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Enantioselective deprotometalation of alkyl ferrocenecarboxylates using bimetallic bases

Gandrath Dayaker,^a William Erb,^{a,*} Madani Hedidi,^{a,b} Floris Chevallier,^{a,*} Marielle Blot,^a Philippe C. Gros,^c Göran Hilmersson,^d Thierry Roisnel,^a Vincent Dorcet,^a Ghenia Bentabed-Ababsa^b and Florence Mongin^{a,*}

 ^a Univ Rennes, CNRS, ISCR (Institut des Sciences Chimiques de Rennes) - UMR 6226, F-35000 Rennes, France
^b Laboratoire de Synthèse Organique Appliquée, Faculté des Sciences Exactes et Appliquées, Université Oran1 Ahmed Ben Bella, BP 1524 El M'Naouer, 31000 Oran, Algeria
^c Université de Lorraine, CNRS, L2CM, F-54000 Nancy, France
^d Department of Chemistry, Göteborg University, 412 96 Göteborg, Sweden

william.erb@univ-rennes1.fr, floris.chevallier@ens-lyon.fr, florence.mongin@univ-rennes1.fr

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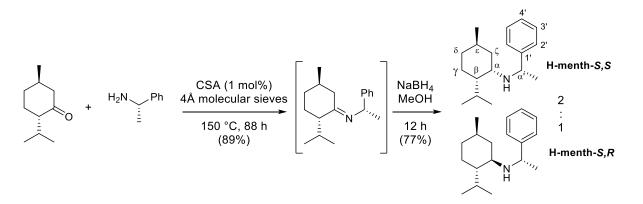
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Synthesis of the secondary amines

General crystallographic details

The X-ray diffraction data of **H-menth-***S*,*S* ·**HCl**, **H-pino-***R*,*R* ·**HCl**, **4-O**₂**NC**₆**H**₄**CO-pino-***S*,*S*, **H-pino-***S*,*R* ·**HCl** and **4-O**₂**NC**₆**H**₄**CO-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

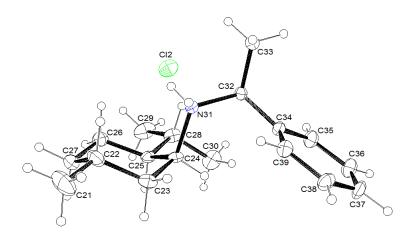
 (αS) - α -Methyl-N-[(1S,2S,5R)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-S,S) and (αS) - α -methyl-N-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]benzylamine (H-menth-S,R)



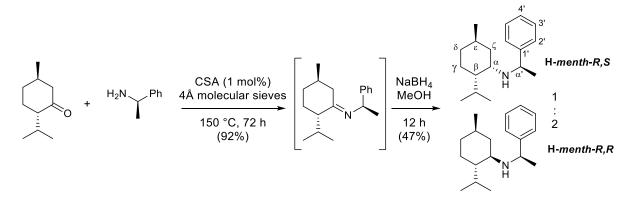
They were prepared by adapting a procedure described.⁴ A mixture of (*S*)- α -methylbenzylamine (5.1 mL, 40 mmol), L- or (–)-menthone (3.1 g, 20 mmol), and camphorsulfonic acid (46 mg, 0.20 mmol) was heated under stirring in the presence of 4Å molecular sieves (7 g) at 150 °C for 4 days. The mixture 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 then heptane-Et₂O 98:2). (aS)-a-Methyl-N-[(1S,2S,5R)-2-isopropyl-5wash methylcyclohexyl]benzylamine (H-menth-S,S)⁵ was first isolated in 50% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 80:20) 0.6; $[\alpha]_D$ -8.0 (c 1.25); ¹H NMR (300 MHz, CDCl₃) δ 0.73 (d, 3H, J = 6.5 Hz, Me-C ϵ), 0.66-0.94 (m, 3H, H β , H δ and H ζ), 0.91 (d, 3H, J = 6.6 Hz, Me₂CH), 0.97 (d, 3H, J = 6.6 Hz, Me_2 CH), 1.01-1.24 (m, 2H, Hy and NH), 1.29 (d, 3H, J = 6.5 Hz, Me-Ca'), 1.49-1.68 (m, 5H, H ζ , H δ , H γ , H ϵ and CHMe₂), 3.05 (q, 1H, J = 2.9 Hz, H α), 3.80 (q, 1H, J = 6.5 Hz, H α '), 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, Me₂CH), 21.6 (CH₃, Me₂CH), 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, Ca), 56.3 (CH, Ca'), 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) & 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: $C_{18}H_{30}ClN$, M = 295.88, 150(2)K, monoclinic, $P 2_1$, a = 11.4383(9), b = 10.9604(14), c = 14.2059(13) Å, $\beta = 98.636(4)$ °, V= 1760.8(3) Å³, Z = 4, d = 1.116 g cm⁻³, μ = 0.210 mm⁻¹. A final refinement on F² with 7320 unique intensities and 369 parameters converged at $\omega R(F^2) = 0.0962$ (R(F) = 0.0533) for 5011 observed

reflections with $I > 2\sigma(I)$. CCDC 2110270. (*aS*)-*a*-Methyl-*N*-[(1*R*,2*S*,5*R*)-2-isopropyl-5methylcyclohexyl]benzylamine (H-menth-*S*,*R*) was next isolated in 27% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 80:20) 0.5; [*a*]_D -54.0 (c 2.1); ¹H NMR (300 MHz, CDCl₃) δ 0.87 (d, 3H, *J* = 6.6 Hz, Me-Cɛ), 0.89 (d, 3H, *J* = 6.7 Hz, *Me*₂CH), 1.03 (d, 3H, *J* = 6.7 Hz, *Me*₂CH), 1.12-1.38 (m, 4H), 1.30 (d, 3H, *J* = 6.6 Hz, *Me*-Cα'), 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, Hα), 3.90 (q, 1H, *J* = 6.6 Hz, Hα'), 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, Cγ), 24.9 (CH₃), 26.7 (CH), 30.2 (CH), 31.5 (CH₂), 35.6 (CH₂), 45.9 (CH), 54.9 (CH, Cα), 55.0 (CH, Cα'), 126.7 (CH, C4'), 126.8 (2CH, C2' and C6'), 128.3 (2CH, C3' and C5'), 146.6 (C, C1'); HRMS (ESI; MeOH), *m/z* 260.2379 (0 ppm) found (calcd for C₁₈H₃₀N, [M+H]⁺, requires 260.23783).



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

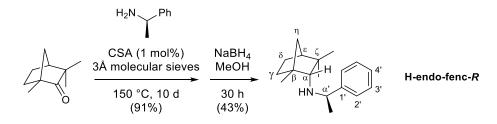


They were prepared by adapting a procedure described:⁴ A mixture of L- or (–)-menthone (3.1 g, 20 mmol), (R)- α -methylbenzylamine (5.1 mL, 40 mmol), and camphorsulfonic acid (46 mg, 0.20

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 heptane-Et₂O silica wash then 98:2). (αR) - α -Methyl-N-[(1S,2S,5R)-2-isopropyl-5methylcvclohexvllbenzvlamine (H-menth-R.S)⁵ was first isolated in 17% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 80:20) 0.7; $[\alpha]_D$ +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, Me_2 CH), 0.92-1.28 (m, 3H, H γ , H δ and NH), 1.32 (d, 3H, J = 6.6 Hz, Me-C α '), 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-Cε), 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, Cζ), 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). (a**R**)-a-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: Rf (heptane-Et₂O 80:20) 0.6; $[\alpha]_D$ +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, Me_2 CH), $0.96-1.12 \text{ (m, 2H)}, 1.14 \text{ (d, 3H, } J = 6.6 \text{ Hz}, Me_2\text{CH}), 1.16-1.26 \text{ (m, 2H)}, 1.27 \text{ (d, 3H, } J = 6.6 \text{ Hz}, Me_2\text{CH})$ Ca'), 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'); ¹³C NMR (75 MHz, CDCl₃) δ 22.3 (CH₃), 22.4 (CH₃), 23.9 (CH₃), 24.6 (CH₃), 25.7 (CH), 26.7 (CH₂, C γ), 30.9 (CH₂), 31.8 (CH), 38.2 (CH₂), 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 C₁₈H₃₀N, [M+H]⁺, requires 260.23783). The corresponding carboxamide [mp ~ 55 °C (gum); [α]_D +119.2 (c 0.65); HRMS (ESI; MeOH), *m*/*z* 431.2308 (1 ppm) found (calcd for C₂₅H₃₂N₂O₃Na, [M+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-(+)-(*aR*)-*N*-(*a*-phenylethyl)fenchylamine (H-endo-fenc-*R*)

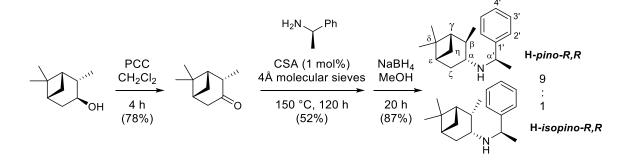


Note that this reaction does not work by using (S)- α -methylbenzylamine instead of the (R).

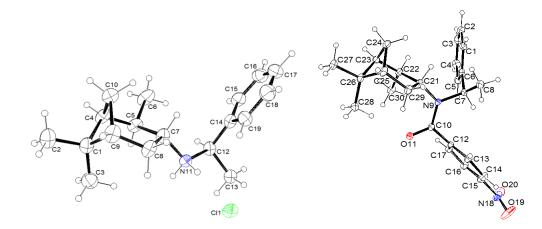
A mixture of (-)-fenchone (3.2 mL, 20 mmol), (*R*)- α -methylbenzylamine (5.1 mL, 40 mmol), and camphorsulfonic acid (47 mg, 0.20 mmol) was heated under stirring in the presence of 3Å molecular sieves (7 g) at 150 °C for 10 days. The mixture was cooled and filtered through celite (washing using 80 mL 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, 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 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 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% 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). *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: $[\alpha]_D$ +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, $Me-C\alpha'$), 1.23-1.51 (m, 4H), 1.58-1.70 (m, 2H), 1.81-2.21 (m, 1H), 3.79 (g, 1H, J = 6.6 Hz, H α '), 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 $C_{18}H_{28}N$, $[M+H]^+$, 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

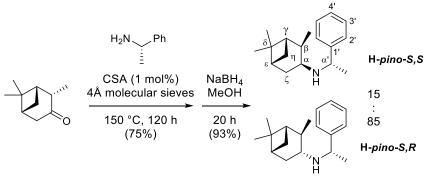
(1S,2R,3R,5R)-2,6,6-Trimethyl-*N*-[(αR)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*R*,*R*) and (1*S*,2*S*,3*R*,5*R*)-2,6,6-Trimethyl-*N*-[(αR)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-isopino-*R*,*R*)



(-)-Isopinocamphone⁷ 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 (-)-isopinocamphone in 78% yield as a colorless liquid: Rf (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 (-)-isopinocamphone (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). (1S,2R,3R,5R)-2,6,6-Trimethyl-N-[(aR)-a-phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-R,R) formed in 78% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 90:10) 0.6; $[\alpha]_D$ -39.6 (c 1.4); ¹H NMR (500 MHz, CDCl₃) δ 0.92 (s, 3H, Me, Me_2 C), 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 α '), 1.48-1.54 (m, 1H, H ζ), 1.71 (td, 1H, J = 5.8 and 1.3 Hz, Hy), 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 α '), 7.28-7.31 (m, 1H, H4'), 7.37-7.40 (m, 2H, H3' and H5'), 7.45-7.47 (m, 2H, H2' and H6'); ¹³C NMR (126 MHz, CDCl₃) δ 20.0 (CH₃, Me-Cβ), 20.1 (CH₃, Me₂C), 23.8 (CH₃, Me-Cα'), 23.9 (CH₂, Cη), 26.6 (CH₃, Me₂C), 34.5 (CH₂, Cζ), 38.7 (CH, Cβ), 39.6 (C, Cδ, CMe₂), 40.7 (CH, Cε), 47.6 (CH, Cγ), 54.2 (CH, Cα), 56.6 (CH, Cα'), 126.7 (CH, C4'), 126.8 (2CH, C2' and C6'), 128.3 (2CH, C3' and C5'), 147.4 (C, C1'); HRMS (ESI; MeOH), *m/z* 258.2220 (1 ppm) found (calcd for C₁₈H₂₈N, [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 hvdrochloride **H-pino-***R*,*R*·**HCl** (white solid; mp 229 °C; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 20.0 (CH₃), 20.6 (CH₃), 21.0 (CH₃), 22.9 (CH₂), 26.2 (CH₃), 30.7 (CH₂), 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: $C_{18}H_{28}CIN, M = 293.86, 150(2)K$, 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. (1S,2S,3R,5R)-2,6,6-Trimethyl-N- $[(\alpha R)-\alpha$ -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, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 16.8 (CH₃), 17.8 (CH₃), 22.8 (CH₃), 27.2 (CH₂), 28.6 (CH₃), 28.8 (CH₂), 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, C=O); HRMS (ESI; MeOH), *m*/*z* 407.2339 (1 ppm) found (calcd for C₂₅H₃₁N₂O₃, [M+H]⁺, requires 407.23347)] formed by reaction of a fraction containing it with 4-nitrobenzoyl chloride. *Crystal data for* **4-O₂NC₆H₄CO-isopino-***R***,***R***: C₂₅H₃₀N₂O₃,** *M* **= 406.51, 150(2)K, orthorhombic,** *P* **2₁ 2₁ 2₁,** *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, μ = 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* **> 2σ(***I***). CCDC 2110269.**



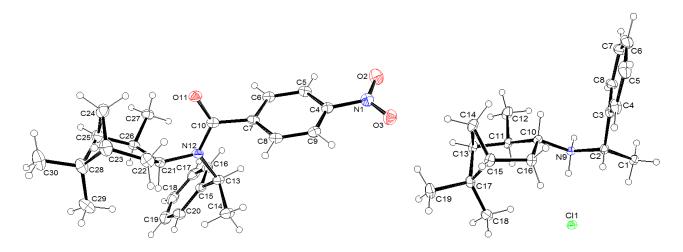
(1S,2R,3S,5R)-2,6,6-Trimethyl-*N*-[(αS)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*S*,*S*) and (1S,2R,3R,5R)-2,6,6-trimethyl-*N*-[(αS)- α -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-*S*,*R*)



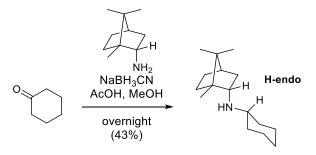
A mixture of (-)-isopinocamphone⁷ (3.7 g, 24.5 mmol), (R)- α -methylbenzylamine (6.3 mL, 49 mmol), and camphorsulfonic acid (57 mg, 0.245 mmol) was heated under stirring in the presence of 4Å molecular sieves (8.5 g) at 150 °C for 5 days. The mixture was cooled and filtered through celite (washing using 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). (1S,2R,3S,5R)-2,6,6-Trimethyl-*N*- $[(\alpha S)-\alpha$ -phenylethyl]bicyclo[3.1.1]heptan-3-amine (H-pino-**S**,**S**) was first isolated in 14% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 90:10) 0.6; $[\alpha]_D$ -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, Ha²), 7.19-7.25 (m, 1H), 7.28-7.38 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 15.5 (CH₃, Me-Cβ), 21.0 (CH₃, Me₂C), 24.1 (CH₃, Me-Cα'), 27.1 (CH₃, Me₂C), 27.5 (CH₂, Cη), 34.5 (CH, Cβ), 37.6 (CH₂, Cζ), 39.0 (C, Cδ, CMe₂), 41.3 (CH, Cε), 48.2 (CH, Cγ), 49.2 (CH, Cα), 57.0 (CH, Cα'), 126.7 (CH, C4'), 126.8 (2CH, C2' and C6'), 128.3 (2CH, C3' and C5'), 147.2 (C, C1'); 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; $[\alpha]_D$ -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); ¹³C NMR (75 MHz, CDCl₃) δ 16.4 (CH₃), 18.4 (CH₃), 21.6 (CH₃), 26.2 (CH₂), 27.6 (CH₃), 31.9 (CH₂), 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 C₂₅H₃₀N₂O₃Na, [M+Na]⁺, requires 429.21541)] formed by reaction of H-pino-S,S with 4-nitrobenzovl chloride. Crystal data for 4-O₂NC₆H₄CO-pino-S,S: C₂₅H₃₀N₂O₃, 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 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*-**[(αS)-α-phenylethyl]bicyclo[3.1.1]heptan-3-amine** (**H-pino-***S*,*R*) was next isolated in 79% yield as a colorless syrupy liquid: Rf (heptane-Et₂O 90:10) 0.6; $[\alpha]_D$ -126.1 (c 4.5); ¹H NMR (500 MHz, CDCl₃) δ 0.87 (d, 3H, J = 6.7 Hz, Me-C β), 0.90 (s, 3H, Me_2 C), 1.10-1.13 (m, 1H, H₁), 1.20 (s, 3H, Me_2C), 1.20-1.30 (br s, 1H, NH), 1.37 (d, 3H, J = 6.6 Hz, Me-Ca'), 1.58 (dd, 1H, J = 11.3 and 6.0 Hz, H ζ), 1.61 (td, 1H, J = 5.8 and 1.1 Hz, H γ), 1.73 (p, 1H, J = 6.8 Hz, H β), 1.89-1.94 (m, 2H, H ϵ and H ζ /H η), 2.16-2.24 (m, 2H, H α and H ζ /H η), 3.95 (q, 1H, J = 6.6 Hz, H α '), 7.24-7.28 (m, 1H, H4'), 7.32-7.37 (m, 4H, H2', H3', H5' and H6'); ¹³C NMR (126 MHz, CDCl₃) δ 19.3 (CH₃, Me-Cβ), 20.2 (CH₃, Me₂C), 23.8 (CH₂, Cη), 25.9 (CH₃, Me-Cα'), 26.6 (CH₃, Me₂C), 33.5 (CH₂, Cζ), 38.1 (CH, Cβ), 39.6 (C, Cδ, CMe₂), 40.7 (CH, Cε), 47.3 (CH, Cγ), 52.3 (CH, Cα), 54.9 (CH, Ca'), 126.8 (2CH, C2' and C6'), 126.9 (CH, C4'), 128.4 (2CH, C3' and C5'), 145.9 (C, C1'); HRMS (ESI; MeOH), m/z 258.2224 (1 ppm) found (calcd for C₁₈H₂₈N, [M+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 $C_{25}H_{31}N_2O_3$, $[M+H]^+$, requires 407.23347)] was prepared by reaction of H**pino-S,** *R* with 4-nitrobenzovl 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: C₁₈H₂₈ClN, M = 293.86, 150(2)K, monoclinic, $P 2_1$, a = 11.2823(3), b = 7.3708(2), c = 11.7289(3) Å, $\beta = 118.3930(10)$ °, V = 858.04(4)

Å³, Z = 2, d = 1.137 g cm⁻³, $\mu = 0.215$ 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 µmol) 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 ($[\alpha]_D$ +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)

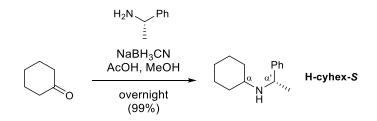
found (calcd for $C_{10}H_{20}N$, $[M+H]^+$, requires 154.15957)), was directly involved in the following step. To a stirred solution of endo-bornylamine (0.77 g, 5.0 mmol) in dry methanol (20 mL) were added cyclohexanone (2.1 mL, 20 mmol) and sodium cyanoborohydride (0.315 g, 5.0 mmol) at room temperature. 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 (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 43% yield as a colorless oil: Rf (heptane-AcOEt 80:20) 0.4; $[\alpha]_{D}$ +71.4 (c 0.35); ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) δ 14.2 (CH₃), 18.8 (CH₃), 20.0 (CH₃), 25.4 (CH₂), 25.5 (CH₂), 26.3 (CH₂), 27.5 (CH₂), 28.6 (CH₂), 34.1 (CH₂), 34.8 (CH₂), 40.2 (CH₂), 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 C₁₆H₃₀N, [M+H]⁺, requires 236.23783).

Exo-N-cyclohexylbornylamine (H-exo)⁹

NaBH₃CN AcOH, MeOH H-exo overniaht (88%)

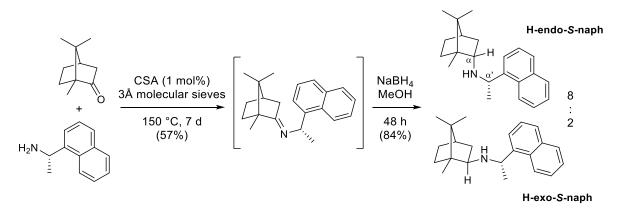
Exo-bornylamine was first prepared from H-exo-born-R as follows. To H-exo-born-R (1.3 g, 5.0 mmol) in ethanol (50 mL) were added 10% Pd(OH)₂ on charcoal (70 mg, 20 µmol) and ammonium formate (1.9 g, 30 mmol) under argon. The reaction mixture was refluxed for 5 h, cooled and filtrated over celite. The 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 $C_{10}H_{20}N$, $[M+H]^+$, 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: Rf (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: Rf (heptane-AcOEt 80:20) 0.2; $[\alpha]_D$ -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, Ha'), 7.20-7.35 (m, 5H, Ph); ¹³C NMR (126 MHz, CDCl₃) & 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

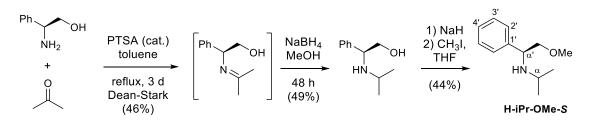
Endo-(1*S*)-*N*-(1-(1-naphthyl)ethyl)bornylamine (H-endo-*S*-naph)



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: Rf (heptane-AcOEt 80:20) 0.5; $[\alpha]_D$ +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, 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, 1.57 (m, 2H), 1.81 - 1.90 (m, 1H), 2.03 - 2.14 (m, 1H), 2.96 (ddd, 1H, J = 10.3, 1.57 (m, 2H), 1.81 - 1.90 (m, 1H), 2.03 - 2.14 (m, 1H), 2.96 (ddd, 1H, J = 10.3, 1.57 (m, 2H), 1.81 - 1.90 (m, 1H), 2.03 - 2.14 (m, 1H), 2.96 (ddd, 1H, J = 10.3, 1.57 (m, 2H), 1.57 - 1.57 (m, 2H), 1.81 - 1.90 (m, 1H), 2.03 - 2.14 (m, 1H), 2.96 (ddd, 1H, J = 10.3, 1.57 (m, 2H), 1.57 - 1.57 (m, 2H),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 found (calcd for $C_{22}H_{30}N$, $[M+H]^{+}$, requires 308.23783). Exo-(1S)-N-(1-(1ppm) 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, $Me-C\alpha$ '), 1.51-1.76 (m, 5H), 3.62 (dd, 1H, J = 6.7 and 4.0 Hz, Ha), 4.51 (q, 1H, J = 6.6 Hz, Ha'), 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).



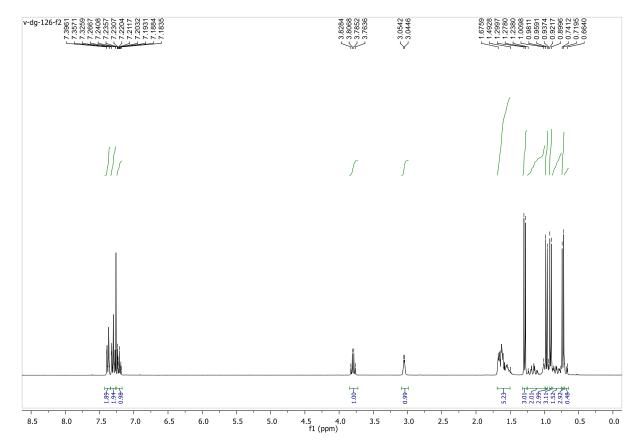


It was prepared by adapting a procedure described.¹¹ A solution of (*S*)-phenylglycinol (2.0 g, 14.8 mmol) and acetone (1.2 mL, 16 mmol) in toluene (30 mL) was treated by a catalytic amount of 4-toluenesulfonic acid. The reaction mixture was heated under reflux for 3 days in the presence of a Dean-Stark 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),

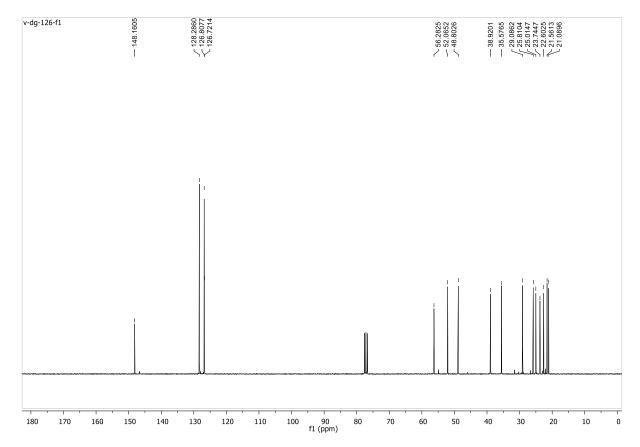
71.8 (CH₂), 95.7 (C), 126.7 (2CH), 127.7 (CH), 128.8 (2CH), 140.4 (C)], was dissolved in MeOH (5 mL) and treated by NaBH₄ (0.15 g, 4.0 mmol) at 0 °C. The mixture was then stirred at room temperature for 2 days. MeOH was removed under reduced pressure and water (5 mL) was added followed by KOH until pH > 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 silica (eluent: heptane-AcOEt-Et₃N, from 98:0:2 to 48:50:2). over gel (S)-N-Isopropylphenylglycinol was isolated in 49% yield as a white solid: Rf (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 = 10.6and 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: Rf (heptane-AcOEt 50:50) 0.4; ¹H NMR $(300 \text{ MHz}, \text{CDCl}_3) \delta 0.99 \text{ (d, 3H, } J = 6.4 \text{ Hz}, Me_2\text{C}), 1.03 \text{ (d, 3H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 1H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{ (br s, 2H, } J = 6.2 \text{ Hz}, Me_2\text{C}), 2.24 \text{$ 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

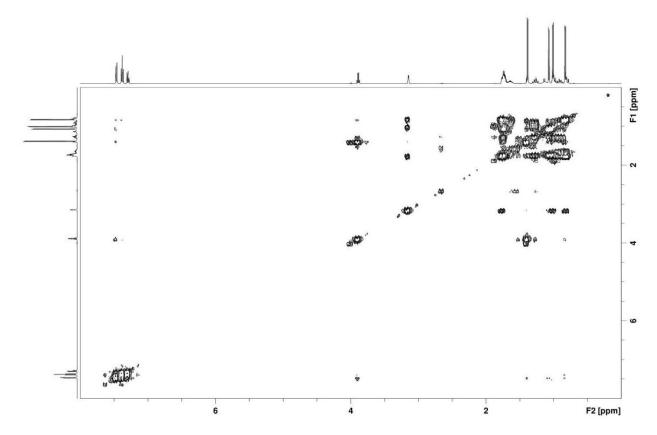
H-menth-S,S

¹H (CDCl₃, 300 MHz)

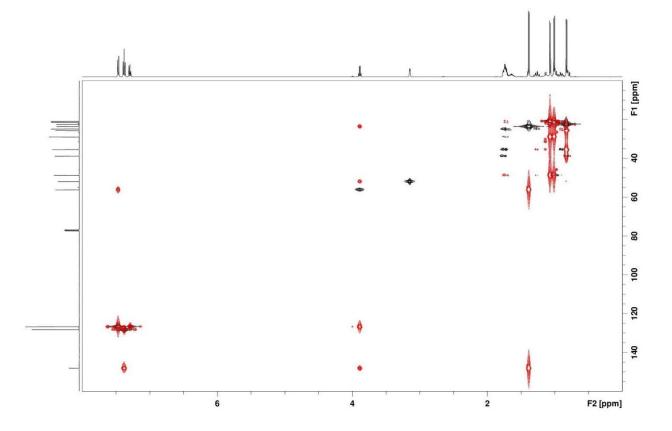


¹³C (CDCl₃, 75 MHz)



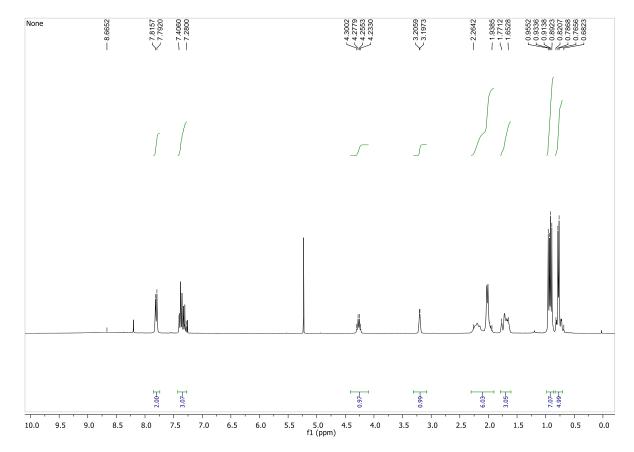


HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)

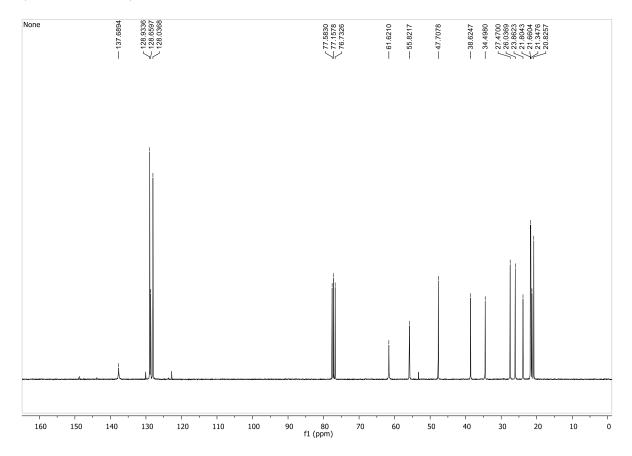


H-menth-S,S·HCl

¹H (CDCl₃, 300 MHz)

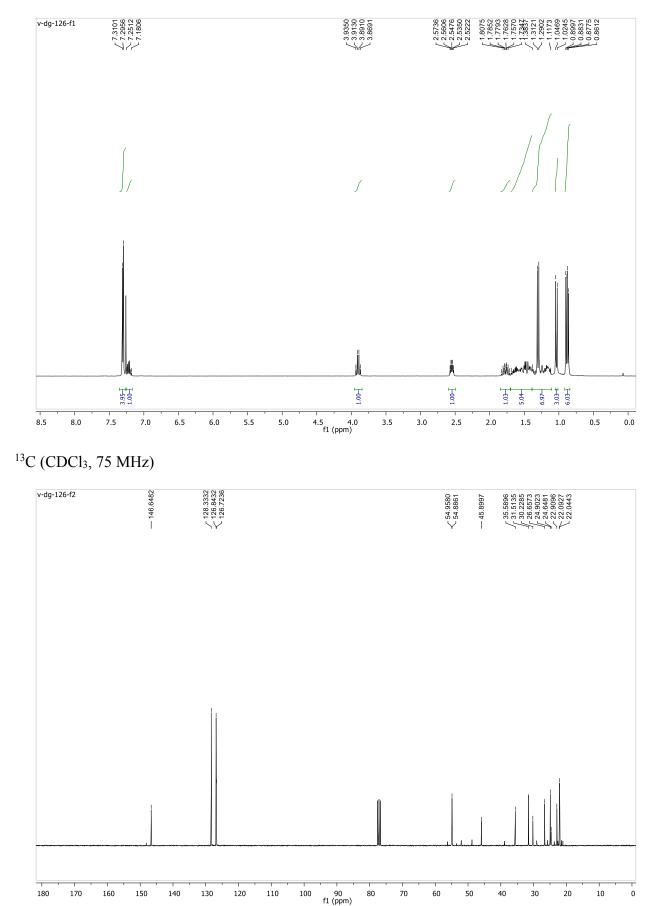


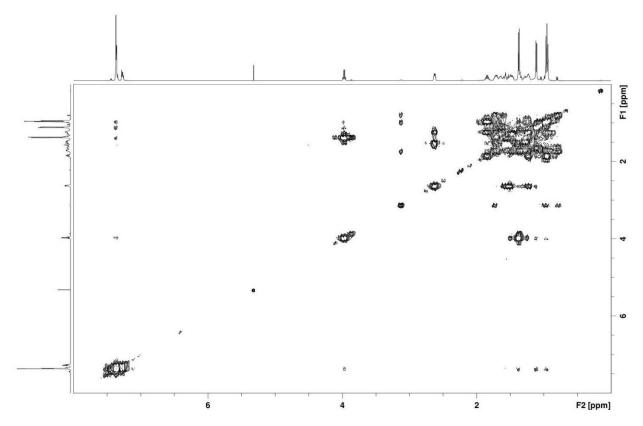
¹³C (CDCl₃, 75 MHz)



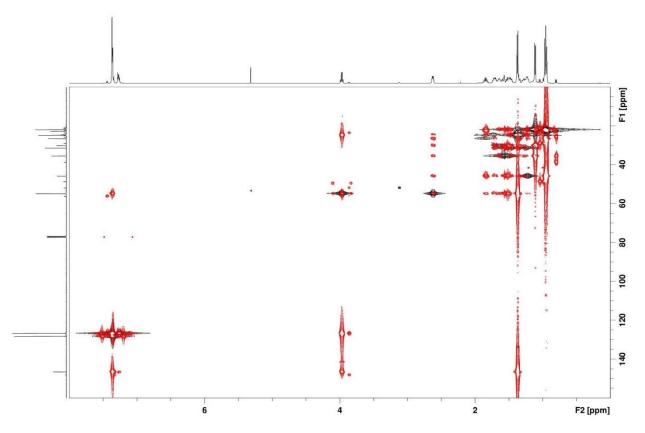
H-menth-S,R

¹H (CDCl₃, 300 MHz)



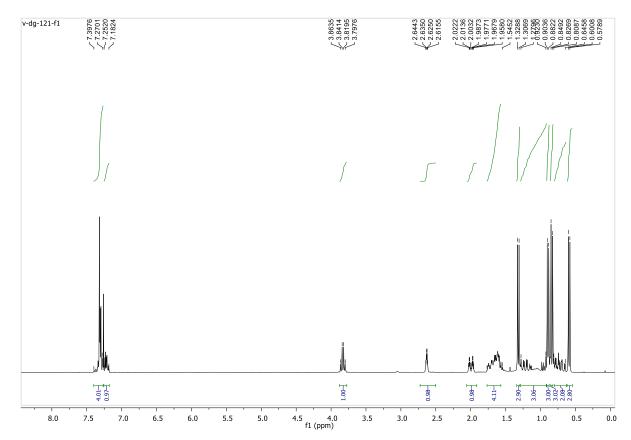


HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)

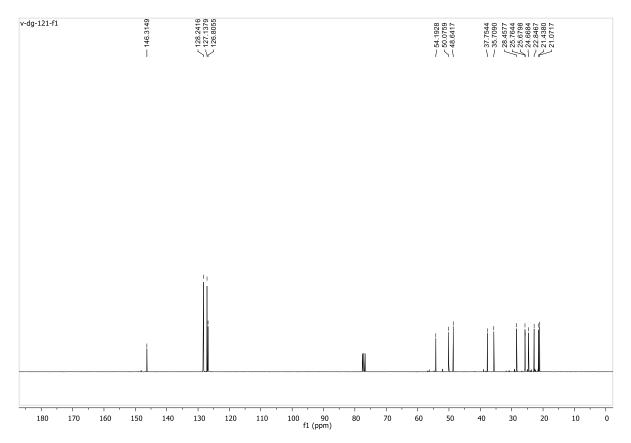


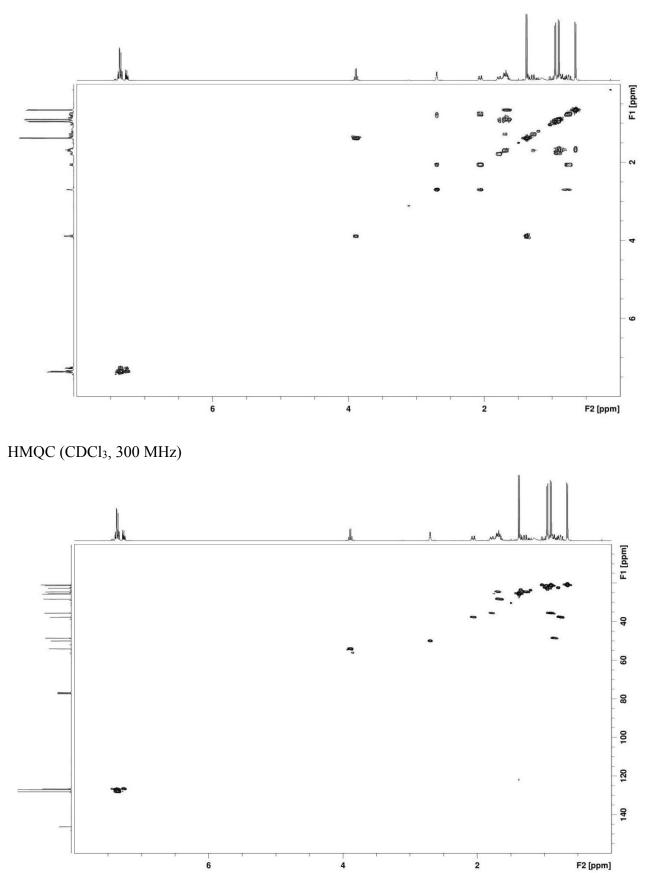
H-menth-*R*,*S*

¹H (CDCl₃, 300 MHz)



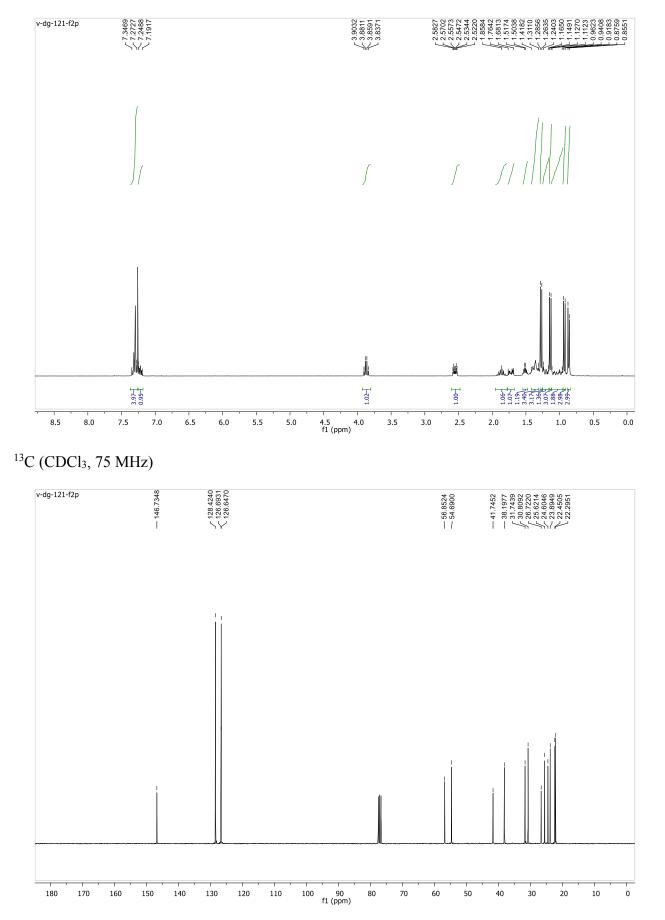
¹³C (CDCl₃, 75 MHz)

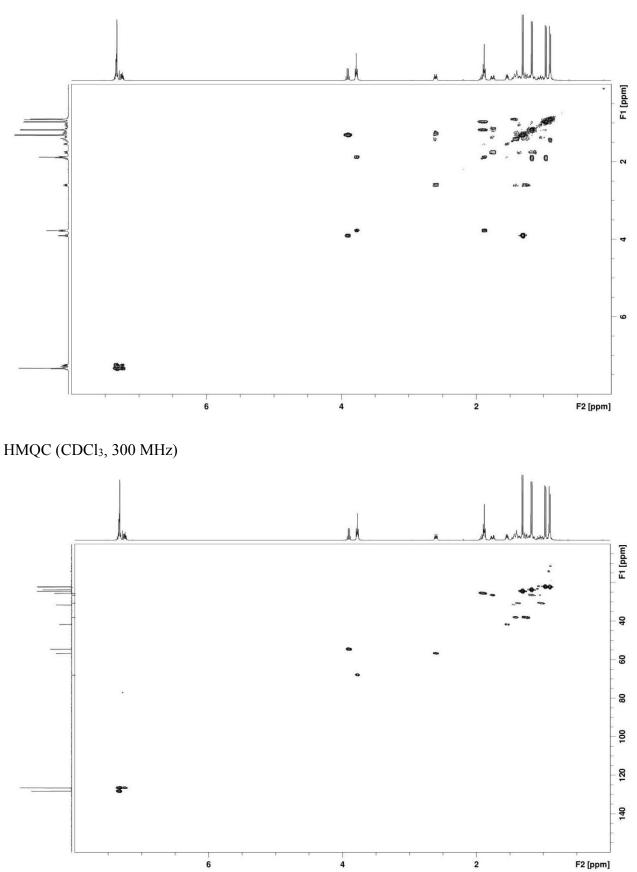




H-menth-*R*,*R*

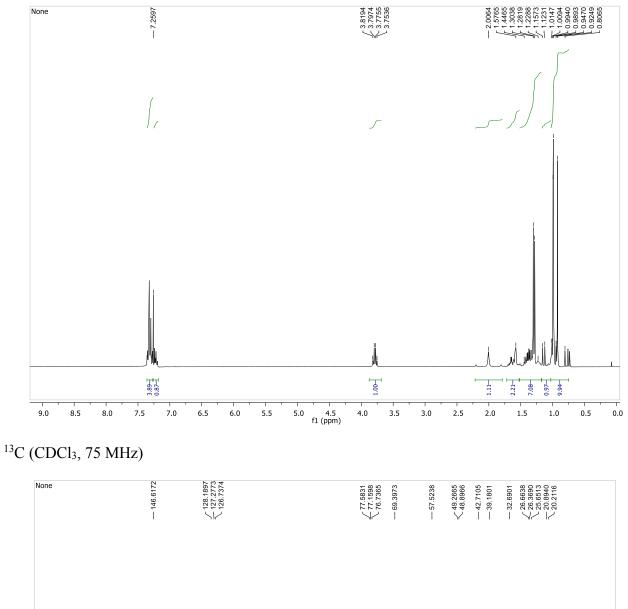
¹H (CDCl₃, 300 MHz)

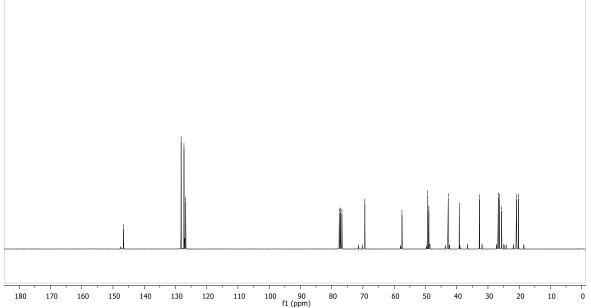




H-endo-fenc-R

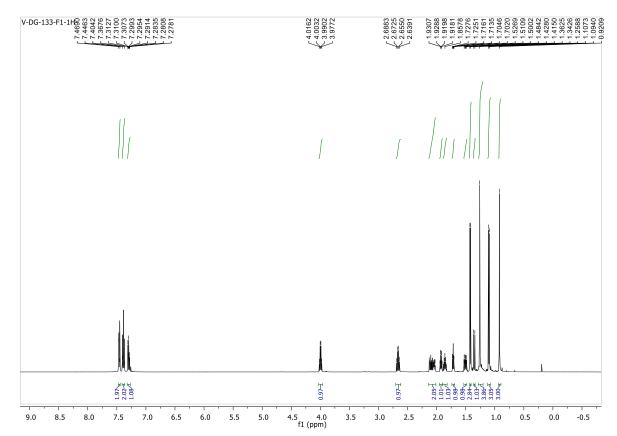
¹H (CDCl₃, 300 MHz)



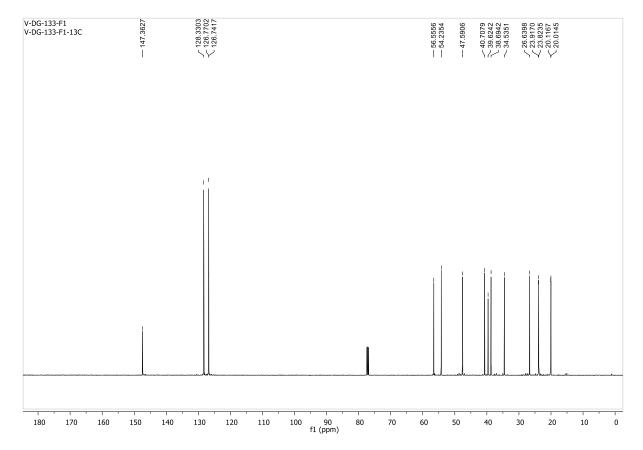


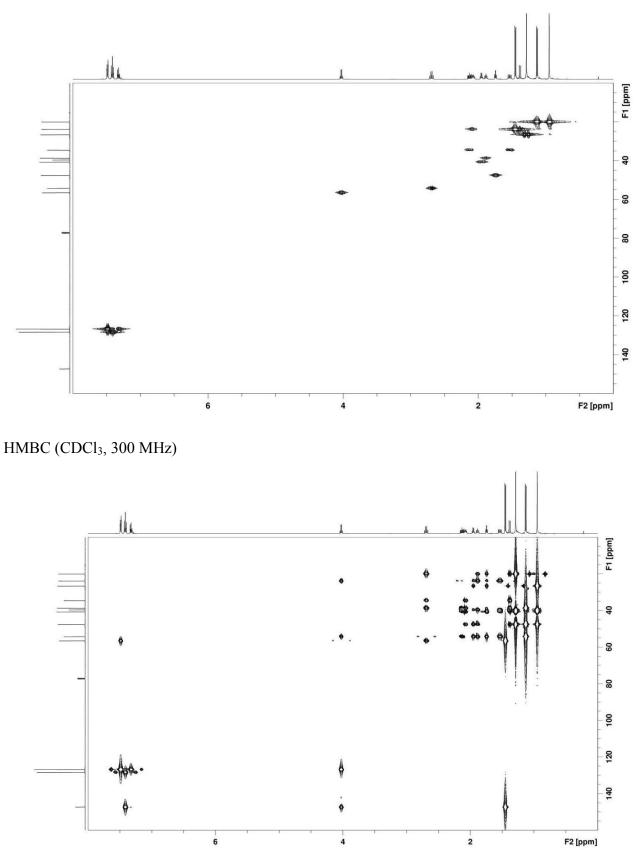
H-pino-*R*,*R*

¹H (CDCl₃, 500 MHz)



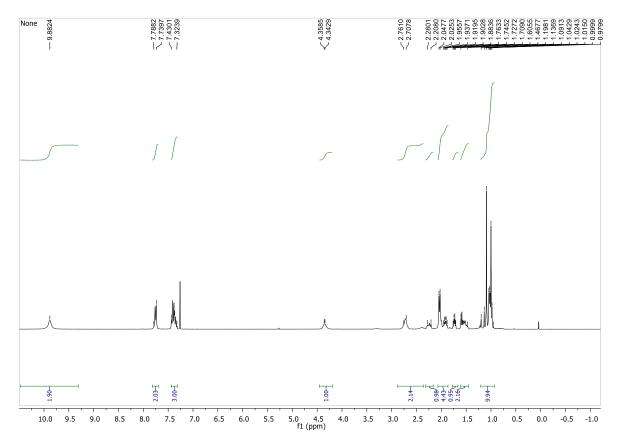
¹³C (CDCl₃, 126 MHz)



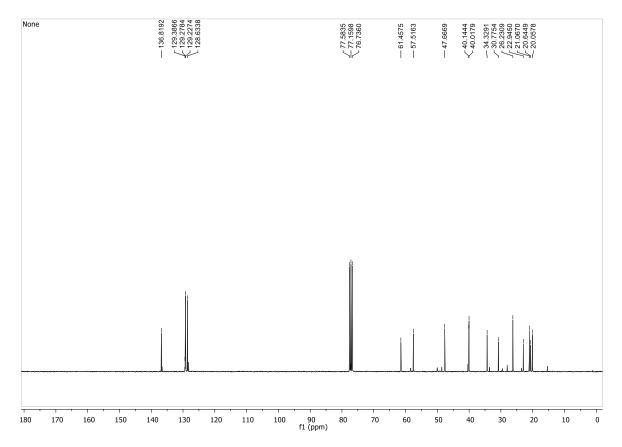


H-pino-R,R·HCl

¹H (CDCl₃, 300 MHz)

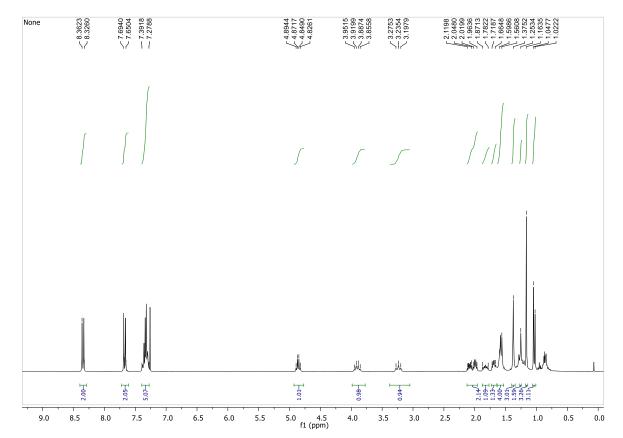


¹³C (CDCl₃, 126 MHz)

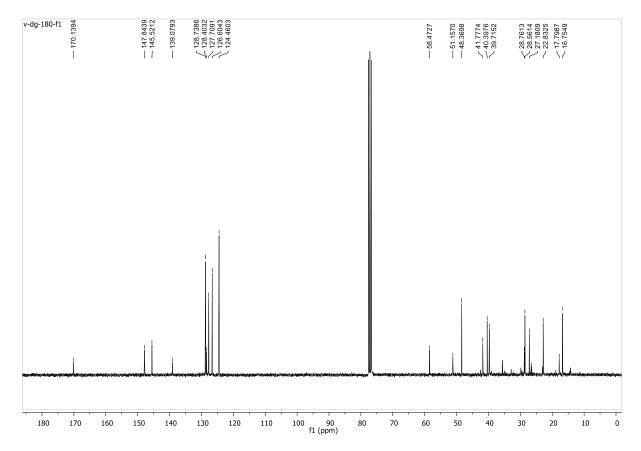


4-O2NC6H4CO-pino-R,R

¹H (CDCl₃, 300 MHz)

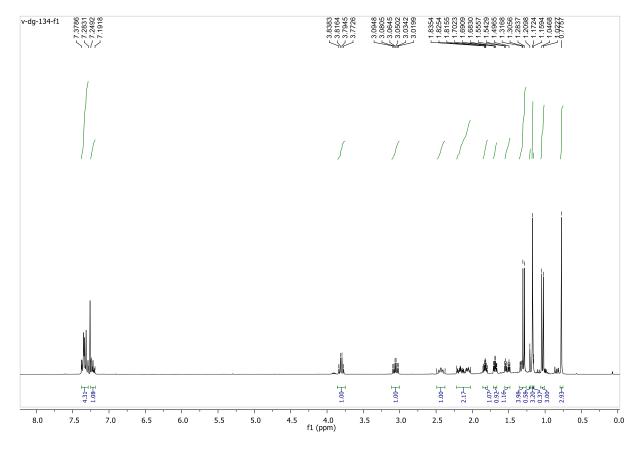


¹³C (CDCl₃, 75 MHz)

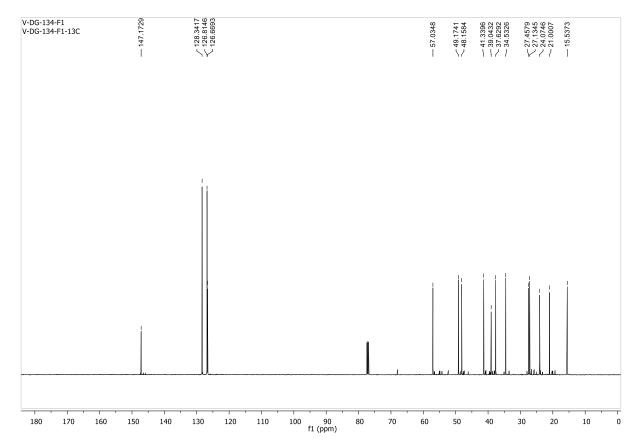


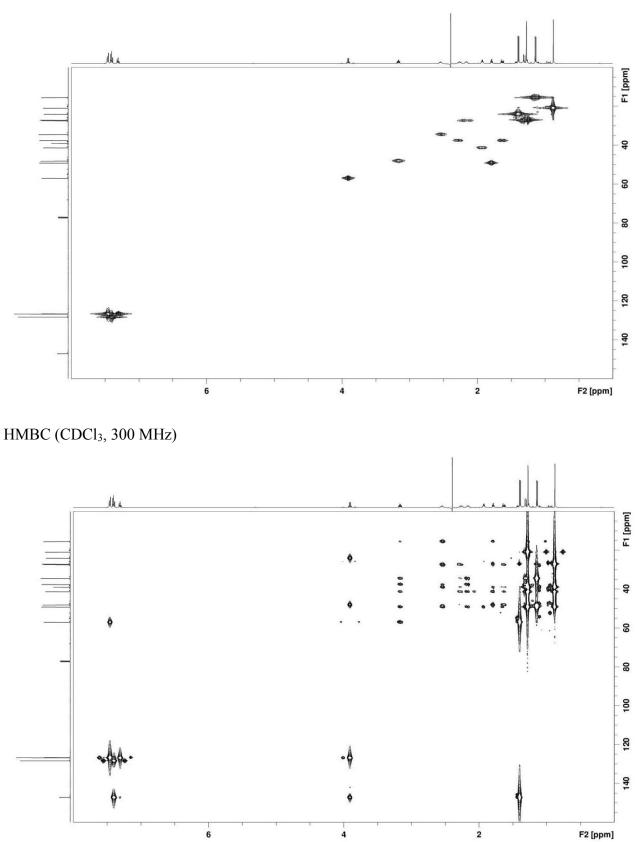
H-pino-S,S

¹H (CDCl₃, 300 MHz)



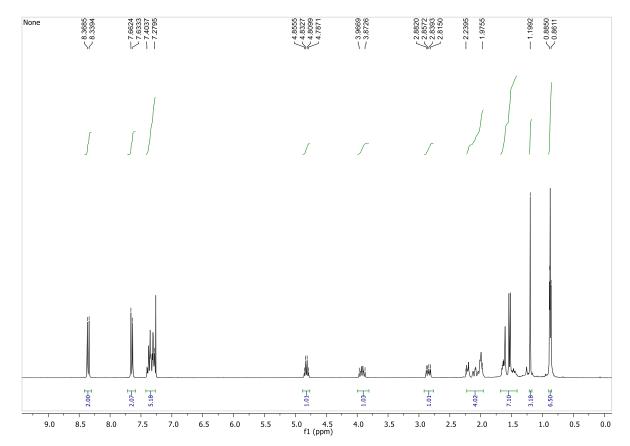
¹³C (CDCl₃, 126 MHz)



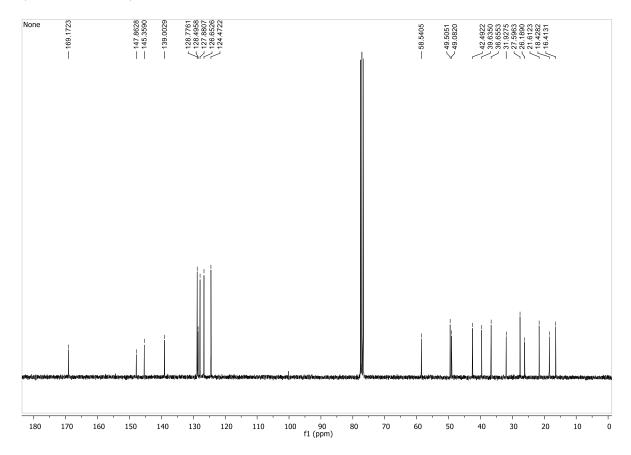


4-O2NC6H4CO-pino-S,S

¹H (CDCl₃, 300 MHz)

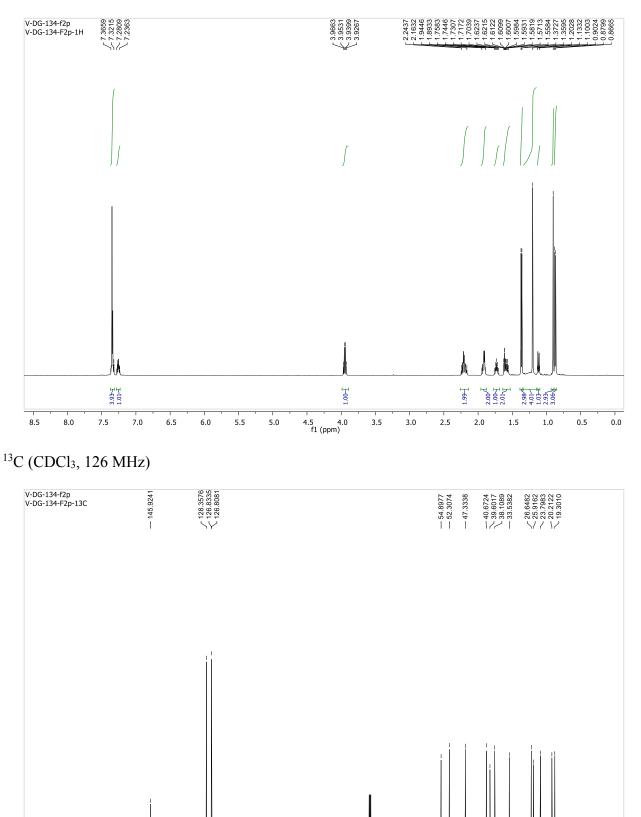


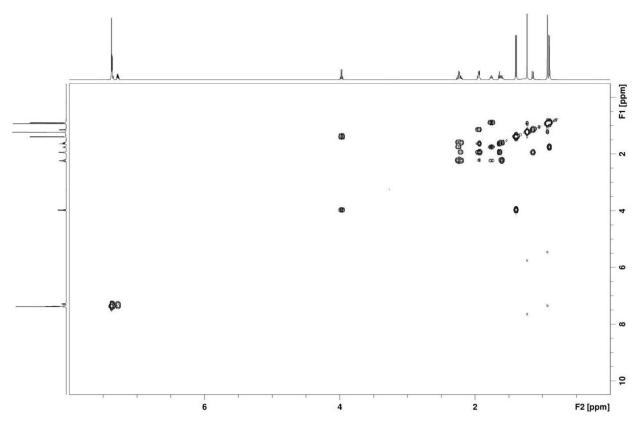
¹³C (CDCl₃, 75 MHz)



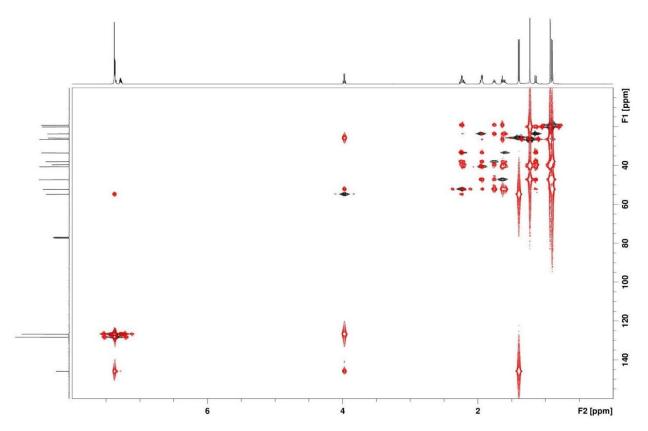
H-pino-S,R

¹H (CDCl₃, 500 MHz)



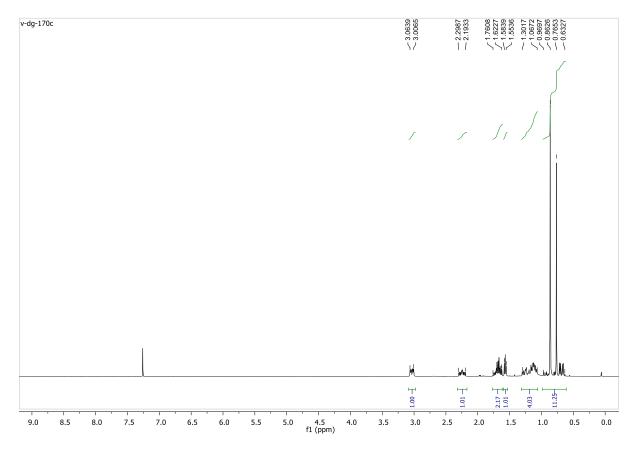
. f1 (ppm) 

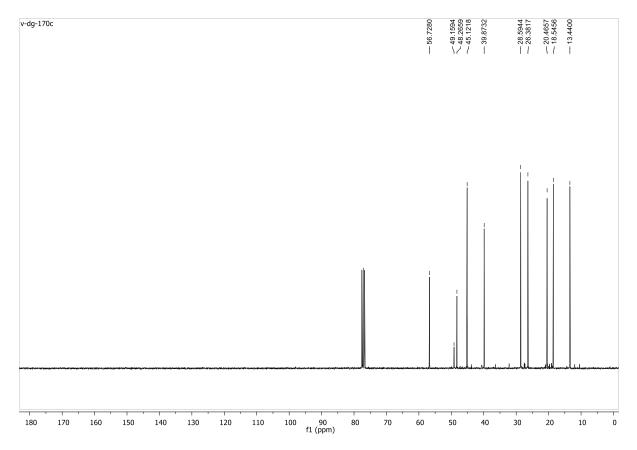
HMQC (black) / HMBC (red) (CDCl₃, 300 MHz)



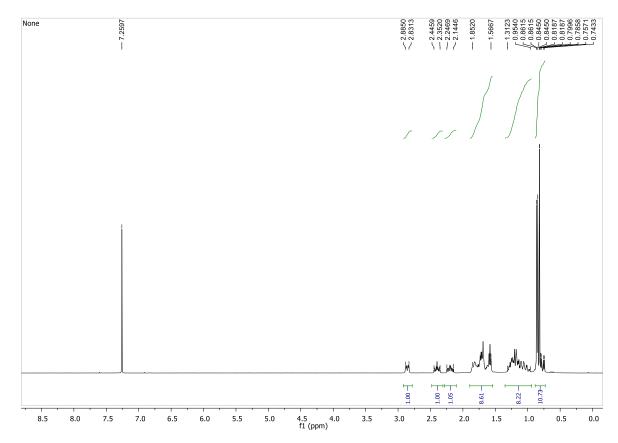
Endo-bornylamine

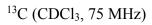
¹H (CDCl₃, 300 MHz)

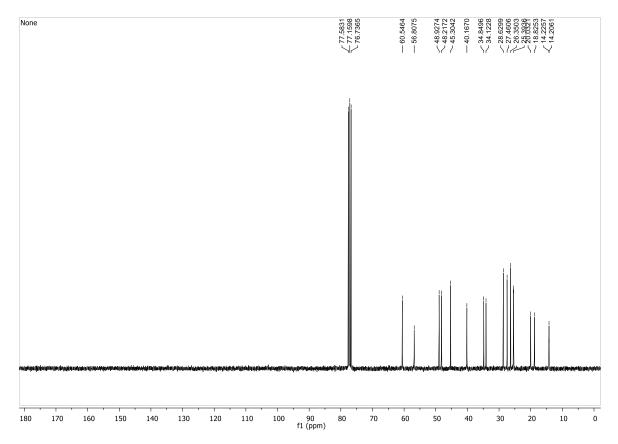




H-endo

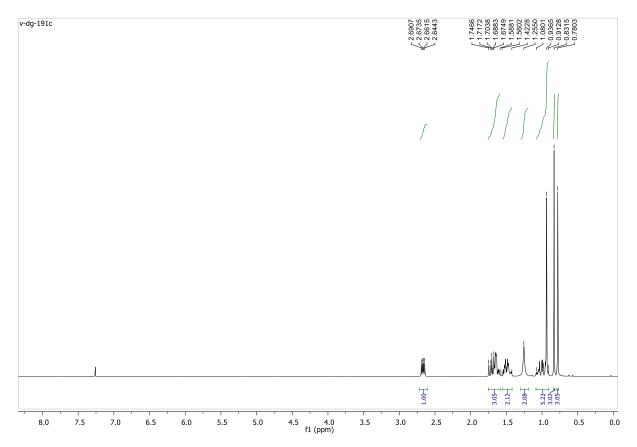


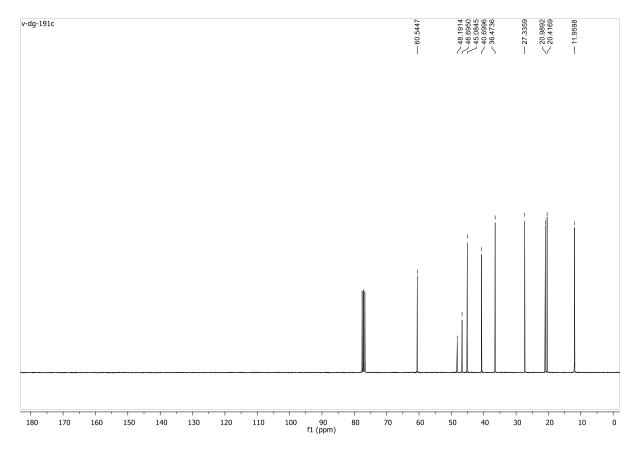




Exo-bornylamine

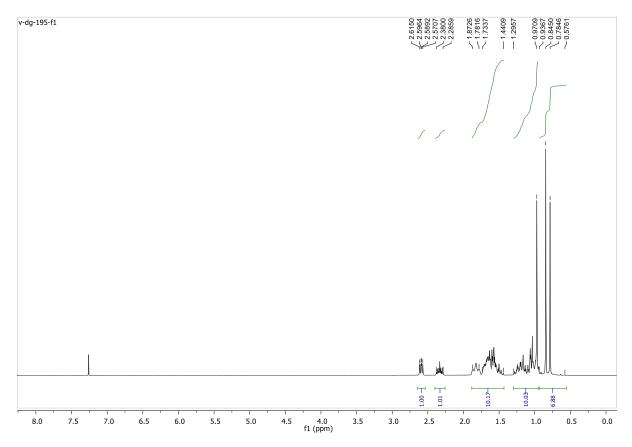
¹H (CDCl₃, 300 MHz)

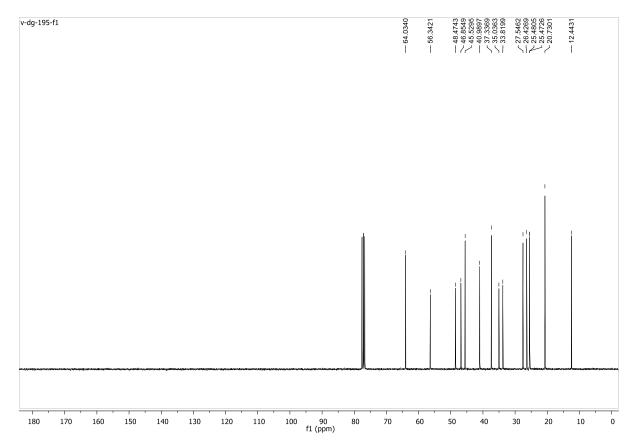




H-exo

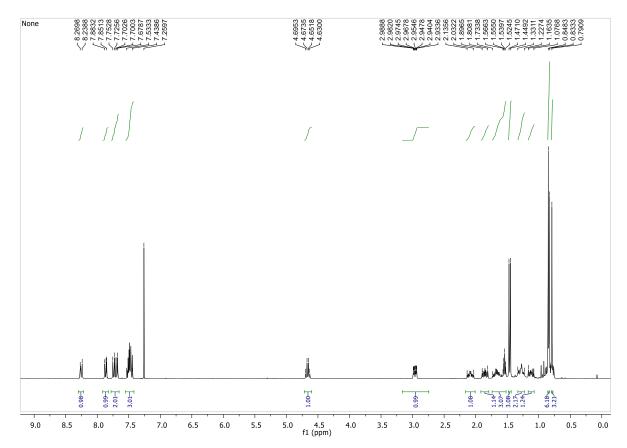
¹H (CDCl₃, 300 MHz)

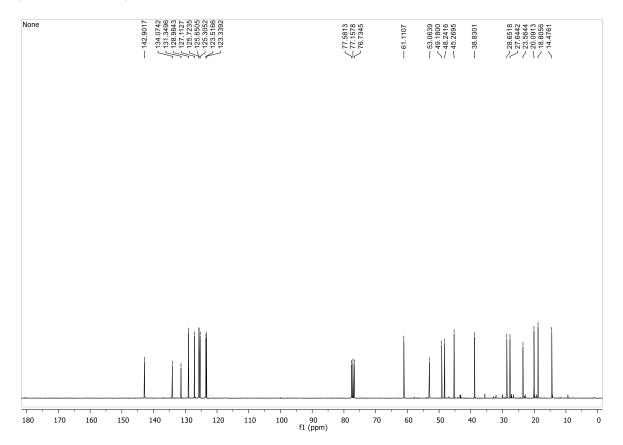




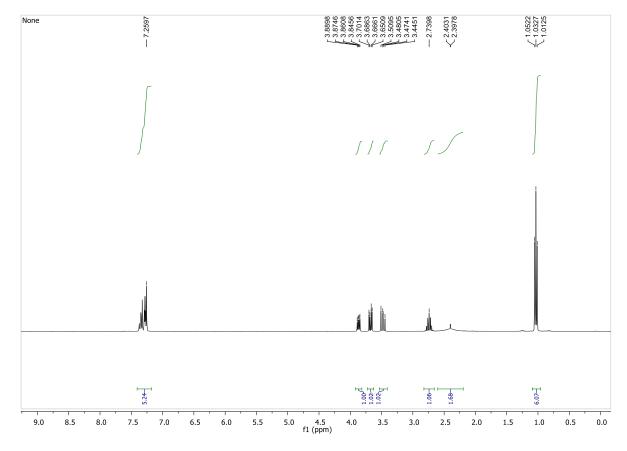
H-endo-S-naph

¹H (CDCl₃, 300 MHz)

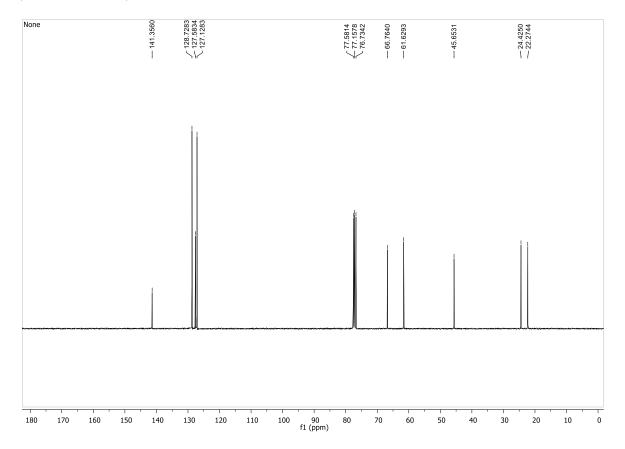




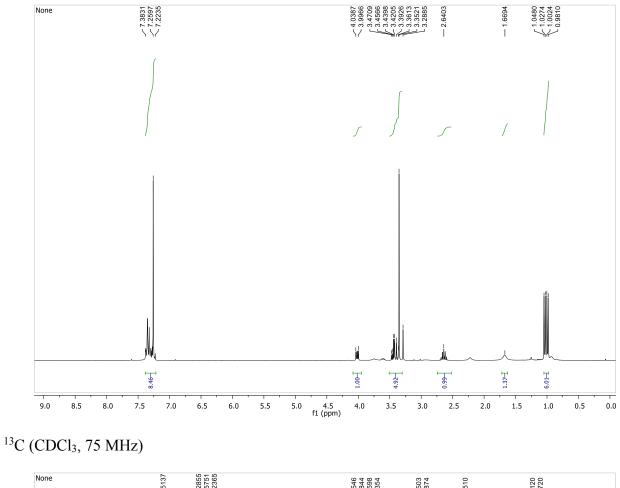
H-iPr-OH-S

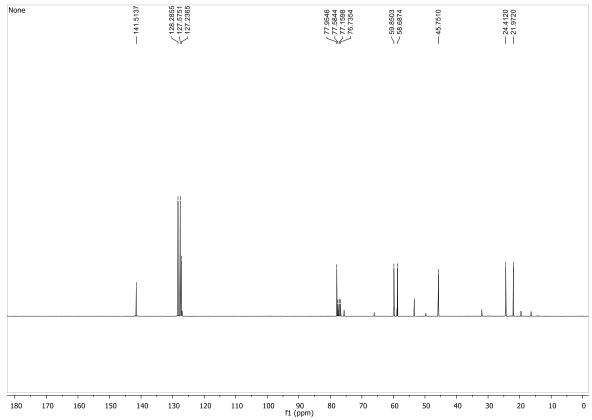


¹³C (CDCl₃, 75 MHz)

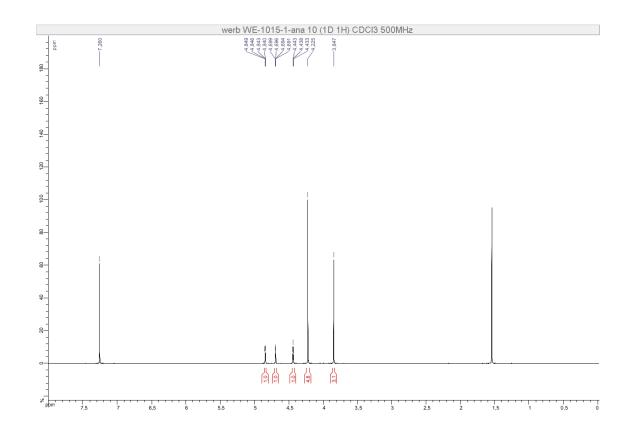


H-iPr-OMe-S

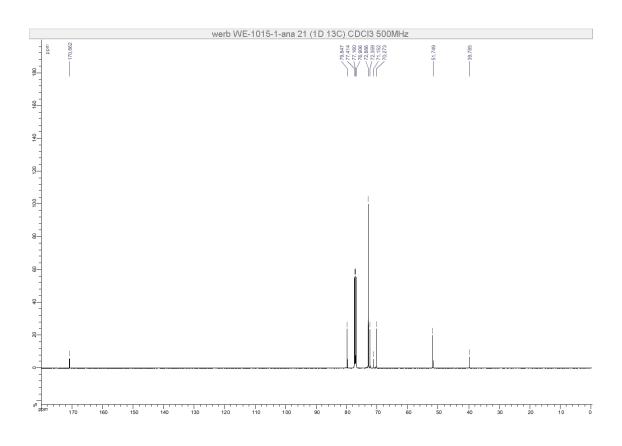




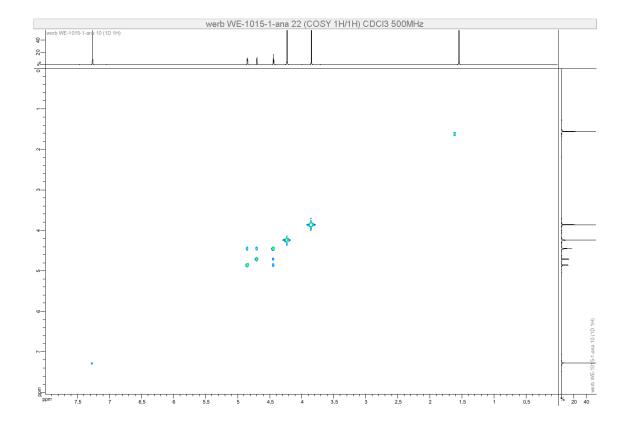
2-Iodo-*O*-methylferrocenecarboxylate (*rac*-1-I)



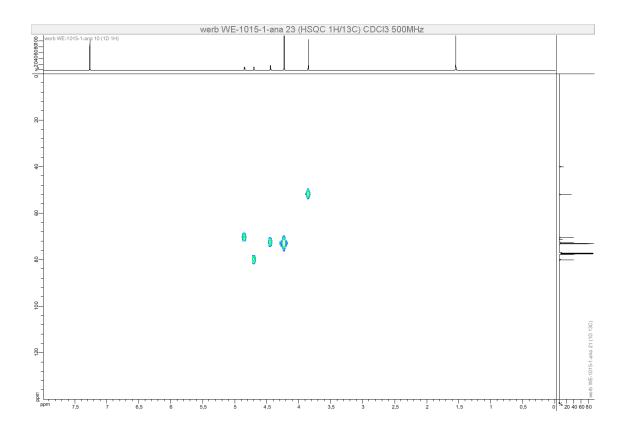
¹³C (CDCl₃, 126 MHz)



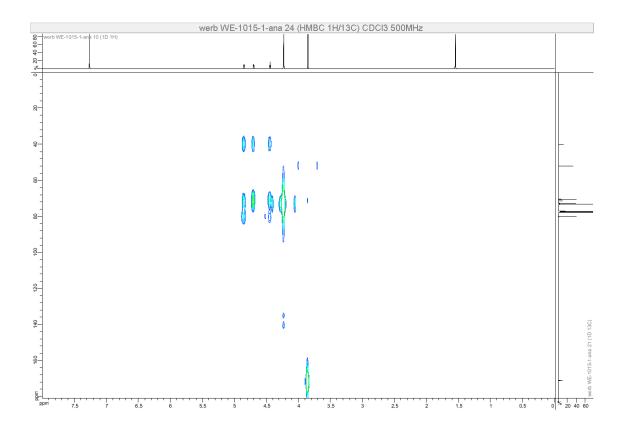
COSY (CDCl₃, 500 MHz)



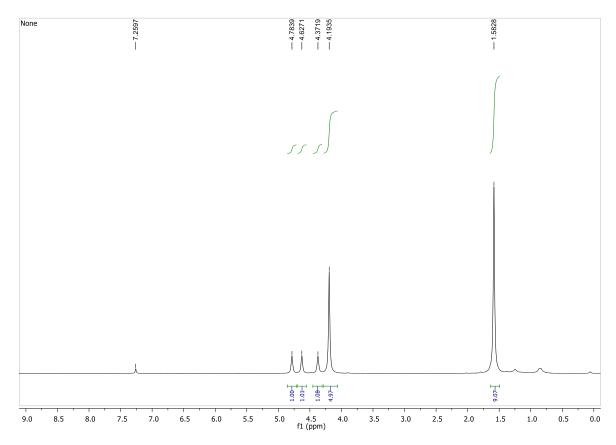
HSQC (CDCl₃, 500 MHz)



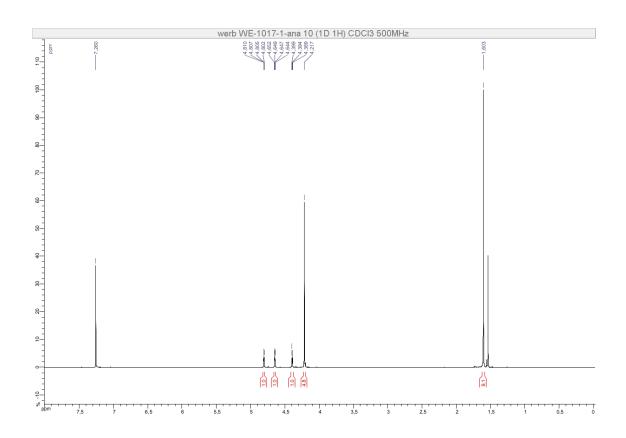
HMBC (CDCl₃, 500 MHz)

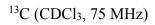


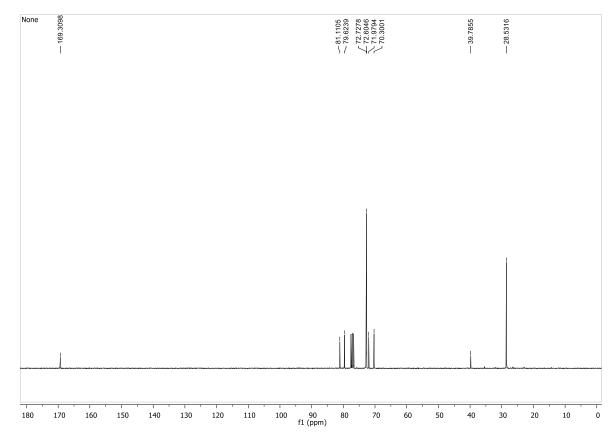
2-Iodo-O-tert-butylferrocenecarboxylate (rac-2-I)



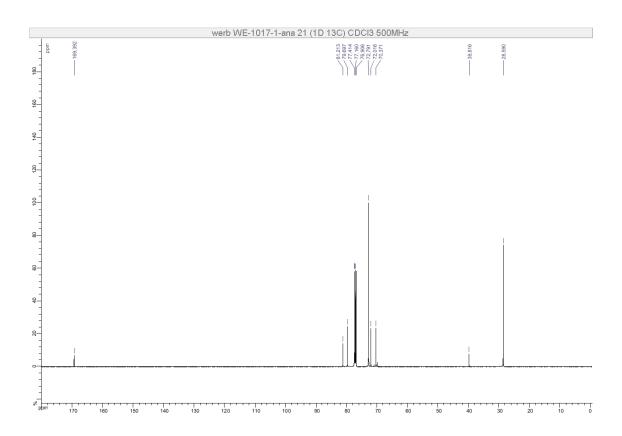
¹H (CDCl₃, 500 MHz)



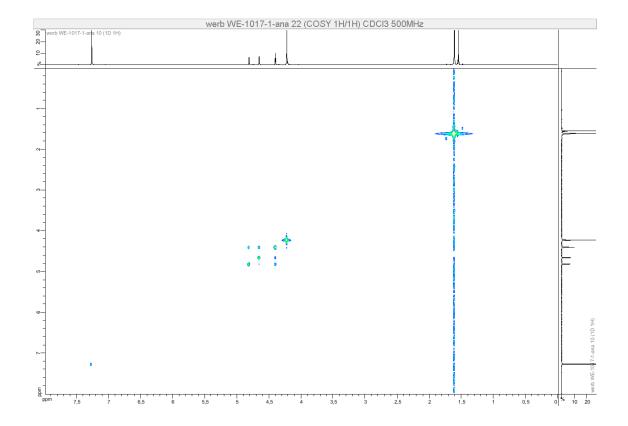




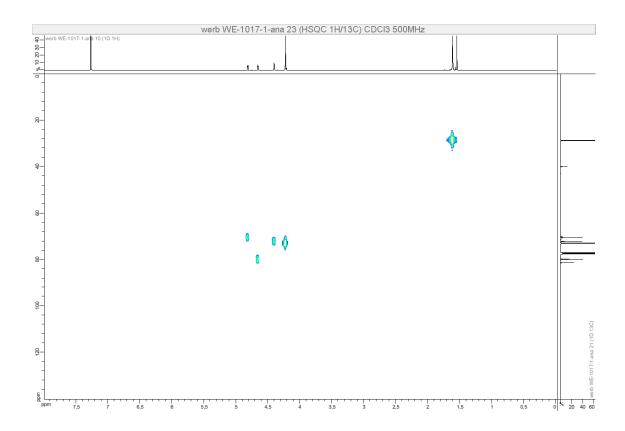
¹³C (CDCl₃, 126 MHz)

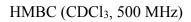


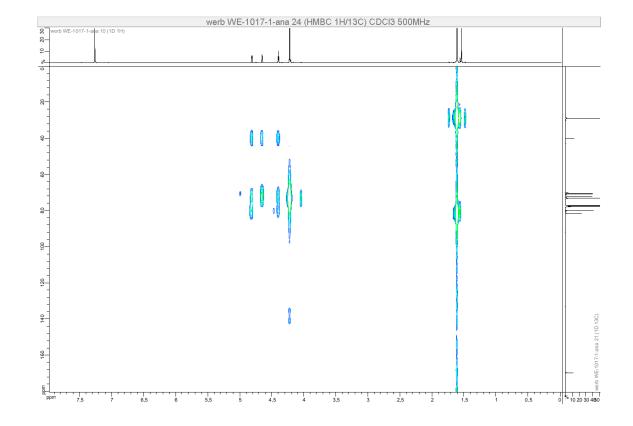
COSY (CDCl₃, 500 MHz)



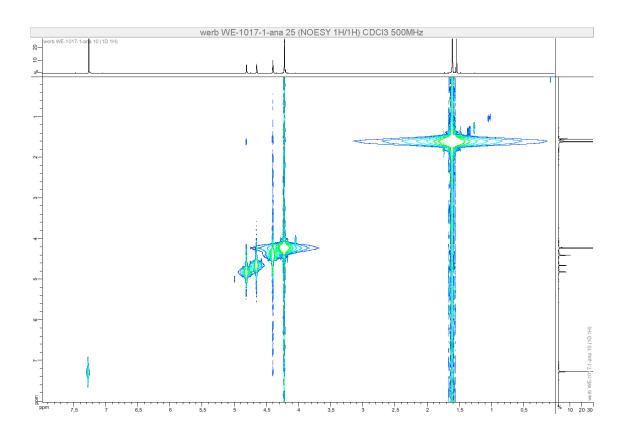
HSQC (CDCl₃, 500 MHz)



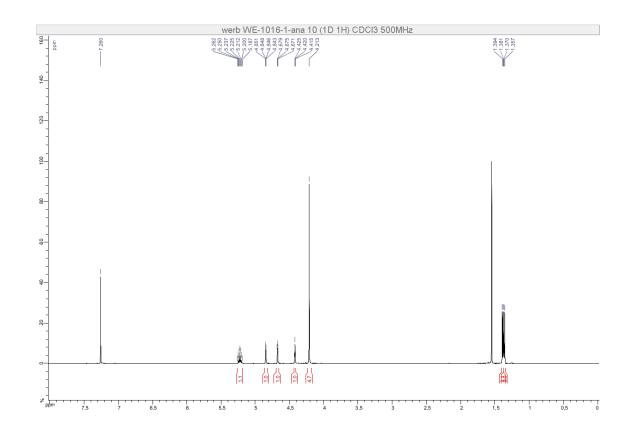




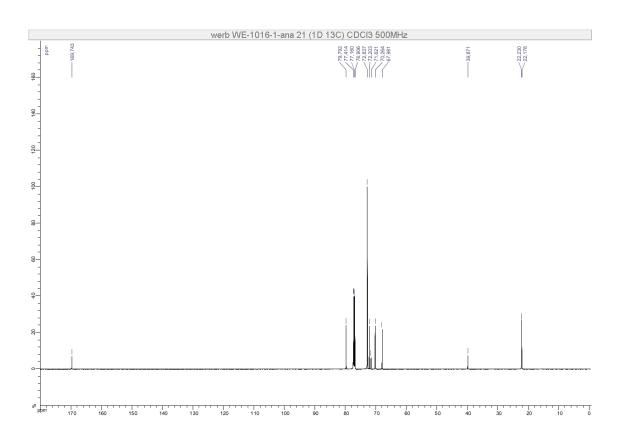
NOESY (CDCl₃, 500 MHz)



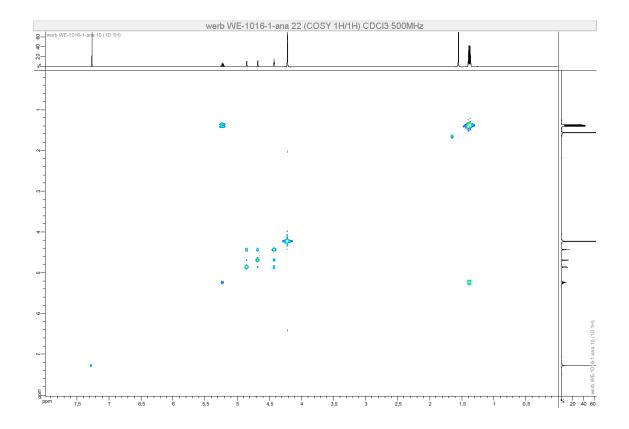
2-Iodo-O-isopropylferrocenecarboxylate (rac-3-I)



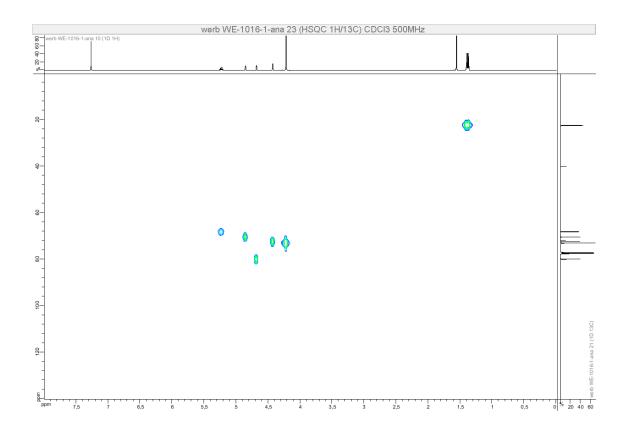
¹³C (CDCl₃, 126 MHz)

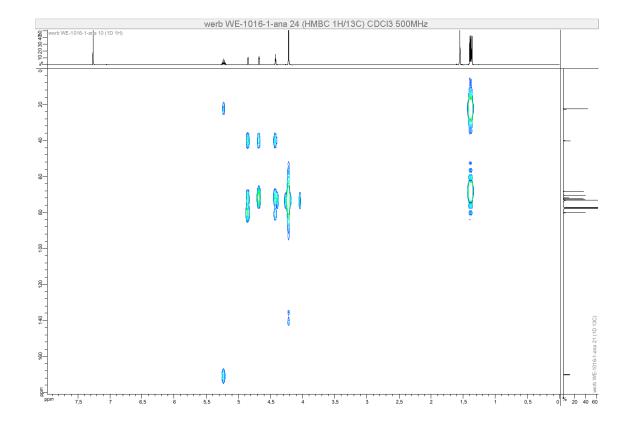


COSY (CDCl₃, 500 MHz)

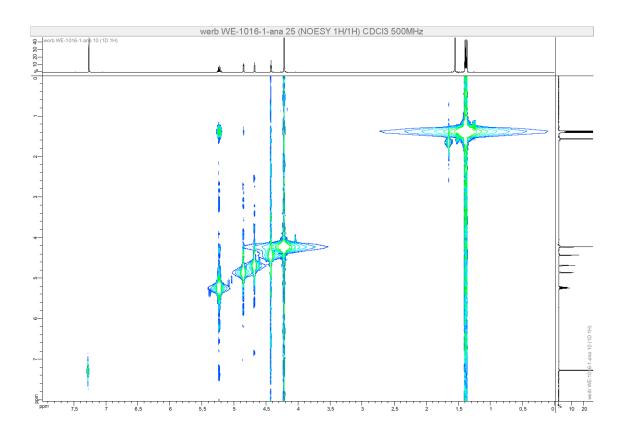


HSQC (CDCl₃, 500 MHz)





NOESY (CDCl₃, 500 MHz)



HPLC Chromatograms

Compound (±)-1-I

		Chromat	ogram and l	Results		
eneral informations						
equence Name:	2021-06-29					
strument:	U3000					
ogiciel used:	Chromeleon					
ograan used: Column used:	CHIRALPAK OF	H DAICEI				
njection Details	of in the rate of	DAIOLL				
jection Name:	WE-1015-1-ODE	1-2021-06-29-95-5-30	min_25°C_254nm	Run Time:	50.00	min
strument Method:		C-254nm-0.5mLmin		Injection Volume:	5.00	
njection Date/Time:	29/juin/21 10:59			Channel:	UV_VIS_1	he
yeenen Dater mine.	20/juli 21 10:00			Wavelength:		nm
nstrument Method De	etails			rear or or origin.	204	
strument Method:		C-254nm-0.5mLmin				
6A Isopropanol		5 %				
6B Hexane		95 %		Température du four:	25.0	°C
Débit:	0.	500 mL/min		Pression:		bars
hromatogram						
間 2021-06-29 #	2 [manually integrated]	WE-1015-1-0DH-2	021-06-29-95-5-30	min-25°C-254nm-0.5m	l min l	JV_VIS_1 WVL:254 nm
1200			1 - 14.020			
1000 800 600 400 200				2 - 18.897		
-200	5.0	10.0	15.0 Time (min)	20.0	25.0	· · · · · 3
eak Results	Detertio T		Develotion (TD)	An and a company	Distant (ED)	l l
o. Peak Name	Retention Tim min	e Width (50%) min	Resolution (EP)	Asymmetry (EP)	Plates (EP)	
	14.020	0.241	10.05	1.20	18819	
	18.897	0.332	n.a.	1.20	17937	

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		14.020	290.852	1125.045	49.75	57.67
2		18.897	293.770	825.750	50.25	42.33
Total:			584.622	1950.795	100.00	100.00

Compound (±)-1-I containing 1-H

			Chromat	ogram and l	Results			
iener	ral informations							
eque	ence Name:	2021-06-29						
nstrur	ment:	U3000						
ogicie	el used:	Chromeleon						
olum	nn used:	CHIRALPAK ODH	DAICEL					
nject	ion Details							
njectio	on Name:	WE-1015-1+G92-1-0	DH-2021-06-29-	95-5-60min-25°C	Run Time:	ţ	50.00 min	
	ment Method:	95-5-50min-25°C-25	4nm-0.5mLmin		Injection Volume:		5.00 µL	
njectio	on Date/Time:	29/juin/21 11:50			Channel:	UV_VIS_1		
					Wavelength:		254 nm	
	ment Method Detail	s						
	ment Method:	95-5-50min-25°C-25						
A	Isopropanol		%					
В	Hexane	95			Température du four:		25.0 °C	
	Débit:	0.500	mL/min		Pression:		18 bars	
nron	natogram							
500	🕺 🛛 2021-06-29 #3 [mar	nually integrated] WE-1	015-1+G92-1-OD	H-2021-06-29-95-5	-60min-25°C-254nm-0.	5mLmin	UV_VIS_1 W	VL:254 n
.300	- - -)- -			1 - 14.150				
200 100	- - - - - - -				2 - 19.07	2		
100 0 -50	- - - - - - -	5'0	10.0	- 150		2	250	
100 0 -50		5.0	10.0	15.0 Time [min]	20.0	2	25.0	
100 0 -50		5.0	10.0			2	25.0	, , , , , , , , , , , , , , , , ,
100 0 -50 eak I		Retention Time	Width (50%)			2 Plates (EP)		•••
100 0 -50	0.0 Results			Time [min]	20.0			· · · ·

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		14.150	70.667	281.049	49.72	57.72
2		19.072	71.470	205.908	50.28	42.28
Total:			142.137	486.957	100.00	100.00

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

		Cl	romatogram and	Results		
Gener	al informations					
	nce Name:	2021-07-01				
Instrur	nent:	U3000				
Logicie	el used:	Chromeleon				
Colum	n used:	CHIRALPAK ODH DAICE	L			
njecti	ion Details					
Injectio	on Name:	WE-1581-1-ODH-2021-07-0	1-95-5-30min-25°C-254nm	Run Time:	30.00	min
Instrur	nent Method:	95-5-30min-25°C-254nm-0.	5mLmin	Injection Volume:	1.00	μL
Injectio	on Date/Time:	01/juil./21 14:29		Channel:	UV_VIS_1	
				Wavelength:	254	nm
	ment Method Deta					
	nent Method:	95-5-30min-25°C-254nm-0.	5mLmin			
%A	Isopropanol	5 %				
%В	Hexane	95 %		Température du four:		
	Débit:	0.500 mL/mii	<u>ا</u>	Pression:	18	bars
Chron	natogram					
220	🗿 2021-07-01 #7 [m	anually integrated] WE-1581	-1-ODH-2021-07-01-95-5-30	min-25°C-254nm-0.5mL	.min l	JV_VIS_1 WVL:254 nm
175 150 125 100 100 75 50 25 0			1 - 14.045	12 - 18.955		
-20	<u>]</u> 0.0	5.0 10.0	15.0 Time [min]	20.0	25.0	3
Peak I	Results		nine (minj			1
No.	Peak Name	Retention Time Widt	h (50%) Resolution (EP)	Asymmetry (EP)	Plates (EP)	
			min			
1			.232 10.52	1.10	20276	1

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		14.045	17.880	71.318	87.84	90.73
2		18.955	2.475	7.284	12.16	9.27
Total:			20.354	78.602	100.00	100.00

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

			Chromat	ogram and F	Results		
iene	ral informations						
	ence Name:	2021-07-08_2					
stru	ment:	U3000 -					
ogici	iel used:	Chromeleon					
-	nn used:	CHIRALPAK ODH	DAICEL				
	tion Details						
njecti	ion Name:	WE-1604-1-ODH-2	21-07-08-95-5-30	min-25°C-254nm/	Run Time:	30.0	0 min
	ment Method:	95-5-30min-25°C-2	54nm-0.5mLmin	1	Injection Volume:	1.0	0 µL
njecti	ion Date/Time:	08/juil./21 18:58		(Channel:	UV_VIS_1	
				I	Wavelength:	25	4 nm
	ument Method Detai						
	ment Method:	95-5-30min-25°C-2					
6A	Isopropanol		%				
6B	Hexane		%		Température du four:		0 °C
	Débit:	0.500	mL/min		Pression:	. 2	0 bars
hro	matogram						
500	_ 🛐 2021-07-08_2 #3 [manually integrated]	VE-1604-1-ODH-20	021-07-08-95-5-30m	nin-25°C-254nm-0.5mL	.min	UV_VIS_1 WVL:254 n
00000000000000000000000000000000000000	-1				12 - 19.120	9	
-50	0.0	5.0	10.0	15.0	20.0	25.	0 ' ' ' :
-50				Time [min]	2010		- "
-50							
	Results						
eak	Results Peak Name	Retention Time	Width (50%)	Resolution (EP)	Asymmetry (EP)	Plates (EP)	
		Retention Time min 14.167	Width (50%) min 0.229	Resolution (EP) 10.74	Asymmetry (EP)	Plates (EP) 21214	

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		14.167	106.313	431.615	83.68	87.54
2		19.120	20.732	61.460	16.32	12.46
Total:			127.045	493.075	100.00	100.00

(±)-2-Iodoferrocenemethanol

		Chroma	atogram and F	Results			
eneral informations							
equence Name:	2021-07-19						_
strument:	U3000						
ogiciel used:	Chromeleon						
olumn used:	CHIRALPAK AS	H DAICEL					
jection Details	01110121711171	Driftee					
jection Name:	WE-666-1-ASH-	2021-07-19-90-10-6	0min-25°C-254nm	Run Time:	3	4.01 min	
strument Method:	90-10-60min-25			Injection Volume:		0.00 µL	
jection Date/Time:	19/juil./21 11:20			Channel:	UV_VIS_1		
poulon Data Anno.	Tonjuli 21 TTi20	,		Wavelength:	01_110_1	254 nm	
strument Method Det	ails			i fut orongun.		2011	
strument Method:	90-10-60min-25	°C-254nm					
A Isopropanol		10 %					
B Hexane		90 %		Température du four:	:	25.0 °C	
Débit:	1.	000 mL/min	1	Pression:		43 bars	
hromatogram							
	nanually integrated]	WE-666-1-ASH-2	2021-07-19-90-10-60r	min-25°C-254nm-1mLn	nin	UV_VIS_1 WVL:25	i4 nr
100-							
1							
1	1 - 14.3	337					
150 -	1						
125 -							
-							
100-			2 - 28.377				
· -			Λ				
75			1				
⁷³ -			1				
1							
50-							
-	11		11				
25							
1	11		1 \				
±1	1 \		1 \				
· · · · · · · · · · · · · · · · · · ·							
-20							
0.0	10.0	20.0	30.0	40.0		50.0	6
			Time [min]				
eak Results							
o. Peak Name	Retention Tim	e Width (50%)	Resolution (EP)	Asymmetry (EP)	Plates (EP)		
	min	min					
	14.337	0.556	11.12	1.33	3684		

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		14.337	96.985	154.835	49.92	61.84
2		28.377	97.303	95.558	50.08	38.16
Total:			194.289	250.393	100.00	100.00

(±)-2-Iodoferrocenemethanol containing ferrocenemethanol

		Chro	natogram and Results		
iener	ral informations				
	ence Name:	2021-07-19			
	ment:	U3000			
	el used:	Chromeleon			
	nn used:	CHIRALPAK ASH DAICEL			
ject	ion Details				
	on Name:	WE-666-1 + WE-091-1-ASH-20	I-07-19-90-10-60min-:Run Time:	60.00 min	
strur	ment Method:	90-10-60min-25°C-254nm	Injection Volume:	20.00 µL	
jectio	on Date/Time:	19/juil./21 11:56	Channel: Wavelength:	UV_VIS_1 254 nm	
stru	iment Method Details		wavelengur.	234 1111	
	ment Method:	90-10-60min-25°C-254nm			
Α	Isopropanol	10 %			
В	Hexane	90 %	Température du fou	r: 25.0 ℃	
	Débit:	1.000 mL/min	Pression:	43 bars	
ron	natogram				
200	2021-07-19 #3 [man	ually integrated]		UV_VIS_1 WVL:2	54 r
		1 - 15.305	12 - 29 222		
-20	0.0	10.0 20.0	30.0 40.0 Time (min)	50.0	
	Description (1)				
	Results			Distant (ED)	
eak I	Peak Name	Retention Time Width (%) Resolution (EP) Asymmetry (EP)	Plates (EP)	
		Retention Time Width (min mir 15.305 0.41	Kesolution (EP) Asymmetry (EP) 12.95 1.16	7451	

Integr	ation Results					
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height
		min	mAU*min	mAU	%	%
1		15.305	52.067	115.412	49.97	66.91
2		29.222	52.134	57.081	50.03	33.09
Total:			104.201	172.493	100.00	100.00

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

			Chromat	ogram and	Results			
Genera	l informations							
	ce Name:	2021-07-20_2						
Instrum		U3000						
Logiciel		Chromeleon						
Column		CHIRALPAK ASH	DAICEI					
		CHINALPAN ASH	DAICEL					
	on Details				<u> </u>		10.00	
Injection		WE-1638-1-ASH-20		min-25°C-254ni			40.00 min	
	ent Method:	90-10-40min-25°C-2	254nm		Injection Volume:		20.00 µL	
Injection	n Date/Time:	20/juil./21 13:51			Channel:	UV_VIS_1		
					Wavelength:		254 nm	
	nent Method Details							
	ent Method:	90-10-40min-25°C-2						
	sopropanol	10						
	Hexane	90	%		Température du four:		25.0 °C	
1	Débit:	1.000	mL/min		Pression:		42 bars	
Chroma	atogram							
	2021-07-20_2 #4 [mar	nually integrated]	VE-1638-1-ASH-20	21-07-20-90-10-6	0min-25°C-254nm-1mL	min	UV_VIS_1 WVL:254 nm	
550		,,						
1								
500 -			1 - 15.3	53				
			Λ					
			11					
-			11					
400 -								
			11					
5 1			11					
₹ 300 -								
- 9			11					
Absorbance [mAU]			11					
ë -			11					
ଞ୍ଚ 200 -			11					
₹ -			11					
-			11					
-			11					
100 -								
-		\	11		\wedge	2 - 29.090		
-					/ \	2 - 20.000		
		1			/	/		
0-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~							
-								
-50								
0	.0 5.0	10.0	15.0	20.0 Time [min]	25.0	30.0	35.0 40.	
Peak Results								
Peak R	esults							
		Retention Time	Width (50%)	Resolution (EP)	Asymmetry (EP)	Plates /EE	2)	
	esults Peak Name	Retention Time	Width (50%)	Resolution (EP)	Asymmetry (EP)	Plates (EF	?)	
No. F		min	min			-	2)	
				Resolution (EP) 8.37 n.a.	Asymmetry (EP) n.a. 1.33	Plates (EF 2454 3173)	

Integr	Integration Results							
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height		
		min	mAU*min	mAU	%	%		
1		15.303	379.356	488.358	85.12	90.38		
2		29.090	66.312	51.955	14.88	9.62		
Total:			445.668	540.313	100.00	100.00		

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

		Chroma	atogram and Results			
General	l informations					
	ce Name:	2021-07-20_2				
nstrume		U3000				
ogiciel u		Chromeleon				
Column i		CHIRALPAK ASH DAICEL				
	n Details					
njection		WE-1637-2-ASH-2021-07-20-90-10-	60min-25°C-254nnRun Time	40.00) min	
	ent Method:	90-10-40min-25°C-254nm	Injection Volume:	20.00		
	Date/Time:	20/juil./21 13:10	Channel:	UV_VIS_1		
.,		2017.00.00	Wavelength:		254 nm	
nstrum	ent Method Details			201		
	ent Method:	90-10-40min-25°C-254nm				
%A Is	sopropanol	10 %				
%В Н	lexane	90 %	Température du fo	our: 25.0	°C	
D	Débit:	1.000 mL/min	Pression:		bars	
hroma	ntogram					
600-	1 2021-07-20_2 #3 [m	anually integrated] WE-1637-2-ASH	-2021-07-20-90-10-60min-25°C-254nm-	1mLmin I	UV_VIS_1 WVL:254 nm	
400 400 100 100 100	M		5.350	12 - 29.098		
Peak Re	20.0 5.0 esults Peak Name	10.0 15.0 Retention Time Width (50%)	20.0 25.0 Time [min]	30.0	35.0 4	
			(Li) (Li)	, , , , , , , , , , , , , , , , , , , ,	1	
NU. F		i min i min				
1		min min 15.350 0.724	8.38 1.37	2492	+	

Integr	Integration Results							
No.	Peak Name	Retention Time	Area	Height	Relative Area	Relative Height		
		min	mAU*min	mAU	%	%		
1		15.350	385.175	500.880	85.45	90.70		
2		29.098	65.568	51.374	14.55	9.30		
Total:			450.743	552.255	100.00	100.00		

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