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$CuFe_2O_4$ nanoparticles catalyzed direct access to 2-azetidinones from alkynes and nitrones

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General

All required chemicals were purchased from Merck, Fluka and Acros chemical companies. The melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. IR spectra were measured on a Galaxy series FT-IR 5000 spectrometer. NMR spectra were recorded in $CDCl_3$ using a Bruker spectrometer (^{1}H NMR 300 MHz, ^{13}C NMR 75 MHz) and coupling constants were given in cycles per second (Hz). Elemental analyses were run on a Vario EL III elemental analyzer. The morphology of nanoparticles was investigated by TEM (Zeiss 906e HT-100kv). The phase composition of nanoparticles was considered by X-ray diffraction (XRD, D8, Advance, Bruker, axs). Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka.

Catalyst preparation.[1] To a solution of $Fe(NO_3)_3.9H_2O$ (3.34 g, 8.2 mmol) and $Cu(NO_3)_2.3H_2O$ (1 g, 4.1 mmol) in 60 mL of distilled water, 3 g (75 mmol) of NaOH dissolved in 20 mL of water was added at room temperature over a period of 25 min. during which black precipitate was formed. Then the reaction mixture was warmed to 90 ^{o}C and stirred. After 3 h, it was cooled to room temperature and the magnetic particles so formed were separated by a magnetic field. It was then washed with water several times. The catalyst was dried in oven at 80 ^{o}C overnight. Then it was ground in a mortar-pestle and kept in a furnace at 700 ^{o}C for 8 h and then cooled to room temperature slowly.

General procedure for the synthesis of 2-azetidinones 3a-p from alkynes and nitrones

Nitrones **2** (1 mmol) was added to a mixture of alkynes **l** (1 mmol), $CuFe_2O_4$ (15 mol%), and Et_2NH (1.1 mmol) in wet CH_3CN (10 mL) at room temperature. The resulting mixture was stirred for 18 hours. Then the catalyst was separated from the reaction mixture with an external magnet and the reaction mixture was extracted was poured to water (15 mL), extracted with chloroform (30 mL), washed with brine (30 mL), and dried over dry Na_2SO_4. The solvent was removed under reduced pressure and pure β-lactams **3a-p** were obtained after purification by crystallization from ethyl acetate. Characterization data for **3a-c** and **3e-l** have been previously reported.[2]

Data for new compound 3d:

1-(4-Chlorophenyl)-3-(hydroxymethyl)-4-(4-methoxyphenyl)azetidin-2-one (3d): Colorless solid, m.p. 114-116 °C. IR (KBr) cm^{-1}: 1756 (CO, β-lactam), 3449 (OH); ^{1}H NMR (300 MHz) δ 1.42 (OH, br, 1H), 3.39-3.55 (H-3 and CH_2O, m, 3H), 3.65 (OMe, s, 3H), 5.13 (H-4, d, 1H, *J*=5.9), 6.90-7.07 (ArH, m, 4H), 7.19-7.38 (ArH, m, 3H), 7.42 (ArH, d, 1H, *J*=8.6); ^{13}C NMR (75 MHz) δ 55.9 (CH_2O), 56.7 (OMe), 58.7 (C-3), 60.7 (C-4), 115.2, 120.4, 125.8, 127.9, 131.8, 133.1, 134.8, 153.4 (aromatic carbons), 161.3 (CO, β-lactam); Elemental anal. calcd for $C_{17}H_{16}ClNO_3$: C, 64.26; H, 5.08; N, 4.41. Found: C, 64.45; H, 5.24; N, 4.59.

1-(4-Chlorophenyl)-3-hydroxymethyl-4-phenyl-2-azetidinone (3m): Colorless solid. m.p: 172-175 ^{o}C. IR (KBr) cm^{-1}: 1749 (CO, β-lactam), 3310 (OH); ^{1}H NMR (300 MHz): δ 1.46 (OH, br, 1H), 3.50-3.68 (CH_2,H-3, m, 3H), 4.98 (H-4, d,1H, *J* = 5.3), 6.91-7.07 (ArH, m, 4H), 7.29-7.41 (ArH, m, 5H); ^{13}C NMR (75 MHz): δ 56.2 (CH_2), 59.5 (C-3), 62.0 (C-4), 116.8, 120.8, 124.1, 126.2, 129.4, 133.6,

134.6, 142.1 (aromatic carbons), 162.3 (CO, β-lactam); Elemental anal. calcd for $C_{16}H_{14}ClNO_2$: C, 66.79; H, 4.90; N, 4.87. Found: C, 66.93; H, 5.11; N, 4.99.

3-Butyl-1-(4-chlorophenyl)-4-phenyl-2-azetidinone (3n): Colorless solid. m.p: 167-169 ^oC. IR (KBr) cm^{-1}: 1742 (CO, β-lactam); ^1H NMR (300 MHz, $CDCl_3$): δ 0.77 (Me, t, 3H, J = 6.9), 1.10-1.19 (CH_2, m, 1H), 1.30-1.39 (CH_2, m, 3H), 1.54-1.73 (CH_2, m, 2H), 3.65 (H-3, dt, 1H, J = 5.7, 7.5), 5.22 (H-4, d, 1H, J = 5.7), 6.94-6.97 (ArH, d, 2H, J = 7.1), 7.06-7.11 (ArH, m, 1H), 7.23-7.36 (ArH, m, 6H); ^{13}C NMR (75 MHz): δ 13.7 (Me), 23.7, 26.2, 30.0 (CH_2), 53.3 (C-3), 59.7 (C-4), 118.4, 122.0, 125.9, 128.6, 130.2, 134.1, 135.6, 139.3 (aromatic carbons), 164.6 (CO, β-lactam); Elemental anal. calcd for $C_{19}H_{20}ClNO$: C, 72.72; H, 6.42; N, 4.46. Found: C, 72.84; H, 6.59; N, 4.61.

4-(4-Chlorophenyl)-3-hydroxymethyl-1-phenyl-2-azetidinone (3o): Colorless solid. m.p: 151-153 ^oC. IR (KBr) cm^{-1}: 1743 (CO, β-lactam), 3346 (OH); ^1H NMR (300 MHz,$CDCl_3$): δ 1.38 (OH, s, 1H), 3.48-3.70 (CH_2, H-3, m, 3H), 4.95 (H-4, d,1H, J = 5.7), 6.92-7.07 (ArH, m, 3H), 7.23-7.45 (ArH, m, 4H), 7.52-7.63 (ArH, m, 2H); ^{13}C NMR (75 MHz): δ 54.3 (CH_2), 60.2 (C-3), 61.9 (C-4), 117.0, 121.0, 125.1, 126.6, 130.4, 132.4, 134.6, 140.8 (aromatic carbons), 162.6 (CO, β-lactam; Elemental anal. calcd for $C_{16}H_{14}ClNO_2$: C, 66.79; H, 4.90; N, 4.87. Found: C, 66.95; H, 5.08; N, 5.01.

3-Butyl-4-(4-chlorophenyl)-1-phenyl-2-azetidinone (3p): Colorless solid. m.p: 157-159 ^oC. IR (KBr) cm^{-1}: 1759 (CO, β-lactam); ^1H NMR (300 MHz, $CDCl_3$): δ 0.78 (Me, t, 3H, J = 7.1), 1.04-1.08 (CH_2, m, 1H), 1.29-1.41 (CH_2, m, 3H), 1.64-1.74 (CH_2, m, 2H), 3.48 (H-3, dt, 1H, J = 6.0, 7.3), 5.04 (H-4, d,1H, J = 6.0), 7.07-7.17 (ArH, m, 2H), 7.28-7.48 (ArH, m, 7H); ^{13}C NMR (75 MHz): δ 14.1 (Me), 24.0, 27.6, 31.2 (CH_2), 54.0 (C-3), 61.7 (C-4), 118.6, 120.5, 124.5, 126.4, 129.2, 132.6, 137.1, 141.0 (aromatic carbons), 165.3 (CO, β-lactam); Elemental anal. calcd for $C_{19}H_{20}ClNO$: C, 72.72; H, 6.42; N, 4.46. Found: C, 72.80; H, 6.62; N, 4.59.

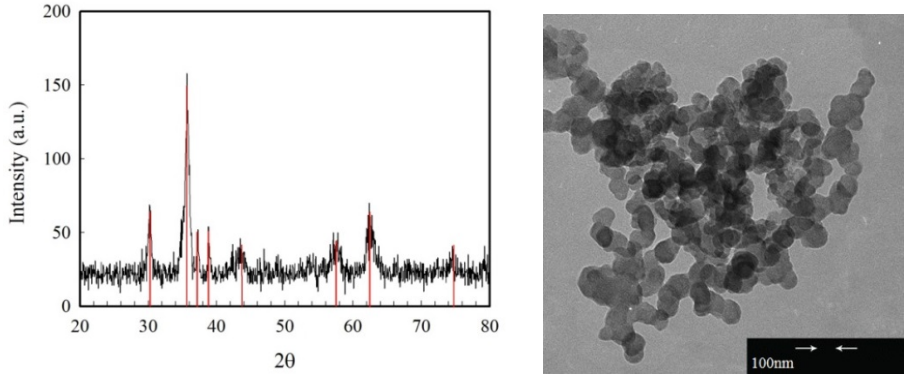


Figure 1. XRD pattern (left) and TEM images (right) of $CuFe_2O_4$ nanoparticles.

Figure 2. Magnetic recoverability of $CuFe_2O_4$ nanocatalyst

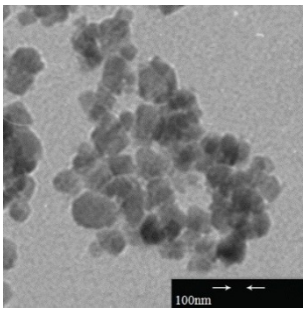
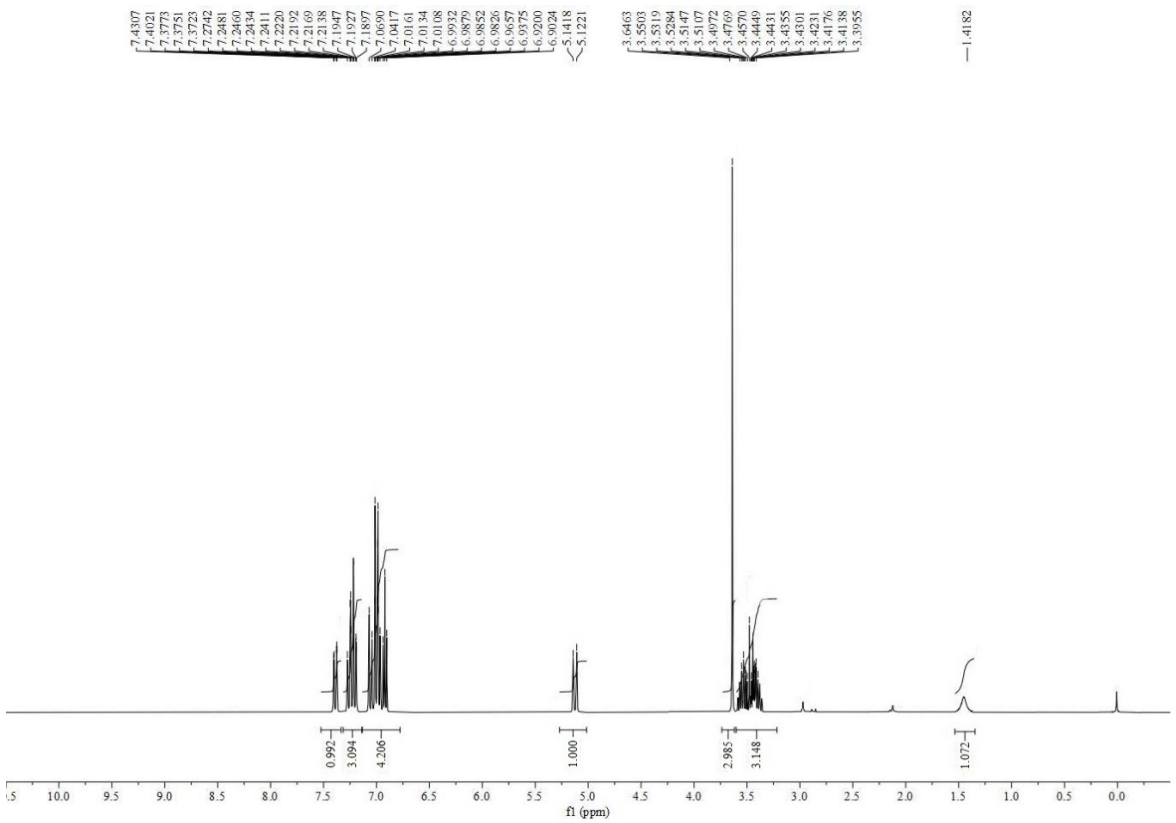
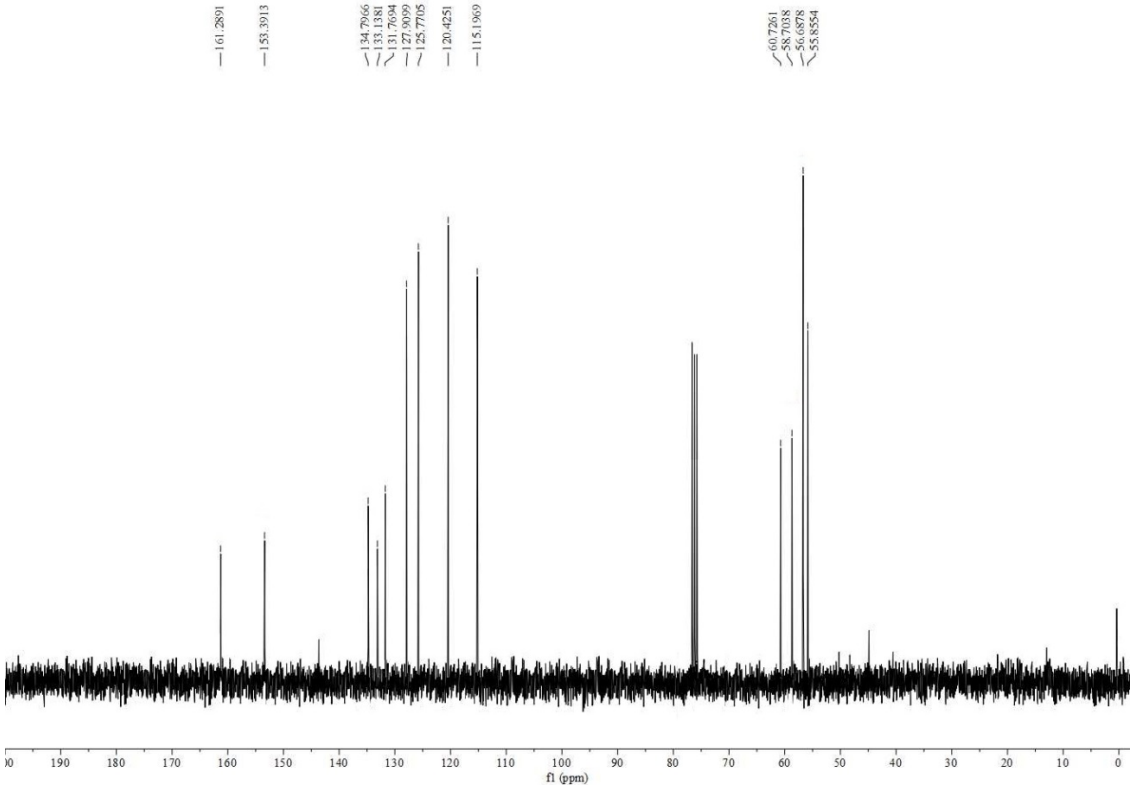


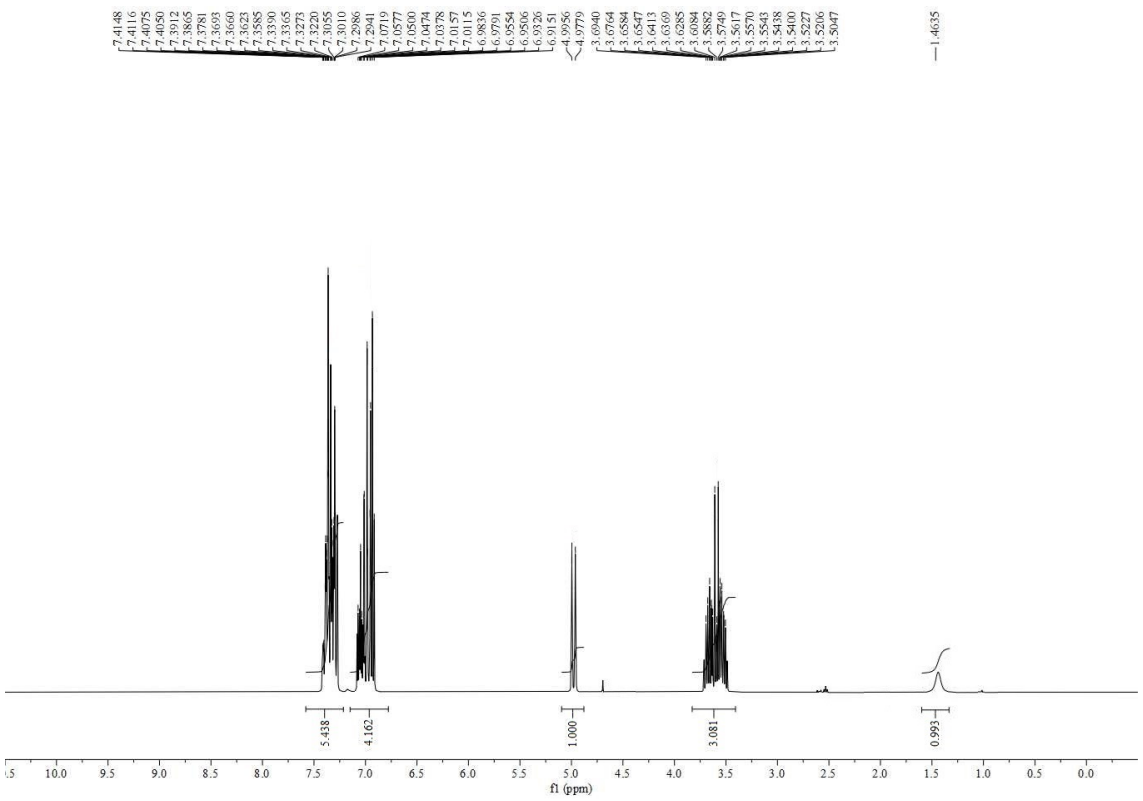
Figure 3. TEM image of used $CuFe_2O_4$ nanoparticles



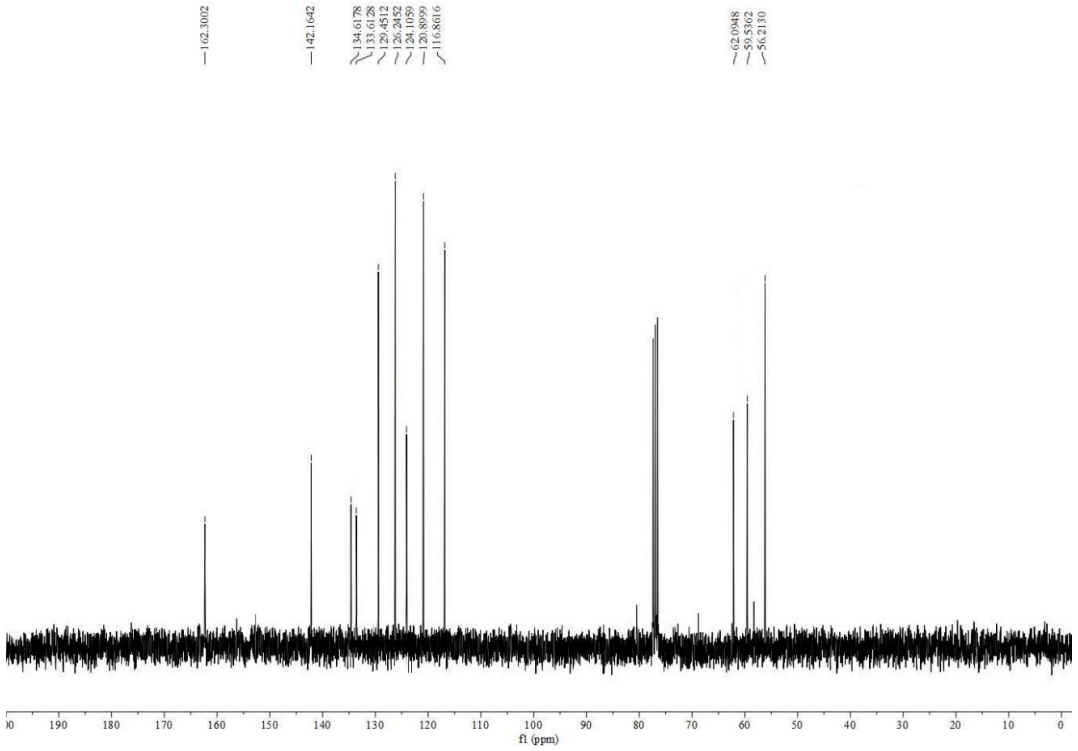
[1]H NMR. 1-(4-Chlorophenyl)-3-(hydroxymethyl)-4-(4-methoxyphenyl)azetidin-2-one (3d)



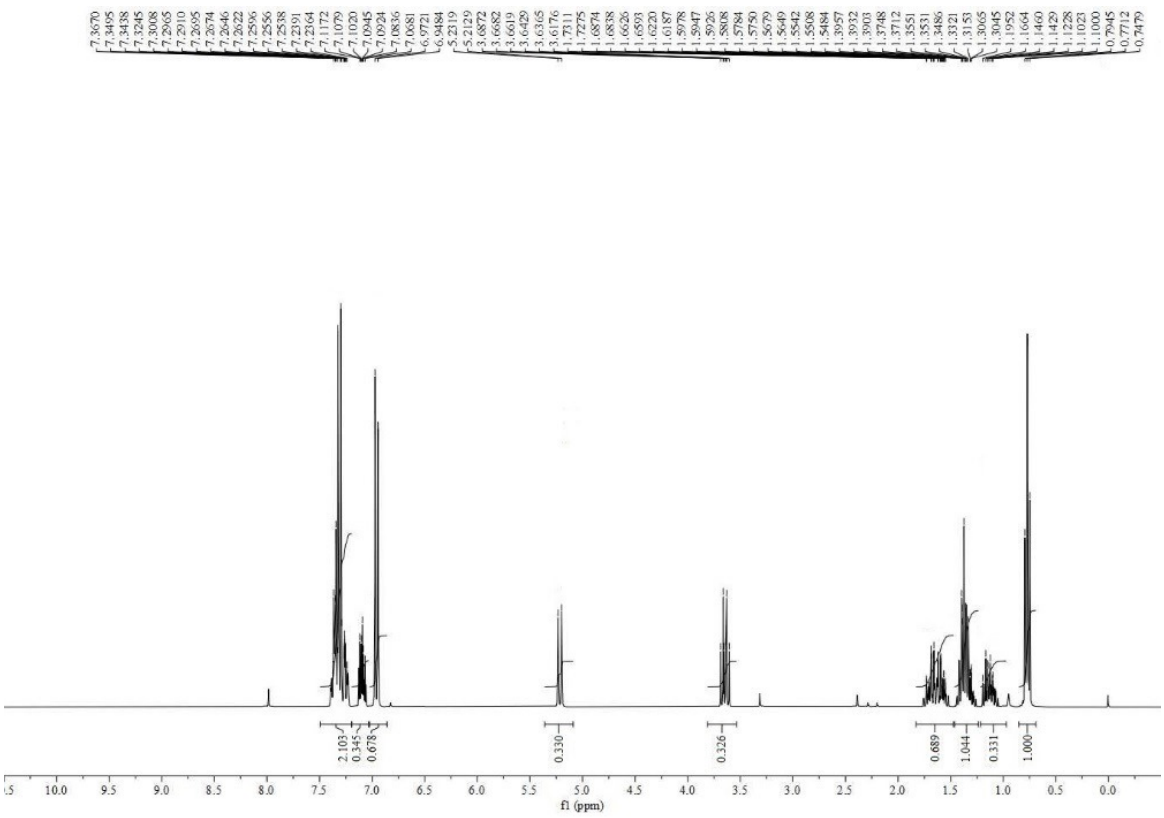
[13]C NMR. 1-(4-Chlorophenyl)-3-(hydroxymethyl)-4-(4-methoxyphenyl)azetidin-2-one (3d)



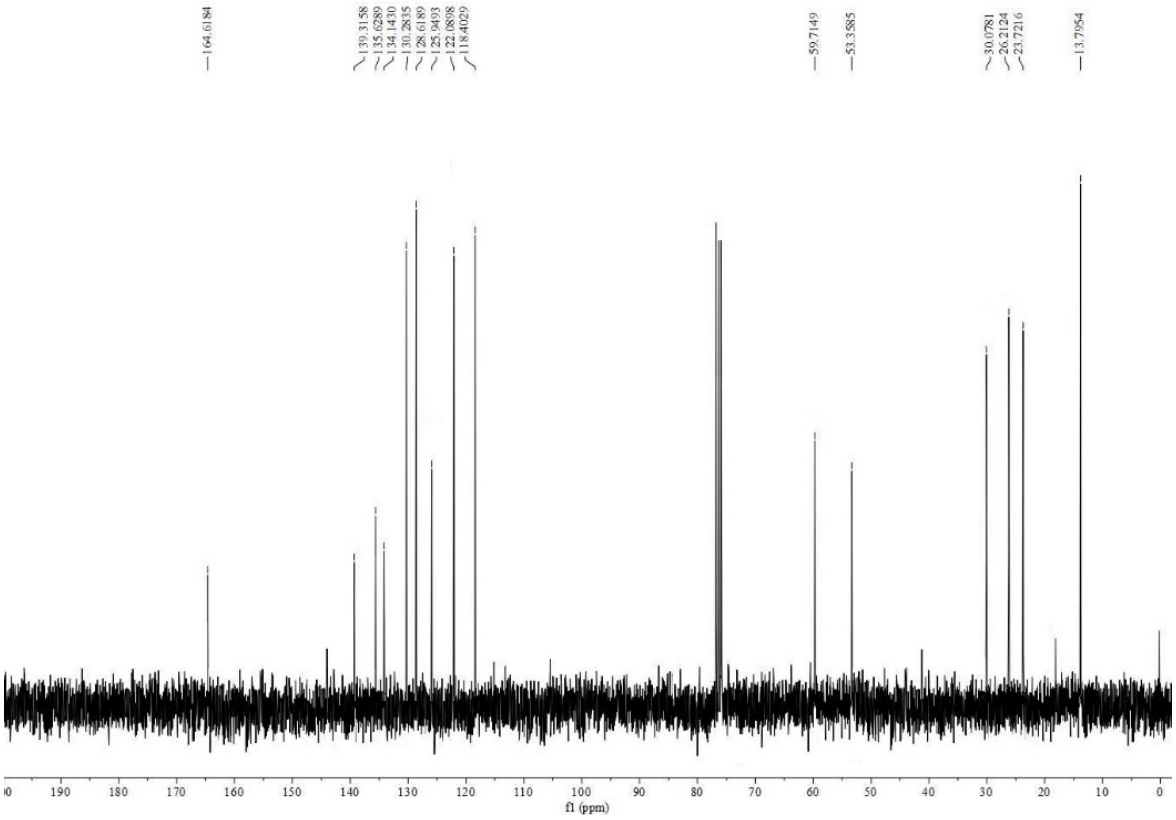
^{1}H NMR: 1-(4-Chlorophenyl)-3-hydroxymethyl-4-phenyl-2-azetidinone (3m)



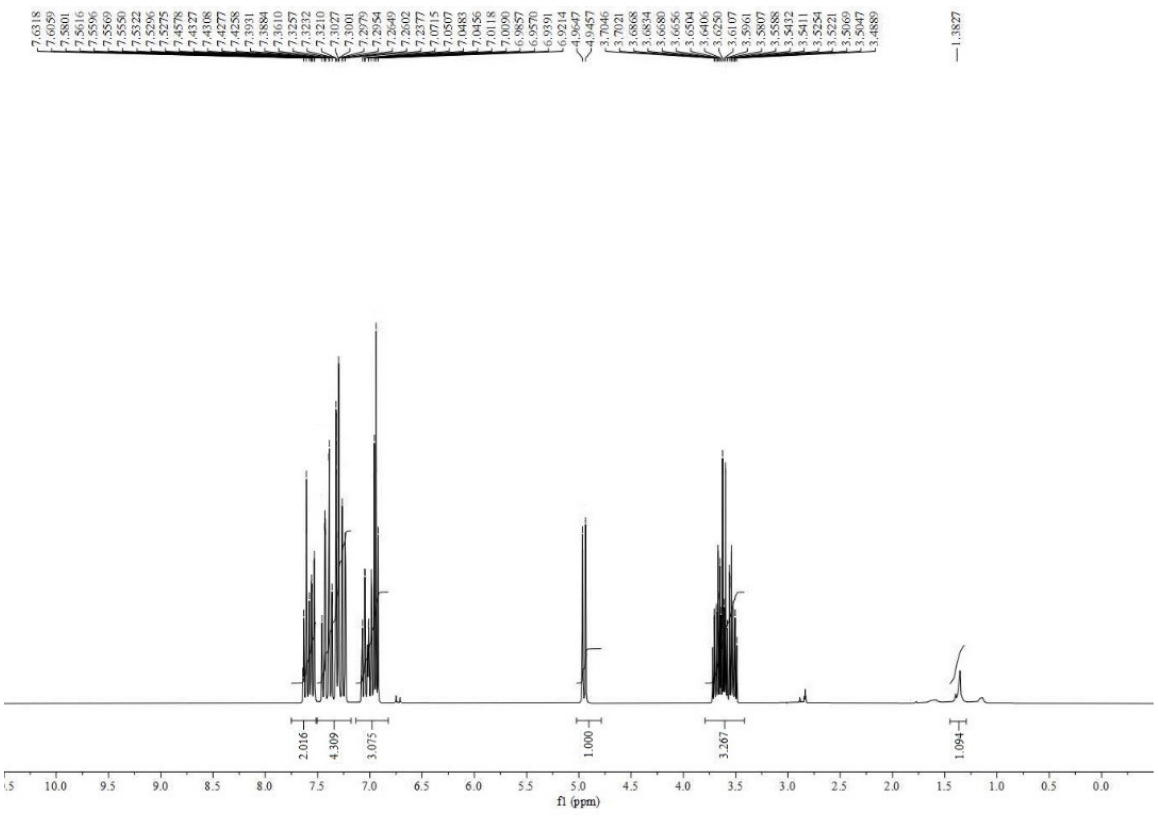
^{13}C NMR: 1-(4-Chlorophenyl)-3-hydroxymethyl-4-phenyl-2-azetidinone (3m)



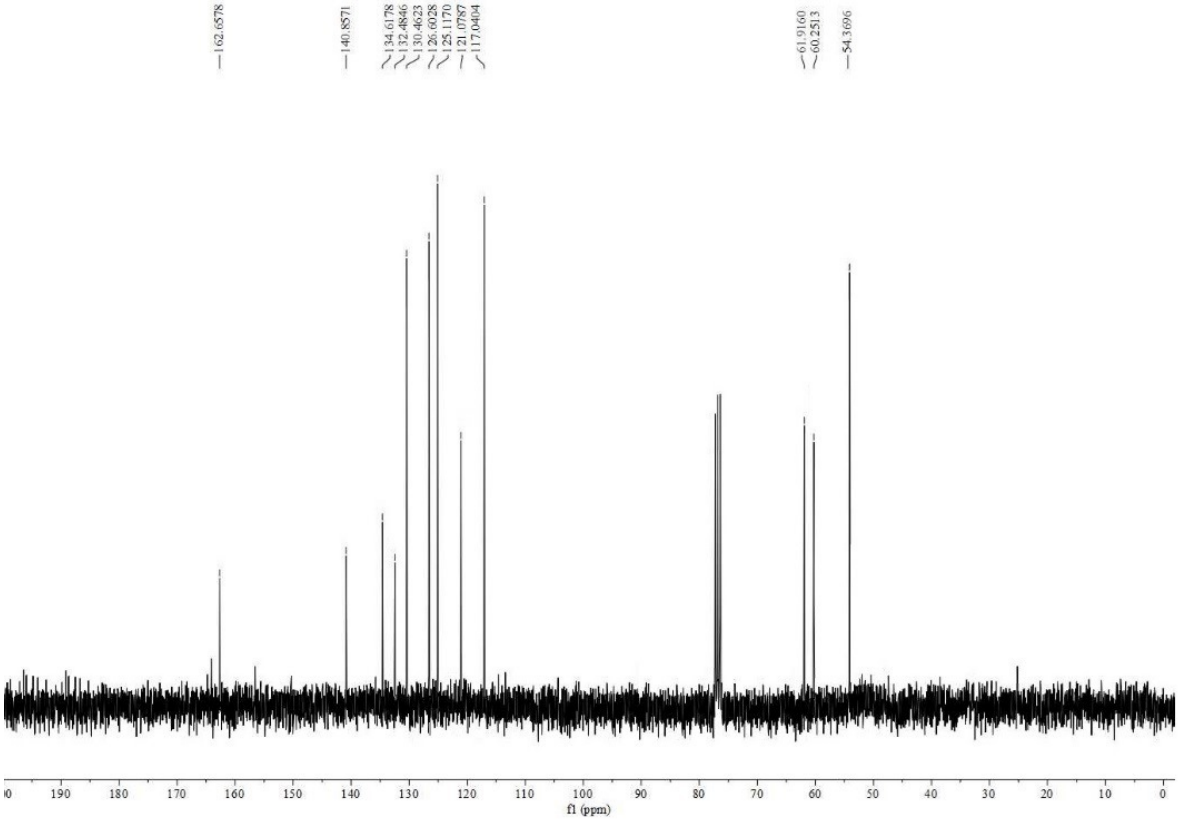
^{1}H NMR: 3-Butyl-1-(4-chlorophenyl)-4-phenyl-2-azetidinone (3n)



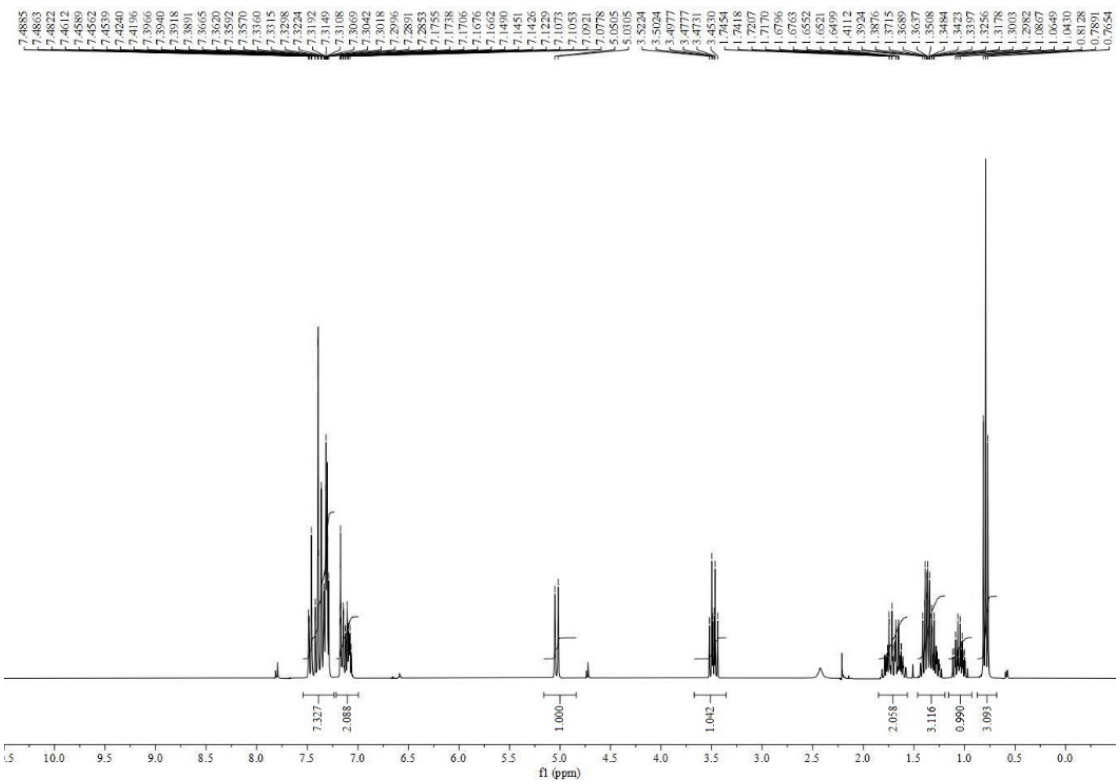
^{13}C NMR: 3-Butyl-1-(4-chlorophenyl)-4-phenyl-2-azetidinone (3n)



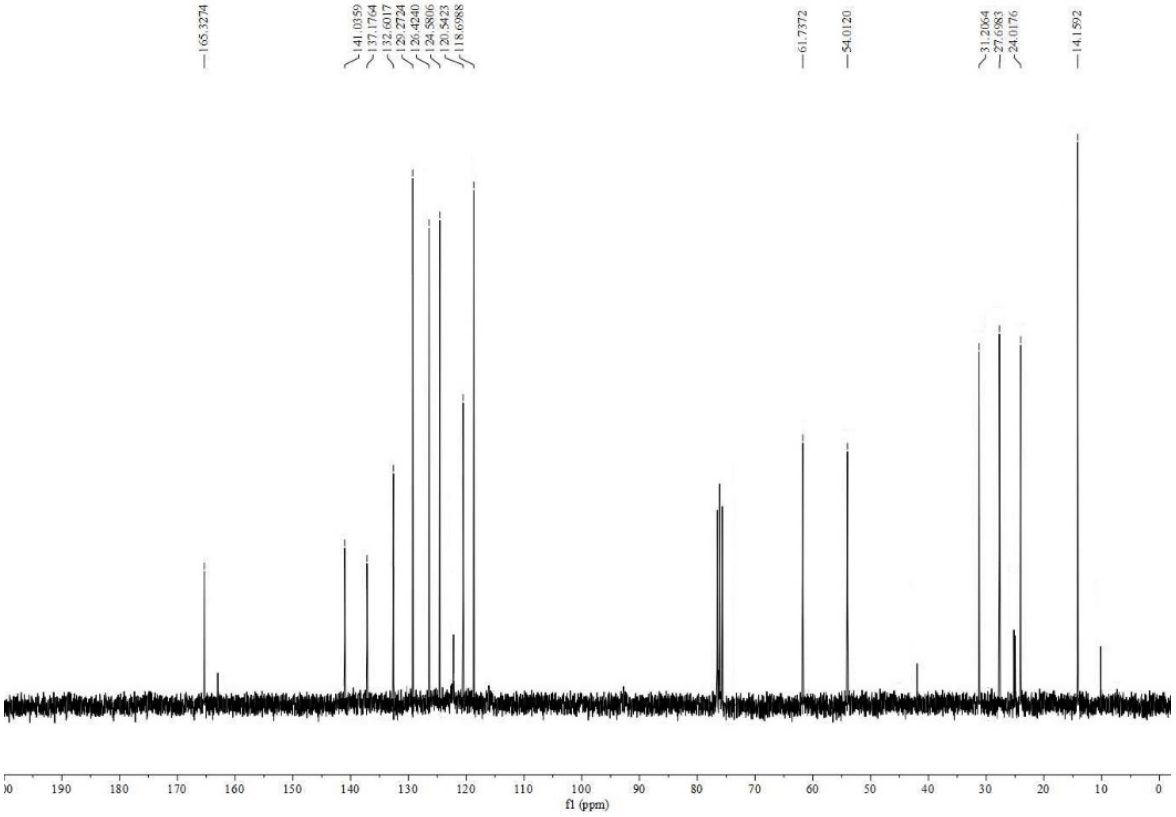
^{1}H NMR: 4-(4-Chlorophenyl)-3-hydroxymethyl-1-phenyl-2-azetidinone (3o)



^{13}C NMR: 4-(4-Chlorophenyl)-3-hydroxymethyl-1-phenyl-2-azetidinone (3o)



^{1}H NMR: 3-Butyl-4-(4-chlorophenyl)-1-phenyl-2-azetidinone (3p)



^{13}C NMR: 3-Butyl-4-(4-chlorophenyl)-1-phenyl-2-azetidinone (3p)

References:

1. N. Panda, A. Kumar Jena, S. Mohapatra, S. Ranjan Rout, *Tetrahedron Lett.*, 2011, **52**, 1924.
2. (a) C. Gluchowski; L. Cooper; D. E. Bergbreiter; M. Newcomb; *J. Org. Chem.*, 1980, **45**, 3413. (b) H. Sterk, G. Uray, E. Ziegler, *Monatsh. Chem.*, 1972, **103**, 544. (c) T. Sheradsky, D. Zbaida, *J. Org. Chem.*, 1980, **45**, 2165. (d) M. V. Diurno, O. Mazzoni, E. Piscopo, A. Bolognese, *IL Farmaco*, 1995, **50**, 143. (e) Y. Kumar, P. Singh, G. Bhargava, *New J. Chem.,* 2016, **40**, 8216. (f) A. Basak, G. Bhattacharya, H. M. M. Bdour, *Tetrahedron*, 1998, **54**, 6529. (g) C. S. Cho, L. H. Jiang, S. C. Shim, *Synth. Commun.*, 1999, **29**, 2695. (h) A. Bolognese, M. V. Diurno, O. Mazzoni, F. Giordano, *Tetrahedron*, 1991, **47**, 7417.