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Highly Enantioselective Synthesis of β -Amino Acid Derivatives by the Lewis Base Catalyzed Hydrosilylation of β -Enamino Esters

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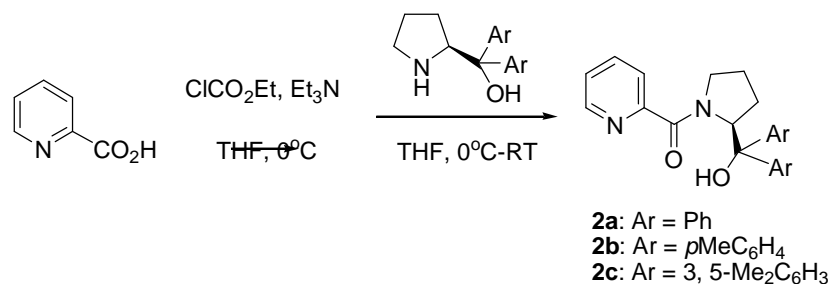
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? .General Information.

All starting materials were of the highest commercially available grade and used without further purification. All solvents used in the reactions were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography using silica gel HSGF254 plates. Flash chromatography (FC) was performed using silica gel HG/T2354-92. ^1H and ^{13}C NMR (300 and 75 MHz, respectively) spectra were recorded in CDCl_3 . ^1H NMR chemical shifts are reported in ppm (**d**) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl_3 , **d** = 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl_3 , **d** = 77.0 ppm). ESI HRMS spectra were recorded on BioTOF Q. HPLC analysis was performed on Waters-Breeze (2487 Dual ? Absorbance Detector and 1525 Binary HPLC Pump). Chiralpak AD, OD and OJ columns were purchased from Daicel Chemical Industries (Hong Kong, China). Optical rotations were measured on a Perkin-Elmer 341 Polarimeter at λ = 589 nm (c g/100ml). All enantiomer ratios have been controlled by coinjections of the pure sample with the racemic substrates.

? . synthesis of catalysts

Synthesis of catalysts 2a, 2b and 2c.



A solution of ethyl chloroformate (0.1 mL, 1 mmol) in dry THF (2 mL) was dropped in a solution of 2-picolinic acid (123 mg, 1 mmol) and triethylamine (0.15 mL, 1 mmol) in dry THF (25 mL) at 0° within 15 min. The resulting mixture was stirred for 1h before 1 mmol of chiral aminoalcohol in dry THF (10 mL) was added dropwisely. The mixture was stirred at 0° for 1h and then at room temperature for overnight. The mixture was quenched with water. The aqueous layer was extracted with ethyl acetate (3×15 mL) and the combined organic layer was dried over MgSO_4 for 2h, filtered and concentrated under reduced pressure. The resulting residue was subject to flash chromatography (eluant: ethyl acetate/petroleum ether = 1/2 to 1/1) to give the pure catalysts.

(S)-(2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (**2a**)^[1]: White solid, prepared from (*S*)- diphenyl(pyrrolidin-2-yl)methanol and 2-picolinic acid, yield 73%. ^1H NMR (300 MHz, CDCl_3 , TMS) **d** = 8.56 and 8.26 (2×br s, 1H), 7.71-7.77 (m, 1H), 7.15-7.52 (m, 12H), 6.69 (s, 1H), 5.42-5.50 (m, 1H), 3.19-3.97 (m, 2H), 2.03-2.14 (m, 2H), 1.50-1.82 (m, 1H), 0.75-1.25 (m, 1H).

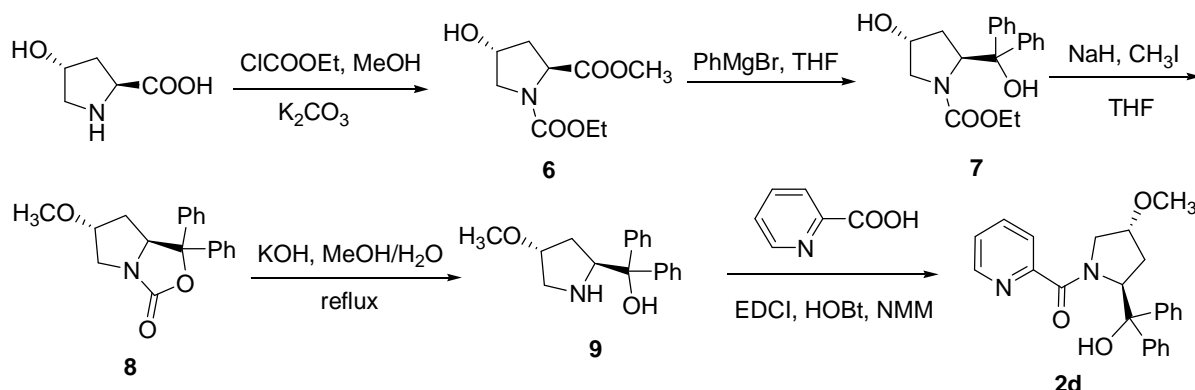
(S)-(2-(hydroxydip-tolylmethyl)pyrrolidin-1-yl)(pyridin-2-yl)methanone (**2b**): Prepared from (*S*)- pyrrolidin-2-yl-di-*p*-tolylmethanol and 2-picolinic acid, yield 76%. White solid , mp =

164.0-165.5 δ , $[\alpha]_D^{20} = -119.2$ ($c = 0.2$, CHCl_3). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 8.56$ and 8.27 (2 \times br s, 1H), 7.70-7.75 (m, 1H), 7.60 (br, 1H), 7.11-7.52 (m, 9H), 6.48 (s, 1H), 5.57 and 5.42 (2 \times br s, 1H), 3.54 and 3.96 (2 \times br s, 1H), 3.17 and 3.31 (2 \times br s, 1H), 2.34 (s, 3H), 2.32 (s, 3H), 2.13 (br s, 1H), 1.97-2.01 (m, 1H), 1.57 (br s, 1H), 1.21 and 0.95 (m, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): $\delta = 20.9$, 21.0, 23.9, 29.3, 48.2, 50.6, 64.9, 67.2, 81.8, 123.3, 124.7, 125.5, 127.1, 127.5, 127.9, 128.2, 128.5, 136.6, 137.3, 140.4, 143.2, 145.8, 148.4, 154.2, 169.9. ESI-HRMS exact mass calcd. for $(\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_2 + \text{Na})^+$ requires m/z 409.1886, found m/z 409.1892.

(S)-(2-(bis(3,5-dimethylphenyl)(hydroxy)methyl)pyrrolidin-1-yl)(pyridin-2-yl)methanone

(2c): Prepared from (S)-bis(3,5-dimethylphenyl)(pyrrolidin-2-yl)methanol and 2-picolinic acid, yield 75%. White solid, mp = 182.0-183.5 δ , $[\alpha]_D^{20} = -83.2$ ($c = 0.2$, CHCl_3). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 8.56$ and 8.30 (2 \times br s, 1H), 7.49-7.72 (br, 2H), 7.25-7.29 (m, 1H), 6.70-7.26 (m, 7H), 5.41-5.57 (br, 1H), 2.80-3.98 (m, 2H), 2.0-2.3 (m, 14H), 1.58 (br s, 1H), 1.0-1.21 (m, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): $\delta = 21.1$, 21.4, 21.7, 23.9, 29.2, 48.1, 50.6, 64.9, 66.9, 82.2, 123.1, 124.5, 125.4, 125.9, 128.6, 136.7, 137.0, 1423.0, 145.7, 148.5, 154.2, 169.8. ESI-HRMS exact mass calcd. for $(\text{C}_{27}\text{H}_{30}\text{N}_2\text{O}_2 + \text{Na})^+$ requires m/z 437.2199, found m/z 437.2200.

Synthesis of catalysts 2d^[2]



Synthesis of (2S,4R)-1-ethyl 2-methyl 4-hydroxypyrrolidine-1,2-dicarboxylate (6)

(2S,4R)-4-hydroxyproline (13.1 g, 0.1 mol), K_2CO_3 (27.5 g, 0.2 mol) and 150 mL of methanol were added into a two necked flask. The mixture was cooled to 0 $^\circ$. Then ethyl chloroformate (29 mL, 0.3 mol) was added dropwise to the mixture. After the addition, the ice bath was removed and the mixture was allowed to stirred at RT for 48h. The solvent was removed at reduced pressure, the residue was dissolved in water and extracted with DCM (3 \times 25 mL). The combined organic layer was dried over Na_2SO_4 . The N,O-protected product **6** was obtained in 98% yield as a slightly yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 4.42$ -4.47 (m, 2H), 4.07-4.14 (m, 2H), 3.70-3.74 (m, 3H), 3.40-3.60 (m, 2H), 3.90 (brs, 1H), 2.20-2.38 (m, 1H), 2.02-2.08 (m, 1H), 1.14-1.28 (m, 3H).

Synthesis of (2S,4R)-ethyl 4-hydroxy-2-(hydroxydiphenylmethyl)pyrrolidine-1-carboxylate (7)

To a solution of PhMgBr (100 mmol) in THF was added **6** (4.34 g, 20 mmol) in 10 mL of THF dropwisely at 0 $^\circ$ for 1h. The mixture was stirred at RT for 8h and quenched with saturated NH_4Cl . The organic phase was separated and dried over anhydrous Na_2SO_4 . Removal of the solvent gave a yellow solid. Recrystallization from EtOAc afforded **7** as a white solid (2.4 g, 37%). $^1\text{H NMR}$ (300 MHz,

CDCl₃, TMS) δ = 7.27-7.42 (m, 10H), 5.05-5.10 (m, 1H), 3.87-4.07 (m, 3H), 3.50-3.54(m, 1H), 2.96-2.99(m, 1H), 2.02-2.16(m, 3H), 1.12(t, $J=7.0$, 3H).

Synthesis of (6*R*,7*aS*)-6-methoxy-1,1-diphenyl-tetrahydropyrrolo[1,2-*c*]oxazol-3(1H)-one (**8**)

A solution of **7** (341 mg, 1 mmol) and CH₃I (0.5 mL, 8 mmol) in THF was cooled to 0°, then NaH (53 mg, 1.3 mmol) was added. After being stirred for 6h, the reaction solution was quenched with saturated NH₄Cl. The organic phase was separated, and the aqueous was extracted with DCM (3×20 mL). The organic phase was combined and dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (1/5 to 1/1 of EtOAc/ hexane as eluent) to give the product **8** as a white solid (260 mg, 84%). ¹H NMR (300 MHz, CDCl₃, TMS) δ = 7.64-7.65 (m, 2H), 7.56-7.62 (m, 2H), 7.29-7.36 (m, 4H), 7.20-7.24 (m, 2H), 4.56 (dd, $J = 6.6\text{Hz}$, $J = 9.8\text{ Hz}$, 1H), 3.83 (br s, 1H), 3.26 (s, 3H), 3.02-3.10 (m, 2H), 1.74-1.79 (m, 1H), 1.60-1.67 (m, 1H).

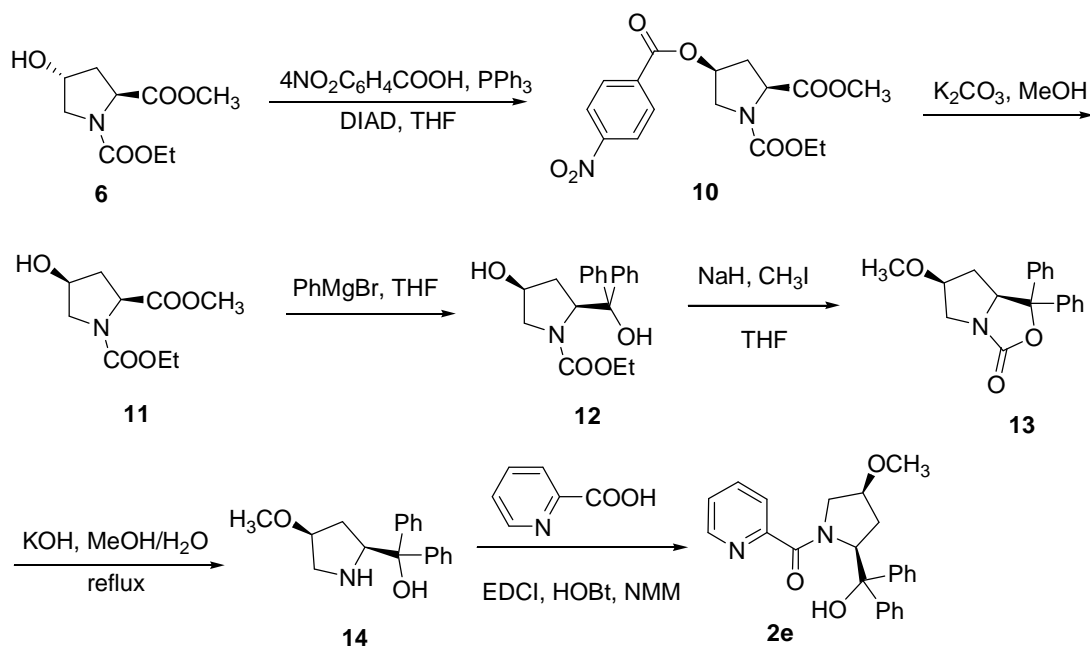
Synthesis of ((2*S*,4*R*)-4-methoxypyrrolidin-2-yl)diphenylmethanol (**9**)

8 (260 mg, 0.84 mmol) and KOH (188 mg, 3.36 mmol) was dissolved in 10 mL of MeOH and 5 mL of H₂O. The mixture was refluxed for 24h. The solvent was removed in vacuo and the residue was extracted with DCM (3×15 mL). The combined organic phase was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give **9** (220 mg, 96%), which was used without further purification.

Synthesis of ((2*S*,4*R*)-2-(hydroxydiphenylmethyl)-4-methoxypyrrolidin-1-yl)(pyridin-2-yl)methanone (**2d**)

To a solution of **9** (174 mg, 0.6 mmol) and 2-picolinic acid (74mg, 0.6mmol) in DCM (20 mL) was added HOBt (175 mg, 1.2 mmol), NMM (1 mL) and EDCI (230 mg, 1.2 mmol) at 0°. After being stirred at room temperature for 12h. The reaction solution was washed with aqueous HCl (1.0N, 10 mL), NaHCO₃ (2N, 10 mL) and brine (10 mL). The organic phase was dried over anhydrous Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give the residue, which was purified through chromatography on silica gel (eluent: hexane/EtOAc = 5/1 to 1/1) to give **2d** (180 mg, 75%) as a white solid. Mp = 200.3-203.0 °C, $[\alpha]_{\text{D}}^{20} = -54.0$ ($c = 0.2$ in CHCl₃). ¹H NMR (300 MHz, CDCl₃, TMS) δ = 8.30-8.54 (m, 1H), 7.70-7.74 (m, 1H), 7.59-7.62 (m, 1H), 7.25-7.56 (m, 12H), 6.42 (br s, 1H), 5.56-5.89 (br, 1H), 3.73-3.76 (m, 1H), 3.19-3.45 (m, 2H), 3.10 (s, 3H), 2.18-2.48 (m, 2H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 35.4, 53.4, 53.8, 55.5, 56.2, 66.1, 77.2, 78.6, 81.8, 123.9, 124.8, 126.1, 126.3, 127.3, 127.4, 127.7, 127.8, 127.9, 128.6, 136.8, 143.1, 145.6, 148.1, 153.6. ESI-HRMS exact mass calcd. for (C₂₄H₂₄N₂O₃ + Na)⁺ requires m/z 411.1679, found m/z 411.1689.

Synthesis of catalyst **2e**



Synthesis of (2*S*,4*R*)-1-ethyl 2-methyl 4-(4-nitrobenzoyloxy)pyrrolidine-1,2-dicarboxylate (**10**)

4-Nitrobenzoic acid (1.2 g, 7 mmol), triphenylphosphine (1.84 g, 7 mmol) and **6** (1.1 g, 5 mmol) were dissolved in 25 mL of anhydrous THF. The solution was cooled to 0°. Then a solution of DIAD (1.42 g, 7 mmol) in 5 mL of THF was added dropwise. After the addition, the mixture was stirred at 0° for 12h. Then the reaction was quenched with aqueous NH₄Cl and extracted with DCM (3×15mL). The organic phase was combined and washed with NaOH (1N), H₂O, brine respectively, then dried over Na₂SO₄. The solvent was removed in vacuo. The residue was purified by recrystallization from EtOH to afford **10** as a yellow solid in 76% yield. ¹H NMR (300 MHz, CDCl₃, TMS) δ = 8.27-8.30 (m, 2H), 8.13-8.16 (m, 2H), 5.60 (br s, 1H), 4.55-4.67 (m, 1H), 4.13-4.22 (m, 2H), 3.80-3.87 (m, 2H), 3.68 (d, *J* = 7.4 Hz, 3H), 2.51-2.56 (m, 2H), 1.21-1.31 (m, 3H).

Synthesis of (2*S*,4*S*)-1-ethyl 2-methyl 4-hydroxypyrrrolidine-1,2-dicarboxylate (**11**)

The mixture of **10** (1.1 g, 3 mmol), K₂CO₃ (1.0 g, 7 mmol) and 20 mL of MeOH was stirred for 6h at RT. Then the mixture was dissolved in water and extracted with DCM (3×20 mL). Removal of the solvent gave the crude product, which was subjected to FC (eluent: petroleum ether/ethyl acetate = 5/1 to 1/1) to give **11** as a colorless oil in 60% yield. ¹H NMR (300 MHz, CDCl₃, TMS) δ = 4.33-4.41 (m, 2H), 4.09-4.17 (m, 2H), 3.76 (d, *J* = 5.8 Hz, 3H), 3.55-3.65 (m, 2H), 3.25-3.48 (m, 1H), 2.30-2.34 (m, 1H), 2.06-2.14 (m, 1H), 1.16-1.27 (m, 3H).

Synthesis of **12-2e**

The procedures of synthesis of **12-2e** are similar to those of **7-2d**.

(2*S*,4*S*)-ethyl 4-hydroxy-2-(hydroxydiphenylmethyl)pyrrolidine-1-carboxylate (12**):** Yield = 33%, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 7.49-7.52 (m, 2H), 7.15-7.41 (m, 8H), 4.96 (d, *J* = 8.6 Hz, 1H), 4.69 (br, 1H), 4.35 (br, 1H), 3.96-4.09 (m, 2H), 3.76 (br, 1H), 3.40-3.44 (m, 1H), 2.26-2.36 (m, 1H), 1.85 (d, *J* = 14.8 Hz, 1H), 0.89 (br, 3H).

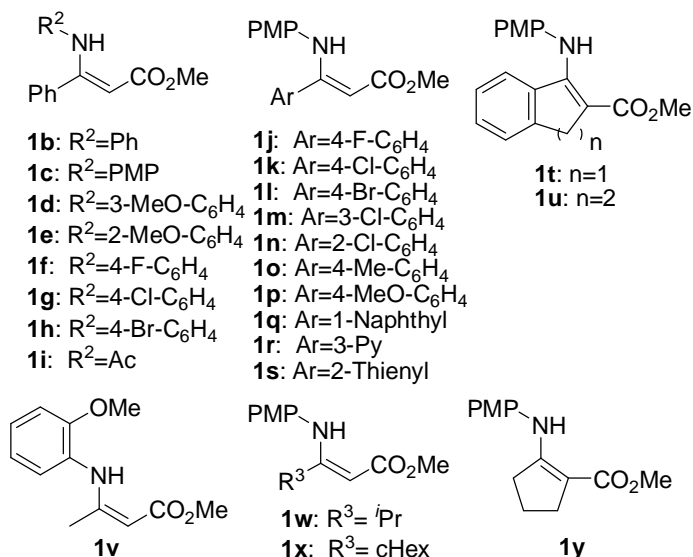
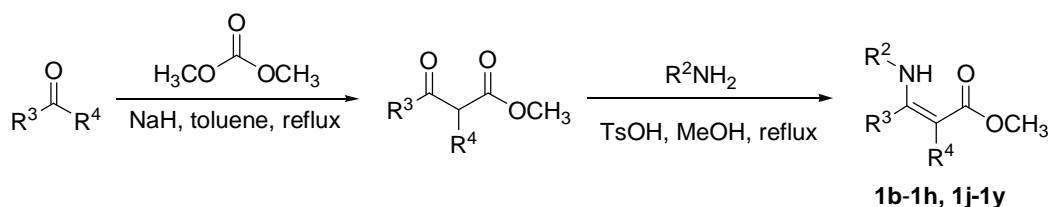
(6*S*,7*aS*)-6-methoxy-1,1-diphenyl-tetrahydropyrrolo[1,2-c]oxazol-3(1H)-one (13**):** Yield = 85%, White solid, mp = 141.0-143.6 °C, [α]_D²⁰ = -230.4 (c = 0.2 in CHCl₃). ¹H NMR (300 MHz,

CDCl₃, TMS) d = 7.50-7.53 (m, 2H), 7.26-7.38 (m, 8H), 4.63 (dd, *J* = 7.4 Hz, *J* = 8.7 Hz, 1H), 4.00-4.02 (m, 1H), 3.88 (dd, *J* = 2.8 Hz, *J* = 12.5 Hz, 1H), 3.02-3.26 (m, 1H), 3.17 (s, 3H), 2.01-2.10 (m, 1H), 1.36-1.43 (m, 1H). ¹³C-NMR (75 MHz, CDCl₃, TMS): d = 35.4, 52.0, 56.9, 67.5, 81.0, 86.2, 125.7, 126.0, 127.8, 128.4, 128.6, 140.0, 143.3, 160.4. ESI-HRMS exact mass calcd. for (C₁₉H₁₉NO₃ + Na)⁺ requires m/z 332.1257, found m/z 332.1248.

((2*S*,4*S*)-2-(hydroxydiphenylmethyl)-4-methoxypyrrolidin-1-yl)(pyridin-2-yl)methanone

(2e): Yield = 54% (two steps) White solid, mp = 190.6-191.8 °C, [α]_D²⁰ = +49.0 (c = 0.2 in CHCl₃). ¹H NMR (300 MHz, [D₆]DMSO, TMS) d = 8.37 and 8.57 (2×brs, 1H), 6.62-7.78 (m, 13H), 6.03 and 6.39 (2×brs, 1H), 5.48 (brs, 1H), 4.12-4.28 (m, 1H), 3.64-3.80 (m, 2H), 3.15-3.25 (m, 3H), 2.31-2.50 (m, 1H), 1.84-1.97 (m, 1H). ¹³C-NMR (75 MHz, [D₆]DMSO, TMS): d = 33.0, 34.1, 53.1, 54.6, 56.4, 63.0, 77.8, 80.1, 123.7, 124.4, 125.9, 126.2, 126.4, 126.8, 127.7, 136.4, 143.8, 145.1, 146.0, 148.0, 153.1, 161.5, 161.5, 165.7, 167.4. ESI-HRMS exact mass calcd. for (C₂₄H₂₄N₂O₃ + Na)⁺ requires m/z 411.1679, found m/z 411.1670.

? . Typical procedure for the synthesis of β-keto esters^[3] and *N*-aryl β-enamino esters^[4].



To a dried three-necked flask equipped with a dropping funnel, a condenser, and a magnetic stirrer was added NaH (7.1 g, 95%, 280 mmol), dimethyl carbonate (18.0 g, 200 mL), and toluene (100 mL). The mixture was heated to reflux. A solution of ketone (100 mmol) in toluene (50 mL) was added dropwise from the dropping funnel over 1-2 h. After the addition, the mixture was heated to reflux until the evolution of hydrogen ceased (15-20 min). When the reaction was cooled to room temperature, glacial acetic acid (30 mL) was added dropwise and a heavy, pasty solid appeared. Ice-water was added until the solid was dissolved completely. The toluene layer was separated, and

the water layer was washed with toluene (3×100 mL). The combined toluene solution was washed with water (100 mL) and brine (100 mL), then dried over Na₂SO₄. After evaporation of the solvent, the mixture was distilled under reduced pressure or subjected chromatography to give the desired β-keto esters in 80-95% yield.

A mixture of β-keto ester (10 mmol), arylamine (10 mmol) and *p*-toluenesulfonic acid monohydrate (0.19 g, 1 mmol) was dissolved in 10 mL of methanol and refluxed overnight. After the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure. The residue was dissolved with 30mL EtOAc and washed with water and brine. The organic phase was separated and dried over Na₂SO₄. The mixture was subsequently filtered and the solvents were removed in vacuo. The crude product was purified by FC to give the pure *N*-arylβ-enamino esters.

(Z)-methyl 3-phenyl-3-(phenylamino)acrylate (1b)^[51]: Yield = 55%, yellow solid, mp = 72.5-73.0 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.28 (br s, 1H), 7.26-7.36 (m, 5H), 7.06-7.11 (m, 2H), 6.88-6.93 (m, 1H), 6.66-6.69 (m, 1H), 5.00 (s, 1H), 3.75 (s, 3H).

(Z)-methyl 3-(4-methoxyphenylamino)-3-phenylacrylate (1c): Yield = 50%, Yellow solid, mp = 94.4-96.7 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.22 (br s, 1H), 7.22-7.34 (m, 5H), 6.63-6.65 (m, 4H), 4.93 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.69 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ¹³C-NMR (75 MHz, CDCl₃): δ = 50.6, 55.3, 88.9, 113.8, 124.3, 128.2, 128.3, 129.2, 133.3, 135.9, 155.8, 160.0, 170.6. ESI-HRMS exact mass calcd. for (C₁₇H₁₇NO₃ + Na)⁺ requires *m/z* 306.1101, found *m/z* 306.1105.

(Z)-methyl 3-(3-methoxyphenylamino)-3-phenylacrylate (1d): Yield = 55%, yellow solid, mp = 48.5-50.6 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.27 (br s, 1H), 7.26-7.37 (m, 5H), 6.99 (t, *J* = 8.1 Hz, 1H), 6.49- 6.50 (m, 1H), 6.28 (m, 1H), 6.17 (t, *J* = 2.2 Hz, 1H), 5.00 (s, 1H), 3.74 (s, 3H), 3.55 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.7, 55.0, 90.8, 107.5, 109.1, 114.5, 128.1, 128.5, 129.3, 129.5, 136.0, 141.4, 159.0, 159.7, 170.4. ESI-HRMS exact mass calcd. for (C₁₇H₁₇NO₃ + Na)⁺ requires *m/z* 306.1101, found *m/z* 306.1104.

(Z)-methyl 3-(2-methoxyphenylamino)-3-phenylacrylate (1e): Yield = 51%, yellow solid, mp = 115.6-117.5 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.27 (br s, 1H), 7.26-7.37 (m, 5H), 6.84-6.87 (m, 2H), 6.51-6.52 (m, 1H), 6.20-6.23 (m, 1H), 5.00 (s, 1H), 3.90 (s, 3H), 3.75 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.7, 55.7, 90.9, 110.4, 119.8, 121.8, 122.9, 127.9, 128.3, 129.3, 129.4, 136.2, 150.4, 158.5, 170.1. ESI-HRMS exact mass calcd. for (C₁₇H₁₇NO₃ + Na)⁺ requires *m/z* 306.1101, found *m/z* 306.1097.

(Z)-methyl 3-(4-fluorophenylamino)-3-phenylacrylate (1f): Yield = 65%, yellow solid, mp = 135.6-138.0 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.25 (br s, 1H), 7.30-7.36 (m, 5H), 7.02-7.05 (m, 2H), 6.57-6.60 (m, 2H), 5.03 (s, 1H), 3.75 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.7, 90.4, 115.2 (d, *J* = 22.5 Hz), 124.1 (d, *J* = 8.0 Hz), 128.3, 128.4, 129.5, 135.6, 136.4 (d, *J* = 2.7 Hz), 158.9 (d, *J* = 241 Hz), 159.4, 170.5. ESI-HRMS exact mass calcd. for (C₁₆H₁₄FNO₂ + Na)⁺ requires *m/z* 294.0901, found *m/z* 294.0910.

(Z)-methyl 3-(4-chlorophenylamino)-3-phenylacrylate (1g): Yield = 60%, yellow solid, mp = 94.7-96.7 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.24 (br s, 1H), 7.30-7.37 (m, 5H), 7.15-7.19 (m, 2H), 6.50-6.54 (m, 2H), 5.03 (s, 1H), 3.74 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.8,

91.4, 123.3, 128.1, 128.2, 128.6, 128.7, 129.6, 135.5, 139.0, 158.7, 170.4. ESI-HRMS exact mass calcd. for (C₁₆H₁₄ClNO₂ + H)⁺ requires m/z 288.0786, found m/z 288.0790.

(Z)-methyl 3-(4-bromophenylamino)-3-phenylacrylate (1h): Yield = 61%, yellow solid, mp = 159.1-161.8 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.24 (br s, 1H), 7.30-7.37 (m, 25H), 7.15-7.19 (m, 2H), 6.50-6.54 (m, 2H), 5.03 (s, 1H), 3.74 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.8, 91.5, 115.8, 123.5, 128.1, 128.6, 129.7, 131.6, 135.4, 139.5, 158.6, 170.3. ESI-HRMS exact mass calcd. for (C₁₆H₁₄BrNO₂ + H)⁺ requires m/z 354.0100, found m/z 354.0092.

(Z)-methyl 3-acetamido-3-phenylacrylate (1i)^[6]: Synthesized according to the literature method.^[5] Yellow oil, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.64 (s, 1H), 7.38-7.40 (m, 5H), 5.28 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.16 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

(Z)-methyl 3-(4-fluorophenyl)-3-(4-methoxyphenylamino)acrylate (1j): Yield = 56%, yellow solid, mp = 92.3-94.1 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.16 (br s, 1H), 7.26-7.31 (m, 2H), 6.91-6.98 (m, 2H), 6.63-6.65 (m, 4H), 4.90 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.3, 89.0, 113.9, 115.4 (d, *J* = 21.6 Hz), 124.5, 130.5 (d, *J* = 8.3 Hz), 131.9 (d, *J* = 3.2 Hz), 133.1, 156.0, 158.9, 161.4, 164.7, 170.5. ESI-HRMS exact mass calcd. for (C₁₇H₁₇NO₃ + Na)⁺ requires m/z 324.1006, found m/z 324.1019.

(Z)-methyl 3-(4-chlorophenyl)-3-(4-methoxyphenylamino)acrylate (1k): Yield = 60%, yellow solid, mp = 123.7-126.0 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.14 (br s, 1H), 7.24-7.26 (m, 4H), 6.63-6.65 (m, 4H), 4.91 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.3, 89.3, 113.9, 124.5, 128.6, 129.6, 133.0, 134.4, 135.2, 156.0, 158.7, 170.4. ESI-HRMS exact mass calcd. For (C₁₇H₁₆ClNO₃ + H)⁺ requires m/z 318.0891, found m/z 318.0889.

(Z)-methyl 3-(4-bromophenyl)-3-(4-methoxyphenylamino)acrylate (1l): Yield = 58%, yellow solid, mp = 133.5-135.6 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.16 (br s, 1H), 7.26-7.31 (m, 2H), 6.92-6.98 (m, 2H), 6.63-6.65 (m, 4H), 4.90 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.7, 55.3, 89.3, 114.0, 123.5, 124.5, 129.9, 131.5, 133.0, 134.9, 156.0, 158.7, 170.4. ESI-HRMS exact mass calcd. for (C₁₇H₁₇BrNO₃ + H)⁺ requires m/z 362.0386, found m/z 362.0387.

(Z)-methyl 3-(3-chlorophenyl)-3-(4-methoxyphenylamino)acrylate (1m): Yield = 52%, viscous liquid, solidified by standing, mp = 75.4-76.8 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.12 (br s, 1H), 7.35-7.36 (m, 1H), 7.26-7.29 (m, 1H), 7.13-7.17 (m, 2H), 6.64-6.66 (m, 4H), 4.92 (s, 1H), 3.73 (s, 3H), 3.73 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.2, 89.6, 113.9, 124.4, 126.5, 128.2, 129.3, 129.4, 132.9, 134.2, 137.7, 156.0, 158.3, 170.3. ESI-HRMS exact mass calcd. for (C₁₇H₁₆ClNO₃ + Na)⁺ requires m/z 340.0771, found m/z 340.0695.

(Z)-methyl 3-(2-chlorophenyl)-3-(4-methoxyphenylamino)acrylate (1n): Yield = 58%, yellow solid, mp = 91.5-93.5 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.35 (br s, 1H), 7.34-7.35 (m, 1H), 7.25-7.30 (m, 3H), 6.61-6.70 (m, 4H), 4.78 (s, 1H), 3.77 (s, 3H), 3.71 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.2, 88.0, 113.7, 124.0, 126.6, 129.8, 130.1, 130.7, 132.5, 135.0, 156.2, 157.7, 170.5. ESI-HRMS exact mass calcd. for (C₁₇H₁₆ClNO₃ + Na)⁺ requires m/z 340.0771, found m/z 340.0693.

(Z)-methyl 3-(4-methoxyphenylamino)-3-p-tolylacrylate (1o): Yield = 50%, yellow solid, mp = 74.5-76.8 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.18 (br s, 1H), 7.18-7.26 (m, 2H), 7.05-7.08 (m, 2H), 6.64-6.66 (m, 4H), 4.92 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.32 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 21.3, 50.5, 55.3, 88.6, 113.8, 124.3, 128.2, 129.0, 132.9, 133.5, 139.4, 155.8, 160.1, 170.6. ESI-HRMS exact mass calcd. For (C₁₈H₁₉NO₃ + H)⁺ requires m/z 298.1438, found m/z 298.1448.

(Z)-methyl 3-(4-methoxyphenyl)-3-(4-methoxyphenylamino)acrylate (1p): Yield = 46%, yellow solid, mp = 91.4-93.0 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.17 (br s, 1H), 7.22-7.26 (m, 2H), 6.75-7.79 (m, 2H), 6.64-6.65 (m, 4H), 4.91 (s, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.5, 55.1, 55.3, 88.3, 113.6, 113.8, 124.3, 128.0, 129.8, 133.6, 155.7, 159.7, 160.3, 170.6. ESI-HRMS exact mass calcd. for (C₁₈H₁₉NO₄ + Na)⁺ requires m/z 336.1206, found m/z 336.1210.

(Z)-methyl 3-(4-methoxyphenylamino)-3-(naphthalen-2-yl)acrylate (1q): Yield = 43%, yellow solid, mp = 92.6-94.7 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.30 (br s, 1H), 7.96 (s, 1H), 7.77-7.83 (m, 2H), 7.66-7.69 (d, *J* = 8.6 Hz, 1H), 7.48-7.51 (m, 2H), 7.28-7.32 (m, 1H), 6.67-6.71 (m, 2H), 6.58-6.62 (m, 2H), 5.09 (s, 1H), 3.77 (s, 3H), 3.66 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.2, 89.4, 113.9, 124.2, 125.6, 126.4, 126.9, 127.6, 127.7, 127.9, 128.3, 132.9, 133.3, 133.4, 133.6, 155.8, 159.8, 170.6. ESI-HRMS exact mass calcd. for (C₂₁H₁₉NO₃ + Na)⁺ requires m/z 356.1257, found m/z 356.1250.

(Z)-methyl 3-(4-methoxyphenylamino)-3-(pyridin-3-yl)acrylate (1r): Yield = 35%, orange solid, mp = 102.8-105.4 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.14 (br s, 1H), 8.58-8.59 (m, 1H), 8.52-8.54 (m, 1H), 7.53-7.56 (m, 1H), 6.64-6.65 (m, 4H), 4.94 (s, 1H), 3.74 (s, 3H), 3.70 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.7, 55.3, 89.9, 114.2, 122.9, 125.1, 131.9, 132.6, 135.7, 149.1, 150.2, 156.6, 156.7, 170.3. ESI-HRMS exact mass calcd. for (C₁₆H₁₆N₂O₃ + Na)⁺ requires m/z 307.1053, found m/z 307.1060.

(Z)-methyl 3-(4-methoxyphenylamino)-3-(thiophen-2-yl)acrylate (1s): Yield = 46%, light yellow solid, mp = 68.5-71.0 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.04 (br s, 1H), 7.26-7.28 (m, 1H), 6.98-7.00 (m, 1H), 6.88-6.90 (m, 1H), 6.80-6.82 (m, 2H), 6.69-6.72 (m, 2H), 5.13 (s, 1H), 3.74 (s, 3H), 3.73 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 50.6, 55.3, 88.9, 113.9, 114.2, 125.3, 127.0, 127.6, 129.0, 133.4, 153.1, 156.5, 170.4. ESI-HRMS exact mass calcd. for (C₁₅H₁₅NO₃ S + Na)⁺ requires m/z 312.0665, found m/z 312.0663.

Methyl 3-(4-methoxyphenylamino)-1H-indene-2-carboxylate (1t): Yield = 45%, yellow solid, mp = 107.0-108.6 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 9.14 (br s, 1H), 7.44-7.46 (d, *J* = 7.6 Hz, 1H), 7.26-7.32 (m, 1H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 4H), 3.85 (s, 3H), 3.83 (s, 3H), 3.63 (s, 2H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 34.6, 50.6, 55.5, 100.2, 114.1, 123.8, 124.6, 125.7, 127.0, 128.2, 133.2, 137.5, 145.1, 156.5, 157.6, 168.6. ESI-HRMS exact mass calcd. for (C₁₈H₁₇NO₃ + Na)⁺ requires m/z 318.1101, found m/z 318.1105.

Methyl 1-(4-methoxyphenylamino)-3,4-dihydronaphthalene-2-carboxylate (1u): Yield = 42%, yellow solid, mp = 92.6-94.7 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.13 (br s, 1H), 7.17-7.22 (m, 3H), 6.96-6.99 (m, 1H), 6.69-6.76 (m, 4H), 3.79 (s, 3H), 3.73 (s, 3H), 2.76-2.86 (m, 2H), 2.56-2.61 (m, 2H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 22.1, 29.0, 51.1, 55.3, 102.6, 114.0, 123.0, 125.5, 127.4, 128.0, 128.9, 129.8, 136.5, 140.1, 151.7, 155.2, 170.4. ESI-HRMS exact mass calcd. for (C₁₉H₁₉NO₃ + Na)⁺ requires m/z 332.1257, found m/z 332.1258.

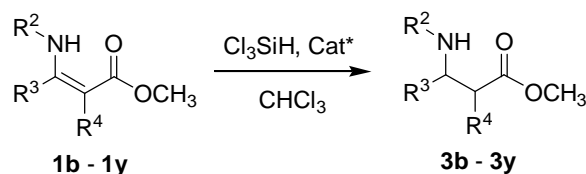
(Z)-methyl 3-(2-methoxyphenylamino)but-2-enoate (1v): Yield = 45%, colorless oil, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.27 (brs, 1H), 7.08-7.14 (m, 2H), 6.87-6.92 (m, 2H), 4.76 (s, 1H), 3.86 (s, 3H), 3.68 (s, 3H), 2.00 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 20.3, 50.2, 55.7, 85.8, 111.0, 120.3, 124.4, 125.4, 128.5, 152.5, 159.0, 170.5. (C₁₇H₁₆ClNO₃ + Na)⁺ requires m/z 244.0944, found m/z 244.0950.

(Z)-methyl 3-(4-methoxyphenylamino)-4-methylpent-2-enoate (1w): Yield = 55%, yellow oil, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.13 (br s, 1H), 7.01-7.05 (m, 2H), 6.85-6.89 (m, 2H), 4.71 (s, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 2.66-2.75 (m, 1H), 1.07 (s, 3H), 1.04 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 21.9, 28.4, 50.2, 55.4, 80.0, 114.3, 127.8, 131.8, 157.8, 171.2, 171.6. ESI-HRMS exact mass calcd. for (C₁₄H₁₉NO₃ + Na)⁺ requires m/z 272.1257, found m/z 272.1260.

(Z)-methyl 3-cyclohexyl-3-(4-methoxyphenylamino)acrylate (1x): Yield = 75%, white solid, mp = 103.8-106.1 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 10.15 (br s, 1H), 6.98-7.26 (m, 2H), 6.83-6.88 (m, 2H), 4.70 (s, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 2.22-2.34 (m, 1H), 1.62-1.78 (m, 5H), 1.13-1.29 (m, 2H), 1.07-1.13 (m, 3H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 25.8, 26.2, 32.4, 50.2, 55.4, 80.9, 114.2, 127.5, 131.7, 157.6, 169.8, 171.6. ESI-HRMS exact mass calcd. for (C₁₇H₂₃NO₃ + Na)⁺ requires m/z 312.1570, found m/z 312.1558.

Methyl 2-(4-methoxyphenylamino)cyclopent-1-enecarboxylate (1y): Yield = 80%, white solid, mp = 67.1-69.6 °C, ¹H NMR (300 MHz, CDCl₃, TMS) δ = 9.29 (br s, 1H), 6.96-7.02 (m, 2H), 6.80-6.85 (m, 2H), 3.80 (s, 3H), 3.72 (s, 3H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 1.78-1.88 (m, 2H). ¹³C-NMR (75 MHz, CDCl₃, TMS): δ = 21.6, 28.8, 33.2, 50.3, 55.4, 95.7, 114.3, 123.8, 133.7, 156.4, 161.9, 168.8. ESI-HRMS exact mass calcd. for (C₁₄H₁₇NO₃ + H)⁺ requires m/z 270.1101, found m/z 270.1092.

? . Typical procedure for asymmetric hydrosilylation of β-enamino esters:



Trichlorosilane (41 μL, 0.40 mmol, 2.0 equiv.) was added to a solution of the catalyst (0.02 mmol) and the corresponding β-enamino ester (0.20 mmol) in 2 mL of dry CHCl₃ at -30 °C. The reaction mixture was stirred at -30 °C for 48h. Then the reaction was quenched with saturated aqueous solution of NaHCO₃. The mixture was extracted with EtOAc and the combined extracts was washed with brine

and dried over anhydrous MgSO₄. Concentration in vacuo followed by flash chromatography on silica gel with hexane/ethyl acetate as the eluent afforded the β -amino acid esters. The ee values were determined using established HPLC techniques with chiral stationary phases.

HPLC separation of chiral β -amino esters

Compound	Column	i-PrOH/n-Hexane	Flow rate (mL/min)	λ (nm)	T (°C)	t_R (min)
3b	AD-H	5%	1	254	25	9.865; 10.998
3c	AD-H	5%	1	254	25	17.956; 19.839
3d	AD-H	5%	1	254	25	17.511; 18.510
3e	AD-H	5%	1	254	25	14.569; 25.438
3f	AD-H	5%	1	254	25	23.162; 27.184
3g	AD-H	5%	1	254	25	25.972; 27.349
3h	OD-H	5%	1	254	25	23.572; 26.103
3j	AD-H	5%	1	254	25	11.318; 13.000
3k	AD-H	5%	1	254	25	9.918; 11.197
3l	AD-H	5%	1	254	25	12.214; 13.683
3m	OD-H	5%	1	254	25	17.540; 19.440
3n	AD-H	5%	1	254	25	13.681; 14.668
3o	OD-H	5%	1	254	25	12.328; 13.914
3p	AD-H	5%	1	254	25	17.889; 19.546
3q	OD-H	5%	1	254	25	25.364; 26.964
3r	OJ-H	30%	1	254	25	14.460; 17.185
3s	AD-H	5%	1	254	25	18.812; 21.107
3t	AD-H	5%	1	254	25	12.579; 24.294
3u	AD-H	5%	1	254	25	11.425; 15.437
3v	AD-H	5%	1	254	25	10.123; 12.073
3w	AD-H	5%	1	254	25	6.774; 7.825
3x	AD-H	5%	1	254	25	8.210; 9.734
3y	AD-H	5%	1	254	25	8.883; 11.071

Methyl 3-phenyl-3-(phenylamino)propanoate (3b): White solid, mp = 103.9-105.4 °C, $[\alpha]_D^{20} = -5.1$ (c = 0.2 in CHCl₃, 95% ee). ¹H NMR (300 MHz, CDCl₃, TMS) δ = 7.31-7.41 (m, 4H), 7.26-7.28 (m, 1H), 7.09-7.15 (m, 2H), 6.68-6.90 (m, 1H), 6.57-6.60 (m, 2H), 4.85 (t, J = 6.7 Hz, 1H), 4.54 (brs, 1H), 3.66 (s, 3H), 2.82 (d, J = 6.0 Hz, 2H).

Methyl 3-(4-methoxyphenylamino)-3-phenylpropanoate (3c): White solid, mp = 62.9-65.6 ? , $[\alpha]_D^{20} = -6.2$ (c = 0.2 in CHCl_3 in 95% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.25-7.41 (m, 5H), 6.71-6.74 (m, 2H), 6.55-6.59 (m, 2H), 4.80 (t, $J = 6.7$ Hz, 1H), 4.47 (brs, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.82 (d, $J = 6.7$ Hz, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.7, 51.8, 55.6, 55.8, 114.7, 115.1, 126.2, 127.4, 128.7, 140.9, 142.3, 152.3, 171.7. ESI-HRMS exact mass calcd. for $(\text{C}_{17}\text{H}_{19}\text{NO}_3 + \text{Na})^+$ requires m/z 308.1257, found m/z 308.1260.

Methyl 3-(3-methoxyphenylamino)-3-phenylpropanoate (3d): White solid, mp = 72.8-74.6 ? , $[\alpha]_D^{20} = -2.3$ (c = 0.2 in CHCl_3 , 96% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.25-7.39 (m, 5H), 7.02 (d, $J = 8.1$ Hz, 1H), 6.20-6.28 (m, 2H), 6.14-6.16 (m, 1H), 5.12 (br s, 1H), 4.83 (t, $J = 6.7$ Hz, 1H), 3.69 (s, 3H), 3.65 (s, 3H), 2.85 (d, $J = 6.7$ Hz, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.4, 51.8, 54.8, 54.9, 99.8, 103.1, 106.8, 126.1, 127.4, 128.7, 129.8, 141.9, 147.9, 160.6, 171.4. ESI-HRMS exact mass calcd. for $(\text{C}_{17}\text{H}_{19}\text{NO}_3 + \text{Na})^+$ requires m/z 308.1257, found m/z 308.1262.

Methyl 3-(2-methoxyphenylamino)-3-phenylpropanoate(3e): White solid, mp = 74.2-76.5 ? , $[\alpha]_D^{20} = +17.7$ (c = 0.2 in CHCl_3 , 92% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.21-7.39 (m, 5H), 6.70-6.78 (m, 2H), 6.60-6.66 (m, 1H), 6.42-6.45 (d, $J = 7.8$ Hz, 1H), 5.02 (brs, 1H), 4.86 (t, $J = 6.7$ Hz, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 2.82 (d, $J = 6.7$, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.9, 51.7, 54.8, 55.5, 109.6, 111.2, 116.9, 121.1, 126.2, 127.3, 128.7, 136.7, 142.3, 146.9, 171.4. ESI-HRMS exact mass calcd. for $(\text{C}_{17}\text{H}_{19}\text{NO}_3 + \text{Na})^+$ requires m/z 308.1257, found m/z 308.1250.

Methyl 3-(4-fluorophenylamino)-3-phenylpropanoate (3f): White solid, mp = 66.0-67.4 ? , $[\alpha]_D^{20} = +2.8$ (c = 0.2 in EtOAc, 92% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.25-7.37 (m, 5H), 6.77-6.83 (m, 2H), 6.46-6.50 (m, 2H), 4.76 (t, $J = 6.7$ Hz, 3H), 4.47 (br s, 1H), 3.66 (s, 3H), 2.73-2.87 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.6, 51.9, 55.6, 114.6 (d, $J = 7.4$ Hz), 115.5 (d, $J = 22.2$ Hz), 126.2, 127.5, 128.8, 141.9, 143.0, 156.0 (d, $J = 234$ Hz), 171.5. ESI-HRMS exact mass calcd. for $(\text{C}_{16}\text{H}_{16}\text{FNO}_2 + \text{Na})^+$ requires m/z 296.1057, found m/z 296.1052.

Methyl 3-(4-chlorophenylamino)-3-phenylpropanoate (3g): White solid, mp = 70.0-72.3 ? , $[\alpha]_D^{20} = +24.2$ (c = 0.2 in EtOAc, 93% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.26-7.34 (m, 5H), 7.03-7.06 (d, $J = 8.3$ Hz, 2H), 6.46-6.49 (d, $J = 8.4$ Hz, 2H), 4.78 (t, $J = 6.7$ Hz, 3H), 4.62 (br s, 1H), 3.66 (s, 3H), 2.74-2.88 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.5, 51.9, 55.0, 114.8, 122.4, 126.1, 127.6, 128.8, 128.9, 141.6, 145.3, 171.5. ESI-HRMS exact mass calcd. for $(\text{C}_{16}\text{H}_{16}\text{ClNO}_2 + \text{Na})^+$ requires m/z 312.0762, found m/z 312.0751.

Methyl 3-(4-bromophenylamino)-3-phenylpropanoate (3h): White solid, mp = 100.3-102.1 ? , $[\alpha]_D^{20} = -3.6$ (c = 0.2 in EtOAc, 92% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.25-7.35 (m, 5H), 7.16-7.20 (m, 2H), 6.42-6.46 (m, 2H), 4.78 (m, 1H), 4.65 (br s, 1H), 3.65 (s, 1H), 2.81 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.5, 51.9, 54.9, 109.5, 115.3, 126.1, 127.6, 128.8, 131.8, 141.5, 145.7, 171.4. ESI-HRMS exact mass calcd. for $(\text{C}_{16}\text{H}_{16}\text{BrNO}_2 + \text{Na})^+$ requires m/z 356.0257, found m/z 356.0267.

Methyl 3-(4-fluorophenyl)-3-(4-methoxyphenylamino)propanoate (3j): Yellow oil, $[\alpha]_D^{20} = +3.4$ (c = 0.2 in EtOAc, 93% ee) , $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) d = 7.31-7.36 (m, 2H), 6.99-7.04 (m, 2H), 6.69-6.72 (m, 2H), 6.50-6.54 (m, 2H), 4.73 (t, $J = 6.7$ Hz, 1H), 4.32 (br s, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 2.77 (d, $J = 6.7$ Hz, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): d = 42.6, 51.8, 55.1, 55.6, 114.7, 115.2, 115.6 (d, $J = 21.3$ Hz), 127.8 (d, $J = 8.0$ Hz), 138.0 (d, $J = 3.1$ Hz), 140.6, 152.4, 161.9

(d, $J = 243.9$ Hz), 171.5. ESI-HRMS exact mass calcd. for $(C_{17}H_{18}FNO_3 + Na)^+$ requires m/z 326.1163, found m/z 326.1164.

Methyl 3-(4-chlorophenyl)-3-(4-methoxyphenylamino)propanoate (3k): Yellow oil, $[a]_D^{20} = -32.0$ ($c = 0.2$ in EtOAc, 92% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.27-7.33$ (m, 4H), 6.68-6.72 (m, 2H), 6.48-6.52 (m, 2H), 4.73 (t, $J = 6.7$ Hz, 1H), 4.30 (br s, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.77 (d, $J = 6.7$ Hz, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 42.5, 51.9, 55.2, 55.6, 114.7, 115.1, 127.7, 128.9, 133.0, 140.5, 140.9, 152.4, 171.4$. ESI-HRMS exact mass calcd. for $(C_{17}H_{18}ClNO_3 + Na)^+$ requires m/z 342.0867, found m/z 342.0865.

Methyl 3-(4-bromophenyl)-3-(4-methoxyphenylamino)propanoate (3l): Yellow oil, $[a]_D^{20} = +3.0$ ($c = 0.2$ in EtOAc, 92% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.42-7.46$ (m, 2H), 7.24-7.26 (m, 2H), 6.68-6.73 (m, 2H), 6.48-6.52 (m, 2H), 4.71 (t, $J = 6.7$ Hz, 1H), 4.31 (br s, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.76 (d, $J = 6.7$ Hz, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 42.4, 51.9, 55.2, 55.6, 114.7, 115.2, 121.1, 128.0, 131.8, 140.5, 141.4, 152.4, 171.4$. ESI-HRMS exact mass calcd. for $(C_{17}H_{18}BrNO_3 + Na)^+$ requires m/z 386.0362, found m/z 386.0360.

Methyl 3-(3-chlorophenyl)-3-(4-methoxyphenylamino)propanoate (3m): Viscous liquid, $[a]_D^{20} = -1.8$ ($c = 0.2$ in EtOAc, 91% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.38$ (s, 1H), 7.23-7.27 (m, 3H), 6.53-6.73 (m, 2H), 6.50-6.53 (m, 2H), 4.72 (t, $J = 6.7$ Hz, 1H), 4.31 (br s, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.77 (d, $J = 6.7$ Hz, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 42.4, 51.9, 55.2, 55.6, 114.7, 115.2, 121.1, 128.0, 131.8, 140.5, 141.4, 152.4, 171.4$. ESI-HRMS exact mass calcd. for $(C_{17}H_{18}ClNO_3 + Na)^+$ requires m/z 342.0867, found m/z 342.0871.

Methyl 3-(2-chlorophenyl)-3-(4-methoxyphenylamino)propanoate (3n): Yellow oil, $[a]_D^{20} = +75.4$ ($c = 0.2$ in EtOAc, 91% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.47-7.49$ (m, 1H), 7.35-7.38 (m, 1H), 7.17-7.20 (m, 5H), 5.16 (m, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 2.96 (dd, $J = 4.4$ Hz, $J = 15.0$ Hz, 1H), 2.77 (dd, $J = 8.3$ Hz, $J = 15.1$ Hz, 1H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 40.1, 51.9, 52.9, 55.6, 114.8, 115.1, 127.3, 128.7, 129.8, 132.8, 139.7, 152.8, 171.4$. ESI-HRMS exact mass calcd. for $(C_{17}H_{18}ClNO_3 + Na)^+$ requires m/z 342.0867, found m/z 342.0870.

Methyl 3-(4-methoxyphenylamino)-3-p-tolylpropanoate (3o): Yellow oil, $[a]_D^{20} = -7.2$ ($c = 0.2$ in EtOAc, 95% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.25-7.27$ (m, 2H), 7.13-7.15 (m, 2H), 6.70-6.73 (m, 2H), 6.53-6.56 (m, 2H), 4.75 (t, $J = 6.7$ Hz, 1H), 4.27 (br s, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.79 (d, $J = 6.7$ Hz, 2H), 2.33 (s, 3H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 42.4, 51.9, 55.2, 55.6, 114.7, 115.2, 121.1, 128.0, 131.8, 140.5, 141.4, 152.4, 171.4$. ESI-HRMS exact mass calcd. for $(C_{18}H_{21}NO_3 + Na)^+$ requires m/z 322.1414, found m/z 322.1413.

Methyl 3-(4-methoxyphenyl)-3-(4-methoxyphenylamino)propanoate (3p): Yellow oil, $[a]_D^{20} = -1.0$ ($c = 0.2$ in EtOAc, 95% ee). 1H NMR (300 MHz, $CDCl_3$, TMS) $\delta = 7.26-7.29$ (m, 2H), 6.84-6.87 (m, 2H), 6.70-6.73 (m, 2H), 6.52-6.56 (m, 2H), 4.73 (t, $J = 6.7$ Hz, 1H), 4.24 (br s, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.65 (s, 3H), 2.79 (d, $J = 6.7$ Hz, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$, TMS): $\delta = 42.6, 51.7, 55.1, 55.6, 114.0, 114.7, 115.1, 127.3, 134.3, 140.9, 152.2, 158.7, 171.7$. ESI-HRMS exact mass calcd. for $(C_{18}H_{21}NO_4 + Na)^+$ requires m/z 338.1363, found m/z 338.1368.

Methyl 3-(4-methoxyphenylamino)-3-(naphthalen-2-yl)propanoate (3q): Solid, mp = 81.1-83.5 °C, $[\alpha]_D^{20} = +7.5$ (c = 0.2 in EtOAc, 95% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 7.82-7.87 (m, 4H), 7.47-7.55 (m, 2H), 6.70-6.74 (m, 2H), 6.60-6.63 (m, 2H), 4.96 (t, $J = 6.8$ Hz, 1H), 4.46 (br s, 1H), 3.70 (s, 3H), 3.68 (s, 3H), 2.90 (d, $J = 6.8$, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 42.6, 51.8, 55.5, 56.0, 114.6, 115.1, 124.3, 125.0, 125.7, 126.1, 127.5, 127.8, 128.6, 132.8, 133.3, 139.8, 140.9, 152.2, 171.6. ESI-HRMS exact mass calcd. for $(\text{C}_{21}\text{H}_{21}\text{NO}_3 + \text{Na})^+$ requires m/z 338.1414, found m/z 338.1410.

Methyl 3-(4-methoxyphenylamino)-3-(pyridin-3-yl)propanoate (3r): Yellow oil, $[\alpha]_D^{20} = -2.5$ (c = 0.2 in EtOAc, 70% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 8.63 (d, $J = 2.0$ Hz, 1H), 8.48 (dd, $J = 1.3$ Hz, $J = 4.8$ Hz, 1H), 7.67 (d, $J = 7.9$ Hz, 4H), 7.19-7.26 (m, 1H), 6.66-6.71 (m, 2H), 6.47-6.53 (m, 2H), 4.80 (t, $J = 6.6$ Hz, 1H), 4.40 (br s, 1H), 3.67 (s, 3H), 3.63 (s, 3H), 2.81 (d, $J = 6.8$ Hz, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 42.0, 51.9, 53.6, 55.6, 114.7, 115.3, 123.5, 133.9, 137.7, 140.2, 148.5, 148.8, 152.6, 171.1. ESI-HRMS exact mass calcd. for $(\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3 + \text{Na})^+$ requires m/z 309.1210, found m/z 309.1212.

Methyl 3-(4-methoxyphenylamino)-3-(thiophen-2-yl)propanoate (3s): Yellow oil, $[\alpha]_D^{20} = -3.7$ (c = 0.2 in EtOAc, 88% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 7.17-7.19 (m, 1H), 6.93-6.98 (m, 2H), 6.74-6.77 (m, 2H), 6.62-6.66 (m, 2H), 5.08 (t, $J = 6.5$ Hz, 1H), 4.19 (br s, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 2.85-2.98 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 42.2, 51.8, 52.0, 55.5, 114.7, 115.7, 123.7, 126.7, 140.4, 147.0, 152.7, 171.3. ESI-HRMS exact mass calcd. for $(\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S} + \text{Na})^+$ requires m/z 314.0821, found m/z 314.0822.

Methyl 1-(4-methoxyphenylamino)-2,3-dihydro-1H-indene-2-carboxylate (3t): Yellow oil, $[\alpha]_D^{20} = +18.6$ (c = 0.2 in EtOAc, 28% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 7.21-7.31 (m, 4H), 6.77-6.81 (m, 2H), 6.69-6.74 (m, 2H), 5.30 (d, $J = 4.6$ Hz, 1H), 3.83 (br s, 3H), 3.77 (s, 3H), 3.62-3.67 (m, 1H), 3.48 (s, 1H), 3.40-3.47 (m, 1H), 3.12 (dd, $J = 8.4$ Hz, $J = 16.3$ Hz, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 33.7, 48.3, 51.4, 55.7, 61.7, 114.7, 115.0, 124.4, 127.0, 128.3, 140.9, 141.3, 142.7, 152.4, 173.5. ESI-HRMS exact mass calcd. for $(\text{C}_{18}\text{H}_{19}\text{NO}_3 + \text{Na})^+$ requires m/z 320.1257, found m/z 320.1251.

Methyl 1-(4-methoxyphenylamino)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3u): Yellow oil, $[\alpha]_D^{20} = -119.4$ (c = 0.2 in EtOAc, 54% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 7.09-7.26 (m, 4H), 6.77-6.80 (m, 2H), 6.68-6.82 (m, 2H), 4.94 (d, $J = 4.6$ Hz, 1H), 3.76 (s, 3H), 3.69 (br s, 1H), 3.61 (s, 3H), 2.98-3.04 (m, 2H), 2.88-2.92 (m, 1H), 2.79-2.82 (m, 1H), 2.10-2.19 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 21.2, 27.8, 44.8, 51.5, 55.0, 55.7, 114.8, 115.8, 126.2, 127.3, 128.4, 128.9, 135.2, 137.8, 141.8, 152.6, 173.7. ESI-HRMS exact mass calcd. for $(\text{C}_{19}\text{H}_{21}\text{NO}_3 + \text{Na})^+$ requires m/z 334.1414, found m/z 334.1420.

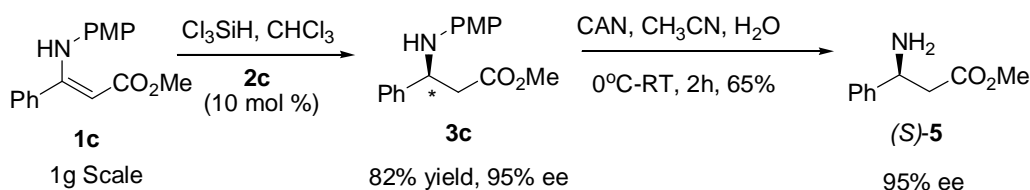
Methyl 3-(2-methoxyphenylamino)butanoate (3v): Yellow oil, $[\alpha]_D^{20} = +12.4$ (c = 0.2 in EtOAc, 17% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) δ = 6.86-6.88 (m, 1H), 6.76-6.80 (m, 1H), 6.65-6.70 (m, 2H), 4.28 (br s, 1H), 3.93-3.99 (m, 1H), 3.84 (s, 1H), 3.69 (s, 1H), 2.73 (dd, $J = 15.0$ Hz, $J = 5.0$ Hz, 1H), 2.39 (dd, $J = 15.0$ Hz, $J = 7.6$ Hz, 1H), 1.30 (d, $J = 6.4$ Hz, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): δ = 20.7, 41.0, 45.5, 51.6, 55.4, 109.7, 110.5, 116.6, 121.3, 136.5, 146.9, 172.3. ESI-HRMS exact mass calcd. for $(\text{C}_{12}\text{H}_{17}\text{NO}_3 + \text{Na})^+$ requires m/z 246.1101, found m/z 246.1107.

Methyl 3-(4-methoxyphenylamino)-4-methylpentanoate (3w): Yellow oil, $[\alpha]_D^{20} = +32.4$ ($c = 0.2$ in EtOAc, 67% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 6.73$ - 6.77 (m, 2H), 6.59 - 6.63 (m, 2H), 3.73 (s, 3H), 3.62 (s, 3H), 3.45 (br s, 1H), 2.39 - 2.54 (m, 2H), 1.87 - 1.93 (m, 1H), 0.98 (d, $J = 6.8$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): $\delta = 18.5$, 18.6 , 31.4 , 36.5 , 51.5 , 55.6 , 57.0 , 114.8 , 114.9 , 141.6 , 152.0 , 172.8 . ESI-HRMS exact mass calcd. for $(\text{C}_{14}\text{H}_{21}\text{NO}_3 + \text{Na})^+$ requires m/z 274.1414, found m/z 274.1420.

Methyl 3-cyclohexyl-3-(4-methoxyphenylamino)propanoate (3x): Yellow oil, $[\alpha]_D^{20} = +5.5$ ($c = 0.2$ in EtOAc, 80% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 6.73$ - 6.77 (m, 2H), 6.72 - 6.75 (m, 1H), 6.59 - 6.63 (m, 2H), 3.73 (s, 3H), 3.61 (s, 1H), 2.43 - 2.57 (s, 3H), 1.77 - 1.78 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): $\delta = 21.2$, 28.8 , 31.2 , 34.1 , 55.5 , 56.3 , 109.8 , 110.2 , 117.3 , 120.0 , 121.0 , 136.5 , 146.9 . ESI-HRMS exact mass calcd. for $(\text{C}_{17}\text{H}_{25}\text{NO}_3 + \text{Na})^+$ requires m/z 314.1727, found m/z 314.1725.

Methyl 2-(4-methoxyphenylamino)cyclopentanecarboxylate (3y): Yellow oil, $[\alpha]_D^{20} = +36.8$ ($c = 0.2$ in EtOAc, 28% ee). $^1\text{H NMR}$ (300 MHz, CDCl_3 , TMS) $\delta = 6.73$ - 6.78 (m, 2H), 6.57 - 6.60 (m, 2H), 4.01 (q, $J = 6.6$ Hz, 1H), 3.73 (s, 3H), 3.53 (s, 3H), 3.06 (q, $J = 7.5$ Hz, 1H), 1.85 - 2.01 (m, 4H), 1.63 - 1.77 (m, 2H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , TMS): $\delta = 22.4$, 27.8 , 32.7 , 47.0 , 51.4 , 55.7 , 58.0 , 114.7 , 114.8 . ESI-HRMS exact mass calcd. for $(\text{C}_{14}\text{H}_{17}\text{NO}_3 + \text{Na})^+$ requires m/z 272.1257, found m/z 272.1249.

V. Experiment in gram scale and deprotection of *N*-PMP group of (*S*)- methyl 3-(4-methoxyphenylamino) -3-phenylpropanoate (3c)^[7]

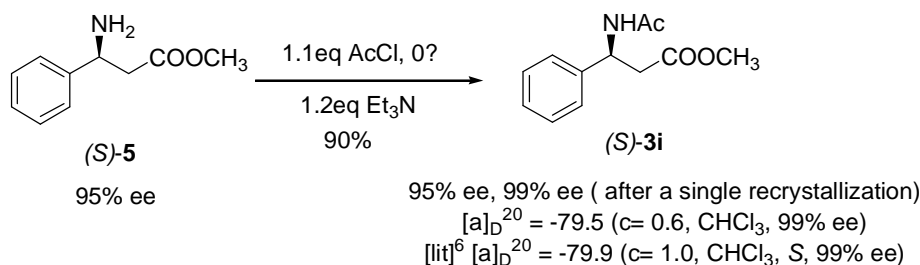


Catalyst **2c** (0.145g, 0.35mmol) and **1c** (1 g, 3.5 mmol) was dissolved in 35 mL of dry CHCl_3 and cooled to -30°C . Trichlorosilane (0.72 mL, 7 mmol) was added to the solution and the reaction mixture was stirred at -30°C for 48h. Then the reaction was quenched with saturated aqueous solution of NaHCO_3 . The mixture was extracted with EtOAc and the combined extract was washed with brine and dried over anhydrous MgSO_4 . Concentration in vacuo followed by flash chromatography on silica gel with hexane/ethyl acetate as the eluent afforded **3c** in 83% yield.

A solution of ammonium cerium nitrate (1.64g, 3 mmol) in water (5 mL) was added slowly to a stirred solution of compound (*S*)- methyl 3-(4-methoxyphenylamino) -3-phenylpropanoate (**3c**) (285mg, 1 mmol) in acetonitrile (10 mL) at 0°C . After 2 hours, a solution of NaHCO_3 (5%) was added until $\text{pH} = 6$. Then sodium sulfite was added until the mixture became a brown suspension. The mixture was then extracted with ethyl acetate (4×30 mL) and the combined organic phase was dried over anhydrous sodium sulfate. The mixture was subsequently filtered and the solvents were removed in vacuo. The crude product was purified through flash column chromatography [petroleum

ether/EtOAc (1/1)] on silica gel to afford (*S*)-**5** as a yellow oil, yield 65%. ¹H NMR (300Hz, CDCl₃, TMS): d = 7.23-7.37 (m, 5H), 4.42 (t, *J* = 6.8 Hz, 1H), 3.68 (s, 3H), 2.66 (d, *J* = 6.7 Hz, 2H), 1.79 (br s, 2H).

VI. Acetylation of the amino group of (*S*)- methyl 3-amino-3- phenylpropanoate (**5**)

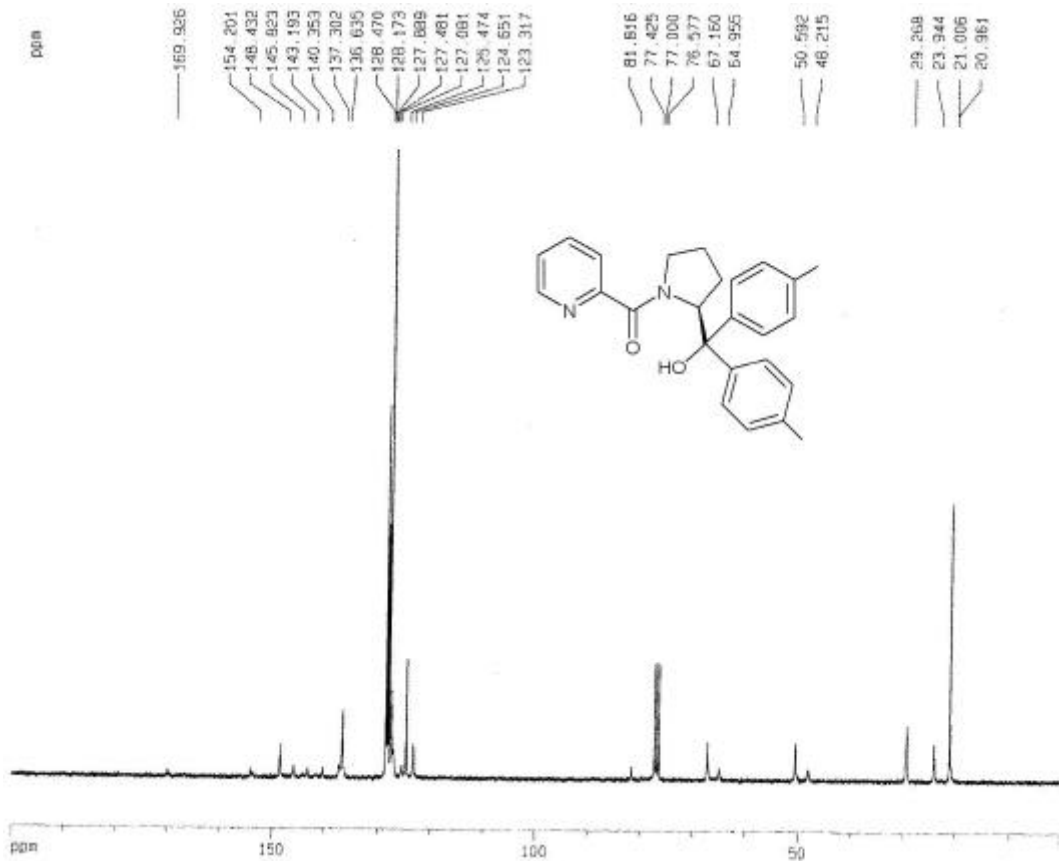
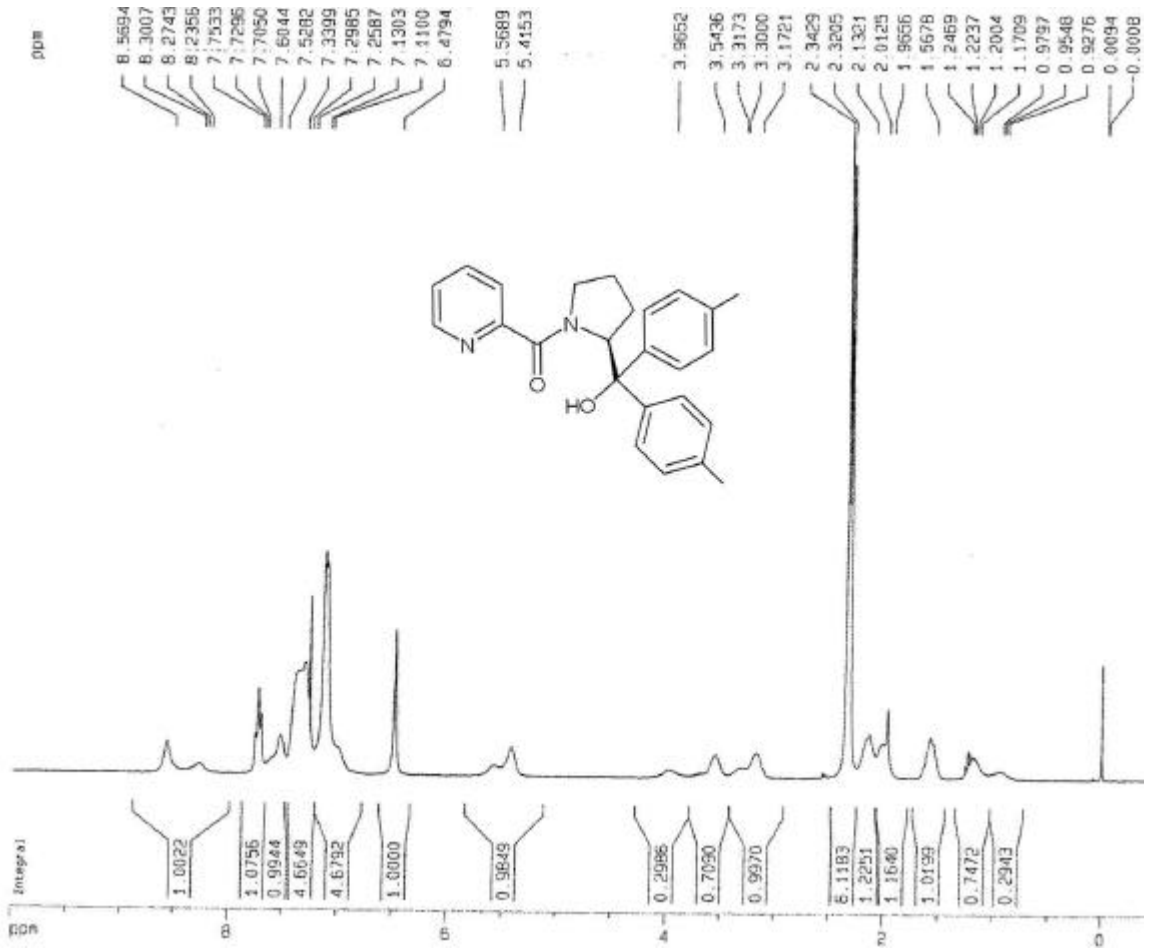


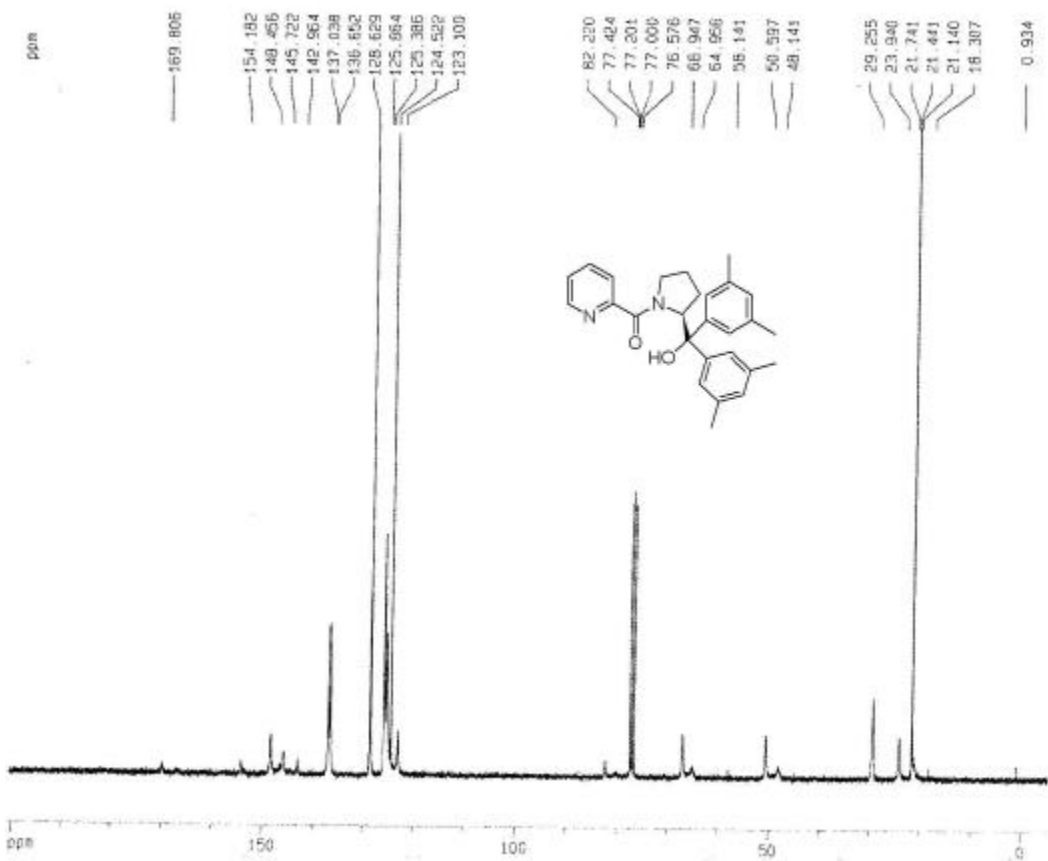
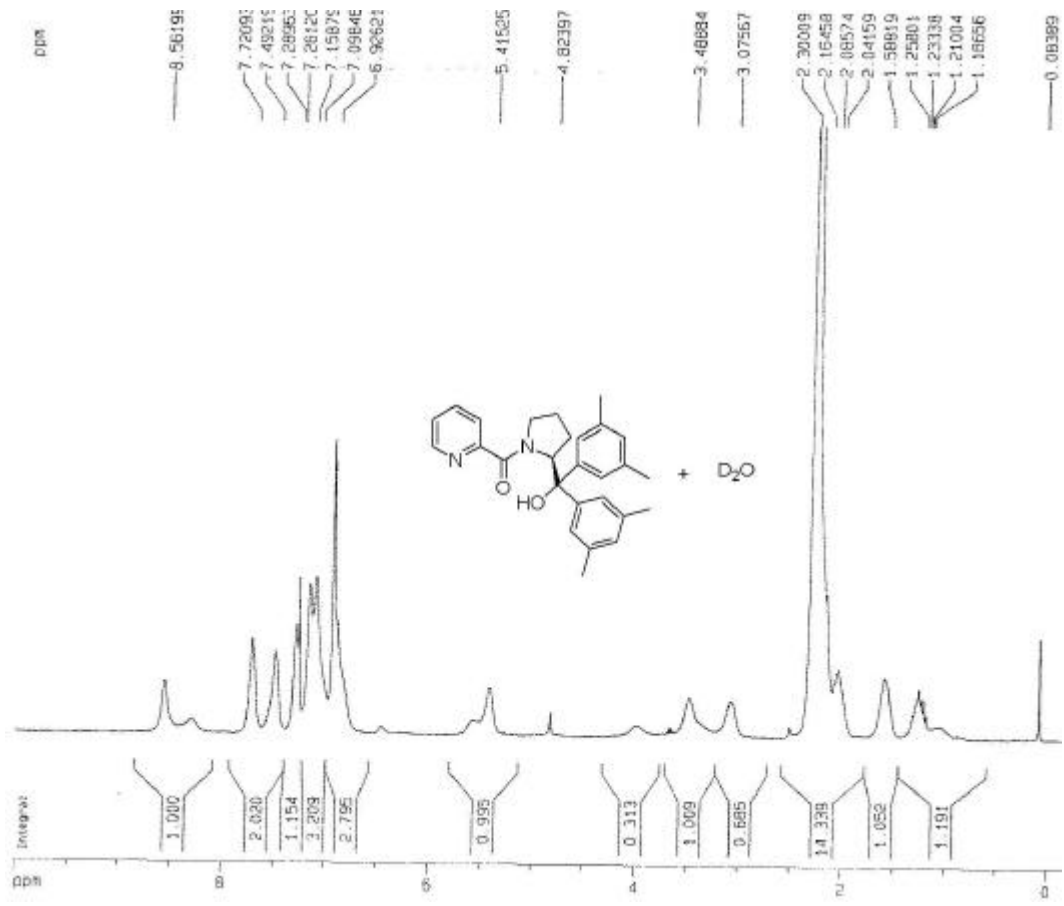
To a solution of (*S*)- methyl 3-amino-3-phenylpropanoate (**5**) (99 mg, 0.5 mmol) and Et₃N (0.1 mL, 0.6 mmol) in CHCl₃ was added CH₃COCl (0.06 mL in 1mL of CHCl₃) dropwise at 0° in 10 mins. The result solution was allowed to warm to RT and stirred for additional two hours. The reaction was quenched with water. Then the organic phase was separated and washed with NaHCO₃ (5%), water, brine respectively. The organic phase was dried over Na₂SO₄. The mixture was subsequently filtered and the solvents were removed in vacuo. The residue was subjected to FC to afford (*S*)- methyl 3-acetamido-3-phenylpropanoate (**3i**) as a white solid, yield 90%. ¹H NMR (300Hz, CDCl₃): d = 7.23-7.35 (m, 5H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.38-5.45 (m, 1H), 3.61 (s, 3H), 2.78-2.97 (m, 2H), 2.00 (s, 3H).

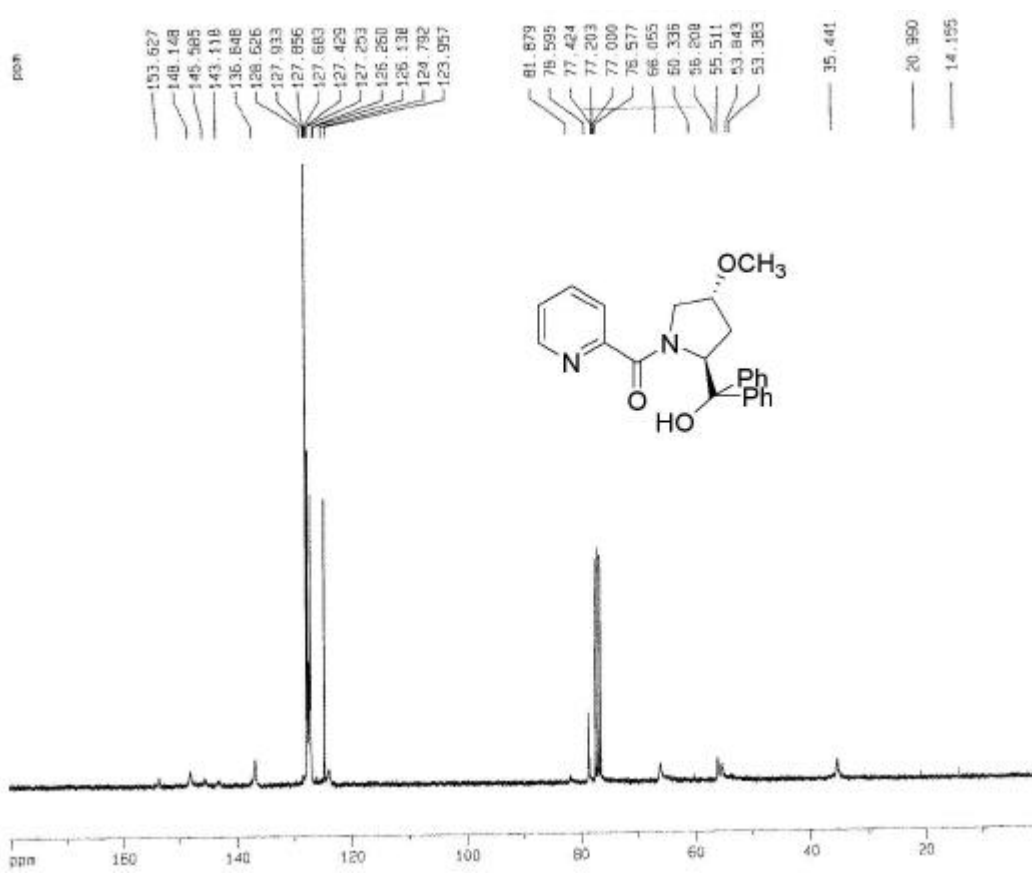
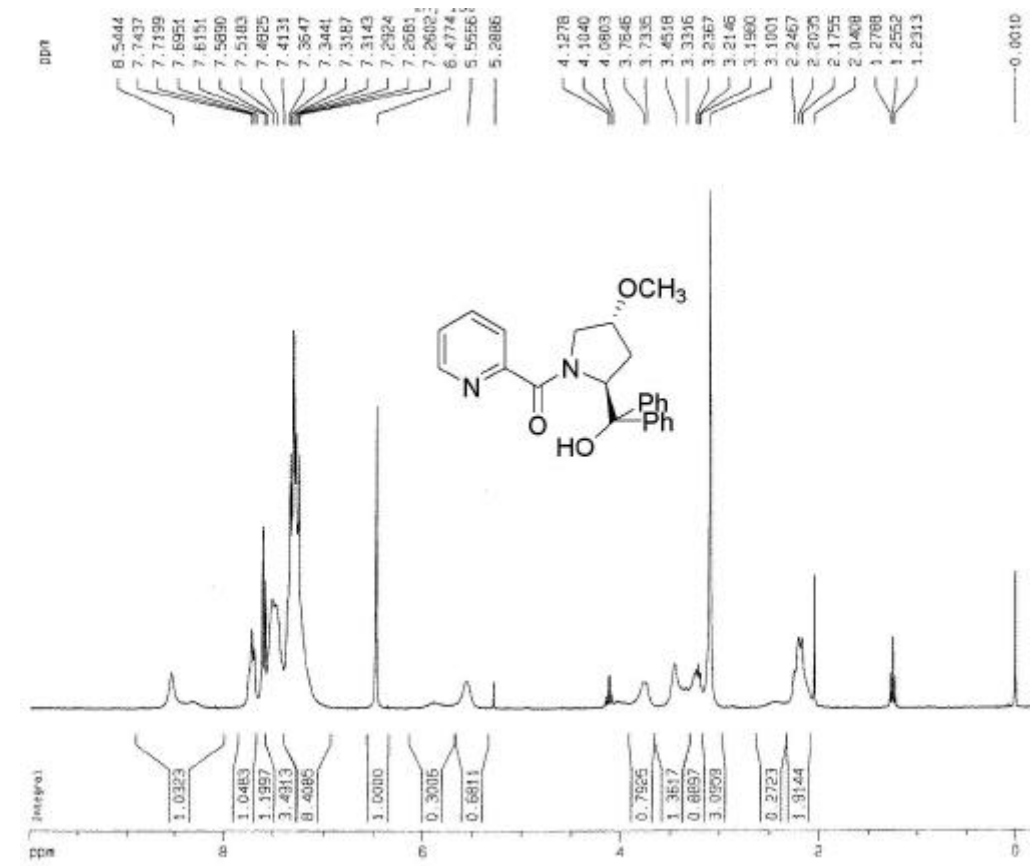
The enantiomers were analyzed by HPLC using a chiral AD-H column (n-heptane/2- propanol = 95/5, flow rate = 1.0 mL/min, wavelength = 220 nm; minor enantiomer: t_R = 27.47 min, major enantiomer: t_R = 30.18 min; $[\alpha]_{\text{D}}^{20} = -79.5$ (c = 0.6 in CHCl₃, 99% ee). Lit.^[6] $[\alpha]_{\text{D}}^{20} = -79.9$ (c = 1.0 in CHCl₃, S, 99% ee).

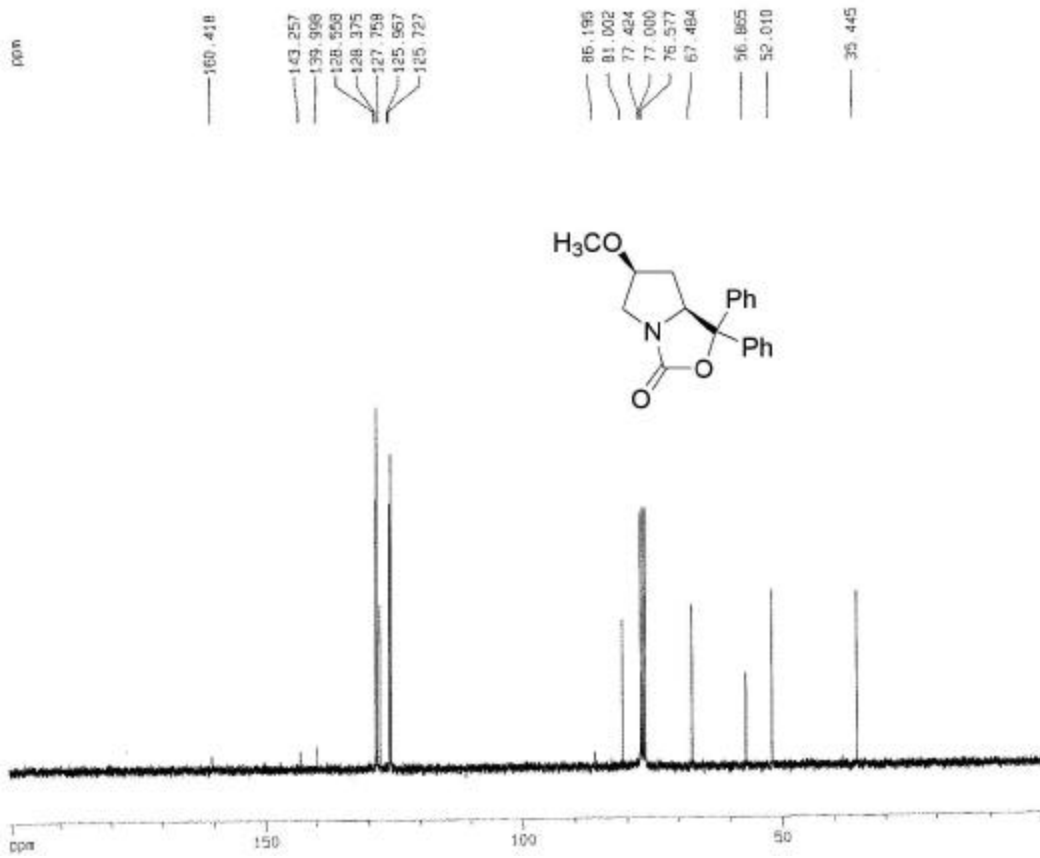
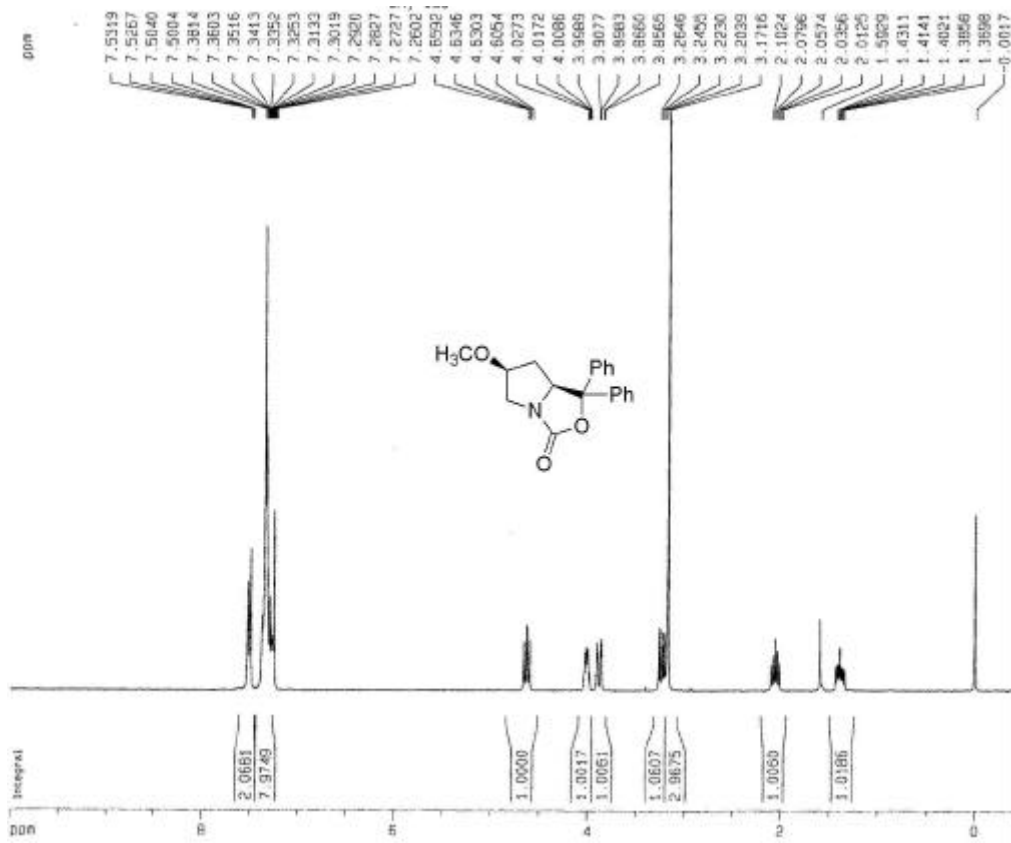
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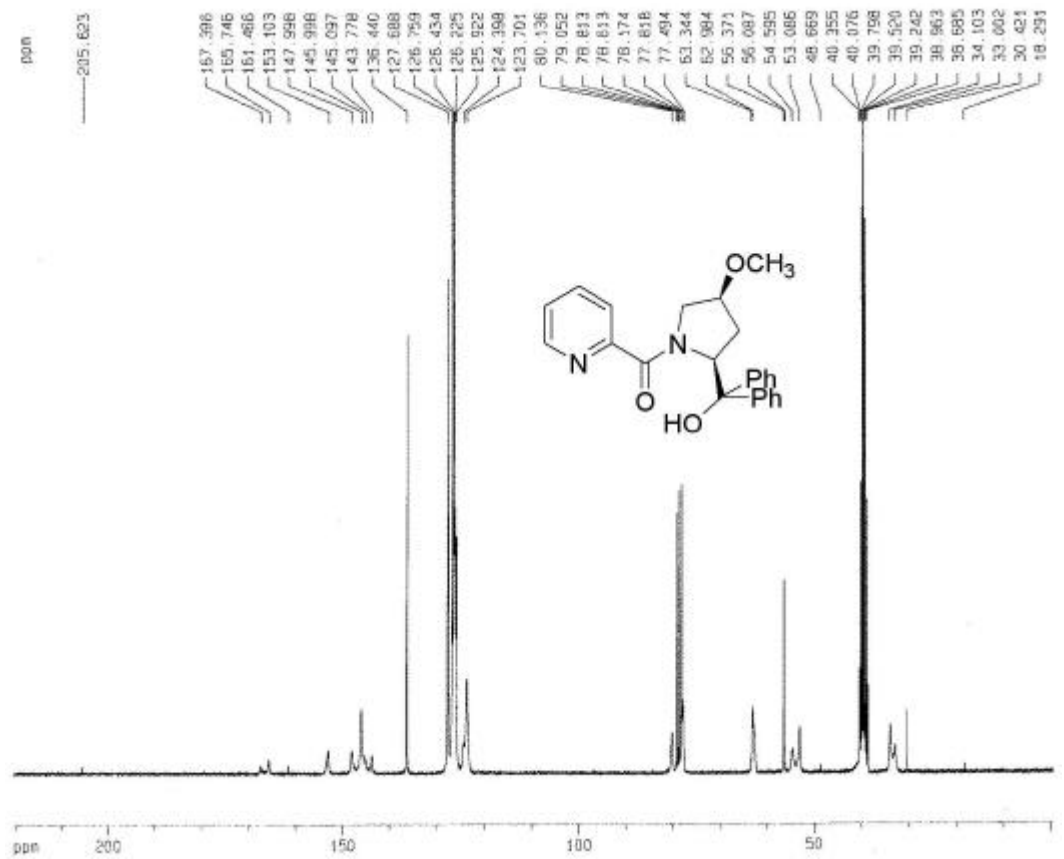
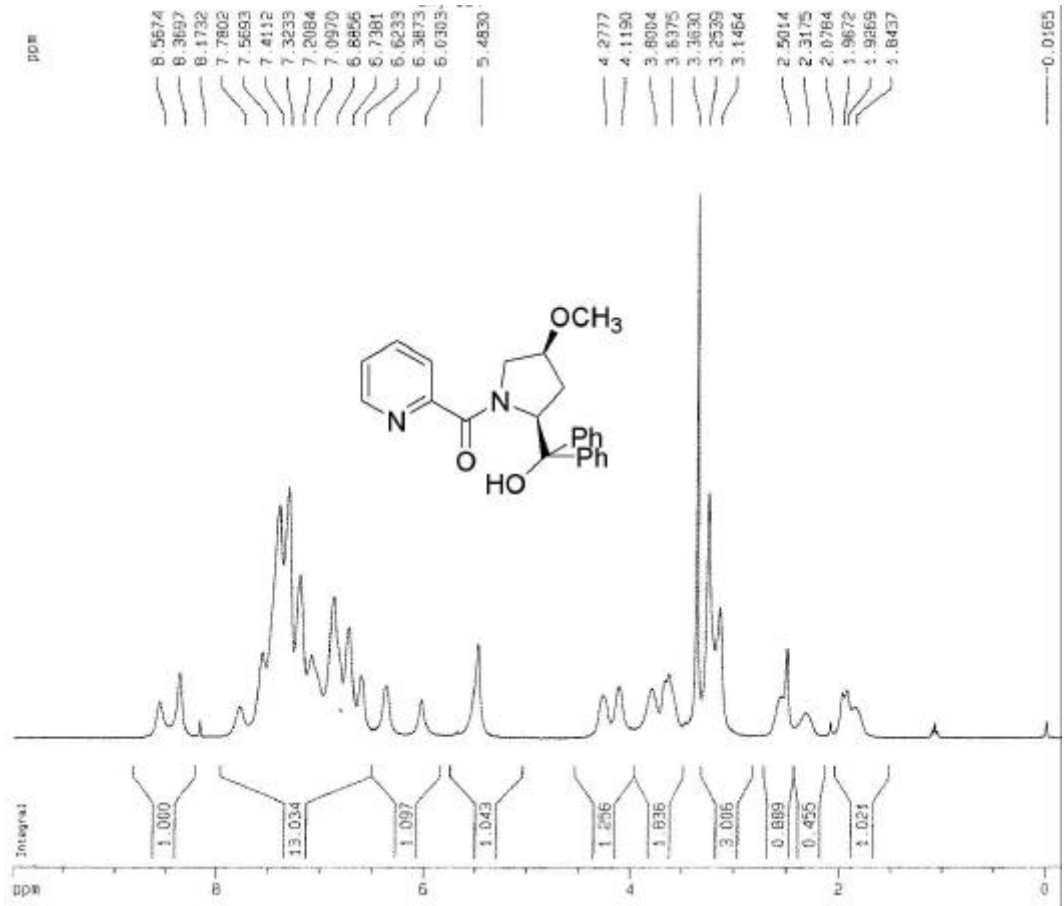
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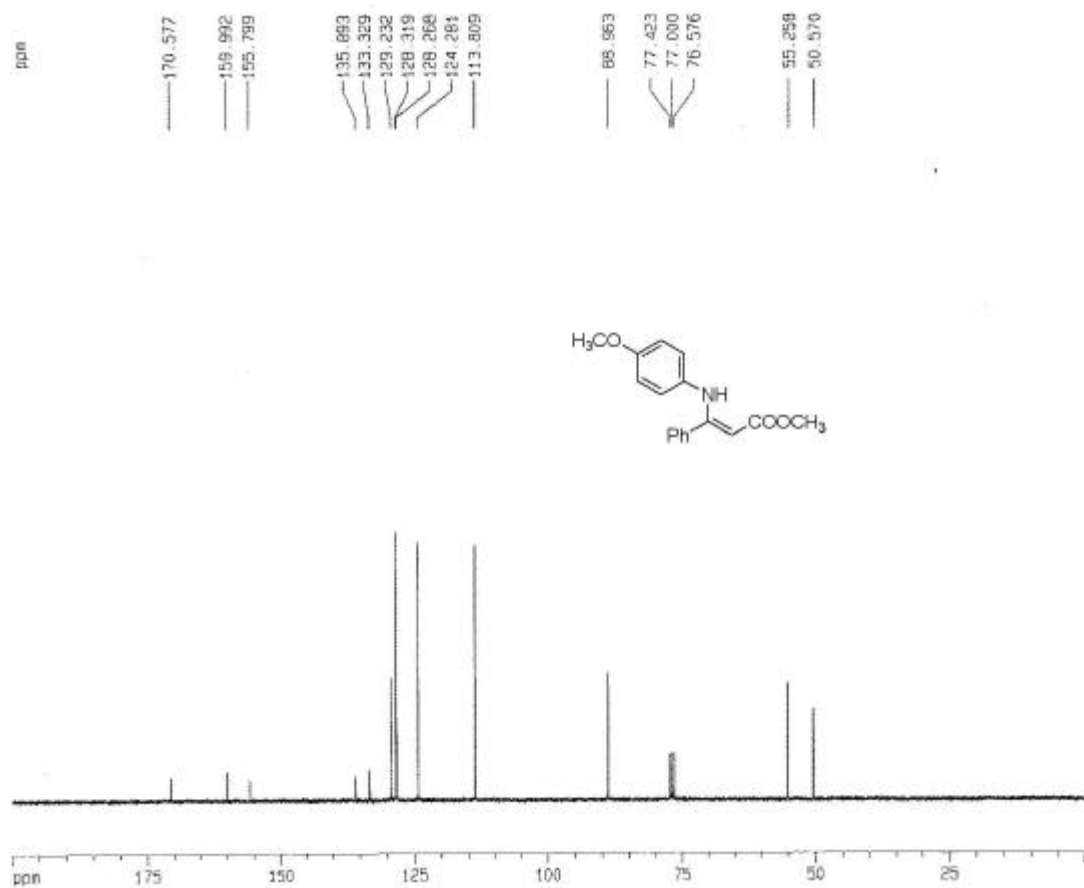
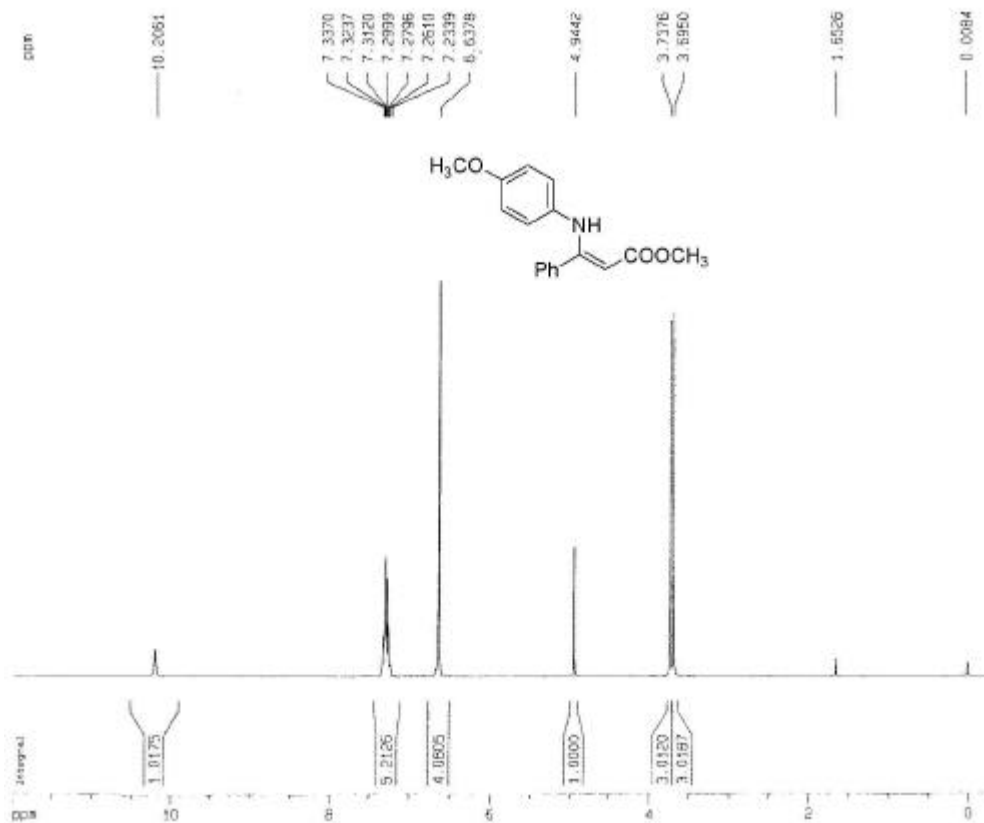


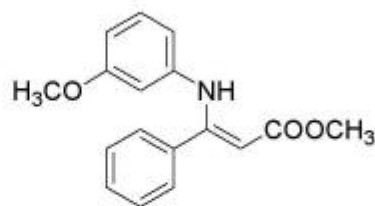
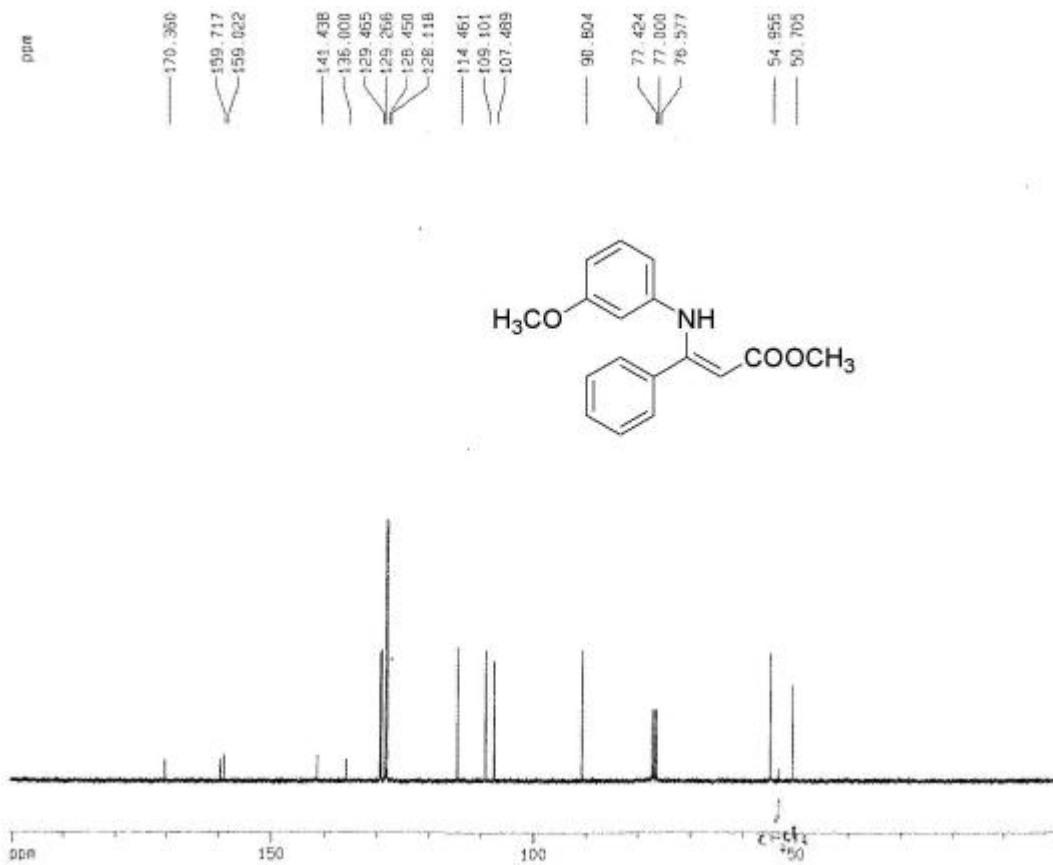
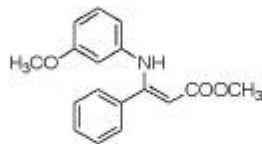
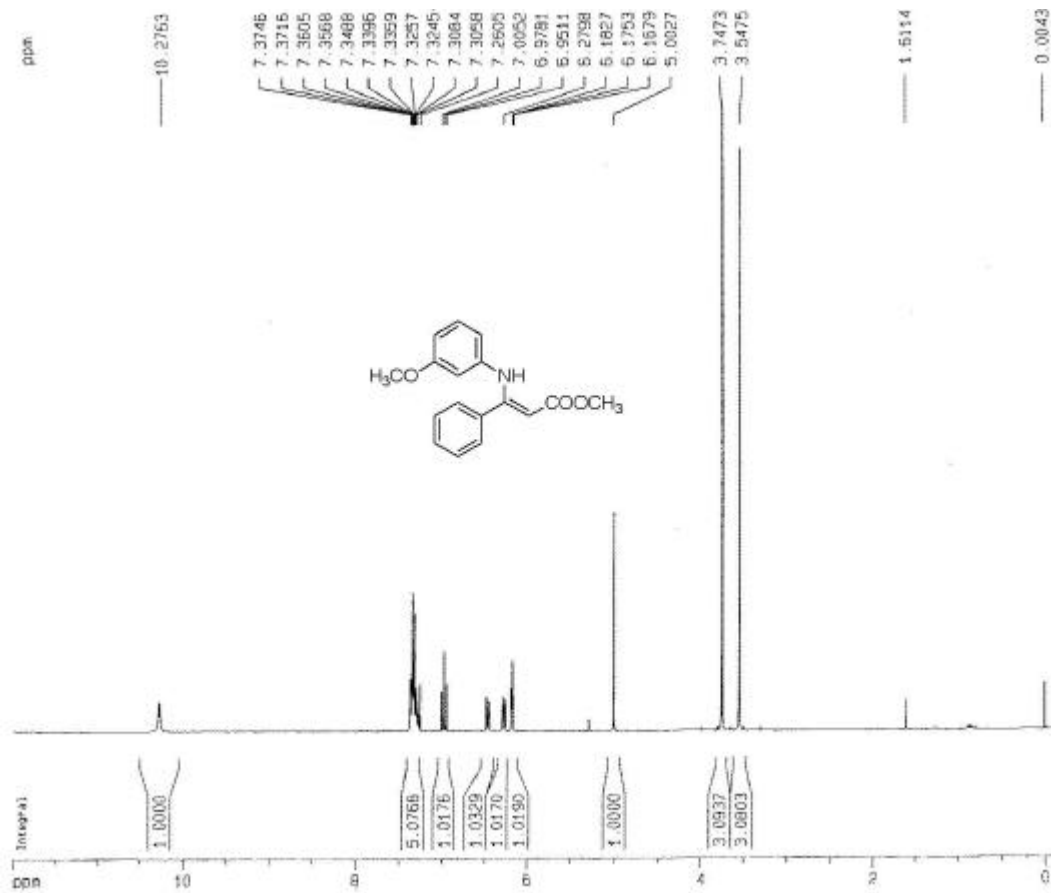


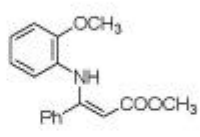
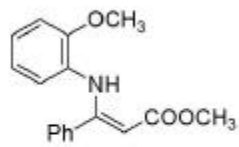
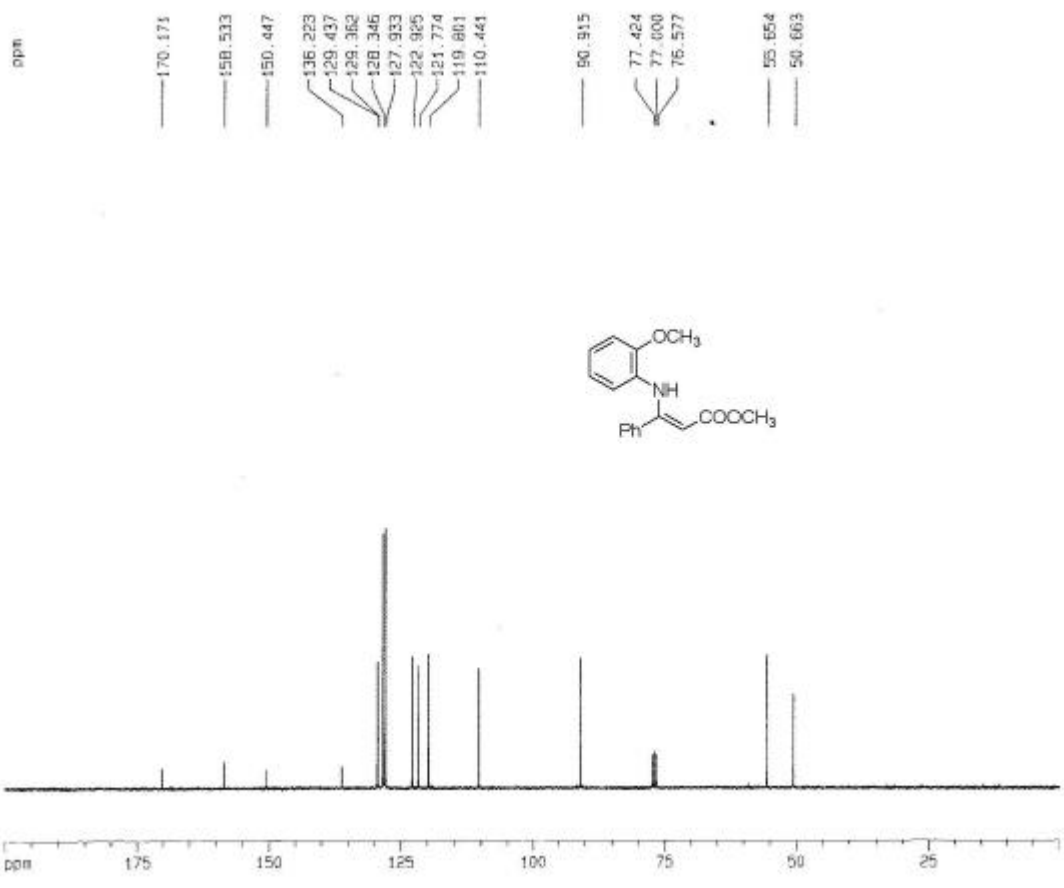
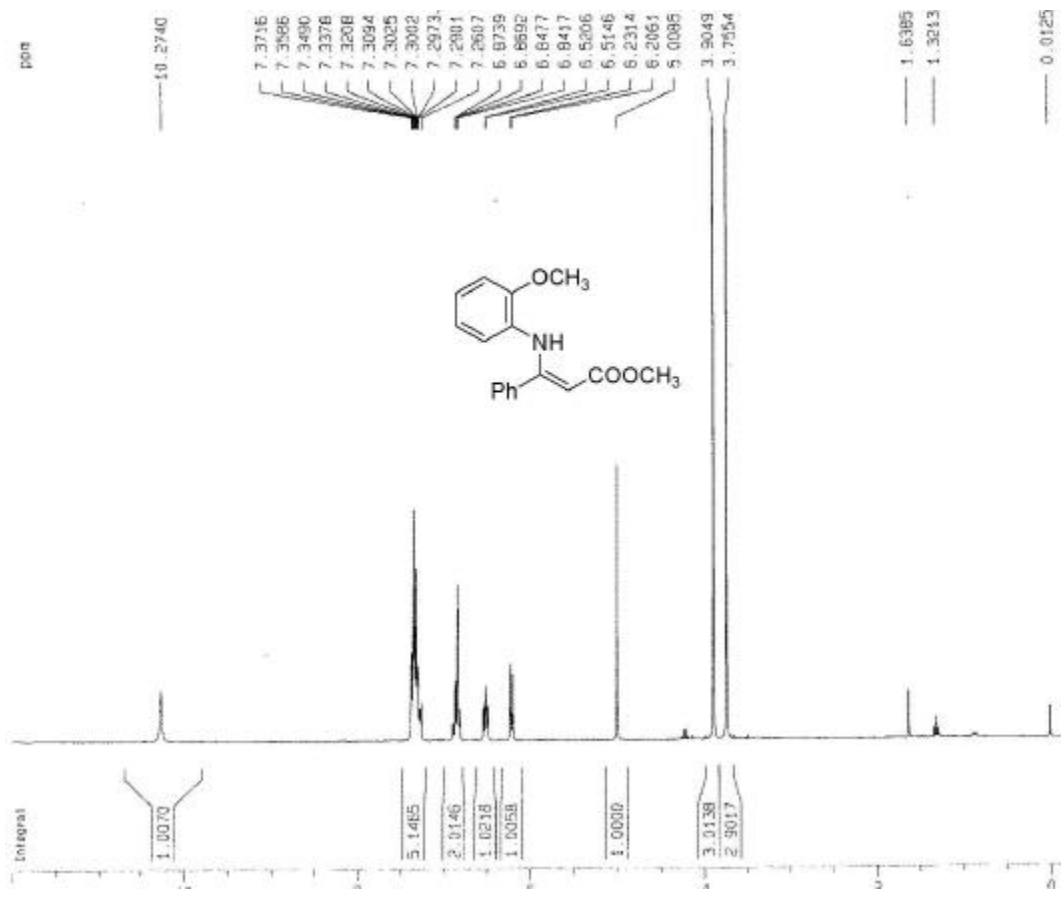


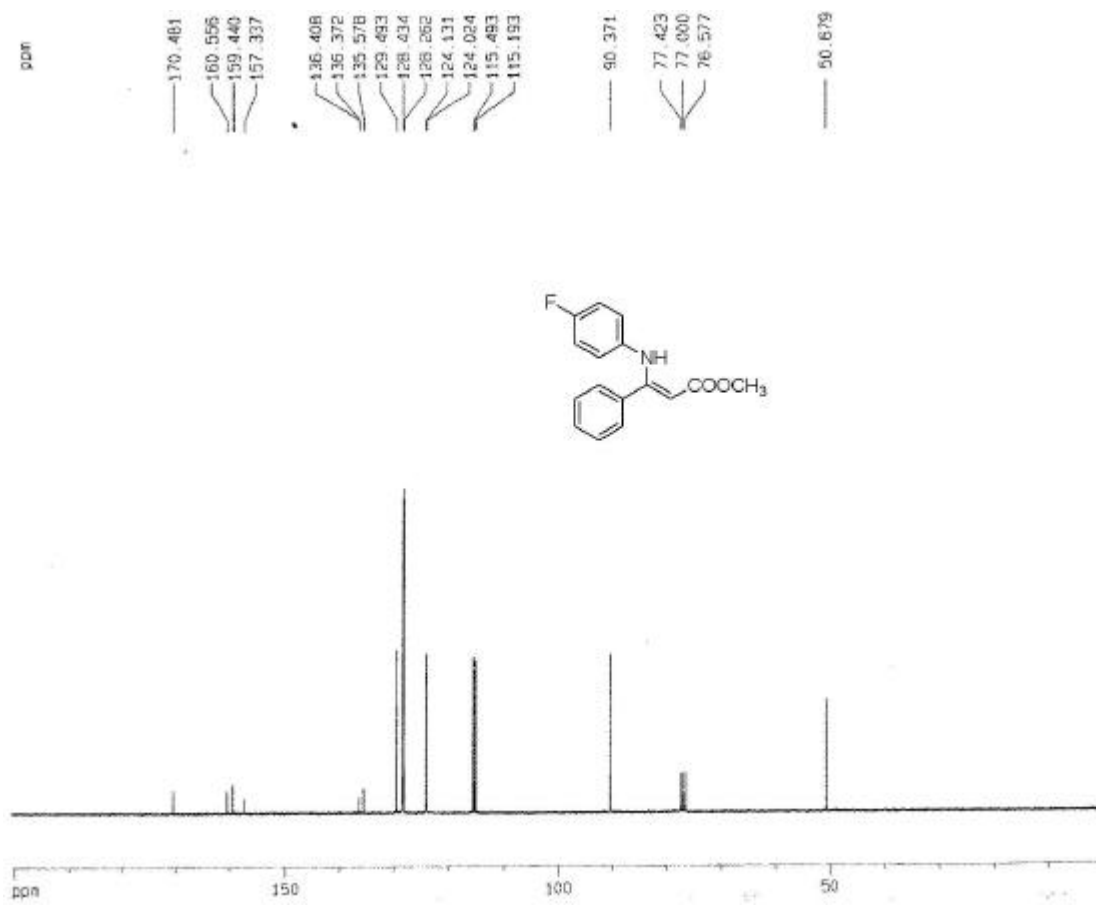
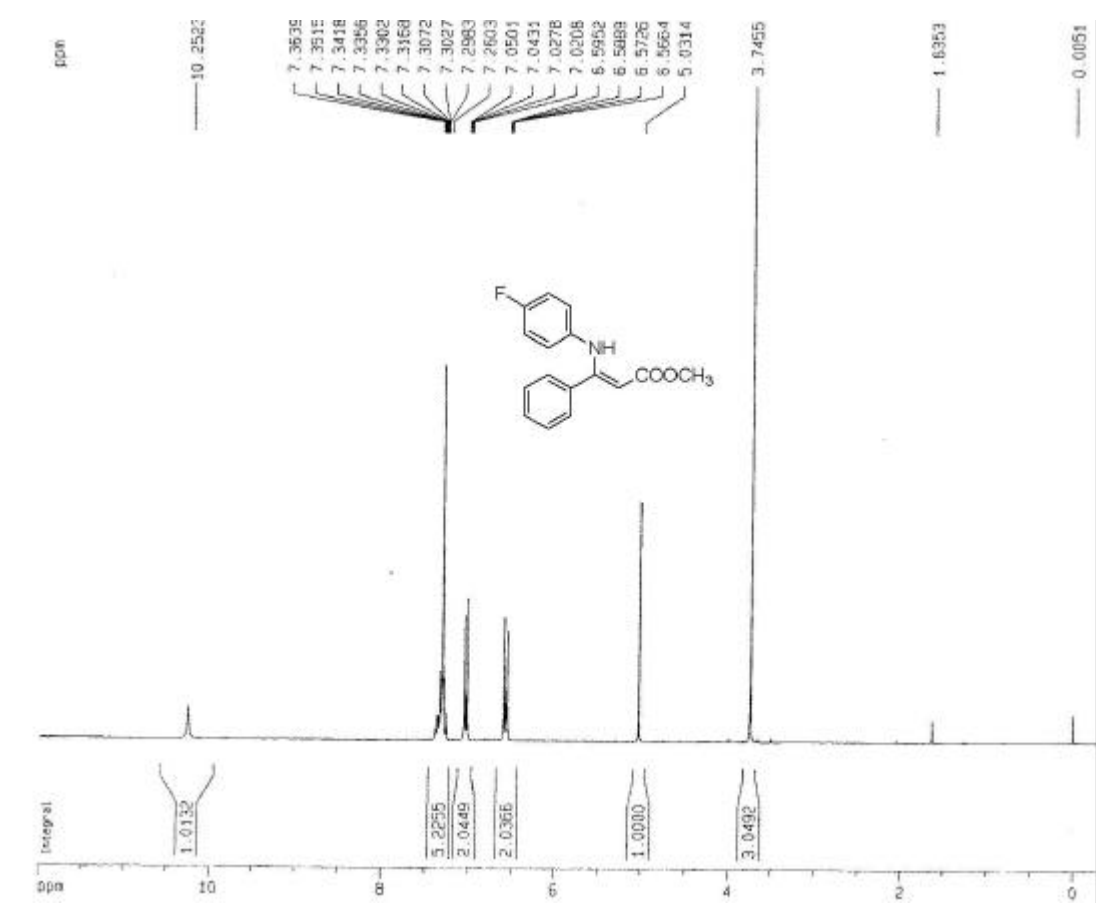


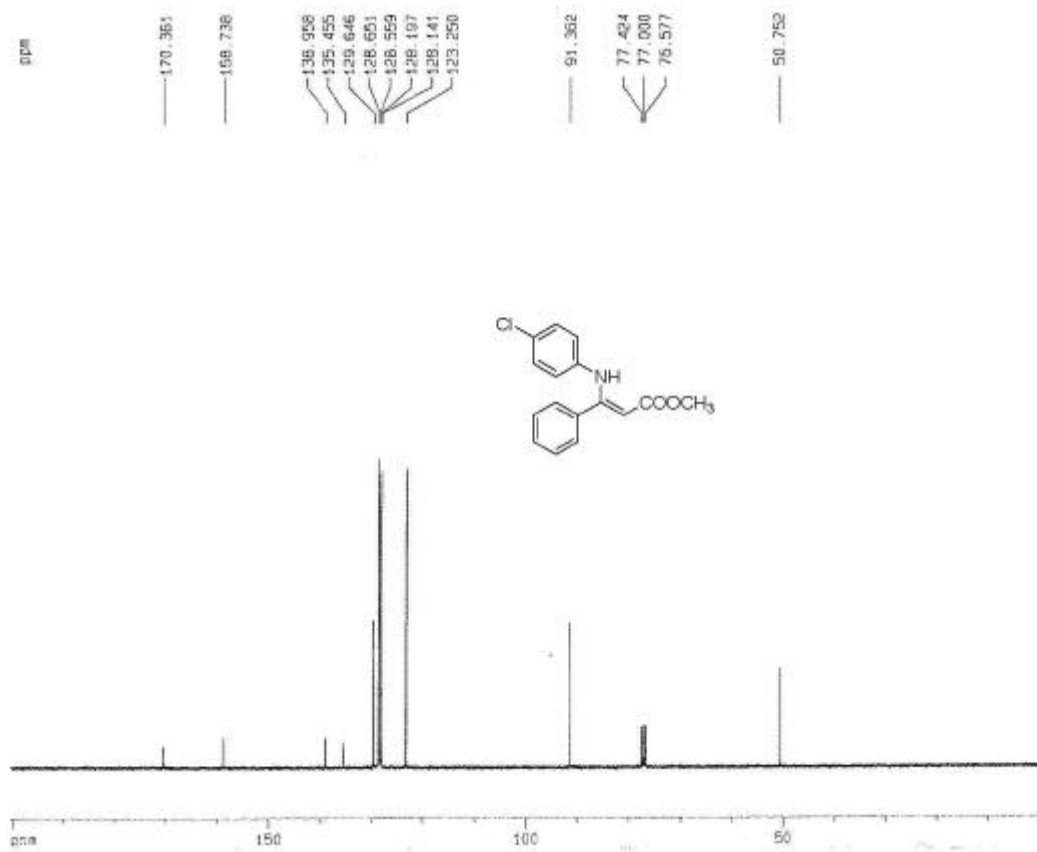
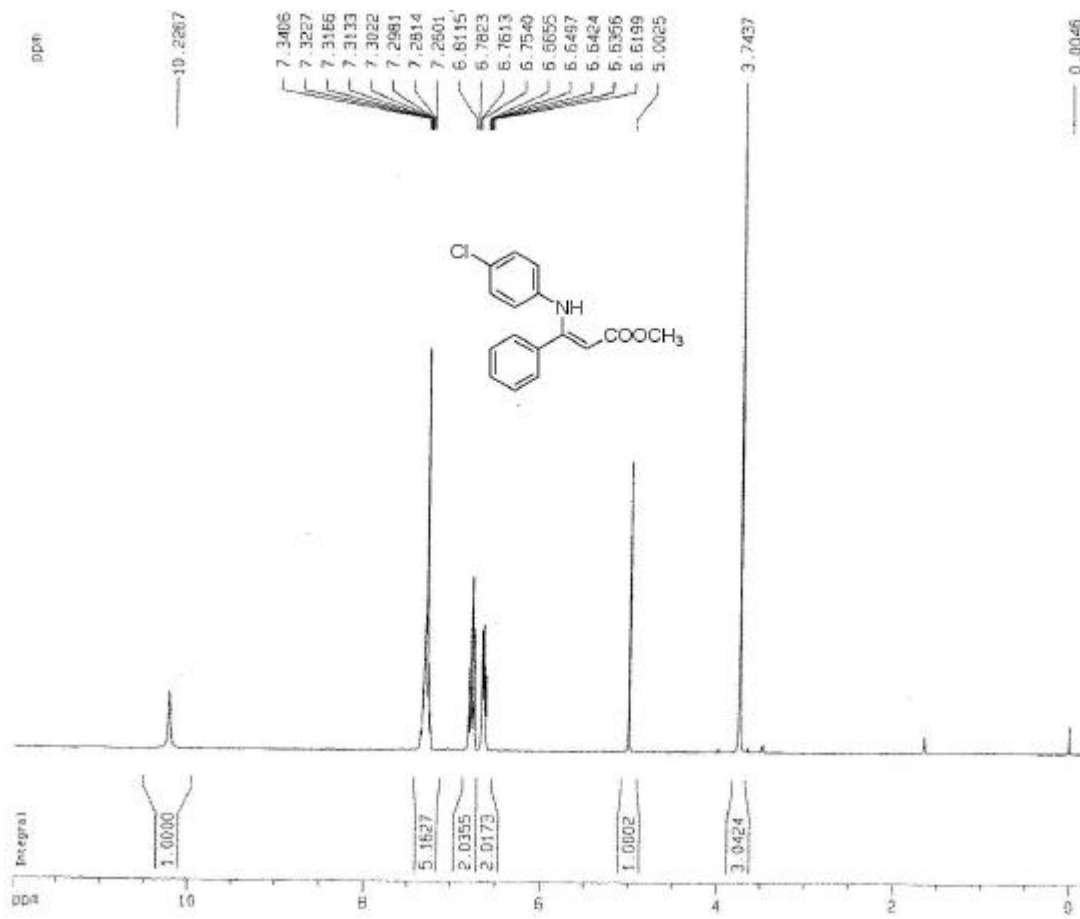


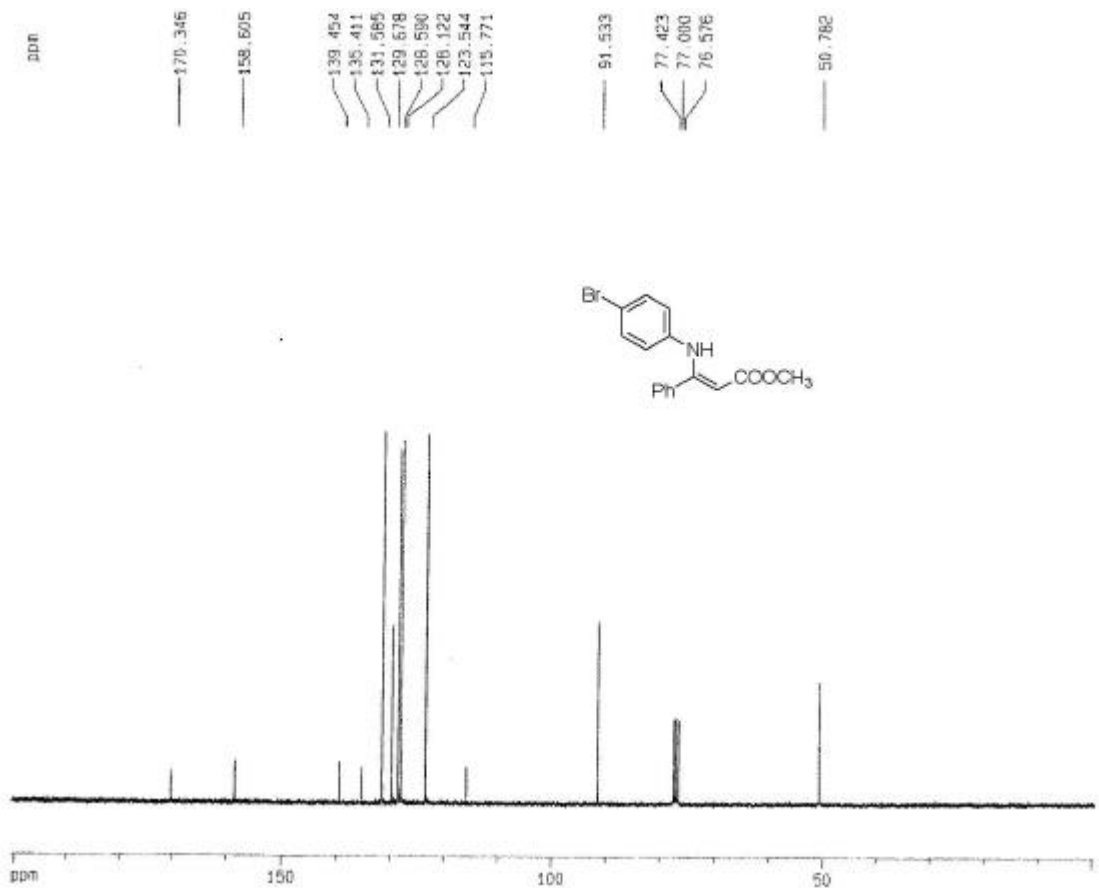
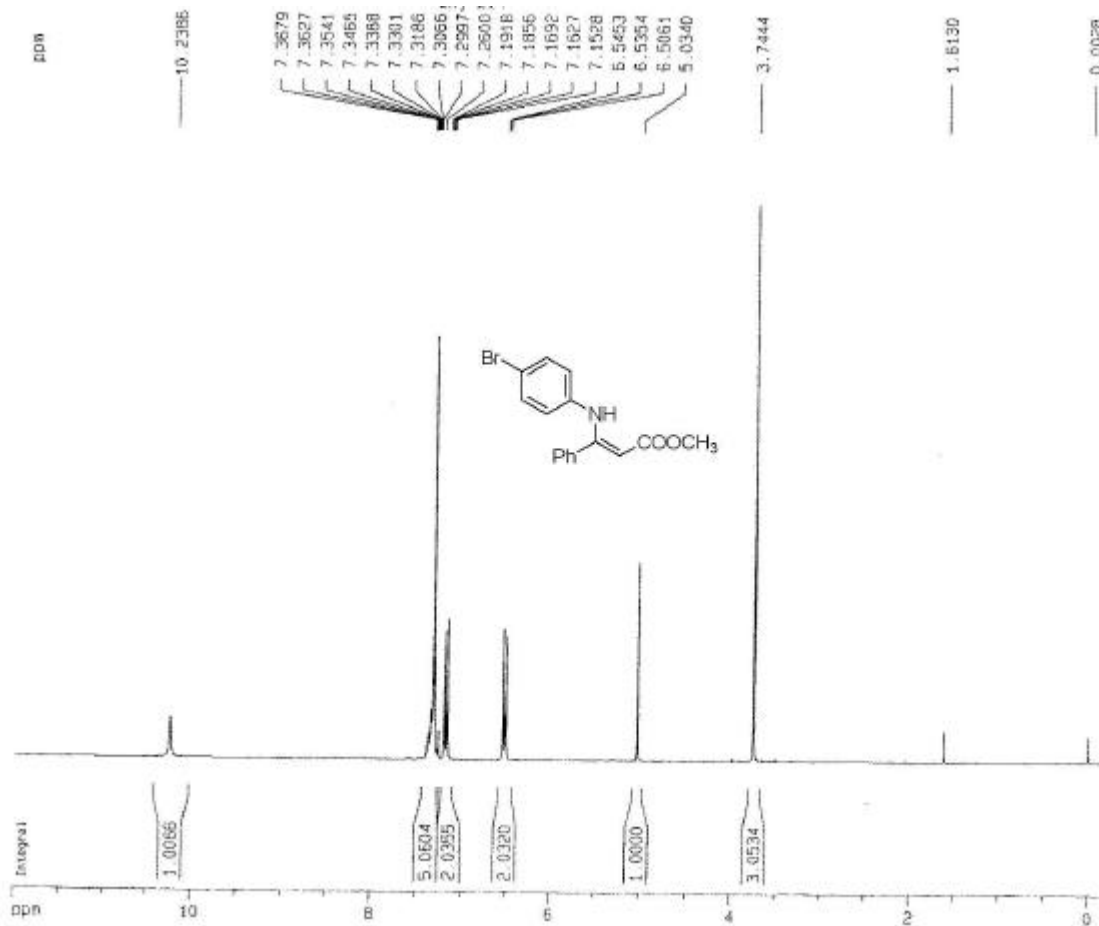


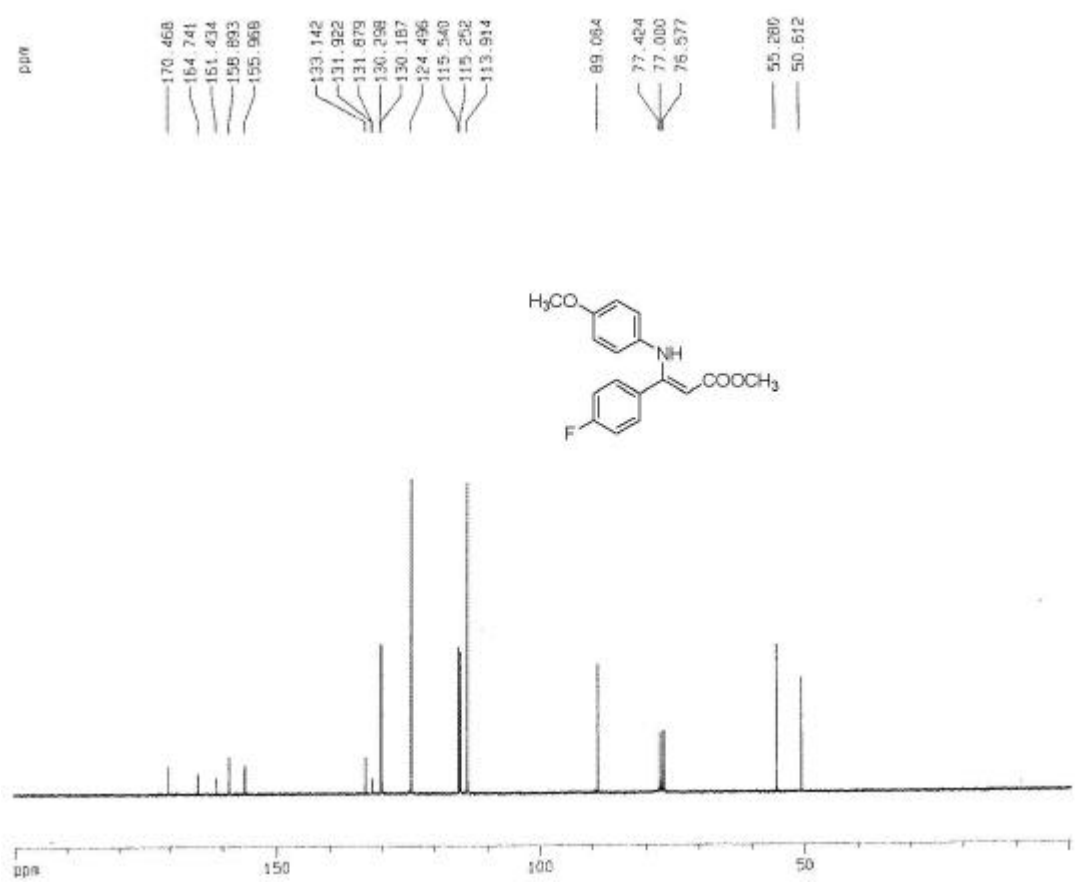
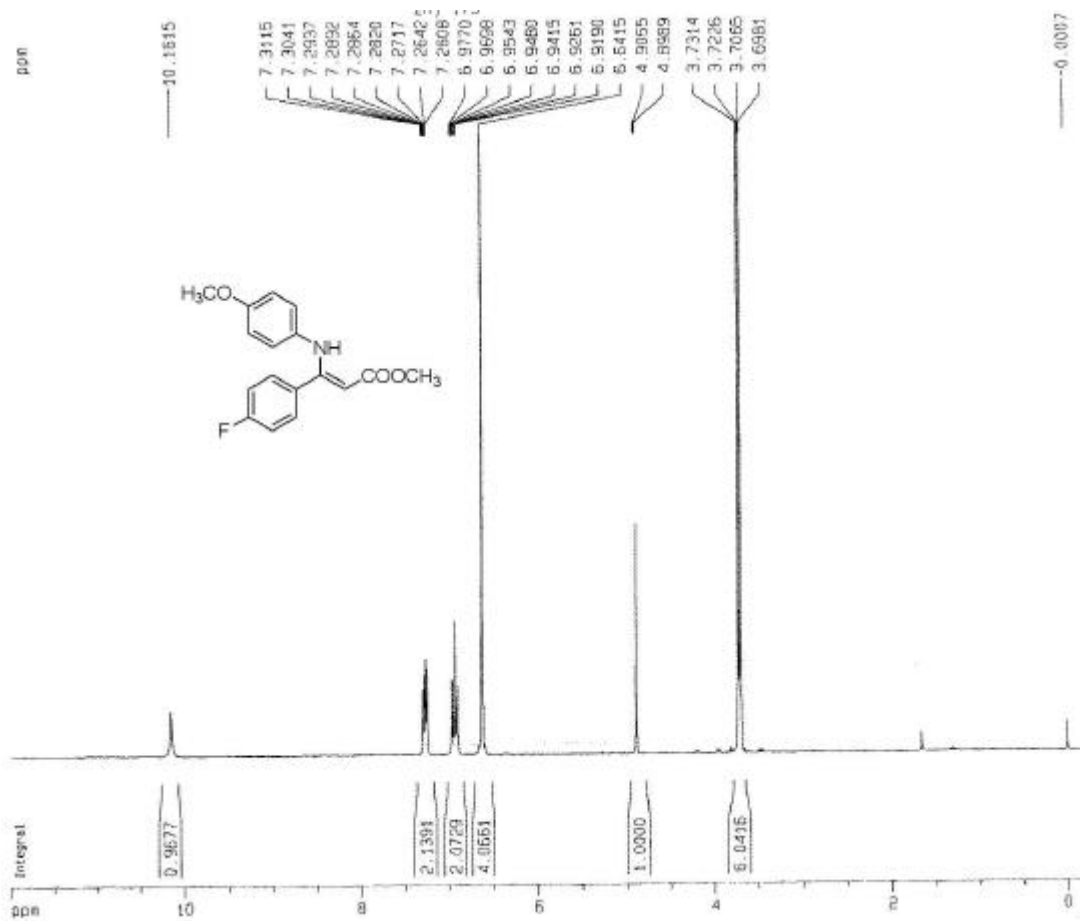




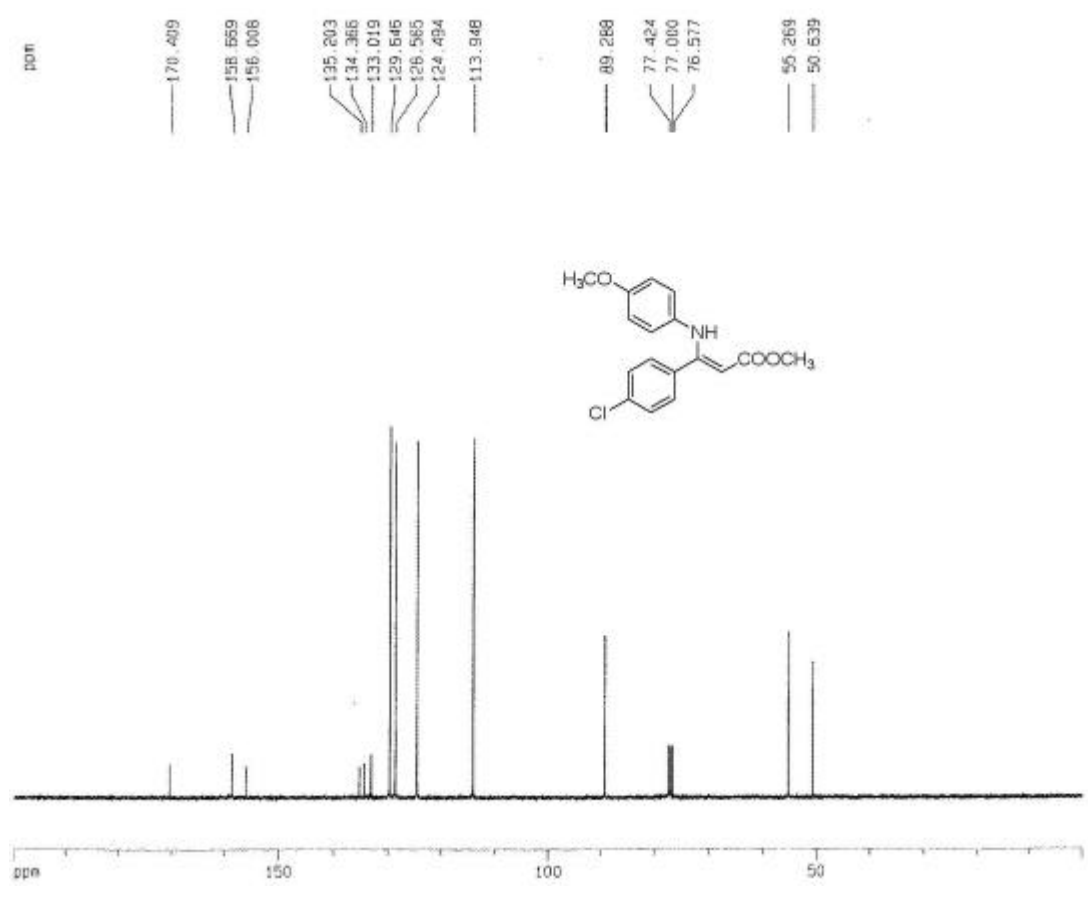
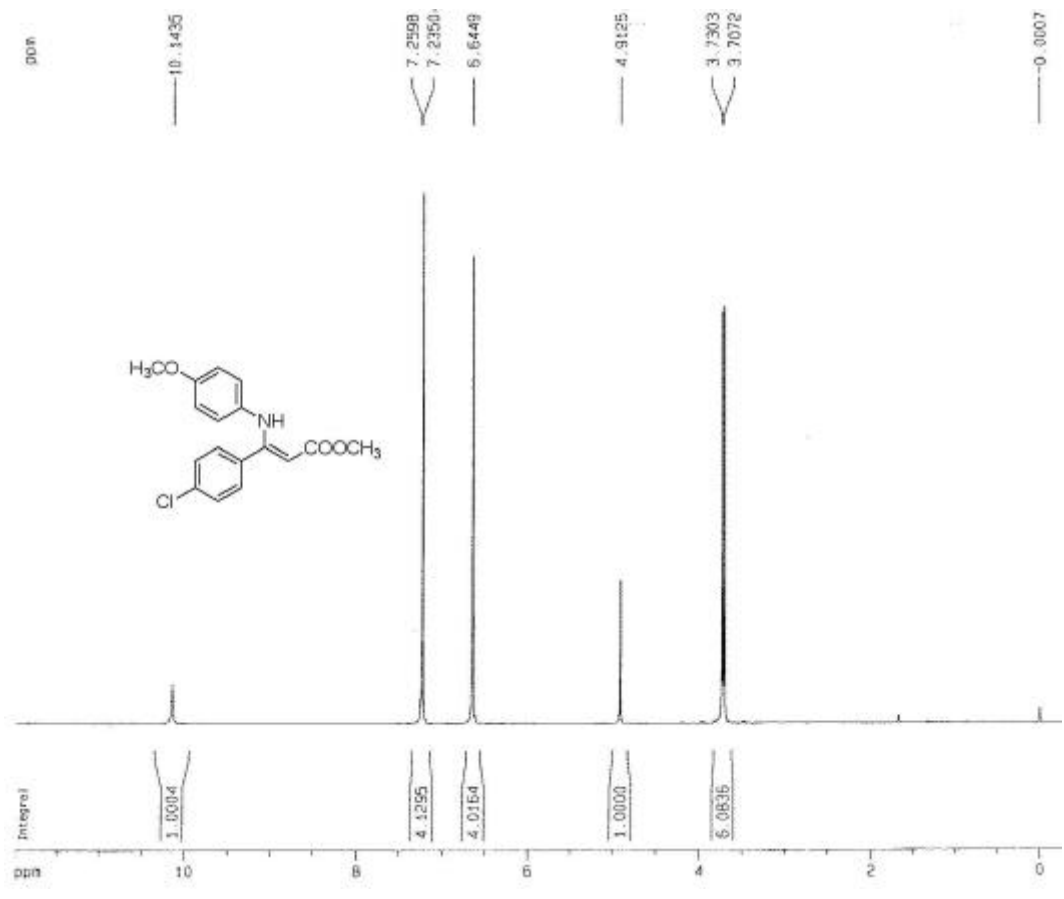


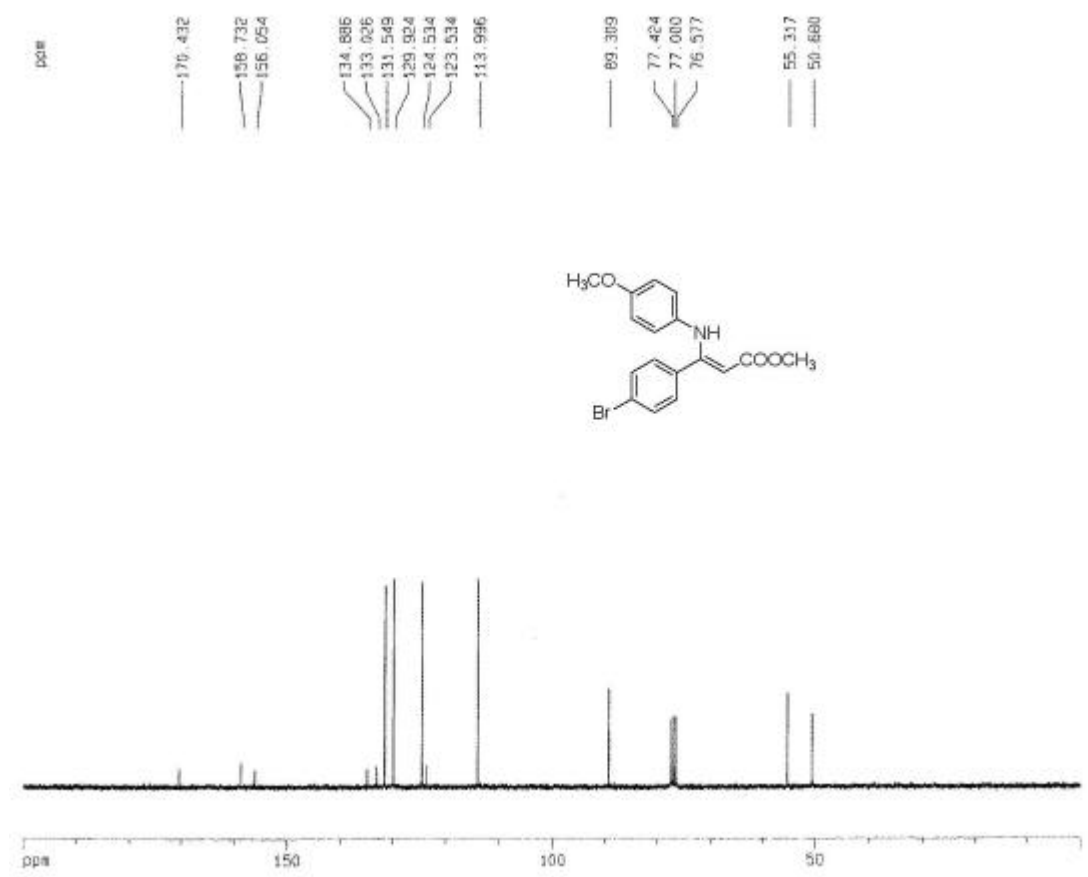
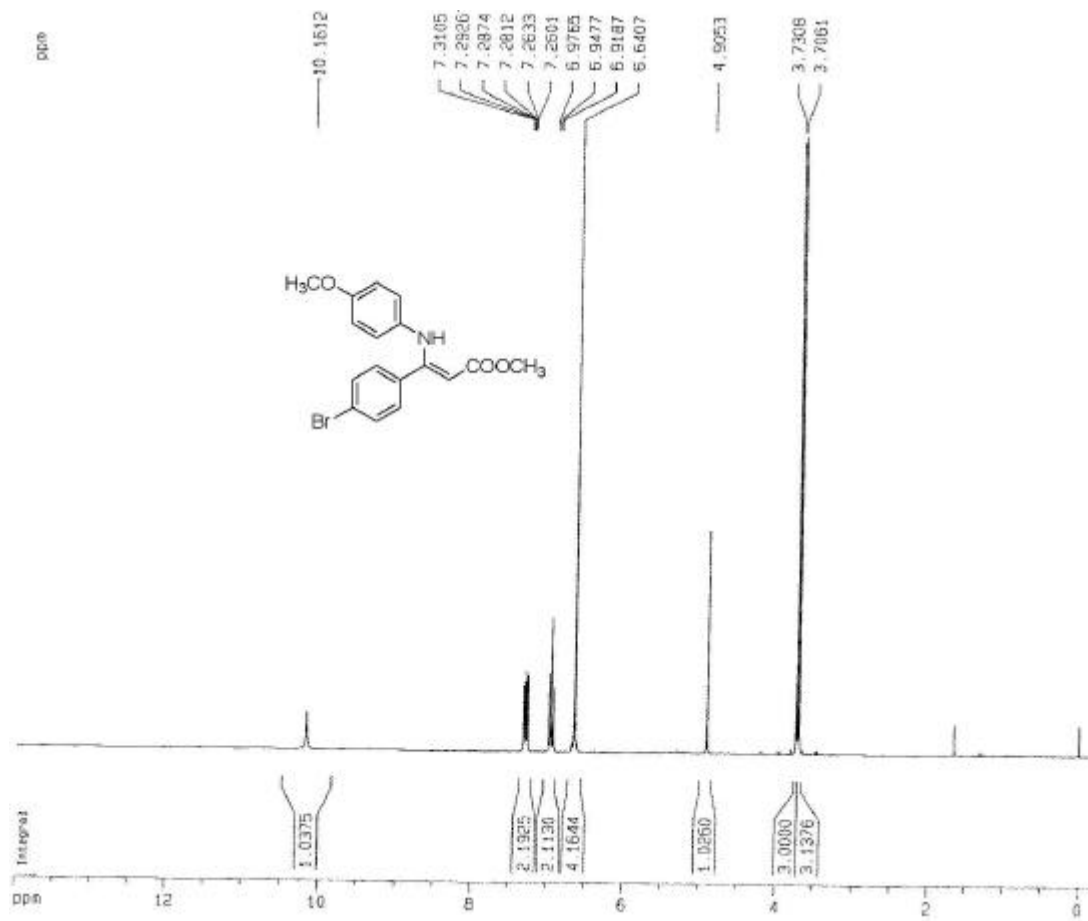


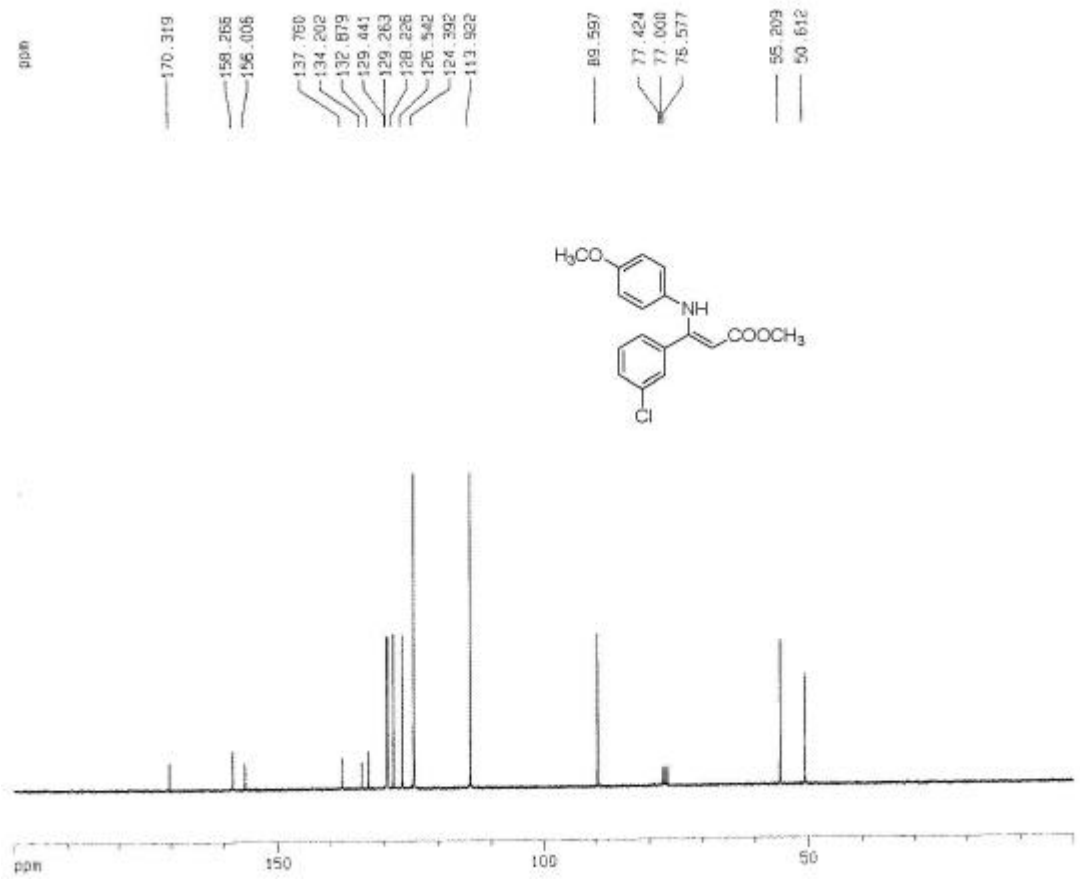
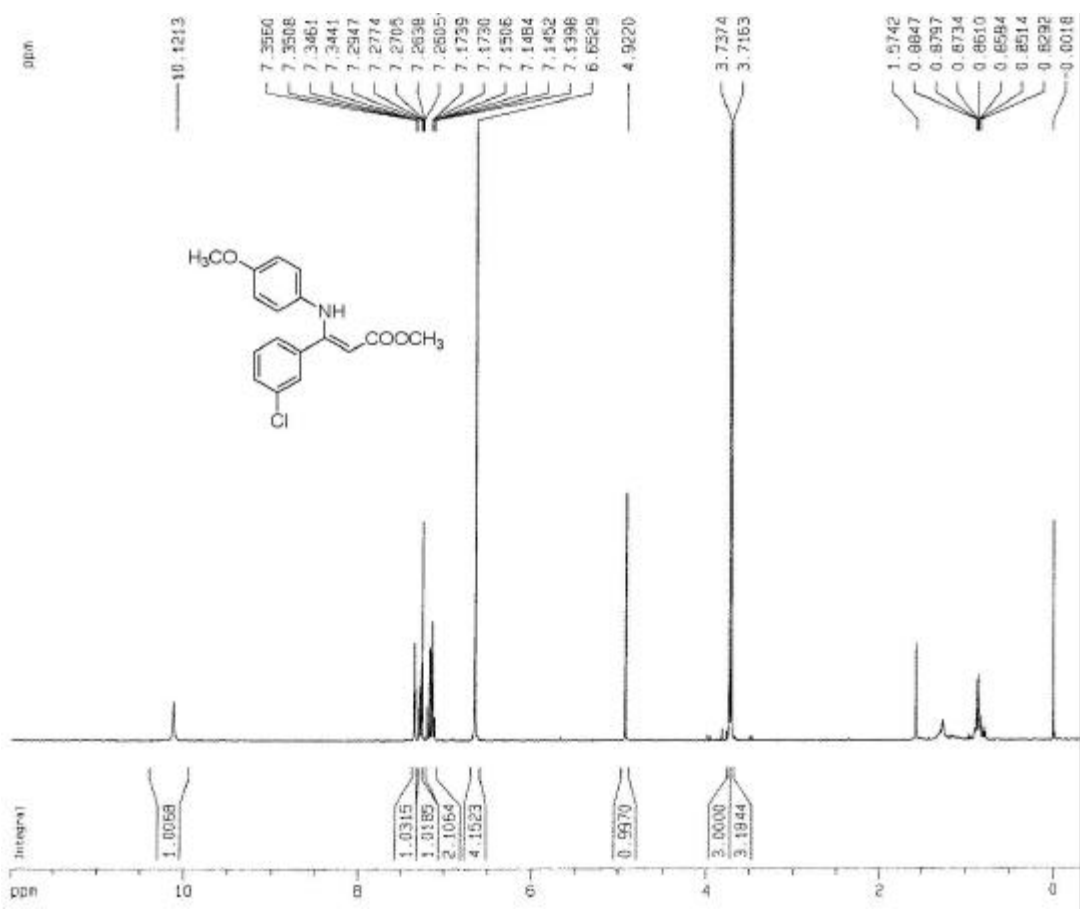


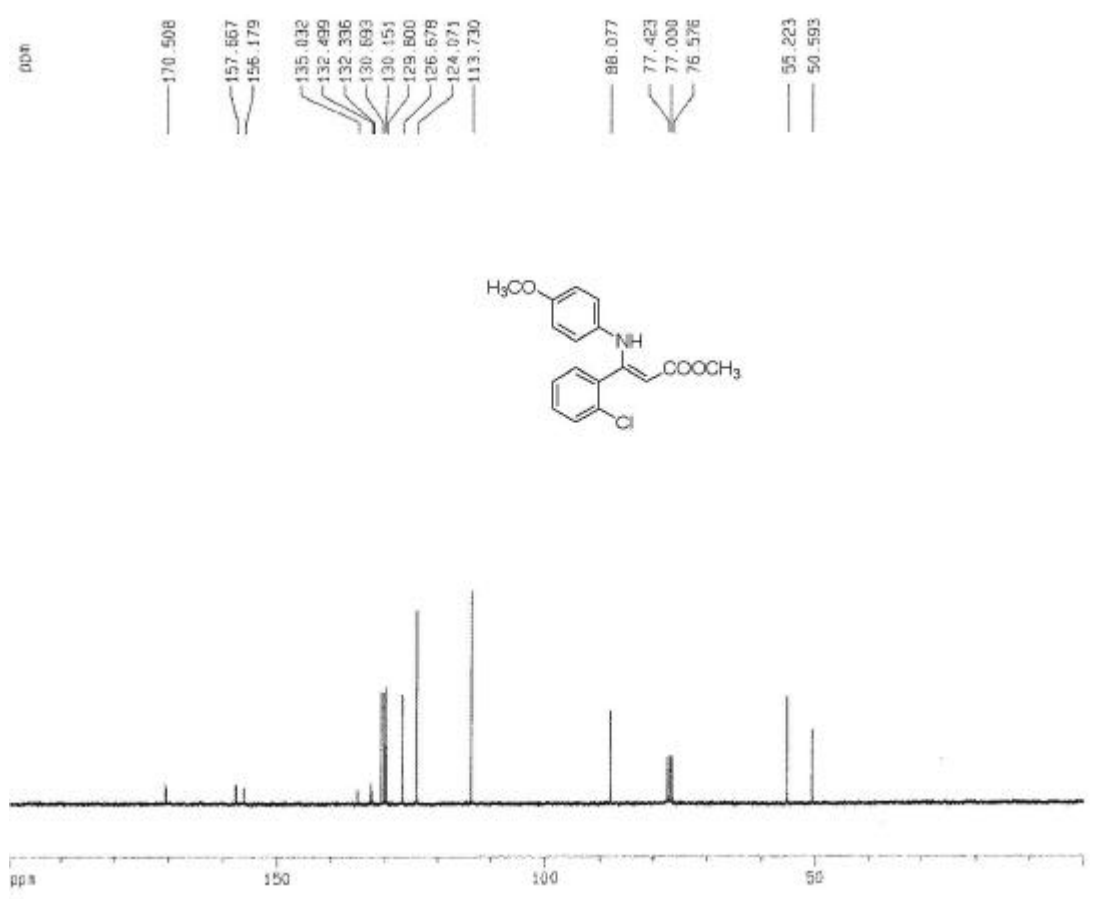
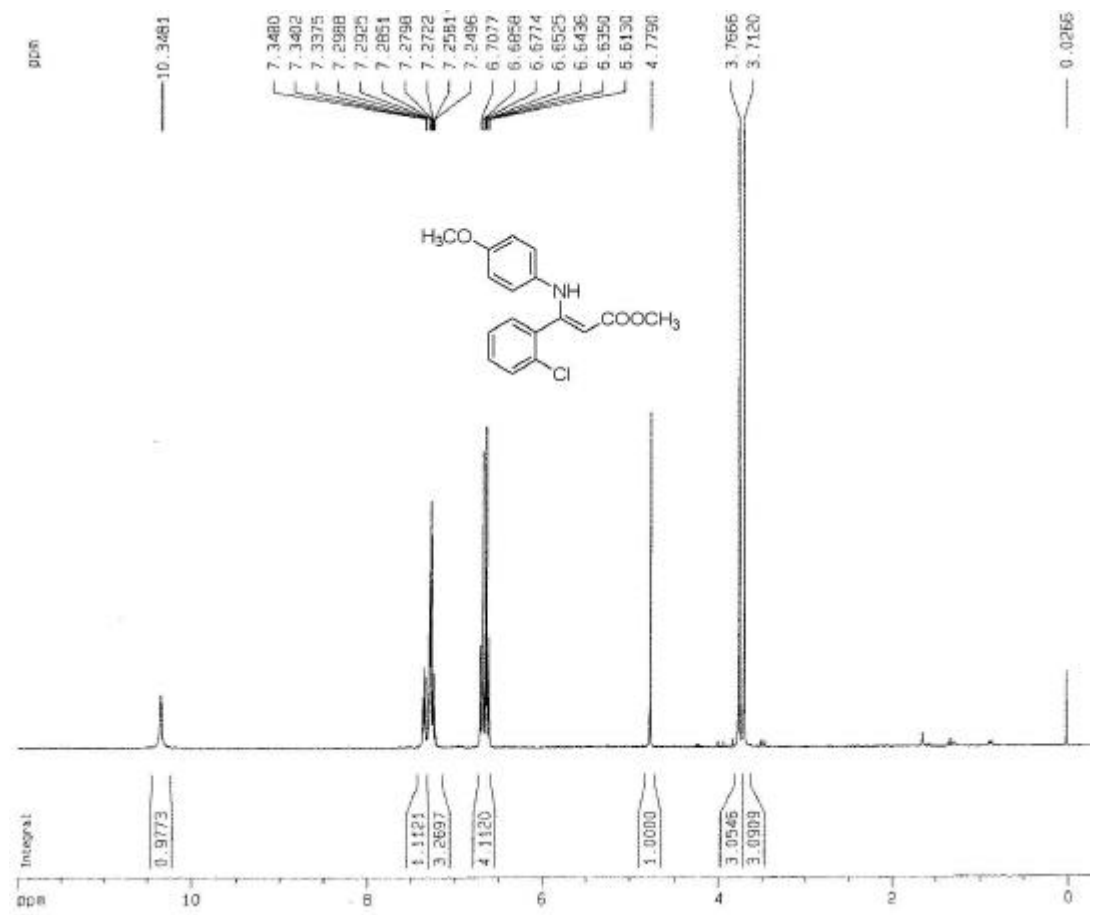


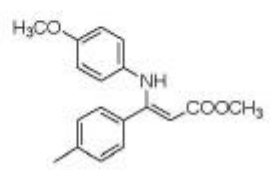
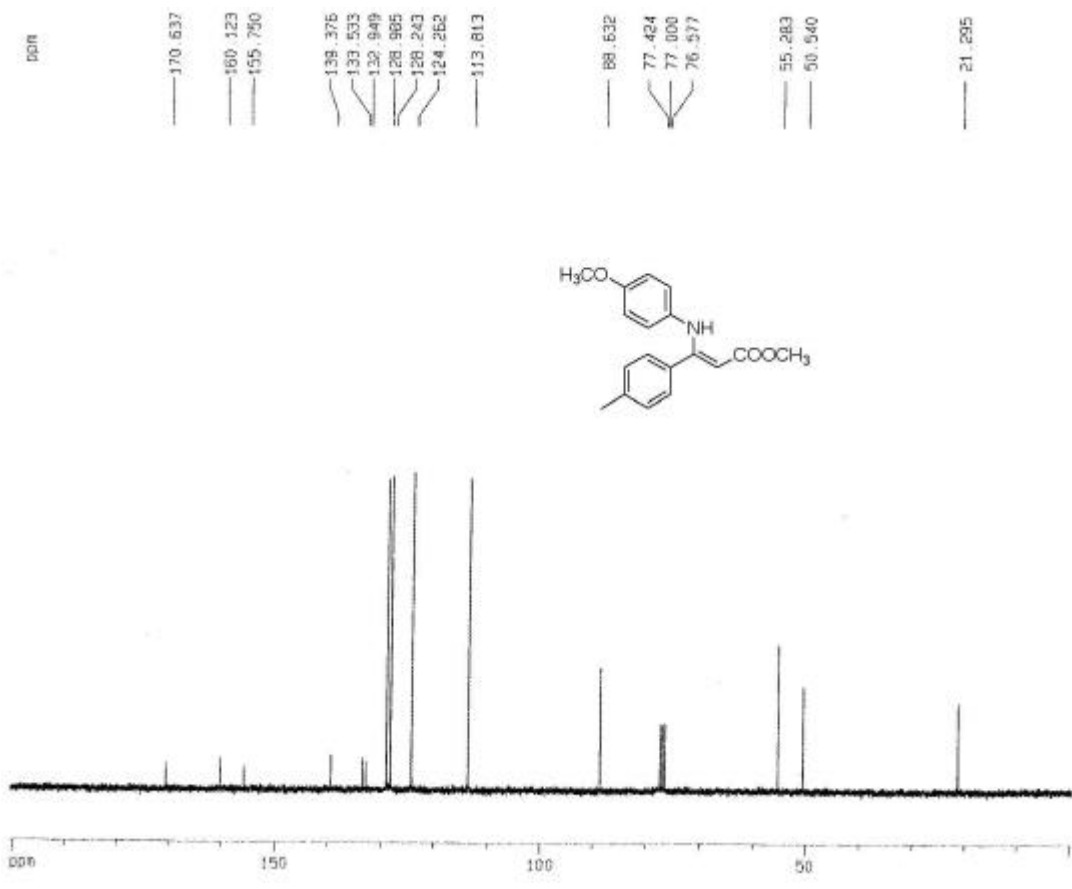
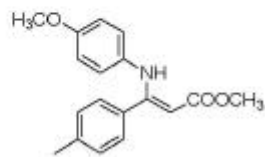
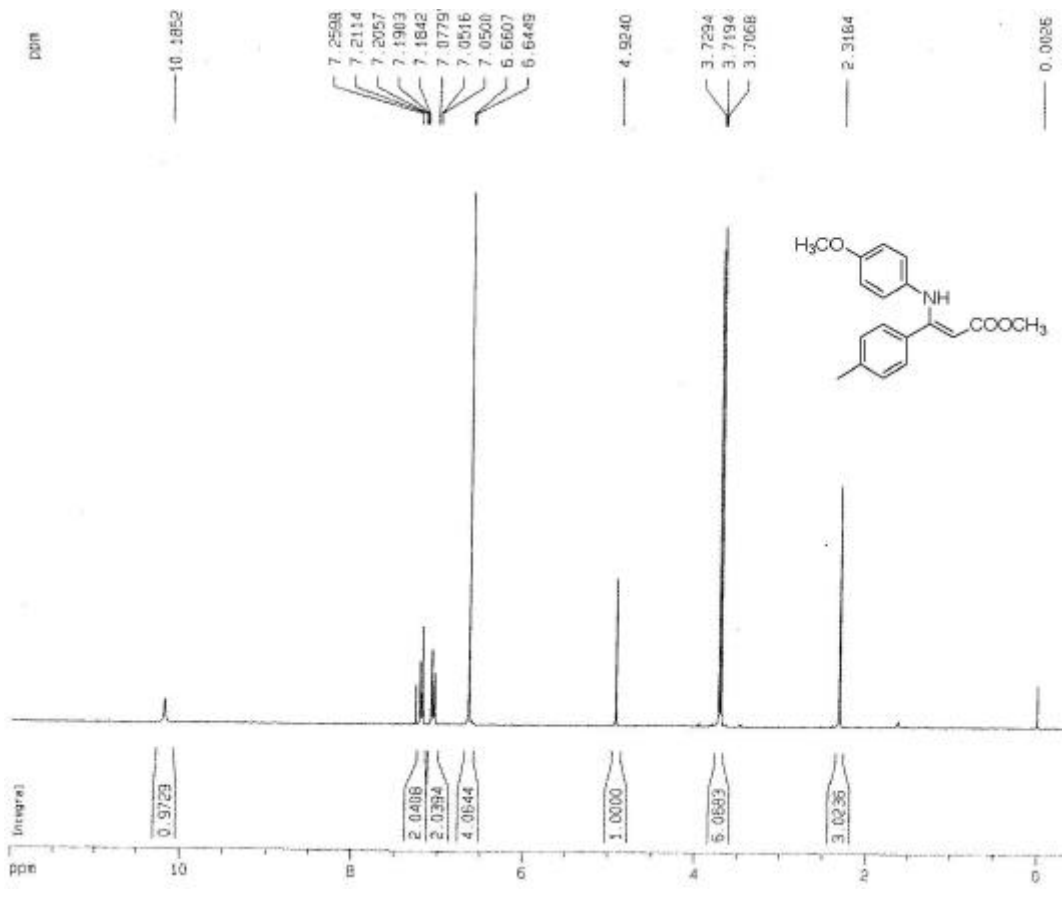
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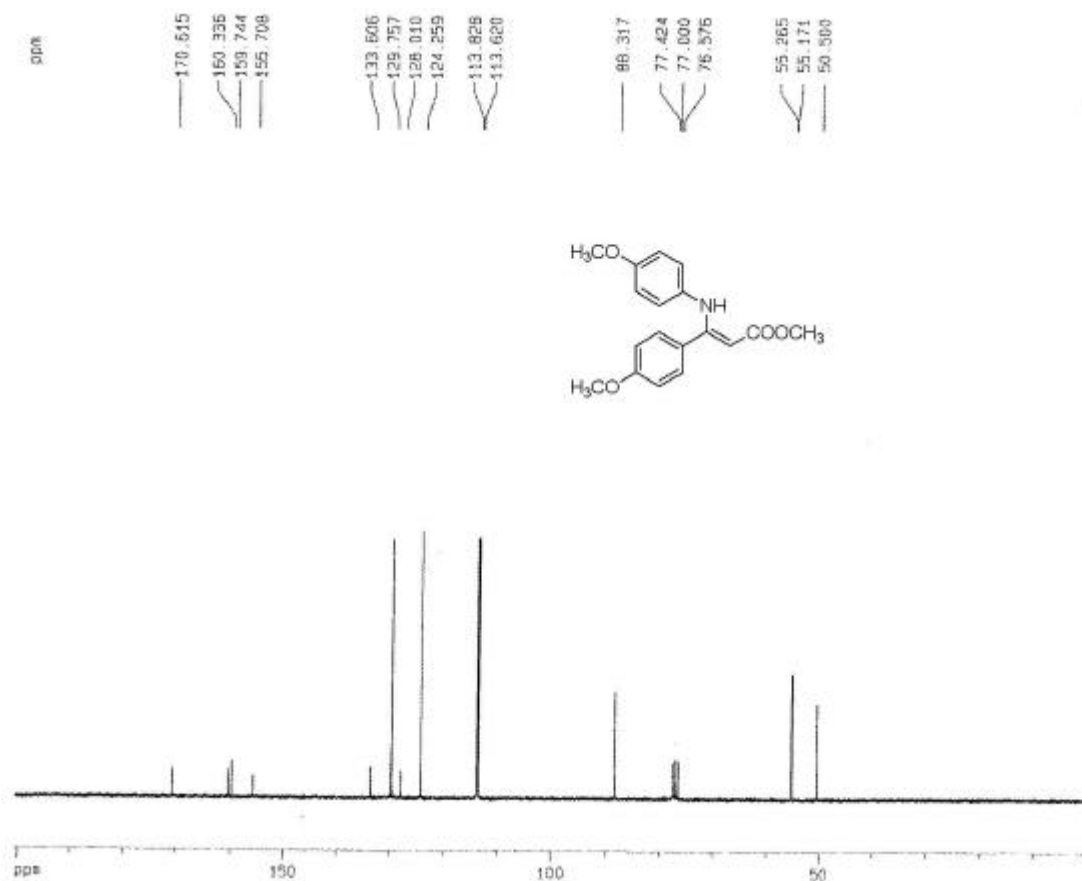
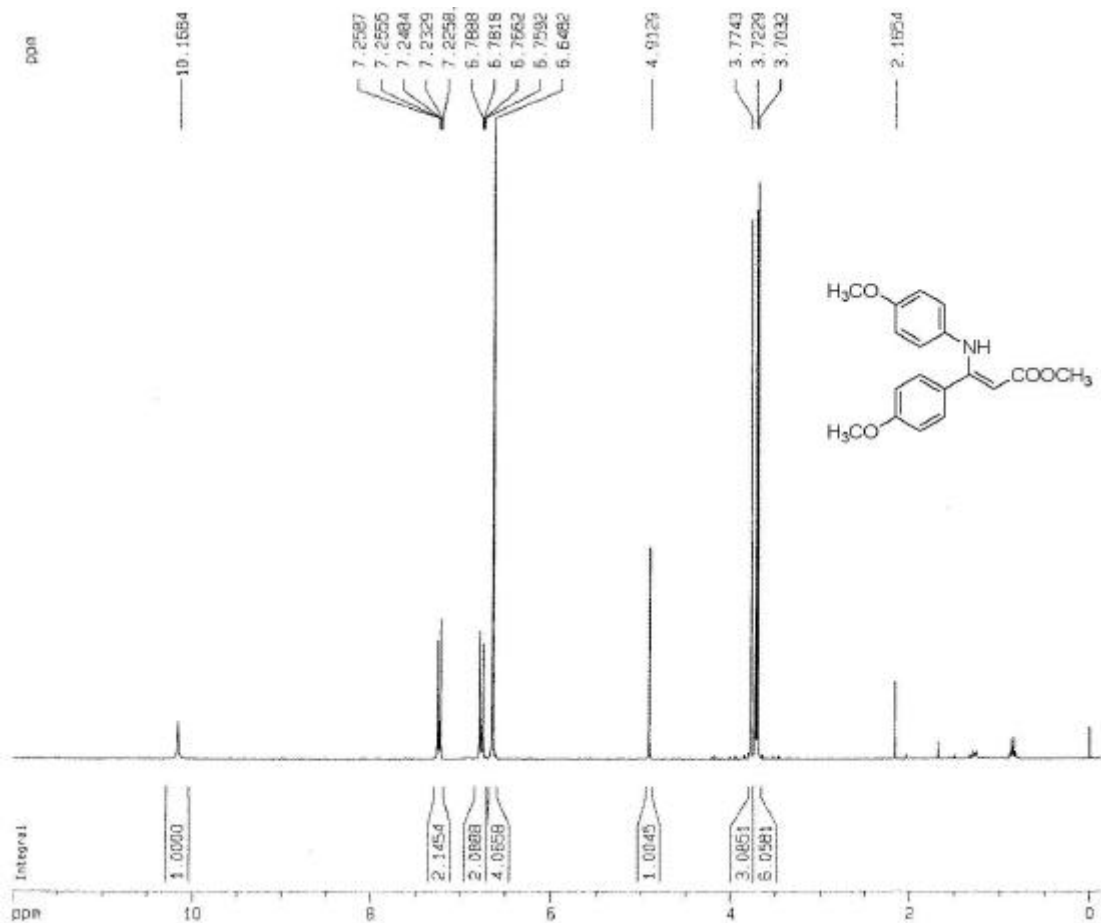


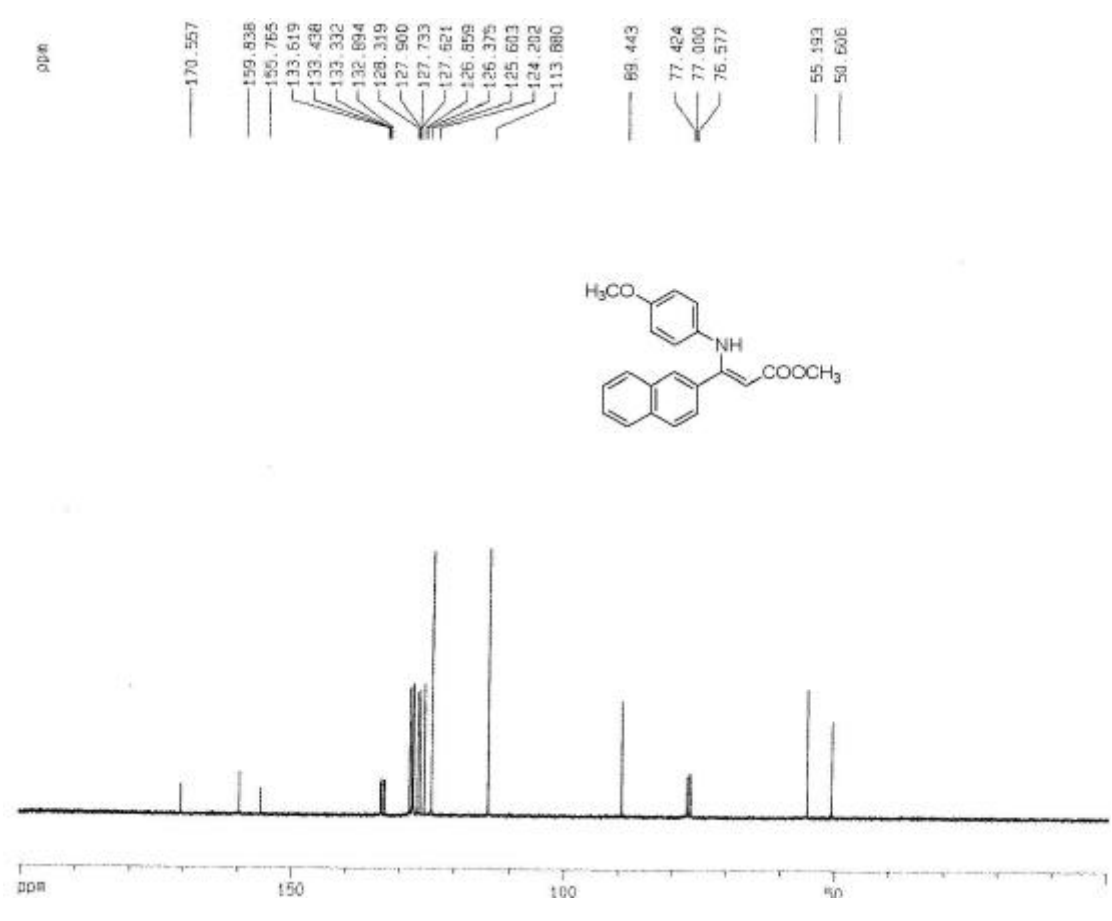
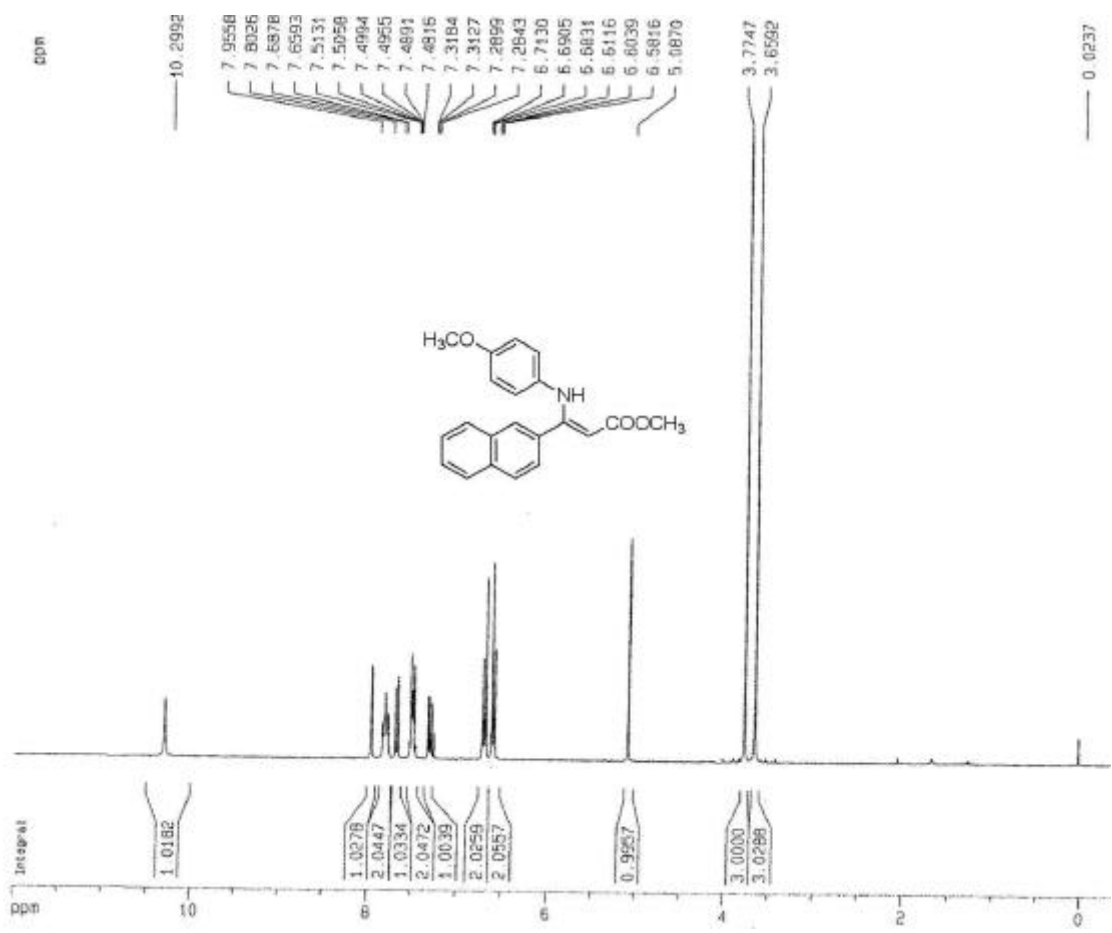


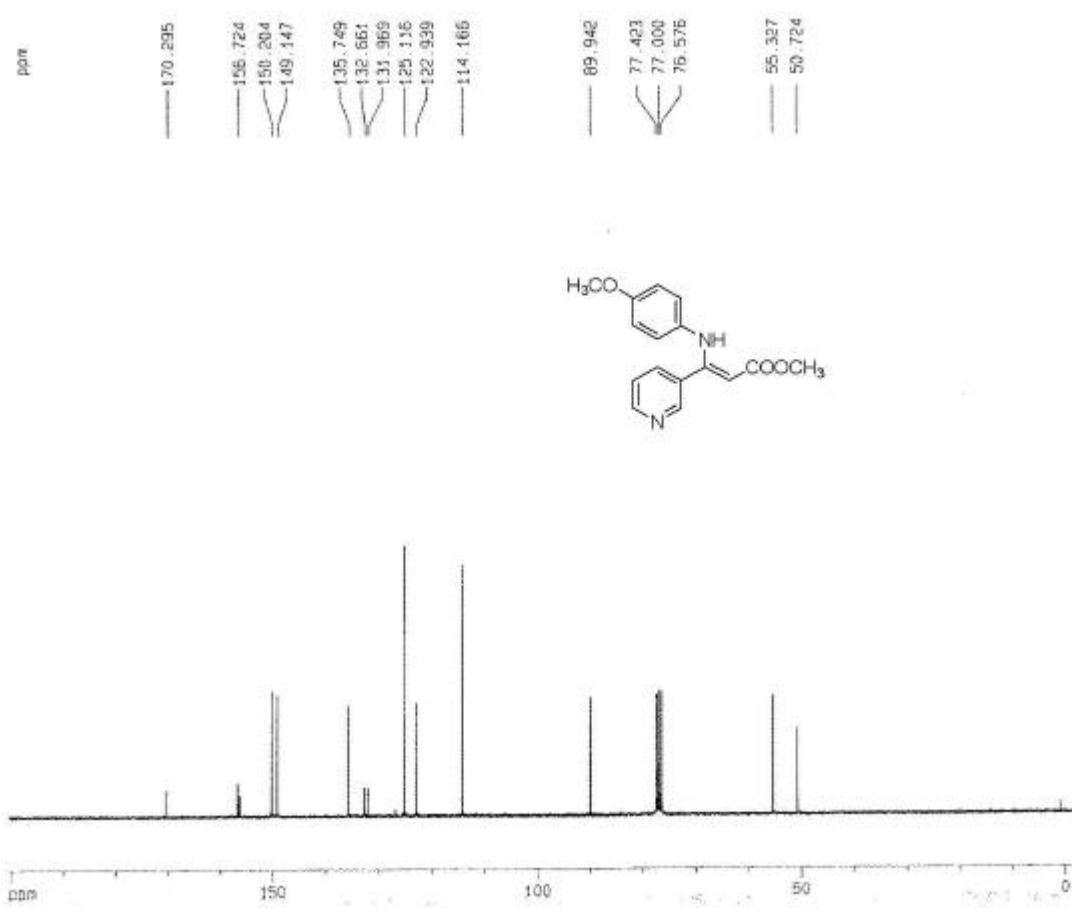
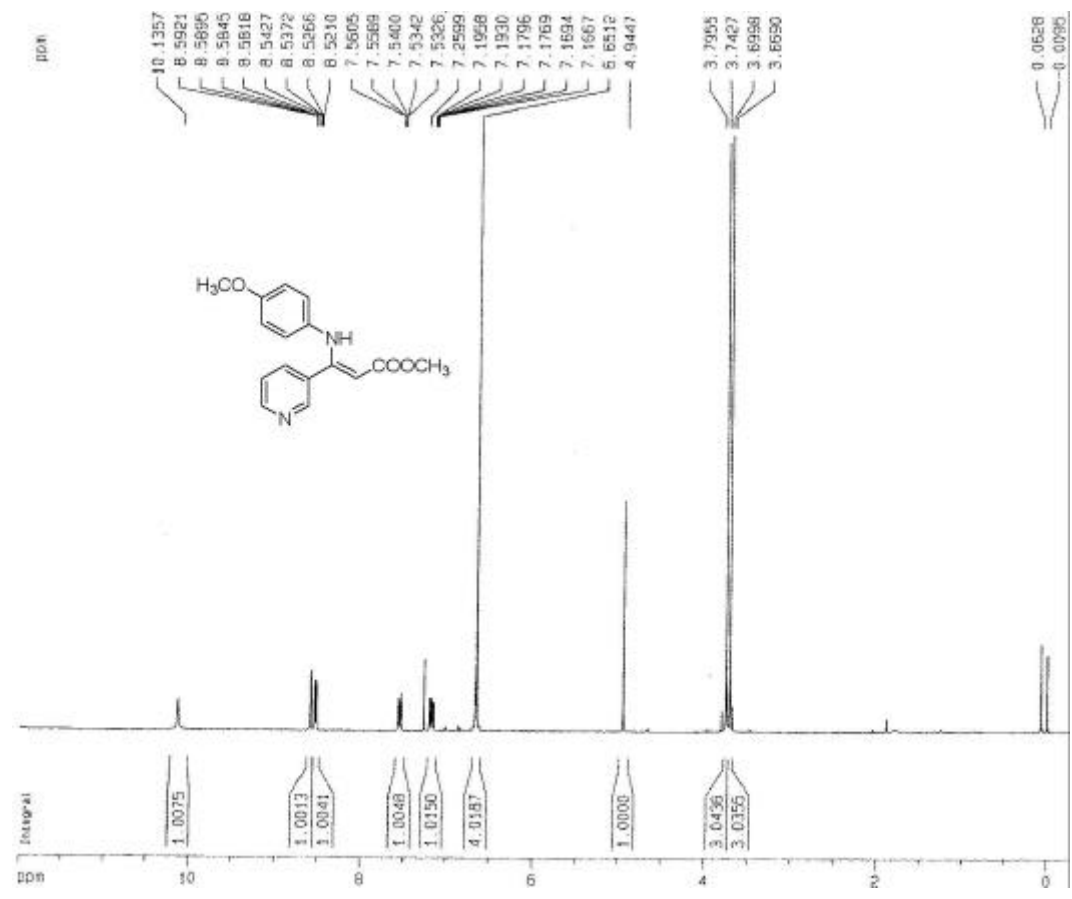


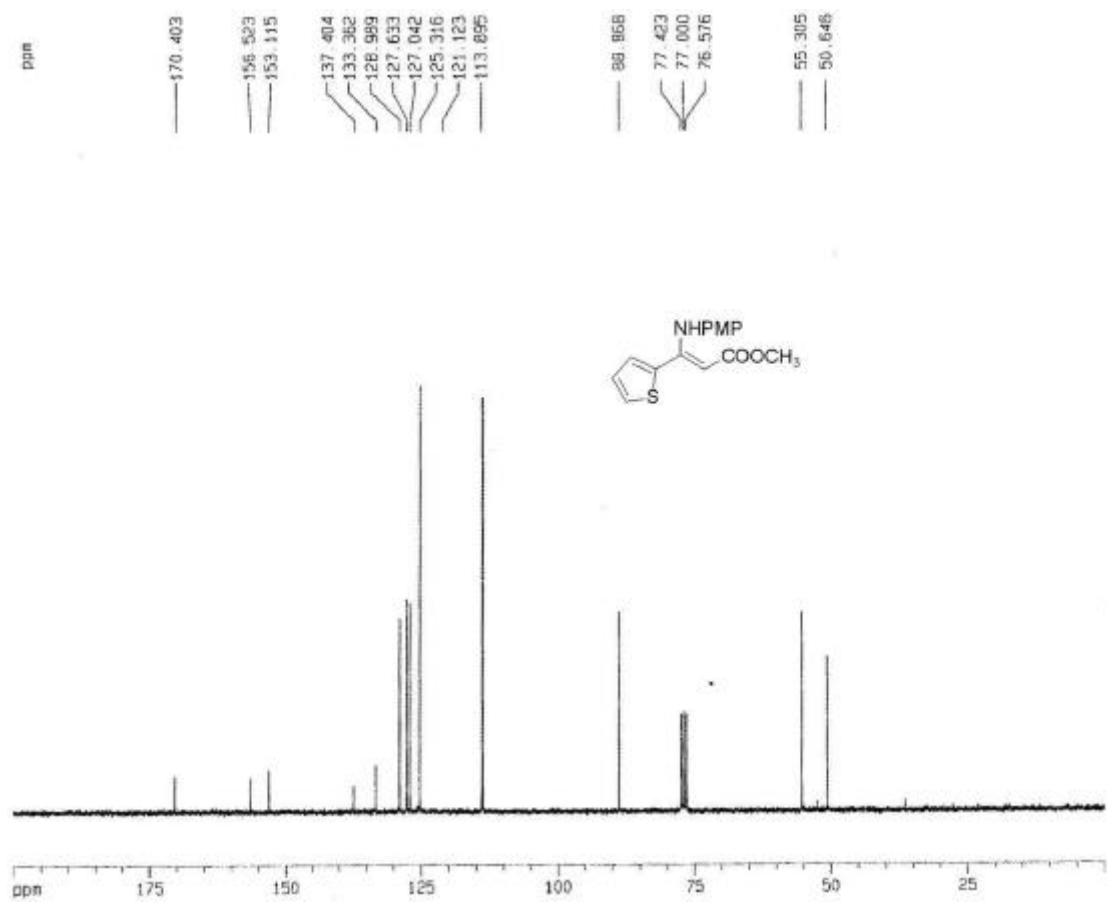
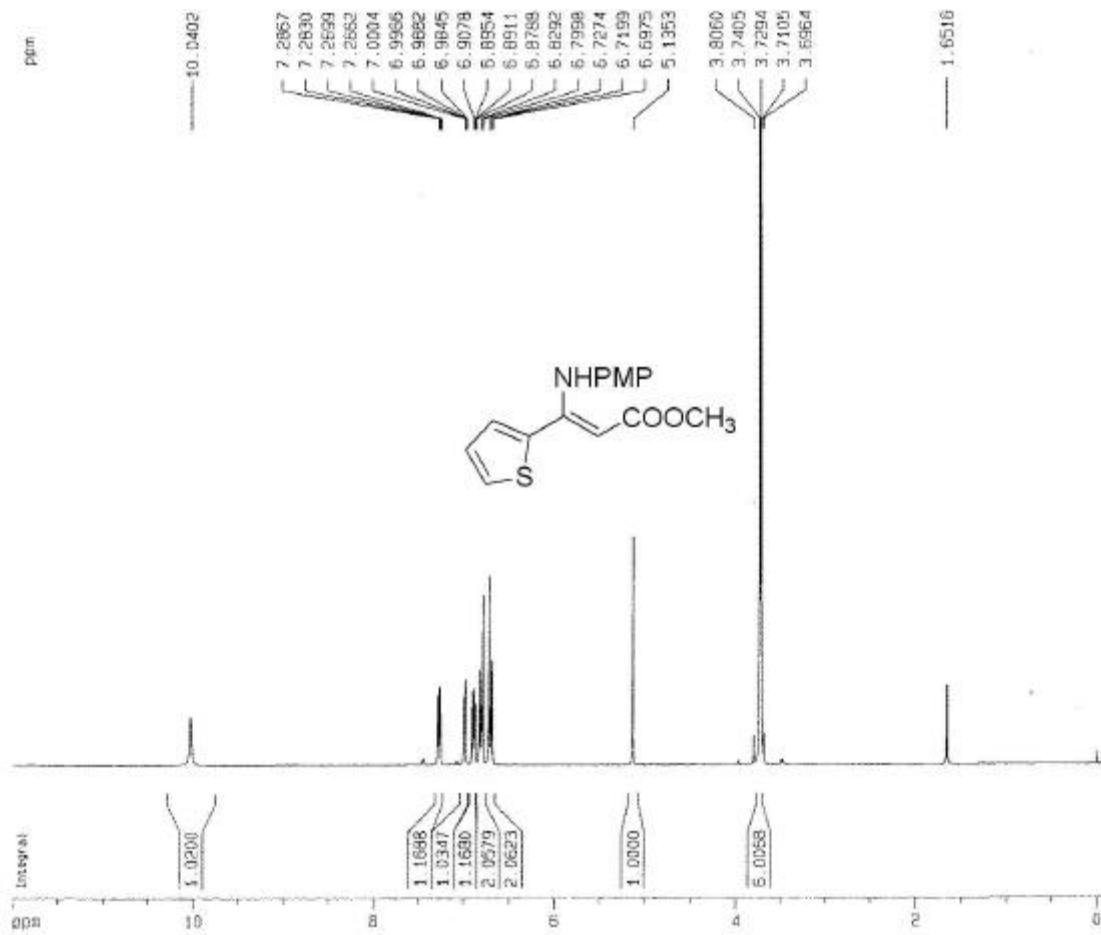


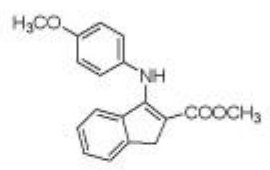
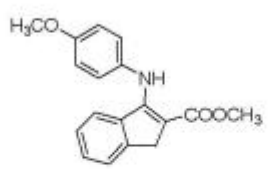
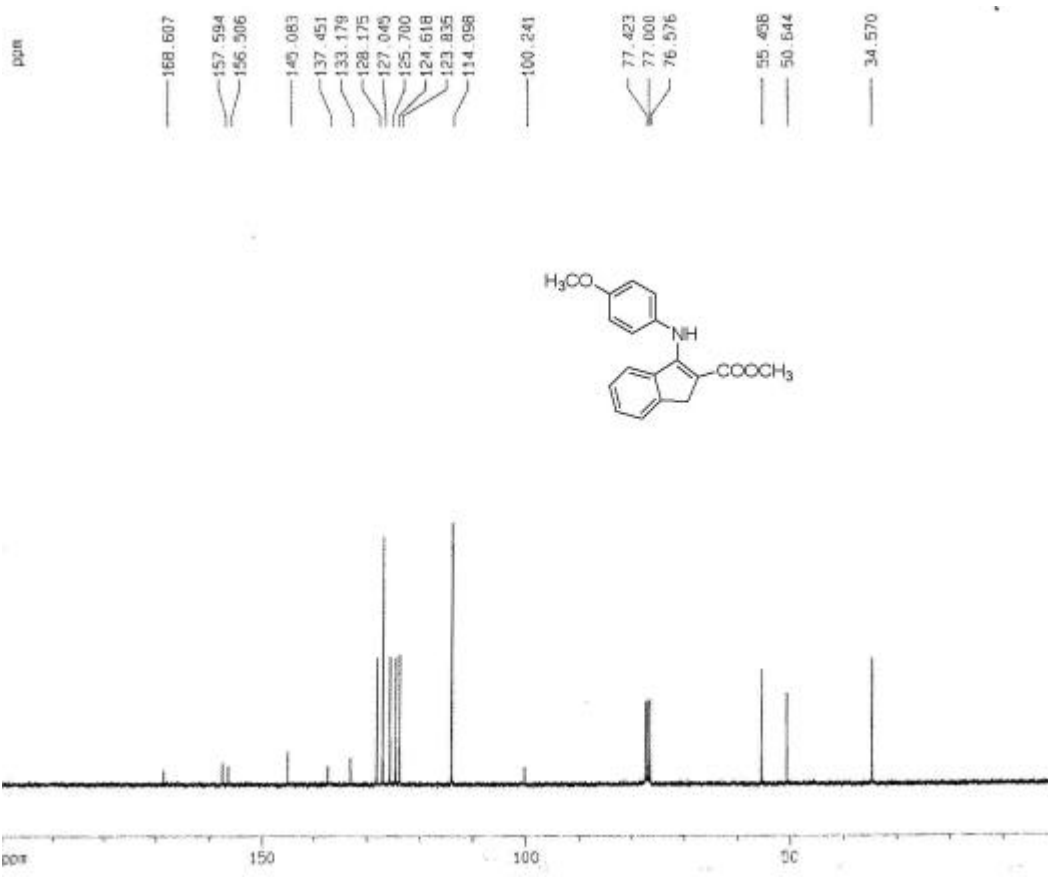
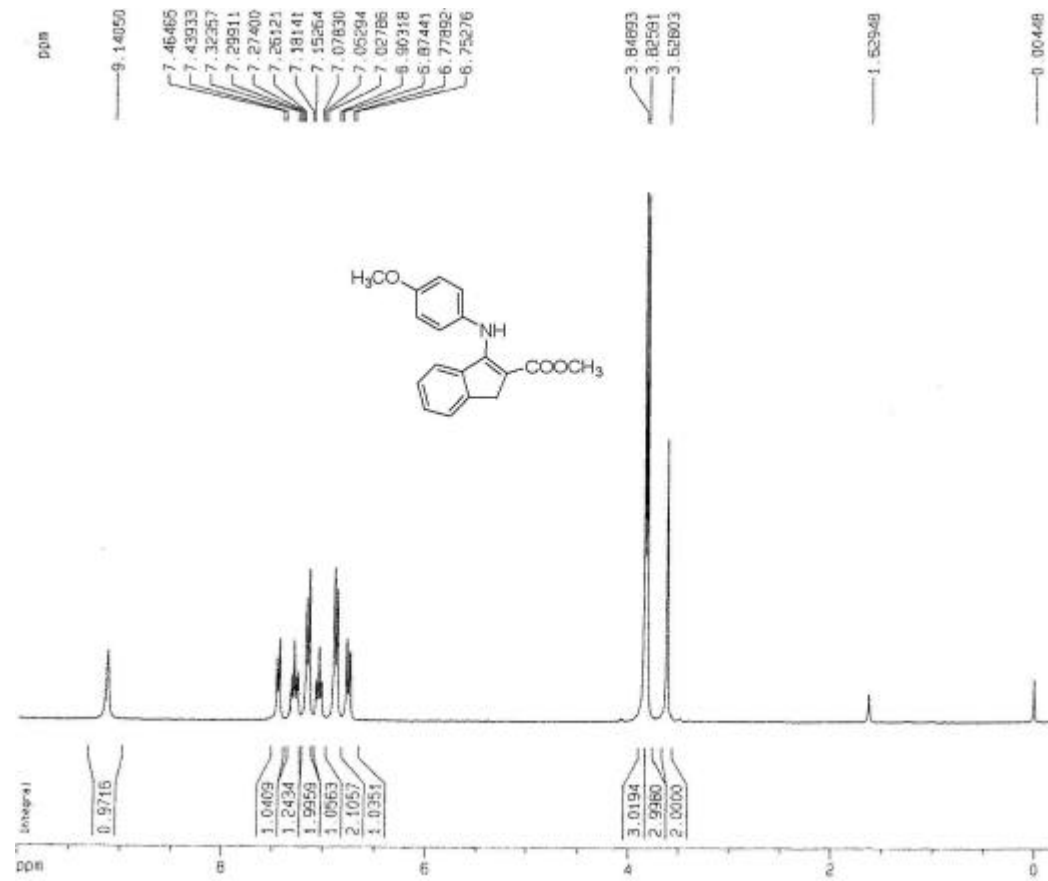


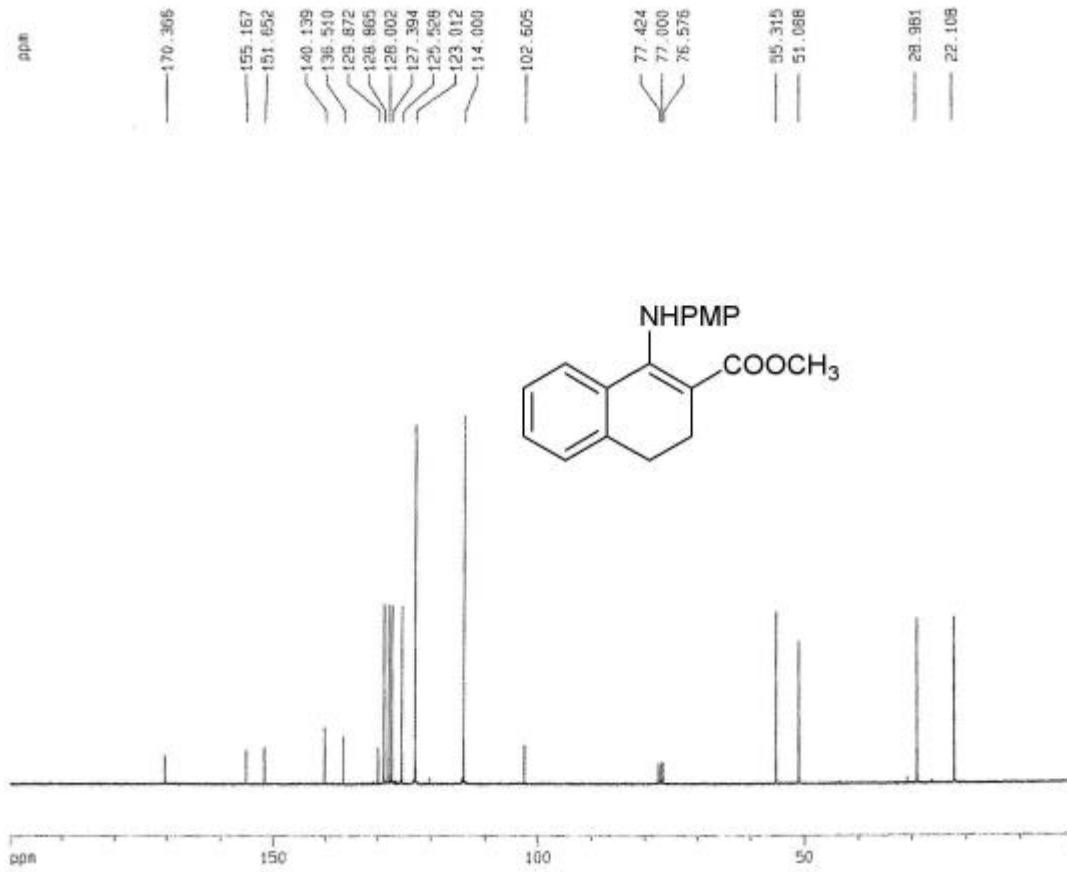
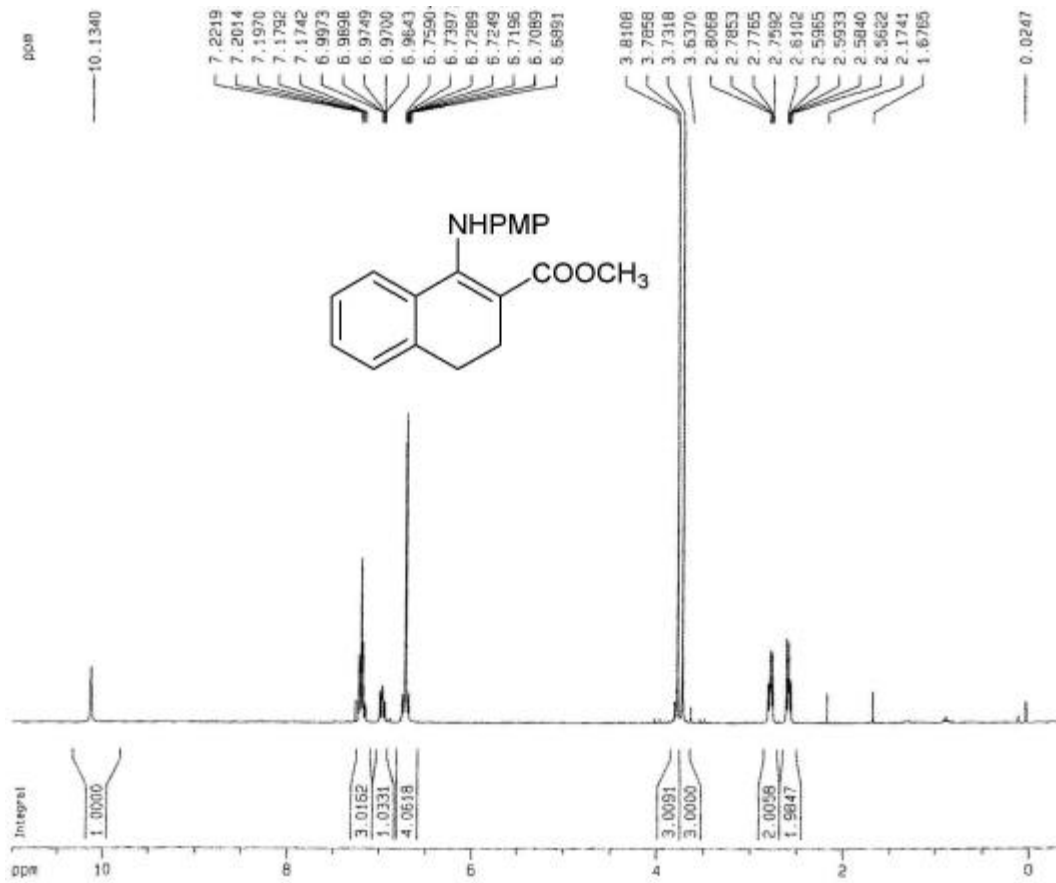


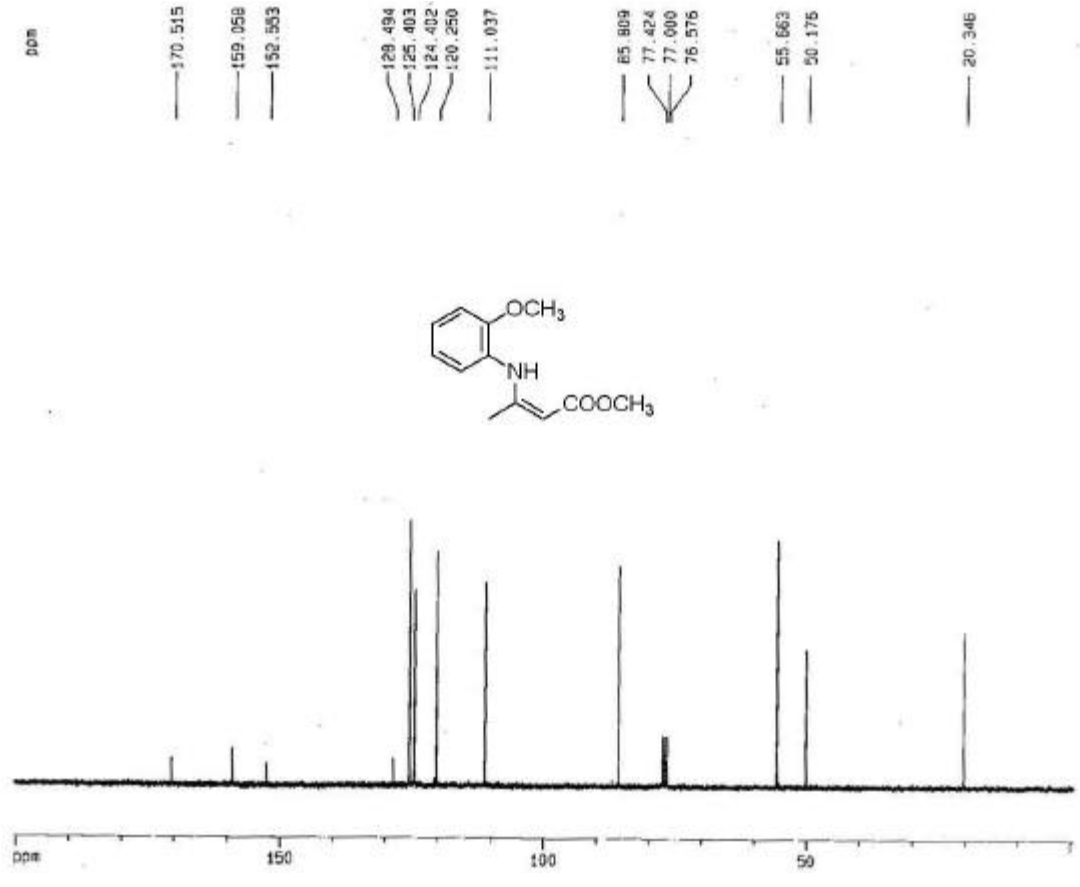
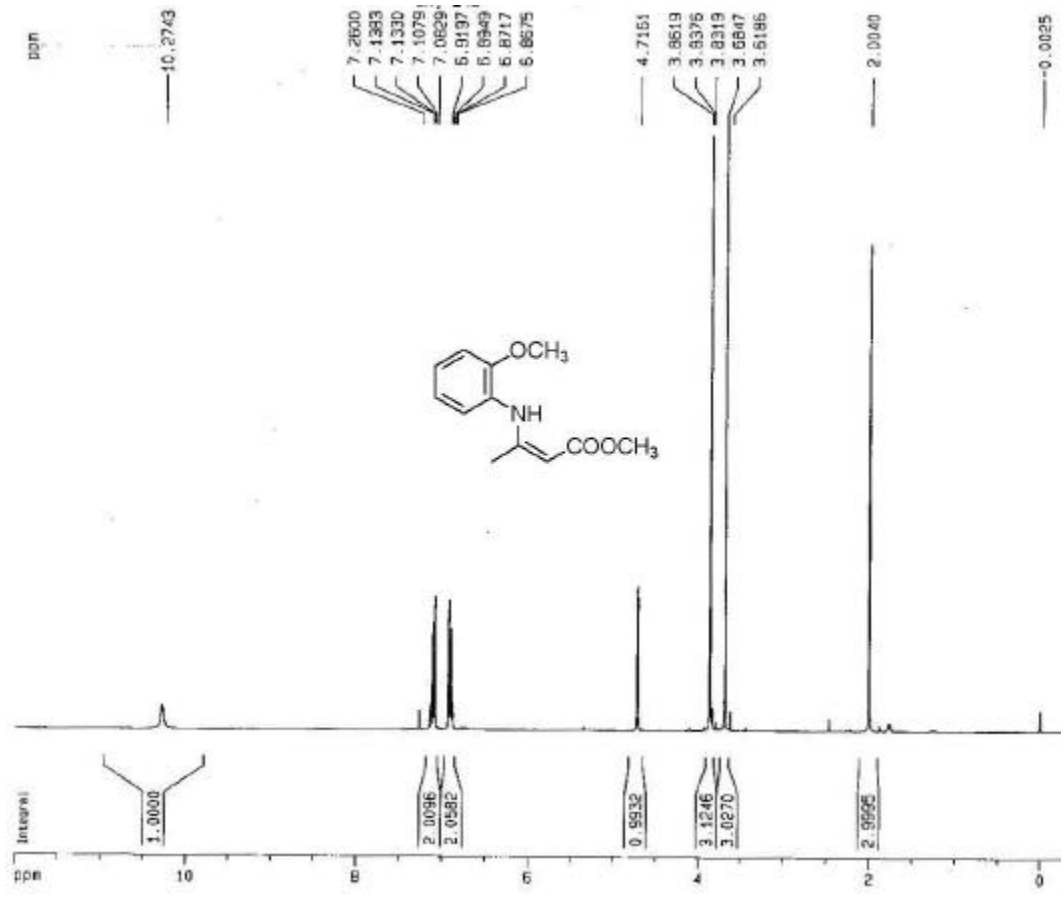


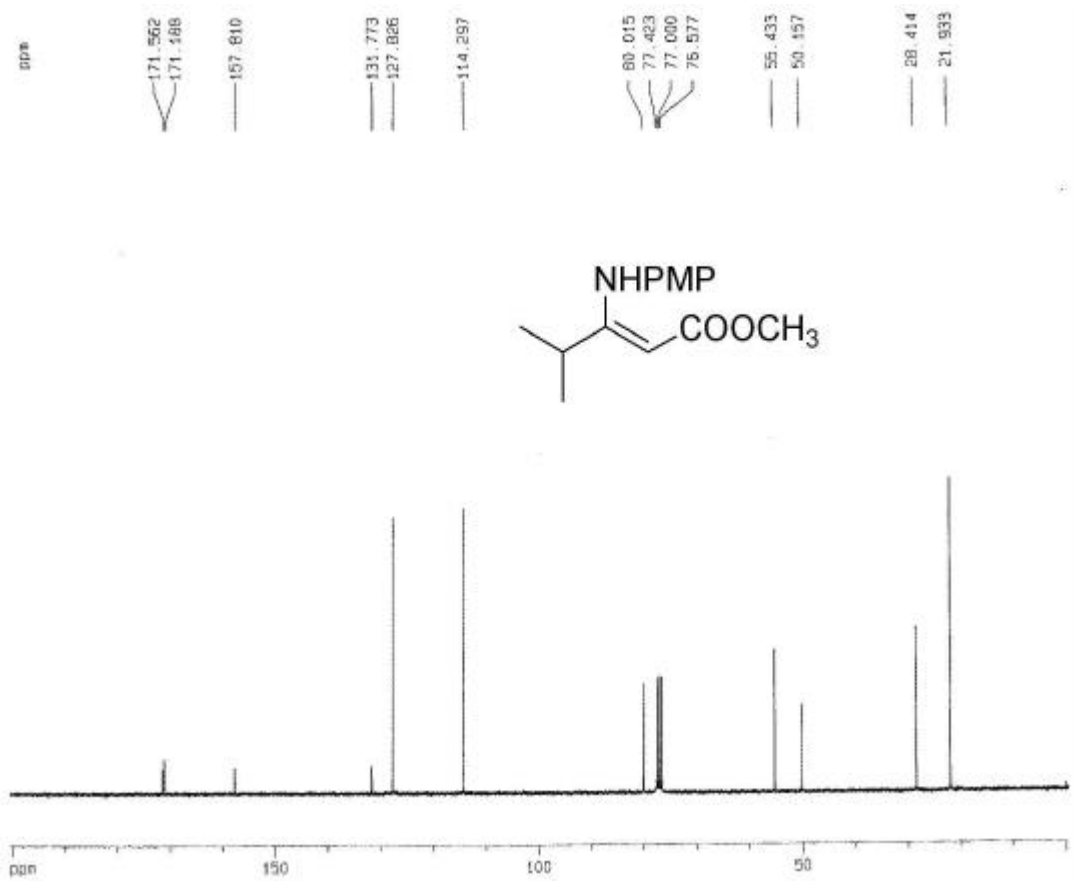
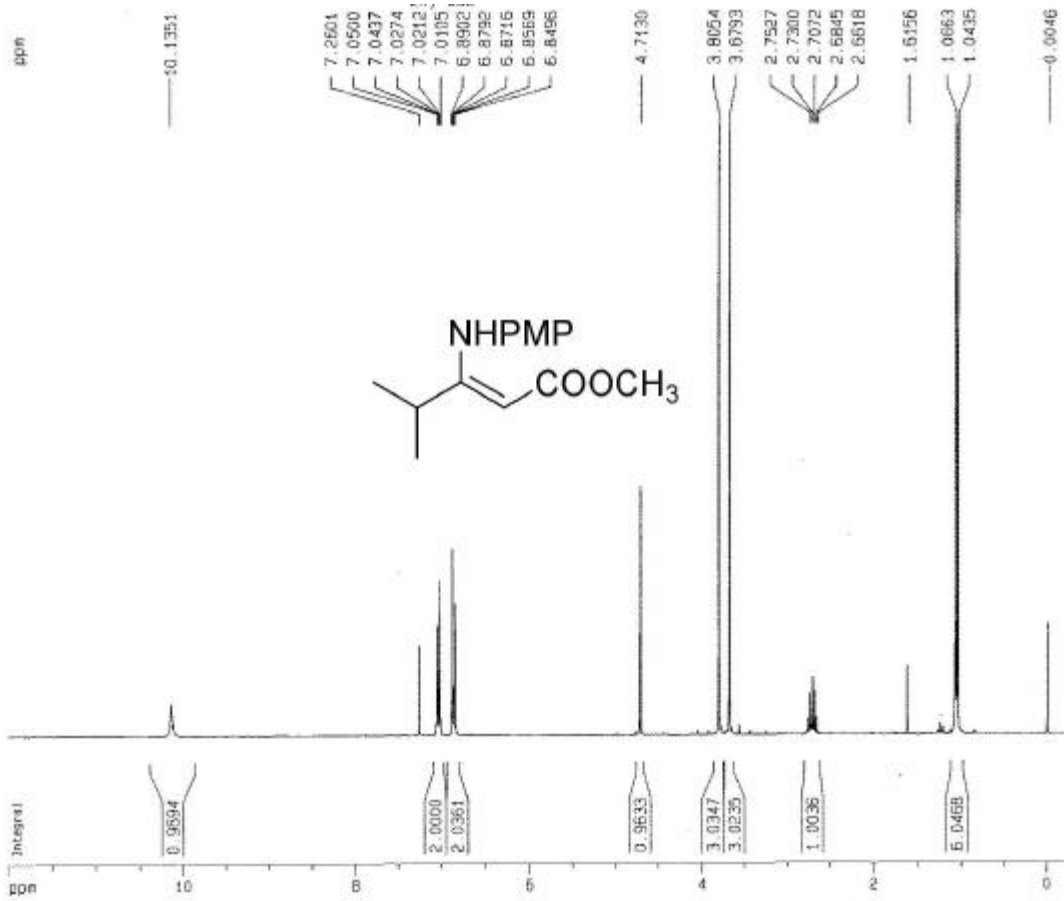


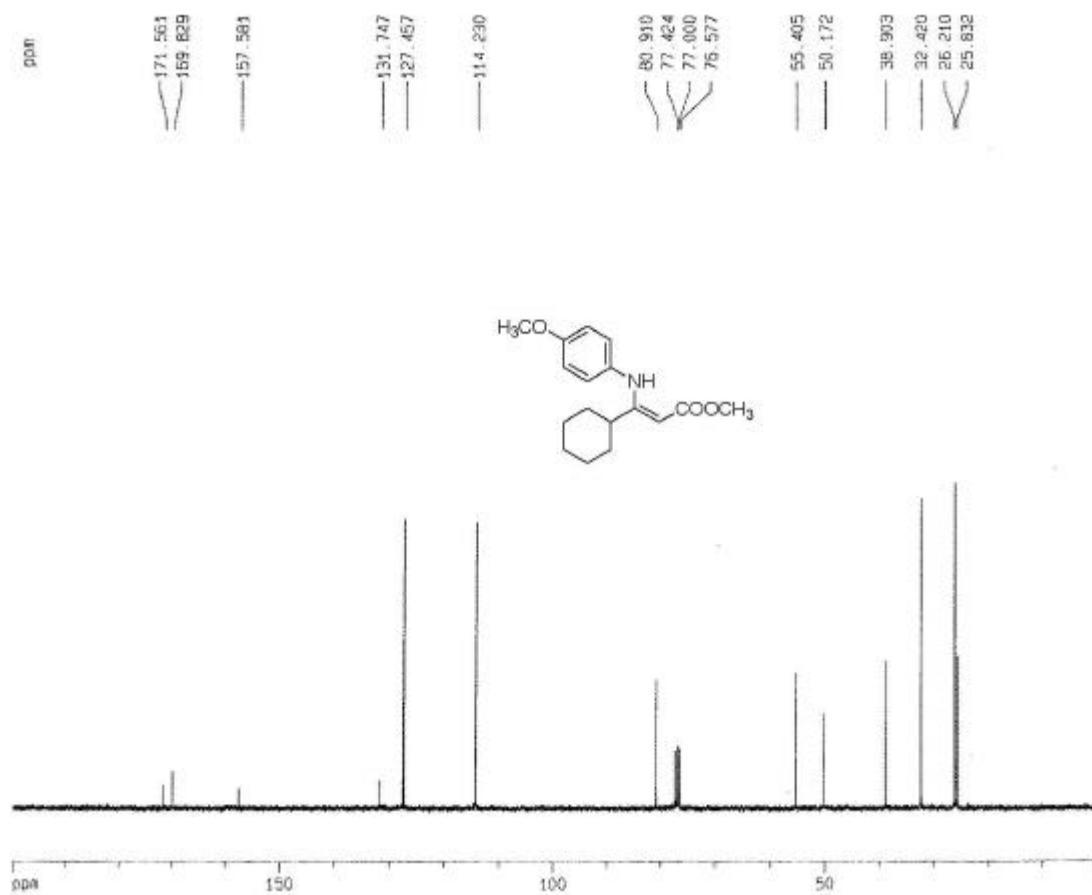
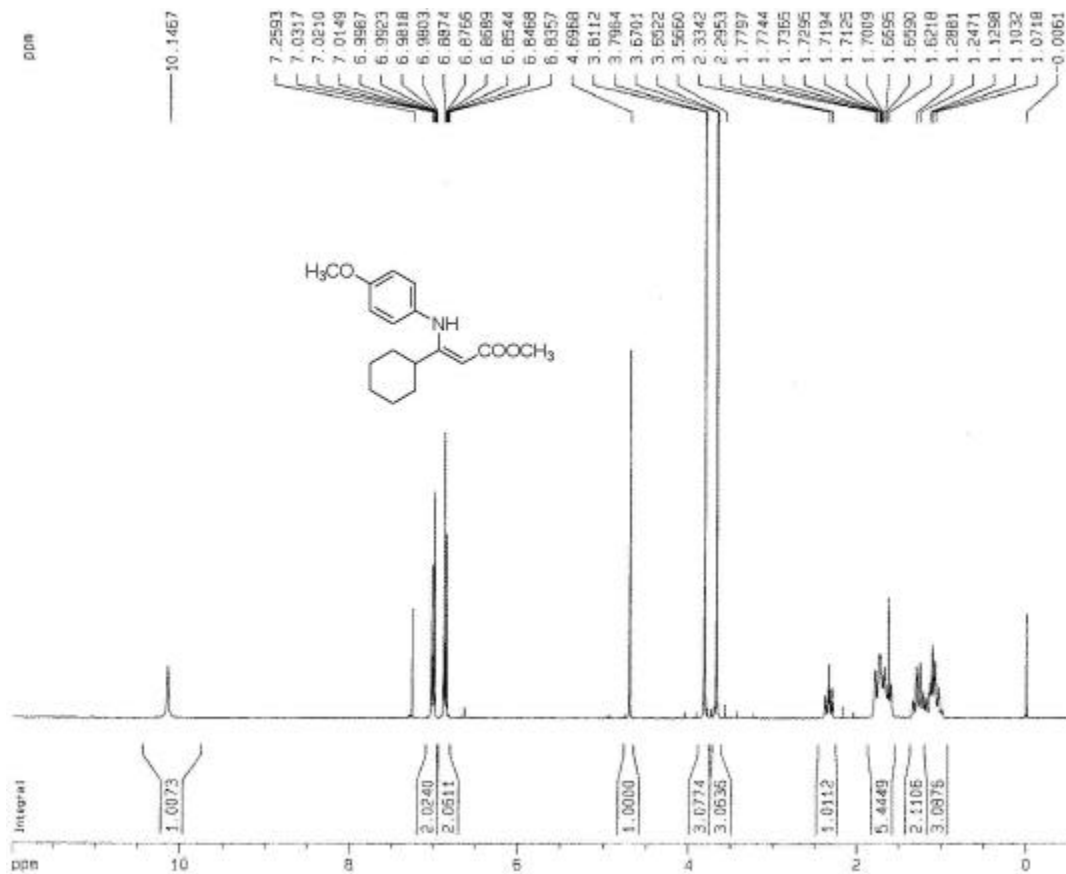


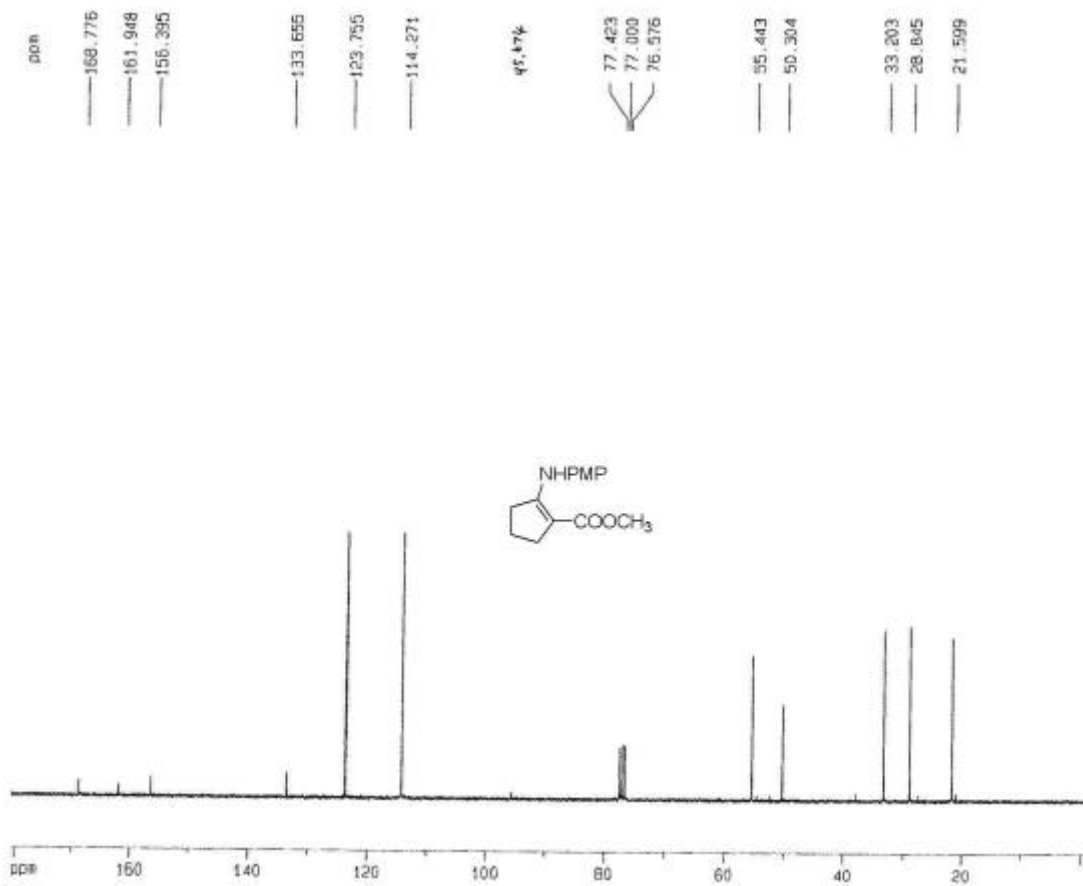
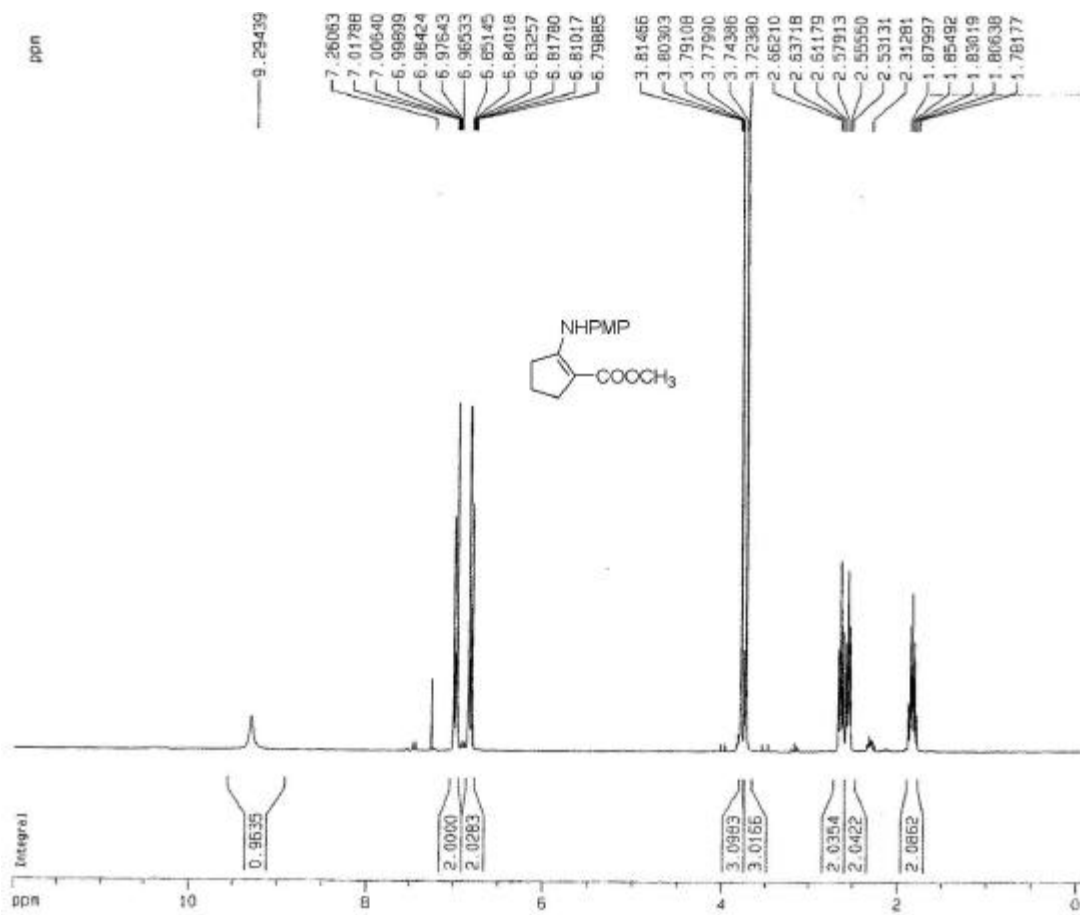


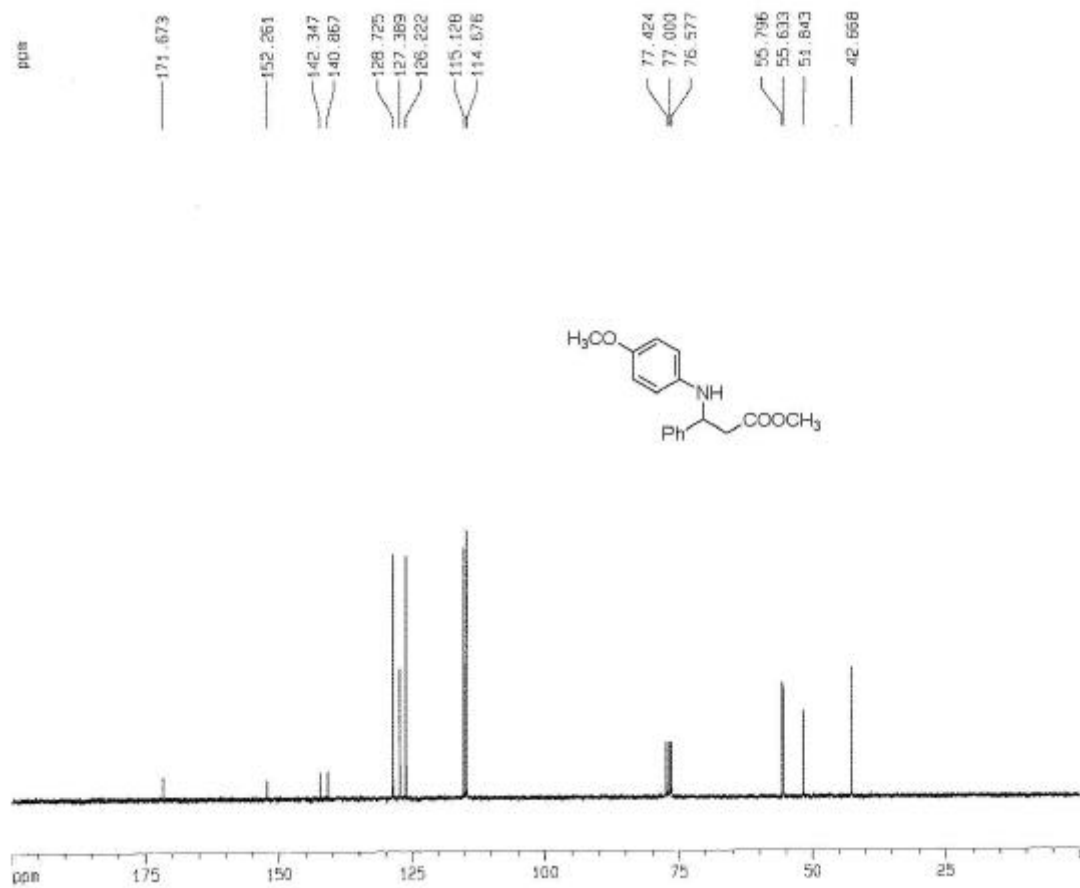
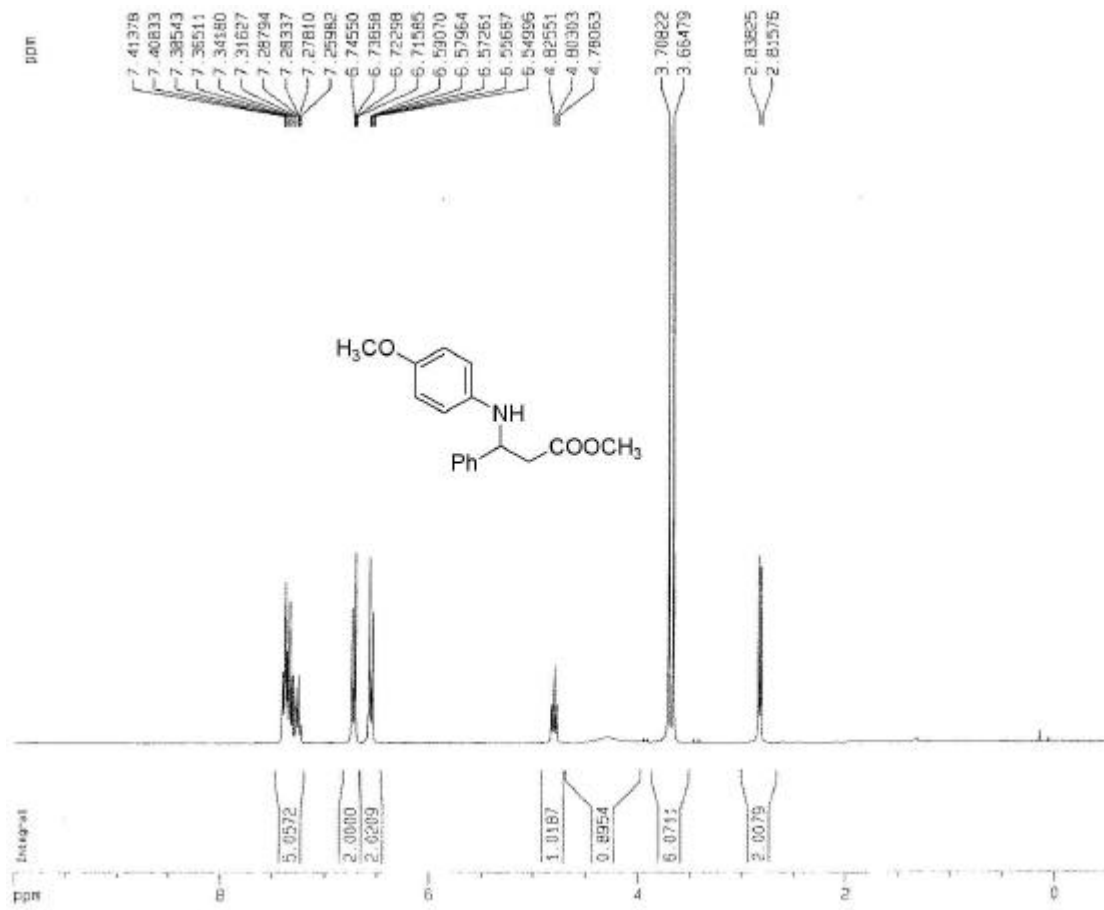


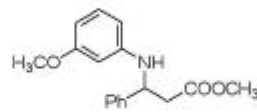
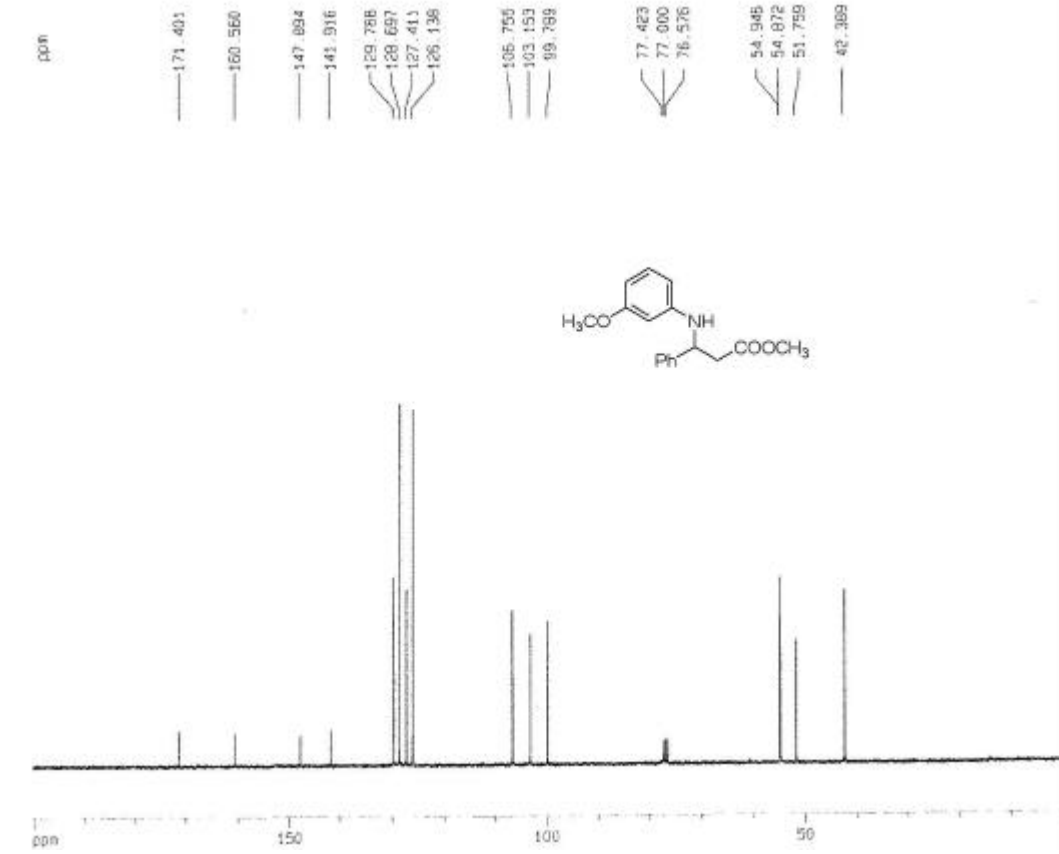
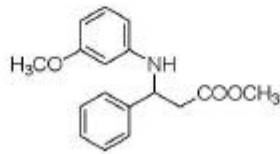
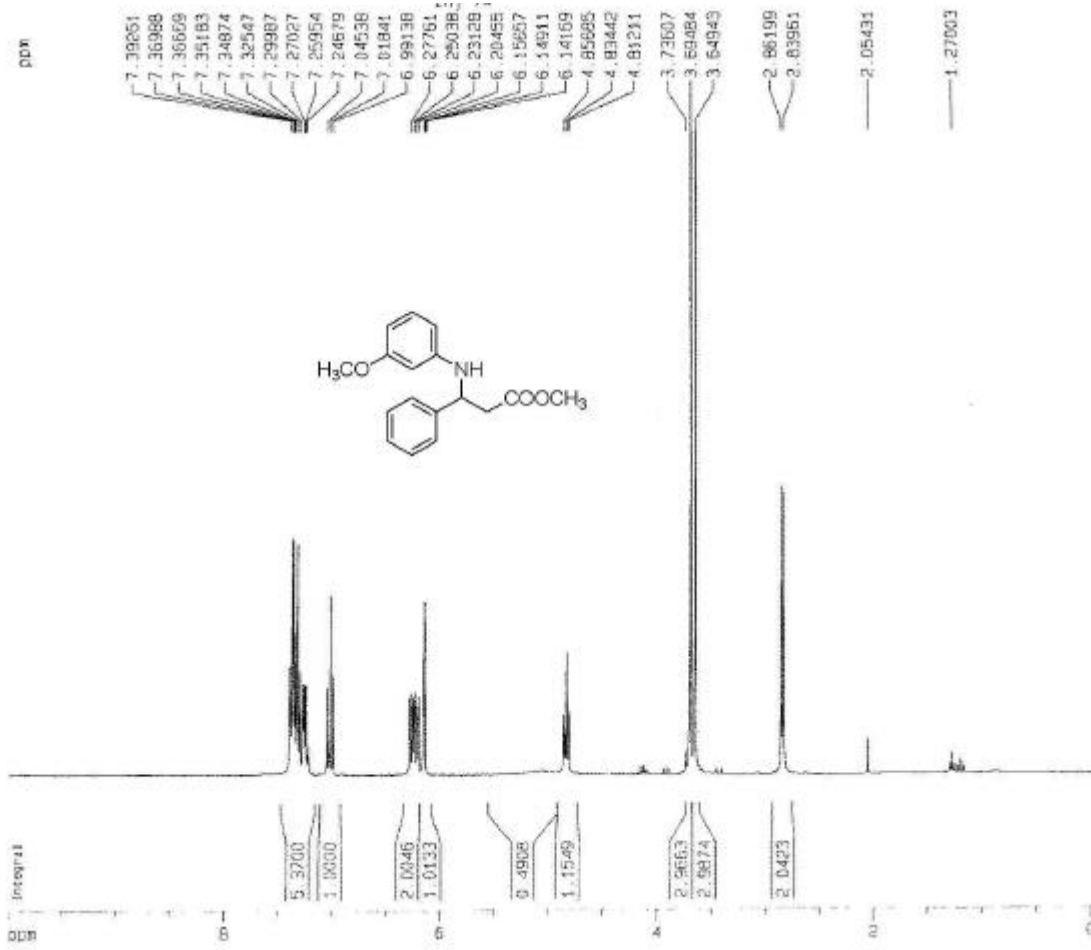


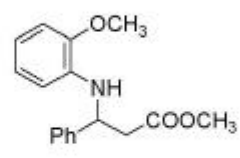
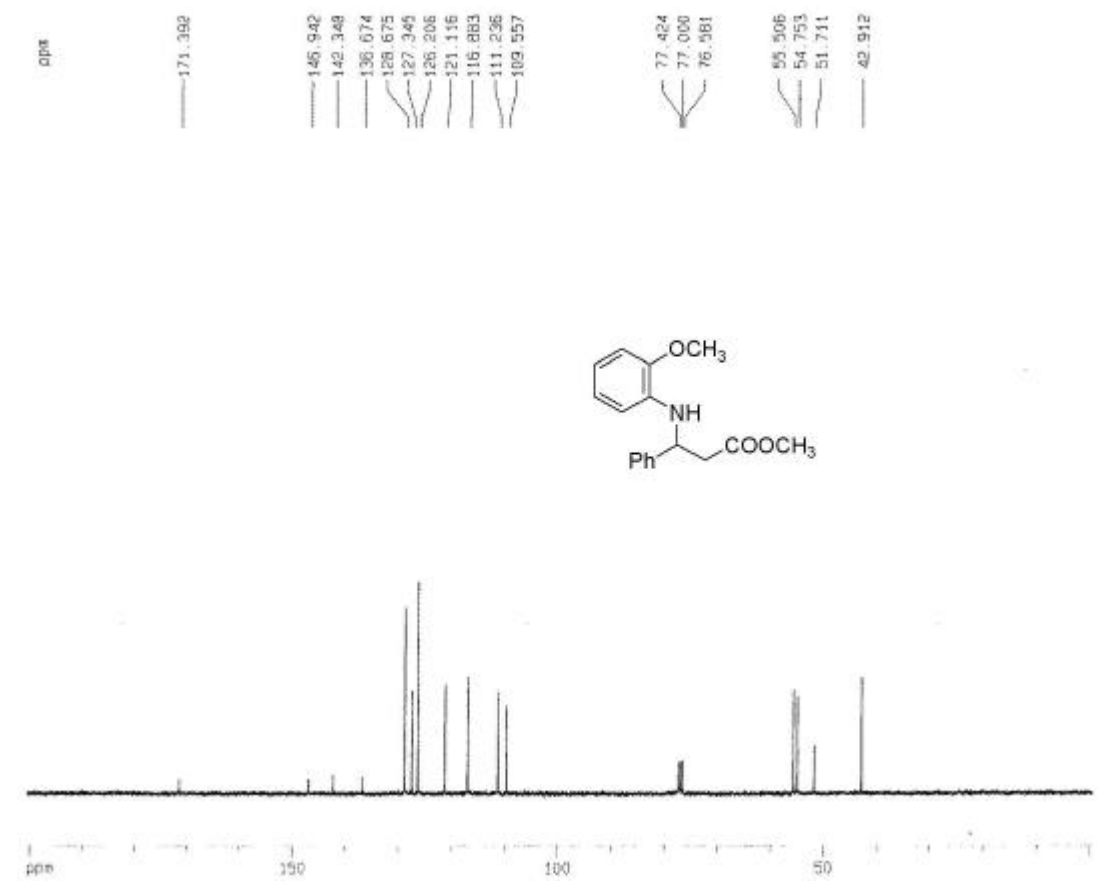
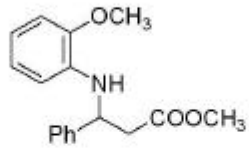
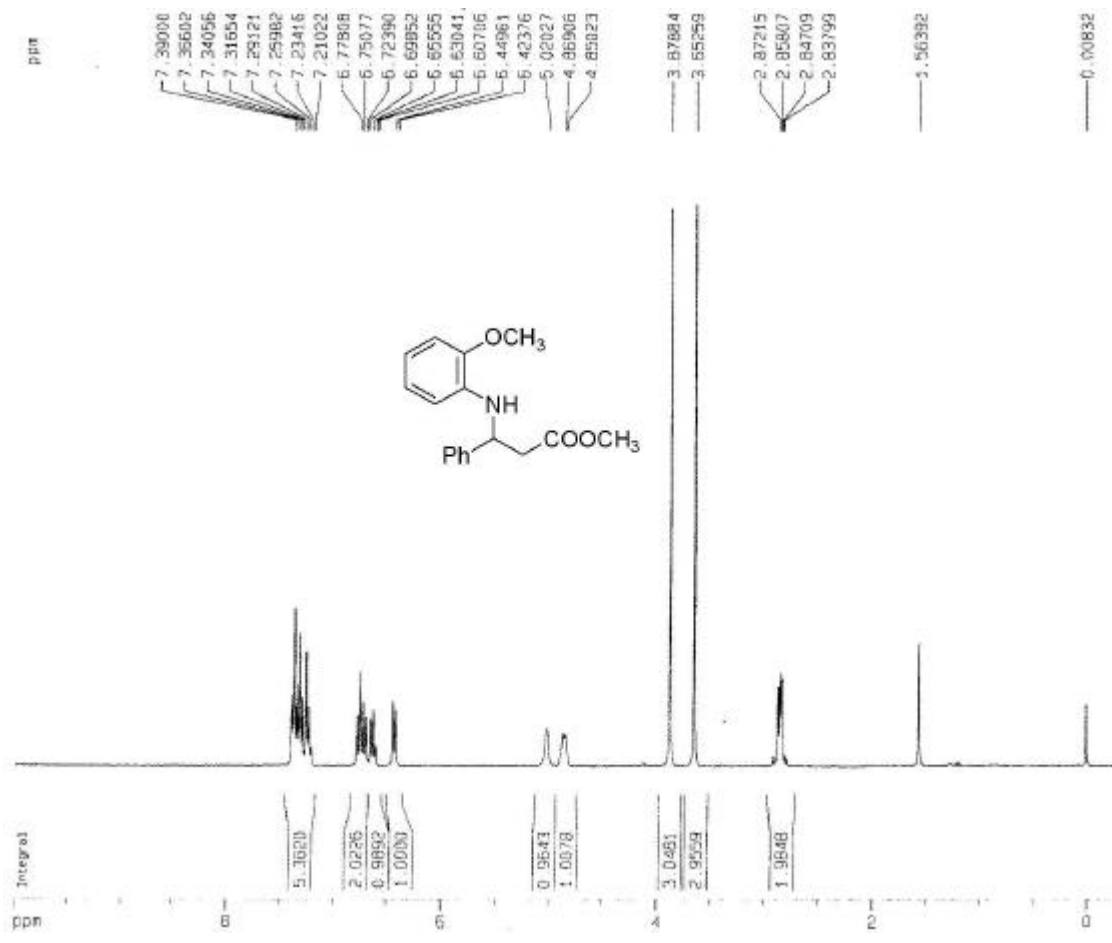


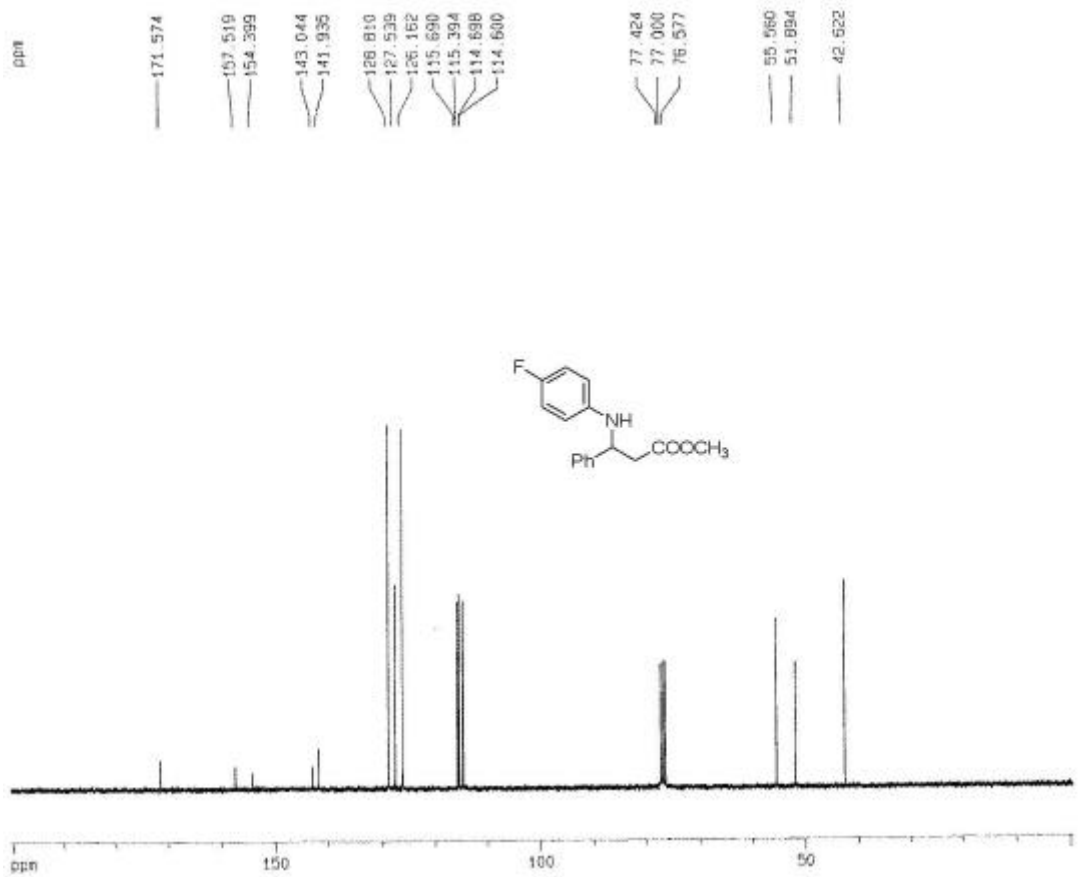
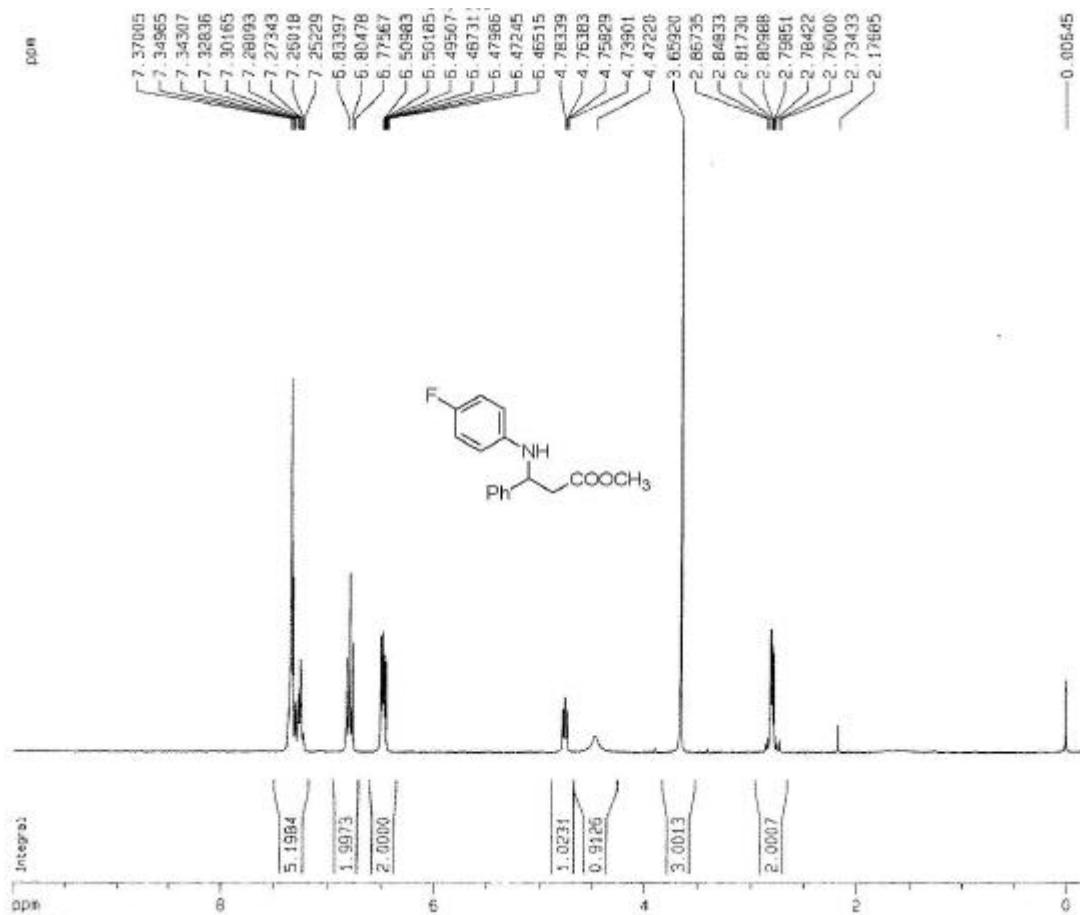


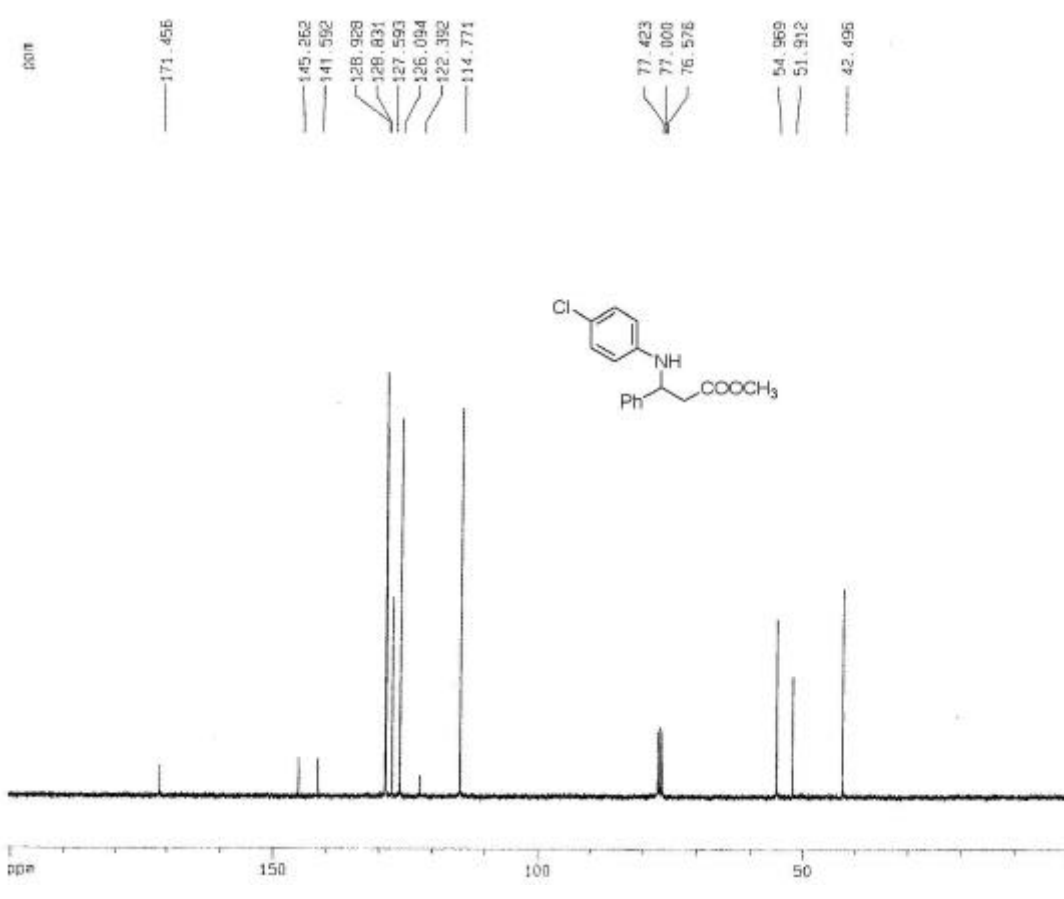
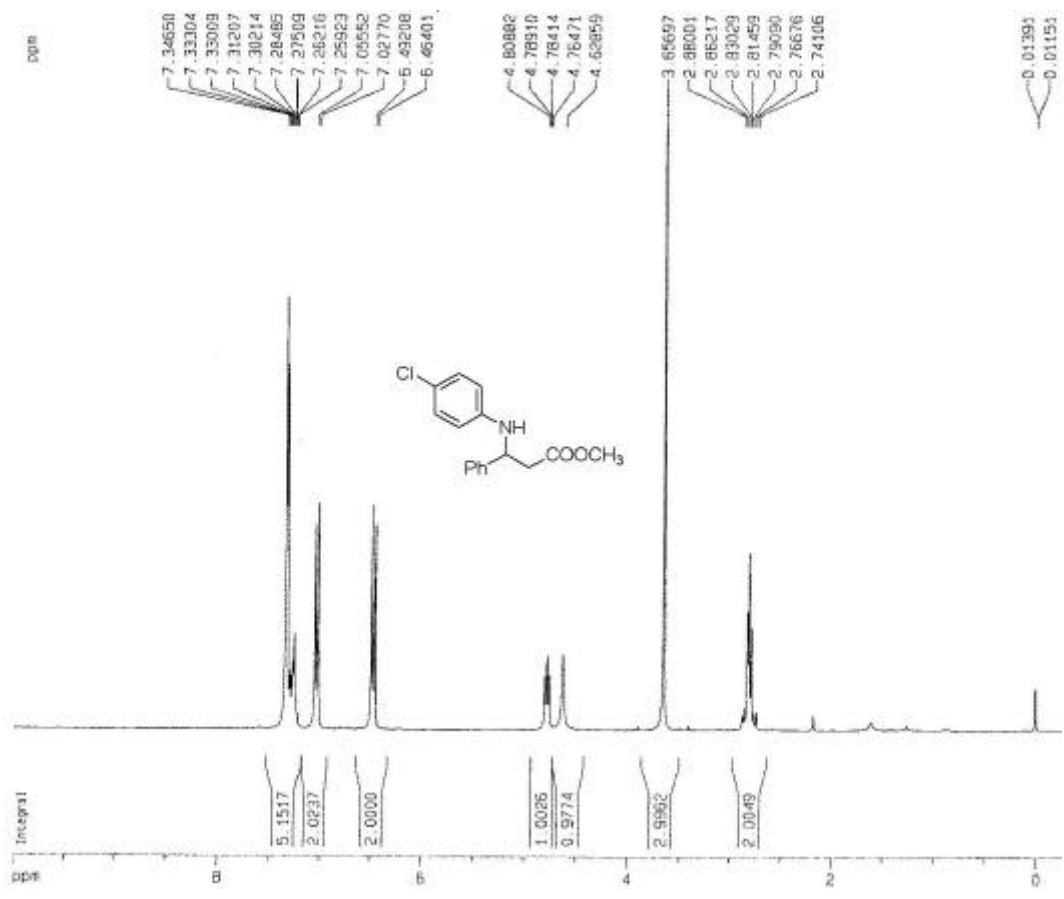


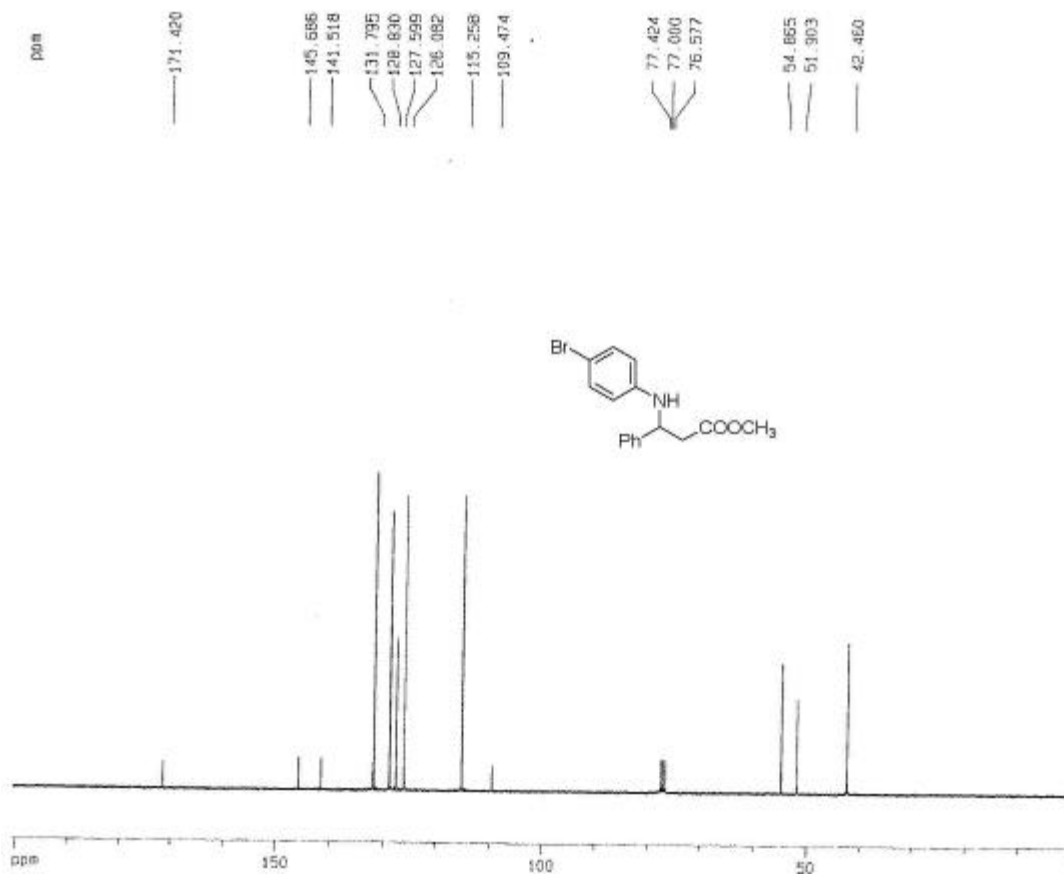
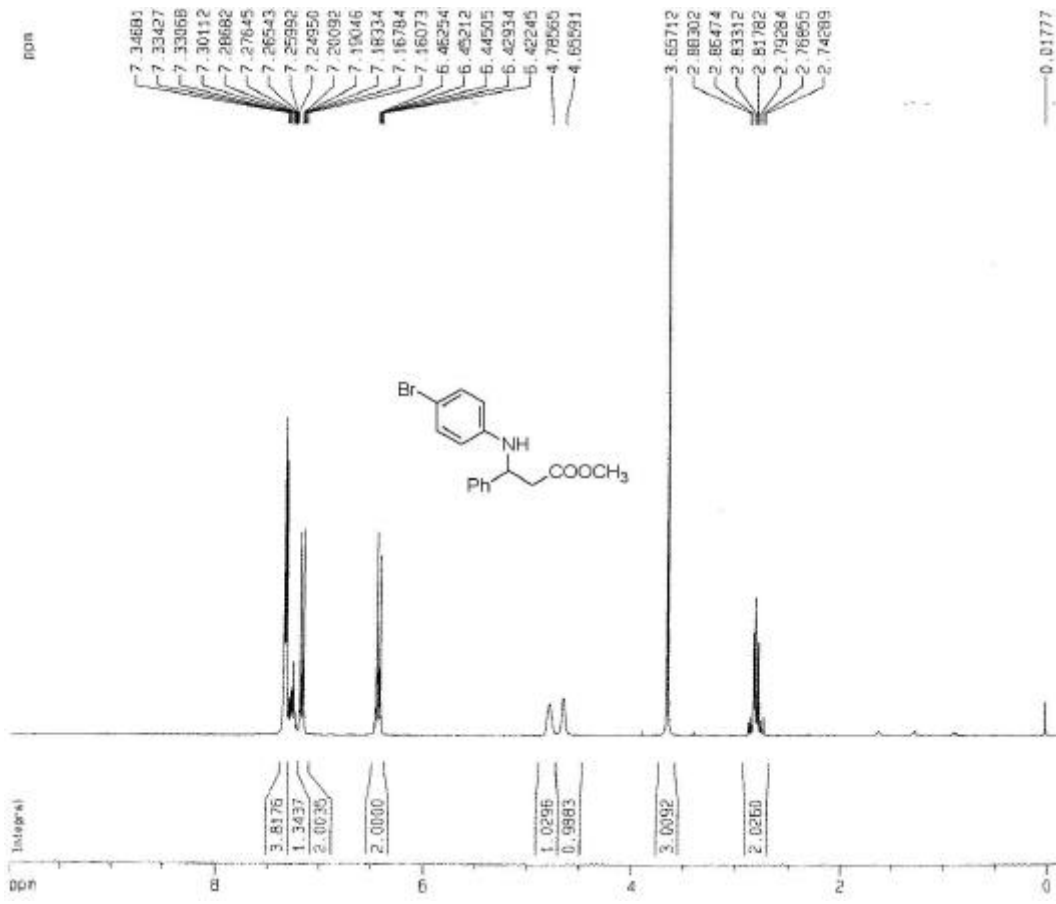


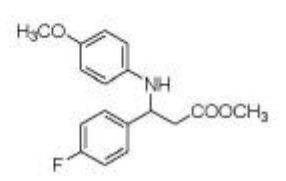
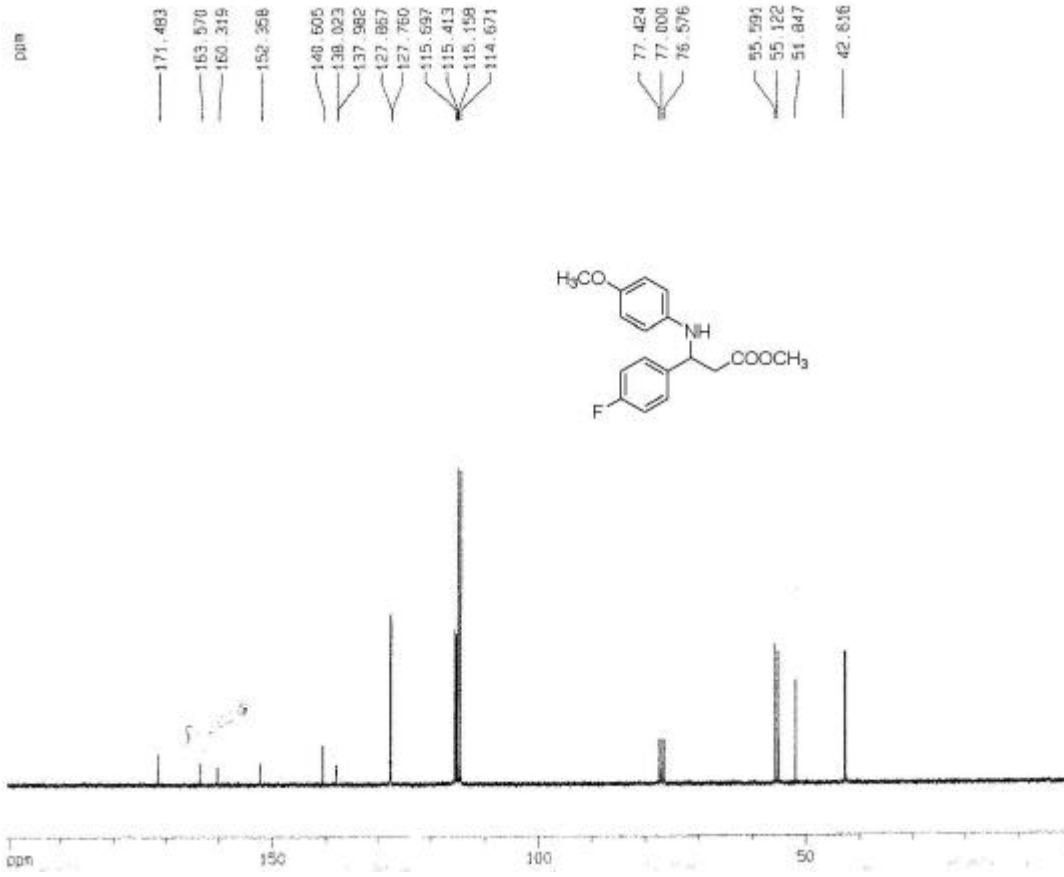
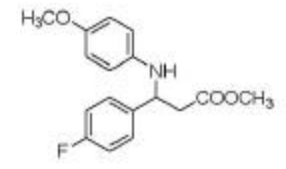
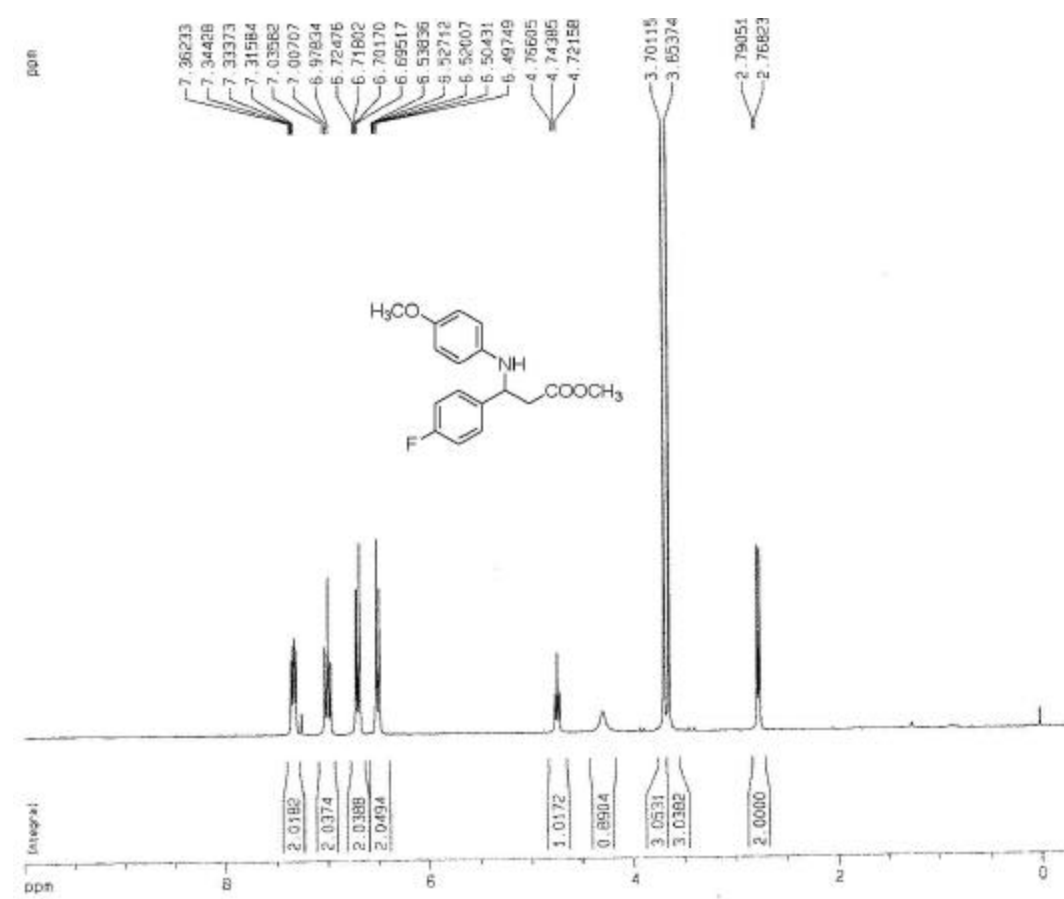


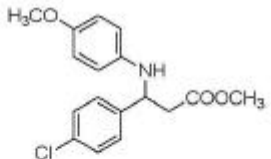
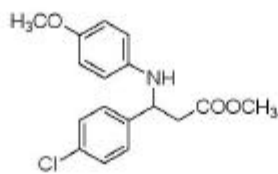
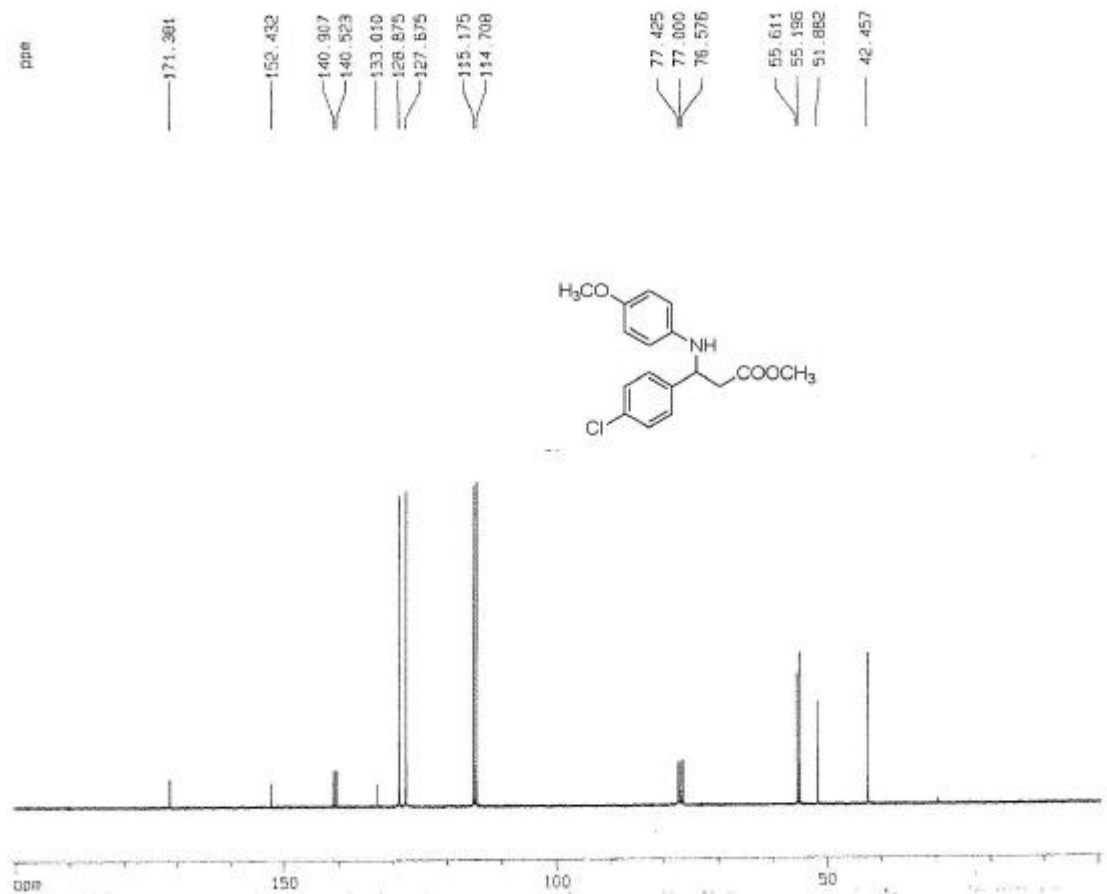
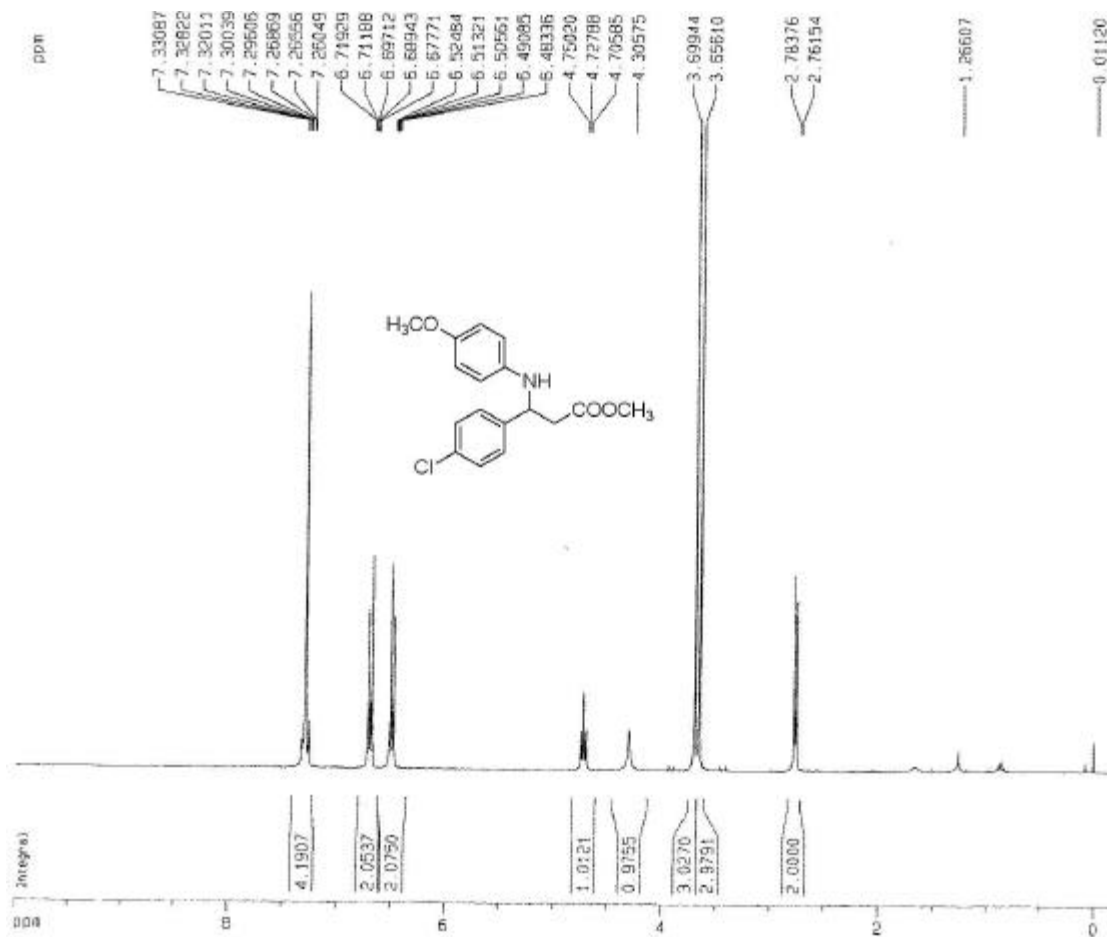


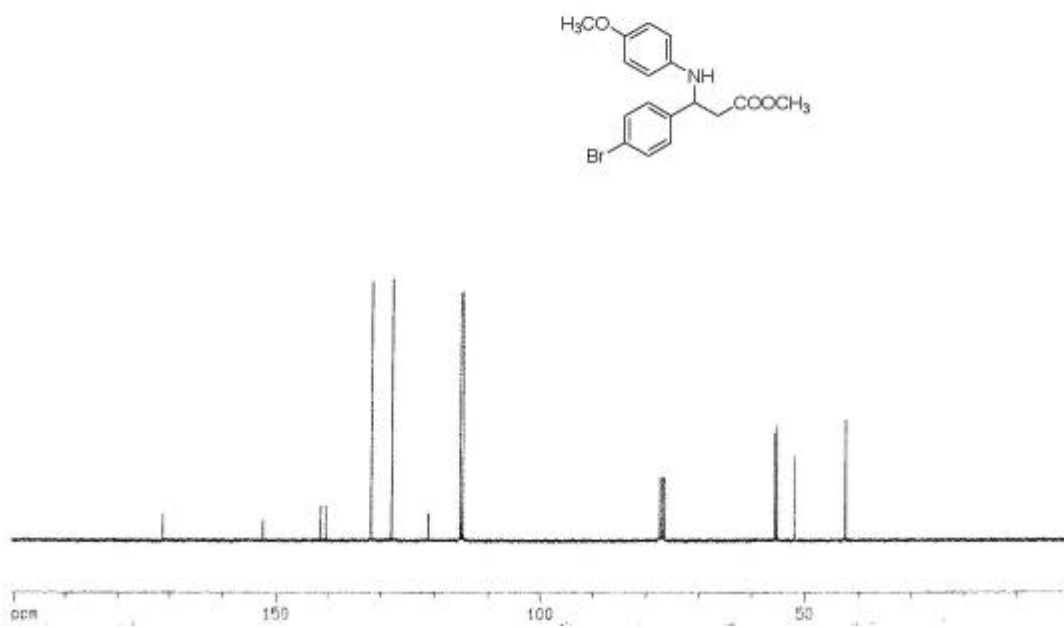
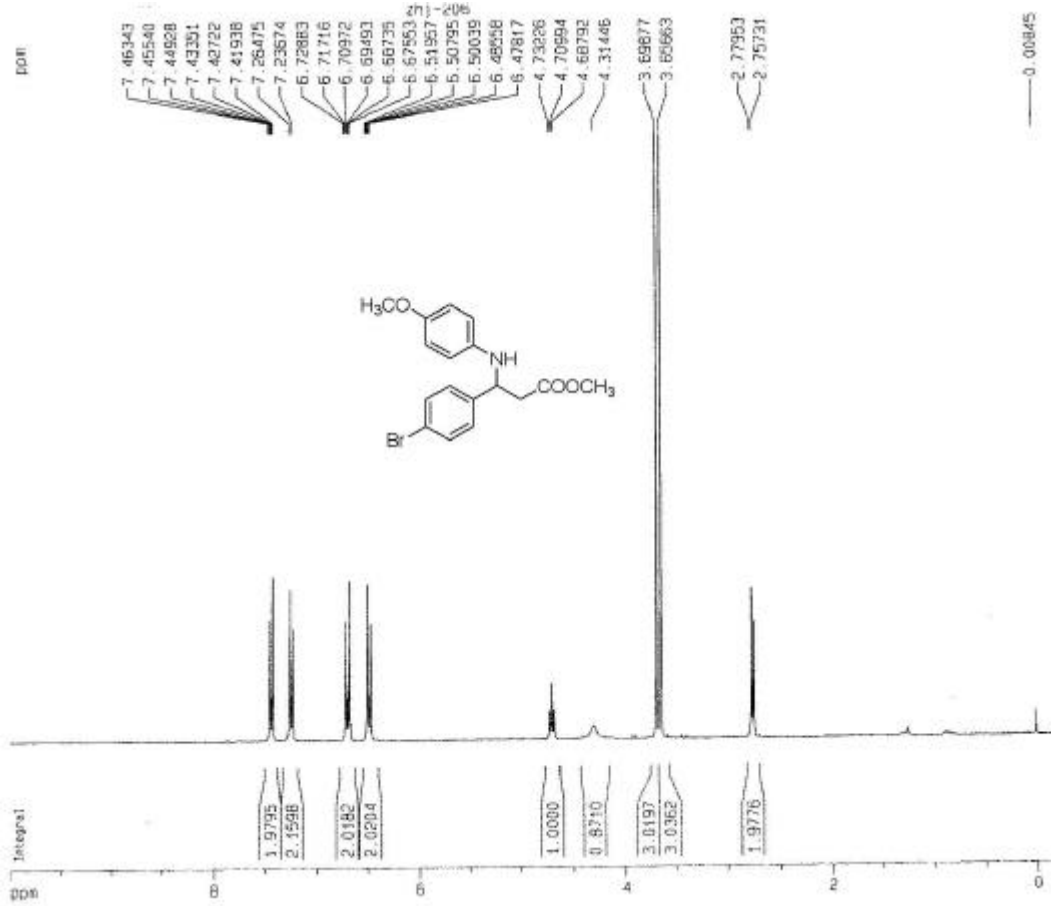


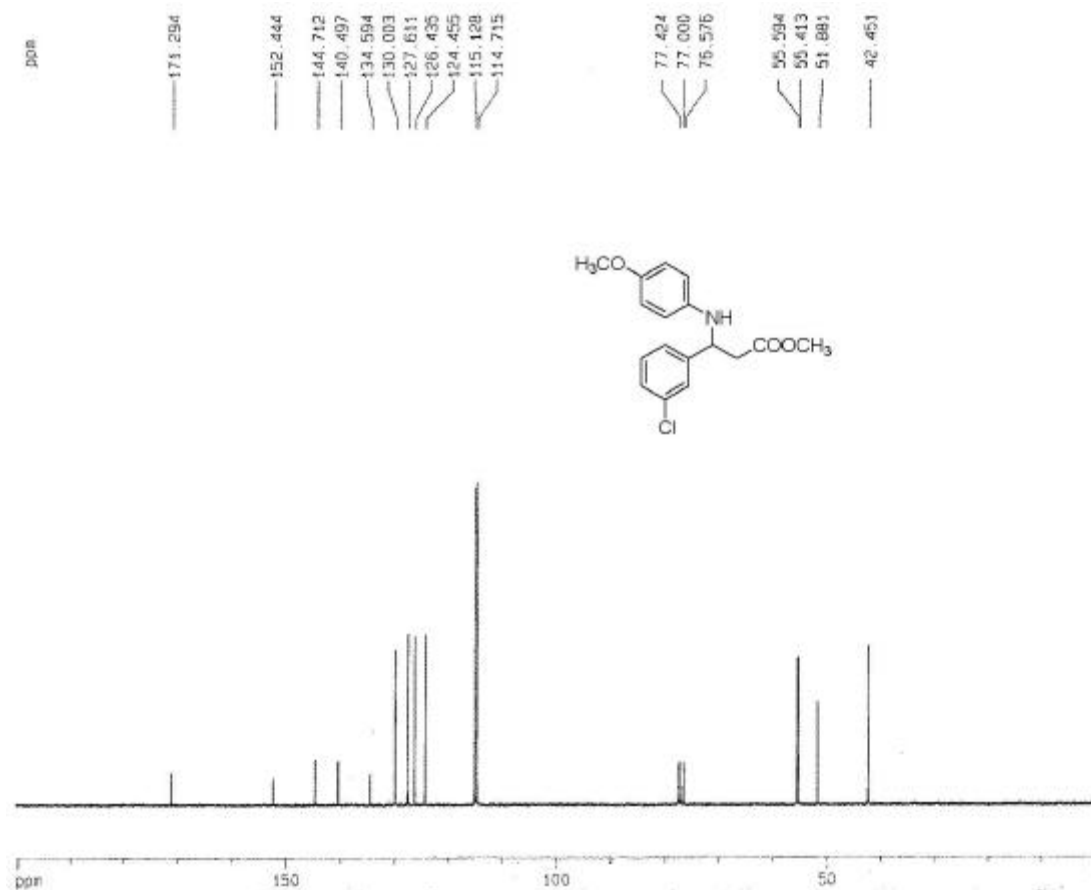
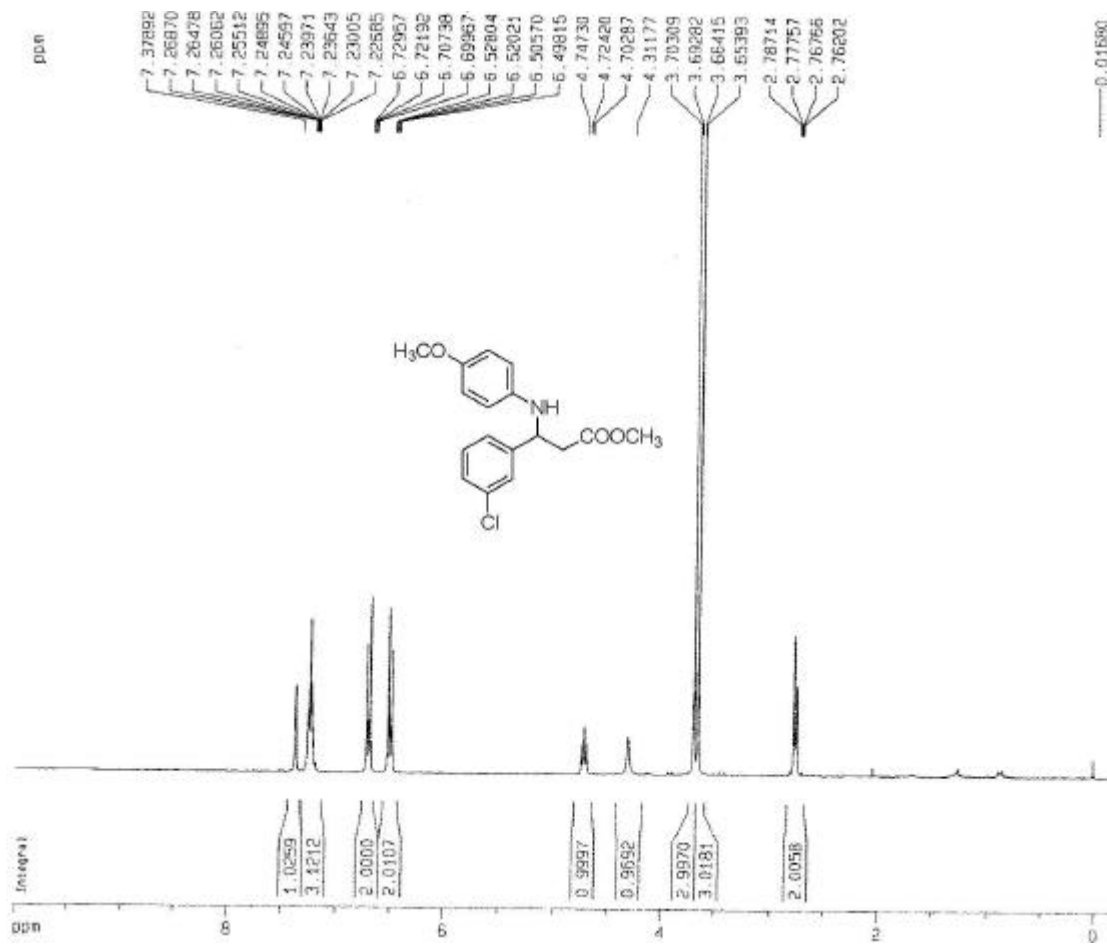




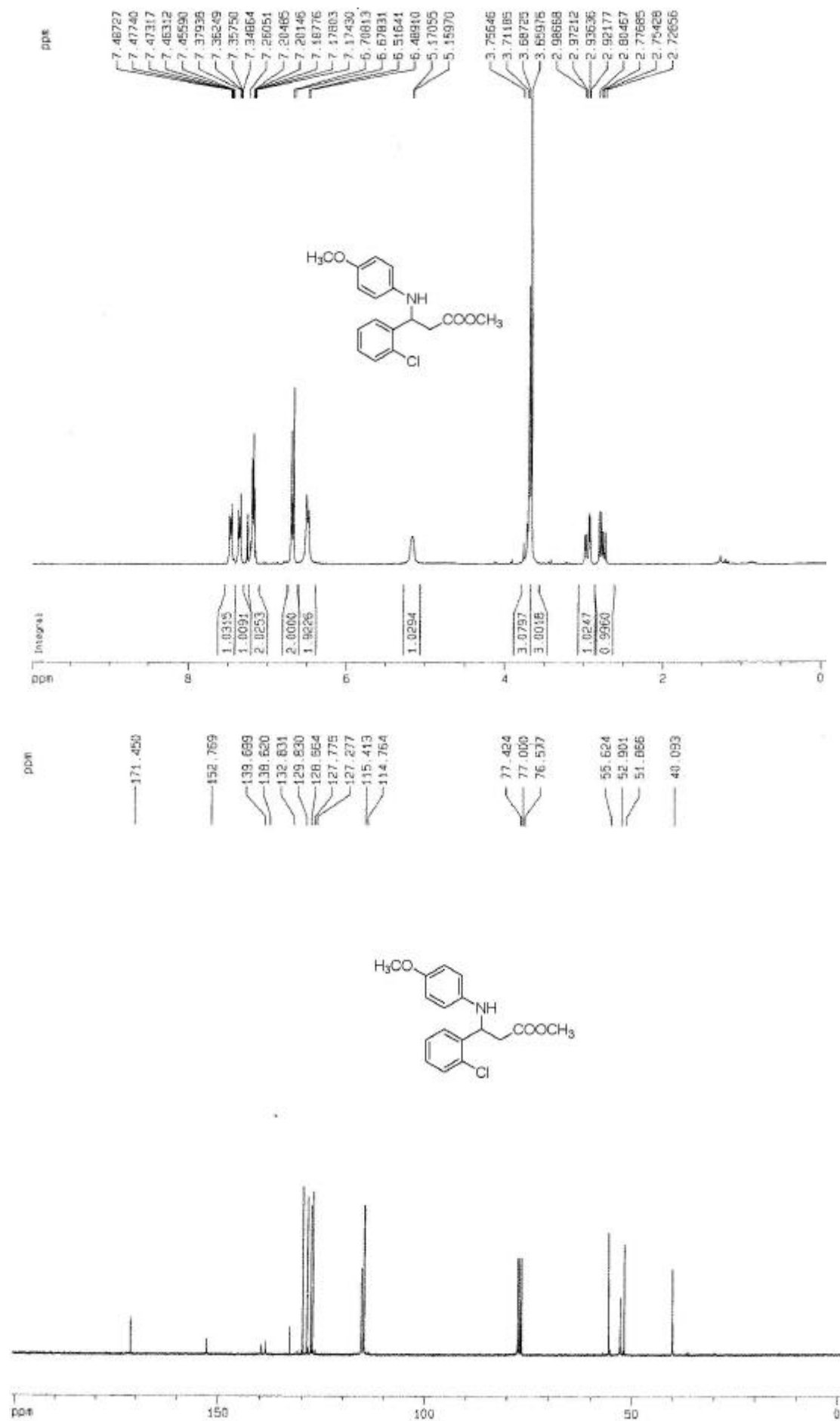


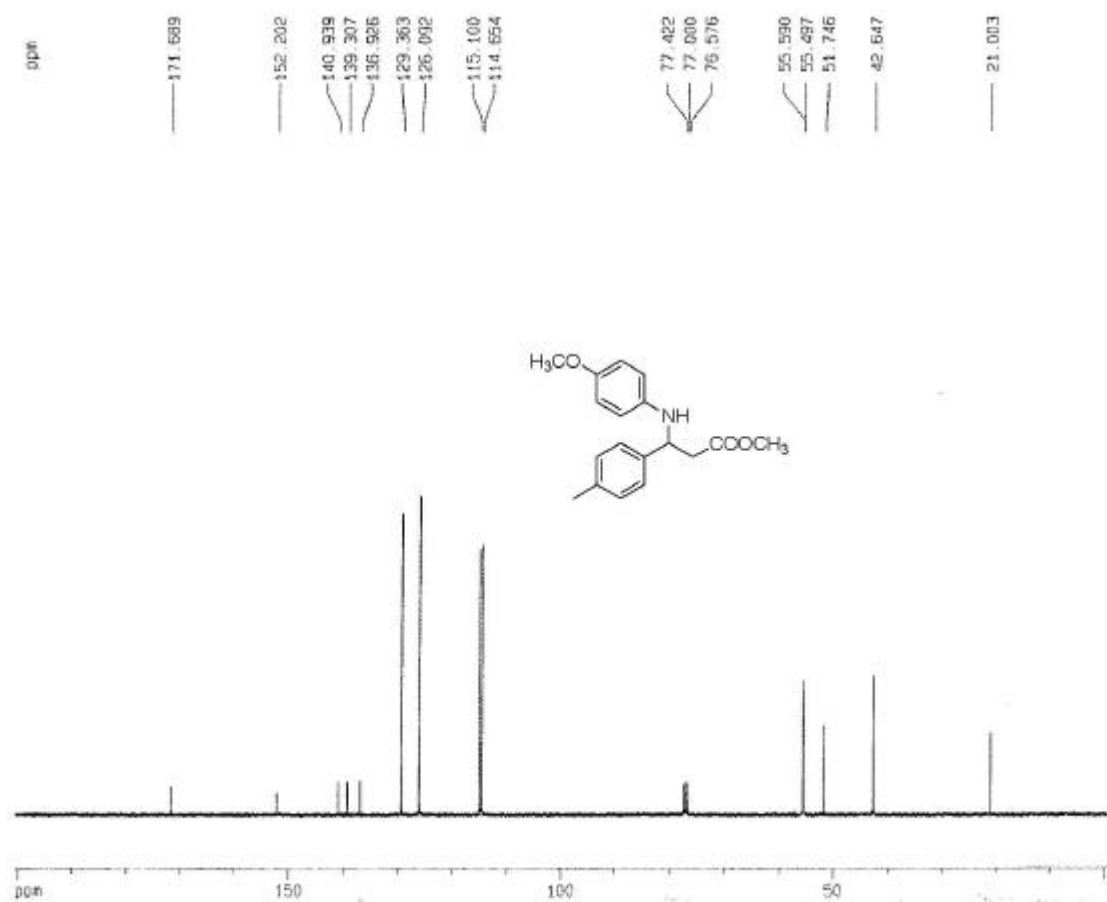
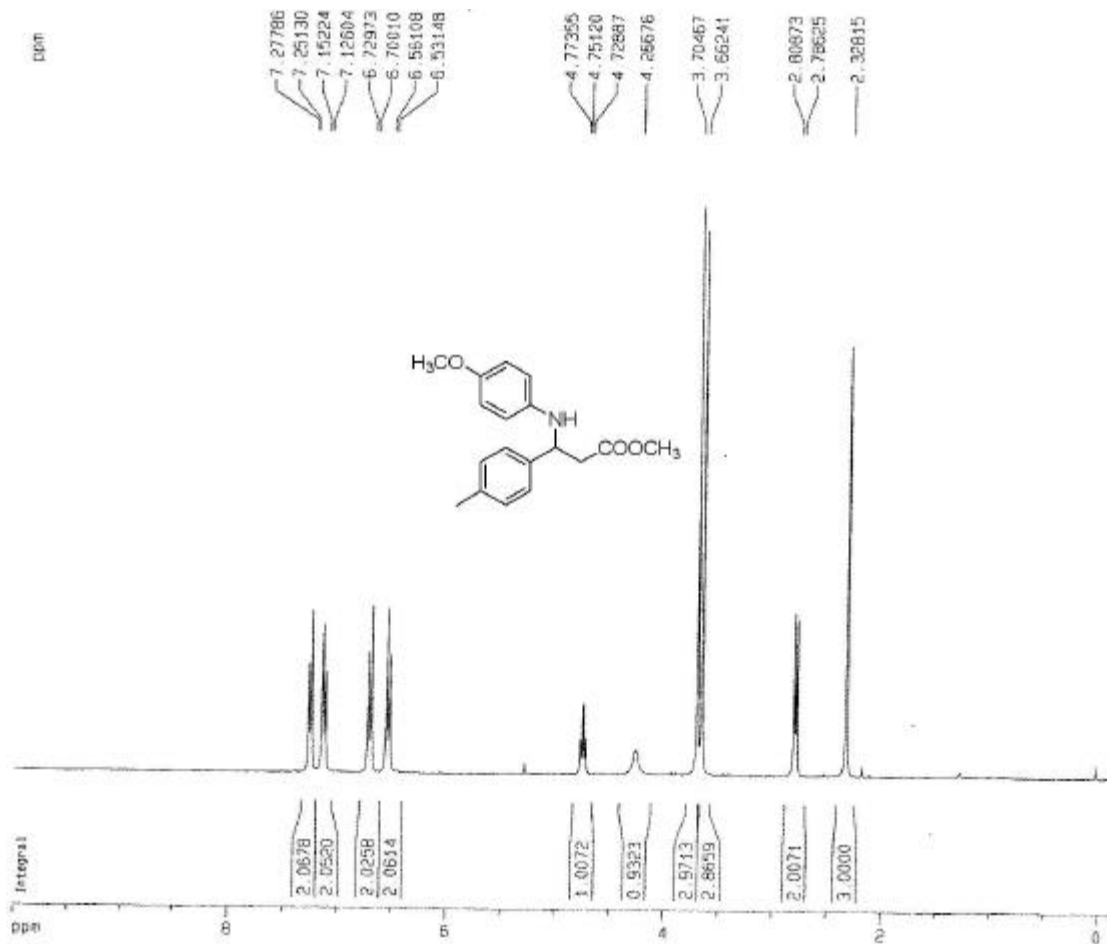


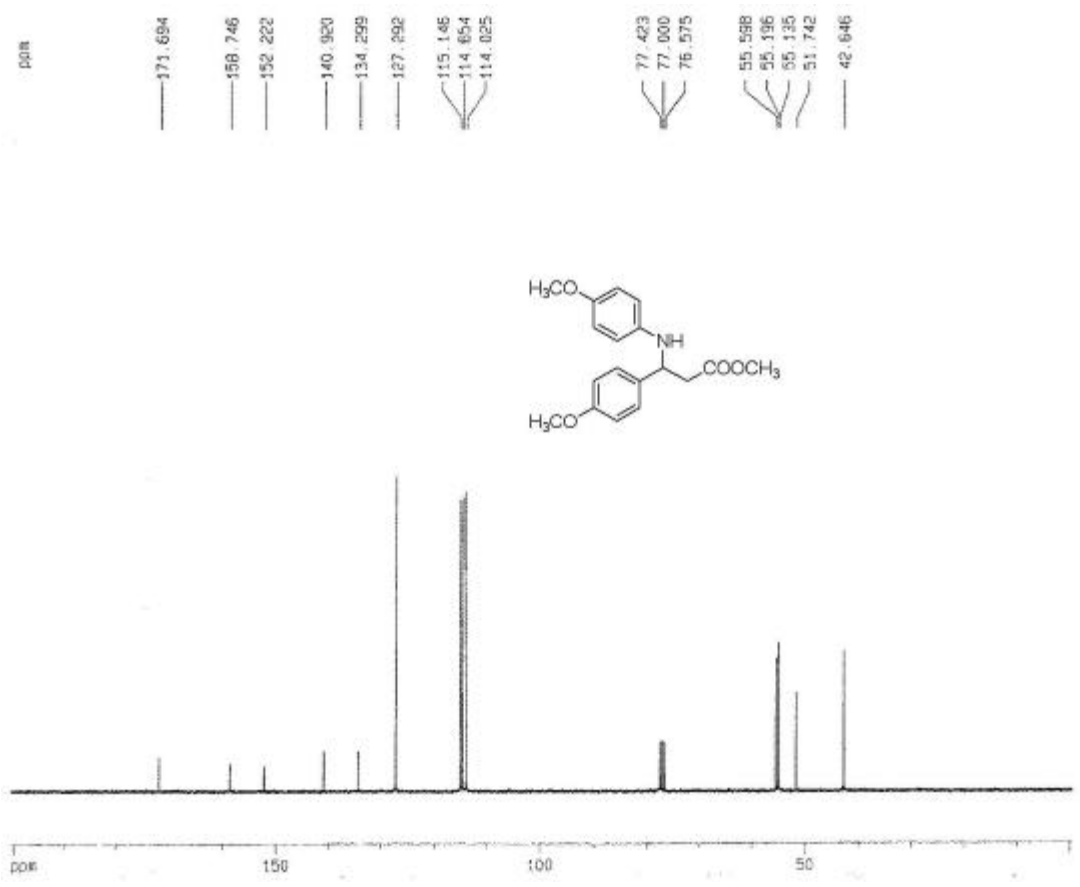
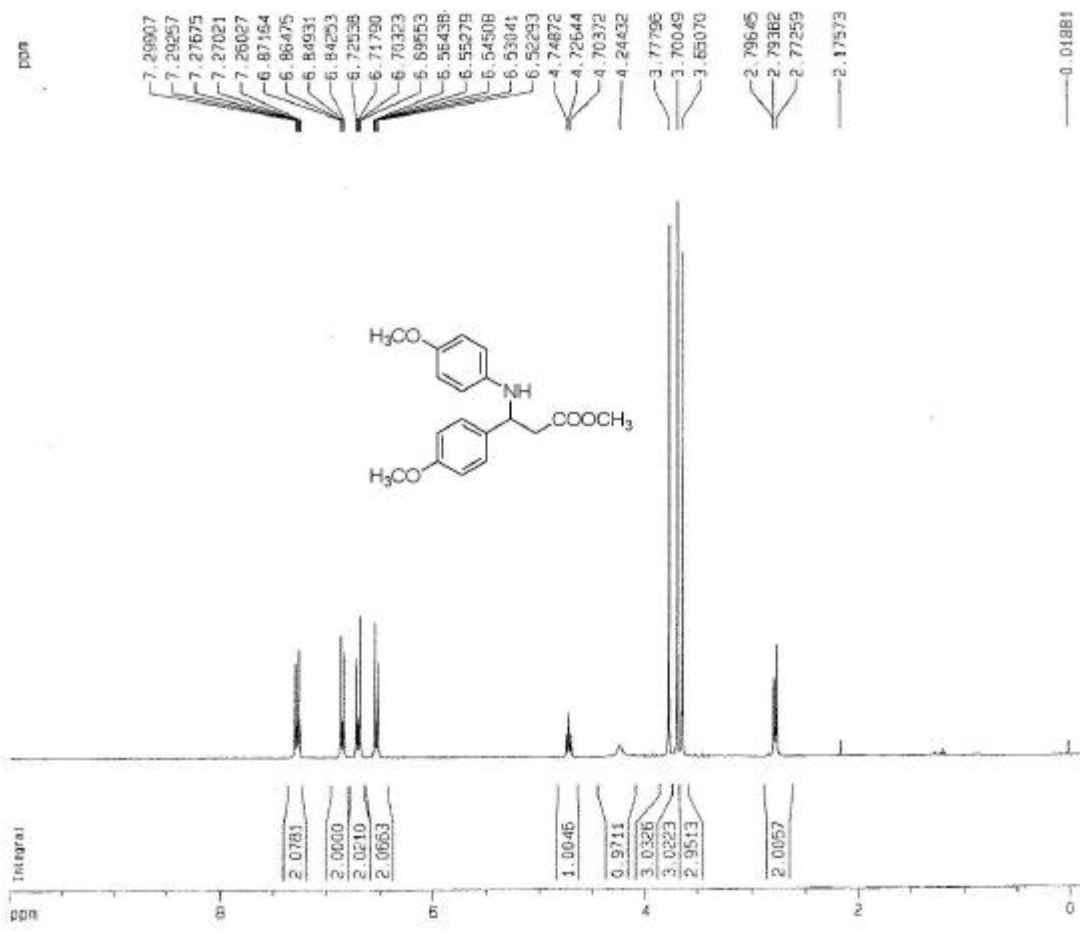




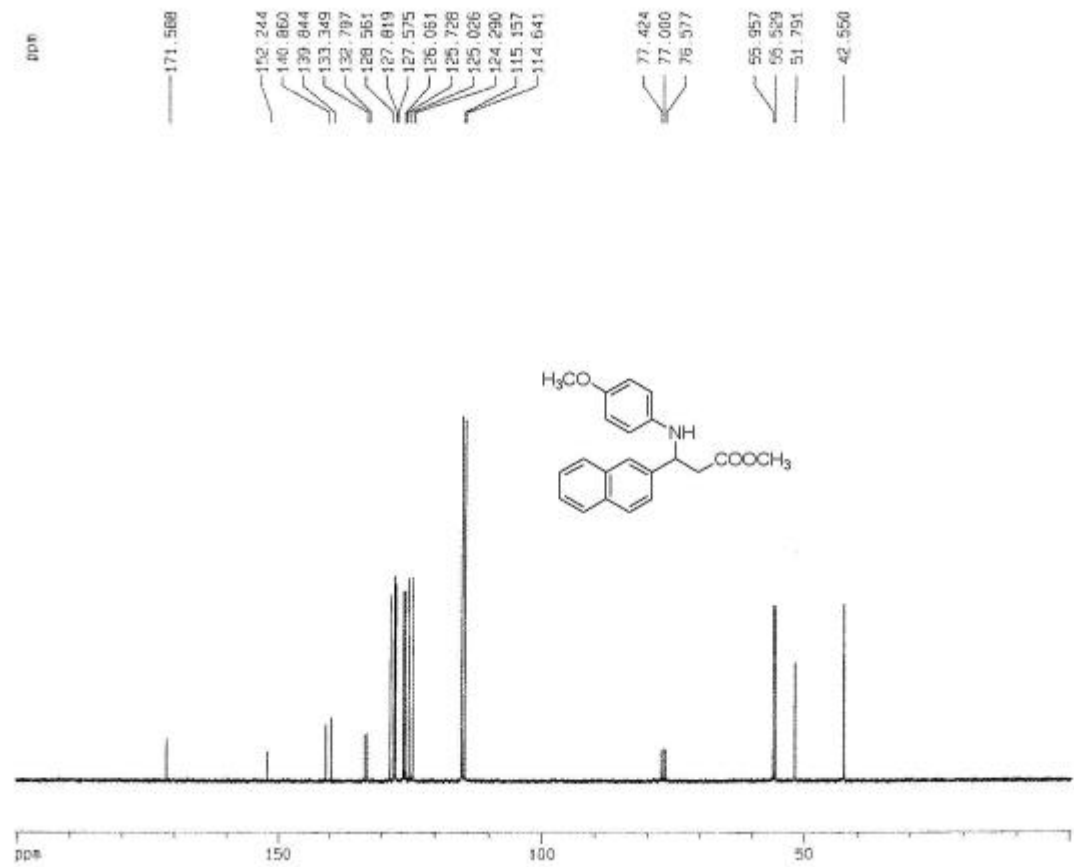
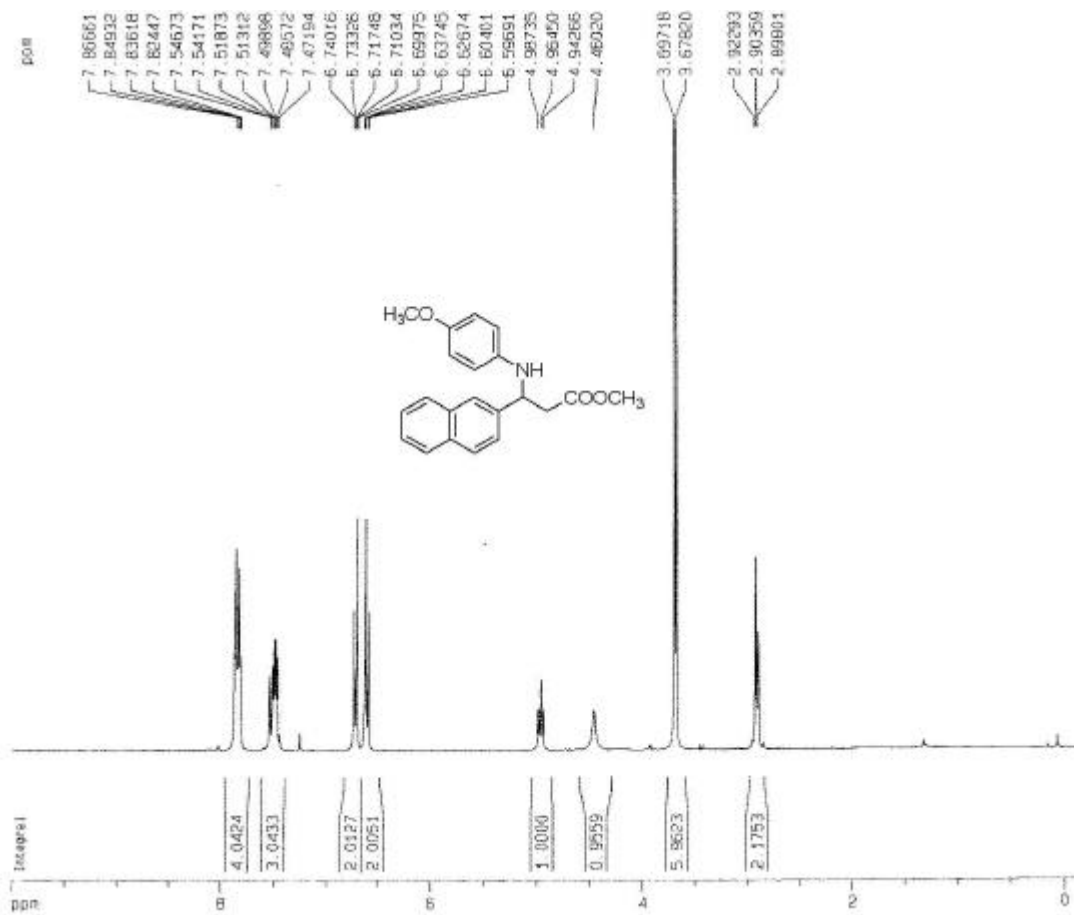
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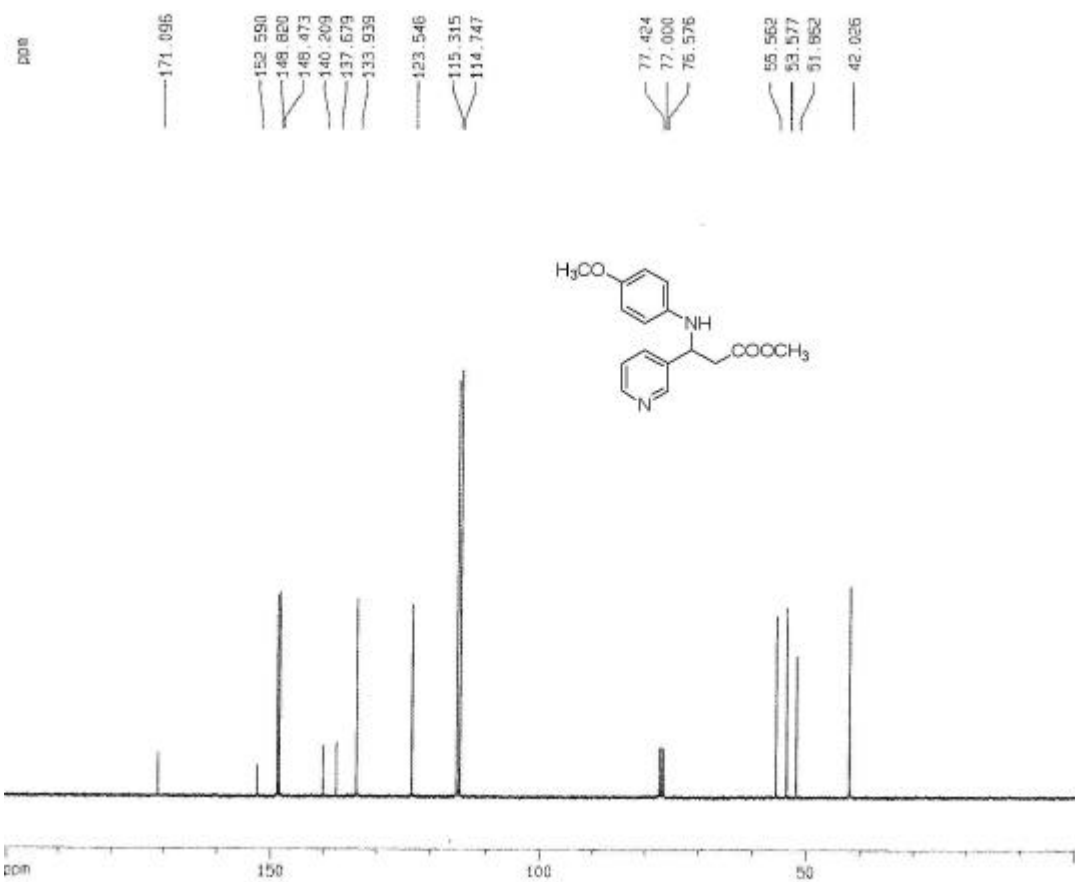
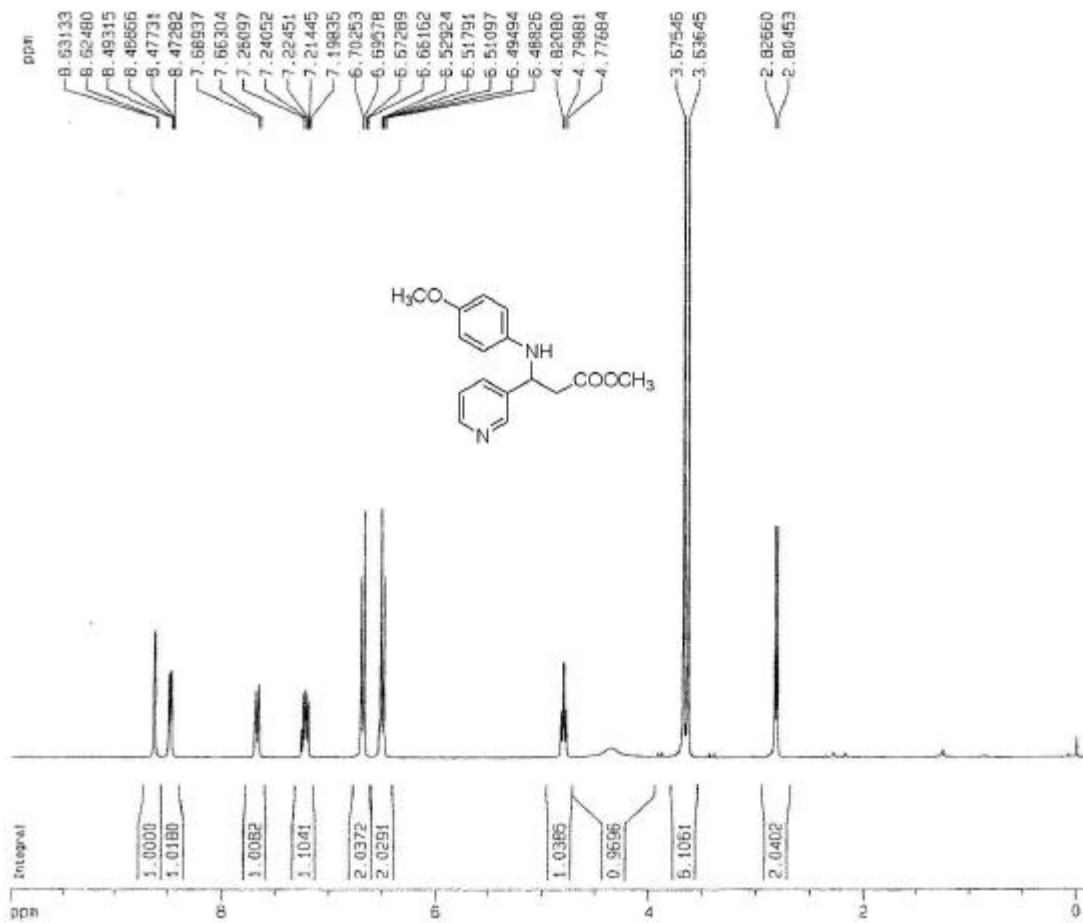


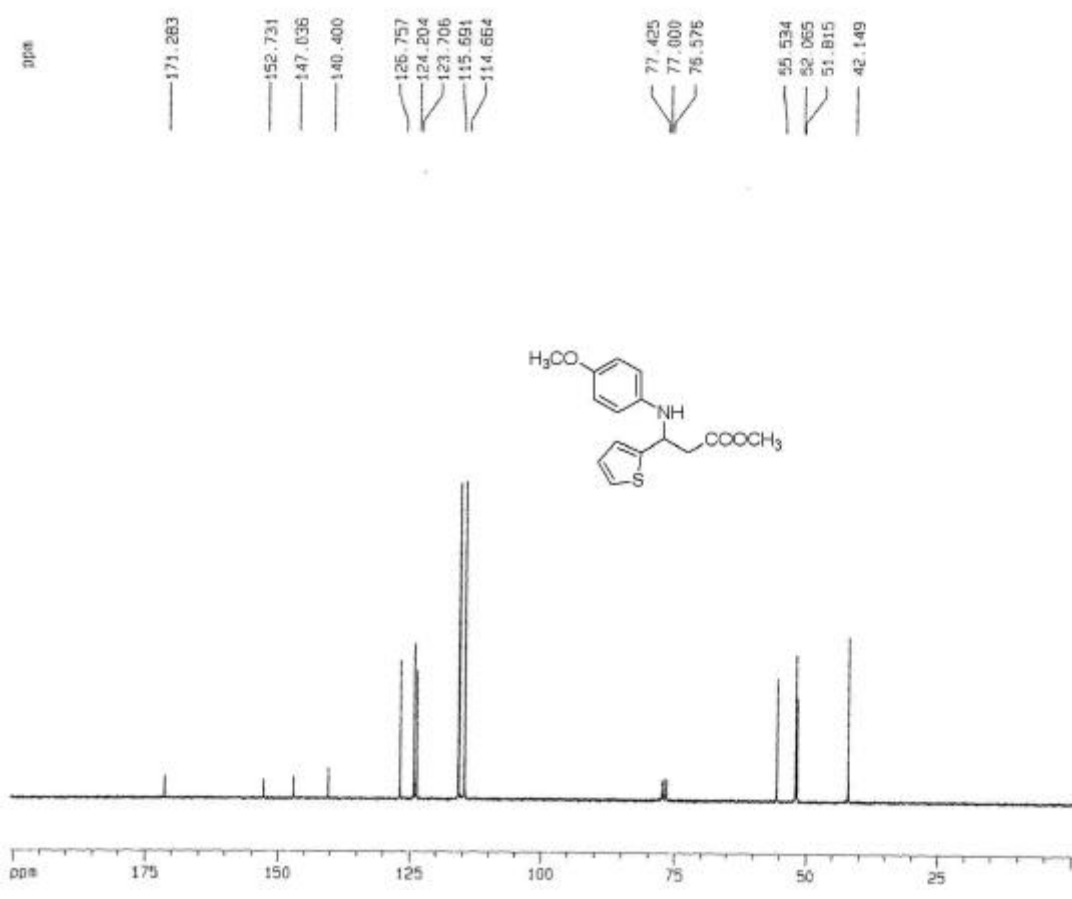
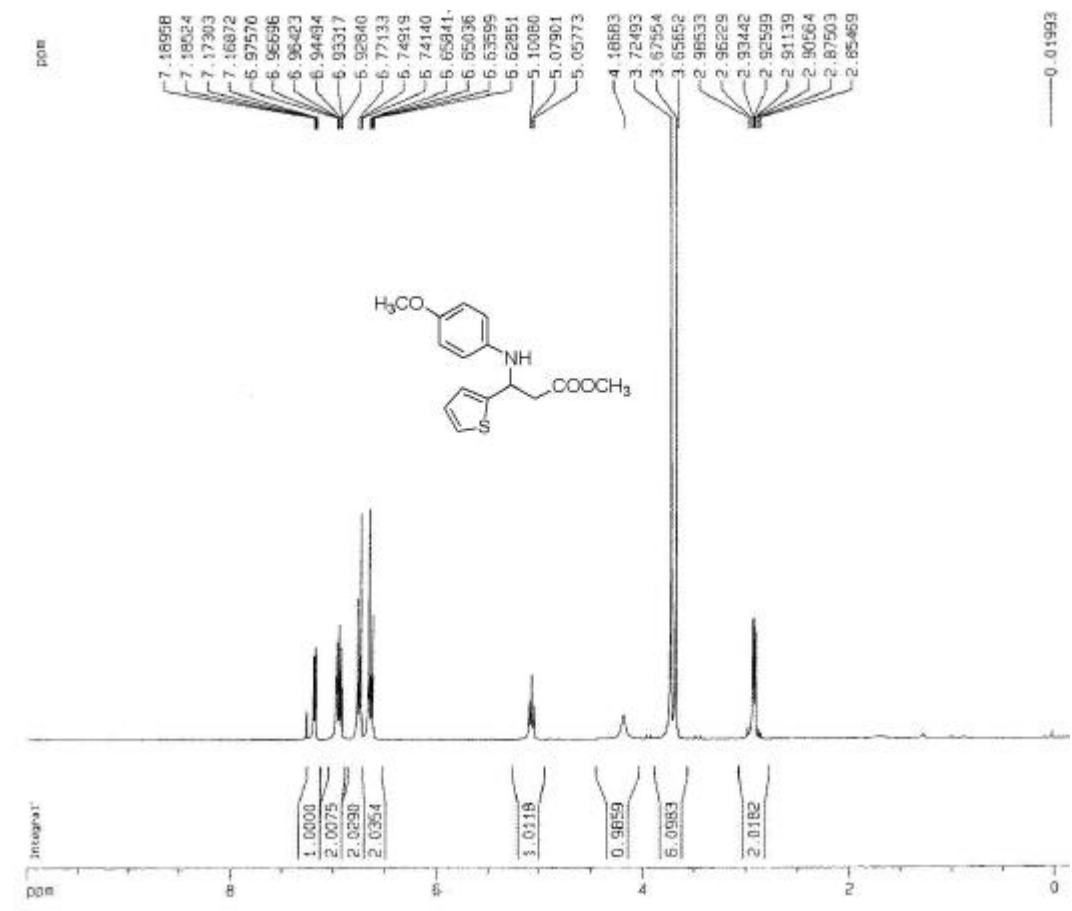


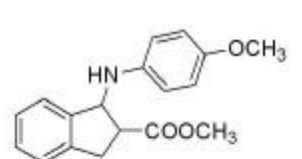
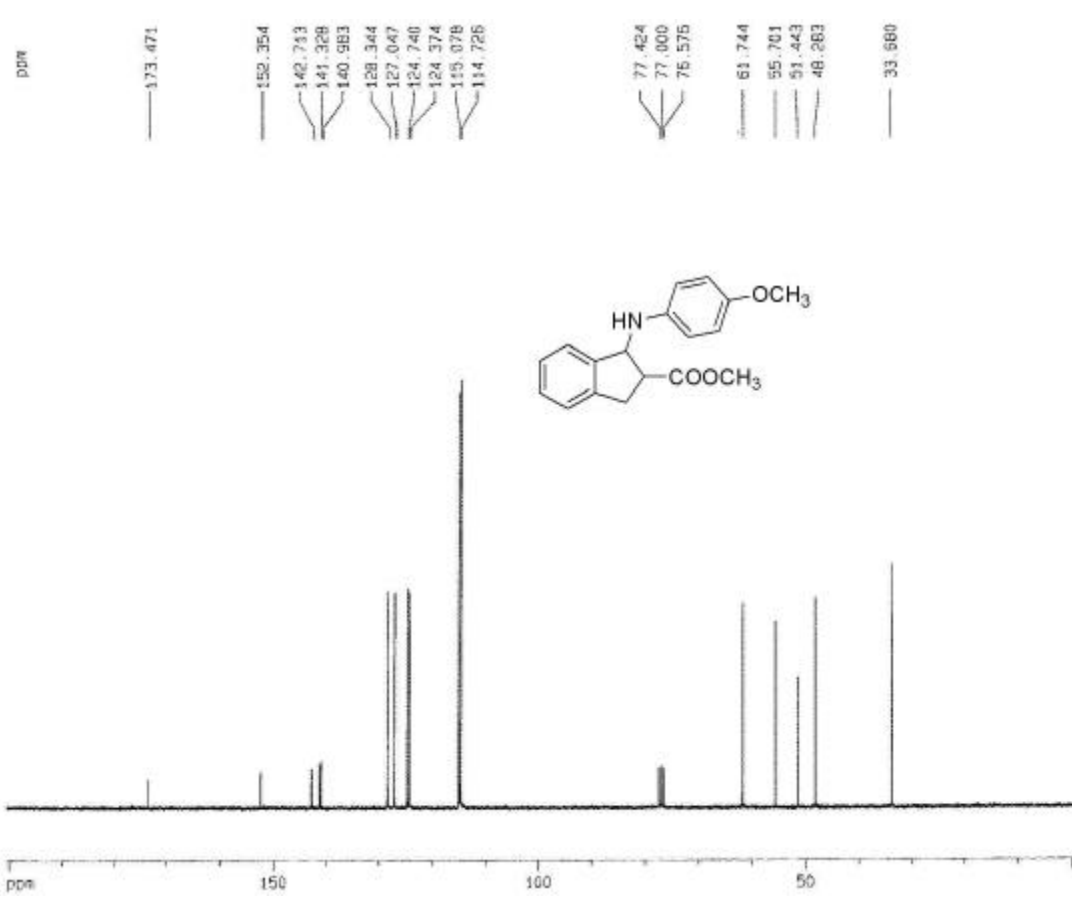
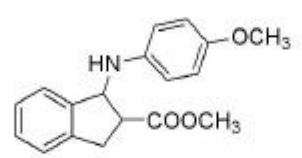
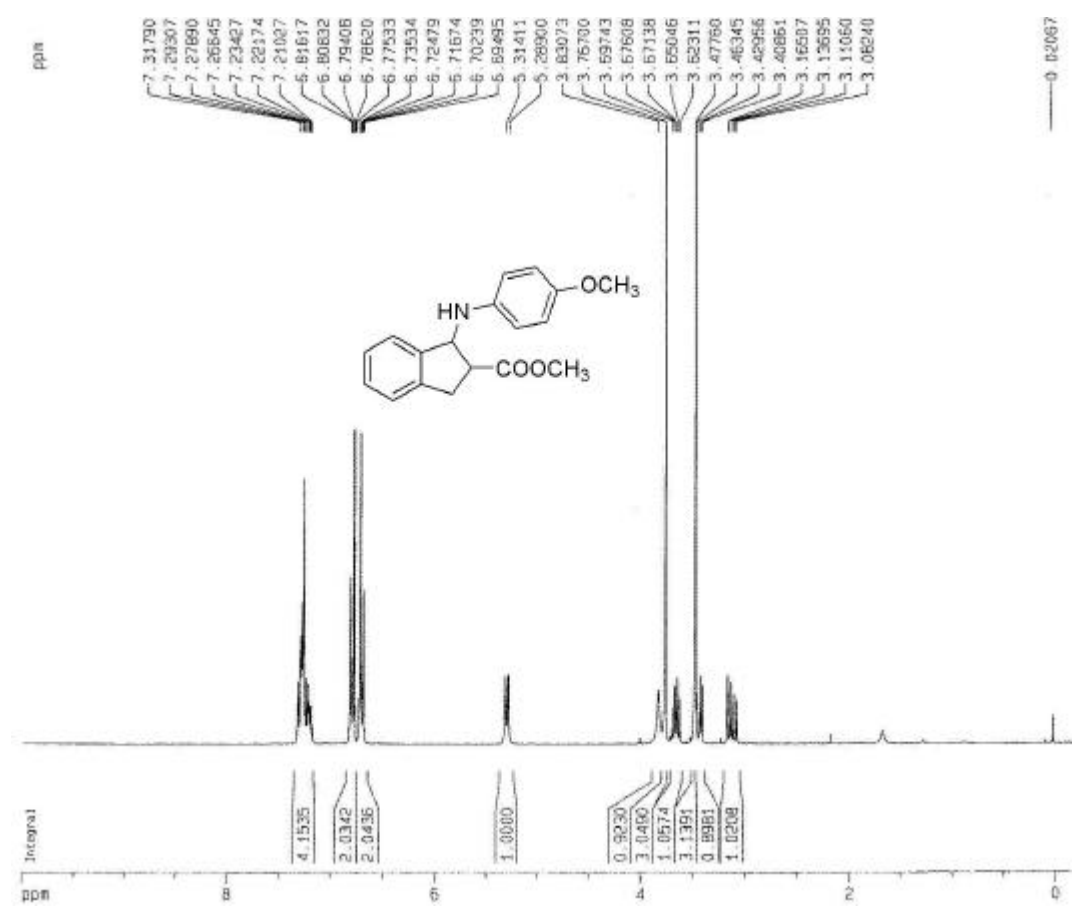


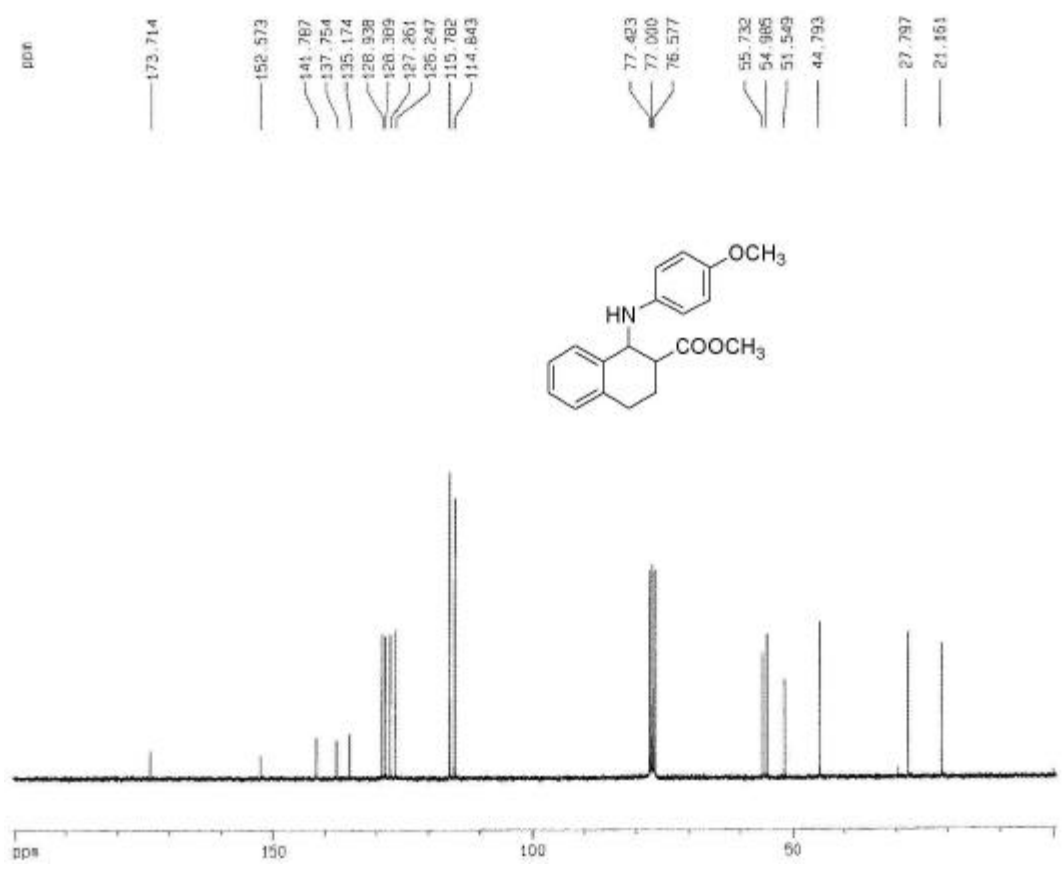
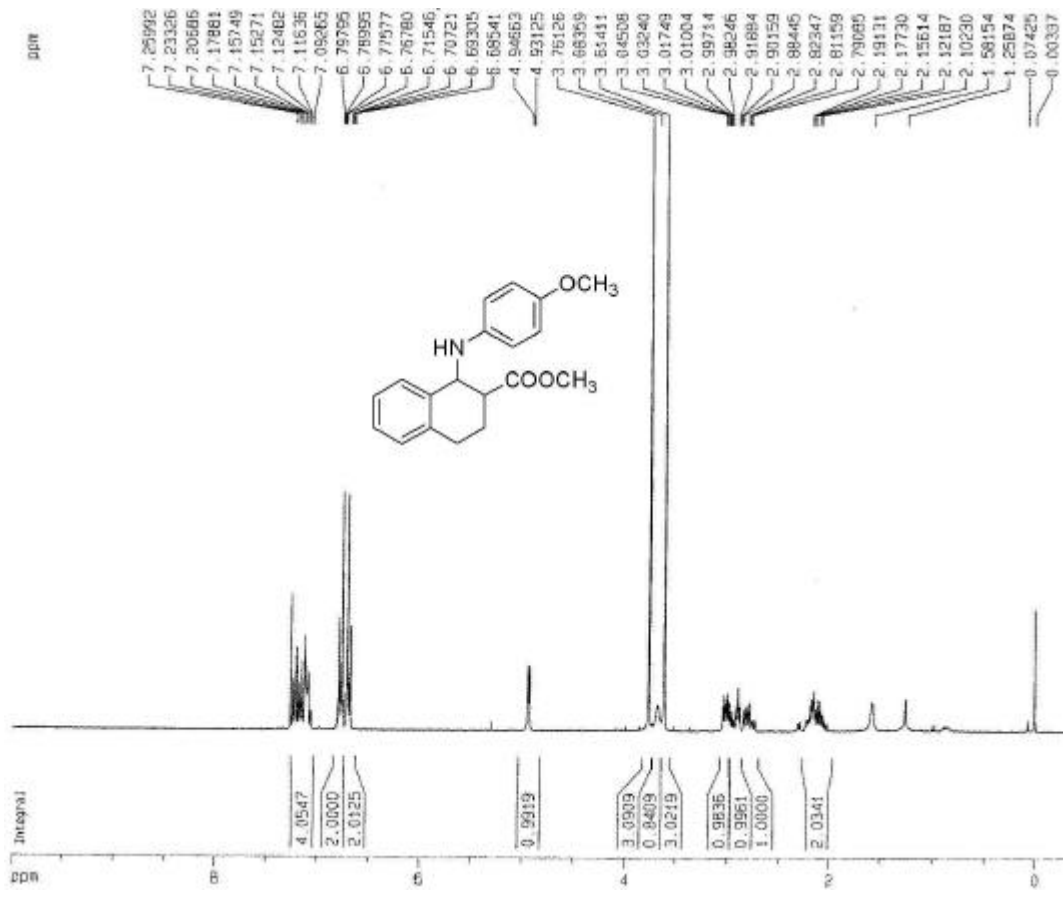
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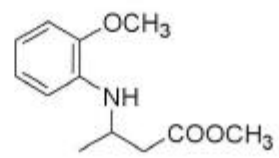
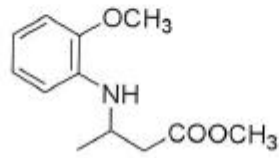
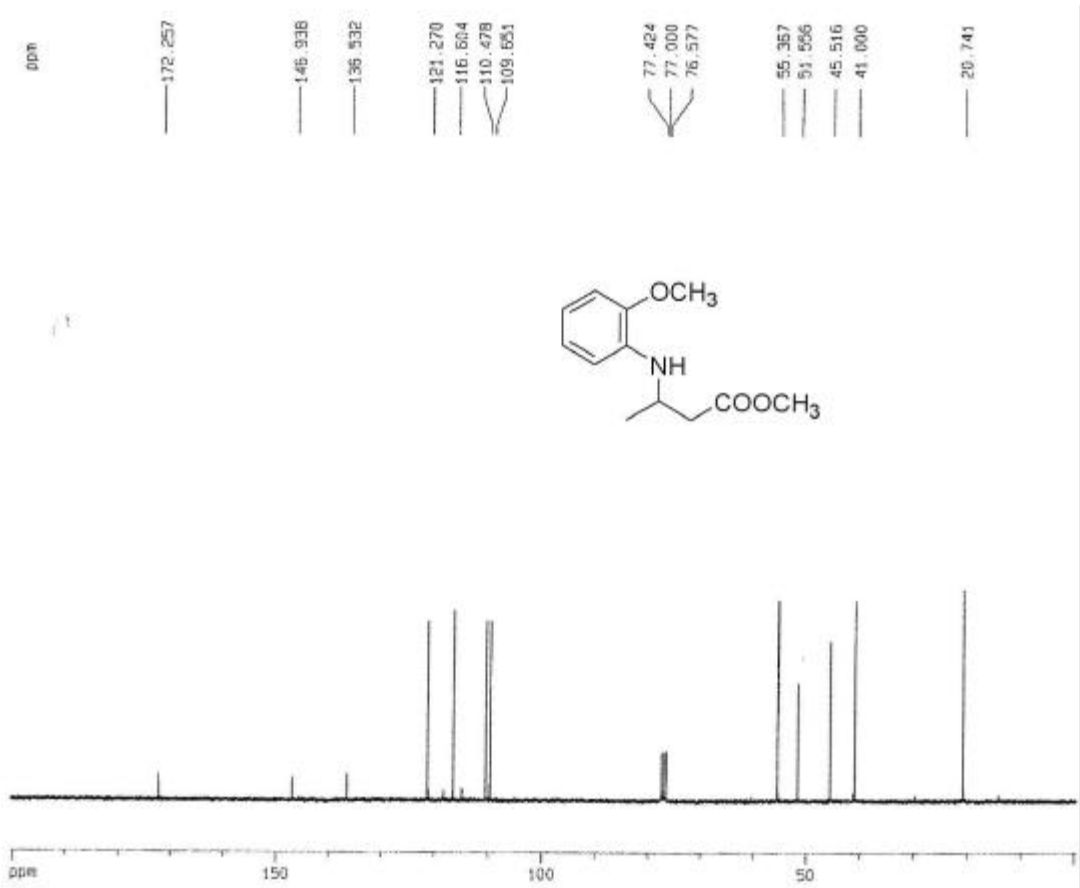
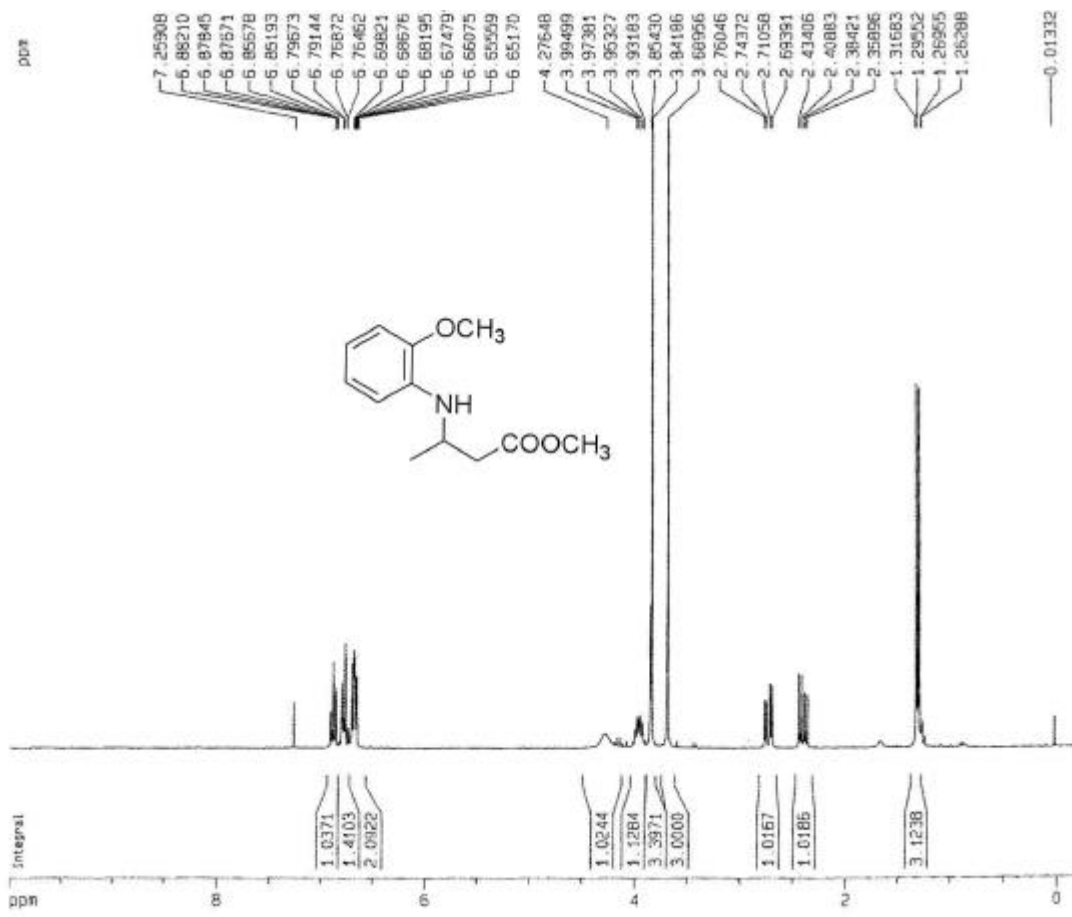


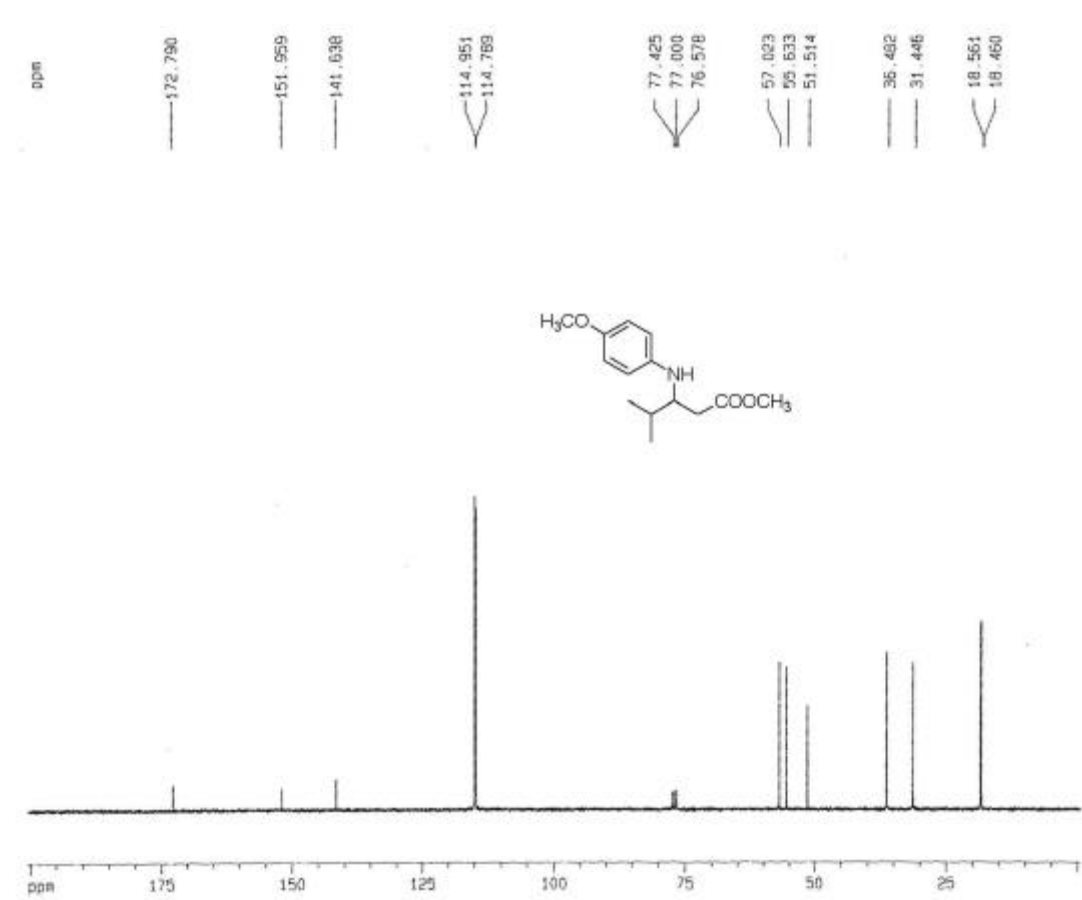
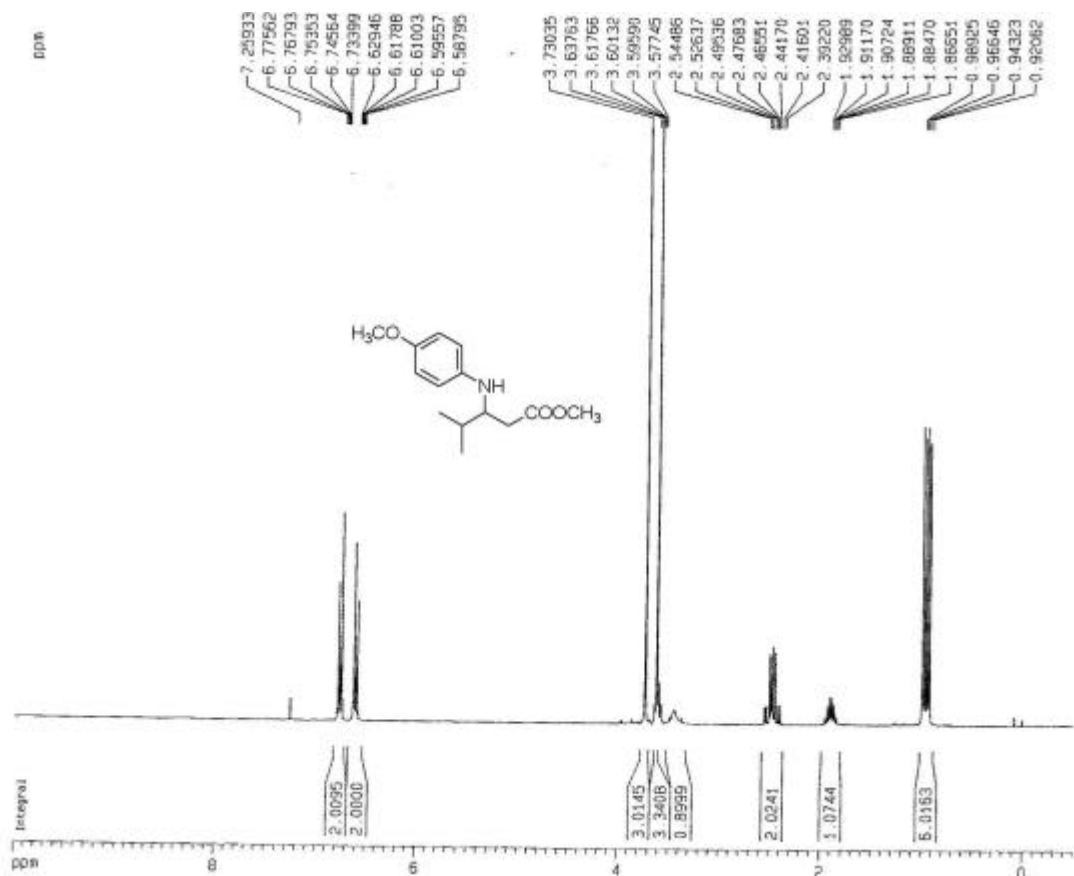


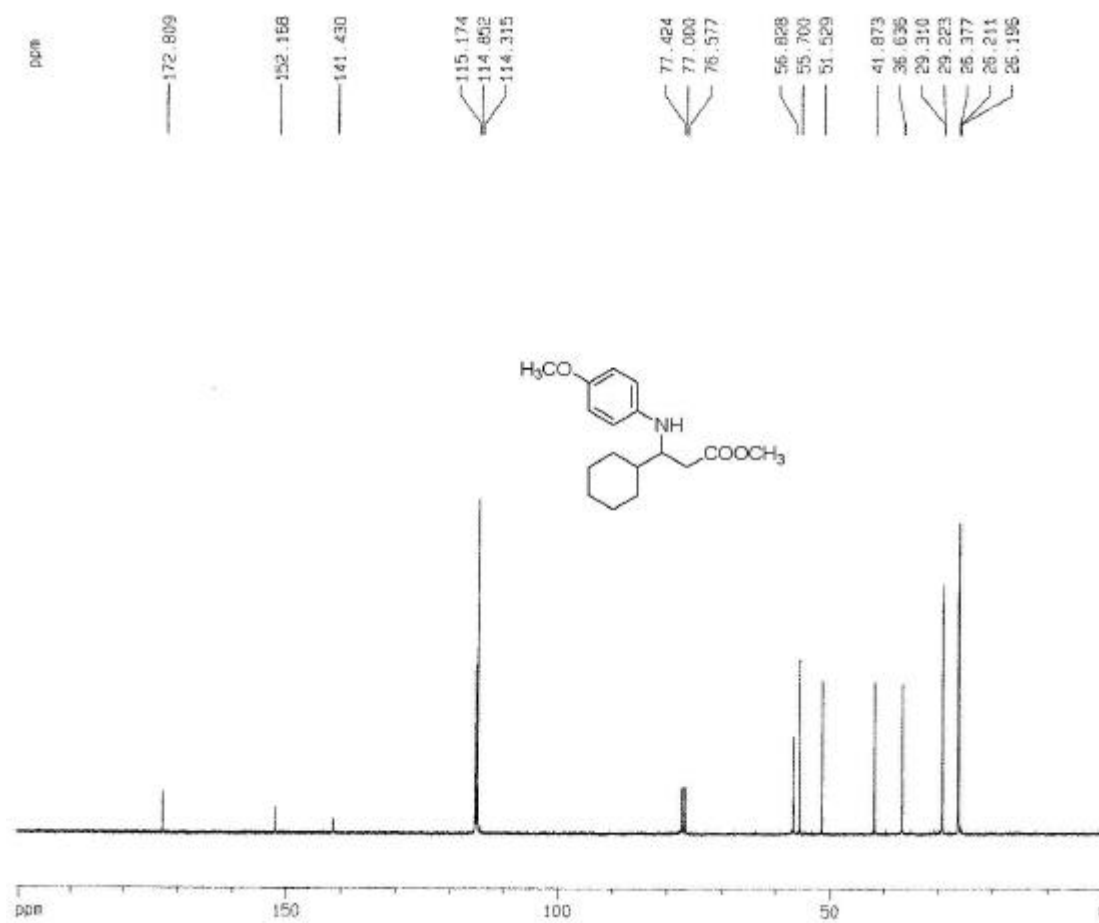
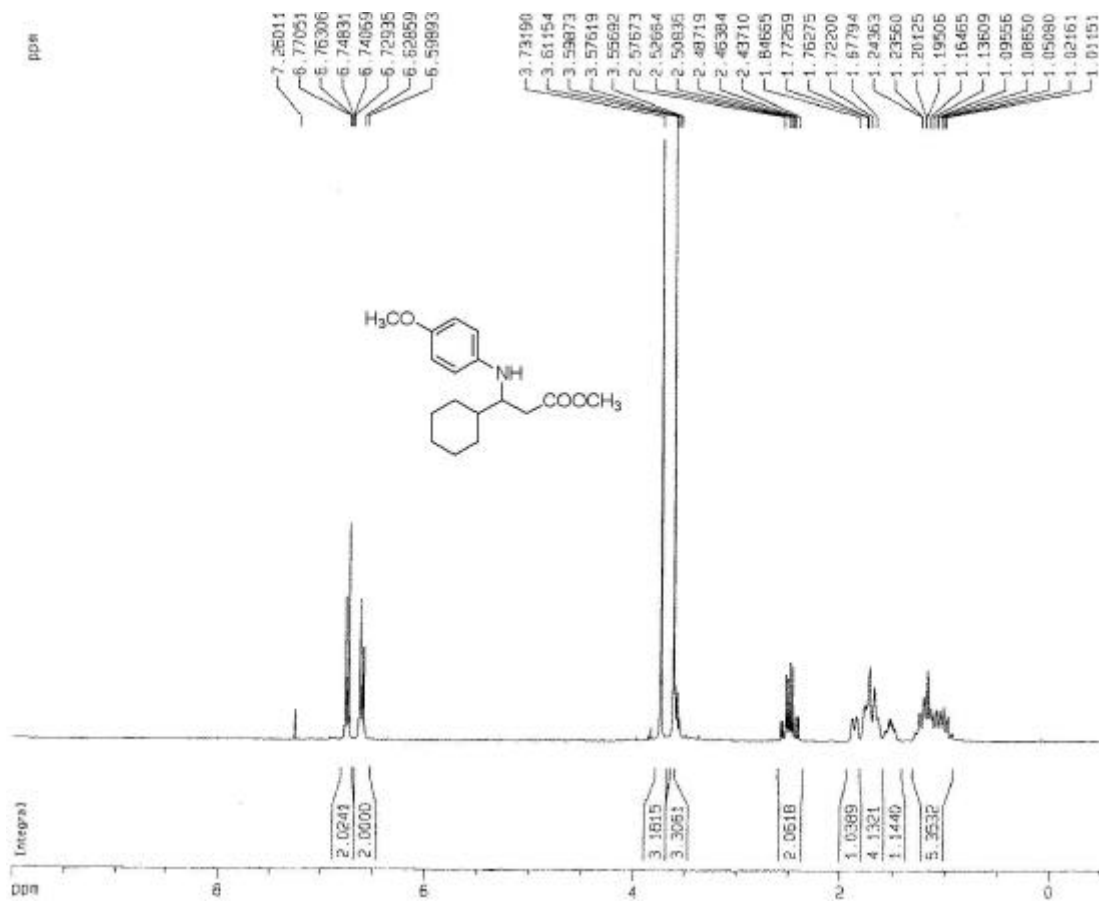


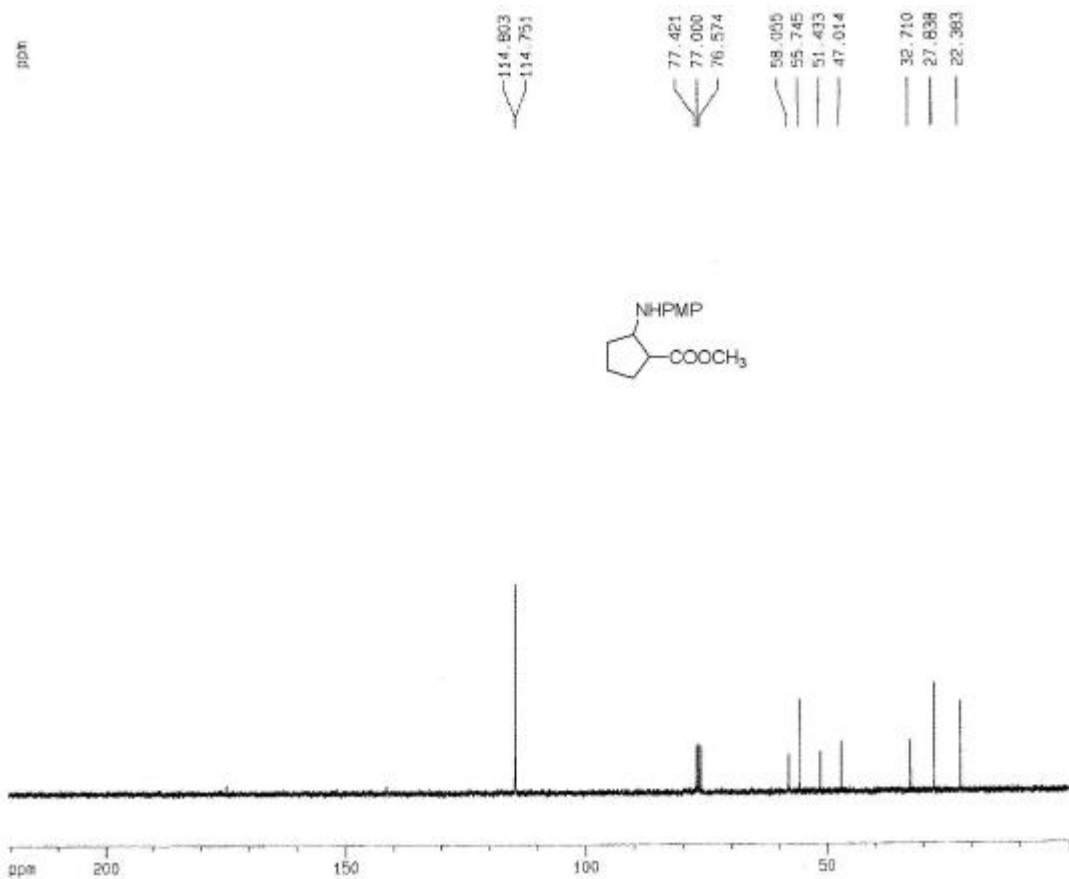
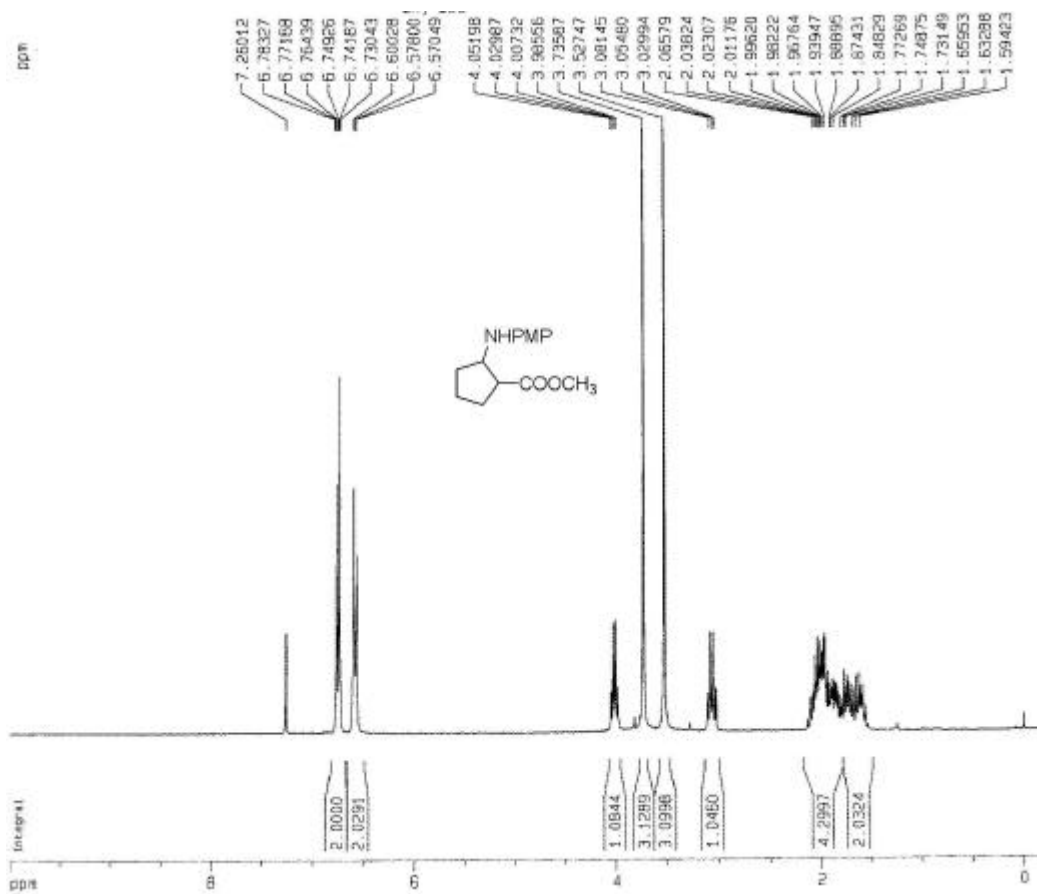


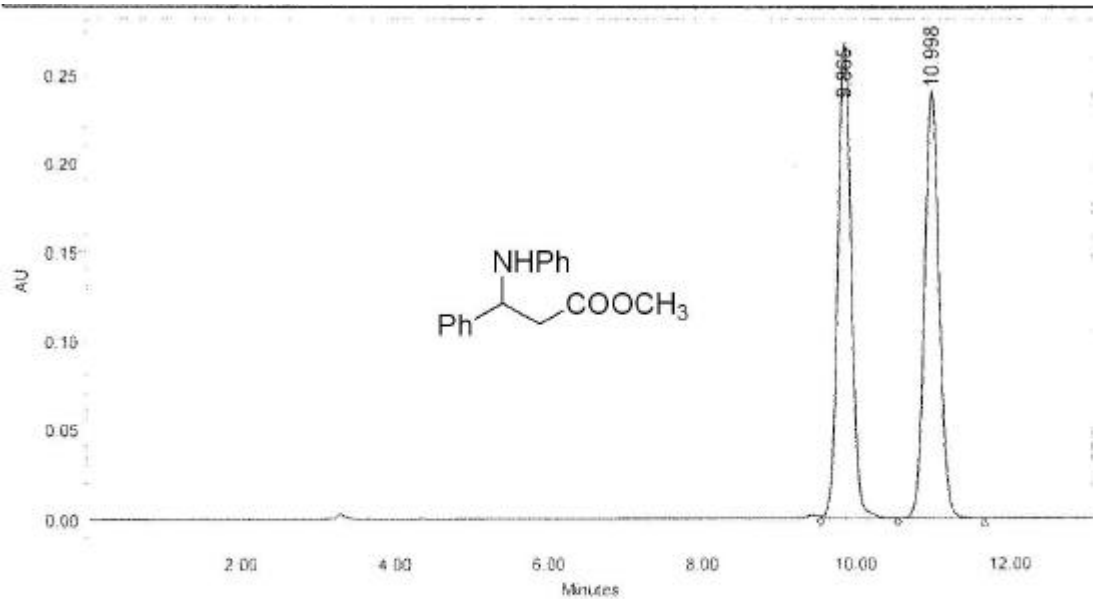




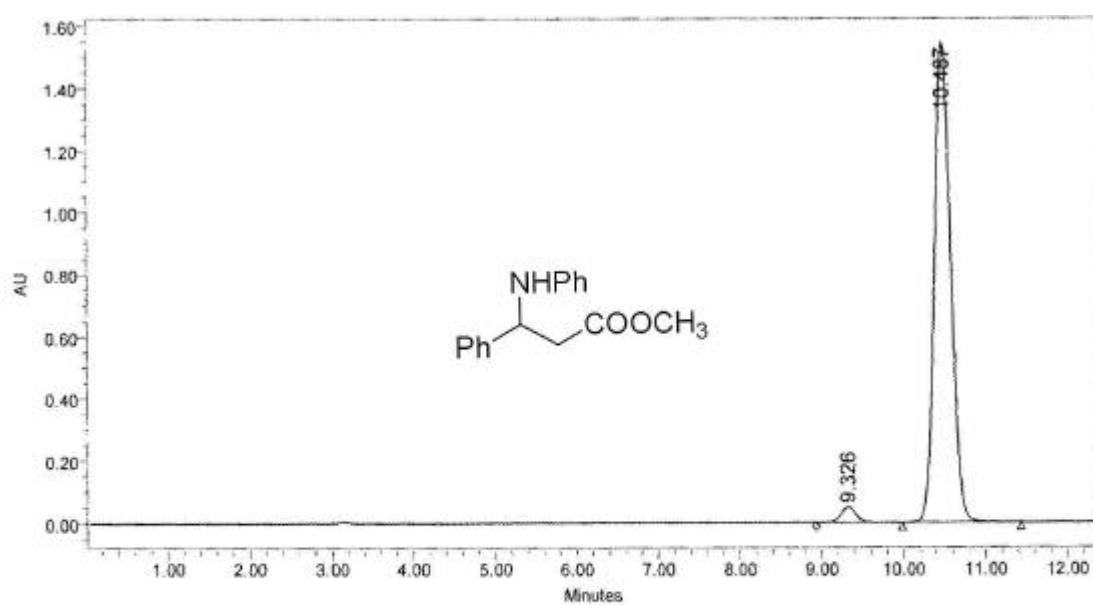




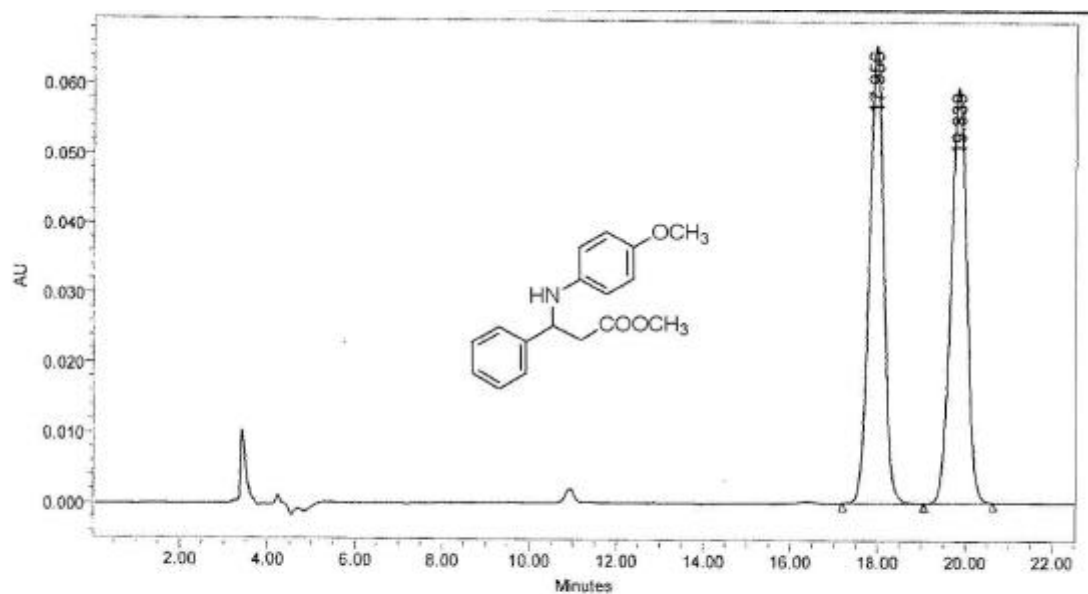




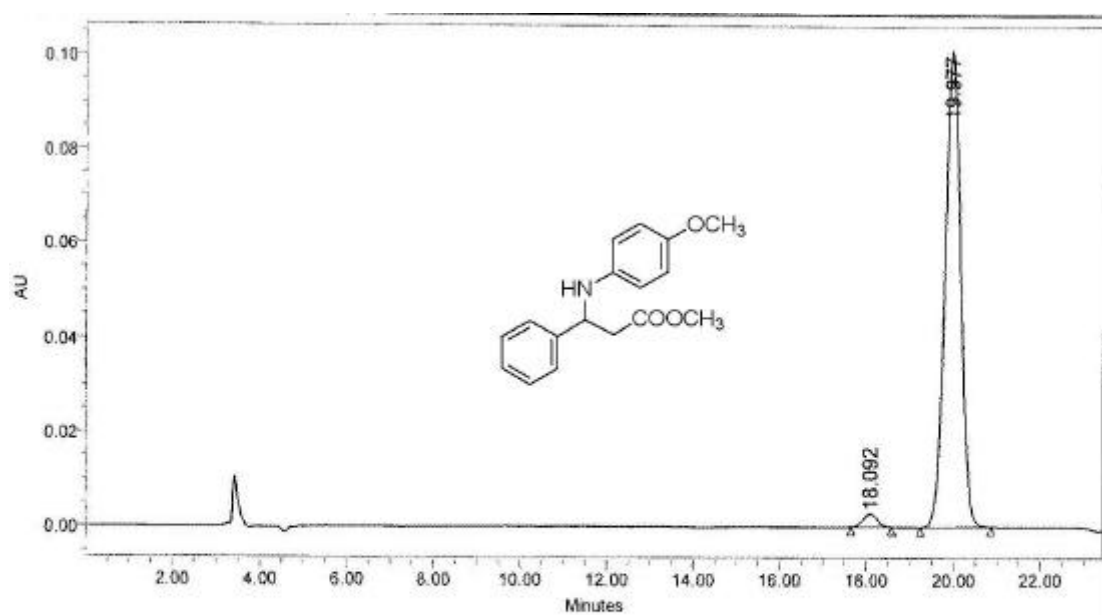
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	9.865	3216164	50.23	267605	52.68
2	10.998	3186117	49.77	240358	47.32



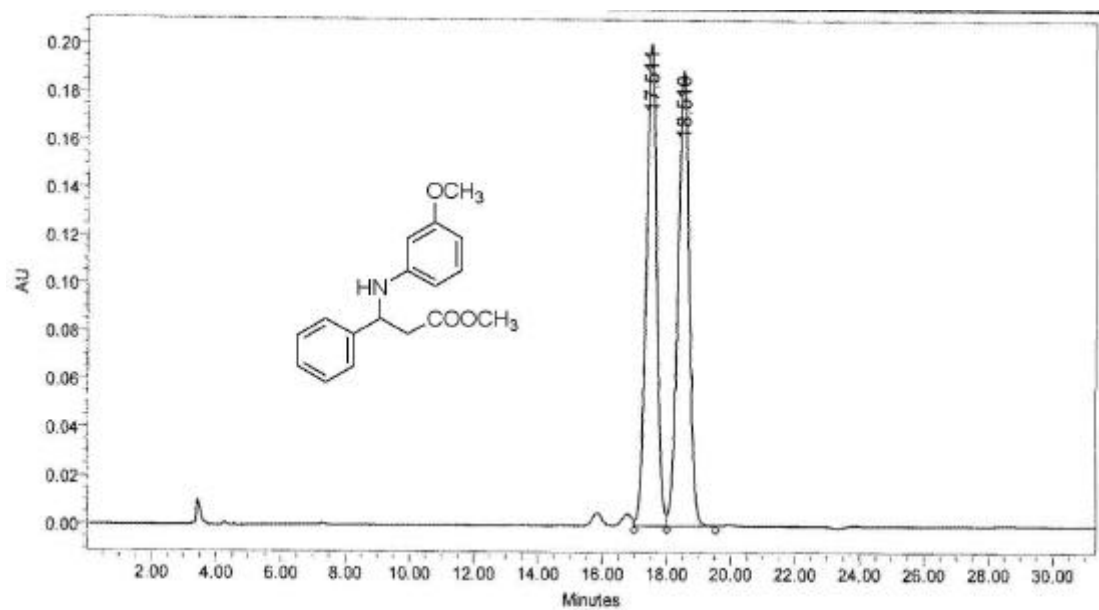
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	9.326	574360	2.63	48067	3.02
2	10.487	21261720	97.37	1541173	96.98



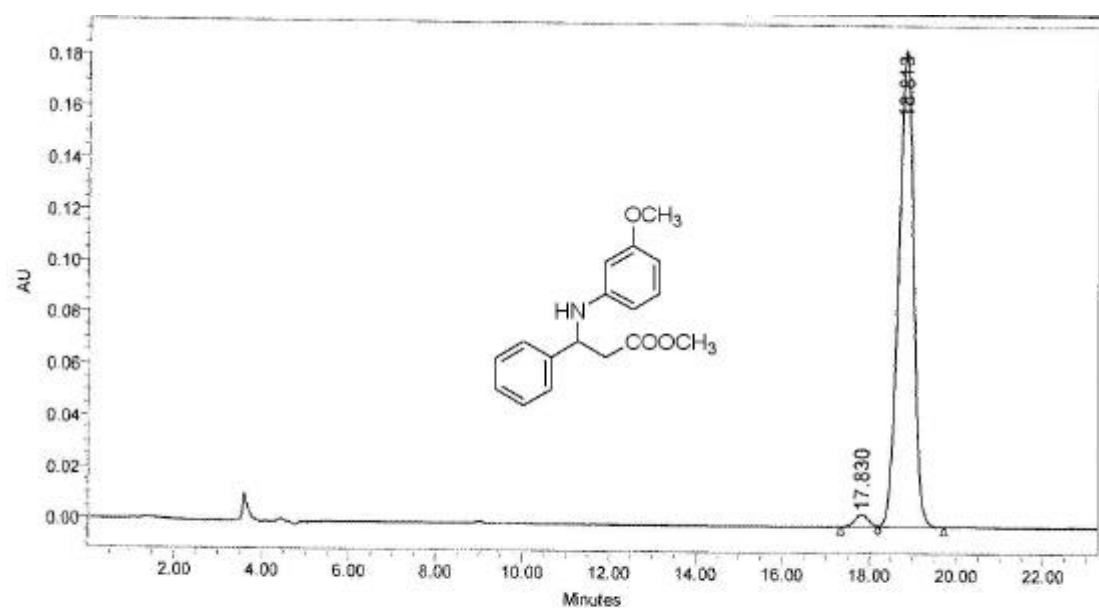
RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	1512297	50.31	65611	52.37
2	1493415	49.69	59581	47.63



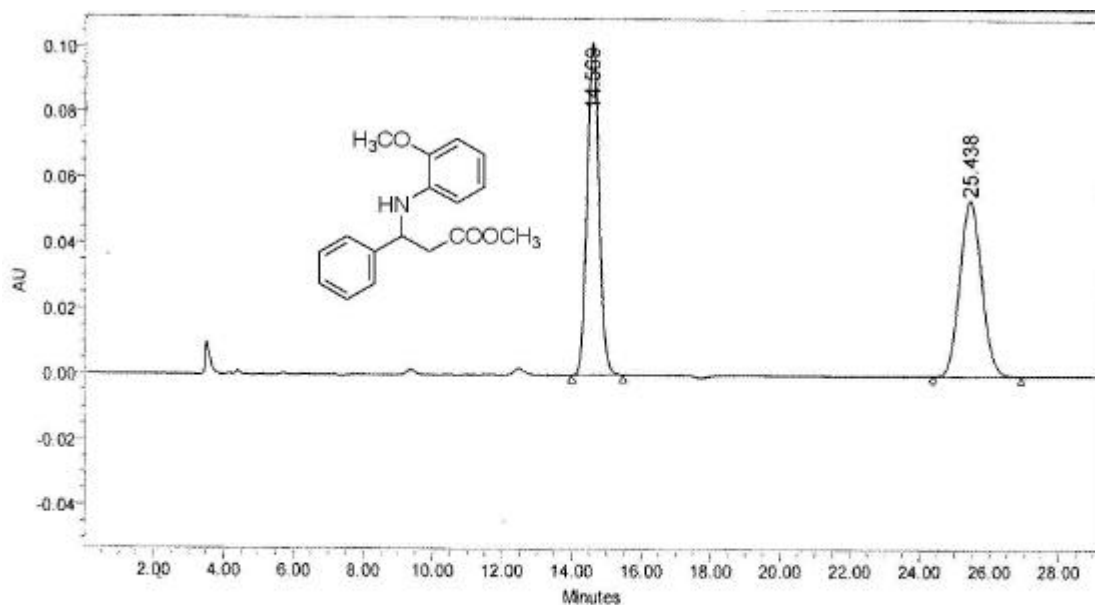
RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	60838	2.34	2749	2.64
2	2535417	97.66	101316	97.36



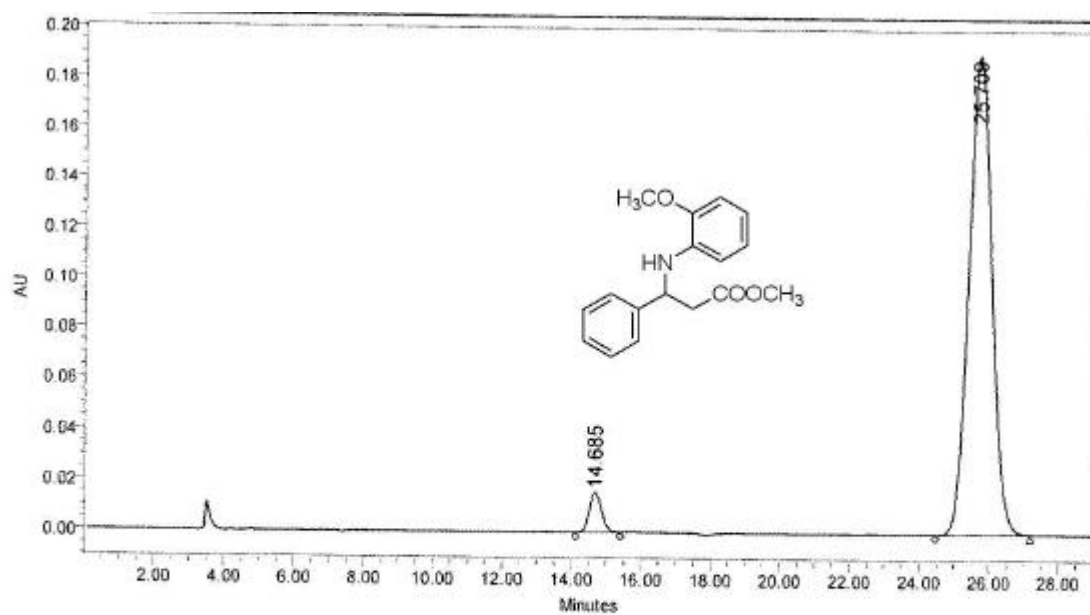
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	17.511	4652158	50.08	200819	51.39
2	18.510	4637990	49.92	189937	48.61



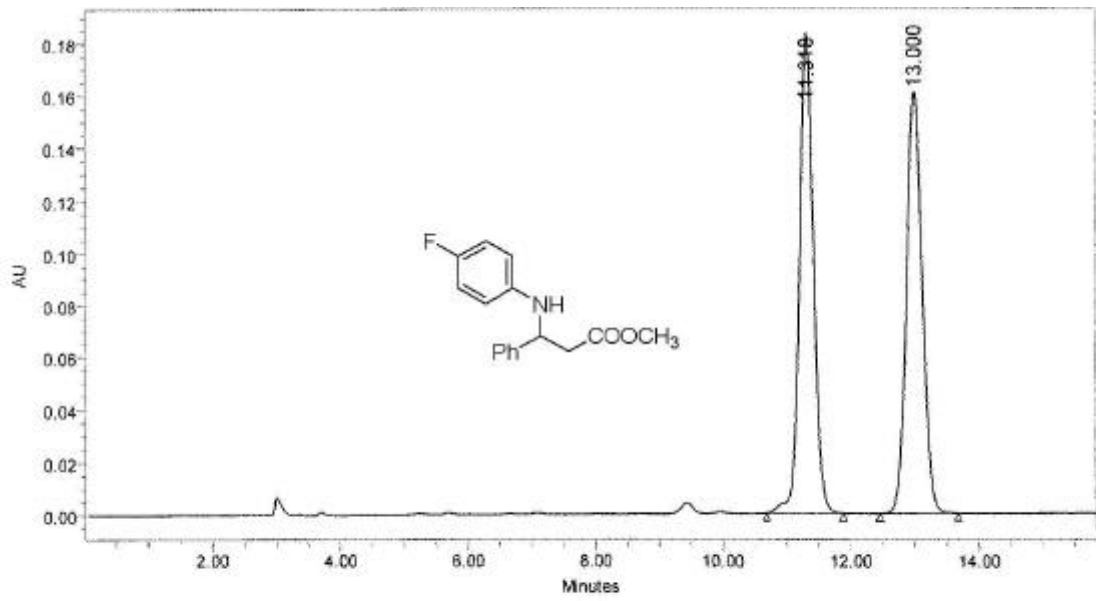
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	17.830	100939	2.23	4652	2.45
2	18.813	4420716	97.77	185536	97.55



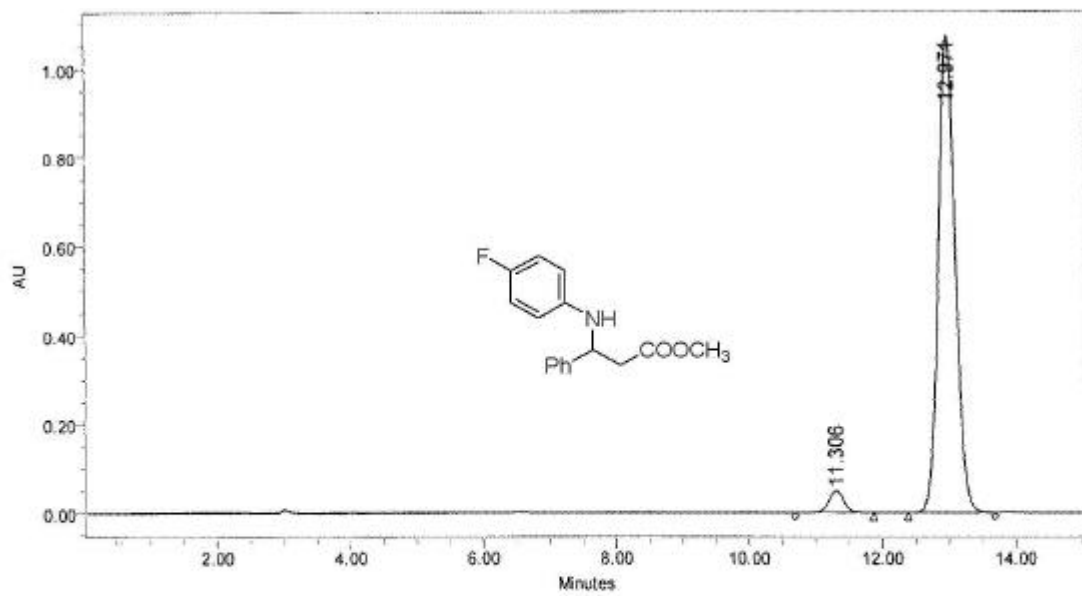
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	14.569	2422795	50.53	101786	85.41
2	25.438	2372117	49.47	53818	34.59



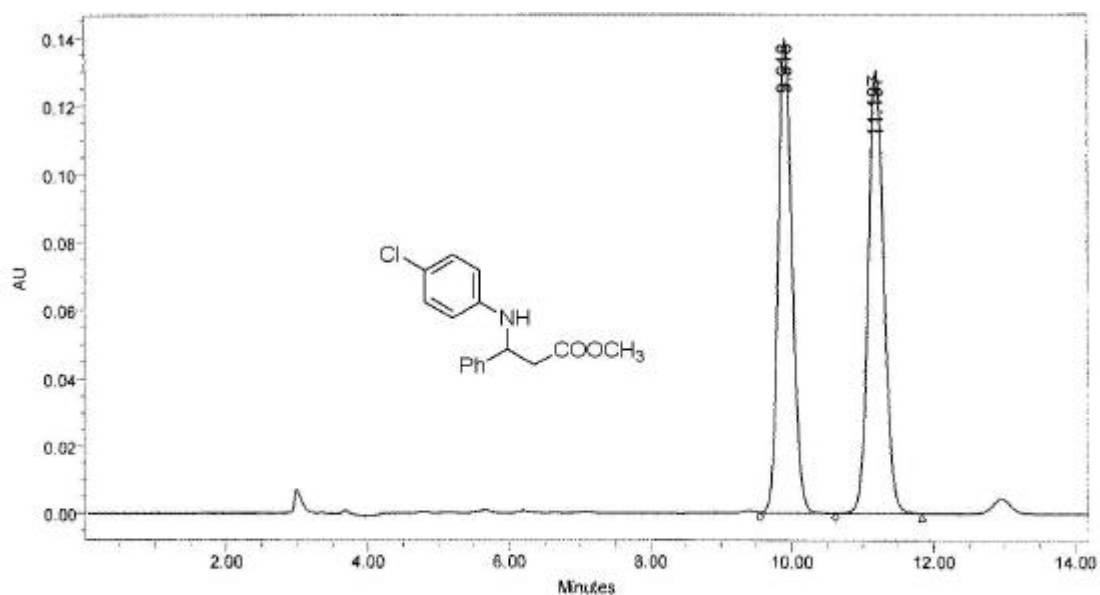
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	14.685	383684	4.24	16003	7.74
2	25.709	8666143	95.76	190818	92.26



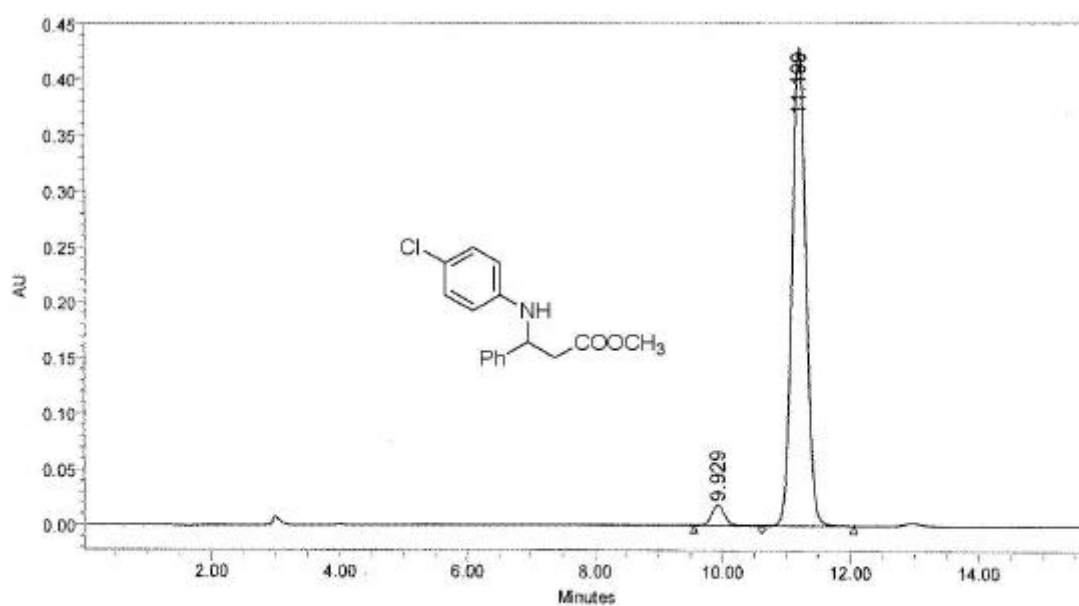
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	11.318	2821723	50.46	183115	53.27
2	13.000	2770587	49.54	160636	46.73



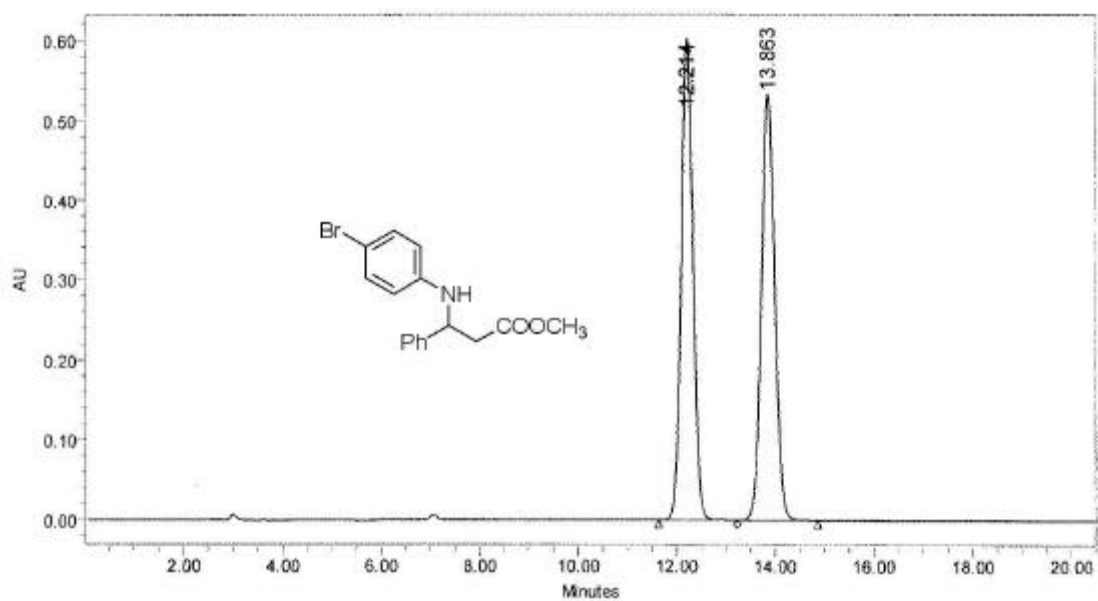
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	11.306	775786	3.94	49839	4.44
2	12.971	18895110	96.06	1071822	95.56



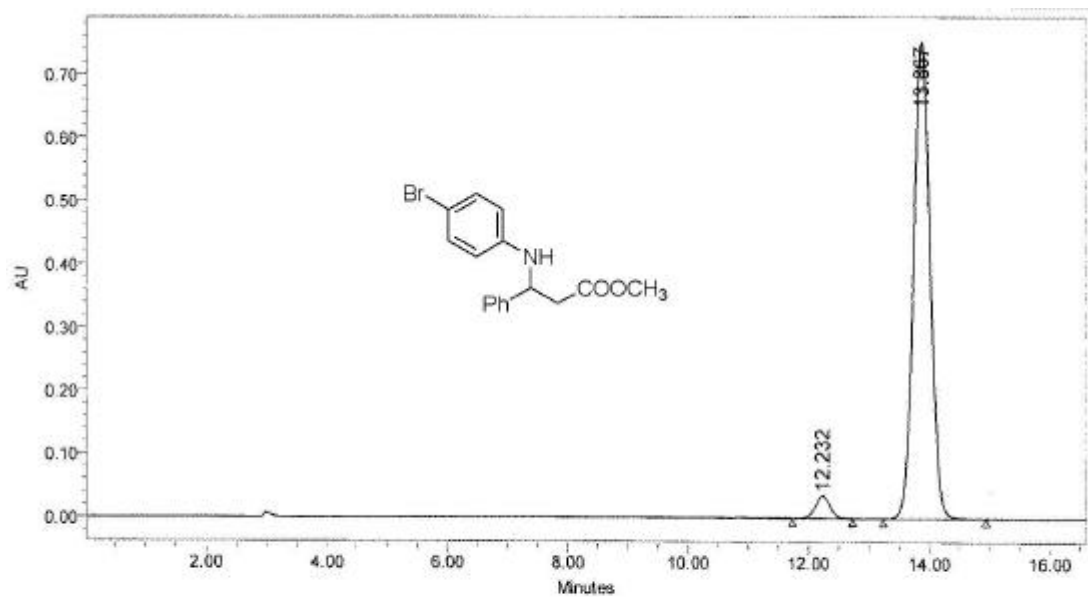
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	9.918	1888863	48.98	139510	51.74
2	11.197	1967526	51.02	130126	48.26



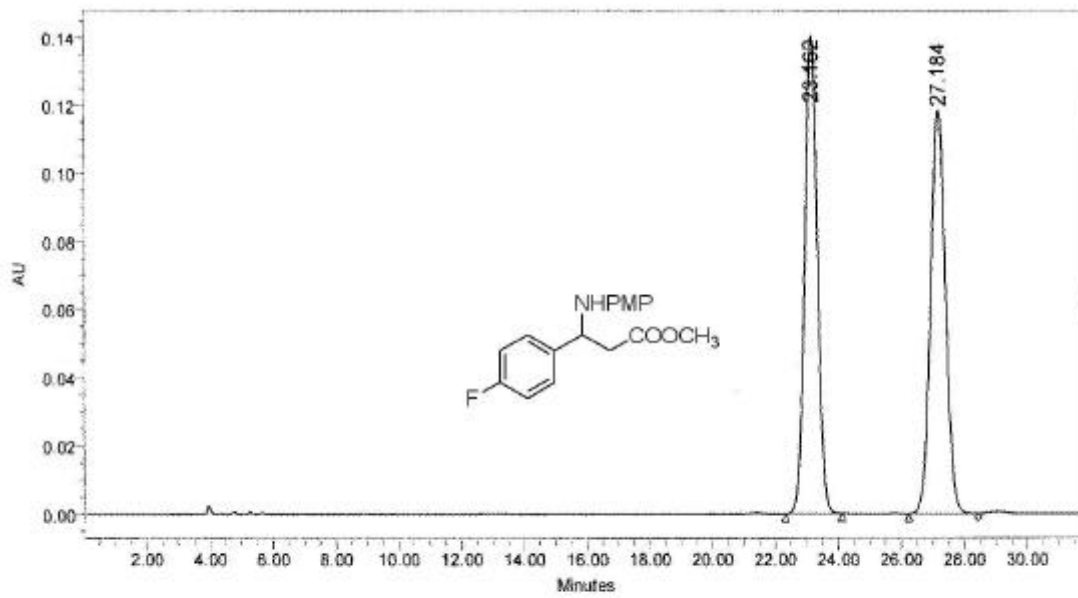
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	9.929	248436	3.72	18325	4.10
2	11.199	6422939	96.28	428612	95.90



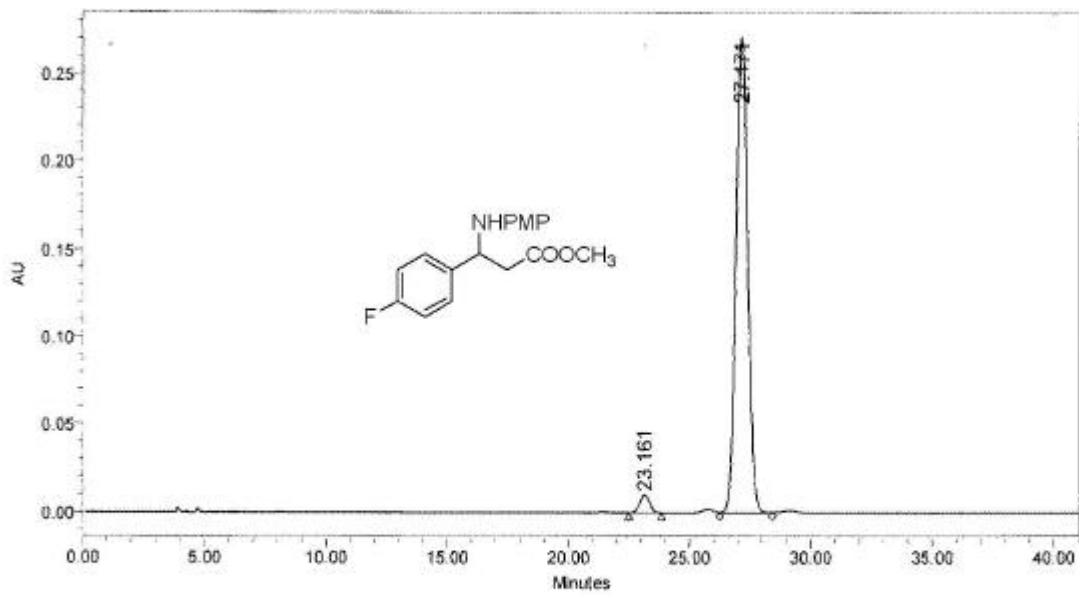
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	12.214	9929154	49.98	600502	53.02
2	13.863	9937356	50.02	532145	46.98



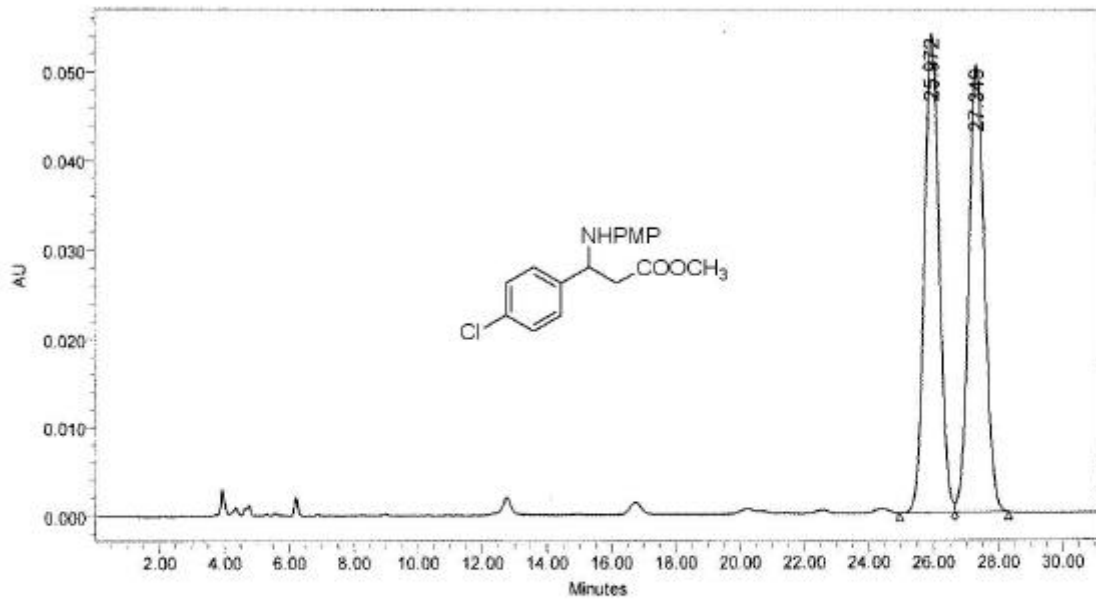
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	12.232	584799	3.97	35436	4.50
2	13.867	14144533	96.03	751827	95.50



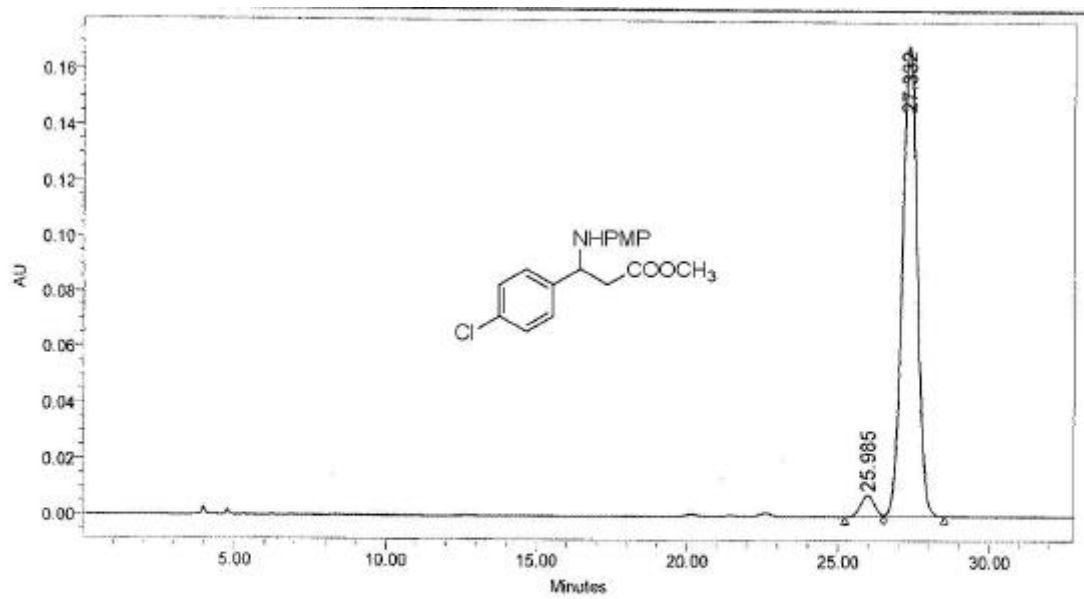
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	23.162	3892777	50.01	140781	54.22
2	27.184	3891422	49.99	118851	45.78



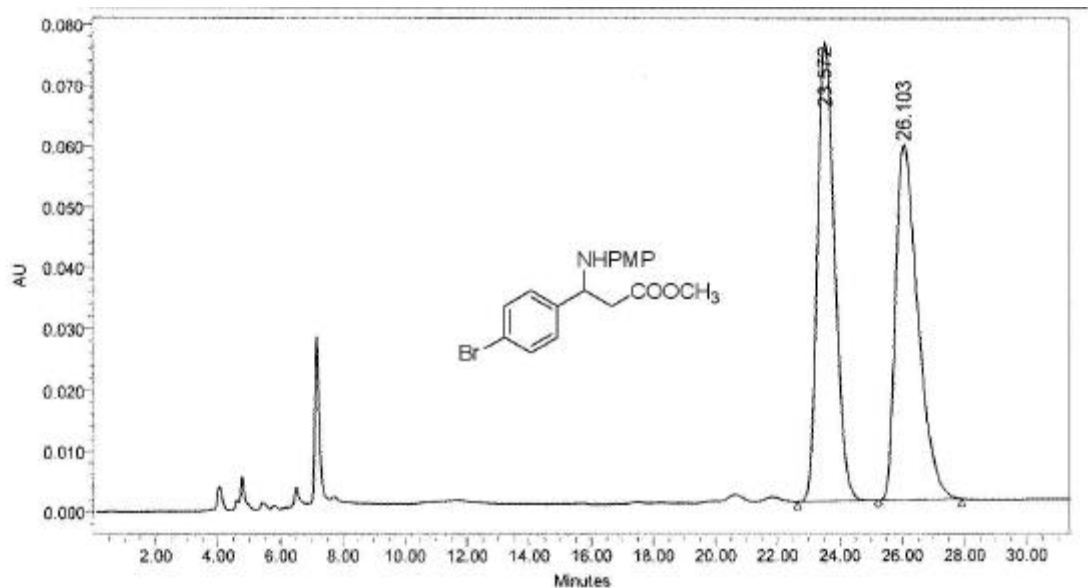
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	23.161	274366	2.95	9927	3.53
2	27.171	9034036	97.05	271450	96.47



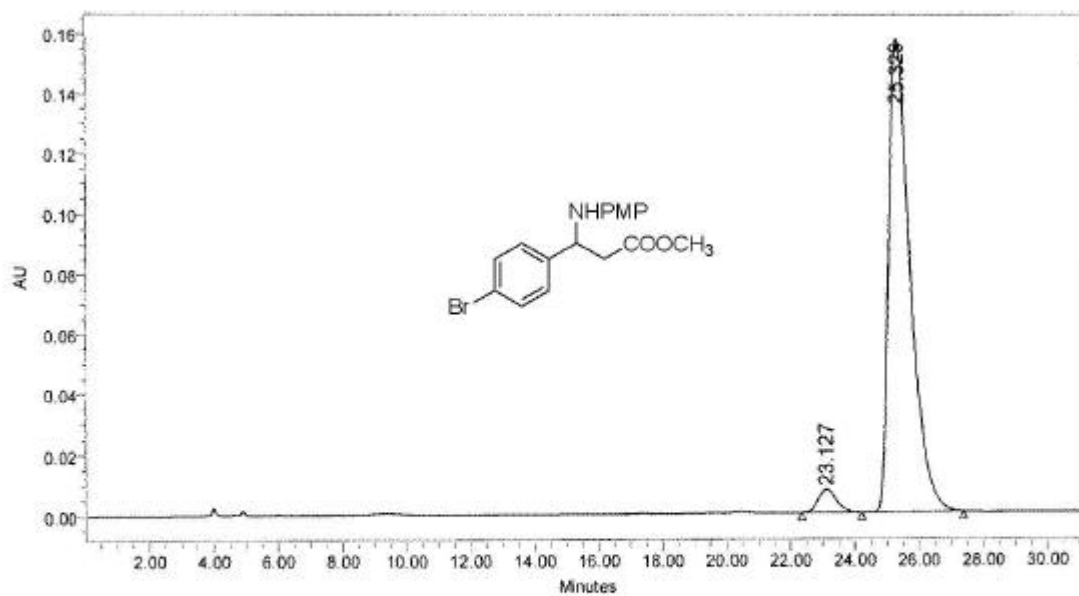
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	25.972	1713272	50.01	54063	51.69
2	27.349	1712485	49.99	50533	48.31



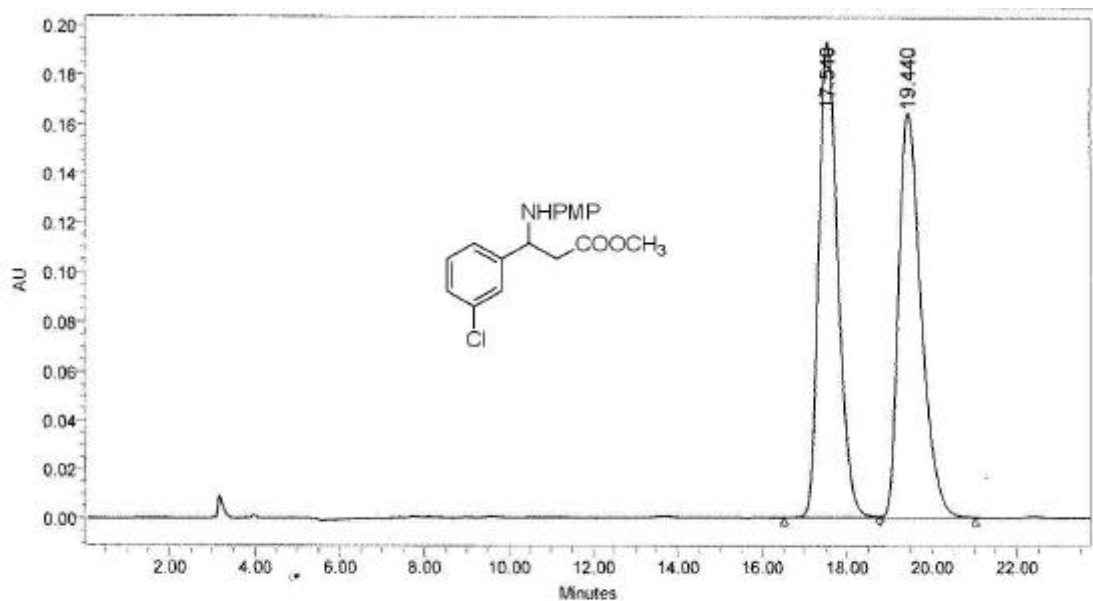
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	25.985	243284	4.05	7694	4.34
2	27.332	5767424	95.95	169655	95.66



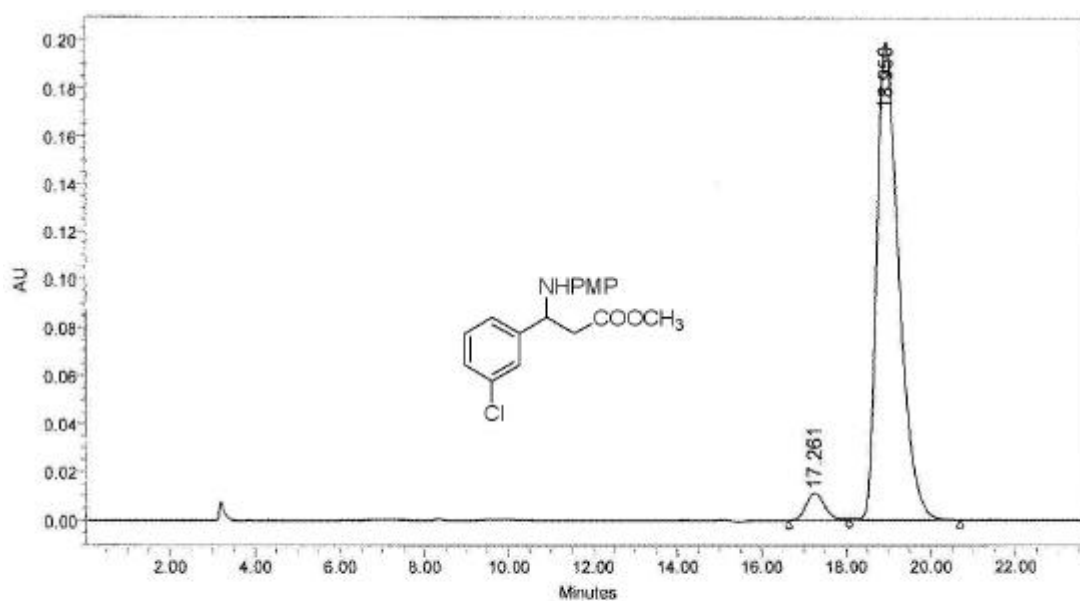
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	23.572	2922825	50.05	75618	56.43
2	26.103	2916685	49.95	58390	43.57



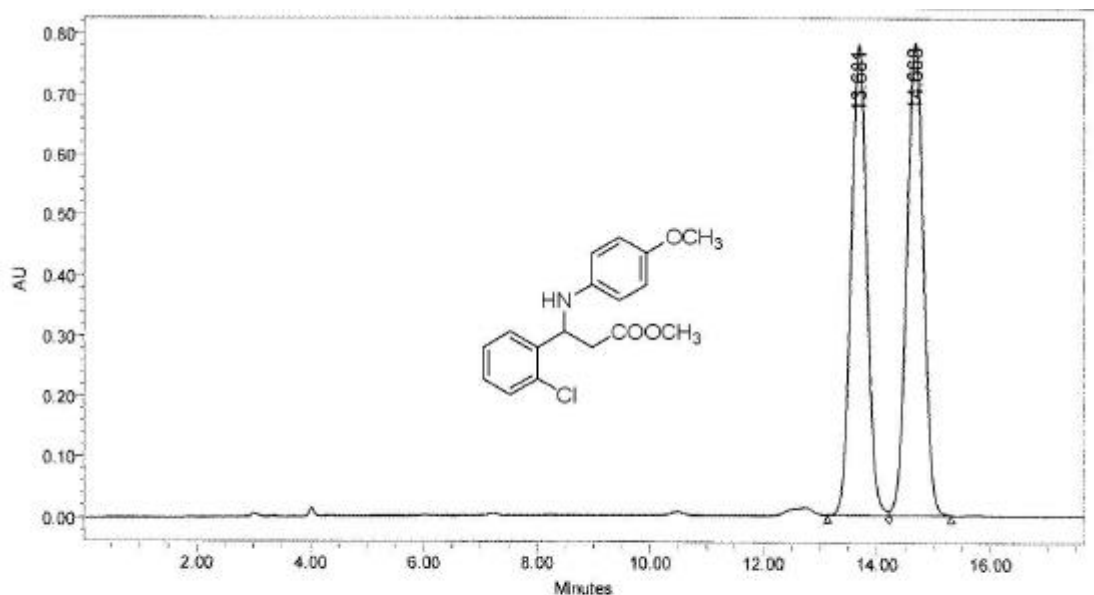
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	23.127	299377	3.94	7622	4.62
2	25.328	7289727	96.06	157494	95.38



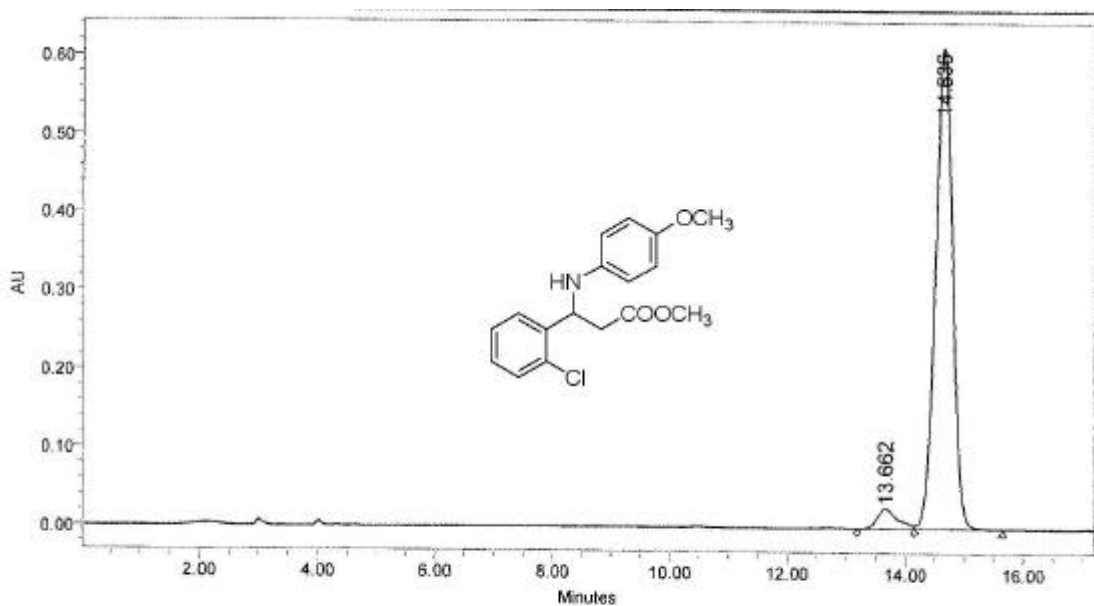
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	17.540	6105994	50.06	193544	54.05
2	19.440	6091847	49.94	164512	45.95



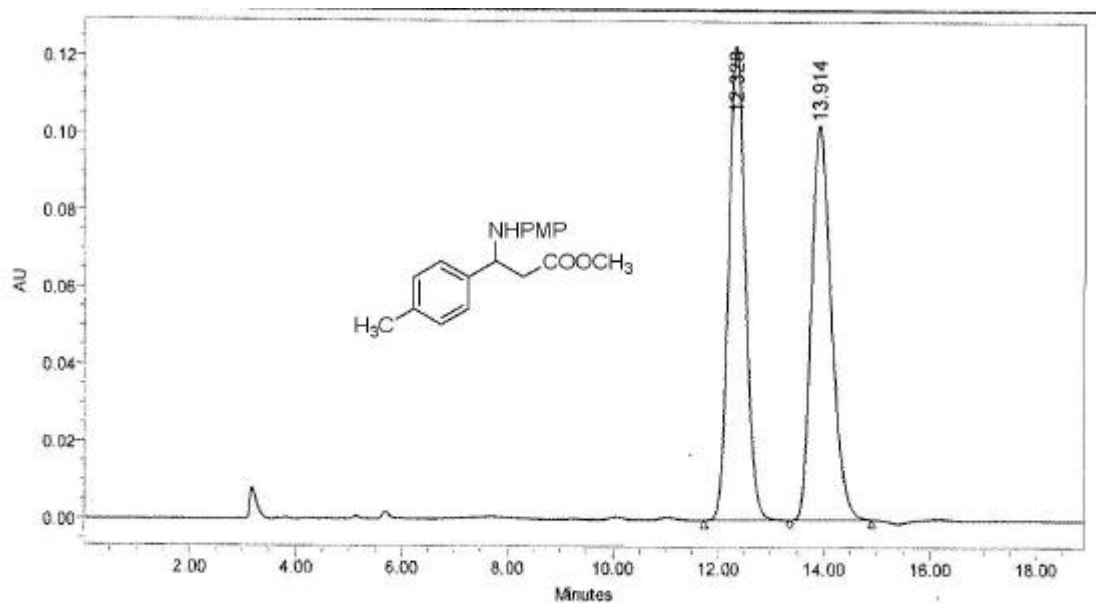
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	17.261	342536	4.50	11148	5.30
2	18.950	7268461	95.50	199281	94.70



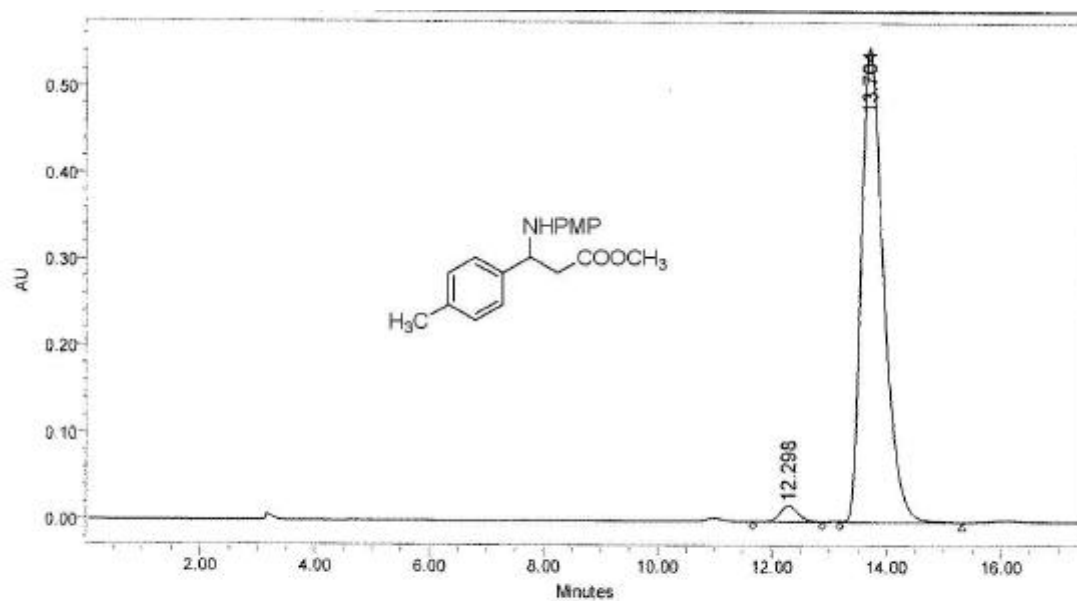
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	13.681	14743441	48.44	776092	49.90
2	14.668	15693476	51.56	779209	50.10



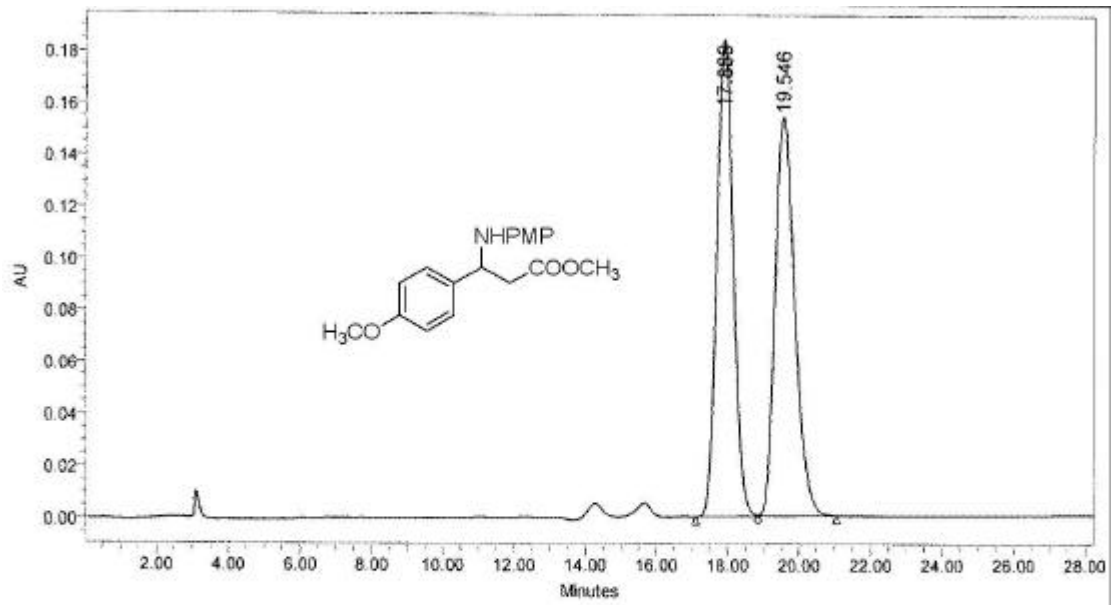
	RT (min)	Area ($\mu V \cdot sec$)	% Area	Height (μV)	% Height
1	13.662	614612	4.77	25956	4.07
2	14.636	12276235	95.23	611842	95.93



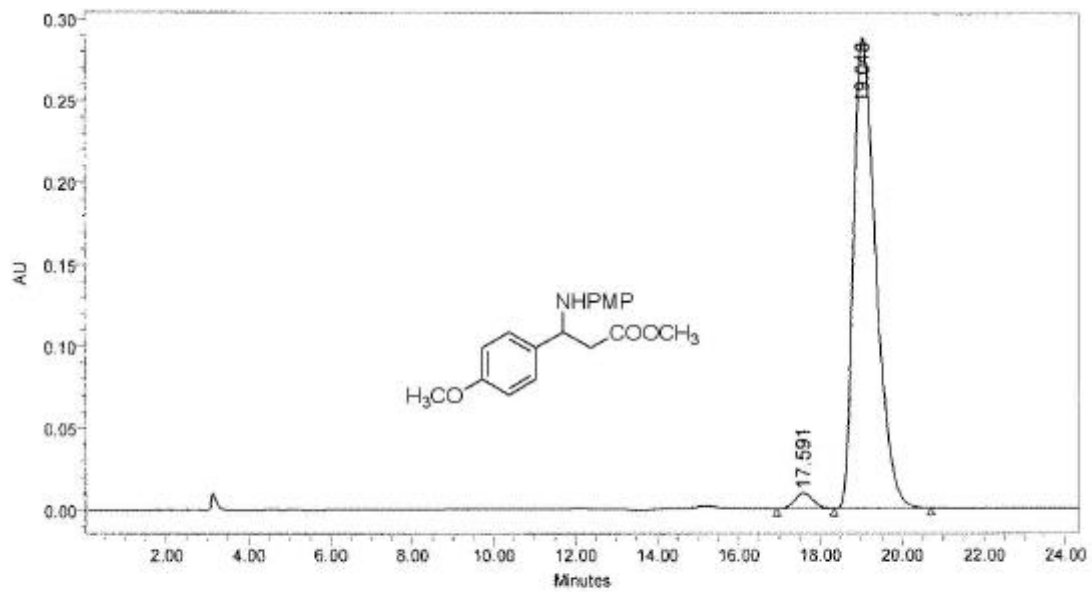
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	12.328	2708435	50.17	123069	54.60
2	13.914	2690376	49.83	102324	45.40



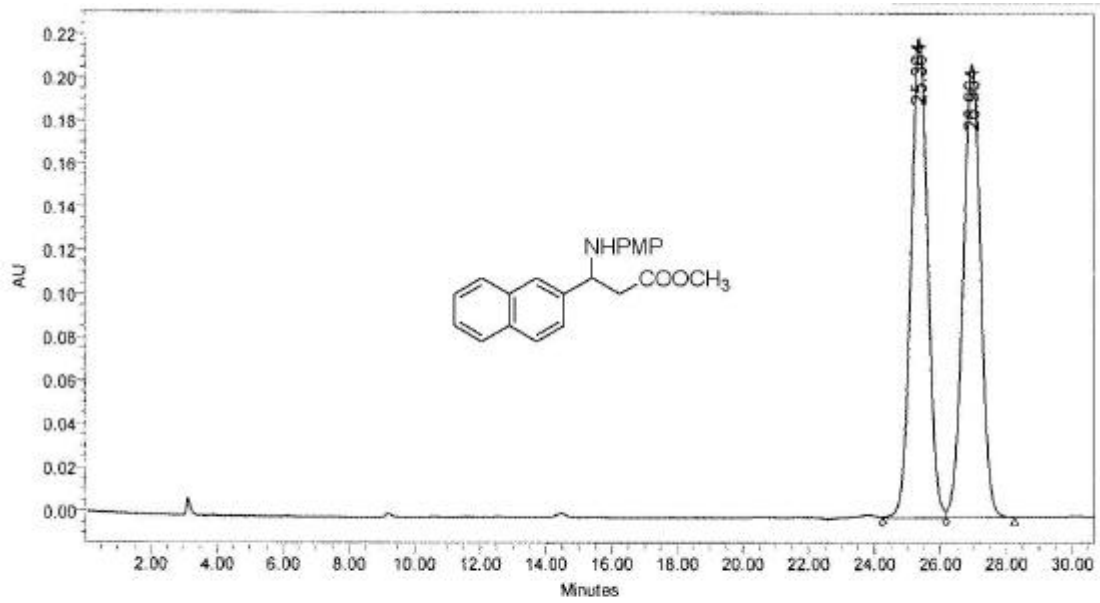
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	12.298	418719	2.75	18859	3.32
2	13.704	14801274	97.25	548742	96.68



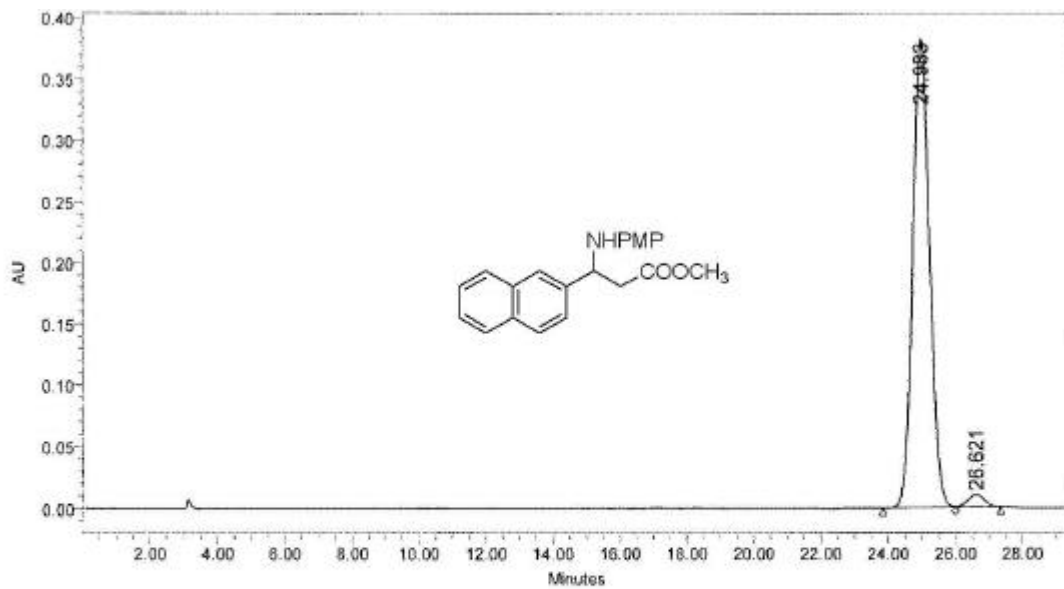
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	17.889	5969818	50.01	184474	54.43
2	19.546	5968515	49.99	154445	45.57



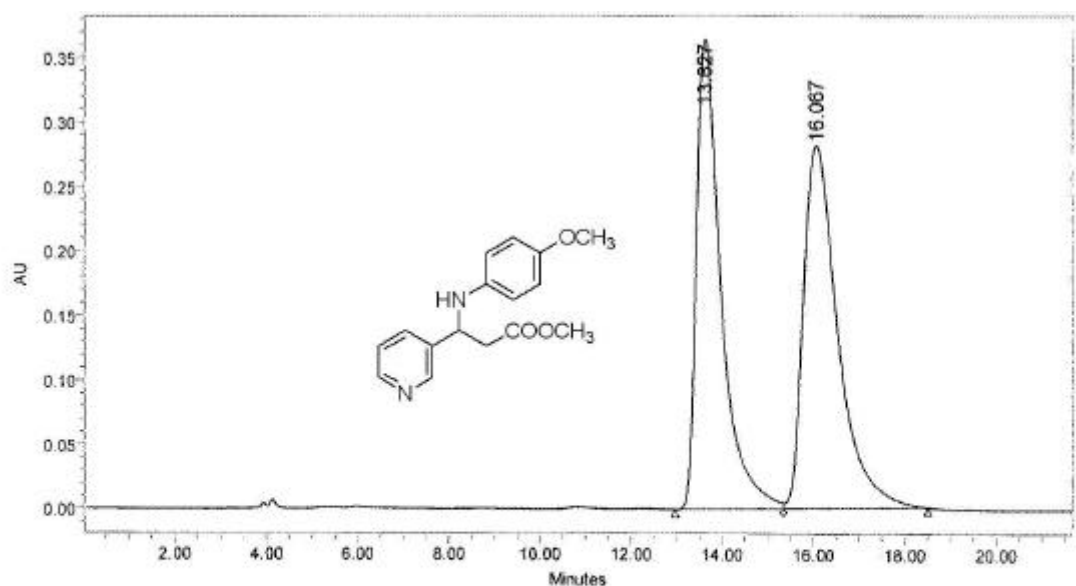
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	17.591	286912	2.55	9389	3.15
2	19.048	10952035	97.45	288617	96.85



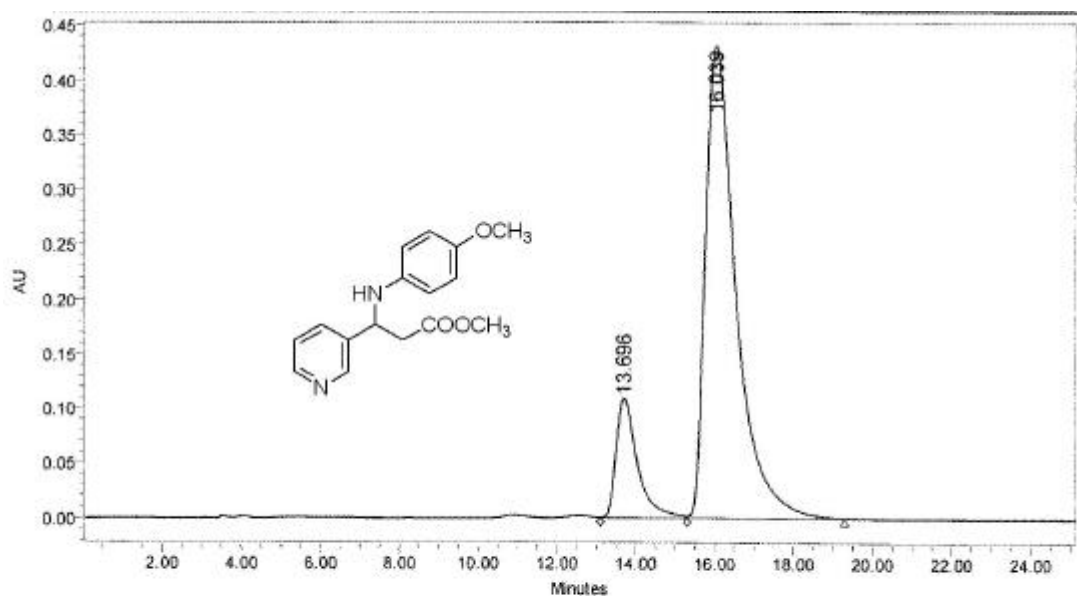
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	25.364	7813669	50.31	222306	51.41
2	26.964	7718866	49.69	210105	48.59



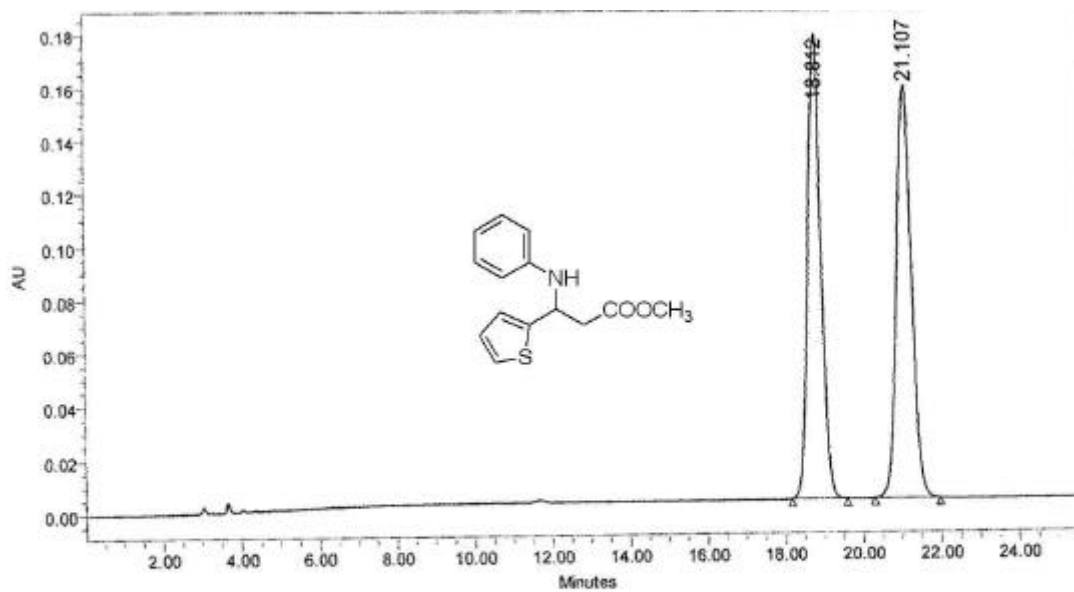
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	24.983	13268707	97.53	383522	97.53
2	26.621	335580	2.47	9711	2.47



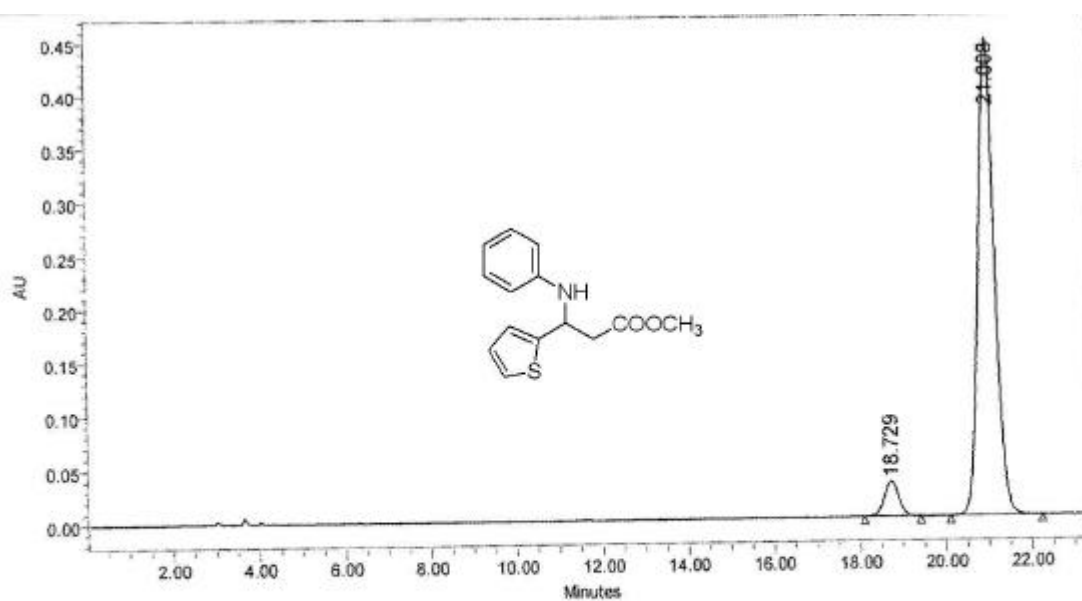
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	13.627	13779894	48.26	364189	56.38
2	16.067	14774186	51.74	281806	43.62



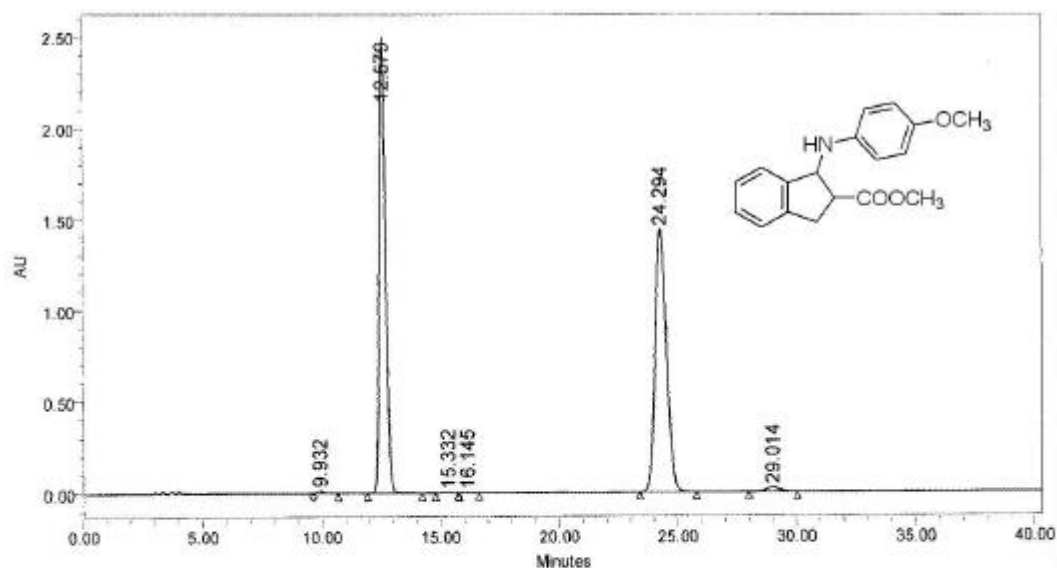
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	13.696	4072706	14.90	108927	20.20
2	16.039	23253643	85.10	430195	79.80



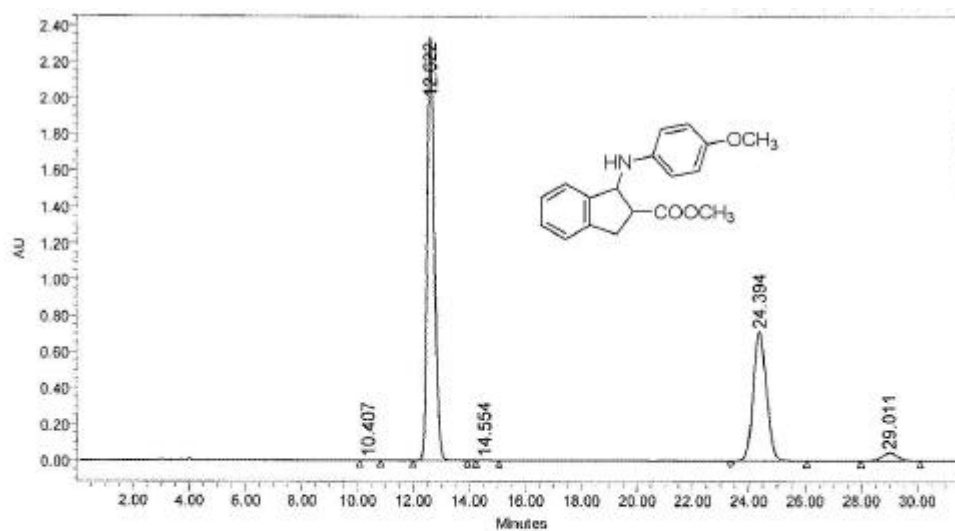
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	18.812	4119622	49.80	175405	52.98
2	21.107	4152883	50.20	155700	47.02



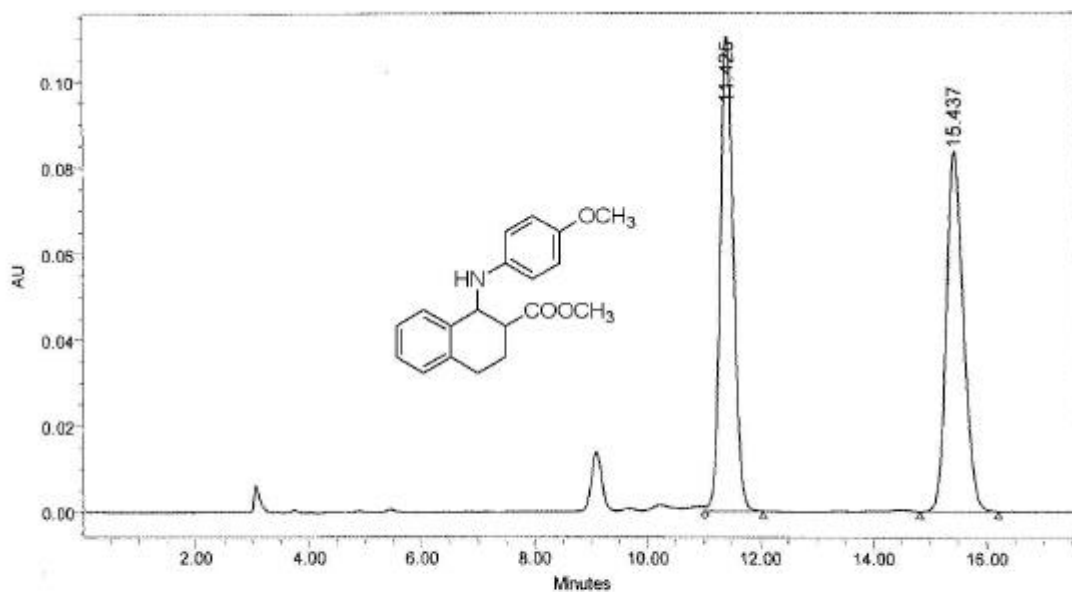
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	18.729	760376	5.96	32672	6.79
2	21.008	11988312	94.04	448393	93.21



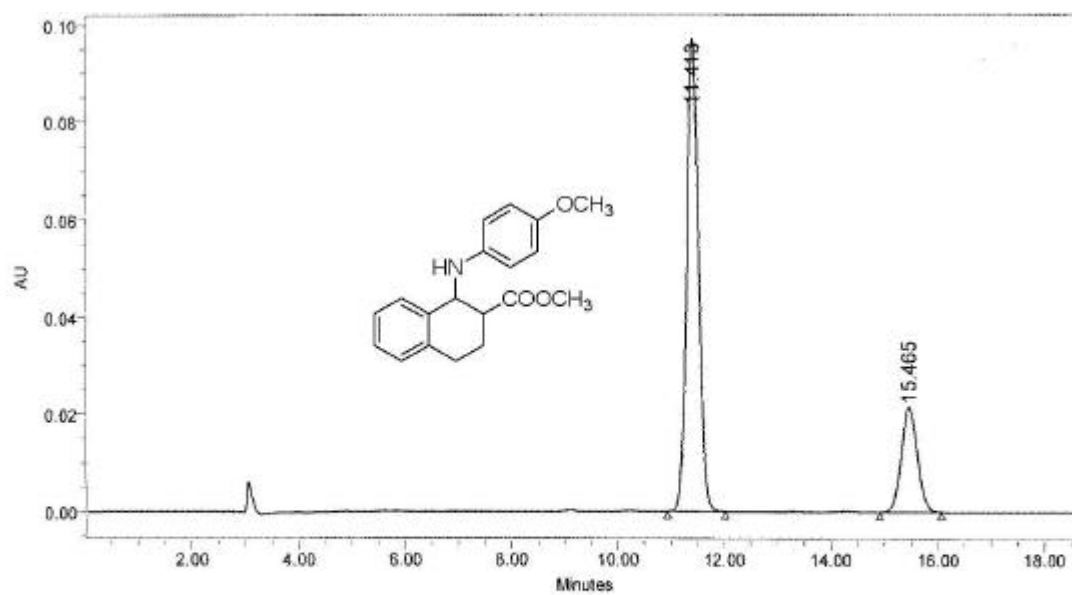
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	9.932	196413	0.21	12078	0.30
2	12.579	46149163	48.56	2496377	62.73
3	15.332	30361	0.03	1196	0.03
4	16.145	25851	0.03	1314	0.03
5	24.294	47705267	50.20	1445023	36.31
6	29.014	928275	0.98	23669	0.59



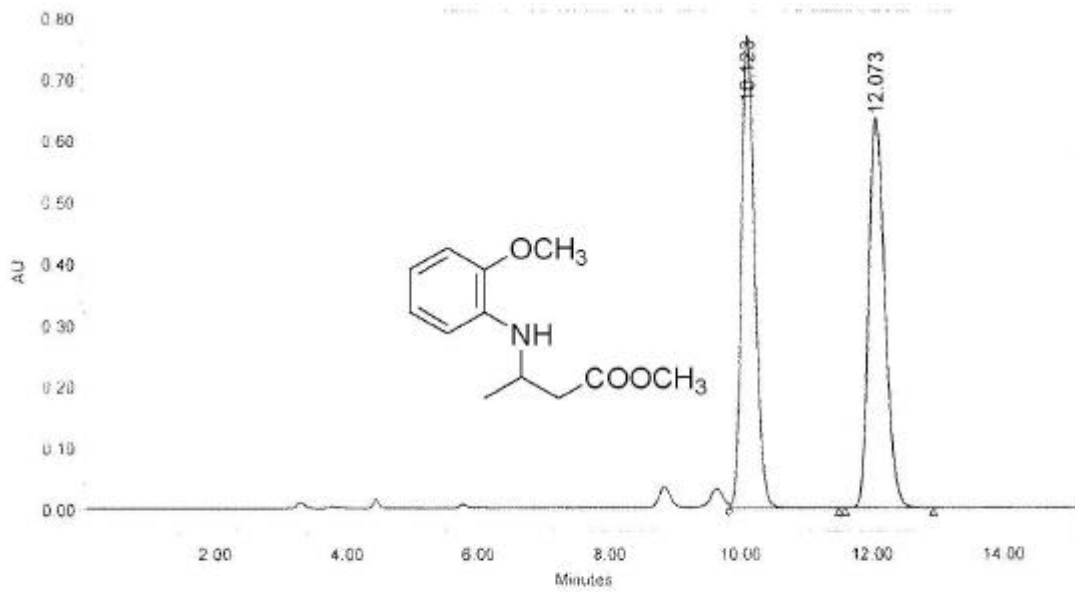
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	10.407	11305	0.02	675	0.02
2	12.622	42037719	62.76	2336270	75.46
3	14.554	46412	0.07	2244	0.07
4	24.394	23190186	34.62	713625	23.05
5	29.011	1691125	2.52	43207	1.40



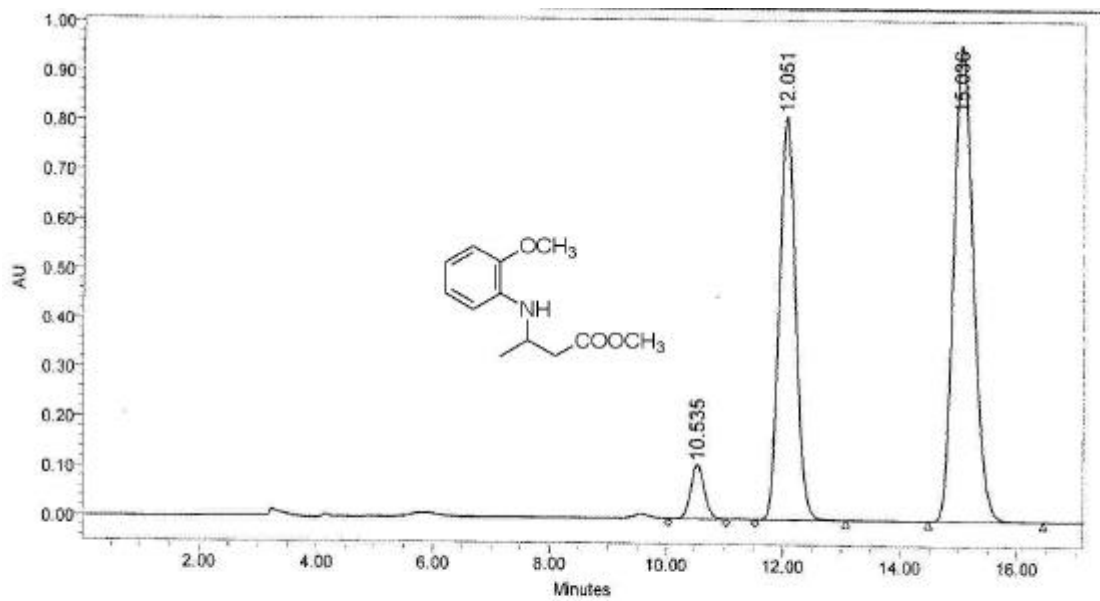
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	11.425	1782808	50.21	110171	56.92
2	15.437	1768049	49.79	83385	43.08



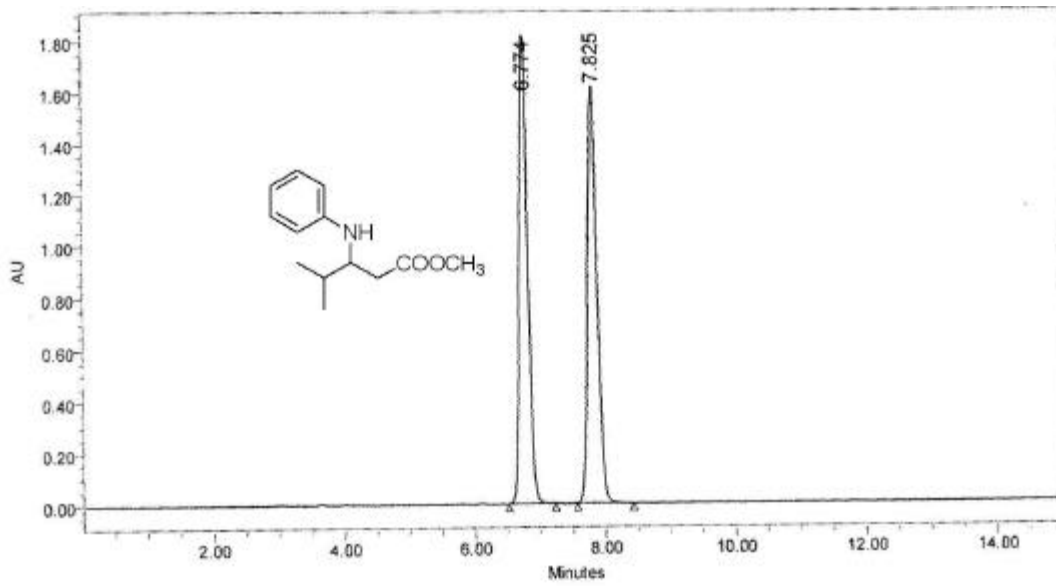
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	11.413	1498255	76.97	97007	81.86
2	15.465	448240	23.03	21497	18.14



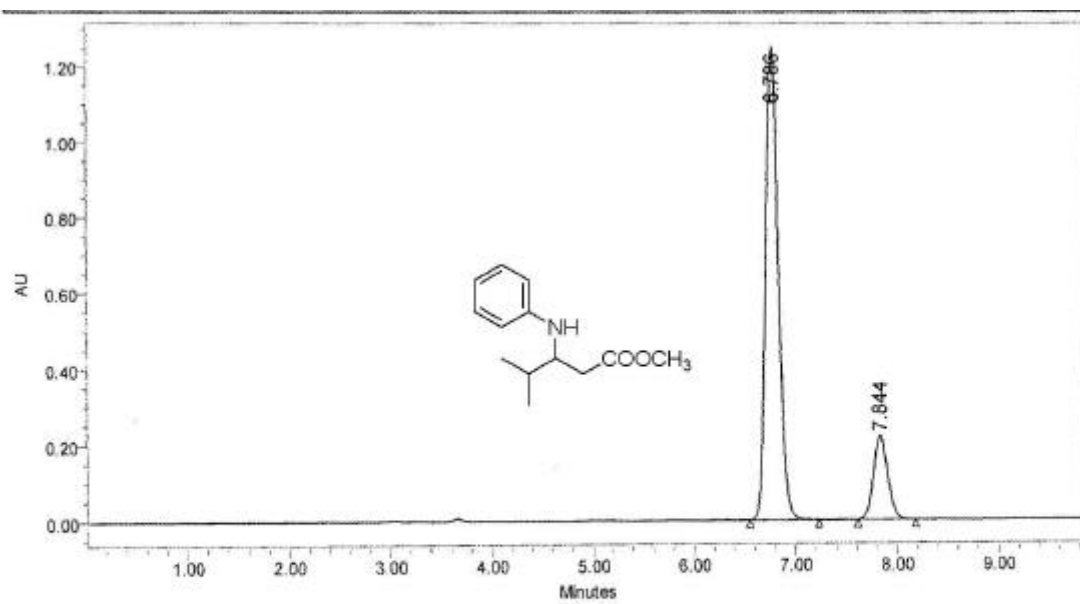
RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	10854693	49.94	773915	54.75
2	10879588	50.06	639663	45.25



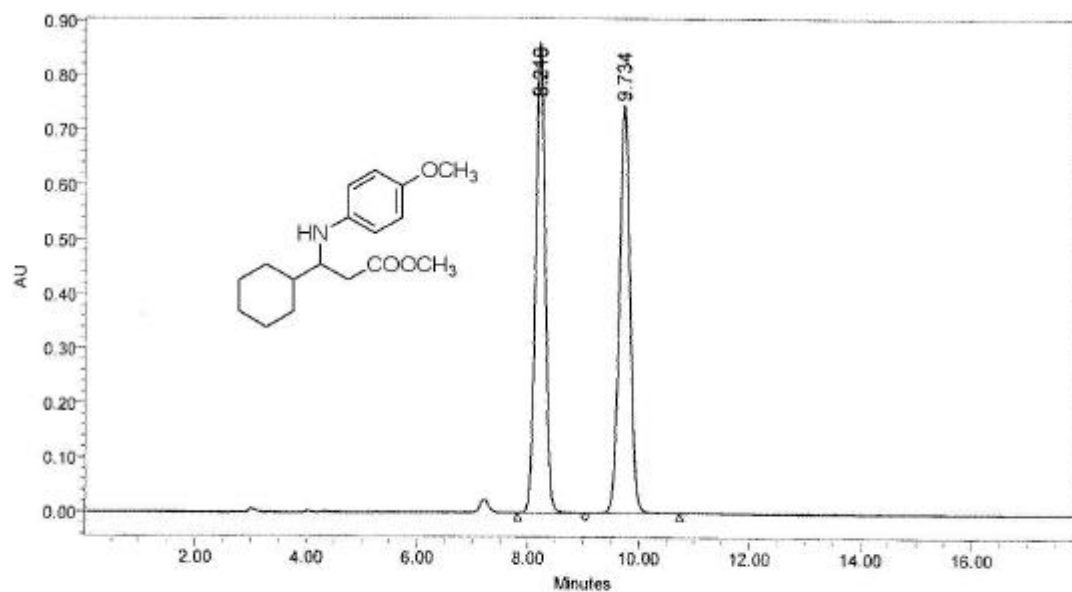
RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	1796030	4.46	109423	5.81
2	15859064	39.40	813477	43.22
3	22594139	56.14	959277	50.97



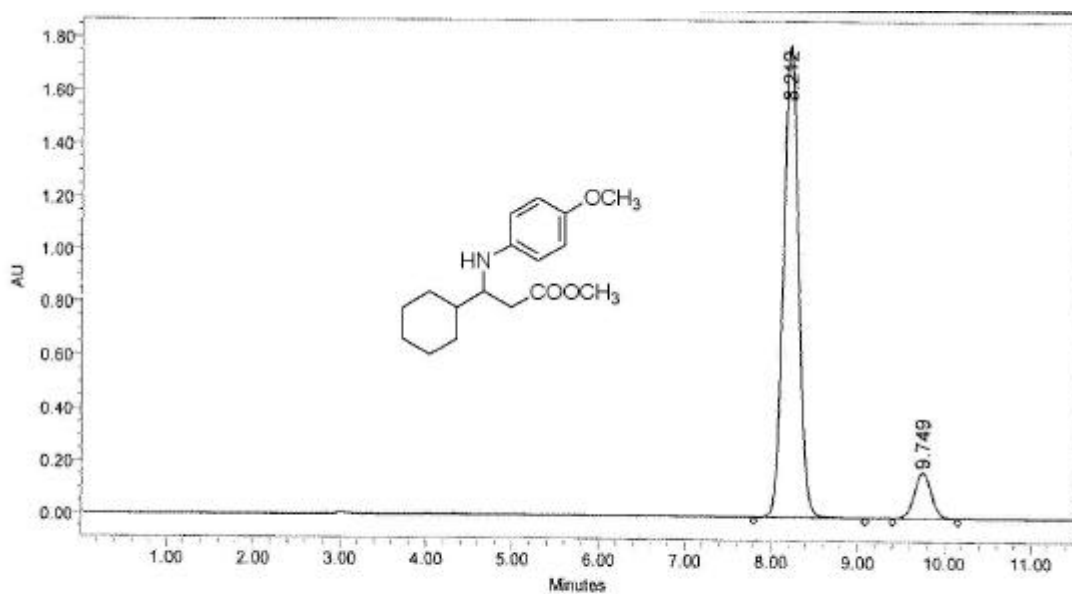
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	6.774	18314505	49.75	1831599	52.89
2	7.825	16475344	50.25	1631382	47.11



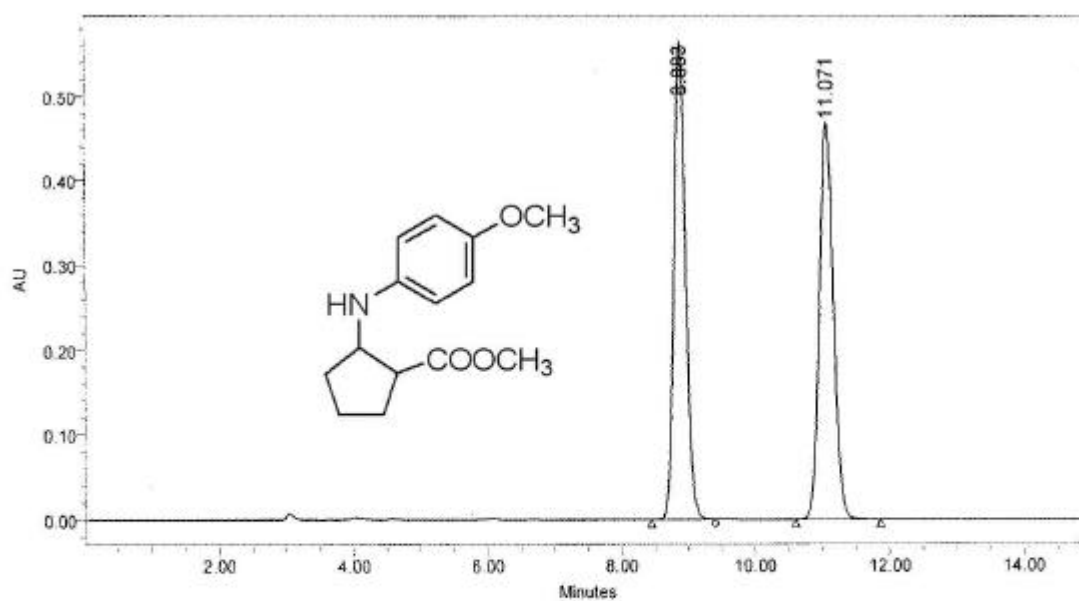
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	6.786	10819182	83.26	1252014	84.86
2	7.844	2175626	16.74	223340	15.14



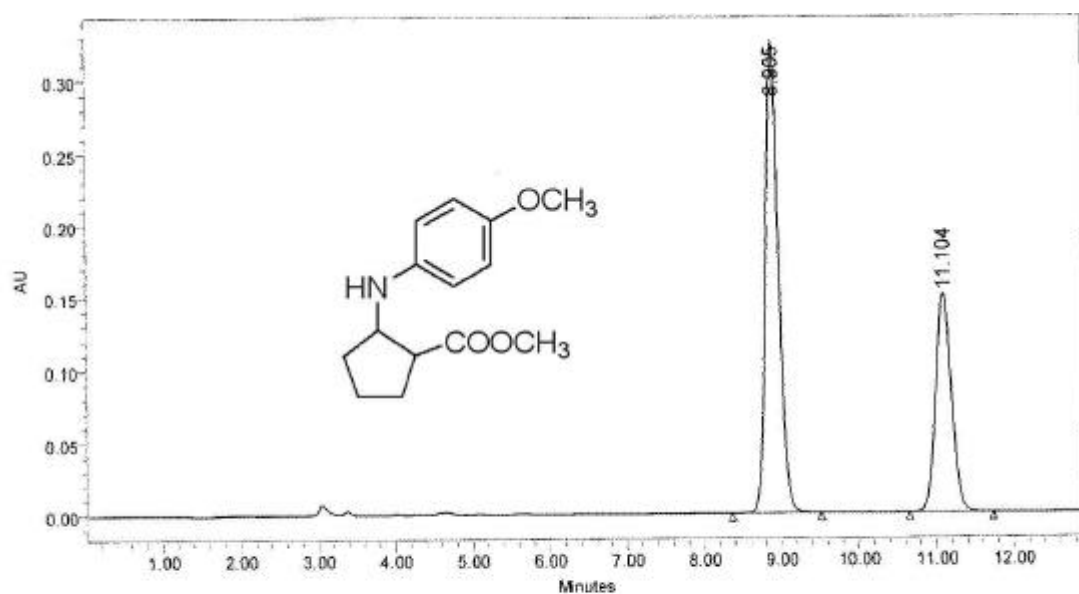
RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1 8.210	10118646	49.95	863528	53.68
2 9.734	10138910	50.05	745134	46.32



RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1 8.212	21556482	90.22	1781636	91.13
2 9.749	2337521	9.78	173308	8.87



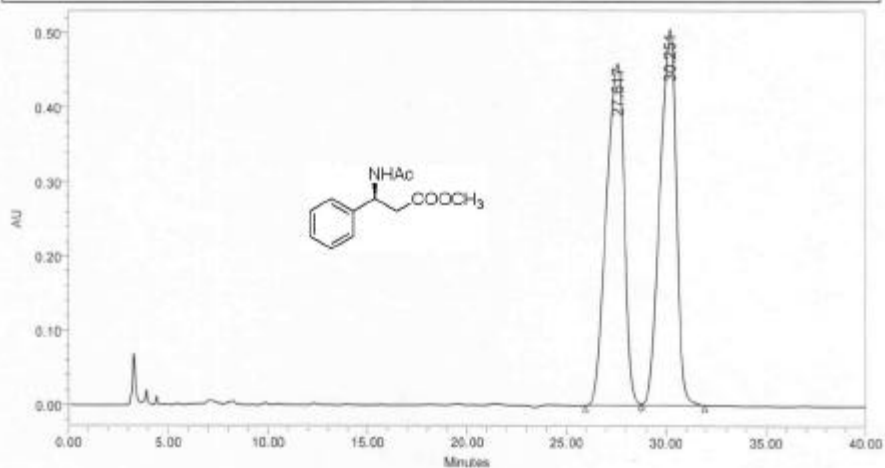
	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	8.883	6707006	49.97	566380	54.67
2	11.071	6714715	50.03	469554	45.33



	RT (min)	Area ($\mu\text{V}\cdot\text{sec}$)	% Area	Height (μV)	% Height
1	8.905	3839693	64.16	327487	68.38
2	11.104	2145098	35.84	151459	31.62

SAMPLE INFORMATION

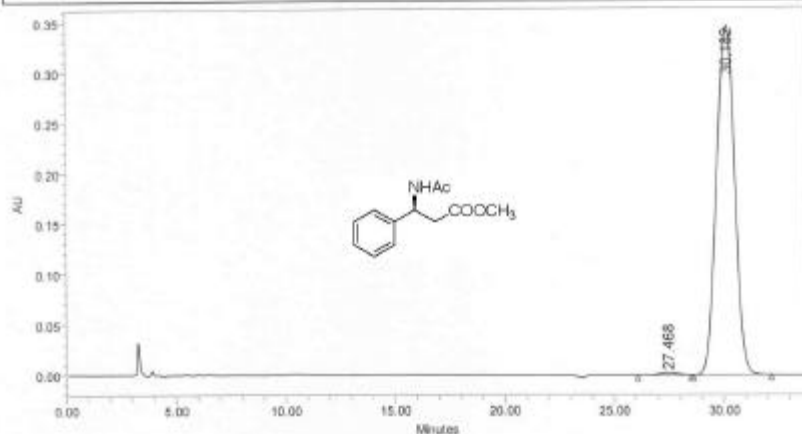
Sample Name: zhj-0	Acquired By: System
Sample Type: Unknown	Date Acquired: 5/4/08 4:15:15 PM
Vial: 1	Acq. Method: 100A220
Injection #: 3	Date Processed: 5/4/08 5:03:40 PM
Injection Volume: 20.00 ul	Channel Name: 2487Channel 1
Run Time: 40.00 Minutes	Sample Set Name:



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	27.617	28762887	49.81	457760	47.60
2	30.251	28998060	50.19	503990	52.40

SAMPLE INFORMATION

Sample Name: zhj	Acquired By: System
Sample Type: Unknown	Date Acquired: 5/4/08 5:06:08 PM
Vial: 1	Acq. Method: 100A220
Injection #: 4	Date Processed: 5/4/08 5:41:05 PM
Injection Volume: 20.00 ul	Channel Name: 2487Channel 1
Run Time: 40.00 Minutes	Sample Set Name:



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	27.468	141976	0.71	2515	0.72
2	30.182	19817701	99.29	345104	99.28