $J = 7.7$ Hz), 1.16 (s, 3H), 1.20-1.28 (m, 1H), 1.38 (s, 3H), 1.57 (d, 3H, $J = 6.8$ Hz), 1.52-1.60 (m, 1H), 1.69 (dd, 1H, $J = 10.2$ and 6.0 Hz), 1.83 (ddd, 1H, $J =$

13.8, 8.6 and 5.5 Hz), 1.99 (dd, 1H, $J = 11.3$ and 5.6 Hz), 2.05-2.12 (m, 1H), 3.24 (t, 1H, $J = 11.6$ Hz), 3.90 (q, 1H, $J = 9.6$ Hz), 4.86 (q, 1H, $J = 6.8$ Hz), 7.28-7.39 (m, 5H), 7.65-7.69 (m, 2H), 8.33-8.36 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 16.8 (CH_3), 17.8 (CH_3), 22.8 (CH_3), 27.2 (CH_2), 28.6 (CH_3), 28.8 (CH_2), 39.7 (CH), 40.4 (C), 41.8 (CH), 48.4 (CH), 51.2 (CH), 58.5 (CH), 124.5 (2CH, Ph), 126.6 (2CH, Ph), 127.7 (2CH, Ph), 128.4 (CH), 128.7 (2CH, Ph), 139.1 (C), 145.5 (C), 147.8 (C), 170.1 (C , $\text{C}=\text{O}$); HRMS (ESI; MeOH), m/z 407.2339 (1 ppm) found (calcd for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_3$, $[\text{M}+\text{H}]^+$, requires 407.23347)] formed by reaction of a fraction containing it with 4-nitrobenzoyl chloride. *Crystal data for 4-O₂NC₆H₄CO-isopino-*R,R**: $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_3$, $M = 406.51$, 150(2)K, orthorhombic, $P 2_1 2_1 2_1$, $a = 7.4497(2)$, $b = 15.2211(5)$, $c = 19.6694(6)$ Å, $V = 2230.37(12)$ Å³, $Z = 4$, $d = 1.211$ g cm⁻³, $\mu = 0.079$ mm⁻¹. A final refinement on F^2 with 4968 unique intensities and 275 parameters converged at $\omega R(F^2) = 0.0888$ ($R(F) = 0.0417$) for 4331 observed reflections with $I > 2\sigma(I)$. CCDC 2110269.



(1*S*,2*R*,3*S*,5*R*)-2,6,6-Trimethyl-*N*-[(α *S*)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*S,S*) and **(1*S*,2*R*,3*R*,5*R*)-2,6,6-trimethyl-*N*-[(α *S*)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*S,R*)**

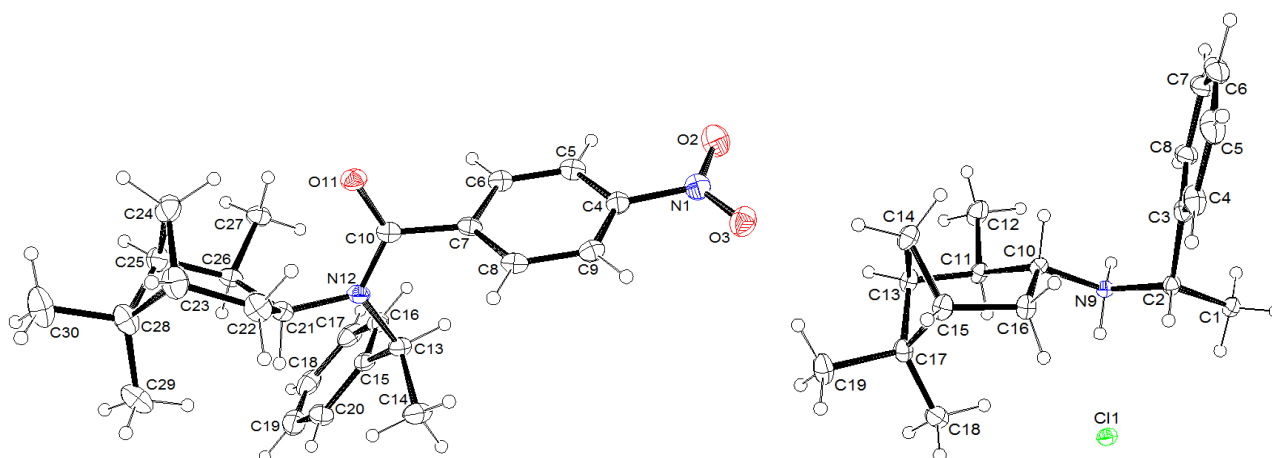


A mixture of (-)-isopinocampone⁷ (3.7 g, 24.5 mmol), (*R*)- α -methylbenzylamine (6.3 mL, 49 mmol), and camphorsulfonic acid (57 mg, 0.245 mmol) was heated under stirring in the presence of 4Å molecular sieves (8.5 g) at 150 °C for 5 days. The mixture was cooled and filtered through celite (washing using 100 mL Et₂O). The organic solution was washed with saturated aqueous NaHCO₃ (2 x 10 mL), saturated aqueous NaHSO₃ (3 x 10 mL), and brine (10 mL). It was then dried (Na₂SO₄) and evaporated. The imine,⁸ obtained in 75% yield, was directly used in the reduction step. A solution of the imine (4.4 g, 17 mmol) in MeOH (25 mL) was progressively treated by NaBH₄ (1.3 g, 34 mmol) at 0 °C over a period of 2-3 h. The mixture was then stirred at room temperature for 20 h. MeOH was removed under reduced pressure and water (30 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 30 mL). The organic solution was washed with 20% FeSO₄ (2 x 30 mL) and brine (30 mL). It was then dried (Na₂SO₄) and evaporated before separation of the 85:15 stereoisomeric mixture by column chromatography over silica gel (eluent: heptane-Et₃N 99:1 for silica wash then heptane-Et₂O 99:1).

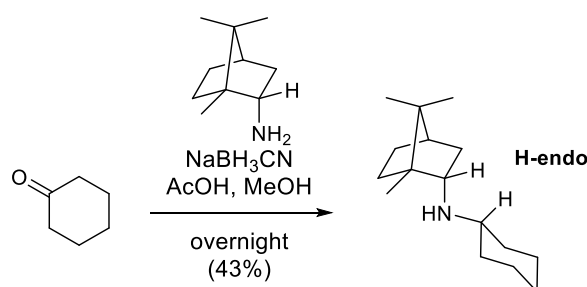
(1*S*,2*R*,3*S*,5*R*)-2,6,6-Trimethyl-*N*-[(α *S*)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*S,S*) was first isolated in 14% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 90:10) 0.6; [α]_D -112.4 (c 2.5); ¹H NMR (300 MHz, CDCl₃) δ 0.78 (s, 3H, Me, Me₂C), 1.03 (d, 3H, *J* = 7.2 Hz, Me-C ζ), 1.17 (s, 3H, Me, Me₂C), 1.16-1.21 (m, 1H, NH), 1.29 (d, 3H, *J* = 6.6 Hz, Me-C α'), 1.32-1.34 (m, 1H, H η), 1.48-1.56 (m, 1H, H ζ), 1.69 (td, 1H, *J* = 5.8 and 2.4 Hz, H γ), 1.83 (ddd, 1H, *J* = 8.9, 5.9 and 3.1 Hz, H β), 2.03-2.49 (m, 3H, H ϵ , H ζ and H η), 3.06 (td, 1H, *J* = 9.1 and 4.3 Hz, H α), 3.81 (q, 1H, *J* = 6.6 Hz, H α'), 7.19-7.25 (m, 1H), 7.28-7.38 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 15.5 (CH₃, Me-C β), 21.0 (CH₃, Me₂C), 24.1 (CH₃, Me-C α'), 27.1 (CH₃, Me₂C), 27.5 (CH₂, C η), 34.5 (CH, C β), 37.6 (CH₂, C ζ), 39.0 (C, C δ , CMe₂), 41.3 (CH, C ϵ), 48.2 (CH, C γ), 49.2 (CH, C α), 57.0 (CH, C α'), 126.7 (CH, C α'), 126.8 (2CH, C $2'$ and C $6'$), 128.3 (2CH, C $3'$ and C $5'$), 147.2 (C, C $1'$); HRMS (ESI; MeOH), *m/z* 258.2221 (0 ppm) found (calcd for C₁₈H₂₈N, [M+H]⁺, requires 258.22218). Its structure was assigned by X-ray diffraction of the corresponding carboxamide **4-O₂NC₆H₄CO-pino-*S,S*** [white solid; mp 153-154 °C; [α]_D -164.3 (c 0.35); ¹H NMR (300 MHz, CDCl₃) δ 0.86 (s, 3H), 0.88 (s, 3H), 1.20 (s, 3H), 1.40-1.65 (m, 5H), 1.93-2.24 (m, 4H), 2.84 (dd, 1H, *J* = 12.8 and 7.4 Hz), 3.87-

3.98 (m, 1H), 4.82 (q, 1H, $J = 6.8$ Hz), 7.26-7.41 (m, 5H), 7.64 (d, 2H, $J = 8.7$ Hz), 8.35 (d, 2H, $J = 8.7$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 16.4 (CH_3), 18.4 (CH_3), 21.6 (CH_3), 26.2 (CH_2), 27.6 (CH_3), 31.9 (CH_2), 36.7 (CH), 39.6 (C), 42.5 (CH), 49.1 (CH), 49.5 (CH), 58.5 (CH), 124.5 (2CH, Ph), 126.7 (2CH, Ph), 127.9 (2CH, Ph), 128.5 (CH , Ph), 128.8 (2CH, Ph), 139.0 (C), 145.4 (C), 147.9 (C), 169.2 (C, C=O); HRMS (ESI; MeOH), m/z 429.2157 (1 ppm) found (calcd for $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_3\text{Na}$, $[\text{M}+\text{Na}]^+$, requires 429.21541)] formed by reaction of **H-pino-S,S** with 4-nitrobenzoyl chloride. *Crystal data for 4-O₂NC₆H₄CO-pino-S,S*: $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_3$, $M = 406.51$, 150(2)K, orthorhombic, $P 2_1 2_1 2_1$, $a = 7.7346(6)$, $b = 14.3407(9)$, $c = 39.815(3)$ Å, $V = 4416.3(6)$ Å³, $Z = 8$, $d = 1.223$ g cm⁻³, $\mu = 0.080$ mm⁻¹. A final refinement on F^2 with 9897 unique intensities and 549 parameters converged at $\omega R(F^2) = 0.0915$ ($R(F) = 0.0450$) for 7802 observed reflections with $I > 2\sigma(I)$. CCDC 2110273. **(1S,2R,3R,5R)-2,6,6-Trimethyl-N-[(α S)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-S,R)** was next isolated in 79% yield as a colorless syrupy liquid: R_f (heptane-Et₂O 90:10) 0.6; $[\alpha]_D -126.1$ (c 4.5); ^1H NMR (500 MHz, CDCl_3) δ 0.87 (d, 3H, $J = 6.7$ Hz, $\text{Me-C}\beta$), 0.90 (s, 3H, Me_2C), 1.10-1.13 (m, 1H, $\text{H}\eta$), 1.20 (s, 3H, Me_2C), 1.20-1.30 (br s, 1H, NH), 1.37 (d, 3H, $J = 6.6$ Hz, $\text{Me-C}\alpha'$), 1.58 (dd, 1H, $J = 11.3$ and 6.0 Hz, $\text{H}\zeta$), 1.61 (td, 1H, $J = 5.8$ and 1.1 Hz, $\text{H}\gamma$), 1.73 (p, 1H, $J = 6.8$ Hz, $\text{H}\beta$), 1.89-1.94 (m, 2H, $\text{H}\epsilon$ and $\text{H}\zeta/\text{H}\eta$), 2.16-2.24 (m, 2H, $\text{H}\alpha$ and $\text{H}\zeta/\text{H}\eta$), 3.95 (q, 1H, $J = 6.6$ Hz, $\text{H}\alpha'$), 7.24-7.28 (m, 1H, $\text{H}4'$), 7.32-7.37 (m, 4H, $\text{H}2'$, $\text{H}3'$, $\text{H}5'$ and $\text{H}6'$); ^{13}C NMR (126 MHz, CDCl_3) δ 19.3 (CH_3 , $\text{Me-C}\beta$), 20.2 (CH_3 , Me_2C), 23.8 (CH_2 , $\text{C}\eta$), 25.9 (CH_3 , $\text{Me-C}\alpha'$), 26.6 (CH_3 , Me_2C), 33.5 (CH_2 , $\text{C}\zeta$), 38.1 (CH , $\text{C}\beta$), 39.6 (C, $\text{C}\delta$, CMe_2), 40.7 (CH , $\text{C}\epsilon$), 47.3 (CH , $\text{C}\gamma$), 52.3 (CH , $\text{C}\alpha$), 54.9 (CH , $\text{C}\alpha'$), 126.8 (2CH, $\text{C}2'$ and $\text{C}6'$), 126.9 (CH , $\text{C}4'$), 128.4 (2CH, $\text{C}3'$ and $\text{C}5'$), 145.9 (C, $\text{C}1'$); HRMS (ESI; MeOH), m/z 258.2224 (1 ppm) found (calcd for $\text{C}_{18}\text{H}_{28}\text{N}$, $[\text{M}+\text{H}]^+$, requires 258.22218). The corresponding carboxamide [white solid; mp 129-130 °C; HRMS (ESI; MeOH), m/z 407.2334 (0 ppm) found (calcd for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_3$, $[\text{M}+\text{H}]^+$, requires 407.23347)] was prepared by reaction of **H-pino-S,R** with 4-nitrobenzoyl chloride, but did not afford suitable crystals for X-ray diffraction. However, the structure of **H-pino-S,R** was confirmed unambiguously by X-ray diffraction of the corresponding hydrochloride. *Crystal data for H-pino-S,R·HCl*: $\text{C}_{18}\text{H}_{28}\text{ClN}$, $M = 293.86$, 150(2)K, monoclinic, $P 2_1$, $a = 11.2823(3)$, $b = 7.3708(2)$, $c = 11.7289(3)$ Å, $\beta = 118.3930(10)^\circ$, $V = 858.04(4)$

\AA^3 , $Z = 2$, $d = 1.137 \text{ g cm}^{-3}$, $\mu = 0.215 \text{ mm}^{-1}$. A final refinement on F^2 with 3854 unique intensities and 185 parameters converged at $\omega R(F^2) = 0.0705$ ($R(F) = 0.0266$) for 3724 observed reflections with $I > 2\sigma(I)$. CCDC 2110272.



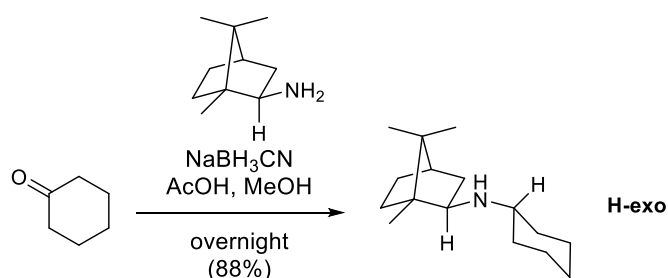
Endo-N-cyclohexylbornylamine (H-endo)⁹



Endo-bornylamine was first prepared from **H-endo-born-S** as follows. To **H-endo-born-S** (1.3 g, 5.0 mmol) in ethanol (50 mL) were added 10% Pd(OH)₂ on charcoal (70 mg, 20 μ mol) and ammonium formate (1.9 g, 30 mmol) under argon. The reaction mixture was refluxed for 2.5 h, cooled and filtrated over celite. The filtrate was concentrated under reduced pressure; the residue was diluted with 40 mL diethyl ether and stirred with 20 mL of a saturated aqueous potassium carbonate solution. The organic phase was filtrated over celite, dried over sodium sulfate, and the solvent was removed under reduced pressure. The white solid, obtained in 87% yield ($[\alpha]_{\text{D}} +37.3$ (c 0.75); ¹H NMR (300 MHz, CDCl₃) δ 0.68 (dd, 1H, $J = 13.0$ and 4.5 Hz), 0.76 (s, 3H, Me), 0.86 (s, 6H, Me), 1.06-1.30 (m, 3H), 1.56 (t, 1H, $J = 4.5$ Hz), 1.61-1.77 (m, 2H), 2.19-2.29 (m, 1H), 3.03 (ddd, 1H, $J = 10.6$, 4.5 and 2.0 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 13.4 (CH₃), 18.5 (CH₃), 20.4 (CH₃), 26.3 (CH₂), 28.5 (CH₂), 39.8 (CH₂), 45.1 (CH), 48.2 (C), 49.1 (C), 56.7 (CH); HRMS (ESI; MeOH), m/z 154.1596 (0 ppm)

found (calcd for $C_{10}H_{20}N$, $[M+H]^+$, requires 154.15957)), was directly involved in the following step. To a stirred solution of *endo*-bornylamine (0.77 g, 5.0 mmol) in dry methanol (20 mL) were added cyclohexanone (2.1 mL, 20 mmol) and sodium cyanoborohydride (0.315 g, 5.0 mmol) at room temperature. The solution was then cooled to 0 °C before addition of acetic acid (to adjust the pH at 6) and the reaction mixture was stirred overnight. Methanol was removed under reduced pressure and 40% aqueous potassium carbonate (30 mL) was added. After extraction with diethyl ether (3 x 25 mL), the organic solution was washed with brine (15 mL). It was then evaporated until a total volume of 6 mL remained. The mixture was acidified at 0 °C by using (~ 3 mL) concentrated hydrochloric acid. The precipitate was filtrated, washed three times with diethyl ether, dissolved in water (30 mL). The aqueous phase was basified with aqueous 2 M sodium hydroxide, and extracted by diethyl ether (3 x 20 mL). The organic phase was washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure before isolation of the product by column chromatography over silica gel (eluent: heptane-AcOEt- Et_3N 97:2:1) in 43% yield as a colorless oil: R_f (heptane-AcOEt 80:20) 0.4; $[\alpha]_D +71.4$ (c 0.35); 1H NMR (300 MHz, $CDCl_3$) δ 0.77 (dd, 1H, $J = 12.7$ and 4.2 Hz), 0.82 (s, 3H, Me), 0.85 (s, 3H, Me), 0.86 (s, 3H, Me), 0.95-1.31 (m, 8H), 1.57-1.88 (m, 8H), 2.20 (dddd, 1H, $J = 12.9$, 10.1, 4.8 and 3.1 Hz), 2.40 (tt, 1H, $J = 10.3$ and 3.7 Hz), 2.86 (ddd, 1H, $J = 10.1$, 4.2 and 1.9 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.2 (CH_3), 18.8 (CH_3), 20.0 (CH_3), 25.4 (CH_2), 25.5 (CH_2), 26.3 (CH_2), 27.5 (CH_2), 28.6 (CH_2), 34.1 (CH_2), 34.8 (CH_2), 40.2 (CH_2), 45.3 (CH), 48.2 (C), 48.9 (C), 56.8 (CH), 60.5 (CH); HRMS (ESI; MeOH), m/z 236.2374 (2 ppm) found (calcd for $C_{16}H_{30}N$, $[M+H]^+$, requires 236.23783).

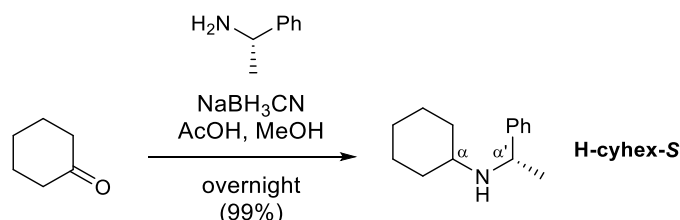
***Exo*-*N*-cyclohexylbornylamine (H-*exo*)⁹**



Exo-bornylamine was first prepared from **H-*exo*-born-*R*** as follows. To **H-*exo*-born-*R*** (1.3 g, 5.0 mmol) in ethanol (50 mL) were added 10% Pd(OH)₂ on charcoal (70 mg, 20 μmol) and ammonium formate (1.9 g, 30 mmol) under argon. The reaction mixture was refluxed for 5 h, cooled and filtrated over celite. The filtrate was concentrated under reduced pressure; the residue was diluted with 40 mL diethyl ether and stirred with 20 mL of a saturated aqueous potassium carbonate solution. The organic phase was filtrated over celite, dried over sodium sulfate, and the solvent was removed under reduced pressure. The white solid, obtained in 85% yield ($[\alpha]_D$ -35.0 (c 0.2); ¹H NMR (300 MHz, CDCl₃) δ 0.78 (s, 3H, Me), 0.83 (s, 3H, Me), 0.94 (s, 3H, Me), 0.91-1.08 (m, 2H), 1.26 (br s, 2H, NH₂), 1.42-1.56 (m, 2H), 1.59-1.70 (m, 2H), 1.71 (dd, 1H, *J* = 12.8 and 8.7 Hz), 2.67 (dd, 1H, *J* = 8.8 and 5.2 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 12.0 (CH₃), 20.4 (CH₃), 21.0 (CH₃), 27.3 (CH₂), 36.5 (CH₂), 40.7 (CH₂), 45.1 (CH), 46.7 (C), 48.2 (C), 60.5 (CH); HRMS (ESI; MeOH), *m/z* 154.1598 (2 ppm) found (calcd for C₁₀H₂₀N, [M+H]⁺, requires 154.15957)), was directly involved in the following step. To a stirred solution of *exo*-bornylamine (0.77 g, 5.0 mmol) in dry methanol (20 mL) were added cyclohexanone (2.1 mL, 20 mmol) and sodium cyanoborohydride (0.315 g, 5.0 mmol) at room temperature. The solution was then cooled to 0 °C before addition of acetic acid (to adjust the pH at 6) and the reaction mixture was stirred overnight. Methanol was removed under reduced pressure and 40% aqueous potassium carbonate (30 mL) was added. After extraction with diethyl ether (3 x 25 mL), the organic solution was washed with brine (15 mL). It was then evaporated until a total volume of 6 mL remained. The mixture was acidified at 0 °C by using (~ 3 mL) concentrated hydrochloric acid. The precipitate was filtrated, washed three times with diethyl ether, dissolved in water (30 mL). The aqueous phase was basified with aqueous 2 M sodium hydroxide, and extracted by diethyl ether (3 x 20 mL). The organic phase was washed with brine, dried (Na₂SO₄) and the solvent was removed under reduced pressure before isolation of the product by column chromatography over silica gel (eluent: heptane-AcOEt-Et₃N 97:2:1) in 88% yield as a colorless oil: *R*_f (heptane-AcOEt 80:20) 0.6; $[\alpha]_D$ -66.5 (c 1.0); ¹H NMR (300 MHz, CDCl₃) δ 0.78 (s, 3H, Me), 0.85 (s, 3H, Me), 0.97 (s, 3H, Me), 0.78-1.29 (m, 8H), 1.44-1.72 (m, 8H), 1.77-1.87 (m, 2H), 2.33 (tt, 1H, *J* = 10.3 and 3.7 Hz), 2.59 (dd, 1H, *J* = 7.8 and 5.5 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 12.4 (CH₃), 20.7 (2CH₃), 25.4

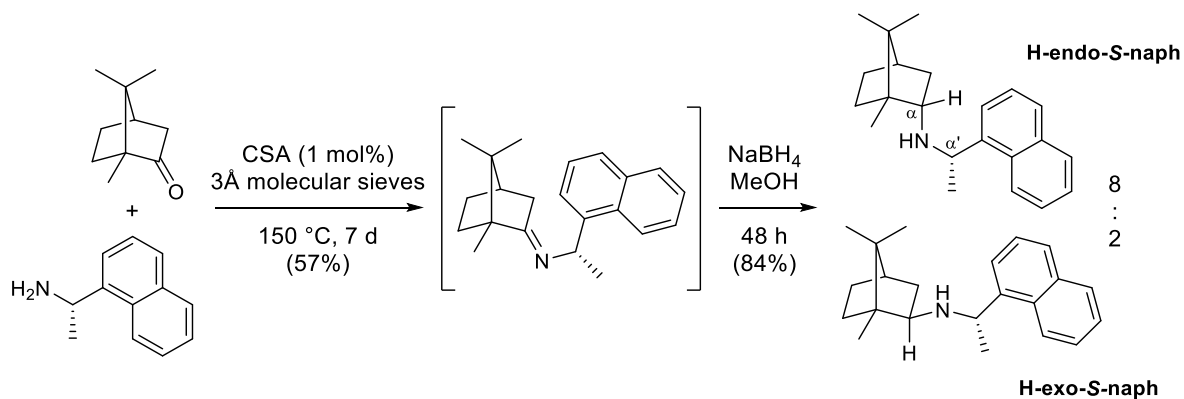
(CH₂), 26.4 (CH₂), 27.5 (CH₂), 33.8 (CH₂), 35.0 (CH₂), 37.3 (CH₂), 40.9 (CH₂), 45.5 (CH), 46.8 (C), 48.4 (C), 56.3 (CH), 64.0 (CH); HRMS (ESI; MeOH), *m/z* 236.2367 (5 ppm) found (calcd for C₁₆H₃₀N, [M+H]⁺, requires 236.23783).

((*S*)- α -phenylethyl)cyclohexylamine (H-cyhex-S**)**



To a stirred solution of (*S*)- α -methylbenzylamine (1.3 mL, 10 mmol) in dry methanol (25 mL) were added cyclohexanone (2.6 mL, 25 mmol) and sodium cyanoborohydride (0.63 g, 10 mmol) at room temperature. The solution was then cooled to 0 °C before addition of acetic acid (to adjust the pH at 6) and the reaction mixture was stirred overnight. Methanol was removed under reduced pressure and 40% aqueous potassium carbonate (40 mL) was added. After extraction with diethyl ether (3 x 30 mL), the organic solution was washed with brine (20 mL). It was then evaporated until a total volume of 8 mL remained. The mixture was acidified at 0 °C by using (~ 4 mL) concentrated hydrochloric acid. The precipitate was filtrated, washed three times with diethyl ether, dissolved in water (40 mL). The aqueous phase was basified with aqueous 2 M sodium hydroxide, and extracted by diethyl ether (3 x 30 mL). The organic phase was washed with brine, dried (Na₂SO₄) and the solvent was removed under reduced pressure before isolation of the product by column chromatography over silica gel (eluent: heptane-Et₂O-Et₃N 88:10:2) as a colorless oil: *R_f* (heptane-AcOEt 80:20) 0.2; [α]_D -68.8 (c 1.0); ¹H NMR (300 MHz, CDCl₃) δ 0.93-1.18 (m, 6H), 1.32 (d, 3H, *J* = 6.6 Hz, Me), 1.52-1.71 (m, 4H), 1.96-2.00 (m, 1H), 2.23-2.31 (m, 1H), 3.95 (q, 1H, *J* = 6.6 Hz, H α '), 7.20-7.35 (m, 5H, Ph); ¹³C NMR (126 MHz, CDCl₃) δ 25.0 (CH₂), 25.1, 25.3 (CH₂), 26.2 (CH₂), 33.3 (CH₂), 34.6 (CH₂), 53.6, 54.5, 126.5 (2CH, C2' and C6'), 126.7 (CH, C4'), 128.4 (2CH, C3' and C5'), 146.4 (C, C1'). The analyses were as reported.¹⁰

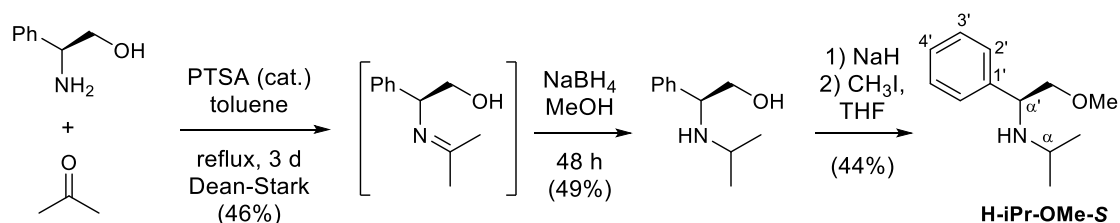
Endo-(1S)-N-(1-(1-naphthyl)ethyl)bornylamine (H-endo-S-naph)



It was prepared by adapting a procedure described:⁴ A mixture of (*S*)- α -methyl-2-naphtylamine (2.4 mL, 15 mmol), D-camphor (1.5 g, 10 mmol), and camphorsulfonic acid (23 mg, 0.10 mmol) was heated under stirring in the presence of 3Å molecular sieves (3 g) at 150 °C for 7 days. The mixture was cooled and filtered through celite (washing using 20 mL Et₂O). The organic solution was washed with saturated aqueous NaHCO₃ (2 x 7 mL), saturated aqueous NaHSO₃ (2 x 7 mL), and brine (7 mL). It was then dried (Na₂SO₄) and evaporated. The imine, obtained in 57% yield, was directly involved in the reduction step. A solution of the imine (1.7 g, 5.7 mmol) in MeOH (15 mL) was treated by NaBH₄ (0.43 g, 11.3 mmol) at 0 °C over a period of 1 h. The mixture was then stirred at room temperature for 2 days. MeOH was removed under reduced pressure and water (5 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 10 mL). The organic solution was washed with 20% FeSO₄ (2 x 10 mL) and brine (10 mL). It was then dried (Na₂SO₄) and evaporated before purification by column chromatography over silica gel (eluent: heptane-AcOEt-Et₃N, from 99:0:1 to 95.5:2.5:2). ***Endo-(1S)-N-(1-(1-naphthyl)ethyl)bornylamine (H-endo-S-naph)*** was first isolated in 70% yield as a colorless syrupy liquid: R_f (heptane-AcOEt 80:20) 0.5; [α]_D +41.4 (c 1.0); ¹H NMR (300 MHz, CDCl₃) δ 0.79 (dd, 1H, *J* = 12.7 and 4.4 Hz), 0.79 (s, 3H, Me), 0.83 (s, 3H, Me), 0.85 (s, 3H, Me), 1.12 (ddd, 1H, *J* = 12.2, 9.5 and 4.6 Hz), 1.23-1.33 (m, 1H), 1.46 (d, 3H, *J* = 6.5 Hz, *Me*-Ca'), 1.54 (t, 1H, *J* = 4.6 Hz), 1.57-1.73 (m, 2H), 1.81-1.90 (m, 1H), 2.03-2.14 (m, 1H), 2.96 (ddd, 1H, *J* = 10.3, 4.3 and 2.0 Hz, H α), 4.66 (q, 1H, *J* = 6.5 Hz, H α'), 7.44-7.53 (m, 3H), 7.69 (dd, 1H, *J* = 7.2 and 0.7 Hz), 7.74 (d, 1H, *J* = 8.2 Hz), 7.85-7.88 (m, 1H), 8.24-8.27 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ

14.5 (CH₃), 18.8 (CH₃), 20.1 (CH₃), 23.6 (CH₃), 27.6 (CH₂), 28.7 (CH₂), 38.8 (CH₂), 45.3 (CH), 48.2 (C), 49.2 (C), 53.1 (CH), 61.1 (CH), 123.3 (CH), 123.5 (CH), 125.3 (CH), 125.6 (CH), 125.7 (CH), 127.1 (CH), 129.0 (CH), 131.4 (C), 134.1 (C), 142.9 (C); HRMS (ESI; MeOH), *m/z* 308.2372 (2 ppm) found (calcd for C₂₂H₃₀N, [M+H]⁺, requires 308.23783). **Exo-(1*S*)-N-(1-(1-naphthyl)ethyl)bornylamine (H-exo-*S*-naph)** was next isolated in 14% yield and identified by NMR: ¹H NMR (300 MHz, CDCl₃) δ 0.83 (s, 3H, Me), 0.92 (s, 3H, Me), 0.85-1.03 (m, 2H), 1.03 (s, 3H, Me), 1.25 (br s, 1H, NH), 1.46 (d, 3H, *J* = 6.6 Hz, Me-Cα'), 1.51-1.76 (m, 5H), 3.62 (dd, 1H, *J* = 6.7 and 4.0 Hz, Hα), 4.51 (q, 1H, *J* = 6.6 Hz, Hα'), 7.18-7.25 (m, 1H), 7.35-7.41 (m, 1H), 7.52 (t, 1H, *J* = 7.6 Hz), 7.72 (t, 3H, *J* = 8.4 Hz), 7.84 (dd, 1H, *J* = 8.1 and 1.3 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 11.4 (CH₃), 20.1 (CH₃), 20.5 (CH₃), 24.5 (CH₃), 27.3 (CH₂), 33.9 (CH₂), 40.4 (CH₂), 45.1 (CH), 46.4 (C), 49.0 (C), 51.3 (CH), 80.0 (CH), 122.7 (CH), 123.1 (CH), 125.2 (CH), 125.5 (CH), 125.7 (CH), 127.1 (CH), 128.7 (CH), 131.5 (C), 133.9 (C), 142.0 (C).

(*S*)-N-Isopropyl-*O*-methylphenylglycinol (H-iPr-OMe-*S*)



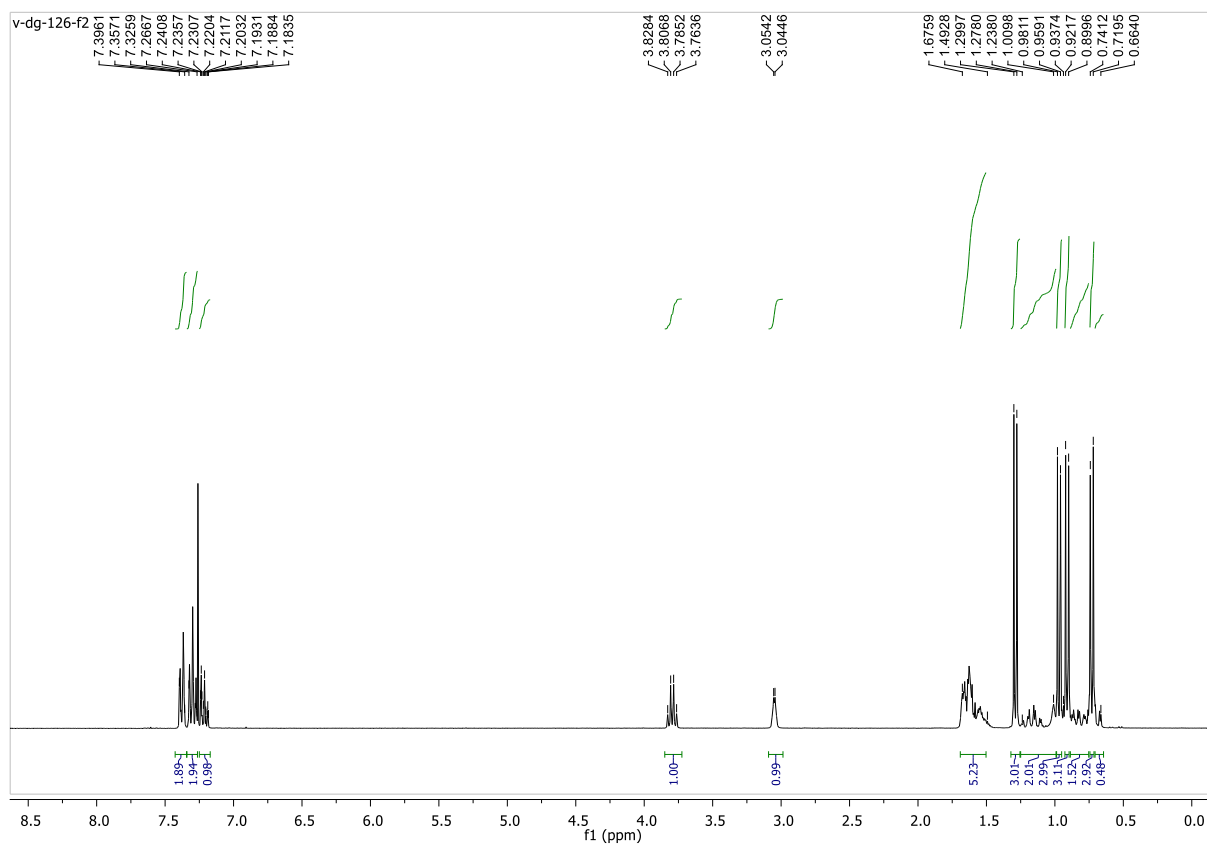
It was prepared by adapting a procedure described.¹¹ A solution of (*S*)-phenylglycinol (2.0 g, 14.8 mmol) and acetone (1.2 mL, 16 mmol) in toluene (30 mL) was treated by a catalytic amount of 4-toluenesulfonic acid. The reaction mixture was heated under reflux for 3 days in the presence of a Dean-Stark trap to remove the formed water. After cooling, the organic phase was washed by a 5% aqueous solution of Na₂CO₃ (20 mL) and brine (20 mL), dried over MgSO₄, and concentrated under vacuum to afford the imine (46% yield), which was directly involved in the reduction step. The imine (0.35 g, 2.0 mmol), obtained as an orange syrupy liquid [¹H NMR (300 MHz, CDCl₃) δ 1.43 (s, 3H, Me), 1.50 (s, 3H, Me), 2.23 (br s, 1H, OH), 3.68 (t, 1H, *J* = 8.0 Hz), 4.26 (t, 1H, *J* = 7.8 Hz), 4.52 (t, 1H, *J* = 7.6 Hz), 7.19-7.39 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 26.8 (CH), 27.7 (CH), 61.7 (CH),

71.8 (CH₂), 95.7 (C), 126.7 (2CH), 127.7 (CH), 128.8 (2CH), 140.4 (C)], was dissolved in MeOH (5 mL) and treated by NaBH₄ (0.15 g, 4.0 mmol) at 0 °C. The mixture was then stirred at room temperature for 2 days. MeOH was removed under reduced pressure and water (5 mL) was added followed by KOH until pH > 10 was attained. The mixture was then saturated with NaCl and extracted with AcOEt (3 x 10 mL). The organic solution was washed with 20% FeSO₄ (2 x 10 mL) and brine (10 mL). It was then dried (Na₂SO₄) and evaporated before purification by column chromatography over silica gel (eluent: heptane-AcOEt-Et₃N, from 98:0:2 to 48:50:2). **(S)-N-Isopropylphenylglycinol** was isolated in 49% yield as a white solid: R_f (heptane-AcOEt 60:40) 0.1; ¹H NMR (300 MHz, CDCl₃) δ 1.03 (t, 6H, *J* = 6.0 Hz, Me₂CH), 2.40 (br s, 2H, OH and NH), 2.74 (hept, 1H, *J* = 6.2 Hz, CHMe₂), 3.47 (dd, 1H, *J* = 10.6 and 8.7 Hz, CHH-OH), 3.67 (dd, 1H, *J* = 10.6 and 4.5 Hz, CHH-OH), 3.86 (dd, 1H, *J* = 8.7 and 4.5 Hz, CHPh), 7.24-7.38 (m, 5H, Ph); ¹³C NMR (75 MHz, CDCl₃) δ 22.3 (CH₃), 24.4 (CH₃), 45.7 (CH), 61.6 (CH), 66.8 (CH₂, CH₂O), 127.1 (2CH), 127.5 (CH, C1'), 127.7 (2CH), 141.3 (C, C4'). These data correspond to those reported for the other enantiomer.¹² By following the reported protocol,¹¹ the aminoalcohol (0.52 g, 2.9 mmol) was next added to washed NaH (0.12 g of a 60% dispersion in oil, 3.2 mmol; washing was carried out by using hexane) in dry THF (5 mL) at 0 °C. After heating for 30 min at 40 °C, and subsequent cooling to room temperature, CH₃I (0.18 mL, 2.9 mmol) was introduced and the reaction mixture was stirred overnight. After slow addition of water (5 mL), extraction was performed by diethyl ether (3 x 10 mL). The combined organic extracts were washed with brine (10 mL) and dried over MgSO₄; the solvent was evaporated before purification by column chromatography over silica gel (eluent: heptane-AcOEt-Et₃N, from 99:0:1 to 89.5:10:0.5). **(S)-N-Isopropyl-O-methylphenylglycinol (H-iPr-OMe-S)** was obtained in 44% yield as a colorless oil: R_f (heptane-AcOEt 50:50) 0.4; ¹H NMR (300 MHz, CDCl₃) δ 0.99 (d, 3H, *J* = 6.4 Hz, Me₂C), 1.03 (d, 3H, *J* = 6.2 Hz, Me₂C), 2.24 (br s, 1H, NH), 2.64 (hept, 1H, *J* = 6.3 Hz, CHMe₂), 3.35 (s, 3H, OMe), 3.39 (dd, 1H, *J* = 9.4 and 8.4 Hz, CHH-OH), 3.45 (dd, 1H, *J* = 9.4 and 4.3 Hz, CHH-OH), 4.01 (dd, 1H, *J* = 8.3 and 4.3 Hz, CHPh), 7.22-7.38 (m, 5H, Ph); ¹³C NMR (75 MHz, CDCl₃) δ 22.0 (CH₃), 24.4 (CH₃), 45.8 (CH), 58.7 (CH₃, OMe),

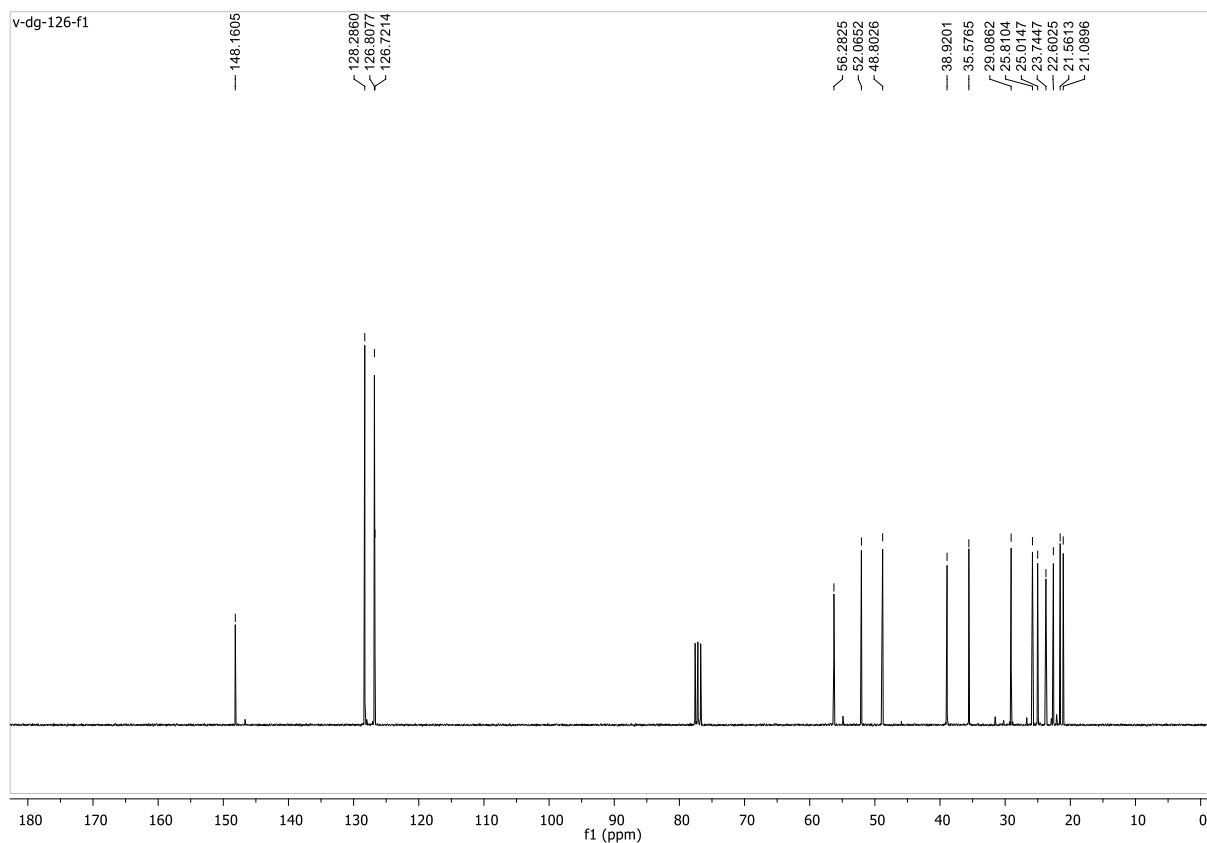
59.9 (CH), 78.0 (CH₂, CH₂O), 127.2 (CH, C4'), 127.6 (2CH), 128.3 (2CH), 141.5 (C, C1'). These data correspond to those reported for the other enantiomer.¹¹

H-menth-*S,S*

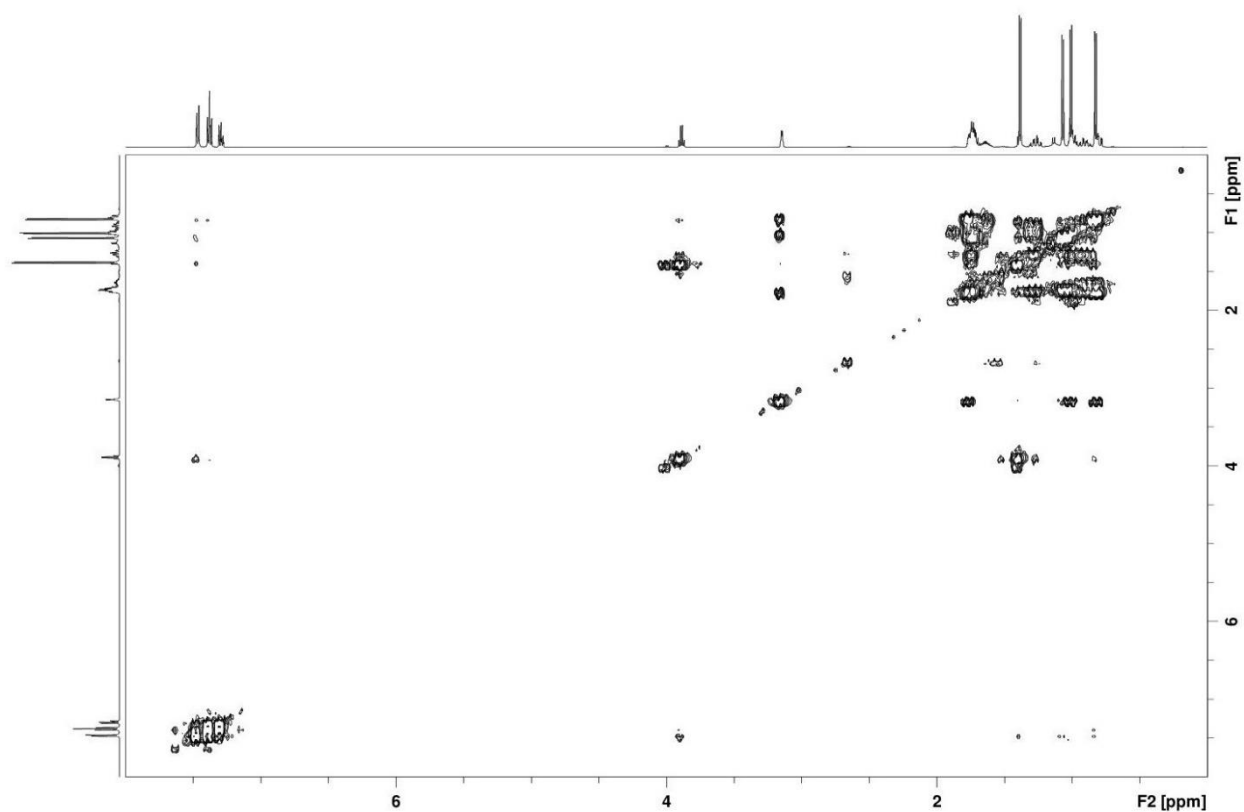
^1H (CDCl_3 , 300 MHz)



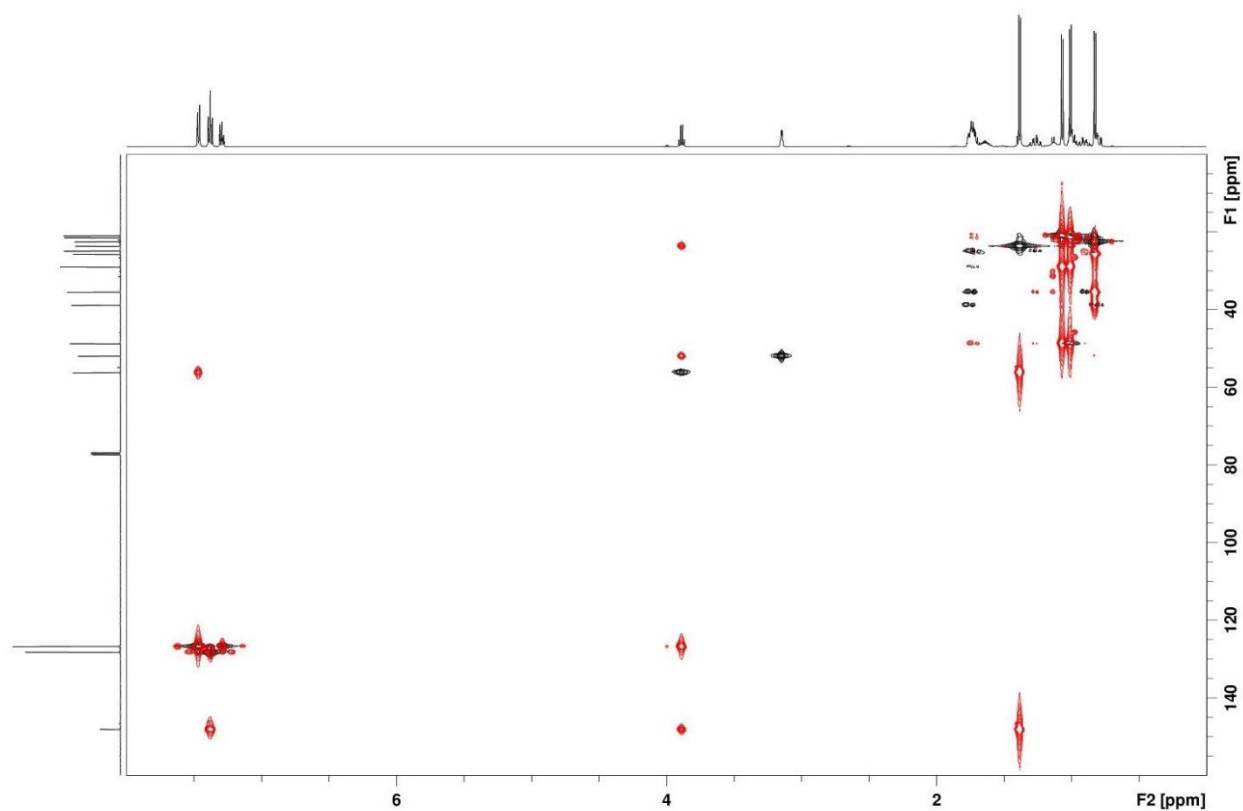
^{13}C (CDCl_3 , 75 MHz)



COSY (CDCl₃, 300 MHz)

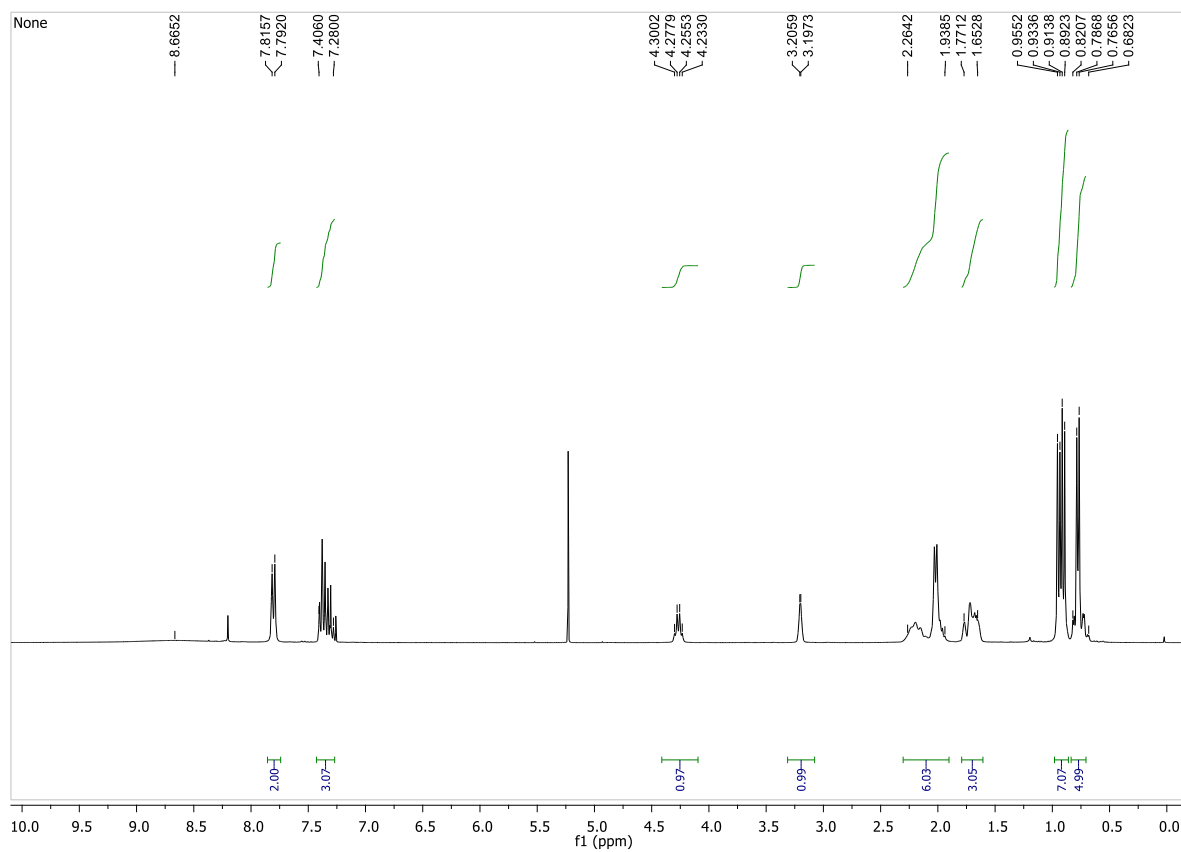


HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)

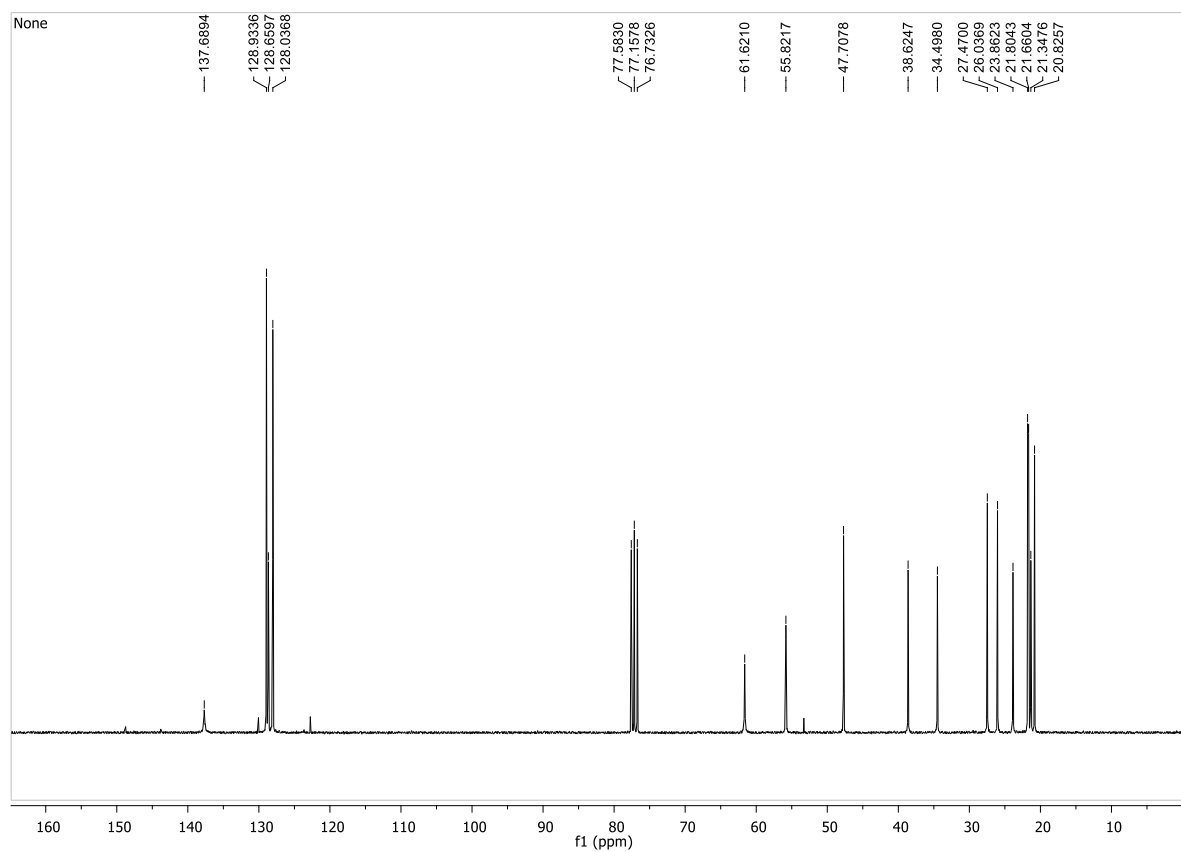


H-menth-*S,S'*-HCl

^1H (CDCl_3 , 300 MHz)

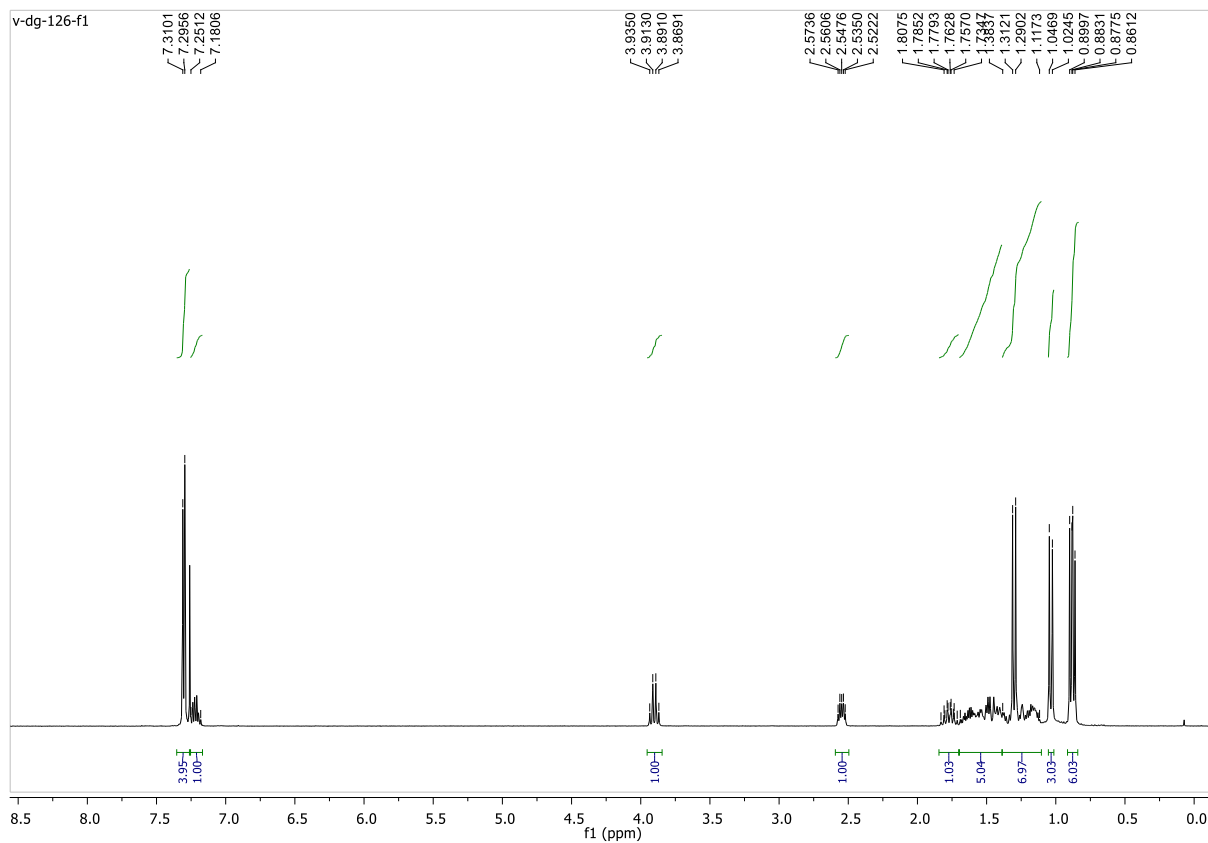


^{13}C (CDCl_3 , 75 MHz)

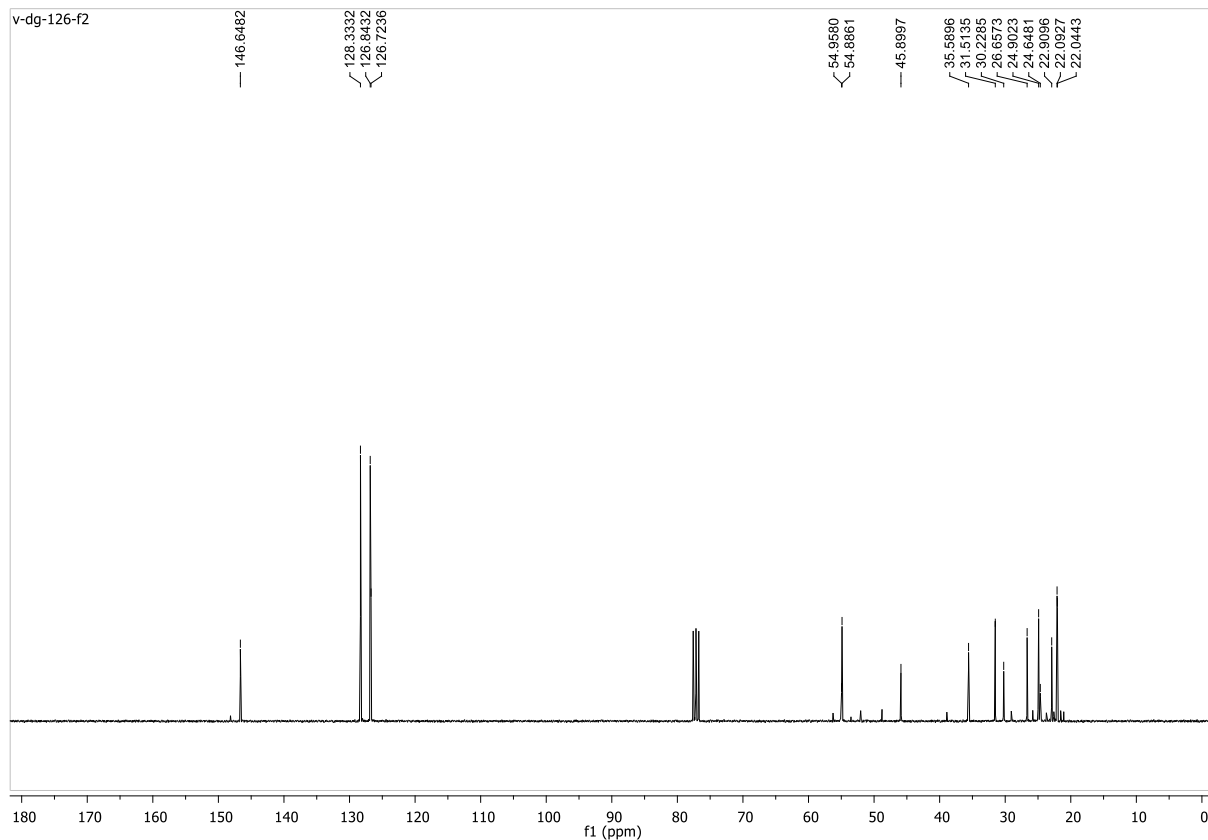


H-menth-*S,R*

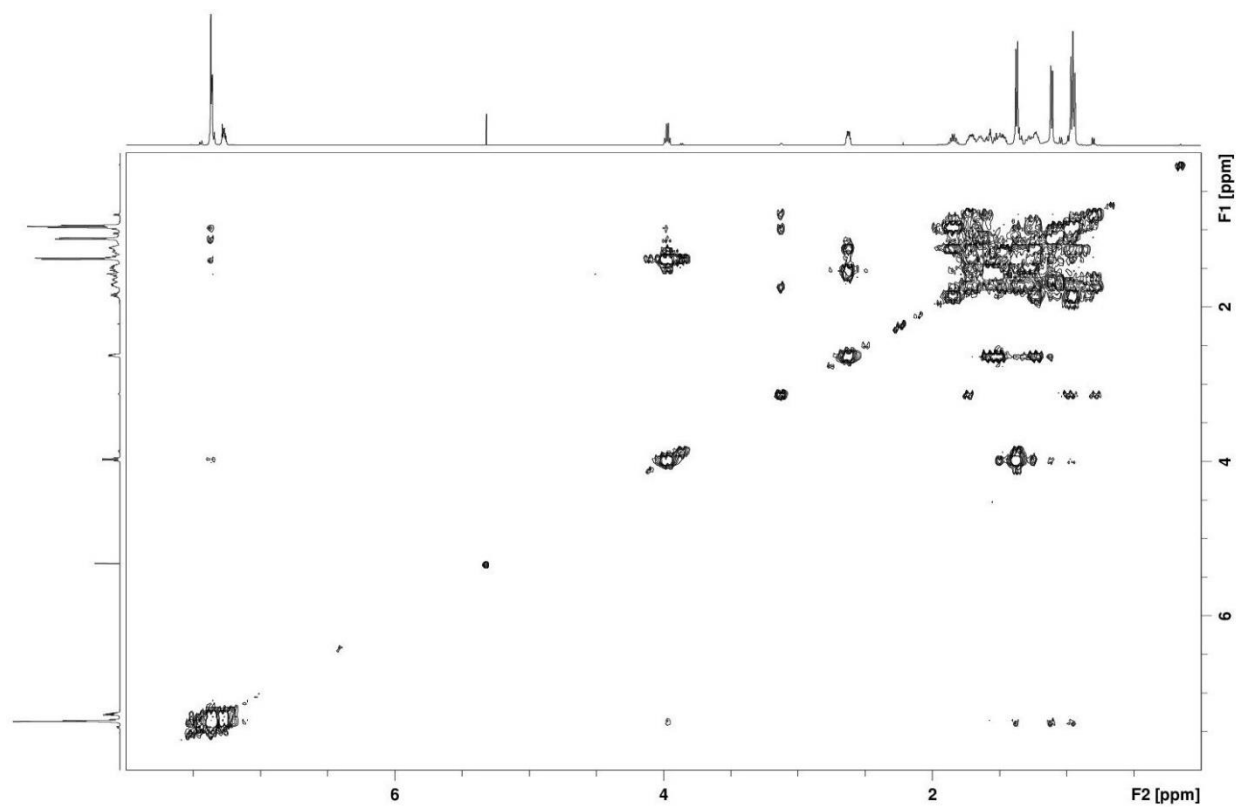
^1H (CDCl_3 , 300 MHz)



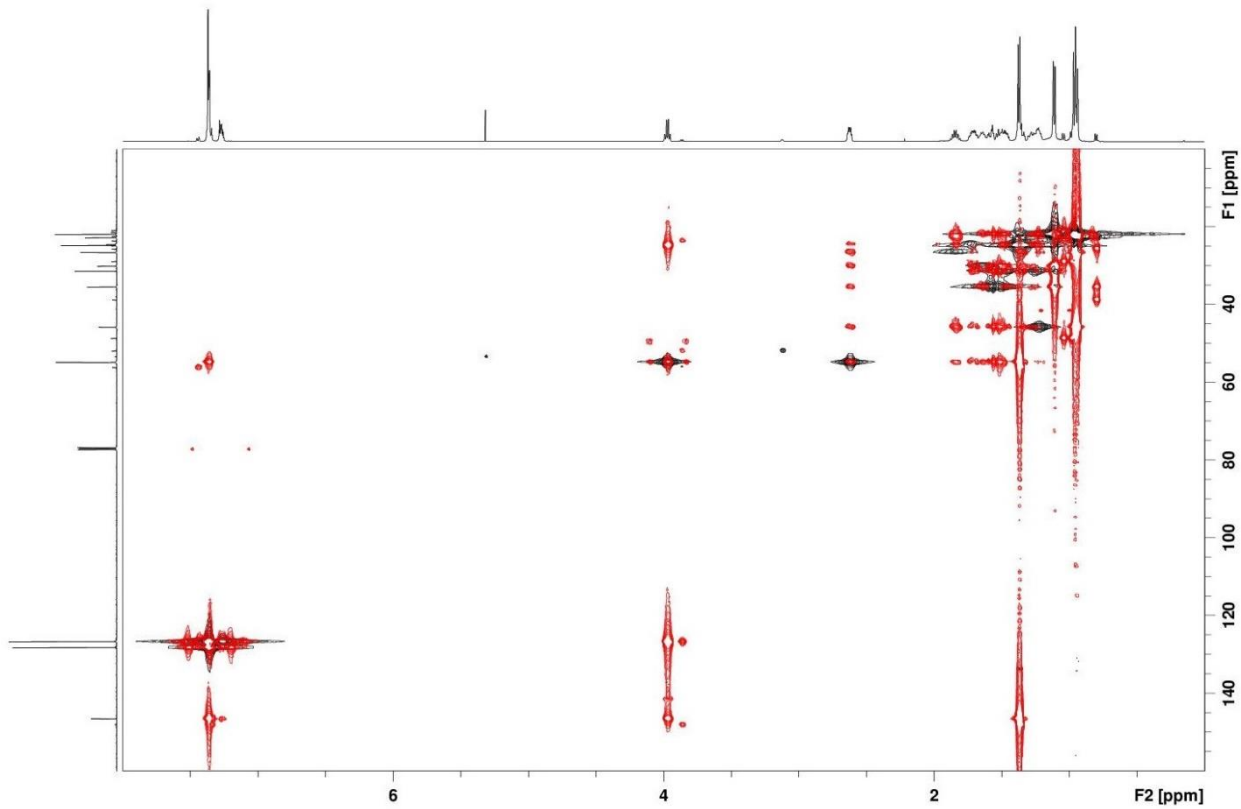
^{13}C (CDCl_3 , 75 MHz)



COSY (CDCl₃, 300 MHz)

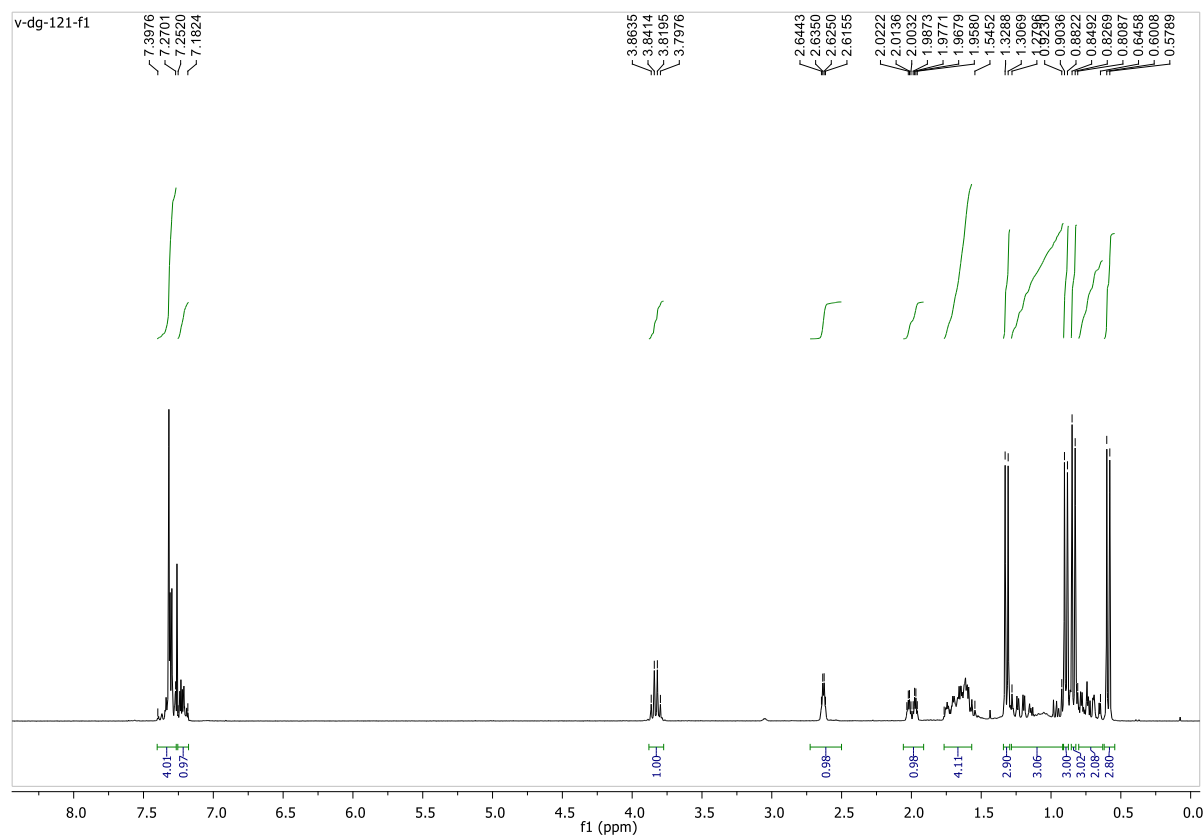


HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)

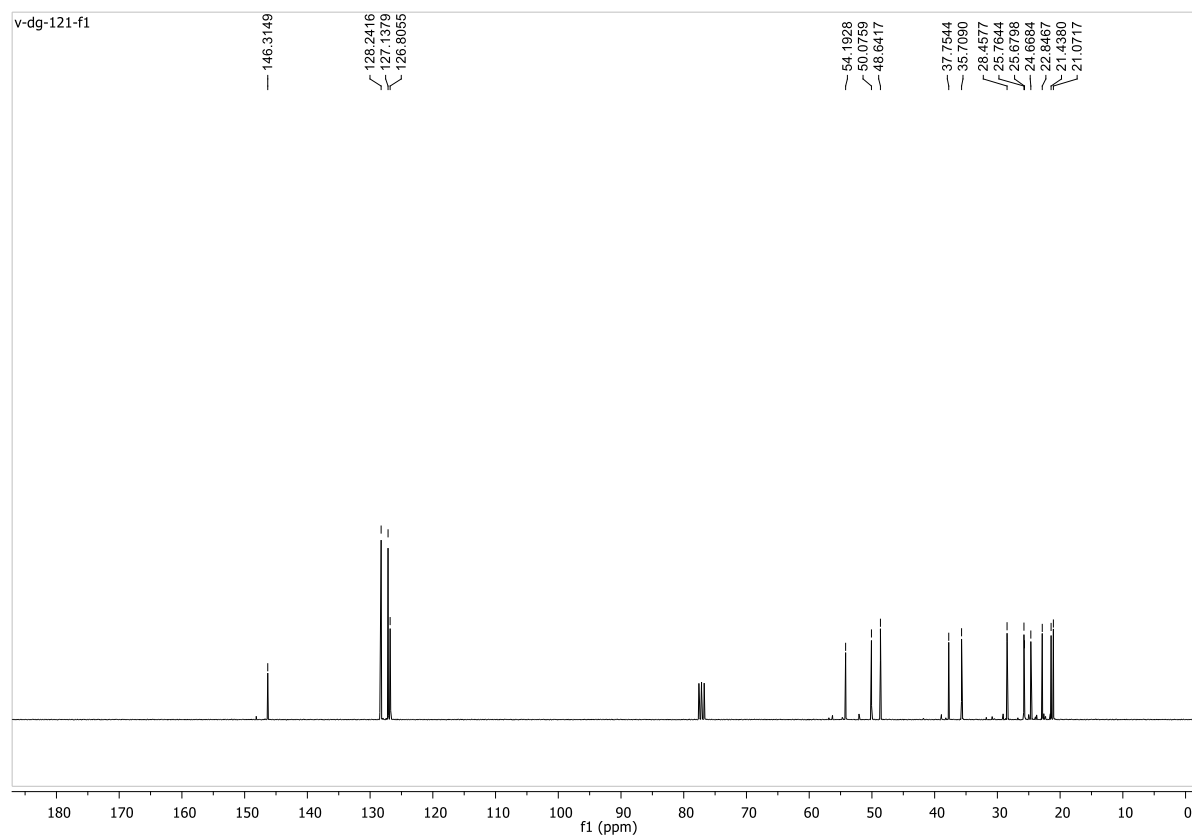


H-menth-*R,S*

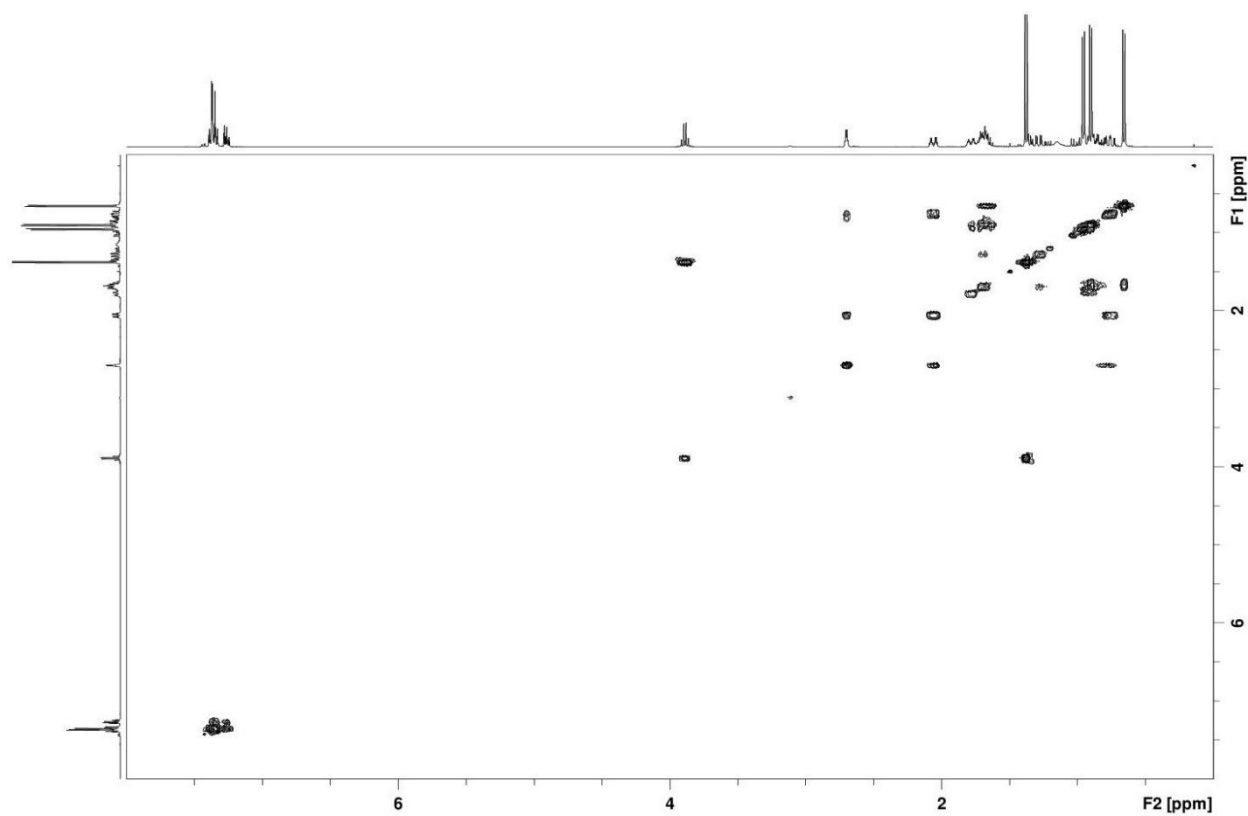
^1H (CDCl_3 , 300 MHz)



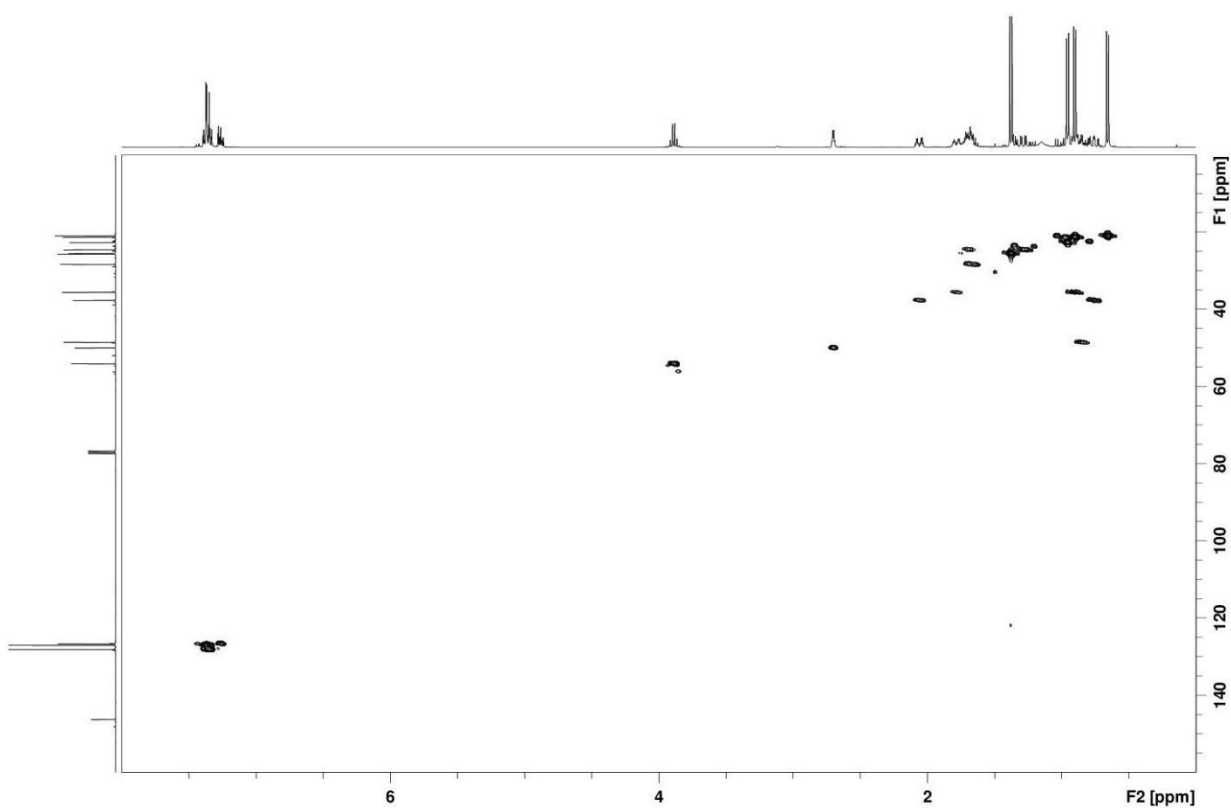
^{13}C (CDCl_3 , 75 MHz)



COSY (CDCl₃, 300 MHz)

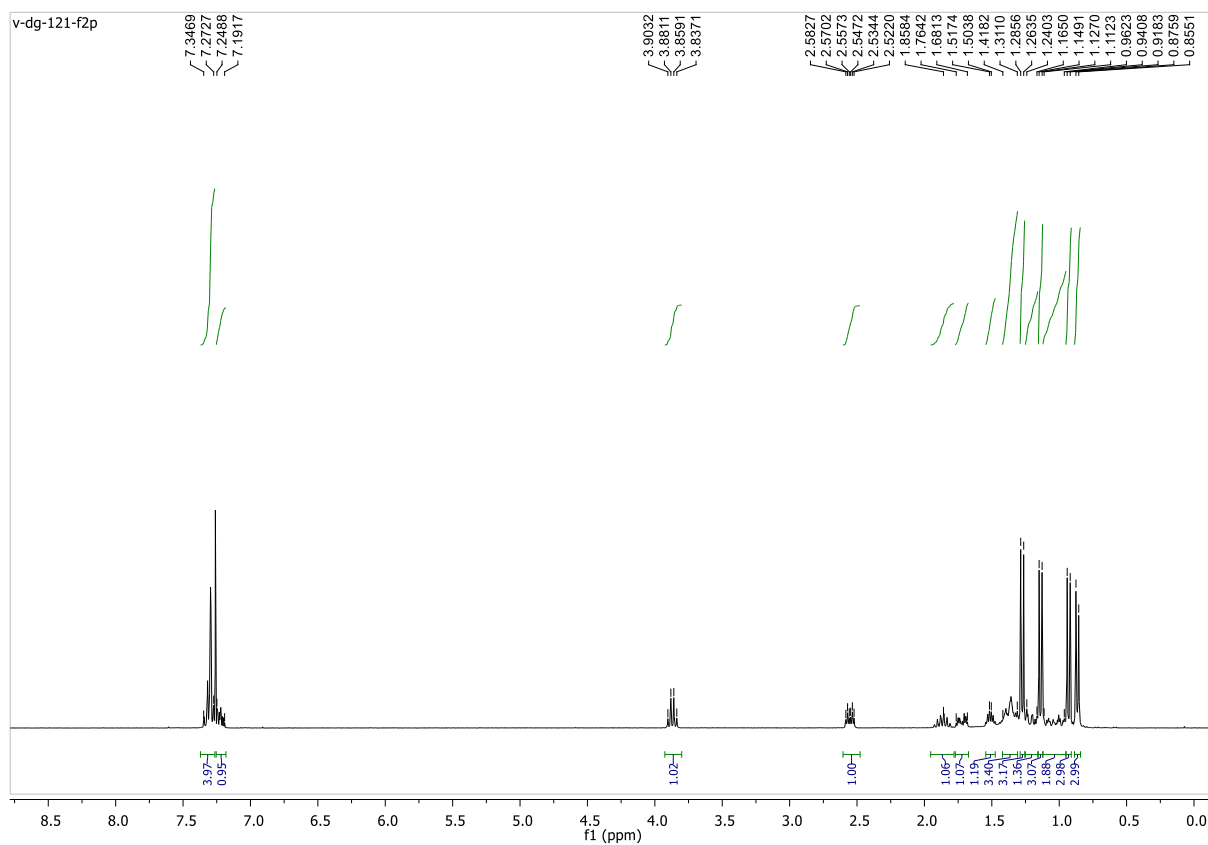


HMQC (CDCl₃, 300 MHz)

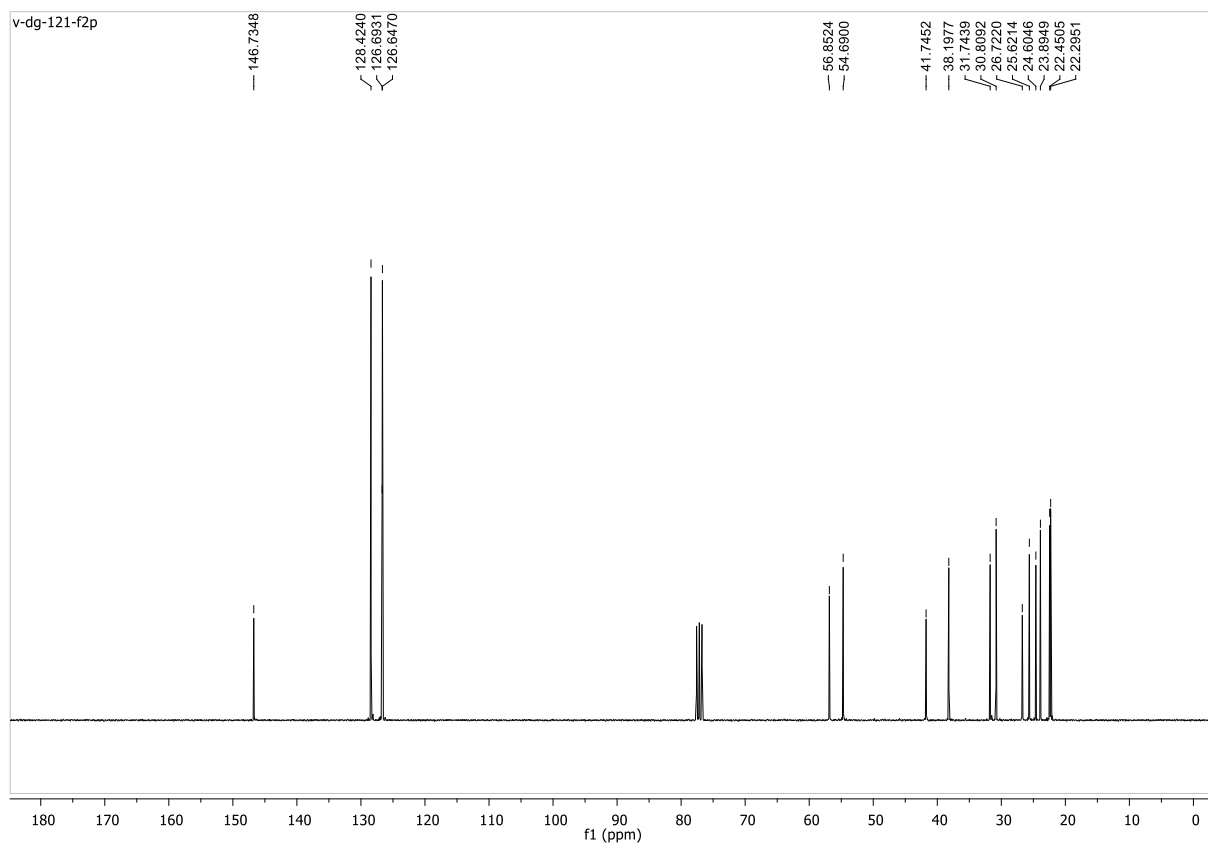


H-menth-*R,R*

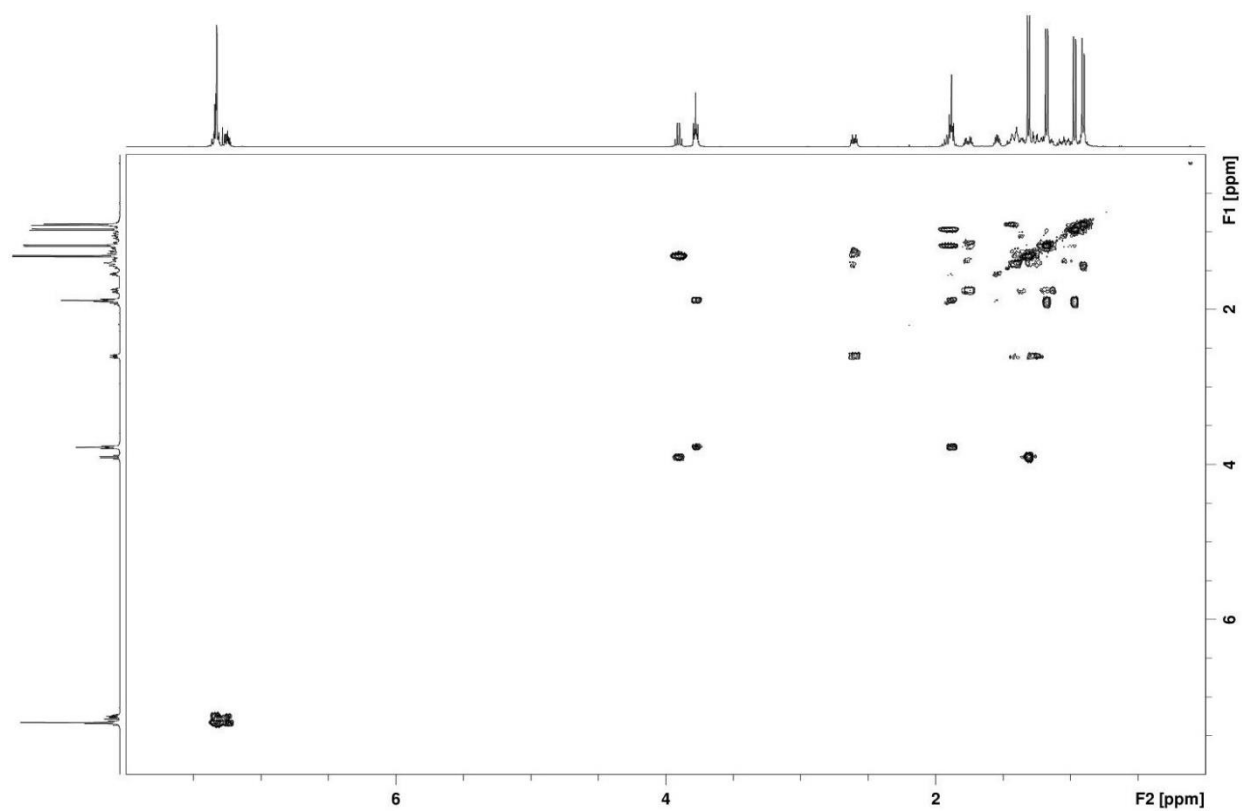
^1H (CDCl_3 , 300 MHz)



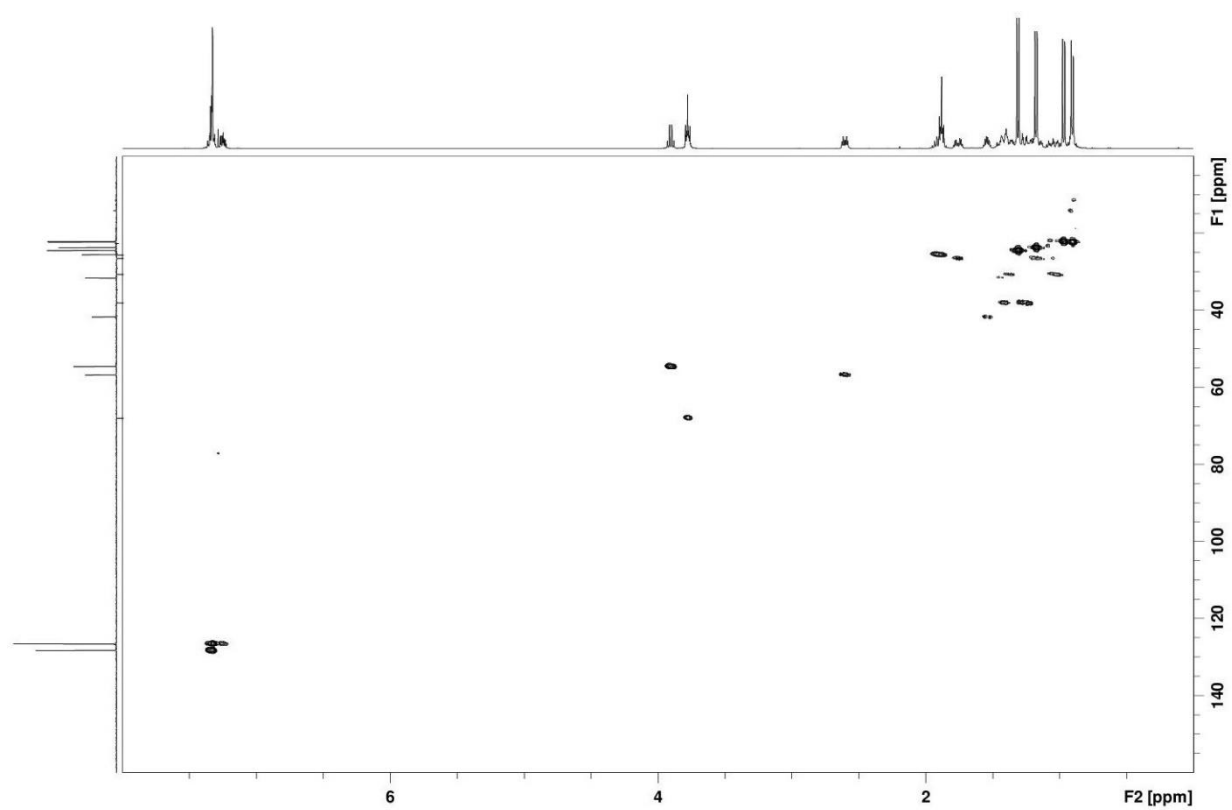
^{13}C (CDCl_3 , 75 MHz)



COSY (CDCl₃, 300 MHz)

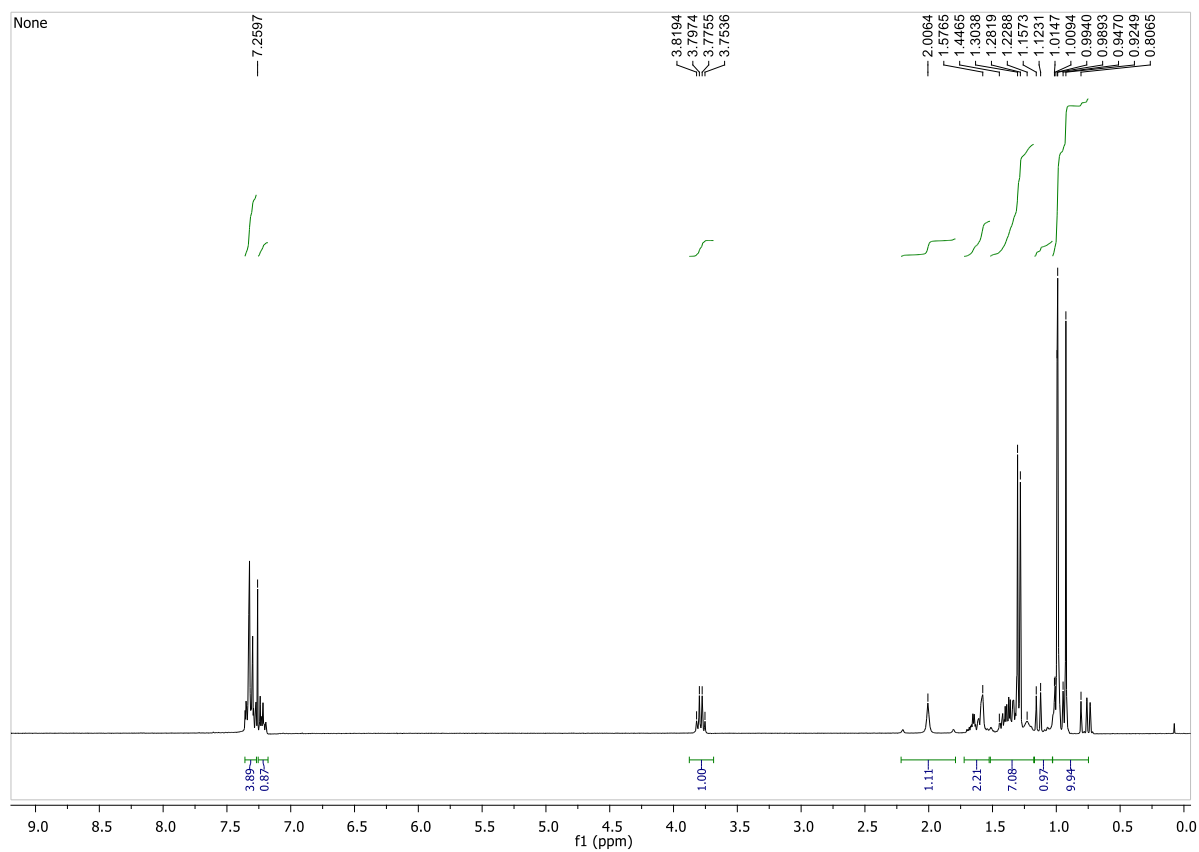


HMQC (CDCl₃, 300 MHz)

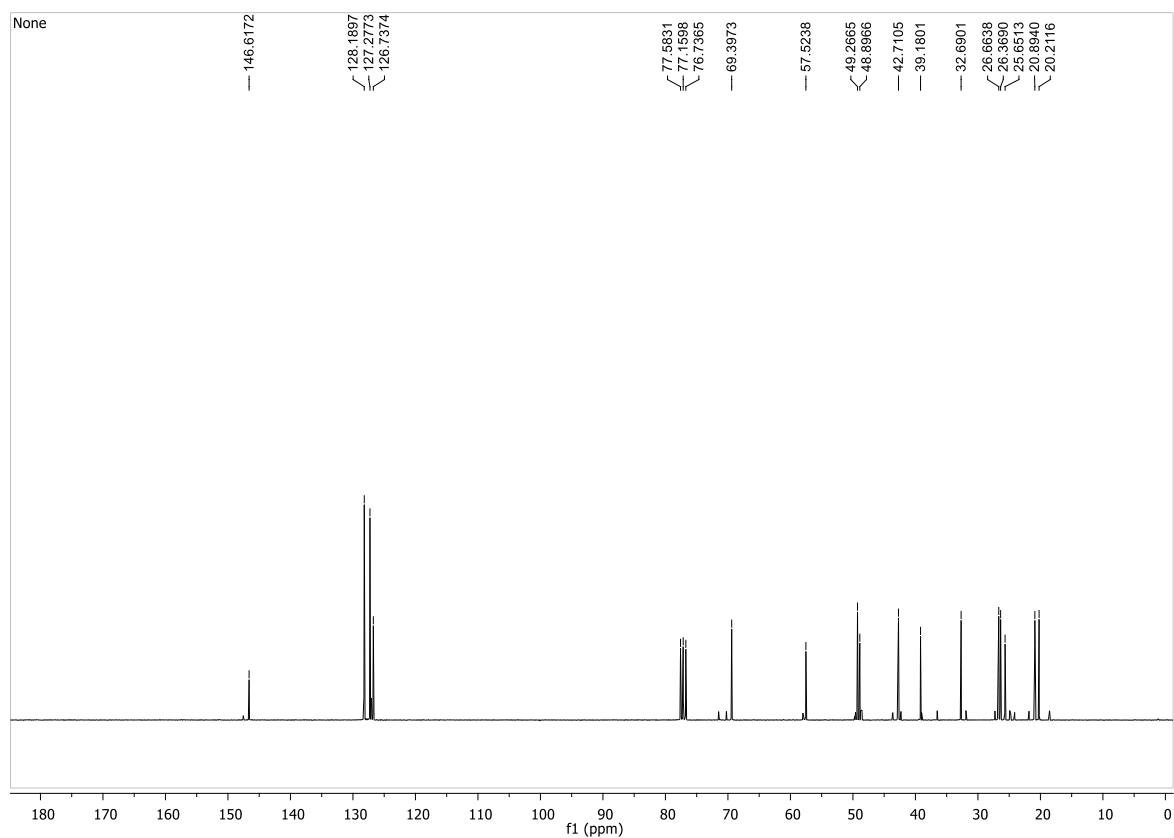


H-endo-fenc-R

^1H (CDCl_3 , 300 MHz)

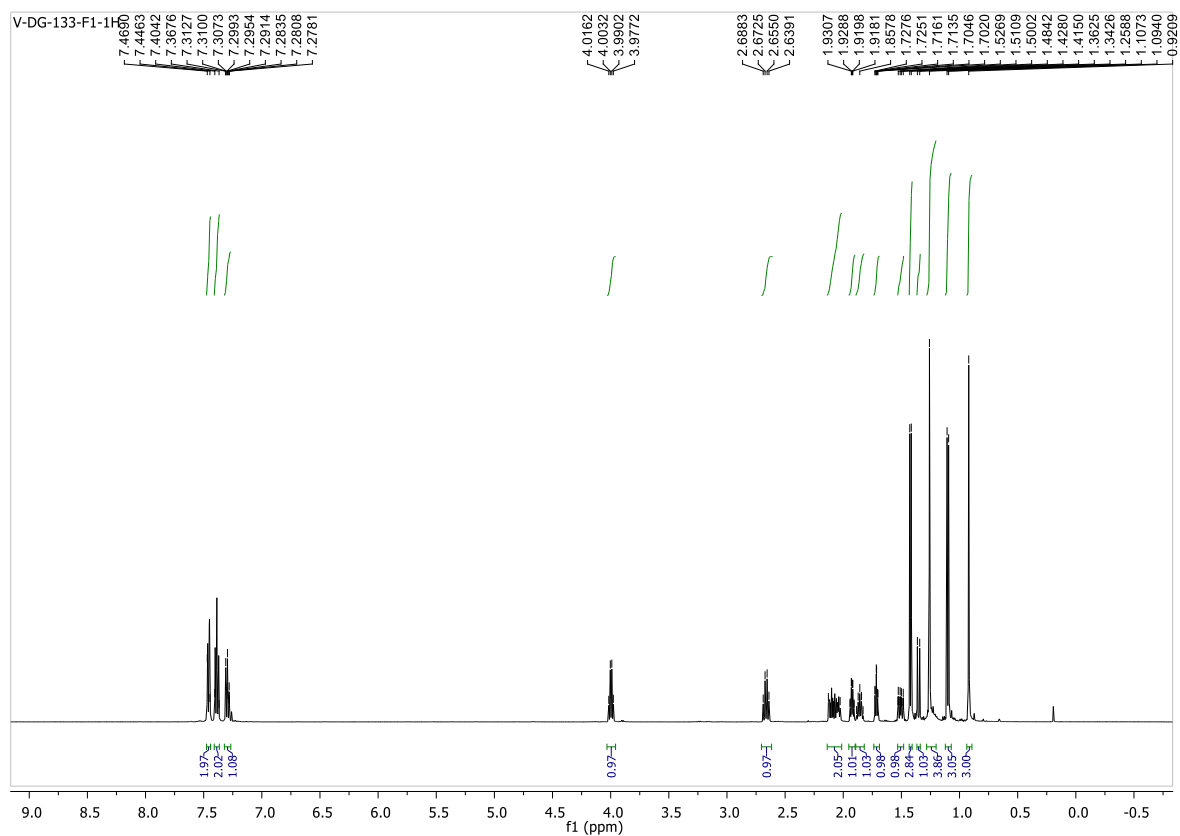


^{13}C (CDCl_3 , 75 MHz)

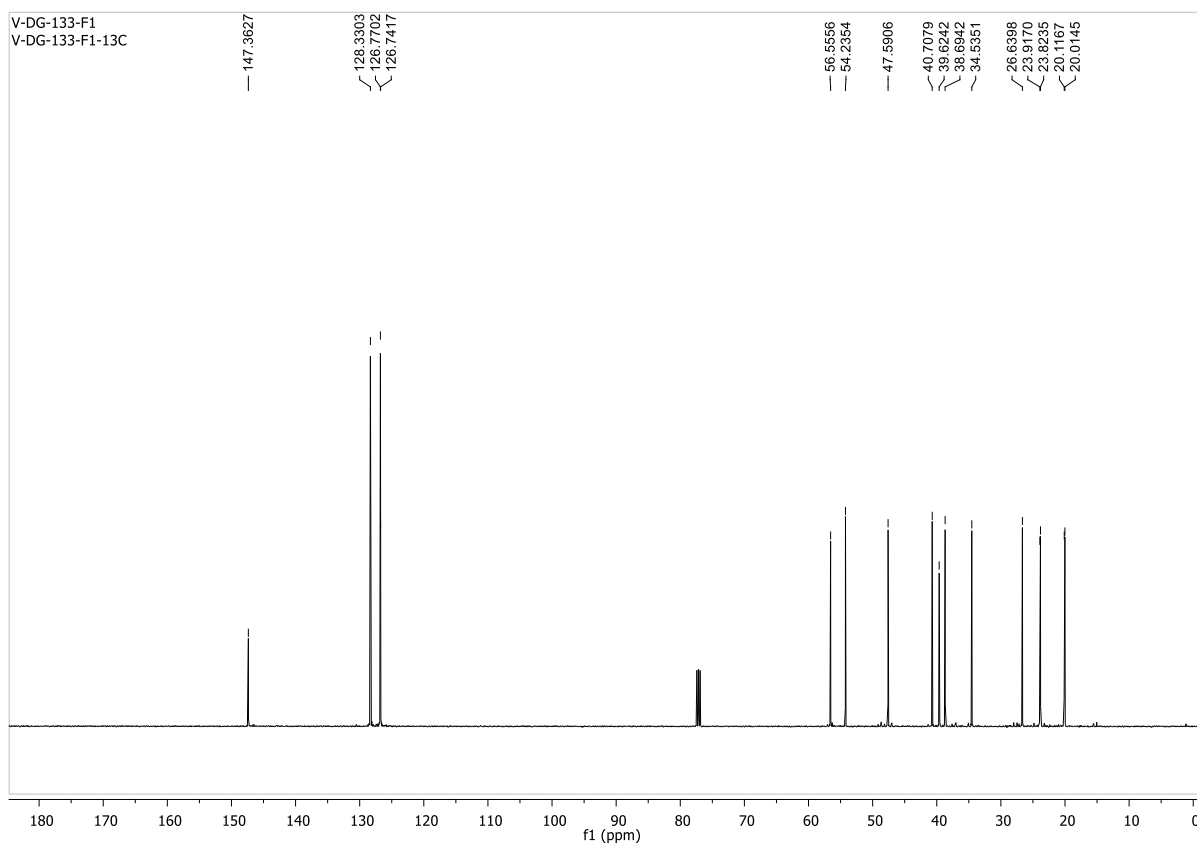


H-pino-*R,R*

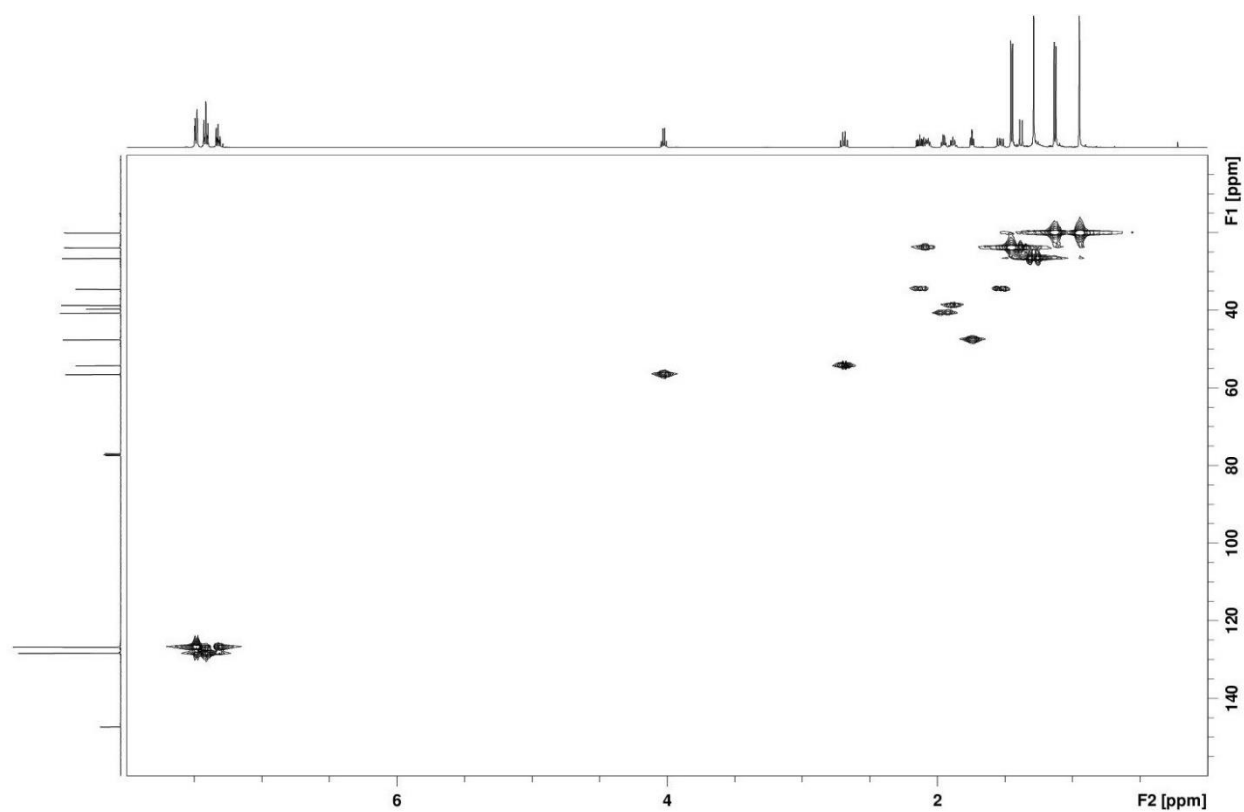
^1H (CDCl_3 , 500 MHz)



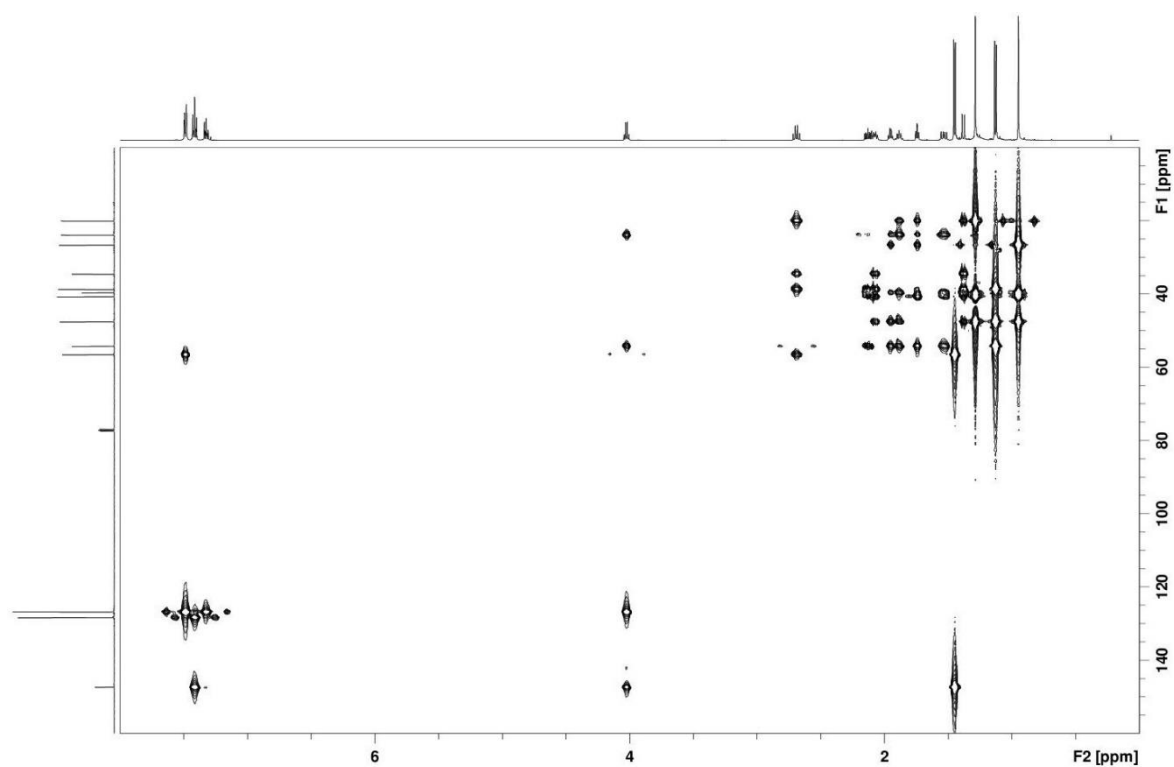
^{13}C (CDCl_3 , 126 MHz)



HMQC (CDCl₃, 300 MHz)

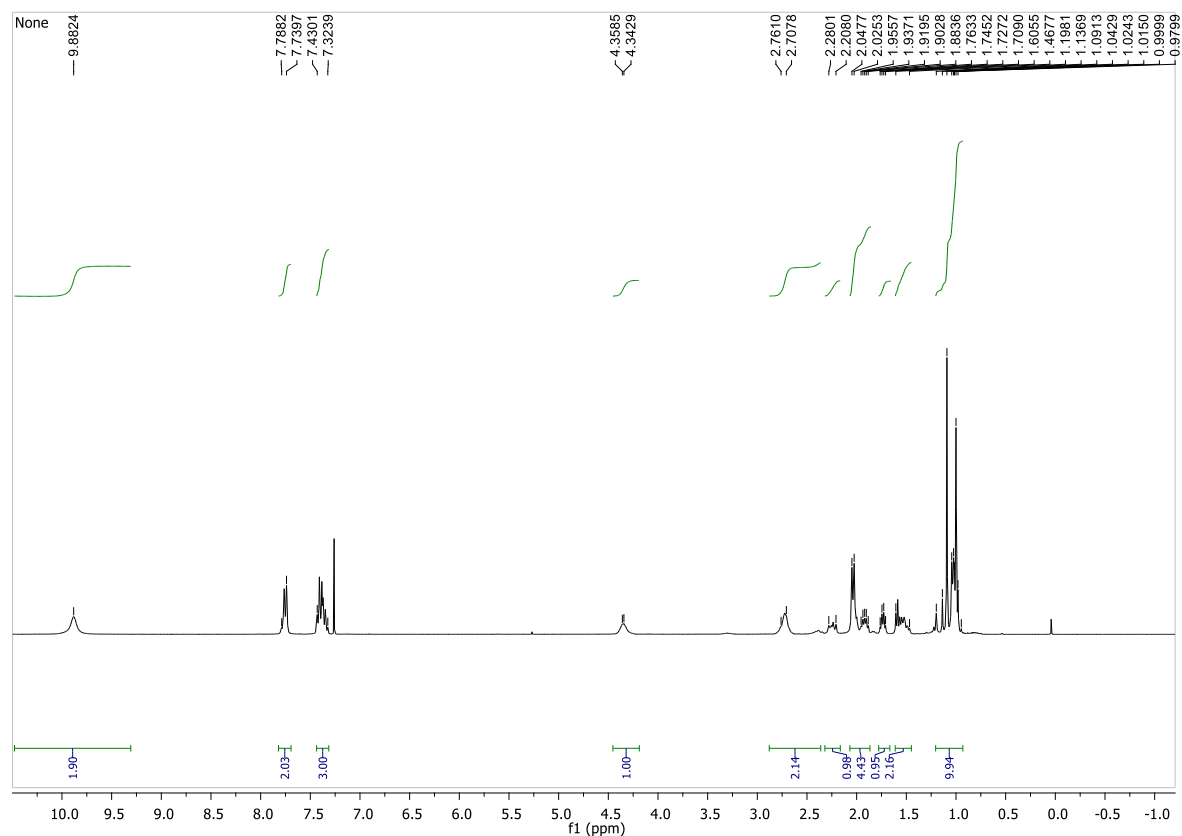


HMBC (CDCl₃, 300 MHz)

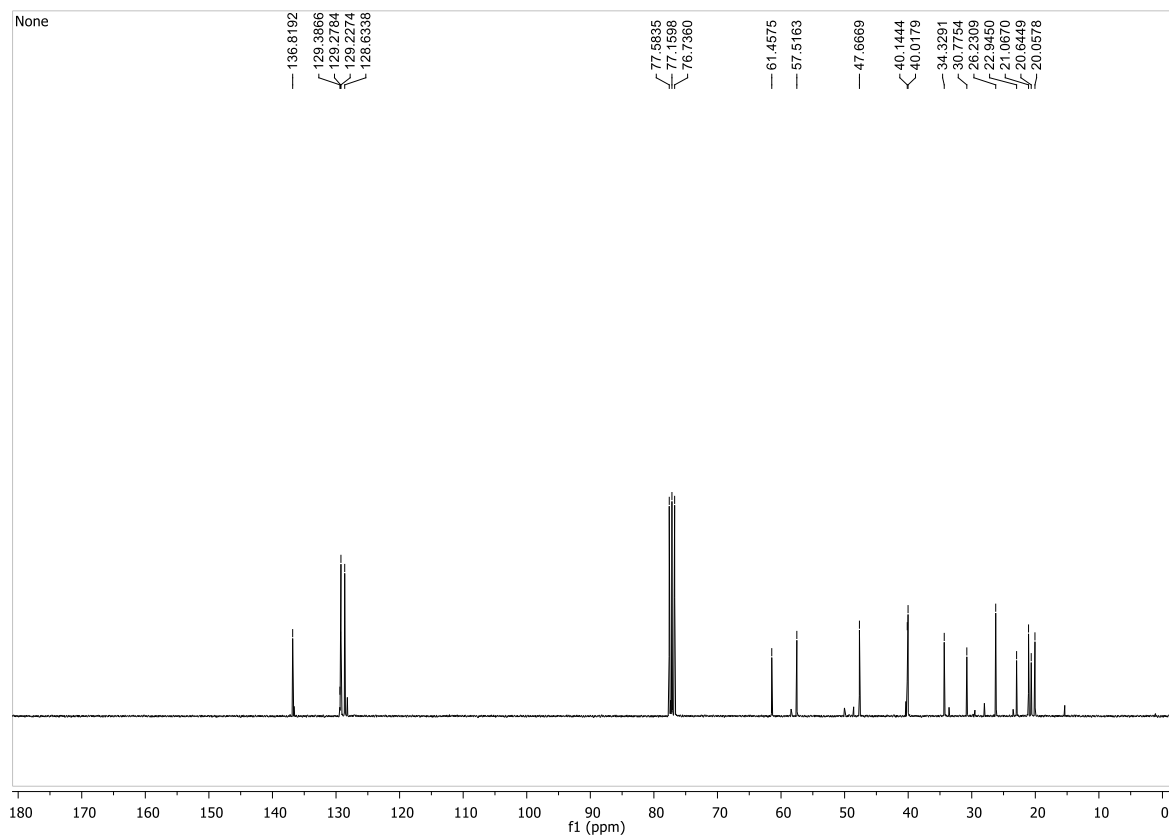


H-pino-*R,R*·HCl

^1H (CDCl₃, 300 MHz)

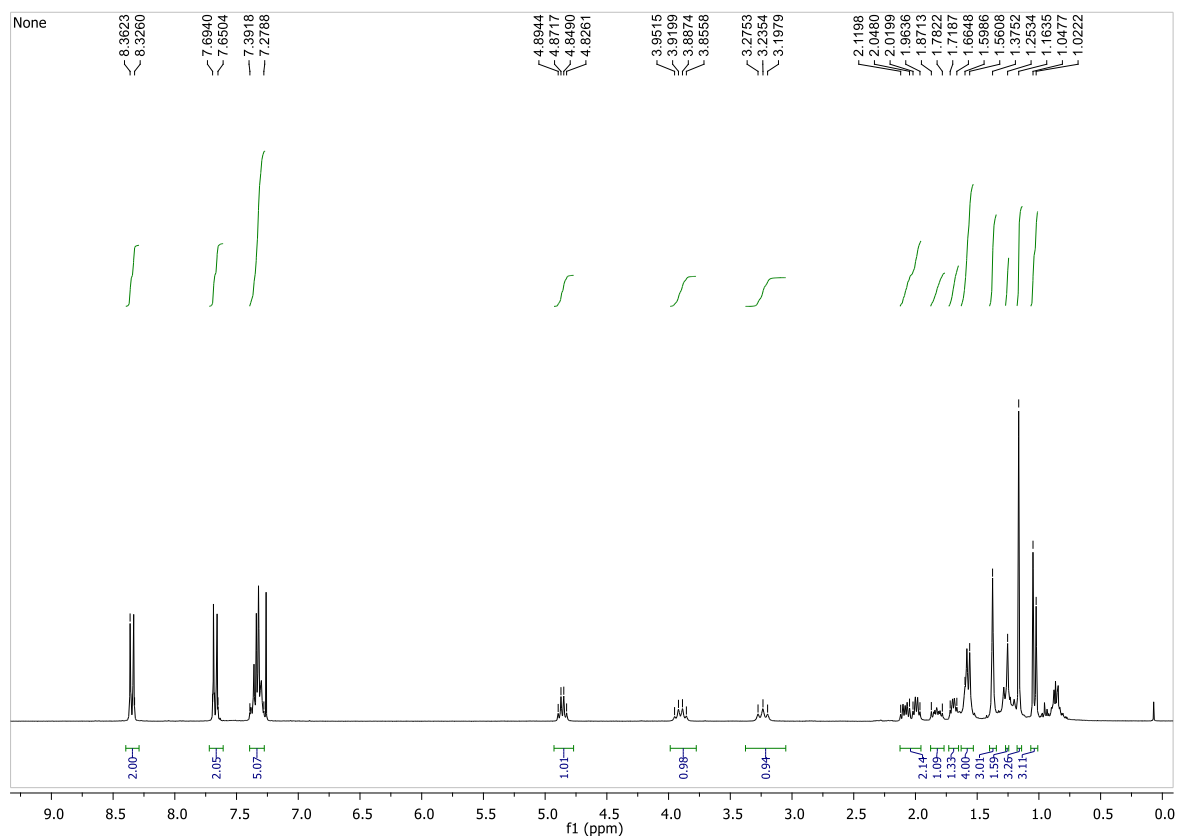


^{13}C (CDCl₃, 126 MHz)

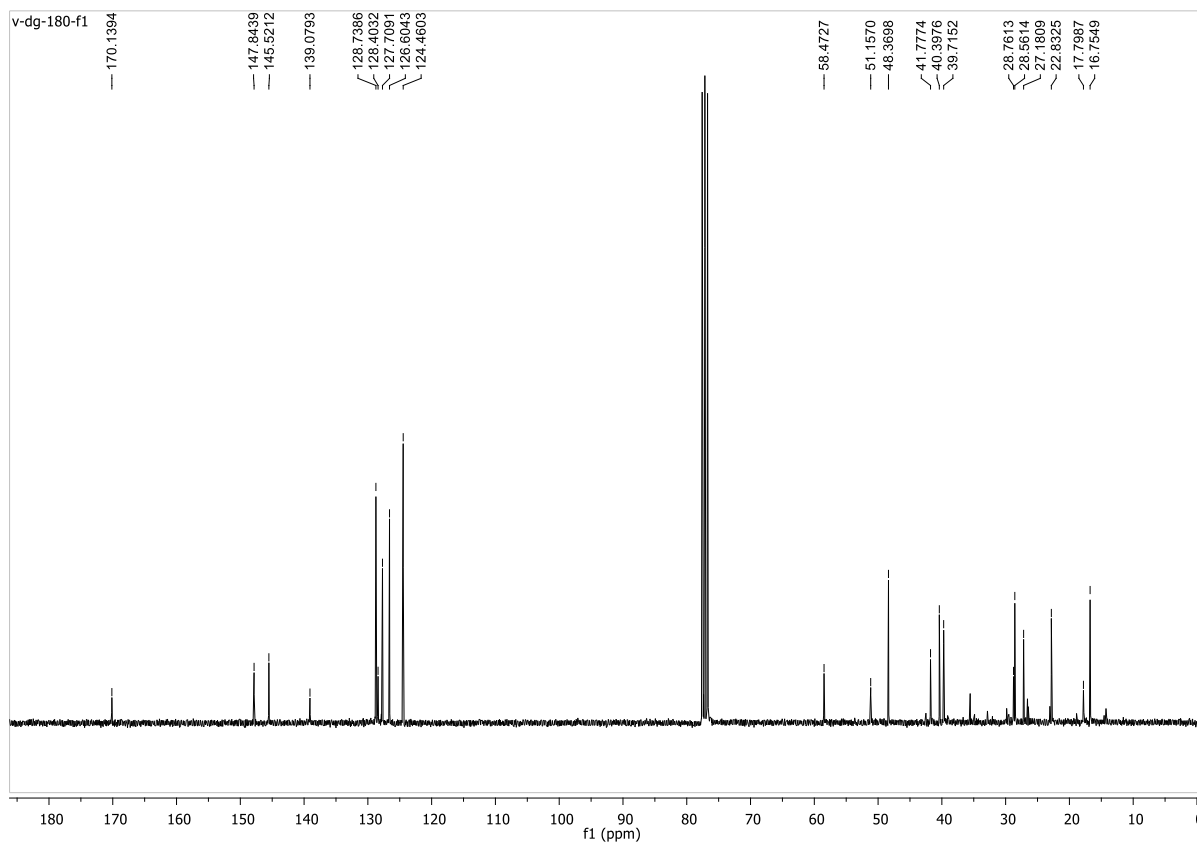


4-O₂NC₆H₄CO-pino-*R,R*

¹H (CDCl₃, 300 MHz)

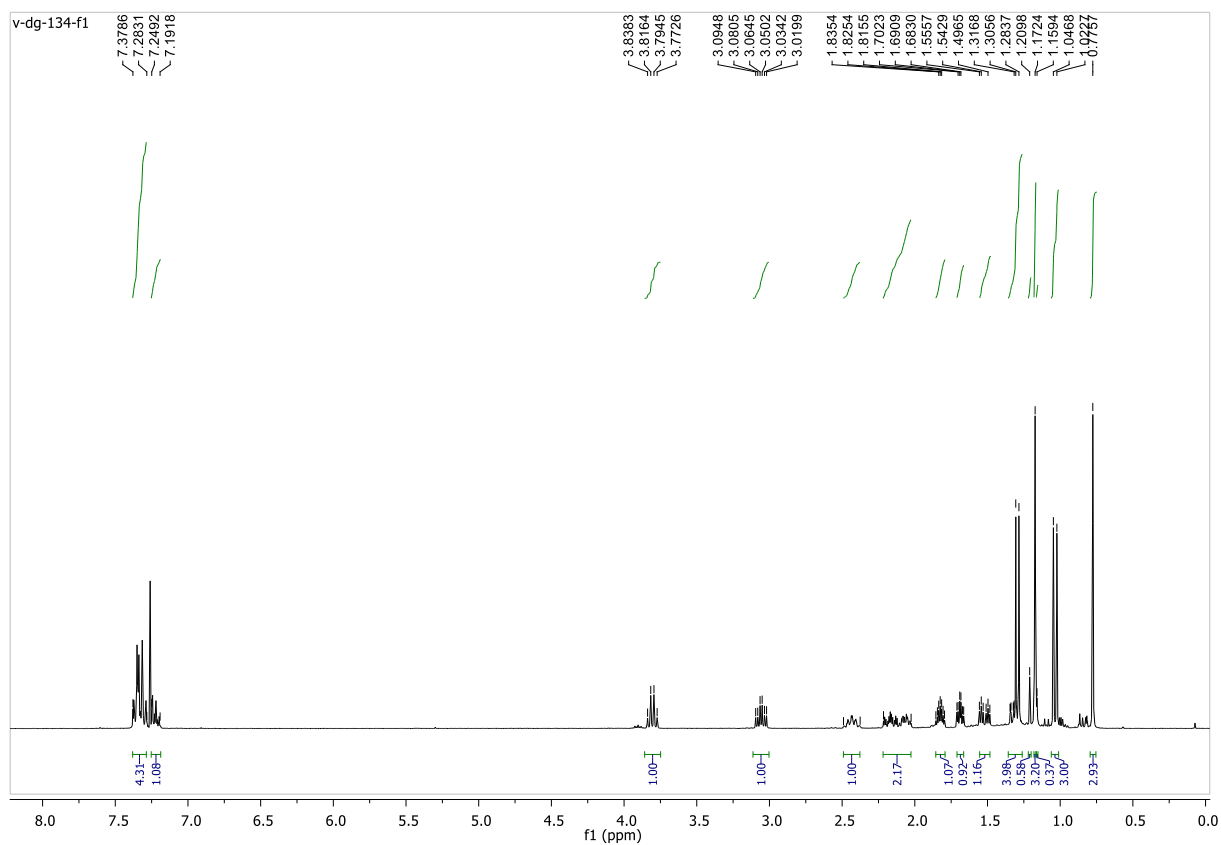


¹³C (CDCl₃, 75 MHz)

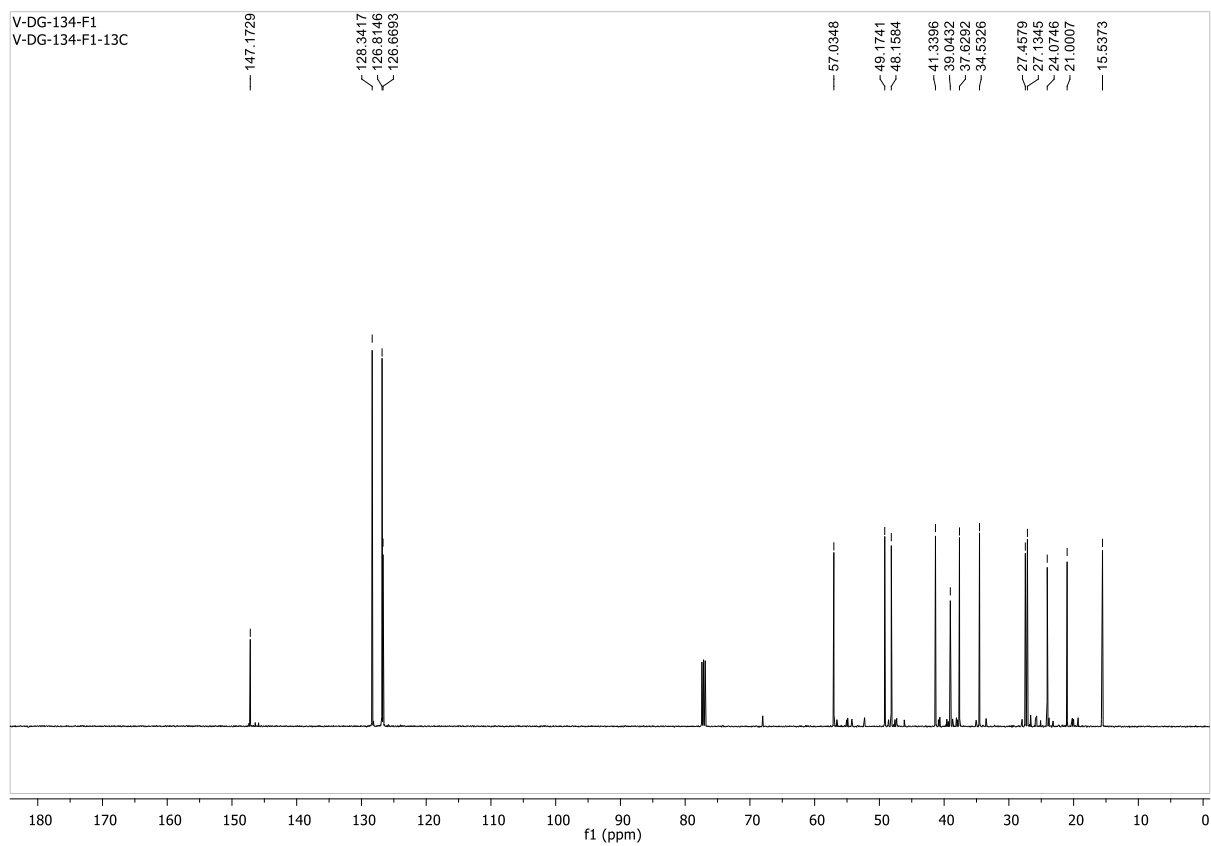


H-pino-*S,S*

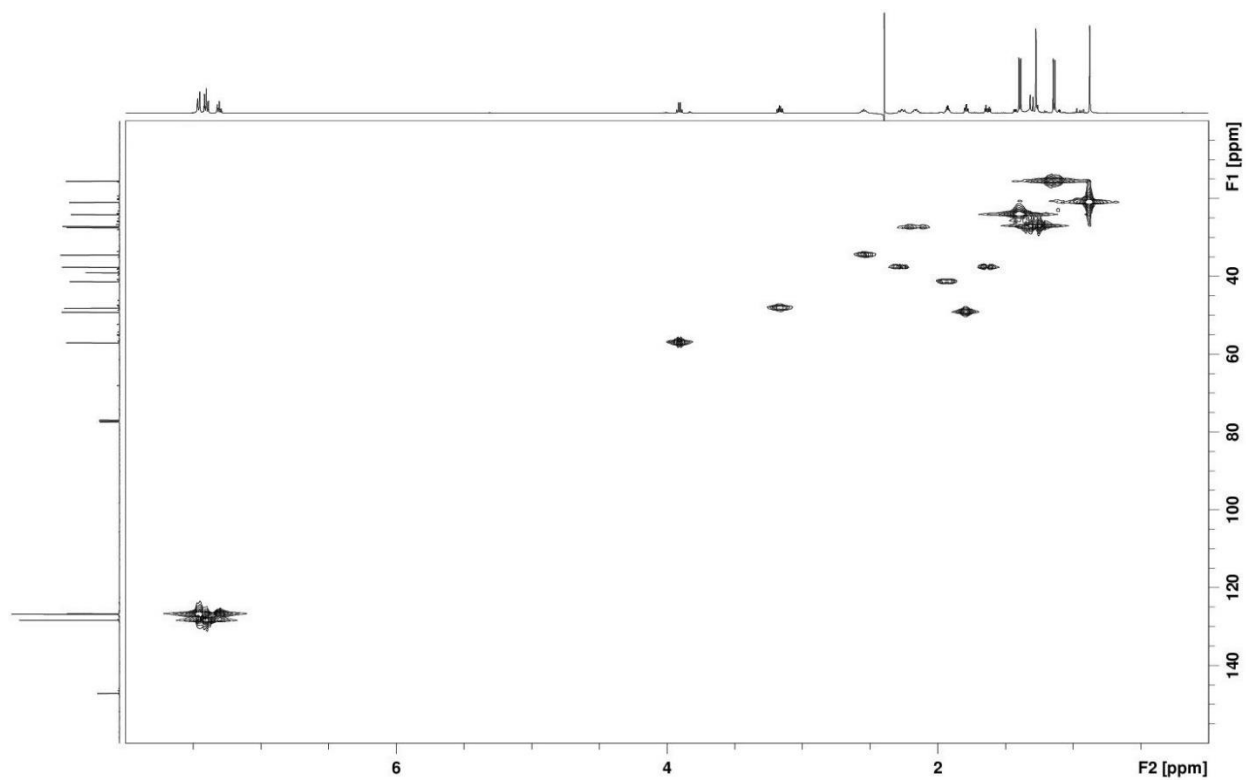
^1H (CDCl_3 , 300 MHz)



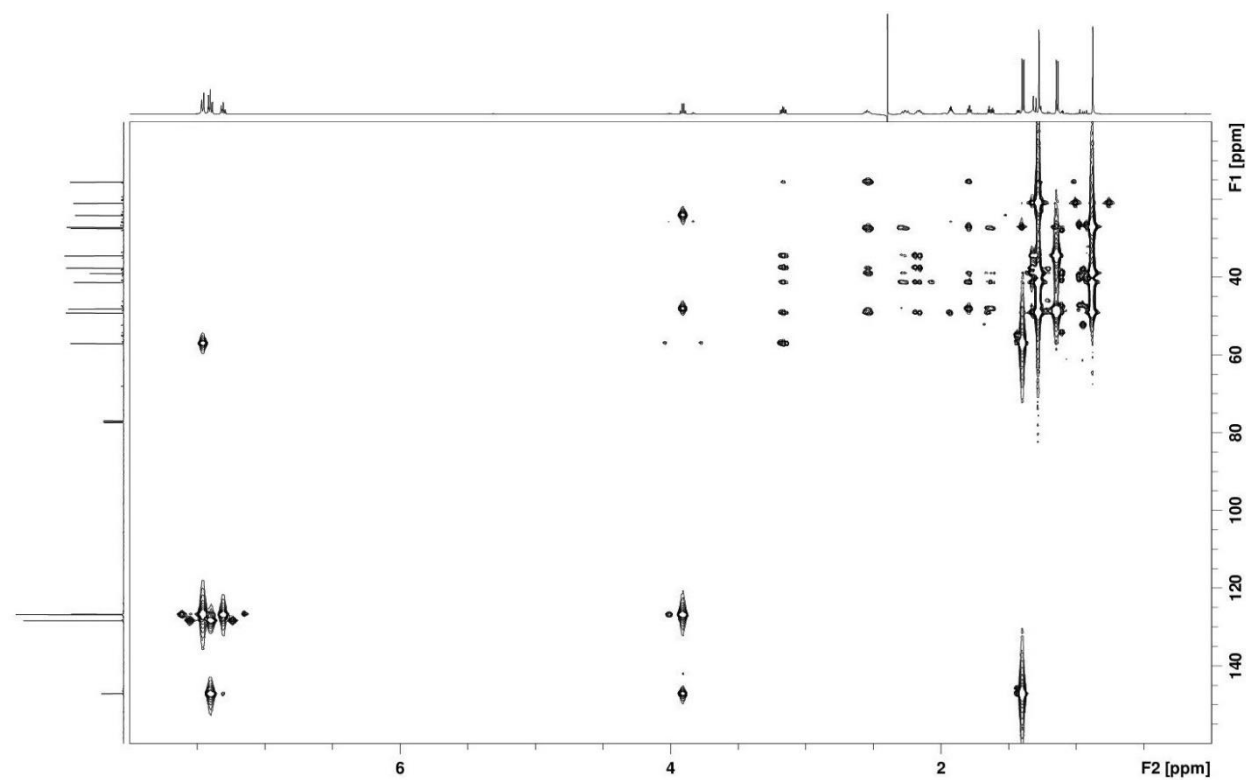
^{13}C (CDCl_3 , 126 MHz)



HMQC (CDCl₃, 300 MHz)

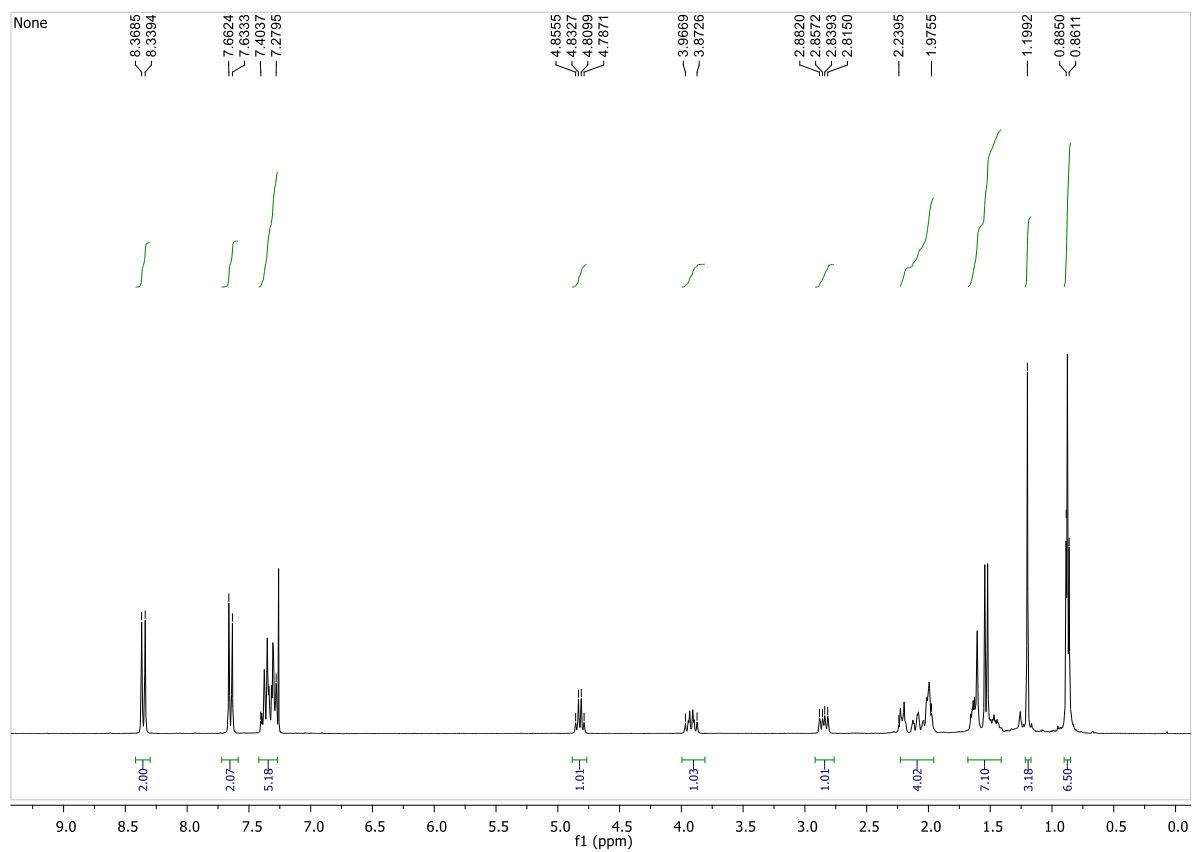


HMBC (CDCl₃, 300 MHz)

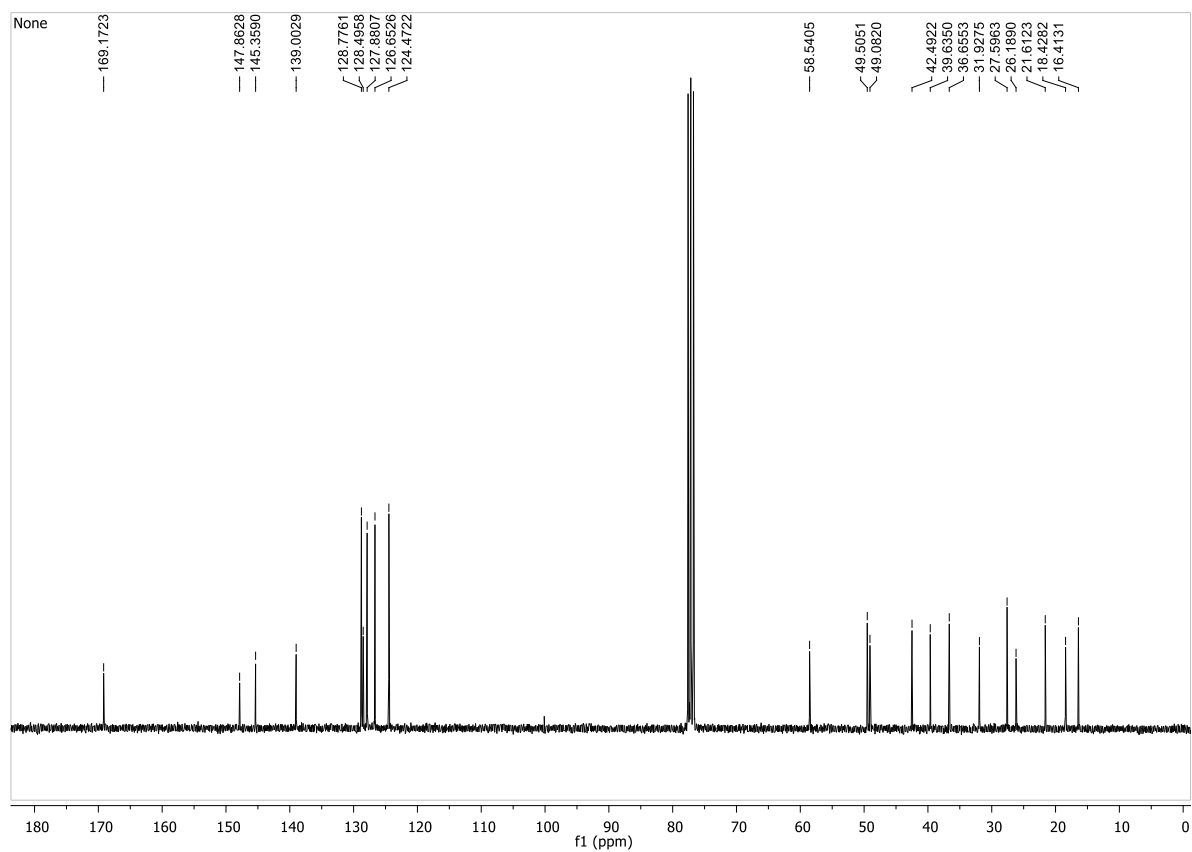


4-O₂NC₆H₄CO-pino-*S,S*

¹H (CDCl₃, 300 MHz)

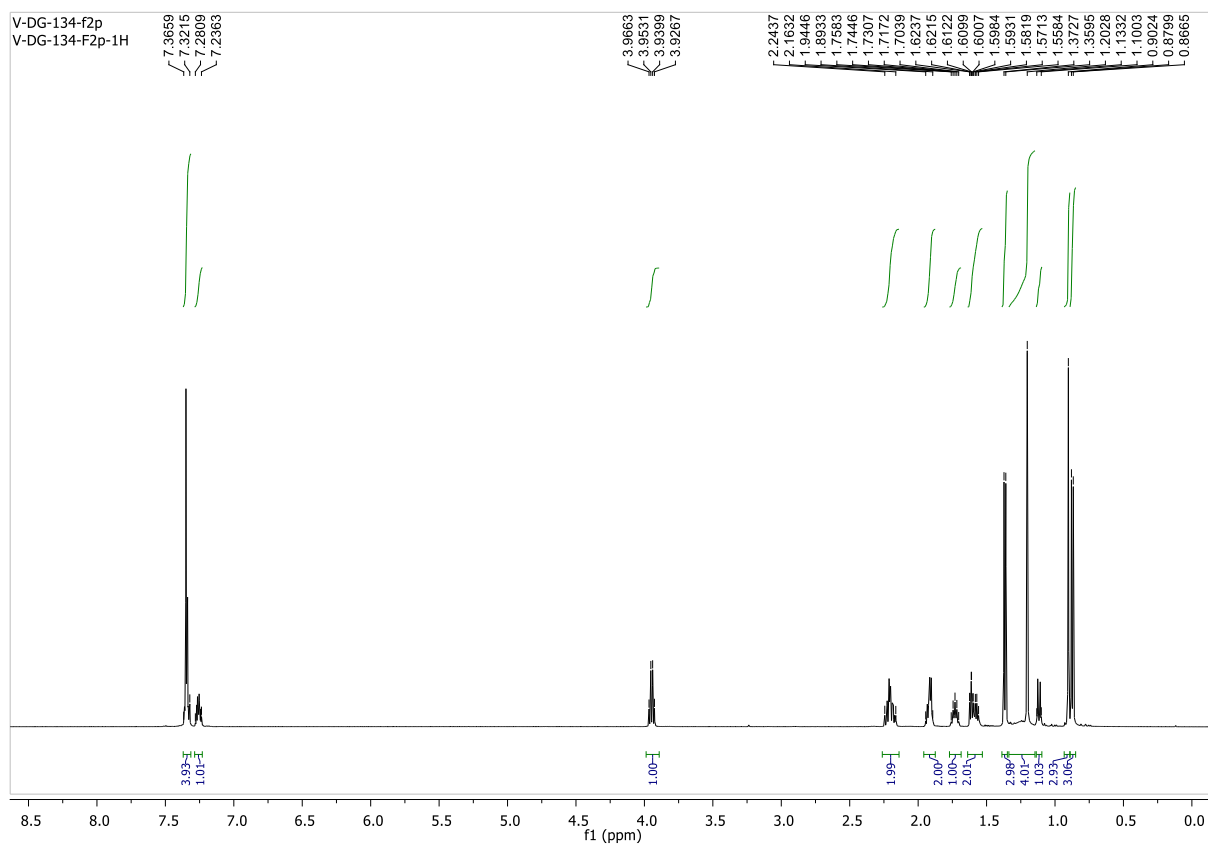


¹³C (CDCl₃, 75 MHz)

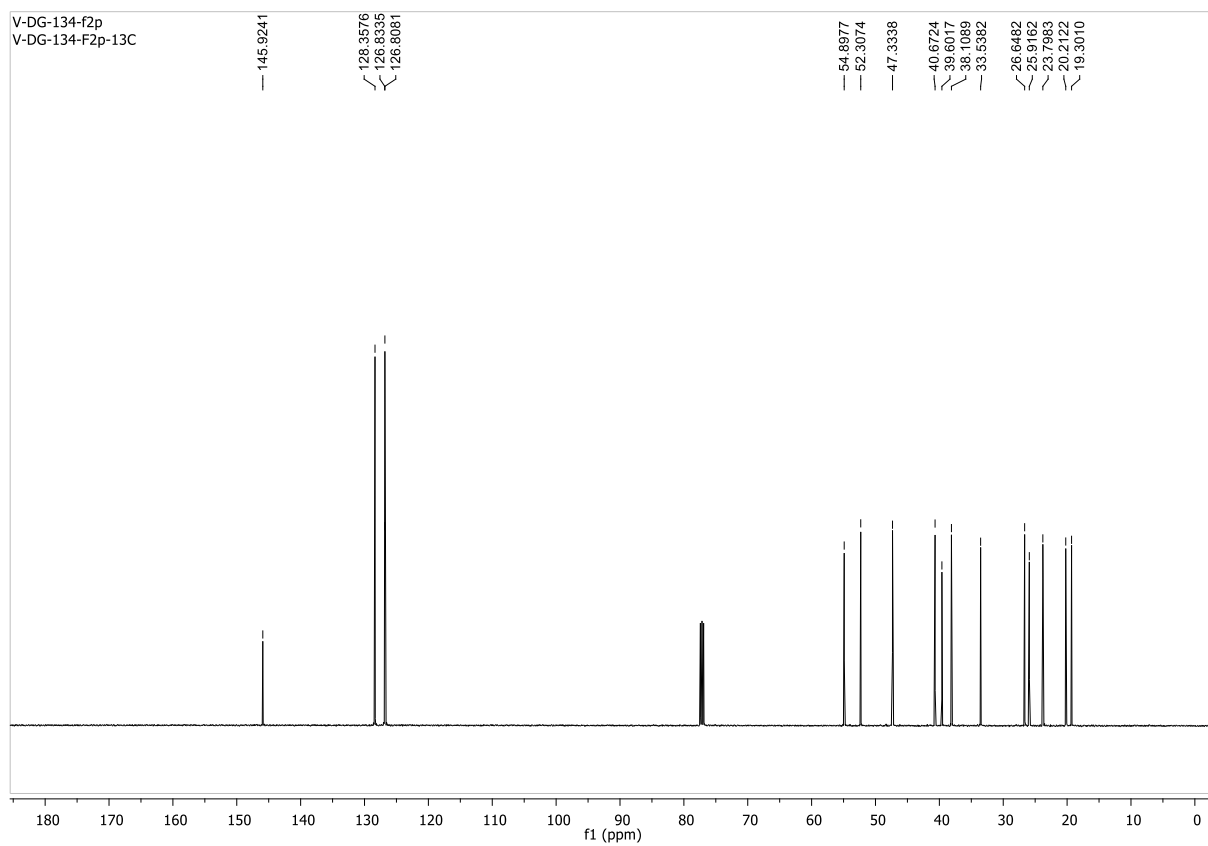


H-pino-*S,R*

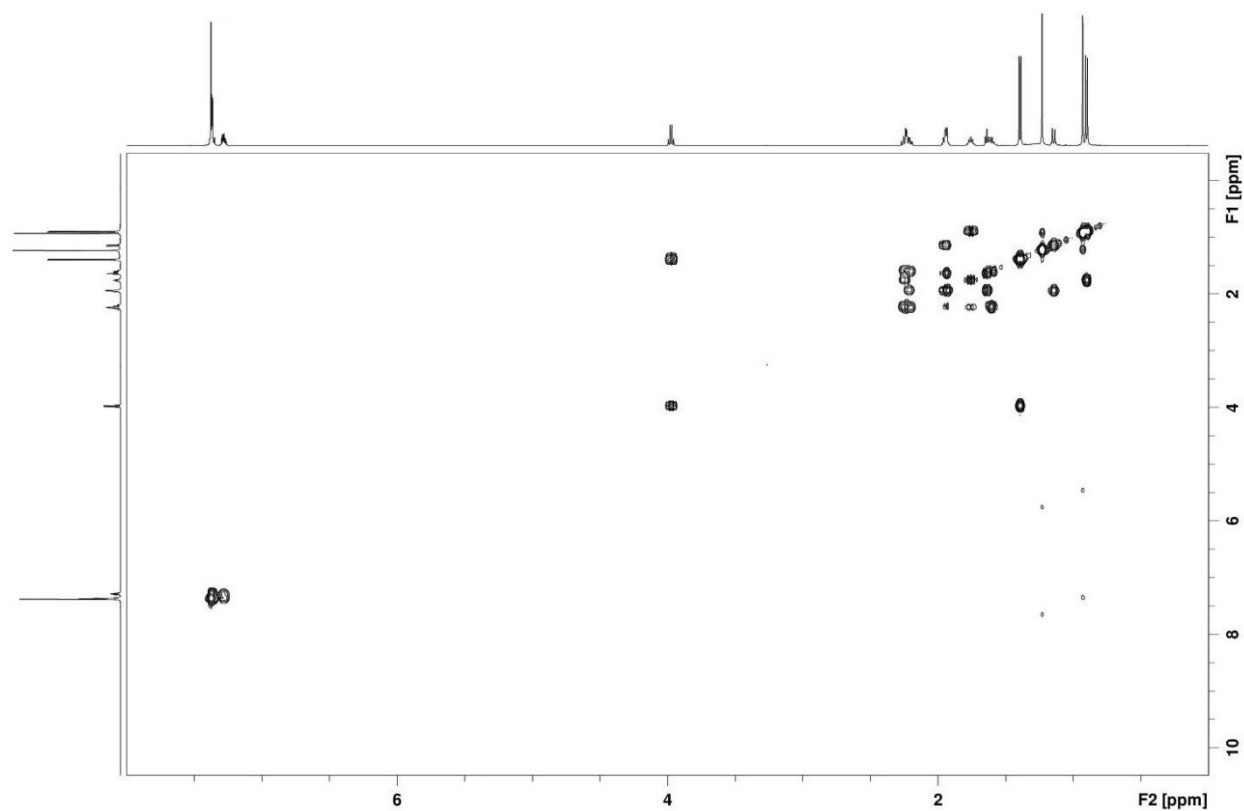
^1H (CDCl_3 , 500 MHz)



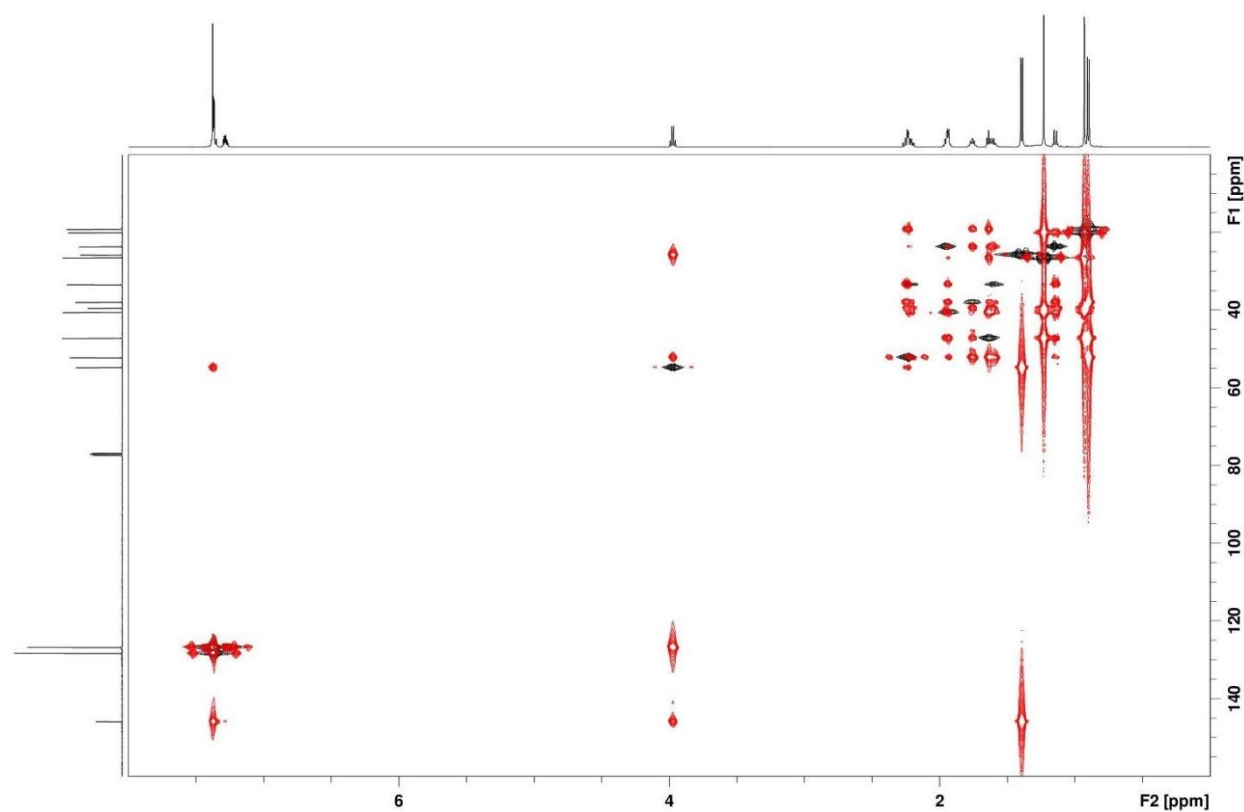
^{13}C (CDCl_3 , 126 MHz)



COSY (CDCl₃, 300 MHz)

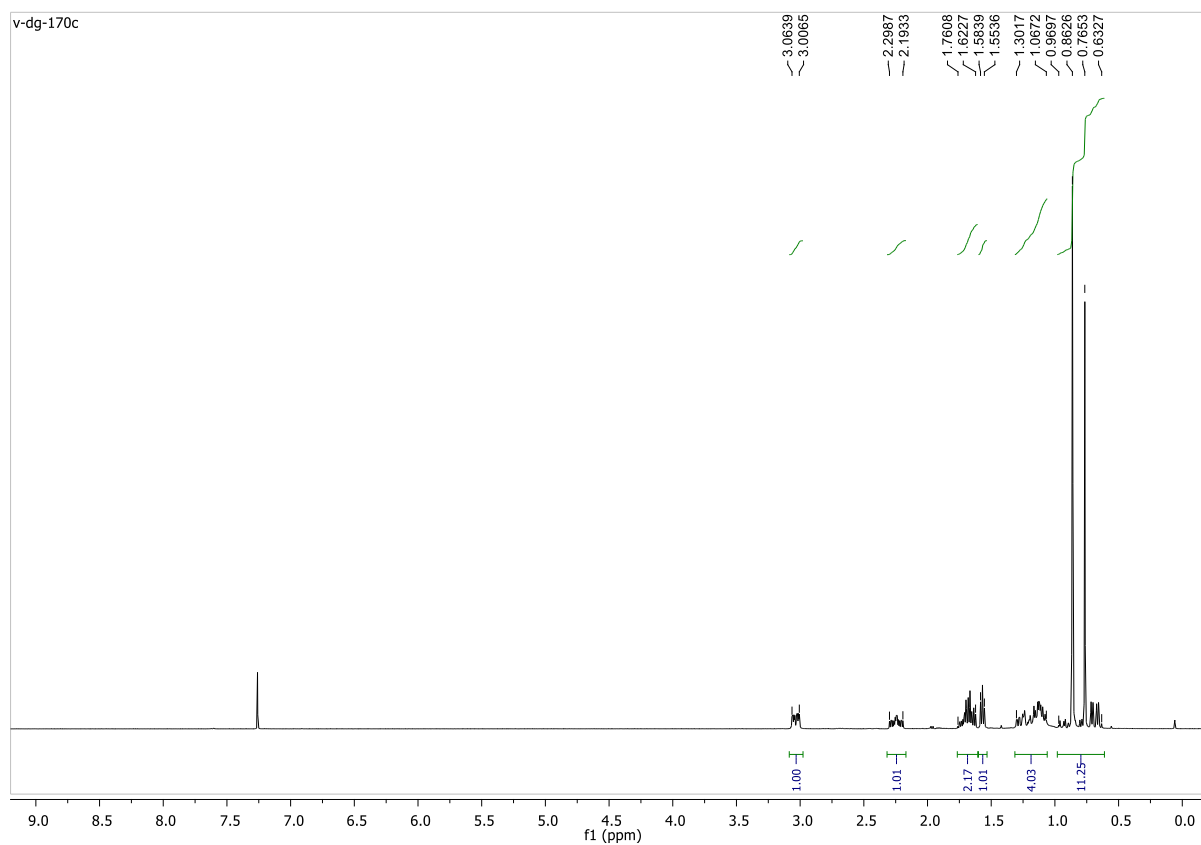


HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)

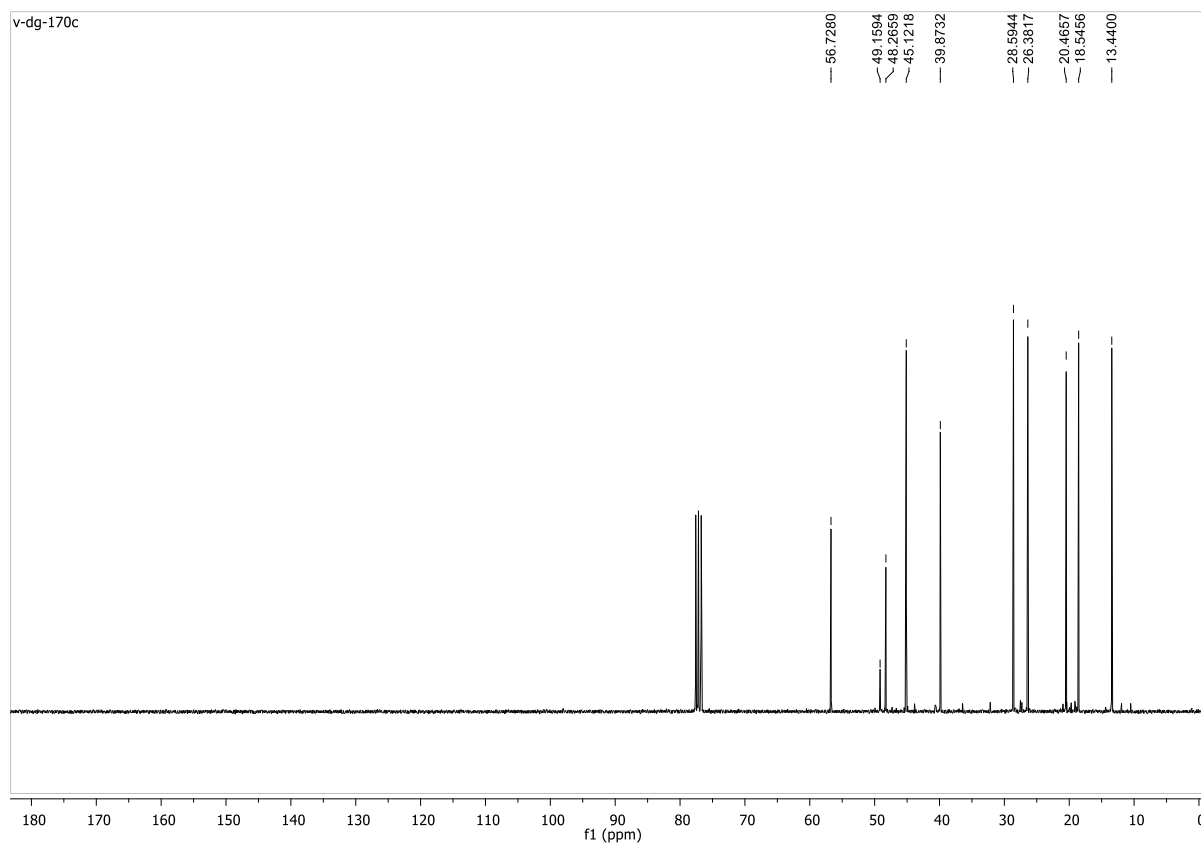


Endo-bornylamine

^1H (CDCl_3 , 300 MHz)

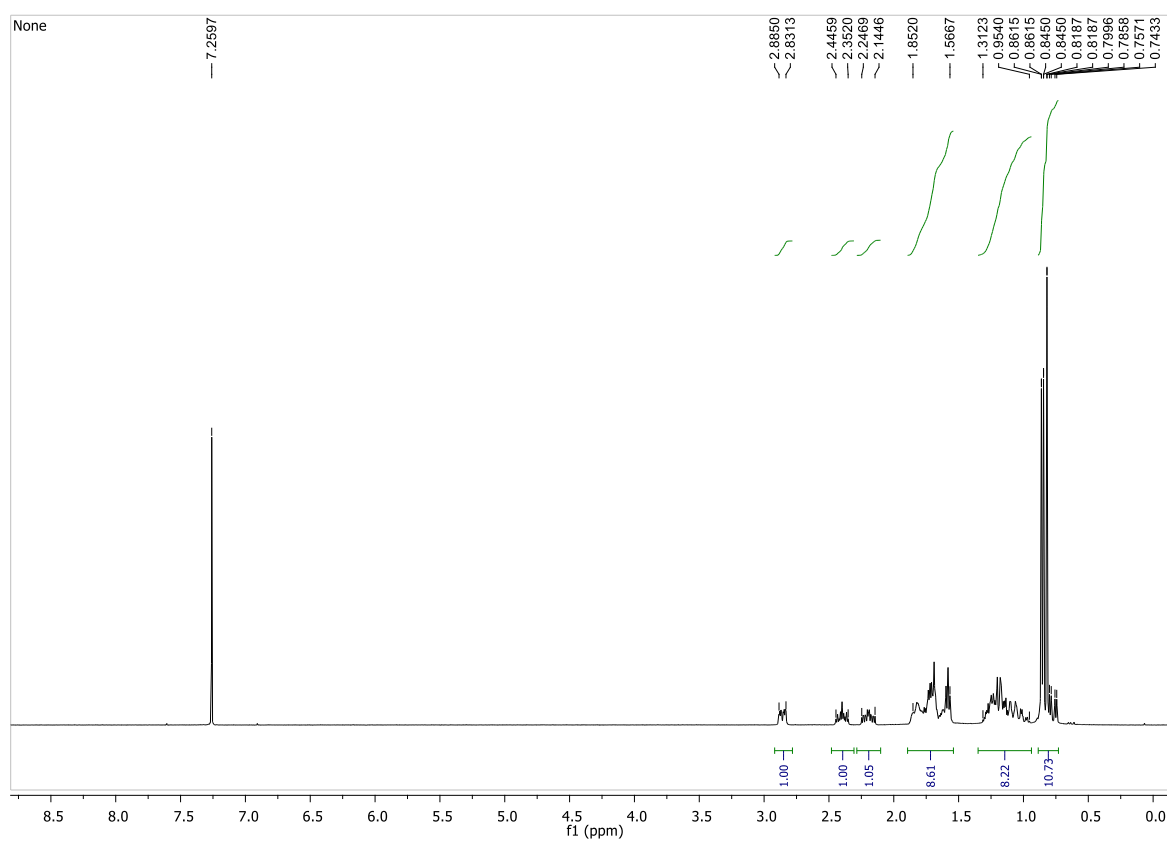


^{13}C (CDCl_3 , 75 MHz)

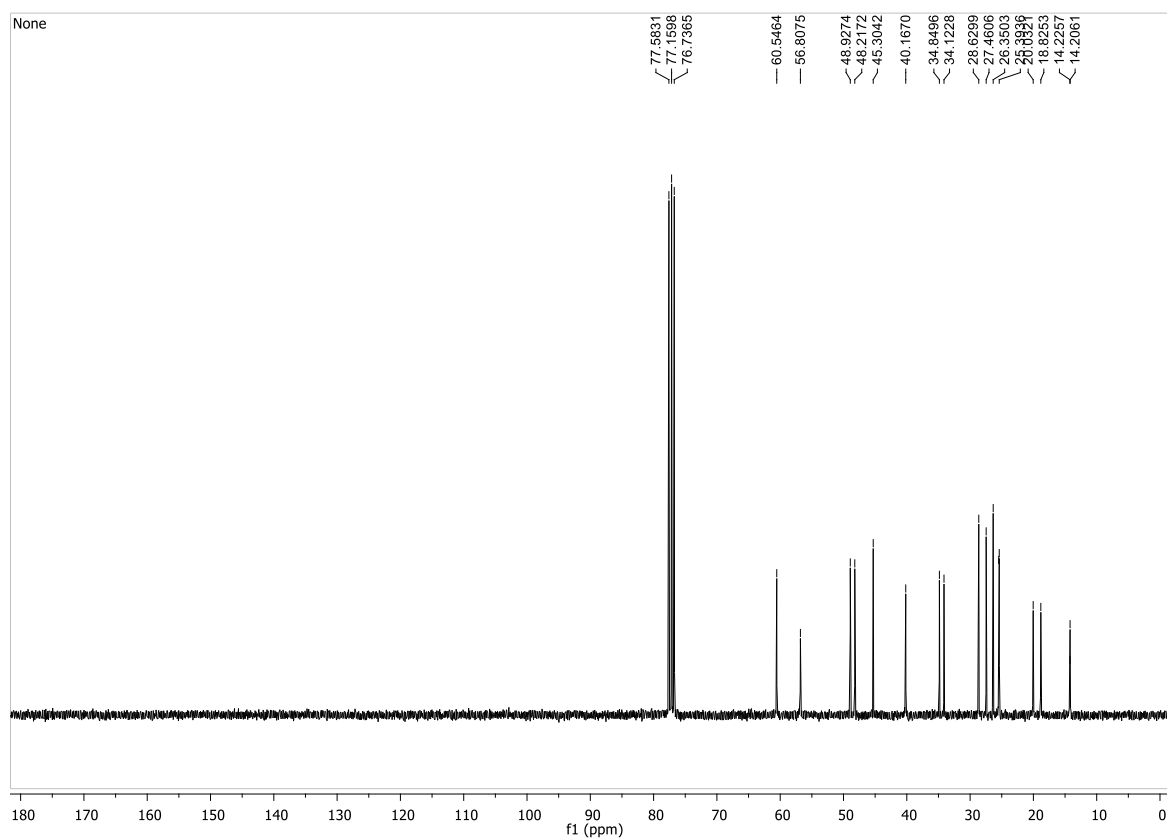


H-endo

^1H (CDCl_3 , 300 MHz)

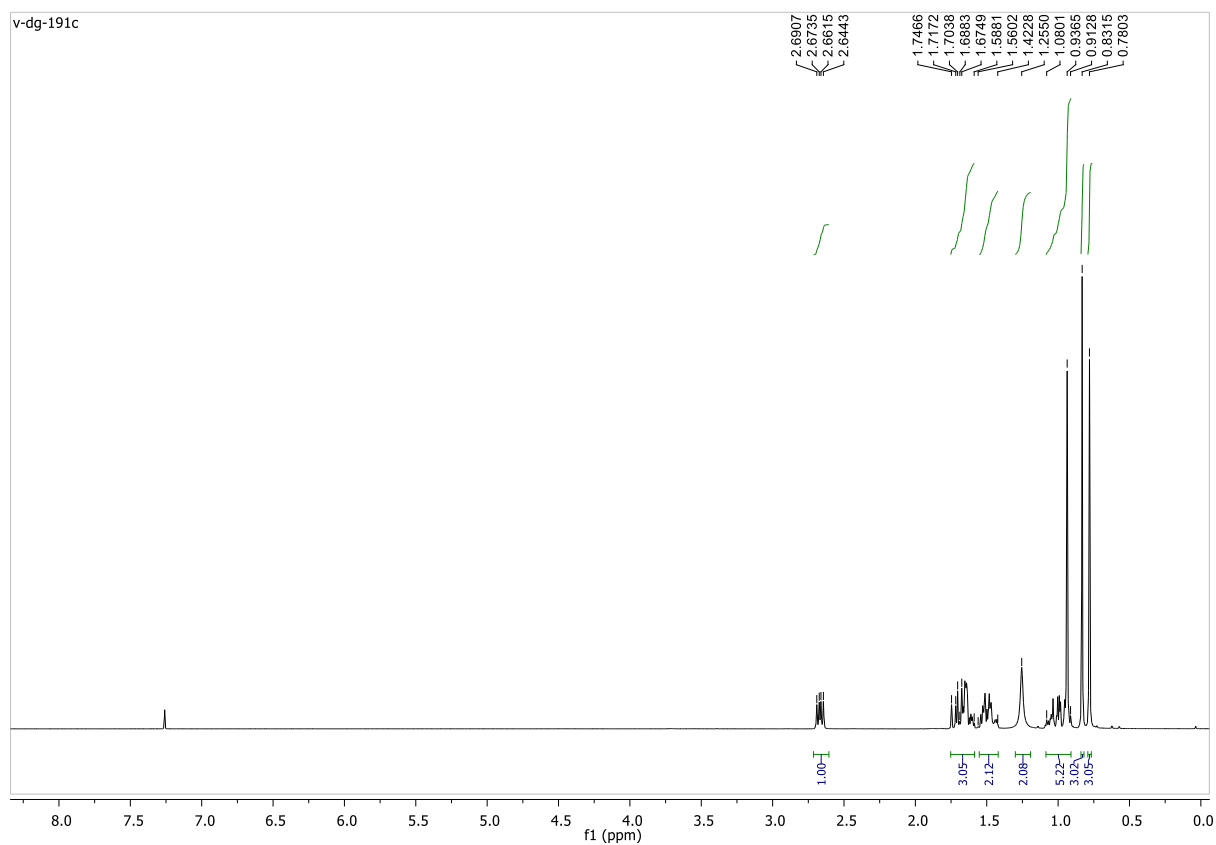


^{13}C (CDCl_3 , 75 MHz)

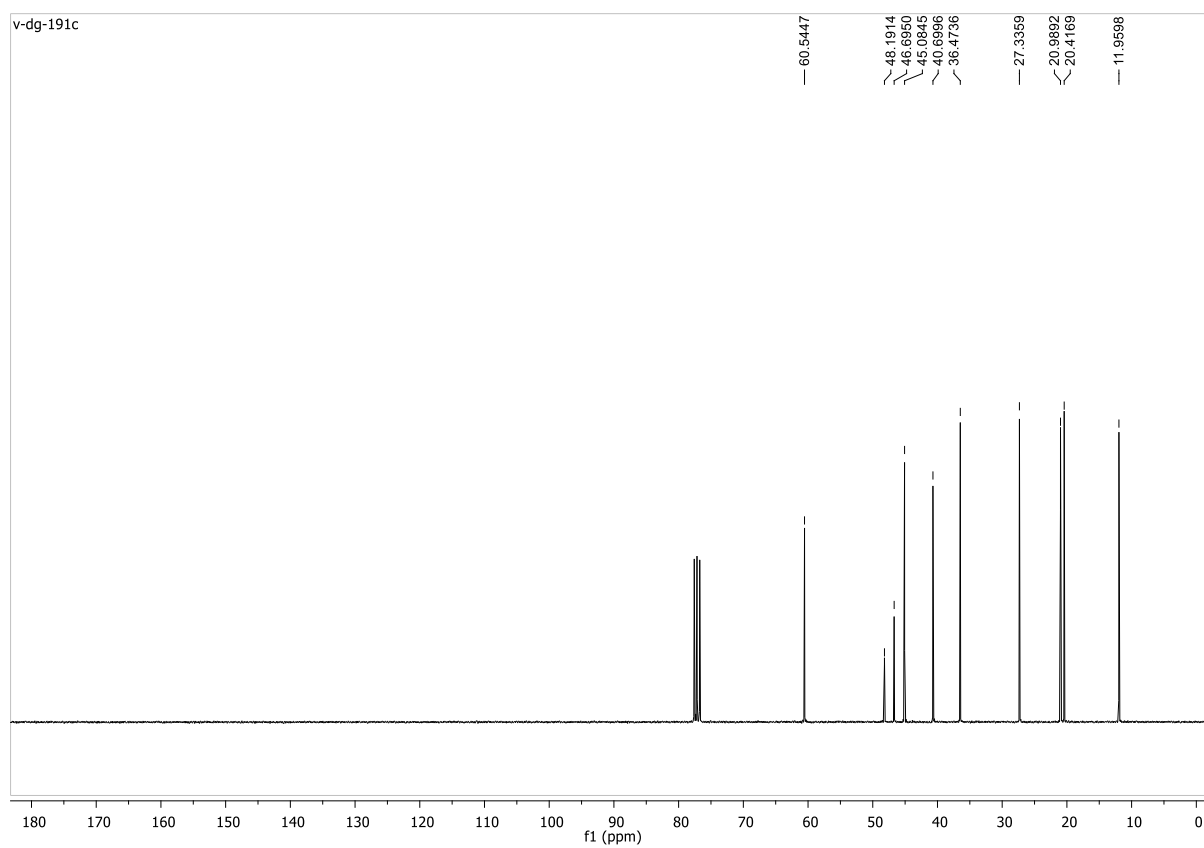


Exo-bornylamine

^1H (CDCl_3 , 300 MHz)

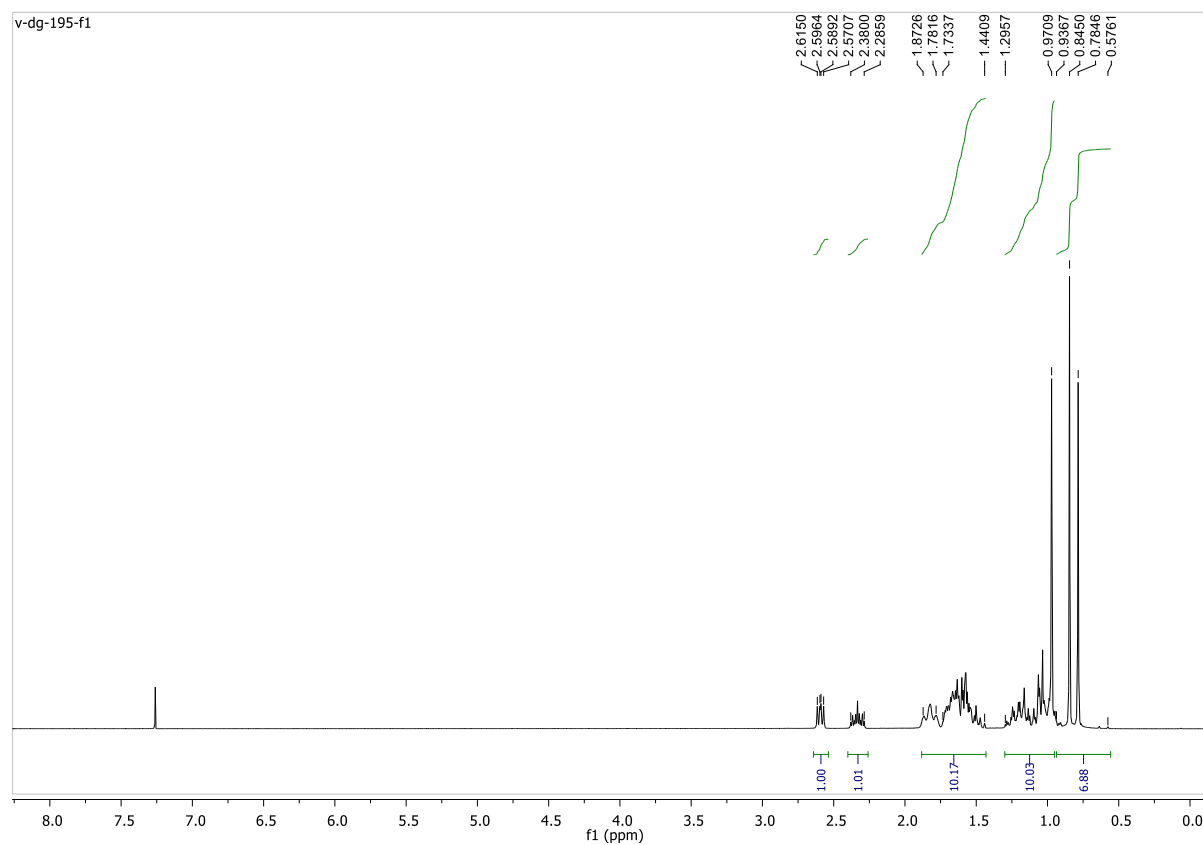


^{13}C (CDCl_3 , 75 MHz)

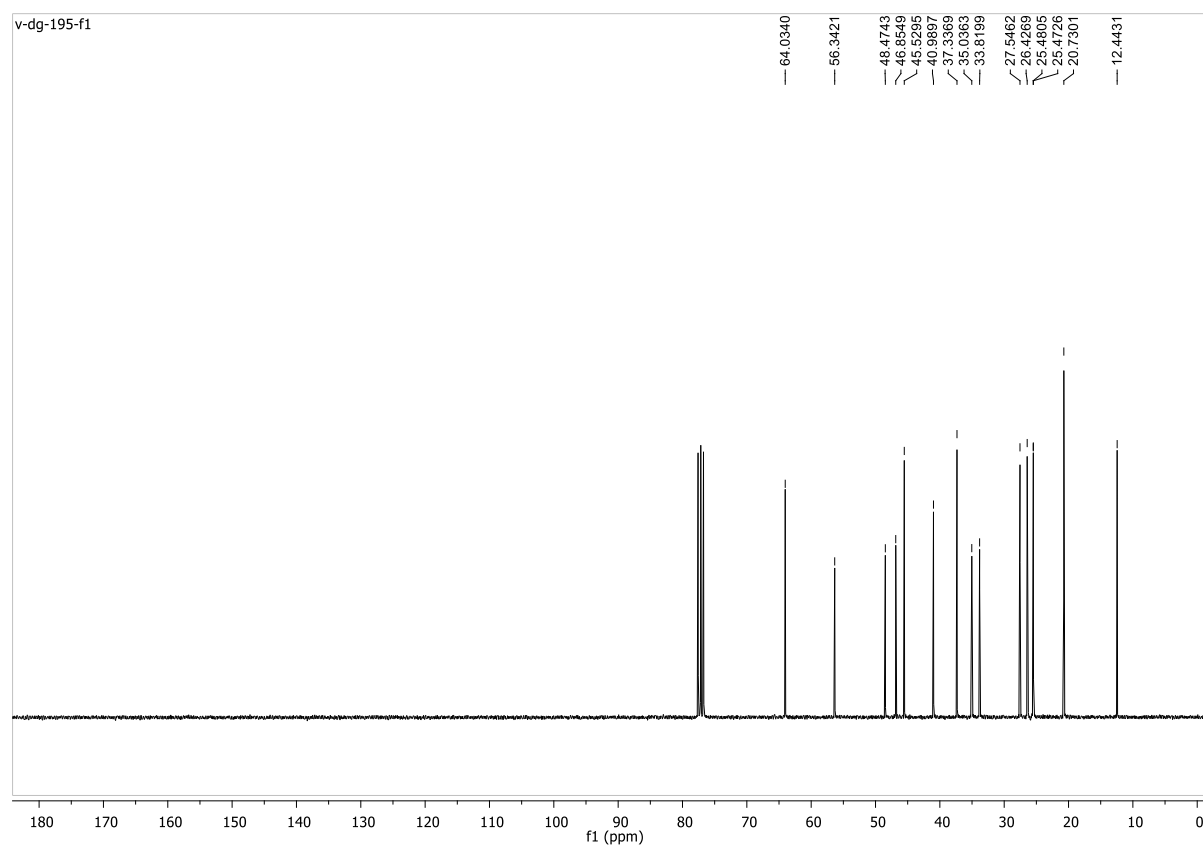


H-exo

^1H (CDCl_3 , 300 MHz)

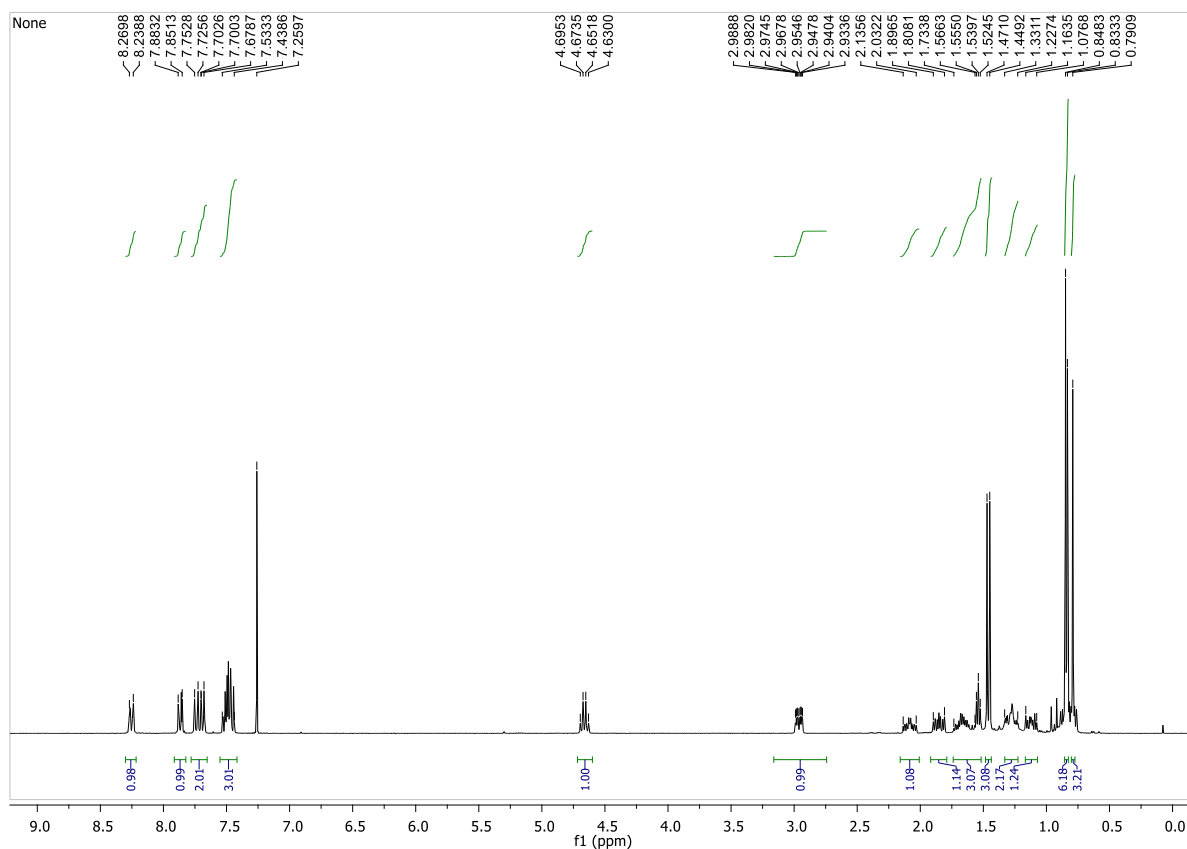


^{13}C (CDCl_3 , 75 MHz)

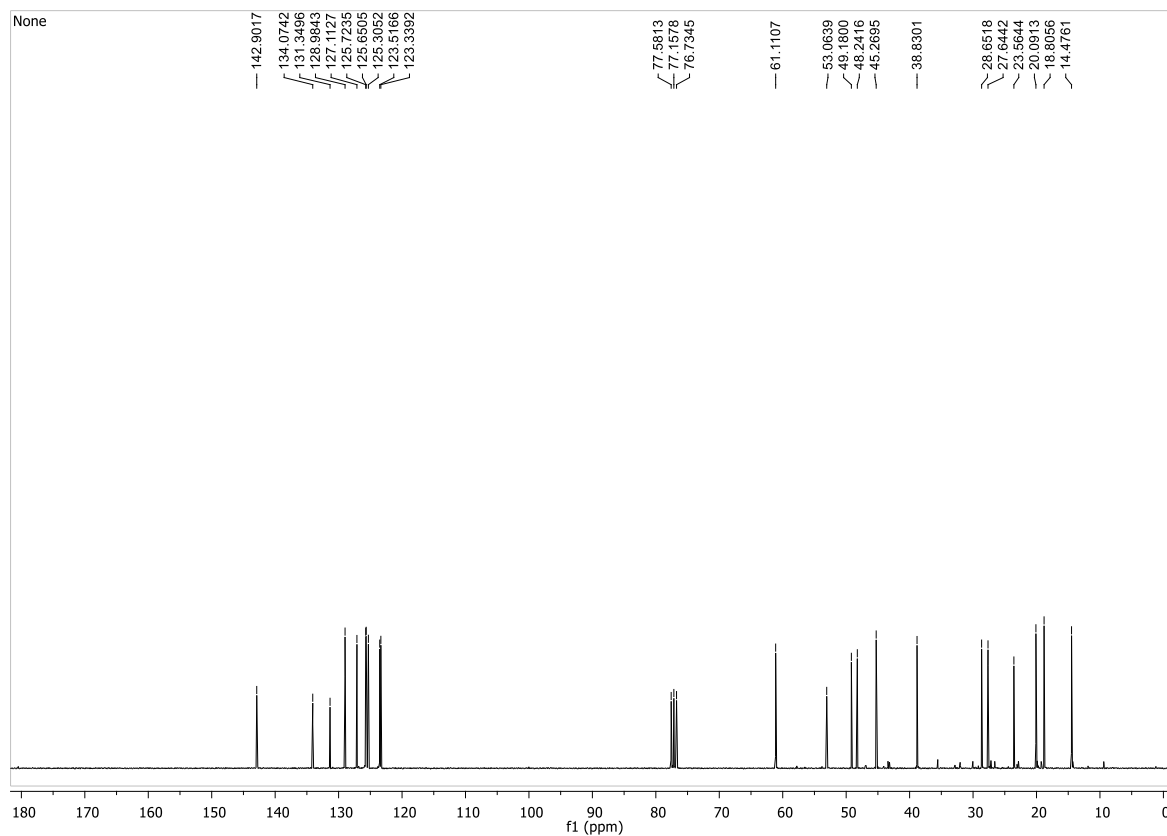


H-endo-S-naph

^1H (CDCl_3 , 300 MHz)

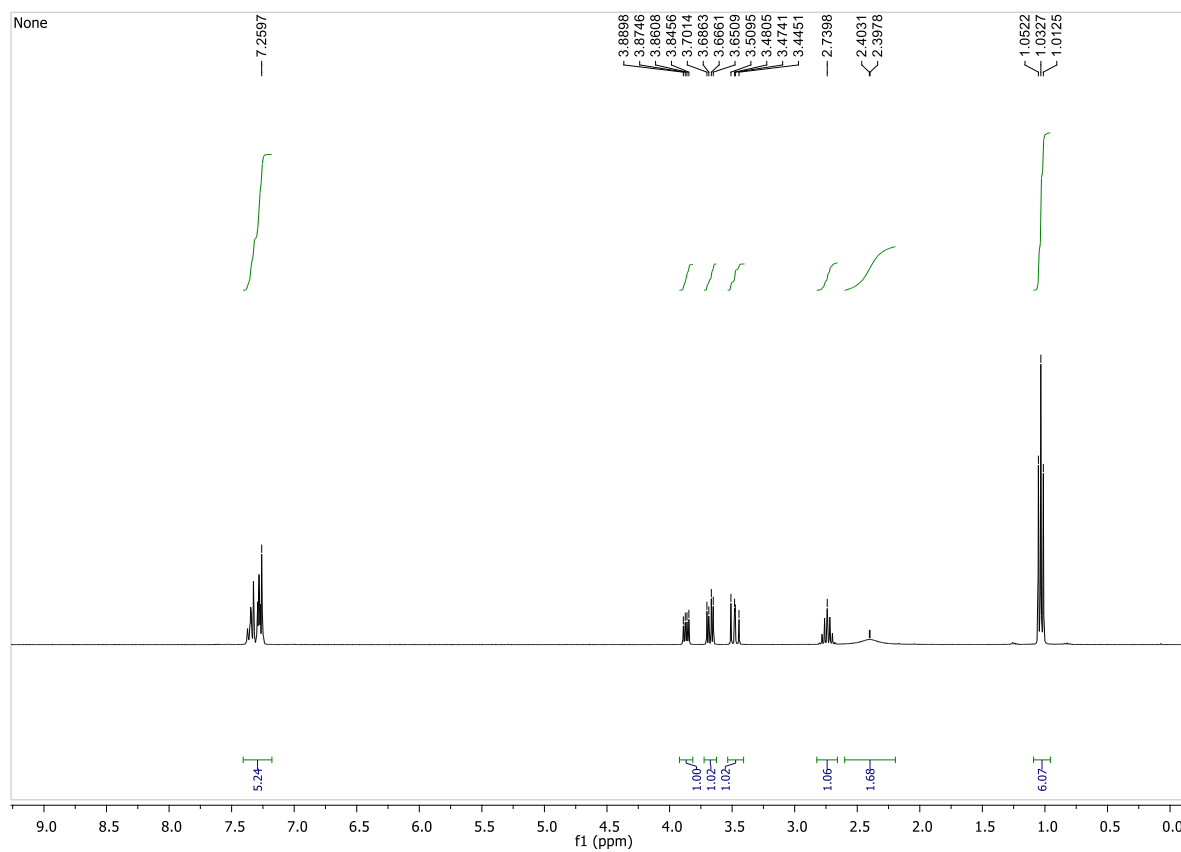


^{13}C (CDCl_3 , 75 MHz)

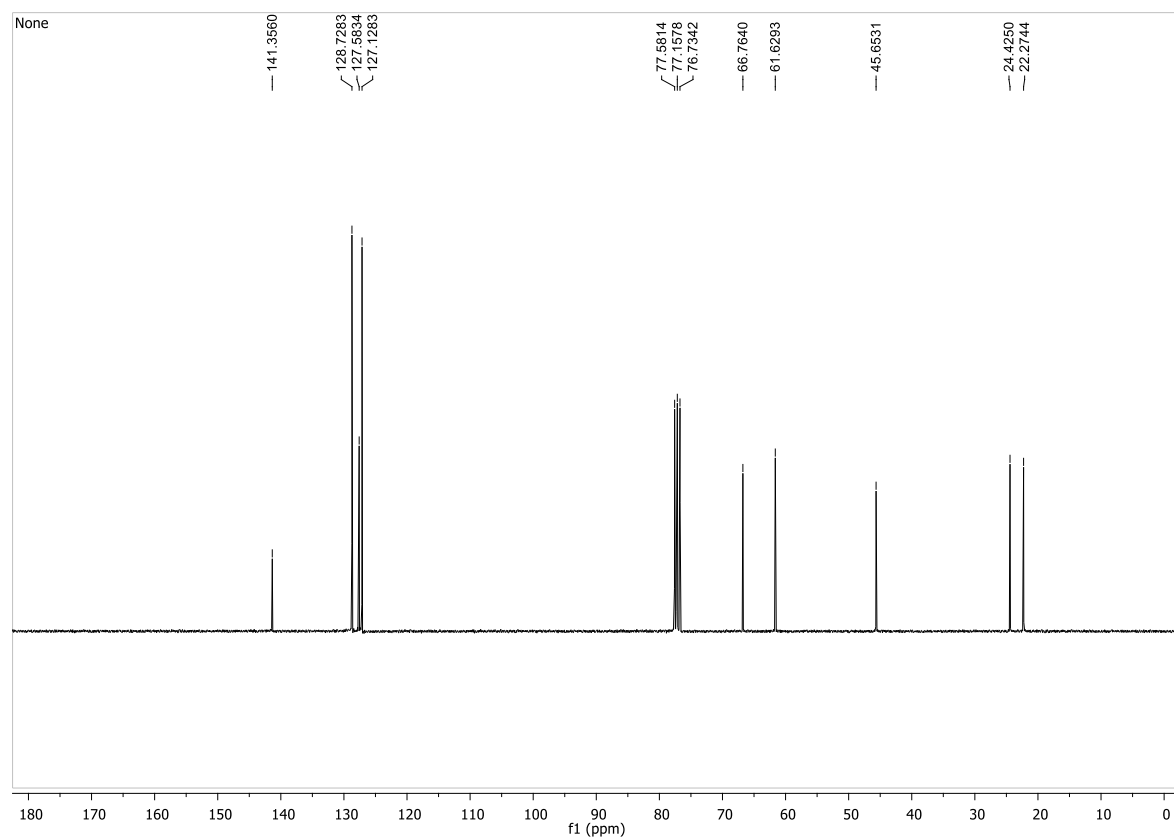


H-iPr-OH-*S*

^1H (CDCl_3 , 300 MHz)

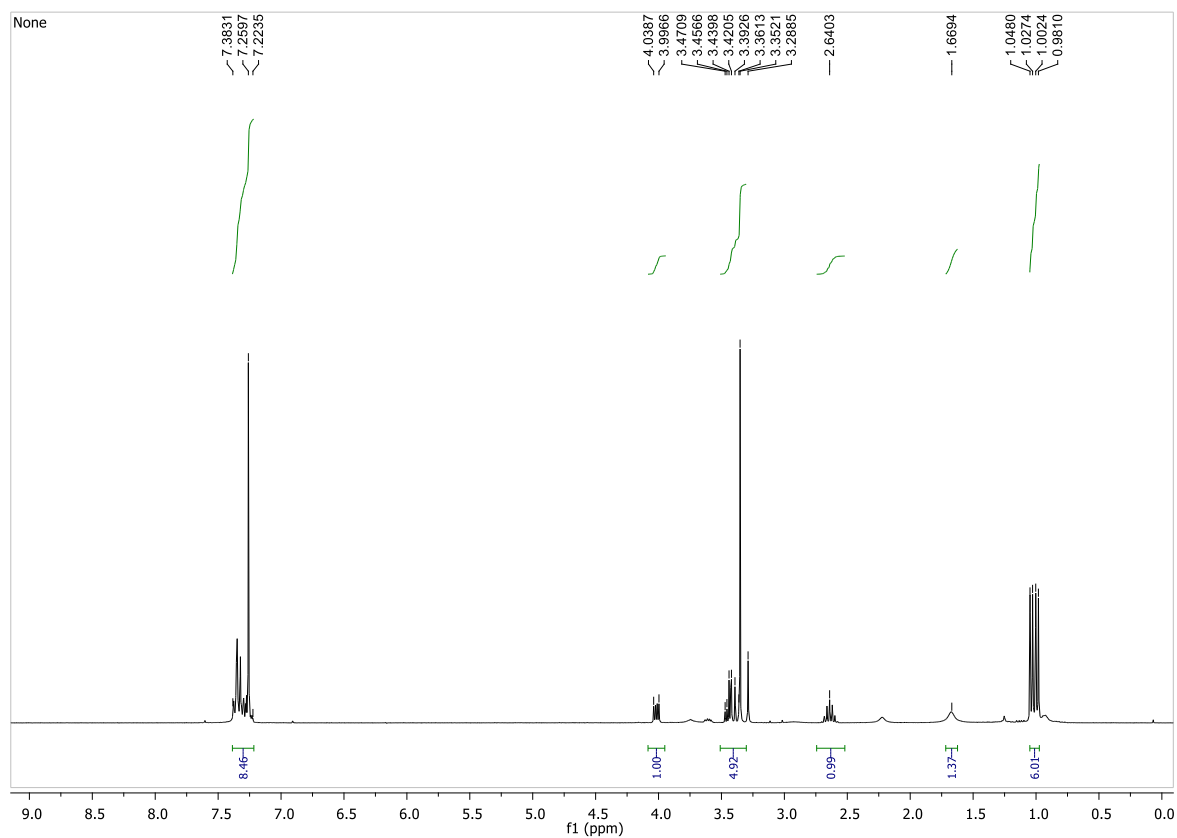


^{13}C (CDCl_3 , 75 MHz)

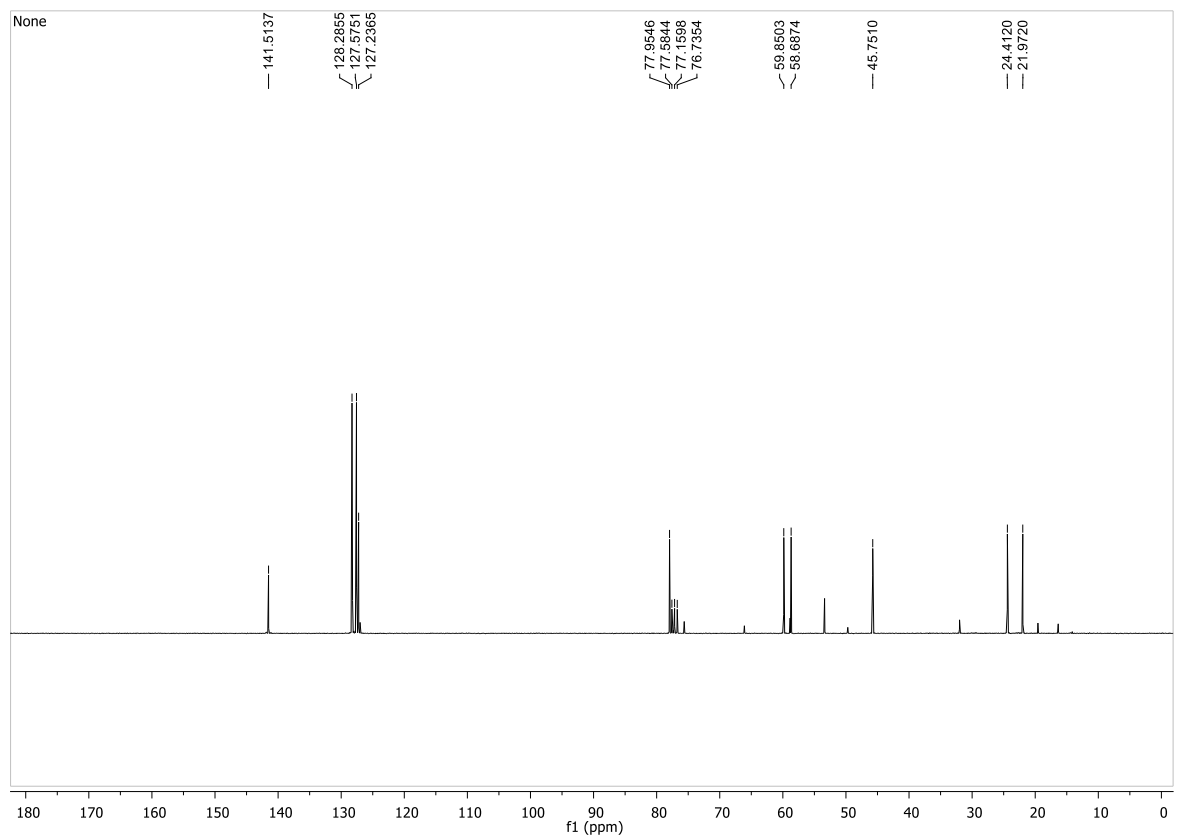


H-iPr-OMe-S

^1H (CDCl_3 , 300 MHz)

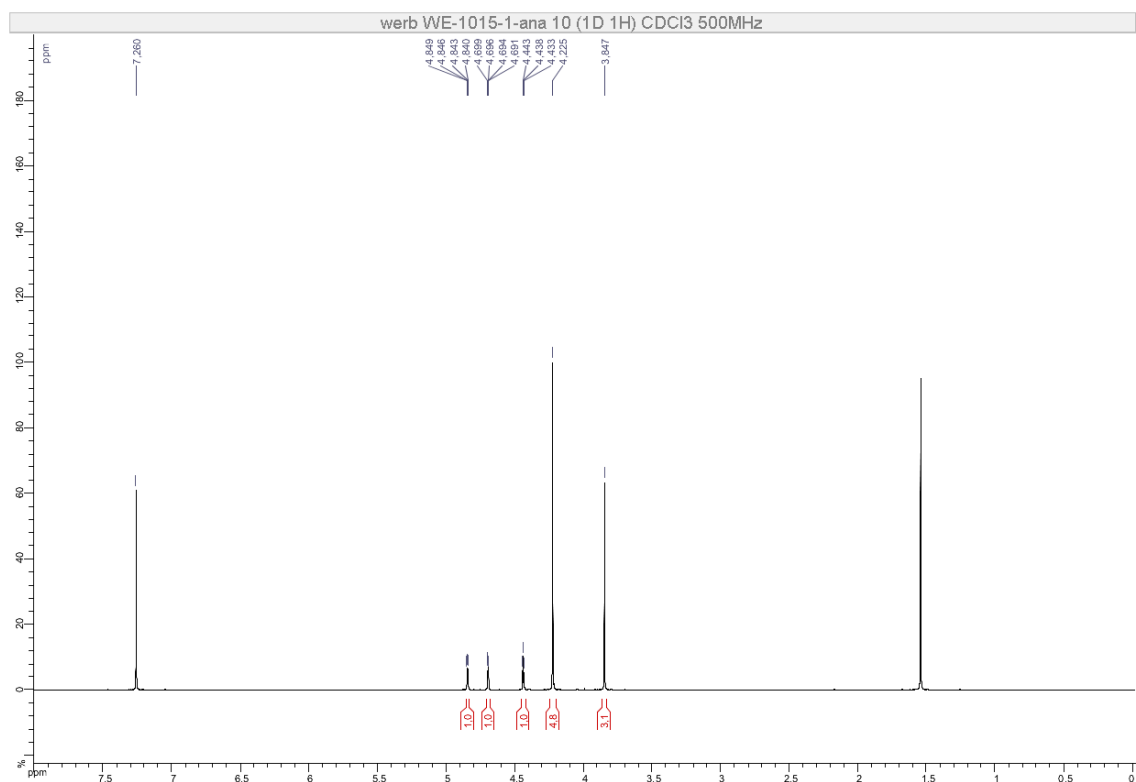


^{13}C (CDCl_3 , 75 MHz)

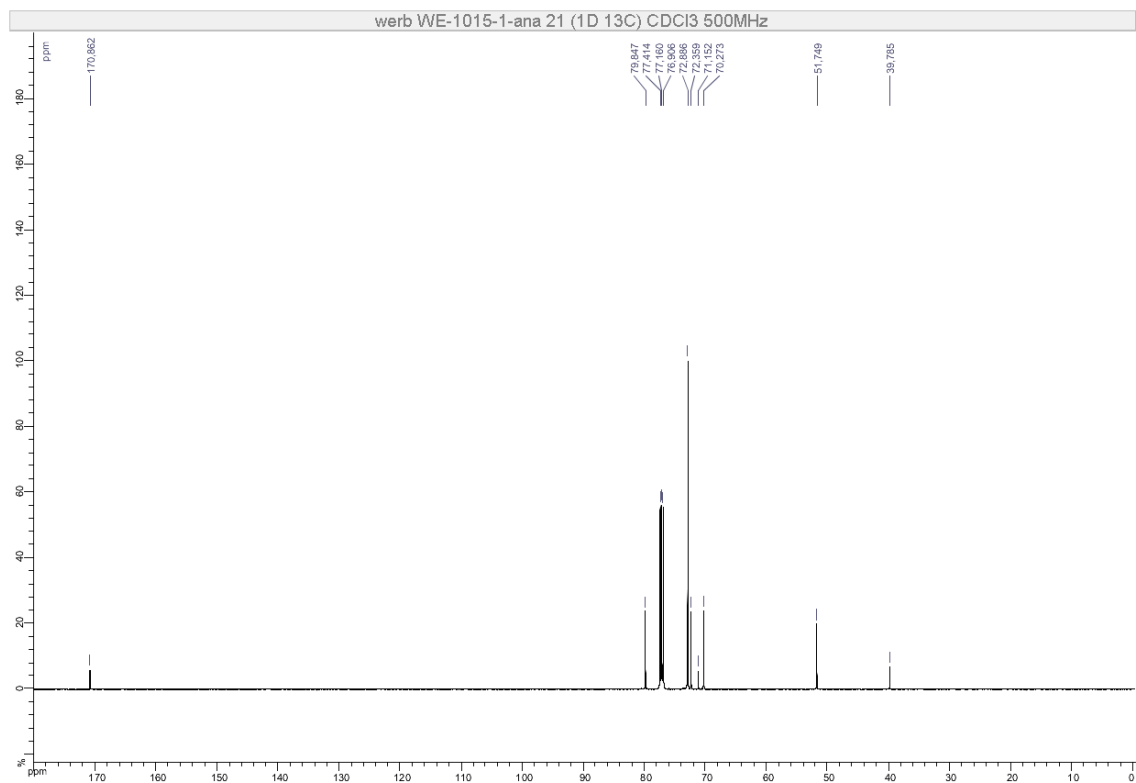


2-Iodo-*O*-methylferrocenecarboxylate (*rac*-1-I)

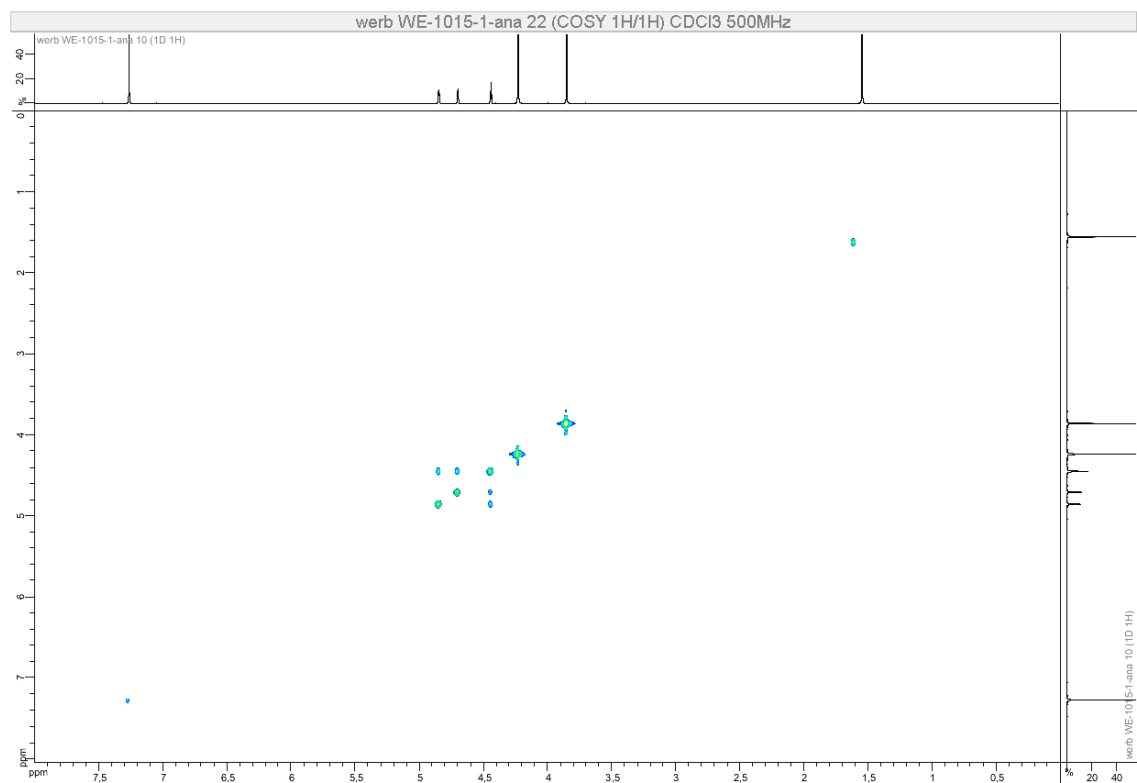
^1H (CDCl_3 , 500 MHz)



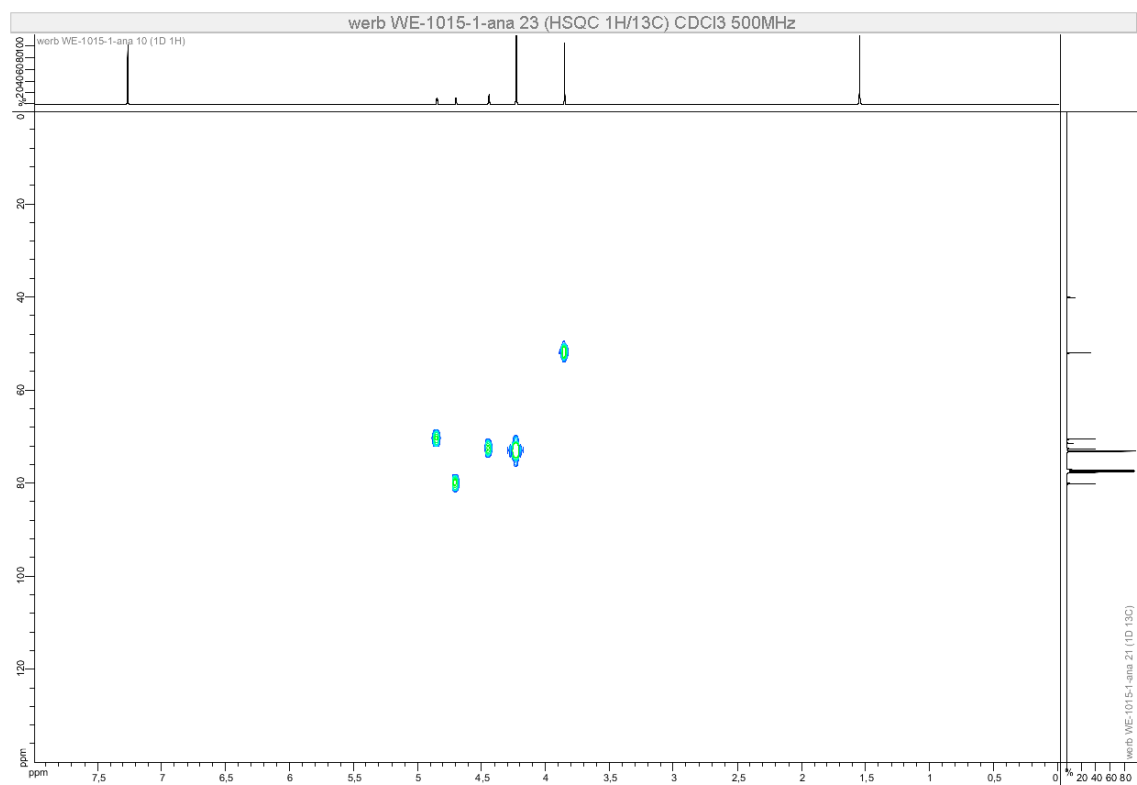
^{13}C (CDCl_3 , 126 MHz)



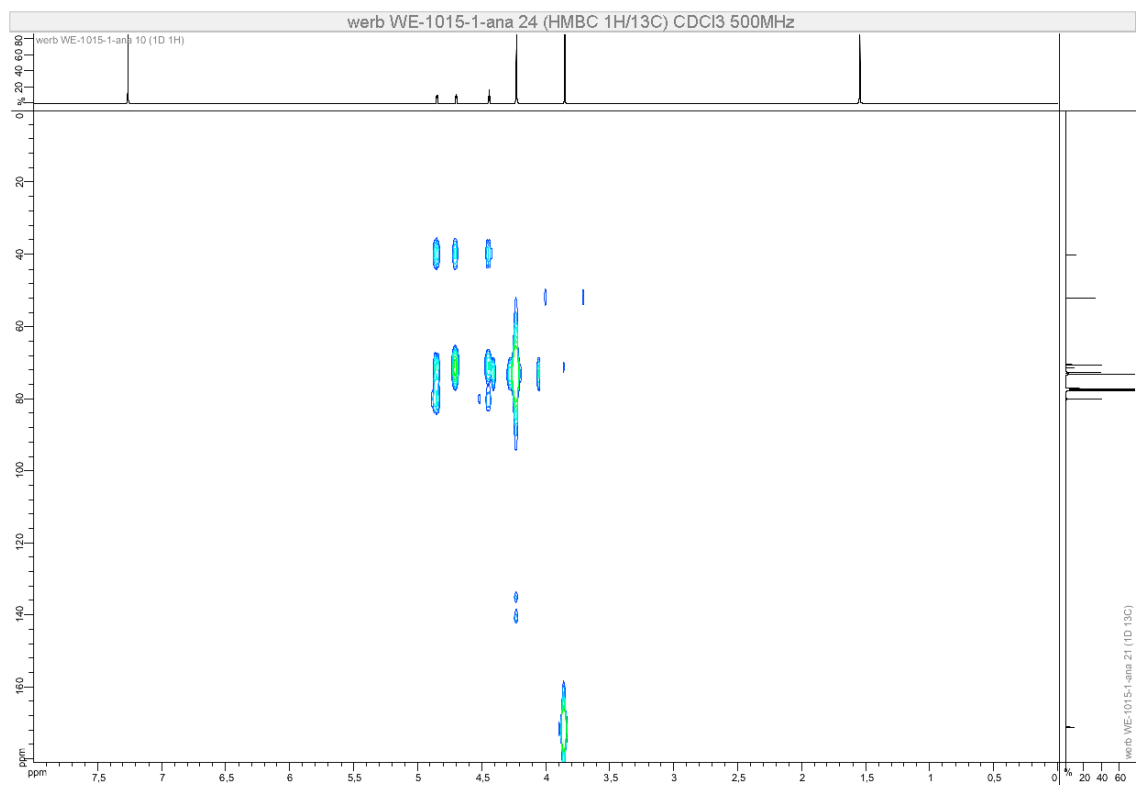
COSY (CDCl₃, 500 MHz)



HSQC (CDCl₃, 500 MHz)

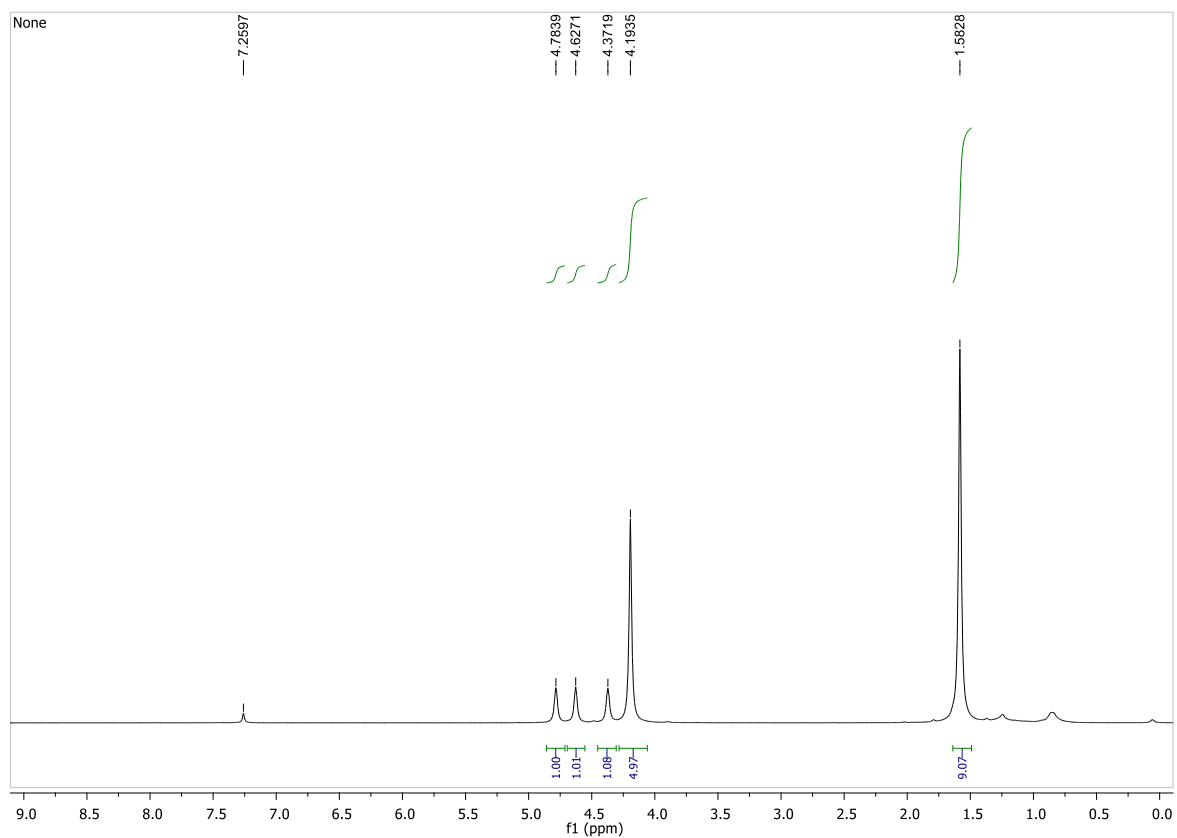


HMBC (CDCl₃, 500 MHz)

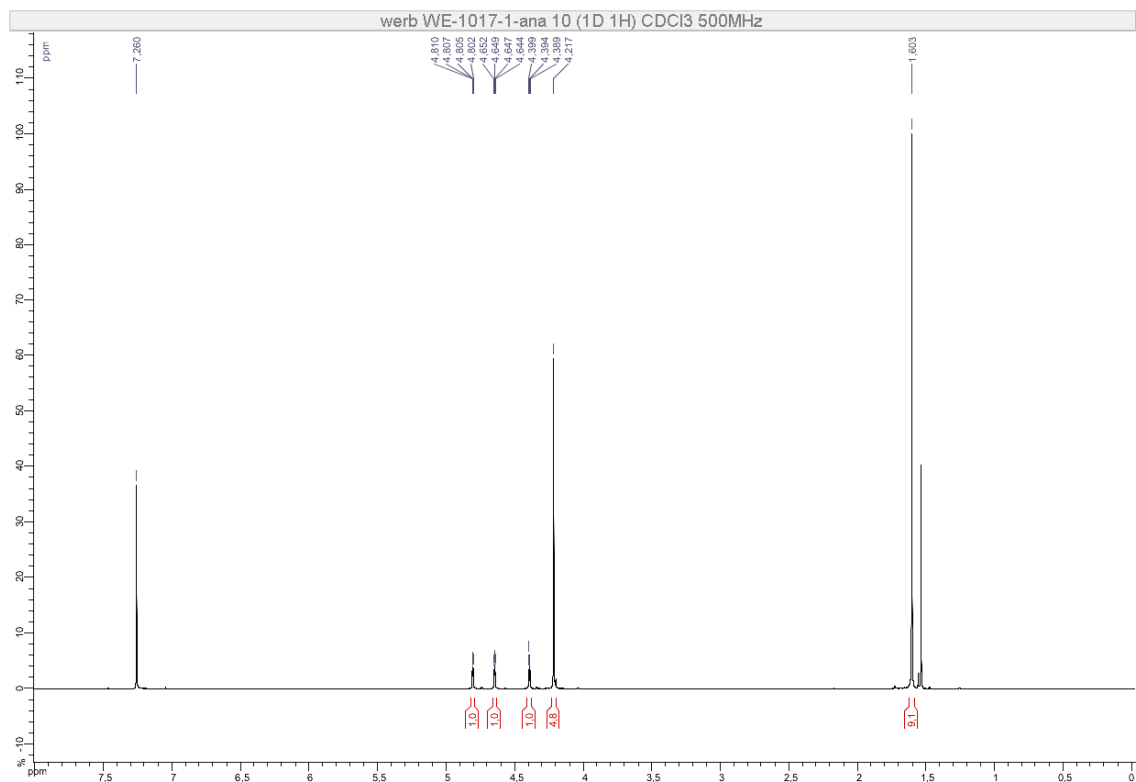


2-Iodo-*O*-*tert*-butylferrocenecarboxylate (*rac*-2-I)

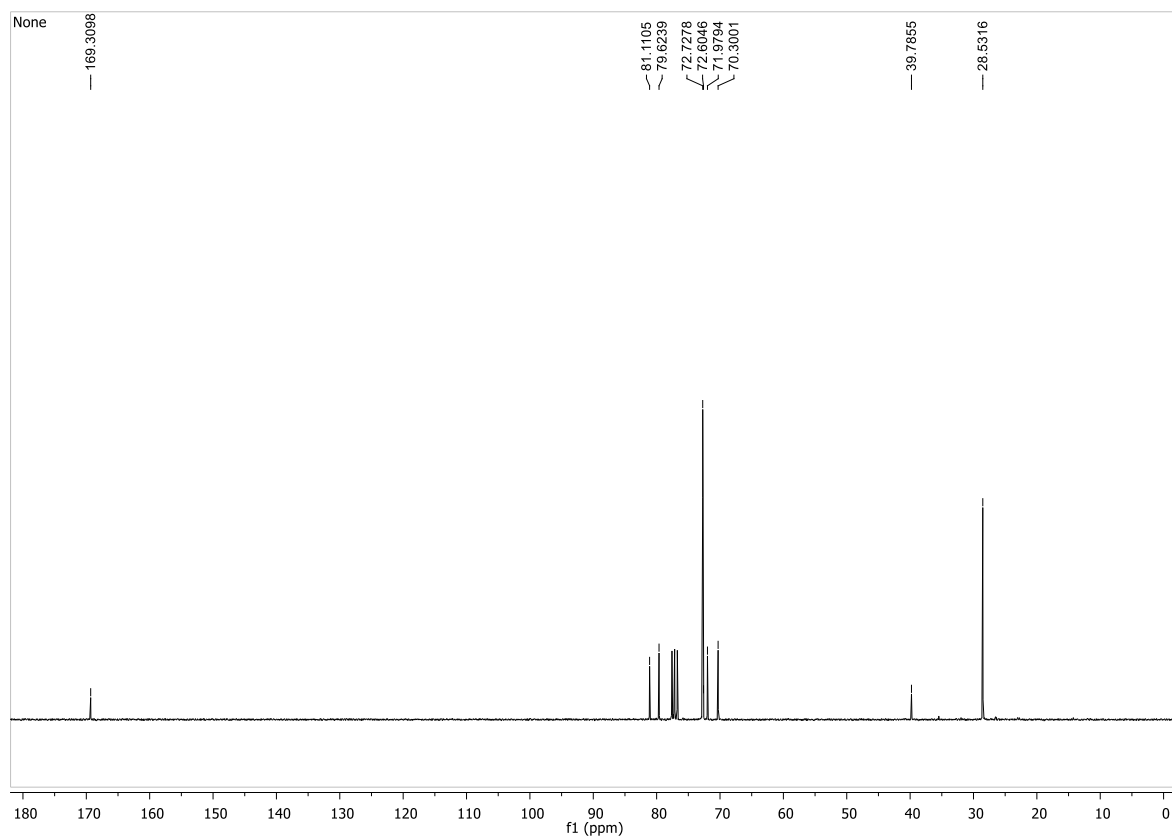
^1H (CDCl_3 , 300 MHz)



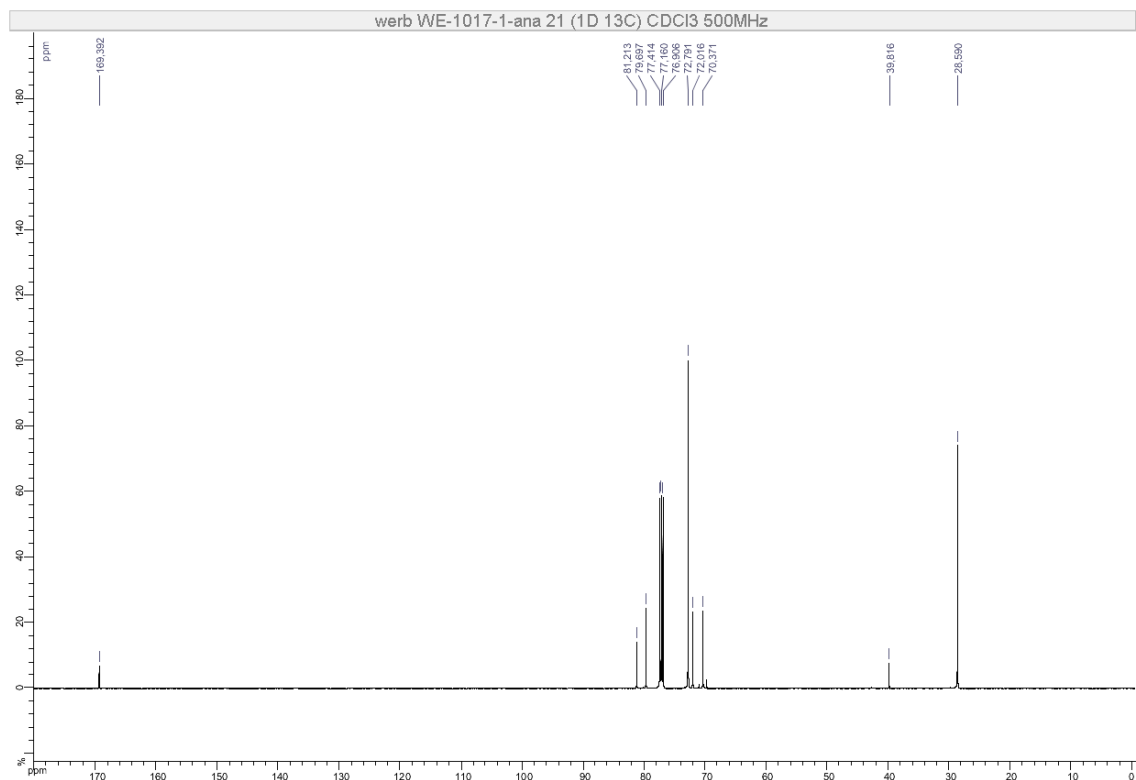
^1H (CDCl_3 , 500 MHz)



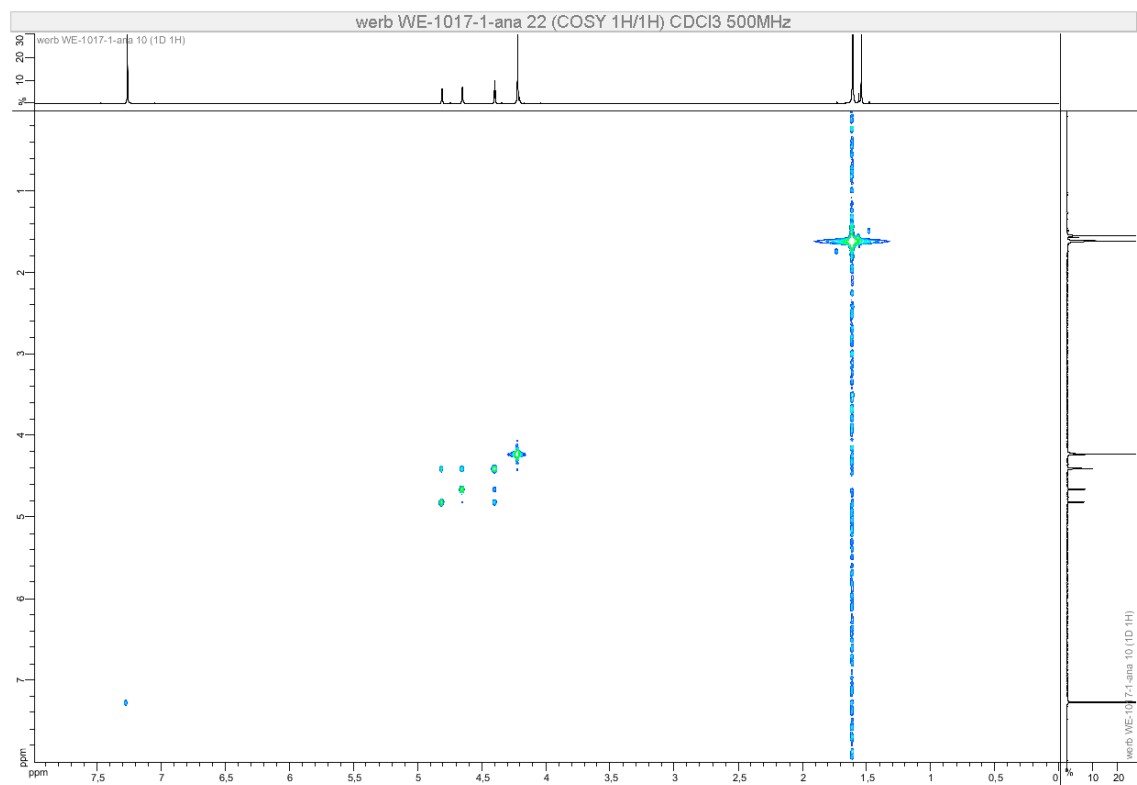
^{13}C (CDCl_3 , 75 MHz)



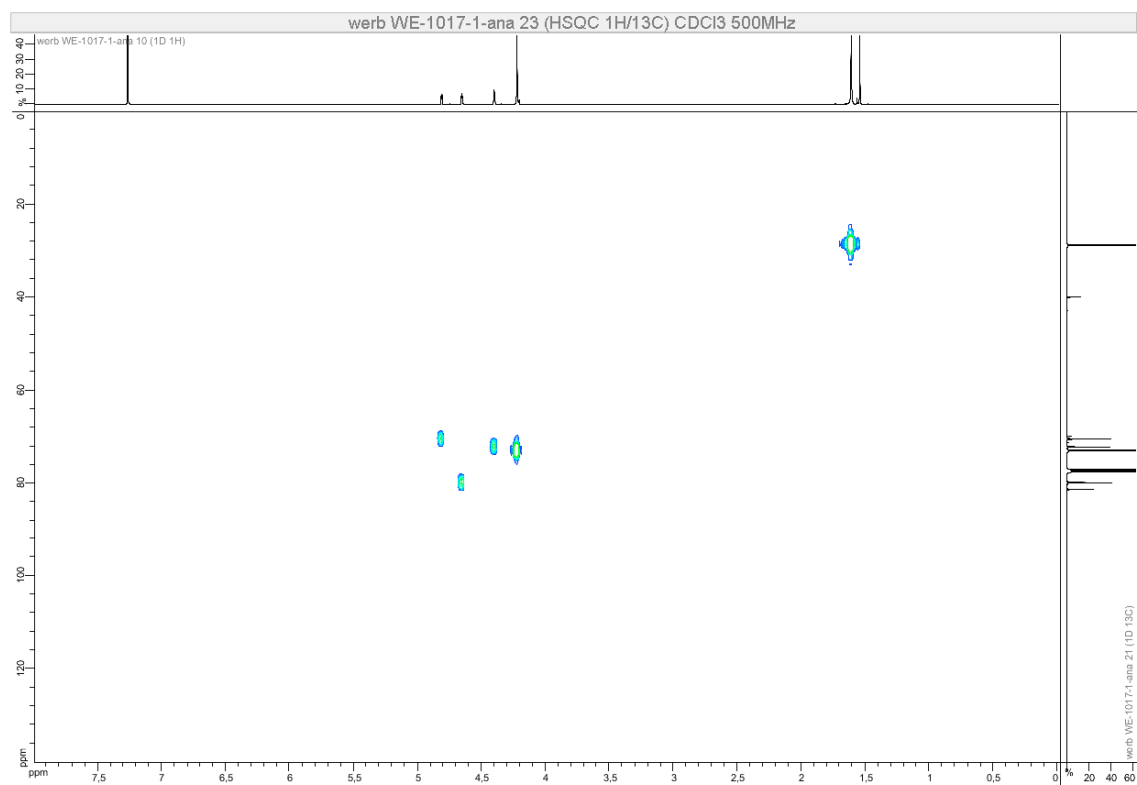
^{13}C (CDCl_3 , 126 MHz)



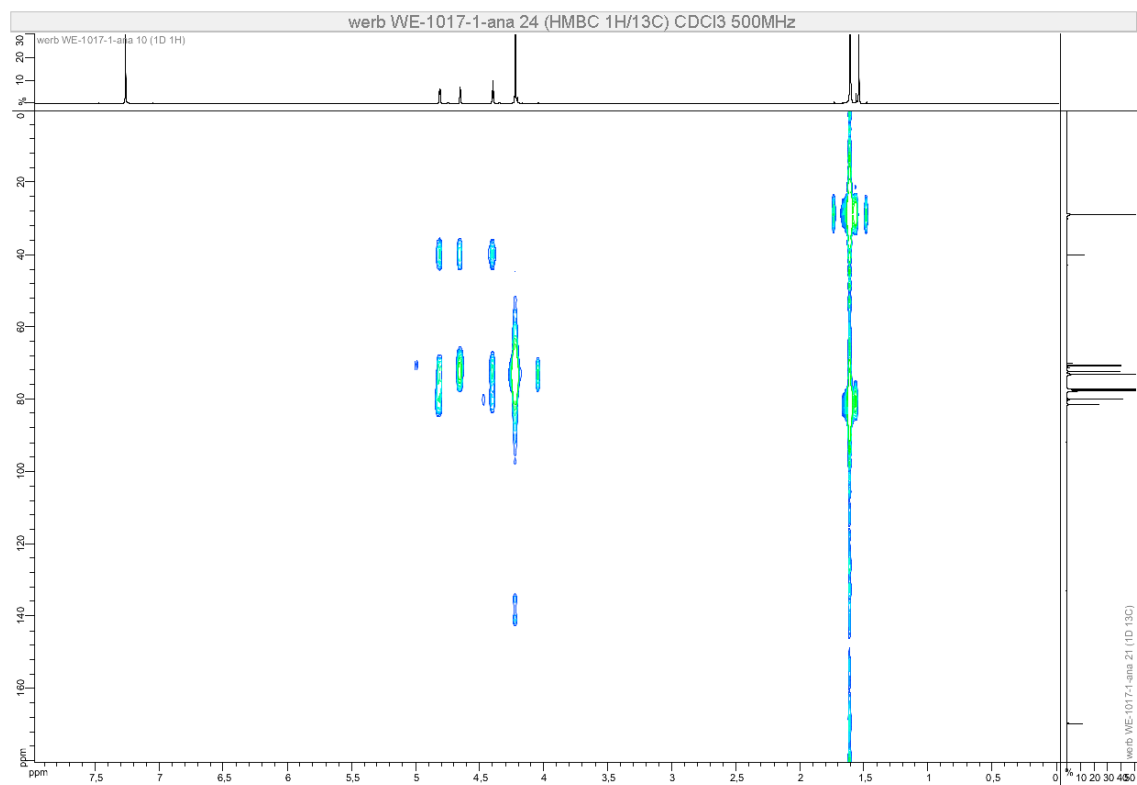
COSY (CDCl₃, 500 MHz)



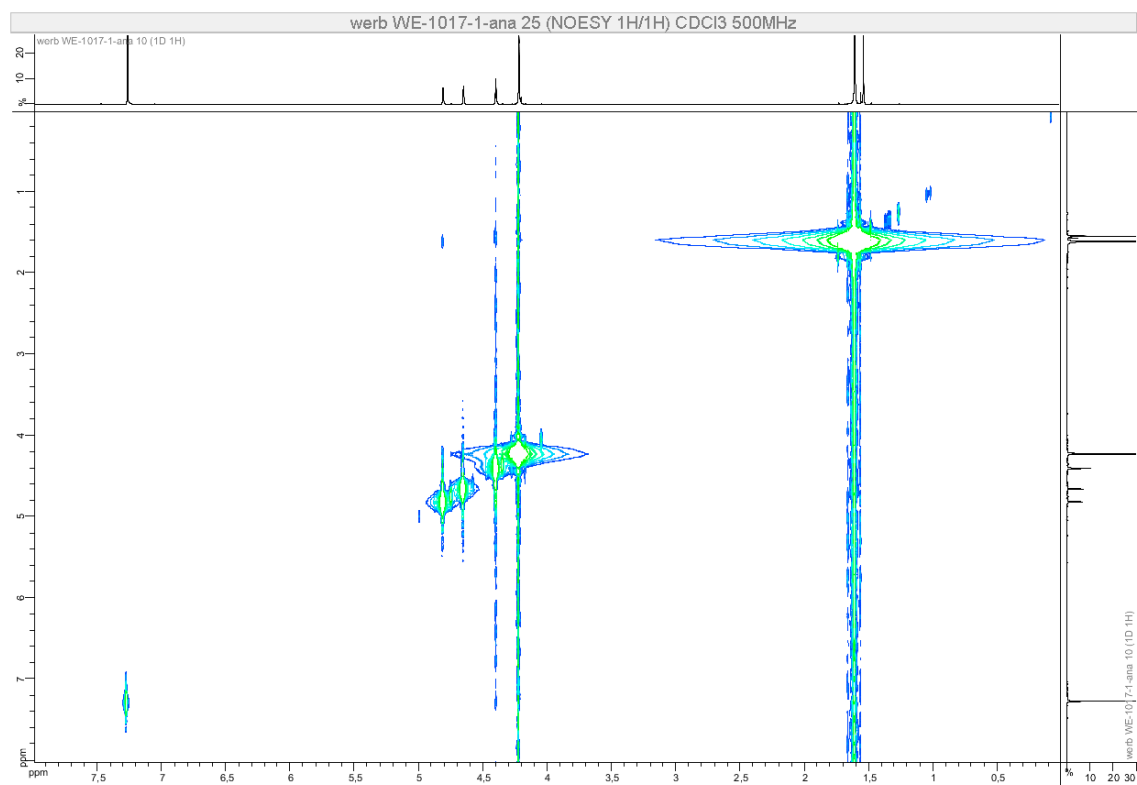
HSQC (CDCl₃, 500 MHz)

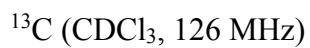


HMBC (CDCl₃, 500 MHz)

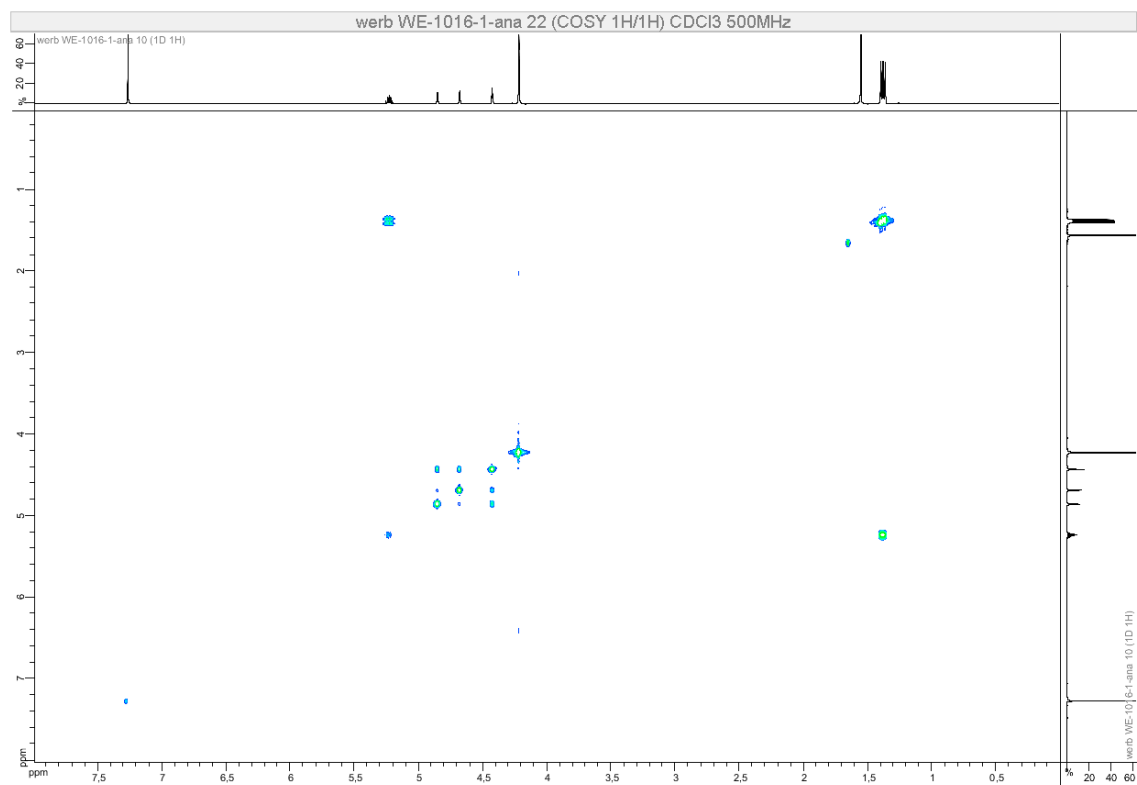


NOESY (CDCl₃, 500 MHz)

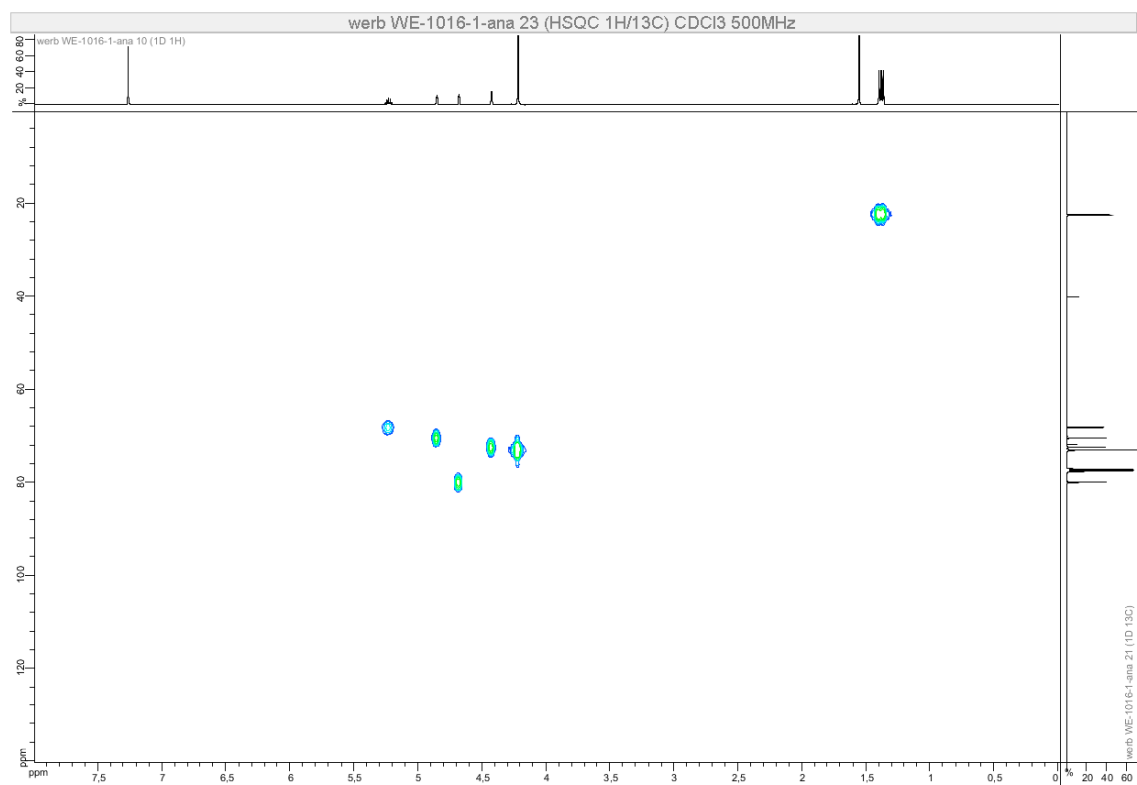


¹H (CDCl₃, 500 MHz)

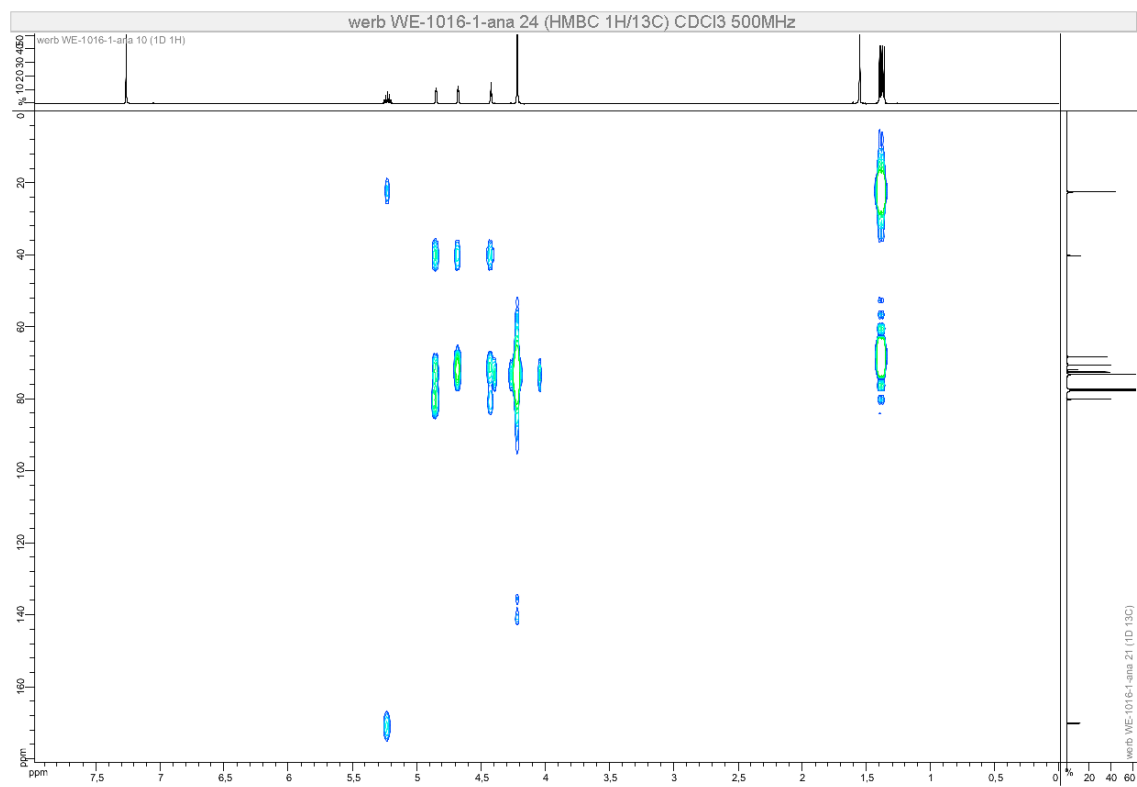
COSY (CDCl₃, 500 MHz)



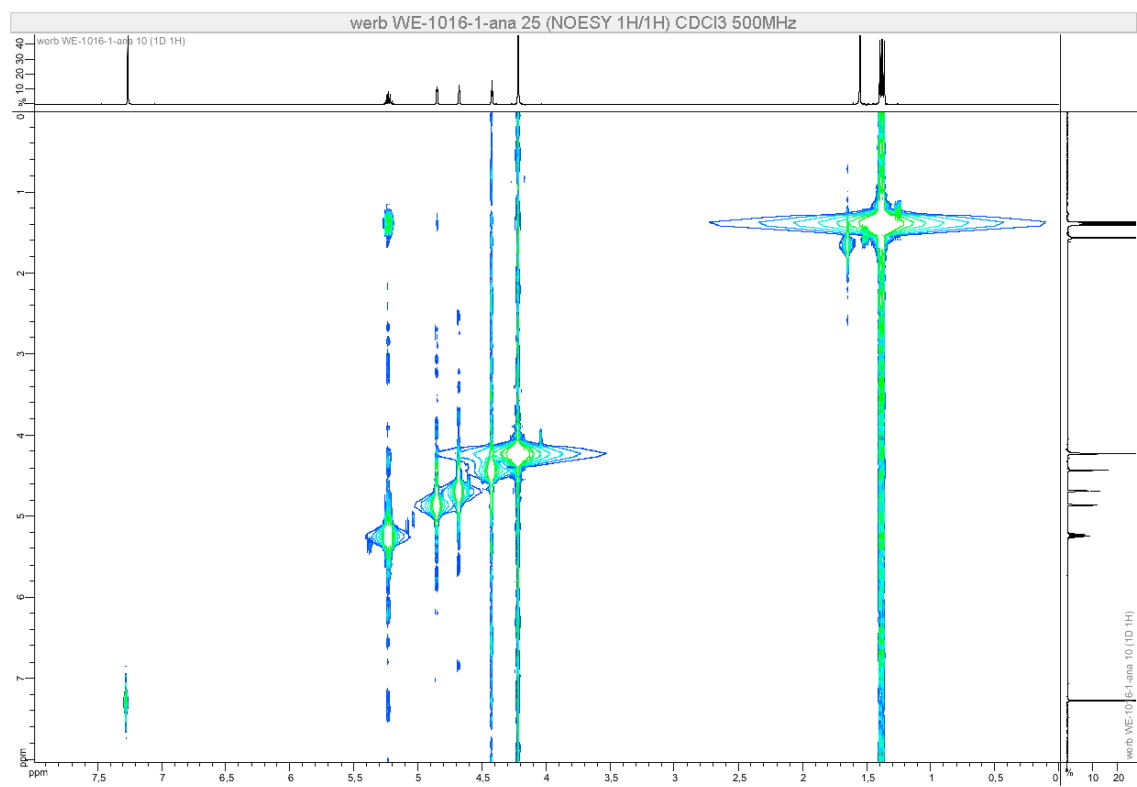
HSQC (CDCl₃, 500 MHz)



HMBC (CDCl₃, 500 MHz)

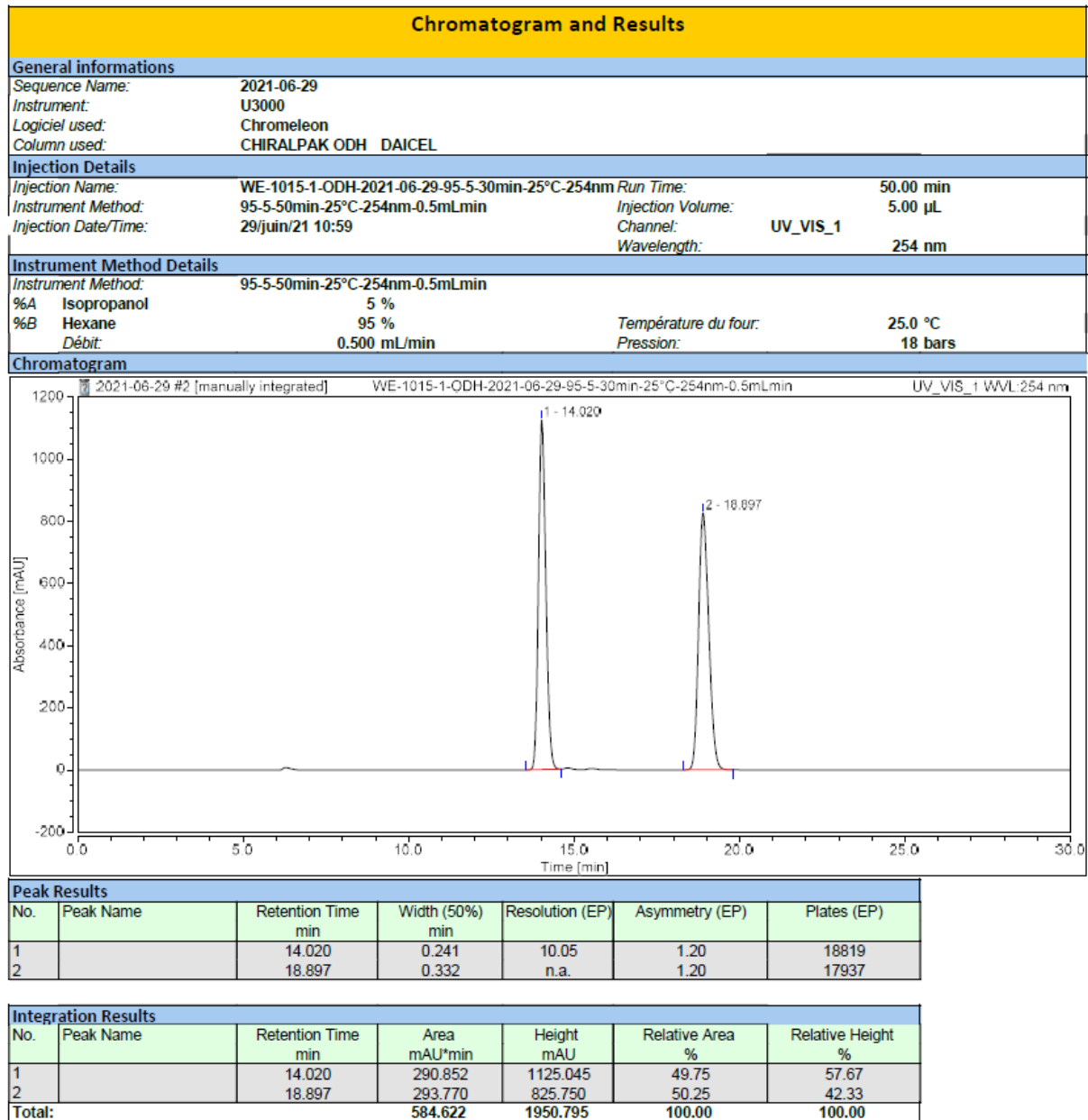


NOESY (CDCl₃, 500 MHz)

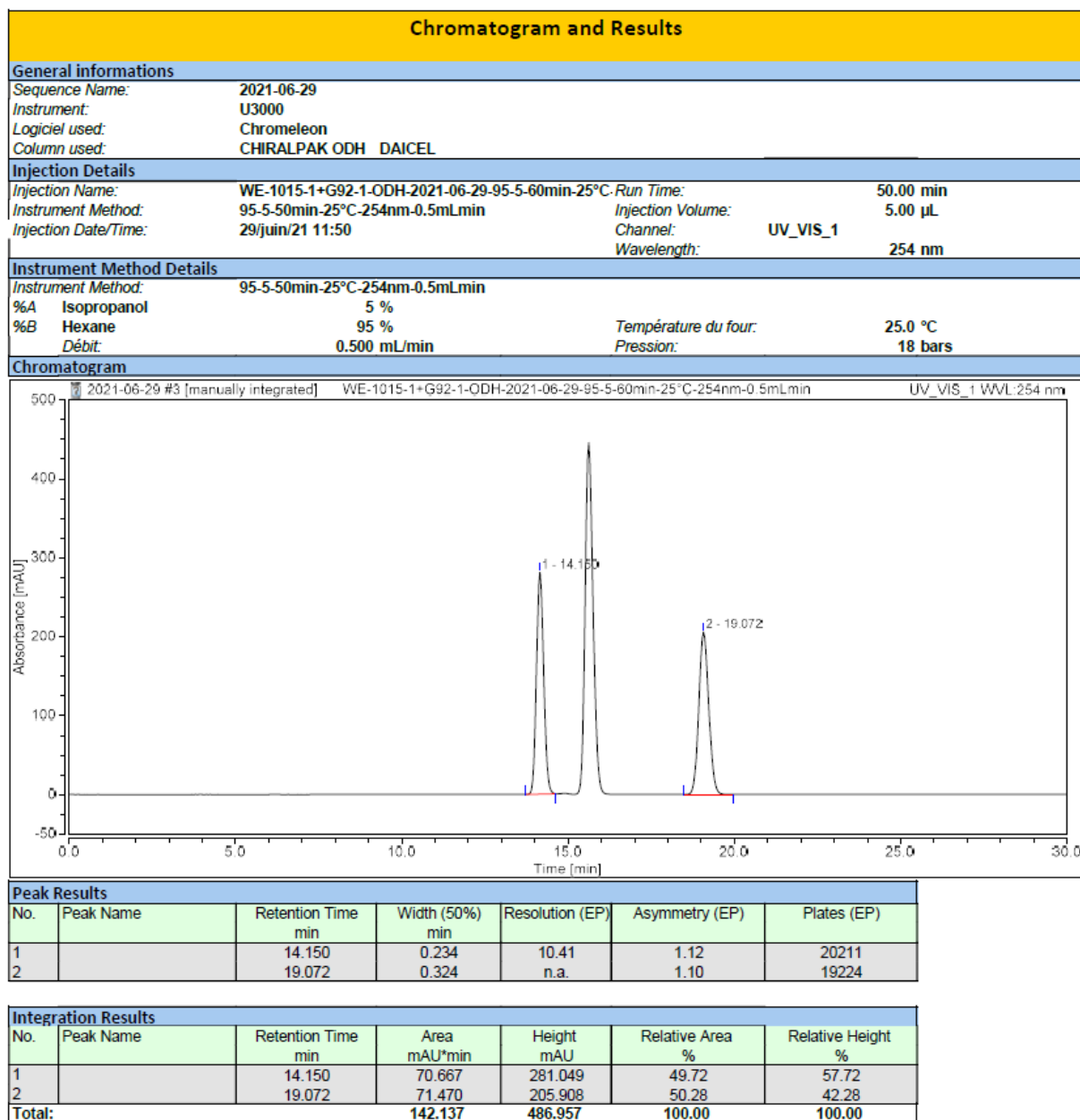


HPLC Chromatograms

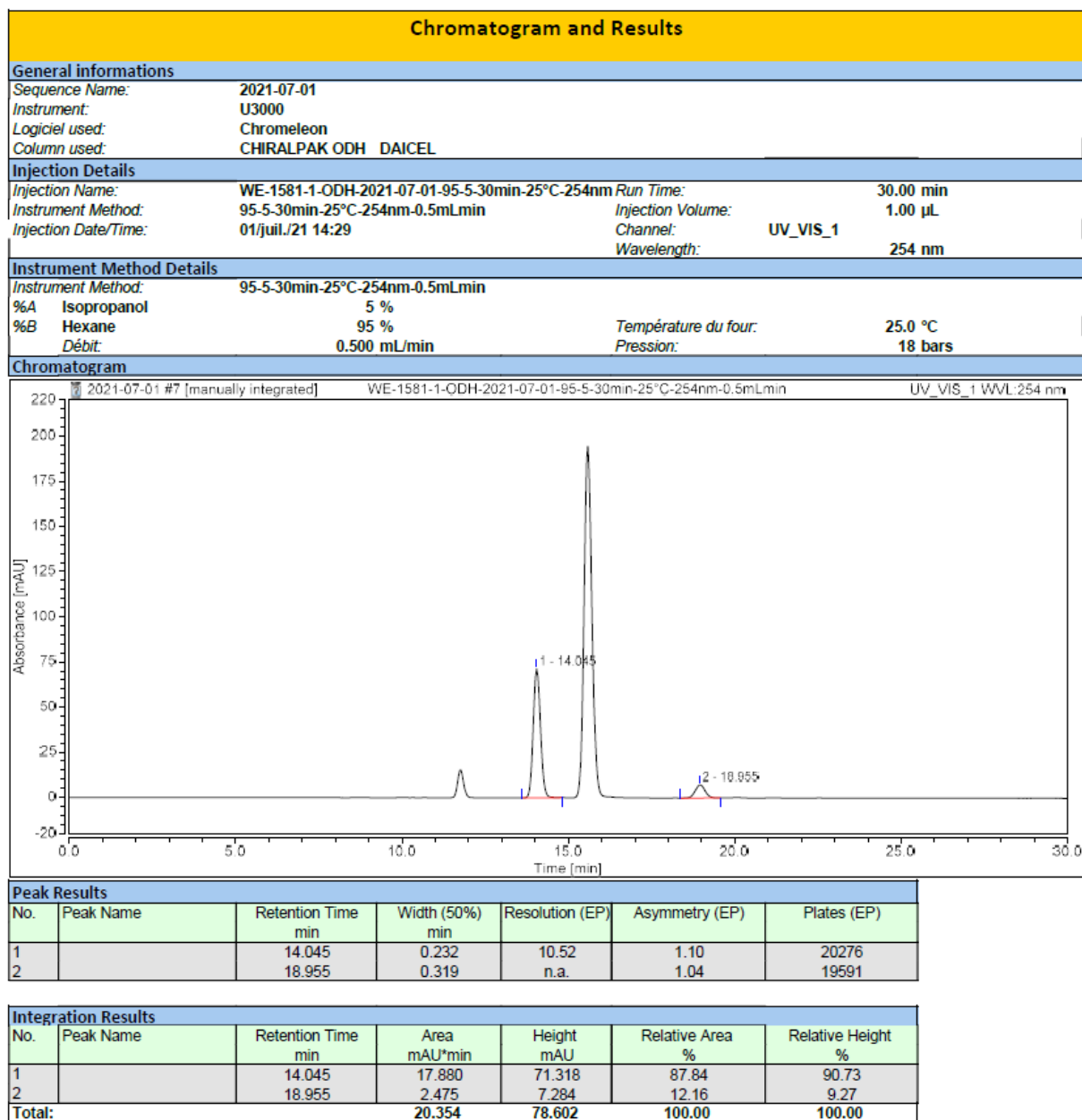
Compound (±)-1-I



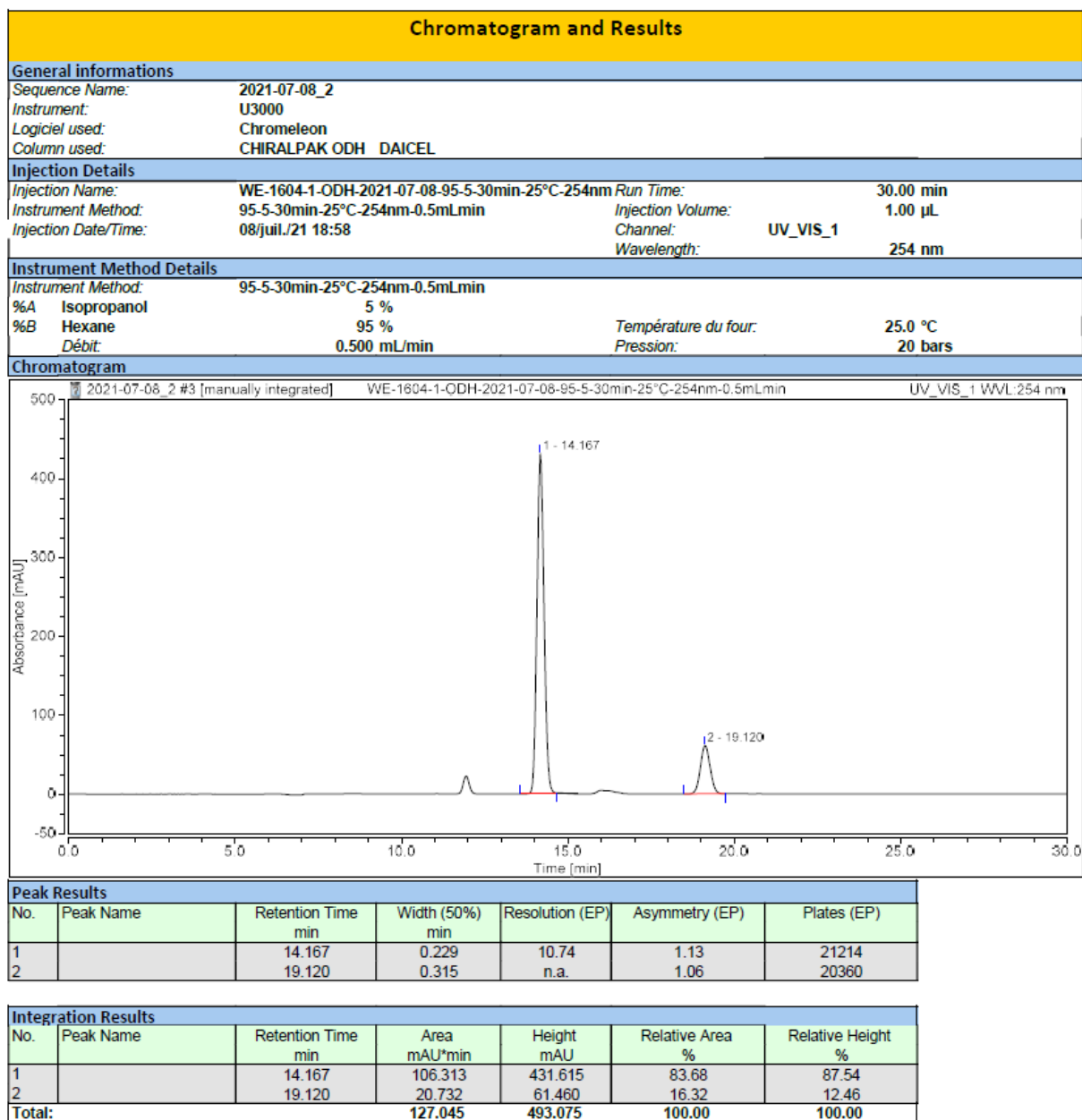
Compound (±)-1-I containing 1-H



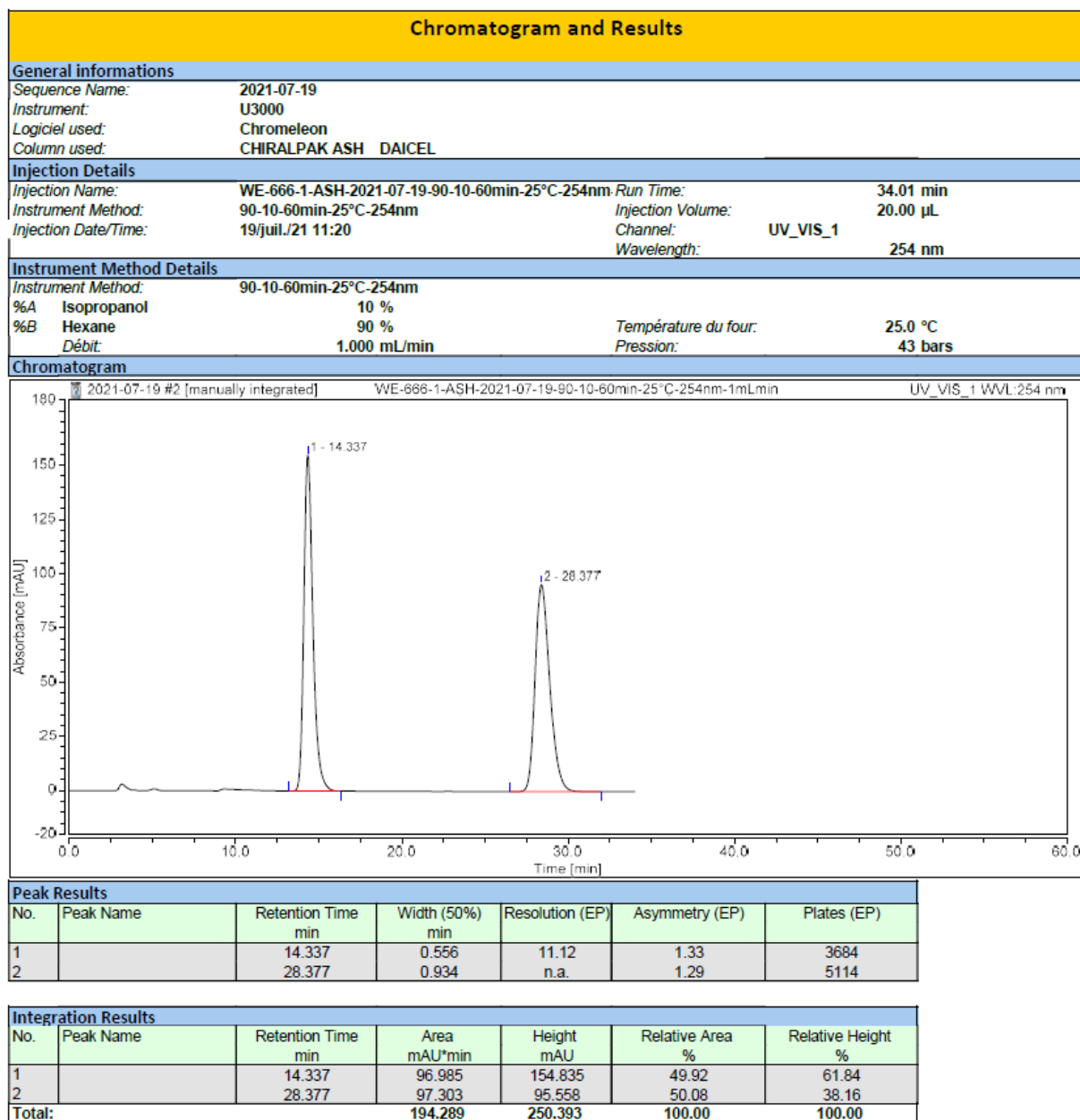
Enantioenriched (*R_p*)-1-I containing 1-H



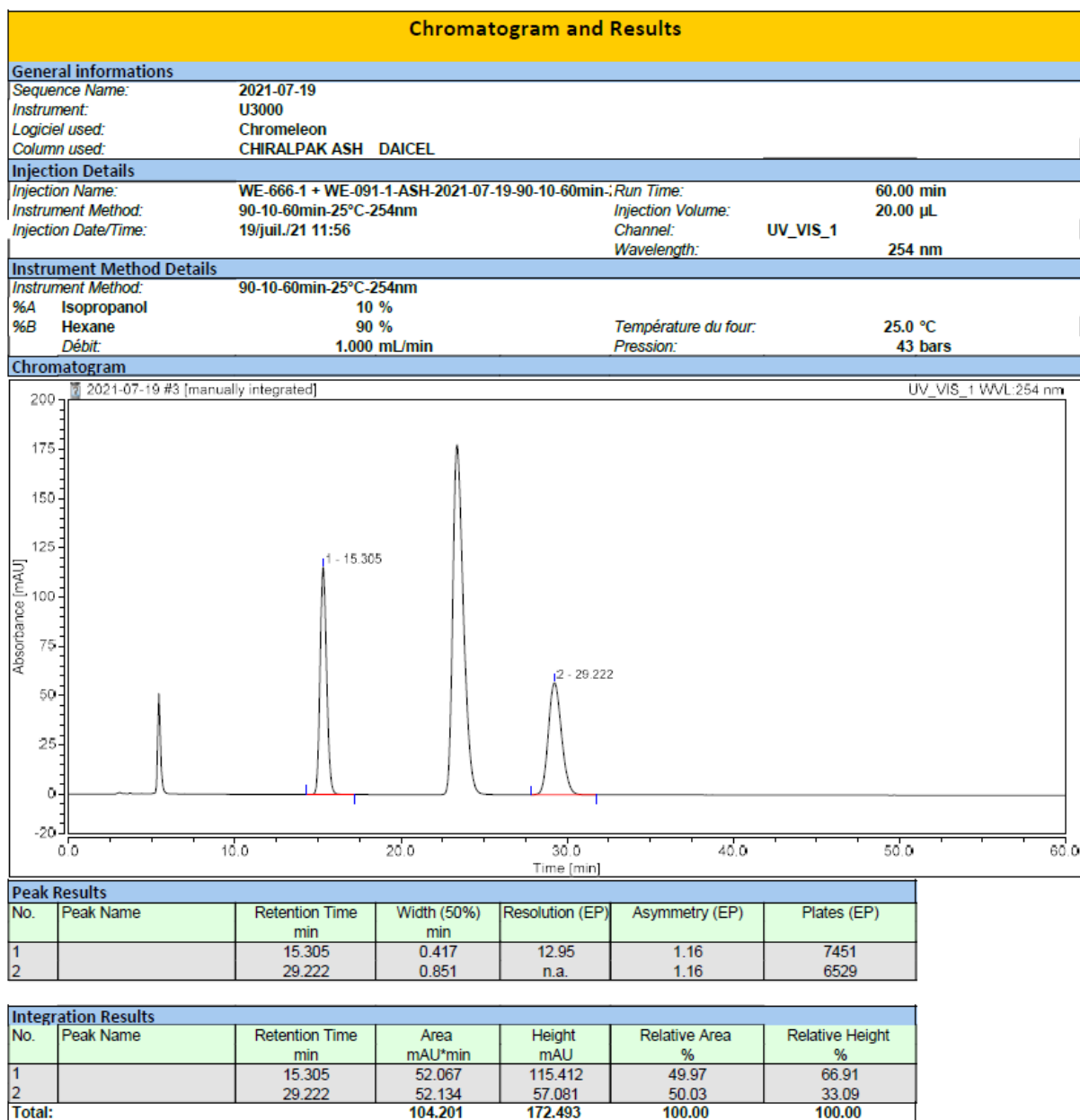
Enantioenriched (*R_p*)-1-I (another one)



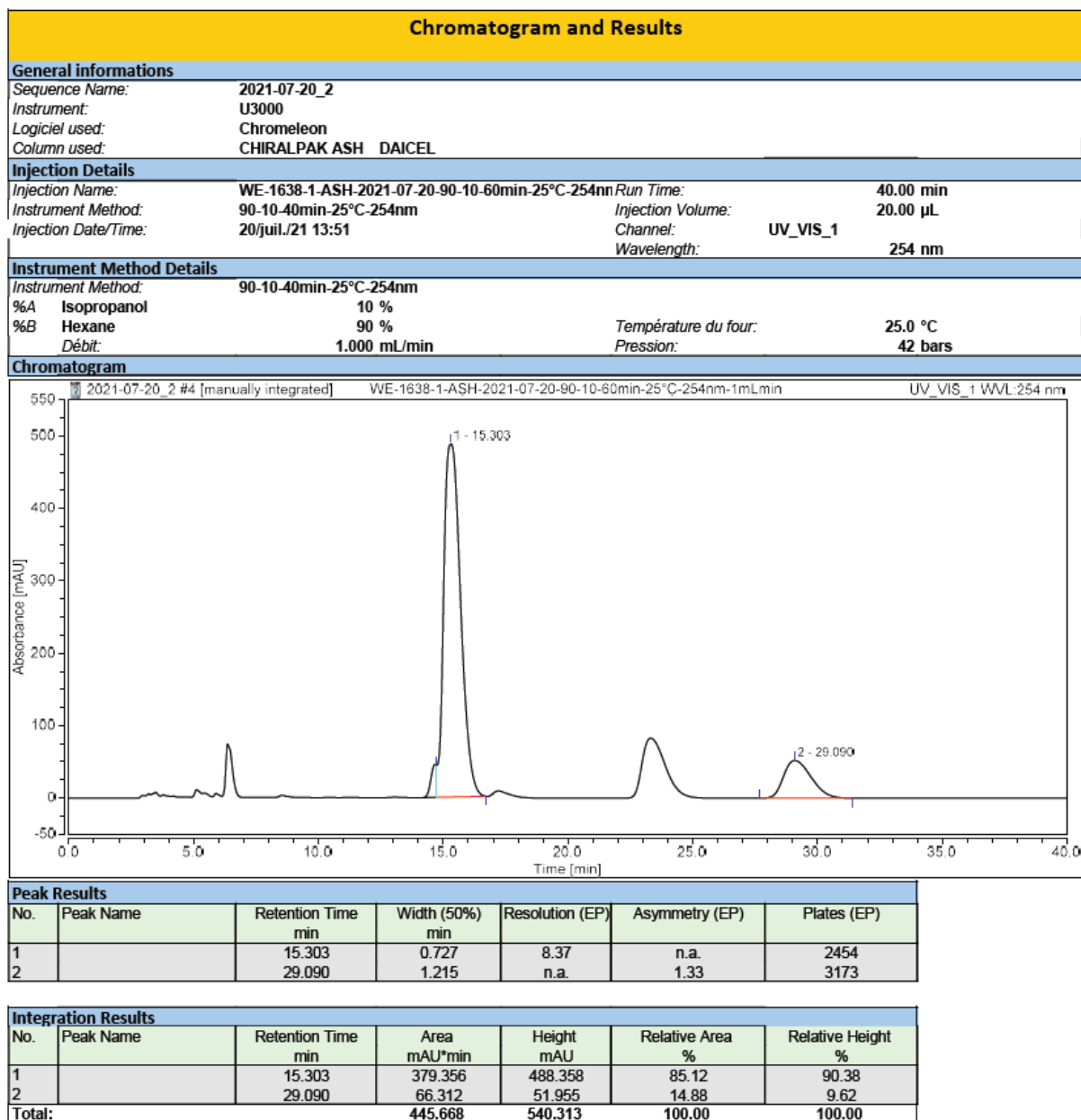
(±)-2-Iodoferrocenemethanol



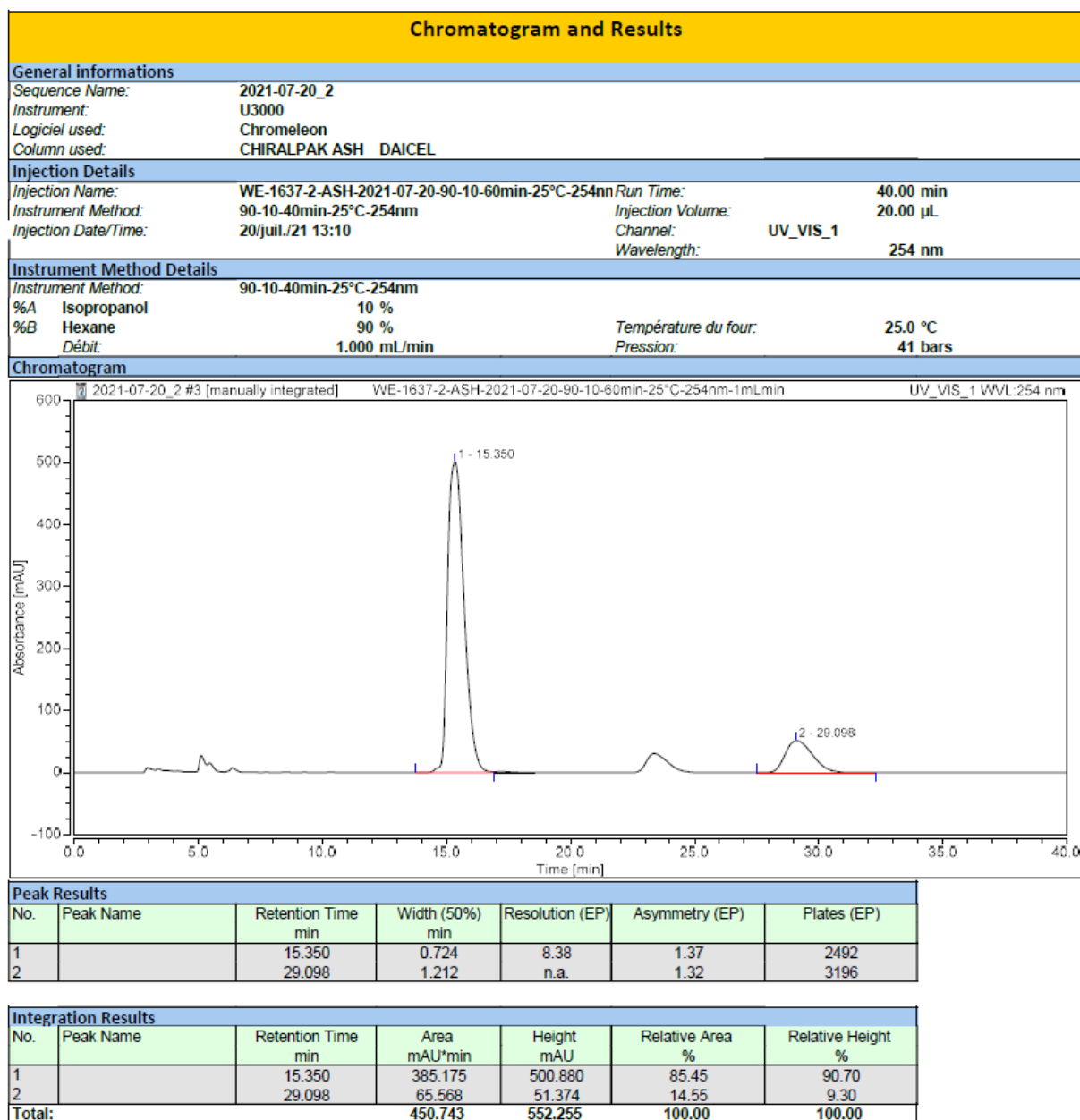
(±)-2-Iodoferrocenemethanol containing ferrocenemethanol



Enantioenriched (*R_p*)-2-iodoferrocenemethanol containing ferrocenemethanol (from 2-I)



Enantioenriched (*R_p*)-2-iodoferrocenemethanol containing ferrocenemethanol (from 3-I)



References

1. A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115-119.
2. G. M. Sheldrick, *Acta Crystallogr. Sect. C: Cryst. Struct. Commun.*, 2015, **C71**, 3-8.
3. L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.
4. C. M. Cain, R. P. C. Cousins, G. Coumbarides and N. S. Simpkins, *Tetrahedron*, 1990, **46**, 523-544.
5. T. Kitagawa, *JP Pat.*, JP1996-1906 09188651, 1997.
6. J. A. Suchocki, E. L. May, T. J. Martin, C. George and B. R. Martin, *J. Med. Chem.*, 1991, **34**, 1003-1010.
7. S. Ganji, F. G. Svensson and C. R. Unelius, *J. Nat. Prod.*, 2020, **83**, 3332-3337.
8. Y. Yang, S. Wang, Y. Li, D. Yuan, B. Zhao, W. Gu and J. Ye, *Huaxue Xuebao*, 2009, **67**, 2463-2474.
9. N. G. Kozlov, T. Pehk and T. Valimae, *Khim. Prir. Soedin.*, 1983, 41-46.
10. M. Majewski and D. M. Gleave, *J. Org. Chem.*, 1992, **57**, 3599-3605.
11. P. I. Arvidsson, G. Hilmersson and Ö. Davidsson, *Chem. Eur. J.*, 1999, **5**, 2348-2355.
12. A. Ando and T. Shioiri, *Tetrahedron*, 1989, **45**, 4969-4988.