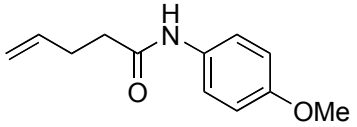
Eur. J. Org. Chem. **2007** · © WILEY-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2007 · ISSN 1434–193X

SUPPORTING INFORMATION

Title: On the Phenyliodine(III)-Bis(trifluoroacetate)-Mediated Olefin Amidohydroxylation Reaction
Author(s): Imanol Tellitu,* Andrea Urrejola, Sonia Serna, Isabel Moreno, M. Teresa Herrero, Esther Domínguez,* Raul SanMartin, Arkaitz Correa
Ref. No.: O200600782

General Methods and Materials. All reagents were purchased and used as received. Melting points were measured using open glass capillaries and are uncorrected. Infrared spectra were recorded as KBr plates or as thin films and peaks are reported in cm^{-1}. Only representative absorptions are given. NMR spectra were recorded on 250 and 500 instruments (250 MHz for ^{1}H and 62.83 MHz for ^{13}C) at 20 ºC. Chemical shifts (δ) were measured in ppm relative to chloroform (δ=7.26 for ^{1}H or 77.00 for ^{13}C) as internal standard. Coupling constants, *J*, are reported in hertz. DEPT experiments were used to assist with the assignation of the signals. HRMS spectra were recorded at the University of the Basque Country (UPV/EHU) and University of Vigo. A Bruker ESP300 spectrometer operating at X band and equipped with standard Oxford low temperature devices was used to record the EPR solution spectra of the amidyl radical **B**. The magnetic field was calibrated by a NMR probe and the frequency inside the cavity was determined with a Hewlett-Packard 5352B microwave frequency counter.

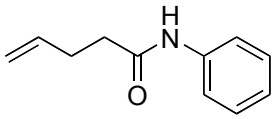
Synthesis of amides 5a–g. Synthesis of *N*-(4-methoxyphenyl)-4-pentenamide (5a). Typical procedure A.



Typical procedure: $(COCl)_2$, (1.0 mL, 12 mmol) was added dropwise to a stirred solution of 4-pentenoic acid (**4b**) (1 g, 10 mmol) in CH_2Cl_2 (10 mL). The solution was magnetically stirred at room temperature for 2 h. Then, the solvent was eliminated under reduced pressure, the so–obtained residue was dissolved in CH_2Cl_2 (15 mL), and a solution of *p*-anisidine (1.5 g, 12 mmol) in 5 mL of the same solvent was added. After cooling the reaction mixture at 0 °C, pyridine (2 mL, 24 mmol) was added dropwise. The reaction was stirred overnight. Then, the crude was washed with saturated aqueous

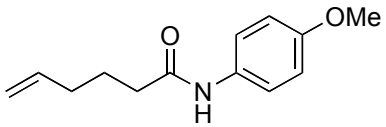
$CuSO_4$ (4x10 mL), saturated aqueous $NaHCO_3$ (2x10 mL), and HCl 5% (1x10 mL). The organic phase was dried over anhydrous Na_2SO_4 and evaporation of the solvent gave an oil which was purified by flash chromatography using hexanes/EtOAc (6:4) as eluent providing amide **5a** as a white solid in 87% yield (1.78 g): mp 86–88 ºC (Et_2O). ^1H NMR ($CDCl_3$) δ 2.37–2.49 (m, 4H), 3.77 (s, 3H), 5.01–5.13 (m, 2H), 5.78–5.94 (m, 1H), 6.83 (d, *J*=9.1, 2H), 7.39 (d, *J*=9.1, 2H), 7.81 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 29.5, 36.4, 55.3, 113.9, 115.6, 121.9, 130.9, 136.8, 156.2, 170.8. IR (KBr) 3425, 1649 cm^{-1}. MS (EI) *m/z* (%) 205 (M^+, 28), 123 (100), 108 (68). HRMS calcd for $C_{12}H_{15}NO_2$ 205.1103, found 205.1105.

***N*-Phenyl-4-pentenamide (5b).**



According to the typical procedure A, amide **5b** was obtained from 4-pentenoic acid (**4b**) and aniline in 82% yield as a white solid after purification by crystallization from Et_2O: mp 89–90 ºC (Et_2O). Lit.[1] 90–91 ºC (Et_2O). All spectroscopic data were in agreement with the literature.[1]

***N*-(4-Methoxyphenyl)-5-hexenamide (5c).**



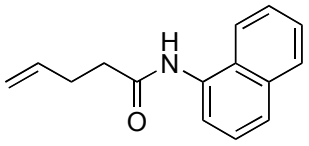
According to the typical procedure A, amide **5c** was obtained from 5-hexenoic acid (**4c**) and *p*-anisidine in 98% yield as a white solid after purification by column chromatography (hexanes/EtOAc, 7:3) followed by crystallization from Et_2O: mp 61–63 ºC (Et_2O). ^1H NMR ($CDCl_3$) δ 1.71–1.82 (m, 2H), 2.04–2.12 (m, 2H), 2.29 (t, *J*=7.5,

---

[1] D. Seebach, M. Pohmakotr, *Tetrahedron* **1981**, *37*, 4047–4058.

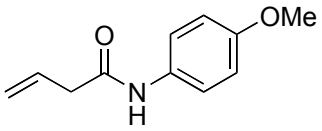
2H), 3.74 (s, 3H), 4.95–5.04 (m, 2H), 5.67–5.84 (m, 1H), 6.79 (d, *J*=8.9, 2H), 7.38 (d, *J*=8.9, 2H), 7.93 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 24.6, 32.9, 36.5, 55.2, 113.7, 115.1, 121.9, 137.7, 131.1, 156.1, 171.6. IR (KBr) 3311, 1650 cm^{-1}. MS (EI) *m/z* (%) 219 (M^+, 24), 165 (23), 123 (100), 108 (64). HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1272.

***N*-(1-Naphthyl)-4-pentenamide (5d).**



According to the typical procedure A, amide **5d** was obtained from carboxylic acid **4b** in 80% yield as a white solid after purification by column chromatography (hexanes/EtOAc, 6:4) followed by crystallization from Et_2O: mp 108–110 ºC (Et_2O). ^{1}H NMR ($CDCl_3$) δ 2.55–2.59 (m, 4H), 5.09–5.20 (m, 2H), 5.91–5.97 (m, 1H), 7.44–7.50 (m, 3H), 7.63 (br s, 1H), 7.66–7.69 (m, 1H), 7.81–7.87 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 29.5, 36.2, 115.8, 121.1, 121.5, 125.4, 125.8, 125.9, 127.5, 128.4, 132.2, 133.9, 136.8, 171.5. IR (KBr) 3252, 1652 cm^{-1}. MS (EI) *m/z* (%) 225 (M^+, 20), 143 (100), 115 (15), 55 (10). HRMS calcd for $C_{15}H_{15}NO$ 225.1157, found 225.1154.

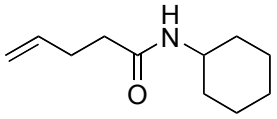
***N*-(4-Methoxyphenyl)-3-butenamide (5e).**



According to the typical procedure A, amide **5e** was obtained from vinylacetic acid and *p*-anisidine in 72% yield as a white solid after purification by column chromatography (hexanes/EtOAc, 6:4) followed by crystallization from Et_2O: mp 76–77 ºC (Et_2O). ^{1}H NMR ($CDCl_3$) δ 3.08 (d, *J*=6.7, 2H), 3.71 (s, 3H), 5.15–5.21 (m, 2H), 5.87–6.04 (m, 1H), 6.76 (d, *J*= 8.9, 2H), 7.37 (d, *J*=8.9, 2H), 8.39 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 41.9, 55.2, 113.7, 119.1, 122.0, 131.1, 130.9, 156.1, 169.4. IR (KBr) 3295, 1654 cm^{-1}. MS

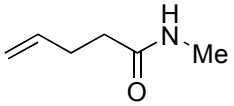
(EI) *m/z* (%) 191 (M^+, 73), 123 (100), 108 (93). HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0949.

_N_-Cyclohexyl-4-pentenamide (5f).



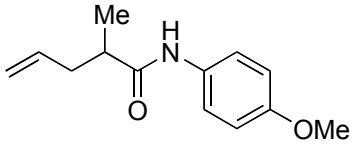
According to the typical procedure A, amide **5f** was obtained from 4-pentenoic acid (**4b**) and cyclohexylamine in 78% yield as a white solid after crystallization from hexanes: mp 59–60 ºC (hexanes). Lit.[2] 67–69 ºC. All spectroscopic data were in agreement with the literature.[2]

_N_-Methyl-4-pentenamide (5g).



According to the typical procedure A, amide **5g** was obtained from 4-pentenoic acid (**4b**) and methylamine in 62% yield as a colourless oil. All spectroscopic data were in agreement with the literature.[3]

Synthesis of amides 8a–e,h,k. Synthesis of _N_-(4-methoxyphenyl)-2-methyl-4-pentenamide (8a). Typical procedure B.



A solution of EDC·HCl (2.53 g, 13.2 mmol) and HOBt (1.63 g, 12.1 mmol) in CH_2Cl_2 (25 mL) was added to a solution of commercially available 2-methyl-4-pentenoic acid

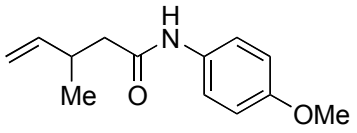
---

[2] J. J. J. de Boer, W. N. Speckamp, *Tetrahedron Lett.* **1975**, *46*, 4039–4042.

[3] M. Buswell, I. Fleming, U. Ghosh, S. Mack, M. Russell, B. P. Clark, *Org. Biomol. Chem*. **2004**, *2*, 3006–3017.

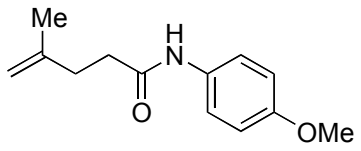
(**7a**) (1.0 g, 8.8 mmol) in the same solvent (11 mL). Then, a solution of *p*-anisidine (1.62 g, 13.2 mmol) in CH_2Cl_2 (11 mL) was added. The mixture was cooled at 0 ^oC and Et_3N (1.8 mL, 13.2 mmol) was added dropwise. After stirring for 2 h, temperature was raised to room temperature, and stirring was continued until the conversion was complete (12 h). Then, H_2O was added, and the aqueous phase was extracted with CH_2Cl_2 (3x15 mL). The combined organic extracts were washed with HCl 1M and with saturated $NaHCO_3$ (aq), dried over Na_2SO_4 and the solvent was evaporated at reduced pressure. The resulting solid was crystallized from hexanes to afford amide **8a** as a white solid (1.54 g, 80%): mp 65–68 ºC (hexanes). ^1H NMR ($CDCl_3$) δ 1.22 (d, *J*=6.7, 3H), 2.16–2.40 (m, 1H), 2.43–2.53 (m, 2H), 3.77 (s, 3H), 5.03–5.13 (m, 2H), 5.72–5.85 (m, 1H), 6.83 (d, *J*=9.1, 2H), 7.30 (br s, 1H), 7.40 (d, *J*=9.1, 2H). ^{13}C NMR ($CDCl_3$) δ 17.3, 38.3, 41.4, 55.2, 113.8, 116.8, 122.0, 131.1, 135.6, 156.1, 174.5. IR (KBr) 3271, 1640 cm^{-1}. MS (EI) *m*/*z* (%) 219 (M^+, 43), 123 (100), 108 (68). HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1273.

***N*-(4-Methoxyphenyl)-3-methyl-4-pentenamide (8b).**



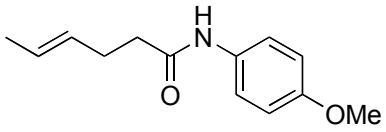
According to the typical procedure B, amide **8b** was obtained from commercially available 3-methyl-4-pentenoic acid (**7b**) and *p*-anisidine in 87% yield: mp 57–60 ºC (hexanes). ^1H NMR ($CDCl_3$) δ 1.07 (d, *J*=6.7, 3H), 2.23–2.39 (m, 2H), 2.70–2.81 (m, 1H), 4.68 (s, 3H), 4.96–5.09 (m, 2H), 5.73–5.87 (m, 1H), 6.80 (d, *J*=8.9, 2H), 7.38 (d, *J*=8.9, 2H), 7.74 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 19.6, 34.8, 44.3, 55.4, 113.9, 122.0, 131.0, 142.6, 156.0, 170.2. IR (KBr) 3280, 1642 cm^{-1}. MS (EI) *m*/*z* (%) 219 (M^+, 17), 123 (100), 108 (60). HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1272.

***N*-(4-Methoxyphenyl)-4-methyl-4-pentenamide (8c).**



According to the typical procedure B, amide **8c** was obtained from 4-methyl-4-pentenoic acid[4] **(7c)**. The resulting residue was purified by crystallization from hexanes to afford amide **8c** as a white solid (92%): mp 83–84 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 3H), 2.45–2.46 (m, 4H), 3.78 (s, 3H), 4.77 (d, *J*=9.5, 2H), 6.83 (d, *J*=8.7, 2H), 7.37–7.40 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 22.4, 33.1, 35.4, 55.4, 110.5, 113.9, 121.9, 131.0, 144.4, 156.2, 171.0; IR 1654 cm^{-1}. MS (EI) *m*/*z* (%) 219 (M^+, 43), 123 (100), 108 (68). HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1265.

***N*-(4-Methoxyphenyl)-4-hexenamide (8d).**

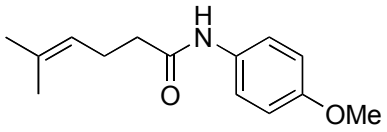


According to the typical procedure B, amide **8d** was obtained from commercially available 4-hexenoic acid (**7d**). The resulting residue was purified by crystallization from hexanes to afford amide **8d** as a grey solid (85%): mp 112–113 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 1.65 (d, *J*=5.8, 3H), 2.35–2.40 (m, 4H), 3.77 (s, 3H), 5.44–5.57 (m, 2H), 6.84 (d, *J*=8.7, 2H), 7.38 (d, *J*=8.7, 2H), 7.49 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 17.9, 28.5, 37.3, 55.4, 114.0, 121.8, 126.6, 129.4, 131.0, 156.2, 170.8; IR 1649 cm^{-1}. MS (EI) *m*/*z* (%) 219 (M^+, 17), 123 (100), 108 (65). HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1294.

***N*-(4-Methoxyphenyl)-5-methyl-4-hexenamide (8e).**

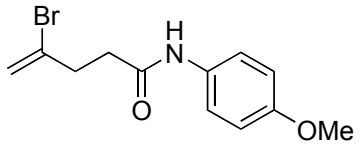
---

[4] H. Hoberg, Y. Peres, C. Krueger, Y. H. Tsay, *Angew. Chem., Int. Ed.* **1987**, *99*, 799–800.



According to the typical procedure B, amide **8e** was obtained from 5-methyl-4-hexenoic acid (**7e**).[5] The resulting residue was purified by crystallization from hexanes to afford amide **8e** as a purple solid (90%): mp 103–104 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 3H), 1.68 (s, 3H), 2.27–2.45 (m, 4H), 3.76 (s, 3H), 5.11–5.14 (m, 1H), 6.80 (d, *J*=9.1, 2H), 7.39 (d, *J*=9.1, 2H), 7.33 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 17.7, 24.2, 25.7, 37.3, 55.3, 113.9, 121.8, 122.6, 131.2, 133.3 156.2, 171.2. IR 1643 cm^{-1}. MS (EI) *m*/*z* (%) 233 (M^+, 15), 123 (100), 108 (52). HRMS calcd for $C_{14}H_{19}NO_2$ 233.1416, found 233.1430.

4-Bromo-*N*-(4-methoxyphenyl)-4-pentenamide (8h).



According to the typical procedure B, amide **8h** was obtained from 4-bromo-4-pentenoic acid (**7h**).[6] The resulting residue was purified by crystallization from hexanes to afford amide **8h** as a white solid (25%): mp 98–99 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.55 (t, *J*=7.4, 2H), 2.79 (t, *J*=7.4, 2H), 3.74 (s, 3H), 5.40 (s, 1H), 5.60 (s, 1H), 6.78 (d, *J*=8.7, 2H), 7.35 (d, *J*=8.7, 2H), 8.11 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 35.5, 37.1, 55.3, 113.9, 117.8 122.2, 130.7, 132.4, 156.3, 169.7. IR 1637 cm^{-1}. MS (EI) *m*/*z* (%) 285 (M^+, 4), 204 (100), 123 (71), 108 (84). HRMS calcd for $C_{12}H_{14}NO_2Br$ 283.0208, found 283.0256.

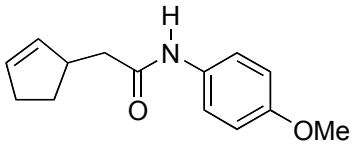
2-(Cyclopent-2-enyl)-*N*-(4-methoxyphenyl)acetamide (8k).[7]

---

[5] D. Cermak, D. Wiemer, K. Lewis, R. Hohl, *Bioorg. Med. Chem.* **2000,** *8*, 2729–2737.

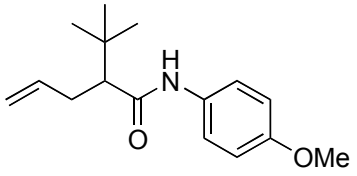
[6] M. Mori, Y. Washioka, T. Urayama, K. Yoshiura, K. Chiba, Y. Ban, *J. Org. Chem.* **1983**, *48*, 4058–4067.

[7] K. C. Nicolaou, P. S. Baran, P. S. Y. –L. Zhong, K. Sugita, *J. Am. Chem. Soc.* **2002**, *124*, 2212–2220.



According to the typical procedure B, amide **8k** was obtained from commercially available 2-(cyclopent-2-enyl)-acetic acid (**7k**). The resulting residue was purified by crystallization from hexanes to afford amide **8k** as a white solid (50%): mp 123–124 ºC (hexanes); Lit.[7] 120-121 ºC (hexanes/AcOEt).

Synthesis of *N*-(4-methoxyphenyl)-2-*tert*-butyl-4-pentenamide (8g).



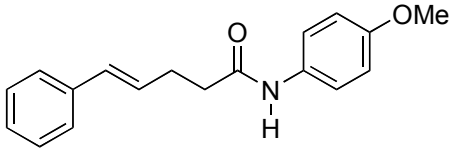
A 2M solution of Me_3Al (2.63 mL, 5.26 mmol) in toluene was slowly added at 0 ^oC to a solution of *p*-anisidine (660 mg, 5.26 mmol) in the same solvent (5.3 mL). After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 2 h. Then, this solution was added to a solution of methyl 2-*tert*-butyl-4-pentenoate[8] (447 mg, 2.63 mmol) in toluene (26 mL). The crude was heated under reflux until conversion was complete. The reaction mixture was cooled to room temperature and carefully quenched with 5% HCl. The organic layer was separated, the aqueous phase was extracted with CH_2Cl_2 (3x 15 mL), the organic extracts were combined, dried over Na_2SO_4, and the solvent was evaporated at reduced pressure. The resulting solid was crystallized from hexanes to afford amide **8g** as a brown solid (364 mg, 53%): mp 132–134 ºC (hexanes). ^{1}HNMR ($CDCl_3$) δ 1.04 (s, 9H), 1.91 (dd, *J*=11.7, 3.0, 1H), 2.21–2.30 (m, 1H), 2.47–2.60 (m, 1H), 3.78 (s, 3H), 4.96–5.13 (m, 2H), 5.70–5.86 (m, 1H), 6.84 (d, *J*=9.1, 2H), 7.00 (br s, 1H NH), 7.38 (d, *J*=9.1, 2H). ^{13}CNMR ($CDCl_3$): δ 27.9, 32.3, 33.3, 55.4, 58.7, 114.0, 116.4, 122.2, 130.8, 136.7, 156.3, 172.4.

---

[8] D.J. Cannes, J. A. Levine, H.–F. Lu, D. F. Covey, *Synth. Comun*. **1990**, *20*, 2065–2073.

IR (KBr): 3287, 1646. MS (EI) *m*/*z* (%) 261 (M^+, 7), 123 (48), 108 (100). HRMS calcd for $C_{16}H_{23}NO_2$ 261.1730, found 261.1729.

Typical procedure for the synthesis of amides 8i–j. Synthesis of *N*-(4-methoxyphenyl)-4-phenyl-4-pentenamide (8i).



The synthesis of this amide started with the condensation of Meldrum's acid and commercially available *trans*-cinnamaldehyde,[9] followed by reduction of the adduct with $NaBH_4$,[10] and transformation into the corresponding carboxylic acid **7i**[4] as previously described.[11] Without further purification carboxylic acid **7i** was transformed into amide **8i** according to typical procedure B. The resulting residue was purified by crystallization from hexanes to afford amide **8i** as a white solid (24% overall yield): mp 222–223 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.46–2.67 (m, 4H), 3.77 (s, 3H), 6.18–6.30 (m, 1H), 6.47 (d, *J*=15.9, 1H), 6.82 (d, *J*=9.1, 2H), 7.20–7.42 (m, 7H). ^{13}C NMR ($CDCl_3$) δ 28.9, 37.0, 55.4 114.0, 121.9, 122.2, 126.0, 127.2, 128.5, 130.8, 131.2. 137.2, 156.3, 170.4. IR 1666 cm^{-1}. MS (EI) *m*/*z* (%) 281 (M^+, 14), 280 (91), 123 (100), 108 (98). HRMS calcd for $C_{18}H_{19}NO_2$ 281.1416, found 281.1414.

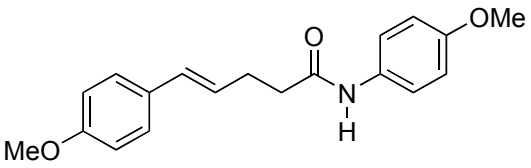
***N*,5-*Bis*-(methoxyphenyl)-4-pentenamide (8j).**

---

[9] F. Bigi, S. Carloni, L. Ferrari, R. Maggi, A. Mazzacani, G. Sartori, *Tetrahedron Lett.* **2001**, *42*, 5203–5205.

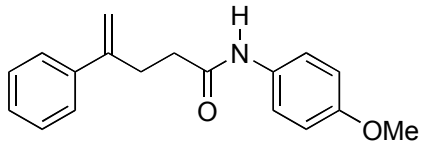
[10] A. D. Wright, M. L. Haslego, F. X. Smith, *Tetrahedron Lett.* **1979**, *25*, 2325–2326.

[11] T. F. Knöpfel, E. M. Carreira, *J. Am. Chem. Soc.* **2003**, *125*, 6054–6055.



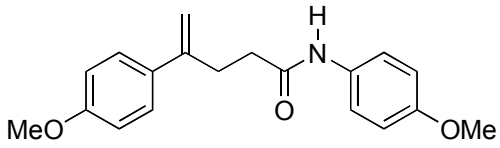
Analogously to amide **8i**, amide **8j** was obtained starting from *trans*-(4'-methoxy)cinnamaldehyde as a white solid (33% overall yield) after crystallization from hexanes: mp 173–178 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.54–2.63 (m, 4H), 3.78 (s, 3H), 3.80 (s, 3H), 6.05–6.17 (m, 1H), 6.43 (d, *J*=15.1, 1H), 6.84 (d, *J*=15.1, 4H), 7.13 (s, 1H), 7.29 (d, *J*=8.7, 2H), 7.38 (d, *J*=8.7, 2H). ^{13}C NMR ($CDCl_3$) δ 28.9, 37.3, 55.2, 55.4, 113.9, 114.1, 121.8, 122.2, 126.3, 127.2, 130.0, 130.7, 156.4, 158.9, 170.4. IR 1649 cm^{-1}. MS (EI) *m*/*z* (%) 311 (M^+, 17), 123 (100), 108 (37). HRMS calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1518.

Typical procedure for the Suzuki coupling reaction. Synthesis of *N*-(4-methoxyphenyl)-4-phenyl-4-pentenamide (8l).



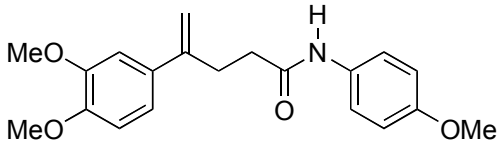
A mixture of $Pd(PPh_3)_4$ (26.13 mg, 0.023 mmol), K_2CO_3 (2M aq solution, 0,35 mL, 0,71 mmol), $PhB(OH)_2$ (53.30 mg, 0.44 mmol) and 4-bromo-*N*-(4-methoxyphenyl)-4-pentenamide **(8h)** (80.0 mg, 0.28 mmol) was diluted with a mixture of DMF/H_2O 4:1 (1 mL). The resulting mixture was then heated to 50 ºC for 48 h. The reaction was quenched with 10 mL of saturated solution of K_2CO_3, and extracted with AcOEt (3x15 mL). The resulting residue was purified by crystallization from hexanes to afford amide **8l** as a white solid (63%): mp 112–114 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.44 (t, *J*=7.6, 2H), 2.93 (t, *J*=7.6, 2H), 3.77 (s, 3H), 5.13 (s, 1H), 5.32 (s, 1H), 6.81 (d, *J*=8.7, 2H), 7.28–7.43 (m, 8H). ^{13}C NMR ($CDCl_3$) δ 31.2, 36.2, 55.5, 113.5, 114.1, 121.7, 126.2, 127.7, 128.5, 130.8, 140.3, 146.9, 156.4, 170.3. IR 1649 cm^{-1}. MS (EI) *m*/*z* (%) 281 (M^+, 17), 123 (100), 108 (47). HRMS calcd for $C_{18}H_{19}NO_2$ 281.1416, found 281.1416.

***N*,4-*Bis*(4-methoxyphenyl)-4-pentenamide (8m).**



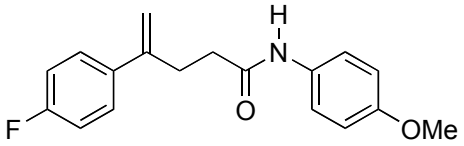
According to the typical procedure, amide **8m** was obtained from 4-bromo-*N*-(4-methoxyphenyl)-4-pentenamide **(8h)**. The resulting residue was purified by crystallization from hexanes to afford amide **8m** as a brown solid (63%): mp 158–160 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.46 (t, *J*=7.5, 2H), 2.92 (t, *J*=7.5, 2H), 3.78 (s, 3H), 3.82 (s, 3H), 5.07 (s, 1H), 5.26 (s, 1H), 6.84 (d, *J*=9.0, 2H), 6.88 (d, *J*=8.8, 2H), 6.98 (s, 1H), 7.35 (d, *J*=9.0, 2H), 7.37 (d, *J*=8.8, 2H). ^{13}C NMR ($CDCl_3$) δ 31.2, 55.3, 55.5, 112.0, 113.8, 114.1, 121.7, 127.3, 130.9, 132.6, 146.2, 156.4, 159.3, 170.4; IR 1655 cm^{-1}. MS (EI) *m*/*z* (%) 311 (M^+, 11), 161 (99), 133 (87), 123 (100), 108 (99). HRMS calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1512.

4-(3,4-Dimethoxyphenyl)-*N*-(4-methoxyphenyl)-4-pentenamide (8n).



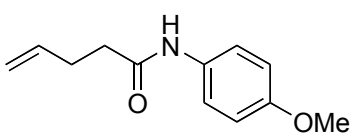
According to the general procedure amide **8n** was obtained from 4-bromo-*N*-(4-methoxyphenyl)-4-pentenamide **(8h)**. The resulting residue was purified by crystallization from hexanes to afford amide **8n** as a white solid (52%): mp 108–110 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.45 (t, *J*=7.4, 2H), 2.90 (t, *J*=7.4, 2H), 3.75 (s, 3H), 3.85 (s, 6H), 5.05 (s, 1H), 5.25 (s, 1H), 6.81 (d, *J*=8.8, 2H), 6.94–6.97 (m, 2H), 7.35 (d, *J*=8.8, 2H), 7.72 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 31.4, 36.4, 55.6, 56.1, 109.6, 111.1, 112.3 114.3, 118.7, 121.9, 131.2, 133.3, 146.7, 148.9, 149.0, 156.5, 170.7. IR 1655 cm^{-1}. MS (EI) *m*/*z* (%) 341 (M^+, 11), 123 (100), 108 (88). HRMS calcd for $C_{20}H_{23}NO_4$ 341.1627, found 341.1630.

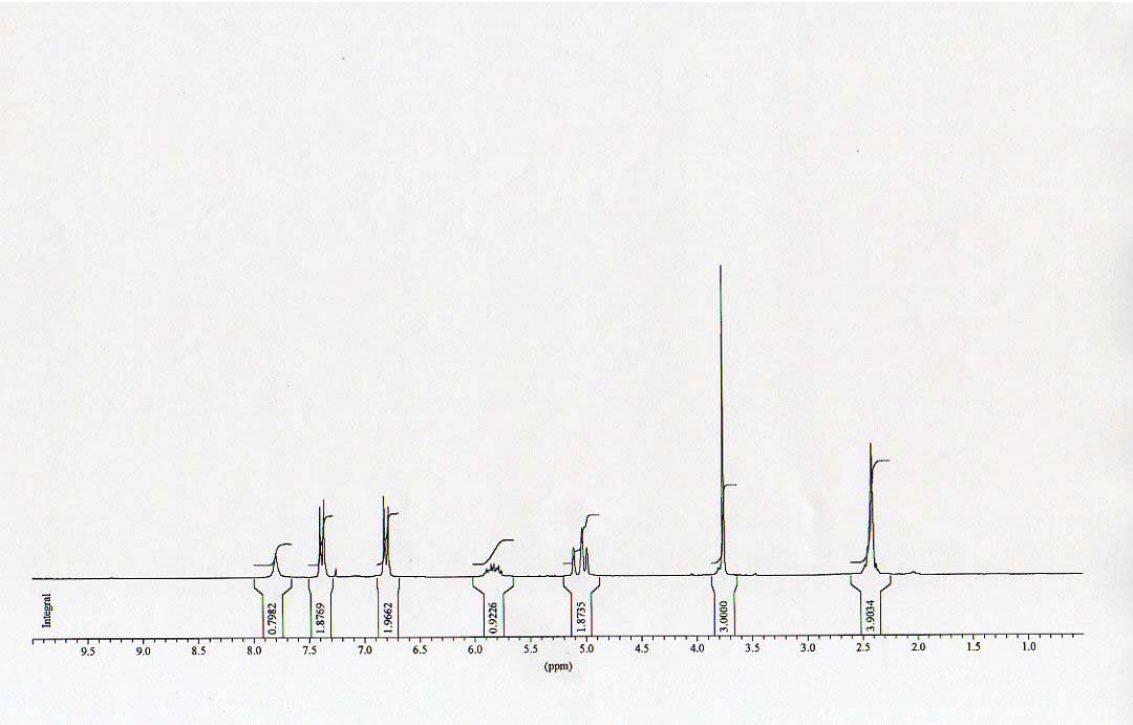
4-(4-Fluorophenyl)-*N*-(4-methoxyphenyl)-4-pentenamide (8o).

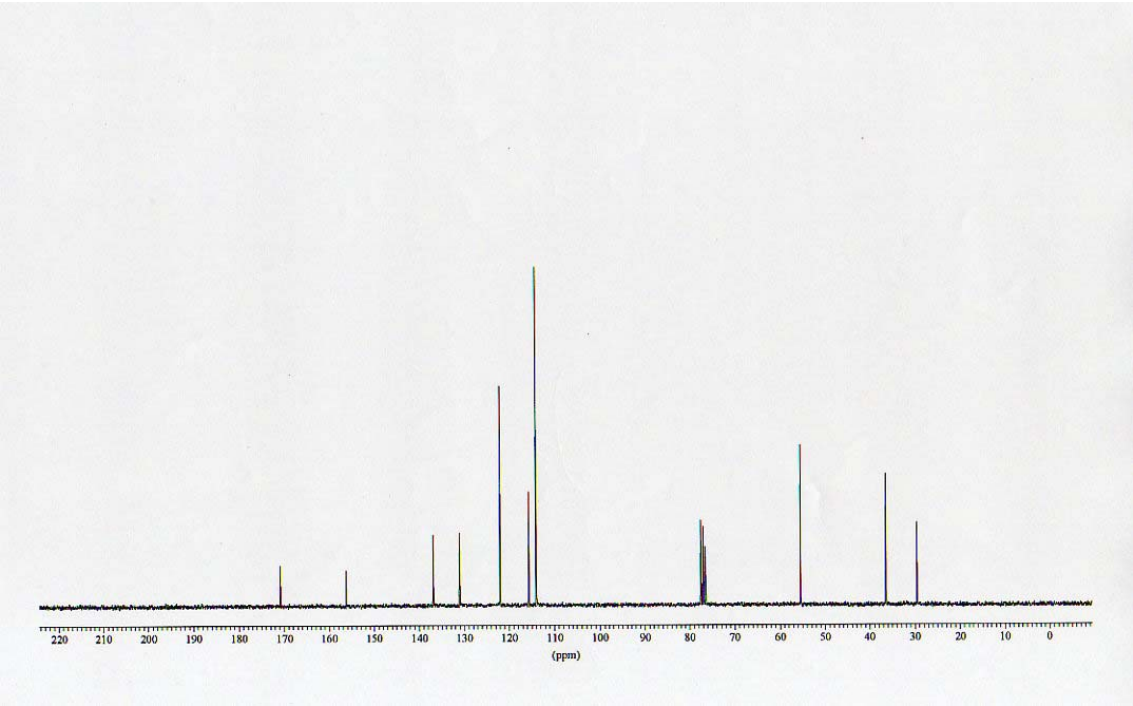


According to the general procedure amide **8o** was obtained from 4-bromo-*N*-(4-methoxyphenyl)-4-pentenamide **(8h)**. The resulting residue was purified by crystallization from hexanes to afford amide **8o** as a white solid (61%): mp 110–111 ºC (hexanes). ^{1}H NMR ($CDCl_3$) δ 2.44 (t, *J*=7.7, 2H), 2.89 (t, *J*=7.7, 2H), 3.77 (s, 3H), 5.10 (s, 1H), 5.26 (s, 1H), 6.82 (d, *J*=8.9, 2H), 7.00 (t, *J*=8.8, 2H), 7.35 (t, *J*=8.8, 2H), 7.33–7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 31.1, 36.1, 55.4, 113.3, 114.1, 115.2 (d, *J*=21.1), 115.4 (d, *J*=21.1), 121.7, 127.7 (d, *J*=8.2), 127.8 (d, *J*=8.2), 130.8, 136.4 (d, *J*=3.7), 136.4 (d, *J*=3.7), 145.9, 156.4, 161.4 (d, *J*=246), 163.4 (d, *J*=246), 170.2. IR 1649 cm^{-1}. MS (EI) *m*/*z* (%) 299 (M^+, 86), 123 (100), 108 (97). HRMS calcd for $C_{18}H_{18}NO_2F$ 299.1322, found 299.1325.

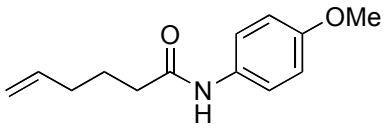
***N*-(4-Methoxyphenyl)-4-pentenamide (5a).**

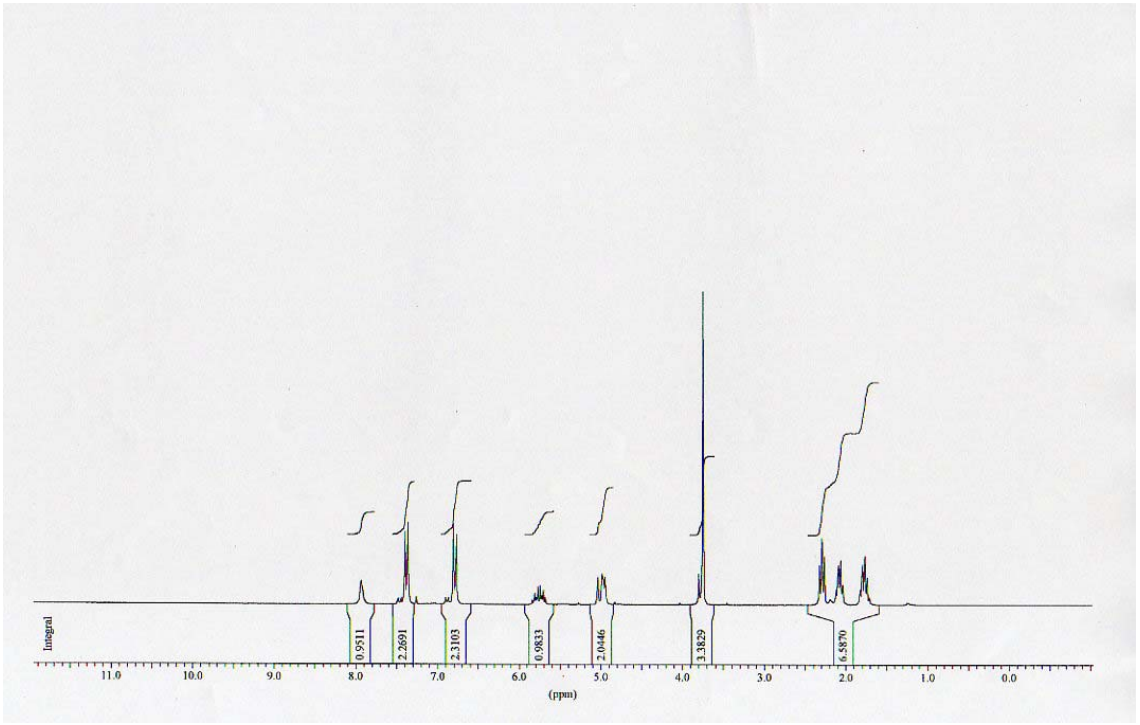


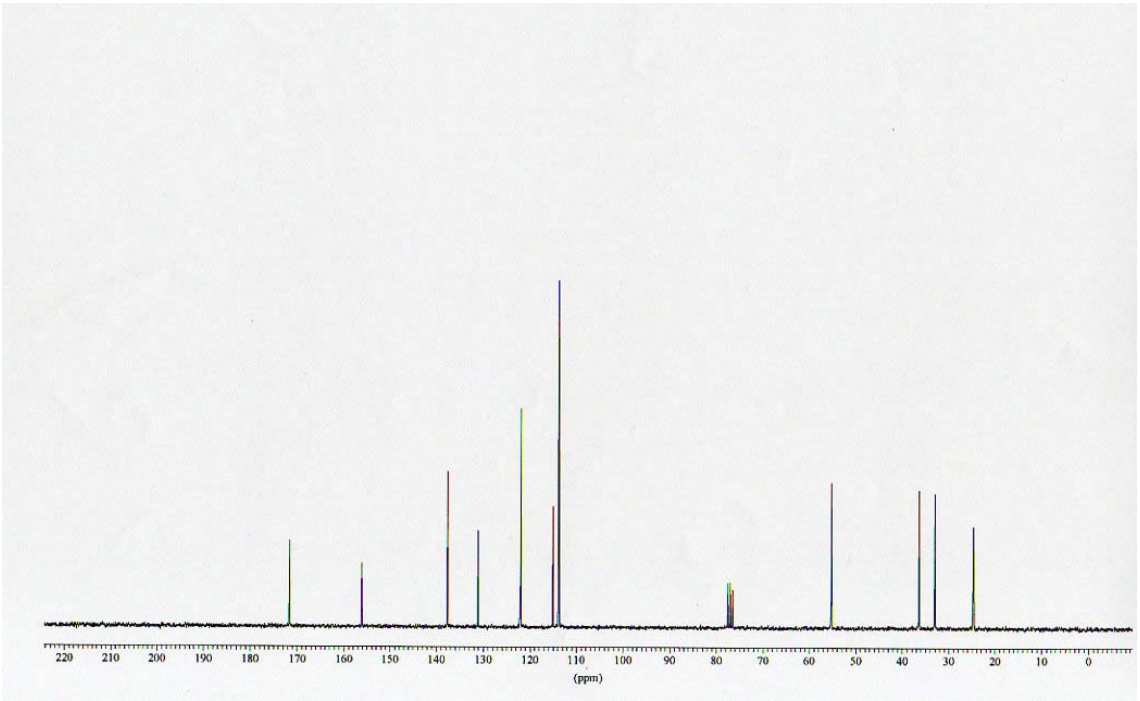

Integral
0.7982
1.8769
1.9662
0.9226
1.8735
3.0000
3.9034
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
(ppm)


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

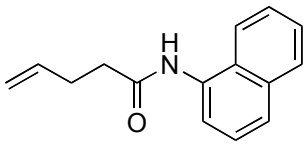
***N*-(4-Methoxyphenyl)-5-hexenamide (5c).**

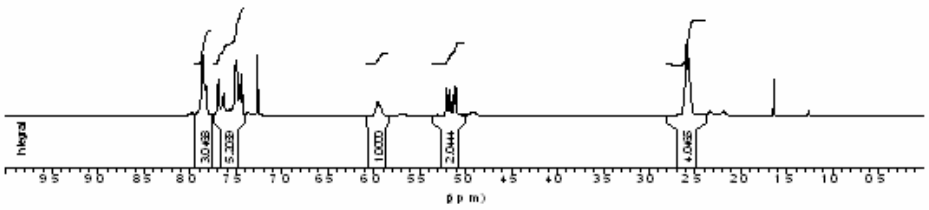


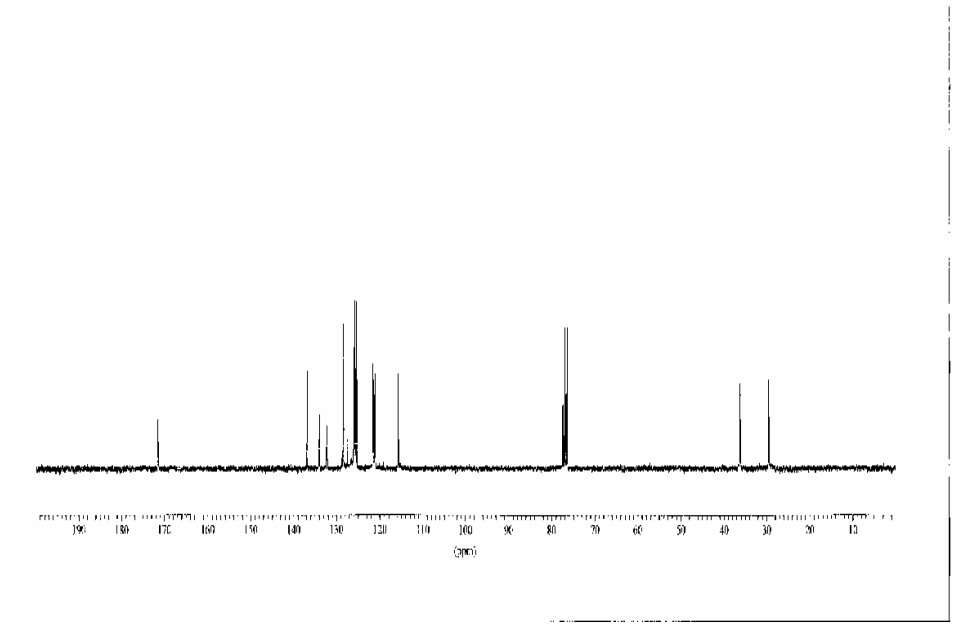




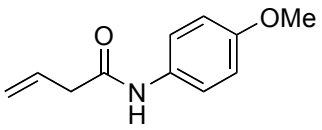
***N*-(1-Naphtyl)-4-pentanamide (5d).**

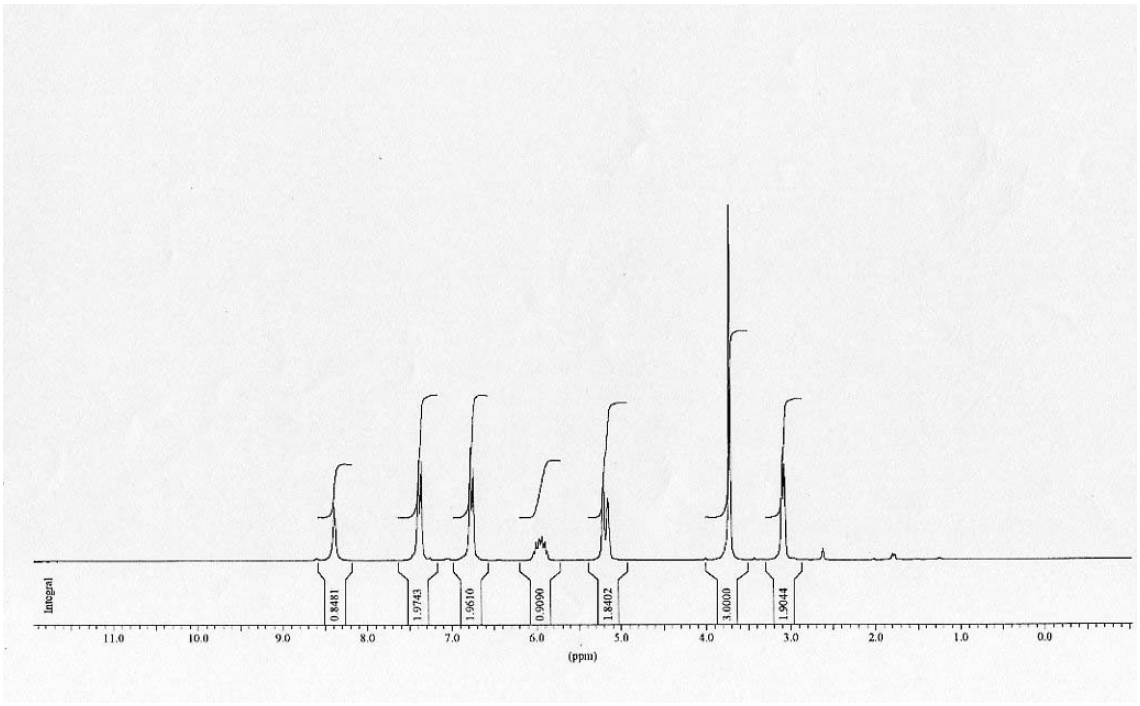


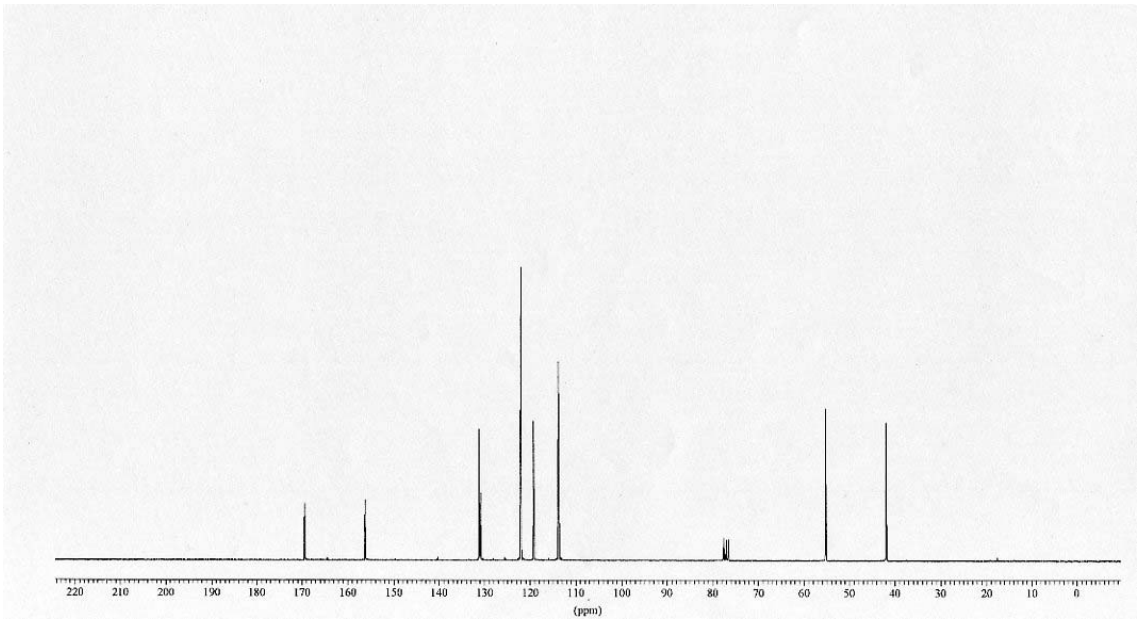




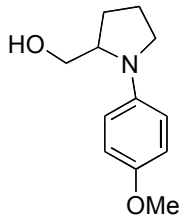
_N_-(4-Methoxyphenyl)-3-butenamide (5e).

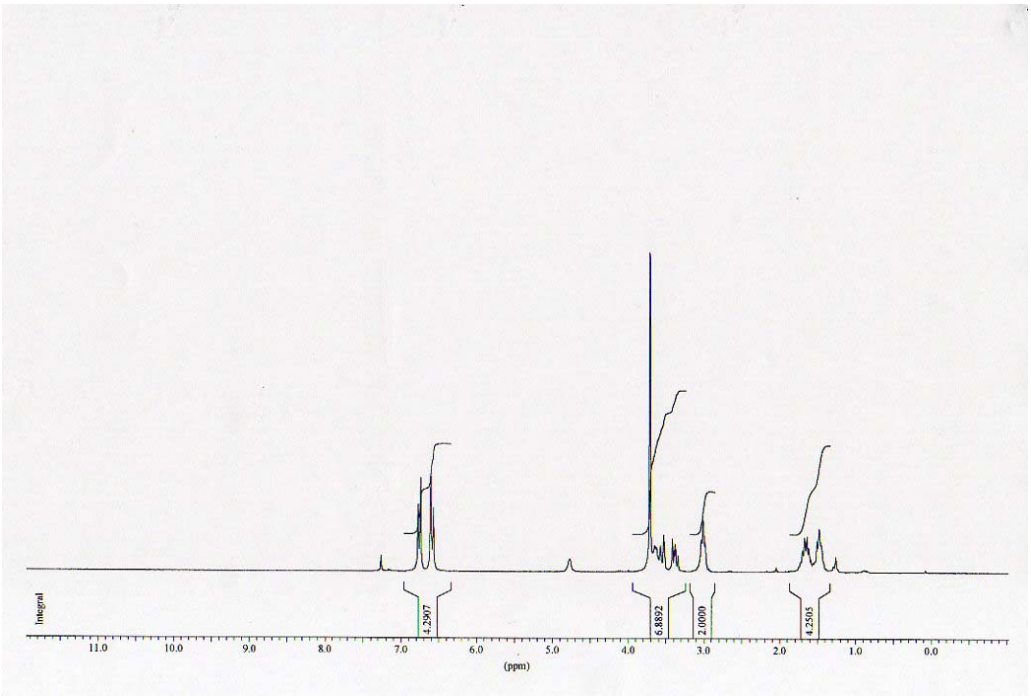


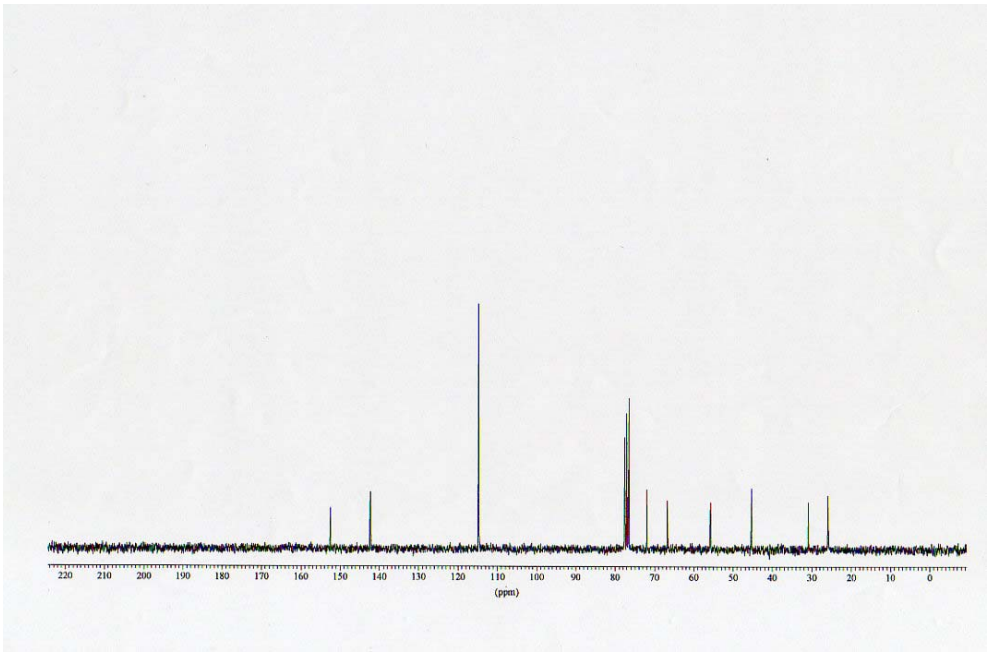




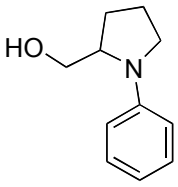
2-(Hydroxymethyl)-*N*-(4-methoxyphenyl)-pyrrolidine (6a).

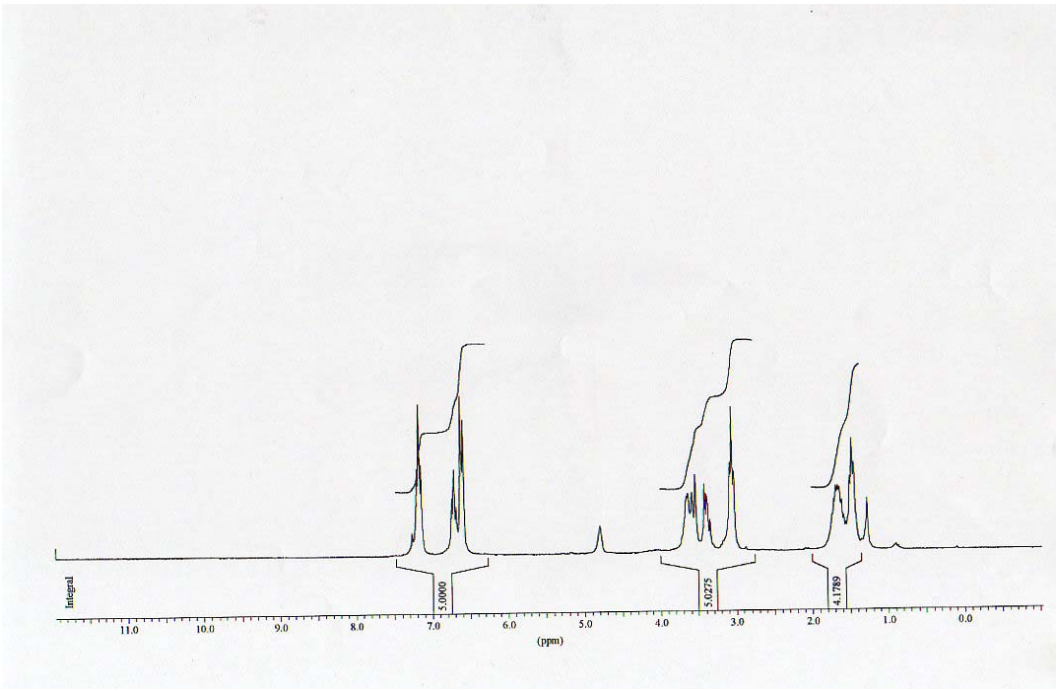


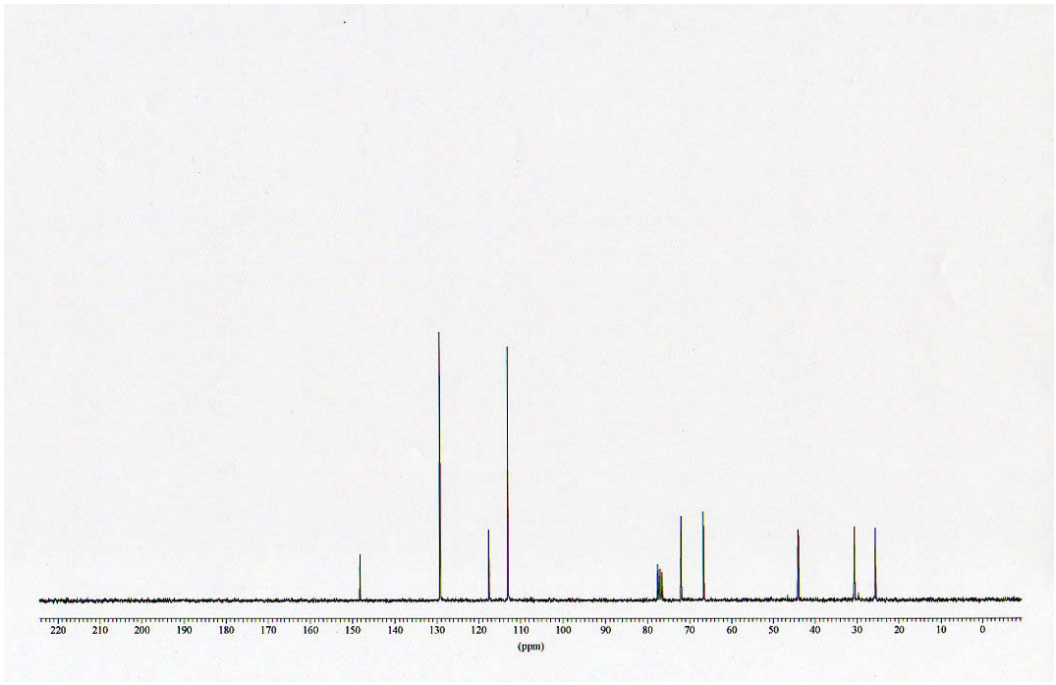




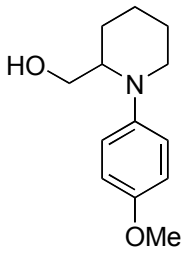
2-Hydroxymethyl-*N*-phenyl-pyrrolidine (6b).

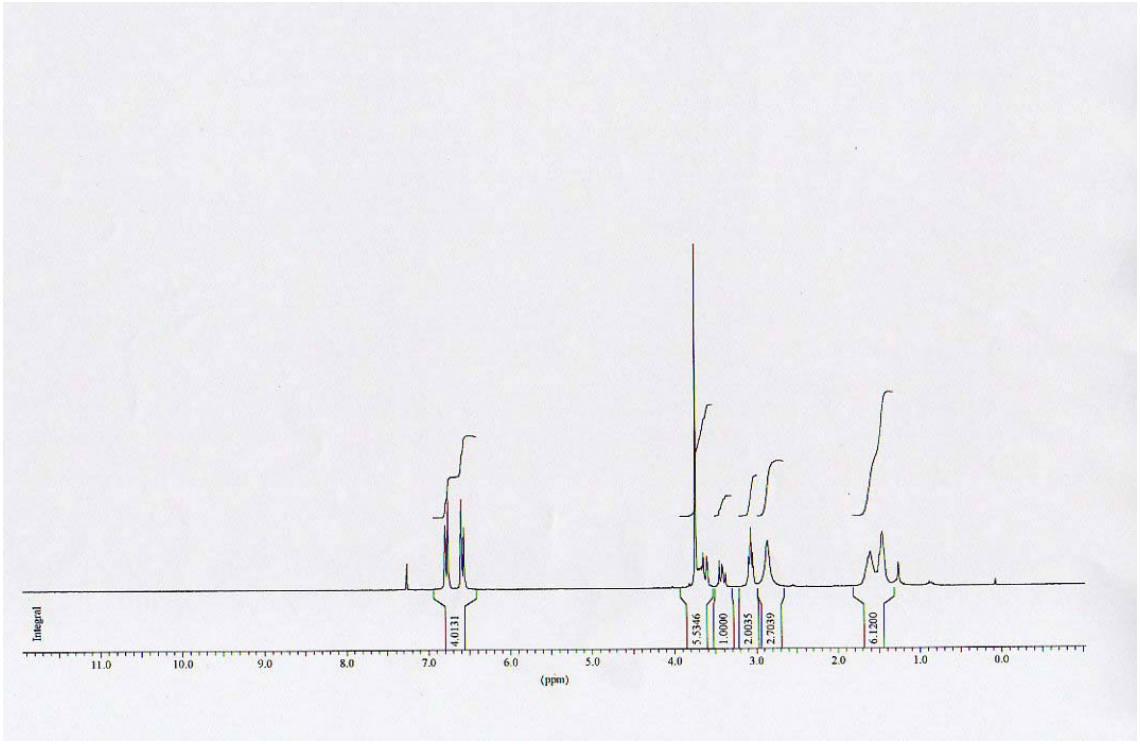


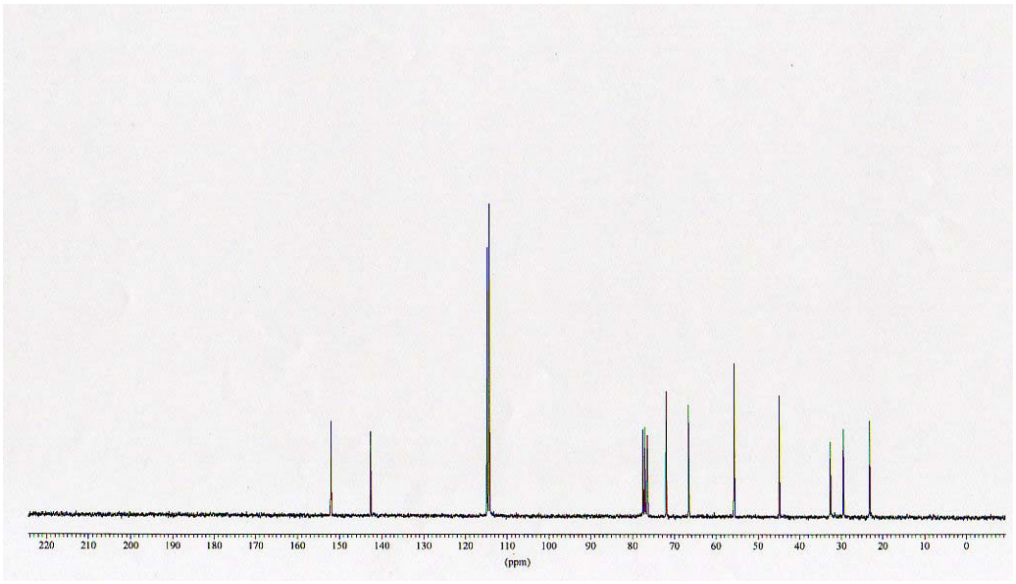




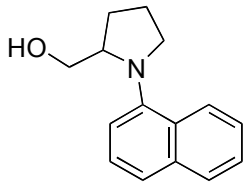
2-Hydroxymethyl-1-(4-methoxyphenyl)piperidine (6c).

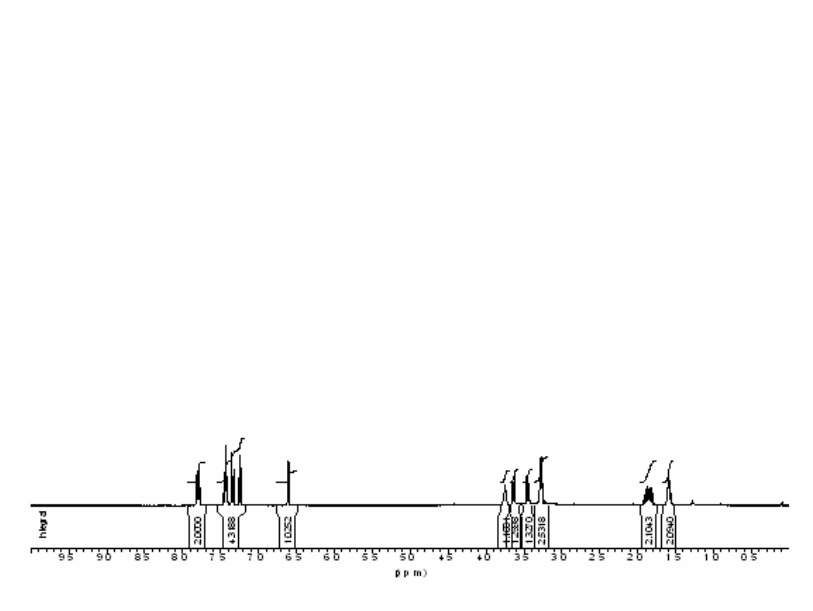


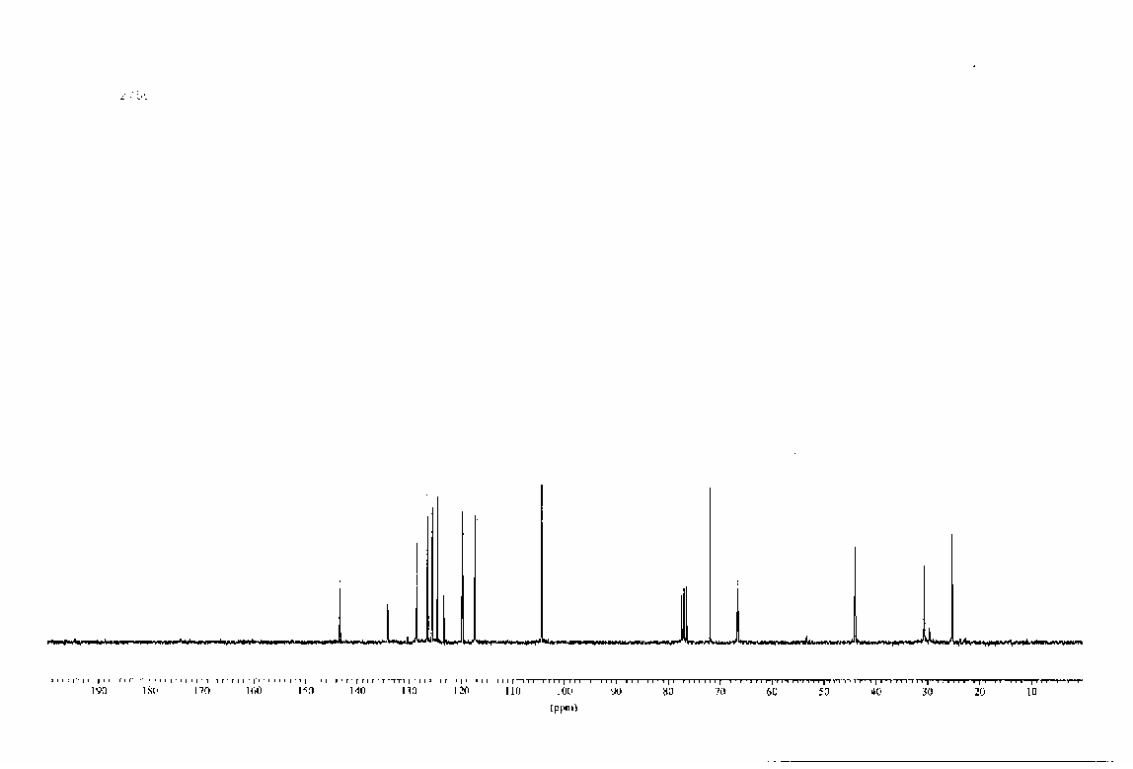




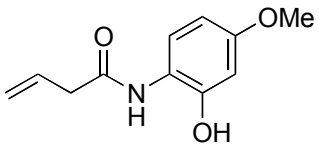
2-Hydroxymethyl-*N*-(1-naphtyl)pyrrolidine (6d).

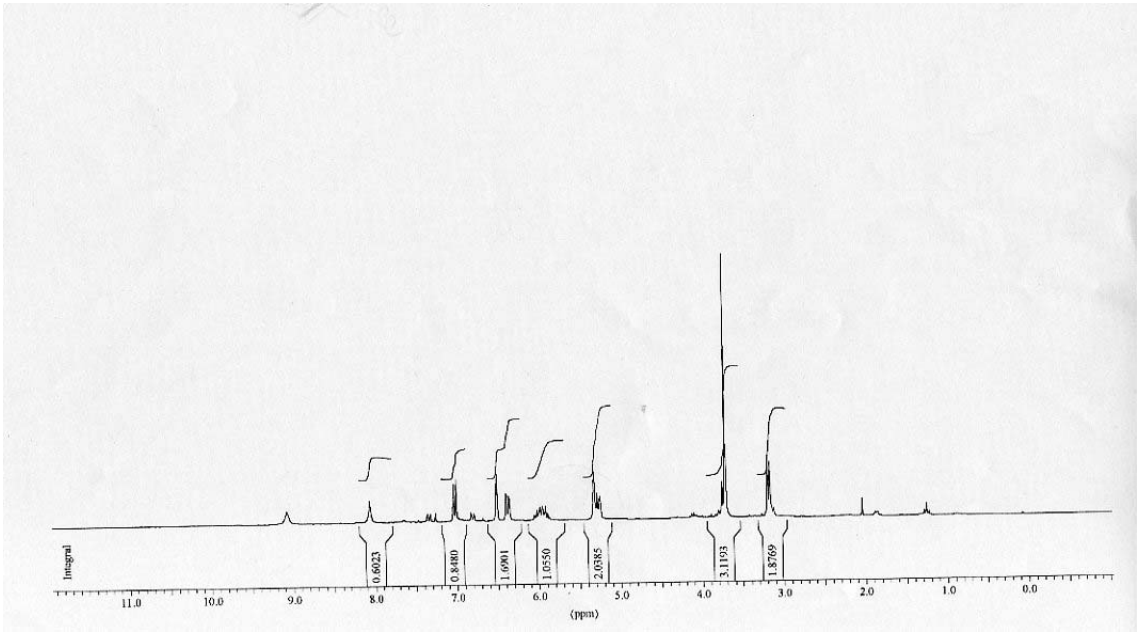


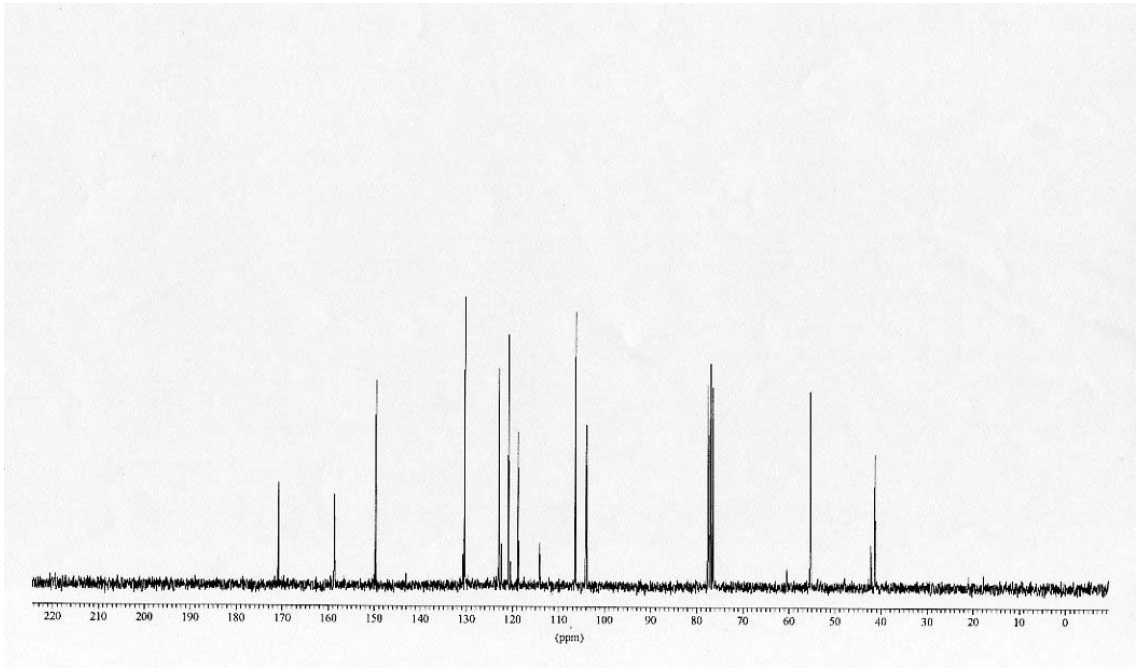




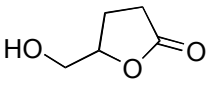
_N_-(2-Hydroxy-4-methoxyphenyl)-3-butenamide (6e').

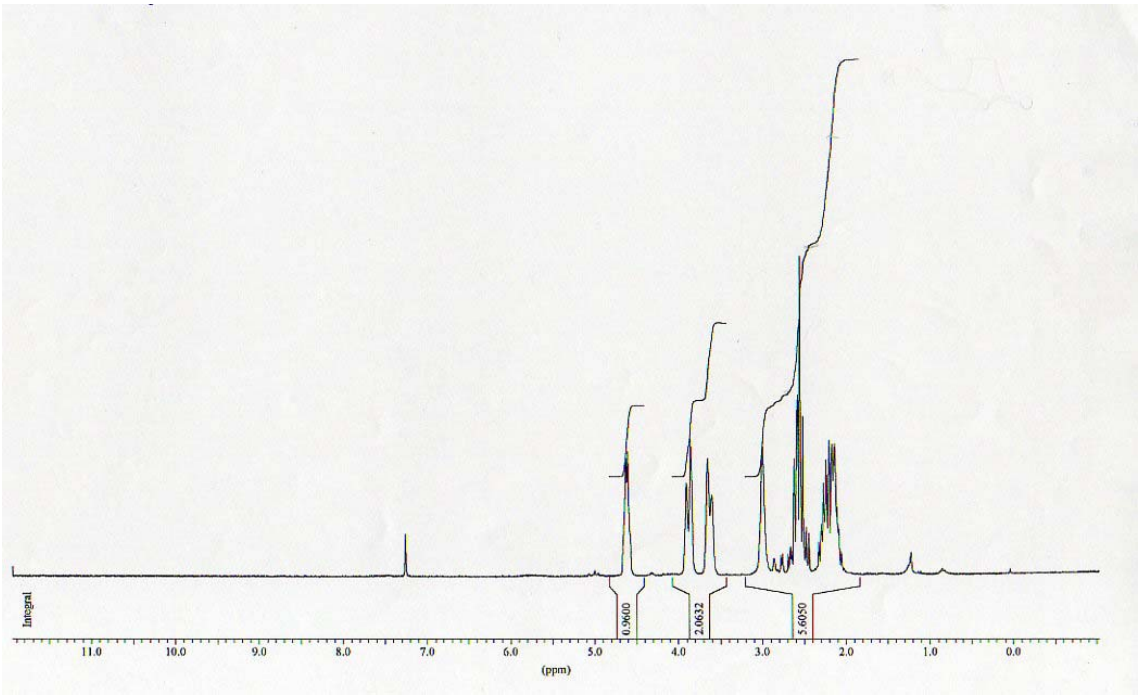


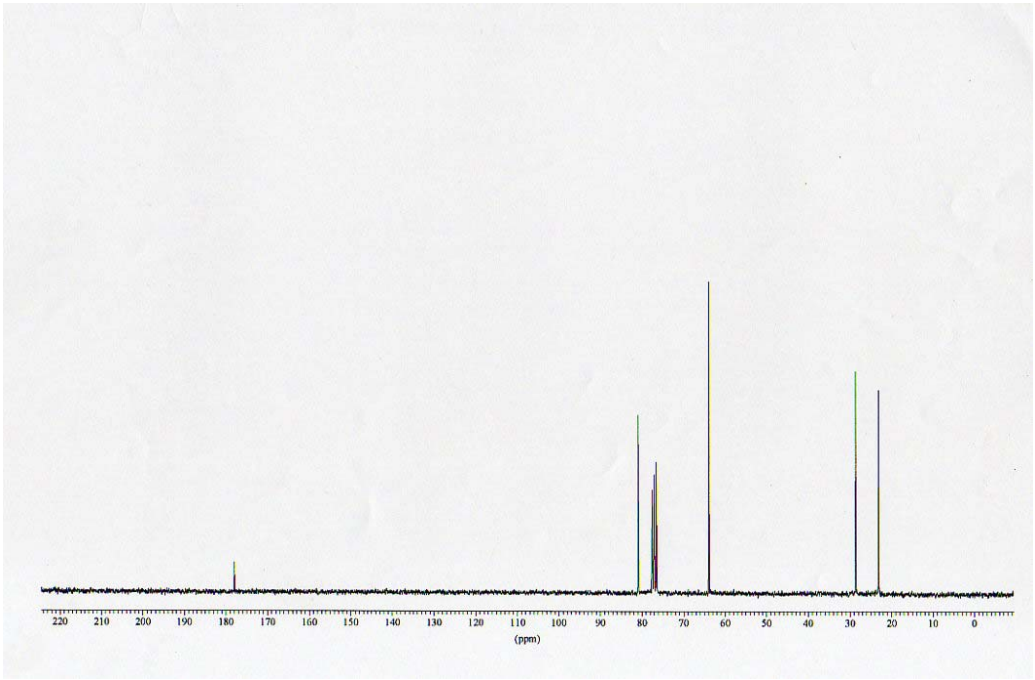




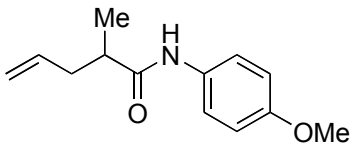
5-Hydroxymethyl-4,5-dihydro-furan-2-one (6f').

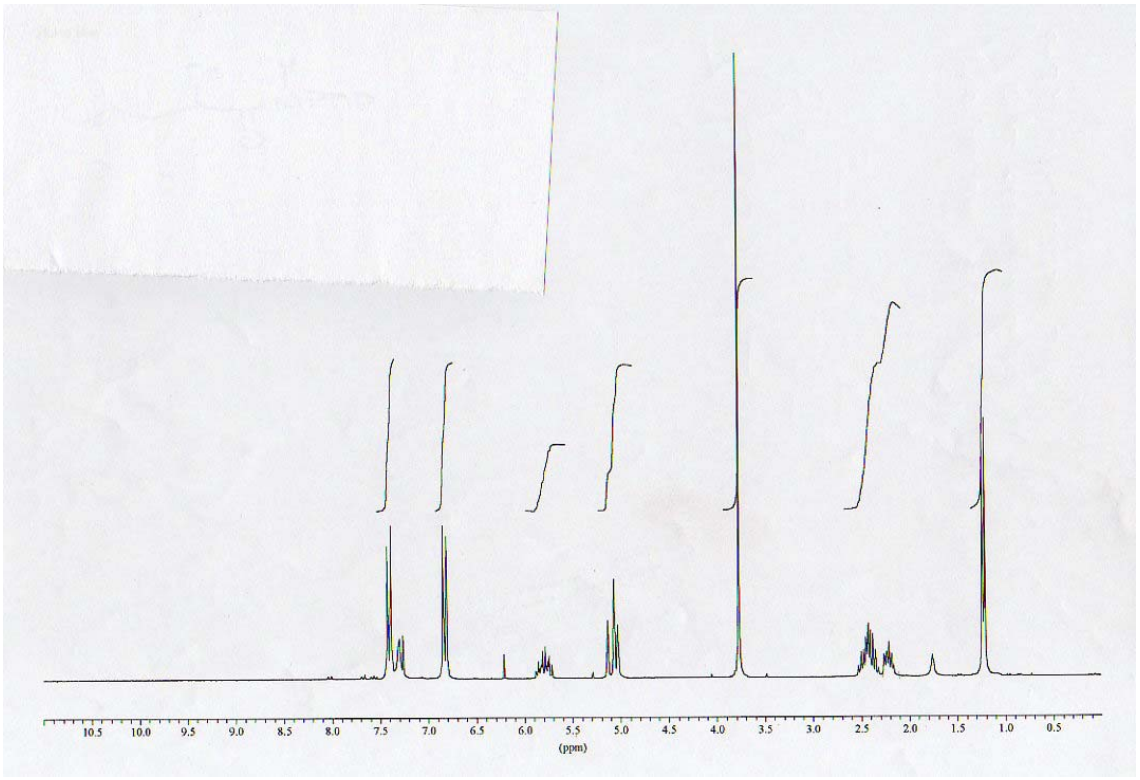


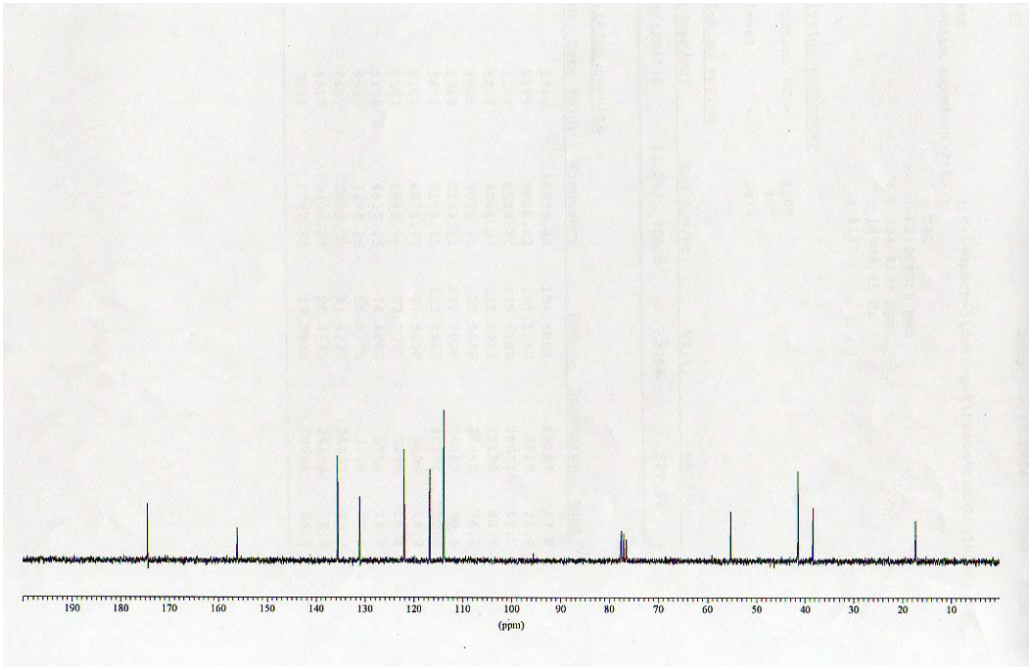




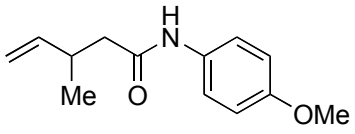
_N_-(4-Methoxyphenyl)-2-methyl-4-pentenamide (8a).

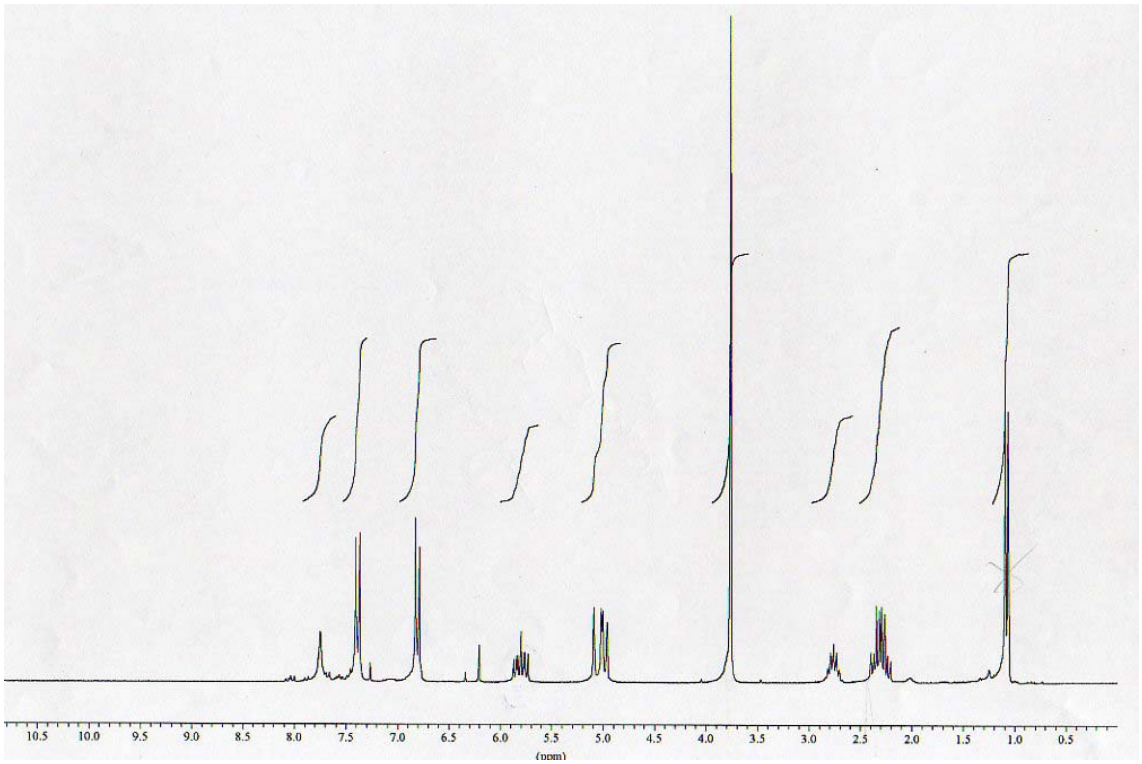


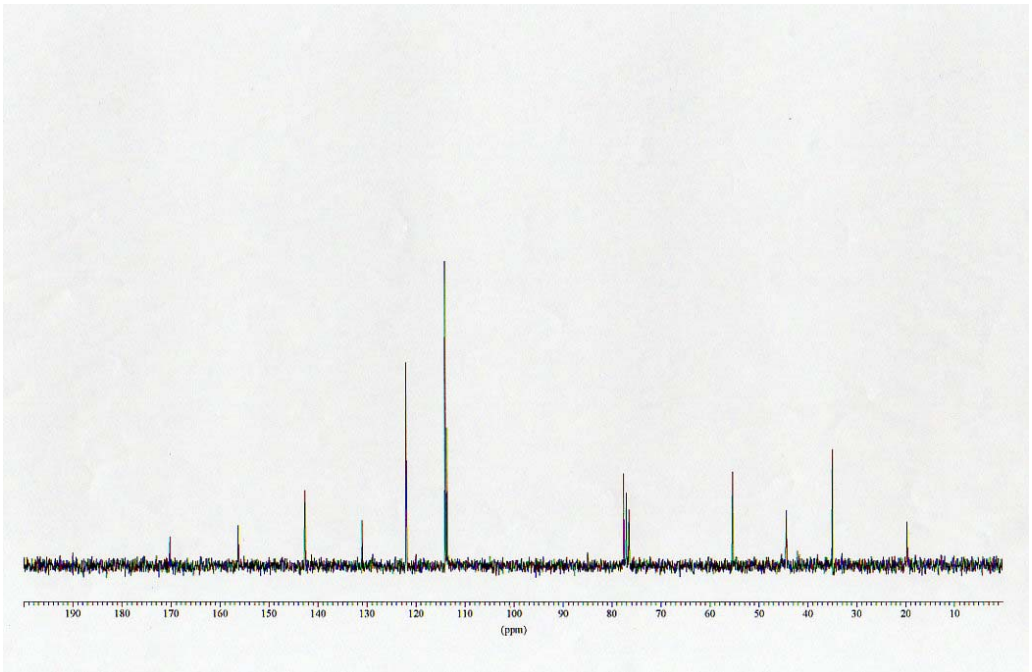




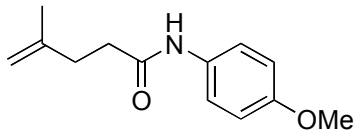
***N*-(4-Methoxyphenyl)-3-methyl-4-pentenamide (8b).**

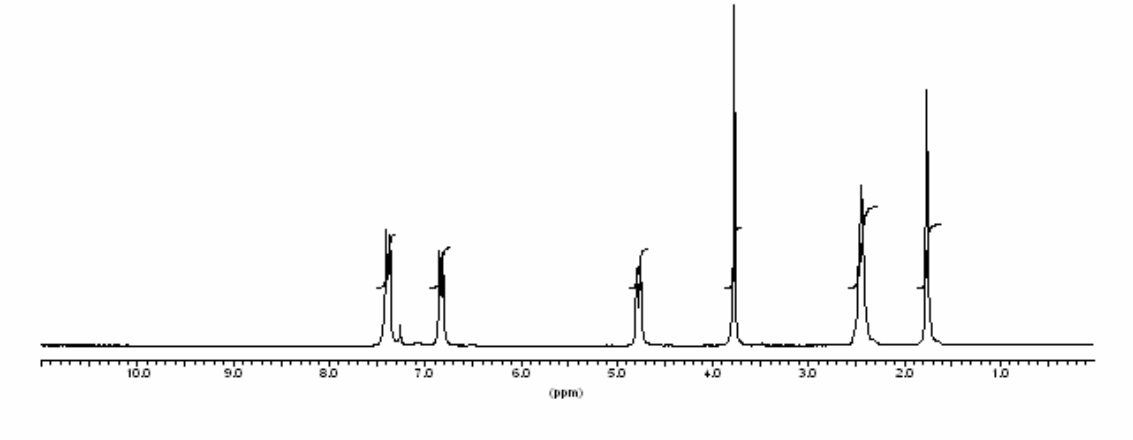


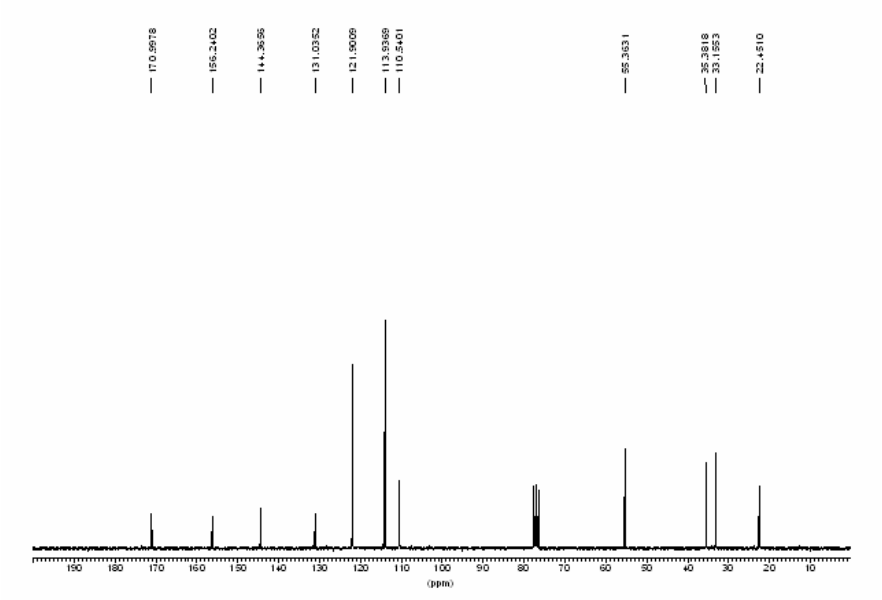




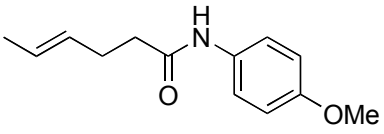
***N*-(4-Methoxyphenyl)-4-methyl-4-pentenamide (8c).**

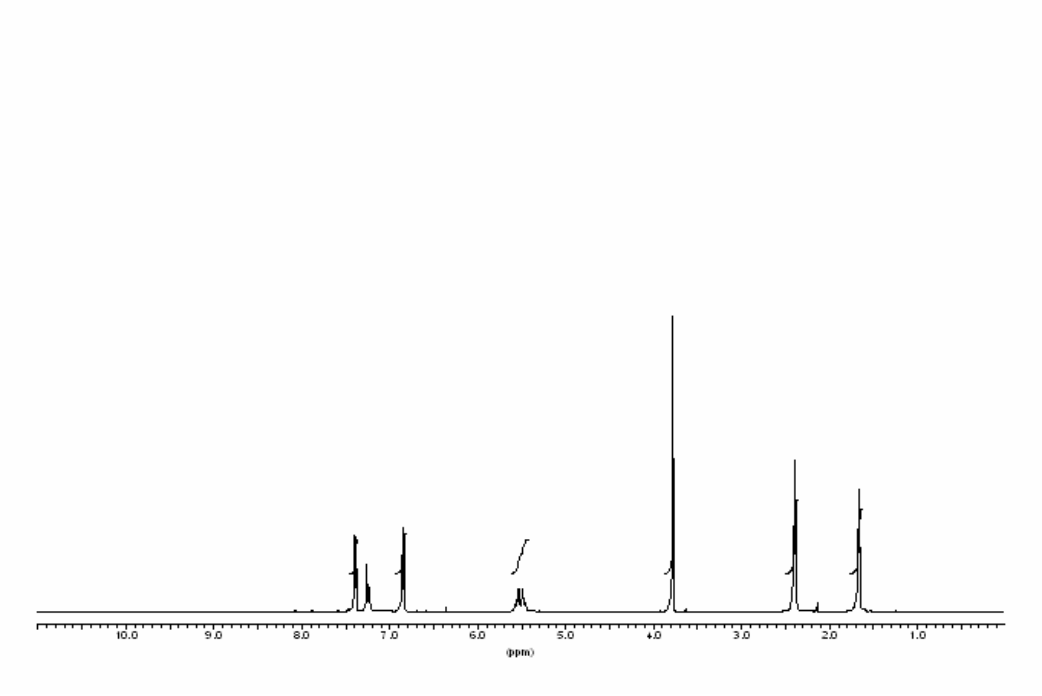


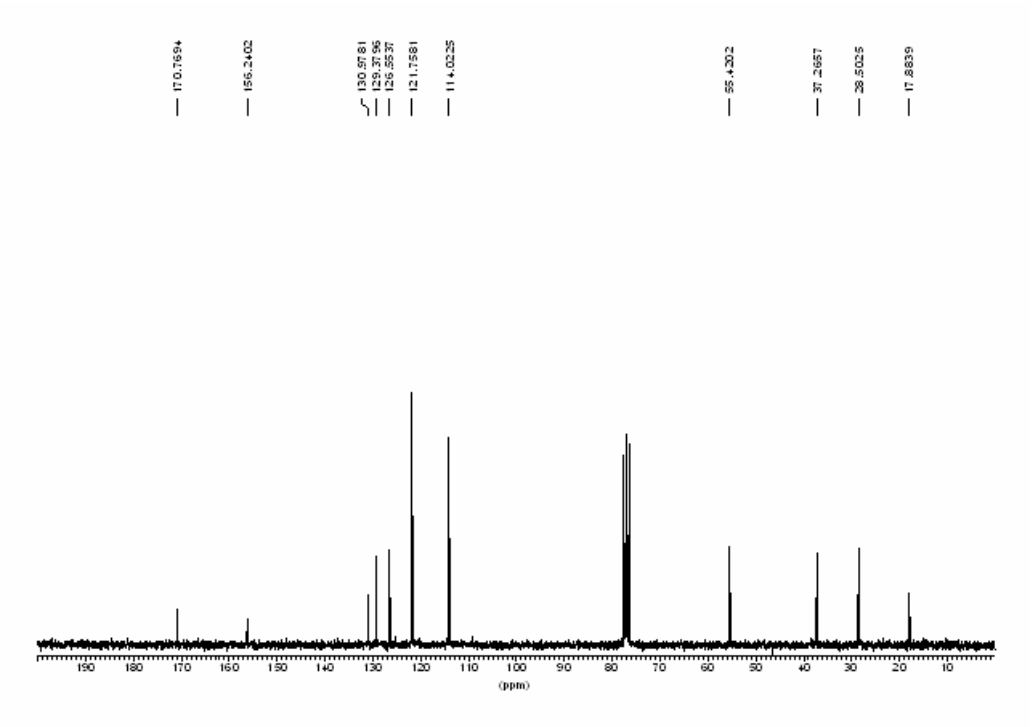




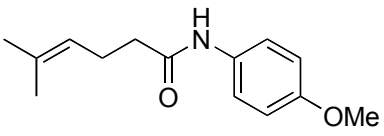
_N_-(4-Methoxyphenyl)-4-hexenamide (8d).

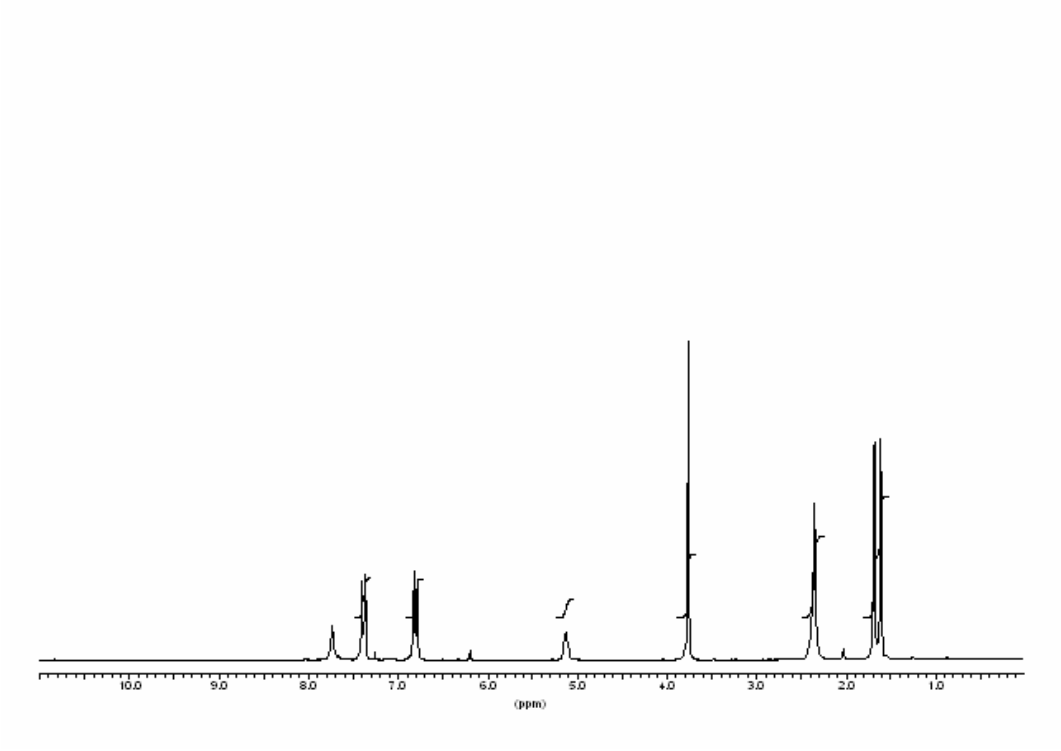


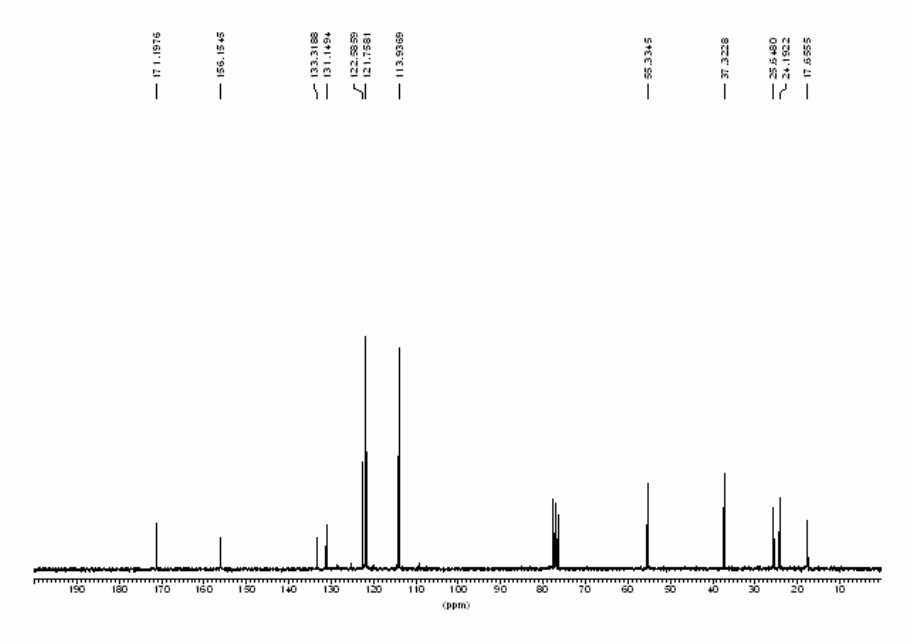




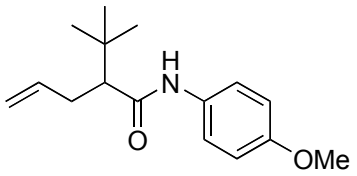
_N_-(4-Methoxyphenyl)-5-methyl-4-hexenamide (8e).

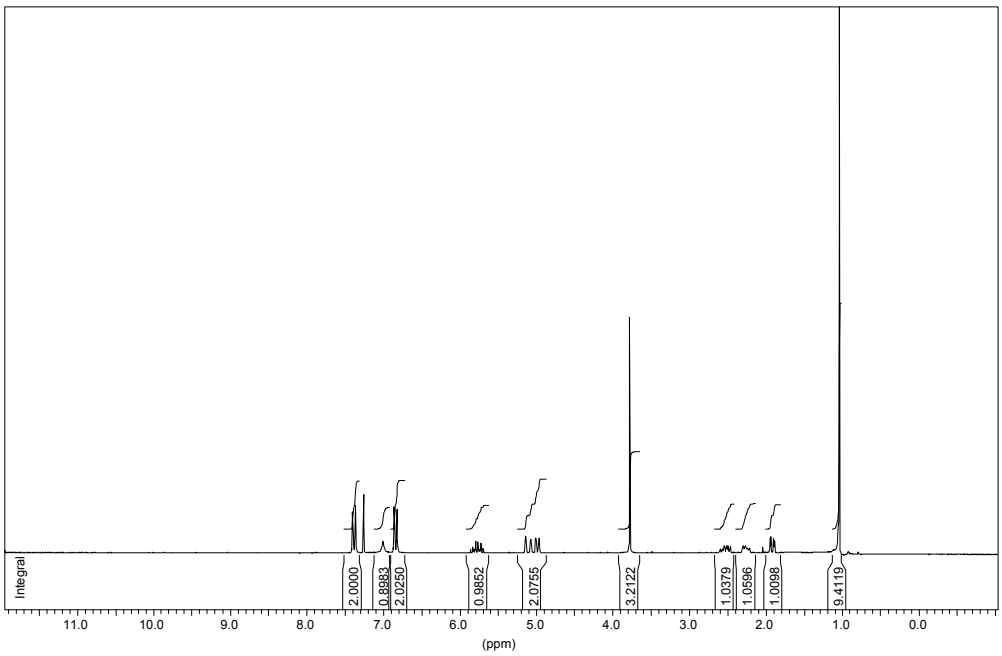


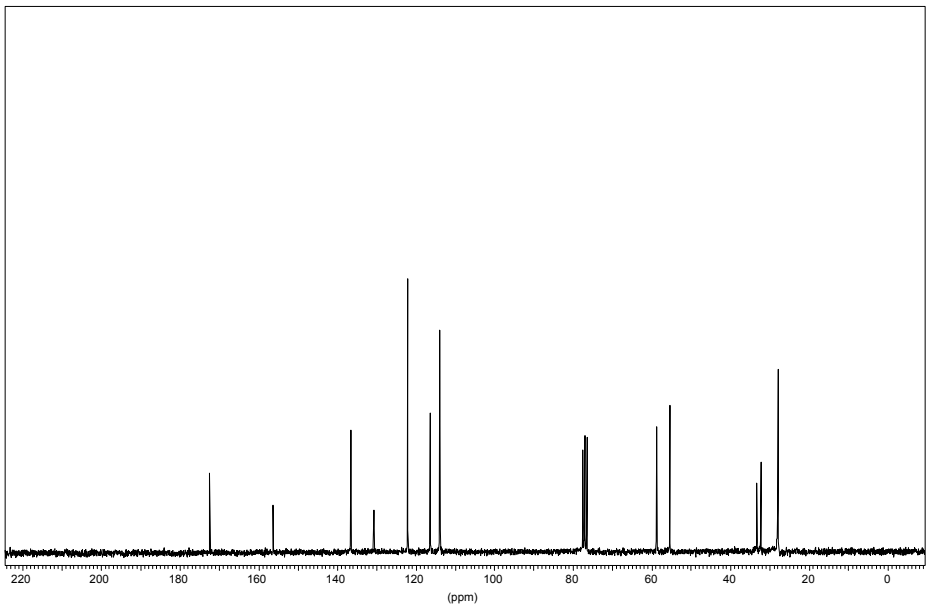




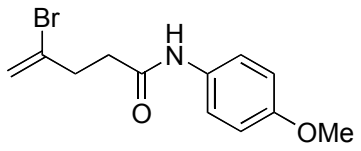
_N_-4-Methoxyphenyl-2-_tert_butyl-4-pentenamide (8g).

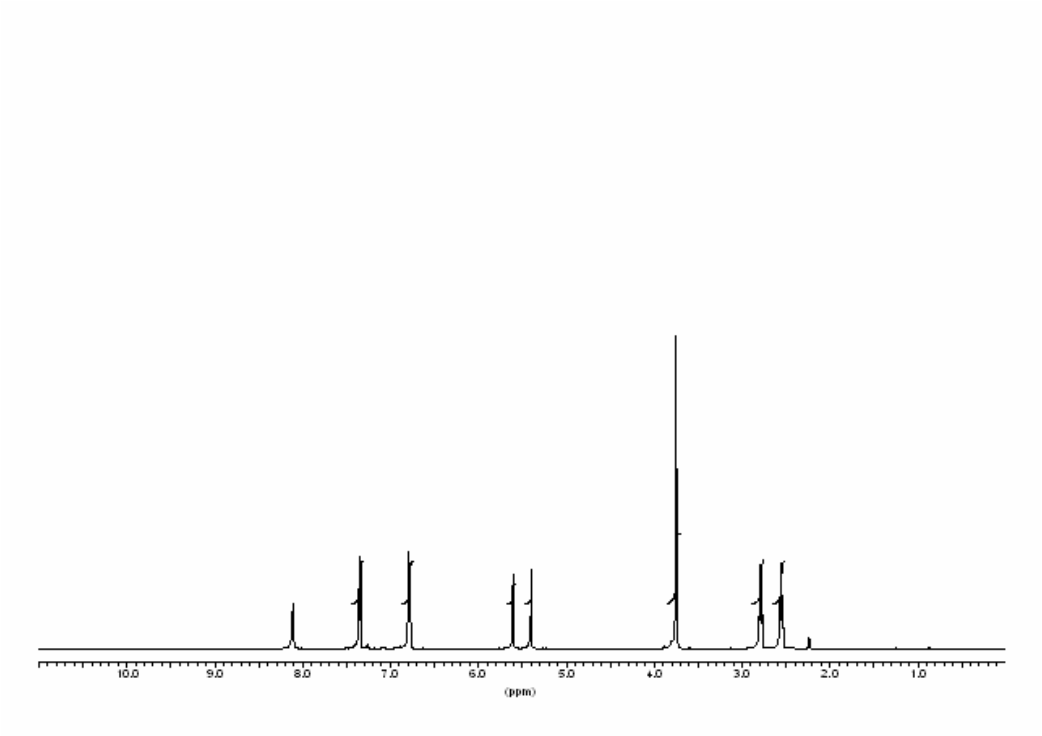


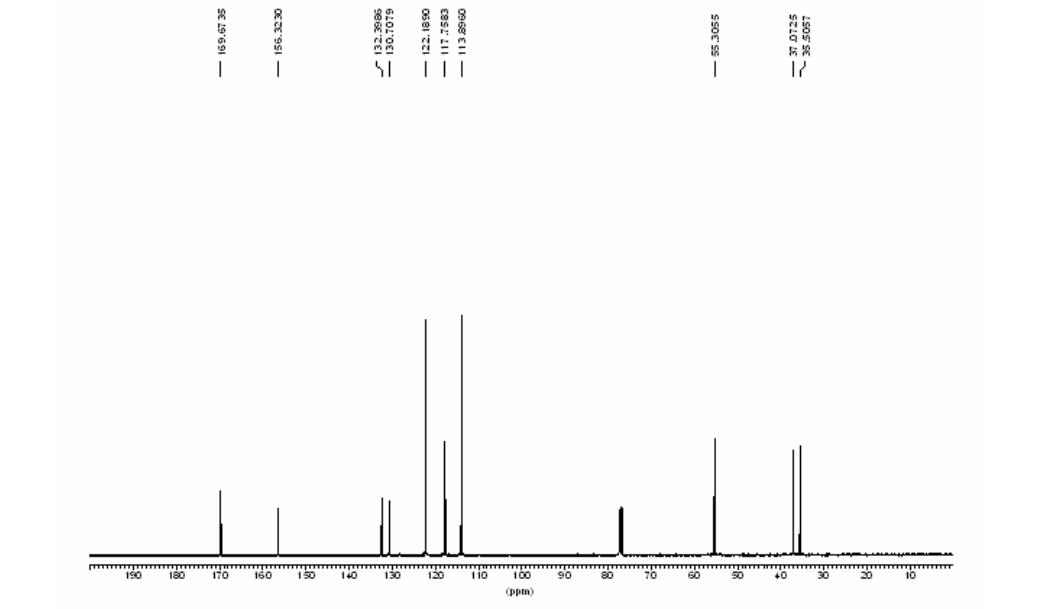




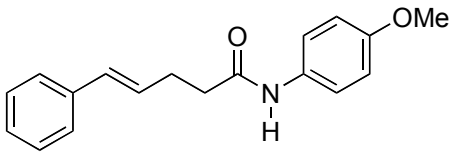
4-Bromo-*N*-(4-methoxyphenyl)-4-pentenamide (8h).

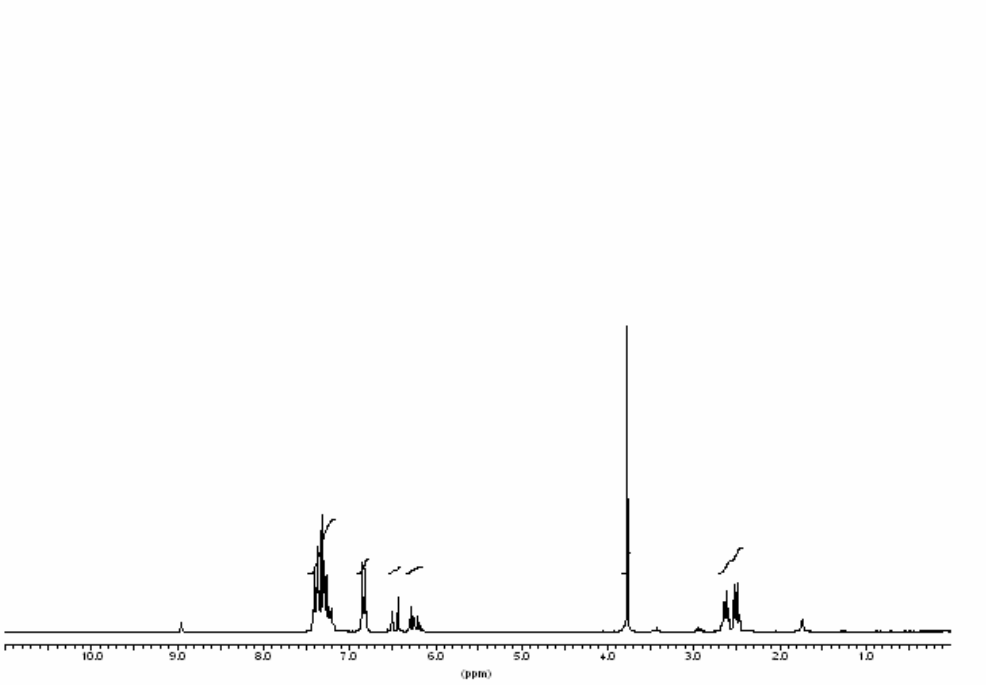


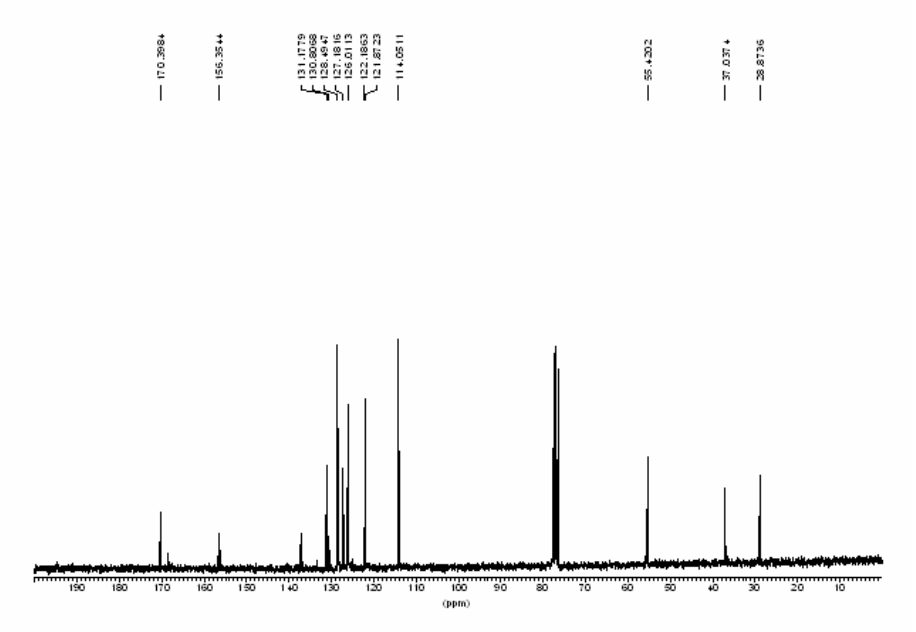




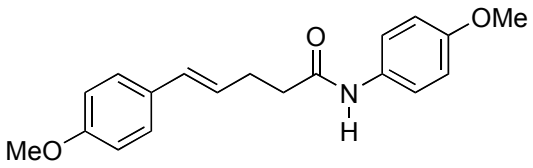
_N_-(4-Methoxyphenyl)-4-phenyl-4-pentenamide (8i).

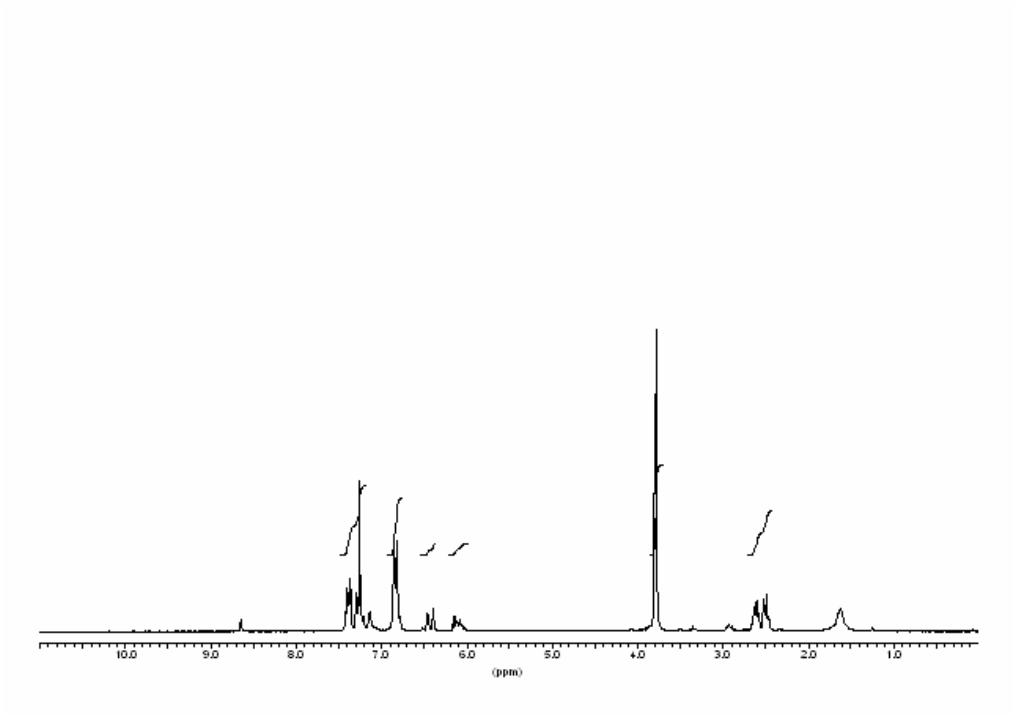


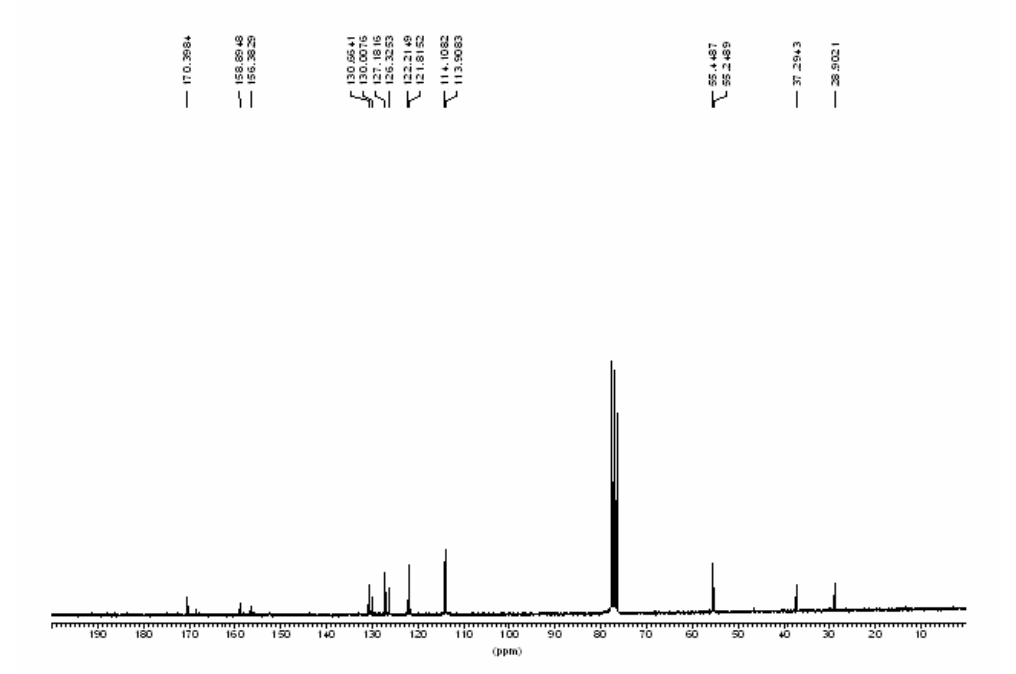




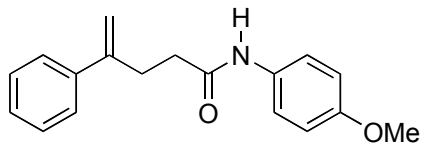
_N_,5-_Bis_-(4-methoxyphenyl)-4-pentenamide (8j).

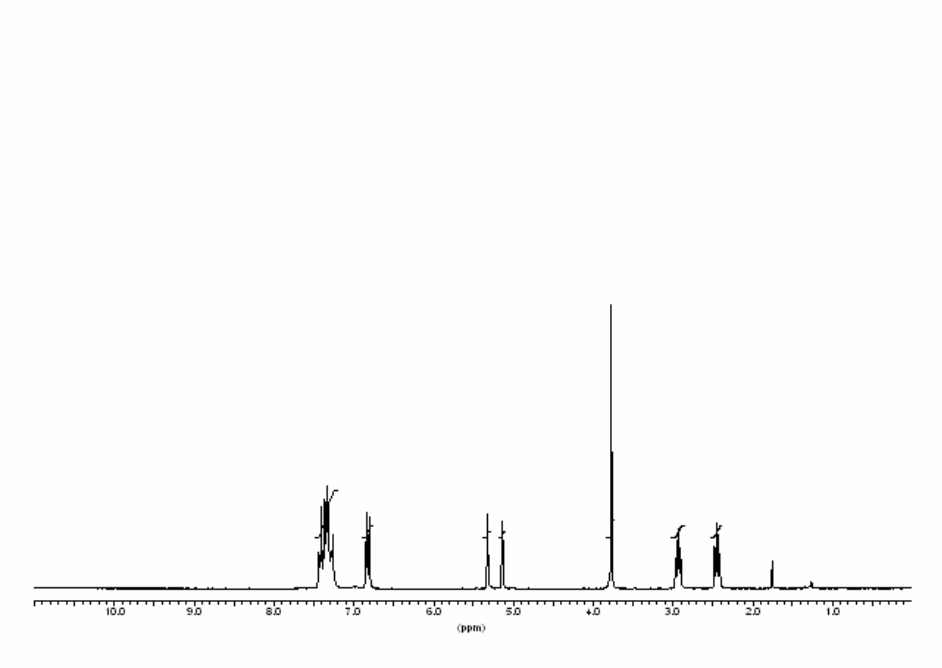


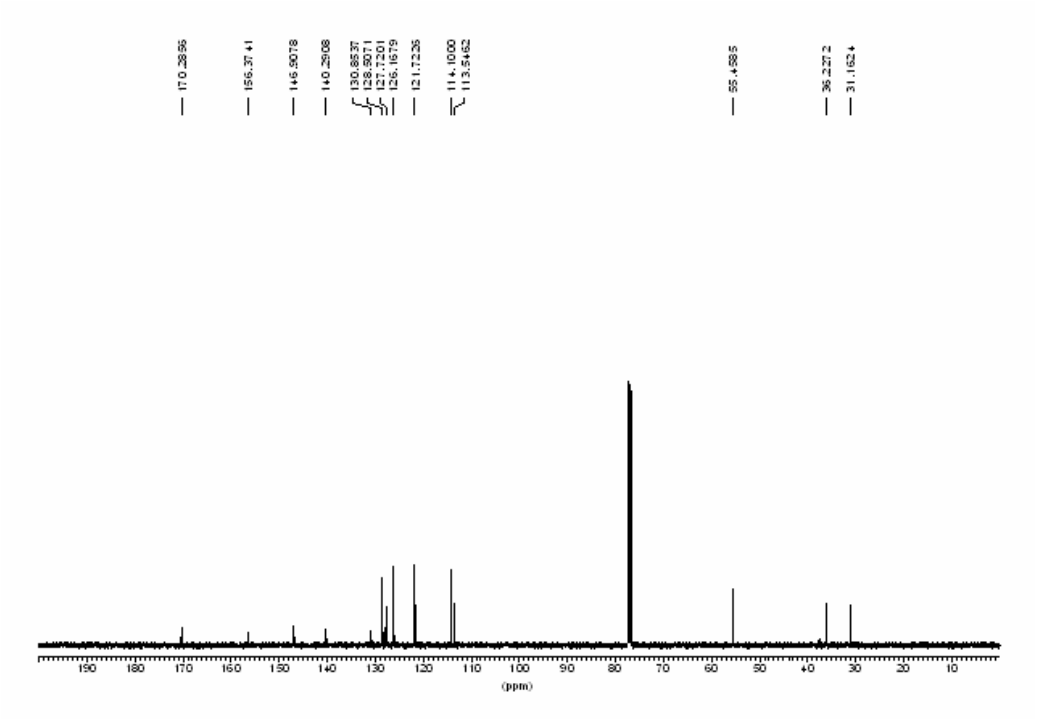




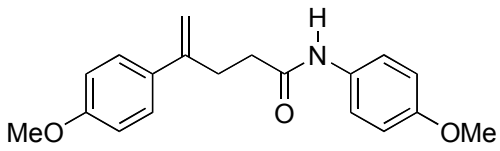
_N_-(4-Methoxyphenyl)-4-phenyl-4-pentenamide (8l).

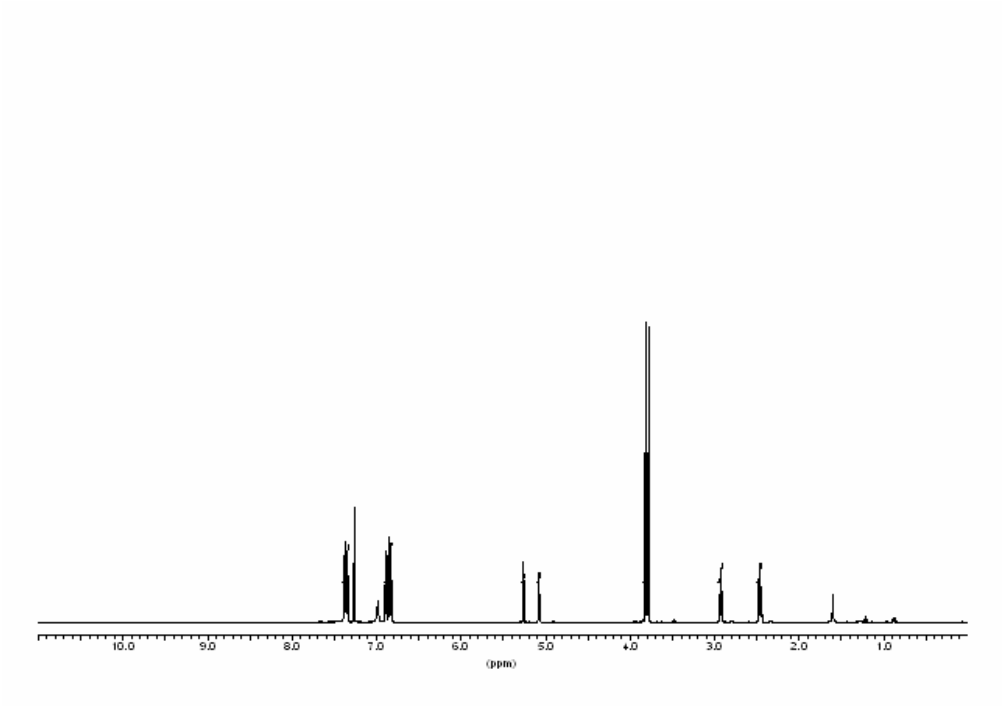


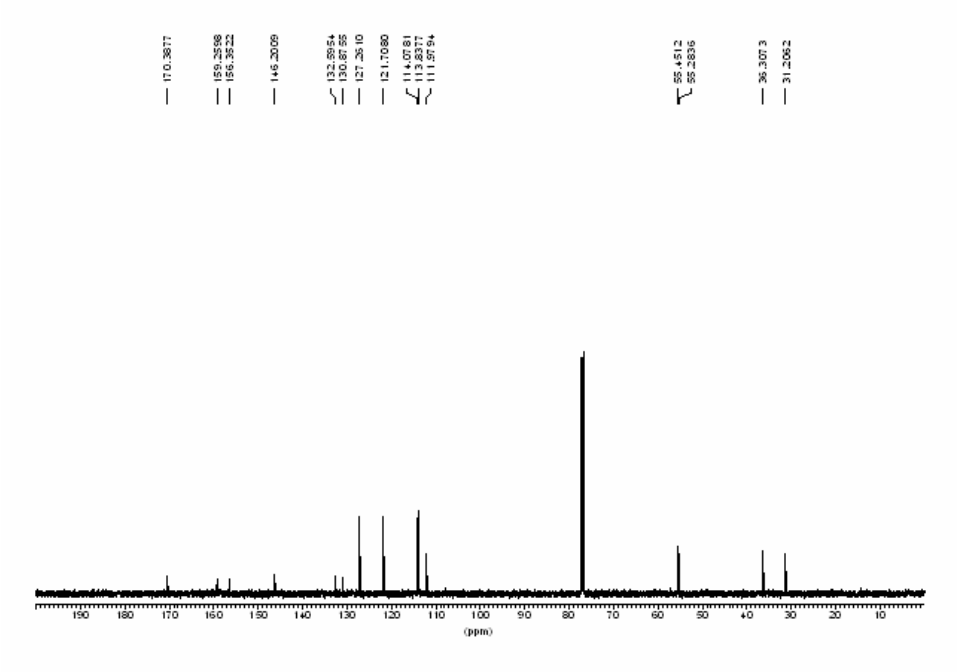




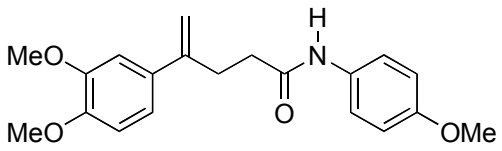
_N_,4-_Bis_(4-methoxyphenyl)-4-pentenamide (8m).

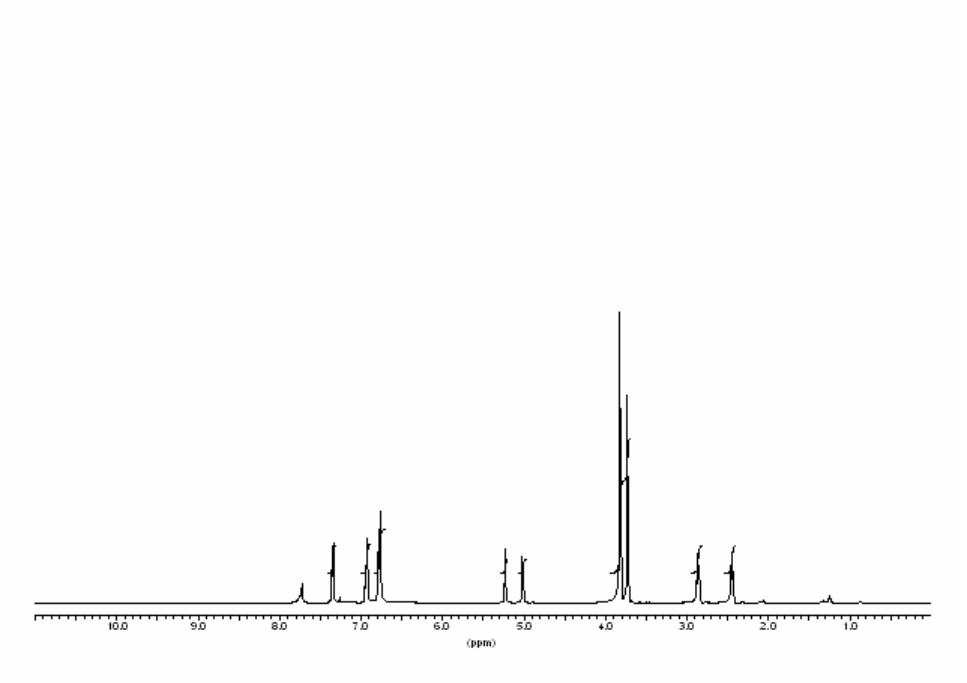


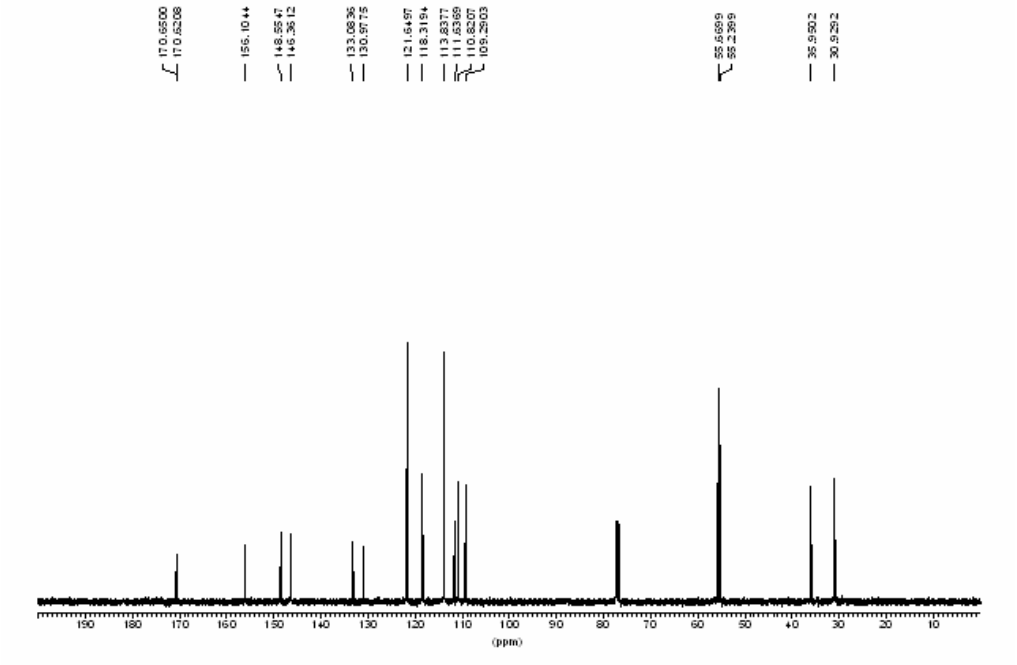




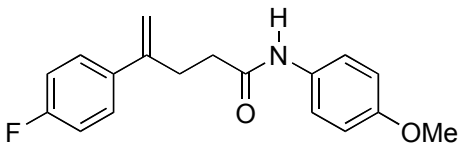
4-(3,4-Dimethoxyphenyl)-*N*-(4-methoxyphenyl)-4-pentenamide (8n).

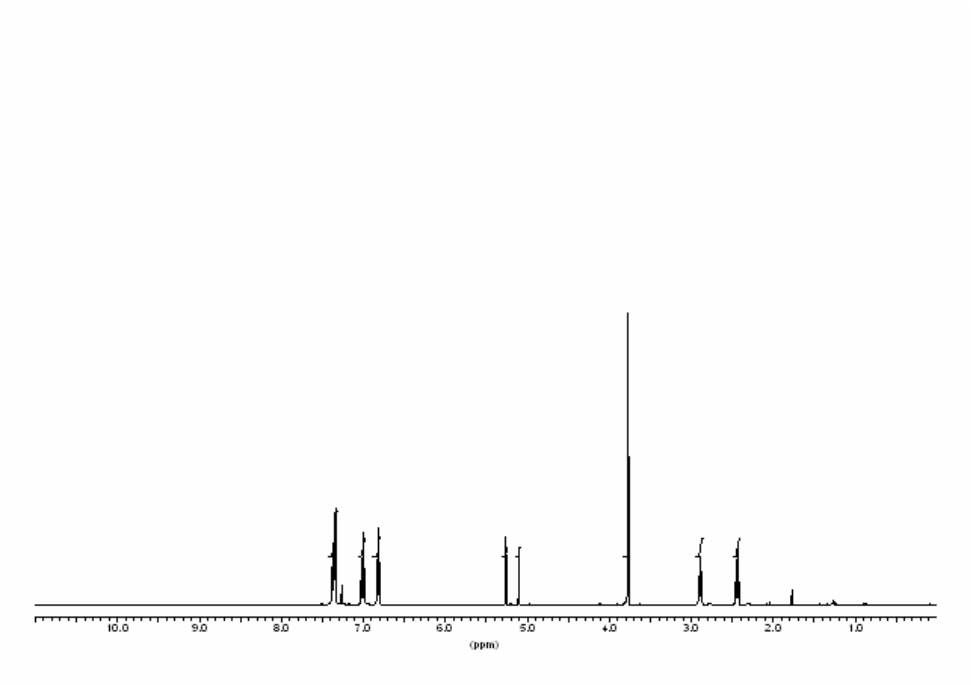


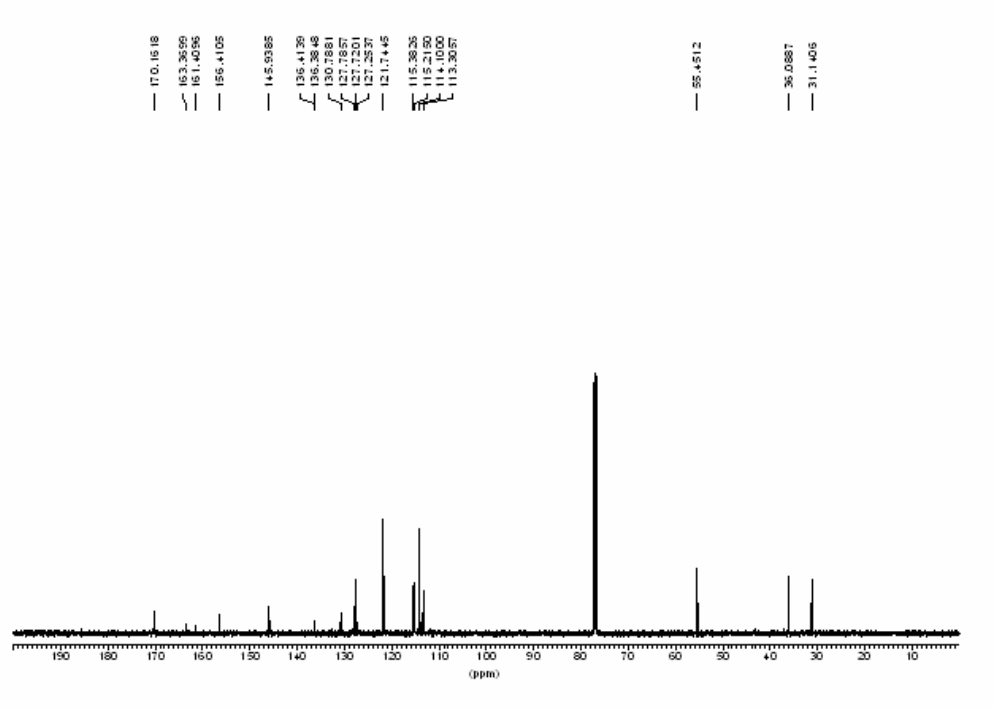




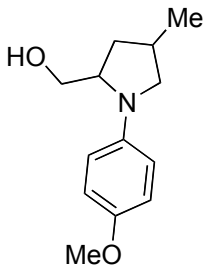
4-(4-Fluorophenyl)-*N*-(4-methoxyphenyl)-4-pentenamide (8o).

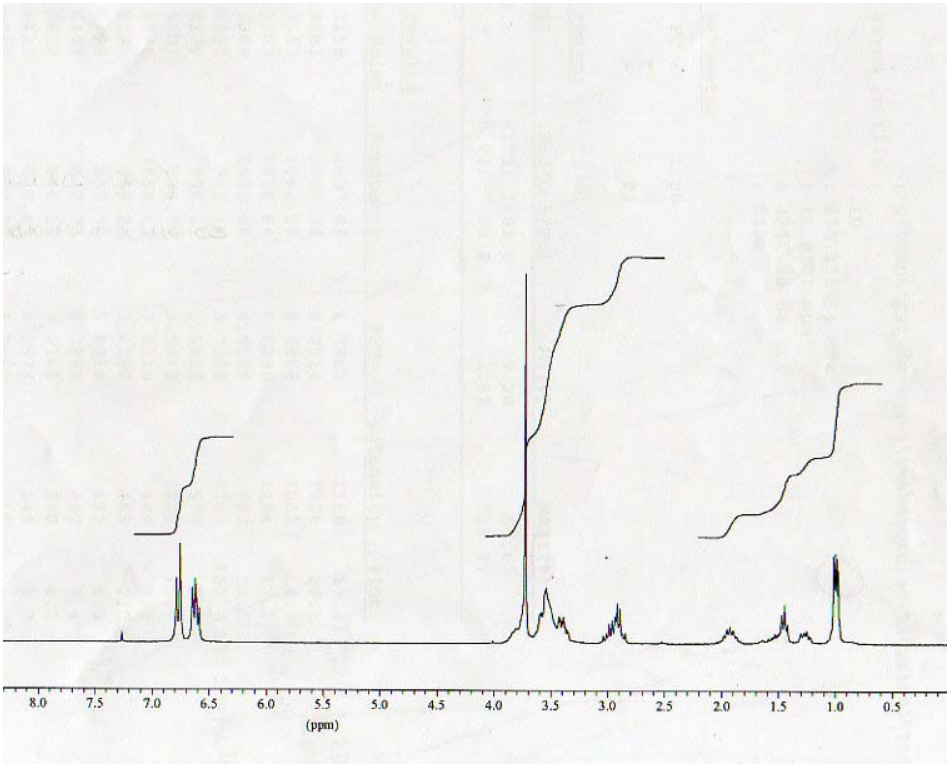


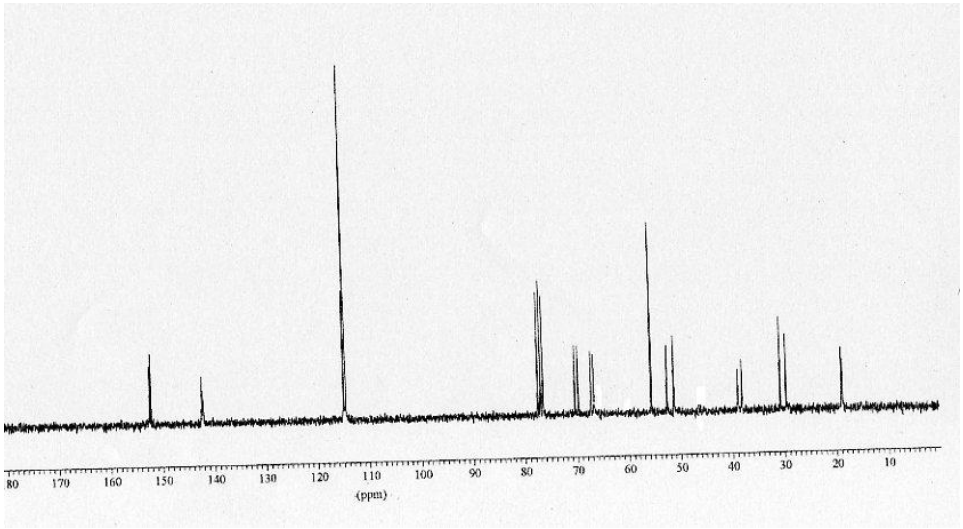




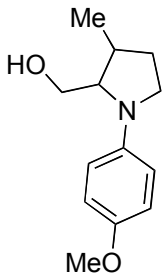
2-(Hydroxymethyl)- *N*-(4-methoxyphenyl)-4-methylpyrrolidine (9a).

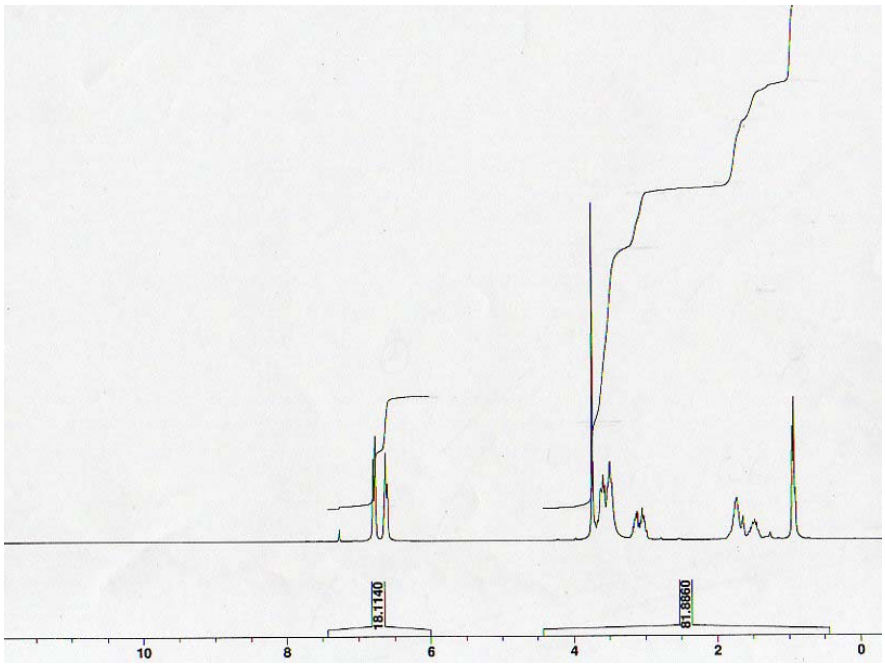


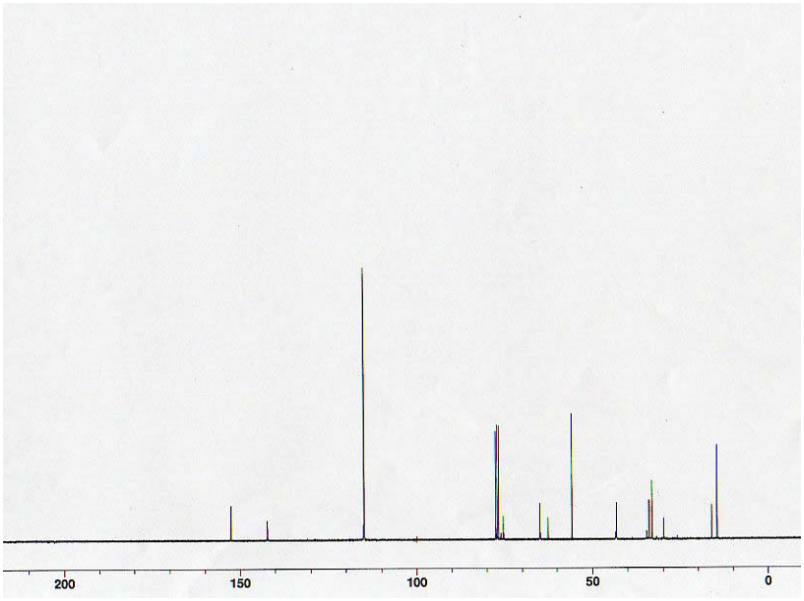




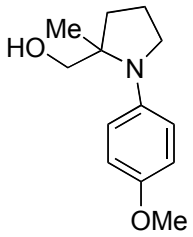
2-(Hydroxymethyl)- *N*-(4-methoxyphenyl)-3-methylpyrrolidine (9b).

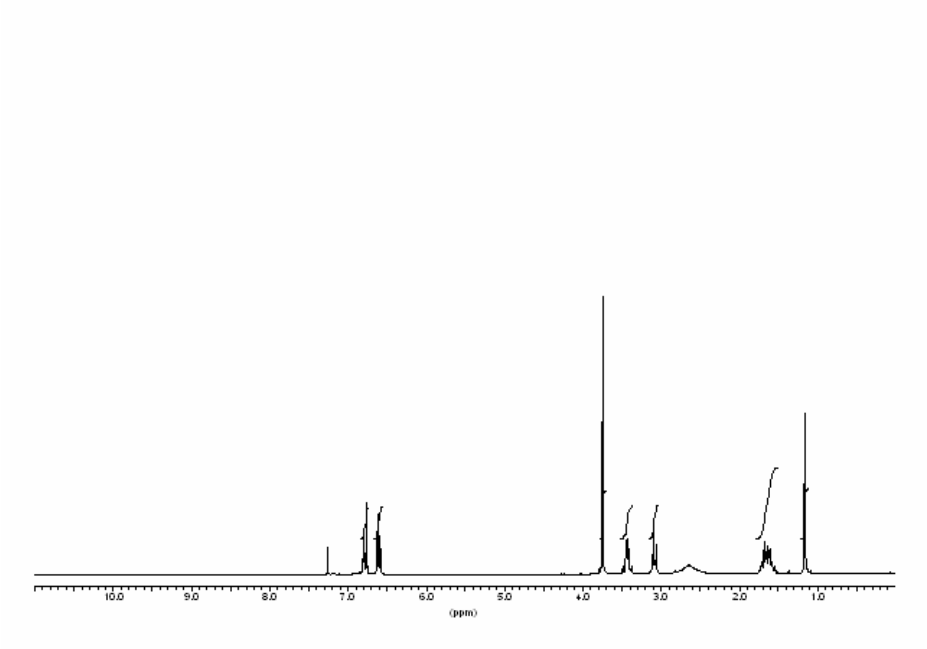


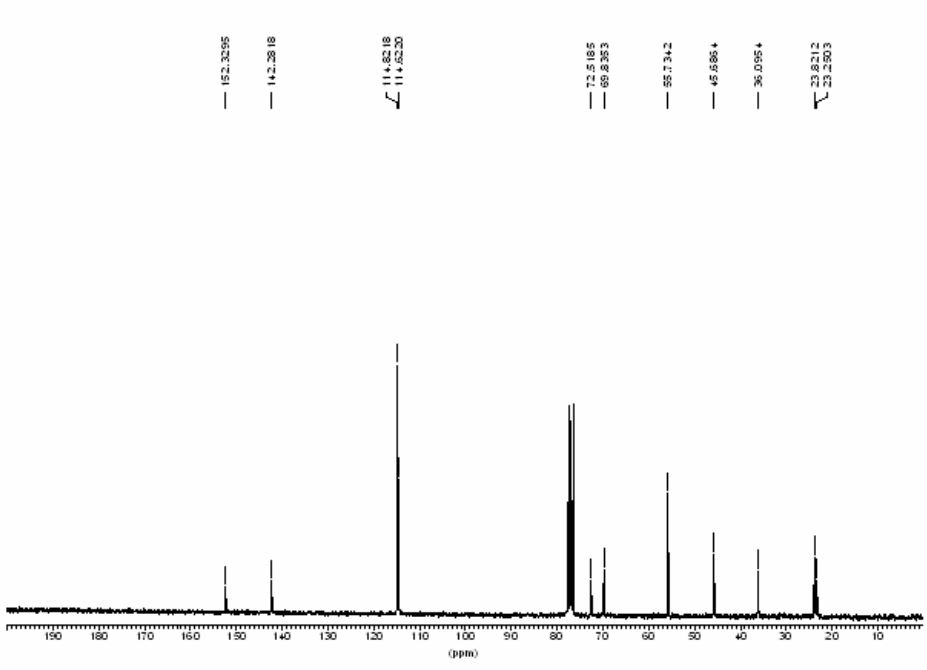




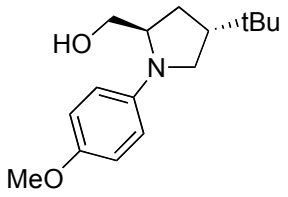
2-(Hydroxymethyl)-*N*-(4-methoxyphenyl)-2-methylpyrrolidine (9c).

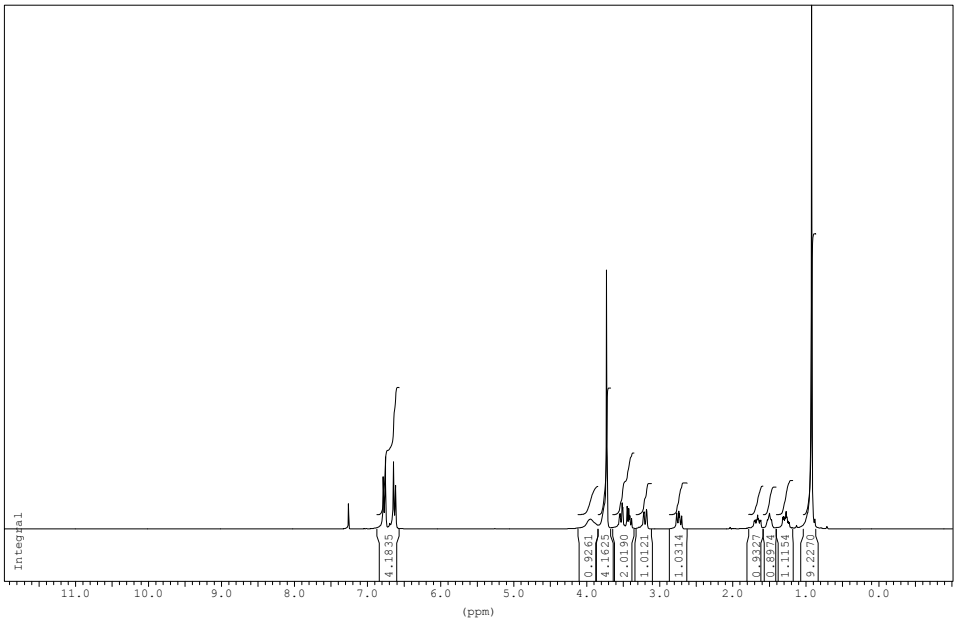


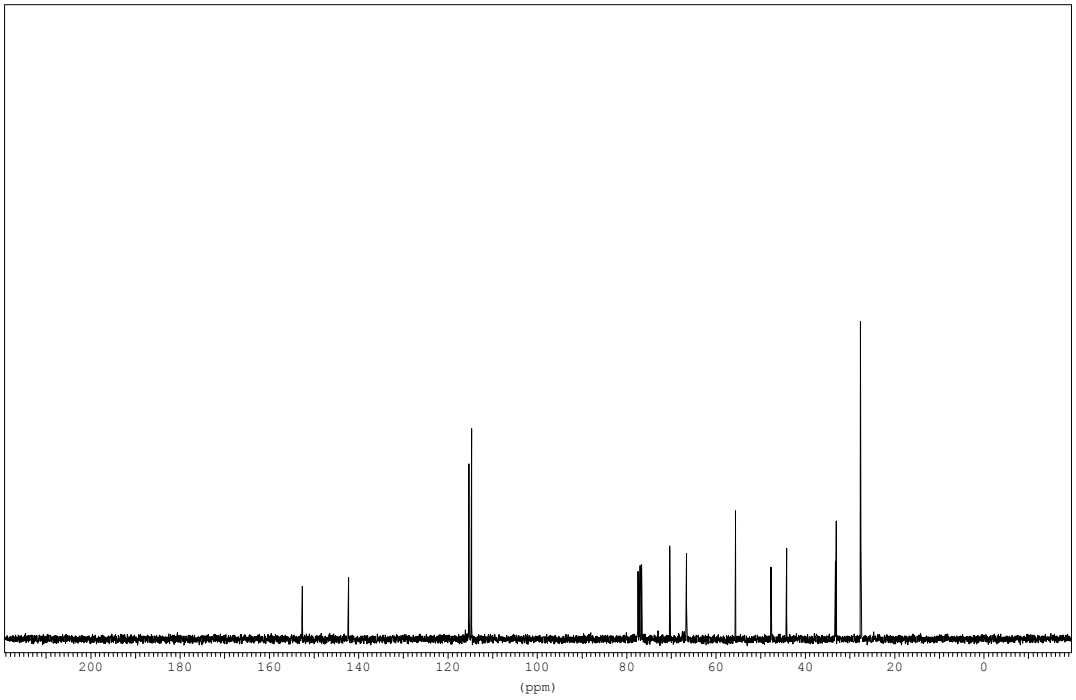




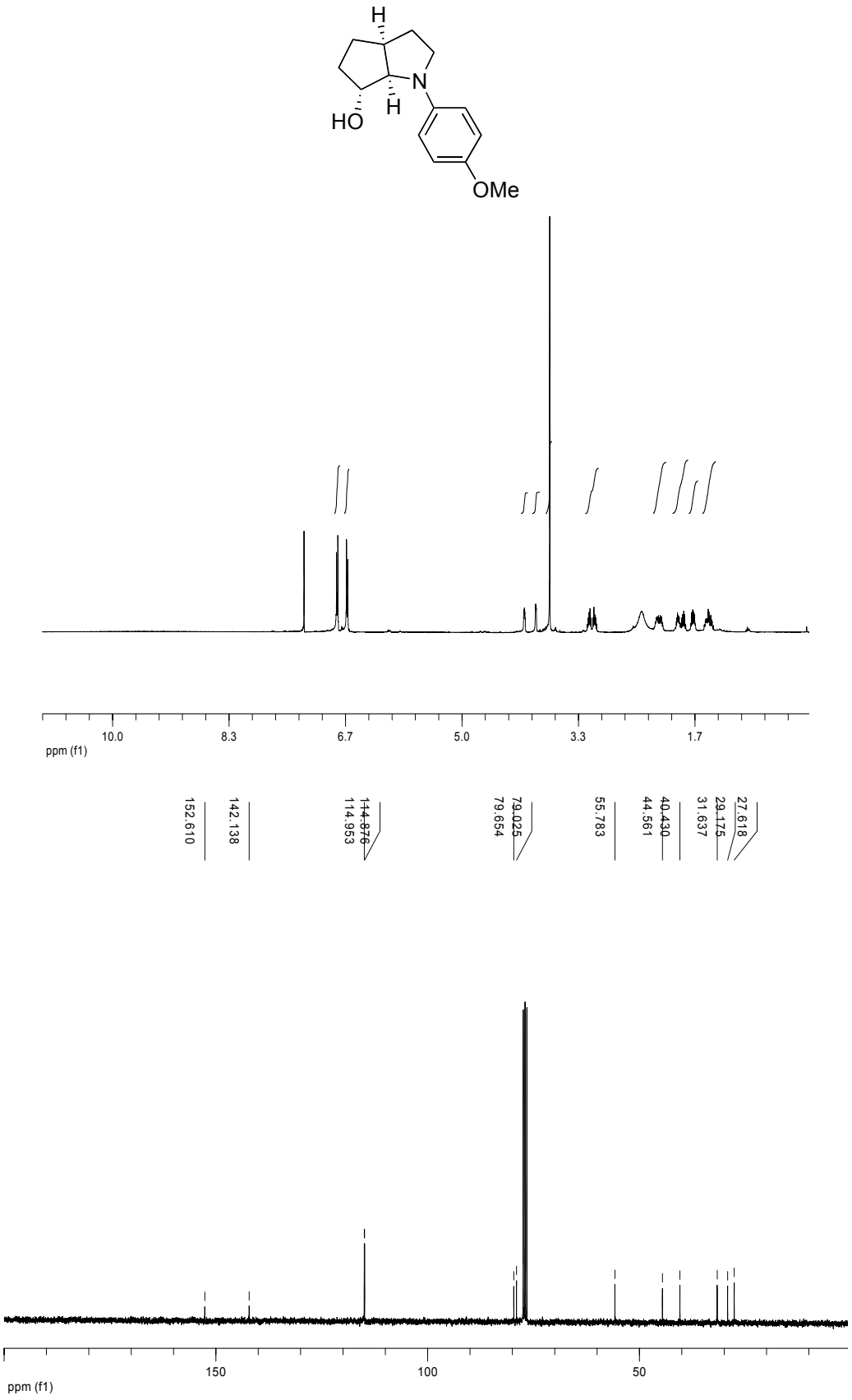
2-Hydroxymethyl-*N*-(4-methoxyphenyl)-4-*tert*butylpyrrolidine (9g).



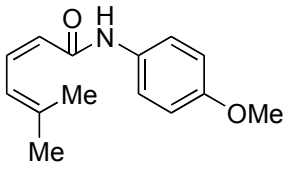


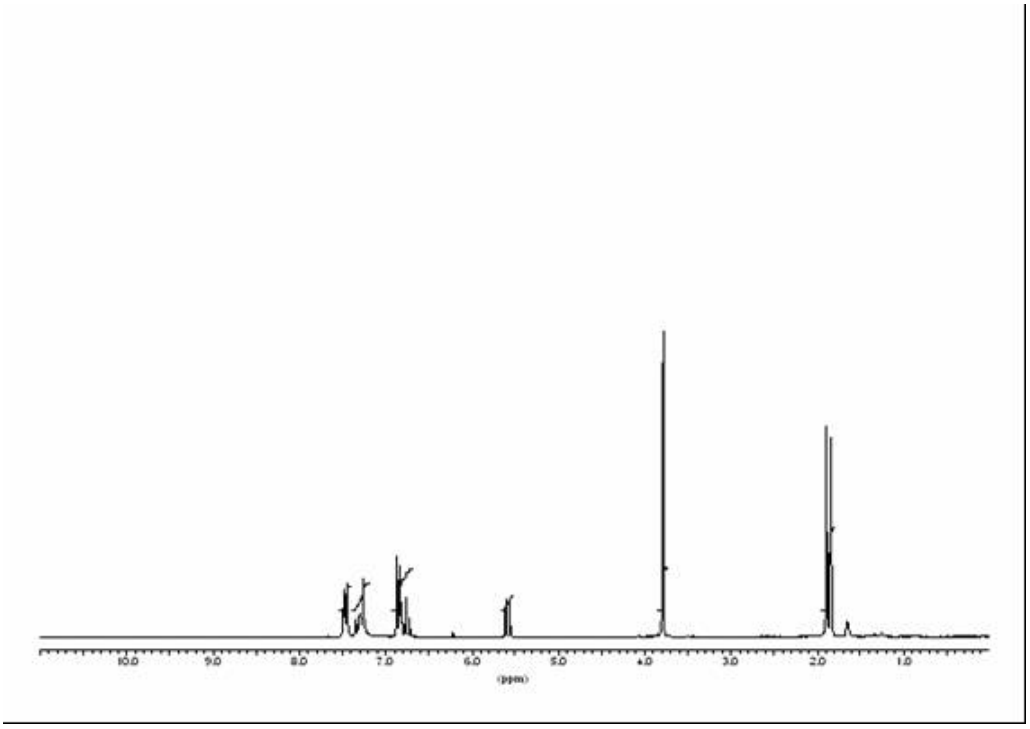


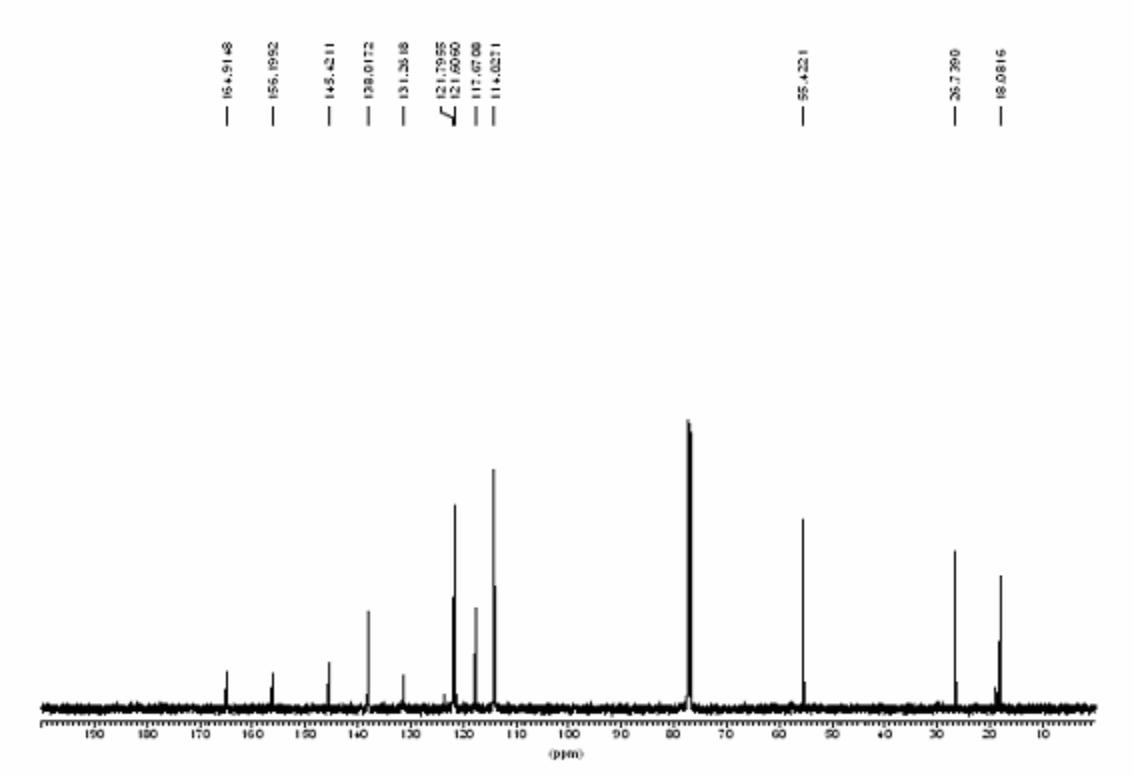
(3a*R*,6*R*,6a*R*)-N-(4-Methoxyphenyl)-octahydrocyclopenta[*b*]pyrrol-6-ol (9k)



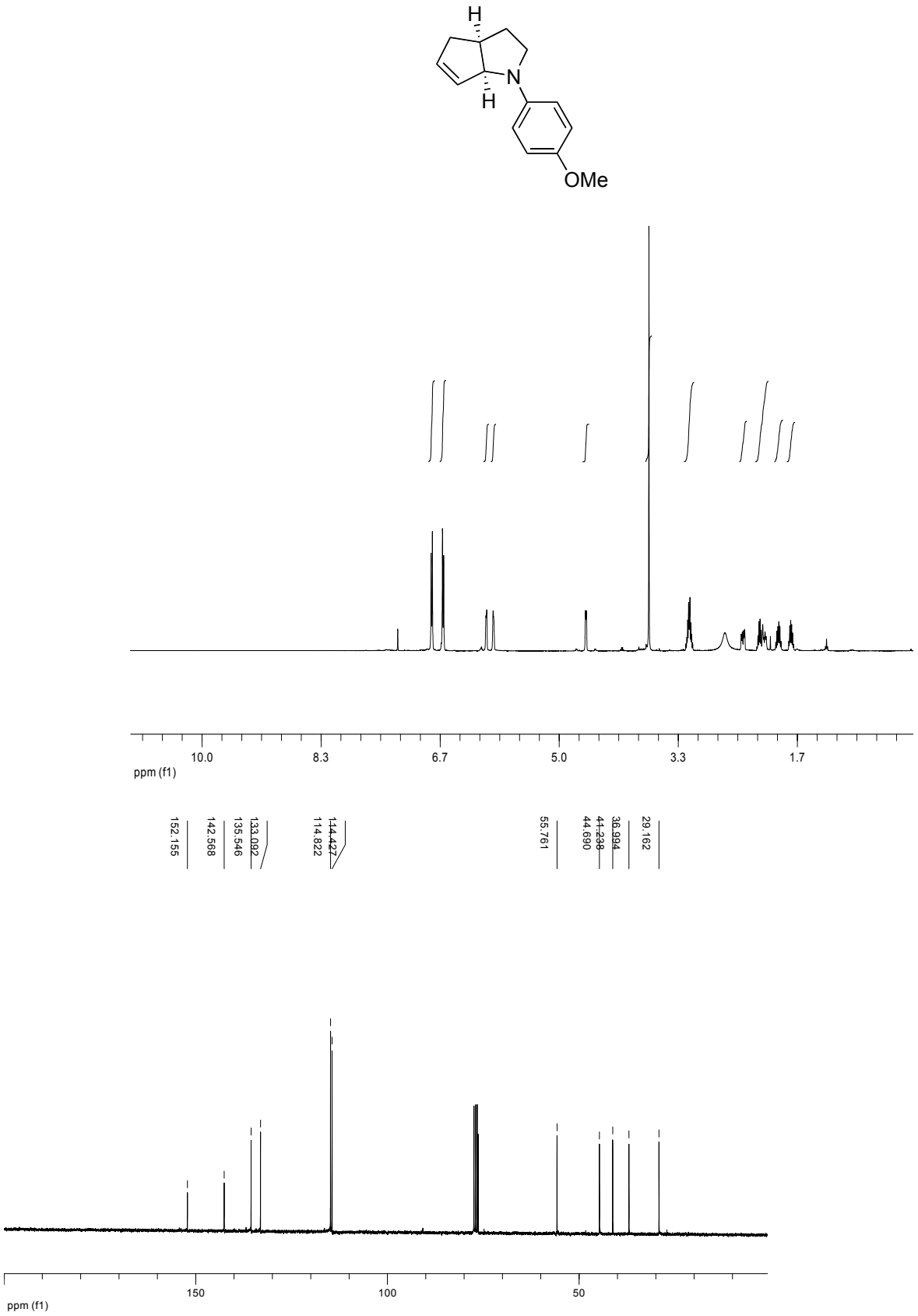
_N_-(4-Methoxyphenyl)-5-methylhexa-2,4-dienamide (10).



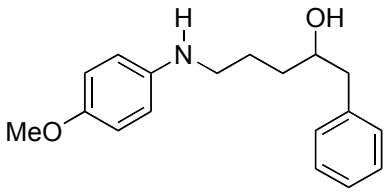


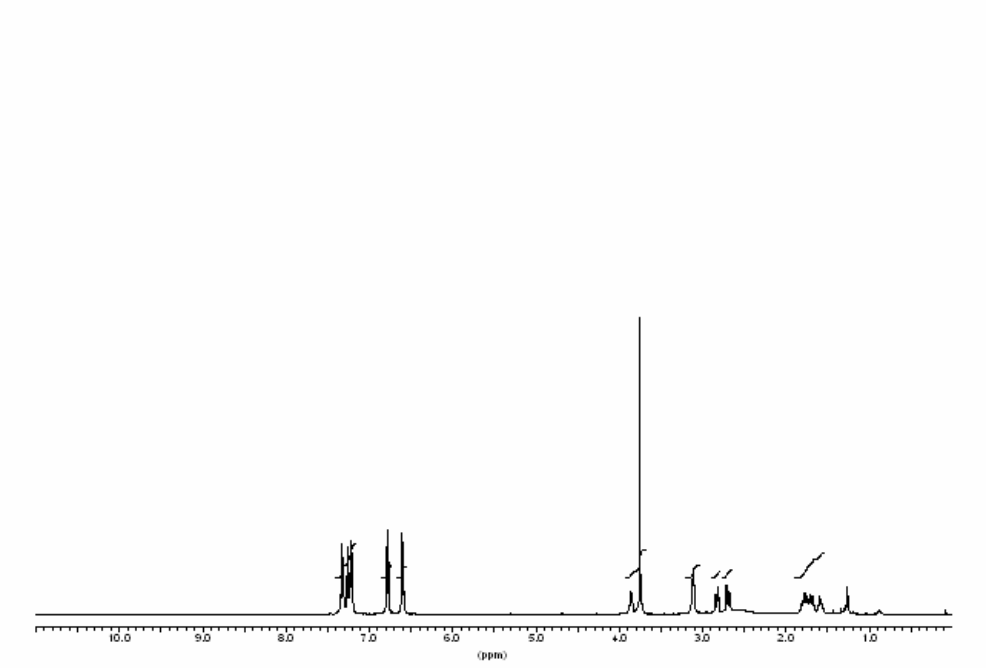


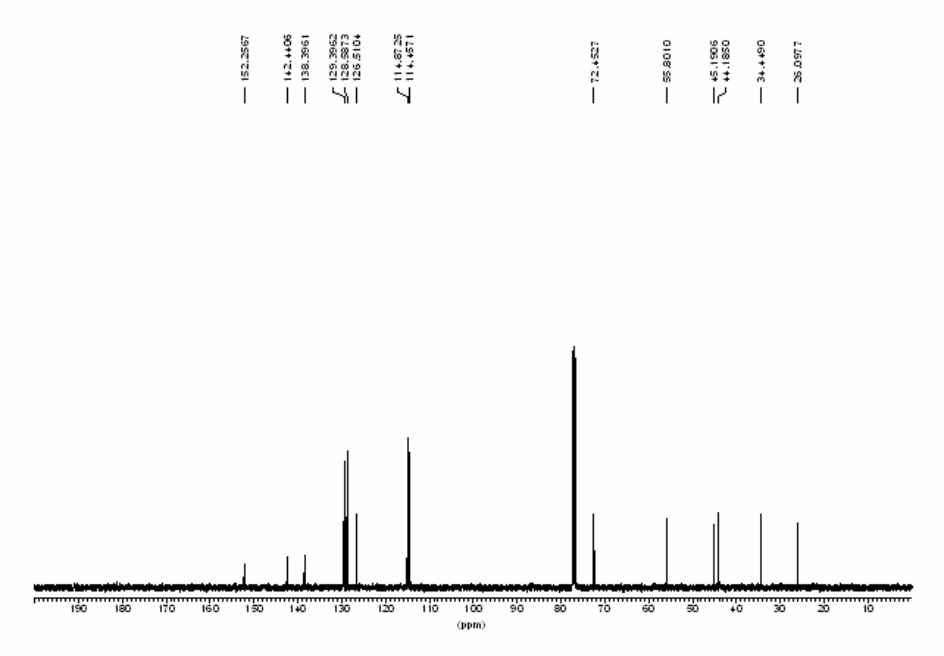
(3a*R*,6a*R*)-*N*-(4-Methoxyphenyl)-1,2,3,3a,4,6a-hexahydrocyclopenta[*b*]pyrrole (11)



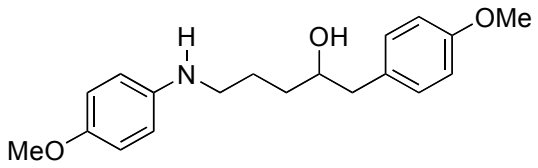
5-(4-Methoxyphenylamino)-1-phenyl-2-pentanol (12a).

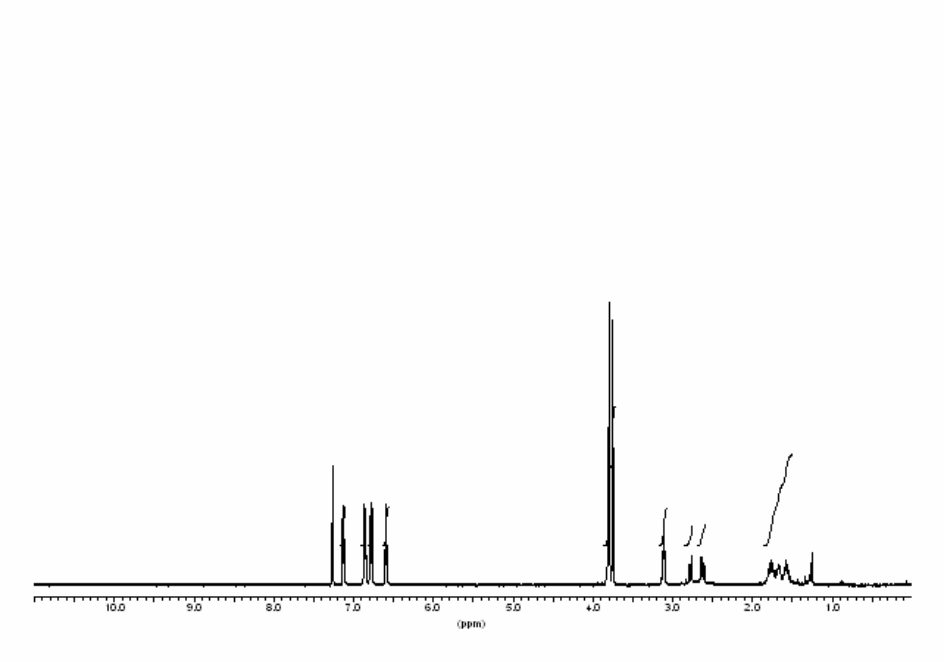


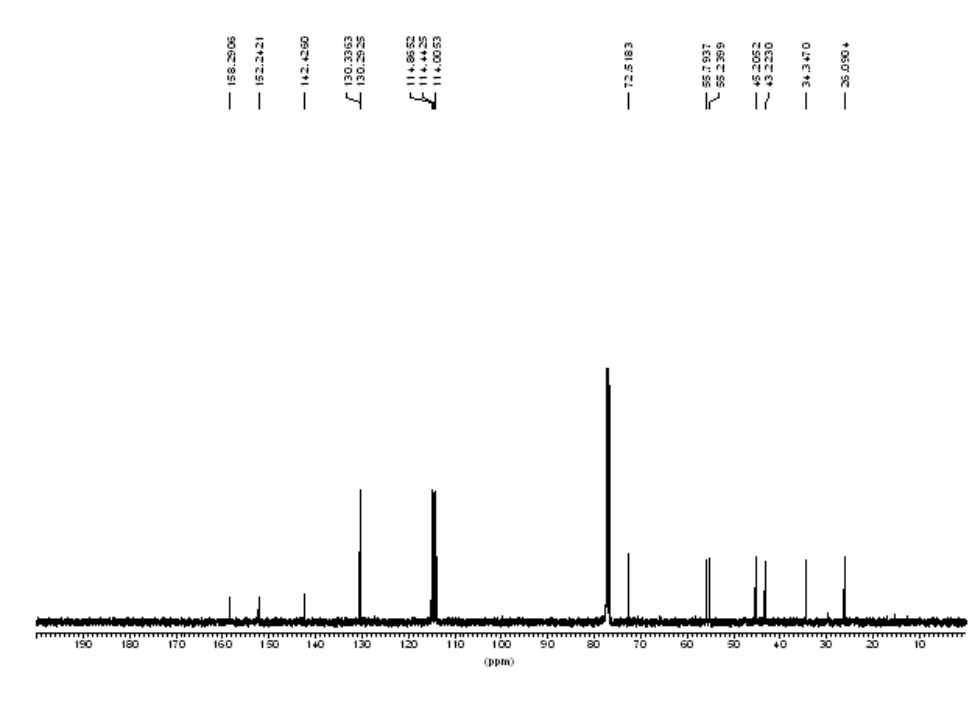




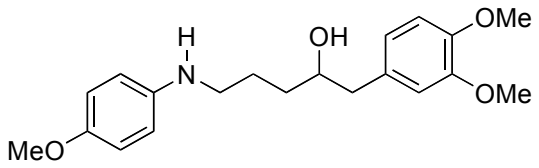
5-(4-Methoxyphenylamino)-1-(4-methoxyphenyl)-2-pentanol (12b).

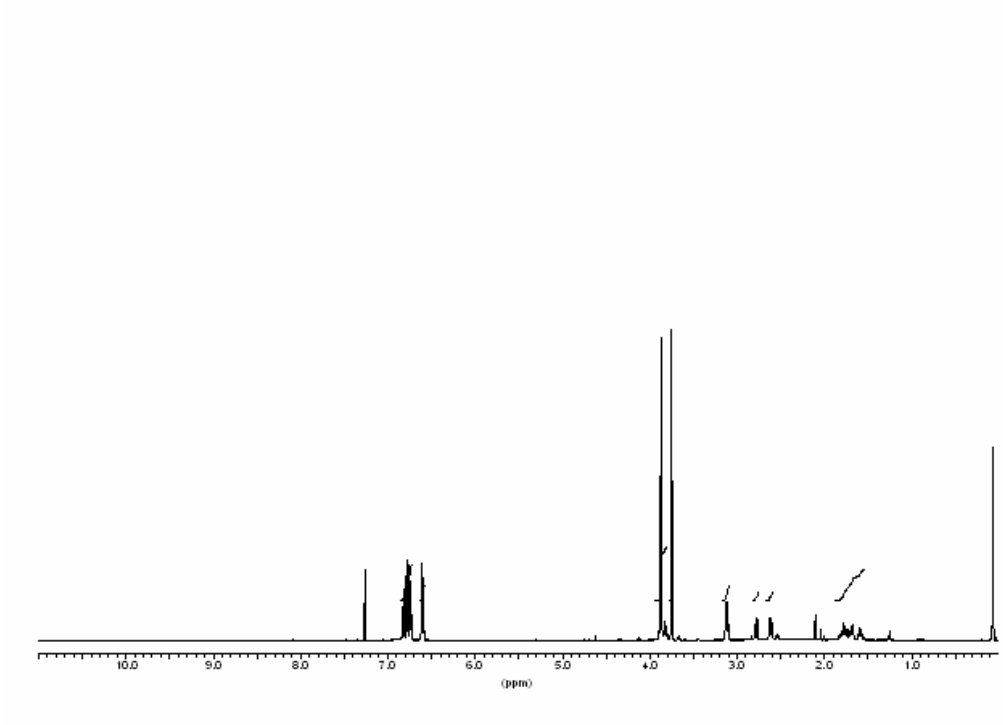


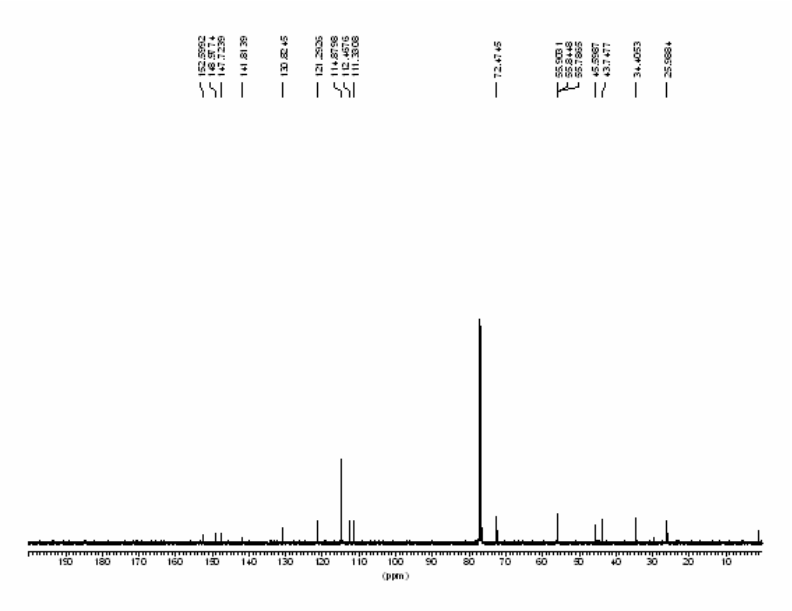




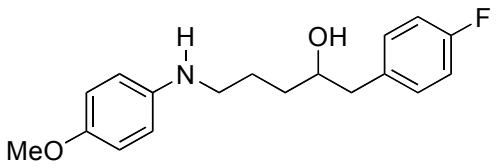
1-(3,4-Dimethoxyphenyl)-5-(4-methoxyphenylamino)-2-pentanol (12c).

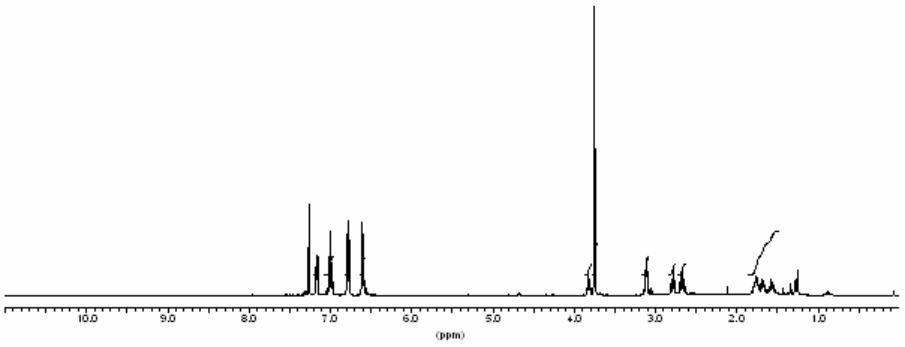


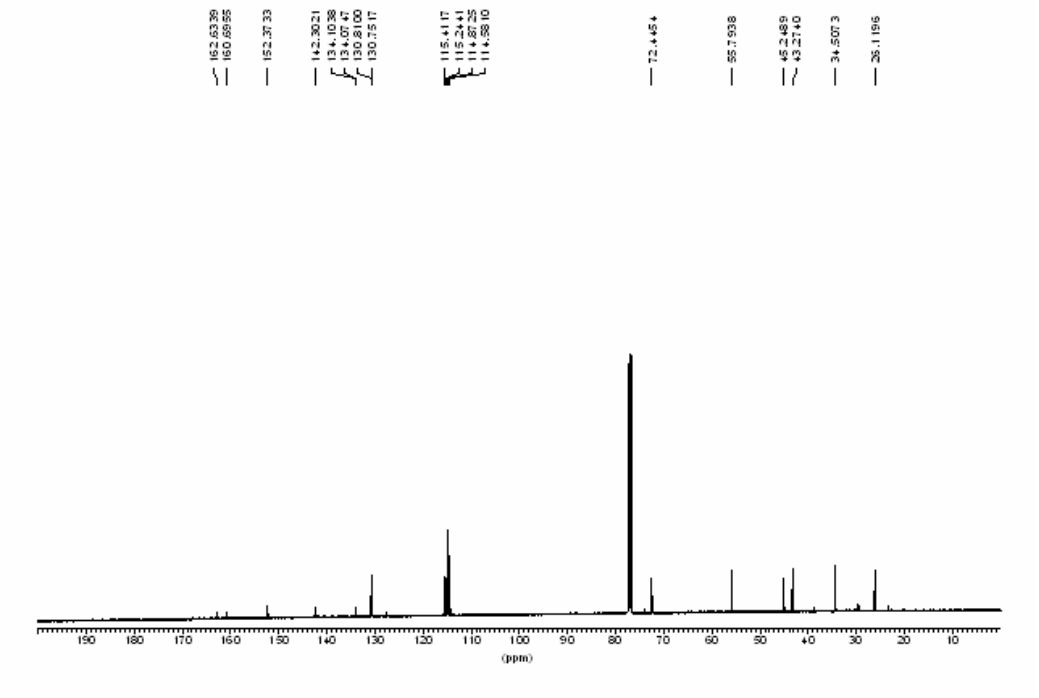




1-(4-Fluorophenyl)-5-(4-methoxyphenylamino)-2-pentanol (12d).


H
N
OH
F
MeO


10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)


162.6339
160.6955
152.3733
142.3021
134.1038
134.0747
130.8100
130.7517
115.4117
115.2441
114.8735
114.5810
72.4454
55.7938
45.2489
43.2740
34.5073
26.1196
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)