

Supporting Information

A New Family of Cinchona-derived Amino Phosphine Pre-catalysts: Application to the Highly Enantio- and Diastereoselective Silver Catalyzed Isocyanoacetate Aldol Reaction

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1. General Experimental

1.1 Solvents and Reagents

All reagents bought from commercial sources were used as sold. Organic solvents were concentrated under reduced pressure using a Büchi rotary evaporator. Syringes, needles and cannulae were oven dried at 140 °C. Anhydrous dichloromethane, toluene, HNiPr₂ were purified by distillation over calcium hydride. Ethyl acetate used for the enantioselective preparation of oxazolines was dried and stored over 4Å MS. Anhydrous TBME was purchased from Aldrich.

1.2 Chromatography

TLC analyses were performed using Merck aluminium-backed or glass-backed plates pre-coated with silica (0.25 mm, 60 F254) and visualized under UV light (254 nm) and/or by the use of *p*-anisaldehyde using the solvent system indicated. Systems using 'petroleum ether (PE)' refer to light petroleum 40-60 °C. Column chromatography was performed on silica Kieselgel 60 (40-60 µm).

1.3 Spectra

Infrared spectra were recorded on an ATI Matison: Genesis Series FTIR spectrometer from a thin film, with absorption maxima (ν_{\max}) recorded in wavenumbers (cm^{-1}). NMR spectra were recorded using a Bruker Avance 400 MHz or 500 MHz spectrometer, chemical shifts (δ) are quoted in parts per million referenced to the residual solvent peak. The multiplicity of each signal is designated using the following abbreviations; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, brs, broad singlet. Coupling constants (J) are reported in Hertz (Hz). High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat 95XP mass spectrometer. Melting points were obtained using a Griffin melting point apparatus and remain uncorrected.

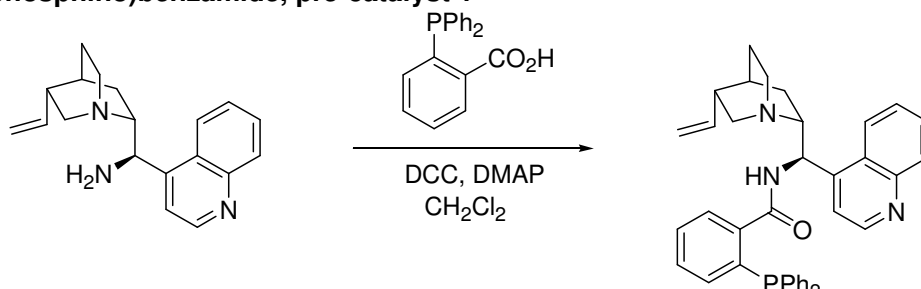
1.4 Starting Materials

Known compounds are indicated by a reference to a previous literature report in their title line. Methyl-isocyano-acetate was purchased from Aldrich. Methyl 2-isocyano-2-phenylacetate **8a** was synthesized by dehydration of the corresponding formamide according to the procedure reported by Zhu et al. for the preparation of methyl 2-isocyano-2-(4-methoxyphenyl)acetate.¹ Methyl 2-isocyano-3-phenylpropanoate **8b** was prepared by dehydration of the corresponding formamide using $\text{POCl}_3/\text{NEt}_3$.

2. Practical Experimental

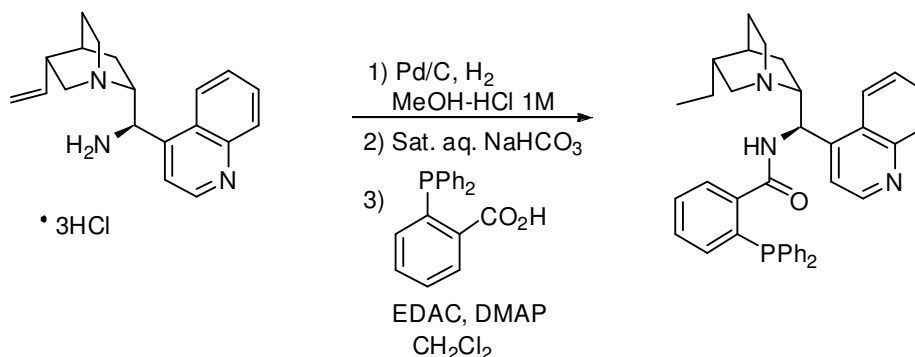
2.1 Preparation of pre-catalysts

2.1.1 Synthesis and characterization of *N*-[(9*R*)-cinchonan-9-yl]-2-(diphenylphosphino)benzamide, pre-catalyst **1**



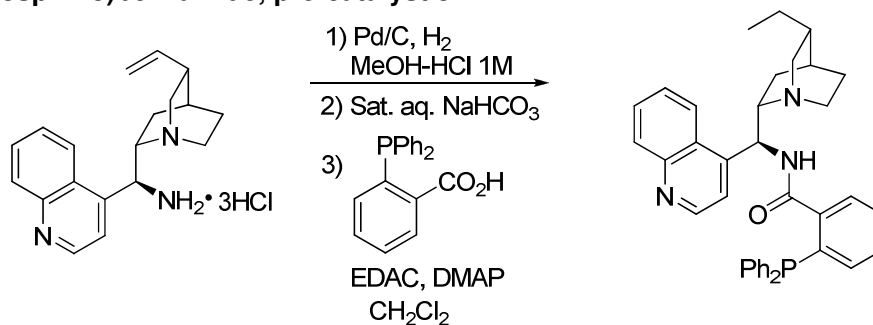
9-Amino(9-deoxy) epicinchonine (120 mg, 0.41 mmol) was dissolved in dry CH_2Cl_2 (2 mL). 2-(diphenylphosphino)benzoic acid (120 mg, 0.39 mmol), 4-dimethylaminopyridine (2.4 mg, 0.020 mmol) and *N,N'*-Dicyclohexylcarbodiimide (88 mg, 0.43 mmol) were sequentially added. The resultant mixture was stirred at room temperature for 24 hours, concentrated under reduced pressure and purified by flash column chromatography (EtOAc/MeOH gradient 100:0 to 100:4) to yield 207 mg (83 %) of **1**. $[\alpha]_D^{28} = +86.0$ (c 0.5, CH_2Cl_2); $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 8.66 (d, $J = 4.5$ Hz, 1 H), 8.28 (d, $J = 8.5$ Hz, 1 H), 8.02 (d, $J = 8.5$ Hz, 1 H), 7.62-7.56 (m, 2 H), 7.49 (t, $J = 7.5$ Hz, 1 H), 7.27-7.16 (m, 12 H), 7.13-7.10 (m, 2 H), 6.83 (dd, $J = 7.4, 4.0$ Hz, 1 H), 5.79 (m, 1 H), 5.32 (brs, 1 H), 5.08 (d, $J = 10.5$ Hz, 1 H), 5.03 (d, $J = 17.5$ Hz, 1 H), 2.83 (brs, 1 H), 2.75-2.66 (m, 4 H), 2.16 (dd, $J = 15.0, 8.0$ Hz, 1 H), 1.52 (s, 1 H), 1.42-1.40 (m, 1 H), 1.36-1.30 (m, 1 H), 1.21-1.16 (m, 1 H), 0.81-0.76 (m, 1 H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) (C-P coupling not removed) δ 168.0, 149.0, 147.4, 140.3, 140.0, 139.0, 136.5, 136.4, 136.0, 135.9, 134.7, 134.4, 133.2, 132.9, 132.7, 132.5, 129.2, 127.9, 127.7, 127.6, 127.5, 127.4, 126.3, 125.4, 124.9, 122.5, 114.0, 59.2, 47.9, 45.7, 38.0, 28.7, 26.2, 25.4, 24.0; $^{31}\text{P-NMR}$ (162 MHz, CDCl_3) δ -10.5; IR $\nu_{\max}/\text{cm}^{-1}$ 2934, 1648, 1508, 1478, 744, 696; MPT 99-101 °C; HRMS (ES+): calcd. for $\text{C}_{38}\text{H}_{37}\text{N}_3\text{O}_1\text{P}_1$ $[\text{M}+\text{H}]^+$ 582.2669, found 582.2658.

2.1.2 Synthesis and characterization of *N*-[(9*R*)-10,11-dihydrocinchonan-9-yl]-2-(diphenylphosphino)benzamide, pre-catalyst **2**



9-Amino(9-deoxy) epicinchonine·3HCl salt (2.024 g, 5.03 mmol) was dissolved in 30 mL of a mixture of 2:1 MeOH/HCl 1M and 10% Pd/C (303 mg) was added. The reaction mixture was stirred under a hydrogen atmosphere for 7 h at room temperature and then filtered through Celite washing with water and MeOH. The filtrate was concentrated under reduced pressure and neutralized with sat. NaHCO₃. The resultant solution was extracted several times with CH₂Cl₂. The combined CH₂Cl₂ extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield a colourless oil which was dissolved in 20 mL of dry CH₂Cl₂. 2-(diphenylphosphino)benzoic acid (1.47 g, 4.80 mmol), 4-dimethylaminopyridine (59 mg, 0.48 mmol) were added. The mixture was cooled to 0 °C, *N*-(3-Dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (920 mg, 4.80 mmol) was added and then the ice bath was removed and the resultant solution was stirred at room temperature for 12 h. CH₂Cl₂ was then removed under reduced pressure and the residue was dissolved in EtOAc and washed with water, 10% NaHCO₃, brine and dried over Na₂SO₄. The organic phase was concentrated under reduced pressure and purified by flash column chromatography (CH₂Cl₂/MeOH 16:1). Impure fractions were further purified by flash column chromatography (EtOAc/CH₂Cl₂/MeOH 5:2:1) to yield 1.70 g (58 %) of **2**. [α]_D²⁵ = + 67.2 (c 0.5, CH₂Cl₂); ¹H-NMR (400 MHz, CDCl₃) δ 8.76 (d, *J* = 4.8 Hz, 1 H), 8.39 (d, *J* = 8.4 Hz, 1 H), 8.12 (d, *J* = 8.4 Hz, 1 H), 7.73-7.58 (m, 4 H), 7.40-7.19 (m, 13 H), 6.92 (dd, *J* = 7.2, 4.0 Hz, 1 H), 5.36 (brs, 1 H), 3.00-2.52 (m, 4 H), 2.49-2.44 (m, 1 H), 1.51 (s, 1H), 1.49-1.30 (m, 5H), 1.29-1.16 (m, 1H), 0.90 (t, *J* = 7.0 Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) (C-P coupling not removed) δ 169.1, 150.1, 148.4, 146.9, 141.4, 141.0, 137.7, 137.6, 137.2, 137.1, 135.9, 135.6, 134.3, 133.9, 133.8, 133.6, 133.5, 130.2, 127.4, 126.5, 123.5, 119.6, 60.3, 51.5, 49.0, 37.2, 27.1, 25.9, 25.7, 25.0, 12.1; ³¹P-NMR (162 MHz, CDCl₃) δ -10.4; IR: ν_{\max} /cm⁻¹ 2933, 2871, 1655, 1458, 744, 696; MPT: 114 °C HRMS (ES⁺): calcd. for C₃₈H₃₉N₃O₁P₁ [M+H]⁺ 584.2825, found 584.2821.

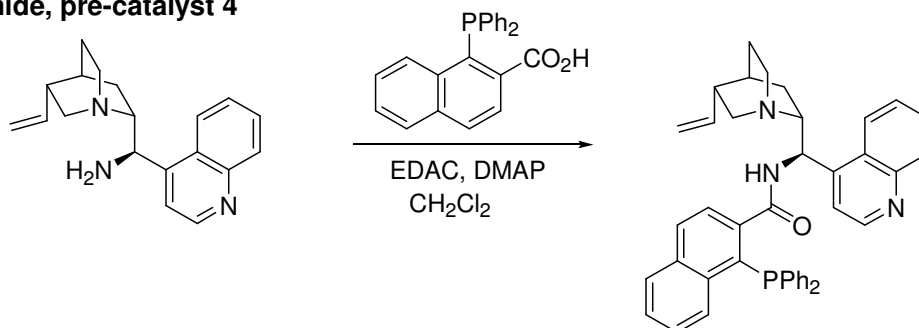
2.1.3 Synthesis and characterization of *N*[(4 β ,8 α ,9S)-10,11-dihydrocinchonan-9-yl]-2-(diphenylphosphino)benzamide, pre-catalyst **3**



9-Amino(9-deoxy) epicinchonine·3HCl salt (1.26 g, 3.13 mmol) was dissolved in 18 mL of a mixture of 2:1 MeOH/HCl 1M and 10% Pd/C (188 mg) was added. The reaction mixture was stirred under a hydrogen atmosphere for 6 h at room temperature and then filtered through Celite washing with water and MeOH. The filtrate was concentrated under reduced pressure and neutralized with sat. NaHCO₃. The resultant solution was extracted several times with CH₂Cl₂. The combined CH₂Cl₂ extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield a colourless oil which was dissolved in 20 mL of dry CH₂Cl₂. 2-(diphenylphosphino)benzoic acid (961 mg, 3.14 mmol), 4-dimethylaminopyridine (38 mg, 0.31 mmol) were added. The mixture was cooled to 0 °C, *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (602 mg, 3.14 mmol) was added

and then the ice bath was removed and the resultant solution was stirred at room temperature for 12 h. CH_2Cl_2 was then removed under reduced pressure and the crude material was dissolved in EtOAc and washed with water, 10% aq. NaHCO_3 , brine and dried over Na_2SO_4 . The organic phase was concentrated under reduced pressure and purified by flash column chromatography (EtOAc to EtOAc/ CH_2Cl_2 /MeOH 5:2:1) to yield 1.20 g (66%, 2 steps) of **3**. $[\alpha]_D^{28} = -4.4$ (c 1, CH_2Cl_2); **$^1\text{H-NMR}$** (400 MHz, CDCl_3) δ 8.78 (d, $J = 4.4$ Hz, 1 H), 8.40 (d, $J = 8.4$ Hz, 1 H), 8.10 (dd, $J = 8.4, 0.8$ Hz, 1 H), 7.70 (t, $J = 6.8$ Hz, 1 H), 7.63 (dd, $J = 6.8, 3.6$ Hz, 1 H), 7.58 (t, $J = 7.2$, 1 H), 7.42-7.21 (m, 12 H), 7.18 (td, $J = 7.2, 1.6$ Hz, 1 H), 6.91 (s, 1 H), 5.36 (brs, 1 H), 3.03 (dd, $J = 13.6, 10$ Hz, 2 H), 2.85 (brs, 1 H), 2.49-2.61 (m, 1 H), 2.11-2.25 (m, 1 H), 1.80-1.60 (m, 4 H), 1.25-1.08 (m, 3 H), 0.91-0.84 (m, 1 H), 0.76 (t, $J = 7.6$ Hz, 3 H); **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3) (C-P coupling not removed) δ 169.1, 150.1, 148.5, 141.4, 141.2, 137.7, 137.5, 137.2, 137.1, 135.8, 135.6, 134.4, 133.8, 133.6, 130.2, 129.0, 128.8, 128.7, 128.6, 128.5, 127.4, 126.6, 123.7, 119.5, 60.2, 57.3, 51.5, 40.9, 37.0, 28.2, 27.3, 25.5, 25.1, 12.0; **$^{31}\text{P-NMR}$** (162 MHz, CDCl_3) δ -10.87; **IR** $\nu_{\text{max}}/\text{cm}^{-1}$ 2360, 1648, 1508, 1458, 744, 696; **MPT** 107-109 °C; **HRMS** (ES+): calcd. for $\text{C}_{38}\text{H}_{39}\text{N}_3\text{O}_1\text{P}_1$ $[\text{M}+\text{H}]^+$ 584.2825, found 584.2815.

2.1.4 Synthesis and characterization of *N*-[(9*R*)-cinchonan-9-yl]-1-(diphenylphosphino)-2-naphthamide, pre-catalyst **4**



9-Amino(9-deoxy) epinonine (270 mg, 0.92 mmol), 1-(diphenylphosphino)-2-naphthoic acidⁱⁱ (258 mg, 0.72 mmol) and 4-dimethylaminopyridine (8.8 mg, 0.072 mmol) were dissolved in dry CH_2Cl_2 (4 mL). The reaction mixture was cooled with an ice/salt bath and solid *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (138 mg, 0.72 mmol) was added. The flask was gently warmed to room temperature and stirred for 16 h. The reaction mixture was diluted with EtOAc, washed with water, brine and dried over Na_2SO_4 . The organic phase was concentrated under reduced pressure and purified by flash column chromatography (CH_2Cl_2 /MeOH 13:1) to yield 248 mg (54 %) of **4**. $[\alpha]_D^{25} = +61.7$ (c 1.75, CH_2Cl_2); **$^1\text{H-NMR}$** (400 MHz, CDCl_3) δ 8.80 (d, $J = 4.4$ Hz, 1 H), 8.38 (d, $J = 8.4$ Hz, 1 H), 8.06 (d, $J = 8.4$ Hz, 1 H), 7.85 (d, $J = 8.4$ Hz, 1 H), 7.70 (d, $J = 8.4$ Hz, 2 H), 7.62 (t, $J = 7.2$ Hz, 1 H), 7.50 (d, $J = 4.4$ Hz, 2 H), 7.34 (q, $J = 6.8$ Hz, 5 H), 7.25 (t, $J = 7.6$ Hz, 1 H), 7.18-7.10 (m, 7 H), 7.01 (t, $J = 8.4$ Hz, 1 H), 5.85-5.76 (m, 1 H), 5.48 (brs, 1 H), 5.09 (d, $J = 10.4$, 1 H), 5.03 (d, $J = 17.6$ Hz, 1 H), 3.20-2.20 (m, 4 H), 2.07 (s, 1 H), 1.51 (s, 1 H), 1.40-1.10 (m, 4 H), 0.83 (s, 1 H); **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3) (C-P coupling not removed) δ 170.1, 150.1, 148.6, 147.3, 146.8, 140.2, 136.4, 136.3, 135.6, 135.5, 134.5, 133.9, 132.2, 131.9, 131.8, 131.6, 131.4, 130.4, 129.1, 129.1, 128.3, 128.2, 127.9, 127.6, 126.4, 126.3, 124.2, 124.1, 123.7, 115.0, 60.29, 49.0, 46.3, 39.0, 29.7, 27.3, 26.5, 25.3; **$^{31}\text{P-NMR}$** (162 MHz, CDCl_3) δ -12.6; **IR** $\nu_{\text{max}}/\text{cm}^{-1}$ 1654, 1508, 1482, 744, 696, 570; **MPT** 108-110 °C; **HRMS** (ES+): calcd. for $\text{C}_{42}\text{H}_{39}\text{N}_3\text{O}_1\text{P}_1$ $[\text{M}+\text{H}]^+$ 632.2825, found 632.2822.

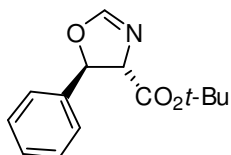
2.2 General procedure for the enantioselective synthesis of oxazolines (**4S**, **5R**)-**7a-7d**, (**4S**, **5R**)-**7f**, (**4R**, **5R**)-**9a**-(**4R**, **5R**)-**9g**

Pre-catalyst **2** (6.7 mg, 0.011 mmol) was dissolved in 0.7 mL of solvent (EtOAc or TBME as specified for each compound) and Ag_2O (1.2 mg, 0.0051 mmol) was added. The heterogeneous mixture was stirred for approximately 2 minutes and then the isocyanoacetate (1.0 equivalents) and powdered 4Å MS were sequentially added. The flask was cooled in a dry ice/acetone bath and the aldehyde (1.2 or 1.7 equivalents as specified for each compound) was added. The flask was then quickly transferred in a -20 °C fridge and the reaction mixture was stirred for the amount of time specified, until all the isocyanoacetate was consumed (typically 16-24 hours as judged by TLC,

p-anisaldehyde). The reaction mixture was then quickly filtered through a short pad of silica (in a glass pipette) and eluted with EtOAc. The filtrate was concentrated under reduced pressure and treated in the way described for each compound.

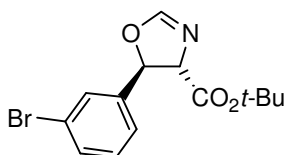
Enantioenriched (4*R*, 5*S*)-**7a** was prepared in identical fashion using pseudo-enantiomeric pre-catalyst **3** instead of pre-catalyst **2**.

2.3 Synthesis and characterization of *tert*-butyl (4*S*,5*R*)-5-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7a**



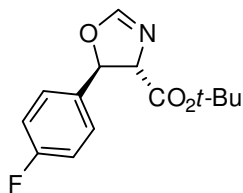
Obtained according to the general procedure, using *tert*-butyl-isocyanoacetate (0.21 mmol, 30 mg) and benzaldehyde (0.25 mmol, 26 μ L) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1) to yield 37 mg (72 %) of product as a colourless oil. $[\alpha]_D^{25} = +99.6$ (c 0.64, CH₂Cl₂); **¹H-NMR** (500 MHz, CDCl₃) δ 7.40-7.20 (m, 5 H, Ar-H), 7.08 (d, $J = 2.0$ Hz, 1 H, N=CH), 5.60 (d, $J = 8.0$, 1 H), 4.51 (dd, $J = 8.0, 2.0$ Hz, 1 H), 1.52 (s, 9 H, ^tBu); **¹³C-NMR** (125 MHz, CDCl₃) δ 169.5 (s, 1C, C=O), 156.0 (d, 1C, C=N), 139.2 (s, 1C, Ph), 128.9 (d, 2C, Ph), 125.6 (d, 2C, Ph), 82.5 (s, 1C, ^tBu), 82.3 (d, 1C), 76.2 (d, 1C), 28.0 (q, 3C, ^tBu); **IR** $\nu_{\max}/\text{cm}^{-1}$ 2978, 1732, 1688, 1626, 1370, 1156, 1106; **HRMS** (ES⁺): calcd. for C₁₄H₁₇N₁O₃Na₁ [M+Na]⁺ 270.1101, found 270.1095. The ee (96%) was calculated after conversion to the *N*-benzoylated amino ester **S1**, using the same procedure described in section 2.18.

2.4 Synthesis and characterization of *tert*-butyl (4*S*,5*R*)-5-(3-bromophenyl)-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7b**



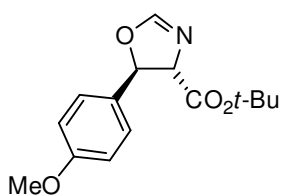
Obtained according to the general procedure, using *tert*-butylisocyanoacetate (0.21 mmol, 30 mg) and 3-bromo-benzaldehyde (0.36 mmol, 42 μ L) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1) to yield 47 mg (69 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 6.23 min., t (minor) = 8.20 min. (92%). $[\alpha]_D^{25} = +168.2$ (c 1, CH₂Cl₂); **¹H-NMR** (500 MHz, CDCl₃) δ 7.41-7.10 (m, 4 H, Ar-H), 7.08 (d, $J = 2.0$ Hz, 1 H, N=CH), 5.60 (d, $J = 8.0$, 1 H), 4.51 (dd, $J = 8.0, 2.0$ Hz, 1 H), 1.52 (s, 9 H, ^tBu); **¹³C-NMR** (125 MHz, CDCl₃) δ 169.2 (s, 1C, C=O), 155.9 (d, 1C, C=N), 141.5 (s, 1C, Ph), 131.7 (d, 1C, Ph), 130.5 (d, 1C, Ph), 128.6 (d, 1C, Ph), 124.1 (d, 1C, Ph), 123.0 (s, 1C, Ph), 82.9 (s, 1C, ^tBu), 81.3 (d, 1C), 76.2 (d, 1C), 28.0 (q, 3C, ^tBu); **IR** $\nu_{\max}/\text{cm}^{-1}$ 2978, 1732, 1626, 1368, 1154, 1102; **HRMS** (ES⁺): calcd. for C₁₄H₁₇BrNO₃ [M+H]⁺ 326.0386, found 326.0382.

2.5 Synthesis and characterization of *tert*-butyl (4*S*,5*R*)-5-(4-fluorophenyl)-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7c**



Obtained according to the general procedure, using *tert*-butylisocyanoacetate (0.21 mmol, 30 mg) and 4-fluoro-benzaldehyde (0.36 mmol, 38 μ L) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc) 3.5:1 to yield 43 mg (77 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 220 nm, 1.0 mL/min] t (major) = 5.75 min., t (minor) = 7.37 min. (92%). $[\alpha]_D^{25} = +248.4$ (c 1.5, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.49-7.45 (m, 2 H, Ar-H), 7.28-7.24 (m, 3 H, Ar-H and N=CH), 5.76 (d, $J = 8.0$ Hz, 1 H), 4.65 (dd, $J = 8.0, 2.0$ Hz, 1 H), 1.70 (s, 9 H, ^tBu); **¹³C-NMR** (125 MHz, CDCl₃) δ 169.3 (s, 1C, C=O), 162.8 (d, $J_{\text{C-F}} = 247.7$ Hz, 1C, C-F), 155.9 (d, 1C, C=N), 135.00 (d, $J_{\text{C-F}} = 3.0$ Hz, 1C, Ph), 127.45 (d, $J_{\text{C-F}} = 8.2$ Hz, 2C, Ph), 115.9 (d, $J_{\text{C-F}} = 21.7$ Hz, 2C, Ph), 82.7 (s, 1C, ^tBu), 81.6 (d, 1C), 76.2 (d, 1C), 27.9 (q, 3C, ^tBu); **IR** $\nu_{\max}/\text{cm}^{-1}$ 1732, 1626, 1512, 1156, 1104; **HRMS** (ES⁺): calcd. for C₁₄H₁₇FNO₃ [M+H]⁺ 266.1187, found 266.1184.

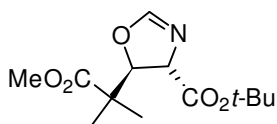
2.6 Synthesis and characterization of *tert*-butyl (4*S*,5*R*)-5-(4-methoxyphenyl)-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7d**



Obtained according to the general procedure, using *tert*-butylisocynoacetate (0.21 mmol, 30 mg) and *p*-anisaldehyde (0.36 mmol, 43 μ L) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 2:1) to yield 35 mg (60 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 7.74 min., t (minor) = 8.95 min. (89%).

$[\alpha]_D^{27} = +118.4$ (c 0.25, CH_2Cl_2); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 7.19-7.16 (m, 2 H, Ar-H), 6.98 (d, $J = 2.0$ Hz, 1 H, N=CH), 6.85-6.83 (m, 2 H, Ar-H), 5.48 (d, $J = 8.0$ Hz, 1 H), 4.41 (dd, $J = 8.0, 2.0$ Hz, 1 H), 3.71 (s, 3 H, O-CH₃), 1.44 (s, 9 H, ^tBu); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 169.6 (s, 1C, C=O), 159.9 (d, 1C, C=N), 156.0 (s, 1C, Ph), 131.1 (s, 1C, Ph), 127.2 (d, 2C, Ph), 114.2 (d, 2C, Ph), 82.4 (s, 1C, ^tBu), 82.3 (d, 1C), 76.0 (d, 1C), 27.9 (q, 3C, ^tBu); **IR** $\nu_{\text{max}}/\text{cm}^{-1}$ 1732, 1624, 1516, 1252, 1156, 1106. **HRMS** (ES⁺): calcd. for $\text{C}_{15}\text{H}_{19}\text{NNaO}_4$ [M+Na]⁺ 300.1206, found 300.1224.

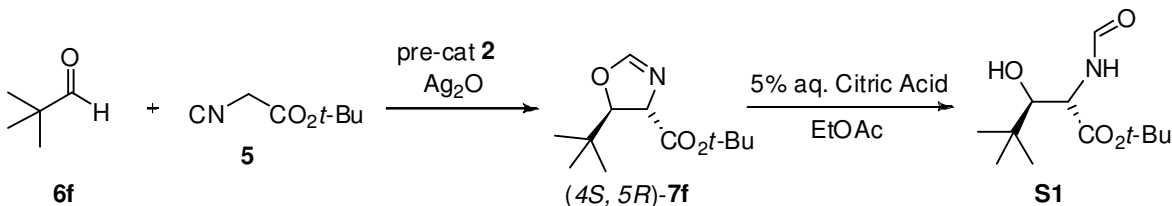
2.7 Synthesis and characterization of *tert*-butyl (4*S*,5*R*)-5-(1-methoxy-2-methyl-1-oxopropan-2-yl)-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7e**



Pre-catalyst **2** (10.2 mg, 0.0175 mmol) was dissolved in 1.2 mL of EtOAc and Ag_2O (2.02 mg, 0.0087 mmol) was added. The heterogeneous mixture was stirred for approximately 2 minutes and isocyanide **5** (50 mg, 0.35 mmol) and powdered 4 \AA MS were sequentially added. The flask was cooled in a ice/NaCl bath and the 2,2-Dimethyl-3-oxo-propionic acid methyl ester (78 mg, 0.60 mmol) was added. The flask was then transferred in a 0 $^\circ\text{C}$ fridge and the reaction mixture was stirred overnight, until all the isocyanide was consumed (TLC, *p*-anisaldehyde). The reaction mixture was then quickly filtered through a short pad of silica (in a glass pipette) and eluted with EtOAc. The filtrate was concentrated under reduced pressure and quickly purified by flash column chromatography (PE/EtOAc 3:1) to yield compound **7e** as a colourless oil (85 mg, 89%). The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 95:5, λ 210 nm, 1.0 mL/min] t (major) = 6.38 min., t (minor) = 7.03 min. (81%); $[\alpha]_D^{25} = +179.4$ (c 0.82, CH_2Cl_2); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 6.88 (d, $J = 2.0$, 1 H, H-C=N), 4.83 (d, $J = 7.3$ Hz, 1 H), 4.32 (dd, $J = 7.3, 2.0$ Hz, 1 H), 3.69 (s, 3 H, CO₂-CH₃), 1.48 (s, 9 H, ^tBu-H), 1.21 (s, 3 H, CH₃), 1.15 (s, 3 H, CH₃); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) 175.0 (s, 1C, ROC=O), 169.8 (s, 1C, ROC=O), 156.1 (d, 1C, C=N), 85.2 (d, 1C), 82.2 (s, 1C, Me₃C-O), 70.0 (d, 1C), 52.2 (q, 1C, CO₂-CH₃), 45.4 (s, 1C, -C(CH₃)₂(CO₂Me)), 27.8 (q, 3C, ^tBu), 20.5 (q, 1C, CO₂MeC-CH₃), 19.8 (q, 1C, CO₂MeC-CH₃); **IR** $\nu_{\text{max}}/\text{cm}^{-1}$ 2980, 1737, 1628, 1157, 1108; **HRMS** (ES⁺): calcd. for $\text{C}_{13}\text{H}_{21}\text{NNaO}_5$ [M+Na]⁺ 294.1312, found 294.1317.

2.8 Synthesis and characterization of (2*S*,3*R*)-*tert*-butyl 2-formamido-3-hydroxy-4,4-dimethylpentanoate, compound **S1**

Due to its instability towards silica gel, compound **7f** was directly converted to the corresponding formamide **S1** and characterized as such.

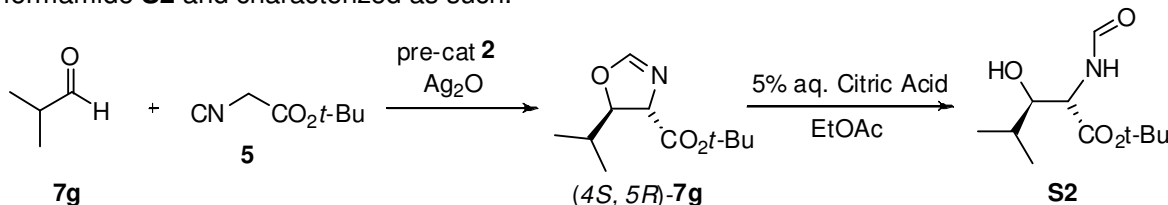


Compound **7f** was obtained according to the general procedure, using *tert*-butylisocynoacetate (0.21 mmol, 30 mg) and pivalaldehyde (0.25 mmol, 27 μ L) as starting materials and EtOAc as solvent. The crude reaction mixture was dissolved in 2.5 mL of EtOAc saturated with 5% solution of Citric acid and stirred until complete conversion of the starting material (TLC, about 6-8 hours). The organic phase was washed with 5% aq. NaHCO_3 sol., dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield 42 mg (81 %) of formamide **S1**. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 80:20, λ 210 nm, 1.0 mL/min] t (minor) = 4.62 min., t (major) = 6.66 min. (91%); $[\alpha]_D^{27} = -20.1$ (c 0.25, CH_2Cl_2); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.21 (s, 1 H, H-

C=O), 6.59 (d, $J = 8.4$ Hz, 1 H, N-H), 4.74 (d, 9.2 Hz, 1 H, C $_{\alpha}$ -H), 3.72 (s, 1 H, C $_{\beta}$ -H), 2.42 (brs, 1 H, O-H), 1.46 (s, 9 H, ^tBu-H), 0.96 (s, 9 H, ^tBu-H); ¹³C-NMR (100 MHz, CDCl₃) 171.1 (s, 1C, ROC=O), 160.9 (d, 1C, HC(O)NH), 82.4 (s, 1C, Me₃C-O), 78.1 (d, 1C, C $_{\beta}$), 51.5 (d, 1C, C $_{\alpha}$), 35.4 (s, 1C, Me₃C-C), 27.9 (q, 3C, ^tBu), 26.0 (q, 3C, ^tBu); IR $\nu_{\max}/\text{cm}^{-1}$ 3384, 2978, 1714, 1656, 1368; HRMS (ES⁺): calcd. for C₁₂H₂₃NNaO₄ [M+Na]⁺ 268.1519, found 268.1515.

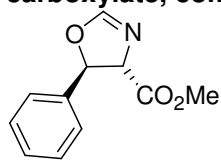
2.9 Synthesis and characterization of (2*S*,3*R*)-*tert*-butyl 2-formamido-3-hydroxy-4-methylpentanoate, compound **S2**

Due to its instability towards silica gel, compound **7g** was directly converted to the corresponding formamide **S2** and characterized as such.



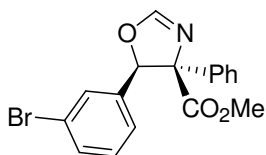
Pre-catalyst **2** (52.0 mg, 0.090 mmol) was dissolved in 1.0 mL of EtOAc and Ag₂O (10.4 mg, 0.045 mmol) was added. The heterogeneous mixture was stirred for approximately 2 minutes and isobutyraldehyde (165 μ L, 1.81 mmol) and powdered 4 \AA MS were sequentially added. The flask was cooled in an ice bath and a solution of *tert*-butyl isocyanoacetate **5** (150 mg, 1.06 mmol) in EtOAc (3 mL) was added over 3 hours via syringe pump. The mixture was then stirred at 0 $^{\circ}$ C for 4.30 h after the addition was finished, until all the isocyanoacetate was consumed (TLC, *p*-anisaldehyde). The reaction mixture was then quickly filtered through a short pad of Celite and eluted with EtOAc to yield crude oxazoline **7g**. The filtrate was concentrated under reduced pressure and dissolved in 20 mL of EtOAc saturated with 5% aq. solution of Citric acid and stirred until complete hydrolysis of the oxazoline **7g** to the corresponding formamide **S2** (TLC, about 6-8 hours). The organic phase was washed with 5% NaHCO₃ sol., dried over Na₂SO₄ and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 1:1) to yield 209 mg (85 %) of formamide. The ee was determined by HPLC using a Chiralpak OD [hexane/*iso*-propanol 90:10, λ 215 nm, 1.0 mL/min] *t* (minor) = 6.41 min., *t* (major) = 9.39 min. (67%); $[\alpha]_{\text{D}}^{25} = -7.50$ (c 1.03, CH₃CN); ¹H-NMR (400 MHz, CDCl₃) δ 8.29 (s, 1 H, H-C=O), 6.37 (d, $J = 8.5$ Hz, 1 H, N-H), 4.79 (dd, $J = 9.4, 4.5$ Hz, 1 H), 3.69 (m, 1 H), 2.27 (d, $J = 4.9$, 1 H, O-H), 1.75-1.60 (m, 1 H, Me₂C-H), 1.49 (s, 9 H, ^tBu-H), 1.03 (d, $J = 8.0$ Hz, 3 H, CH₃-CH-CH₃), 0.96 (3 H, $J = 8.0$ Hz, 3 H, CH₃-CH-CH₃); ¹³C-NMR (100 MHz, CDCl₃); 170.5 (s, 1C, ROC=O), 161.2 (d, 1C, HC(O)NH), 82.7 (s, 1C, Me₃C-O), 77.7 (d, 1C, C $_{\beta}$), 53.3 (d, 1C, C $_{\alpha}$), 30.9 (d, 1C, Me₂CH-C), 28.0 (q, 3C, ^tBu), 18.9 (q, 2C, Me₂CH-C); IR $\nu_{\max}/\text{cm}^{-1}$ 3351, 1735, 1662, 1159; MPT 85-87 $^{\circ}$ C; HRMS (ES⁺): calcd. for C₁₁H₂₁NNaO₄ [M+Na]⁺ 254.1363, found 254.1363.

2.10 Synthesis and characterization of methyl (4*S*,5*R*)-5-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **7h**



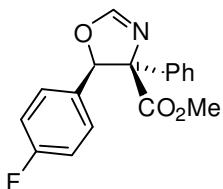
Obtained according to the general procedure, methyl-isocyano-acetate (0.55 mmol, 50 μ L) and benzaldehyde (0.937 mmol, 95 μ L) as starting materials and EtOAc (1.8 mL) as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:2) to yield 83 mg (73 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak AD [hexane/*iso*-propanol 90:10, λ 220 nm, 1.0 mL/min] *t* (minor) = 8.43 min., *t* (major) = 11.72 min. (81%); $[\alpha]_{\text{D}}^{25} = 166.6$ (c 0.80, THF); ¹H-NMR (400 MHz, CDCl₃) δ 7.43-7.31 (m, 5 H), 7.27 (s, 1 H), 7.11 (d, $J = 2.3$ Hz, 1 H), 5.70 (d, $J = 7.8$ Hz, 1 H), 4.64 (dd, $J = 2.3, 7.8$ Hz, 1 H), 3.85 (s, 3 H); ¹³C-NMR (100 MHz, CDCl₃); 170.9 (s, 1C, ROC=O), 156.3 (d, 1C, C=N), 138.9 (s, 1C, Ph), 129.0 (d, 2C, Ph), 128.8 (s, 1C, Ph), 125.6 (d, 2C, Ph), 82.1 (d, 1C), 75.3 (d, 1C), 52.9 (q, 1C, Me); IR $\nu_{\max}/\text{cm}^{-1}$ 1741, 1626, 1105; HRMS (ES⁺): calcd. for [M+Na]⁺ C₁₁H₁₁NNaO₃ 228.0631, found 228.0633.

2.11 Synthesis and characterization of methyl (4*R*,5*R*)-5-(3-bromophenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound **9a**



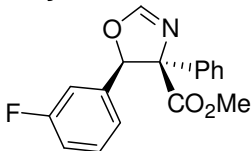
Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (1.71 mmol, 300 mg) and 3-bromo-benzaldehyde (2.90 mmol, 537 mg) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3.5:1) to yield 554 mg (90 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 10.06 min., t (minor) = 12.53 min. (97%); $[\alpha]_D^{25} = +138.6$ (c 1.12, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.31-7.59 (m, 2 H, Ar-H), 7.45-7.42 (m, 2 H, Ar-H), 7.37-7.19 (m, 6 H, Ar-H+N=CH), 5.62 (s, 1 H, C _{β} -H), 3.21 (s, 3 H, OCH₃); **¹³C-NMR** (100 MHz, CDCl₃) δ 169.4 (s, 1C, C=O), 155.4 (d, 1C, C=N), 141.1 (s, 1C), 138.6 (s, 1C), 132.1 (d, 1C), 130.0 (d, 1C), 129.6 (d, 1C), 128.5 (d, 2C), 128.3 (d, 1C), 126.6 (d, 2C), 125.3 (d, 1C), 122.5 (s, 1C), 88.8 (d, 1C, C _{β}), 84.4 (s, 1C, C _{α}), 52.4 (q, 1C, OCH₃); **IR** $\nu_{\max}/\text{cm}^{-1}$ 1738, 1638, 1238, 1104, 694; **HRMS** (ES+): calcd. for C₁₇H₁₅O₃N₁Br₁ [M+H]⁺ 360.0230, found 360.0231.

2.12 Synthesis and characterization of methyl (4*R*,5*R*)-5-(4-fluorophenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound 9b



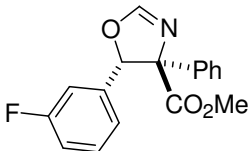
Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (0.21 mmol, 37 mg) and 4-fluoro-benzaldehyde (0.36 mmol, 38 μ L) as starting materials and TBME as solvent. The crude reaction mixture was quickly purified by flash column chromatography (PE/EtOAc 3:1) to yield 49 mg (78 %) of product. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 10.37 min., t (minor) = 11.61 min. (94%); $[\alpha]_D^{27} = +158.0$ (c 2.6, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.69-7.66 (m, 2 H, Ar-H), 7.44-7.33 (m, 5 H, Ar-H), 7.31 (s, 1 H, N=CH), 7.12-7.09 (m, 2 H, Ar-H), 5.75 (s, 1 H, C _{β} -H), 3.25 (s, 3 H, OCH₃); **¹³C-NMR** (100 MHz, CDCl₃) δ 169.6 (s, 1C, C=O), 162.9 (d, $J_{C-F} = 248.50$ Hz, 1C), 155.4 (d, C=N), 141.3 (s, 1C), 132.2 (d, $J_{C-F} = 3.4$ Hz, 1C), 128.5 (d, 3C), 128.3 (d, $J_{C-F} = 17.4$ Hz, 2C), 126.6 (d, 2C), 115.5 (d, $J_{C-F} = 21.8$ Hz, 2C), 89.1 (d, 1C, C _{β}), 84.2 (s, 1C, C _{α}), 52.3 (q, 1C, OCH₃); **IR** $\nu_{\max}/\text{cm}^{-1}$ 2362, 1740, 1638, 1512, 1228, 1104, 698; **HRMS** (ES+): calcd. for C₁₇H₁₅O₃N₁F₁ [M+H]⁺ 300.1030, found 300.1032.

2.13 Synthesis and characterization of methyl (4*R*,5*R*)-5-(3-fluorophenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound (4*R*,5*R*)-9c



Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (0.85 mmol, 150 mg) and 3-fluoro-benzaldehyde (1.45 mmol, 154 μ L) as starting materials and TBME as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3.5:1) to yield 236 mg (93 %) of product. Relative stereochemistry was confirmed by single crystal X-ray analysis (see attached CIF file). The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 9.07 min., t (minor) = 10.61 min. (97%); $[\alpha]_D^{30} = +157.8$ (c 1.9, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.70-7.68 (m, 2 H, Ar-H), 7.44-7.34 (m, 4 H, Ar-H), 7.32 (s, 1 H, N=CH), 7.16 (d, $J = 8.0$ Hz, 1 H, aromatic proton), 7.11-7.04 (m, 2 H, Ar-H), 5.73 (s, 1 H, C _{β} -H), 3.26 (s, 3 H, OCH₃); **¹³C-NMR** (100 MHz, CDCl₃) δ 169.4 (s, 1C, C=O), 162.6 (d, $J_{C-F} = 247.2$ Hz, 1C, C-F), 155.3 (d, 1C, C=N), 141.1 (s, 1C), 138.8 (d, $J_{C-F} = 7.1$ Hz, 1C), 130.0 (d, $J_{C-F} = 8.1$ Hz, 1C), 128.5 (d, 2C), 128.3 (s, 1C), 126.6 (d, 2C), 122.3 (d, $J_{C-F} = 2.9$ Hz, 1C), 115.9 (d, $J_{C-F} = 21.1$ Hz, 1C), 113.7 (d, $J_{C-F} = 22.7$ Hz, 1C), 88.9 (d, 1C, C _{β}), 84.4 (s, 1C, C _{α}), 52.3 (q, 1C, OCH₃); **IR** $\nu_{\max}/\text{cm}^{-1}$ 2930, 1731, 1626, 1131; **HRMS** (ES+): calcd. for C₁₇H₁₅O₃N₁F₁ [M+H]⁺ 300.1030, found 300.1030.

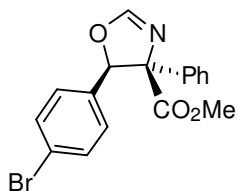
Minor diastereoisomer, Compound (4*R**,5*S**)-9c



¹H-NMR (400 MHz, CDCl₃) δ 7.36 (s, 1 H), 7.09 - 6.99 (m, 4 H), 6.97 - 6.92 (m, 2 H), 6.80 (d, $J = 7.8$ Hz, 1 H), 6.75 (dt, $J = 2.7, 8.4$ Hz, 1 H), 6.66 (td, $J = 1.9, 9.8$ Hz, 1 H), 6.33 (s, 1 H), 3.82 (s, 3 H); **¹³C-NMR** (100 MHz, CDCl₃) δ 172.6 (s, 1C, C=O), 162.4 (s, $J_{C-F} = 245.5$ Hz, 1C), 156.0 (d, 1C, C=N), 137.8 (s, $J_{C-F} = 8.0$ Hz, 1C), 135.6 (s, 1C), 129.3 (d, $J_{C-F} = 9.0$ Hz, 1C), 127.9 (d, 1C), 127.7 (d, 2C), 126.2 (d, 2C), 122.7 (d, 1C), 114.9 (d, $J_{C-F} = 20.1$ Hz, 1C), 114.0 (d, $J_{C-F} = 23.1$ Hz, 1C), 85.4 (d, C _{β} , 1C),

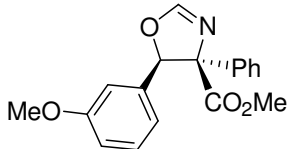
83.5 (s, C_α, 1C) 53.4 (q, CO₂CH₃, 1C); IR ν_{max}/cm⁻¹ 2930, 1738, 1620; HRMS (ES⁺): calcd. for C₁₇H₁₅O₃N₁F₁ [M+H]⁺ 300.1030, found 300.1036.

2.14 Synthesis and characterization of methyl (4*R*,5*R*)-5-(4-bromophenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound 9d



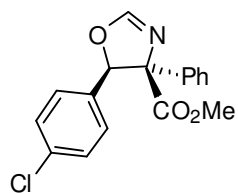
Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (1.71 mmol, 300 mg) and 4-bromo-benzaldehyde (2.91 mmol, 538 mg) as starting materials and EtOAc as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3.5:1) to yield 524 mg (85 %) of product. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 13.69 min., t (minor) = 15.57 min. (98%); [α]_D²⁵ = +197.8 (c 1.60, CH₂Cl₂); ¹H-NMR (400 MHz, CDCl₃) δ 7.61-7.59 (m, 2 H, Ar-H), 7.47-7.45 (m, 2 H, Ar-H), 7.36-7.17 (m, 6 H, Ar-H+N=CH), 5.64 (s, 1 H, C_β-H), 3.18 (s, 3 H, OCH₃); ¹³C-NMR (100 MHz, CDCl₃) δ 169.5 (s, 1C, C=O) 155.4 (d, C=N), 141.1 (s, 1C), 135.3 (s, 1C), 131.6 (d, 2C), 128.5 (d, 3C), 128.3 (d, 2C), 126.6 (d, 2C), 123.1 (s, 1C), 89.0 (d, 1C, C_β), 84.2 (s, 1C, C_α), 52.4 (q, 1C, OCH₃); IR ν_{max}/cm⁻¹ 1736, 1638, 1240, 1106, 1072, 700; HRMS (ES⁺): calcd. for C₁₇H₁₅O₃N₁Br₁ [M+H]⁺ 360.0230, found 360.0233.

2.15 Synthesis and characterization of methyl (4*R*,5*R*)-5-(3-methoxyphenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound 9e



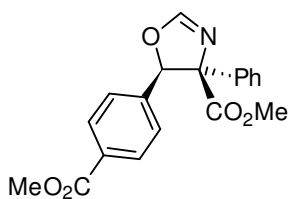
Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (0.21 mmol, 37 mg) and 3-methoxy-benzaldehyde (0.36 mmol, 43 μL) as starting materials and TBME as solvent. The crude reaction mixture was purified by flash column chromatography (PE/EtOAc 3:1) to yield 33 mg (50 %) of product as a colourless oil. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 12.46 min., t (minor) = 14.15 min. (93%); [α]_D²⁸ = +154.0 (c 1, CH₂Cl₂); ¹H-NMR (400 MHz, CD₂Cl₂) δ 7.60-7.58 (m, 2 H, Ar-H), 7.35-7.20 (m, 5 H, Ar-H+N=CH), 6.88-6.80 (m, 3 H), 5.64 (s, 1 H, C_β-H), 3.74 (s, 3 H, OCH₃), 3.11 (s, 3 H, OCH₃); ¹³C-NMR (100 MHz, CD₂Cl₂) δ 170.1 (s, 1C, C=O), 160.1 (s, 1C), 155.7 (d, 1C, N=CH), 142.1 (s, 1C), 138.4 (s, 1C), 129.8 (d, 1C), 128.7 (d, 2C), 128.4 (d, 1C), 127.2 (d, 2C), 119.3 (d, 1C), 114.6 (d, 1C), 112.7 (d, 1C), 89.6 (d, 1C, C_β), 84.8 (s, 1C, C_α), 55.7 (q, 1C, OCH₃), 52.4 (q, 1C, OCH₃); IR ν_{max}/cm⁻¹ 1740, 1638, 1238, 1108, 742, 698; HRMS (ES⁺): calcd. for C₁₈H₁₇O₄N₁Na₁ [M+Na]⁺ 334.1050, found 334.1050.

2.16 Synthesis and characterization of methyl (4*R*,5*R*)-5-(4-chlorophenyl)-4-phenyl-4,5-dihydro-1,3-oxazole-4-carboxylate, compound 9f



Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (0.21 mmol, 37 mg) and 4-chloro-benzaldehyde (0.36 mmol, 50 mg) as starting materials and TBME as solvent. The crude reaction mixture was purified by quick flash column chromatography (PE/EtOAc 3.5:1) to yield 37mg (56 %) of product. The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 95:5, λ 230 nm, 1.0 mL/min] t (major) = 13.99 min., t (minor) = 15.87 min. (96%); [α]_D³⁰ = +222.6 (c 1.50, CH₂Cl₂); ¹H-NMR (400 MHz, CDCl₃) δ 7.68-7.66 (m, 2 H, Ar-H), 7.43-7.30 (m, 8 H, Ar-H+N=CH), 5.73 (s, 1 H, C_β-H), 3.25 (s, 3 H, OCH₃); ¹³C-NMR (100 MHz, CDCl₃) δ 169.5 (s, 1C, C=O) 155.4 (d, C=N), 141.1 (s, 1C), 134.9 (s, 1C), 134.8 (s, 1C), 128.6 (d, 2C), 128.5 (d, 2C), 128.3 (d, 1C), 128.0 (d, 2C), 126.6 (d, 2C), 89.0 (d, 1C, C_β), 84.3 (s, 1C, C_α), 52.4 (q, 1C, OCH₃); IR ν_{max}/cm⁻¹ 1738, 1637, 1493, 1241, 1108, 1091; HRMS (ES⁺): calcd. for C₁₇H₁₄O₃N₁Cl₁Na₁ [M+Na]⁺ 338.0554, found 338.0559.

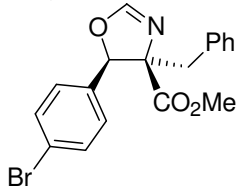
2.17 Synthesis and characterization of methyl (4*R*,5*R*)-5-[4 (methoxycarbonyl)phenyl]-4-phenyl-4,5-dihydro-1,3-oxazole-4-Carboxylate, compound 9g



Obtained according to the general procedure, using methyl 2-isocyano-2-phenylacetate (0.21 mmol, 37 mg) and 4-Formyl-benzoic acid methyl ester (0.36 mmol, 58 mg) as starting materials and TBME as solvent. The crude reaction mixture was diluted with Et₂O, washed with NaHSO₃ 1M (3x), NaHCO₃ sat. (1x), dried over K₂CO₃ and quickly purified by flash column chromatography (Et₂O/PE 4:1) to yield 41 mg (57 %) of product.

The ee was determined by HPLC using a Chiralpak OD [hexane/iso-propanol 90:10, λ 230 nm, 1.0 mL/min] t (major) = 15.39 min., t (minor) = 20.37 min. (93%); [α]_D²⁴ = +173.3 (c 1.50, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 8.07 (d, *J* = 8.4, 2 H, Ar-H), 7.70-7.68 (m, 2 H, Ar-H), 7.46-7.36 (m, 5 H, Ar-H), 7.34 (s, 1 H, N=C-H), 5.79 (s, 1 H, C_β-H), 3.93 (s, 3 H, OCH₃), 3.19 (s, 3 H, OCH₃); **¹³C-NMR** (100 MHz, CDCl₃) δ 169.4 (s, 1C, C=O) 166.5 (s, 1C, C=O), 155.4 (d, 1C, C=N), 141.2 (s, 1C) 141.1 (s, 1C), 130.7 (s, 1C), 129.7 (d, 2C), 128.6 (d, 2C), 128.3 (d, 2C), 126.6 (d, 2C), 89.1 (d, 1C, C_β), 84.6 (s, 1C, C_α), 52.4 (q, 1C, OCH₃), 52.3 (q, 1C, OCH₃); **IR** ν_{max}/cm⁻¹ 1724, 1638, 1436, 1280, 1106, 700; **HRMS** (ES⁺): calcd. for C₁₉H₁₇O₅N₁Na₁ [M+Na]⁺ 362.0999, found 362.0991.

2.18 Synthesis and characterization of methyl (4*R*,5*R*)-4-benzyl-5-(4-bromophenyl)-4,5-dihydro-1,3-oxazole-4-carboxylate, compound 9h



Obtained according to the general procedure, using methyl 2-isocyano-3-phenylpropanoate (0.21 mmol, 40 mg) and *p*-Br-benzaldehyde (0.357 mmol, 66 mg) as starting materials and TBME as solvent. The crude reaction mixture was purified by quick flash column chromatography (PE/EtOAc 3:1) to yield 57 mg (72%) of product. The ee was determined by HPLC using a Chiralpak OD-H [hexane/iso-propanol 95:05, λ 230 nm, 1.0 mL/min] t (minor) = 20.07 min., t (major) = 28.79 min. (71%); [α]_D²⁰ = -46.7 (c 0.86, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.50-7.44 (m, 2 H), 7.34-7.23 (m, 4 H), 7.12-7.07 (m, 3 H), 5.29 (s, 1 H), 3.49 (d, *J* = 13.6 Hz, 1 H), 3.24 (d, *J* = 13.6 Hz, 1 H), 3.21 (s, 3 H); **¹³C-NMR** (100 MHz, CDCl₃) δ 170.0, 155.6, 134.9, 134.8, 131.3, 130.9, 128.2, 127.7, 127.1, 122.6, 85.3, 82.7, 51.9, 43.8; **IR** ν_{max}/cm⁻¹ 1737.3, 1635.7, 1092.7, 701.1; **HRMS** (ES⁺): calcd. for C₁₈H₁₆BrNNaO₃ [M+Na]⁺ 396.0206, found 396.0209.

2.19 Preparation of racemic compounds

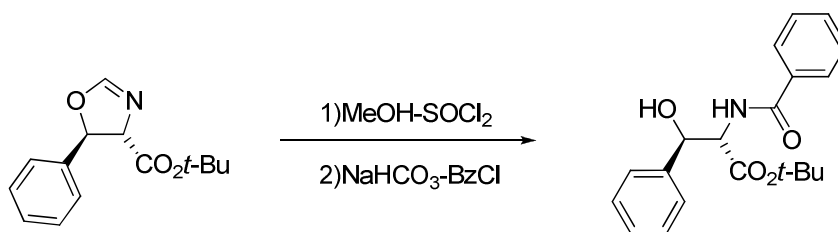
2.19.1 Racemic oxazolines deriving from *tert*-butylisocyanoacetate

Racemic oxazolines derived from *tert*-butylisocyanoacetate were obtained by dissolving 1 equivalent of isocyanide and 1.2 equivalents of the corresponding aldehyde in dry CH₂Cl₂ (approximately 5 mL/mmol) at 0°C and adding 10 mol % of DBU as catalyst. The reaction mixture was then stirred at 0°C until TLC indicated complete consumption of the isocyanide (2-16 hours). The resultant solution was then diluted with CH₂Cl₂, washed with water, dried over Na₂SO₄ and concentrated under reduce pressure. The crude obtained was purified using the same method described for the enantioenriched examples.

2.19.2 Racemic oxazolines deriving from isocyano-phenyl-acetic acid methyl ester

Racemic oxazolines derived from methyl 2-isocyano-2-phenylacetate were obtained by dissolving 1 equivalent of isocyanide and 1.2 equivalents of the corresponding aldehyde in dry CH₂Cl₂ (approximately 5 mL/mmol) at 0°C and adding 10 mol% of DBU and 5 mol% of Ag₂O. The reaction mixture was then gently warmed at room temperature until TLC indicated complete consumption of the isocyanide (2-16 hours). The resultant solution was then concentrated under reduced pressure and purified using the same method described for the enantioenriched examples.

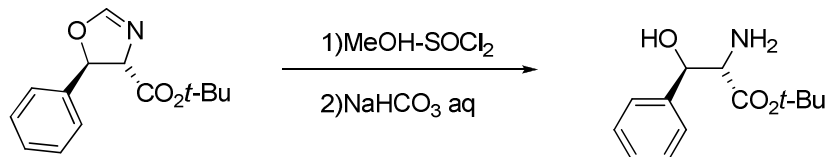
2.20 Direct conversion of oxazoline 7a to *tert*-butyl (β*R*)-*N*-benzoyl-β-hydroxy-L-phenylalaninate S3



Crude oxazoline **7a** prepared according to general procedure **2.2** from *tert*-butyl-isocyanoacetate (0.21 mmol, 30 mg) and benzaldehyde (0.25 mmol, 26 μ L) was dried in vacuo and dissolved in 1.5 mL of anhydrous MeOH. The reaction mixture was cooled to 0 $^{\circ}$ C and 1.5 mL of 1M solution of SOCl₂ in MeOH (2M HCl) were added drop wise. The solution was stirred 1 h 45' at 0 $^{\circ}$ C and then the solvent was removed under reduced pressure. The resultant oil was dissolved in CH₂Cl₂ (2 mL) and few drops of sat. NaHCO₃ solution were added under vigorous stirring until pH 8 (pH paper). The flask was cooled to 0 $^{\circ}$ C and 1 equivalent (0.21 mmol) of benzoyl chloride was added. After 20 minutes the ice bath was removed and the reaction mixture was stirred further 40 minutes. The suspension was partitioned between CH₂Cl₂ and water. The organic extracts were dried over Na₂SO₄ and purified by flash column chromatography (PE/EtOAc 3.5:1) to yield 52 mg (72 %, 3 steps) of derivative **S3** as a single diastereoisomer. The ee was determined by HPLC using a Chiralpak AD [hexane/*iso*-propanol 80:20, λ 230 nm, 1.0 mL/min] t (minor) = 7.98 min., t (major) = 23.05 min. (96%); $[\alpha]_D^{25} = +60.4$ (c 0.5, CHCl₃); **¹H-NMR** (500 MHz, CDCl₃) δ 7.70 (d, $J = 7.0$ Hz, 2 H, Ar-H), 7.48 (t, $J = 7.5$ Hz, 1 H, aromatic proton), 7.41-7.38 (m, 4 H, Ar-H), 7.32 (t, $J = 7.0$ Hz, 2 H), 7.29-7.25 (m, 1 H, aromatic proton), 6.92 (d, $J = 8.0$ Hz, 1 H, N-H), 5.26 (d, $J = 4.0$ Hz, 1 H), 4.96 (dd, $J = 8.5, 4.0$ Hz, 1 H), 3.32 (brs, 1 H, O-H), 1.42 (s, 9 H, ^tBu); **HRMS** (ES⁺): calcd. for C₂₀H₂₃O₄N₁Na₁ [M+Na]⁺ 364.1519, found 364.1510.

Spectroscopic data were consistent with previously reported data for this compound.ⁱⁱⁱ

2.21 Synthesis and characterization of compound 10



Oxazoline **7a**, prepared according to general procedure **2.2** from *tert*-butyl-isocyanoacetate (0.21 mmol, 30 mg) and benzaldehyde (0.25 mmol, 26 μ L), was dissolved in 1.5 mL of dry MeOH. The reaction mixture was cooled to 0 $^{\circ}$ C and 1.5 mL of 1M solution of SOCl₂ in MeOH (2M HCl) were added drop wise. The solution was stirred 1 h 45' at 0 $^{\circ}$ C and then the solvent was removed under reduced pressure. The resultant oil was dissolved in CH₂Cl₂ (2 mL) and few drops of sat. NaHCO₃ solution were added under vigorous stirring until pH 8 (pH paper). The mixture was further diluted with CH₂Cl₂ and dried with Na₂SO₄. The insoluble were filtered off and the resultant solution was concentrated under reduced pressure and the crude was purified by FCC (AcOEt/P.E. 2:1) to yield amino-ester **10** (85%) **¹H-NMR** (400 MHz, CDCl₃) δ 7.35-7.27 (m, 5 H, Ar-H), 4.73 (d, $J = 5.2$ Hz, 1H), 3.51 (d, $J = 4.4$ Hz, 1 H), 2.51 (brs, 3 H, NH₂ and O-H), 1.34 (s, 9 H, ^tBu); **¹³C-NMR** (100 MHz, CDCl₃) δ 172.3 (s, 1C, C=O), 140.8 (s, 1C, quaternary Ph), 128.2 (d, 2C, aromatic C-H), 127.7 (d, 1C, aromatic C-H), 126.5 (d, 2C, aromatic C-H), 81.7 (s, 1C, Me₃C-O), 74.6 (d, 1C), 60.9 (d, 1C), 27.8 (q, 3C; ^tBu); **HRMS** (ES⁺): calcd. for C₁₃H₂₀O₃N [M+H]⁺ 238.1438, found 238.1436. The process was confirmed to be "racemization-free" by analyzing the enantiomeric excess of the benzoylated derivative **S3** (96% ee).

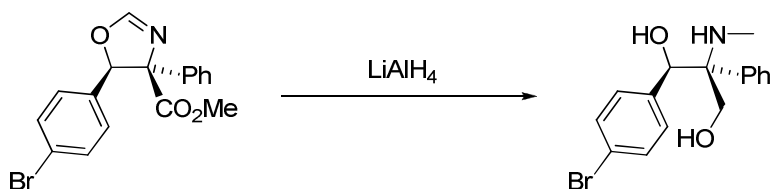
2.22 Synthesis and characterization of compound 11



Amino ester **10** (38 mg, 0.16 mmol, 91% ee) was dissolved in 6M HCl (3 mL) and the mixture was stirred at room temperature for 4 hours. Removal of volatiles under reduced pressure yielded the corresponding amino acid as the HCl salt, in quantitative yield.

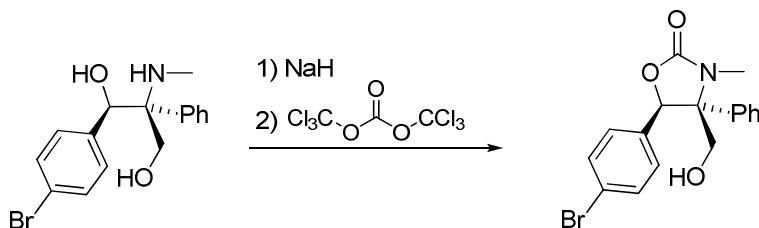
$[\alpha]_D^{25} = -43.6$ (c 1.1, 6M HCl); **¹H-NMR** (500 MHz, D₂O) δ 7.41-7.35 (m, 5 H, Ar-H), 5.34 (d, $J = 4.0$ Hz, 1 H), 4.15 (d, $J = 4.0$ Hz, 1 H); **¹³C-NMR** (500 MHz, D₂O) δ 170.4 (s, 1C), 138.2 (s, 1C), 128.8 (d, 2C, Aromatic C-H), 125.8 (d, 2C, aromatic C-H), 70.7 (d, 1C), 59.4 (d, 1C); **HRMS** (ES+): calcd. for C₉H₁₁NNaO₃ [M+Na]⁺ 204,0631, found 204,0635. Spectroscopic data were consistent with previously reported data for this compound.^{iv}

2.23 Synthesis and characterization of (1R,2S)-1-(4-bromophenyl)-2-(methylamino)-2-phenylpropane-1,3-diol, compound **12**



LiAlH₄ (1.25 g, 33.06 mmol) was suspended in THF (25 mL). The suspension was cooled to -78 °C and oxazoline **9d** (2.38 g, 6.61 mmol) in THF (20 mL) was added during 5 minutes. The reaction mixture was gently warmed to room temperature without removing the dry ice bath and left stirring overnight. The reaction mixture was then cooled to 0 °C and quenched by sequential addition of H₂O (1.25 mL), 15% NaOH (1.25 mL) and H₂O (3.7 mL). The resultant suspension was diluted with Et₂O, dried by addition of Na₂SO₄ and filtered through Celite. Solvents were removed under reduced pressure and the crude product was purified by flash column chromatography (CH₂Cl₂/MeOH 30:1). Impure fractions were combined and further purified by flash column chromatography (CH₂Cl₂/MeOH 20:1). All pure fractions were concentrated under reduced pressure to yield compound **12** as a white solid (1.68 g, 75%). $[\alpha]_D^{25} = +30.9$ (c 1.0, MeOH); **¹H-NMR** (400 MHz, CDCl₃) δ 7.29-2.25 (m, 2 H, Ar-H), 7.22-7.14 (m, 3 H, Ar-H), 7.02-7.00 (m, 2 H, Ar-H), 6.81(d, $J = 6.81$ Hz, 2 H, Ar-H), 4.99 (s, 1 H, Ar-C-H), 4.41 (d, $J = 11.4$, 1H, one of CH₂-OH), 3.86 (d, $J = 11.4$, 1H, one of CH₂-OH), 3.00-2.20 (brs, 3H, 2 x O-H and N-H), 2.23 (s, 3H, N-CH₃); **¹³C-NMR** (100 MHz, CDCl₃) δ 138.6 (s, 1C), 137.8 (s, 1C), 130.5 (d, 2C), 129.1 (d, 2C), 128.1 (d, 2C), 127.5 (d, 1C), 127.5 (d, 2C), 121.6 (s, 1C), 80.6 (d, 1C, Ar-CH-OH), 64.9 (t, 1C, CH₂-OH), 60.2 (s, C $_{\alpha}$ -N), 28.6 (q, N-CH₃); **IR** ν_{max}/cm^{-1} 3251, 2942, 1486, 1072, 700; **MPT** 55 °C; **HRMS** (ES+): calcd. for C₁₆H₁₉BrN₁O₂ [M+H]⁺ 336.0594, found 336.0595.

2.24 Synthesis and characterization of (4S,5R)-5-(4-bromophenyl)-4-(hydroxymethyl)-3-methyl-4-phenyl-1,3-oxazolidin-2-one, compound **13**

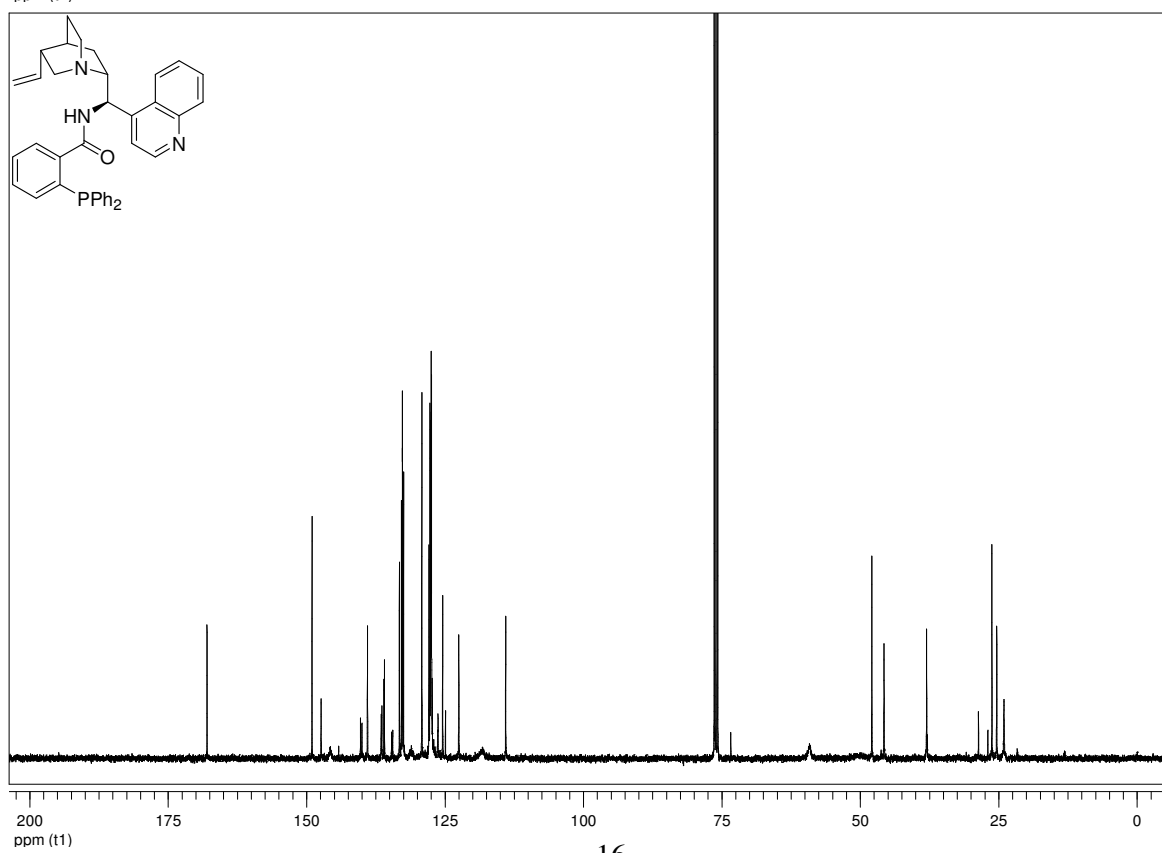
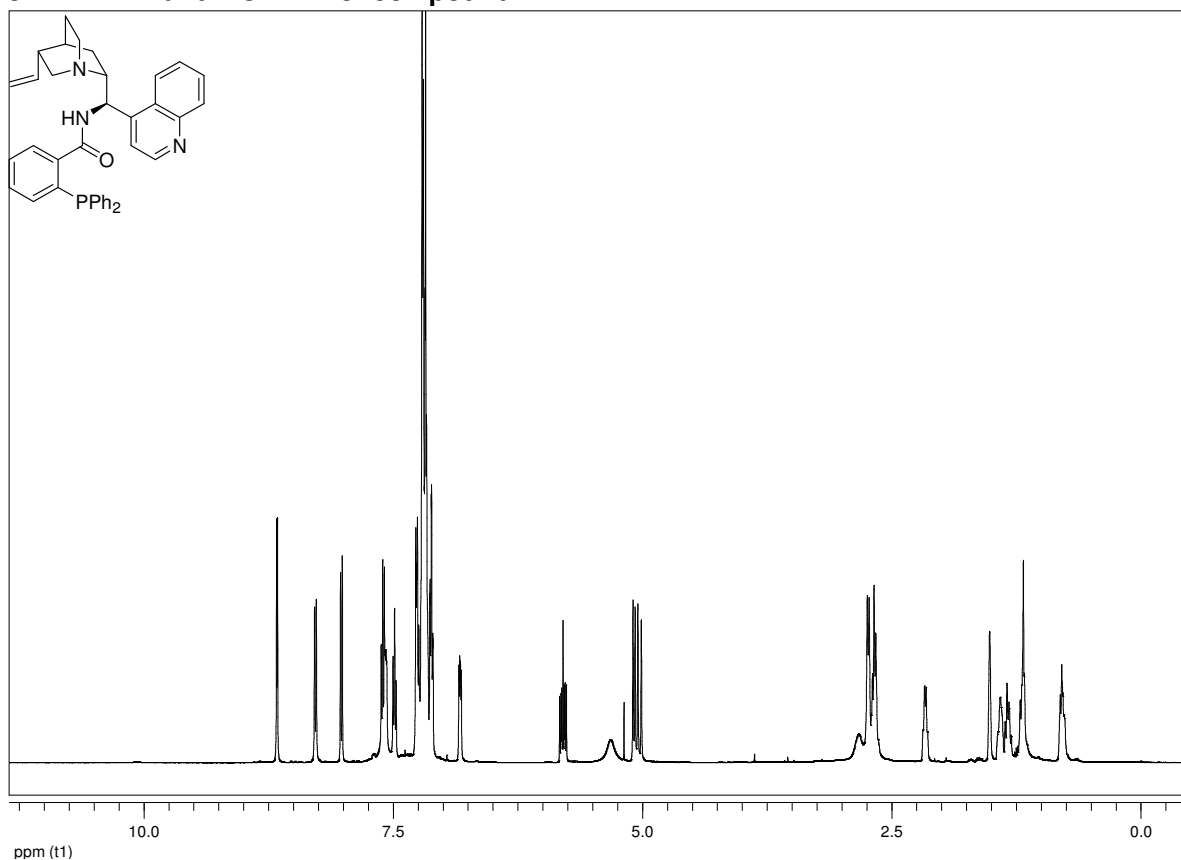


NaH (60% suspension in mineral oil) was suspended in THF (8 mL). Alcohol **12** (180 mg, 0.53 mmol) was added and the resultant mixture was stirred at room temperature for 1 hour and 30 minutes. The reaction mixture was cooled to 0 °C and a solution of triphosgene (63 mg, 0.21 mmol) in CH₂Cl₂ (10 mL) was added drop wise over 10 minutes.

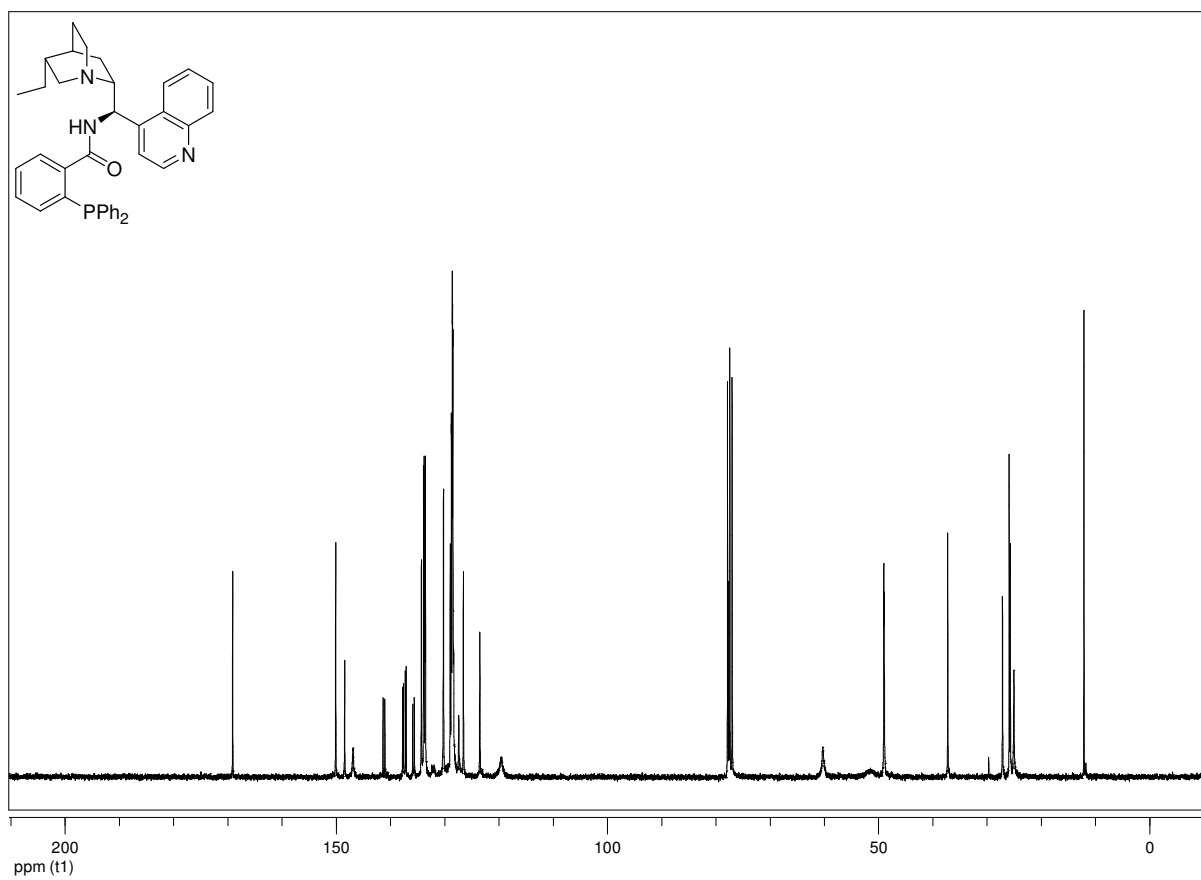
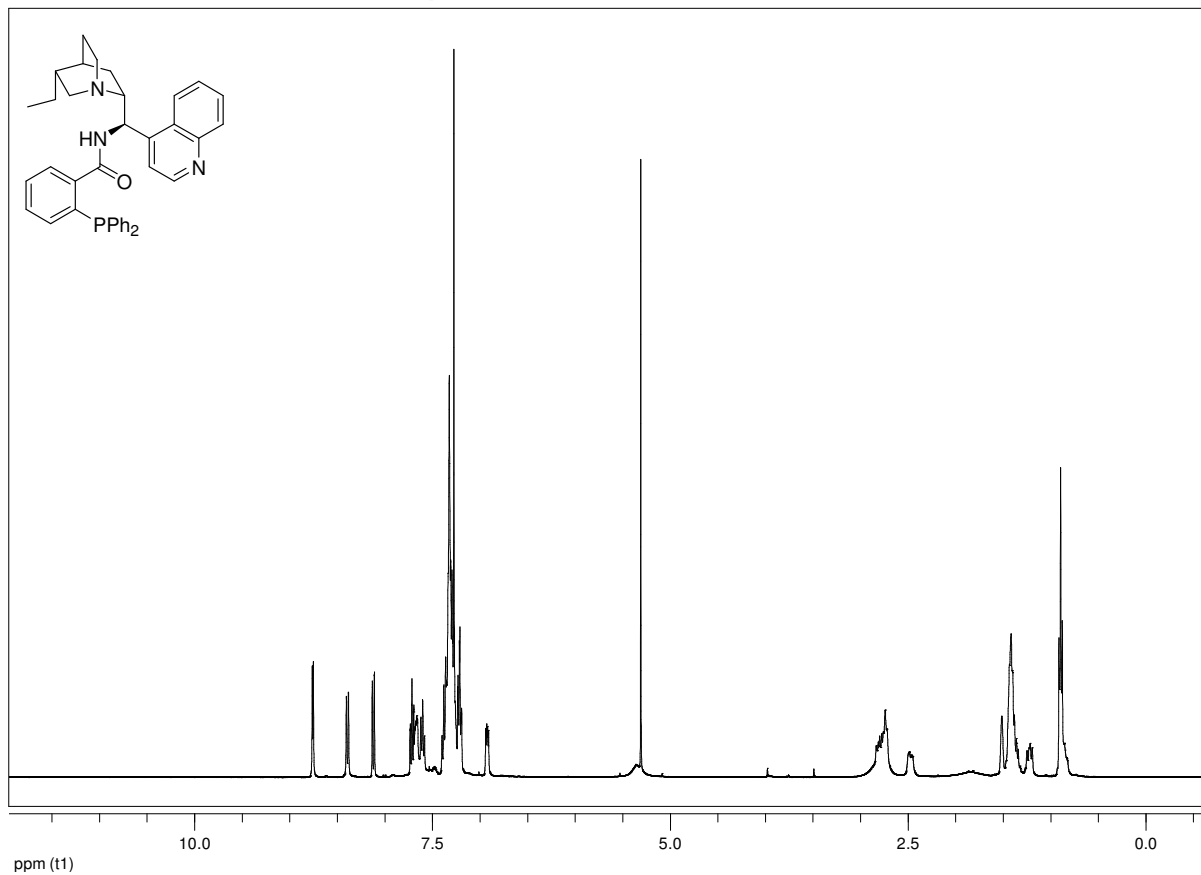
The reaction mixture was stirred for 1 hour at 0 °C and then 8 hour at room temperature. The resultant suspension was diluted with EtOAc and washed with water, brine and dried over anhydrous Na₂SO₄. Solvents were removed under reduced pressure and the crude product was purified by flash column chromatography (PE/EtOAc 3:2) to yield **13** as a white solid (163 mg, 85%). The product was recrystallised from EtOAc/Cyclohexane. Absolute stereochemistry was confirmed by single crystal X-ray analysis (see attached CIF file). The ee was determined by HPLC using a Chiralpak AD [hexane/iso-propanol 80:20, λ 220 nm, 1.0 mL/min] t (major) = 6.13 min., t (minor) = 7.85 min. (97%); [α]_D²⁵ = -5.4 (c 0.58, CH₂Cl₂); **¹H-NMR** (400 MHz, CDCl₃) δ 7.50-7.47 (m, 4 H, Ar-H), 7.44-7.40 (m, 1 H, Ar-H), 7.27 (d, J = 10.0 Hz, 2 H, Ar-H), 7.12 (d, J = 10.0 Hz, 1 H, Ar-H), 5.32 (s, 1 H, Ar-C-H), 3.83 (s, 2 H, CH₂-O), 2.82 (s, 3 H, N-CH₃), 1.99 (brs, 1 H, O-H); **¹³C-NMR** (500 MHz, CDCl₃) δ 159.0 (s, 1C, carbamate), 137.9 (s, 1C), 132.6 (s 1C), 131.6 (d, 2C), 129.5 (d, 2C), 128.8 (d, 1C), 127.9 (d, 2C), 126.2 (d, 2C), 122.8 (s, 1C), 85.9 (d, 1C, Ar-CH-O), 70.9 (s, 1C, C_α-N), 60.7 (t, 1C, CH₂-O), 28.0 (q, 1C, N-CH₃); **IR** ν_{max}/cm⁻¹ 3422, 1742, 1383, 1071, 1040; **MPT** 189 °C; **HRMS** (ES⁺): calcd. for C₁₇H₁₆BrN₁Na₁O₃ [M+Na]⁺ 384.0206, found 384.0203.

3. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ Spectra of pre-catalysts

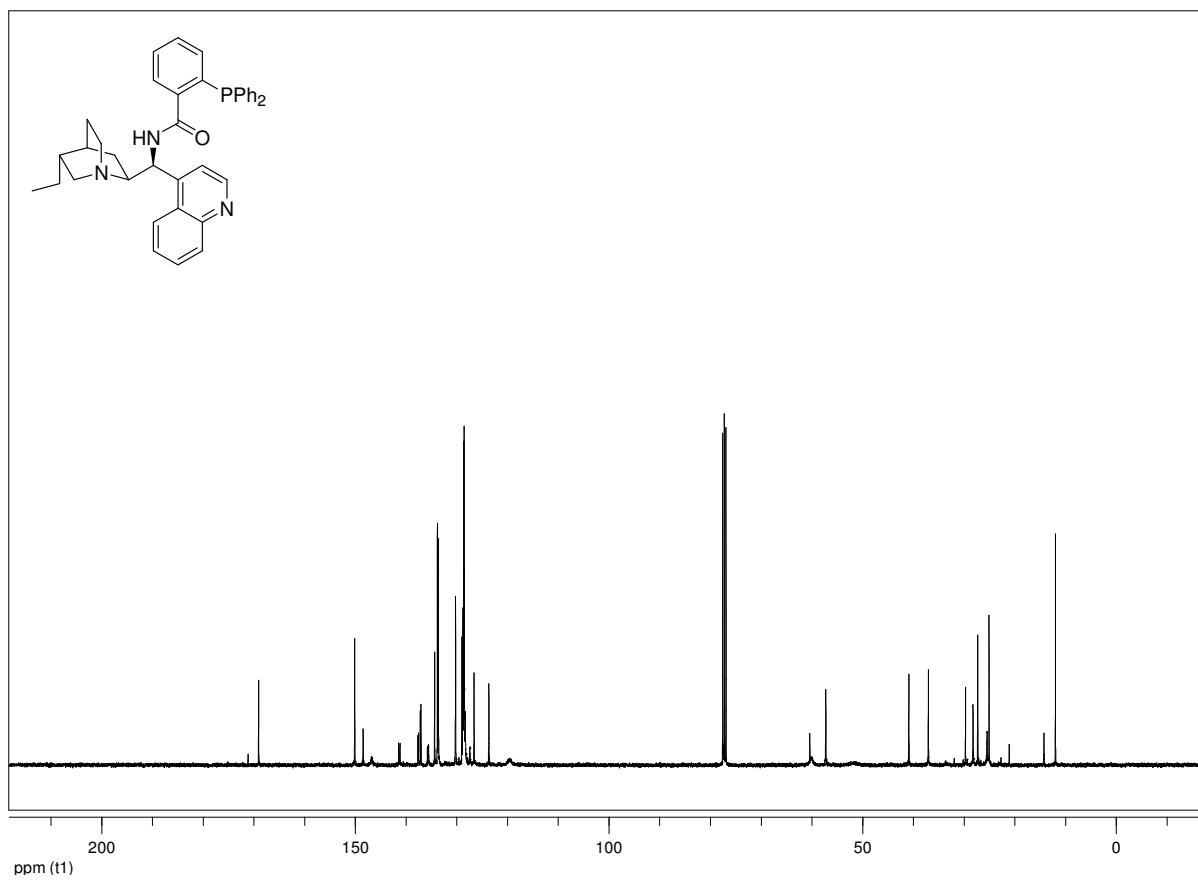
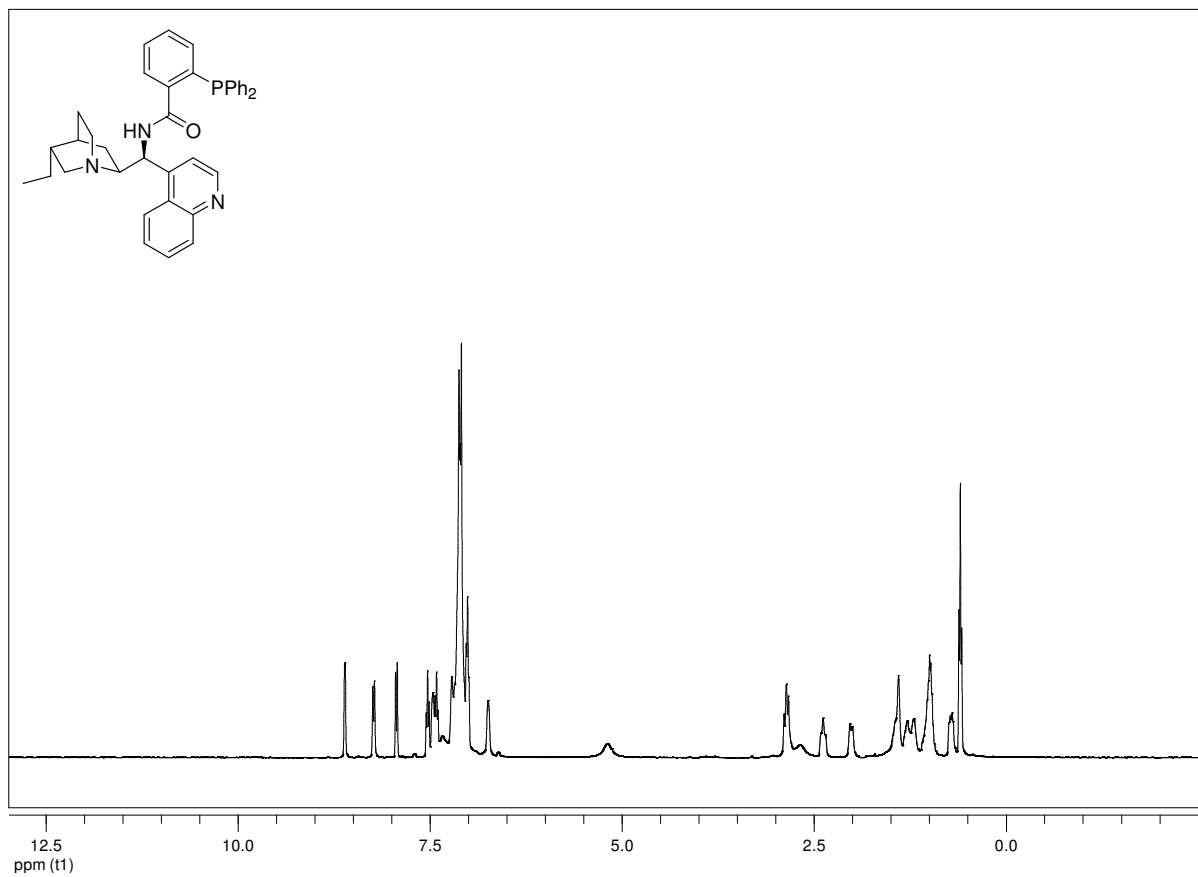
3.1 $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of compound 1



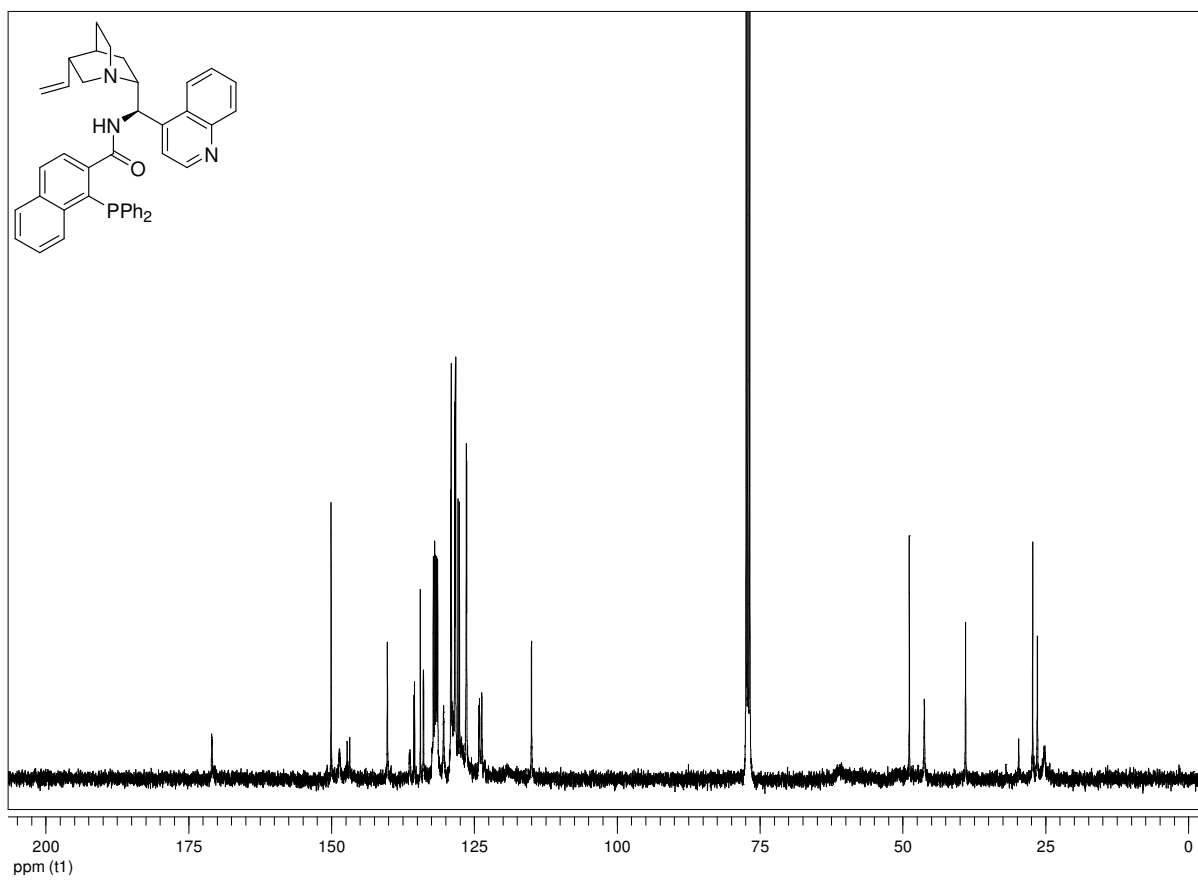
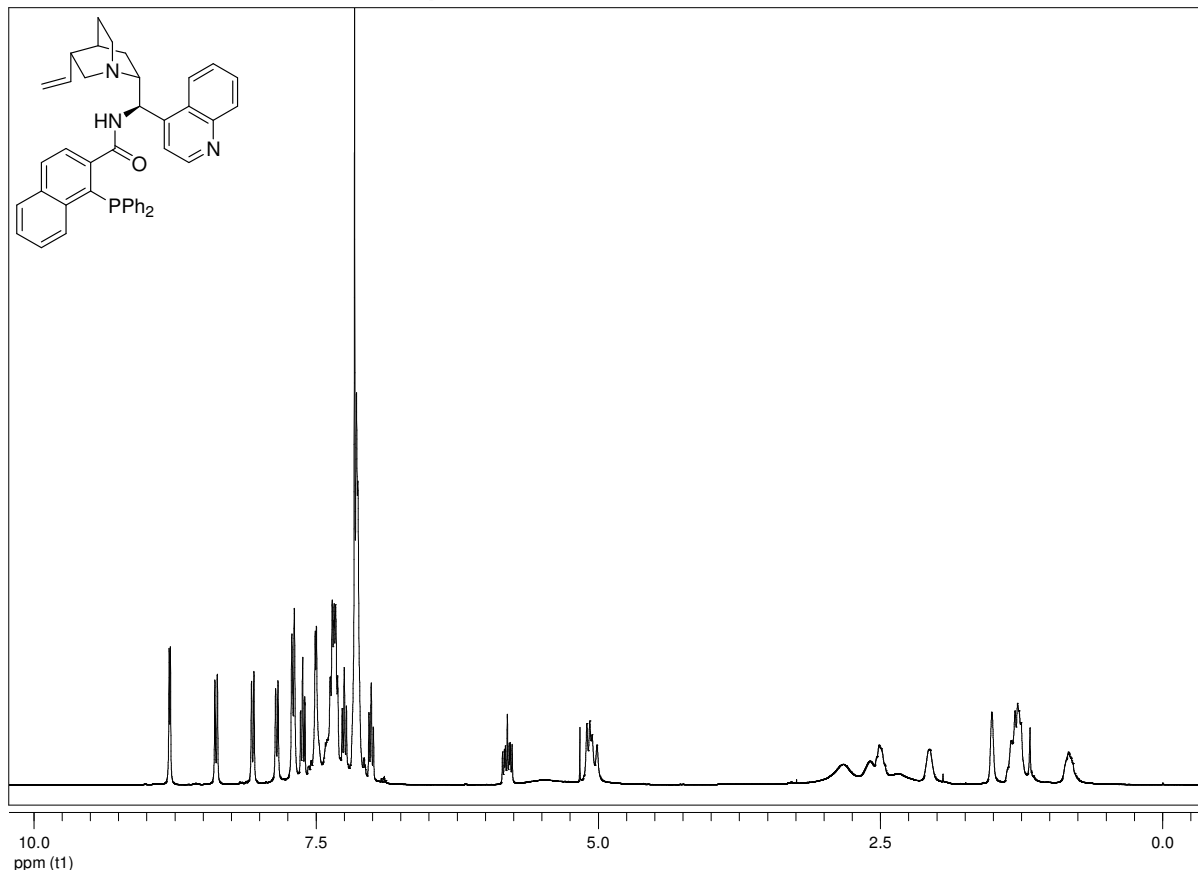
3.2 $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of compound 2



3.3 $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of compound 3

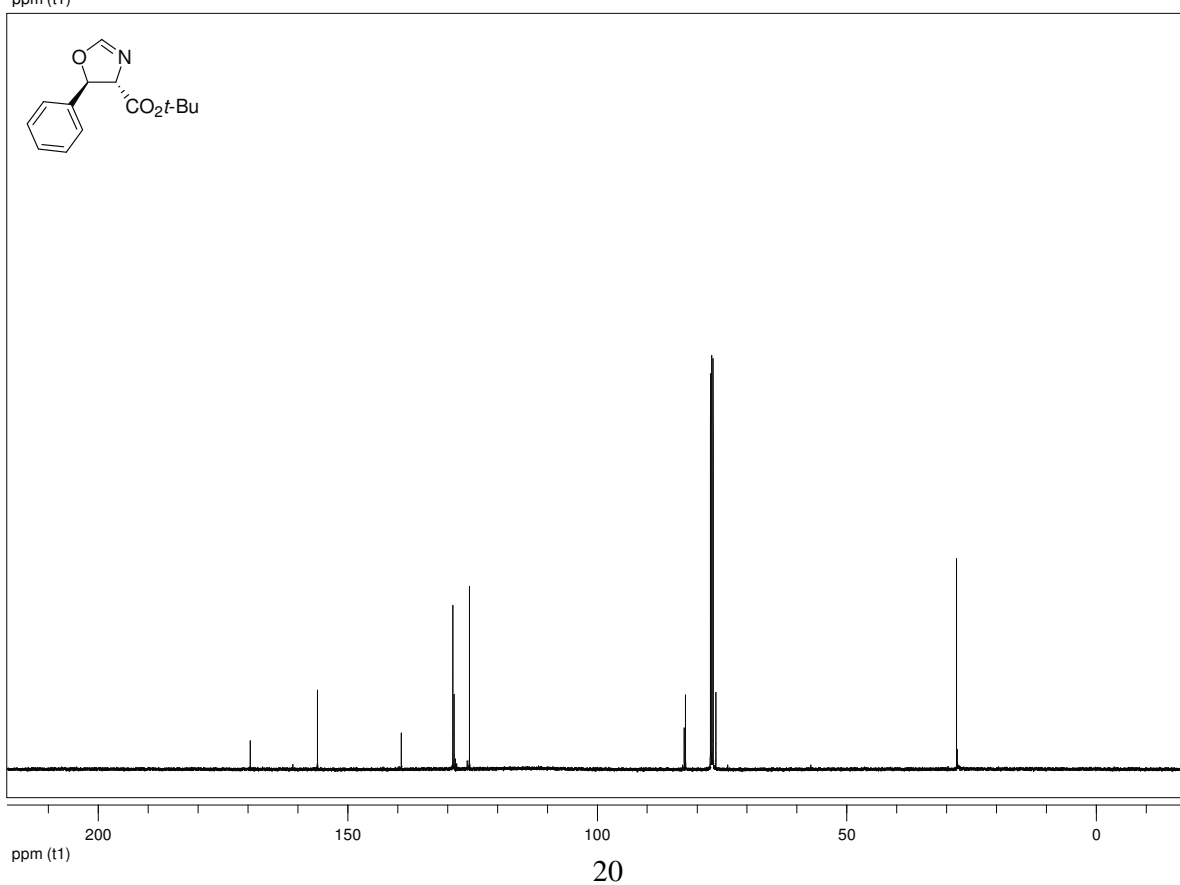
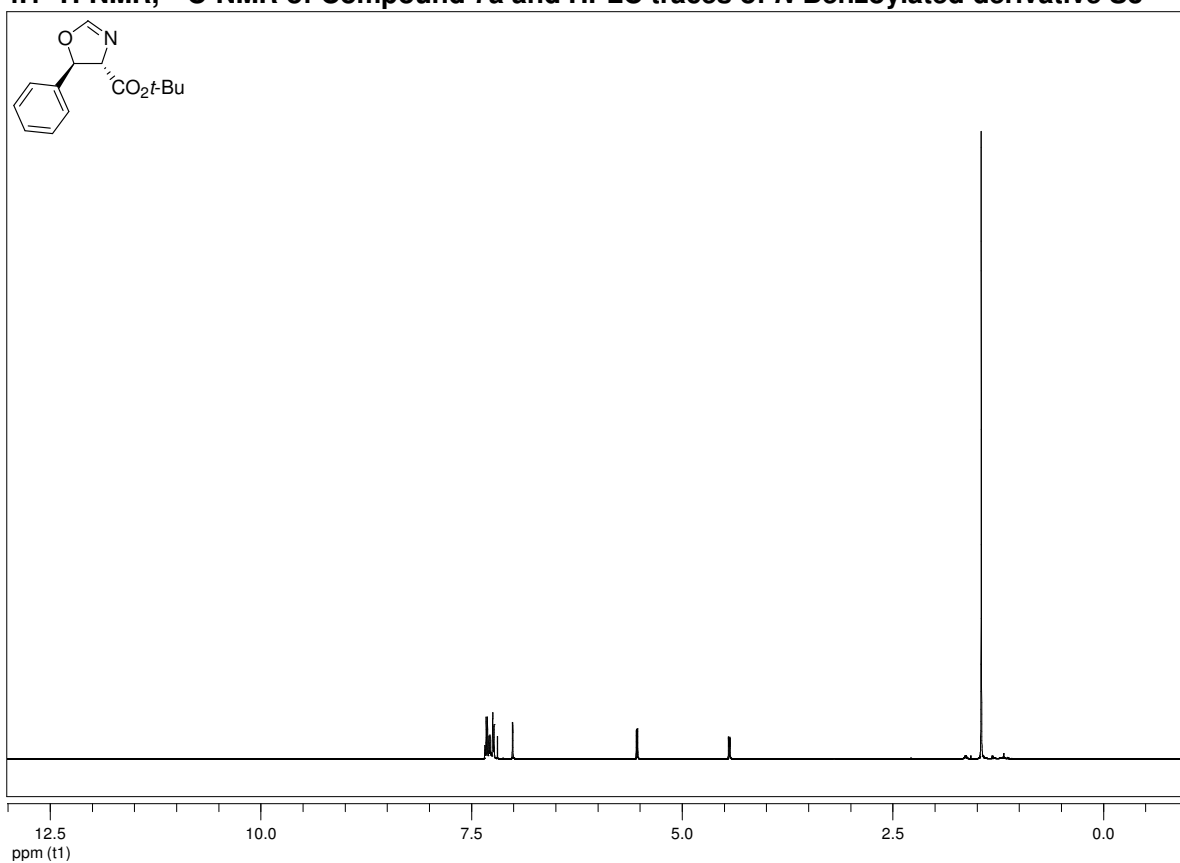


3.4 $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of compound 4



4. $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ Spectra and HPLC traces of oxazoline and hydrolyzed derivatives

4.1 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ of Compound 7a and HPLC traces of *N*-Benzoylated derivative S3



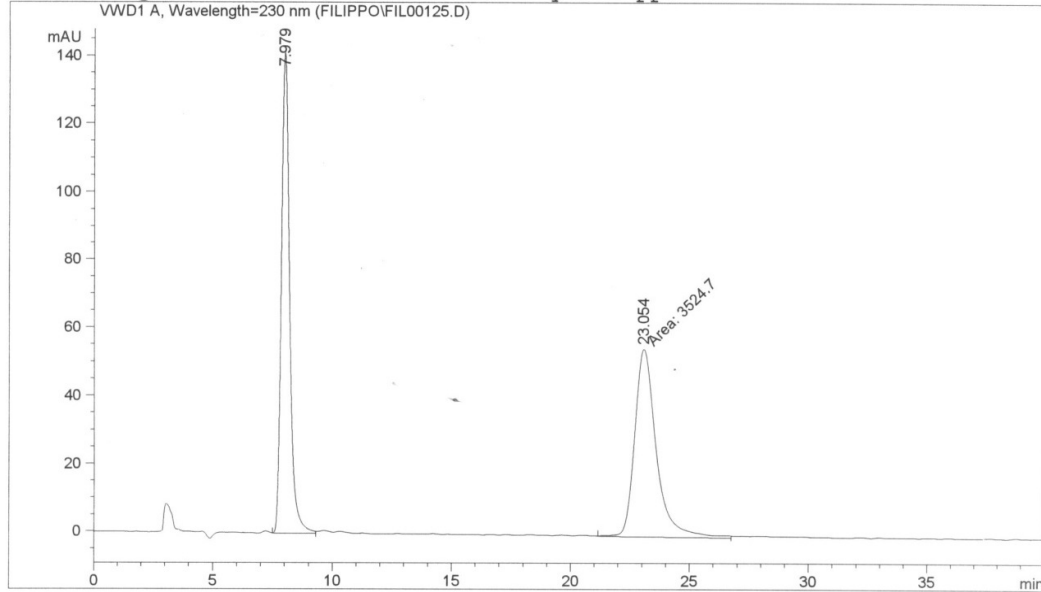
Racemate

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LSD-59, AD COLUMN, 80-20, 230 NM

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Acq. Method    : C:\HPCHEM\1\METHODS\80_20.M
Last changed   : 8/26/08 12:23:47 PM by FILIPPO
Analysis Method : C:\HPCHEM\1\METHODS\80HEX230.M
Last changed   : 6/30/08 4:44:14 PM by Filippo
=====
```



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.979	VB	0.3699	3416.90967	141.42903	49.2236
2	23.054	MM	1.0634	3524.69580	55.24395	50.7764

Totals : 6941.60547 196.67298

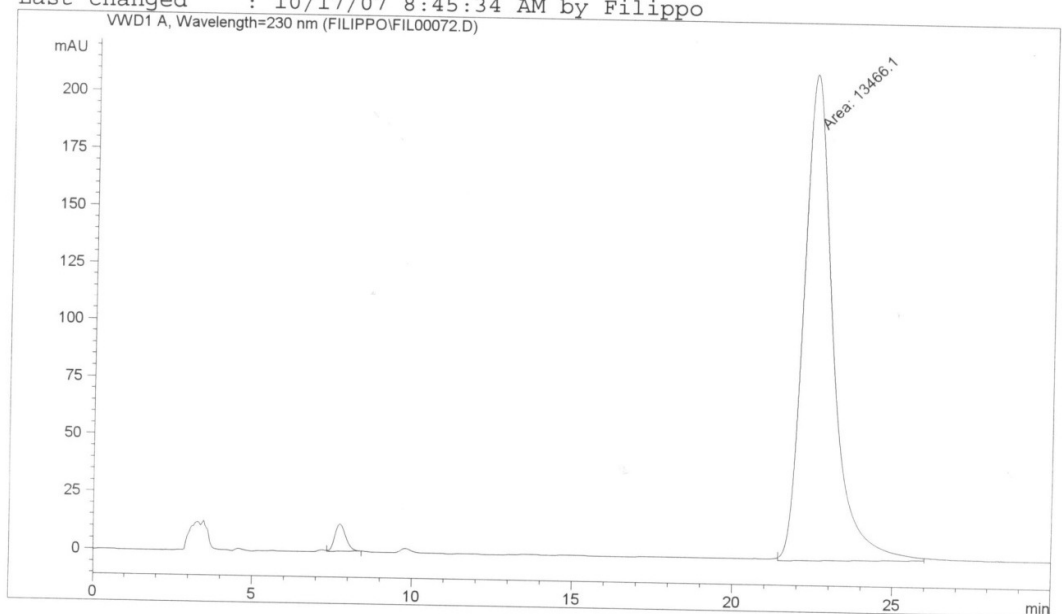
Results obtained with enhanced integrator!

=====
*** End of Report ***

Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00072.D Sample Name: LSD_160-500+MS

```
=====
Injection Date   : 3/12/08 6:21:06 PM           Seq. Line :    2
Sample Name     : LSD_160-500+MS                Vial      :   10
Acq. Operator  : FILIPPO                        Inj       :    1
                                                    Inj Volume: 25 µl
Acq. Method    : C:\HPCHEM\1\METHODS\80HEX230.M
Last changed   : 2/28/08 6:32:32 PM by Filippo
Analysis Method: C:\HPCHEM\1\METHODS\65HEX220.M
Last changed   : 10/17/07 8:45:34 AM by Filippo
=====
```



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=230 nm

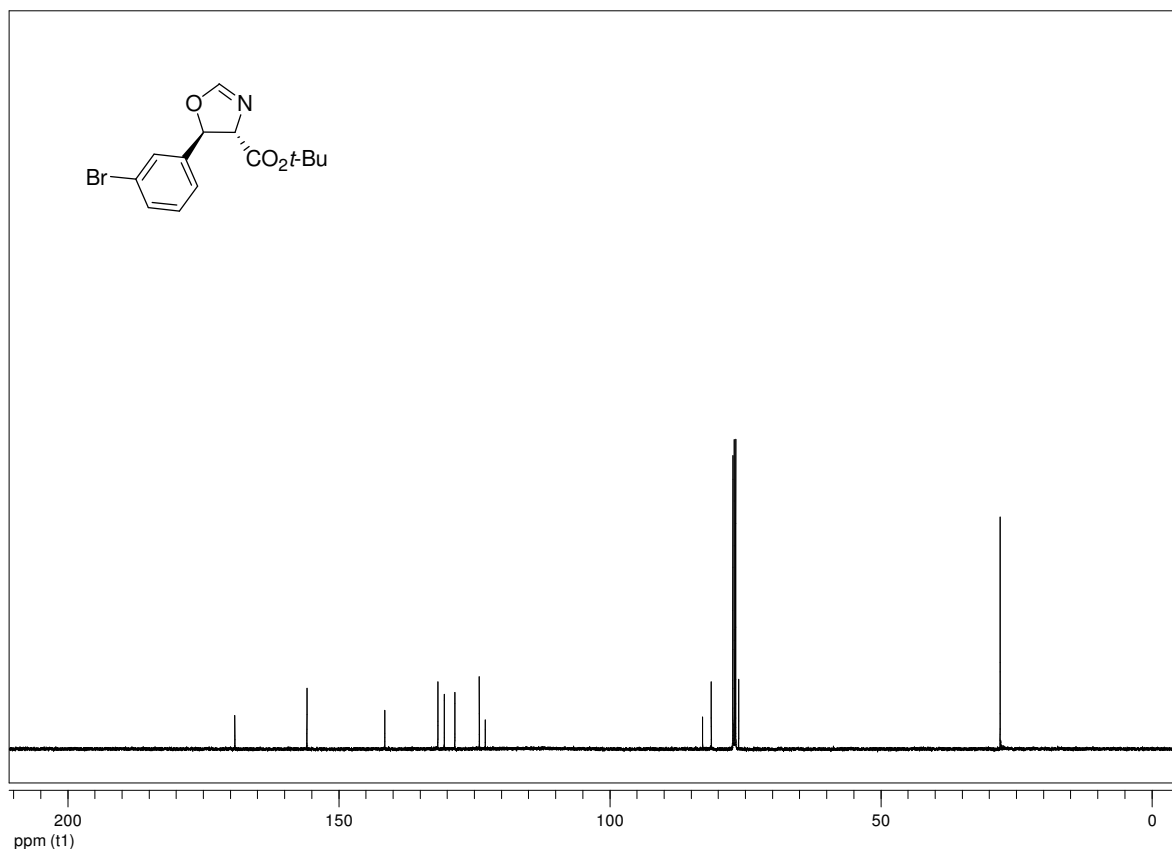
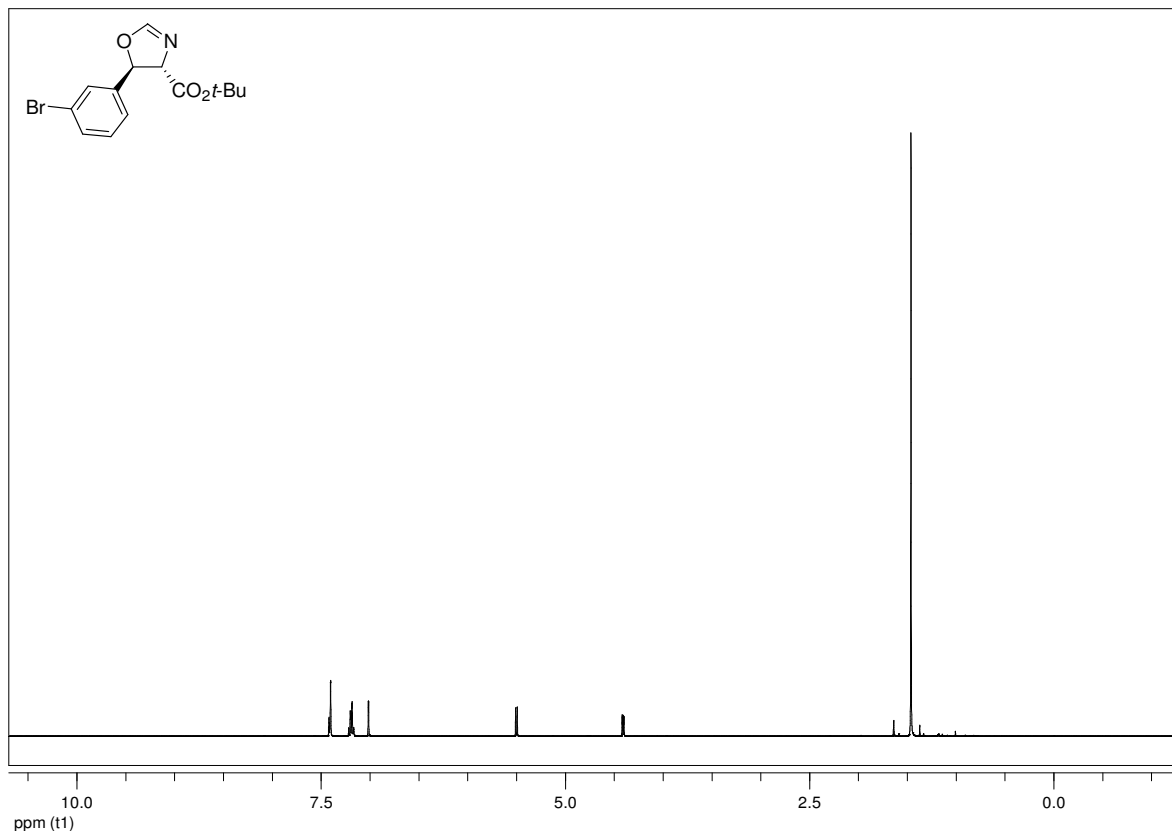
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.733	VB	0.3309	283.02994	11.71446	2.0585
2	22.446	MM	1.0590	1.34661e4	211.93782	97.9415

Totals : 1.37492e4 223.65228

Results obtained with enhanced integrator!

=====
*** End of Report ***

4.2 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ -NMR and HPLC traces of compound 7b



Enantioenriched

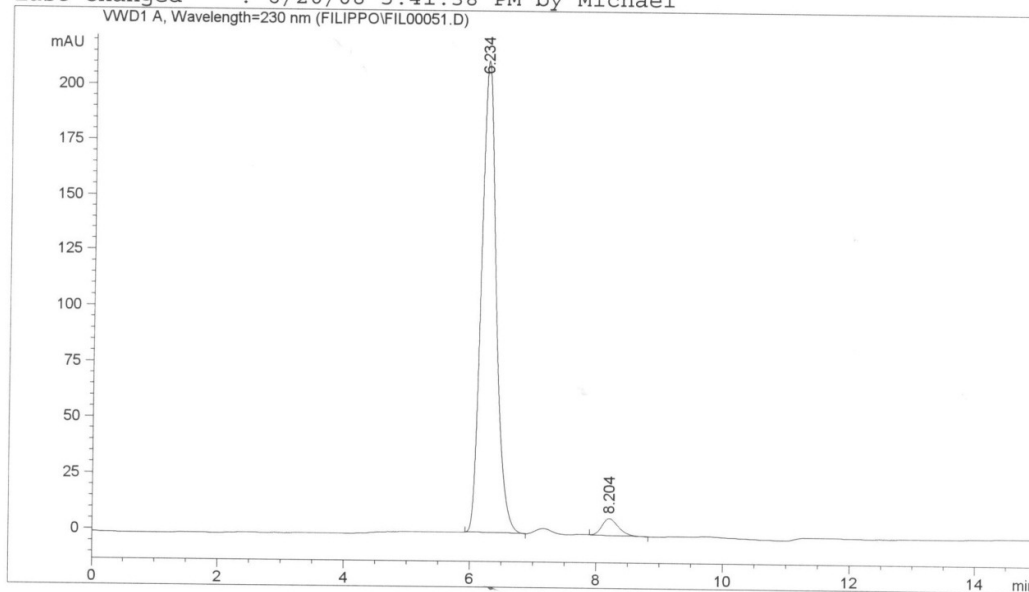
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00051.D

Sample Name: LSD_270-3

LSD_270-3, OD COLUMN, 90-1-, 220 NM

```
=====
Injection Date   : 6/24/08 6:37:27 PM           Seq. Line :    4
Sample Name     : LSD_270-3                     Vial      :   10
Acq. Operator   : filippo                       Inj       :    1
                                                    Inj Volume: 20 µl

Acq. Method     : C:\HPCHEM\1\METHODS\90HEX.M
Last changed    : 6/24/08 5:49:01 PM by filippo
Analysis Method : C:\HPCHEM\1\METHODS\80_20.M
Last changed    : 6/20/08 5:41:38 PM by Michael
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

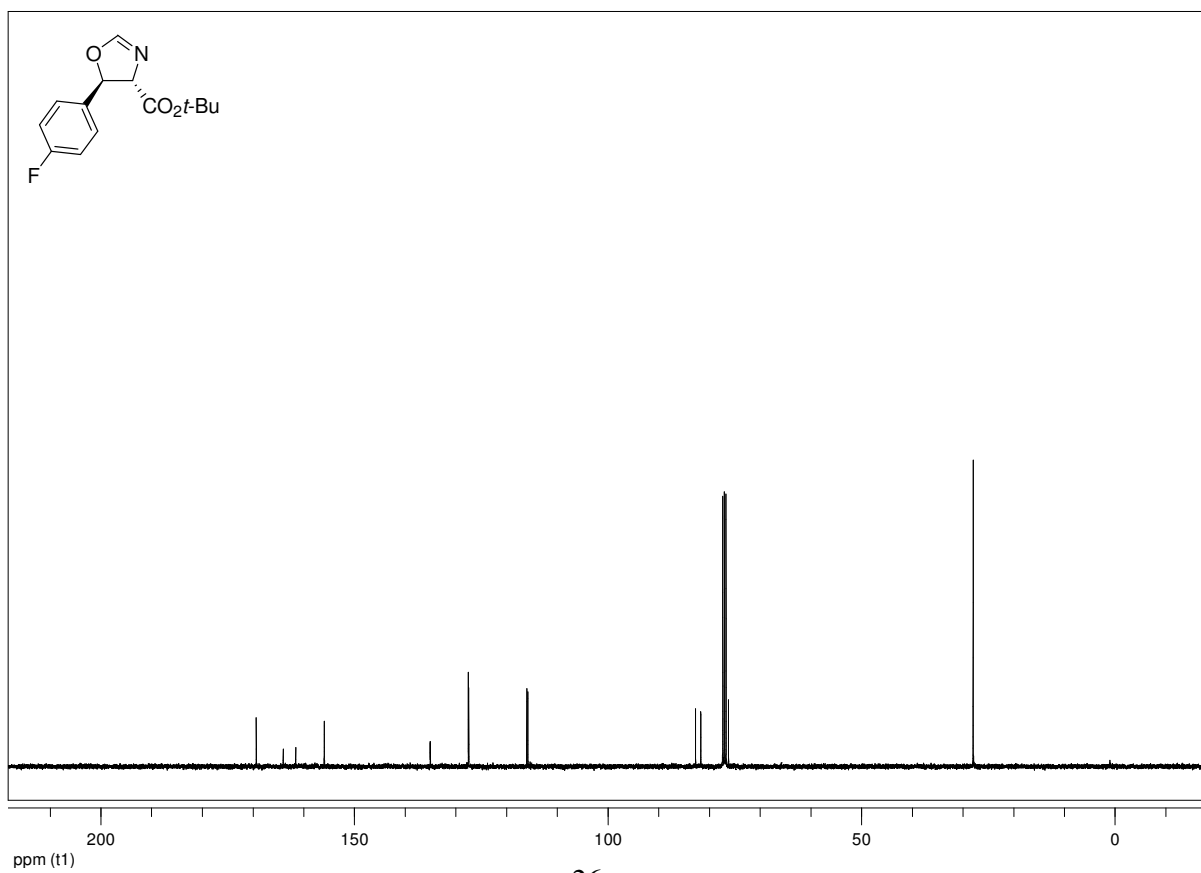
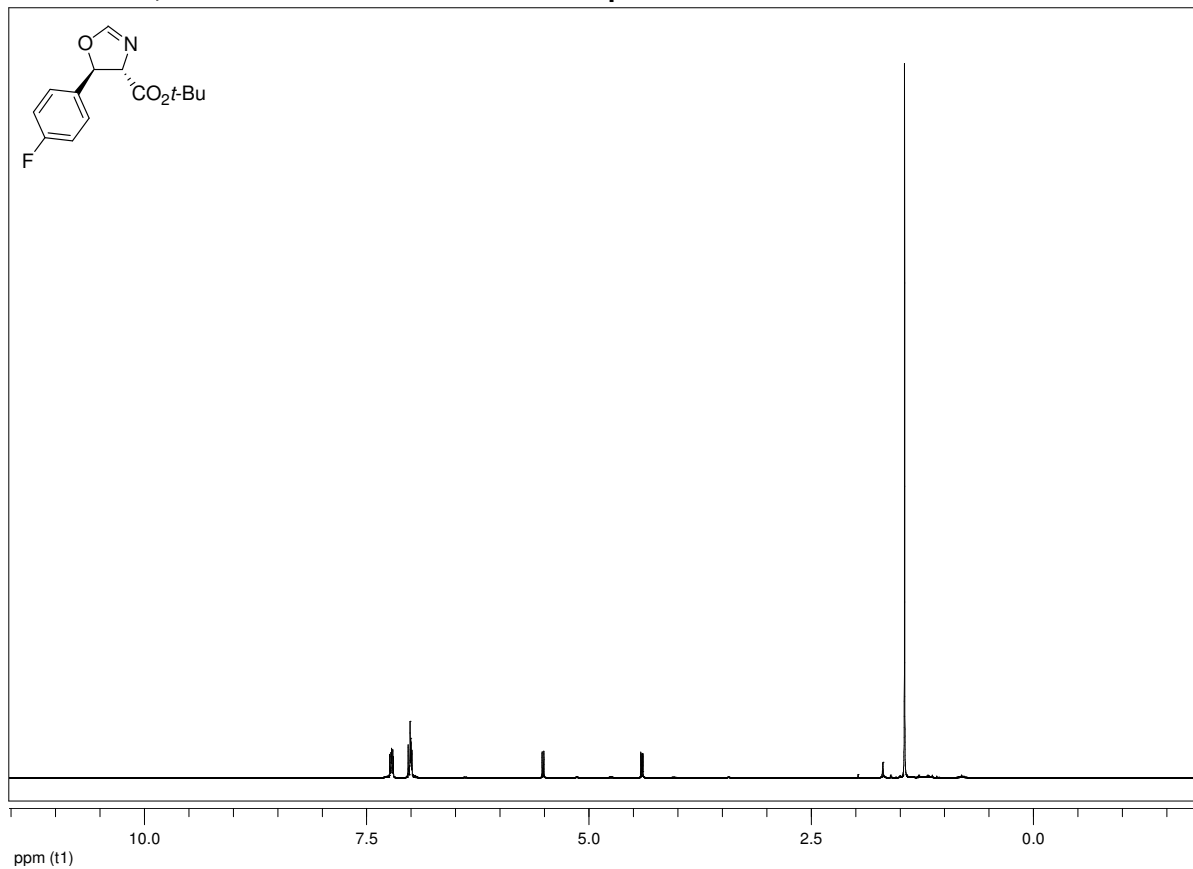
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.234	BP	0.2495	3444.48730	212.09233	95.9660
2	8.204	BP	0.2240	144.79216	7.74844	4.0340

Totals : 3589.27946 219.84077

Results obtained with enhanced integrator!

*** End of Report ***

4.3 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 7c



Racemate

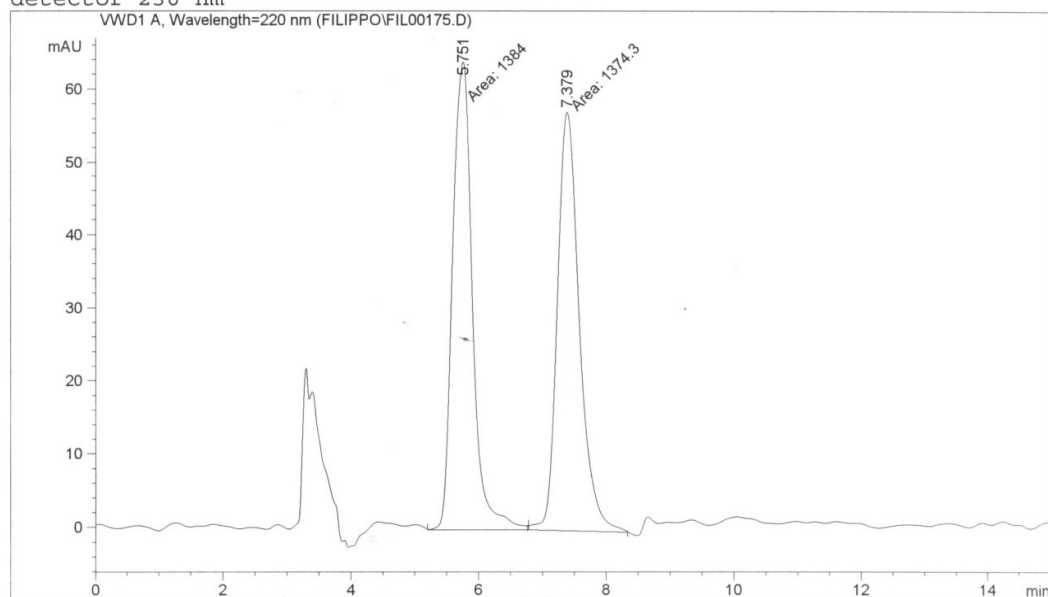
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00175.D

Sample Name: lsd_290

lsd_290
OD Column, 220 nm, 90-10 Hex:IPA

```
=====
Injection Date   : 7/9/08 6:35:56 PM           Seq. Line :    1
Sample Name      : lsd_290                     Vial       :    9
Acq. Operator    : filippo                     Inj        :    1
                                                    Inj Volume : 20 µl

Acq. Method      : C:\HPCHEM\1\METHODS\90HEX220.M
Last changed     : 7/9/08 6:28:36 PM by filippo
Analysis Method  : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed     : 7/8/08 6:41:34 PM by filippo
90% hexane+10% isopropanol
detector 230 nm
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.751	MM	0.3602	1384.00378	64.04493	50.1759
2	7.379	MM	0.3995	1374.30237	57.33828	49.8241

Totals : 2758.30615 121.38321

Results obtained with enhanced integrator!

*** End of Report ***

Instrument 1 7/10/08 8:52:13 AM filippo

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Enantioenriched

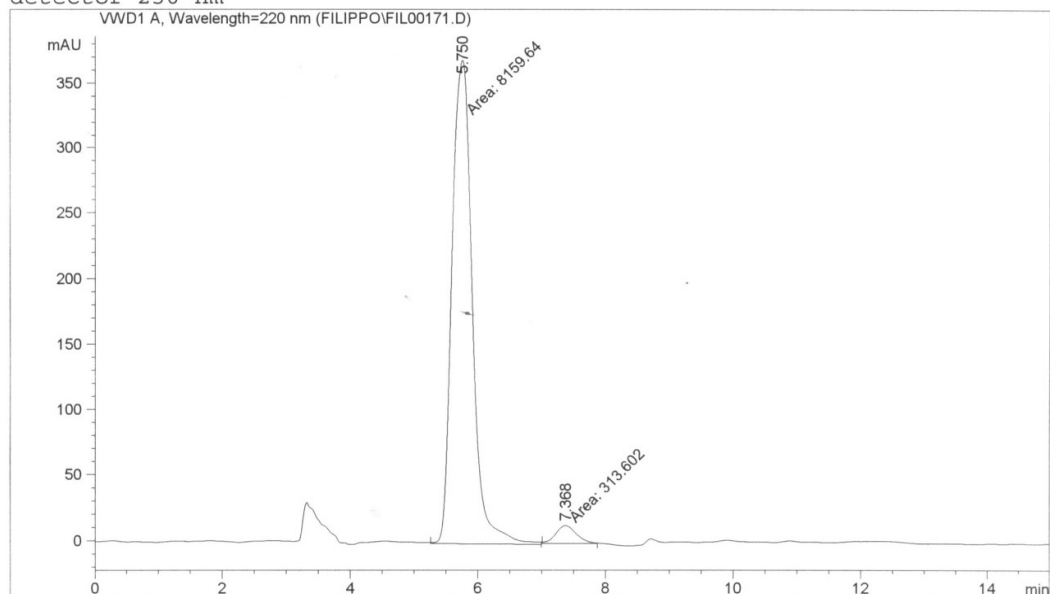
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00171.D

Sample Name: lsd_289

lsd_289
OD Column, 220 nm, 90-10 Hex:IPA

```
=====
Injection Date   : 7/9/08 2:36:45 PM           Seq. Line :    1
Sample Name     : lsd_289                     Vial      :   12
Acq. Operator   : filippo                     Inj       :    1
                                                    Inj Volume: 20 µl

Acq. Method     : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed    : 7/9/08 2:37:02 PM by filippo
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed    : 7/8/08 6:41:34 PM by filippo
90% hexane+10% isopropanol
detector 230 nm
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.750	MM	0.3676	8159.63721	369.96783	96.2989
2	7.368	MM	0.3831	313.60168	13.64374	3.7011

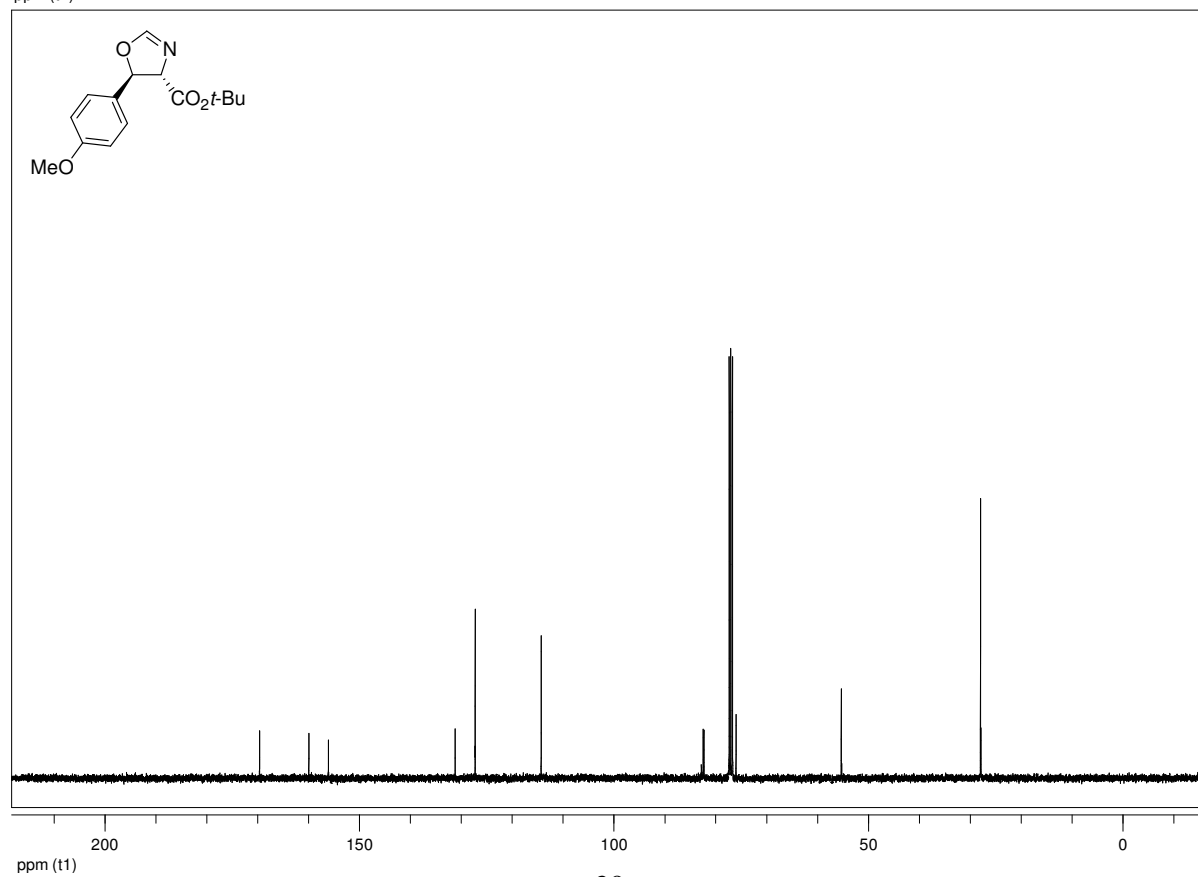
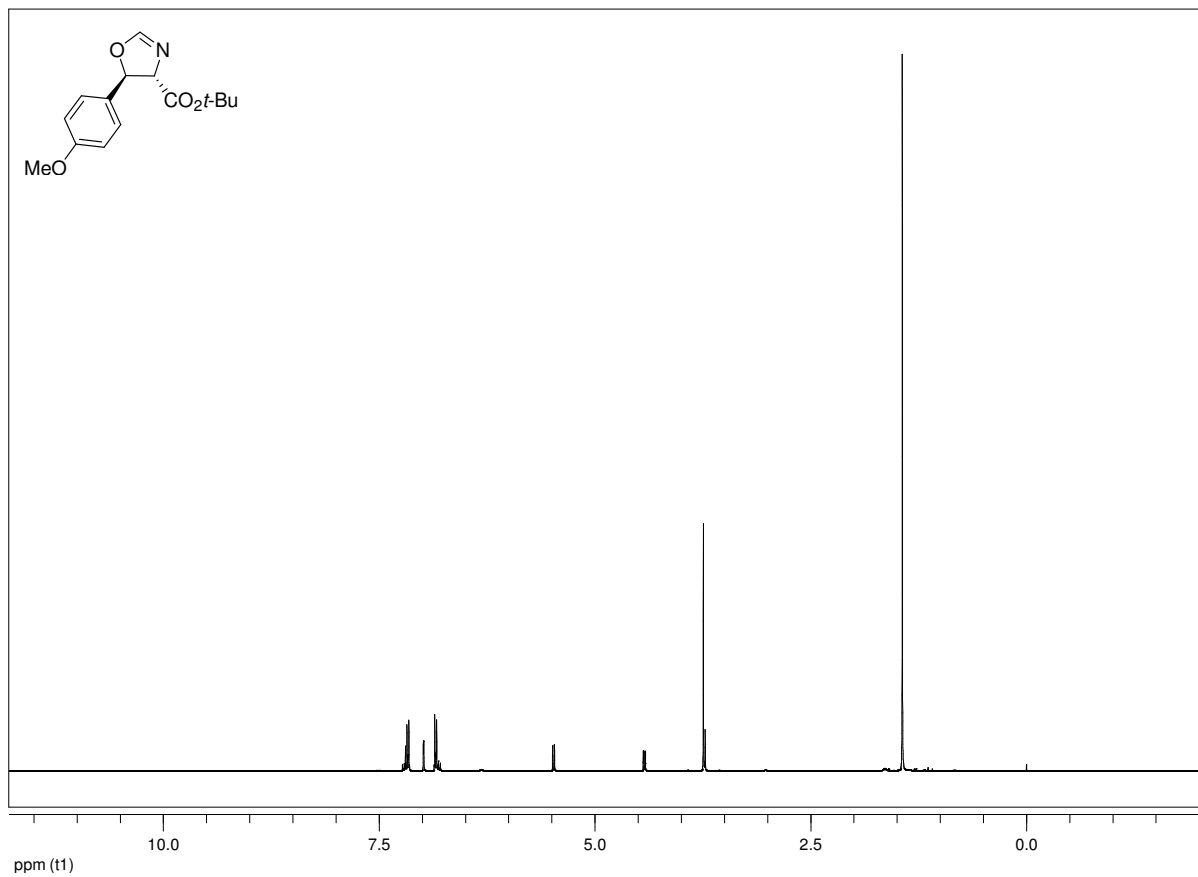
Totals : 8473.23889 383.61158

Results obtained with enhanced integrator!

Instrument 1 7/9/08 6:09:20 PM filippo

Page 1 of 1

4.4 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 7d



Racemate

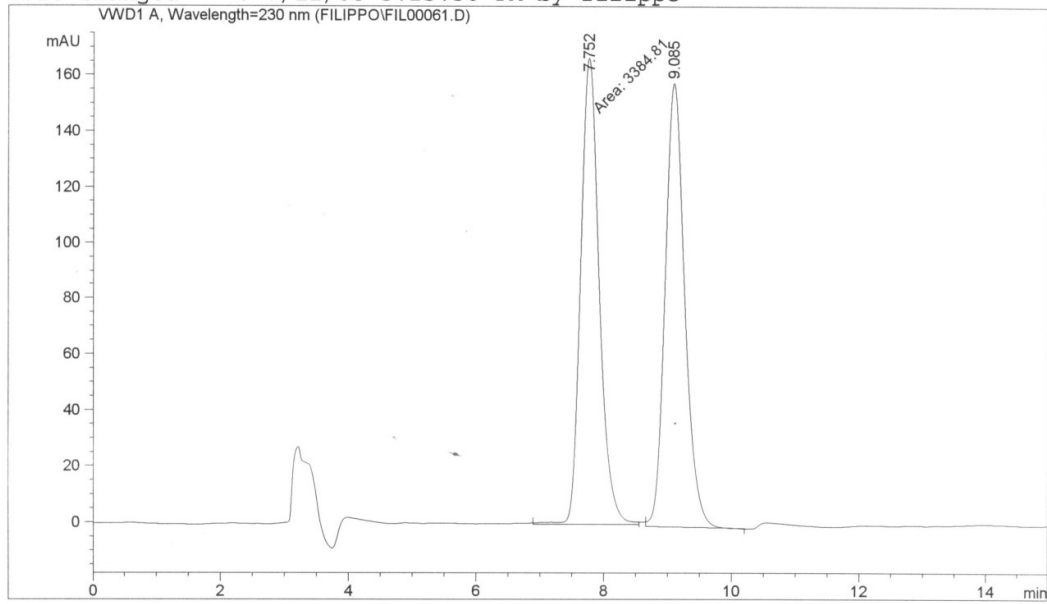
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00061.D

Sample Name: LSD_294

LSD_294, OD COLUMN, 230 NM, 90-10

```
=====
Injection Date   : 7/11/08 4:06:01 PM           Seq. Line :    3
Sample Name     : LSD_294                       Vial      :   13
Acq. Operator  : filippo                        Inj       :    1
                                                    Inj Volume: 20 µl

Method          : C:\HPCHEM\1\METHODS\90HEX.M
Last changed   : 7/11/08 3:25:30 PM by filippo
=====
```



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=230 nm

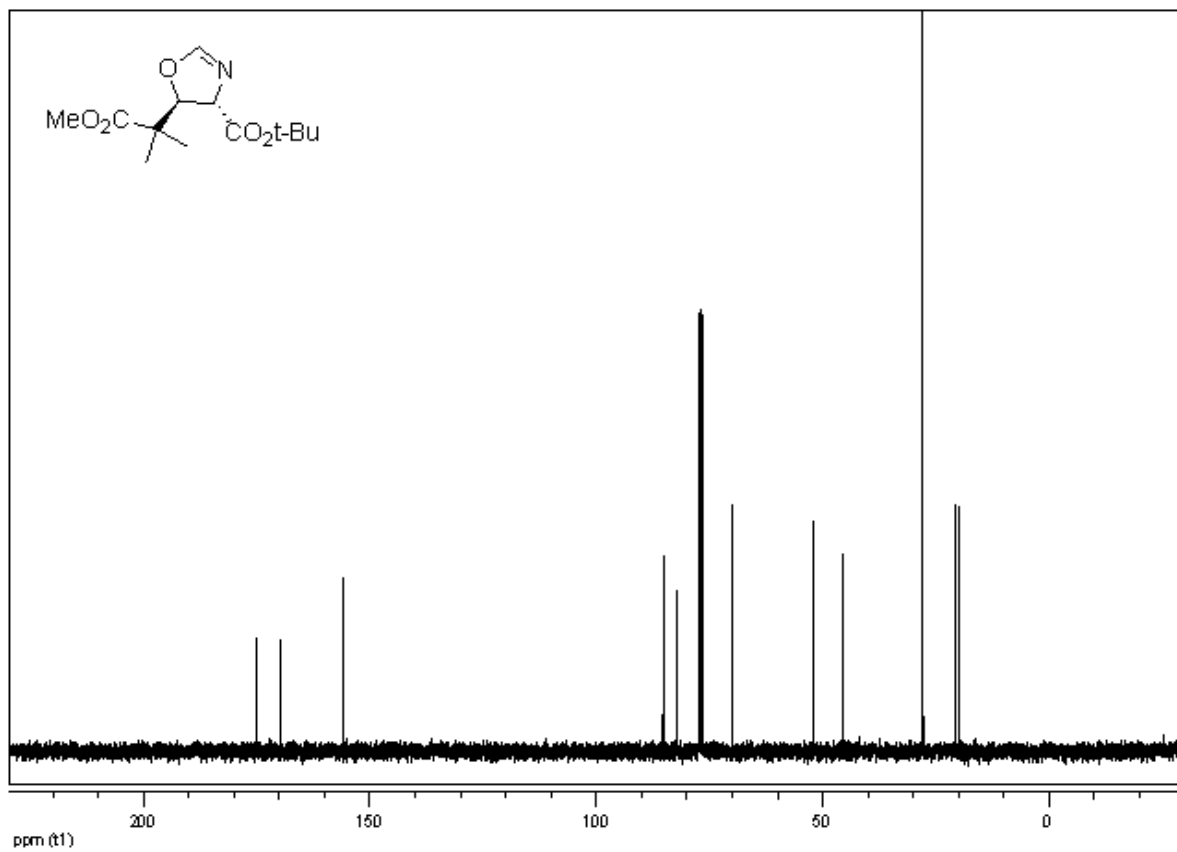
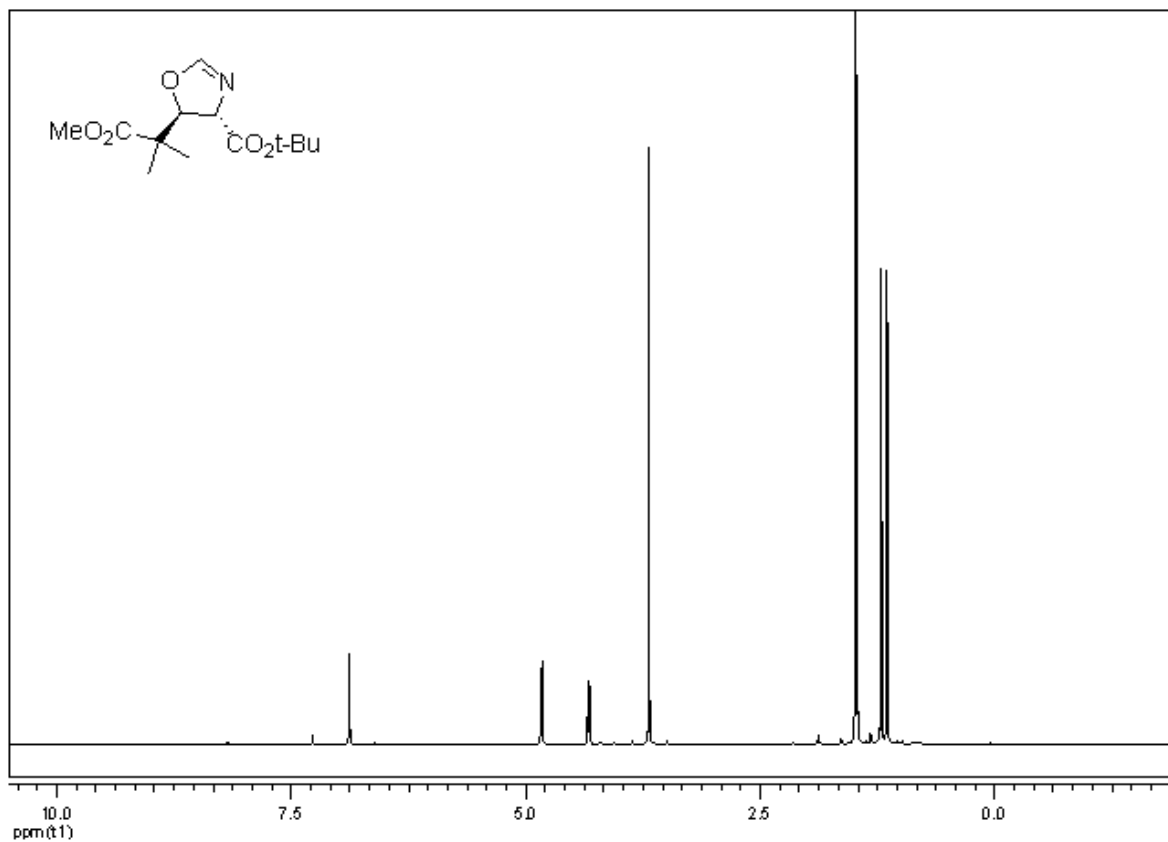
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.752	MM	0.3376	3384.80640	167.11002	49.9058
2	9.085	BP	0.3254	3397.58643	158.94487	50.0942

Totals : 6782.39282 326.05489

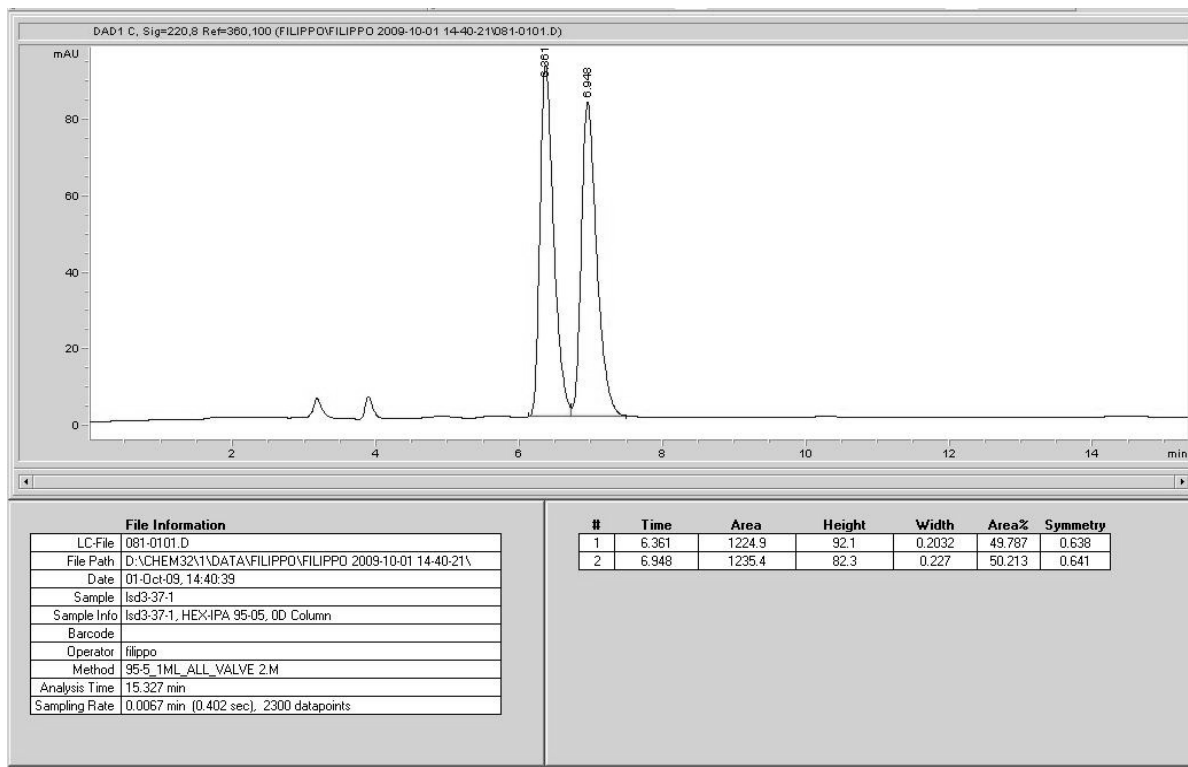
Results obtained with enhanced integrator!

=====
*** End of Report ***

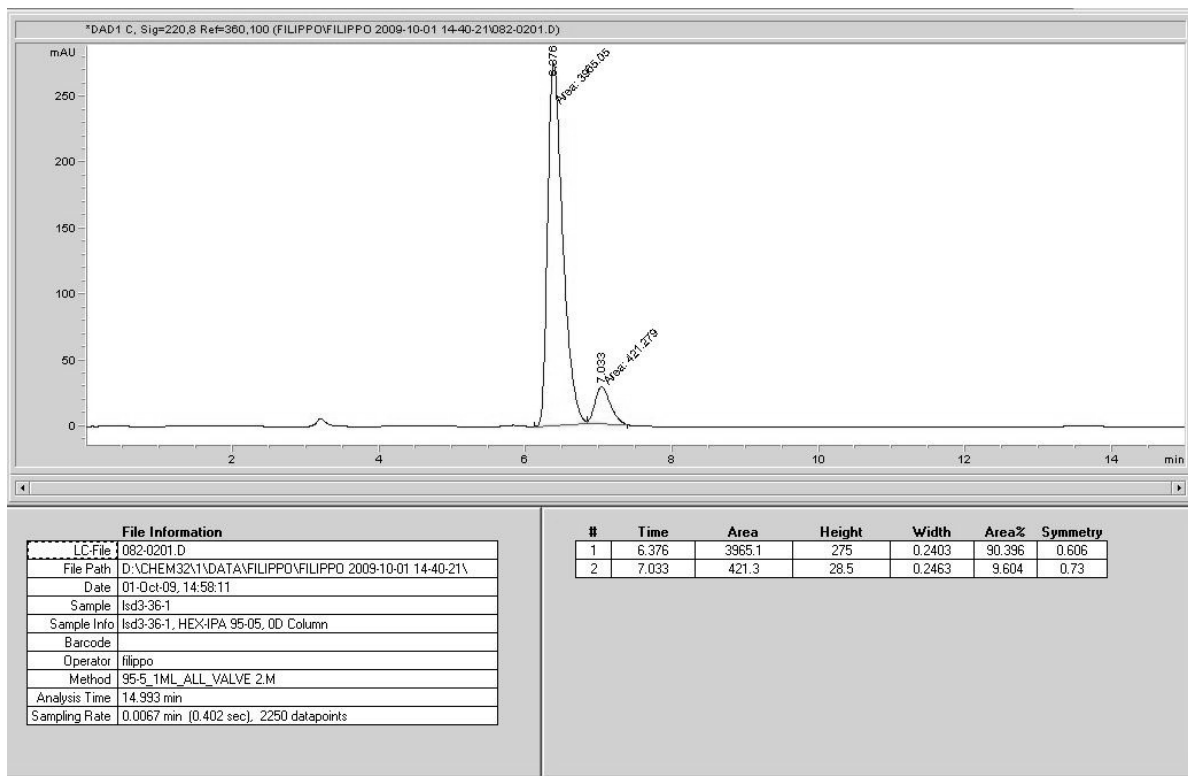
4.5 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 7e



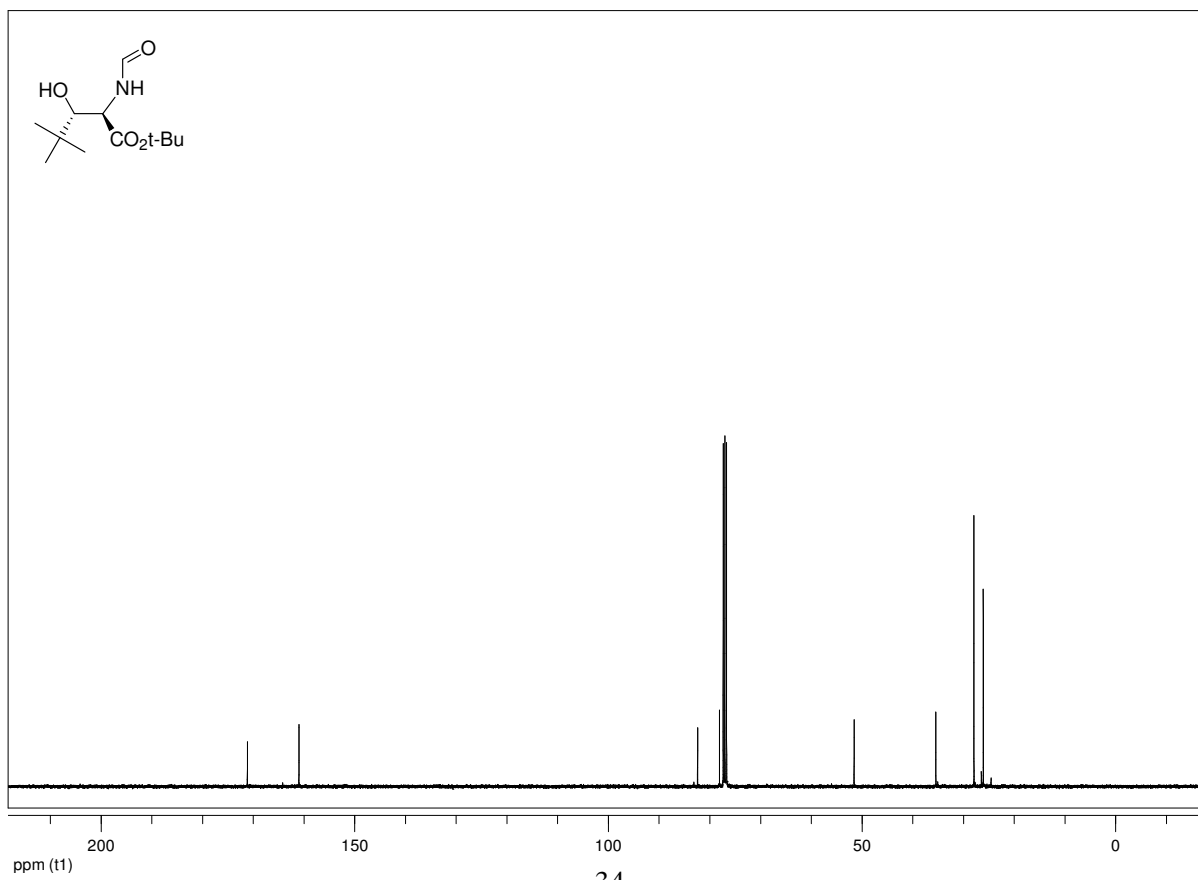
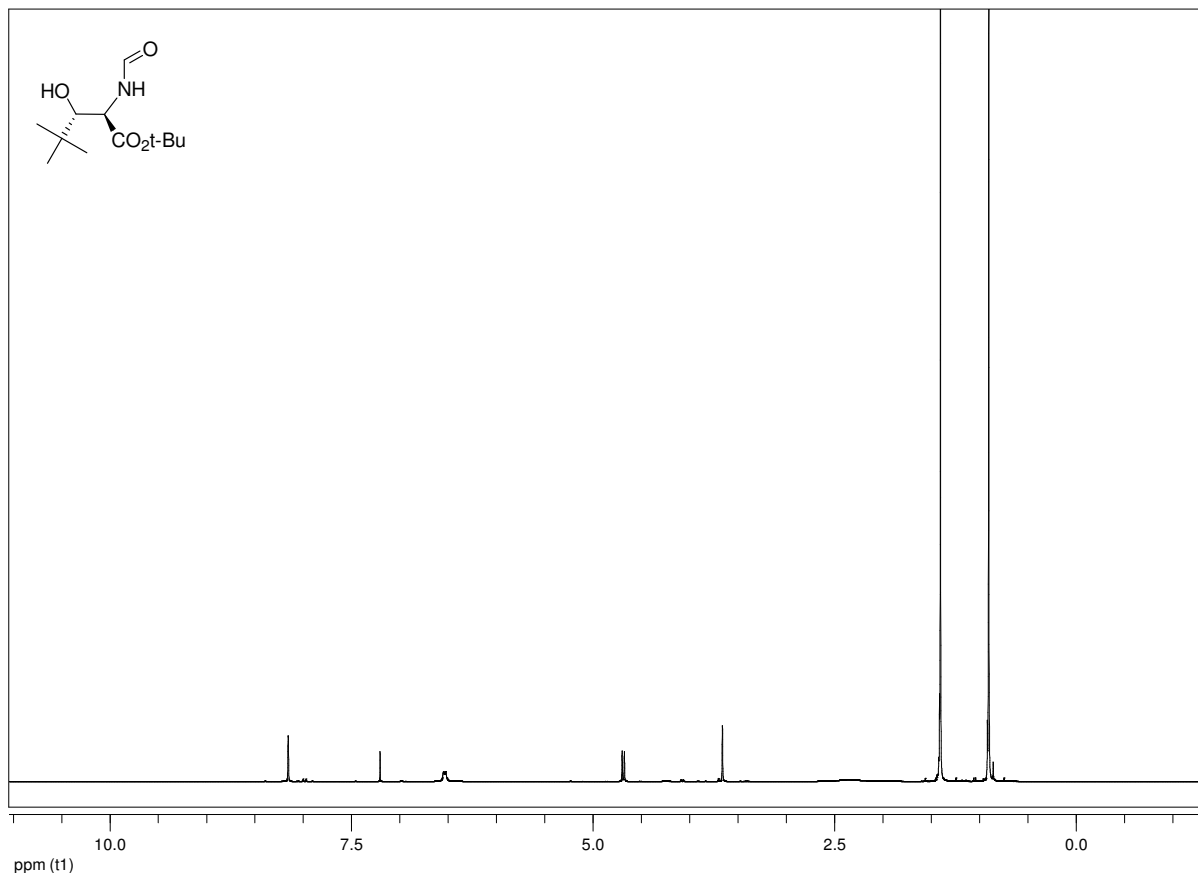
Racemate



Enantioenriched



4.6 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound S1



Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00087.D

Sample Name: LSD_159

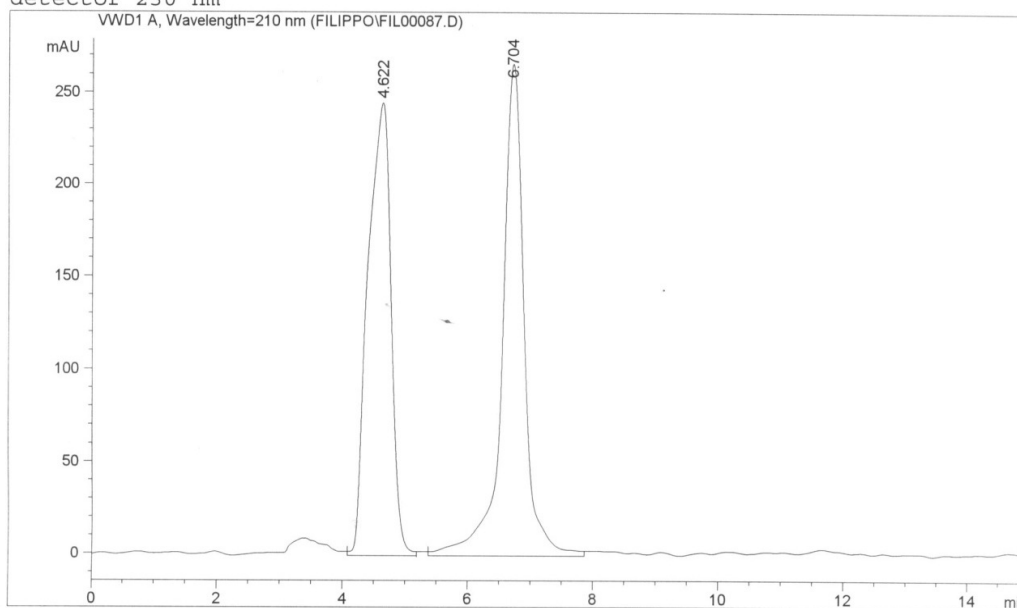
lsd_181

```
=====
Injection Date   : 4/6/08 5:54:54 PM           Seq. Line :    2
Sample Name     : LSD_159                     Vial      :    6
Acq. Operator   : filippo                     Inj       :    1
                                                    Inj Volume: 20 µl
```

```
Acq. Method     : C:\HPCHEM\1\METHODS\80HEX210.M
Last changed    : 4/6/08 5:54:17 PM by filippo
                (modified after loading)
```

```
Analysis Method : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed    : 8/24/08 2:09:12 PM by ting
                (modified after loading)
```

90% hexane+10% isopropanol
detector 230 nm



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.622	VV	0.3512	6297.33301	245.56668	49.0575
2	6.704	VV	0.3449	6539.31250	266.85794	50.9425

Totals : 1.28366e4 512.42462

Results obtained with enhanced integrator!

Instrument 1 8/24/08 2:09:18 PM ting

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Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00086.D

Sample Name: LSD_181

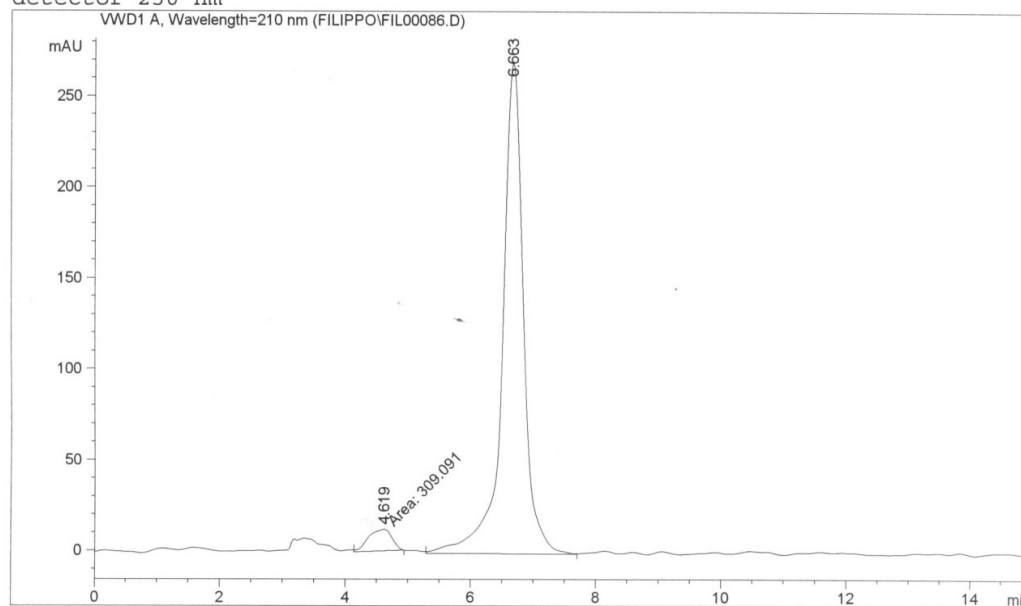
lsd_181

```
=====  
Injection Date : 4/6/08 5:24:10 PM          Seq. Line : 1  
Sample Name    : LSD_181                    Vial       : 7  
Acq. Operator  : filippo                    Inj        : 1  
                                           Inj Volume : 20 µl
```

```
Acq. Method    : C:\HPCHEM\1\METHODS\80HEX210.M  
Last changed   : 4/6/08 5:50:51 PM by filippo  
                (modified after loading)
```

```
Analysis Method : C:\HPCHEM\1\METHODS\90HEX230.M  
Last changed   : 8/24/08 2:06:50 PM by ting  
                (modified after loading)
```

90% hexane+10% isopropanol
detector 230 nm



Area Percent Report

```
=====  
Sorted By      : Signal  
Multiplier     : 1.0000  
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.619	MM	0.4351	309.09128	11.83919	4.6439
2	6.663	VV	0.3369	6346.69287	270.29636	95.3561

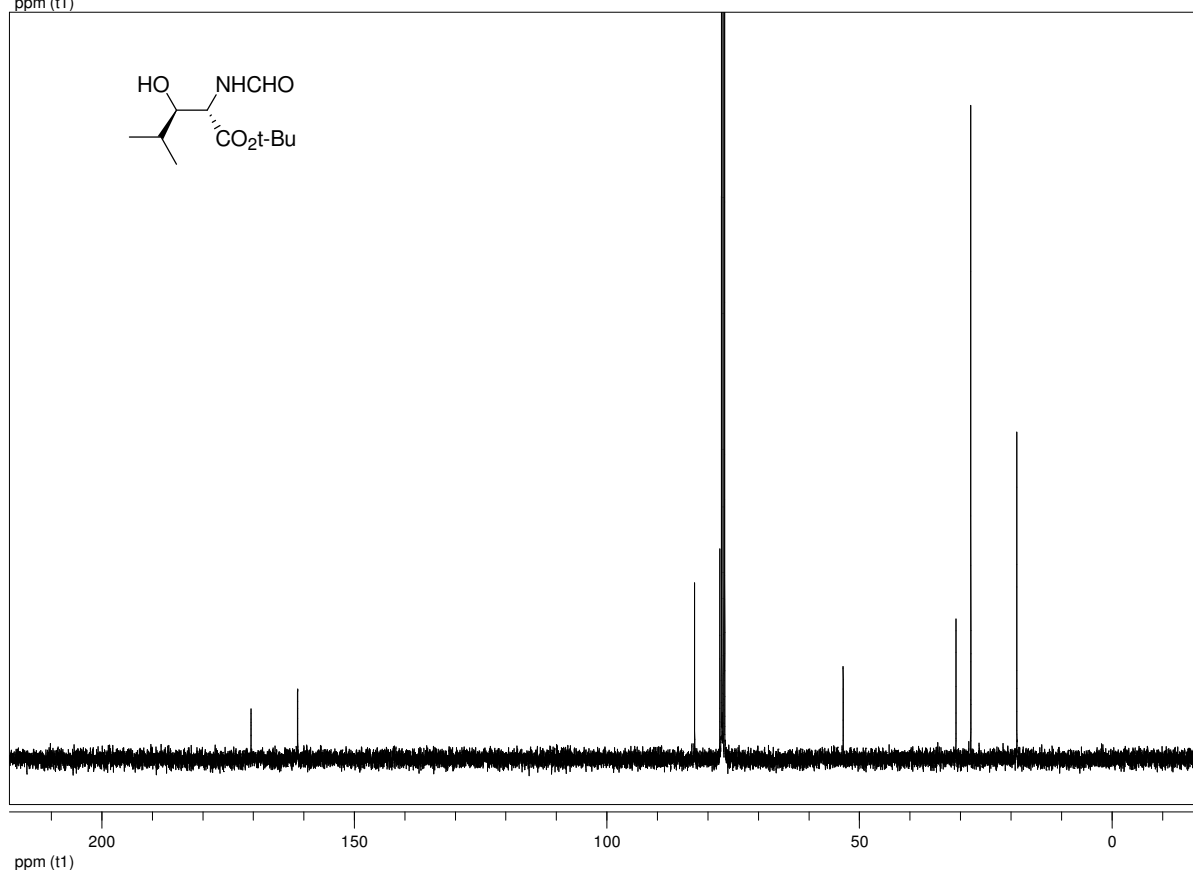
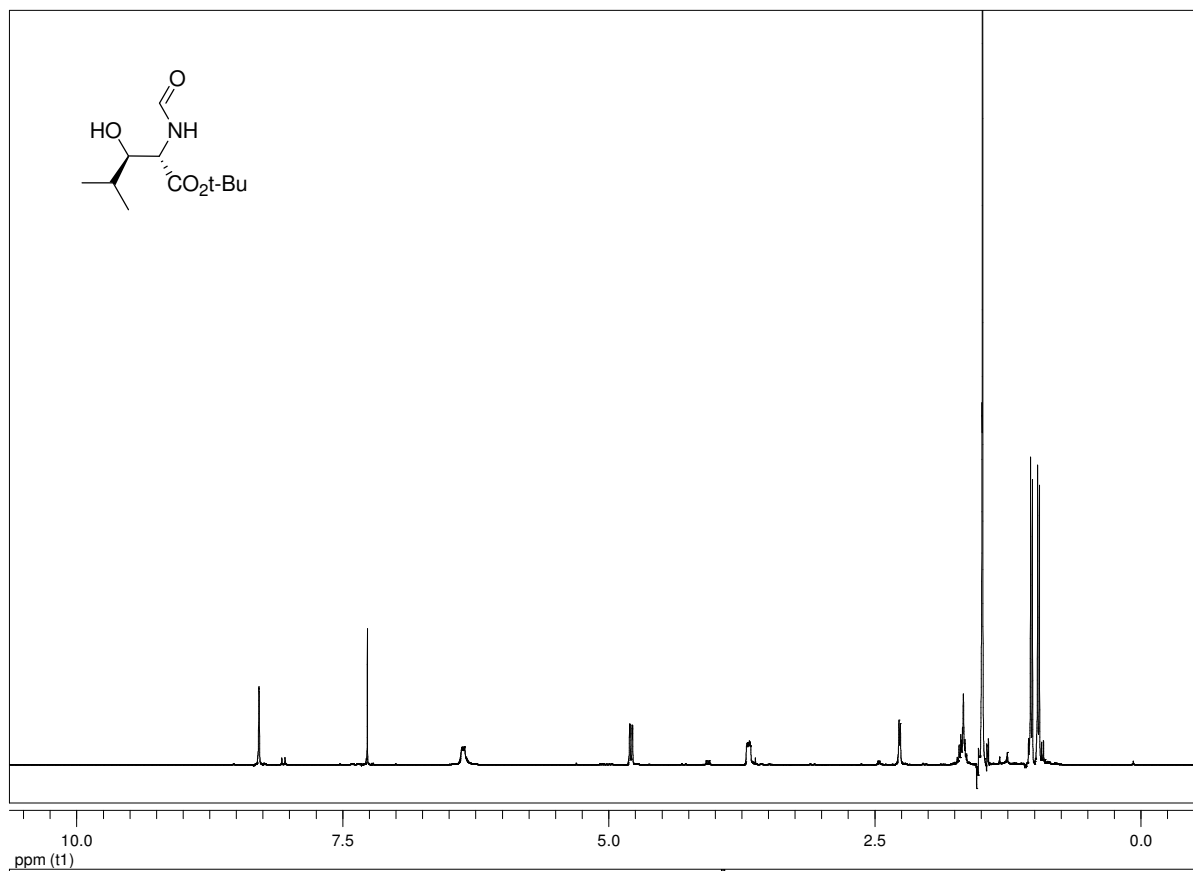
Totals : 6655.78415 282.13554

Results obtained with enhanced integrator!

Instrument 1 8/24/08 2:07:36 PM ting

Page 1 of 1

4.7 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound S2



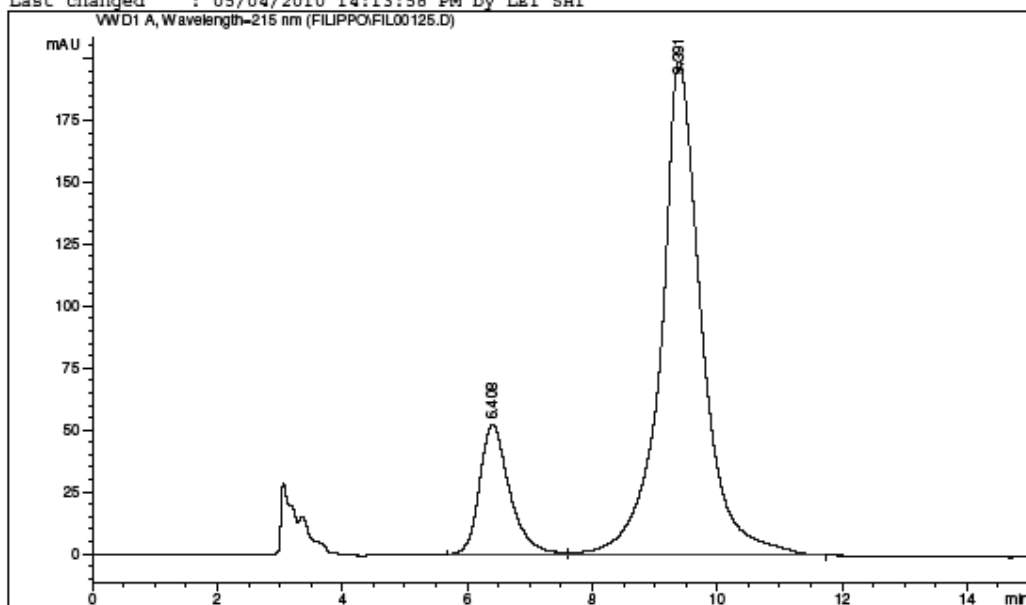
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00125.D

Sample Name: lsd3-74

LSD3-74, OD Column, 90-10, 215 nm, 1 ML/MIN

```
=====
Injection Date : 07/01/2010 09:18:35 PM      Seq. Line : 2
Sample Name    : lsd3-74                      Location  : Vial 9
Acq. Operator  : filippo                      Inj       : 1
Acq. Instrument : Instrument 1                 Inj Volume: 20 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\90HEX215.M
Last changed   : 07/01/2010 09:17:06 PM by filippo
                (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\80HEX220.M
Last changed   : 05/04/2010 14:13:58 PM by LEI SHI
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=215 nm

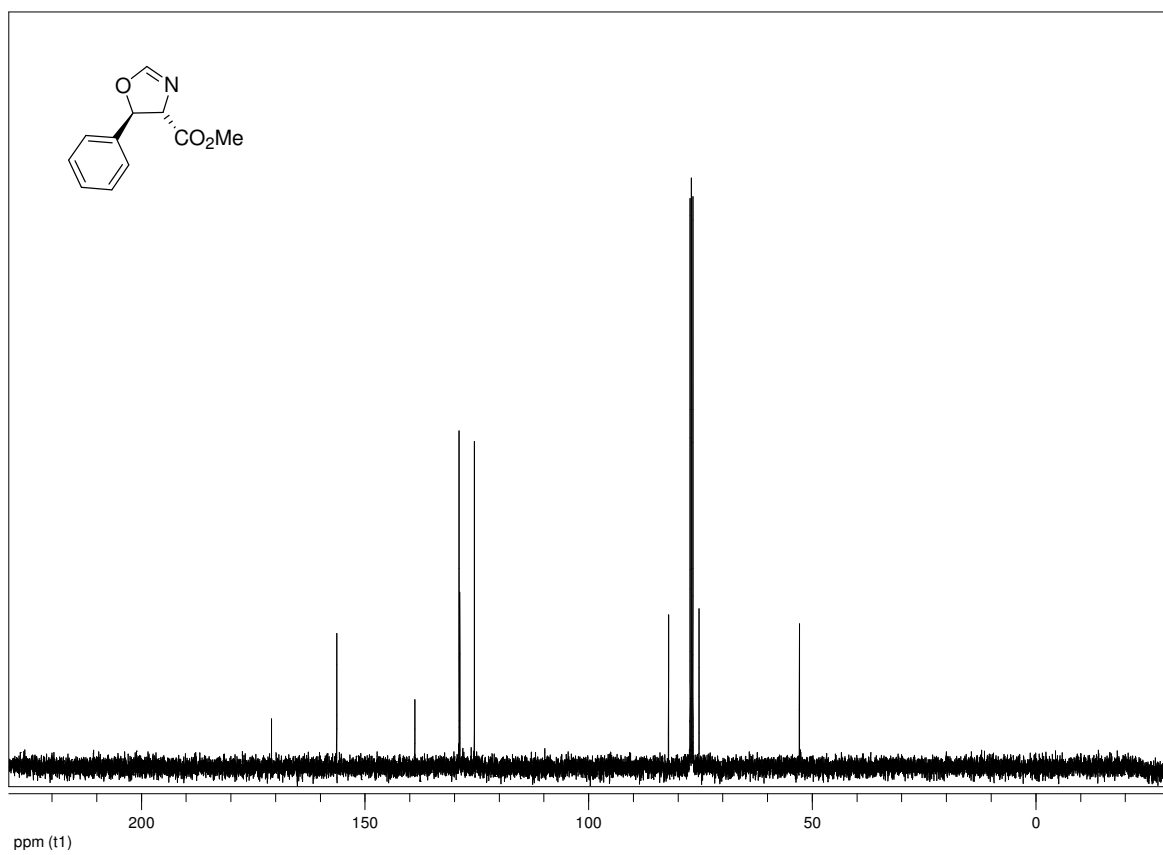
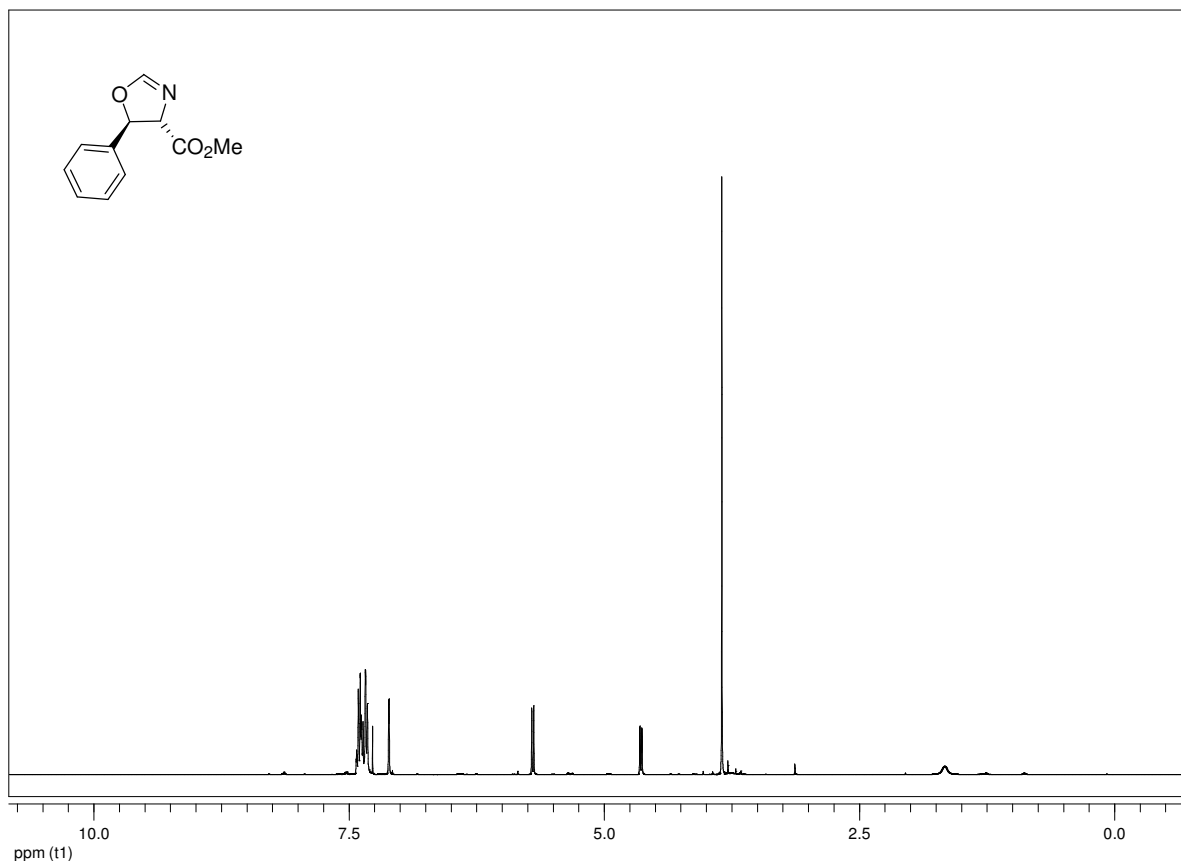
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.408	BV	0.5146	1784.32129	52.48695	16.5349
2	9.391	VB	0.6577	9006.95410	199.11411	83.4651

Totals : 1.07913e4 251.60106

Results obtained with enhanced integrator!

*** End of Report ***

4.8 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 7h



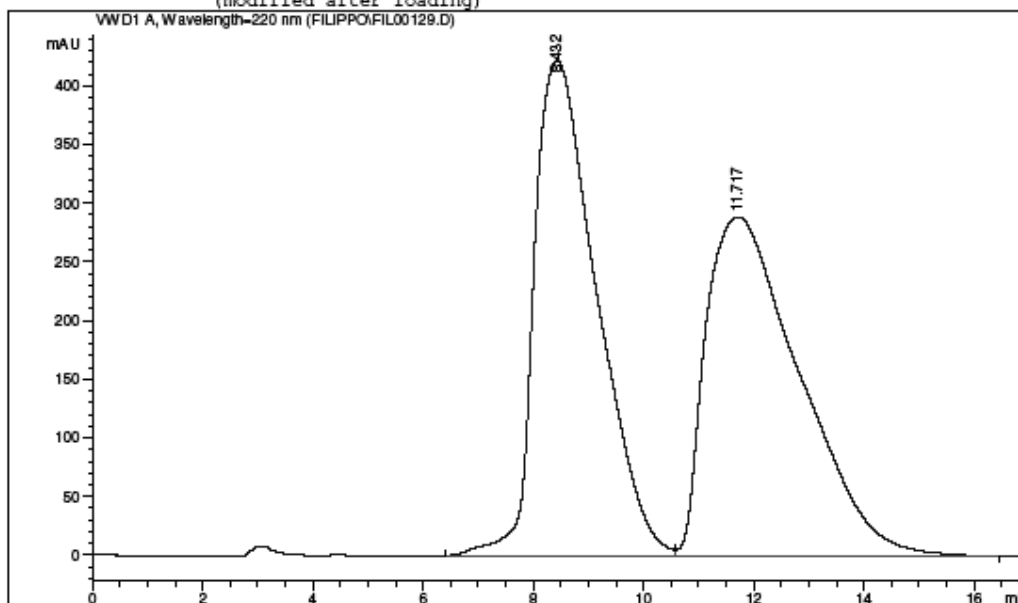
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00129.D

Sample Name: lsd7-45

LSD7-45, AD Column, 90-10, 220 nm, 1 ML/MIN

```
=====
Injection Date : 05/09/2010 15:44:32 PM      Seq. Line : 1
Sample Name    : lsd7-45                      Location  : Vial 13
Acq. Operator  : filippo                      Inj       : 1
Acq. Instrument : Instrument 1                 Inj Volume: 20 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\90HEX220.M
Last changed   : 05/09/2010 16:01:19 PM by filippo
                (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\90HEX220.M
Last changed   : 06/09/2010 19:29:04 PM by filippo
                (modified after loading)
=====
```



Area Percent Report

```
=====
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
=====
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.432	BV	1.1813	3.32171e4	422.48746	49.3017
2	11.717	VB	1.7706	3.41580e4	289.06854	50.6983

Totals : 6.73751e4 711.55600

Results obtained with enhanced integrator!

*** End of Report ***

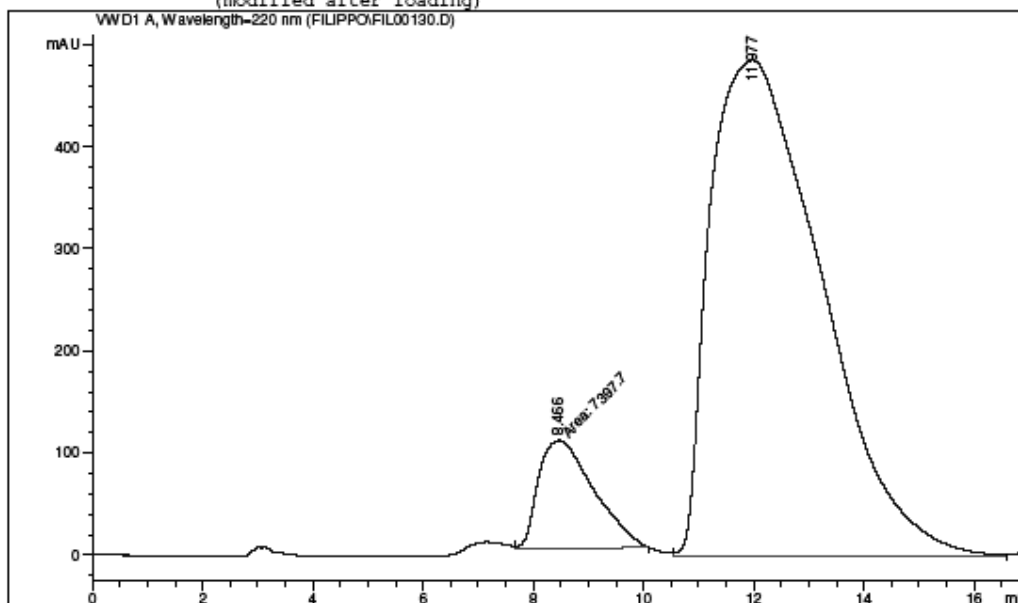
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00130.D

Sample Name: lsd7-47

LSD7-47, AD Column, 90-10, 220 nm, 1 ML/MIN

```
=====
Injection Date : 06/09/2010 19:06:12 PM      Seq. Line : 1
Sample Name    : lsd7-47                      Location  : Vial 12
Acq. Operator  : filippo                      Inj       : 1
Acq. Instrument : Instrument 1                 Inj Volume: 20 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJ26\90HEX220.M
Last changed   : 06/09/2010 19:29:56 PM by filippo
                (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DJ26\90HEX220.M
Last changed   : 07/09/2010 08:54:42 PM by filippo
                (modified after loading)
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=220 nm

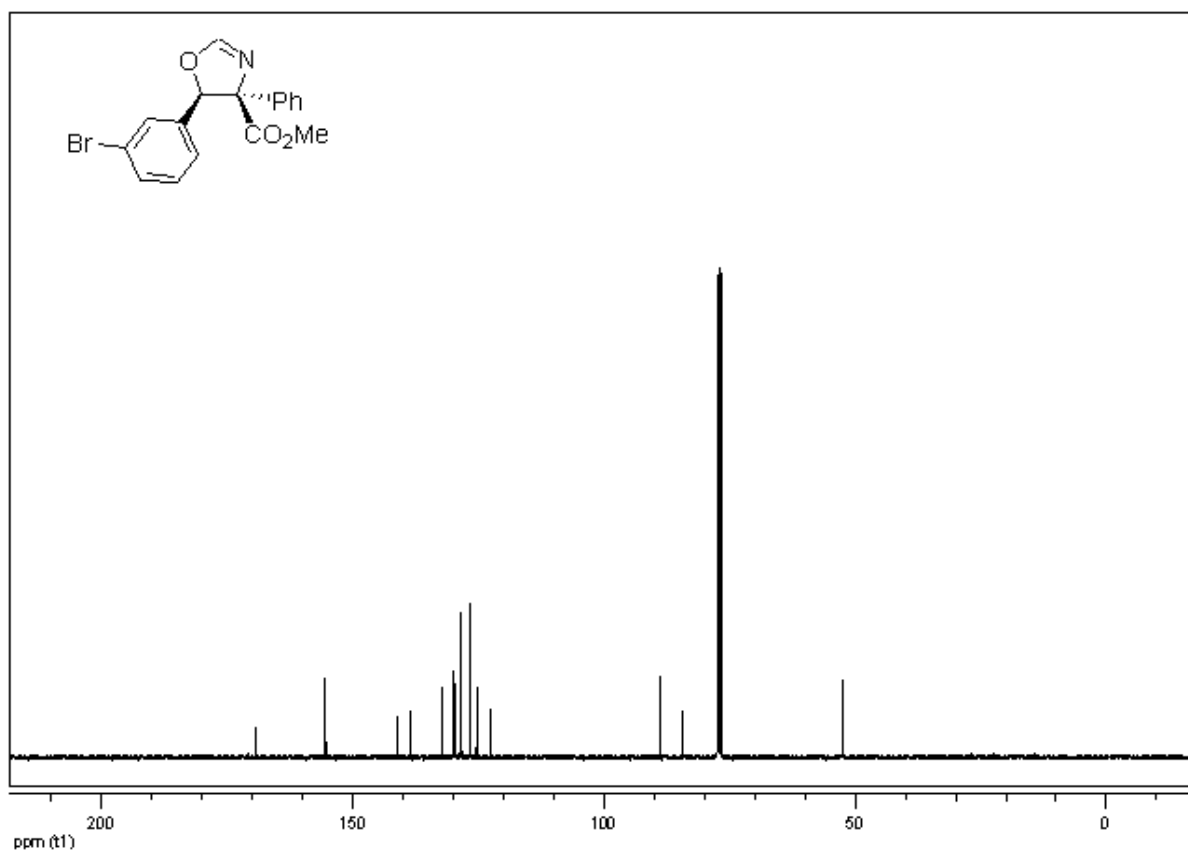
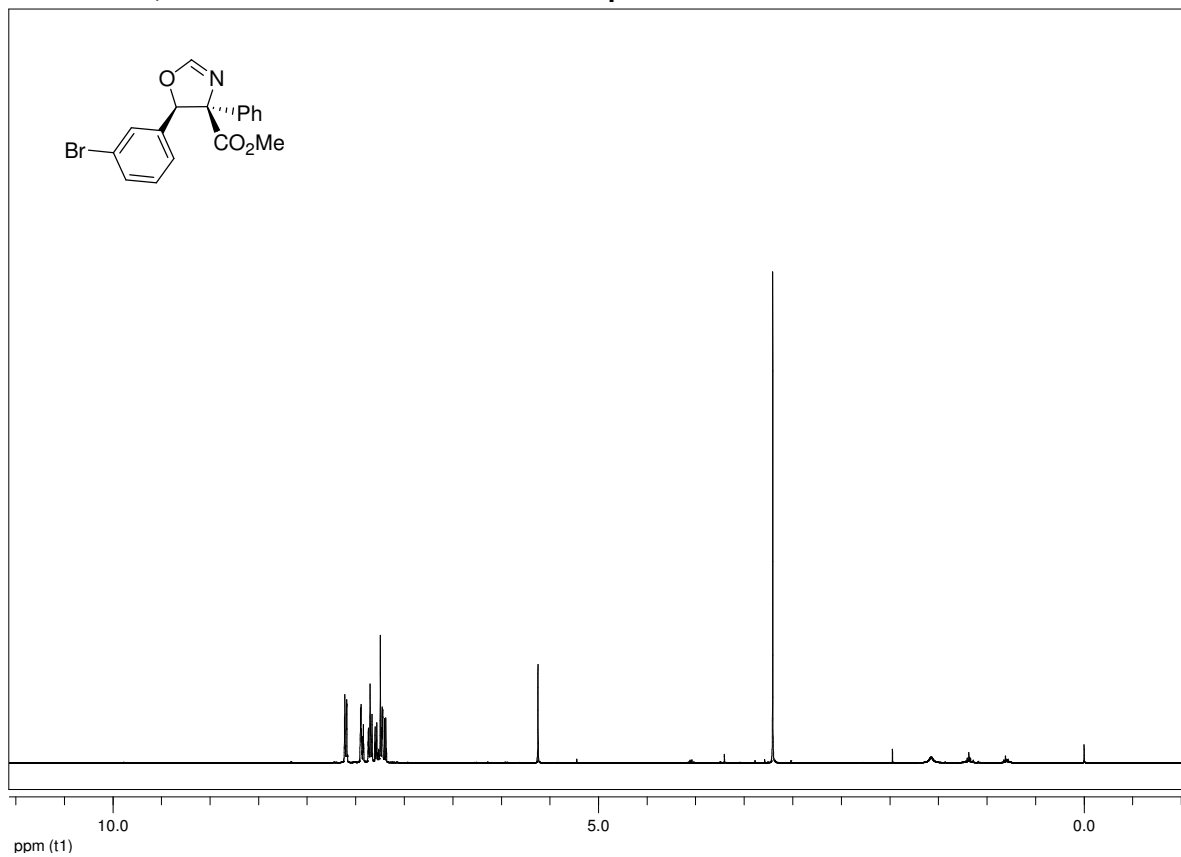
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.466	MM	1.1636	7397.70215	105.96352	9.7579
2	11.977	VV	2.0865	6.84144e4	485.94919	90.2421

Totals : 7.58121e4 591.91270

Results obtained with enhanced integrator!

*** End of Report ***

4.9 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9a



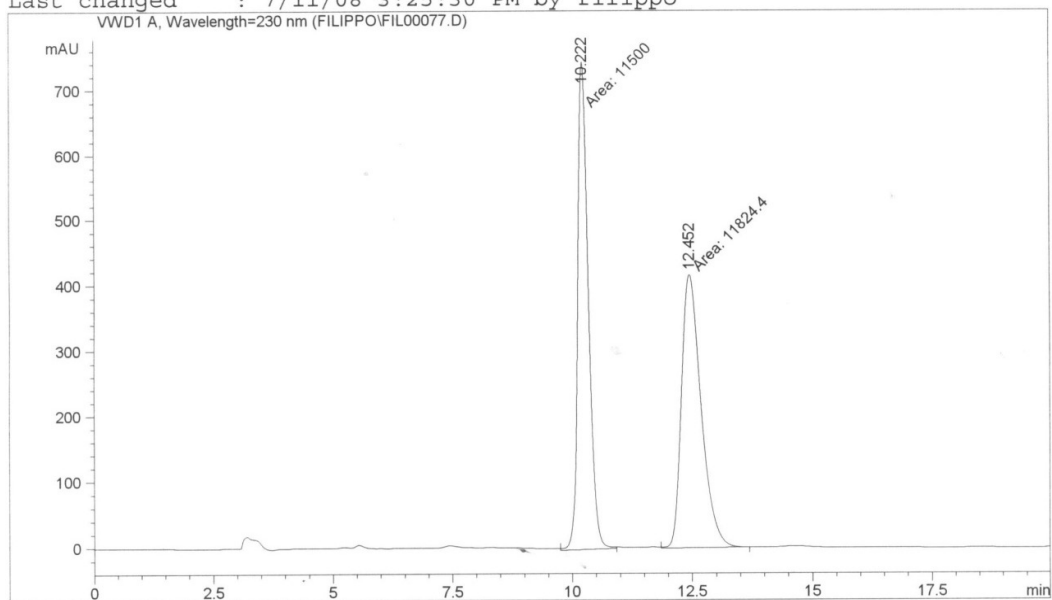
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00077.D

Sample Name: LSD_306

LSD_306, od COLUMN, 230 NM, 90-10

```
=====  
Injection Date : 7/17/08 8:50:12 PM      Seq. Line : 2  
Sample Name    : LSD_306                  Vial : 10  
Acq. Operator  : filippo                  Inj : 1  
                                           Inj Volume : 20 µl  
  
Acq. Method    : C:\HPCHEM\1\METHODS\90HEX230.M  
Last changed   : 7/17/08 8:54:54 PM by filippo  
                (modified after loading)  
Analysis Method : C:\HPCHEM\1\METHODS\90HEX.M  
Last changed   : 7/11/08 3:25:30 PM by filippo  
=====
```



Area Percent Report

```
=====  
Sorted By      :      Signal  
Multiplier     :      1.0000  
Dilution       :      1.0000  
=====
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.222	MM	0.2568	1.15000e4	746.38428	49.3045
2	12.452	MM	0.4733	1.18244e4	416.42099	50.6955

Totals : 2,33244e4 1162.80527

Results obtained with enhanced integrator!

=====
*** End of Report ***

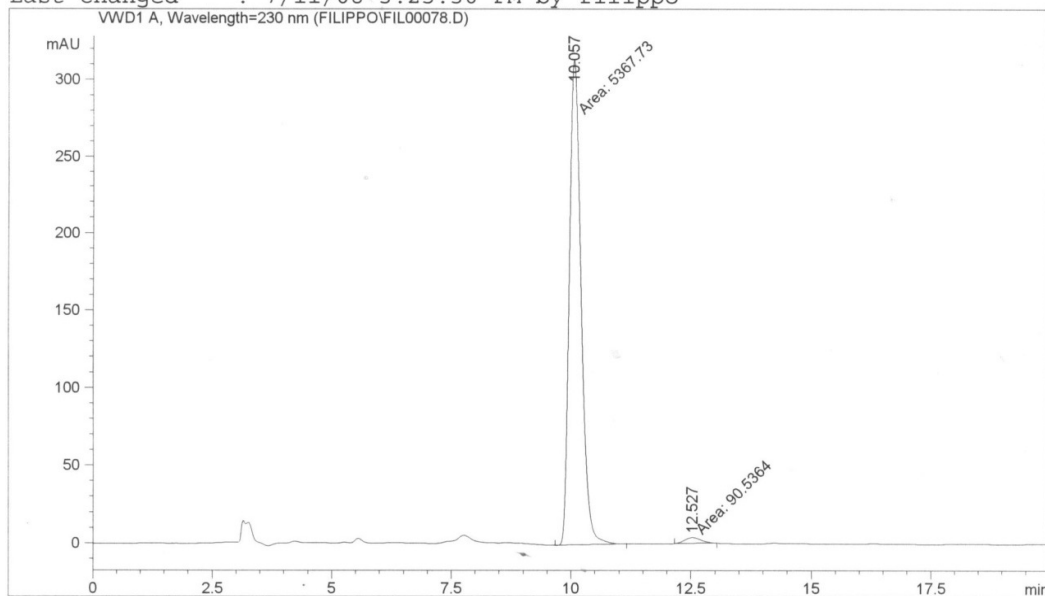
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00078.D

Sample Name: LSD_304

LSD_304, od COLUMN, 230 NM, 90-10

```
=====
Injection Date : 7/17/08 9:10:51 PM      Seq. Line : 3
Sample Name    : LSD_304                  Vial : 11
Acq. Operator  : filippo                  Inj : 1
                                           Inj Volume : 10 µl
Acq. Method    : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed   : 7/17/08 9:10:17 PM by filippo
                 (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\90HEX.M
Last changed   : 7/11/08 3:25:30 PM by filippo
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.057	MM	0.2847	5367.73340	314.24094	98.3413
2	12.527	MM	0.4000	90.53645	3.77271	1.6587

Totals : 5458.26984 318.01364

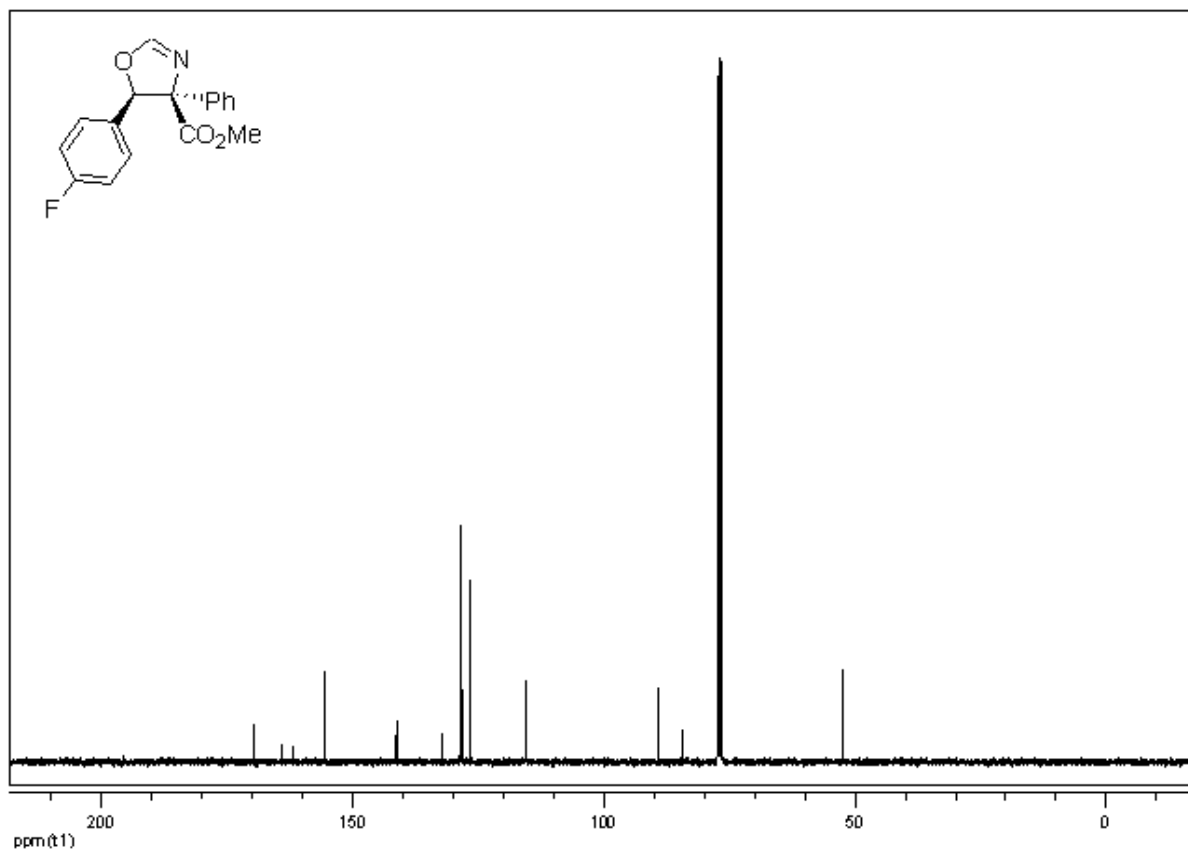
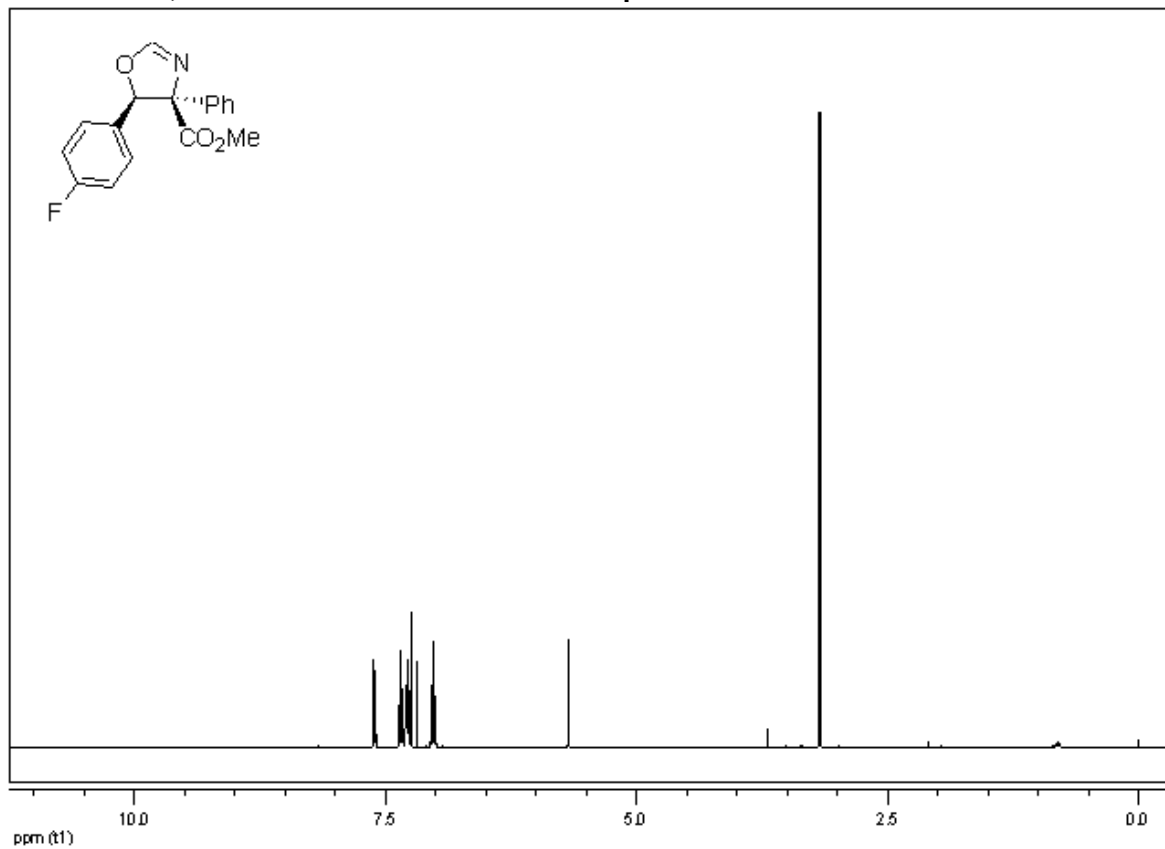
Results obtained with enhanced integrator!

*** End of Report ***

Instrument 1 7/17/08 9:38:58 PM filippo

Page 1 of 1

4.10 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9b



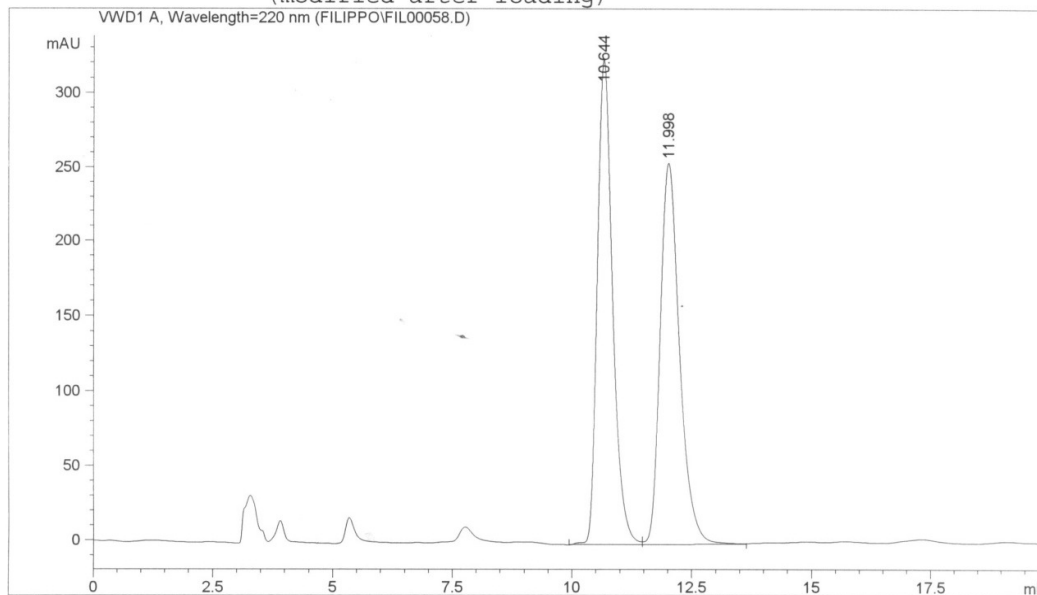
Racemate

lsd_287, OD Column, 220 nm, 90-10 IPA, Hex

```
=====
Injection Date : 7/8/08 9:12:36 AM          Seq. Line : 1
Sample Name    : LSD_287                    Vial : 10
Acq. Operator  : filippo                    Inj : 1
                                           Inj Volume : 20 µl

Acq. Method    : C:\HPCHEM\1\METHODS\90HEX220.M
Last changed   : 7/8/08 9:12:31 AM by filippo
                (modified after loading)

Analysis Method : C:\HPCHEM\1\METHODS\90HEX.M
Last changed   : 7/8/08 9:11:24 AM by filippo
                (modified after loading)
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.644	VV	0.3441	7239.39063	324.74503	50.1065
2	11.998	VB	0.4331	7208.60693	255.53934	49.8935

Totals : 1.44480e4 580.28436

Results obtained with enhanced integrator!

*** End of Report ***

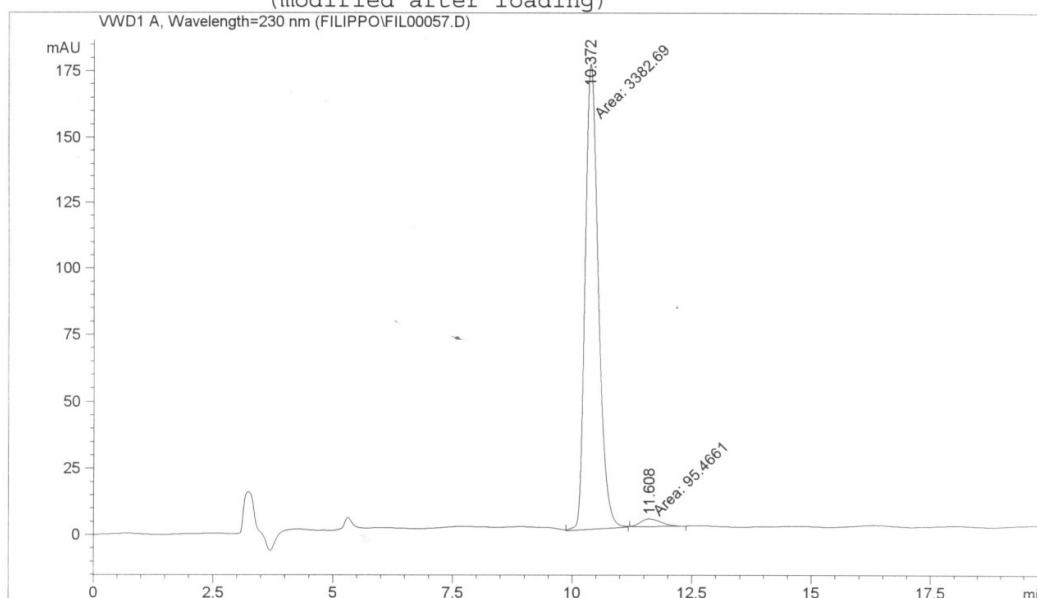
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00057.D

Sample Name: LSD_285

lsd_285, OD Column, 230 nm, 90-10 IPA,Hex

```
=====  
Injection Date   : 7/7/08 5:51:00 PM           Seq. Line :    1  
Sample Name     : LSD_285                     Vial      :    9  
Acq. Operator   : filippo                     Inj       :    1  
                                           Inj Volume: 10 µl  
  
Acq. Method     : C:\HPCHEM\1\METHODS\90HEX230.M  
Last changed    : 7/7/08 6:09:49 PM by filippo  
                (modified after loading)  
Analysis Method : C:\HPCHEM\1\METHODS\90HEX.M  
Last changed    : 7/7/08 4:49:10 PM by filippo  
                (modified after loading)
```



Area Percent Report

```
=====  
Sorted By      : Signal  
Multiplier    : 1.0000  
Dilution      : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.372	MM	0.3205	3382.68872	175.90138	97.2553
2	11.608	MM	0.5335	95.46614	2.98222	2.7447

Totals : 3478.15486 178.88360

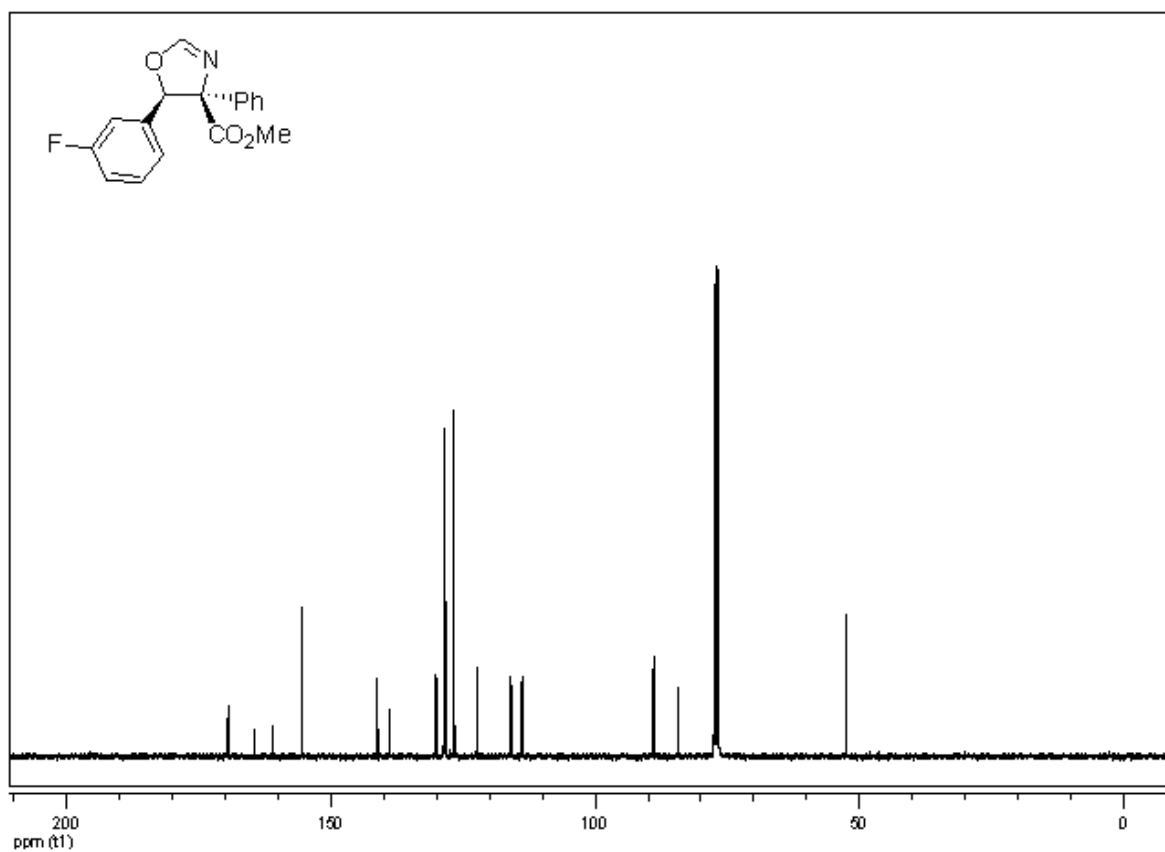
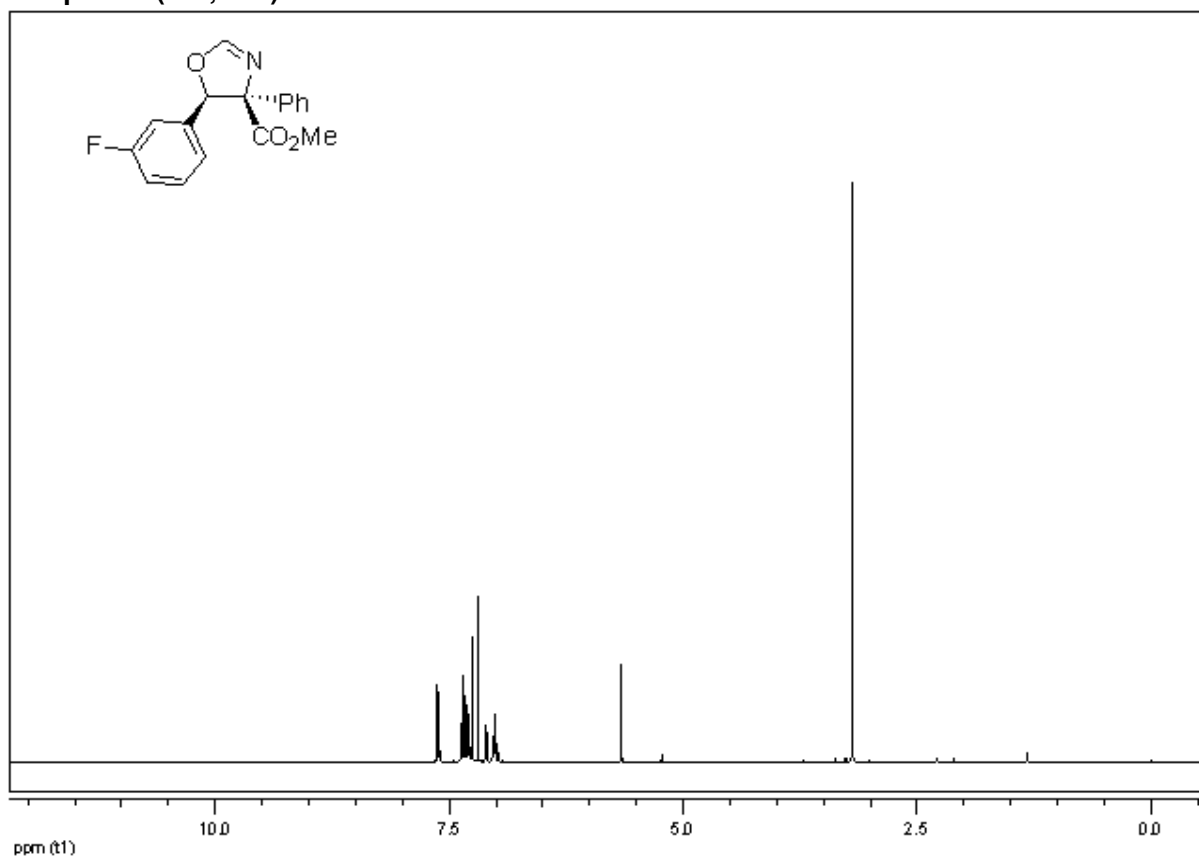
Results obtained with enhanced integrator!

*** End of Report ***

Instrument 1 7/7/08 6:14:32 PM filippo

Page 1 of 1

4.11 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound (*4R*, *5R*)-9c and $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ of compound (*4S^**, *5R^**)-9c.



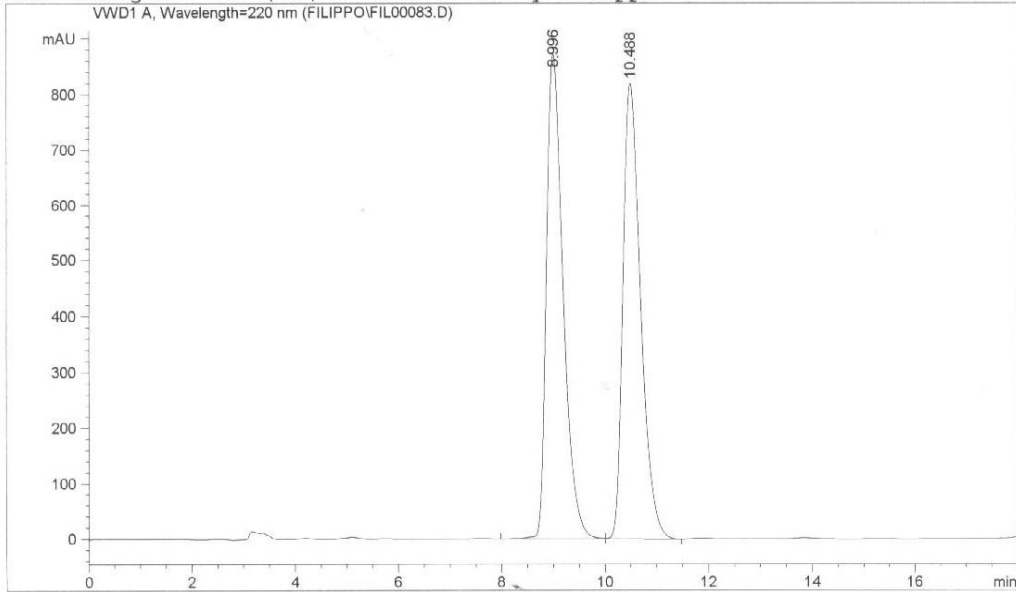
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00083.D

Sample Name: LSD_322

LSD_322, 90-10, 220 NM, OD COLUMN

=====
Injection Date : 7/24/08 7:36:18 PM Seq. Line : 1
Sample Name : LSD_322 Vial : 7
Acq. Operator : filippo Inj : 1
 Inj Volume : 20 µl
Acq. Method : C:\HPCHEM\1\METHODS\90HEX220.M
Last changed : 7/24/08 7:35:29 PM by filippo
Analysis Method : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed : 7/17/08 8:26:16 PM by filippo



=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.996	VV	0.3418	1.95700e4	872.21729	50.1456
2	10.488	VP	0.3648	1.94564e4	819.93701	49.8544

Totals : 3.90264e4 1692.15430

Results obtained with enhanced integrator!

=====
*** End of Report ***

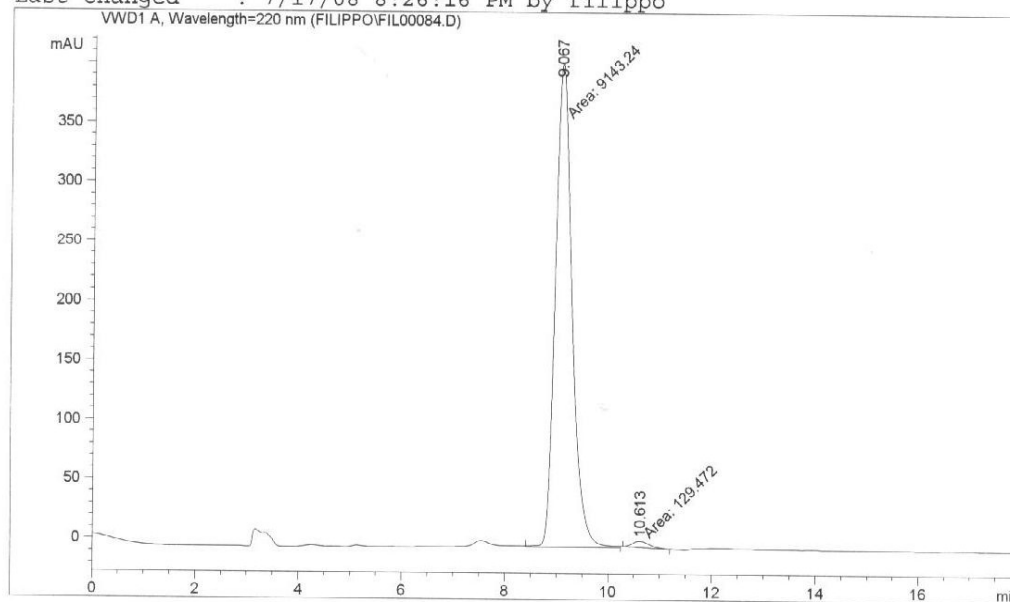
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00084.D

Sample Name: LSD_321-2

LSD_321-2 90-10, 220 NM, OD COLUMN

```
=====  
Injection Date : 7/24/08 7:55:00 PM          Seq. Line :    2  
Sample Name    : LSD_321-2                  Vial       :    8  
Acq. Operator  : filippo                    Inj        :    1  
                                           Inj Volume : 20 µl  
  
Acq. Method    : C:\HPCHEM\1\METHODS\90HEX220.M  
Last changed   : 7/24/08 7:35:29 PM by filippo  
Analysis Method : C:\HPCHEM\1\METHODS\90HEX230.M  
Last changed   : 7/17/08 8:26:16 PM by filippo  
=====
```



Area Percent Report

```
=====  
Sorted By      :      Signal  
Multiplier    :      1.0000  
Dilution       :      1.0000  
=====
```

Signal 1: VWD1 A, Wavelength=220 nm

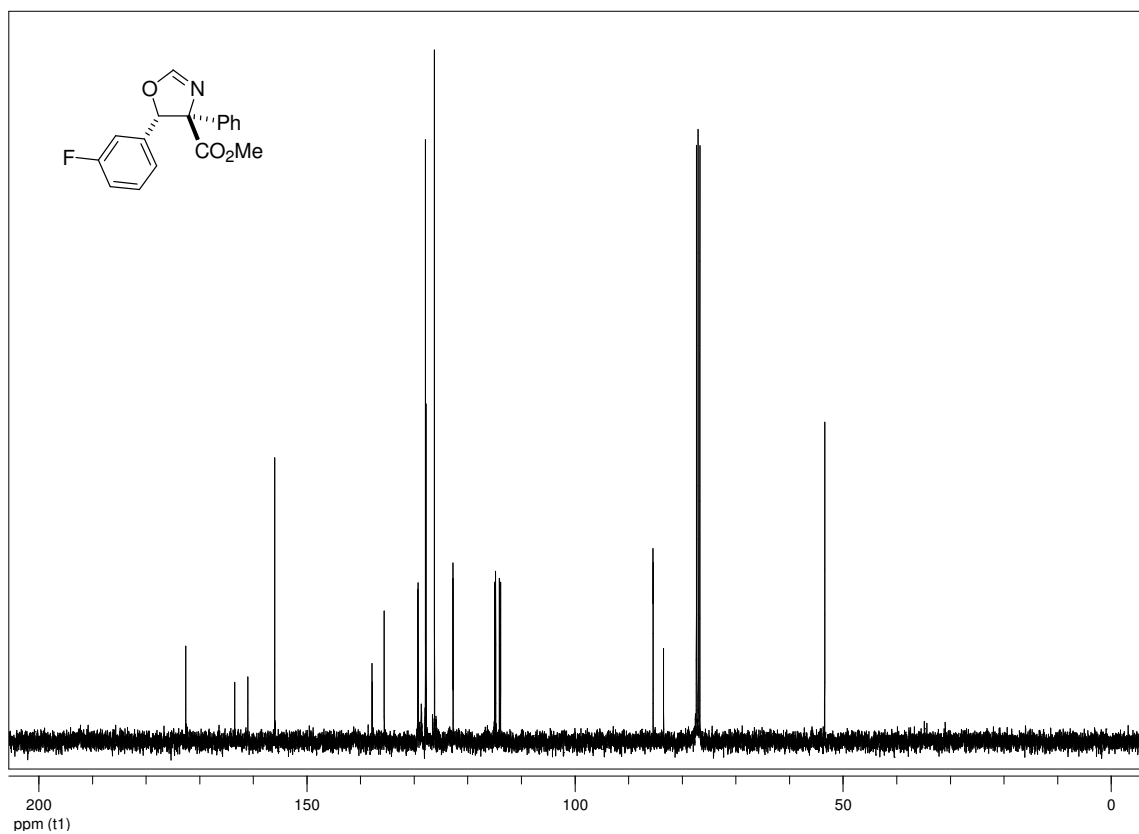
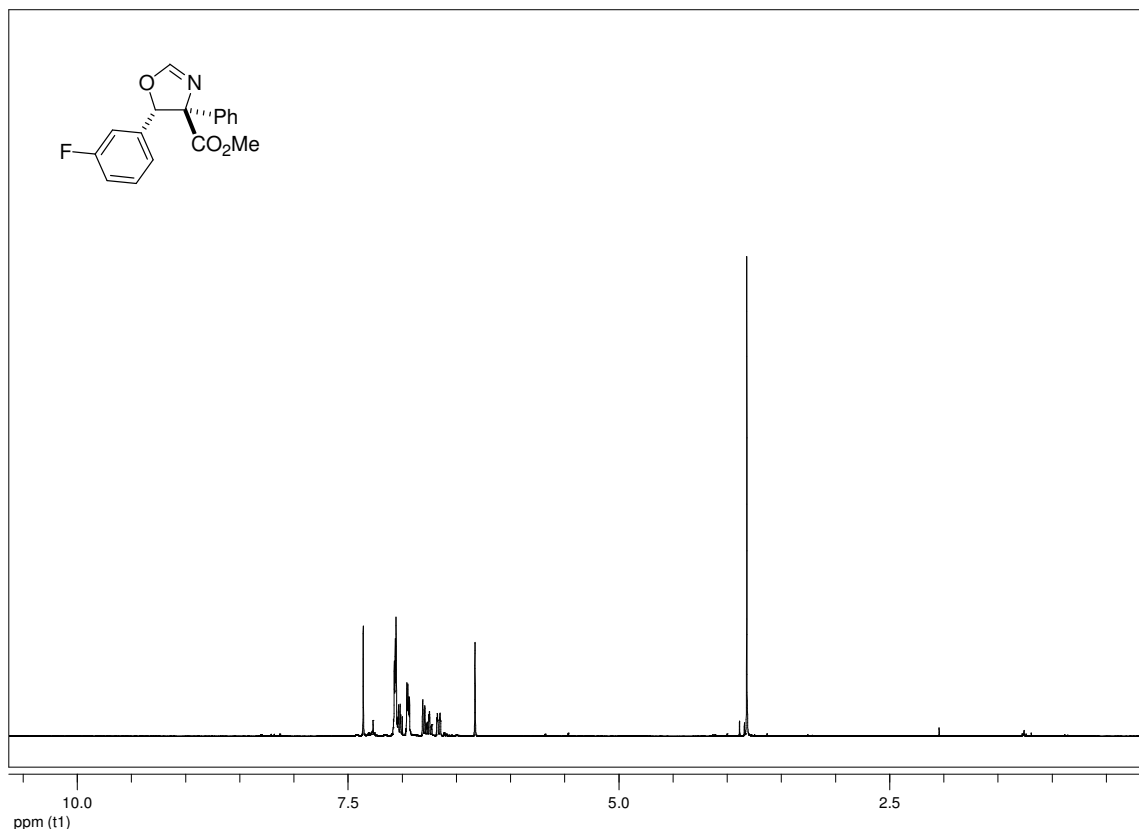
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.067	MM	0.3747	9143.23730	406.70877	98.6037
2	10.613	MM	0.4141	129.47179	5.21072	1.3963

Totals : 9272.70909 411.91950

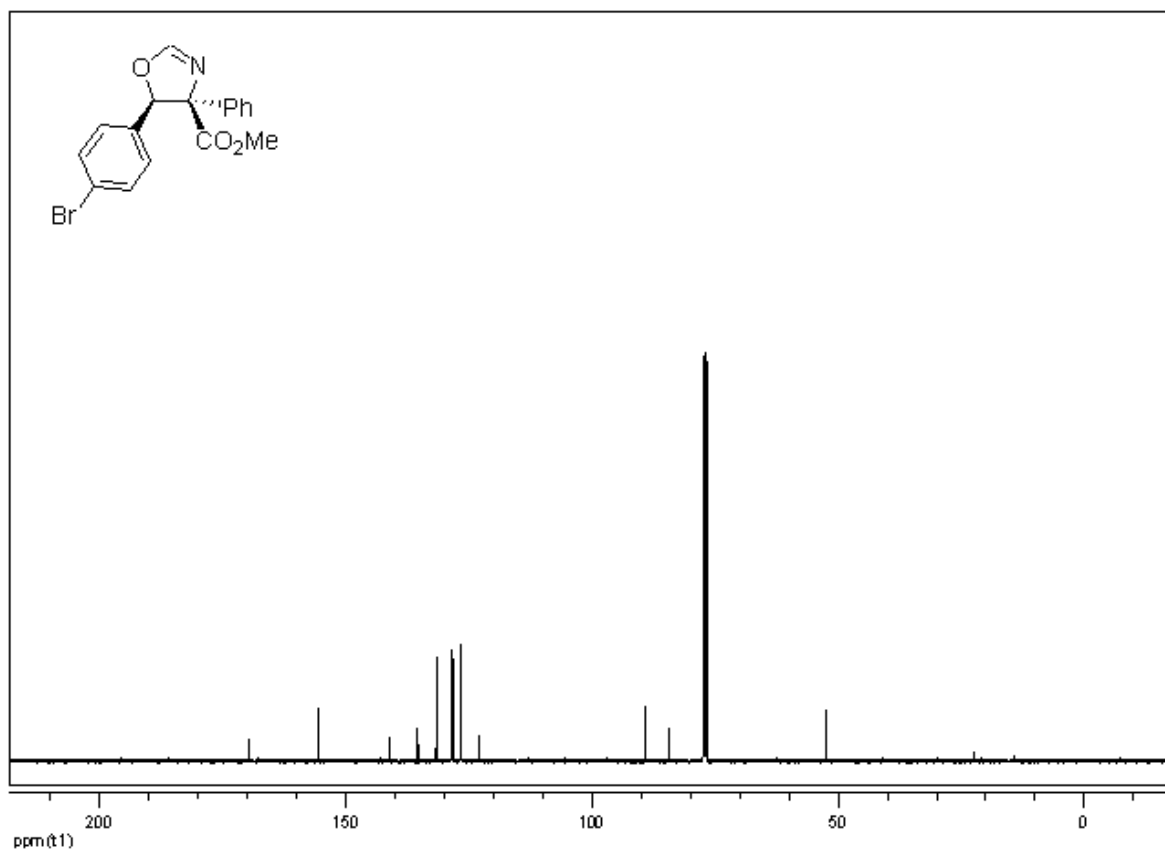
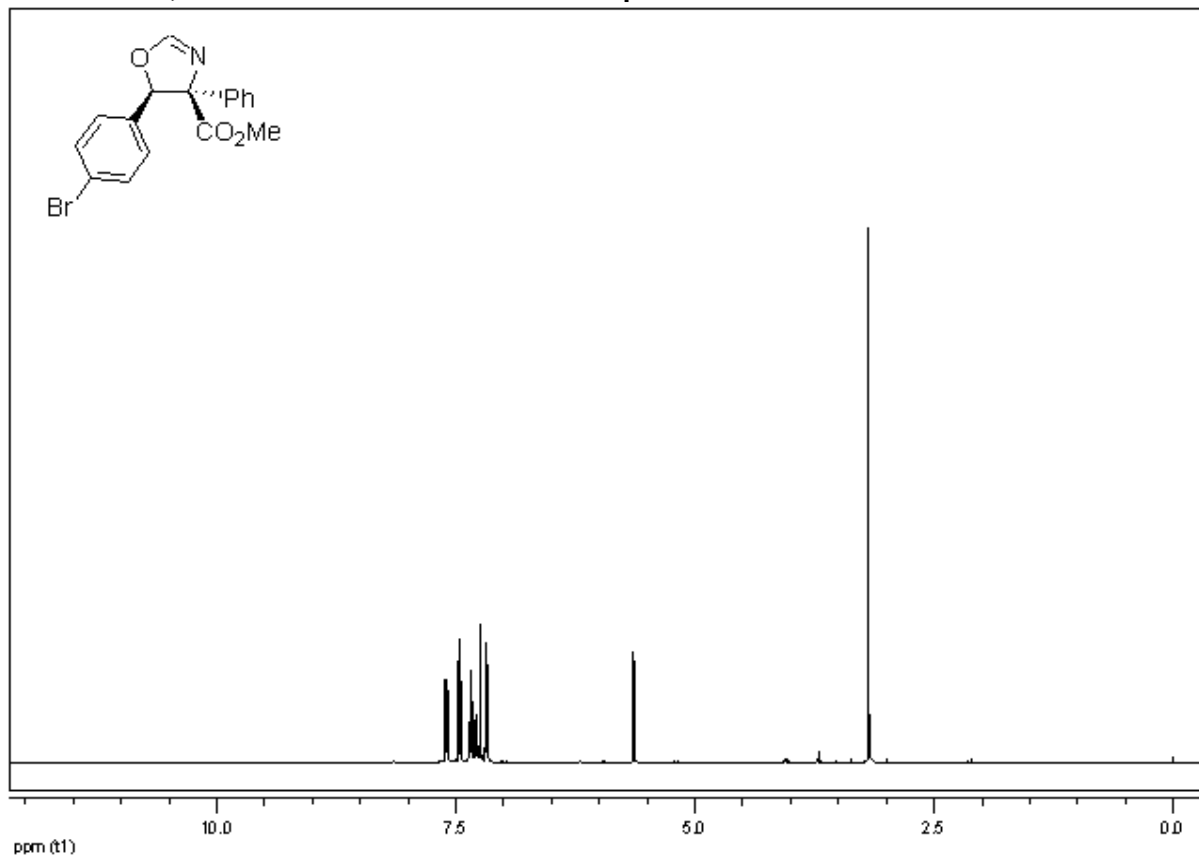
Results obtained with enhanced integrator!

=====
*** End of Report ***

$^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ of minor diastereoisomer ($4R^*$, $5S^*$ -9c)



4.12 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9d



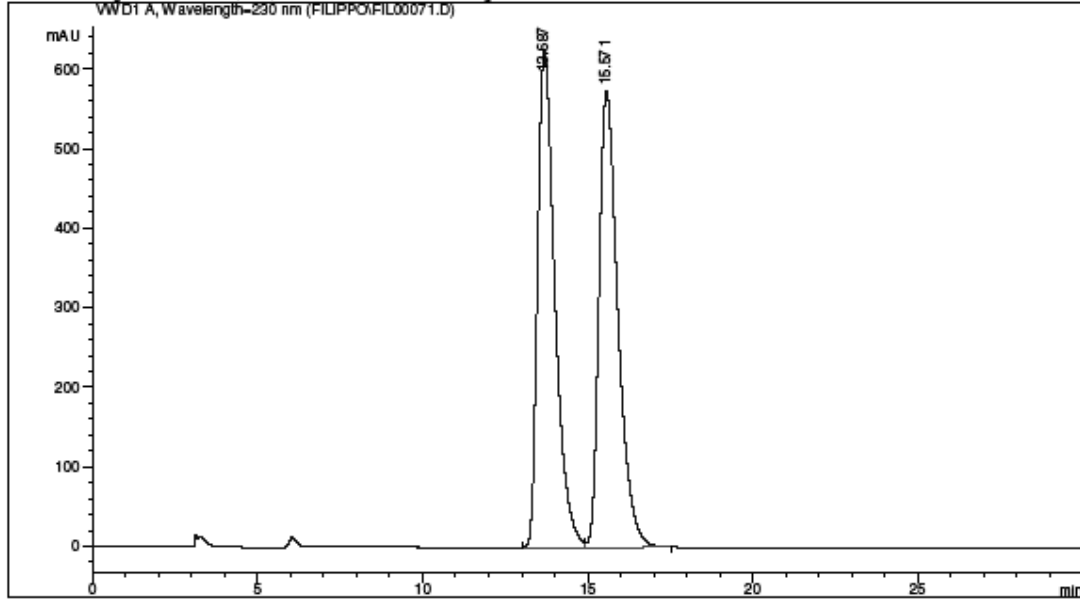
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00071.D

Sample Name: LSD2-68

LSD2-68, 95-05, OD COLUMN, 230 nm

```
=====
Injection Date : 31/07/2009 14:53:11 PM      Seq. Line : 1
Sample Name    : LSD2-68                      Location  : Vial 12
Acq. Operator  : FILIPPO                      Inj       : 1
Acq. Instrument : Instrument 1                 Inj Volume: 20 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\95HEX230.M
Last changed   : 31/07/2009 14:44:01 PM by Kath
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\85HEX215.M
Last changed   : 24/07/2009 14:52:29 PM by Kath
=====
```



```
=====
                          Area Percent Report
=====
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type Width Area Height Area
# [min] [min] [mAU*s] [mAU] %
-----|-----|-----|-----|-----|-----|
1 13.687 BV 0.5548 2.27216e4 622.63159 49.8955
2 15.571 VB 0.5996 2.28168e4 574.16553 50.1045

Totals : 4.55385e4 1196.79712

Results obtained with enhanced integrator!
=====
*** End of Report ***
=====
```

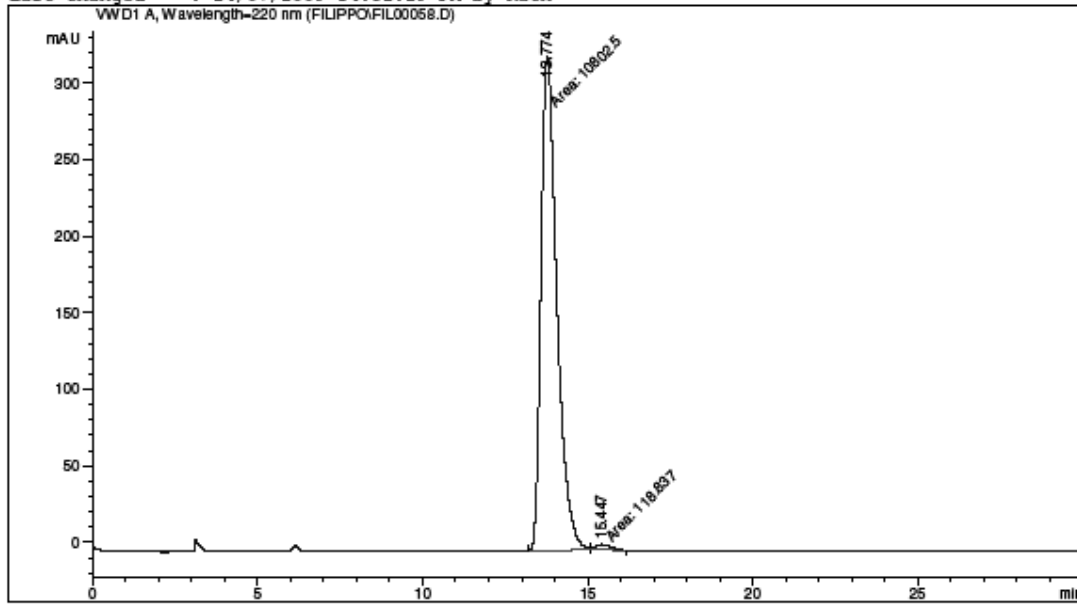
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00058.D

Sample Name: lsd_95

lsd_95 od column, 95-05, 220 nm

```
=====  
Injection Date : 11/06/2009 14:38:57 PM      Seq. Line : 1  
Sample Name    : lsd_95                      Location  : Vial 12  
Acq. Operator  : FILIPPO                     Inj       : 1  
Acq. Instrument : Instrument 1                Inj Volume: 10 µl  
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\95HEX220.M  
Last changed   : 11/06/2009 14:52:28 PM by FILIPPO  
                (modified after loading)  
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\85HEX215.M  
Last changed   : 24/07/2009 14:52:29 PM by Kath  
=====
```



Area Percent Report

```
=====  
Sorted By      : Signal  
Multiplier     : 1.0000  
Dilution       : 1.0000  
Use Multiplier & Dilution Factor with ISTDs  
=====
```

Signal 1: VWD1 A, Wavelength=220 nm

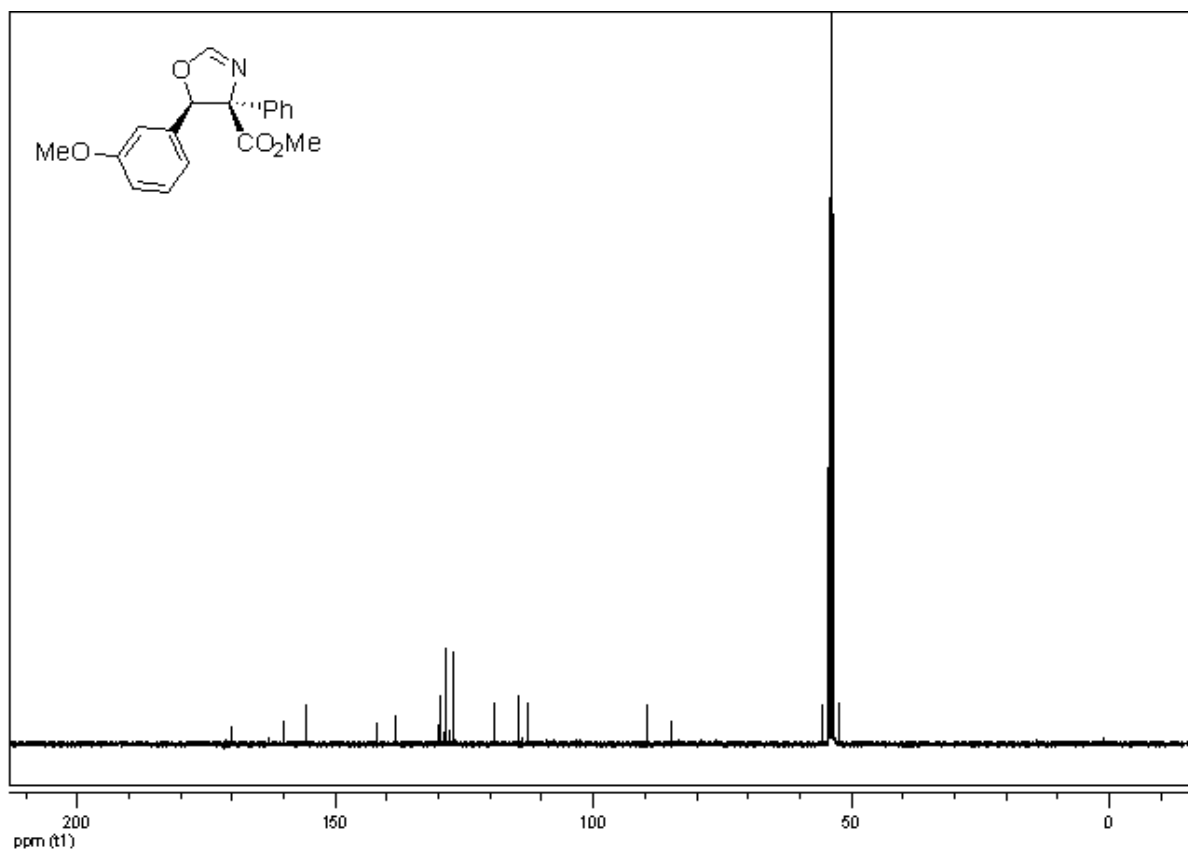
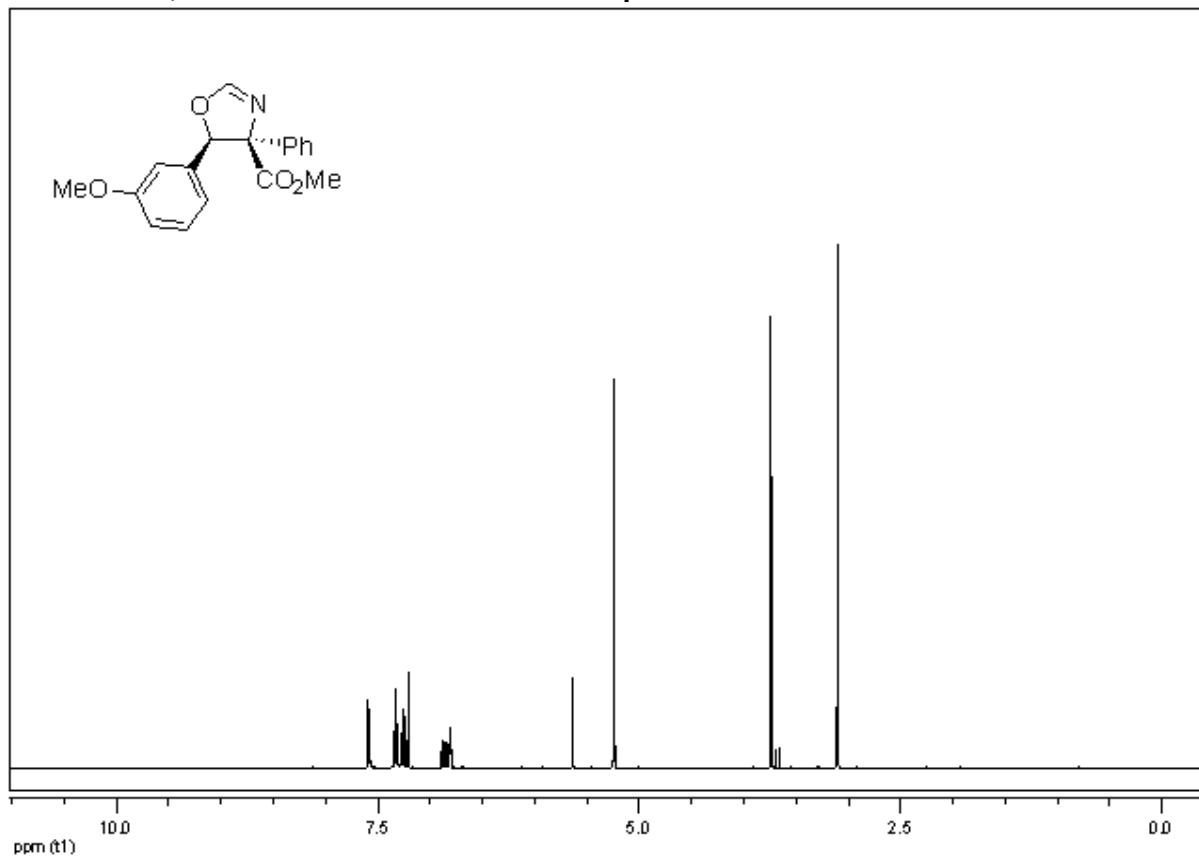
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.774	MM	0.5561	1.08025e4	323.73483	98.9119
2	15.447	MM	0.5619	118.83664	3.52496	1.0881

Totals : 1.09214e4 327.25979

Results obtained with enhanced integrator!

*** End of Report ***

4.13 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9e



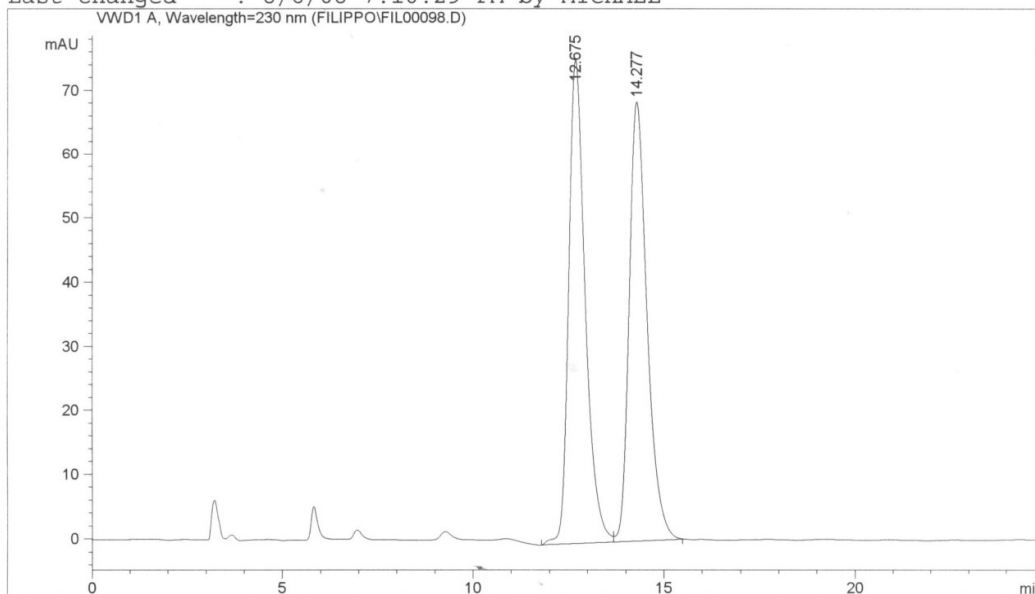
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00098.D

Sample Name: LSD-330

LSD_330 (RAC), OD COLUMN, 90-10, 230 nm

```
=====
Injection Date   : 8/7/08 5:50:39 PM           Seq. Line :    3
Sample Name     : LSD-330                     Vial      :   15
Acq. Operator   : FILIPPO                     Inj       :    1
                                           Inj Volume: 10 µl
Acq. Method     : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed    : 8/7/08 5:50:07 PM by FILIPPO
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\80_20.M
Last changed    : 8/6/08 7:10:29 PM by MICHAEL
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.675	PV	0.4438	2277.83105	75.54282	50.5596
2	14.277	VB	0.4839	2227.40625	68.58606	49.4404

Totals : 4505.23730 144.12888

Results obtained with enhanced integrator!

*** End of Report ***

Enantioenriched

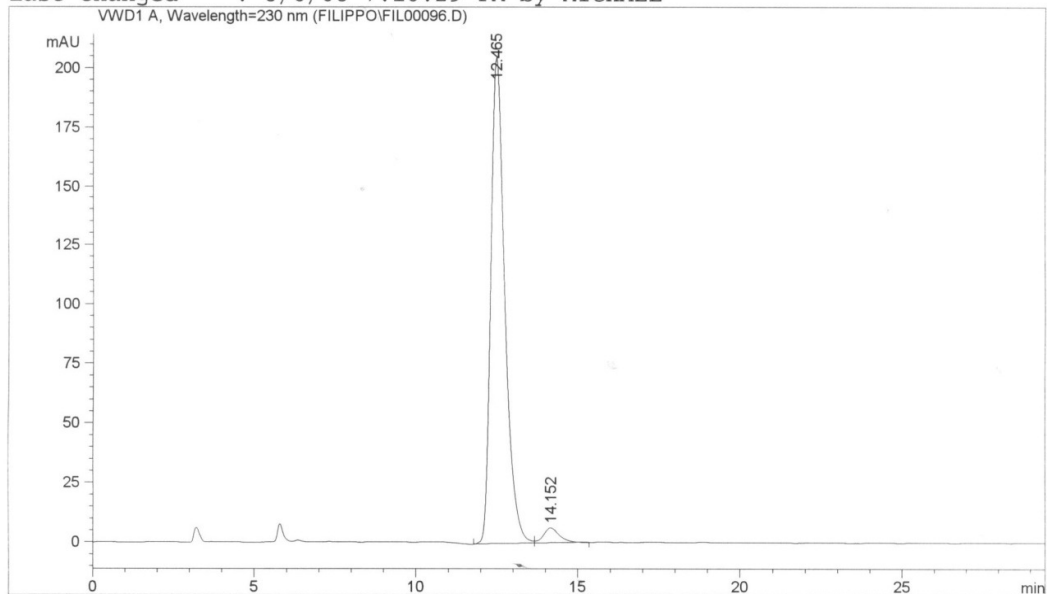
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00096.D

Sample Name: LSD-335-3

LSD_335-3, OD COLUMN, 90-10, 230 nm

```
=====
Injection Date   : 8/7/08 4:54:59 PM           Seq. Line :    1
Sample Name      : LSD-335-3                   Vial       :   14
Acq. Operator    : FILIPPO                     Inj        :    1
                                                    Inj Volume : 10 µl

Acq. Method      : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed     : 8/7/08 5:24:26 PM by FILIPPO
                  (modified after loading)
Analysis Method  : C:\HPCHEM\1\METHODS\80_20.M
Last changed     : 8/6/08 7:10:29 PM by MICHAEL
=====
```



Area Percent Report

```
Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

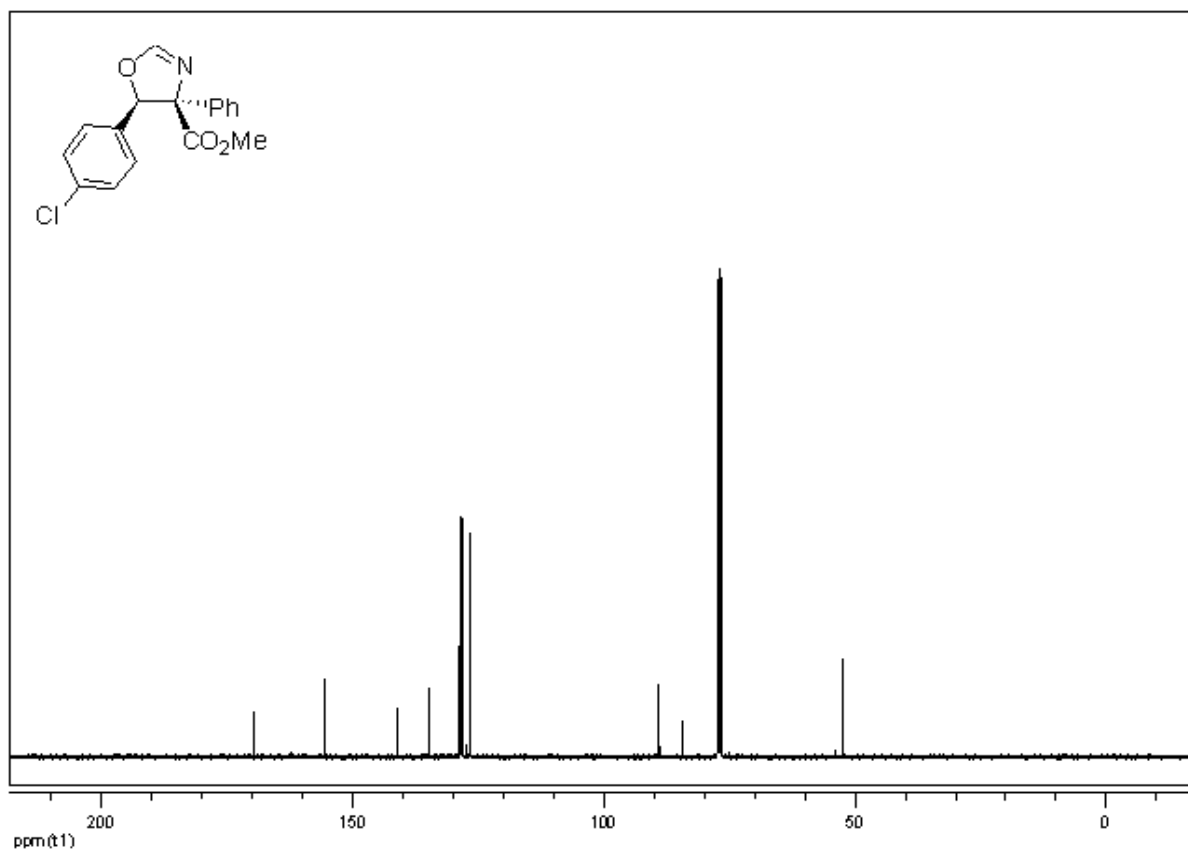
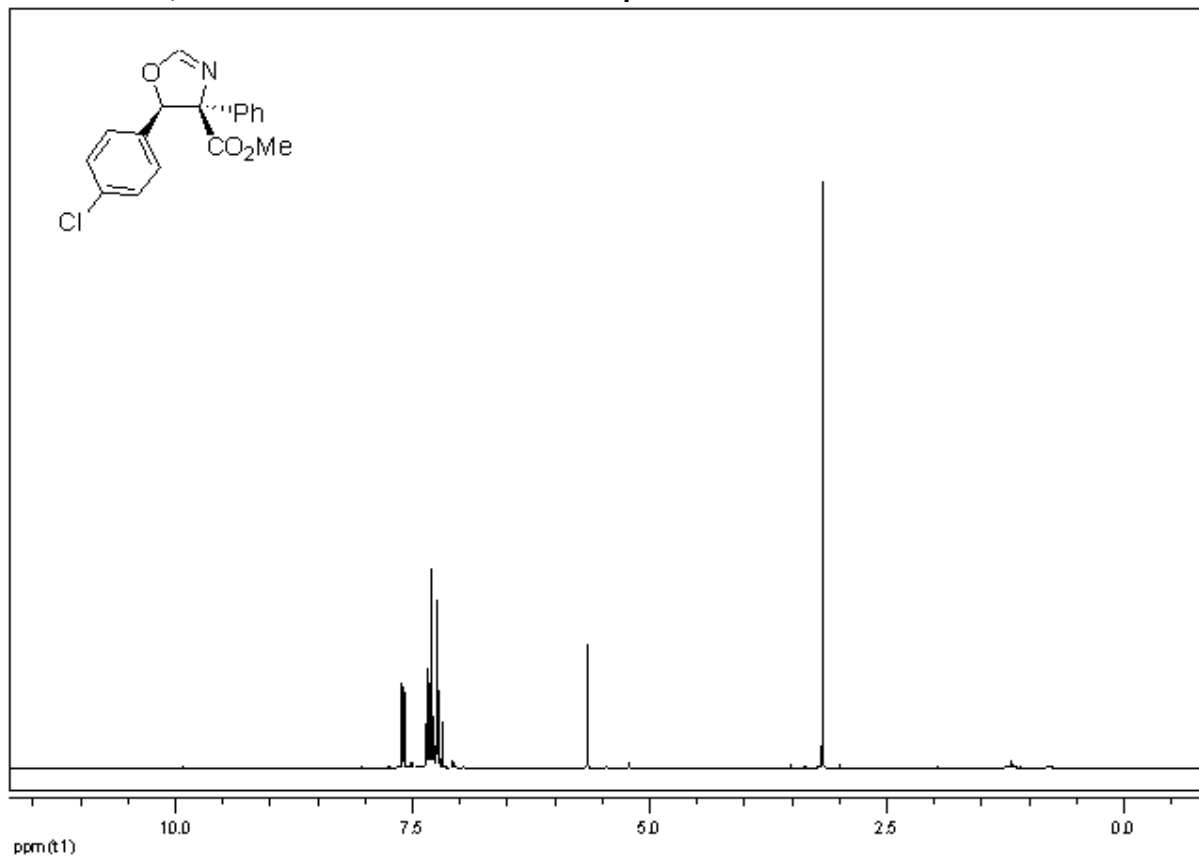
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.465	PB	0.4505	6140.06299	204.97763	96.5475
2	14.152	BP	0.4078	219.56563	6.35891	3.4525

Totals : 6359.62862 211.33654

Results obtained with enhanced integrator!

*** End of Report ***

4.14 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9f



Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00085.D

Sample Name: LSD_323-3

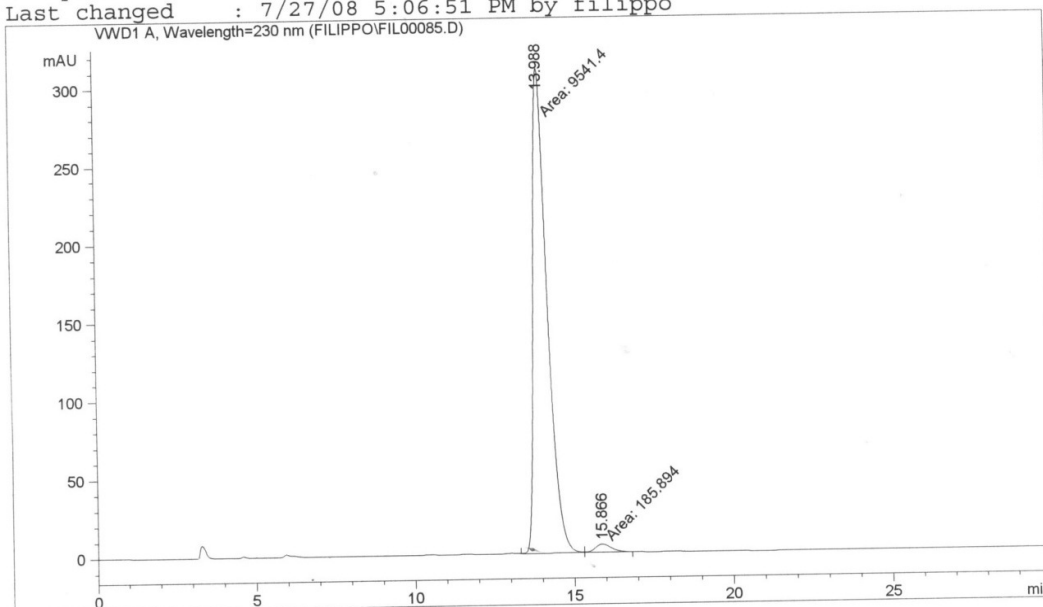
LSD_323-3, OD COLUMN, 230 NM
95-05 hex-ipa

```

=====
Injection Date   : 7/27/08 5:07:36 PM           Seq. Line :    1
Sample Name     : LSD_323-3                     Vial      :   10
Acq. Operator   : filippo                       Inj       :    1
                                                    Inj Volume: 10 µl

Acq. Method     : C:\HPCHEM\1\METHODS\95HEX230.M
Last changed    : 7/27/08 5:19:48 PM by filippo
                  (modified after loading)

Analysis Method : C:\HPCHEM\1\METHODS\95HEX230.M
Last changed    : 7/27/08 5:06:51 PM by filippo
    
```



=====
Area Percent Report
=====

```

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
    
```

Signal 1: VWD1 A, Wavelength=230 nm

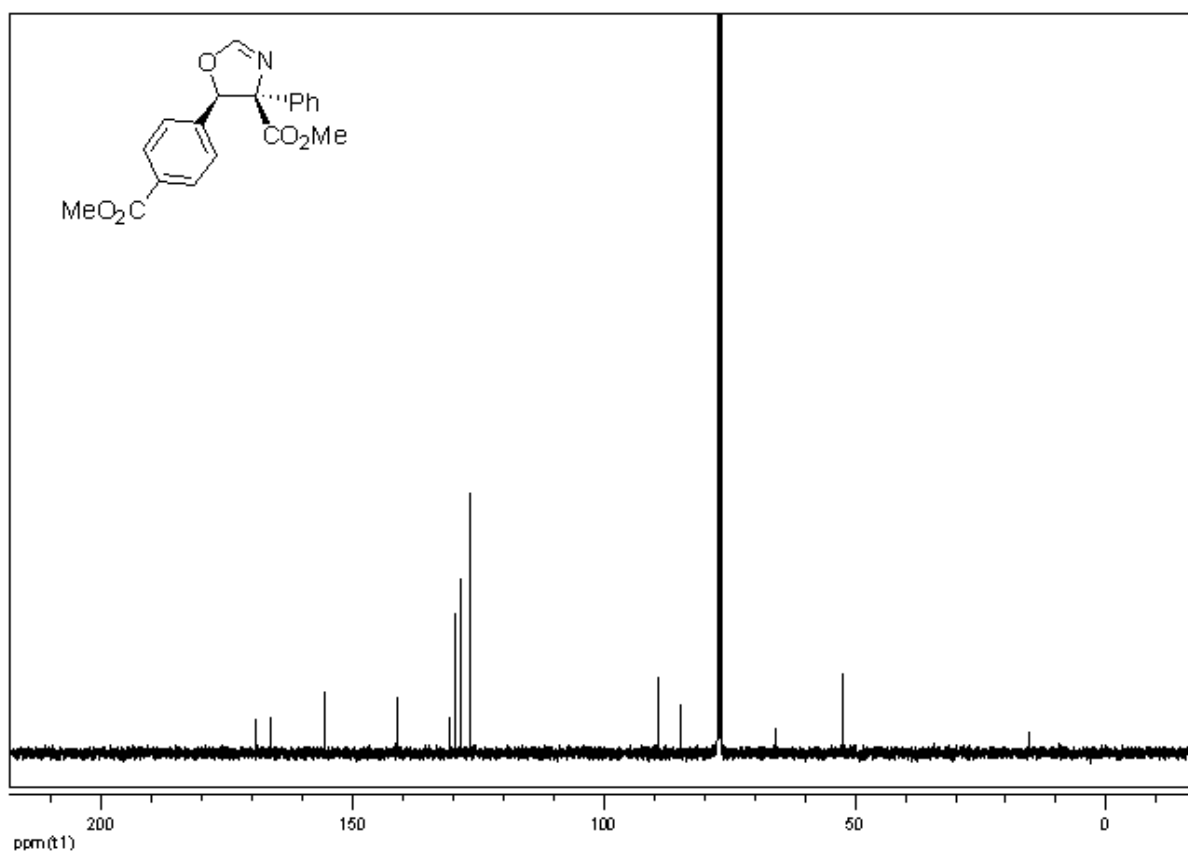
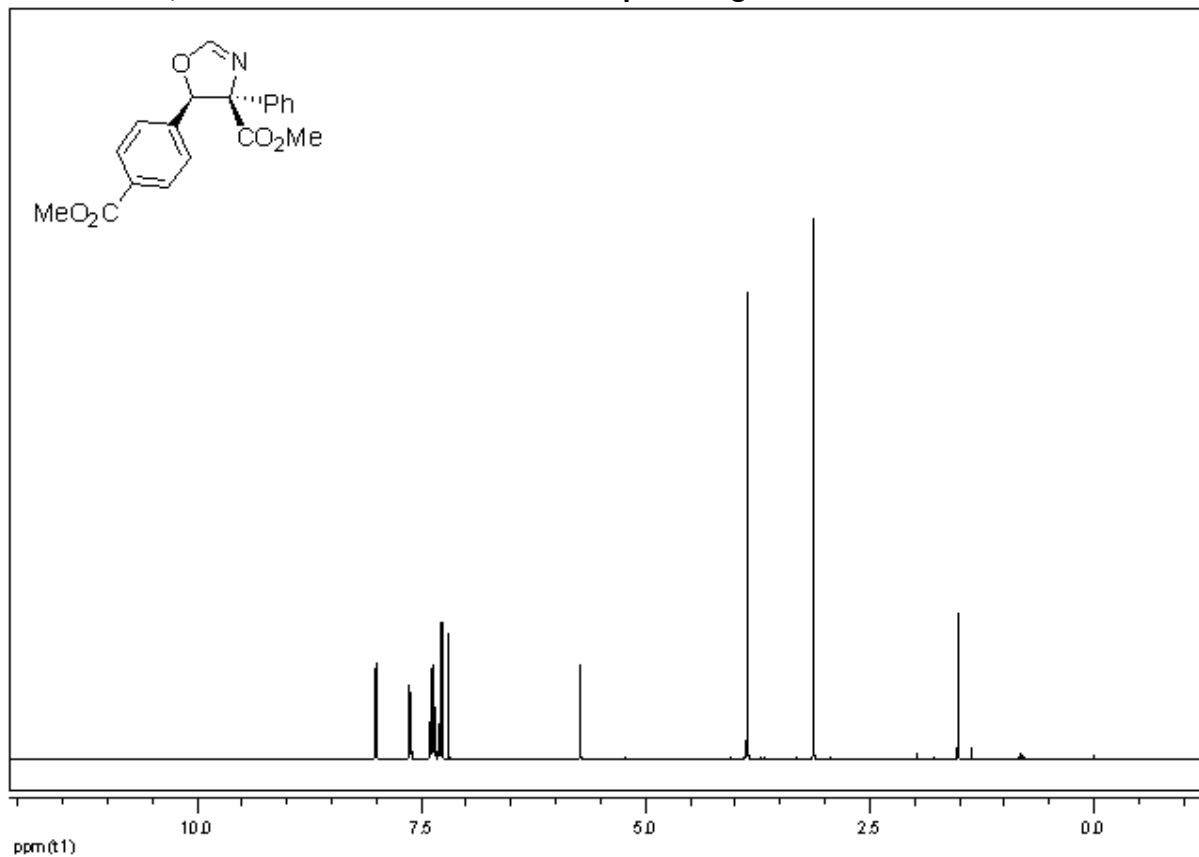
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.988	MM	0.5123	9541.39746	310.42279	98.0889
2	15.866	MM	0.5958	185.89392	5.20006	1.9111

Totals : 9727.29138 315.62285

Results obtained with enhanced integrator!

=====
*** End of Report ***

4.15 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9g



Racemate

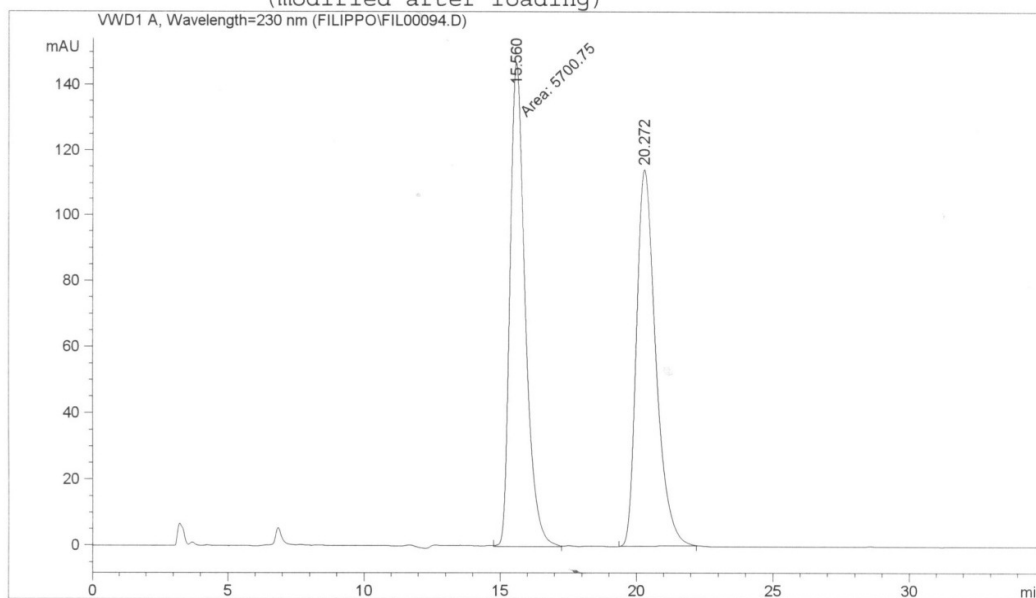
Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00094.D

Sample Name: LSD_325

LSD_325 RAC, 90-10, OD COLUMN, 230 nm

```
=====
Injection Date : 8/4/08 6:43:27 PM          Seq. Line : 1
Sample Name    : LSD_325                    Vial      : 15
Acq. Operator  : FILIPPO                    Inj       : 1
                                           Inj Volume: 10 µl

Acq. Method    : C:\HPCHEM\1\METHODS\90HEX230.M
Last changed   : 8/4/08 6:28:49 PM by FILIPPO
Analysis Method: C:\HPCHEM\1\METHODS\80_20.M
Last changed   : 8/4/08 7:55:35 PM by MICHAEL
                (modified after loading)
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.560	MM	0.6452	5700.75439	147.26953	50.3668
2	20.272	BB	0.6968	5617.73193	114.41761	49.6332

Totals : 1.13185e4 261.68714

Results obtained with enhanced integrator!

*** End of Report ***

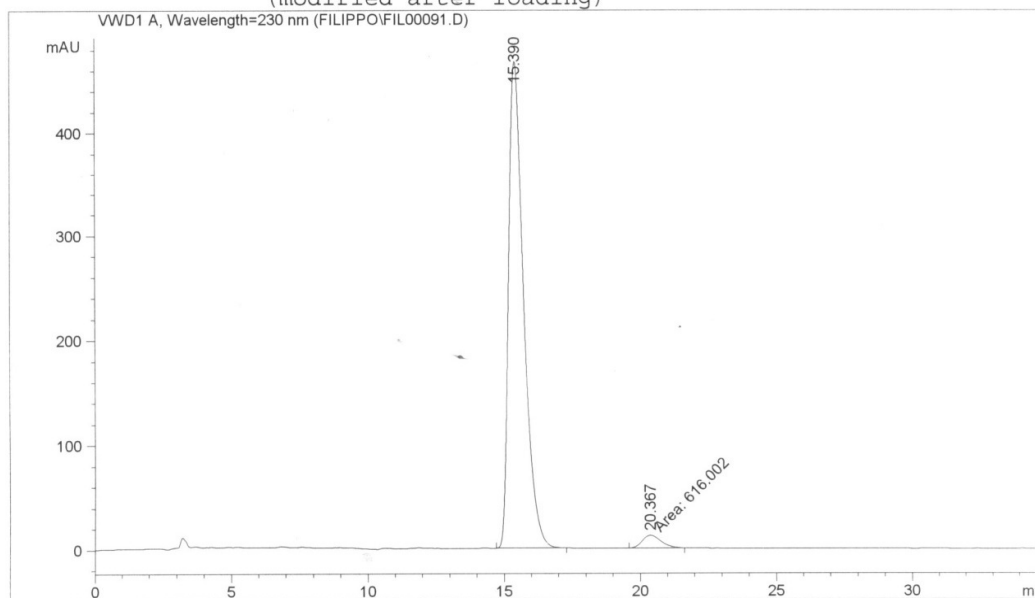
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00091.D

Sample Name: LSD_334

LSD_334, OD COLUMN, 90-10, 230 NM

```
=====  
Injection Date : 8/3/08 6:22:32 PM      Seq. Line : 1  
Sample Name    : LSD_334                 Vial : 9  
Acq. Operator  : FILIPPO                 Inj : 1  
                                           Inj Volume : 10 µl  
  
Acq. Method    : C:\HPCHEM\1\METHODS\90HEX230.M  
Last changed   : 8/3/08 6:46:36 PM by FILIPPO  
                (modified after loading)  
Analysis Method : C:\HPCHEM\1\METHODS\90HEX.M  
Last changed   : 8/1/08 6:42:30 PM by MICHAEL  
                (modified after loading)
```



Area Percent Report

```
=====  
Sorted By      : Signal  
Multiplier     : 1.0000  
Dilution       : 1.0000
```

Signal 1: VWD1 A, Wavelength=230 nm

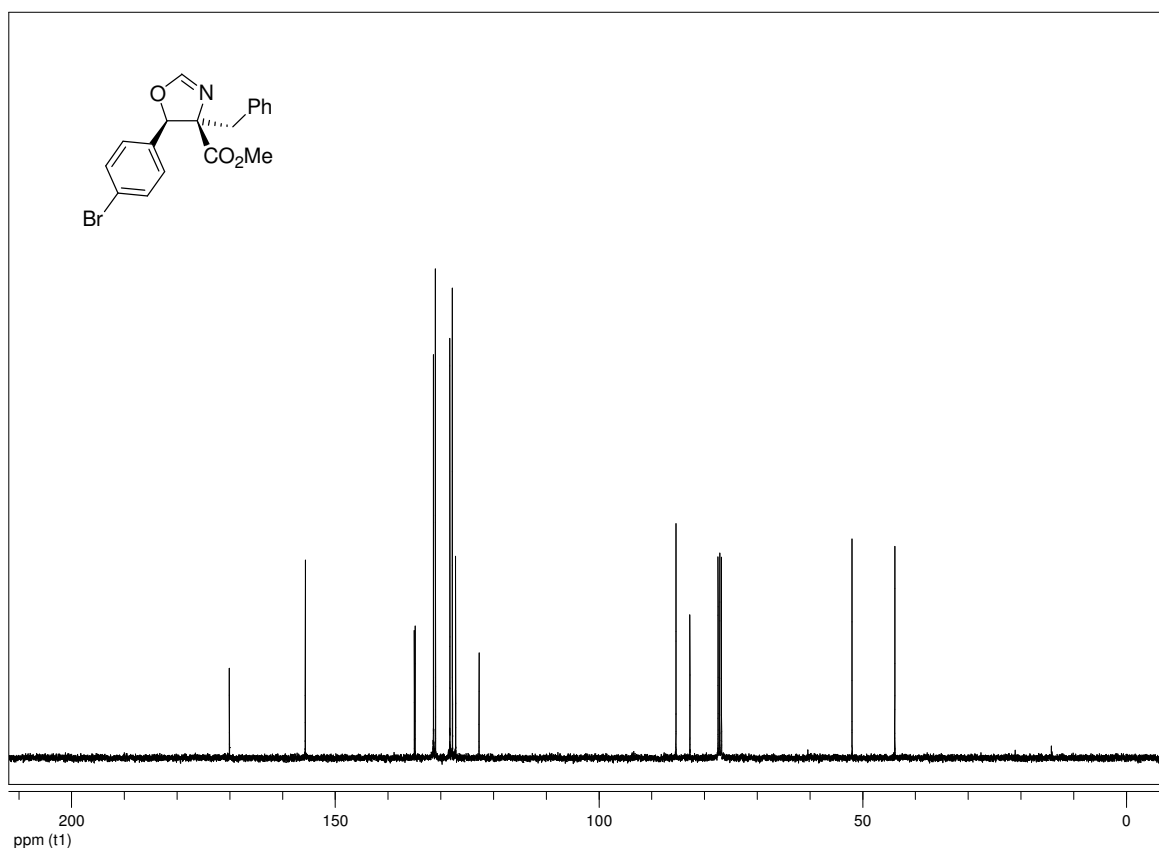
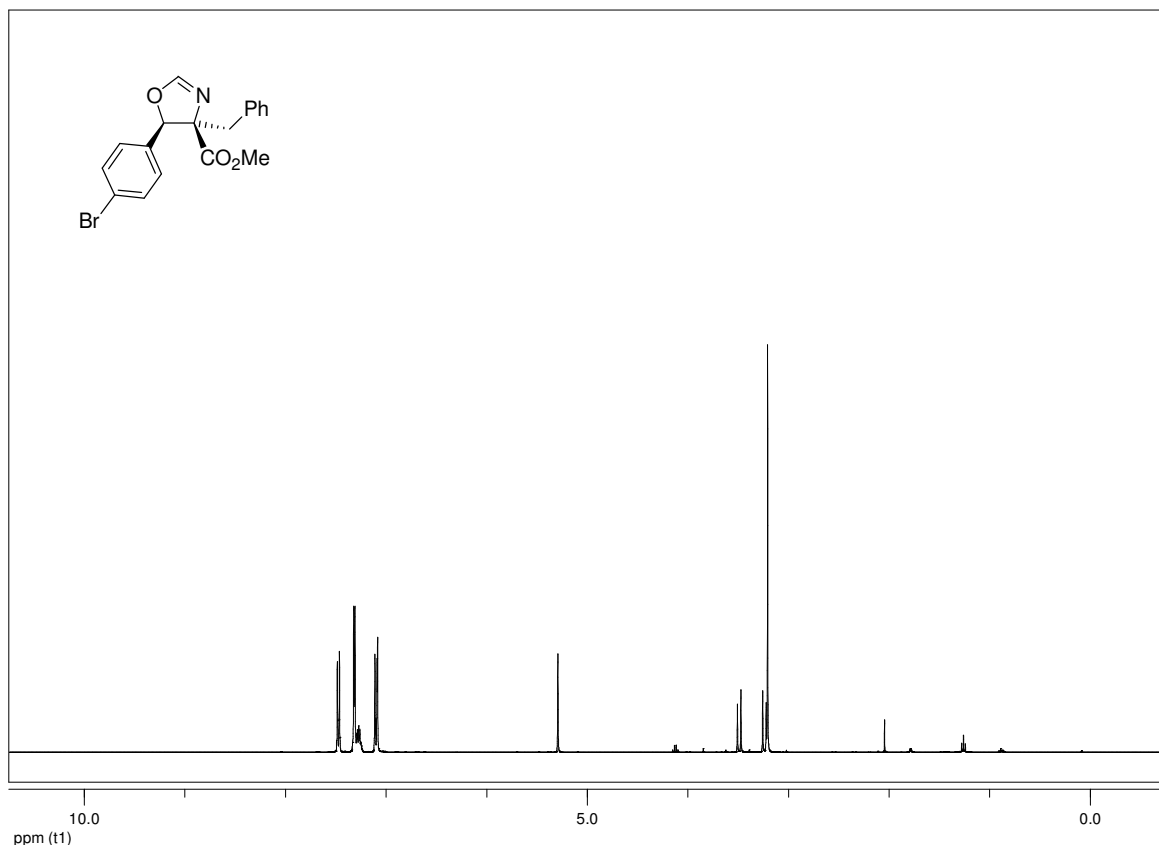
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.390	BB	0.5848	1.78257e4	467.53723	96.6597
2	20.367	MM	0.8114	616.00220	12.65295	3.3403

Totals : 1.84417e4 480.19018

Results obtained with enhanced integrator!

*** End of Report ***

4.16 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 9h



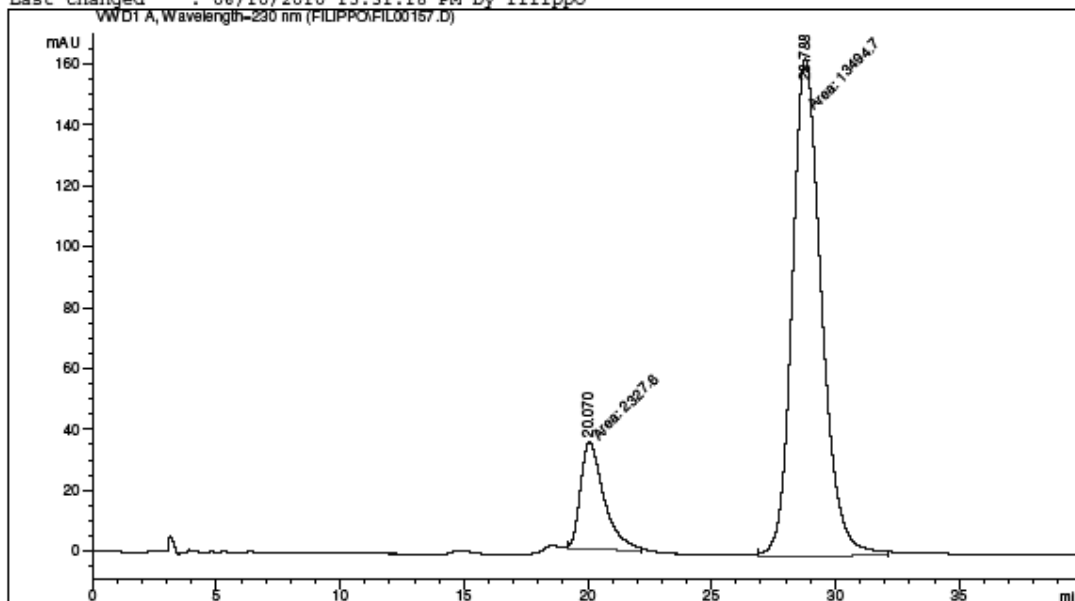
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00157.D

Sample Name: lsd7-89

LSD7-89 OD-H Column, 95-05, 230 nm, 1 ML/MIN

```
=====
Injection Date : 14/10/2010 17:44:33 PM      Seq. Line : 1
Sample Name    : lsd7-89                    Location  : Vial 11
Acq. Operator  : filippo                    Inj      : 1
Acq. Instrument : Instrument 1              Inj Volume : 8 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\95HEX230.M
Last changed   : 14/10/2010 17:42:35 PM by filippo
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\95HEX230.M
Last changed   : 06/10/2010 15:31:18 PM by filippo
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=230 nm

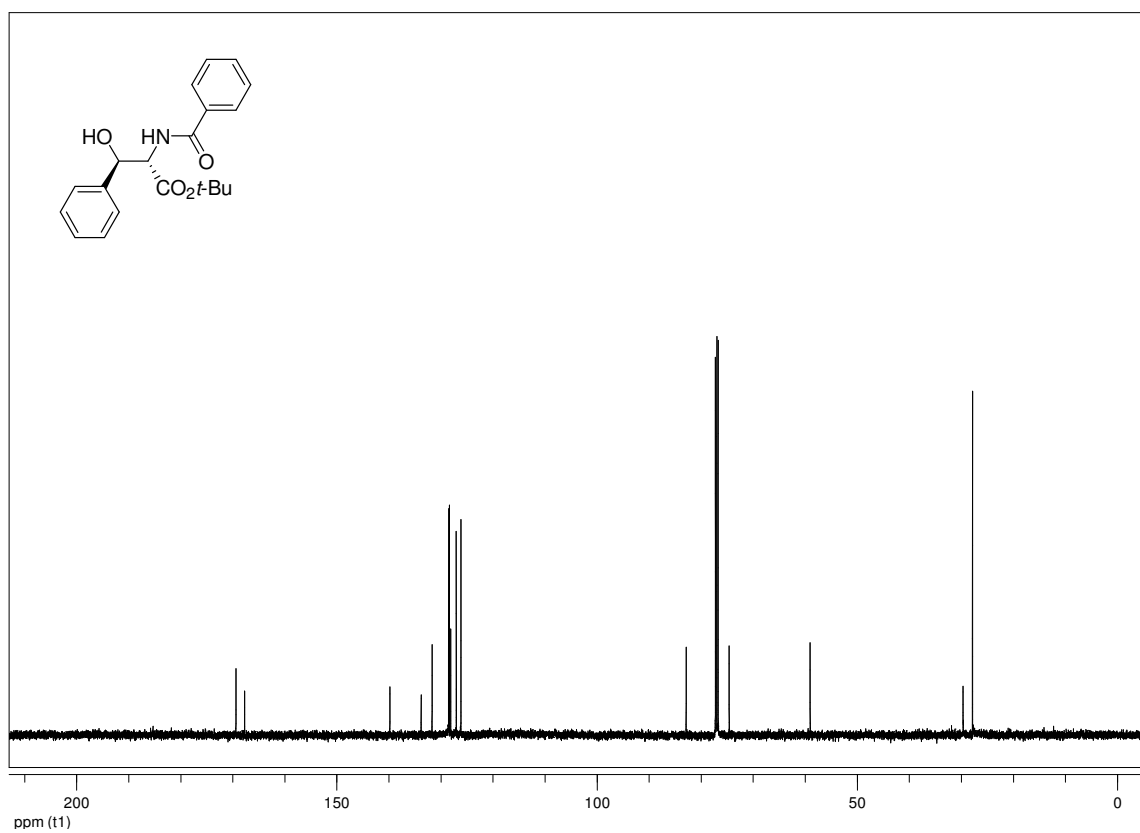
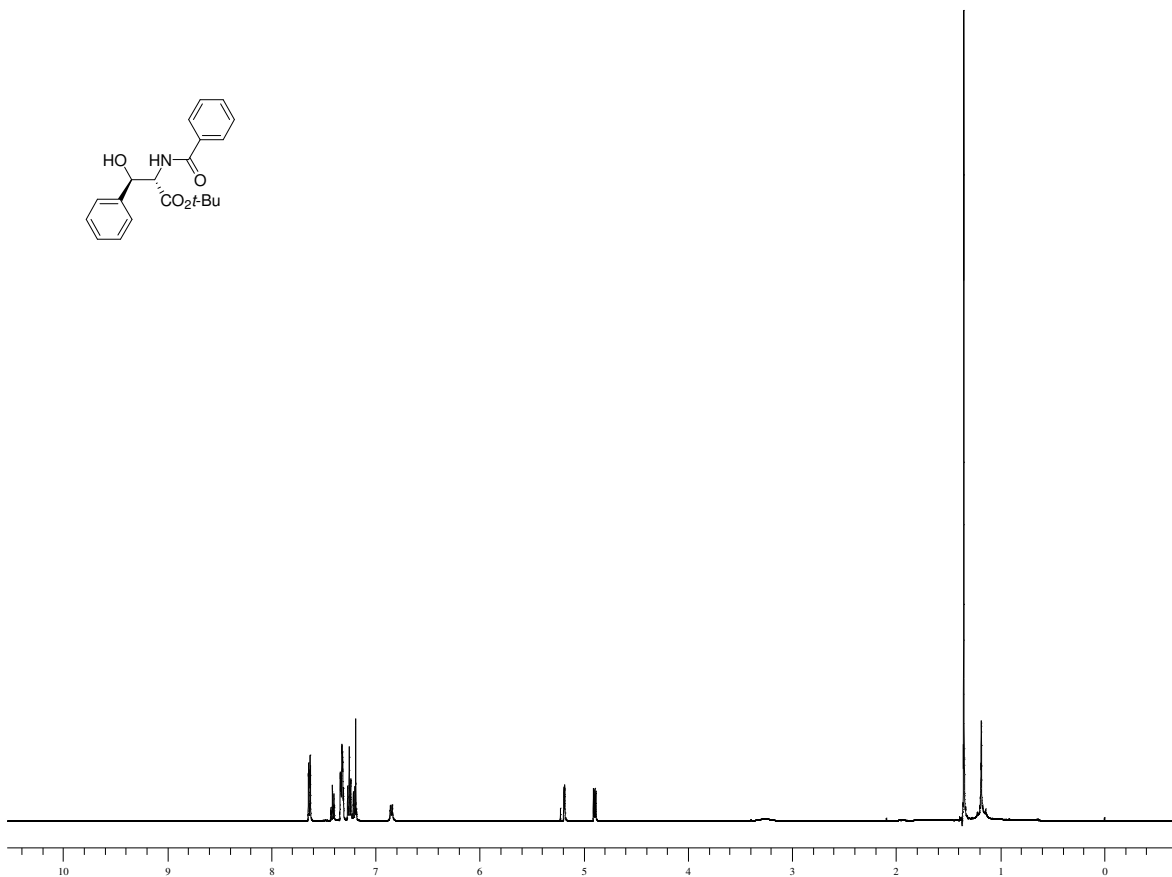
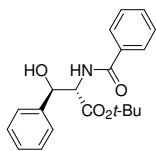
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.070	MM	1.1086	2327.59839	34.99245	14.7109
2	28.788	MM	1.3756	1.34947e4	163.50107	85.2891

Totals : 1.58223e4 198.49352

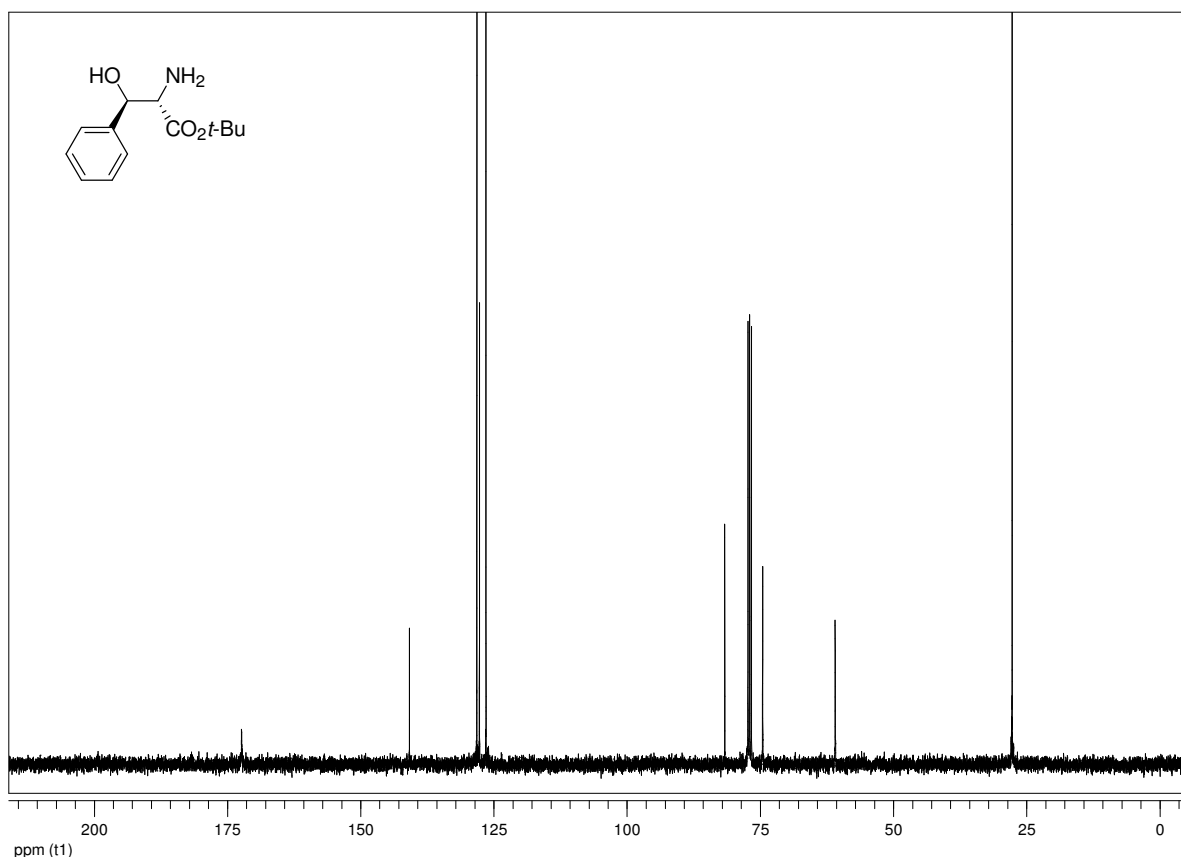
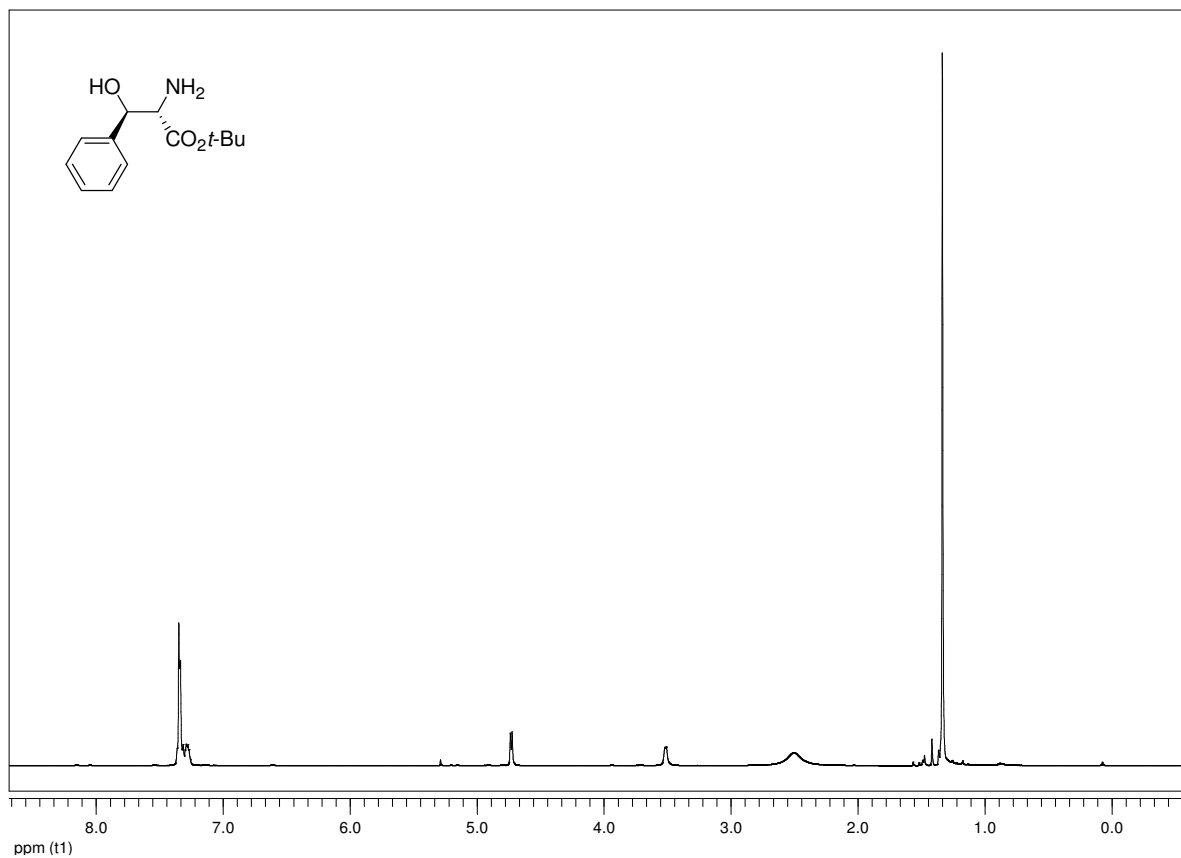
Results obtained with enhanced integrator!

*** End of Report ***

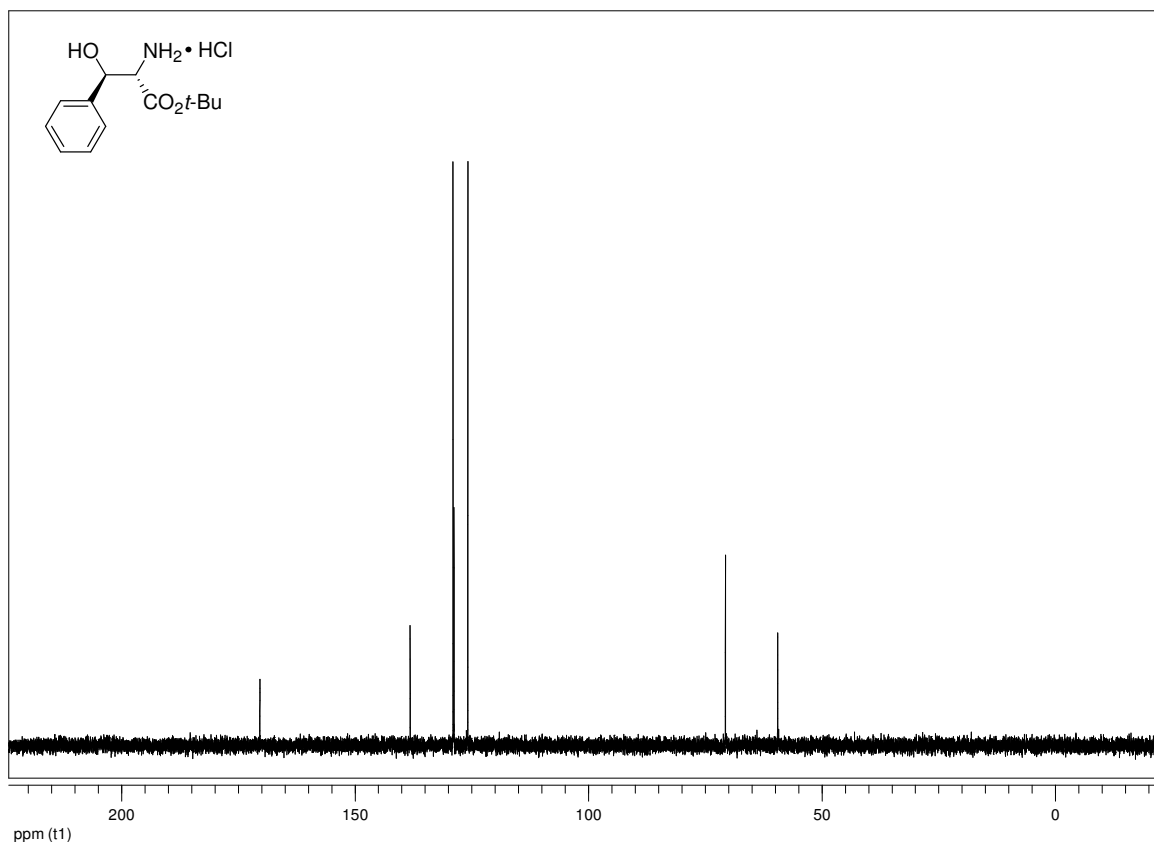
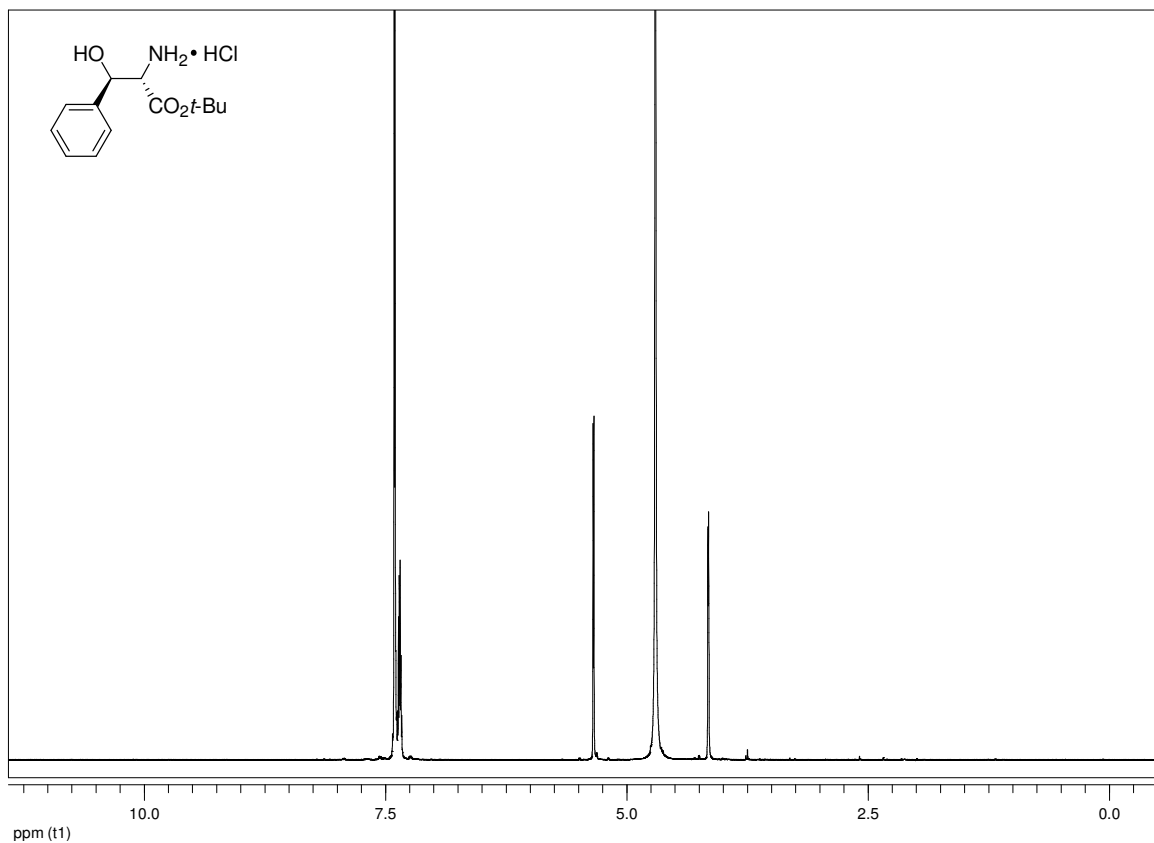
4.17 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ of compound S3



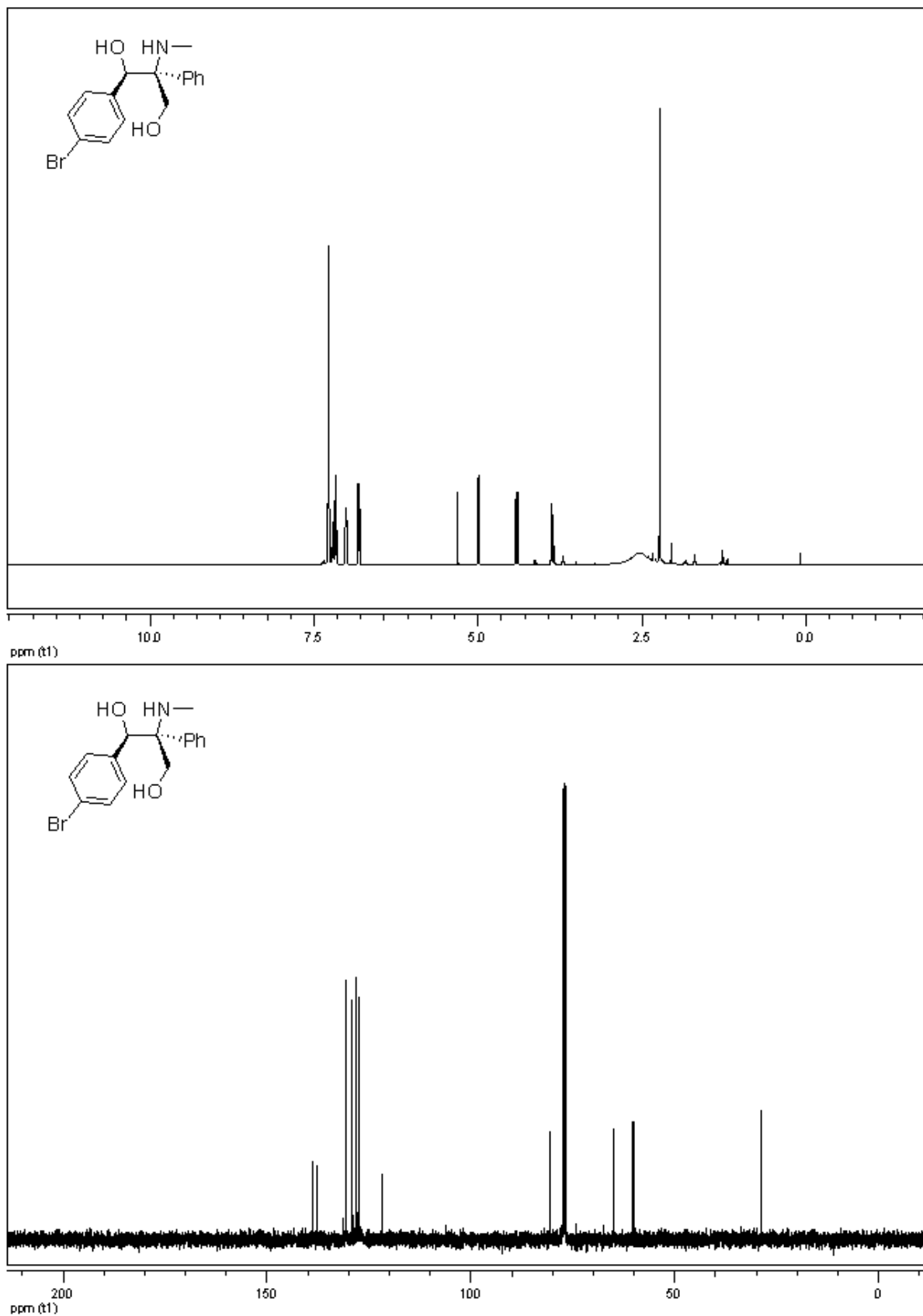
4.18 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ of compound 10



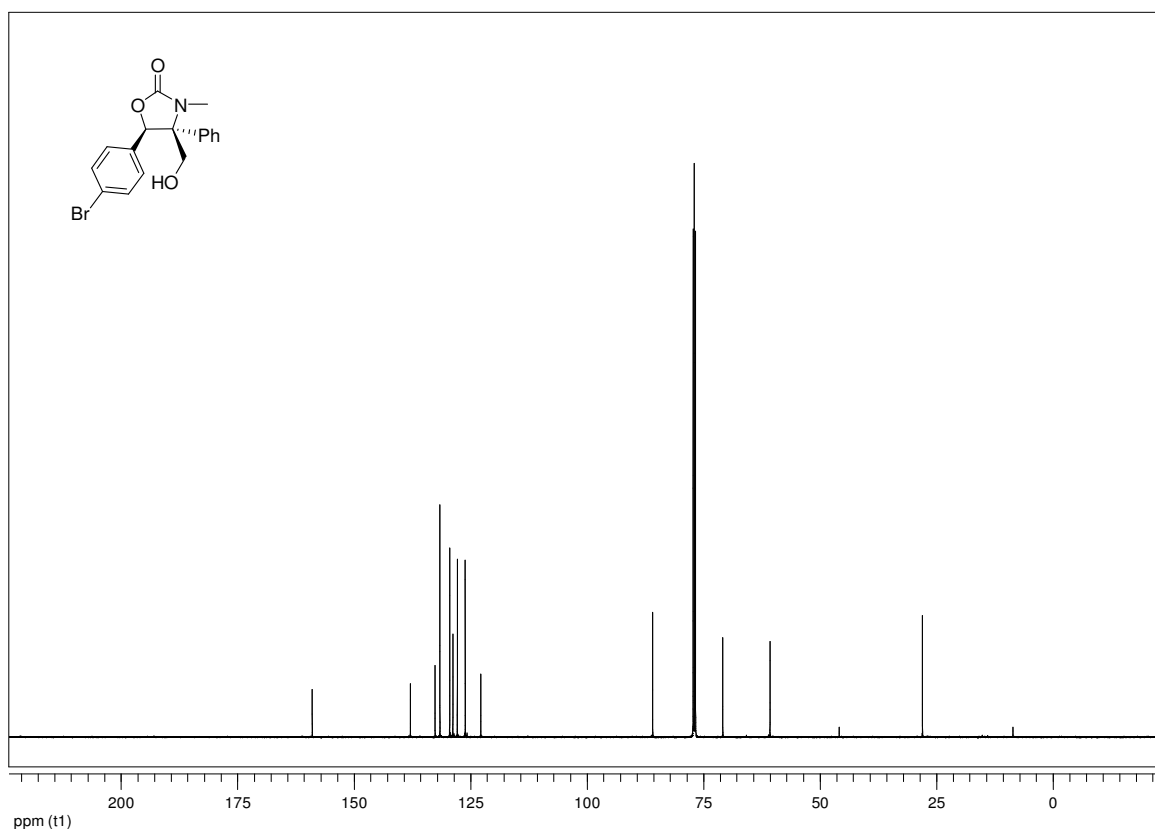
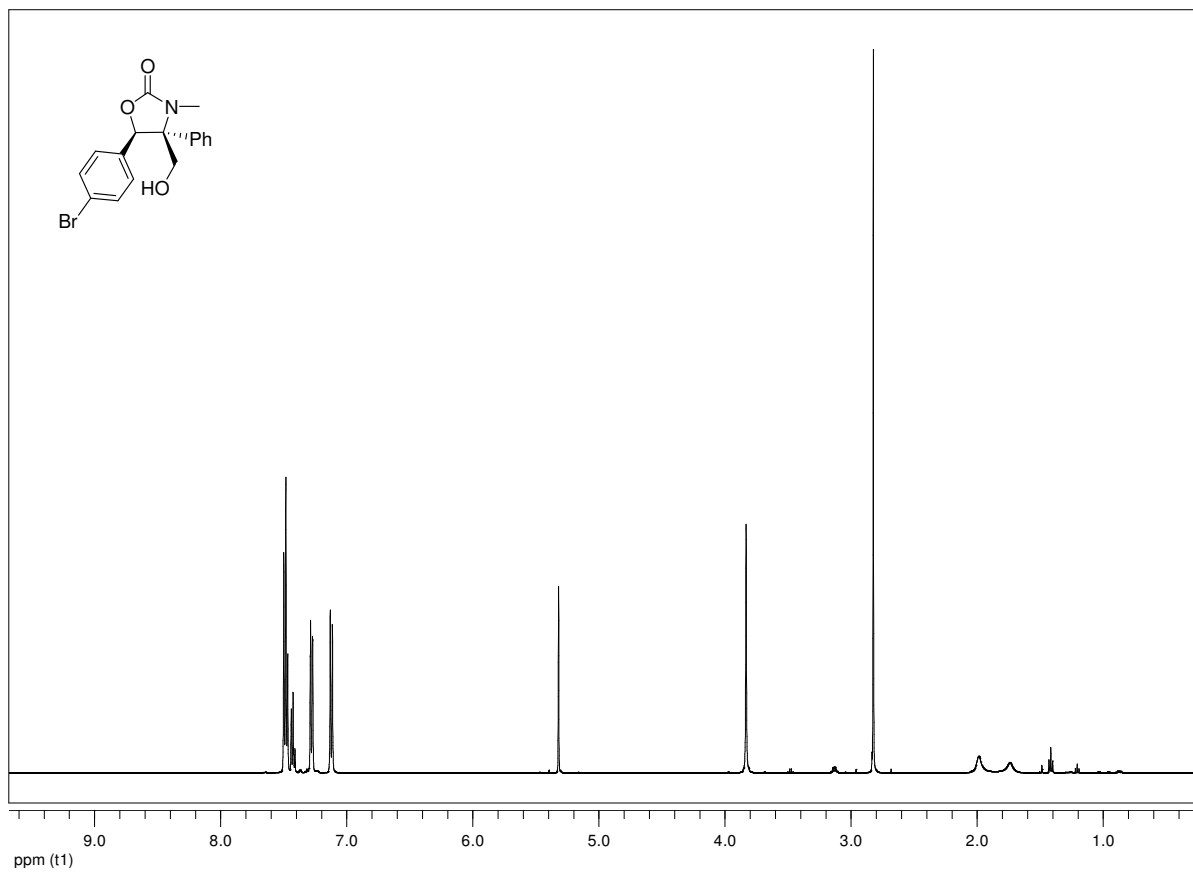
4.19 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ of compound 11



4.20 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 12



4.21 $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and HPLC traces of compound 13



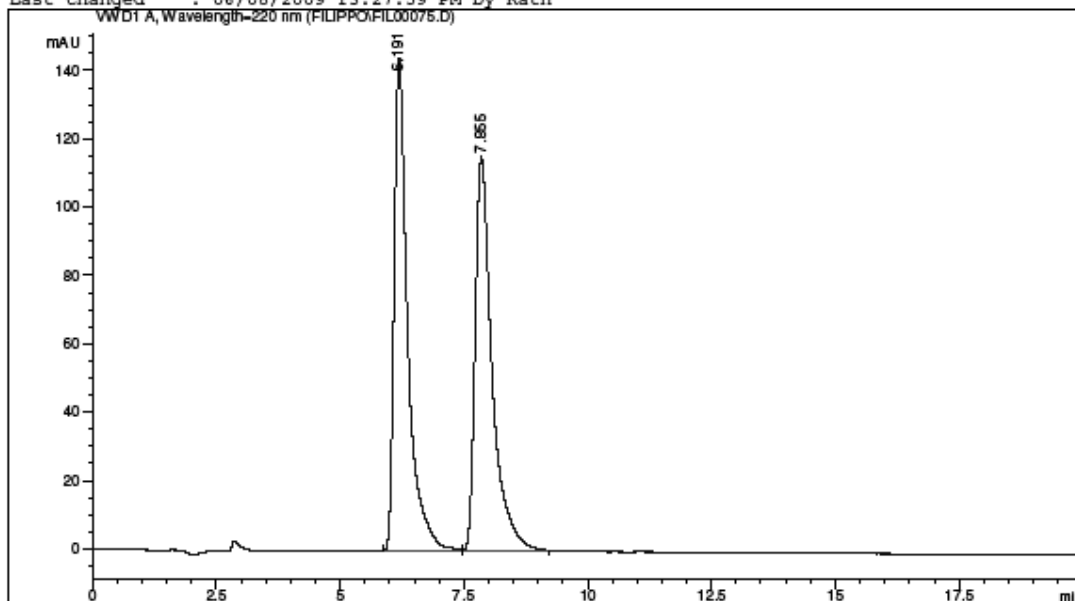
Racemate

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00075.D

Sample Name: LSD2-65

LSD_2-65, AD, Column, 80-20, 220 nm

```
=====
Injection Date : 18/08/2009 17:08:43 PM      Seq. Line : 1
Sample Name    : LSD2-65                      Location  : Vial 10
Acq. Operator  : FILIPPO                      Inj      : 1
Acq. Instrument : Instrument 1                 Inj Volume : 5 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\80HEX220.M
Last changed   : 18/08/2009 17:07:39 PM by FILIPPO
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\85HEX215.M
Last changed   : 06/08/2009 13:27:59 PM by Kath
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.191	BV	0.2814	2758.75684	144.08948	50.2047
2	7.855	VB	0.3481	2736.26025	115.21459	49.7953

Totals : 5495.01709 259.30407

Results obtained with enhanced integrator!

*** End of Report ***

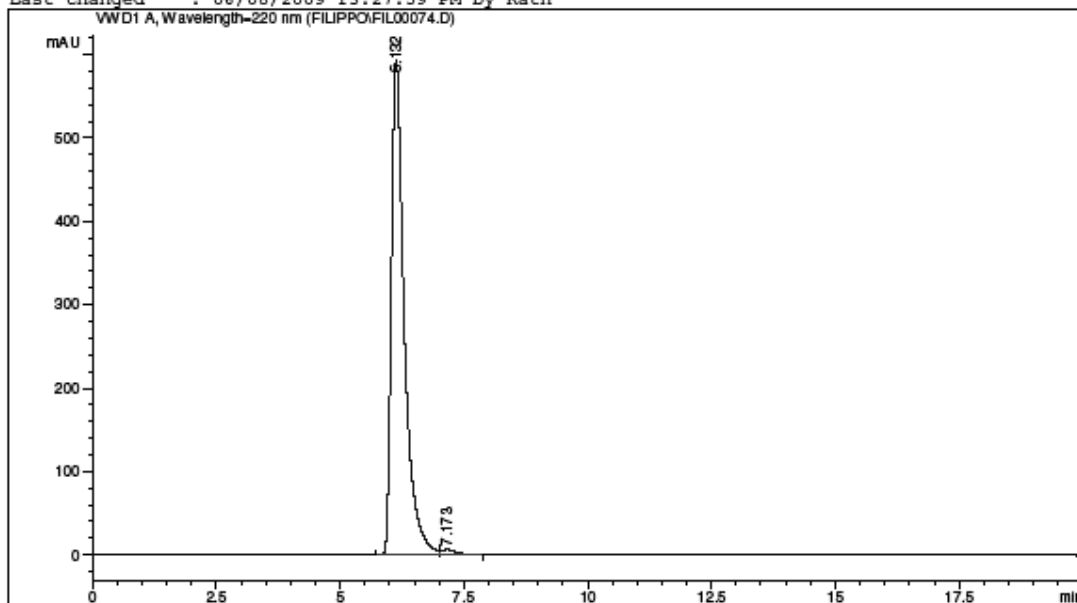
Enantioenriched

Data File C:\HPCHEM\1\DATA\FILIPPO\FIL00074.D

Sample Name: LSD2-55

LSD_2-65, AD, Column, 80-20, 220 nm

```
=====
Injection Date : 10/08/2009 18:05:14 PM      Seq. Line : 3
Sample Name    : LSD2-55                      Location  : Vial 11
Acq. Operator  : FILIPPO                      Inj       : 1
Acq. Instrument : Instrument 1                 Inj Volume: 2 µl
Acq. Method    : C:\HPCHEM\1\METHODS\DJD26\80HEX220.M
Last changed   : 10/08/2009 18:05:30 PM by FILIPPO
                (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DJD26\85HEX215.M
Last changed   : 06/08/2009 13:27:59 PM by Kath
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.132	VV	0.2677	1.07376e4	594.54590	98.6625
2	7.173	VB	0.2734	145.56152	6.32686	1.3375

Totals : 1.08832e4 600.87275

Results obtained with enhanced integrator!

*** End of Report ***

5. References

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- ⁱBonne, D.; Dekhane, M.; Zhu, J. *J. Am. Chem. Soc.*, **2005**, *127*, 6926-6927.
- ⁱⁱTrost, M.B.; Bunt, R.C.; Lemoine, C.R.; Calkins, L.T. *J. Am. Chem. Soc.*, **2000**, *122*, 5968-5976.
- ⁱⁱⁱ Hasegawa, K.; Arai, S.; Nishida, A. *Tetrahedron*, **2006**, *62*, 1390-1401.
- ^{iv} (a) Ito, Y.; Sawamura, M.; Hayashy, T. *J. Am. Chem. Soc.*, **1986**, *108*, 6405-6406. (b) Fones, *Journal Biol. Chem.*, **1953**, *204*, 323-325. (c) Easton, J.C.; Hutton, A.C.; Roselt, D.P.; Tiekink, R.T.E. *Tetrahedron*, **1994**, *50*, 7327-7340.