

(+)-Camphor- Mediated Kinetic Resolution of Allylalanines: A Strategy Towards Enantio-Enriched Cyclohex-2-en-1-ylalane

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Electronic Supporting Information

p. 2-11 : Experimental procedures and characterization of compounds

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Experimental procedures and characterization of compounds.

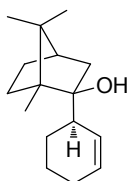
All reactions involving organometallics were conducted under an atmosphere of argon.

^1H and ^{13}C NMR spectra were recorded in CDCl_3 , on a Bruker AC-250, coupling constant (J) values are reported in Hz.

Mass spectra were recorded on a Micromass Q-TOF micro MS spectrometer.

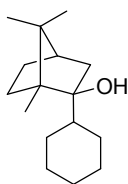
X-ray diffraction measurement was performed on a Bruker D8 Venture diffractometer equipped with a kappa goniometer and a PHOTON100 CMOS detector and using Cu K α radiation (from a microsource tube with multi-layer mirror focalizing opticals). Data were collected using Bruker Apex2 software, on the full sphere, with omega and phi scans, $1^\circ/\text{frame}$, 25 s/frame, with the detector placed at 35mm. The sample temperature was maintained at 100K using a Cryostream700 (Oxford Cryosystems).

(1S,2S,4R)-2-[(R)-Cyclohex-2-en-1-yl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol **1b**



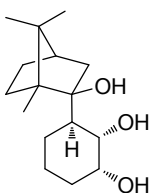
To a solution of Cp_2TiCl_2 (50 mg, 0.2 mmol) and 1,3-cyclohexadiene (0.4 mL) in THF (5 mL), was slowly added a solution of DIBAL-H (1 M in THF, 2.2 mL, 2.2 mmol) at rt. The resulting mixture was stirred for 4 h at 40°C , then cooled down to -30°C . A solution of (+)-camphor (152 mg, 1 mmol) in THF (1 mL) was added. The resulting mixture was stirred for 2 h at -30°C ; then, an aqueous solution of NaOH (10%, 5 mL) was added. After 2 h of stirring, the organic layer was collected, the aqueous phase was extracted with Et_2O (2 x 5 mL), the organic phases were combined, washed with brine (5 mL) dried over Na_2SO_4 , filtered and concentrated. The residue was purified by column chromatography on silica gel eluting with a mixture of PE and AcOEt to give **1b** (192 mg, 82%) as a colorless oil. $[\alpha]_D = +15.3$ (c 1, CH_2Cl_2); ^1H NMR (250 MHz, CDCl_3) δ : 5.96 (dt, $J = 10.5, 3.3$ Hz, 1 H), 5.67 (d, $J = 10.2$ Hz, 1 H), 2.34 (m, 1 H), 2.07-1.66 (m, 7 H), 1.58-1.39 (m, 6 H), 1.09-1.01 (m, 4 H), 0.94 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (62.5 MHz, CDCl_3) δ : 132.1, 128.1, 81.4, 52.1, 50.4, 46.9, 44.6, 29.7, 27.6, 25.4, 25.0, 22.0, 21.4, 20.8, 12.3; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{26}\text{ONa}$: 257.1881; found: 257.1886.

(1S,2S,4R)-2-Cyclohexyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol 1'b



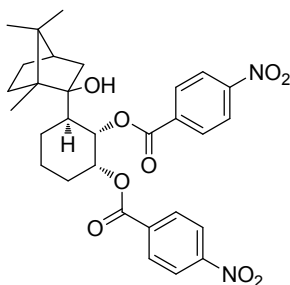
A mixture of **1b** (185 mg, 0.79 mmol) and Pd/C (10%, 30 mg) in EtOH (5 mL) was stirred under an atmosphere of H₂ for 1 h. The resulting mixture was filtrated through a plug of celite. The filtrate was concentrated to give **1'b** (183 mg, 98%) as pale yellow solid. Mp 58°C; [α]_D = +16.7 (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 1.93-1.60 (m, 8 H), 1.50-1.14 (m, 10 H), 1.09-1.01 (m, 4 H), 0.93 (s, 3 H), 0.82 (s, 3 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 82.3, 52.2, 50.4, 48.3, 46.4, 44.4, 29.2, 28.4, 27.7, 27.6, 26.9, 26.5, 26.4, 21.3, 20.9, 12.4.

(1R,2S,3R)-3-[(1S,2S,4R)-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl]cyclohexane-1,2-diol



To a solution of **1b** (204 mg, 0.87 mmol) in a 10:1 mixture of acetone/water (17 mL) was added a solution of OsO₄ (4% in H₂O, 0.4 mL) and NMO (205, mg, 1.75 mmol) and the resulting mixture was stirred at rt for 24 h. Sodium bisulfite (200 mg) was added and the stirring was continued for 1 h. The solid was filtered off. The filtrate was diluted with CH₂Cl₂ (20 mL), the aqueous layer was discarded, and the organic phase was dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel eluting with a 1:1 mixture of PE and AcOEt to give the triol (193 mg, 83%) as a colorless oil. ¹H NMR (250 MHz, CDCl₃) δ : 4.07 (m, 1 H), 3.79 (dd, *J* = 9.4, 2.3Hz, 1 H), 2.47 (br s, 3 H), 2.03-1.36 (m, 13 H), 1.13 (m, 1 H), 1.07 (s, 3 H), 0.96 (s, 3 H), 0.82 (s, 3 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 82.1, 74.3, 71.2, 53.1, 49.9, 48.1, 44.6, 30.8, 28.9, 27.8, 27.4, 21.4, 20.8, 20.0, 12.5; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₁₆H₂₈O₃Na: 291.1936; found: 291.1930.

(1R,2S,3R)-3-[(1S,2S,4R)-2-Hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl]cyclohexane-1,2-diyl bis(4-nitrobenzoate) 1''c



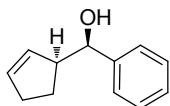
To a solution of the above triol (113 mg, 0.42 mmol) in pyridine (2 mL) was added 4-nitrobenzoyl chloride (175 mg, 0.94 mmol) and DMAP (25 mg, 0.2 mmol) and the resulting mixture was stirred for 24 h at rt. The reaction mixture was diluted with CH₂Cl₂ (10 mL) washed with an aqueous solution of HCl (1 M, 3 x 2 mL) dried with Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel eluting with a 7:1 mixture of PE and AcOEt to give **1''c** (152 mg, 64%) as a white solid which was allowed to crystallized from a mixture of Et₂O and AcOEt. Mp 140°C; [α]_D = -151 (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 8.34 (d, *J* = 8.8 Hz, 2 H), 8.25 (d, *J* = 8.9 Hz, 2 H), 8.19 (d, *J* = 8.9 Hz, 2 H), 8.10 (d, *J* = 8.9 Hz, 2 H), 5.77 (dt, *J* = 5.4, 2.8 Hz, 1 H), 5.65 (dd, *J* = 9.1, 2.8 Hz, 1 H), 2.34 (dt, *J* = 9.9, 4.8 Hz, 1 H), 2.11 (m, 1 H), 1.93-1.46 (m, 12 H), 1.08 (m, 1 H), 1.03 (s, 3 H), 1.00 (s, 3 H), 0.83 (s, 3 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 164.2, 163.9, 150.6, 150.6, 135.7, 135.5, 130.8, 130.5, 123.8, 123.6, 80.9, 75.6, 73.4, 53.3, 50.0, 49.6, 48.2, 44.4, 29.2, 28.6, 27.8, 27.0, 21.3, 20.8, 20.3, 12.5; HRMS-ESI : *m/z* [M+Na]⁺calcd for C₃₀H₃₄N₂O₉Na: 589.2162; found: 589.2166.

General procedure for the synthesis of alcohols 2 (GP1).

To a solution of Cp₂TiCl₂ (50 mg, 0.2 mmol) and 1,3-cyclohexadiene (0.3 mL) in THF (5 mL) under argon, was slowly added a solution of DIBAL-H (1 M in THF, 2 mL, 2 mmol) at rt. The resulting mixture was stirred for 4 h at 40°C, then cooled down to -30°C. A solution of (+)-camphor (152 mg, 1 mmol) in THF (1 mL) was slowly added. The resulting mixture was stirred for 2 h at -30°C, then, a solution of aldehyde (0.8 mmol) in THF (1 mL) was added. The reaction was quenched after 2 h of stirring by adding an aqueous solution of NaOH (10%, 5 mL). After 2 h of stirring, the organic layer was collected and the aqueous phase was extracted with Et₂O (2 x 5 mL). The organic phases were combined, washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel, eluting with a mixture of PE and AcOEt, to give **2**.

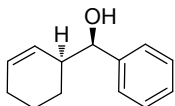
(R)-[(S)-Cyclopent-2-en-1-yl](phenyl)methanol 4a¹

¹ Y. Sasaki, C. Zhong, M. Sawamura, H. Ito, *J. Am. Chem. Soc.* **2010**, *132*, 1226-1227



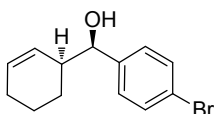
Yield = 85%. Colorless oil; ee = 48%, $[\alpha]_D = -15.1$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.35-7.25 (m, 5 H), 5.84 (m, 1 H), 5.38 (m, 1 H), 4.56 (d, $J = 6.5$ Hz, 1 H), 3.09 (m, 1 H), 2.43-2.23 (m, 2 H), 2.01-1.77 (m, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 143.4, 133.6, 131.2, 128.2, 127.3, 126.3, 76.9, 53.9, 32.2, 25.0.

(R)-[(S)-Cyclohex-2-en-1-yl](phenyl)methanol 3a²



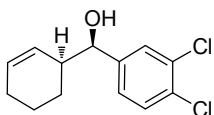
Yield = 85%. Colorless oil; ee = 89%; $[\alpha]_D = -9.1$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.40-7.30 (m, 5 H), 5.82 (dq, $J = 10.1, 3.4$ Hz, 1 H), 5.47 (dt, $J = 10.6, 2.6$ Hz, 1 H), 4.53 (d, $J = 6.6$ Hz, 1 H), 2.44 (m, 1 H), 2.05-1.89 (m, 3 H), 1.84-1.71 (m, 2 H), 1.55-1.44 (m, 2 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 142.9, 130.3, 128.2, 128.0, 127.3, 126.5, 77.3, 42.9, 25.2, 23.8, 21.1.

(R)-(4-Bromophenyl) [(S)-cyclohex-2-en-1-yl]methanol 3b³



Yield = 89%. Colorless oil; ee = 84%; $[\alpha]_D = -7.1$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.45 (d, $J = 8.4$ Hz, 2 H), 7.22 (d, $J = 8.3$ Hz, 2 H), 5.83 (dq, $J = 10.0, 3.4$ Hz, 1 H), 5.36 (dt, $J = 10.2, 2.4$ Hz, 1 H), 4.54 (d, $J = 6.2$ Hz, 1 H), 2.44 (m, 1 H), 2.06-1.92 (m, 3 H), 1.83-1.38 (m, 4 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 141.7, 131.2, 130.8, 128.2, 128.0, 127.5, 121.0, 76.6, 42.9, 25.1, 23.5, 21.0.

(R)- [(S)-Cyclohex-2-en-1-yl](3,4-dichlorophenyl)methanol 3c



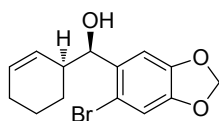
Yield = 55%. Colorless oil; ee = 87%; $[\alpha]_D = -8.3$ (c 0.9, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.44 (d, $J = 1.4$ Hz, 1 H), 7.40 (d, $J = 8.2$ Hz, 1 H), 7.15 (dd, $J = 8.3, 2.1$ Hz, 1 H), 5.87 (dq, $J = 10.0, 3.4$ Hz, 1 H), 5.39 (dd, $J = 9.7, 3.1$ Hz, 1 H), 4.58 (d, $J = 5.8$ Hz, 1 H), 2.45 (m, 1 H), 2.11-1.92 (m, 3 H), 1.83-1.39 (m, 4 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ :

² Y. Yoshimura, M. Ohta, T. Imahori, T. Imamichi, H. Takahata, *Org. Lett.* **2008**, *10*, 3449-3452.

³ A. Flahaut, K. Toutah, P. Mangeney, S. Rolan, *Eur. J. Inorg. Chem.* **2009**, 5422-5432.

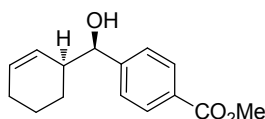
143.0, 132.2, 131.4, 131.0, 130.0, 128.4, 128.2, 127.2, 125.7, 75.9, 42.9, 25.1, 23.2, 21.0;
HRMS-ESI : m/z [M]⁻ calcd for C₁₃H₁₃Cl₂O: 255.0343; found: 255.0340.

(R)-(6-Bromobenzo[d][1,3]dioxol-5-yl)[(S)-cyclohex-2-en-1-yl]methanol 3d



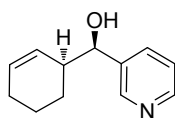
Yield = 82%. Colorless oil; ee = 84%; $[\alpha]_D = -21.1$ (c 1, Et₂O); ¹H NMR (250 MHz, CDCl₃) δ : 7.02 (s, 1 H), 6.94 (s, 1 H), 5.96 (s, 2 H), 5.86 (dt, $J = 10.2, 3.4$ Hz, 1 H), 5.45 (m, 1 H), 4.93 (d, $J = 5.4$ Hz, 1 H), 2.56 (m, 1 H), 2.19 (br s, 1 H), 2.04-1.93 (m, 2 H), 1.76 (m, 1 H), 1.58-1.43 (m, 3 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 147.3, 134.9, 130.8, 127.8, 112.4, 112.2, 108.2, 101.6, 75.2, 41.0, 25.1, 23.0, 21.2; HRMS-ESI : m/z [M+Na]⁺ calcd for C₁₄H₁₅BrO₃Na: 333.0102; found: 333.0106.

Methyl 4-[(R)-[(S)-cyclohex-2-en-1-yl](hydroxymethyl)]benzoate 3e⁴



Yield = 75%. White solid; mp 62°C; ee = 87%; $[\alpha]_D = -7.0$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 8.02 (d, $J = 8.2$ Hz, 2 H), 7.42 (d, $J = 8.1$ Hz, 2 H), 5.93-5.77 (m, 1 H), 5.41 (d, $J = 10.0$ Hz, 1 H), 4.70 (d, $J = 5.8$ Hz, 1 H), 3.91 (s, 3 H), 2.51 (m, 1 H), 2.03-1.94 (m, 2 H), 1.88 (br s, 1 H), 1.63 (m, 1 H), 1.62-1.44 (d, $J = 7.8$ Hz, 3 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 147.9, 131.2, 129.5, 129.1, 127.5, 126.4, 76.7, 52.05, 43.0, 25.1, 23.3, 21.0, 1 C is missing.

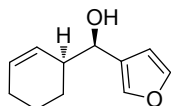
(R)- [(S)-Cyclohex-2-en-1-yl](pyridin-3-yl)methanol 3f



Yield = 50%. Colorless oil; ee = 88%; $[\alpha]_D = -7.5$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 8.57-8.20 (m, 2 H), 7.71 (d, $J = 7.9$ Hz, 1 H), 7.20 (m, 1 H), 5.83 (dq, $J = 9.8, 3.3$ Hz, 1 H), 5.39 (dd, $J = 9.9, 2.8$ Hz, 1 H), 4.63 (d, $J = 6.3$ Hz, 1 H), 3.21 (s, 1 H), 2.50 (m, 1 H), 2.02-1.92 (m, 2 H), 1.78-1.42 (m, 4 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 148.0, 134.5, 130.7, 129.9, 127.2, 126.7, 74.7, 42.8, 42.7, 25.1, 23.7, 20.9; HRMS-ESI : m/z [M+H]⁺ calcd for C₁₂H₁₆NO: 190.1232; found: 190.1235.

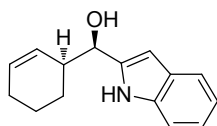
(R)- [(S)-Cyclohex-2-en-1-yl](furan-3-yl)methanol 3g

⁴ G. P. Howell, A. J. Minnaard, B. L. Feringa, *Org. Biomol. Chem.* **2006**, *4*, 1278-1283.



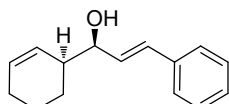
Yield = 83%. Colorless oil; ee = 87%; $[\alpha]_D = -39.6$ (c 1, Et₂O); ¹H NMR (250 MHz, CDCl₃) δ : 7.38 (s, 2 H), 6.39 (s, 1 H), 5.81 (m, 1 H), 5.47 (d, *J* = 9.8 Hz, 1 H), 4.53 (d, *J* = 6.6 Hz, 1 H), 2.44 (m, 1 H), 2.04-1.93 (m, 3 H), 1.84-1.72 (m, 2 H), 1.57-1.42 (m, 2 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 143.0, 139.7, 130.2, 127.7, 127.2, 108.8, 70.2, 41.9, 25.1, 24.1, 21.1; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₁₁H₁₄O₂Na: 201.0891; found: 201.0899.

(R)-1-[(S)-Cyclohex-2-en-1-yl](1H-indol-2-yl)methanol 3h



Yield = 64%. White solid; mp 129°C; ee = 84%; $[\alpha]_D = -46$ (c 0.4, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 8.41 (s, 1 H), 7.56 (d, *J* = 7.6 Hz, 1 H), 7.32 (d, *J* = 7.8 Hz, 1 H), 7.21-7.02 (m, 2 H), 6.35 (m, 1 H), 5.87 (dq, *J* = 9.9, 3.3 Hz, 1 H), 5.51 (m, 1 H), 4.79 (d, *J* = 6.3 Hz, 1 H), 2.62 (m, 1 H), 2.16 (br s, 1 H), 2.03-1.45 (m, 6 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 139.5, 135.6, 130.9, 130.6, 128.1, 127.2, 127.2, 121.2, 120.3, 119.7, 110.9, 99.7, 71.8, 67.9, 41.9, 25.1, 24.2, 21.0; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₁₅H₁₇NONa: 250.1208; found: 250.1203.

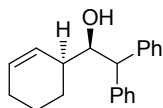
(S,E)-1-[(S)-Cyclohex-2-en-1-yl]-3-phenylprop-2-en-1-ol 3i⁵



Yield = 80%. Colorless oil; ee = 87%; $[\alpha]_D = -81$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 7.45-7.15 (m, 5 H), 6.58 (d, *J* = 16.0 Hz, 1 H), 6.23 (dd, *J* = 15.9, 6.9 Hz, 1 H), 5.84 (dq, *J* = 10.1, 3.3 Hz, 1 H), 5.64 (d, *J* = 10.1 Hz, 1 H), 4.18 (t, *J* = 6.4 Hz, 1 H), 2.36 (m, 1 H), 2.06-1.93 (m, 2 H), 1.80 (m, 3 H), 1.62-1.39 (m, 2 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 136.7, 131.4, 130.5, 130.1, 128.5, 127.60, 127.6, 126.4, 76.0, 41.8, 25.2, 24.1, 21.2.

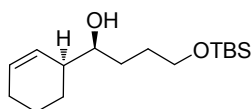
(R)-1-[(S)-Cyclohex-2-en-1-yl]-2,2-diphenylethanol 3j

⁵ E. González, L. Muñoz-Hernández, E. Alicea, B. Singaram, G. W. Kabalka, J. A. Soderquist, *Org. Lett.* **2015**, *17*, 4368-4371.



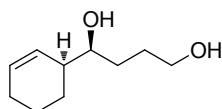
Yield = 58%. Pale yellow solid; mp 58°C; ee = 82%; $[\alpha]_D = +2.1$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 7.61-7.05 (m, 10 H), 5.91 (dq, *J* = 10.1, 3.1 Hz, 1 H), 5.68-5.51 (d, *J* = 10.1 Hz, 1 H), 4.44 (dd, *J* = 9.2, 3.7 Hz, 1 H), 4.12 (d, *J* = 9.2 Hz, 1H), 2.26 (m, 1 H), 2.07-1.96 (m, 2 H), 1.88-1.67 (m, 3 H), 1.60 (br s, 1 H), 1.44 (m, 1 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 142.2, 141.8, 130.4, 129.4, 128.6 (3 C), 128.1, 126.6, 126.5, 76.3, 54.8, 37.9, 25.0, 21.4, 21.3; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₂₀H₂₂ONa 301.1568; found: 301.1565.

(S)-4-[(Tert-Butyldimethylsilyloxy)-1-[(S)-cyclohex-2-en-1-yl]butan-1-ol 3k



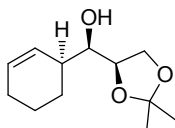
Yield = 66%. Colorless oil; ee = 89%; $[\alpha]_D = -31.9$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 5.83 (dq, *J* = 9.9, 3.2 Hz, 1 H), 5.58 (d, *J* = 8.5 Hz, 1 H), 3.67 (t, *J* = 5.2 Hz, 2 H), 3.55 (m, 1 H), 2.35 (s, 1 H), 2.22 (s, 1 H), 1.99 (m, 2 H), 1.81-1.43 (m, 8 H), 0.90 (s, 9 H), 0.07 (s, 6 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 129.8, 128.8, 74.2, 63.4, 41.3, 30.9, 29.4, 25.9, 23.2, 21.4, 18.3, -5.4, -5.4; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₁₆H₃₂O₂SiNa 307.2069; found: 307.2077.

(S)-1-[(S)-Cyclohex-2-en-1-yl]butane-1,4-diol



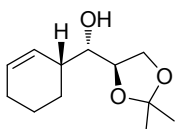
To a solution of **2ak** (104 mg, 0.37 mmol) in THF (5 mL), was added TBAF·H₂O (184 mg, 0.66 mmol) and the resulting solution was stirred at rt for 2 h; then the solvent was removed under reduced pressure. The residue was diluted with Et₂O (10 mL), washed with water (2 x 1 mL), dried over Na₂SO₄, filtered and concentrated to give the title diol as a colorless oil (53 mg, 86%). ee = 89%; $[\alpha]_D = -36.7$ (c 1, CH₂Cl₂); ¹H NMR (250 MHz, CDCl₃) δ : 5.86 (m, 1 H), 5.56 (d, *J* = 8.5 Hz, 1 H), 3.75-3.54 (m, 3 H), 2.69 (m, 2 H), 2.23 (m, 1 H), 1.99 (br s, 2 H), 1.83-1.41 (m, 8 H); ¹³C NMR (62.5 MHz, CDCl₃) δ : 130.4, 128.4, 74.6, 62.9, 41.6, 30.9, 29.7, 25.2, 23.0, 21.3; HRMS-ESI : *m/z* [M+Na]⁺ calcd for C₁₀H₁₈O₂Na 193.1204; found: 193.1207.

(R)-[(S)-cyclohex-2-en-1-yl][(R)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol 3l



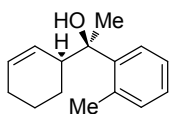
Prepared according to GP1 using (+)-camphor (152 mg, 1 mmol). Colorless oil; $de = 86\%$; $[\alpha]_D = -30.3$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 5.84 (dq, $J = 10.1, 2.2$ Hz, 1 H), 5.57 (dt, $J = 10.0, 2.3$ Hz, 1 H), 4.22 (m, 1H), 4.03 (dd, $J = 8.1, 6.4$ Hz, 1 H), 3.77 (t, $J = 7.6$ Hz, 1 H), 3.44 (t, $J = 5.7$ Hz, 1 H), 2.22 (m, 1 H), 2.08 (br s, 1 H), 2.00 (m, 2 H), 1.80-1.64 (m, 3 H), 1.56 (m, 1 H), 1.44 (s, 3 H), 1.38 (s, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 130.2, 127.5, 109.2, 76.6, 74.5, 66.4, 39.0, 26.6, 25.3, 25.0, 23.5, 20.6; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{20}\text{O}_3\text{Na}$ 235.1310; found: 235.1308.

(S)-1-[(R)-cyclohex-2-en-1-yl]-(R)-2,2-dimethyl-1,3-dioxolan-4-ylmethanol 3m



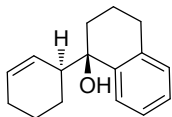
Prepared according to GP1 using (-)-camphor (152 mg, 1 mmol). Colorless oil; $de = 88\%$; $[\alpha]_D = +38.5$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 5.89 (dq, $J = 9.8, 2.5$ Hz, 1 H), 5.50 (d, $J = 10.0$ Hz, 1 H), 4.16 (q, $J = 6.2$ Hz, 1 H), 4.04 (t, $J = 7.1$ Hz, 1 H), 3.95 (t, $J = 7.5$ Hz, 1 H), 3.70 (t, $J = 5.6$ Hz, 1 H), 2.36 (br s, 1 H), 2.08-1.86 (m, 3 H), 1.83-1.70 (m, 2 H), 1.65-1.50 (m, 2 H), 1.43 (s, 3 H), 1.37 (s, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 131.1, 127.3, 108.7, 76.2, 73.8, 65.6, 37.9, 26.6, 25.4, 25.1, 23.0, 20.8; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{20}\text{O}_3\text{Na}$ 235.1310; found: 235.1303.

(R)-1-[(S)-Cyclohex-2-en-1-yl]-1-(o-tolyl)ethanol 3n



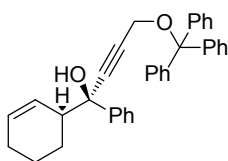
Yield = 58%. Colorless oil; $ee = 86\%$; $[\alpha]_D = +38.8$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.52 (m, 1 H), 7.18-7.10 (m, 3 H), 5.92 (dq, $J = 10.3, 3.5$ Hz, 1 H), 5.64 (d, $J = 10.3$ Hz, 1 H), 2.89 (m, 1 H), 2.51 (s, 3 H), 1.97 (m, 2 H), 1.80 (br s, 1 H), 1.73 (m, 1 H), 1.64 (s, 3 H), 1.54-1.24 (m, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 144.7, 134.7, 132.4, 131.3, 126.65, 126.60, 126.55, 125.4, 77.1, 43.7, 27.0, 25.1, 24.2, 22.6, 22.0; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{20}\text{ONa}$ 239.1412; found: 239.1411.

(R)-1-[(S)-cyclohex-2-en-1-yl]-1,2,3,4-tetrahydronaphthalen-1-ol 3o



Yield = 53%. Colorless oil; $ee = 86\%$; $[\alpha]_D = -17.4$ (c 0.7, CH_2Cl_2); 1H NMR (250 MHz, $CDCl_3$) δ : 7.53 (dd, $J = 7.2, 2.0$ Hz, 1H), 7.27-7.14 (m, 2H), 7.07 (d, $J = 7.3$ Hz, 1 H), 5.63 (dq, $J = 10.3, 3.4$ Hz, 1H), 5.00 (dt, $J = 10.3, 2.1$ Hz, 1H), 2.91 (m, 1 H), 2.79-2.55 (m, 2 H), 2.05-1.44 (m, 12 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ : 141.1, 138.1, 129.0, 128.7, 128.2, 126.9, 126.5, 126.3, 74.0, 46.3, 33.0, 30.2, 25.3, 23.4, 22.3, 19.2; HRMS-ESI : m/z $[M+Na]^+$ calcd for $C_{16}H_{20}ONa$ 251.1412; found: 251.1410.

(R)-1-[(S)-cyclohex-2-en-1-yl]-1-phenyl-4-(trityloxy)but-2-yn-1-ol 3p

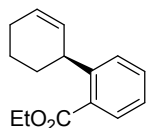


Yield = 55%. Yellow oil; dr *syn* / *anti* = 89:11, ee (*syn*) = 86%; 1H NMR (250 MHz, $CDCl_3$) δ : 7.57 (d, $J = 7.2$ Hz, 2 H), 7.48 (d, $J = 7.4$ Hz, 6 H), 7.37 – 7.16 (m, 12 H), 5.89 (dq, $J = 10.2, 3.3$ Hz, 1 H), 5.75 (d, $J = 10.3$ Hz, 1 H), 3.89 (s, 2 H), 2.63 (m, 1 H), 2.31 (br s, 1 H), 1.95 (m, 2 H), 1.74 (m, 1 H), 1.63-1.34 (m, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ : 143.6, 142.9, 131.3, 128.6, 127.9, 127.8, 127.4, 127.1, 126.6, 126.1, 87.8, 87.6, 82.9, 75.1, 53.4, 48.1, 25.1, 23.7, 21.6; HRMS-ESI : m/z $[M+Na]^+$ calcd for $C_{35}H_{32}O_2Na$ 507.2300; found: 507.2295.

General procedure for the palladium-mediated retroallylation / coupling reaction. Synthesis of compounds 5 (GP2).

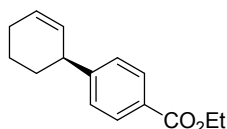
A dry flask was loaded with anhydrous Cs_2CO_3 (279 mg, 0.85 mmol) and heated with a heat gun for 2 min under reduced pressure. $Pd(OAc)_2$ (19 mg, 0.08 mmol) was next added and the flask was filled with argon by using the standard Schlenk technique. Tritolylphosphine (104 mg, 0.34 mmol) in toluene (1 mL) was added and the resulting mixture was stirred for 10 min. A solution of **1c** (100 mg, 0.43 mmol) and aryl bromide (0.43 mmol) in toluene (1 mL) was added and the mixture was stirred at reflux for 12 h. the mixture was cooled down to rt, then water (2 mL) and hexane (2 x 2 mL) were added. The aqueous layer was extracted with Et_2O (2 x 5 mL), the organic phases were combined, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give **3**.

(S)-Ethyl 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxylate 5a.



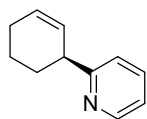
Yield = 55%; colorless oil; $[\alpha]_D = -35$ (c 0.5, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.79 (d, $J = 7.7$ Hz, 1 H), 7.43 (dt, $J = 7.4, 2.0$ Hz, 1 H), 7.36 (d, $J = 7.3$ Hz, 1 H), 7.23 (td, $J = 7.4, 2.1$ Hz, 1 H), 5.91 (dq, $J = 10.1, 3.0$ Hz, 1 H), 5.65 (d, $J = 10.1$ Hz, 1H), 4.36 (q, $J = 7.0$ Hz, 2 H), 4.25 (m, 1 H), 2.22-2.04 (m, 3 H), 1.79-1.59 (m, 2 H), 1.50 (m, 1 H), 1.39 (t, $J = 7.0$ Hz, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 168.1, 147.3, 131.5, 130.4, 130.2, 130.0, 128.9, 128.4, 125.7, 60.9, 37.9, 32.2, 25.0, 21.3, 14.2; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2\text{Na}$ 253.1204; found: 253.1198.

(S)-Ethyl 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-carboxylate 5b



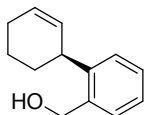
Yield = 66%; colorless oil; $[\alpha]_D = -62.5$ (c 1, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 8.00 (d, $J = 8.2$ Hz, 2 H), 7.31 (d, $J = 8.2$ Hz, 3H), 5.96 (dq, $J = 9.8, 3.1$ Hz, 1 H), 5.72 (d, $J = 10.0$ Hz, 1 H), 4.39 (q, $J = 7.1$ Hz, 2 H), 3.49 (m, 1 H), 2.18-1.99 (m, 3 H), 1.84-1.53 (m, 3 H), 1.41 (t, $J = 7.1$ Hz, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 166.7, 152.0, 129.6, 129.2, 129.0, 128.3, 127.7, 77.1, 60.7, 41.8, 24.9, 21.0, 14.3; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2\text{Na}$ 253.1204; found: 253.1207.

(S)-2-(Cyclohex-2-en-1-yl)pyridine 5c.



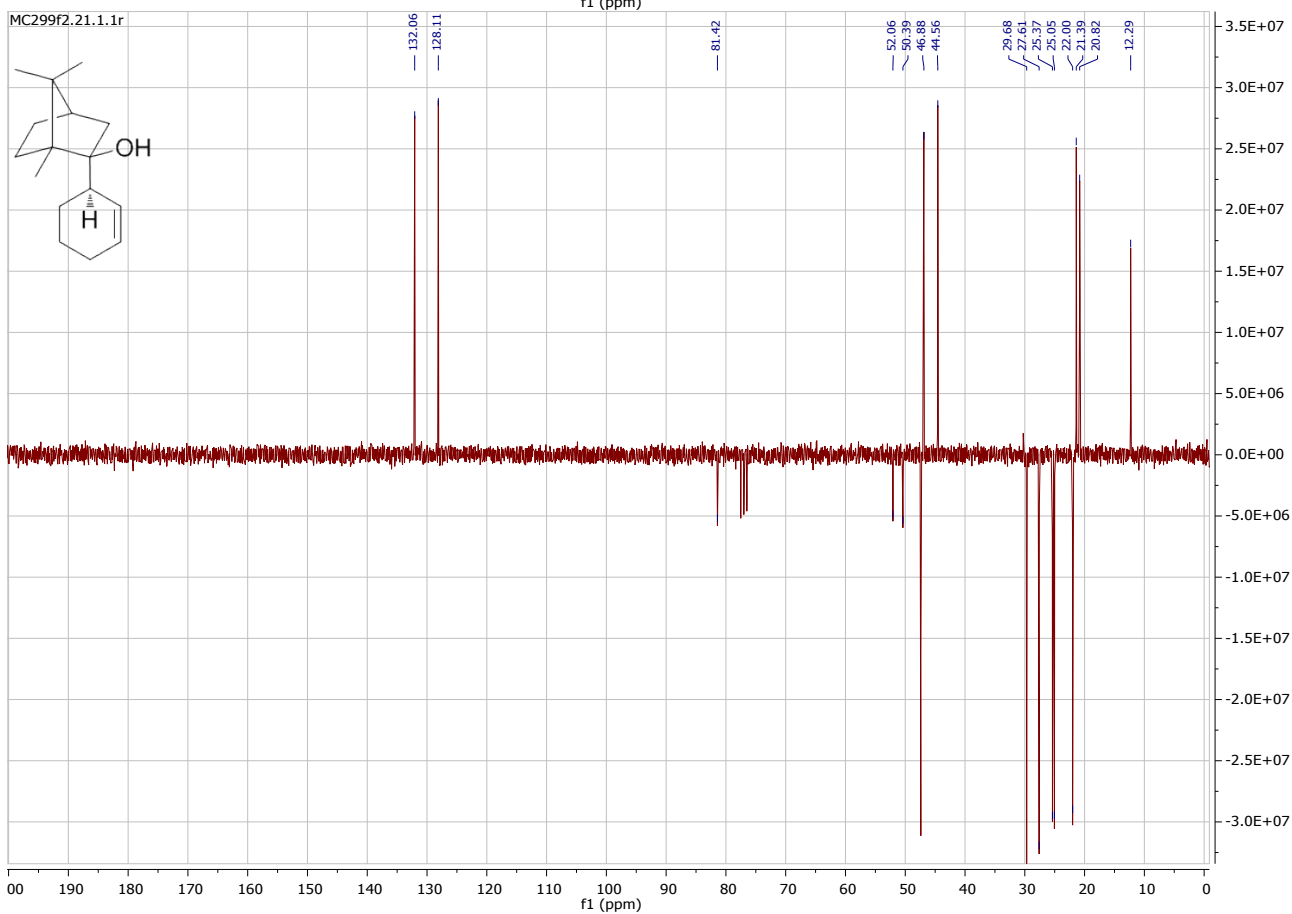
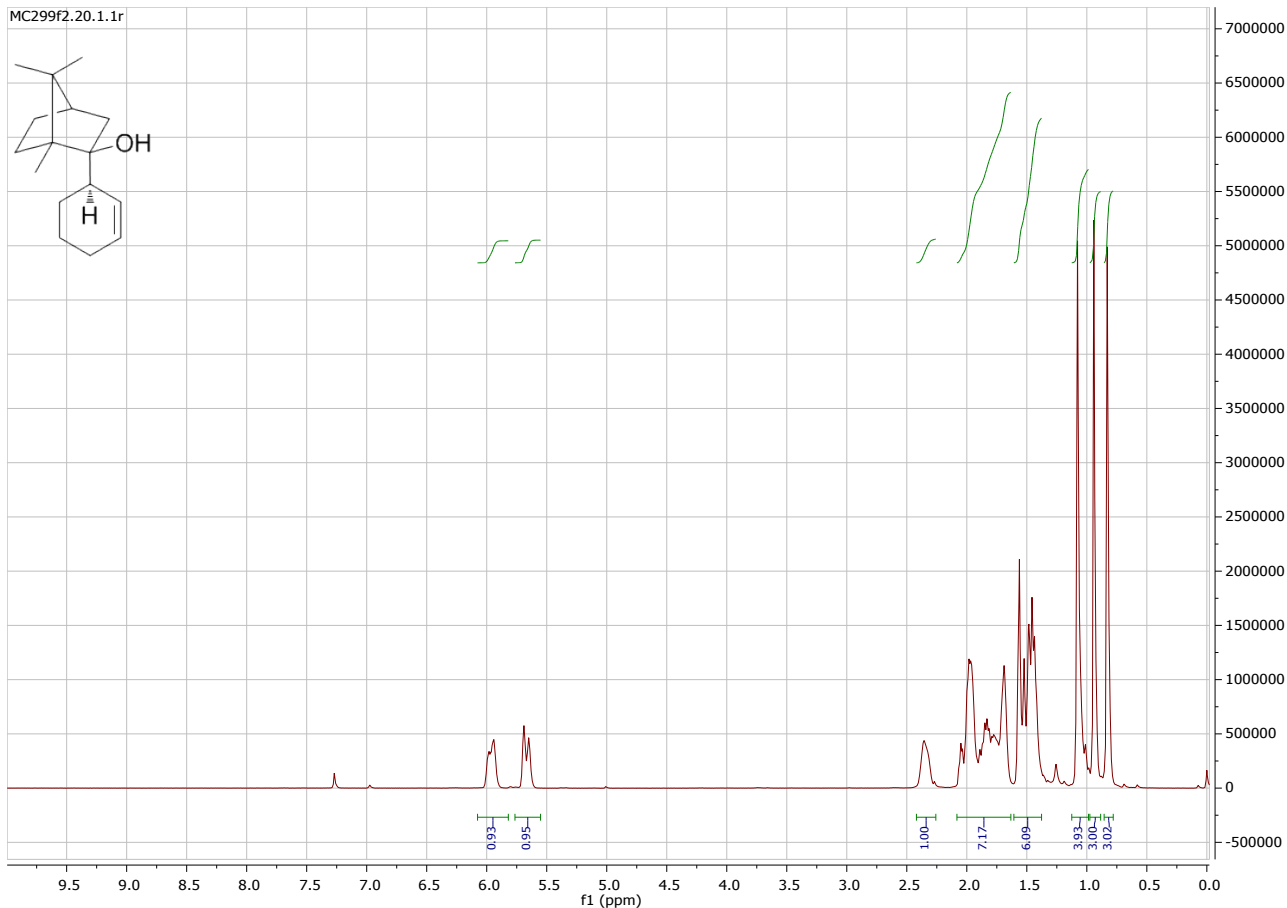
Yield = 46% ; colorless oil; $[\alpha]_D = -64.5$ (c 0.5, CH_2Cl_2); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 8.55 (d, $J = 3.9$ Hz, 1 H), 7.61 (td, $J = 7.7, 1.9$ Hz, 1 H), δ 7.20 (d, $J = 7.8$ Hz, 1 H), 7.11 (m, 1 H), 5.95 (dq, $J = 7.6, 2.3$ Hz, 1 H), 5.80 (d, $J = 10.0$ Hz, 1 H), 3.60 (m, 1 H), 2.17-2.01 (m, 3 H), 1.81-1.61 (m, 3 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 165.3, 149.2, 136.3, 128.8, 128.6, 121.7, 121.0, 43.9, 30.6, 24.9, 21.0; HRMS-ESI : m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{14}\text{N}$ 160.1126; found: 160.1120.

(S)-(1',2',3',4'-Tetrahydro-[1,1'-biphenyl]-2-yl)methanol 5'a

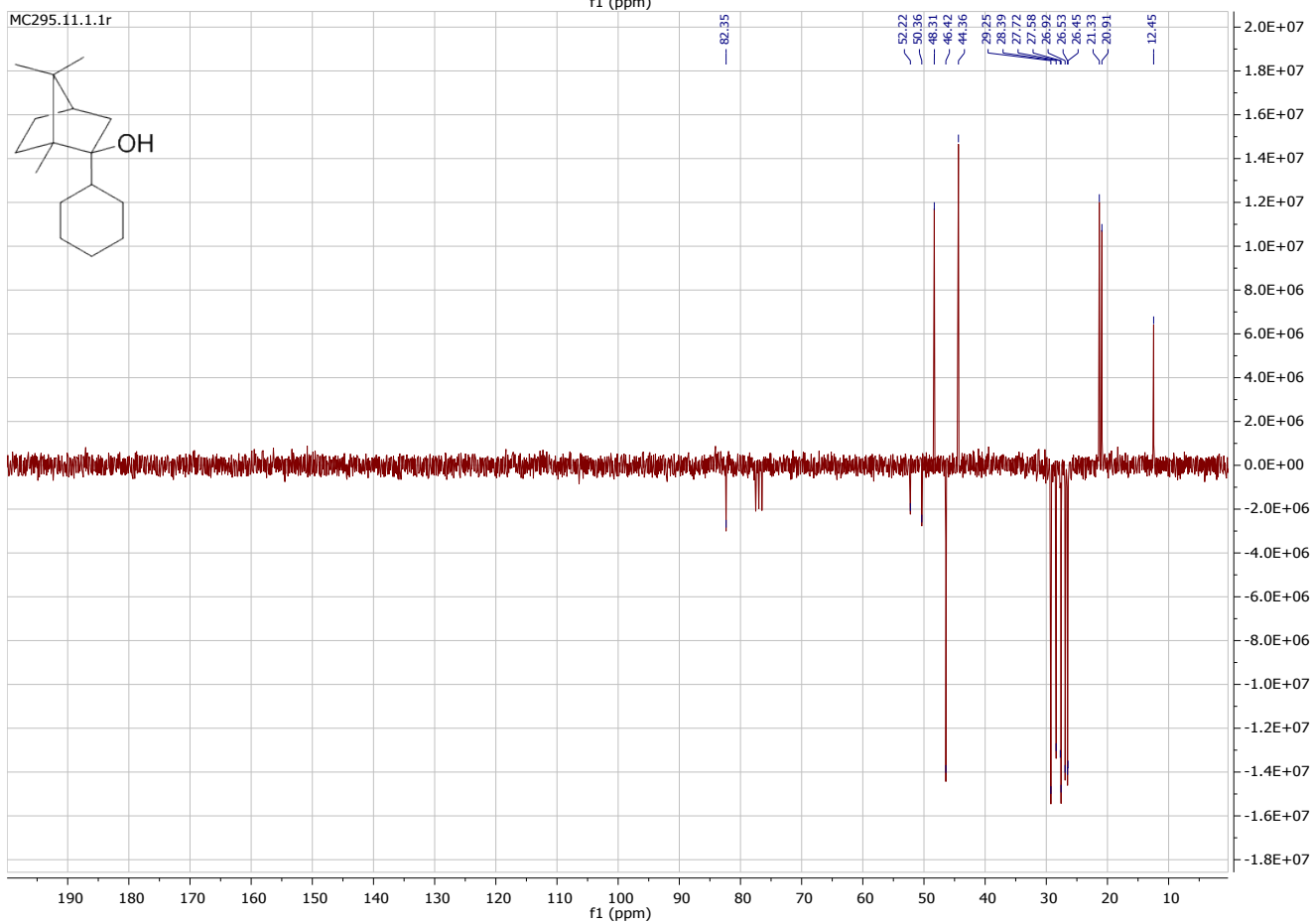
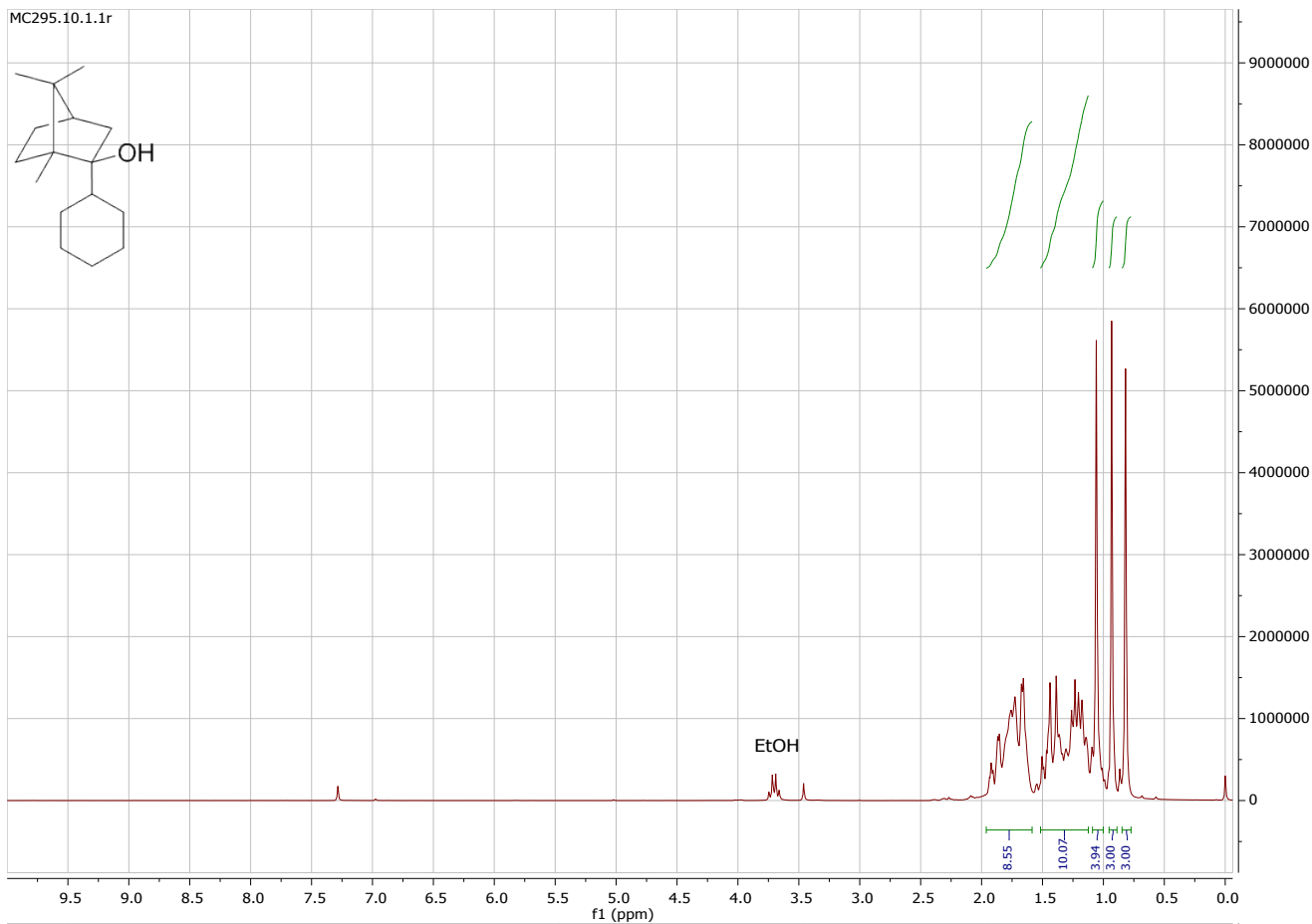


To a suspension of LiAlH_4 (22 mg, 0.58 mmol) in Et_2O (2 mL) was slowly added a solution of **5c** (67 mg, 0.29 mmol) in Et_2O (2 mL) at 0°C , and the resulting mixture was stirred for 2 h at rt. An aqueous solution of NaOH (10%, 2 mL) was carefully added at 0°C . The aqueous layer was extracted with AcOEt (3 x 2 mL), the organic phases were combined, dried over Na_2SO_4 , filtered and concentrated. The residue was purified by flash column chromatography to give **5'a** (45 mg, 85%) as a white solid, mp 59°C ; $[\alpha]_{\text{D}} = -72$ (c 0.2, CHCl_3); $^1\text{H NMR}$ (250 MHz, CDCl_3) δ : 7.37 (d, $J = 7.0$ Hz, 1 H), 7.32-7.16 (m, 3 H), 5.92 (dq, $J = 10.0, 3.4$ Hz, 1 H), 5.65 (d, $J = 10.2$ Hz, 1 H), 4.78 (d, $J = 12.5$ Hz, 1 H), 4.71 (d, $J = 12.4$ Hz, 1 H), 3.73 (m, 1 H), 2.08 (m, 3 H), 1.85-1.41 (m, 4 H); $^{13}\text{C NMR}$ (62.5 MHz, CDCl_3) δ : 144.7, 137.8, 130.4, 128.4, 128.2, 128.0, 126.2, 63.0, 37.2, 32.0, 24.9, 21.4; HRMS-ESI : m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{16}\text{ONa}$ 211.1099; found: 211.1096.

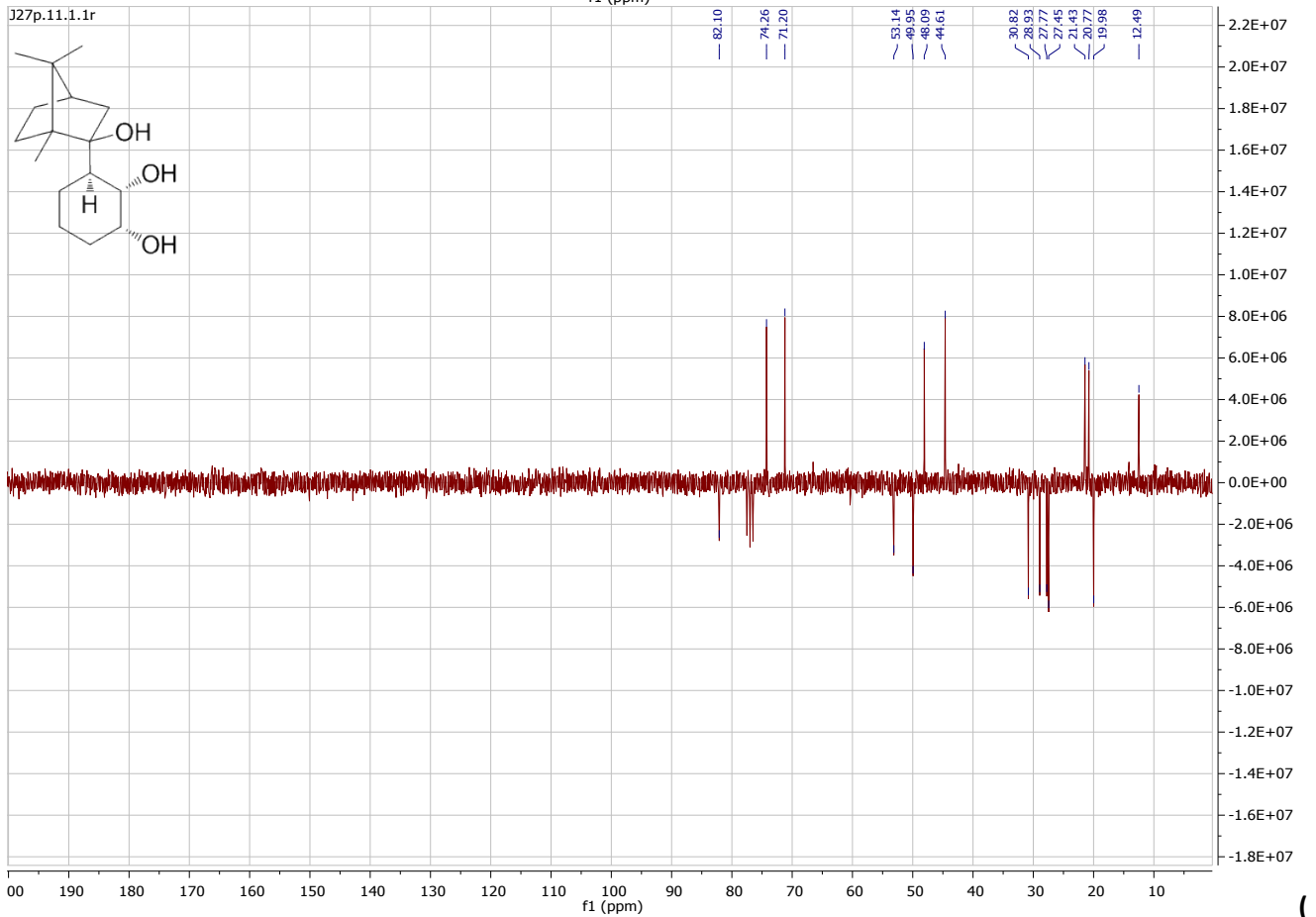
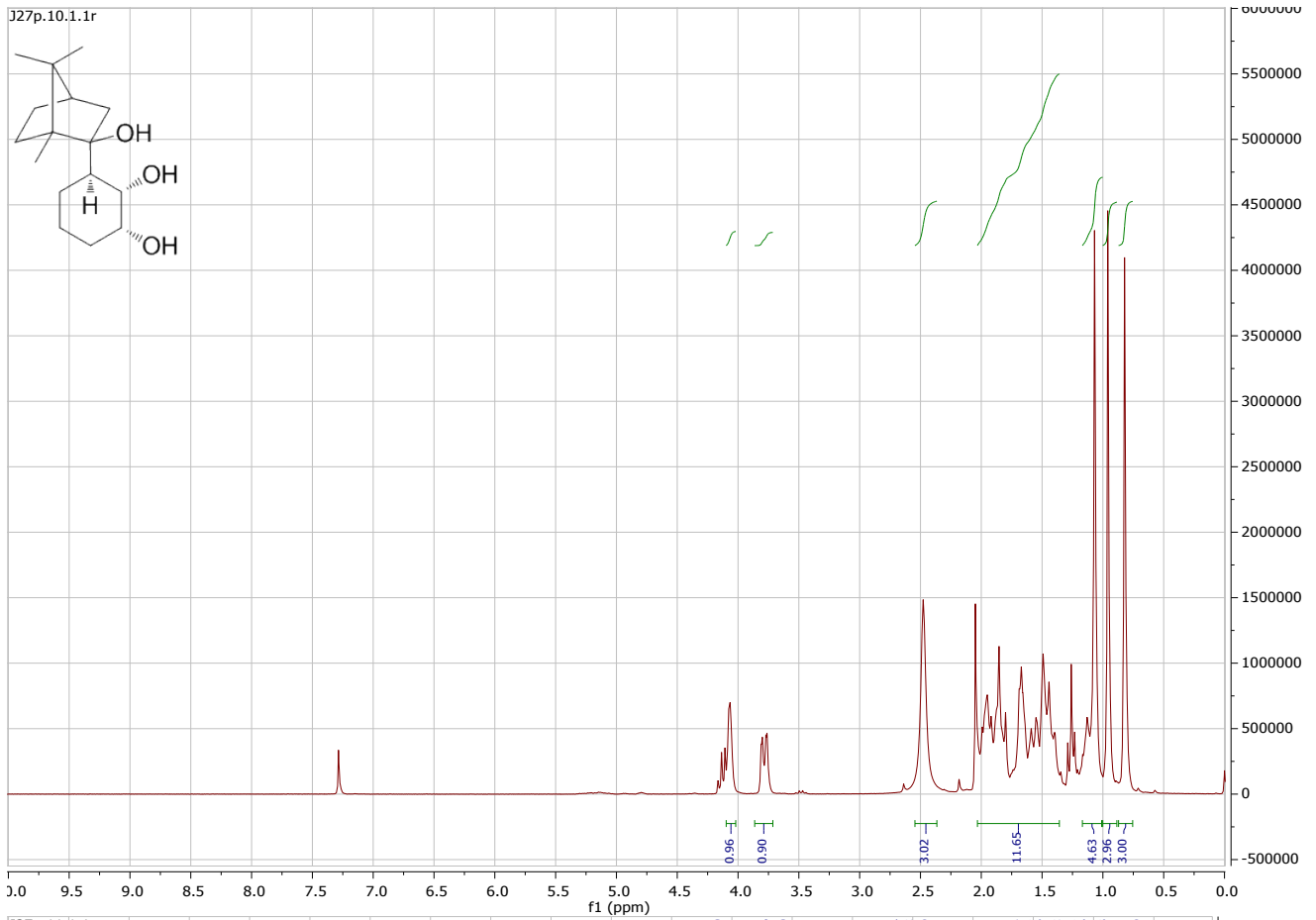
(1S,2S,4R)-2-[(R)-Cyclohex-2-en-1-yl]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol 1b



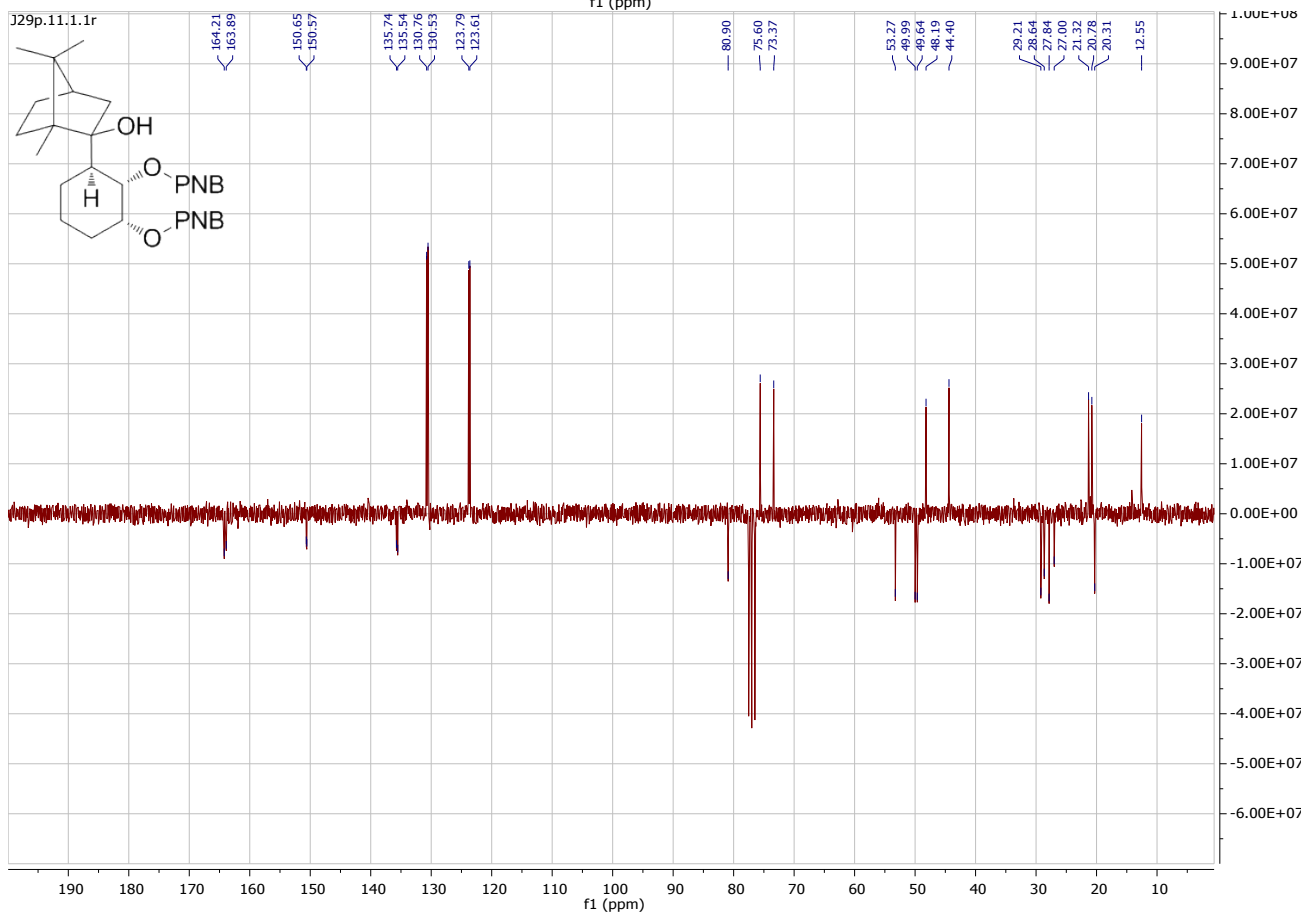
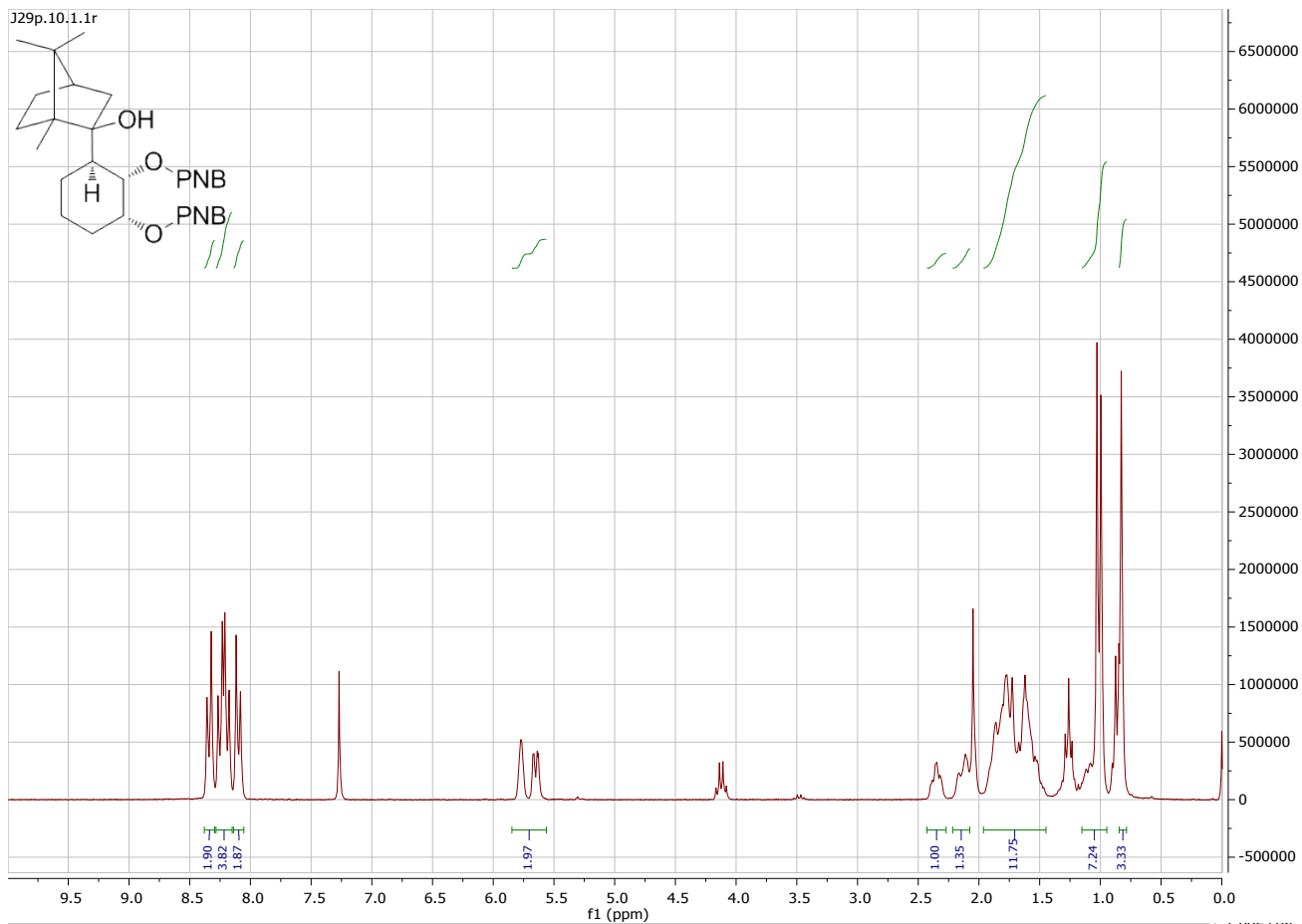
(1S,2S,4R)-2-Cyclohexyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol 1'b



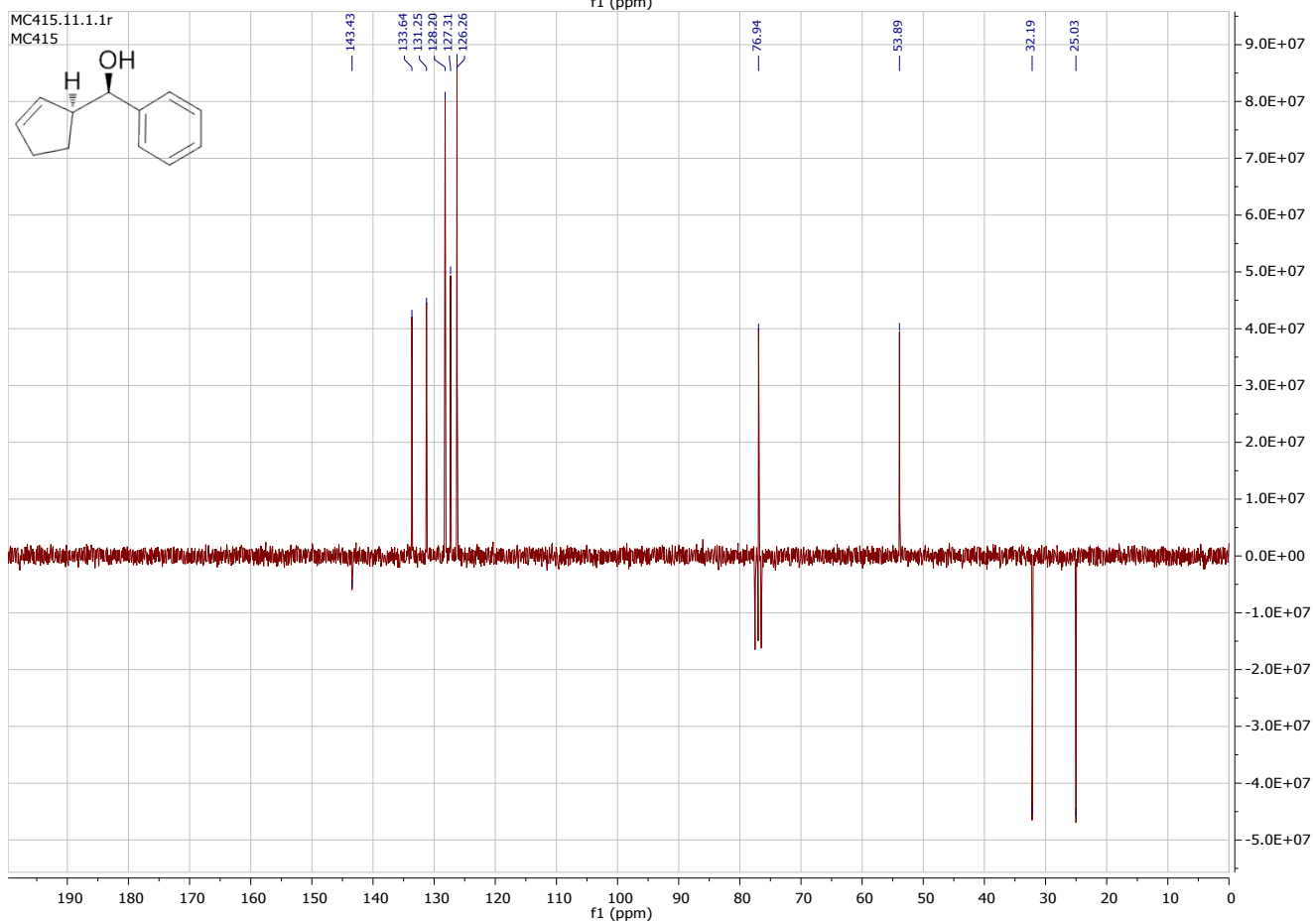
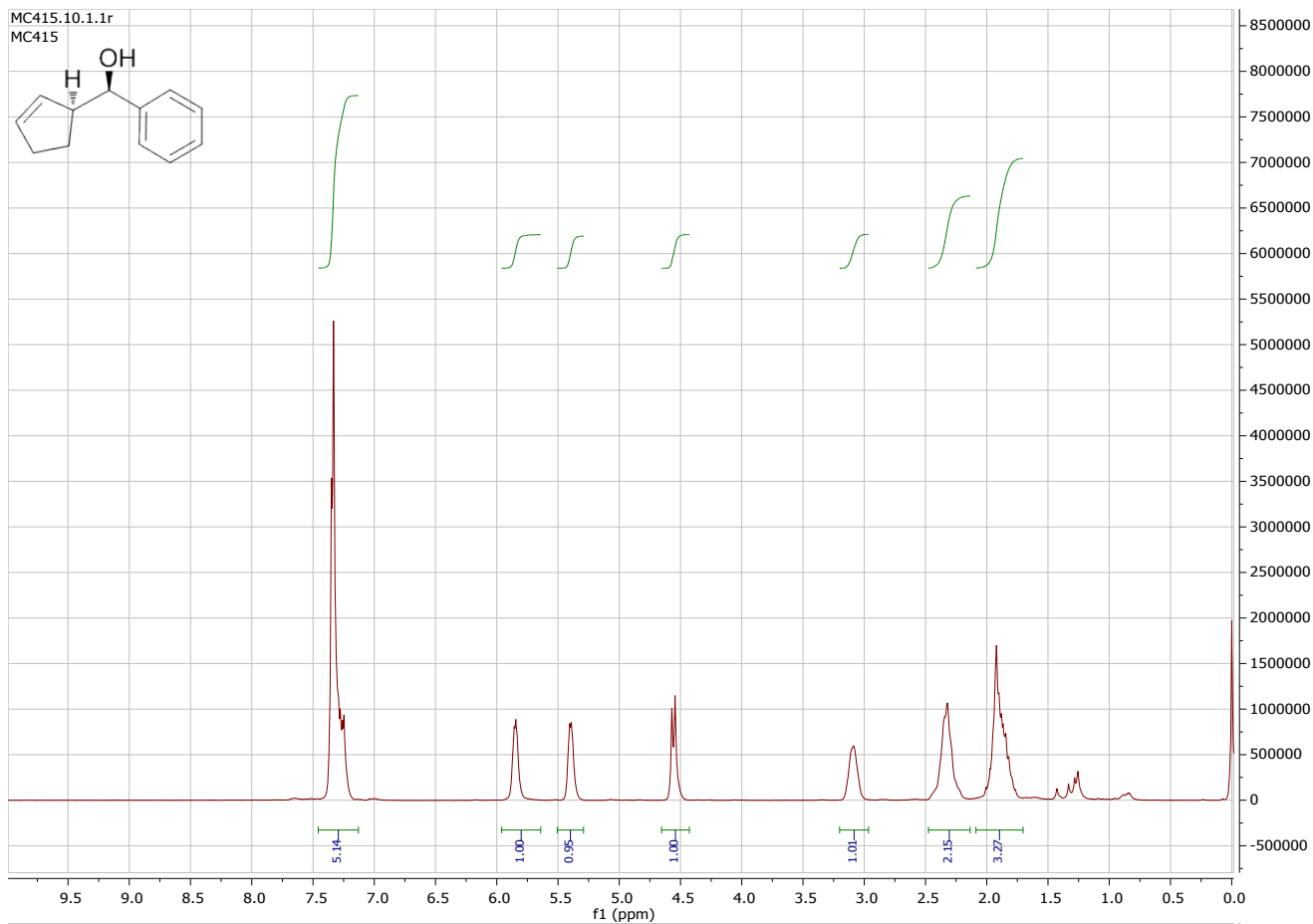
(1R,2S,3R)-3-[(1S,2S,4R)-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl]cyclohexane-1,2-diol



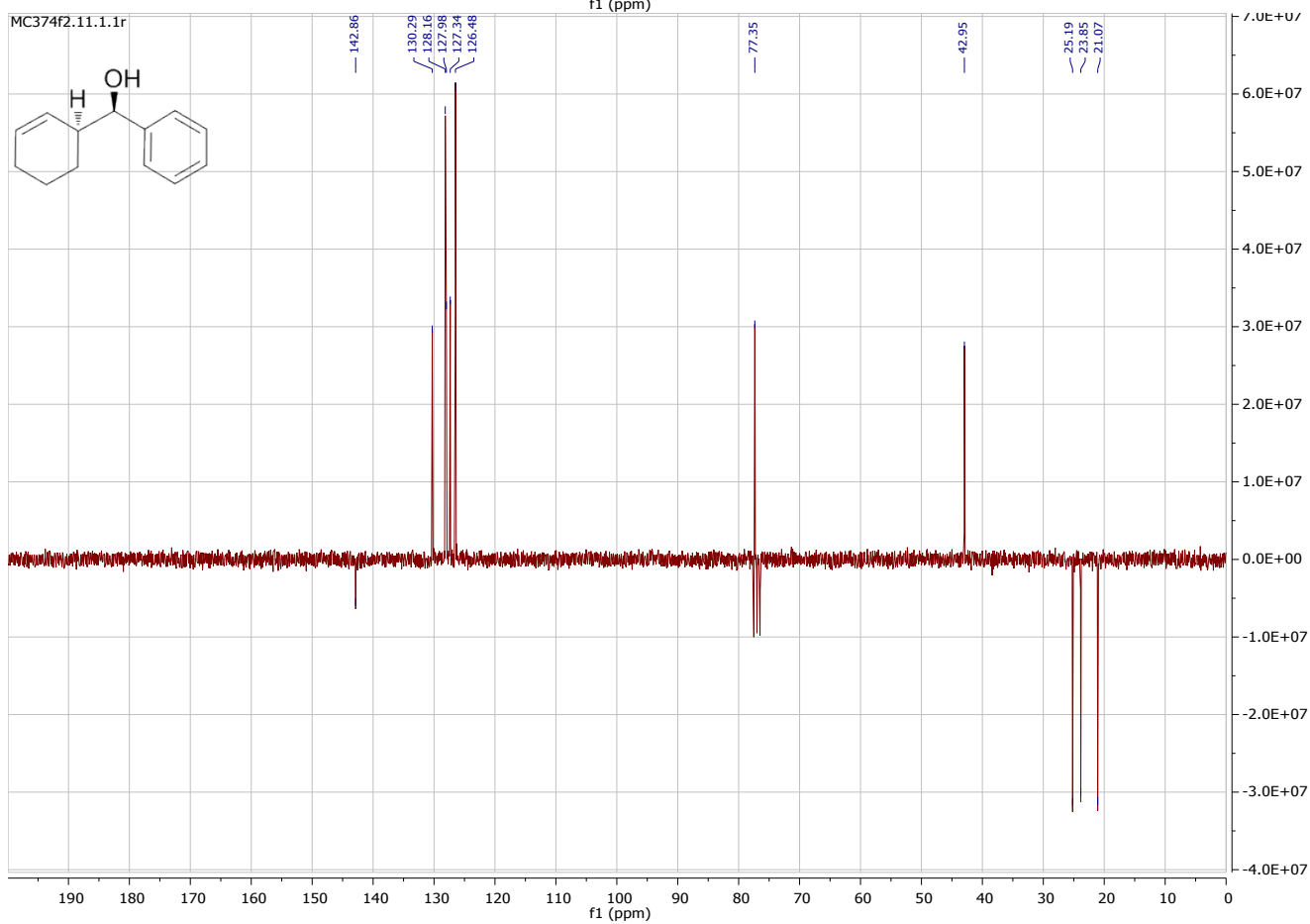
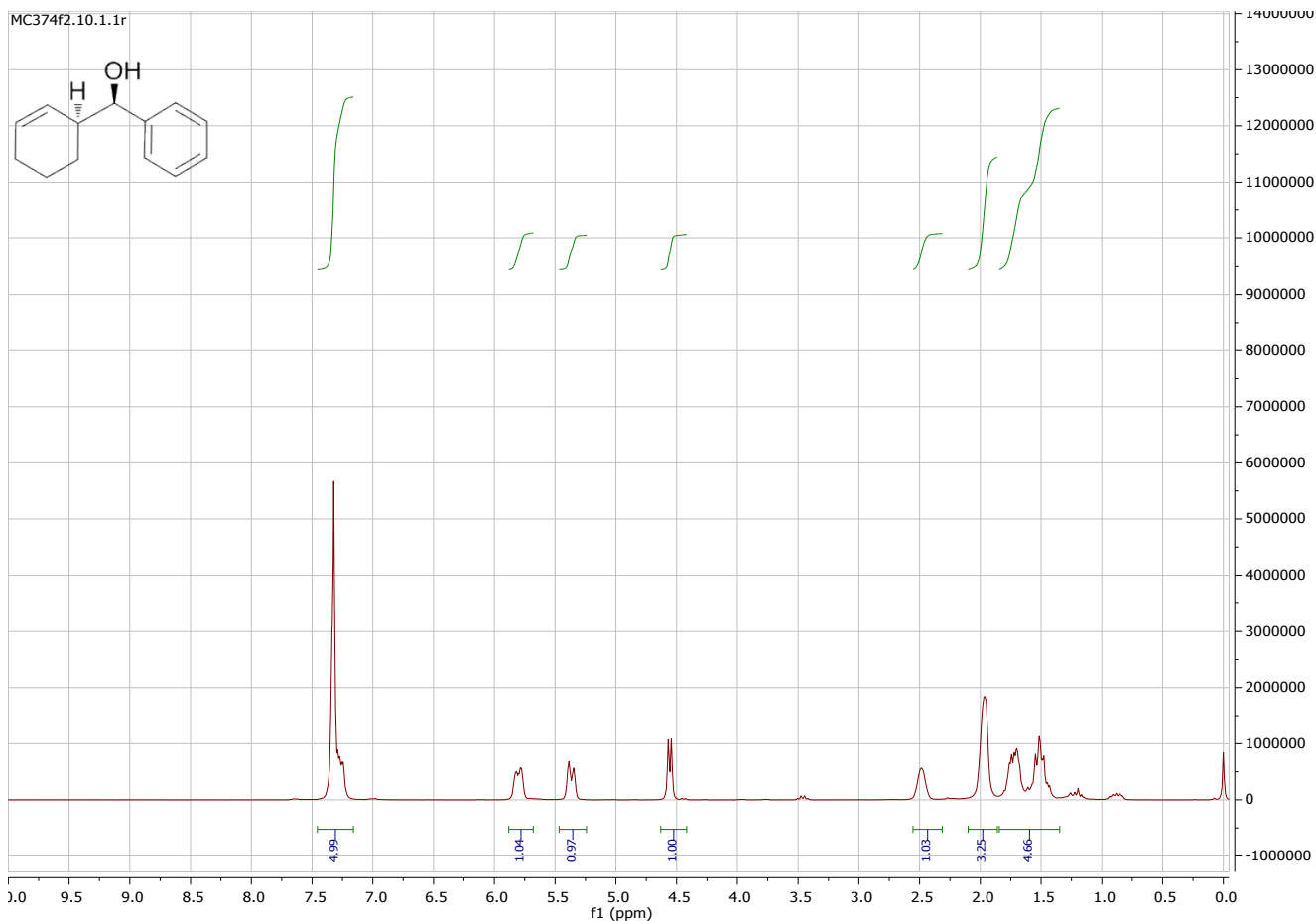
1R,2S,3R)-3-[(1S,2S,4R)-2-Hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl]cyclohexane-1,2-diyl bis(4-nitrobenzoate) 1''b



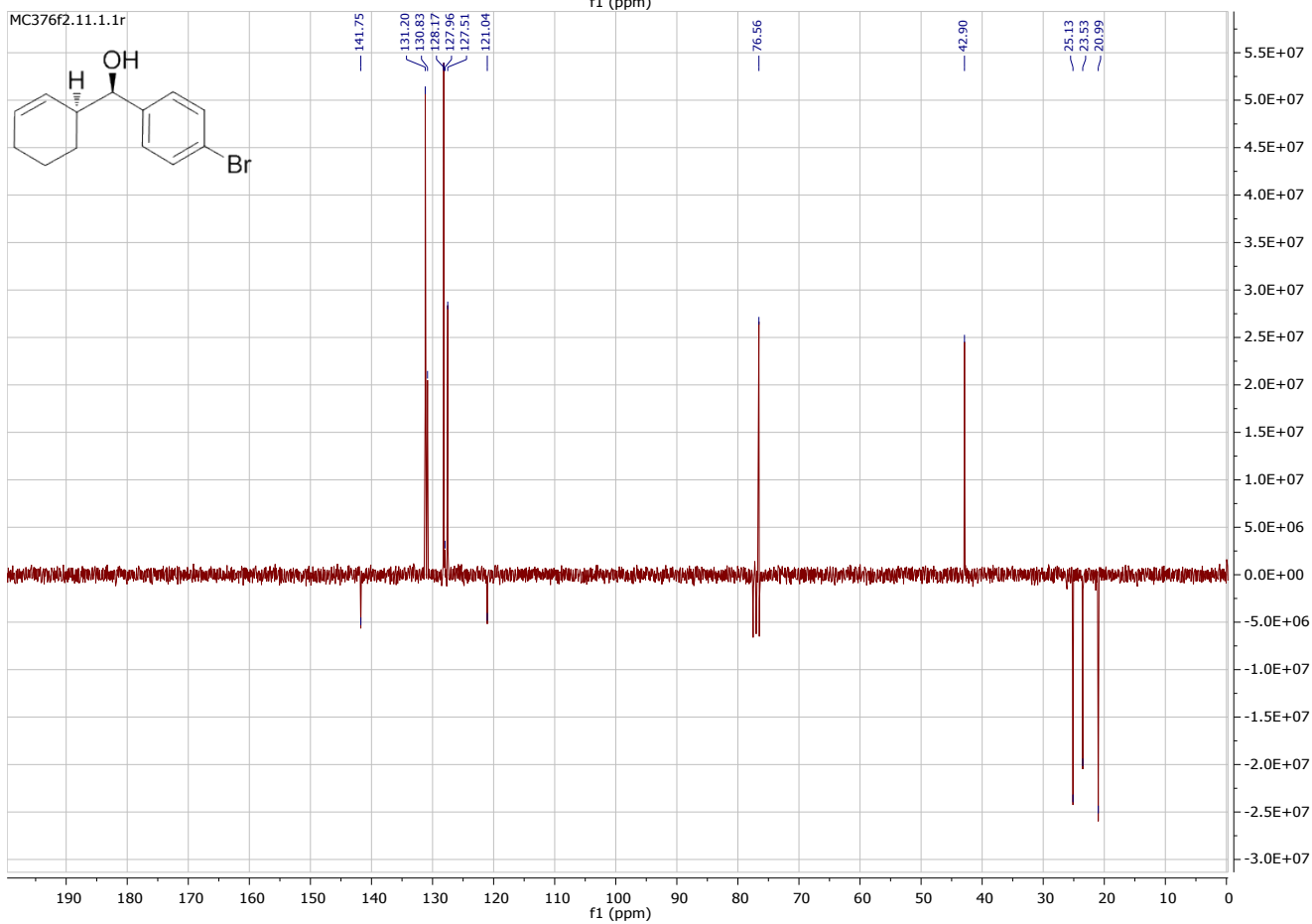
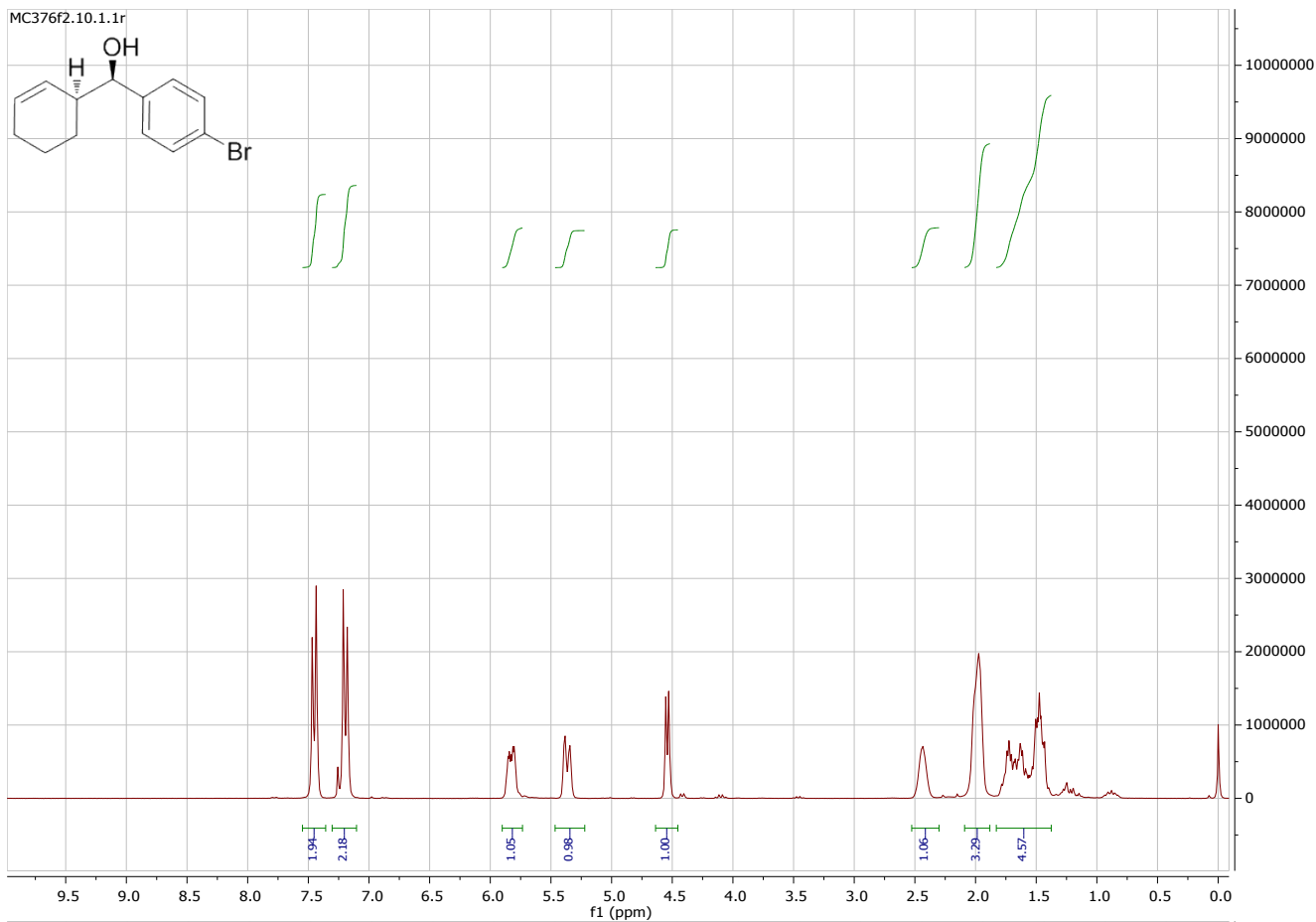
(R)-[(S)-Cyclopent-2-en-1-yl](phenyl)methanol 4a



(R)-[(S)-Cyclohex-2-en-1-yl](phenyl)methanol 3a

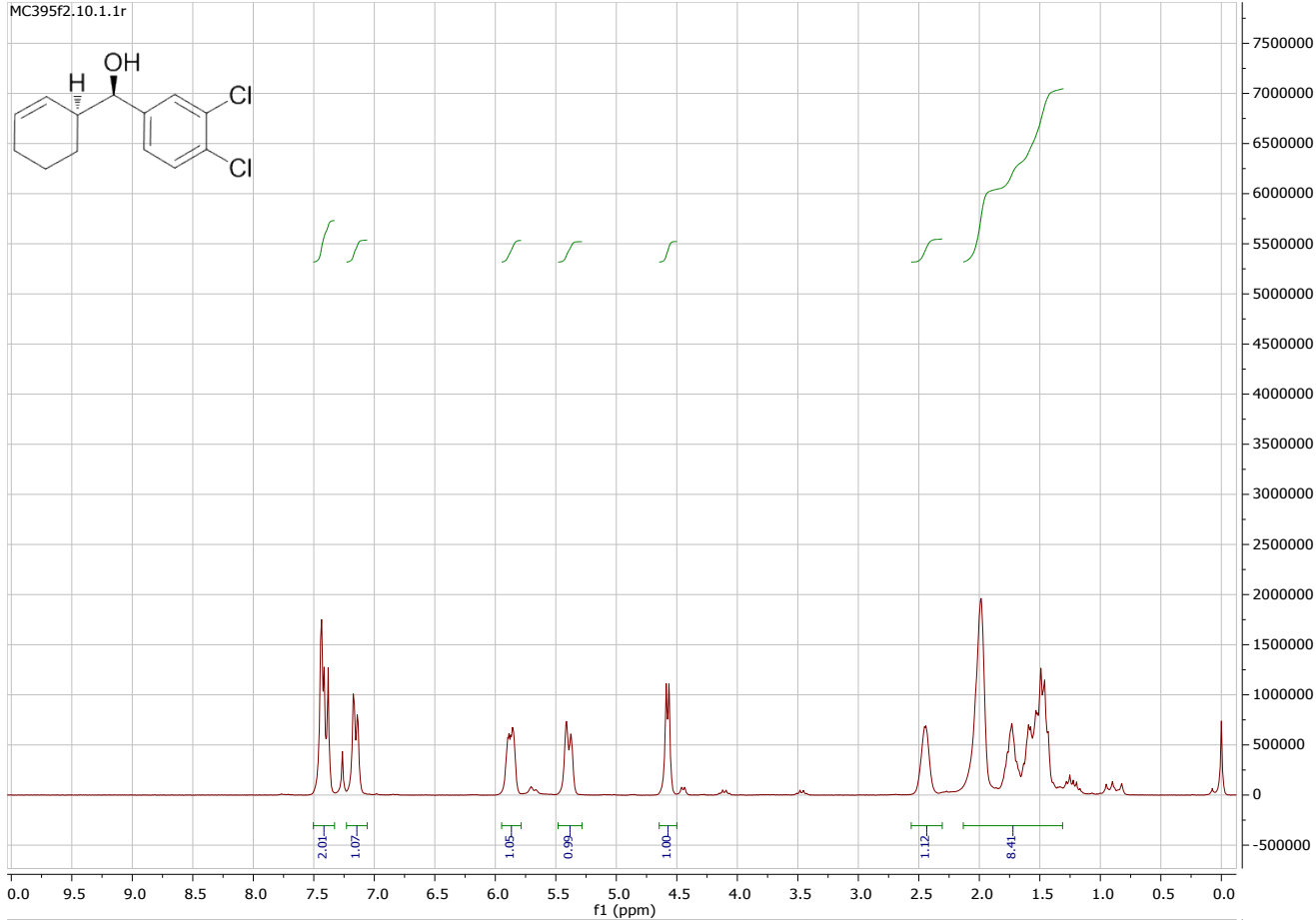
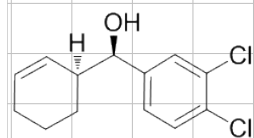


(R)-(4-Bromophenyl) [(S)-cyclohex-2-en-1-yl]methanol 3b

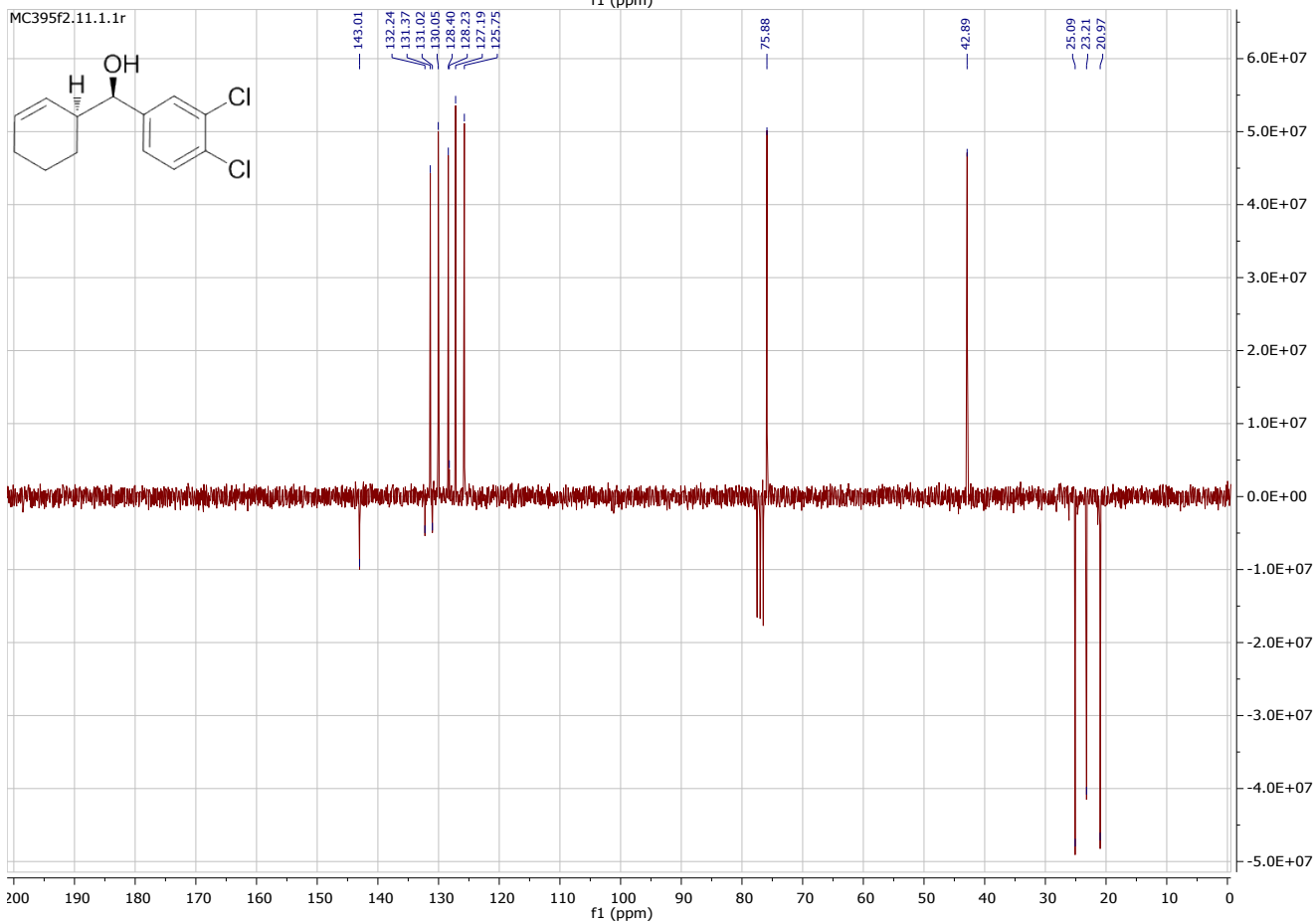
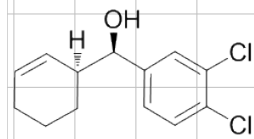


(R)- [(S)-Cyclohex-2-en-1-yl](3,4-dichlorophenyl)methanol 3c

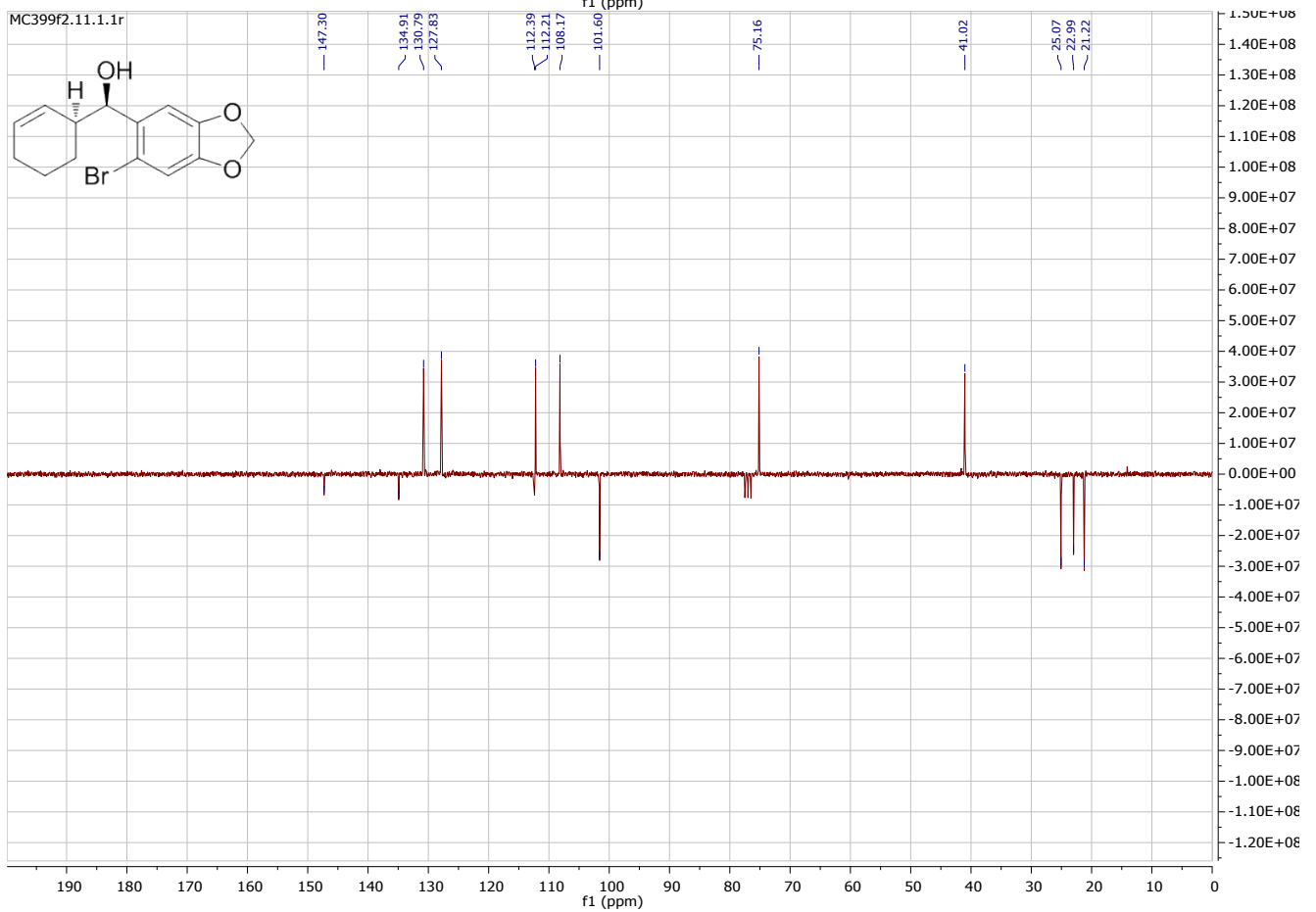
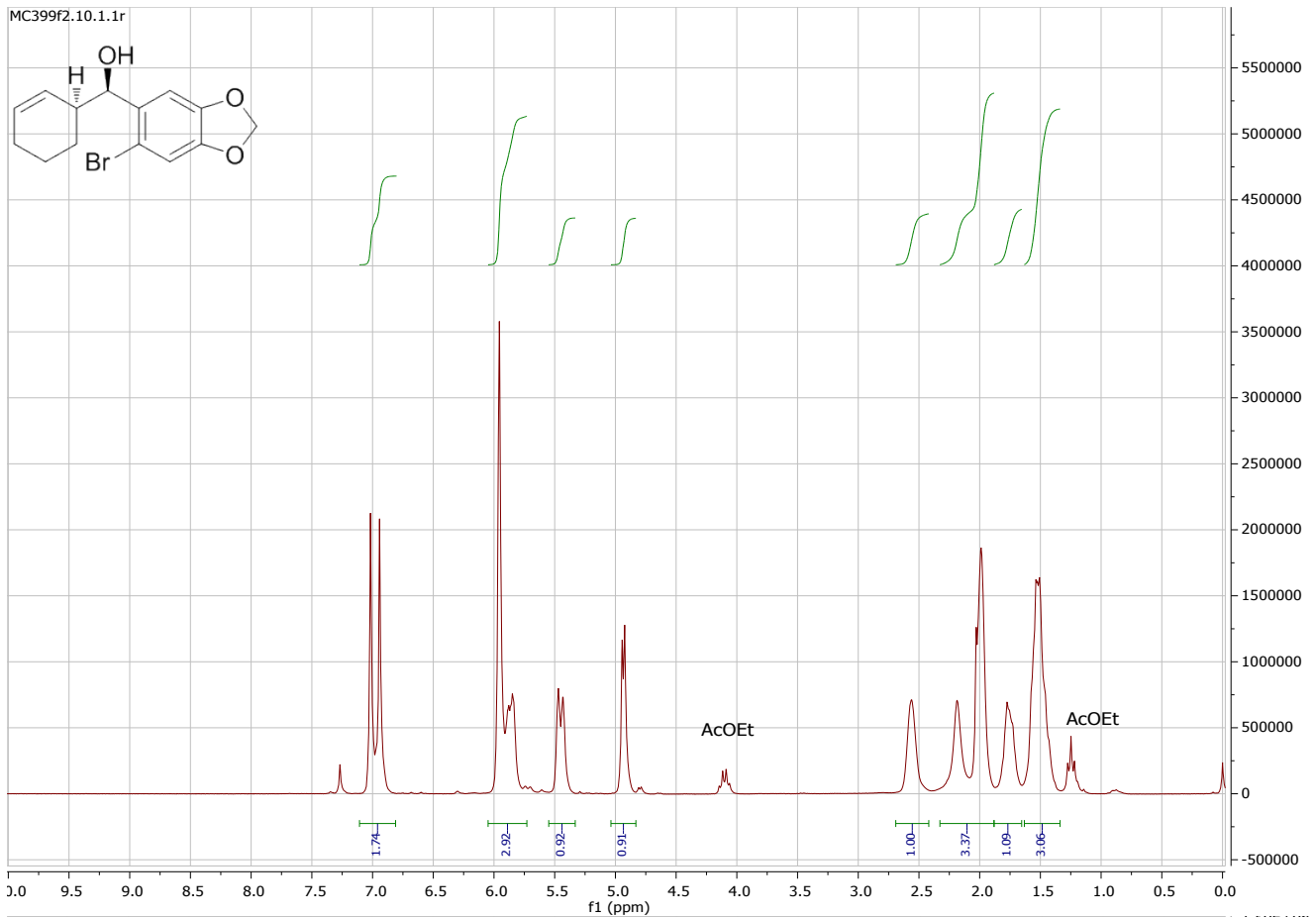
MC395f2.10.1.1r



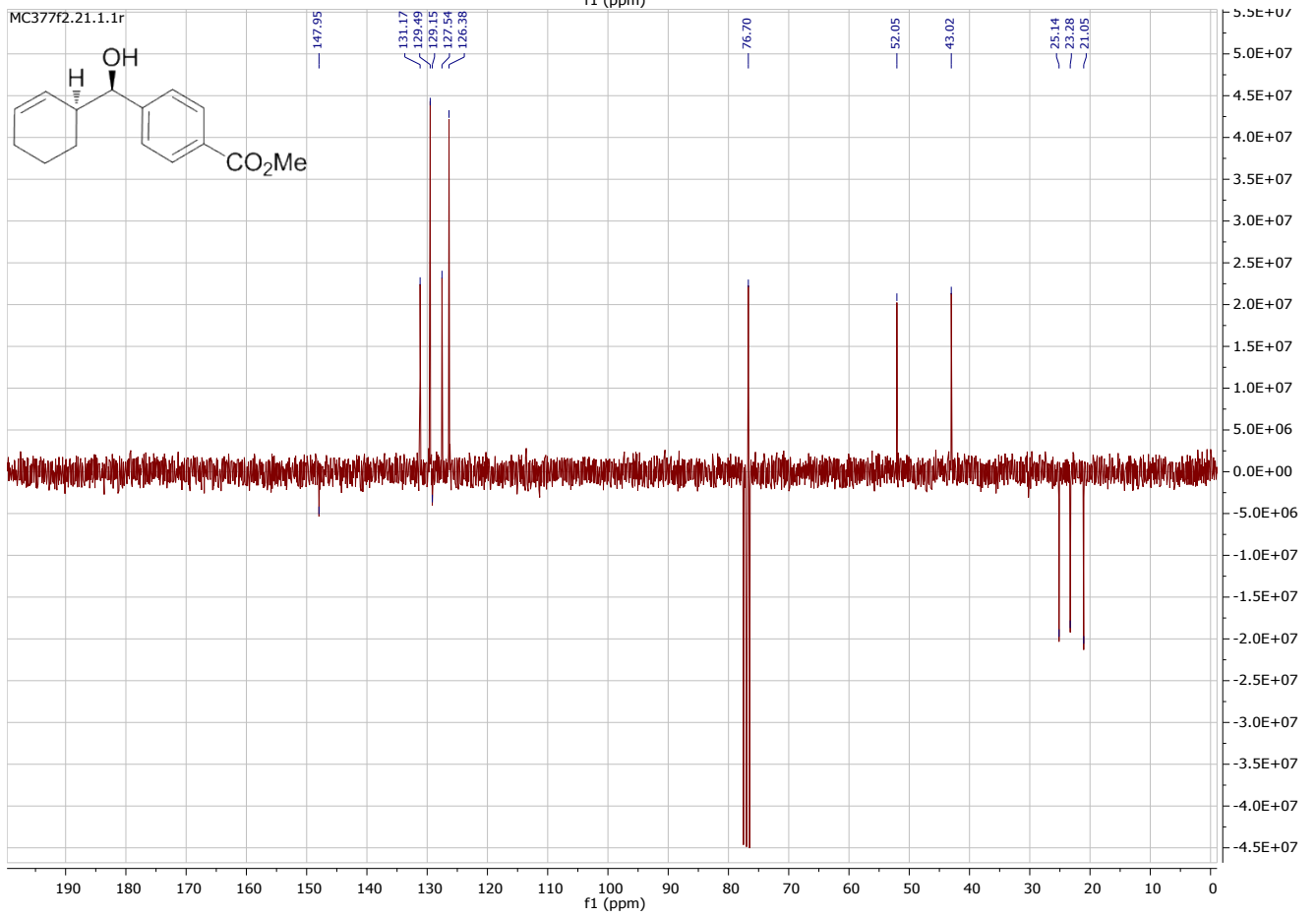
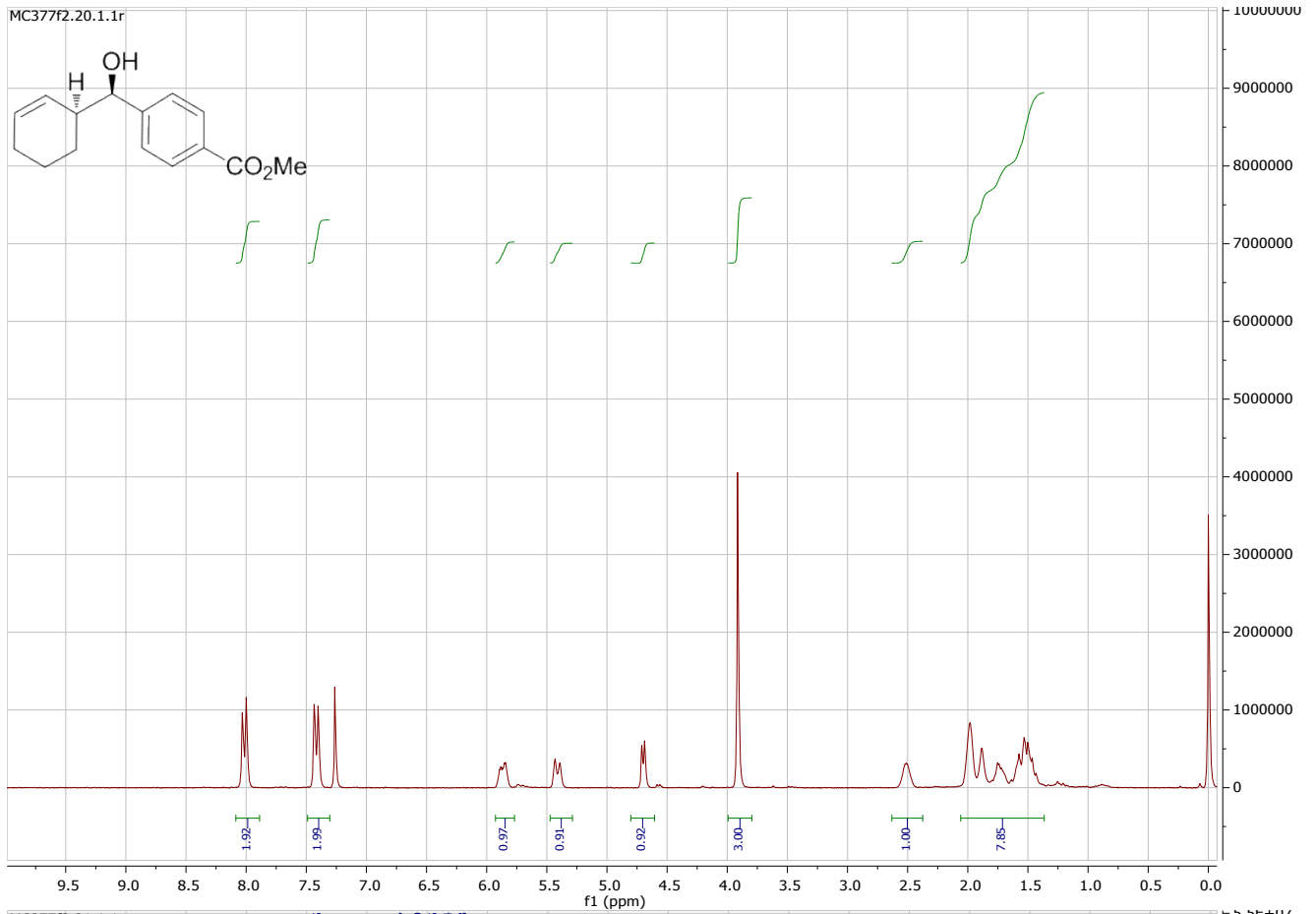
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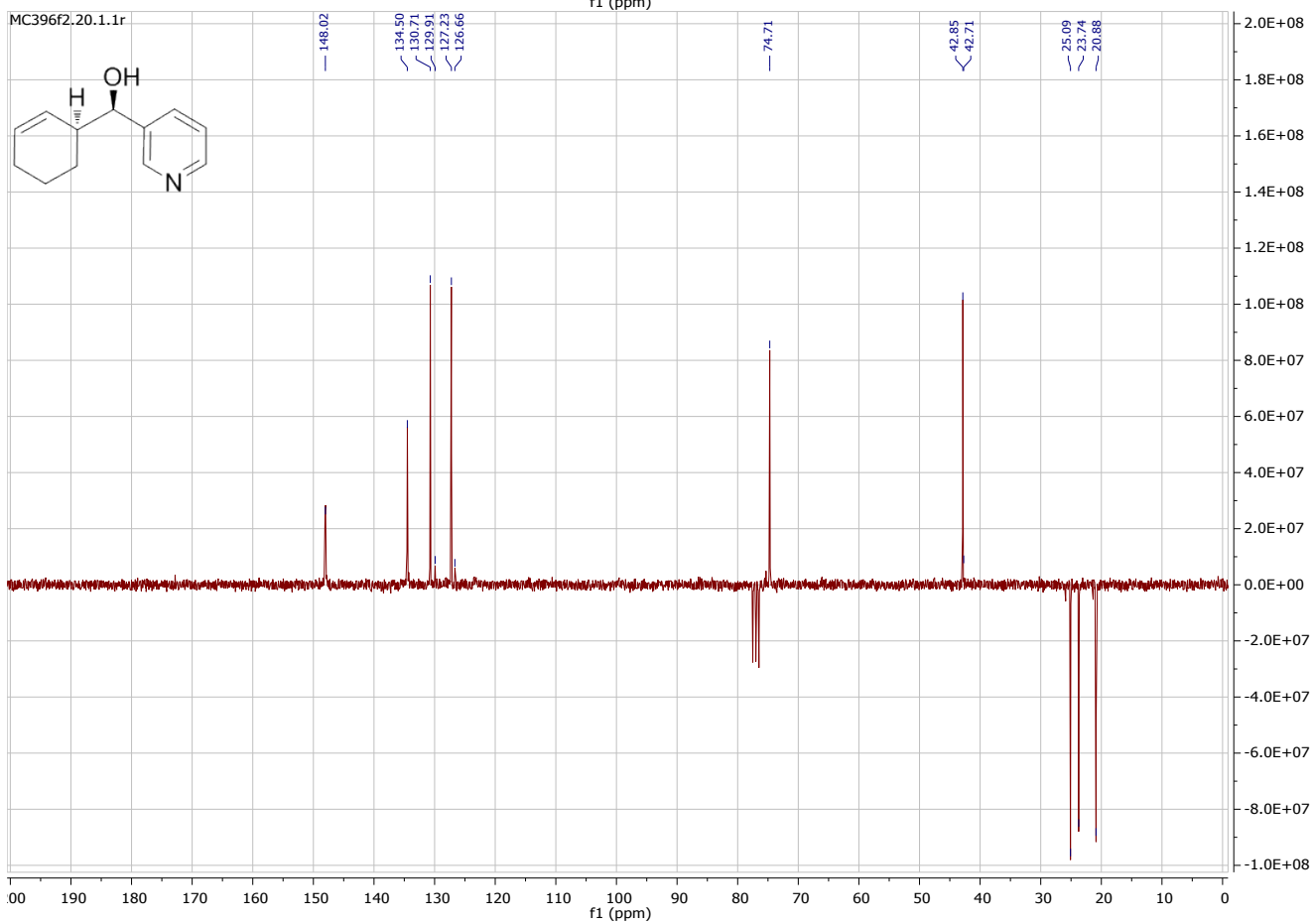
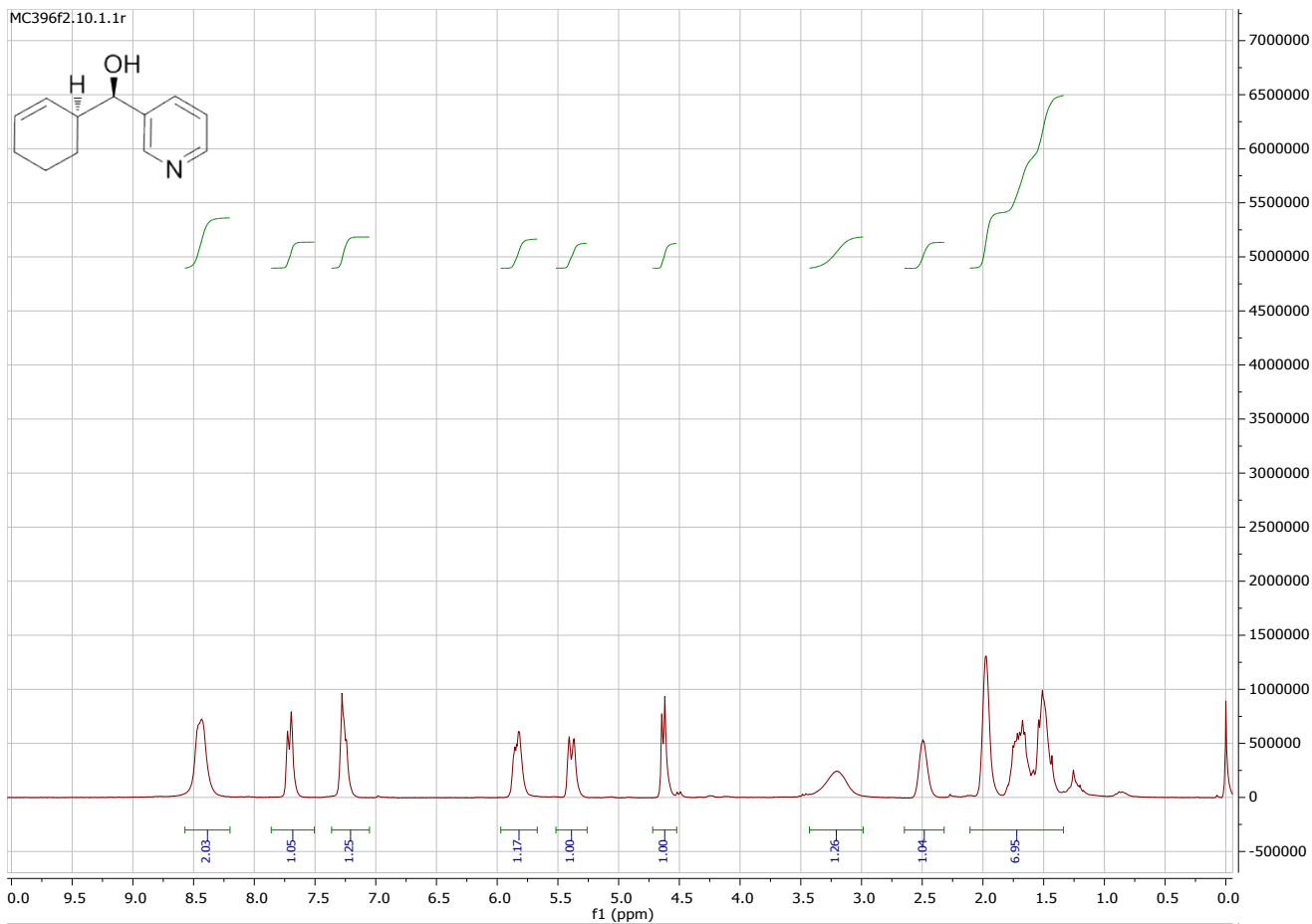
(R)-(6-Bromobenzo[d][1,3]dioxol-5-yl)((S)-cyclohex-2-en-1-yl)methanol 3d



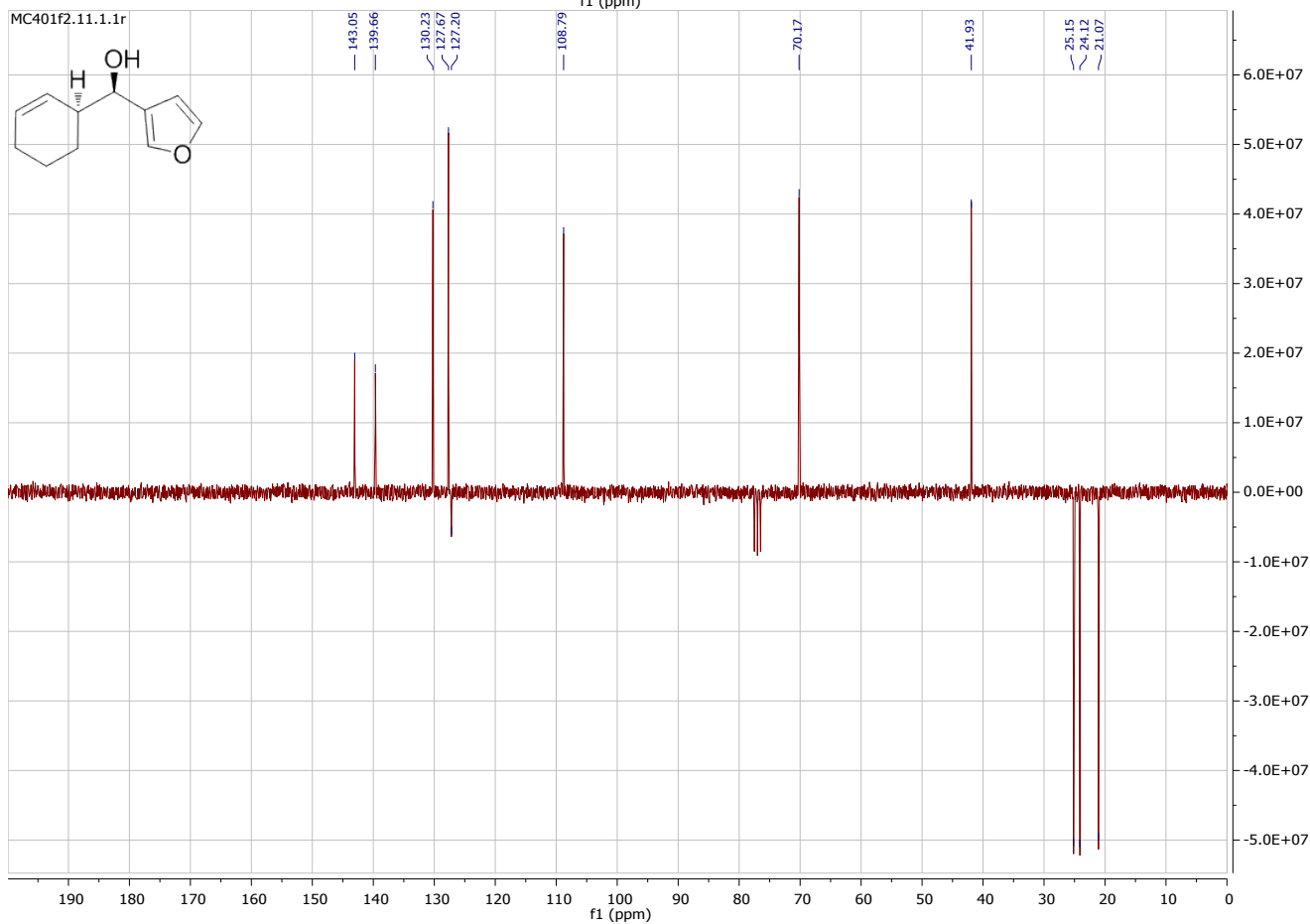
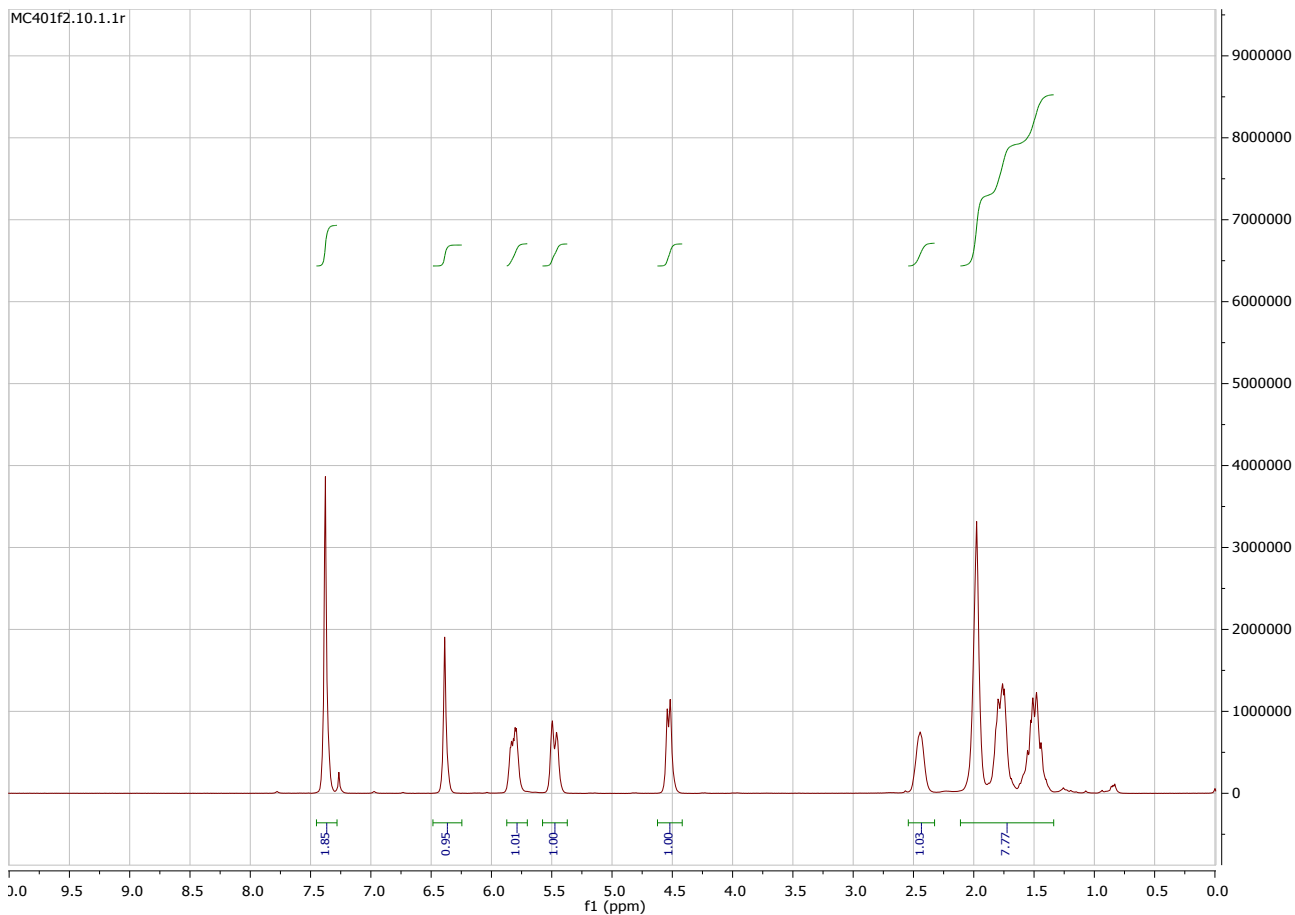
Methyl 4-[(R)-[(S)-cyclohex-2-en-1-yl](hydroxy)methyl]benzoate 3e



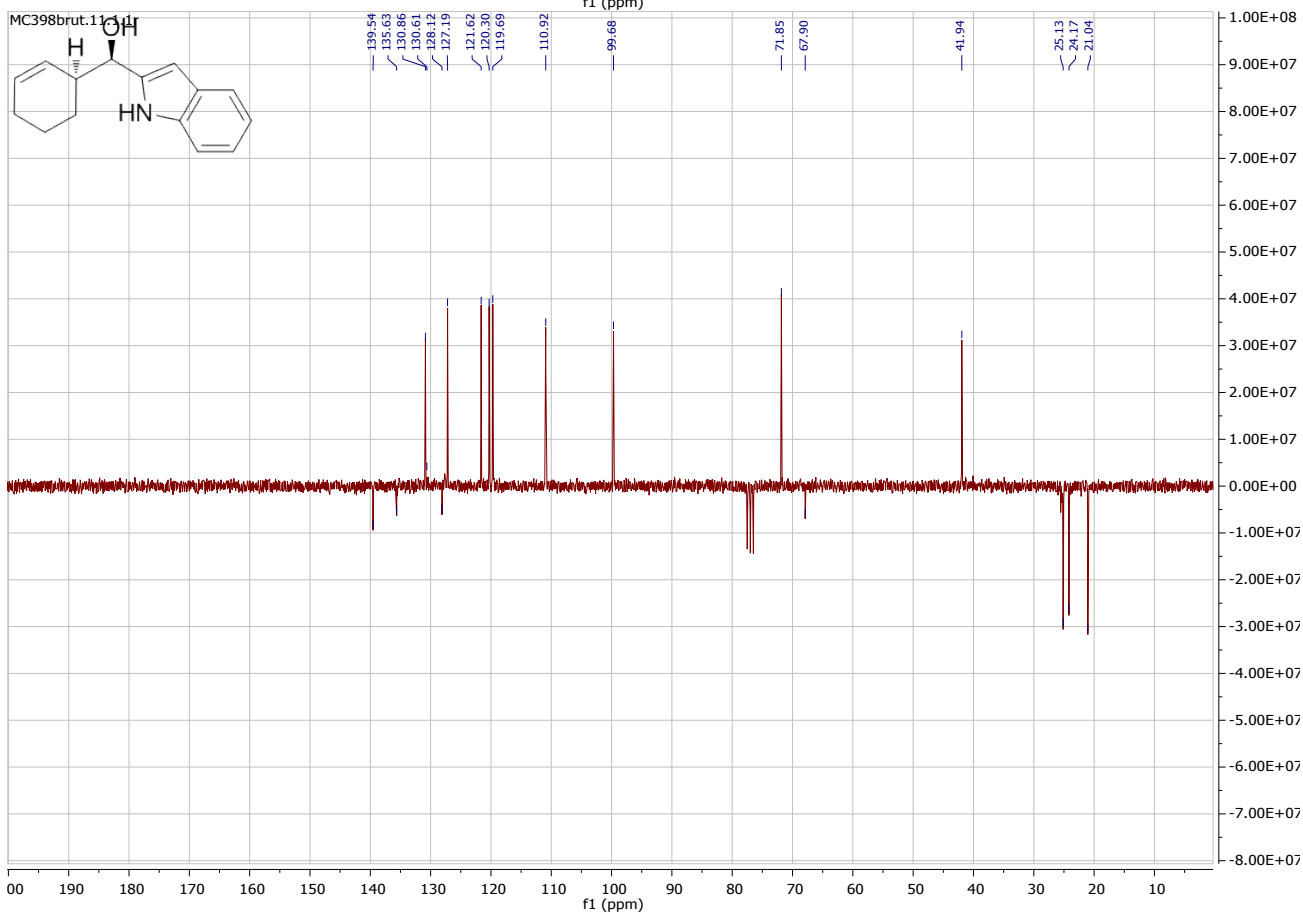
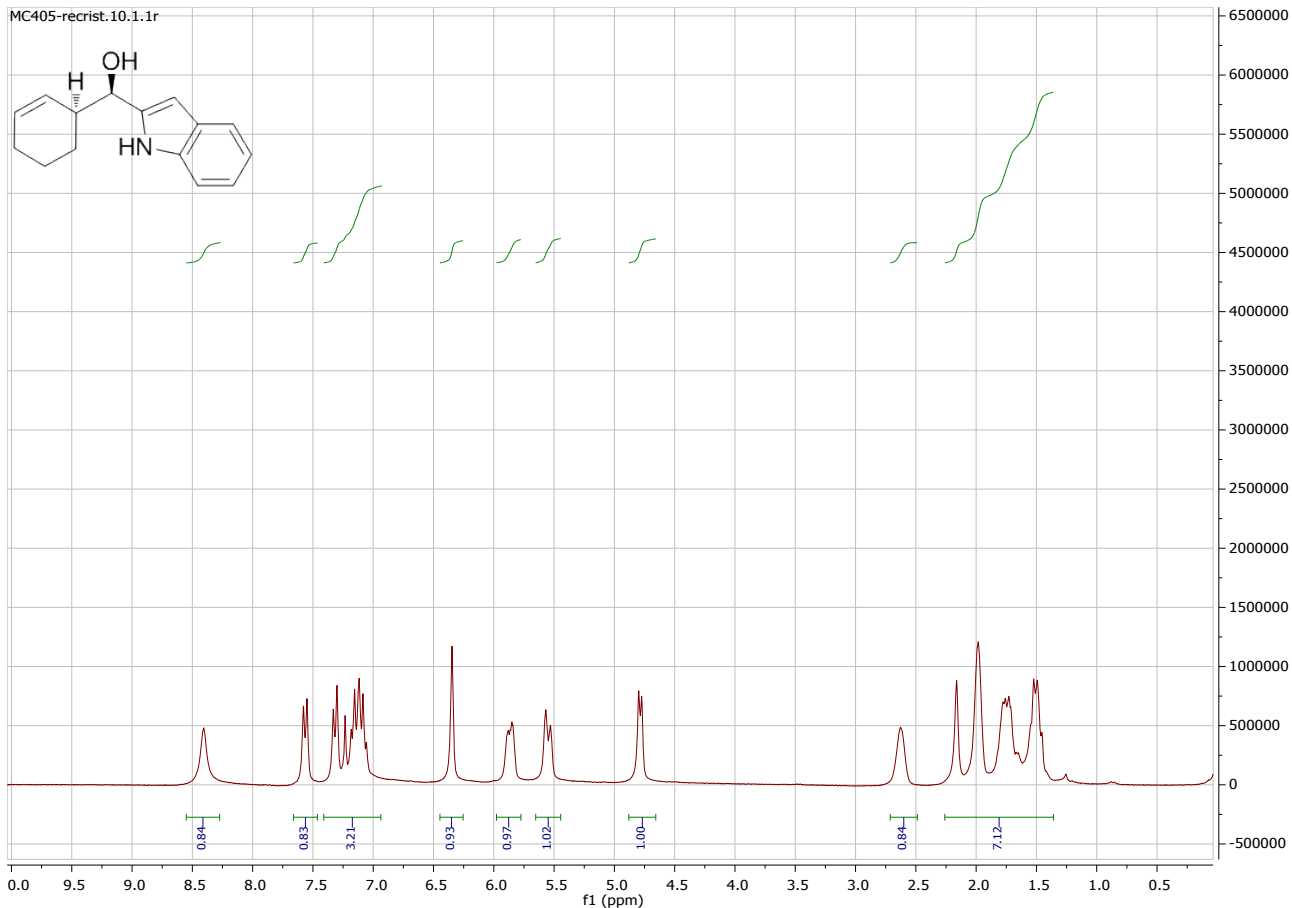
(R)- [(S)-Cyclohex-2-en-1-yl](pyridin-3-yl)methanol 3f



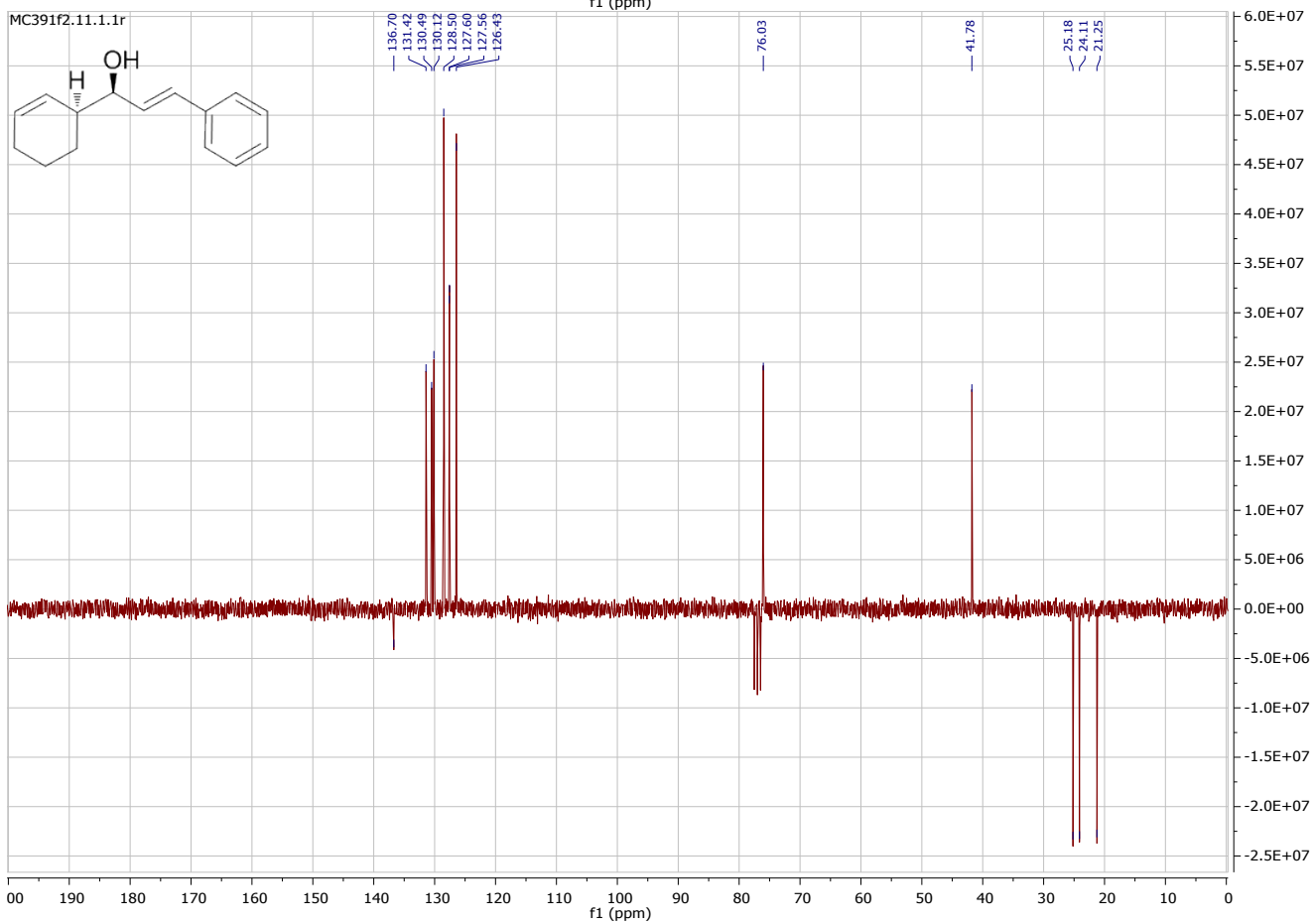
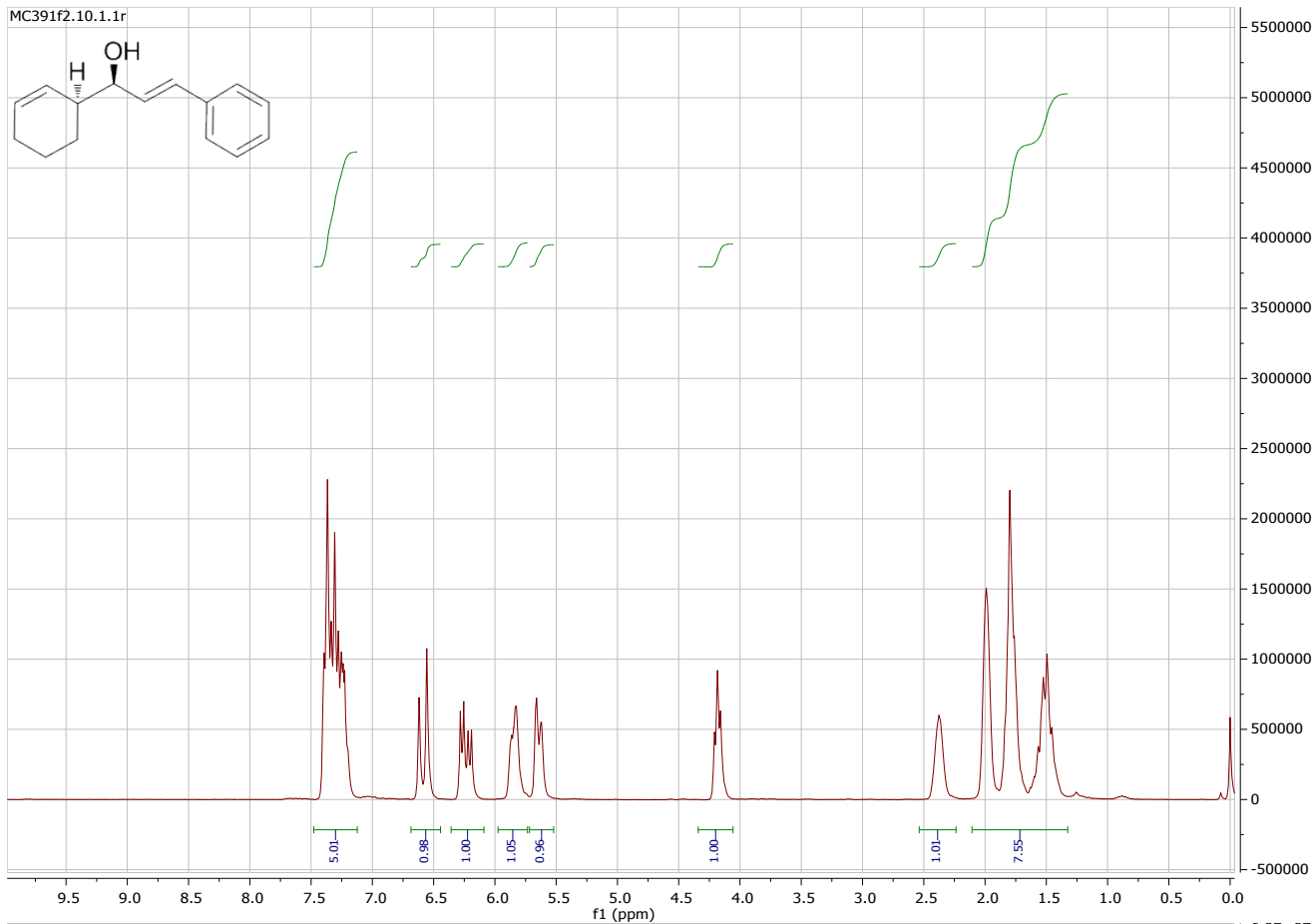
(R)- [(S)-Cyclohex-2-en-1-yl](furan-3-yl)methanol 3g



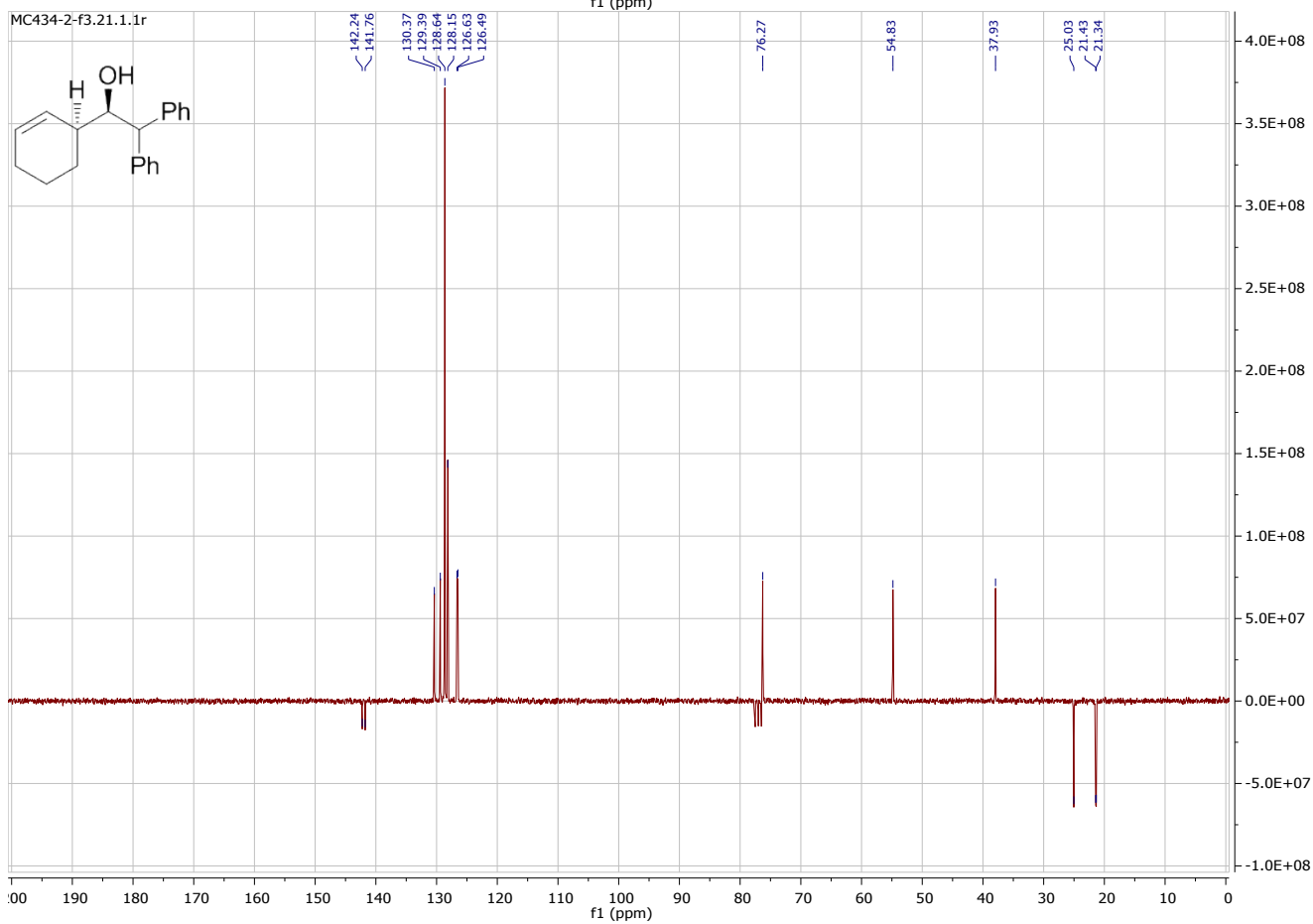
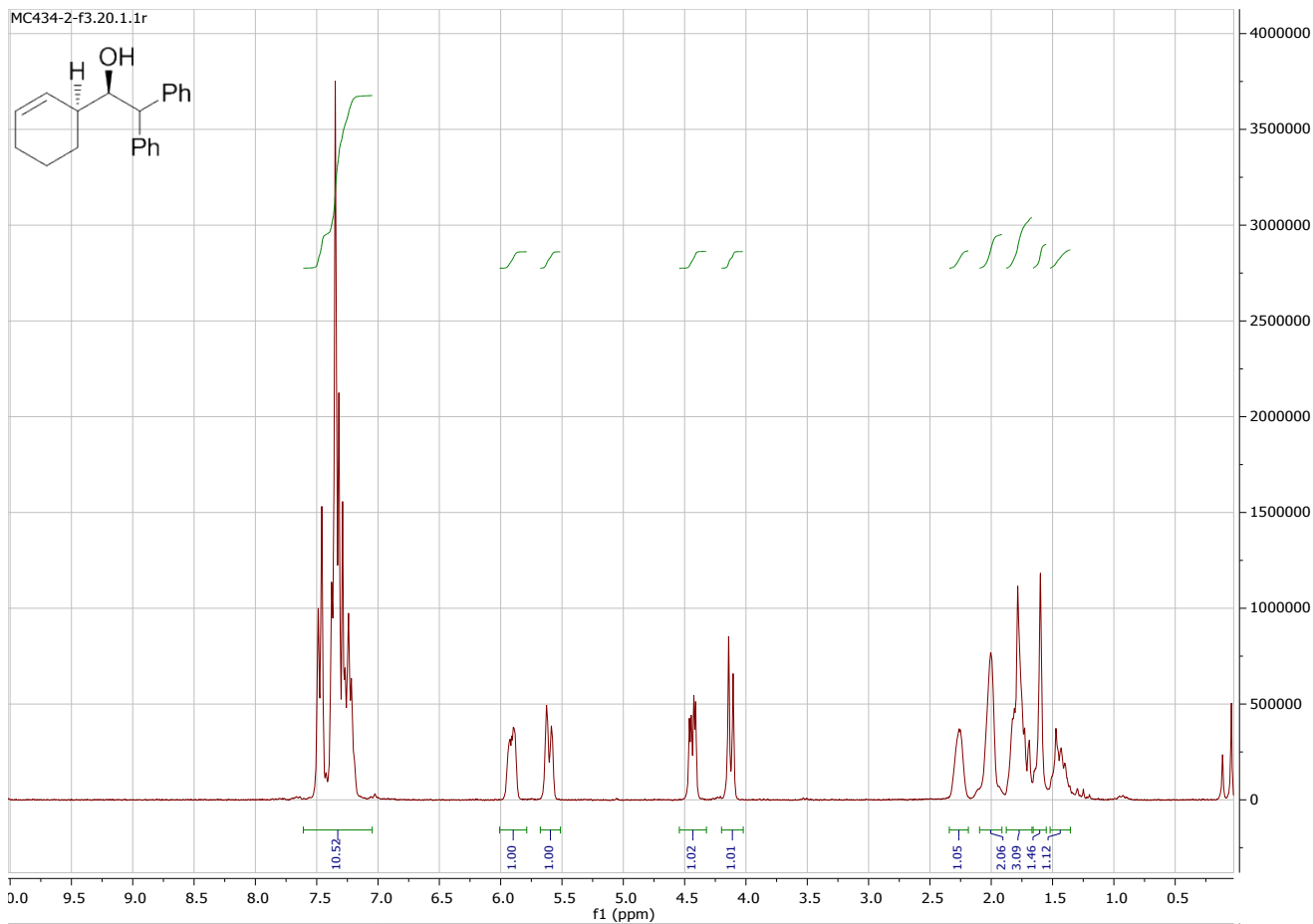
(R)- [(S)-Cyclohex-2-en-1-yl](1H-indol-2-yl)methanol 3h



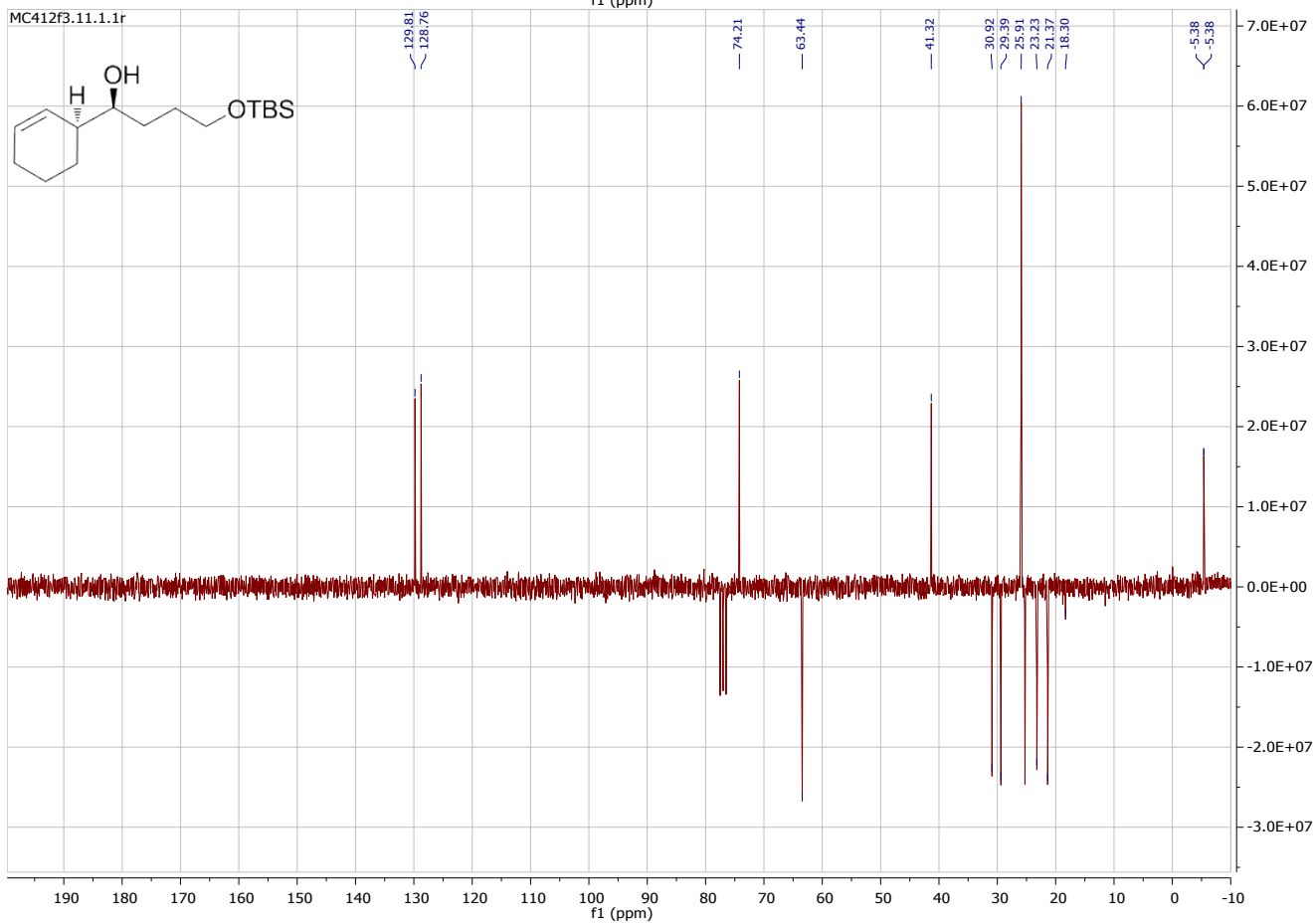
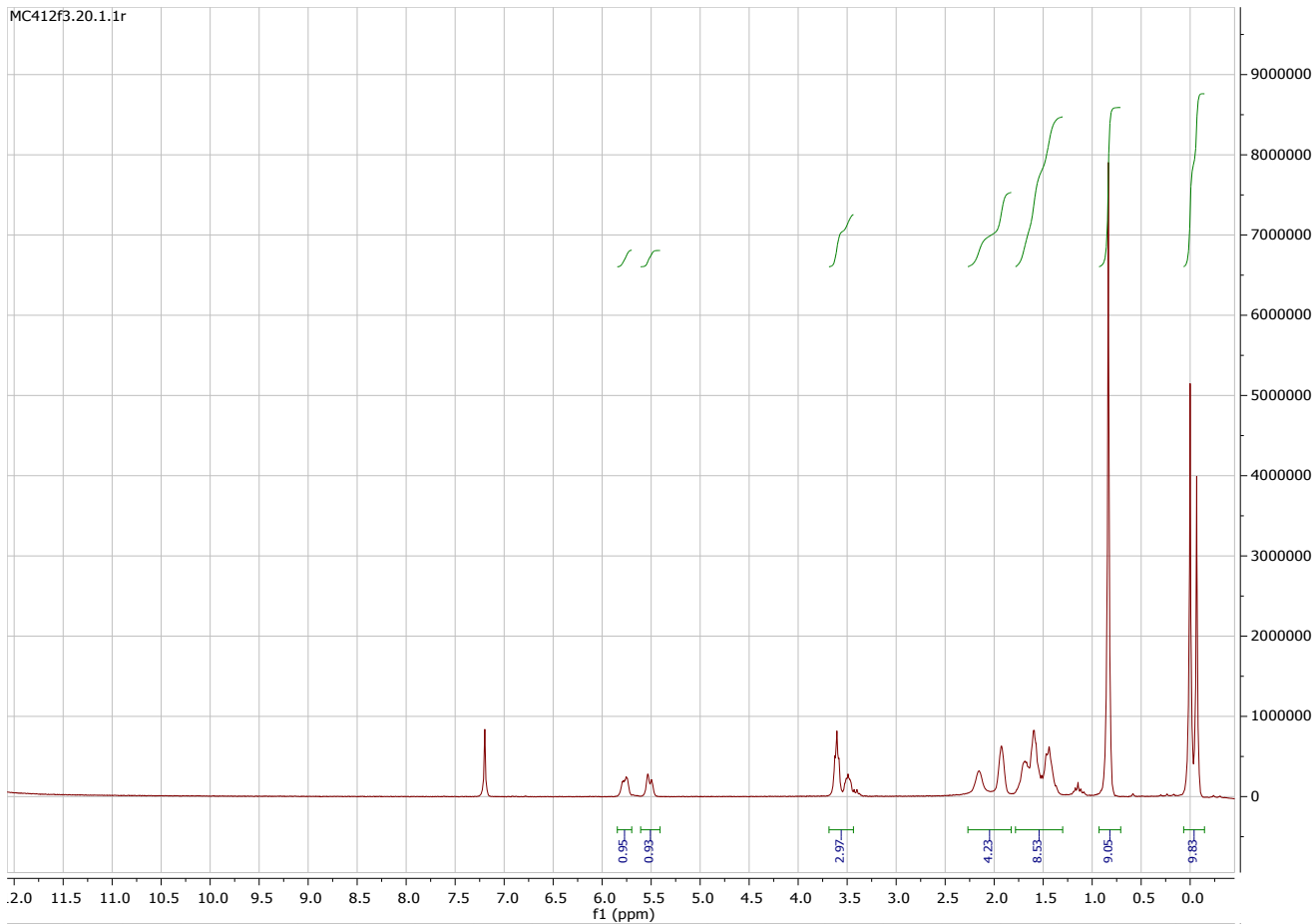
(*S,E*)-1-[(*S*)-Cyclohex-2-en-1-yl]-3-phenylprop-2-en-1-ol 3i



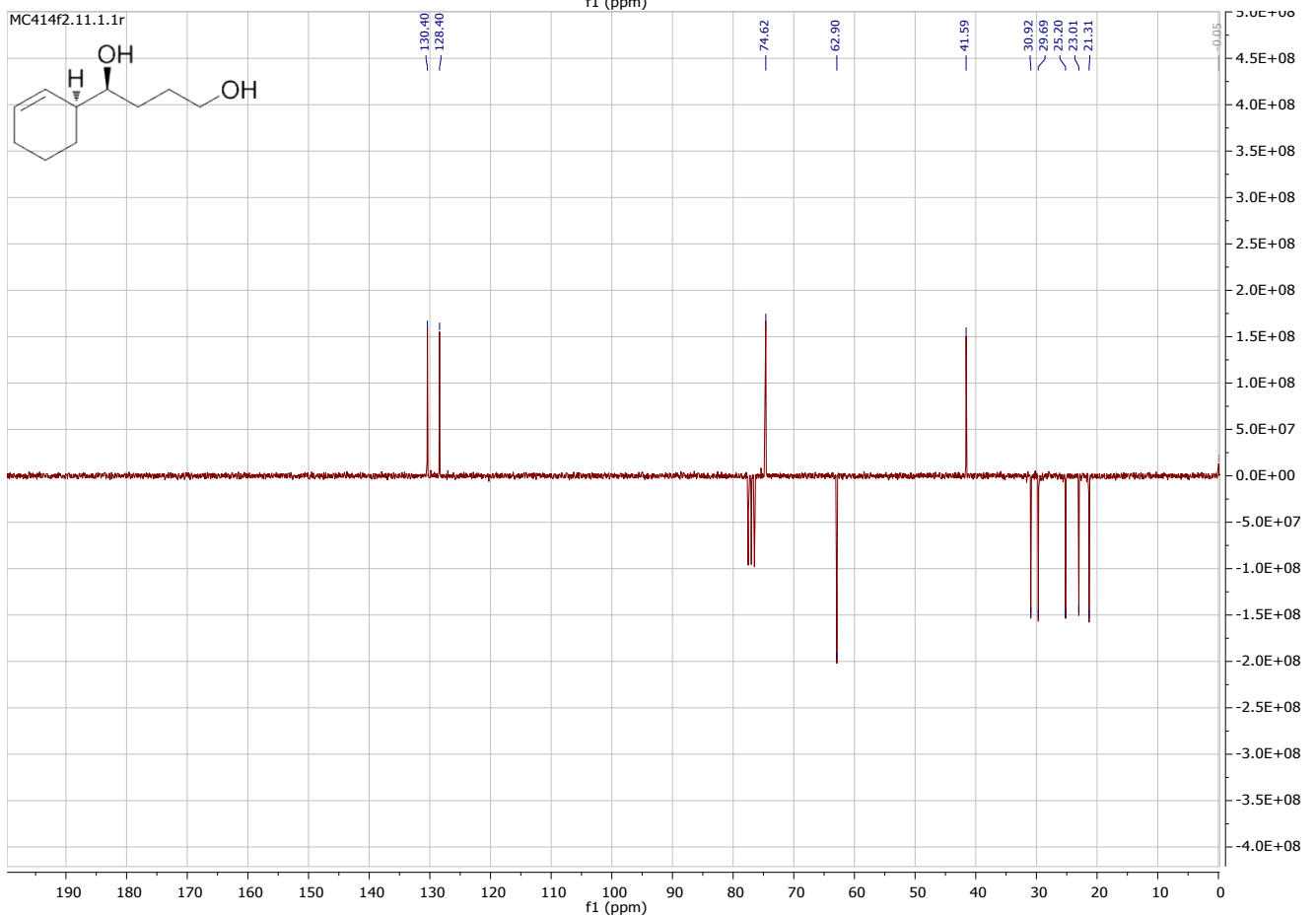
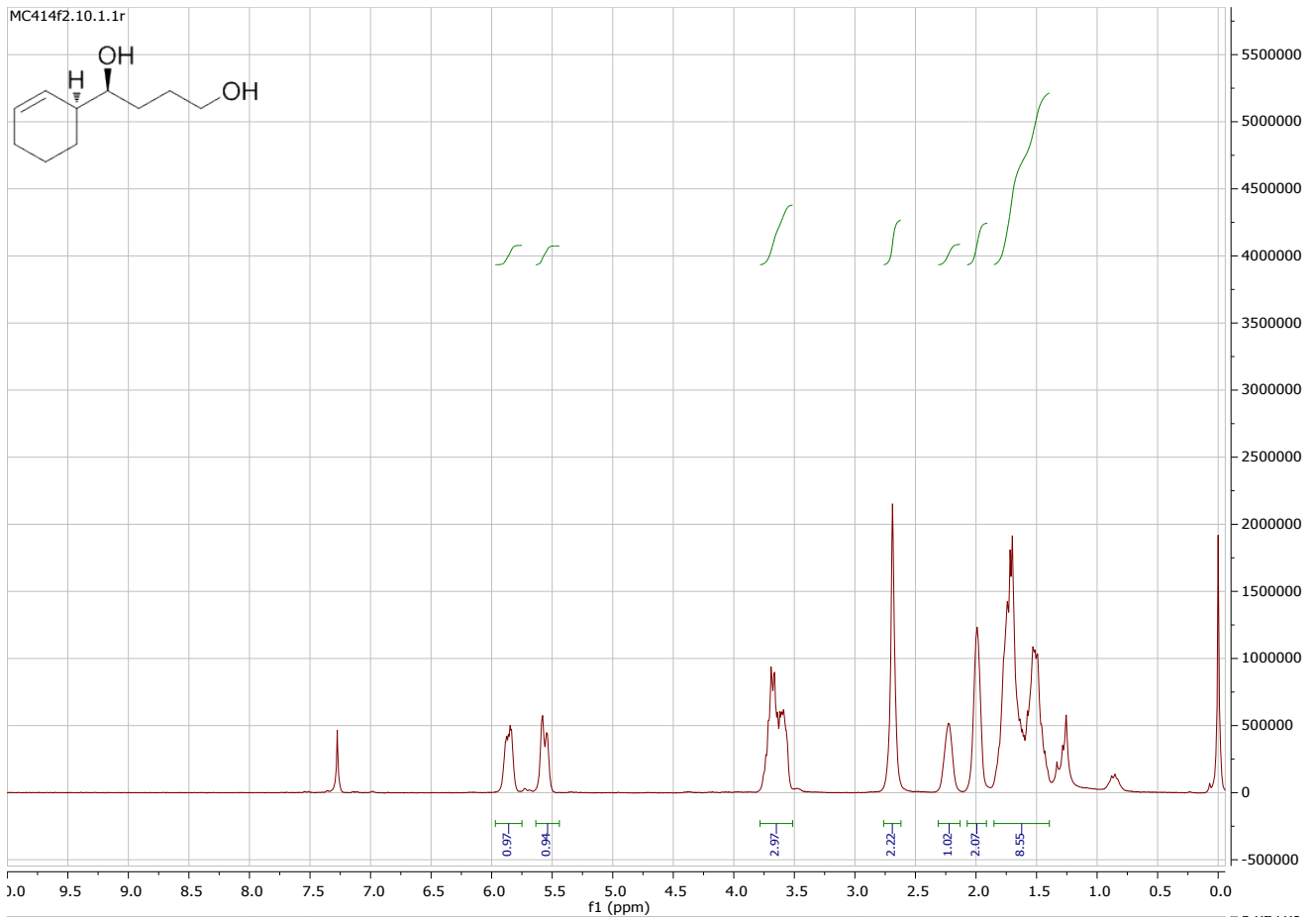
(R)-1-[(S)-Cyclohex-2-en-1-yl]-2,2-diphenylethanol 3j



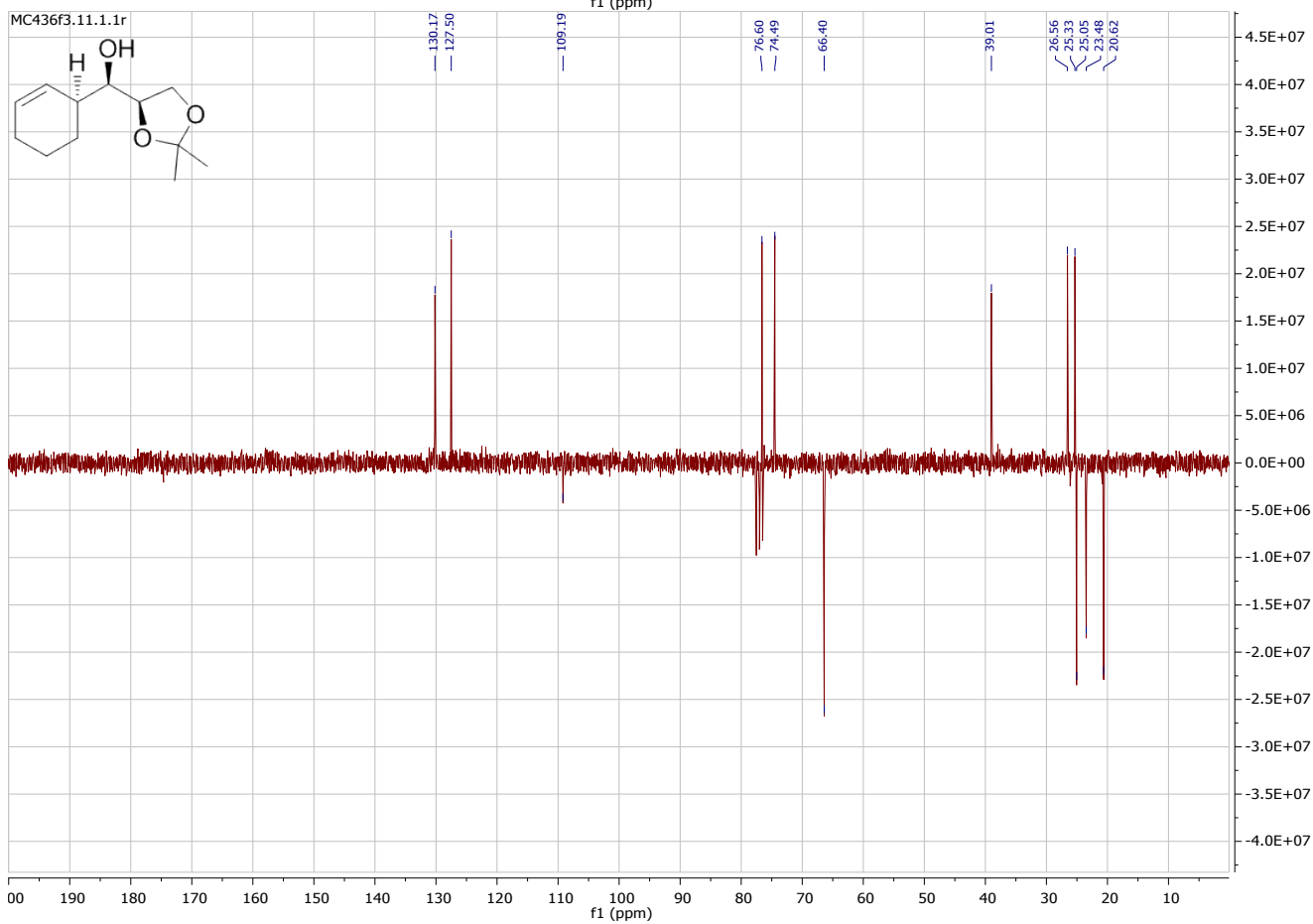
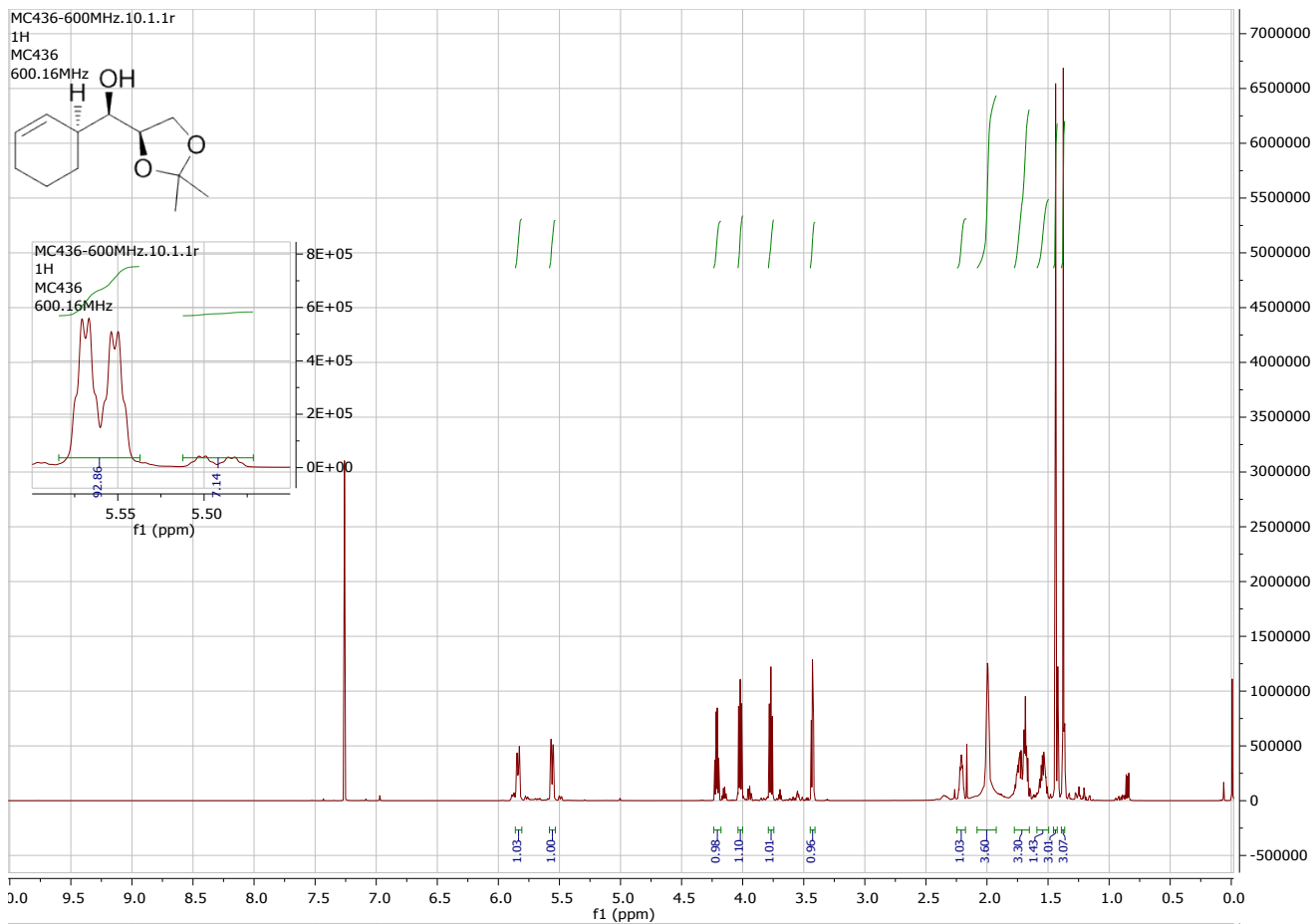
(S)-4-((Tert-Butyldimethylsilyl)oxy)-1-[(S)-cyclohex-2-en-1-yl]butan-1-ol 3k



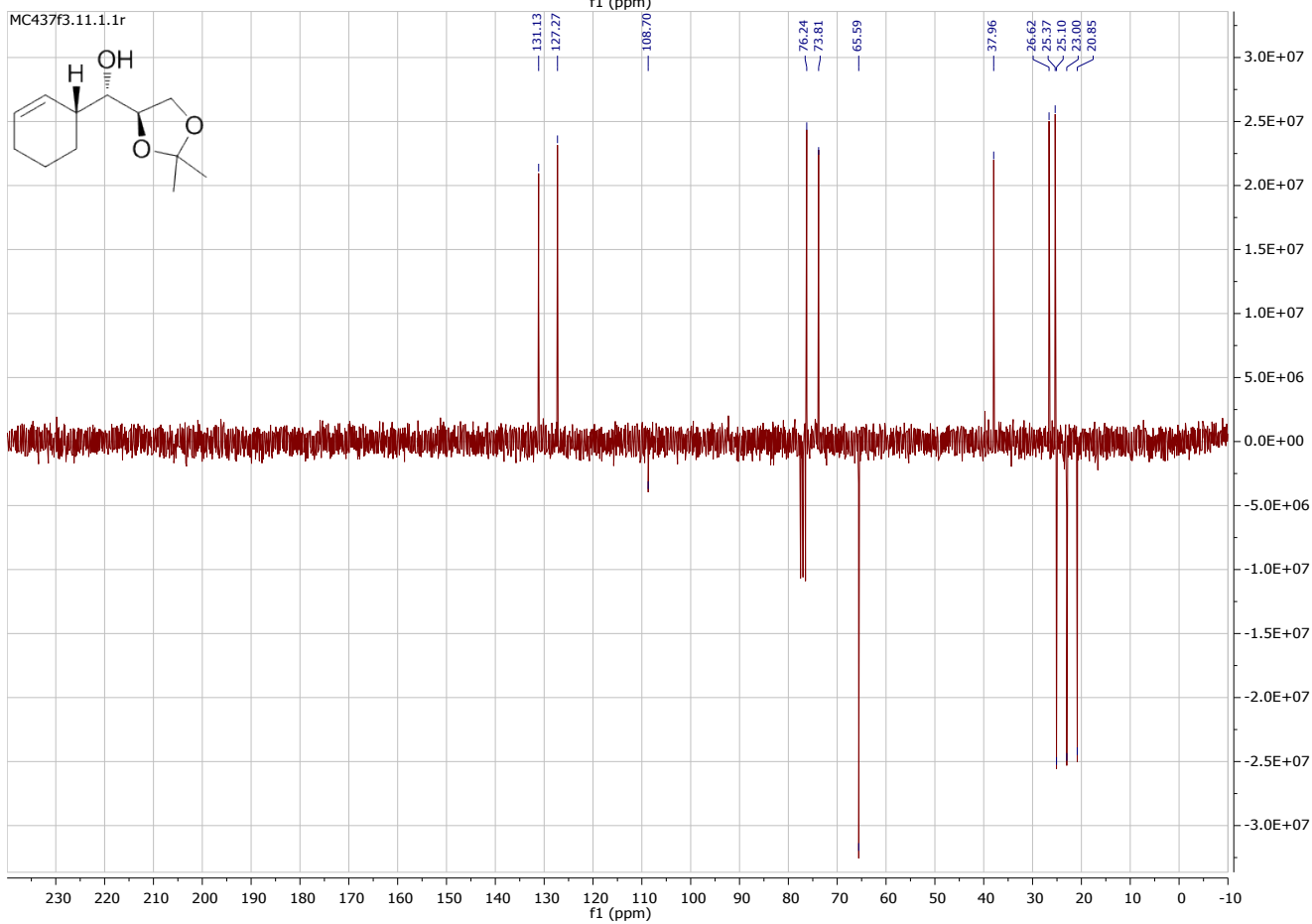
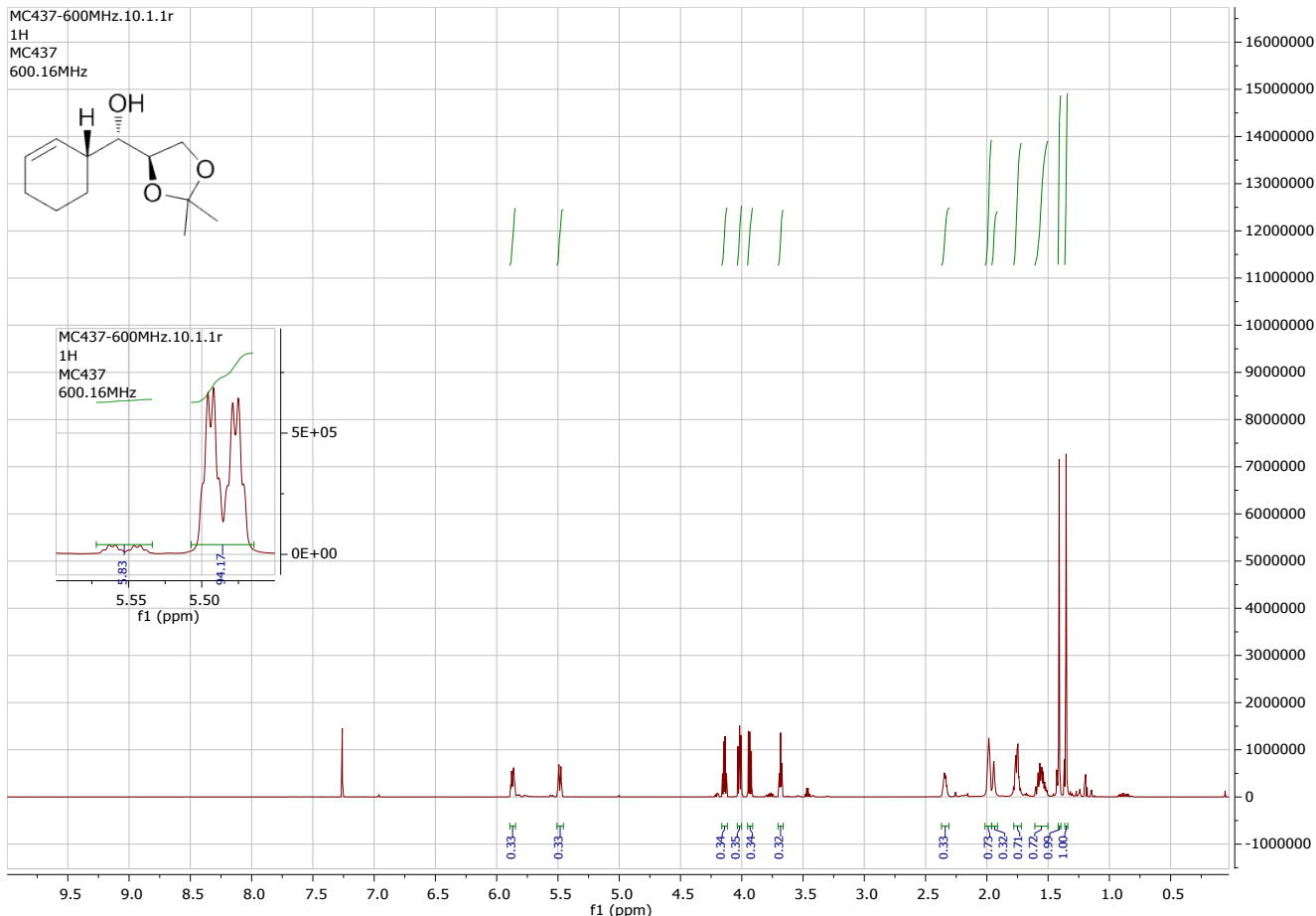
(S)-1-[(S)-Cyclohex-2-en-1-yl]butane-1,4-diol



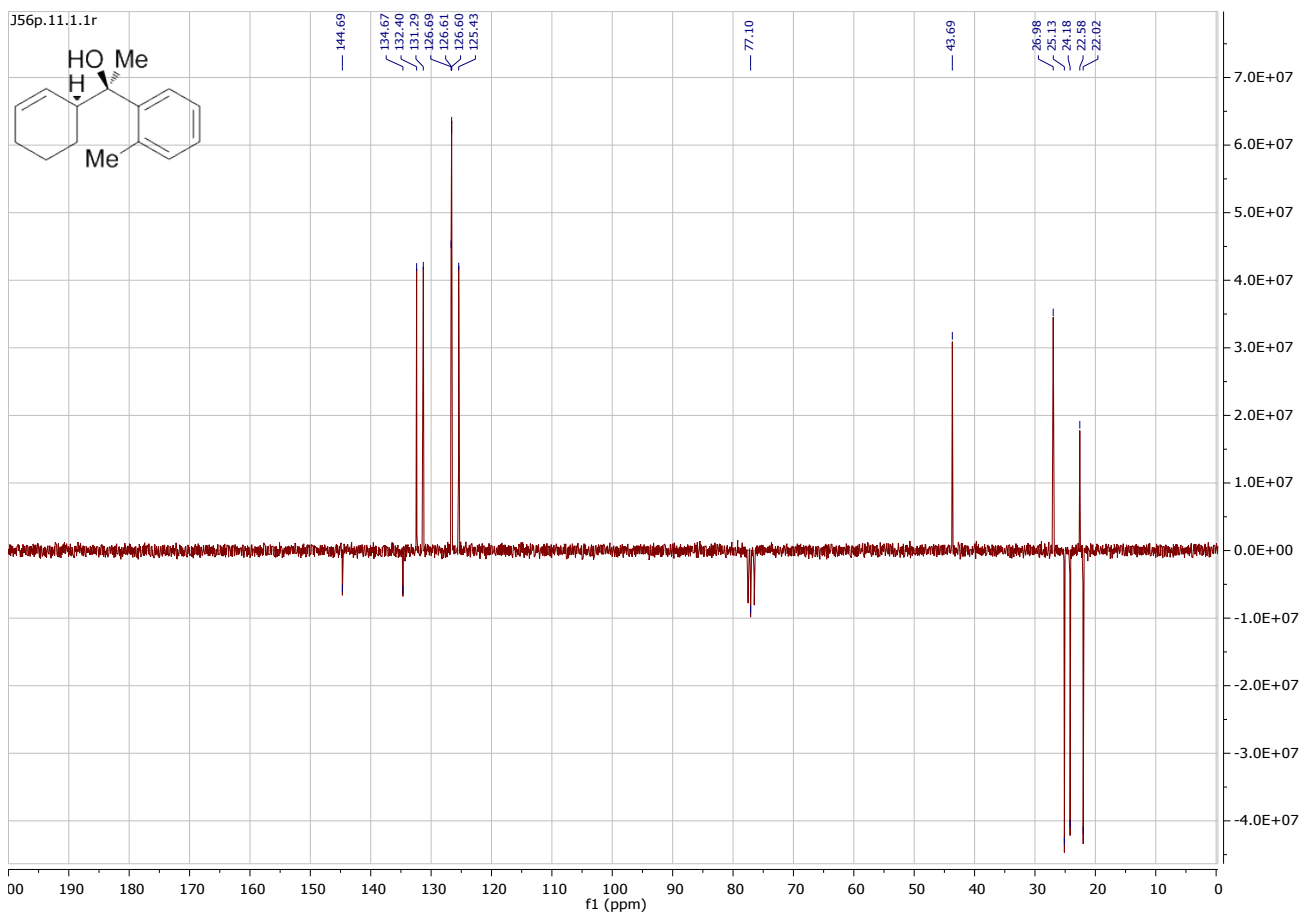
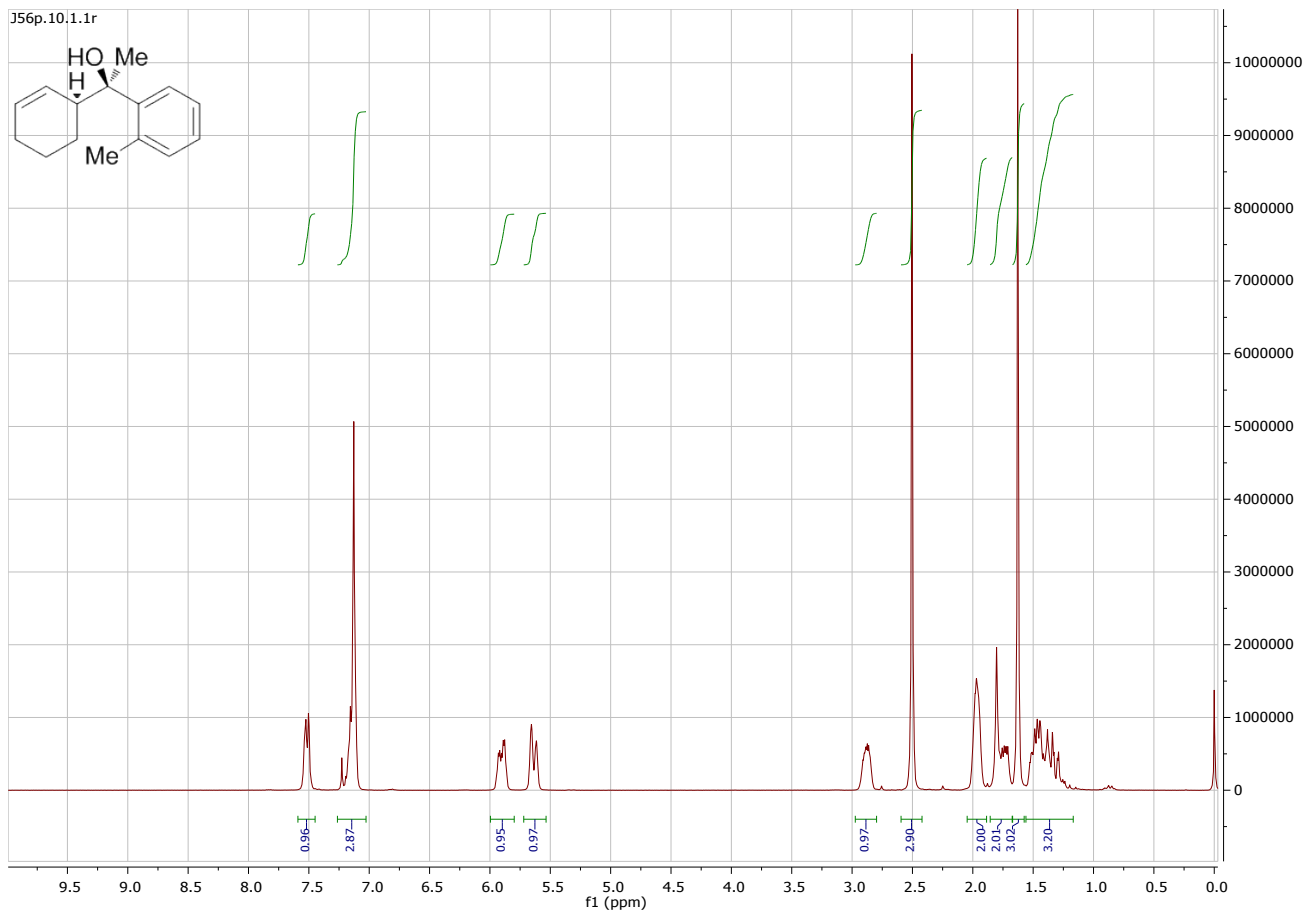
(R)-[(S)-cyclohex-2-en-1-yl][(R)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol 3l



(S)-[*(R)*-cyclohex-2-en-1-yl][*(R)*-2,2-dimethyl-1,3-dioxolan-4-yl]methanol 3m

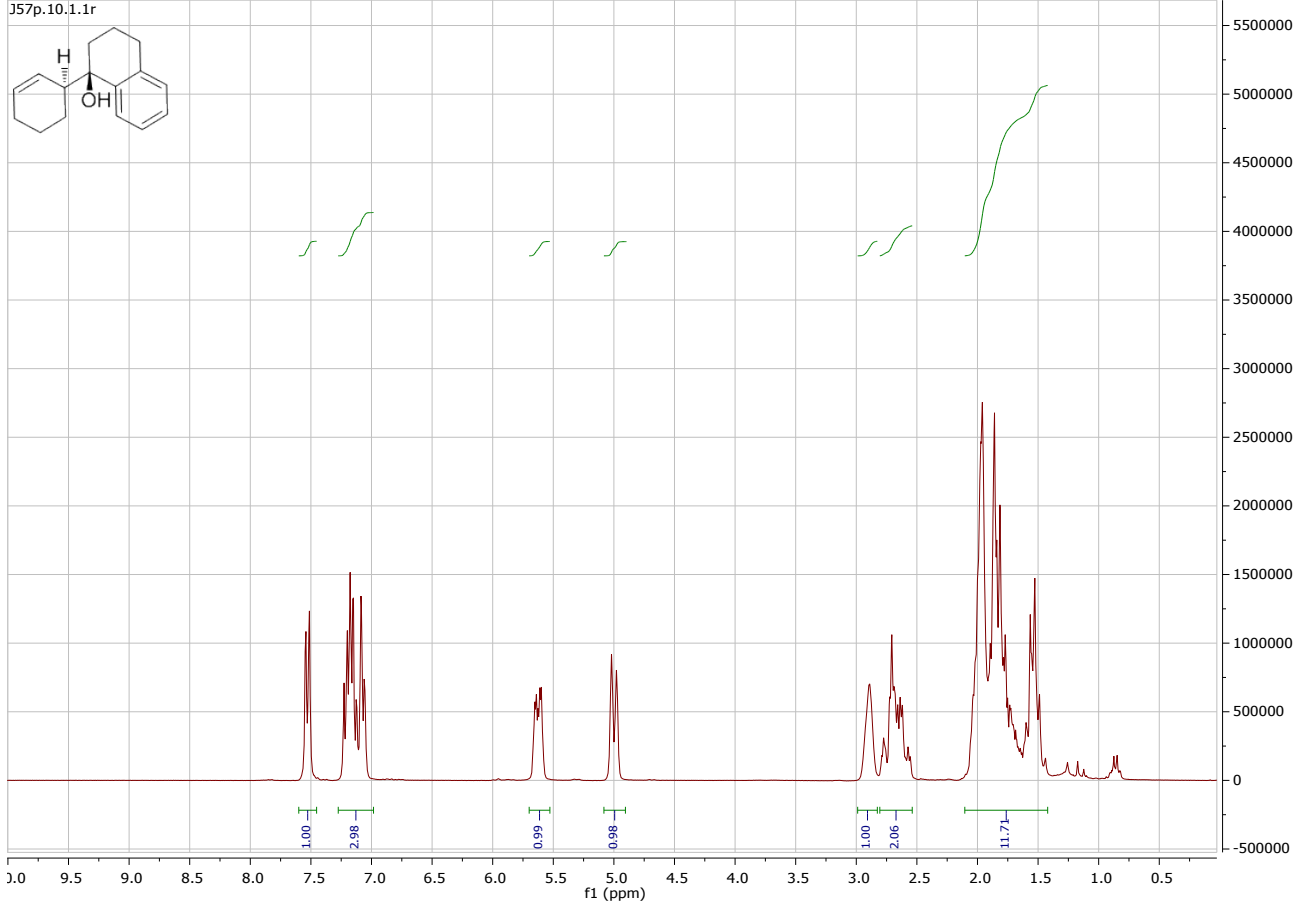
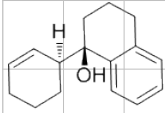


(R)-1-[(S)-Cyclohex-2-en-1-yl]-1-(o-tolyl)ethanol 3n

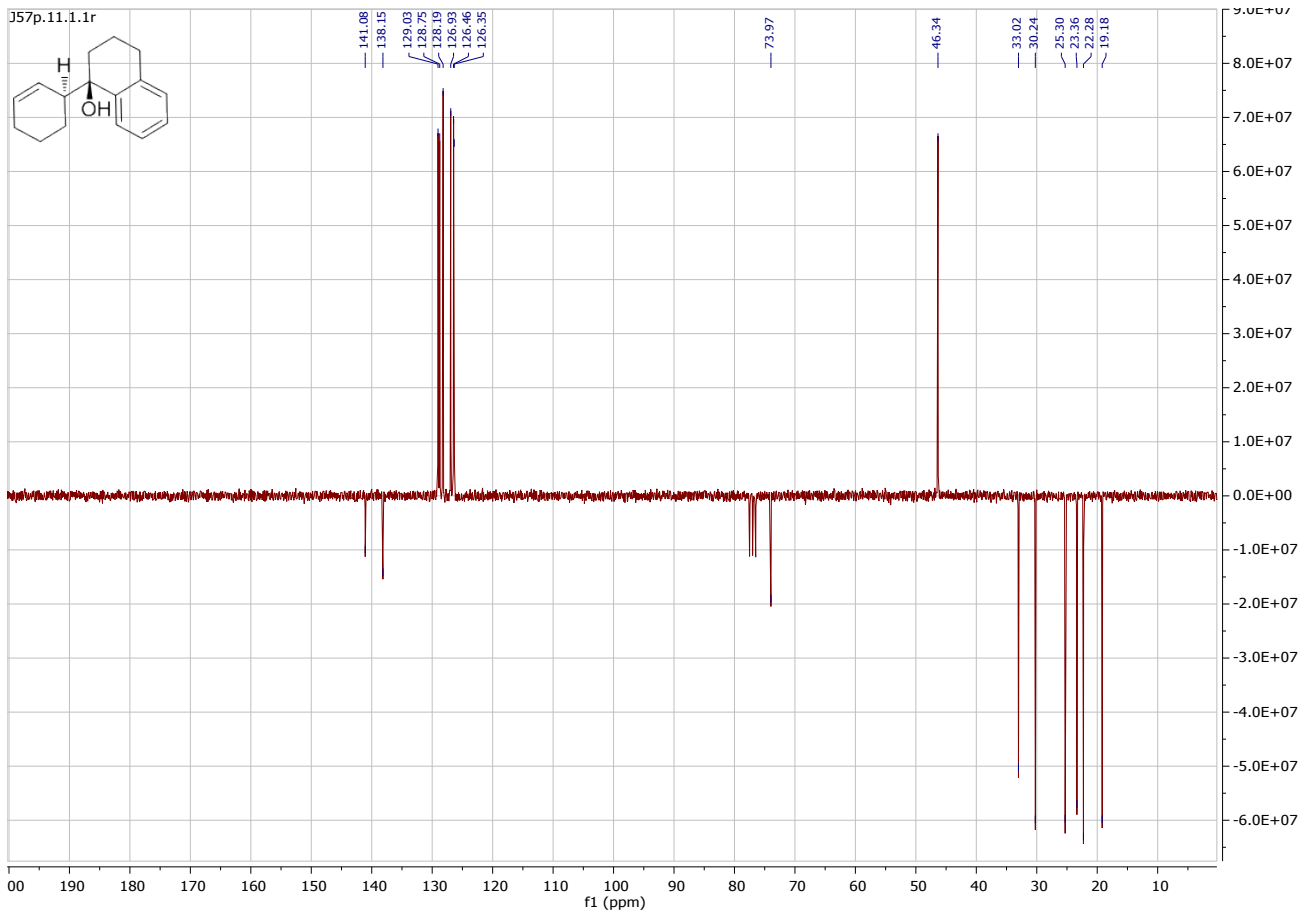
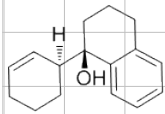


(R)-1-[(S)-cyclohex-2-en-1-yl]-1,2,3,4-tetrahydronaphthalen-1-ol 3o

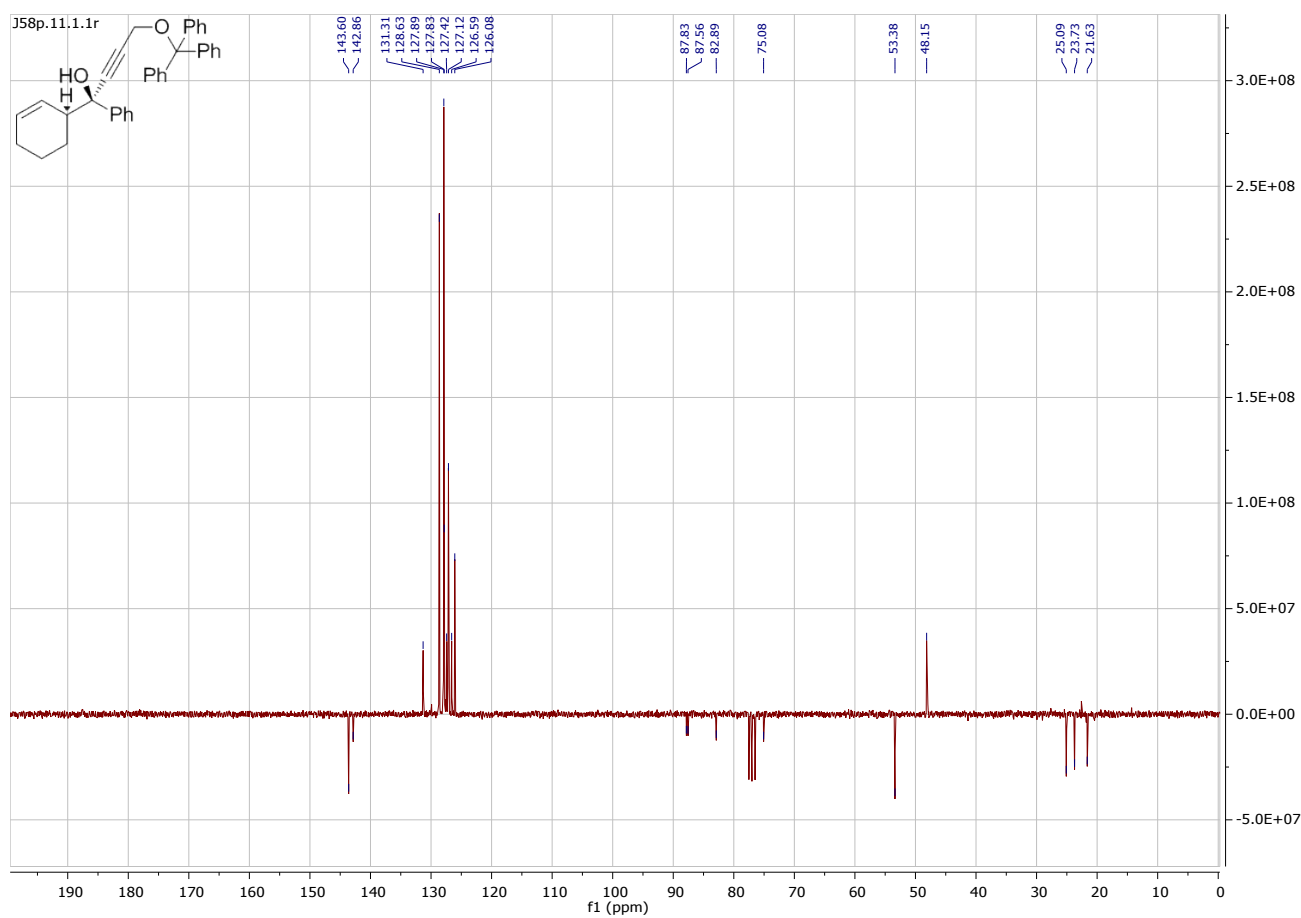
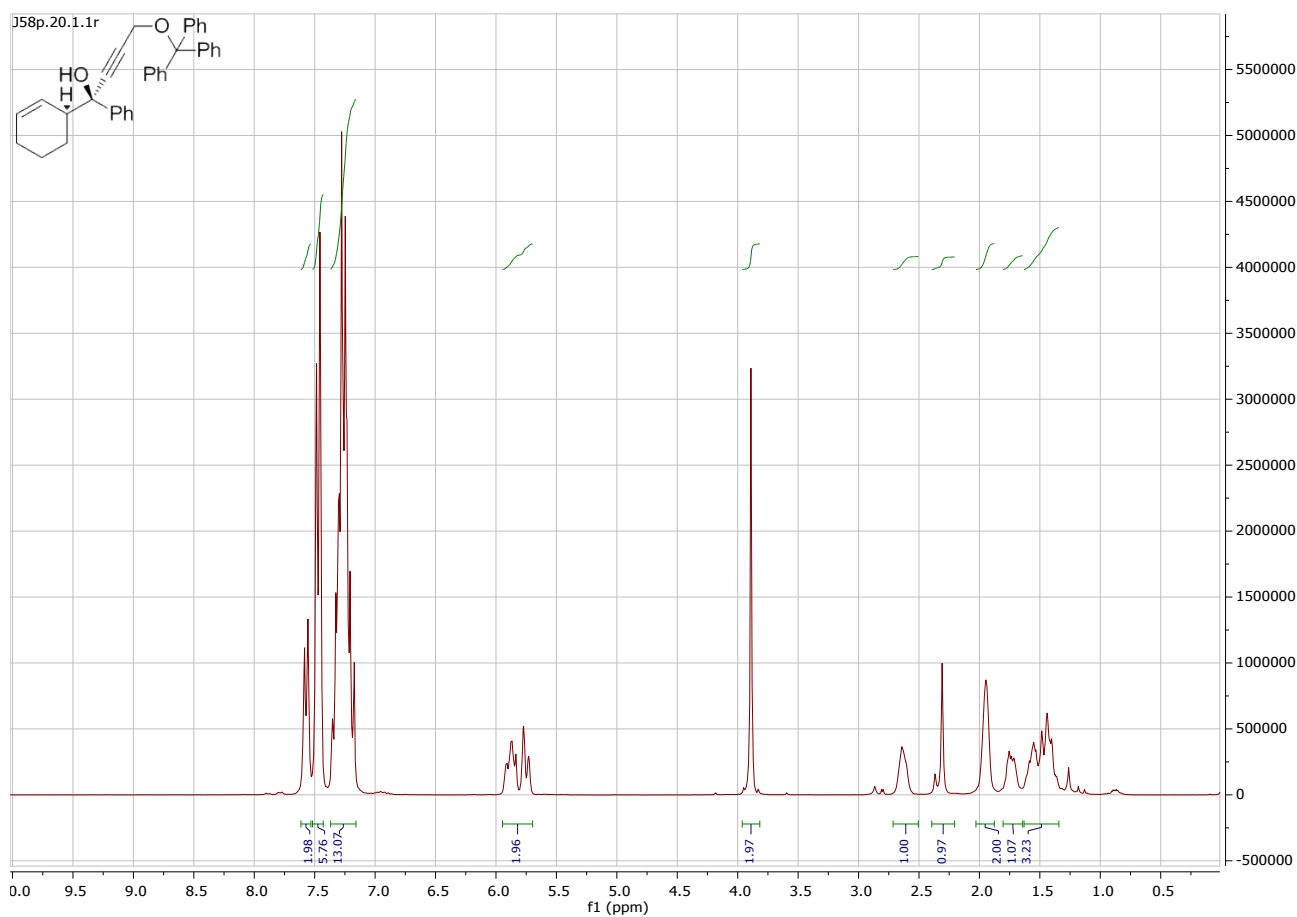
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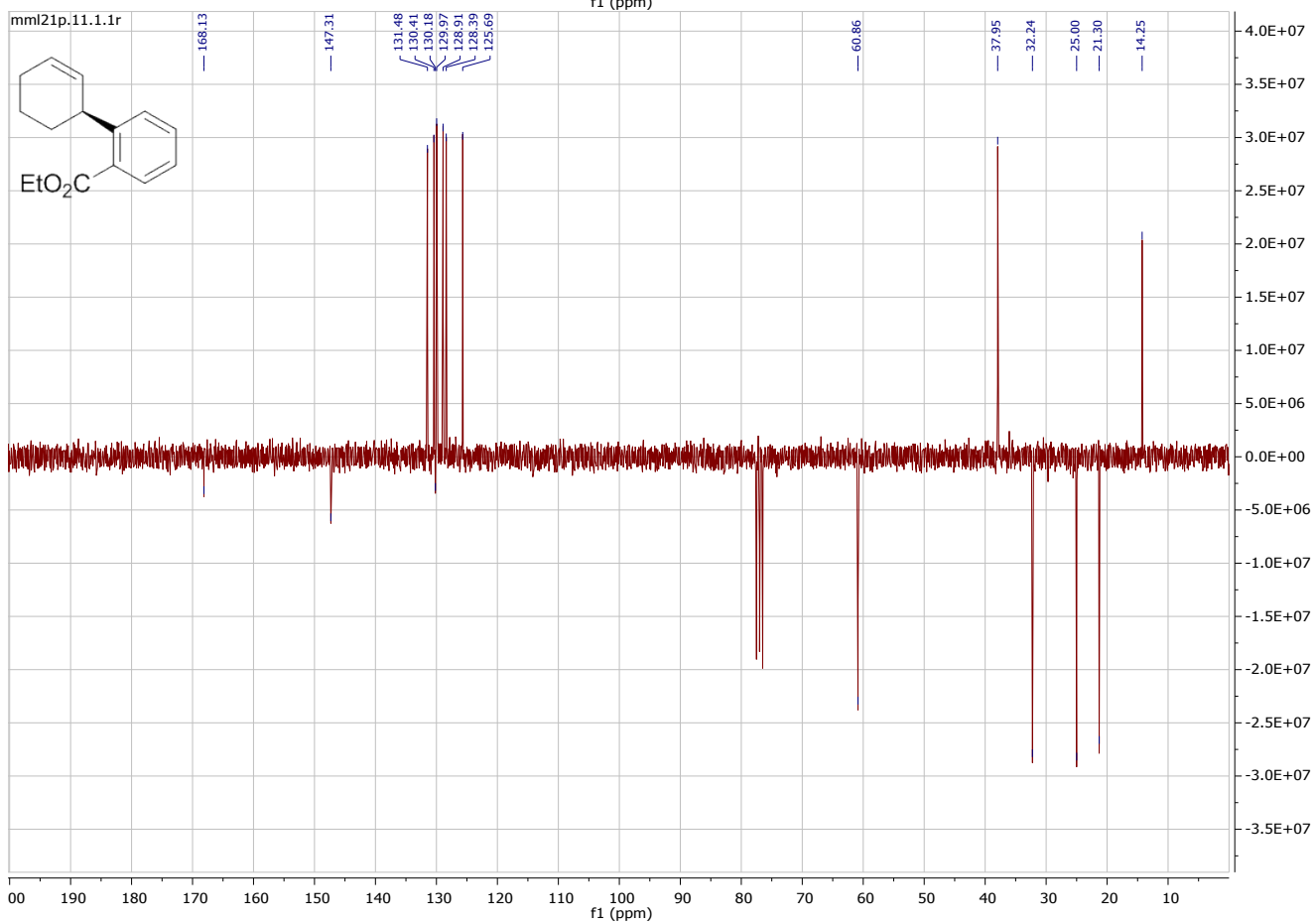
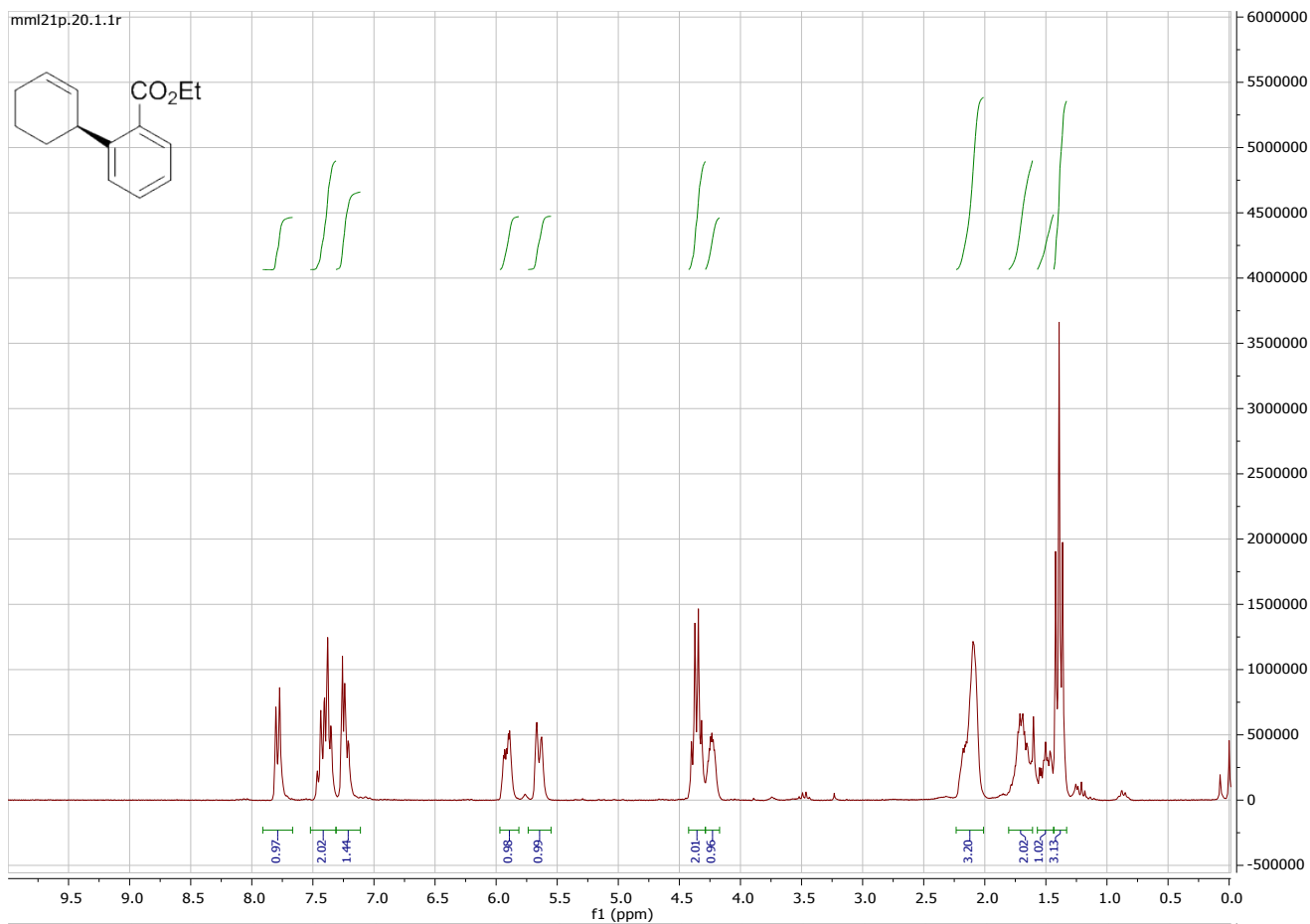
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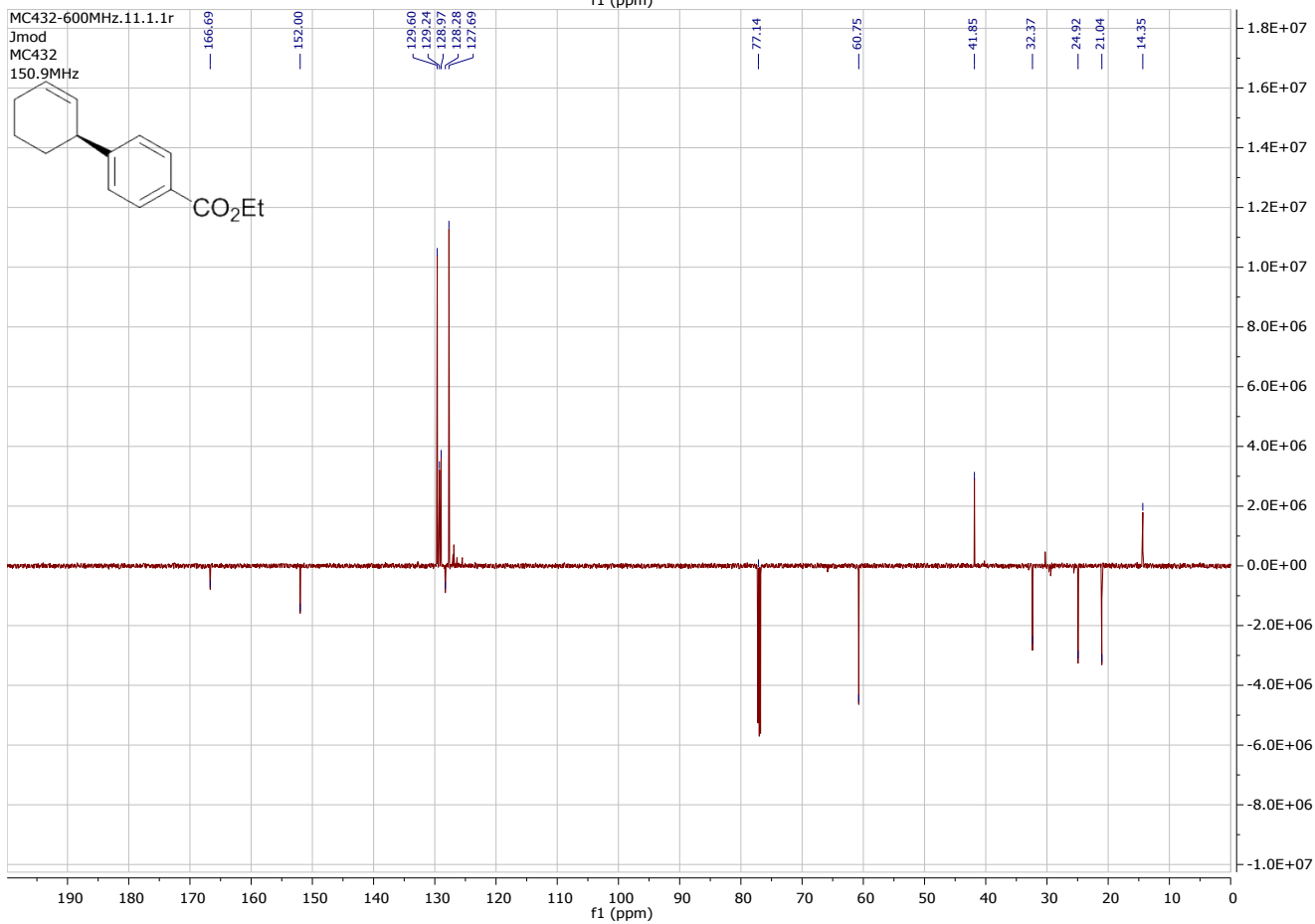
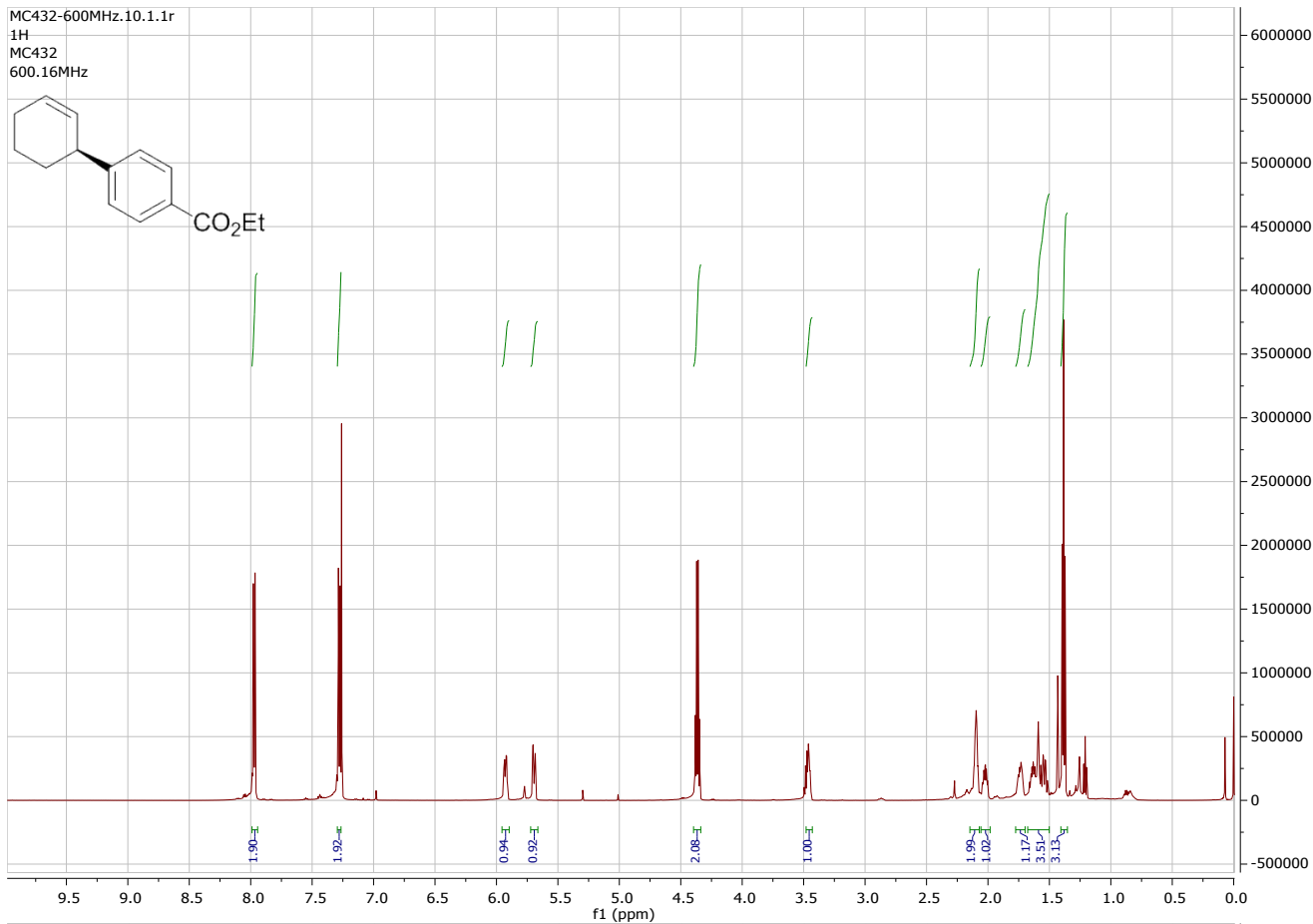
(R)-1-[(S)-cyclohex-2-en-1-yl]-1-phenyl-4-(trityloxy)but-2-yn-1-ol 3p



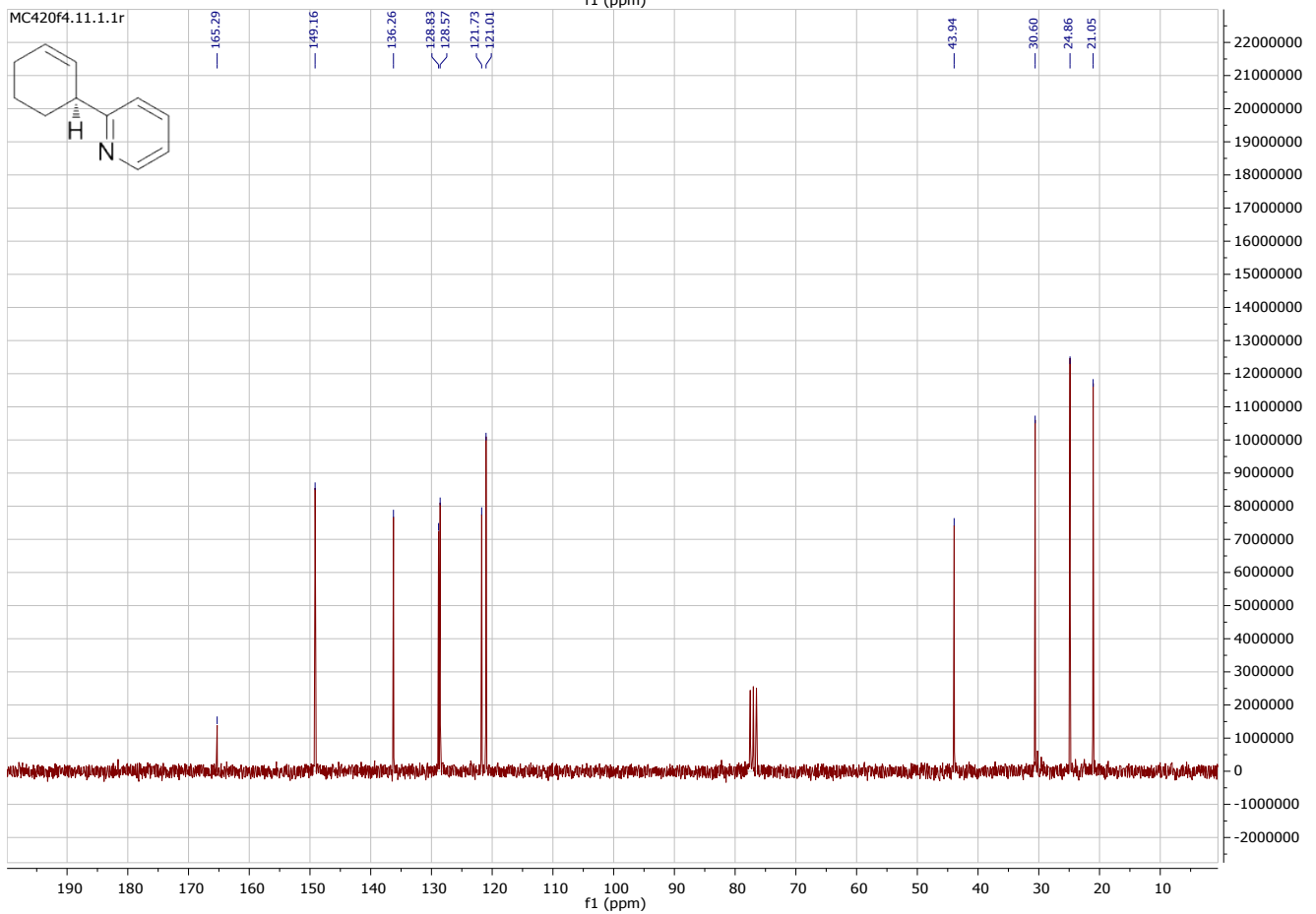
(S)-Ethyl 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2-carboxylate 5a.



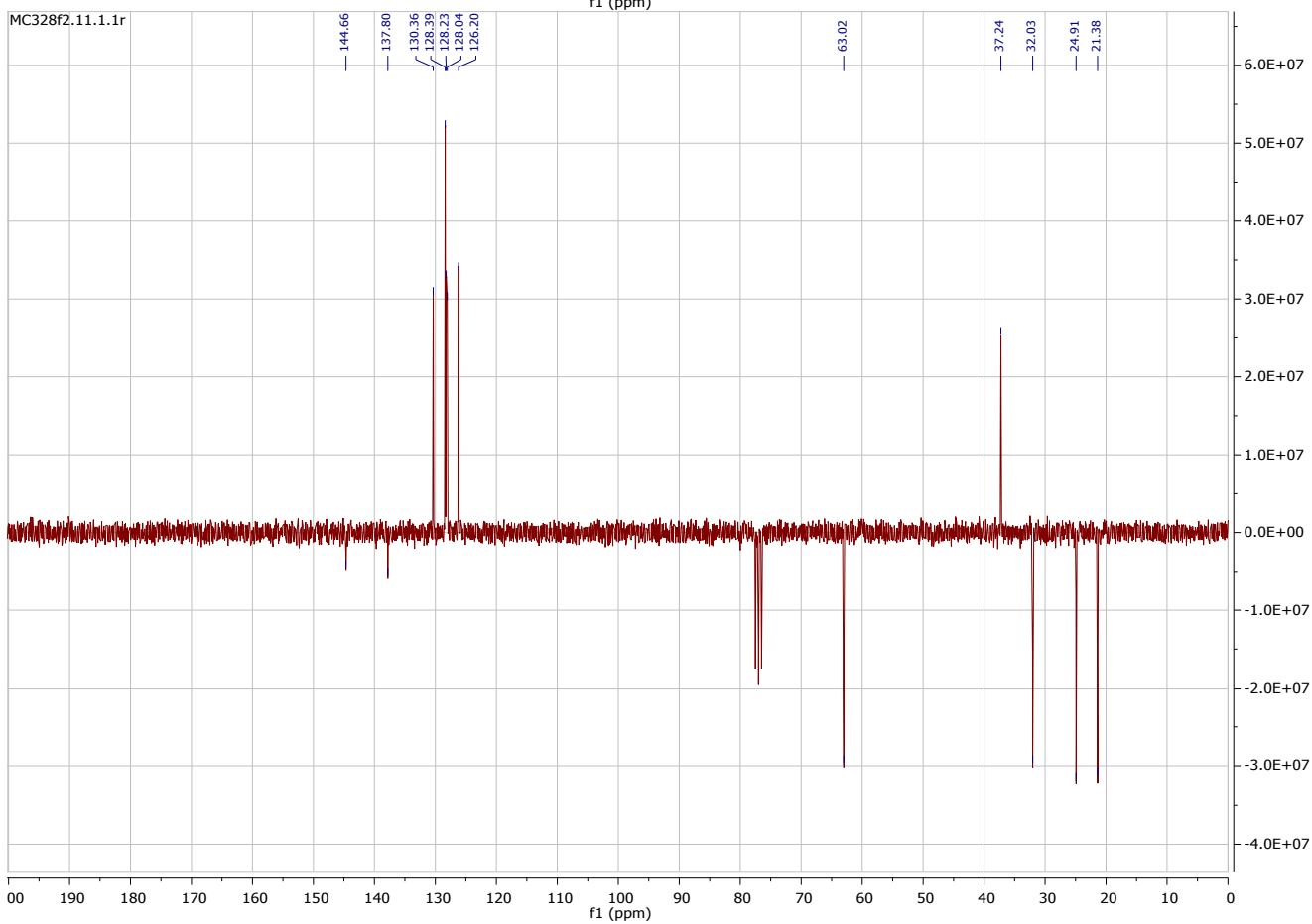
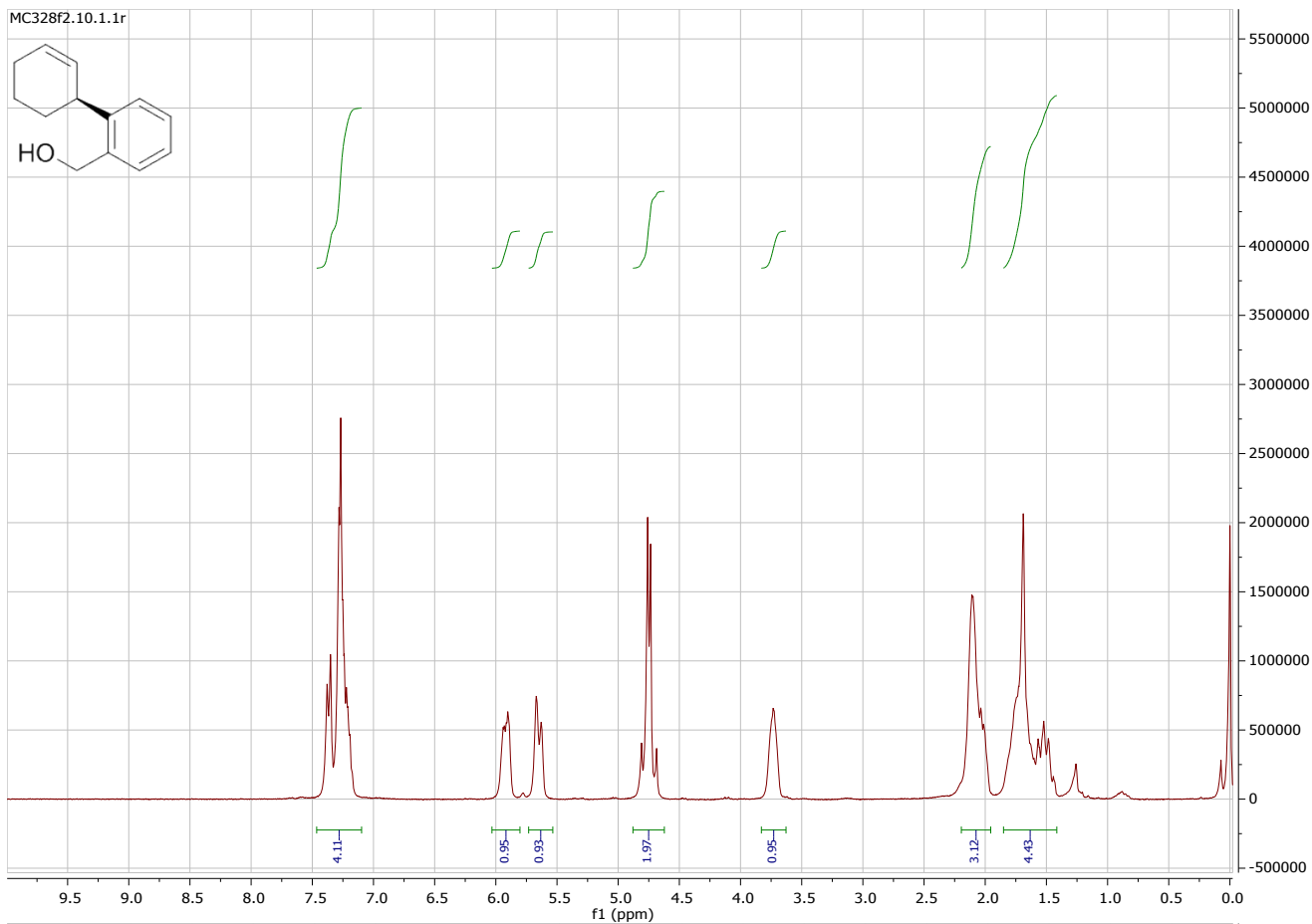
(S)-Ethyl 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-carboxylate 5b



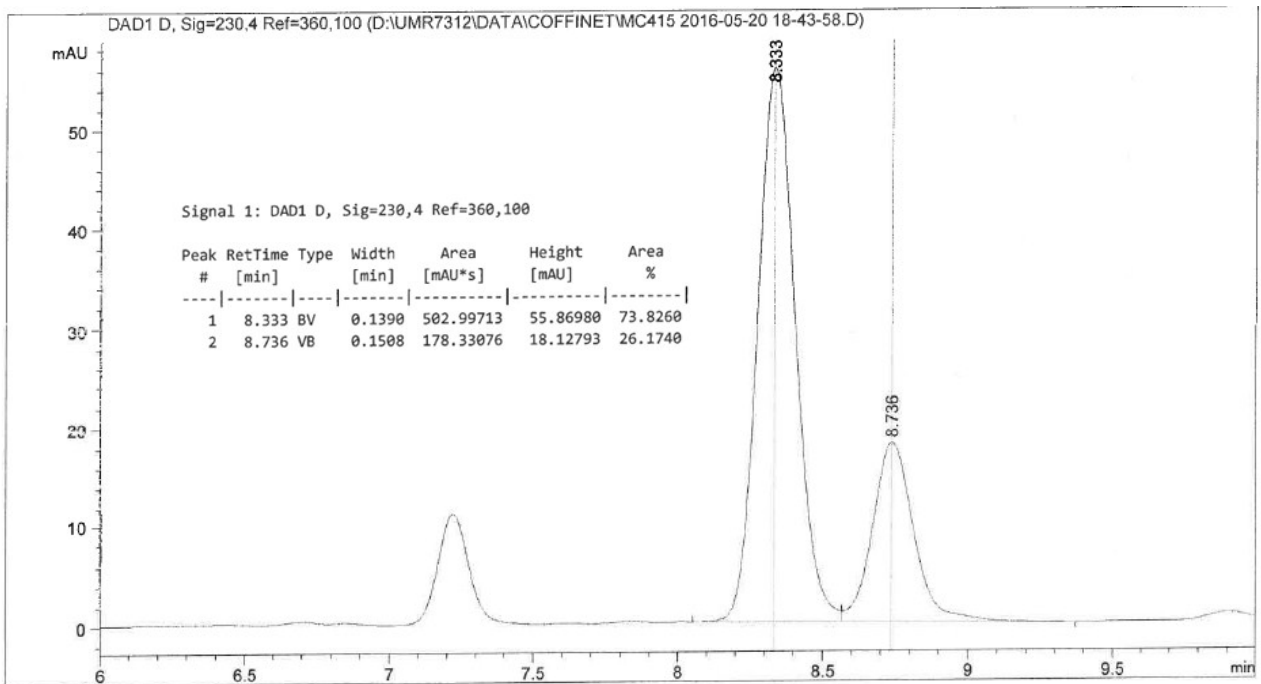
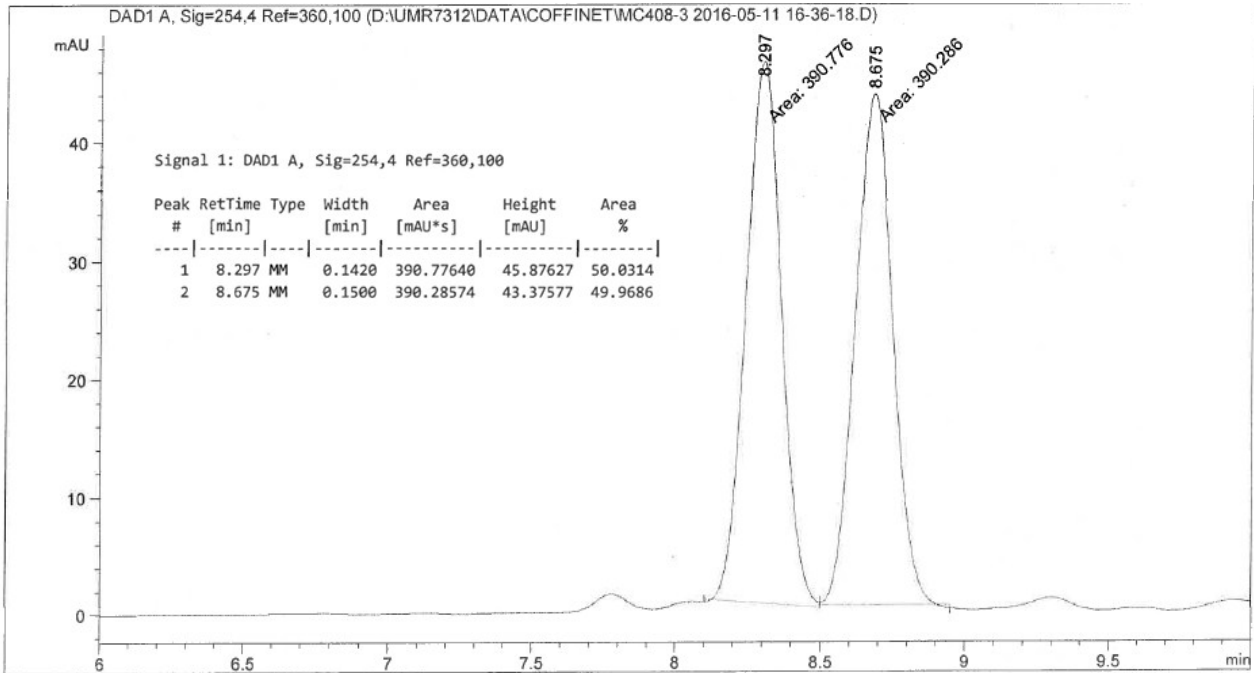
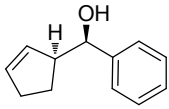
(S)-2-(Cyclohex-2-en-1-yl)pyridine 5c.



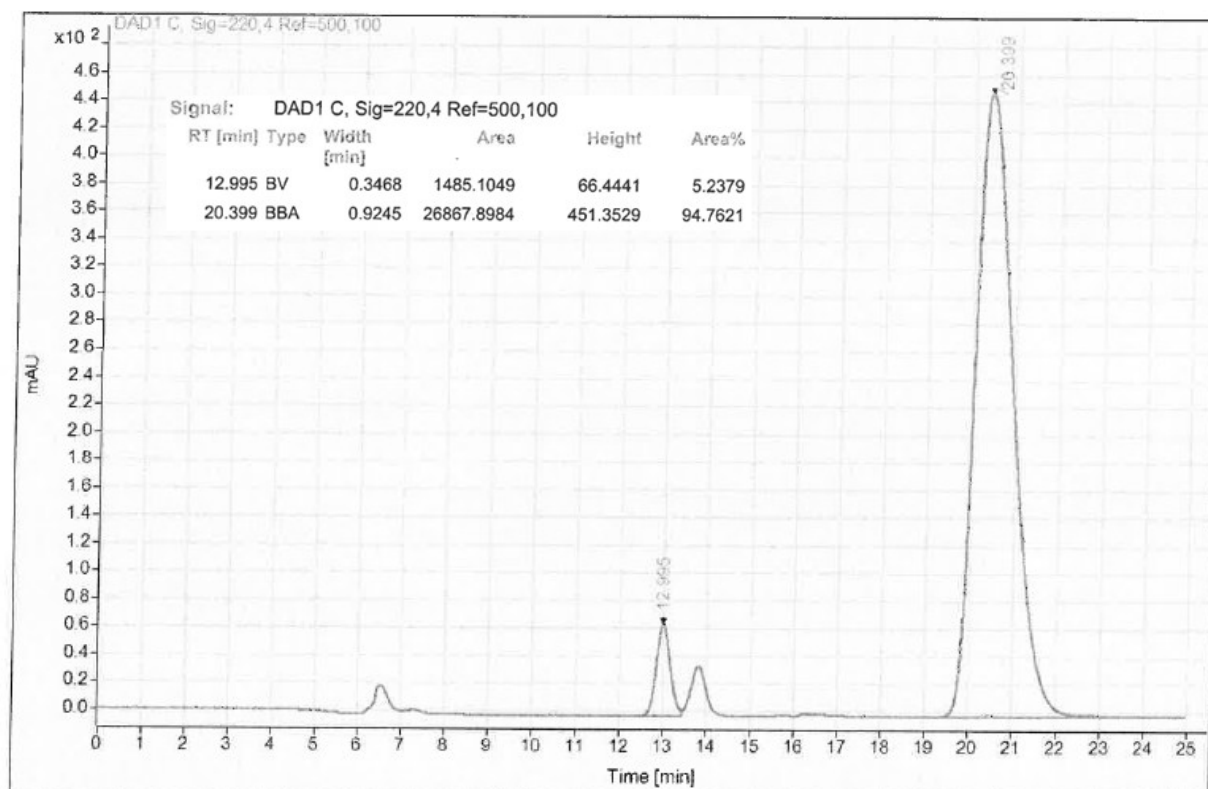
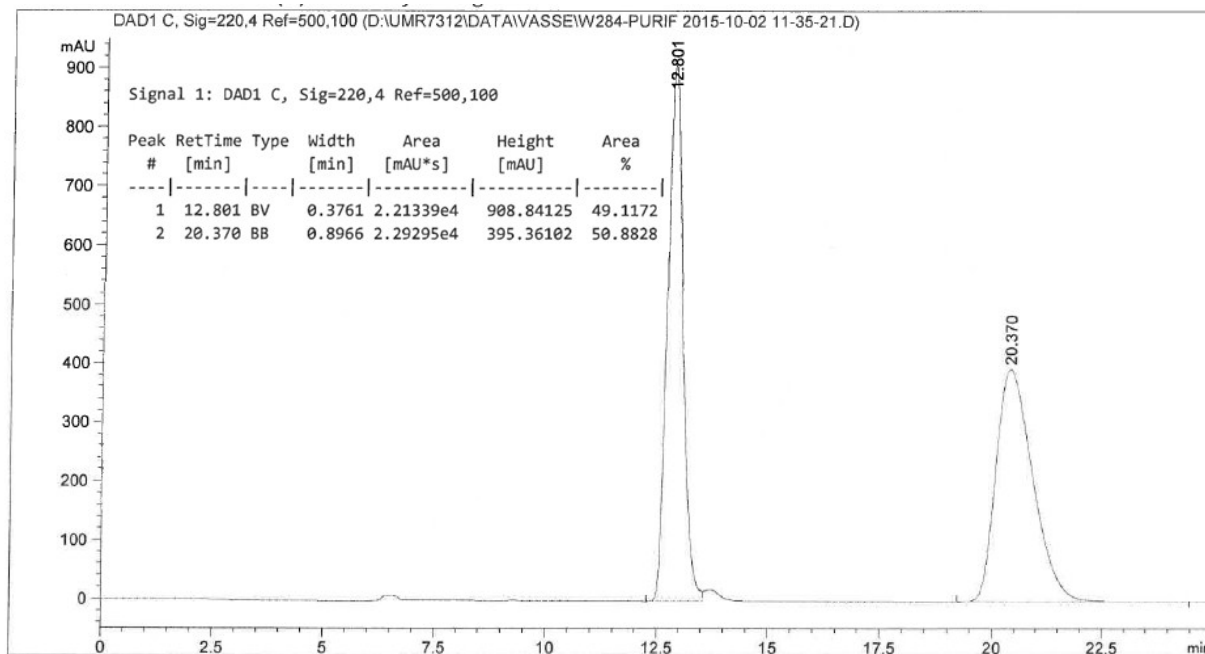
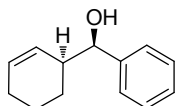
(S)-(1',2',3',4'-Tetrahydro-[1,1'-biphenyl]-2-yl)methanol 5'a



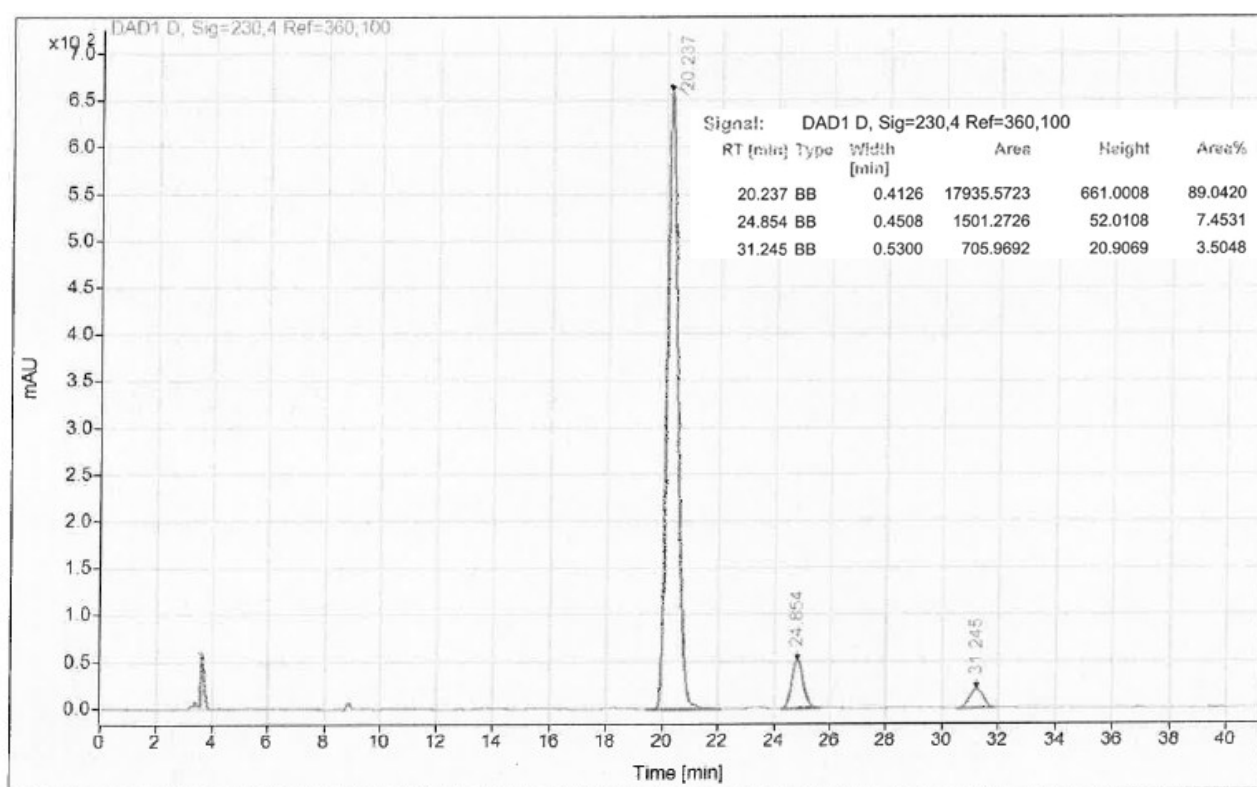
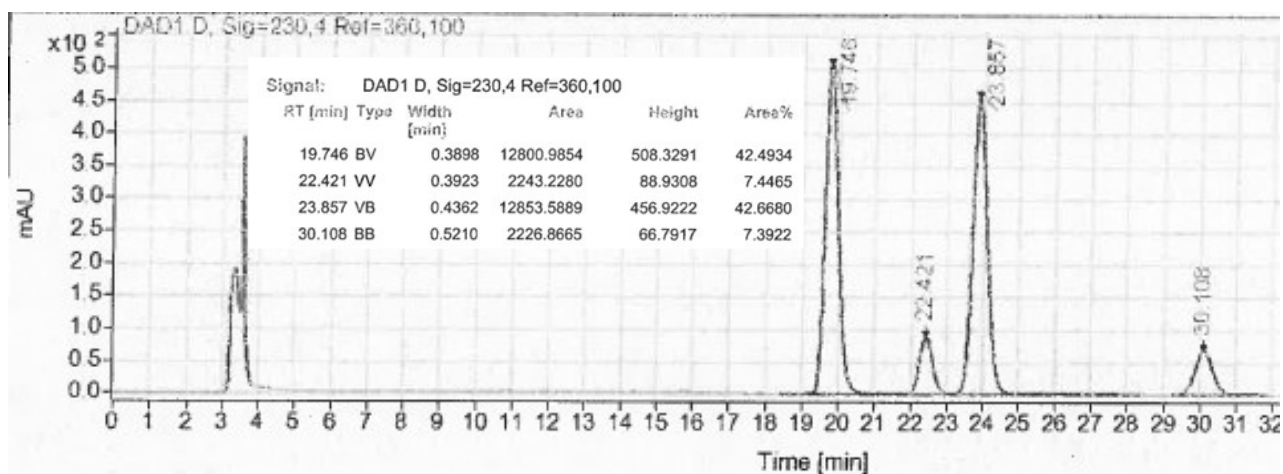
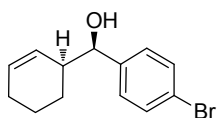
(R)-[(S)-Cyclopent-2-en-1-yl](phenyl)methanol 4a



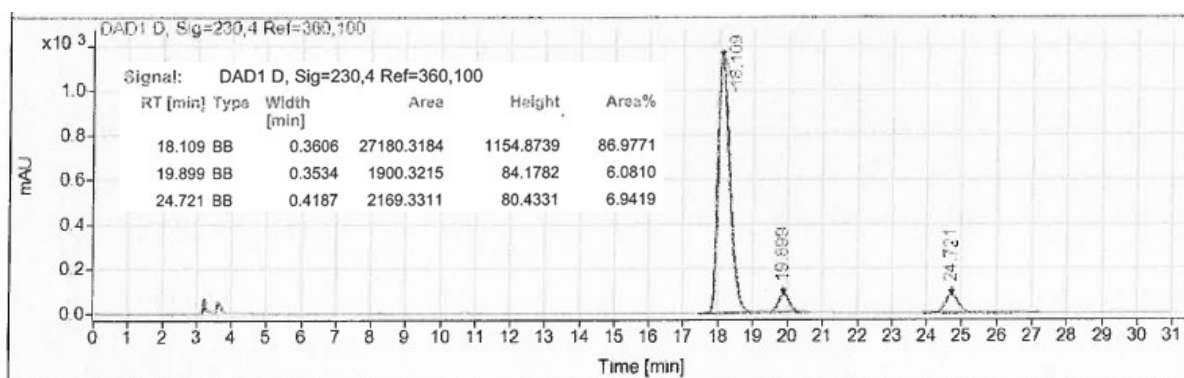
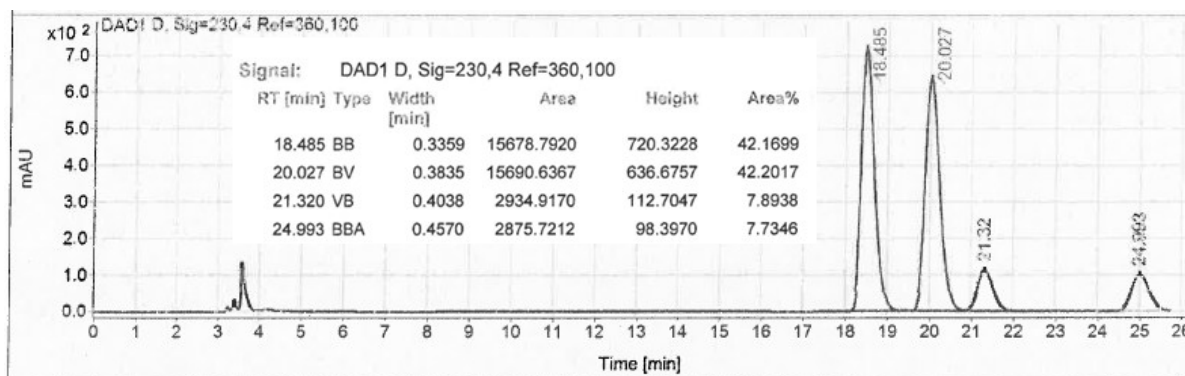
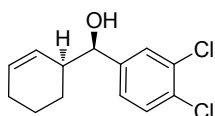
(R)-[(S)-Cyclohex-2-en-1-yl](phenyl)methanol 3a



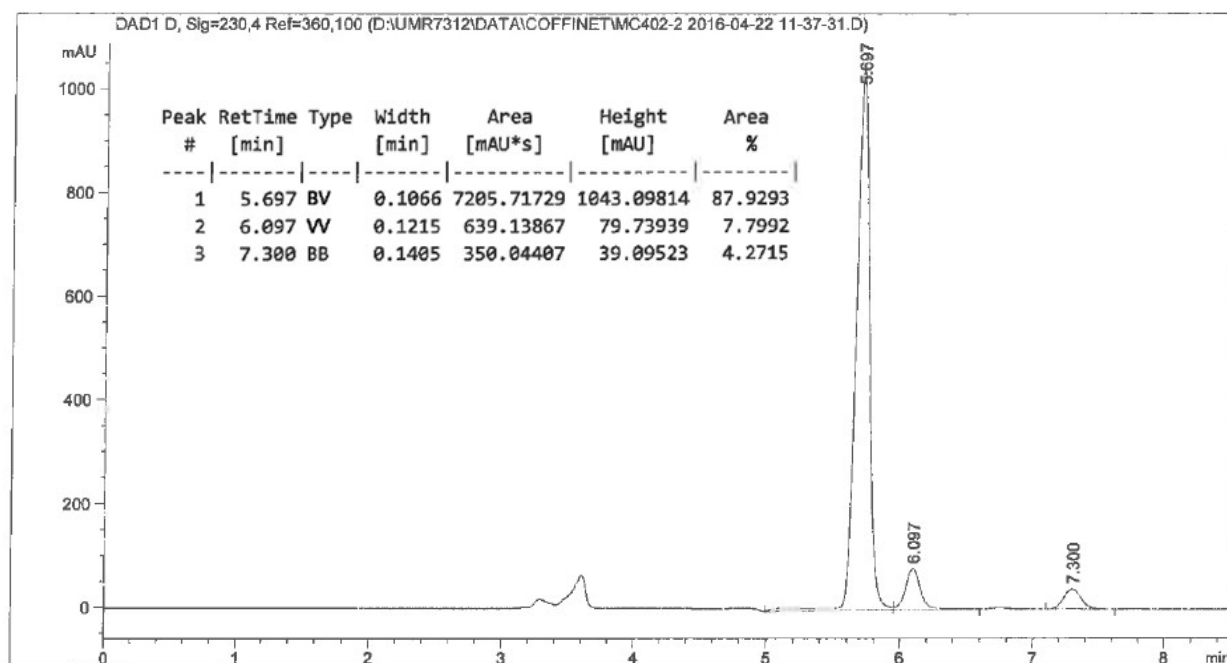
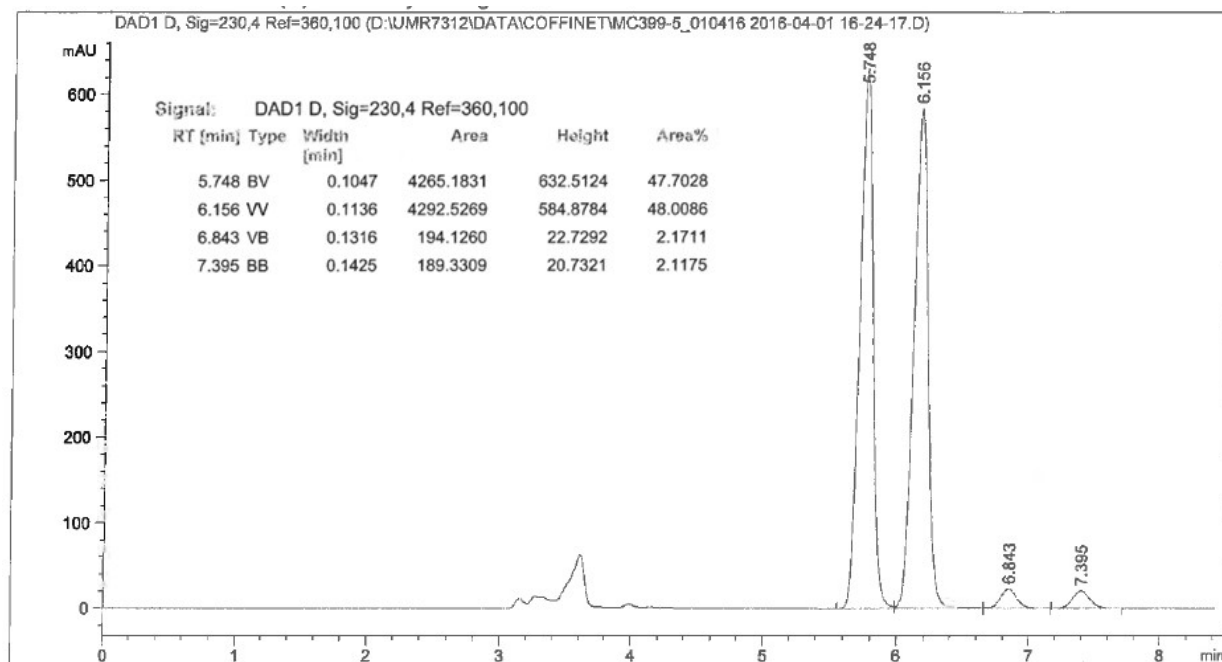
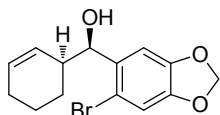
(R)-(4-Bromophenyl) [(S)-cyclohex-2-en-1-yl]methanol 3b



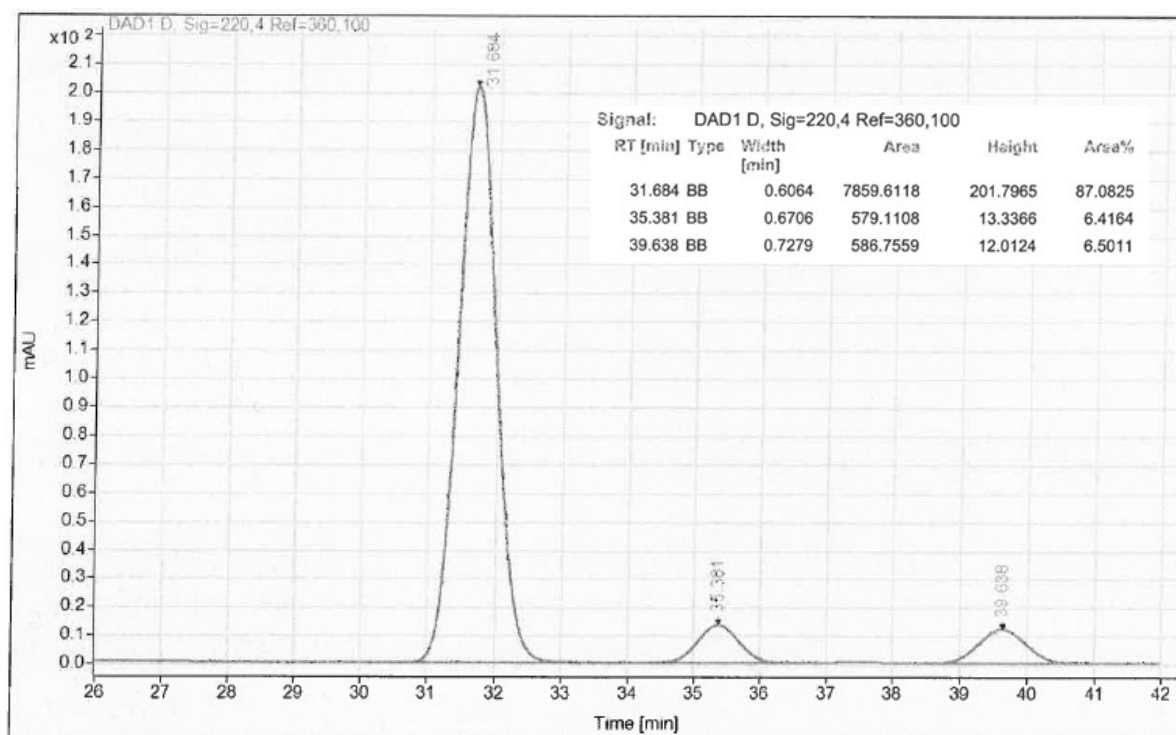
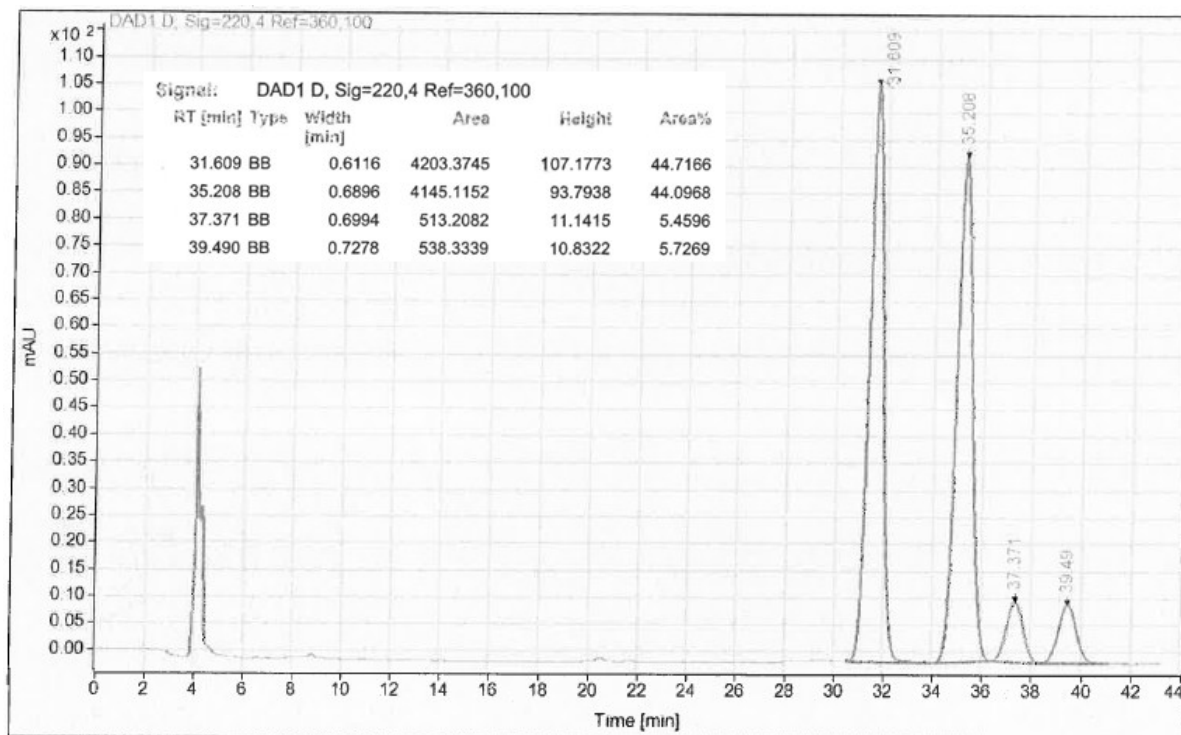
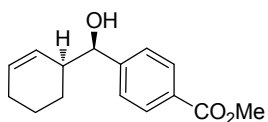
(R)- [(S)-Cyclohex-2-en-1-yl](3,4-dichlorophenyl)methanol 3c



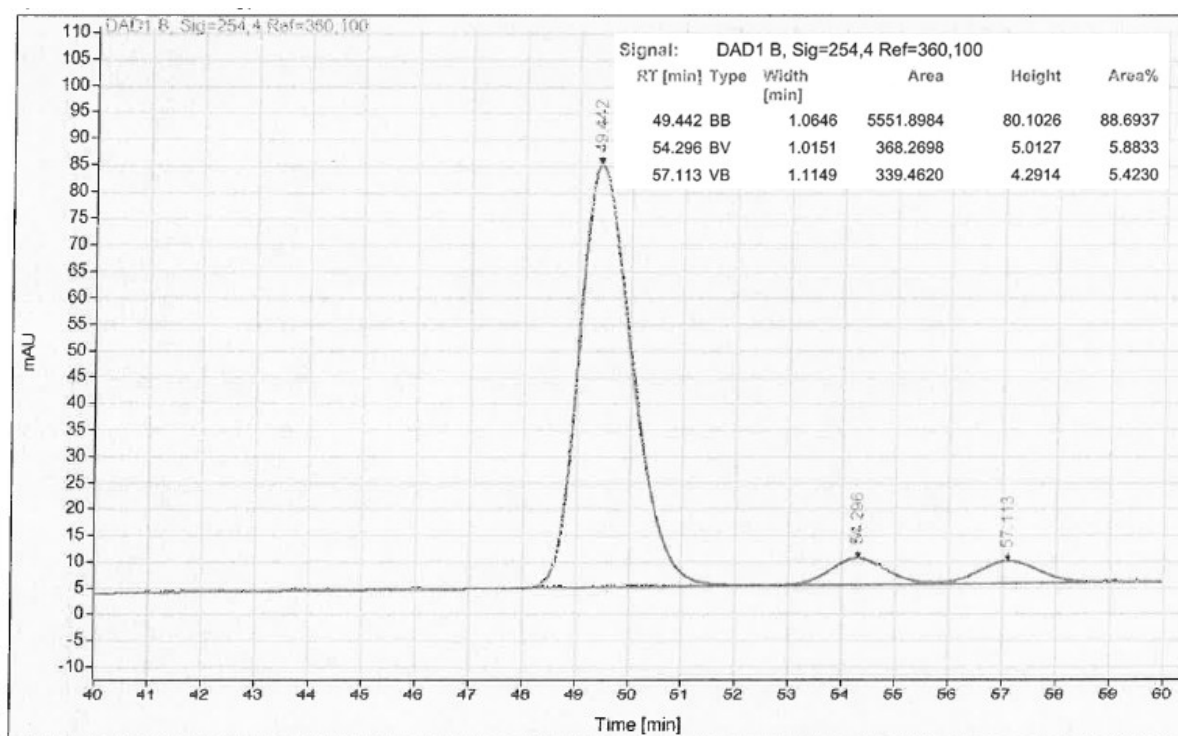
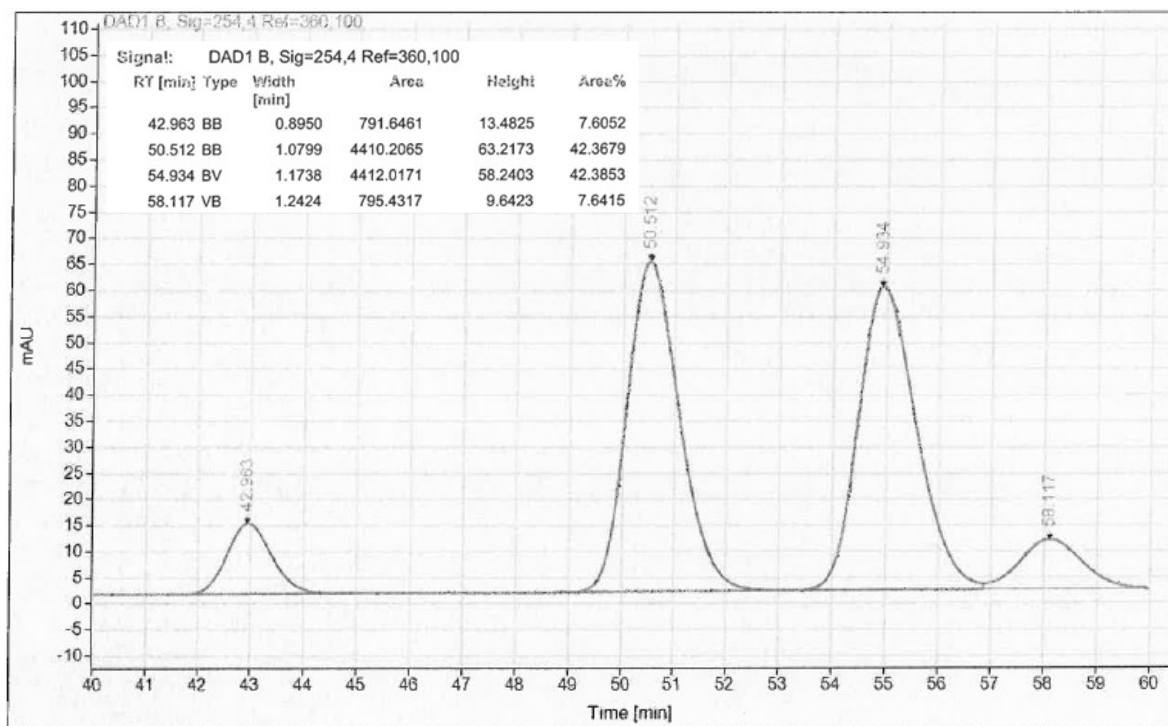
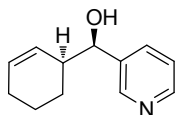
(R)-(6-Bromobenzo[d][1,3]dioxol-5-yl)[(S)-cyclohex-2-en-1-yl]methanol 3d



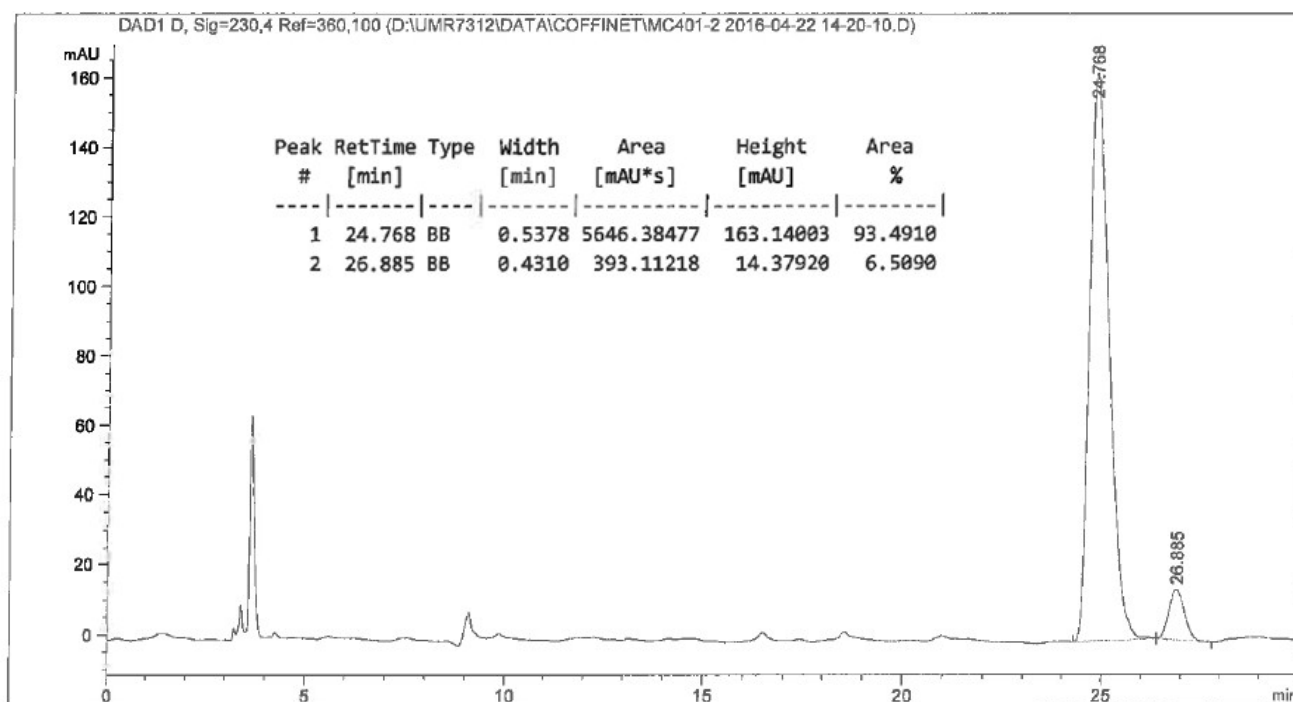
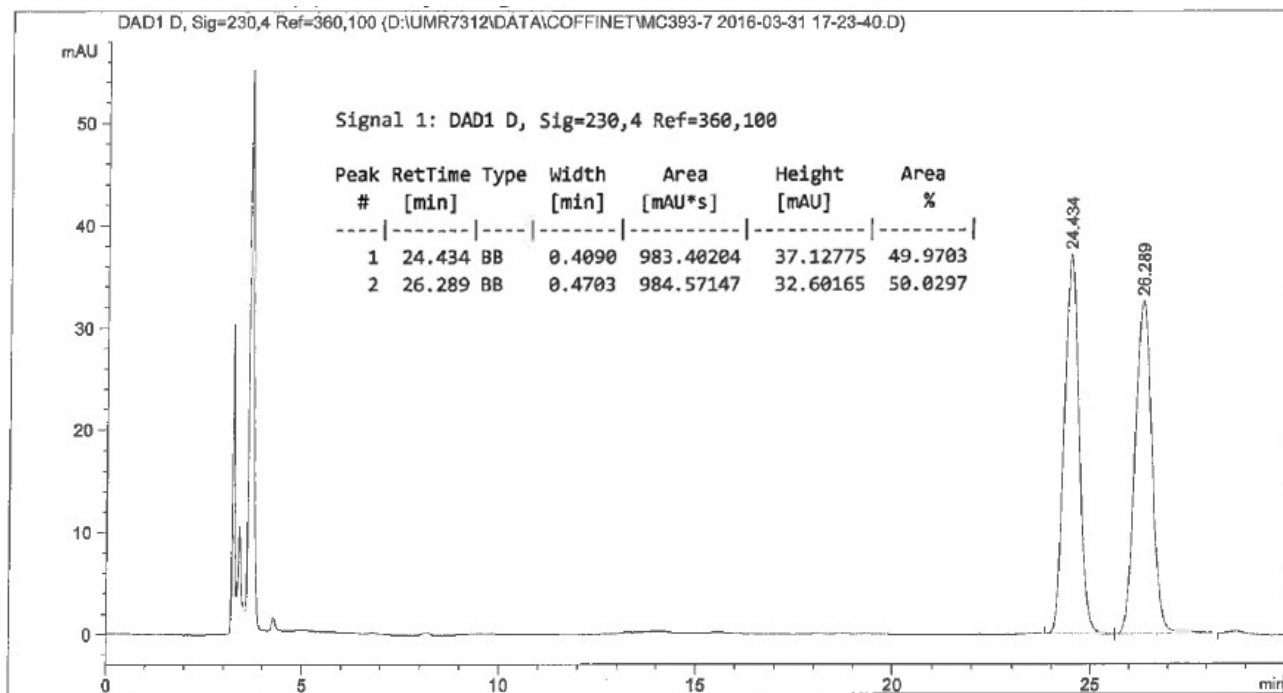
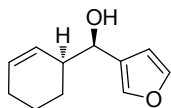
Methyl 4-[(*R*)-[(*S*)-cyclohex-2-en-1-yl](hydroxy)methyl]benzoate 3e



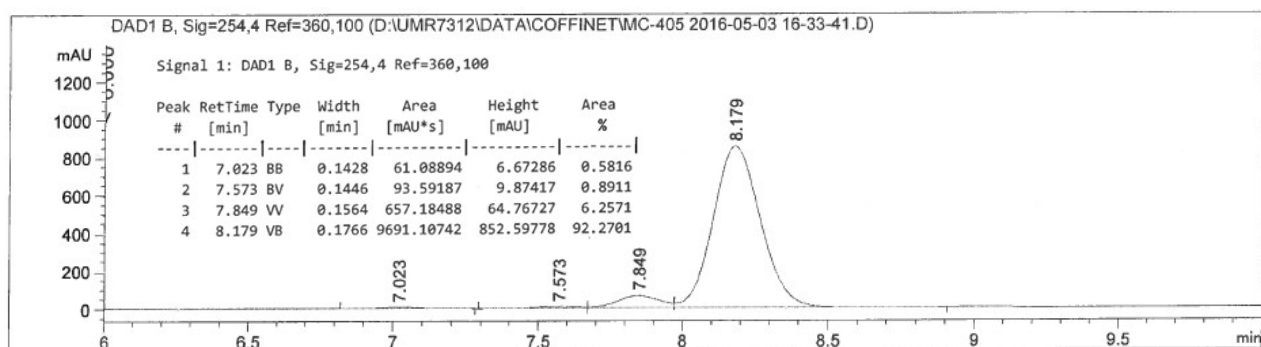
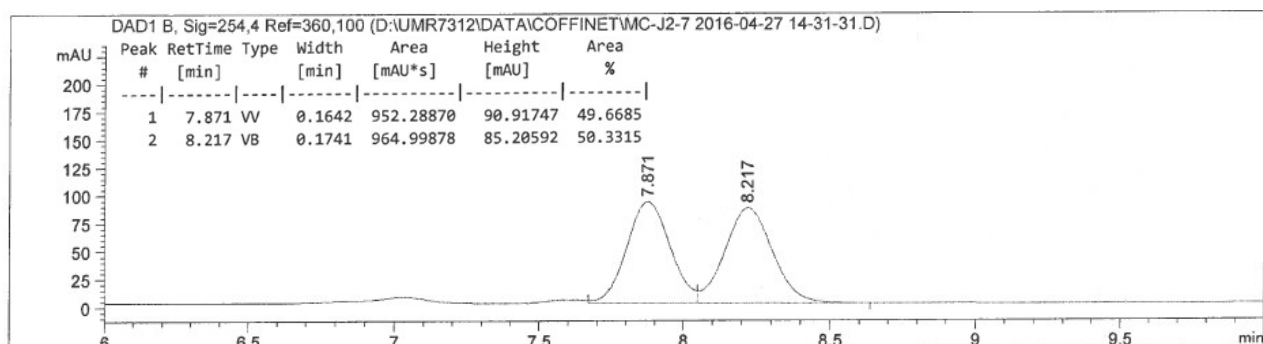
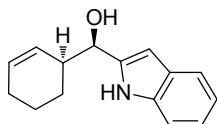
(R)- [(S)-Cyclohex-2-en-1-yl](pyridin-3-yl)methanol 3f



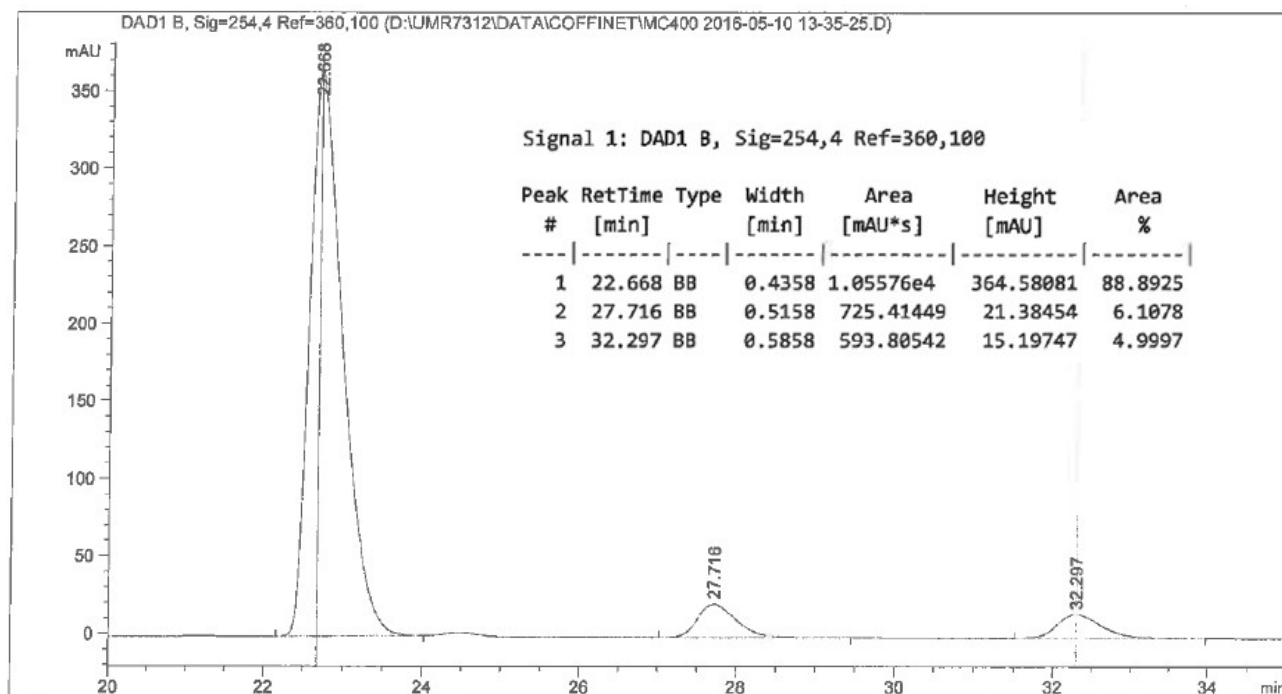
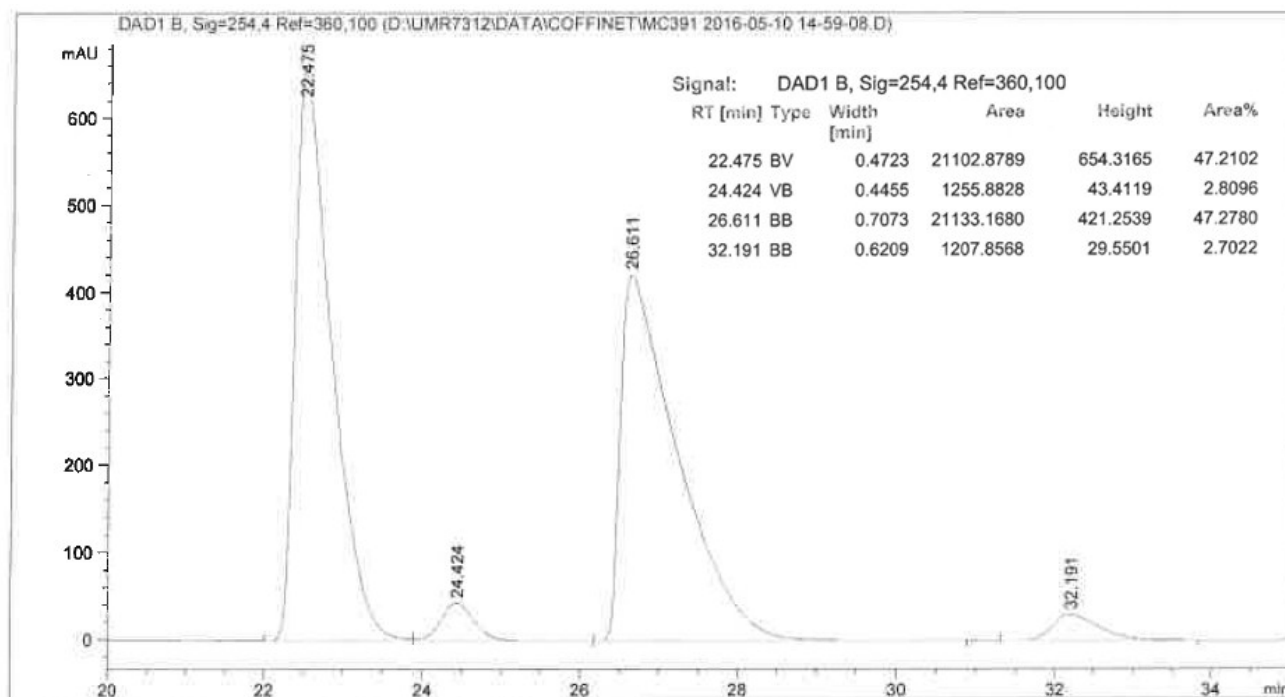
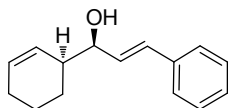
(R)- [(S)-Cyclohex-2-en-1-yl](furan-3-yl)methanol 3g



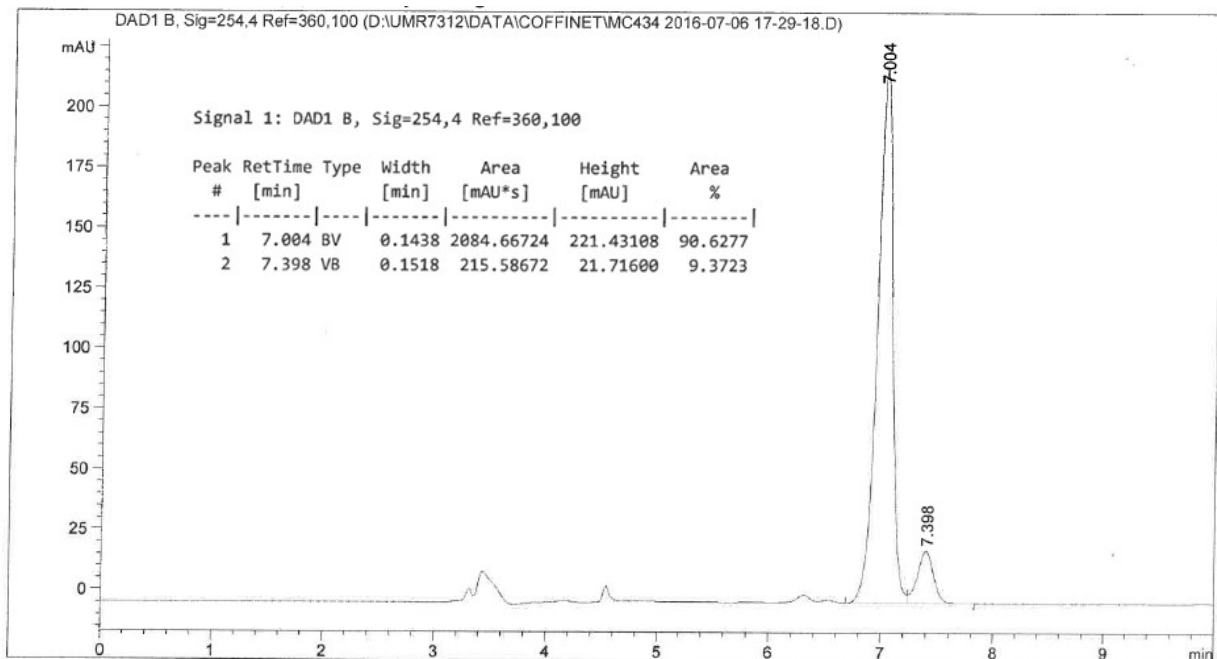
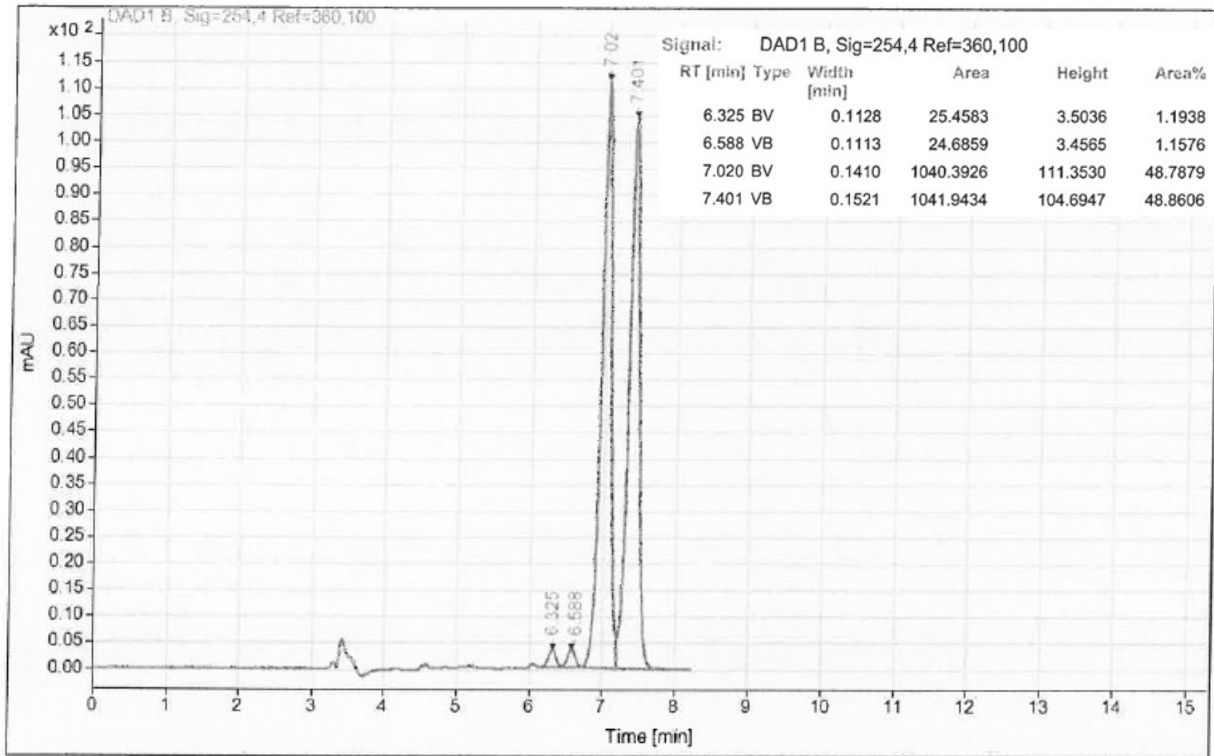
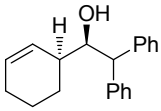
(R)- [(S)-Cyclohex-2-en-1-yl](1H-indol-2-yl)methanol 3h



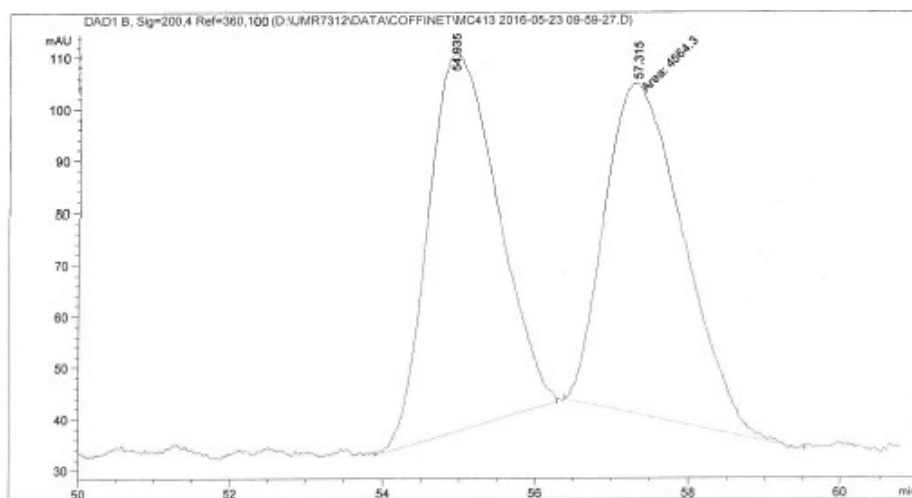
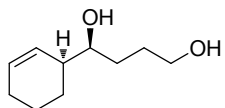
(*S,E*)-1-[(*S*)-Cyclohex-2-en-1-yl]-3-phenylprop-2-en-1-ol 3i



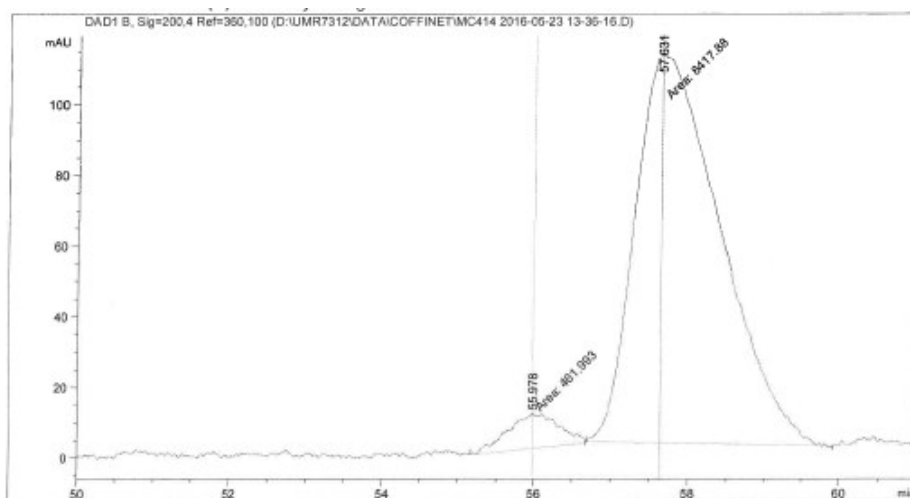
(R)-1-[(S)-Cyclohex-2-en-1-yl]-2,2-diphenylethanol 3j



(S)-1-[(S)-Cyclohex-2-en-1-yl]butane-1,4-diol



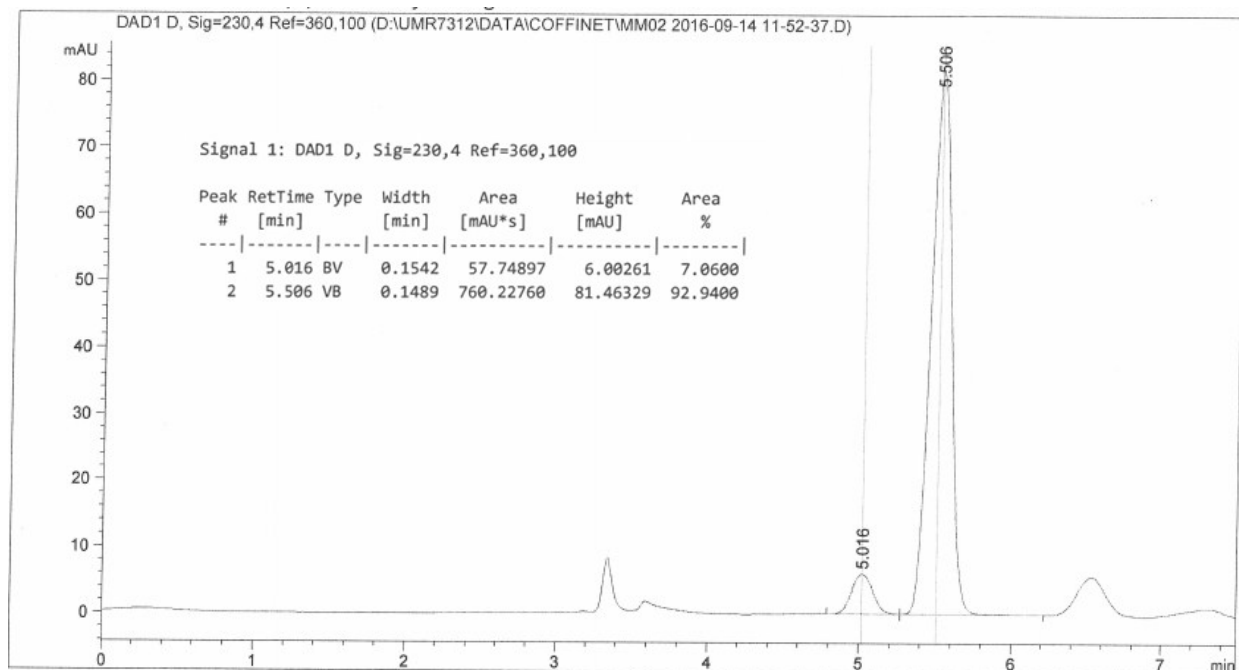
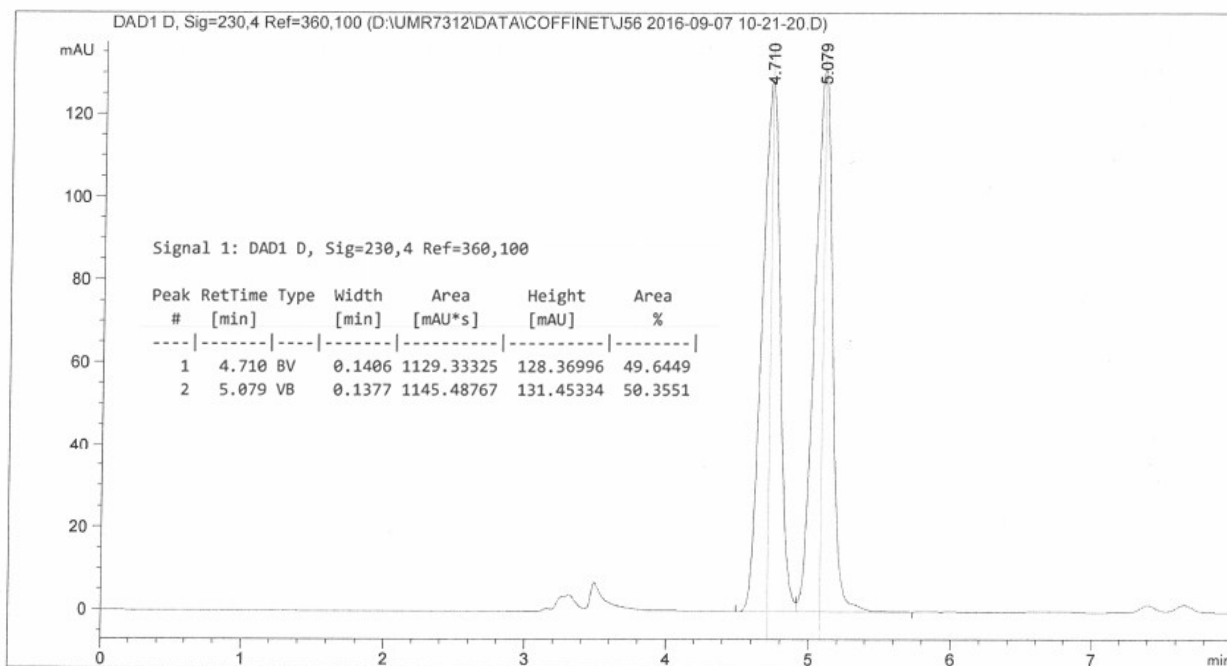
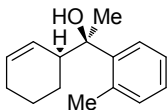
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	54.935	BV	0.7513	4678.54199	73.43497	50.6180
2	57.315	MM T	1.1878	4564.29834	64.04315	49.3820



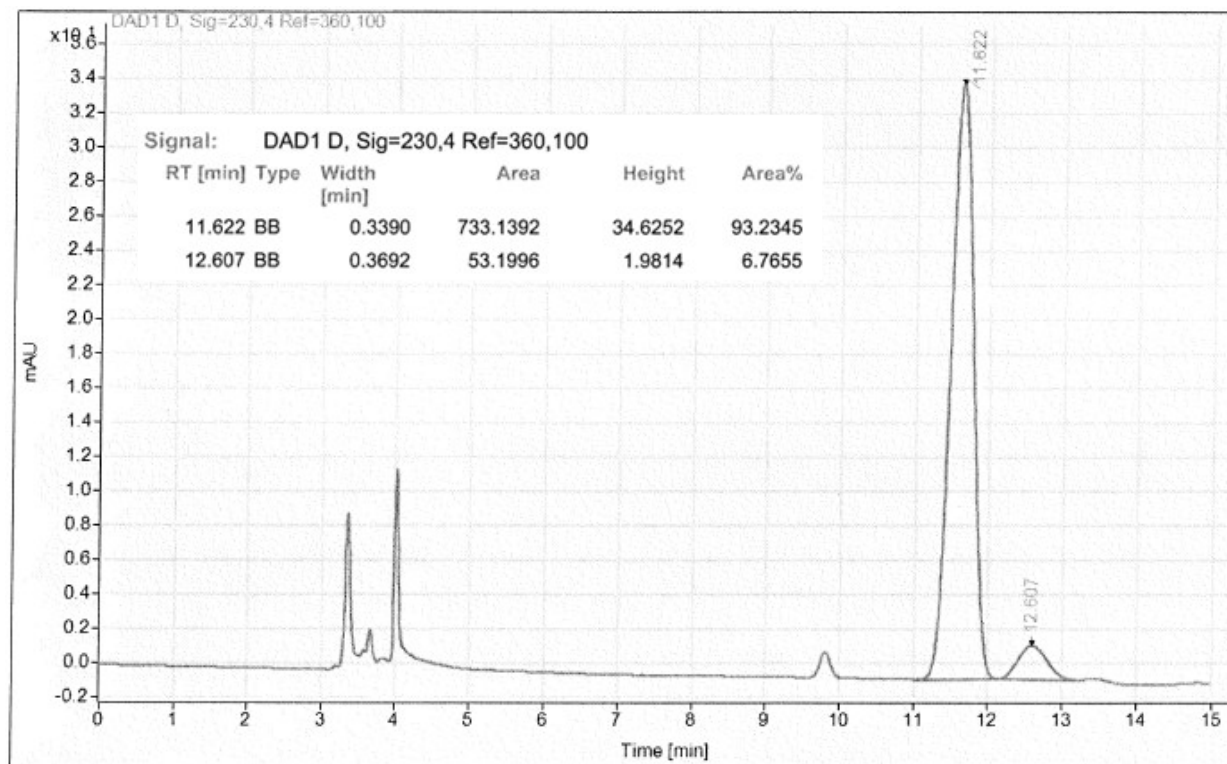
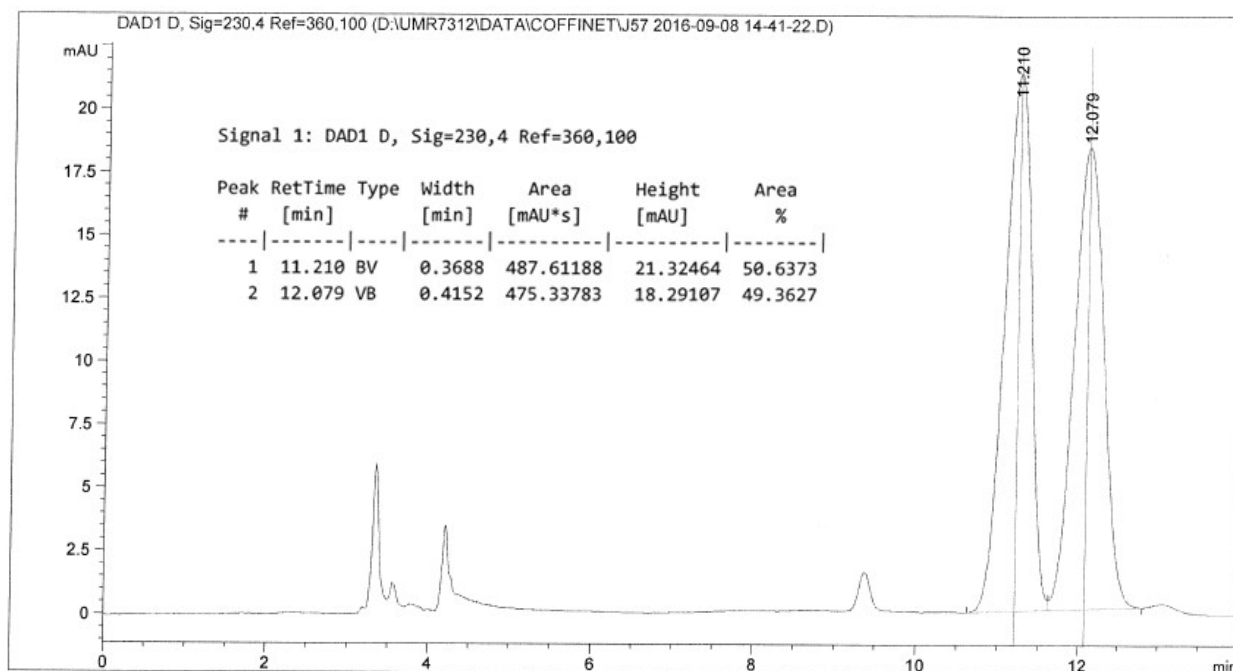
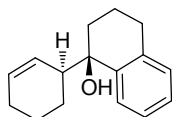
Signal 1: DAD1 B, Sig=200,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	55.978	MM T	0.7912	461.99271	9.73145	5.2027
2	57.631	MM T	1.2817	8417.87793	109.46446	94.7973

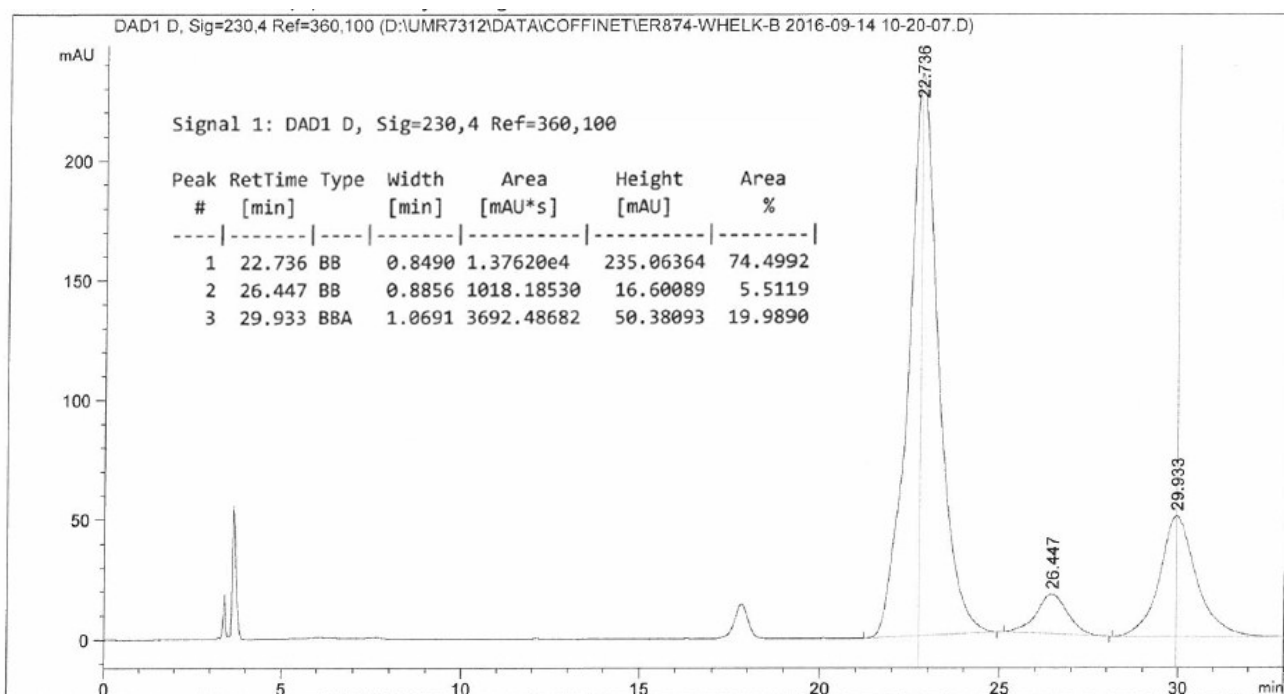
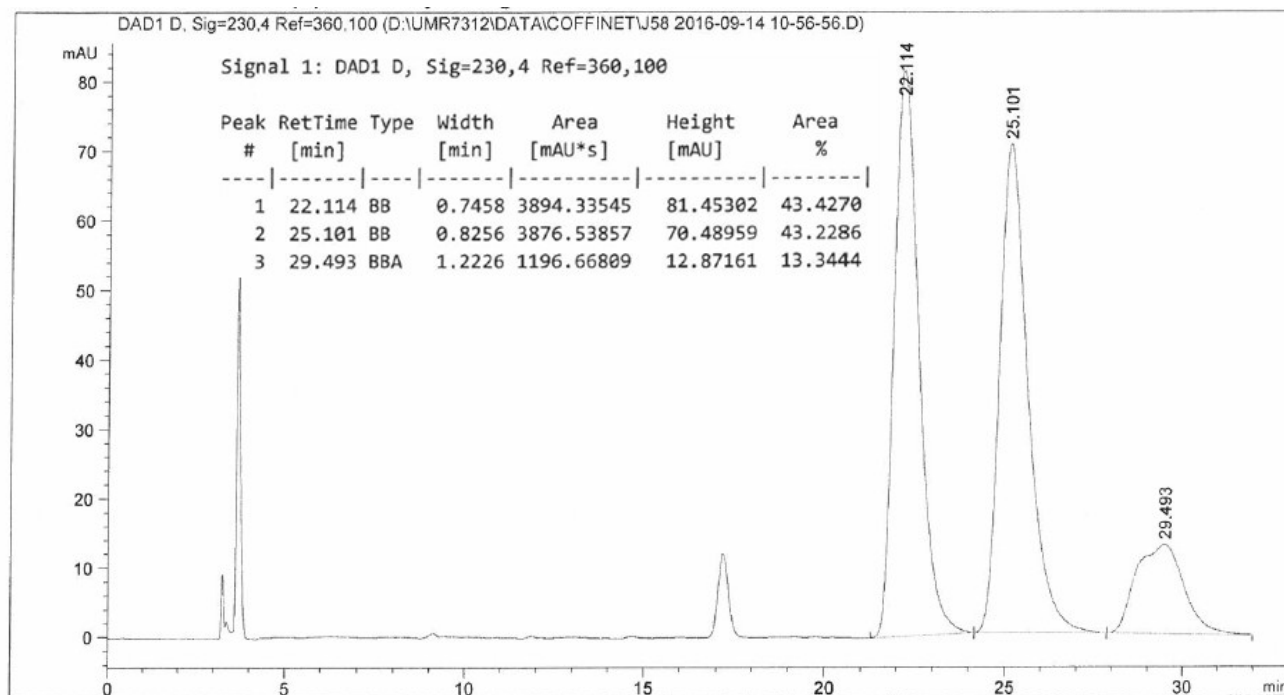
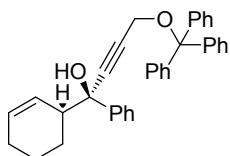
(R)-1-[(S)-Cyclohex-2-en-1-yl]-1-(o-tolyl)ethanol 3n



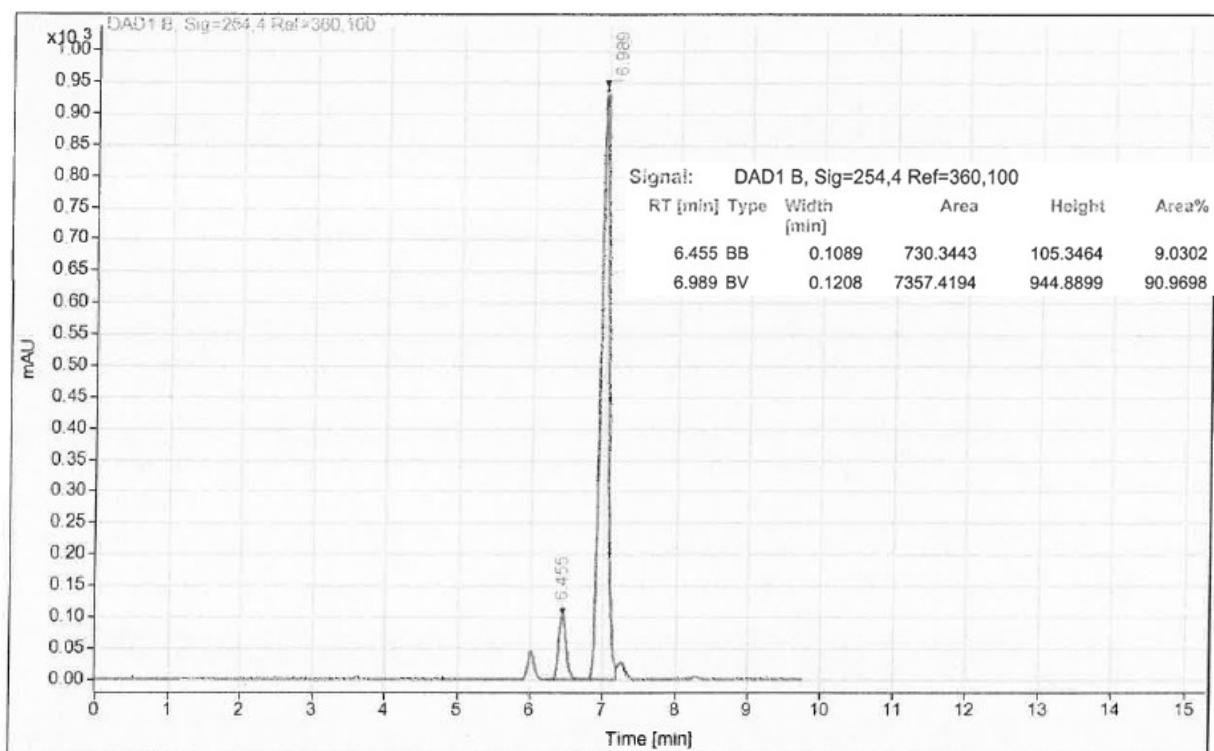
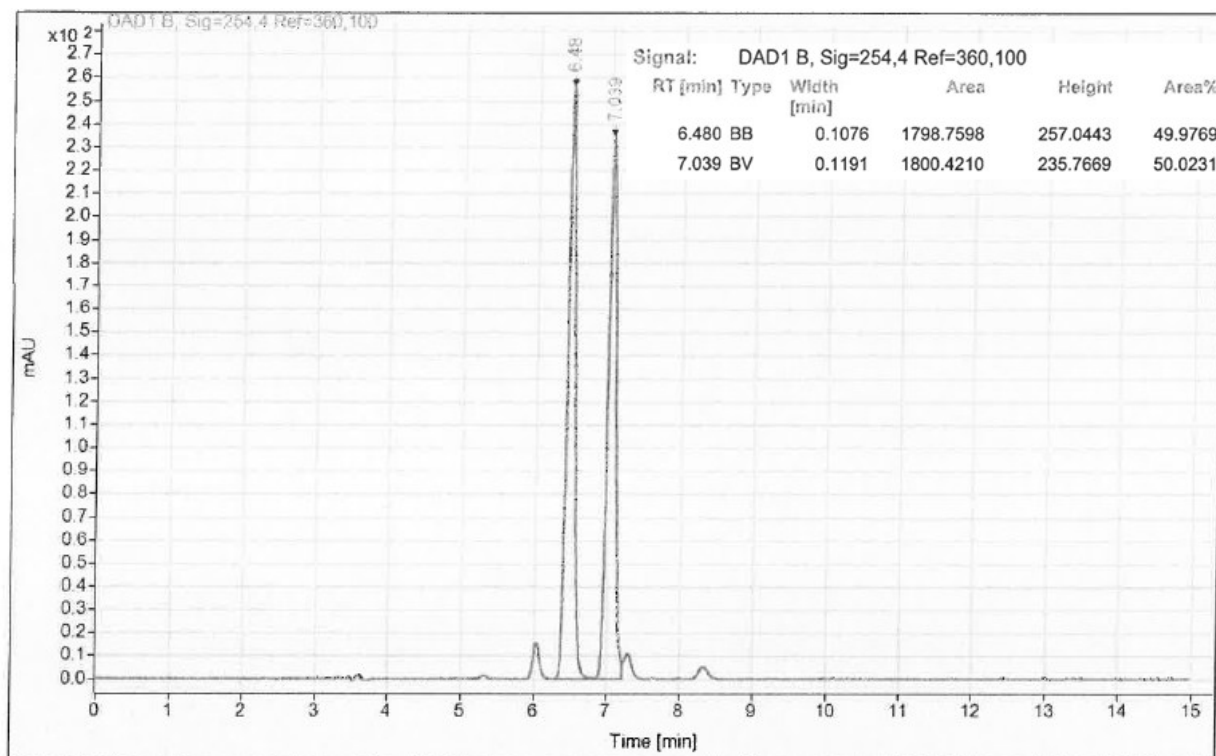
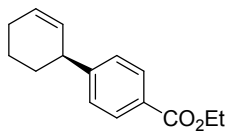
(R)-1-[(S)-cyclohex-2-en-1-yl]-1,2,3,4-tetrahydronaphthalen-1-ol 3o



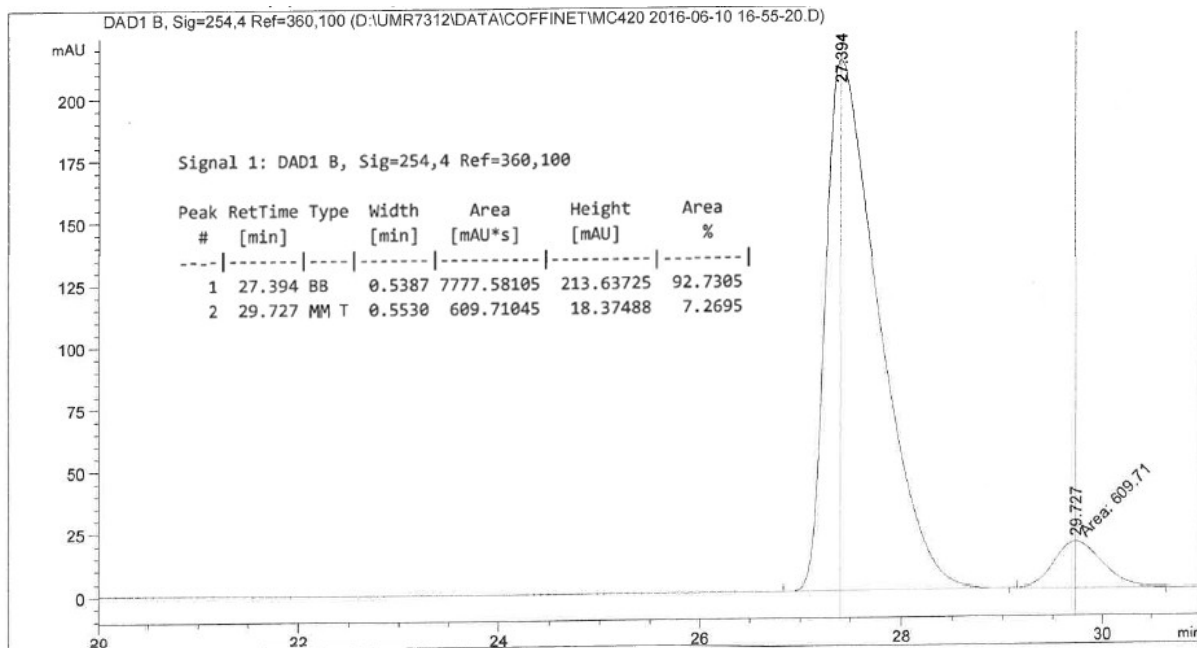
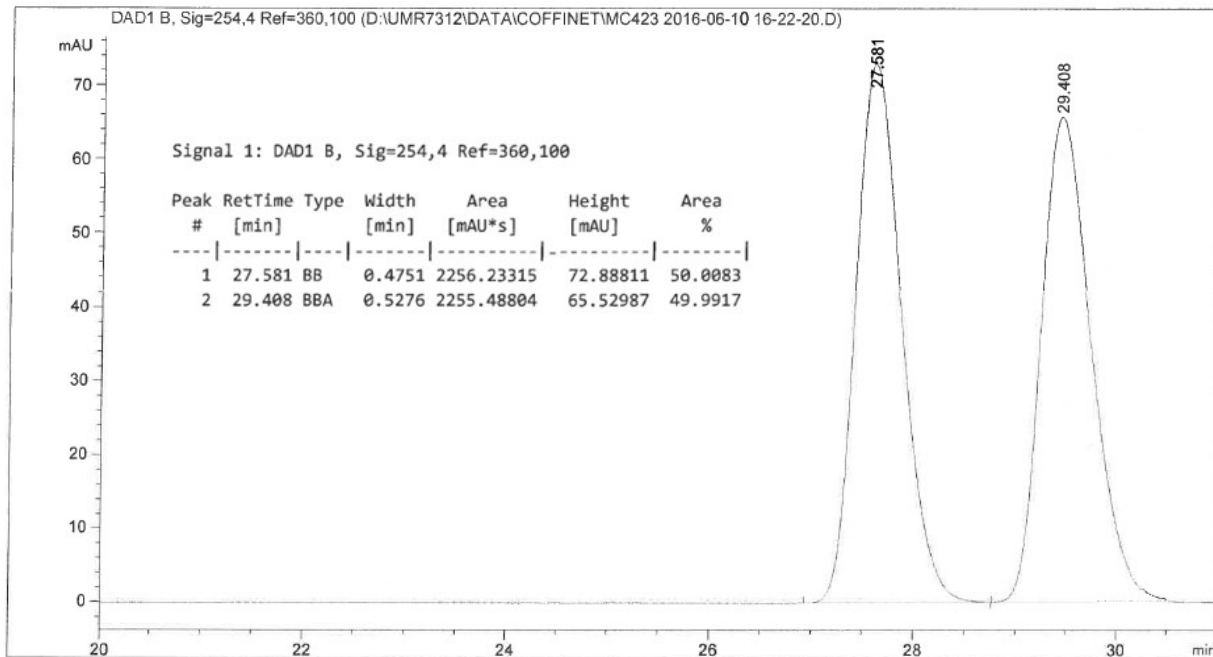
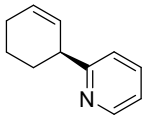
(R)-1-[(S)-cyclohex-2-en-1-yl]-1-phenyl-4-(trityloxy)but-2-yn-1-ol 3p



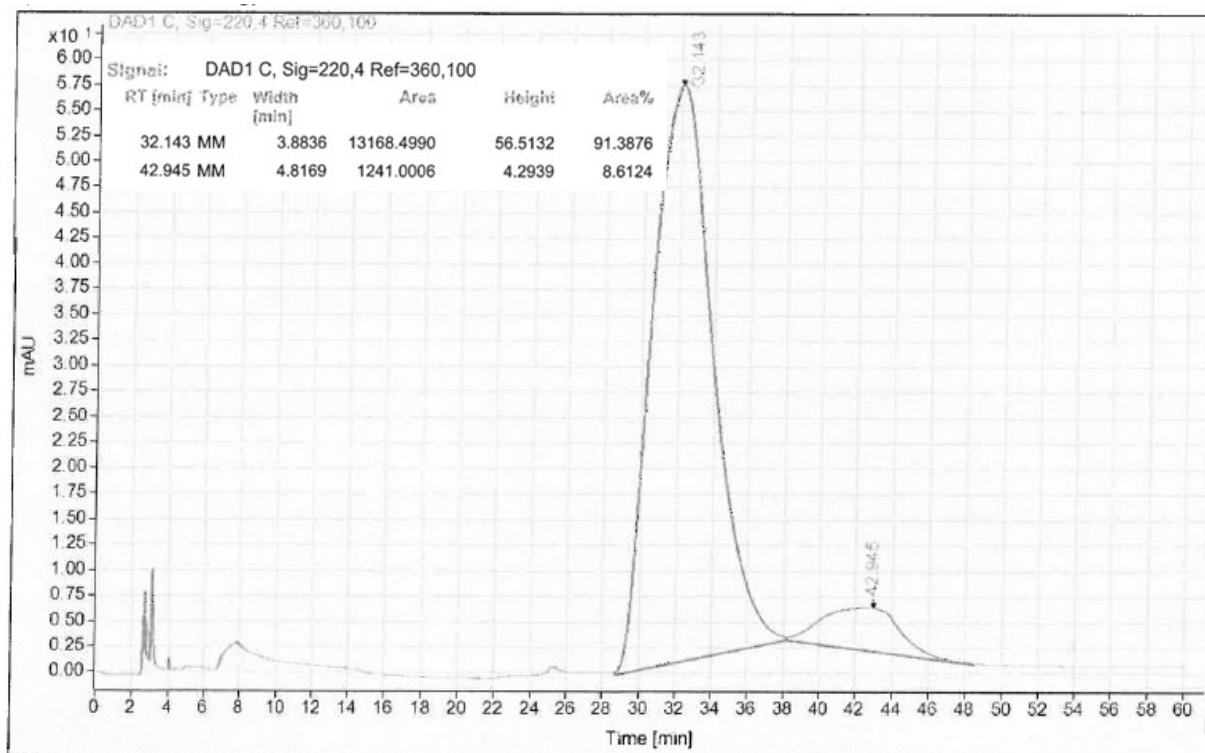
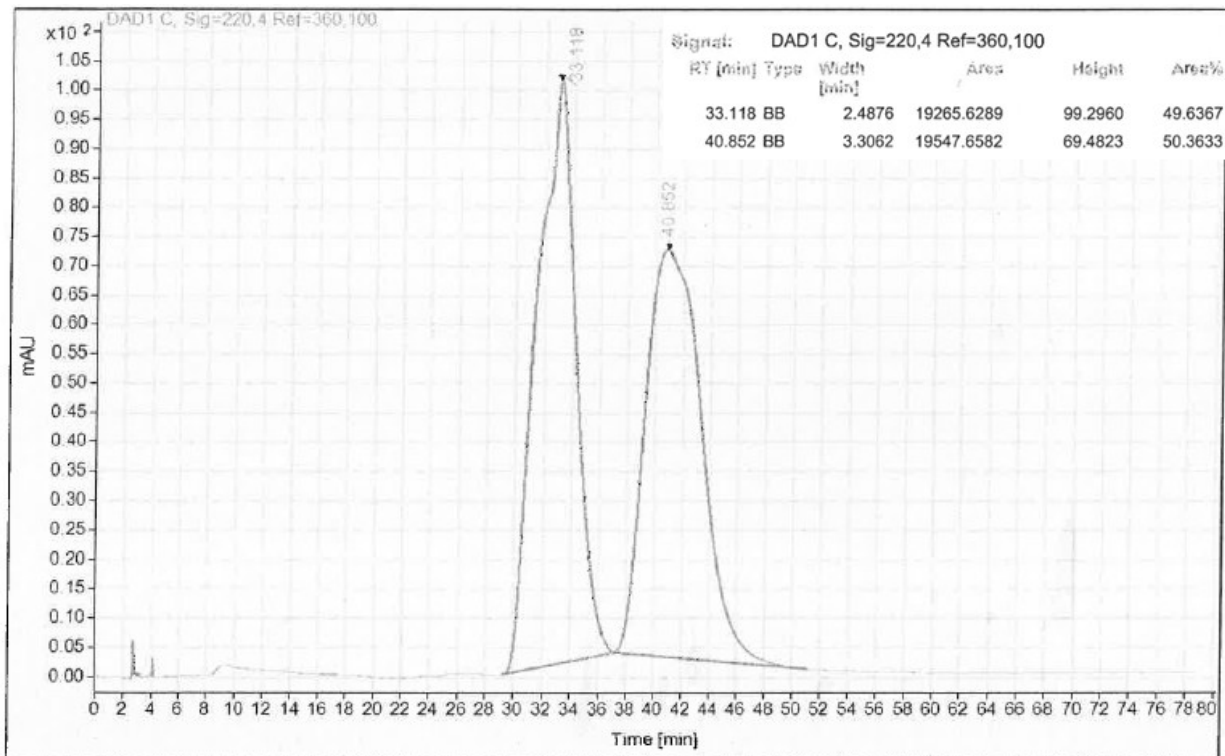
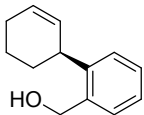
(S)-Ethyl 1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-carboxylate 5b



(S)-2-(Cyclohex-2-en-1-yl)pyridine 5c.



(S)-(1',2',3',4'-Tetrahydro-[1,1'-biphenyl]-2-yl)methanol 5'a



ORTEP diagram of 1''b

