Supporting Information

Acid-ionic polymer as recyclable catalyst for one-pot three-component Mannich reaction

Warapong Senapak, Rungnapha Saeeng, Uthaiwan Sirion*

Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Burapha University, Sangesook, ChonBuri 20131, Thailand.

***Corresponding Author** *Department of Chemistry and Center for Innovation in Chemistry, Faculty of Science, Burapha University, Sangsook, Chonburi 20131, Thailand.*
E-mail: uthaiwan@buu.ac.th, Fax: +66-3-839-3494; Tel: +66-98-026-2181

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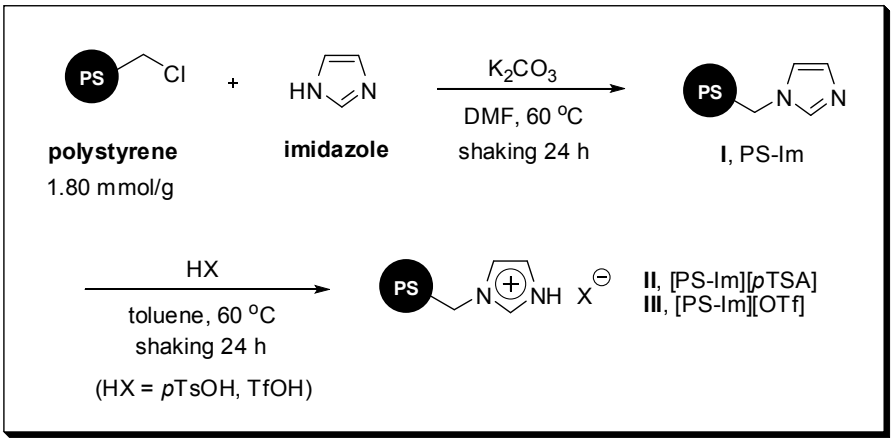
General remarks

All chemicals were purchased from commercial sources and used without further purification. The reactions were carried out using a shaker, VORTEMP 1550. ^{1}H and ^{13}C NMR spectra were recorded using a BRUKER AVANC (400 MHz). High-resolution mass spectra (HRMS) data were recorded at Mahidol University using a Bruker Daltonics - micrOTOF-Q. Infrared spectra were determined on a PERKIN ELMER FT/IR-2000S spectrophotometer. Analytical

thin-layer chromatrography (TLC) was conducted on pre-coated TLC plates; silica gel 60F-254 [E. Merck, Darmstadt, Germany]. Open-column chromatography was carried out using silica gel 60 PF254 [E. Merck, Darmstadt, Germany]. Melting points were measured using a Melting point apparatus (Griffin) and are uncorrected.

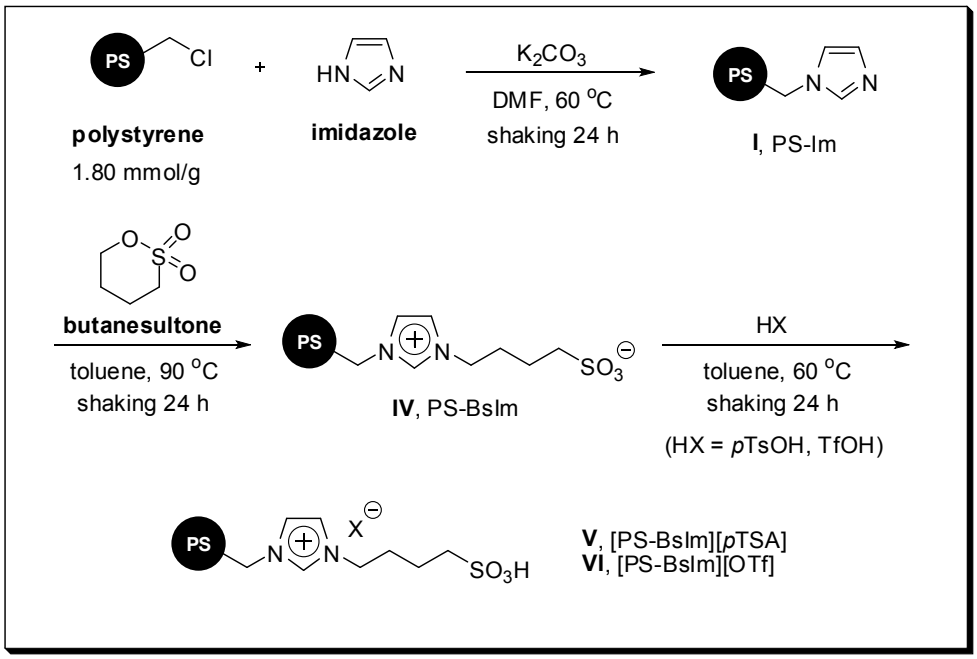
General procedure for the preparation of acid-functionalized ionic polymers



PS-Im (I): Chloromethyl Merrifield resin (5.0023 g, 1.80 mmol/g Cl loading) was placed in a vial (50 mL) pretreated with Sigmacote® and DMF (27.0 mL) was added. The suspension was shaken until resin was fully swollen. Then, imidazole (1.2230 g, 17.96 mmol) and K_2CO_3 (3.7211 g, 26.92 mmol) were added to the suspension, respectively. The mixture suspension was continually shaken at 60°C using a shaker with a speed of 800 r.p.m. for 24 h. The resulting resin was cooled and collected into a plastic syringe equipped with polyethylene frit, and wash with water, methanol and diethyl ether respectively, and dried under reduced pressure to give **PS-Im (I)** in >99% (5.6385 g, 1.80 mmol/g Cl loading).

[Ps-Im][X] (II, III): Resin **PS-Im (I)** (1.0000 g, 1.80 mmol/g Cl loading) was placed in a vial (50 mL) pretreated with Sigmacote® and toluene (3.0 mL) was added. Then, *para*-toluenesulfonic acid (*p*TsOH) (0.7228 g, 3.8 mmol) or trifluoromethanesulfonic acid (TfOH) (318 μL, 3.6 mmol) was added to the suspension. The mixture suspension was continually

shaken at 60°C using a shaker with a speed of 800 r.p.m. for 24 h. The resulting resin was cooled and collected into a plastic syringe equipped with polyethylene frit, and wash with acetone, methanol and diethyl ether respectively, and dried under reduced pressure to give **[PS-Im][*p*TSA] (II)** in 95% (1.2771 g, 1.71 mmol/g Cl loading) or **[PS-Im][OTf] (III)** in >99% (1.4970 g, 1.80 mmol/g Cl loading).



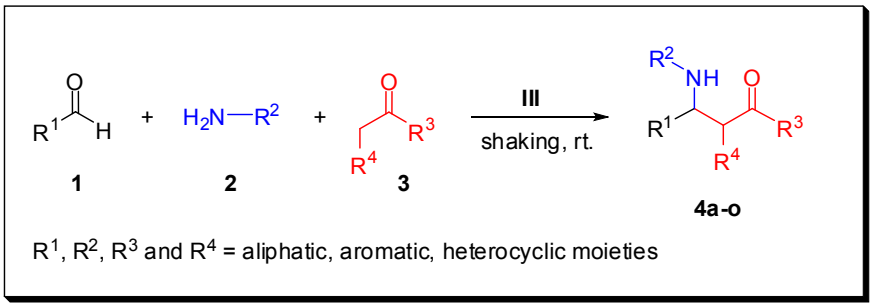
PS-Im (I): Chloromethyl Merrifield resin (5.0023 g, 1.80 mmol/g Cl loading) was placed in a vial (50 mL) pretreated with Sigmacote® and DMF (27.0 mL) was added. The suspension was shaken until resin was fully swollen. Then, imidazole (1.2230 g, 17.96 mmol) and K_2CO_3 (3.7211 g, 26.92 mmol) were added to the suspension, respectively. The mixture suspension was continually shaken at 60°C using a shaker with a speed of 800 r.p.m. for 24 h. The resulting resin was cooled and collected into a plastic syringe equipped with polyethylene frit, and wash with water, methanol and diethyl ether respectively, and dried under reduced pressure to give **PS-Im (I)** in quantitative yield (5.6385 g, 1.80 mmol/g Cl loading).

PS-BsIm (IV): Resin **PS-Im (I)** (2.0000 g, 1.80 mmol/g Cl loading) was placed in a vial (50 mL) pretreated with Sigmacote® and toluene (7.0 mL) was added. The suspension was added

1,4-butanesultone (1.50 mL, 14.68 mmol) in portion at room temperature. The mixture suspension was continually shaken at 90°C using a shaker with a speed of 800 r.p.m. for 24 h. The resulting resin was cooled and collected into a plastic syringe equipped with polyethylene frit, and wash with toluene, methanol and diethyl ether respectively, and dried under reduced pressure to give **PS-BsIm (IV)** in most-quantitative yield (2.5064 g, 1.80 mmol/g Cl loading).

[PS-BsIm][X] (V, VI): Resin **PS-BsIm (IV)** (0.5000 g, 1.80 mmol/g Cl loading) was placed in a vial (20 mL) pretreated with Sigmacote® and toluene (3.0 mL) was added. Then, *para*-toluenesulfonic acid (*p*TsOH) (0.3493 g, 1.8 mmol) or trifluoromethanesulfonic acid (TfOH) (159 μL, 1.8 mmol) was added to the suspension. The mixture suspension was continually shaken at 60°C using a shaker with a speed of 800 r.p.m. for 24 h. The resulting resin was cooled and collected into a plastic syringe equipped with polyethylene frit, and wash with acetone, methanol and diethyl ether respectively, and dried under reduced pressure to give **[PS-BsIm][*p*TSA] (V)** in 69% (0.4630 g, 1.24 mmol/g Cl loading) or **[PSSIM][OTf] (VI)** in 72% (0.4593 g, 1.30 mmol/g Cl loading).

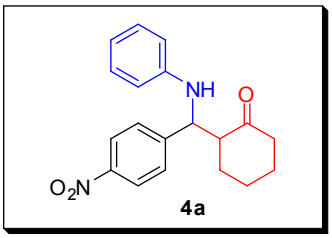
General procedure for one-pot three-component Mannich-type reaction



A mixture of aldehyde **(1)** (1.0 mmol), amine **(2)** (1.0 mmol) and catalyst **III** (10 mol%) in MeCN (3.0 mL) was suspended at room temperature, then ketone **(3)** (1.2 mmol) was added. The mixture suspension was shaken at room temperature using a shaker with a speed of 800 r.p.m. and monitored by TLC. After complete conversion, the solution was separated from

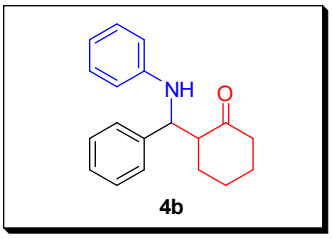
resin catalyst using filtration, a plastic syringe equipped with polyethylene frit and washed with ethyl acetate (4×5 mL). The filtered resin catalyst was dried under reduced pressure for the next experiment. The combine filtrate was concentrated using a rotary evaporator, and purified by column chromatography (SiO_2, 10-20% ethyl acetate/n-hexane as eluent) to give the desired products **4a-o** in 24-96% yields.

Physical and Spectral data of Mannich products



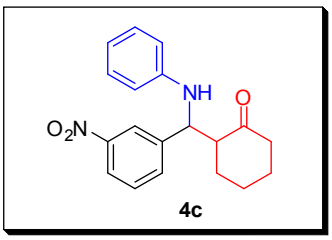
4a

2-[(4-nitrophenyl)(phenylamino)methyl]-cyclohexanone (4a):[9f,18d,15] 93% yield (0.3002 g) as a yellow solid (*syn*:*anti* = 33:67); m.p. 94-98 ^{o}C; R_f = 0.20 (20% EtOAc/*n*-hexane); IR (Neat): 3403, 2938, 1706, 1601, 1518, 1345, 751, 693 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.68-1.79 (m, 3H, CH_2), 1.90-2.10 (m, 3H, CH_2), 2.29-2.46 (m, 2H, CH_2), 2.79-2.96 (m, 1H, CH), 4.70 (d, 0.77H, *J* = 7.0 Hz, *anti*-CH), 4.85 (d, 0.24H, *J* = 5.5 Hz, *syn*-CH), 6.48-6.56 (m, 2H, ArH), 6.70 (t, 1H, *J* = 7.0 Hz, ArH), 7.06-7.13 (m, 2H, ArH), 7.57 (d, 2H, *J* = 8.5 Hz, ArH), 8.15 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.46 (*anti*), 24.91 (*syn*), 27.01 (*syn*), 27.74 (*anti*), 29.05 (*syn*), 31.99 (*anti*), 42.38 (*anti*), 42.42 (*syn*), 56.18 (*syn*), 56.92 (*anti*), 57.22 (*syn*), 57.92 (*anti*), 113.61 (2C, *anti*), 114.04 (2C, *syn*), 118.26 (*anti*), 118.39 (*syn*), 123.60 (2C, *syn*), 123.65 (2C, *anti*), 128.27 (2C, *anti*), 128.59 (2C, *syn*), 129.14 (2C, *syn*), 129.25 (2C, *anti*), 146.45 (*anti*), 146.57 (*syn*), 147.03 (*syn*, *anti*), 149.51 (*syn*), 149.65 (*anti*), 210.60 (*syn*), 211.79 (*anti*).



4b

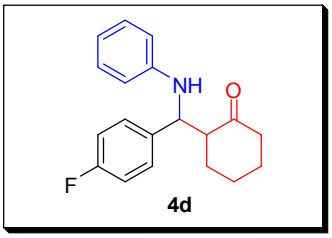
2-[phenyl(phenylamino)methyl]-cyclohexanone (4b):[8b,9a,10a,13a,13b,15,16,18d] 73% yield (0.2050 g) as a yellow solid (*syn*:*anti* = 26:74); m.p.102-106 ^{o}C; R_f = 0.41 (20% EtOAc/*n*-hexane); IR (Neat): 3399, 2936, 1702, 1602, 1505, 1451, 1317, 749, 702 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.63-1.73 (m, 2H, CH_2), 1.80-1.96 (m, 4H, CH_2), 2.29-2.48 (m, 2H, CH_2), 2.75-2.85 (m, 1H, CH), 4.61 (d, 0.77H, *J* = 7.0 Hz, *anti*-CH), 4.80 (d, 0.28H, *J* = 4.5 Hz, *syn*-CH), 6.56 (dd, 2H, *J* = 3.0, 7.5 Hz, ArH), 6.65 (t, 1H, *J* = 7.5 Hz, ArH), 7.04-7.10 (m, 2H, ArH), 7.17-7.24 (m, 1H, ArH), 7.27-7.33 (m, 2H, ArH), 7.33-7.41 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.61 (*anti*), 24.80 (*syn*), 26.96 (*syn*), 27.84 (*anti*), 28.63 (*syn*), 31.25 (*anti*), 41.73 (*anti*), 42.36 (*syn*), 56.56 (*anti*), 57.23 (*syn*), 57.38 (*anti*), 58.06 (*syn*), 113.68 (2C, *anti*), 114.04 (2C, *syn*), 117.59 (*anti*), 117.65 (*syn*), 126.96 (*syn*), 127.15 (*anti*), 127.24 (2C, *anti*), 127.48 (2C, *syn*), 128.33 (2C, *syn*), 128.43 (2C, *anti*), 128.96 (2C, *syn*), 129.02 (2C, *anti*), 141.50 (*syn*), 141.55 (*anti*), 147.04 (*anti*), 147.42 (*syn*), 211.29 (*syn*), 212.84 (*anti*).



4c

2-[(3-nitrophenyl)(phenylamino)methyl]-cyclohexanone (4c): [9f,18d] 89% yield (0.2285 g) as a yellow solid (*syn*:*anti* = 46:54); m.p. 104-106 ^{o}C; R_f = 0.19 (10% EtOAc/*n*-hexane); IR (Neat): 3406, 2939, 1706, 1602, 1527, 1349, 751, 692 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ

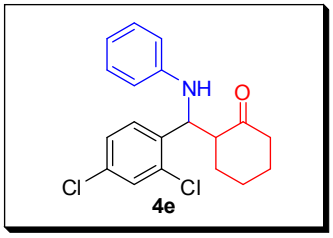
1.60-1.85 (m, 3H, CH_2), 1.90-2.15 (m, 3H, CH_2), 2.28-2.48 (m, 2H, CH_2), 2.82-2.90 (m, 1H, CH), 4.70 (d, 0.67H, J = 5.0 Hz, *anti*-CH), 4.85 (d, 0.47H, J = 4.5 Hz, *syn*-CH), 6.52 (d, 2H, J = 7.5 Hz, ArH), 6.64-6.71 (m, 1H, ArH), 7.06-7.12 (m, 2H, ArH), 7.46 (t, 1H, J = 8.0 Hz, ArH), 7.74-7.80 (m, 1H, ArH), 8.04-8.10 (m, 1H, ArH), 8.21-8.26 (m, 1H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.40 (*anti*), 24.88 (*syn*), 27.07 (*syn*), 27.76 (*anti*), 29.22 (*syn*), 31.97 (*anti*), 42.36 (*anti*), 42.42 (*syn*), 56.23 (*anti*), 57.02 (*syn, anti*), 57.61 (*syn*), 113.44 (2C, *anti*), 113.94 (2C, *syn*), 118.00 (*anti*), 118.24 (*syn*), 122.17 (*anti*), 122.20 (*syn*), 122.24 (*anti*), 122.46 (*syn*), 129.14 (2C, *syn*), 129.22 (2C, *anti*), 129.25 (*syn*), 129.31 (*anti*), 133.57 (*anti*), 134.13 (*syn*), 144.11 (*syn*), 144.45 (*anti*), 146.58 (*syn*), 146.65 (*anti*), 148.37 (*syn, anti*), 210.70 (*syn*), 211.86 (*anti*).



4d

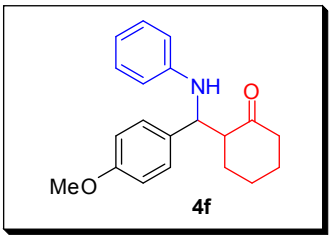
2-[(4-fluorophenyl)(phenylamino)methyl]-cyclohexanone (4d): 76% yield (0.2263 g) as a yellow solid (*syn*:*anti* = 26:74); m.p. 98-102 ^{o}C; R_f = 0.38 (20% EtOAc/*n*-hexane); IR (Neat): 3397, 2938, 1705, 1603, 1507, 1222, 838, 750, 693 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.55-1.75 (m, 2H, CH_2), 1.75-2.09 (m, 4H, CH_2), 2.29-2.47 (m, 2H, CH_2), 2.74-2.84 (m, 1H, CH), 4.60 (d, 0.78H, J = 6.5 Hz, *anti*-CH), 4.74 (d, 0.27H, J = 4.5 Hz, *syn*-CH), 6.53 (dd, 2H, J = 4.5, 8.0 Hz, ArH), 6.66 (t, 1H, J = 8.0 Hz, ArH), 6.94-7.01 (m, 2H, ArH), 7.08 (t, 2H, J = 8.0 Hz, ArH), 7.30-7.38 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.84 (*anti*), 24.83 (*syn*), 26.98 (*syn*), 27.81 (*anti*), 28.95 (*syn*), 31.36 (*anti*), 41.93 (*anti*), 42.42 (*syn*), 56.45 (*syn*), 56.89 (*syn*), 57.34 (*anti*), 57.57 (*anti*), 113.77 (2C, *anti*), 114.05 (2C, *syn*), 115.16 (d, J = 21 Hz, 2×*syn*-C-F), 115.31 (d, J = 21 Hz, 2×*anti*-C-F), 117.87 (*syn*, *anti*), 128.81 (d, J = 8.0

Hz, 2×*anti*-C-F), 129.02 (2C, *syn*), 129.08 (2C, *anti*), 129.12 (d, *J* = 8.0 Hz, 2×*syn*-C-F), 137.00 (d, *J* = 3.0 Hz, *syn*-C-F), 137.20 (d, *J* = 3.0 Hz, *anti*-C-F), 146.79 (*anti*), 147.16 (*syn*), 161.85 (d, *J* = 244 Hz, *syn*-, *anti*-C-F), 211.30 (*syn*), 212.65 (*anti*); HRMS (ESI) *m/z* $C_{19}H_{20}FNO$ $[M+Na]^+$ calcd 320.1421, found 320.1423.



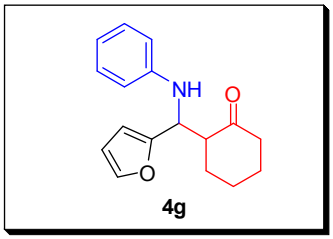
4e

2-[(2,4-dichlorophenyl)(phenylamino)methyl]-cyclohexanone (4e):[13a] 96% yield (0.3319 g) as a yellow oil (*syn*:*anti* = 41:59); R_f = 0.64 (20% EtOAc/*n*-hexane); IR (Neat): 3396, 2938, 1706, 1603, 1505, 1468, 749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.55-1.80 (m, 3H, CH_2), 1.89-2.14 (m, 3H, CH_2), 2.26-2.51 (m, 2H, CH_2), 2.84-2.98 (m, 1H, CH), 4.83 (d, 0.54H, *J* = 4.5 Hz, *anti*-CH), 5.26 (d, 0.37H, *J* = 3.5 Hz, *syn*-CH), 6.48 (d, 1H, *J* = 8.0 Hz, ArH), 6.52 (d, 1H, *J* = 7.5 Hz, ArH), 6.65-6.70 (m, 1H, ArH), 7.06-7.13 (m, 2H, ArH), 7.16 (dd, 1H, *J* = 2.0, 8.5 Hz, ArH), 7.34 (d, 0.54H, *J* = 2.0 Hz, *anti*-ArH), 7.38 (d, 0.36H, *J* = 2.0 Hz, *syn*-ArH), 7.46 (d, 0.59H, *J* = 8.5 Hz, *anti*-ArH), 7.56 (d, 0.41H, *J* = 8.5 Hz, *syn*-ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.90 (*anti*), 27.04 (*syn*), 27.59 (*syn*), 28.03 (*anti*), 29.67 (*syn*), 32.82 (*anti*), 42.30 (*syn*), 42.93 (*anti*), 53.14 (*syn*), 53.95 (*anti*), 54.98 (*anti*), 55.32 (*syn*), 113.45 (2C, *syn*), 114.06 (2C, *anti*), 117.98 (*syn*), 118.27 (*anti*), 127.29 (*syn*), 127.39 (*anti*), 128.99 (*anti*), 129.06 (2C, *syn*), 129.22 (2C, *anti*), 129.54 (*syn*), 130.08 (*anti*), 130.58 (*syn*), 133.21 (*anti*), 133.26 (*syn*), 133.33 (*syn*), 133.79 (*anti*), 137.31 (*anti*), 137.70 (*syn*), 146.40 (*syn*), 146.78 (*anti*), 210.59 (*syn*), 213.04 (*anti*).



4f

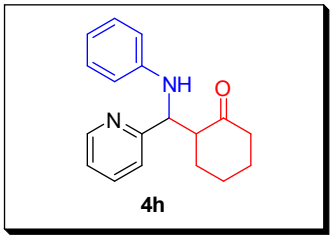
2-[(4-methoxyphenyl)(phenylamino)methyl]-cyclohexanone (4f):[10a,15,18d] 61% yield (0.1887 g) as a yellow oil (*syn*:*anti* = 28:72); R_f = 0.34 (20% EtOAc/*n*-hexane); IR (Neat): 3386, 2935, 1702, 1603, 1509, 1249, 1177, 1032, 833, 750, 693, 511 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.55-1.76 (m, 3H, CH_2), 1.76-1.96 (m, 3H, CH_2), 2.25-2.47 (m, 2H, CH_2), 2.65-2.74 (m, 1H, CH), 3.76 (s, 3H, OMe), 4.58 (d, 0.79H, *J* = 7.0 Hz, *anti*-CH), 4.72 (d, 0.30H, *J* = 4.0 Hz, *syn*-CH), 6.49-6.57 (m, 2H, ArH), 6.59-6.66 (m, 1H, ArH), 6.83 (d, 2H, *J* = 8.5 Hz, ArH), 7.01-7.10 (m, 2H, ArH), 7.28 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.48 (*anti*), 24.75 (*syn*), 26.96 (*syn*), 27.82 (*anti*), 28.94 (*syn*), 31.04 (*anti*), 41.63 (*anti*), 42.38 (*syn*), 55.15 (OMe, *syn*, *anti*), 56.57 (*syn*), 56.83 (*syn*), 57.31 (*anti*), 57.59 (*anti*), 113.62 (2C, *anti*), 113.69 (2C, *syn*), 113.83 (2C, *anti*), 114.01 (2C, *syn*), 117.42 (*anti*), 117.55 (*syn*), 128.23 (2C, *anti*), 128.57 (2C, *syn*), 128.95 (2C, *syn*), 128.99 (2C, *anti*), 133.35 (*syn*), 133.58 (*anti*), 147.22 (*anti*), 147.47 (*syn*), 158.61 (*anti*), 159.68 (*syn*), 211.60 (*syn*), 212.99 (*anti*).



4g

2-[(Furan-2-yl)(phenylamino)methyl]-cyclohexanone (4g):[8b,9a,13b] 80% yield (0.2148 g) as a brown solid (*syn*:*anti* = 26:74); m.p. = 82-84 ^oC; R_f = 0.50 (20% EtOAc/*n*-hexane); IR (Neat): 3387, 2937, 1706, 1602, 1505, 1316, 1149, 1009, 749, 692, 598 cm^{-1}; ^{1}H-NMR (400

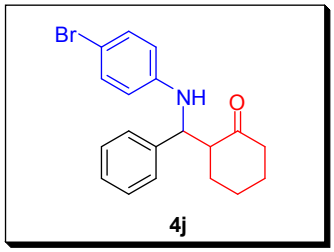
MHz, $CDCl_3$): δ 1.60-1.77 (m, 3H, CH_2), 1.84-2.06 (m, 3H, CH_2), 2.30-2.47 (m, 2H, CH_2), 2.89-3.05 (m, 1H, CH), 4.81 (d, 0.67H, *J* = 5.5 Hz, *anti*-CH), 4.87 (d, 0.24H, *J* = 4.5 Hz, *syn*-CH), 6.18-6.21 (m, 1H, Het-H), 6.24-6.28 (m, 1H, Het-H), 6.62-6.74 (m, 3H, ArH), 7.11-7.17 (m, 2H, ArH), 7.28-7.31 (m, 1H, Het-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.25 (*anti*), 24.67 (*syn*), 26.84 (*syn*), 27.58 (*anti*), 29.65 (*syn*), 30.78 (*anti*), 42.06 (*anti*), 42.20 (*syn*), 51.91 (*syn*), 52.17 (*anti*), 54.03 (*syn*), 54.42 (*anti*), 106.86 (*anti*), 107.15 (*syn*), 110.30 (*syn*, *anti*), 113.69 (2C, *anti*), 113.99 (2C, *syn*), 118.00 (*anti*), 118.15 (*syn*), 129.13 (2C, *syn*), 129.15 (2C, *anti*), 141.14 (*syn*), 141.26 (*anti*), 147.10 (*syn*), 147.13 (*anti*), 154.58 (*anti*), 154.85 (*syn*), 211.00 (*syn*), 211.84 (*anti*).



4h

2-[(pyridin-2-yl)(phenylamino)methyl]-cyclohexanone (*syn*-4h):[8b,10a] 15% yield (0.0410 g) of *syn*-isomer as a brown solid; m.p. = 138-140 ^{o}C; R_f = 0.29 (20% EtOAc/*n*-hexane); IR (Neat): 3392, 3051, 2929, 2859, 1704, 1602, 1505, 1470, 1434, 1317, 749, 692 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.65-1.82 (m, 4H, CH_2), 1.88-2.15 (m, 2H, CH_2), 2.31-2.37 (m, 2H, CH_2), 3.30-3.38 (m, 1H, CH), 4.79 (d, 1H, *J* = 4.0 Hz, CH), 6.60 (d, 2H, *J* = 7.5 Hz, ArH), 6.66 (t, 1H, *J* = 7.5 Hz, ArH), 7.09-7.15 (m, 3H, ArH, Pyr-H), 7.48 (d, 1H, *J* = 7.5 Hz, Pyr-H), 7.59 (td, 1H, *J* = 1.0, 7.5 Hz, Pyr-H), 8.52 (brd, 1H, *J* = 4.5 Hz, Pyr-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.63, 27.71, 31.62, 42.47, 55.41, 58.68, 113.11 (2C), 117.34, 121.81, 121.91, 129.27 (2C), 136.47, 147.35, 148.69, 161.25, 213.10; HRMS (ESI) *m/z* $C_{18}H_{20}N_2O$ $[M+Na]^+$ calcd 303.1473, found 303.1472.

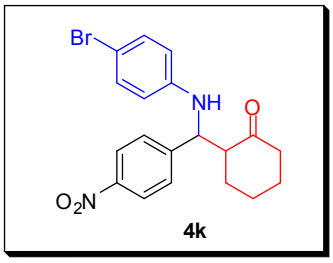
2-[(pyridin-2-yl)(phenylamino)methyl]-cyclohexanone (*anti*-4h):[8b,10a] 11% yield (0.0304 g) of *anti*-isomer as a yellow solid; m.p. = 112-114 ^{o}C; R_f = 0.07 (20% EtOAc/*n*-hexane); IR (Neat): 3378, 2938, 1706, 1602, 1505, 1434, 1261, 749, 693 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.60-1.73 (m, 3H, CH_2), 1.85-1.99 (m, 1H, CH_2), 2.00-2.09 (m, 1H, CH_2), 2.23-2.40 (m, 3H, CH_2), 3.06-3.14 (m, 1H, CH_2), 4.96 (d, 1H, *J* = 6.5 Hz, CH), 6.61-6.69 (m, 3H, ArH), 7.07-7.16 (m, 3H, ArH, Pyr-H), 7.43 (d, 1H, *J* = 7.5 Hz, Pyr-H), 7.59 (t, 1H, *J* = 7.5 Hz, Pyr-H), 8.53 (d, 1H, *J* = 4.0 Hz, Pyr-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.98, 27.64, 29.79, 42.45, 56.02, 57.84, 113.95 (2C), 117.73, 121.97, 123.08, 129.11 (2C), 136.29, 147.59, 148.97, 161.48, 211.64; HRMS (ESI) *m/z* $C_{18}H_{20}N_2O$ $[M+H]^+$ calcd 281.1654, found 281.1666.



4j

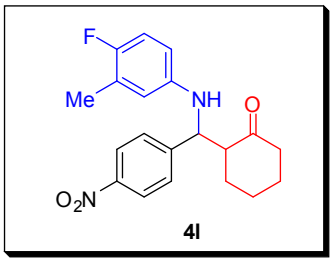
2-[(phenyl)(4-bromophenylamino)methyl]-cyclohexanone (4j): 96% yield (0.3433 g) as a yellow solid (*syn*:*anti* = 28:72); m.p. 108-111 ^{o}C; R_f = 0.36 (20% EtOAc/*n*-hexane); IR (Neat): 3398, 2937, 1702, 1592, 1495, 813, 702 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.54-1.74 (m, 3H, CH_2), 1.76-2.07 (m, 3H, CH_2), 2.30-2.47 (m, 2H, CH_2), 2.75-2.87 (m, 1H, CH), 4.52 (d, 0.71H, *J* = 7.0 Hz, *anti*-CH), 4.73 (d, 0.27H, *J* = 4.0 Hz, syn-CH), 6.40-6.48 (m, 2H, ArH), 7.14 (d, 2H, *J* = 8.5 Hz, ArH), 7.20-7.37 (m, 5H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.3 (*anti*), 24.81 (*syn*), 26.87 (*syn*), 27.89 (*anti*), 28.48 (*syn*), 31.52 (*anti*), 41.94 (*anti*), 42.34 (*syn*), 56.33 (*syn*), 57.21 (*anti*), 57.36 (*syn*), 58.40 (*anti*), 109.41 (*syn, anti*), 115.40 (2C, *anti*), 115.69 (2C, *syn*), 127.16 (*syn*), 127.20 (2C, *anti*), 127.35 (*anti*), 127.43 (2C, *syn*), 128.43 (2C, *syn*), 128.53 (2C, *anti*), 131.67 (2C, *syn*), 131.74 (2C, *anti*), 140.86 (*syn*), 140.97

(*anti*), 146.03 (*anti*), 146.42 (*syn*), 211.26 (*syn*), 212.77 (*anti*); HRMS (ESI) *m/z* $C_{19}H_{20}BrNO$ $[M+Na]^+$ calcd 380.0620, found 380.0621.



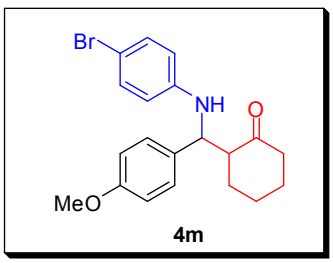
4k

2-[(4-nitrophenyl)(4-bromophenylamino)methyl]-cyclohexanone (4k): 91% yield (0.3675 g) as a yellow solid (*syn*:*anti* = 38:62); m.p. 66-70 ^oC; R_f = 0.16 (20% EtOAc/*n*-hexane); IR (Neat): 3403, 2939, 1706, 1594, 1516, 1346, 814 cm^{-1}; ^1H-NMR (400 MHz, $CDCl_3$): δ 1.50-1.80 (m, 3H, CH_2), 1.89-2.11 (m, 3H, CH_2), 2.28-2.48 (m, 2H, CH_2), 2.79-2.96 (m, 1H, CH), 4.62 (d, 0.64H, *J* = 5.5 Hz, *anti*-CH), 4.79 (d, 0.39H, *J* = 4.0 Hz, *syn*-CH), 6.36-6.45 (m, 2H, ArH), 7.14-7.19 (m, 2H, ArH), 7.50-7.58 (m, 2H, ArH), 8.16 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.57 (*anti*), 24.88 (*syn*), 26.91 (*syn*), 27.79 (*anti*), 28.92 (*syn*), 32.21 (*anti*), 42.38 (*syn*), 42.50 (*anti*), 55.96 (*syn*), 56.80 (*anti*), 57.32 (*syn*), 58.16 (*anti*), 110.02 (*syn*), 110.20 (*anti*), 115.24 (2C, *anti*), 115.64 (2C, *syn*), 123.68 (2C, *syn*), 123.73 (2C, *anti*), 128.21 (2C, *anti*), 128.55 (2C, *syn*), 131.88 (2C, *syn*), 131.98 (2C, *anti*), 145.52 (*syn*), 145.62 (*anti*), 147.13 (*anti*), 147.17 (*syn*), 148.82 (*syn*), 149.05 (*anti*), 210.57 (*syn*), 211.77 (*anti*); HRMS (ESI) *m/z* $C_{19}H_{19}BrN_2O_3$ $[M+Na]^+$ calcd 425.0471, found 425.0479.



4l

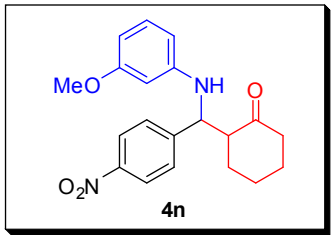
2-[(4-nitrophenyl)(4-fluoro-3-methylphenylamino)methyl]-cyclohexanone (4l): 82% yield (0.2920 g) as a orange vicous oil (*syn*:*anti* = 31:69); R_f = 0.18 (20% EtOAc/*n*-hexane); IR (Neat): 3457, 2937, 1706, 1516, 1345, 1217, 855 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.51-1.82 (m, 4H, CH_2), 1.90-2.00 (m, 2H, CH_2), 2.12 (brs, 3H, Me), 2.30-2.45 (m, 2H, CH_2), 2.77-2.85 (m, 1H, CH), 4.61 (d, 0.82H, *J* = 5.5 Hz, *anti*-CH), 4.78 (d, 0.29H, *J* = 4.5 Hz, *syn*-CH), 6.18-6.25 (m, 1H, ArH), 6.30-6.35 (m, 1H, ArH), 6.71 (t, 1H, *J* = 9.0 Hz, ArH), 7.55 (d, 2H, *J* = 8.5 Hz, ArH), 8.16 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 14.72 (d, *J* = 3.0 Hz, *syn*-, *anti*-Me-F), 24.47 (*anti*), 24.90 (*syn*), 27.00 (*syn*), 27.75 (*anti*), 28.79 (*syn*), 32.00 (*anti*), 40.40 (*syn*), 42.39 (*anti*), 56.21 (*syn*), 57.01 (*anti*), 57.78 (*syn*), 58.46 (*anti*), 111.61 (d, *J* = 7.0 Hz, *anti*-C-F), 112.20 (d, *J* = 7.0 Hz, *syn*-C-F), 115.14 (d, *J* = 23 Hz, *syn*-C-F), 115.22 (d, *J* = 23 Hz, *anti*-C-F), 116.38 (d, *J* = 4.0 Hz, *anti*-C-F), 116.96 (d, *J* = 4.0 Hz, *syn*-C-F), 123.60 (2C, *syn*), 123.64 (2C, *anti*), 125.20 (d, *J* = 18.0 Hz, *syn*-C-F), 125.30 (d, *J* =18 Hz, *anti*-C-F), 128.23 (2C, *anti*), 128.49 (2C, *syn*), 142.71 (d, *J* = 3.0 Hz, *anti*-C-F, *syn*, *anti*), 147.04 (d, *J* = 3.0 Hz, *syn*-C-F), 149.49 *(syn)*, 149.78 (*anti*), 154.73 (d, *J* = 234 Hz, *anti*-C-F), 154.90 (d, *J* = 234 Hz, *syn*-C-F), 210.66 (*syn*), 211.78 (*anti*); HRMS (ESI) *m/z* $C_{20}H_{21}FN_2O_3$ $[M+Na]^+$ calcd 379.1428, found 379.1430.



4m

2-[(4-methoxyphenyl)(4-bromophenylamino)methyl]-cyclohexanone (4m): 76% yield (0.2940 g) as a yellow oil (*syn*:*anti* = 25:75); R_f = 0.34 (20% EtOAc/*n*-hexane); IR (Neat): 3391, 2934, 1702, 1594, 1510, 1247, 1177, 1033, 814, 503 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.47-1.65 (m, 3H, CH_2), 1.70-1.91 (m, 3H, CH_2), 2.20-2.39 (m, 2H, CH_2), 2.58-

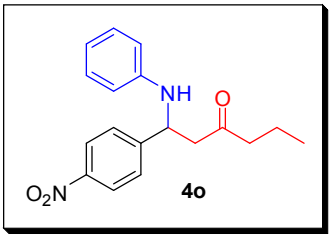
2.66 (m, 1H, CH), 3.70 (s, 3H, OMe), 4.42 (d, 0.77H, *J* = 7.0 Hz, *anti*-CH), 4.58 (d, 0.28H, *J* = 4.0 Hz, *syn*-CH), 6.30-6.36 (m, 2H, ArH), 6.73-6.79 (m, 2H, ArH), 7.03-7.09 (m, 2H, ArH), 7.14-7.19 (m, 2H, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 23.66 (*anti*), 24.73 (*syn*), 26.84 (*syn*), 27.85 (*anti*), 28.75 (*syn*), 31.27 (*anti*), 41.80 (*anti*), 42.34 (*syn*), 55.15 (*syn*, *anti*-OMe), 56.31 (*syn*), 56.92 (*syn*), 57.43 (*anti*), 57.54 (*anti*), 109.08 (*anti*), 109.25 (*syn*), 113.76 (2C, *syn*), 113.89 (2C, *anti*), 115.26 (2C, *anti*), 115.62 (2C, *syn*), 128.17 (2C, *anti*), 128.52 (2C, *syn*), 131.65 (2C, *syn*, *anti*), 132.53 (syn), 132.99 (*anti*), 146.27 (*anti*), 146.50 (*syn*), 158.59 (*syn*), 158.69 (*anti*), 211.55 (*syn*), 212.90 (*anti*); HRMS (ESI) *m/z* $C_{20}H_{22}BrNO_2$ $[M+Na]^+$ calcd 410.0732, found 410.0728.



4n

2-[(4-nitrophenyl)(3-methoxyphenylamino)methyl]-cyclohexanone (4n): 29% yield (0.1016 g) as a yellow oil (*syn*:*anti* = 34:66); R_f = 0.19 (20% EtOAc/*n*-hexane); IR (Neat): 3392, 2938, 1706, 1598, 1518, 1346, 1210, 1163, 855, 736, 702, 689 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.53-1.67 (m, 3H, CH_2), 1.68-1.85 (m, 2H, CH_2), 1.88-1.98 (m, 1H, CH_2), 2.27-2.47 (m, 2H, CH_2), 2.79-2.88 (m, 1H, CH), 3.69 (s, 3H, OMe), 4.68 (d, 0.65H, *J* = 5.0 Hz, *anti*-CH), 4.82 (d, 0.45H, *J* = 4.0 Hz, *syn*-CH), 6.03 (t, 1H, *J* = 2.0 Hz, ArH), 6.12 (brd, 1H, *J* = 7.5 Hz, ArH), 6.23 (ddd, 1H, *J* = 2.0, 5.0, 7.5 Hz, ArH), 6.99 (td, 1H, *J* = 2.0, 8.0 Hz, ArH), 7.53-7.58 (m, 2H, ArH), 8.15 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 24.44 (*anti*), 24.89 (*syn*), 26.97 (*syn*), 27.75 (*anti*), 29.16 (*syn*), 32.04 (*anti*), 42.39 (*syn*, *anti*), 54.98 (*syn*, *anti*-OMe), 56.07 (*syn*), 56.97 (*anti*), 57.25 (*syn*), 57.79 (*anti*), 99.67 (*anti*), 100.23 (*syn*), 103.00 (*anti*), 103.33 (*syn*), 106.51 (*anti*), 107.02 (*syn*), 123.60 (2C, *syn*),

123.66 (2C, *anti*), 128.14 (2C, *anti*), 128.58 (2C, *syn*), 129.91 (*syn*), 130.02 (*anti*), 147.01 (*syn*), 147.06 (*anti*), 148.00 (*syn*), 148.07 (*anti*), 149.41 (*syn*), 149.79 (*anti*), 160.61 (*syn*), 160.70 (*anti*), 210.60 (*syn*), 211.79 (*anti*); HRMS (ESI) *m/z* $C_{20}H_{22}BrN_2O_4$ $[M+Na]^+$ calcd 377.1477, found 377.1482.

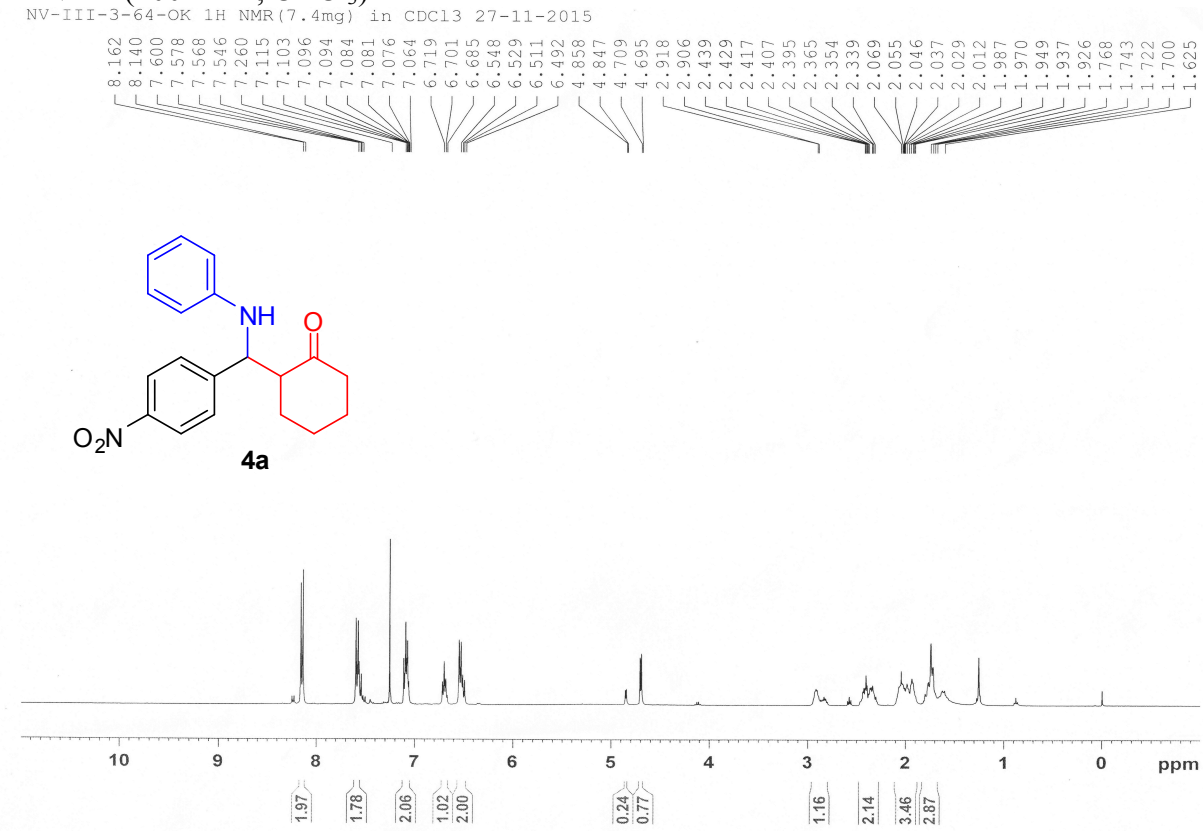


1-(4-nitroyphenyl)(phenylamino)hexan-3-one (4o): 24% yield (0.0749 g) as a yellow oil; R_f = 0.34 (20% EtOAc/*n*-hexane); IR (Neat): 3395, 2963, 1709, 1602, 1519, 1345, 750, 694 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J* = 7.0 Hz), 1.55 (hex, 2H, *J* = 7.0 Hz, CH_2), 2.31-2.38 (m, 2H, CH_2), 2.94 (d, 2H, *J* = 6.0 Hz, CH_2), 4.93 (t, 1H, *J* = 6.0 Hz, CH), 6.49 (d, 2H, *J* = 7.5 Hz, ArH), 6.70 (t, 1H, *J* = 7.5 Hz, ArH), 7.10 (t, 2H, *J* = 7.5 Hz, ArH), 7.56 (d, 2H, *J* = 8.5 Hz, ArH), 8.17 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 13.54, 16.88, 45.53, 49.58, 53.89, 113.78 (2C), 118.46, 124.04 (2C), 127.36 (2C), 129.26 (2C), 146.16, 147.25, 150.54, 208.42; HRMS (ESI) *m/z* $C_{18}H_{20}N_2O_3$ $[M+Na]^+$ calcd 313.1552, found 313.1550.

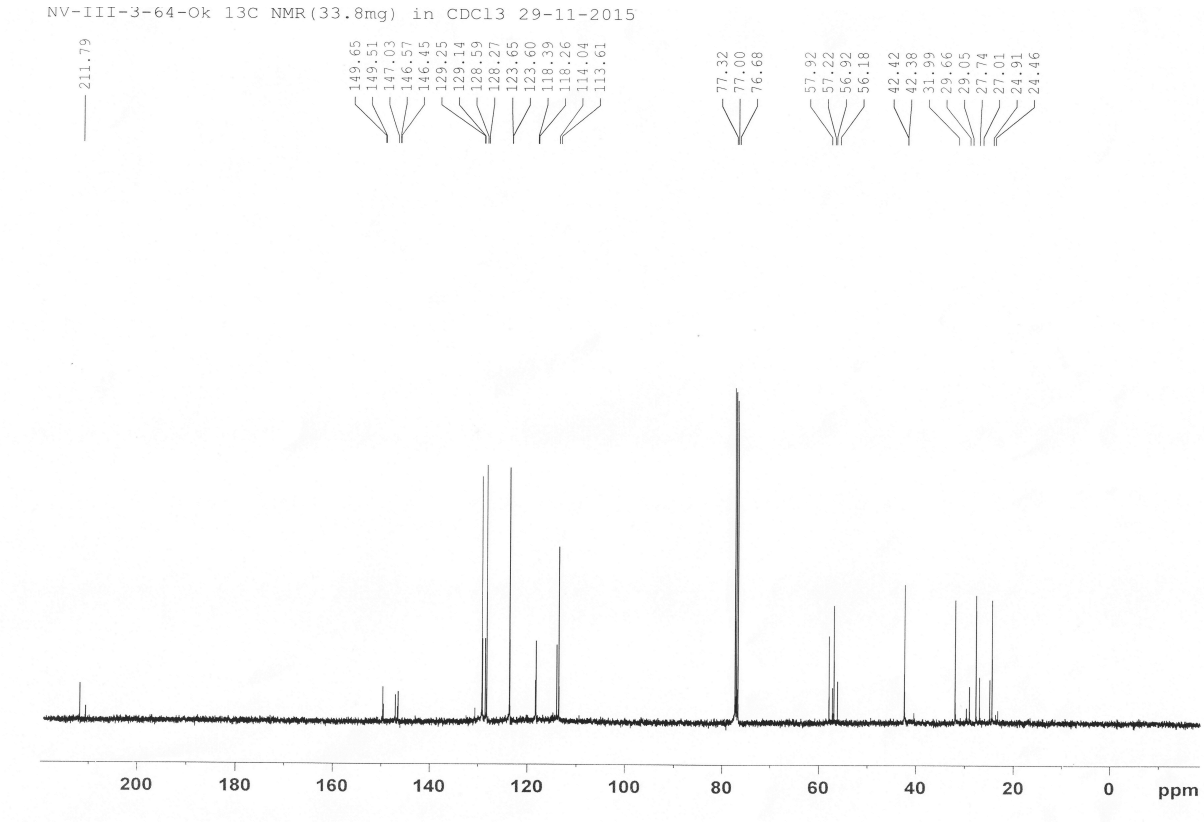
^{1}H and ^{13}C NMR spectra of *β*-amino carbonyl compounds

2-[(4-nitrophenyl)(phenylamino)methyl]-cyclohexanone (4a):

^{1}H-NMR (400 MHz, $CDCl_3$)

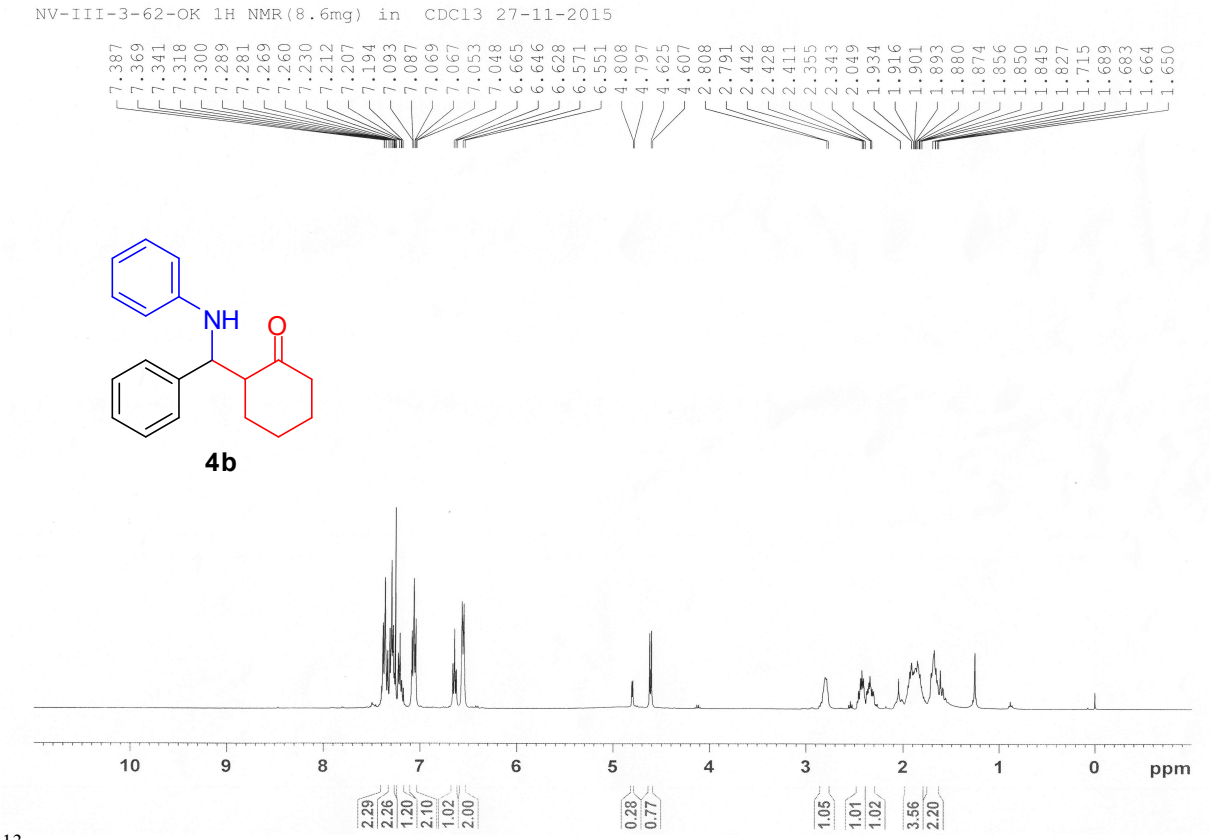


^{13}C-NMR (100 MHz, $CDCl_3$)

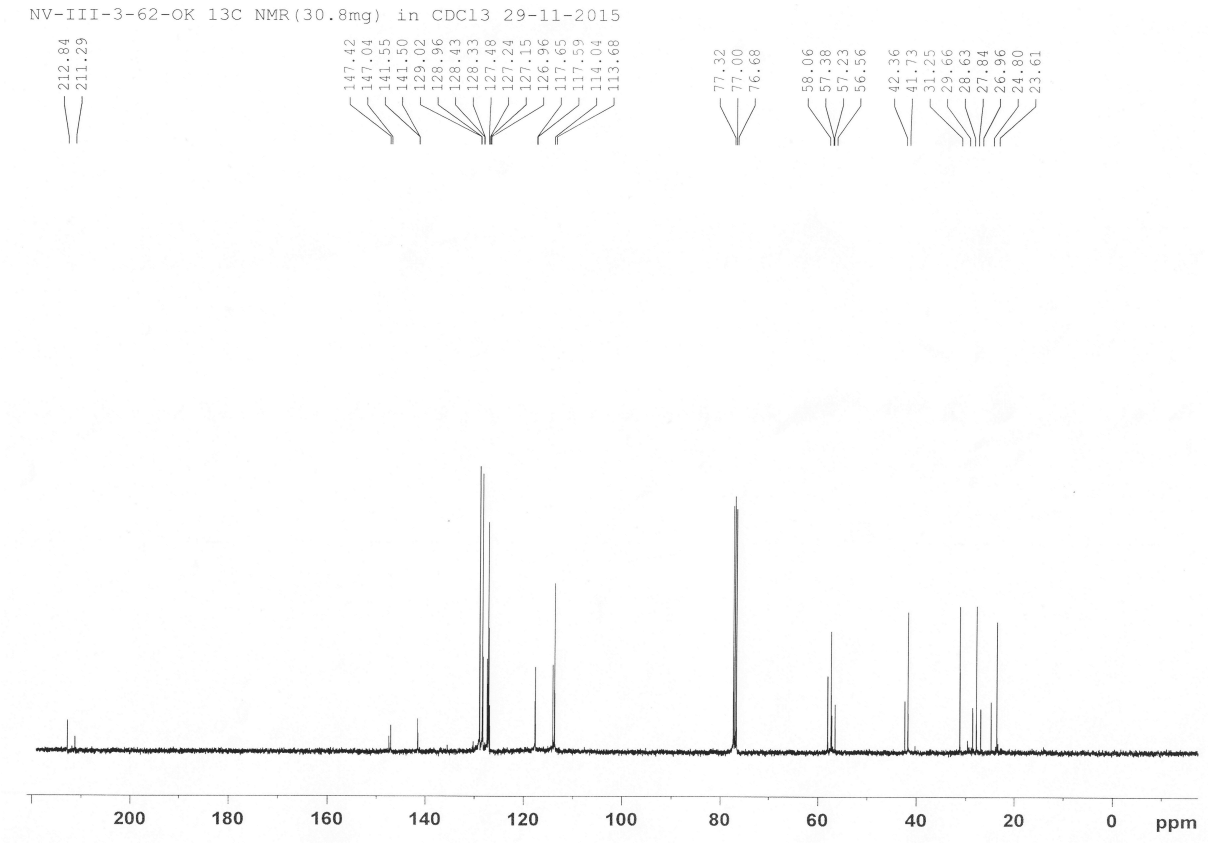


2-[phenyl(phenylamino)methyl]-cyclohexanone (4b):

^{1}H-NMR (400 MHz, $CDCl_3$)

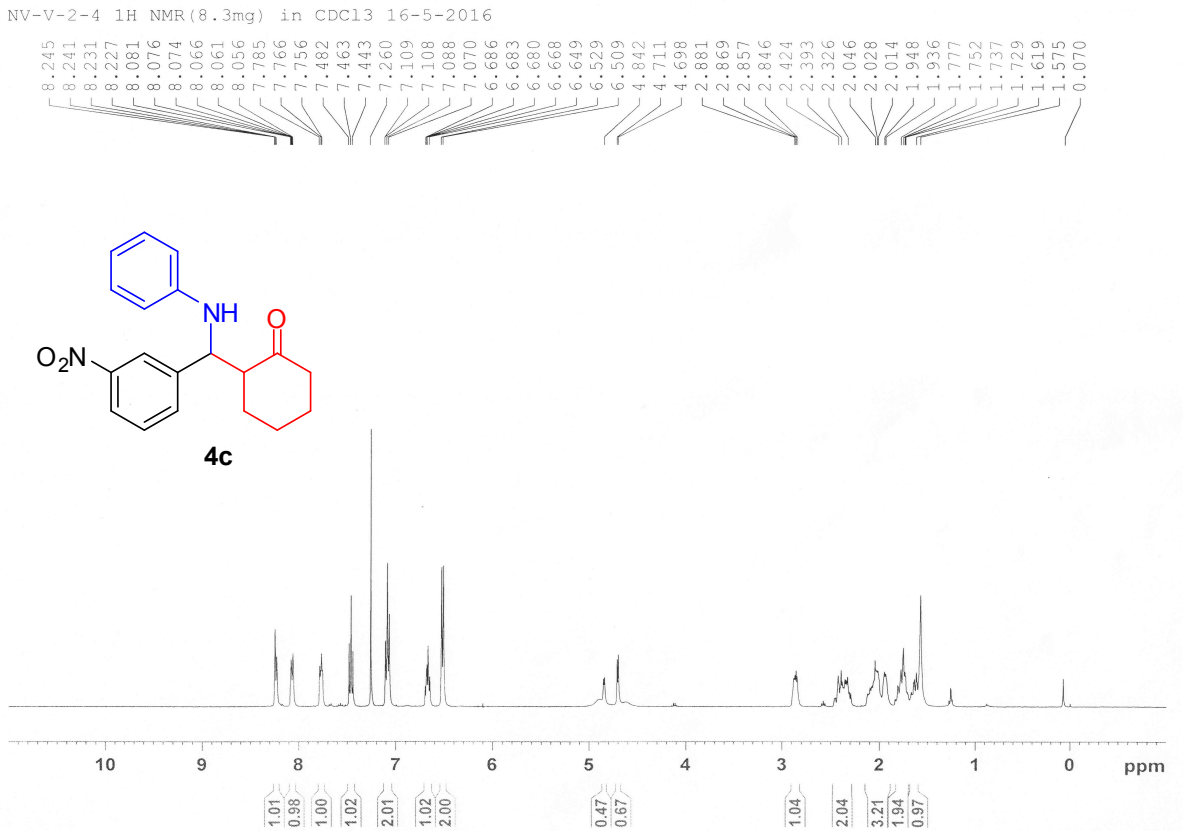


^{13}C-NMR (100 MHz, $CDCl_3$)

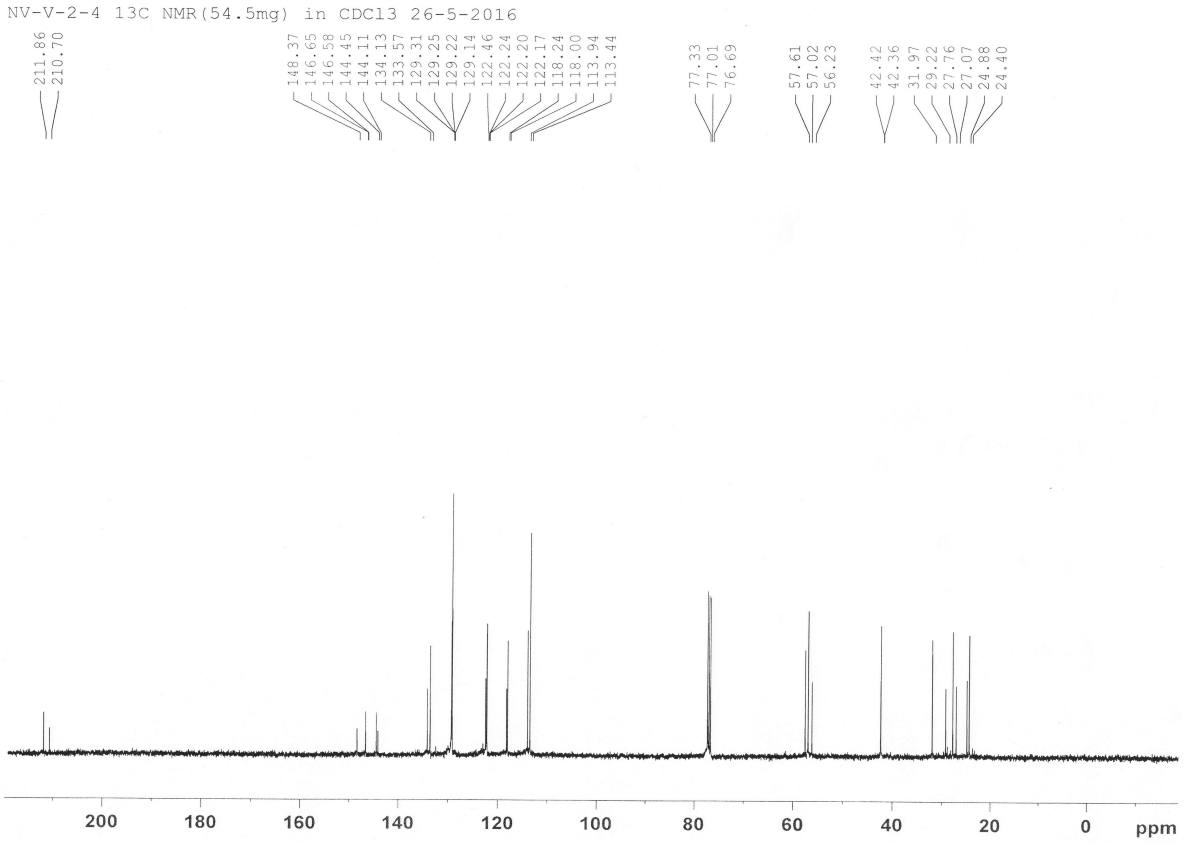


2-[(3-nitrophenyl)(phenylamino)methyl]-cyclohexanone (4c):

^{1}H-NMR (400 MHz, $CDCl_3$)

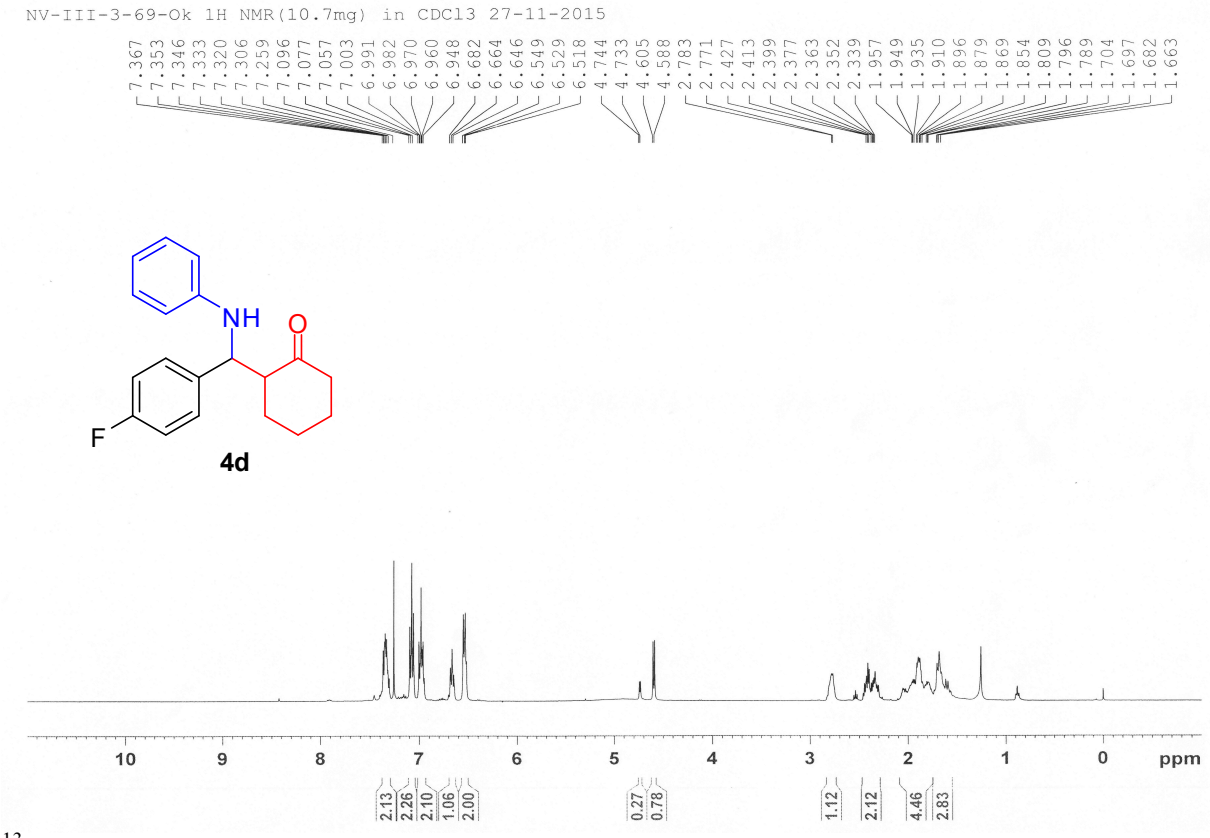


^{13}C-NMR (100 MHz, $CDCl_3$)

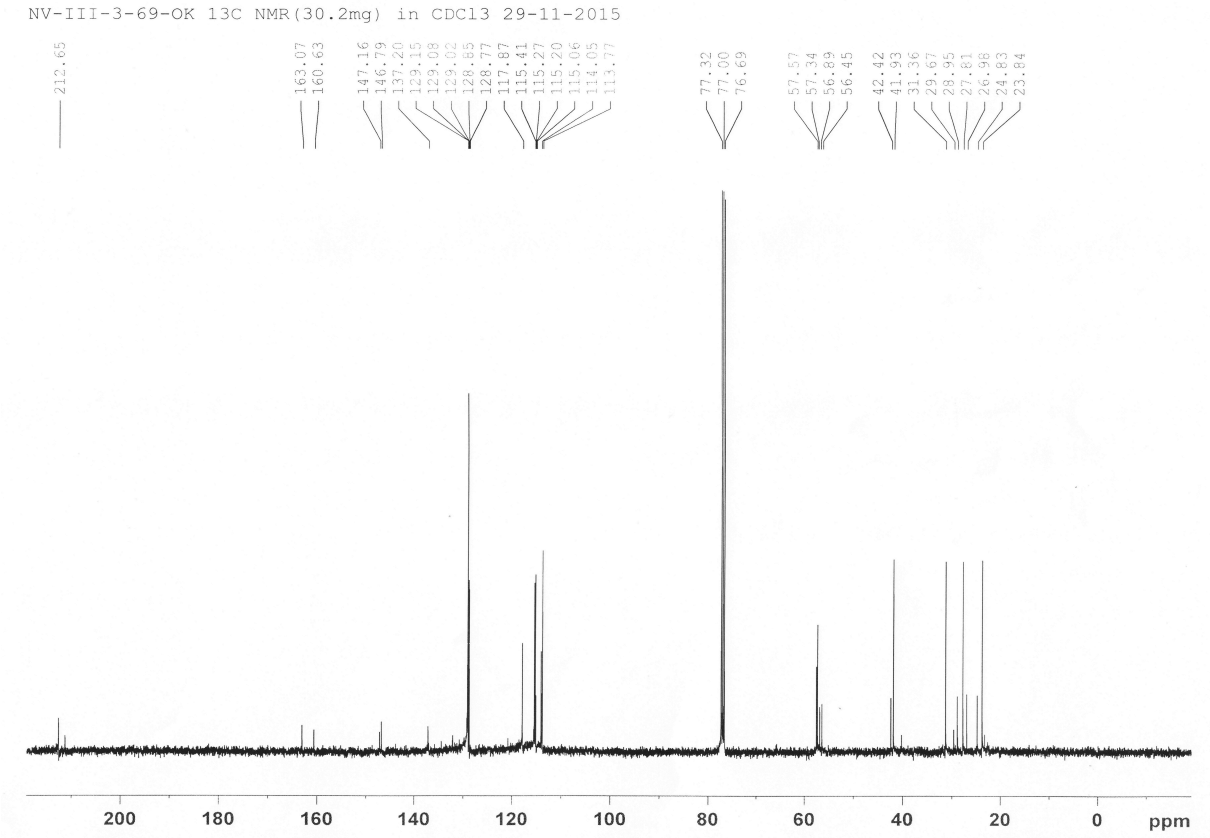


2-[(4-fluorophenyl)(phenylamino)methyl]-cyclohexanone (4d):

^{1}H-NMR (400 MHz, $CDCl_3$)

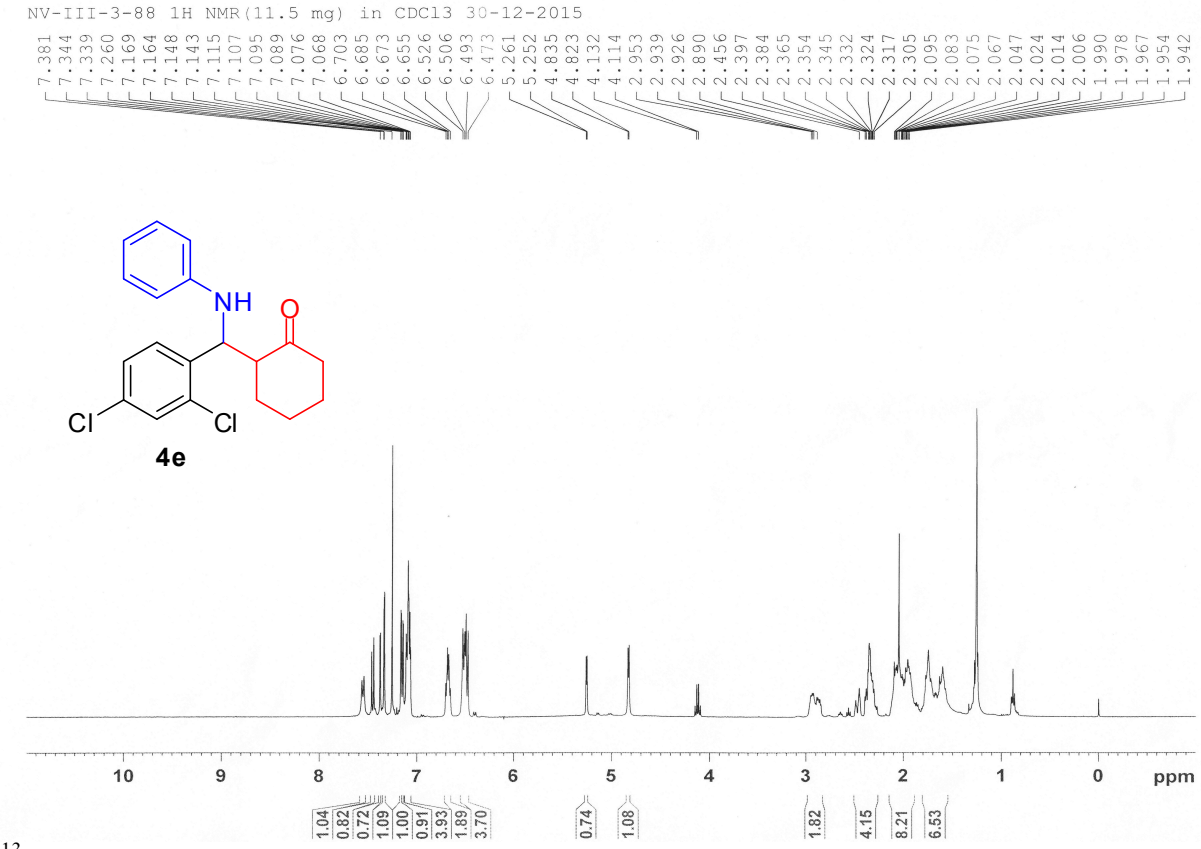


^{13}C-NMR (100 MHz, $CDCl_3$)

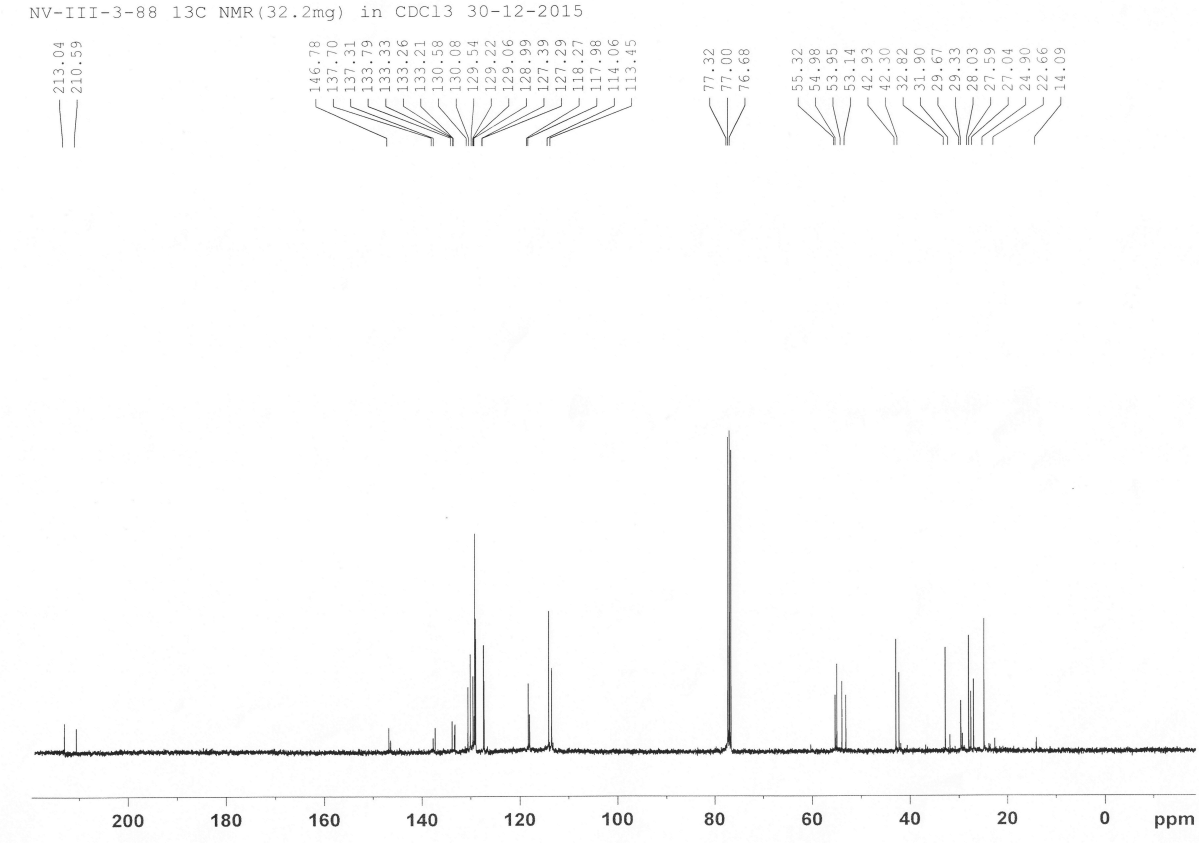


2-[(2,4-dichlorophenyl)(phenylamino)methyl]-cyclohexanone (4e):

^{1}H-NMR (400 MHz, $CDCl_3$)

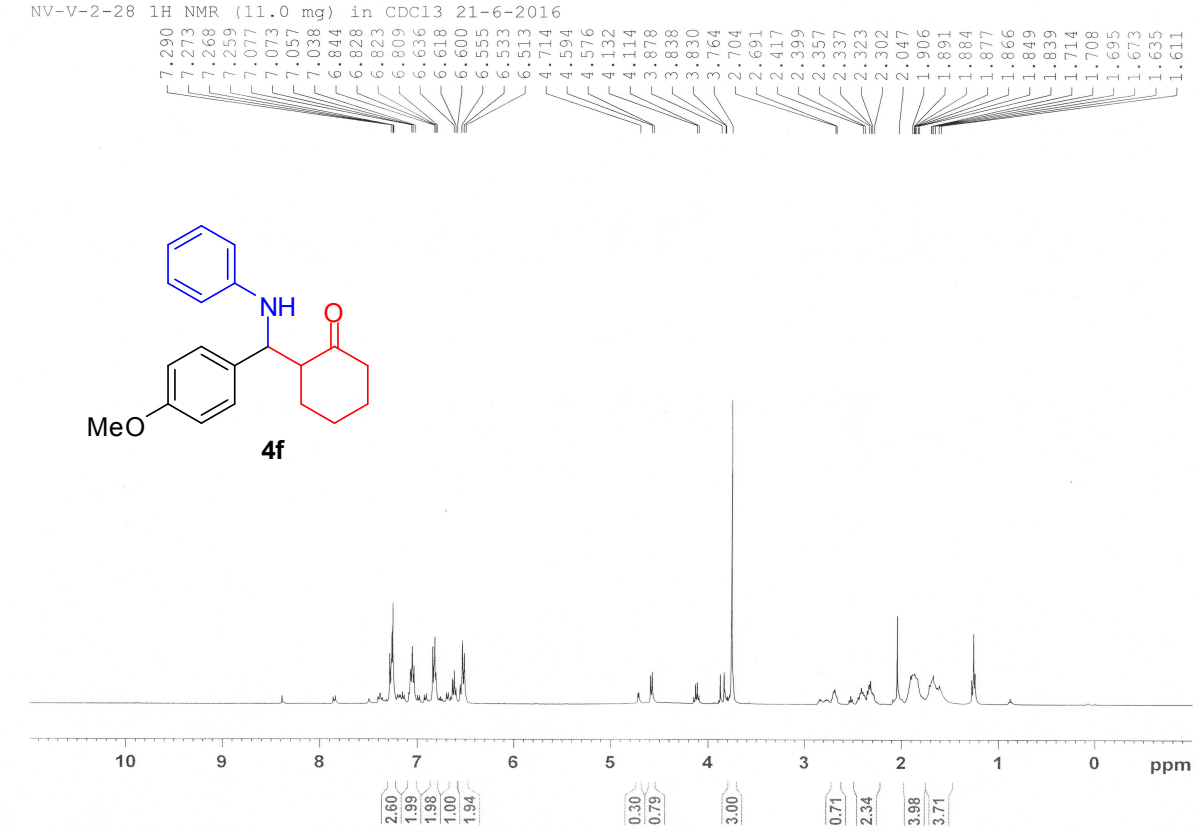


^{13}C-NMR (100 MHz, $CDCl_3$)

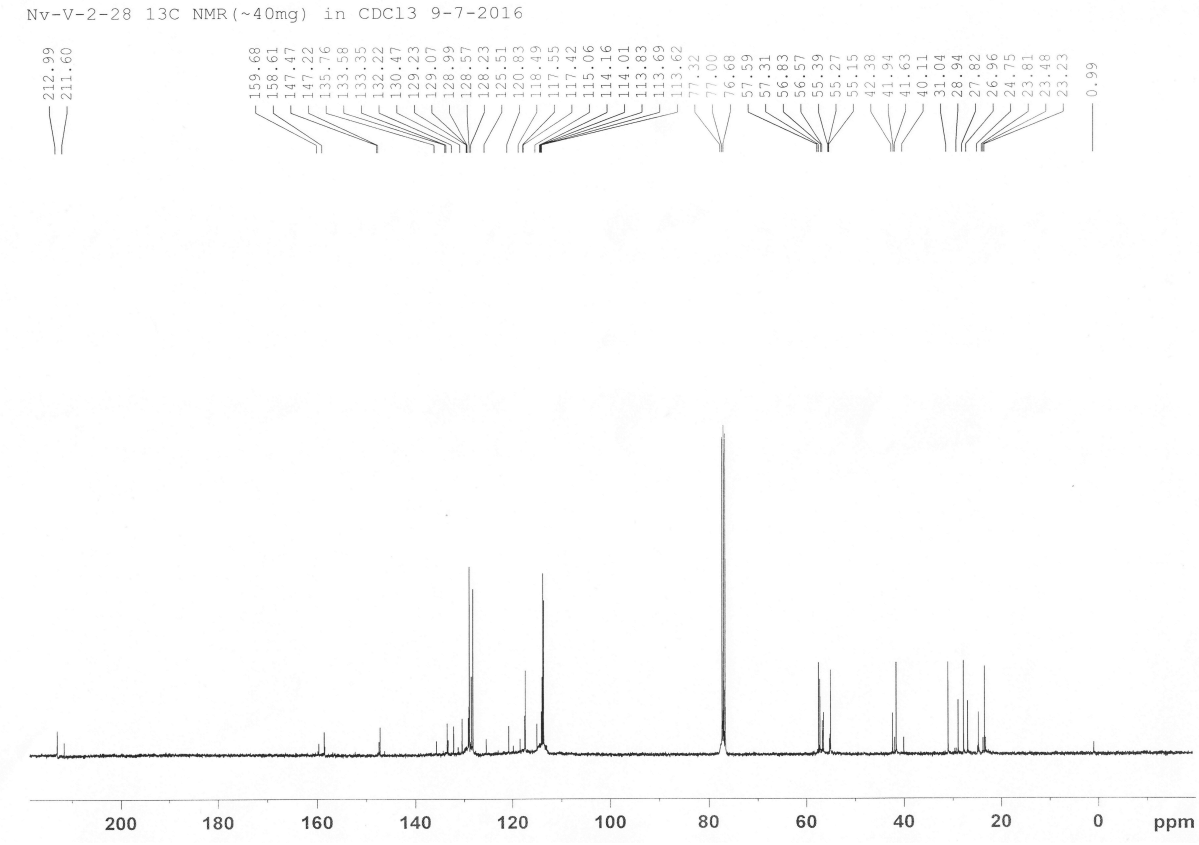


2-[(4-methoxyphenyl)(phenylamino)methyl]-cyclohexanone (4f):

^{1}H-NMR (400 MHz, $CDCl_3$)

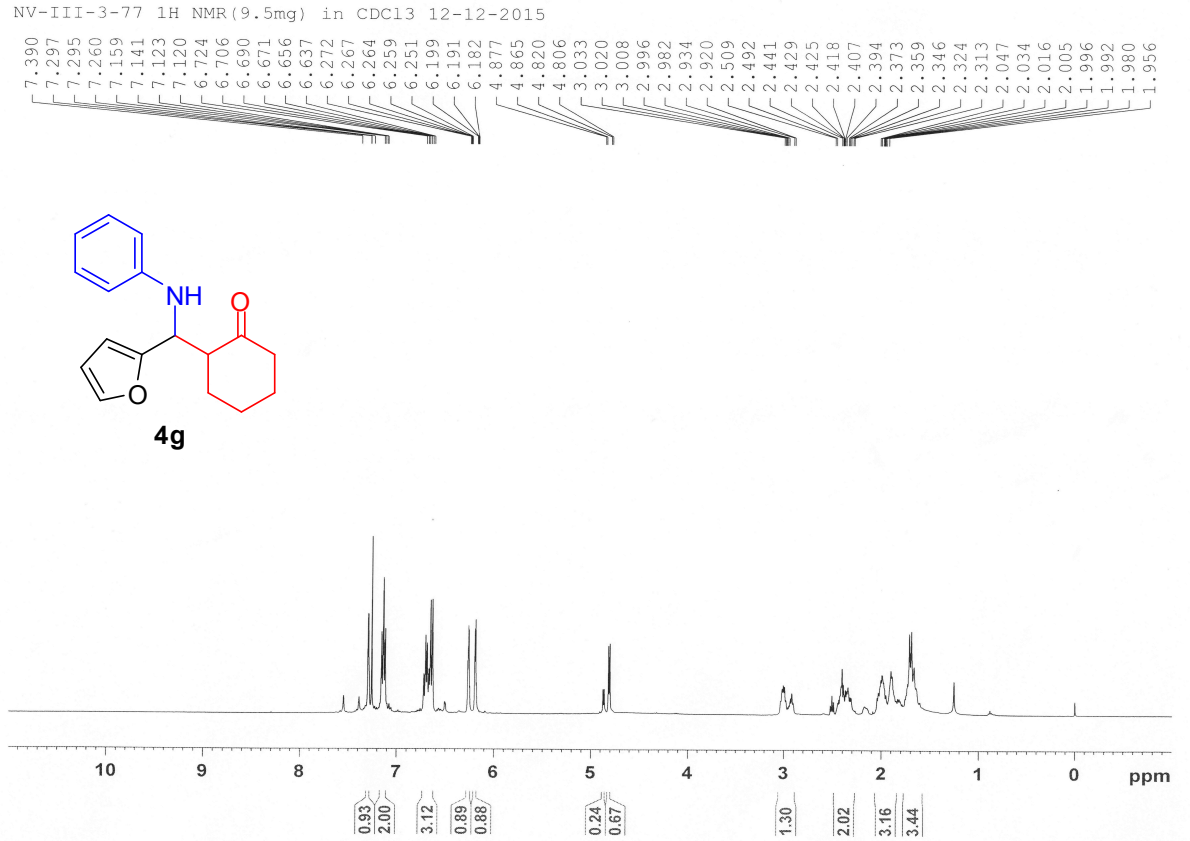


^{13}C-NMR (100 MHz, $CDCl_3$)

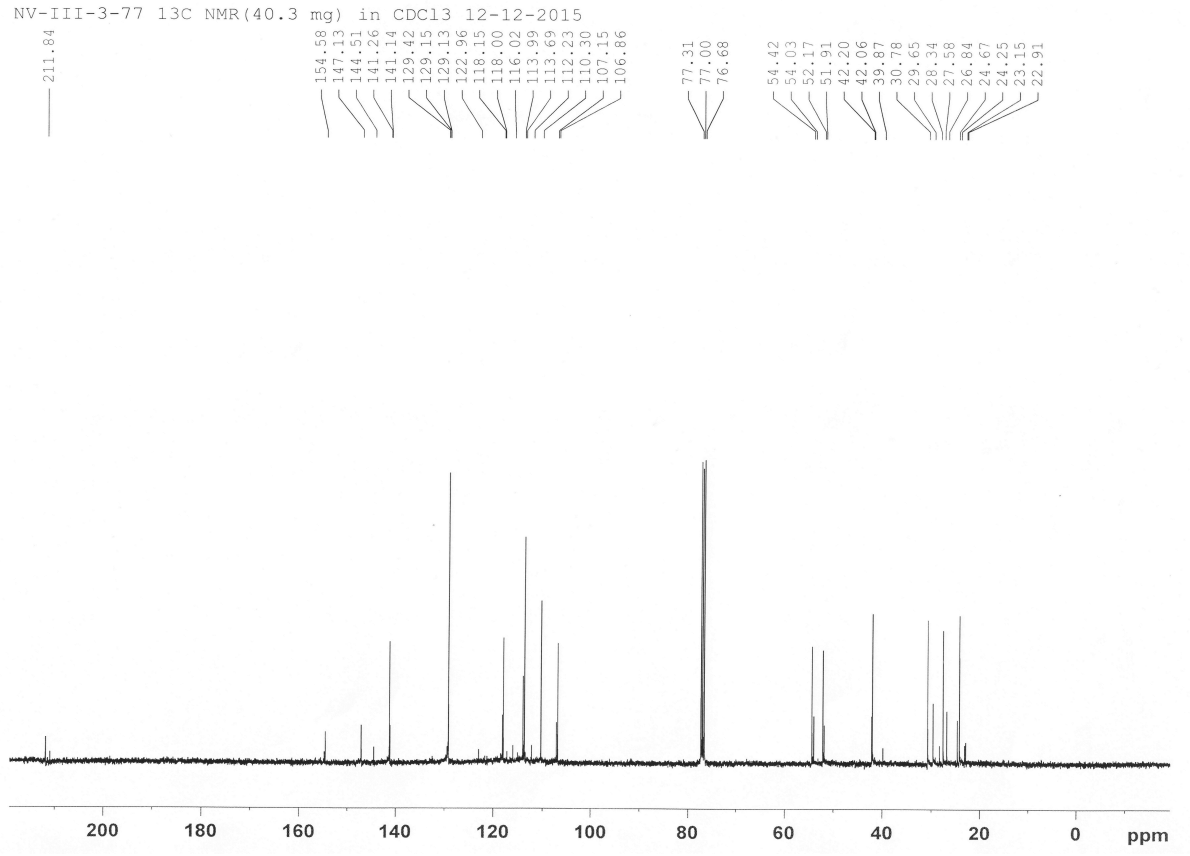


2-[(Furan-2-yl)(phenylamino)methyl]-cyclohexanone (4g):

^{1}H-NMR (400 MHz, $CDCl_3$)

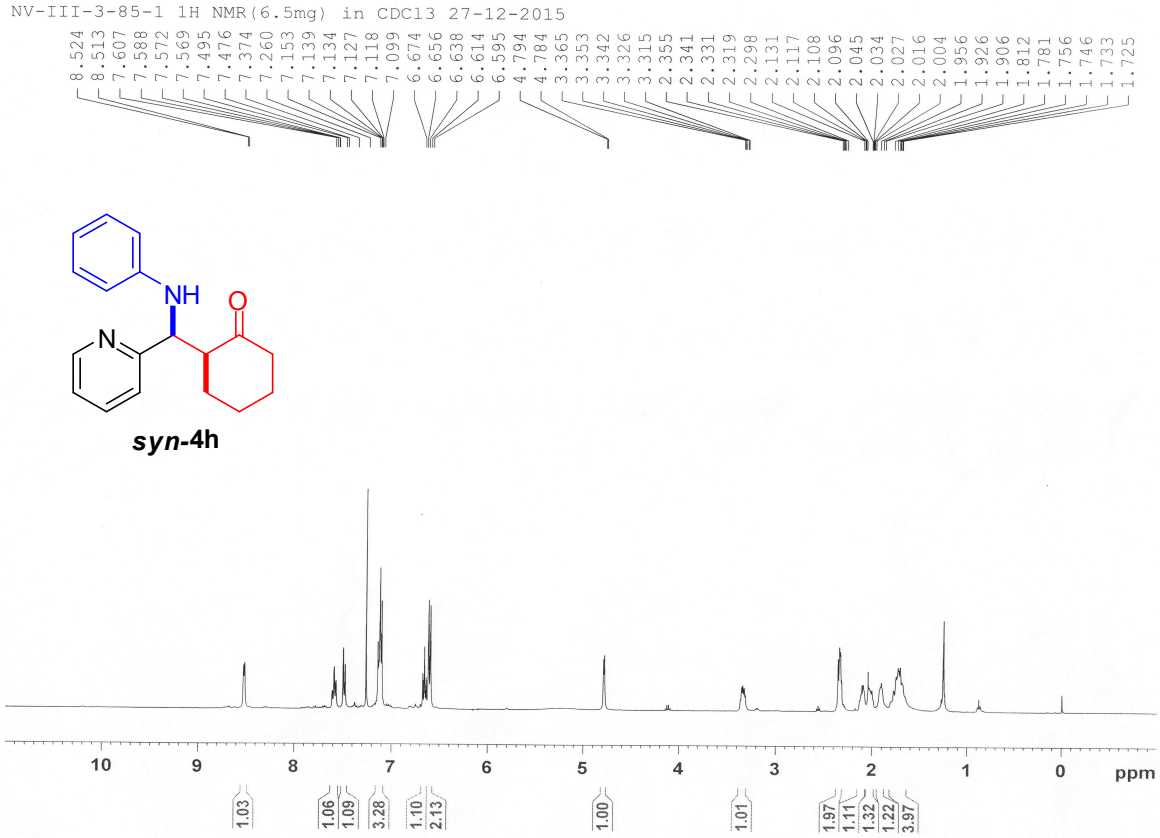


^{13}C-NMR (100 MHz, $CDCl_3$)

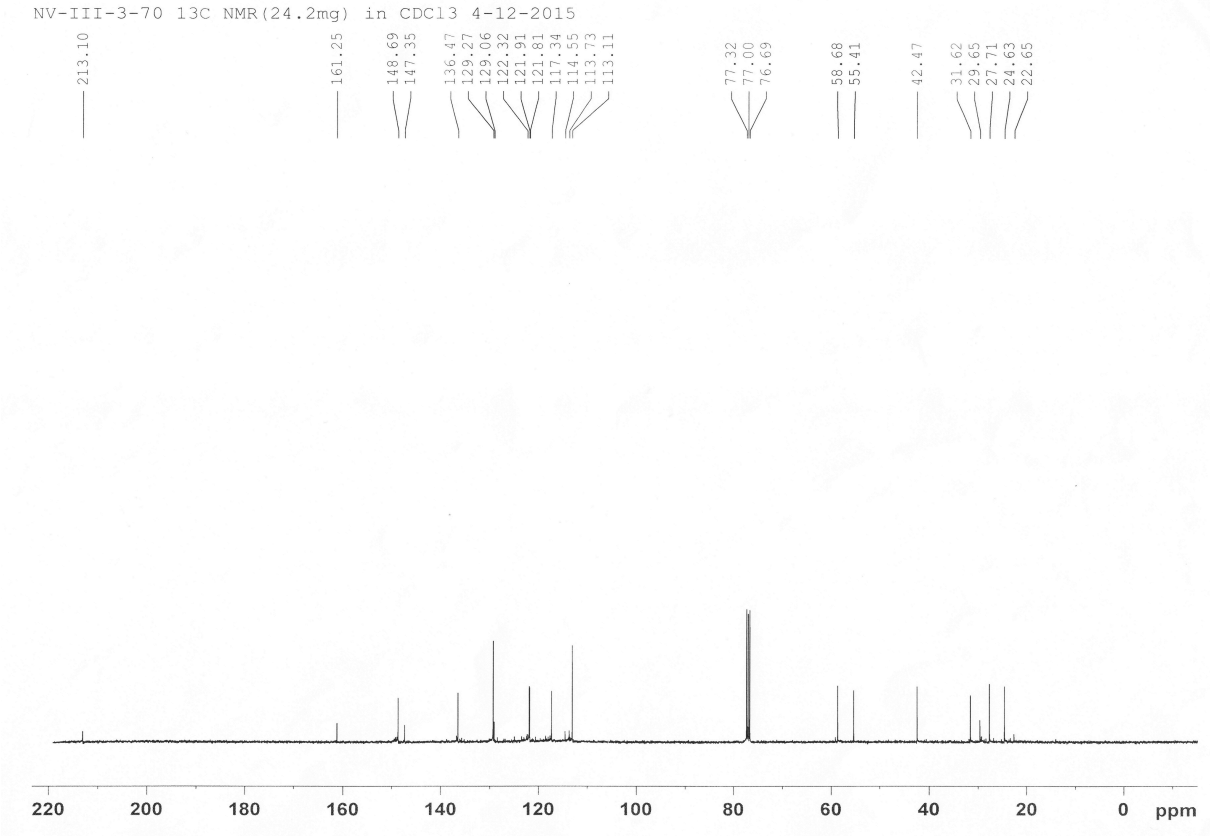


syn-2-[(pyridin-2-yl)(phenylamino)methyl]-cyclohexanone (_syn_-4h):

^{1}H-NMR (400 MHz, $CDCl_3$)

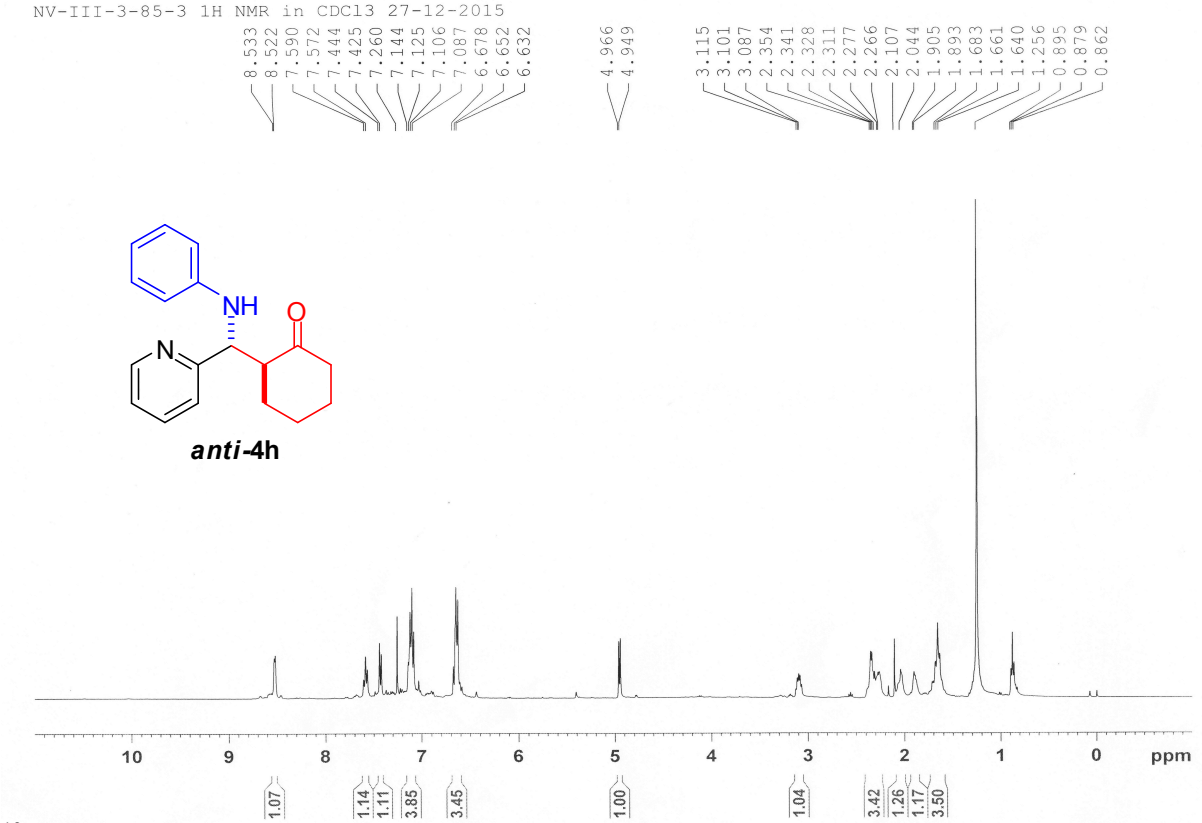


^{13}C-NMR (100 MHz, $CDCl_3$)

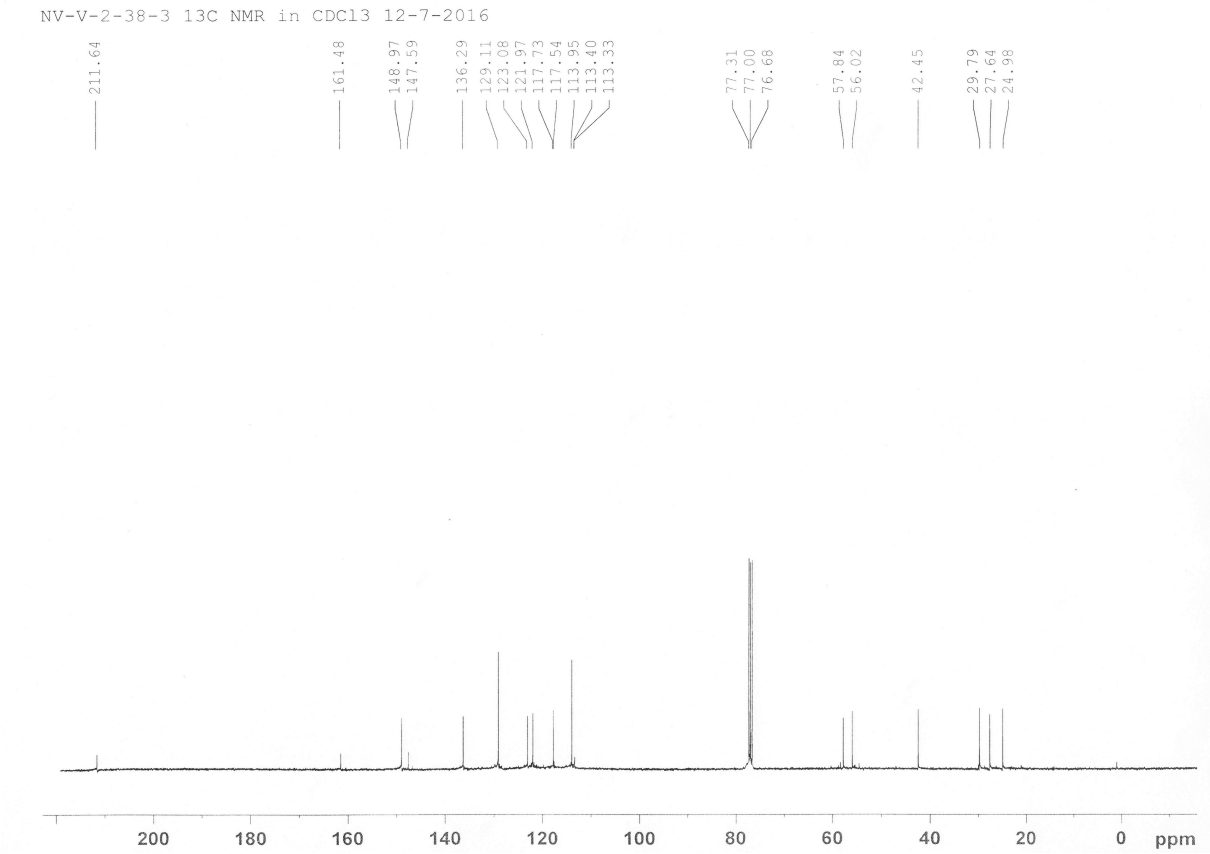


anti-2-[(pyridin-2-yl)(phenylamino)methyl]-cyclohexanone (_anti_-4h):

^{1}H-NMR (400 MHz, $CDCl_3$)

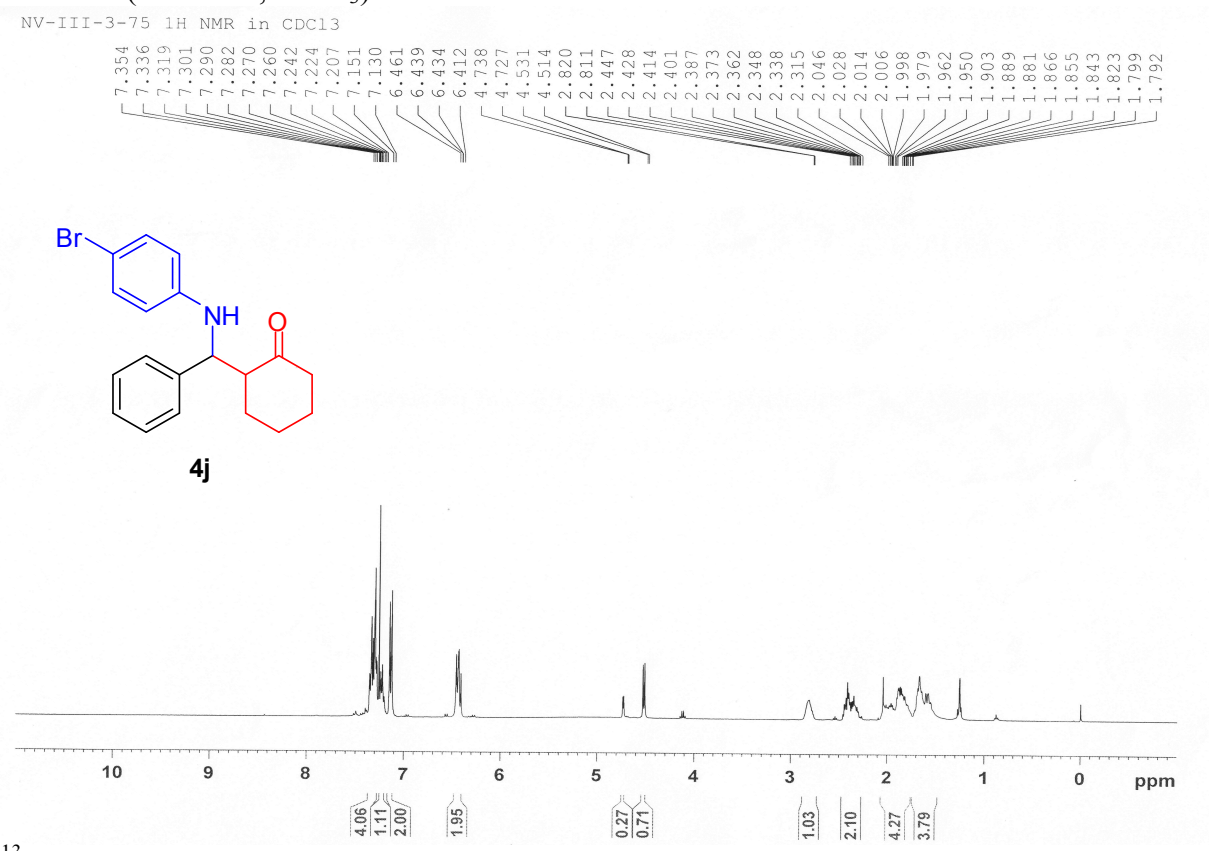


^{13}C-NMR (100 MHz, $CDCl_3$)

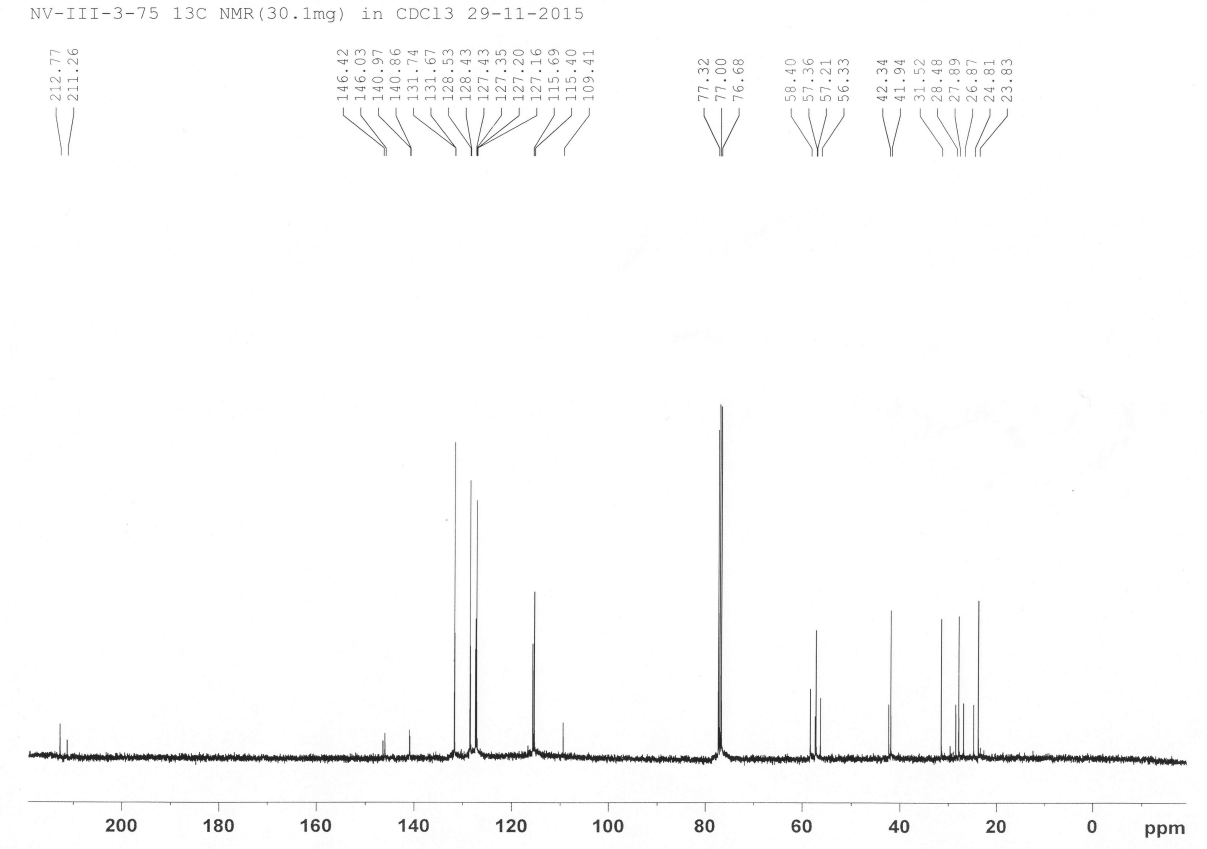


2-[(phenyl)(4-bromophenylamino)methyl]-cyclohexanone (4j):

^{1}H-NMR (400 MHz, $CDCl_3$)

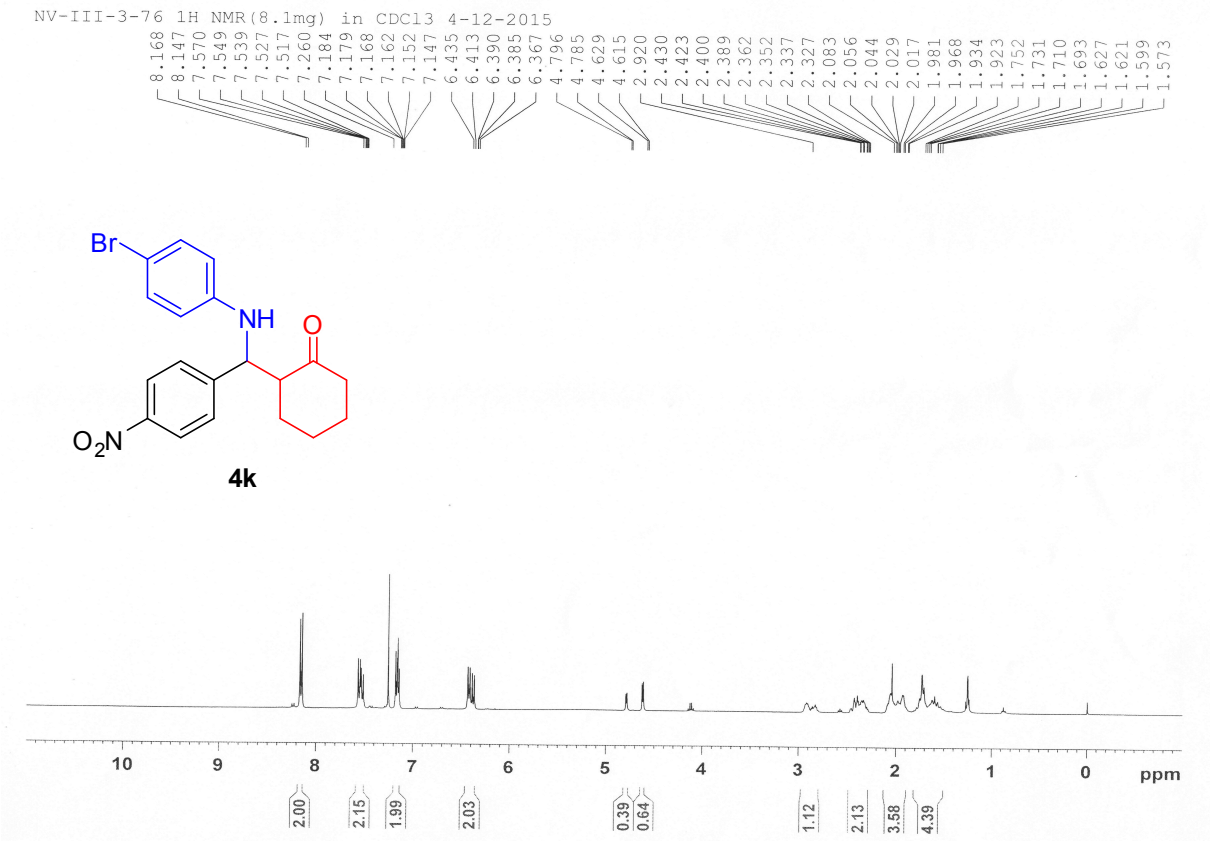


^{13}C-NMR (100 MHz, $CDCl_3$)

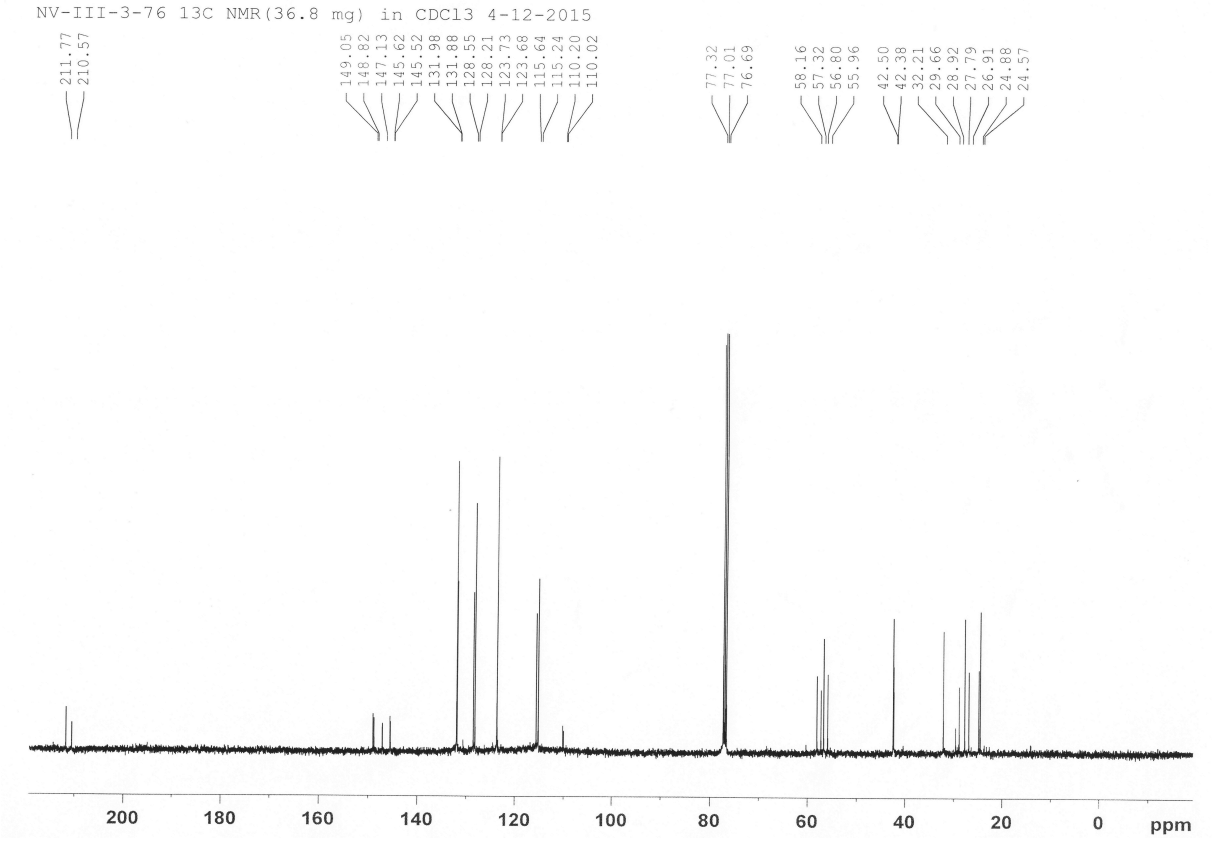


2-[(4-nitrophenyl)(4-bromophenylamino)methyl]-cyclohexanone (4k):

^{1}H-NMR (400 MHz, $CDCl_3$)

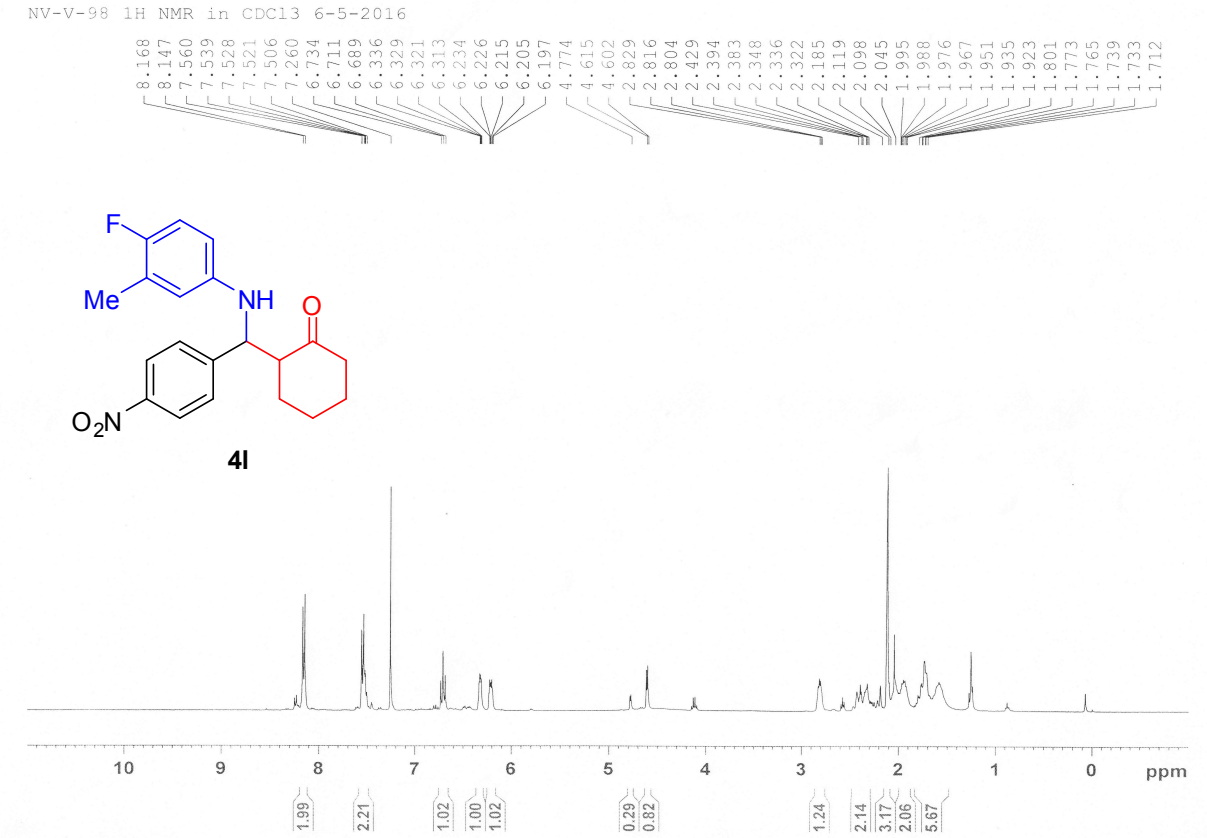


^{13}C-NMR (100 MHz, $CDCl_3$)

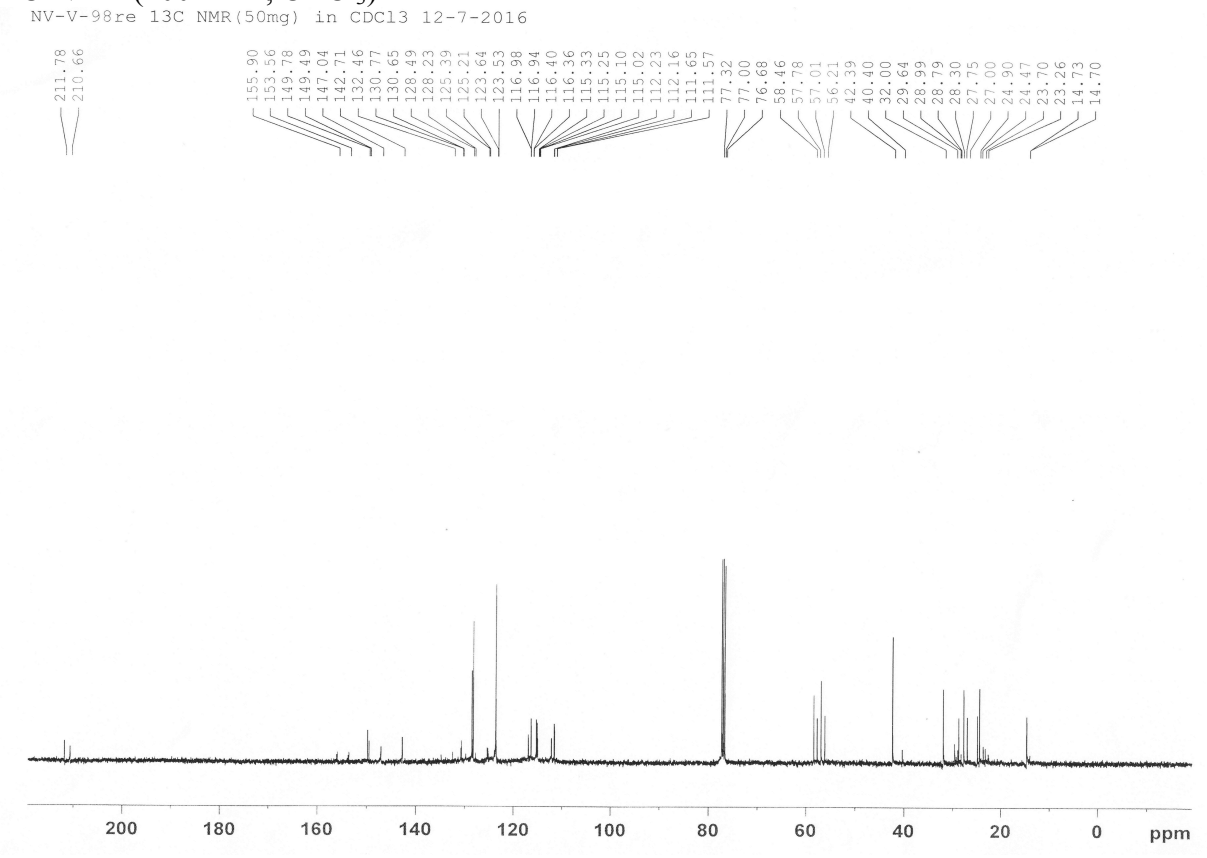


2-[(4-nitrophenyl)(4-fluoro-3-methylphenylamino)methyl]-cyclohexanone (4l):

^{1}H-NMR (400 MHz, $CDCl_3$)

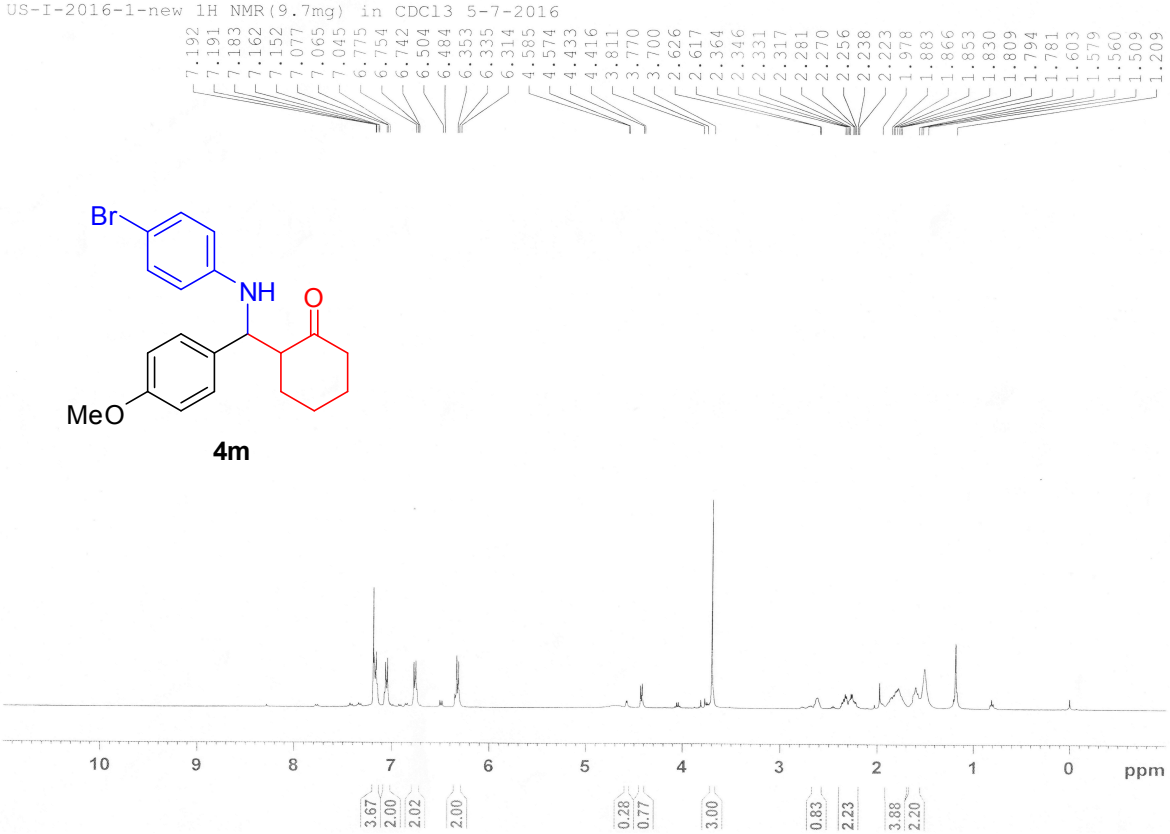


^{13}C-NMR (100 MHz, $CDCl_3$)

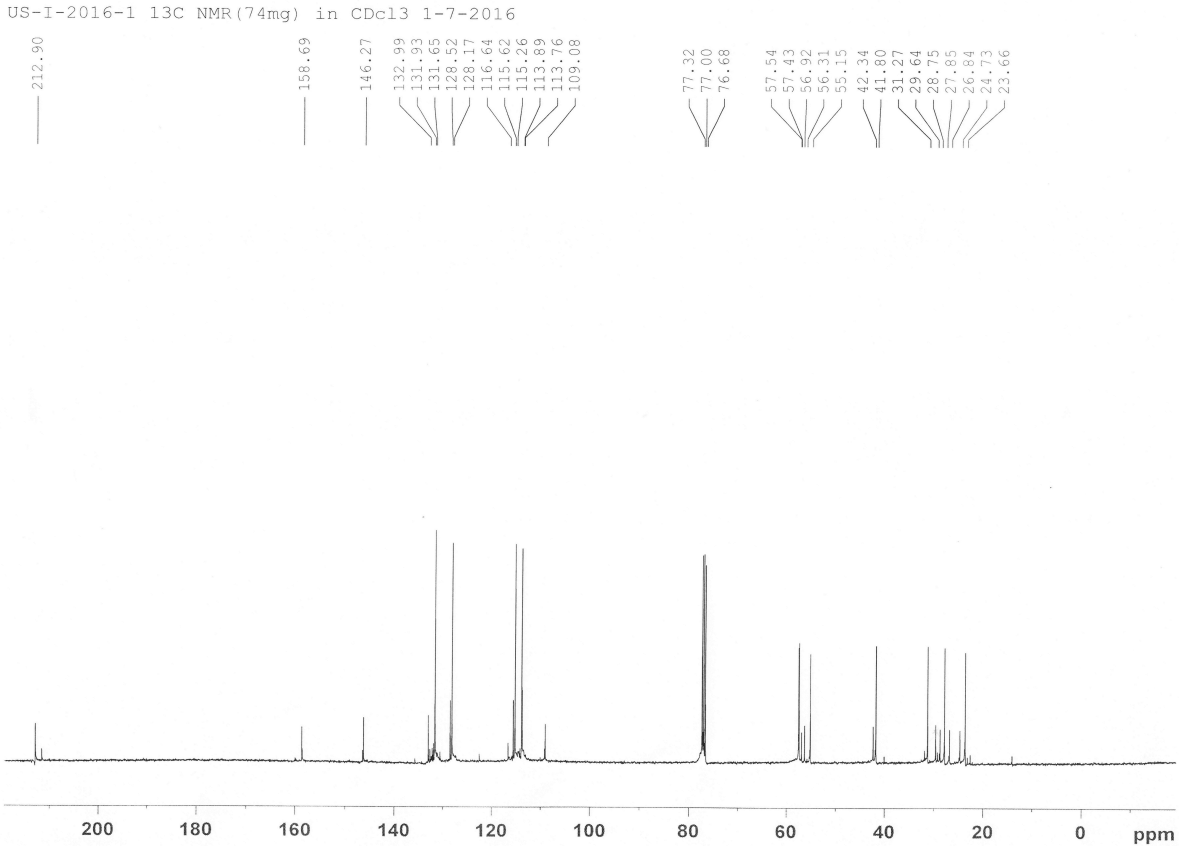


2-[(4-methoxyphenyl)(4-bromophenylamino)methyl]-cyclohexanone (4m):

^{1}H-NMR (400 MHz, $CDCl_3$)

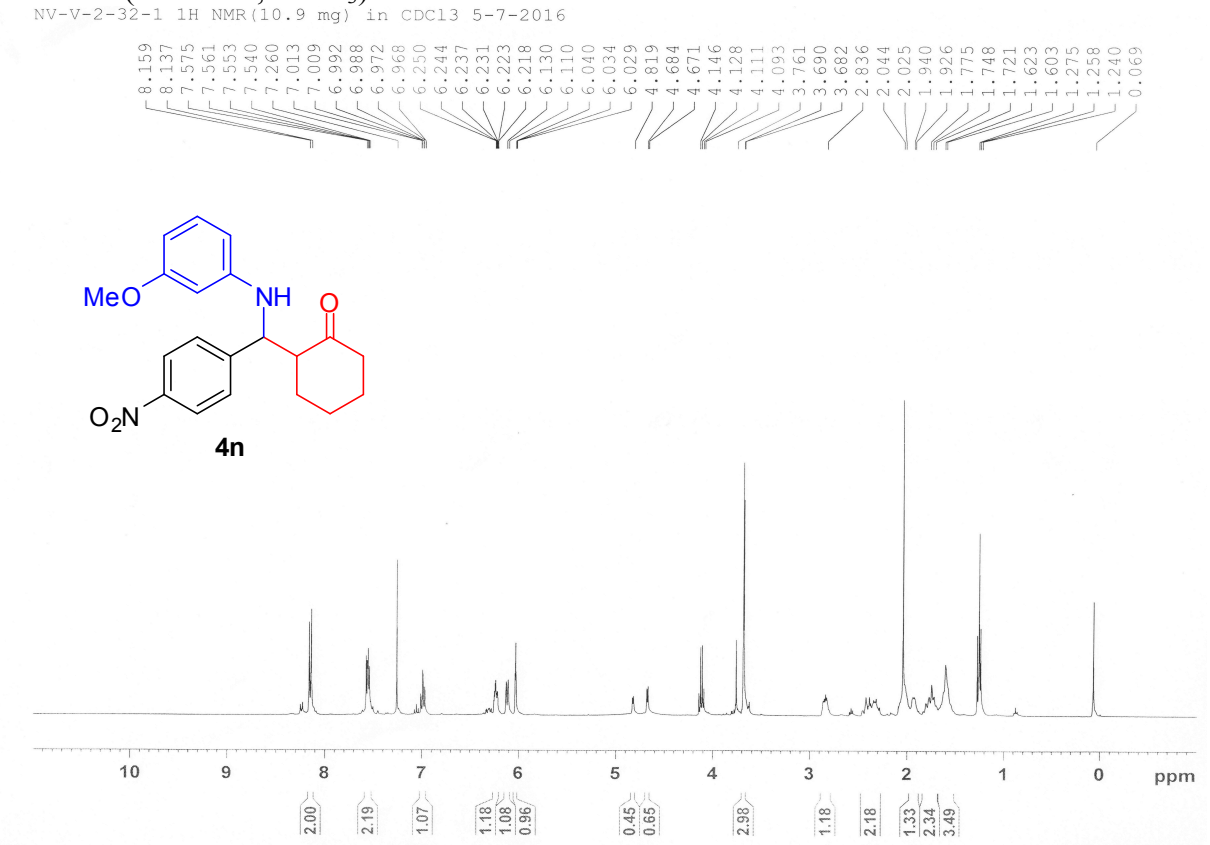


^{13}C-NMR (100 MHz, $CDCl_3$)

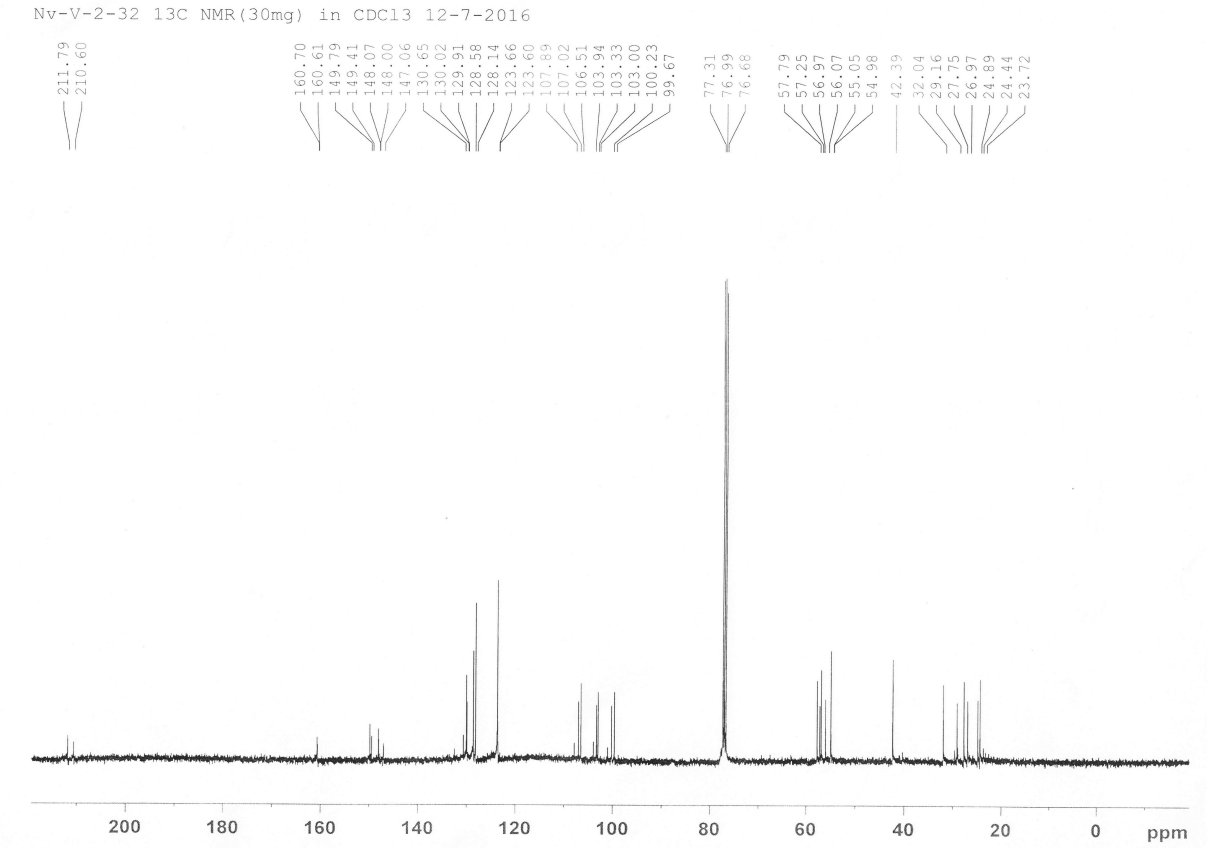


2-[(4-nitrophenyl)(3-methoxyphenylamino)methyl]-cyclohexanone (4n):

^{1}H-NMR (400 MHz, $CDCl_3$)

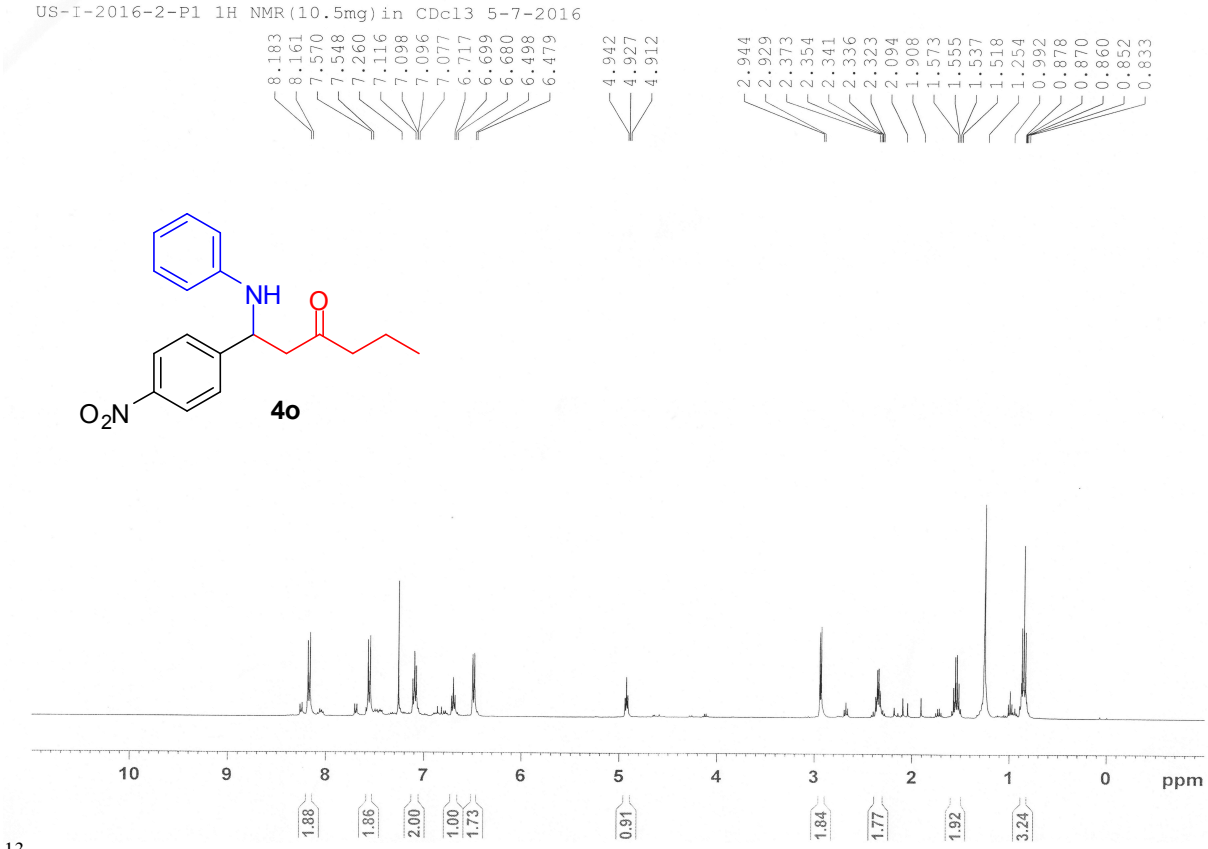


^{13}C-NMR (100 MHz, $CDCl_3$)



1-(4-nitroyphenyl)(phenylamino)hexan-3-one (4o):

^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (100 MHz, $CDCl_3$)