

Supporting Information

Chitosan: an efficient recyclable catalyst for transamidation of carboxamides with amines under neat conditions

Sadu Nageswara Rao, Darapaneni Chandra Mohan and Subbarayappa Adimurthy *

Central Salt & Marine Chemicals Research Institute, Council of Scientific & Industrial Research, G.B. Marg, Bhavnagar-364 002. Gujarat (INDIA); Fax: +91-278-2567562

adimurthy@csmcri.org

Table of Contents

General Experimental	S2
General experimental procedure	S2
The catalyst recycling experiment	S2
Characterization data of the new compounds	S5-S7
^1H & ^{13}C- NMR Spectra of products	S8-S15

I. General Experimental Section:

General: All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^1H and ^{13}C NMR spectra were recorded at 500/200, and 125/50 MHz, respectively. The spectra were recorded in CDCl_3 as solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc. and coupling constants (J) were given in Hz. Chemical shifts are reported in ppm relative to TMS as an internal standard. The peaks around delta values of ^1H NMR (7.2), and ^{13}C NMR (77.0) are correspond to deuterated solvents chloroform. Mass spectra were obtained using electron impact (EI) ionization method. Progress of the reactions was monitored by thin layer chromatography (TLC). All products were purified through column chromatography using silica gel 200-400 mesh size using dichloromethane (DCM)/ethyl acetate as (80:20) eluent unless otherwise indicated.

General experimental procedure:

A mixture of amide (1 mmol), amine (2 mmol) and chitosan (20 wt. %; 24 mg) was stirred in sealed tube at indicated temperature for indicated reaction time (See Table 1 and Schemes 2-4). After being cooled to room temperature, the reaction mixture was dissolved with DCM (15 mL). After removal of solvent, the crude reaction mixture left out was purified by silica gel (200-400 mesh) column chromatography (eluted with dichloromethane and ethyl acetate). The yields are mentioned in Schemes 2-4.

The catalyst recycling experiment

The transamidation reaction was repeated up to five consecutive cycles with the chitosan catalyst, which was recovered after each reaction. Reactions were carried out for 36 h. After completion of the reaction, the catalyst was filtered off, washed with dichloromethane and then dried in oven for 30 min and catalyst was reused accordingly.

ICP-OES analysis of Chitosan:

The concentration of copper, Iron, Mercury, and Zinc elements were determined by ICP-OES instrument (Perkin Elmer, USA, and Optima 2000 DV) after acid digestion of the chitosan sample. The concentration of copper, Iron, Mercury, and Zinc elements were found in the chitosan are below detection limit. This experiment indicate that chitosan has metal ions less than 0.05 ppm level. Hence there is no effect of metals in the transamidation reaction.

TON number calculation:

The mass average weight of Chitosan calculated by using GPC was found to be = 286020 g/mol.

(Mw = 286 K Da)

NO. of monomeric units present in chitosan polymer

Wt. of de acetylated monomeric unit mass = 179.17

Wt. of acetylated monomeric unit mass = 221.0

Purity of the chitosan catalyst average = 80% (Chitosan medium molecular weight

Sigma Aldrich 448877-250 G

CAS 9012-76-4;

Bach: 03318 AJ.)

$80/100 \times 286020 = 228816$ g/mol of the Wt. of de acetylated of chitosan

NO. of monomeric units present in chitosan polymer = $228816/179.17 = 1277.08$

Therefore 1277.08 units present in 80% of deacetylated of chitosan.

20 % of acetylated units which is equivalent to 258.8416 acetylated units.

Total active sites including acetylated and deacetylated units = 1535.9216 units

Wt. of Chitosan used = 0.024 g (see experimental section)

0.024 g of chitosan contains 0.128 m moles

So, NO. of active site in the 0.024 g of the chitosan catalyst = **0.128 m moles**

TON = NO. of moles of product formed/ NO. of moles of active sites present in the catalyst

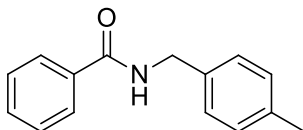
$$= 0.990/0.128$$

$$\mathbf{TON} = 7.734 (\sim 8)$$

Therefore, based on above calculated **TON** it is concluded that, chitosan is not a promoter, it is catalyst.

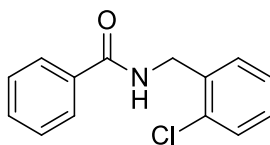
Characterization data of unknown compounds

N-(4-Methylbenzyl) benzamide (3b)



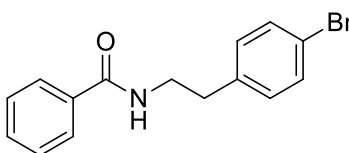
(Eluent: 20% EtOAc in DCM); white solid; 83% yield (201 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.78 (d, $J = 7.5$ Hz, 2H), 7.49 (t, $J = 7.0$ Hz, 1H), 7.41 (t, $J = 7.0$ Hz, 2H), 7.25 (d, $J = 8.5$ Hz, 2H), 7.17 (d, $J = 7.5$ Hz, 2H), 6.37 (br s, 1H, NH), 4.60 (d, $J = 5.5$ Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3) δ 167.2, 137.3, 135.1, 134.4, 131.5, 129.4, 128.5, 127.9, 126.9, 43.5, 21.1. HRMS calcd for $\text{C}_{15}\text{H}_{16}\text{NO}$: 226.1232. Found: 226.1221.

N-(2-Chlorobenzyl)benzamide (3c)



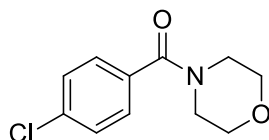
(Eluent: 20% EtOAc in DCM); white solid; 89% yield (218 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.79 (d, $J = 7.0$ Hz, 2H), 7.51-7.38 (m, 5H), 7.26-7.24 (m, 2H), 6.68 (br s, 1H, NH), 4.74 (d, $J = 6.0$ Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3) δ 163.3, 134.5, 133.2, 132.6, 130.6, 129.4, 128.4, 128.0, 127.5, 126.1, 125.9, 41.0. LRMS calculated for $\text{C}_{14}\text{H}_{12}\text{ClNO}$ ($\text{M}+\text{Na}$) 268.05; found: 268.11.

N-(4-Bromophenethyl) benzamide (3k)



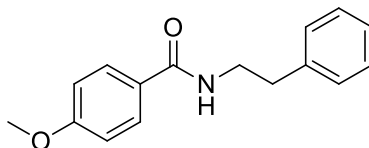
(Eluent: 20% EtOAc in DCM); white solid; 76% yield (116 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.70 (d, $J = 7.0$ Hz, 2H), 7.48 (t, $J = 7.0$ Hz, 1H), 7.40-7.39(m, 4H), 7.10(d, $J = 7.0$ Hz, 2H), 6.26 (br s, 1H, NH), 3.68 (q, $J = 6.5$ Hz, 2H), 2.88 (t, $J = 7.0$ Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3) δ 166.5, 136.8, 133.4, 130.7, 129.5, 127.5, 125.7, 119.4, 39.9, 34.1. HRMS calcd for $\text{C}_{15}\text{H}_{15}\text{NOBr}$: 304.0337, found: 304.0338.

(4-Chlorophenyl)(morpholino)methanone (3t)



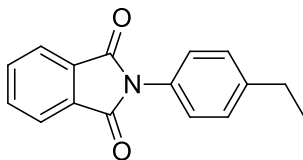
(Eluent: 20% EtOAc in DCM); 76% yield (153 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.40-7.35(m, 4H), 3.75-3.65(m, 6H) 3.41 (s, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 168.3, 134.9, 132.5, 127.8, 127.6, 65.7, 47.2, 41.5. HRMS calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_2\text{Cl}$: 226.0635, found: 226.0628.

4-methoxy-N-phenethylbenzamide (3v)



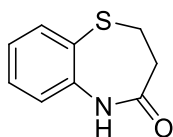
(Eluent: 20% EtOAc in DCM); white solid; 82% yield (208 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, $J = 8.0$ Hz, 2H), 7.48 (t, $J = 6.0$ Hz, 3H), 6.90(d, $J = 9.0$ Hz, 2H), 6.03 (br s, 1H, NH), 3.83 (s, 3H), 3.71 (q, $J = 7.0$ Hz, 2H). 2.92 (t, $J = 6.5$ Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3) δ 166.9, 162.0, 139.0, 128.8, 128.6, 128.5, 126.5, 113.7, 55.3, 41.0, 35.7. HRMS calcd for $\text{C}_{16}\text{H}_{18}\text{NO}_2$: 256.1338, found: 256.1336.

2-(4-Ethylphenyl) isoindoline-1,3-dione (6g)



(Eluent: DCM); white solid; 75% yield (188 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.95 (q, $J = 5.5$ Hz, 2H), 7.78 (q, $J = 3.0$ Hz, 2H), 7.33 (s, 4H), 2.71 (q, $J = 8.0$ Hz, 2H), 1.27 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (50 MHz, CDCl_3) δ 167.4, 144.3, 134.2, 131.8, 128.6, 126.4, 123.6, 28.5, 15.4. HRMS calcd. for $\text{C}_{17}\text{H}_{16}\text{NO}_2$: 266.1181. Found: 266.1173.

(2,3-Dihydrobenzo[b][1,4]thiazepin-4(5H)-one (12)¹

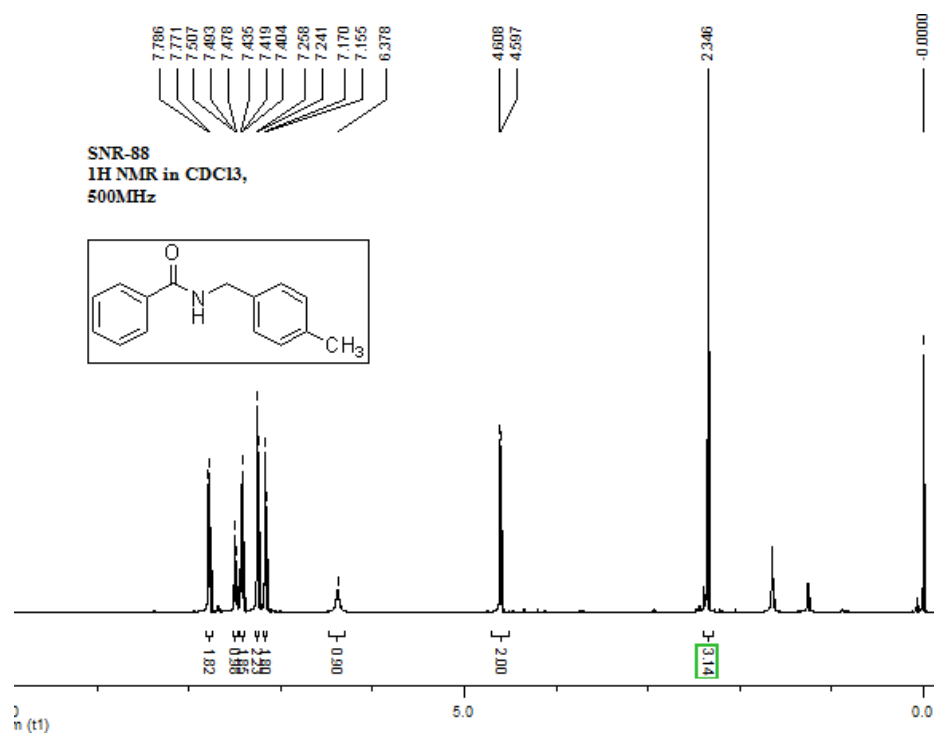


(Eluent: 40% EtOAc in DCM); Brown solid; 74% yield (132 mg); ^1H NMR (500 MHz, CDCl_3) δ 7.90(s, 1H), 7.61(d, $J = 7.5$ Hz, 1H), 7.37-7.34(m, 1H), 7.19(t, $J = 8.0$ Hz, 1H), 7.11 (d, $J = 7.5$ Hz, 1H), 3.45 (t, $J = 7.0$ Hz, 2H), 2.63 (t, $J = 7.0$ Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3) δ 172.4, 140.2, 134.5, 128.5, 125.9, 125.5, 122.2, 33.2, 32.4.

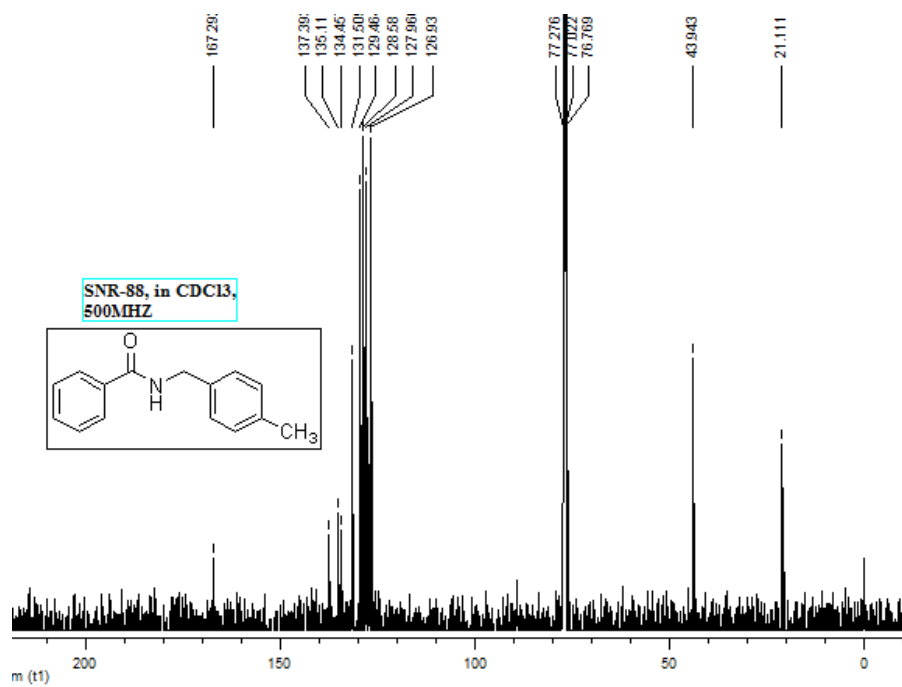
Reference

1. Lillian, B-F.; Andrea, O-P.; Diego, G.-S. *J. Org. Chem.* **2014**, 79, 4544.

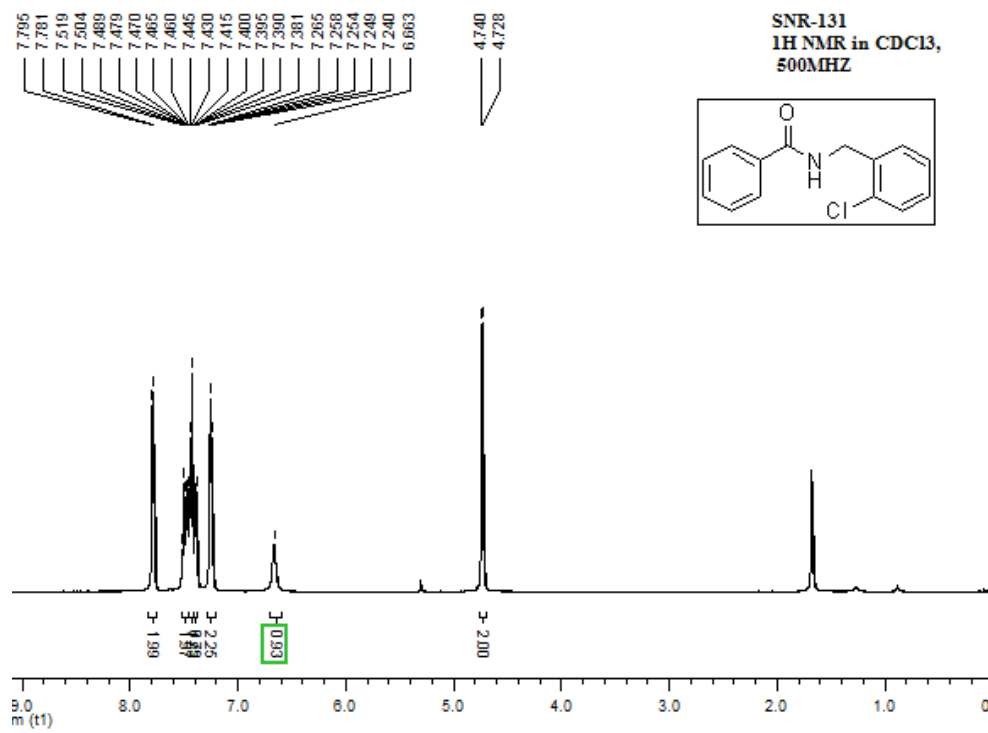
Copies of ^1H and ^{13}C NMR spectra



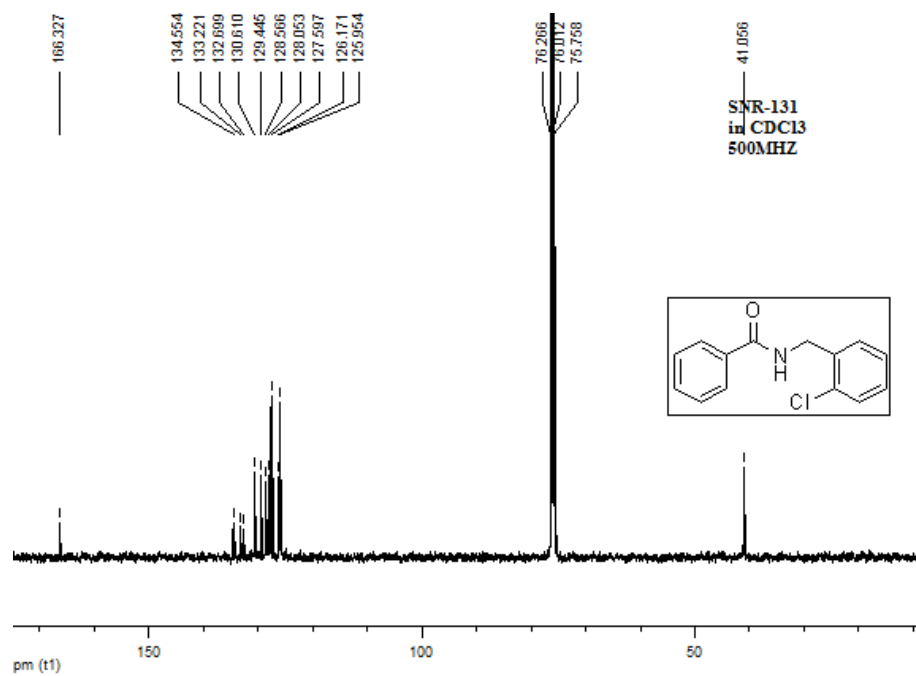
¹H NMR of 3b



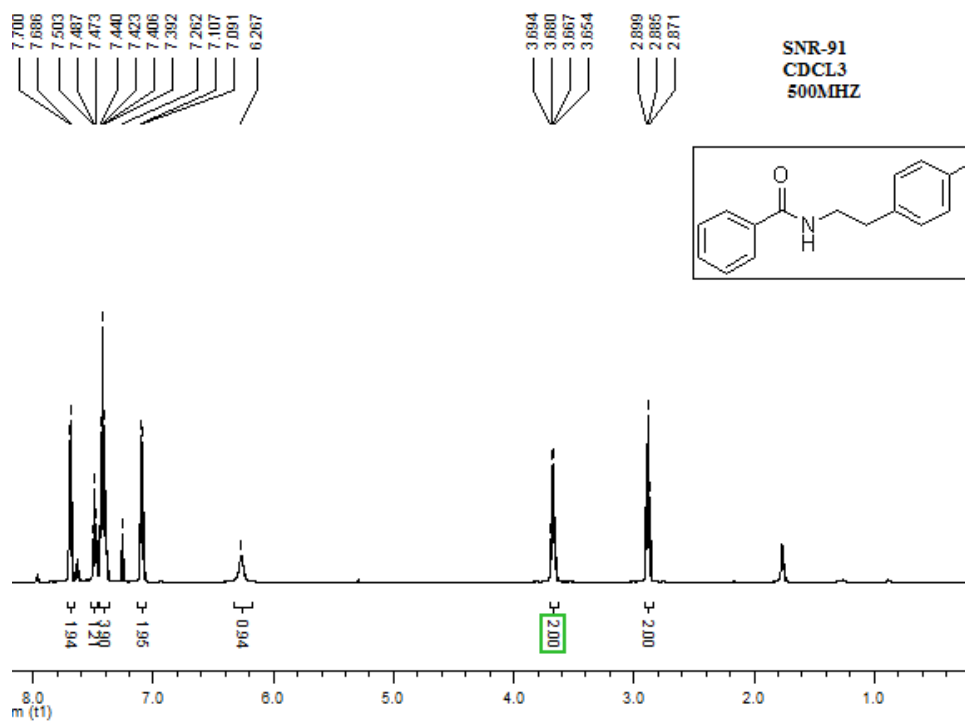
¹³C NMR of 3b



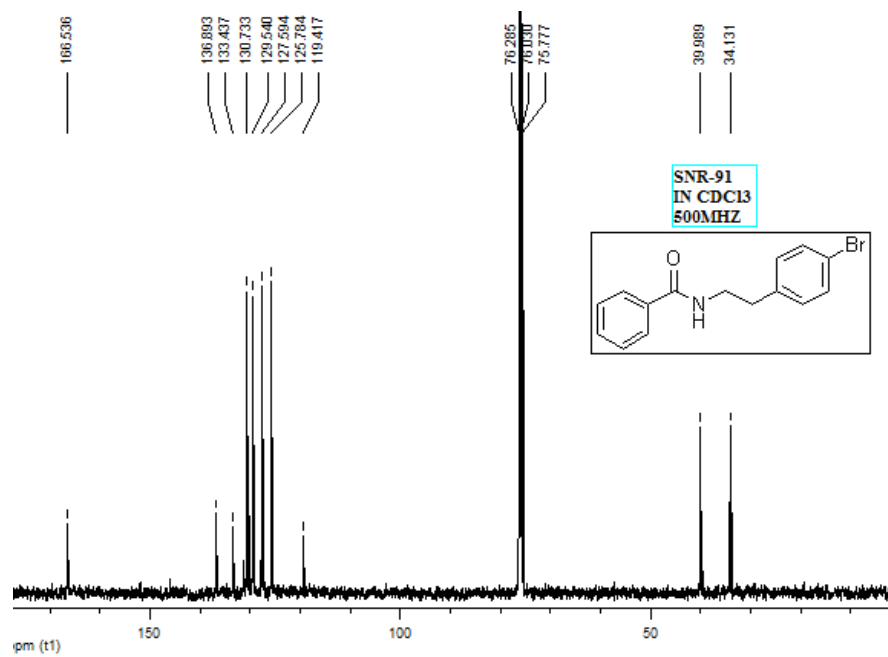
¹H NMR of 3c



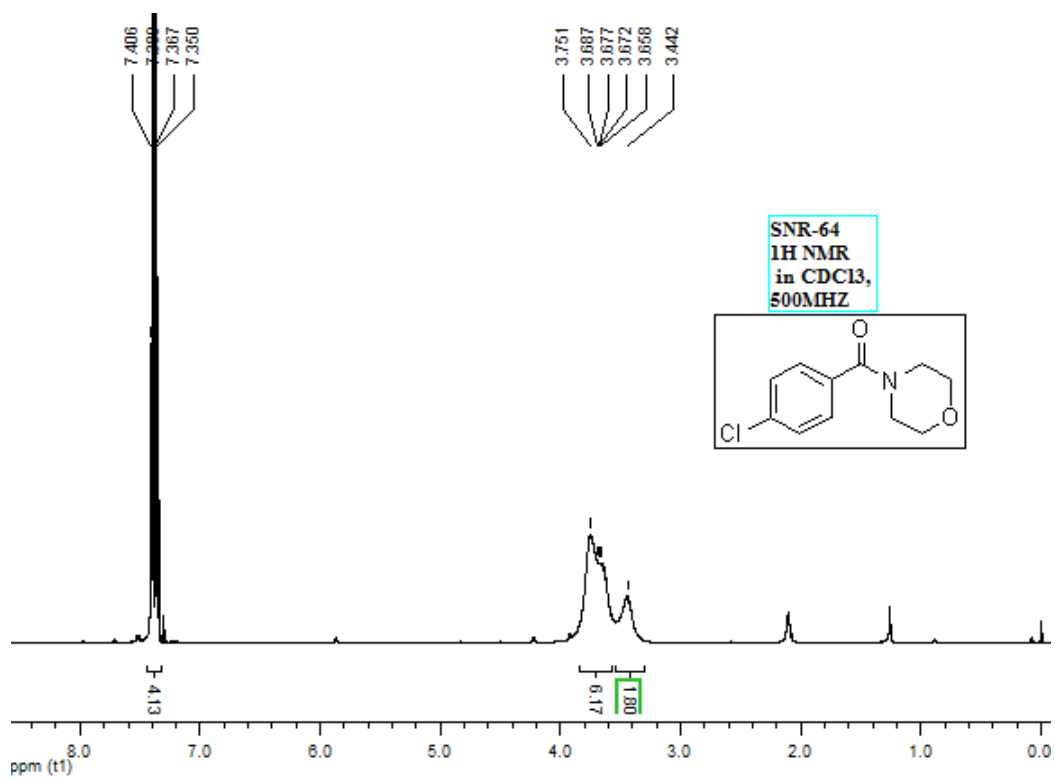
¹³C NMR of 3c



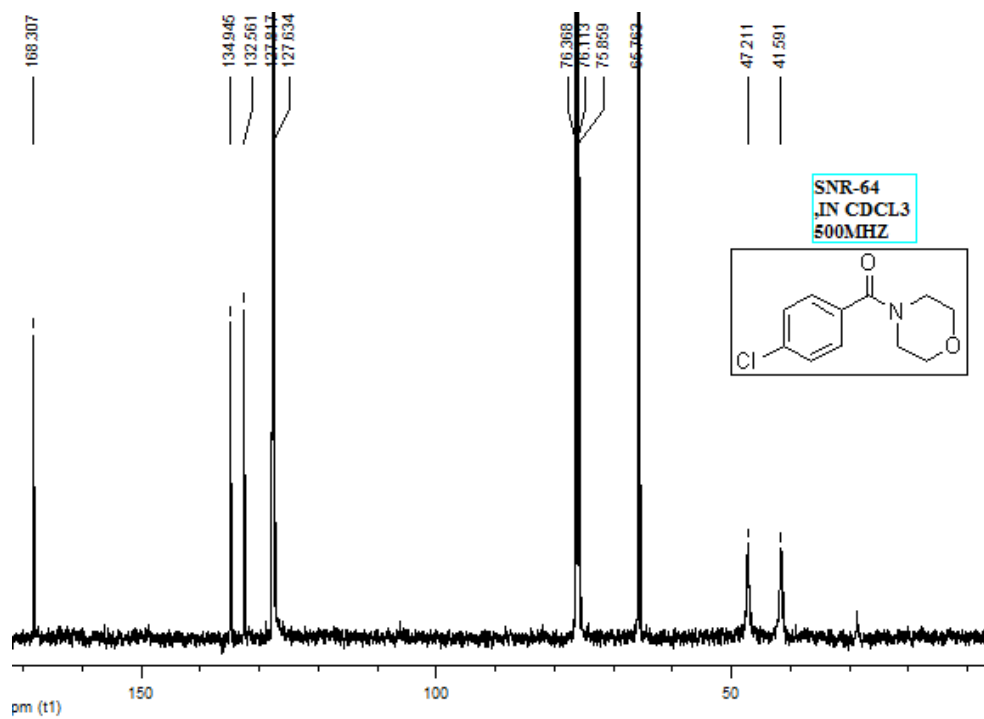
¹H NMR of 3k



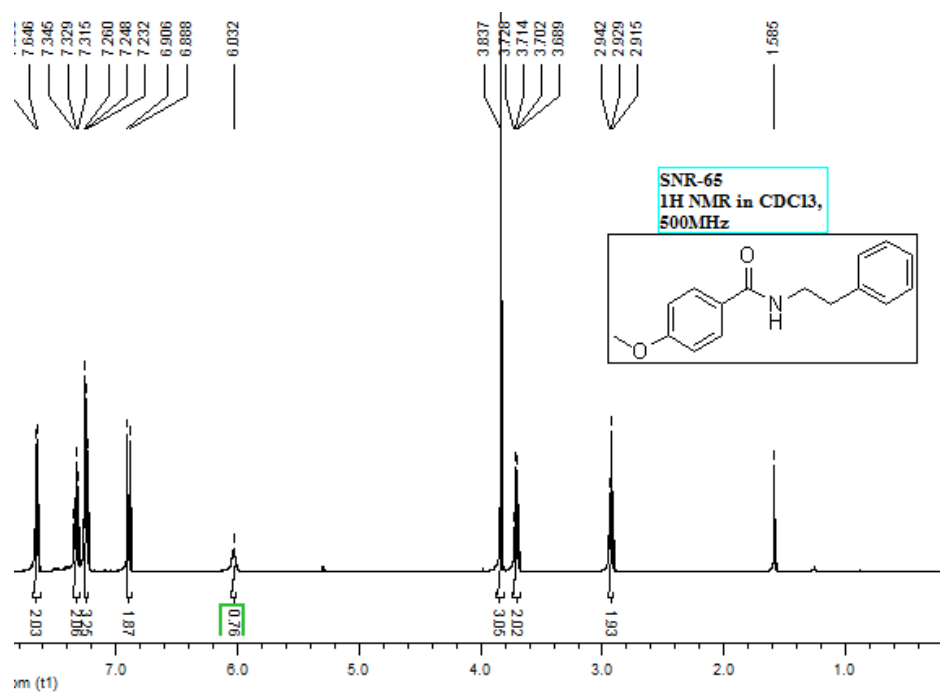
¹³C NMR of 3k



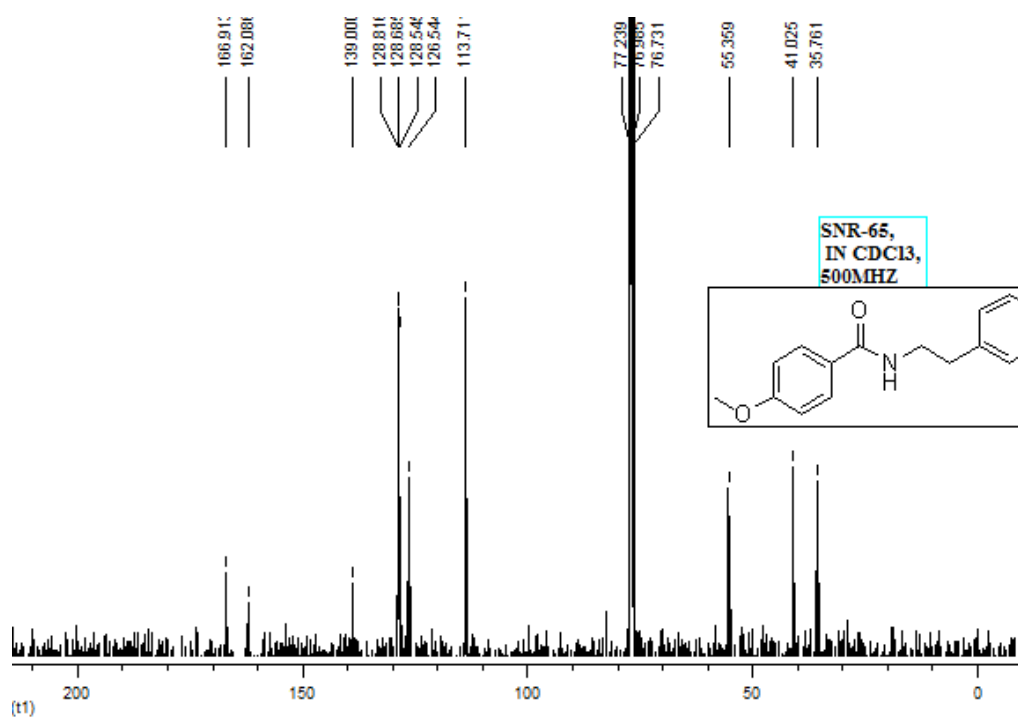
¹H NMR of 3t



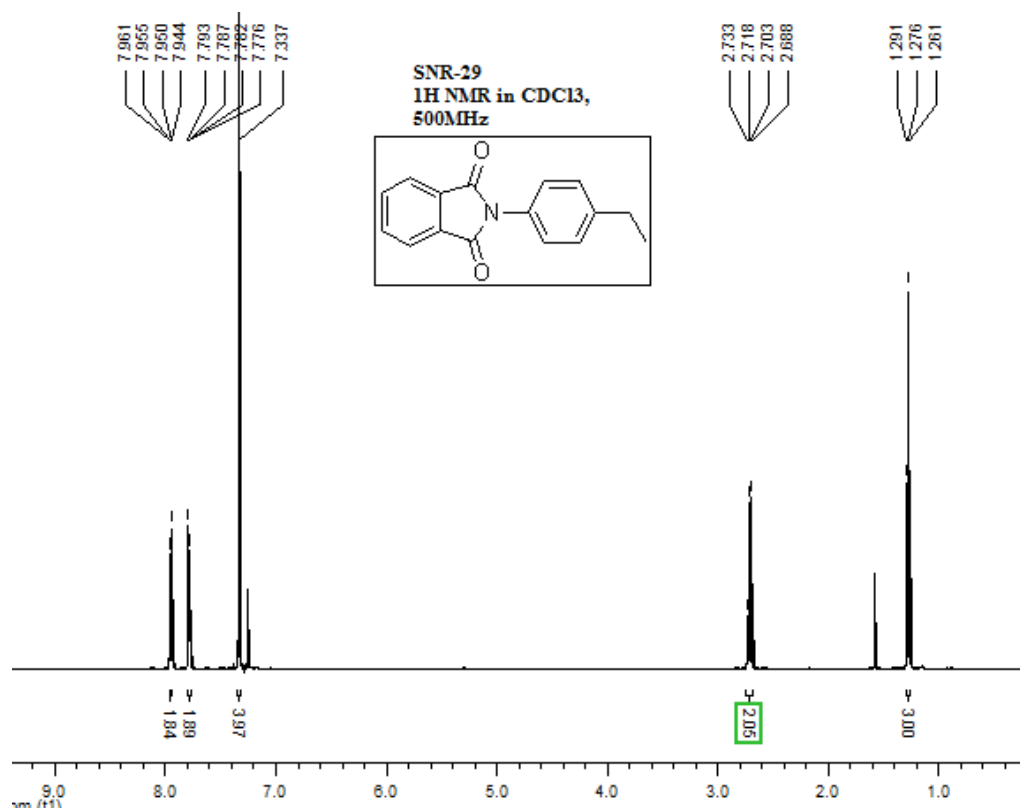
¹³C NMR of 3t



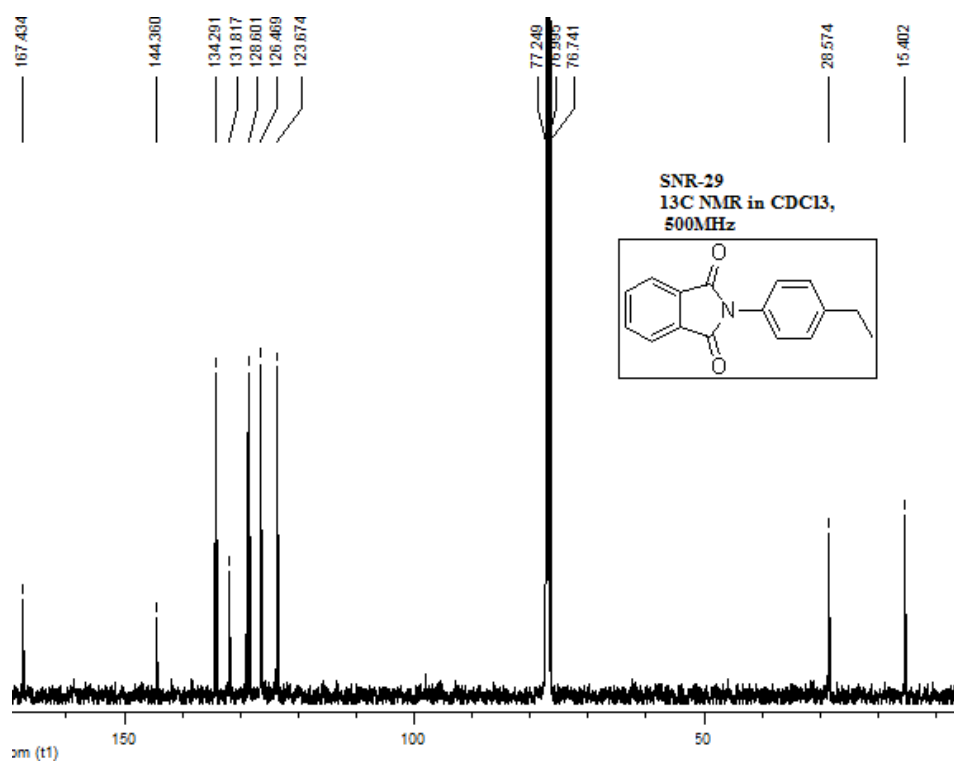
¹H NMR of 3v



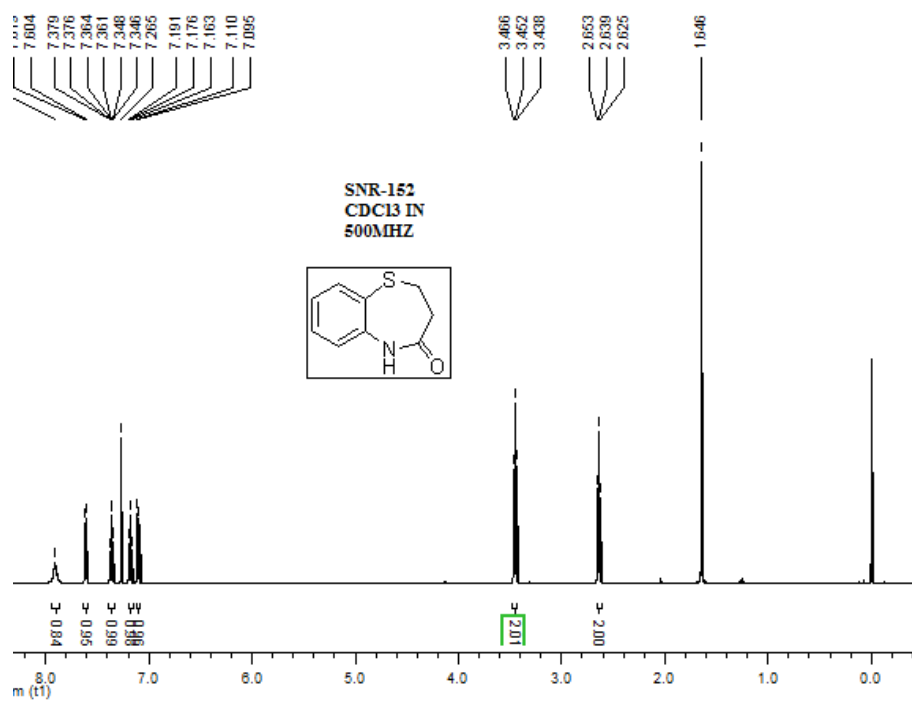
¹³C NMR of 3v



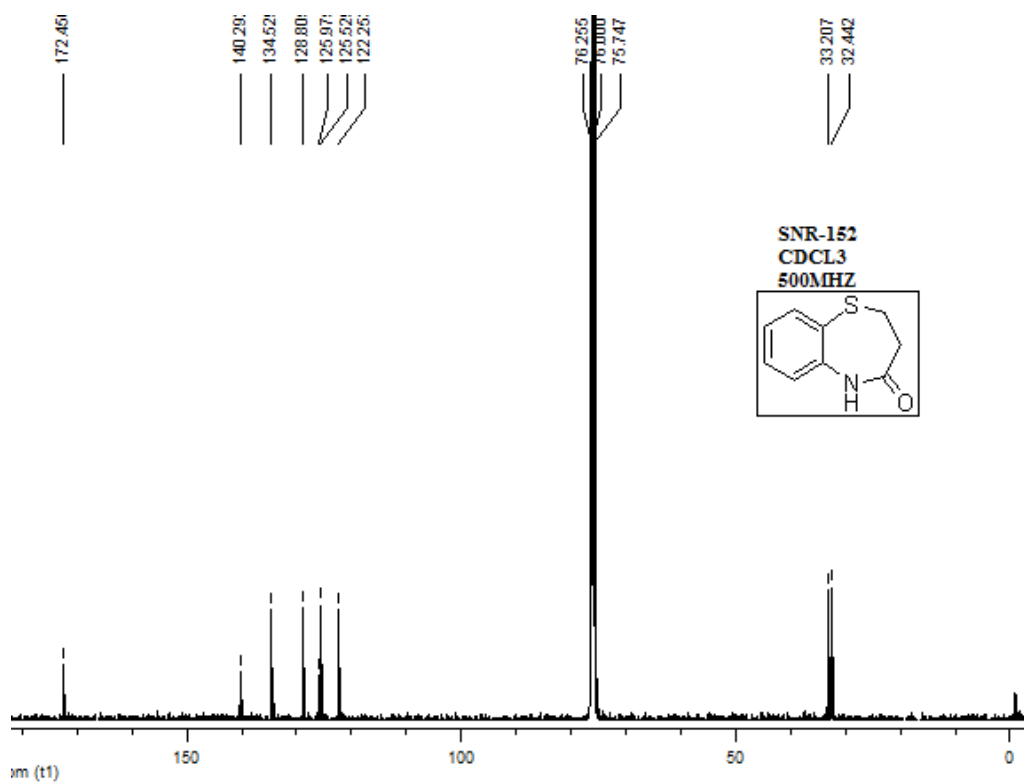
¹H NMR of 6g



¹³C NMR of 6g



¹H NMR of 13



¹³C NMR of 13