Eur. J. Org. Chem. **2008** · © WILEY-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2008 · ISSN 1434–193X

SUPPORTING INFORMATION

Title: Oxidative Amidation of Aldehydes and Alcohols with Primary Amines Catalyzed by KI-TBHP
Author(s): K. Rajender Reddy,* C. Uma Maheswari, M. Venkateshwar, M. Lakshmi Kantam
Ref. No.: O200800454

General Information

^{1}H NMR spectra were recorded on a Gemini-200 MHz or an Avance-300 MHz spectrometer in $CDCl_3$ with TMS as an internal standard. GC were recorded on Schimadzu using BP-01 (30M X 0.25 mm X 1.0 μm) column. GC-MS spectra were recorded on Trace DSQ GC-MS spectrometer using BP-01 (30M X 0.25 mm X 1.0 μm) column.

General Procedure For synthesis of Amide from Amines:

To a solution of aldehyde (1.0 mmol), potassium iodide (0.05 mmol) and amine (1.2 mmol) in 3 mL of water was added a solution of 70% aqueous TBHP (2.2 mmol) dropwise over a period of 30 min and stirred at 80 ^{o}C. Progress of the reaction was monitored by TLC and after completion of the reaction; mixture was quenched with saturated aqueous $Na_2S_2O_3$, washed with brine, extracted with ethyl acetate and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography using hexane/ethyl acetate mixture and was analyzed by ^{1}H NMR, GC and GC-MS. Similar procedure was followed for synthesis of amides from benzyl alcohol with primary amines.

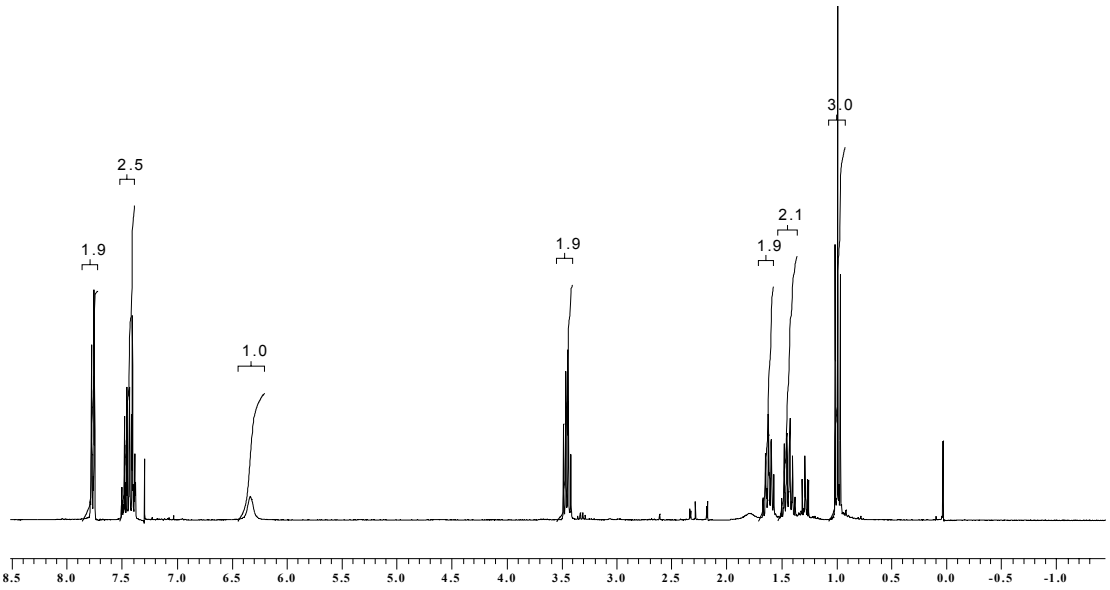
General Procedure for the synthesis of Amide from Amino acid derivatives:

To a solution of potassium iodide (0.20 mmol) and amino acid derivative (1.1 mmol) in 3 mL of acetonitrile was added , a solution of 70% aqueous TBHP (2.2 mmol) dropwise over a period of 30 min at room temperature. Then aldehyde (1.0 mmol) was added slowly for 1 h and stirred at 80 ^{o}C. Progress of the reaction was monitored by TLC and after completion of the reaction; mixture was quenched with saturated aqueous $Na_2S_2O_3$, washed with brine, extracted with ethyl acetate and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography using hexane/ethyl acetate mixture and was analyzed by ^{1}H NMR, GC and GC-MS.

^{1}H NMR and Mass spectral Data

Table 2, Entry 1
N-Butyl-benzamide (3a):

Isolated yield = 75%; ^{1}H NMR δ(300 MHz, $CDCl_3$) 7.76 (d, *J* = 8.3 Hz, Ar, 2H), 7.37 - 7.51 (m, Ar, 3H), 6.35(br, s, -*NH*, 1H,), 3.45 (q, *J* = 12.84, NH-C*H*$_2$, 2H,), 1.62 (q, *J* = 14.35, NH-CH_2-C*H*$_2$, 2H,), 1.38-1.50(m, NH-CH_2- CH_2- C*H*$_2$, 2H,), 0.99 (t, J = 6.79, -C*H*$_3$, 3H).



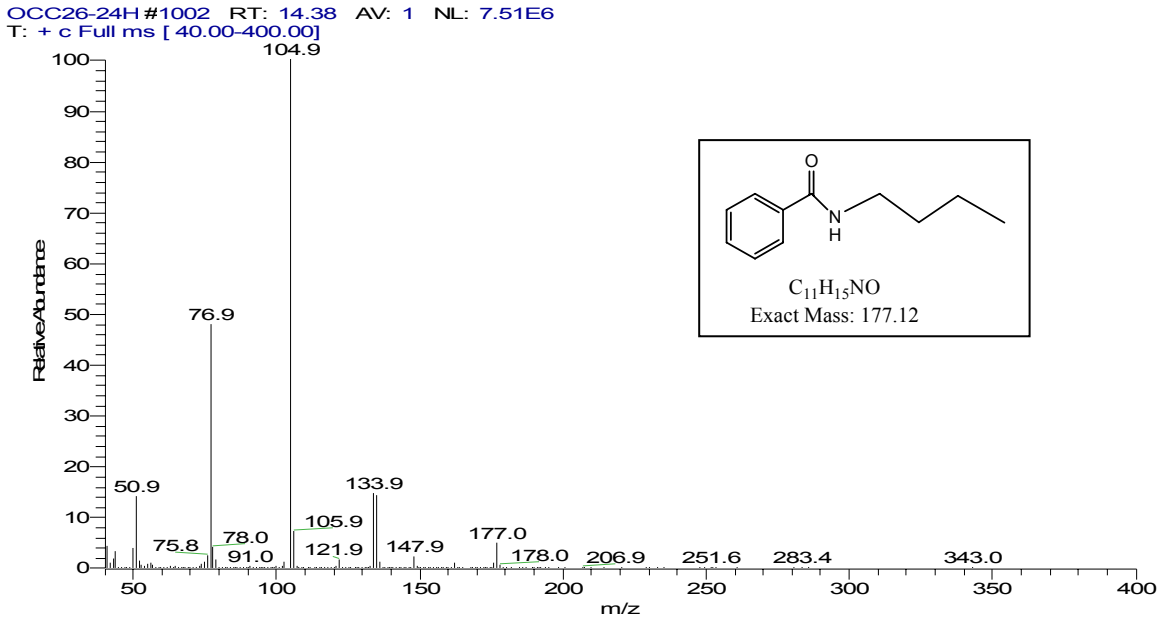
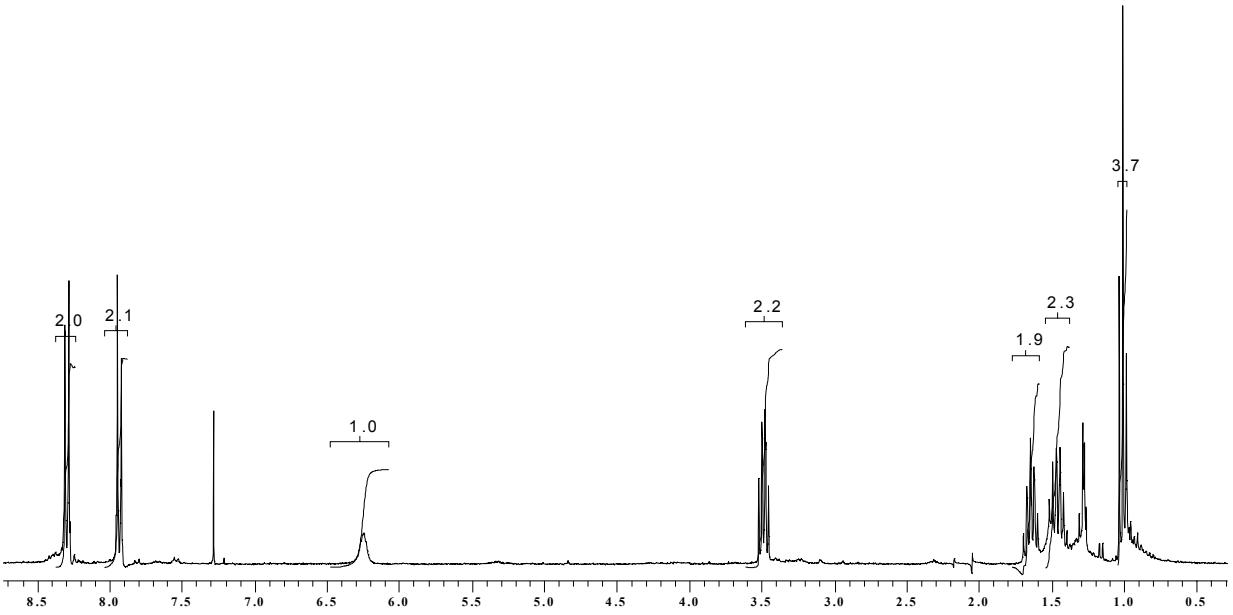


Table 2,Entry 2

N-Butyl-4-nitro-benzamide (3b):

Isolated yield = 32%;H NMR δ(300 MHz,$CDCl_3$) 8.3 (d, *J* = 8.3 Hz, 2H, Ar), 7.92 (d, *J* = 8.3, 2H, Ar), 6.25 (br, s, -N*H*, 1H), 3.48 (q, *J* = 12.84, NH-CH_2, 2H), 1.65 (quin, *J* = 6.79, NH-CH_2-CH_2, 2H), 1.38 - 1.52 (m, NH-CH_2- CH_2- CH_2, 2H), 1.0(t, *J* = 6.55,-CH_3, 3H)



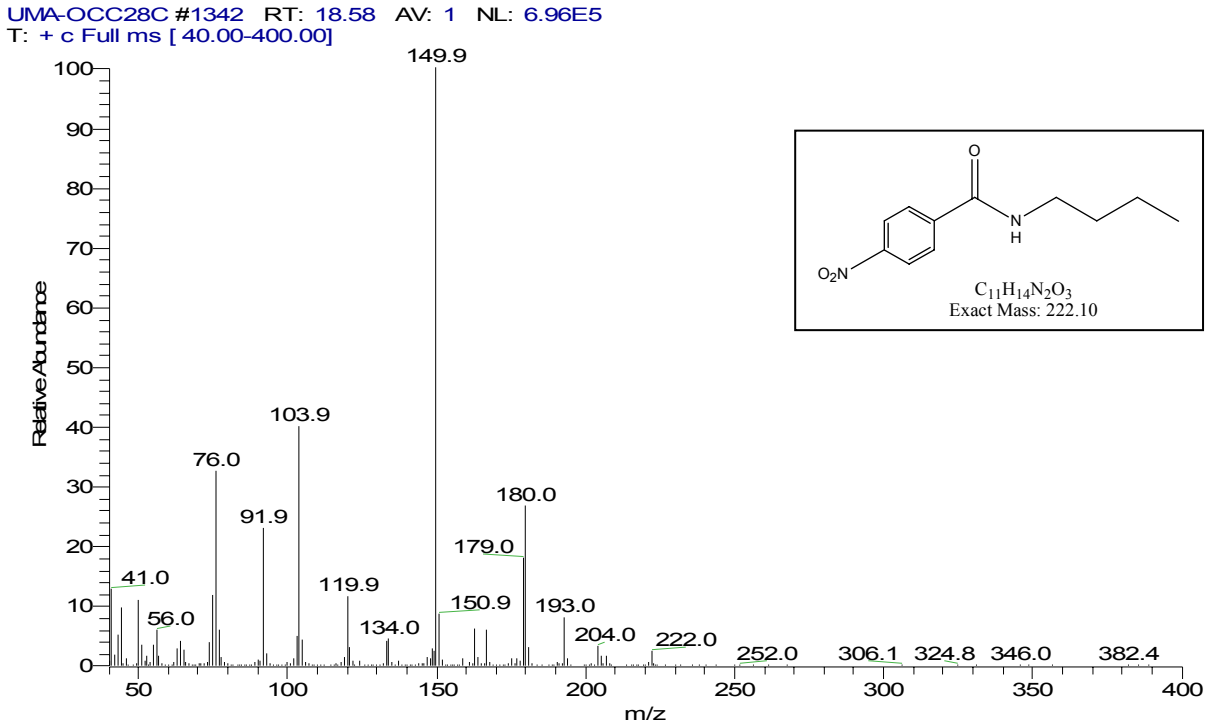
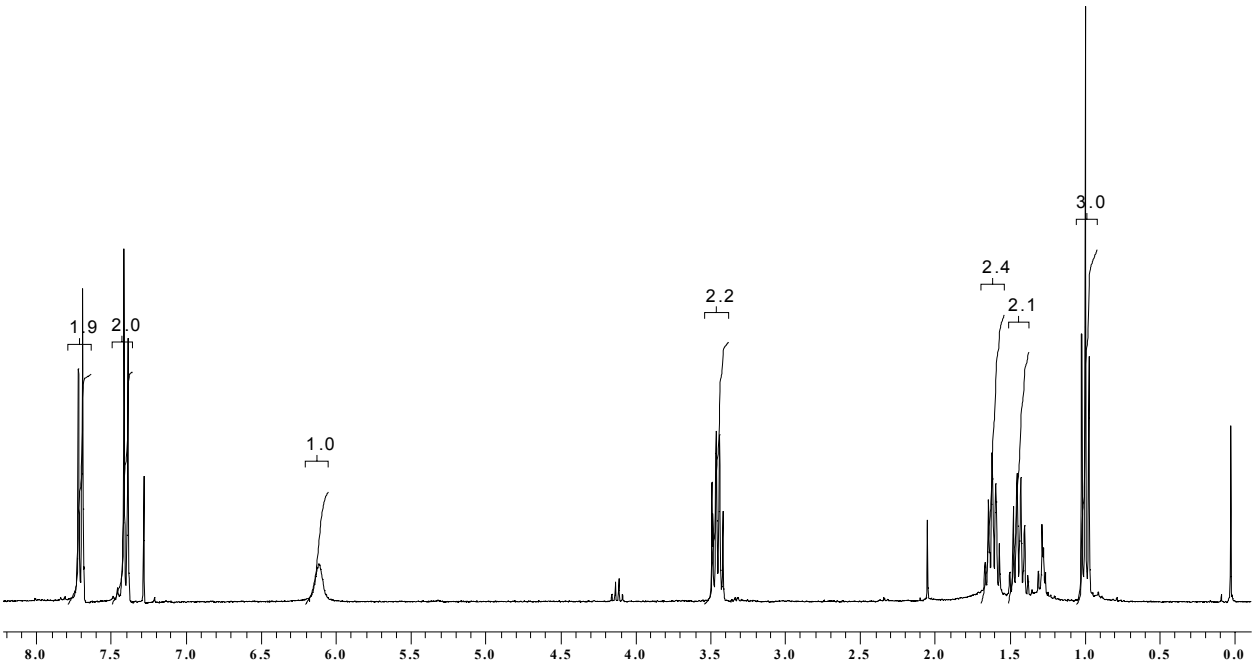


Table 2,Entry 3

N-Butyl-4-chloro-benzamide (3c):

Isolated yield-77%.^{1}H NMR δ(300 MHz,$CDCl_3$) 7.70 (d, *J* = 9.0Hz, 2H, Ar), 7.40 (d, *J* = 8.3, 2H, Ar), 6.15 (br, s, -N*H*, 1H), 3.45 (q, *J* = 12.84, NH-CH_2, 2H), 1.62 (quin, *J* = 14.35, NH-CH_2-CH_2, 2H),1.38-1.50 (m, NH-CH_2- CH_2- CH_2, 2H),1.0 (t,*J* = 6.80 , -CH_3 , 3H).



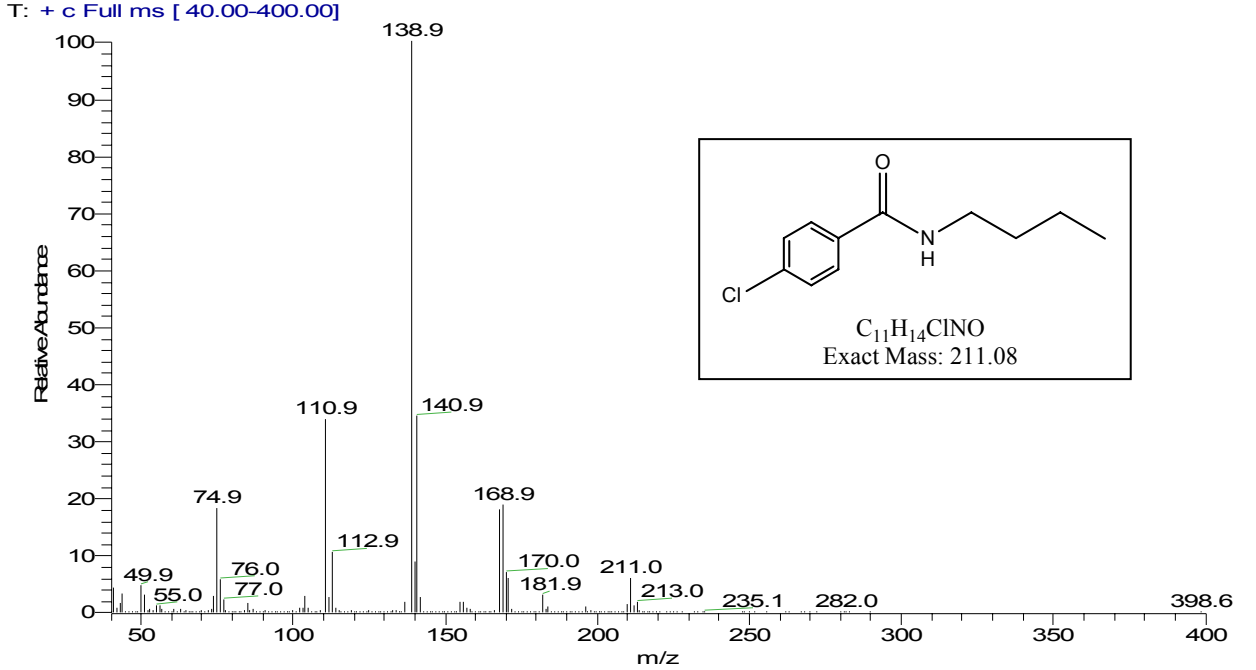
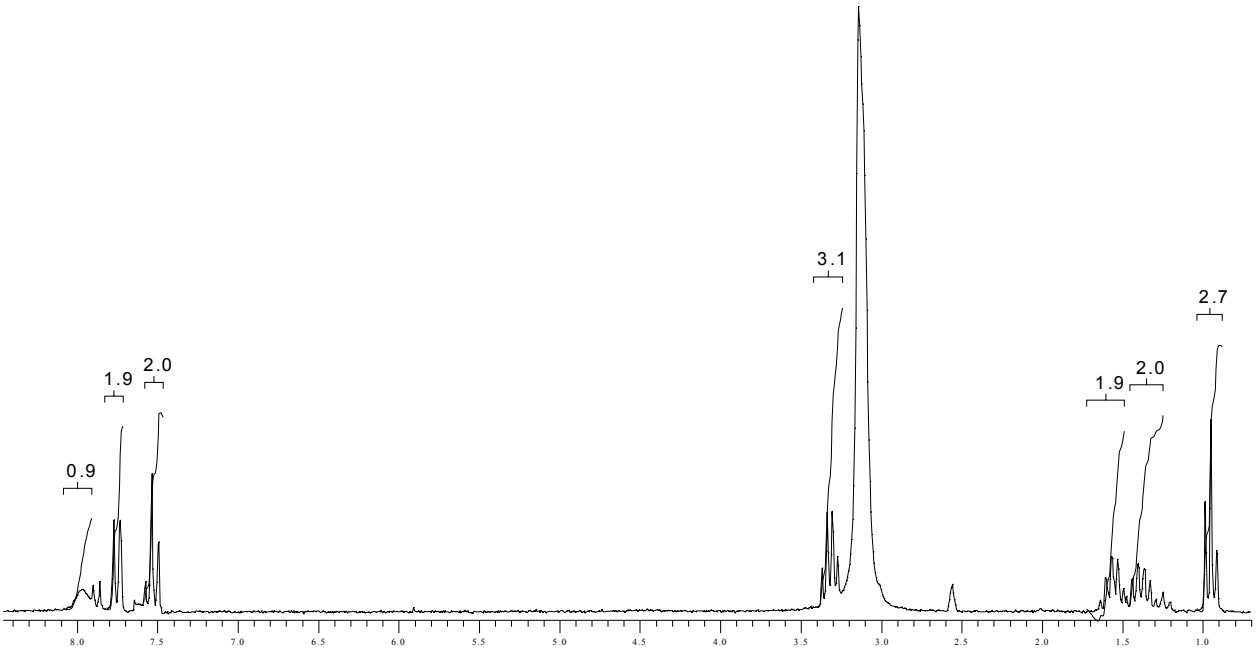


Table 2, Entry 4

N-Butyl-4-Bromo-benzamide (3d):

Isolated yield-44%.^{1}H NMR δ(300 MHz,$CDCl_3$ + DMSO) 8.00(s, broad, 1H, -N*H*), 7.75 (d, 2H, *J* = 7.6, Ar), 7.50 (d, *J* = 8.8, Ar, 2H), 3.30 (q, *J* = 12.84, NH-CH_2, 2H),1.55 (quin, *J* = 14.30 NH-CH_2-CH_2, 2H), 1.20 - 1.48 (m, NH-CH_2-CH_2-C*H*, 2H), 0.95 (t, J = 6.79, -CH_3, 3H).



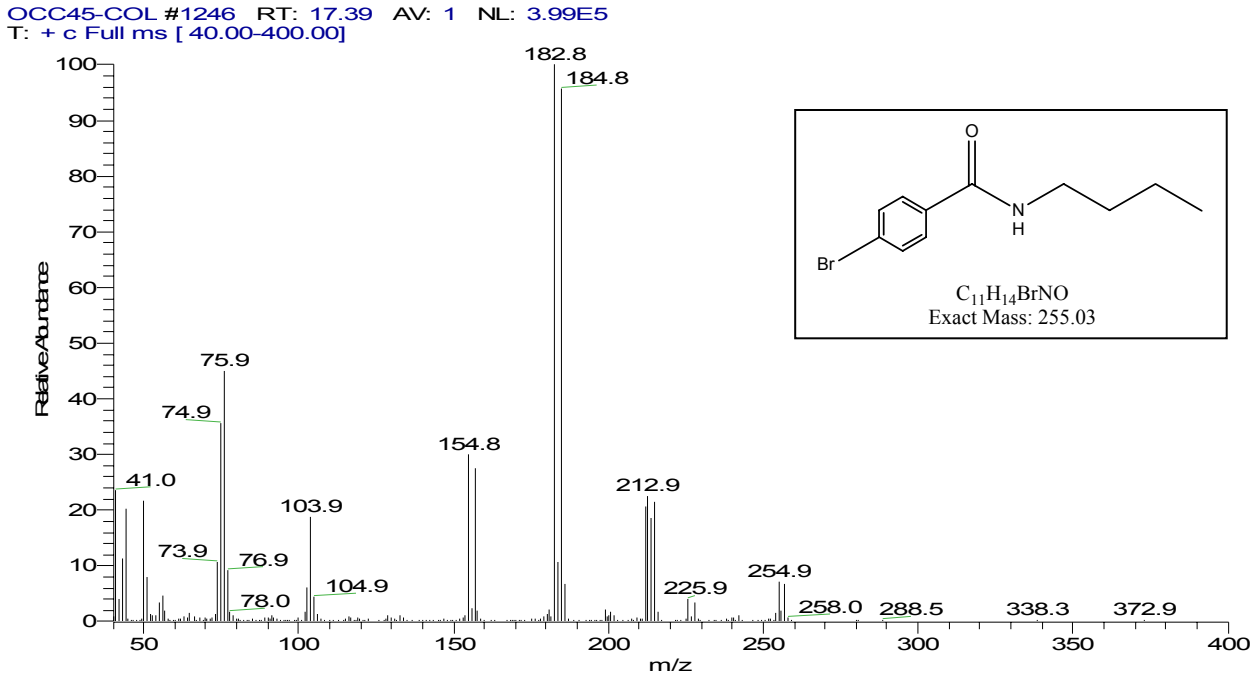
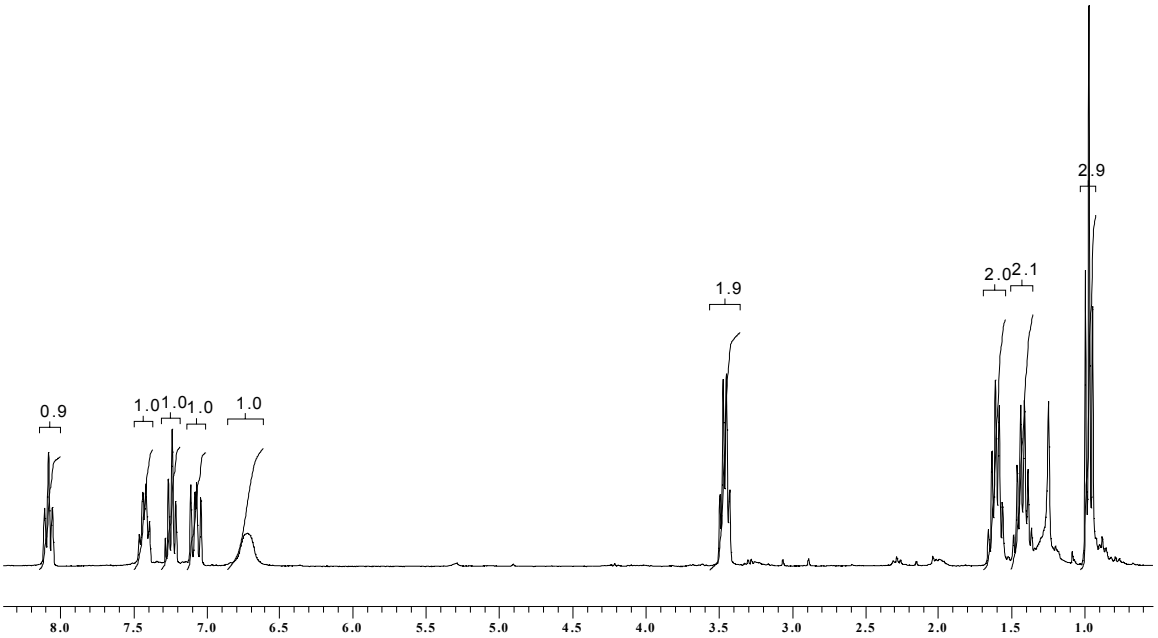


Table 2,Entry 5

N-Butyl-4-fluoro-benzamide (3e):

Isolated yield= 72%.^{1}H NMR δ(300 MHz,$CDCl_3$) 8.10 (t, *J* = 15.10, Ar, 1H), 7.40 (q, *J* = 13.59, Ar, 1H), 7.25 (q, J = 13.59, Ar, 1H), 7.10 (q, *J* = 12.08, Ar, 1H), 6.75 (br s, -N*H*, 1H), 3.45 (q, *J* = 13.59, NH-CH_2, 2H), 1.62 (quin, *J* = 14.35, NH-CH_2-CH_2, 2H),1.35 - 1.48 (m, NH-CH_2- CH_2- CH_2, 2H), 0.95 (t,*J* = 6.79, -CH_3, 3H).



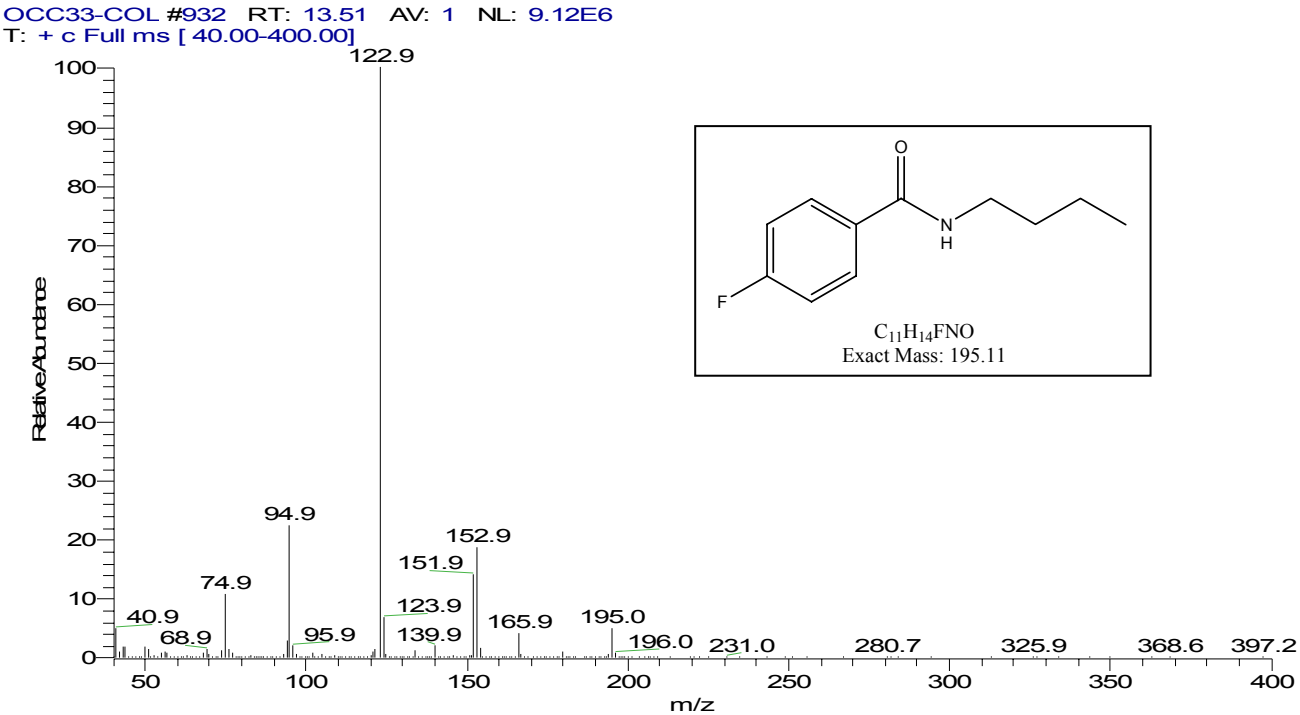
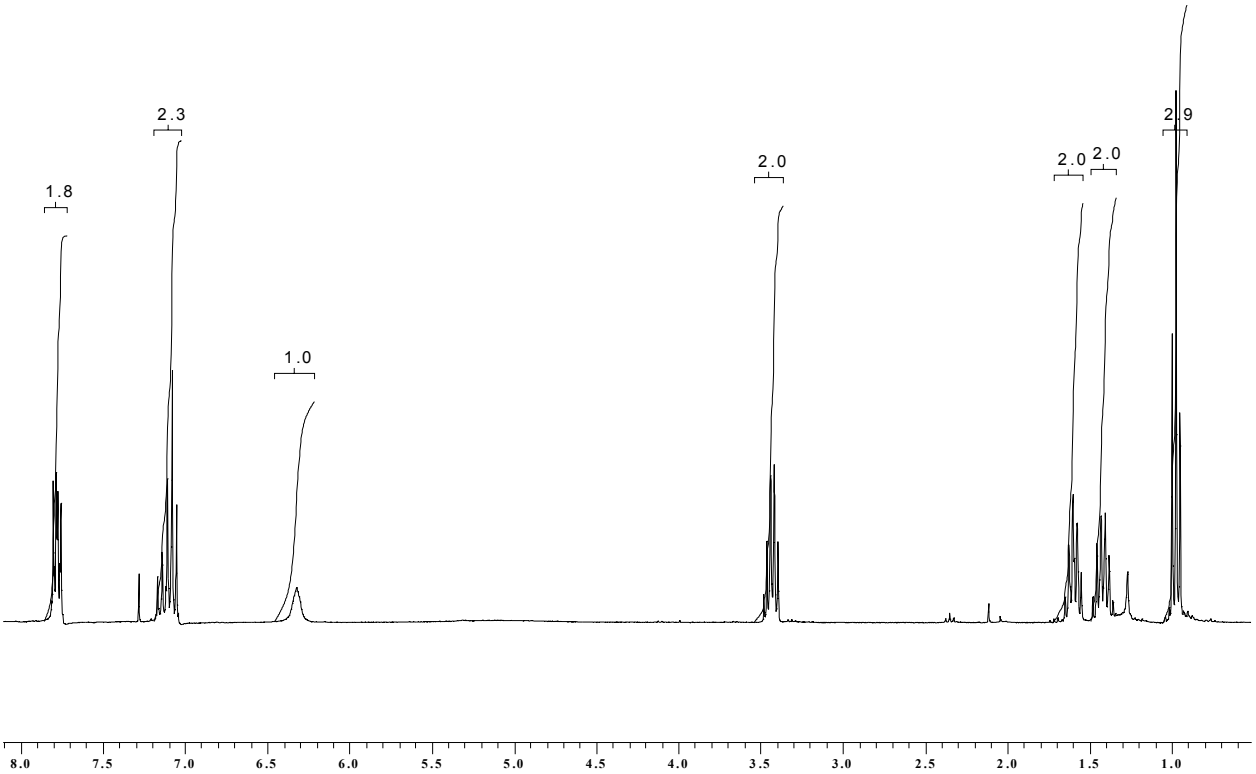


Table 2, Entry 6

N-Butyl-2-fluoro-benzamide (3f):

Isolated yield-63%.^{1}H NMR δ(300 MHz,$CDCl_3$) 7.75-7.81 (m, Ar, 2H), 7.04-7.17(m, Ar, 3H), 6.35 (br, s, -N*H*, 1H), 3.45(q, *J* = 12.84, NH-CH_2, 2H), 1.60 (quin,*J* = 14.35, NH-CH_2-CH_2, 2H),1.35-1.48 (m, NH-CH_2- CH_2- CH_2, 2H), 0.98 (t,J = 6.80, -CH_3,3H).



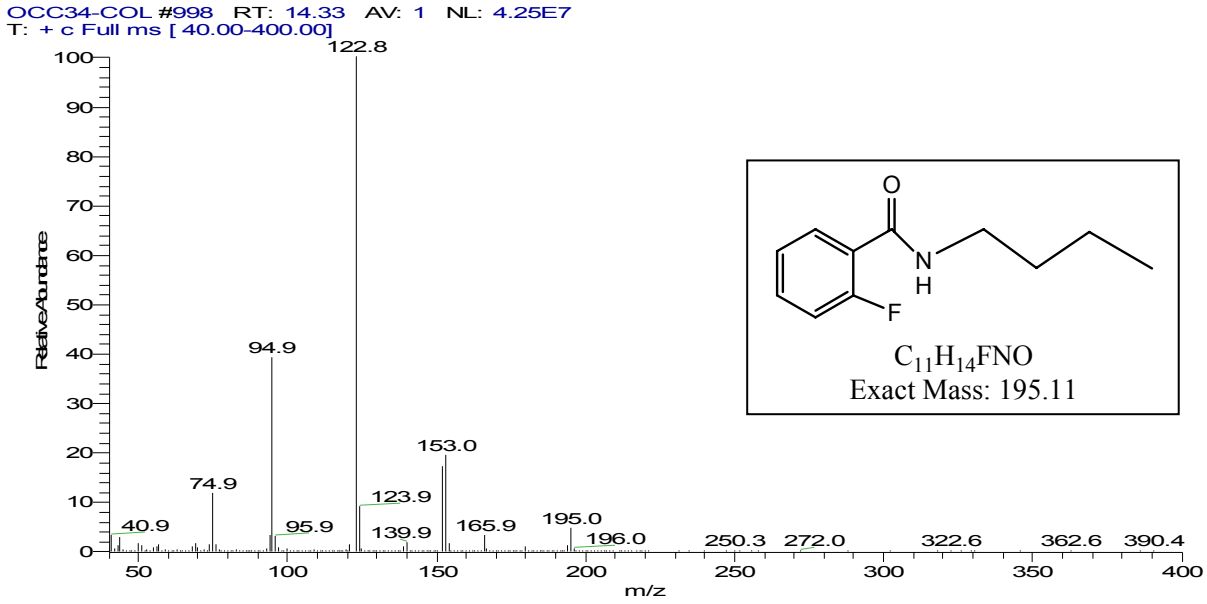
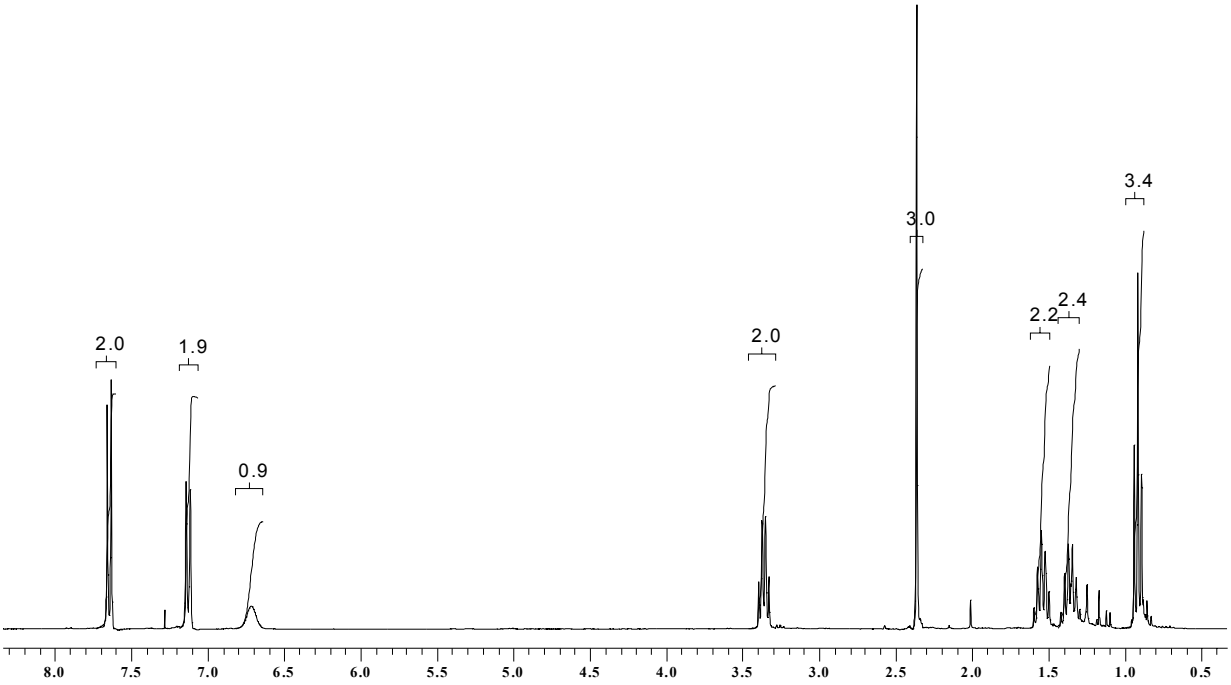


Table 2,Entry 7

N-Butyl-4-Methyl-benzamide (3g):

Isolated yield= 80%;^{1}H NMR δ(300 MHz,$CDCl_3$) 7.65 (d, *J* = 8.3 Hz, Ar, 2H), 6.13 (d, *J*= 8.3, Ar, 2H), 6.7(br, s, -N*H*, 1H), 3.36(q, *J*=12.84,NH-C*H*$_2$,2H), 2.36(s,C*H*$_3$,3H),1.55(quin, *J* = 15.10, NH-CH_2-C*H*$_2$, 2H), 1.30 -1.42 (m, NH-CH_2- CH_2- C*H*$_2$, 2H), 0.92 (t, *J* = 6.79, -C*H*$_3$, 3H).



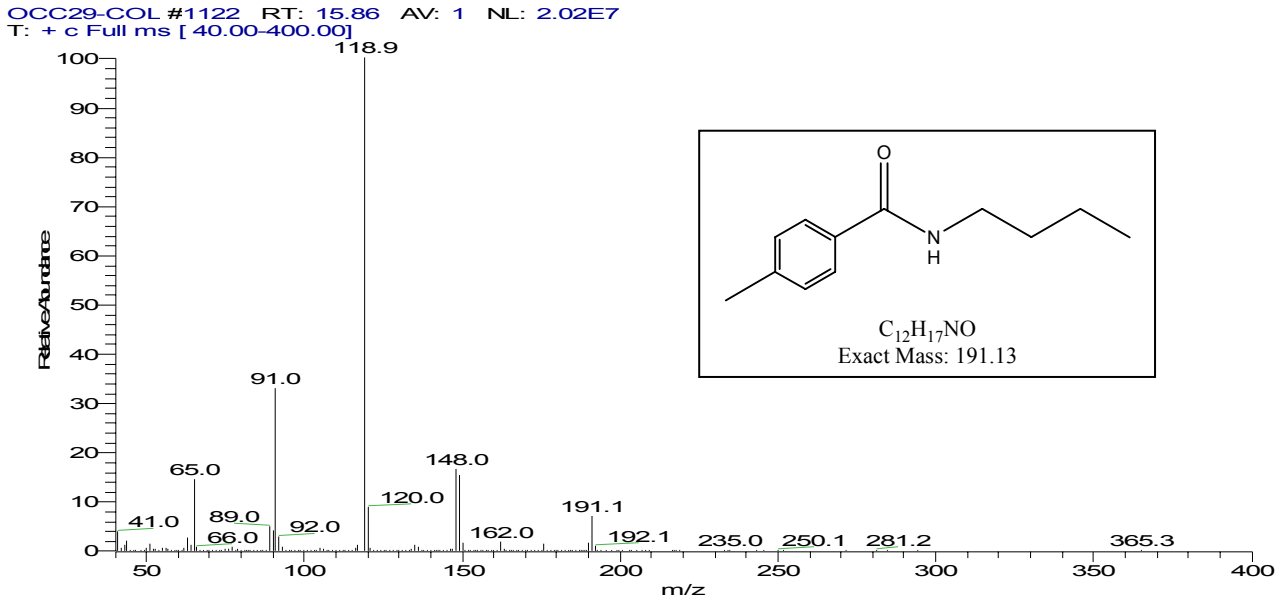
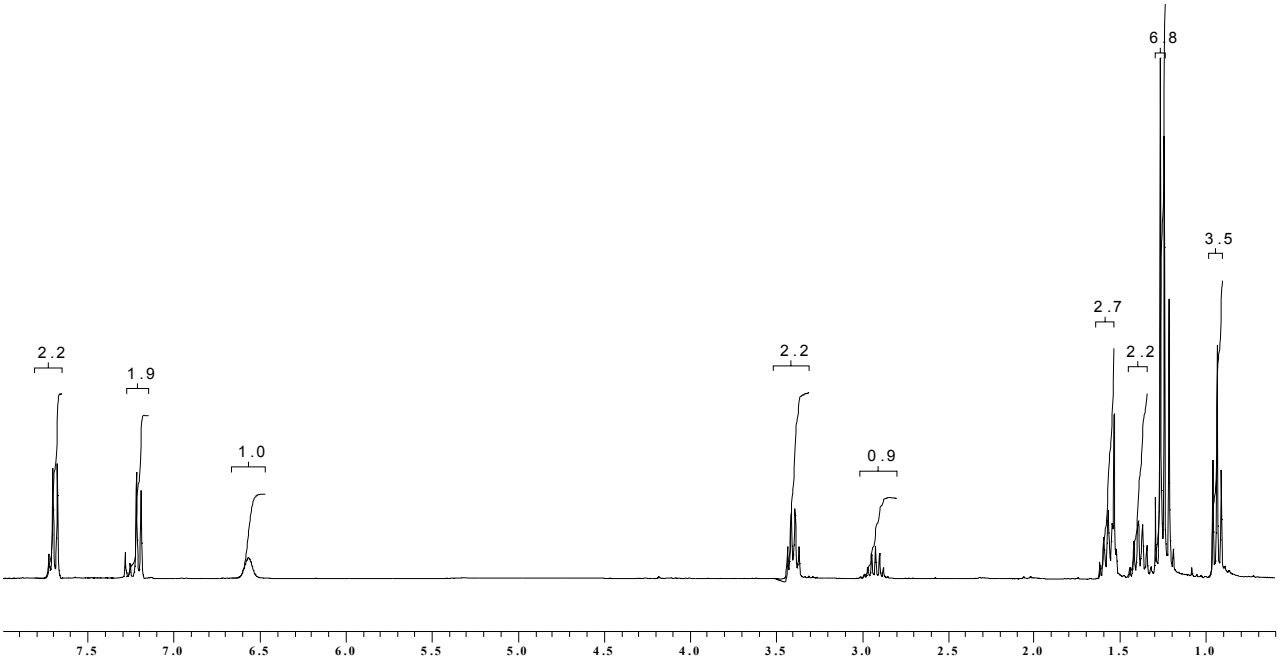


Table 2,Entry 8

N-Butyl-4-Isopropyl-benzamide (3h):

Isolated yield-50%;^{1}H NMR δ(300 MHz,$CDCl_3$) 7.70 (d, *J* = 8.30, Ar, 1H), 7.2 (d, *J* = 8.30, Ar, 2H), 6.5 (br, s, 1H, -N*H*), 3.40 (q, *J* = 13.59, NH-CH_2, 2H), 2.9(m, -C*H*$(CH_3)_2$, 1H), 1.51 – 1.62 (m, NH-CH_2-CH_2, 2H), 1.32 – 1.46 (m, NH-CH_2- CH_2- CH_2, 2H), 1.20 – 1.32 (m, -CH(CH_3)$_2$, 6H), 0.95 (t, J = 6.79, -CH_3, 3H).



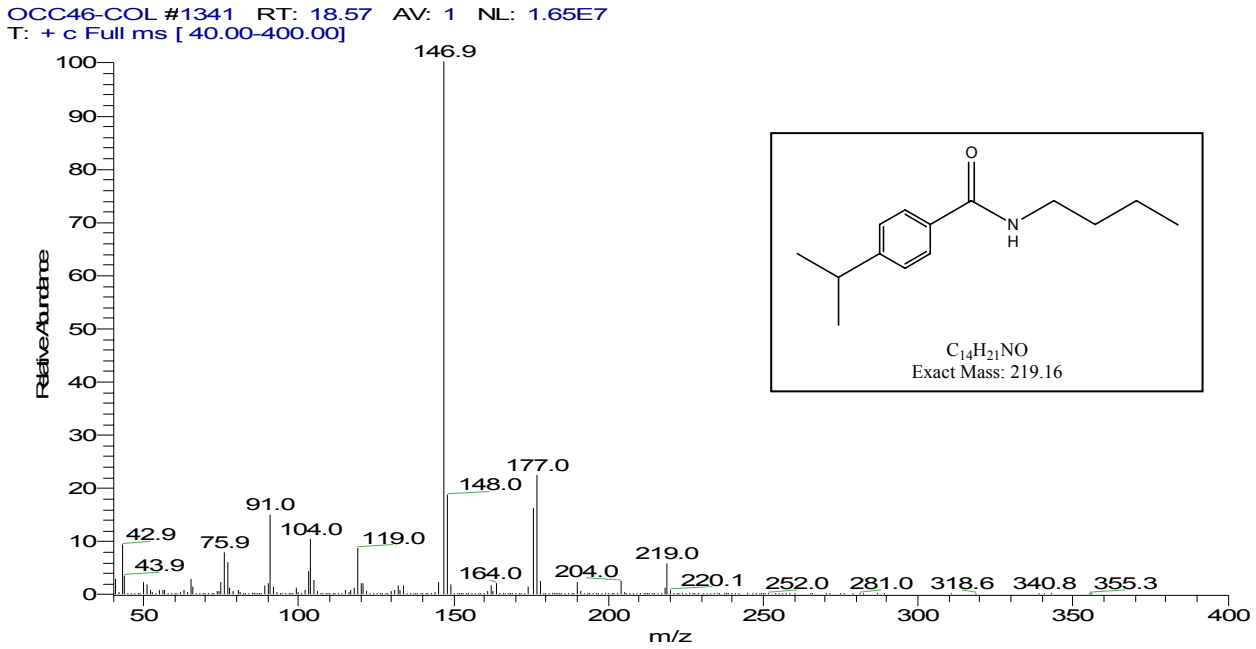
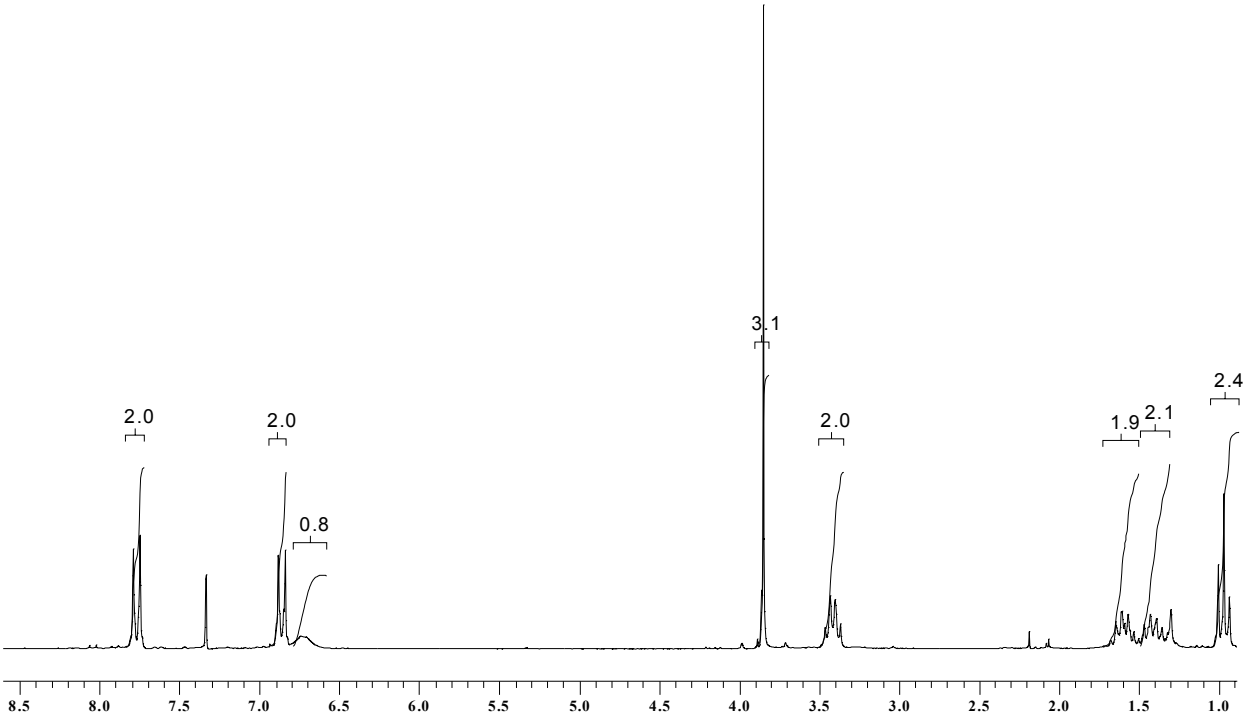


Table 2,Entry 9

N-Butyl-4-methoxy-benzamide (3i):

Isolated yield-80%; ^{1}H NMR δ(300 MHz,$CDCl_3$) 7.7 (d, *J* = 8.6 Hz, Ar, 2H), 6.9 (d, *J*= 9.1, Ar, 2H), 6.7 (br, s, -N*H*, 1H), 3.85 (s, -OC*H*$_3$, 3H), 3.41 (q, *J* = 13.28, NH-C*H*$_2$, 2H), 1.6 (quin, *J* = 14.85, NH-CH_2-C*H*$_2$, 2H),1.28-1.48 (m, NH-CH_2- CH_2- C*H*$_2$, 2H), 0.97 (t, *J* = 6.70, -C*H*$_3$, 3H).



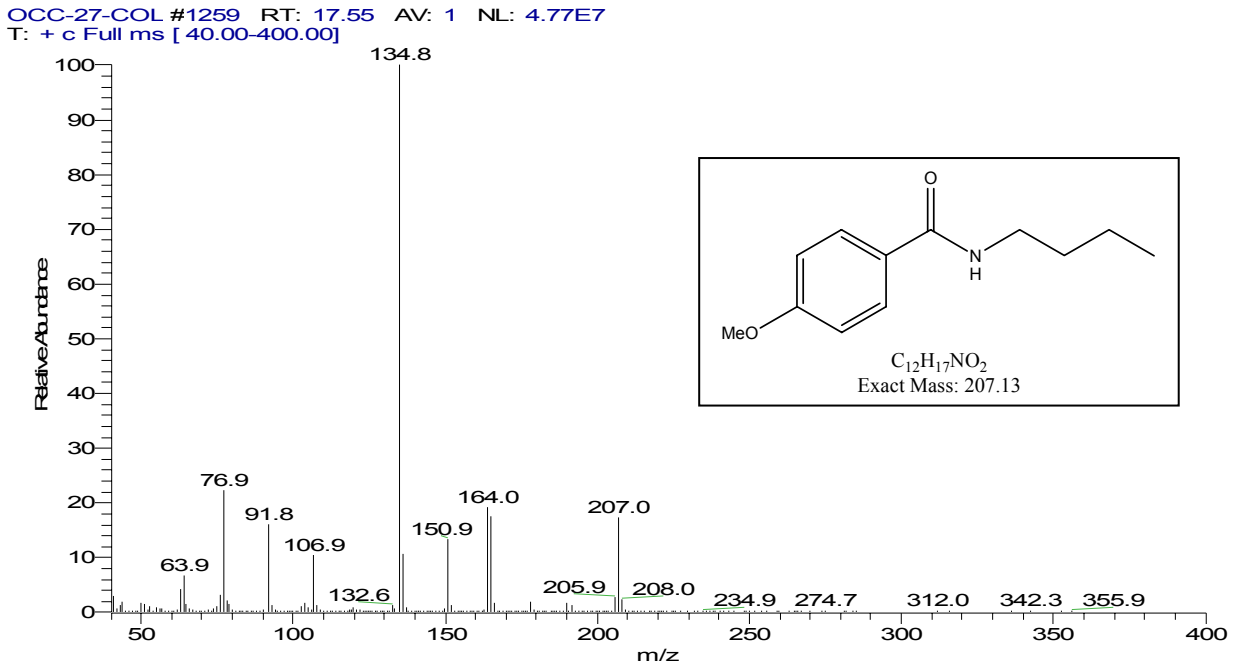
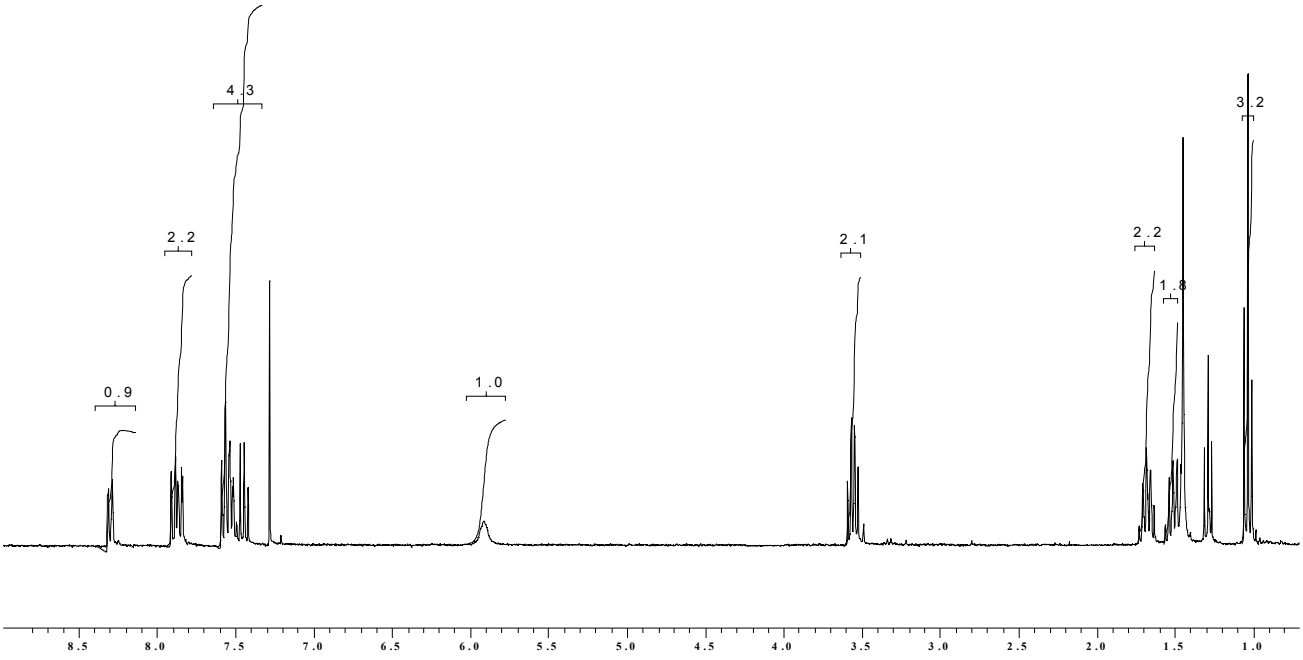


Table 2,Entry 10

Naphthalene-2-carboxylic acid butylamide (j):

Isolated yield = 61%; ^{1}H NMR δ(300 MHz,$CDCl_3$) 8.30 (d, *J* = 9.00, Ar, 1H), 7.82 - 7.92 (m, Ar, 2H), 7.40 - 7.58 (m, Ar, 4H), 5.9 (br, s, 1H, -N*H*), 3.55 (q, *J* = 12.8, NH-CH_2, 2H), 1.62 (quin, *J* = 12.84, NH-CH_2-CH_2 ,2H), 1.40 - 1.58 (m, NH-CH_2- CH_2- CH_2, 2H), 0.95 (t , J = 14.3, -CH_3, 3H).



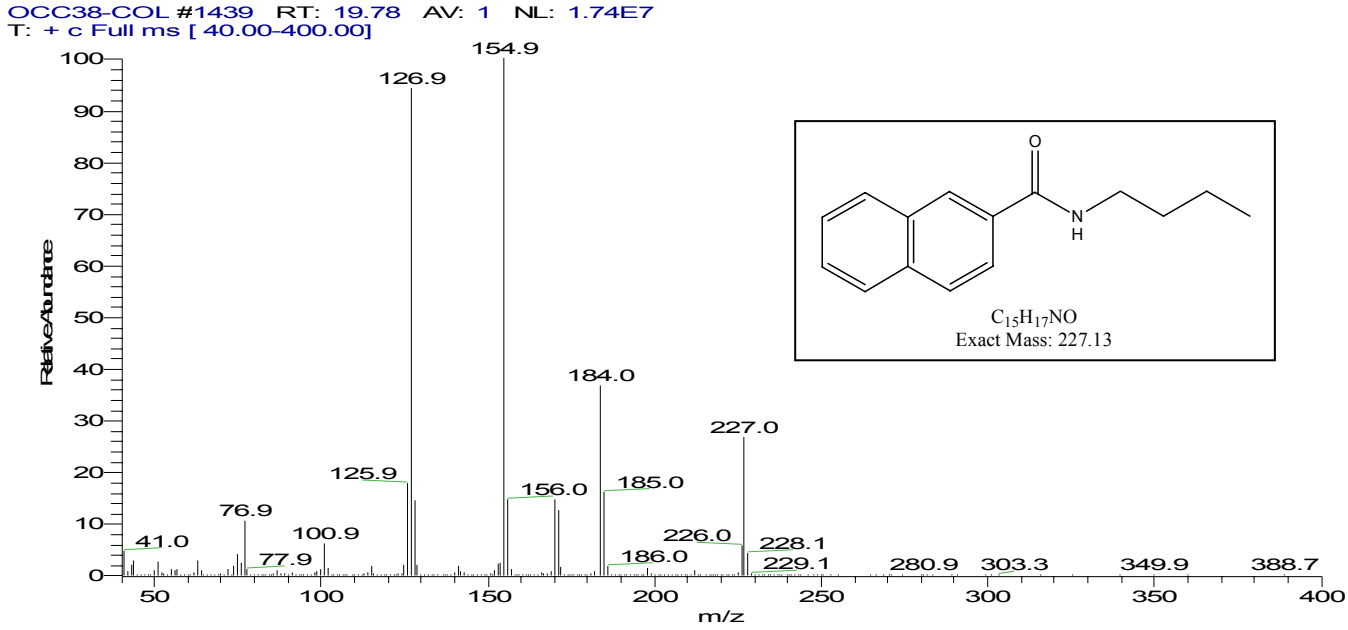
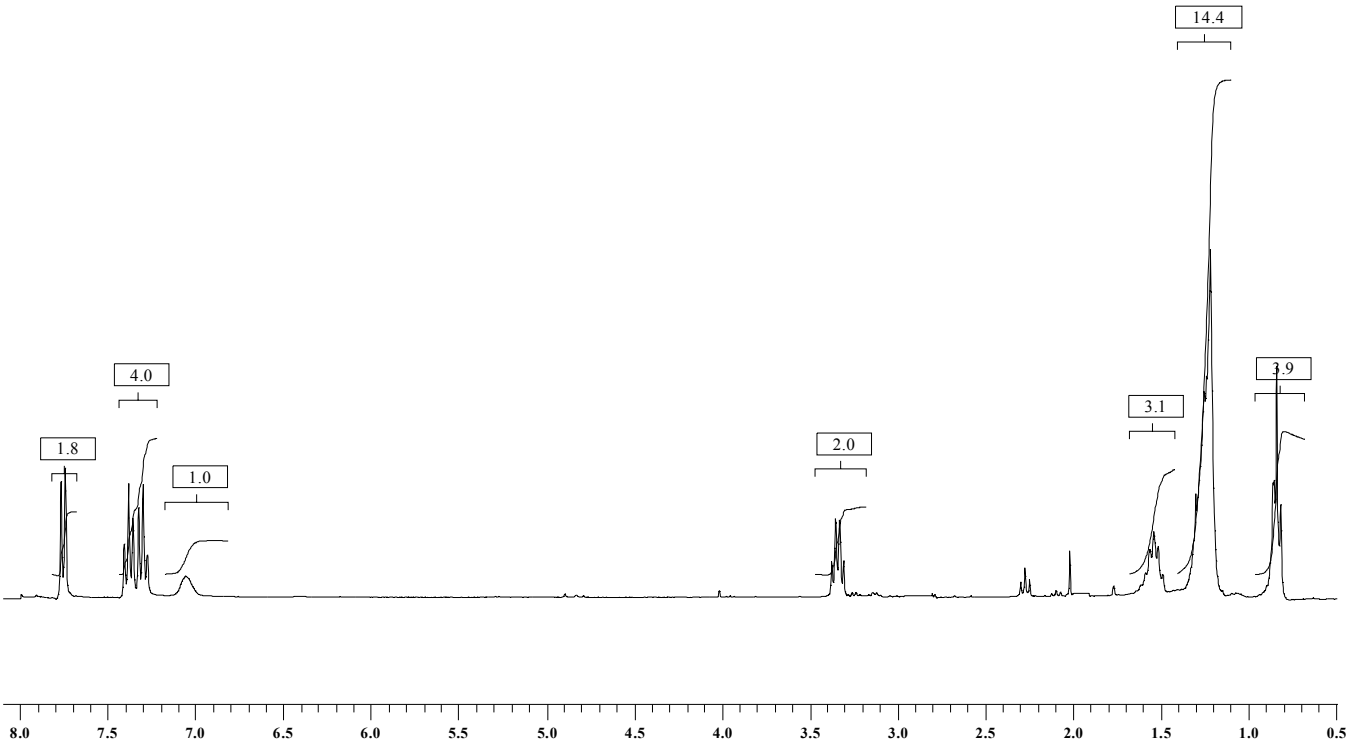


Table 2,Entry 11

N-Octyl-benzamide (3k):

Isolated yield = 51%; ^{1}H NMR δ(300 MHz,$CDCl_3$) 7.7 (d, *J* = 8.3 Hz, Ar, 2H), 7.24 -7.42 (m, Ar,3H), 7.0 (br, s, -N*H*, 1H), 3.32 (q, *J* = 13.59, NH-CH_2, 2H), 1.6 (m, NH-CH_2-CH_2, 2H), 1.18 - 1.32 (m, *alp* CH_2 ,10H), 0.82 (t,*J* = 6.80, -CH_3, 3H).



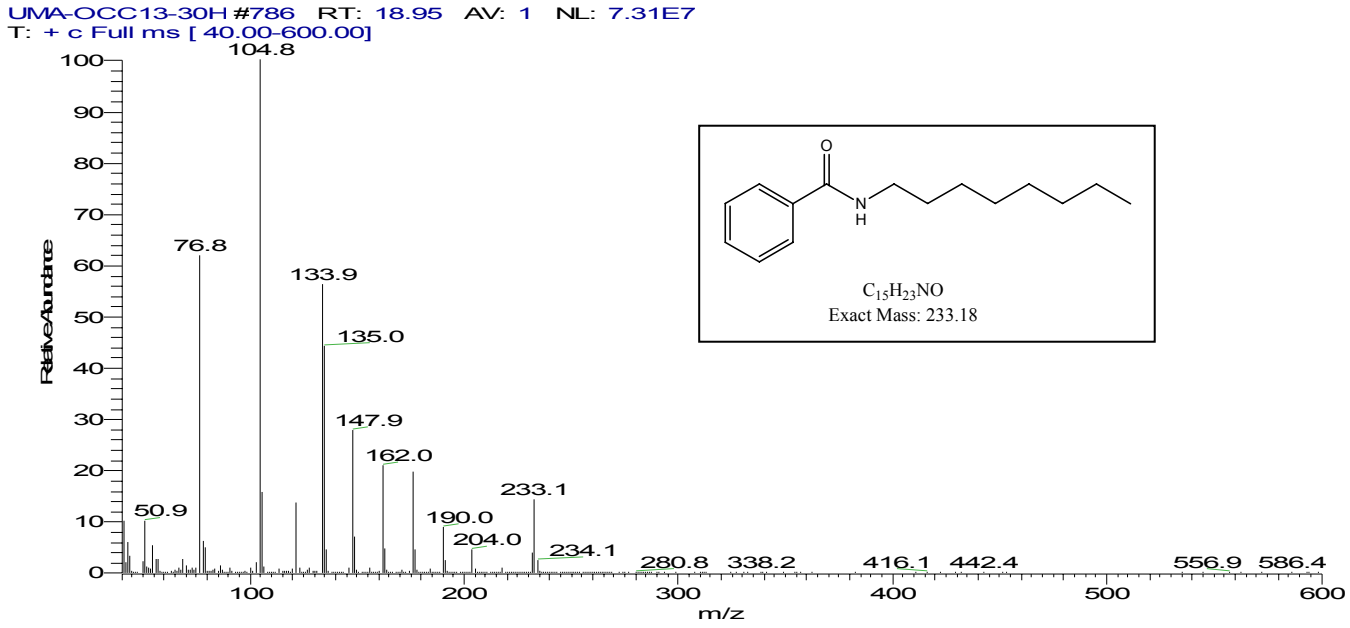
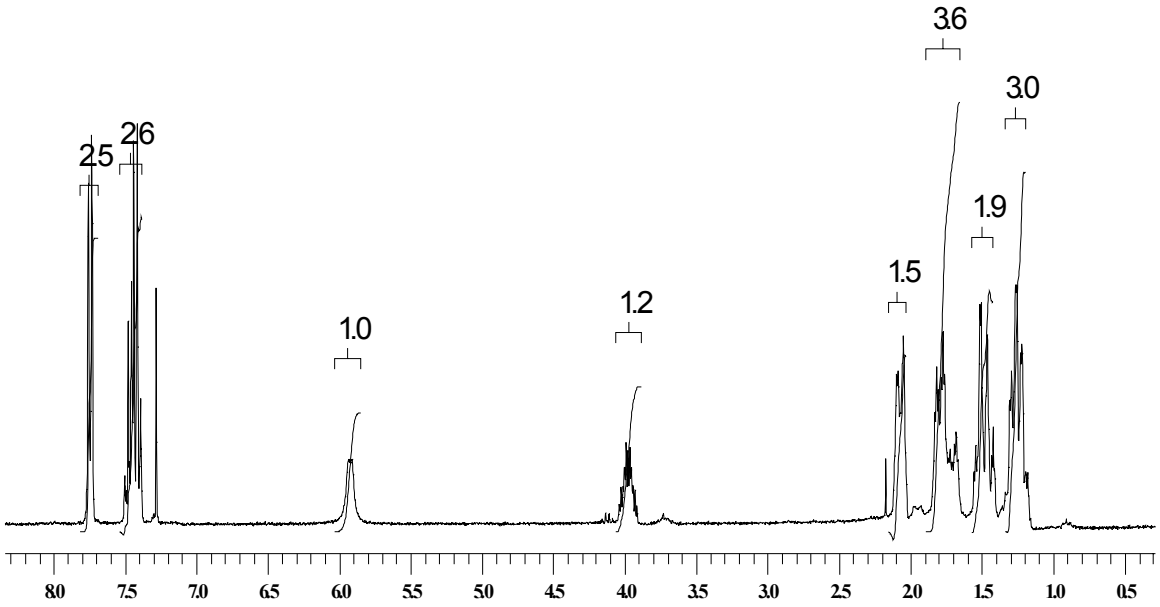


Table 2,Entry 12

N-Cyclohexyl-benzamide (3l):

Isolated yield = 63%; ^{1}H NMR δ(300 MHz,$CDCl_3$) 7.7 (d, *J* = 6.8 Hz, Ar, 2H), 7.32-7.52 (m, Ar, 3H), 5.93 (br, s, -N*H*, 1H), 3.92 - 4.04, (m, NH-C*H*, 1H), 1.20 –2.10 (m, NH-CH-(CH_2)$_5$, 10 H).



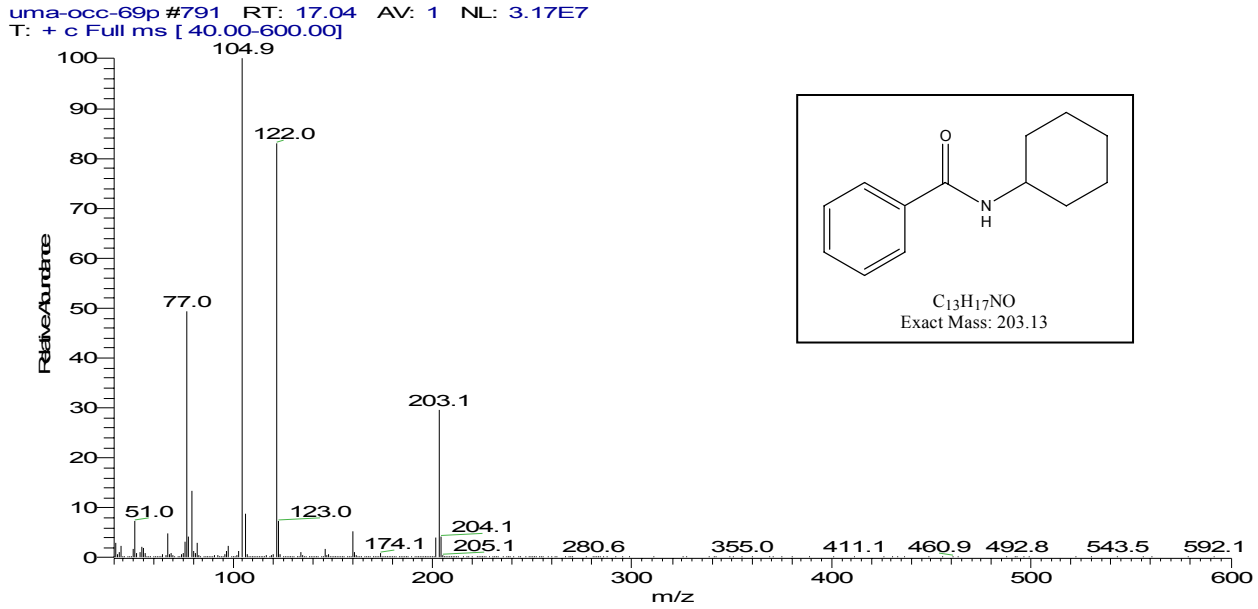
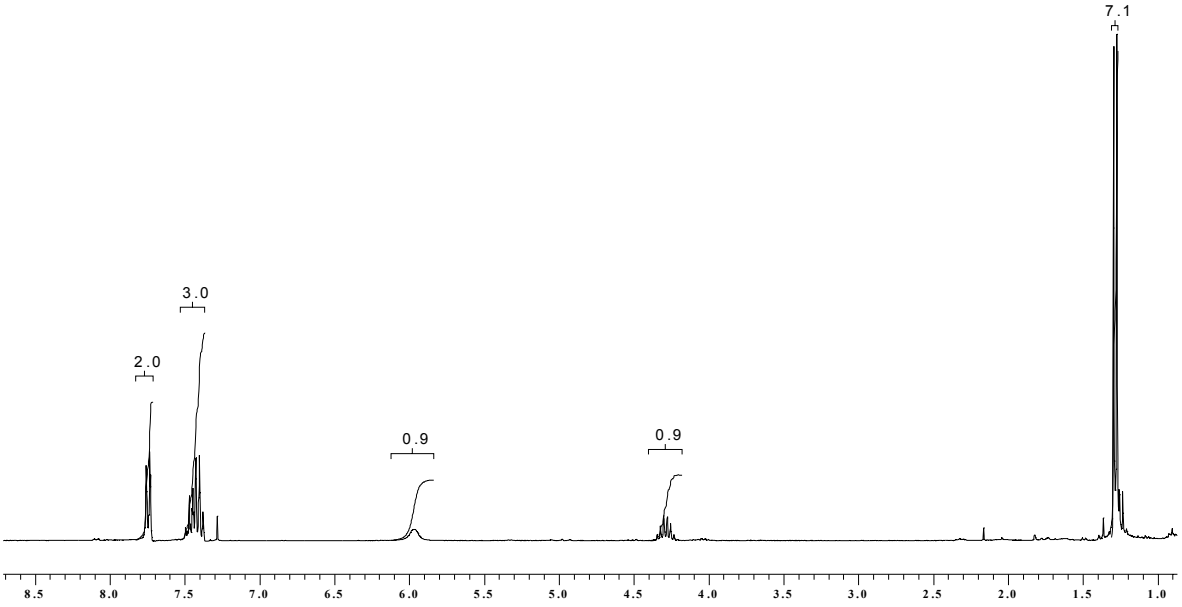


Table 2,Entry 13

N-Isopropyl-benzamide (3m)

Isolated yield =57%; ^{1}H NMR δ(300 MHz, $CDCl_3$) 7.76 (d, *J* = 8.3 Hz, Ar, 2H), 7.37 - 7.50 (m, Ar, 3H), 6.00(br, s, -*NH*, 1H,), 4.30 (m, NH-C*H*, 1H,), 1.28 (d, *J* =6.04, NH-CH-($C\mathit{H_3}$)$_2$, 6H).



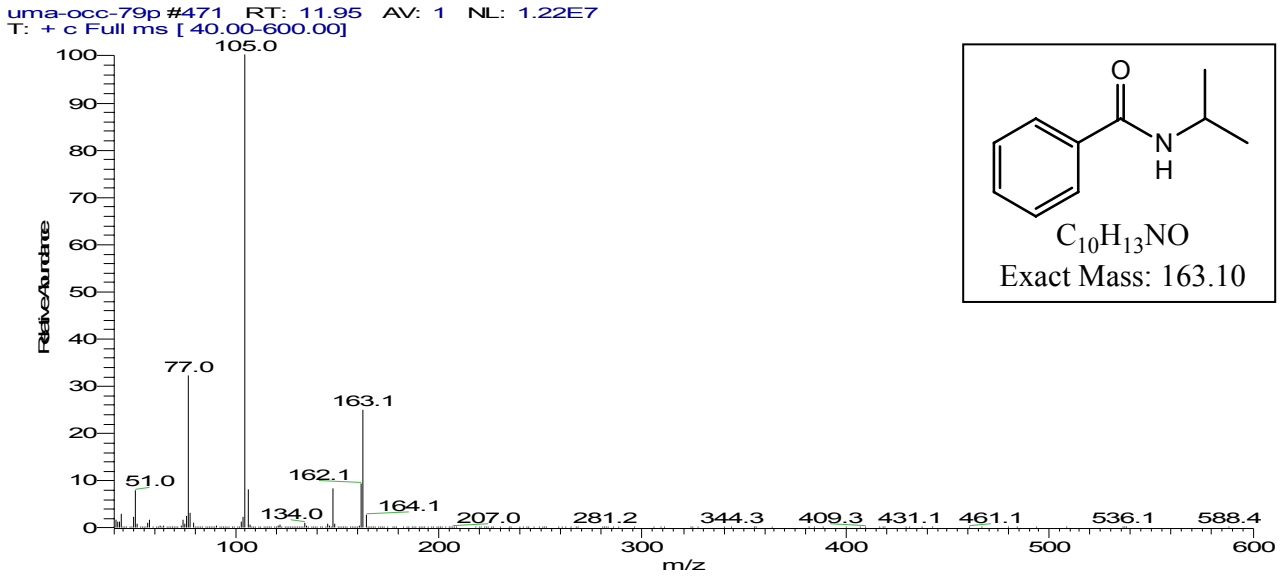
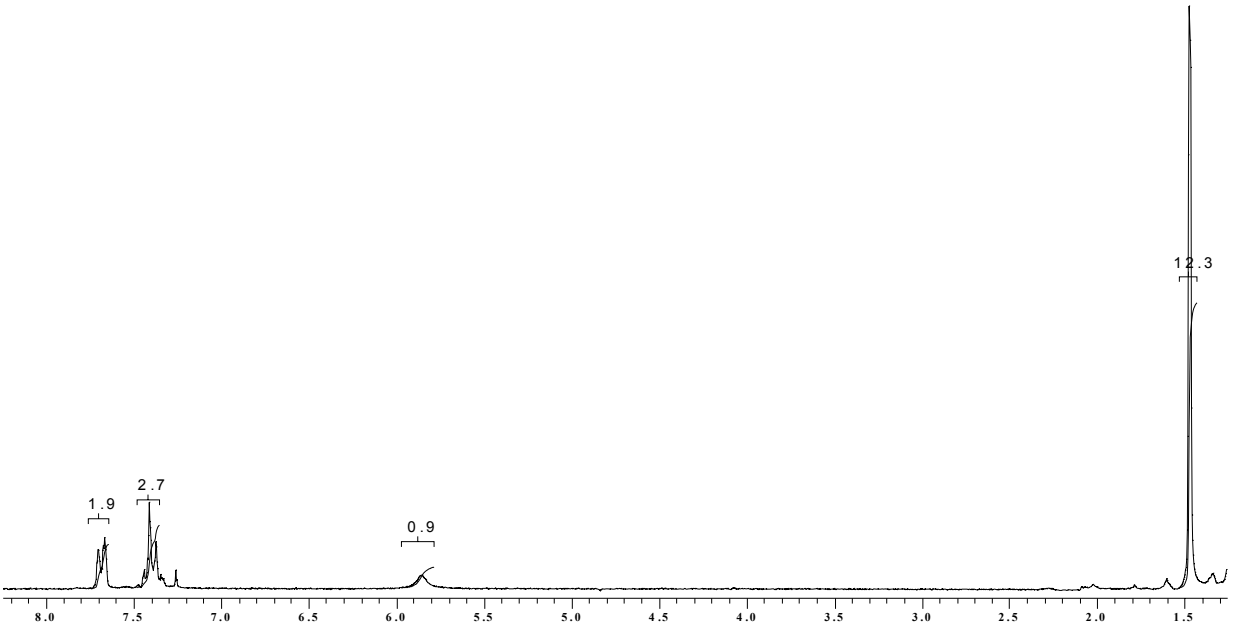


Table 2,Entry 14

N-tert-Butyl-benzamide (3n):

Isolated yield =42%; ^{1}H NMR δ(300 MHz, $CDCl_3$) 7.70 (d, *J* = 8.1 Hz, Ar, 2H), 7.37 - 7.45 (m, Ar, 3H), 5.86 (br, s, -*NH*, 1H,), 1.48 (s, NH-(C*H*$_3$)$_3$, 9H).



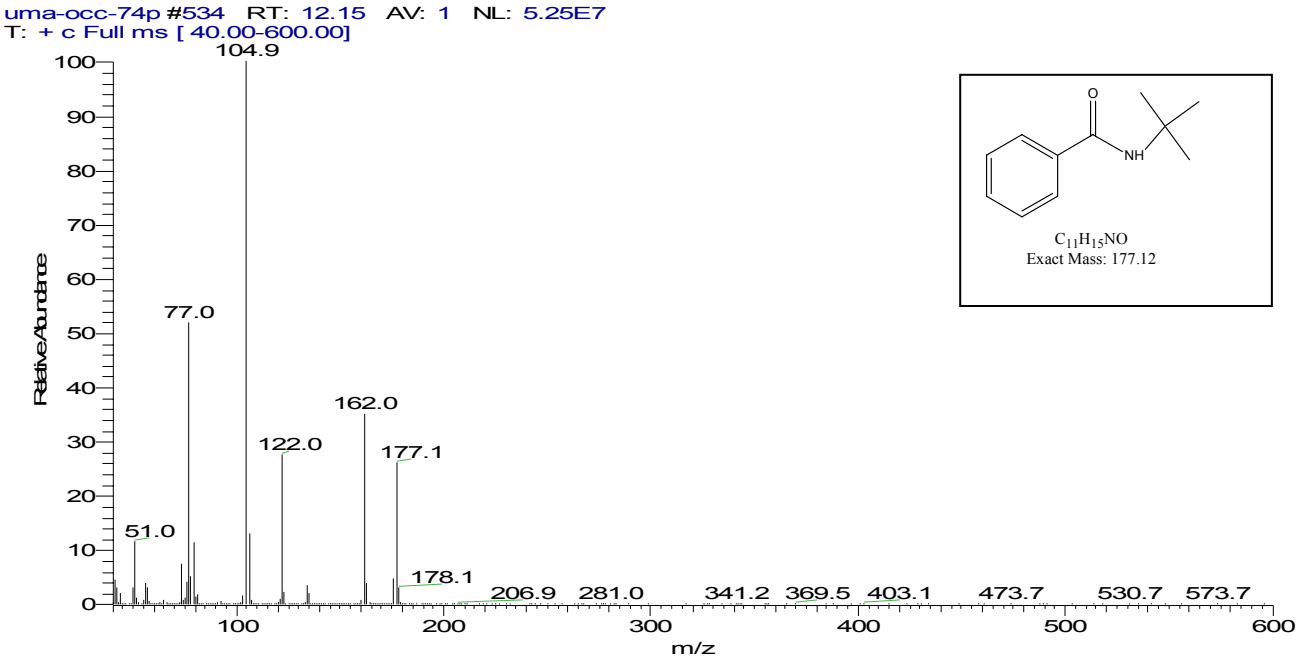
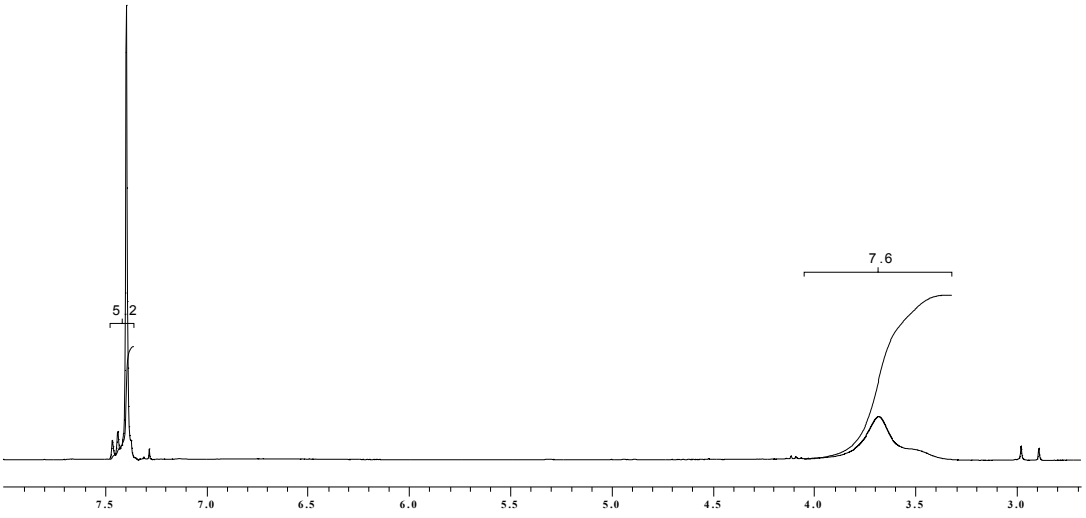


Table 2,Entry 15

Morpholin-4-yl-phenyl-methanone (3o)

Isolated yield =63%; ^{1}H NMR δ(300 MHz, $CDCl_3$) 7.40 (s, Ar, 5H), 3.60-3.81 (s, aliphatic CH_2, 8H).



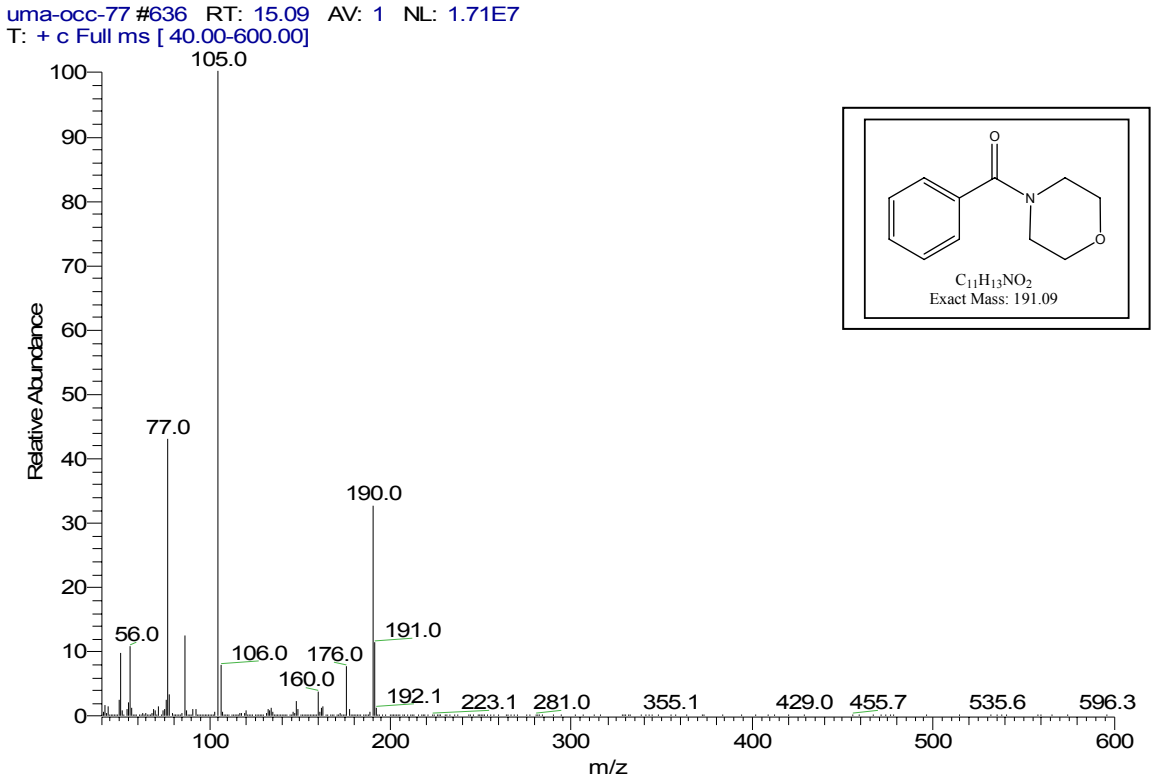
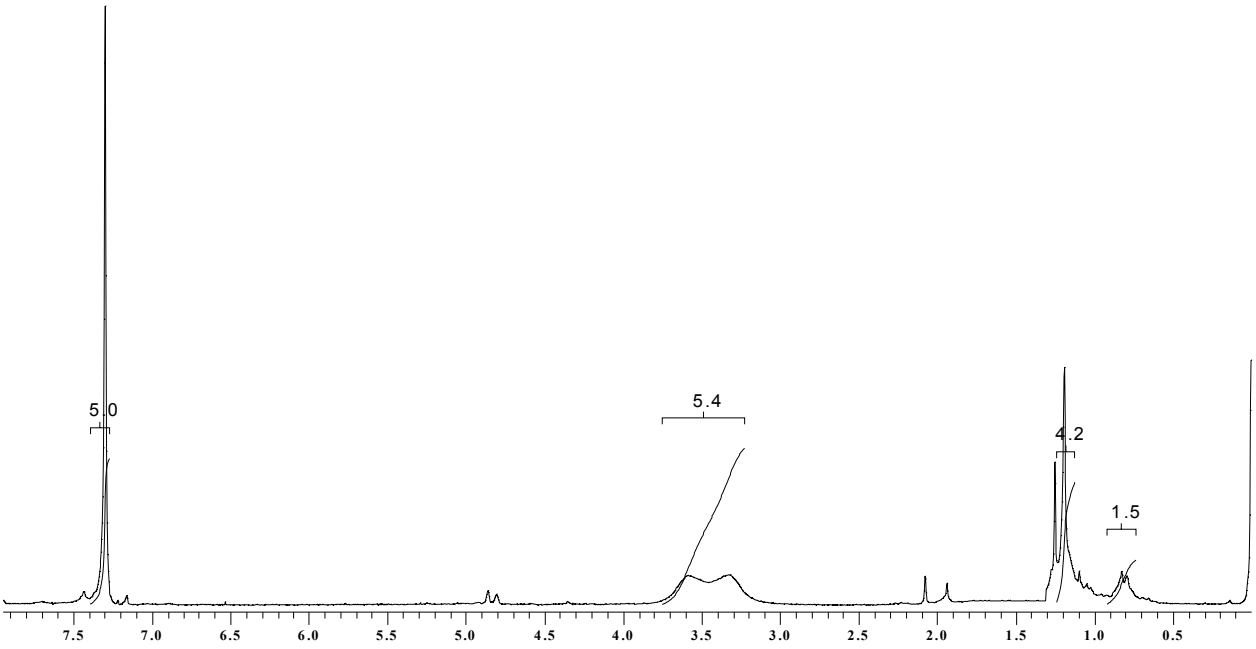


Table 2,Entry 16

Phenyl-piperidin-1-yl-methanone (3p) :

Isolated yield =61%; ^{1}H NMR δ(300 MHz, $CDCl_3$) 7.30 (s, Ar, 5H), 3.20-3.71 (broad, s, CH_2- N-CH_2, 4H) , 1.10-1.32 (broad, m, 4H), 0.75-0.85 (broad, m, 2H)



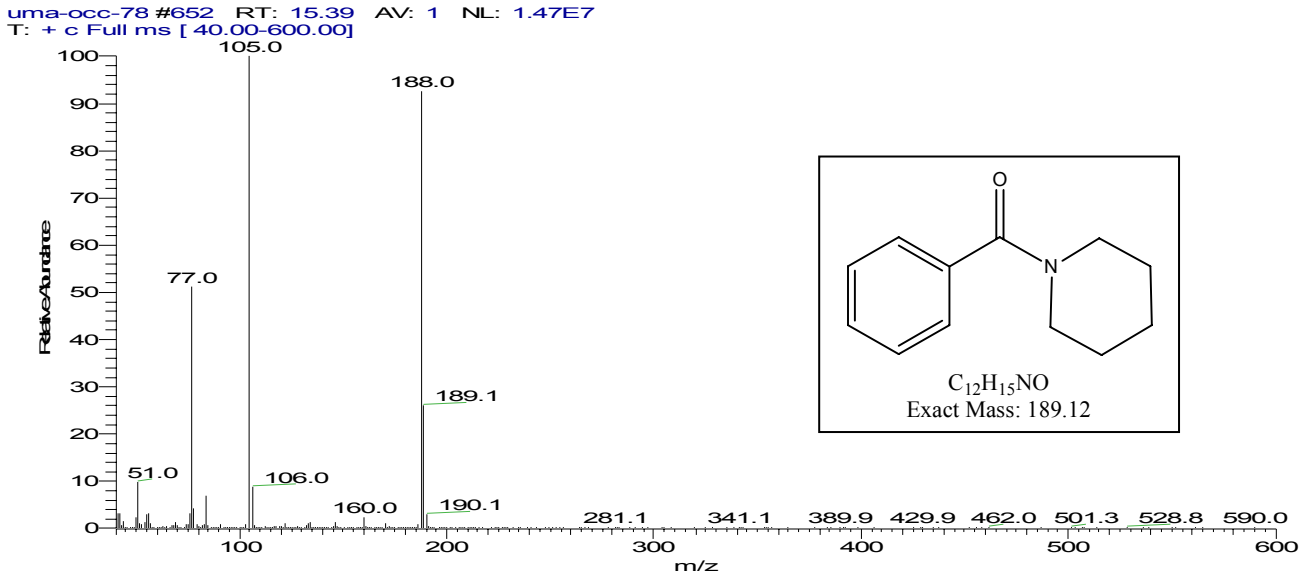
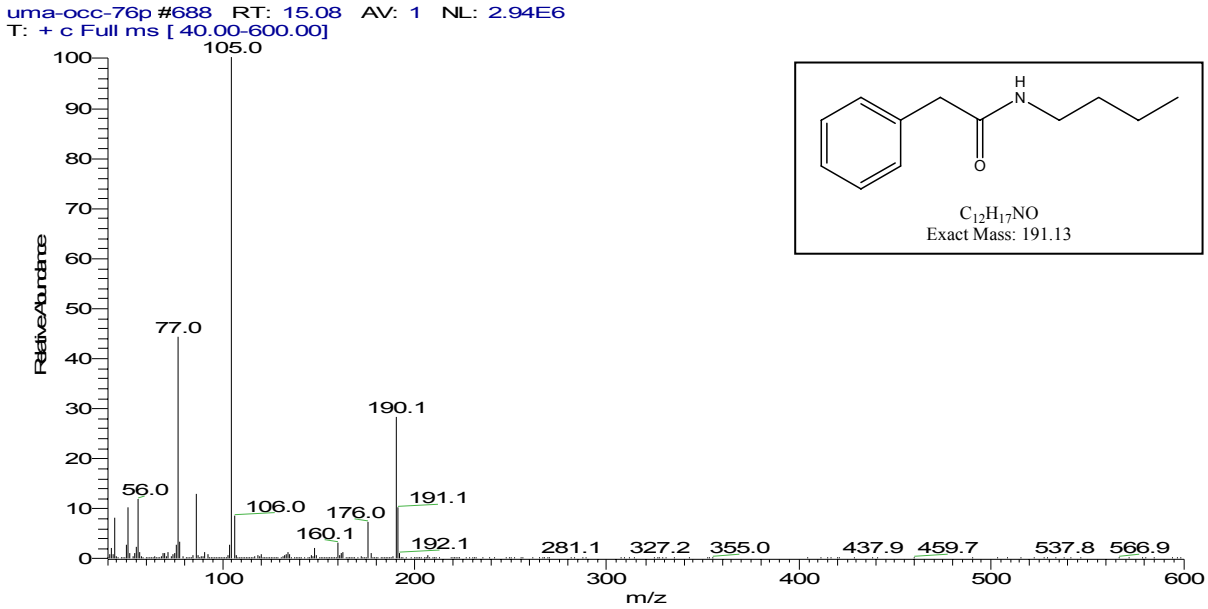


Table 2,Entry 19

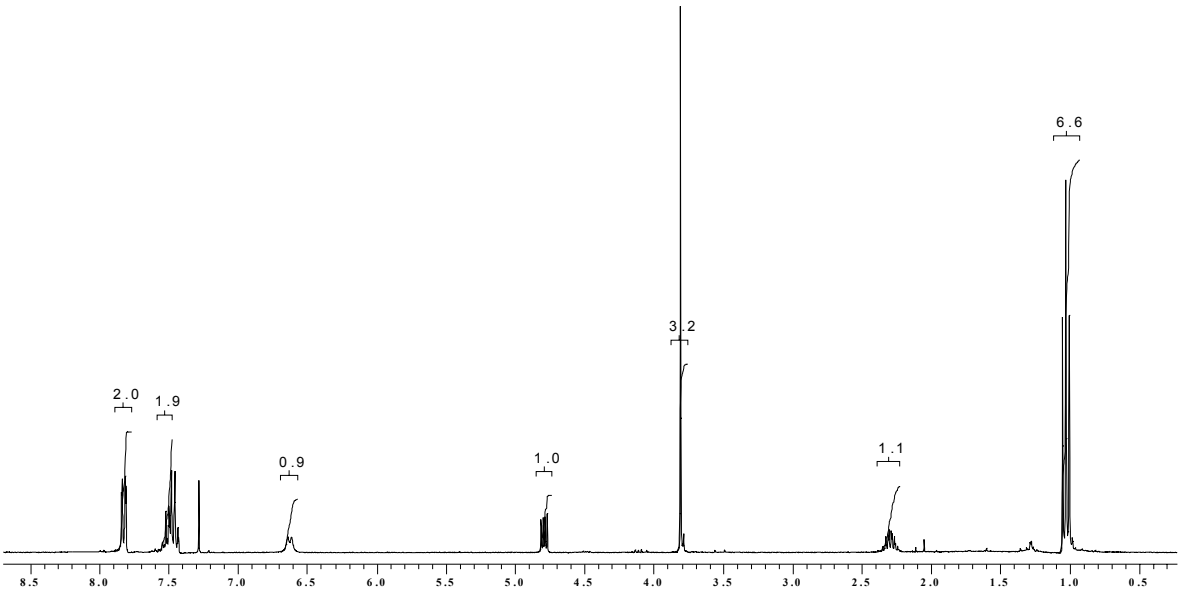
N-Butyl-2-phenyl-acetamide (3s) ;

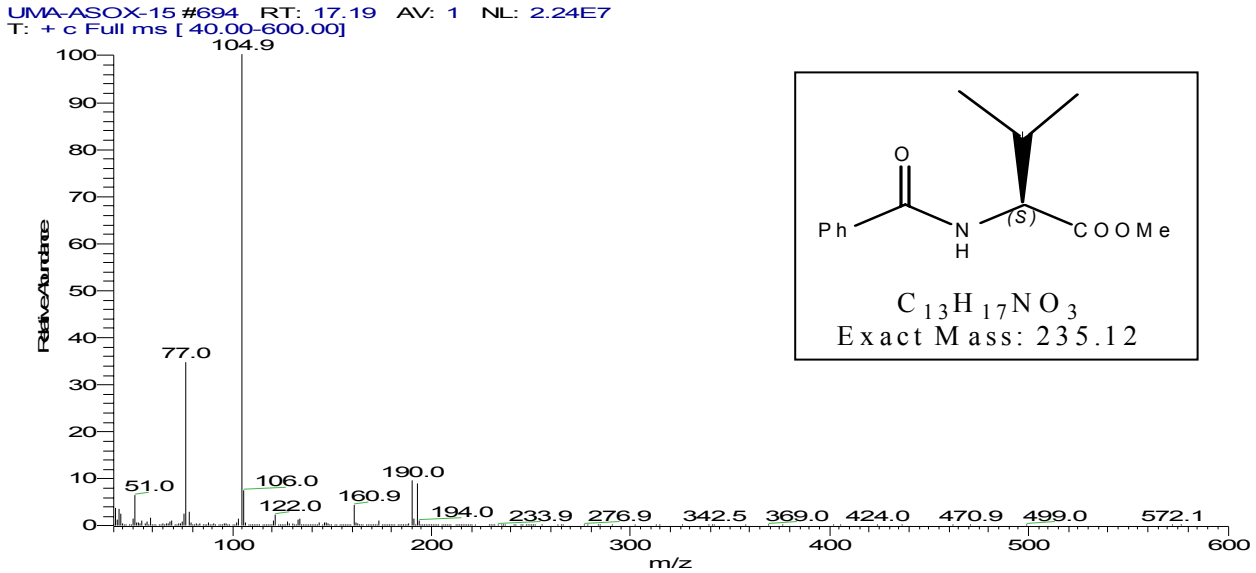


Scheme 1,compound 1

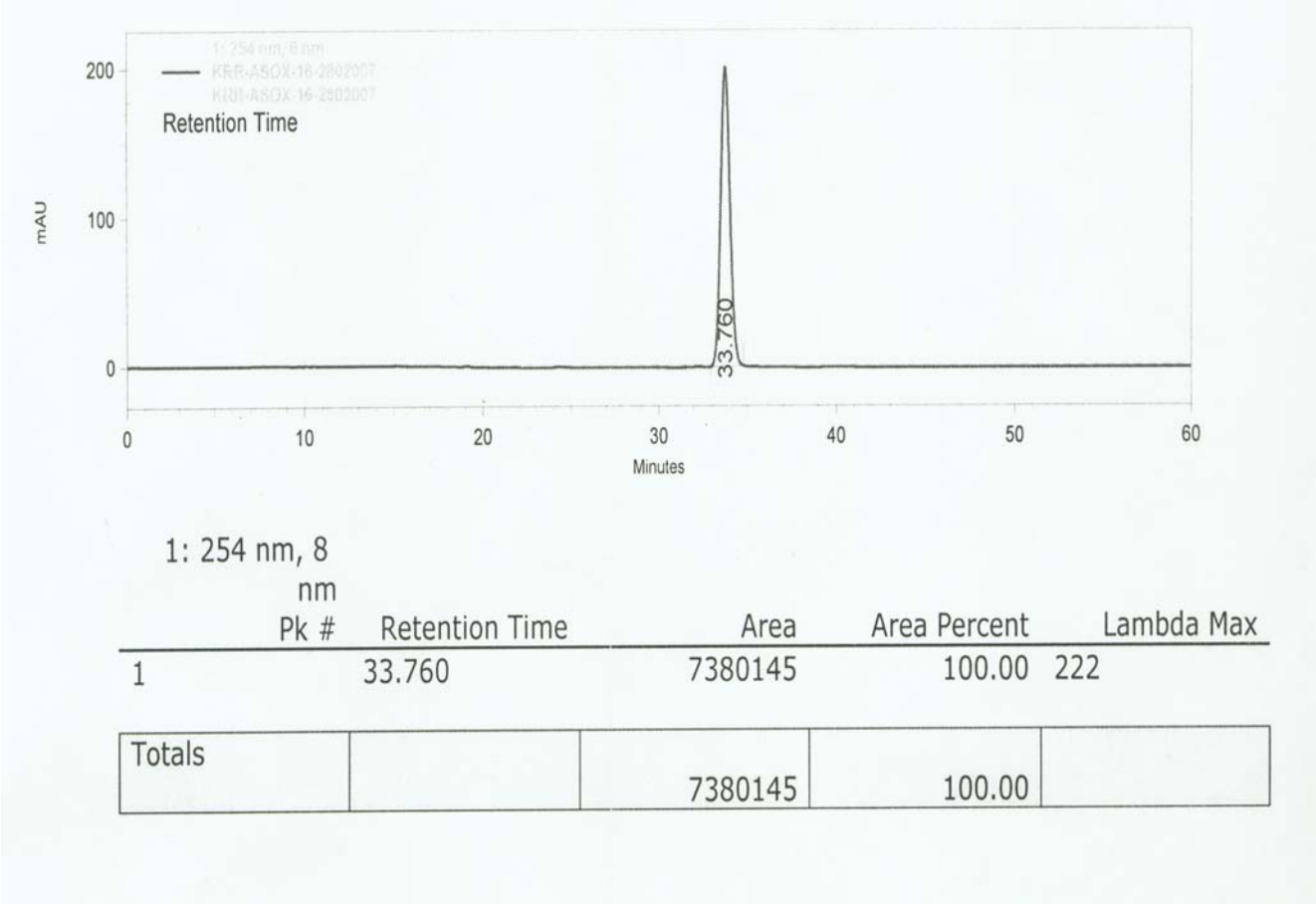
(S)-2-Benzoylamino-3-methyl-butyric acid methyl ester:

Isolated yield = 81%; ^{1}H NMR δ(300 MHz,$CDCl_3$) 7.82 (d, *J* = 8.30, Ar, 2H),
7.42 -7.52 (m, Ar, 3H), 6.62 (br, d, *J* =
8.31, 1H, -N*H*), 4.78 (dd, J = 8.3, 1H, NH-*CH*), 3.8 (s, -OCH_3,3H),2.34-2.44 (m, C*H*-$(CH_3)_2$, 1H), 1.04
(t, *J* = 7.44, CH-(CH_3)$_2$, 6H).Optical rotation: [α] = -7.8, c = 5 in MeOH)[1].





HPLC Data for (S)-**2-Benzoylamino-3-methyl-butyric acid methyl ester:** AD-H column, Hexane/Isopropanol = 95 : 5, flow rate = 0.5 mL/min.[2]



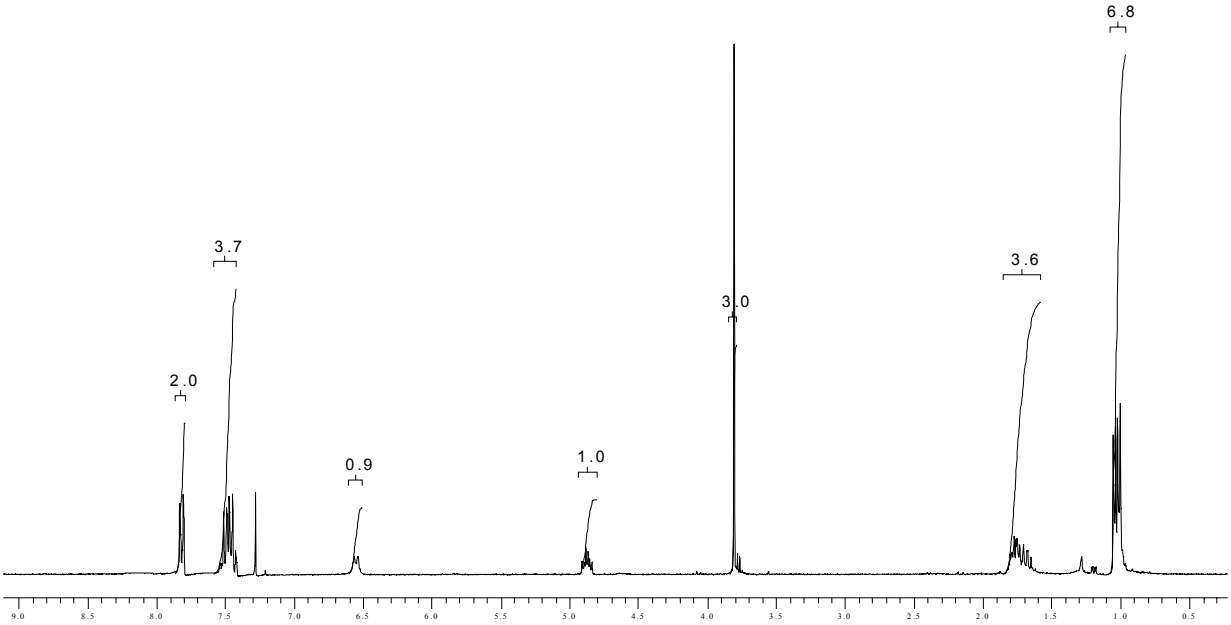
1: 254 nm, 8 nm

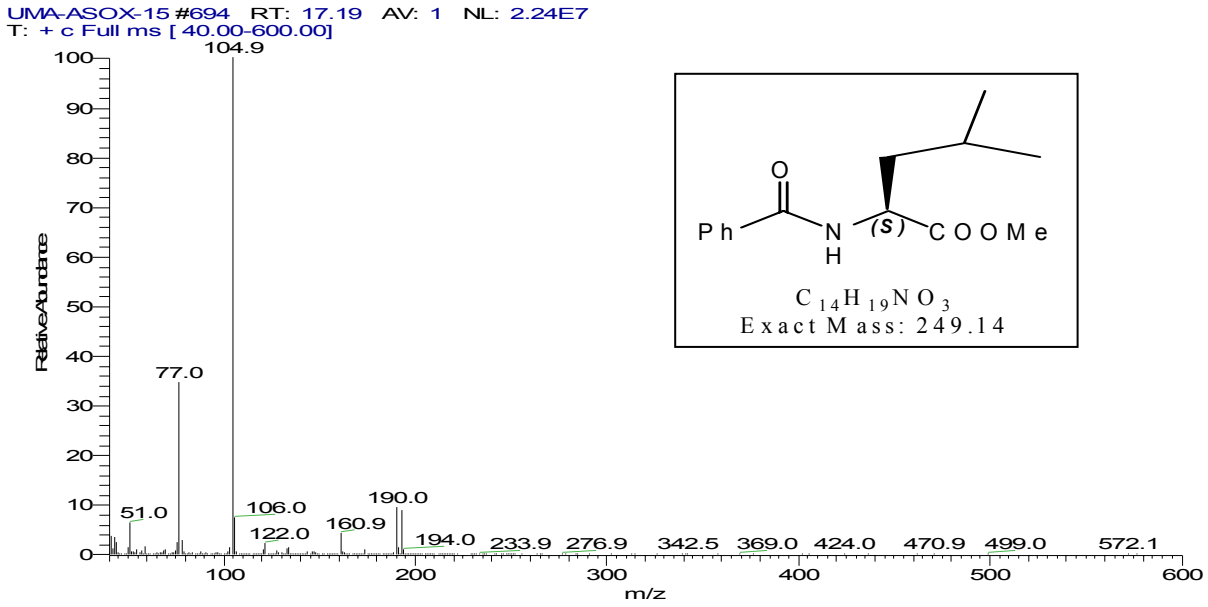
Pk #	Retention Time	Area	Area Percent	Lambda Max
1	33.760	7380145	100.00	222
Totals		7380145	100.00	

Scheme 1,Compound 2:

(S)-2-Benzoylamino-4-methyl-pentanoic acid methyl ester:

Isolated yield-78%;^{1}H NMR δ(300 MHz,$CDCl_3$) 7.80 (d, *J* = 6.80, Ar, 2H), 7.40 - 7.58 (m, Ar, 3H), 6.62 (br, d, *J* = 7.55, -N*H*, 1H), 4.86 - 4.92 (m, NH-*CH*, 1H), 3.8 (s, -OCH_3, 3H), 1.64 - 1.80 (m, C*H*-CH_2(CH_3)$_2$,3H), 0.98 -1.06 (m, -CH_2(CH_3)$_2$, 6H). [α] = - 22.8, c = 0.8 in MeOH)[3]

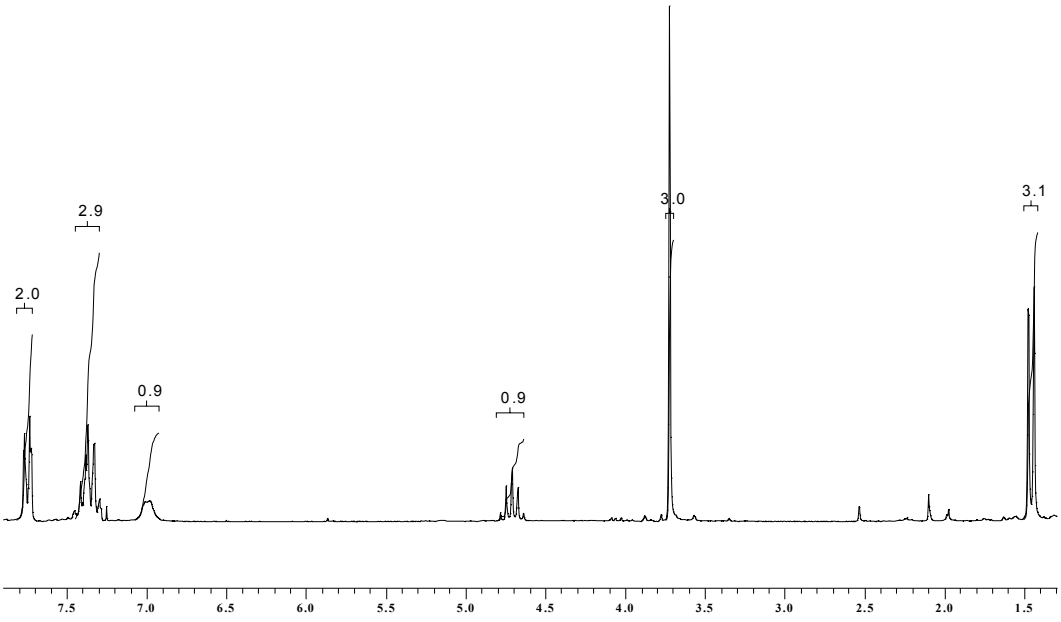


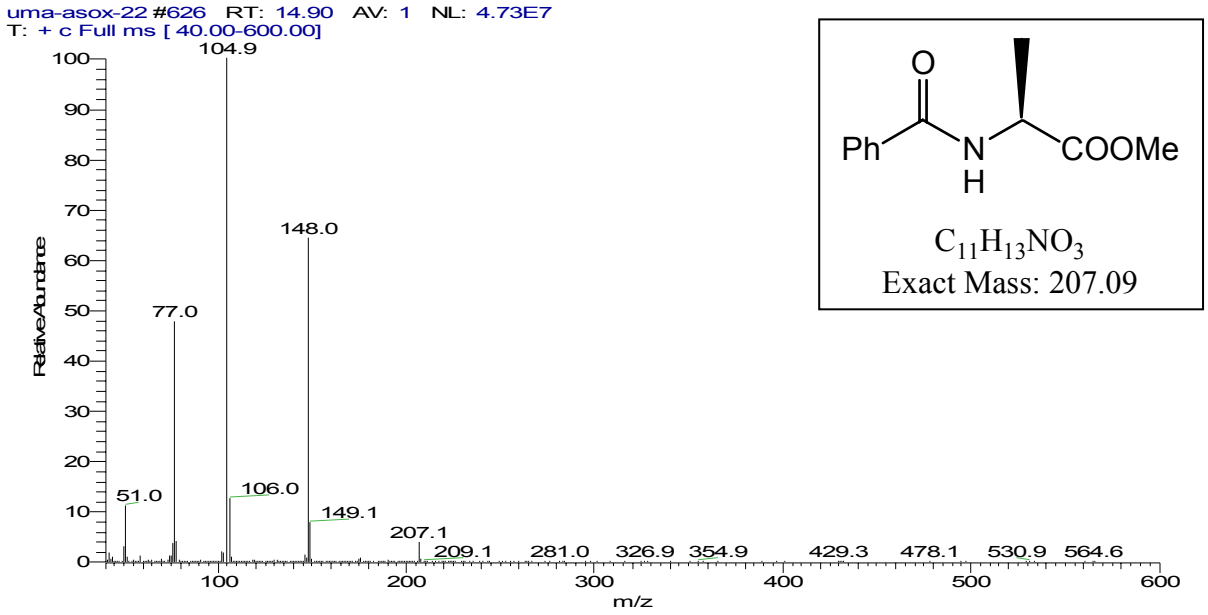


Scheme 1,Compound 3:

(S)-2-Benzoylamino-propionic acid methyl ester:

Isolated yield - 65%; ^{1}H NMR δ (300 MHz,$CDCl_3$) 7.70 (d, *J* = 8.02, Ar, 2H), 7.28 - 7.42 (m, Ar, 3H), 7.00 (br, s, N*H*, 1H), 4.64 - 4.78 (m, NHC*H*, 1H), 3.72 (s, OCH_3, 3H), 1.45 (d, *J* = 7.28, 3H). Optical rotation: [α] = - 25.0, c = 1 in $CHCl_3$.[4]



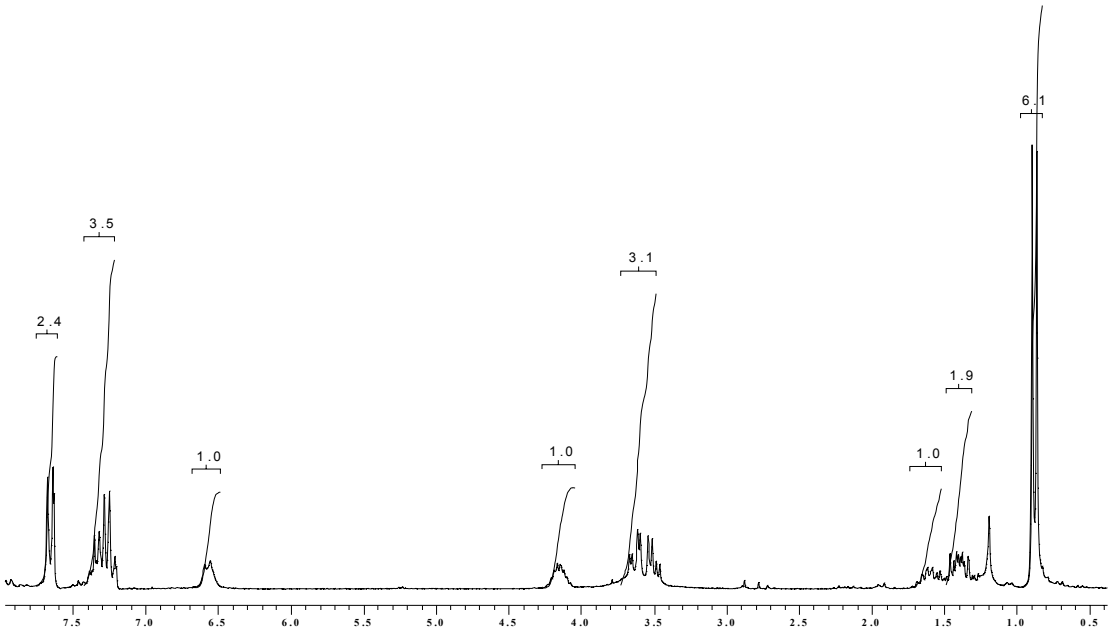


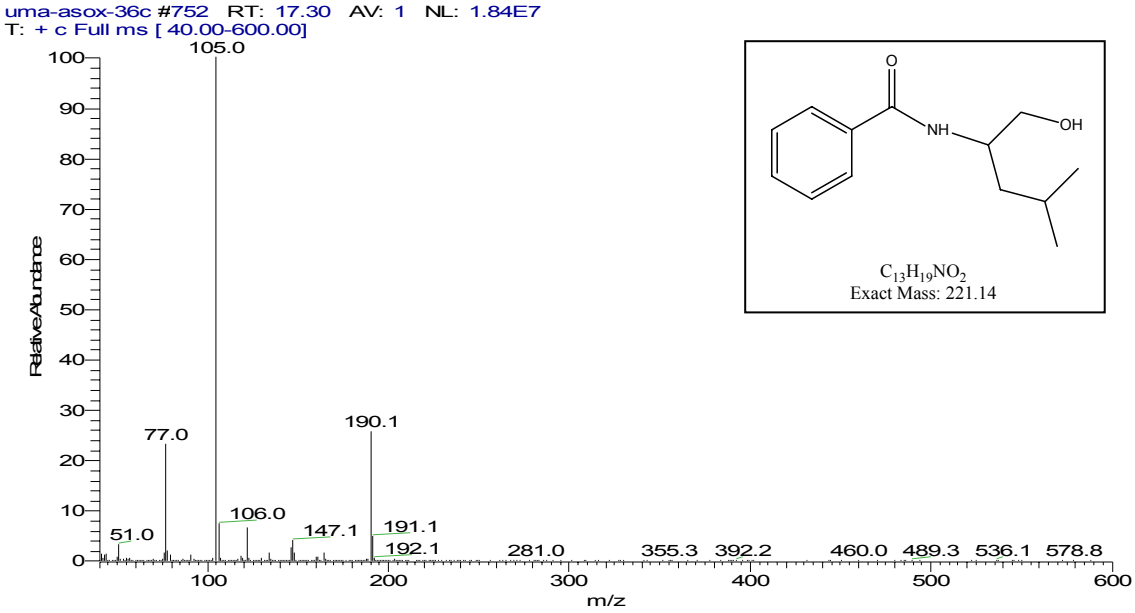
$C_{11}H_{13}NO_3$
Exact Mass: 207.09

Scheme 1,Compound 4:

N-((S)-1-Hydroxymethyl-3-methyl-butyl)-benzamide:

Isolated yield-34%;^{1}H NMR δ(300 MHz,$CDCl_3$) 7.80 (d, *J* = 7.03, Ar, 2H), 7.20 - 7.38 (m, Ar, 3H), 6.60 (br, d, *J* = 7.81, -N*H*, 1H), 4.20(b,m, 1H) , 3.42-3.62 (m, 2H),1.32-1.62 (m, 3H), 0.88 (dd, *J*= 2.0 Hz, -CH-(C*H*$_3$)$_2$, 6H). [α] = -31.3 ^{o}, c = 1.0 in MeOH)[5]





Reference:

1. B. M. Dean, M. P. V. Mijovi , J. Walker**, *J. Chem. Soc.***, 1961, 3394 – 3400
2. W. J. Yoo, C. J. Li, *J. Am. Chem. Soc.* **2006**, *128*, 13064-13065.
3. M. W. Williams, G. T. Young**, *J. Chem. Soc.***, 1963, 881 – 889.
4. K. Nadia, B. Malika, K. Nawel, B. Md. Yazid, R. Zine, N.-E. Aouf, *J. Heterocyclc. Chem*, **2004**, 41, 57-60.
5. K. Y. Lee, Y. H. Kim, M. S. Park, C. Y. Oh, W. H. Ham, *J. Org. Chem.* . **1999**, *64,* 9450-9458.