Supporting Information for

Ruthenium Catalyzed Redox-Neutral and Single-Step Amide Synthesis from Alcohol and Nitrile with Complete Atom Economy

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Content

1. Experimental section

General Considerations

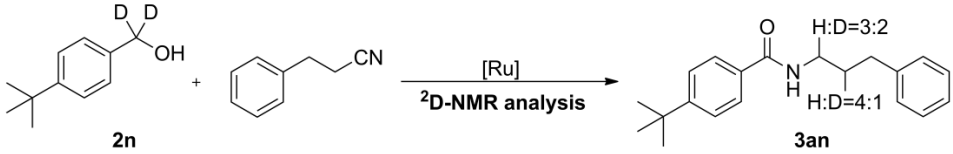
Unless otherwise noted, all reactions were carried out using standard Schlenk techniques or in an argon-filled glove box. Dichloromethane, diethyl ether and toluene were dried over Pure Solv solvent purification system. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and Sigma-Aldrich Corporation. NMR spectra were recorded in $CDCl_3$ or benzene-d_6 using Bruker DPX300, AMX400, Agilent 400-MR, JEOL ECA400, or JEOL ECA400SL spectrometer, and TMS (tetramethylsilane) was used as a reference. Chemical shifts were reported in ppm and coupling constant in Hz. High Resolution Mass Spectrometry (HRMS) was performed by the Korea Basic Science Institute Daegu Center. GC analysis was carried out with 7980A GC system from Agilent Technologies, equipped with an HP-5 column and FID detector. $RuH_2(PPH_3)_4$,[1] $RuH_2(CO)(PPh_3)_3$,[2] imidazolium salt **4**,[3] and other metal reagents were prepared by literature procedures or purchased from Strem Chemicals, Inc. ^{13}C (99 atom % ^{13}C), ^{15}N (98 atom % ^{15}N), and ^{13}C–^{15}N (99 atom % ^{13}C, 99 atom % ^{15}N) isotope labeled potassium cyanide were purchased from Cambridge Isotope Laboratories, Inc. and Sigma-Aldrich Corporation, and corresponding isotope labeled nitriles were synthesized based on literature procedure.[4] Other chemicals were purchased from commercial suppliers and used as received without further purification.

General procedure for amide synthesis

Inside an argon-filled glove box, $RuH_2(CO)(PPh_3)_3$ (45.9 mg, 0.05 mmol), 1,3-diisopropylimidazolium bromide (11.7 mg, 0.05 mmol), NaH (2.4 mg, 0.10 mmol), and toluene (0.6 mL) were added to an oven-dried 4 mL vial equipped with septum screw cap. If solid nitrile (0.50 mmol) or alcohol (0.55 mmol) substrates were used, they were also added to the reaction mixture inside the glove box. Liquid alcohol or nitrile substrates were added into the vial using micro-syringe under Ar flow after the vial was taken out of the glove box.

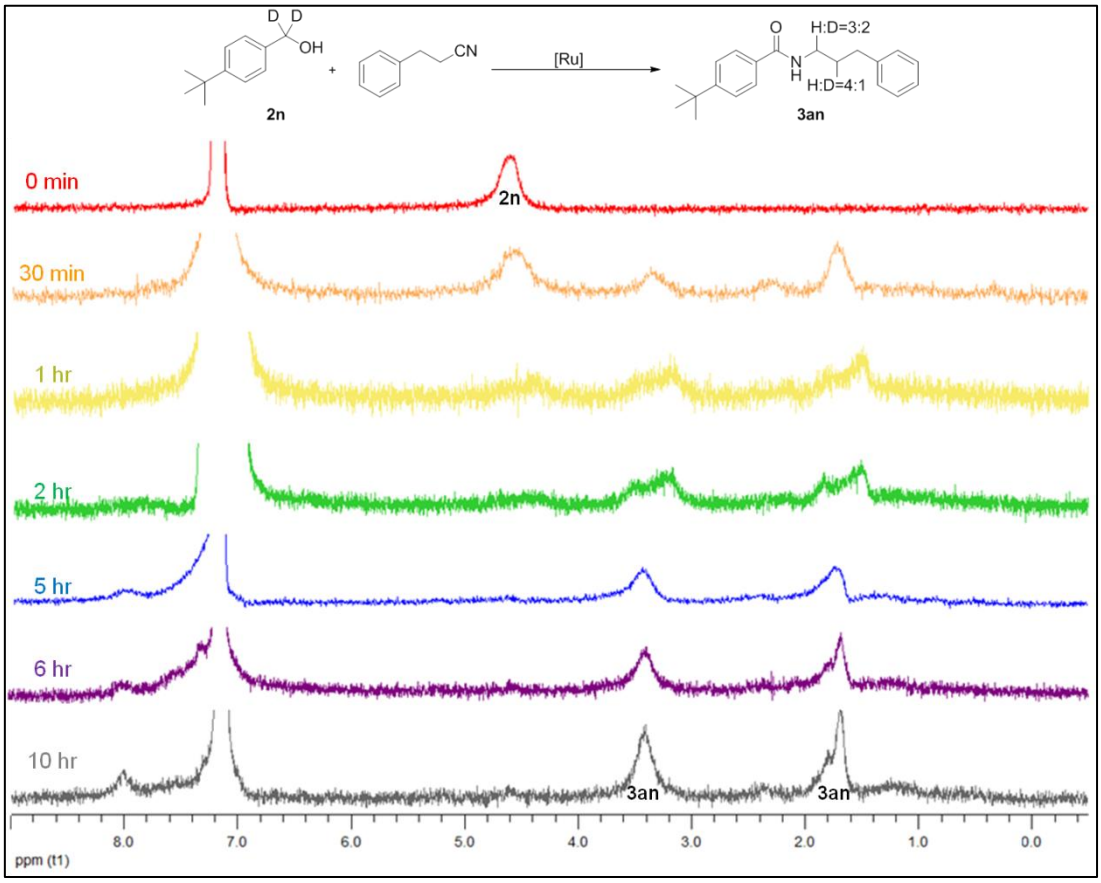
Then the overall reaction media was stirred at 110 ℃ for 48 h before being cooled down to room temperature. All the volatiles were removed under vacuum. Purification of the crude product was performed with silica gel column chromatography using hexane and ethyl acetate solvent mixture as an eluent to afford the corresponding amide.

^{2}D labeling study

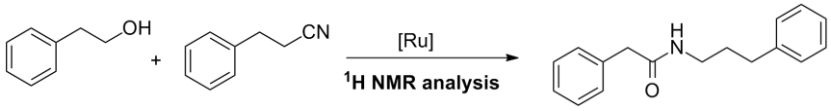


3-Phenylpropionitrile (65.5 μL, 0.5 mmol), **2n** (98.5 μL, 0.55 mmol), $RuH_2(CO)(PPh_3)_3$ (22.9 mg, 0.025 mmol), 1,3-diisopropylimidazolium bromide **4** (5.8 mg, 0.025 mmol), NaH (2.4 mg, 0.10 mmol), and toluene (0.6 mL) were placed in an oven dried 4 mL vial inside an argon-filled glove box. Small amount of benzene-d_6 (10 μL) was also added, and stirred for a minute. The reaction mixture was transferred to a screw-cap NMR tube inside the glove box and was taken out of the box. Then the tube was heated to 110 ℃, and ^{2}D NMR spectra were taken after 0 min, 30 min, 1 hr, 2 hr, 5 hr, 6 hr, and 10 hr, respectively (Figure S1). The product was purified with silica gel column chromatography after the reaction for 48 hr. Deuterium exchange ratios were determined based on the integration values in ^{1}H NMR.

Figure S1. ^{2}D NMR spectral changes in a reaction between **2n** and **1a**

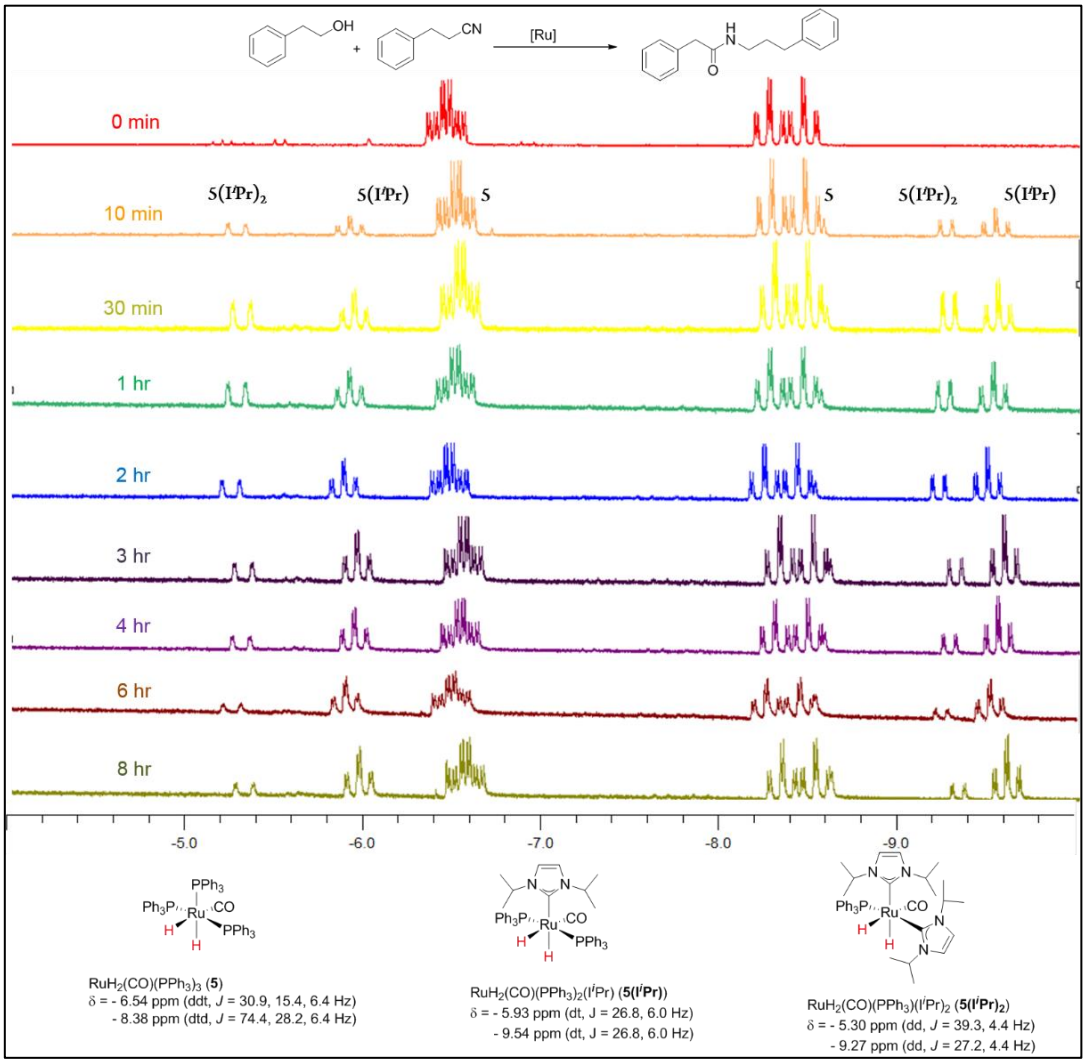


^{1}H NMR spectroscopic investigation for catalytic intermediate observation



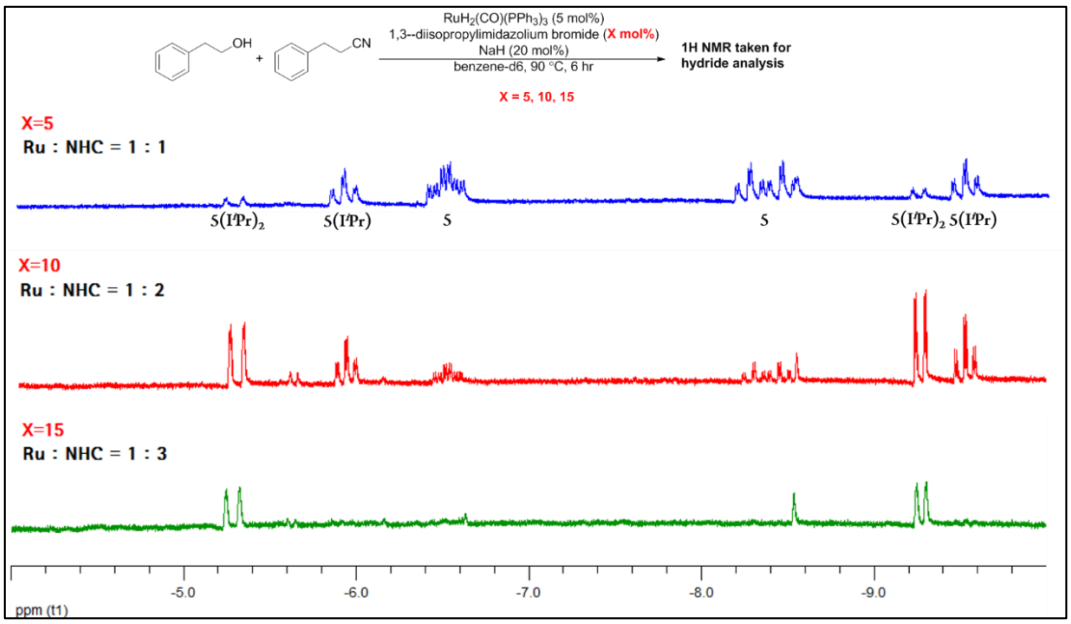
3-Phenylpropionitrile (32.5 μL, 0.25 mmol), 2-phenylethanol (32.8 μL, 0.275 mmol), $RuH_2(CO)(PPh_3)_3$ (11.5 mg, 0.0125 mmol), 1,3-diisopropylimidazolium bromide **4** (2.9 mg, 0.0125 mmol), NaH (1.2 mg, 0.05 mmol), and benzene-d_6 (0.6 mL) were placed in an oven dried 4 mL vial inside a argon-filled glove box. The reaction mixture was transferred to a screw-cap NMR tube inside the glove box. Then the tube was taken out of the glove box and was heated to 90 ℃. ^{1}H NMR spectra were taken at room temperature after 0 min, 10 min, 30 min, 1 hr, 2 hr, 3 hr, 4 hr, 6 hr, and 8 hr, respectively (Figure S2).

Figure S2. ^{1}H NMR spectra for investigation of catalytic intermediates



A NHC-Ru hydride complex, $RuH_2(CO)(PPh_3)_2(I^iPr)$ (**5(I^{i}Pr)**) (I^iPr = 1,2-diisopropylimidazol-2-ylidene), was identified based on literature data.[5] Formation of $RuH_2(CO)(PPh_3)(I^iPr)_2$ (**5(I^{i}Pr)$_2$**) was proposed based on the similar spectral data, such as ^1H chemical shifts and coupling constants, with $RuH_2(CO)(PPh_3)(ICy)_2$ (ICy = 1,2-dicyclohexylimidazol-2-ylidene) reported by Whittlesey and Williams. To verify it further, ^1H NMR spectroscopic investigations with 2.0 equiv. (5.8 mg, 0.025 mmol) or 3.0 equiv. (8.7 mg, 0.038 mmol) of 1,3-diisopropylimidazolium bromide were performed (Figure S3). Especially with 3.0 equiv of the NHC precursor, the identical equivalence of NHC for the synthesis of $RuH_2(CO)(PPh_3)(ICy)_2$ in the report by Whittlesey and Williams, the complex which has hydride peaks at –5.3 and –9.3 ppm was formed as a major species. This highly indicates that the minor hydride complex formed during the reaction is highly likely to be $RuH_2(CO)(PPh_3)(I^iPr)_2$.

Figure S3. ^1H NMR analysis for verification of formation of $RuH_2(CO)(PPh_3)(I^iPr)_2$



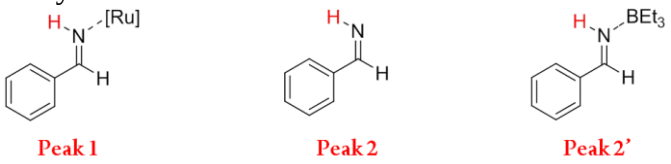
^{1}H NMR experiment for benzaldimine intermediate observation

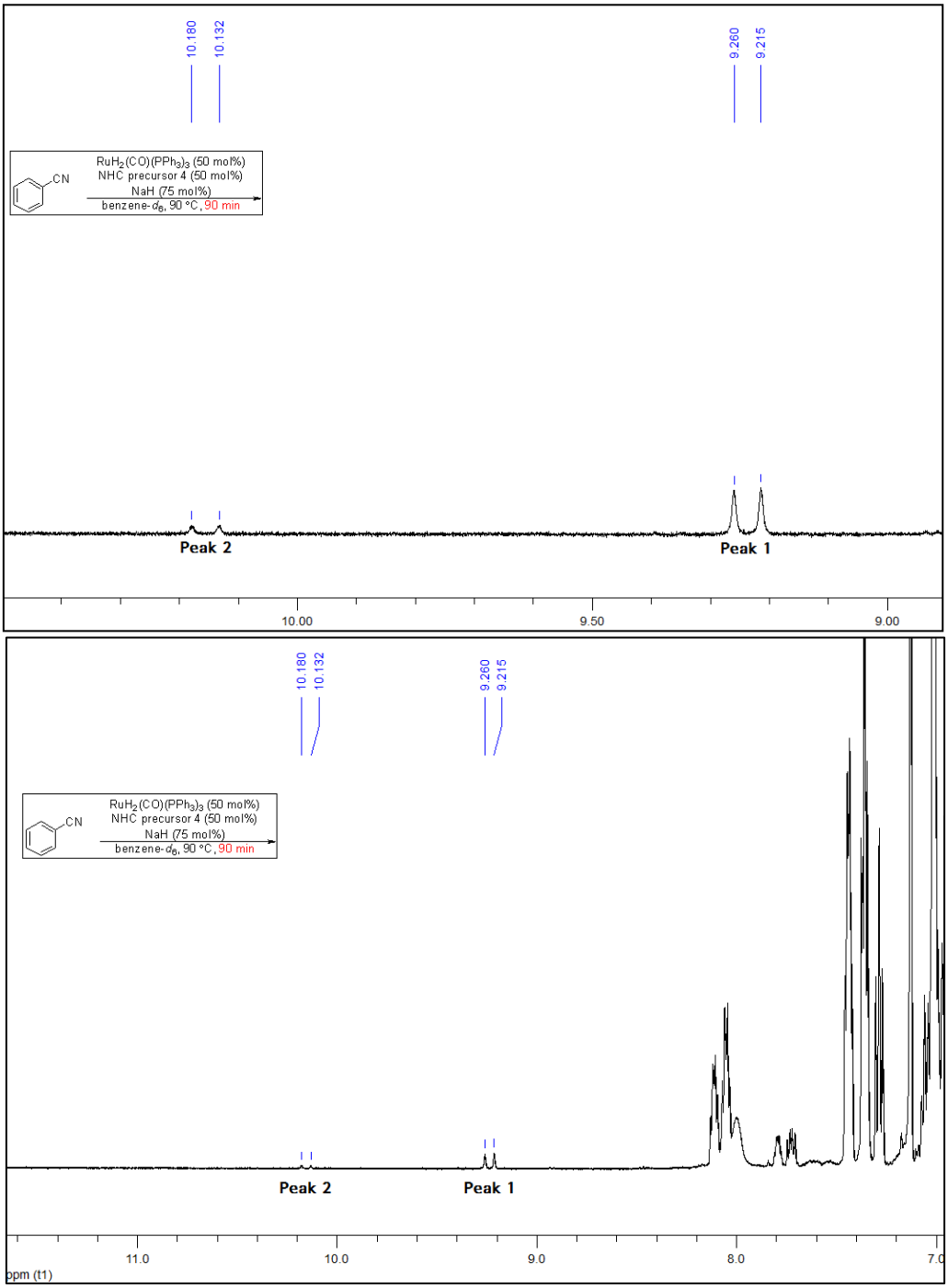
Benzonitrile (2.6 μL, 0.025 mmol) was added to a mixture of $RuH_2(CO)(PPh_3)_3$ (11.5 mg, 0.0125 mmol), 1,3-diisopropylimidazolium bromide **4** (2.9 mg, 0.0125 mmol), sodium hydride (0.45 mg, 0.0188 mmol), and benzene-d_6 (0.6 mL) inside a argon-filled glove box. The reaction mixture was transfered to a screw-cap NMR tube. Then the tube was taken out of the glove box and was heated to 90 ℃. ^{1}H NMR spectra were taken at room temperature after 0 min, 5 min, 10 min, 20 min, 30 min, 45 min, 60 min, and 95 min, respectively. After 5 min, small portion of clear doublet (J = 22.9 Hz) was appeared at 9.2 ppm (**peak 1**). Further heating induces another doublet (J = 23.5 Hz) at 10.2 ppm (**peak 2**). Even after 90 min, the intensities of these two peaks were not diminished. Then, we added 10 mol % of 2-phenylethanol into the NMR tube, and the tube was heated to 90 ℃ for 60 min. Two peaks remained with slight decrease of intensity. Finally, 100 mol % of 2-phenylethanol was added into the reaction mixture. The reaction progress was monitored by ^{1}H NMR spectroscopy, which shows that intensities of **peak 1** and **peak 2** were decreased. After 2 hr, **peak 1** and **peak 2** were completely disappeared.

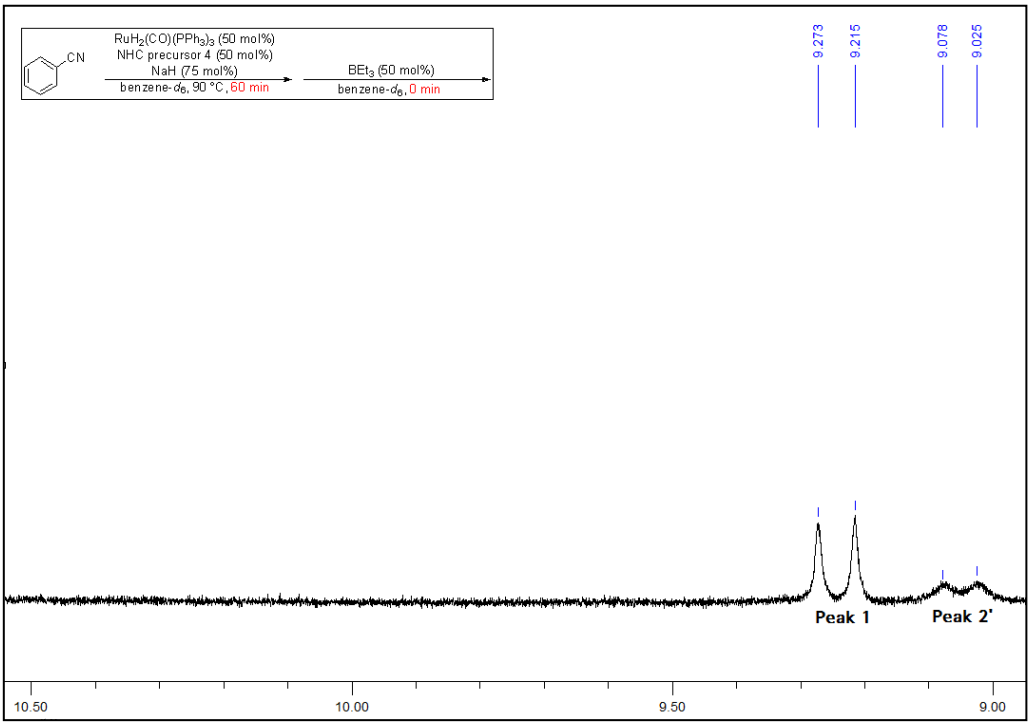
With its characteristic chemical shift and an unusually big coupling constant, **peak 2** was interpreted as N-**H** hydrogen of *trans*-benzaldimine following the literature report.[6] **Peak 1** could be ruthenium coordinated *trans*-benzaldimine. This type of upfield shift of the imine hydrogen peak in ^{1}H NMR spectra has been also observed in the case of BEt_3-bound benzaldimine complex.[6]

To make sure that **peak 1** is derived from imine, an additional experiment was performed. **Peak 1** and **peak 2** were generated again by the same procedure, and 0.0125 mmol of BEt_3 (12.5 μL, 1.0 M solution in hexane) was added to the reaction mixture. Immediately, **peak 2** was shifted to 9.0 ppm with a similar coupling constant of 21.5 Hz (**peak 2'**), due to BEt_3 coordination to free imine. This experiment shows that **peak 1** is likely to be derived from ruthenium coordinated *trans*-benzaldimine and **peak 2** is free *trans*-benzaldimine.

Figure S4. ^{1}H NMR study for benzaldimine intermediate identification



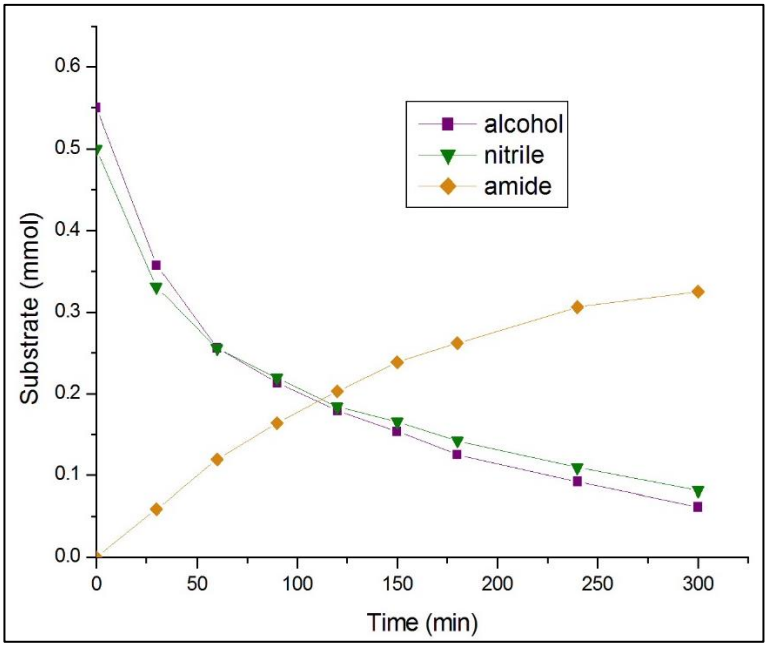



CN
RuH2(CO)(PPh3)3 (50 mol%)
NHC precursor 4 (50 mol%)
NaH (75 mol%)
benzene-d6, 90 °C, 60 min
BEt3 (50 mol%)
benzene-d6, 0 min
9.273
9.215
9.078
9.025
Peak 1
Peak 2'
10.50
10.00
9.50
9.00

GC analysis for reaction intermediate detection

$RuH_2(CO)(PPh_3)_3$ (22.9 mg, 0.05 mmol), 1,3-diisopropylimidazolium bromide **4** (5.8 mg, 0.05 mmol), NaH (2.4 mg, 0.10 mmol), and toluene (0.6 mL) were placed in an oven dried 25 mL Schlenk tube inside an argon-filled glove box. The Schlenk tube was taken out of the box. 2-Phenylethanol (65.8 μL, 0.55 mmol), 3-phenylpropionitrile (65.5 μL, 0.50 mmol), and dodecane (56.8 μL, 0.25 mmol) as an internal standard were added to the reaction mixture under Ar flow. The reaction tube was heated at 110 ℃. Small portion of reaction medium (about 10 μL) was sampled by micro-syringe under Ar flow after 0 min, 30 min, 60 min, 90 min, 120 min, 150 min, 180 min, 240 min, and 300 min. The sample was diluted with dichloromethane, filtered with celite, analysed with GC.

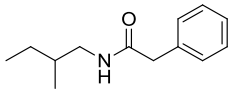
Figure S5. Reaction profiles for the amide synthesis from 2-phenylethanol and 3-phenylpropionitrile (average of 3 runs)



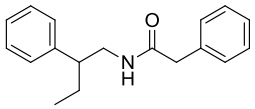
2. Characterization Data

The reaction was performed in 0.50 mmol scale. All reported compounds, **3aa** (129.8 mg, 0.512 mmol, >99%,),[7] **3ca** (99.3 mg, 0.453 mmol, 91%),[8] **3da** (46.1 mg, 0.282 mmol, 56%),[9] **3ja** (100.3 mg, 0.445 mmol, 89%),[7] **3ab** (109.6 mg, 0.410 mmol, 82%),[10] **3ae** (80.7 mg, 0.397 mmol, 79%),[11] **3af** (68.2 mg, 0.278 mmol, 56%),[11] **3ag** (96.9 mg, 0.405 mmol, 81%),[12] **3aj** (108.6 mg, 0.403 mmol, 81%)[13] were identified by spectral comparison with literature data or with analogous literature data.

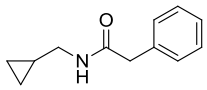
Characterization of amides, 3ba, 3ea, 3fa, 3ga, 3ha, 3ia, 3ka, 3ac, 3ad, 3ah, 3ai, 3ak, 3al, 3am, 3la, 3ma, 3na



***N*-(2-Methylbutyl)-2-phenylacetamide (3ba):** white solid (99.3 mg, 0.484 mmol, 97%); ^{1}H NMR ($CDCl_3$) δ = 0.78 (t, J = 6.4 Hz, 3H), 0.84 (d, J = 7.2 Hz, 3H), 1.02–1.11 (m, 1H), 1.22–1.31 (m, 1H), 1.42–1.50 (m, 1H), 2.98–3.05 (m, 1H), 3.12–3.18 (m, 1H), 3.58 (s, 2H), 5.34 (bs, 1H), 7.25–7.32 (m, 3H), 7.35–7.39 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 170.9, 135.1, 129.5, 129.1, 127.4, 45.2, 44.0, 34.8, 26.9, 17.0, 11.2; HRMS(ESI) calcd for $C_{13}H_{19}NO$: 205.1467. Found: 205.1471 [MH^+].

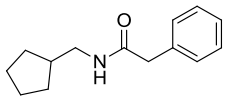


***N*-(2-Phenylbutyl)-2-phenylacetamide (3ea):** colorless oil (112.2 mg, 0.420 mmol, 84%); ^{1}H NMR ($CDCl_3$) δ = 0.78 (t, J = 7.2 Hz, 3H), 1.49–1.68 (m, 2H), 2.54–2.59 (m, 1H), 3.10–3.17 (m, 1H), 3.45 (s, 2H), 3.63–3.69 (m, 1H), 5.14 (bs, 1H), 6.96–7.05 (m, 4H), 7.17–7.25 (m, 6H); ^{13}C NMR ($CDCl_3$) δ = 170.8, 142.2, 134.7, 129.3, 128.9, 128.6, 127.7, 127.2, 126.6, 47.3, 44.8, 43.8, 26.4, 11.9; HRMS(ESI) calcd for $C_{18}H_{21}NO$: 267.1623. Found: 267.1625 [MH^+].

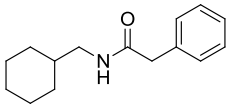


***N*-(Cyclopropylmethyl)-2-phenylacetamide (3fa):** white solid (79.5 mg, 0.420 mmol,

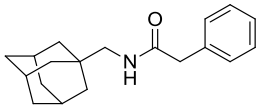
84%); ^{1}H NMR ($CDCl_3$) δ = 0.12 (q, J = 4.4 Hz, 2H), 0.41–0.46 (m, 2H), 0.83–0.90 (m, 1H), 3.08 (t, J = 5.6 Hz, 2H), 3.58 (s, 2H), 5.46 (bs, 1H), 7.28–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 170.8, 135.1, 129.4, 129.0, 127.3, 44.3, 43.9, 10.6, 3.2; HRMS(ESI) calcd for $C_{12}H_{15}NO$: 189.1154. Found: 189.1161 [MH^+].



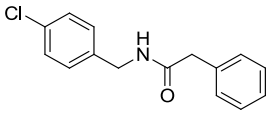
***N*-(Cyclopentylmethyl)-2-phenylacetamide (3ga):** white solid (89.7 mg, 0.413 mmol, 83%); ^{1}H NMR ($CDCl_3$) δ = 1.05–1.12 (m, 2H), 1.46–1.66 (m, 6H), 1.92 (q, J = 7.6 Hz, 1H), 3.15 (t, J = 7.2 Hz, 2H), 3.58 (s, 2H), 5.35 (bs, 1H), 7.25–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 170.9, 135.1, 129.5, 129.0, 127.4, 44.5, 44.0, 39.6, 30.1, 25.1; HRMS(ESI) calcd for $C_{14}H_{19}NO$: 217.1467. Found: 217.1471 [MH^+].



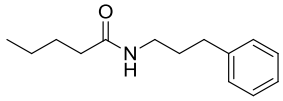
***N*-(Cyclohexylmethyl)-2-phenylacetamide (3ha):** white solid (96.2 mg, 0.416 mmol, 83 %); ^{1}H NMR ($CDCl_3$) δ = 0.77-0.87 (m, 2H), 1.08-1.22 (m, 3H), 1.34-1.40 (m, 1H), 1.56-1.59 (m, 5H), 3.04 (t, J = 8.0 Hz, 2H), 3.58 (s, 2H), 5.39 (bs, 1H), 7.25-7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 170.9, 135.1, 129.5, 129.0, 127.3, 45.8, 44.0, 37.8, 30.7, 26.4, 25.8; HRMS(ESI) calcd for $C_{15}H_{21}NO$: 231.1623. Found: 231.1629 [MH^+].



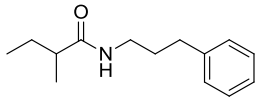
***N*-(Adamantan-1-ylmethyl)-2-phenylacetamide (3ia)**: white solid (126.2 mg, 0.445 mmol, 89%); ^{1}H NMR($CDCl_3$) δ = 1.33 (bs, 6H), 1.52-1.56 (bs, 3H), 1.65-1.69 (bs, 3H), 1.91 (bs, 3H), 2.89 (d, J = 6.3 Hz, 2H), 3.60 (s, 2H), 5.33 (bs, 1H), 7.26-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 171.0, 135.2, 129.5, 129.0, 127.4, 50.9, 44.0, 40.0, 36.8, 33.7, 28.0; HRMS(ESI) calcd for $C_{19}H_{25}NO$: 283.1936. Found: 283.1938 [MH^+].



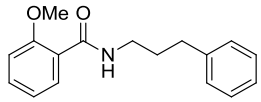
***N*-(4-Chlorobenzyl)-2-phenylacetamide (3ka):** white solid (68.3 mg, 0.263 mmol, 53%); ^{1}H NMR ($CDCl_3$) δ = 3.63 (s, 2H), 4.38 (d, J = 6.0 Hz, 2H), 5.74 (bs, 1H), 7.11 (d, J = 8.4 Hz, 2H), 7.27 (m, 4H), 7.31 (m, 1H), 7.37 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 170.9, 136.7, 134.6, 133.2, 129.4, 129.1, 128.8, 128.7, 127.5, 43.8, 42.9; HRMS(ESI) calcd for $C_{15}H_{14}ClNO$: 259.0764. Found: 259.0764 [MH^+].



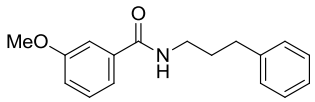
***N*-(3-Phenylpropyl)-pentanamide (3ac):** yellow liquid (87.4 mg, 0.399 mmol, 80%); ^{1}H NMR ($CDCl_3$) δ = 0.98 (t, J = 7.3 Hz, 3H), 1.40 (m, 2H), 1.65 (m, 2H), 1.91 (m, 2H), 2.20 (t, J = 7.73 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H), 3.36 (q, J = 6.8 Hz, 2H), 5.60 (bs, 1H), 7.24 (m, 3H), 7.33 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 173.3, 141.5, 128.4, 128.3, 126.0, 39.2, 36.5, 33.3, 31.2, 27.9, 22.4, 13.8; HRMS(ESI) calcd for $C_{14}H_{21}NO$: 219.1623. Found: 219.1620 [MH^+].



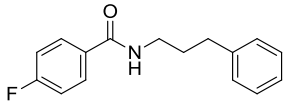
2-Methyl-*N*-(3-phenylpropyl)-butanamide (3ad): colorless oil (68.0 mg, 0.310 mmol, 62%); ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 7.2 Hz, 3H), 1.10 (d, J = 7.2 Hz, 3H), 1.38–1.45 (m, 1H), 1.57–1.68 (m, 1H), 1.80–1.87 (m, 2H), 1.98–2.08 (m, 1H), 2.65 (t, J = 7.6 Hz, 2H), 3.22–3.36 (m, 2H), 5.53 (bs, 1H), 7.17–7.20 (m, 3H), 7.27–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 176.4, 141.6, 128.5, 128.4, 126.0, 43.3, 39.1, 33.4, 31.4, 27.4, 17.5, 12.0; HRMS(ESI) calcd for $C_{14}H_{21}NO$: 219.1623. Found: 219.1711 [MH^+].



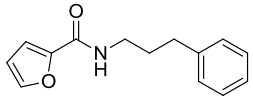
2-Methoxy-*N*-(3-phenylpropyl)-benzamide (3ah): colorless oil (107.3 mg, 0.399 mmol, 80%); ^{1}H NMR ($CDCl_3$) δ = 1.91–2.00 (m, 2H), 2.71 (t, J = 7.6 Hz, 2H), 3.49 (q, J = 7.2 Hz, 2H), 3.93 (s, 3H), 6.95 (d, J = 8.0 Hz, 1H), 7.04–7.08 (m, 1H), 7.16–7.21 (m, 3H), 7.25–7.30 (m, 2H), 7.40–7.44 (m, 1H), 7.89 (bs, 1H), 8.21 (q, J = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 165.3, 157.4, 141.6, 132.7, 132.2, 128.5, 126.0, 121.7, 121.3, 111.3, 56.0, 39.3, 33.4, 31.3; HRMS(ESI) calcd for $C_{17}H_{19}NO_2$: 269.1416. Found: 269.1418 [MH^+].



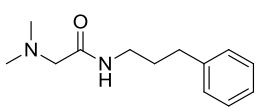
3-Methoxy-*N*-(3-phenylpropyl)-benzamide (3ai): colorless oil (110.1 mg, 0.409 mmol, 82%); ^{1}H NMR ($CDCl_3$) δ = 1.88 (m, 2H), 2.64 (t, J = 7.6 Hz, 2H), 3.40 (q, J = 6.9 Hz, 2H), 3.75 (s, 3H), 6.11 (bs, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.07–7.14 (m, 4H), 7.18–7.24 (m, 4H); ^{13}C NMR ($CDCl_3$) δ = 167.3, 159.8, 141.4, 136.2, 129.4, 128.5, 128.4, 126.0, 118.5, 117.5, 112.3, 55.4, 39.8, 33.5, 31.1; HRMS(ESI) calcd for $C_{17}H_{19}NO_2$: 269.1416. Found: 269.1418 [MH^+].



4-Fluoro-*N*-(3-phenylpropyl)-benzamide (3ak): colorless oil (67.6 mg, 0.263 mmol, 53%); ^{1}H NMR ($CDCl_3$) δ = 1.94–2.01 (m, 2H), 2.73 (t, J = 7.2 Hz, 2H), 3.49 (q, J = 6.8 Hz, 2H), 6.01 (bs, 1H), 7.03–7.09 (m, 2H), 7.19–7.32 (m, 5H), 7.62–7.64 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 166.3, 165.9, 141.5, 129.1, 128.6, 128.4, 126.1, 115.6, 115.4, 40.0, 33.6, 31.1; HRMS(ESI) calcd for $C_{16}H_{16}FNO$: 257.1216. Found: 257.1226 [MH^+].

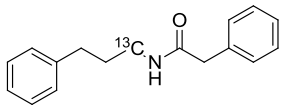


***N*-(3-Phenylpropyl)-2-furancarboxamide (3al):** yellow oil (87.5 mg, 0.382 mmol, 76%); ^{1}H NMR ($CDCl_3$) δ = 1.90–1.98 (m, 2H), 2.71 (t, J = 7.6 Hz, 2H), 3.46 (q, J = 7.2 Hz, 2H), 6.36 (bs, 1H), 6.48 (d, J = 1.6 Hz, 1H), 7.08 (q, J = 0.4 Hz, 1H), 7.17–7.21 (m, 3H), 7.26–7.30 (m, 2H), 7.41 (d, J = 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 158.4, 148.1, 143.7, 141.3, 128.5, 128.4, 126.0, 114.0, 112.0, 38.8, 33.3, 31.3; HRMS(ESI) calcd for $C_{14}H_{15}NO_2$: 229.1103. Found: 229.1105 [MH^+].

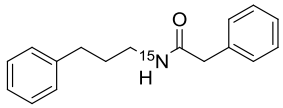


2-(Dimethylamino)-*N*-(3-phenylpropyl)-acetamide (3am): yellow oil (80.7 mg, 0.366

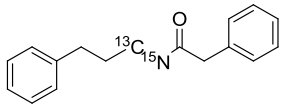
mmol, 73%); ^{1}H NMR ($CDCl_3$) δ = 1.82–1.89 (m, 2H), 2.27 (s, 6H), 2.66 (t, J = 7.6 Hz, 2H), 2.92 (s, 2H), 3.31 (q, J = 6.8 Hz, 2H), 7.17–7.20 (m, 4H), 7.27–7.30 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 170.6, 141.5, 128.5, 128.4, 126.0, 63.2, 46.0, 38.5, 33.3, 31.3; HRMS(ESI) calcd for $C_{13}H_{20}N_2O$: 220.1576. Found: 217.1577 [MH^+].



***N*-(3-Phenylpropyl)-benzeneacetamide (^{13}C labeled) (3la):** white solid (111.4 mg, 0.438 mmol, 88%); ^{1}H NMR ($CDCl_3$) δ = 1.77 (m, 2H), 2.55 (m, 2H), 3.00 (dd, J = 7.0, 13.2 Hz, 1H), 3.46 (dd, J = 7.0, 13.2 Hz, 1H), 3.55 (s, 2H), 5.32 (bs, 1H), 7.08-7.11 (m, 2H), 7.17-7.28 (m, 5H), 7.30-7.39 (m, 3H); ^{13}C NMR (32 scans, $CDCl_3$) δ = 39.2; HRMS(ESI) calcd for $C_{16}{}^{13}CH_{17}NO$: 254.1500. Found: 254.1503 [MH^+]



***N*-(3-Phenylpropyl)-benzeneacetamide (^{15}N labeled) (3ma):** white solid (120.1 mg, 0.472 mmol, 94%); ^{1}H NMR ($CDCl_3$) δ = 1.76 (m, 2H), 2.55 (t, J = 7.4 Hz, 2H), 3.23 (q, J = 6.5 Hz, 2H), 3.55 (s, 2H), 5.17 (t, J = 5.9 Hz, 0.5 H), 5.47 (t, J = 5.9 Hz, 0.5 H), 7.08-7.11 (m, 2H), 7.17-7.28 (m, 5H), 7.30-7.39 (m, 3H); ^{15}N NMR ($CDCl_3$) δ = -262.4; HRMS(ESI) calcd for $C_{17}H_{17}{}^{15}NO$: 254.1437. Found: 254.1440 [MH^+]



***N*-(3-Phenylpropyl)-benzeneacetamide (^{13}C, ^{15}N labeled) (3na):** white solid (122.9 mg, 0.481 mmol, 96%); ^{1}H NMR ($CDCl_3$) δ = 1.76 (m, 2H), 2.56 (m, 2H), 3.00 (dd, J = 6.19, 13.17 Hz, 1H), 3.46 (dd, J = 6.2, 13.2 Hz, 1H), 3.55 (s, 2H), 5.17 (m, 0.5 H), 5.47 (m, 0.5 H), 7.08-7.11 (m, 2H), 7.17-7.28 (m, 5H), 7.30-7.39 (m, 3H); ^{13}C NMR (100 scans, $CDCl_3$) δ = 39.2, 39.1; ^{15}N NMR ($CDCl_3$) δ = -262.3, -262.5; HRMS(ESI) calcd for $C_{16}{}^{13}CH_{17}{}^{15}NO$: 255.1471. Found: 255.1472 [MH^+]

3. References

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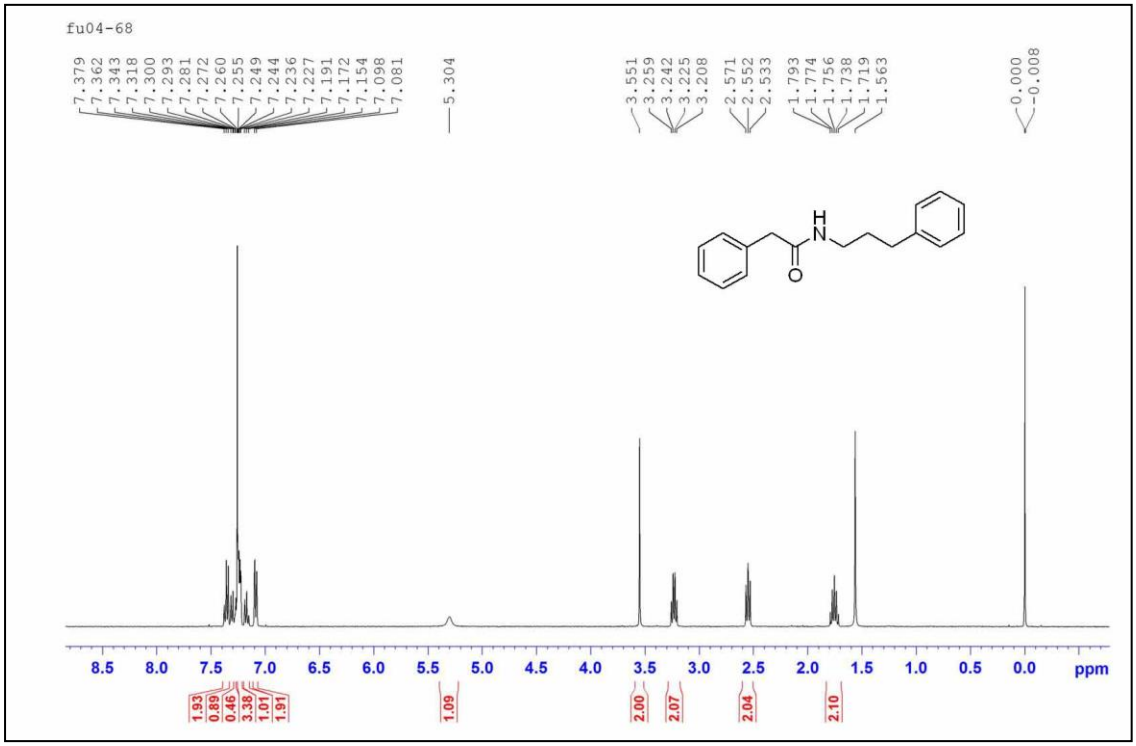
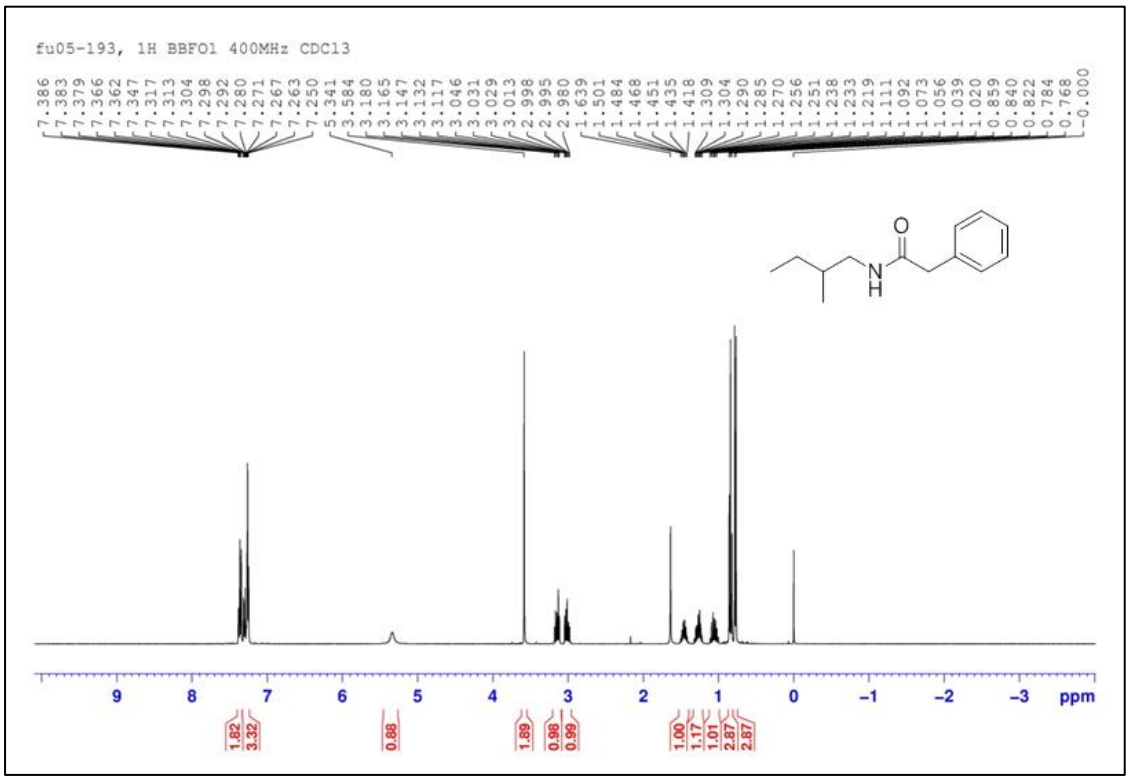
4. ^{1}H and ^{13}C NMR spectra

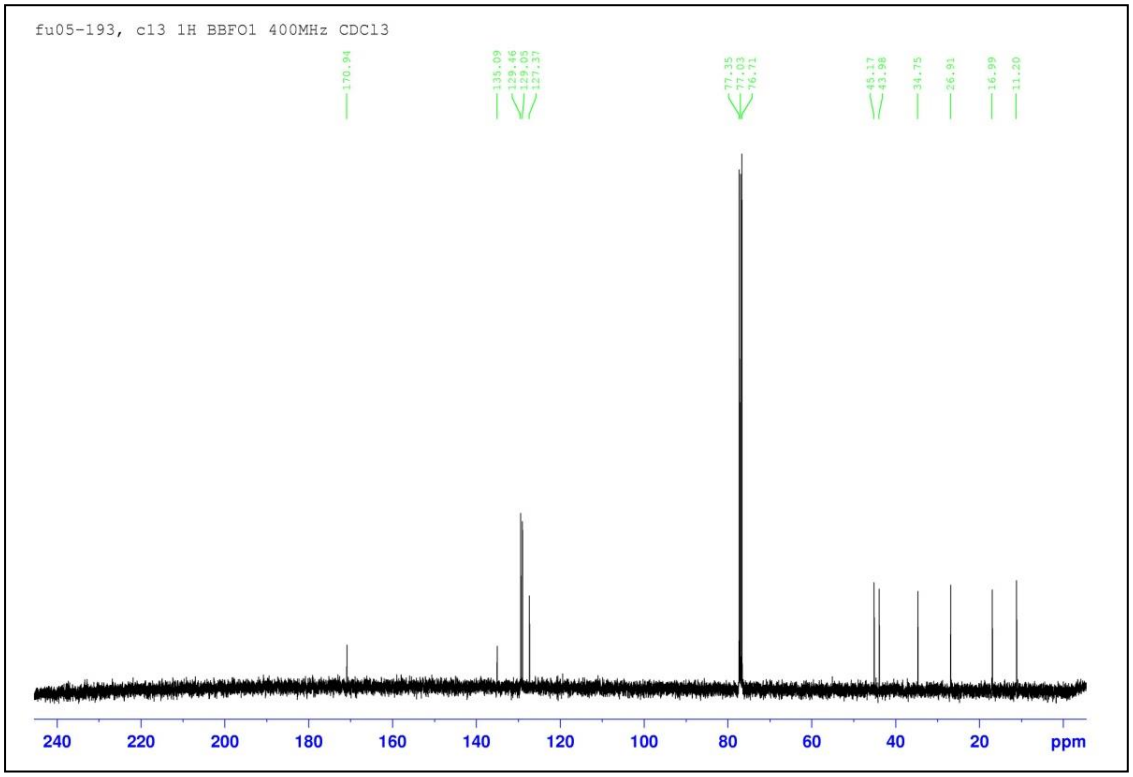
^{1}H NMR (**3aa**) ($CDCl_3$)



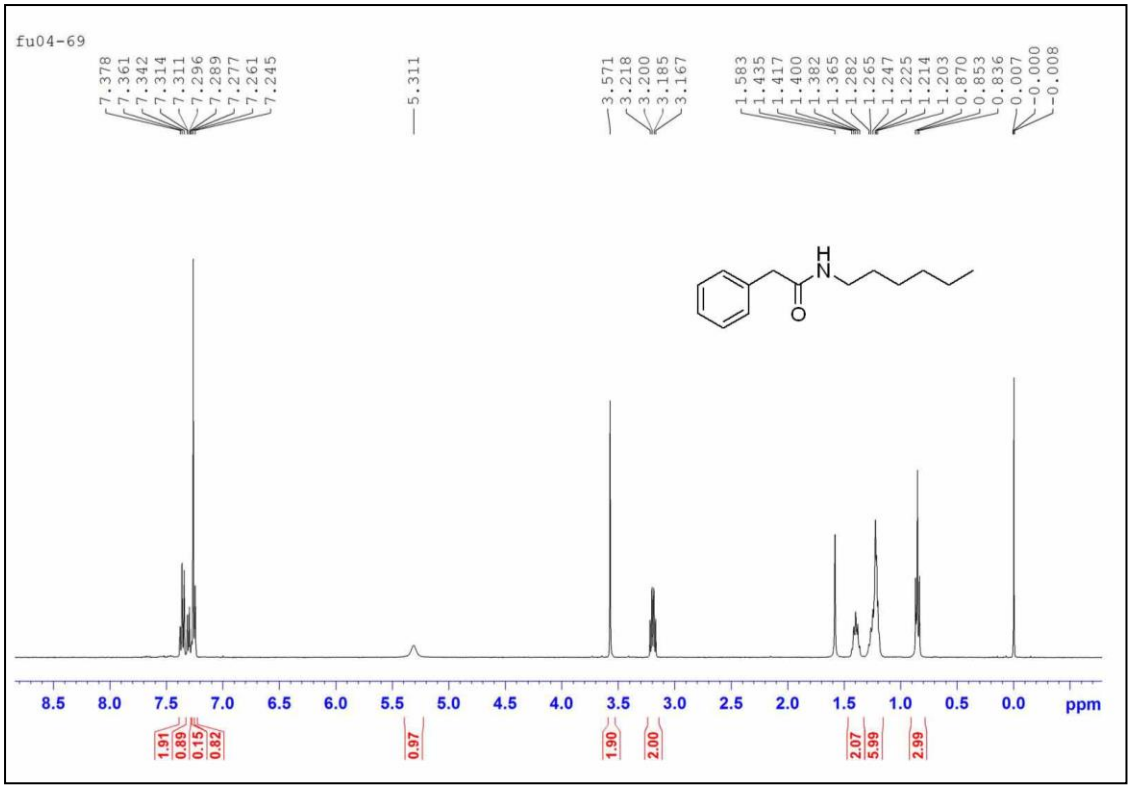
^{1}H NMR (**3ba**) ($CDCl_3$)



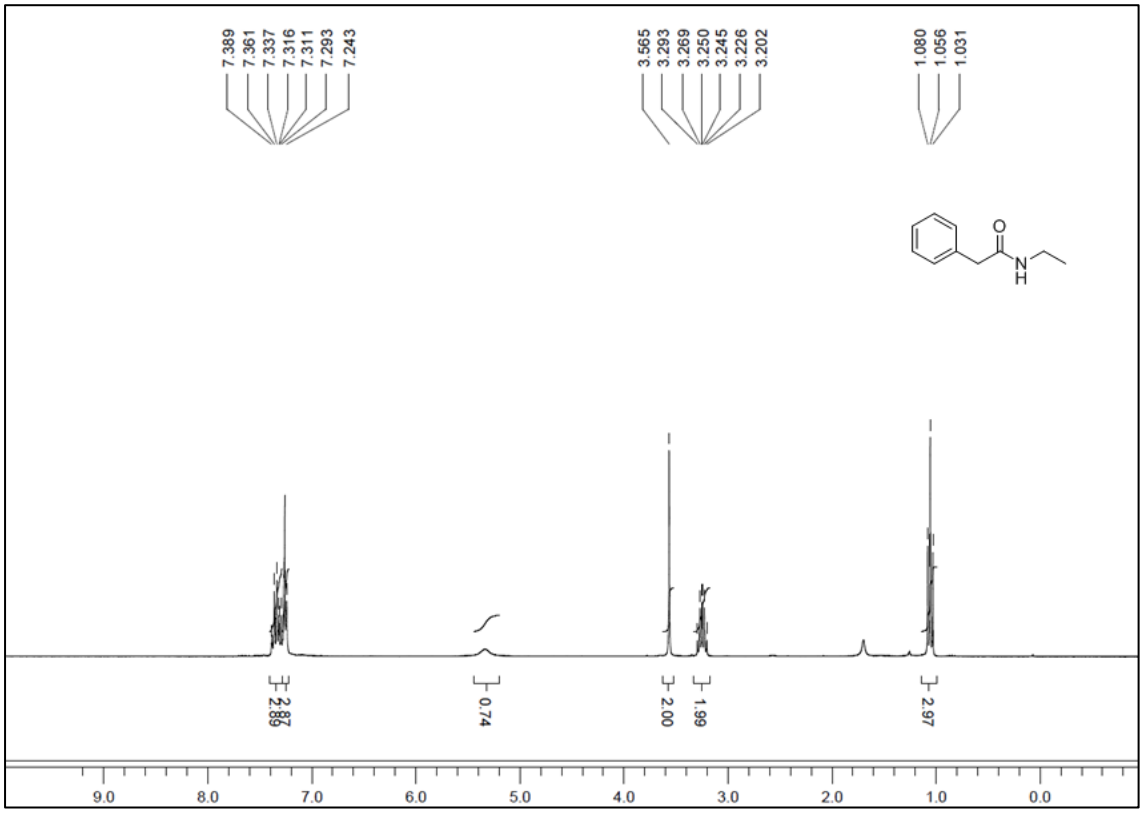
^{13}C NMR (**3ba**) ($CDCl_3$)



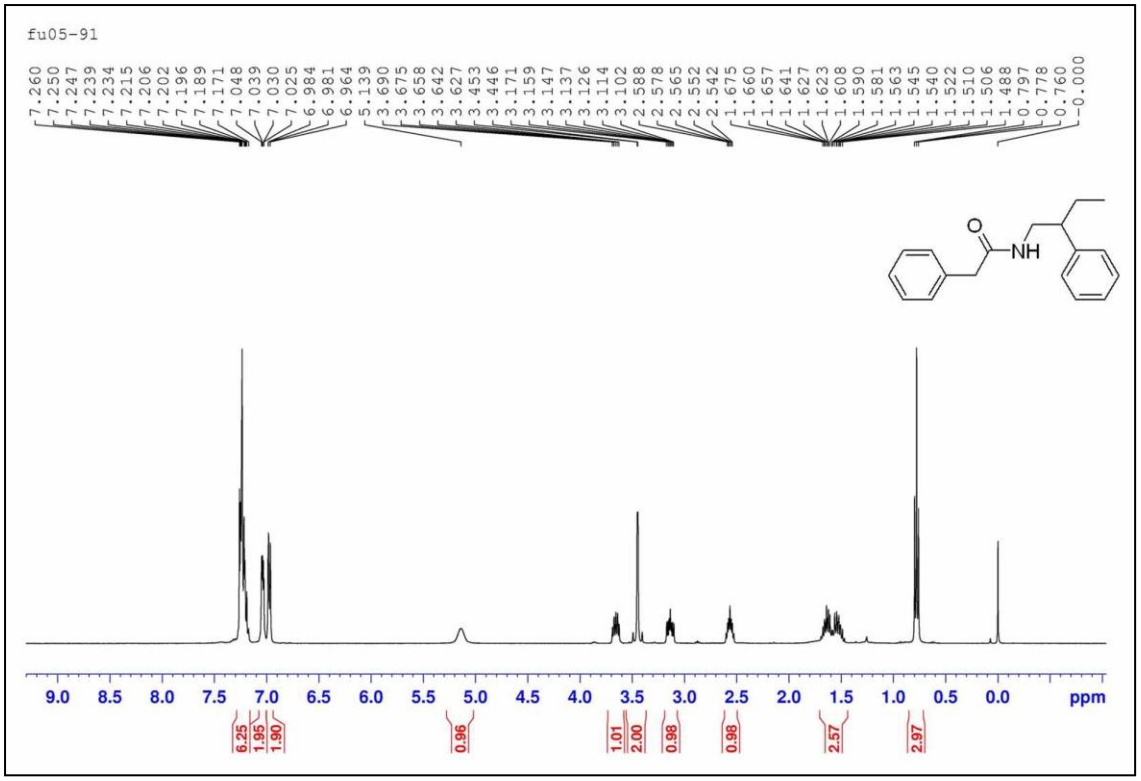
^{1}H NMR (**3ca**) ($CDCl_3$)



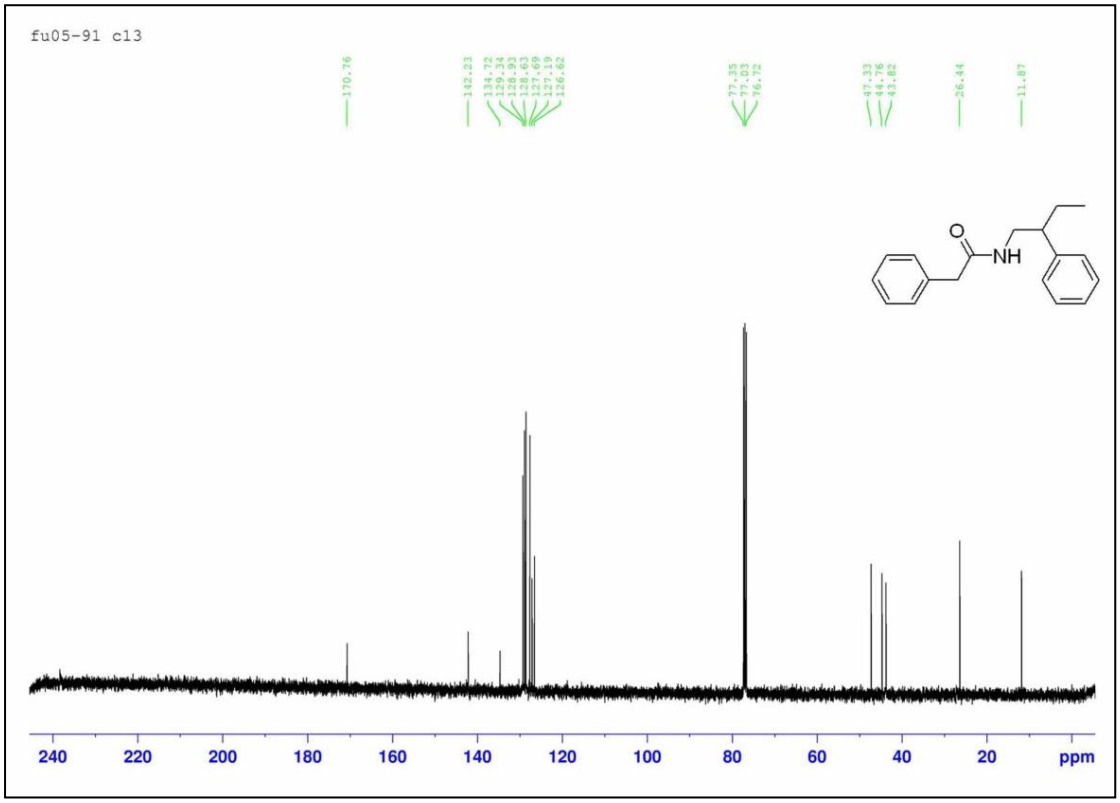
^{1}H NMR (**3da**) ($CDCl_3$)



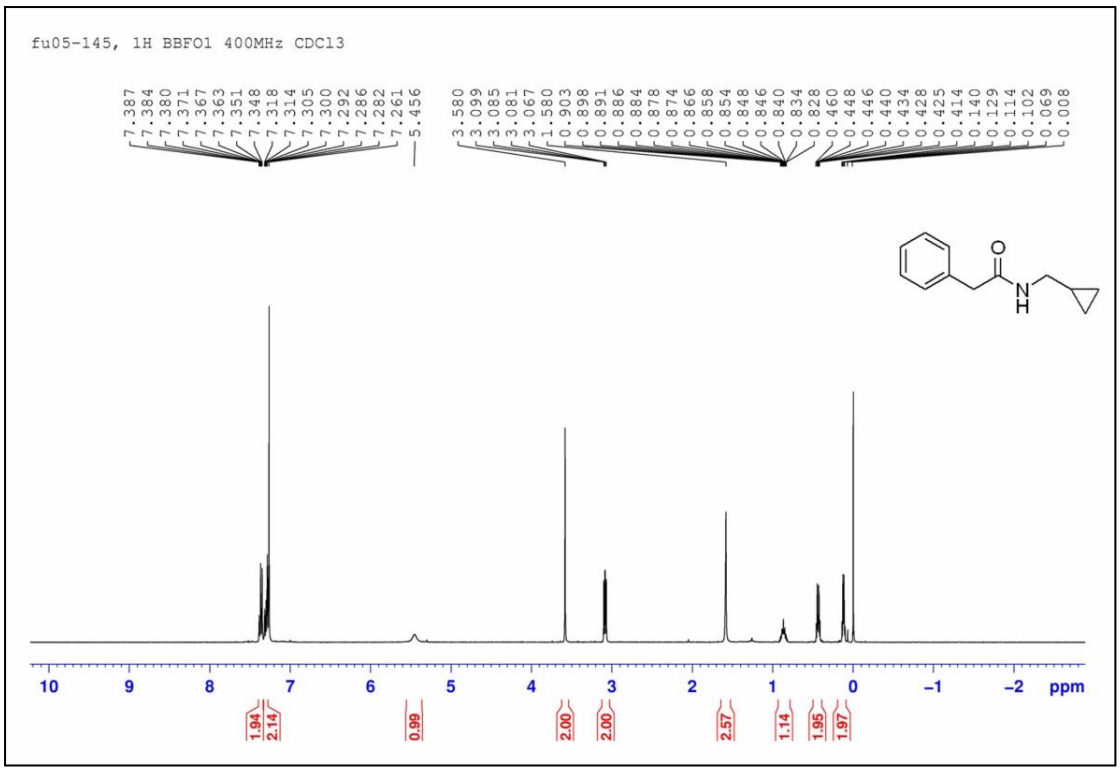
^{1}H NMR (**3ea**) ($CDCl_3$)



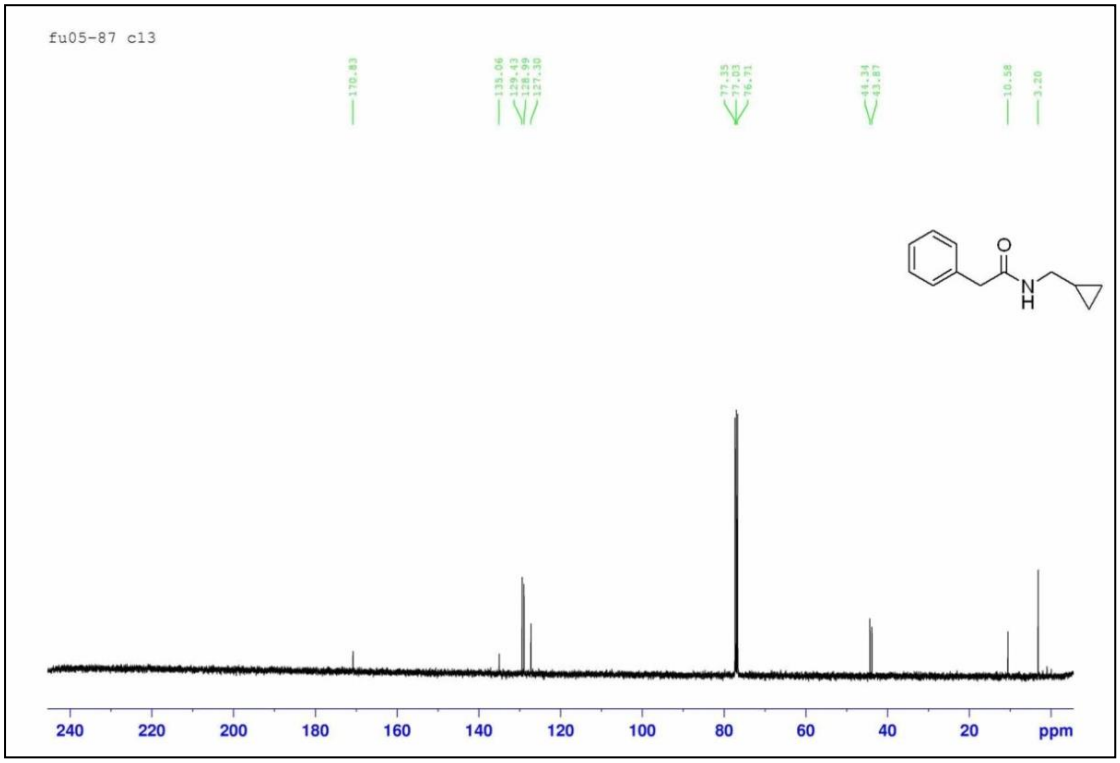
^{13}C NMR (**3ea**) ($CDCl_3$)



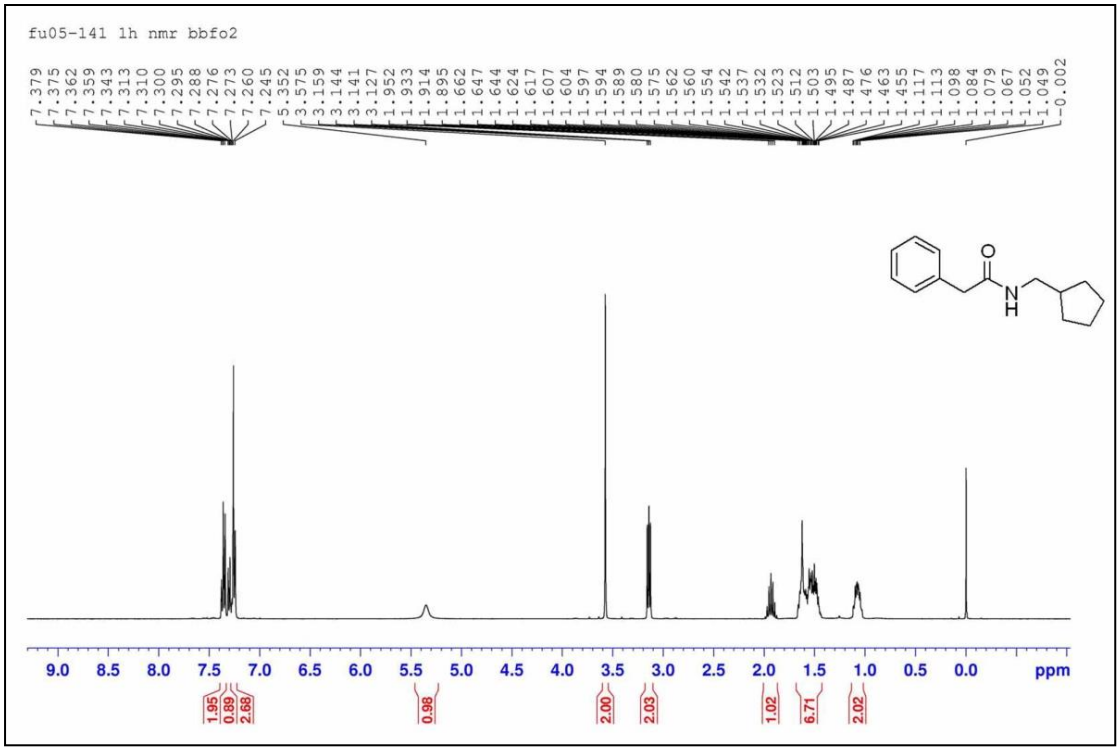
^{1}H NMR (**3fa**) ($CDCl_3$)



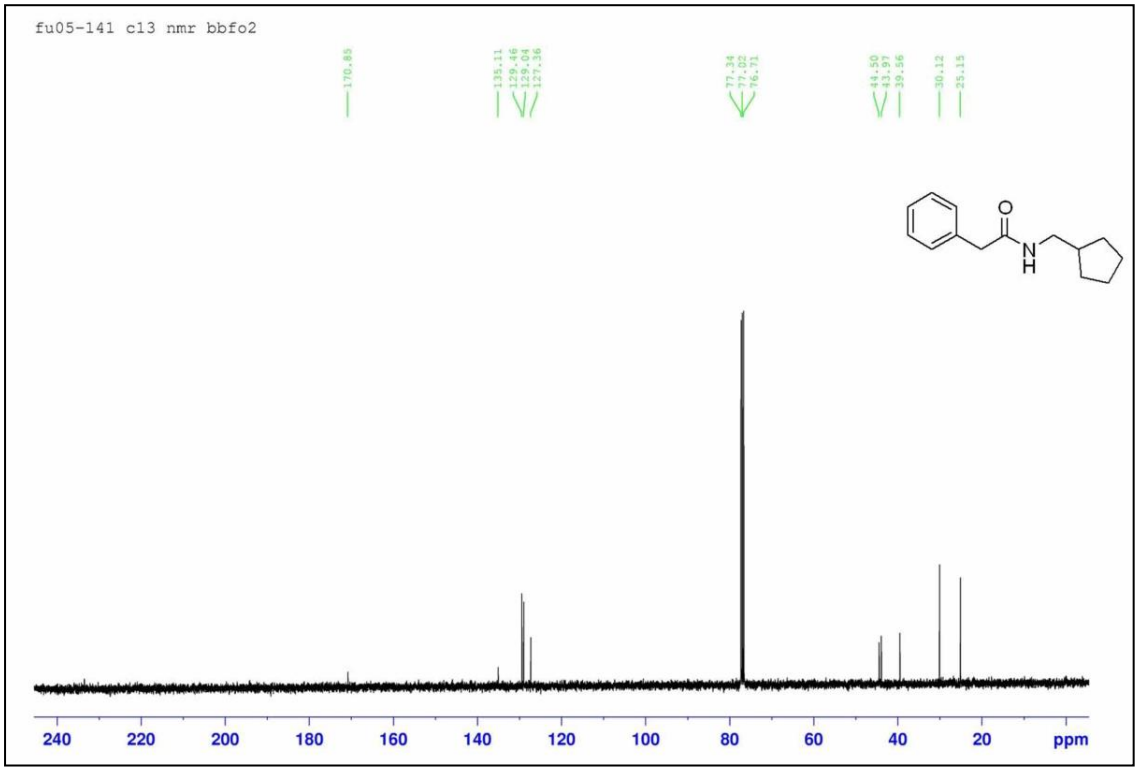
^{13}C NMR (**3fa**) ($CDCl_3$)



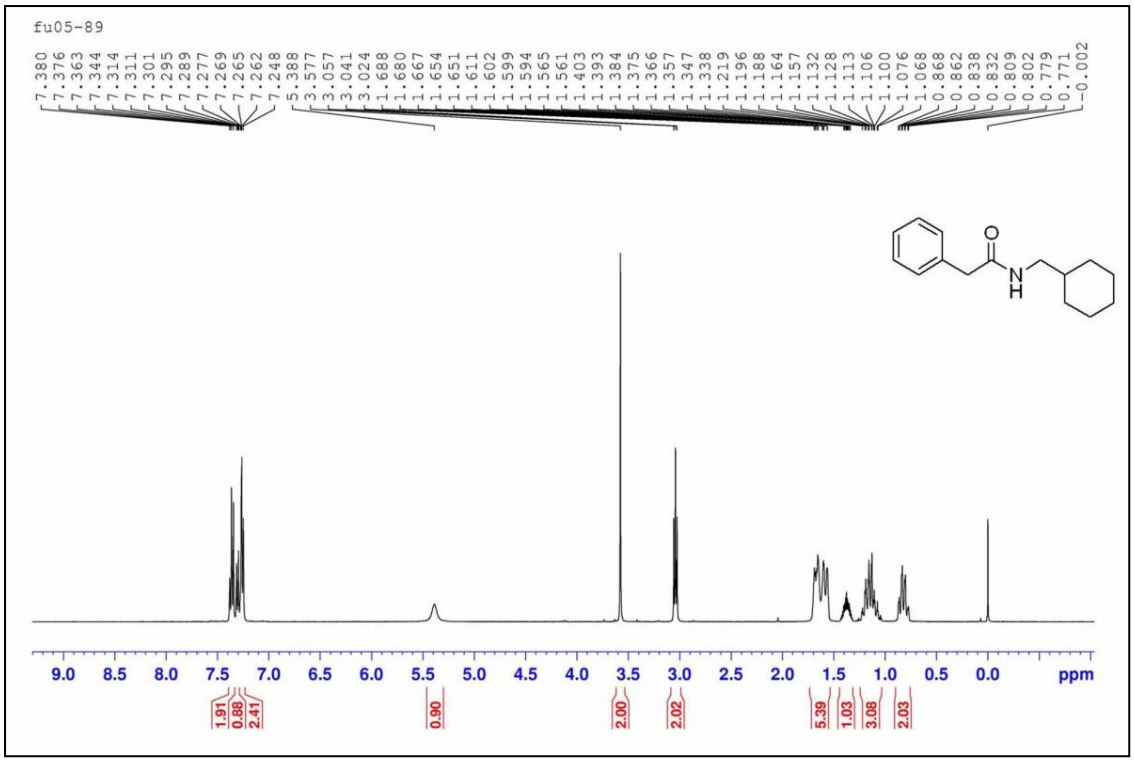
^{1}H NMR (**3ga**) ($CDCl_3$)



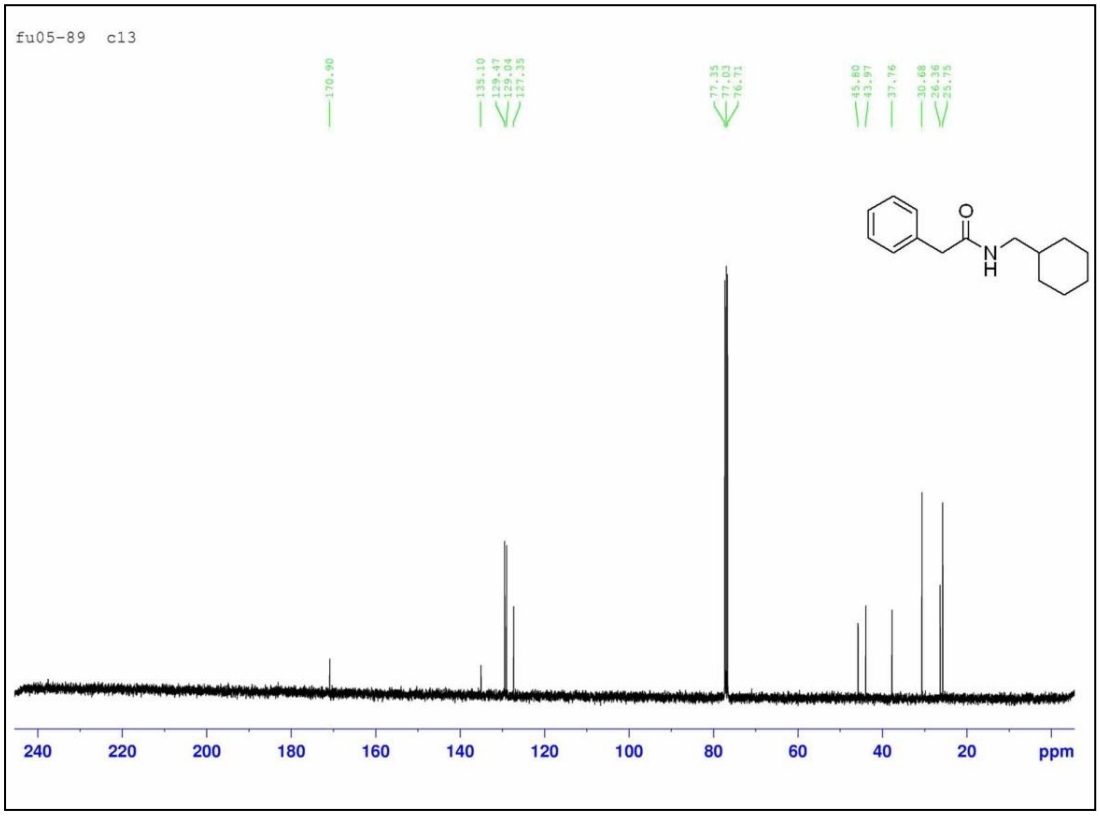
^{13}C NMR (**3ga**) ($CDCl_3$)



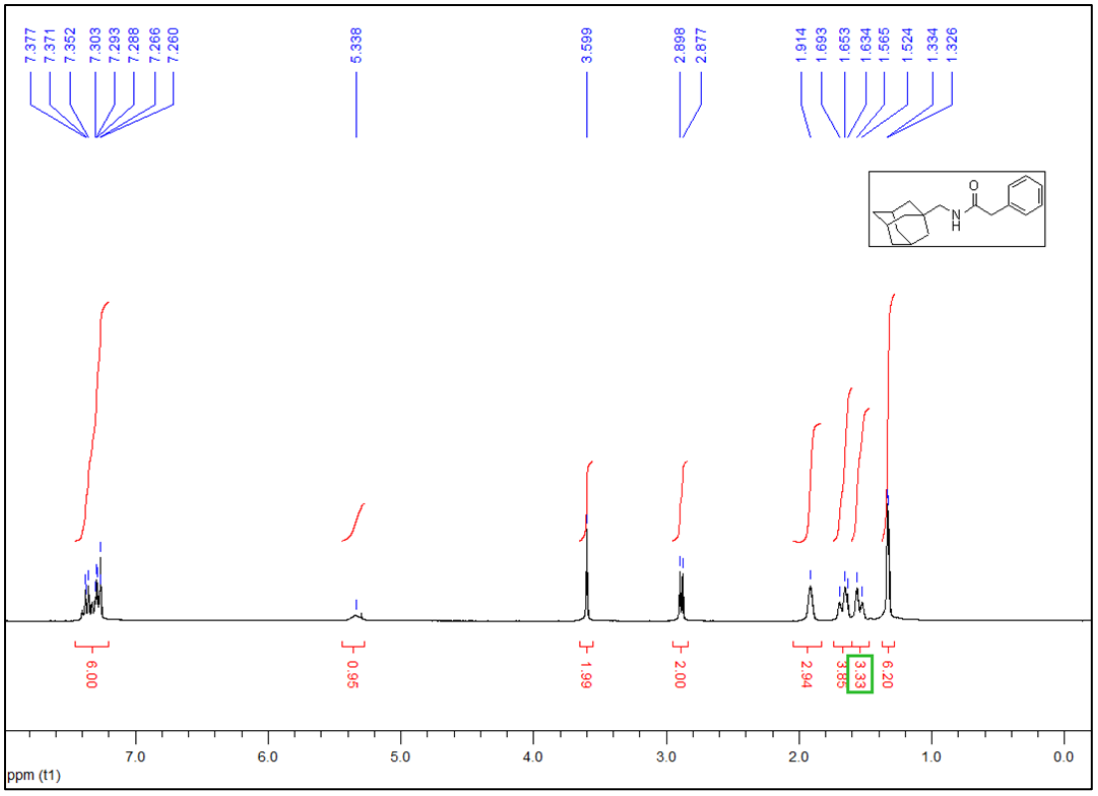
^{1}H NMR (**3ha**) ($CDCl_3$)



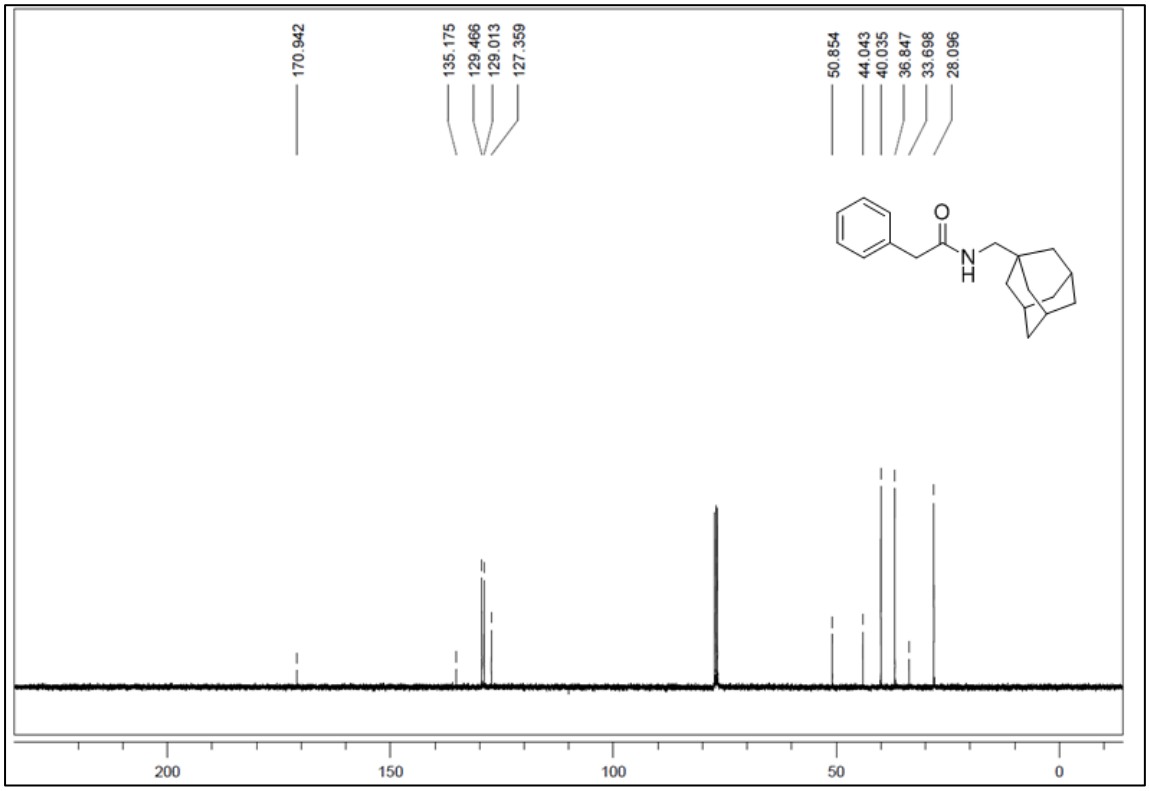
^{13}C NMR (**3ha**) ($CDCl_3$)



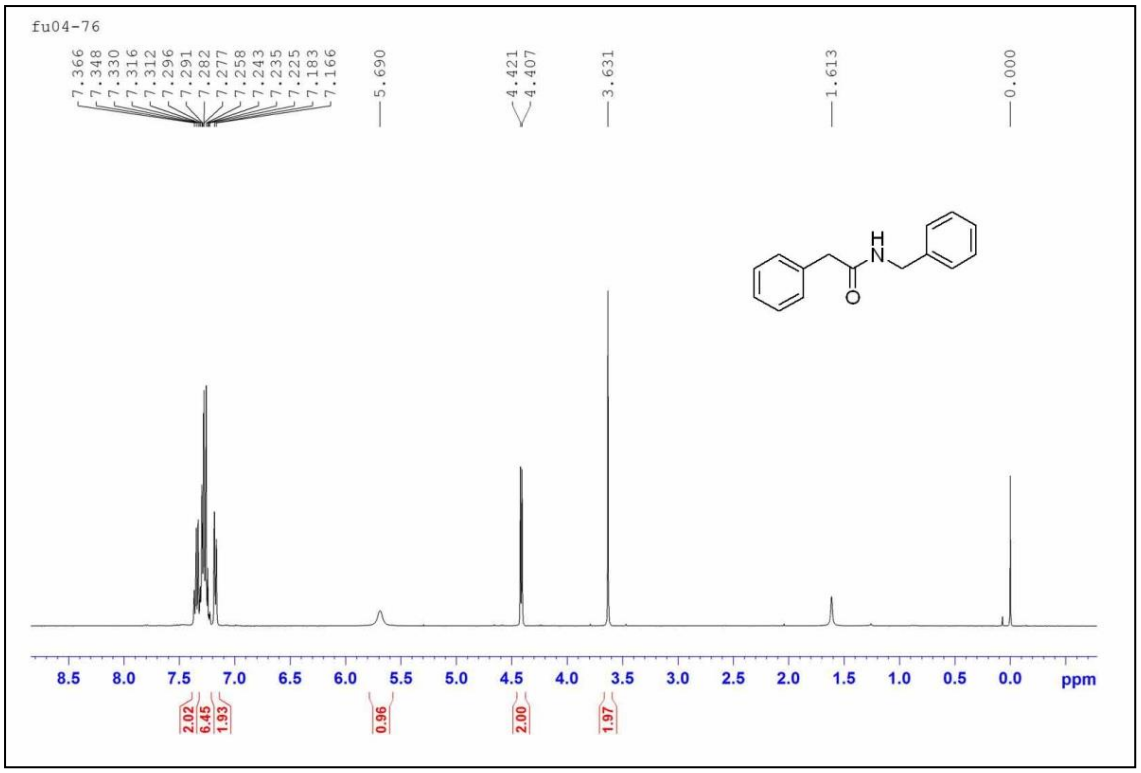
^{1}H NMR (**3ia**) ($CDCl_3$)



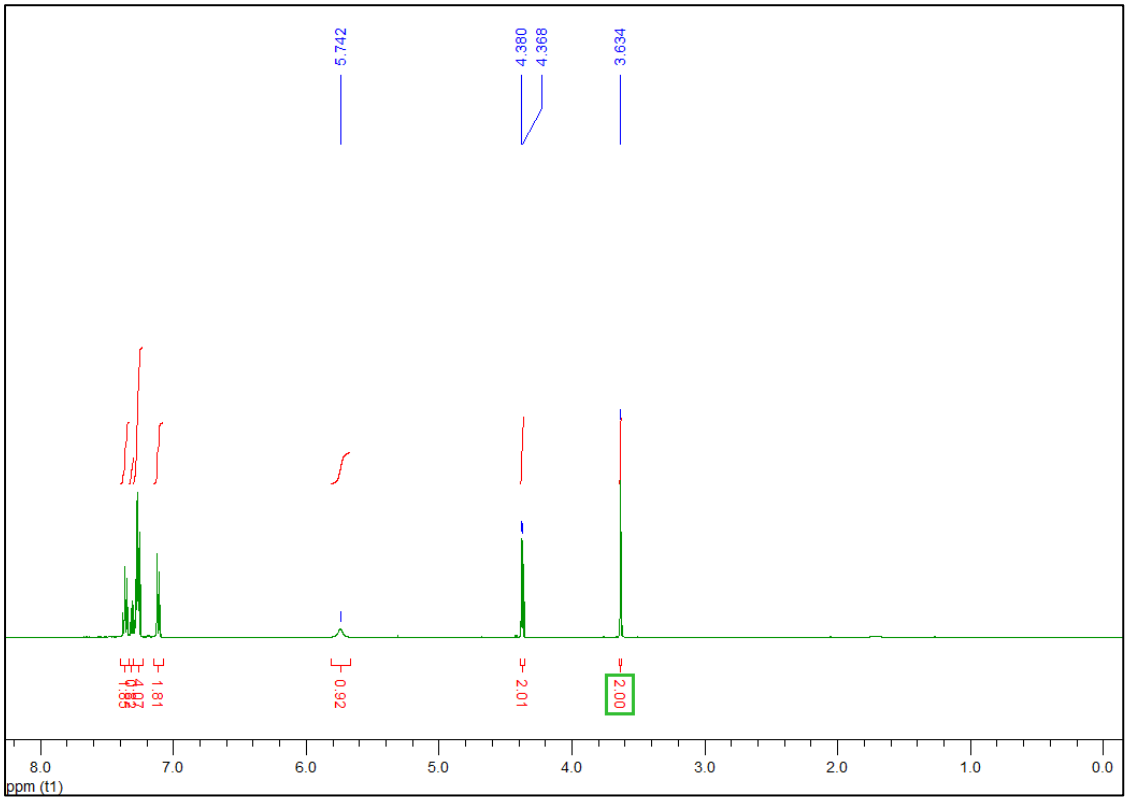
^{13}C NMR (**3ia**) ($CDCl_3$)



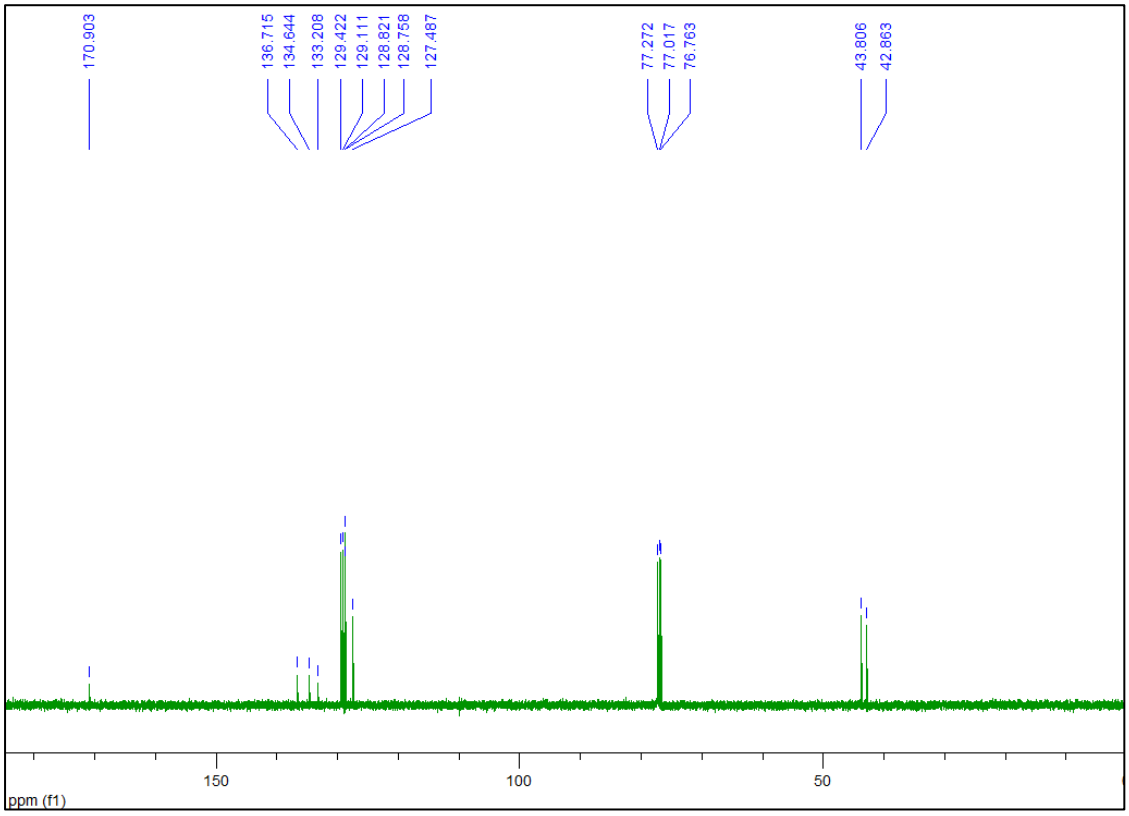
^{1}H NMR (**3ja**) ($CDCl_3$)



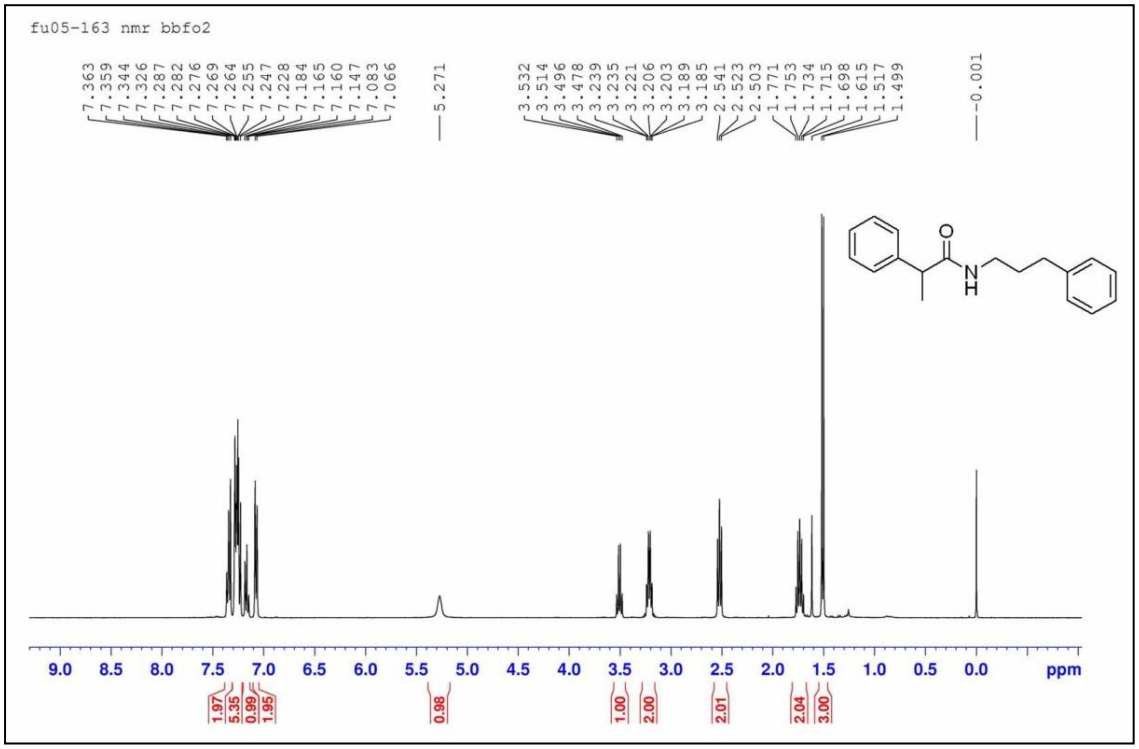
^{1}H NMR (**3ka**) ($CDCl_3$)



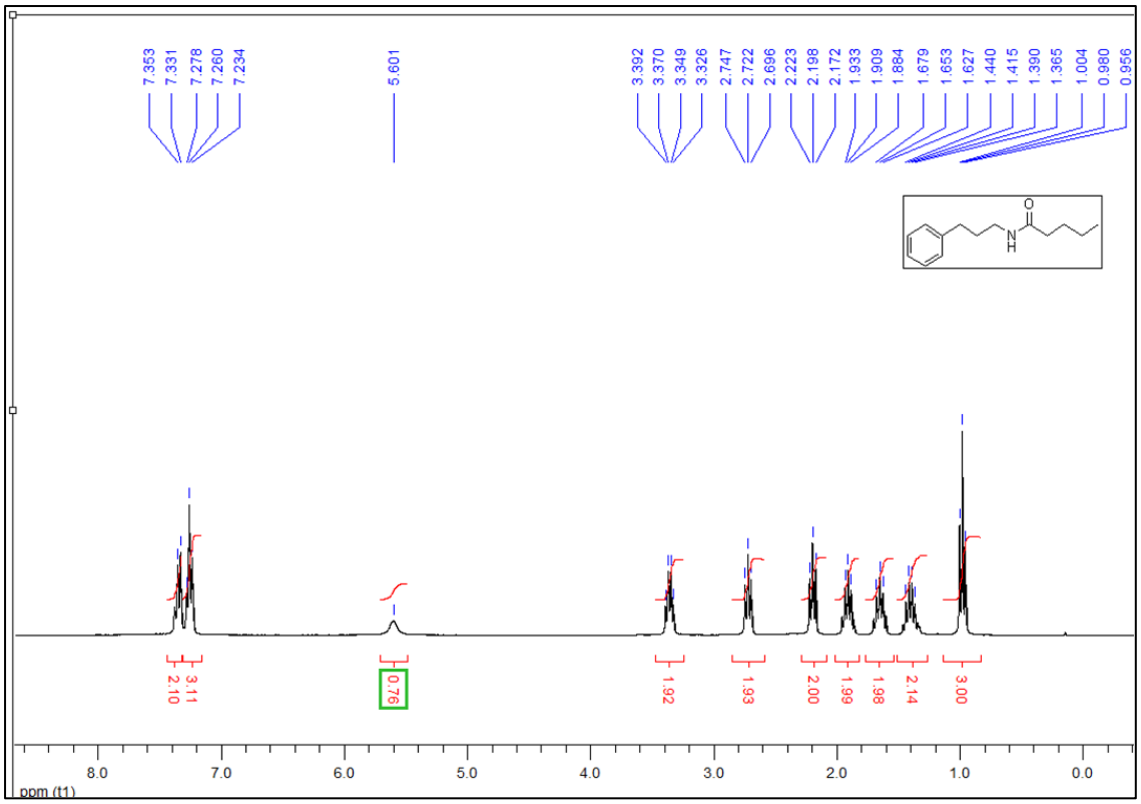
^{13}C NMR (**3ka**) ($CDCl_3$)



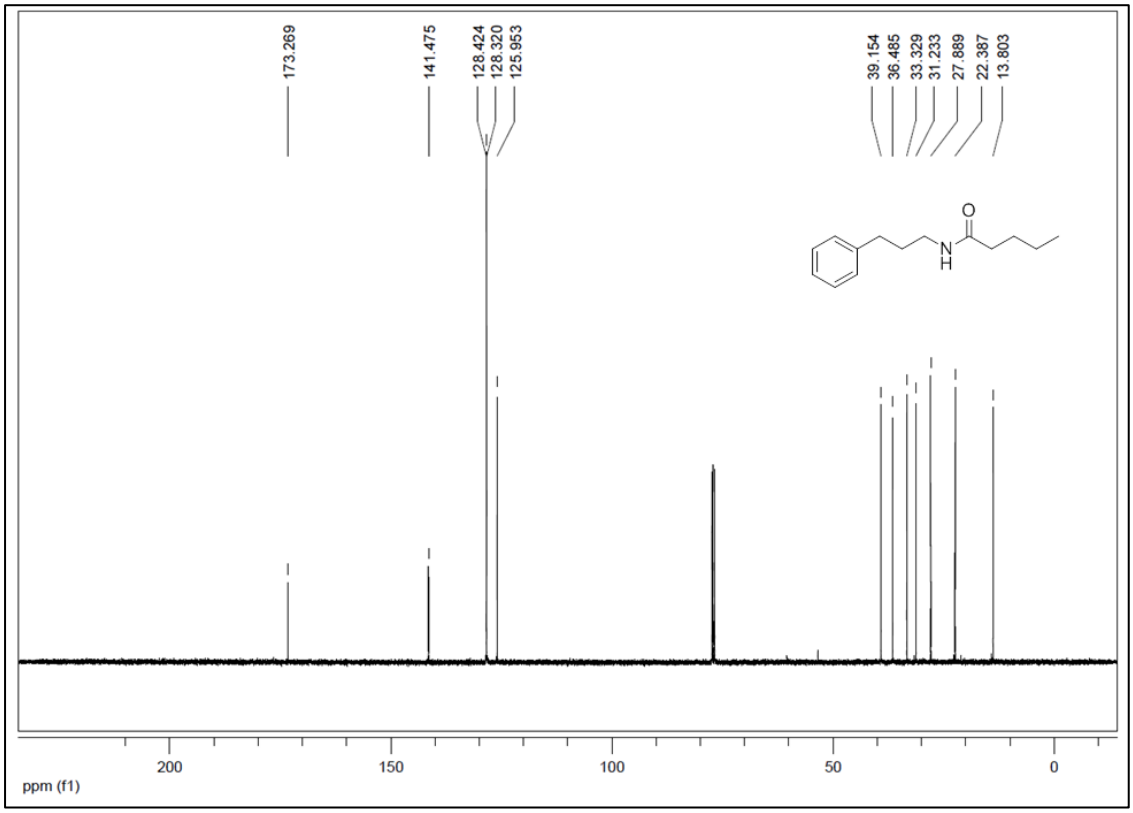
^{1}H NMR (**3ab**) ($CDCl_3$)



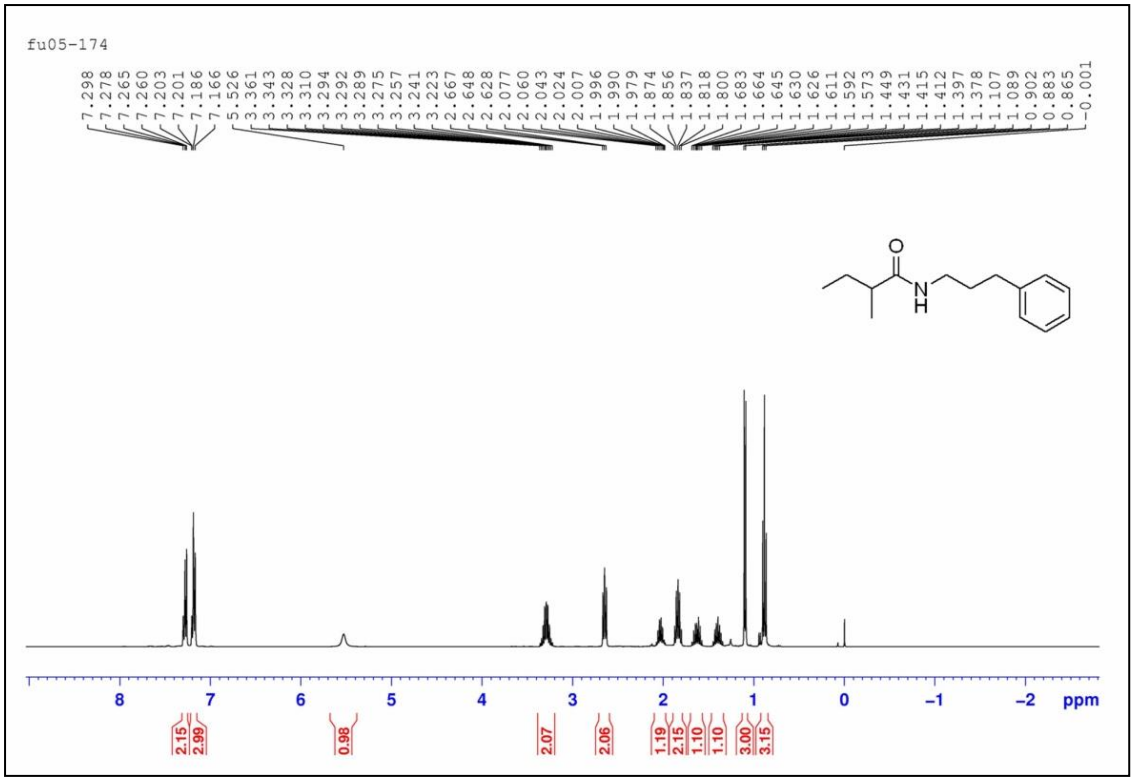
^{1}H NMR (**3ac**) ($CDCl_3$)



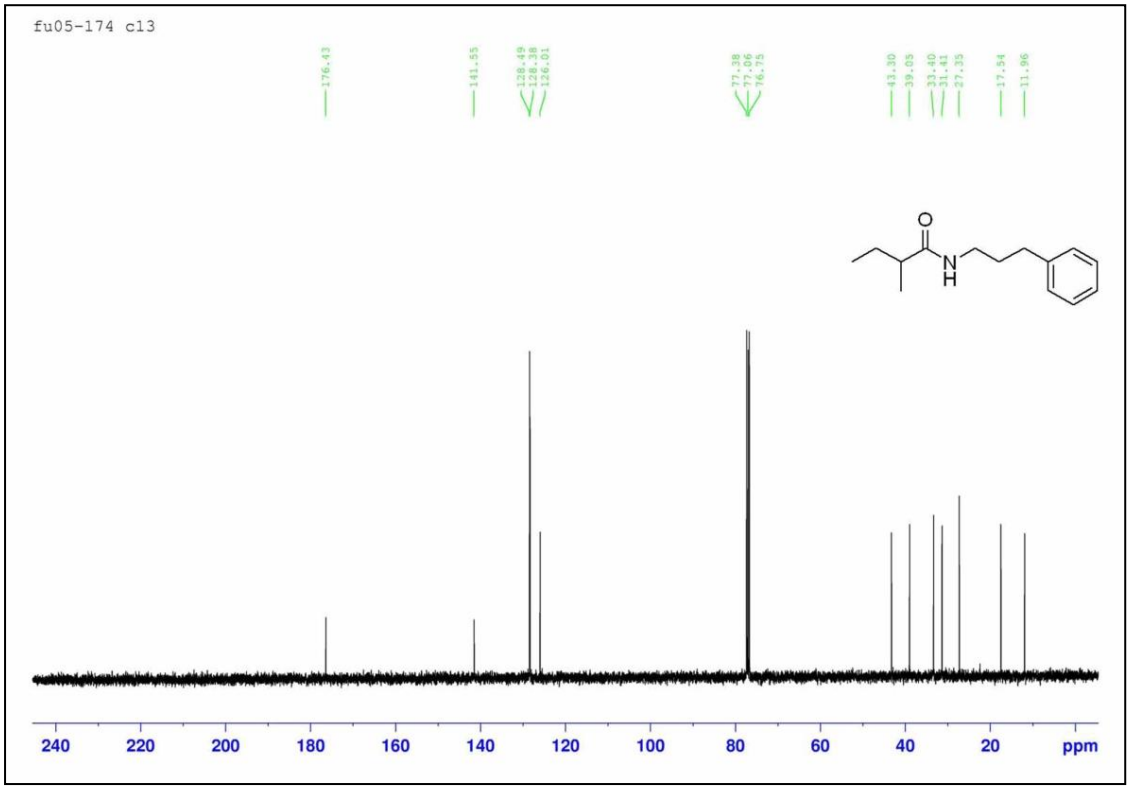
^{13}C NMR (**3ac**) ($CDCl_3$)



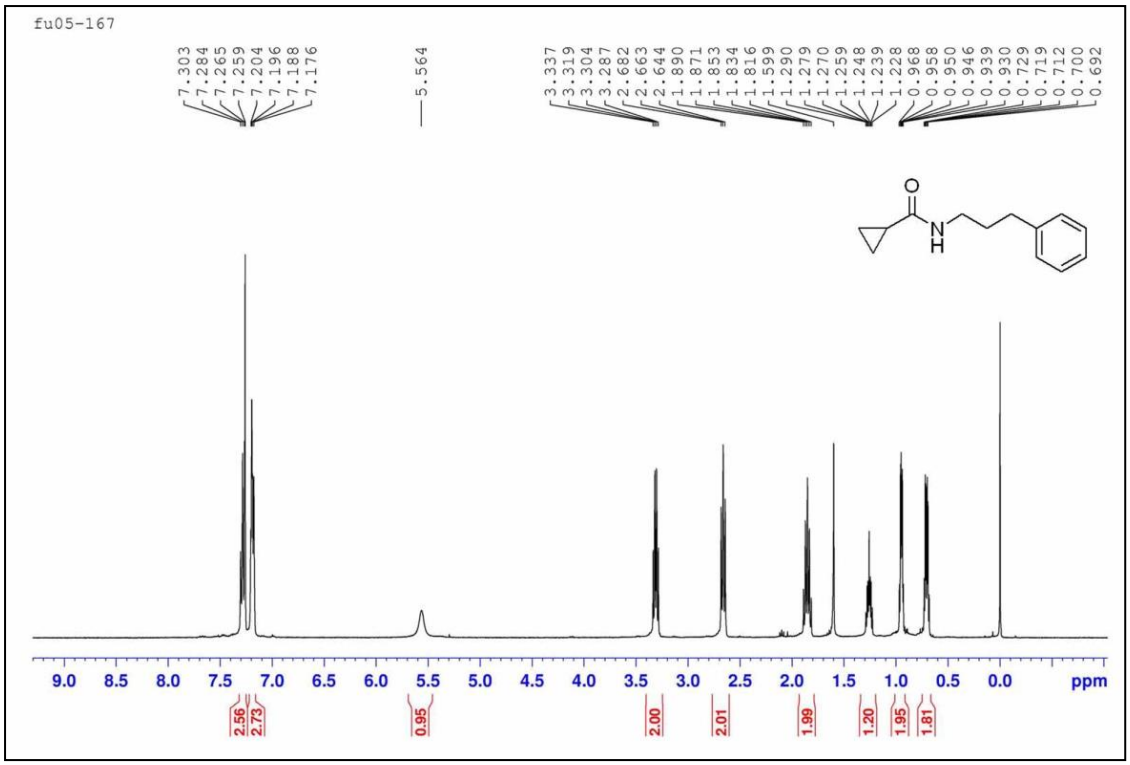
^{1}H NMR (**3ad**) ($CDCl_3$)



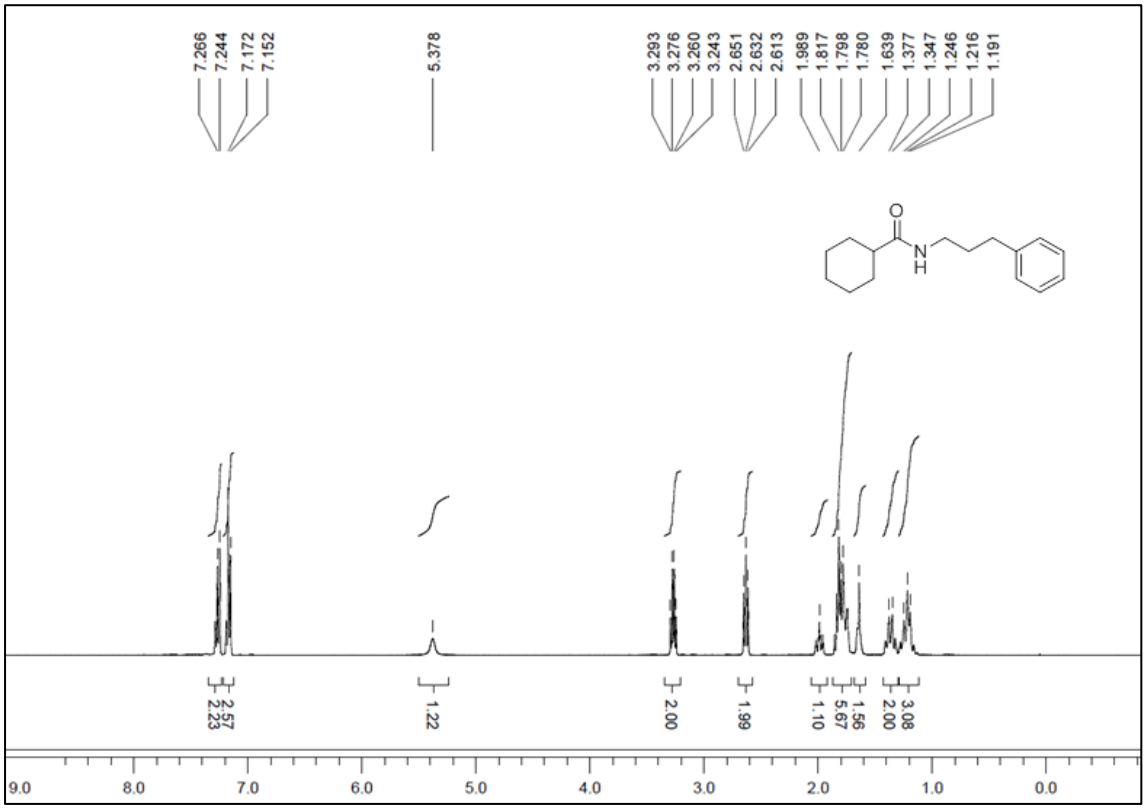
^{13}C NMR (**3ad**) ($CDCl_3$)



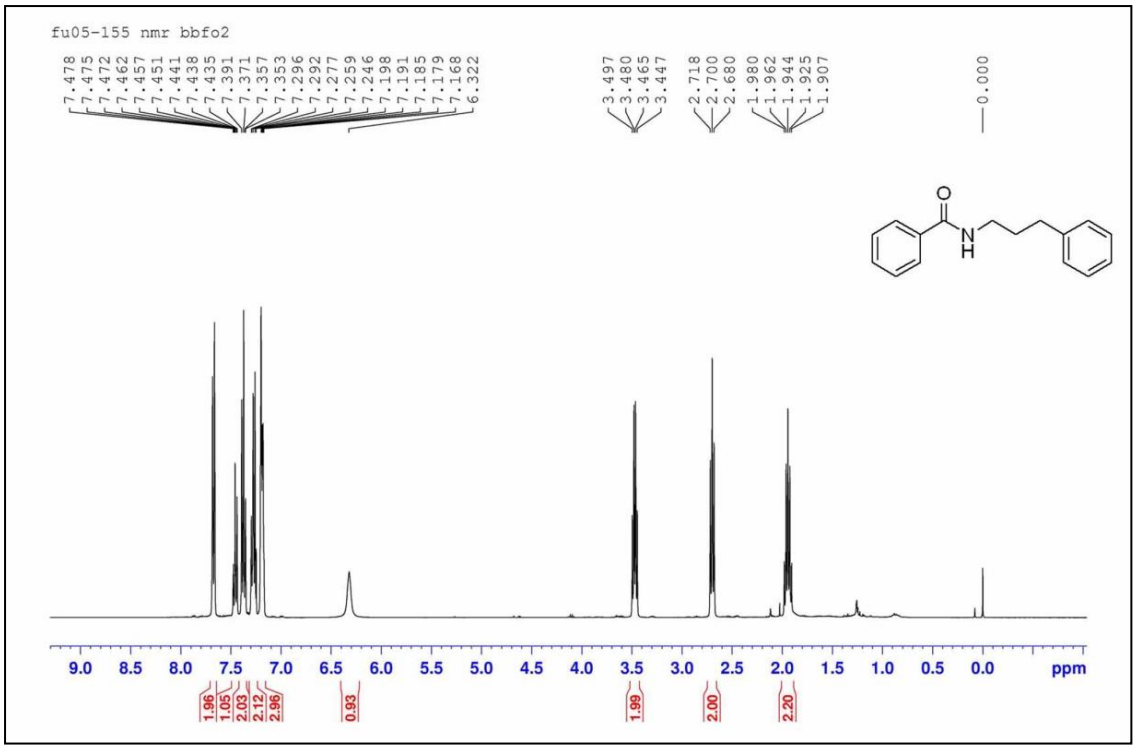
^{1}H NMR (**3ae**) ($CDCl_3$)



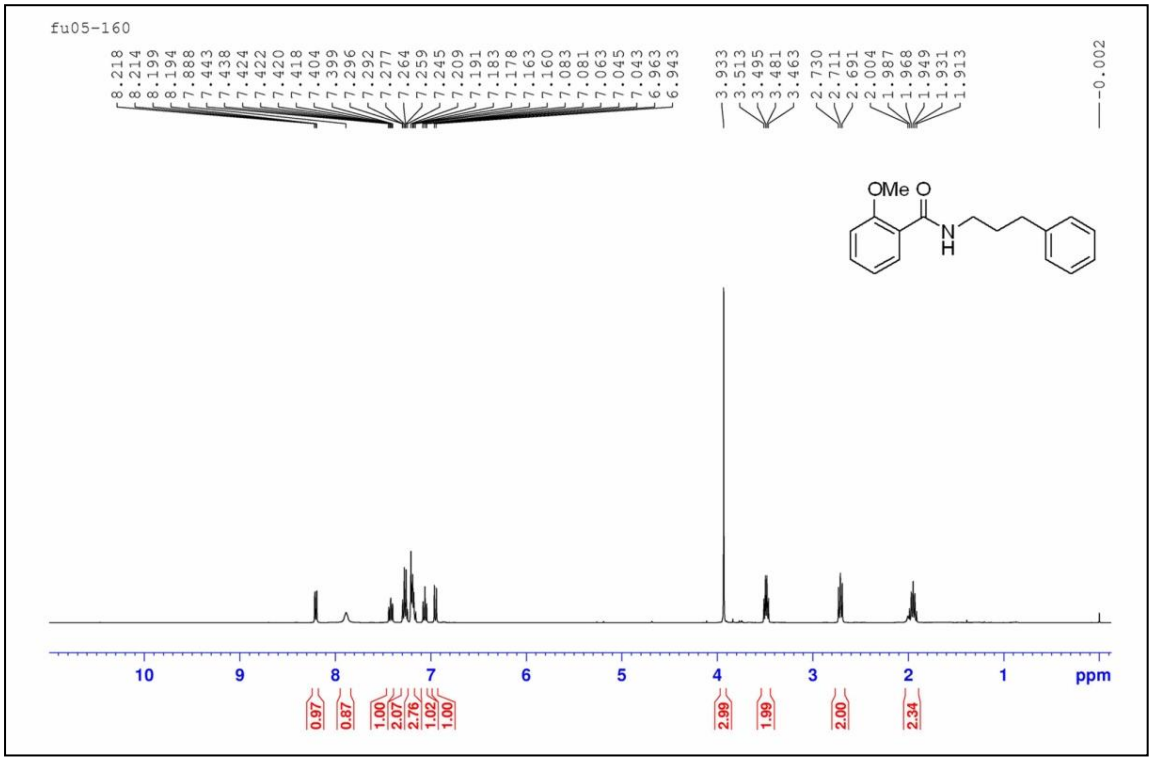
^{1}H NMR (**3af**) ($CDCl_3$)



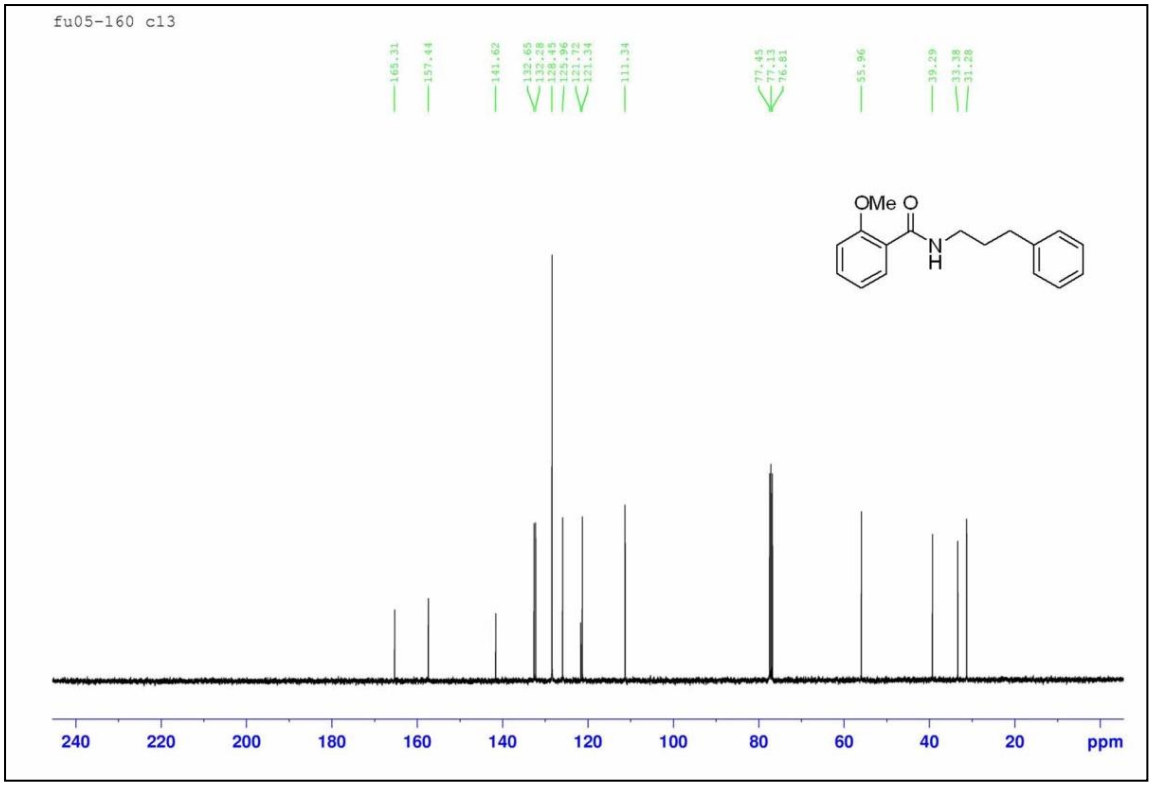
^{1}H NMR (**3ag**) ($CDCl_3$)



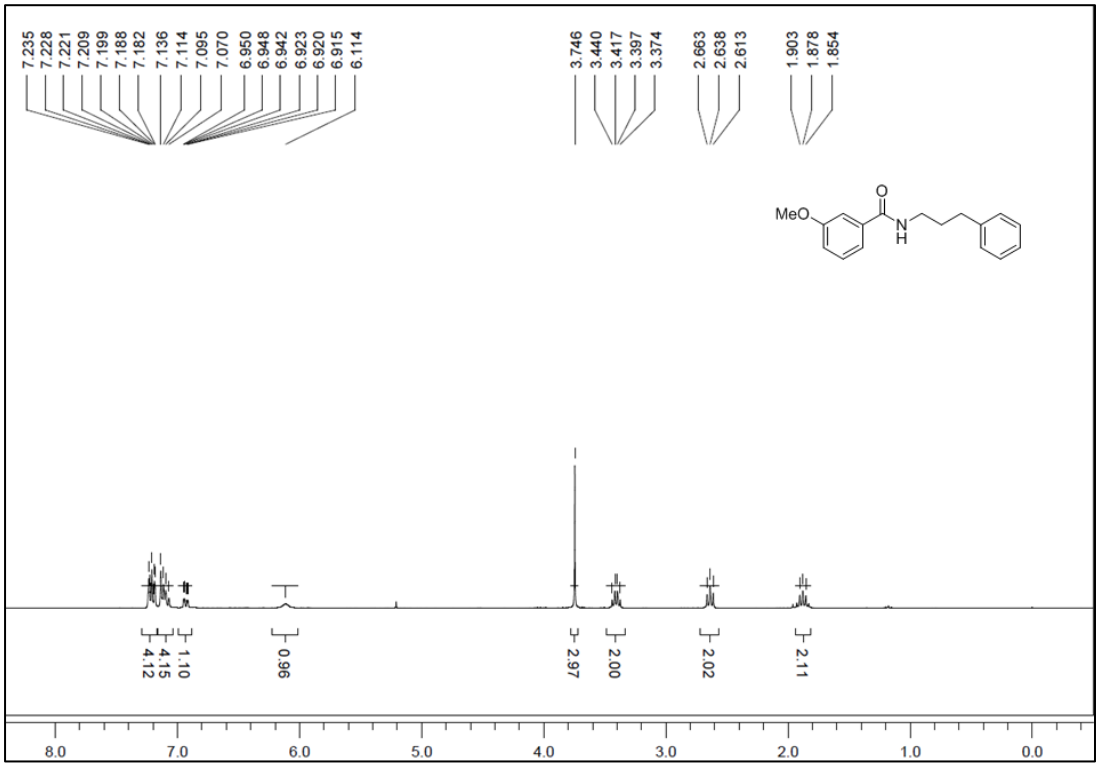
^{1}H NMR (**3ah**) ($CDCl_3$)



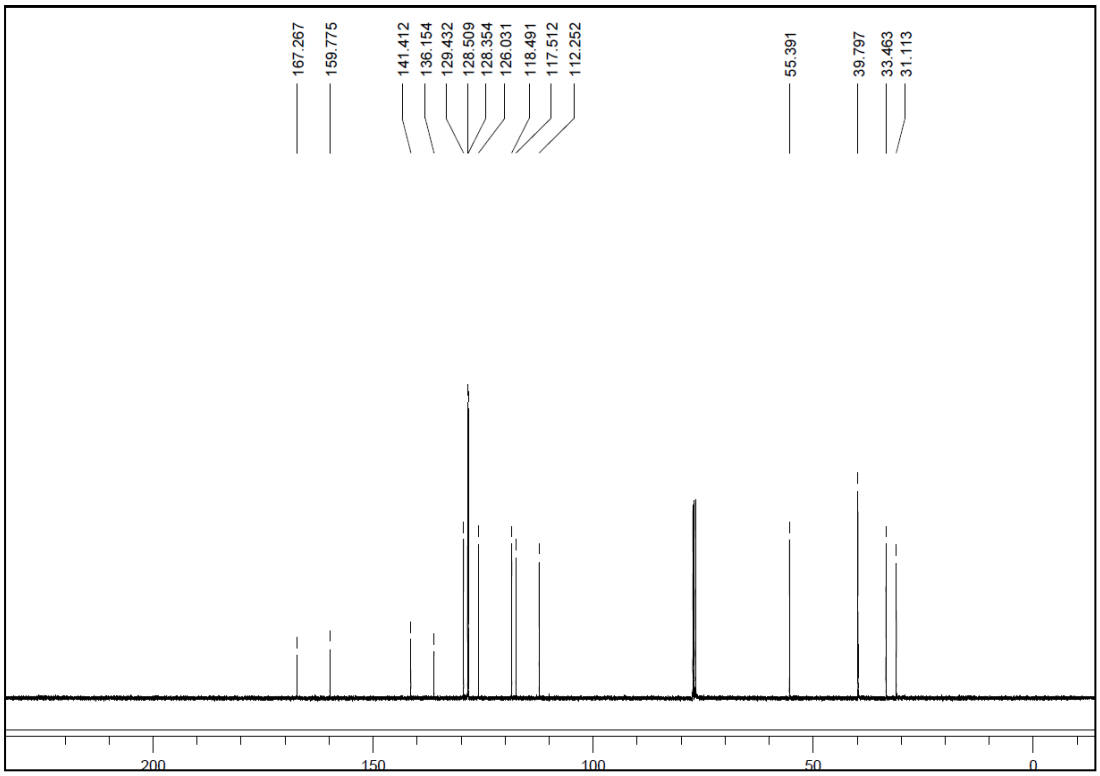
^{13}C NMR (**3ah**) ($CDCl_3$)



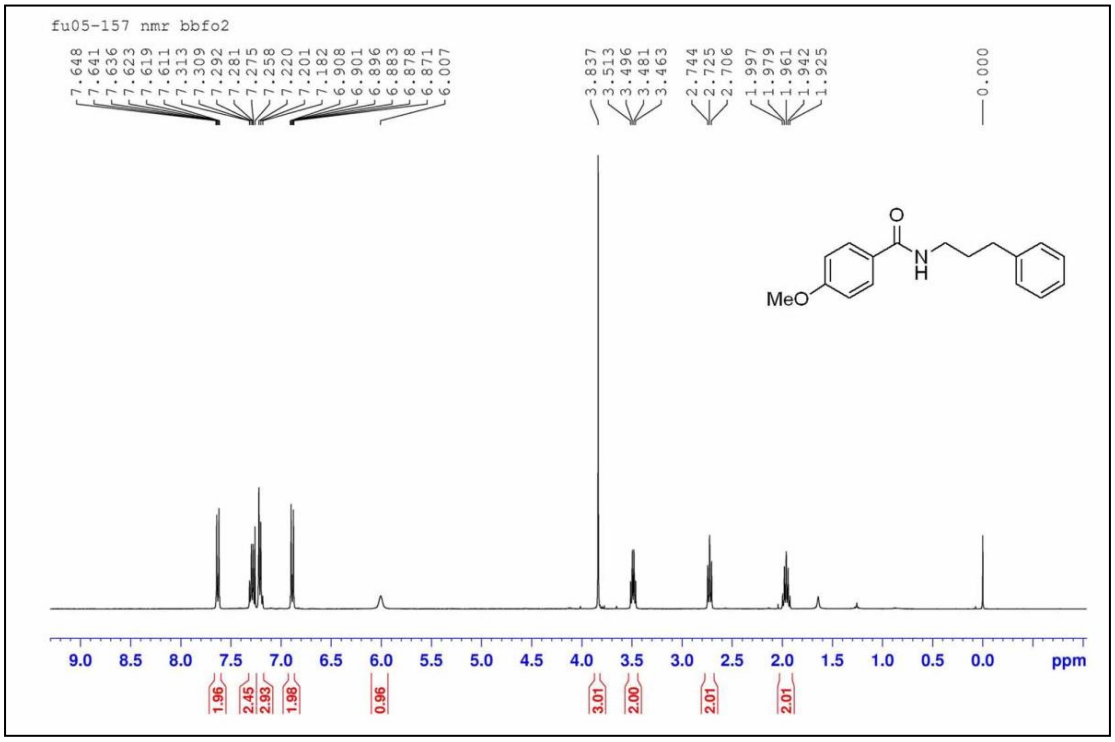
^{1}H NMR (**3ai**) ($CDCl_3$)



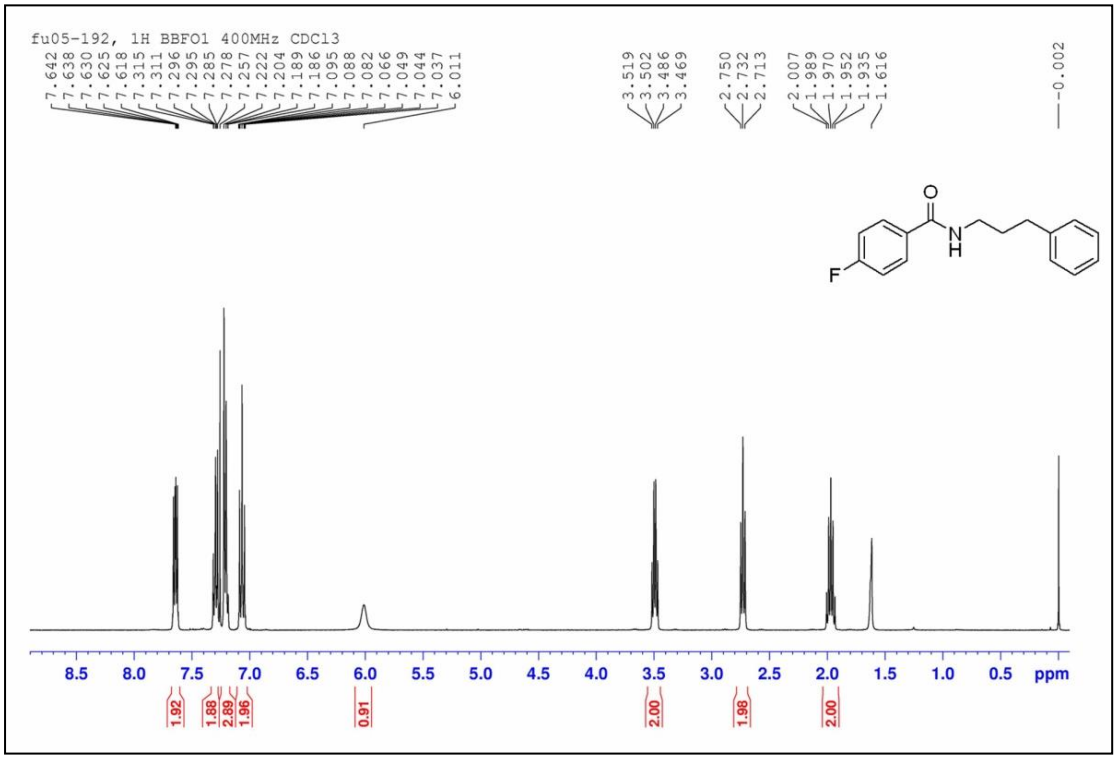
^{13}C NMR (**3ai**) ($CDCl_3$)



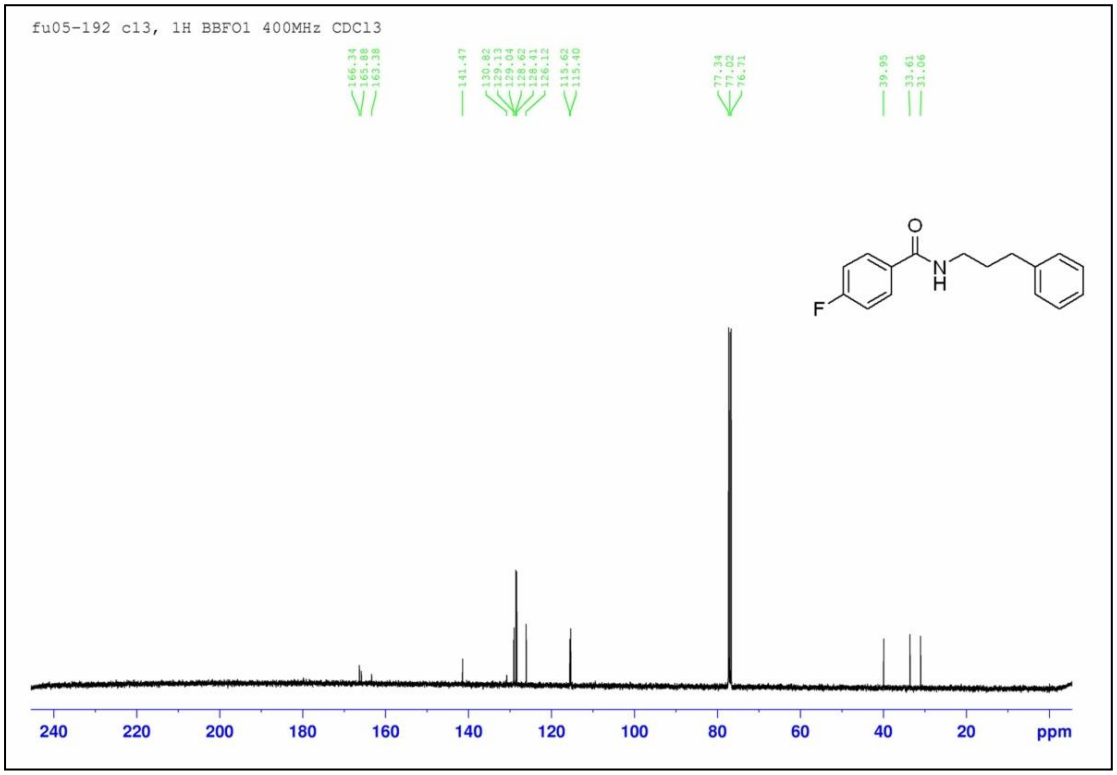
^{1}H NMR (**3aj**) ($CDCl_3$)



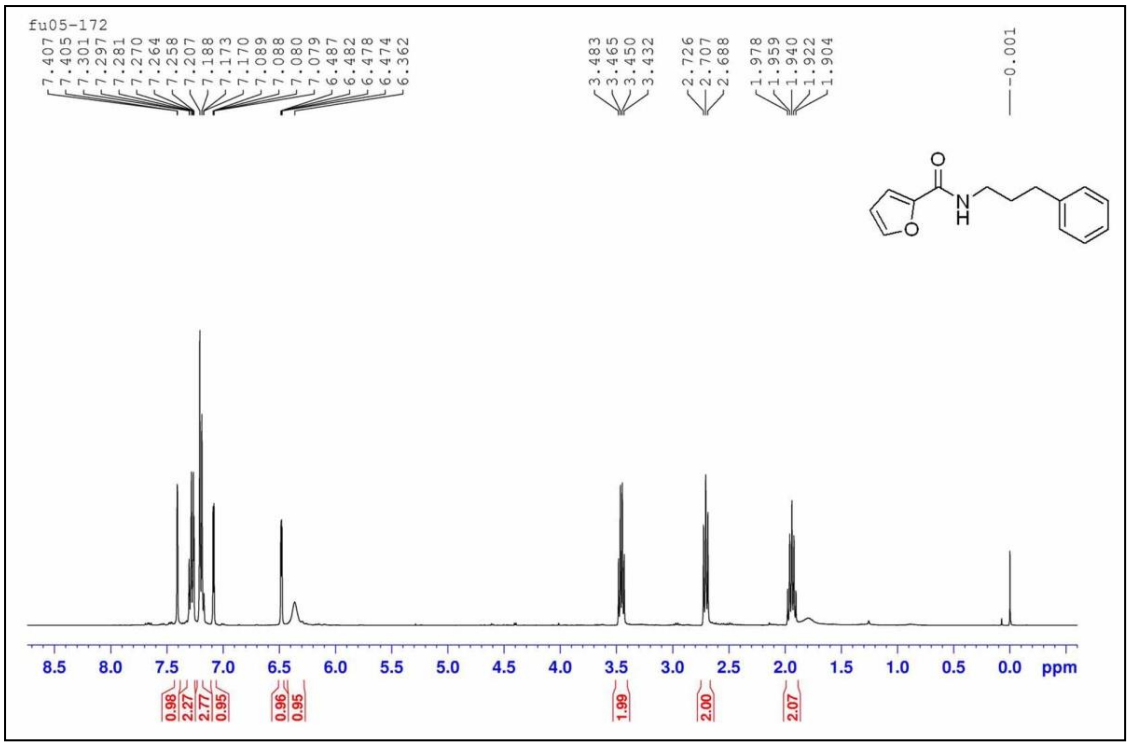
^{1}H NMR (**3ak**) ($CDCl_3$)



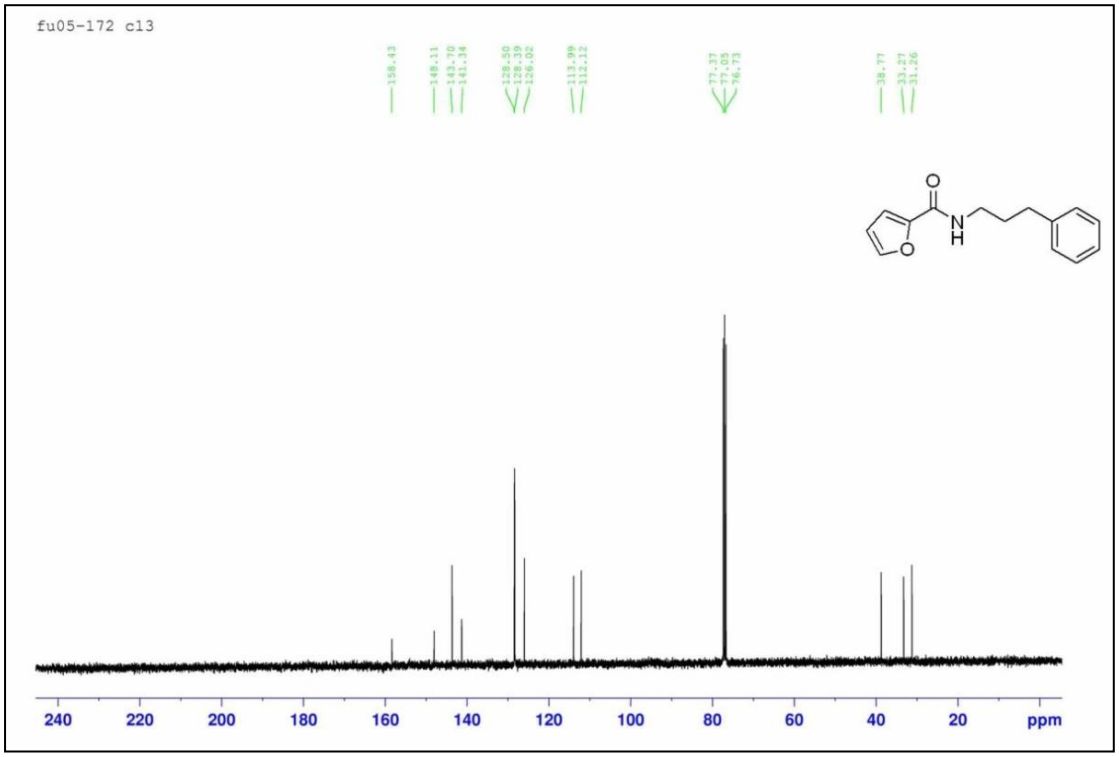
^{13}C NMR (**3ak**) ($CDCl_3$)



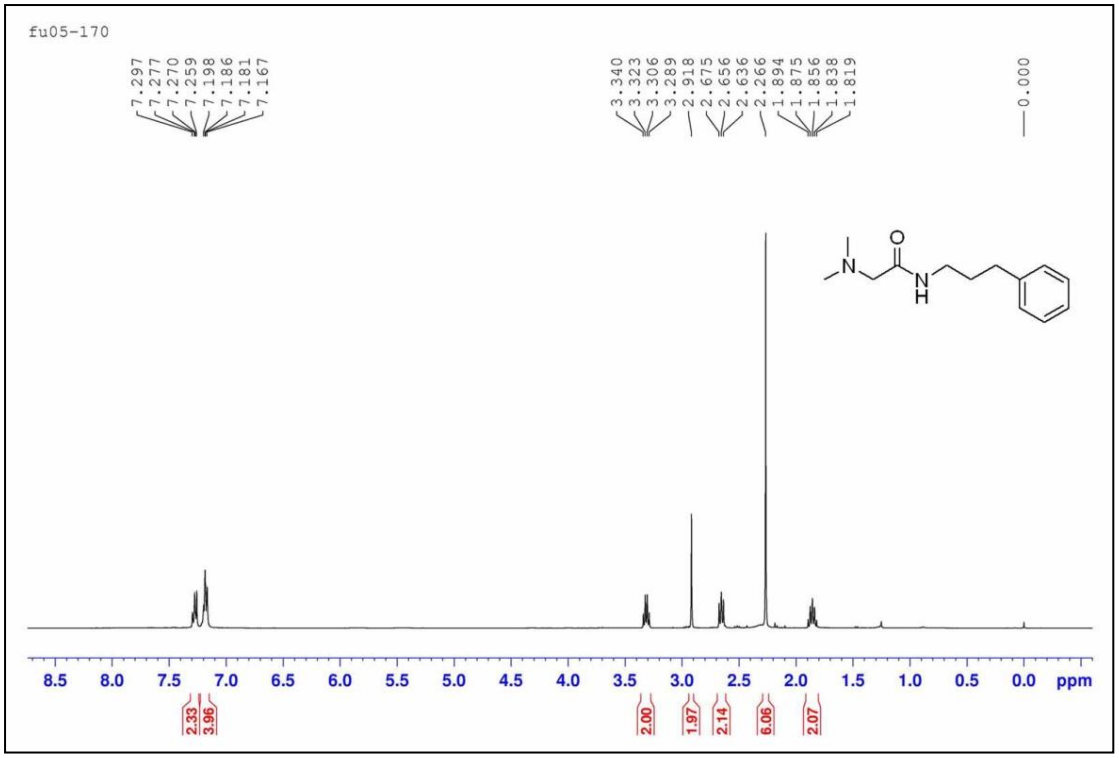
^{1}H NMR (**3al**) ($CDCl_3$)



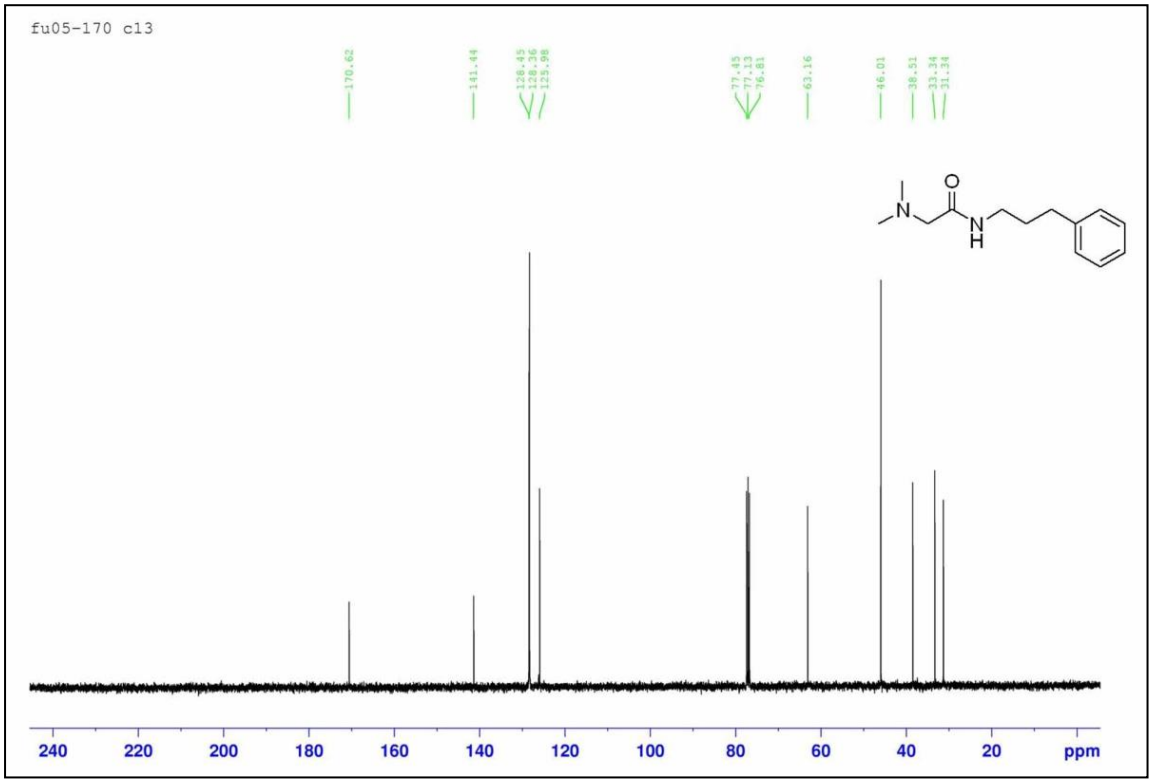
^{13}C NMR (**3al**) ($CDCl_3$)



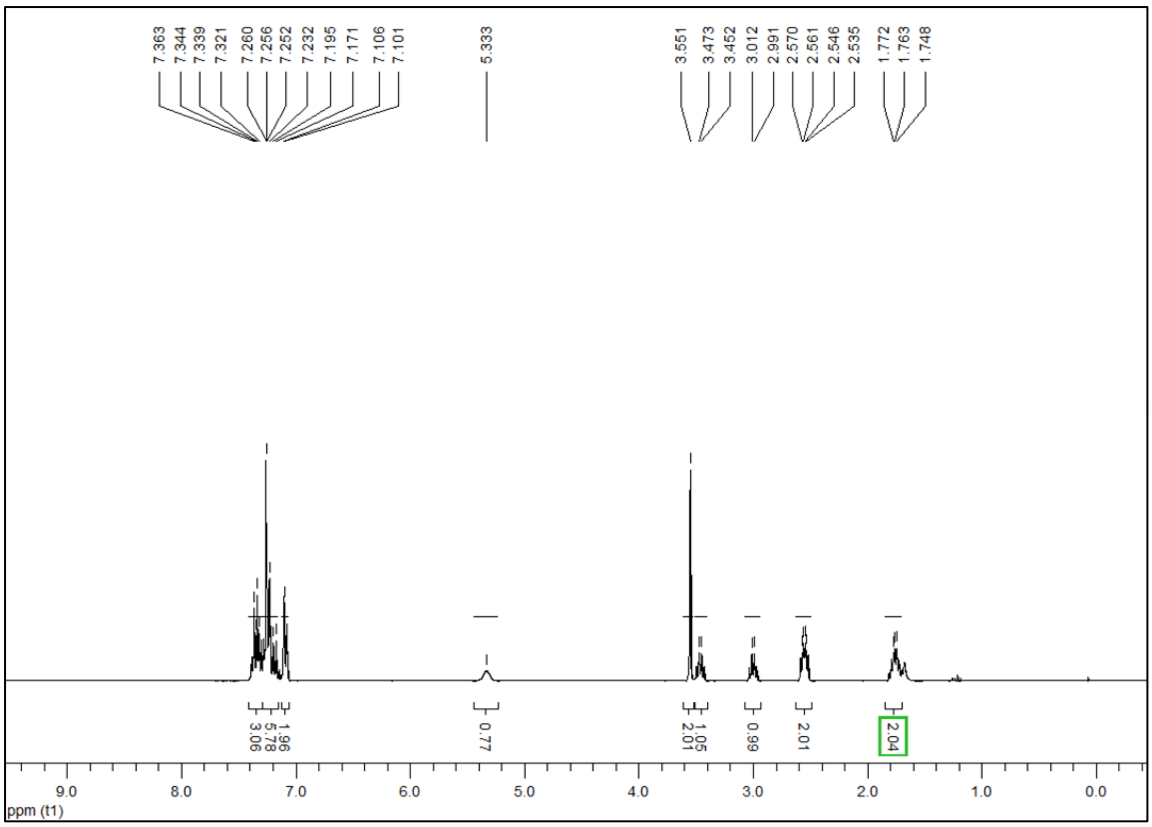
^{1}H NMR (**3am**) ($CDCl_3$)



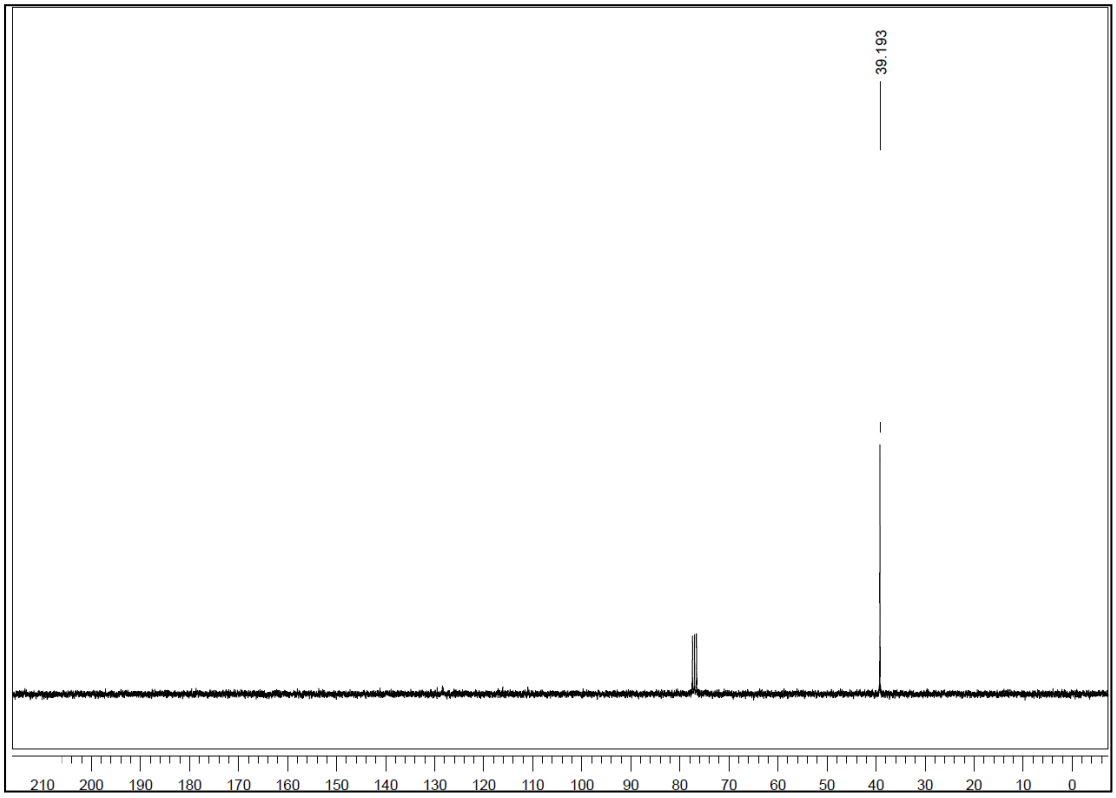
^{13}C NMR (**3am**) ($CDCl_3$)



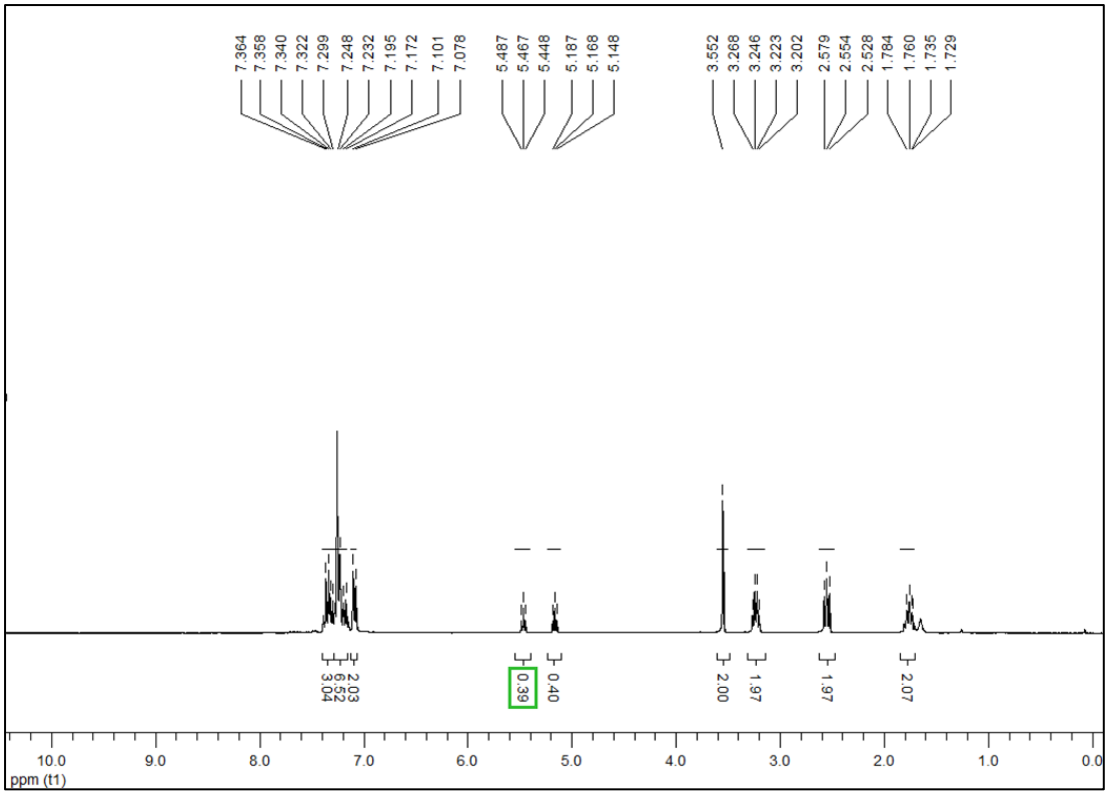
^{1}H NMR (**3la**) ($CDCl_3$)



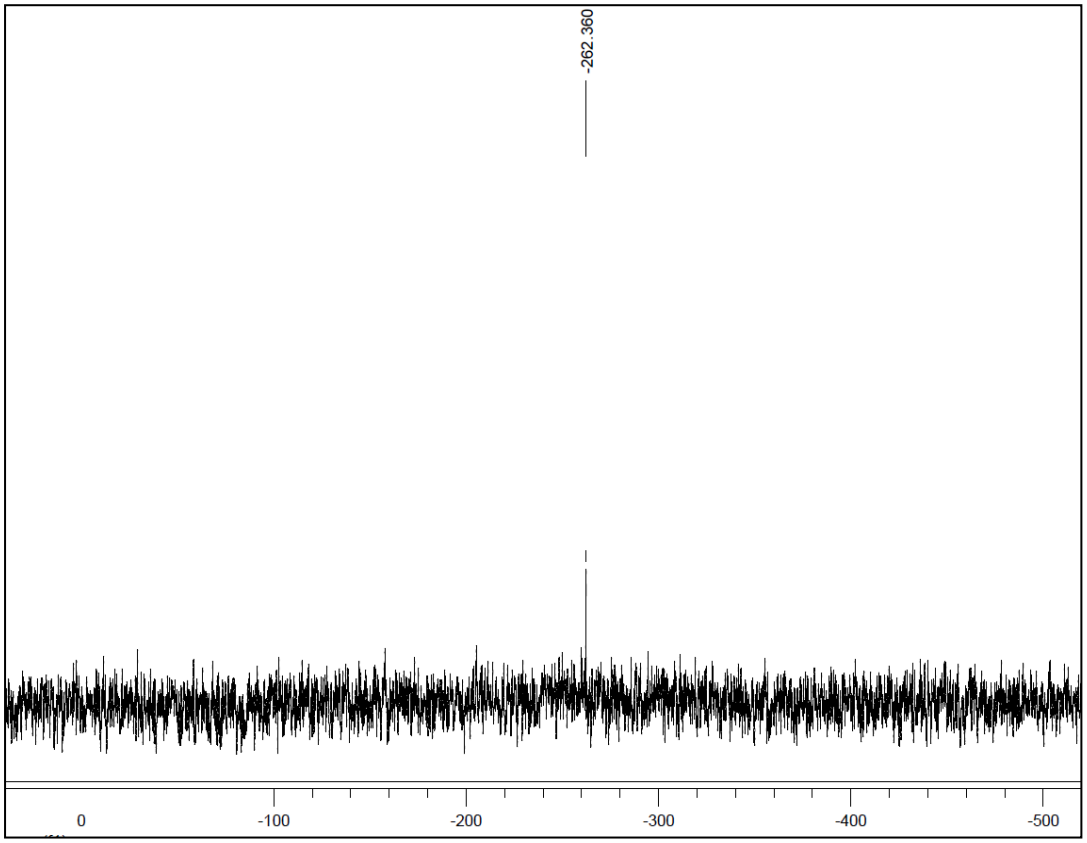
^{13}C NMR (**3la**) ($CDCl_3$)



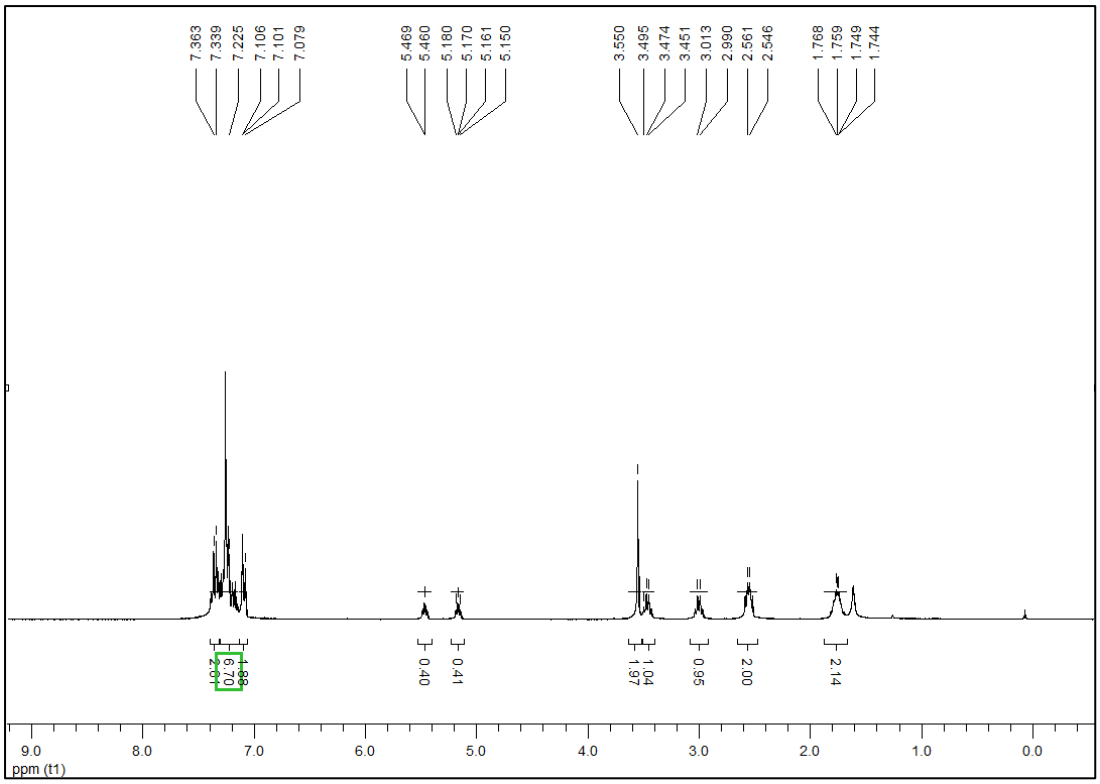
^{1}H NMR (**3ma**) ($CDCl_3$)



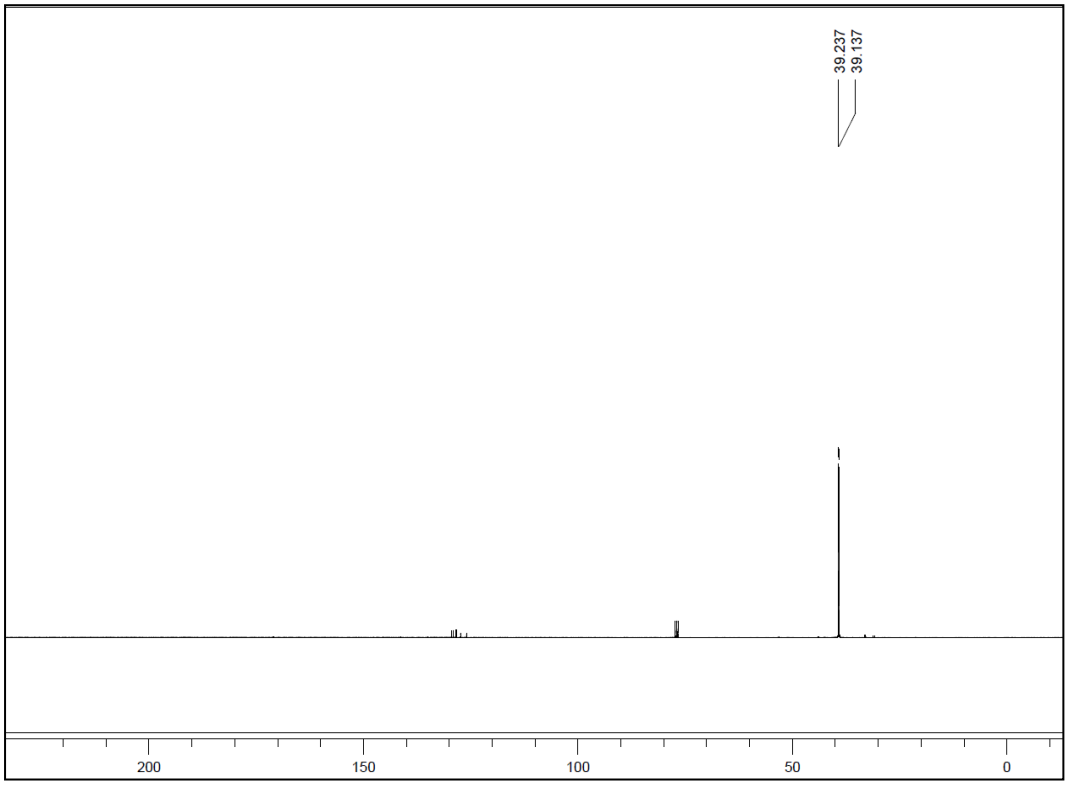
^{15}N NMR (**3ma**) ($CDCl_3$)



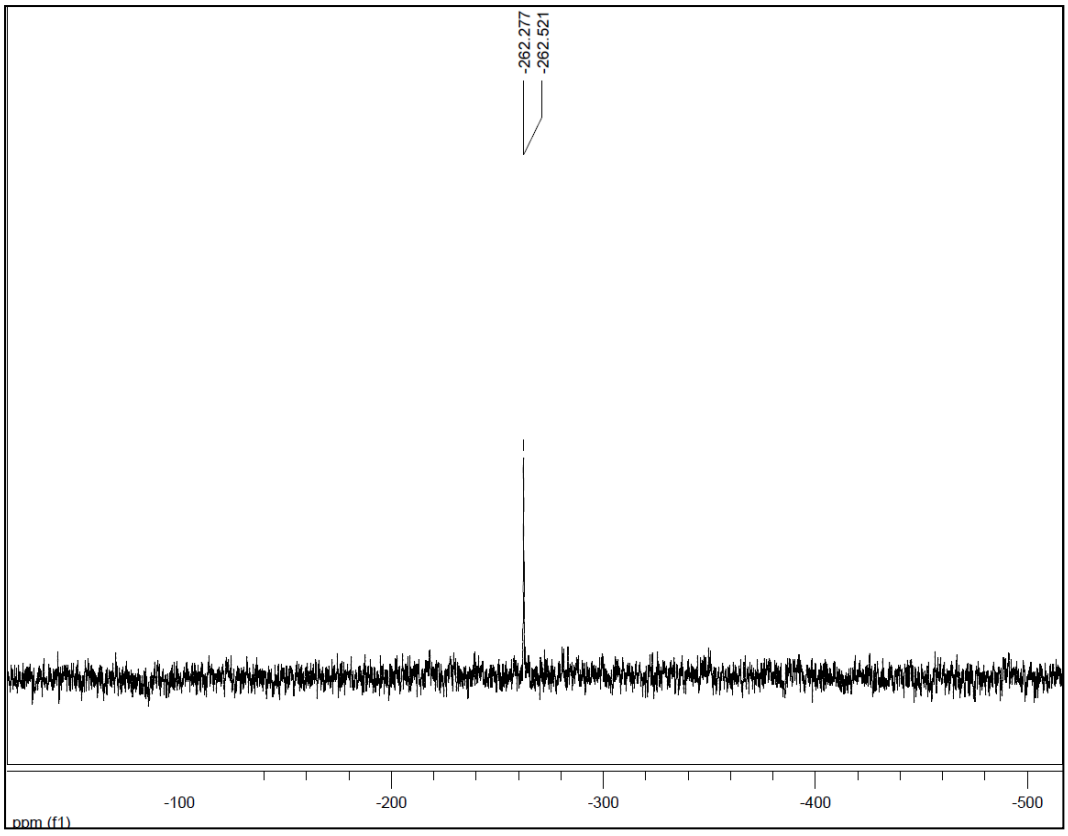
^{1}H NMR (**3na**) ($CDCl_3$)



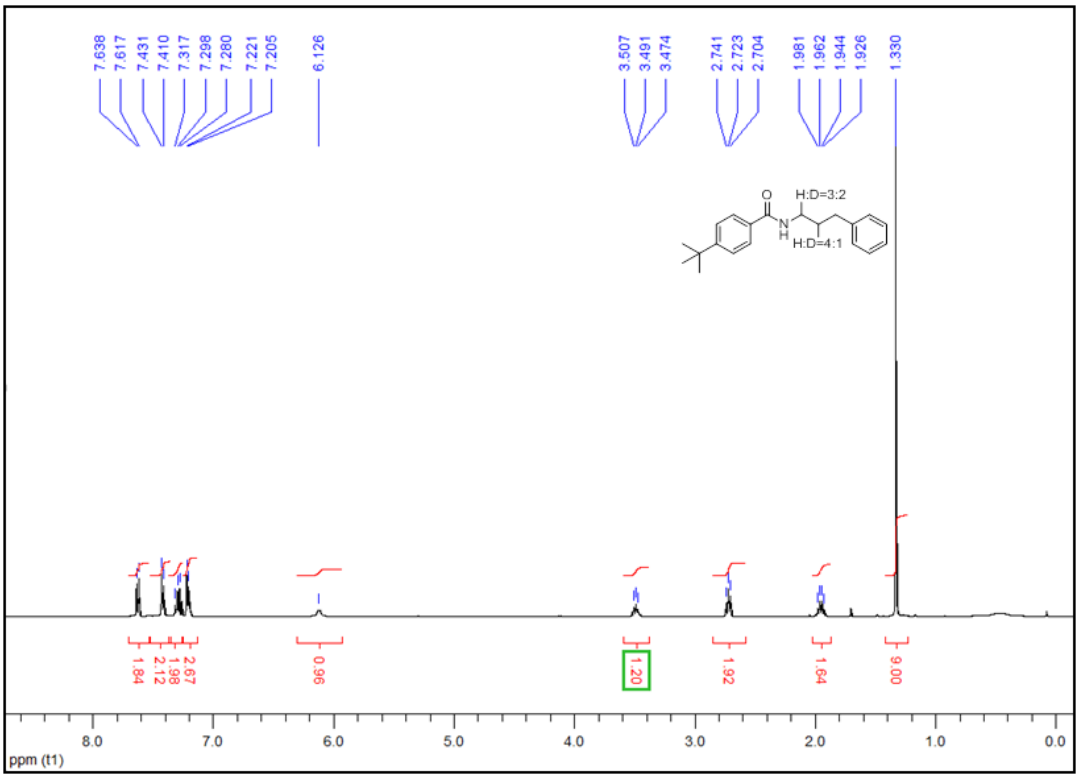
^{13}C NMR (**3na**) ($CDCl_3$)



^{15}N NMR (**3na**) ($CDCl_3$)



^{1}H NMR (**3an**) ($CDCl_3$)



^{13}C NMR (**3an**) ($CDCl_3$)