Solid-Supported Ruthenium(0): an Efficient Heterogeneous Catalyst for Hydration of Nitriles to Amides under Microwave Irradiation

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Methods and materials

Reagents of high quality were purchased from Sigma Aldrich. Amberlite® IRA 900 resin used as solid support (Chloride form) was purchased from Acros Organics. Silica gel (60-120 mesh size) for column chromatography was procured from Sd Fine-chem Ltd. Commercial reagents and solvents were of analytical grade and were purified by standard procedures prior to use. Thin layer chromatography was performed using pre coated silica gel plates 60 F254 (Merck) in UV light detector. GC-MS analysis was carried out on a Shimadzu (QP 2010) series GC-MS (Tokyo, Japan), equipped with a FID, AOC 5000 autosampler, DB-5MS capillary column (30 m × 0.25 mm i.d. with film thickness 0.25 µm).The X-ray diffraction (XRD) studies were carried on X-ray Spectrometer (Bruker AXS, D8 Advance) with Fek-Alpha radiation and magnetic measurements were made on a vibrating sample magnetometer (VSM) (155, PAR).^{1}H and ^{13}C NMR spectra were recorded using a Bruker Avance 300 spectrometer operating at 300 MHz (^{1}H) and 75 MHz (^{13}C). Spectra were recorded at 25 °C in $CDCl_3$ [residual $CHCl_3$ (δ_H 7.26 ppm) or $CDCl_3$ (δ_C 77.00 ppm), CD_3OD [residual CH_3 and OH (δ_H 3.33, 4.87 ppm) and CD_3OD (δ_c 48.01) , DMSO-d_6 (δ_H 2.50 ppm, δ_C 40.35) , pyridine-d_5 (δ_H 7.38, 7.75, 8.59 ppm, δ_C 123.90, 135.90, 150.04 ppm) [residual (as international standard] with TMS as internal standard. Chemical shifts were recorded in δ (ppm) relative to the TMS and NMR solvent signal, coupling constants (J) are given in Hz and multiplicities of signals are reported as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad singlet. All experiments were performed on CEM Discover focused microwave (2450 MHz, 300W). The temperature of reactions in monomode microwave experiments was measured by an inbuilt infrared temperature probe that determined the temperature on the surface of reaction flask. The sensor is attached in a feedback loop with an on-board microprocessor to control the rate of temperature rise. HRMS-ESI spectra were analyzed using micromass Q-TOF ultima spectrometer.

Preparation of SS-Ru catalyst

Formation of catalytic quantity borohydride exchanged amberlite resin

The solution of 100 mg of $NaBH_4$ in 30 ml of water was added in 4 g of Amberlite® IRA 900 (Chloride form) (Across, BE) in 100 ml flask. The mixture was stirred for 4h at room temperature. Then the resin was washed with water till pH became neutral and then with acetone to remove water from the solid surface. The resin beads (borohydride exchanged) were dried under reduced pressure.

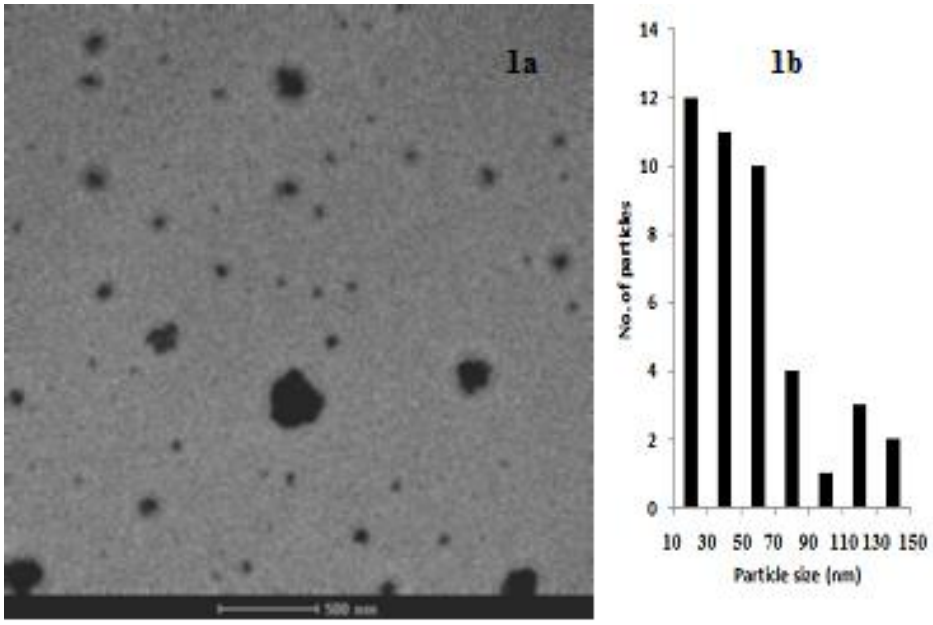
Procedure for SS-Ru (0) preparation

Initially, the amberlite IRA 900 chloride form resin as a solid surface was treated with catalytic quantity of $NaBH_4$ to exchange partial chloride ions by BH_4^- ions and then treated with $RuCl_3.H_2O$ in DMF at 100 ^oC for 1h. The white solid surface of resin soon found to be turned grey after complete impregnation of Ru. After complete immobilization of Ru over solid surface, the resin was washed with water, then with acetone and dried under reduced pressure. The SS-Ru(0) thus obtained could be useful in several catalytic reactions without loss of activity.

Characterization data (UV-Visible, TEM and XRD spectra) for SS-Ru(0)

(a) Transmission electron microscopy analysis of SS-Ru(0):

SS-Ru(0) catalyst was prepared as described in manuscript. To access the most metal particle dense surface of resin matrix, we follow grinding and water suspension method. 500 mg of SS-Ru (2.36 mg of Ru(0)) was grinded in a mortar and suspended in 50 ml of water. The mixture was left overnight to settle down the heavy inner part of the resin bead. The upper portion of the suspension was applied on carbon coated copper grid (Electron Microscopy Science, CF 300-Cu, CARBON FILM, on 300 squre mesh copper grid) and analyzed for Transmission electron microscopy (FEI Tecnoi G^{20}, 200KV, Netherlands). The TEM image, particle size distribution and EDX spectrum of of Ru(0) particles on solid support is as given below.



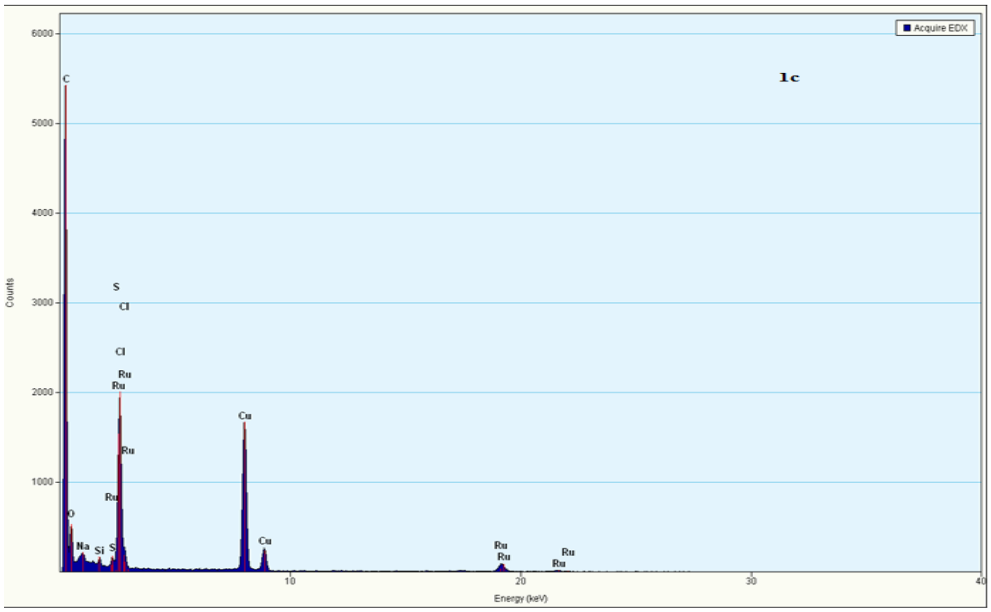


Figure. 1a; TEM image, 1b; particle size distribution, 1c; EDX spectrum of SS-Ru(0) catalyst

UV-Visible and XRD studies are as reported in previous paper.[1]

(b) XRD of SS-Ru after seven runs:

The XRD analysis of SS-Ru catalyst was performed after seven cycle (Figure 2). The XRD data was found to be same as previously reported data for the fresh SS-Ru(0) catalyst.[1]

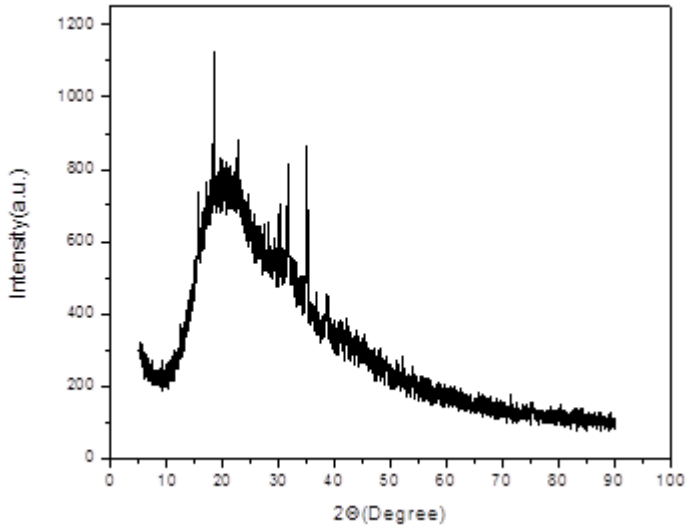


Figure 2. XRD specta of SS-Ru (0) after seven runs.

Typical experimental procedure for microwave-assisted hydration of organonitriles using SS-Ru catalyst

4-Bromo Benzamide (2a)

4- Bromobenzonitrile (100 mg, 0.55 mmol), water (8.0 ml) and SS-Ru (230 mg, 2 mol% Ru) were taken in an oven dried reaction tube equipped with screw cap. The reaction mixture was then irradiated in a microwave apparatus at 130 ^{o}C, 100W for 1 hour with a pressure of 80 psi. After cooling to ambient temperature in the microwave cavity the reaction mixture was extracted with ethyl acetate (5x20 ml). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. GCMS of crude sample give 100% 4-Bromo Benzamide (**2a**). The reaction mixture after washing with hexane yielded 4-Bromo Benzamide as white solid (94 mg, 85%).

Catalyst recovery from reaction mixture

The SS-Ru(0) catalyst remains settled down after the reaction. The crystallized amides can be separated by decantation or by extraction with ethylacetate.

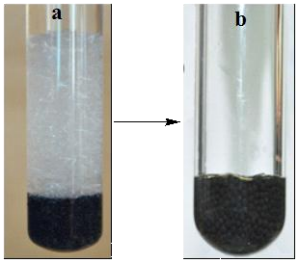
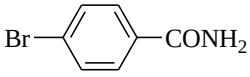


Figure a: SS-Ru(0) + 4-bromobenzamide, b: SS- Ru(0) catalyst recovered for reuse.

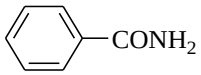
Synthesis and characterization data for the products of Table-1 and 2

4-Bromobenzamide (2a) (Table-1, entry 3)[2]



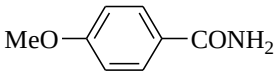
^{1}H NMR (300 MHz; CD_3OD) δ = 7.62-7.65 (d, *J* = 8.53 Hz, 2H), 7.78-7.81 (d, *J* = 8.48 Hz, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 127.85, 130.54 (2C), 133.22 (2C), 134.58, 171.72. HREIMS C_7H_6BrNO calculated 199.9633 obsvd 199.9619.

Benzamide (2b) (Table-2, entry 1)[2]



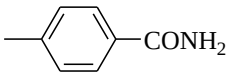
Prepared as described for 4-bromobenzonitrile starting from **1b** (100 mg, 0.970 mmol) gave, after washing with hexane **2b** as white solid (101 mg, 86%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.43-7.48 (m, 2H), 7.51-7.57 (m, 1H), 7.87-7.91 (m, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 129.38 (2C), 130.26 (2C), 133.67, 135.68, 173.18. HREIMS C_7H_7NO calculated 122.0528 obsvd 122.0509.

4-Methoxybenzamide (2c) (Table-2, entry 2) [3], [4]



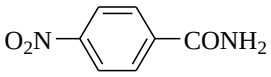
Prepared as described for 4-bromobenzonitrile starting from **1c** (100 mg, 0.752 mmol) gave, after column chromatography (Hexane:EtOAc:: 6:4) **2c** as white solid (94 mg, 83%); ^{1}H NMR (300 MHz; CD_3OD) δ = 3.85 (s, 3H), 6.96-6.99 (d, *J* = 8.87 Hz, 2H), 7.84-7.87 (d, *J* = 8.85 Hz, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 56.38, 115.13 (2C), 133.67, 135.68, 173.18. HREIMS $C_8H_9NO_2$ calculated 152.0633 obsvd 152.0625.

4-Methylbenzamide (2d) (Table-2, entry 3) [3], [4]



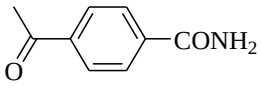
Prepared as described for 4-bromobenzonitrile starting from **1d** (100 mg, 0.854 mmol) gave, after (Hexane:EtOAc:: 6:4) **2d** as white solid (101 mg, 86%); ^{1}H NMR (300 MHz; CD_3OD) δ = 2.38 (s, 3H), 7.25-7.27 (d, *J* = 7.98 Hz, 2H), 7.76-7.80 (d, *J* = 8.12 Hz, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 20.47, 127.73 (2C), 129.13 (2C), 131.05, 142.66, 171.45. HREIMS C_8H_9NO calculated 136.0684 obsvd 136.0669.

4-Nitrobenzamide (2e) (Table-2, entry 4) [2]



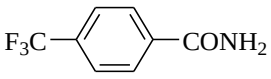
Prepared as described for 4-bromobenzonitrile starting from **1e** (100 mg, 0.676 mmol) gave, after washing with hexane **2e** as white solid (99 mg, 88%); ^{1}H NMR (300 MHz; CD_3OD) δ = 8.08-8.11 (d, *J* = 11.08 Hz , 2H), 8.32-8.35 (d, *J* = 8.87 Hz , 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 125.06 (2C), 130.47 (2C), 141.37, 151.69, 170.62. HREIMS $C_7H_6N_2O_3$ calculated 167.0378 obsvd 167.0329.

4-Acetylbenzamide (2f) (Table-2, entry 5) [4]



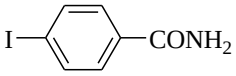
Prepared as described for 4-bromobenzonitrile starting from **1f** (100 mg, 0.690 mmol) gave, after column chromatography with (Hexane:EtOAc:: 6:4) **2f** as white solid (89 mg, 79%); ^{1}H NMR (300 MHz; C_5D_5N) δ = 3.67 (s, 3H), 9.25-9.27 (d, *J* = 8.28 Hz, 2H), 9.53-9.56 (d, *J* = 8.40 Hz, 2H); ^{13}C NMR (75 MHz; C_5D_5N) δ = 28.05, 129.79, 130.01, 140.66, 140.80, 170.19, 198.73. HREIMS $C_9H_9NO_2$ calculated 164.0633 obsvd 164.0651.

4-(Trifluoromethyl)benzamide (2g) (Table-2, entry 6)[4]



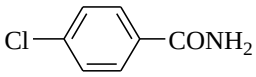
Prepared as described for 4-bromobenzonitrile starting from **1g** (100 mg, 0.585 mmol) gave, after column chromatography with (Hexane:EtOAc:: 6:4) **2g** as white solid (94 mg, 85%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.60-7.79 (d, *J* = 8.16 Hz, 2H), 8.04-8.06 (d, *J* = 8.60 Hz, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 123.68, 126.64 (2C), 129.58 (2C), 134.25, 139.00, 171.03. HREIMS $C_8H_6F_3NO$ calculated 190.0401 obsvd 190.0383.

4-Iodobenzamide (2h) (Table-2, entry 7)[2]



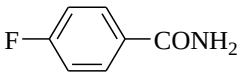
Prepared as described for 4-bromobenzonitrile starting from **1h** (100 mg, 0.437 mmol) gave, after column chromatography with (Hexane:EtOAc:: 6:4) **2h** as white solid (91 mg, 84%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.62-7.65 (d, *J* =8.42, 2H), 7.84-7.87 (d, *J* =8.44, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 99.71, 130.55, 134.79, 139.08, 171.68. HREIMS C_7H_6INO calculated 247.9494 obsvd 247.9475.

4-Chlorobenzamide (2i) (Table-2, entry 8) [3]



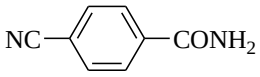
Prepared as described for 4-bromobenzonitrile starting from **1i** (100 mg, 0.730 mmol) after washing with Hexane gave **2i** as white solid (89 mg, 79%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.44-7.48 (d, *J* = 13.45 Hz , 2H), 7.84-7.89 (d, *J* = 13.45 Hz , 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 129.85 (2C), 130.54 (2C), 133.78, 139.17, 171.31. HREIMS C_7H_6ClNO calculated 156.0138 obsvd 156.0121.

4-fluorobenzamide (2j) (Table-2, entry 9)



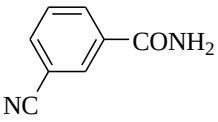
Prepared as described for 4-bromobenzonitrile starting from **1j** (100 mg, 0.826 mmol) after washing with Hexane gave **2j** as white solid (98 mg, 86%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.15-7.20 (m, 2H), 7.91-7.96 (m, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 113.66, 113.96, 128.74 (2C) 162.19, 165.51, 168.67. HREIMS C_7H_6FNO calculated 140.0433 obsvd 140.0421.

4-Cyanobenzamide (2k) (Table-2, entry 10)



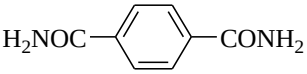
Prepared as described for 4-bromobenzonitrile starting from **1k** (100 mg, 0.781 mmol) after column chromatography with (Hexane:EtOAc:: 6:4) **2k** as white solid (88 mg, 77%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.84-7.87 (m, *J* =8.47, 2H), 8.01-8.04 (d, *J* =8.46, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 116.74, 119.54, 129.98, 133.98, 139.80, 170.87. HREIMS $C_8H_6N_2O$ calculated 147.0480 obsvd 147.0449.

3-cyanobenzamide (2l) (Table-2, entry 11) [2]



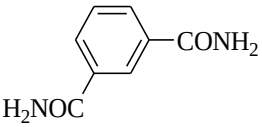
Prepared as described for 4-bromobenzonitrile starting from **1l** (100 mg, 0.781 mmol) after column chromatography with (Hexane:EtOAc:: 6:4) **2l** as white solid (83 mg, 73%); ^{1}H NMR (300 MHz; DMSO-d_6) δ = 7.66-7.71 (t, *J* =7.82, 1H), 7.99-8.01 (d, *J* =7.74, 1H), 8.16-8.19 (d, *J* =9.03, 1H), 8.28 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6) δ = 111.47, 118.39, 129.74, 131.08, 132.23, 134.74, 135.30, 166.04. HREIMS $C_8H_6N_2O$ calculated 147.0480 obsvd 147.0461.

Terephthalimide (2m) (Table-2, entry 12)[5]



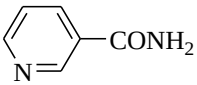
The hydration of **1m** (100 mg, 0.781 mmol) at 150^{o}C for 2h followed by drying the solvent under reduced pressure and washing with CH_2Cl_2 yielded **2m** as white solid (102 mg, 80%); ^{1}H NMR (300 MHz; DMSO-d_6) δ = 7.53 (s, 2H), 7.93 (s, 4H), 8.10 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6) δ = 127.68, 136.86, 167.60. HREIMS $C_8H_8N_2O_2$ calculated 165.0586 obsvd 165.0569.

Isophthalimide (2n) (Table-2, entry 13)



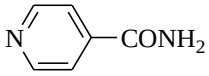
Prepared as described for **2m** after washing with CH_2Cl_2 gave **2n** as white solid (105 mg, 82%); ^{1}H NMR (300 MHz; DMSO-d_6) δ = 7.49-7.56 (m, 4H), 7.97-8.00 (m, 3H), 8.37 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6) δ = 126.84, 128.30, 130.09, 134.45, 167.58. HREIMS $C_8H_8N_2O_2$ calculated 165.0586 obsvd 165.0574.

Nicotinamide (2o) (Table-2, entry 14)[3]



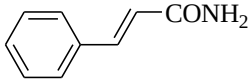
Prepared as described for 4-bromobenzonitrile starting from **1o** (100 mg, 0.961 mmol) after washing with Hexane afforded **2o** as white solid (87 mg, 84%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.52-7.57 (m, 1H), 8.28-8.31 (m, 1H), 8.68-8.70 (m, 1H), 9.04-9.05 (m, 1H); ^{13}C NMR (75 MHz; CD_3OD) δ = 125.55, 131.85, 137.76, 149.92, 153.28, 170.28. HREIMS $C_6H_6N_2O$ calculated 123.0480 obsvd 123.0455.

Isonicotinamide (2p) (Table-2, entry 15)



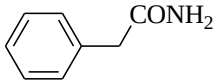
Prepared as described for 4-bromobenzonitrile starting from **1p** (100 mg, 0.961 mmol) after washing with Hexane gave **2p** as white solid (103 mg, 88%); ^{1}H NMR (300 MHz; CD_3OD) δ = 7.82-7.84 (m, 2H), 8.70-8.72 (m, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 122.11, 142.44, 149.97, 168.75, 139.80, 170.87. HREIMS $C_6H_6N_2O$ calculated 123.0480 obsvd 123.0455.

(E)-cinnamamide (2q) (Table-2, entry 16) [3], [4a]



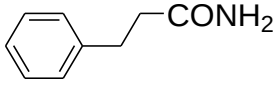
Prepared as described for 4-bromobenzonitrile starting from **1q** (100 mg, 0.775 mmol) after column chromatography with (Hexane:EtOAc:: 1:1) gave **2q** as white solid (92 mg, 80%); ^{1}H NMR (300 MHz; CD_3OD) δ = 6.63-6.69 (d, *J*= 15.89 Hz, 1H), 7.36-7.40 (m, 3H), 7.54-7.60 (m, 3H); ^{13}C NMR (75 MHz; CD_3OD) δ = 120.43, 127.54 (2C), 128.64 (2C), 129.95, 135.16, 141.75, 144.33, 169.98. HREIMS C_9H_9NO calculated 148.0684 obsvd 148.0205.

Phenylacetamide (2r) (Table-2, entry 17)



Prepared as described for 4-bromobenzonitrile starting from **1r** (100 mg, 0.854 mmol) after column chromatography with (Hexane:EtOAc:: 6:4) gave **2r** as white solid (98 mg, 85%); ^{1}H NMR (300 MHz; CD_3OD) δ = 3.52 (s, 2H), 7.29-7.32 (m, 5H); ^{13}C NMR (75 MHz; CD_3OD) δ = 42.43, 126.91, 128.57 (2C) 129.16 (2C), 135.92, 175.97. HREIMS C_8H_9NO calculated 136.0684 obsvd 136.0659.

Phenylpropionamide (2s) (Table-2, entry 18)[3]



Prepared as described for 4-bromobenzonitrile starting from **1s** (100 mg, 0.854 mmol) for 2h after washing with Hexane gave **2s** as white solid (82 mg, 72%);^{1}H NMR (300 MHz; CD_3OD) δ = 2.48-2.51 (t, *J*= 7.40, 2H), 2.89-2.94 (t, *J*=7.43, 2H), 7.15-7.31 (m, 5H); ^{13}C NMR (75 MHz; CD_3OD) δ = 33.23, 38.83, 127.65, 129.82, 142.70, 179.65. HREIMS $C_8H_{11}NO$ calculated 150.0841 obsvd 150.0825.

Propionamide (2t) (Table-2, entry 19)[3]

$CH_3CH_2CONH_2$ Prepared by reacting (100 mg, 1.817 mmol) of **1t** extraction with CH_2Cl_2 (5*20ml) followed by washing with hexane gave **2t** as white solid (79 mg, 60%); ^{1}H NMR (300 MHz; CD_3OD) δ = 1.11-1.16 (t, *J* =7.65, 3H), 2.19-2.27 (quartet, *J* =7.65, 2H); ^{13}C NMR (75 MHz; CD_3OD) δ = 10.82, 30.07, 180.54. HREIMS C_3H_7NO calculated 74.0528 obsvd 74.0517.

References

[1] P. Das, N. Aggarwal and N. R. Guha, *Tetrahedron Lett*., 2013, **54**, 2924.

[2] The compounds are commercially available.

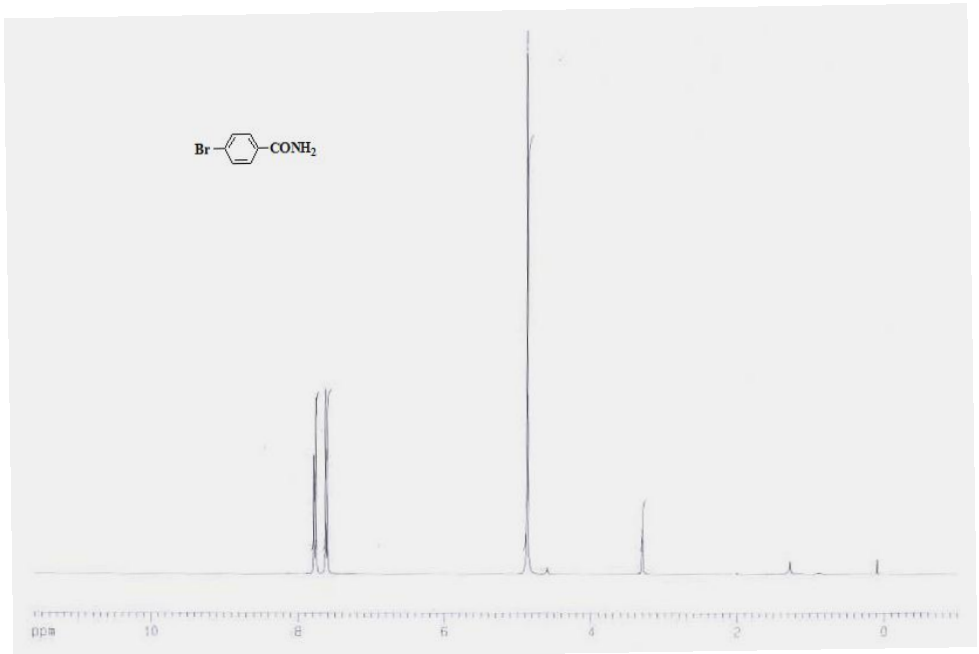
[3] (a) R. G. Alaverz, A. E. D. Alaverz, J. Borge, P. Crochet and V. Cadierno, Organometallics, 2012, **31**, 6482; (b) N. A. Owston, A. J. Parker and J. M. J. Williams, *Org. Lett.*, 2007, **9**, 73.

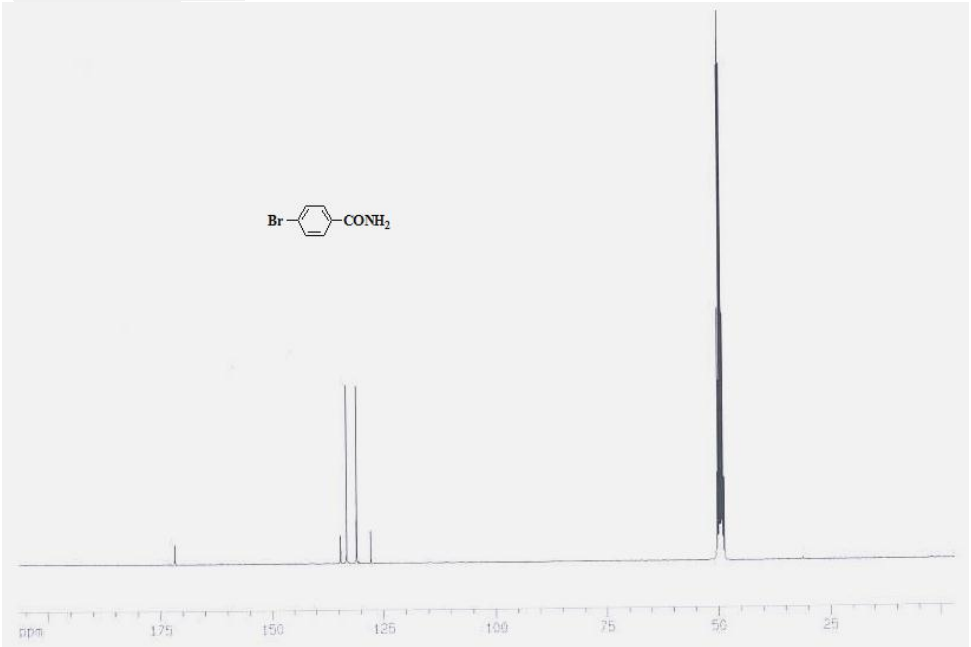
[4] (a) A. Schnyder, M. Beller, G. Mehltretter, T. Nsenda, M. Studer and A. F. Indolese, *J. Org. Chem.*, 2001, **66**, 4311; (b) J. Lee, M. Kim, S. Chang and H. Y. Lee, *Org. Lett.*, 2009, **11**, 5598.

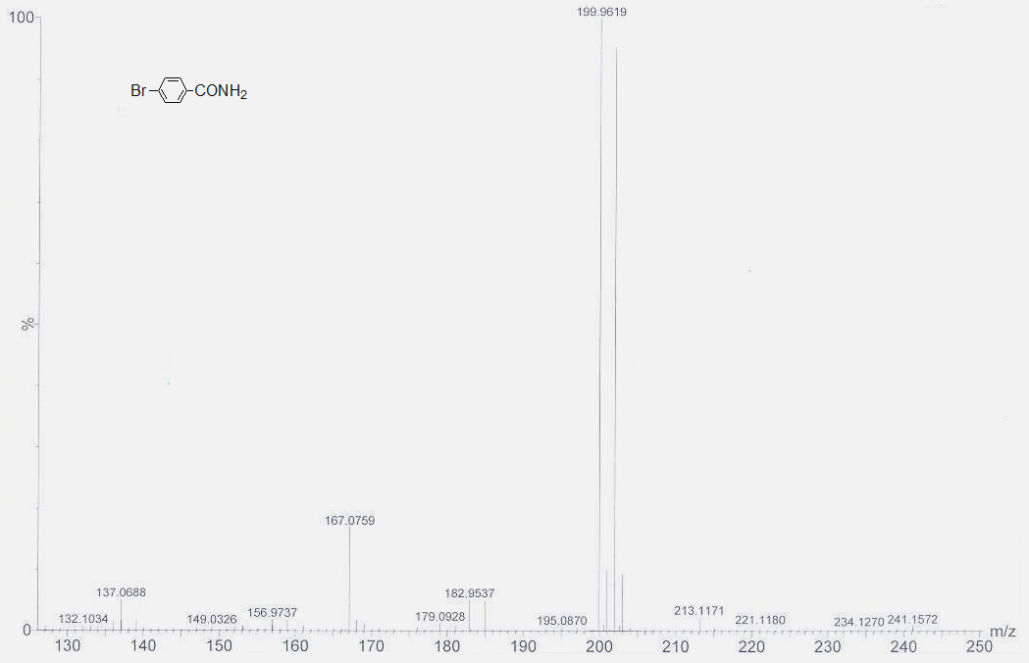
[5] T. Tu, Z. Wang, Z. Liu, X. Feng and Q. Wang, *Green Chem*., 2012, **14**, 921.

^{1}H, ^{13}C NMR and HRMS Spectra for the amides obtained from hydration of organonitriles

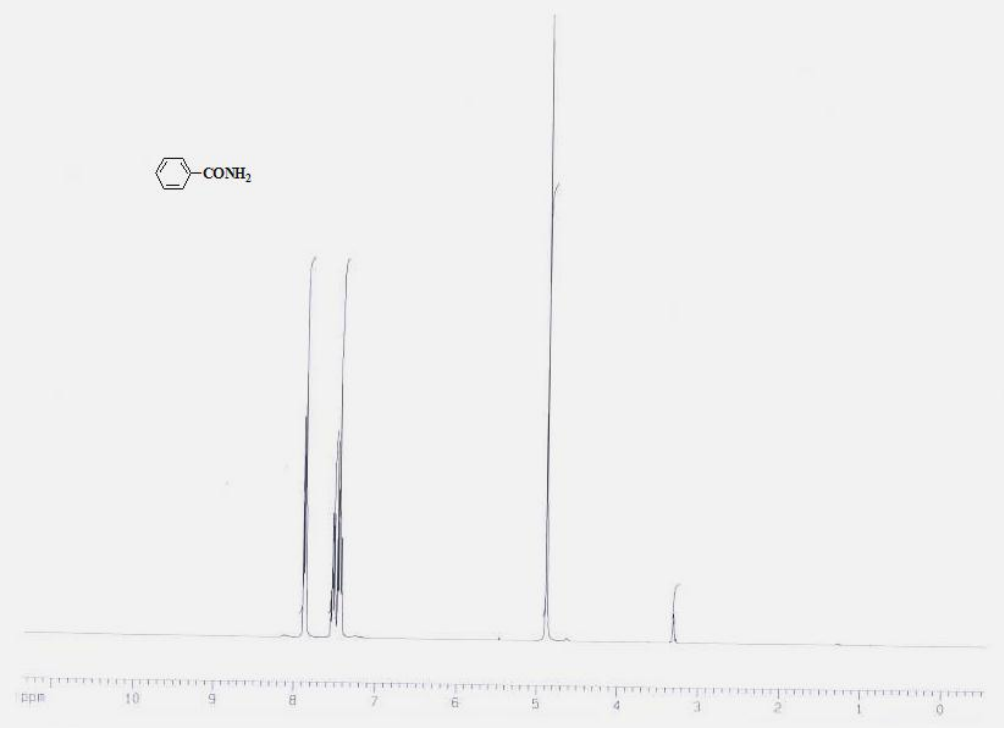
4-bromobenzamide (2a)

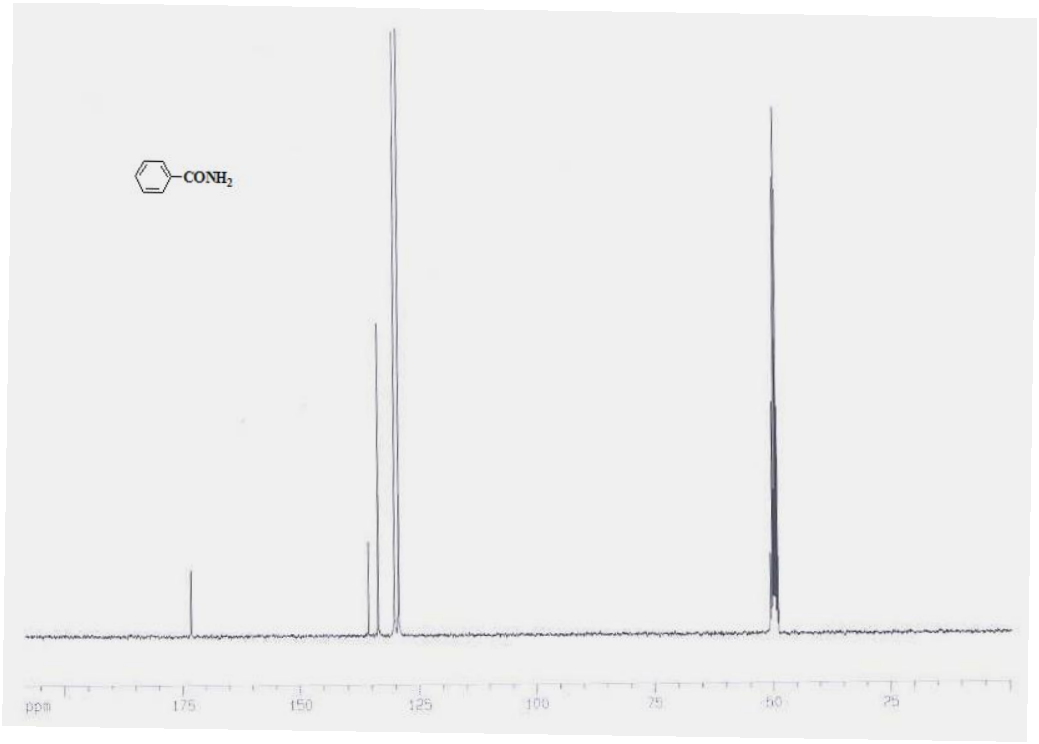


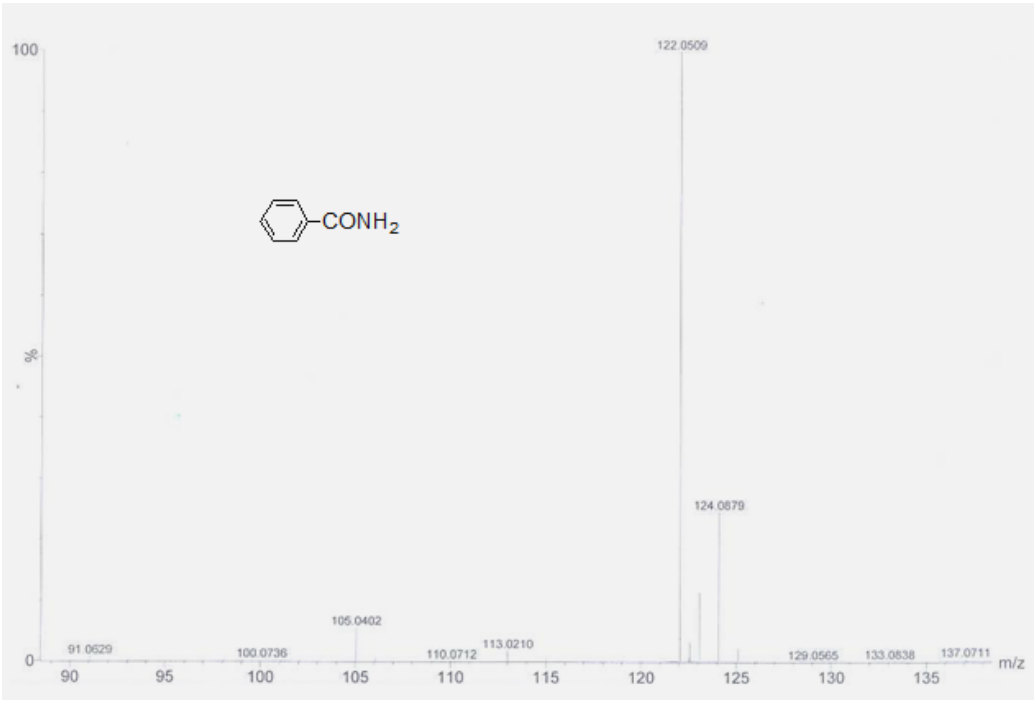




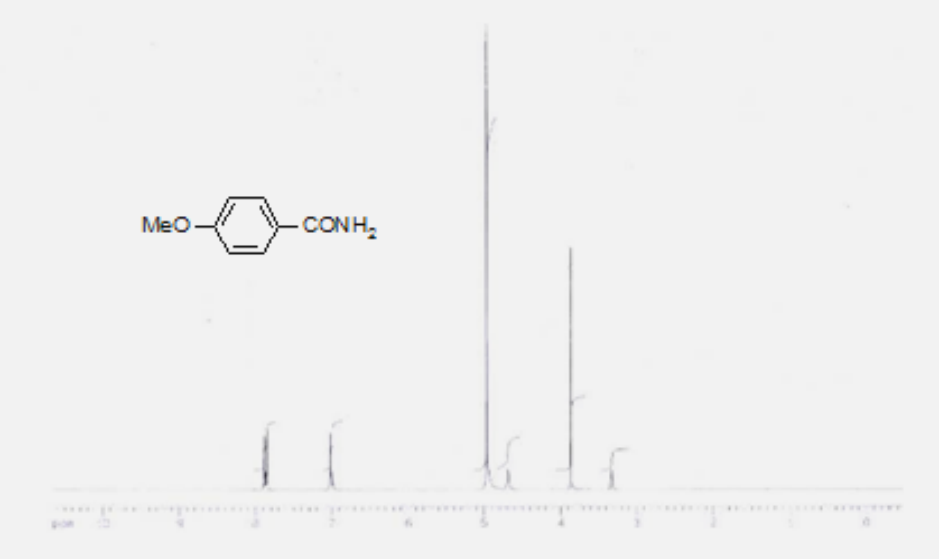
Benzamide (**2b**, Table 2, entry 1)

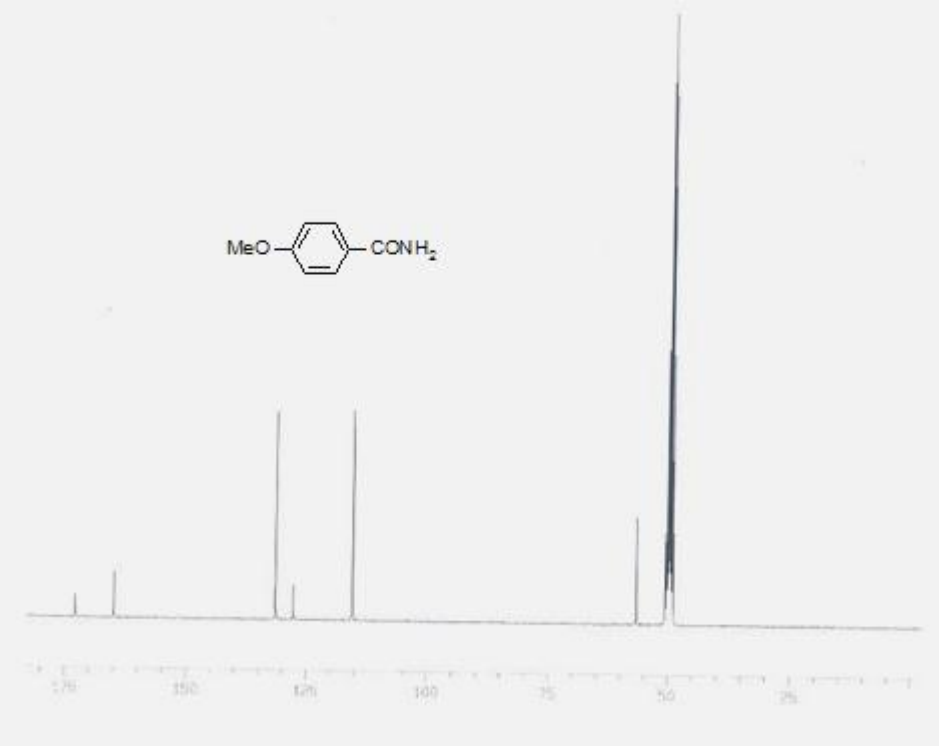


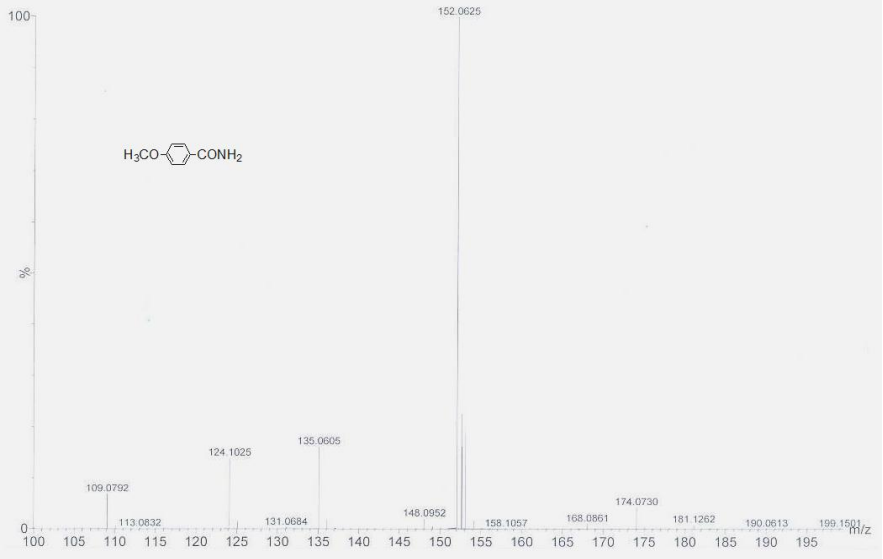




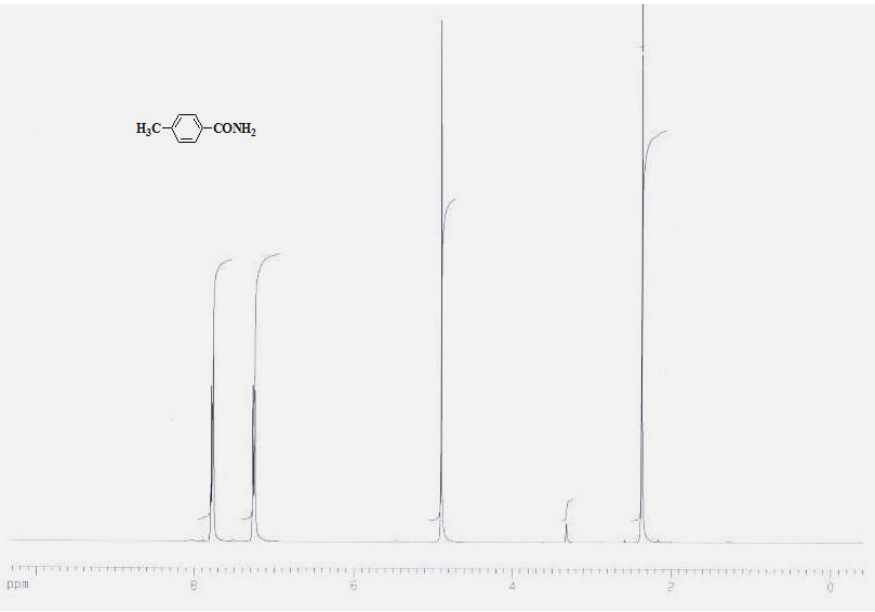
4-Methoxybenzamide (**2c**, Table 2, entry 2)

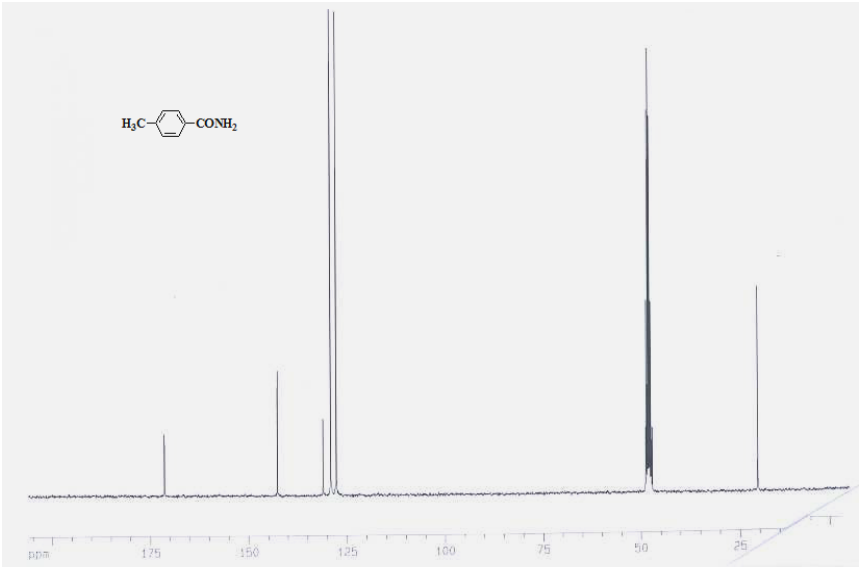


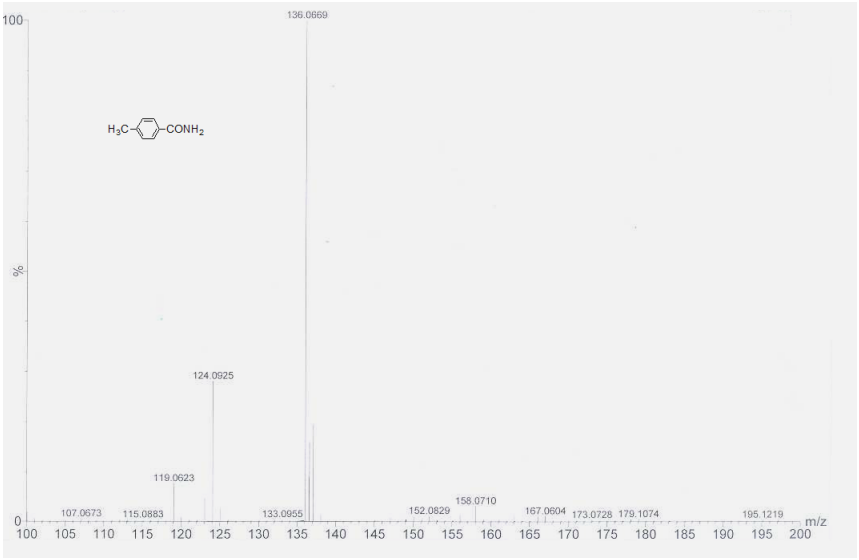


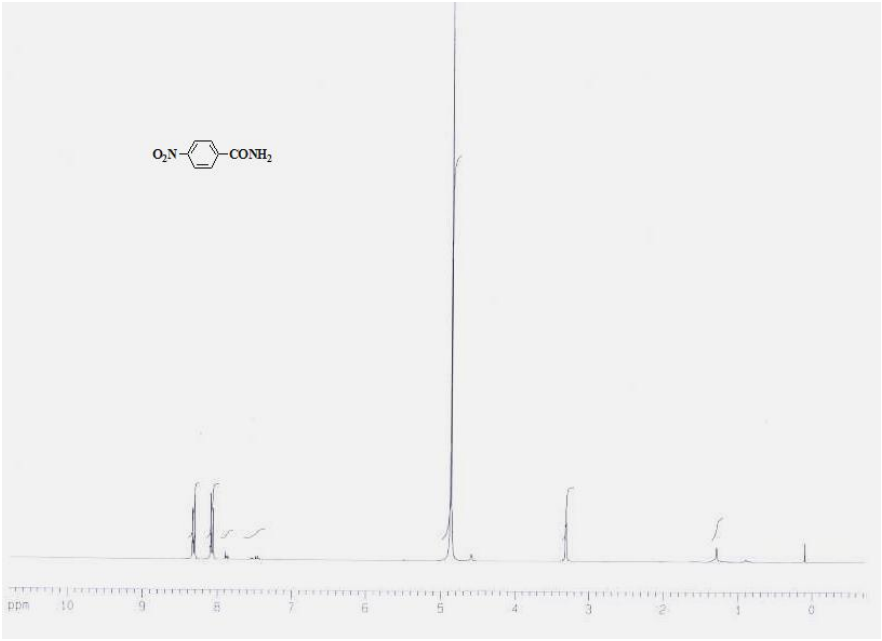


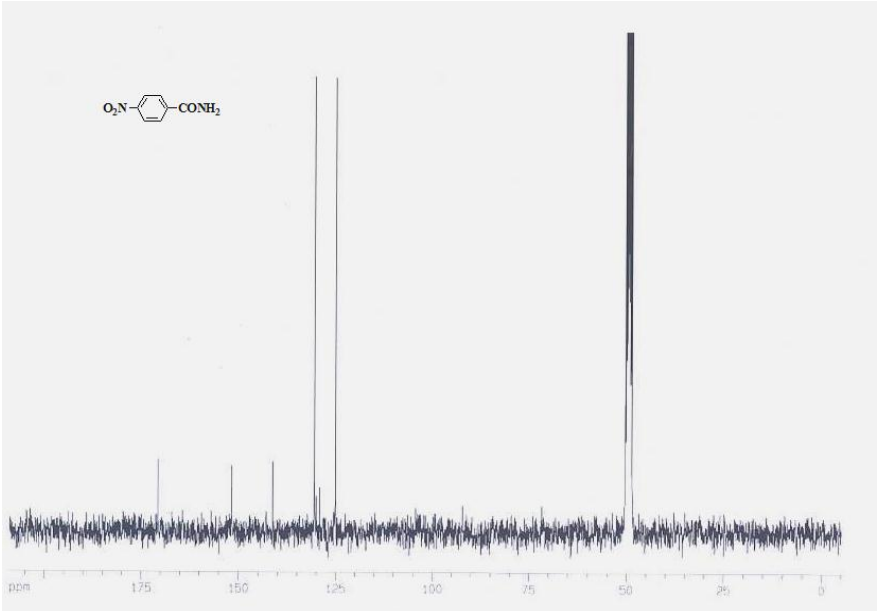
4-Methylbenzamide (**2d**, Table 2, entry 3)

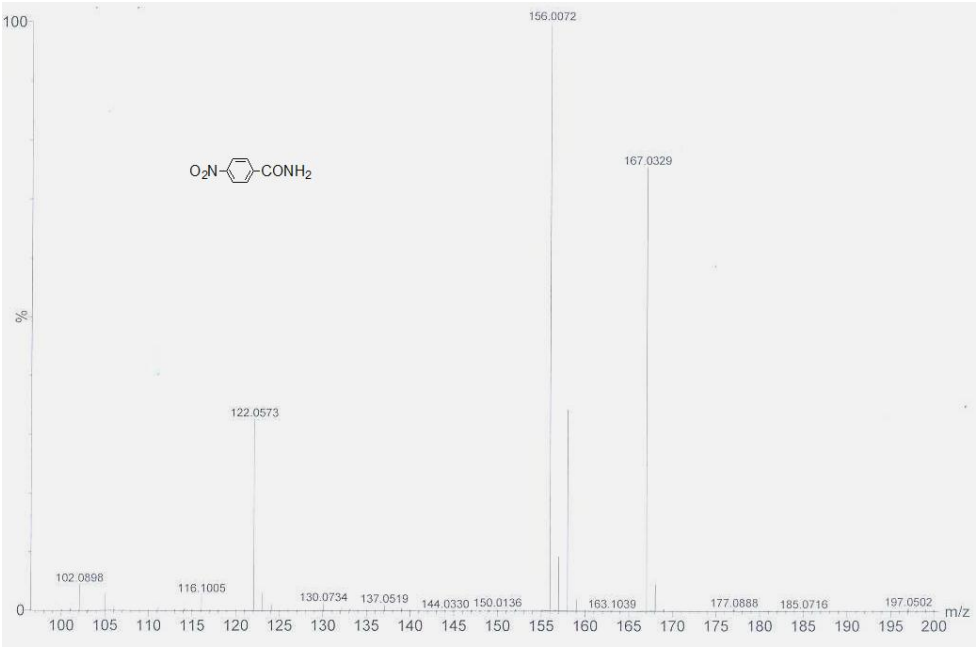




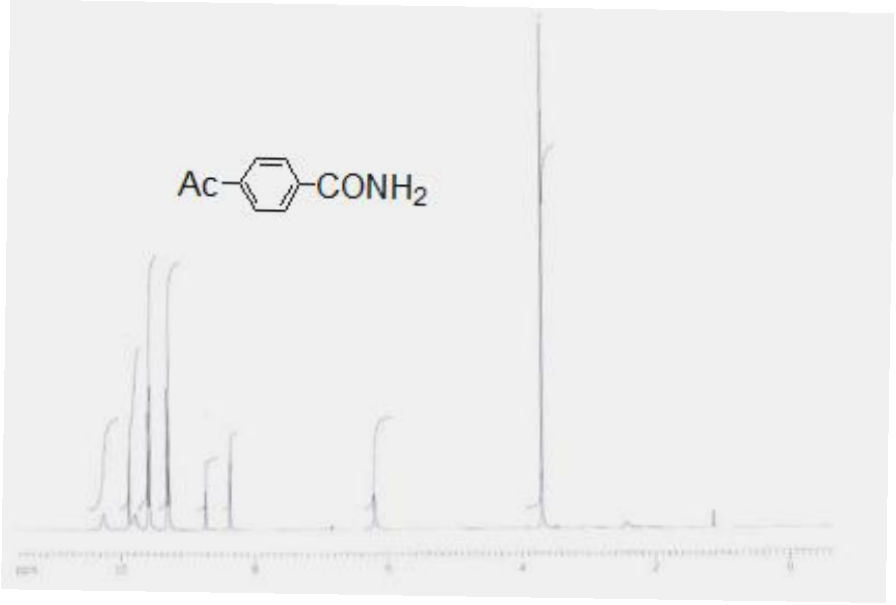


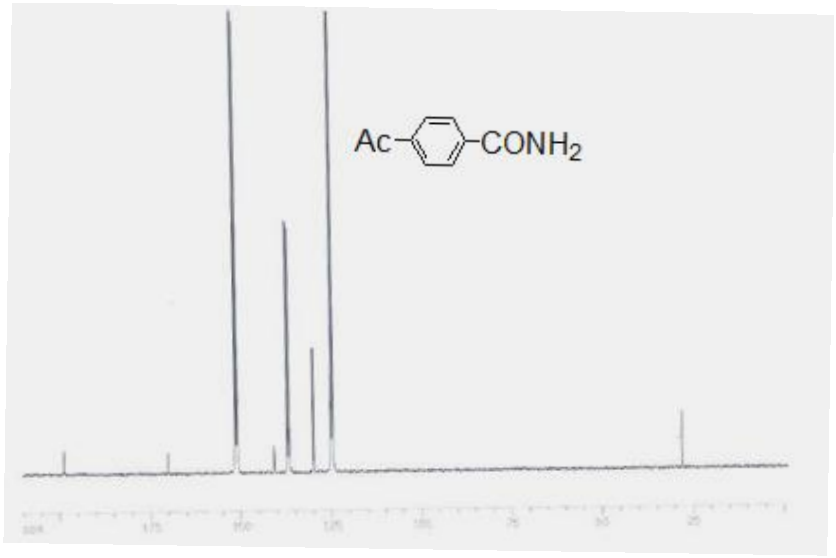


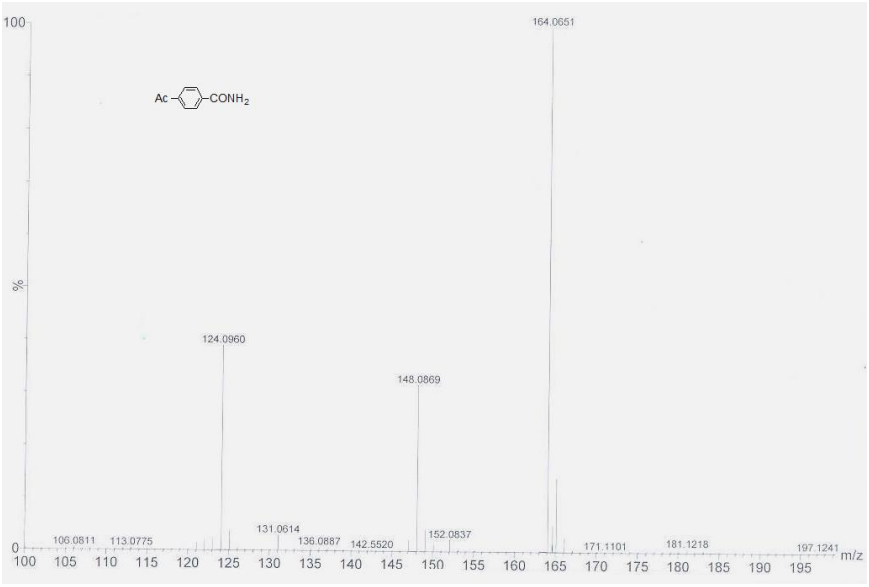




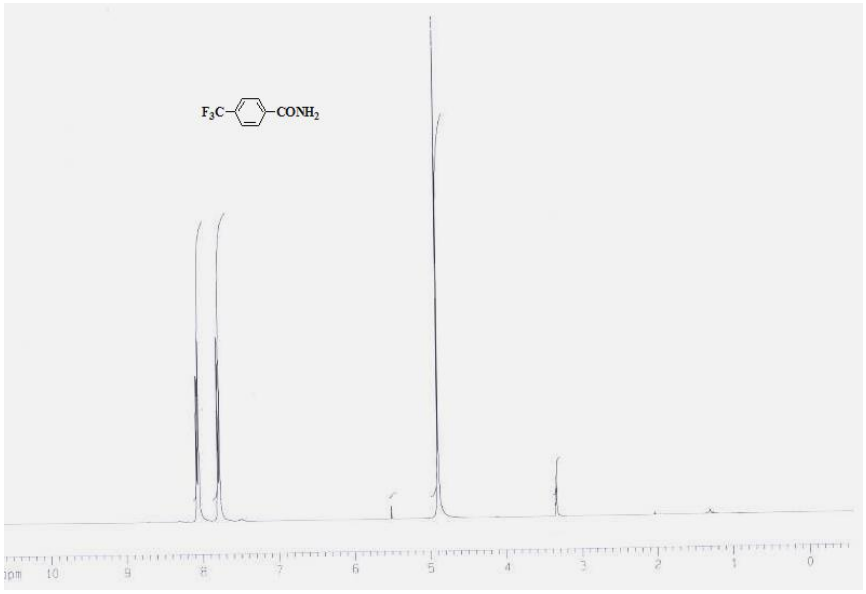
4-Acetylbenzamide (**2f**, Table 2, entry 5)

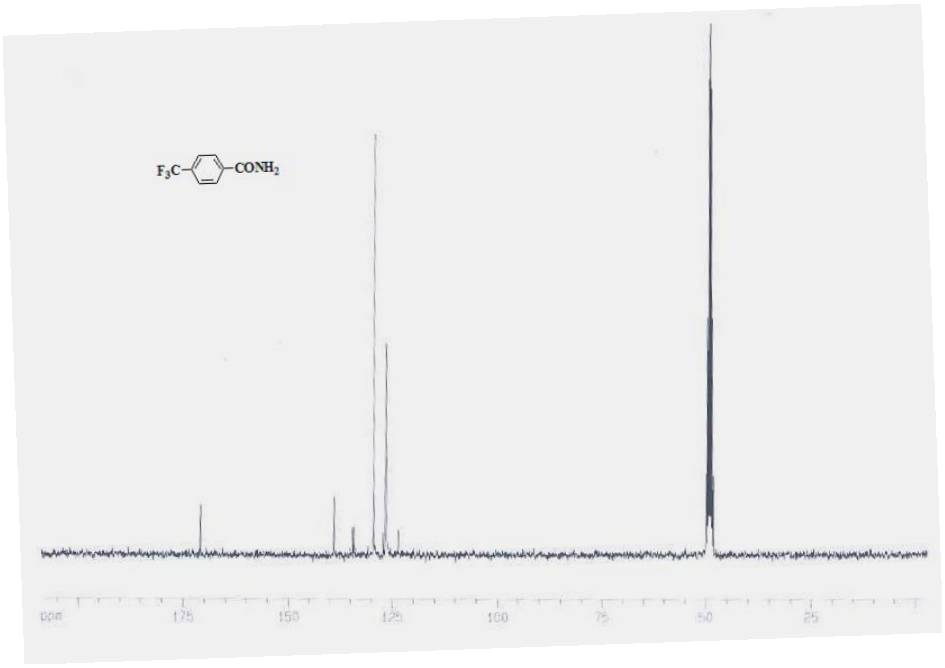


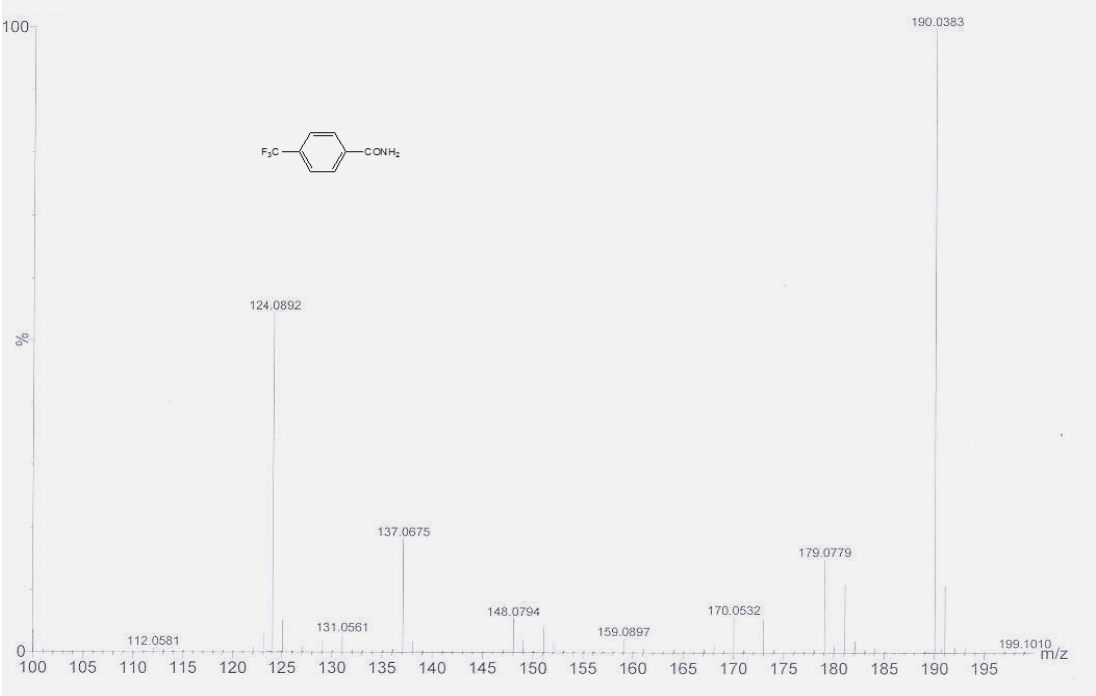




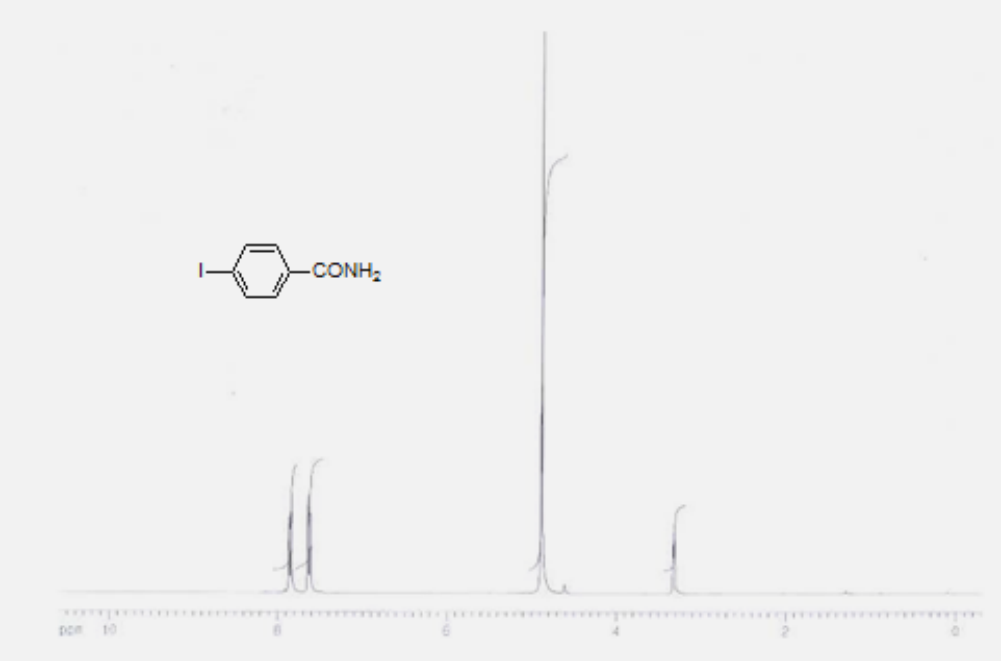
4-Trifluoromethylbenzamide (**2g**, Table 2, entry 6)

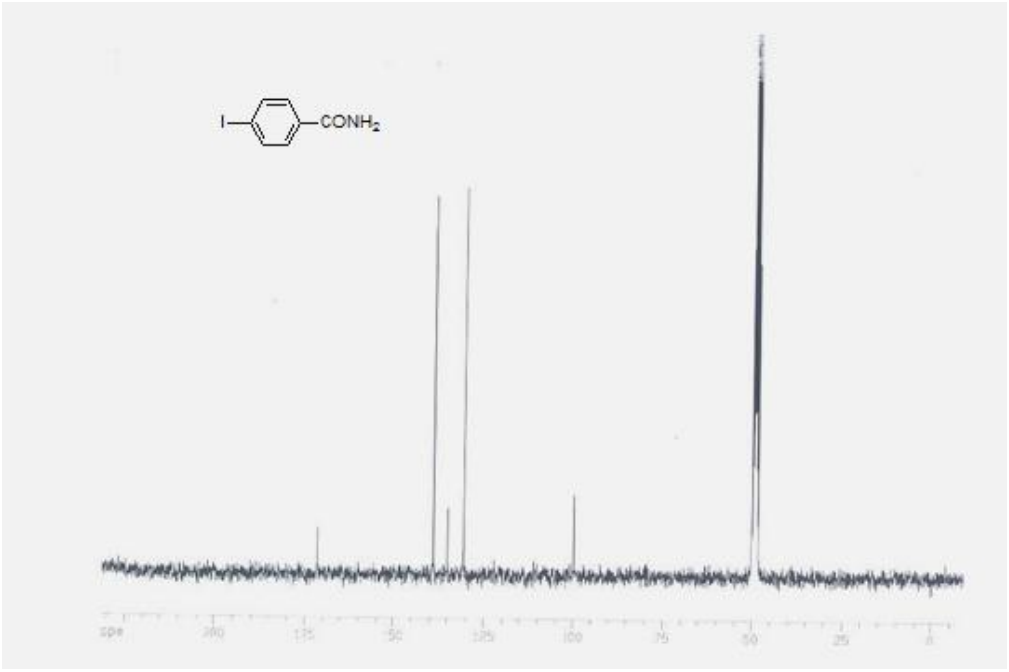


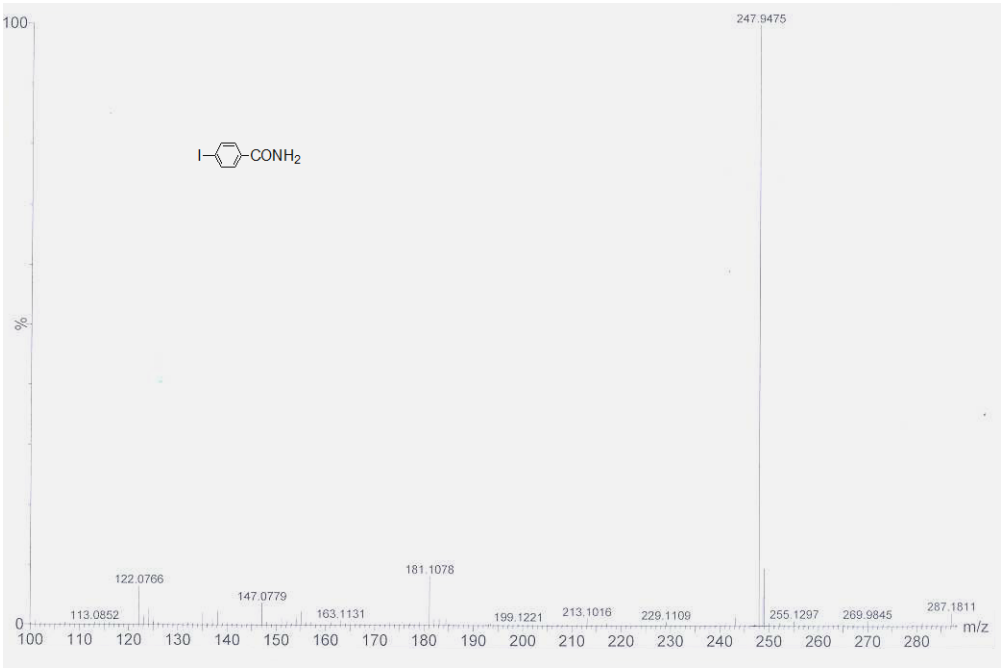




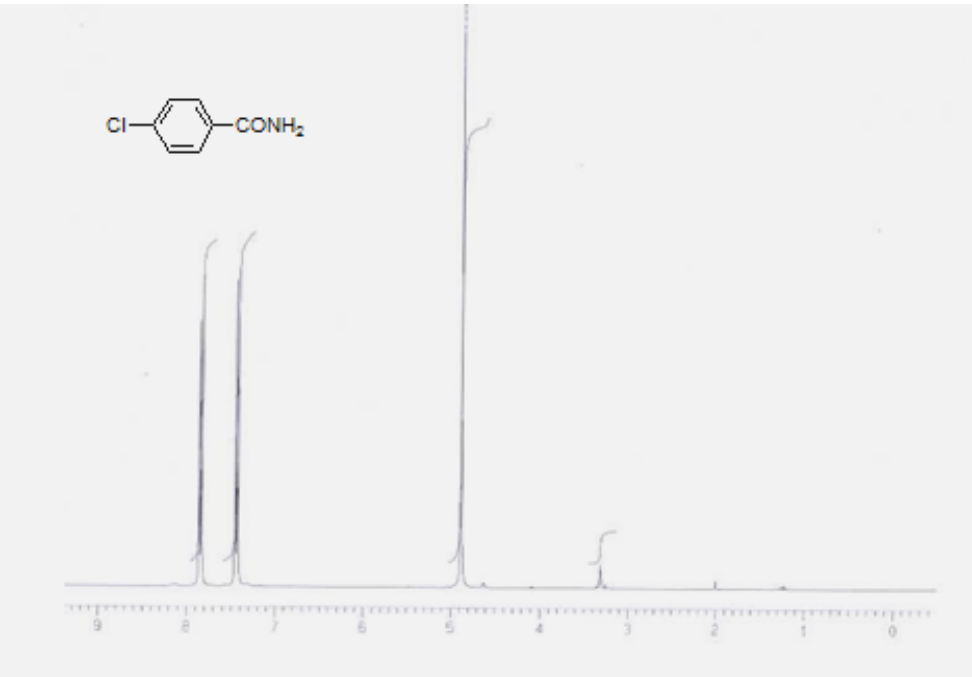
4-Iodobenzamide (**2h**, Table 2, entry 7)

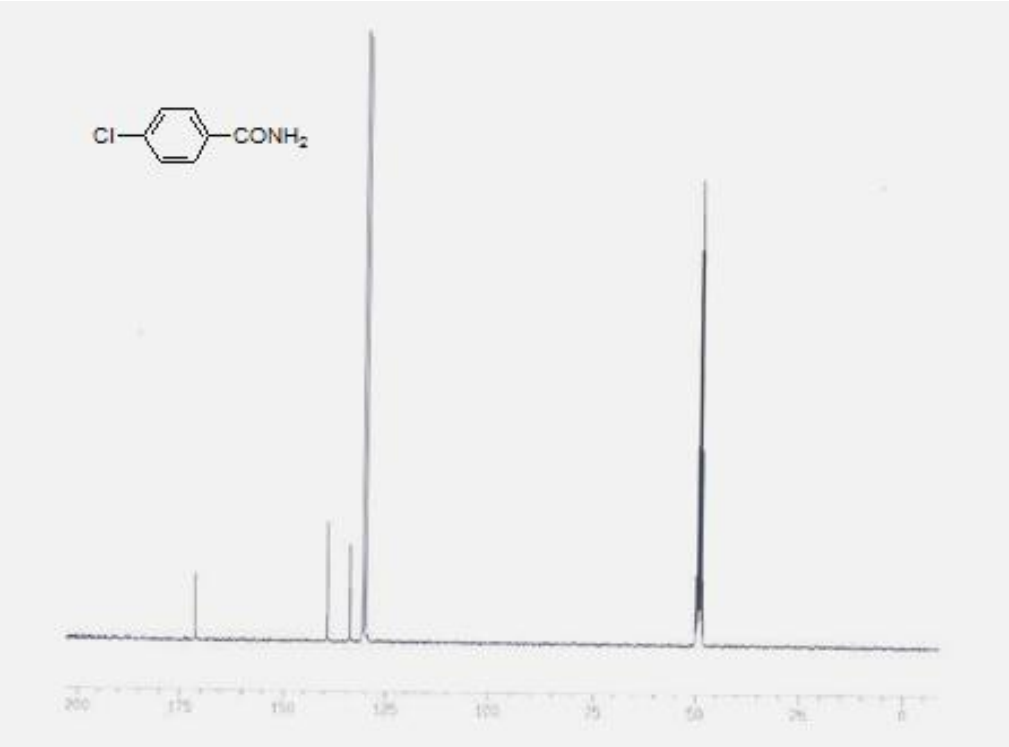


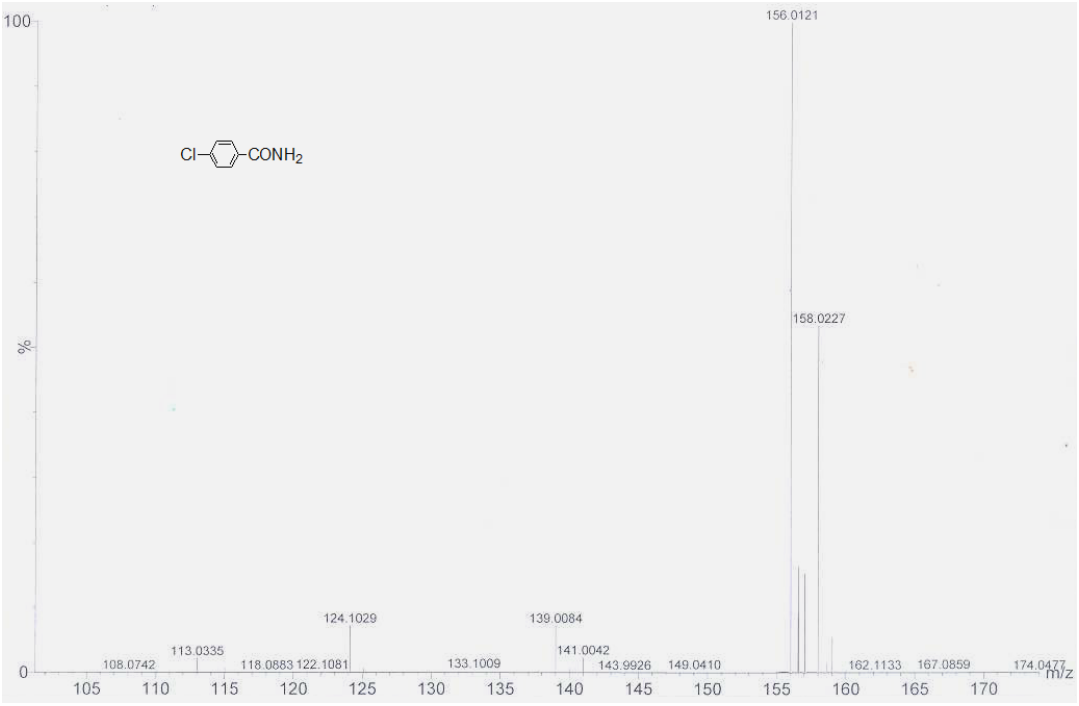




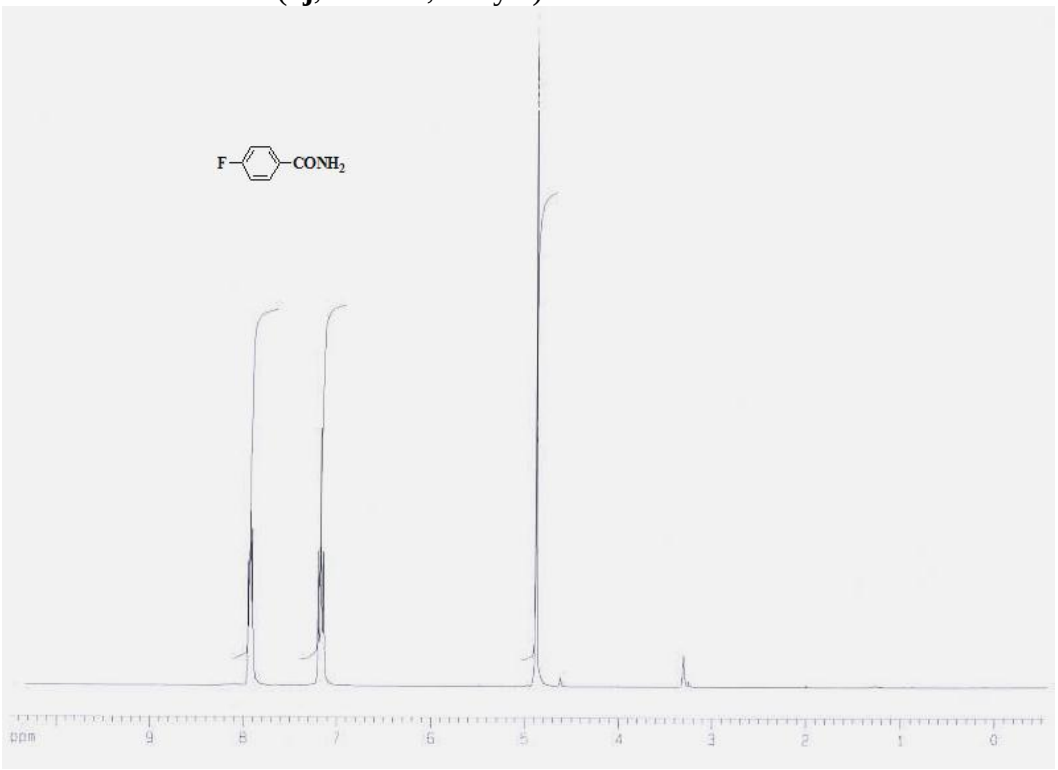
4-Chlorobenzamide (**2i**, Table 2, entry 8)

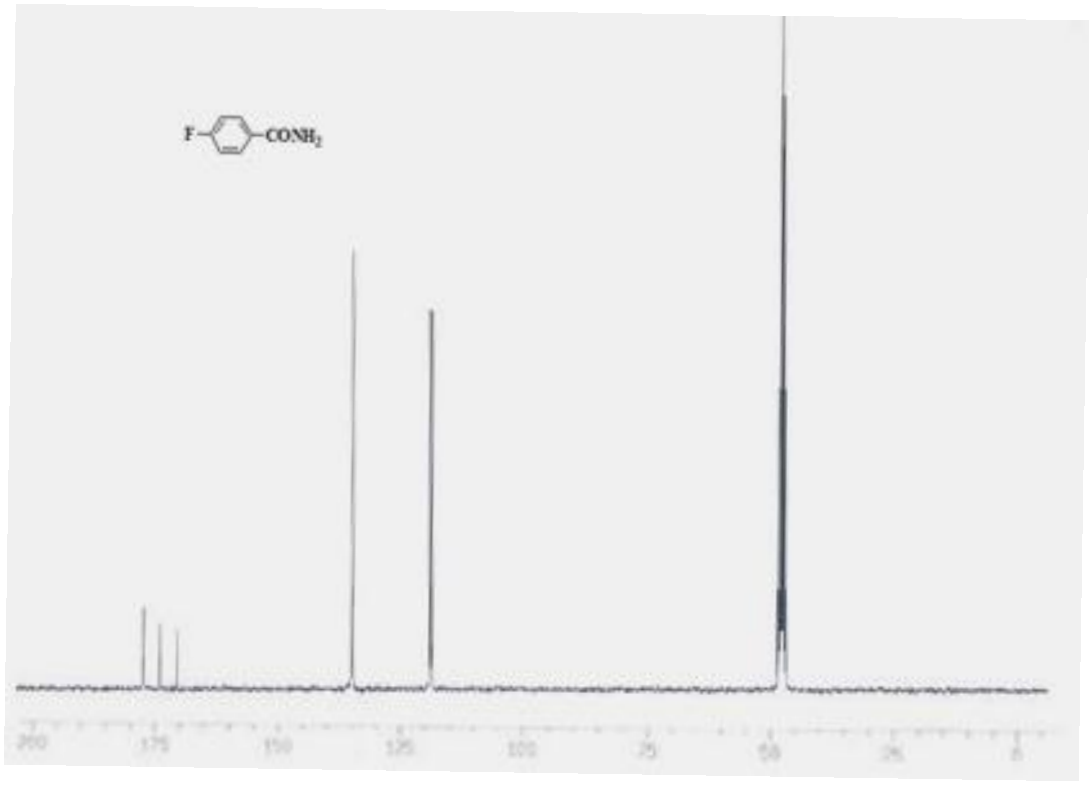


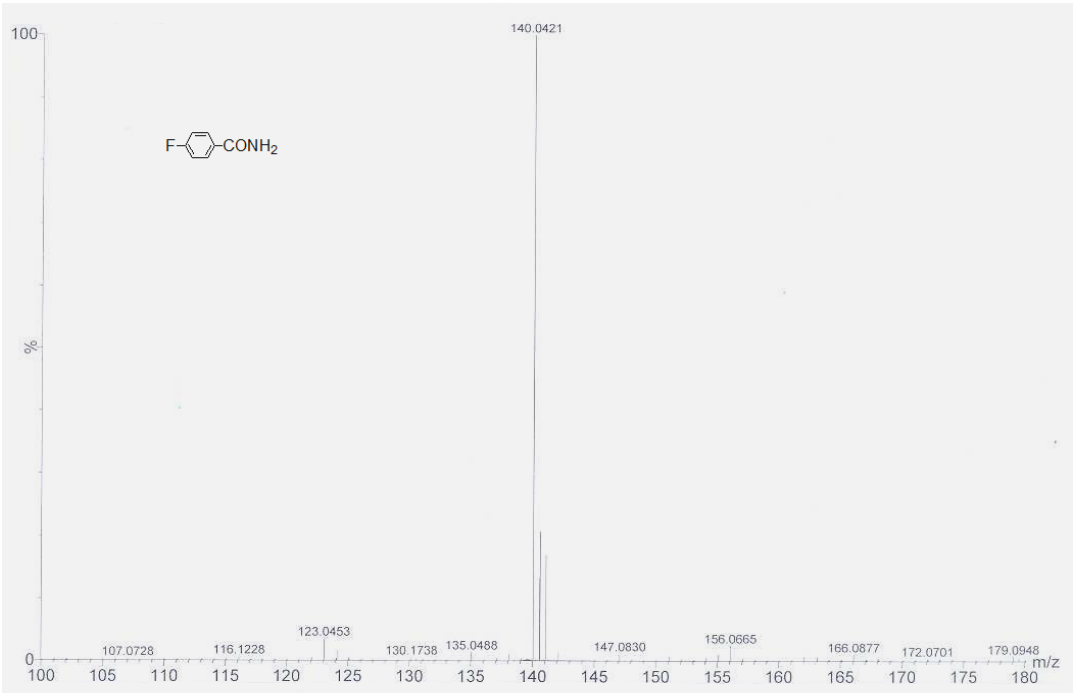




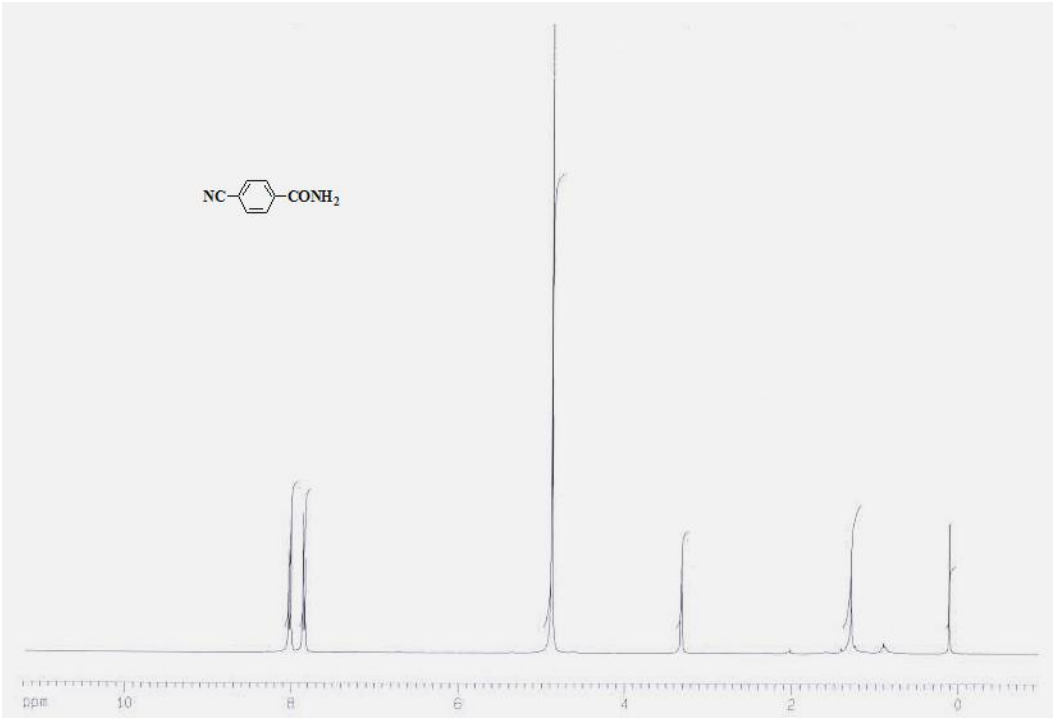
4-Fluorobenzamide (**2j**, Table 2, entry 9)

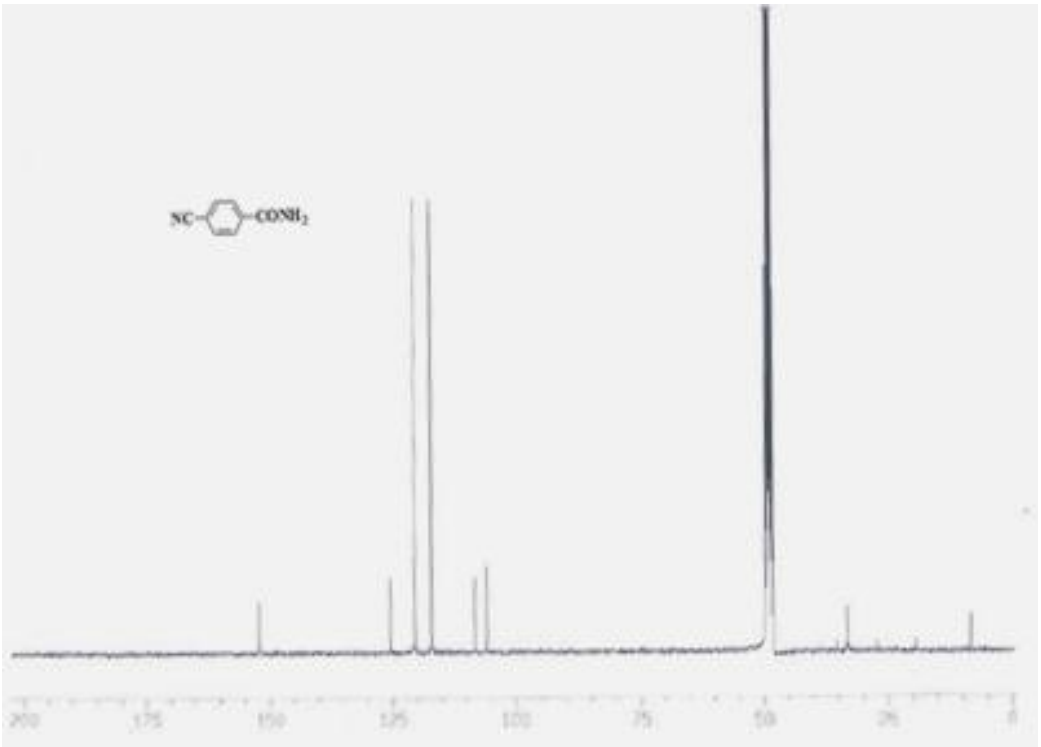


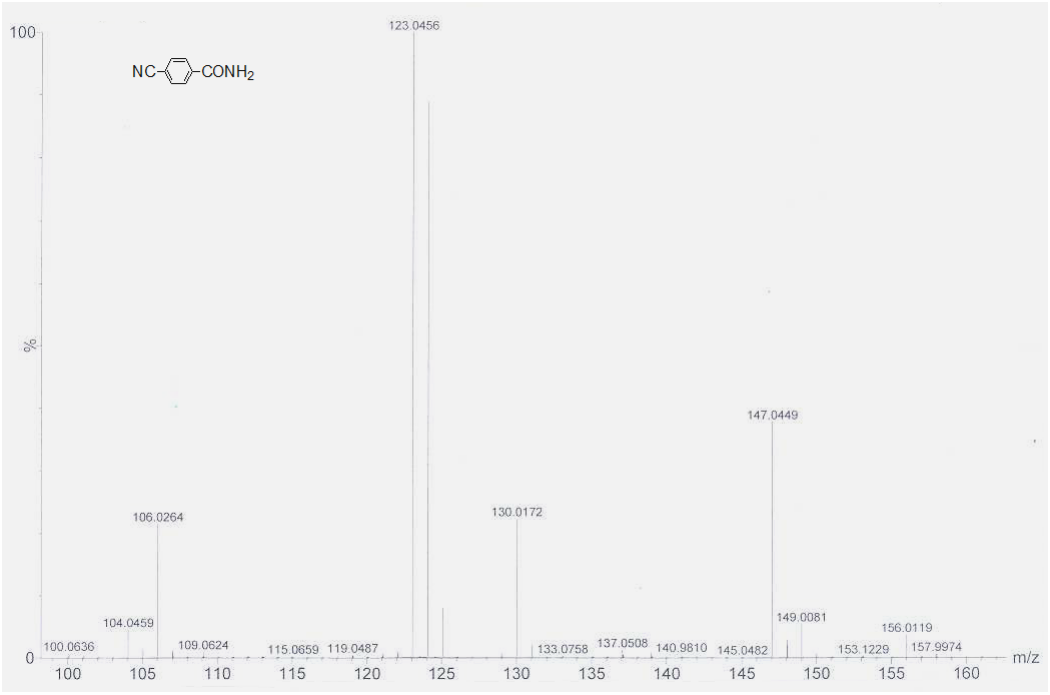




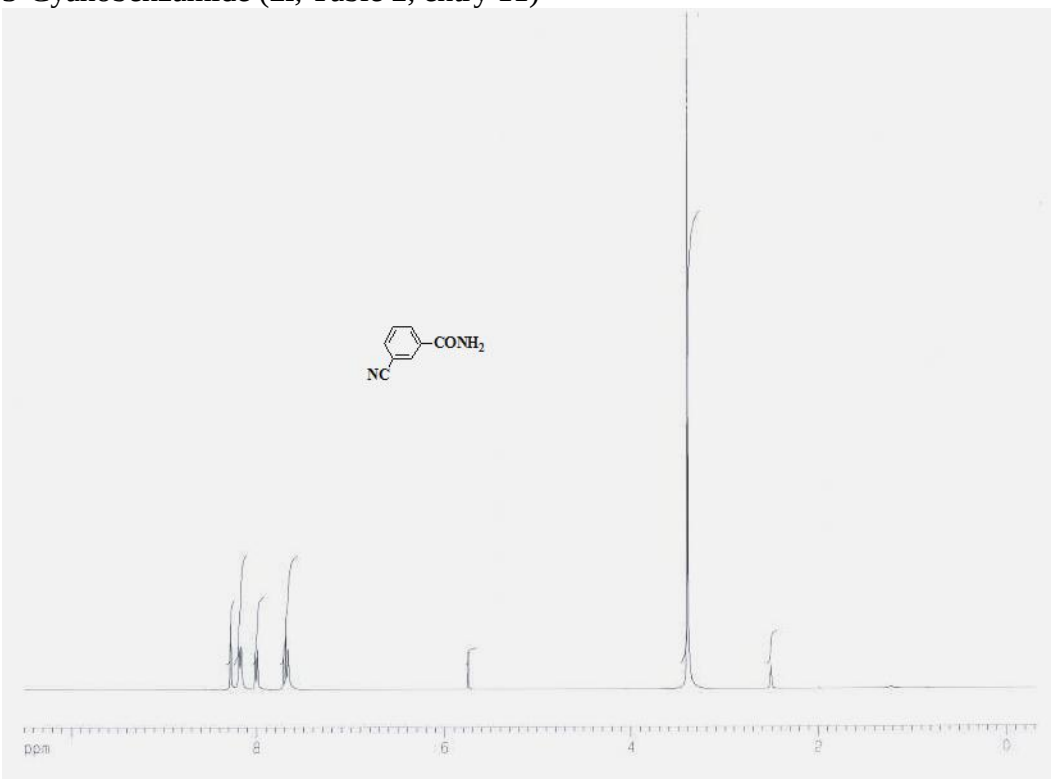
4-Cyanobenzamide (**2k**, Table 2, entry 10)

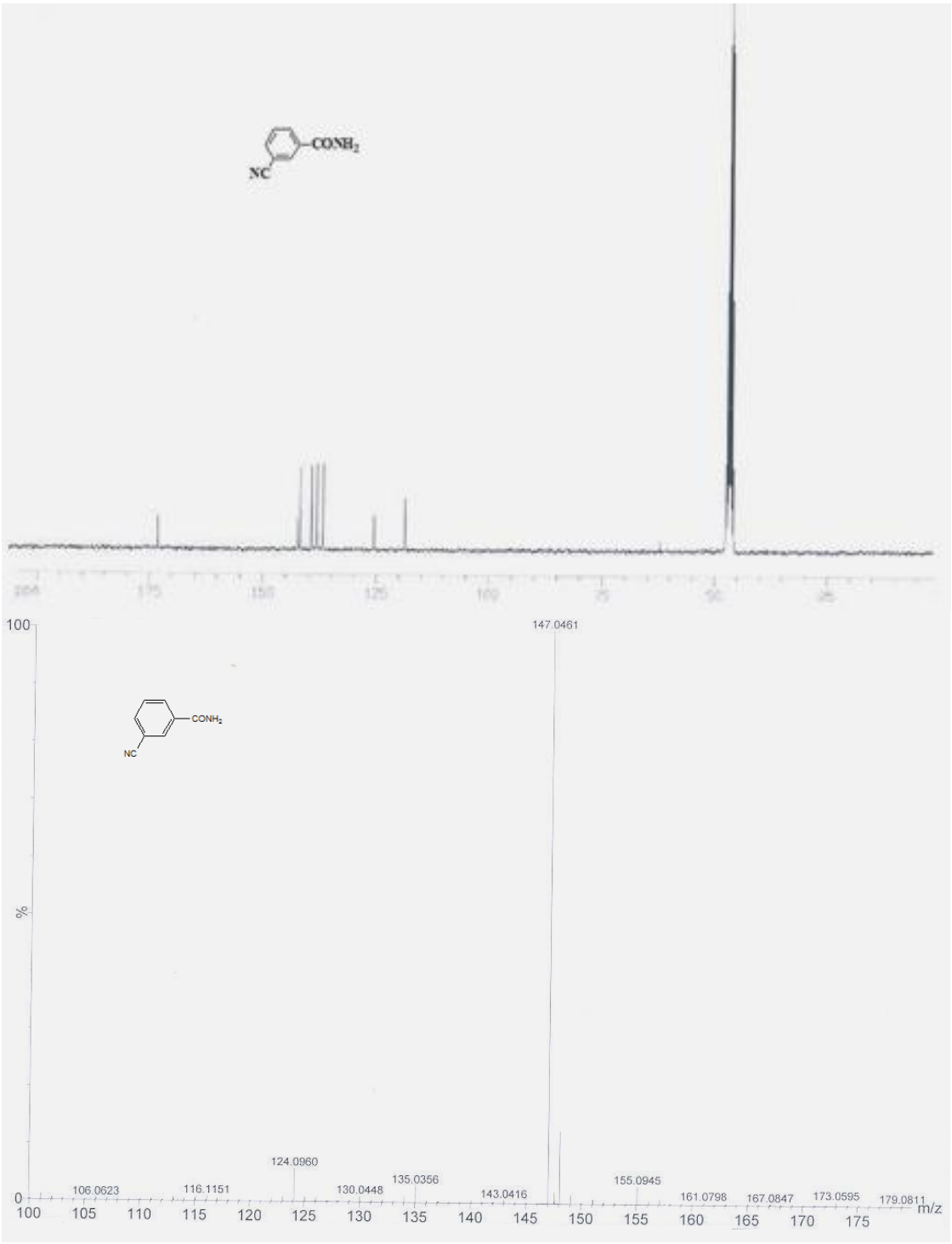




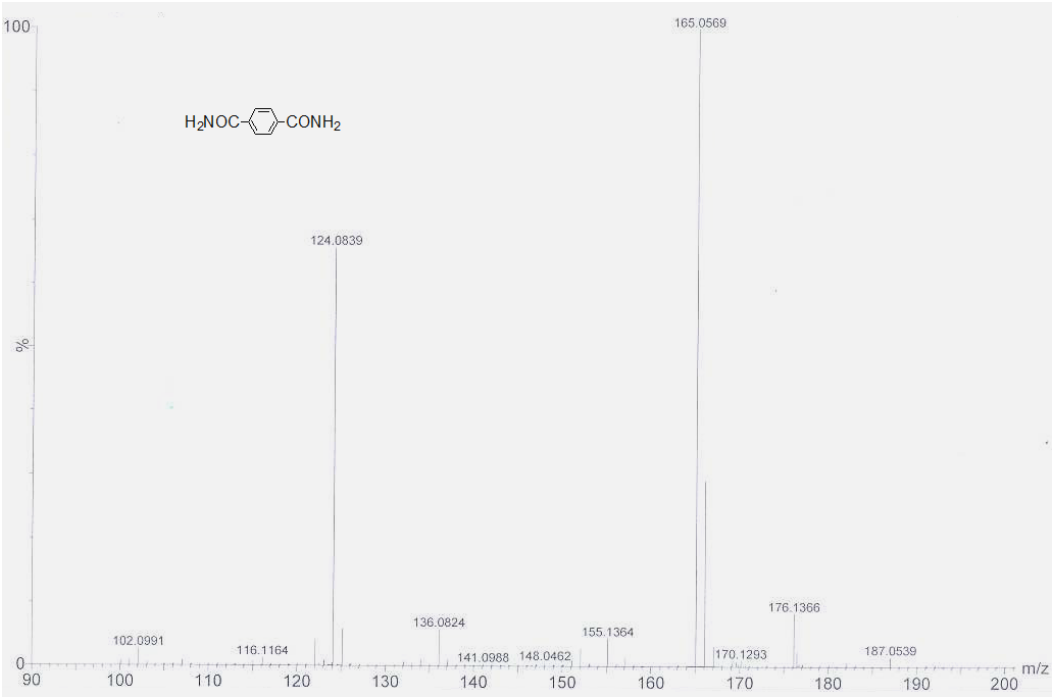


3-Cyanobenzamide (**2l**, Table 2, entry 11)

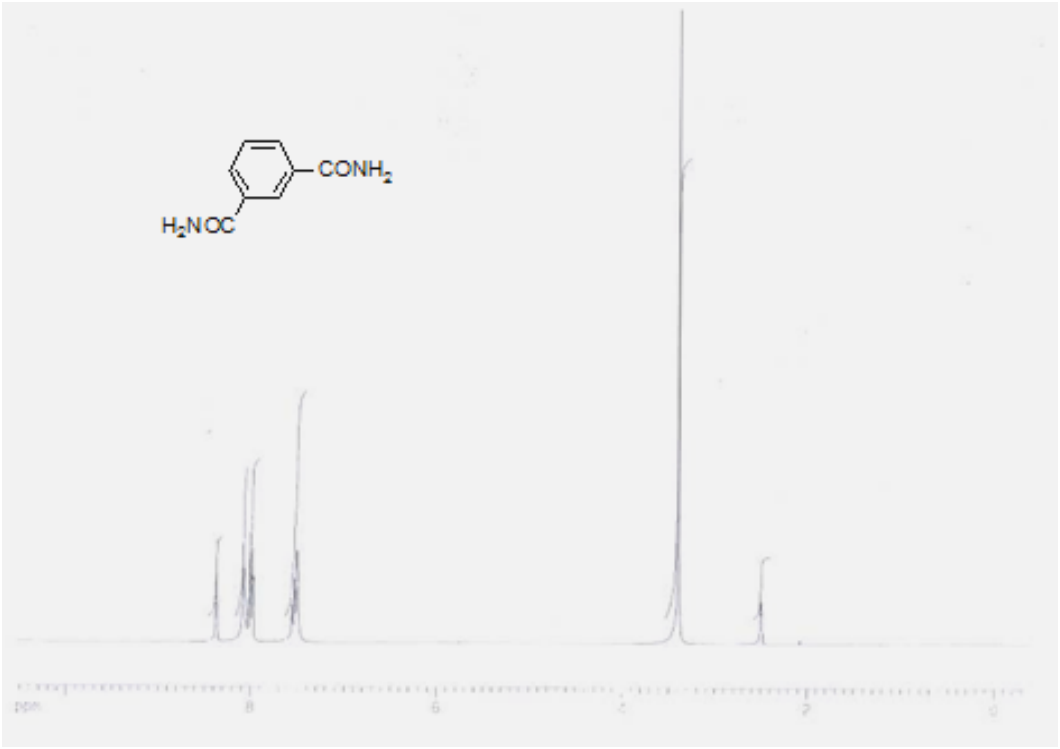


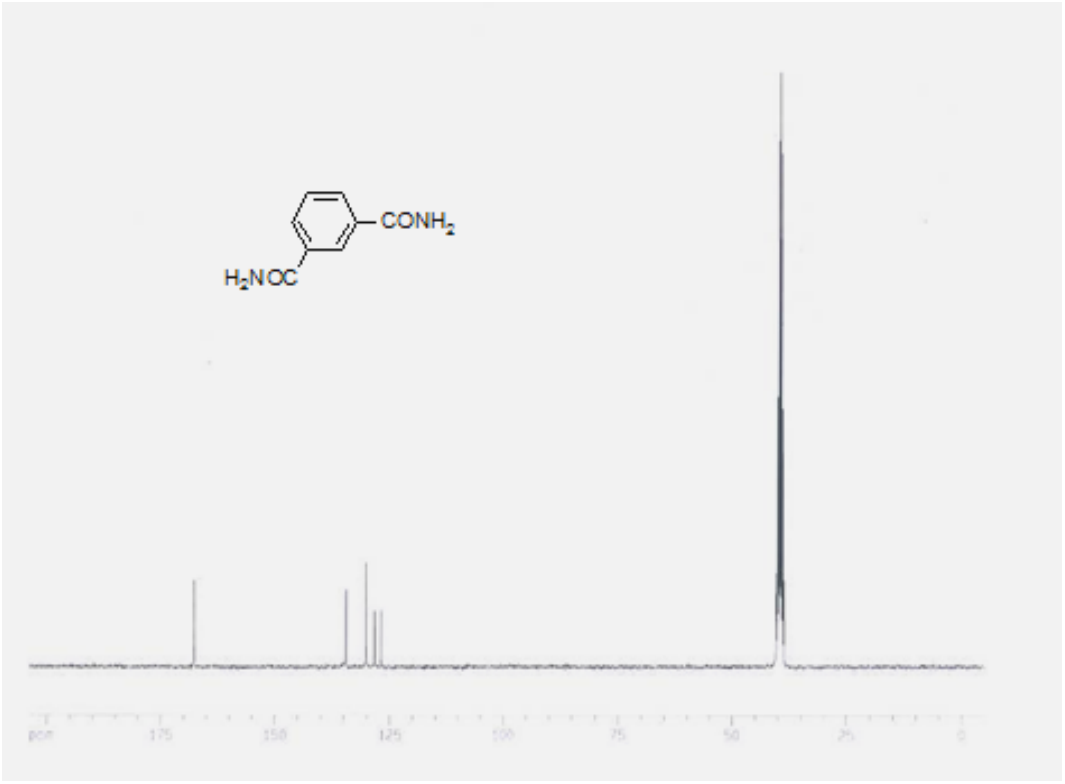


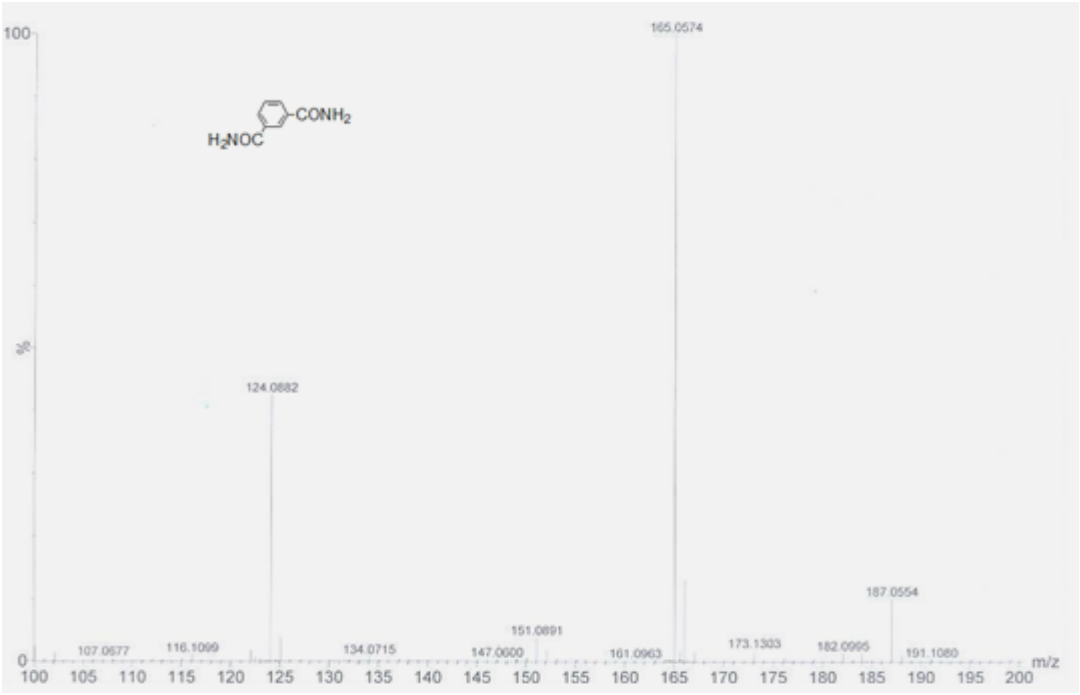
Terephthalimide (**2m**, Table 2, entry 12)



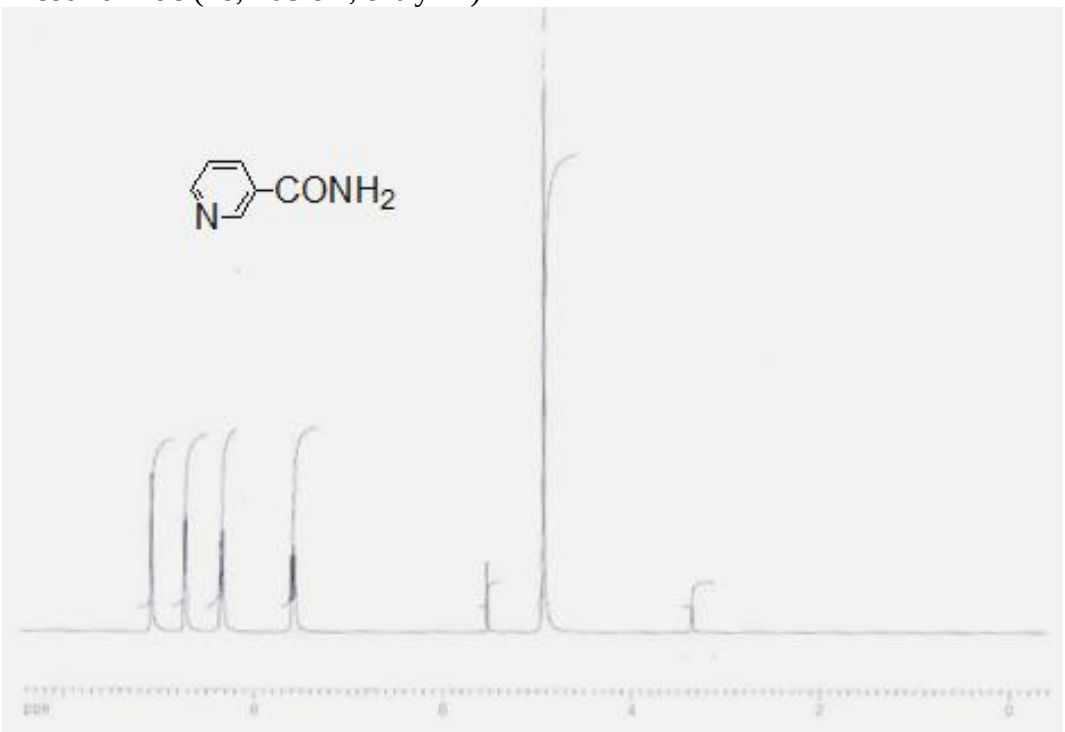
Isophthalimide (**2n**, Table 2, entry 13)

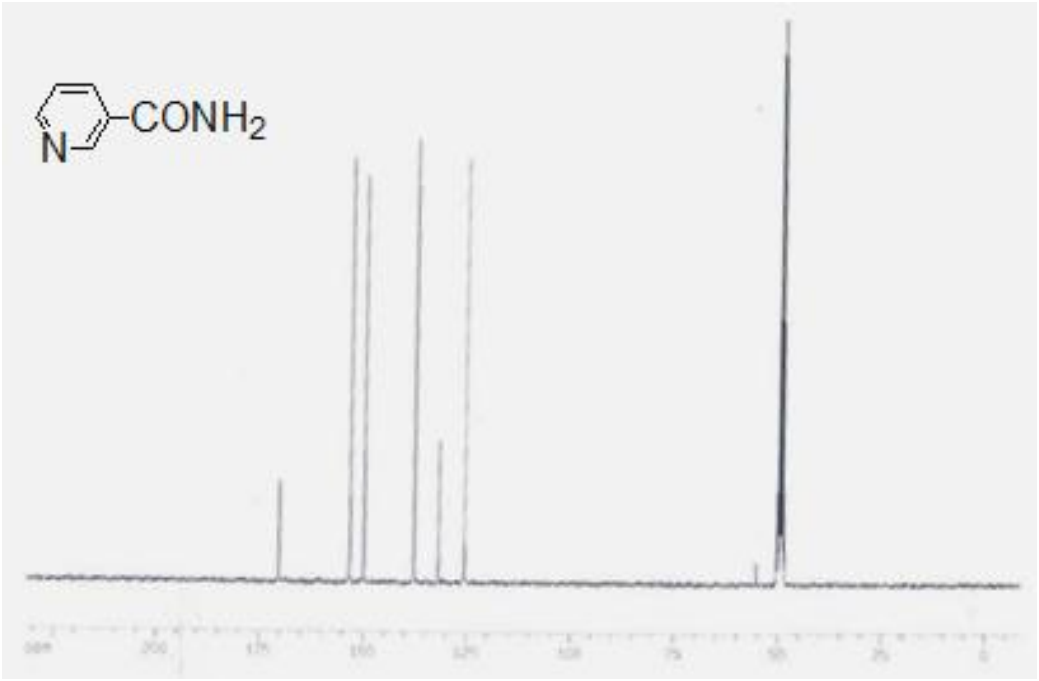


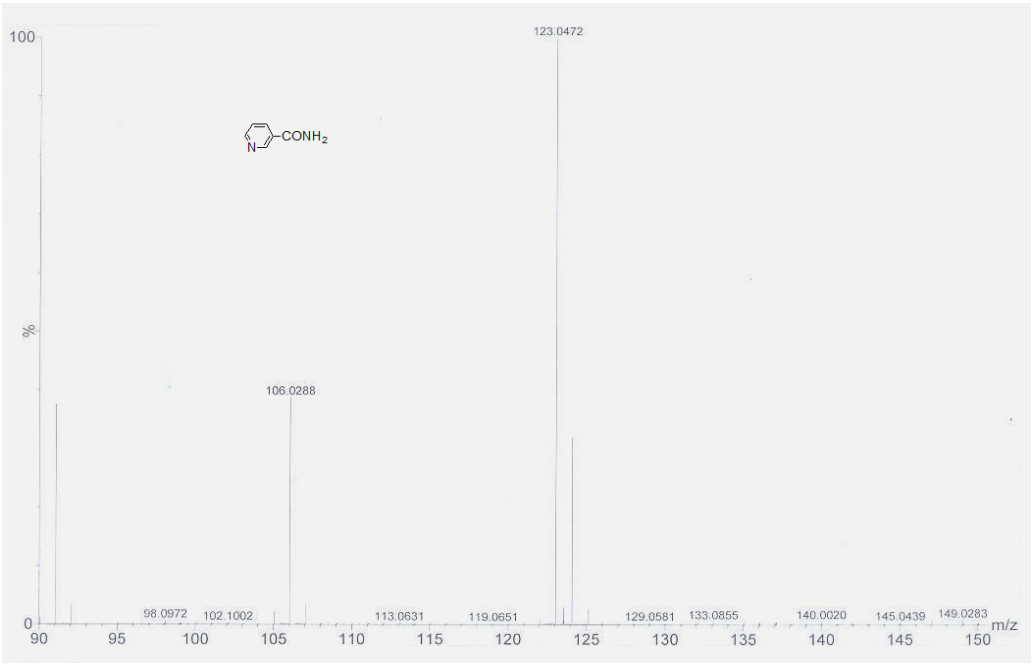




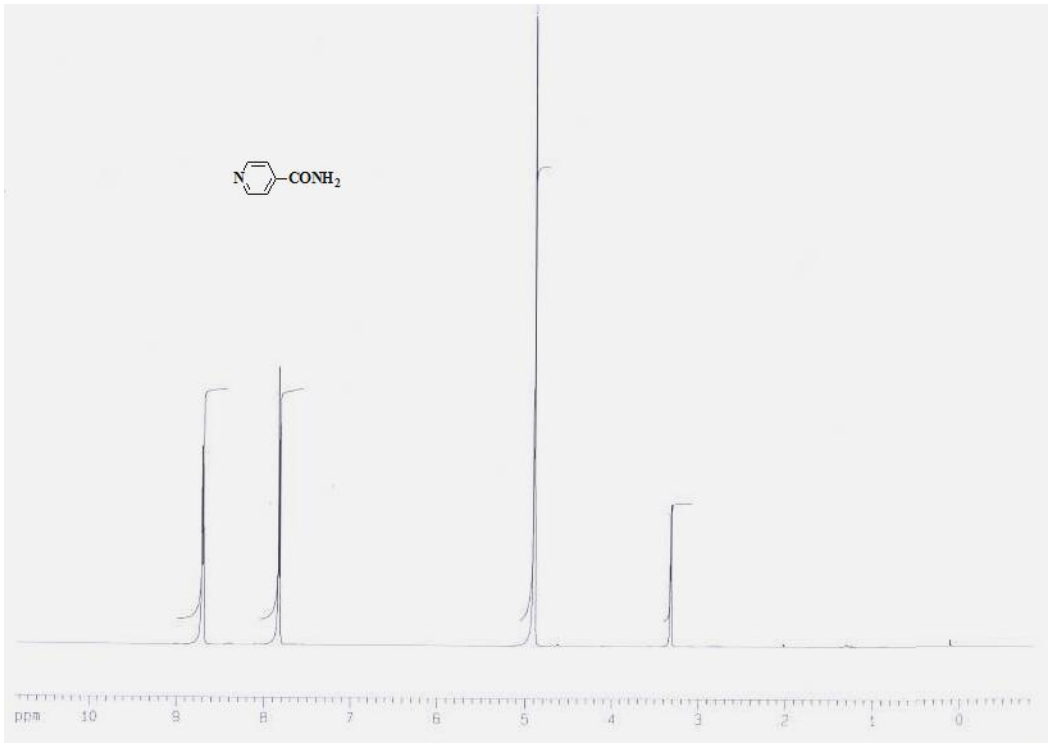
Nicotinamide (**2o**, Table 2, entry 14)

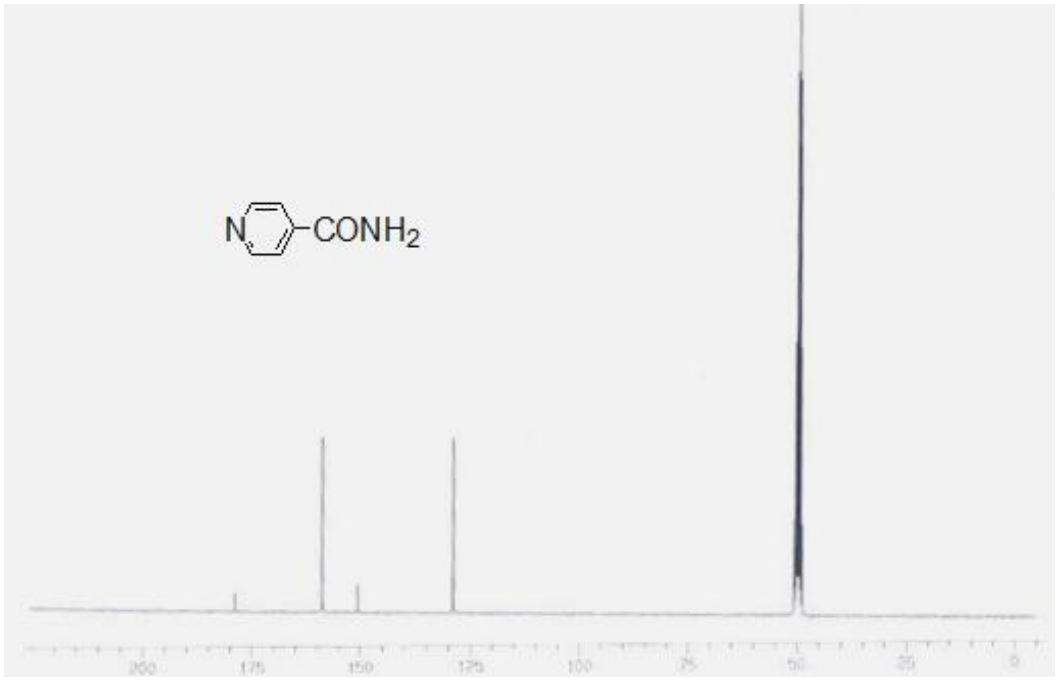


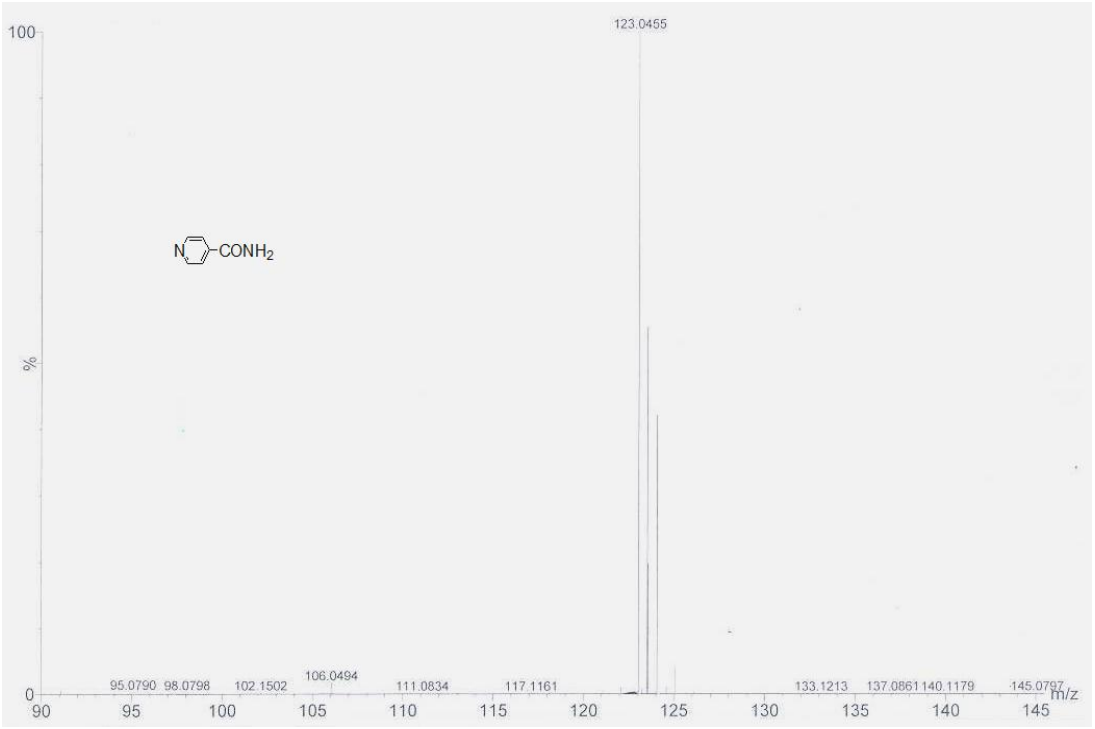




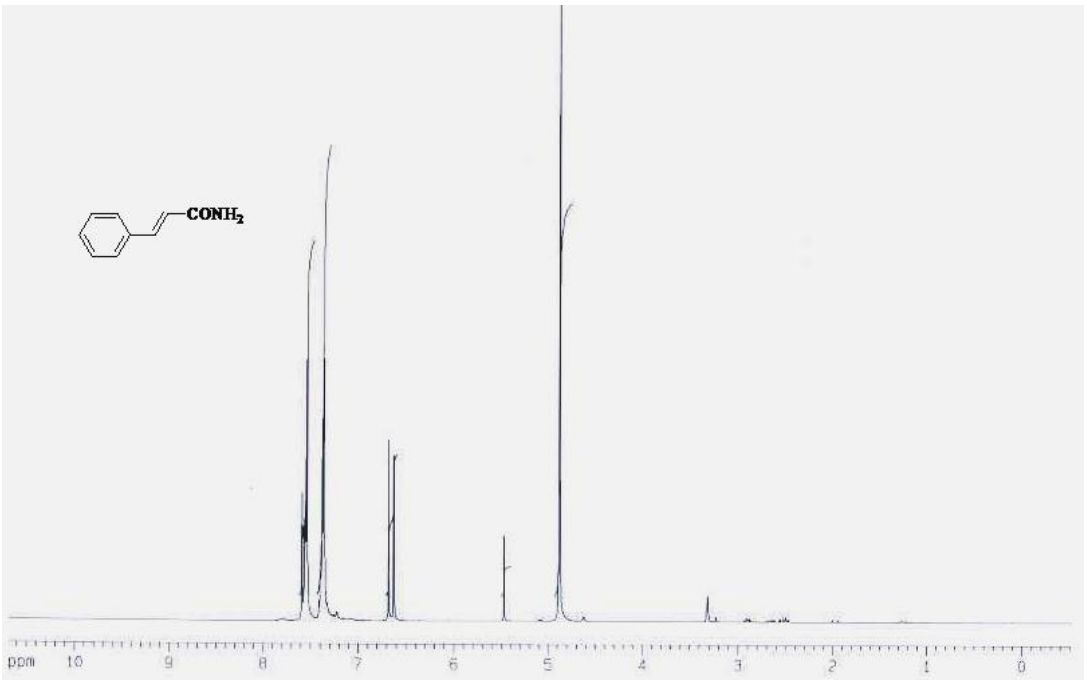
Isonicotinamide (**2p**, Table 2, entry 15)

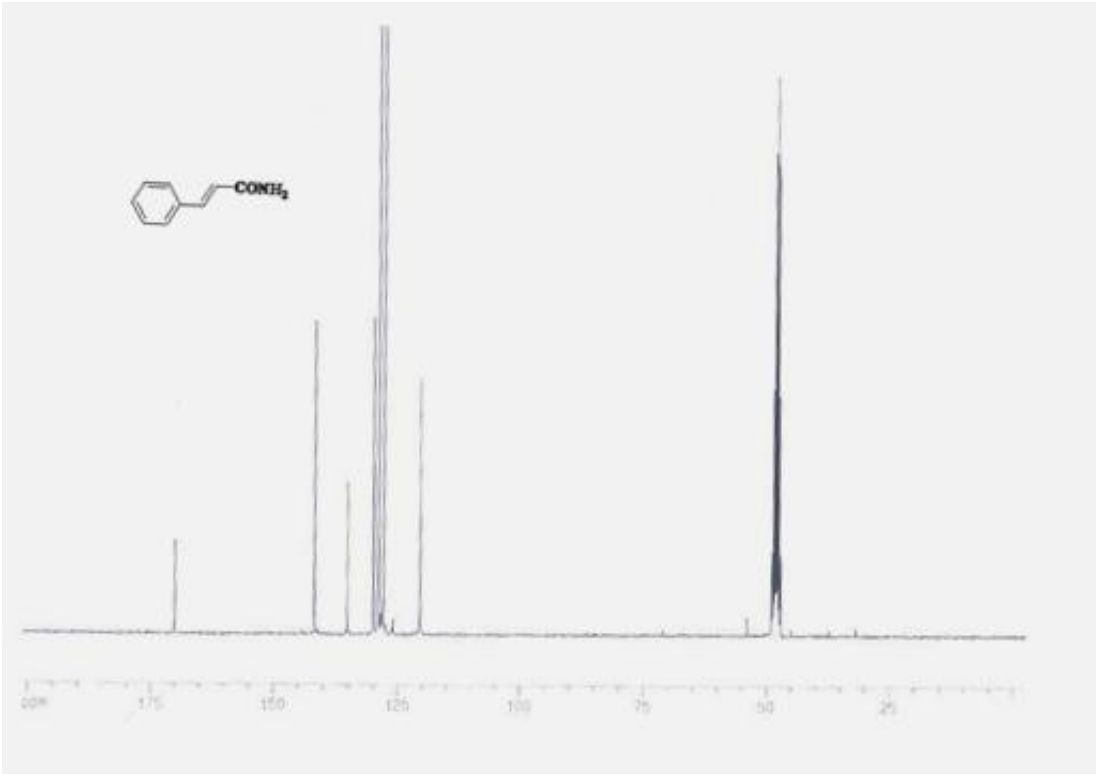


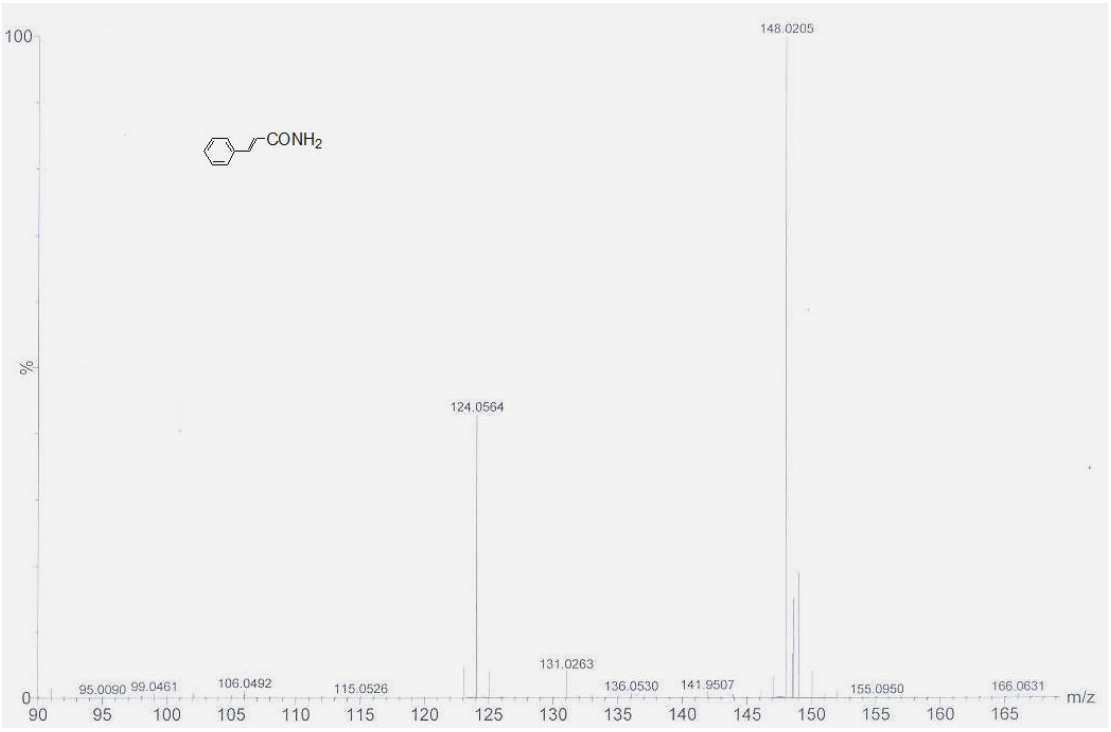




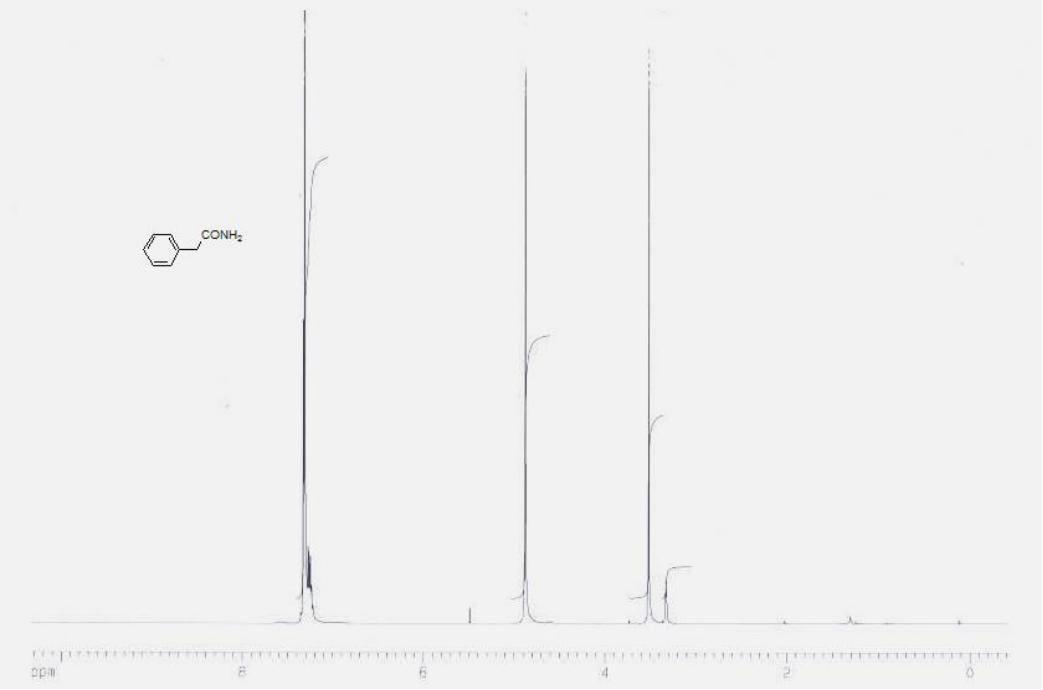
E-cinnamide (**2q**, Table 2, entry 16)

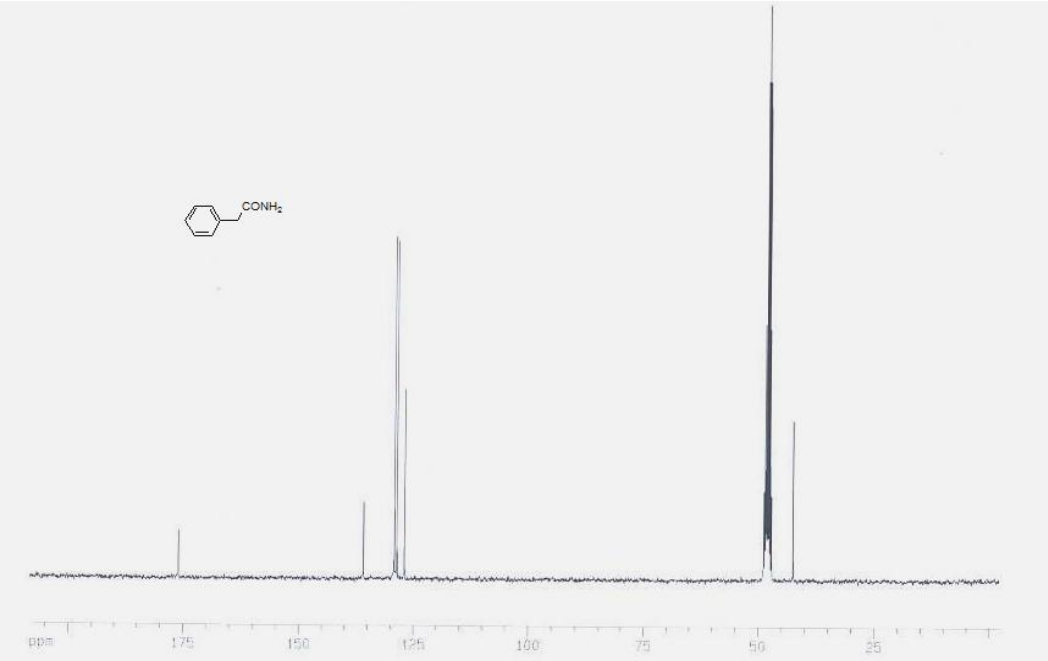


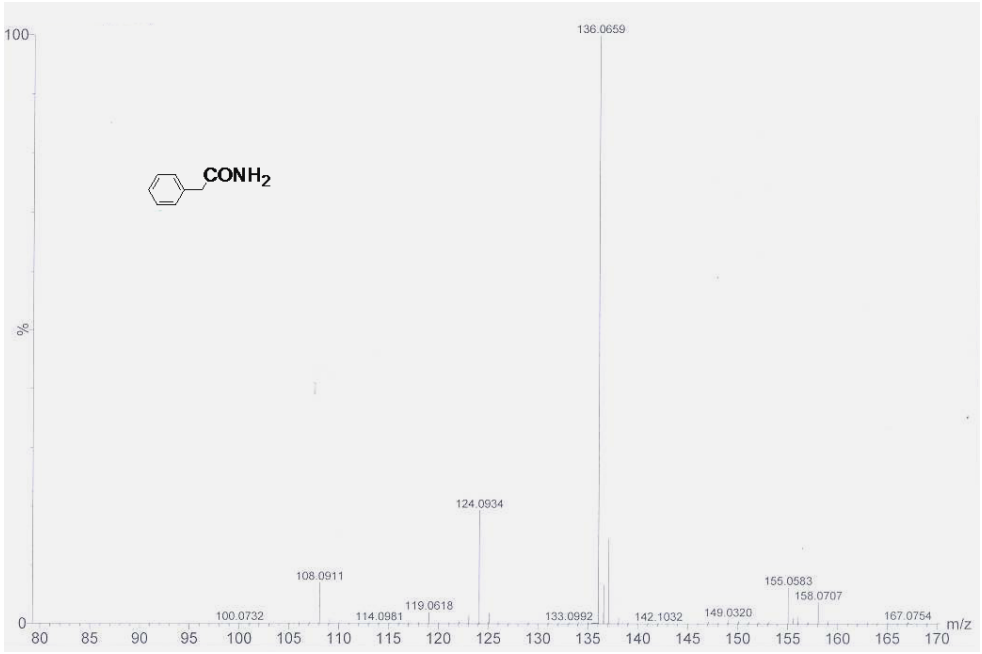




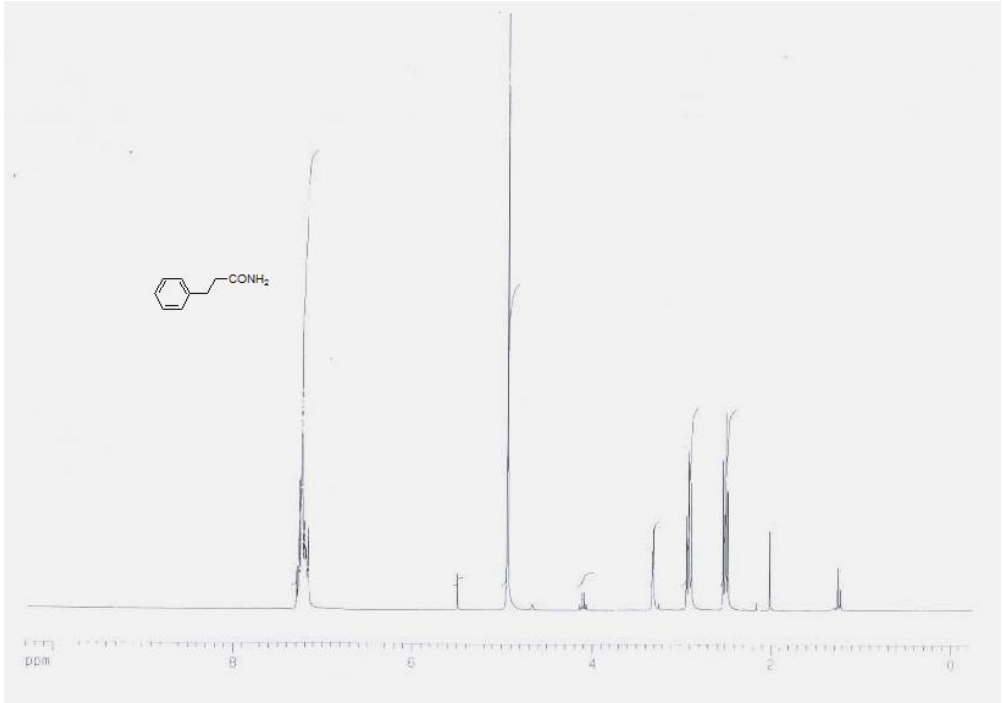
2-Phenylacetamide (**2r**, Table 2, entry 17)

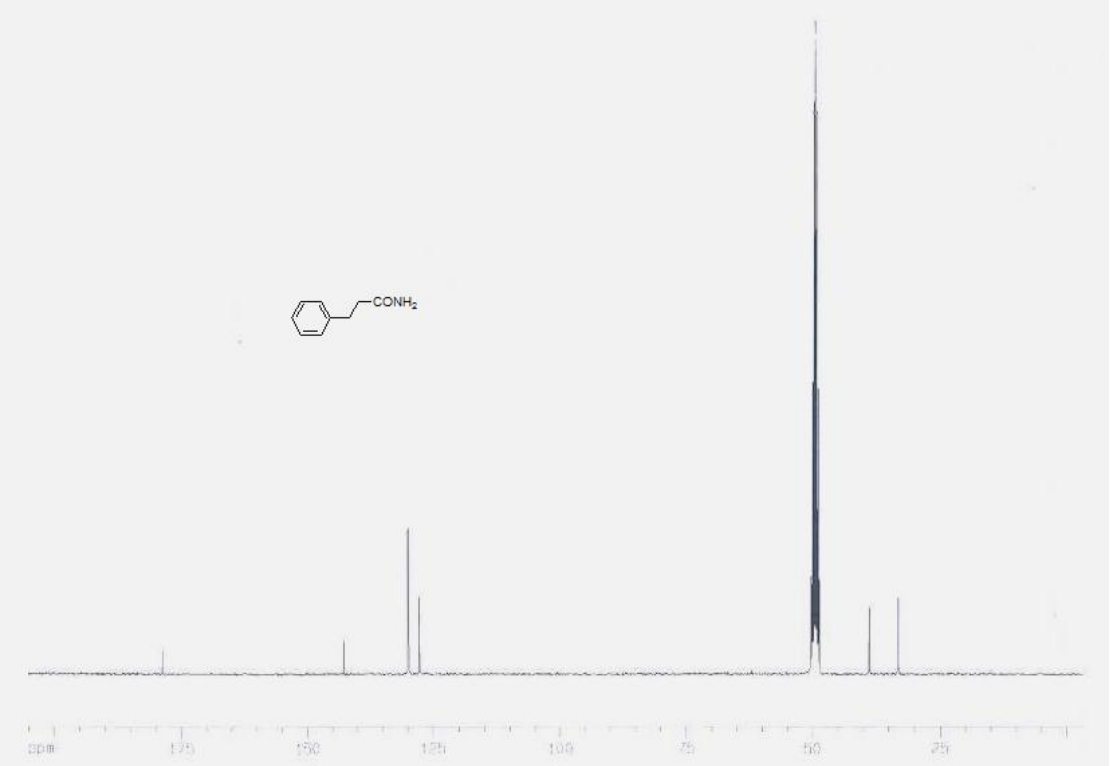


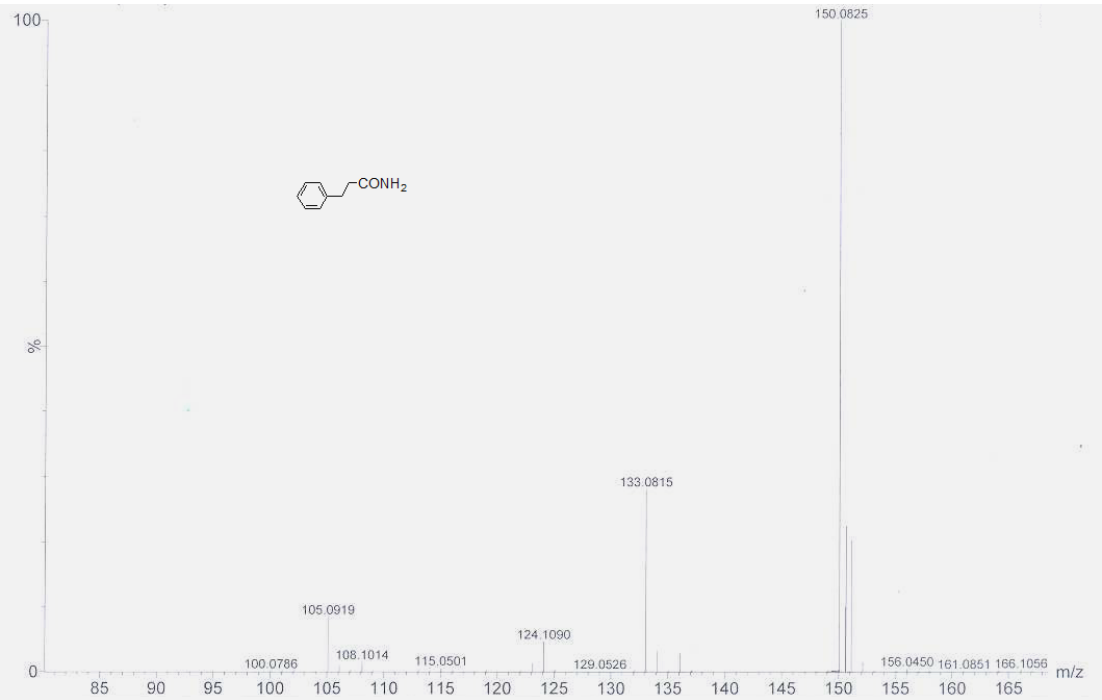




3-Phenylpropionamide (**2s**, Table 2, entry 18)







Propionamide (**2t**, Table 2, entry 19)