N-Heterocyclic Carbene and Brønsted Acid Cooperative Catalysis: Asymmetric Synthesis of *trans*-*γ*-Lactams

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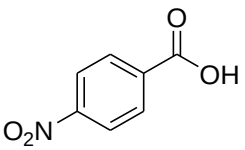
1. General considerations

Commercial reagents were purchased from Sigma-Aldrich or Alfa Aesar and used without further purification unless otherwise indicated. KHMDS refers to potassium hexamethyldisilazide. All catalytic reactions were carried out under Ar with oven-dried glassware. Dichloromethane was degassed with argon and passed through two columns of neutral alumina. Acetontrile and propionitrile were distilled from CaH_2 prior to use. Ethyl *trans*-4-oxo-2-butenoate (**2a**) was distilled and stored in the refrigerator before use. Thin layer chromatography was performed on 0.25 mm silica gel 60-F plates from Silicycle Inc. Column chromatography was performed on silica gel 60 (230-400 mesh) from Silicycle Inc.

^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra were recorded on a Varian 300 or 400 spectrometer at ambient temperature. All NMR spectra are referenced to TMS or the residual solvent signal. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Data for ^{13}C{^{1}H} NMR are reported as follows: chemical shift (δ ppm). Data for ^{19}F NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration.

High resolution mass spectra (HRMS) were recorded on an Agilent Technologies 6210 Time of Flight LC/MS. HPLC spectra were obtained on an Agilent 1100 series system. Optical rotation was obtained with an Autopol-III automatic polarimeter.

All imines were synthesized from the corresponding aldehydes and amines. The triazolium salts **C1**-**C6** were prepared according to our previous procedure.[1] Enals **2b**[2] and **2d**[3] were synthesized according to known procedures. Acids **AA3** and **AA4** were prepared from amino acids by known procedures.[4] Sodium salts **A1**-**A4** were easily prepared from the corresponding acids **AA1**-**AA4** with stoichometric sodium hydroxide, respectively. **AA1** and **AA2** are commercially available. Imines **2f**[5] and **2g**[6], azoliums **C1**,[7] **C2**,[8] **C5**[8] and **C6**,[1] enals **2b**[2] and **2d**[3], acids **AA3**[4] and **AA4**[9] are known compounds and were identified by NMR comparison to reported data.



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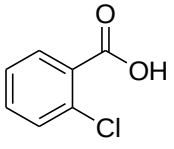

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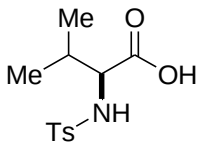

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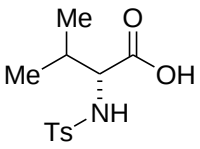

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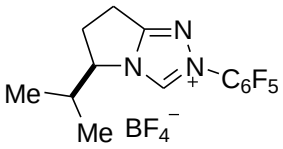
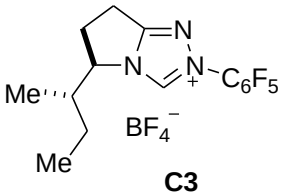
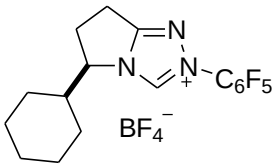
C1



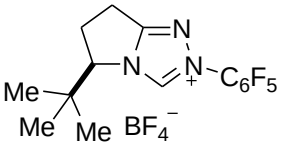
C2



C3



C4



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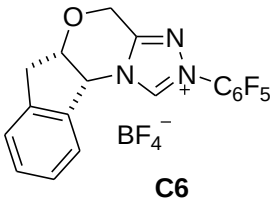

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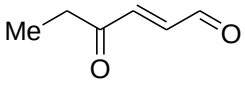

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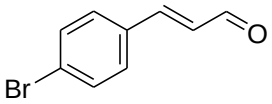
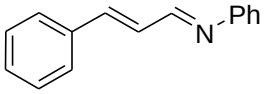
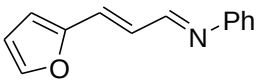


2d



2f



2g

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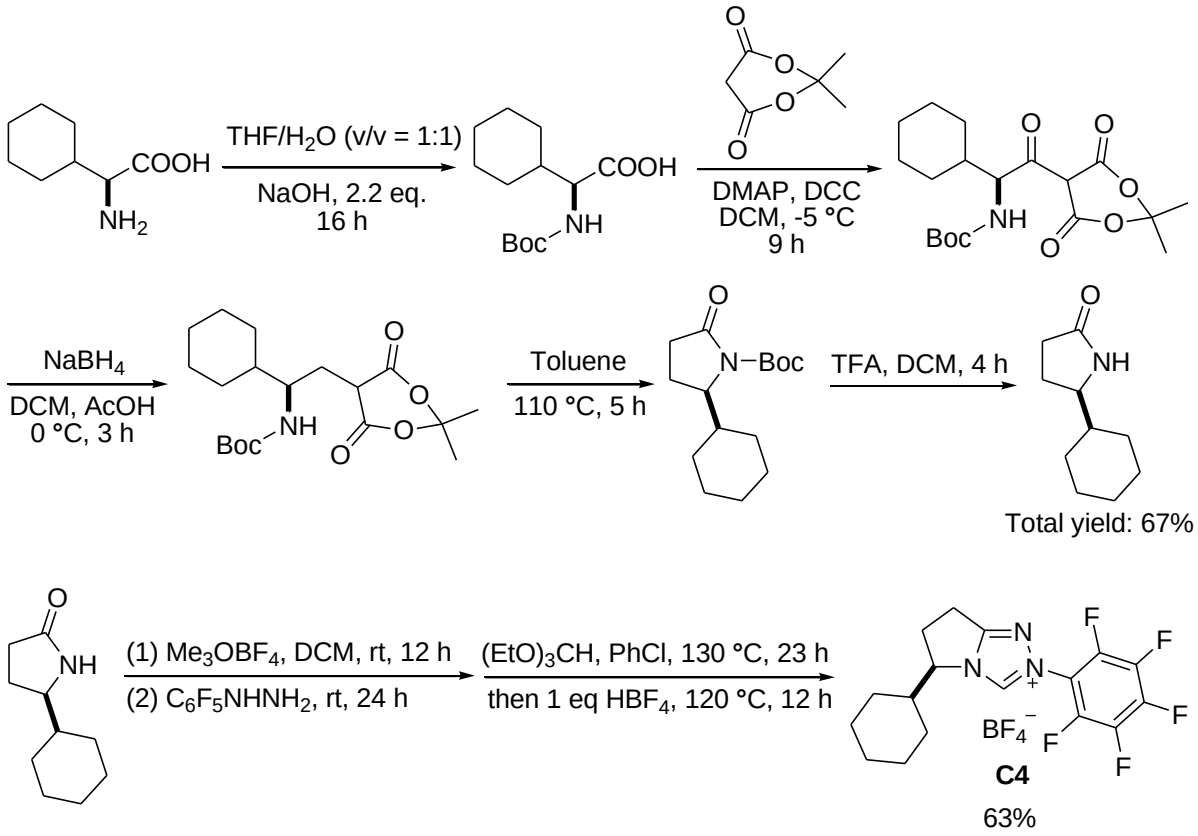
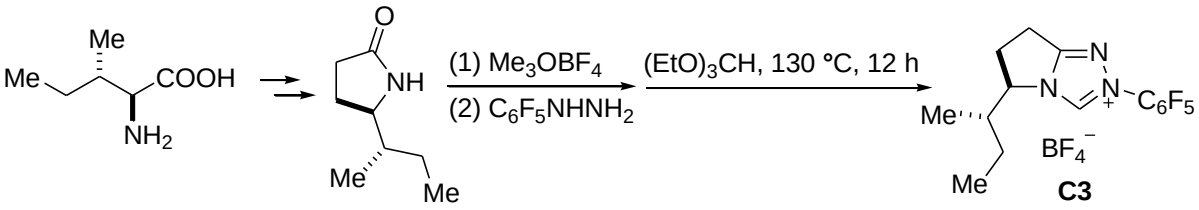
2. Experimental procedures

2.1. Synthesis of Triazolium Salts



Triazolium salt **C4**: Synthesized by a modification to the known procedure.[1] In a 20-mL vial was added (R)-5-cyclohexylpyrrolidin-2-one (0.5 g, 2.99 mmol) and dichloromethane (15 mL). Subsequently, trimethyloxonium tetrafluoroborate (0.443 g, 2.99 mmol) was added. The vial was sealed with white cap and the mixture was stirred at room temperature for 12 h, then, pentafluorophenyl hydrazine (0.593 g, 2.99 mmol) was added. The resulting solution was stirred at room temperature for 24 hours and then transferred to a 100 mL round-bottomed flask. All volatiles were removed under reduced pressure, and triethyl orthoformate (4 mL, 24.0 mmol) and chlorobenzene (20 mL) were subsequently added to the flask, and the solution was heated at 130 ℃ for 23 h. The resulting dark brown solution was concentrated. Chlorobenzene (20 mL) and HBF_4 (0.41 mL, 2.99 mmol) were added to the residue, and the resulting solution was stirred at 120 ℃ for 12 h. The dark solution was cooled to room temperature, and concentrated under reduced pressure. The residue was purified by silica gel column chromatoghy (eluent: DCM/acetone = 15/1 to 10/1, v/v) to afford a brown solid. The

solid was dissolved into dichloromethane (0.5 mL) in a vial, and ether was added in order to precipitate the azolium salt. The solution was poured out, and the remaining solid was washed with ether (5 mL x 3) to give a white solid **C4** (0.834 g, 63%). Triazolium salt **C4**: White solid. M.p.: 180-181 °C. $[\alpha]^{20}_{D}$ = +43.6 ° (c = 0.005 g/mL, MeOH). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 10.37 (s, 1H), 5.00 (td, J = 5.9, 8.1 Hz, 1H), 3.51-3.36 (m, 2H), 3.14-3.04 (m, 1H), 2.91-2.84 (m, 1H), 2.21-2.13 (m, 1H), 1.94-1.91 (m, 1H), 1.82-1.79 (m, 2H), 1.75-1.67 (m, 2H), 1.38-1.17 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.2, 143.5, 67.0, 40.3, 29.9, 28.5, 27.3, 25.6, 25.4, 25.3, 21.4. HRMS (ESI) *m/z* calc'd for $C_{17}H_{17}F_5N_3$ $[M\text{-}BF_4]^+$: 358.1337; found: 358.1355.



Triazolium salt **C3**: Synthesized according to a modification to the known procedure.[1] To a flame-dried flask with magnetic stir bar was added (R)-5-((*S*)-*sec*-butyl)pyrrolidin-2-one (1.0 g, 7.08 mmol). The flask was then evacuated and back-filled with argon. Dichloromethane (35 mL) and trimethyloxonium tetrafluoroborate (1.05 g, 7.08 mmol) were then added via powder funnel. The heterogeneous mixture was stirred at room temperature until the reaction was homogeneous (about 6 hours). Pentafluorophenyl hydrazine (1.40 g, 7.08 mmol) was added in one portion and the mixture was stirred for 18 hours at which point dichloromethane was removed *in vacuo*. Triethylorthoformate (20.0 mL) was then added and the solution transferred to a 75 mL pressure flask and heated in a 130 °C oil bath for 12 h. The resulting dark brown solution was then concentrated *in vacuo* to leave a semi-solid which was then triturated with diethyl ether, filtered and washed with diethyl ether. The resulting off-white powder was dried under vacuum for 12 h to give triazolium salt **C3** (1.04 g, 35%) as an off-white solid. Triazolium salt **C3**: White solid. $[\alpha]^{20}_{D}$ = +35.6 ° (c = 0.00458 g/mL, MeOH). M.p.: 176-178 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H), 5.20-5.15 (m, 2H), 3.46 (ddd, J = 4.0, 6.6, 8.5 Hz, 2H), 3.06 (dtd, J = 6.5, 8.5, 13.5 Hz, 1H), 2.89-2.82 (m, 1H), 2.46-2.36 (m, 1H), 1.71-1.60 (m, 1H), 1.46-1.35 (m, 1H), 1.03-0.99 (m, 6H). ^{13}C{^{1}H} NMR

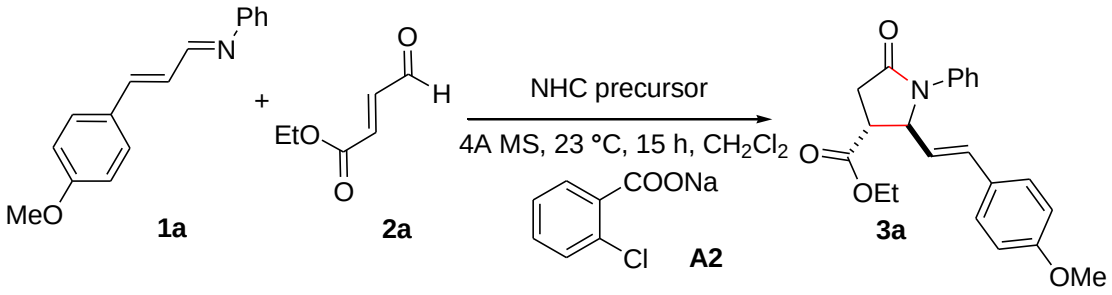
(101 MHz, $CDCl_3$) δ 164.2, 143.4, 66.2, 36.9, 28.5, 25.3, 21.6, 12.5, 10.6. HRMS (ESI) *m/z* calc'd for $C_{15}H_{15}F_5N_3$ $[M\text{-}BF_4]^+$: 332.1181; found: 332.1171.

2.2. Synthesis of Imines

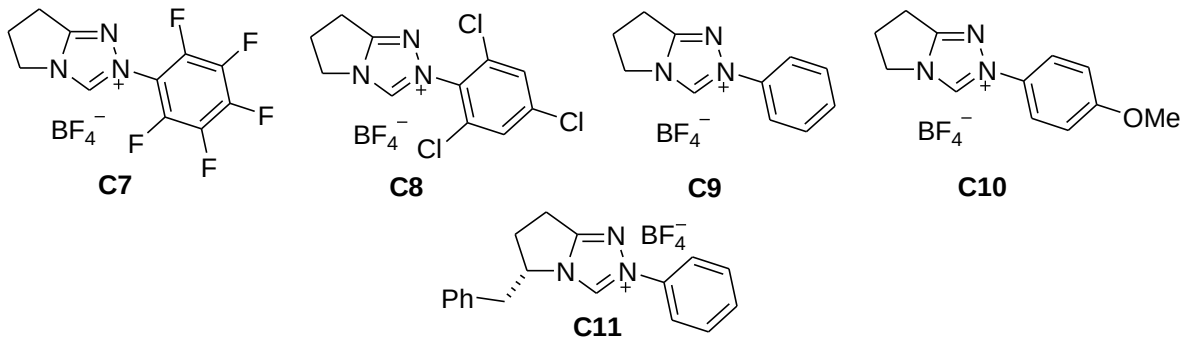
General procedure: To a 100 mL round-bottomed flask was added α,*β*-unsaturated aldehyde, amine (1 eq.) and 3A molecular sieves. The mixture was stirred at room temperature for 12 h. Then, the mixture was fitered and concentrated to give the corresponding imine. The generated imine is typically pure. If necessary, it can be purified by recrystallization from toluene or hexanes.

2.3. Catalyst Screen

Achiral catalysts bearing varying *N*-aryl substituents were examined under the optimized reaction conditions and the results are reported below. Chiral azolium catalyst bearing an *N*-phenyl group was also examined.



entry	NHC precursor	yield (%)[a]	dr[b]	ee of trans/cis (%)[c]
1	**C7**	>99	3.5/1	---
2	**C8**	84	2/1	---
3	**C9**	20	3/1	---
4	**C10**	14	2.5/1	---
5	**C11**	13	2.3/1	-55/-66



Conditions: **2a**, 0.2 mmol; **1a**, 0.1 mmol; **A2**, 20 mol%; NHC precursor, 20 mol%; CH_2Cl_2, 1 mL; 4A MS under Ar. [a] NMR yields of *trans* and *cis*-diastereomers (internal standard). [b] The ratio of *trans*/*cis* determined by ^1H NMR. [c] Determined by chiral HPLC.

2.3. Synthesis of *trans*-*γ*-Lactam Using Chiral Carbenes and Achiral Bases

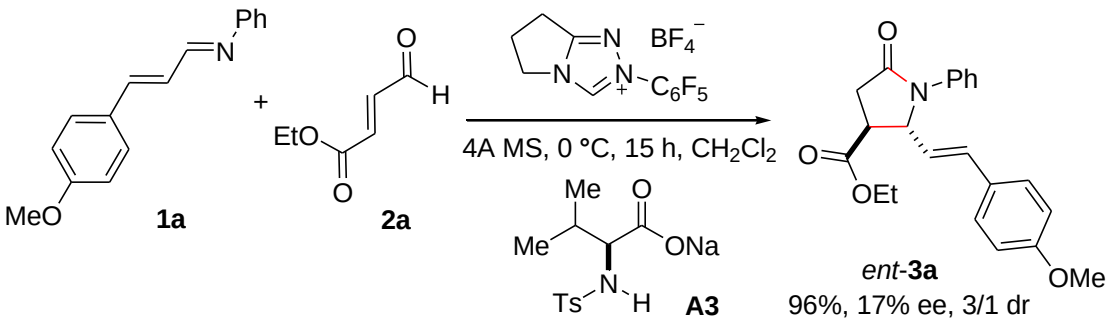
General procedure for cyclization of N-(4-methoxycinnamylidene)aniline (1a) with ethyl trans-4-oxo-2-butenoate (2a): In a 10 mL tube was subsequently added *N*-(4-methoxycinnamylidene)aniline (**1a**) (23.7 mg, 0.1 mmol), triazoliun salt **C4** (8.9 mg, 0.02 mmol, 20 mol%) and sodium *o*-chlorobenzoate (3.6 mg, 0.02 mmol, 20 mol%). The tube was moved into glovebox. Then, ethyl *trans*-4-oxo-2-butenoate (**2a**) (25.6 mg, 0.2 mmol) and 4A molecular sieves (50 mg) were added. The tube was sealed with a septum and removed from the glovebox. Acrylonitrile (1 mL) was added, and the mixture was stirred at 0 ℃ for 15 h, then filtered through Celite and concentrated. The resulting residue was analyzed by proton NMR using 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as an internal standard to determine NMR yield (*trans* and *cis* isomers, 96%) and the diastereoselectivity (*trans*/*cis* = 11/1).

In order to obtain isolated yield, the NMR solution was diluted with 40 mL EtOAc and washed with 1M HCl (5 mL), water (5 mL), $NaHCO_3$ (sat., 5 mL) and brine (10 mL). The organic phase was dried over Na_2SO_4, concentrated *in vacuo* and the resulting residue was purified by silica gel column chromatography (eluent: hexanes/EtOAc = 3:1 to 2/1, v/v) to afford the *trans*-*γ*-lactam product **3a** as a yellow viscous oil (34.0 mg, 93% yield and 91% ee for *trans*-lactam).

Experimental procedure for synthesis of lactam 3m with ethyl trans-4-oxo-2-butenoate (2a) and aniline in one pot: In a 10 mL tube was subsequently added aniline (**1a**) (9.3 mg, 0.1 mmol), triazoliun salt **C4** (8.9 mg, 0.02 mmol, 20 mol%) and sodium *o*-chlorobenzoate (3.6 mg, 0.02 mmol, 20 mol%). The tube was moved into a glovebox, then, ethyl *trans*-4-oxo-2-butenoate (**2a**) (38.4 mg, 0.3 mmol) and 4A molecular sieves (50 mg) were added. The tube was sealed with a septum and removed from glovebox. Acrylonitrile (0.8 mL) was added, and the mixture was stirred at 0 ℃ for 15 h, then filtered through Celite and concentrated. The resulting residue was analyzed to determine the disatereoselectivity (*trans*/*cis* = 8/1). To isolate the product, the NMR solution was diluted with 40 mL EtOAc and washed with 1M HCl (5 mL), water (5 mL), $NaHCO_3$ (sat., 5 mL) and brine (10 mL). The organic phase was dried over Na_2SO_4, concentrated in vacuo and the resulting residue

was purified by silica gel column chromatography (eluent: hexanes/EtOAc = 3:1, v/v) to afford the *trans*-*γ*-lactam product **3m** as a yellow viscous oil (28.1 mg, 85% yield and 92% ee for *trans*-lactam).

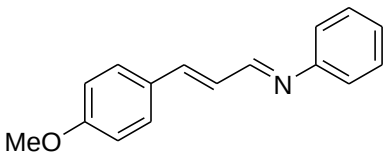
2.4. Synthesis of *trans*-*γ*-Lactam Using Achiral Carbene and Chiral Base



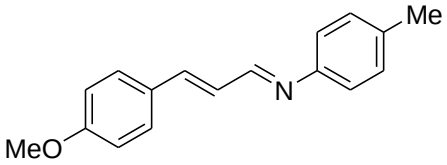
In a 10 mL tube was subsequently added *N*-(4-methoxycinnamylidene)aniline (**1a**) (23.7 mg, 0.1 mmol), 2-pentafluorophenyl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium *tetrafluoroborate* (7.5 mg, 0.02 mmol, 20 mol%) and base **A3** (2.9 mg, 0.02 mmol, 20 mol%). The tube was moved into glovebox. Then, ethyl *trans*-4-oxo-2-butenoate (**2a**) (25.6 mg, 0.2 mmol) and 4A molecular sieves (50 mg) were added. The tube was sealed with a septum and removed from golvebox. Dichloromethane (1 mL) was added. The mixture was stirred at 0 ℃ for 15 h, then filtered through Celite and concentrated to give a residue. It was analyzed by proton NMR to determine the diastereoselectivity (*trans*/*cis* = 3/1). The NMR solution was concentrated and directly purified by silica gel column chromatography (eluent: hexanes/EtOAc = 3:1 to 2/1, v/v) to afford the *trans*-*γ*-lactam product *ent*-**3a** as a yellow viscous oil (35.0 mg, 96% yield and 17% ee for *trans*-lactam). For HPLC trace, see page S76.

3. Analytical data

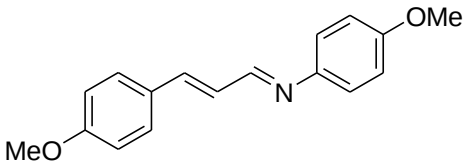
Starting material imines



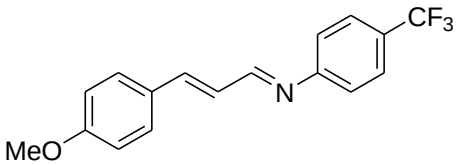
***N*-(4-Methoxycinnamylidene)aniline (1a)**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 78.24 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.38 (t, J = 7.7 Hz, 2H), 7.24-6.91 (m, 7H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 161.8, 160.8, 151.8, 143.7, 129.1, 129.0, 128.3, 126.4, 125.8, 120.8, 114.3, 55.3. HRMS (ESI) *m/z* calc'd for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1226; found: 238.1200.



***N*-(4-Methoxycinnamylidene)-4-methylaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.5 Hz, 1H), 7.45 (d, J = 8.7 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.09-7.04 (m, 3H), 6.97 (dd, J = 8.4, 15.8 Hz, 1H), 6.89 (d, J = 8.7 Hz, 2H), 3.81 (s, 3H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.9, 160.7, 149.2, 143.2, 135.7, 129.7, 128.9, 128.4, 126.5, 120.7, 114.3, 55.3, 20.9. HRMS (ESI) *m/z* calc'd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1383; found: 252.1388.

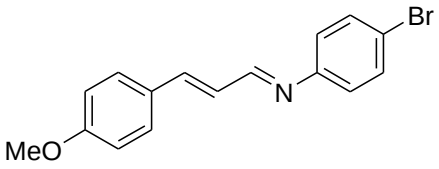


***N*-(4-Methoxycinnamylidene)-4-methoxylaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.9 Hz, 2H), 7.04 (d, J = 15.9 Hz, 1H), 6.96 (dd, J = 8.5, 15.9 Hz, 1H), 6.90-6.88 (m, 4H), 3.82 (s, 3H), 3.80 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 159.8, 158.1, 144.7, 142.7, 128.8, 128.5, 126.6, 122.1, 114.4, 114.3, 55.4, 55.3. HRMS (ESI) *m/z* calc'd for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338; found: 268.1340.

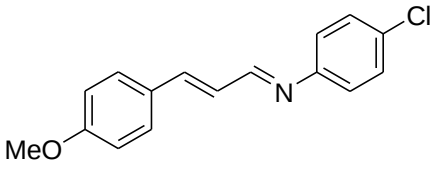


***N*-(4-Methoxycinnamylidene)-4-trifluoromethylaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.9 Hz, 1H), 7.59 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.24-7.11 (m, 3H), 6.96 (dd, J = 8.9, 15.9 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.4, 161.1, 155.0, 145.2,

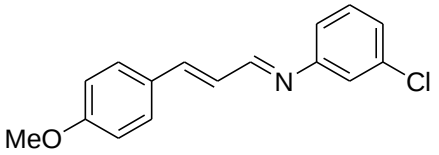
129.2, 128.0, 126.3 (q, J = 3.8 Hz), 125.9, 120.9, 114.4, 55.3. HRMS (ESI) *m/z* calc'd for $C_{17}H_{15}F_3NO$ $[M+H]^+$: 306.1100; found: 306.1108.



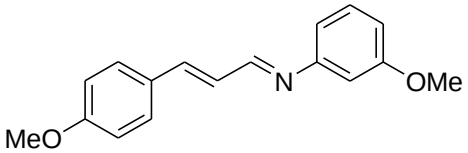
***N*-(4-Methoxycinnamylidene)-4-bromoaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 8.8 Hz, 1H), 7.50-7,46 (m, 4H), 7.12 (d, J = 15.9 Hz, 1H), 7.04 (d, J = 8.6 Hz, 2H), 7.01-6.91 (m, 3H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 162.2, 160.9, 150.8, 144.4, 132.1, 129.1, 128.2, 126.1, 122.5, 119.1, 114.4, 55.3. HRMS (ESI) *m/z* calc'd for $C_{16}H_{15}BrNO$ $[M+H]^+$: 316.0332; found: 316.0333.



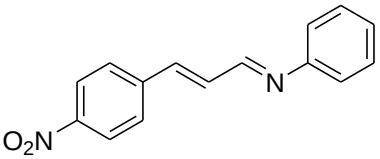
***N*-(4-Methoxycinnamylidene)-4-chloroaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H), 7.11-7.07 (m, 3H), 6.94 (dd, J = 8.8, 15.9 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.1, 160.9, 150.3, 144.3, 131.2, 129.1, 129.0, 128.2, 126.1, 122.1, 114.3, 55.3. HRMS (ESI) *m/z* calc'd for $C_{16}H_{15}ClNO$ $[M+H]^+$: 272.0837; found: 272.0833.



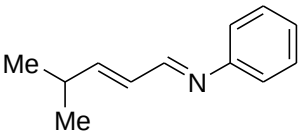
***N*-(4-Methoxycinnamylidene)-3-chloroaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 8.6 Hz, 2H), 7.26 (dd, J = 5.9, 13.8 Hz, 1H), 7.16-7.08 (m, 3H), 7.02 (d, J = 7.9 Hz, 1H), 6.97-6.89 (m, 3H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.8, 161.0, 153.2, 144.7, 134.6, 130.1, 129.1, 128.1, 126.0, 125.6, 120.7, 119.5, 114.4, 55.3. HRMS (ESI) *m/z* calc'd for $C_{16}H_{15}ClNO$ $[M+H]^+$: 272.0842; found: 272.0843.



***N*-(4-Methoxycinnamylidene)-3-methoxylaniline**: Prepared by general procedure. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.7 Hz，1H), 7.45 (d, J = 8.7 Hz, 2H), 7.25 (t, J = 8.0 Hz, 1H), 7.06 (d, J = 15.9 Hz, 1H), 6.96 (dd, J = 8.7, 15.9 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.76-6.72 (m, 3H), 3.80 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.8, 160.7, 160.2, 153.2, 143.8, 129.7, 128.9, 128.2, 126.2, 114.2, 112.8, 111.6, 106.6, 55.2, 55.1. HRMS (ESI) *m/z* calc'd for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338; found: 268.1336.



***N*-(4-Nitrocinnamylidene)aniline**: Prepared by a modification to general procedure. Dichloromethane and toluene were used as mixed solvents instead of toluene because of the solubility of imine in toluene. Yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.4 Hz, 1H), 8.23 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.7 Hz, 2H), 7.38 (t, J = 7.8 Hz, 2H), 7.26-7.22 (m, 1H), 7.20-7.14 (m, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.2, 151.1, 141.7, 140.4, 132.5, 129.2, 127.9, 126.7, 124.2, 120.9. HRMS (ESI) *m/z* calc'd for $C_{15}H_{13}N_2O_2$ $[M+H]^+$: 253.0972; found: 253.0981.



***N*-(4-Methylpent-2-enylidene)aniline**: Prepared by general procedure. Yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 3.0, 5.3 Hz, 1H), 7.35-7.31 (m, 2H), 7.17 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 7.2 Hz, 2H), 6.39-6.37 (m, 2H), 2.58-2.49 (m, 1H), 1.09 (d, J = 6.8 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.4, 155.1, 151.9, 129.0, 128.4, 125.6, 120.7, 31.4, 21.5. HRMS (ESI) *m/z* calc'd for $C_{12}H_{16}N$ $[M+H]^+$: 174.1277; found: 174.1272.

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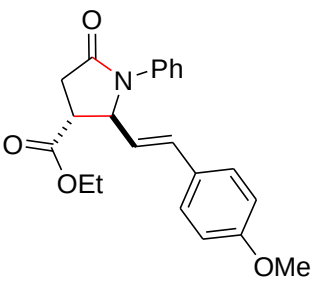
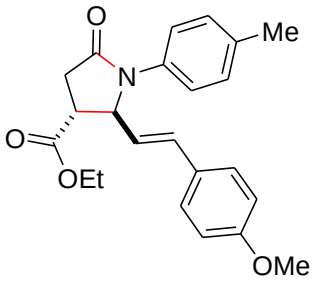
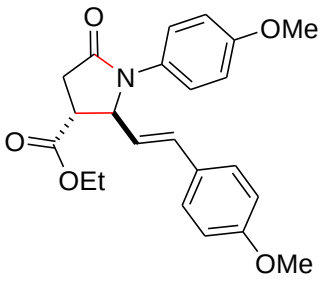


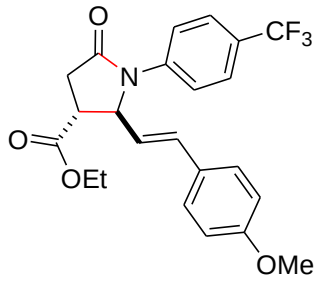
(2S,3R)-Ethyl 2-(4-methoxystyryl)-5-oxo-1-phenylpyrrolidine-3-carboxylate (**3a**): Yellow viscous oil. 93% yield, 91% ee and 11/1 dr. $[\alpha]^{20}_{D}$ = -15.2 °(c = 0.094 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 18.93 min, minor: 24.56 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 7.5 Hz, 2H), 7.34-7.29 (m, 2H), 7.22 (d, J =8.7 Hz, 2H), 7.16-7.11 (m, 1H), 6.80 (d, J = 8.7 Hz, 2H), 6.52 (d, J = 15.8 Hz, 1H), 5.92 (dd, J = 7.8, 15.8 Hz, 1H), 5.05 (dd, J = 5.5, 7.5 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 3.14-3.07 (m, 1H), 3.00-2.83 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.7, 171.2, 159.2, 137.0, 132.7, 128.4, 127.9, 127.4, 125.3, 124.4, 123.0, 113.6, 64.3, 61.1, 54.8, 43.8, 33.9, 13.7. HRMS (ESI) *m/z* calc'd for $C_{22}H_{24}NO_4$ $[M+H]^+$: 366.1700; found: 366.1697.



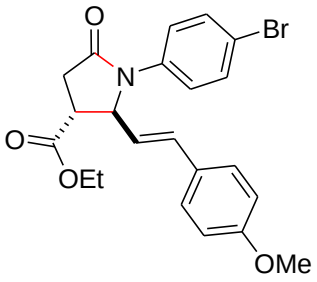
(2S,3R)-Ethyl 2-(4-methoxystyryl)-5-oxo-1-*p*-tolylpyrrolidine-3-carboxylate (**3b**): Yellow viscous oil. 86% yield, 89% ee and 9/1 dr. $[\alpha]^{20}_{D}$ = -5.4 °(c = 0.0236 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 21.98 min, minor: 29.88 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.29-7.22 (m, 4H), 7.13 (d, J = 8.3 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 6.50 (d, J = 15.8 Hz, 1H), 5.90 (dd, J = 7.9, 15.8 Hz, 1H), 4.99 (dd, J = 5.6, 7.8 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.13-3.06 (m, 1H), 2.99-2.82 (m, 2H), 2.28 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.1, 171.5, 159.6, 135.6, 134.6, 133.1, 129.4, 128.3, 127.8, 124.9, 123.7, 113.9, 64.8, 61.5, 55.2, 44.2, 34.3, 20.9, 14.1. HRMS (ESI) *m/z* calc'd for $C_{23}H_{26}NO_4$ $[M+H]^+$: 380.1856; found: 380.1865.



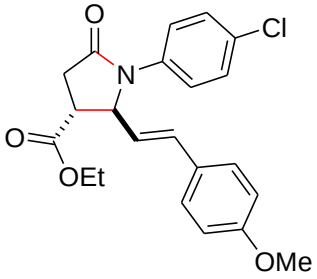
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(4-methoxyphenyl)-5-oxopyrrolidine-3-carboxylate (**3c**): Yellow viscous oil. 35% yield, 86% ee and 6/1 dr in acrylonitrile; 87% yield, 81% ee and 4/1 dr in dichloromethane. $[\alpha]^{20}_{D}$ = +5.3 ° (c = 0.0233 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 75:25 hexanes/isopropanol, 1.0 mL/min, major: 11.78 min, minor: 15.57 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.29-7.22 (m, 4H), 6.87-6.80 (m, 4H), 6.48 (d, J = 15.8 Hz, 1H), 5.89 (dd, J = 8.1, 15.8 Hz, 1H), 4.93 (dd, J = 5.7, 8.0 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.75 (s, 3H), 3.13-3.06 (m, 1H), 2.99-2.82 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.2, 171.6, 159.6, 157.5, 133.3, 130.0, 128.3, 127.8, 125.6, 124.9, 114.1, 113.9, 65.2, 61.5, 55.2, 44.2, 34.2, 14.1. HRMS (ESI) *m/z* calc'd for $C_{23}H_{26}NO_5$ $[M+H]^+$: 396.1805; found: 396.1808.



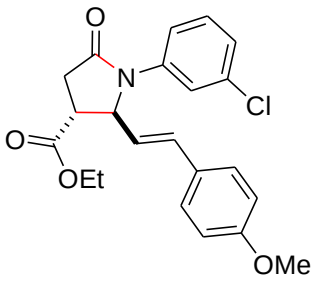
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(4-(trifluoromethyl)phenyl)-5-oxopyrrolidine-3-carboxylate (**3d**) Yellow viscous oil. 76% yield, 86% ee and 10/1 dr. $[\alpha]^{20}_{D}$ = -24.0 °(c = 0.021 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 95:5 hexanes/isopropanol, 1.0 mL/min, major: 29.87 min, minor: 38.57 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.9 Hz, 2H), 7.58 (d, J = 9.0 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 6.55 (d, J = 15.9 Hz, 1H), 5.92 (dd, J = 7.5, 15.9 Hz, 1H), 5.12 (dd, J = 5.1, 7.3 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.15-3.08 (m, 1H), 2.94 (dq, J = 7.9, 17.2 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.9, 159.8, 140.5, 133.4, 127.9, 125.9 (q, J = 3.1 Hz), 124.0, 122.3, 114.0, 64.1, 61.7, 55.3, 44.0, 34.3, 14.1.^{19}F NMR (282 MHz, $CDCl_3$) δ -62.7. HRMS (ESI) *m/z* calc'd for $C_{23}H_{23}F_3NO_4$ $[M]^+$: 434.1574; found: 434.1578.



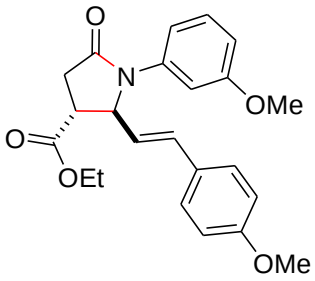
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(4-bromophenyl)-5-oxopyrrolidine-3-carboxylate (**3e**): Yellow viscous oil. 96% yield, 89% ee and 10/1 dr. $[\alpha]^{20}_{D}$ = +2.62 ° (c = 0.029 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 23.07 min, minor: 29.59 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 8.8 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.51 (d, J = 15.8 Hz, 1H), 5.88 (dd, J = 7.8, 15.8 Hz, 1H), 5.02 (dd, J = 5.5, 7.6 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.13-3.06 (m, 1H), 2.99-2.82 (m, 2H), 1.28 (t, J =7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.0, 171.6, 159.8, 136.4, 133.4, 131.8, 128.0, 127.8, 124.7, 124.2, 118.7, 114.0, 64.4, 61.6, 55.3, 44.0, 34.3, 14.1. HRMS (ESI) *m/z* calc'd for $C_{22}H_{23}BrNO_4$ $[M+H]^+$: 444.0805; found: 444.0810.



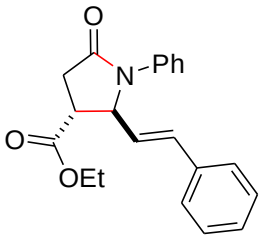
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(4-chlorophenyl)-5-oxopyrrolidine-3-carboxylate (**3f**): Yellow viscous oil. 79% yield, 92% ee and 9/1 dr. $[\alpha]^{20}_{D}$ = -3.2 ° (c = 0.0248 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 97:3 hexanes/isopropanol, 1.0 mL/min, major: 63.66 min, minor: 84.75 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.51 (d, J = 15.8 Hz, 1H), 5.88 (dd, J = 7.8, 15.8 Hz, 1H), 5.02 (dd, J = 5.5, 7.6 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.13-3.06 (m, 1H), 3.00-2.83 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.0, 171.6, 159.8, 135.9, 133.4, 130.9, 128.9, 128.1, 127.9, 124.5, 124.3, 114.0, 64.5, 61.7, 55.3, 44.1, 34.3, 14.1. HRMS (ESI) *m/z* calc'd for $C_{22}H_{23}ClNO_4$ $[M+H]^+$: 400.1310; found: 400.1321.



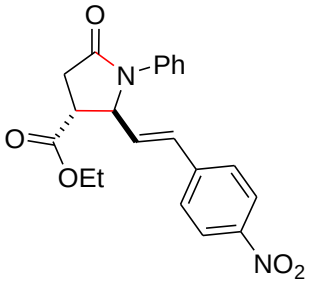
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(3-chlorophenyl)-5-oxopyrrolidine-3-carboxylate (**3g**): Yellow viscous oil. 91% yield, 90% ee and 9/1 dr. $[\alpha]^{20}_{D}$ = -17.6 ° (c = 0.0238 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 98:2 hexanes/isopropanol, 1.0 mL/min, major: 57.29 min, minor: 87.01 min, 280 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.34-7.22 (m, 4H), 7.11 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.52 (d, J = 15.8 Hz, 1H), 5.90 (dd, J = 7.6, 15.8 Hz, 1H), 5.04 (dd, J = 5.1, 7.4 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.13-3.06 (m, 1H), 3.00-2.83 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.9, 171.7, 159.7, 138.6, 134.4, 133.3, 129.7, 128.1, 127.9, 125.6, 124.2, 123.2, 120.9, 114.0, 64.4, 61.7, 55.3, 44.1, 34.3, 14.1. HRMS (ESI) *m/z* calc'd for $C_{22}H_{23}ClNO_4$ $[M+H]^+$: 400.1310; found: 400.1310.



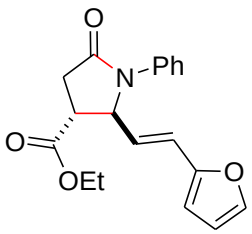
(2S,3R)-Ethyl 2-(4-methoxystyryl)-1-(3-methoxyphenyl)-5-oxopyrrolidine-3-carboxylate (**3h**): Yellow viscous oil. 64% yield, 85% ee and 9/1 dr. $[\alpha]^{20}_{D}$ = -18.1 ° (c = 0.0181 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 21.28 min, minor: 34.42 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.26-7.22 (m, 3H), 7.08-7.07 (m, 1H), 6.99 (d, J = 8.0 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.70 (dd, J = 2.4, 8.3 Hz, 1H), 6.52 (d, J = 15.8 Hz, 1H), 5.93 (dd, J = 7.7, 15.8 Hz, 1H), 5.03 (dd, J = 5.2, 7.6 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.76 (s, 3H), 3.12-3.05 (m, 1H), 3.00-2.83 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.1, 171.6, 159.7, 159.6, 138.5, 132.9, 129.4, 128.3, 127.8, 124.7, 115.5, 113.9, 111.3, 109.3, 64.7, 61.5, 55.2, 44.1, 34.3, 14.1. HRMS (ESI) *m/z* calc'd for $C_{23}H_{26}NO_5$ $[M+H]^+$: 396.1805; found: 396.1797.



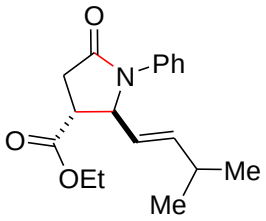
(2S,3R)-Ethyl 5-oxo-1-phenyl-2-styrylpyrrolidine-3-carboxylate (**3i**): Yellow viscous oil. 92% yield, 92% ee and 14/1 dr. $[\alpha]^{20}_{D}$ = -21.4 ° (c = 0.031 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 13.42 min, minor: 16.92 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 7.7 Hz, 2H), 7.31-7.24 (m, 7H), 7.16 (t, J = 7.3 Hz, 1H), 6.59 (d, J = 15.9 Hz, 1H), 6.07 (dd, J = 7.7, 15.9 Hz, 1H), 5.09 (dd, J = 5.4, 7.5 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.12 (dt, J = 5.4, 8.1 Hz, 1H), 3.02-2.85 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.0, 171.6, 137.2, 135.5, 133.6, 128.8, 128.5, 128.2, 127.1, 126.5, 125.7, 123.4, 64.4, 61.6, 44.0, 34.3, 14.1. HRMS (ESI) *m/z* calc'd for $C_{21}H_{22}NO_3$ $[M+H]^+$: 336.1594; found: 336.1602.



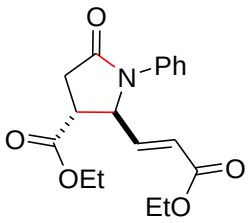
(2S,3R)-Ethyl 2-(4-nitrostyryl)-5-oxo-1-phenylpyrrolidine-3-carboxylate (**3j**): Yellow viscous oil. 95% yield, 93% ee and >20/1 dr. $[\alpha]^{20}_{D}$ = -20.5 ° (c = 0.0198 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 80:20 hexanes/isopropanol, 1.0 mL/min, major: 18.12 min, minor: 21.45 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J = 8.7 Hz, 2H), 7.44-7.32 (m, 6H), 7.17 (t, J = 7.2 Hz, 1H), 6.65 (d, J = 15.9 Hz, 1H), 6.27 (dd, J = 7.5, 15.9 Hz, 1H), 5.15 (dd, J = 5.8, 7.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.14 (dt, J = 5.5, 8.2 Hz, 1H), 3.03-2.87 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.7, 171.4, 147.2, 141.8, 137.0, 132.1, 131.5, 129.0, 127.2, 126.0, 124.0, 123.2, 63.9, 61.8, 43.6, 34.2, 14.2. HRMS (ESI) *m/z* calc'd for $C_{21}H_{21}N_2O_5$ $[M+H]^+$: 381.1445; found: 381.1457.



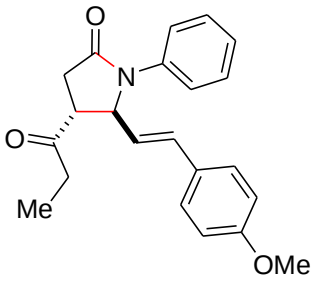
(2S,3R)-Ethyl 2-((*E*)-2-(furan-2-yl)vinyl)-5-oxo-1-phenylpyrrolidine-3-carboxylate (**3k**): Yellow viscous oil. 93% yield, 89% ee and 12/1 dr. $[\alpha]^{20}_{Dv}$= -16.4 °(c = 0.026 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 85:15 hexanes/isopropanol, 1.0 mL/min, major: 9.87 min, minor: 12.68 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.0 Hz, 2H), 7.39-7.31 (m, 3H), 7.16 (t, J = 7.3 Hz, 1H), 6.39-6.32 (m, 2H), 6.21 (d, J = 3.2 Hz, 1H), 6.02 (dd, J = 7.6, 15.8 Hz, 1H), 5.04 (dd, J = 5.2, 7.6 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.13-3.06 (m, 1H), 2.91 (dq, J = 8.0, 17.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.0, 171.6, 151.2, 142.5, 137.3, 128.9, 125.8, 125.4, 123.3, 121.6, 111.4, 109.4, 64.1, 61.6, 44.0, 34.2, 14.1. HRMS (ESI) *m/z* calc'd for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1387; found: 326.1385.



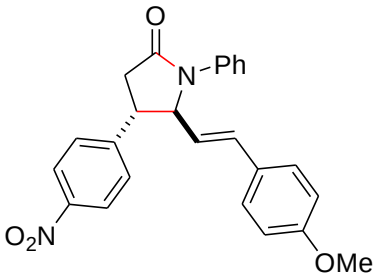
(2S,3R)-Ethyl 2-((E)-3-methylbut-1-enyl)-5-oxo-1-phenylpyrrolidine-3-carboxylate (**3l**): Yellow viscous oil. 49% yield, 90% ee and >20/1 dr in acrylonitrile; 73% yield, 88% ee and >15/1 dr in dichloromethane. $[\alpha]^{20}_{D}$ = -38.5 ° (c = 0.0160 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 98:2 hexanes/isopropanol, 1.0 mL/min, major: 23.20 min, minor: 35.12 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.45-7.30 (m, 4H), 7.18-7.15 (m, 1H), 5.63 (dd, J = 6.7, 15.3 Hz, 1H), 5.23 (dd, J = 8.0, 15.4 Hz, 1H), 4.78 (t, J = 6.7 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.00-2.96 (m, 1H), 2.87-2.85 (m, 2H), 2.21 (qd, J = 6.6, 13.4 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0.89-0.81 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.3, 171.6, 143.1, 137.2, 128.6, 125.7, 124.7, 123.9, 64.7, 61.4, 44.25, 34.4, 30.7, 21.9, 14.2. HRMS (ESI) *m/z* calc'd for $C_{18}H_{24}NO_3$ $[M+H]^+$: 302.1751; found: 302.1759.



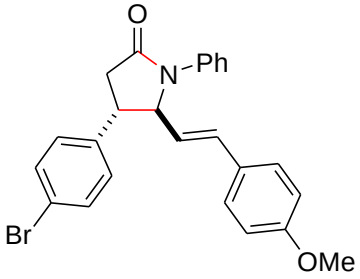
(2S,3R)-Ethyl 2-((*E*)-2-(ethoxycarbonyl)vinyl)-5-oxo-1-phenylpyrrolidine-3-carboxylate (**3m**): Yellow viscous oil. 85% yield, 92% ee and 8/1 dr. $[\alpha]^{20}_{D}$ = -36.5 ° (c = 0.0203 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 17.34 min, minor: 20.08 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.44-7.31 (m, 4H), 7.21-7.16 (m, 1H), 6.82 (dd, J = 7.0, 15.7 Hz, 1H), 5.97 (d, J = 15.3 Hz, 1H), 5.14-5.10 (m, 1H), 4.23 (q, J = 7.2 Hz, 2H), 4.12 (q, J = 7.0 Hz, 2H), 3.10-3.03 (m, 1H) ppm 2.98-2.83 (m, 2H), 1.32-1.22 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.3, 171.3, 165.2, 144.3, 136.9, 129.0, 125.9, 124.2, 122.7, 62.3, 61.9, 60.8, 42.6, 33.9, 14.0. HRMS (ESI) *m/z* calc'd for $C_{18}H_{22}NO_5$ $[M+H]^+$: 332.1492; found: 332.1497.



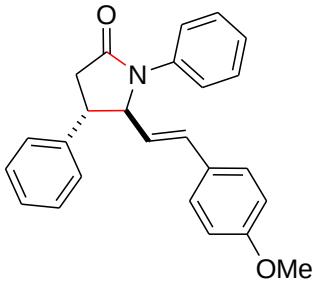
(4R,5S)-5-(4-Methoxystyryl)-1-phenyl-4-propionylpyrrolidin-2-one (**3n**): Yellow viscous oil. 62% yield, 66% ee and 11/1 dr. $[\alpha]^{20}_{D}$ = -42.0 ° (c = 0.0131 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 19.98 min, minor: 26.12 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.39 (d, J = 7.7 Hz, 2H), 7.35-7.30 (m, 2H), 7.22 (d, J = 8.7 Hz, 2H), 7.17-7.12 (m, 1H), 6.81 (d, J = 8.7 Hz, 2H), 6.49 (d, J = 15.8 Hz, 1H), 5.88 (dd, J = 8.2, 15.8 Hz, 1H), 5.00 (dd, J = 6.1, 8.0 Hz, 1H), 3.78 (s, 3H), 3.30-3.22 (m, 1H), 2.91 (dd, J = 9.4, 17.0 Hz, 1H), 2.77 (dd, J = 8.1, 17.0 Hz, 1H), 2.64-2.47 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 208.7, 171.3, 159.7, 137.2, 133.3, 128.8, 128.2, 127.8, 125.8, 125.3, 123.8, 114.0, 63.8, 55.3, 50.3, 36.0, 34.1, 7.5. HRMS (ESI) *m/z* calc'd for $C_{22}H_{24}NO_3$ $[M+H]^+$: 350.1751; found: 350.1751.



(4S,5S)-5-(4-Methoxystyryl)-4-(4-nitrophenyl)-1-phenylpyrrolidin-2-one (**3o**): White solid. 99% yield, 93% ee and 14/1 dr. M.p.: 77-79 ℃. $[\alpha]^{20}_{D}$ = -150.3 ° (c = 0.0239 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IA column, 90:10 hexanes/isopropanol, 1.0 mL/min, major: 55.19 min, minor: 42.59 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 8.7 Hz, 2H), 7.50-7.43 (m, 4H), 7.37-7.32 (m, 2H), 7.21-7.14 (m, 3H), 6.81 (d, J = 8.7 Hz, 2H), 6.30 (d, J = 15.9 Hz, 1H), 5.96 (dd, J = 7.9, 15.8 Hz, 1H), 4.71 (dd, J = 5.9, 7.6 Hz, 1H), 3.78 (s, 3H), 3.54 (dd, J = 8.0, 14.0 Hz, 1H), 3.17 (dd, J = 8.8, 17.2 Hz, 1H), 2.81 (dd, J = 7.6, 17.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.1, 159.8, 148.6, 147.3, 137.4, 133.4, 128.9, 128.2, 128.1, 127.8, 125.8, 124.4, 124.2, 123.3, 114.0, 69.8, 55.3, 45.4, 38.4. HRMS (ESI) *m/z* calc'd for $C_{25}H_{23}N_2O_4$ $[M+H]^+$: 415.1652; found: 415.1661.

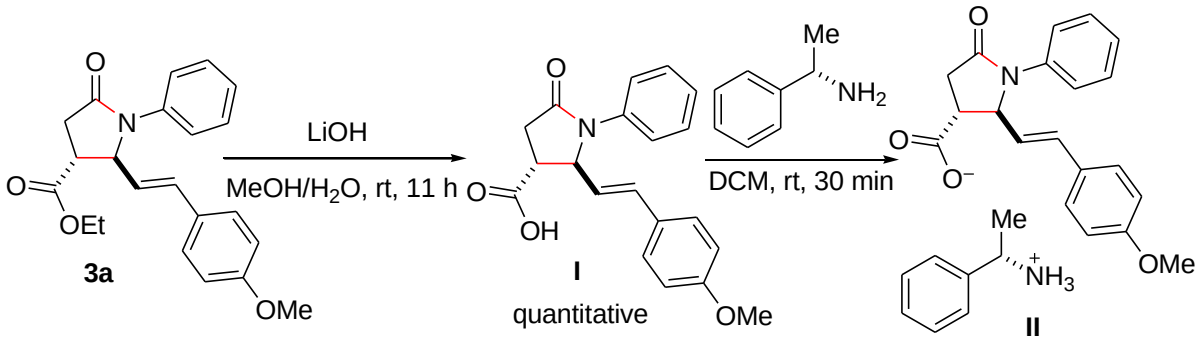


(4S,5S)-5-(4-Methoxystyryl)-4-(4-bromophenyl)-1-phenylpyrrolidin-2-one (**3p**): White solid. 58% yield, 91% ee and 17/1 dr. M.p.: 56-58 ℃. $[\alpha]^{20}_{D}$ = -117.8 ° (c = 0.0157 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IC column, 50:50 hexanes/isopropanol, 1.0 mL/min, major: 17.30 min, minor: 28.03 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.49-7.43 (m, 4H), 7.36-7.31 (m, 2H), 7.24-7.13 (m, 5H), 6.81 (d, J = 7.3 Hz, 2H), 6.29 (d, J =15.8 Hz, 1H), 5.94 (dd, J = 7.8, 15.9 Hz, 1H), 4.66 (t, J = 6.7 Hz, 1H), 3.78 (s, 3H), 3.37 (dd, J = 7.6, 14.1 Hz, 1H), 3.11 (dd, J = 8.8, 17.1 Hz, 1H), 2.76 (dd, J = 7.5, 17.2 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 172.7, 159.6, 140.1, 137.6, 132.9, 132.0, 129.0, 128.8, 128.3, 127.8, 125.6, 124.9, 123.3, 121.2, 114.0, 70.1, 55.3, 45.0, 38.5. HRMS (ESI) *m/z* calc'd for $C_{25}H_{23}BrNO_2$ $[M+H]^+$: 448.0907; found: 448.0918.



(4S,5S)-5-(4-Methoxystyryl)-1,4-diphenylpyrrolidin-2-one (**3q**): White solid. 48% yield, 90% ee and 20/1 dr. M.p.: 49-51 ℃. $[\alpha]^{20}_{D}$ = -94.6 ° (c = 0.0121 g/mL, $CHCl_3$). HPLC analysis–Chiralcel IC column, 50:50 hexanes/isopropanol, 1.0 mL/min, major: 15.86 min, minor: 16.99 min, 254 nm. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 8.1 Hz, 2H), 7.39-7.29 (m, 7H), 7.22-7.12 (m, 3H), 6.81 (d, J = 8.7 Hz, 2H), 6.29 (d, J = 15.9 Hz, 1H), 5.98 (dd, J = 7.7, 15.9 Hz, 1H), 4.72 (dd, J = 5.6, 7.6 Hz, 1H), 3.78 (s, 3H), 3.41 (dd, J = 8.0, 13.6 Hz, 1H), 3.13 (dd, J = 8.8, 17.2 Hz, 1H), 2.82 (dd, J = 7.3, 17.2 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 173.1, 159.5, 141.3, 137.8, 132.6, 128.9, 128.8, 128.6, 127.7, 127.3, 127.2, 125.5, 125.4, 123.3, 113.9, 70.2, 55.3, 45.4, 38.8. HRMS (ESI) *m/z* calc'd for $C_{25}H_{24}NO_2$ $[M+H]^+$: 370.1802; found: 370.1797.

4. Absolute configuration assignment



In a 20-mL vial was added ester **3a** (33.0 mg, 0.09 mmol), MeOH (3 mL) and H_2O (1 mL). LiOH (10.8 mg, 0.45 mmol) was then added. The solution was stirred at room temperature for 11 h. MeOH was removed under reduced pressure. The aqueous solution was acidified with 1 M HCl until pH = 2~3. The resulting mixture was extracted with EtOAc (4 mL x 3), dried over Na_2SO_4, filtered and concentrated to give slightly yellow solid residue, which was purified by silica gel column chromatoghy (eluent: EtOAc) to quantitatively give the desired product acid **I** as a white solid. Acid **I**: White solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.72 (br,

1H), 7.41 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.24-7.14 (m, 3H), 6.81 (d, J = 8.6 Hz, 2H), 6.53 (d, J = 15.8 Hz, 1H), 5.92 (dd, J = 7.8, 15.8 Hz, 1H), 5.07 (dd, J = 5.1, 7.6 Hz, 1H), 3.78 (s, 3H), 3.18-3.12 (m, 1H), 3.08-2.90 (m, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 176.3, 172.1, 159.7, 137.0, 133.5, 128.8, 128.2, 127.9, 126.1, 124.3, 123.7, 114.0, 64.8, 55.2, 43.9, 34.1. Treatment of obtained acid **I** with 1 eq. (s)-1-phenylethylamine afforded counterion **II**. Crude ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.59 (br, 3H), 7.42 (d, J = 8.1 Hz, 2H), 7.32-7.15 (m, 9H), 7.08 (t, J = 7.3 Hz, 1H), 6.78 (d, J = 8.6 Hz, 2H), 6.34 (d, J = 15.9 Hz, 1H), 5.81 (dd, J = 7.2, 15.9 Hz, 1H), 4.89 (dd, J = 4.1, 6.9 Hz, 1H), 4.12-3.99 (m, 1H), 3.75 (s, 3H), 2.61-2.36 (m, 3H), 1.38 (d, J = 6.6 Hz, 3H) (Note: the spectra are on page S41). A single crystal of **II** suitable for X-ray analysis was obtained by slow volatilization of its DCM/EtOAc solution.

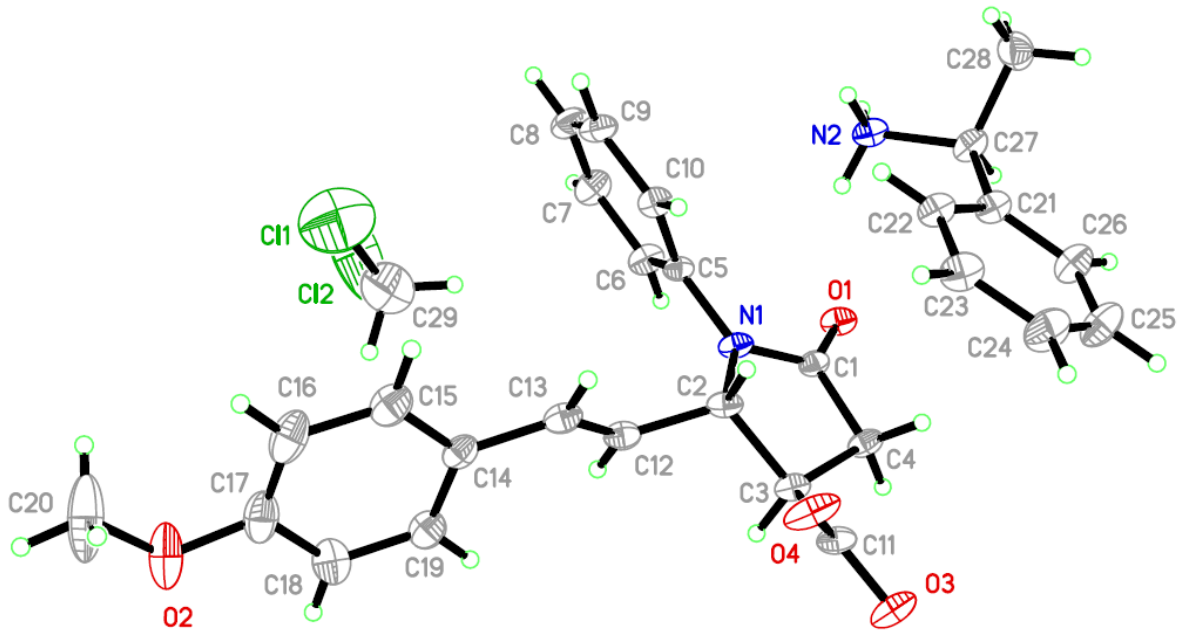


Table 1. Crystal data and structure refinement for rovis125.

Identification code	rovis125
Empirical formula	$C_{29}H_{32}Cl_2N_2O_4$
Formula weight	543.47
Temperature	120 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 6.0055(2) Å = 90°.

	b = 27.8264(8) Å = 99.216(2)°.
	c = 8.3886(2) Å = 90°.
Volume	1383.74(7) $Å^3$
Z	2
Density (calculated)	1.304 Mg/m^3
Absorption coefficient	0.272 mm^{-1}
F(000)	572
Crystal size	0.25 x 0.14 x 0.13 mm^3
Theta range for data collection	2.46 to 28.33 °.
Index ranges	-6<=h<=8, -37<=k<=35, -11<=l<=11
Reflections collected	24033
Independent reflections	6583 [R(int) = 0.0384]
Completeness to theta = 28.33 °	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9661 and 0.9357
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6583 / 1 / 338
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0589, wR2 = 0.1588
R indices (all data)	R1 = 0.0774, wR2 = 0.1787
Absolute structure parameter	0.13(11)
Largest diff. peak and hole	0.459 and -0.741 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for rovis125. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	1863(5)	2009(1)	5135(3)	17(1)
C(2)	5441(5)	2326(1)	6283(3)	18(1)

C(3)	4442(5)	2079(1)	7641(3)	17(1)
C(4)	2505(5)	1762(1)	6743(3)	19(1)
C(5)	3534(5)	2591(1)	3482(3)	17(1)
C(6)	1679(5)	2866(1)	2827(3)	23(1)
C(7)	1724(6)	3117(1)	1389(4)	26(1)
C(8)	3599(6)	3093(1)	636(3)	27(1)
C(9)	5450(6)	2823(1)	1293(3)	24(1)
C(10)	5428(5)	2568(1)	2709(3)	20(1)
C(11)	6158(5)	1808(1)	8852(3)	20(1)
C(12)	6259(5)	2827(1)	6714(3)	21(1)
C(13)	8312(5)	2990(1)	6664(3)	23(1)
C(14)	9162(5)	3472(1)	7138(3)	22(1)
C(15)	11057(6)	3653(1)	6588(4)	30(1)
C(16)	11912(6)	4110(1)	7032(5)	36(1)
C(17)	10840(6)	4391(1)	8044(5)	33(1)
C(18)	8956(6)	4215(1)	8606(4)	32(1)
C(19)	8130(6)	3764(1)	8154(4)	26(1)
C(20)	13554(7)	5026(2)	8155(9)	66(2)
C(21)	2809(5)	941(1)	3081(3)	22(1)
C(22)	4922(5)	1158(1)	3455(3)	22(1)
C(23)	6412(5)	1024(1)	4844(4)	28(1)
C(24)	5769(6)	669(1)	5851(4)	35(1)
C(25)	3691(6)	455(1)	5495(4)	35(1)
C(26)	2208(6)	588(1)	4119(4)	29(1)
C(27)	1158(5)	1067(1)	1574(3)	22(1)
C(28)	1447(7)	759(1)	118(4)	34(1)
C(29)	5684(11)	4041(2)	3524(7)	74(2)
Cl(1)	8191(3)	4076(1)	2820(2)	93(1)
Cl(2)	3567(3)	4372(1)	2335(4)	129(1)
N(1)	3506(4)	2334(1)	4948(3)	17(1)
N(2)	1327(4)	1581(1)	1106(3)	20(1)
O(1)	193(3)	1923(1)	4130(2)	20(1)
O(2)	11530(5)	4840(1)	8580(4)	47(1)
O(3)	5437(4)	1601(1)	9984(2)	28(1)
O(4)	8174(4)	1819(1)	8644(2)	31(1)

Table 3. Bond lengths [Å] and angles [°] for rovis125.

C(1)-O(1)	1.225(3)
C(1)-N(1)	1.366(4)
C(1)-C(4)	1.509(4)
C(2)-N(1)	1.480(4)
C(2)-C(12)	1.503(4)
C(2)-C(3)	1.534(4)
C(3)-C(11)	1.524(4)
C(3)-C(4)	1.555(4)
C(5)-C(6)	1.390(4)
C(5)-C(10)	1.398(4)
C(5)-N(1)	1.425(3)
C(6)-C(7)	1.398(4)
C(7)-C(8)	1.379(5)
C(8)-C(9)	1.382(5)
C(9)-C(10)	1.385(4)
C(11)-O(3)	1.247(3)
C(11)-O(4)	1.251(4)
C(12)-C(13)	1.321(4)
C(13)-C(14)	1.466(4)
C(14)-C(15)	1.389(4)
C(14)-C(19)	1.393(4)
C(15)-C(16)	1.400(5)
C(16)-C(17)	1.387(6)
C(17)-O(2)	1.368(4)
C(17)-C(18)	1.383(5)
C(18)-C(19)	1.381(5)
C(20)-O(2)	1.419(5)
C(21)-C(22)	1.395(4)
C(21)-C(26)	1.399(4)
C(21)-C(27)	1.518(4)
C(22)-C(23)	1.401(4)
C(23)-C(24)	1.393(5)
C(24)-C(25)	1.372(6)
C(25)-C(26)	1.390(5)
C(27)-N(2)	1.491(4)
C(27)-C(28)	1.525(4)
C(29)-Cl(1)	1.706(6)
C(29)-Cl(2)	1.749(7)

O(1)-C(1)-N(1)	125.2(2)
O(1)-C(1)-C(4)	126.2(2)
N(1)-C(1)-C(4)	108.6(2)
N(1)-C(2)-C(12)	110.8(2)
N(1)-C(2)-C(3)	102.4(2)
C(12)-C(2)-C(3)	112.9(2)
C(11)-C(3)-C(2)	114.4(2)
C(11)-C(3)-C(4)	114.6(2)
C(2)-C(3)-C(4)	104.3(2)
C(1)-C(4)-C(3)	103.8(2)
C(6)-C(5)-C(10)	120.1(2)
C(6)-C(5)-N(1)	119.9(2)
C(10)-C(5)-N(1)	120.0(2)
C(5)-C(6)-C(7)	119.4(3)
C(8)-C(7)-C(6)	120.1(3)
C(7)-C(8)-C(9)	120.5(3)
C(8)-C(9)-C(10)	120.2(3)
C(9)-C(10)-C(5)	119.7(3)
O(3)-C(11)-O(4)	125.4(3)
O(3)-C(11)-C(3)	117.1(3)
O(4)-C(11)-C(3)	117.5(2)
C(13)-C(12)-C(2)	125.6(3)
C(12)-C(13)-C(14)	126.3(3)
C(15)-C(14)-C(19)	117.4(3)
C(15)-C(14)-C(13)	120.6(3)
C(19)-C(14)-C(13)	122.0(3)
C(14)-C(15)-C(16)	121.7(3)
C(17)-C(16)-C(15)	119.3(3)
O(2)-C(17)-C(18)	115.6(3)
O(2)-C(17)-C(16)	124.8(3)
C(18)-C(17)-C(16)	119.6(3)
C(19)-C(18)-C(17)	120.4(3)
C(18)-C(19)-C(14)	121.5(3)
C(22)-C(21)-C(26)	118.7(3)
C(22)-C(21)-C(27)	122.4(3)
C(26)-C(21)-C(27)	118.8(3)
C(21)-C(22)-C(23)	120.5(3)

C(24)-C(23)-C(22)	119.4(3)
C(25)-C(24)-C(23)	120.4(3)
C(24)-C(25)-C(26)	120.3(3)
C(25)-C(26)-C(21)	120.6(3)
N(2)-C(27)-C(21)	112.3(2)
N(2)-C(27)-C(28)	107.9(2)
C(21)-C(27)-C(28)	113.2(3)
Cl(1)-C(29)-Cl(2)	111.9(3)
C(1)-N(1)-C(5)	122.7(2)
C(1)-N(1)-C(2)	113.4(2)
C(5)-N(1)-C(2)	123.0(2)
C(17)-O(2)-C(20)	118.5(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for rovis125. The anisotropic displacement factor exponent takes the form: $-2\ ^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	16(1)	20(1)	15(1)	2(1)	4(1)	3(1)
C(2)	12(1)	26(1)	13(1)	0(1)	1(1)	2(1)
C(3)	10(1)	26(1)	14(1)	2(1)	1(1)	3(1)
C(4)	14(1)	29(1)	15(1)	5(1)	0(1)	-1(1)
C(5)	19(2)	21(1)	12(1)	1(1)	1(1)	1(1)
C(6)	18(2)	29(2)	22(1)	4(1)	4(1)	4(1)
C(7)	22(2)	31(2)	24(1)	8(1)	-2(1)	5(1)
C(8)	30(2)	33(2)	18(1)	7(1)	2(1)	-3(1)
C(9)	22(2)	35(2)	16(1)	-1(1)	5(1)	-4(1)
C(10)	15(2)	26(1)	18(1)	1(1)	0(1)	0(1)
C(11)	16(1)	30(1)	14(1)	1(1)	1(1)	4(1)
C(12)	19(2)	27(1)	16(1)	1(1)	2(1)	3(1)
C(13)	23(2)	29(2)	16(1)	3(1)	2(1)	2(1)
C(14)	17(2)	27(1)	20(1)	6(1)	0(1)	0(1)
C(15)	22(2)	37(2)	32(2)	5(1)	6(1)	-1(1)
C(16)	22(2)	37(2)	50(2)	14(2)	7(2)	-3(1)

C(17)	27(2)	24(2)	47(2)	9(1)	-1(2)	0(1)
C(18)	26(2)	27(2)	41(2)	0(1)	4(1)	2(1)
C(19)	20(2)	30(2)	29(1)	2(1)	6(1)	-1(1)
C(20)	25(2)	32(2)	139(5)	10(3)	8(3)	-8(2)
C(21)	18(2)	27(1)	21(1)	4(1)	3(1)	4(1)
C(22)	16(2)	29(1)	22(1)	4(1)	3(1)	4(1)
C(23)	20(2)	37(2)	24(1)	5(1)	-3(1)	5(1)
C(24)	33(2)	41(2)	29(2)	13(2)	-2(1)	11(2)
C(25)	31(2)	40(2)	34(2)	18(2)	4(2)	4(2)
C(26)	25(2)	34(2)	29(2)	9(1)	4(1)	0(1)
C(27)	16(2)	30(1)	20(1)	6(1)	-1(1)	-4(1)
C(28)	44(2)	28(2)	27(2)	-1(1)	-2(1)	0(2)
C(29)	91(4)	67(3)	67(3)	-13(3)	25(3)	-13(3)
Cl(1)	77(1)	113(1)	91(1)	9(1)	20(1)	22(1)
Cl(2)	65(1)	66(1)	236(3)	-49(1)	-36(1)	9(1)
N(1)	11(1)	27(1)	12(1)	2(1)	-1(1)	1(1)
N(2)	14(1)	28(1)	16(1)	4(1)	0(1)	4(1)
O(1)	13(1)	31(1)	16(1)	1(1)	-2(1)	0(1)
O(2)	35(2)	23(1)	81(2)	5(1)	4(1)	-5(1)
O(3)	18(1)	44(1)	22(1)	15(1)	4(1)	2(1)
O(4)	14(1)	61(2)	20(1)	16(1)	4(1)	8(1)

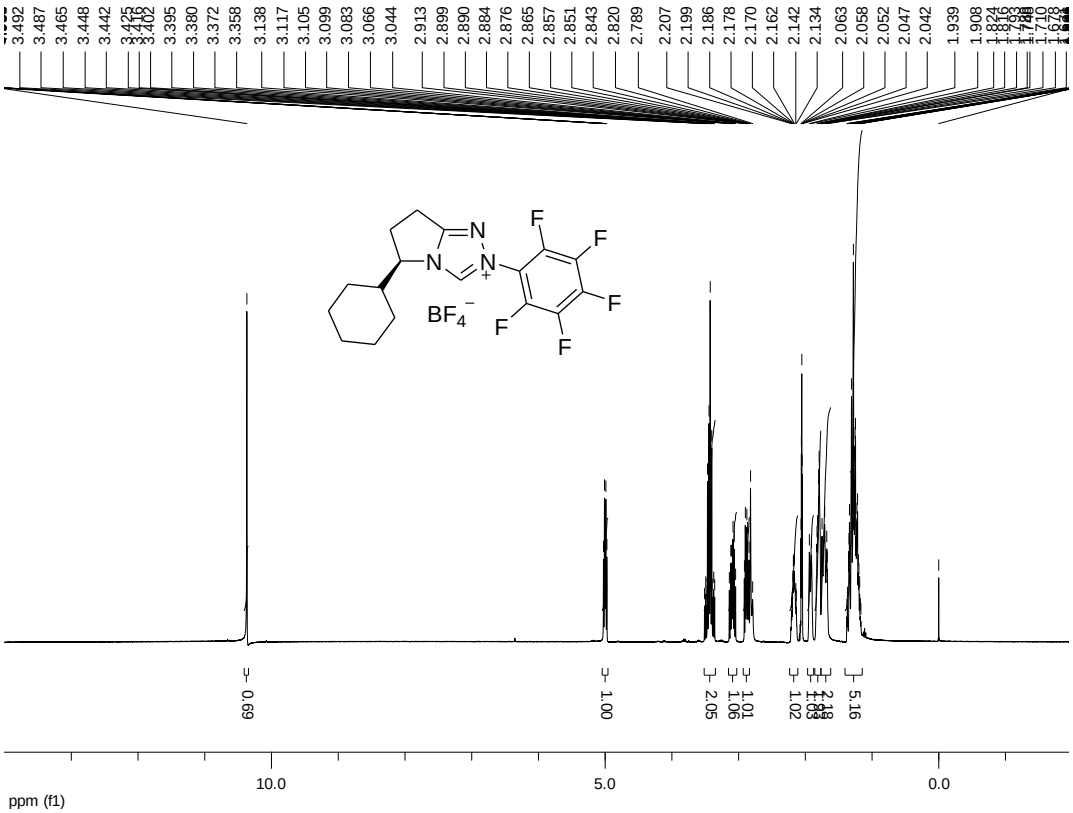
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for rovis125.

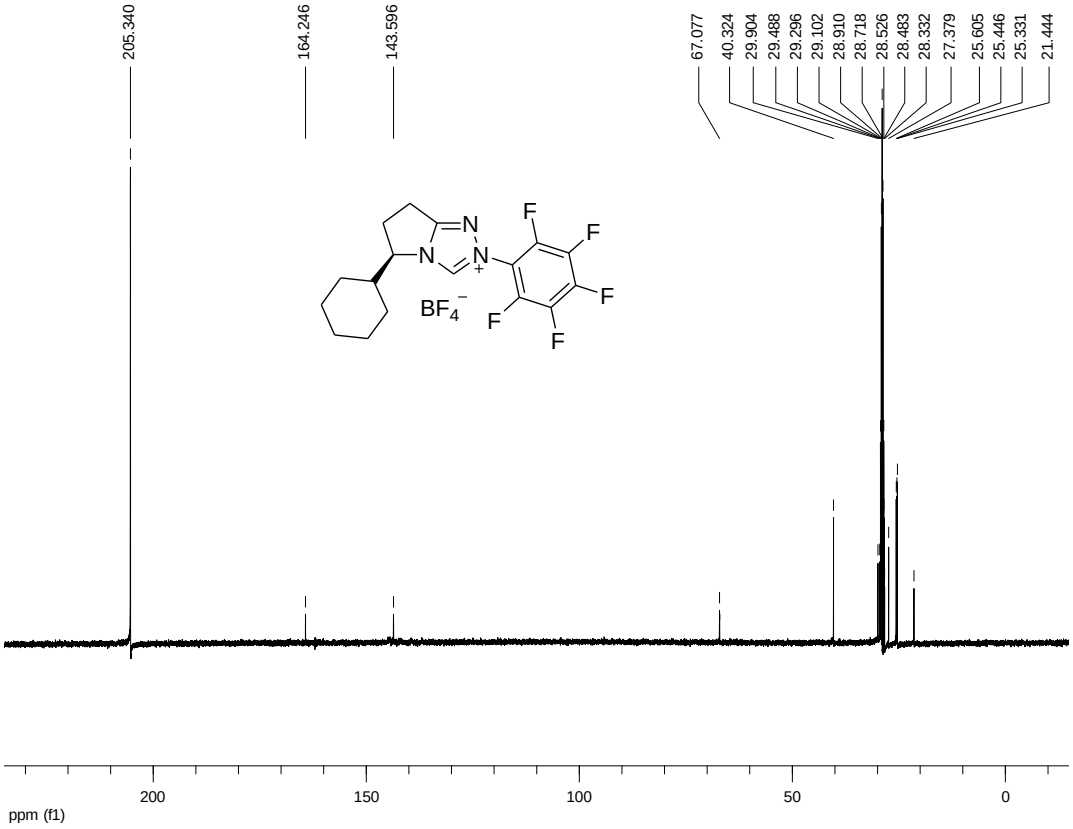
	x	y	z	U(eq)
H(2)	6669	2132	5981	21
H(3)	3758	2327	8233	20
H(4A)	3022	1436	6603	23
H(4B)	1238	1751	7329	23
H(6)	419	2882	3340	28
H(7)	487	3301	941	32
H(8)	3618	3260	-323	33
H(9)	6716	2812	784	29
H(10)	6667	2383	3144	24
H(12)	5231	3041	7045	25

H(13)	9315	2779	6293	27
H(15)	11777	3465	5907	36
H(16)	13185	4224	6651	43
H(18)	8240	4402	9292	38
H(19)	6855	3652	8537	31
H(20A)	14812	4840	8671	99
H(20B)	13738	5354	8502	99
H(20C)	13483	5010	7005	99
H(22)	5345	1394	2778	26
H(23)	7817	1170	5091	33
H(24)	6755	577	6770	42
H(25)	3273	220	6177	42
H(26)	803	440	3888	35
H(27)	-369	1013	1809	27
H(28A)	287	837	-770	50
H(28B)	1340	426	389	50
H(28C)	2898	821	-181	50
H(29A)	5882	4160	4624	88
H(29B)	5222	3707	3539	88
H(2A)	1344	1767	1972	30
H(2B)	145	1658	367	30
H(2C)	2591	1626	698	30

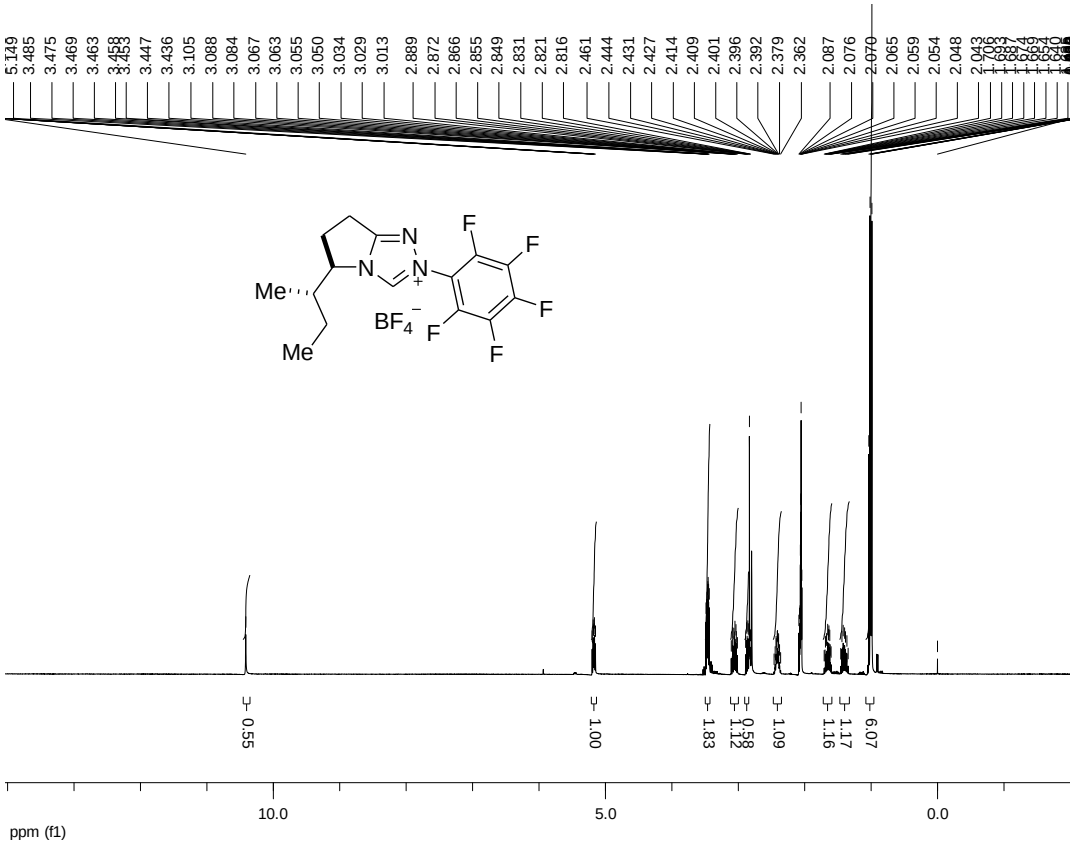
5. NMR spectra for new compounds

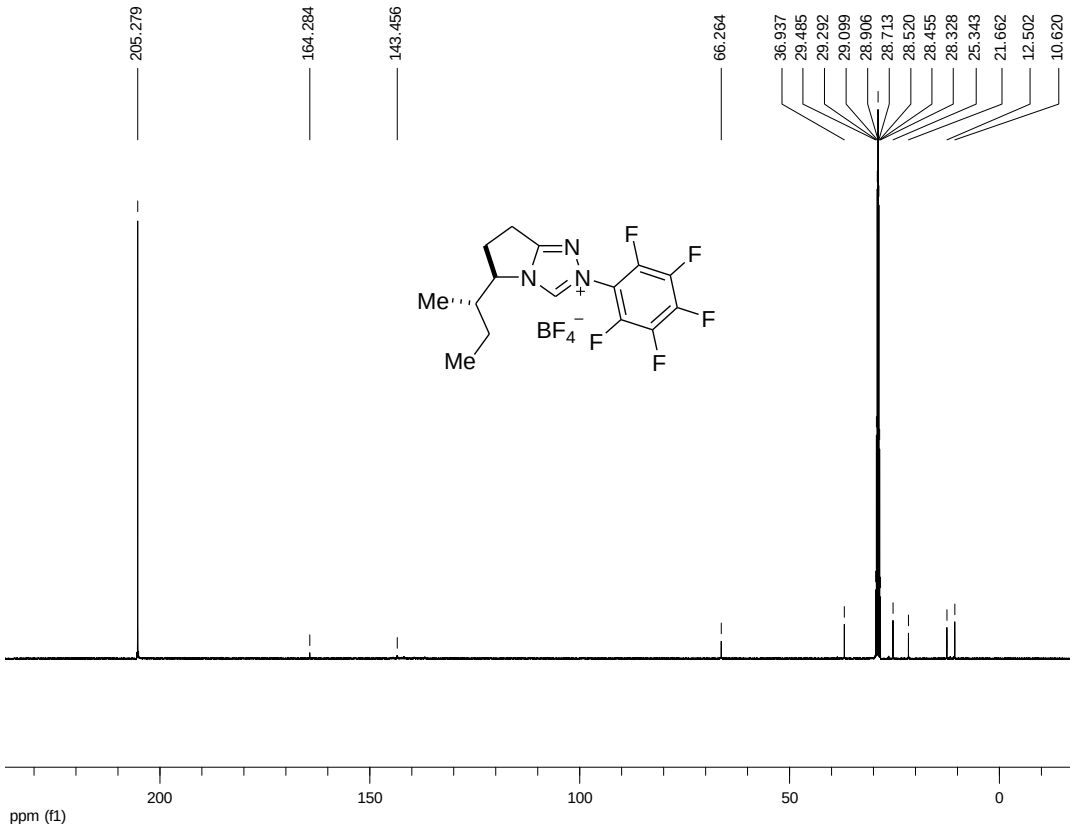
NMR Spectra of Triazolium Salt C4



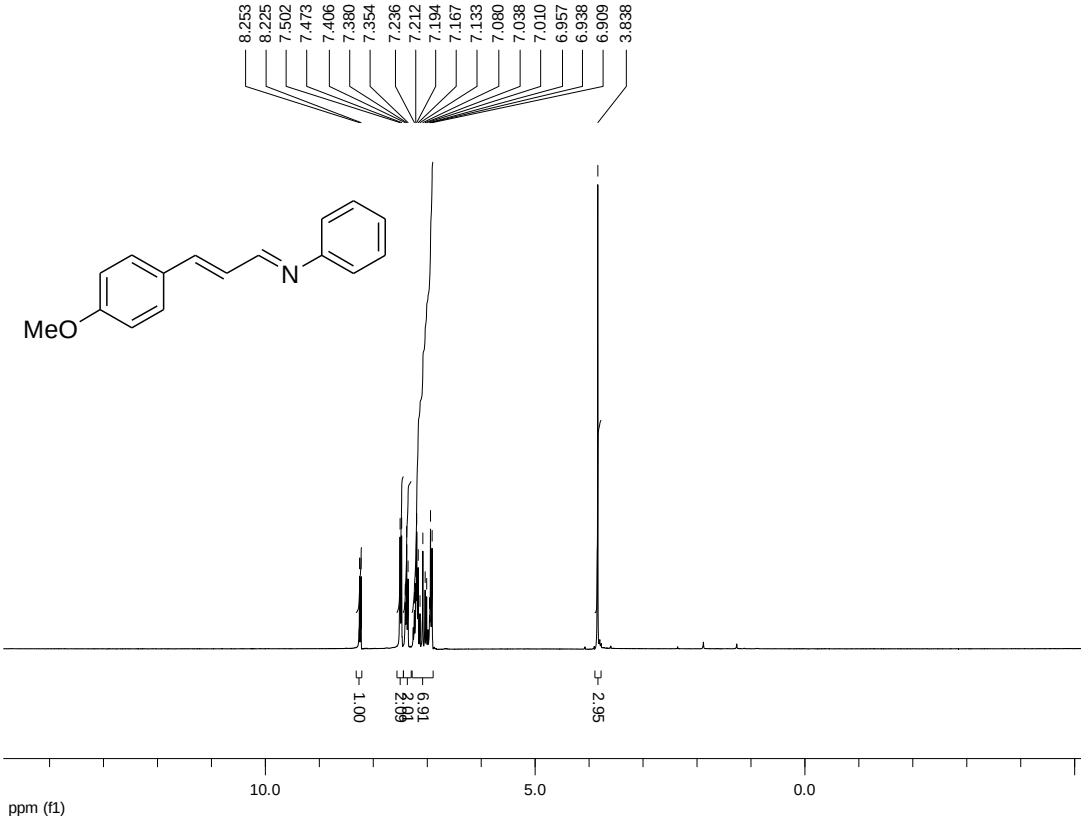


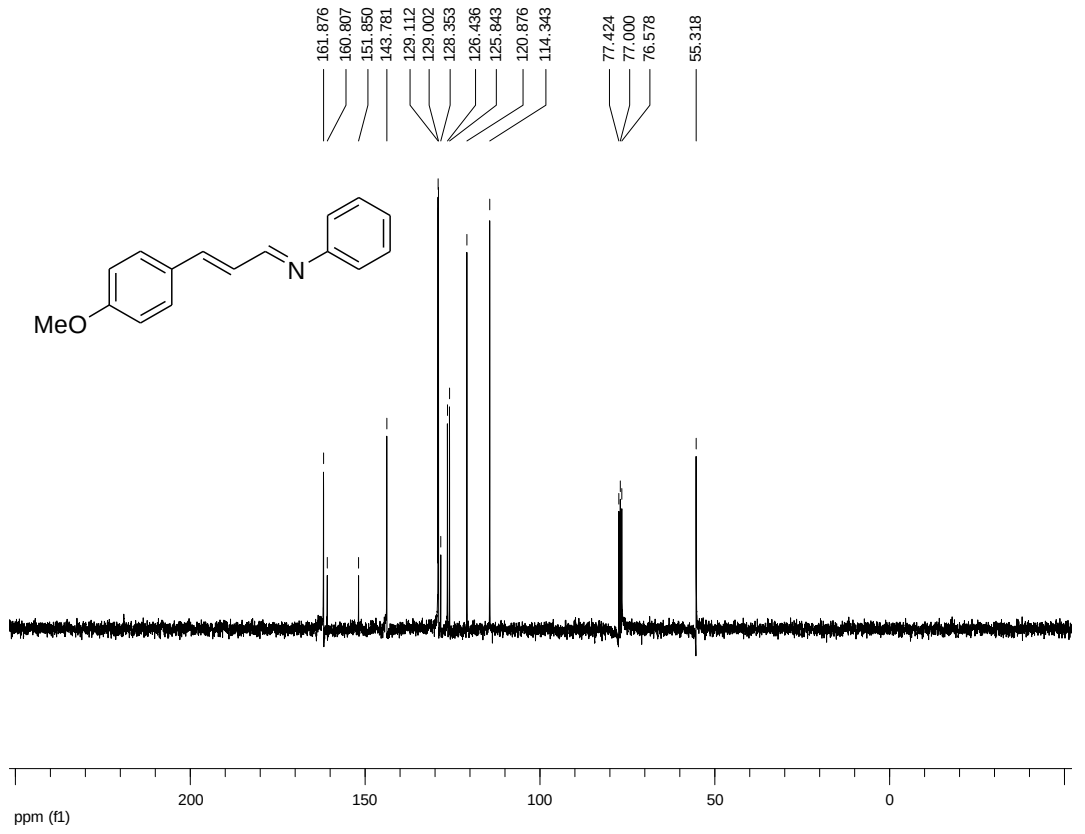
NMR Spectra of Triazolium Salt C3



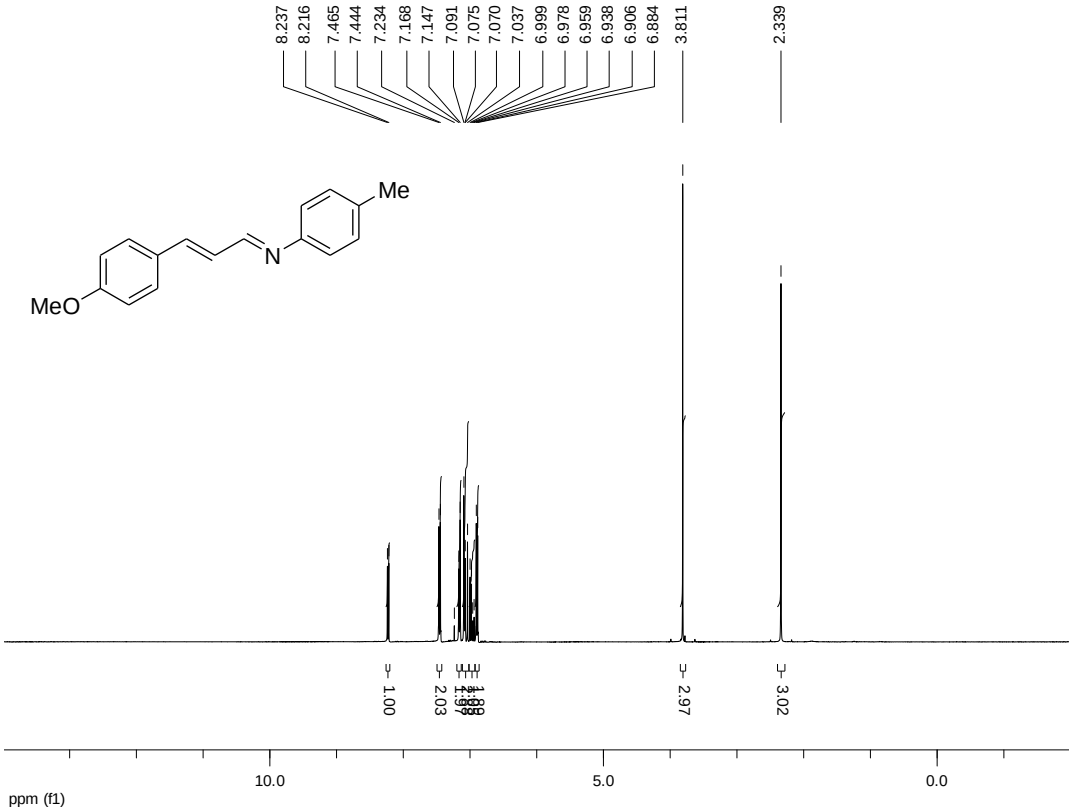


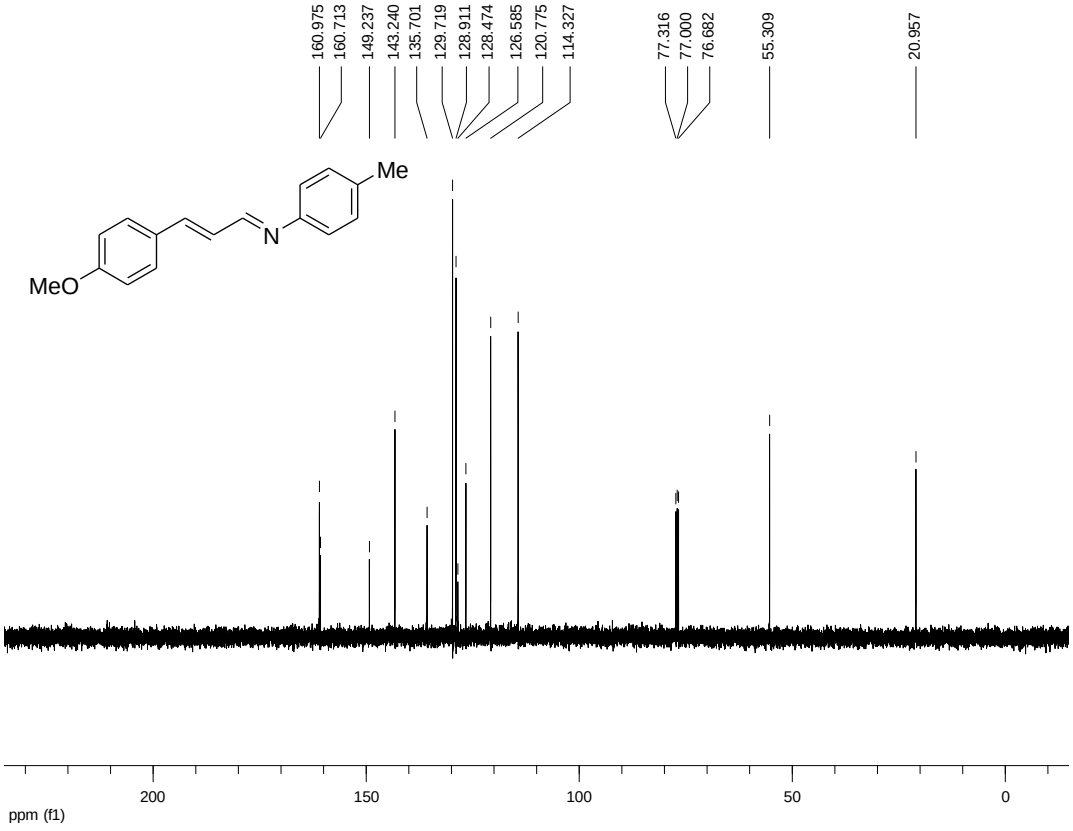
NMR Spectra of *N*-(4-Methoxycinnamylidene)aniline (1a)



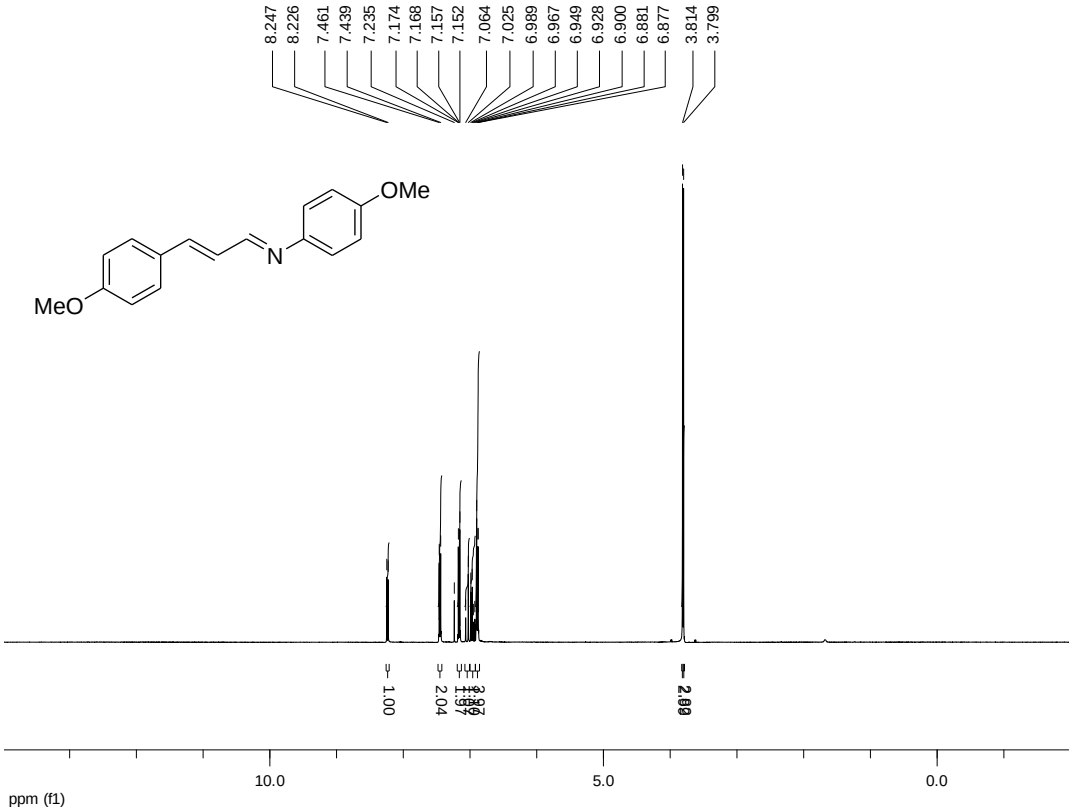


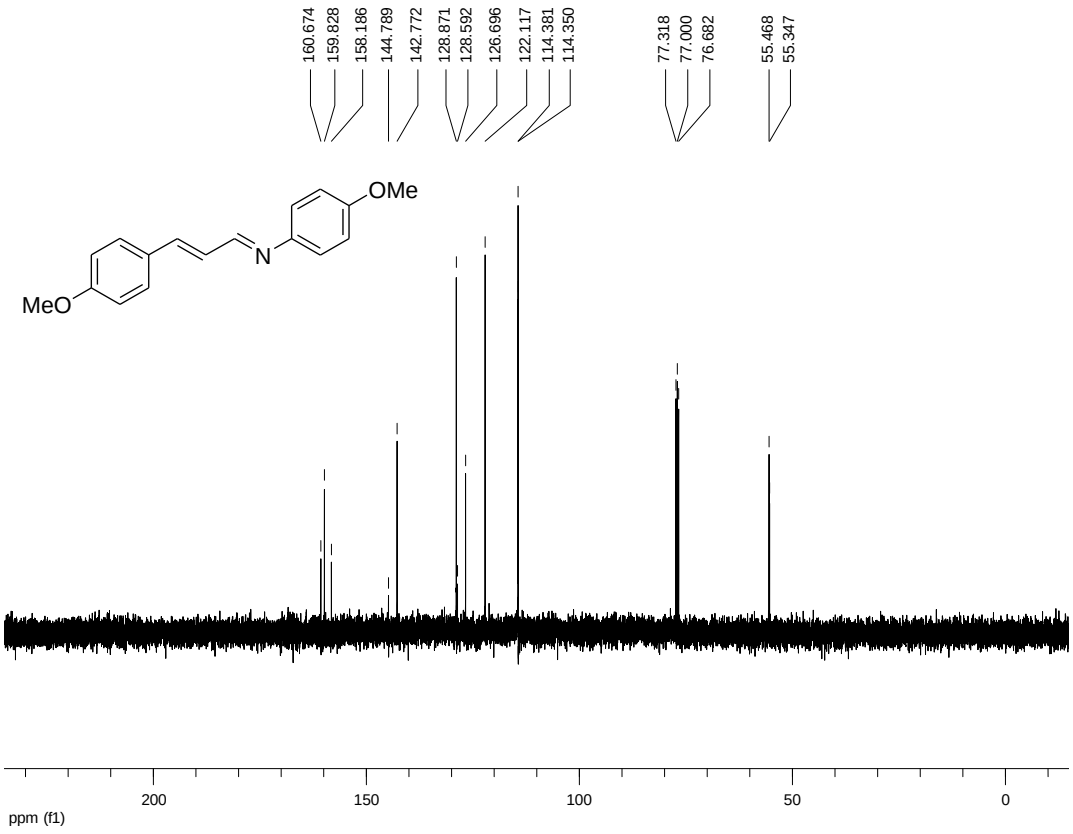
NMR Spectra of *N*-(4-Methoxycinnamylidene)-4-methylaniline



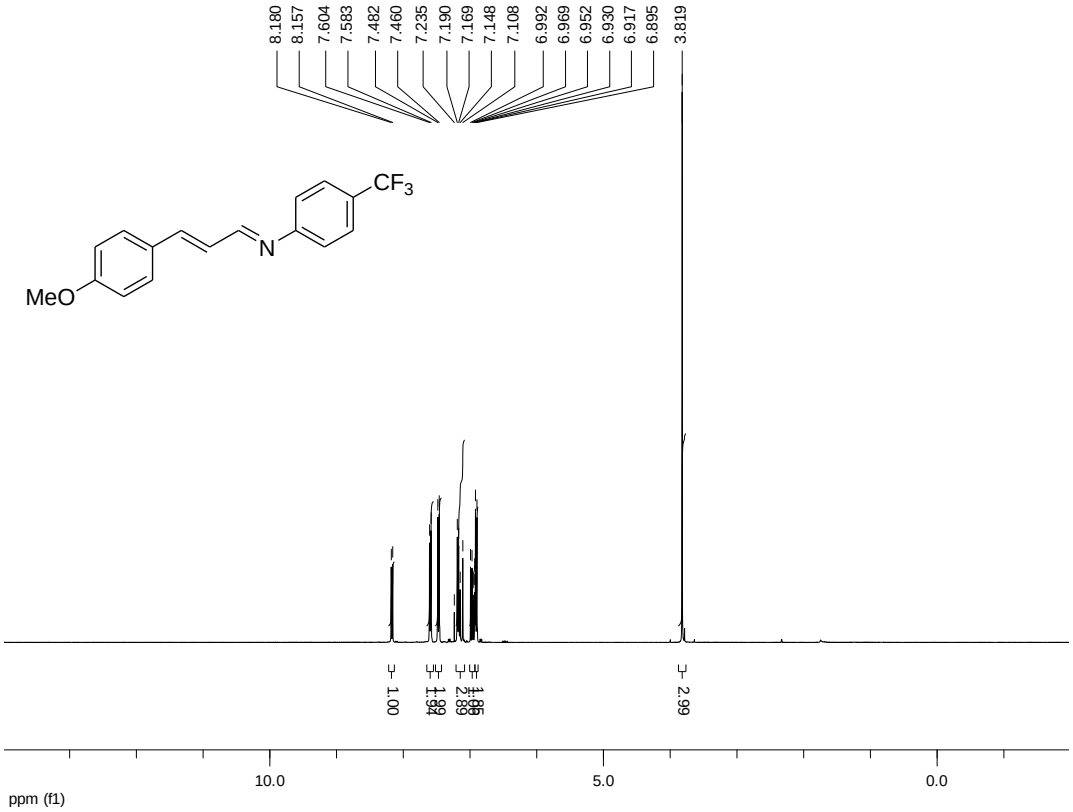


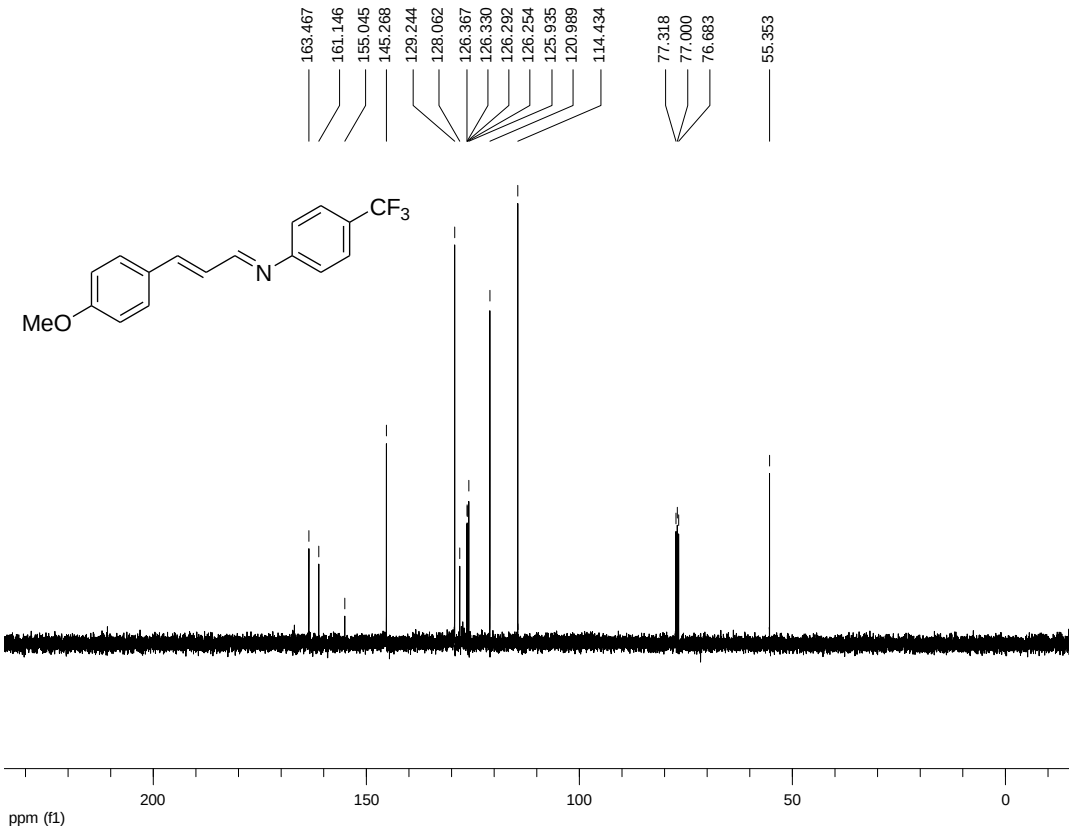
NMR Spectra of *N*-(4-Methoxycinnamylidene)-4-methoxylaniline



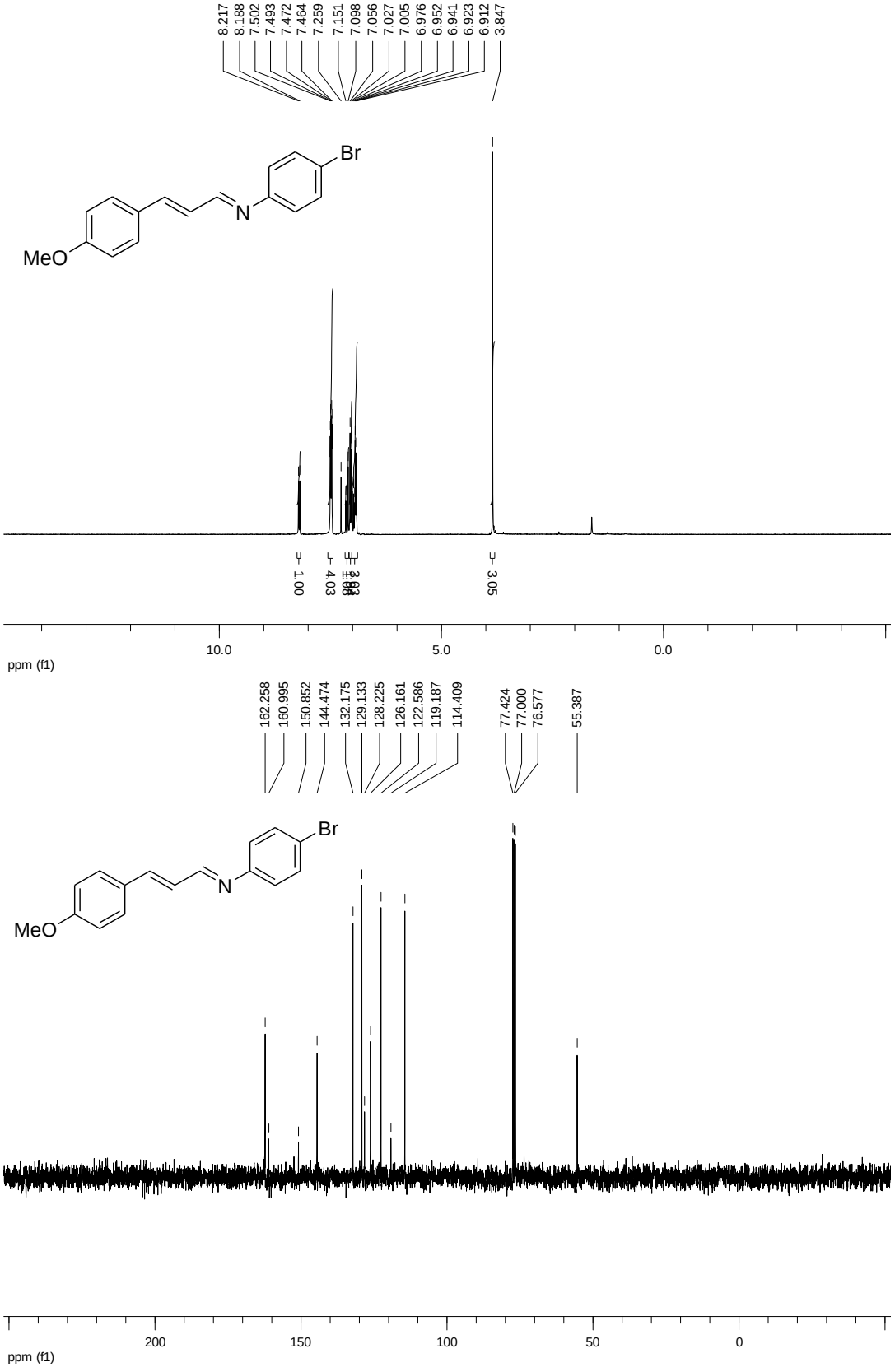


NMR Spectra of *N*-(4-Methoxycinnamylidene)-4-trifluoromethylaniline

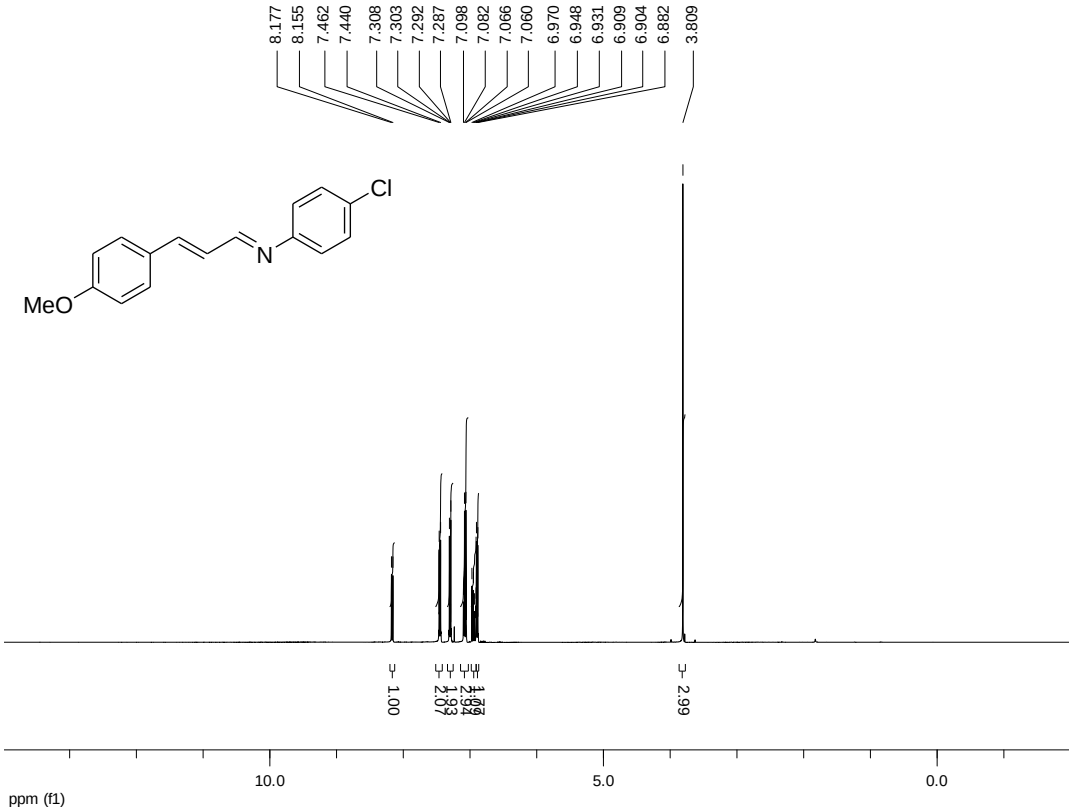


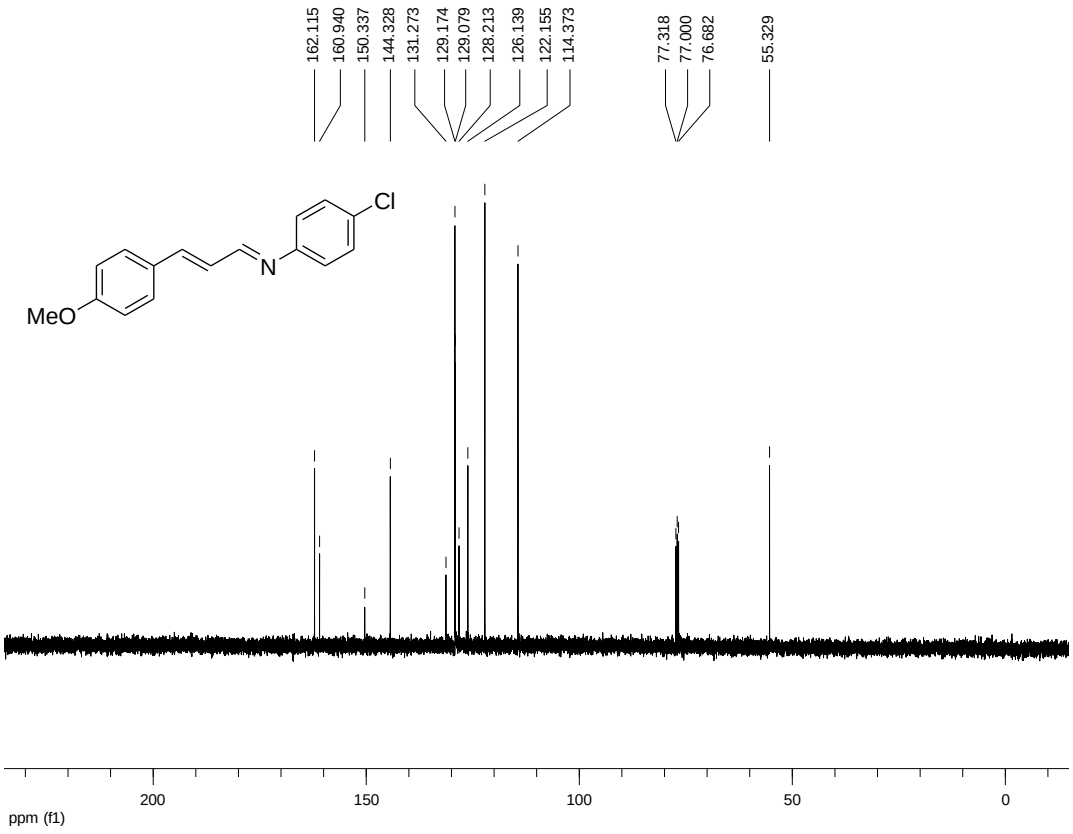


NMR Spectra of *N*-(4-Methoxycinnamylidene)-4-bromoaniline

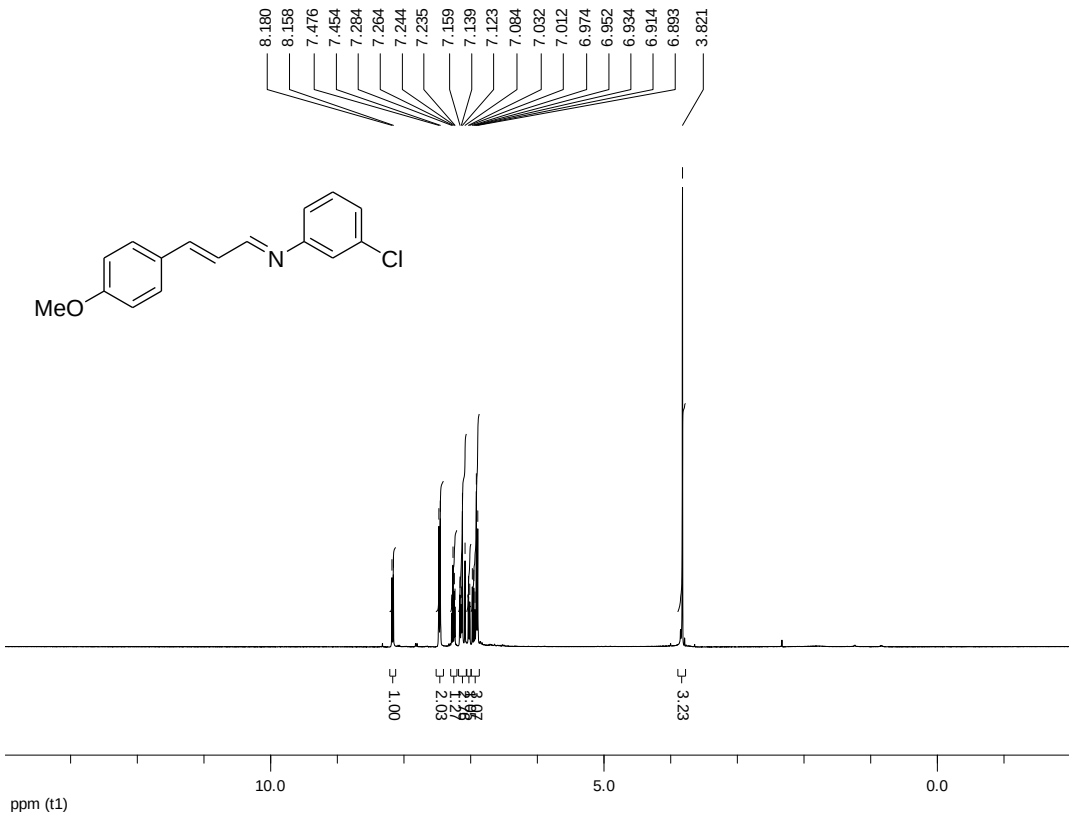


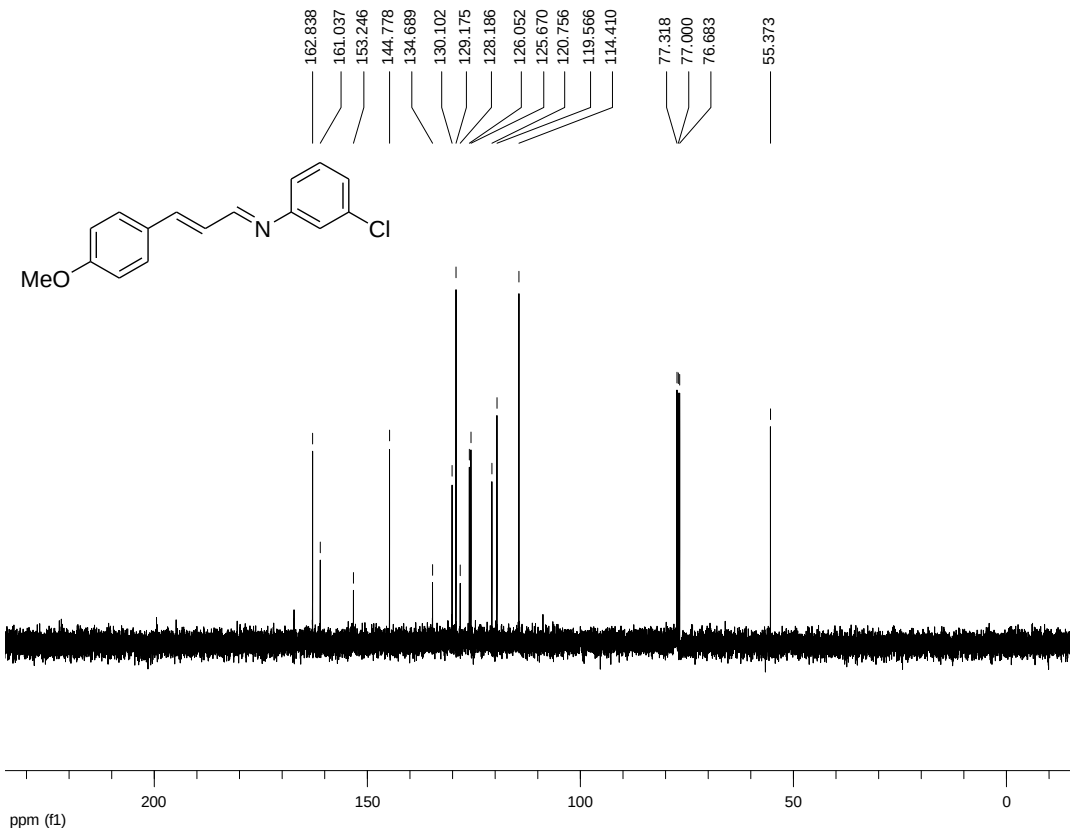
NMR Spectra of *N*-(4-Methoxycinnamylidene)-4-chloroaniline



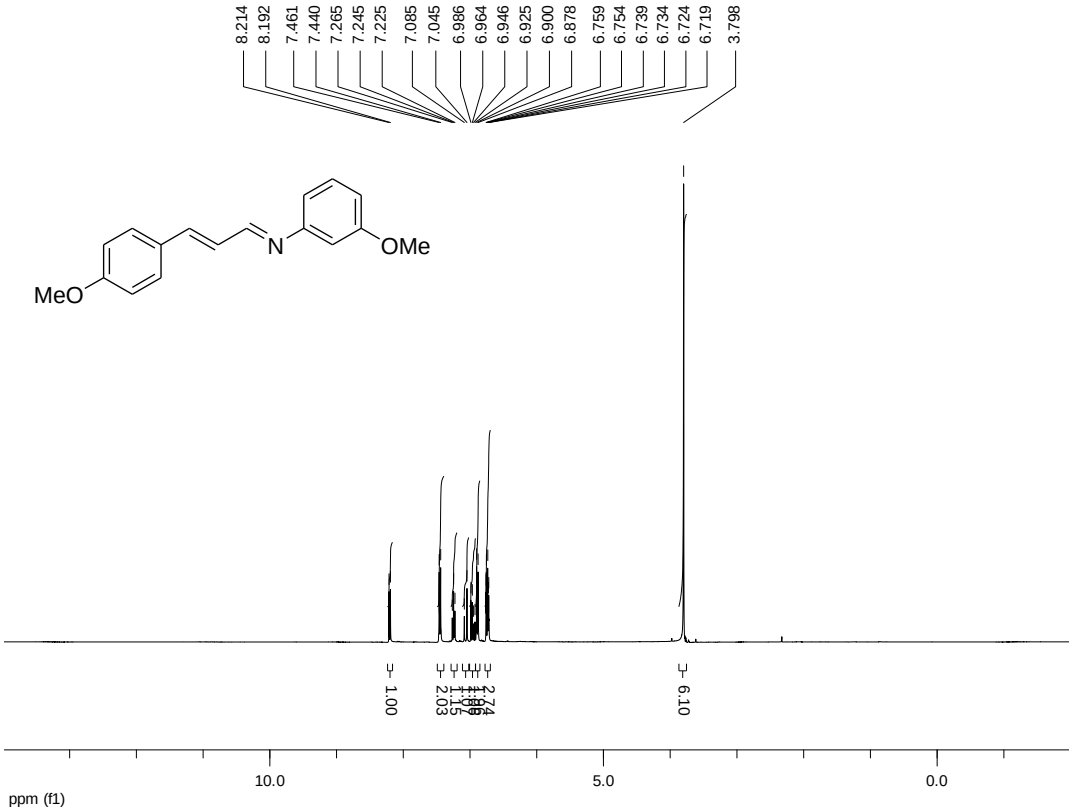


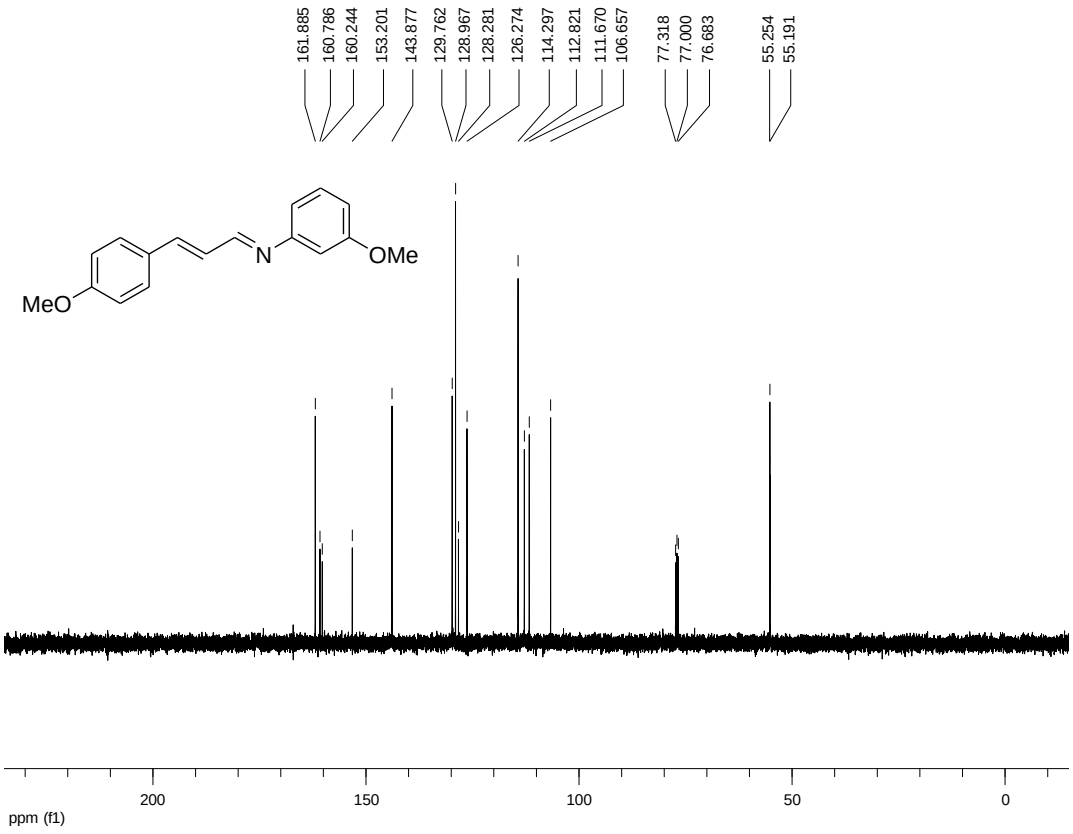
NMR Spectra of *N*-(4-Methoxycinnamylidene)-3-chloroaniline



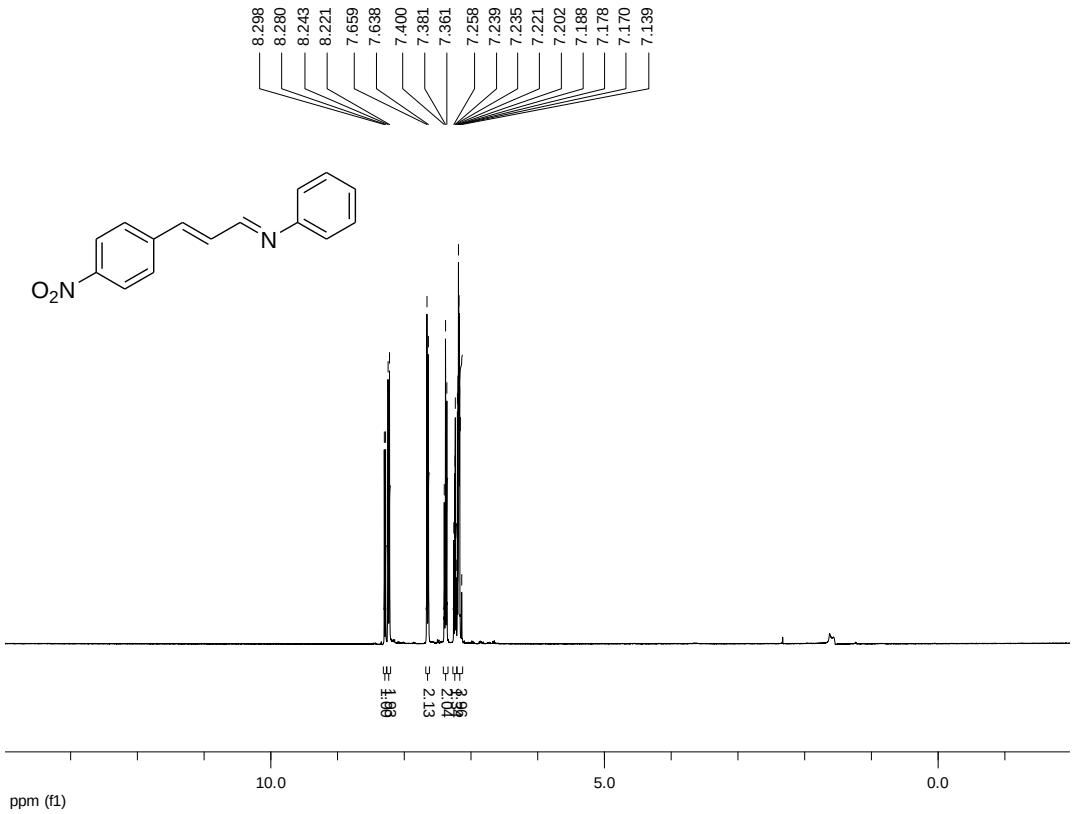


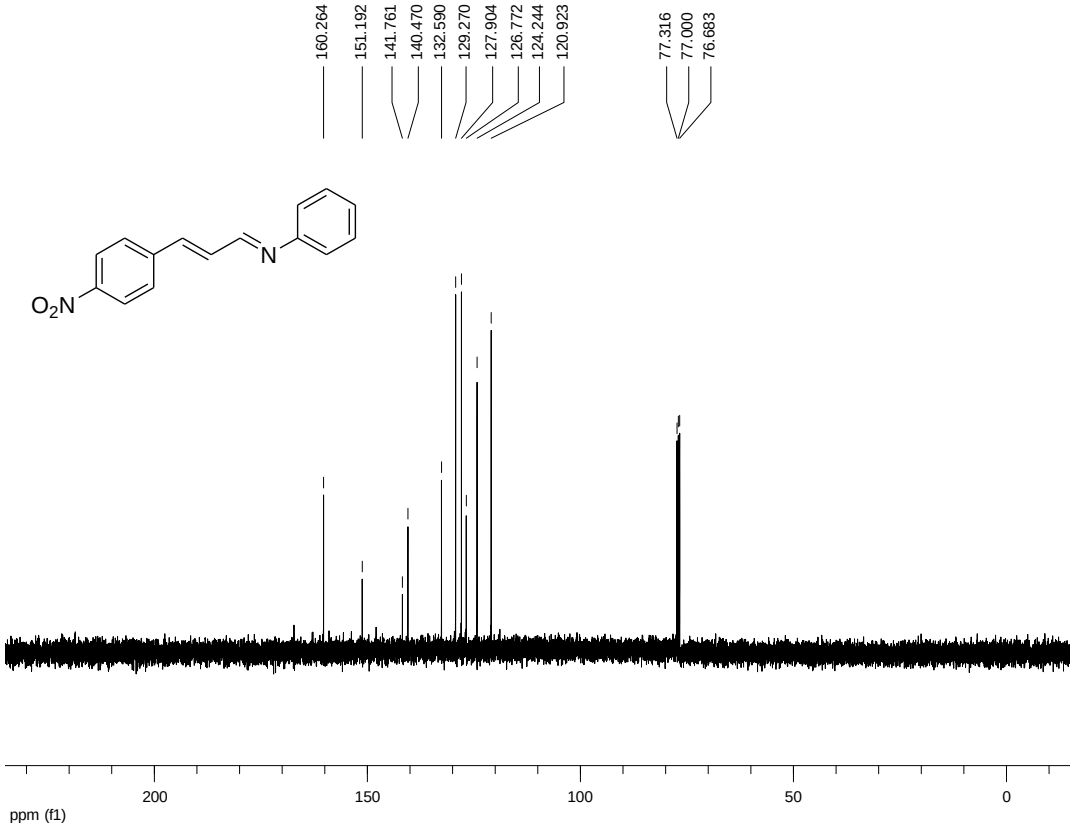
NMR Spectra of *N*-(4-Methoxycinnamylidene)-3-methoxylaniline



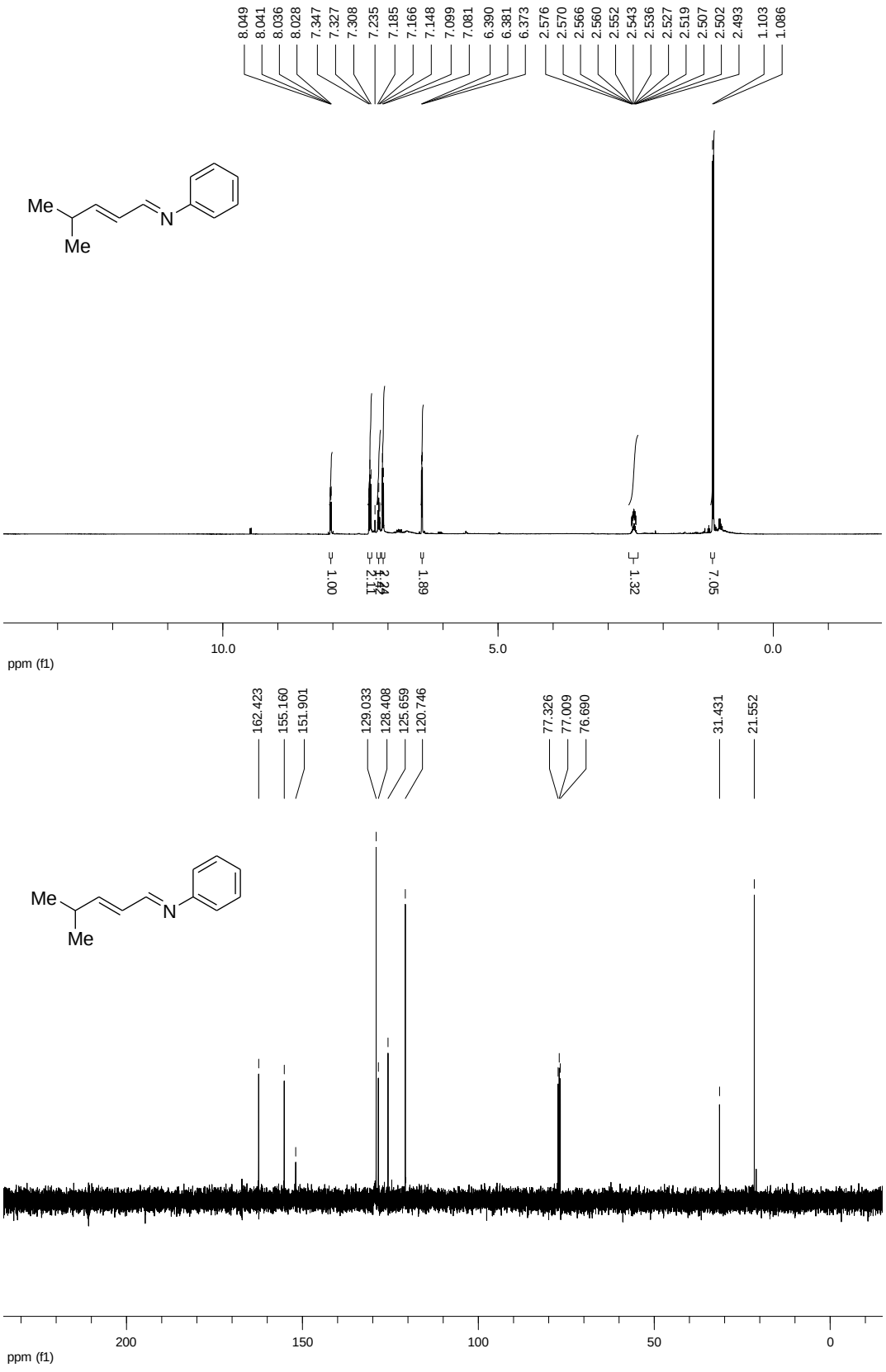


NMR Spectra of *N*-(4-Nitrocinnamylidene)aniline

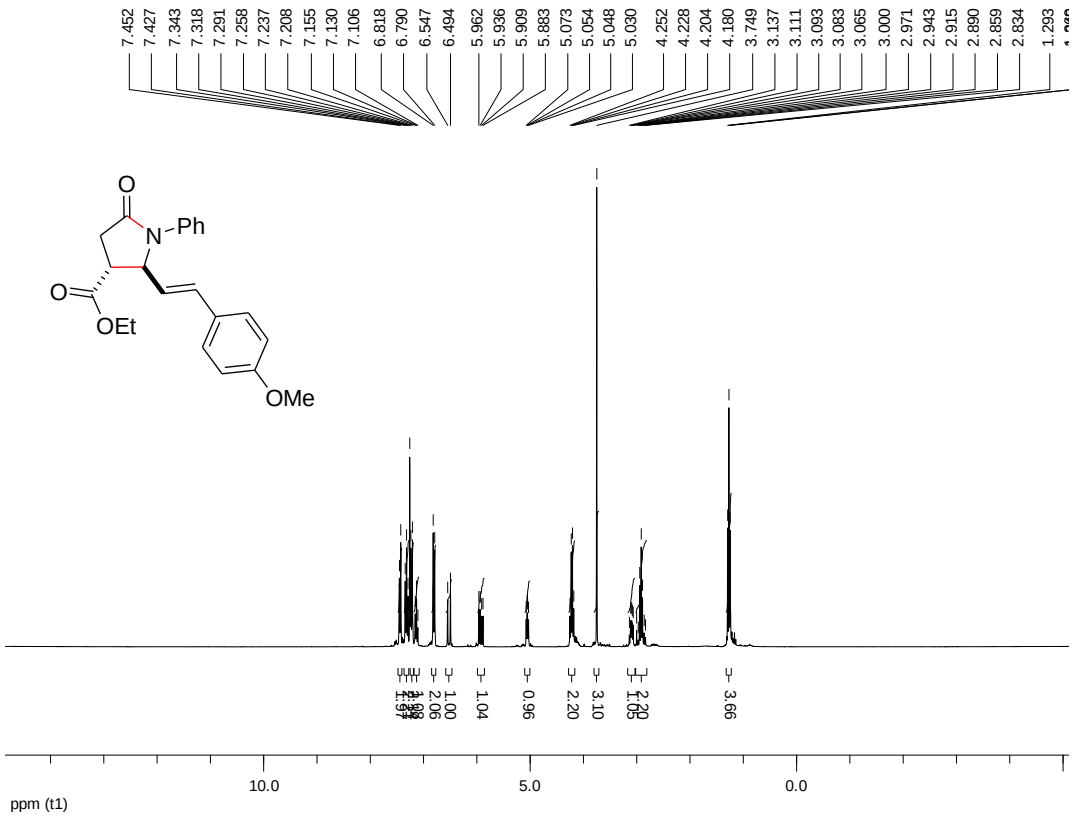


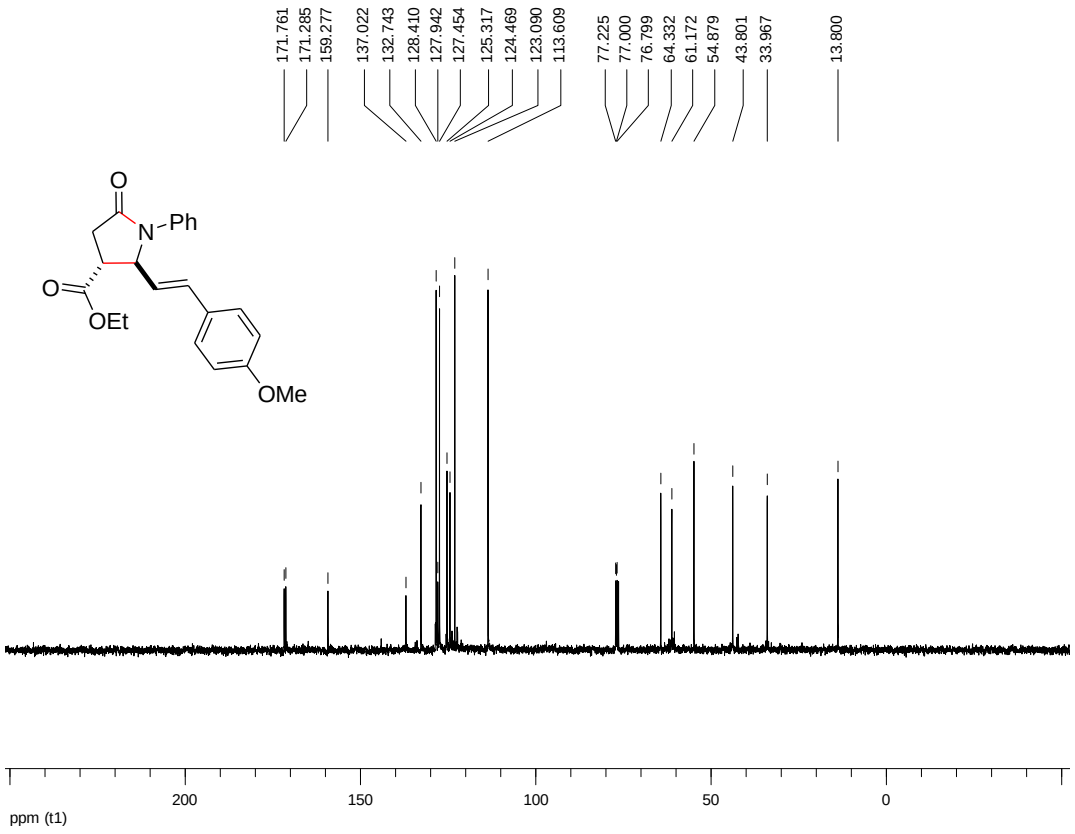


NMR Spectra of *N*-(4-Methylpent-2-enylidene)aniline

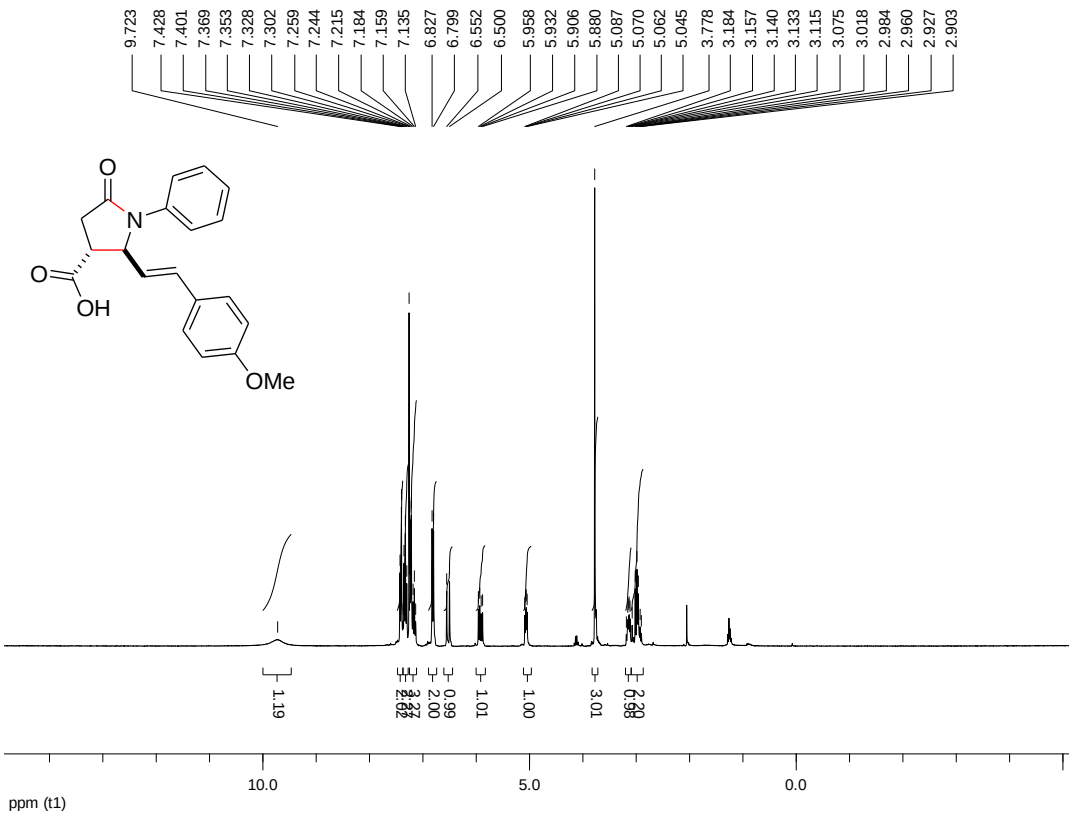


NMR Spectra of Product 3a

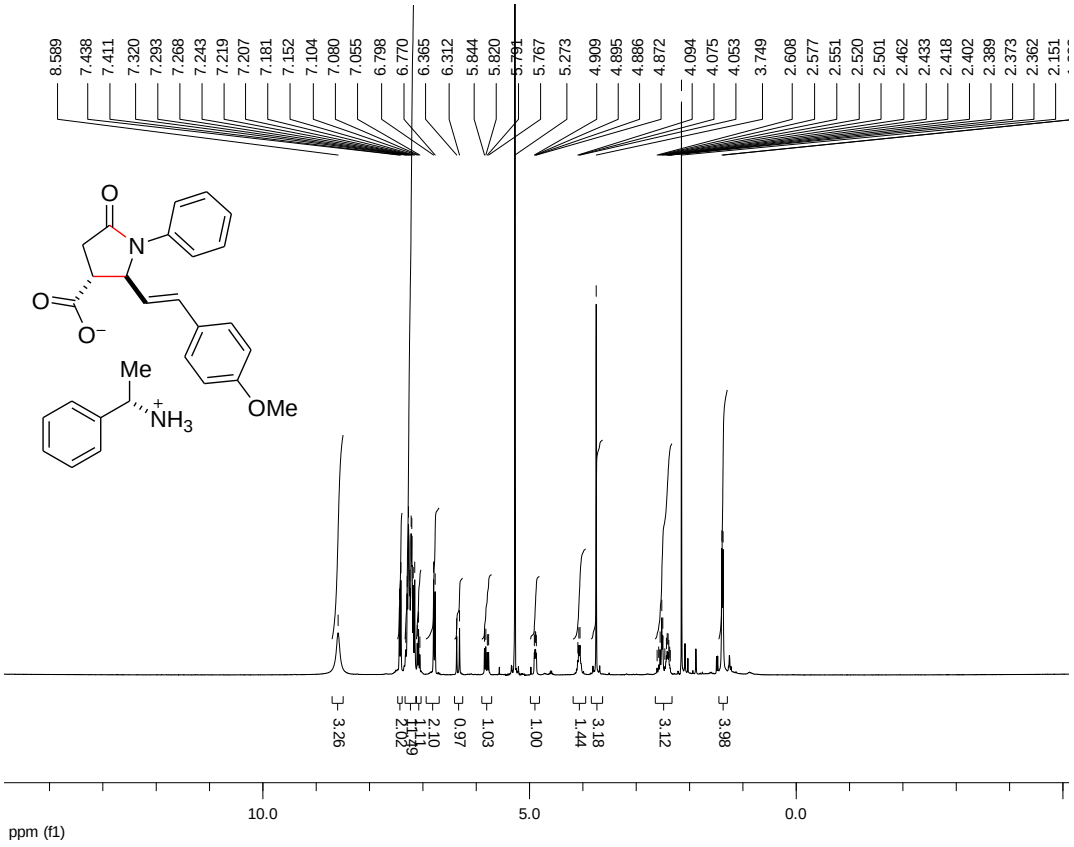




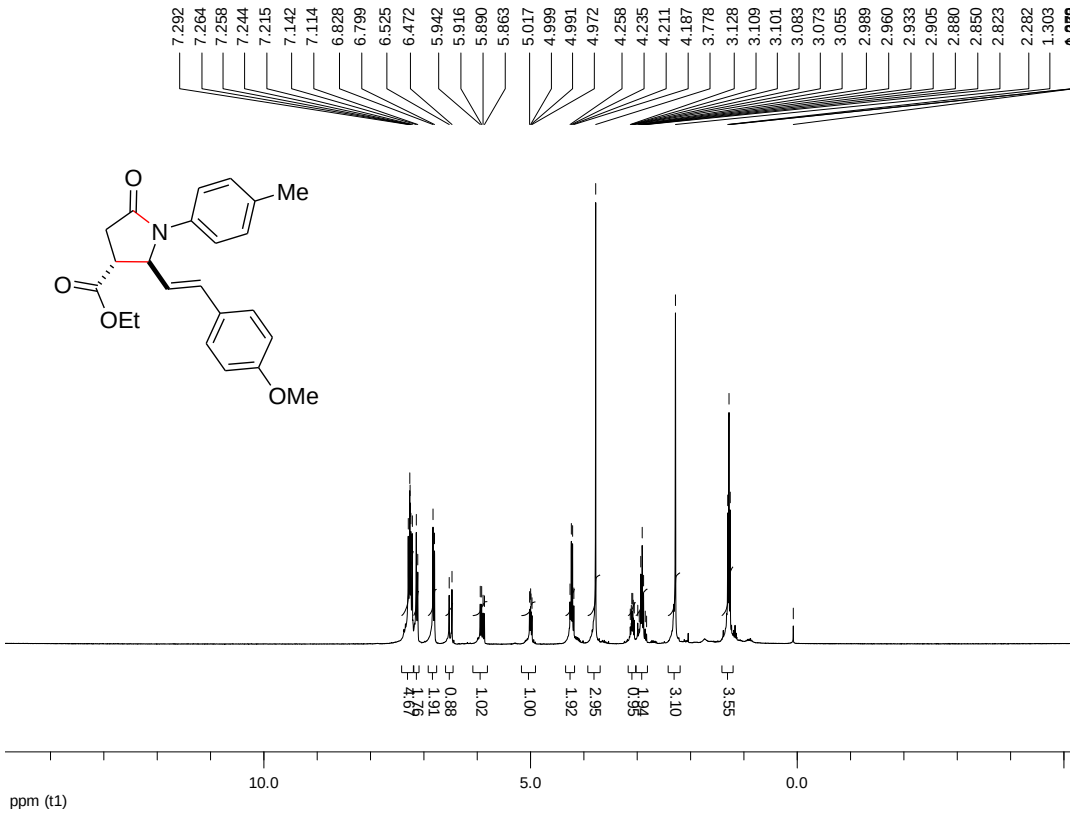
^{1}H NMR Spectrum of Acid I from Product 3a

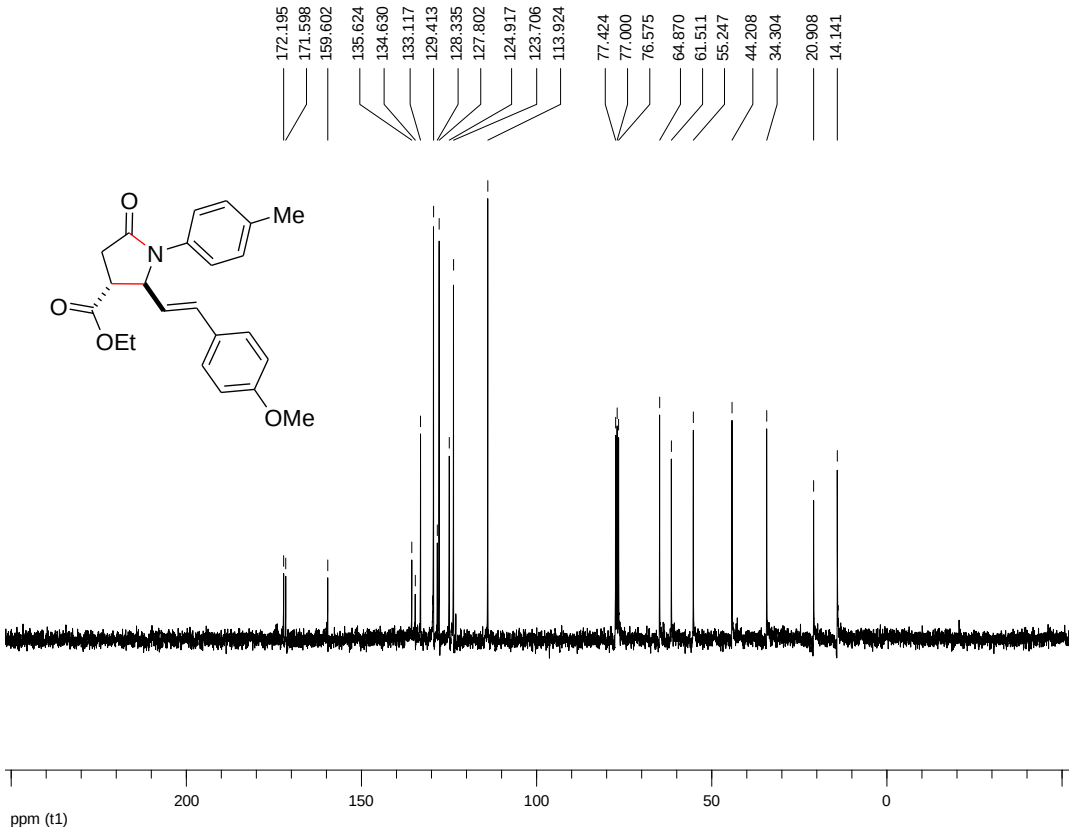


^{1}H NMR Spectrum of Crude Counterion II

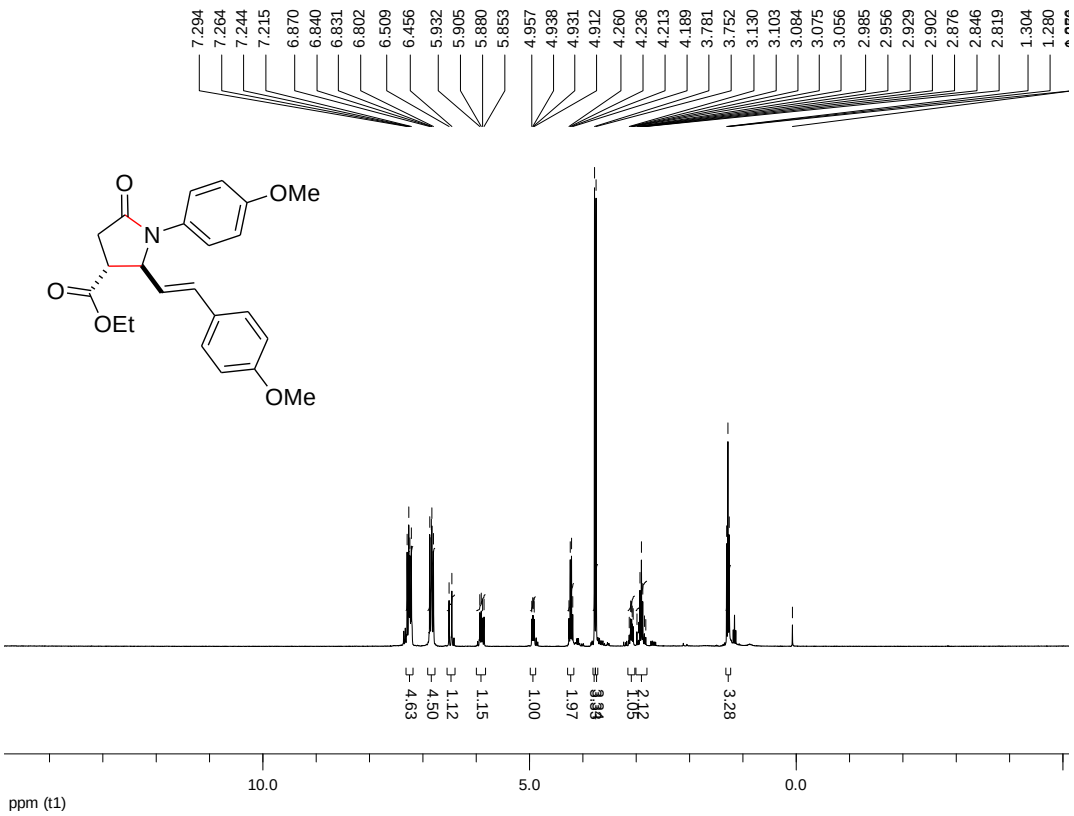


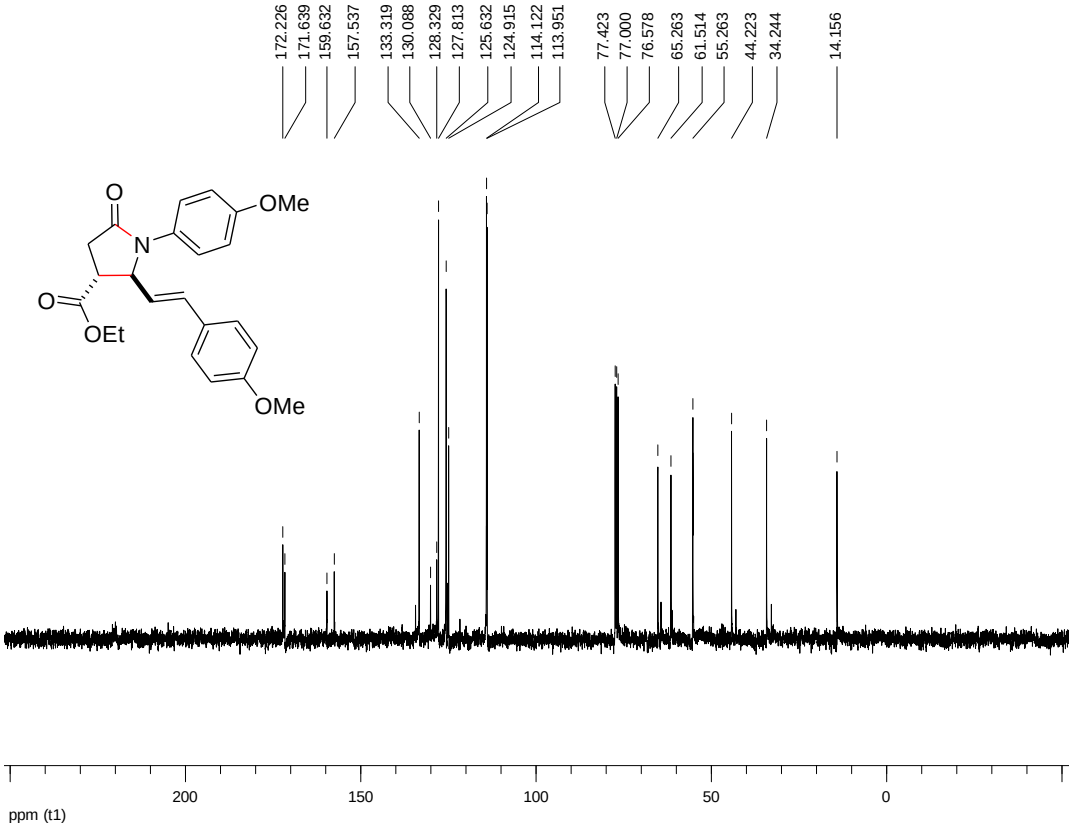
NMR Spectra of Product 3b



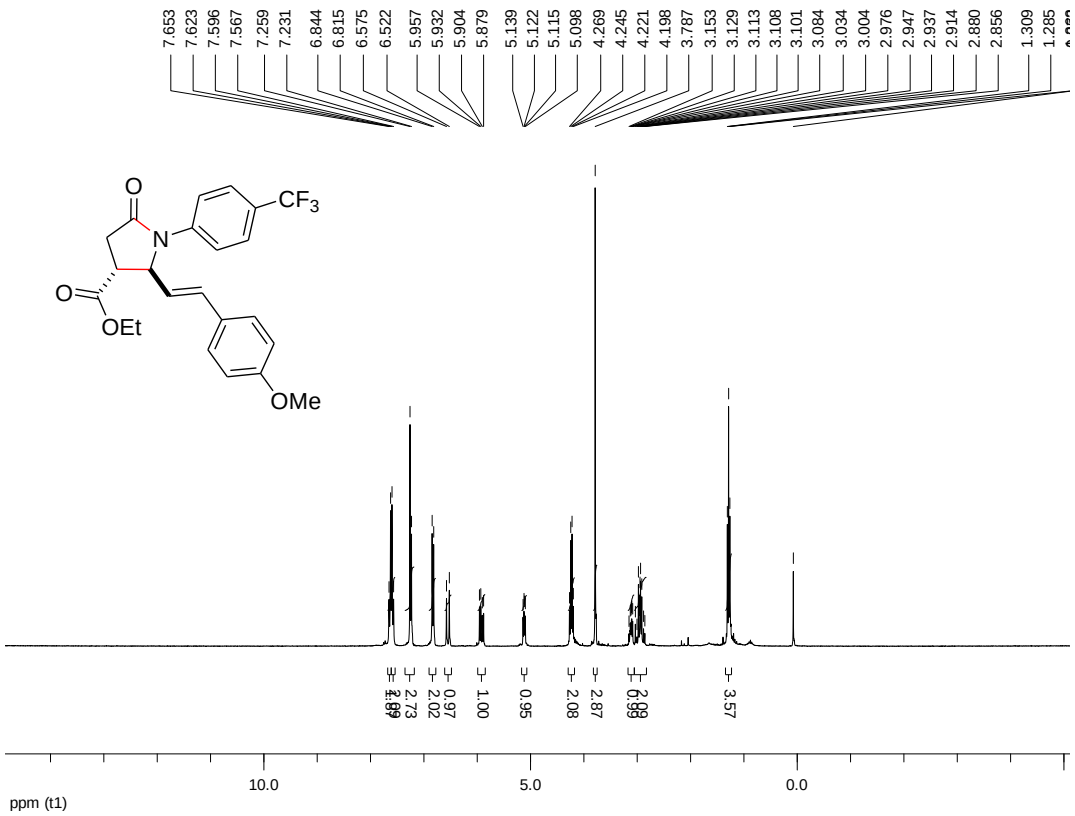


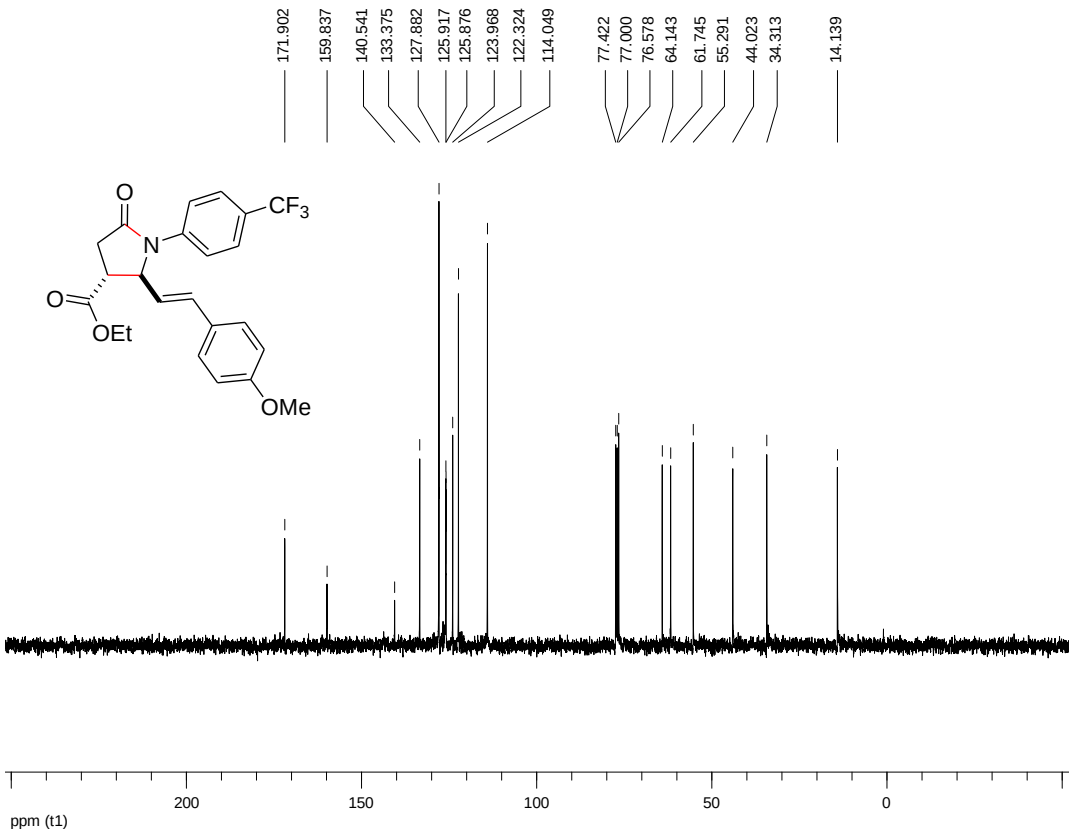
NMR Spectra of Product 3c



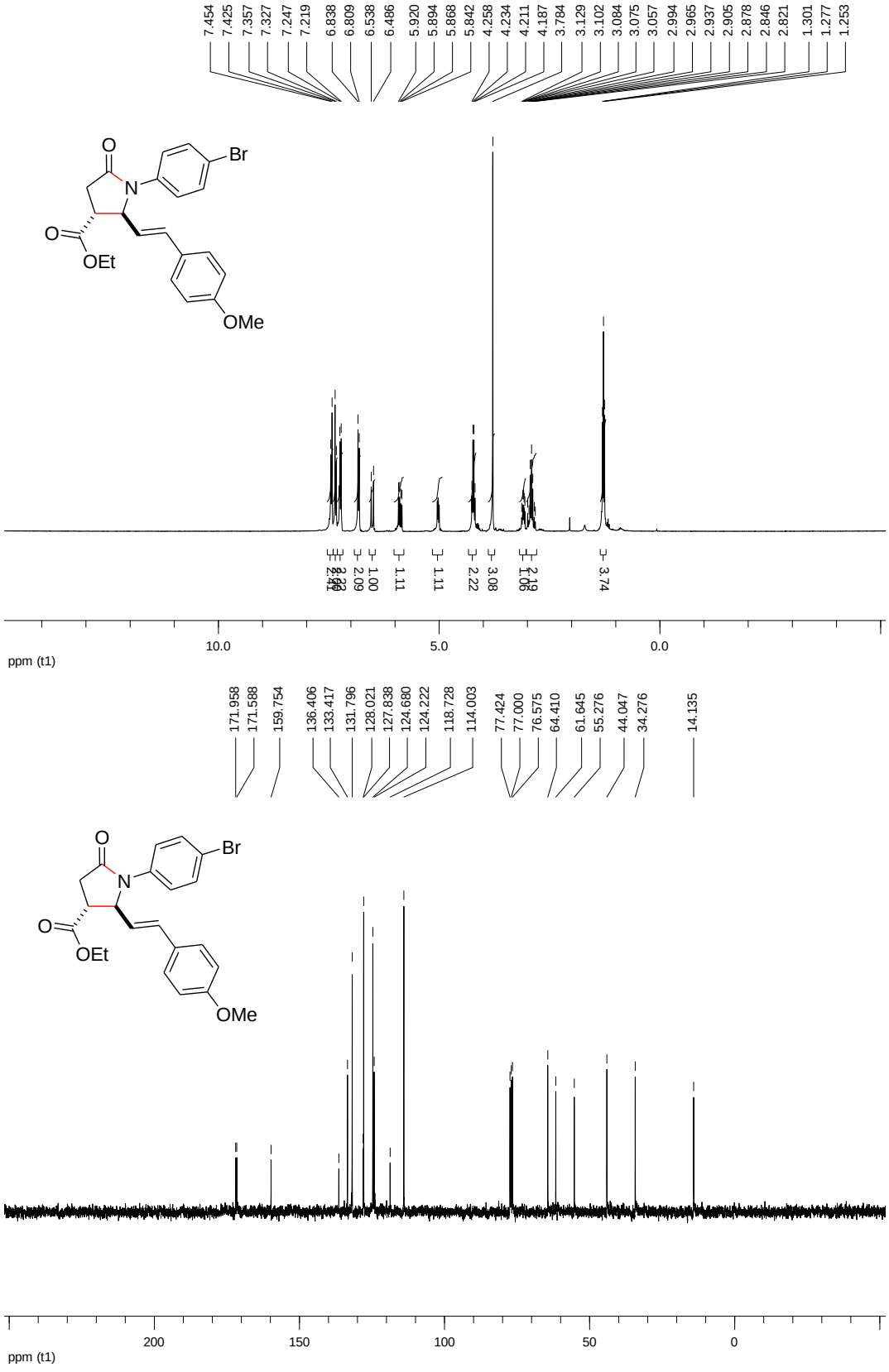


NMR Spectra of Product 3d

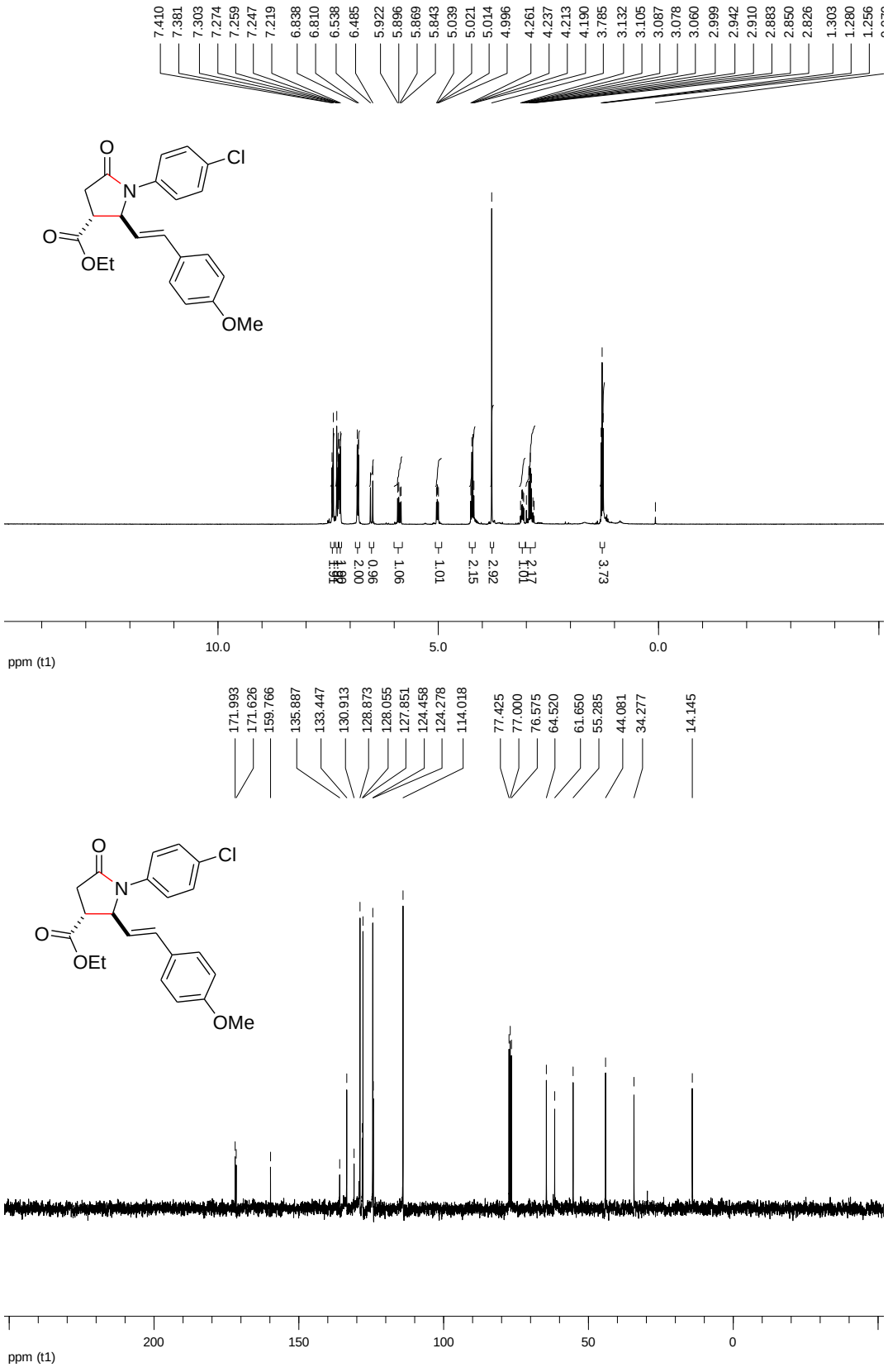




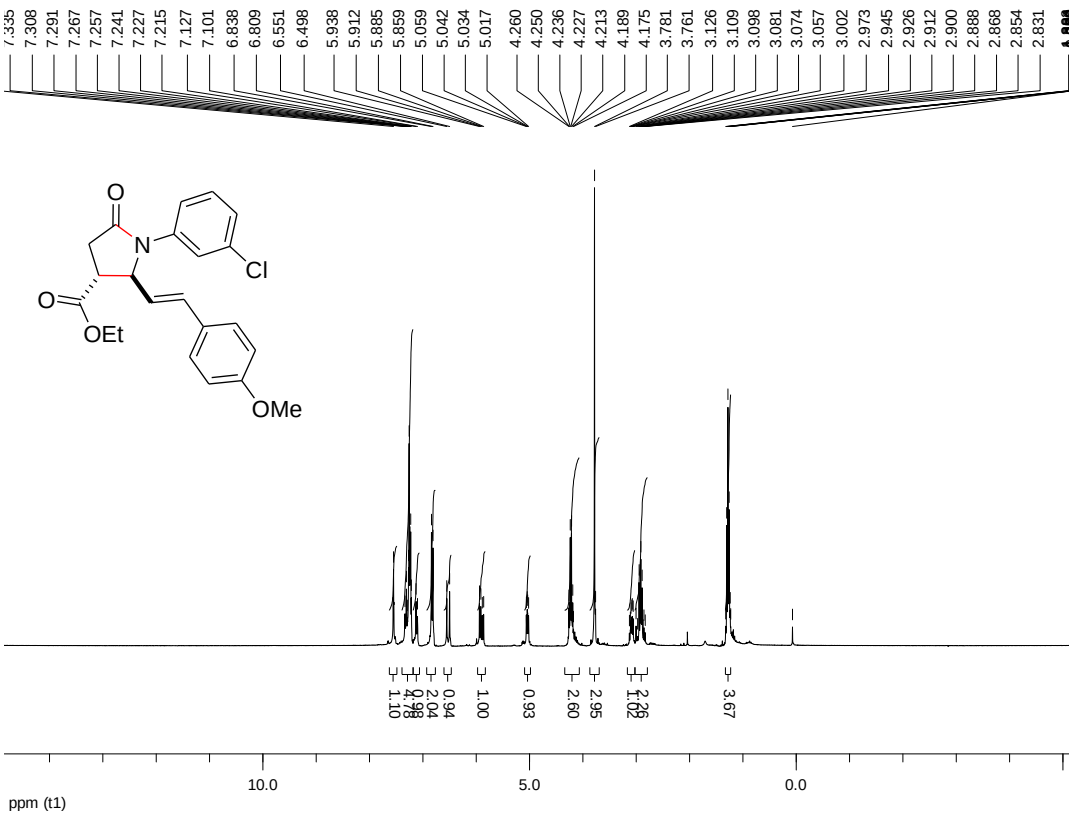
NMR Spectra of Product 3e

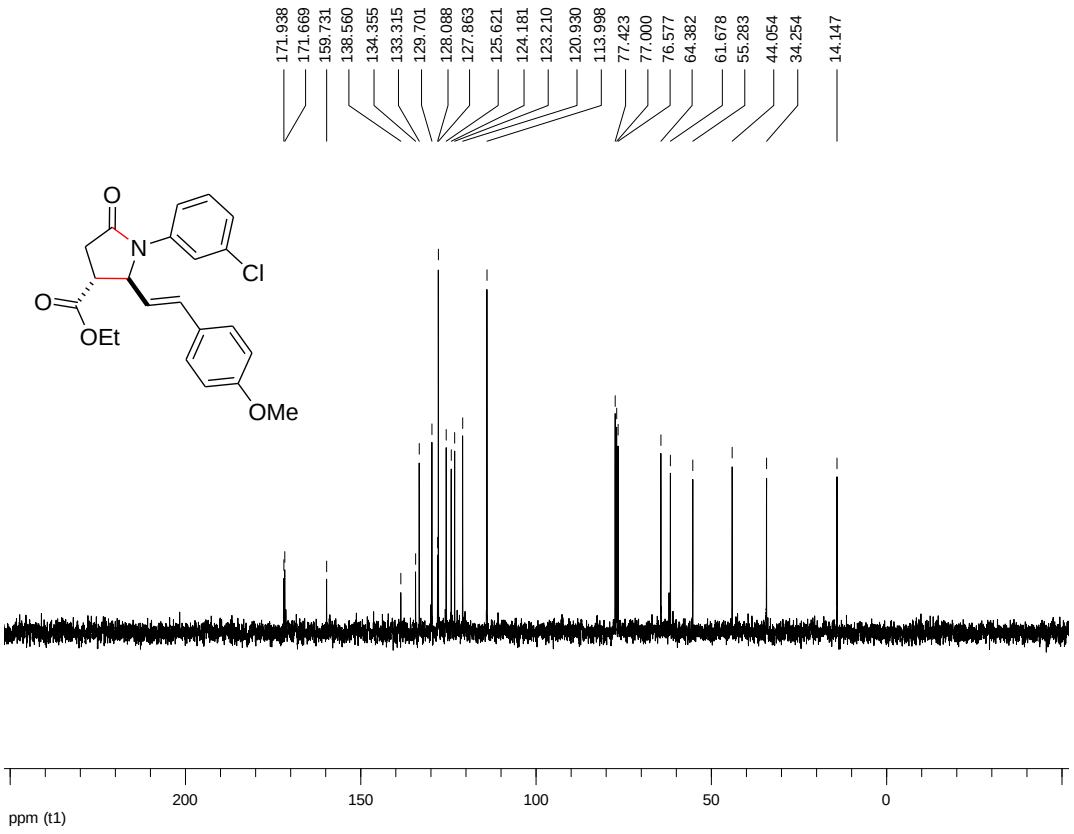


NMR Spectra of Product 3f

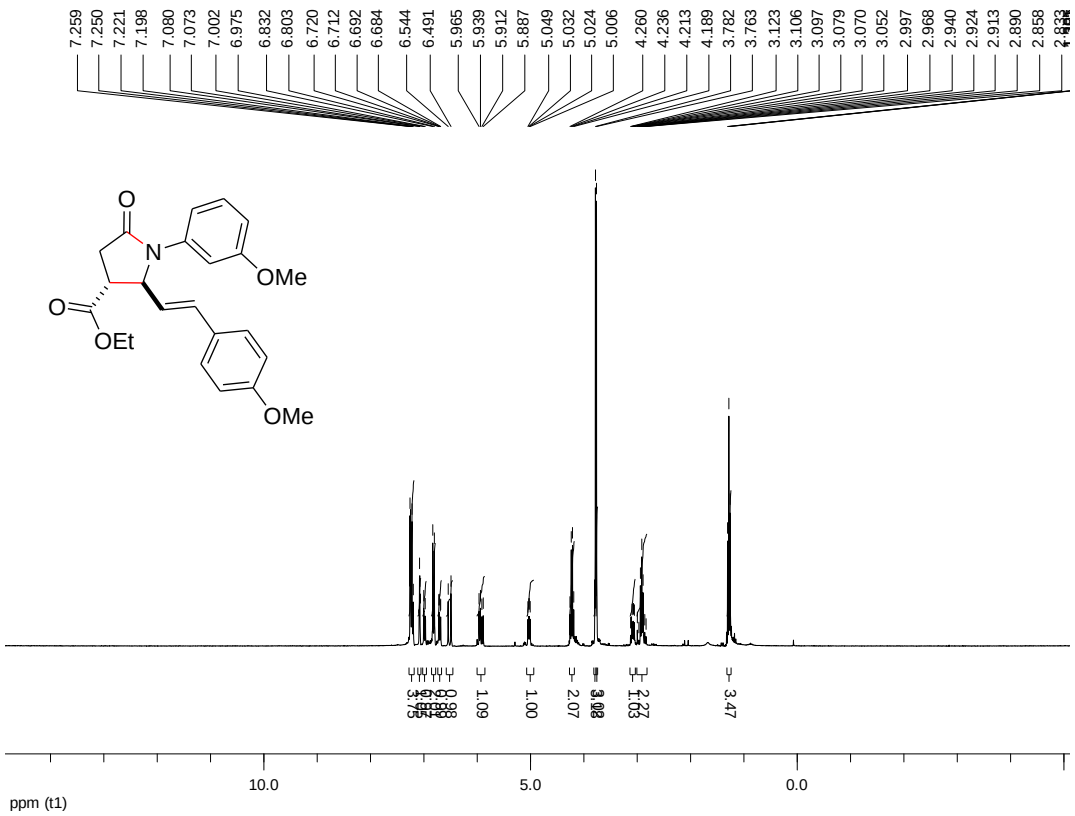


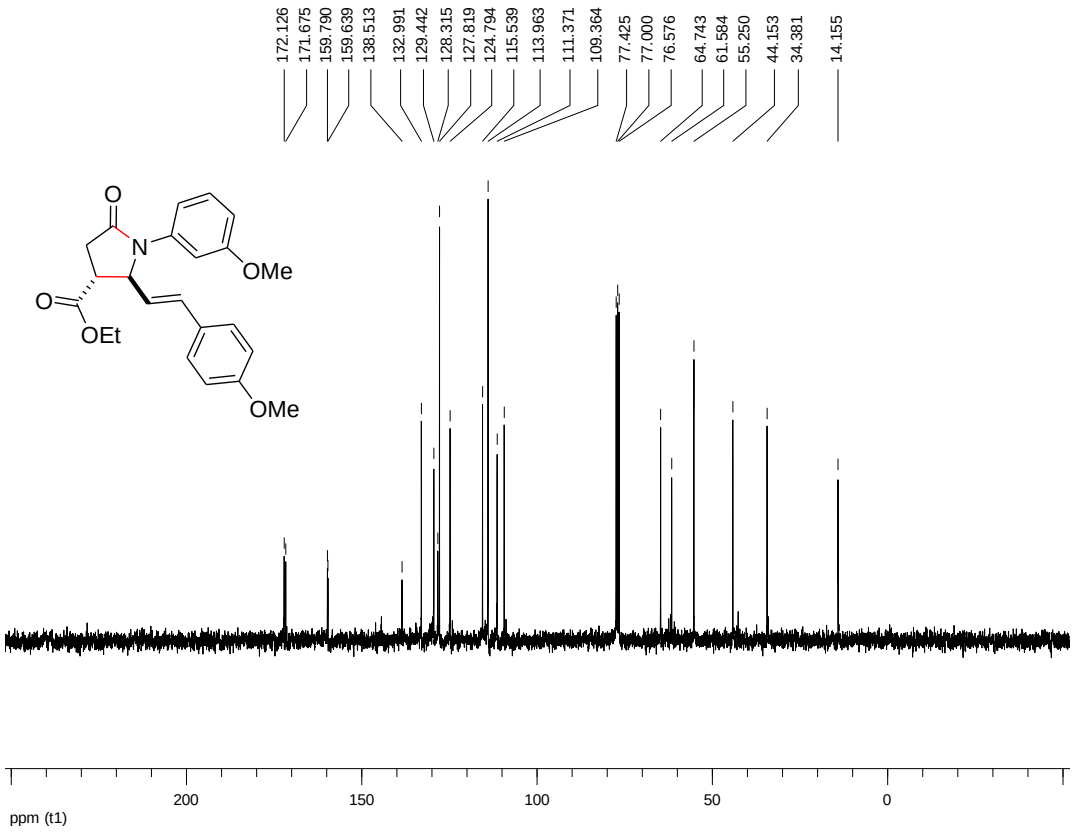
NMR Spectra of Product 3g



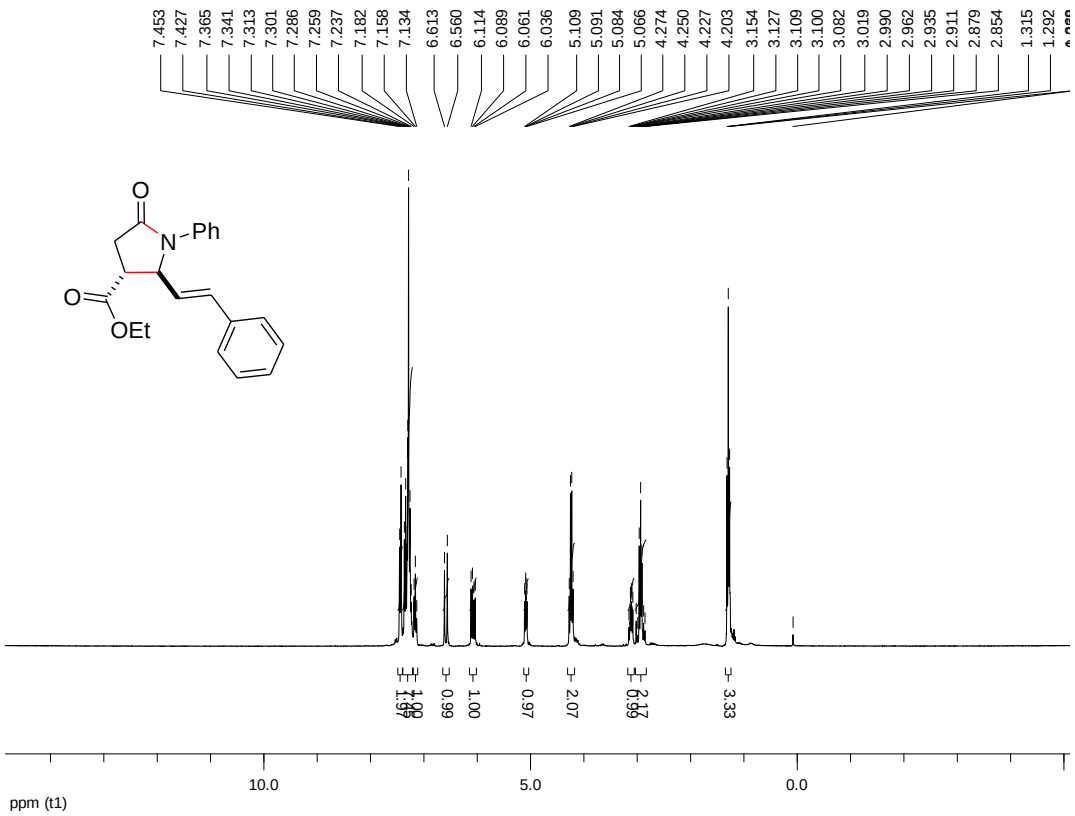


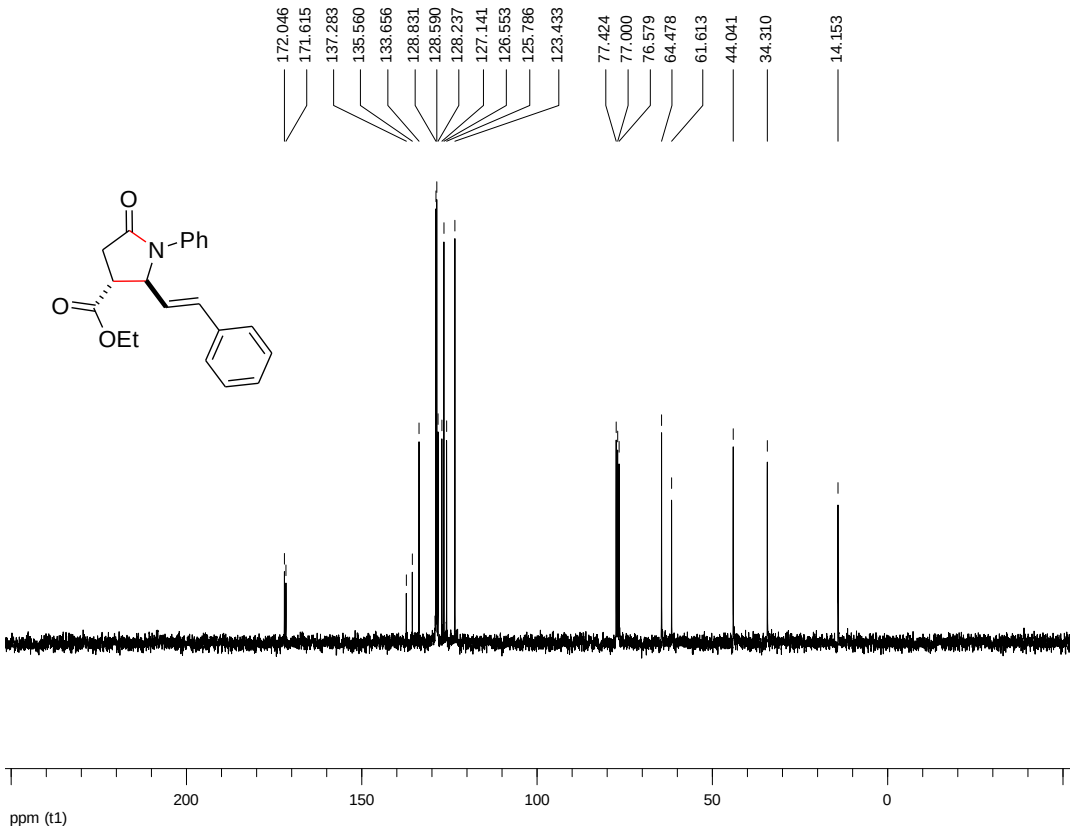
NMR Spectra of Product 3h



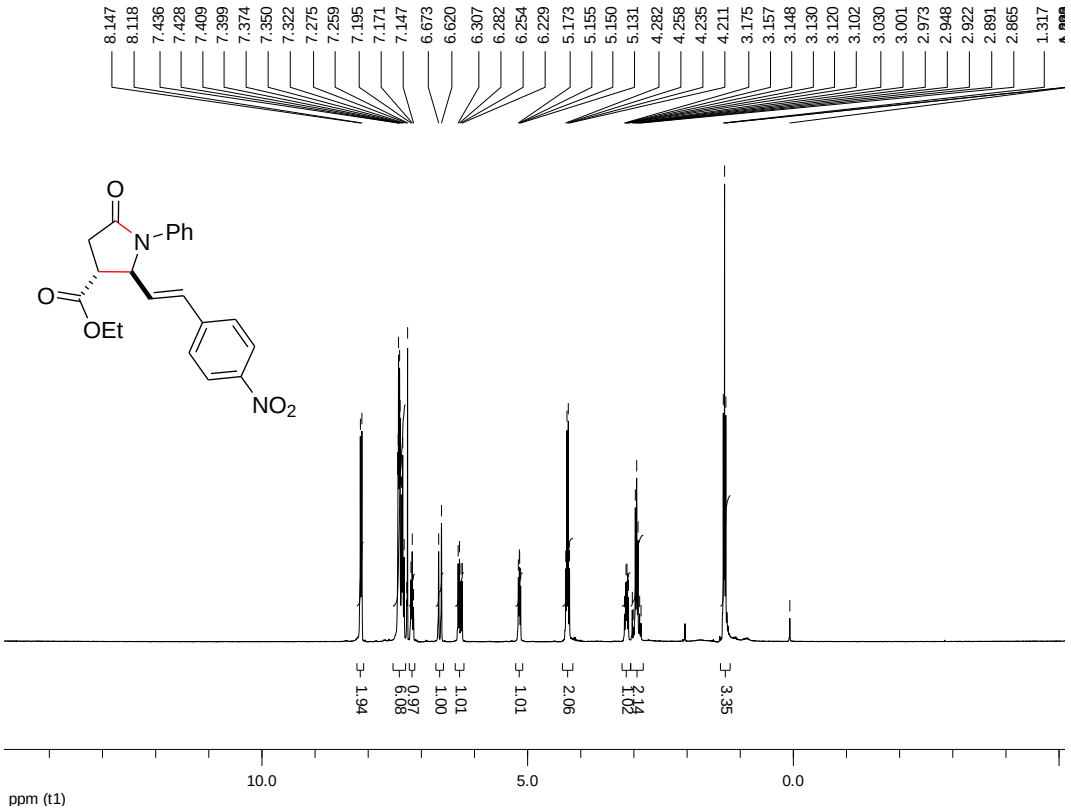


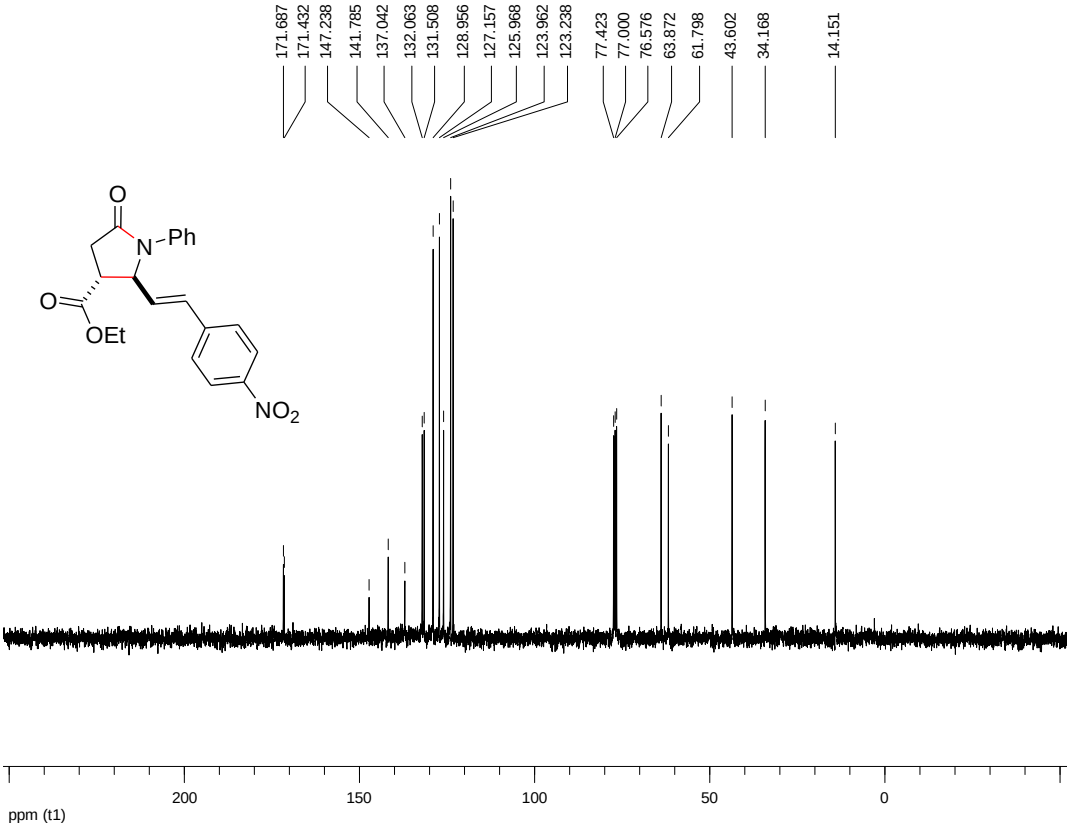
NMR Spectra of Product 3i



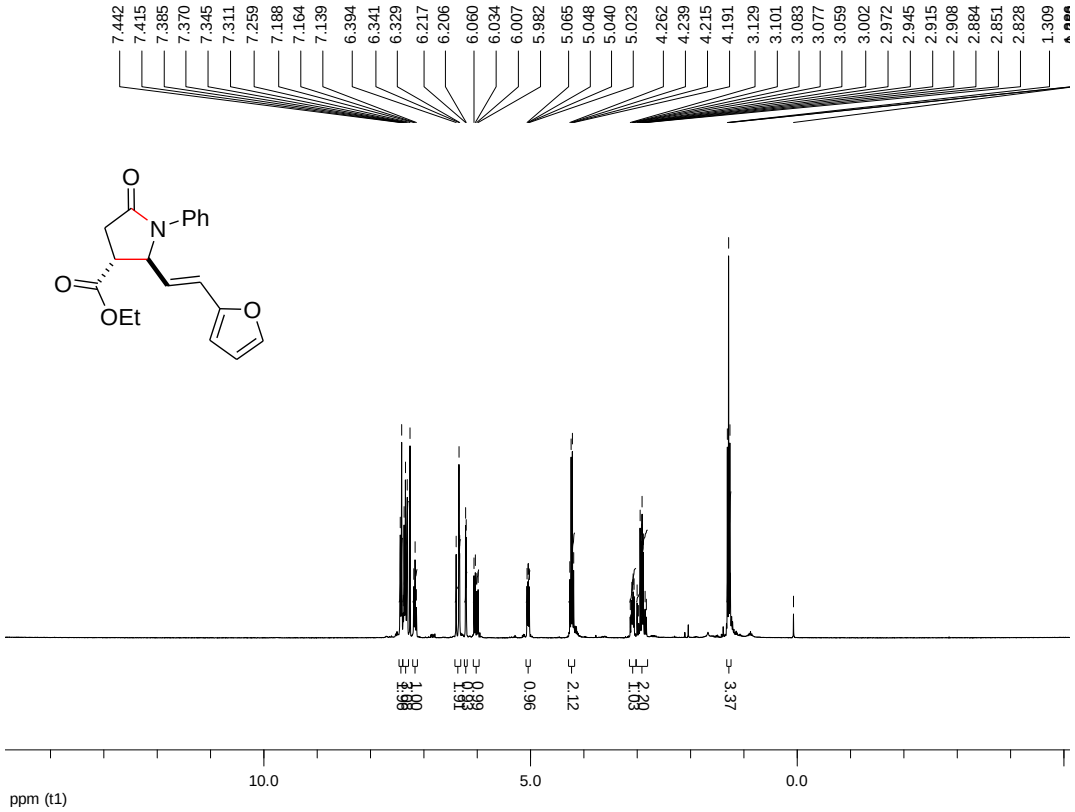


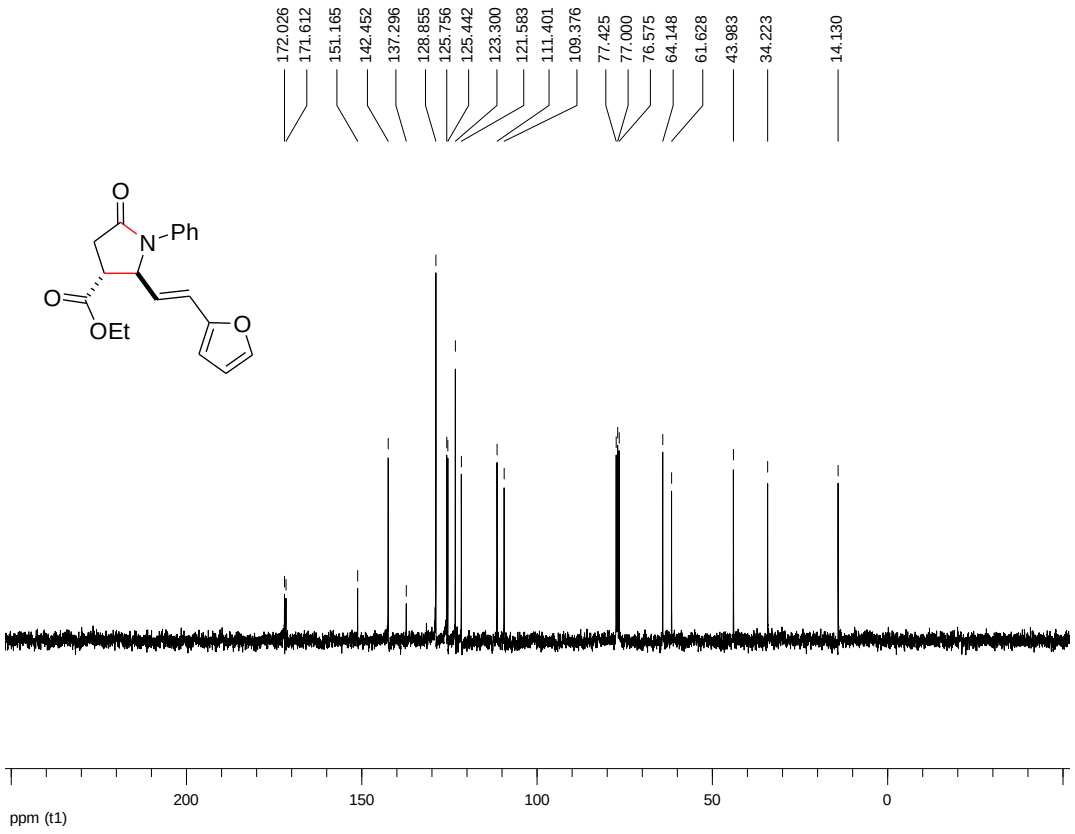
NMR Spectra of Product 3j



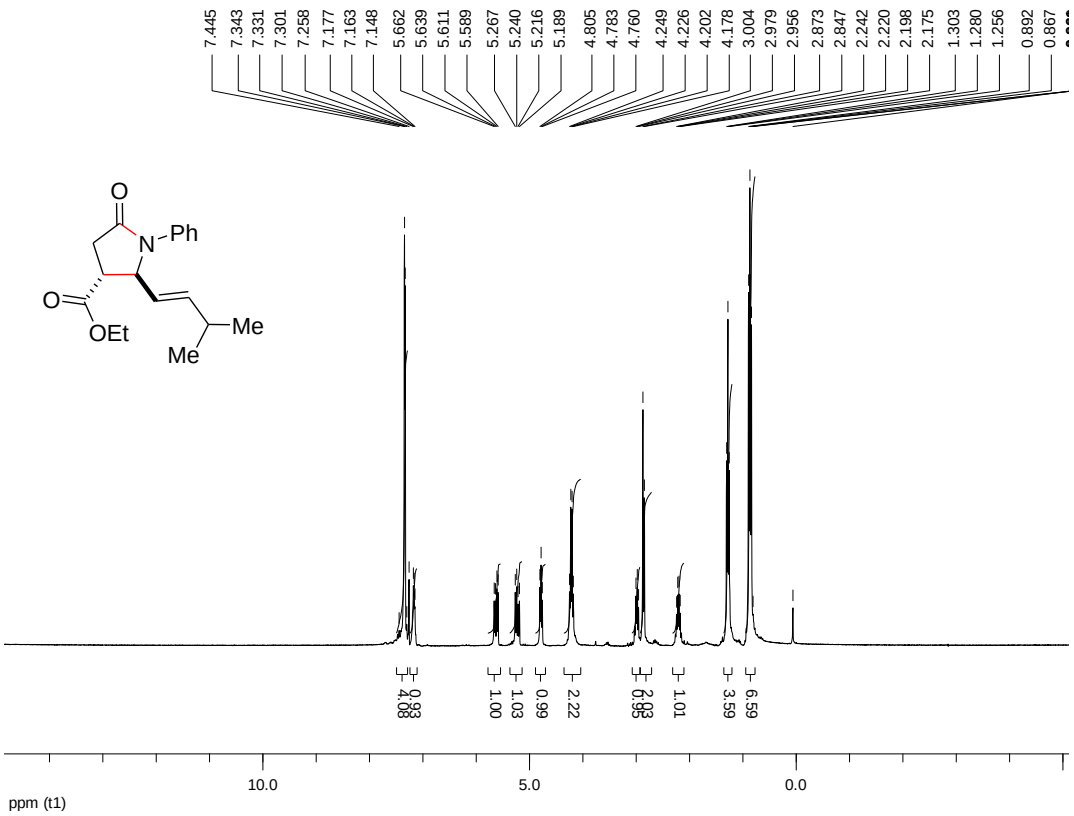


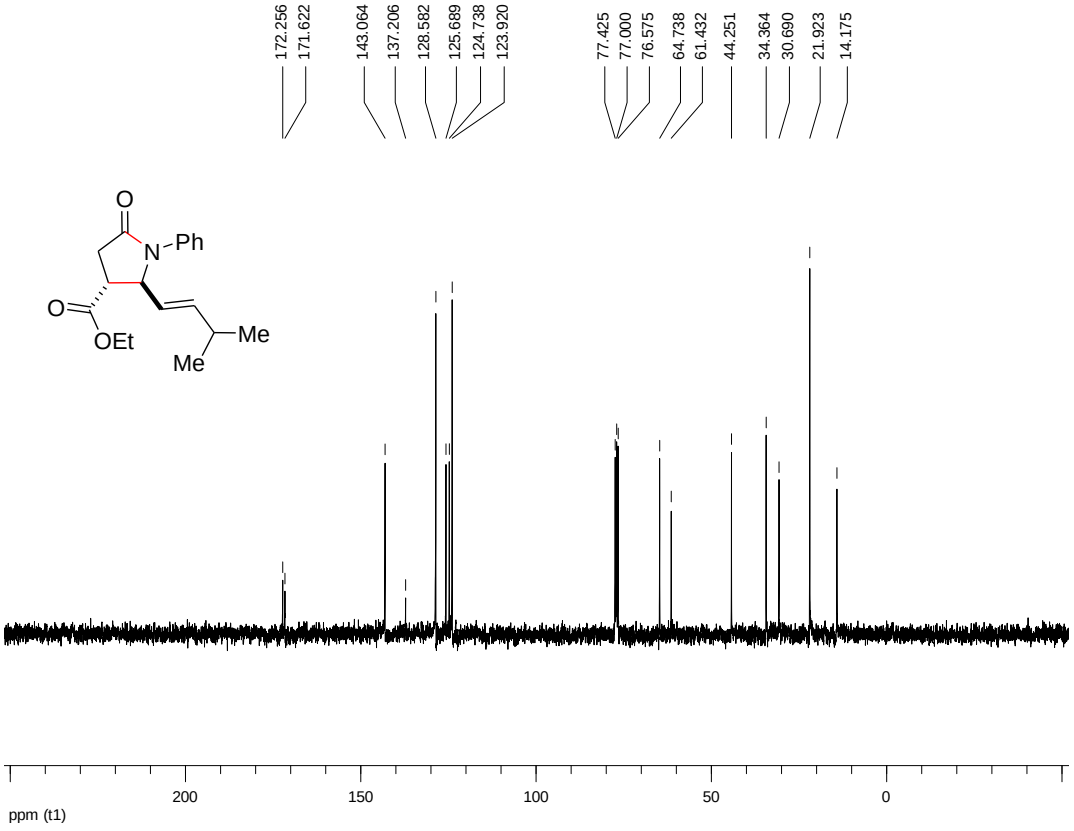
NMR Spectra of Product 3k



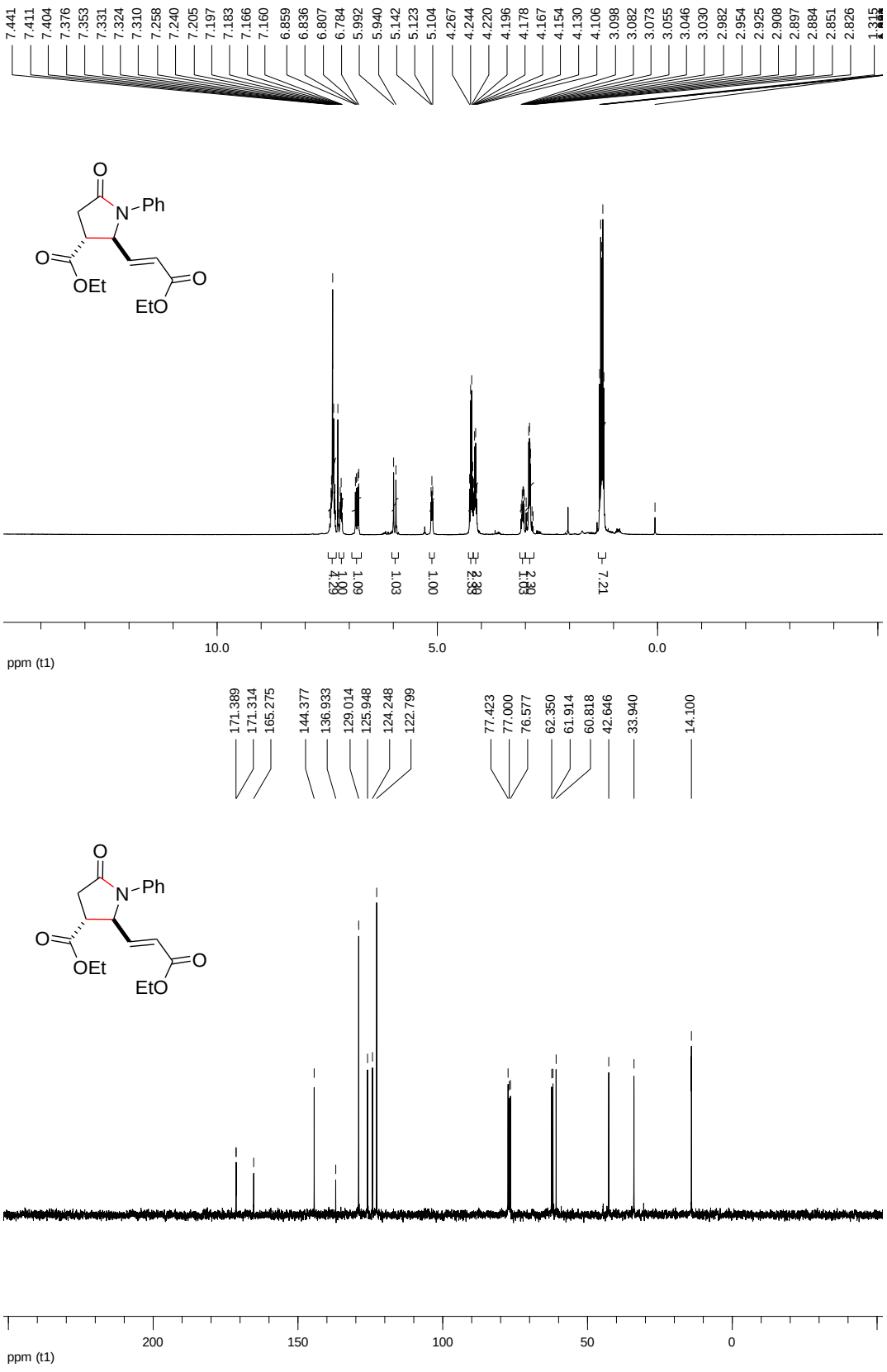


NMR Spectra of Product 3l

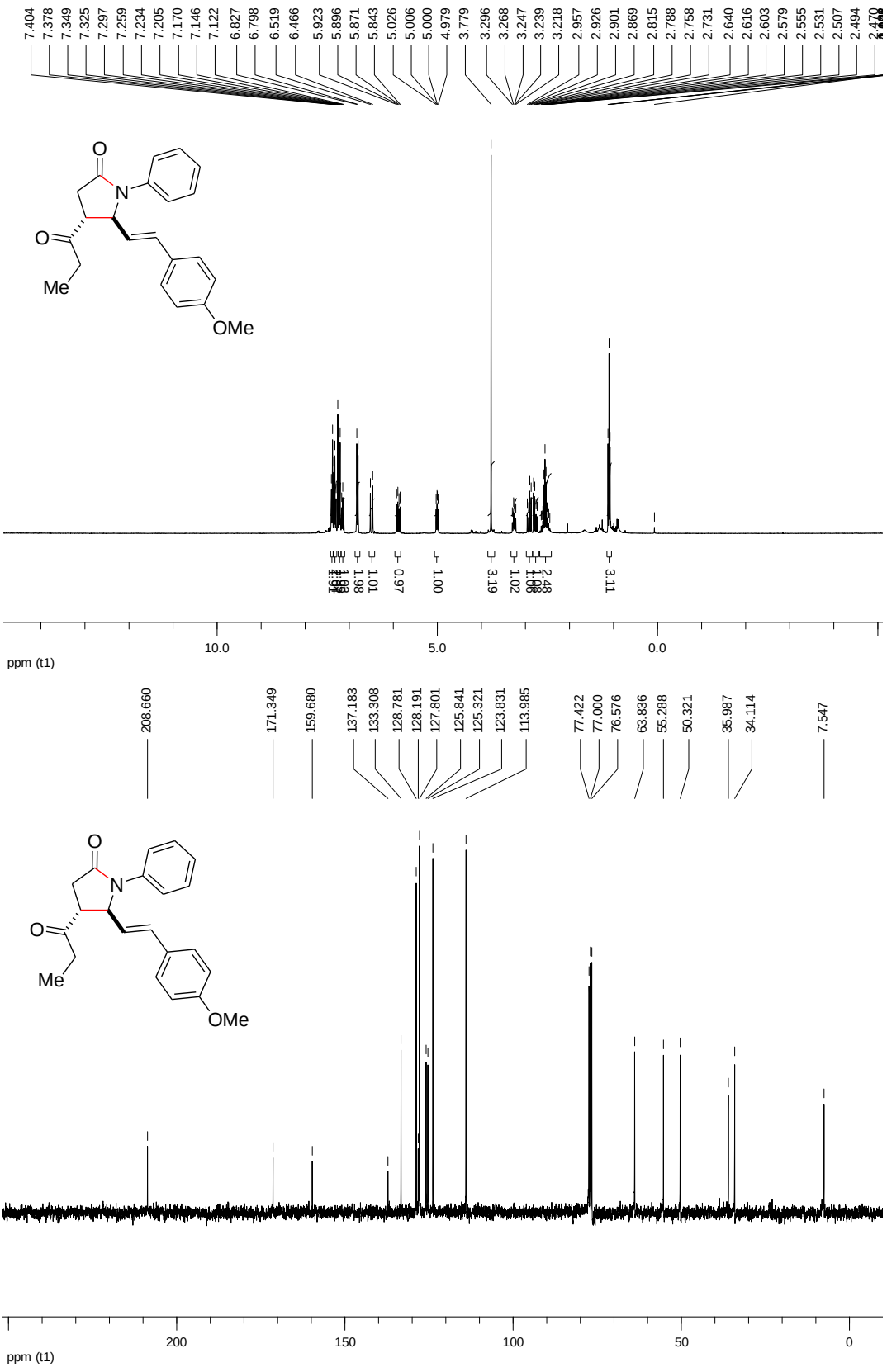




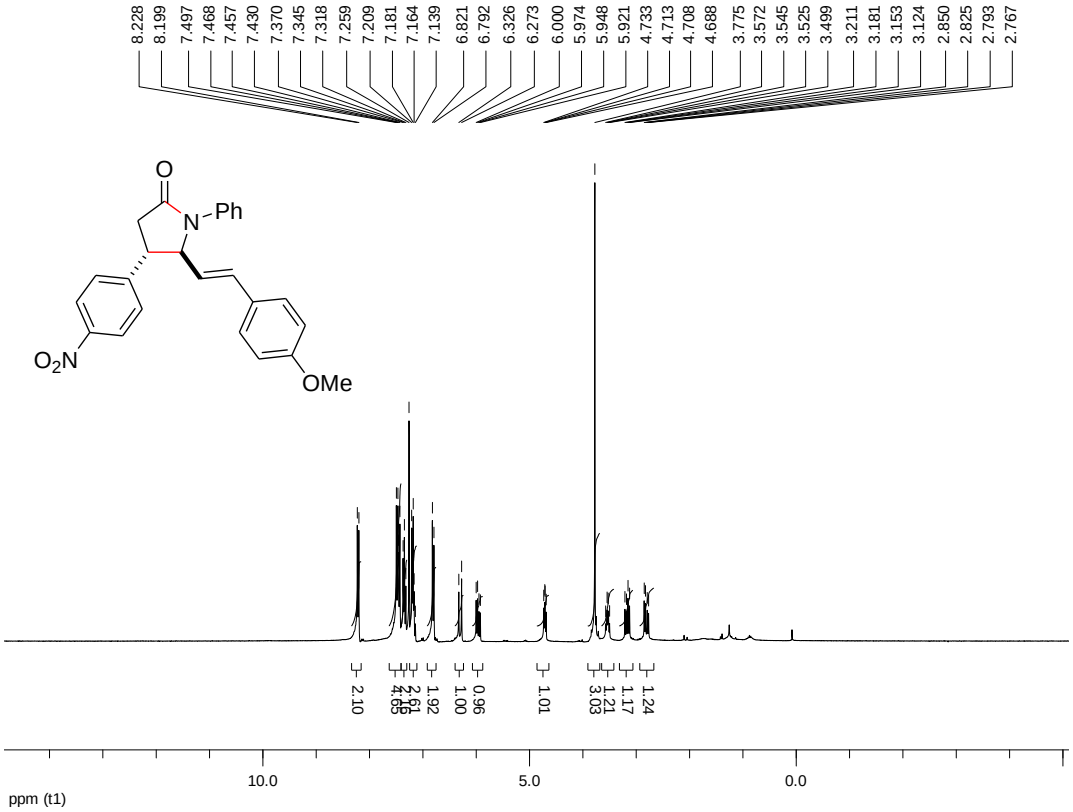
NMR Spectra of Product 3m

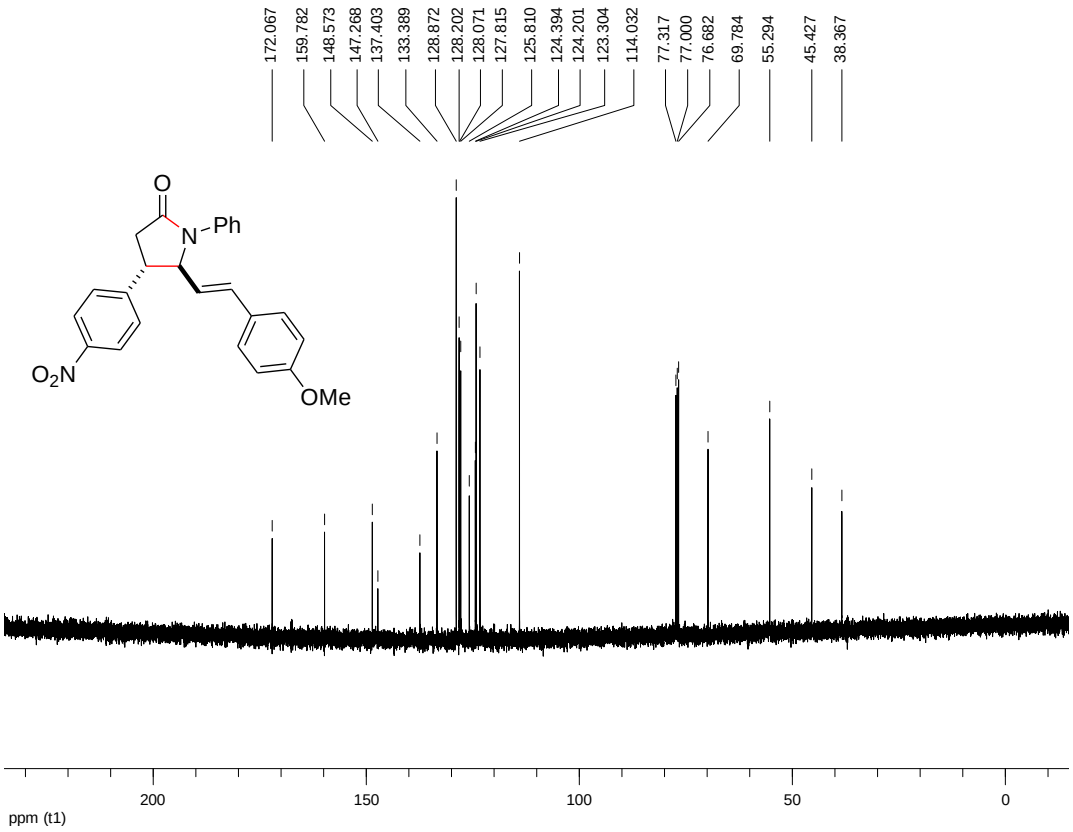


NMR Spectra of Product 3n

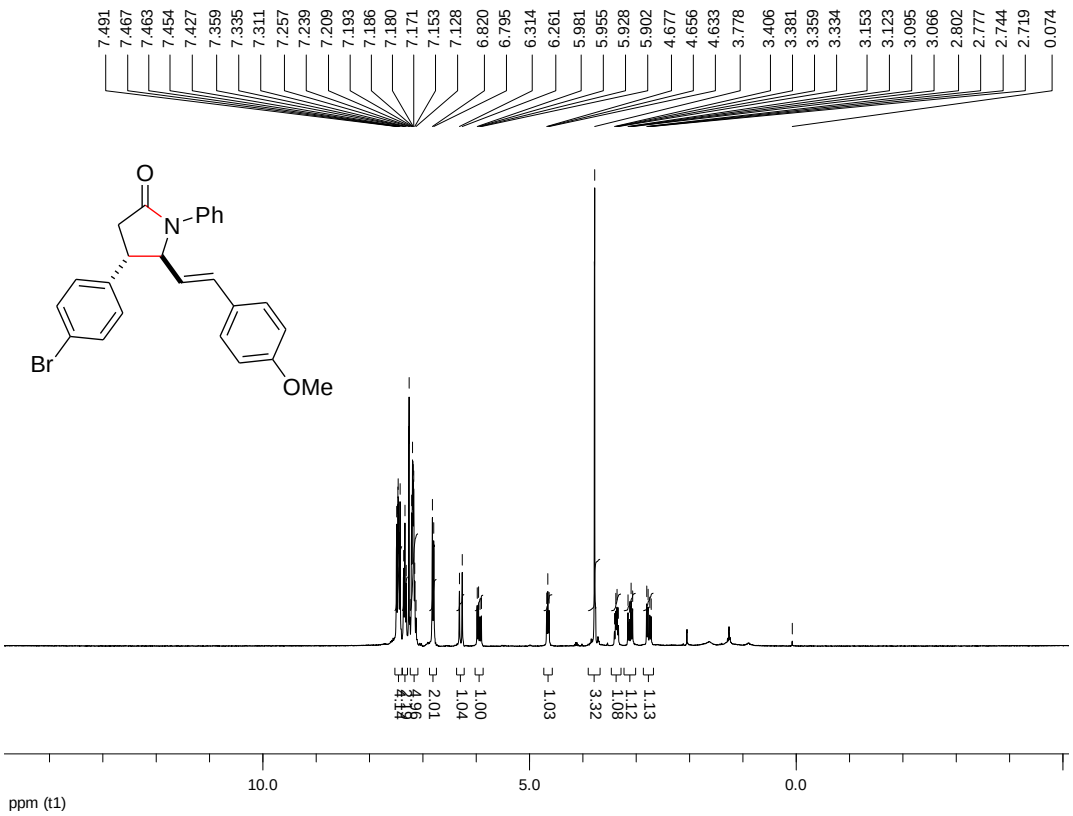


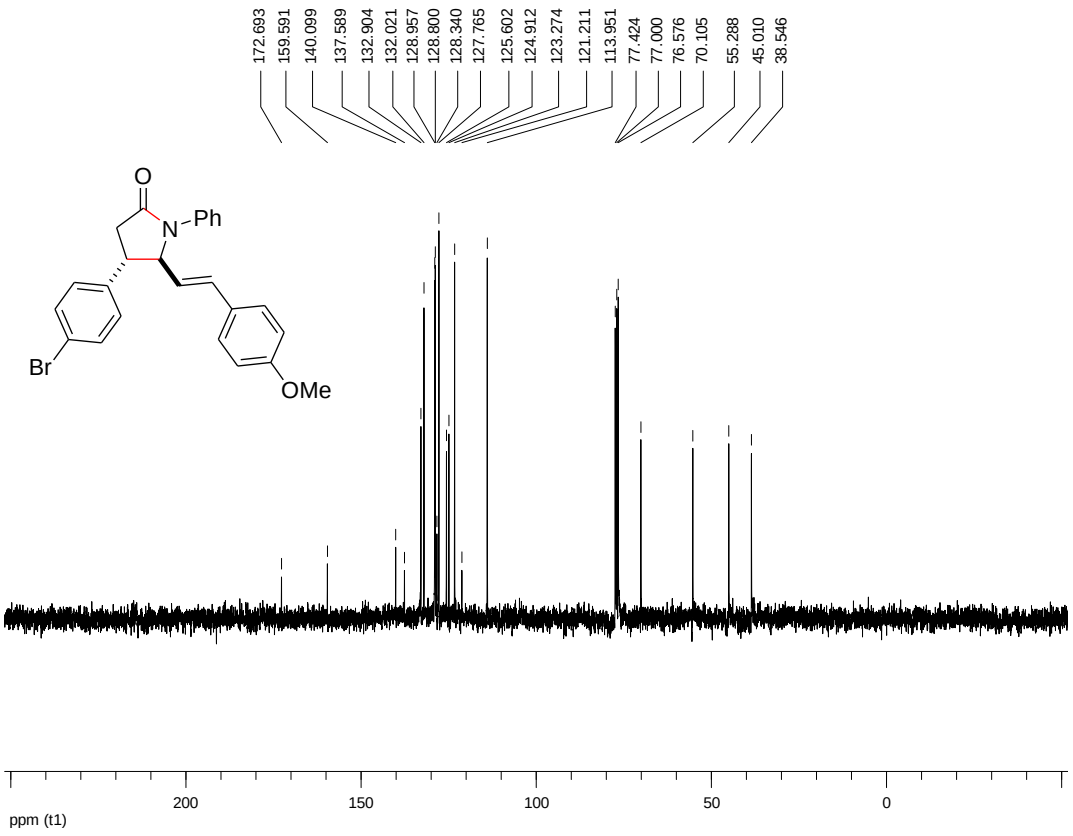
NMR Spectra of Product 3o



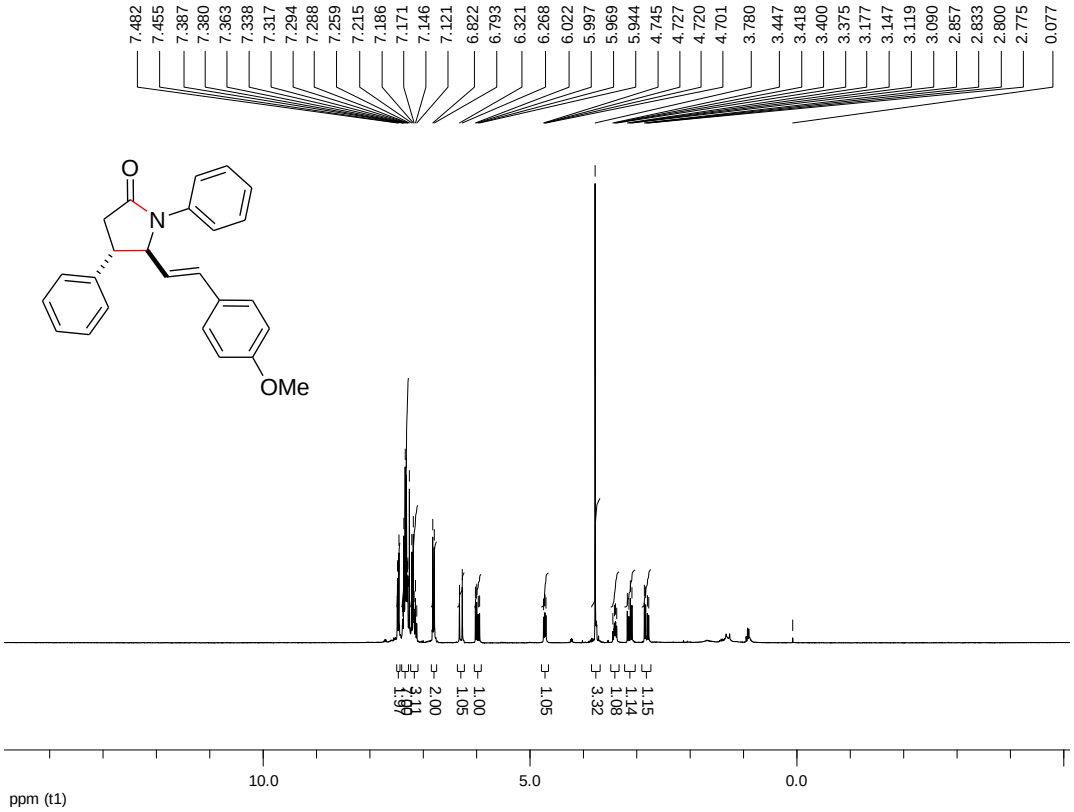


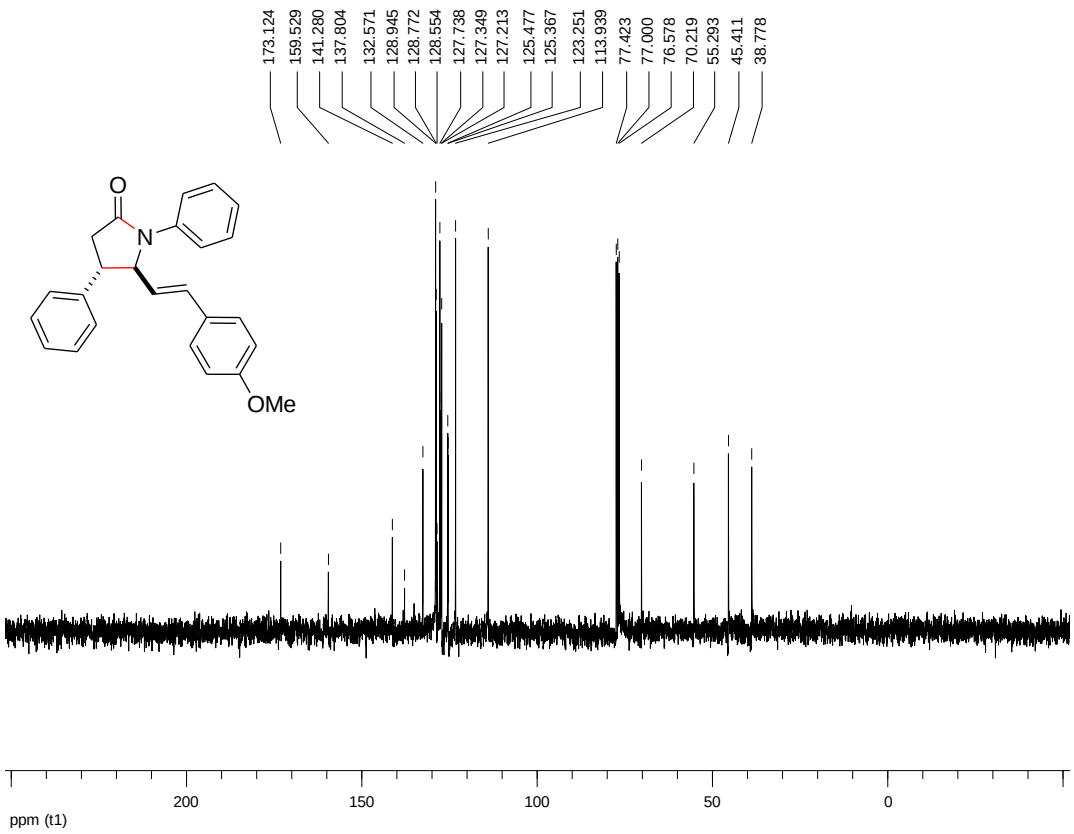
NMR Spectra of Product 3p



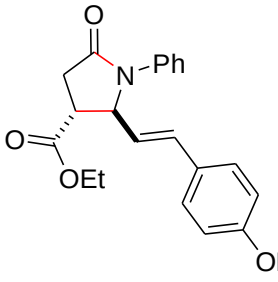


NMR Spectra of Product 3q





6. HPLC spectra for products



3a

```
=====================================================================
Injection Date  : 12/21/2010 12:43:18 PM          Seq. Line :   2
Sample Name     : CSUzxd-295                       Location : Vial 9
Acq. Operator   : Rovis Group                         Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:52:57 PM by Rovis Group
                  (modified after loading)
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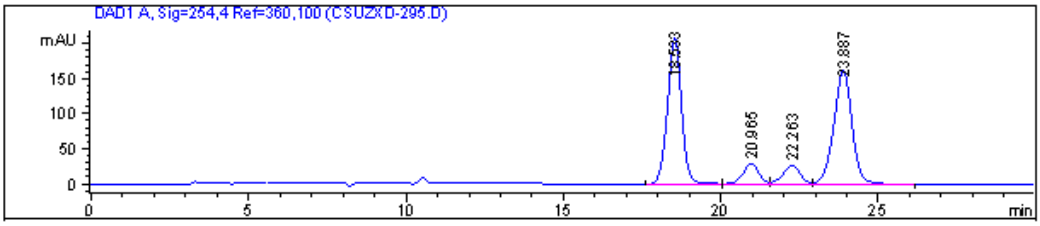

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.533	VV	0.4757	6499.29004	208.48705	42.8600
2	20.965	VV	0.5404	1039.62891	29.41075	6.8559
3	22.263	VV	0.5878	1050.91370	27.13725	6.9303
4	23.887	VV	0.6067	6574.17090	162.96042	43.3538

```
=====================================================================
Injection Date  : 2/23/2011 9:37:31 PM           Seq. Line :   1
Sample Name     : CSUzxd-367                       Location : Vial 1
Acq. Operator   : Rovis Group                         Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:52:57 PM by Rovis Group
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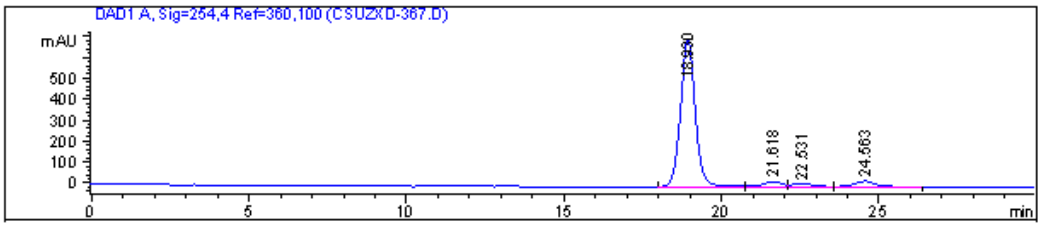
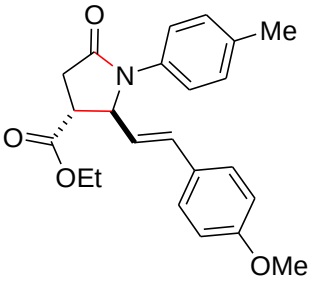


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.930	BV	0.4884	2.27257e4	704.31970	89.1647
2	21.618	VV	0.5821	975.44342	25.06002	3.8272
3	22.531	VV	0.7148	609.73468	13.00988	2.3923
4	24.563	VB	0.6654	1176.46277	26.73501	4.6159



3b

```
======================================================================
Injection Date  : 3/17/2011 10:53:04 AM          Seq. Line :   1
Sample Name     : CSUzxd-409                      Location : Vial 4
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:48:02 PM by Rovis Group
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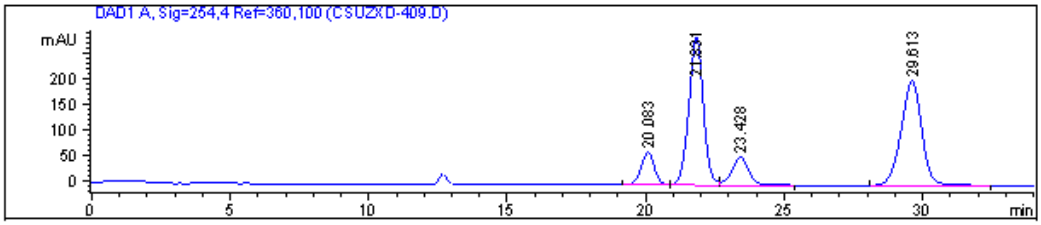

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.083	BV	0.5107	2185.18066	65.24619	8.4900
2	21.831	VV	0.5616	1.06049e4	290.68579	41.2025
3	23.428	VB	0.6418	2330.92432	54.63216	9.0562
4	29.613	BB	0.7848	1.06174e4	206.17418	41.2513

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======================================================================
Injection Date  : 3/17/2011 12:15:41 PM          Seq. Line :   2
Sample Name     : CSUzxd-400-2                    Location : Vial 7
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:48:02 PM by Rovis Group
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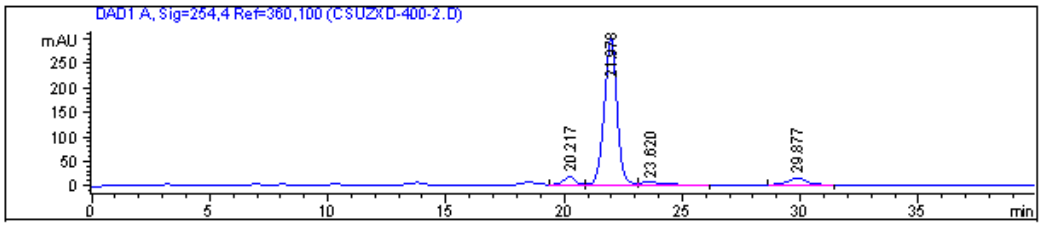
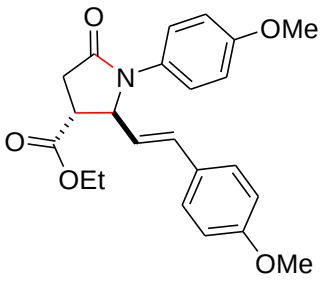


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.217	VV	0.5639	636.83850	17.04400	4.9313
2	21.978	VV	0.5651	1.12218e4	299.49097	86.8949
3	23.620	VB	0.8370	346.07196	5.75987	2.6798
4	29.877	BB	0.7933	709.51196	13.58589	5.4940



3c

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=====================================================================
Injection Date  : 3/18/2011 10:44:13 AM          Seq. Line :   1
Sample Name     : CSUzxd-410-7                    Location : Vial 5
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-75-25 1ML 25MIN.M
Last changed    : 9/27/2010 9:36:11 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:36:45 PM by Rovis Group
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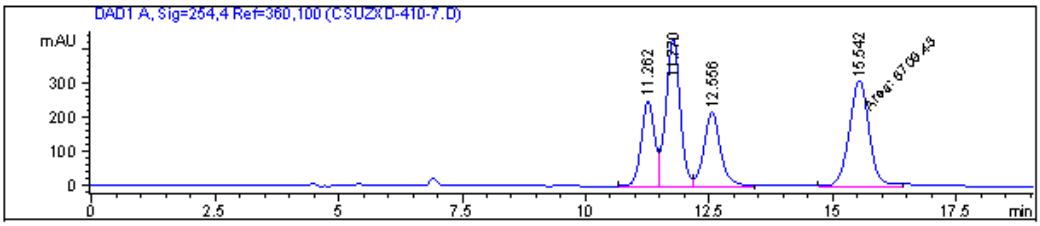

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.262	BV	0.2802	4615.64453	249.02686	17.0568
2	11.770	VV	0.3053	8632.49414	431.74124	31.9009
3	12.556	VV	0.3552	5102.79834	216.33461	18.8571
4	15.542	MM	0.4661	8709.43359	311.45889	32.1852

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=====================================================================
Injection Date  : 4/4/2011 1:10:15 PM           Seq. Line :   1
Sample Name     : CSUzxd-404-2                    Location : Vial 2
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-75-25 1ML 25MIN.M
Last changed    : 9/27/2010 9:36:11 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:46:28 PM by Rovis Group
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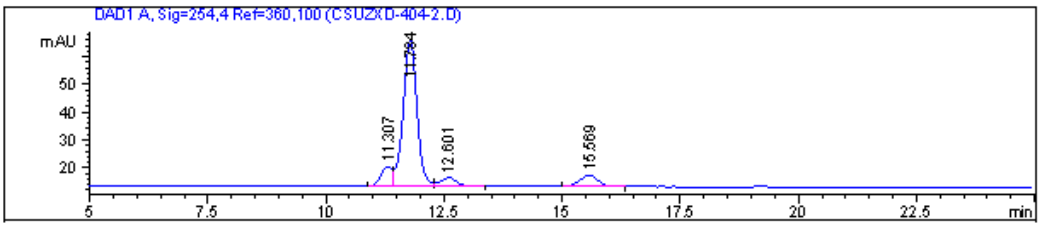
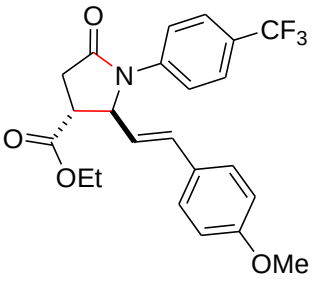


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.307	BV	0.2554	116.09611	7.07822	8.3553
2	11.784	VV	0.3105	1082.53906	52.96441	77.9088
3	12.601	VB	0.3688	77.69789	3.13838	5.5918
4	15.569	BB	0.4275	113.16182	4.08086	8.1441



3d

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=====================================================================
Injection Date  : 3/28/2011 12:28:39 PM          Seq. Line :   2
Sample Name     : CSUzxd-426-1                    Location : Vial 2
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-95-5 1ML 60 MIN.M
Last changed    : 3/17/2011 4:16:47 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:13:53 PM by Rovis Group
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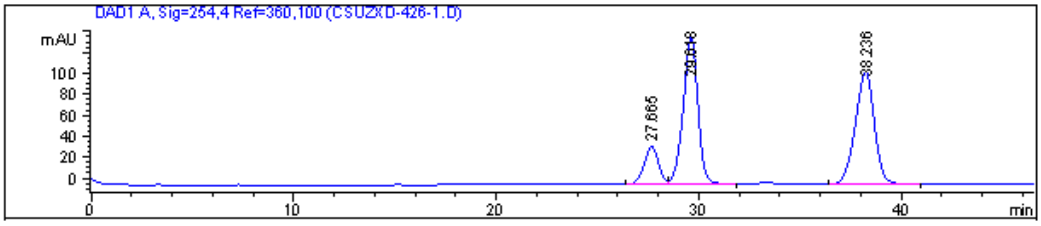

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.665	BV	0.7509	1790.74451	36.33751	11.1594
2	29.618	VB	0.7692	7147.93799	140.57462	44.5439
3	38.236	BB	1.0109	7108.27051	107.57991	44.2967

```
=====================================================================
Injection Date  : 3/28/2011 1:19:39 PM           Seq. Line :   1
Sample Name     : CSUzxd-418-2                    Location : Vial 7
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-95-5 1ML 60 MIN.M
Last changed    : 3/17/2011 4:16:47 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:13:53 PM by Rovis Group
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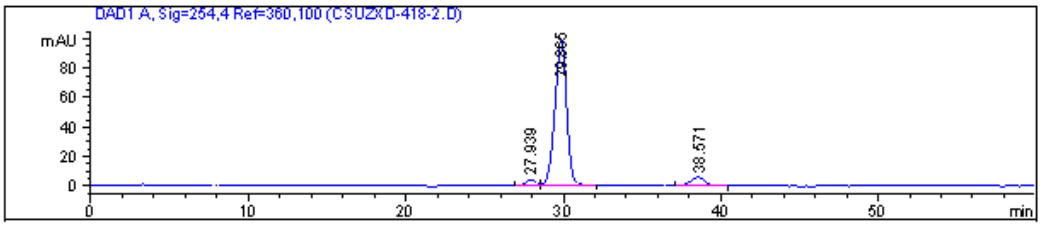
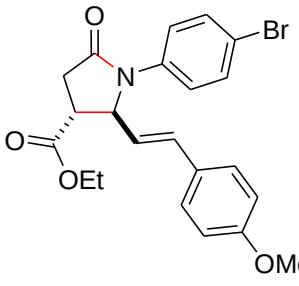


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.939	BV	0.7293	205.18219	4.38992	3.5292
2	29.865	VB	0.7915	5210.50098	100.05789	89.6223
3	38.571	BB	1.0398	398.16263	5.92628	6.8485



3e

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==================================================================
Injection Date  : 5/24/2011 10:52:13 AM          Seq. Line :   2
Sample Name     : CSUzxd-506                      Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 5/24/2011 11:24:09 AM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/10/2011 10:21:47 PM by Rovis Group
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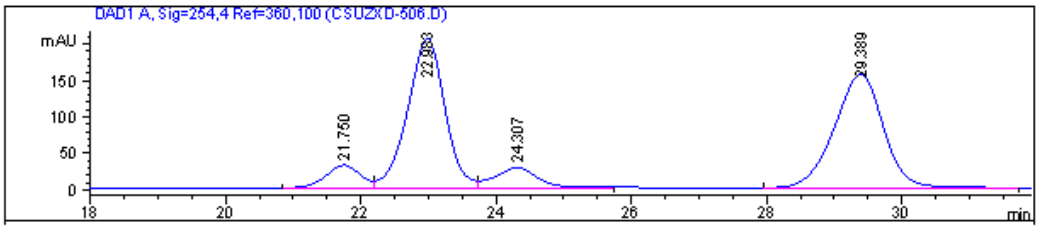

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.750	VV	0.5419	1103.40234	31.10537	6.1408
2	22.983	VV	0.5816	7821.12695	204.78281	43.5269
3	24.307	VB	0.6601	1215.39746	27.47562	6.7640
4	29.389	BB	0.7609	7828.57910	156.16014	43.5683

```
==================================================================
Injection Date  : 5/25/2011 12:19:31 PM          Seq. Line :   1
Sample Name     : CSUzxd-508                      Location : Vial 4
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/10/2011 10:40:24 PM by Rovis Group
                  (modified after loading)
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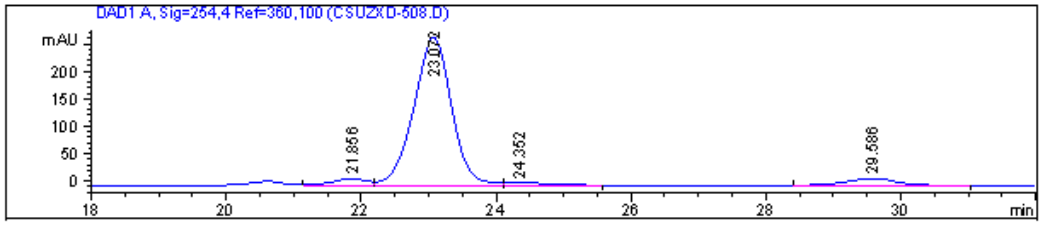
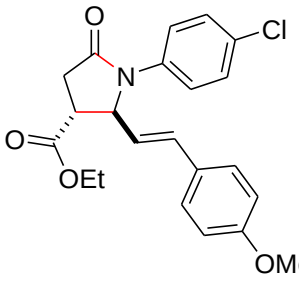


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.856	VV	0.5332	416.62830	11.99605	3.5660
2	23.072	VV	0.5892	1.04511e4	269.06799	89.4525
3	24.352	VB	0.6001	187.97130	4.72520	1.6089
4	29.586	BB	0.7801	627.70709	12.45283	5.3726



3f

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==================================================================
Injection Date  : 4/8/2011 9:57:07 AM            Seq. Line :   1
Sample Name     : CSUzxd-432-3                    Location : Vial 1
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-97-3 1ML 60 MIN.M
Last changed    : 4/8/2011 11:22:20 AM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:59:31 PM by Rovis Group
                  (modified after loading)
==================================================================
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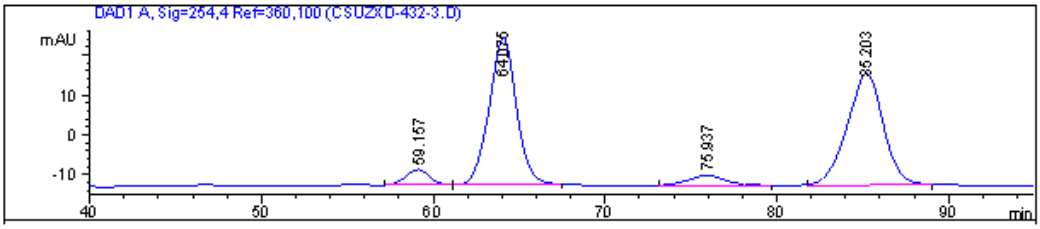

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	59.157	BV	1.3016	366.65134	3.82759	4.1007
2	64.075	VB	1.6785	4091.94238	36.87767	45.7654
3	75.937	BB	1.8549	377.93146	2.46203	4.2269
4	85.203	BB	2.1438	4104.60742	27.97445	45.9070

```
==================================================================
Injection Date  : 4/8/2011 12:59:24 PM          Seq. Line :   2
Sample Name     : CSUzxd-433                     Location : Vial 2
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                 Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 8 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-97-3 1ML 60 MIN.M
Last changed    : 4/8/2011 1:17:28 PM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:59:31 PM by Rovis Group
                  (modified after loading)
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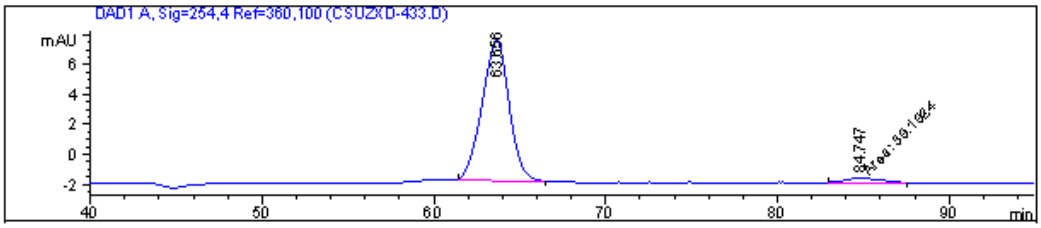
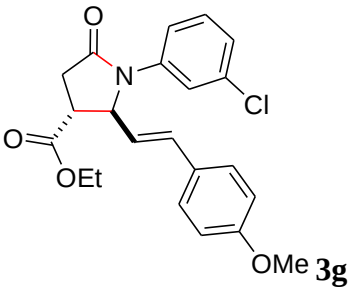


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	63.656	BB	1.5215	1030.68420	9.50179	96.3367
2	84.747	MM	2.0696	39.19243	3.15618e-1	3.6633



3g

```
=====================================================================
Injection Date  : 4/7/2011 11:03:01 PM          Seq. Line :   1
Sample Name     : CSUzxd-440-4                   Location : Vial 2
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-98-2 1ML 60 MIN.M
Last changed    : 4/8/2011 12:25:23 AM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:37:11 PM by Rovis Group
                  (modified after loading)
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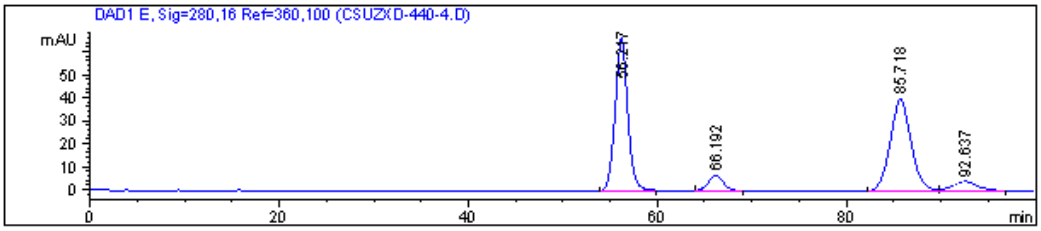

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	56.217	BB	1.3625	6121.42188	66.21866	44.6241
2	66.192	BB	1.5934	741.90442	6.63051	5.4084
3	85.718	BB	2.1154	6109.00781	40.14426	44.5336
4	92.637	BB	2.3002	745.40149	4.10951	5.4339

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=====================================================================
Injection Date  : 4/9/2011 11:49:11 PM          Seq. Line :   1
Sample Name     : CSUzxd-442                     Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 1 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-98-2 1ML 60 MIN.M
Last changed    : 4/9/2011 11:45:04 PM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:54:27 PM by Rovis Group
                  (modified after loading)
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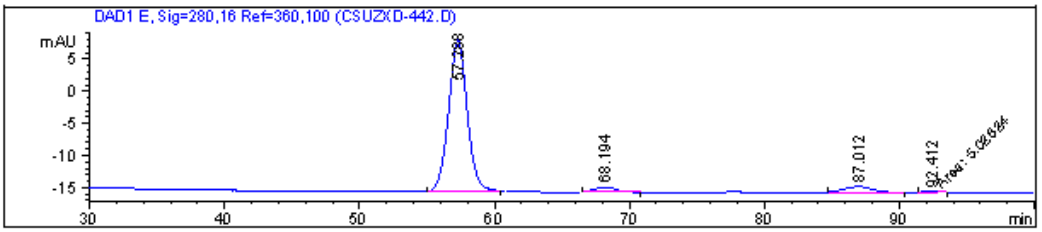
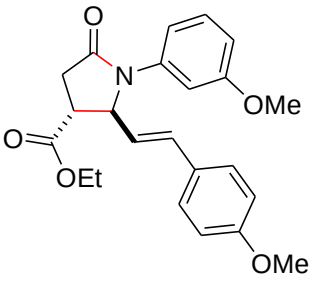


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	57.288	BB	1.4906	2268.14917	23.57191	91.4641
2	68.194	BB	1.3352	85.21616	8.02295e-1	3.4364
3	87.012	BB	1.6756	121.43230	8.8567le-1	4.8968
4	92.412	MM	1.6237	5.02624	5.1592le-2	0.2027



3h

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==================================================================
Injection Date  : 4/7/2011 3:53:52 PM            Seq. Line :   1
Sample Name     : CSUzxd-439-1                    Location : Vial 1
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:36:45 PM by Rovis Group
                  (modified after loading)
==================================================================
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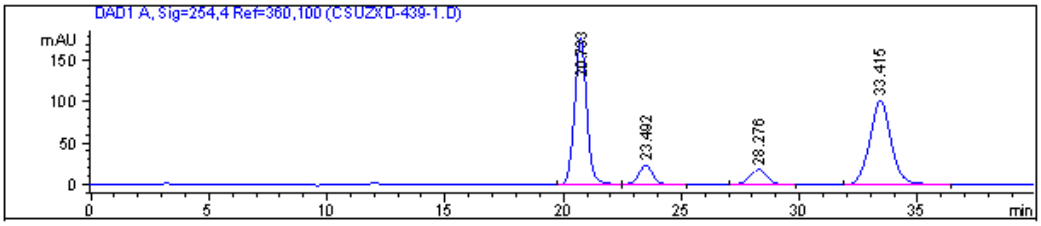

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.733	BV	0.5480	6432.87305	178.67545	43.4656
2	23.492	VB	0.6543	1005.56335	23.35649	6.7944
3	28.276	BB	0.7802	941.40942	18.17768	6.3609
4	33.415	BB	0.9389	6420.08398	102.48081	43.3792

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==================================================================
Injection Date  : 4/9/2011 4:08:37 PM            Seq. Line :   2
Sample Name     : CSUzxd-441-1                    Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:36:45 PM by Rovis Group
                  (modified after loading)
==================================================================
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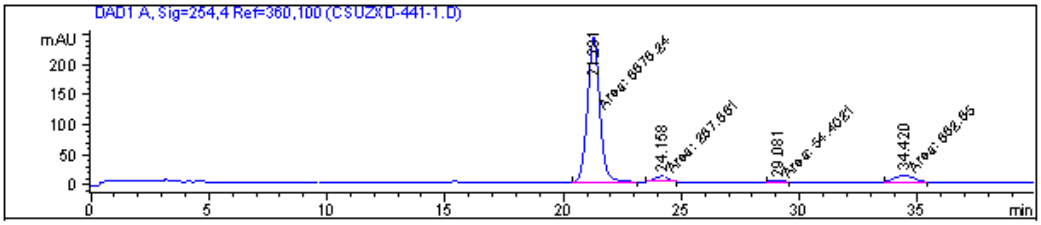
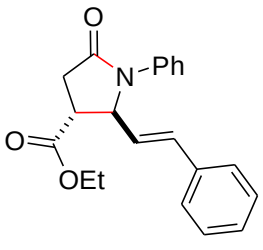


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.281	MM	0.6102	8878.24219	242.50221	89.6487
2	24.158	MM	0.5769	287.88129	8.31754	2.9069
3	29.081	MM	0.6111	54.40211	1.48366	0.5493
4	34.420	MM	0.9587	682.84955	11.87061	6.8951



3i

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================================================================================
Injection Date  : 3/1/2011 9:12:24 PM            Seq. Line :   1
Sample Name     : CSUzxd-375                      Location : Vial 2
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:52:57 PM by Rovis Group
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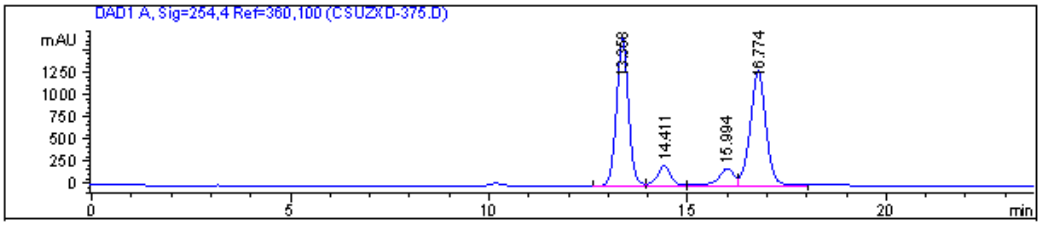

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.358	VV	0.3250	3.48158e4	1657.86182	43.0116
2	14.411	VV	0.3543	5268.65918	224.06734	6.5089
3	15.994	VV	0.4109	5374.14746	194.16936	6.6393
4	16.774	VV	0.4177	3.54864e4	1286.87939	43.8402

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================================================================================
Injection Date  : 3/11/2011 11:26:12 AM          Seq. Line :   1
Sample Name     : CSUzxd-396                      Location : Vial 1
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:52:57 PM by Rovis Group
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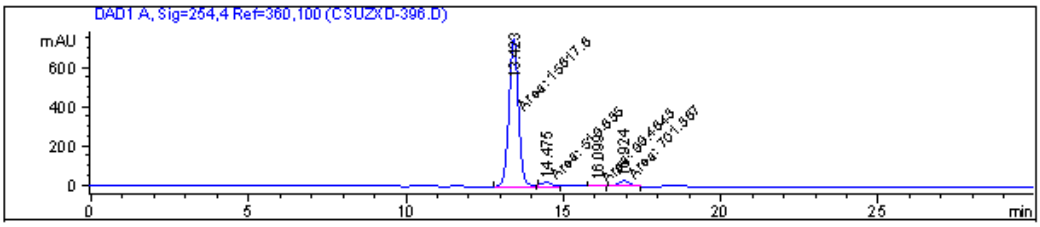
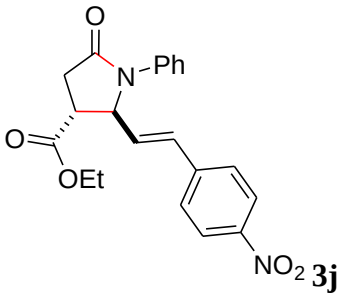


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.423	MM	0.3483	1.58178e4	756.93011	92.2951
2	14.475	MM	0.3960	519.63495	21.87186	3.0320
3	16.099	MM	0.3578	99.48429	4.63368	0.5805
4	16.924	MM	0.4354	701.36731	26.84999	4.0924



3j

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=====================================================================
Injection Date  : 3/30/2011 6:22:20 PM          Seq. Line :   1
Sample Name     : CSUzxd-431                     Location : Vial 2
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-80-20 1ML 40MIN.M
Last changed    : 3/18/2011 9:51:10 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:09:38 PM by Rovis Group
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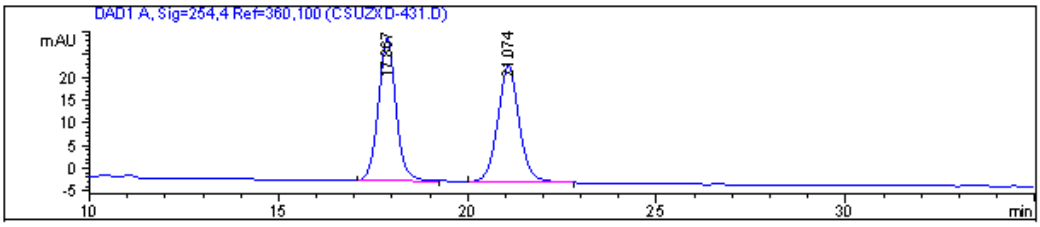

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.867	BB	0.5014	1023.28595	31.30357	50.2275
2	21.074	BB	0.5974	1014.01544	25.64235	49.7725

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=====================================================================
Injection Date  : 3/30/2011 8:31:08 PM          Seq. Line :   1
Sample Name     : CSUzxd-428                     Location : Vial 1
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-80-20 1ML 40MIN.M
Last changed    : 3/18/2011 9:51:10 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:11:29 PM by Rovis Group
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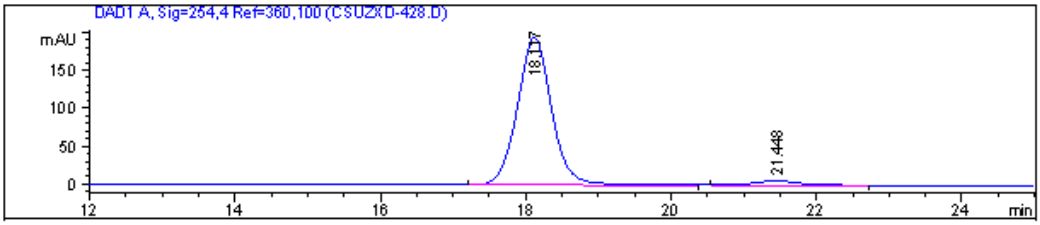
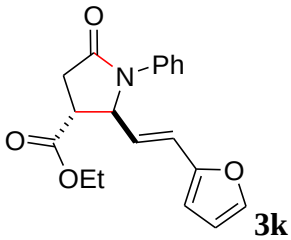


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.117	BB	0.5021	6363.49658	194.31239	96.3565
2	21.448	BB	0.6438	240.62164	5.70832	3.6435



3k

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=====================================================================
Injection Date  : 3/28/2011 11:57:37 AM          Seq. Line :   1
Sample Name     : CSUzxd-425-1                    Location : Vial 1
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-85-15 1ML 25MIN.M
Last changed    : 3/28/2011 11:27:28 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:13:53 PM by Rovis Group
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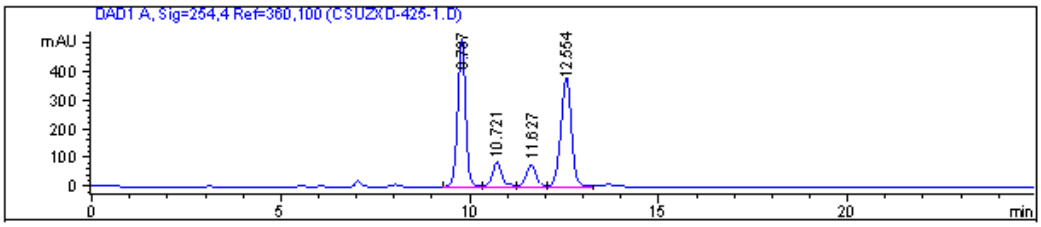

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.787	VV	0.2261	7458.71484	511.64975	41.8280
2	10.721	VV	0.2704	1518.28455	85.83617	8.5144
3	11.627	VV	0.2836	1445.84033	76.81924	8.1082
4	12.554	VV	0.3003	7409.04883	378.59149	41.5494

```
=====================================================================
Injection Date  : 3/28/2011 11:32:38 AM          Seq. Line :   1
Sample Name     : CSUzxd-422-2                    Location : Vial 6
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-85-15 1ML 25MIN.M
Last changed    : 3/28/2011 11:27:28 AM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:13:53 PM by Rovis Group
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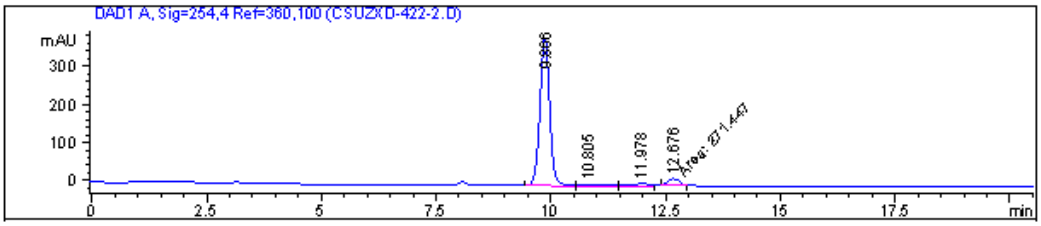
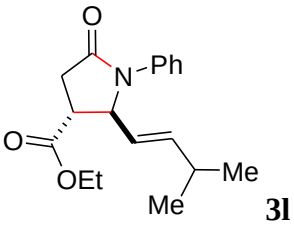


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.866	BV	0.2289	5731.96240	386.86972	92.2289
2	10.805	VV	0.3652	80.71348	3.04590	1.2987
3	11.978	VV	0.3284	130.80730	5.95292	2.1047
4	12.676	MM	0.2813	271.44690	16.08284	4.3677



3l

```
=====================================================================
Injection Date  : 4/26/2011 1:25:57 PM          Seq. Line :   3
Sample Name     : CSUzxd-470-3                   Location : Vial 1
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-98-2 1ML 60 MIN.M
Last changed    : 4/7/2011 6:01:37 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:22:49 PM by Rovis Group
                  (modified after loading)
=====================================================================
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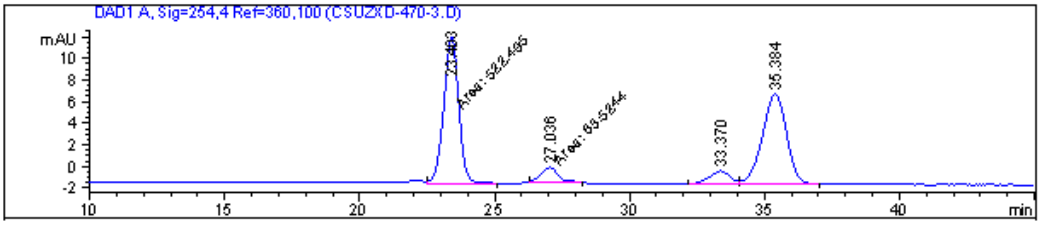

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.403	MM	0.6434	522.49506	13.53495	44.8728
2	27.036	MM	0.7547	63.52445	1.40282	5.4556
3	33.370	BV	0.8097	63.46736	1.18335	5.4507
4	35.384	VB	0.9627	514.90356	8.31217	44.2209

```
=====================================================================
Injection Date  : 4/27/2011 12:50:09 PM          Seq. Line :   1
Sample Name     : CSUzxd-475                     Location : Vial 1
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-98-2 1ML 60 MIN.M
Last changed    : 4/7/2011 6:01:37 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:22:49 PM by Rovis Group
                  (modified after loading)
=====================================================================
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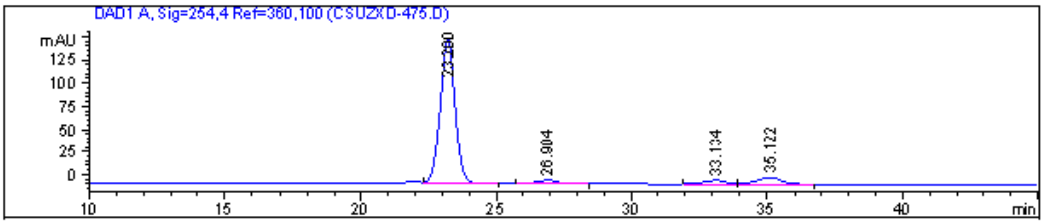
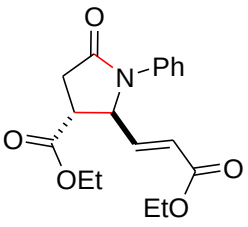
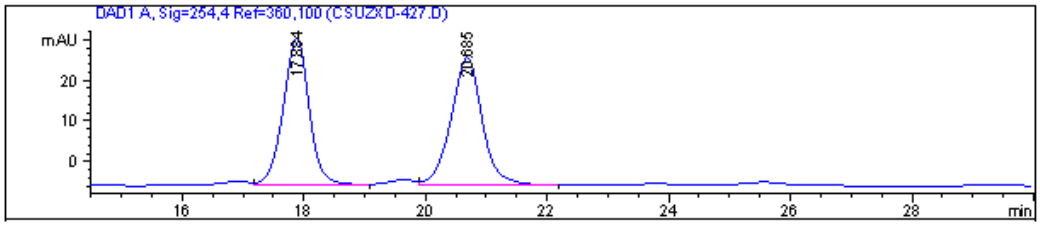


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.200	VB	0.5806	6024.03027	158.07256	87.5346
2	26.904	BB	0.8556	216.80142	3.85824	3.1503
3	33.134	BV	0.8467	212.23572	3.92621	3.0840
4	35.122	VB	0.9027	428.81522	7.28517	6.2311



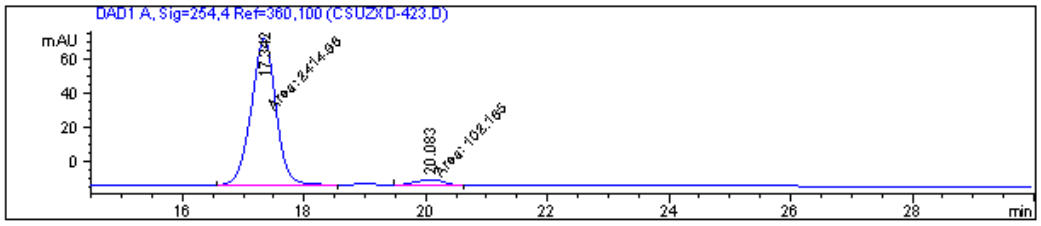
3m

```
=====================================================================
Injection Date  : 3/28/2011 12:20:06 AM          Seq. Line :   3
Sample Name     : CSUzxd-427                      Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:27:24 PM by Rovis Group
                  (modified after loading)
=====================================================================
```

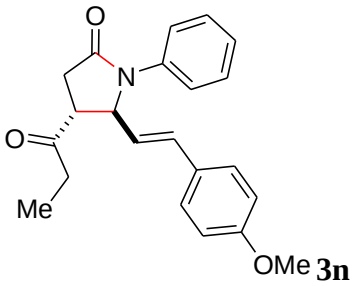


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.884	VB	0.4531	1082.12878	36.16209	49.1514
2	20.685	VB	0.5379	1119.49487	31.25508	50.8486

```
=====================================================================
Injection Date  : 3/25/2011 5:27:02 PM          Seq. Line :   1
Sample Name     : CSUzxd-423                      Location : Vial 7
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 7/16/2010 3:53:17 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 35MIN.M
Last changed    : 6/13/2011 9:27:24 PM by Rovis Group
                  (modified after loading)
=====================================================================
```



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.342	MM	0.4691	2414.97607	85.80814	95.9405
2	20.083	MM	0.5065	102.18536	3.36251	4.0595



3n

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==================================================================
Injection Date  : 5/9/2011 10:43:18 AM          Seq. Line :   1
Sample Name     : CSUzxd-494                     Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 5/9/2011 11:11:48 AM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:14:36 PM by Rovis Group
                  (modified after loading)
==================================================================
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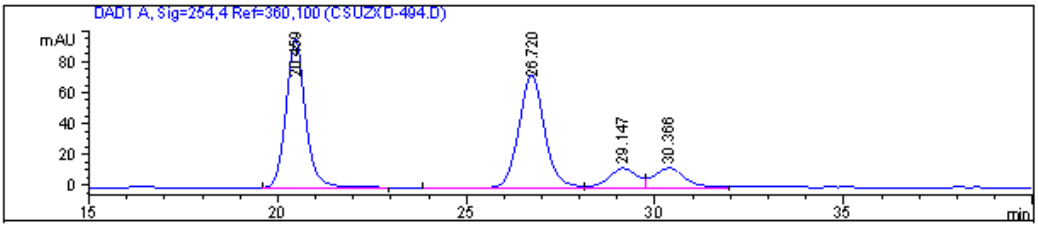

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.459	BB	0.5478	3572.74805	97.44020	42.2696
2	26.720	BV	0.7169	3497.96265	73.27803	41.3848
3	29.147	VV	0.7788	659.21631	12.59132	7.7993
4	30.366	VV	0.8581	722.36108	12.65187	8.5463

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==================================================================
Injection Date  : 5/9/2011 7:33:28 PM            Seq. Line :   2
Sample Name     : CSUzxd-496                     Location : Vial 4
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 10/9/2010 6:21:21 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:14:36 PM by Rovis Group
                  (modified after loading)
==================================================================
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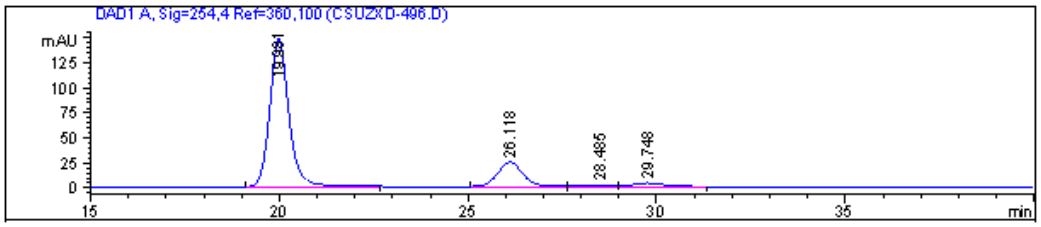
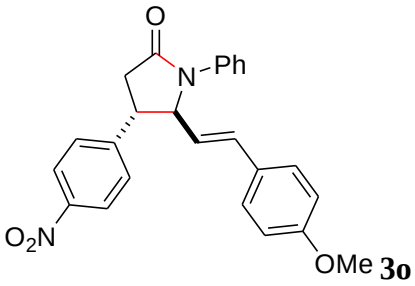


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.981	BB	0.5308	5207.87695	147.90758	78.4536
2	26.118	BV	0.7067	1134.47778	24.57097	17.0902
3	28.485	VV	0.7453	90.07835	1.74788	1.3570
4	29.748	VB	0.8629	205.73003	3.57735	3.0992



3o

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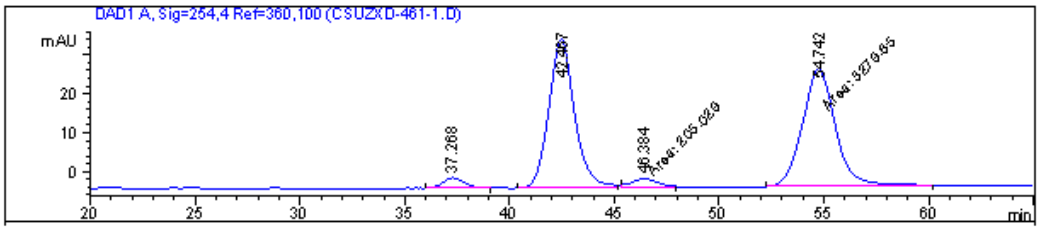
=====================================================================
Injection Date  : 4/19/2011 2:33:17 PM          Seq. Line :   2
Sample Name     : CSUzxd-461-1                   Location : Vial 3
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 40MIN.M
Last changed    : 4/19/2011 3:24:24 PM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:31:24 PM by Rovis Group
                  (modified after loading)
=====================================================================
```



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.268	BB	1.0860	195.02414	2.66417	2.8031
2	42.467	BV	1.2450	3277.79150	38.35566	47.1117
3	46.384	MM	1.5421	205.02927	2.21593	2.9469
4	54.742	MM	1.8068	3279.64526	30.25341	47.1383

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=====================================================================
Injection Date  : 4/19/2011 3:44:20 PM          Seq. Line :   3
Sample Name     : CSUzxd-455-2                   Location : Vial 4
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 3 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 65MIN.M
Last changed    : 4/19/2011 3:29:29 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\XD ODH 80-20 1ML 30MIN.M
Last changed    : 6/13/2011 8:31:24 PM by Rovis Group
                  (modified after loading)
=====================================================================
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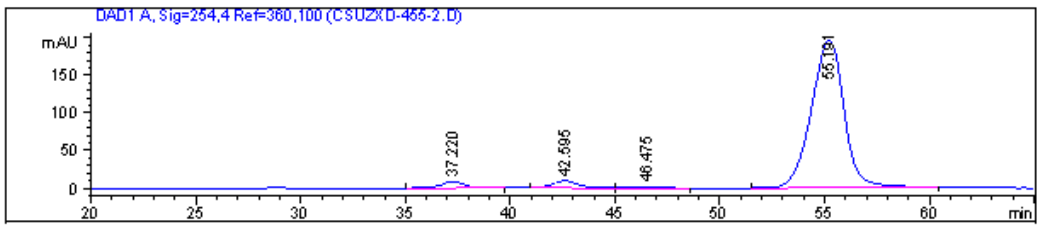
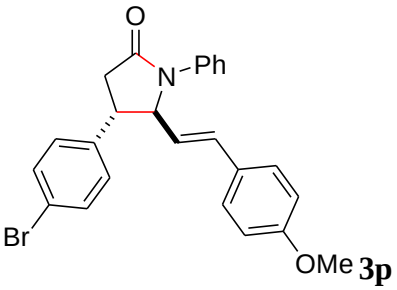


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.220	BB	1.2305	692.66302	8.43110	2.9875
2	42.595	BB	1.2901	823.07715	9.58276	3.5500
3	46.475	BV	1.1780	163.94576	1.72933	0.7071
4	55.191	BB	1.6106	2.15053e4	196.84256	92.7553



3p

```
=====================================================================
Injection Date  : 4/30/2011 8:55:35 PM          Seq. Line :   1
Sample Name     : CSuzxd-484-6                   Location : Vial 1
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD IC 50-50 1ML 40 MIN.M
Last changed    : 4/30/2011 8:50:32 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/10/2011 11:16:13 PM by Rovis Group
                  (modified after loading)
=====================================================================
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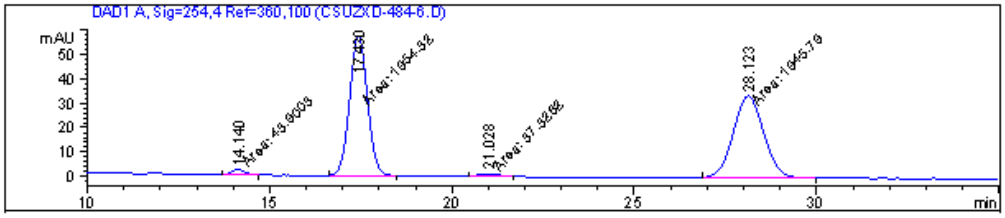

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.140	MM	0.3974	43.90025	1.84128	1.1027
2	17.430	MM	0.5684	1954.32080	57.30454	49.0870
3	21.028	MM	0.5932	37.32821	1.04873	0.9376
4	28.123	MM	0.9671	1945.79114	33.53290	48.8728

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=====================================================================
Injection Date  : 4/30/2011 9:38:32 PM          Seq. Line :   1
Sample Name     : CSUzxd-479-1                   Location : Vial 3
Acq. Operator   : Rovis Group                       Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD IC 50-50 1ML 40 MIN.M
Last changed    : 4/30/2011 8:50:32 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/10/2011 11:21:04 PM by Rovis Group
                  (modified after loading)
=====================================================================
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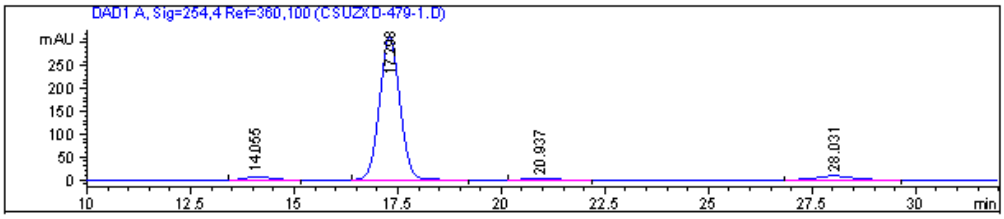
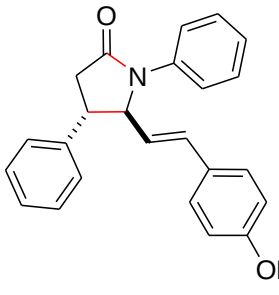


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.055	BB	0.5571	251.51779	6.59292	2.1839
2	17.298	BB	0.5258	1.06925e4	313.58862	92.8415
3	20.937	BB	0.7252	88.70139	1.85717	0.7702
4	28.031	BB	0.9115	484.21878	8.41345	4.2044



3q

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======================================================================
Injection Date  : 4/30/2011 10:22:11 PM          Seq. Line :   1
Sample Name     : CSUzxd-485-1                    Location : Vial 2
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD IC 50-50 1ML 40 MIN.M
Last changed    : 4/30/2011 8:50:32 PM by Rovis Group
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/11/2011 11:07:26 AM by Rovis Group
                  (modified after loading)
======================================================================
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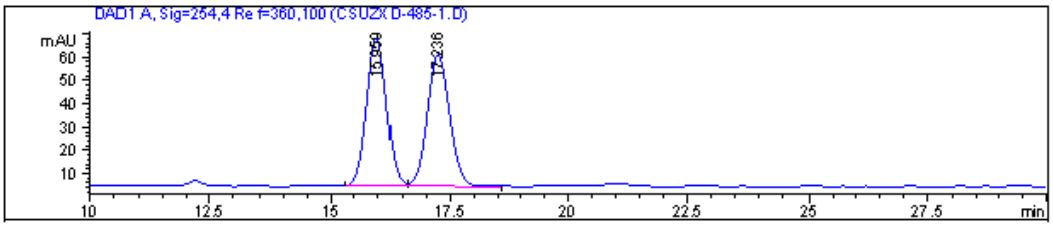

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.959	BV	0.4529	1853.68237	63.43568	49.8904
2	17.236	VB	0.5125	1861.82971	56.48634	50.1096

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======================================================================
Injection Date  : 5/2/2011 12:05:18 PM          Seq. Line :   2
Sample Name     : CSUzxd-480                      Location : Vial 4
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                  Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 6 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD IC 50-50 1ML 40 MIN.M
Last changed    : 5/2/2011 12:11:56 PM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\IA 99-1 1ML 35MIN.M
Last changed    : 6/11/2011 11:11:23 AM by Rovis Group
                  (modified after loading)
======================================================================
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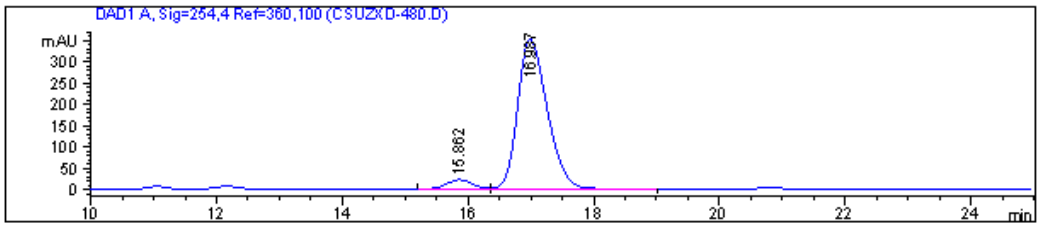
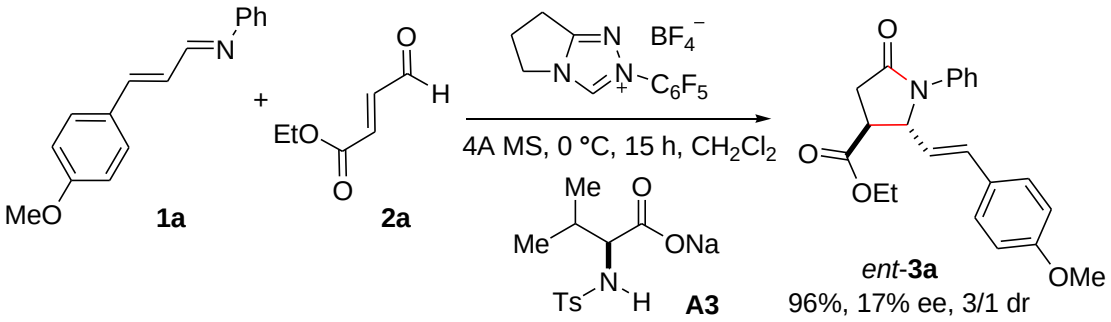
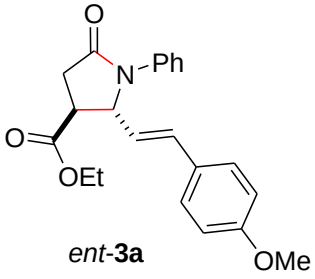


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.862	BV	0.4426	598.80872	21.13406	4.9966
2	16.987	VB	0.4990	1.13856e4	350.45380	95.0034



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======================================================================
Injection Date  : 5/23/2011 11:43:25 AM          Seq. Line :   1
Sample Name     : CSUzxd-502                      Location : Vial 1
Acq. Operator   : Rovis Group                        Inj :   1
Acq. Instrument : Instrument 1                   Inj Volume : 10 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 4 µl
Acq. Method     : D:\AGILENT HPLC\METHODS\XD-IA-90-10 1ML 30MIN.M
Last changed    : 5/23/2011 11:39:42 AM by Rovis Group
                  (modified after loading)
Analysis Method : D:\AGILENT HPLC\METHODS\IA 97-3 1ML 60MIN.M
Last changed    : 7/10/2011 3:42:12 PM by Rovis Group
                  (modified after loading)
======================================================================
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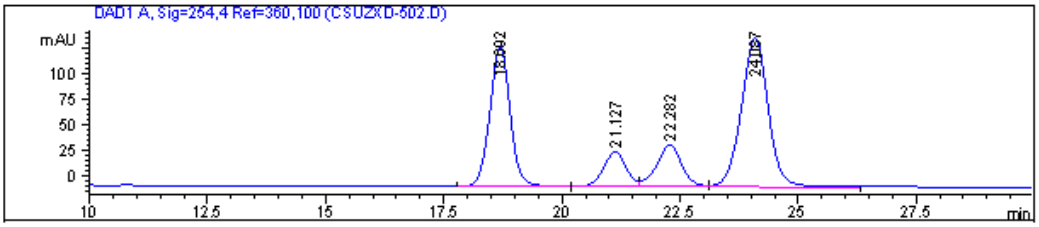

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.692	BV	0.4606	4063.42578	136.00938	32.5937
2	21.127	VV	0.5159	1143.66064	33.70366	9.1736
3	22.282	VV	0.5649	1510.32776	40.33284	12.1147
4	24.087	VV	0.6085	5749.48193	144.42230	46.1180