Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Cu(I)-Catalyzed Amidation/Imidation of *N*-Arylglycine Ester Derivatives via C-N Coupling under Mild conditions

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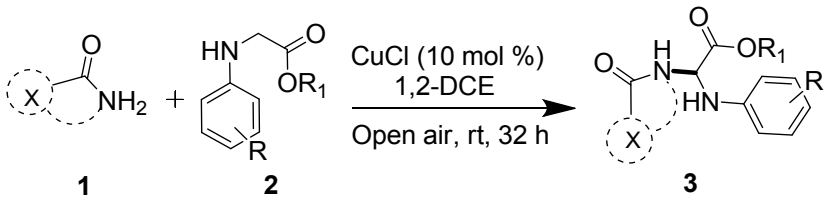
1. General information

All commercially available chemicals were used as received. Purification of products was carried out by column chromatography using commercial column chromatography grade silica gel (60-120 & 100-200 mesh) and a mixture of ethyl acetate and hexane as eluting agent. The ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ solvent. ^{1}H spectra were recorded on 300, 400 and 500 MHz spectrometers and ^{13}C NMR spectra were recorded on 75, 100 and 125 MHz spectrometers with tetramethylsilane and chloroform-d as the internal reference respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal for $CDCl_3$ (δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR) and for DMSO-d6 (δ = 2.50 for ^{1}H NMR and δ = 39.0 for ^{13}C NMR). Data for ^{1}H NMR are reported as follows: chemical shift (multiplicity, coupling constant, number of hydrogens). Multiplicity is abbreviated as follows: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), m (multiplet). Mass spectra were carried out using Quattro LC triple-quadrupole mass spectrometer (Micromass, Manchester, UK). High-resolution mass spectra were determined using Quadrupole time-of-flight (Q-TOF) mass spectrometer (QSTARXL, Applied Biosystems/MDS Sciex, Foster city, USA).

2. Experimental procedure

General procedure for the copper catalyzed direct C-N bond reaction between *N*-aryl glycine esters 2 and amide/imide/carbamates (1, 4): A mixture of *N*-aryl glycine esters **2** (1 mmol), amide/imide/carbamate (1 mmol) and CuCl (0.1 mmol, 10 mol %) in a DCE (2 mL) solvent was stirred under open air reaction at room temperature until the reaction was completed. The resulting mixture was concentrated under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate as an eluent) to afford the desired coupling products **3a**-**3zb** and **5b**.

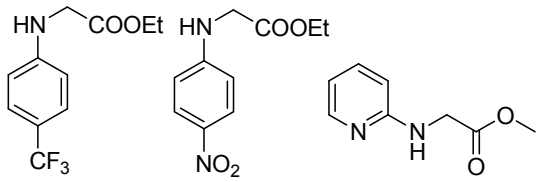
3. Substrates resistant to C-N coupling



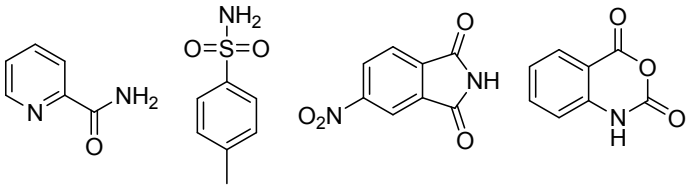
1 **2** **3**

The following carbon- and nitrogen- partners found to be resistant to the C-N coupling under standard reaction conditions.

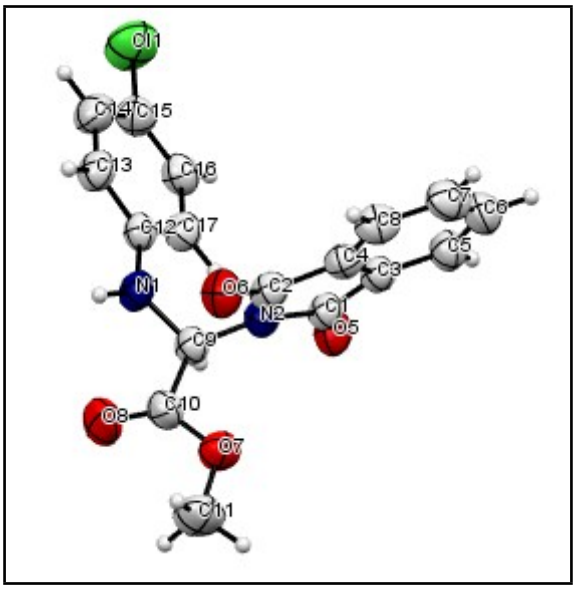
C- partner



N- partner



4. X-ray crystal analysis of product 3e



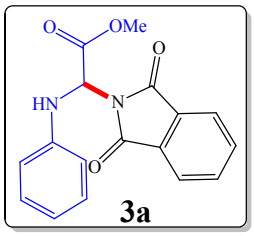
ORTEP diagram of compound **3e**

CCDC No. 1576573 (**3e**) contains the supplementary crystallographic data for this paper. The crystal data can be obtained free of charge from the Cambridge Crystallographic Data Centre through www.ccdc.cam.ac.uk/data_request/cif.

Table: Crystallographic data of compound **3e**

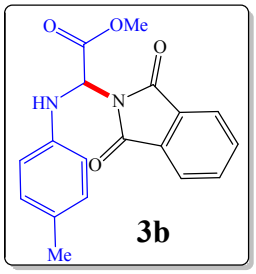
CCDC number	1576573
Empirical formula	$C_{17}H_{13}N_2O_4Cl$
Formula weight	344.76
Temperature (K)	150
Crystal system	Triclinic
Space group	P-1
a/Å	10.1754(7)
b/Å	13.7004(8)
c/Å	13.8309(10)
α/°	119.490(7)
β/°	102.929(6)
γ/°	92.342(5)
Volume (Å^3)	1609.7(2)
Z	4
ρ_{calc}/mg mm^{-3}	1.4255
Absorption coefficient (μ/mm^{-1})	2.321
F(000)	715.8
Reflections collected	10894
R_{int}	0.0231
GOF on F^2	1.146
R_1 ($I>2\sigma(I)$)	0.0468
wR_2 ($I>2\sigma(I)$)	0.1497
R_1 values (all data)	0.0570
R_2 values (all data)	0.1676

5. Spectral data of all compounds



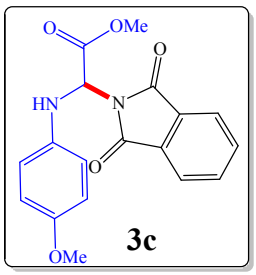
3a

(R)-methyl 2-(1,3-dioxoisoindolin-2-yl)-2-(phenylamino)acetate **3a:** Brown solid 52 % yield; m.p 65-67; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.88-7.83 (m, 2H), 7.77-7.71 (m, 2H), 7.20-7.16 (m, 3H), 6.83-6.76 (m, 2H), 6.25-6.23 (d, *J* = 9.2 Hz, 1H), 5.33-5.30 (d, *J* = 9.2 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.9, 167.4, 143.7, 134.2, 132.6, 131.6, 129.4, 123.5, 119.6, 113.7, 59.7, 53.6; ESI-MS m/z 311 $[M+H]^+$.



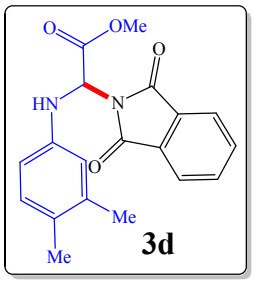
3b

(R)-methyl 2-(1,3-dioxoisoindolin-2-yl)-2-(p-tolylamino)acetate **3b:** Yellow solid 85 % yield; m.p 129-131; ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.84- 7.82 (m, 2H), 7.72-7.71 (m, 2H), 6.99-6.98 (d, *J* = 8.2 Hz, 2H), 6.74-6.72 (d, *J* = 8.5 Hz, 2H), 6.22-6.20 (d, *J* = 9.6 Hz, 1H), 5.18-5.16 (d, *J* = 9.6 Hz, 1H), 3.82 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.6, 167.4, 141.3, 134.3, 131.6, 129.9, 128.9, 123.6, 123.5, 113.9, 60.1, 53.5, 20.3; ESI-MS m/z 347 $[M+Na]^+$.



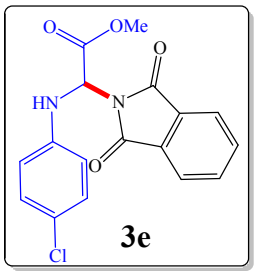
3c

(R)-methyl 2-(1,3-dioxoisoindolin-2-yl)-2-((4-methoxyphenyl)amino)acetate **3c:** Brown solid 81 % yield; m.p 98-100; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.88-7.82 (m, 2H), 7.77-7.71 (m, 2H), 6.79-6.74 (m, 4H), 6.17-6.15 (d, *J* = 9.9 Hz, 2H), 5.07-5.05 (d, *J* = 9.9 Hz, 2H), 3.82 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.6, 167.4, 153.5, 137.5, 134.3, 134.2, 131.5, 123.6, 123.5, 115.4, 114.8, 60.9, 55.5, 53.5;



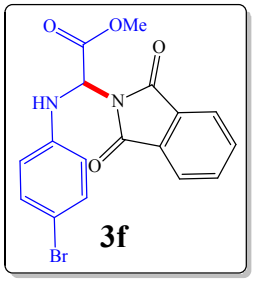
3d

(R)-methyl 2-((3,4-dimethylphenyl)amino)-2-(1,3-dioxoisoindolin-2-yl)acetate **3d:** Yellow solid 80 % yield; m.p 115-117; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.88-7.82 (m, 2H), 7.76-7.70 (m, 2H), 6.94-6.92 (d, *J* = 8.1 Hz, 1H), 6.64-6.63, 6.59- 6.57, 6.23-6.20 (d, *J* = 9.7 Hz, 1H), 5.15-5.13 (d, *J* = 9.7 Hz, 1H), 3.82 (s, 3H), 2.16 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 167.6, 167.4, 141.6, 137.5, 134.2, 131.6, 130.3, 127.5, 123.5, 115.6, 110.9, 60.0, 53.5, 19.8, 18.6;



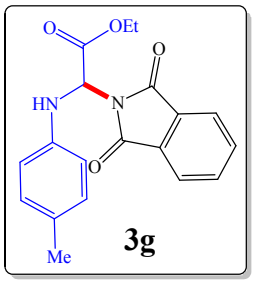
3e

(R)-methyl 2-((4-chlorophenyl)amino)-2-(1,3-dioxoisoindolin-2-yl)acetate **3e:** White solid 79 % yield; m.p 133-135; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.88-7.84 (m, 2H), 7.77-7.73 (m, 2H), 7.14-7.11 (d, *J* = 8.8 Hz, 2H), 6.76-6.74 (d, *J* = 8.9 Hz, 2H), 6.18-6.15 (d, *J* = 9.2 Hz, 1H), 5.34-5.31 (d, *J* = 9.2 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.8, 167.3, 142.3, 134.5, 134.2, 132.6, 131.5, 129.3, 124.4, 123.8, 123.5, 121.0, 114.9, 59.6, 53.7; ESI-MS m/z 345 $[M+H]^+$; HRMS (ESI) calcd for $C_{17}H_{14}ClN_2O_4$ $(M + H)^+$: 345.0634; found: 345.0636.



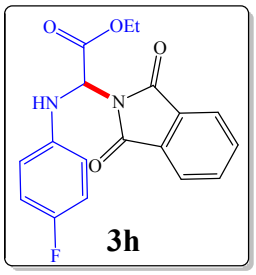
3f

(R)-methyl 2-((4-bromophenyl)amino)-2-(1,3-dioxoisoindolin-2-yl)acetate **3f:** White solid 73 % yield; m.p 144-146; ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.88-7.87 (m, 2H), 7.77-7.75 (m, 2H), 7.27-7.25 (m, 2H), 6.71-6.69 (d, *J* = 8.8 Hz, 2H), 6.17-6.15 (d, *J* = 9.1 Hz, 2H), 5.35-5.33 (d, *J* = 9.3 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.9, 167.3, 142.8, 134.5, 134.2, 132.6, 132.2, 131.5, 123.8, 123.5, 115.4, 111.6, 59.4, 53.7; ESI-MS m/z 389 $[M+H]^+$; HRMS (ESI) calcd for $C_{17}H_{14}BrN_2O_4$ $(M + H)^+$: 389.0131; found: 389.0137.



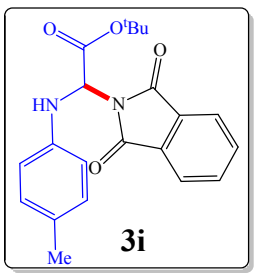
3g

(R)-ethyl 2-(1,3-dioxoisoindolin-2-yl)-2-(p-tolylamino)acetate **3g:** Brown solid 70 % yield; m.p ; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.83-7.81 (m, 2H), 7.70-6.99 (m, 2H), 6.97-6.75 (d, *J* = 8.1 Hz, 2H), 6.72-6.20 (d, *J* = 8.4 Hz, 2H), 6.18-5.21 (d, *J* = 9.5 Hz, 1H), 5.19-4.32 (d, *J* = 9.5 Hz, 1H), 4.30-4.26 (q, *J* = 7.2, 14.3 Hz, 2H), 2.19 (s, 3H), 1.26-1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.4, 167.0, 141.4, 134.2, 131.5, 129.8, 128.7, 123.5, 113.8, 62.8, 60.2, 20.2, 13.9; ESI-MS m/z 377 $[M+H]^+$.



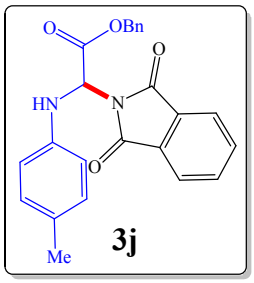
3h

(R)-ethyl 2-(1,3-dioxoisoindolin-2-yl)-2-((4-fluorophenyl)amino)acetate **3h:** White solid 86 % yield; m.p 145-147; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 8.87 (s, 1H), 7.88-7.86 (m, 2H), 7.77-7.75 (m, 2H), 7.63-7.60 (m, 2H), 7.09-7.05 (m, 2H), 4.44-4.40 (q, *J* = 7.1, 14.3 Hz, 2H), 1.45-1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.9, 160.9, 153.8, 134.3, 132.6, 123.5, 121.6, 121.5, 116.0, 115.8, 63.8, 13.9; ESI-MS m/z 381 $[M+K]^+$.



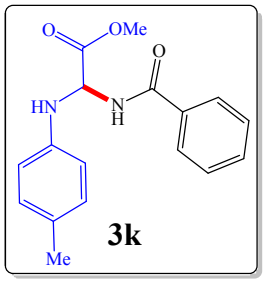
3i

(R)-tert-butyl 2-(1,3-dioxoisoindolin-2-yl)-2-(p-tolylamino)acetate **3i:** Pale yellow solid 88 % yield; m.p 130-132; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.86-7.82 (m, 2H), 7.73-7.69 (m, 2H), 6.99-6.97 (d, *J* = 8.2 Hz, 2H), 6.73-6.71 (d, *J* = 8.3 Hz, 2H), 6.08-6.06 (d, *J* = 9.1 Hz, 1H), 5.15-5.13 (d, *J* = 9.1 Hz, 1H), 2.19 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.5, 165.9, 141.7, 134.2, 131.6, 129.8, 128.5, 123.5, 113.8, 83.8, 60.7, 27.7, 20.3; ESI-MS m/z 311 $[M+H]^+$.



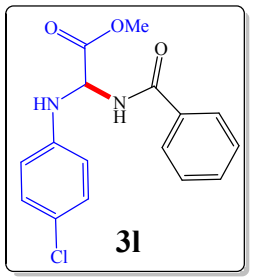
3j

***(R)-benzyl 2-(1,3-dioxoisoindolin-2-yl)-2-(p-tolylamino)acetate* 3j:** Brown solid 83 % yield; m.p 97-99; ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.81-7.79 (m, 2H), 7.70- 7.68 (m, 2H), 7.29-7.25 (m, 5H), 6.98-6.97 (d, J = 8.2 Hz, 2H), 6.73-6.72 (d, J = 8.5 Hz, 2H), 6.25-6.23 (d, J = 9.6 Hz, 1H), 5.29-5.21 (q, J = 14.3, 27.1 Hz, 2H), 5.20-5.18 (d, J = 9.6 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 167.4, 167.0, 141.3, 134.6, 134.2, 131.5, 129.9, 128.8, 128.4, 128.2, 123.6, 113.9, 68.3, 60.3, 20.3; ESI-MS m/z 423 $[M+Na]^+$; HRMS (ESI) calcd for $C_{24}H_{20}N_2O_4Na$ $(M + Na)^+$: 423.1317; found: 423.1315.



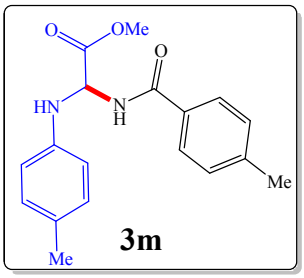
3k

***(R)-methyl 2-benzamido-2-(p-tolylamino)acetate* 3k:** Brown solid 83 % yield; m.p ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.76-7.73 (m, 2H), 7.51-7.48 (m, 1H), 7.42-7.39 (m, 2H), 7.02-6.97 (d, J = 8.2 Hz, 2H), 6.68-6.65 (d, J = 8.3 Hz, 2H), 6.15-6.10 (d, J = 5.6 Hz, 1H), 4.85 (s, 1H), 3.84 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 170.4, 167.1, 141.5, 133.2, 132.0, 129.9, 128.9, 128.6, 127.1, 114.2, 61.1, 53.3, 20.4; ESI-MS m/z 299 $[M+H]^+$.



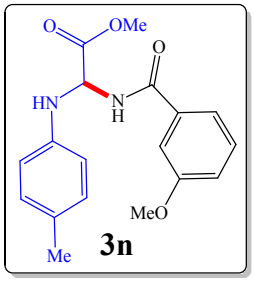
3l

***(R)-methyl 2-benzamido-2-((4-chlorophenyl)amino)acetate* 3l:** Pale pink solid 80 % yield; m.p 178-180;^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.76-7.75 (m, 2H), 7.53-7.50 (s, 1H), 7.44-7.41 (s, 2H), 7.15-7.13 (d, J = 8.8 Hz, 2H), 6.74-6.72 (d, J = 8.0 Hz, 1H), 6.69-6.68 (d, J = 8.8 Hz, 2H), 6.13-6.10 (t, J = 7.6 Hz, 1H), 5.01-4.99 (d, J = 7.0 Hz, 1H), 3.85 (s, 3H); NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ_{ppm}: 169.1, 166.5, 142.9, 132.6, 130.9, 128.1, 127.5, 126.7, 122.1, 114.3, 59.7, 52.1; ESI-MS m/z 319 $[M+H]^+$.



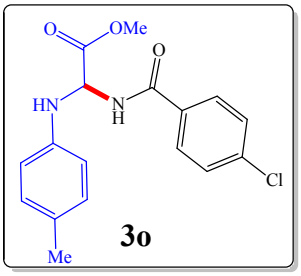
3m

(R)-methyl 2-(4-methylbenzamido)-2-(p-tolylamino)acetate **3m:** ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.65-7.63 (d, *J* = 8.1 Hz, 2H), 7.17-7.15 (d, *J* = 7.7 Hz, 2H), 6.98-6.96 (d, *J* = 8.1 Hz, 2H), 6.66-6.64 (d, *J* = 8.4 Hz, 2H), 6.10-6.08 (d, *J* = 7.4 Hz, 1H), 4.91 (s, br, 1H), 3.80 (s, 3H), 2.35 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 170.5, 167.1, 142.5, 141.6, 130.3, 129.9, 129.1, 128.7, 127.1, 114.2, 61.1, 53.1, 21.4, 20.3; ESI-MS m/z 313 $[M+H]^+$.



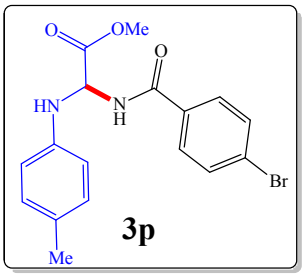
3n

(R)-methyl 2-(3-methoxybenzamido)-2-(p-tolylamino)acetate **3n:** ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.36-7.28 (m, 2H), 7.25-7.23 (m, 1H), 7.04-6.99 (m, 3H), 6.71-6.65 (m, 2H), 6.11-6.09 (d, *J* = 7.9 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 2.22 (s, 3H); ESI-MS m/z 329 $[M+H]^+$.



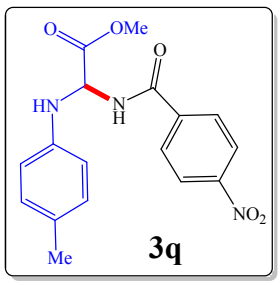
3o

(R)-methyl 2-(4-chlorobenzamido)-2-(p-tolylamino)acetate **3o:** ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.69-7.67 (d, *J* = 8.2 Hz, 2H), 7.38-7.37 (d, *J* = 8.3 Hz, 2H), 7.00-6.99 (d, *J* = 8.0 Hz, 2H), 6.66-6.64 (d, *J* = 8.2 Hz, 2H), 6.09-6.07 (d, *J* = 7.3 Hz, 2H), 4.86-4.80 (d, *J* = 6.2 Hz, 2H), 3.85 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 170.3, 166.1, 141.4, 138.3, 131.5, 129.9, 129.0, 128.8, 128.5, 114.2, 61.2, 53.3, 20.3; ESI-MS m/z 333 $[M+H]^+$.



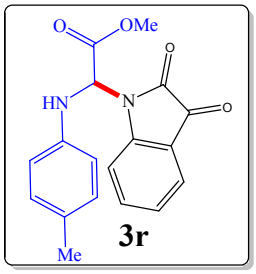
3p

(R)-methyl 2-(4-bromobenzamido)-2-(p-tolylamino)acetate **3p:** ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.62-7.52 (m, 4H), 7.00-6.98 (m, 2H), 6.83-6.60 (m, 3H), 6.12-6.02 (m, 1H), 3.84 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 170.2, 166.2, 141.4, 132.0, 131.8, 129.9, 129.0, 128.7, 126.8, 114.2, 61.2, 53.3, 20.3; ESI-MS m/z 377 $[M+H]^+$.



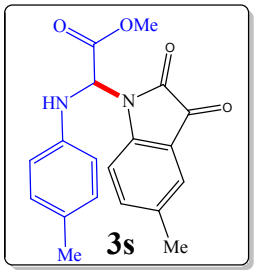
3q

(R)-methyl 2-(4-nitrobenzamido)-2-(p-tolylamino)acetate **3q:** ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 8.24-8.22 (d, J = 7.1 Hz, 2H), 7.91-7.89 (d, J = 8.6 Hz, 2H), 7.01-6.99 (d, J = 8.2 Hz, 2H), 6.66-6.64 (d, J = 8.3 Hz, 2H), 6.10-6.09 (d, J = 7.7 Hz, 1H), 3.86 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 170.0, 165.3, 149.8, 141.3, 138.7, 130.0, 129.2, 128.3, 123.7, 114.1, 61.4, 53.4, 20.3; ESI-MS m/z 344 $[M+H]^+$.



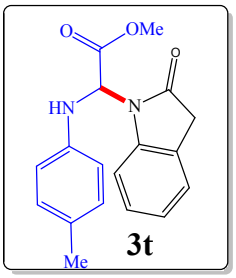
3r

(R)-methyl 2-(2,3-dioxoindolin-1-yl)-2-(p-tolylamino)acetate **3r:** ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.62-7.59 (m, 1H), 7.54-7.51 (m, 1H), 7.13-7.11 (d, J = 7.7 Hz, 2H), 7.00-6.98 (d, J = 8.2 Hz, 2H), 6.66-6.63 (d, J = 8.4 Hz, 2H), 6.40-6.39 (d, J = 5.2 Hz, 1H), 5.10-5.09 (d, J = 5.0 Hz, 1H), 3.83 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm}: 182.3, 168.2, 157.9, 148.5, 140.7, 138.2, 130.0, 129.3, 125.5, 124.1, 121.6, 119.8, 118.0, 113.7, 112.0, 61.9, 53.9, 20.3;



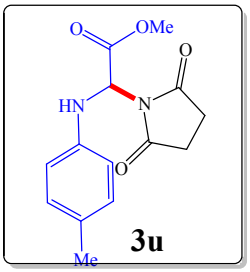
3s

(R)-methyl 2-(5-methyl-2,3-dioxoindolin-1-yl)-2-(p-tolylamino)acetate **3s:** ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.43-7.40 (m, 1H), 7.33-7.31 (m, 1H), 7.01-6.97 (m, 3H), 6.65-6.62 (m, 2H), 6.38-6.36 (d, *J* = 5.2 Hz, 1H), 5.08-5.07 (d, *J* = 5.1 Hz, 1H), 3.82 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 182.6, 168.3, 158.1, 146.3, 140.7, 138.7, 134.0, 130.0, 129.2, 125.8, 118.1, 113.7, 111.8, 61.8, 53.9, 20.5, 20.3;



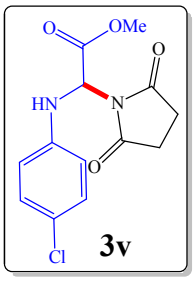
3t

(R)-methyl 2-(2-oxoindolin-1-yl)-2-(p-tolylamino)acetate **3t:** ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.21-7.17 (m, 2H), 7.02-6.96 (m, 4H), 6.69-6.67 (d, *J* = 8.3 Hz, 2H), 6.45-6.44 (d, *J* = 5.7 Hz, 1H), 5.16-5.14 (d, *J* = 5.5 Hz, 1H), 3.78 (s, 3H), 3.58 (s, 2H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 175.0, 168.9, 141.7, 141.3, 129.9, 128.5, 127.7, 124.4, 124.1, 122.6, 113.6, 109.9, 61.1, 53.6, 35.5, 20.3; ESI-MS m/z 311 $[M+H]^+$.

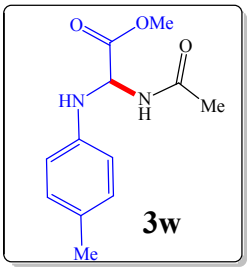


3u

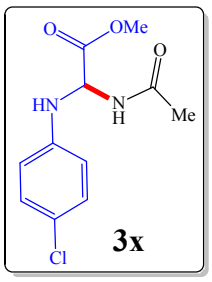
(R)-methyl 2-(2,5-dioxopyrrolidin-1-yl)-2-(p-tolylamino)acetate **3u:** Brown solid 78 % yield; m.p 142-144; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.01-6.99 (d, *J* = 8.0 Hz, 2H), 6.68-6.65 (d, *J* = 8.4 Hz, 2H), 6.06-6.04 (d, *J* = 9.7 Hz, 1H), 5.11-5.08 (d, *J* = 9.9 Hz, 1H), 3.82 (s, 3H), 2.72-2.68 (d, *J* = 1.5 Hz, 4H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 176.3, 167.2, 141.2, 129.9, 128.9, 113.8, 60.7, 53.5, 27.9, 20.3;



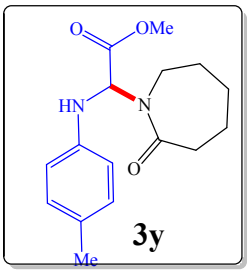
(R)-methyl 2-((4-chlorophenyl)amino)-2-(2,5-dioxopyrrolidin-1-yl)acetate **3v:** Brown solid 79 % yield; m.p 167-169; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.15-7.13 (d, *J* = 8.9 Hz, 2H), 6.70-6.67 (d, *J* = 8.9 Hz, 2H), 6.01-5.99 (d, *J* = 8.5 Hz, 1H), 5.24-5.22 (d, *J* = 9.0 Hz, 1H), 3.83 (s, 3H), 2.72 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 176.2, 166.9, 142.3, 129.3, 124.5, 114.9, 60.2, 53.7, 28.0; ESI-MS m/z 319 $[M+Na]^+$.



(R)-methyl 2-acetamido-2-(p-tolylamino)acetate **3w:** Pale pink solid 75 % yield; m.p 109-111; ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm}: 7.04-7.00 (d, *J* = 8.0 Hz, 2H), 6.61-6.59 (d, *J* = 8.3 Hz, 2H), 6.13-6.05 (d, *J* = 4.5 Hz, 1H), 5.92-5.88 (d, *J* = 8.2 Hz, 1H), 3.82 (s, 3H), 2.24 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 170.3, 170.0, 141.4, 129.9, 128.8, 114.1, 60.4, 53.1, 23.1, 20.4; ESI-MS m/z 237 $[M+H]^+$.

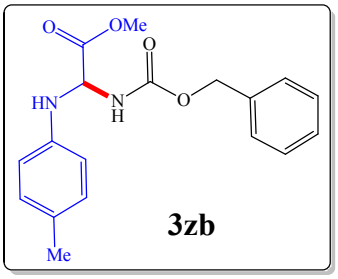


(R)-methyl 2-acetamido-2-((4-chlorophenyl)amino)acetate **3x:** Pink solid 82 % yield; m.p 160-162; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ_{ppm}: 8.35 (s, br., 1H), 7.09-7.06 (d, *J* = 8.8 Hz, 2H), 6.70-6.67 (d, *J* = 8.8 Hz, 2H), 5.76-5.74 (d, *J* = 6.0 Hz, 1H), 3.78 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ_{ppm}: 169.7, 169.1, 142.8, 128.1, 122.1, 114.1, 58.9, 52.0, 21.9; ESI-MS m/z 257 $[M+H]^+$.



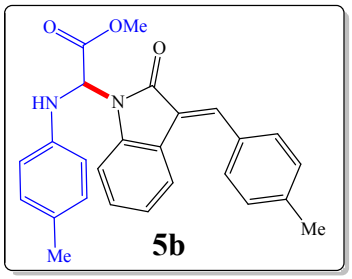
3y

***(R)-methyl 2-(2-oxoazepan-1-yl)-2-(p-tolylamino)acetate* 3y:** ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 6.99-6.96 (d, *J* = 8.1 Hz, 2H), 6.60-6.57 (d, *J* = 8.4 Hz, 2H), 6.54-6.52 (d, *J* = 5.8 Hz, 1H), 5.00-4.91 (d, *J* = 5.7 Hz, 1H), 3.80 (s, 3H), 3.33-3.16 (m, 2H), 2.63-2.52 (m, 2H), 2.22 (s, 3H), 1.73-1.28 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm}: 176.3, 169.9, 141.6, 129.8, 127.9, 113.4, 63.2, 52.9, 43.2, 37.4, 29.8, 28.0, 23.0, 20.3; ESI-MS m/z 291 $[M+H]^+$.



3zb

***(R)-methyl 2-(((benzyloxy)carbonyl)amino)-2-(p-tolylamino)acetate* 3zb:** Brown solid 58 % yield; m.p ; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.38-7.28 (m, 5H), 7.01-6.99 (d, *J* = 7.9 Hz, 2H), 6.64-6.62 (d, *J* = 7.7 Hz, 2H), 5.67 (s, 1H), 5.41 (s, 1H), 5.12 (s, 2H), 4.67 (s, 1H), 3.81 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 170.1, 155.5, 141.5, 135.9, 129.8, 128.8, 128.4, 128.1, 128.0, 114.3, 67.1, 62.5, 53.1, 20.4;



5b

***(R,E)-methyl 2-(3-(4-methylbenzylidene)-2-oxoindolin-1-yl)-2-(p-tolylamino)acetate* 5b:** Yellow solid 67 % yield; m.p ; ^{1}H NMR (400 MHz, $CDCl_3$) δ_{ppm}: 7.91 (s, 1H), 7.69-7.67 (d, *J* = 7.5 Hz, 1H), 7.56-7.54 (m, 2H), 7.28-7.27 (m, 1H), 7.19-7.15 (m, 1H), 7.02-6.98 (m, 3H), 6.88-6.84 (m, 1H), 6.74-6.72 (m, 2H), 6.55-6.54 (d, *J* = 5.6 Hz, 1H), 5.18-5.17 (d, *J* = 5.5 Hz, 1H), 3.79 (s, 3H), 2.42 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{ppm}: 169.1, 168.5, 141.5, 140.7, 140.1, 138.6, 138.2, 132.2, 131.7, 129.9, 129.4, 129.3, 129.1, 128.5, 125.6, 122.7, 122.0, 121.5, 118.9, 113.6, 110.0, 109.6, 61.3, 53.6, 21.5, 20.3; ESI-MS m/z 435 $[M+Na]^+$.

6. ^{1}H & ^{13}C NMR of all compounds

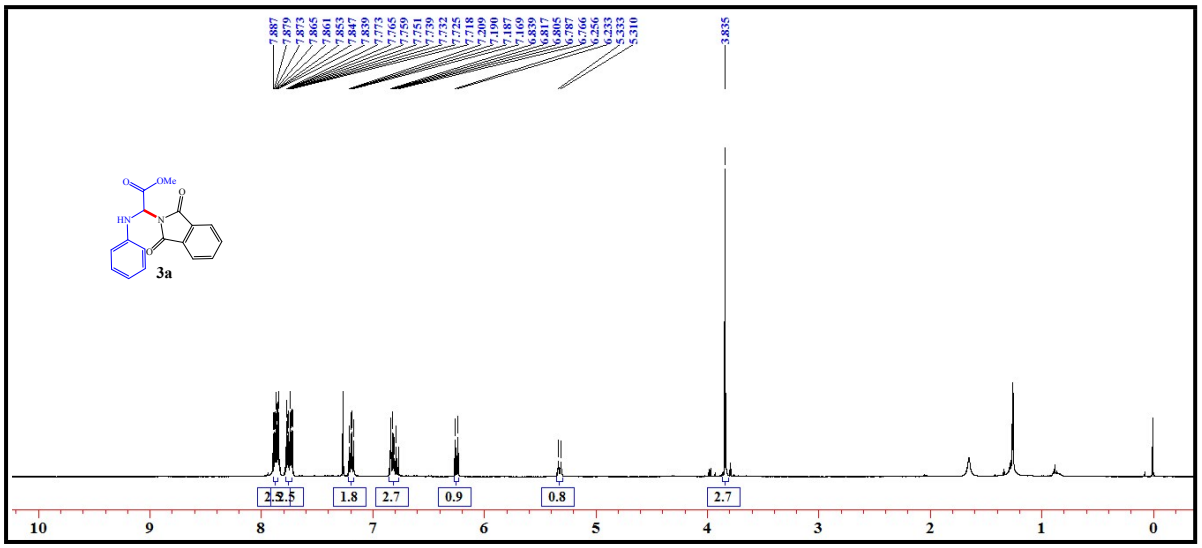


Figure S1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3a**

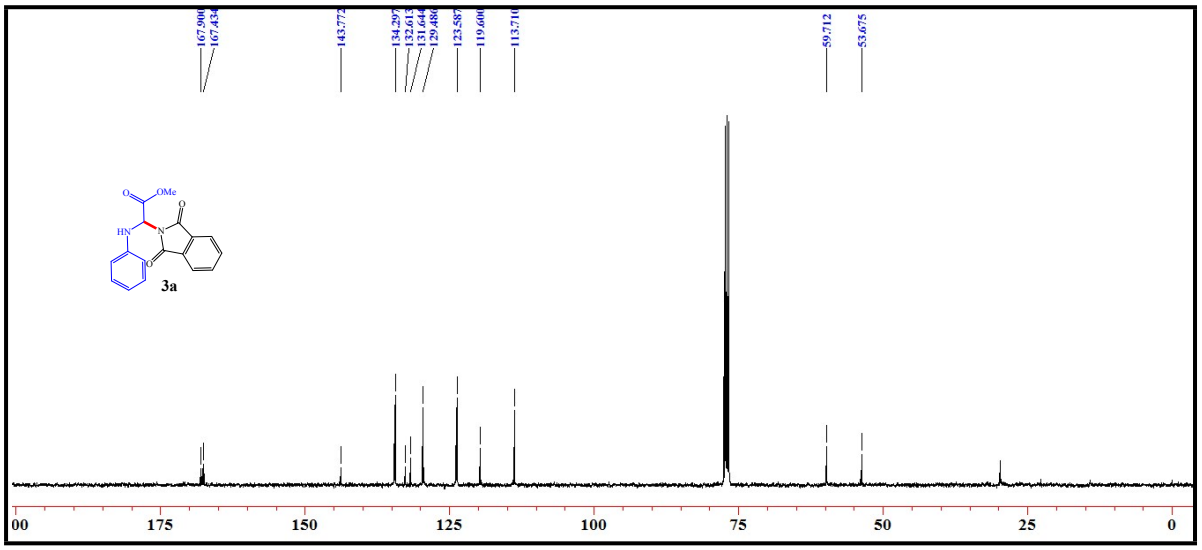


Figure S2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3a**

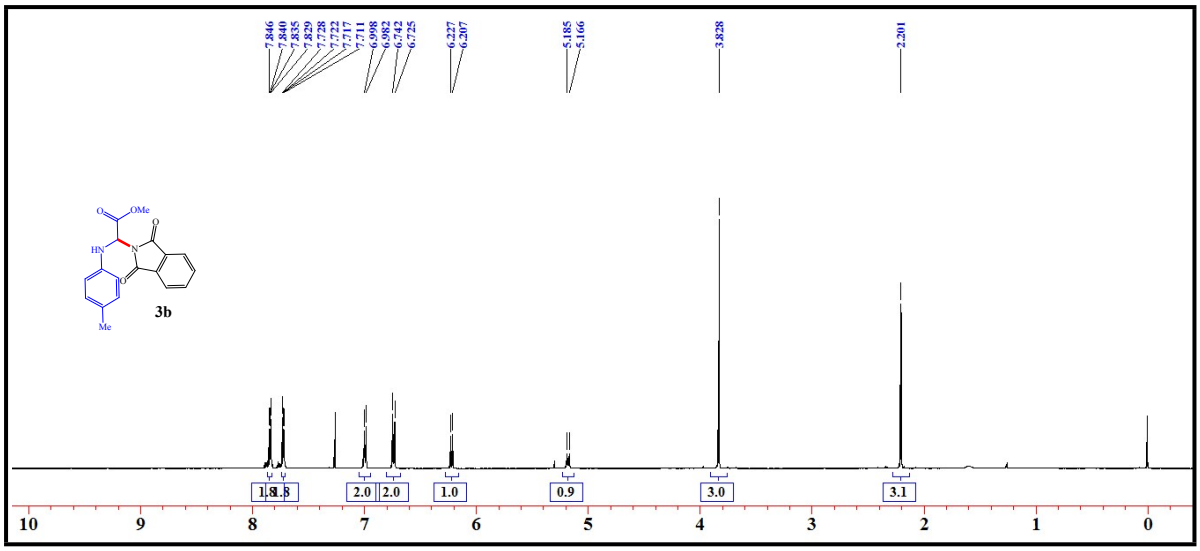


Figure S3. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3b**

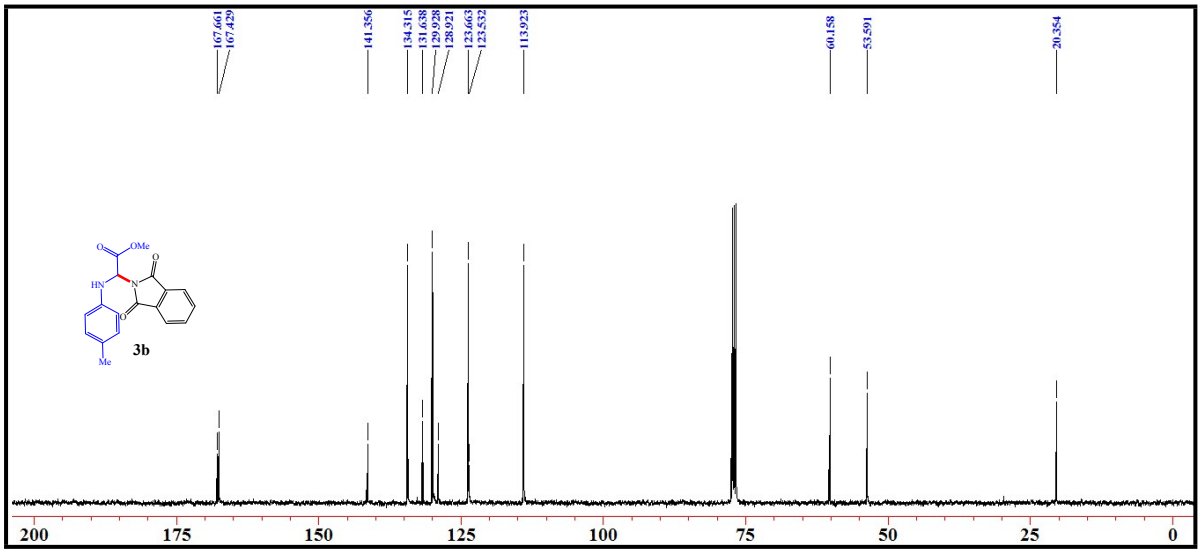


Figure S4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3b**

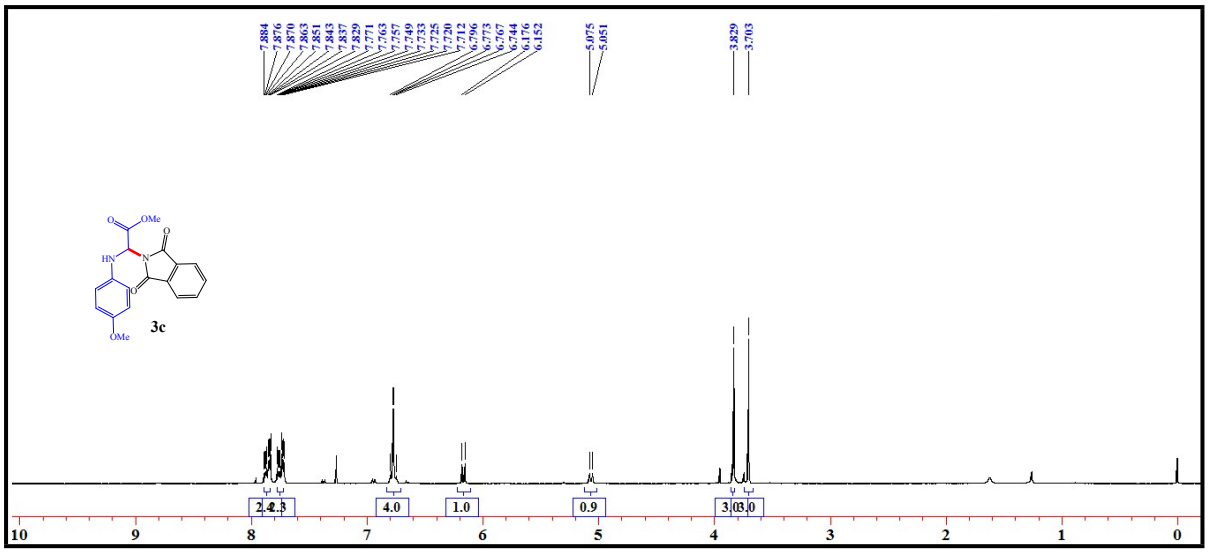


Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3c**

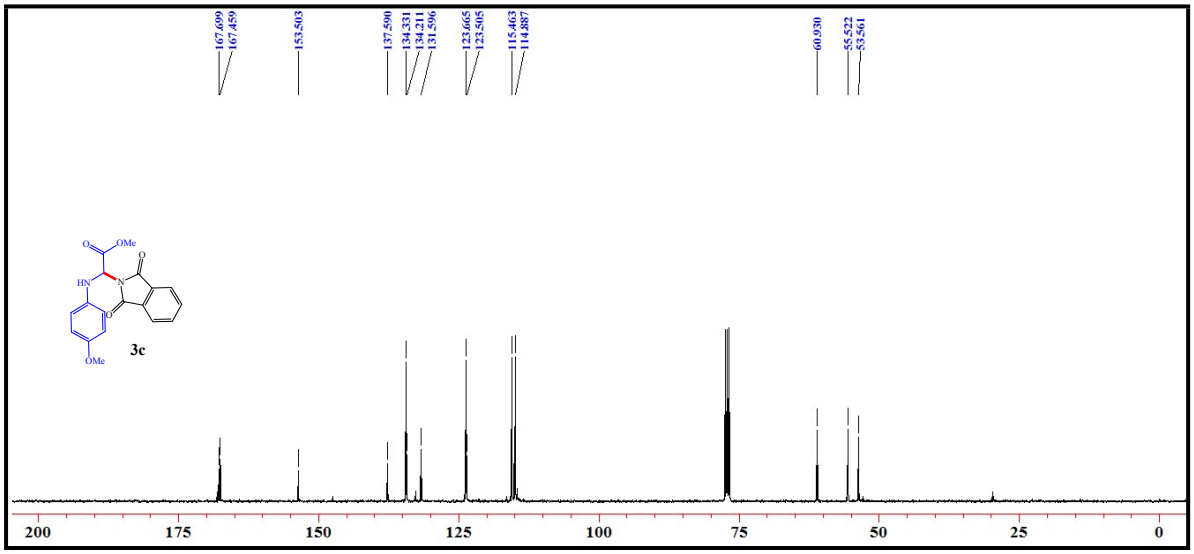


Figure S6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3c**

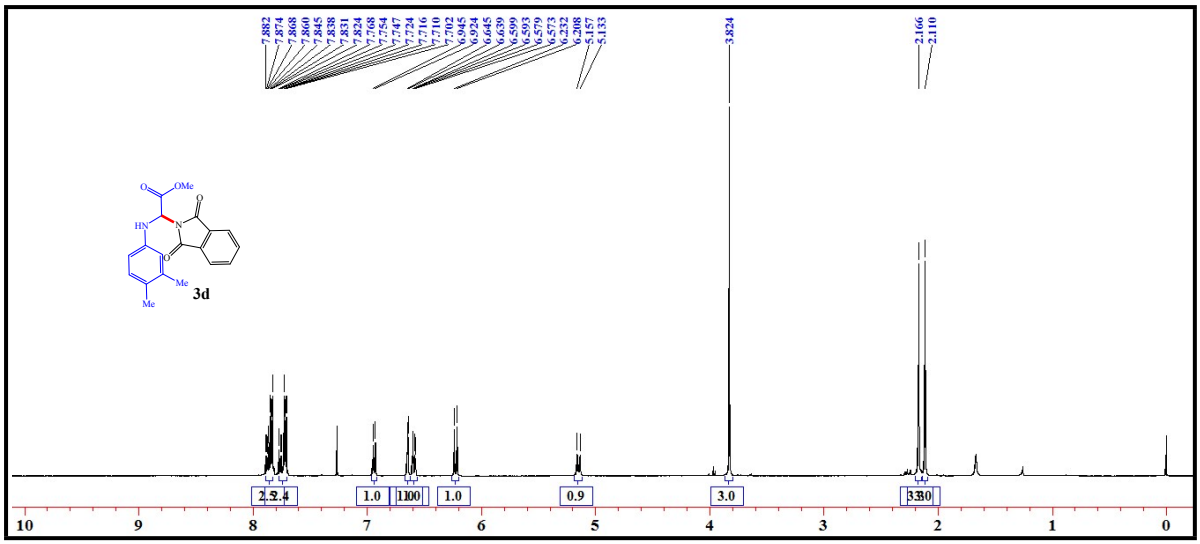


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3d**

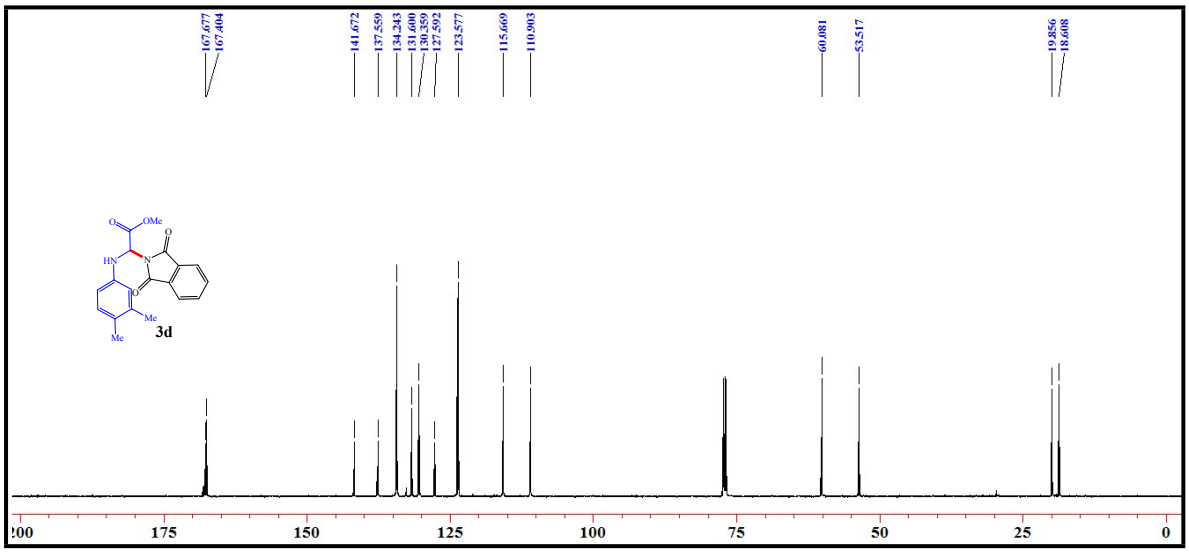


Figure S8. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3d**

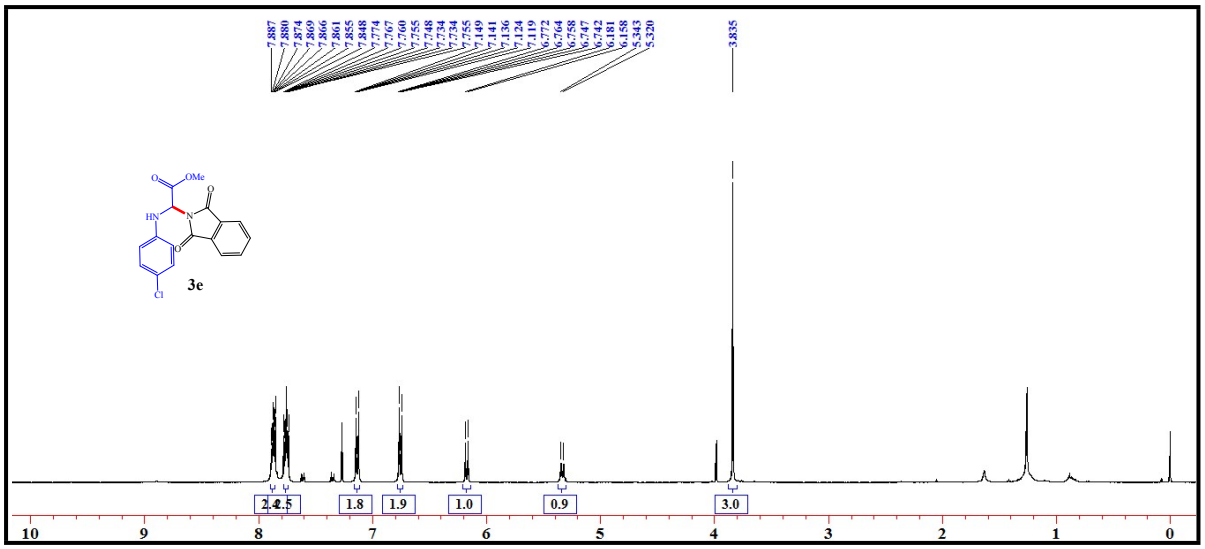


Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3e**

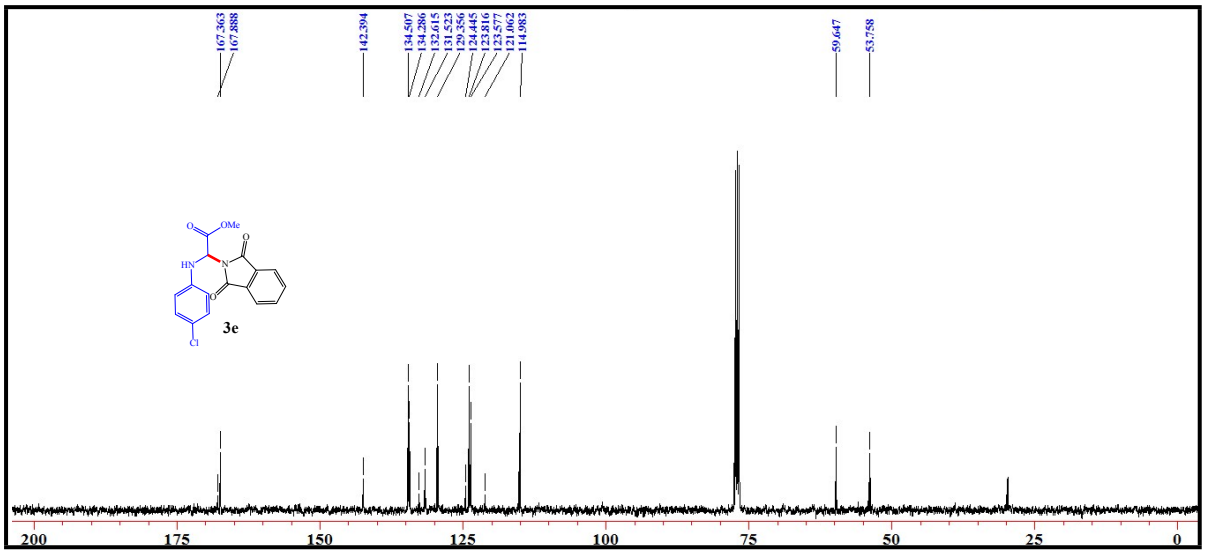


Figure S10. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3e**

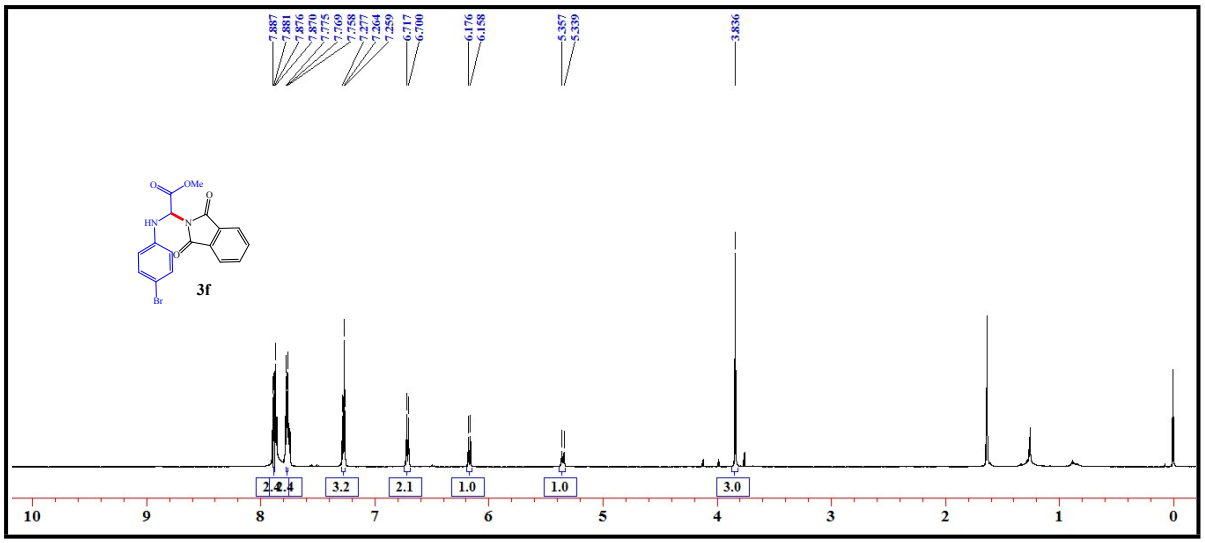


Figure S11. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3f**

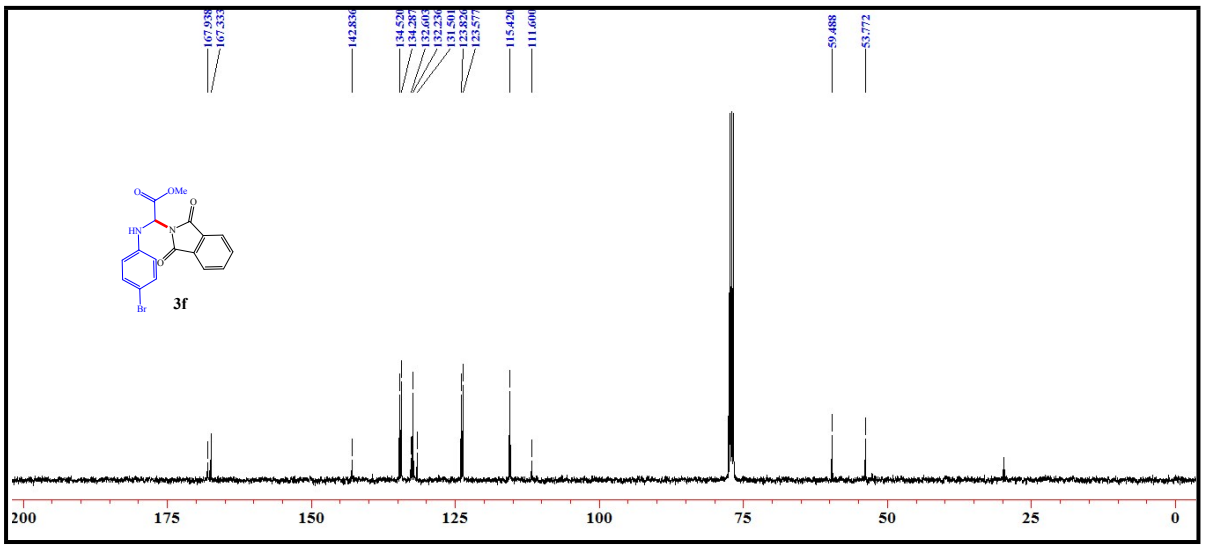


Figure S12. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3f**

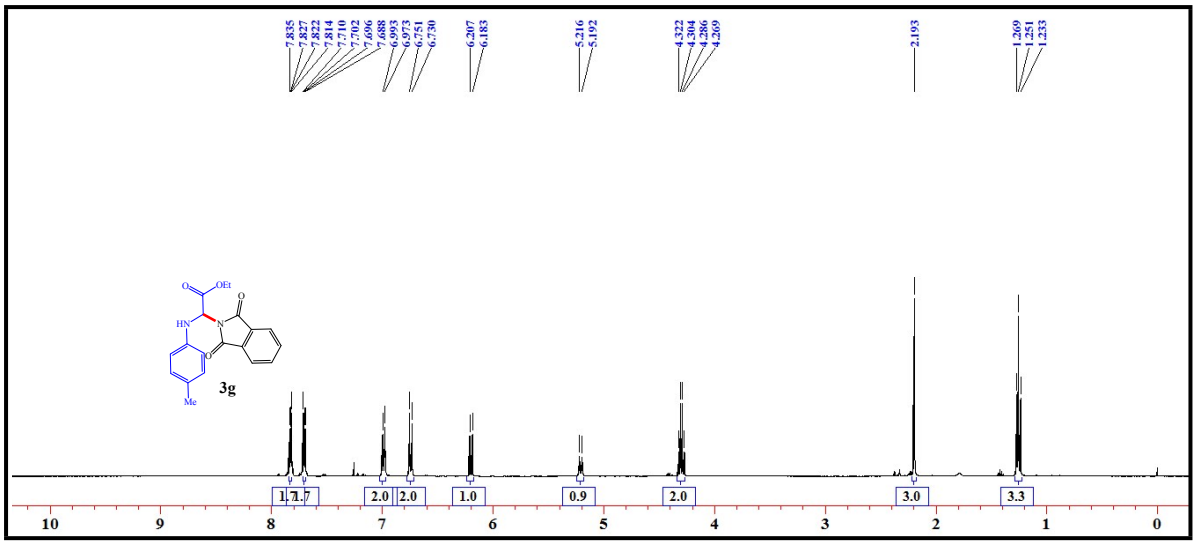


Figure S13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3g**

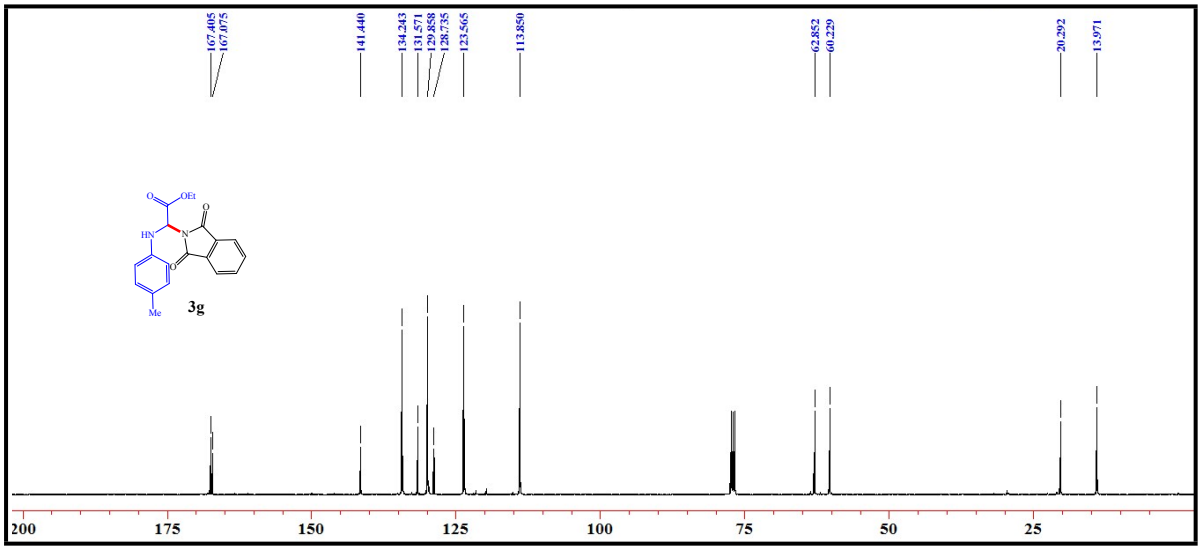


Figure S14. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3g**

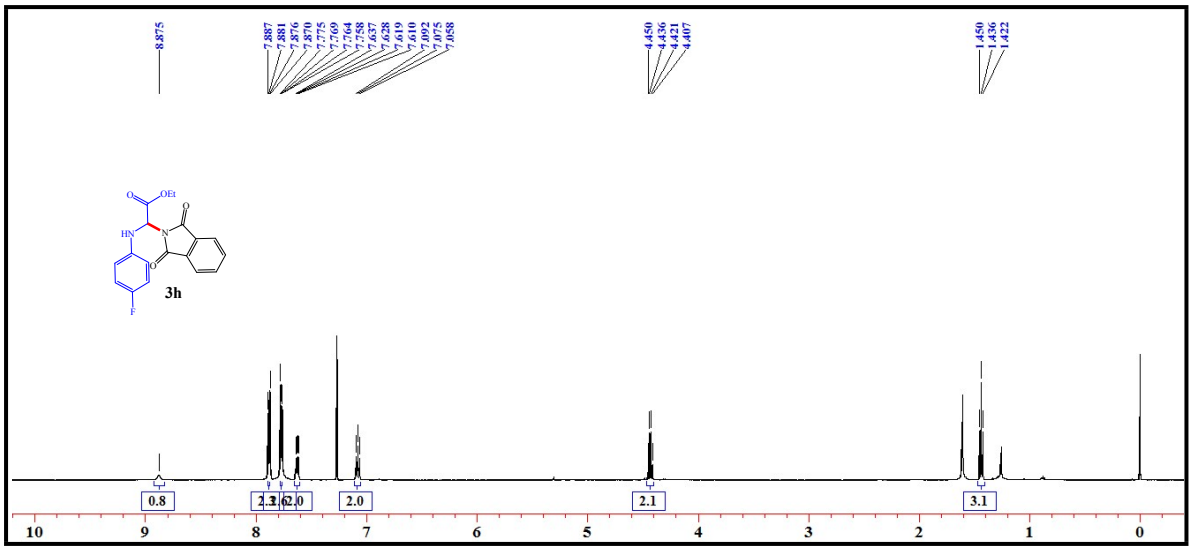


Figure S15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3h**

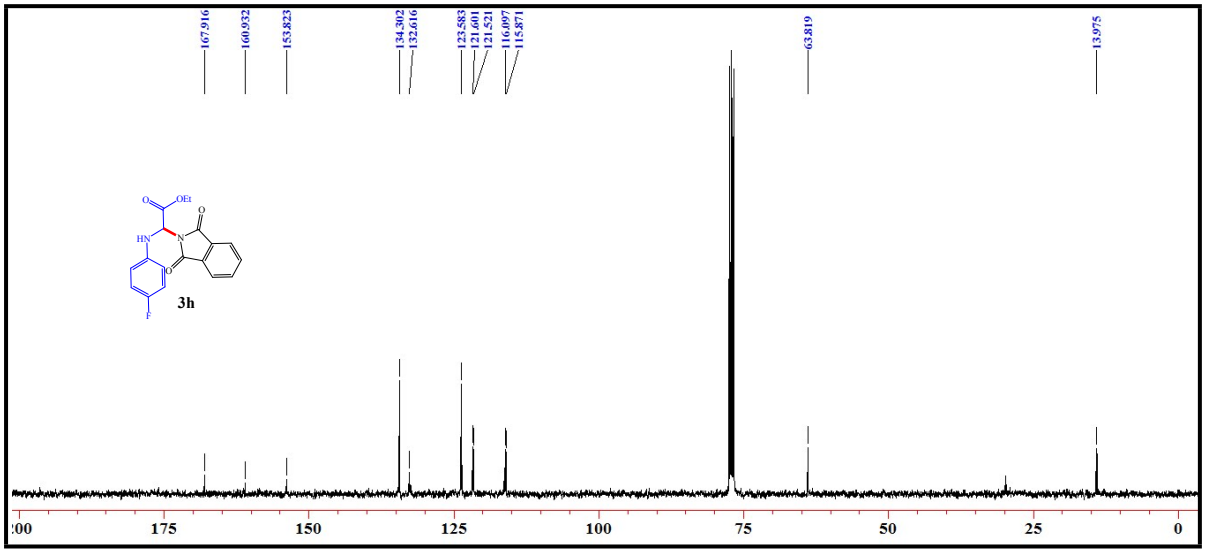


Figure S16. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3h**

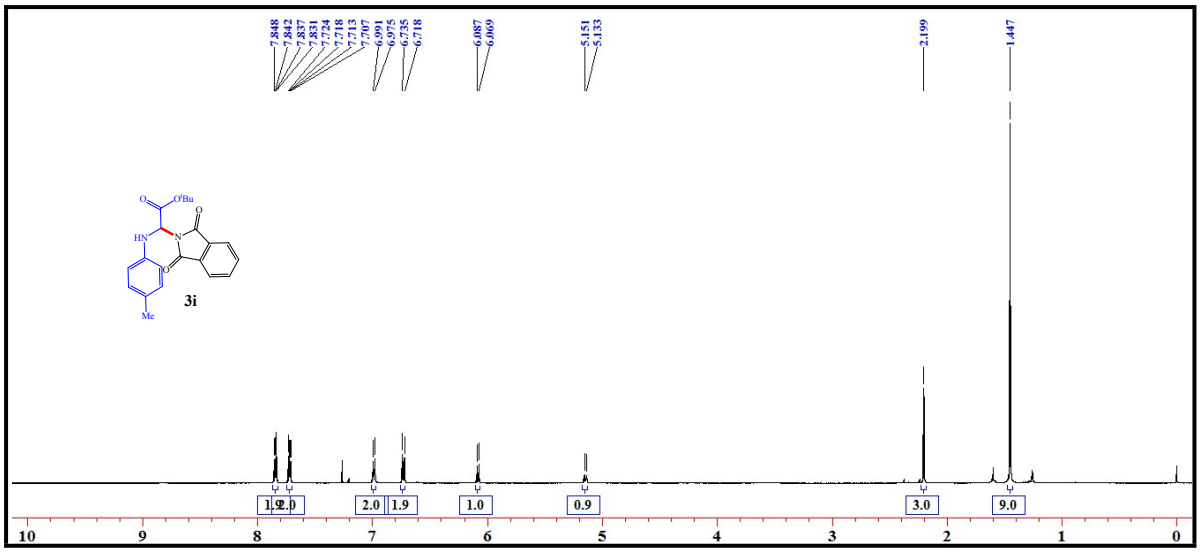


Figure S17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3i**

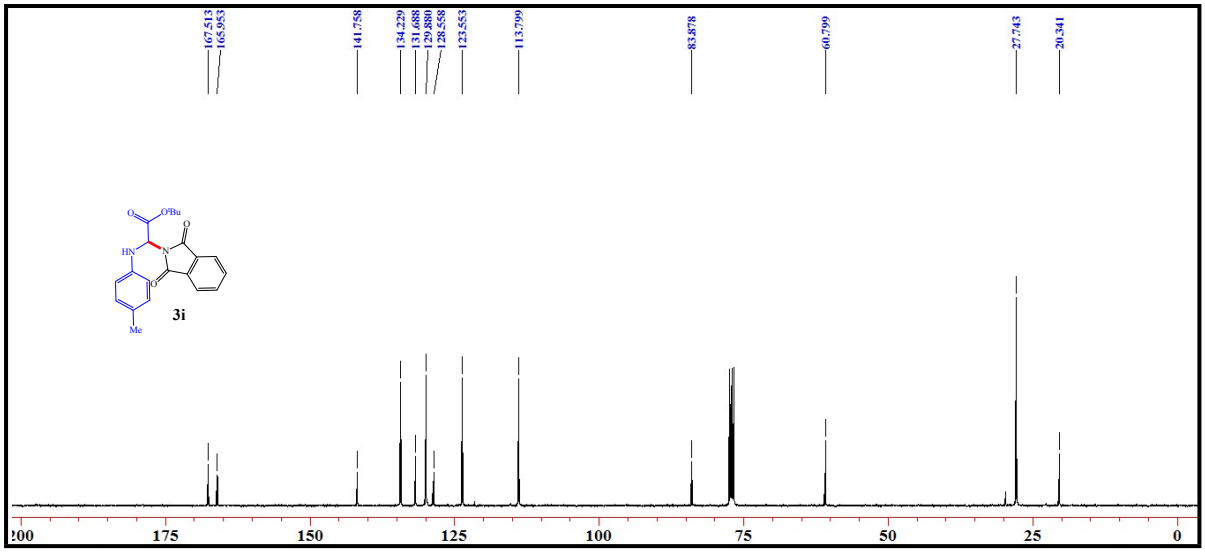


Figure S18. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3i**

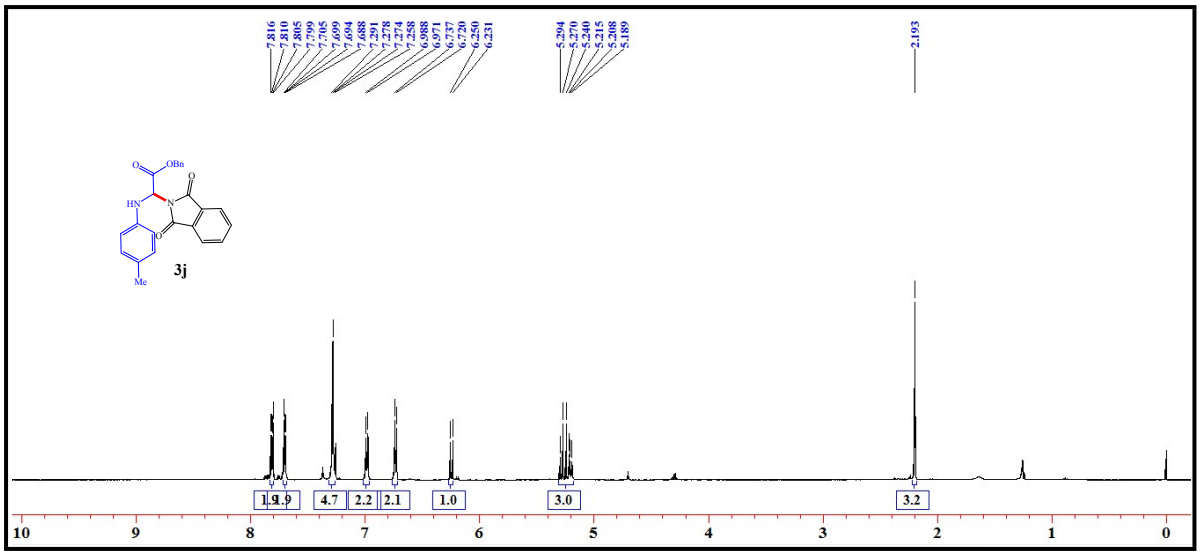


Figure S19. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3j**

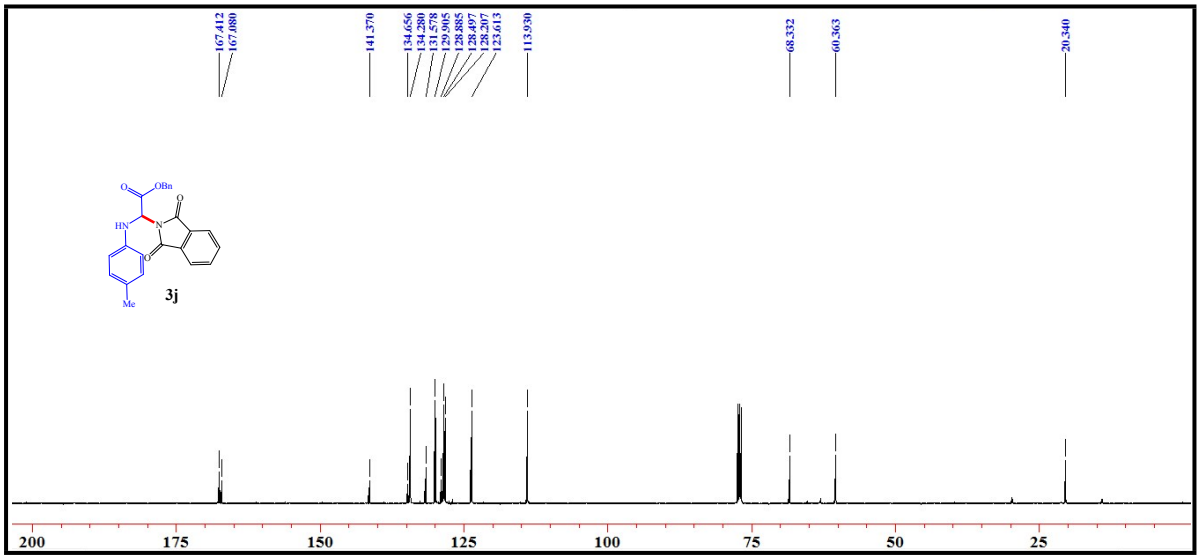


Figure S20. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3j**

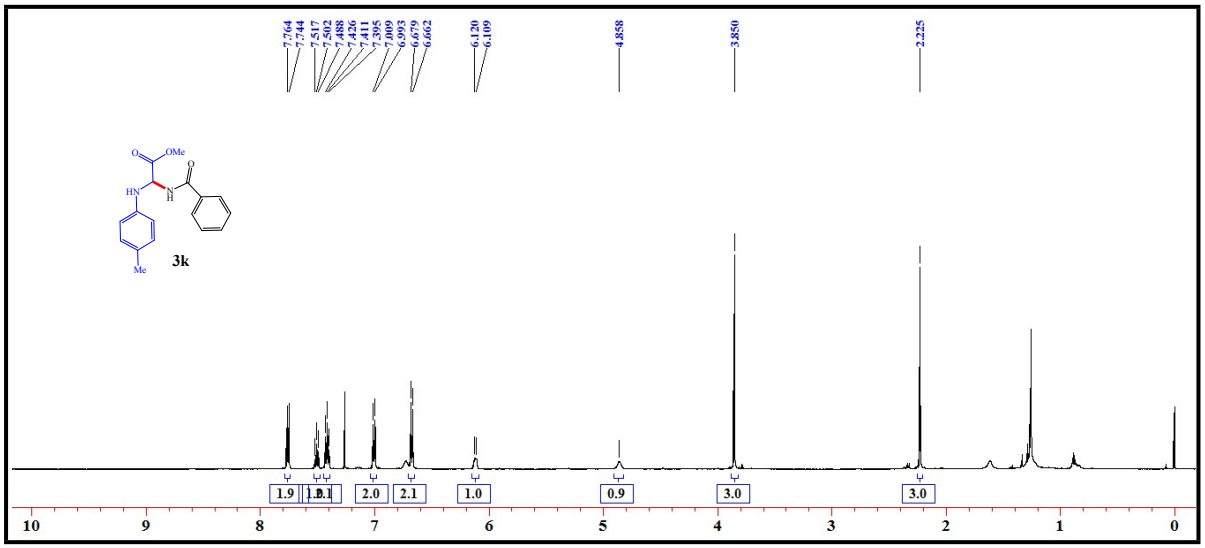


Figure S21. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3k**

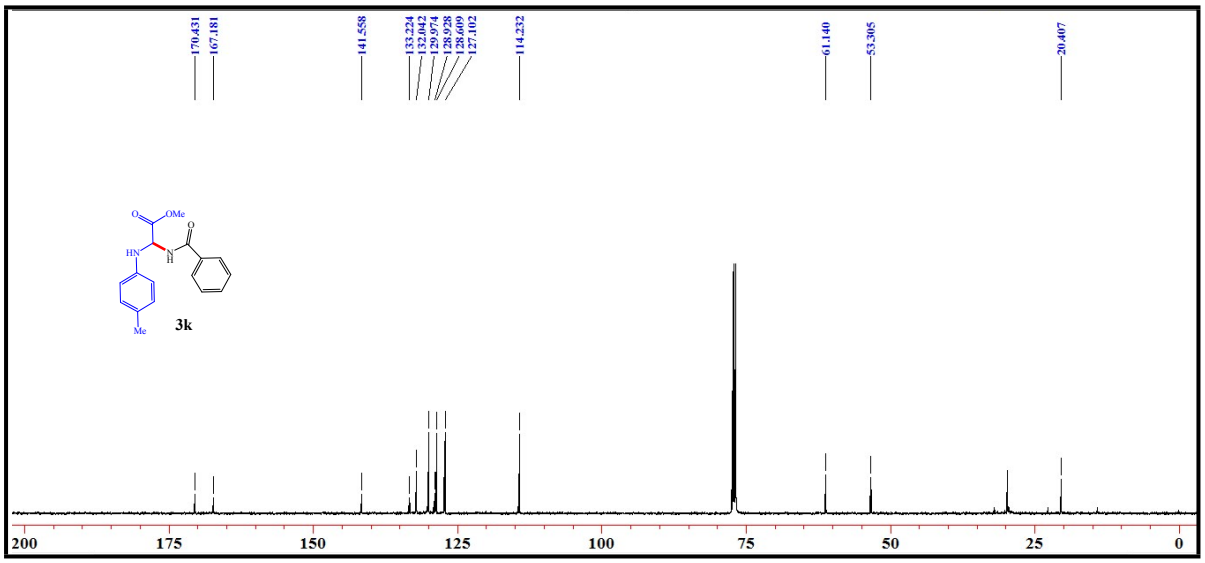


Figure S22. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3k**

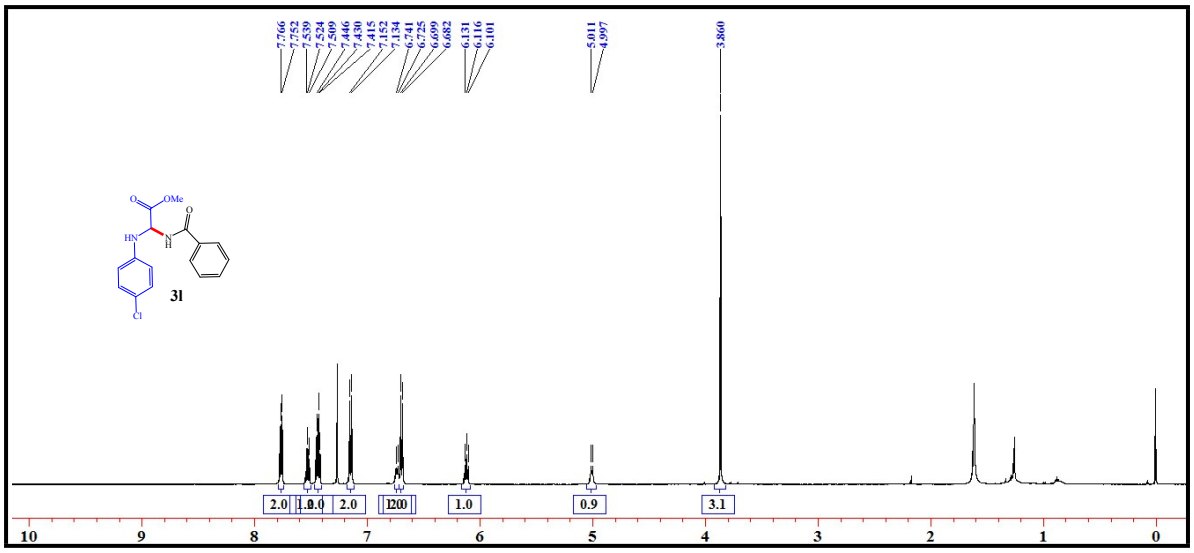


Figure S23. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3l**

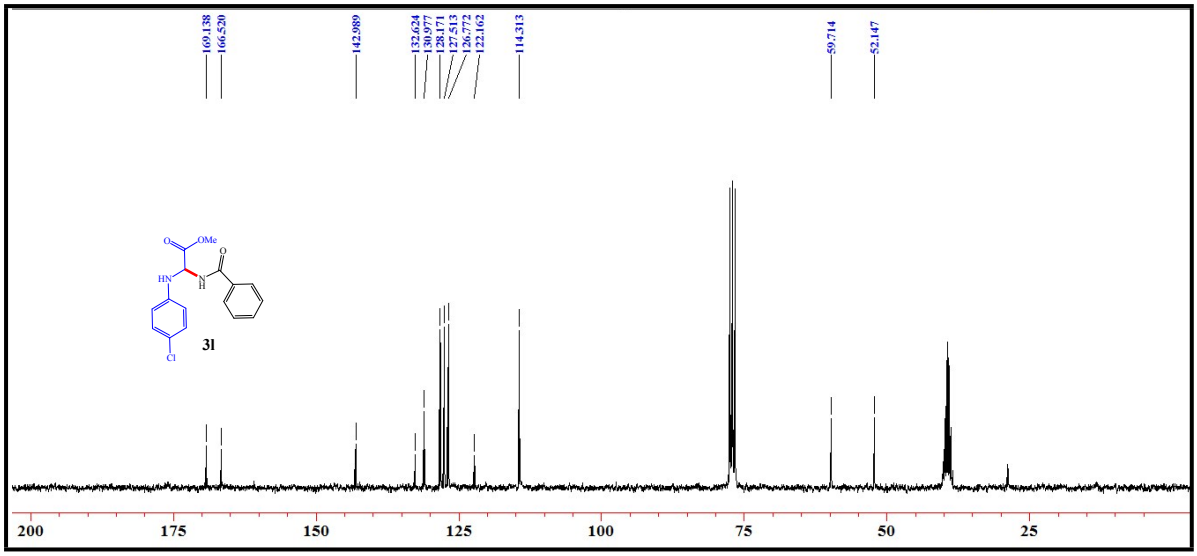


Figure S24. ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) spectrum of **3l**

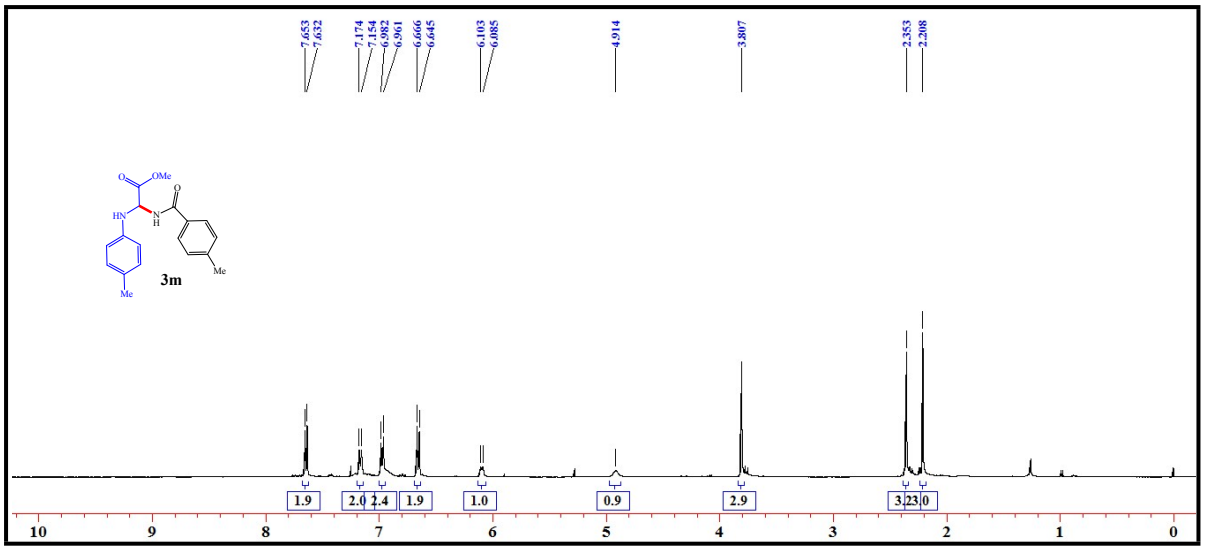


Figure S25. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3m**

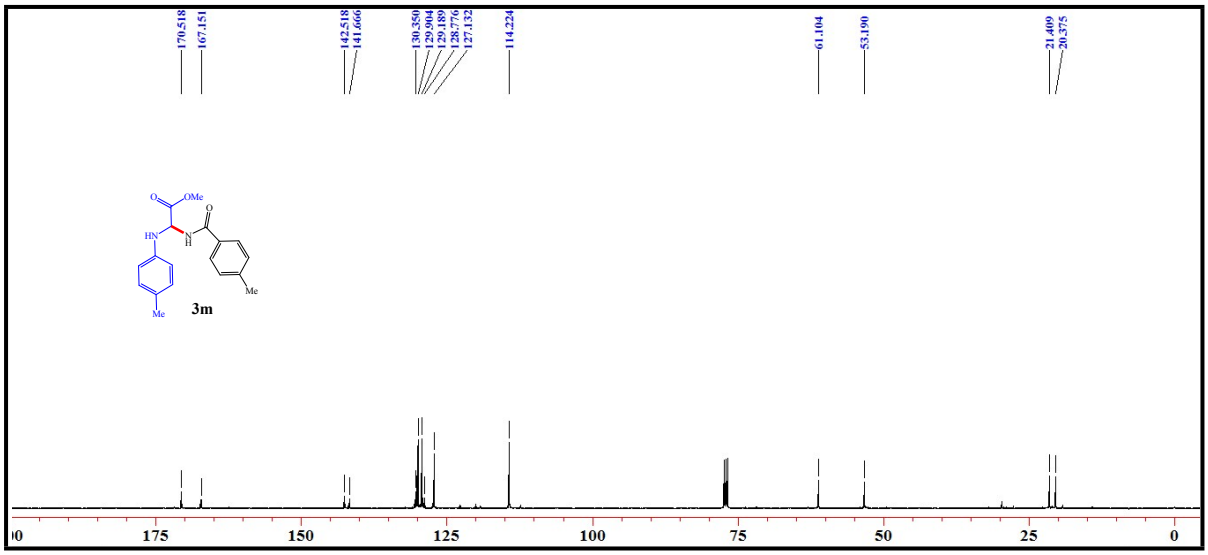


Figure S26. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3m**

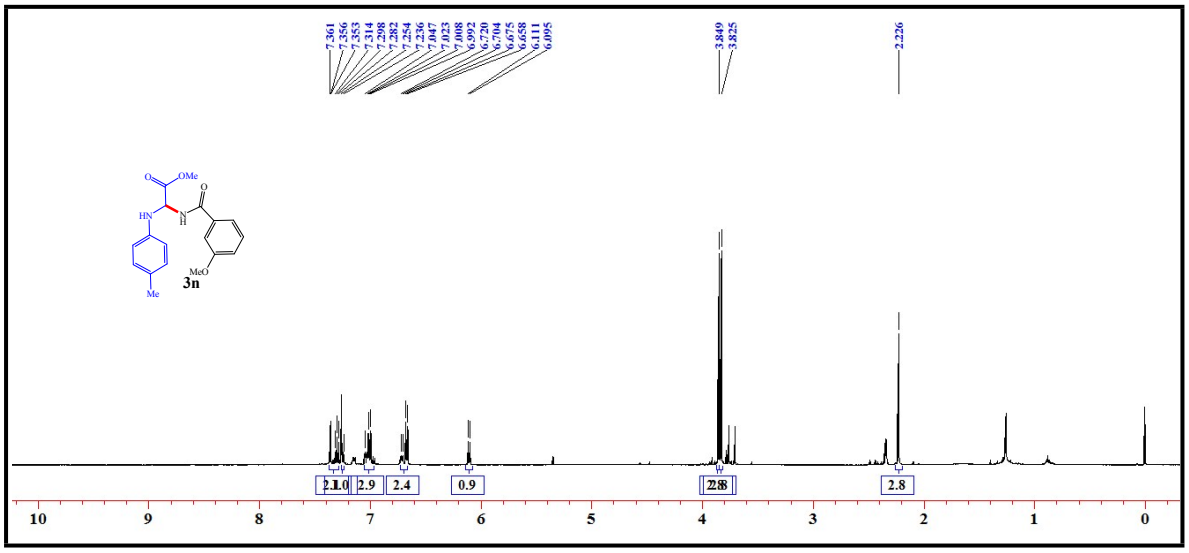


Figure S27. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3n**

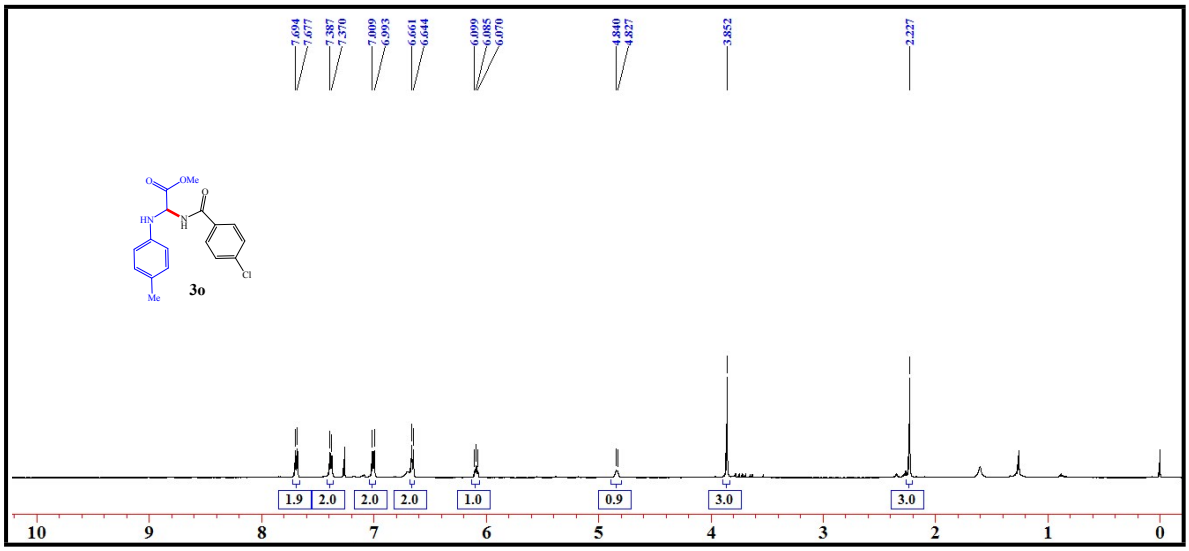


Figure S28. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3o**

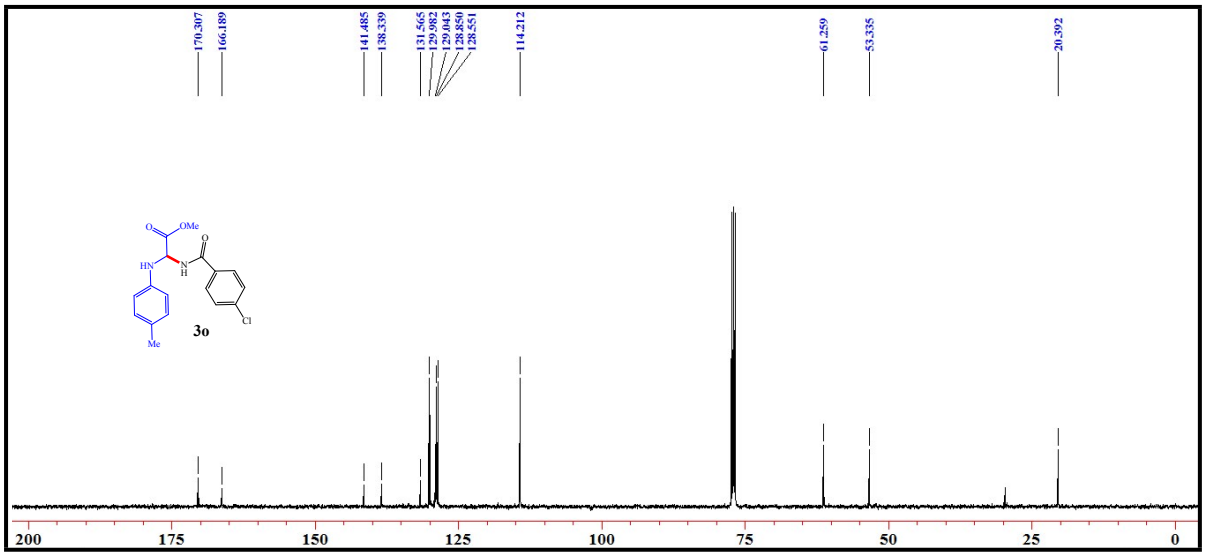


Figure S29. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3o**

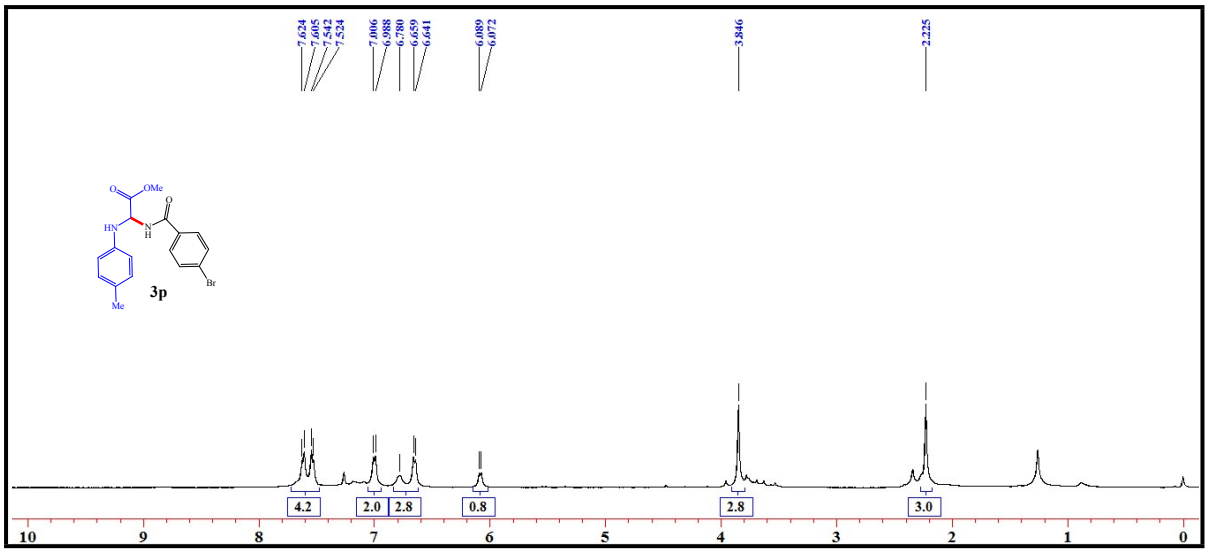


Figure S30. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3p**

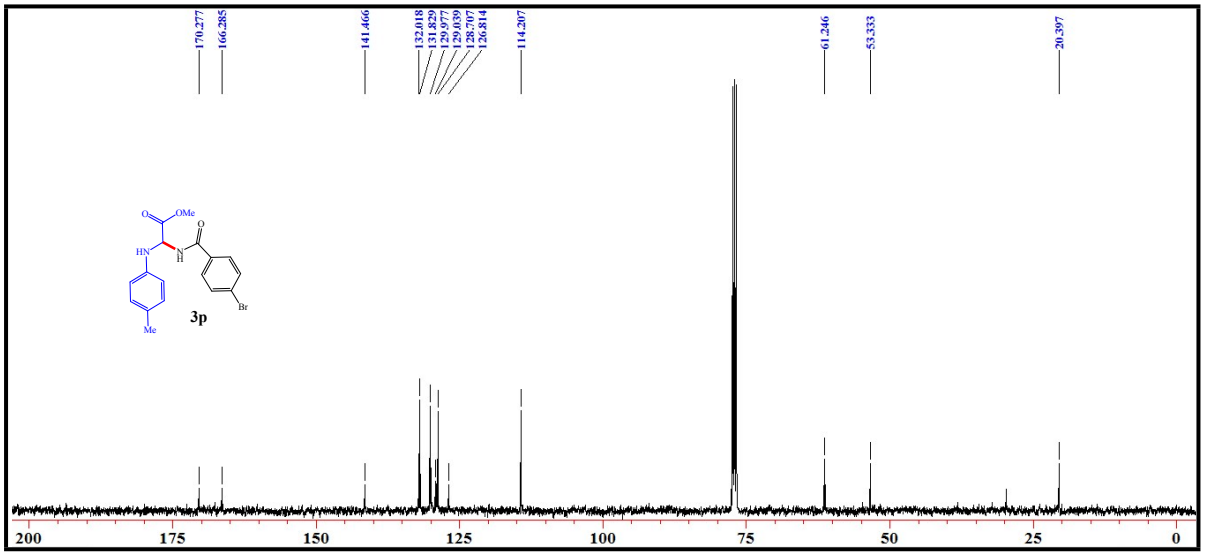


Figure S31. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3p**

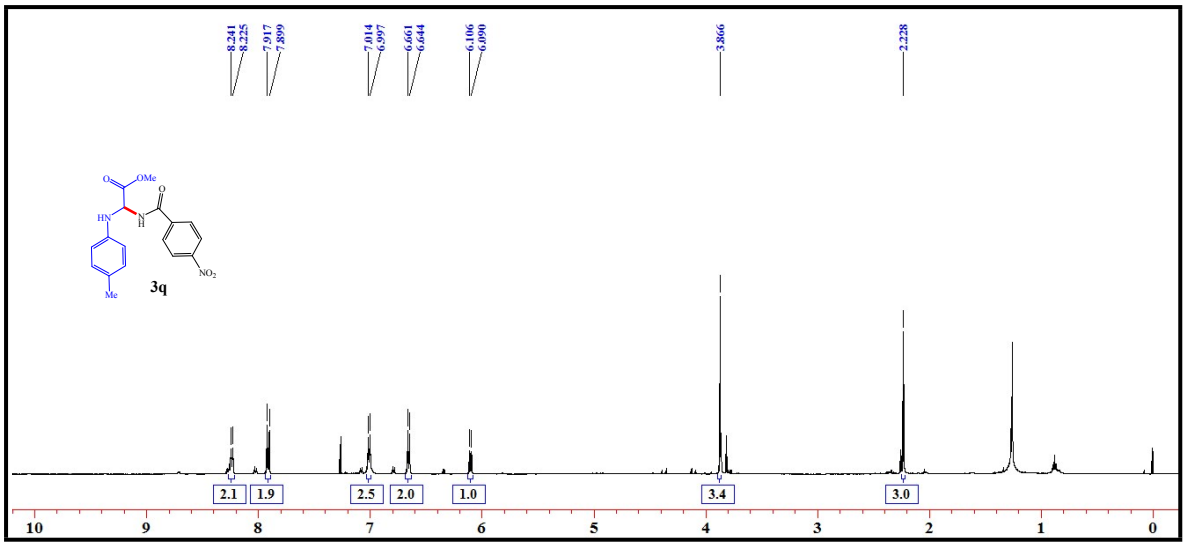


Figure S32. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3q**

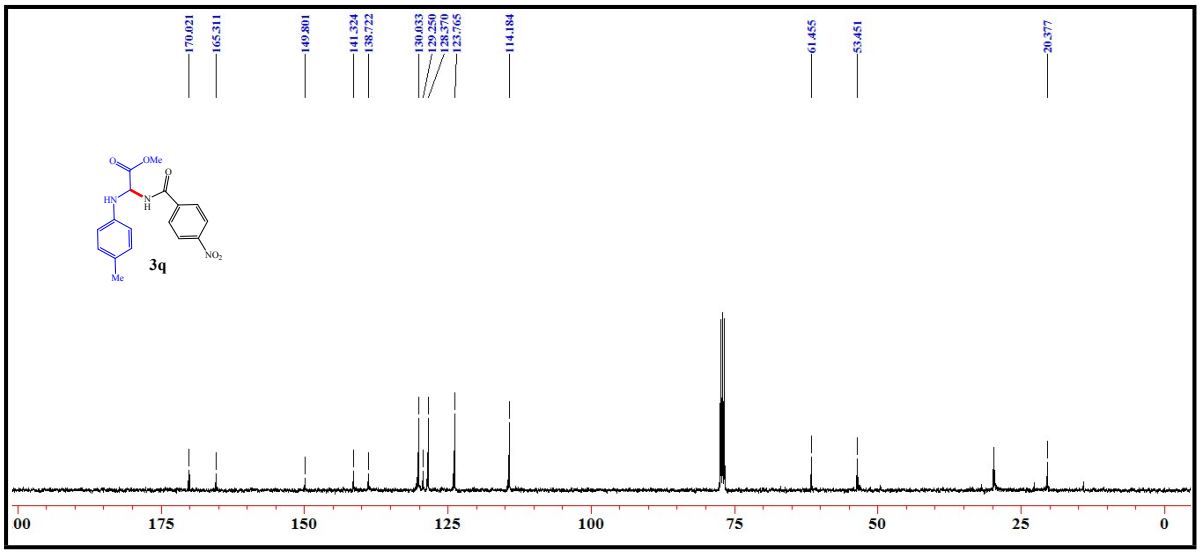


Figure S33. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3q**

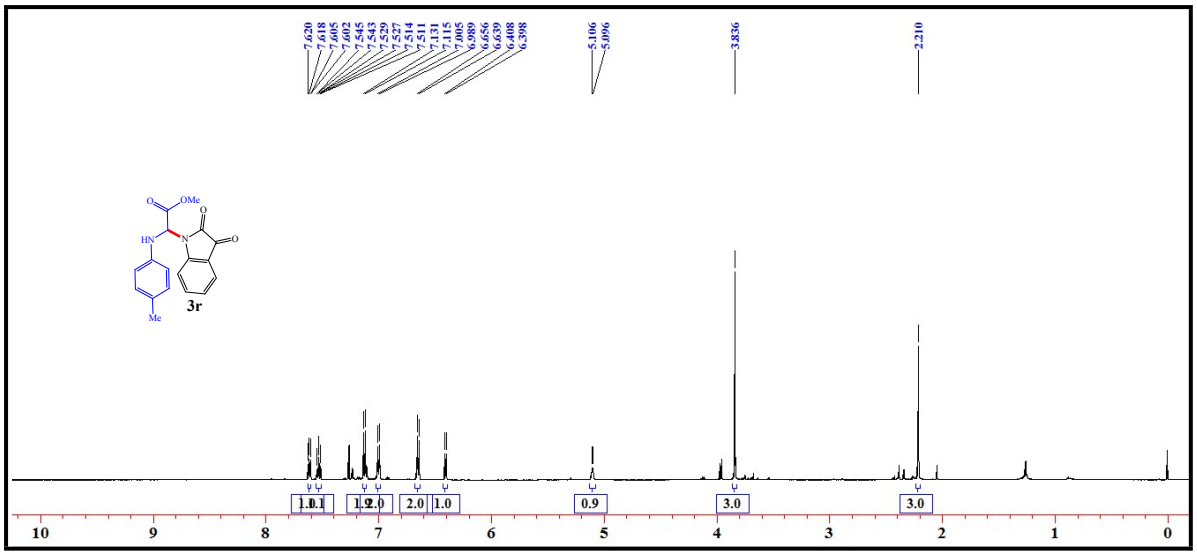


Figure S34. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3r**

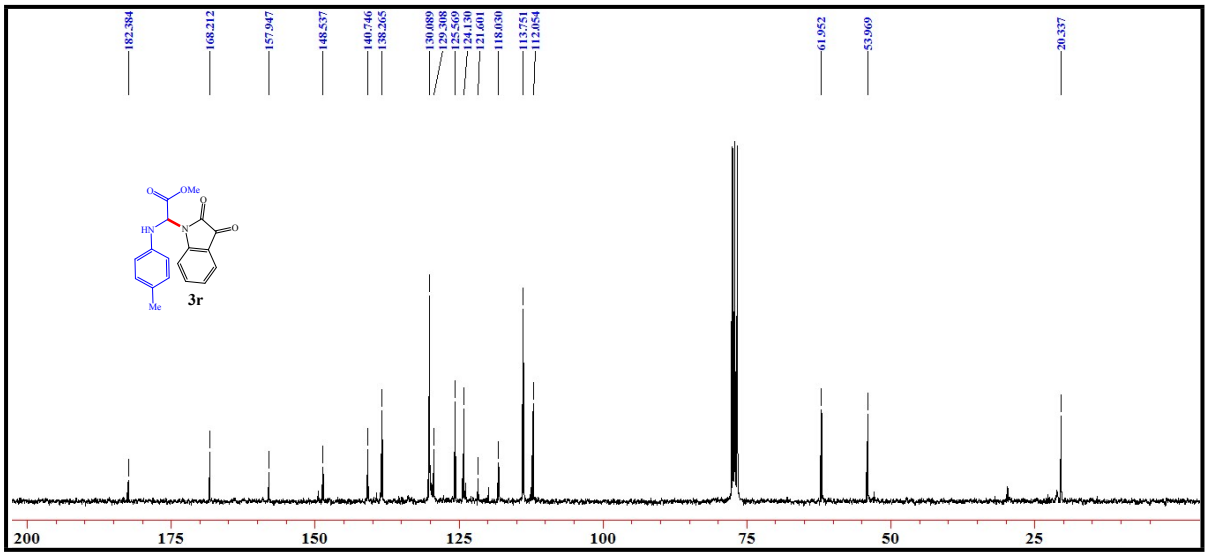


Figure S35. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of **3r**

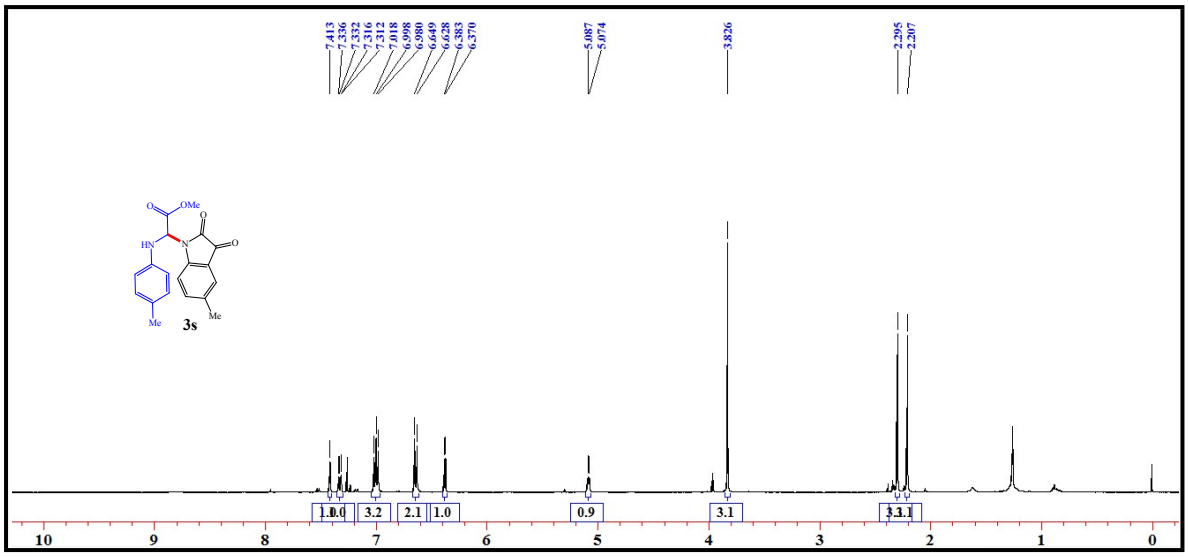


Figure S36. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3s**

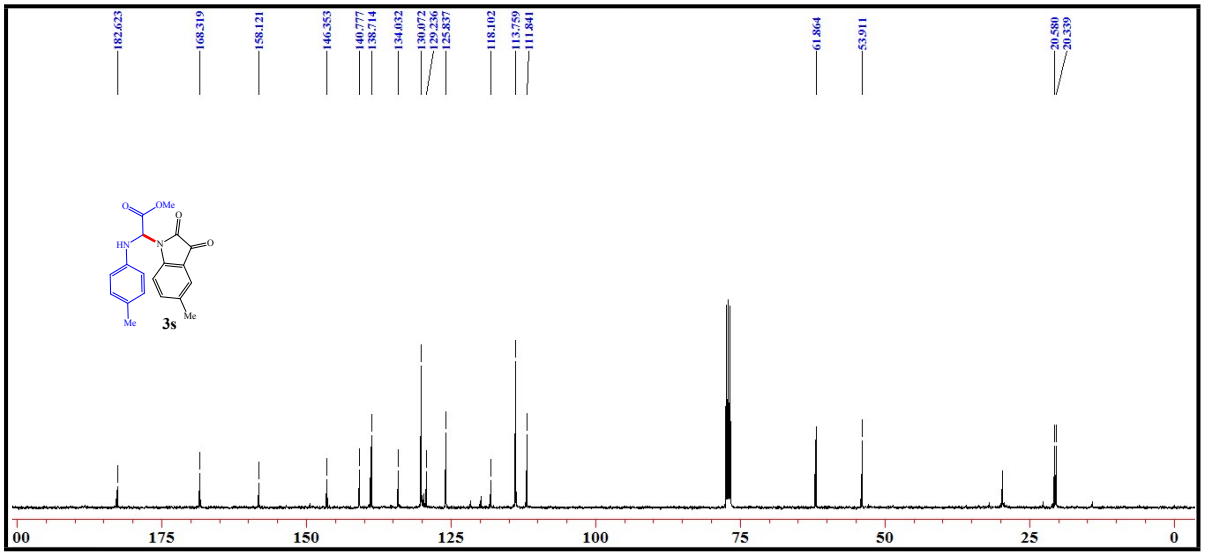


Figure S37. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3s**

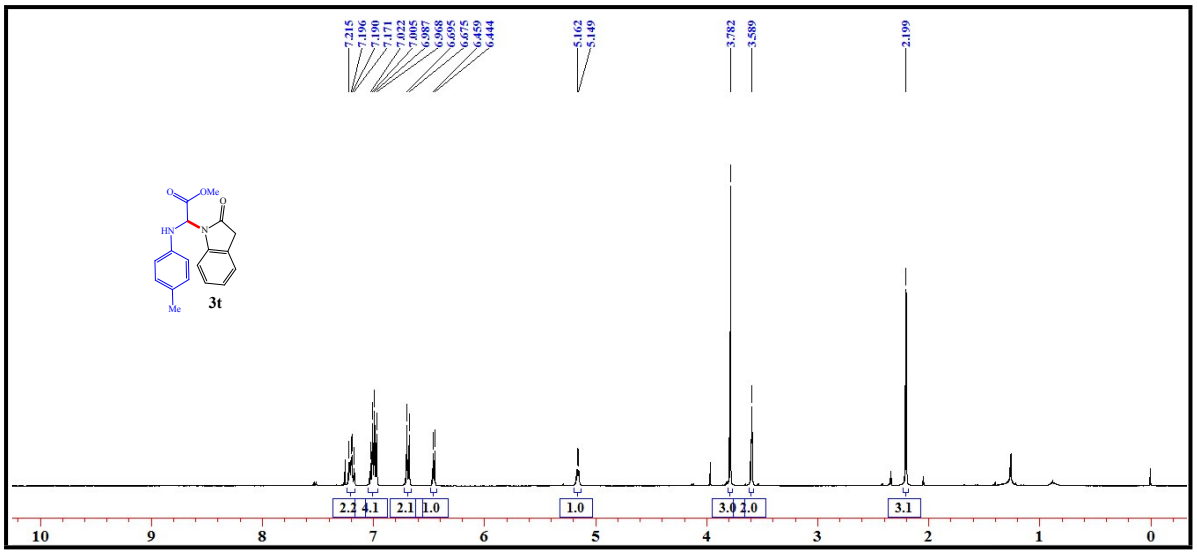


Figure S38. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3t**

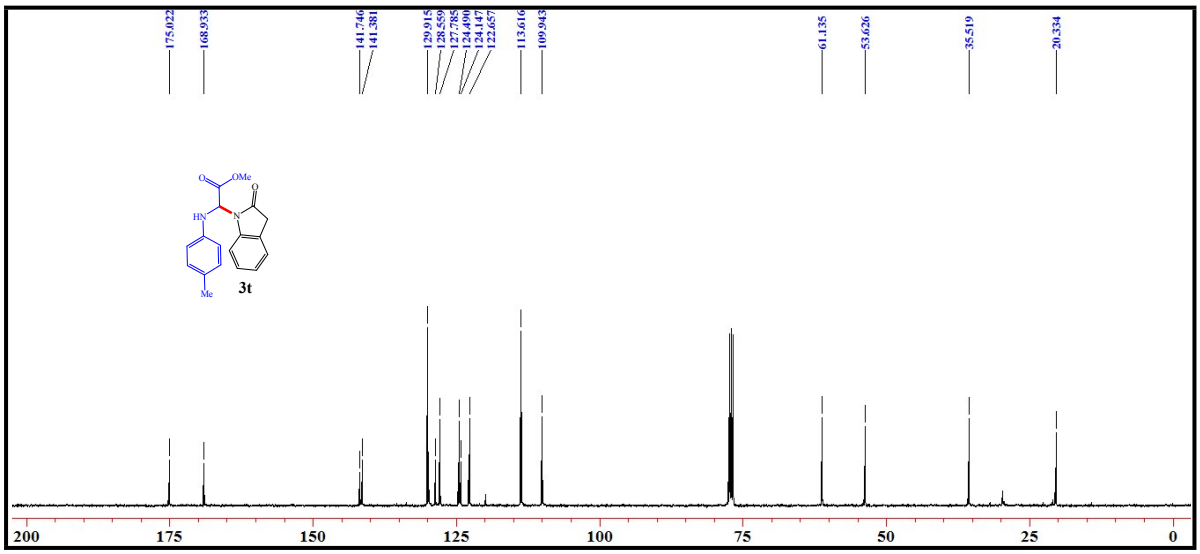


Figure S39. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3t**

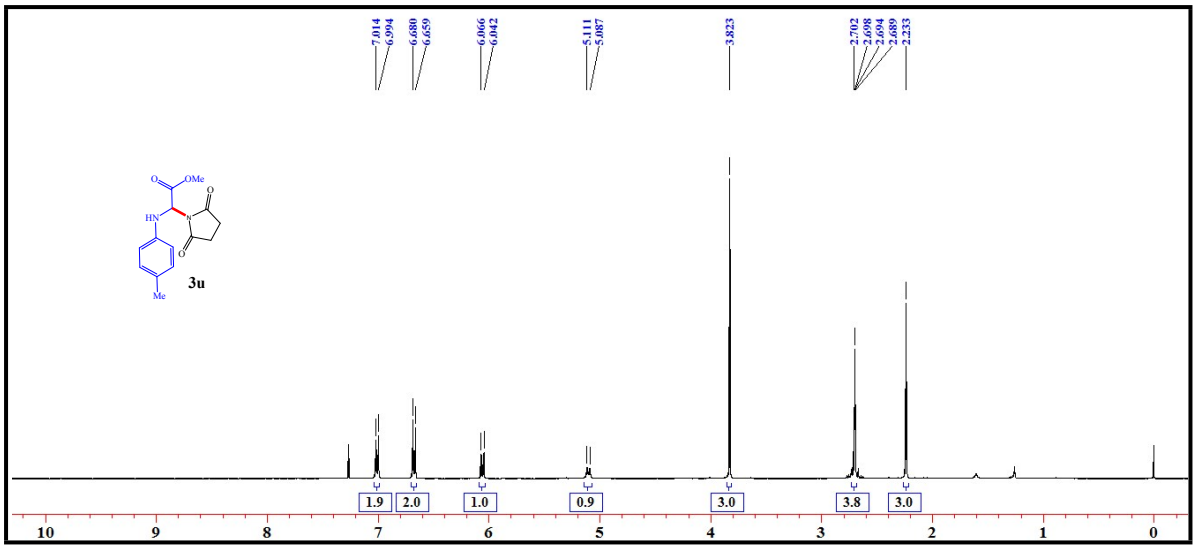


Figure S40. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3u**

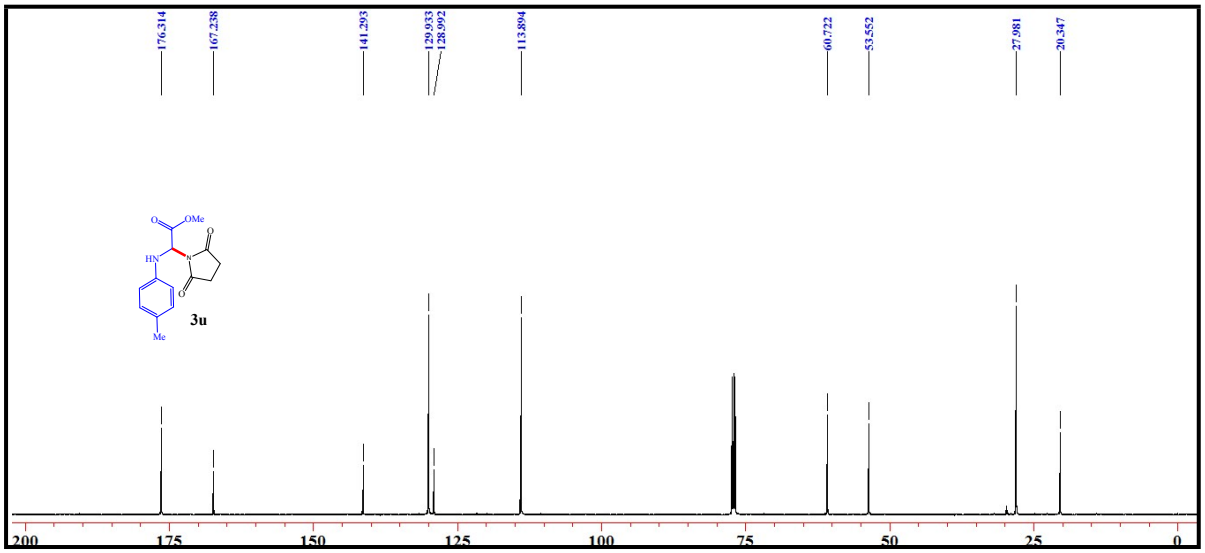


Figure S41. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3u**

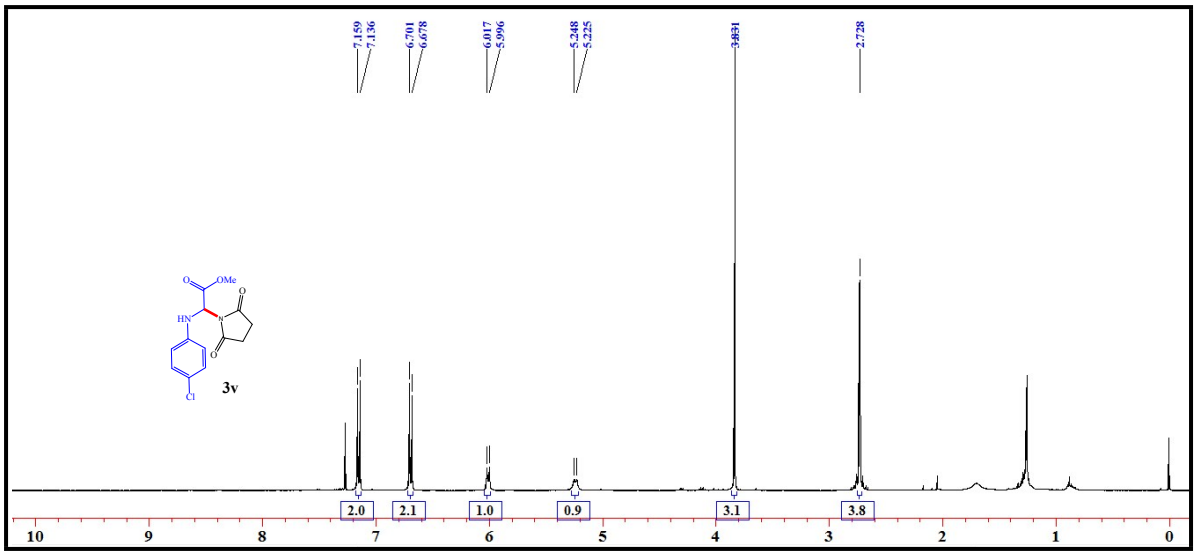


Figure S42. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3v**

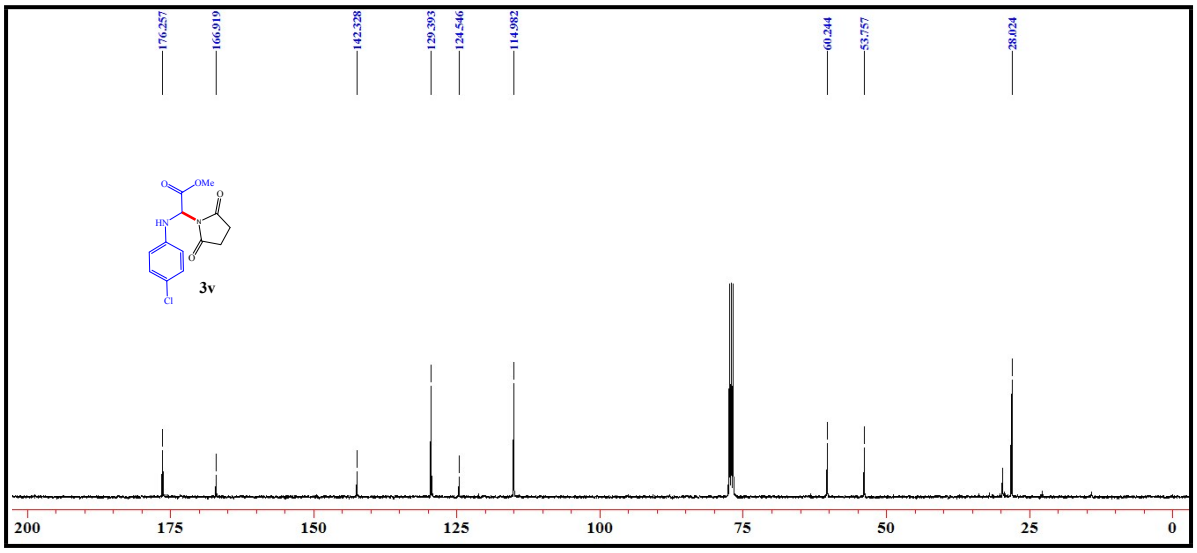


Figure S43. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3v**

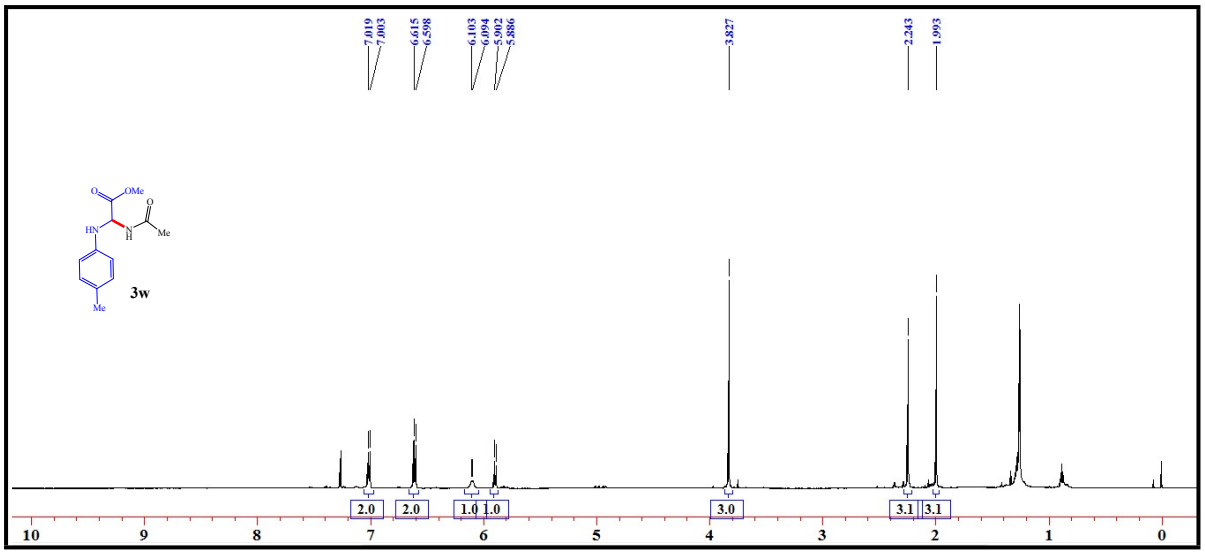


Figure S44. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3w**

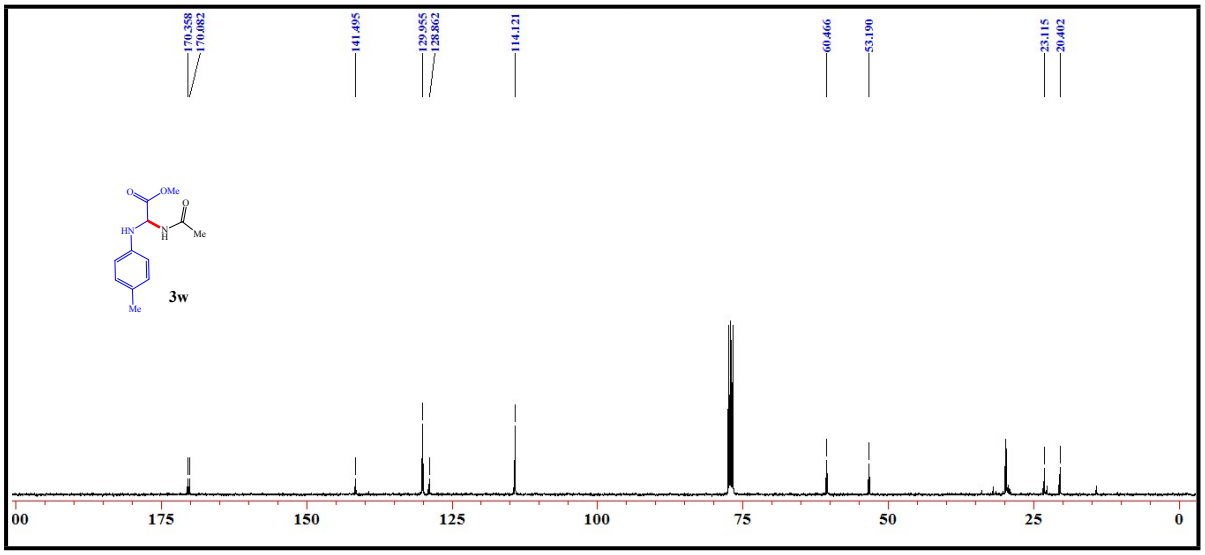


Figure S45. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3w**

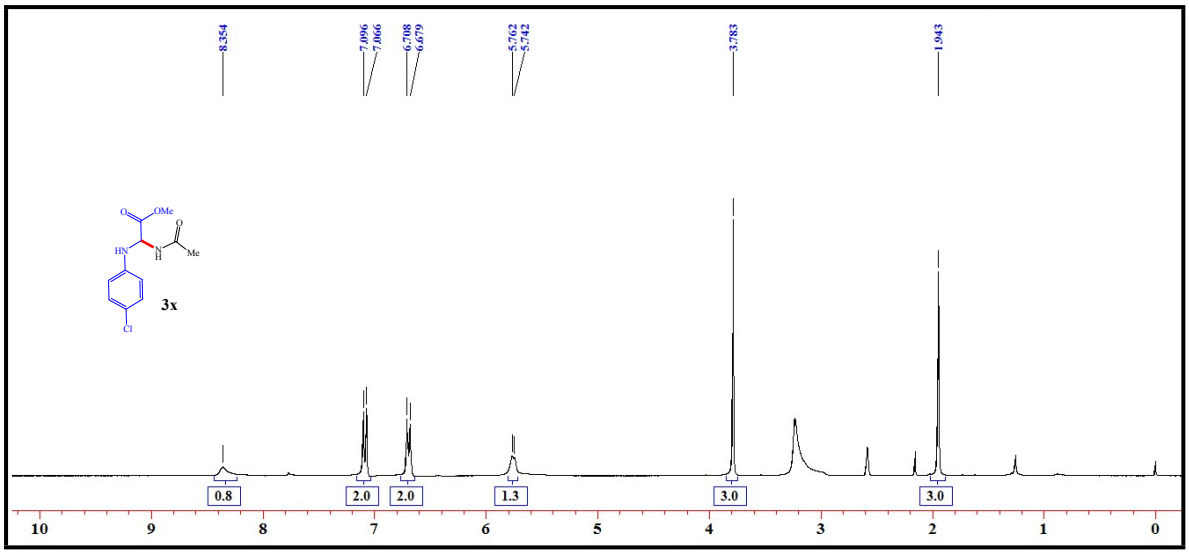


Figure S46. ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6) spectrum of **3x**

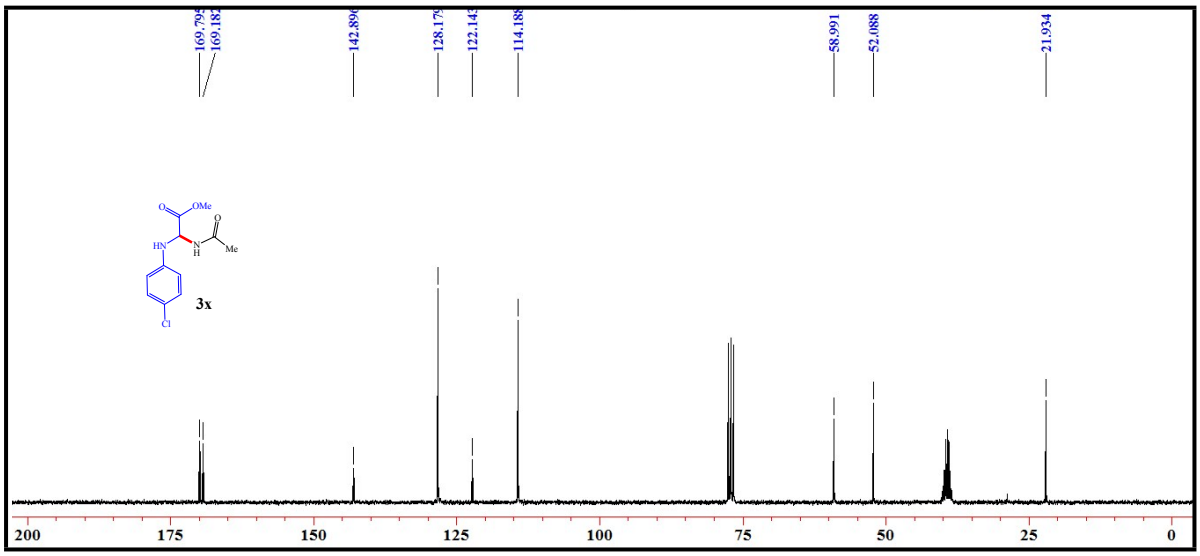


Figure S47. ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) spectrum of **3x**

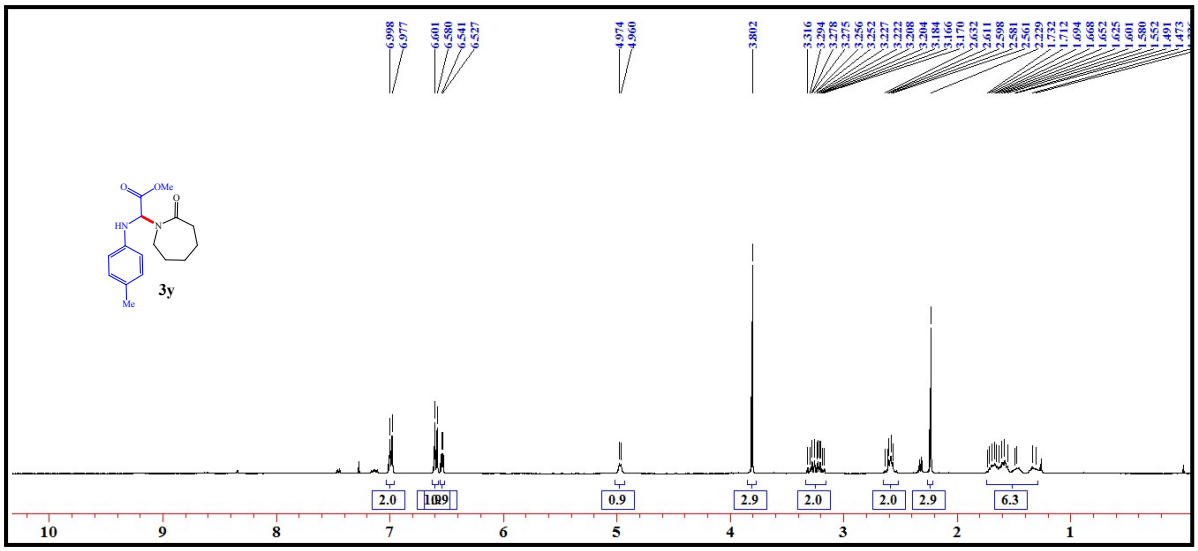


Figure S48. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3y**

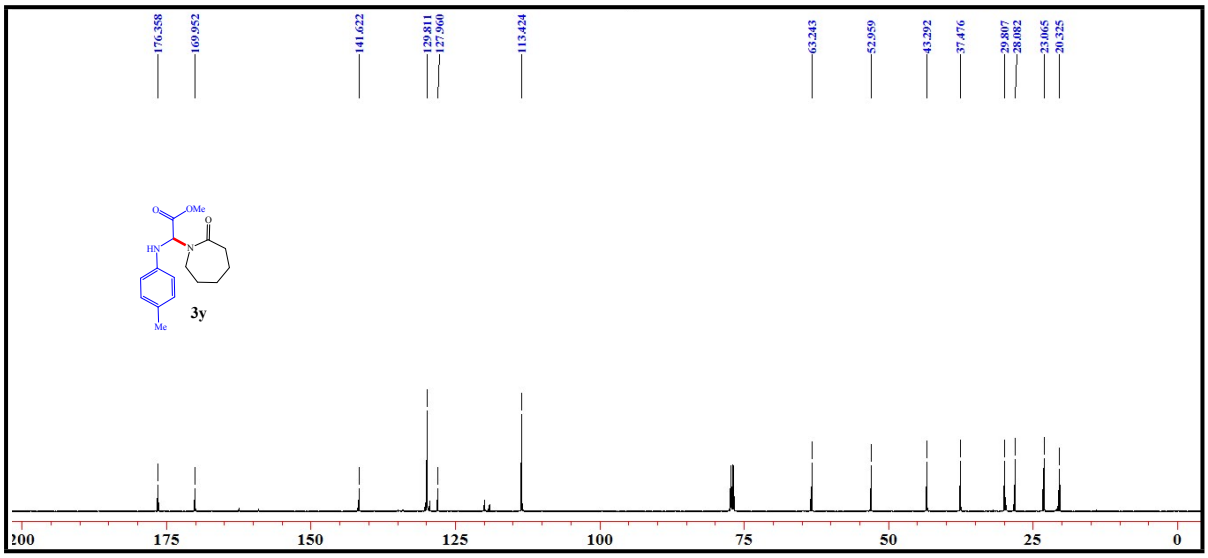


Figure S49. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3y**

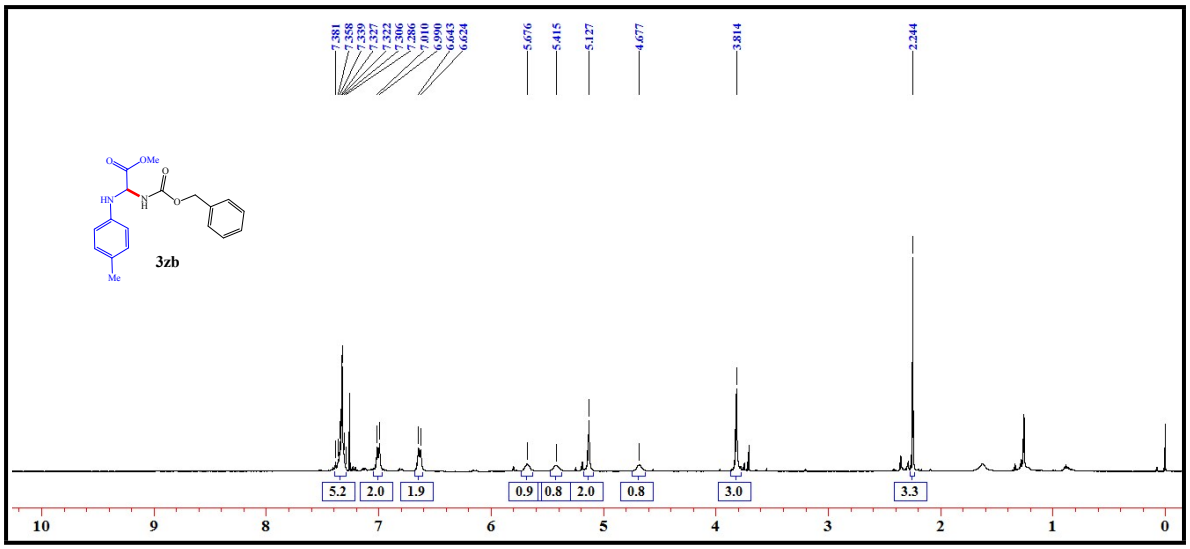


Figure S52. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3zb**

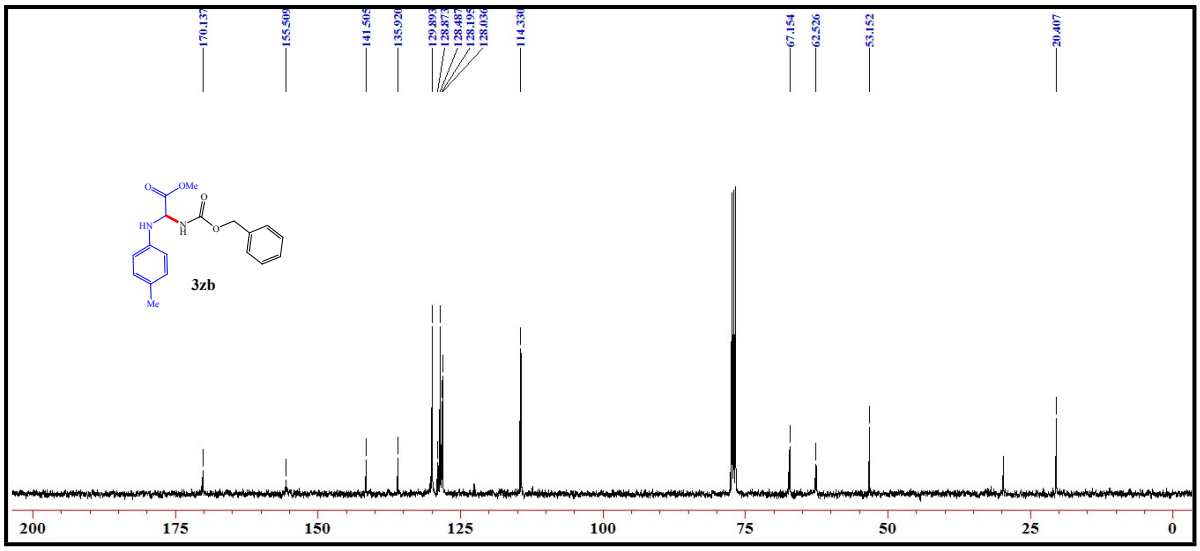


Figure S53. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3zb**

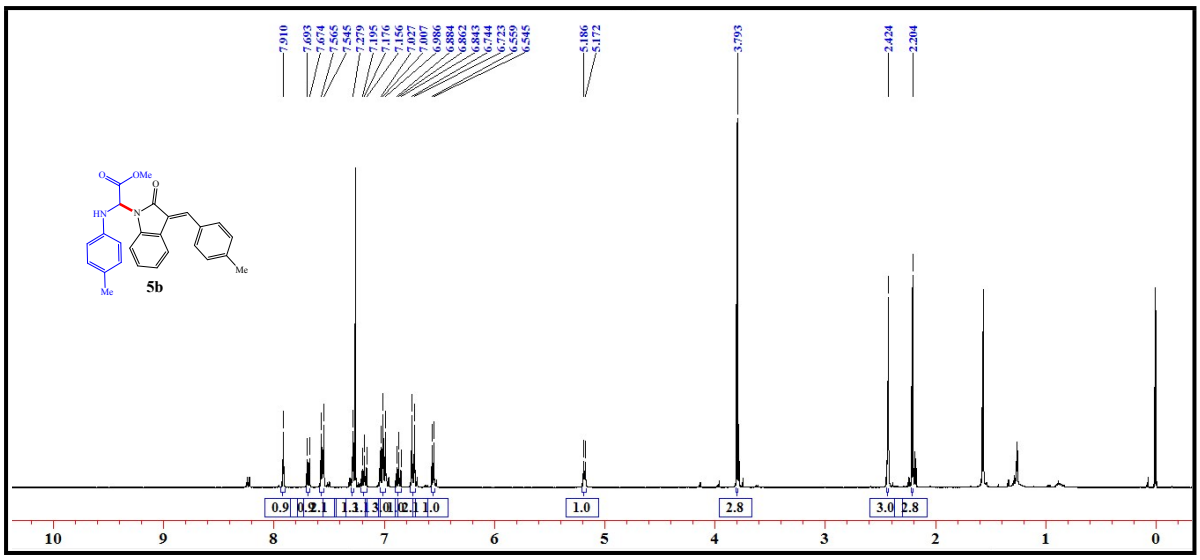


Figure S50. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **5b**

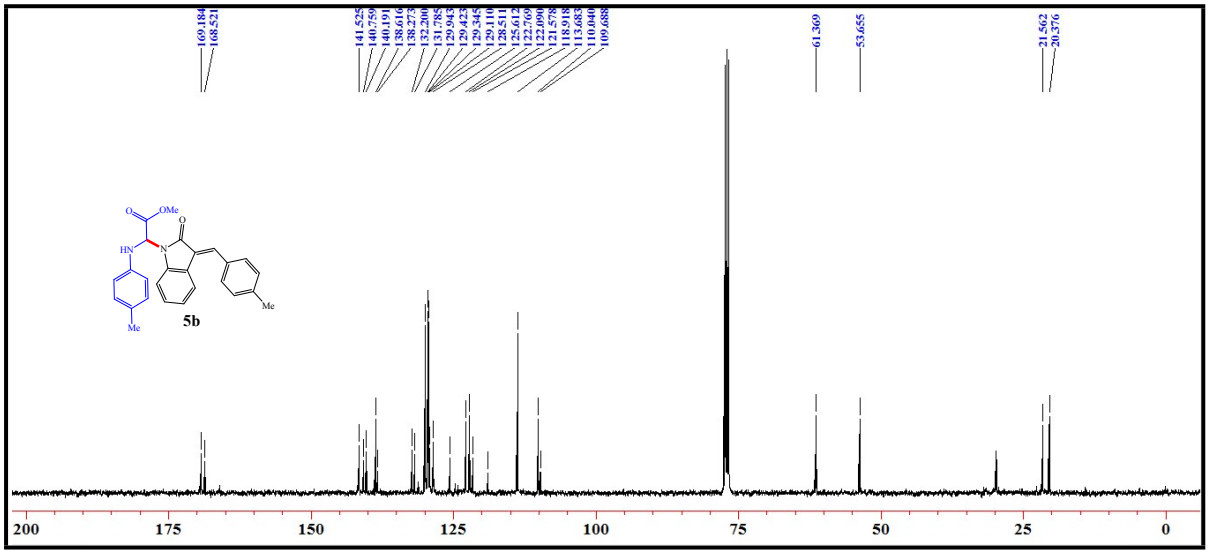


Figure S51. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **5b**