SUPPORTING INFORMATION

Stereospecific Intramolecular Arylation of 2- and 3-Pyridyl Substituted Alkylamines via Configurationally Stable α-Pyridyl Organolithiums

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General Information

All reactions were performed under a nitrogen or argon atmosphere in flame-dried apparatus. All reagents and chemicals were bought from chemical suppliers and used without further purification (unless otherwise stated). Tetrahydrofuran (THF) was distilled under nitrogen from sodium wire using benzophenone as an indicator. Triethylamine was stored over KOH. All solvents were removed under vacuum using a rotary evaporator. Pet.Ether indicates fractions of petroleum ether boiling at 40-60 °C. LDA was used as a solution in THF/heptane/ethylbenzene (2.0 M from sigma Aldrich) or prepared by General procedure 6. -78 °C, -40 °C and other low temperatures were reached using a Thermo Scientific Haake Immersion Cooler EK90.

Thin layer chromatography (TLC) was performed using commercially available pre-coated plates (Macherey-Nagel alugram SIL G/UV254). Visualisation was Via UV light (at 254 nm) or by staining with phosphomolybdic acid or 'Seebach' dip (2.50 g phosphomolybdic acid hydrate, 1.00 g cerium (IV) sulphate tetrahydrate, 3.20 mL conc. H_2SO_4, 90.50 mL H_2O) then heating. Flash column chromatography used chromatography grade silica, 60 Å particle size, 40-63 microns from Aldrich and compounds were loaded as saturated solutions in the correct solvents.

Capillary melting points were determined on a Stuart Scientific melting point SMP 10 apparatus and are uncorrected. Optical rotations $[\alpha]_{\lambda}^{T}$ were recorded on an AA-100 polarimeter using a cell with a pathlength of 0.25 dm at 18-22 °C with the solvent and concentration (*c*) quoted in g/100 mL.

Nuclear Magnetic Resonance (NMR) spectra (1H NMR and 13C NMR) were recorded on either Bruker Ultrashield 300 (Avance), 400 (Avance III or Avance III HD fitted with nitrogen cooled prodigy cold probe) or 500 MHz (Avance II) spectrometers. The residual solvent peak for $CDCl_3$ (δ_H: 7.26 ppm; δ_C: 77.16 ppm), CD_3OD (δ_H: 3.31 ppm; δ_C: 49.00 ppm) were used as internal standards when assigning NMR spectra.[1]

Chemical shifts, δ, are quoted in parts per million (ppm) downfield of trimethylsilane. Coupling constants (*J*) are reported to the nearest 0.1 Hz. The splitting patterns for the spectra assignment are abbreviated to: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin.), septet (sept.), multiplet (m), broad (br.) and some as a combination of these.

Infrared spectra were recorded on a Thermo Scientific iD5 ATR, FT-IR spectrometer, using a Universal ATR accessory for sampling, with absorption of most relevance quoted as vin cm^{-1} and the samples were run as solids or evaporated films.

Low and high resolution mass spectra were recorded mainly by staff at the University of Manchester. ESI were recorded on a Micromass Platform II or Waters QTOF; high resolution mass spectra (HRMS) were recorded on a Thermo Finnigan MAT95XP mass spectrometer or Waters.

[1] Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512

General Experimental Procedure

General procedure 1: *Urea formation from carbamoyl chloride (**9**, **10**, **17** and **18**)*

The pyridine-derived amine **5** or **6** (1.0 equiv), anhydrous acetonitrile (0.4 M) and triethylamine (1.1 equiv) were combined and stirred for 10 minutes under nitrogen at room temperature. The carbamoyl chloride (1.0 equiv) was added. The reaction mixture was heated to reflux overnight. The reaction mixture was cooled to room temperature and quenched with saturated aqueous $NaHCO_3$ solution. The organic layer was removed and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with NH_4Cl and brine and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

General procedure 2: *Methylation of ureas (**7** and **8**)*

A – in THF as a solvent

The urea derivative **17** (1.0 equiv) was dissolved in anhydrous THF (0.4 M) and methyl iodide (1.2 eq) was added. The solution was cooled to 0 °C before sodium hydride (1.3 equiv, (60% suspension in oil)) was added. The reaction was allowed to warm to room temperature, monitored by TLC and worked up when complete (between 2 hours and overnight). The reaction mixture was quenched with MeOH and saturated aqueous NH_4Cl solution was added before being extracted three times with ethyl acetate. The combined organic extracts were washed twice with water and once with brine then dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

B – in DMF as a solvent

To a solution of the urea derivative **18** (1.0 equiv) in anhydrous DMF (0.1 M) at 0 °C was added sodium hydride (1.5 equiv, (60% suspension in oil)). The reaction mixture was stirred at 0 °C for 15 min, then methyl iodide was added dropwise. The reaction was allowed to warm to room temperature, monitored by TLC and worked up when complete (1 h - overnight). The reaction mixture was quenched with H_2O. The solvent was evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and extracted from H_2O three times. The combined organic phase was washed three times with 5% aqueous LiCl solution and once with brine, then dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure 3: *LDA-mediated rearrangement of ureas (**11**, **13**, **14** and **15**)*

A solution of a pyridine derivative (1.0 equiv) in anhydrous THF (0.1 M) was cooled to -78 °C and LDA (2.5 equiv) was added dropwise. After stirring at -78 °C for 3-18 h the reaction mixture was quenched with NH_4Cl or MeOH. The mixture was extracted three times with ethyl acetate, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

General procedure 4: *Hydrolysis of ureas (**12** and **16**)*

A solution of a pyridine derivative (1.0 equiv), aqueous NaOH (2.0 M) and EtOH (1.2 M) was microwaved at 130 °C for 3 h. The reaction mixture was concentrated and extracted with ethyl acetate, dried over $MgSO_4$, and concentrated under reduced pressure.

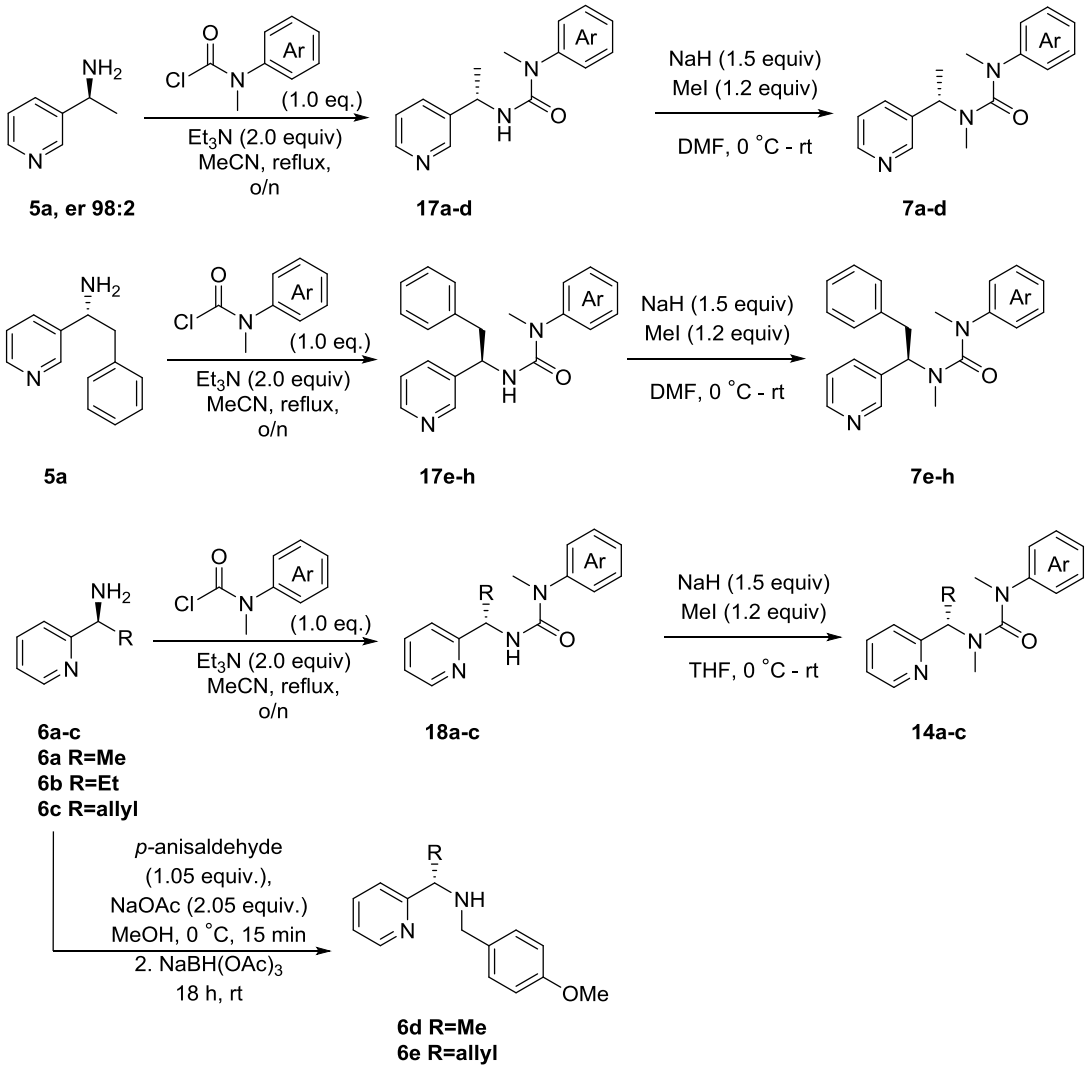
General procedure 5: *Amine protection*

To a solution of aminopyridine (1.0 equiv) in methanol (0.2 M) were added *p*-anisaldehyde (1.05 equiv) and NaOAc (2.05 quiv) and stirred at room temperature for 15 minutes. The reaction mixture was cooled to 0 °C and $NaBH(OAc)_3$ (2.05 equiv) was added portionwise. After stirring for 18 h at room temperature, the solvent was evaporated. The crude mixture was dissolved in EtOAc, washed (with $NaHCO_3$ and brine), dried over $MgSO_4$, and concentrated under reduced pressure.

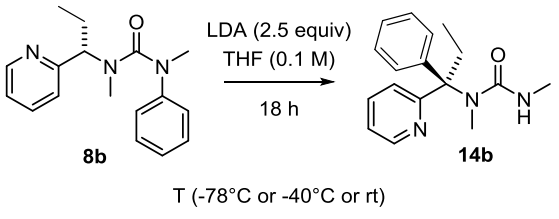
General procedure 6: *Preparation of LDA*

To a cooled solution of distilled diisopropylamine (1.0 equiv.) in THF (0.75 M) at 0 °C was added *n*-BuLi (1.0 equiv.) The reaction mixture was stirred at 0 °C for 20 min before immediate use.

For clarity, compounds **6d**, **6e**, **17a-h** and **18a-c** were not included in the main text, but were isolated and purified before **7a-h** were made.



Effect of the temperature reaction on the er (HPLC traces of **14b** in HPLC part)



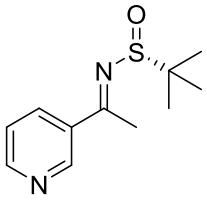
- Conditions A : LDA (2.5 equiv) in THF at **-78 °C** for 18 hours =>***er > 99:1***

- Conditions B : LDA (2.5 equiv) in THF at **-40 °C** for 18 hours => ***er = 98:2***

- Conditions C : LDA (2.5 equiv) in THF at **room temperature** for 18 hours => ***er = 86:4***

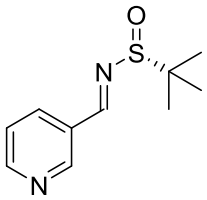
Synthetic procedures

(*R*,*E*)-2-methyl-*N*-(1-(pyridin-3-yl)ethylidene)propane-2-sulfinamide ((*R*)-1)[2]



Procedure by Chellucci *et al.* was followed.[2] A solution of 1-(pyridin-3-yl)ethan-1-one (4.54 mL, 41.27 mmol), (*R*)-(+)-2-methylpropane-2-sulfinamide (5.0 g, 41.27 mmol) and $Ti(OEt)_4$ (18.8 g, 82.6 mmol) in CH_2Cl_2 (165 mL) was refluxed for 72 h. The reaction mixture was allowed to cool down to room temperature, then it was concentrated *in vacuo*. The residue was dissolved in EtOAc (200 mL). The solution was stirred vigorously and brine was added (150 mL) slowly. After 15 min, the mixture was filtered over a pad of Celite, and the filter cake was washed with copious amounts of EtOAc. The filtrate was dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the crude was purified by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH) to give **(*R*)-1** as yellow oil (5.73 g, 61%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 9.14-9.03 (1H, m, =C*H*), 8.71 (1H, dd, *J* = 4.8, 1.7, =C*H*), 8.16 (1H, ddd, *J* = 8.1, 2.4, 1.6, =C*H*), 7.38 (1H, ddd, *J* = 8.0, 4.8, 0.9, =C*H*), 2.80 (3H, s, N=C-CH_3), 1.33 (9H, s, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 174.4 (*C*=N), 152.4 (=*C*H), 148.8 (=*C*H), 134.6 (=*C*H), 134.4 (=*C*), 123.5 (=*C*H), 58.0 (*C*(CH$_3$)$_3$), 22.7 (C(*C*H$_3$)$_3$), 19.8 (N=C-*C*H$_3$).

(*R*,*E*)-2-methyl-*N*-(pyridin-3-ylmethylene)propane-2-sulfinamide ((*R*)-2)[3]



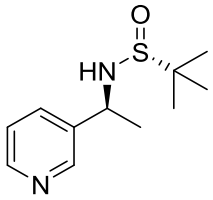
Literature procedure was followed.[3] To a solution of 3-pyridinecarboxaldehyde (6.00 mL, 63.58 mmol) and (*R*)-(+)-2-methylpropane-2-sulfinamide (7.72 g, 63.58 mmol) in anhydrous THF was added $Ti(OEt)_4$ (29.00 g, 127.2 mmol). The reaction mixture turned instantly orange and was stirred at room temperature overnight. Brine (100 mL) was added to the vigorously stirred reaction mixture. The suspension was filtered through a pad of Celite. The filter cake was washed with copious amount of EtOAc. The organic phase was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo*. The crude was purified by flash column chromatography (SiO_2, 60:40 to 100:0 EtOAc:Petrol) to give **(*R*)-2** as yellow oil (5.73 g, 61%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ = 9.03 (1H, dd, *J* = 2.1, 0.9, =C*H*), 8.74 (1H, dd, *J* = 4.8, 1.7, =C*H*), 8.65 (1H, s, =C*H*), 8.17 (1H,

[2] Data in agreement with the literature (Reference: Chelucci, G.; Baldino, S.; Chessa, S.; Pinna, G. A.; Soccolini, F.; *Tetrahedron: Asymmetry*, **2006**, *17*, 3163)

[3] Data in accordance with the literature (Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. *J. Org. Chem.*, **1999**, *64*, 1278)

dt, *J* = 8.0, 1.9, =C*H*), 7.46 – 7.40 (1H, m, =C*H*), 1.28 (9H, s, (C(CH_3)$_3$)). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.5 (N=*C*H), 153.0 (=*C*H), 151.1 (=*C*H), 135.9 (=*C*H), 129.9 (=*C*), 124.1 (=*C*H), 58.3 (*C*(CH_3)$_3$, 22.8 (C(*C*H_3)$_3$).

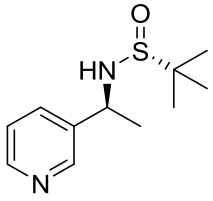
(*R*)-2-methyl-*N*-((*S*)-1-(pyridin-3-yl)ethyl)propane-2-sulfinamide (3a, dr 98:2)[2]



Procedure by Chellucci *et al.* was followed.[2] To a solution of **1** (2.01 g, 8.96 mmol) in anhydrous THF (90 mL) at -78 °C was added dropwise tri-*sec*-butylborohydride (L-Selectride) (1.0 M solution in THF, 8.96 mL, 8.96 mmol). The reaction mixture was stirred at -78 °C overnight, then allowed to warm up to room temperature, quenched with saturated aqueous solution of NH_4Cl. The organic and aqueous phases were separated, the aqueous layer was extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to yield a crude brown oil, which was purified by flash column chromatography (SiO_2, 95:5 CH_2Cl_2:MeOH) to yield **3a** as a yellow oil (1.46 g, 72%, >95:5 d.r. (R_S,*S*):(*R*,*R*)). The exact diastereomeric ratio (d.r. 98:2) was later confirmed by er of **7b** and **7c**, which were determined by chiral HPLC.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.58 (1H, d, *J* = 2.3, =C*H*), 8.50 (1H, dd, *J* = 4.8, 1.6, =C*H*), 7.62 (1H, dt, *J* = 7.9, 2.0, =C*H*), 7.25 (1H, dd, *J* = 7.9, 4.8, =C*H*), 4.59 (1H, qd, *J* = 6.7, 3.4, C*H*-CH_3), 3.40 (1H, d, *J* = 2.7, N*H*), 1.55 (3H, d, *J* = 6.7, CH-CH_3), 1.18 (9H, s, C(CH_3)$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 149.0 (=*C*H), 148.8 (=*C*H), 138.80 (=*C*), 134.6 (=*C*H), 123.5 (=*C*H), 55.8 (*C*(CH_3)$_3$), 52.5 (*C*H-CH_3), 24.9 (CH-*C*H_3), 22.5 (C(*C*H_3)$_3$). **HRMS** (ESI^+): *m/z* calcd for $C_{11}H_{19}N_2OS$ $[M+H]^+$ 227.1213, found 227.1213.

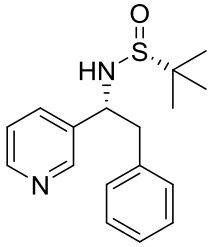
(*R*)-2-methyl-*N*-((*S*)-1-(pyridin-3-yl)ethyl)propane-2-sulfinamide (3a, dr 73:27)[2]



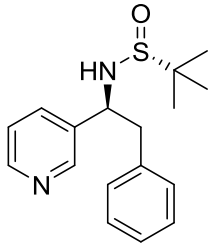
To a solution of **2** (6.00 g, 28.54 mmol) in CH_2Cl_2 (140 mL) at -40 °C was added dropwise methylmagnesium bromide (3.0 M solution in Et_2O, 19.1 mL, 57.12 mmol). The reaction mixture was stirred overnight at -40 °C, then warmed up to room temperature, quenched with saturated aqueous solution of NH_4Cl . The organic and aqueous phases were separated, the aqueous layer was extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to give a crude mixture of diastereoisomers **3a** (d.r. 73:27) that was used without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.62-8.59 (1H, m, =C*H,* major and minor isomer), 8.55 (0.27H, dd, *J* = 4.9, 1.8, =C*H,* minor

isomer), 8.53 (0.73H, dd, *J* = 4.8, 1.7, =C*H*, major isomer), 7.68 (0.27H, dt, *J* = 7.9, 2.0, =C*H*, minor isomer), 7.64 (0.73H, dt, *J* = 7.9, 2.0 Hz, =C*H*, major isomer), 7.31 – 7.24 (1H, m, =C*H,* major and minor isomer), 4.66 – 4.54 (1H, m, C*H*-CH_3, major and minor isomer), 3.42 (0.27H, d, *J* = 2.9, N*H*, minor isomer), 3.34 (0.73H, d, *J* = 3.4, major isomer), 1.57 (2.19H, d, *J* = 6.7, CH-CH_3, major isomer), 1.55 (0.81H, d, *J* = 6.7, CH-CH_3, minor isomer), 1.24 (2.43H, s, C(CH_3)$_3$, minor isomer), 1.20 (6.57H, s, C(CH_3)$_3$, major isomer).

(*R*)-2-methyl-*N*-((*R*)-2-phenyl-1-(pyridin-3-yl)ethyl)propane-2-sulfinamide (R_S,*R*-3b)[4] and (*R*)-2-methyl-*N*-((*S*)-2-phenyl-1-(pyridin-3-yl)ethyl)propane-2-sulfinamide (R_S,*S*-3b))



(R_S,*R*)-3b



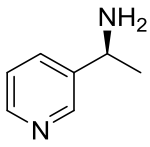
(R_S,*S*)-3b

To a solution of **2** (3.46 g, 16.45 mmol) in CH_2Cl_2 (97 mL) at -40 °C was added dropwise benzylmagnesium chloride (2.0 M solution in THF, 16.5 mL, 32.90 mmol). The reaction mixture was stirred overnight at -40 °C, then warmed up to room temperature, quenched with saturated aqueous solution of NH_4Cl . The organic and aqueous phases were separated, the aqueous layer was extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to give a crude mixture of diastereoisomers (72:28 ratio of (R_S,*R*)-**3b** to (R_S,*S*)-**3b** determined by ^{1}H NMR) that was separated by flash column chromatography (SiO_2, EtOAc, then 90:10 CH_2Cl_2:MeOH) to yield (R_S,*R*)-**3b** as a yellow oil (3.21 g, 64%) and (R_S,*S*)-**3b** as a white solid (0.92 g, 19%). (R_S,*R*)-**3b: R_f** 0.1 (EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.45 (1H, d, *J* = 2.3, =C*H*), 8.41 (1H, dd, *J* = 4.8, 1.6, =C*H*), 7.51 (1H, dt, *J* = 8.0, 2.0, =C*H*), 7.22 – 7.04 (4H, m, 4 x =C*H*), 6.98 – 6.92 (2H, m, 2 x =C*H*), 4.55 (1H, td, *J* = 7.2, 4.9, C*H*NH), 3.80 (1H, d, *J* = 5.1, CHN*H*), 3.26 (1H, dd, *J* = 13.5, 6.9, CH_AH$_B$Bn), 2.95 (1H, dd, *J* = 13.5, 7.5, CH$_A$$H_B$Bn), 1.07 (9H, s, C(C$H_3$)$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 148.9 (=*C*H), 148.7 (=*C*H), 137.6 (=*C*), 136.7 (=*C*), 135.5 (=*C*H), 129.7 (=*C*H), 128.5 (=*C*H), 126.9 (=*C*H), 123.6 (=*C*H), 59.1 (C*H*-Bn), 56.4 (*C*(CH$_3$)$_3$), 43.5 (*C*H$_2$Ph), 22.6 (C(*C*H$_3$)$_3$).

(R_S,*S*)-**3b: R_f** 0.3 (EtOAc). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.52 – 8.42 (2H, m, 2 x =C*H*), 7.49 (1H, dt, *J* = 7.9, 2.0, =C*H*), 7.26 – 7.12 (4H, m, 4 x =C*H*), 7.05 – 6.99 (2H, m, 2 x =C*H*), 4.62 (1H, ddd, *J* = 8.4, 6.5, 2.3, C*H*NH), 3.55 (1H, d, *J* = 2.3, CHN*H*), 3.10 – 2.92 (2H, m, C*H*$_2$Ph), 1.08 (9H, s, (C(CH_3)$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 149.5 (=*C*H), 149.2 (=*C*H), 136.9 (=*C*), 136.0 (=*C*), 135.7 (=*C*H), 129.6 (=*C*H), 129.0 (=*C*H), 127.4 (=*C*H), 123.4 (=*C*H), 57.3 (*C*H-Bn), 55.9 (*C*(CH$_3$)$_3$), 45.3 (*C*H$_2$Ph), 22.6 (C(*C*H$_3$)$_3$). **Mp** = 112-114 °C. **IR** (film, cm^{-1}): ν_{max} = 3194, 3028, 1578, 1454, 1428, 1363, 1057. $[\alpha]_D^{25}$ = -20 (c = 1.00; CH_2Cl_2). **HRMS** (ESI$^+$): *m/z* calcd for $C_{17}H_{23}N_2OS$ $[M+H]^+$ 303.1526, found 303.1525.

[4] Data for (R_S,*R*)-**3b** in accordance with the literature (Reference: Buesking, A. W.; Baguley, T. D.; Ellman, J. A.; *Org. Lett.*, 2011, 13, 964}

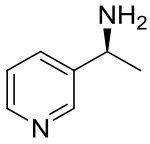
(*S*)-1-(pyridin-3-yl)ethan-1-amine (5a, er 98:2)[5]



To a solution of **3aa** (4.50 g, 19.88 mmol) in anhydrous MeOH (100 mL) was added HCl in dioxane (4.0 M, 24.9 mL, 99.4 mmol). Reaction mixture was stirred for 2 h, evaporated *in vacuo* and the solid residue was washed with Et_2O and then dissolved in 1 M aqueous KOH solution until pH was higher than 10. The aqueous phase was extracted three times with EtOAc. The combined organic extract was dried over $MgSO_4$ and evaporated *in vacuo* to give **5a (er 98:2)** as brown oil (1.60 g, 66%) that was used without further purification.

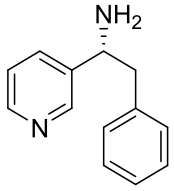
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.53 (1H, t, *J* = 1.9, =C*H*), 8.48 – 8.37 (1H, m, =C*H*), 7.70 – 7.60 (1H, m, =C*H*), 7.27 – 7.13 (1H, m, =C*H*), 4.12 (1H, q, *J* = 6.7, C*H*-CH_3), 1.50 (2H, s, NH_2), 1.34 (3H, d, *J* = 6.6, CH-CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 148.6 (=*C*H), 148.2 (=*C*H), 142.7 (=*C*), 133.4 (=*C*H), 123.6 (=*C*H), 49.2 (*C*H-CH_3), 25.8 (CH-*C*H_3). **HRMS** (ESI^+): *m/z* calcd for $C_7H_{11}N_2$ $[M+H]^+$ 123.0917, found 123.0920.

(*S*)-1-(pyridin-3-yl)ethan-1-amine (5a, er 73:27)



Same procedure and data as for **5a (er 98:2)**, **(3a, dr 73:27)** used as the starting material instead.

(*R*)-2-phenyl-1-(pyridin-3-yl)ethan-1-amine (5b)[5]



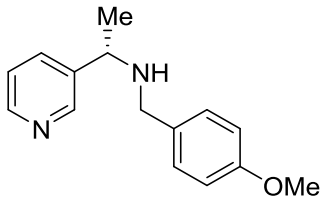
To a solution of (R_S,*R*)-**3b** (5.20 g, 17.19 mmol) in anhydrous MeOH (85 mL) was added HCl in dioxane (4.0 M, 21.5 mL, 86.0 mmol). Reaction mixture was stirred for 2 h, evaporated *in vacuo* and the solid residue was washed with Et_2O and then dissolved in 1 M aqueous KOH solution until pH was higher than 10. The aqueous phase was extracted three times with EtOAc. The combined organic extract was dried over $MgSO_4$ and evaporated *in vacuo* to give **5b** as brown oil (2.90 g, 85%) that was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (1H, d, *J* = 2.2, =C*H*), 8.44 (1H, dd, *J* = 4.8, 1.7, =C*H*), 7.63 (1H, ddd, *J* = 7.9, 2.3, 1.6, =C*H*), 7.29 – 7.12 (4H, m, 4 x =C*H*), 7.10 – 7.06 (2H, m, 2 x =C*H*), 4.18 (1H, dd, *J* = 8.7, 5.2, C*H*-CH_2), 2.92 (1H, dd, *J* = 13.4, 5.2, CH-C$H_A$$H_B$), 2.78 (1H, dd, *J* = 13.3, 8.7, CH-CH$_A$$H_B$), 1.50 (2H, s, N$H_2$). **^{13}C NMR**

[5] The data are in agreement with the literature (Reference: Baucom, K. D.; Guram, A. S.; Borths, C. J. *Synlett*, 2015, 26, 201).

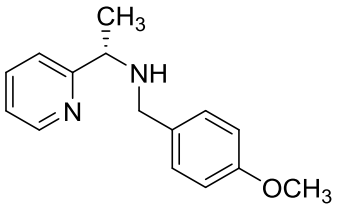
(101 MHz, $CDCl_3$) δ = 148.8 (2 x =C*H*), 140.8 (=*C*) , 138.3 (=*C*), 134.2 (=*C*H), 129.5 (=*C*H), 128.7 (=*C*H), 126.8 (=*C*H), 123.5 (=*C*H), 55.4 (N-*C*H-CH_2), 46.4 (N-CH-*C*H_2). **HRMS** (ESI^+): *m/z* calcd for $C_{13}H_{15}N_2$ $[M+H]^+$ 199.1230, found 199.1230.

(*S*)-N-(4-methoxybenzyl)-1-phenyl-1-(pyridin-3-yl)ethan-1-amine (5c)



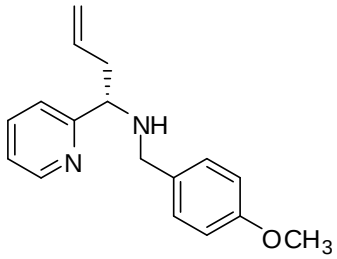
Following General procedure 5, aminopyridine **5a, er 73:27** (2.075 g, 16.99 mmol), *p*-anisaldehyde (2.17 mL, 17.83 mmol), NaOAc (2.86 g, 34.82 mmol) and $NaBH(OAc)_3$ (7.38 g, 34.82 mmol) in MeOH (77 ml) gave after purification by flash column chromatography (SiO_2, 95:5 CH_2Cl_2:MeOH) **5c** as an oil (2.27 g, 55%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.57 (1H, d, *J* = 2.2, =C*H*), 8.51 (1H, dd, *J* = 4.8, 1.7, =C*H*), 7.73 (1H, dt, *J* = 8.0, 2.0, =C*H*), 7.30 – 7.24 (1H, m, =C*H*), 7.20 – 7.16 (2H, m, 2 x =C*H*), 6.87 – 6.81 (2H, m, 2 x =C*H*), 3.84 (1H, q, *J* = 6.6, C*H*-CH_3), 3.79 (3H, s, OCH_3), 3.58 (1H, d, *J* = 13.0, NHC$H_A$$H_B$), 3.53 (1H, d, *J* = 13.0, NHC$H_A$$H_B$), 1.68 (1H, br s, N*H*), 1.37 (3H, d, *J* = 6.6, CH-CH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 158.8 (=*C*), 149.2 (=*C*H), 148.7 (=*C*H), 140.8 (=*C*), 134.4 (=*C*H), 132.4 (=*C*), 129.4 (=*C*H), 123.7 (=*C*H), 114.0 (=*C*H), 55.4 (O*C*H_3), 55.2 (*C*H-CH_3), 51.2 (NH-*C*H_2), 24.5 (CH-*C*H_3). **$[\alpha]_D^{23}$** = -31.7 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3357, 2930, 1365, 1168. **HRMS** (ESI^+): *m/z* calcd for $C_{15}H_{19}N_2O$ $[M+H]^+$ 243.1492, found 243.1497.

[(4-Methoxyphenyl)methyl][(1S)-1-(pyridin-2-yl)ethyl]amine (6d)



Following General procedure 5, aminopyridine **6a** (440 mg, 3.60 mmol), *p*-anisaldehyde (0.46 ml), NaOAc (605 mg) and $NaBH(OAc)_3$ (1.56 g) in MeOH (16.4 ml) gave **6d** as an oil (477 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.63-8.54 (1H, m, =C*H*), 7.65 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.34 (1H, d, *J* = 7.8, =C*H*), 7.24-7.20 (2H, m, 2 x =C*H*), 7.16 (1H, ddd, *J* = 14.3, 4.9 and 1.1, =C*H*), 6.90-6.77 (2H, m, 2 x =C*H*), 3.90 (1H, q, *J* = 6.7, NC*H*CH_3), 3.79 (3H, s, OCH_3), 3.57 (2H, AB pattern, *J* = 12.9, Δν = 9.0, NHCH_2), 1.88 (1H, brs, N*H*), 1.39 (3H, d, *J* = 6.7, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.8 (=*C*), 158.6 (=*C*), 149.5 (=*C*H), 136.7 (=*C*H), 132.7 (=*C*), 129.5 (=*C*H), 122.0 (=*C*H), 121.4 (=*C*H), 113.8 (2 x =*C*H), 58.7 (N*C*H), 55.4 (O*C*H_3), 51.3 (*C*H_2), 23.1 (*C*H_3). **$[\alpha]_D^{20}$** = -159 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2975, 1214, 1041, 748. **HRMS** (ESI^+): *m/z* calcd for $C_{15}H_{19}N_2O$ $[M+H]^+$ 243.1419, found 243.1495.

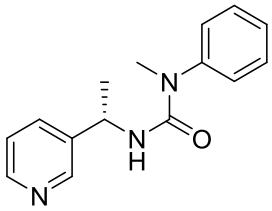
[(4-Methoxyphenyl)methyl][(1S)-1-(pyridin-2-yl)but-3-en-1-yl]amine (6e)



Following General procedure 5, aminopyridine **6c** (200 mg, 1.35 mmol), *p*-anisaldehyde (0.17 ml), NaOAc (227 mg) and $NaBH(OAc)_3$ (0.59 mg) in MeOH (6.13 ml) gave **6e** as an oil (90 mg, 25%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.63-8.51 (1H, m, =C*H*), 7.66 (1H, td, *J* = 7.6 and 1.8, =C*H*), 7.37 (1H, d, *J* = 7.8, =C*H*), 7.23-7.13 (3H, m, 3 x =C*H*), 6.88-6.79 (2H, m, 2 x =C*H*), 5.79-5.65 (1H, m, CH_2=C*H*CH_2), 5.10-4.97 (1H, m, CH_2=CH), 3.82 (1H, dd, *J* = 7.7 and 5.9, NHC*H*CH_2), 3.79 (3H, s, OCH_3), 3.61 (1H, d, *J* = 12.9, NHC$H_A$$H_B$), 3.51 (1H, d, *J* = 13.0, $NHCH_AH_B$), 2.63-2.35 (2H, m, CHCH_2CH=), 1.92 (1H, brs, N*H*). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.4 (=*C*), 158.7 (=*C*), 149.5 (=*C*H), 136.4 (=*C*H), 135.4 (=*C*H), 132.7 (=*C*), 129.4 (=*C*H), 122.1 (=*C*H), 122.0 (=*C*H), 117.6 (=*C*H_2), 113.8 (=*C*H), 63.0 (N*C*H), 55.4 (O*C*H_3), 51.3 (*C*H_2), 41.7 (*C*H_2). **$[\alpha]_D^{20}$** = -64 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3010, 2957, 1639, 1245, 1037, 750. **HRMS** (ESI^+): *m/z* calcd for $C_{17}H_{21}N_2O$ $[M+H]^+$ 269.1648, found 269.1650.

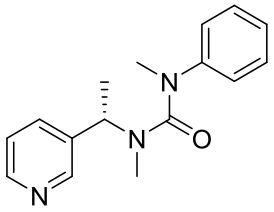
- Urea formation

(*S*)-1-methyl-1-phenyl-3-(1-(pyridin-3-yl)ethyl)urea (17a)



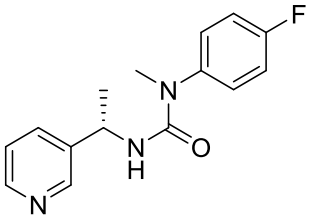
Following General procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (416 mg, 2.456 mmol, 1.2 eq.), 3-pyridine **5a (er 98:2)** (250 mg, 2.036 mmol, 1.0 eq.) and Et_3N (570 µl, 4.072 mmol, 2.0 eq.) in acetonitrile (20.0 ml) gave after 20 h heating at reflux a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to obtain **17a** as a brown oil (239 mg, 46%). **R_f** 0.21 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.50 (1H, d, *J* = 2.3, =C*H*), 8.47 (1H, dd, *J* = 4.8, 1.6, =C*H*), 7.54 (1H, dt, *J* = 7.9, 1.8, =C*H*), 7.47 – 7.42 (2H, m, 2 x =C*H*), 7.36 – 7.30 (1H, m, =C*H*), 7.28 – 7.24 (2H m, 2 x =C*H*), 7.22 (ddd, *J* = 7.9, 4.8, 0.7 Hz, 1H, =C*H*), 5.03 (quin, *J* = 7.1 Hz, 1H, NHC*H*CH_3), 4.54 (d, *J* = 7.2 Hz, 1H, N*H*$CHCH_3$), 3.25 (s, 3H, NCH_3), 1.36 (d, *J* = 7.0 Hz, 3H, $NHCHCH_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 156.4 (*C*=O), 148.5 (=*C*H), 147.9 (=*C*H), 143.3 (=*C*), 140.0 (=*C*), 133.9 (=*C*H), 130.4 (=*C*H), 127.7 (=*C*H), 127.5 (=*C*H), 123.5 (=*C*H), 48.3 (NH*C*HCH_3), 37.4 (NCH_3), 22.5 ($NHCHCH_3$). **$[\alpha]_D^{25}$** = +90 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3327, 2979, 1650, 1495, 1346. **HRMS** (ESI^+): *m/z* calcd for $C_{15}H_{18}N_3O$ $[M+H]^+$ 256.1444, found 256.1447.

(*S*)-1,3-dimethyl-3-phenyl-1-(1-(pyridin-3-yl)ethyl)urea (7a)



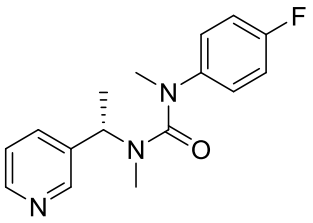
Following general procedure 2B, urea **17a** (193 mg, 0.715 mmol), NaH (43 mg, 1.073 mmol), MeI (53 µL, 0.858 mmol) in DMF (10.0 ml) gave after 2.5 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to obtain **7a** as a yellow oil (173 mg, 85%). $\mathbf{R_f}$ 0.25 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.52 (1H, d, *J* = 2.3, =C*H*), 8.49 (1H, dd, *J* = 4.8, 1.4, =C*H*), 7.66 – 7.58 (1H, m, =C*H*), 7.37 – 7.29 (2H, m, 2 x =C*H*), 7.24 (1H, ddd, *J* = 7.9, 4.9, 0.7, =C*H*), 7.15 – 7.07 (3H, m, 3 x =C*H*), 5.57 (1H, q, *J* = 7.1, NC*H*CH_3), 3.25 (3H, s, C*H*$_3$N-C=CH), 2.21 (3H, s, C*H*$_3$NCHCH_3), 1.45 (3H, d, *J* = 7.1, NCHC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 162.3 (*C*=O), 149.0 (=*C*H), 148.6 (=*C*H), 147.0 (=*C*), 136.7 (=*C*), 135.2 (=*C*H), 129.7 (=*C*H), 125.1 (=*C*H), 124.6 (=*C*H), 123.4 (=*C*H), 52.3 (N*C*HCH_3), 40.4 (*C*H$_3$NCHCH_3), 31.1 (C*H*$_3$NC=CH), 15.6 (NCH*C*H_3). $\mathbf{[\alpha]_D^{25}}$ = -10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 2973, 1637, 1439, 1338, 1119, 760, 698.

(*S*)-1-(4-fluorophenyl)-1-methyl-3-(1-(pyridin-3-yl)ethyl)urea (17b)



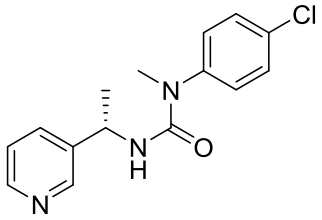
Following General procedure 1, *N*-methyl-*N*-(4-fluorophenyl) carbamoyl chloride (461 mg, 2.456 mmol, 1.2 eq.), 3-pyridine **5a (er 98:2)** (250 mg, 2.036 mmol, 1.0 eq.) and Et_3N (570 µl, 4.072 mmol, 2.0 eq.) in acetonitrile (20.0 ml) gave after 20 h heating at reflux a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to yield **17b** as a yellow oil (261 mg, 47%). $\mathbf{R_f}$ 0.28 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.58 – 8.41 (2H, m, 2 x =C*H*), 7.50 – 7.44 (1H, m, =C*H*), 7.35 – 7.03 (5H, m, 5 x =C*H*), 5.01 (1H, quint, *J* = 7.1, NHC*H*CH_3), 4.44 (1H, d, *J* = 6.8, N*H*CHCH_3), 3.21 (3H, s, NC*H*$_3$), 1.37 (3H, d, *J* = 7.0, NHCHC*H*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 161.7 (d, $^1J_{CF}$ = 248.3 Hz, =*C*F), 156.4 (*C*=O), 148.6 (=*C*H), 147.9 (=*C*H), 139.9 (=*C*-CHCH_3), 139.2 (d, $^4J_{CF}$ = 3.4 Hz, N-*C*=CH), 133.8 (=*C*H), 129.4 (d, $^3J_{CF}$ = 8.7 Hz, =*C*H), 123.5 (=*C*H), 117.3 (d, $^2J_{CF}$ = 22.6 Hz, =*C*H), 48.4 (NH*C*HCH_3), 37.6 (NC*H*$_3$), 22.5 (NHCH*C*H_3). $\mathbf{[\alpha]_D^{25}}$ = +90 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3326, 2976, 1649, 1507, 1220, 843. **HRMS** (ESI$^+$): *m/z* calcd for $C_{15}H_{16}N_3OFNa$ $[M+Na]^+$ 296.1170, found 296.1156.

((*S*)-1-(4-fluorophenyl)-1,3-dimethyl-3-(1-(pyridin-3-yl)ethyl)urea (7b)



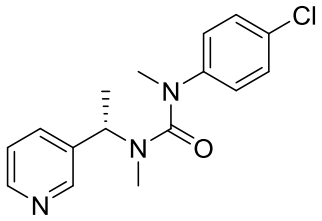
Following general procedure 2B, urea **17b** (223 mg, 0.817 mmol), NaH (49 mg, 1.226 mmol), MeI (61 µL, 0.981 mmol) in DMF (12.0 ml) gave after 3 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to yield **7b** as a yellow oil (186 mg, 79%). $\mathbf{R_f}$ 0.29 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.59 – 8.42 (1H, m, 2 x =C*H*), 7.66 – 7.54 (1H, m, =C*H*), 7.27 – 7.21 (2H, m, 2 x =C*H*), 7.11 – 6.98 (3H, m, 3 x =C*H*), 5.55 (1H, q, *J* = 7.1, NC*H*CH_3), 3.20 (3H, s, C*H*$_3$NC=CH), 2.22 (3H, s, C*H*$_3$NCHCH_3), 1.45 (3H, d, *J* = 7.1, NCHC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 162.3 (*C*=O), 160.0 (d, $^1J_{CF}$ = 245.3 Hz, =*C*F), 149.0 (=*C*H), 148.7 (=*C*H), 143.1 (d, $^4J_{CF}$ = 3.4 Hz = 3.0 Hz, N-*C*=CH), 136.6 (=*C*-CHCH_3), 135.1 (=*C*H), 126.4 (d, $^3J_{CF}$ = 8.1 Hz, =*C*H), 123.4 (=*C*H), 116.5 (d, $^2J_{CF}$ = 22.6 Hz, =*C*H), 52.4 (N*C*HCH_3), 40.8 (*C*H$_3$NCHCH_3), 31.1 (C*H*$_3$NC=CH), 15.7 (NCH*C*H$_3$). $\mathbf{[\alpha]_D^{25}}$ = -10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 2923, 1639, 1507, 1331, 1218, 1120, 716. **HRMS** (ESI$^+$): *m/z* calcd for $C_{16}H_{19}N_3OF$ $[M+H]^+$ 288.1507, found 288.1494.

(*S*)-1-(4-chlorophenyl)-1-methyl-3-(1-(pyridin-3-yl)ethyl)urea (17c)



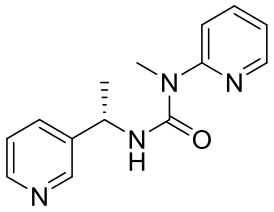
Following general procedure 1, *N*-methyl-*N*-(4-chlorophenyl) carbamoyl chloride (501 mg, 2.456 mmol, 1.2 eq.), 3-pyridine **5a (er 98:2)** (250 mg, 2.036 mmol, 1.0 eq.) and Et_3N (570 µl, 4.072 mmol, 2.0 eq.) in acetonitrile (20.0 ml) gave after 20 h heating at reflux a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to yield **17c** as a brown solid (248 mg, 42%). $\mathbf{R_f}$ 0.31 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.51 (1H, d, *J* = 2.2, =C*H*), 8.48 (1H, dd, *J* = 4.8, 1.5, =C*H*), 7.55 (1H, dt, *J* = 7.9, 1.8, =C*H*), 7.43 – 7.38 (2H, m, 2 x =C*H*), 7.25 – 7.17 (3H, m, 3 x =C*H*), 5.02 (1H, quint, *J* = 7.1, NHC*H*CH_3), 4.49 (1H, d, *J* = 7.3, N*H*CHCH_3), 3.22 (3H, s, NC*H*$_3$), 1.38 (3H, d, *J* = 7.0, NHCHC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 156.1 (*C*=O), 148.6 (=*C*H), 147.9 (=*C*H), 141.9 (=*C*), 139.8 (=*C*), 133.9 (=*C*H), 133.4 (=*C*), 130.5 (=*C*H), 128.8 (=*C*H), 123.5 (=*C*H), 48.4 (NH*C*HCH_3), 37.4 (NC*H*$_3$), 22.4 (NHCH*C*H$_3$). **Mp** = 110-112 °C. $\mathbf{[\alpha]_D^{25}}$ = +60 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3319, 2975, 1647, 1516, 1492, 1341, 1091, 714. **HRMS** (ESI$^+$): *m/z* calcd for $C_{15}H_{17}N_3OCl$ $[M+H]^+$ 290.1055, found 290.1058.

(*S*)-1-(4-chlorophenyl)-1,3-dimethyl-3-(1-(pyridin-3-yl)ethyl)urea (7c)



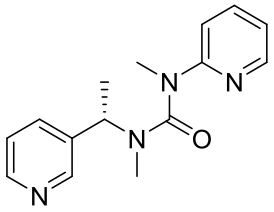
Following general procedure 2B, urea **17c** (248 mg, 0.856 mmol), NaH (51 mg, 1.283 mmol), MeI (64 µL, 1.027 mmol) in DMF (15.0 ml) gave after 3 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to yield **7c** as a yellow oil (215 mg, 83%). $\mathbf{R_f}$ 0.22 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.54 (1H, d, *J* = 1.5 Hz, =C*H*), 8.50 (1H, d, *J* = 3.8 Hz, =C*H*), 7.61 (1H, d, *J* = 7.9 Hz, =C*H*), 7.31 – 7.22 (4H, m, 4 x =C*H*), 7.04 – 6.99 (2H, m, 2 x =C*H*), 5.56 (1H, q, *J* = 7.1, NC*H*CH_3), 3.21 (3H, s, C*H*$_3$NC=CH), 2.24 (3H, s, C*H*$_3$NCHCH_3), 1.46 (3H, d, *J* = 7.1, NCHC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 161.9 (*C*=O), 149.0 (=*C*H), 148.8 (=*C*H), 145.4 (=*C*), 136.5 (=*C*), 135.1 (=*C*H), 130.3 (=*C*), 129.8 (=*C*H), 125.6 (=*C*H), 123.4 (=*C*H), 52.3 (N*C*HCH_3), 40.2 (*C*H$_3$NCHCH_3), 31.2 (C*H*$_3$NC=CH), 15.6 (NCH*C*H_3). **Mp** = 77-78 °C. $\mathbf{[\alpha]_D^{25}}$ = -10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 2974, 1642, 1492, 1330, 1120, 834, 715. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{19}N_3OCl$ $[M+H]^+$ 304.1211, found 304.1214.

(*S*)-1-methyl-1-(pyridin-2-yl)-3-(1-(pyridin-3-yl)ethyl)urea (17d)



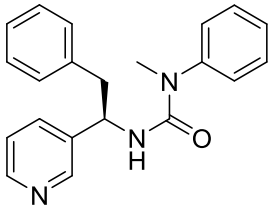
Following general procedure 1, *N*-methyl-*N*-(3-pyridyl) carbamoyl chloride (419 mg, 2.456 mmol, 1.2 eq.), 3-pyridine **5a (er 98:2)** (250 mg, 2.036 mmol, 1.0 eq.) and Et_3N (570 µl, 4.072 mmol, 2.0 eq.) in acetonitrile (20.0 ml) gave after 2 h heating at reflux a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to yield **17d** as a brown oil (203 mg, 39%). $\mathbf{R_f}$ 0.24 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.89 (1H, d, *J* = 6.7, N*H*CH_3), 8.65 (1H, d, *J* = 2.2, =C*H*), 8.48 (1H, dd, *J* = 4.8, 1.5, =C*H*), 8.31 – 8.24 (1H, m, =C*H*), 7.75 – 7.65 (2H, m, 2 x =C*H*), 7.26 – 7.22 (1H, m, =C*H*), 7.01 – 6.95 (2H, m, 2 x =C*H*), 5.13 (1H, quint, *J* = 7.0, NC*H*CH_3), 3.38 (3H, s, *J* = 8.4, NC*H*$_3$), 1.57 (3H, d, *J* = 7.0, NHCHC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 156.2 (*C*=O), 155.9 (=*C*), 148.4 (=*C*H), 148.2 (=*C*H), 140.4 (=*C*), 138.9 (=*C*H), 133.9 (=*C*H), 123.5 (=*C*H), 117.1 (=*C*H), 111.6 (=*C*H), 48.6 (NH*C*HCH_3), 32.9 (NC*H*$_3$), 23.2 (NHCH*C*H_3). $\mathbf{[\alpha]_D^{25}}$ = +110 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3172, 2972, 1666, 1529, 1435, 1317, 777. **HRMS** (ESI^+): *m/z* calcd for $C_{14}H_{17}N_4O$ $[M+H]^+$ 257.1397, found 257.1400.

(*S*)-1,3-dimethyl-3-(pyridin-2-yl)-1-(1-(pyridin-3-yl)ethyl)urea (7d)



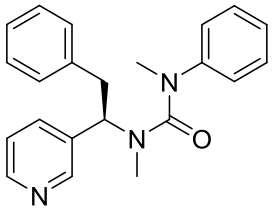
Following general procedure 2B, urea **17d** (248 mg, 0.856 mmol), NaH (51 mg, 1.283 mmol), MeI (64 µL, 1.027 mmol) in DMF (15.0 ml) gave after 3 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to yield **7d** as a yellow oil (215 mg, 74%). $\mathbf{R_f}$ 0.28 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.64 (1H, s, =C*H*), 8.52 (1H, d, *J* = 4.2, =C*H*), 8.32 (1H, dd, *J* = 4.8, 1.3, =C*H*), 7.74 (1H, d, *J* = 7.9, =C*H*), 7.61 – 7.53 (1H, m, =C*H*), 7.33 – 7.22 (1H, m, =C*H*), 6.94 – 6.84 (2H, m, =C*H*), 5.69 (1H, q, *J* = 7.1, NC*H*CH_3), 3.33 (3H, s, CH_3NC=CH), 2.42 (3H, s, CH_3NCHCH_3), 1.59 (3H, d, *J* = 7.1, NCHCH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.3 (*C*=O), 157.5 (=*C*), 149.1 (=*C*H), 148.8 (=*C*H), 148.6 (=*C*H), 137.9 (=*C*H), 136.2 (=*C*), 135.3 (=*C*H), 123.5 (=*C*H), 117.8 (=*C*H), 114.3 (=*C*H), 52.3 (N*C*HCH_3), 36.5 (*C*H_3NCHCH_3), 30.7 (CH_3NC=CH), 15.7 (NCH*C*H_3). $\mathbf{[\alpha]_D^{25}}$ = +10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 2978, 1651, 1589, 1477, 1428, 1332, 1104, 775. **HRMS** (ESI$^+$): *m/z* calcd for $C_{15}H_{18}N_4ONa$ $[M+Na]^+$ 293.1373, found 293.1365.

(*R*)-1-methyl-1-phenyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (17e)



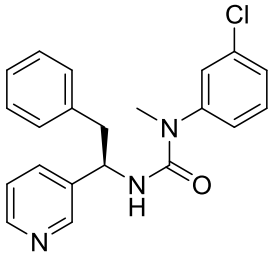
Following general procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (0.308 g, 1.816 mmol, 1.2 eq.), 3-pyridine **5b** (300 mg, 1.513 mmol, 1.0 eq.) and Et_3N (422 µl, 3.026 mmol, 2.0 eq.) in acetonitrile (15.0 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to yield **17e** as a brown oil (261 mg, 52%). $\mathbf{R_f}$ 0.18 (95:5 CH_2Cl_2:MeOH).**^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.46 (1H, dd, *J* = 4.8, 1.6, =C*H*), 8.41 (1H, d, *J* = 2.2, =C*H*), 7.47 – 7.29 (4H, m, 4 x =C*H*), 7.23 – 7.14 (4H, m, 4 x =C*H*), 7.09 – 7.03 (2H, m, 2 x =C*H*), 6.88 – 6.80 (2H, m, 2 x =C*H*), 5.12 (1H, dd, *J* = 14.6, 6.5, NHC*H*CH_2), 4.65 (1H, d, *J* = 6.8, N*H*CHCH_2), 3.17 (3H, s, N-CH_3), 3.00 (1H, dd, *J* = 13.8, 6.0, NHCHC$H_A$$H_B$), 2.80 (1H, dd, *J* = 13.8, 8.2, NHCHC$H_A$$H_B$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 156.4 (*C*=O), 148.4 (=*C*H), 148.1 (=*C*H), 143.0 (=*C*), 138.6 (=*C*), 136.6 (=*C*), 134.3 (=*C*H), 130.3 (=*C*H), 129.3 (=*C*H), 128.7 (=*C*H), 127.7 (=*C*H), 127.5 (=*C*H), 126.9 (=*C*H), 123.3 (=*C*H), 53.8 (NH*C*HCH_2), 43.0 (NHCH*C*H_2), 37.1 (NCH_3). $\mathbf{[\alpha]_D^{25}}$ = -10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3337, 3028, 2926, 1656, 1495. **HRMS** (ESI$^+$): *m/z* calcd for $C_{21}H_{21}N_3ONa$ $[M+Na]^+$ 354.1577, found 354.1561.

(*R*)-1,3-dimethyl-3-phenyl-1-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (7e)



Following general procedure 2B, urea **17e** (224 mg, 0.677 mmol), NaH (41 mg, 1.016 mmol), MeI (51 µL, 0.813 mmol) in DMF (6.8 ml) gave after 2 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to obtain **7e** as an orange oil (211 mg, 90%). $\mathbf{R_f}$ 0.18 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.66 (1H, d, *J* = 2.2, =C*H*), 8.51 (1H, dt, *J* = 18.8, 9.4, =C*H*), 7.80 (1H, dt, *J* = 7.9, 1.7, =C*H*), 7.44 – 7.23 (6H, m, 6 x =C*H*), 7.10 – 6.95 (3H, m, 3 x =C*H*), 6.48 – 6.40 (2H, m, 2 x =C*H*), 6.02 (1H, dd, *J* = 11.4, 5.5, NC*H*CH_2), 3.34 (1H, dd, *J* = 14.4, 5.5 Hz, NCHCH_AH_B), 3.12 (3H, s, =CH-NCH_3), 3.09 (1H, dd, *J* = 14.4, 11.4, NCHCH_AH_B), 2.23 (3H, s, CH_2CHNCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.1 (*C*=O), 149.2 (=*C*H), 148.9 (=*C*H), 146.5 (=*C*), 137.9 (=*C*), 135.9 (2 peaks, =*C*H, =*C*), 129.6 (=*C*H), 129.1 (=*C*H), 129.0 (=*C*H), 126.9 (=*C*H), 124.5 (=*C*H), 124.3 (=*C*H), 123.5 (=*C*H), 57.1 (N*C*HCH$_2$), 40.5 (=CH-N*C*H$_3$), 36.6 (NCH*C*H$_2$), 31.6 (CH_2CHN*C*H$_3$). $\mathbf{[\alpha]_D^{25}}$ = +95 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3029, 2931, 1634, 1494, 1342, 1118. **HRMS** (ESI$^+$): *m/z* calcd for $C_{22}H_{24}N_3O$ $[M+H]^+$ 346.1914, found 346.1900.

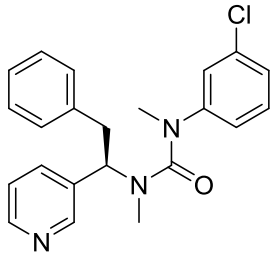
(*R*)-1-(3-chlorophenyl)-1-methyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (17f)



Following general procedure 1, *N*-methyl-*N*-(3-chlorophenyl) carbamoyl chloride (0.371 g, 1.816 mmol, 1.2 eq.), 3-pyridine **5b** (300 mg, 1.513 mmol, 1.0 eq.) and Et_3N (420 µL, 3.026 mmol, 2.0 eq.) in acetonitrile (11.0 ml) gave, after 2 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 97:3 to 95:5 CH_2Cl_2:MeOH) to yield **17f** as a brown oil (474 mg, 86%). $\mathbf{R_f}$ 0.23 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.41 (1H, dd, *J* = 4.8, 1.6, =C*H*), 8.37 (1H, d, *J* = 2.3, =C*H*), 7.41 – 7.35 (1H, m, =C*H*), 7.26 – 7.22 (2H, m, 2 x =C*H*), 7.18 – 7.10 (4H, m, 4 x =C*H*), 7.05 (1H, dt, *J* = 2.0, 0.9, =C*H*), 6.89 – 6.85 (1H, m, =C*H*), 6.85 – 6.78 (2H, m, 2 x =C*H*), 5.06 (1H, dt, *J* = 8.2, 6.4, NHC*H*CH_2), 4.56 (1H, d, *J* = 6.7, N*H*CHCH$_2$), 3.09 (3H, s, NCH_3), 2.99 (1H, dd, *J* = 13.9, 5.9, NHCHCH_AH_B), 2.76 (1H, dd, *J* = 13.9, 8.4, NHCHCH$_A$*H*$_B$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 155.9 (*C*=O), 148.6 (=*C*H), 148.1 (=*C*H), 144.3 (=*C*), 138.4 (=*C*), 136.5 (=*C*), 135.6 (=*C*), 134.3 (=*C*H), 131.2 (=*C*H), 129.3 (=*C*H), 128.8 (=*C*H), 127.9 (=*C*H), 127.8 (=*C*H), 127.1 (=*C*H), 125.6 (=*C*H), 123.4 (=*C*H), 53.9 (NH*C*HCH$_2$), 42.9 (NHCH*C*H$_2$), 37.2 (N*C*H$_3$). $\mathbf{[\alpha]_D^{25}}$ = -10 (c = 1.00;

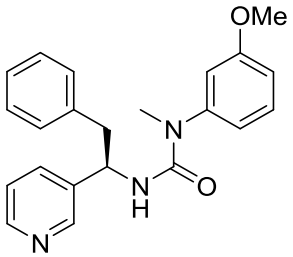
CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3310, 3028, 1656, 1591, 1509, 1337. **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{21}N_3OCl$ $[M+H]^+$ 366.1368, found 366.1354.

(*R*)-1-(3-chlorophenyl)-1,3-dimethyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (7f)



Following general procedure 2B, urea **17f** (282 mg, 0.772 mmol), NaH (51 mg, 1.278 mmol), MeI (64 µL, 1.02 mmol) in DMF (8.5 ml) gave gave after 2 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH),to obtain **7f** as a yellow oil (282 mg, 96%). $\mathbf{R_f}$ 0.18 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.61 (1H, d, *J* = 1.5, =C*H*), 8.47 (1H, d, *J* = 3.6 Hz, =C*H*), 7.75 – 7.69 (1H, m, =C*H*), 7.35 – 7.17 (6H, m, =C*H*), 6.93 – 6.75 (3H, m, =C*H*), 5.96 – 5.88 (2H, m, =C*H* and NC*H*CH_2), 3.28 (1H, dd, *J* = 14.5, 5.7, NCHC$H_A$$H_B$), 3.12 – 3.04 (1H, m, NCHC$H_A$$H_B$), 3.02 (3H, s, =CH-NC$H_3$), 2.23 (3H, s, CH_2CHNCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.6 (*C*=O), 149.2 (=*C*H), 149.1 (=*C*H), 147.6 (s), 137.7 (=*C*), 135.9 (=*C*H), 135.5 (=*C*), 134.8 (=*C*), 130.6 (=*C*H), 129.0 (2 x =*C*H), 127.0 (=*C*H), 124.5 (=*C*H), 123.8 (=*C*H), 123.6 (=*C*H), 121.8 (=*C*H), 57.4 (N*C*HCH_2), 40.0 (=CH-N*C*H_3), 36.5 (NCH*C*H_2), 31.8 (CH_2CHN*C*H_3). $\mathbf{[\alpha]_D^{25}}$ = +110 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3028, 2925, 1640, 1591, 1478, 1330, 1099. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{23}N_3OCl$ $[M+H]^+$ 380.1524, found 380.1511.

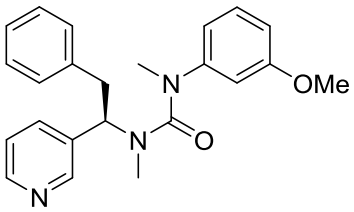
(*R*)-1-(3-methoxyphenyl)-1-methyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (17g)



Following general procedure 1, *N*-methyl-*N*-(3-methoxyphenyl) carbamoyl chloride (0.302 g, 1.513 mmol, 1.2 eq.), 3-pyridine **5b** (250 mg, 1.261 mmol, 1.0 eq.) and Et_3N (350 µl, 2.522 mmol, 2.0 eq.) in acetonitrile (13.0 ml) gave, after 2 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH) to yield **17g** as a brown oil (313 mg, 69%). $\mathbf{R_f}$ 0.17 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.46 (1H, dd, *J* = 4.8, 1.5, =C*H*), 8.41 (1H, d, *J* = 2.1, =C*H*), 7.42 (1H, dt, *J* = 7.8, 1.8, =C*H*), 7.33 – 7.24 (2H, m, 2 x =C*H*), 7.22 – 7.13 (3H, m, 3 x =C*H*), 6.91 – 6.81 (3H, m, 3 x =C*H*), 6.67 – 6.60 (2H, m, 2 x =C*H*), 5.11 (1Hz, dd, *J* = 6.8, 6.6, NHC*H*CH_2), 4.75 (1H, d, *J* = 6.8, N*H*CHCH_2), 3.79 (3H, s, OCH_3), 3.16 (3H, s, N-CH_3), 3.00 (1H, dd, *J* = 13.8, 6.1, NHCHC$H_A$$H_B$), 2.82 (1H, dd, *J* = 13.8, 8.1,

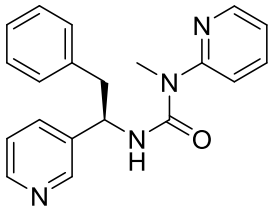
NHCHCH$_A$H$_B$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.0 (*C*=O), 156.3 (=*C*-OCH$_3$), 148.5 (=*C*H), 148.2 (=*C*H), 144.2 (=*C*), 138.6 (=*C*), 136.6 (=*C*), 134.3 (=*C*H), 131.0 (=*C*H), 129.3 (=*C*H), 128.7 (=*C*H), 126.9 (=*C*H), 123.4 (=*C*H), 119.5 (=*C*H), 113.5 (=*C*H), 113.0 (=*C*H), 55.5 (O*C*H$_3$), 53.8 (NH*C*HCH$_2$), 43.0 (NHCH*C*H$_2$), 37.1 (N*C*H$_3$). **IR** (film, cm^{-1}): ν_{max} = 3322, 3028, 2935, 1659, 1598, 1489. **HRMS** (ESI$^+$): *m/z* calcd for $C_{22}H_{24}N_3O_2$ $[M+H]^+$ 362.1863, found 362.1848.

(*R*)-1-(3-methoxyphenyl)-1,3-dimethyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)urea (7g)



Following general procedure 2B, urea **17g** (236 mg, 0.653 mmol), NaH (39 mg, 0.979 mmol), MeI (49 µL, 0.784 mmol) in DMF (7.0 ml) gave after 2 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), to obtain **7g** as a yellow oil (86mg, 35%). **R$_f$** 0.27 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.63 (1H, br s, =*C*H), 8.50 (1H, d, *J* = 4.1, =*C*H), 7.75 (1H, d, *J* = 7.9, =*C*H), 7.34 (2H, t, *J* = 7.4, 2 x =*C*H), 7.30 – 7.22 (3H, m, 3 x =*C*H), 6.91 (1H, t, *J* = 8.1, =*C*H), 6.60 – 6.53 (1H, m, =*C*H), 6.45 (1H, t, *J* = 2.2, =*C*H), 5.94 (1H, dd, *J* = 10.3, 6.2, =*C*H), 5.86 (1H, d, *J* = 7.9, =*C*H), 3.70 (3H, s, OC*H*$_3$), 3.32 (1H, dd, *J* = 14.4, 6.2, NCHC*H*$_A$H$_B$), 3.17 – 3.12 (1H, m, NCHCH$_A$*H*$_B$), 3.10 (3H, s, CH$_2$CHNC*H*$_3$), 2.32 (3H, s, =CH-NC*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 161.9 (*C*=O), 160.5 (=*C*), 149.3 (=*C*H), 148.9 (=*C*H), 147.7 (=*C*), 137.8 (=*C*), 135.9 (=*C*H), 135.6 (=*C*), 130.3 (=*C*H), 129.0 (=*C*H), 128.9 (=*C*H), 126.8 (=*C*H), 123.5 (=*C*H), 116.6 (=*C*H), 110.3 (=*C*H), 109.8 (=*C*H), 57.5 (N*C*HCH$_2$), 55.3 (O*C*H$_3$), 40.3 (=CH-N*C*H$_3$), 36.6 (NCH*C*H$_2$), 31.6 (CH$_2$CHN*C*H$_3$). **$[\alpha]_D^{25}$** = +65 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 2938, 1637, 1594, 1487, 1328, 1111, 1042, 699. **HRMS** (ESI$^+$): *m/z* calcd for $C_{23}H_{26}N_3O_2$ $[M+H]^+$ 376.2020, found 376.2025.

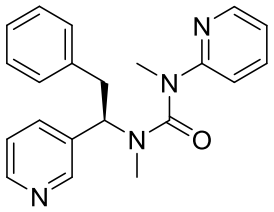
(*R*)-1-methyl-3-(2-phenyl-1-(pyridin-3-yl)ethyl)-1-(pyridin-2-yl)urea (17h)



Following general procedure 1, *N*-methyl-*N*-(3-pyridyl)) carbamoyl chloride (310 mg, 1.816 mmol, 1.2 eq.), 3-pyridine **5b** (300 mg, 1.513 mmol, 1.0 eq.) and Et_3N (420 µl, 3.026 mmol, 2.0 eq.) in acetonitrile (15.0 ml) gave after 2 h heating at reflux a crude product that was purified by flash column chromatography (SiO_2, 97:3 CH_2Cl_2:MeOH) to yield **17h** as a brown oil (450 mg, 90%). **R$_f$** 0.15 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.10 (1H, d, *J* = 7.0 Hz, N*H*CHCH$_2$), 8.51 (1H, d, *J* = 2.2 Hz, =C*H*), 8.46 (1H, dd, *J* = 4.8, 1.6 Hz,

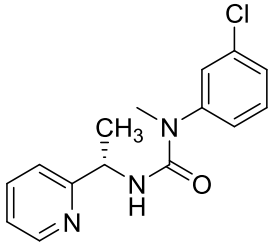
=C*H*), 8.19 (1H, ddd, *J* = 5.0, 2.0, 0.8 Hz, =C*H*), 7.70 (1H, ddd, *J* = 8.6, 7.4, 2.0 Hz, =C*H*), 7.48 (1H, dt, *J* = 7.9, 1.8 Hz, =C*H*), 7.28 – 7.15 (4H, m, 4 x =C*H*), 7.08 – 7.03 (2H, m, 2 x =C*H*), 6.99 – 6.93 (2H, m, 2 x =C*H*), 5.32 (1H, q, *J* = 6.8 Hz, NHC*H*CH_2), 3.33 (3H, s, N-CH_3), 3.18 – 3.13 (2H, m, NHCHCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 156.0 (*C*=O and N=*C*-N), 148.6 (=*C*H), 148.4 (=*C*H), 145.7 (=*C*H), 138.9 (=*C*H), 138.5 (=*C*), 137.1 (=*C*), 134.5 (=*C*H), 129.9 (=*C*H), 128.4 (=*C*H), 126.8 (=*C*H), 123.2 (=*C*H), 117.1 (=*C*H), 111.5 (=*C*H), 54.7 (NH*C*HCH$_2$), 43.6 (NHCH*C*H$_2$), 32.7 (N*C*H$_3$). $[\alpha]_D^{25}$ = -5 (c = 1.00; CH_2Cl_2). **Mp** = 85-86 °C. **IR** (film, cm^{-1}): ν_{max} = 3028, 1665, 1521, 1434, 1316. **HRMS** (ESI^+): *m/z* calcd for $C_{20}H_{21}N_4O$ $[M+H]^+$ 333.1710, found 333.1705.

(*R*)-1,3-dimethyl-1-(2-phenyl-1-(pyridin-3-yl)ethyl)-3-(pyridin-2-yl)urea (7h)



Following general procedure 2B, urea **17h** (330 mg, 0.993 mmol), NaH (60 mg, 1.490 mmol), MeI (74 µL, 1.192 mmol) in DMF (10.0 ml) gave after 2.5 h of stirring at room temperature a crude product that was purified by flash column chromatography (SiO_2, 97:3 CH_2Cl_2:MeOH), to obtain **7h** as a yellow oil (286 mg, 83%). **R_f** 0.21 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.75 (1H, d, *J* = 2.0, =C*H*), 8.56 (1H, dd, *J* = 4.7, 1.3, =C*H*), 8.24 (1H, ddd, *J* = 5.0, 2.0, 0.8 Hz, =C*H*), 7.87 (1H, dt, *J* = 7.9, 1.7 Hz, =C*H*), 7.45 – 7.28 (6H, m, 6 x =C*H*), 7.21 (1H, ddd, *J* = 8.3, 7.3, 2.0, =C*H*), 6.78 (1H, ddd, *J* = 7.3, 4.9, 0.9, =C*H*), 6.06 (1H, dd, *J* = 11.4, 5.6, NC*H*CH_2), 5.89 (1H, d, *J* = 8.3, =C*H*), 3.43 (1H, dd, *J* = 14.5, 5.6, NCHCH_AH_B), 3.23 (1H, dd, *J* = 14.5, 11.5, NCHCH_AH_B), 3.14 (3H, s, CH_2CHNCH_3), 2.45 (3H, s, =CH-NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 161.5 (*C*=O), 157.1 (=*C*), 149.2 (2 x =*C*H), 148.4 (=*C*H), 137.9 (=*C*H), 137.7 (=*C*), 135.9 (=*C*H), 135.3 (=*C*), 129.1 (2 x =*C*H), 123.6 (=*C*H), 117.5 (=*C*H), 114.8 (=*C*H), 57.2 (N*C*HCH$_2$), 36.6 (NCH*C*H$_2$), 36.1 (=CH-N*C*H$_3$), 31.4 (CH_2CHN*C*H$_3$). $[\alpha]_D^{25}$ = +90 (c = 1.00; CH_2Cl_2). **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{23}N_4O$ $[M+H]^+$ 347.1866, found 347.1851.

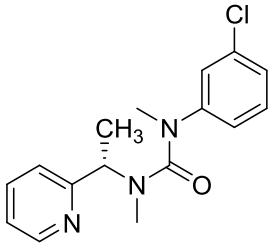
1-(3-Chlorophenyl)-1-methyl-3-[(1*S*)-1-phenylethyl]urea (18a)



Following general procedure 1, *N*-methyl-*N*-(3-chlorophenyl) carbamoyl chloride (1.40 g), 2-pyridine **6a** (835 mg, 6.87 mmol), synthesized from **4**, Et_3N (1.05 ml) and DMAP (cat) in dichloroethane (17.20 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH) to yield the title compound as an oil (1.28 g, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ =

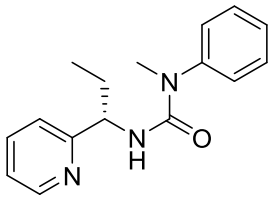
8.50-8.38 (1H, m, =C*H*), 7.64 (1H, td, *J* = 7.7 and 1.4, =C*H*), 7.35 (1H, t, *J* = 7.9, =C*H*), 7.30-7.21 (3H, m, 3 x =C*H*), 7.20-7.09 (2H, m, 2 x =C*H*), 5.97-5.79 (1H, brd, CHN*H*), 5.05 (1H, q, *J* = 6.9, NHC*H*CH_3), 3.27 (3H, s, NCH_3), 1.41 (3H, d, *J* = 6.8, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.8 (*C*=O), 156.3 (=*C*), 148.9 (=*C*H), 144.9 (=*C*), 137.0 (=*C*H), 135.2 (=*C*), 130.8 (=*C*H), 127.3 (=*C*H), 127.1 (=*C*H), 125.2 (=*C*H), 122.3 (=*C*H), 121.5 (=*C*H), 51.2 (N*C*H), 37.2 (NCH_3), 23.1 (CH_3). **$[\alpha]_D^{20}$** = -137 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3320, 2971, 2928, 1642. **HRMS** (ESI^+): *m/z* calcd for $C_{15}H_{16}ClN_3ONa$ $[M+Na]^+$ 312.0880, found 312.0871.

1-(3-Chlorophenyl)-1,3-dimethyl-3-[(1S)-1-phenylethyl]urea (8a)



Following general procedure 2A, urea **18a** (689 mg, 2.38 mmol), MeI (0.18 ml), NaH (124 mg) in THF (5.95 ml) gave, after purification by flash column chromatography (SiO_2, 80:20 to 0:100 Pet.Ether:EtOAc), **8a** as an oil (720 mg, 99%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.61-8.52 (1H, m, =C*H*), 7.65 (1H, td, *J* = 7.7 and 1.7, =C*H*), 7.32 (1H, d, *J* = 7.9, =C*H*), 7.21 (1H, t, *J* = 8.1, =C*H*), 7.18-7.10 (2H, m, 2 x =C*H*), 7.06-7.01 (1H, m, =C*H*), 7.00-6.95 (1H, m, =C*H*), 5.25 (1H, q, *J* = 7.1, NC*H*CH_3), 3.23 (3H, s, NCH_3), 2.38 (3H, s, NCH_3), 1.52 (3H, d, *J* = 7.1, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.6 (*C*=O), 160.2 (=*C*), 149.0 (=*C*H), 147.9 (=*C*), 136.7 (=*C*H), 134.9 (=*C*), 130.4 (=*C*H), 124.3 (=*C*H), 123.8 (=*C*H), 122.5 (=*C*H), 122.3 (=*C*H), 121.6 (=*C*H), 56.0 (N*C*H), 39.7 (NCH_3), 31.6 (NCH_3), 15.5 (CH_3). **$[\alpha]_D^{20}$** = -237 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2992, 2945, 1639. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{18}ClN_3ONa$ $[M+H]^+$ 326.1036, found 326.1048.

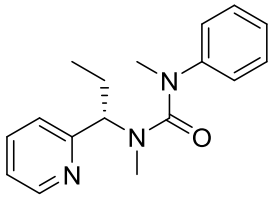
1,3-dimethyl-1-phenyl-3-[(1S)-1-(pyridin-2-yl)propyl]urea (18b)



Following general procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (477 mg), 2-pyridine **6b** (383 mg, 2.81 mmol), synthesized from **4**, and Et_3N (431 µl) in acetonitrile (7.00 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH) to yield **18b** as an oil (280 mg, 37%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.45-8.37 (1H, m, =C*H*), 7.60 (1H, td, *J* = 7.6 and 1.8, =C*H*), 7.47-7.38 (2H, m, 2 x =C*H*), 7.34-7.23 (3H, m, 3 x =C*H*), 7.22-7.18 (1H, m, =C*H*), 7.11 (1H, ddd, *J* = 7.5, 4.9 and 1.1, =C*H*), 5.50 (1H, d, *J* = 8.0, CHN*H*), 4.87 (1H, dt, *J* = 7.8 and 6.9, NHC*H*CH_2), 3.26 (3H, s, NCH_3), 1.85-1.63 (2H, m, CHC$H_2$$CH_3$), 0.78 (3H, t, *J* = 7.4, CH_2CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.3 (*C*=O), 157.0 (=*C*), 149.2 (=*C*H), 143.5 (=*C*), 136.5 (=*C*H), 130.0 (=*C*H), 127.3 (=*C*H), 127.2 (=*C*H), 122.2 (=*C*H),

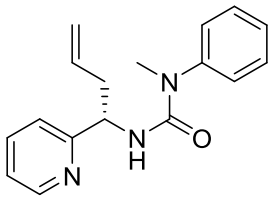
122.1 (=*C*H), 56.8 (N*C*H), 37.3 (N*C*H_3), 29.5 (*C*H_2), 10.3 (*C*H_3). **[α]$_D^{20}$** = -151 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3421, 2965, 2931, 1658, 750. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{20}N_3O$ $[M+H]^+$ 270.1601, found 270.1607.

1,3-dimethyl-1-phenyl-3-[(1S)-1-(pyridin-2-yl)propyl]urea (8b)



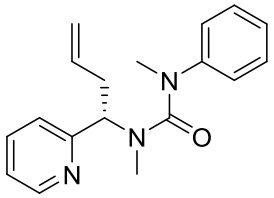
Following General procedure 2A, urea **18b** (230 mg, 0.85 mmol), MeI (0.06 ml), NaH (45 mg) in THF (2.13 ml) gave, after purification by flash column chromatography (SiO_2, 80:20 to 0:100 Pet.Ether:EtOAc), **8b** as an oil (230 mg, 95%).**^{1}H NMR** (400 MHz, $CDCl_3$) *δ* = 8.57-8.47 (1H, m, =C*H*), 7.62 (1H, td, *J* = 10.7 and 1.8, =C*H*), 7.34 (1H, d, *J* =, =C*H*), 7.31-7.25 (2H, m, 2 x =C*H*), 7.14 (1H, ddd, *J* = 7.5, 4.9 and 1.1, =C*H*), 7.11-7.05 (3H, m, 3 x =C*H*), 5.25 (1H, dd, *J* = 8.9 and 6.7, NC*H*CH_2), 3.21 (3H, s, NCH_3), 2.43 (3H, s, NCH_3), 2.13 (1H, dquint, *J* = 14.4 and 7.3, CHC$H_A$$H_B$$CH_3$), 1.83 (1H, ddq, *J* = 14.0, 8.9 and 7.5, $CHCH_AH_BCH_3$), 0.91 (3H, t, *J* = 7.4, CH_2CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* = 162.7 (*C*=O), 160.0 (=*C*), 148.8 (=*C*H), 147.1 (=*C*), 136.5 (=*C*H), 129.5 (=*C*H), 124.7 (=*C*H), 124.6 (=*C*H), 123.6 (=*C*H), 122.2 (=*C*H), 61.9 (N*C*H), 40.4 (N*C*H_3), 31.5 (N*C*H_3), 23.3 (*C*H_2), 11.5 (*C*H_3). **[α]$_D^{20}$** = -88 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2968, 2931, 1641. **HRMS** (ESI^+): *m/z* calcd for $C_{17}H_{22}N_3O$ $[M+H]^+$ 284.1757, found 284.1760.

1,3-dimethyl-1-phenyl-3-[(1S)-1-(pyridin-2-yl)but-3-en-1-yl]urea (18c)



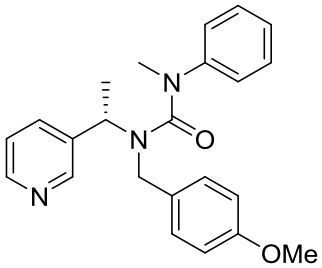
Following general procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (230 mg), 2-pyridine **6c** (200 mg, 1.35 mmol), synthesized from **4**, and Et_3N (207 µl) in acetonitrile (3.40 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH) to yield **18c** as an oil (270 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* = 8.48-8.37 (1H, m, =C*H*), 7.60 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.47-7.37 (2H, m, 2 x =C*H*), 7.35-7.23 (3H, m, 3 x =C*H*), 7.20 (1H, d, *J* = 7.8, =C*H*), 7.11 (1H, ddd, *J* = 7.5, 4.8 and 1.0, =C*H*), 5.61 (1H, ddt, *J* = 17.1, 10.4 and 7.2, CH_2CH=CH_2), 5.43 (1H, d, *J* = 7.7, CHN*H*), 5.01 (1H, dt, *J* = 7.1 and 6.8, NHC*H*CH_2), 4.97-4.83 (2H, m, =CH_2), 3.26 (3H, s, NCH_3), 2.61-2.39 (2H, m, CHCH_2CH=). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* = 160.9 (*C*=O), 156.8 (=*C*), 149.2 (=*C*H), 143.5 (=*C*), 136.5 (=*C*H), 134.4 (=*C*H), 130.0 (=*C*H), 127.4 (=*C*H), 127.3 (=*C*H), 122.1 (=*C*H), 121.9 (=*C*H), 117.9 (=*C*H_2), 55.1 (N*C*H), 40.7 (*C*H_2), 37.3 (N*C*H_3). **[α]$_D^{20}$** = +40 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3080, 2946, 1656, 1493. **HRMS** (ESI^+): *m/z* calcd for $C_{17}H_{20}N_3O$ $[M+H]^+$ 282.1601, found 282.1602.

1,3-dimethyl-1-phenyl-3-[(1S)-1-(pyridin-2-yl)but-3-en-1-yl]urea (8c)



Following General procedure 2A, urea **18c** (260 mg, 0.92 mmol), MeI (0.07 mL), NaH (48 mg) in THF (2.30 mL) gave, after purification by flash column chromatography (SiO_2, 80:20 to 0:100 Pet.Ether:EtOAc), **8c** as an oil (230 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.58-8.45 (1H, m, =C*H*), 7.62 (1H, td, *J* = 7.8 and 1.8, =C*H*), 7.37 (1H, d, *J* = 7.9, =C*H*), 7.30-7.21 (2H, m, 2 x =C*H*), 7.13 (1H, ddd, *J* = 7.5, 4.9 and 0.8, =C*H*), 7.12-7.03 (3H, m, 3 x =C*H*), 5.82 (1H, dddd, *J* = 17.2, 10.2, 8.2 and 5.6, CH_2=C*H*CH_2), 5.53 (1H, dd, *J* = 9.7 and 5.9, NC*H*CH_2), 5.17-4.99 (2H, m, =C*H*$_2$), 3.22 (3H, s, NC*H*$_3$), 2.95-2.82 (1H, m, CHC*H*$_A$H$_B$CH=), 2.70-2.54 (1H, m, CHCH$_A$*H*$_B$CH=), 2.41 (3H, s, NC*H*$_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.5 (*C*=O), 159.6 (=*C*), 148.8 (=*C*H), 146.9 (=*C*), 136.6 (=*C*H), 135.8 (=*C*H), 129.4 (=*C*H), 124.7 (2 x =*C*H), 123.6 (=*C*H), 122.4 (=*C*H), 117.3 (=*C*H$_2$), 60.0 (N*C*H), 40.4 (N*C*H$_3$), 34.6 (*C*H$_2$), 31.8 (N*C*H$_3$). **$[\alpha]_D^{20}$** = -96 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3064, 3005, 2925, 1640. **HRMS** (ESI$^+$): *m/z* calcd for $C_{18}H_{22}N_3O$ $[M+H]^+$ 296.1757, found 296.1761.

(*S*)-1-(4-methoxybenzyl)-3-methyl-3-phenyl-1-(1-(pyridin-3-yl)ethyl)urea (9), er 73:27

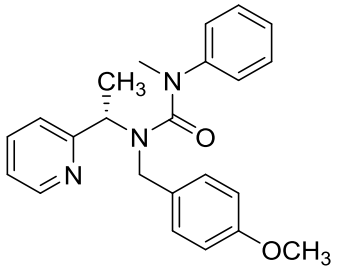


To a solution of **5c** (1.299 g, 5.36 mmol) in CH_2Cl_2 (54 mL) at room temperature was added phenyl isocyanate (0.58 mL, 5.36 mmol) and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was evaporated *in vacuo*. The residue was dissolved in anhydrous DMF (54 mL), and the solution was cooled down to 0 °C. To the solution was added in portions NaH (60% suspension in oil, 0.43 g, 10.72 mmol). The reaction mixture was stirred at 0 °C for 15 min, then MeI (0.500 mL, 8.04 mmol) was added dropwise. The reaction mixture was allowed to warm up to room temperature and was stirred overnight. Then it was quenched at room temperature with water and evaporated *in vacuo*. The residue was dissolved in ethyl acetate and extracted from water three times. The combined organic layer was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash column chromatography (50:50 Petrol-EtOAc, then 0:100) to give **9** as a brown oil (1.48 g, 74%, er 73:27).

R$_f$ 0.37 (100% EtOAc). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.48 (1H, dd, *J* = 4.7, 1.6, =C*H*), 8.41 (1H, d, *J* = 2.3, =C*H*), 7.52 (1H, dt, *J* = 8.0, 1.9, =C*H*), 7.35 – 7.29 (2H, m, 2 x =C*H*), 7.25 – 7.13 (2H, m, 2 x =C*H*), 6.99 – 6.93 (2H, m, 2 x =C*H*), 6.92 – 6.86 (2H, m, 2 x =C*H*), 6.80 – 6.74 (2H, m, 2 x =C*H*), 5.26 (1H, q, *J* = 7.0, C*H*-CH$_3$), 3.87 (1H, d, *J* = 15.5, NHC*H*$_A$H$_B$), 3.77 (3H, s, OC*H*$_3$), 3.71 (1H, d, *J* = 15.5, NHCH$_A$*H*$_B$), 3.10 (3H, s, NC*H*$_3$), 1.37

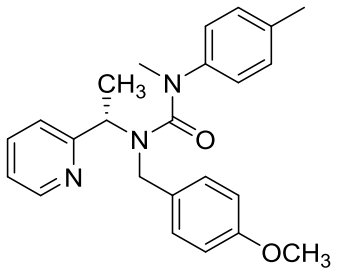
(3H, d, *J* = 7.0, CH-C*H*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 162.5 (*C*=O), 158.6 (=*C*), 149.2 (=C*H*), 148.7 (=C*H*), 146.4 (=*C*), 136.9 (=*C*), 135.2 (=C*H*), 130.8 (=C), 129.6 (=C*H*), 128.7 (=C*H*), 125.5 (=C*H*), 125.0 (=C*H*), 123.3 (=C*H*), 113.6 (=C*H*), 55.3 (O*C*H$_3$), 54.4 (*C*H-CH$_3$), 47.3 (NH*C*H$_2$), 39.9 (N*C*H$_3$), 16.5 (CH-*C*H$_3$). **IR** (film, cm^{-1}): ν_{max} = 2996, 2928, 2835, 1644, 1495, 1243. $[\alpha]_D^{23}$ = +11.9 (c = 1.00; CH_2Cl_2); **HRMS** (ESI$^+$): *m/z* calcd for $C_{23}H_{26}N_3O_2$ $[M+H]^+$ 376.2020, found 376.2007.

1-[(4-[Methoxyphenyl)methyl]-3,3-dimethyl-1-[(1S)-1-(pyridin-2-yl)ethyl]urea (10a)



Following General procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (77 mg), 2-pyridine **6d** (100 mg, 0.41 mmol) and Et_3N (63 µl) in acetonitrile (1.03 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10a** as an oil (155 mg, quant.). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.55-8.44 (1H, m, =C*H*), 7.66-7.53 (1H, m, =C*H*), 7.33-7.06 (5H, m, 5 x =C*H*), 6.99-6.82 (4H, m, 4 x =C*H*), 6.81-6.66 (2H, m, 2 x =C*H*), 5.39-5.19 (1H, m, NC*H*CH$_3$), 4.06 (1H, d, *J* = 15.7, NCH_AH$_B$), 3.85-3.64 (1H, superimposed d, NCH$_A$$H_B$), 3.78 (3H, s, OC$H_3$), 3.08 (3H, s, NC$H_3$), 1.39 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.5 (*C*=O), 160.6 (=*C*), 158.4 (=*C*), 149.0 (=*C*H), 146.4 (=*C*), 136.5 (=*C*H), 131.5 (=*C*), 129.4 (=*C*H), 128.7 (=*C*H), 125.0 (=*C*H), 124.6 (=*C*H), 123.0 (=*C*H), 122.4 (=*C*H), 113.5 (=*C*H), 57.9 (N*C*H), 55.4 (O*C*H$_3$), 47.0 (*C*H$_2$), 39.6 (N*C*H$_3$), 16.2 (*C*H$_3$). $[\alpha]_D^{20}$ = +90 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2941, 2928, 1644, 1247. **HRMS** (ESI$^+$): *m/z* calcd for $C_{23}H_{26}N_3O_2$ $[M+H]^+$ 376.2025, found 376.2026.

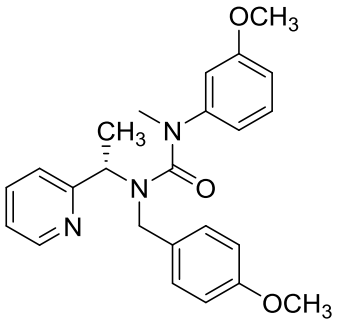
3-[(4-[Methoxyphenyl)methyl]-1-methyl-1-(4-methylphenyl)-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10b)



Following General procedure 1, *N*-methyl-*N*-(4-methylphenyl) carbamoyl chloride (39 mg), 2-pyridine **6d** (50 mg, 0.21 mmol) and Et_3N (32 µl) in acetonitrile (0.52 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10b** as an oil (52 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.57-8.44 (1H, m, =C*H*), 7.66-7.54 (1H, m, =C*H*), 7.24-7.05 (4H, m, 4 x =C*H*), 6.96-6.81 (4H, m, 4 x =C*H*), 6.80-6.70 (2H, m, 2 x =C*H*), 5.34 (1H, q, *J* = 7.0,

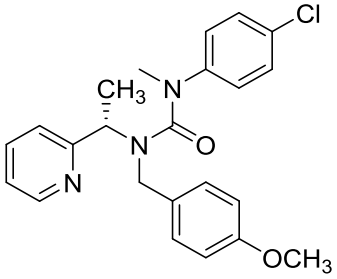
NC*H*CH_3), 4.07 (1H, d, *J* = 15.5, NCH_AH_B), 3.77 (1H, d, *J* = 15.4, NCH_AH_B), 3.77 (3H, s, OCH_3), 3.06 (3H, s, NCH_3), 2.32 (3H, s, CH_3), 1.60 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.6 (*C*=O), 160.8 (=*C*), 158.4 (=*C*), 149.0 (=*C*H), 143.9 (=*C*), 136.4 (=*C*H), 134.8 (=*C*), 131.6 (=*C*), 130.0 (=*C*H), 128.7 (=*C*H), 124.7 (=*C*H), 123.0 (=*C*H), 122.3 (=*C*H), 113.5 (=*C*H), 57.9 (N*C*H), 55.3 (OCH_3), 47.0 (CH_2), 39.9 (NCH_3), 21.0 (CH_3), 16.2 (CH_3). $[\alpha]_D^{20}$ = +20 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2976, 1646, 1245, 1038. **HRMS** (ESI^+): *m/z* calcd for $C_{24}H_{28}N_3O_2$ $[M+H]^+$ 390.2176, found 390.2181.

1-(3-Methoxyphenyl)-3-[(4-[methoxyphenyl)methyl]-1-methyl-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10c)



Following General procedure 1, *N*-methyl-*N*-(3-methoxyphenyl) carbamoyl chloride (82 mg), 2-pyridine **6d** (100 mg, 0.41 mmol) and Et_3N (63 µl) in acetonitrile (1.03 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10c** as an oil (64 mg, 38%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.56-8.45 (1H, m, =C*H*), 7.60 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.23-7.10 (3H, m, 3 x =C*H*), 6.97-6.89 (2H, m, 2 x =C*H*) , 6.78-6.71 (2H, m, 2 x =C*H*), 6.66 (1H, dd, *J* = 8.3 and 1.9, =C*H*), 6.61-6.54 (1H, m, =C*H*), 6.53-6.47 (1H, m, =C*H*), 5.35 (1H, q, *J* = 7.0, NC*H*CH_3), 4.14 (1H, d, *J* = 15.5, NCH_AH_B), 3.84 (1H, d, *J* = 15.5, NCH_AH_B), 3.75 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 3.08 (3H, s, NCH_3), 1.43 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.3 (*C*=O), 160.6 (=*C*), 160.4 (=*C*), 158.4 (=*C*), 149.0 (=*C*H), 147.6 (=*C*), 136.5 (=*C*H), 131.6 (=*C*), 130.0 (=*C*H), 128.7 (=*C*H), 122.9 (=*C*H), 122.3 (=*C*H), 116.6 (=*C*H), 113.5 (=*C*H), 110.7 (=*C*H), 109.8 (=*C*H), 57.9 (N*C*H), 55.3 (2 x OCH_3), 47.0 (CH_2), 39.5 (NCH_3), 16.4 (CH_3). $[\alpha]_D^{20}$ = -34 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2973, 2918, 1652, 1250, 1034. **HRMS** (ESI^+): *m/z* calcd for $C_{24}H_{28}N_3O_3$ $[M+ H]^+$ 406.2125, found 406.2130.

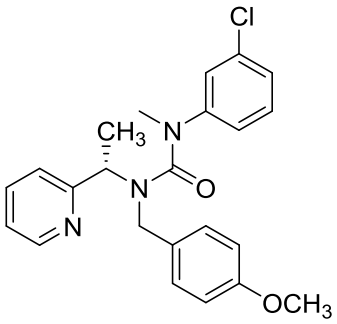
1-(4-Chlorophenyl)-3-[(4-[methoxyphenyl)methyl]-1-methyl-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10d)



Following general procedure 1, *N*-methyl-*N*-(4-chlorophenyl) carbamoyl chloride (43 mg), 2-pyridine **6d** (50 mg, 0.21 mmol) and Et_3N (32 µl) in acetonitrile (0.52 ml) gave, after 20 h heating at reflux, a crude product

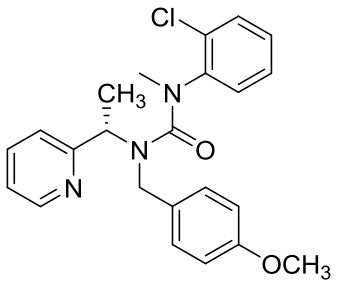
that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10d** as an oil (48 mg, 56%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.89-8.48 (1H, m, =C*H*), 7.64 (1H, td, *J* = 7.6 and 1.8, =C*H*), 7.29-7.20 (3H, m, 3 x =C*H*), 7.18-7.10 (1H, m, =C*H*), 6.95-6.82 (4H, m, 4 x =C*H*), 6.79-6.69 (2H, m, 2 x =C*H*), 5.35 (1H, q, *J* = 6.9, NC*H*CH_3), 4.05 (1H, d, *J* = 15.7, NC$H_A$$H_B$), 3.80 (1H, d, *J* = 15.7, NC$H_A$$H_B$), 3.77 (3H, s, OC$H_3$), 3.02 (3H, s, NC$H_3$), 1.45 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.1 (*C*=O), 160.4 (=*C*), 158.5 (=*C*), 149.2 (=C*H*), 144.8 (=*C*), 136.6 (=C*H*), 131.3 (=*C*), 129.9 (=*C*), 129.4 (=C*H*), 128.5 (=C*H*), 125.2 (=C*H*), 122.7 (=C*H*), 122.5 (=C*H*), 113.6 (=C*H*), 57.9 (N*C*H), 55.4 (OCH_3), 47.2 (CH_2), 39.2 (NCH_3), 16.5 (CH_3). **$[\alpha]_D^{20}$** = +16 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2978, 1648, 1245, 1040. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{24}ClN_3O_2Na$ $[M+Na]^+$ 432.1449, found 432.1448.

1-(3-Chlorophenyl)-3-[(4-[methoxyphenyl)methyl]-1-methyl-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10e)



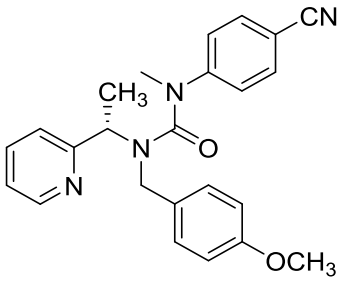
Following General procedure 1, *N*-methyl-*N*-(3-chlorophenyl) carbamoyl chloride (84 mg), 2-pyridine **6d** (100 mg, 0.41 mmol), Et_3N (63 µl) and DMAP (cat.) in dichloroethane (1.03 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10e** as an oil (78 mg, 46%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.61-8.52 (1H, m, =C*H*), 7.65 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.28-7.14 (3H, m, 3 x =C*H*), 7.06 (1H, ddd, *J* = 8.0, 1.9 and 0.9, =C*H*), 7.00-6.96 (1H, m, =C*H*), 6.92-6.86 (2H, m, 2 x =C*H*), 6.82 (1H, ddd, *J* = 8.1, 2.2 and 0.9, =C*H*), 6.80-6.73 (2H, m, 2 x =C*H*), 5.36 (1H, q, *J* = 7.0, NC*H*CH_3), 4.03 (1H, d, *J* = 15.6, NC$H_A$$H_B$), 3.81 (1H, d, *J* = 15.7, NC$H_A$$H_B$), 3.78 (3H, s, OC$H_3$), 3.02 (3H, s, NC$H_3$), 1.48 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.8 (*C*=O), 160.3 (=*C*), 158.5 (=*C*), 149.3 (=C*H*), 147.3 (=*C*), 136.7 (=C*H*), 134.7 (=*C*), 131.1 (=*C*), 130.2 (=C*H*), 128.5 (=C*H*), 124.4 (=C*H*), 123.9 (=C*H*), 122.7 (=C*H*), 122.5 (=C*H*), 121.5 (=C*H*), 113.6 (=C*H*), 57.8 (N*C*H), 55.4 (OCH_3), 47.3 (CH_2), 38.9 (NCH_3), 16.4 (CH_3). **$[\alpha]_D^{20}$** = +36.6 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2985, 1642, 1239, 1043. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{25}ClN_3O_2$ $[M+H]^+$ 410.1635, found 410.1638.

1-(2-Chlorophenyl)-3-[(4-[methoxyphenyl)methyl]-1-methyl-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10f)



Following General procedure 1, *N*-methyl-*N*-(2-chlorophenyl) carbamoyl chloride (43 mg), 2-pyridine **6d** (50 mg, 0.21 mmol), Et_3N (32 µl) and DMAP (cat.) in dichloroethane (0.52 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10f** as an oil (83 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.53-8.42 (1H, m, =C*H*), 7.57 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.48-7.38 (1H, m, =C*H*), 7.22-7.15 (2H, m, 2 x =C*H*), 7.14-7.07 (2H, m, 2 x =C*H*), 7.05-6.97 (2H, m, 2 x =C*H*), 6.93-6.85 (1H, m, =C*H*), 6.82-6.69 (2H, m, 2 x =C*H*), 4.95 (1H, q, *J* = 7.0, NC*H*CH_3), 4.12 (1H, d, *J* = 15.0, NCH_AH_B), 3.85 (1H, d, *J* = 15.0, NCH_AH_B), 3.77 (3H, s, OCH_3), 3.08 (3H, s, NCH_3), 1.22 (3H, d, *J* = 7.0, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.9 (*C*=O), 160.4 (=*C*), 158.4 (=*C*), 148.8 (=*C*H), 143.7 (=*C*), 136.5 (=*C*H), 131.8 (=*C*), 131.1 (=*C*), 130.8 (=*C*H), 129.4 (=*C*H), 129.3 (=*C*H), 128.0 (=*C*H), 127.9 (=*C*H), 122.9 (=*C*H), 122.3 (=*C*H), 113.4 (=*C*H), 58.3 (N*C*H), 55.3 (O*C*H_3), 47.1 (*C*H_2), 38.4 (N*C*H_3), 15.9 (*C*H_3). **$[\alpha]_D^{20}$** = -16 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2993, 1640, 1235, 1039. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{24}ClN_3O_2Na$ $[M+Na]^+$ 432.1449, found 432.1443.

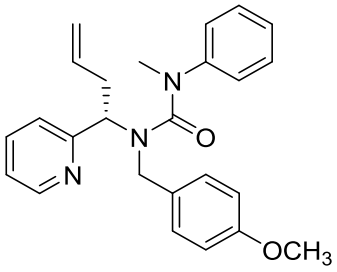
1-(4-Cyanophenyl)-3-[(4-[methoxyphenyl)methyl]-1-methyl-3-[(1S)-1-(pyridin-2-yl)ethyl]urea (10g)



Following general procedure 1, *N*-methyl-*N*-(4-cyanophenyl) carbamoyl chloride (41 mg), 2-pyridine **6d** (50 mg, 0.21 mmol) and Et_3N (32 µl) in acetonitrile (0.52 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10g** as an oil (84 mg, quant. yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.60-8.50 (1H, m, =C*H*), 7.68 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.55-7.45 (2H, m, 2 x =C*H*), 7.36-7.29 (1H, m, =C*H*), 7.21 (1H, ddd, *J* = 7.5, 4.8 and 1.0, =C*H*), 7.01-6.91 (2H, m, 2 x =C*H*), 6.85-6.68 (4H, m, 4 x =C*H*), 5.46 (1H, q, *J* = 7.1, NC*H*CH_3), 4.10 (1H, d, *J* = 15.8, NCH_AH_B), 3.91 (1H, d, *J* = 15.8, NCH_AH_B), 3.76 (3H, s, OCH_3), 2.95 (3H, s, NCH_3), 1.60 (3H, d, *J* = 7.1, CHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 160.9 (*C*=O), 159.8 (=*C*), 158.8 (=*C*), 149.4 (=*C*H), 149.2 (=*C*), 136.8 (=*C*H), 133.2 (=*C*H), 130.7 (=*C*), 128.1 (=*C*H), 122.7 (=*C*H), 122.5 (=*C*H), 120.1 (=*C*H), 119.2 (=*C*), 113.8 (=*C*H), 105.1 (*C*N), 57.7

(N*C*H), 55.4 (O*C*H_3), 47.7 (*C*H_2), 37.2 (N*C*H_3), 16.8 (*C*H_3). $[\alpha]_D^{20}$ = +12 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2935, 2221, 1657, 1245, 1034. **HRMS** (ESI^+): *m/z* calcd for $C_{24}H_{24}N_4O_2Na$ $[M+Na]^+$ 423.1791, found 423.1791.

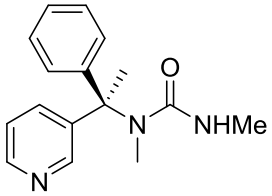
1-[(4-[Methoxyphenyl)methyl]-3-methyl-3-phenyl-1-[(1S)-1-(pyridin-2-yl)but-3-en-1-yl]urea (10h)



Following general procedure 1, *N*-methyl-*N*-phenyl carbamoyl chloride (58 mg), 2-pyridine **6e** (90 mg, 0.34 mmol) and Et_3N (52 µl) in acetonitrile (0.84 ml) gave, after 20 h heating at reflux, a crude product that was purified by flash column chromatography (SiO_2, 80:20 to 20:80 Pet.Ether:EtOAc) to yield **10h** as an oil (80 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.50-8.41 (1H, m, =C*H*), 7.57 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.32-7.22 (2H, m, 2 x =C*H*), 7.16-7.02 (3H, m, 3 x =C*H*), 6.95-6.88 (2H, m, =C*H*), 6.68 (4H, s, 4 x =C*H*), 5.67 (1H, dddd, *J* = 17.1, 10.0, 7.6 and 6.4, CH_2=C*H*CH_2), 5.30 (1H, t, *J* = 7.6, C*H*CH_2), 5.09-4.90 (2H, m, =CH_2), 4.23 (1H, d, *J* = 15.5, NC$H_A$$H_B$), 3.94 (1H, d, *J* = 15.5, NC$H_A$$H_B$), 3.75 (3H, s, OC$H_3$), 3.04 (3H, s, NC$H_3$), 2.94-2.79 (1H, m, C$H_A$$CH_B$CH=), 2.68-2.52 (1H, m, CH_ACH_BCH=). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.4 (*C*=O), 158.9 (=*C*), 158.3 (=*C*) 149.0 (=*C*H), 143.4 (=*C*), 136.5 (=*C*H), 135.3 (=*C*H), 131.5 (=*C*), 129.4 (=*C*H), 128.5 (=*C*H), 124.9 (=*C*H), 124.7 (=*C*H), 124.5 (=*C*H), 122.6 (=*C*H), 117.5 (=*C*H_2), 113.4 (=*C*H), 61.9 (N*C*H), 55.3 (O*C*H_3), 46.6 (*C*H_2), 39.6 (N*C*H_3), 35.5 (*C*H_2). $[\alpha]_D^{20}$ = -40 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3064, 2930, 1642, 1244, 1036. **HRMS** (ESI^+): *m/z* calcd for $C_{25}H_{28}N_3O_2$ $[M+H]^+$ 402.2176, found 402.2178.

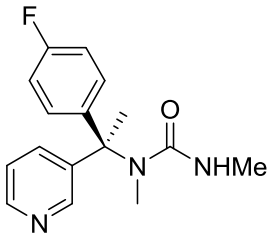
- LDA-mediated rearrangement of ureas and their hydrolysis

(*R*)-1,3-dimethyl-1-(1-phenyl-1-(pyridin-3-yl)ethyl)urea (11a)[6]



Following General procedure 3, urea **7a** (72 mg, 0.266 mmol), freshly prepared LDA (0.75 M in THF, 0.89 ml, 0.666 mmol) and THF (2.7 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), **11a** as a yellow solid (47 mg, 65%). $\mathbf{R_f}$ 0.14 (95:5 CH_2Cl_2:MeOH); ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 8.52 (1H, br s, =C*H*), 8.42 (1H, br s, =C*H*), 7.56 – 7.48 (m, 1H, =C*H*), 7.32 – 7.14 (6H, m, 6 x =C*H*), 4.13 (1H, br s, N*H*CH_3), 2.83 (3H, s, $CH_3CNC\mathit{H}_3$), 2.55 (3H, d, *J* = 4.6 Hz, NHCH_3), 2.08 (3H, s, CH_3CNCH_3). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ = 159.7 (*C*=O), 148.6 (=C*H*), 147.9 (=C*H*), 144.7, 141.3, 134.6 (=C*H*), 128.9 (=C*H*), 127.6 (=C*H*), 127.1 (=C*H*), 123.2 (=C*H*), 66.2 ($CH_3\mathit{C}NCH_3$), 34.6 (CH_3CNCH_3), 29.8 ($\mathit{C}H_3CNCH_3$), 27.7 (NH$\mathit{C}H_3$). **Mp** = 145-146 °C. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{20}N_3O$ $[M+H]^+$ 270.1601, found 270.1625.

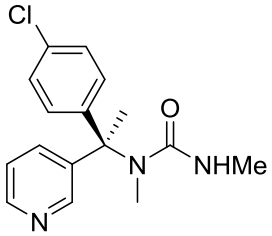
(*R*)-1-(1-(4-fluorophenyl)-1-(pyridin-3-yl)ethyl)-1,3-dimethylurea (11b)



Following general procedure 3, urea **7b** (94 mg, 0.328 mmol), freshly prepared LDA (0.75 M in THF, 1.09 ml, 0.819 mmol) and THF (3.3 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **11b** as a white solid (70 mg, 74%). $\mathbf{R_f}$ 0.14 (95:5 CH_2Cl_2:MeOH). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 8.59 – 8.35 (2H, m, 2 x =C*H*), 7.52 – 7.47 (1H, m, =C*H*), 7.23 – 7.15 (3H, m, 3 x =C*H*), 7.00 – 6.92 (2H, m, 2 x =C*H*), 4.24 (1H, dd, *J* = 8.7, 4.4, N*H*CH_3), 2.79 (3H, s, CH_3-C-N-CH_3), 2.59 (3H, d, *J* = 4.6, NHCH_3), 2.06 (3H, s, CH_3-C-N-CH_3). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ = 161.8 (d, $^{1}J_{CF}$ = 247.2 Hz, =*C*-F), 159.6 (*C*=O), 148.3 (=C*H*), 147.8 (=C*H*), 141.5 (=*C*), 140.5 (d, $^{4}J_{CF}$ = 3.4 Hz, =*C*), 134.5 (=C*H*), 128.8 (d, $^{3}J_{CF}$ = 8.0 Hz, =C*H*), 123.3 (=C*H*), 115.6 (d, $^{2}J_{CF}$ = 21.3 Hz, =*C*H), 65.8 ($CH_3\mathit{C}$-N-CH_3), 34.7 (CH_3C-NCH_3), 29.7 ($\mathit{C}H_3$C-N-CH_3), 27.7 (NH$\mathit{C}H_3$). **Mp** = 126-127 °C. $\mathbf{[\alpha]_D^{25}}$ = +10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3345, 2946, 1635, 1507, 1323, 1226, 1163, 1081, 814, 728. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{19}N_3OF$ $[M+H]^+$ 288.1507, found 288.1492.

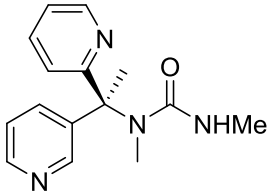
[6] Data in agreement with the literature (reference: Clayden, J.; Hennecke, U. *Org. Lett.* **2008**, *10*, 3567).

(*R*)-1-(1-(4-chlorophenyl)-1-(pyridin-3-yl)ethyl)-1,3-dimethylurea (11c)



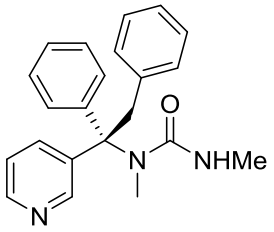
Following general procedure 3, urea **7c** (91 mg, 0.298 mmol), freshly prepared LDA (0.75 M in THF, 0.99 ml, 0.750 mmol) and THF (3.0 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **11c** as a white solid (57 mg, 63%). $\mathbf{R_f}$ 0.12 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.64 – 8.43 (2H, m, 2 x =C*H*), 7.56 (1H, ddd, *J* = 8.1, 2.3, 1.5, =C*H*), 7.33 – 7.19 (5H, m, 6 x =C*H*), 4.28 (1H, dd, *J* = 8.4, 4.1, N*H*CH_3), 2.86 (3H, s, CH_3C-NC*H*$_3$), 2.67 (3H, d, *J* = 4.7 Hz, NHC*H*$_3$), 2.12 (3H, s, C*H*$_3$C-NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 159.6 (*C*=O), 148.4 (=C*H*), 148.0 (=C*H*), 143.5 (=*C*), 141.2 (=*C*), 134.5 (=*C*), 133.3 (=C*H*), 128.9 (=C*H*), 128.5 (=C*H*), 123.3 (=C*H*), 65.9 (CH_3*C*-NCH_3), 34.8 (CH_3C-N*C*H_3), 29.4 (*C*H_3C-NCH_3), 27.7 (NH*C*H_3). **Mp** = 58-59 °C. $\mathbf{[\alpha]_D^{25}}$ = +20 (c = 2.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} =3345, 2948, 1639, 1532, 1491, 1415, 1326, 1095, 729. **HRMS** (ESI^+): *m/z* calcd for $C_{16}H_{18}N_3OCl$ $[M+H]^+$ 304.1211, found 304.1207.

(*S*)-1,3-dimethyl-1-(1-(pyridin-2-yl)-1-(pyridin-3-yl)ethyl)urea (11d)



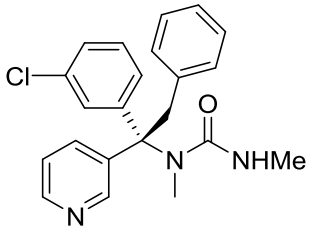
Following General procedure 3, urea **7d** (92 mg, 0.302 mmol), freshly prepared LDA (0.75 M in THF, 1.01 ml, 0.756 mmol) and THF (3.0 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **11d** as a yellow oil (61 mg, 76%). $\mathbf{R_f}$ 0.10 (95:5 CH_2Cl_2:MeOH); **^{1}H NMR (**400 MHz, $CDCl_3$) δ = 8.56 (1H, d, *J* = 2.4, =C*H*), 8.55 – 8.52 (1H, m, =C*H*), 8.47 (1H, dd, *J* = 4.7, 0.9, =C*H*), 7.72 – 7.64 (2H, m, 2 x =C*H*), 7.39 (1H, d, *J* = 8.1, =C*H*), 7.27 – 7.22 (1H, m, =C*H*), 7.17 (1H, dd, *J* = 7.4, 4.8, =C*H*), 5.00 (1H, br s, N*H*CH_3), 3.01 (3H, s, CH_3C-NC*H*$_3$), 2.55 (3H, d, *J* = 4.6, NHC*H*$_3$), 2.08 (3H, s, C*H*$_3$C-NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 163.4 (=*C*), 159.7 (*C*=O), 149.0 (=C*H*), 148.5 (=C*H*), 148.0 (=C*H*), 140.4 (=*C*), 137.0 (=C*H*), 135.0 (=C*H*), 123.0 (=C*H*), 122.1 (=C*H*), 121.5 (=C*H*), 66.9 (CH_3*C*-NCH_3), 33.5 (CH_3C-N*C*H_3), 28.9 (*C*H_3C-NCH_3), 27.5 (NH*C*H_3). **Mp** = 111-113 °C. **IR** (film, cm^{-1}): ν_{max} = 3350, 2924, 1640, 1533, 1329, 1082, 714. **HRMS** (ESI^+): *m/z* calcd for $C_{15}H_{19}N_4O$ $[M+H]^+$ 271.1553, found 271.1541.

(*S*)-1-(1,2-diphenyl-1-(pyridin-3-yl)ethyl)-1,3-dimethylurea (11e)



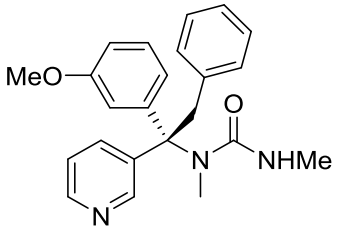
Following General procedure 3, urea **7e** (85 mg, 0.246 mmol), freshly prepared LDA (0.75 M in THF, 0.82 ml, 0.615 mmol) and THF (2.5 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **11e** as a yellow solid (62 mg, 87%). $\mathbf{R_f}$ 0.19 (95:5 CH_2Cl_2:MeOH). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 8.62 – 8.31 (2H, m, 2 x =C*H*), 7.60 (1H, d, *J* = 8.1 Hz, =C*H*), 7.38 – 7.08 (9H, m, 9 x =C*H*), 6.88 (2H, dd, *J* = 7.9, 1.4, 2 x =C*H*), 4.36 (1H, dd, *J* = 9.0, 4.7, N*H*CH_3), 4.19 – 4.11 (2H, m, CH_2Ph), 2.72 (3H, d, *J* = 4.6, NHCH_3), 2.63 (3H, s, CH_2C-NCH_3). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ = 160.3 (*C*=O), 148.8 (=*C*H), 147.4 (=*C*H), 143.1 (=*C*), 140.7 (=*C*), 137.1 (=*C*), 135.0 (=*C*H), 131.2 (=*C*H), 128.3 (=*C*H), 128.0 (2 x =*C*H), 127.2 (=*C*H), 126.8 (=*C*H), 71.3 (N*C*-CH_2), 43.4 (NC-*C*H_2), 37.0 (CH_2C-N*C*H_3), 27.7 (NH*C*H_3). **Mp** = 150-151 °C. $\mathbf{[\alpha]_D^{25}}$ = +37 (c = 2.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3362, 2924, 1636, 1527, 1414, 1319. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{24}N_3O$ $[M+H]^+$ 346.1914, found 346.1899.

(*S*)-1-(1-(3-chlorophenyl)-2-phenyl-1-(pyridin-3-yl)ethyl)-1,3-dimethylurea (11f)



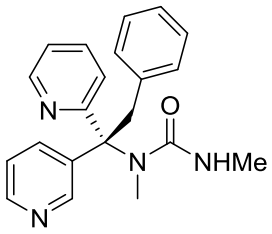
Following General procedure 3, urea **7f** (87 mg, 0.230 mmol), freshly prepared LDA (0.75 M in THF, 0.76 ml, 0.573mmol) and THF (2.3 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), **11f** as a yellow solid (19 mg, 22%). $\mathbf{R_f}$ 0.19 (95:5 CH_2Cl_2:MeOH). ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 8.51 (1H, d, *J* = 1.0, =C*H*), 8.43 (1H, d, *J* = 4.1 Hz, =C*H*), 7.59 (1H, ddd, *J* = 8.1, 2.3, 1.5, =C*H*), 7.27 – 7.10 (8H, m, 8 x =C*H*), 6.89 – 6.84 (2H, m, 2 x =C*H*), 4.51 (1H, dd, *J* = 9.3, 5.3, N*H*CH_3), 4.13 (2H, s, CH_2Ph), 2.75 (3H, d, *J* = 4.6, NHCH_3), 2.59 (3H, s, CH_2C-NCH_3). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ = 160.1 (*C*=O), 148.8 (=*C*H), 147.7 (=*C*H), 145.8 (=*C*), 139.9 (=*C*), 136.7 (=*C*), 135.1 (=*C*H), 134.1 (=*C*H), 131.1 (=*C*H), 129.5 (=*C*H), 128.1 (=*C*H), 127.9 (=*C*H), 127.2 (=*C*H), 126.9 (=*C*H), 125.8 (=*C*H), 122.9 (=*C*H), 71.0 (N*C*CH_2), 43.0 (NC*C*H_2), 37.2 (CH_2C-N*C*H_3), 27.7 (NH*C*H_3). **Mp** = 88-90 °C. $\mathbf{[\alpha]_D^{25}}$ = +20 (c = 2.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3349, 2953, 1639, 1529, 1413, 1309, 907, 725, 700. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{23}N_3OCl$ $[M+H]^+$ 380.1524, found 380.1520.

(*S*)-1-(1-(3-methoxyphenyl)-2-phenyl-1-(pyridin-3-yl)ethyl)-1,3-dimethylurea (11g)



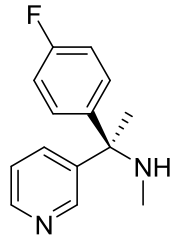
Following General procedure 3, urea **7g** (68 mg, 0.181 mmol), freshly prepared LDA (0.75 M in THF, 0.61 ml, 0.453 mmol) and THF (1.8 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 97:3 CH_2Cl_2:MeOH), **11g** as a yellow solid (18 mg, 26%). $\mathbf{R_f}$ 0.15 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.52 (1H, br s, =C*H*), 8.40 (1H, br d, *J* = 4.1, =C*H*), 7.58 (1H, ddd, *J* = 8.0, 2.2, 1.5, =C*H*), 7.24 – 7.10 (5H, m, 5 x =C*H*), 6.95 – 6.89 (3H, m, 3 x =C*H*), 6.85 (1H, t, *J* = 2.1, =C*H*), 6.76 (1H, dd, *J* = 8.2, 2.3, =C*H*), 4.37 (1H, dd, *J* = 8.5, 4.2, N*H*CH_3), 4.15 (1H, d, *J* = 13.6, C$H_A$$H_B$Ph), 4.11 (1H, d, *J* = 13.6, C$H_A$$H_B$Ph), 3.70 (3H, s, OC$H_3$), 2.72 (3H, d, *J* = 4.6, NHCH_3), 2.64 (3H, s, CH_2C-NCH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (*C*=O), 159.4 (=*C*-OCH_3), 148.9 (=C*H*), 147.5 (=C*H*), 144.9 (=*C*), 140.6 (=*C*), 137.2 (=*C*), 134.9 (=C*H*), 131.3 (=C*H*), 129.3 (=C*H*), 128.1 (=C*H*), 126.8 (=C*H*), 122.7 (=C*H*), 120.3 (=C*H*), 114.6 (=C*H*), 112.1 (=C*H*), 71.2 (N*C*-CH_2), 55.3 (OCH_3), 43.3 (NC-*C*H_2), 37.2 (CH_2C-NCH_3), 27.7 (NH*C*H_3). **Mp** = 71-73 °C. $\mathbf{[\alpha]_D^{25}}$ = +10 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3349, 2953, 1640, 1530, 1315, 724. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{25}N_3O_2Na$ $[M+Na]^+$ 398.1839, found 398.1842.

(*R*)-1,3-dimethyl-1-(2-phenyl-1-(pyridin-2-yl)-1-(pyridin-3-yl)ethyl)urea (11h)



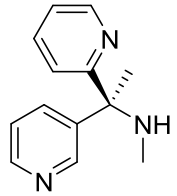
Following General procedure 3, urea **7h** (96 mg, 0.276 mmol), freshly prepared LDA (0.75 M in THF, 0.92 ml, 0.691 mmol) and THF (2.8 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **11h** as a yellow solid (84 mg, 88%). $\mathbf{R_f}$ 0.21 (95:5 CH_2Cl_2:MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.54 (1H, ddd, *J* = 4.8, 1.8, 0.9, =C*H*), 8.47 (1H, d, *J* = 2.2, =C*H*), 8.37 (1H, dd, *J* = 4.7, 1.4, =C*H*), 7.66 (1H, ddd, *J* = 8.1, 7.5, 1.9, =C*H*), 7.60 – 7.53 (2H, m, 2 x =C*H*), 7.20 – 7.06 (5H, m, 5 x =C*H*), 6.90 (2H, dd, *J* = 7.9, 1.5, 2 x =C*H*), 4.71 (1H, dd, *J* = 8.5, 4.0, N*H*CH_3), 4.28 (1H, d, *J* = 13.1, C$H_A$$H_B$Ph), 4.04 (1H, d, *J* = 13.1, C$H_A$$H_B$Ph), 2.73 (3H, d, *J* = 5.3, NHCH_3), 2.64 (3H, d, *J* = 4.6, CH_2C-NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 162.1 (=*C*), 159.8 (*C*=O), 149.1 (=*C*H), 148.1 (=*C*H), 147.4 (=*C*H), 139.4 (=*C*), 137.0 (=*C*), 136.7 (=*C*H), 135.2 (=*C*H), 131.2 (=*C*H), 128.1 (=*C*H), 126.8 (=*C*H), 123.0 (=*C*H), 122.5 (=*C*H), 122.1 (=*C*H), 71.9 (N*C*CH_2), 42.5 (NC*C*H_2), 35.8 (CH_2C-N*C*H_3), 27.6 (NH*C*H_3). **Mp** = 166-168 °C. $\mathbf{[\alpha]_D^{25}}$ = +5 (c = 2.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3349, 2923, 1640, 1533, 1319, 730. **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{23}N_4O$ $[M+H]^+$ 347.1866, found 347.1851.

1-(4-fluorophenyl)-N-methyl-1-(pyridin-3-yl)ethan-1-amine (12b)



Following General procedure 4, urea **11b** (32 mg, 0.111 mmol), 10% aqueous NaOH solution (0.45 mL, 1.11 mmol), EtOH (0.89 mL) gave **12b** as a yellow oil (23 mg, 88%) without further purification. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.61 (1H, d, *J* = 2.0, =C*H*), 8.47 (1H, dd, *J* = 4.7, 1.3, =C*H*), 7.63 (1H, ddd, *J* = 8.0, 2.3, 1.7, =C*H*), 7.33 – 7.27 (2H, m, 2 x =C*H*), 7.22 (1H, ddd, *J* = 8.1, 4.7, 0.5, =C*H*), 7.03 – 6.95 (2H, m, 2 x =C*H*), 2.20 (3H, s, N-C-CH_3), 1.79 (3H, s, NHCH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 161.7 (d, $^{1}J_{CF}$ = 245.2 Hz, =*C*F), 149.0 (=*C*H), 148.0 (=*C*H), 143.1 (=*C*), 142.5 (d, $^{4}J_{CF}$ = 3.1 Hz, =*C*), 134.8 (=*C*H), 128.8 (d, $^{3}J_{CF}$ = 7.7 Hz, =*C*H), 123.1 (=*C*H), 115.1 (d, $^{2}J_{CF}$ = 20.4 Hz, =*C*H), 61.5 (CH_3NH-*C*-CH_3), 29.8 (CH_3NH-C-*C*H_3), 26.9 (*C*H_3NH-C-CH_3). **IR** (film, cm^{-1}): ν_{max} = 3289, 2981, 1506, 1414. **$[\alpha]_D^{23}$** = -5.0 (c = 1.00; CH_2Cl_2). **HRMS** (ESI^+): *m/z* calcd for $C_{14}H_{16}N_2F$ $[M+H]^+$ 231.1292, found 231.1289.

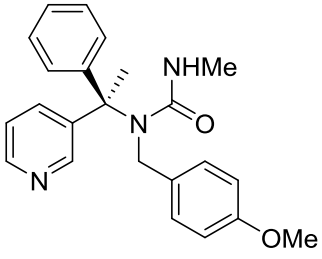
(*R*)-1-(4-fluorophenyl)-N-methyl-1-(pyridin-3-yl)ethan-1-amine (12d)



Following general procedure 4, urea **11d** (27 mg, 0.098 mmol), 10% aqueous NaOH solution (0.39 mL, 0.98 mmol), EtOH (0.78 mL) gave **12d** as a yellow oil (14 mg, 64%) without further purification.

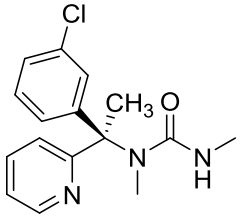
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.58 – 8.47 (2H, m, 2 x =C*H*), 8.42 – 8.35 (1H, m, =C*H*), 7.66 (1H, dq, *J* = 8.1, 1.8, =C*H*), 7.55 (1H, tt, *J* = 7.8, 1.7, =C*H*), 7.22 – 7.13 (2H, m, 2 x =C*H*), 7.10 – 7.06 (1H, m, =C*H*), 2.16 (3H, s, N-C-CH_3), 1.79 (3H, s, NHCH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 165.1 (=*C*), 149.2 (=*C*H), 149.1 (=*C*H), 148.0 (=*C*H), 142.4 (=*C*), 136.5 (=*C*H), 134.9 (=*C*H), 123.2 (=*C*H), 121.9 (=*C*H), 121.6 (=*C*H), 63.1 (CH_3NH-*C*-CH_3), 29.7 (CH_3NH-C-*C*H_3), 25.1 (*C*H_3NH-C-CH_3). **IR** (film, cm^{-1}): ν_{max} = 3304, 2983, 2923, 1587, 1430, 1414. **$[\alpha]_D^{23}$** = +8.7 (c = 1.00; CH_2Cl_2). **HRMS** (ESI^+): *m/z* calcd for $C_{13}H_{16}N_3$ $[M+H]^+$ 214.1339, found 214.1324.

(*R*)-1-(4-methoxybenzyl)-3-methyl-1-(1-phenyl-1-(pyridin-3-yl)ethyl)urea (13)



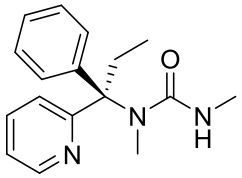
Following General procedure 3, urea **9** (0.995 g, 2.65 mmol), freshly prepared LDA (0.75 M in THF, 8.84 ml, 6.627 mmol) and THF (26.5 ml) gave after purification by flash column chromatography (SiO_2, 99:1 to 95:5 CH_2Cl_2:MeOH), **13** as a yellow solid (0.845 g, 85%). $\mathbf{R_f}$ 0.26 (95:5 CH_2Cl_2:MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.54 (1H, d, *J* = 2.5, =C*H*), 8.39 (1H, dd, *J* = 4.7, 1.5, =C*H*), 7.48 (1H, ddd, *J* = 8.1, 2.5, 1.5, =C*H*), 7.27 – 7.10 (8H, m, 8 x =C*H*), 6.86 – 6.80 (2H, m, 2 x =C*H*), 4.44 (1H, d, *J* = 17.5, NHCH_AH_B), 4.35 (1H, d, *J* = 17.5 Hz, NHCH$_A$$H_B$), 4.24 (1H, q, *J* = 4.7 Hz, C*H*-CH_3), 3.75 (3H, s, OCH_3), 2.51 (3H, d, *J* = 4.5, CH-CH_3), 2.02 (3H, s, NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 160.3 (=*C*), 158.8 (=*C*), 148.8 (=*C*H), 147.8 (=*C*H), 144.2 (=*C*), 141.6 (=*C*), 134.9 (=*C*H), 131.5 (=*C*H), 128.6 (=*C*H), 127.5 (3x =*C*H), 123.0 (=*C*H), 114.4 (=*C*H), 67.2 (NH-*C*-CH_3), 55.4 (O*C*H_3), 50.5 (NH*C*H_2), 31.0 (NH-C-*C*H_3), 27.7 (NH*C*H_3). **Mp** = 56-58 °C. $\mathbf{[\alpha]_D^{25}}$ = +0.25 (c = 1.00; CH_2Cl_2). **IR** (film, cm^{-1}): ν_{max} = 3440, 2951, 1645, 1510, 1243. **HRMS** (ESI$^+$): *m/z* calcd for $C_{23}H_{26}N_3O_2$ $[M+H]^+$ 376.2020, found 376.2003.

1-[(1R)-1-(3-Chlorophenyl)-1-(pyridine-2-yl)ethyl]-1,3-dimethylurea (14a)



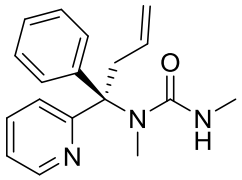
Following general procedure 3, LDA (0.21 ml), urea **8a** (50 mg, 0.17 mmol) and THF (1.56 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **14a** as an oil (48 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.58-8.49 (1H, m, =C*H*), 7.69-7.58 (1H, m, =C*H*), 7.37-7.09 (6H, m, 6 x =C*H*), 5.08-4.85 (1H, brs, N*H*CH_3), 2.95 (3H, s, NCH_3), 2.55 (3H, d, *J* = 4.6, NHCH_3), 2.06 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.5 (*C*=O), 159.9 (=*C*), 148.4 (=*C*H), 147.2 (=*C*), 136.8 (=*C*H), 134.1 (=*C*), 129.5 (=*C*H), 127.5 (=*C*H), 127.1 (=*C*H), 125.5 (=*C*H), 121.9 (=*C*H), 121.5 (=*C*H), 68.1 (N*C*), 33.7 (NCH_3), 28.6 (NCH_3), 27.4 (CH_3). $\mathbf{[\alpha]_D^{20}}$ = -53 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3337, 2980, 2935, 1630. **HRMS** (ESI$^+$): *m/z* calcd for $C_{16}H_{18}ClN_3ONa$ $[M+Na]^+$ 326.1036, found 326.1043.

1,3-Dimethyl-1-[(1R)-1-phenyl-1(pyridin-2-yl)propyl]urea (14b)



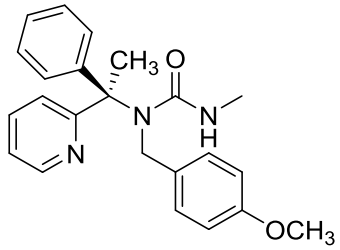
Following general procedure 3, LDA (0.44 ml), urea **8b** (100 mg, 0.35 mmol) and THF (3.53 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **14b** as an oil (88 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.58-8.53 (1H, m, =C*H*), 7.69 (1H, td, *J* = 7.9 and 1.8, =C*H*), 7.52-7.44 (1H, m, =C*H*), 7.35-7.27 (4H, m, 4 x =C*H*), 7.24-7.14 (2H, m, 2 x =C*H*), 5.82-5.63 (1H, m, N*H*CH_3), 3.03 (3H, m, NCH_3), 2.65-2.52 (2H, m, C$H_2$$CH_3$), 2.51 (3H, d, *J* = 4.6, NHCH_3), 0.76 (3H, t, *J* = 7.3, CH_2CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.6 (*C*=O), 160.3 (=*C*), 148.3 (=*C*H), 142.8 (=*C*), 136.6 (=*C*H), 128.3 (2 x =*C*H), 127.7 (=*C*H), 126.8 (=*C*H), 122.0 (=*C*H), 70.9 (N*C*), 33.5 (N*C*H_3), 33.1 (*C*H_2), 27.3 (N*C*H_3), 10.1 (*C*H_3). $[\alpha]_D^{20}$ = -80 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3341, 2970, 2937, 1635. **HRMS** (ESI^+): *m/z* calcd for $C_{17}H_{21}N_3ONa$ $[M+Na]^+$ 306.1577, found 306.1581.

1,3-Dimethyl-1-[(1R)-1-phenyl-1(pyridin-2-yl)but-3-en-1-yl]urea (14c)



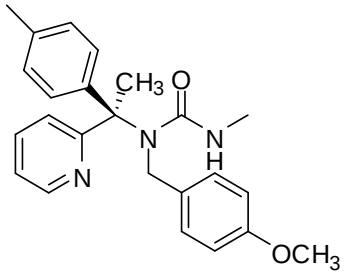
Following general procedure 3, LDA (0.42 ml), urea **8c** (100 mg, 0.34 mmol) and THF (3.39 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **14c** as an oil (67 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.59-8.46 (1H, m, =C*H*), 7.63 (1H, td, *J* = 8.0 and 1.8, =C*H*), 7.44 (1H, d, *J* = 8.1, =C*H*), 7.38-7.31 (2H, m, 2 x =C*H*), 7.30-7.23 (2H, m, 2 x =C*H*), 7.22-7.16 (1H, m, =C*H*), 7.12 (1H, ddd, *J* = 7.4, 4.8 and 0.8, =C*H*), 5.71 (1H, ddt, *J* = 17.1, 10.2 and 6.9, CH_2=C*H*CH_2), 5.23-5.08 (1H, m, N*H*CH_3), 5.08-4.91 (2H, m, =CH_2) 3.51 (1H, dd, *J* = 14.6 and 6.8, C$H_A$$CH_B$CH=), 3.41 (1H, dd, *J* = 14.6 and 7.0, CH_ACH_BCH=), 2.97 (3H, s, NCH_3), 2.56 (3H, d, *J* = 4.6, NHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.2 (*C*=O), 160.1 (=*C*), 148.3 (=*C*H), 143.0 (=*C*), 136.3 (=*C*H), 134.7 (=*C*H), 128.1 (=*C*H), 128.0 (=*C*H), 127.0 (=*C*H), 122.1 (=*C*H), 121.7 (=*C*H), 118.3 (=*C*H_2), 71.0 (N*C*), 44.0 (*C*H_2), 34.9 (*C*H_3), 27.4 (N*C*H_3). $[\alpha]_D^{20}$ = -36 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3345, 3060, 2925, 1635, 1218, 1081. **HRMS** (ESI^+): *m/z* calcd for $C_{18}H_{21}N_3ONa$ $[M+Na]^+$ 318.1577, found 318.1577.

1-[(4-Methoxyphenyl)methyl]- 3-methyl-1-[(1R)-1-phenyl-1-(pyridin-2-yl)ethyl]urea (15a)



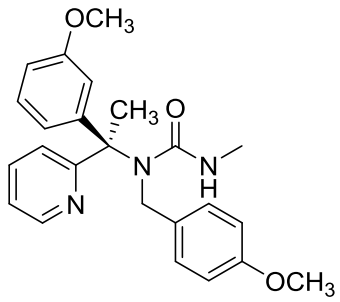
Following General procedure 3, LDA (0.48 ml), urea **10a** (145 mg, 0.39 mmol) and THF (3.86 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15a** as an oil (138 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.62-8.50 (1H, m, =C*H*), 7.59 (1H, td, *J* = 7.9 and 1.8, =C*H*), 7.35-7.18 (8H, m, 8 x =C*H*), 7.15 (1H, ddd, *J* = 7.4, 4.9 and 0.7, =C*H*), 6.89-6.79 (2H, m, 2 x =C*H*), 5.42-5.26 (1H, m, N*H*CH_3), 4.77 (1H, d, *J* = 17.0, NC$H_A$$H_B$), 4.49 (1H, d, *J* = 17.1, NC$H_A$$H_B$), 3.81 (3H, s, OC$H_3$), 2.51 (3H, d, *J* = 4.6, NHCH_3), 2.04 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.4 (*C*=O), 160.7 (=*C*), 158.5 (=*C*), 148.2 (=*C*H), 145.1 (=*C*), 136.5 (=*C*H), 132.7 (=*C*), 128.2 (=*C*H), 128.1 (=*C*H), 127.4 (2 x =*C*H), 127.0 (=*C*H), 122.2 (=*C*H), 121.8 (=*C*H), 114.0 (=*C*H), 69.2 (N*C*), 55.4 (O*C*H_3), 49.7 (*C*H_2), 30.8 (N*C*H_3), 27.5 (*C*H_3). $[\alpha]_D^{20}$ = -44 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2990, 2937, 1641. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{26}N_3O_2$ $[M+H]^+$ 376.2025, found 376.2025.

1-[(4-Methoxyphenyl)methyl]-3-methyl-1-[(1R)-1-(4-methylphenyl)-1-(pyridin-2-yl)ethyl]urea (15b)



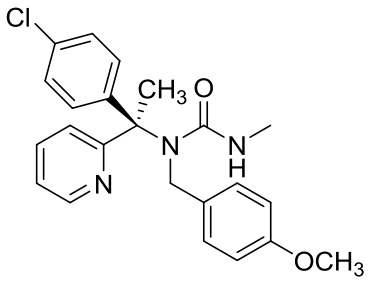
Following general procedure 3, LDA (0.14 ml), urea **10b** (45 mg, 0.12 mmol) and THF (1.16 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15b** as an oil (44 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.55 (1H, ddd, *J* = 4.8, 1.9 and 0.7, =C*H*), 7.58 (1H, td, *J* = 7.7 and 1.8, =C*H*), 7.33-7.27 (3H, m, 3 x =C*H*), 7.16-7.11 (3H, m, 3 x =C*H*), 7.10-7.04 (2H, m, 2 x =C*H*), 6.89-6.81 (2H, m, 2 x =C*H*), 5.18 (1H, q, *J* = 4.6, N*H*CH_3), 4.76 (1H, d, *J* = 17.0, NC$H_A$$H_B$), 4.47 (1H, d, *J* = 17.0, NC$H_A$$H_B$), 3.80 (3H, s, OC$H_3$), 2.51 (3H, d, *J* = 4.6, NHCH_3), 2.31 (3H, s, CH_3), 2.03 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.6 (*C*=O), 160.7 (=*C*), 158.5 (=*C*), 148.2 (=*C*H), 141.9 (=*C*), 136.7 (=*C*H), 136.4 (=*C*), 132.8 (=*C*), 128.9 (=*C*H), 128.2 (=*C*H), 127.4 (*C*H), 122.2 (=*C*H), 121.7 (=*C*H), 114.0 (=*C*H), 69.1 (N*C*), 55.4 (O*C*H_3), 49.8 (*C*H_2), 30.7 (N*C*H_3), 27.5 (*C*H_3), 21.1 (*C*H_3). $[\alpha]_D^{20}$ = -48 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2924, 1641, 1243, 1034, 748. **HRMS** (ESI^+): *m/z* calcd for $C_{24}H_{27}N_3O_2Na$ $[M+Na]^+$ 412.1995, found 412.1994.

1-[(1R)-1-(3-Methoxyphenyl)-1-(pyridin-2-yl)ethyl]-1-[(4-[methoxyphenyl)methyl]-3-methylurea (15c)



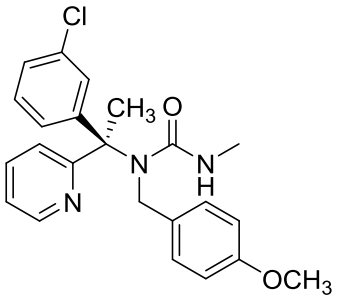
Following general procedure 3, LDA (0.19 ml), urea **10c** (63 mg, 0.16 mmol) and THF (1.55 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15c** as an oil (64 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.57 (1H, dd, *J* = 4.7 and 0.9, =C*H*), 7.59 (1H, td, *J* = 7.9 and 1.8, =C*H*), 7.36-7.24 (3H, m, 3 x =C*H*), 7.18 (1H, t, *J* = 8.0, =C*H*), 7.14 (1H, dd, *J* = 7.4 and 5.5, =C*H*), 6.90-6.70 (5H, m, 5 x =C*H*), 5.37-5.22 (1H, brq, N*H*CH_3), 4.69 (1H, d, *J* = 17.0, NC$H_A$$H_B$), 4.51 (1H, d, *J* = 17.1, NCH_AH_B), 3.80 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 2.53 (3H, d, *J* = 4.6, NHCH_3), 2.06 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.2 (*C*=O), 160.6 (=*C*), 159.4 (=*C*), 159.5 (=*C*), 148.3 (=*C*H), 147.0 (=*C*), 136.4 (=*C*H), 132.6 (=*C*), 129.1 (=*C*H), 128.1 (2 x =*C*H), 122.1 (=*C*H), 121.8 (=*C*H), 119.8 (=*C*H), 114.0 (2 x =*C*H), 113.7 (=*C*H), 112.1 (=*C*H), 69.3 (N*C*), 55.4 (O*C*H_3), 55.2 (O*C*H_3), 49.9 (*C*H_2), 30.4 (N*C*H_3), 27.5 (*C*H_3). $[\alpha]_D^{20}$ = -28 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2957, 2924, 1670, 1250, 1034. **HRMS** (ESI^+): *m/z* calcd for $C_{24}H_{28}N_3O_3$ $[M+H]^+$ 406.2125, found 406.2111.

1-[(1R)-1-(4-Chlorophenyl)-1-(pyridin-2-yl)ethyl]-1-[(4-[methoxyphenyl)methyl]-3-methylurea (15d)



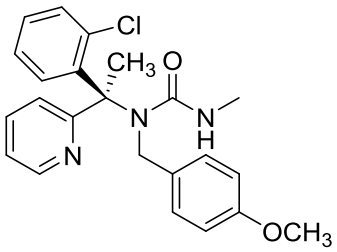
Following general procedure 3, LDA (0.13 ml), urea **10d** (41 mg, 0.10 mmol) and THF (1.00 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15d** as an oil (35 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.55 (1H, ddd, *J* = 4.8, 1.9 and 0.9, =C*H*), 7.59 (1H, td, *J* = 7.6 and 1.9, =C*H*), 7.32-7.17 (7H, m, 7 x =C*H*), 7.15 (1H, ddd, *J* =7.5, 4.8 and 0.8, =C*H*), 6.92-6.76 (2H, m, 2 x =C*H*), 5.34 (1H, q, *J* = 4.5, N*H*CH_3), 4.76 (1H, d, *J* = 17.1, NC$H_A$$H_B$), 4.44 (1H, d, *J* = 17.1, NCH_AH_B), 3.80 (3H, s, OCH_3), 2.53 (3H, d, *J* = 4.6, NHCH_3), 2.01 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.0 (*C*=O), 160.5 (=*C*), 158.7 (=*C*), 148.4 (=*C*H), 143.8 (=*C*), 136.6 (=*C*H), 132.7 (=*C*), 132.3 (=*C*), 128.9 (2 x =*C*H), 128.2 (2 x =*C*H), 128.1 (2 x =*C*H), 122.1 (=*C*H), 122.0 (=*C*H), 114.1 (2 x =*C*H), 68.8 (N*C*), 55.4 (O*C*H_3), 49.7 (*C*H_2), 30.5 (N*C*H_3), 27.5 (*C*H_3). $[\alpha]_D^{20}$ = +16 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2980, 1642, 1215, 1038, 747. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{24}ClN_3O_2Na$ $[M+Na]^+$ 432.1449, found 432.1437.

1-[(1R)-1-(3-Chlorophenyl)-1-(pyridin-2-yl)ethyl]-1-[(4-[methoxyphenyl)methyl]-3-methylurea (15e)



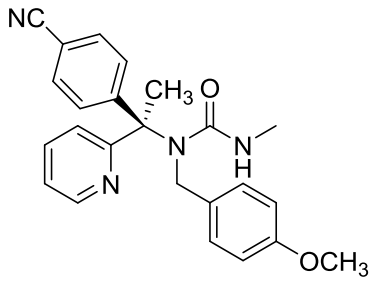
Following general procedure 3, LDA (0.21 ml), urea **10e** (70 mg, 0.17 mmol) and THF (1.71 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15e** as an oil (67 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.62-8.51 (1H, m, =C*H*), 7.60 (1H, td, *J* = 7.9 and 1.7, =C*H*), 7.35-7.23 (8H, m, 8 x =C*H*), 6.90-6.80 (2H, m, 2 x =C*H*), 5.47-5.34 (1H, m, N*H*CH_3), 4.76 (1H, d, *J* = 17.1, NC$H_A$$H_B$), 4.45 (1H, d, *J* = 17.1, NC$H_A$$H_B$), 3.80 (3H, s, OC$H_3$), 2.53 (3H, d, *J* = 4.6, NHCH_3), 2.01 (3H, m, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.4 (*C*=O), 160.4 (=*C*), 158.6 (=*C*), 148.3 (=*C*H), 147.4 (=*C*), 136.7 (=*C*H), 134.0 (=*C*), 132.2 (=*C*), 129.4 (=*C*H), 128.1 (2 x =*C*H), 127.6 (=*C*H), 127.1 (=*C*H), 125.6 (=*C*H), 122.2 (=*C*H), 122.1 (=*C*H), 114.1 (2 x =*C*H), 68.9 (N*C*), 55.4 (O*C*H_3), 49.7 (*C*H_2), 30.5 (N*C*H_3), 27.5 (*C*H_3). **$[\alpha]_D^{20}$** = -53 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2985, 1653, 1207, 1036, 751. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{25}ClN_3O_2$ $[M+H]^+$ 410.1635, found 410.1637.

1-[(1R)-1-(2-Chlorophenyl)-1-(pyridin-2-yl)ethyl]-1-[(4-[methoxyphenyl)methyl]-3-methylurea (15f)



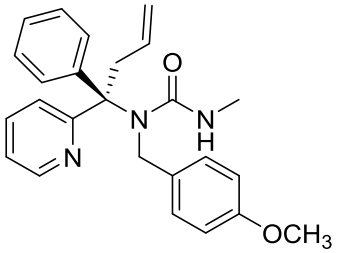
Following general procedure 3, LDA (0.23 ml), urea **10f** (74 mg, 0.18 mmol) and THF (1.81 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15f** as an oil (49 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.56-8.38 (1H, m, =C*H*), 7.61-7.51 (1H, m, =C*H*), 7.38-7.31 (1H, m, =C*H*), 7.27-7.17 (6H, m, 6 x =C*H*), 7.16-7.10 (1H, m, =C*H*), 6.87-6.71 (2H, m, 2 x =C*H*), 6.23-6.02 (1H, m, N*H*CH_3), 5.11 (1H, d, *J* = 16.9, NC$H_A$$H_B$), 4.45 (1H, d, *J* = 16.9, NC$H_A$$H_B$), 3.80-3.75 (3H, m, OC$H_3$), 2.59-2.46 (3H, m, NHC$H_3$), 2.21-2.07 (3H, m, C$H_3$). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.5 (*C*=O), 160.4 (=*C*), 158.4 (=*C*), 147.2 (=*C*H), 141.9 (=*C*), 136.7 (=*C*H), 132.9 (=*C*), 132.8 (=*C*), 132.0 (=*C*H), 129.0 (=*C*H), 128.3 (=*C*H), 128.2 (2 x =*C*H), 126.7 (=*C*H), 122.9 (=*C*H), 122.2 (=*C*H), 113.9 (2 x =*C*H), 69.4 (N*C*), 55.4 (O*C*H_3), 49.3 (*C*H_2), 27.4 (N*C*H_3), 27.3 (*C*H_3). **$[\alpha]_D^{20}$** = -28 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3017, 1628, 1215, 1035, 745. **HRMS** (ESI^+): *m/z* calcd for $C_{23}H_{24}ClN_3O_2Na$ $[M+Na]^+$ 432.1449, found 432.1447.

1-[(1R)-1-(4-Cyanophenyl)-1-(pyridin-2-yl)ethyl]-1-[(4-[methoxyphenyl)methyl]-3-methylurea (15g)



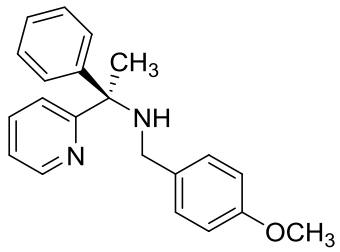
Following general procedure 3, LDA (0.24 ml), urea **10g** (78 mg, 0.20 mmol) and THF (1.95 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15g** as an oil (66 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.57 (1H, ddd, *J* = 4.8, 1.9 and 0.9, =C*H*), 7.55 (1H, ddd, *J* = 9.4, 7.5 and 1.9, =C*H*), 7.58-7.53 (2H, m, 2 x =C*H*), 7.41-7.35 (2H, m, 2 x =C*H*), 7.32-7.26 (3H, m, 3 x =C*H*), 7.18 (1H, ddd, *J* =7.5, 4.8 and 1.0, =C*H*), 6.89-6.83 (2H, m, 2 x =C*H*), 5.46 (1H, q, *J* = 4.3, N*H*CH_3), 4.73 (1H, d, *J* = 17.3, NC$H_A$$H_B$), 4.42 (1H, d, *J* = 17.3, NC$H_A$$H_B$), 3.81 (3H, s, OC$H_3$), 2.53 (3H, d, *J* = 4.6, NHCH_3), 2.01 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.9 (*C*=O), 160.3 (=*C*), 158.8 (=*C*), 151.4 (=*C*), 148.4 (=*C*H), 136.8 (=*C*H), 131.9 (2 x =*C*H), 131.7 (=*C*), 128.0 (2 x =*C*H), 127.9 (2 x =*C*H), 122.4 (=*C*H), 122.3 (=*C*H), 119.1 (=*C*), 114.3 (2 x =*C*H), 110.4 (*C*N), 69.1 (N*C*), 55.5 (O*C*H_3), 49.7 (*C*H_2), 30.1 (N*C*H_3), 27.4 (*C*H_3). **$[\alpha]_D^{20}$** = -56 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2999, 2227, 1647, 1244, 1033, 749. **HRMS** (ESI$^+$): *m/z* calcd for $C_{24}H_{24}N_4O_2Na$ $[M+Na]^+$ 423.1791, found 423.1793.

1-[(4-Methoxyphenyl)methyl]-3-methyl-1-[(1R)-1-phenyl-1-(pyridin-2-yl)but-3-en-1-yl]urea (15h)



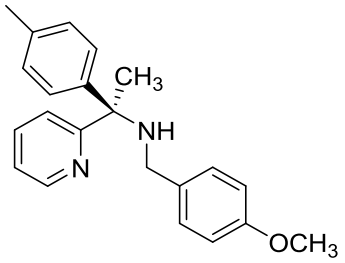
Following general procedure 3, LDA (0.24 ml), urea **10h** (77 mg, 0.19 mmol) and THF (1.92 ml) gave, after purification by flash column chromatography (SiO_2, 99:1 to 90:10 DCM:MeOH), **15h** as an oil (70 mg, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.58-8.50 (1H, m, =C*H*), 7.54 (1H, td, *J* = 8.0 and 1.9, =C*H*), 7.34-7.29 (1H, m, =C*H*), 7.28-7.15 (7H, m, 7 x =C*H*), 6.85-6.76 (2H, m, 2 x =C*H*), 7.22-7.16 (1H, m, =C*H*), 7.12 (1H, ddd, *J* = 7.4, 4.8 and 0.9, =C*H*), 5.76-5.67 (1H, m, N*H*CH_3), 5.59 (1H, ddt, *J* = 17.1, 10.2 and 6.8, CH_2=C*H*CH_2), 5.03-4.87 (2H, m, =CH_2) 3.80 (3H, s, OCH_3), 3.49 (1H, dd, *J* = 14.5 and 6.8, C$H_A$$CH_B$CH=), 3.40 (1H, dd, *J* = 14.5 and 7.5, CH_ACH_BCH=), 2.52 (3H, d, *J* = 4.6, NHCH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.3 (*C*=O), 160.6 (=*C*), 158.5 (=*C*) 148.1 (=*C*H), 143.1 (=*C*), 136.1 (=*C*H), 134.8 (=*C*H), 132.4 (=*C*), 128.1 (2 x =*C*H), 128.0 (2 x =*C*H), 127.8 (2 x =*C*H), 126.9 (=*C*H), 122.7 (=*C*H), 121.7 (=*C*H), 118.3 (=CH_2), 114.0 (2 x =*C*H), 71.8 (N*C*), 55.4 (O*C*H_3), 50.3 (*C*H_2), 44.8 (*C*H_2), 27.4 (N*C*H_3). **$[\alpha]_D^{20}$** = -36 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3441, 3064, 2930, 1645, 1244, 1036. **HRMS** (ESI$^+$): *m/z* calcd for $C_{25}H_{28}N_3O_2$ $[M+H]^+$ 402.2182, found 402.2174.

[(4-[Methoxyphenyl)methyl][(1R)-1-phenyl-1-(pyridin-2-yl)ethyl]amine (16a)



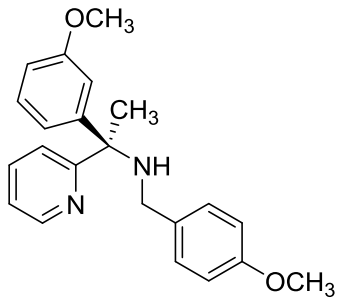
Following general procedure 4, urea **15a** (130 mg, 0.35 mmol) gave **16a** as an oil (100 mg, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.61-8.53 (1H, m, =C*H*), 7.58 (1H, td, *J* = 7.8 and 1.9, =C*H*), 7.53-7.46 (2H, m, 2 x =C*H*), 7.35-7.29 (2H, m, 2 x =C*H*), 7.28-7.25 (3H, m, 3 x =C*H*), 7.25-7.19 (1H, m, =C*H*), 7.11 (1H, ddd, *J* = 7.5, 4.8 and 1.1, =C*H*), 6.92-6.78 (2H, m, 2 x =C*H*), 3.79 (3H, s, OCH_3), 3.50 (2H, AB pattern, *J* = 12.2, Δν = 18.8, NHCH_2), 2.95-2.21 (1H, brs, N*H*CH_2), 1.95 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.4 (=*C*), 158.6 (=*C*), 148.8 (=*C*H), 147.1 (=*C*), 136.3 (=*C*H), 133.6 (=*C*), 129.5 (2 x =*C*H), 128.3 (2 x =*C*H), 127.3 (2 x =*C*H), 126.7 (=*C*H), 121.7 (=*C*H), 121.5 (=*C*H), 113.9 (2 x =*C*H), 64.3 (N*C*), 55.4 (OCH_3), 46.9 (*C*H_2), 26.2 (*C*H_3). $[\alpha]_D^{20}$ = -49 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2.954, 2931, 1241. **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{23}N_2O_1$ $[M+H]^+$ 319.1805, found 319.1809.

[(4-[Methoxyphenyl)methyl][(1R)-1-(4-methylphenyl)-1-(pyridin-2-yl)ethyl]amine (16b)



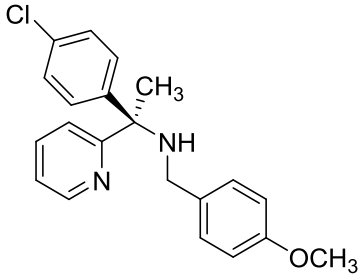
Following general procedure 4, urea **15b** (37 mg, 0.09 mmol) gave **16b** as an oil (28 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.63-8.50 (1H, m, =C*H*), 7.63-7.50 (1H, m, =C*H*), 7.42-7.32 (2H, m, 2 x =C*H*) , 7.30-7.21 (3H, m, 3 x =C*H*), 7.17-7.03 (3H, m, 3 x =C*H*), 6.89-6.77 (2H, m, 2 x =C*H*), 3.79 (3H, s, OCH_3), 3.50 (2H, AB pattern, *J* = 12.1, Δν = 12.6, NHCH_2), 2.73-2.37 (1H, brs, N*H*), 2.32 (3H, s, CH_3), 1.93 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.4 (=*C*), 158.6 (=*C*), 148.7 (=*C*H), 143.9 (=*C*), 136.3 (=*C*H), 136.2 (=*C*), 133.5 (=*C*), 129.5 (2 x =*C*H), 129.0 (2 x =*C*H), 127.2 (2 x =*C*H), 121.6 (=*C*H), 121.5 (=*C*H), 113.8 (2 x =*C*H), 64.1 (N*C*), 55.4 (OCH_3), 46.9 (*C*H_2), 26.2 (*C*H_3), 21.1 (*C*H_3). $[\alpha]_D^{20}$ = -24 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2926, 1246, 1036. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{25}N_2O$ $[M+H]^+$ 333.1961, found 333.1961.

[(1R)-1-(3-Methoxyphenyl)-1-(pyridin-2-yl)ethyl][(4-[methoxyphenyl)methyl]amine (16c)



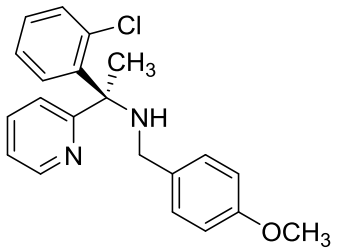
Following general procedure 4, urea **15c** (57 mg, 0.14 mmol) gave **16c** as an oil (28 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.61-8.54 (1H, m, =C*H*), 7.58 (1H, td, *J* = 7.9 and 1.8, =C*H*), 7.32-7.20 (4H, m, 4 x =C*H*), 7.15-7.10 (2H, m, 2 x =C*H*) , 7.09-7.02 (1H, m, =C*H*), 6.89-6.82 (2H, m, 2 x =C*H*), 6.78 (1H, ddd, *J* = 7.1, 1.5 and 0.6, =C*H*), 3.80 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.51 (2H, AB pattern, *J* = 15.5, Δν = 18.4, NHCH_2), 2.58-2.31 (1H, brs, N*H*), 1.94 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.1 (=*C*), 159.6 (=*C*), 158.6 (=*C*), 148.8 (=*C*), 148.7 (=*C*H), 136.3 (=*C*H), 133.5 (=*C*), 129.5 (2 x =*C*H), 129.2 (=*C*H), 121.6 (=*C*H), 121.5 (=*C*H), 119.9 (=*C*H), 113.8 (2 x =*C*H), 113.5 (=*C*H), 111.8 (=*C*H), 64.2 (N*C*), 55.4 (O*C*H_3), 55.3 (O*C*H_3), 46.9 (*C*H_2), 26.2 (*C*H_3). $[\alpha]_D^{20}$ = -9.4 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3011, 2960, 1246, 1037. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{25}N_2O_2$ $[M+H]^+$ 349.1911, found 349.1914.

[(1R)-1-(4-Chlorophenyl)-1-(pyridin-2-yl)ethyl][(4-[methoxyphenyl)methyl]amine (16d)



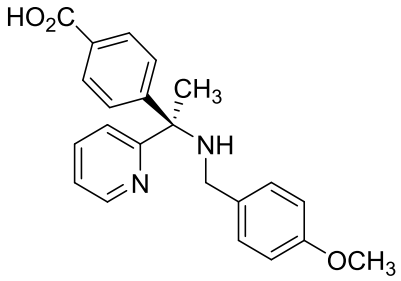
Following general procedure 4, urea **15d** (30 mg, 0.07 mmol) gave **16d** as an oil (25 mg, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.65-8.50 (1H, m, =C*H*), 7.60 (1H, td, *J* = 7.6 and 1.4, =C*H*), 7.49-7.39 (2H, m, 2 x =C*H*), 7.30-7.22 (5H, m, 5 x =C*H*) , 7.13 (1H, dd, *J* = 7.1 and 4.9, =C*H*), 6.92-6.76 (2H, m, 2 x =C*H*), 3.79 (3H, s, OCH_3), 3.48 (2H, AB pattern, *J* = 12.1, Δν = 15.9, NHCH_2), 2.71-2.40 (1H, brs, N*H*), 1.92 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.8 (=*C*), 158.7 (=*C*), 149.0 (=*C*H), 145.7 (=*C*), 136.4 (=*C*H), 133.2 (=*C*), 132.5 (=*C*), 129.4 (2 x =*C*H), 128.8 (2 x =*C*H), 128.4 (2 x =*C*H), 121.7 (=*C*H), 121.4 (=*C*H), 113.9 (2 x =*C*H), 64.0 (N*C*), 55.4 (O*C*H_3), 46.9 (*C*H_2), 26.2 (*C*H_3). $[\alpha]_D^{20}$ = -48 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 3002, 2934, 1238, 1042, 767. **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{22}ClN_2O$ $[M+H]^+$ 353.1415, found 353.1421.

[(1R)-1-(2-Chlorophenyl)-1-(pyridin-2-yl)ethyl][(4-[methoxyphenyl)methyl]amine (16e)



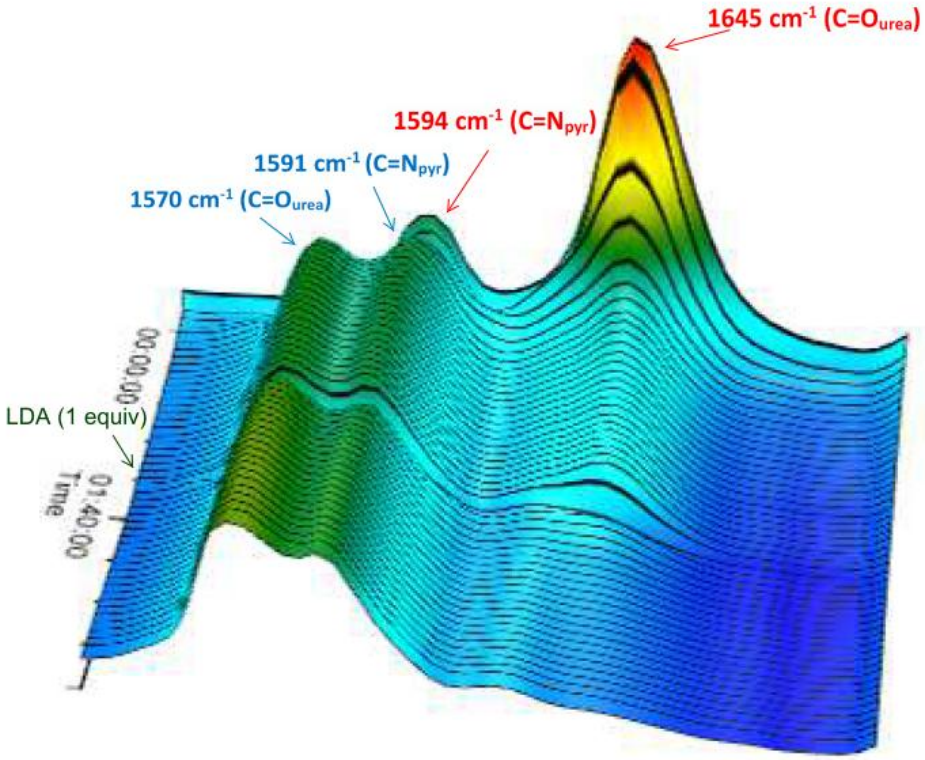
Following general procedure 4, urea **15f** (41 mg, 0.10 mmol) gave **16e** as an oil (32 mg, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.56-8.46 (1H, m, =C*H*), 7.87 (1H, d, *J* = 7.9, =C*H*), 7.60 (1H, td, *J* = 8.0 and 1.7, =C*H*), 7.46 (1H, d, *J* = 8.0, =C*H*), 7.39-7.33 (1H, m, =C*H*), 7.32-7.28 (1H, m, =C*H*), 7.27-7.23 (1H, m, =C*H*), 7.22-7.16 (2H, m, 2 x =C*H*), 7.15-7.06 (1H, m, =C*H*), 6.89-6.75 (2H, m, 2 x =C*H*), 3.78 (3H, s, OCH_3), 3.54 (1H, d, *J* = 12.0, NHC$H_A$$H_B$), 3.28 (1H, d, *J* = 12.0, NHC$H_A$$H_B$), 2.98-2.59 (1H, brs, N*H*), 1.91 (3H, s, CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.4 (=*C*), 158.7 (=*C*), 157.5 (=*C*), 148.7 (=*C*H), 146.2 (=*C*), 136.2 (=*C*H), 133.3 (=*C*), 131.5 (=*C*H), 129.6 (3 x =*C*H), 128.5 (=*C*H), 126.8 (=*C*H), 121.4 (=*C*H), 121.1 (=*C*H), 113.9 (2 x =*C*H), 65.3 (N*C*), 55.4 (O*C*H_3), 47.1 (*C*H_2), 26.7 (*C*H_3). **$[\alpha]_D^{20}$** = -36 (c = 1.00; $CHCl_3$). **IR** (film, cm^{-1}): ν_{max} = 2929, 1245, 1034, 750. **HRMS** (ESI^+): *m/z* calcd for $C_{21}H_{22}ClN_2O_1$ $[M+H]^+$ 353.1415, found 353.1416.

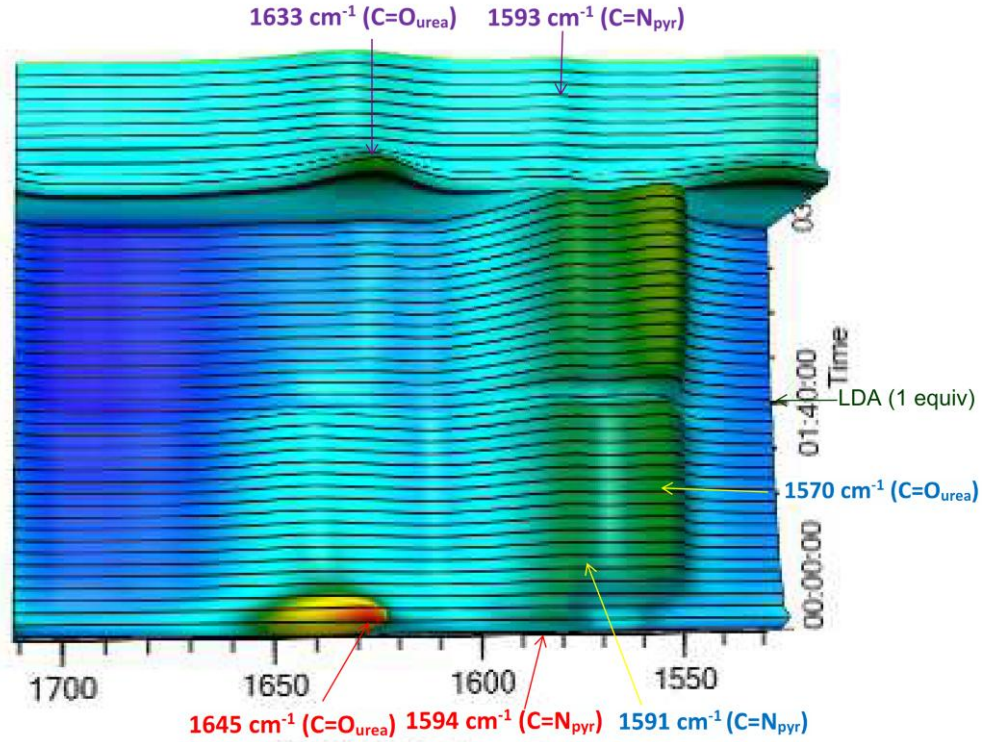
4-[(1R)-1-{[(4-Methoxyphenyl)methyl]amino}-1-(pyridin-2-yl)ethyl]benzoic acid (16f)

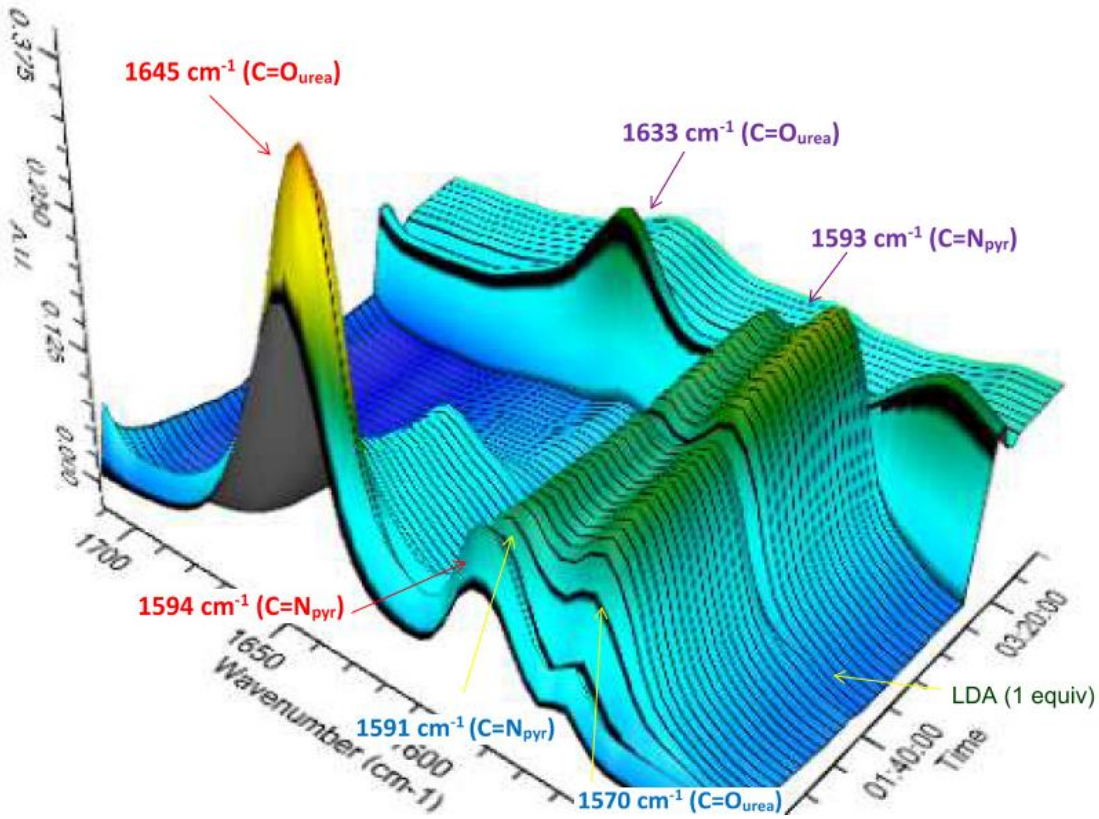


A solution of urea **15g** (62 mg, 0.16 mmol), aqueous NaOH (2.0 M) and EtOH (1.2 M) was microwaved at 130 °C for 3 h. The reaction mixture was concentrated and extracted with ethyl acetate. The aqueous phase was acidified with conc. HCl (pH = 1) and concentrated under reduced pressure. The amine **16f** was obtained by filtration on acidic Dowx ion exchange column (32 mg, 57%). **^{1}H NMR** (400 MHz, MeOD) δ = 8.78-8.66 (1H, m, =C*H*), 8.10-7.95 (2H, m, 2 x =C*H*), 7.84 (1H, td, *J* = 7.8 and 1.6, =C*H*), 7.58-7.48 (2H, m, 2 x =C*H*), 7.46-7.38 (1H, m, =C*H*), 7.36-7.29 (2H, m, 2 x =C*H*) , 7.27 (1H, d, *J* = 8.1, =C*H*), 6.98-6.87 (2H, m, 2 x =C*H*), 3.83 (2H, s, NHCH_2), 3.79 (3H, s, OCH_3), 2.18 (3H, s, CH_3). **^{13}C NMR** (100 MHz, MeOD) δ = 164.3 (=*C*), 164.1 (=*C*), 159.1 (=*C*), 151.9 (=*C*H), 145.5 (=*C*), 141.5 (=*C*H), 140.3 (=*C*), 134.9 (2 x =*C*H), 133.5 (2 x =*C*H), 131.3 (2 x =*C*H), 128.7 (=*C*), 127.1 (=*C*H), 126.0 (=*C*H), 117.8 (2 x =*C*H), 70.9 (N*C*), 58.3 (O*C*H_3), 50.7 (*C*H_2), 26.8 (*C*H_3). **$[\alpha]_D^{20}$** = -68 (c = 1.00; MeOH). **IR** (film, cm^{-1}): ν_{max} = 3317, 2947, 2834, 1652, 1253. **HRMS** (ESI^+): *m/z* calcd for $C_{22}H_{23}N_2O_3$ $[M+H]^+$ 363.1703, found 363.1699.

React-IR experiments pictures



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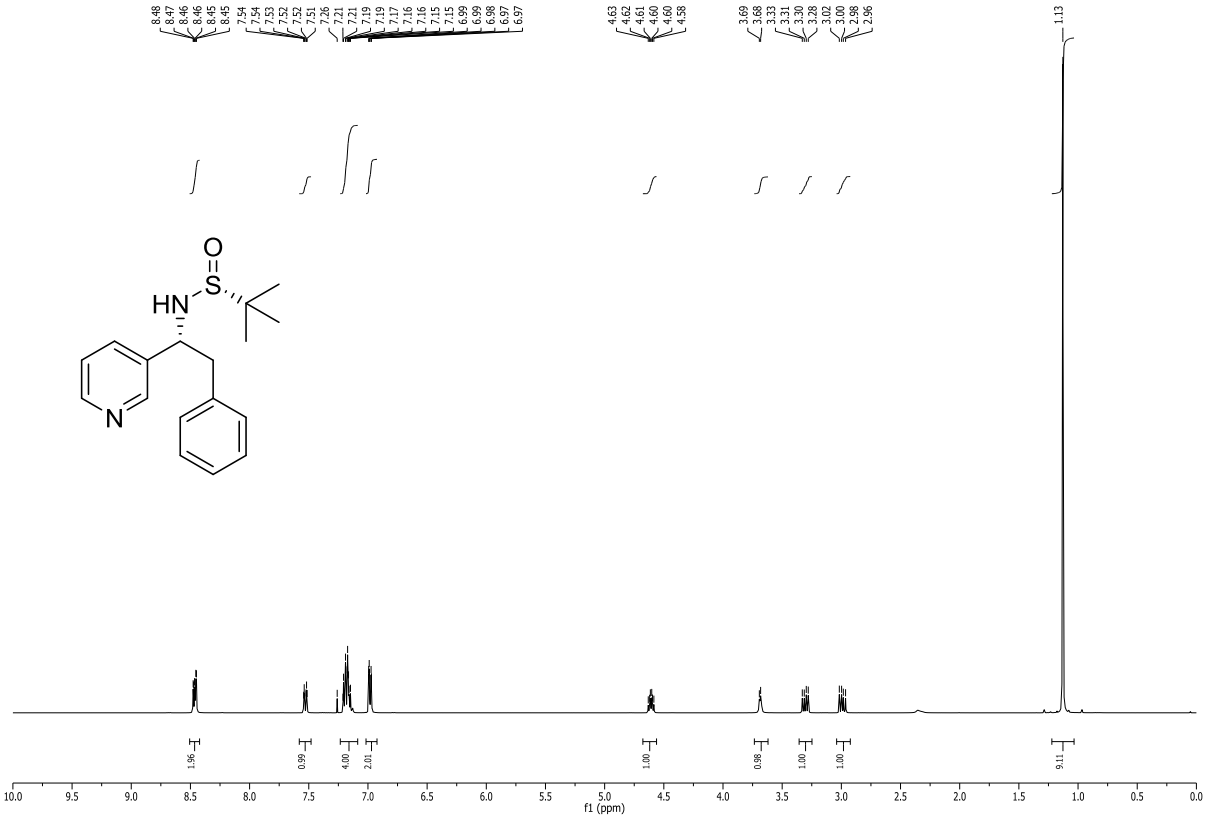
1633 cm-1 (C=Ourea)
1593 cm-1 (C=Npyr)
1594 cm-1 (C=Npyr)
1591 cm-1 (C=Npyr)
1570 cm-1 (C=Ourea)
LDA (1 equiv)
0.375
0.250
0.125
0.000
A.U.
1700
1650
1600
Wavenumber (cm-1)
01:40:00
03:20:00
Time

NMR

(R_S,R)-**3b**


8.48
8.47
8.46
8.46
8.45
8.45
7.54
7.54
7.53
7.52
7.52
7.51
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7.21
7.21
7.19
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7.17
7.16
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7.15
7.15
6.99
6.99
6.98
6.97
6.97
4.63
4.62
4.61
4.60
4.60
4.58
3.69
3.68
3.33
3.31
3.30
3.28
3.02
3.00
2.98
2.96
1.13
O
S
HN
N
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0.99
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2.01
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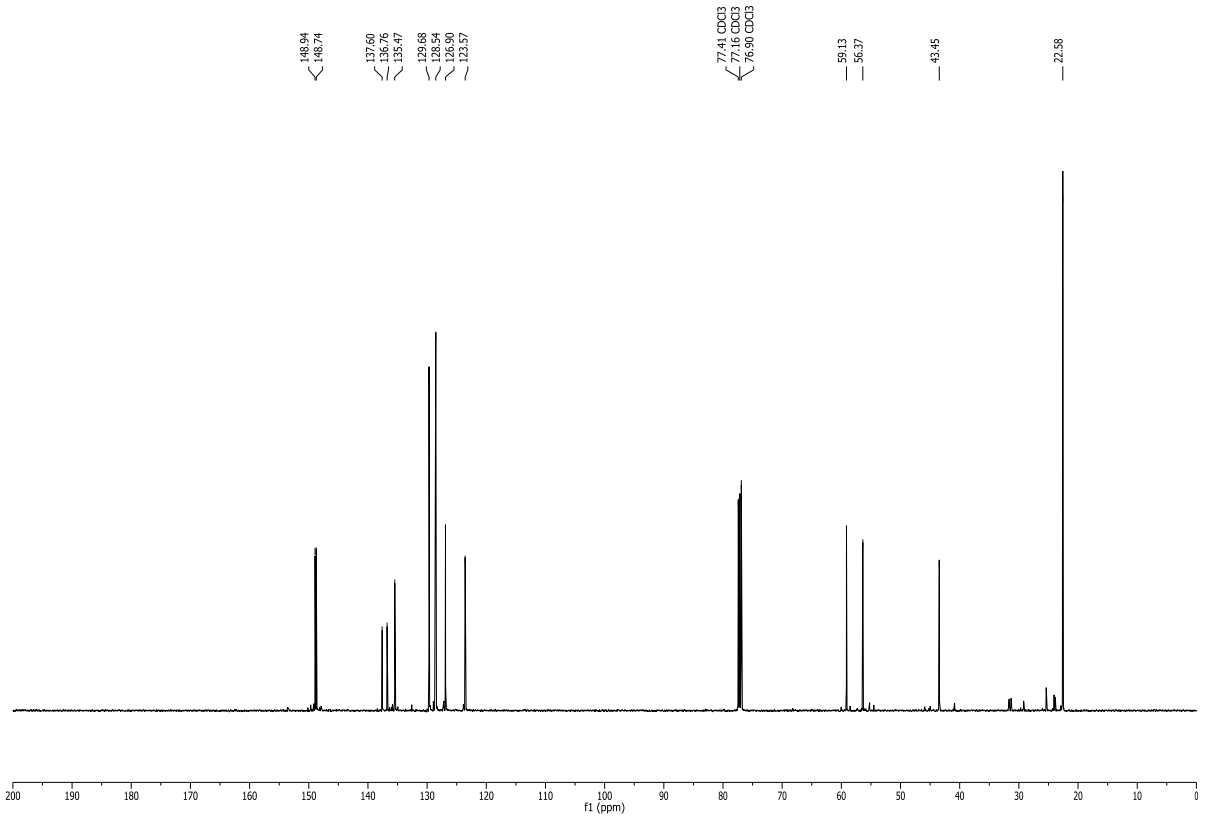
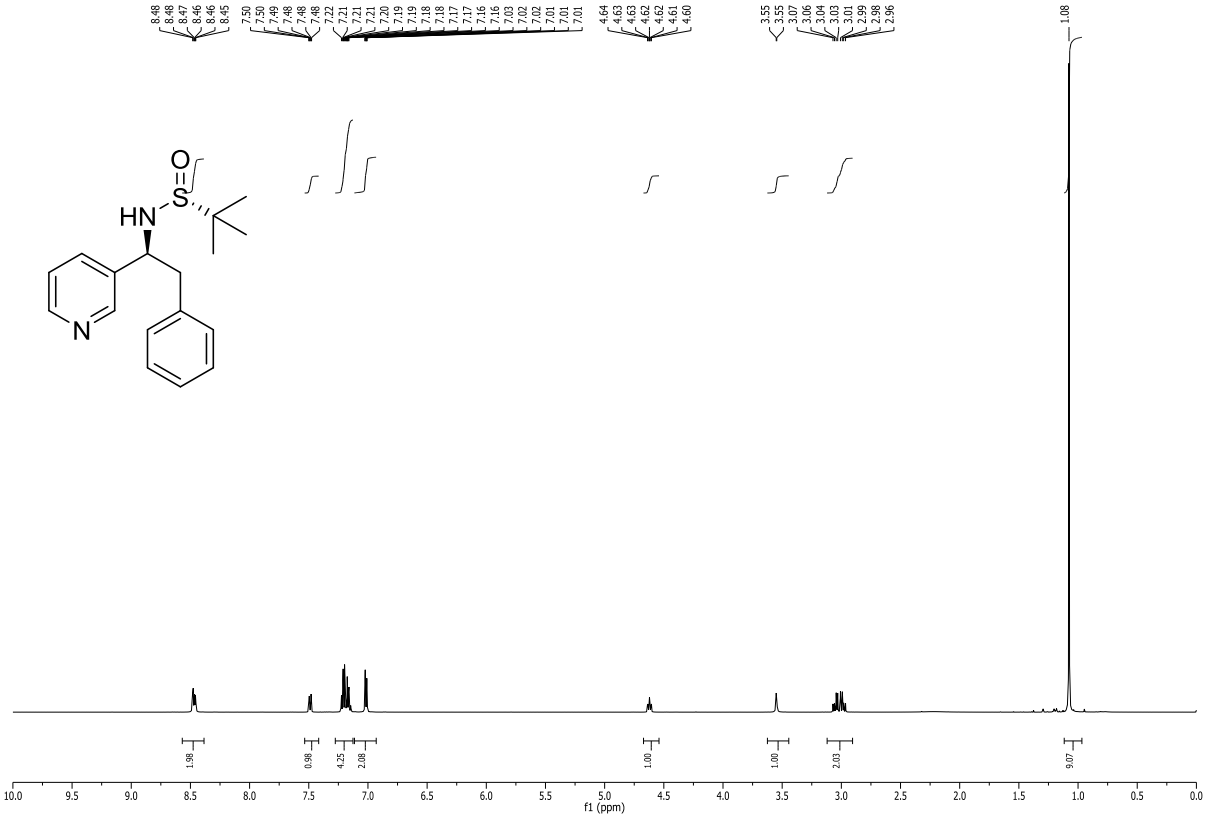
0.98
1.00
1.00
9.11
f1 (ppm)


148.94
148.74
137.60
136.76
135.47
129.68
128.54
126.90
123.57
77.41 CDCl3
77.16 CDCl3
76.90 CDCl3
59.13
56.37
43.45
22.58
f1 (ppm)

(R_S,S)-**3b**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8.48
8.47
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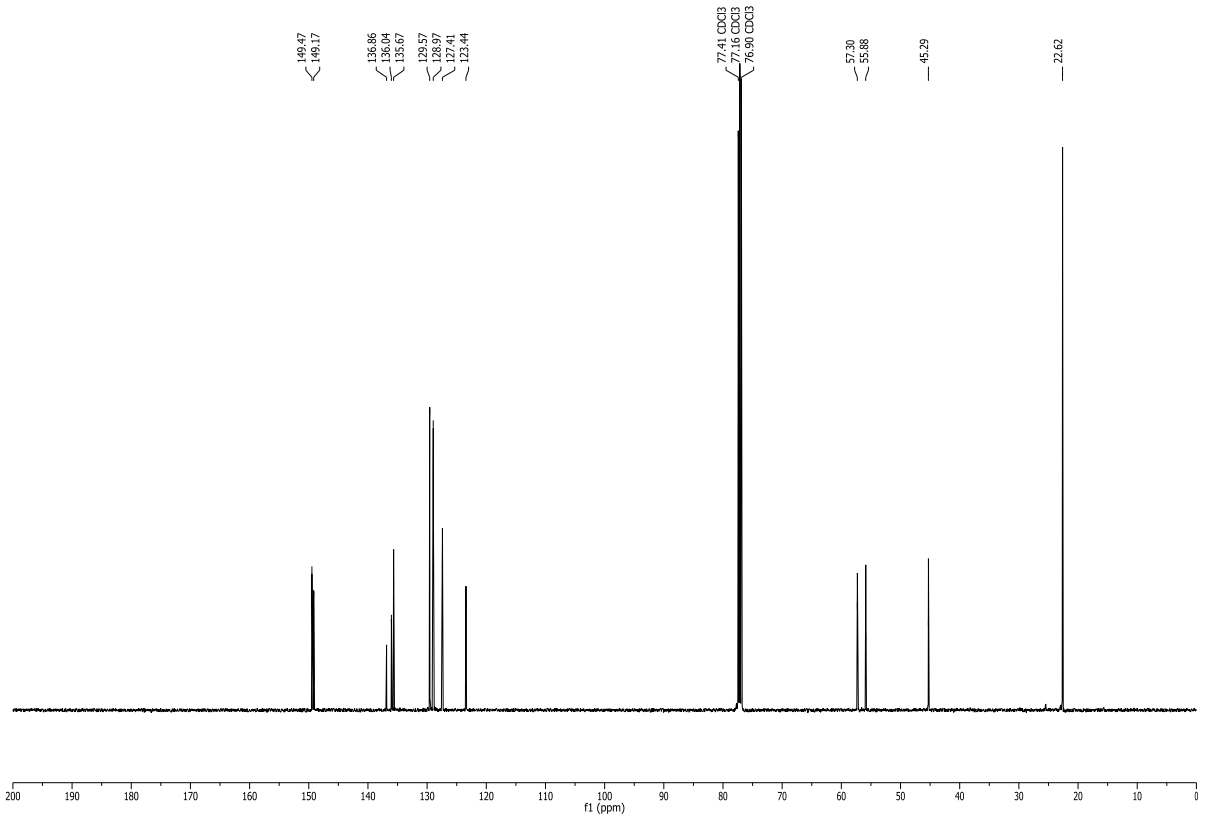
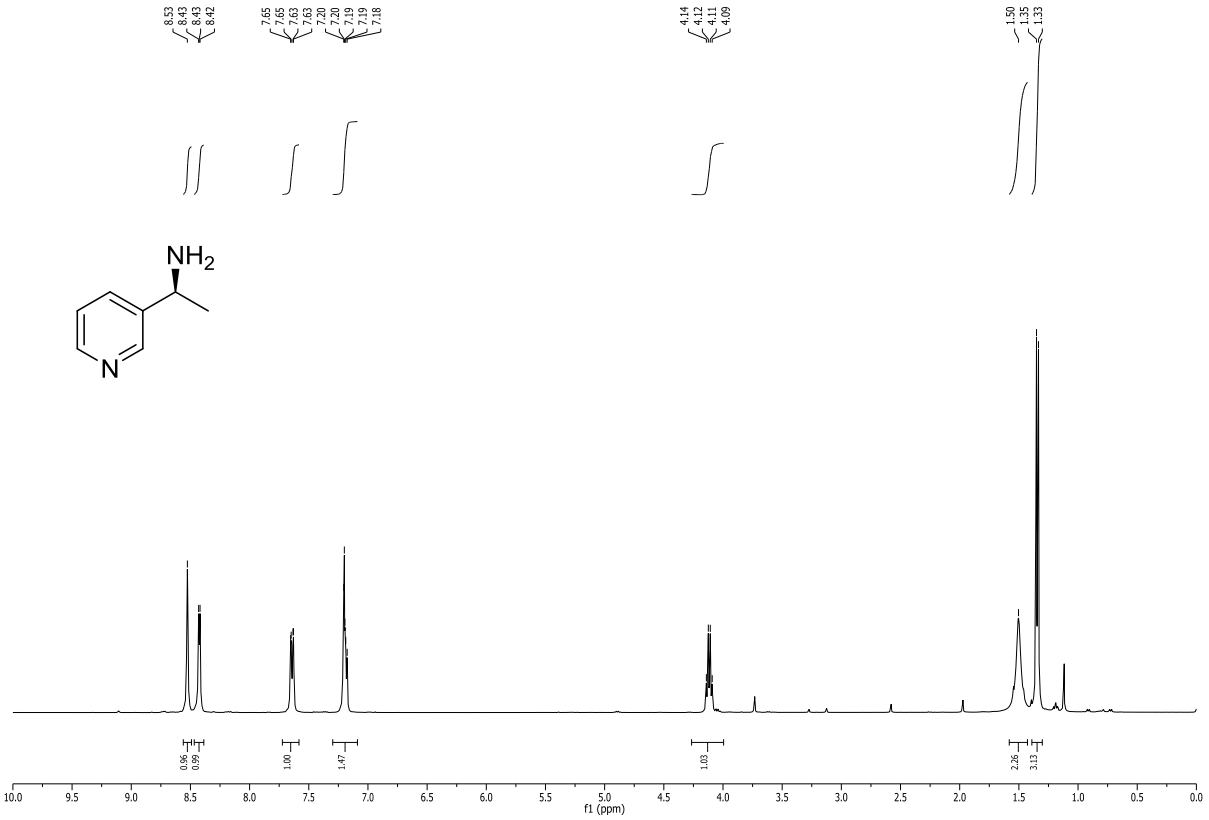
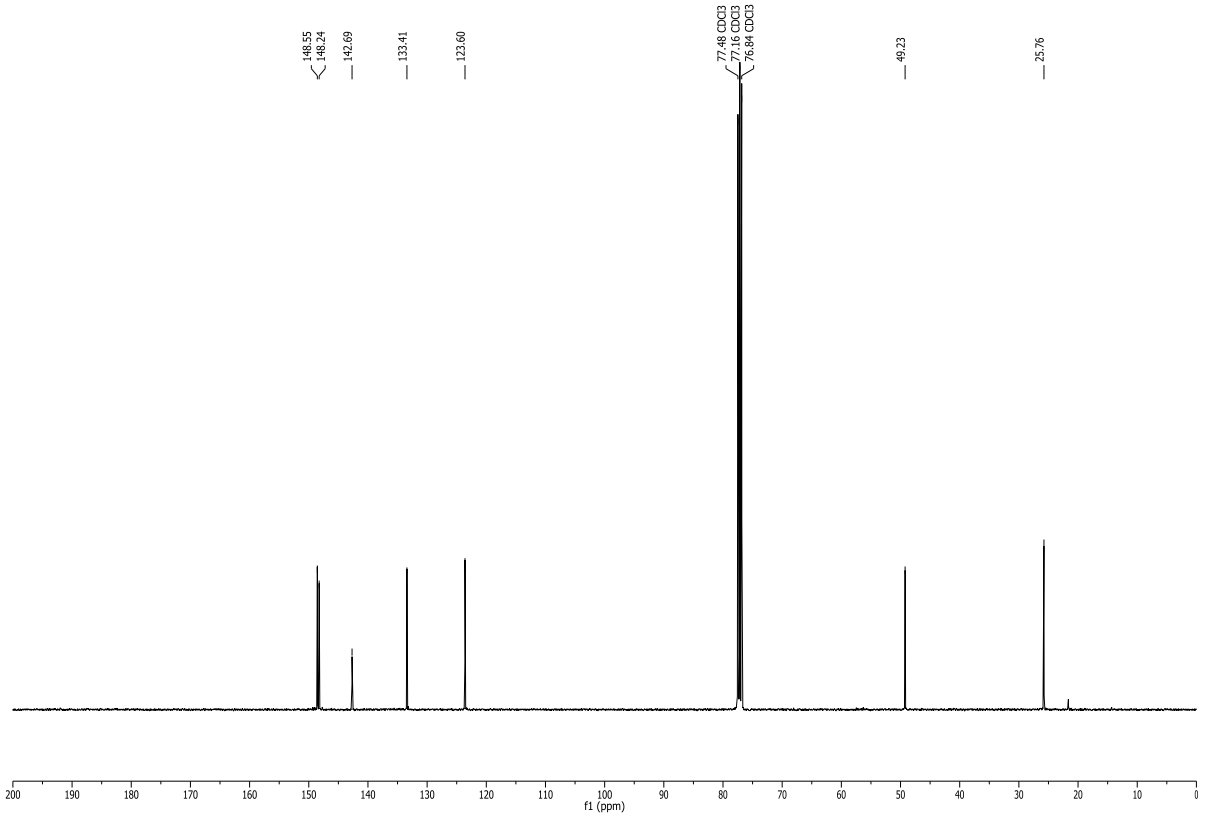
8.46
8.45
7.50
7.50
7.49
7.48
7.48
7.48
7.22
7.21
7.21
7.21
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.17
7.16
7.16
7.03
7.02
7.01
7.01
7.01
4.64
4.63
4.63
4.62
4.62
4.61
4.60
3.55
3.55
3.07
3.06
3.04
3.03
3.01
2.99
2.98
2.96
1.08
O
S
HN
N
1.98
0.98
4.25
2.08
1.00
1.00
2.03
9.07
f1 (ppm)

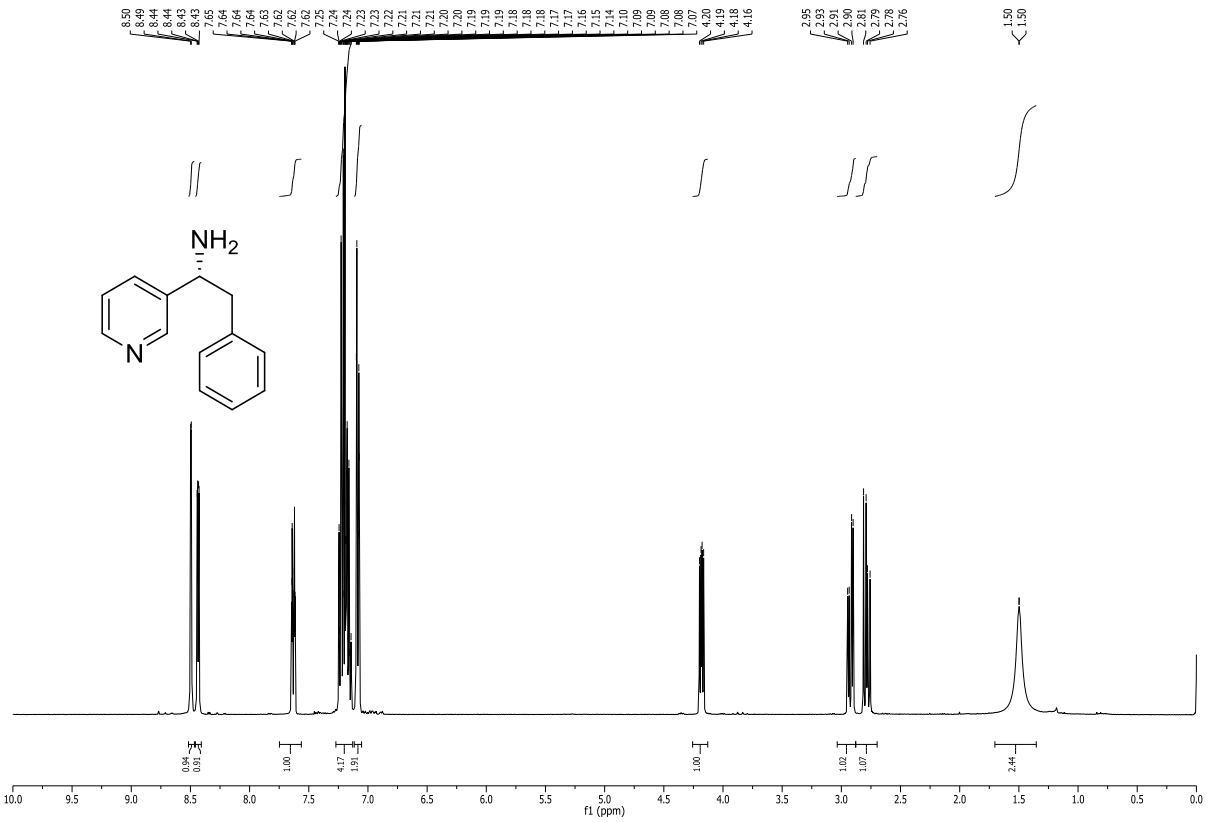

149.47
149.17
136.86
136.04
135.67
129.57
128.97
127.41
123.44
77.41 CDCl3
77.16 CDCl3
76.90 CDCl3
57.30
55.88
45.29
22.62
f1 (ppm)

5a


8.53
8.43
8.43
8.42
7.65
7.65
7.63
7.63
7.20
7.20
7.19
7.19
7.18
4.14
4.12
4.11
4.09
1.50
1.35
1.33
NH2
N
0.96
0.99
1.00
1.47
1.03
2.26
3.13
f1 (ppm)


148.55
148.24
142.69
133.41
123.60
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
49.23
25.76
f1 (ppm)

5b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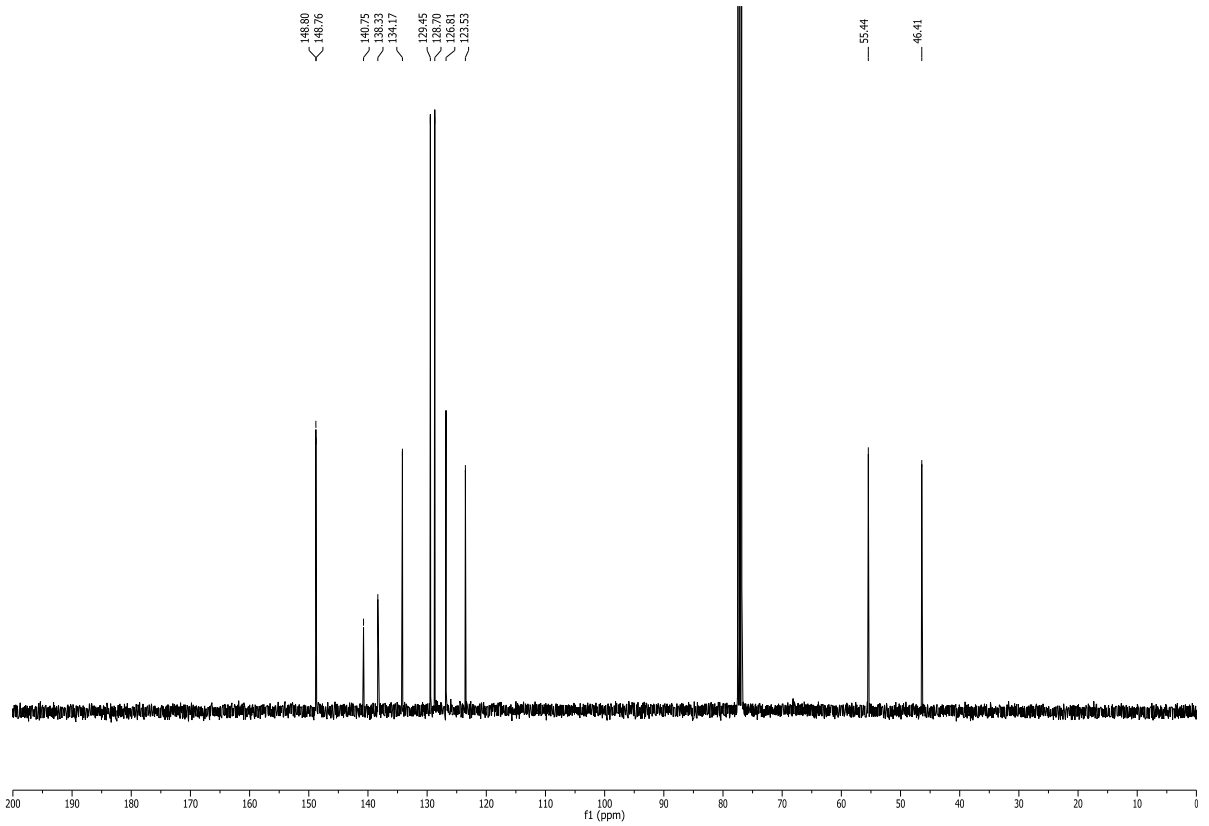
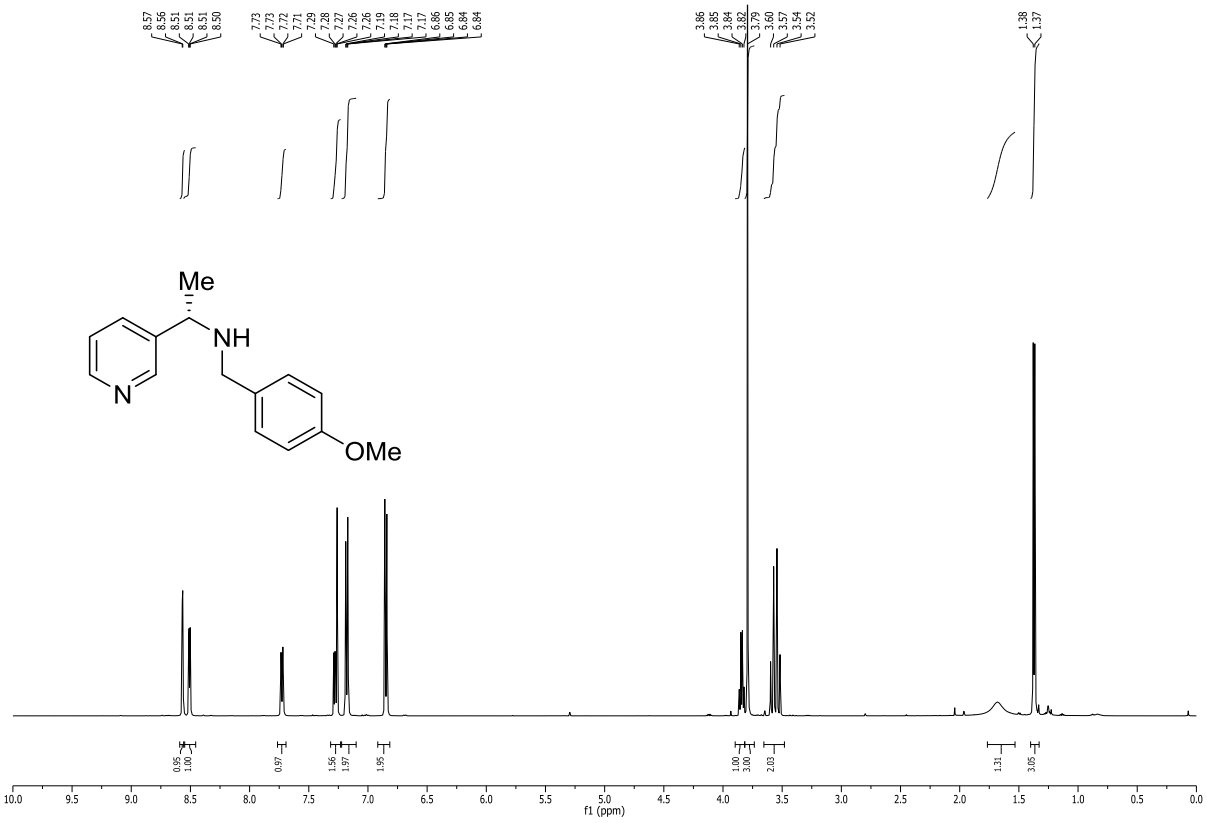
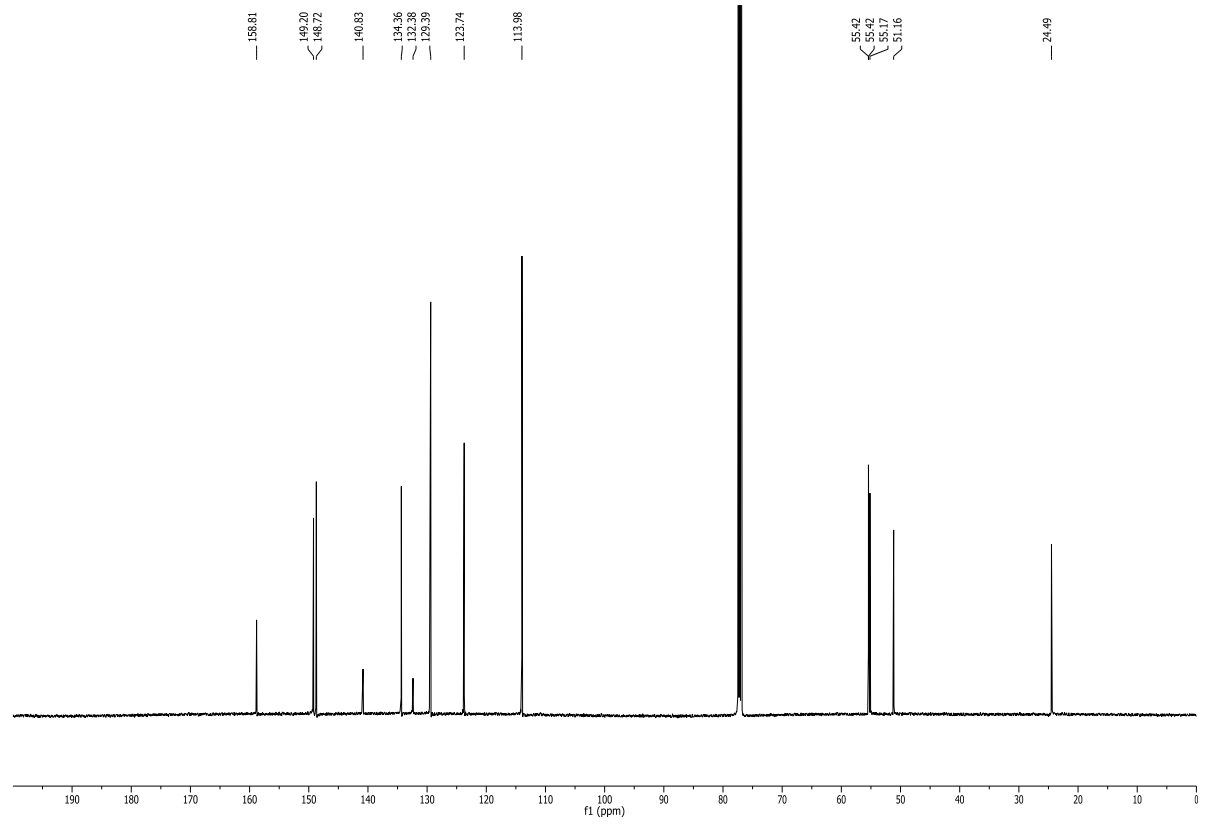
8.49
8.44
8.44
8.43
8.43
7.65
7.64
7.64
7.64
7.63
7.62
7.62
7.62
7.25
7.24
7.24
7.23
7.23
7.22
7.21
7.21
7.21
7.20
7.20
7.19
7.19
7.19
7.18
7.18
7.18
7.17
7.17
7.16
7.15
7.14
7.10
7.09
7.09
7.08
7.08
7.07
4.20
4.19
4.18
4.16
2.95
2.93
2.91
2.90
2.81
2.79
2.78
2.76
1.50
1.50
NH2
N
0.94
0.91
1.00
4.17
1.91
1.00
1.02
1.07
2.44
f1 (ppm)

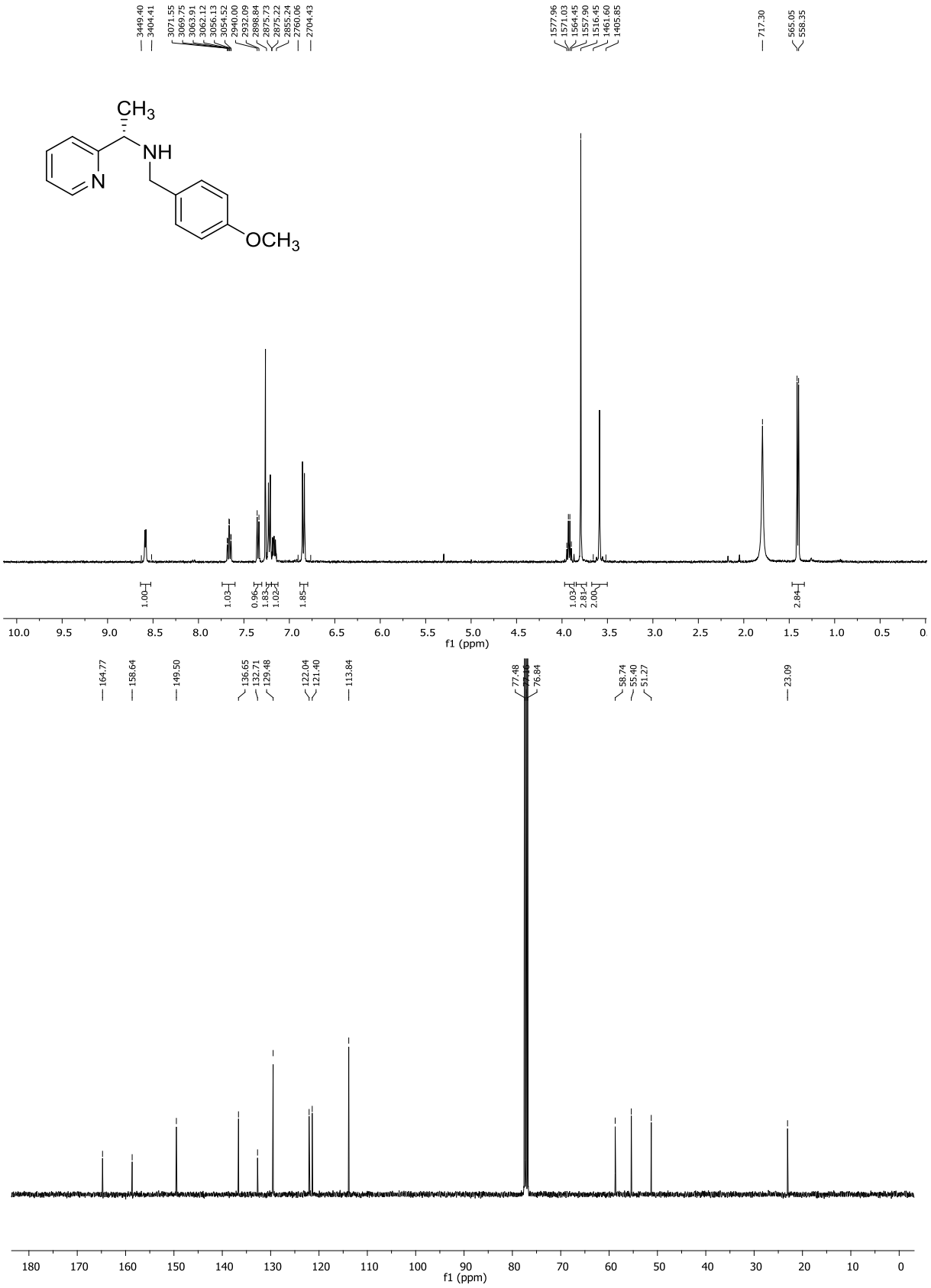

148.80
148.76
140.75
138.33
134.17
129.45
128.70
126.81
123.53
55.44
46.41
f1 (ppm)

5c

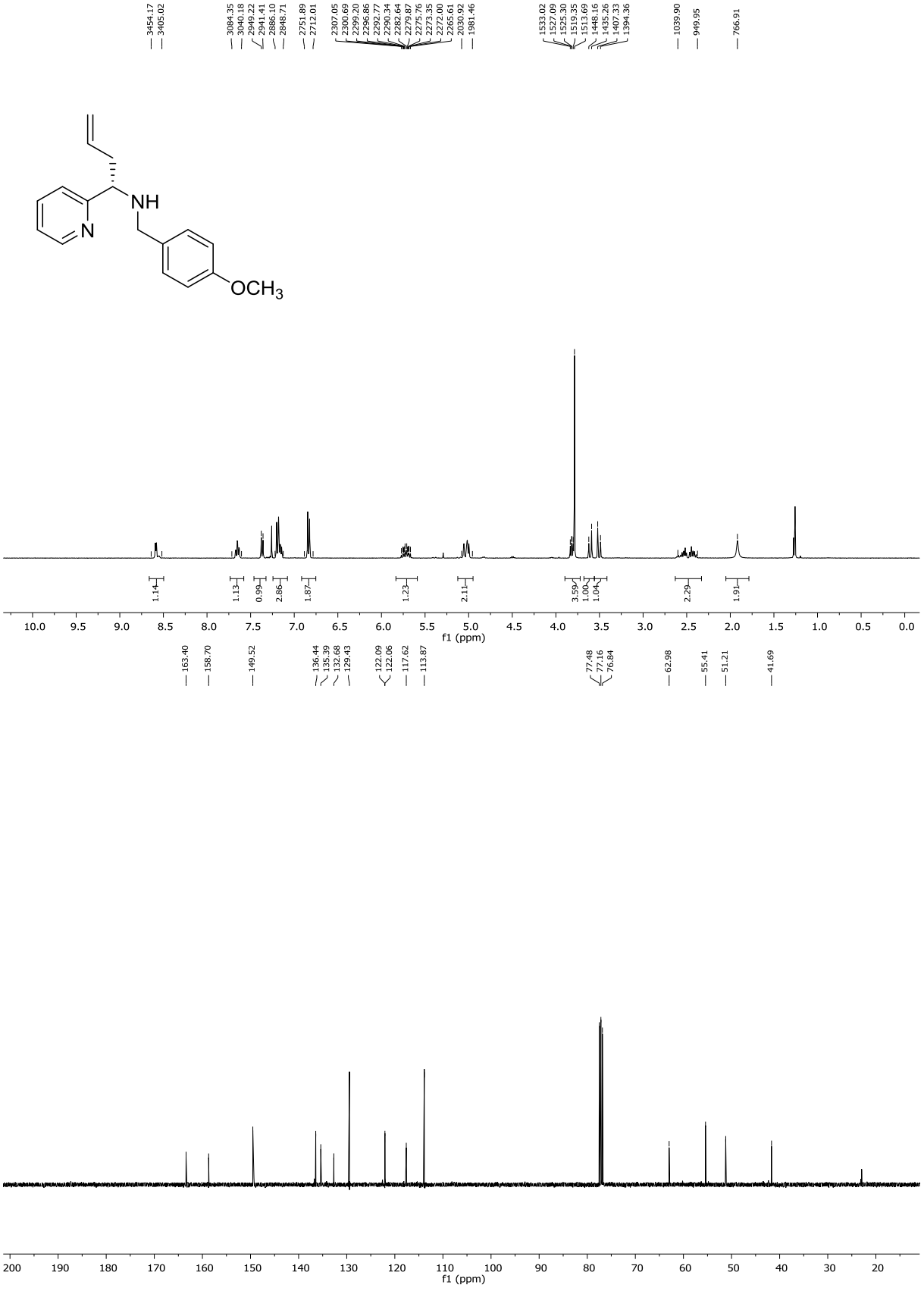

8.57
8.56
8.51
8.51
8.51
8.50
7.73
7.73
7.72
7.71
7.29
7.28
7.27
7.26
7.26
7.19
7.18
7.17
7.17
6.86
6.85
6.84
6.84
3.86
3.85
3.84
3.82
3.79
3.60
3.57
3.54
3.52
1.38
1.37
Me
NH
N
OMe
0.95
1.00
0.97
1.56
1.97
1.95
1.00
3.08
2.03
1.31
3.05
f1 (ppm)


158.81
149.20
148.72
140.83
134.36
132.38
129.39
123.74
113.98
55.42
55.42
55.17
51.16
24.49
f1 (ppm)

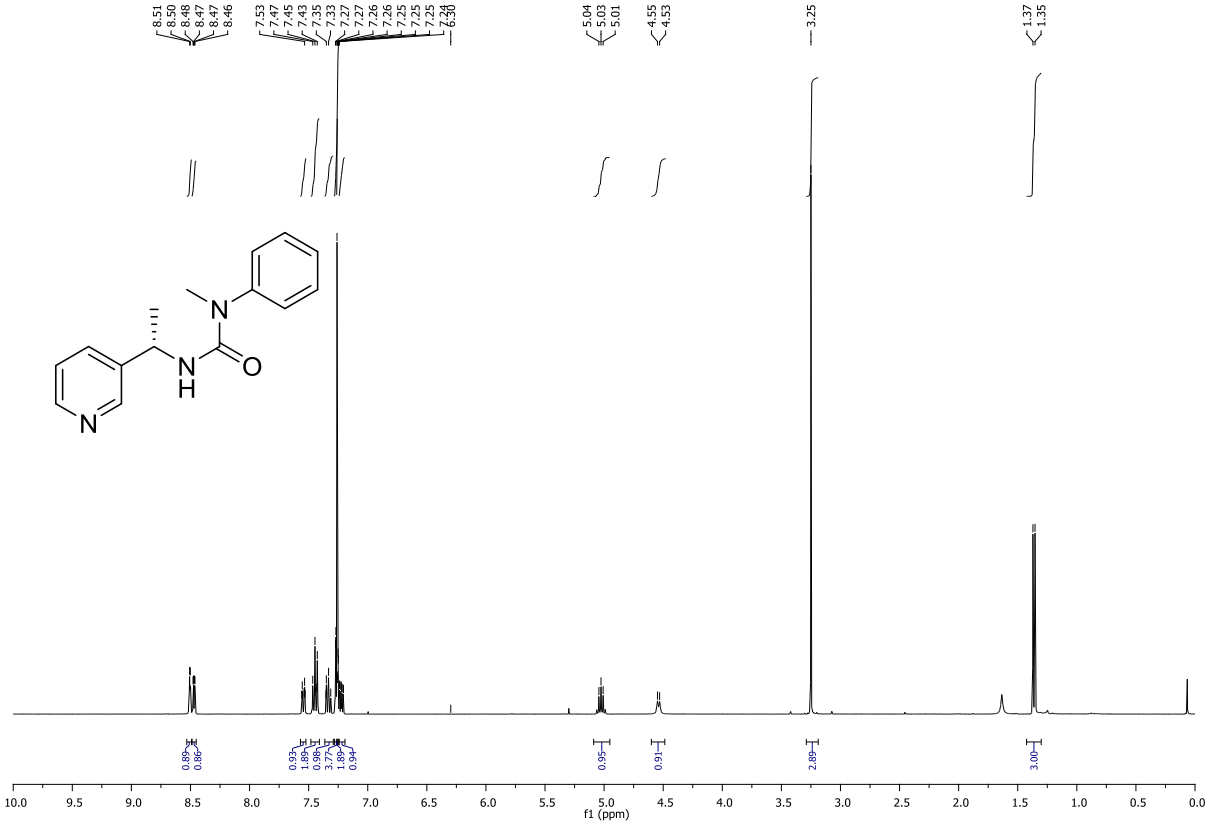
6d

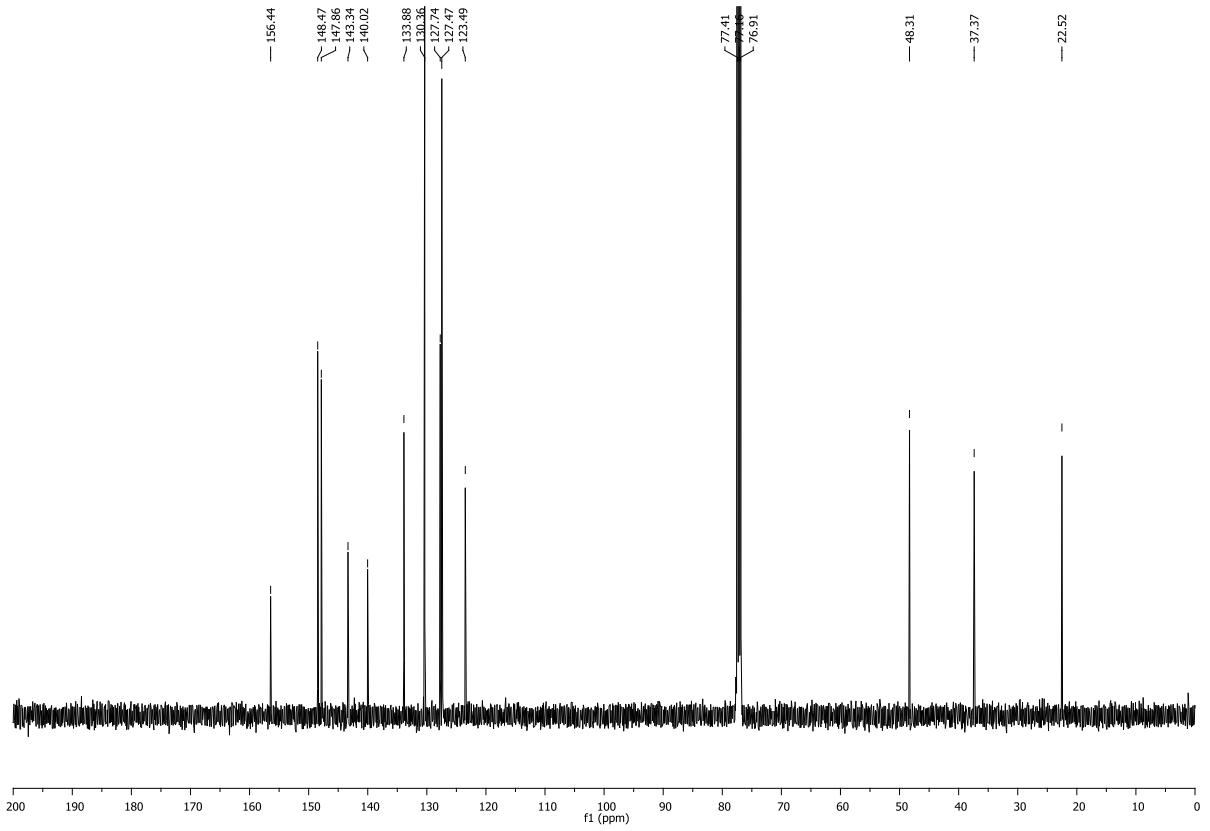

3449.40
3404.41
3071.55
3069.75
3063.91
3062.12
3056.13
3054.52
2940.00
2932.09
2898.84
2875.73
2875.22
2855.24
2760.06
2704.43
1577.96
1571.03
1564.45
1557.90
1516.45
1461.60
1405.85
717.30
565.05
558.35
CH3
NH
N
OCH3
1.00
1.03
0.96
1.83
1.02
1.85
1.03
2.81
2.00
2.84
f1 (ppm)
164.77
158.64
149.50
136.65
132.71
129.48
122.04
121.40
113.84
77.48
77.16
76.84
58.74
55.40
51.27
23.09
f1 (ppm)

6e

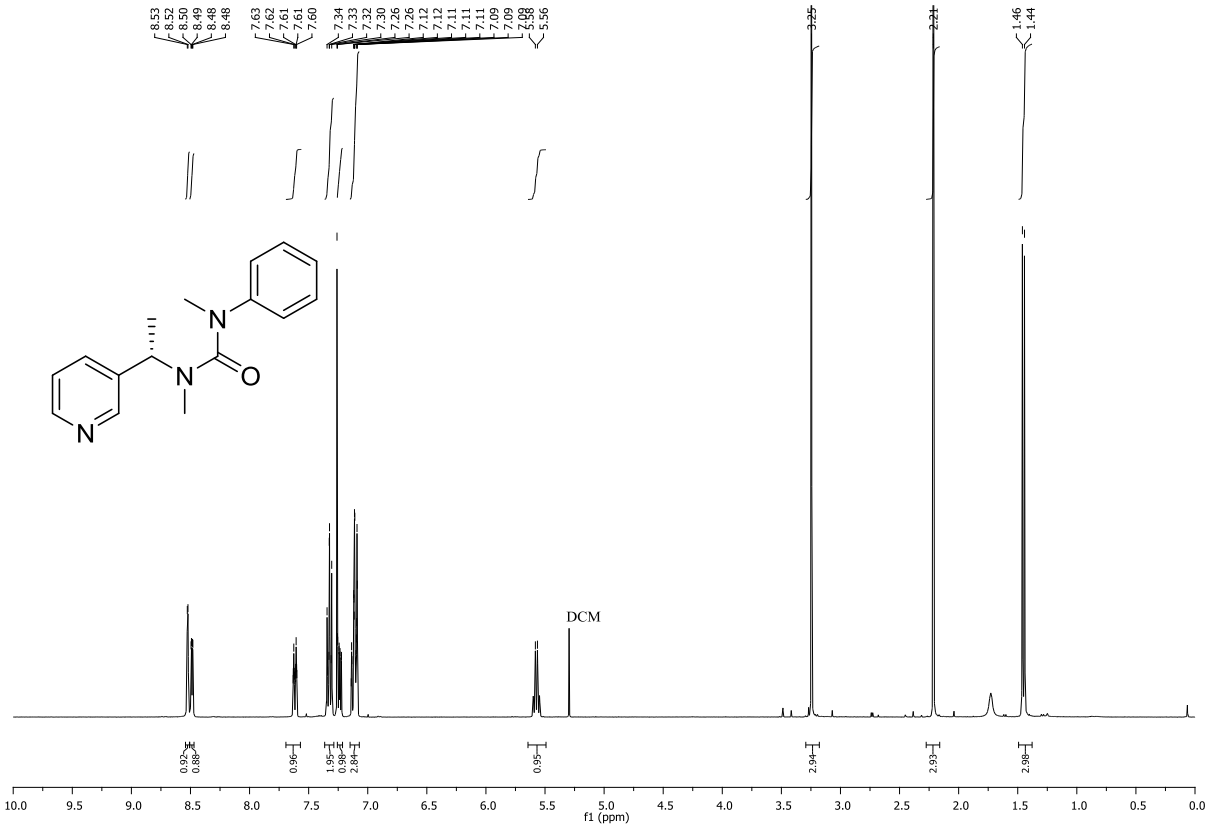

3454.17
3405.02
3084.35
3040.18
2999.22
2941.41
2886.10
2848.71
2751.89
2712.01
2307.05
2300.69
2293.20
2286.86
2282.77
2280.54
2279.87
2275.76
2273.35
2272.00
2265.61
2030.92
1981.46
1533.02
1527.09
1525.30
1519.35
1513.69
1448.16
1435.26
1407.33
1394.36
1039.90
949.95
766.91
NH
N
OCH3
1.14
1.13
0.99
2.86
1.87
1.23
2.11
3.59
1.00
1.04
2.29
1.91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
163.40
158.70
149.52
136.44
135.39
132.68
129.43
122.09
122.06
117.62
113.87
77.48
77.16
76.84
62.98
55.41
51.21
41.69
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

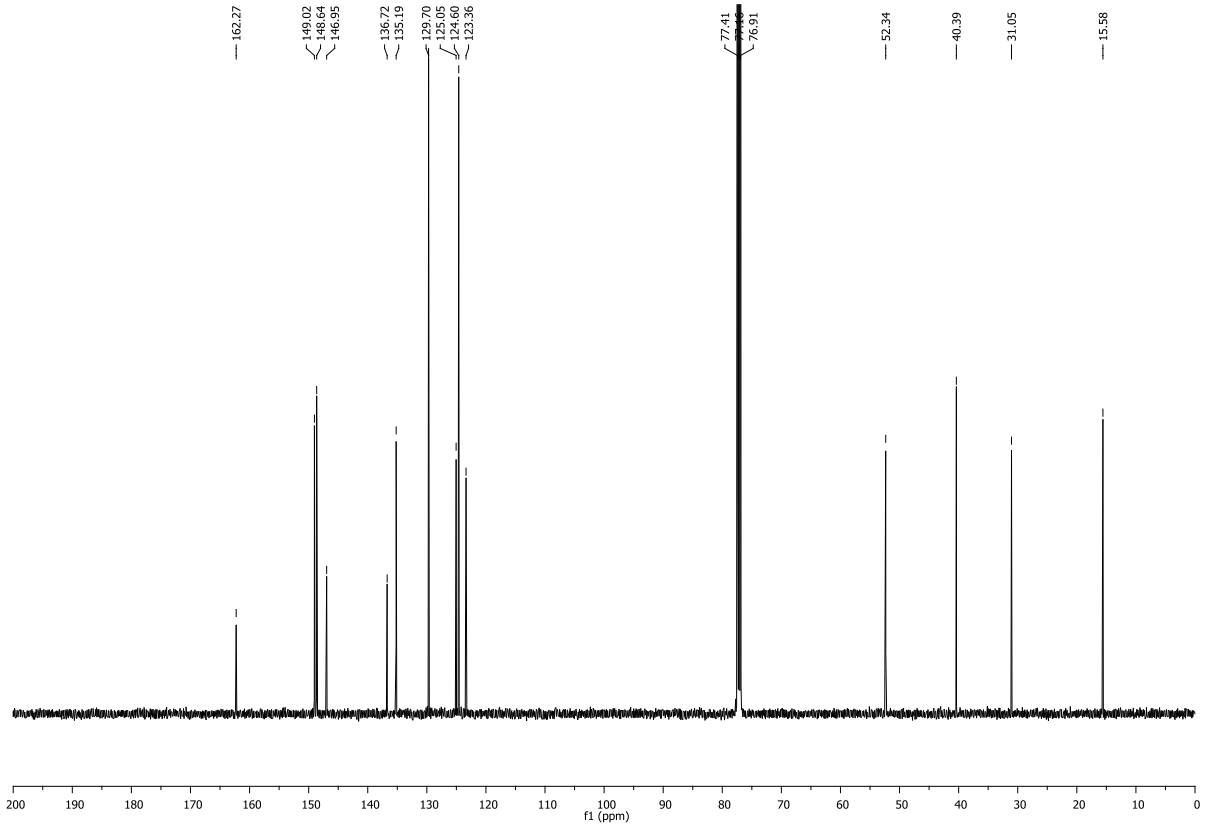
17a


8.51
8.50
8.48
8.47
8.47
8.46
7.53
7.47
7.45
7.43
7.35
7.33
7.27
7.27
7.26
7.26
7.25
7.25
7.25
7.24
6.30
5.04
5.03
5.01
4.55
4.53
3.25
1.37
1.35
N
N
H
O
N
0.89
0.86
0.93
1.89
0.98
3.77
1.94
0.94
0.95
0.91
2.89
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

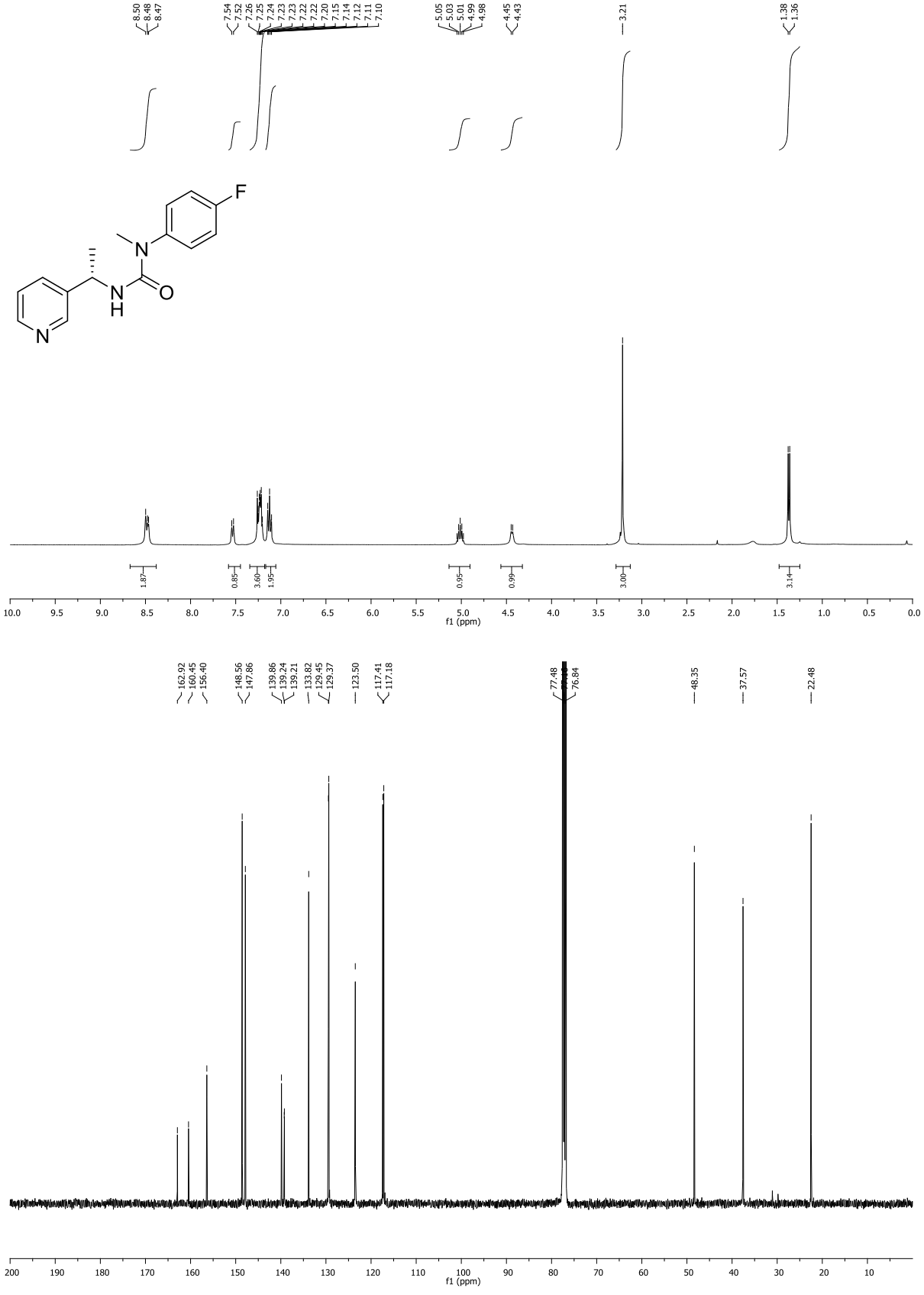

156.44
148.47
147.86
143.34
140.02
133.88
130.36
127.74
127.47
123.49
77.41
77.16
76.91
48.31
37.37
22.52
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

7a

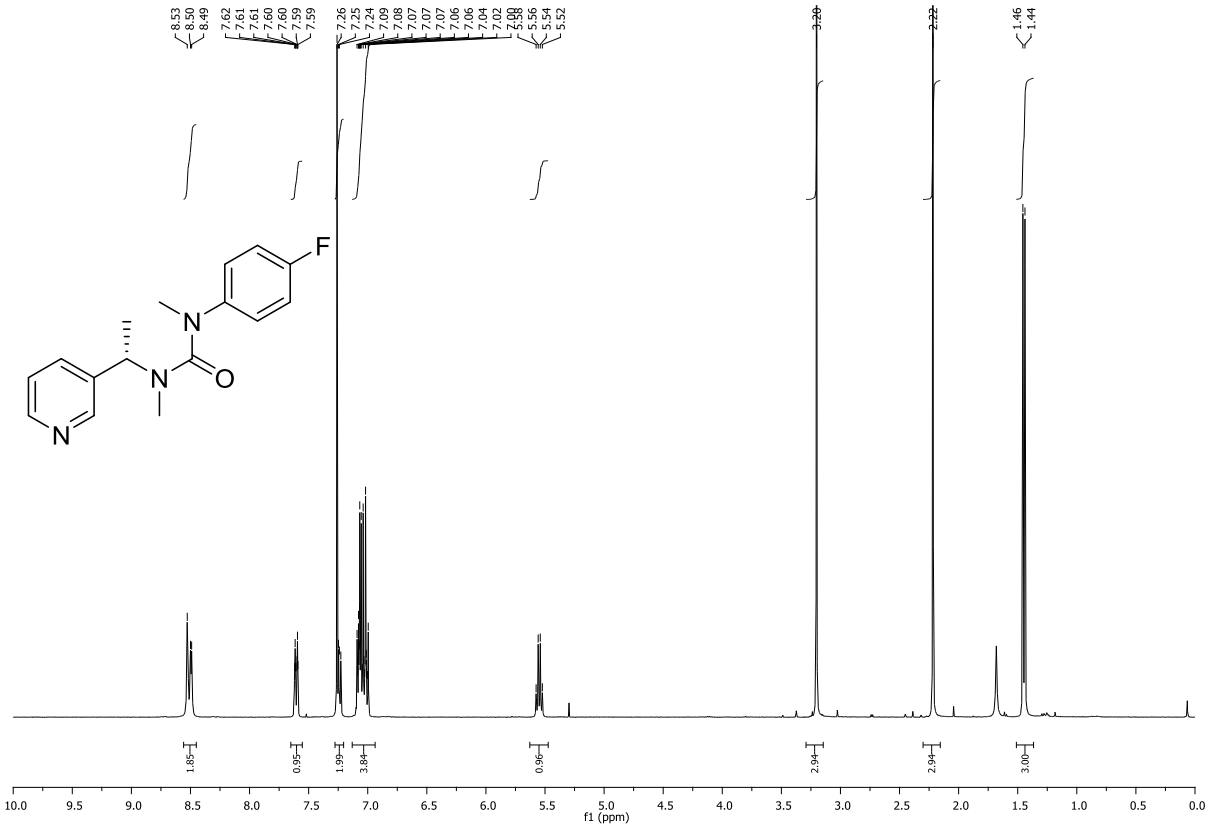

8.53
8.52
8.50
8.49
8.48
8.48
8.48
7.63
7.62
7.61
7.61
7.60
7.34
7.33
7.32
7.30
7.26
7.26
7.12
7.12
7.11
7.11
7.11
7.09
7.09
5.58
5.56
3.25
2.21
1.46
1.44
DCM
0.92
0.88
0.96
1.95
0.98
2.04
0.95
2.94
2.93
2.98
f1 (ppm)

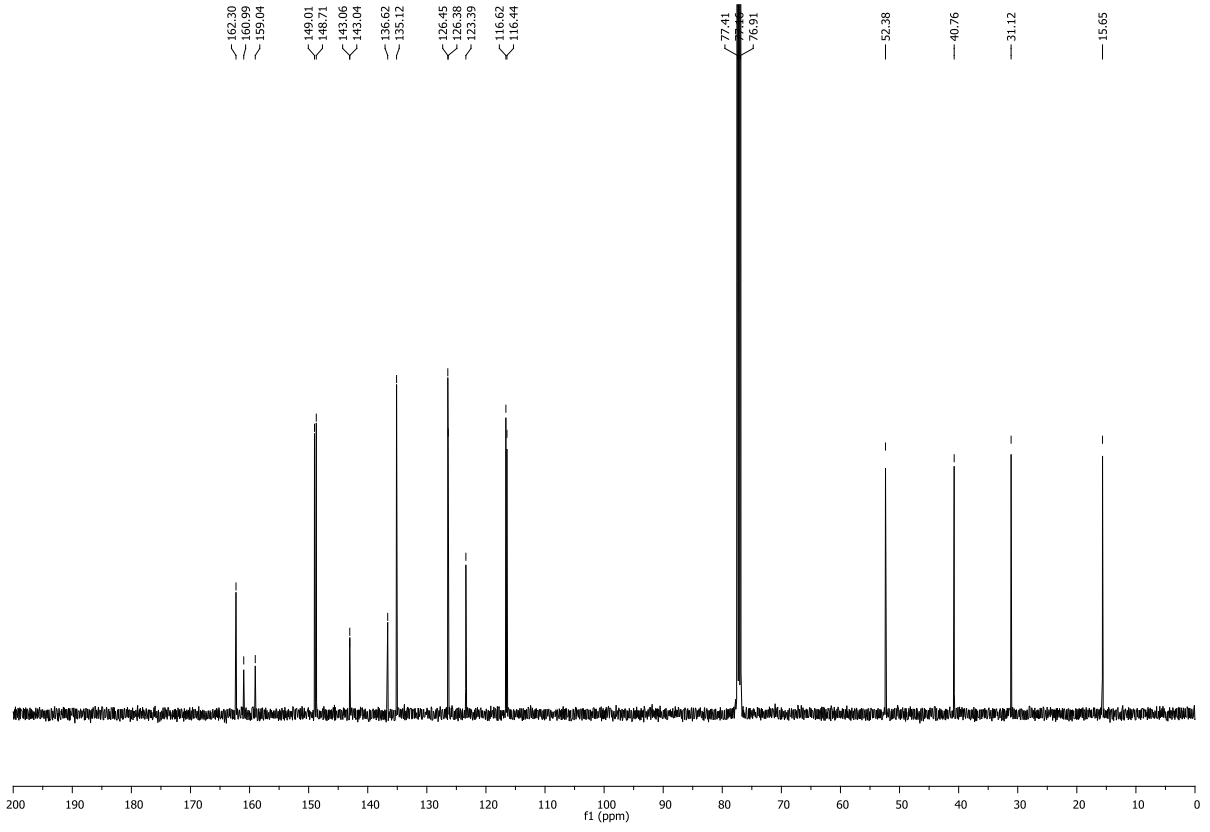

162.27
149.02
148.64
146.95
136.72
135.19
129.70
125.05
124.60
123.36
77.41
77.16
76.91
52.34
40.39
31.05
15.58
f1 (ppm)

17b

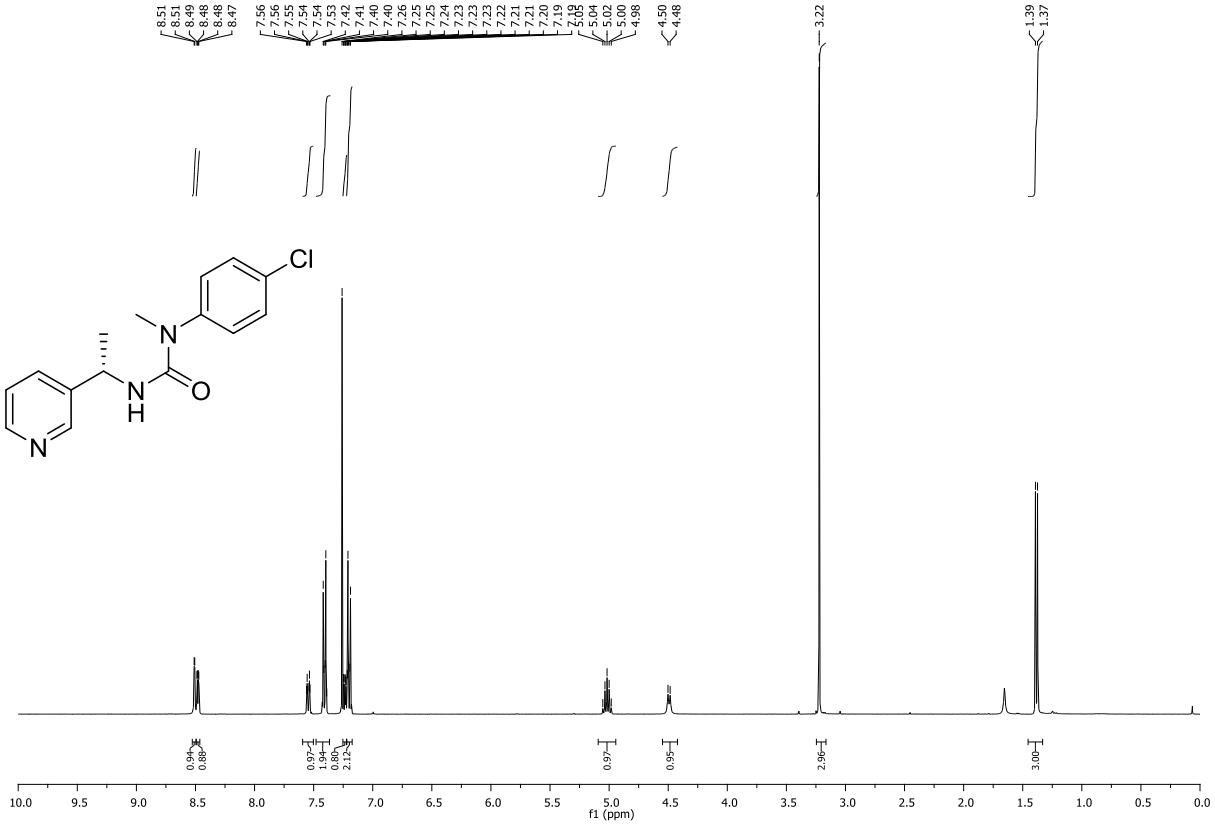

8.50
8.48
8.47
7.54
7.52
7.26
7.25
7.24
7.23
7.23
7.22
7.22
7.20
7.15
7.14
7.12
7.11
7.10
5.05
5.03
5.01
4.99
4.98
4.45
4.43
3.21
1.38
1.36
F
N
N
H
O
N
1.87
0.85
3.60
1.95
0.95
0.99
3.00
3.14
f1 (ppm)
162.92
160.45
156.40
148.56
147.86
139.86
139.24
139.21
133.82
129.45
129.37
123.50
117.41
117.18
77.48
76.84
48.35
37.57
22.48
f1 (ppm)

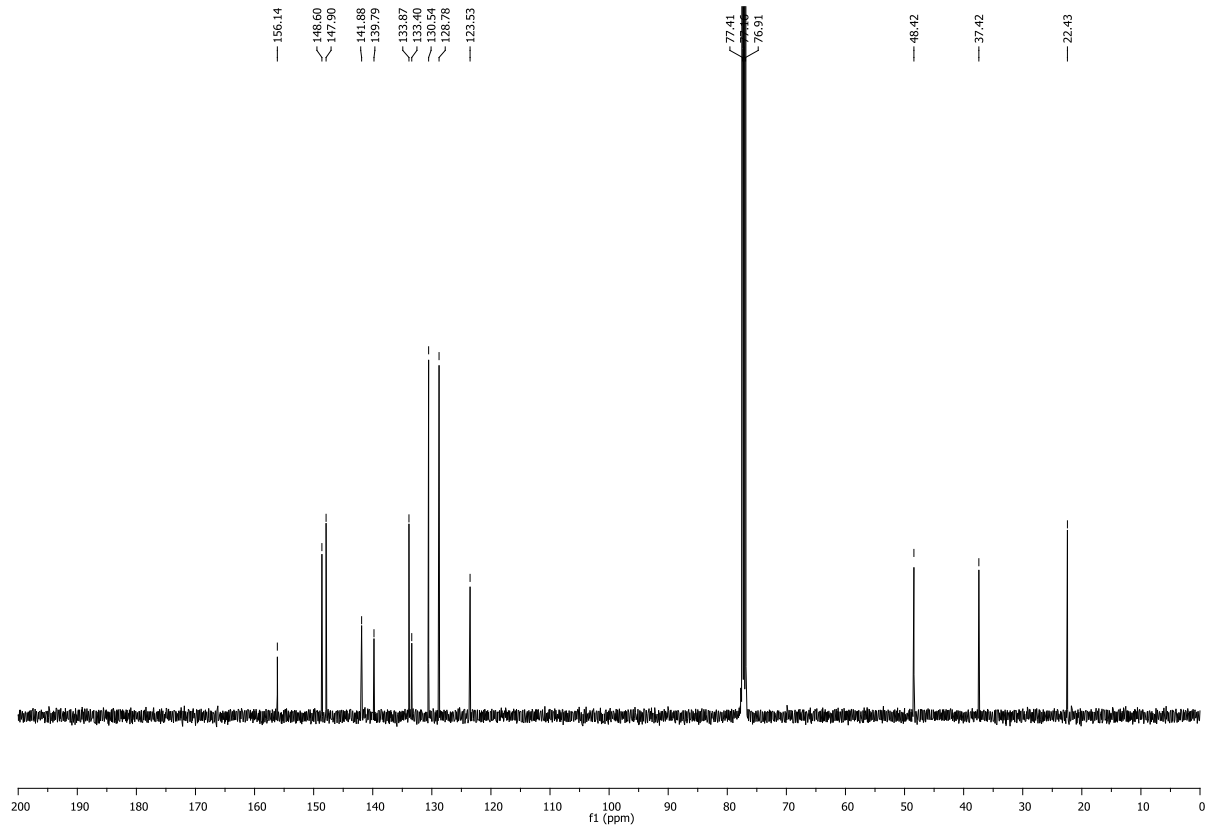
7b


8.53
8.50
8.49
7.62
7.61
7.61
7.60
7.60
7.59
7.59
7.26
7.25
7.24
7.09
7.08
7.07
7.07
7.07
7.06
7.06
7.04
7.02
5.58
5.56
5.54
5.52
3.20
2.22
1.46
1.44
F
N
N
O
N
1.85
0.95
1.99
3.84
0.96
2.94
2.94
3.00
f1 (ppm)

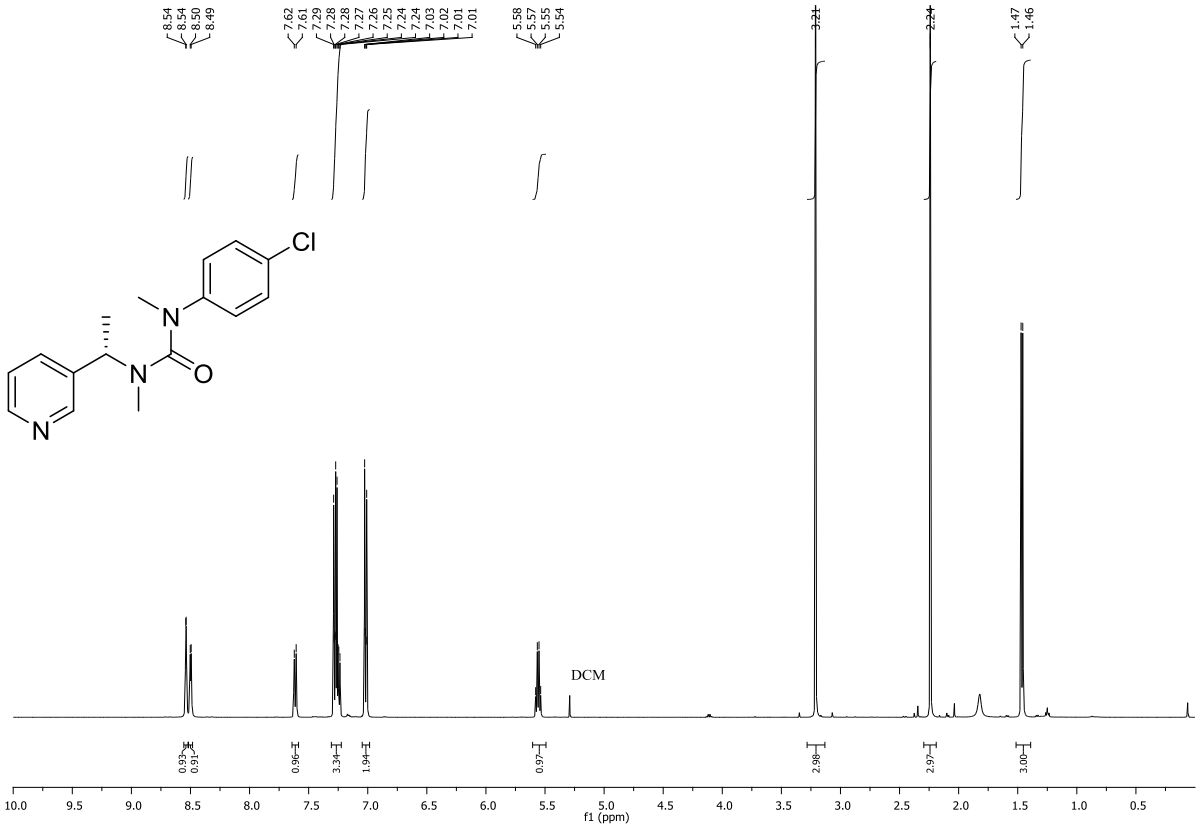

162.30
160.99
159.04
149.01
148.71
143.06
143.04
136.62
135.12
126.45
126.38
123.39
116.62
116.44
77.41
76.91
52.38
40.76
31.12
15.65
f1 (ppm)

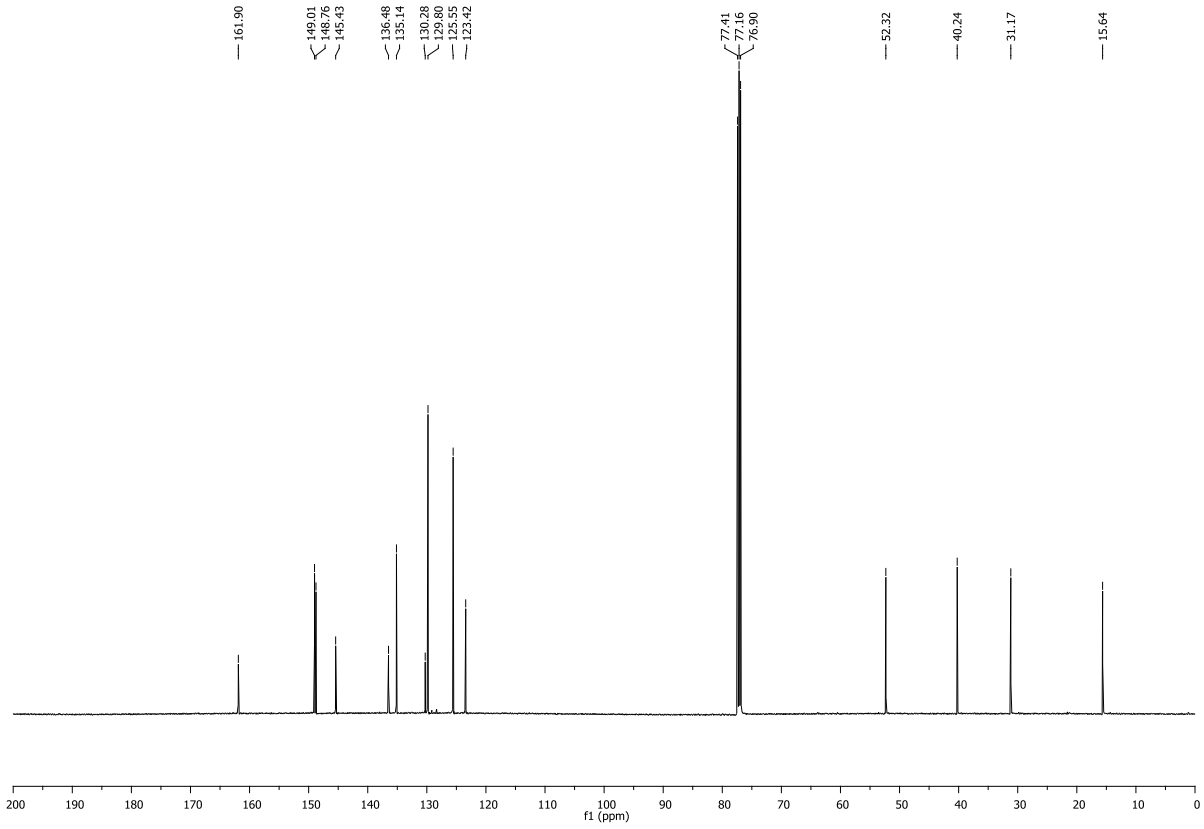
17c


8.51
8.51
8.49
8.48
8.48
8.47
7.56
7.56
7.55
7.54
7.54
7.53
7.42
7.41
7.40
7.40
7.26
7.25
7.25
7.24
7.23
7.23
7.23
7.22
7.21
7.21
7.20
7.19
5.04
5.02
5.00
4.98
4.50
4.48
3.22
1.39
1.37
Cl
N
N
H
O
N
0.94
0.88
0.97
1.94
0.80
2.12
0.97
0.95
2.96
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

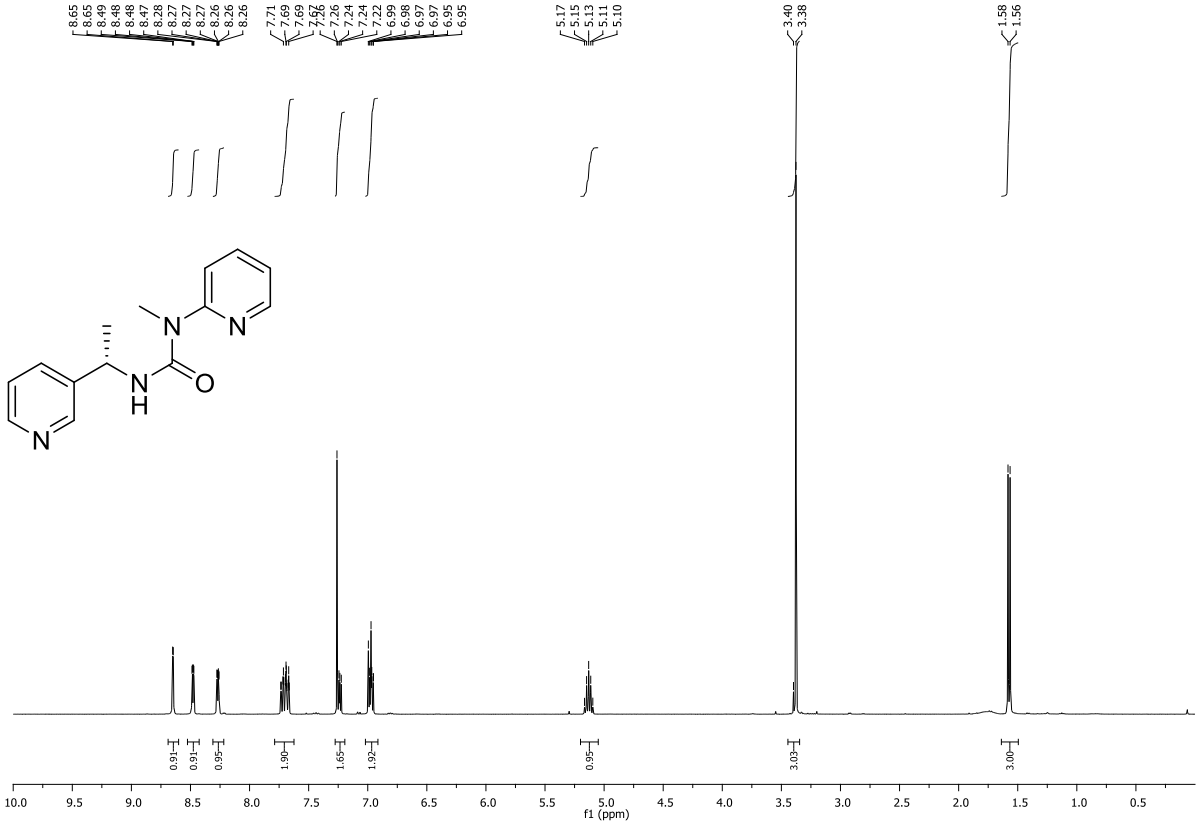

156.14
148.60
147.90
141.88
139.79
133.87
133.40
130.54
128.78
123.53
77.41
77.16
76.91
48.42
37.42
22.43
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

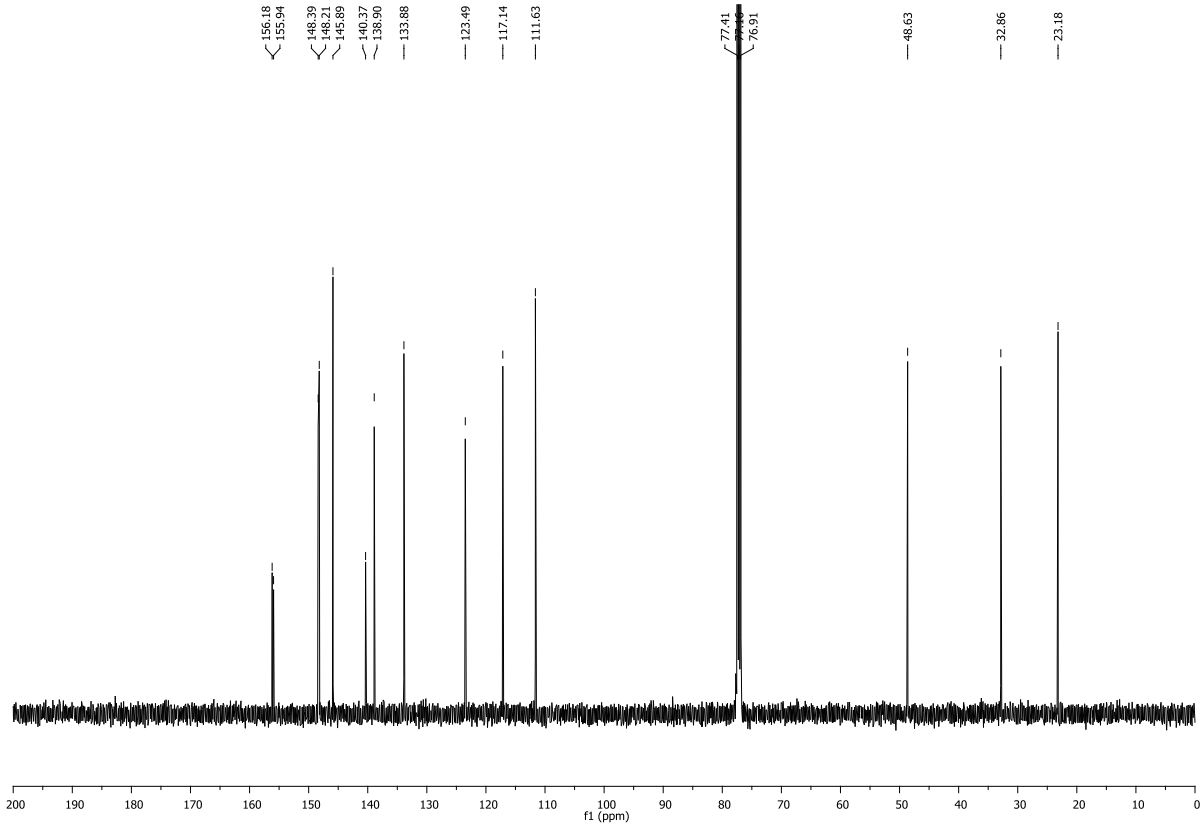
7c


8.54
8.54
8.50
8.49
7.62
7.61
7.29
7.28
7.28
7.27
7.26
7.25
7.24
7.24
7.03
7.02
7.01
7.01
5.58
5.57
5.55
5.54
3.21
2.24
1.47
1.46
Cl
N
N
O
N
DCM
0.93
0.91
0.96
3.34
1.94
0.97
2.98
2.97
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


161.90
149.01
148.76
145.43
136.48
135.14
130.28
129.80
125.55
123.42
77.41
77.16
76.90
52.32
40.24
31.17
15.64
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

17d


8.65
8.65
8.49
8.48
8.48
8.47
8.28
8.27
8.27
8.26
8.26
8.26
7.71
7.69
7.69
7.26
7.26
7.24
7.24
7.22
6.99
6.98
6.97
6.97
6.95
6.95
5.17
5.15
5.13
5.11
5.10
3.40
3.38
1.58
1.56
N
N
N
H
O
N
0.91
0.91
0.95
1.90
1.65
1.92
0.95
3.03
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


156.18
155.94
148.39
148.21
145.89
140.37
138.90
133.88
123.49
117.14
111.63
77.41
77.16
76.91
48.63
32.86
23.18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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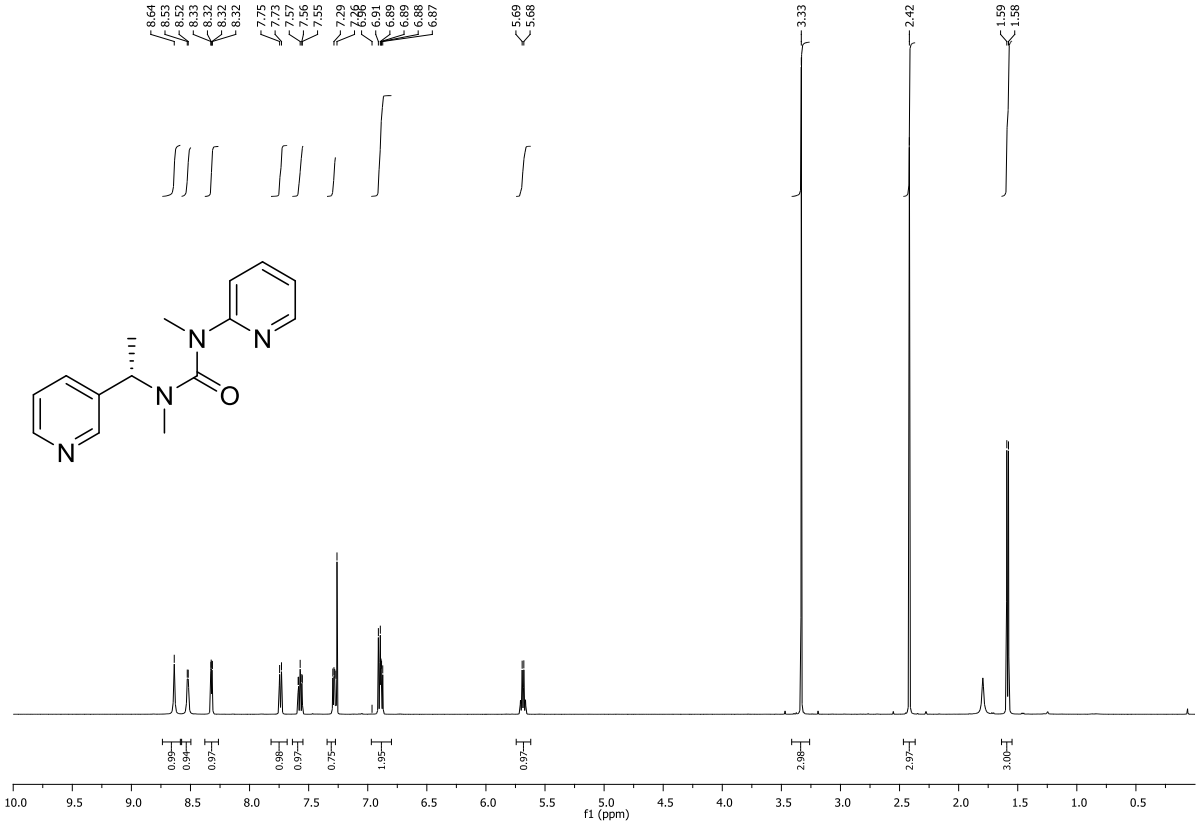
40
30
20
10
0
f1 (ppm)

7d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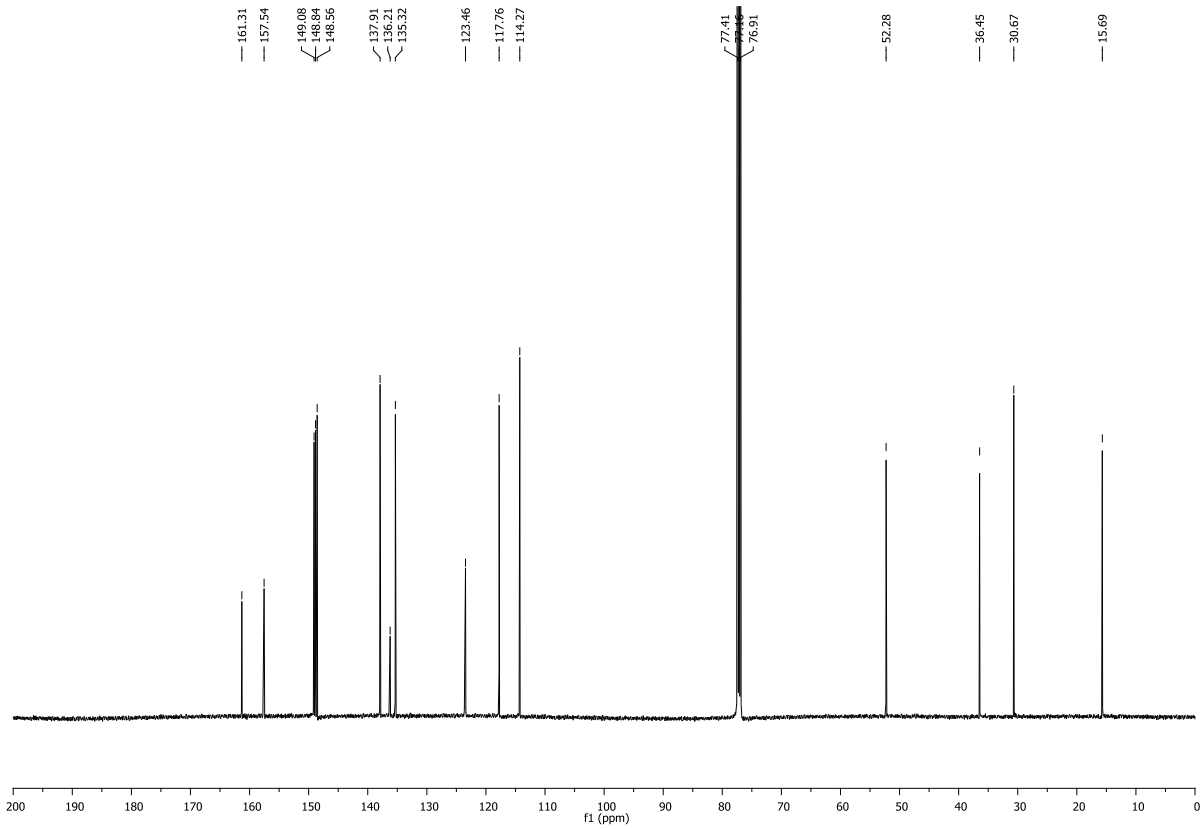
8.32
8.32
8.32
7.75
7.73
7.57
7.56
7.55
7.29
6.91
6.89
6.89
6.88
6.87
5.69
5.68
3.33
2.42
1.59
1.58
0.99
0.94
0.97
0.98
0.97
0.75
1.95
0.97
2.98
2.97
3.00
f1 (ppm)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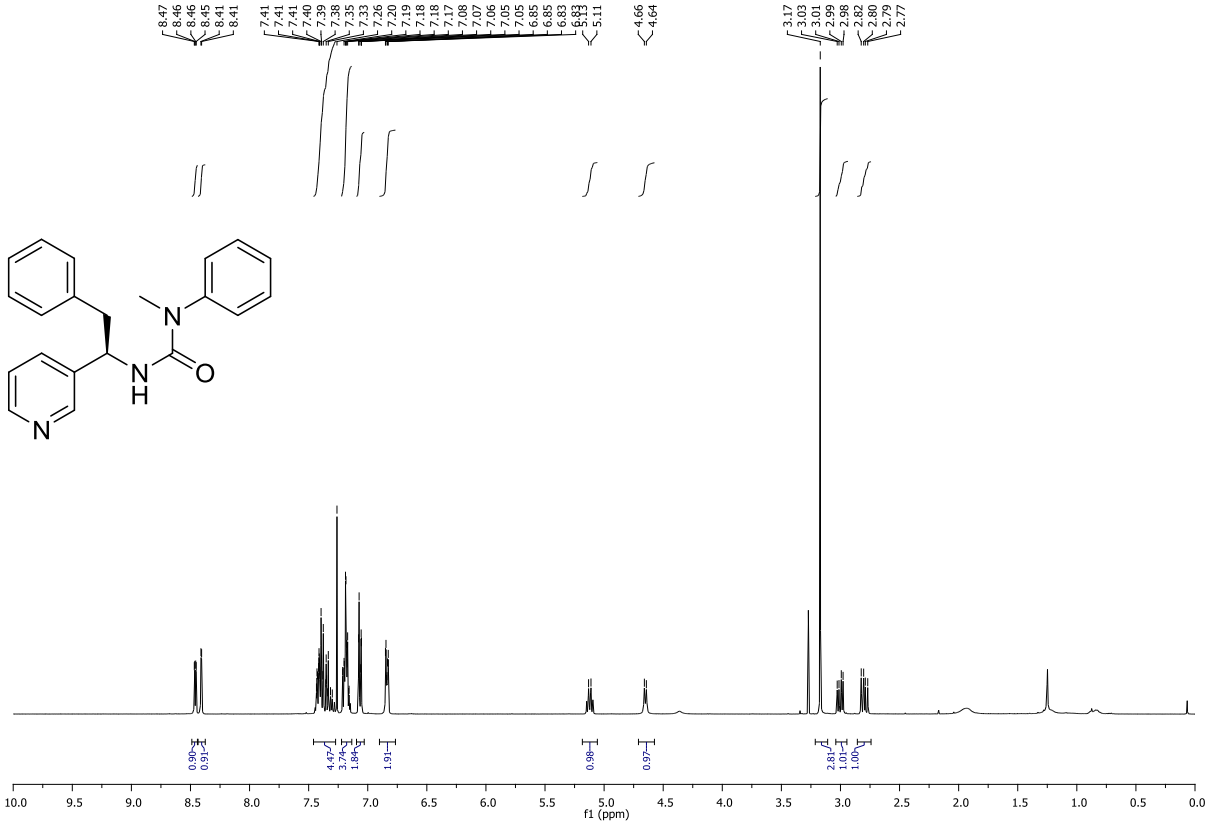
148.84
148.56
137.91
136.21
135.32
123.46
117.76
114.27
77.41
77.16
76.91
52.28
36.45
30.67
15.69
f1 (ppm)

17e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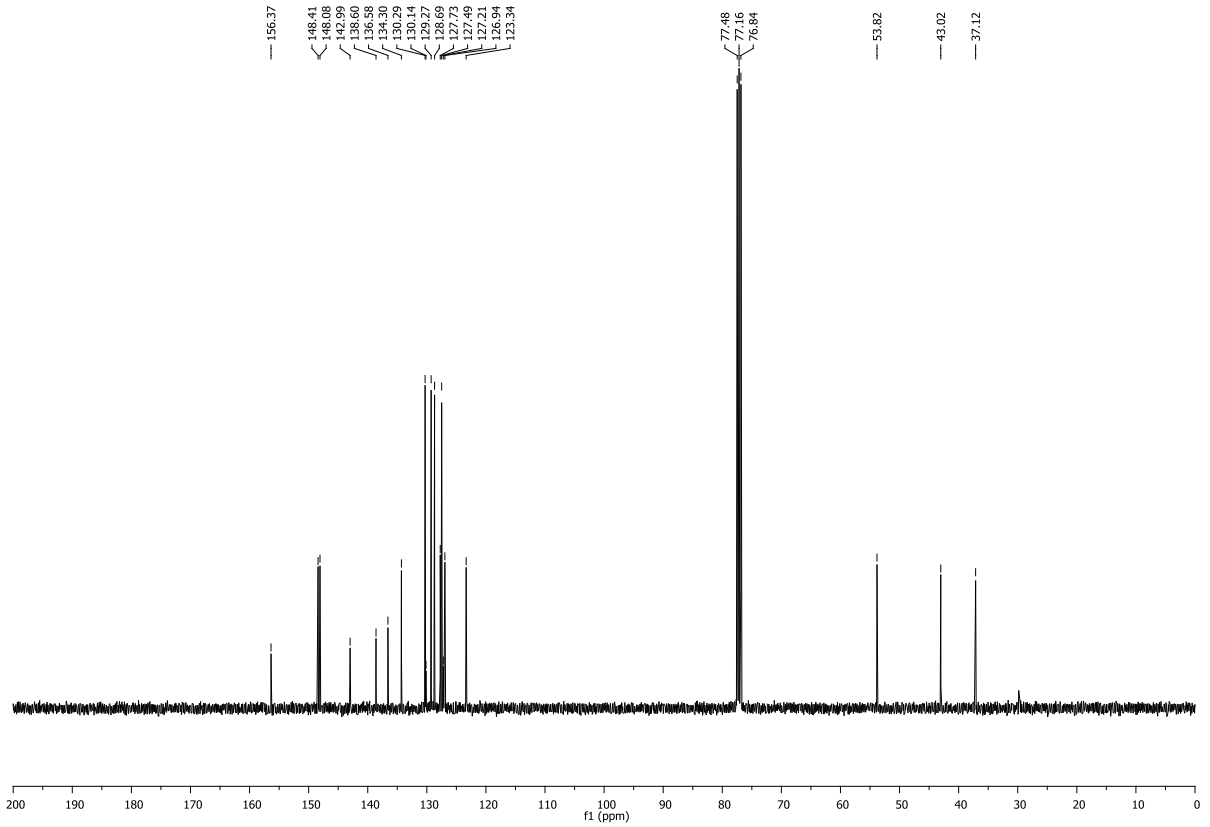
8.41
7.41
7.41
7.41
7.40
7.39
7.38
7.35
7.33
7.26
7.20
7.19
7.18
7.18
7.17
7.08
7.07
7.06
7.05
7.05
6.85
6.85
6.83
6.83
5.13
5.11
4.66
4.64
3.17
3.03
3.01
2.99
2.98
2.82
2.80
2.79
2.77
N
N
H
O
N
0.90
0.91
4.47
3.70
1.84
1.91
0.98
0.97
2.81
1.01
1.00
f1 (ppm)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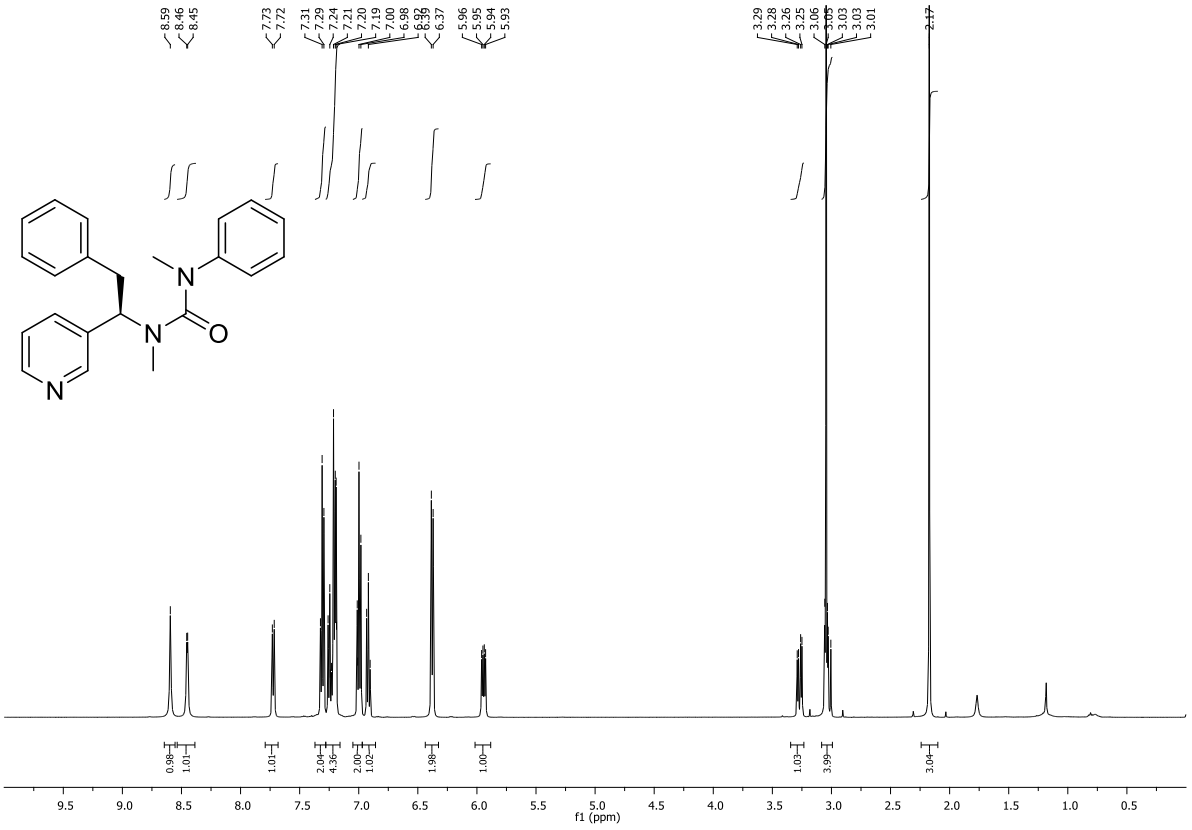
136.58
134.30
130.29
130.14
129.27
128.69
127.73
127.49
127.21
126.94
123.34
77.48
77.16
76.84
53.82
43.02
37.12
f1 (ppm)

7e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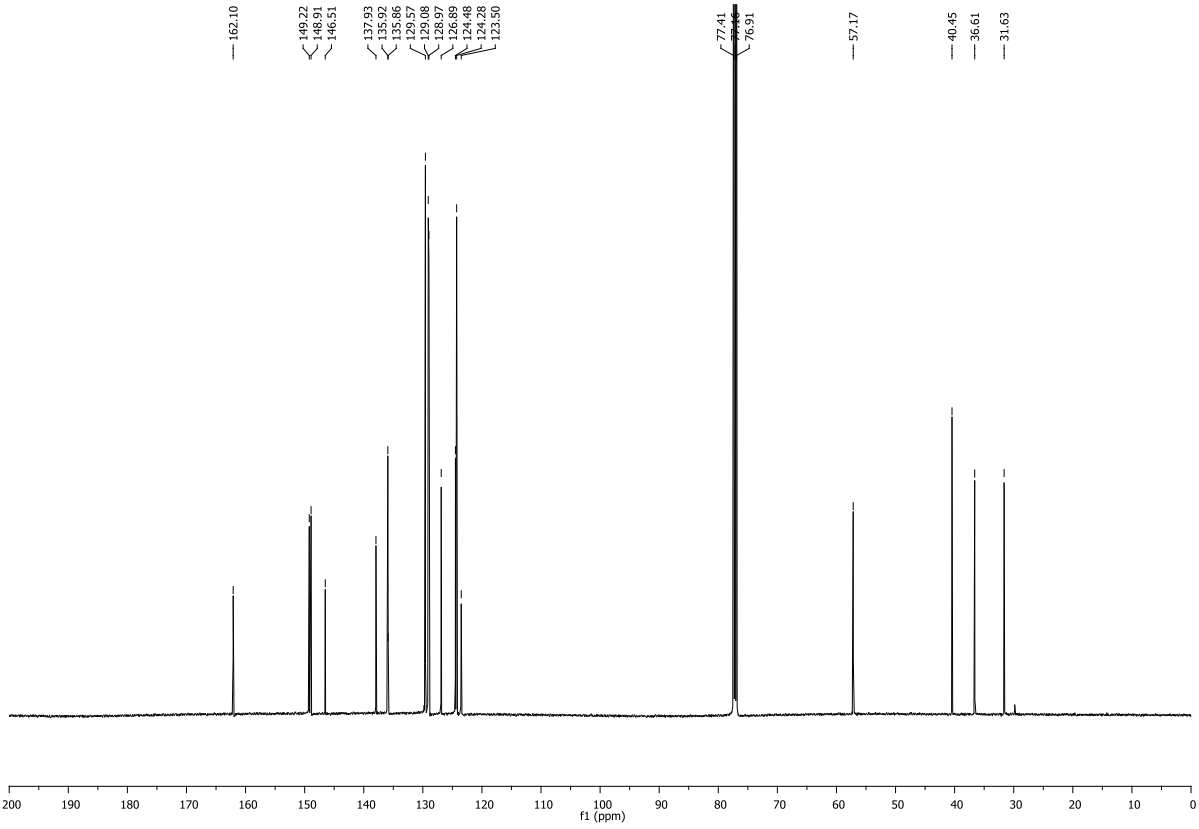
8.46
8.45
7.73
7.72
7.31
7.29
7.24
7.21
7.20
7.19
7.00
6.98
6.39
6.37
5.96
5.95
5.94
5.93
3.29
3.28
3.26
3.25
3.06
3.05
3.03
3.03
3.01
2.17
N
N
O
N
0.98
1.01
1.01
2.04
4.36
2.00
1.02
1.98
1.00
1.03
3.99
3.04
f1 (ppm)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149.22
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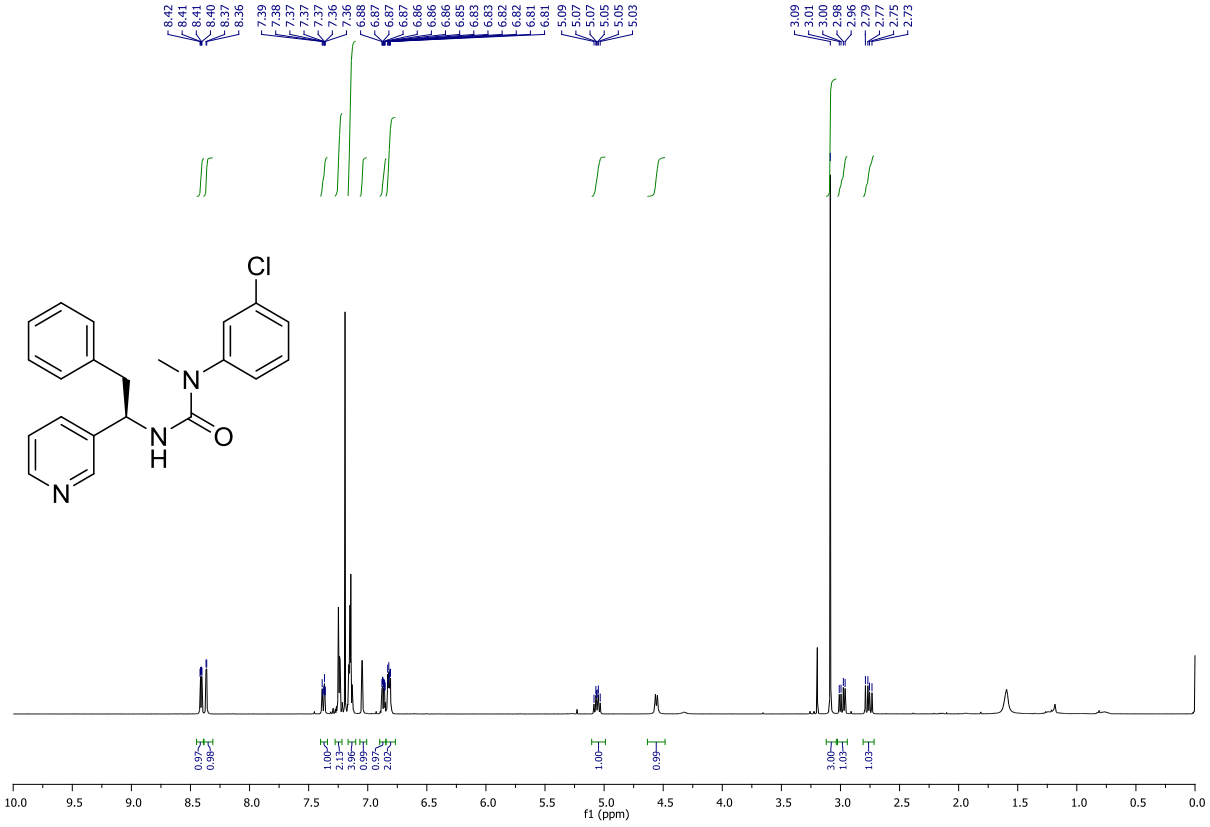
135.92
135.86
129.57
129.08
128.97
126.89
124.48
124.28
123.50
77.41
77.16
76.91
57.17
40.45
36.61
31.63
f1 (ppm)

17f


8.42
8.41
8.41
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8.36
7.39
7.38
7.37
7.37
7.37
7.36
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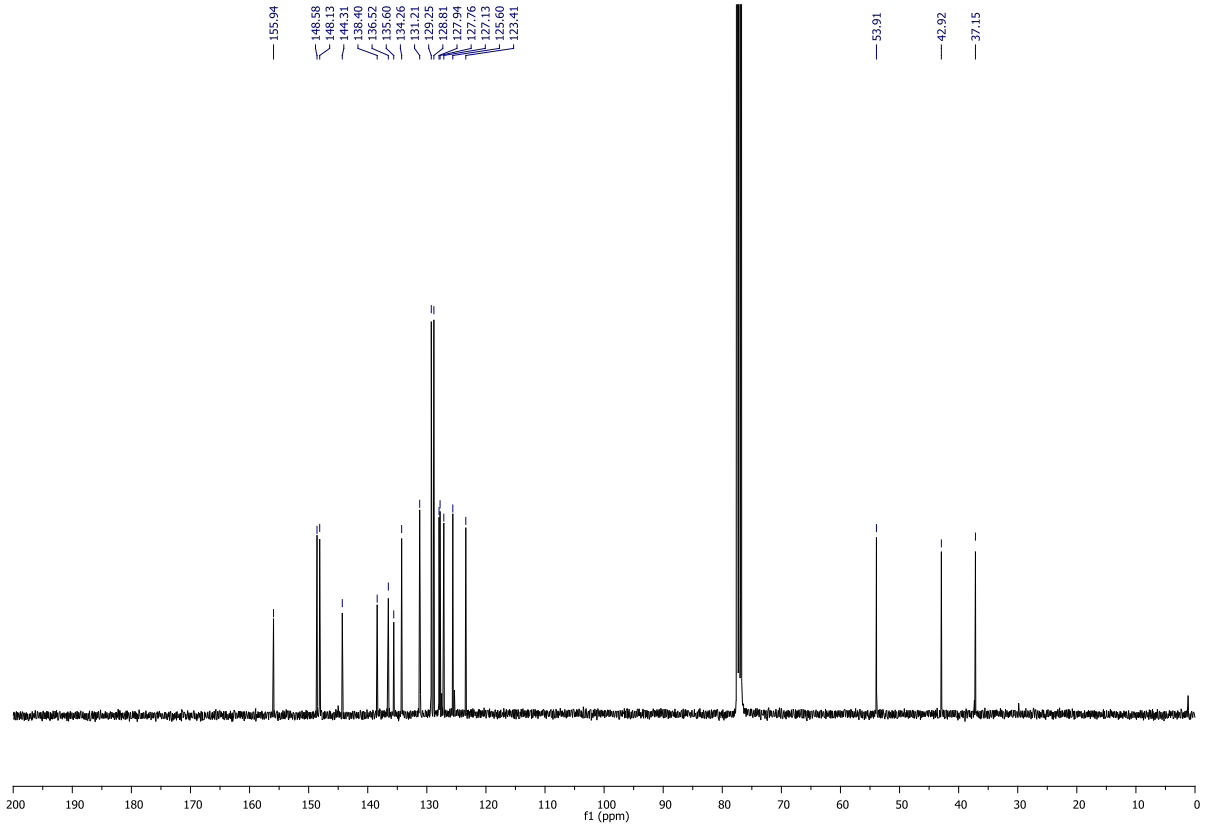
6.88
6.87
6.87
6.87
6.86
6.86
6.86
6.85
6.83
6.83
6.82
6.82
6.81
6.81
5.09
5.07
5.07
5.05
5.05
5.03
3.09
3.01
3.00
2.98
2.96
2.79
2.77
2.75
2.73
Cl
N
N
H
O
N
0.97
0.98
1.00
2.19
3.96
0.99
0.97
2.02
1.00
0.99
3.00
1.03
1.03
f1 (ppm)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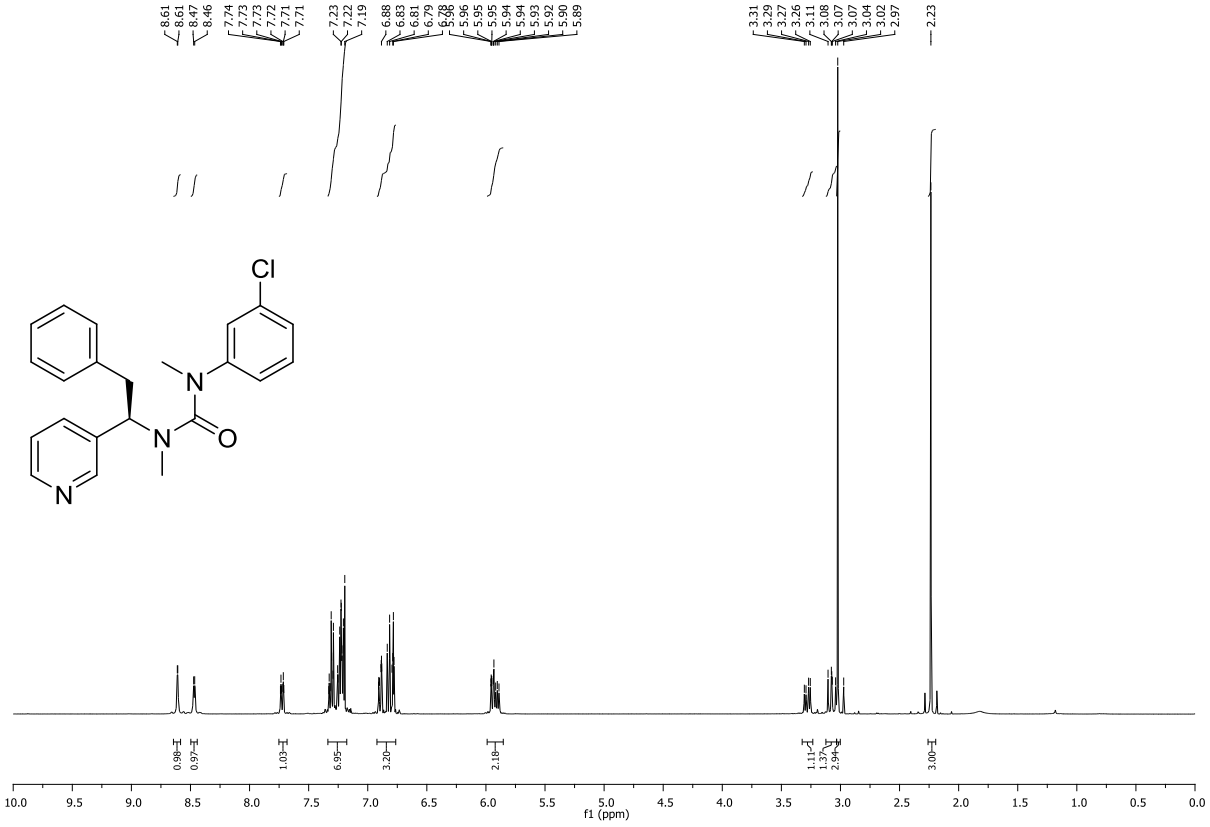
148.58
148.13
144.31
138.40
136.52
135.60
134.26
131.21
129.25
128.81
127.94
127.76
127.13
125.60
123.41
53.91
42.92
37.15
f1 (ppm)

7f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8.61
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8.46
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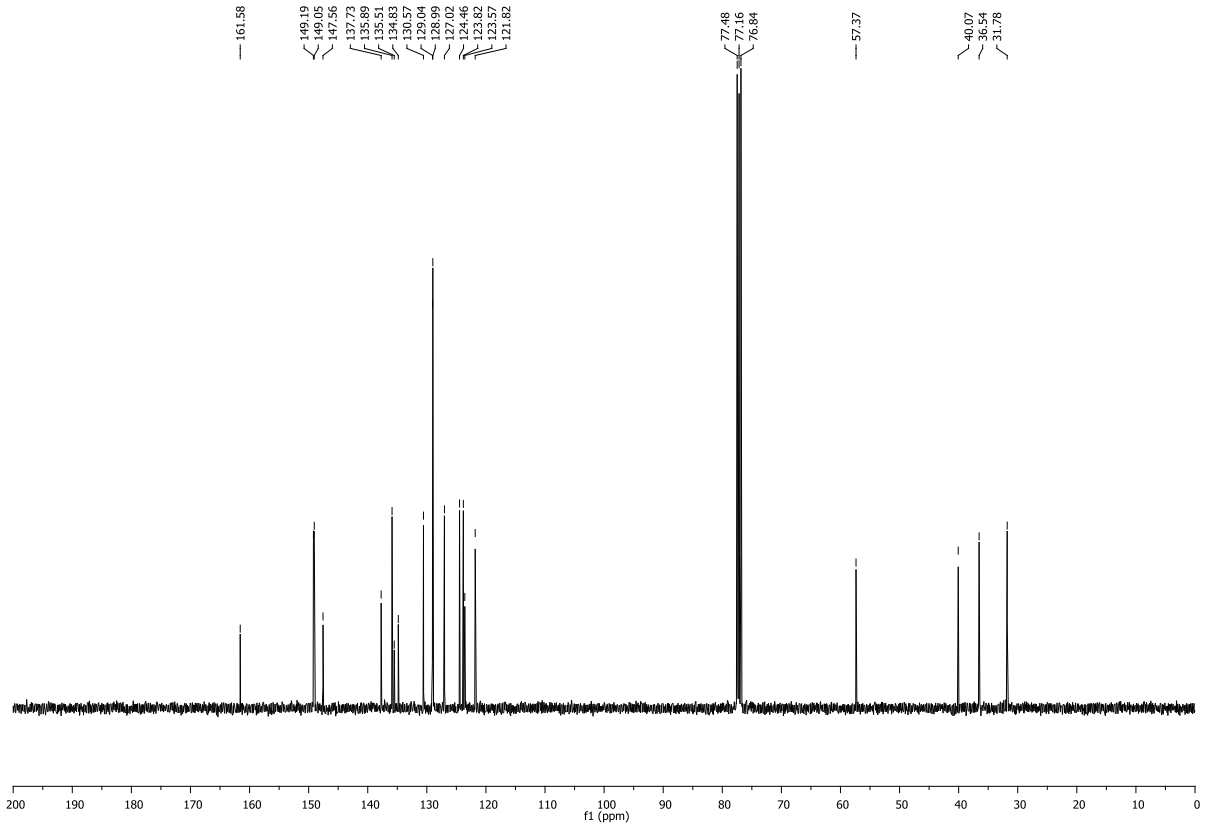
7.73
7.73
7.72
7.71
7.71
7.23
7.22
7.19
6.88
6.83
6.81
6.79
5.96
5.95
5.95
5.94
5.94
5.93
5.92
5.90
5.89
3.31
3.29
3.27
3.26
3.11
3.08
3.07
3.07
3.04
3.02
2.97
2.23
Cl
N
N
O
N
0.98
0.97
1.03
6.95
3.20
2.18
1.11
1.37
2.94
3.00
f1 (ppm)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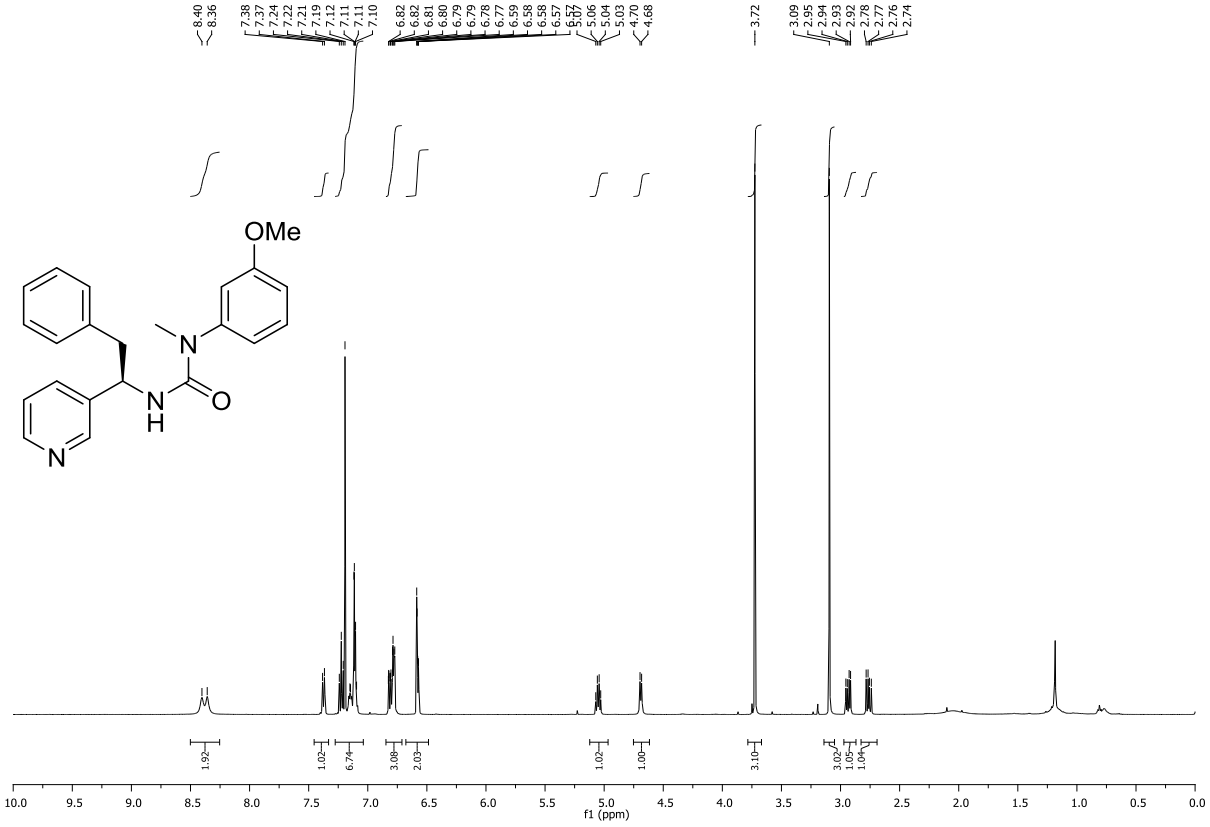
149.19
149.05
147.56
137.73
135.89
135.51
134.83
130.57
129.04
128.99
127.02
124.46
123.82
123.57
121.82
77.48
77.16
76.84
57.37
40.07
36.54
31.78
f1 (ppm)

17g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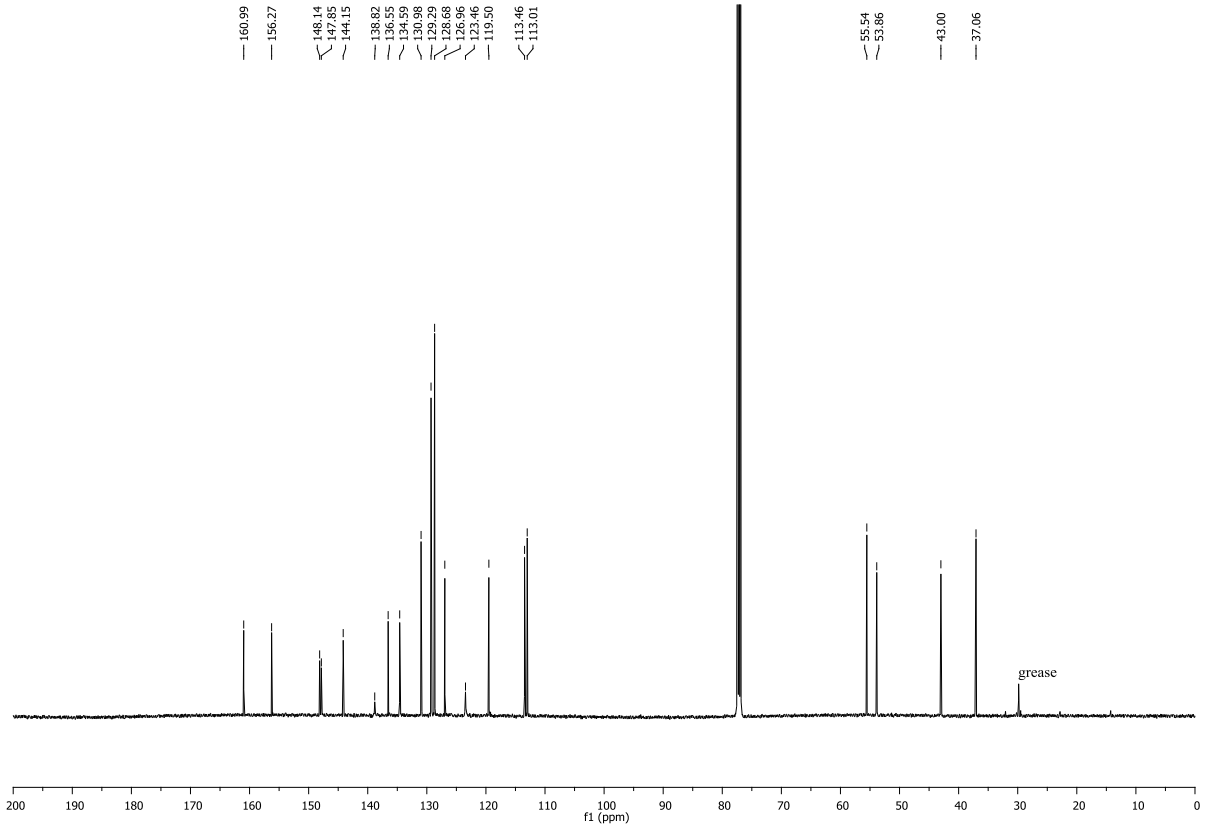
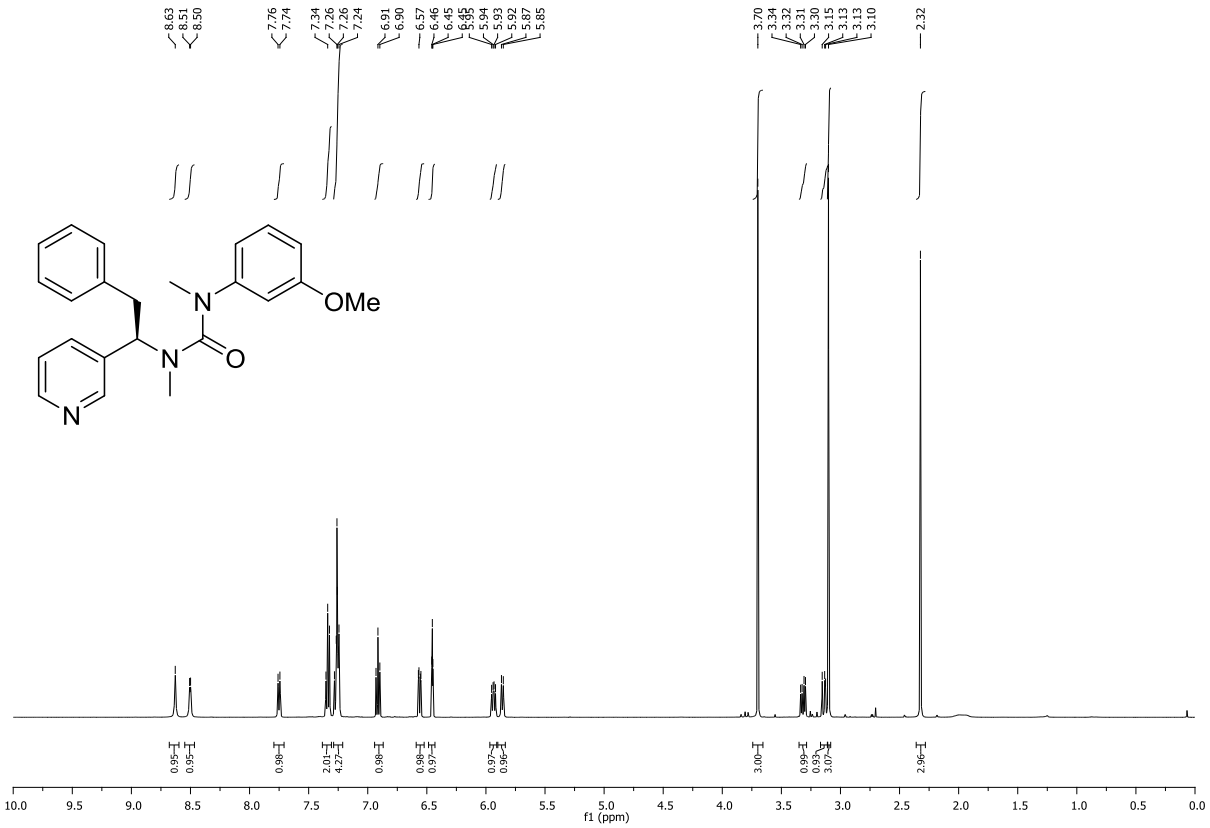
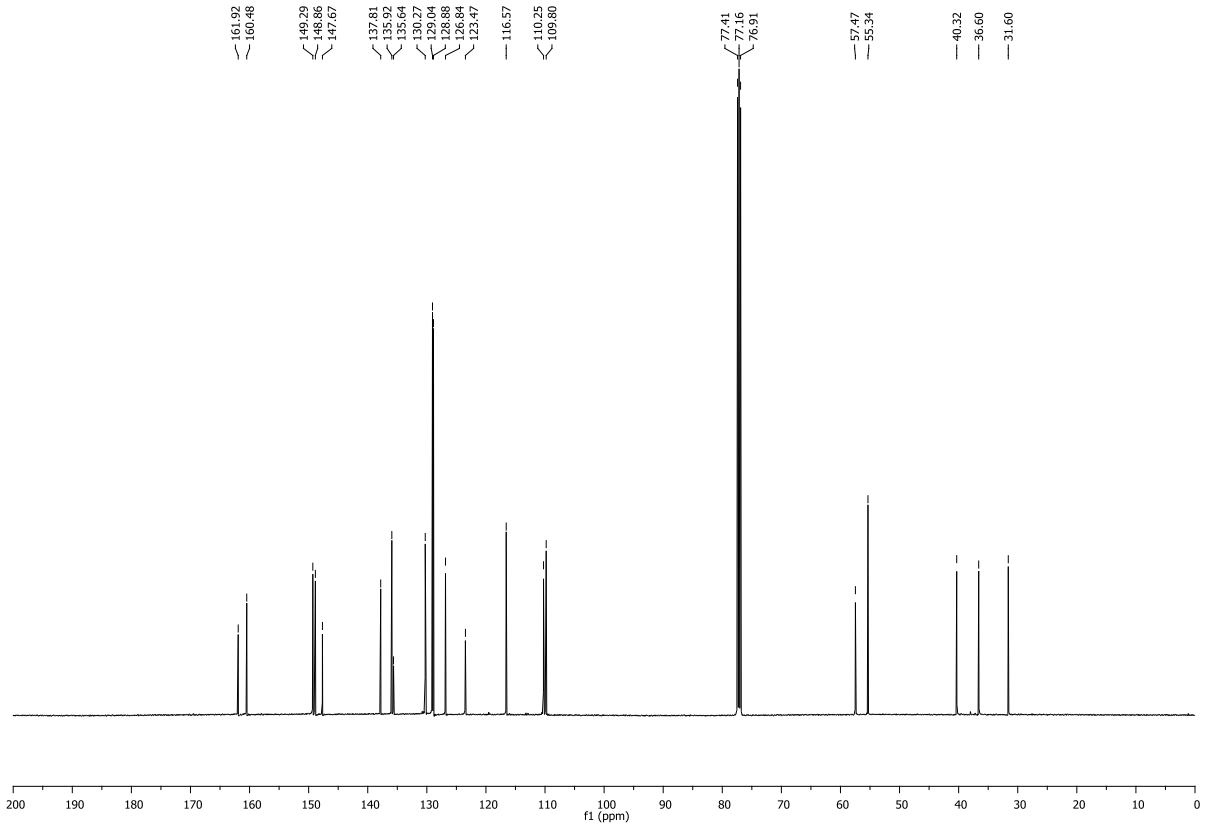
8.36
7.38
7.37
7.24
7.22
7.21
7.19
7.12
7.11
7.11
7.10
6.82
6.82
6.81
6.80
6.79
6.79
6.78
6.77
6.59
6.58
6.58
6.57
5.07
5.06
5.04
5.03
4.70
4.68
3.72
3.09
2.95
2.94
2.93
2.92
2.78
2.77
2.76
2.74
OMe
N
N
H
O
N
1.92
1.02
6.74
3.08
2.03
1.02
1.00
3.10
3.02
1.05
1.04
f1 (ppm)


160.99
156.27
148.14
147.85
144.15
138.82
136.55
134.59
130.98
129.29
128.68
126.96
123.46
119.50
113.46
113.01
55.54
53.86
43.00
37.06
grease
f1 (ppm)

7g


8.63
8.51
8.50
7.76
7.74
7.34
7.26
7.26
7.24
6.91
6.90
6.57
6.46
6.45
5.94
5.93
5.92
5.87
5.85
3.70
3.34
3.32
3.31
3.30
3.15
3.13
3.10
2.32
OMe
N
N
O
N
f1 (ppm)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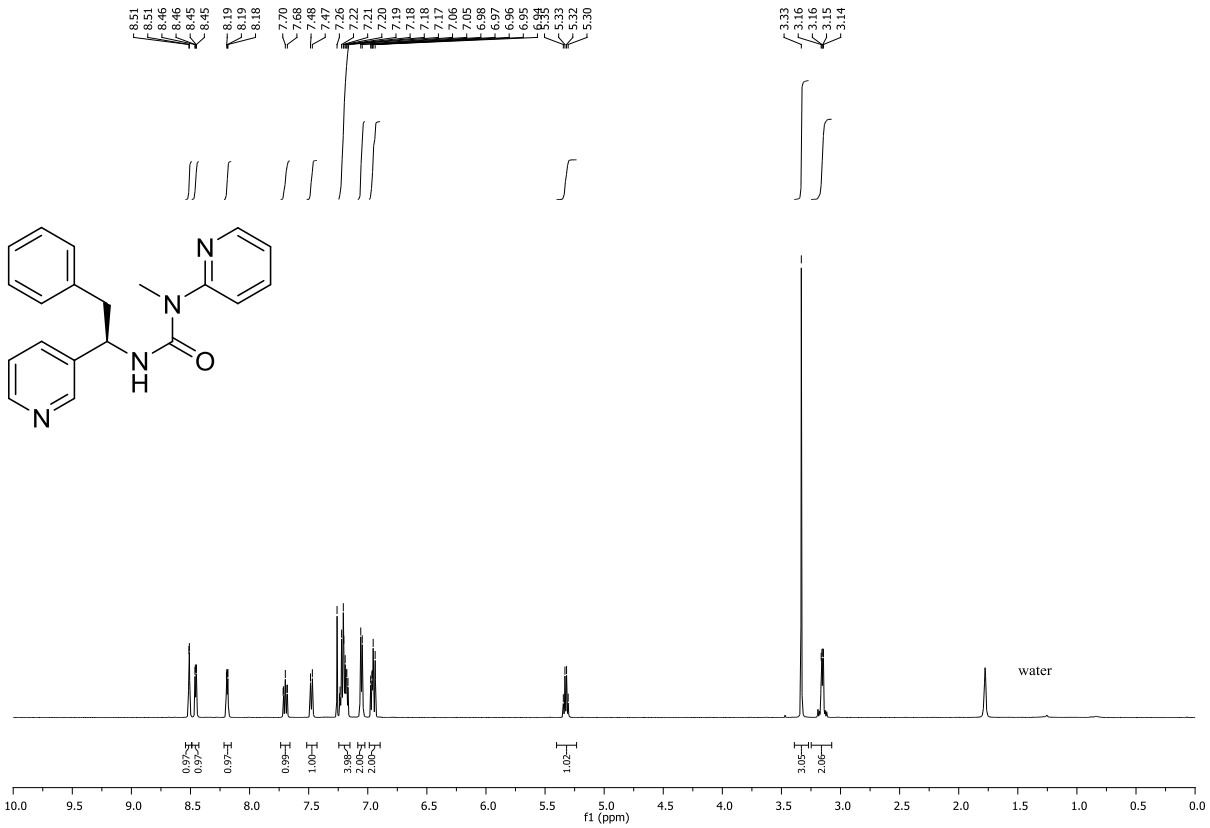
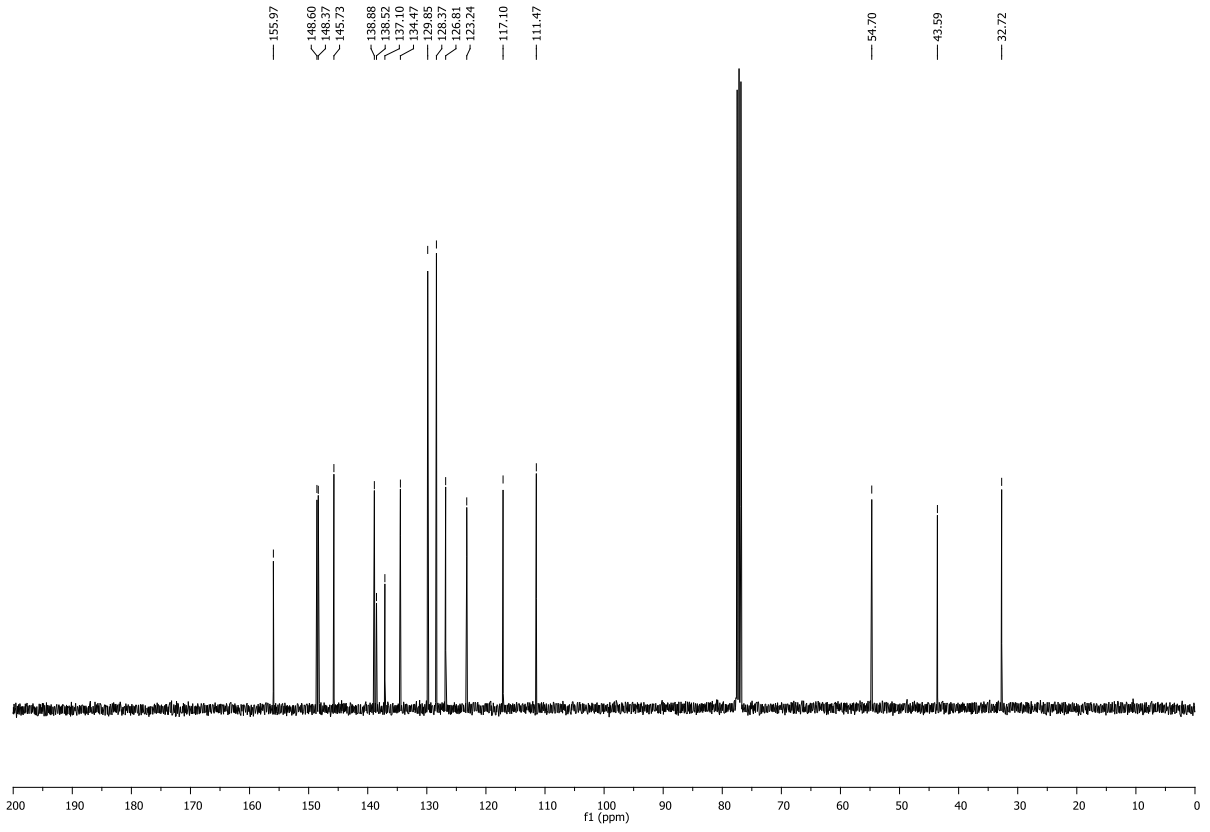
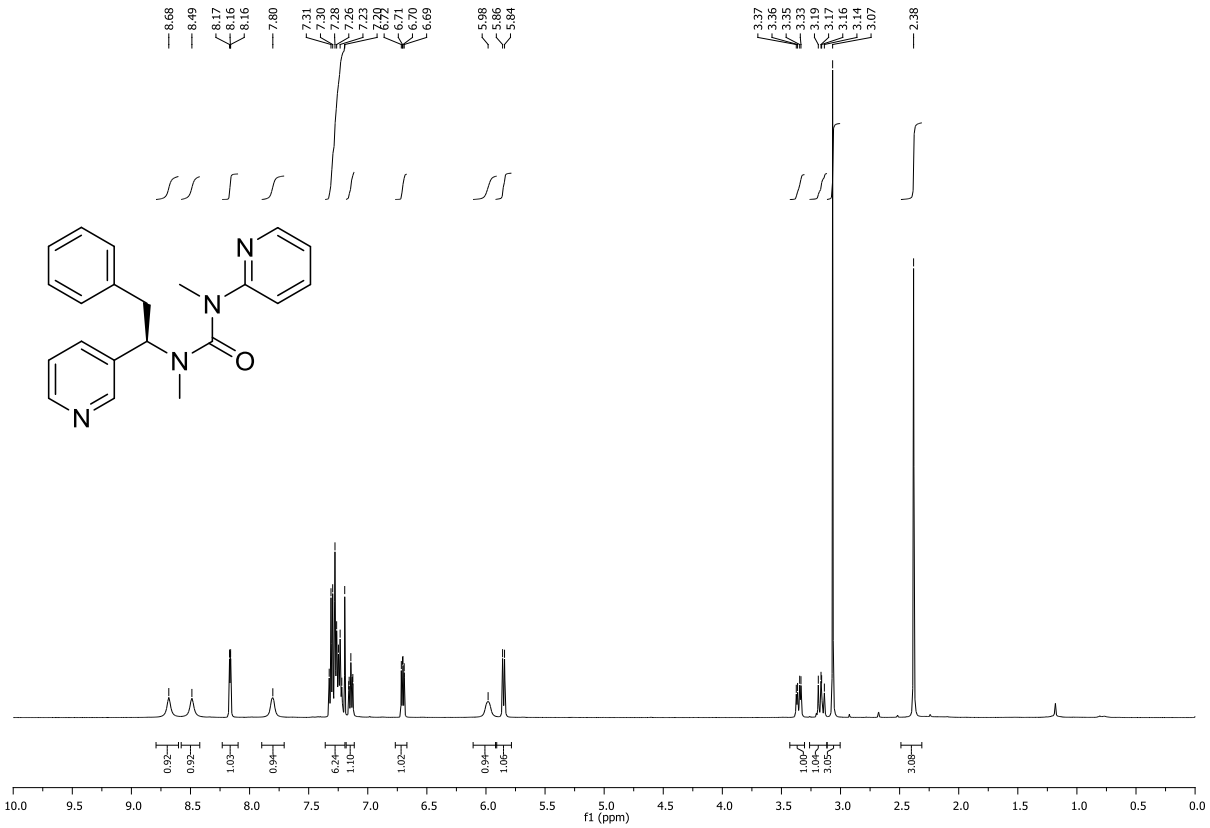
160.48
149.29
148.86
147.67
137.81
135.92
135.64
130.27
129.04
128.88
126.84
123.47
116.57
110.25
109.80
77.41
77.16
76.91
57.47
55.34
40.32
36.60
31.60
f1 (ppm)

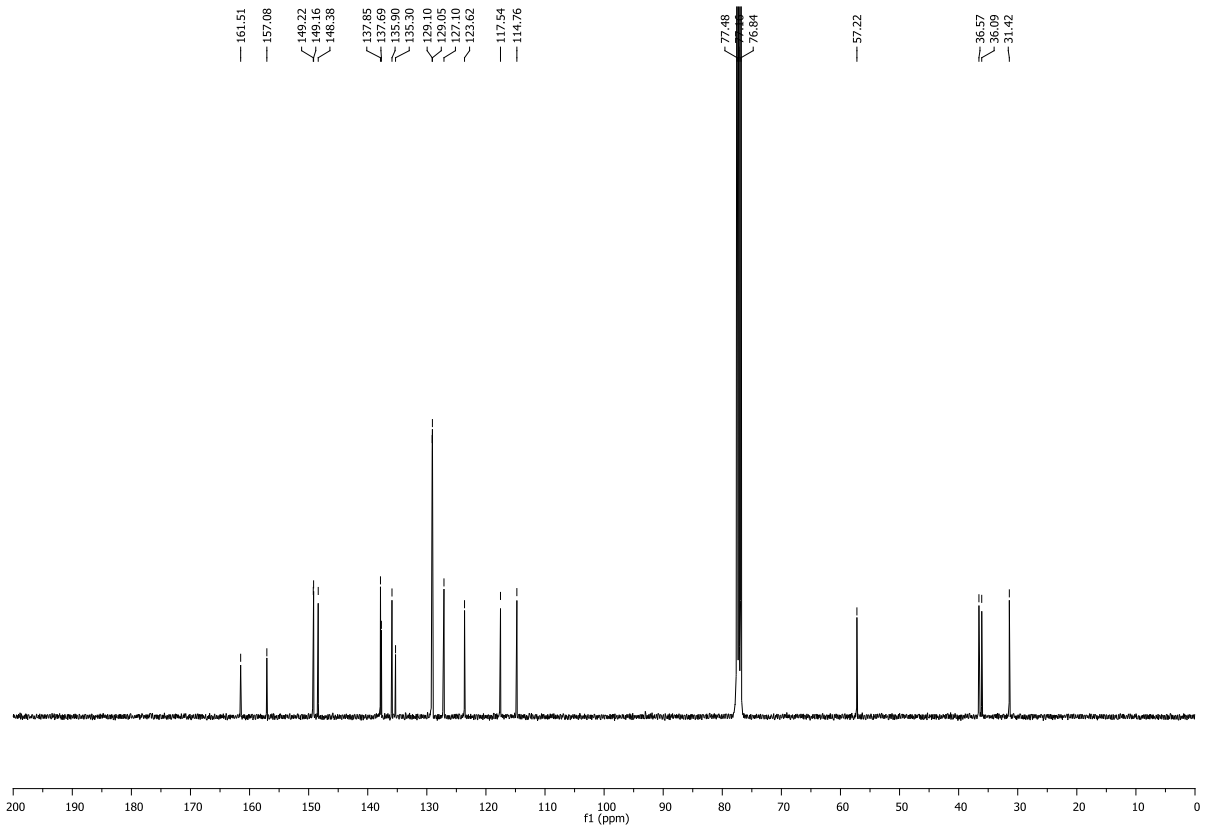
17h


8.51
8.51
8.46
8.46
8.45
8.45
8.19
8.19
8.18
7.70
7.68
7.48
7.47
7.26
7.22
7.21
7.20
7.19
7.18
7.17
7.06
7.05
6.98
6.97
6.96
6.95
5.33
5.32
5.30
3.33
3.16
3.16
3.15
3.14
water
0.97
0.97
0.97
0.99
1.00
3.98
2.00
2.00
1.02
3.05
2.06
f1 (ppm)

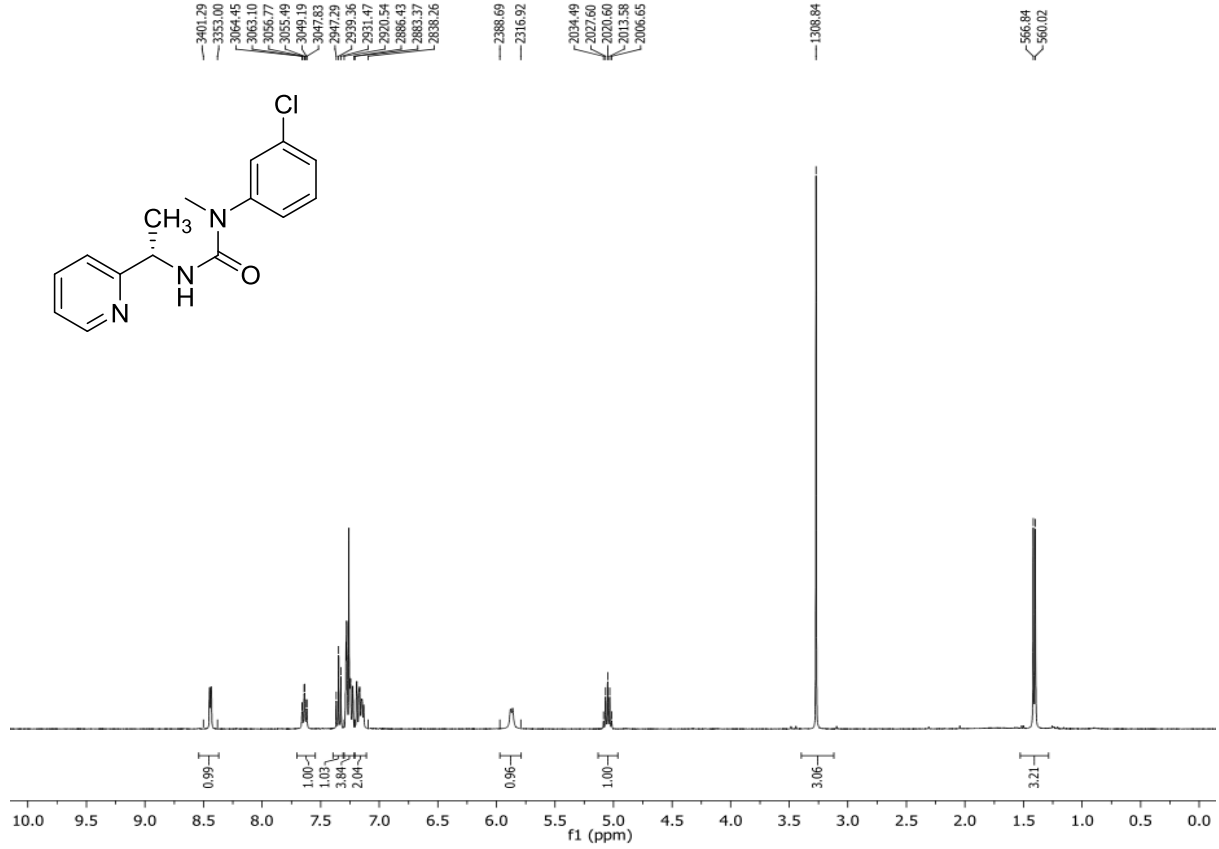

155.97
148.60
148.37
145.73
138.88
138.52
137.10
134.47
129.85
128.37
126.81
123.24
117.10
111.47
54.70
43.59
32.72
f1 (ppm)

7h


8.68
8.49
8.17
8.16
8.16
7.80
7.31
7.30
7.28
7.26
7.23
7.20
6.72
6.71
6.70
6.69
5.98
5.86
5.84
3.37
3.36
3.35
3.33
3.19
3.17
3.16
3.14
3.07
2.38
N
N
N
O
N
0.92
0.92
1.03
0.94
6.24
1.10
1.02
0.94
1.06
1.09
1.04
3.05
3.08
f1 (ppm)


161.51
157.08
149.22
149.16
148.38
137.85
137.69
135.90
135.30
129.10
129.05
127.10
123.62
117.54
114.76
77.48
76.84
57.22
36.57
36.09
31.42
f1 (ppm)

18a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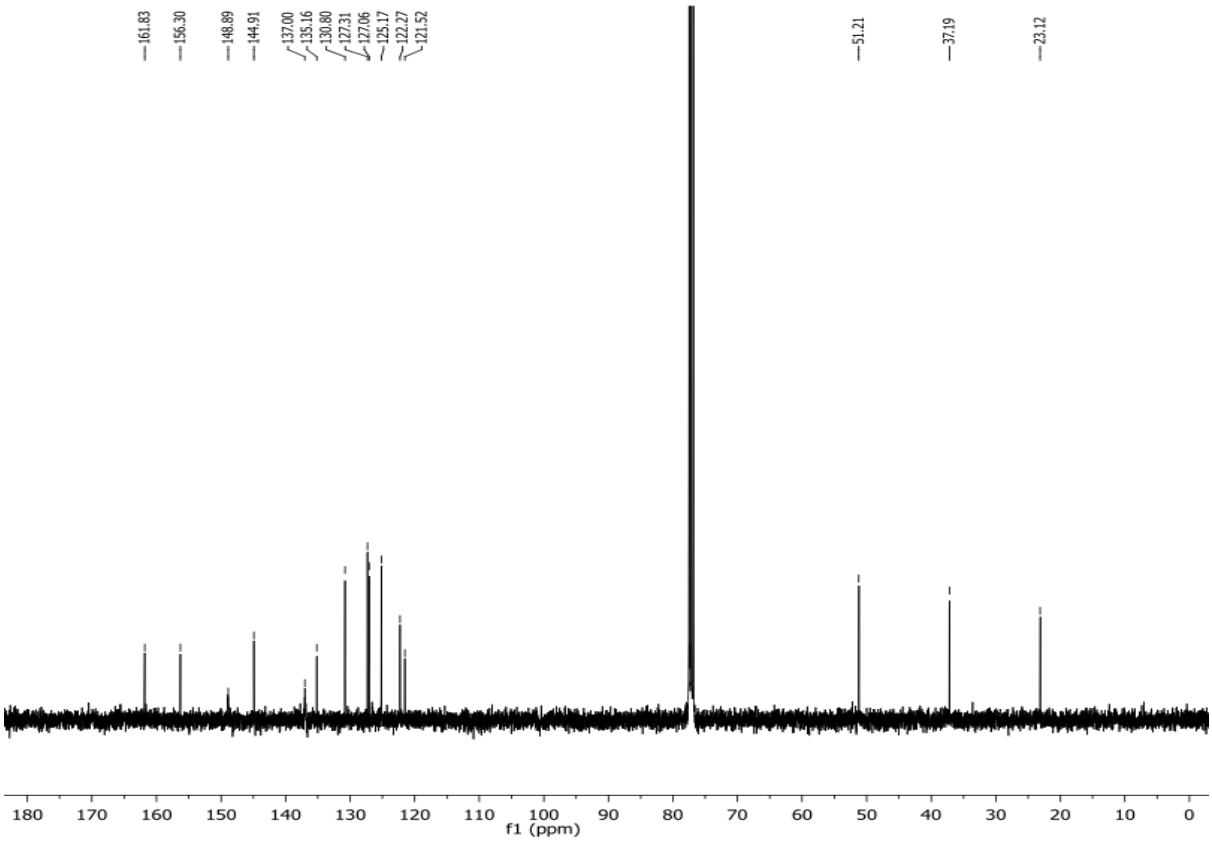
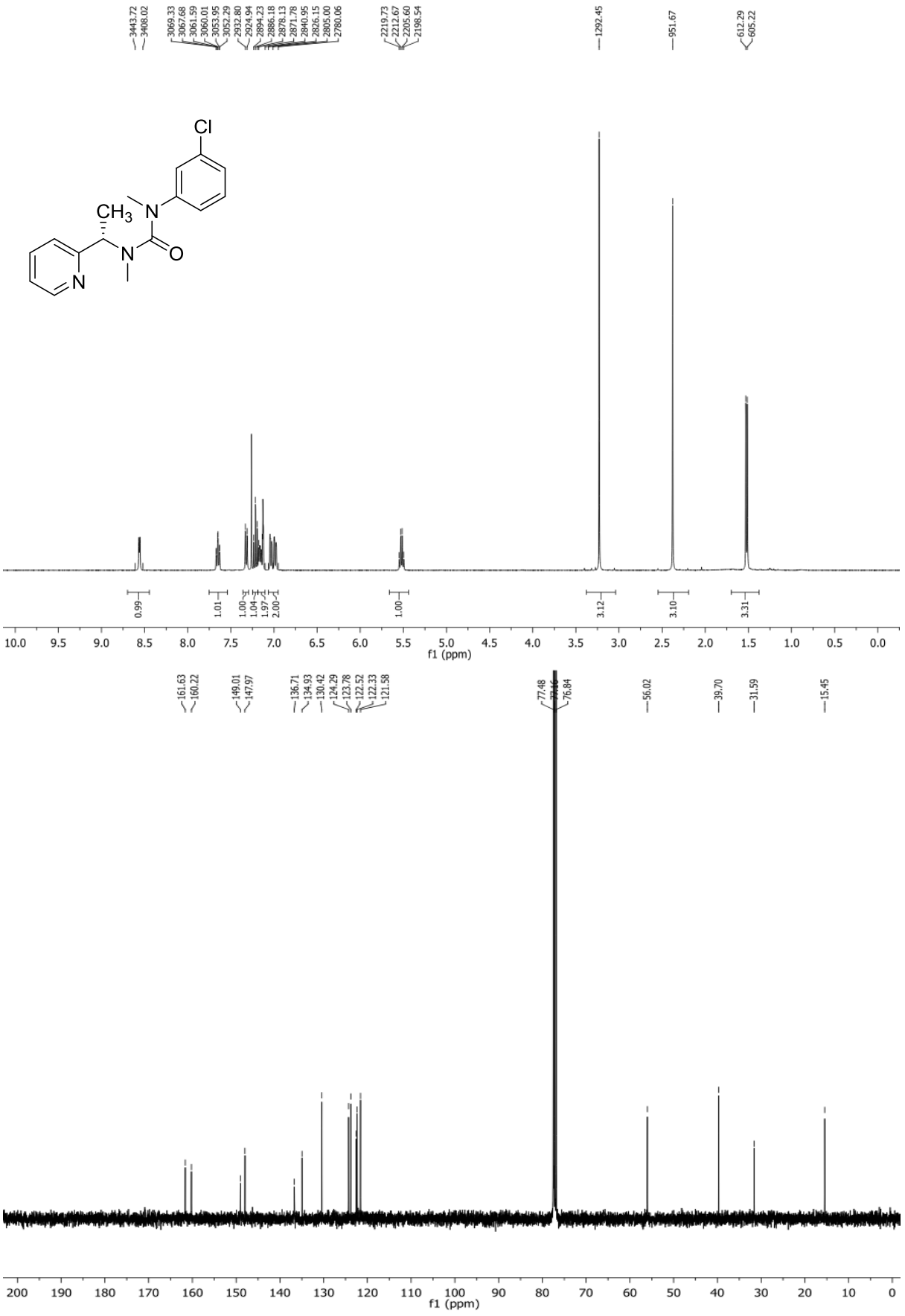
3353.00
3064.45
3063.10
3056.77
3055.49
3049.19
3047.83
2947.29
2939.36
2931.47
2920.54
2886.43
2883.37
2838.26
2388.69
2316.92
2034.49
2027.60
2020.60
2013.58
2006.65
1308.84
566.84
560.02
Cl
CH3
N
N
H
O
N
0.99
1.00
1.03
3.84
2.04
0.96
1.00
3.06
3.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


161.83
156.30
148.89
144.91
137.00
135.16
130.80
127.31
127.06
125.17
122.27
121.52
51.21
37.19
23.12
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

8a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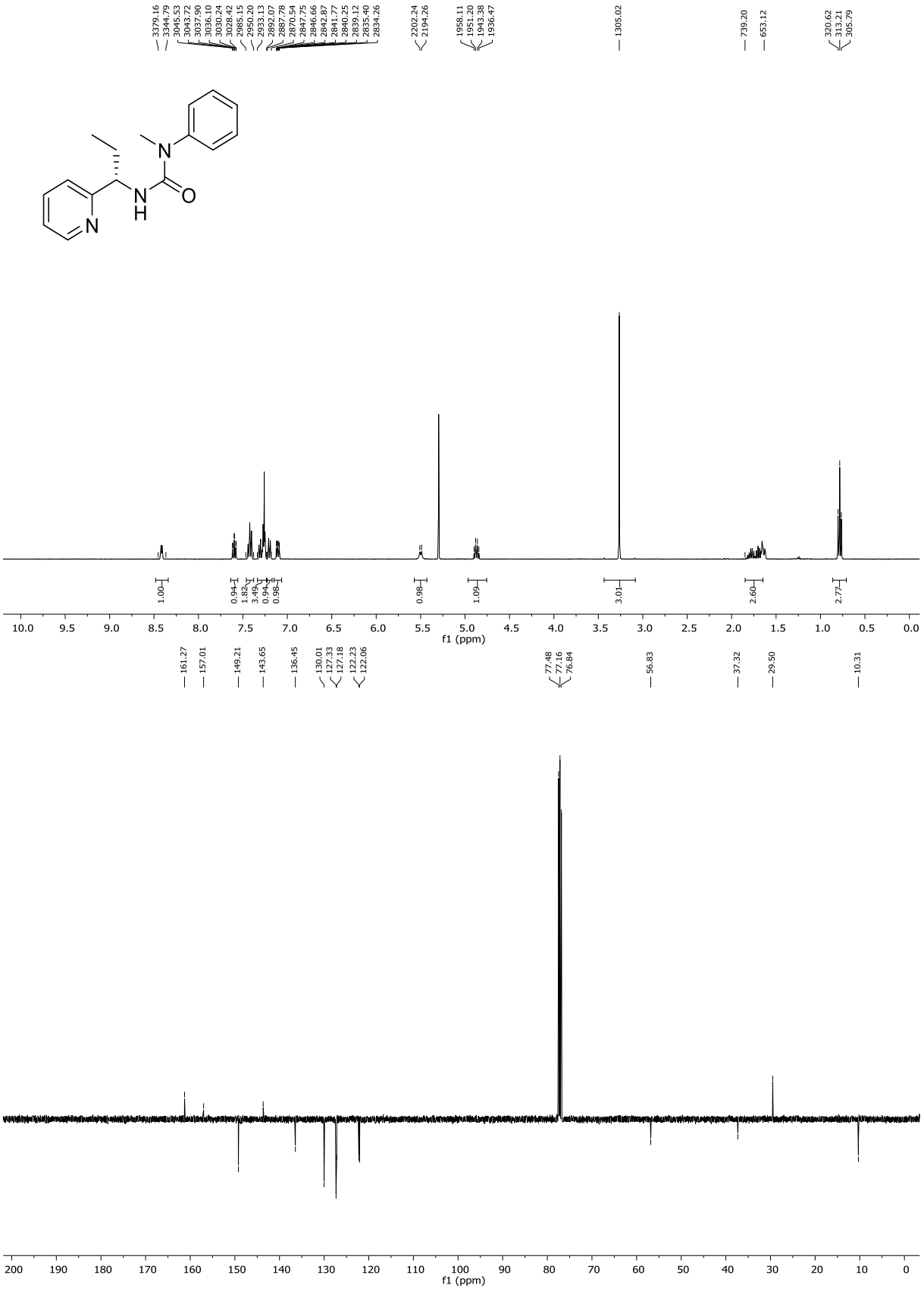
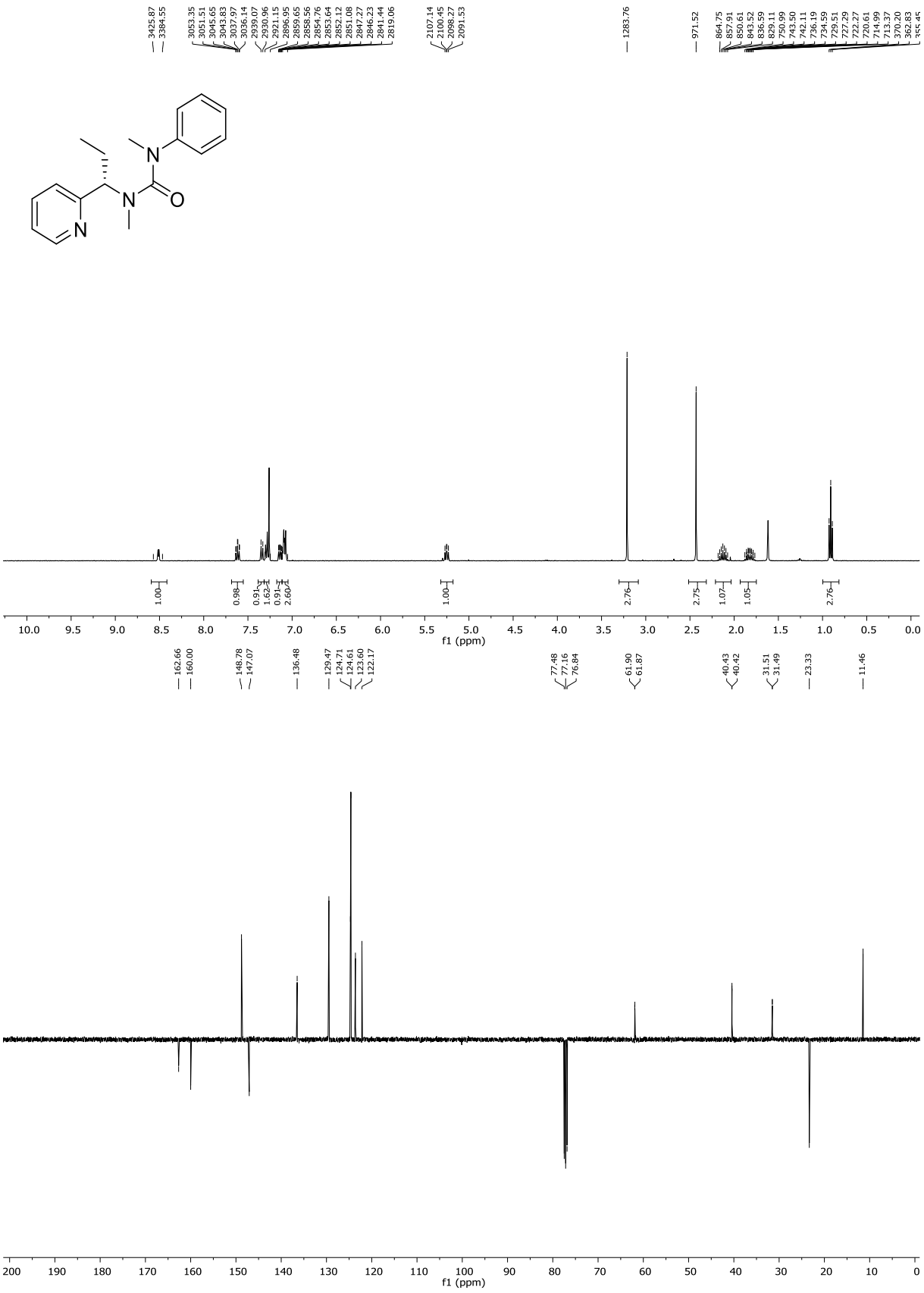
3408.02
3069.33
3067.68
3061.59
3060.01
3053.95
3052.29
2932.80
2924.94
2894.23
2886.18
2878.13
2871.78
2840.95
2826.15
2805.00
2780.06
2219.73
2212.67
2205.60
2198.54
1292.45
951.67
612.29
605.22
Cl
CH3
N
N
O
N
0.99
1.01
1.00
1.04
1.97
2.00
1.00
3.12
3.10
3.31
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
161.63
160.22
149.01
147.97
136.71
134.93
130.42
124.29
123.78
122.52
122.33
121.58
77.48
77.16
76.84
56.02
39.70
31.59
15.45
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

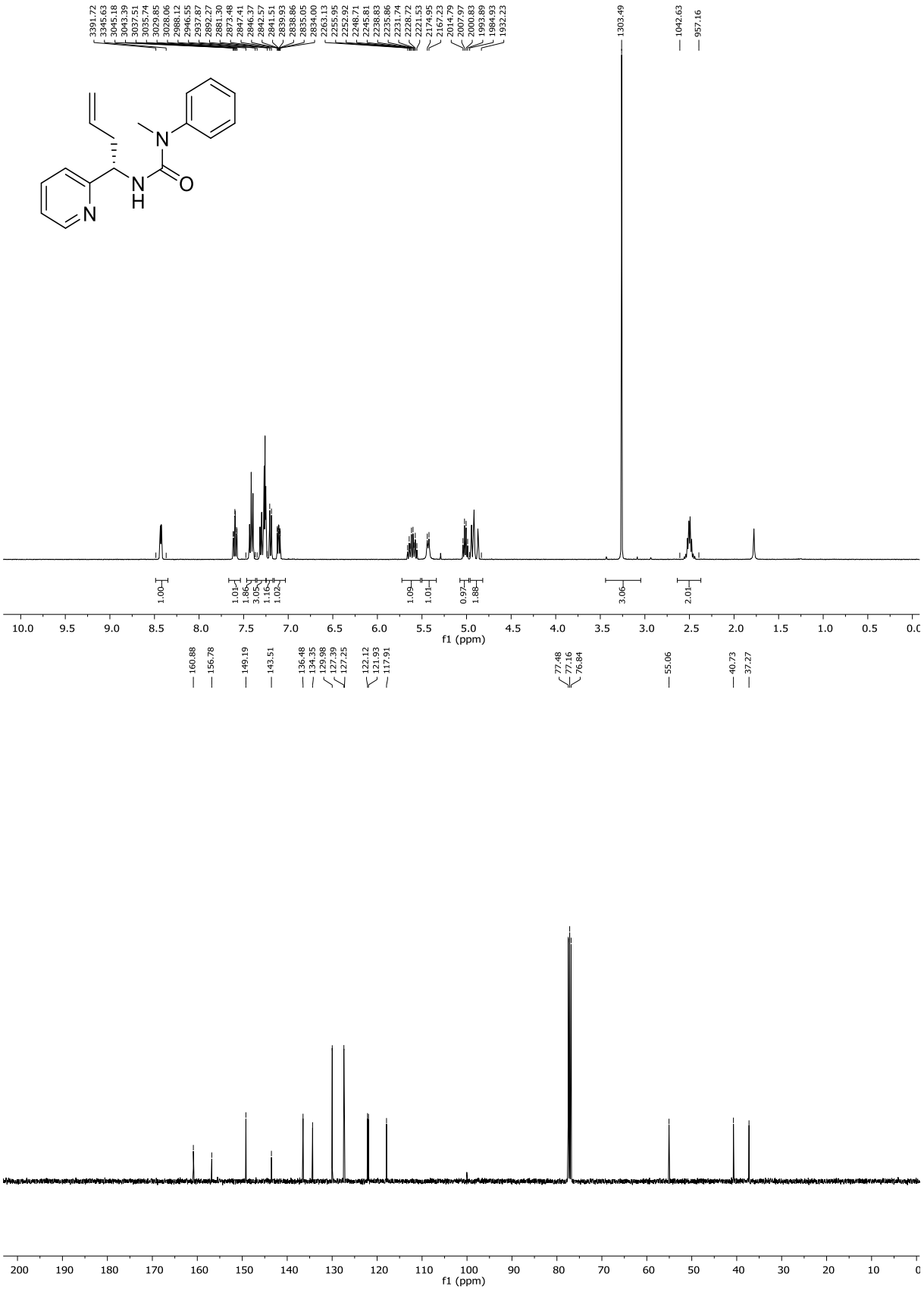
18b


3379.16
3344.79
3045.53
3043.72
3037.90
3036.10
3030.24
3028.42
2985.15
2950.20
2933.13
2892.07
2870.54
2847.75
2846.66
2842.87
2841.77
2840.25
2839.12
2835.40
2834.26
2202.24
2194.26
1958.11
1951.20
1943.38
1936.47
1305.02
739.20
653.12
320.62
313.21
305.79
N
N
H
O
N
1.00
0.94
1.82
3.49
0.94
0.98
0.98
1.09
3.01
2.60
2.77
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
161.27
157.01
149.21
143.65
136.45
130.01
127.33
127.18
122.23
122.06
77.48
77.16
76.84
56.83
37.32
29.50
10.31
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

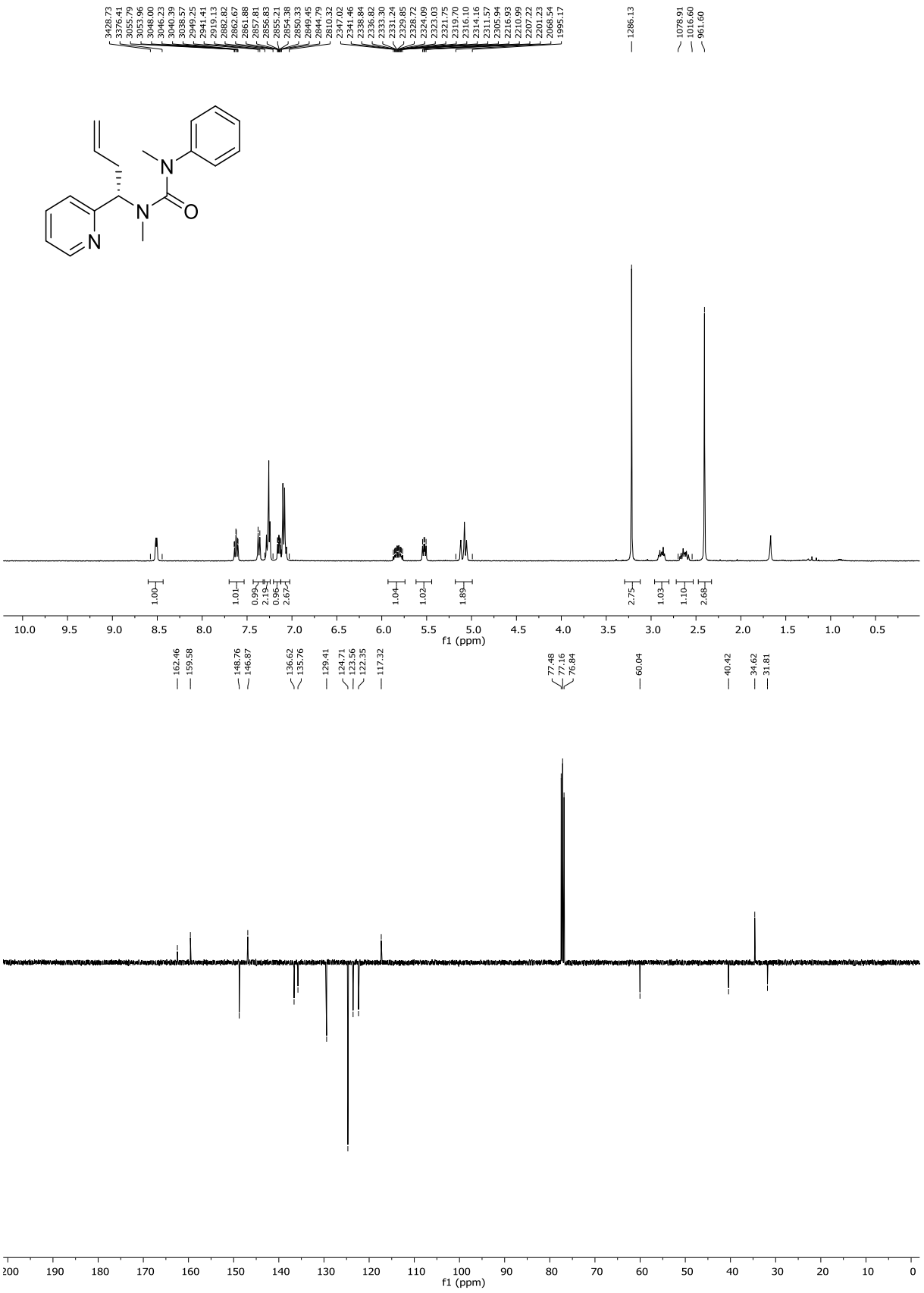
8b


3425.87
3384.55
3053.35
3051.51
3045.65
3043.83
3037.97
3036.14
2939.07
2930.96
2921.15
2896.95
2859.65
2858.56
2854.76
2853.64
2852.12
2851.08
2847.27
2846.23
2841.44
2819.06
2107.14
2100.45
2098.27
2091.53
1283.76
971.52
864.75
857.91
850.61
843.52
836.59
829.11
750.99
743.50
742.11
736.19
734.59
729.51
727.29
722.27
720.61
714.99
713.37
370.20
362.83
355.45
N
N
O
N
1.00
0.98
0.91
1.62
0.91
2.60
1.00
2.76
2.75
1.07
1.05
2.76
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
162.66
160.00
148.78
147.07
136.48
129.47
124.71
124.61
123.60
122.17
77.48
77.16
76.84
61.90
61.87
40.43
40.42
31.51
31.49
23.33
11.46
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

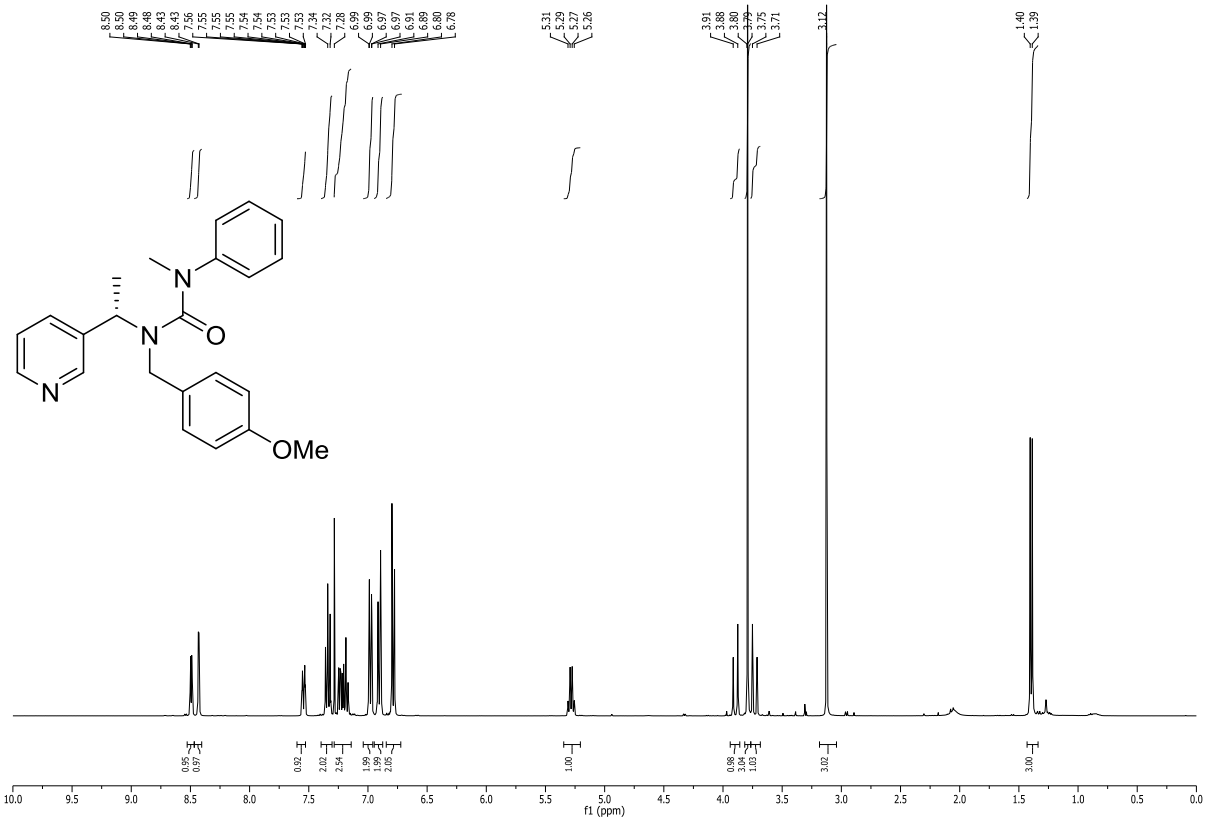
18c

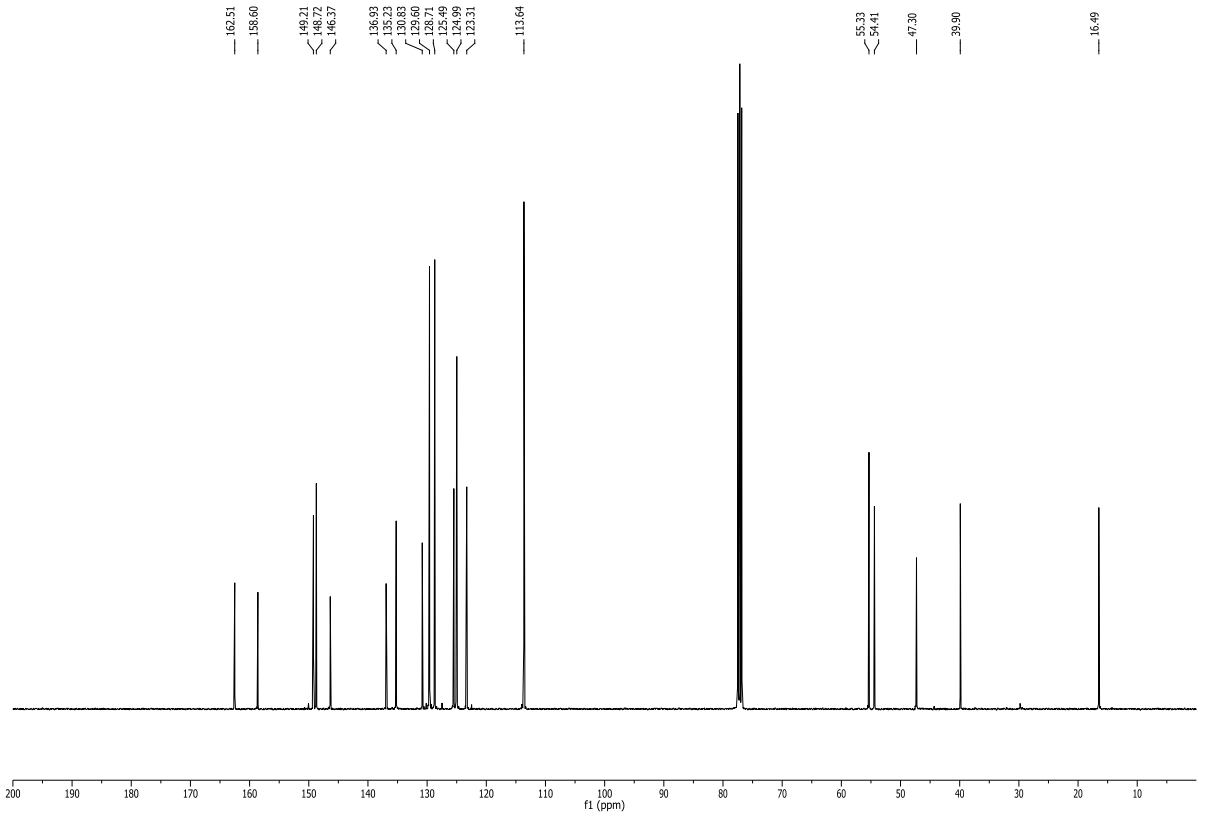

3391.72
3345.63
3045.18
3043.39
3037.51
3035.74
3029.85
3028.06
2988.12
2946.55
2937.87
2892.27
2881.30
2873.48
2847.41
2846.37
2842.57
2841.51
2839.93
2838.86
2835.05
2834.00
2263.13
2255.95
2252.92
2248.71
2245.81
2238.83
2235.96
2231.74
2228.72
2221.53
2174.95
2167.23
2014.79
2007.97
2000.83
1993.89
1984.93
1932.23
1303.49
1042.63
957.16
N
N
H
O
N
1.00
1.01
1.86
3.05
1.16
1.02
1.09
1.01
0.97
1.88
3.06
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
160.88
156.78
149.19
143.51
136.48
134.35
129.98
127.39
127.25
122.12
121.93
117.91
77.48
77.16
76.84
55.06
40.73
37.27
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

8c

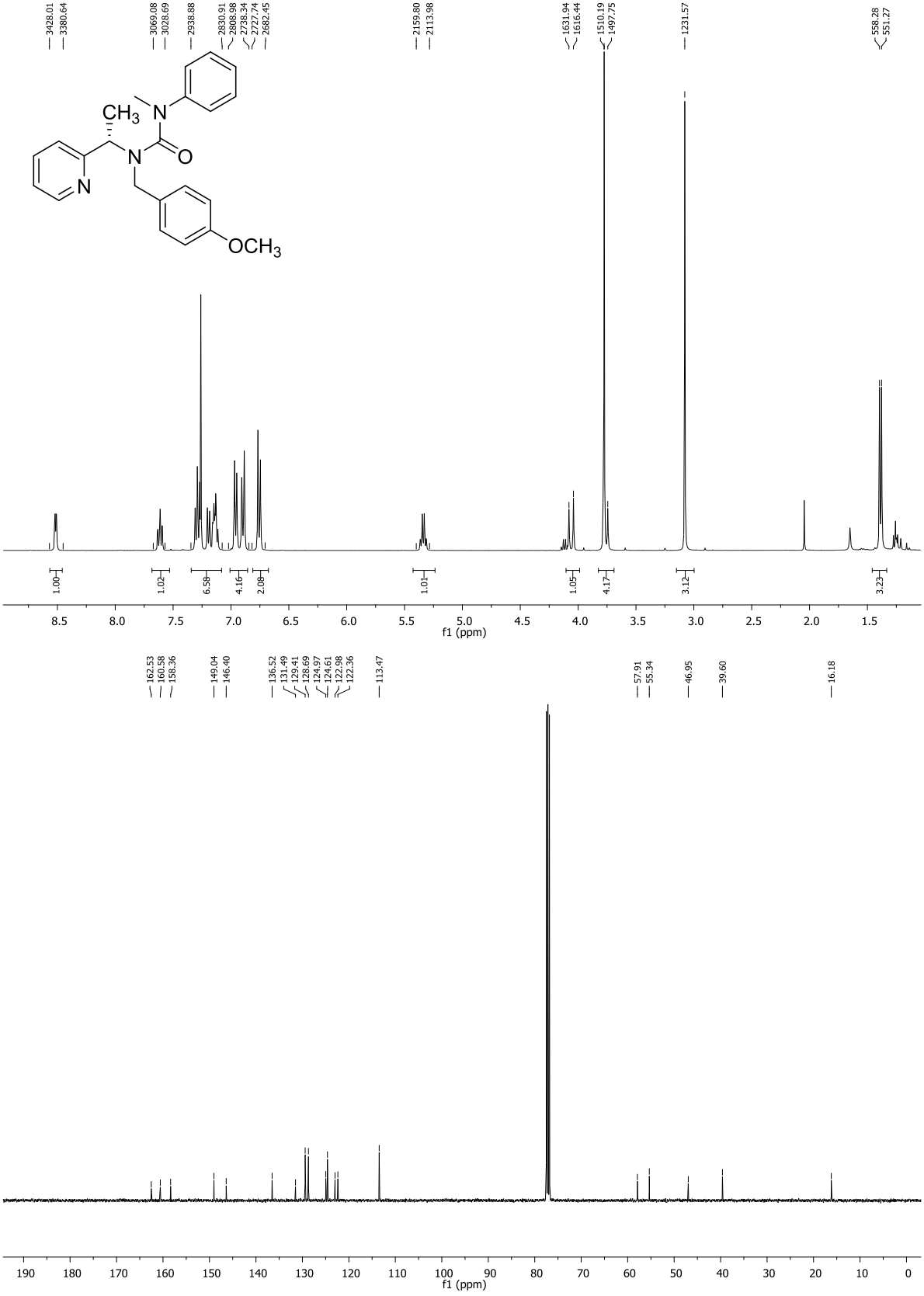

3428.73
3376.41
3055.79
3053.96
3048.00
3046.23
3040.39
3038.57
2949.25
2941.41
2919.13
2882.82
2862.67
2861.88
2857.81
2856.83
2855.21
2854.38
2850.33
2849.45
2844.79
2810.32
2347.02
2341.46
2338.84
2336.82
2333.30
2331.24
2329.85
2328.72
2324.09
2323.03
2321.75
2319.70
2316.10
2314.16
2311.57
2305.94
2216.93
2210.99
2207.22
2201.23
2068.54
1995.17
1286.13
1078.91
1016.60
961.60
N
N
O
N
1.00
1.01
0.99
2.19
0.96
2.67
1.04
1.02
1.89
2.75
1.03
1.10
2.68
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
162.46
159.58
148.76
146.87
136.62
135.76
129.41
124.71
123.56
122.35
117.32
77.48
77.16
76.84
60.04
40.42
34.62
31.81
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

9

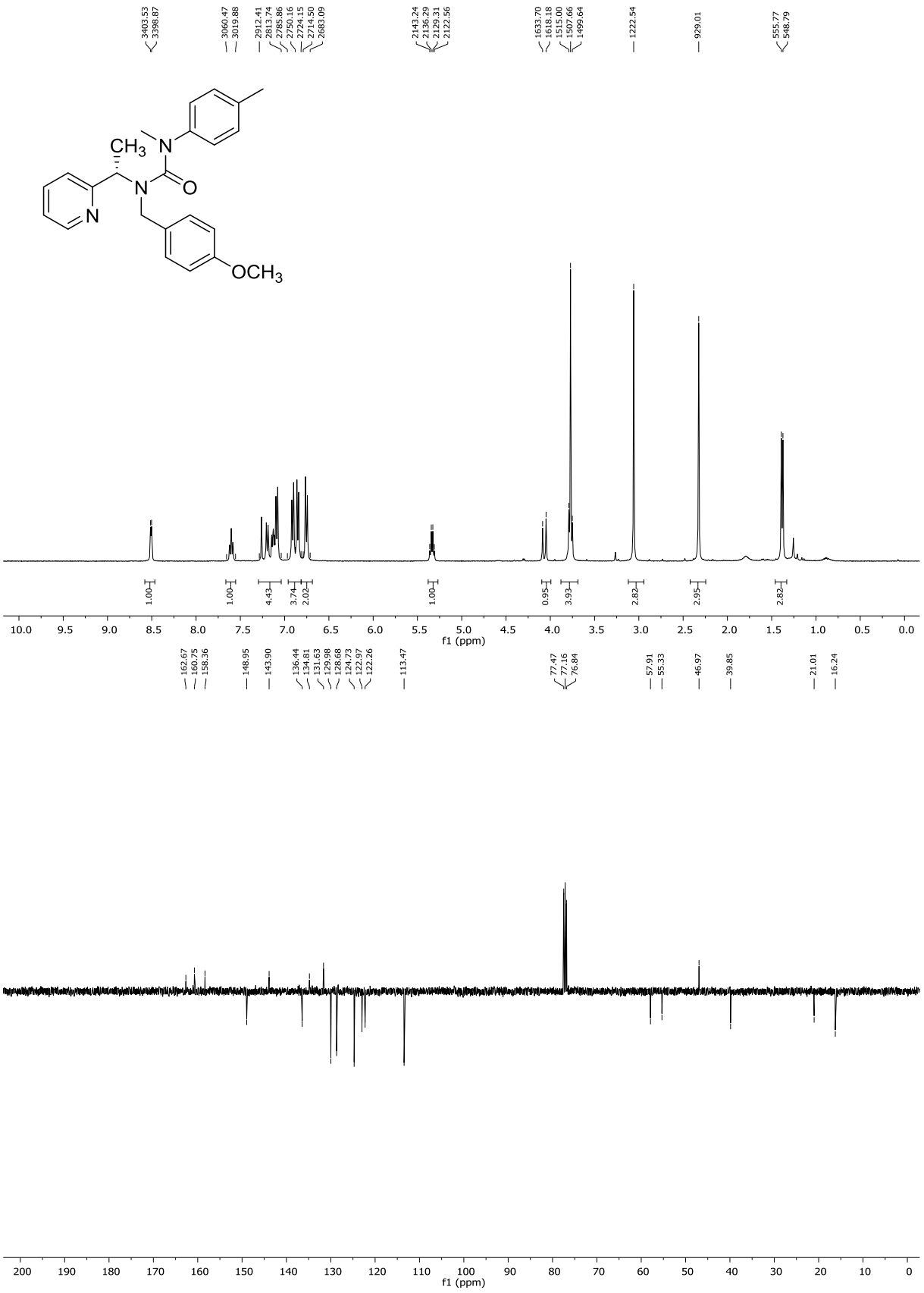

8.50
8.50
8.49
8.48
8.43
8.43
7.56
7.55
7.55
7.55
7.54
7.54
7.53
7.53
7.34
7.32
7.28
6.99
6.97
6.97
6.91
6.89
6.80
6.78
5.31
5.29
5.27
5.26
3.91
3.88
3.80
3.79
3.75
3.71
3.12
1.40
1.39
N
N
O
N
OMe
0.95
0.97
0.92
2.02
2.54
1.99
1.99
2.05
1.00
0.98
3.04
1.03
3.02
3.00
f1 (ppm)


162.51
158.60
149.21
148.72
146.37
136.93
135.23
130.83
129.60
128.71
125.49
124.99
123.31
113.64
55.33
54.41
47.30
39.90
16.49
f1 (ppm)

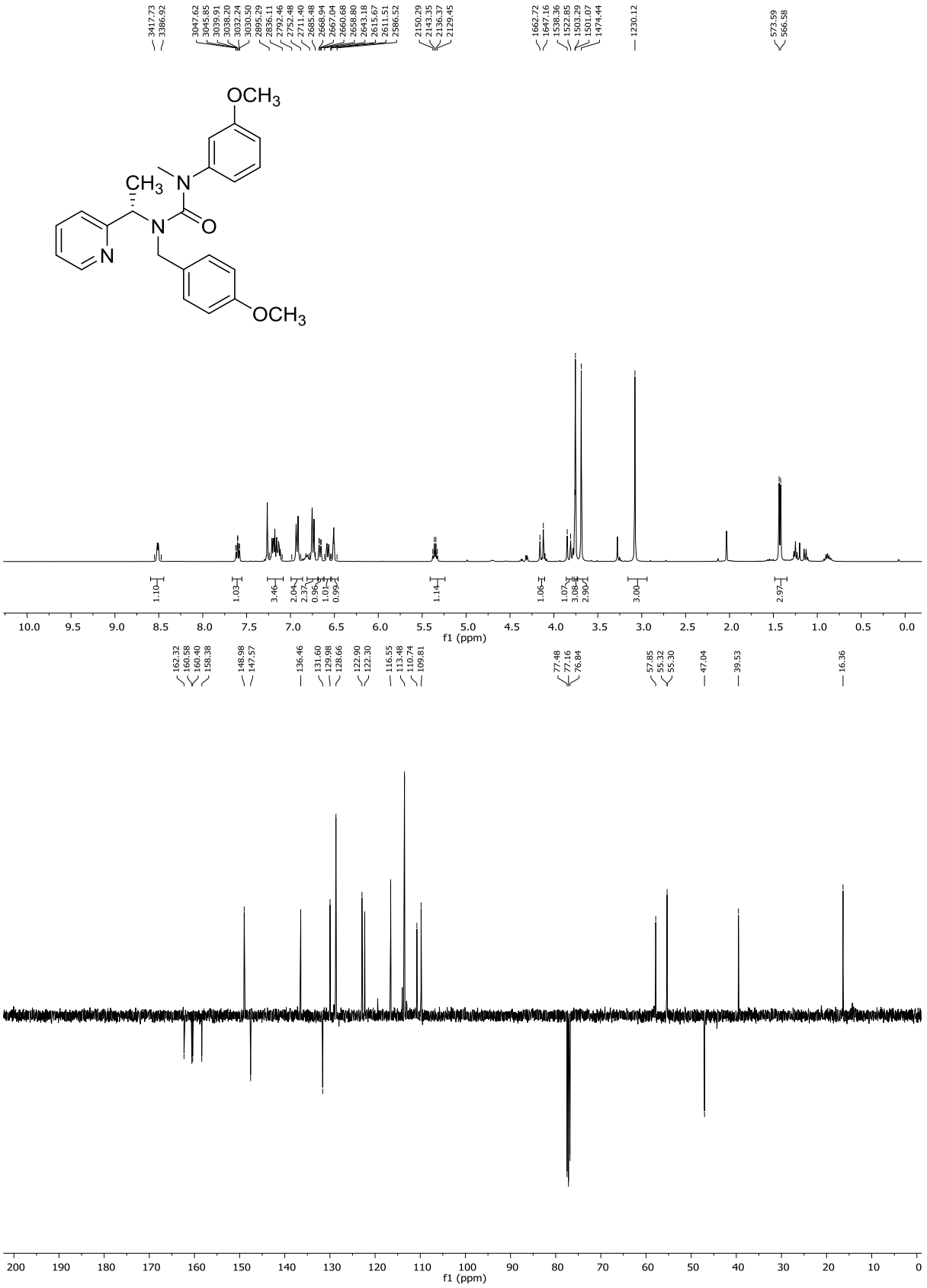
10a


3428.01
3380.64
3069.08
3028.69
2938.88
2830.91
2808.98
2738.34
2727.74
2682.45
2159.80
2113.98
1631.94
1616.44
1510.19
1497.75
1231.57
558.28
551.27
CH3
N
N
O
N
OCH3
1.00
1.02
6.58
4.16
2.08
1.01
1.05
4.17
3.12
3.23
f1 (ppm)
162.53
160.38
158.36
149.04
146.40
136.52
131.49
129.41
128.69
124.97
124.61
122.98
122.36
113.47
57.91
55.34
46.95
39.60
16.18
f1 (ppm)

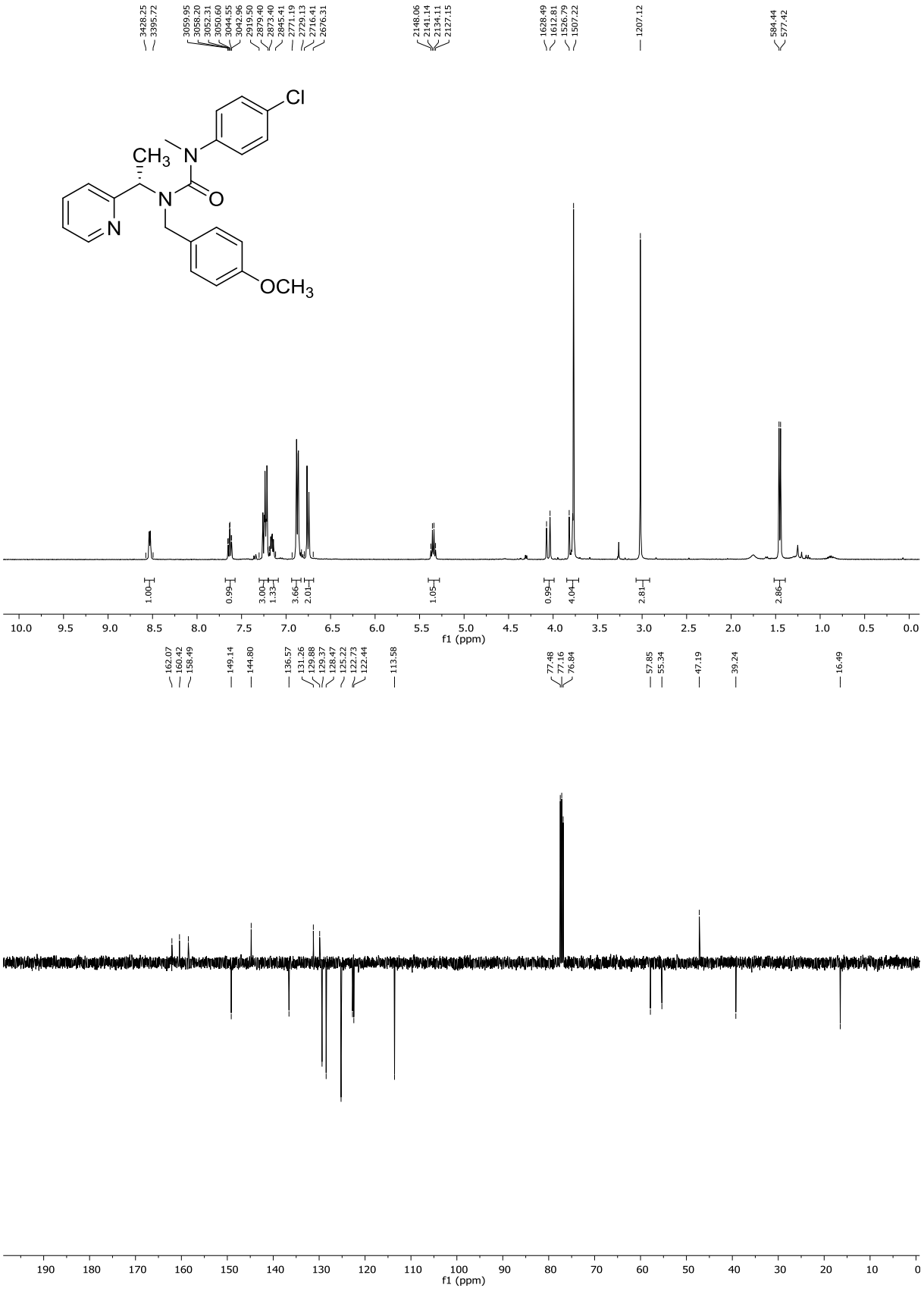
10b


3403.53
3398.87
3060.47
3019.88
2912.41
2813.74
2785.86
2750.16
2724.15
2714.50
2683.09
2143.24
2136.29
2129.31
2122.56
1633.70
1618.18
1515.00
1507.66
1499.64
1222.54
929.01
555.77
548.79
CH3
N
N
O
N
OCH3
1.00
1.00
4.43
3.74
2.02
1.00
0.95
3.93
2.82
2.95
2.82
f1 (ppm)
162.67
160.75
158.36
148.95
143.90
136.44
134.81
131.63
129.98
128.68
124.73
122.97
122.26
113.47
77.47
77.16
76.84
57.91
55.33
46.97
39.85
21.01
16.24
f1 (ppm)

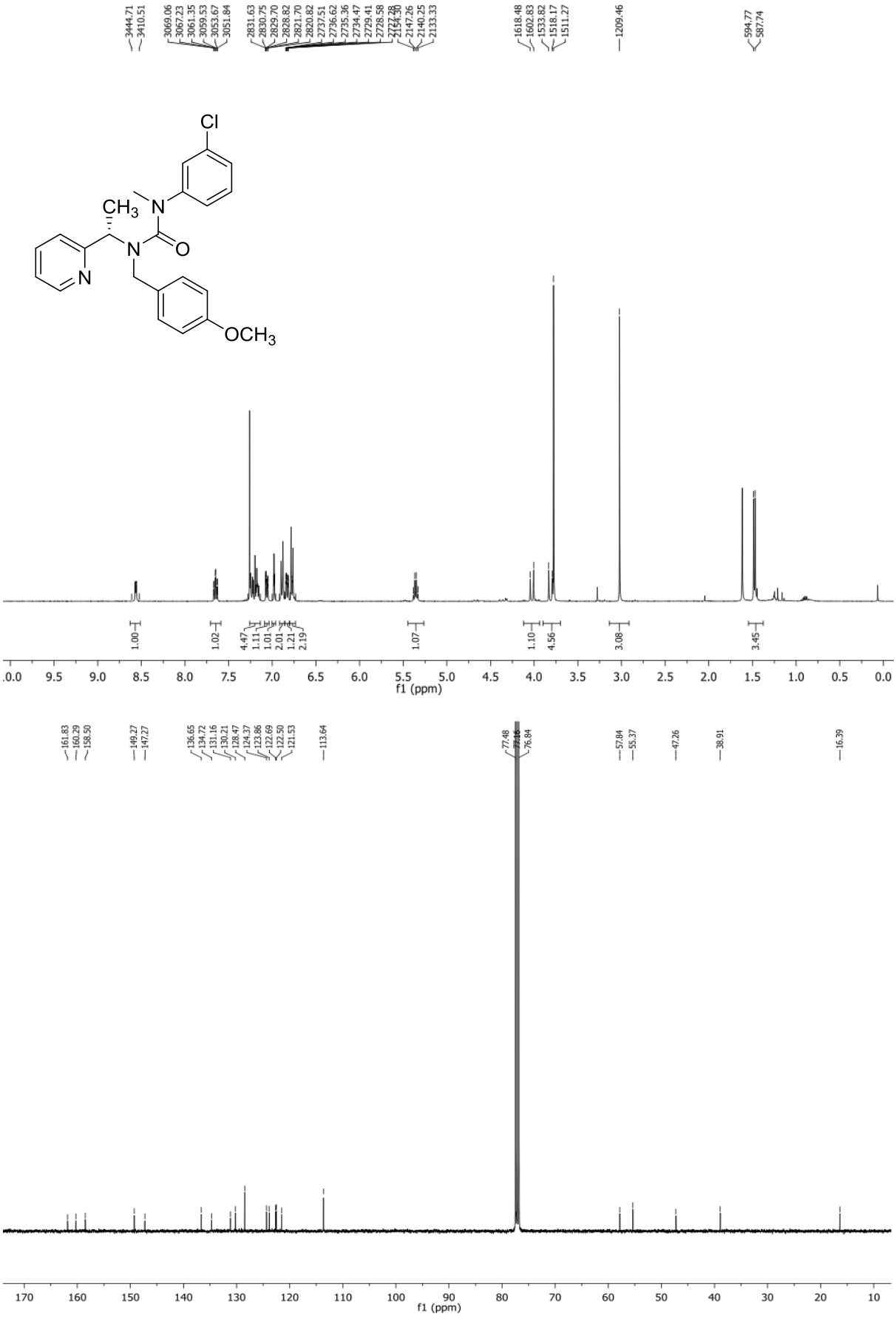
10c


3417.73
3386.92
3047.62
3045.85
3039.91
3038.20
3032.24
3030.50
2895.29
2836.11
2792.46
2752.48
2711.40
2685.48
2668.94
2667.04
2660.68
2658.80
2643.18
2615.67
2611.51
2586.52
2150.29
2143.35
2136.37
2129.45
1662.72
1647.16
1538.36
1522.85
1503.29
1501.07
1474.44
1230.12
573.59
566.58
OCH3
CH3
N
N
O
N
OCH3
1.10
1.03
3.46
2.04
2.37
0.96
1.01
0.99
1.14
1.06
1.07
3.08
2.90
3.00
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
162.32
160.58
160.40
158.38
148.98
147.57
136.46
131.60
129.98
128.66
122.90
122.30
116.55
113.48
110.74
109.81
77.48
77.16
76.84
57.85
55.32
55.30
47.04
39.53
16.36
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

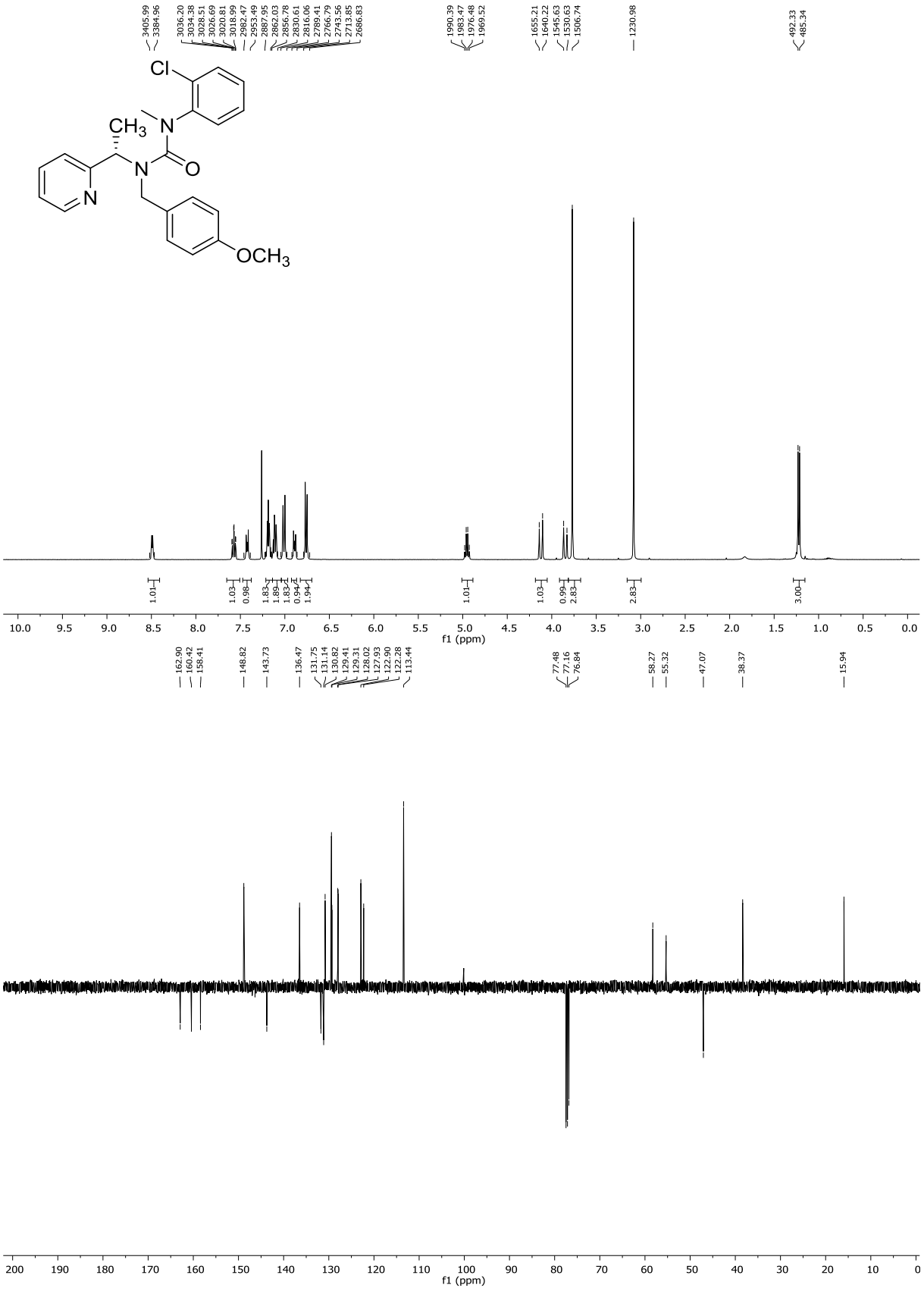
10d


3428.25
3395.72
3059.95
3058.20
3052.31
3050.60
3044.55
3042.96
2919.50
2879.40
2873.40
2835.41
2771.19
2716.41
2676.31
2148.06
2141.14
2134.11
2127.15
1628.49
1612.81
1526.79
1507.22
1207.12
584.44
577.42
Cl
CH3
N
N
O
N
OCH3
1.00
0.99
3.00
1.33
3.66
2.01
1.05
0.99
4.04
2.81
2.86
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
162.07
160.42
158.49
149.14
144.80
136.57
131.26
129.88
129.37
128.47
125.22
122.73
122.44
113.58
77.48
77.16
76.84
57.85
55.34
47.19
39.24
16.49
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

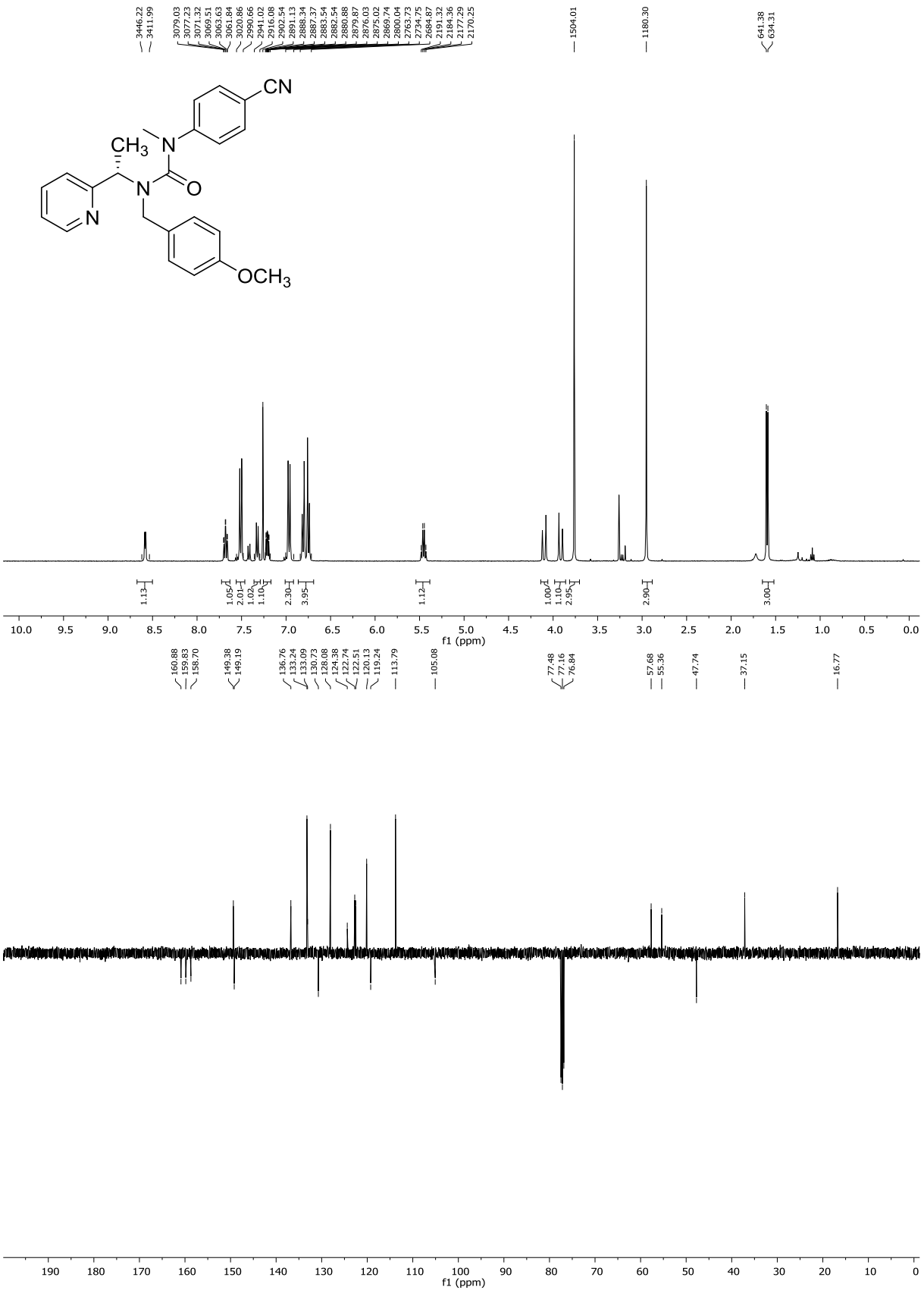
10e


3444.71
3410.51
3069.06
3067.23
3061.35
3059.53
3053.67
3051.84
2831.63
2830.75
2829.70
2828.82
2821.70
2820.82
2737.51
2736.62
2735.36
2734.47
2729.41
2728.58
2147.26
2140.25
2133.33
1618.48
1602.83
1533.82
1518.17
1511.27
1209.46
594.77
587.74
Cl
CH3
N
N
O
N
OCH3
1.00
1.02
4.47
1.11
1.01
2.01
1.21
2.19
1.07
1.10
4.56
3.08
3.45
f1 (ppm)
161.83
160.29
158.50
149.27
147.27
136.65
134.72
131.16
130.21
128.47
124.37
123.86
122.69
122.50
121.53
113.64
77.48
77.16
76.84
57.84
55.37
47.26
38.91
16.39
f1 (ppm)

10f


3405.99
3384.96
3036.20
3034.38
3028.51
3026.69
3020.81
3018.99
2982.47
2953.49
2887.95
2862.03
2856.78
2830.61
2816.06
2789.41
2766.79
2743.56
2713.85
2686.83
1990.39
1983.47
1976.48
1969.52
1655.21
1640.22
1545.63
1530.63
1506.74
1230.98
492.33
485.34
Cl
CH3
N
N
O
N
OCH3
1.01
1.03
0.98
1.83
1.89
1.83
0.94
1.94
1.01
1.03
0.99
2.83
2.83
3.00
f1 (ppm)
162.90
160.42
158.41
148.82
143.73
136.47
131.75
131.14
130.82
129.41
129.31
128.02
127.93
122.90
122.28
113.44
77.48
77.16
76.84
58.27
55.32
47.07
38.37
15.94
f1 (ppm)

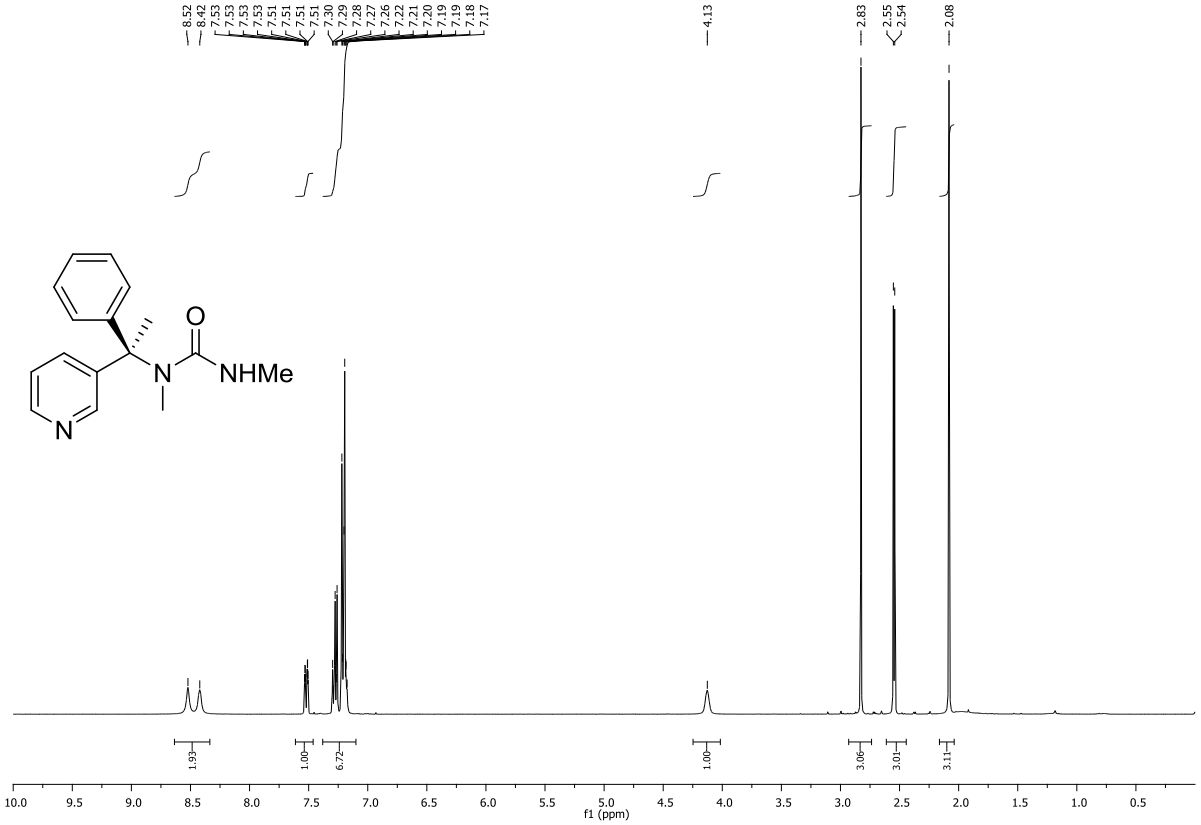
10g

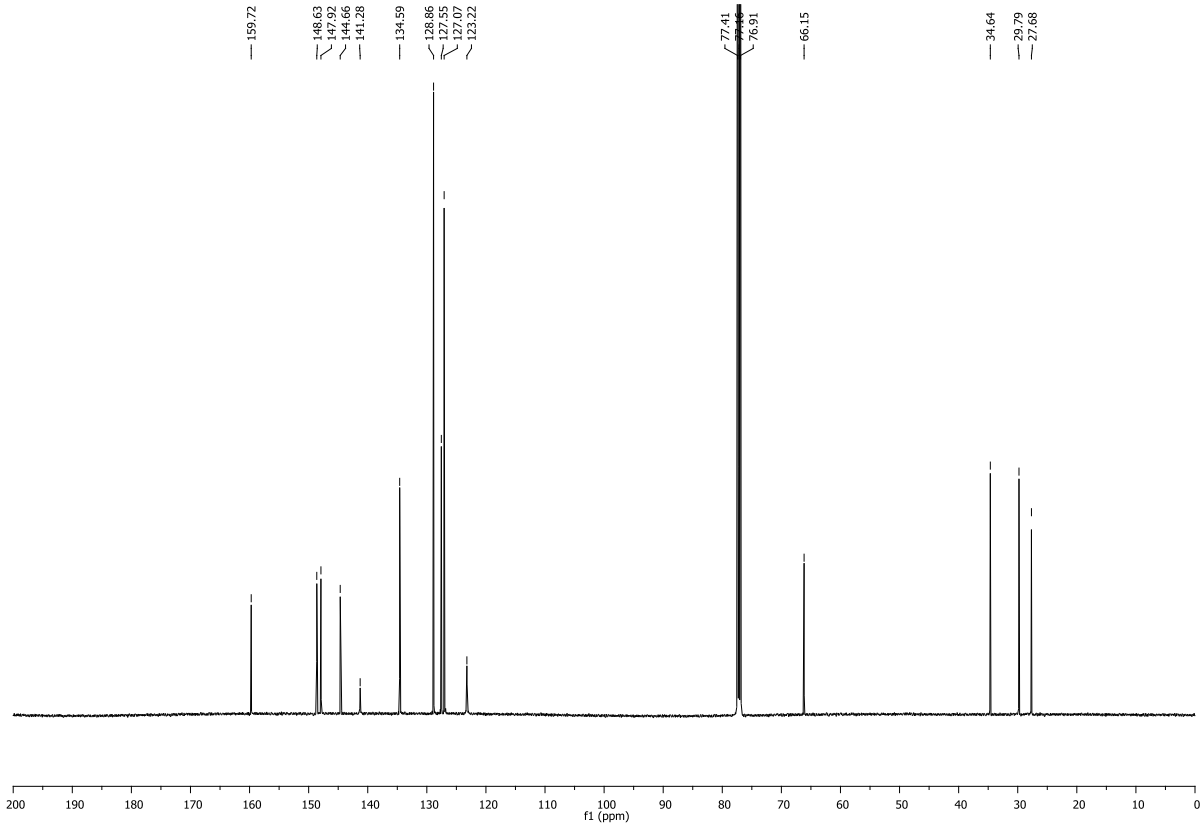

3446.22
3411.99
3079.03
3077.23
3071.32
3069.51
3063.63
3061.84
3020.86
2990.66
2941.02
2916.08
2902.54
2891.13
2888.34
2887.37
2883.54
2882.54
2880.88
2879.87
2876.03
2875.02
2869.74
2800.04
2763.73
2734.75
2684.87
2191.32
2184.36
2177.29
2170.25
1504.01
1180.30
641.38
634.31
CN
CH3
N
N
O
N
OCH3
1.13
1.05
2.01
1.02
1.10
2.30
3.95
1.12
1.00
1.10
2.95
2.90
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
160.88
159.83
158.70
149.38
149.19
136.76
133.24
133.09
130.73
128.08
124.38
122.74
122.51
120.13
119.24
113.79
105.08
77.48
77.16
76.84
57.68
55.36
47.74
37.15
16.77
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

10h

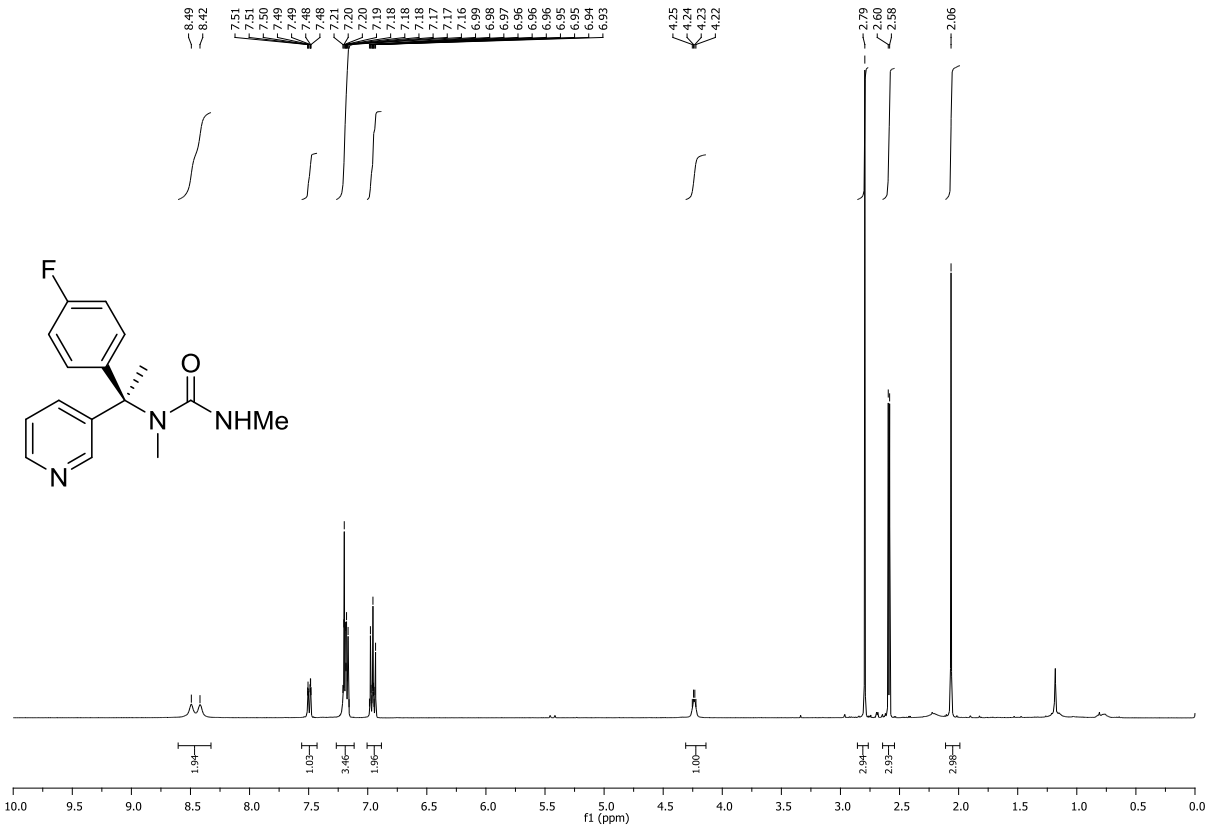

3402.87
3365.50
3037.61
3035.83
3029.91
3028.20
3022.27
3020.49
2925.12
2890.16
2865.63
2810.04
2782.65
2751.93
2673.83
2287.95
2281.53
2280.39
2277.79
2274.04
2270.82
2263.75
2260.77
2256.98
2254.45
2253.12
2246.77
2127.10
2119.48
2111.83
1701.12
1685.59
1583.49
1567.98
1500.31
1215.09
1174.51
1112.04
1077.65
1007.16
N
N
O
N
OCH3
1.02
1.06
4.02
2.14
1.13
2.18
4.18
1.07
1.07
2.09
1.07
1.08
3.17
3.24
1.11
1.10
f1 (ppm)
162.40
158.86
158.29
148.96
146.36
136.47
135.32
131.53
129.37
128.48
124.88
124.65
124.52
122.61
117.51
113.37
77.41
77.16
76.91
61.89
55.33
46.60
39.61
35.52
f1 (ppm)

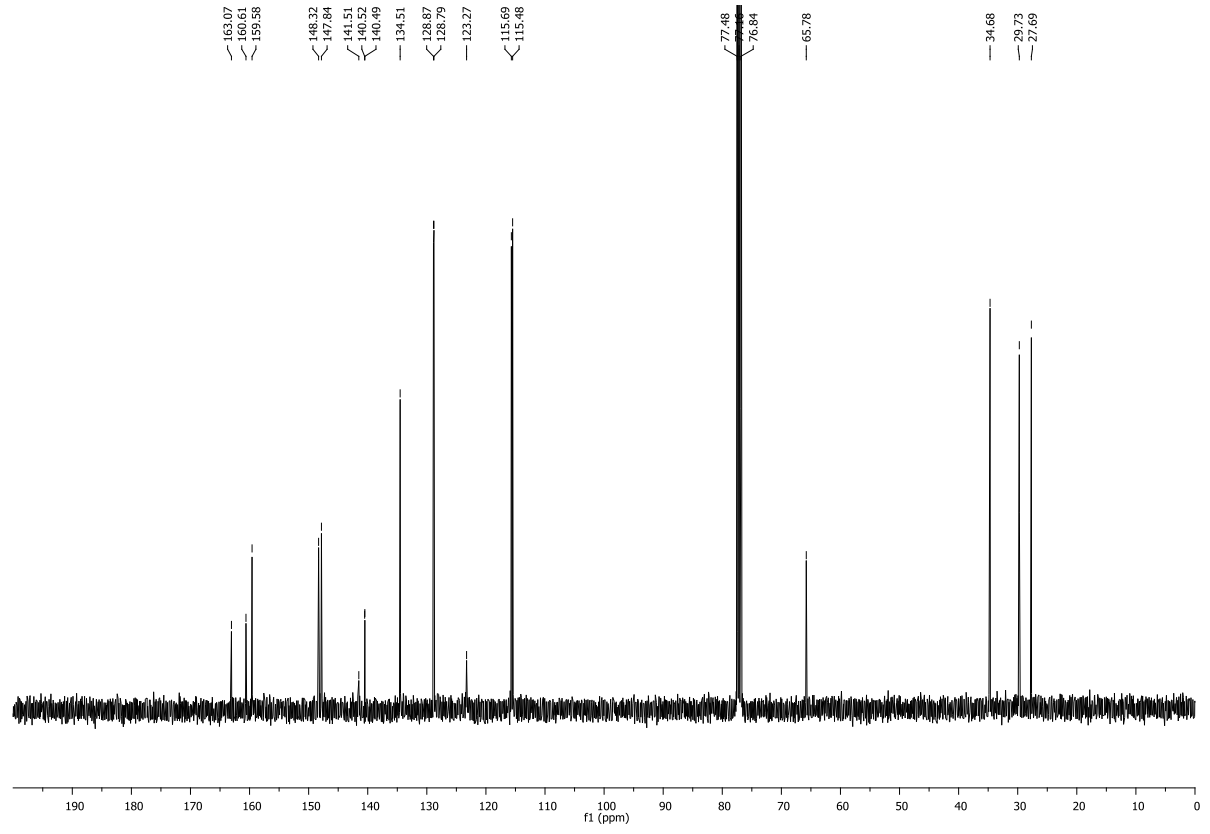
11a


8.52
8.42
7.53
7.53
7.53
7.53
7.51
7.51
7.51
7.51
7.30
7.29
7.28
7.27
7.26
7.22
7.21
7.20
7.19
7.19
7.18
7.17
4.13
2.83
2.55
2.54
2.08
O
N
NHMe
N
1.93
1.00
6.72
1.00
3.06
3.01
3.11
f1 (ppm)

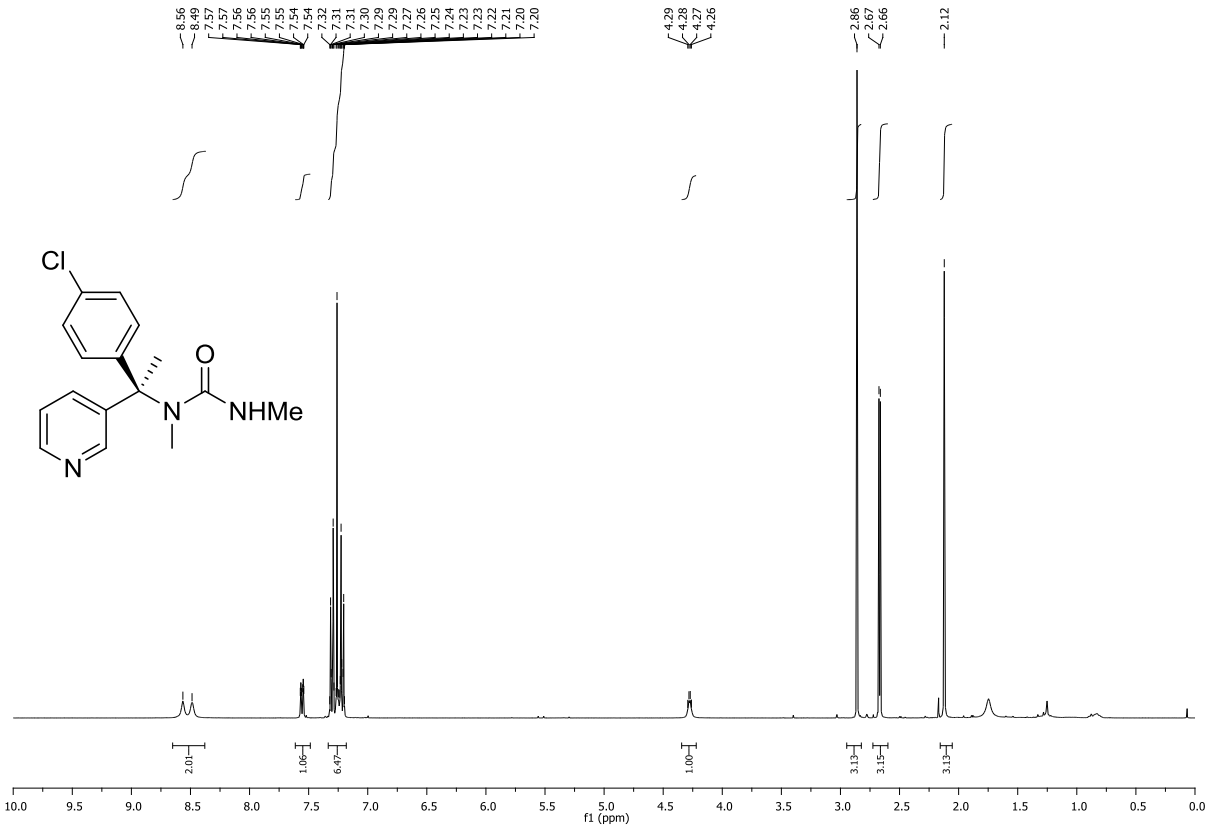

159.72
148.63
147.92
144.66
141.28
134.59
128.86
127.55
127.07
123.22
77.41
77.16
76.91
66.15
34.64
29.79
27.68
f1 (ppm)

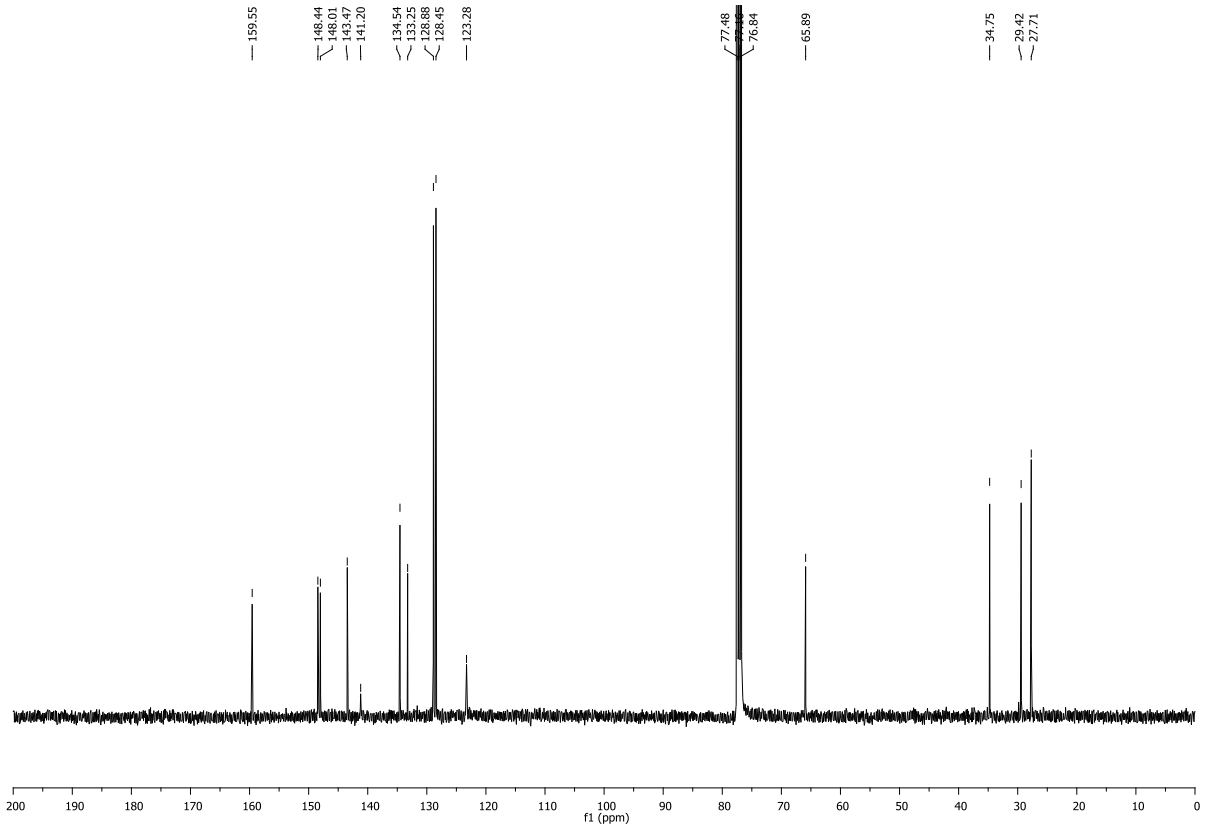
11b


8.49
8.42
7.51
7.51
7.50
7.49
7.49
7.48
7.48
7.21
7.20
7.20
7.19
7.18
7.18
7.18
7.17
7.17
7.16
6.99
6.98
6.97
6.96
6.96
6.96
6.96
6.95
6.95
6.94
6.93
4.25
4.24
4.23
4.22
2.79
2.60
2.58
2.06
F
O
N
NHMe
N
1.94
1.03
3.46
1.96
1.00
2.94
2.93
2.98
f1 (ppm)

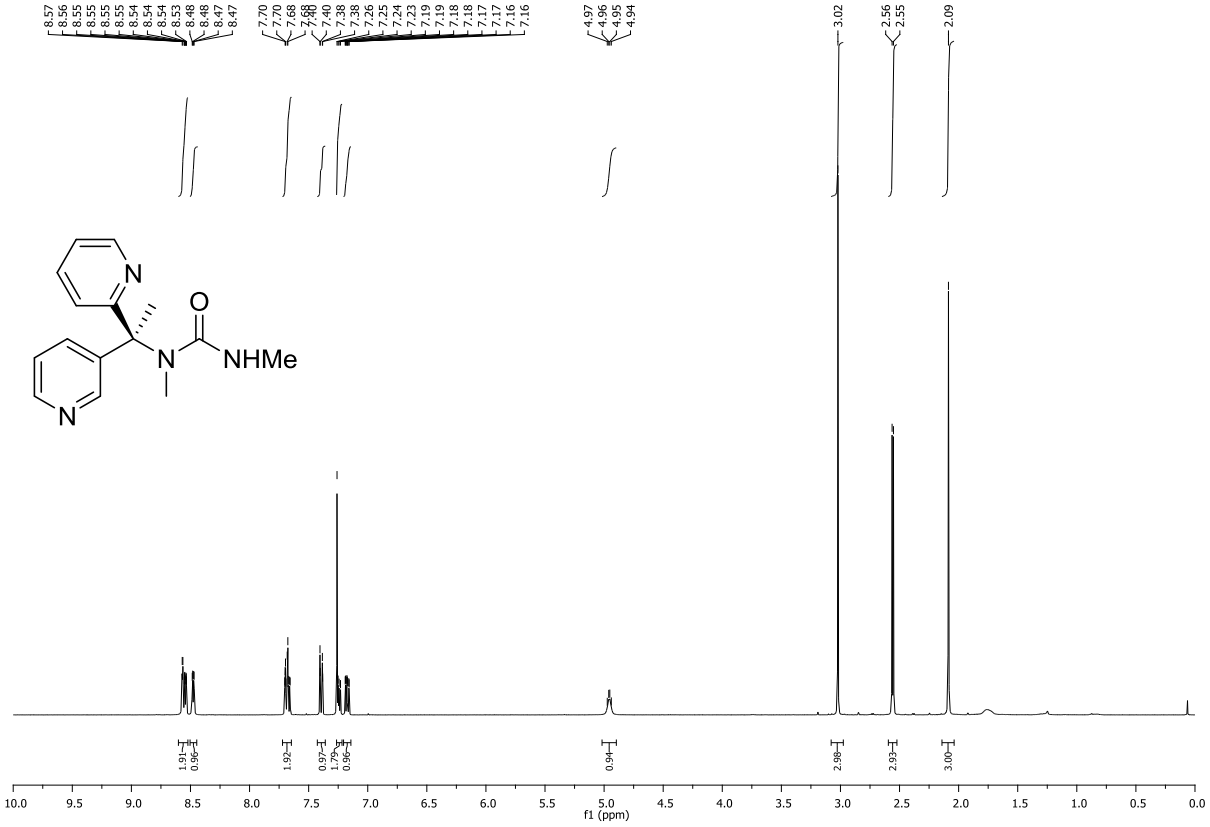

163.07
160.61
159.58
148.32
147.84
141.51
140.52
140.49
134.51
128.87
128.79
123.27
115.69
115.48
77.48
76.84
65.78
34.68
29.73
27.69
f1 (ppm)

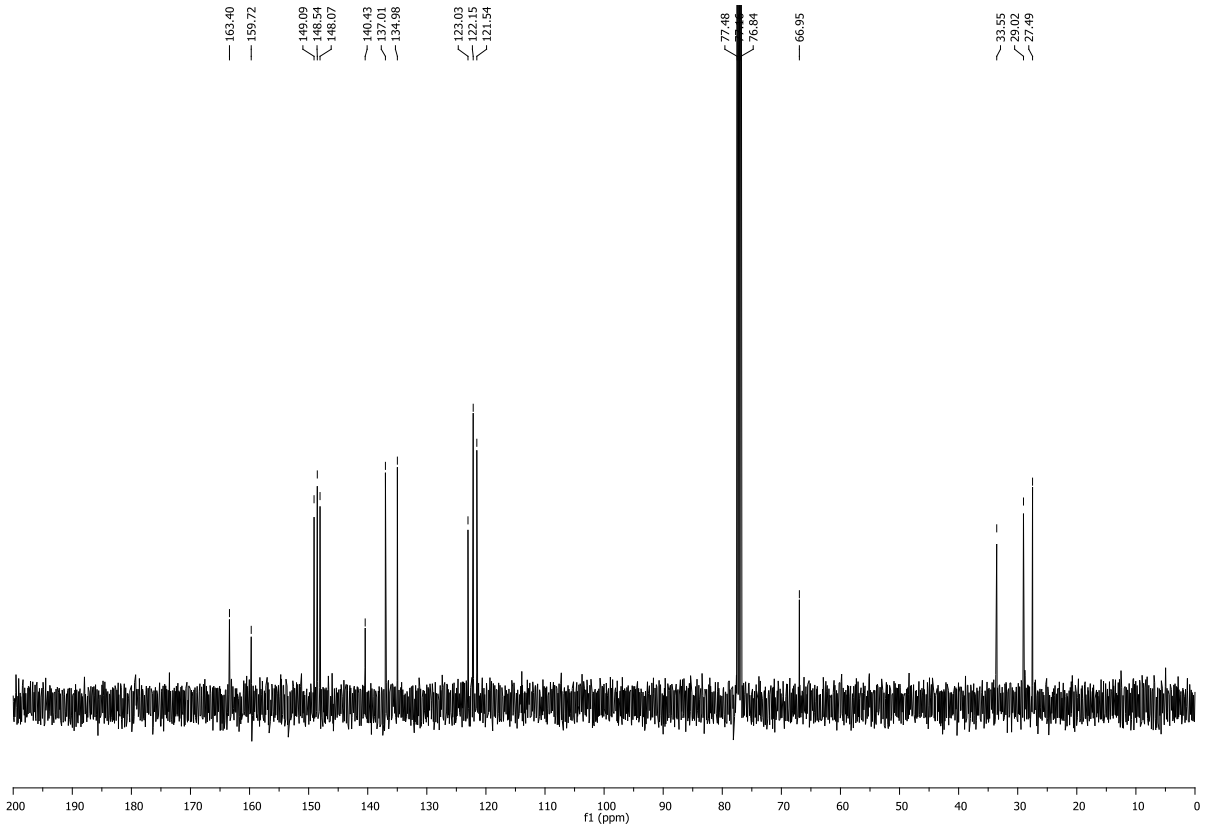
11c


8.56
8.49
7.57
7.57
7.56
7.56
7.55
7.55
7.54
7.54
7.32
7.31
7.31
7.30
7.29
7.29
7.27
7.26
7.25
7.24
7.23
7.23
7.22
7.21
7.20
7.20
4.29
4.28
4.27
4.26
2.86
2.67
2.66
2.12
Cl
O
N
NHMe
N
2.01
1.06
6.47
1.00
3.13
3.15
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

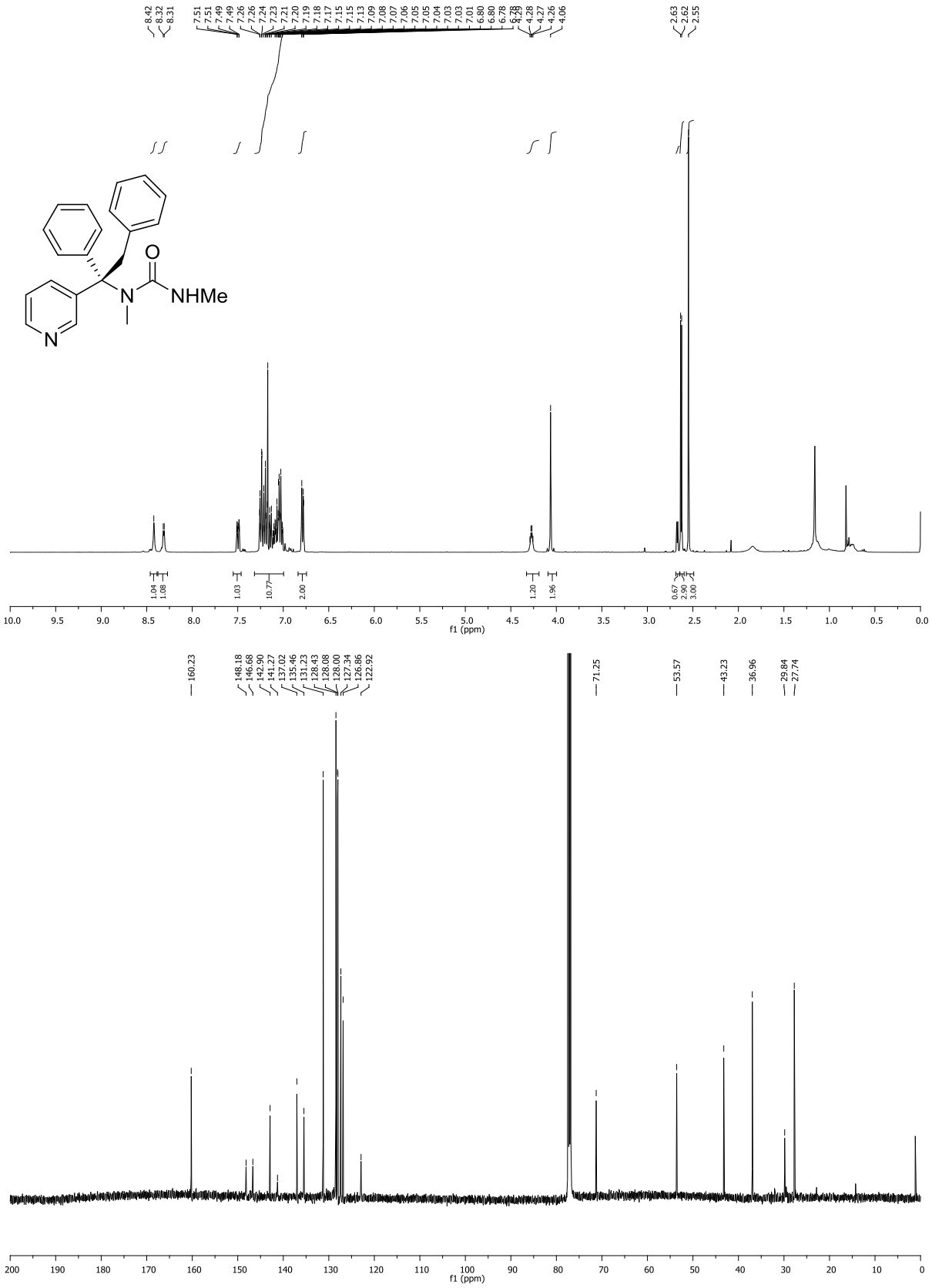

159.55
148.44
148.01
143.47
141.20
134.54
133.25
128.88
128.45
123.28
77.48
77.16
76.84
65.89
34.75
29.42
27.71
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

11d

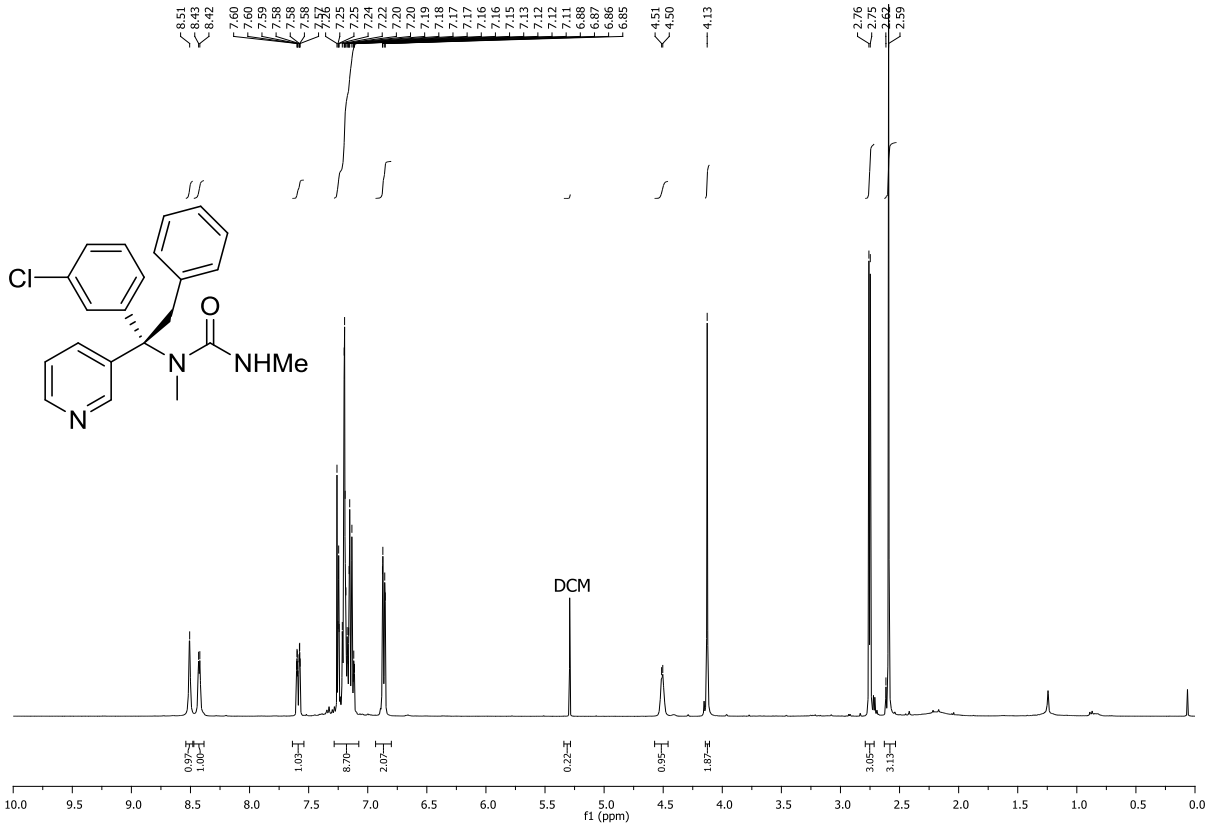

8.57
8.56
8.55
8.55
8.55
8.55
8.54
8.54
8.54
8.53
8.48
8.48
8.47
8.47
7.70
7.70
7.68
7.68
7.40
7.38
7.38
7.26
7.25
7.24
7.23
7.19
7.19
7.18
7.18
7.17
7.17
7.16
7.16
4.97
4.96
4.95
4.94
3.02
2.56
2.55
2.09
N
O
N
NHMe
N
1.91
0.96
1.92
0.97
1.79
0.96
0.94
2.98
2.93
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

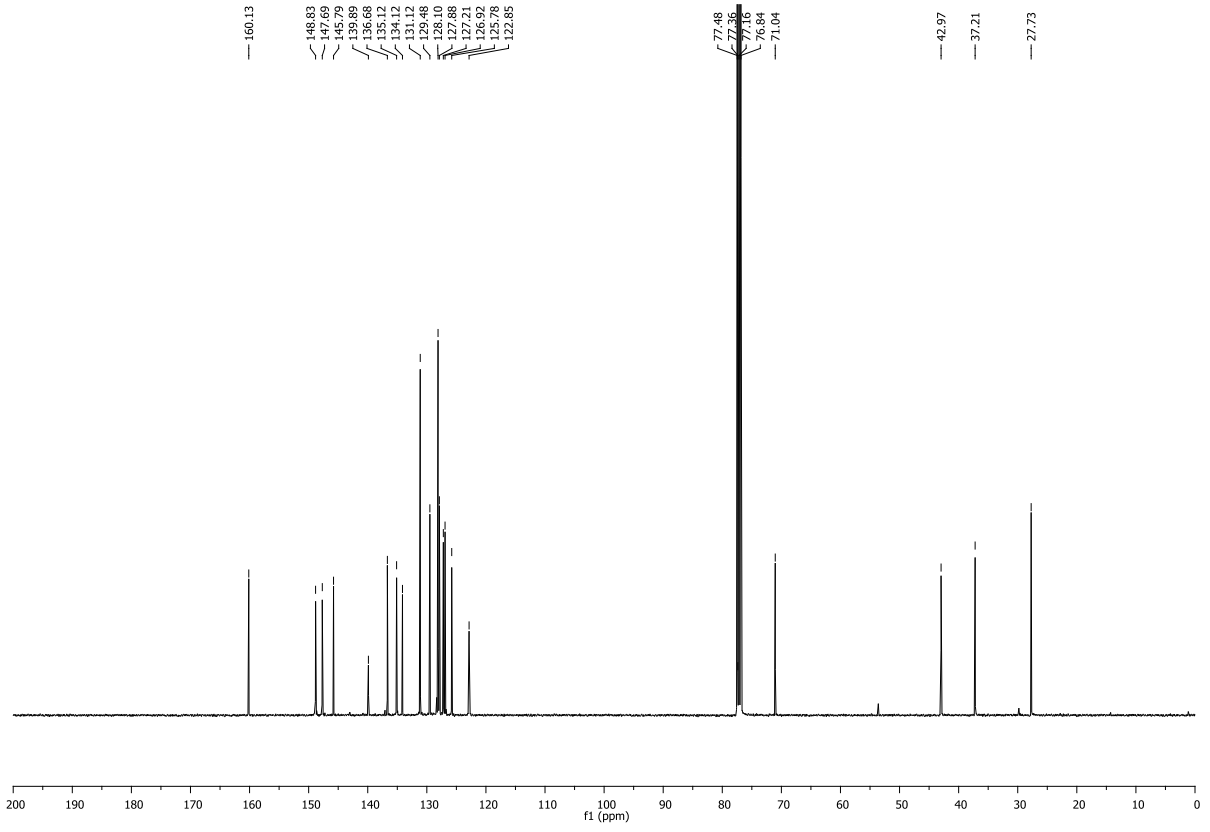

163.40
159.72
149.09
148.54
148.07
140.43
137.01
134.98
123.03
122.15
121.54
77.48
76.84
66.95
33.55
29.02
27.49
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

11e

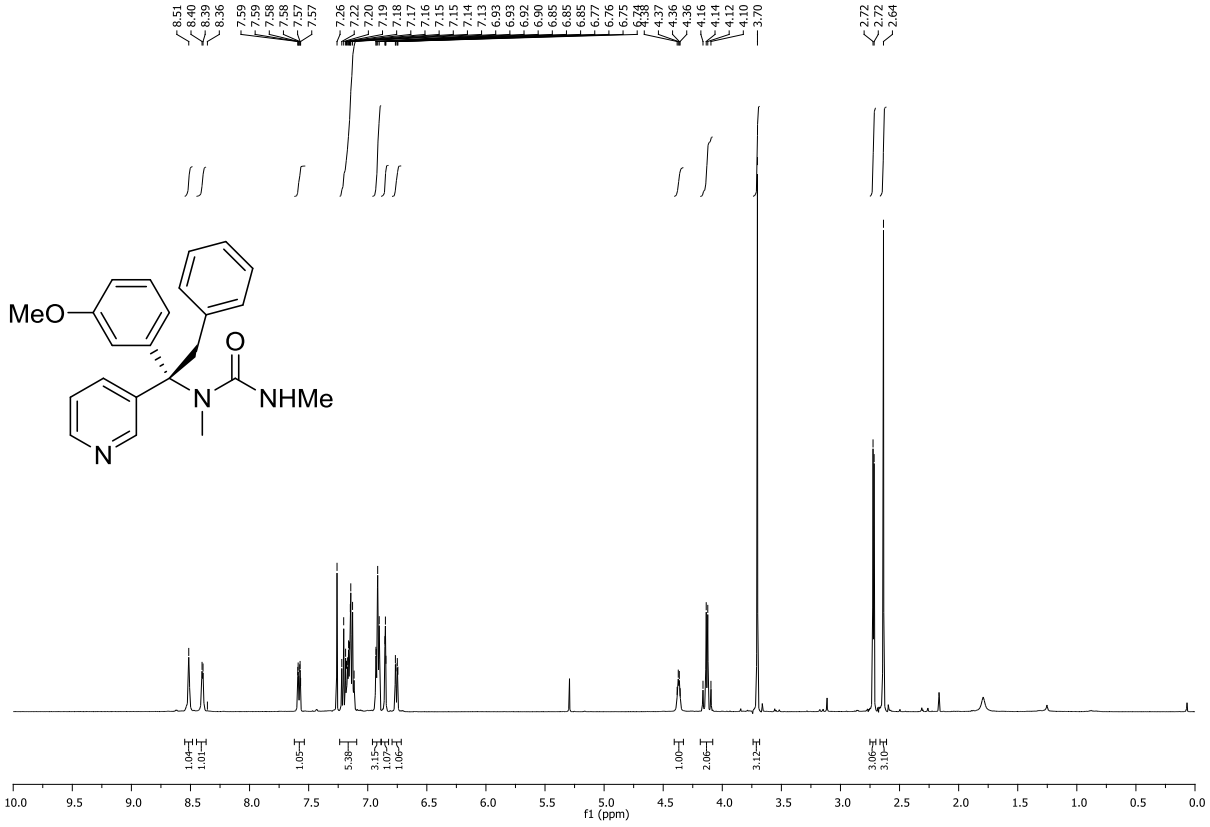

8.42
8.32
8.31
7.51
7.51
7.49
7.49
7.26
7.26
7.24
7.23
7.21
7.20
7.19
7.18
7.17
7.15
7.15
7.13
7.09
7.08
7.07
7.06
7.05
7.05
7.04
7.03
7.03
7.01
6.80
6.78
4.28
4.27
4.26
4.06
2.63
2.62
2.55
O
N
NHMe
N
1.04
1.08
1.03
10.77
2.00
1.20
1.96
0.67
2.90
3.00
f1 (ppm)
160.23
148.18
146.68
142.90
141.27
137.02
135.46
131.23
128.43
128.08
128.00
127.34
126.86
122.92
71.25
53.57
43.23
36.96
29.84
27.74
f1 (ppm)

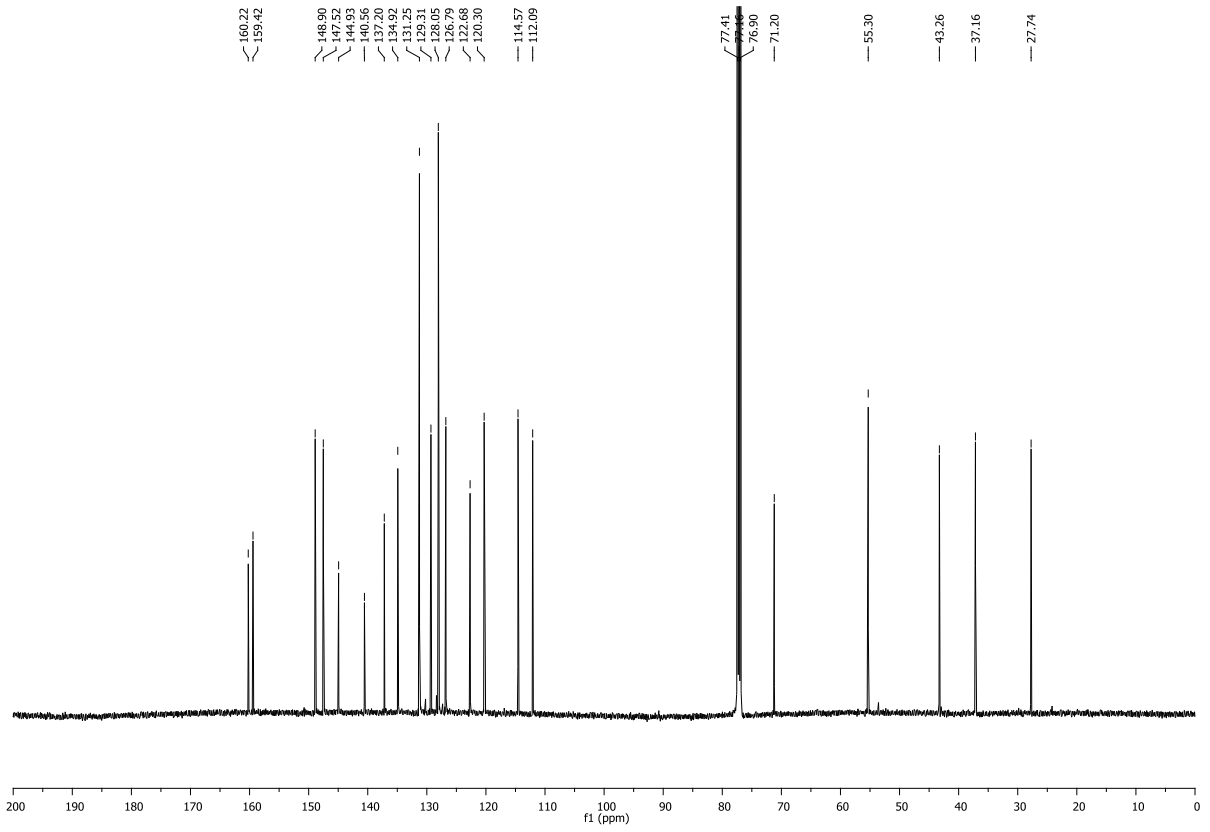
11f


8.51
8.43
8.42
7.60
7.60
7.59
7.58
7.58
7.58
7.57
7.56
7.25
7.24
7.22
7.20
7.20
7.19
7.18
7.17
7.17
7.16
7.16
7.15
7.13
7.12
7.12
7.11
6.88
6.87
6.86
6.85
4.51
4.50
4.13
2.76
2.75
2.62
2.59
Cl
O
N
NHMe
N
DCM
0.97
1.00
1.03
8.70
2.07
0.22
0.95
1.87
3.05
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

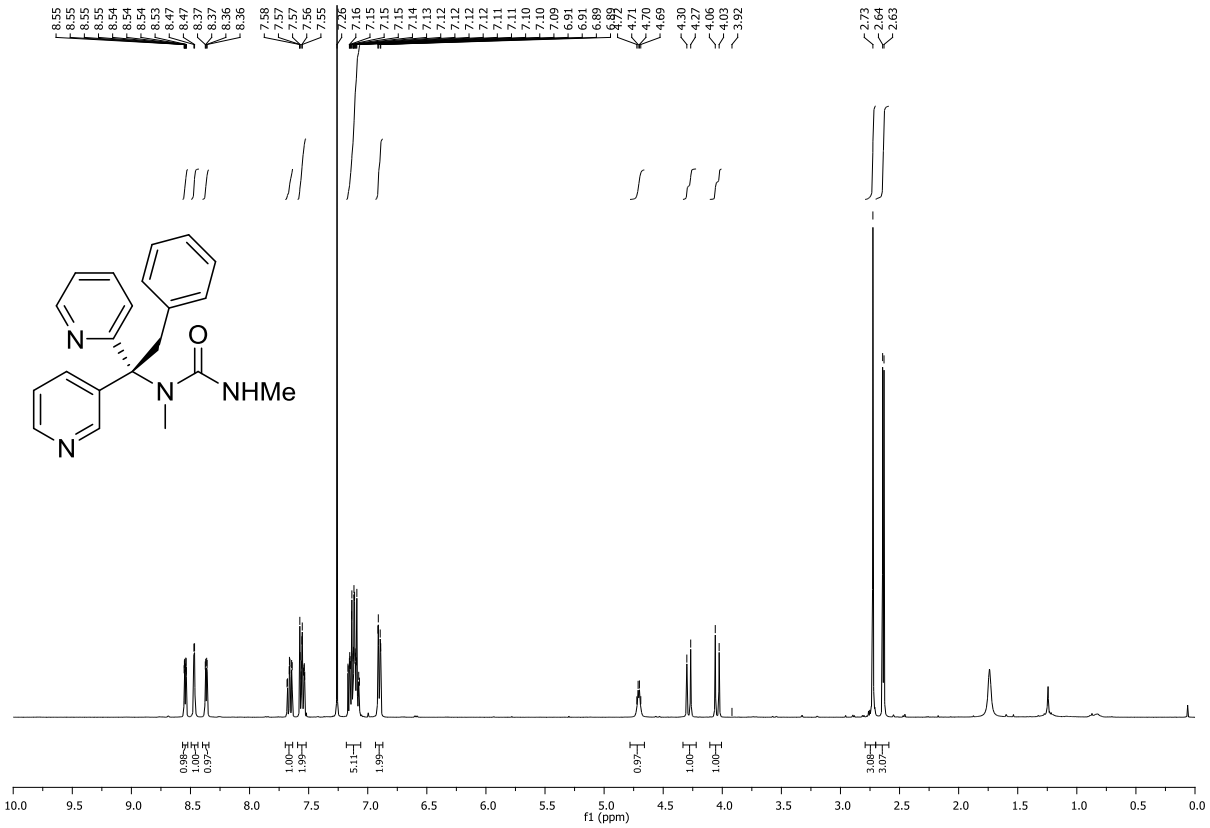

160.13
148.83
147.69
145.79
139.89
136.68
135.12
134.12
131.12
129.48
128.10
127.88
127.21
126.92
125.78
122.85
77.48
77.36
77.16
76.84
71.04
42.97
37.21
27.73
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

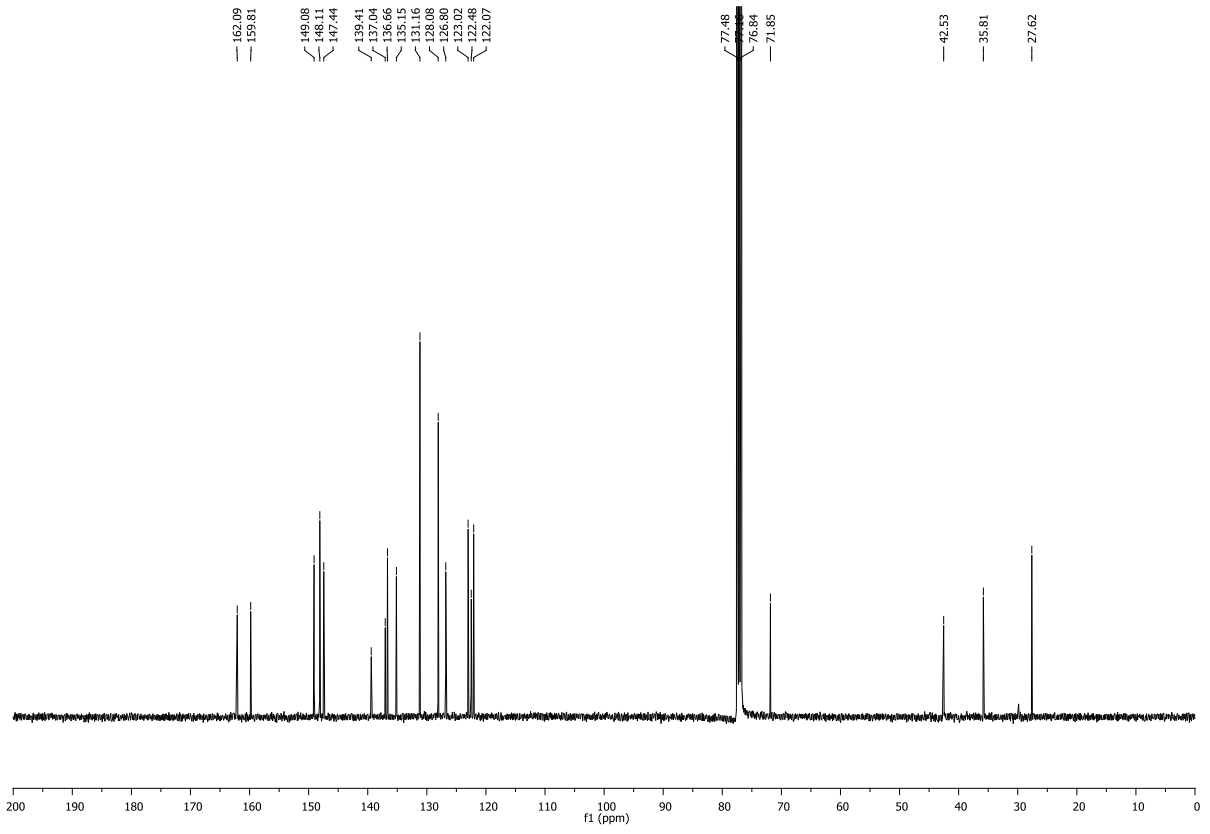
11g


8.51
8.40
8.39
8.36
7.59
7.59
7.58
7.58
7.57
7.57
7.26
7.22
7.20
7.19
7.18
7.17
7.16
7.15
7.15
7.14
7.13
6.93
6.93
6.92
6.90
6.85
6.85
6.85
6.77
6.76
6.75
4.38
4.37
4.36
4.36
4.16
4.14
4.12
4.10
3.70
2.72
2.72
2.64
MeO
O
N
NHMe
N
1.04
1.01
1.05
5.38
3.15
1.07
1.06
1.00
2.06
3.12
3.06
3.10
f1 (ppm)

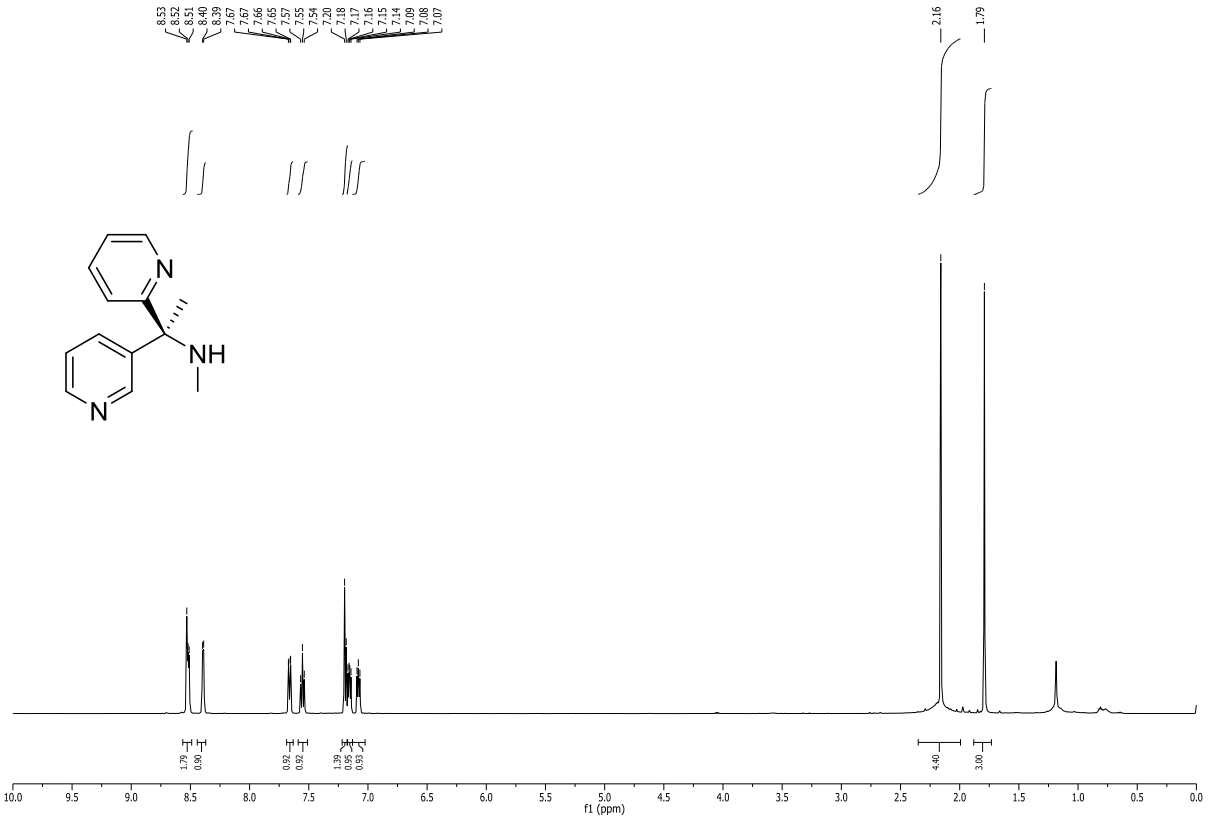

160.22
159.42
148.90
147.52
144.93
140.56
137.20
134.92
131.25
129.31
128.05
126.79
122.68
120.30
114.57
112.09
77.41
77.16
76.90
71.20
55.30
43.26
37.16
27.74
f1 (ppm)

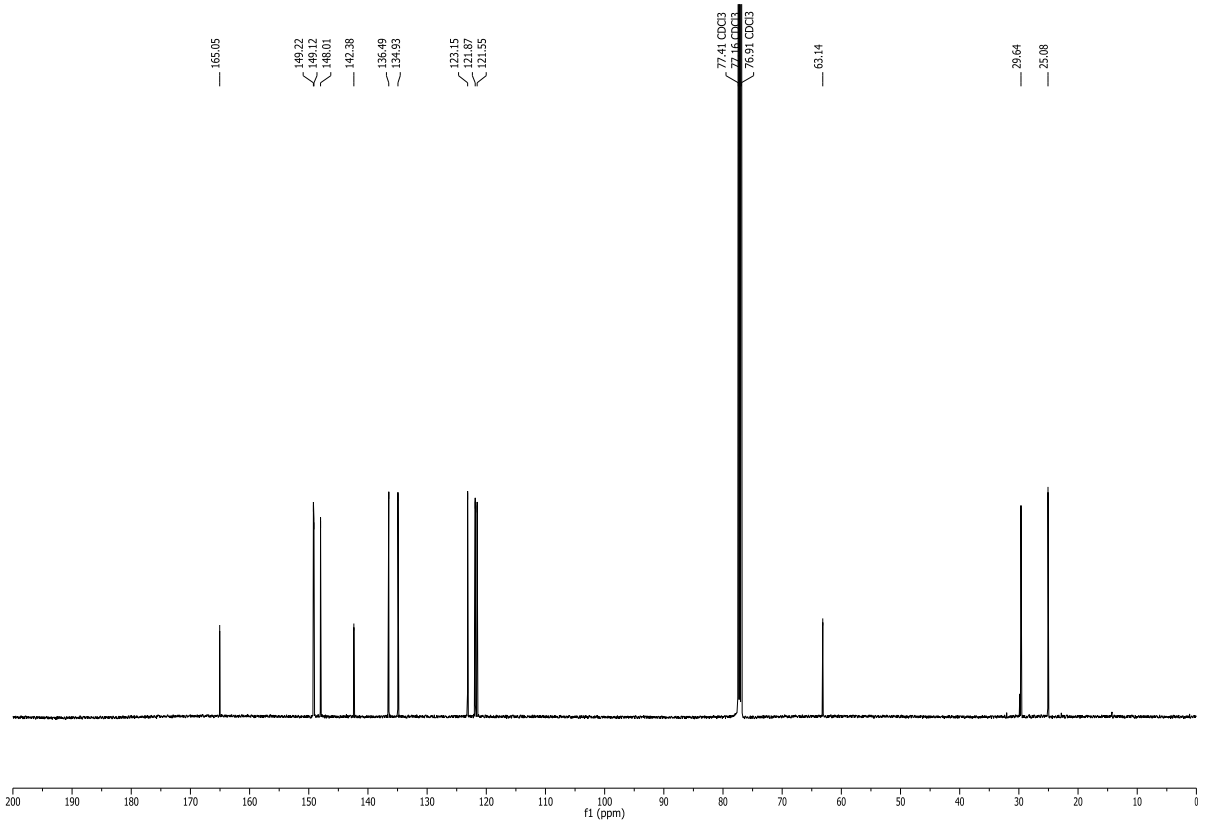
11h


8.55
8.55
8.55
8.55
8.54
8.54
8.54
8.53
8.47
8.47
8.37
8.37
8.36
8.36
7.58
7.57
7.57
7.57
7.56
7.55
7.26
7.16
7.15
7.15
7.15
7.14
7.13
7.12
7.12
7.12
7.12
7.11
7.11
7.10
7.10
7.09
6.91
6.91
6.89
4.71
4.70
4.69
4.30
4.27
4.06
4.03
3.92
2.73
2.64
2.63
N
O
N
NHMe
N
0.98
1.00
0.97
1.00
1.99
5.11
1.99
0.97
1.00
1.00
3.08
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

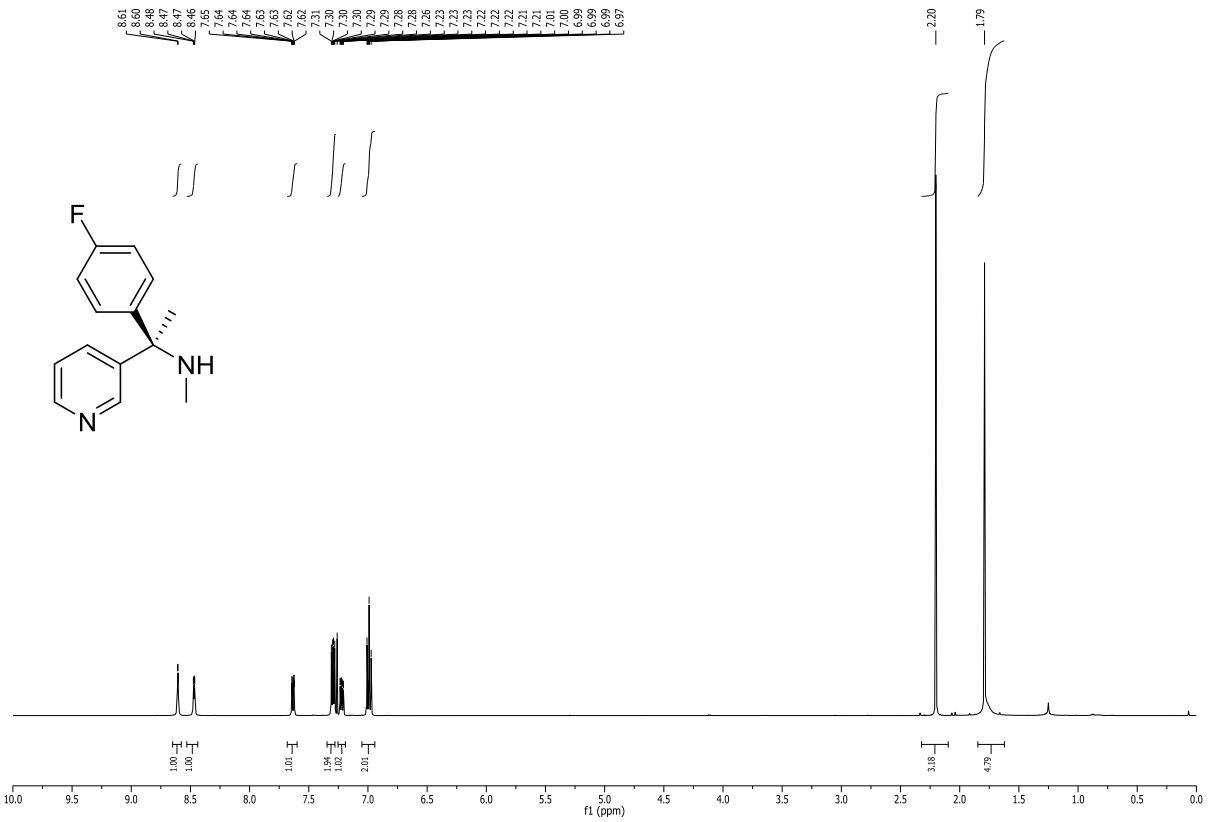

162.09
159.81
149.08
148.11
147.44
139.41
137.04
136.66
135.15
131.16
128.08
126.80
123.02
122.48
122.07
77.48
77.16
76.84
71.85
42.53
35.81
27.62
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

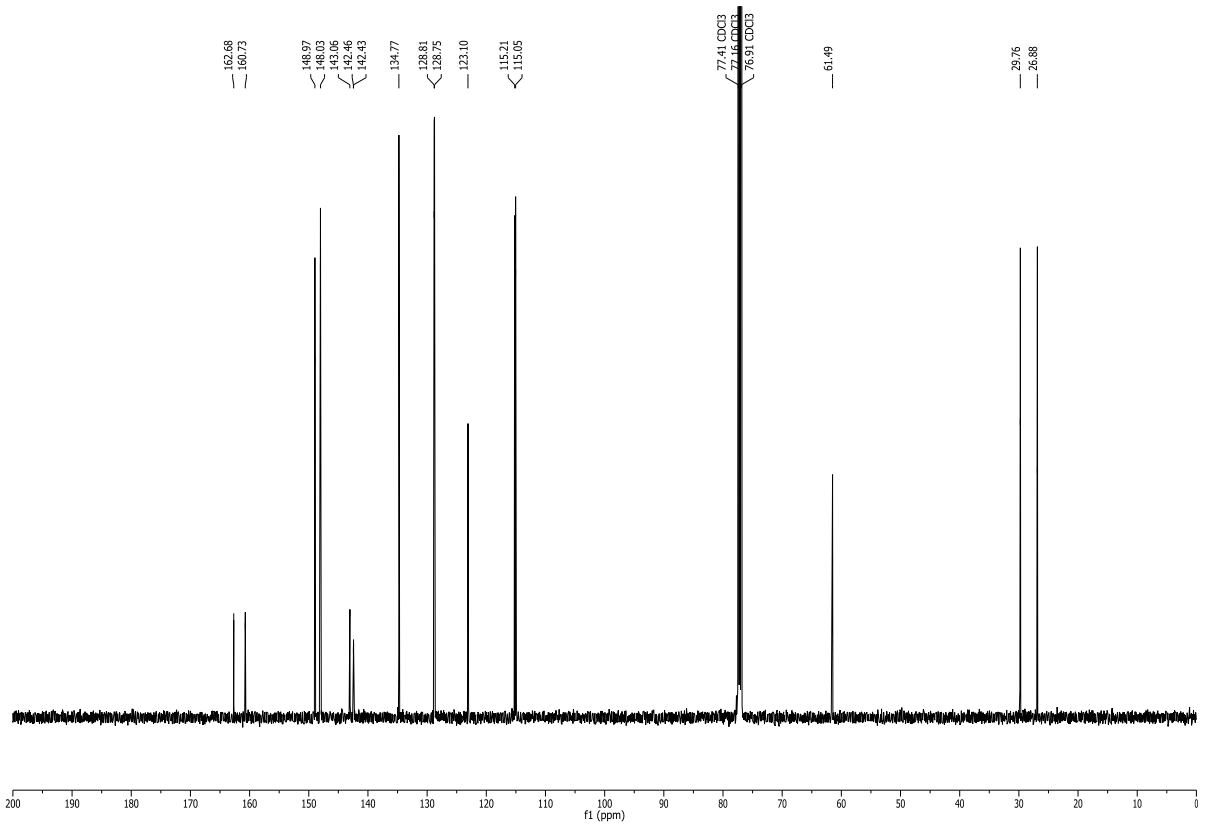
12b


8.53
8.52
8.51
8.40
8.39
7.67
7.67
7.66
7.65
7.57
7.55
7.54
7.20
7.18
7.17
7.16
7.15
7.14
7.09
7.08
7.07
2.16
1.79
N
NH
N
1.79
0.90
0.92
0.92
1.39
0.95
0.93
4.40
3.00
f1 (ppm)

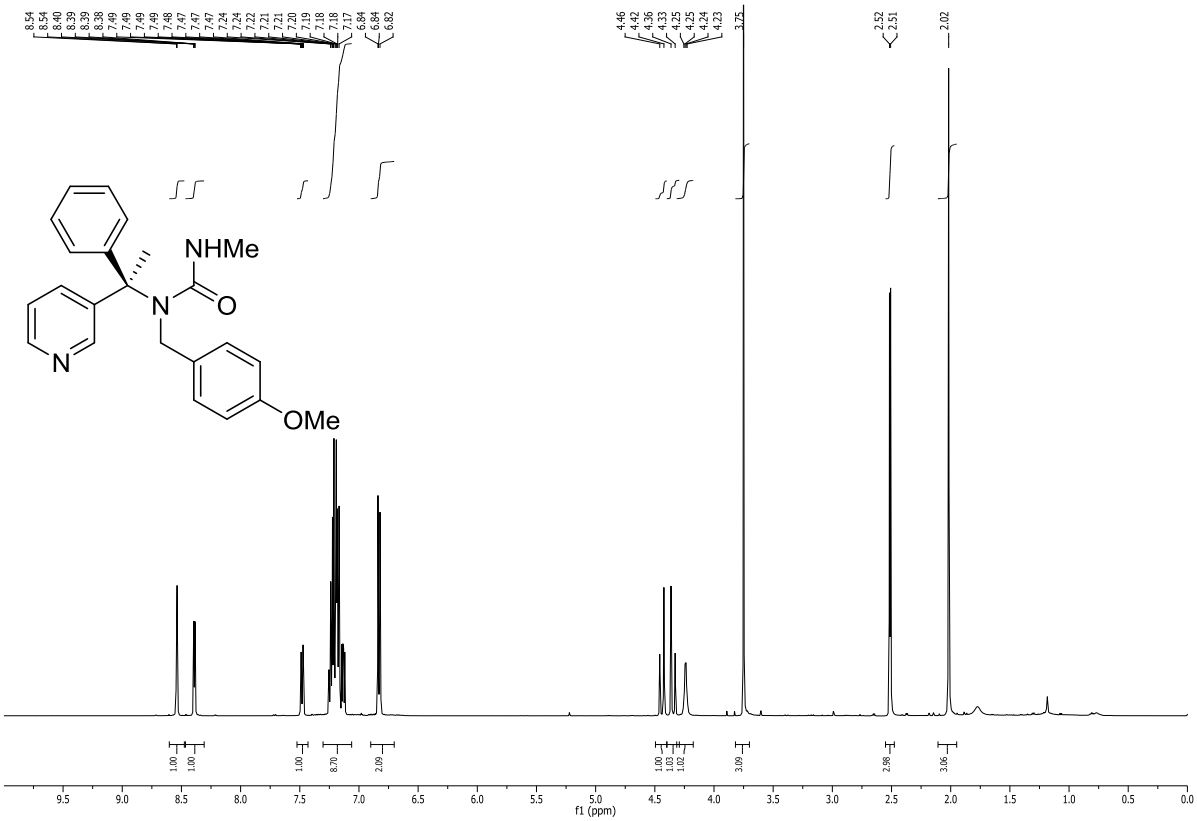

165.05
149.22
149.12
148.01
142.38
136.49
134.93
123.15
121.87
121.55
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
63.14
29.64
25.08
f1 (ppm)

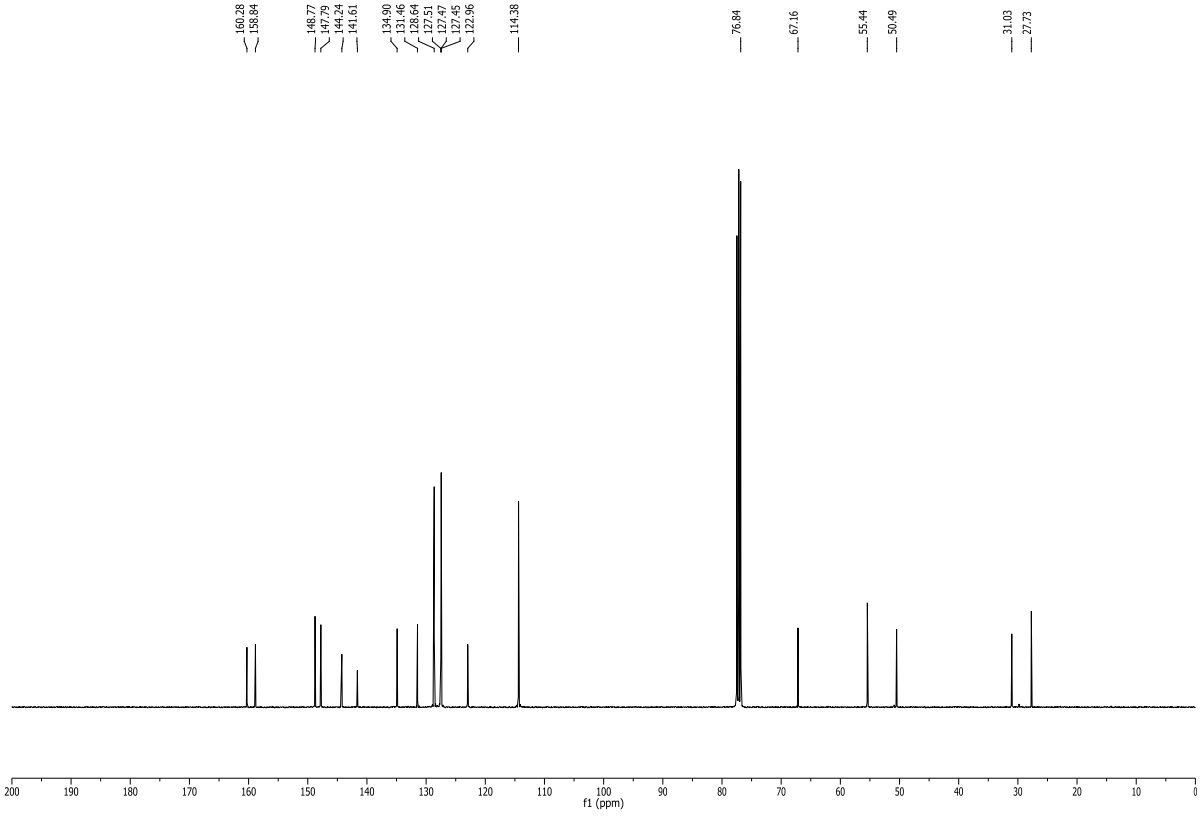
12d


8.61
8.60
8.48
8.47
8.47
8.47
8.46
7.65
7.64
7.64
7.64
7.63
7.63
7.62
7.62
7.31
7.30
7.30
7.30
7.29
7.29
7.28
7.28
7.26
7.23
7.23
7.23
7.22
7.22
7.22
7.21
7.21
7.01
7.00
6.99
6.99
6.99
6.97
2.20
1.79
F
NH
N
1.00
1.00
1.01
1.94
1.02
2.01
3.18
4.79
f1 (ppm)

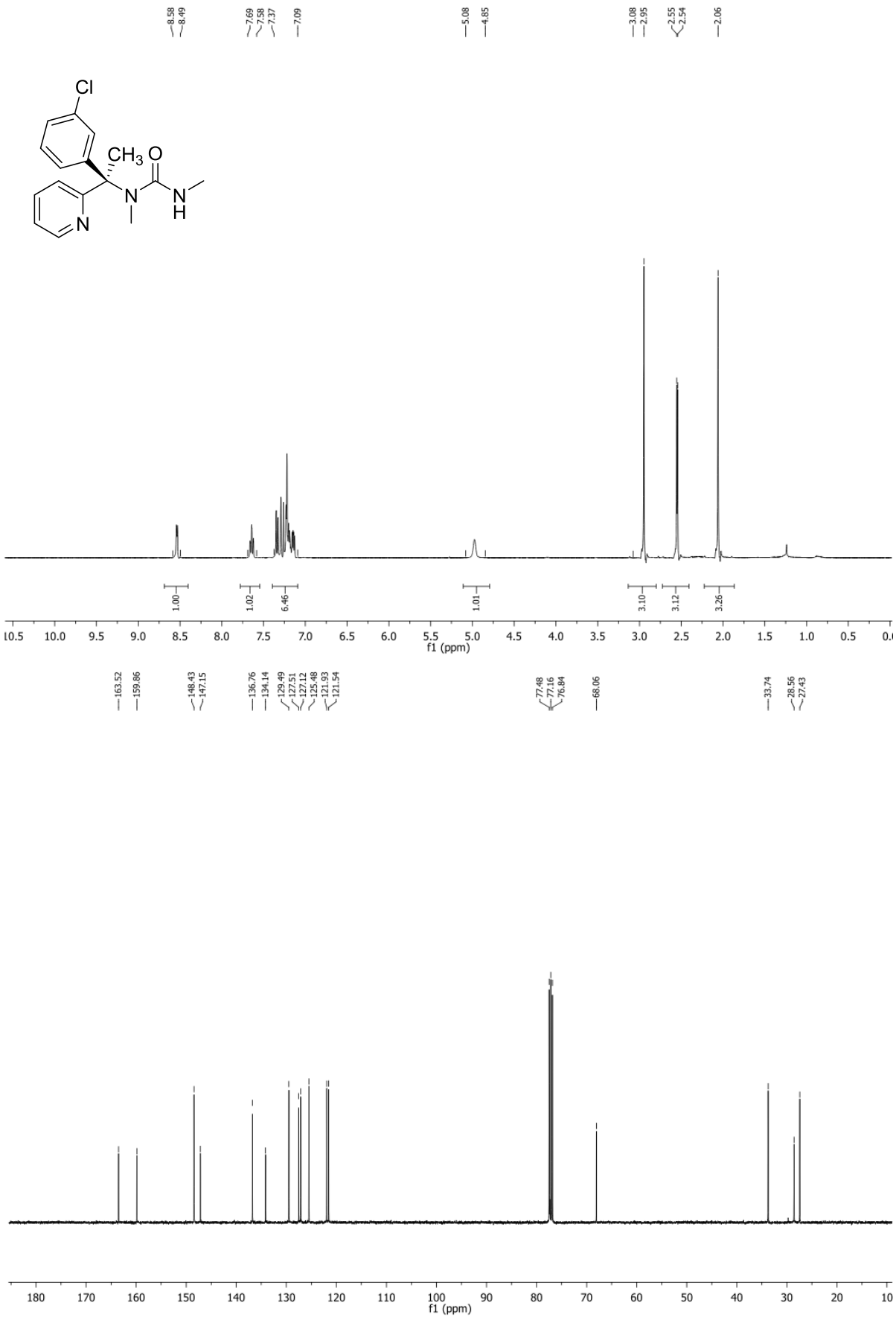

162.68
160.73
148.97
148.03
143.06
142.46
142.43
134.77
128.81
128.75
123.10
115.21
115.05
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
61.49
29.76
26.88
f1 (ppm)

13

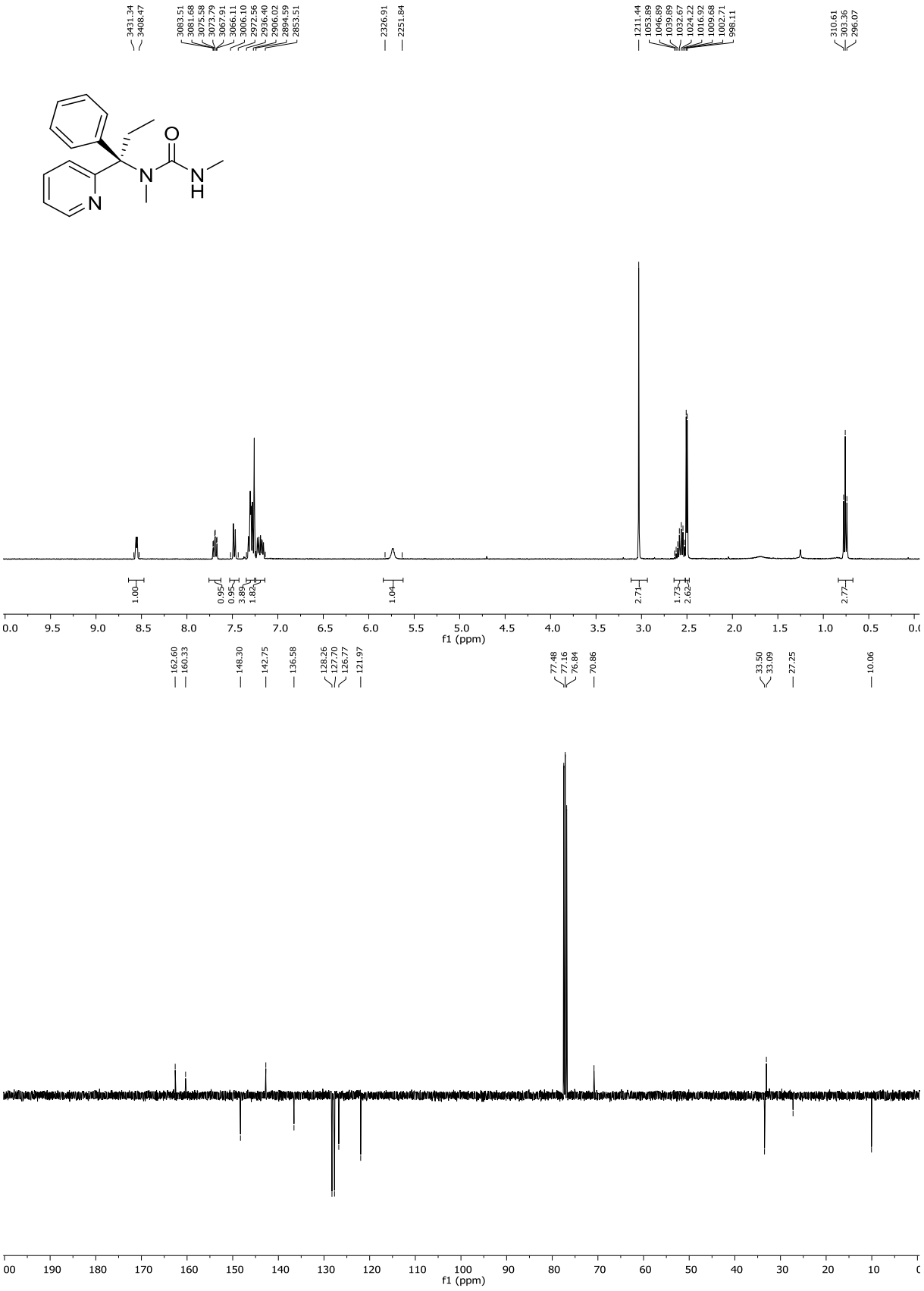




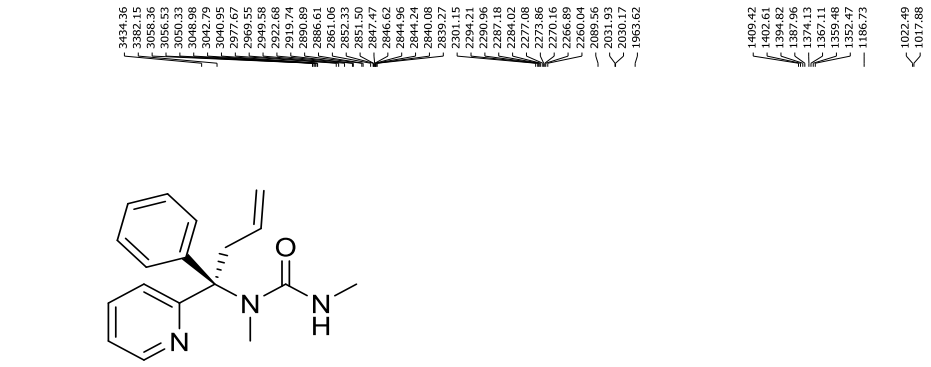
14a


8.58
8.49
7.69
7.58
7.37
7.09
5.08
4.85
3.08
2.95
2.55
2.54
2.06
Cl
CH3
O
N
N
H
N
1.00
1.02
6.46
1.01
3.10
3.12
3.26
f1 (ppm)
163.52
159.86
148.43
147.15
136.76
134.14
129.49
127.51
127.12
125.48
121.93
121.54
77.48
77.16
76.84
68.06
33.74
28.56
27.43
f1 (ppm)

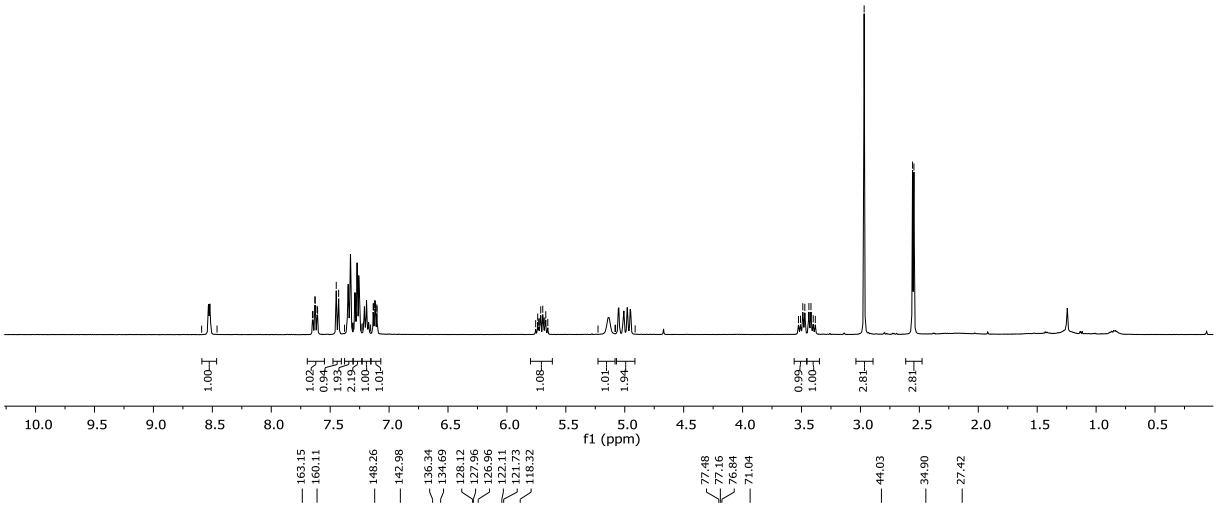
14b

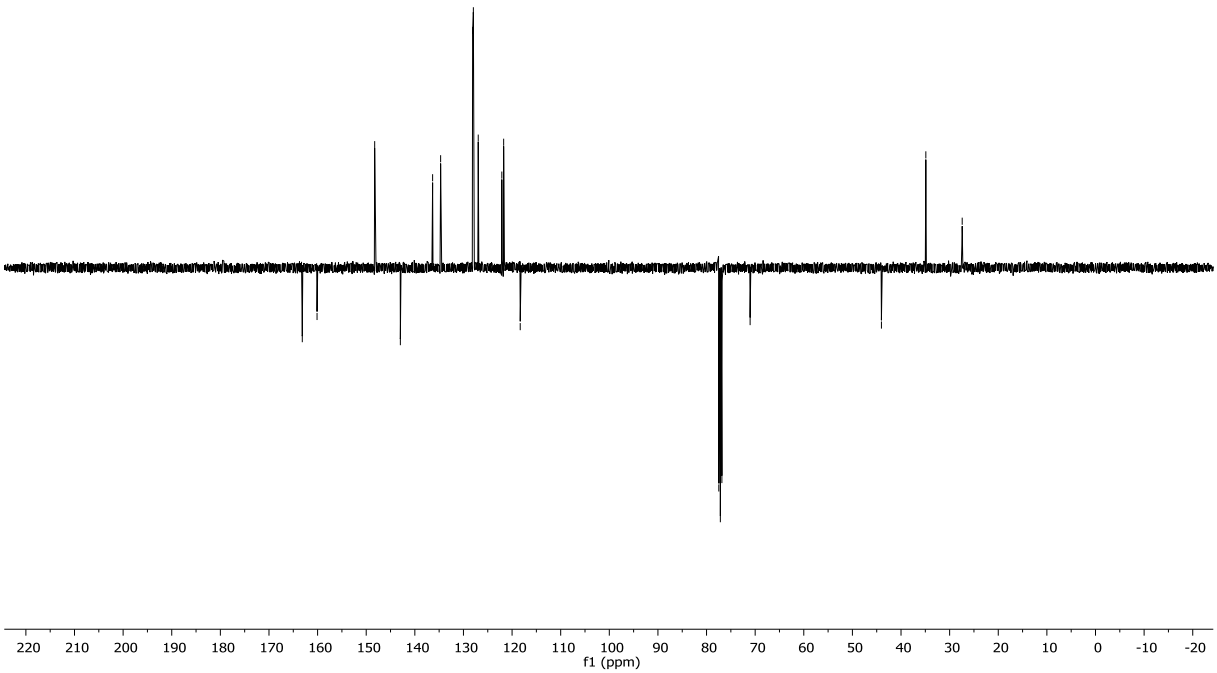

3431.34
3408.47
3083.51
3081.68
3075.58
3073.79
3067.91
3066.11
3006.10
2972.56
2936.40
2906.02
2894.59
2853.51
2326.91
2251.84
1211.44
1053.89
1046.89
1039.89
1032.67
1024.22
1016.92
1009.68
1002.71
998.11
310.61
303.36
296.07
O
N
N
H
N
1.00
0.95
0.95
3.85
1.82
1.04
2.71
1.73
2.62
2.77
f1 (ppm)
162.60
160.33
148.30
142.75
136.58
128.26
127.70
126.77
121.97
77.48
77.16
76.84
70.86
33.50
33.09
27.25
10.06
f1 (ppm)

14c

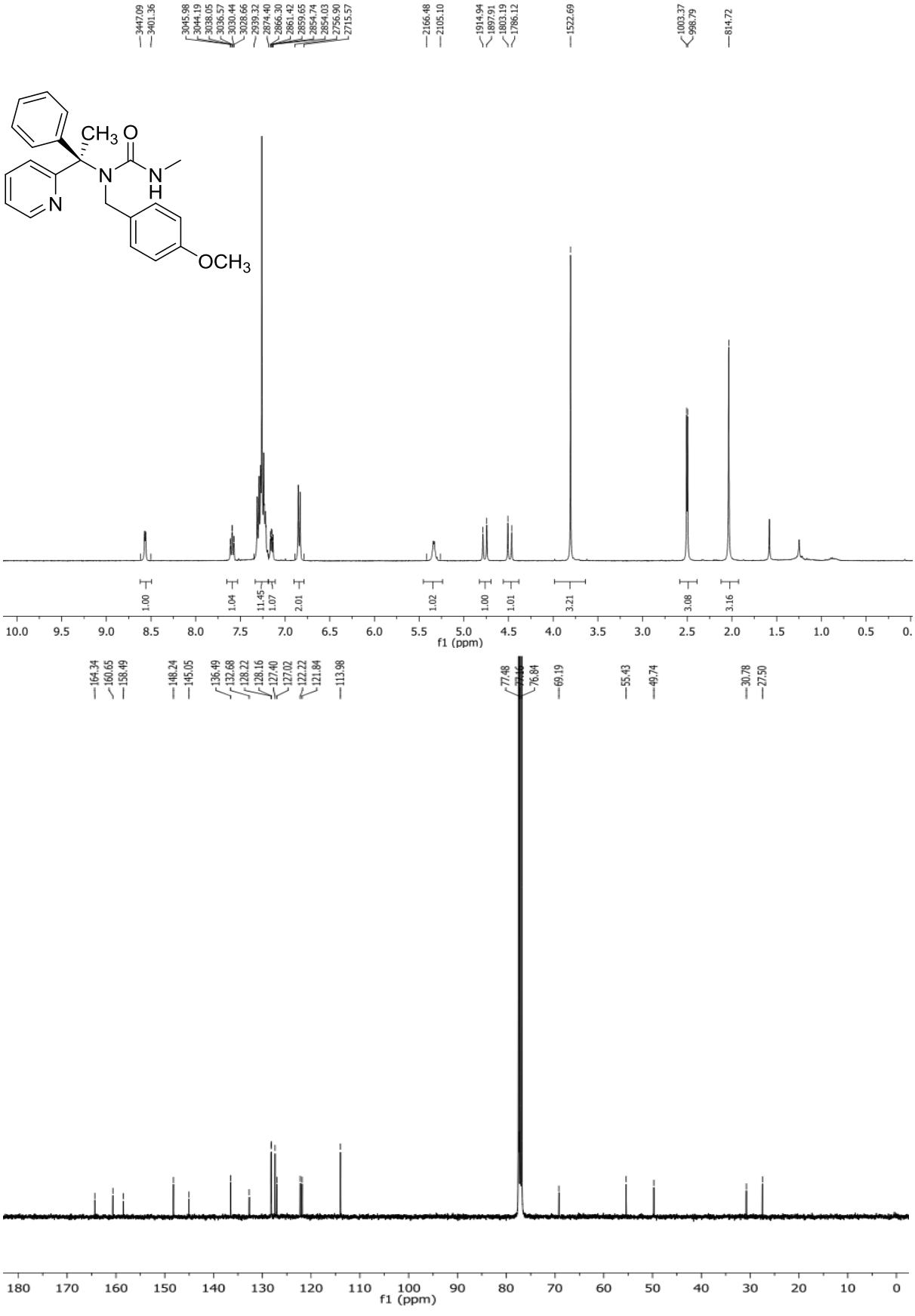

3434.36
3382.15
3058.36
3056.53
3050.33
3048.98
3042.79
3040.95
2977.67
2969.55
2949.58
2922.68
2919.74
2890.89
2886.61
2861.06
2852.33
2851.50
2847.47
2846.62
2844.96
2844.24
2840.08
2839.27
2301.15
2294.21
2290.96
2287.18
2284.02
2277.08
2273.86
2270.16
2266.04
2089.56
2031.93
2030.17
1963.62
1409.42
1402.61
1394.82
1387.96
1374.13
1367.11
1359.48
1352.47
1186.73
1022.49
1017.88

O
N
N
H
N

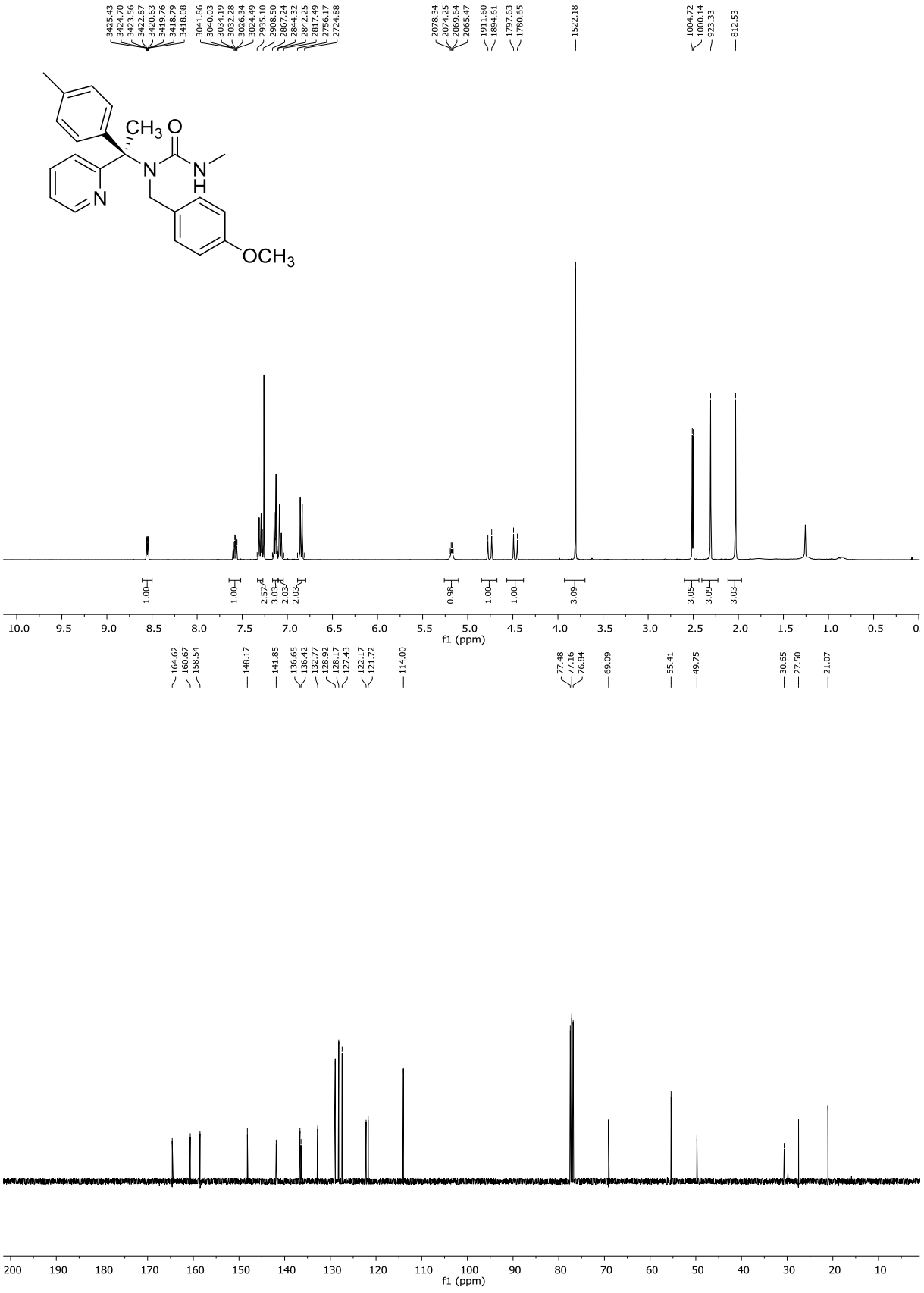

1.00
1.02
0.94
1.93
2.19
1.00
1.01
1.08
1.01
1.94
0.99
1.00
2.81
2.81
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
163.15
160.11
148.26
142.98
136.34
134.69
128.12
127.96
126.96
122.11
121.73
118.32
77.48
77.16
76.84
71.04
44.03
34.90
27.42


220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

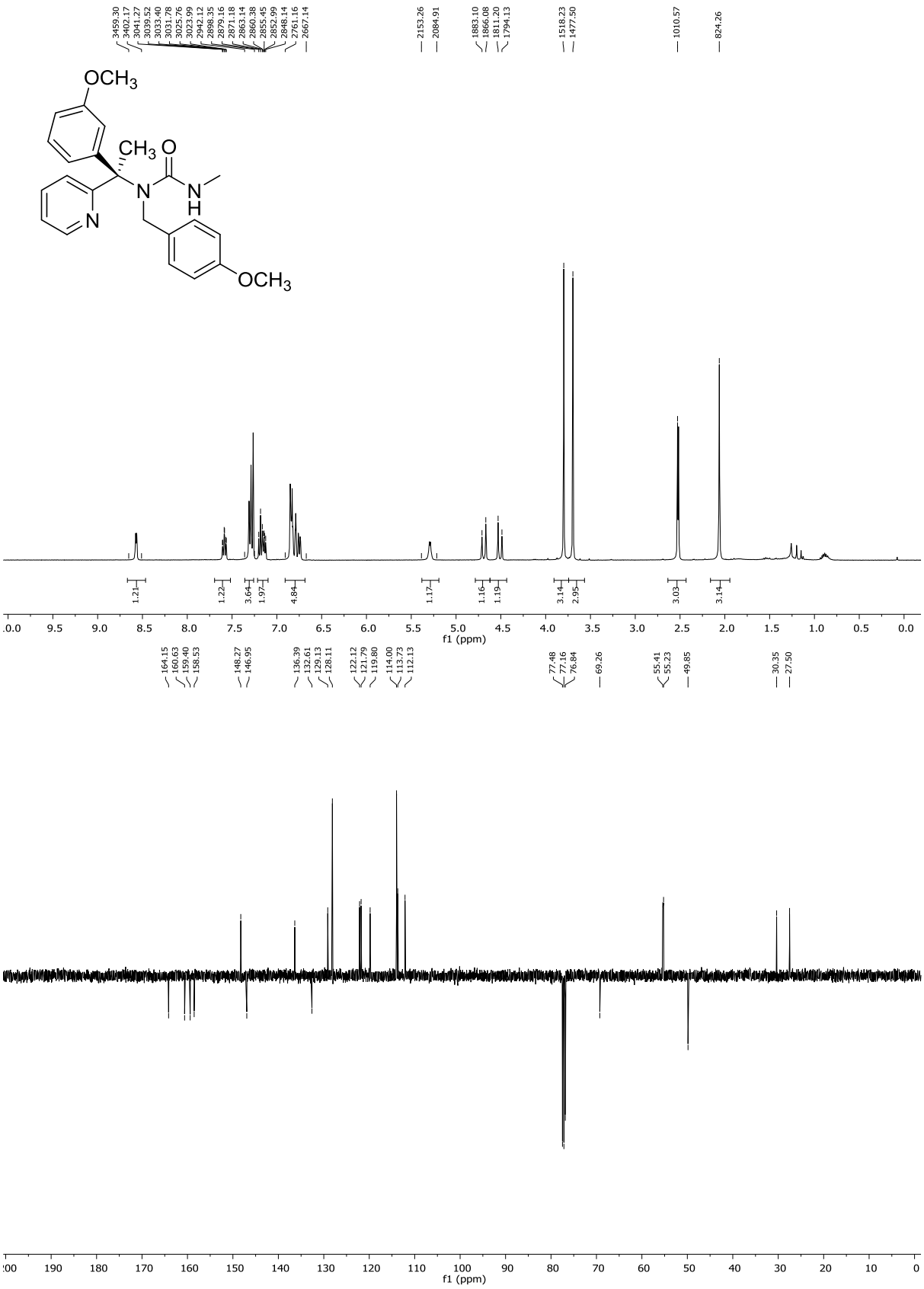
15a


3447.09
3401.36
3045.98
3044.19
3038.05
3036.57
3030.44
3028.66
2939.32
2874.40
2866.30
2861.42
2859.65
2854.74
2854.03
2756.90
2715.57
2166.48
2105.10
1914.94
1897.91
1803.19
1786.12
1522.69
1003.37
998.79
814.72
CH3
O
N
N
H
N
OCH3
1.00
1.04
11.45
1.07
2.01
1.02
1.00
1.01
3.21
3.08
3.16
f1 (ppm)
164.34
160.65
158.49
148.24
145.05
136.49
132.68
128.22
128.16
127.40
127.02
122.22
121.84
113.98
77.48
77.16
76.84
69.19
55.43
49.74
30.78
27.50
f1 (ppm)

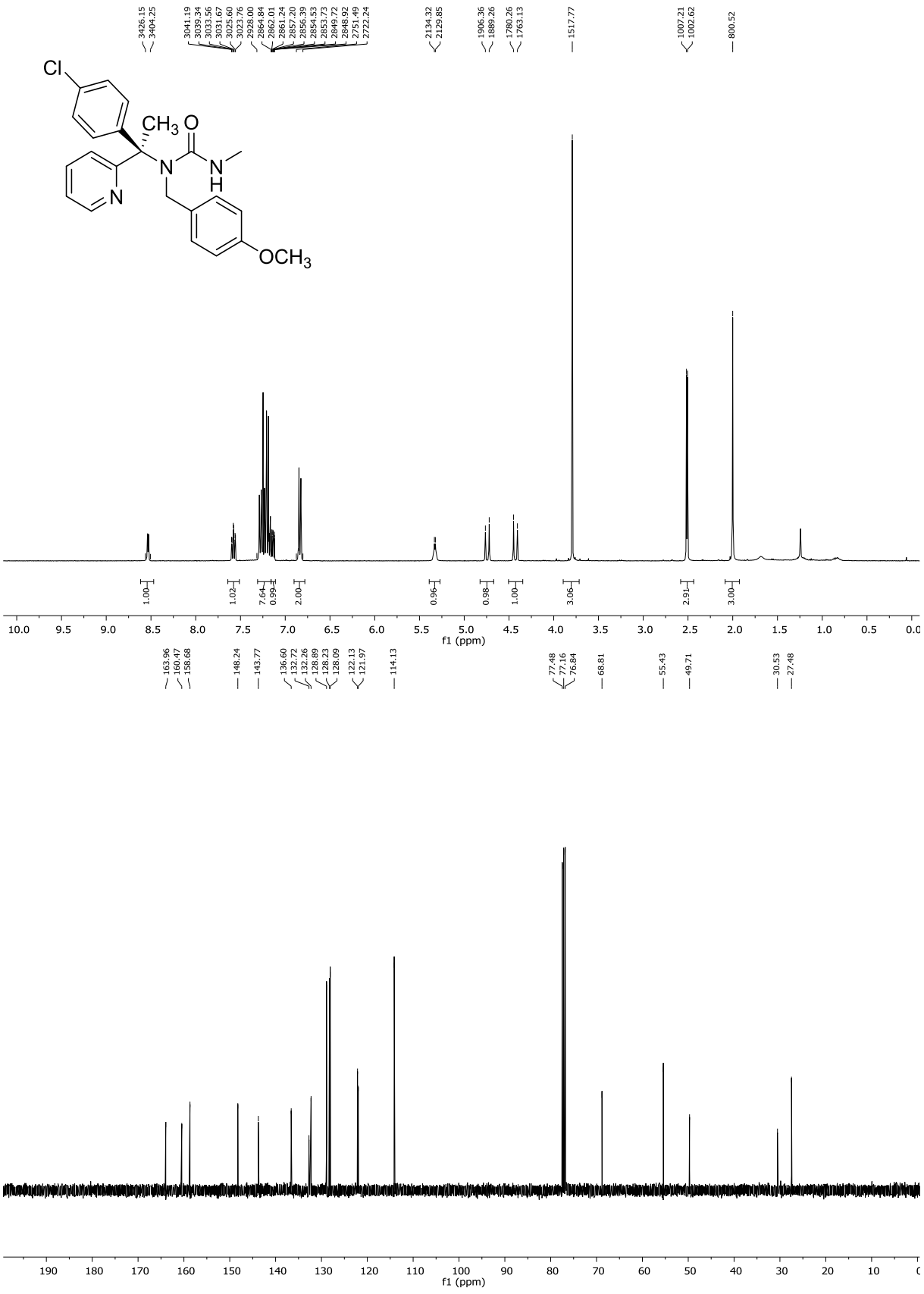
15b


3425.43
3424.70
3423.56
3422.87
3420.63
3419.76
3418.79
3418.08
3041.86
3040.03
3034.19
3032.28
3026.34
3024.49
2935.10
2908.50
2867.24
2844.32
2842.25
2817.49
2756.17
2724.88
2078.34
2074.25
2069.64
2065.47
1911.60
1894.61
1797.63
1780.65
1522.18
1004.72
1000.14
923.33
812.53
CH3
O
N
N
H
N
OCH3
1.00
1.00
2.57
3.03
2.03
2.03
0.98
1.00
1.00
3.09
3.05
3.09
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)
164.62
160.67
158.54
148.17
141.85
136.65
136.42
132.77
128.92
128.17
127.43
122.17
121.72
114.00
77.48
77.16
76.84
69.09
55.41
49.75
30.65
27.50
21.07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

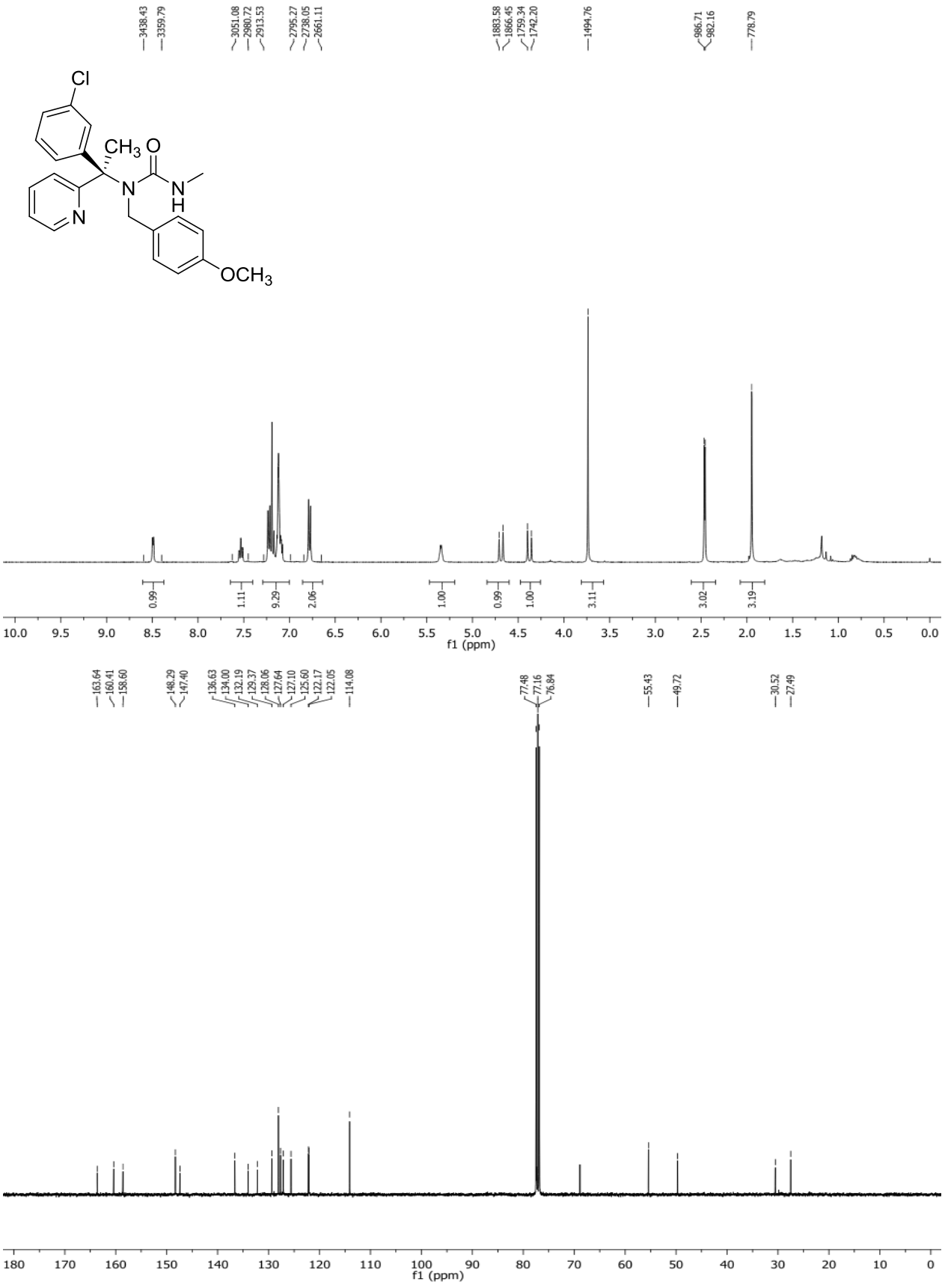
15c


3459.30
3402.17
3041.27
3039.52
3033.40
3031.78
3025.76
3023.99
2942.12
2898.35
2879.16
2871.18
2863.14
2860.38
2855.45
2852.99
2848.14
2761.16
2667.14
2153.26
2084.91
1883.10
1866.08
1811.20
1794.13
1518.23
1477.50
1010.57
824.26
OCH3
CH3
O
N
N
H
N
OCH3
1.21
1.22
3.64
1.97
4.84
1.17
1.16
1.19
3.14
2.95
3.03
3.14
f1 (ppm)
164.15
160.63
159.40
158.53
148.27
146.95
136.39
132.61
129.13
128.11
122.12
121.79
119.80
114.00
113.73
112.13
77.48
77.16
76.84
69.26
55.41
55.23
49.85
30.35
27.50
f1 (ppm)

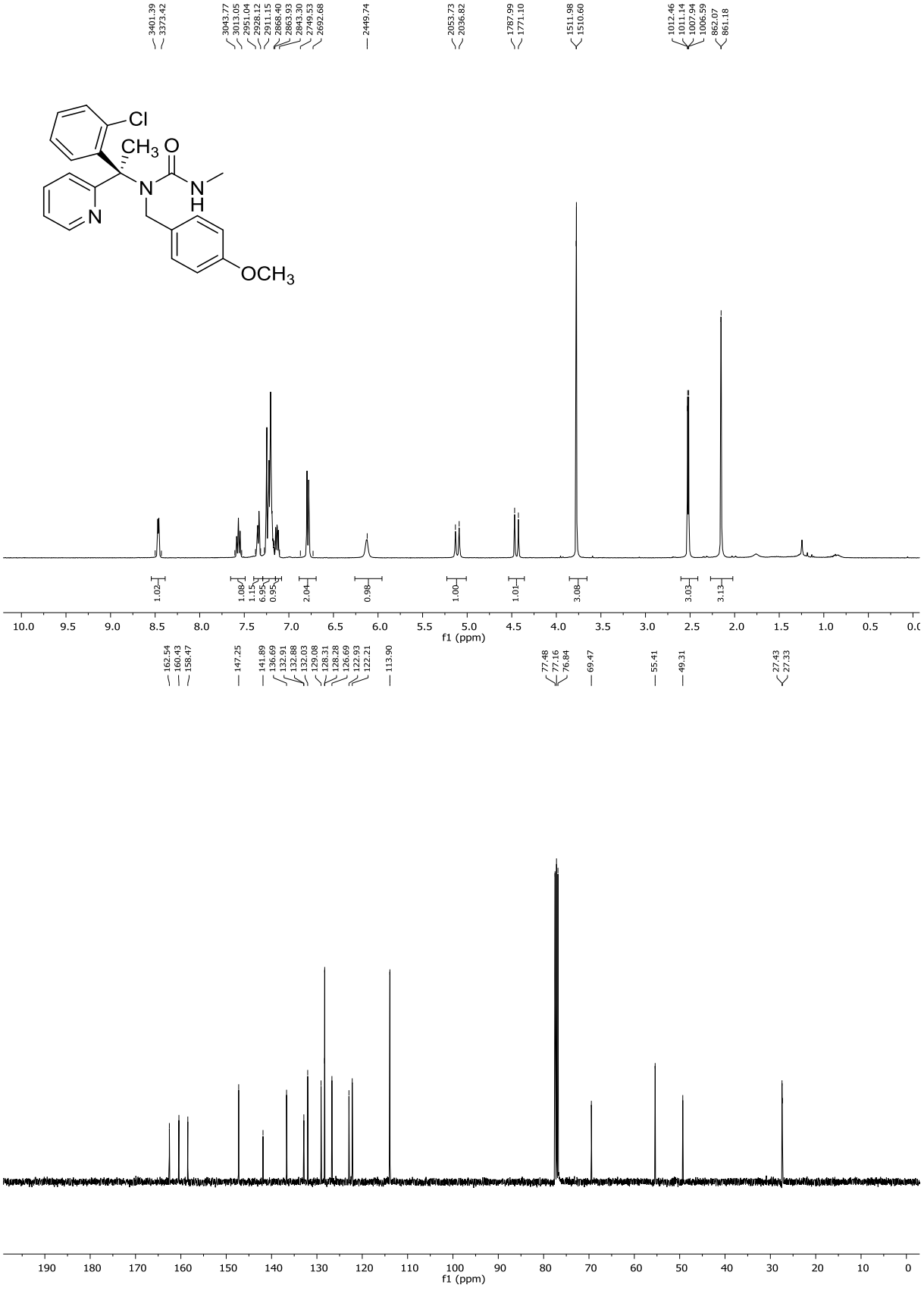
15d


3426.15
3404.25
3041.19
3039.34
3033.56
3031.67
3025.60
3023.76
2928.00
2864.84
2862.01
2861.24
2857.20
2856.39
2854.53
2853.73
2849.72
2846.92
2751.49
2722.24
2134.32
2129.85
1906.36
1889.26
1780.26
1763.13
1517.77
1007.21
1002.62
800.52
Cl
CH3
O
N
N
H
N
OCH3
1.00
1.02
7.64
0.99
2.00
0.96
0.98
1.00
3.06
2.91
3.00
f1 (ppm)
163.96
160.47
158.68
148.24
143.77
136.60
132.72
132.26
128.89
128.23
128.09
122.13
121.97
114.13
77.48
77.16
76.84
68.81
55.43
49.71
30.53
27.48
f1 (ppm)

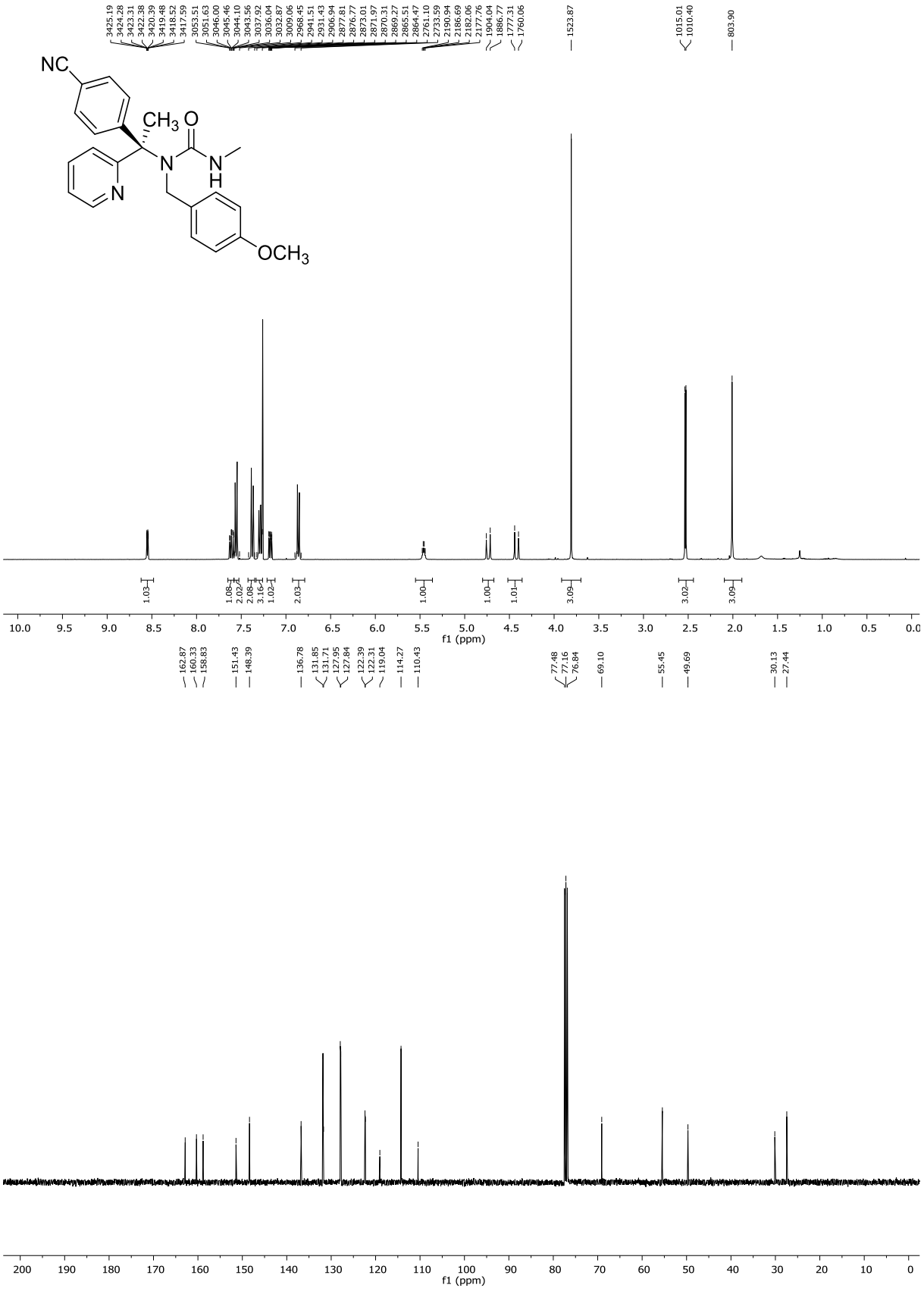
15e


3438.43
3359.79
3051.08
2980.72
2913.53
2795.27
2738.05
2661.11
1883.58
1866.45
1759.34
1742.20
1494.76
986.71
982.16
778.79
Cl
CH3
O
N
N
H
N
OCH3
0.99
1.11
9.29
2.06
1.00
0.99
1.00
3.11
3.02
3.19
f1 (ppm)
163.64
160.41
158.60
148.29
147.40
136.63
134.00
132.19
129.37
128.06
127.64
127.10
125.60
122.17
122.05
114.08
77.48
77.16
76.84
55.43
49.72
30.52
27.49
f1 (ppm)

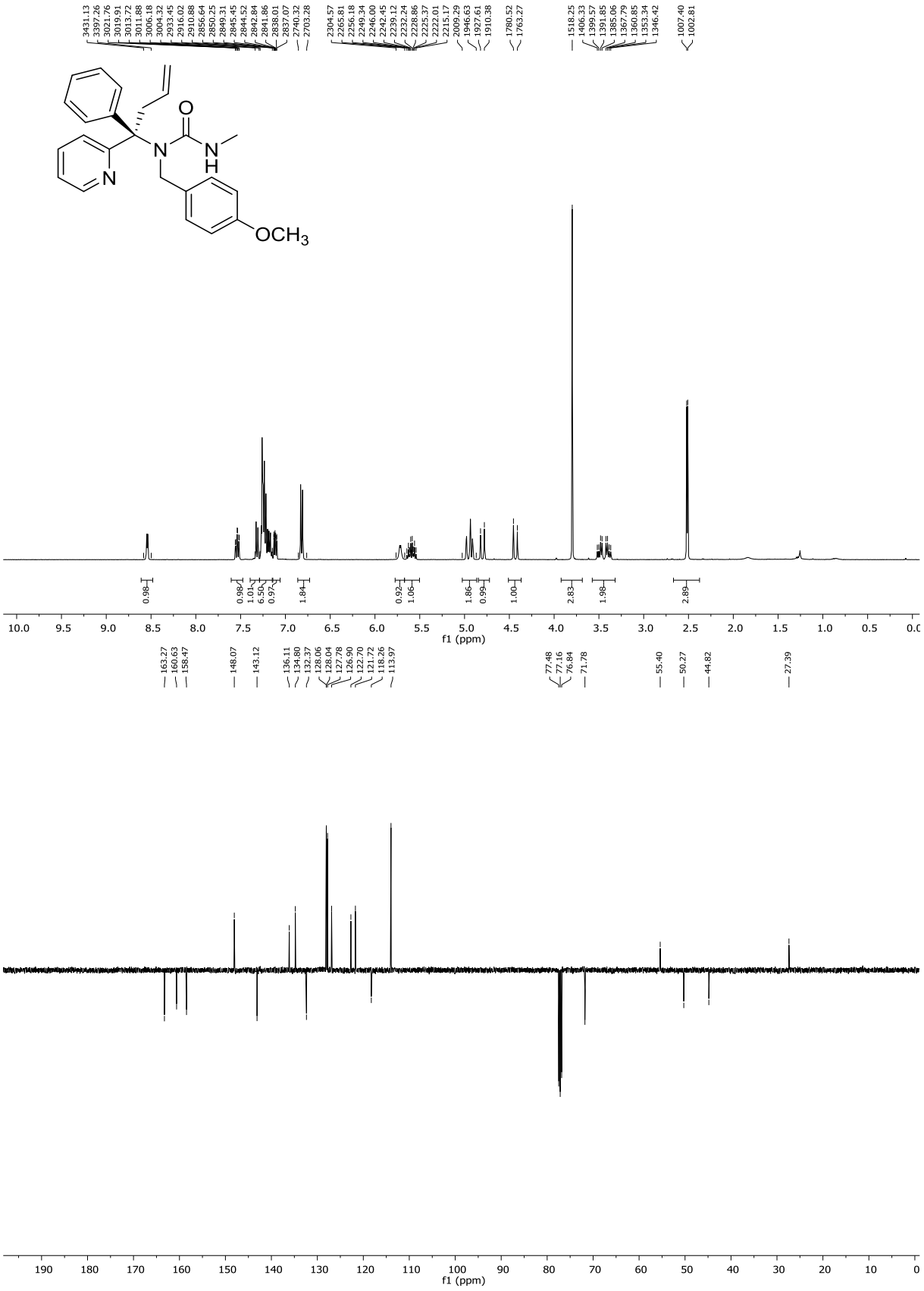
15f


3401.39
3373.42
3043.77
3013.05
2951.04
2928.12
2911.15
2868.40
2863.93
2843.30
2749.53
2692.68
2449.74
2053.73
2036.82
1787.99
1771.10
1511.98
1510.60
1012.46
1011.14
1007.94
1006.59
862.07
861.18
Cl
CH3
O
N
N
H
N
OCH3
1.02
1.08
1.15
6.95
0.95
2.04
0.98
1.00
1.01
3.08
3.03
3.13
f1 (ppm)
162.54
160.43
158.47
147.25
141.89
136.69
132.91
132.88
132.03
129.08
128.31
128.28
126.69
122.93
122.21
113.90
77.48
77.16
76.84
69.47
55.41
49.31
27.43
27.33
f1 (ppm)

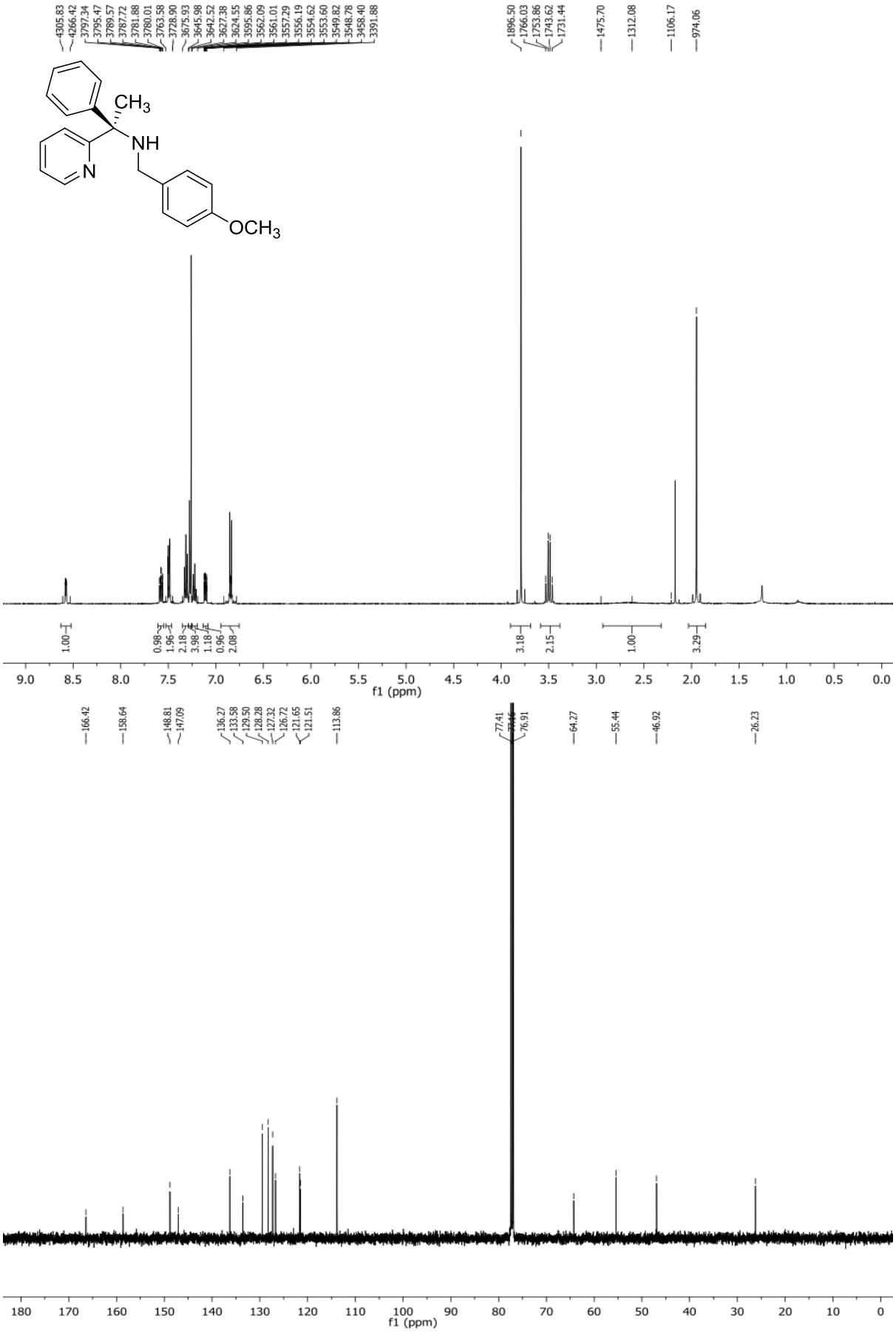
15g



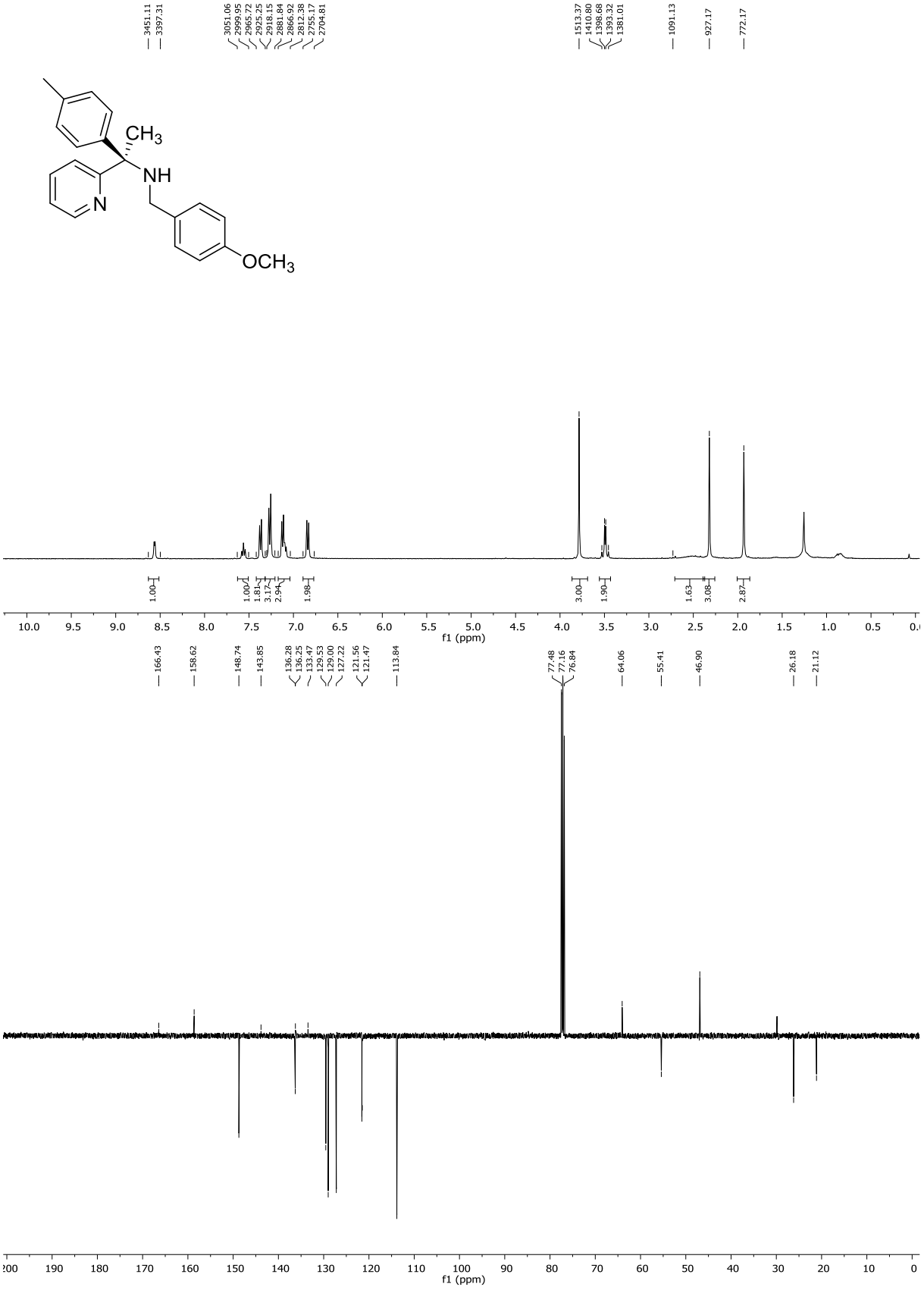
15h


3431.13
3397.26
3021.76
3019.91
3013.72
3011.88
3006.18
3004.32
2933.45
2916.02
2910.88
2856.64
2850.25
2849.31
2845.45
2844.52
2842.84
2841.86
2838.01
2837.07
2740.32
2703.28
2304.57
2265.81
2256.18
2249.34
2246.00
2242.45
2239.12
2232.24
2228.86
2225.37
2222.01
2215.17
2009.29
1946.63
1927.61
1910.38
1780.52
1763.27
1518.25
1406.33
1399.57
1391.85
1385.06
1367.79
1360.85
1353.34
1346.42
1007.40
1002.81
O
N
N
H
N
OCH3
0.98
0.99
1.01
6.50
0.97
1.84
0.92
1.06
1.86
0.99
1.00
2.83
1.98
2.89
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
163.27
160.63
158.47
148.07
143.12
136.11
134.80
132.37
128.06
128.04
127.78
126.90
122.70
121.72
118.26
113.97
77.48
77.16
76.84
71.78
55.40
50.27
44.82
27.39
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

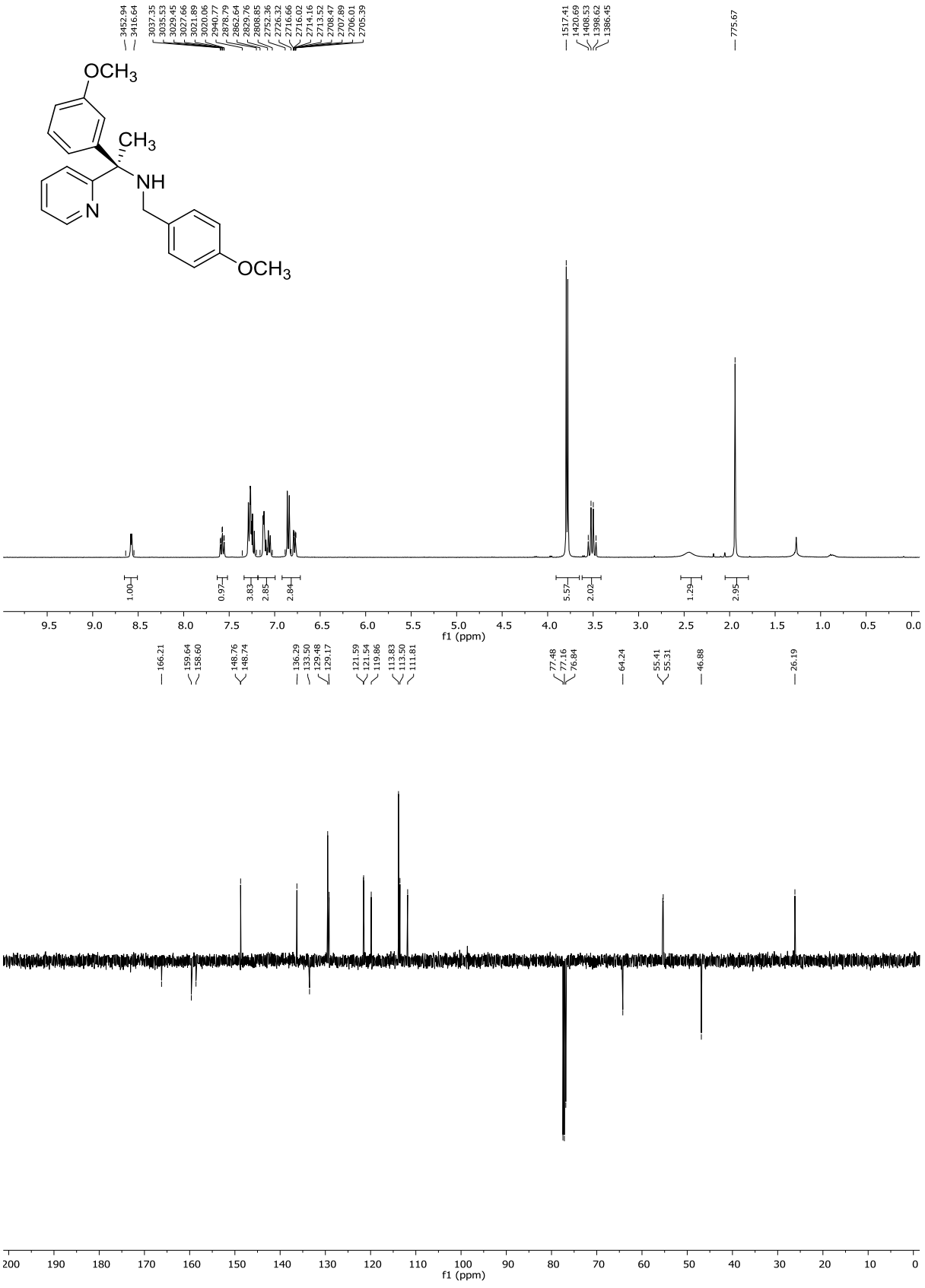
16a


4305.83
4266.42
3797.34
3795.47
3789.57
3787.72
3781.88
3780.01
3763.58
3728.90
3675.93
3645.98
3642.52
3627.38
3624.55
3595.86
3562.09
3561.01
3557.29
3556.19
3554.62
3553.60
3549.82
3548.78
3458.40
3391.88
1896.50
1766.03
1753.86
1743.62
1731.44
1475.70
1312.08
1106.17
974.06
CH3
NH
N
OCH3
1.00
0.98
1.96
2.18
3.98
1.18
0.96
2.08
3.18
2.15
1.00
3.29
f1 (ppm)
166.42
158.64
148.81
147.09
136.27
133.58
129.50
128.28
127.32
126.72
121.65
121.51
113.86
77.41
77.16
76.91
64.27
55.44
46.92
26.23
f1 (ppm)

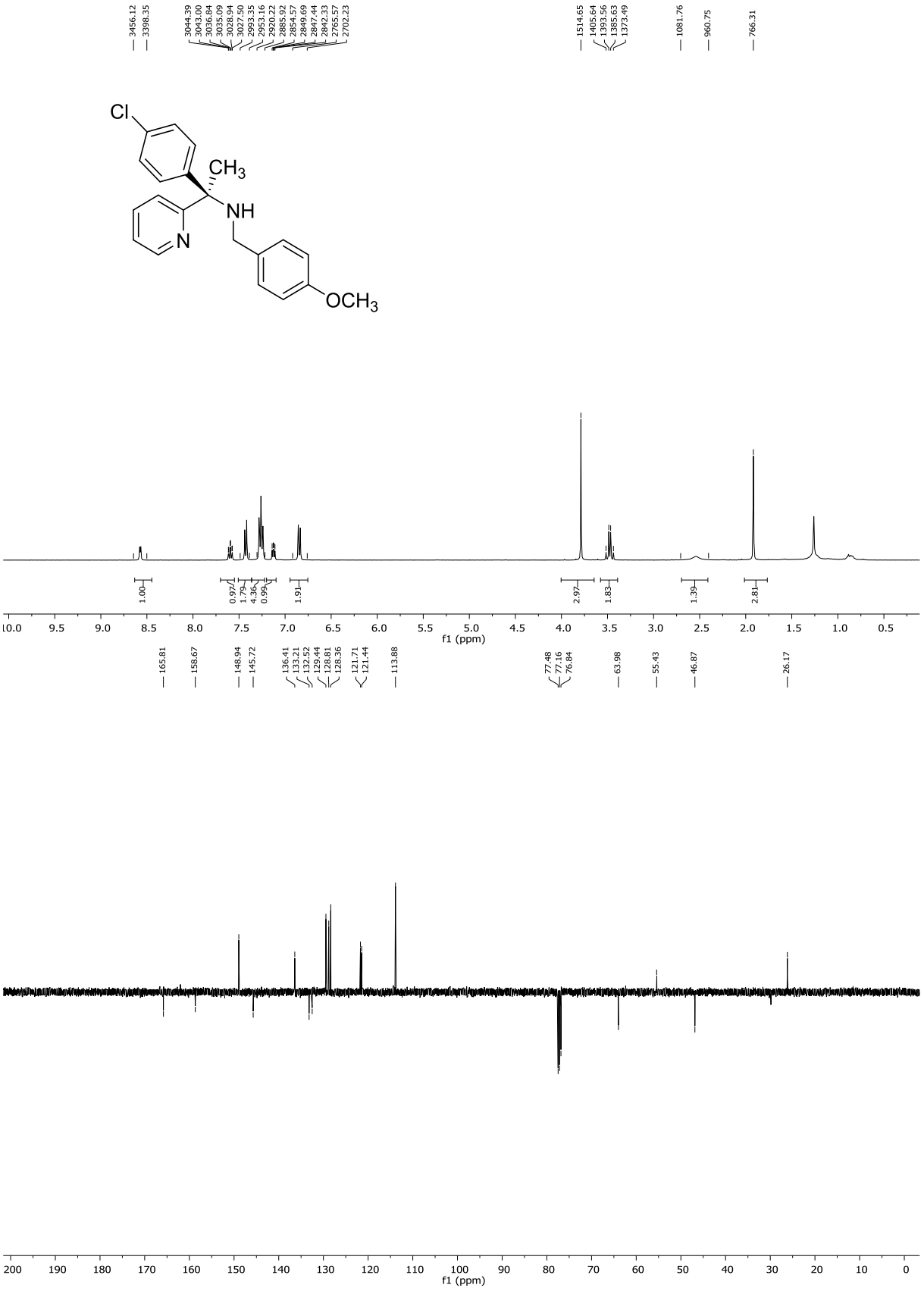
16b


3451.11
3397.31
3051.06
2999.95
2965.72
2925.25
2918.15
2881.84
2866.92
2812.38
2755.17
2704.81
1513.37
1410.80
1398.68
1393.32
1381.01
1091.13
927.17
772.17
CH3
NH
N
OCH3
1.00
1.00
1.81
3.17
2.94
1.98
3.00
1.90
1.63
3.08
2.87
f1 (ppm)
166.43
158.62
148.74
143.85
136.28
136.25
133.47
129.53
129.00
127.22
121.56
121.47
113.84
77.48
77.16
76.84
64.06
55.41
46.90
26.18
21.12
f1 (ppm)

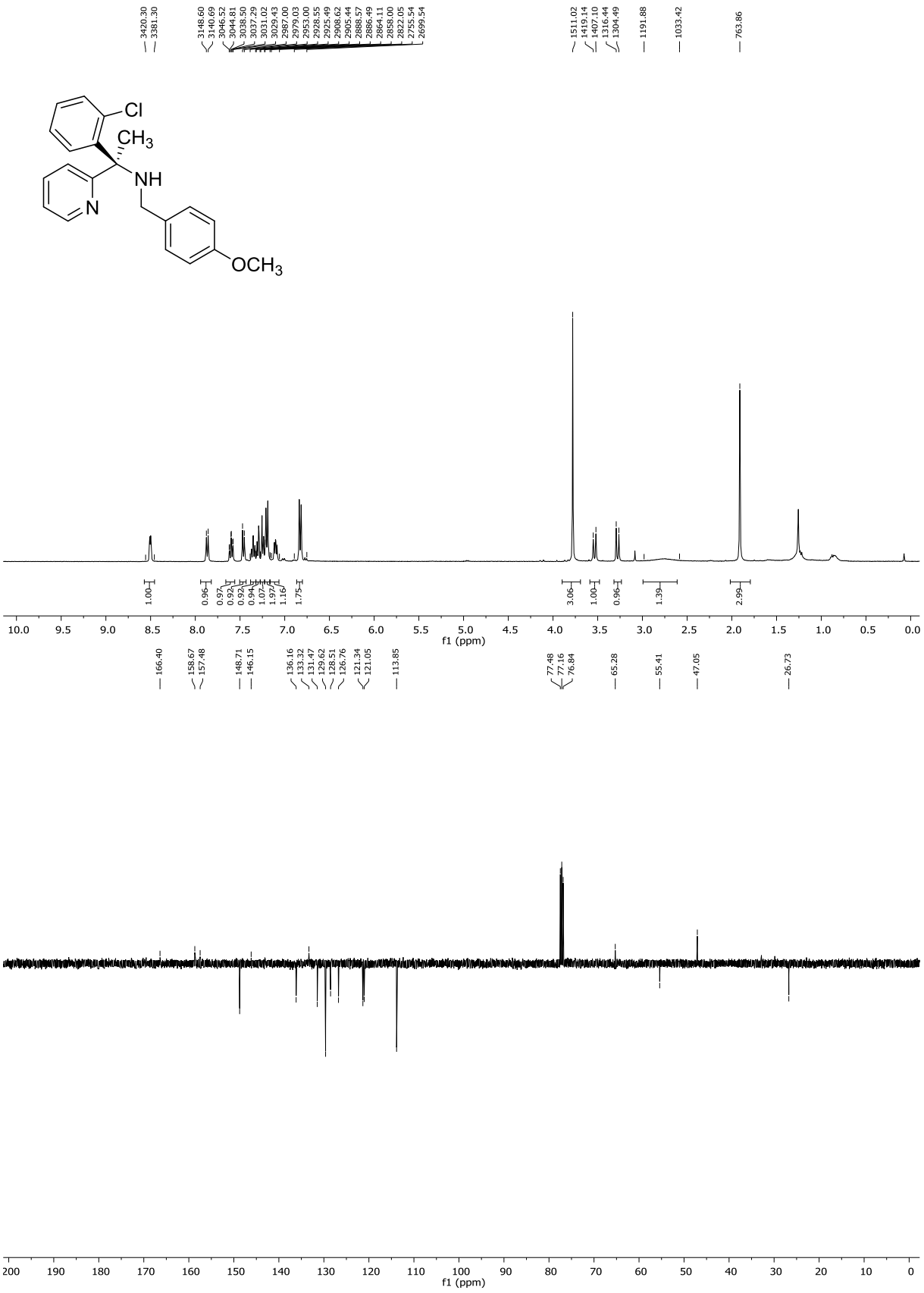
16c


3452.94
3416.64
3037.35
3035.53
3029.45
3027.66
3021.89
3020.06
2940.77
2878.79
2862.64
2829.76
2808.85
2752.36
2726.32
2716.66
2716.02
2714.16
2713.52
2708.47
2707.89
2706.01
2705.39
1517.41
1420.69
1408.53
1398.62
1386.45
775.67
OCH3
CH3
NH
N
OCH3
1.00
0.97
3.83
2.85
2.84
5.57
2.02
1.29
2.95
f1 (ppm)
166.21
159.64
158.60
148.76
148.74
136.29
133.50
129.48
129.17
121.59
121.54
119.86
113.83
113.50
111.81
77.48
77.16
76.84
64.24
55.41
55.31
46.88
26.19
f1 (ppm)

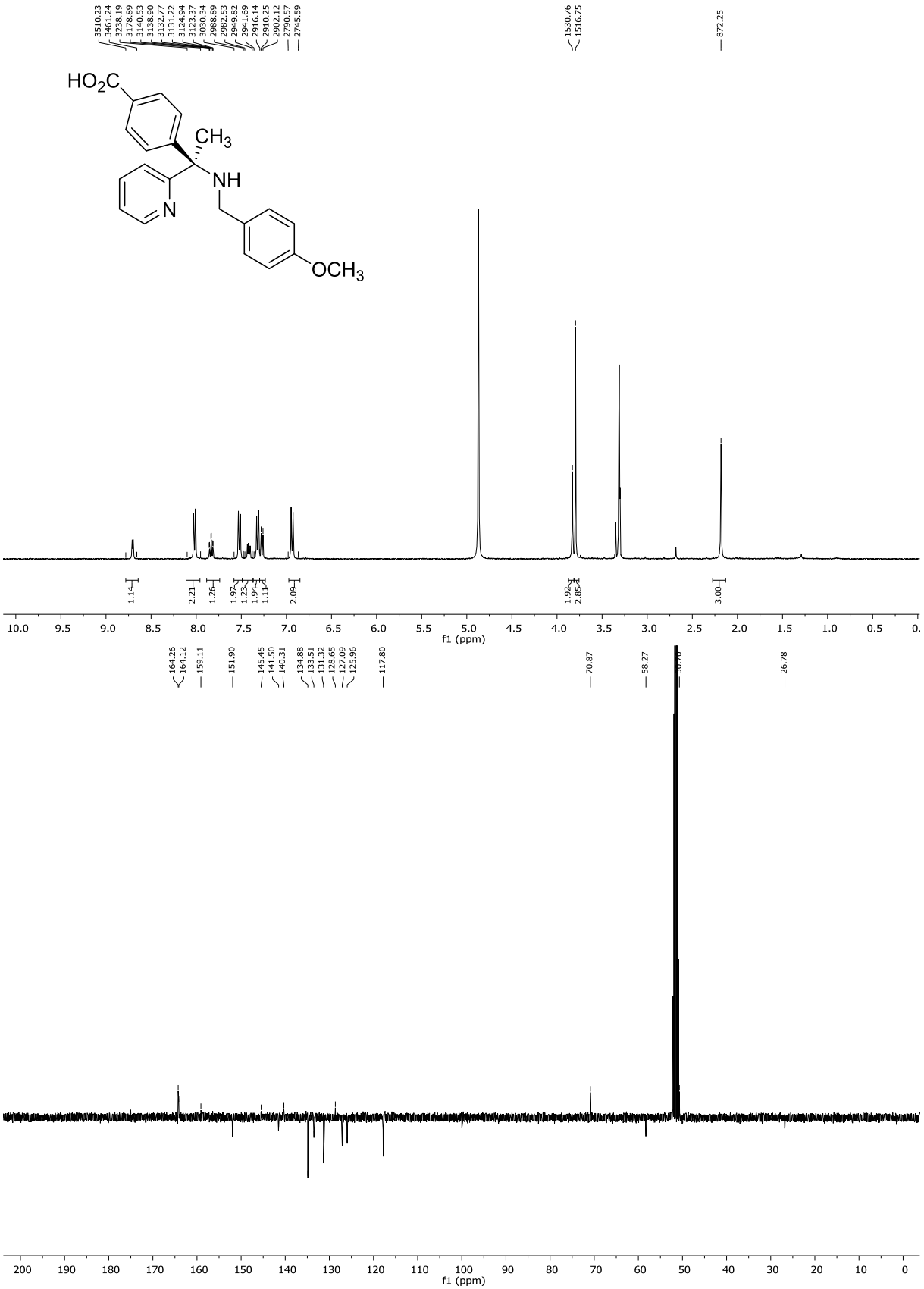
16d


3456.12
3398.35
3044.39
3043.00
3036.84
3035.09
3028.94
3027.50
2993.35
2953.16
2920.22
2885.92
2854.57
2849.69
2847.44
2842.33
2765.57
2702.23
1514.65
1405.64
1393.56
1385.63
1373.49
1081.76
960.75
766.31
Cl
CH3
NH
N
OCH3
1.00
0.97
1.79
4.36
0.99
1.91
2.97
1.83
1.39
2.81
f1 (ppm)
165.81
158.67
148.94
145.72
136.41
133.21
132.52
129.44
128.81
128.36
121.71
121.44
113.88
77.48
77.16
76.84
63.98
55.43
46.87
26.17
f1 (ppm)

16e

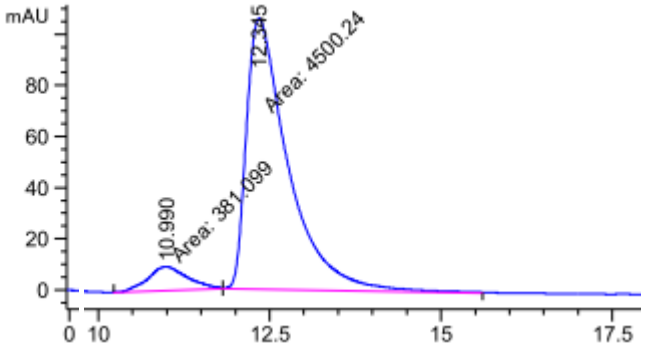

3420.30
3381.30
3148.60
3140.69
3046.52
3044.81
3038.50
3037.29
3031.02
3029.43
2987.00
2979.03
2953.00
2928.55
2925.49
2908.62
2905.44
2888.57
2886.49
2864.11
2858.00
2822.05
2755.54
2699.54
1511.02
1419.14
1407.10
1316.44
1304.49
1191.88
1033.42
763.86
Cl
CH3
NH
N
OCH3
1.00
0.96
0.97
0.92
0.92
0.94
1.07
1.97
1.16
1.75
3.06
1.00
0.96
1.39
2.99
f1 (ppm)
166.40
158.67
157.48
148.71
146.15
136.16
133.32
131.47
129.62
128.51
126.76
121.34
121.05
113.85
77.48
77.16
76.84
65.28
55.41
47.05
26.73
f1 (ppm)

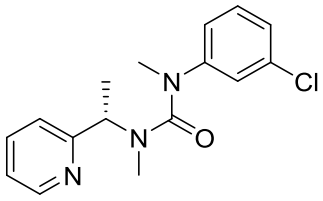
16f


3510.23
3461.24
3238.19
3178.89
3140.53
3138.90
3132.77
3131.22
3124.94
3123.37
3030.34
2988.89
2982.53
2949.82
2941.69
2916.14
2910.25
2902.12
2790.57
2745.59
1530.76
1516.75
872.25
HO2C
CH3
NH
N
OCH3
1.14
2.21
1.26
1.97
1.23
1.94
1.11
2.09
1.92
2.85
3.00
f1 (ppm)
164.26
164.12
159.11
151.90
145.45
141.50
140.31
134.88
133.51
131.32
128.65
127.09
125.96
117.80
70.87
58.27
26.78
f1 (ppm)

HPLC data

8a : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

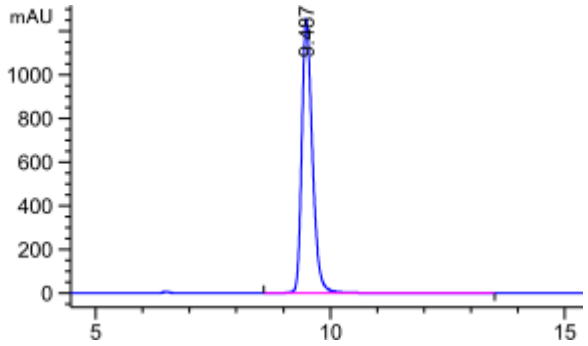


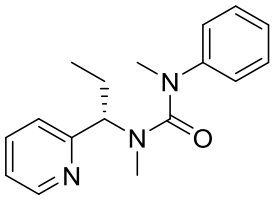


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.990	MM	0.6792	381.09869	9.35218	7.8073
2	12.345	MM	0.7080	4500.23926	105.93288	92.1927

8b : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

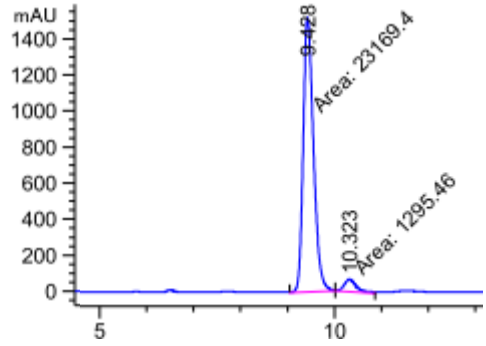


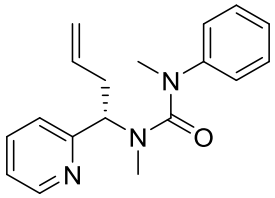


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.487	BB	0.2424	1.98642e4	1256.81714	100.0000

8c : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

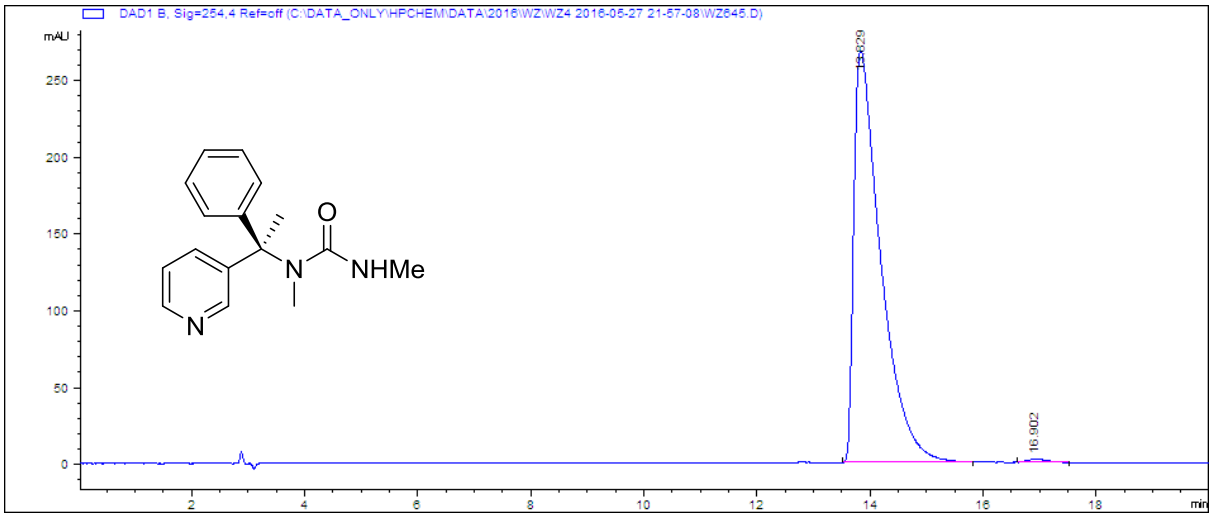




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

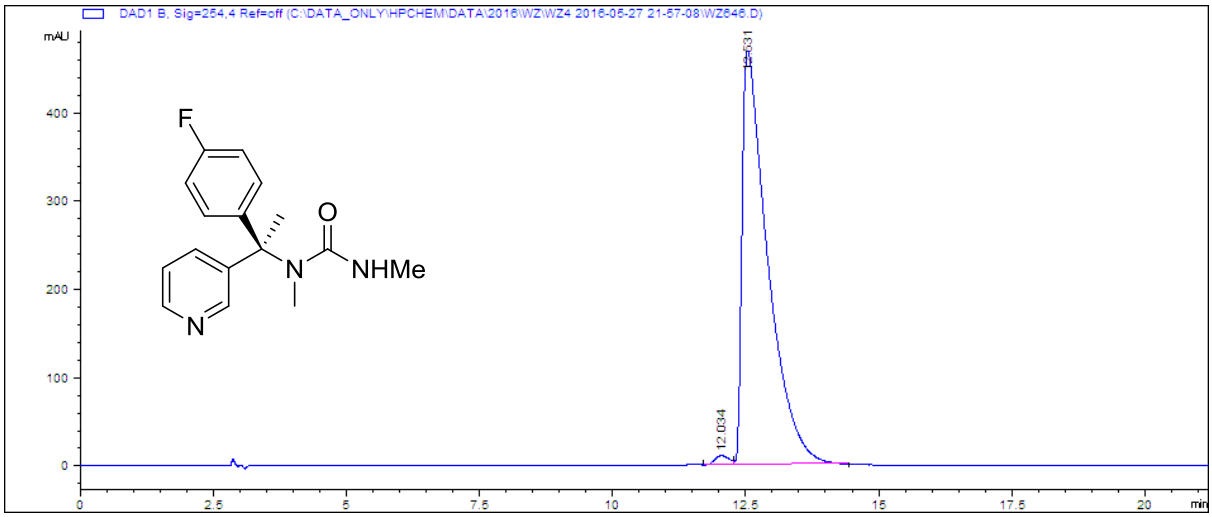
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.428	MM	0.2546	2.31694e4	1516.86768	94.7048
2	10.323	MM	0.3179	1295.46326	67.91454	5.2952

11a : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



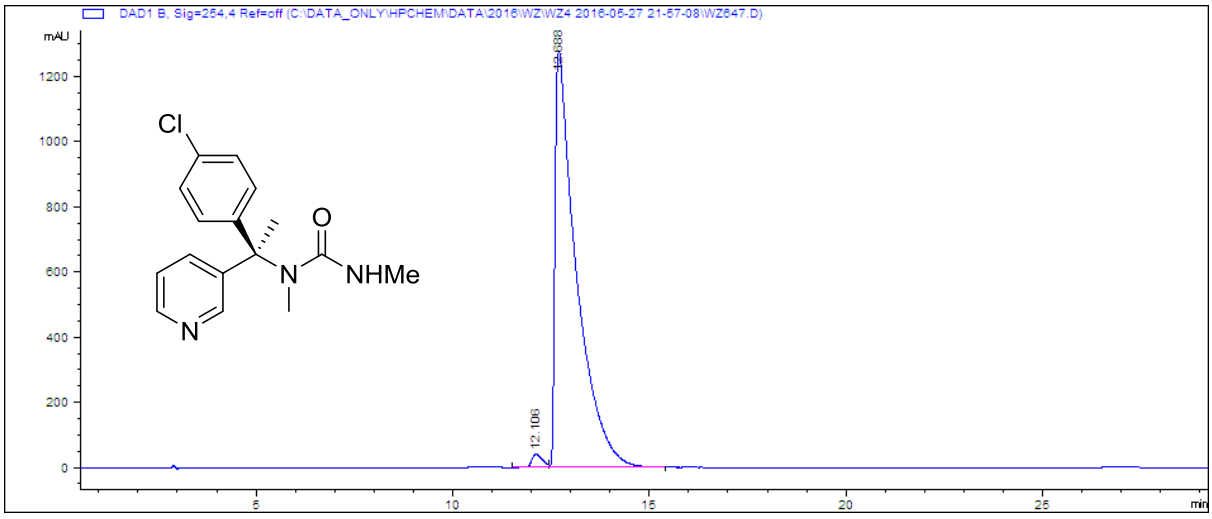
#	Time	Area	Height	Width	Area%	Symmetry
1	13.829	8886.2	268.3	0.4644	99.399	0.32
2	16.902	53.7	2.2	0.3035	0.601	0.588

11b : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



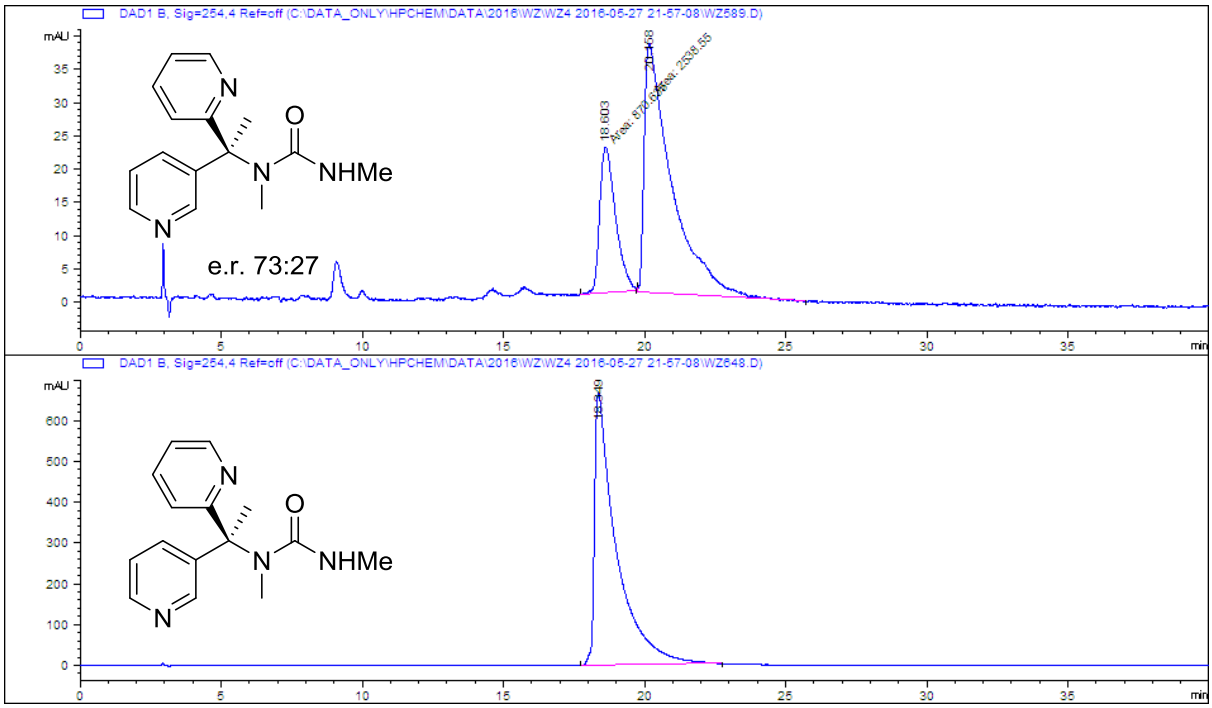
#	Time	Area	Height	Width	Area%	Symmetry
1	12.034	196.5	10.4	0.2675	1.234	0.829
2	12.531	15732.6	469.1	0.4692	98.766	0.26

11c : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



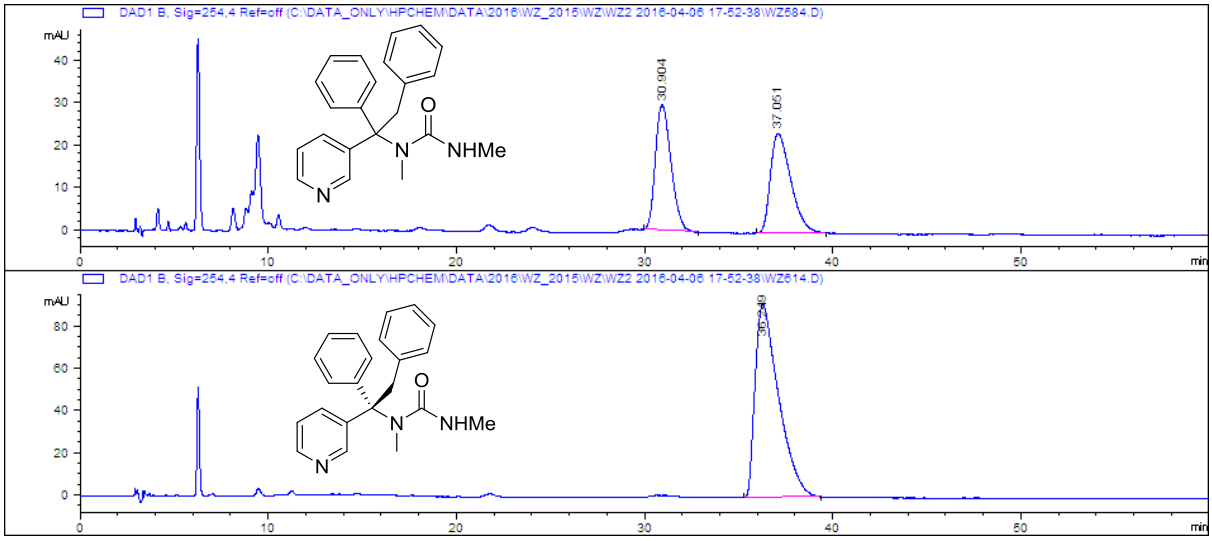
#	Time	Area	Height	Width	Area%	Symmetry
1	12.106	796.7	40.1	0.2915	1.634	0.646
2	12.688	47945.1	1279.3	0.4972	98.366	0.199

11d : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



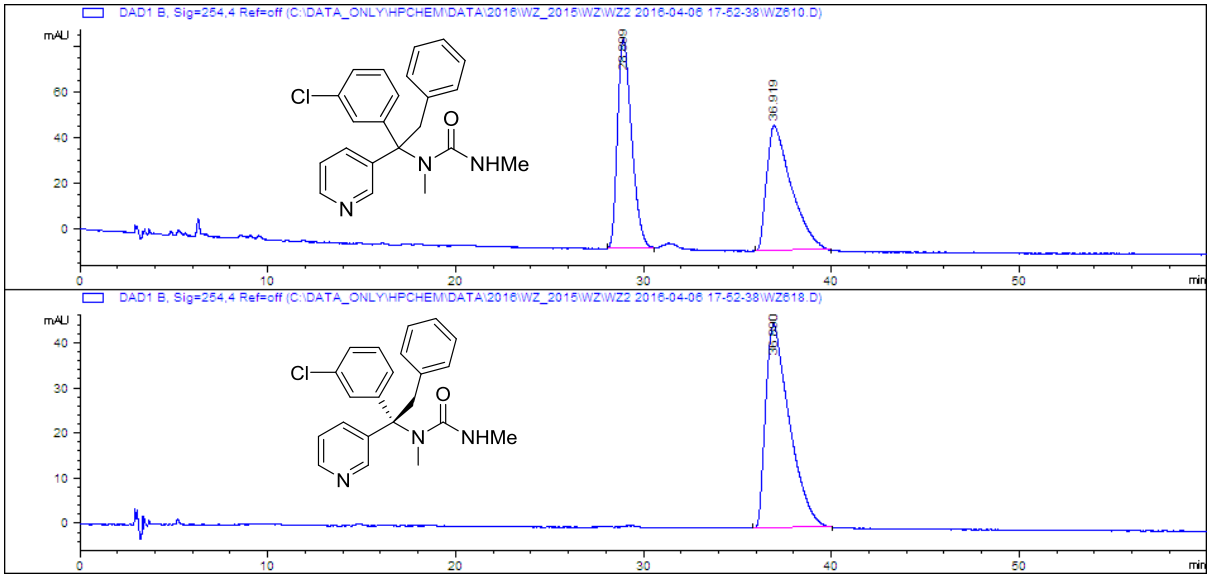
#	Time	Area	Height	Width	Area%	Symmetry
1	18.603	870.6	22	0.6583	25.538	0.584
2	20.158	2538.6	37.5	1.1268	74.462	0.227

11e : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

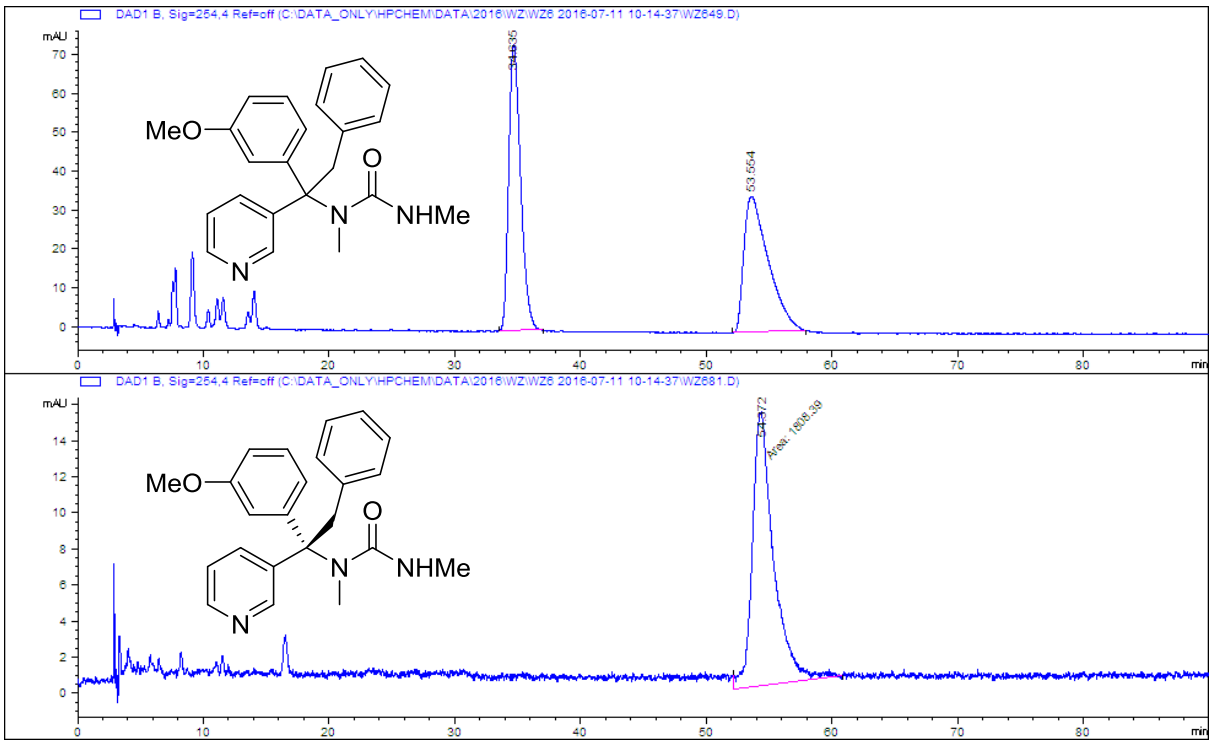


#	Time	Area	Height	Width	Area%	Symmetry
1	30.904	1715	29.5	0.7738	49.206	0.717
2	37.051	1770.3	23.5	0.9315	50.794	0.527

11f : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

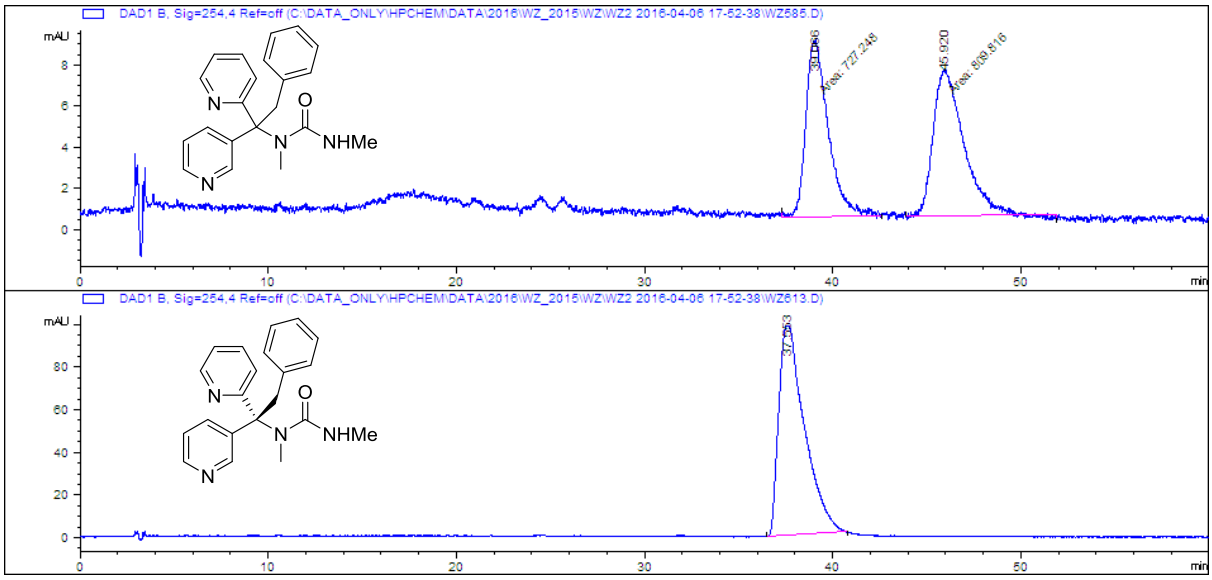


11g : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



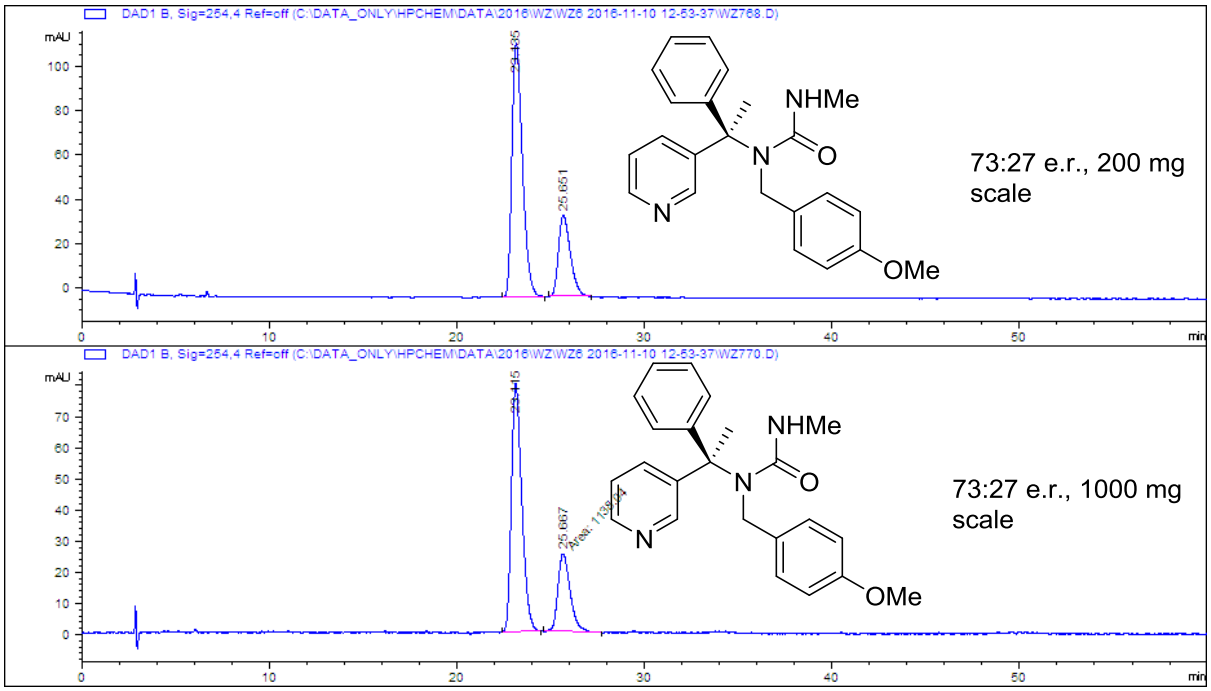
#	Time	Area	Height	Width	Area%	Symmetry
1	37.163	4098.4	55.3	0.873	54.364	0.617
2	58.026	3440.4	25	1.6159	45.636	0.517

11h : Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	39.066	727.2	8.6	1.4106	47.314	0.739
2	45.92	809.8	7.1	1.896	52.686	0.589

13: Phenomenex LUX® 5 µm Amylose-1 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



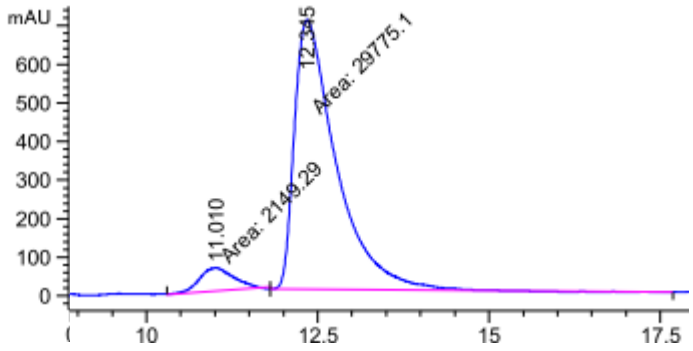
200 mg scale

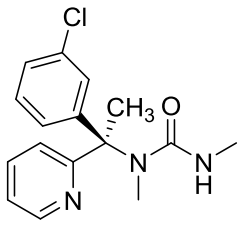
#	Time	Area	Height	Width	Area%	Symmetry
1	23.135	4458.8	114.2	0.5996	73.306	0.636
2	25.651	1623.6	36.6	0.6299	26.694	0.653

1.00 g scale

#	Time	Area	Height	Width	Area%	Symmetry
1	23.115	3072.9	79.8	0.5615	72.974	0.681
2	25.667	1138	24.9	0.7607	27.026	0.645

14a : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 85:15 hexane-IPA, 1 mL/min, 210 nm

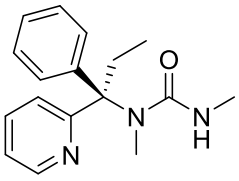




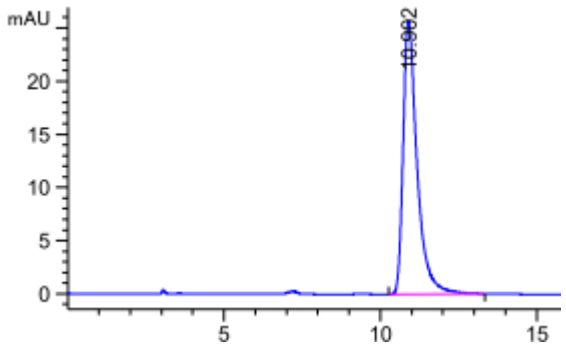
Signal 2: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.010	MM	0.5926	2149.28882	60.44871	6.7324
2	12.345	MM	0.7126	2.97751e4	696.35681	93.2676

14b : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



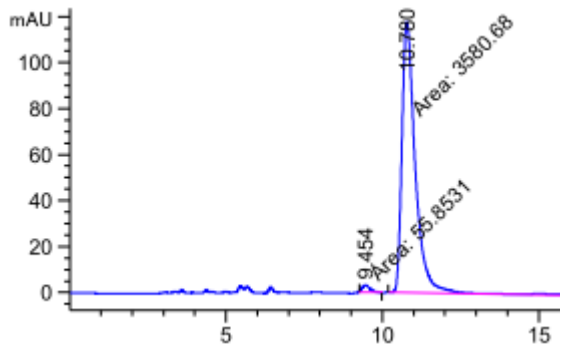
At -78 °C :



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.902	BB	0.4629	3812.61108	122.56915	100.0000

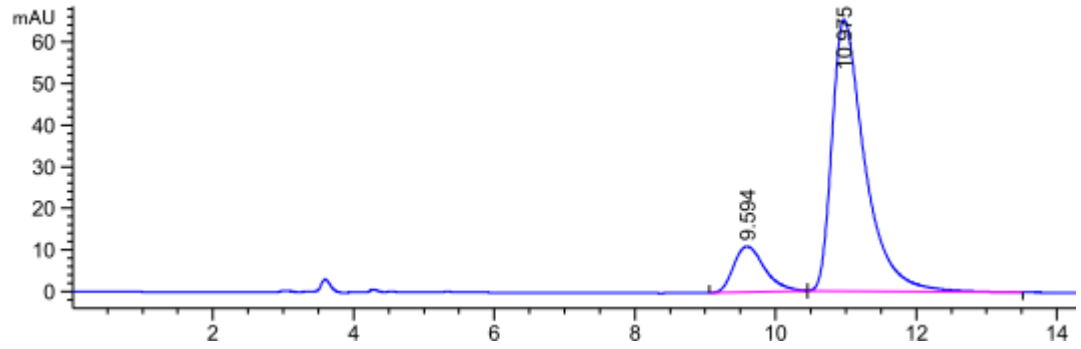
At -40°C :



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.452	MM	0.4783	325.75943	11.35186	1.9338
2	10.780	MM	0.4935	1.65200e4	557.91547	98.0662

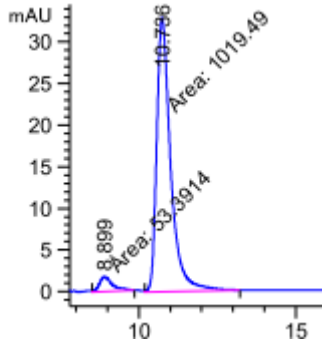
At –RT :

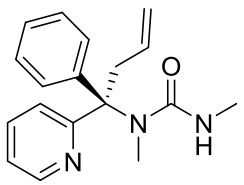


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.594	BV	0.4888	1686.06079	53.04249	14.1670
2	10.975	VB	0.4911	1.02153e4	309.43759	85.8330

14c : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

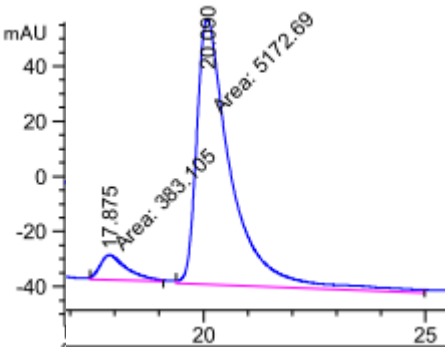


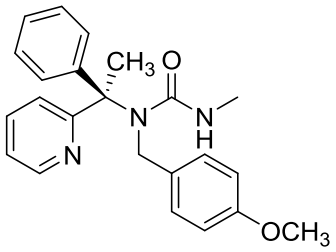


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.899	MM	0.4987	53.39144	1.78439	4.9764
2	10.736	MM	0.5158	1019.49408	32.94215	95.0236

15a : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

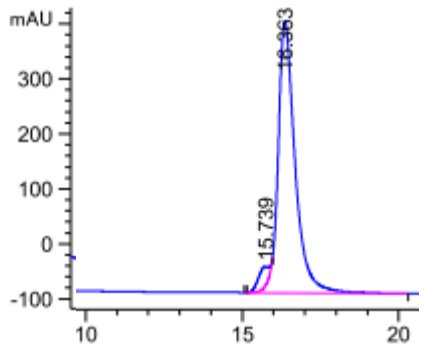


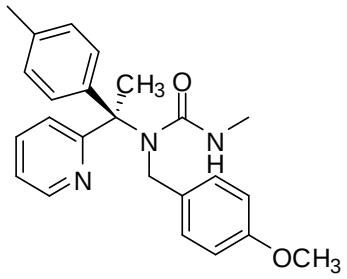


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.875	MM	0.7054	383.10529	9.05111	6.8956
2	20.090	MM	0.8961	5172.68652	96.20653	93.1044

15b : CHIRALPAK® AD-H 5 µm Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 210.4 nm

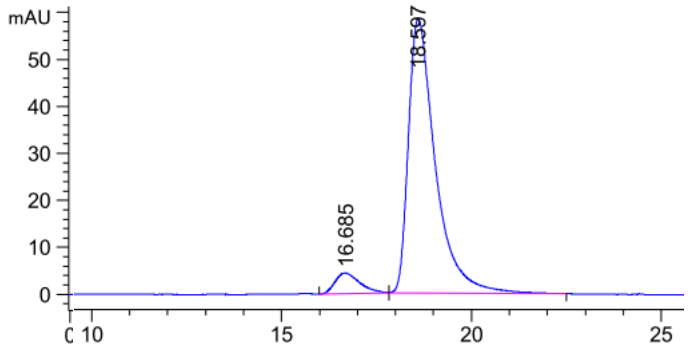


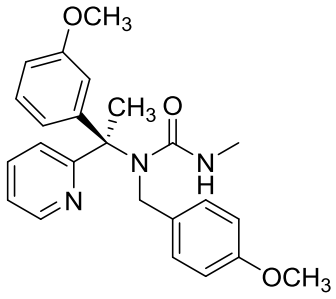


Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.739	BV E	0.3682	846.94214	34.76965	4.3293
2	16.363	VB R	0.5629	1.87161e4	492.98035	95.6707

15c : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

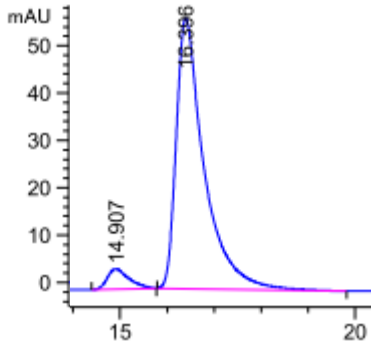


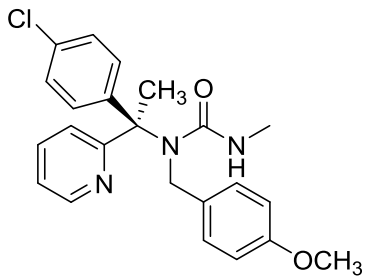


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.685	BB	0.5405	195.72812	4.35365	6.3669
2	18.597	BB	0.7201	2878.44189	58.28962	93.6331

15d : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

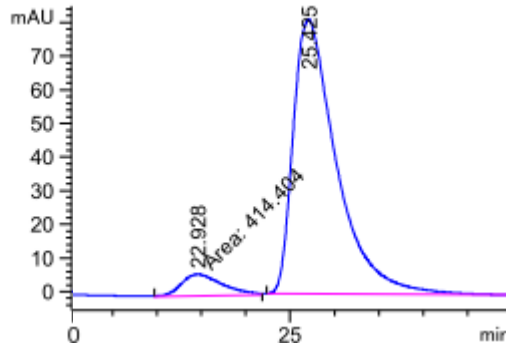


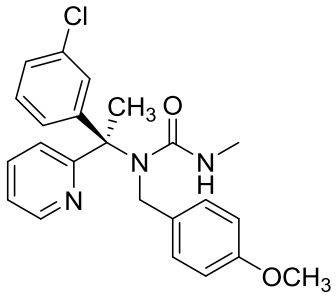


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.907	BB	0.4735	135.96097	4.24698	5.4596
2	16.396	BB	0.5971	2354.35156	56.85265	94.5404

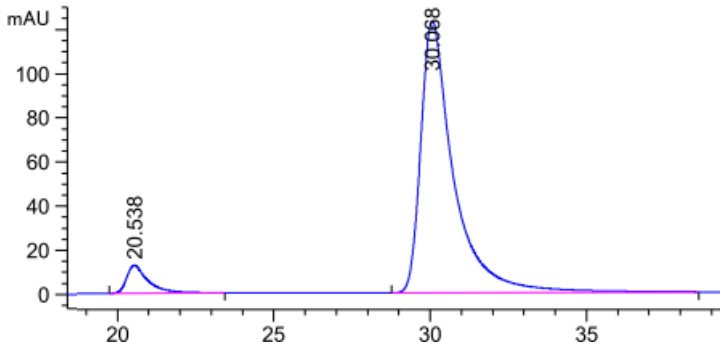
15e : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 85:15 hexane-IPA, 1 mL/min, 254 nm

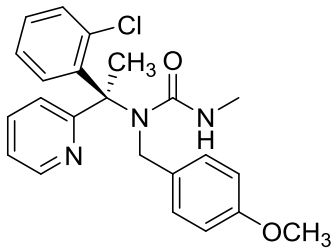




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.928	MM	1.0764	414.40408	6.41670	6.9338
2	25.425	BBA	1.0069	5562.18359	81.64005	93.0662

15f : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 230.4 nm

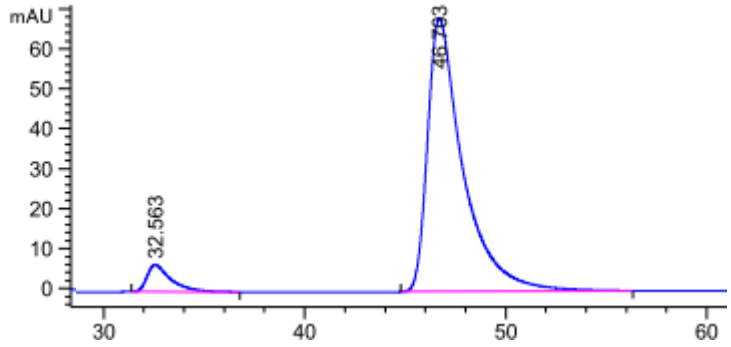


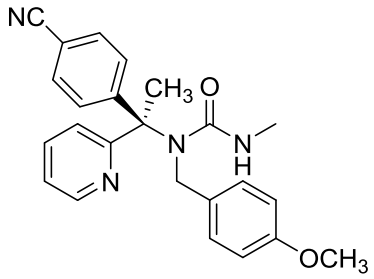


Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.538	BB	0.6862	601.03552	12.56179	6.2515
2	30.068	BB	1.0576	9013.16895	122.89481	93.7485

15g : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm

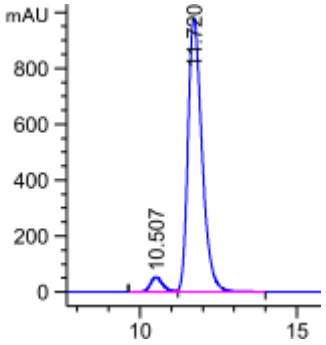


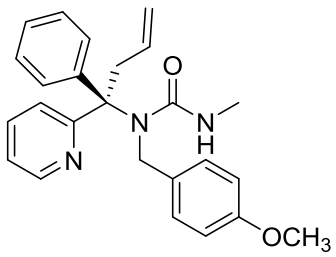


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.563	BB	1.1684	561.90320	6.78379	6.2634
2	46.703	BB	1.7692	8409.32227	68.36113	93.7366

15h : CHIRALPAK® AD-H 5 µm LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 210.4 nm





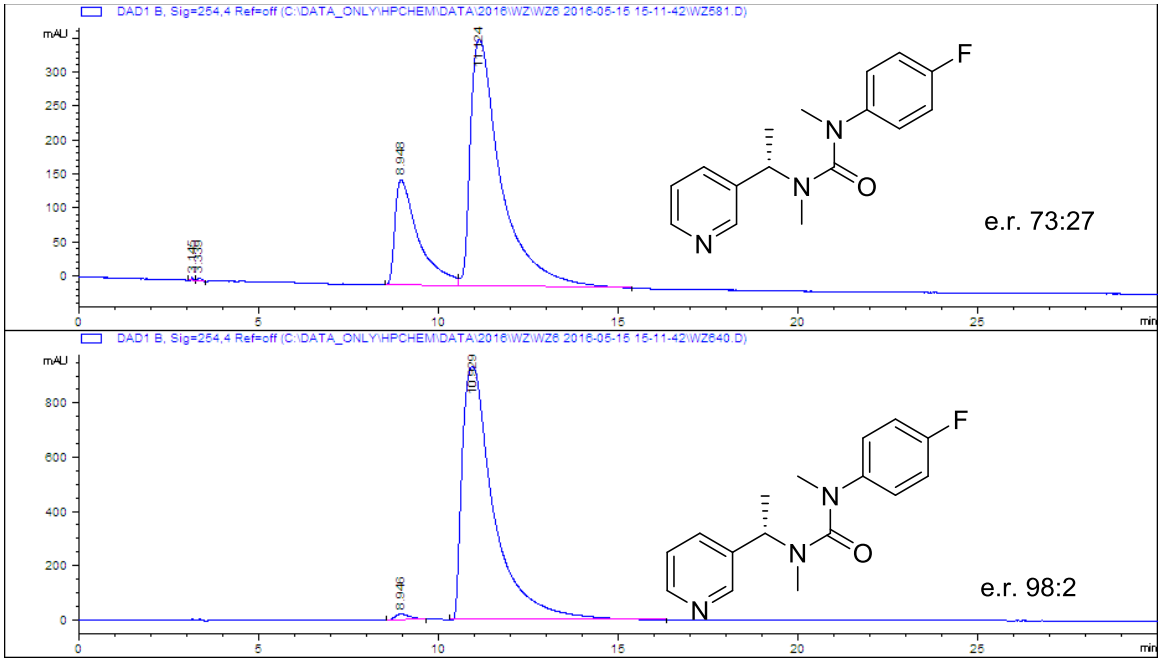
Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.507	BV E	0.4170	1762.75281	64.86910	4.5262
2	11.720	VB R	0.4768	3.71832e4	1195.57593	95.4738

Determination of d.r. in 3aa, and e.r. in the corresponding compounds 17a-d and 7a-d

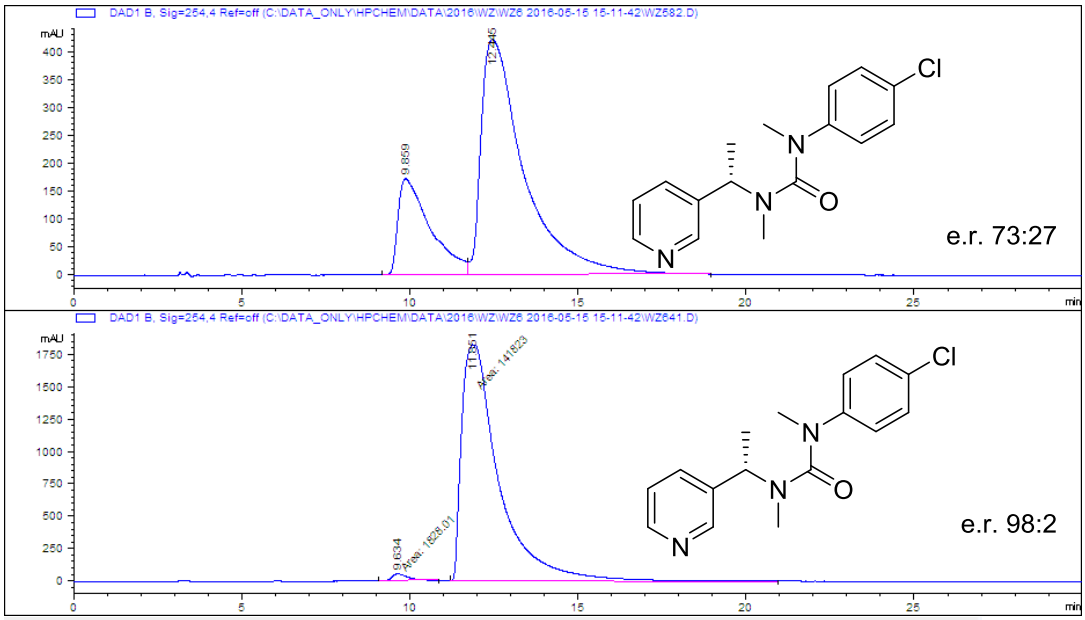
To determine the exact diastereomeric ratio in **3a**, at a later stage of the synthesis **5a** was converted to **7b** and **7c** and the e.r. of the compounds was measured by chiral HPLC.

Phenomenex LUX® 5 µm Cellulose-3 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	8.946	1024	23.7	0.7215	1.728	0.364
2	10.929	58247.6	936.4	1.0367	98.272	0.425

Phenomenex LUX® 5 µm Cellulose-3 LC Column 250 x 4.6 mm, 90:10 hexane-IPA, 1 mL/min, 254 nm



#	Time	Area	Height	Width	Area%	Symmetry
1	9.634	1860	52.9	0.586	1.368	0.516
2	11.851	134068.5	1823.2	1.2256	98.632	0.414

X-RAY

Table 1. Crystallographic data and structure refinement for compound (*R*)-**11c**; the Cambridge Crystallographic Data Centre (CCDC) code is 1519696

Identification code	1519696	
Empirical formula	C16 H18 Cl N3 O	
Formula weight	303.78	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.54450(10) Å	α= 90°.
	b = 9.1514(2) Å	β= 90°.
	c = 19.7296(4) Å	γ = 90°.
Volume	1542.74(5) $Å^3$	
Z	4	
Density (calculated)	1.308 Mg/m^3	
Absorption coefficient	2.207 mm^{-1}	
F(000)	640	
Crystal size	0.250 x 0.150 x 0.080 mm^3	
Theta range for data collection	4.482 to 72.143°.	
Index ranges	-10<=h<=10, -11<=k<=11, -23<=l<=17	
Reflections collected	18119	
Independent reflections	3026 [R(int) = 0.0404]	
Completeness to theta = 67.679°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.843 and 0.767605	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3026 / 0 / 197	
Goodness-of-fit on F^2	1.040	
Final R indices [I>2sigma(I)]	R1 = 0.0247, wR2 = 0.0617	
R indices (all data)	R1 = 0.0261, wR2 = 0.0623	
Absolute structure parameter	0.031(6)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.184 and -0.257 $e.Å^{-3}$	