Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Supporting Information

## Facile Construction of Peptidomimetics by Sequential C-S/C-N Bond Activation of Ugi-Adducts

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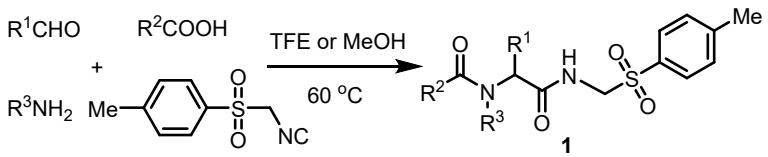
Contents

# 1. General information

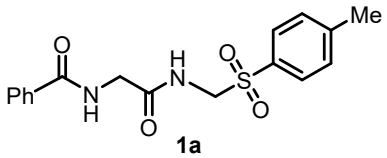
Commercially available reagents were used without additional purification. Column chromatography was performed with silica gel (70-230 mesh). $^{1}H$ and $^{13}C$ NMR spectra were recorded on a Bruker AM (300 or 400 MHz) spectrometer at ambient temperature using $CDCl_3$ or DMSO-$d_6$ or MeOH-$d_4$ as solvent. HRMS (ESI) spectrometry data were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer [Synapt G2 high definition mass spectrometer (HDMS), Waters, Milford, MA]. Samples were infused at 3 μL $min^{-1}$, and spectra were obtained in the positive ionization mode with a resolution of 15000 [full width at half maximum (FWHM)] with leucine encephalin as lock mass. Melting points were recorded on a Reichert Thermovar apparatus and were uncorrected.

# 2. General procedure for the synthesis of Ugi adducts




To a solution of aldehyde (For the HCHO: formaldehyde solution 37 wt. % in $H_2O$ was used) (1.0 mmol, 1.0 equiv) in MeOH (1.0 mL) were added successively amine (1.2 mmol, 1.2 equiv), acid (1.2mmol, 1.2 equiv) and isonitrile (1.2 mmol, 1.2 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred in an oil bath at 60 °C for 12 h in a closed vial. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: *n*-heptane/ethyl acetate = 1:4 v/v) to afford the desired Ugi products **1** (when ammonia solution (7 N in methanol: 2.0 equiv) was used, TFE would be the solvent instead of MeOH).

## 3. Characterization of Ugi adducts



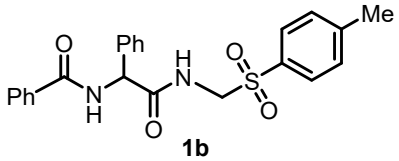
**1a**

**1a** was obtained as a white solid. Yield 70% (243 mg). Melting point 171 – 173 °C.

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 8.99 – 8.91 (m, 1H), 8.77 – 8.70 (m, 1H), 7.90 – 7.83 (m, 2H), 7.72 (d, $J$ = 8.2 Hz, 2H), 7.58 – 7.52 (m, 1H), 7.51 – 7.44 (m, 2H), 7.39 (d, $J$ = 8.0 Hz, 2H), 4.67 (d, $J$ = 6.4 Hz, 2H), 3.83 (d, $J$ = 5.9 Hz, 2H), 2.37 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 170.0, 167.1, 145.1, 135.4, 134.5, 132.0, 130.4, 129.1, 128.9, 128.0, 60.9, 43.0, 21.8.

HRMS (ESI, m/z) calcd for $C_{17}H_{18}N_2O_4S$ ([M+Na]$^+$): 369.0879, found 369.0861.



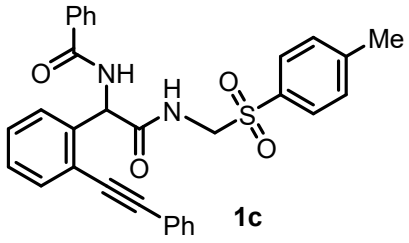
**1b**

**1b** was obtained as a white solid. Yield 65% (275 mg). Melting point 265 – 267 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.39 – 9.32 (m, 1H), 8.74 (d, $J$ = 8.1 Hz, 1H), 7.89 (d, $J$ = 7.3 Hz, 2H), 7.57 – 7.51 (m, 1H), 7.50 – 7.40 (m, 6H), 7.39 – 7.33 (m, 3H), 7.20 (d, $J$ = 8.0 Hz, 2H), 5.74 (d, $J$ = 8.2 Hz, 1H), 4.83 – 4.76 (m, 1H), 4.67 – 4.59 (m, 1H), 2.28 (s, 3H).

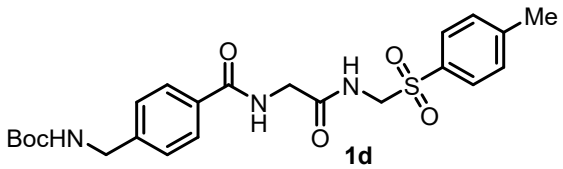
$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 170.7, 166.7, 144.9, 138.1, 135.0, 134.3, 132.1, 130.2 129.0, 128.9, 128.8, 128.4, 128.4, 60.7, 57.2, 21.7.

HRMS (ESI, m/z) calcd for $C_{23}H_{22}N_2O_4S$ ([M+Na]$^+$): 445.1192, found 445.1186.



**1c**

**1c** was obtained as a yellow solid according to literature [1]



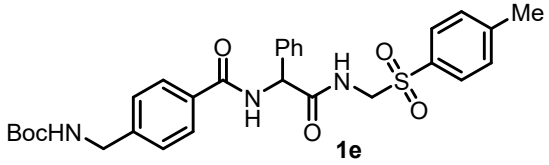

**1d**

**1d** was obtained as a white solid. Yield 75% (357 mg). Melting point 175 – 177 °C.

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 8.98 – 8.89 (m, 1H), 8.72 – 8.63 (m, 1H), 7.88 (d, $J$ = 7.9 Hz, 1H), 7.81 (d, $J$ = 7.9 Hz, 1H), 7.71 (d, $J$ = 8.0 Hz, 2H), 7.47 – 7.42 (m, 1H), 7.39 (d, $J$ = 8.0 Hz, 2H), 7.32 (d, $J$ = 8.1 Hz, 2H), 4.67 (d, $J$ = 6.4 Hz, 2H), 4.17 (d, $J$ = 5.1 Hz, 2H), 3.82 (d, $J$ = 5.6 Hz, 2H), [2.37 (s), 2.28 (s), 3H], [1.39 (s), 1.30 (s), 9H]. Mixture of rotamers (~6.5:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.8, 168.7, 168.5, 145.3, 136.5, 136.1, 135.2, 130.3, 129.1, 129.0, 127.1, 60.6, 53.1, 51.2, 48.5, 47.5, 21.7. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{23}H_{29}N_3O_6S$ ([M+Na]$^+$): 498.1669, found 498.1680.



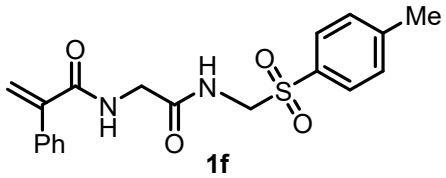

**1e**

**1e** was obtained as a white solid. Yield 60% (331 mg). Melting point 226 – 228 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.34 – 9.29 (m, 1H), 8.63 (d, $J$ = 8.1 Hz, 1H), 7.83 (d, $J$ = 8.0 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.43 – 7.38 (m, 3H), 7.37 – 7.33 (m, 3H), 7.31 (d, $J$ = 8.1 Hz, 2H), 7.20 (d, $J$ = 8.2 Hz, 2H), 5.72 (d, $J$ = 8.1 Hz, 1H), 4.82 – 4.75 (m, 1H), 4.67 – 4.57 (m, 1H), 4.17 (d, $J$ = 6.2 Hz, 2H), 2.29 (s, 3H), 1.39 (s, 9H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 170.7, 166.5, 156.4, 144.9, 144.4, 138.1, 135.0, 132.7, 130.1, 128.9, 128.8, 128.3, 127.1, 78.5, 60.7, 57.1, 43.8, 28.8, 21.6.

HRMS (ESI, m/z) calcd for $C_{29}H_{33}N_3O_6S$ ([M+Na]$^+$): 574.1982, found 574.1962.



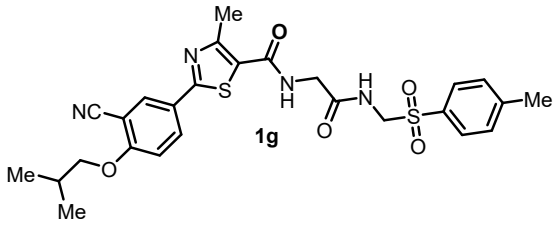
**1f**

**1f** was obtained as a white solid. Yield 72% (268 mg). Melting point 134 – 136 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.00 – 8.93 (m, 1H), 8.33 – 8.27 (m, 1H), 7.74 (d, $J$ = 8.1 Hz, 2H), 7.46 – 7.40 (m, 4H), 7.35 (d, $J$ = 7.5 Hz, 2H), 5.77 (s, 1H), 5.68 (s, 1H), 4.72 (d, $J$ = 6.3 Hz, 2H), 3.82 – 3.75 (m, 2H), 2.38 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.8, 169.1, 145.4, 145.2, 137.2, 135.4, 130.5, 129.1, 128.9, 128.8, 127.9, 118.9, 60.9, 42.6, 21.8.

HRMS (ESI, m/z) calcd for $C_{19}H_{20}N_2O_4S$ ([M+Na]$^+$): 395.1036, found 395.1029.



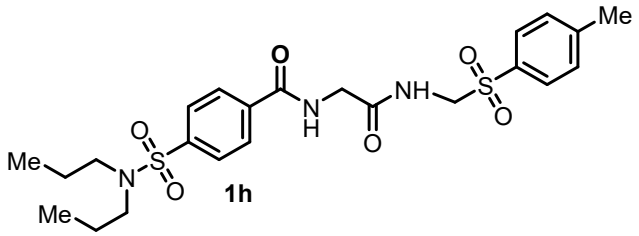
**1g**

**1g** was obtained as a yellow solid. Yield 20% (119 mg). Melting point 164 – 166 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.07 – 9.02 (m, 1H), 8.44 – 8.39 (m, 1H), 8.24 – 8.12 (m, 2H), 7.78 – 7.64 (m, 2H), 7.41 (d, $J$ = 8.1 Hz, 1H), 7.38 – 7.31 (m, 2H), 4.70 (d, $J$ = 6.5 Hz, 2H), [3.98 (d, $J$ = 6.3 Hz), 3.83 (d, $J$ = 5.8 Hz), 4H], [2.64 (s), 2.59 (s), 3H], [2.38 (s,), 2.29 (s), 3H] 2.12 – 2.05 (m, 1H), 1.02 (s, 3H), 1.00 (s, 3H). Mixture of rotamers (~1.5:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 169.6, 164.6, 162.5, 161.8, 155.9, 145.2, 135.3, 133.5, 131.8, 130.4, 129.1, 126.8, 126.1, 116.1, 114.6, 102.2, 75.7, 60.9, 43.0, 28.2, 21.8, 19.4, 17.7. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{26}H_{28}N_4O_5S_2$ ([M+Na]$^+$): 563.1393, found 563.1397.

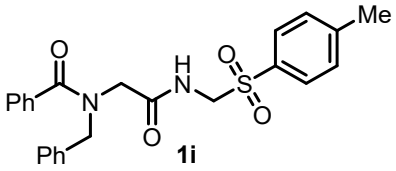



**1h** was obtained as a yellow solid. Yield 76% (387 mg). Melting point 109 – 111 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ [8.13 (d, J = 8.1 Hz), 7.92 (d, *J* = 8.5 Hz), 2H], 7.98 – 7.93 (m, 1H), [7.86 (d, J = 8.4 Hz), 7.80 (d, *J* = 8.3 Hz), 2H], 7.72 (d, *J* = 8.2 Hz, 2H), 7.67 – 7.63 (m, 1H), [7.32 (d, J = 8.0 Hz), 7.25 (d, J = 8.3 Hz), 2H], 4.68 (d, *J* = 6.7 Hz, 2H), 4.14 (d, *J* = 5.4 Hz, 2H), [3.12 – 3.08 (m), 3.07 – 3.03 (m), 4H], [2.41 (s), 2.34 (s), 3H], [1.59 – 1.54 (m), 1.53 – 1.46 (m), 4H], [0.88 – 0.85 (m), 0.84 – 0.80 (m), 6H]. Mixture of rotamers (~6.5:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 166.7, 145.7, 143.4, 136.6, 133.8, 130.2, 128.8, 128.2, 127.3, 60.6, 50.1, 43.7, 22.0, 21.8, 11.2. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{23}H_{31}N_3O_6S_2$ ($[M+Na]^+$): 532.1546, found 532.1560.

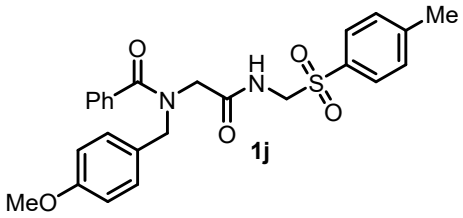



**1i** was obtained as a brown solid. Yield 85% (371 mg). Melting point 144 – 146 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ [8.02 (d, J = 7.5 Hz), 7.76 (d, *J* = 7.7 Hz), 2H], 7.95 – 7.83 (m, 1H), 7.46 (d, *J* = 6.8 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.35 (d, *J* = 7.0 Hz, 2H), 7.32 (d, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 4H), 7.11 (d, *J* = 6.2 Hz, 1H), 4.64 (d, *J* = 6.5 Hz, 2H), [4.55 (s), 4.47 (s), 2H], [4.00 (s), 3.69 (s), 2H], 2.39 (s, 3H). Mixture of rotamers (~5.7:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) δ 173.2, 168.6, 145.3, 135.6, 134.7, 134.3, 130.5, 130.0, 129.1, 128.9, 128.7, 128.1, 127.1, 60.4, 54.0, 48.4, 21.8. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{24}H_{24}N_2O_4S$ ($[M+Na]^+$): 459.1349, found 459.1353.



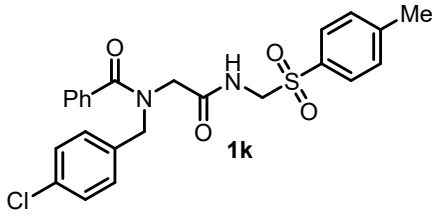

**1j**

**1j** was obtained as a white solid. Yield 76% (355 mg). Melting point 74 –76 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.86 – 7.73 (m, 3H), 7.51 – 7.45 (m, 2H), 7.44 – 7.36 (m, 4H), 7.30 (d, $J$ = 8.1 Hz, 2H), 7.10 – 7.00 (m, 1H), 6.89 – 6.86 (m, 2H), 4.66 (d, $J$ = 6.7 Hz, 2H), 4.43 (s, 2H), 4.02 (s, 2H), 3.79 (s, 3H), 2.42 (s, 3H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 168.6, 159.4, 145.2, 135.0, 134.3, 133.2, 130.3, 130.0, 128.9, 128.6, 128.5, 127.0, 114.4, 60.4, 55.3, 53.4, 48.0, 21.7.

HRMS (ESI, m/z) calcd for $C_{25}H_{26}N_2O_5S$ ([M+Na]$^+$): 467.1635, found 467.1654.



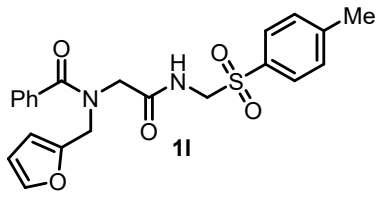

**1k**

**1k** was obtained as a white solid. Yield 68% (320 mg). Melting point 172 – 174 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.01 (s, 1H), 7.71 (d, $J$ = 6.7 Hz, 2H), 7.42 (s, 7H), 7.36 – 7.28 (m, 3H), 7.21 – 7.12 (m, 1H), 4.72 (s, 2H), [4.40 (s), 4.31 (s), 2H], [3.90 (s), 3.72 (s), 2H], 2.41 (s, 3H). Mixture of rotamers (~1.5:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.8, 168.7, 145.3, 136.5, 136.1, 135.2, 132.5, 130.3, 130.3, 129.2, 129.1, 129.0, 127.1, 60.7, 53.1, 51.2, 48.5, 47.5, 21.7. Mixture of rotamers

HRMS (ESI, m/z) calcd for $C_{24}H_{23}ClN_2O_4S$ ([M+Na]$^+$): 493.0959, found 493.0936.



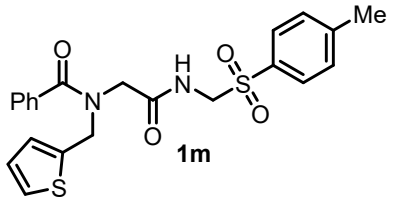

**1l**

**1l** was obtained as a white solid. Yield 68% (290 mg). Melting point 152 – 154 °C.

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 7.9 Hz, 2H), 7.64 – 7.54 (m, 3H), 7.48 – 7.38 (m, 5H), 7.29 (d, $J$ = 8.0 Hz, 2H), 6.34 – 6.32 (m, 1H), 6.21 (s, 1H), 4.65 (d, $J$ = 6.7 Hz, 2H), 4.37 (s, 1H), 4.03 (s, 1H), 2.40 (s, 3H).

$^{3}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.9, 168.5, 149.0, 145.4, 143.3, 134.2, 130.6, 130.1, 128.9, 128.7, 127.5, 110.6, 109.7, 60.4, 48.4, 47.3, 21.8.

HRMS (ESI, m/z) calcd for $C_{22}H_{22}N_2O_5S$ ([M+Na]$^+$): 449.1142, found 449.1139.



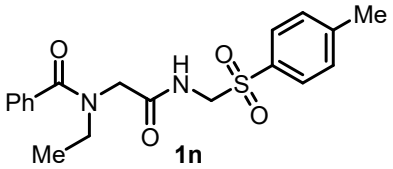

**1m**

**1m** was obtained as a brown solid. Yield 45% (199 mg). Melting point 136 – 138 °C.

$^{1}$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.11 (t, J = 6.5 Hz, 1H), [8.04 – 7.92 (m), 7.79 – 7.58 (m), 3H], 7.53 – 7.38 (m, 7H), 7.29 (d, J = 7.4 Hz, 1H), 7.05 – 6.99 (m, 1H), 4.75 (d, J = 6.5 Hz, 2H), [4.53 (s), 4.44 (s), 2H], [3.93 (s), 3.73 (s), 2H], [2.41 (s), 2.39 (s), 3H]. Mixture of rotamers (~6:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.3, 168.7, 145.3, 139.5, 135.9, 135.2, 133.4, 130.4, 129.8, 129.1, 127.9, 127.1, 60.7, 50.6, 44.0, 21.7. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{22}H_{22}N_2O_4S_2$ ([M+Na]$^+$): 465.0913, found 465.0919.



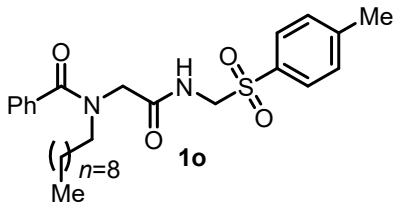

**1n**

**1n** was obtained as a white solid. Yield 78% (292 mg). Melting point 120 – 122 °C.

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.90 – 7.85 (m, 1H), 7.82 – 7.73 (m, 2H), 7.44 (s, 5H), 7.34 – 7.27 (m, 2H), 4.67 (d, $J$ = 6.9 Hz, 2H), 4.07 (s, 2H), 3.33 – 3.18 (m, 2H), 2.39 (s, 3H), 1.07 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.1, 169.1, 160.5, 145.4, 135.3, 134.4, 130.0, 128.9, 128.7, 126.8, 60.4, 49.1, 45.6, 21.8, 13.7.

HRMS (ESI, m/z) calcd for $C_{19}H_{22}N_2O_4S$ ([M+Na]$^+$): 397.1192, found 397.1183.



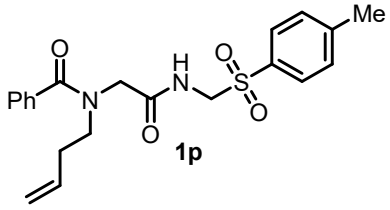

**1o**

**1o** was obtained as a yellow solid. Yield 40% (195 mg). Melting point 74 – 76 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 6.9 Hz, 1H), 7.78 (d, $J$ = 7.5 Hz, 2H), 7.42 – 7.37 (m, 5H), 7.29 – 7.25 (m, 2H), 4.67 (d, $J$ = 6.1 Hz, 2H), 4.26 – 3.61 (m, 2H), 3.38 – 3.08 (m, 2H), 2.37 (s, 3H), 1.49 – 1.41 (m, 2H), 1.28 – 1.24 (m, 4H), 1.23 – 1.14 (m, 8H), 1.09 – 1.02 (m, 2H), 0.86 (t, $J$ = 6.9 Hz, 3H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.9, 168.9, 145.1, 135.3, 134.3, 129.8, 128.8, 128.5 , 126.7, 67.0, 60.4, 50.7, 49.0, 31.8, 29.4, 29.2, 28.9, 28.1, 26.4, 22.6, 21.7, 14.1.

HRMS (ESI, m/z) calcd for $C_{27}H_{38}N_2O_4S$ ([M+Na]$^+$): 509.2444, found 509.2447.



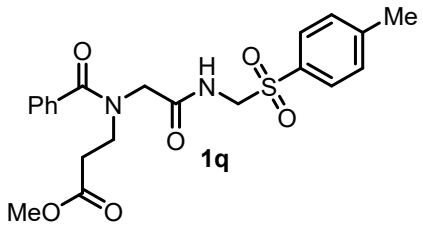

**1p**

**1p** was obtained as a brown solid. Yield 45% (180 mg). Melting point 136 – 138 °C. ). Mixture of rotamers (~6:1).

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 – 7.85 (m, 1H), 7.80 – 7.75 (m, 2H), 7.43 – 7.38 (m, 5H), 7.28 (d, $J$ = 8.0 Hz, 2H), 5.54 – 5.44 (m, 1H), 5.11 – 4.90 (m, 2H), 4.67 (d, $J$ = 6.5 Hz, 2H), 4.25 – 3.68 (m, 2H), 3.29 – 3.19 (m, 2H), [2.41 (s), 2.38 (s), 3H], 2.23 – 2.16 (m, 2H). Major rotamer.

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.2, 168.9, 145.3, 135.2, 134.2, 133.8, 130.0, 128.9, 128.7, 126.8, 117.8, 60.4, 50.2, 49.4, 32.7, 21.8. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{21}H_{24}N_2O_4S$ ([M+Na]$^+$): 423.1349, found 423.1335**.**



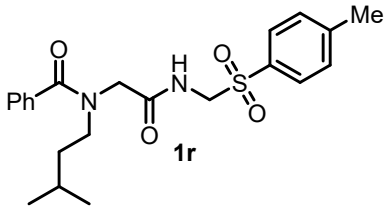

**1q**

**1q** was obtained as a yellow oil. Yield 52% (225 mg).

1H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 – 7.74 (m, 3H), 7.44 – 7.35 (m, 5H), 7.32 – 7.28 (m, 2H), 4.72 – 4.61 (m, 2H), 4.05 (s, 2H), [3.73 – 3.70 (m), 3.57 – 3.51 (m), 2H], 3.62 (s, 3H), 2.66 – 2.66 – 2.44 (m, 2H), [2.42 (s), 2.41 (s), 3H]. Mixture of rotamers (~9:1).

13C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 172.6, 171.2, 168.7, 160.4, 145.7, 145.5, 145.4, 135.1, 134.3, 133.7, 130.3, 130.1, 130.0, 128.9, 128.9, 128.8, 126.8, 60.5, 60.3, 58.8, 58.6, 55.1, 52.2, 52.0, 50.6, 32.6, 21.8. Mixture of rotamers.

HRMS (ESI, m/z) calcd for $C_{21}H_{24}N_2O_6S$ ([M+Na]+): 455.1247, found 455.1248.



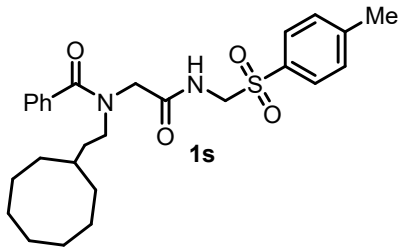

**1r**

**1r** was obtained as a brown solid. Yield 70% (292 mg). Melting point 103 – 105 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.07 – 9.00 (m, 1H), 7.99 – 7.57 (m, 2H), 7.53 – 7.35 (m, 5H), 7.33 – 7.22 (m, 2H), 4.75 – 4.69 (m, 2H), [4.00 (s), 3.78 (s), 2H], [3.20 – 3.14 (m), 3.05 – 2.97 (m), 2H], 2.39 (d, $J$ = 12.2 Hz, 3H), 1.62 – 1.44 (m, 1H), [1.41 – 1.35 (m), 1.30 – 1.25 (m), 2H], [0.91 (d, $J$ = 6.3 Hz), 0.64 (d, $J$ = 4.7 Hz), 6H]. Mixture of rotamers (~1:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.4, 171.4, 169.1, 168.9, 145.3, 145.1, 137.0, 136.8, 135.2, 130.4, 129.9, 129.9, 129.2, 129.2, 129.0, 129.0, 128.9, 127.0, 60.8, 60.6, 51.5, 48.6, 47.8, 44.5, 37.1, 35.7, 26.2, 25.7, 23.1, 22.7, 21.8. Mixture of rotamers.

HRMS (ESI, m/z) calcd for $C_{22}H_{28}N_2O_4S$ ([M+Na]$^+$): 439.1662, found 439.1660.



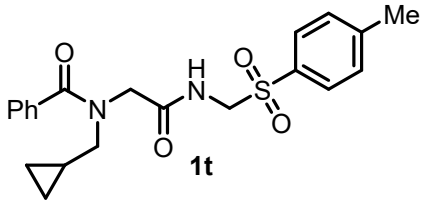

**1s**

**1s** was obtained as a white solid. Yield 77% (373 mg). Melting point 52 – 54 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 – 7.82 (m, 1H), 7.78 (d, $J$ = 7.9 Hz, 2H), 7.46 – 7.39 (m, 5H), 7.28 (d, $J$ = 8.1 Hz, 2H), 4.67 (d, $J$ = 6.6 Hz, 2H), 4.06 (s, 2H), 3.20 – 3.11 (m, 2H), 2.39 (s, 3H), 1.57 – 1.46 (m, 5H), 1.45 – 1.36 (m, 6H), 1.34 – 1.22 (m, 4H), 1.16 – 1.04 (m, 2H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.2, 169.1, 145.3, 135.2, 134.4, 130.0, 128.9, 128.6, 126.8, 60.4, 49.7, 49.5, 36.4, 35.1, 32.0, 27.2, 26.1, 25.3, 21.8.

HRMS (ESI, m/z) calcd for $C_{27}H_{36}N_2O_4S$ ([M+Na]$^+$): 507.2288, found 507.2303.



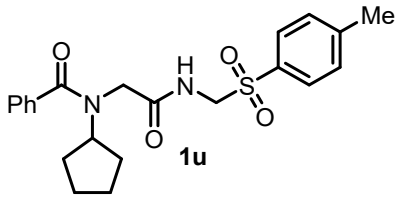

**1t**

**1t** was obtained as a yellow solid. Yield 62% (248 mg). Melting point 99 – 101 °C.

1H NMR (400 MHz, $CDCl_3$) $\delta$ 8.39 – 7.90 (m, 2H), 7.85 – 7.61 (m, 2H), [7.57 – 7.33 (m), 7.25 – 7.19 (m), 6H], 4.69 (s, 2H), [4.27 (s), 3.93 (s), 2H], 3.36 – 2.96 (m, 2H), 2.34 (s, 3H), [1.38 – 1.14 (m), 1.01 – 0.59 (m), 1H], 0.49 – 0.39 (m, 2H), 0.21 – -0.04 (m, 2H). Mixture of rotamers (~3:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.6, 169.3, 168.9, 145.3, 145.1, 135.1, 134.0, 132.9, 130.2, 129.8, 128.7, 128.7, 128.6, 128.4, 128.2, 126.8, 60.3, 58.8, 54.9, 48.3, 45.4, 21.5, 9.4, 8.4, 3.6. Mixture of rotamers (~3:1).

HRMS (ESI, m/z) calcd for $C_{21}H_{24}N_2O_4S$ ([M+Na]$^+$): 423.1349, found 423.1335.



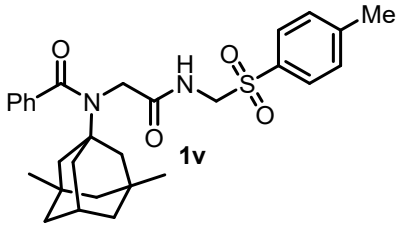

**1u**

**1u** was obtained as a brown solid. Yield 56% (232 mg). Melting point 165 – 167 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 – 7.87 (m, 1H), 7.78 – 7.70 (m, 2H), 7.41 – 7.33 (m, 5H), 7.28 – 7.23 (m, 2H), [4.66 (d, J = 6.7 Hz), 4.60 (d, J = 6.9 Hz), 2H], [4.01 (s), 3.92 (s), 2H], [2.38 (s), 2.35 (s), 3H], 2.36 (s, 1H), 1.75 – 1.52 (m, 4H), 1.46 – 1.15 (m, 4H). Mixture of rotamers (~9:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 169.7, 145.2, 134.3, 129.9, 129.9, 128.9, 128.8, 128.6, 126.6, 60.5, 58.9, 46.0, 29.8, 24.0, 21.7. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{22}H_{26}N_2O_4S$ ([M+Na]$^+$): 437.1505, found 437.1499.




**1v**

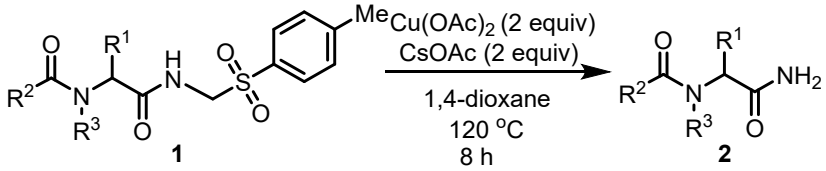
**1v** was obtained as a yellow solid. Yield 50% (254 mg). Melting point 115 – 117 °C.

$^1$H NMR (400 MHz, MeOH-$d_4$) $\delta$ [8.05 – 7.99 (m), 7.74 – 7.70 (m), 2H], 7.48 – 7.32 (m, 6H), 7.28 – 7.25 (m, 2H), [4.64 (s), 4.53 (s), 2H], [4.00 (s), 3.96 (s), 2H], [3.22 (s), 2.45 (s), 3H], 2.18 – 2.14 (m, 1H), 1.99 (d, $J$ = 11.6 Hz, 4H), 1.86 (d, $J$ = 11.4 Hz, 2H), 1.41 (d, $J$ = 11.8 Hz, 2H), 1.31 (d, $J$ = 12.2 Hz, 2H), 1.22 – 1.12 (m, 2H), 0.87 (s, 6H). Mixture of rotamers (~6:1).

$^{13}$C NMR (101 MHz, DMSO-*d*) $\delta$ 173.0, 172.9, 171.5, 170.7, 145.1, 140.2, 140.1, 135.6, 130.4, 129.9, 129.1, 129.1, 128.9, 128.9, 128.8, 126.2, 79.8, 71.0, 60.4, 55.6, 50.8, 50.6, 49.8, 49.6, 45.3, 45.1, 42.9, 42.8, 37.8, 33.0, 33.0, 31.0, 30.9, 30.7, 21.8. Mixture of rotamers (~6:1).

HRMS (ESI, m/z) calcd for $C_{29}H_{36}N_2O_4S$ ([M+Na]$^+$): 531.2288, found 531.2285.

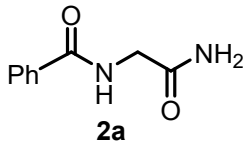
## 4. Copper-catalyzed reaction




**1** **2**

**1** (0.1 mmol, 1.0 equiv), CsOAc (0.2 mmol, 2.0 equiv) and $Cu(OAc)_2$ (0.2 mmol, 2.0 equiv) were placed to the screw cap vial followed by addition of 1,4-dioxane (1.0 mL) The resulting mixture was sealed and stirred in an oil bath at 120 °C for 8 h. After completion of the reaction, the mixture was evaporated under reduced pressure to obtain residue which was purified by a silica gel column chromatography (eluent: DCM/MeOH = 20:1 v/v) to afford the desired products **2**.

## 5. Characterization of products



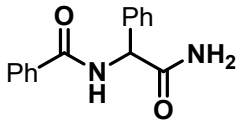

**2a**

**2a** was obtained as a white solid. Yield 80% (14.3 mg). Melting point 210 – 212 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.68 – 8.62 (m, 1H), 7.90 – 7.87 (m, 2H), 7.56 – 7.51 (m, 1H), 7.49 – 7.44 (m, 2H), 7.38 (s, 1H), 7.04 (s, 1H), 3.82 (d, *J* = 5.9 Hz, 2H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.7, 167.0, 134.7, 131.9, 128.9, 128.0, 43.1.

HRMS (ESI, m/z) calcd for $C_9H_{10}N_2O_2$ ([M+Na]$^+$): 201.0634, found 201.0630.



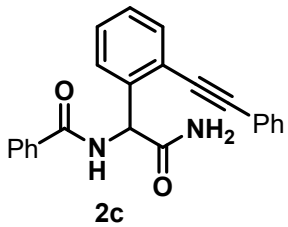
**2b**

**2b** was obtained as a white solid. Yield 50% (12.7 mg). Melting point 180 – 182 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.69 (d, J = 7.9 Hz, 1H), 7.97 – 7.86 (m, 2H), 7.74 – 7.63 (m, 1H), 7.59 – 7.49 (m, 3H), 7.49 – 7.41 (m, 2H), 7.41 – 7.26 (m, 3H), 7.25 – 7.17 (m, 1H), 5.63 (d, J = 8.0 Hz, 1H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 172.3, 166.6, 139.4, 134.6, 132.0, 128.9, 128.8, 128.2, 128.1, 128.1, 57.4.

HRMS (ESI, m/z) calcd for $C_{15}H_{14}N_2O_2$ ([M+Na]$^+$): 277.0947, found 277.0944.



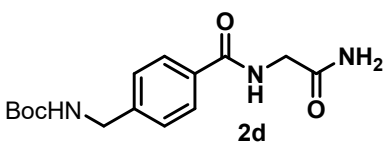
**2c**

**2c** was obtained as a yellow solid. Yield 58% (20.6 mg). Melting point 145 – 147 °C.

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.86 (d, $J$ = 7.3 Hz, 3H), 7.63 – 7.59 (m, 3H), 7.54 – 7.46 (m, 2H), 7.42 (d, $J$ = 7.7 Hz, 2H), 7.40 – 7.36 (m, 4H), 7.34 – 7.29 (m, 1H), 6.24 (s, 1H), 6.18 (d, $J$ = 6.0 Hz, 1H), 5.63 (s, 1H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 171.6, 166.4, 139.9, 133.8, 133.2, 131.9, 131.8, 129.5, 129.2, 128.7, 128.7, 128.4, 127.3, 127.0, 122.4, 121.9, 95.8, 87.3, 55.9.

HRMS (ESI, m/z) calcd for $C_{23}H_{18}N_2O_2$ ([M+Na]$^+$): 377.1260, found 377.1269.



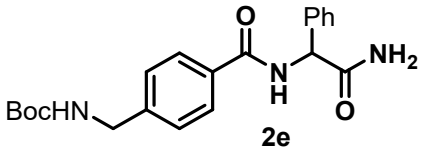
**2d**

**2d** was obtained as a white solid. Yield 62% (19 mg). Melting point 134 – 136 °C.

1H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.60 (t, J = 5.9 Hz, 1H), 7.86 – 7.80 (m, 2H), 7.44 (t, J = 6.2 Hz, 1H), 7.39 – 7.24 (m, 3H), 7.02 (s, 1H), 4.17 (d, J = 6.2 Hz, 2H), 3.80 (d, J = 5.9 Hz, 2H), 1.39 (s, 9H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 171.7, 166.8, 156.5, 144.2, 133.2, 128.0, 127.2, 78.6, 43.8, 43.0, 28.9.

HRMS (ESI, m/z) calcd for $C_{15}H_{21}N_3O_4$ ([M+H]$^+$): 308.1605, found 308.1590.



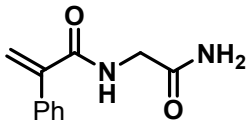

**2e**

**2e** was obtained as a white solid. Yield 50% (19.2 mg). Melting point 95 – 97 °C.

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.79 – 7.74 (m, 2H), 7.61 (d, $J$ = 6.5 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.39 – 7.33 (m, 3H), 7.33 – 7.30 (m, 2H), 6.06 (s, 1H), 5.76 – 5.72 (m, 1H), 5.69 (d, $J$ = 6.5 Hz, 1H), 4.99 (s, 1H), 4.33 (d, $J$ = 6.1 Hz, 2H), 1.45 (s, 9H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.4, 169.4, 166.6, 156.1, 143.3, 138.0, 132.8, 129.3, 127.9, 127.7, 127.6, 79.9, 57.3, 44.4, 28.5.

HRMS (ESI, m/z) calcd for $C_{21}H_{25}N_3O_4$ ([M+Na]$^+$): 406.1737, found 406.1735.



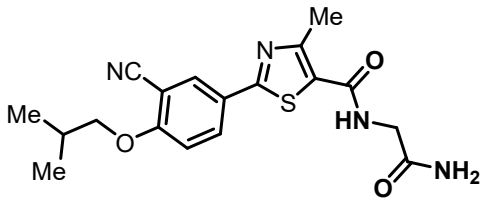

**2f**

**2f** was obtained as a white solid. Yield 52% (10.6 mg). Melting point 79 – 81 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 – 7.35 (m, 5H), 6.67 (s, 1H), 6.55 (s, 1H), 6.12 (s, 1H), 5.88 (s, 1H), 5.66 (s, 1H), 4.03 (d, $J$ = 4.9 Hz, 2H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 171.3, 168.1, 144.2, 136.7, 128.9, 128.2, 43.3.

HRMS (ESI, m/z) calcd for $C_{11}H_{12}N_2O_2$ ([M+Na]$^+$): 227.0791, found 227.0813.



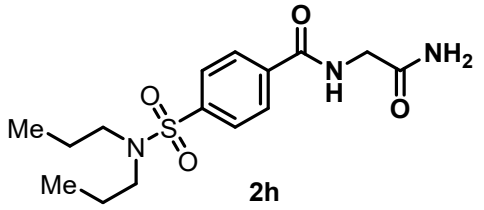
**2g**

**2g** was obtained as a yellow solid. Yield 53% (20 mg). Melting point 168 – 170 °C.

1H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.32 – 8.28 (m, 1H), 8.24 (d, J = 2.3 Hz, 1H), 8.20 – 8.16 (m, 1H), 7.44 – 7.35 (m, 2H), 7.07 (s, 1H), 4.00 (d, J = 6.5 Hz, 2H), 3.80 (d, J = 5.8 Hz, 2H), 2.63 (s, 3H), 2.13 – 2.06 (m, 1H), 1.03 (s, 3H), 1.01 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 171.1, 164.5, 162.5, 161.7, 155.6, 133.5, 131.9, 127.1, 126.2, 116.1, 114.6, 102.2, 75.7, 43.1, 28.2, 19.4, 17.7.

HRMS (ESI, m/z) calcd for $C_{18}H_{20}N_4O_3S$ ([M+H]$^+$): 373.1329, found 373.1330.



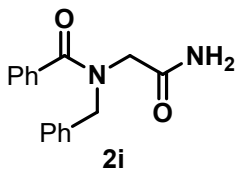
**2h**

**2h** was obtained as a white solid. Yield 66% (22.6 mg). Melting point 120 – 122 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 7.1 Hz, 2H), 7.83 (d, $J$ = 6.6 Hz, 2H), 7.57 (s, 1H), 6.53 (s, 1H), 6.10 (s, 1H), 4.13 (s, 2H), 3.12 – 3.03 (m, 4H), 1.56 – 1.50 (m, 4H), 0.85 (t, $J$ = 6.1 Hz, 6H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 171.5, 166.6, 143.4, 137.0, 128.1, 127.4, 50.1, 43.4, 22.1, 11.3.

HRMS (ESI, m/z) calcd for $C_{15}H_{23}N_3O_4S$ ([M+H]$^+$): 342.1482, found 342.1470.



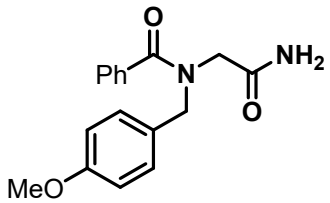
**2i**

**2i** was obtained as a yellow solid. Yield 55% (14.8 mg). Melting point 109 – 111 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.50 (d, J = 7.3 Hz, 2H), 7.46 – 7.28 (m, 7H), 7.23 – 7.15 (m, 1H), [6.36 (s), 5.85 (s), 1H], [5.64 (s), 5.54 (s), 1H], [4.83 (s), 4.66 (s), 2H], [4.09 (s), 3.81 (s), 2H] Mixture of rotamers (~7:3).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 171.0, 130.4, 129.1, 128.8, 128.1, 127.2, 127.0, 54.2, 48.7. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{16}H_{16}N_2O_2$ ($[M+H]^+$): 269.1285, found 269.1275.

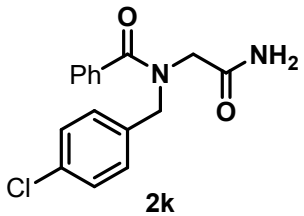



**2j**

**2j** was obtained as a yellow solid. Yield 85% (25.4 mg). Melting point 158 – 160 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.49 (d, *J* = 6.9 Hz, 2H), 7.43 – 7.36 (m, 4H), 7.10 – 7.07 (m, 1H), 6.88 – 6.85 (m, 2H), [6.46 (s), 6.20 (s), 1H], [5.98 (s), 5.83 (s), 1H], 4.72 (d, *J* = 6.4 Hz, 1H), 4.57 (s, 2H), 4.05 (s, 1H), 3.79 (s, 3H). Mixture of rotamers (~7:3).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.9, 171.3, 159.4, 130.3, 128.7, 128.7, 127.0, 114.4, 55.4, 53.7, 48.4. Major rotamer.



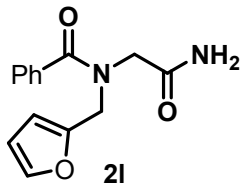

**2k**

**2k** was obtained as a white solid. Yield 84% (25.5 mg). Melting point 161 – 163 °C.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.54 – 7.30 (m, 8H), [7.25 (s), 7.23 (s), 1H], [7.13 (s), 7.09 (s), 1H], [4.61 (s), 4.48 (s), 2H], [3.89 (s), 3.68 (s), 2H]. Mixture of rotamers (~3:1).

$^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 172.1, 171.9, 170.2, 170.0, 136.9, 136.7, 136.5, 132.5, 130.4, 130.2, 129.4, 129.3, 129.1, 129.0, 127.2, 53.2, 51.3, 48.8, 47.7. Mixture of rotamers (~3:1).

HRMS (ESI, m/z) calcd for $C_{16}H_{15}ClN_2O_2$ ([M+Na]$^+$): 325.0714, found 325.0710.



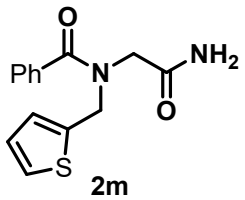

**2l**

**2l** was obtained as a white solid. Yield 48% (12.4 mg). Melting point 161 – 163 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.66 – 7.54 (m, 2H), 7.50 – 7.36 (m, 5H), 6.38 – 6.32 (m, 1H), 6.28 (s, 1H), 5.65 (s, 1H), 4.55 (s, 2H), 4.11 (s, 2H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.9, 171.1, 143.2, 130.5, 128.7, 127.5, 110.7, 109.9, 48.7, 47.5.

HRMS (ESI, m/z) calcd for $C_{14}H_{14}N_2O_3$ ([M+Na]$^+$): 281.0897, found 281.0902.



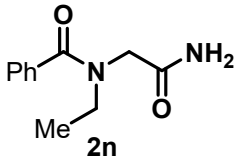

**2m**

**2m** was obtained as a yellow solid. Yield 78% (21.4 mg). Melting point 162 – 164 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ [8.11 – 7.99 (m), 7.50 – 7.16 (m), 5H], 7.65 – 7.51 (m, 1H), 7.05 – 6.84 (m, 2H), [6.46 (s), 6.38 (s), 1H], [6.10 (s), 5.92 (s), 1H], [4.89 (s), 4.75 (s), 2H], [4.11 (s), 3.84 (s), 2H]. Mixture of rotamers (~3:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.7, 171.2, 138.8, 135.0, 130.4, 128.8, 127.2, 127.0, 125.9, 49.5, 48.0. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{14}H_{14}N_2O_2S$ ([M+Na]$^+$): 297.0668, found 297.0662.



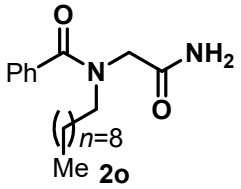
**2n**

**2n** was obtained as a white solid. Yield 98% (20.1 mg). Melting point 76 – 78 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 – 7.37 (m, 5H), 6.71 (s, 1H), 5.87 (s, 1H), 4.12 (s, 2H), 3.39 (s, 2H), 1.16 (t, $J$ = 7.2 Hz, 3H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.8, 172.0, 135.6, 130.1, 128.7, 126.7, 49.5, 45.8, 29.8, 13.9.

HRMS (ESI, m/z) calcd for $C_{11}H_{14}N_2O_2$ ([M+Na]$^+$): 229.0947, found 229.0946.



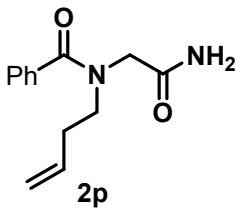
**2o**

**2o** was obtained as a white solid. Yield 93% (30 mg). Melting point 148 – 150 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51 – 7.32 (m, 5H), [6.77 (s), 6.64 (s), 1H], [6.25 (s), 6.02 (s),1H], [4.11 (s), 3.86 (s), 2H], [3.50 – 3.25 (m), 3.23 – 3.08 (m), 2H], 1.67 – 1.43 (m, 2H), 1.34 – 1.20 (m, 6H), 1.20 – 0.97 (m, 8H), 0.86 (t, $J$ = 6.9 Hz, 3H). Mixture of rotamers (~9:1).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.8, 172.0, 135.6, 129.9, 128.6, 126.7, 51.1, 49.8, 31.9, 29.5, 29.5, 29.3, 29.1, 28.4, 26.5, 22.7, 14.2. Major rotamer.

HRMS (ESI, m/z) calcd for $C_{19}H_{30}N_2O_2$ ([M+Na]$^+$): 341.2199, found 341.2193.



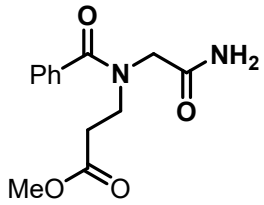
**2p**

**2p** was obtained as a yellow solid. Yield 90% (21 mg). Melting point 210 – 212 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51 – 7.36 (m, 5H), 6.64 (s, 1H), 5.56 (s, 2H), 5.03 (d, $J$ = 9.6 Hz, 2H), 4.14 (s, 2H), 3.45 (s, 2H), 2.36 (s, 2H).

$^{13}$C NMR (151 MHz, $CDCl_3$) $\delta$ 173.1, 171.7, 135.5, 133.9, 130.2, 128.7, 126.9, 118.0, 50.7, 33.0, 29.8.

HRMS (ESI, m/z) calcd for $C_{13}H_{16}N_2O_2$ ([M+Na]$^+$): 255.1104, found 255.1106.



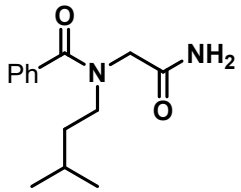

**2q**

**2q** was obtained as a white solid. Yield 77% (20.4 mg). Melting point 90 – 92 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41 (s, 5H), 6.50 (s, 1H), 5.78 (s, 1H), 4.08 (s, 2H), 3.75 – 3.71 (m, 2H), 3.65 (s, 3H), 2.68 (s, 2H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 171.3, 171.3, 135.4, 130.2, 128.8, 126.8, 52.0, 32.9, 22.8, 14.2.

HRMS (ESI, m/z) calcd for $C_{13}H_{16}N_2O_4$ ([M+Na]$^+$): 287.1002, found 287.1006.



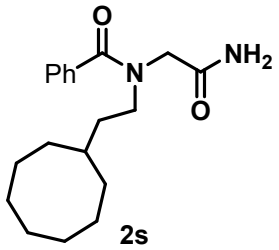

**2r**

**2r** was obtained as a white solid. Yield 98% (24.3 mg). Melting point 64 – 66 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.52 – 7.34 (m, 5H), 6.72 (s, 1H), 5.75 (s, 1H), 4.13 (s, 2H), 3.36 – 3.30 (m, 2H), 1.49 – 1.45 (m, 2H), 1.42 – 1.32 (m, 1H), 0.78 – 0.66 (m, 6H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 172.9, 172.1, 135.6, 130.1, 128.6, 126.8, 50.1, 49.8, 37.4, 25.8, 22.3.

HRMS (ESI, m/z) calcd for $C_{14}H_{20}N_2O_2$ ([M+Na]$^+$): 271.1417, found 271.1423.



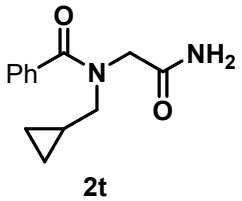
**2s**

**2s** was obtained as a yellow solid. Yield 74% (23.4 mg).

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42 – 7.38 (m, 5H), 6.71 (s, 1H), 5.82 (s, 1H), 4.12 (s, 2H), 3.33 (s, 2H), 1.63 – 1.43 (m, 9H), 1.41 – 1.26 (m, 6H), 1.16 – 1.06 (m, 2H).

$^{13}$C NMR (151 MHz, $CDCl_3$) $\delta$ 172.9, 172.0, 135.6, 130.1, 128.6, 126.8, 50.3, 49.9, 36.6, 35.0, 32.0, 27.2, 26.2, 25.3.

HRMS (ESI, m/z) calcd for $C_{19}H_{28}N_2O_2$ ([M+H]$^+$): 317.2224, found 317.2224.



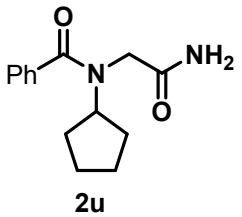
**2t**

**2t** was obtained as a yellow oil. Yield 62% (14.4 mg).

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51 – 7.36 (m, 5H), 6.67 (s, 1H), 5.78 (s, 1H), 4.31 (s, 2H), 3.27 (s, 2H), 1.00 – 0.93 (m, 1H), 0.64 – 0.47 (m, 2H), 0.16 – 0.07 (m, 2H)

$^{13}$C NMR (101 MHz, $CDCl_3$) δ 172.7, 172.1, 135.6, 130.1, 128.7, 127.0, 55.5, 49.6, 9.9, 4.0.

HRMS (ESI, m/z) calcd for $C_{13}H_{16}N_2O_2$ ([M+Na]$^+$): 255.1104, found 255.1111.



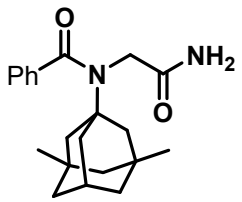
**2u**

**2u** was obtained as a yellow oil. Yield 92% (23 mg).

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.48 – 7.34 (m, 5H), 6.85 (s, 1H), 5.92 (s, 1H), 4.13 – 4.07 (m, 1H), 4.03 (s, 2H), 1.79 – 1.75 (m, 2H), 1.71 – 1.51 (m, 4H), 1.44 – 1.41 (m, 2H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 173.0, 171.1, 136.0, 129.9, 128.7, 126.6, 60.9, 46.3, 29.9, 24.0.

HRMS (ESI, m/z) calcd for $C_{14}H_{18}N_2O_2$ ([M+Na]$^+$): 269.1260, found 269.1274.



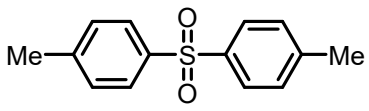

**2v**

**2v** was obtained as a white solid. Yield 53% (18 mg). Melting point 168 – 170 °C.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36 – 7.33 (m, 5H), 5.85 (s, 1H), 5.58 (s, 1H), 3.95 (s, 2H), 2.22 – 2.17 (m, 1H), 2.12 (d, $J$ = 2.5 Hz, 2H), 1.95 – 1.91 (m, 3H), 1.65 (s, 1H), 1.47 – 1.37 (m, 2H), 1.34 – 1.30 (m, 1H), 1.30 – 1.26 (m, 1H), 1.25 – 1.19 (m, 1H), 1.18 – 1.11 (m, 1H), 0.87 (s, 6H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 174.0, 172.8, 139.1, 129.4, 128.8, 126.1, 61.6, 50.6, 50.2, 45.8, 42.7, 38.4, 33.1, 30.8, 30.5.

HRMS (ESI, m/z) calcd for $C_{21}H_{28}N_2O_2$ ([M+Na]$^+$): 363.2043, found 363.2031.

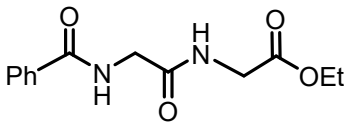



**3**

**3** was obtained as a white solid[2]

$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.81 (d, $J$ = 8.0 Hz, 4H), 7.28 (d, $J$ = 8.1 Hz, 4H), 2.39 (s, 6H).

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 144.0, 139.2, 130.0, 127.7, 21.7.



**4**

**4** was obtained according to literature[3].

# 6. References

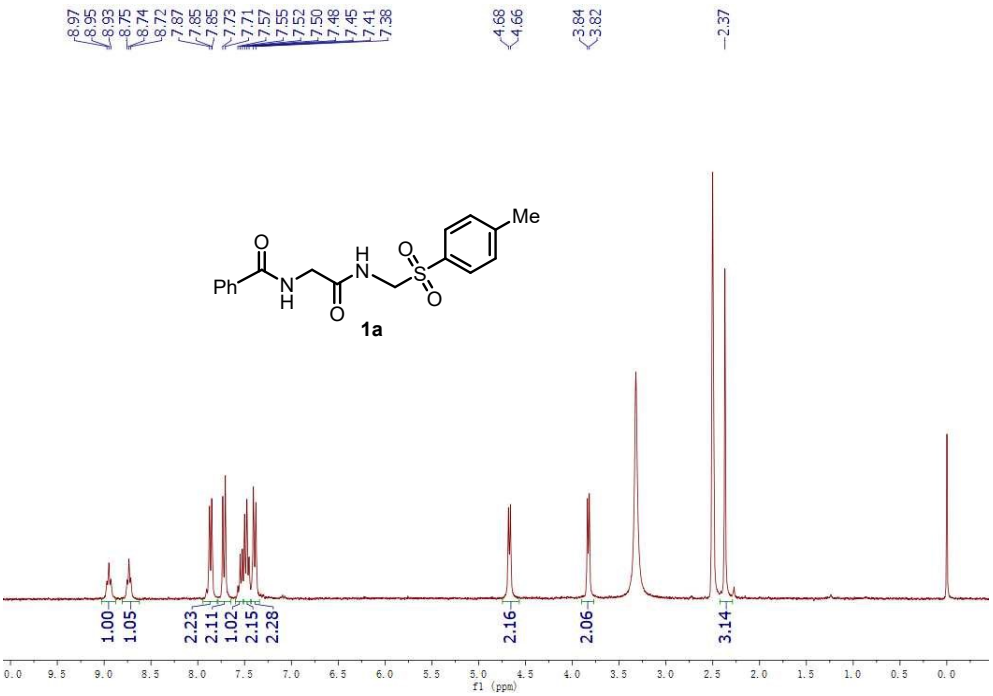

[1] Song, L., Tian, G., Blanpain, A., Van Meervelt, L. and Van der Eycken, E.V. *Adv. Synth. Catal.* **2019**, *361*, 4442 – 4447.

[2] Yang, Y., Chen, Z., Rao, Y. *Chem. Commun.*, **2014**, *50*, 15037 – 15040.

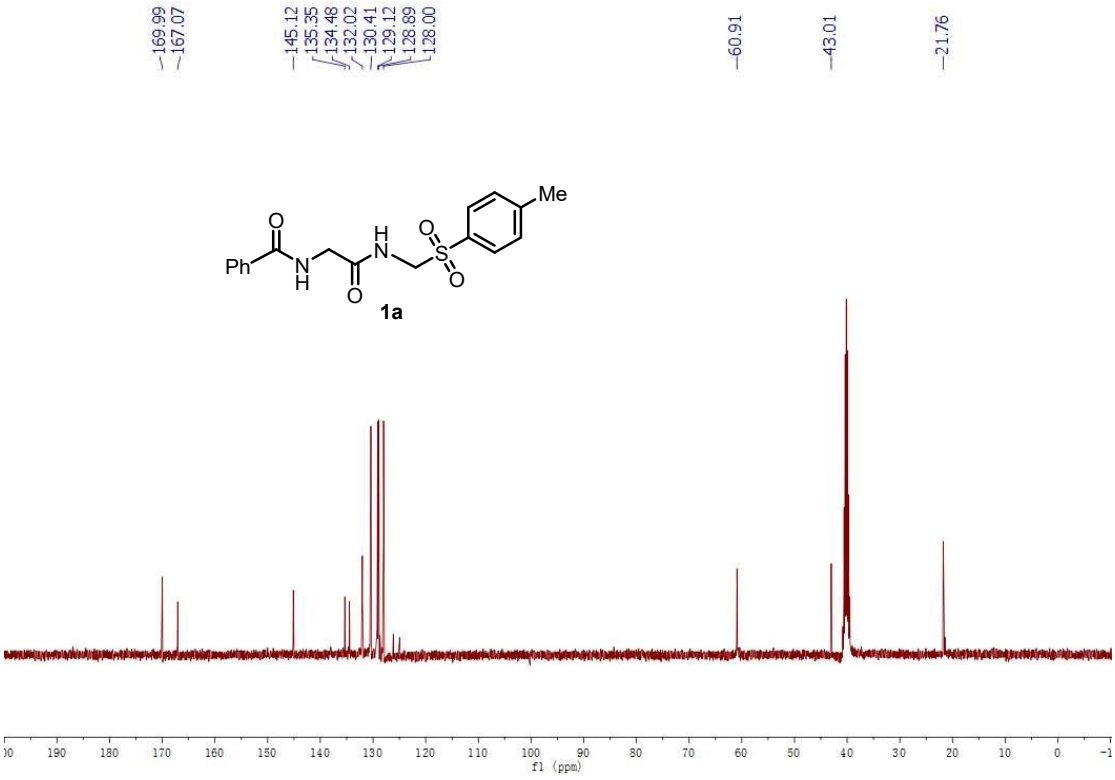
[3] Pick, R., Bauer, M., Kazmaier, U., Hebach, C. **2005**. *Synlett*, *05*, 0757-0760.

# 7. NMR Spectra

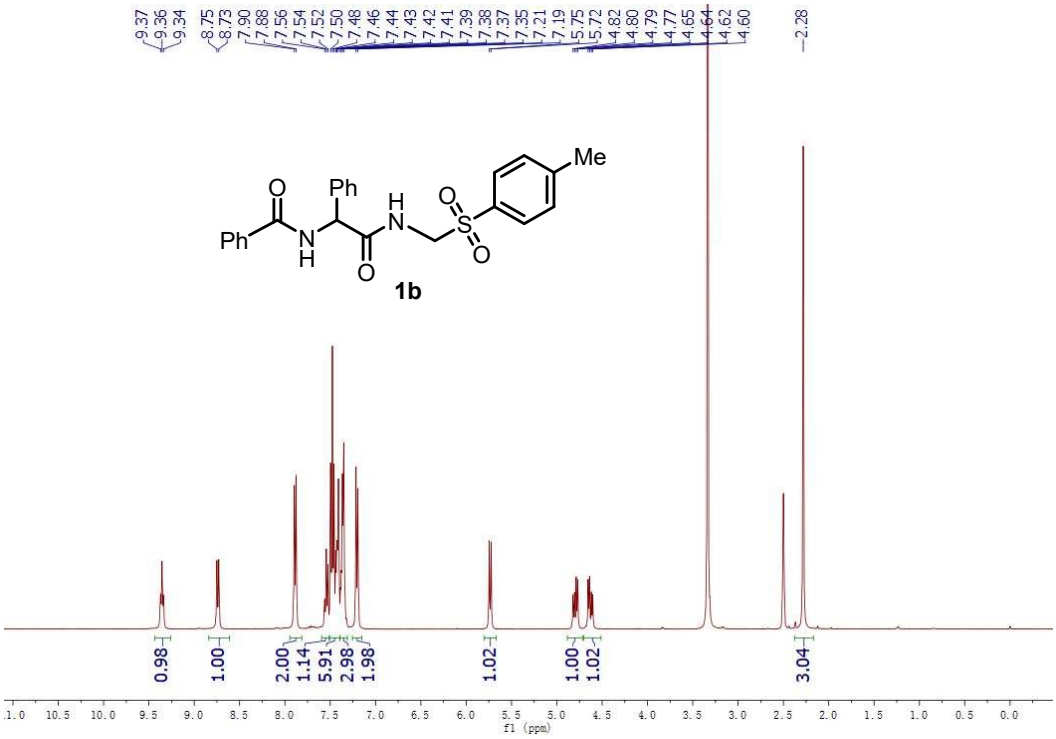
$^{1}$H spectra of compound **1a** (300 MHz, DMSO-$d_6$)



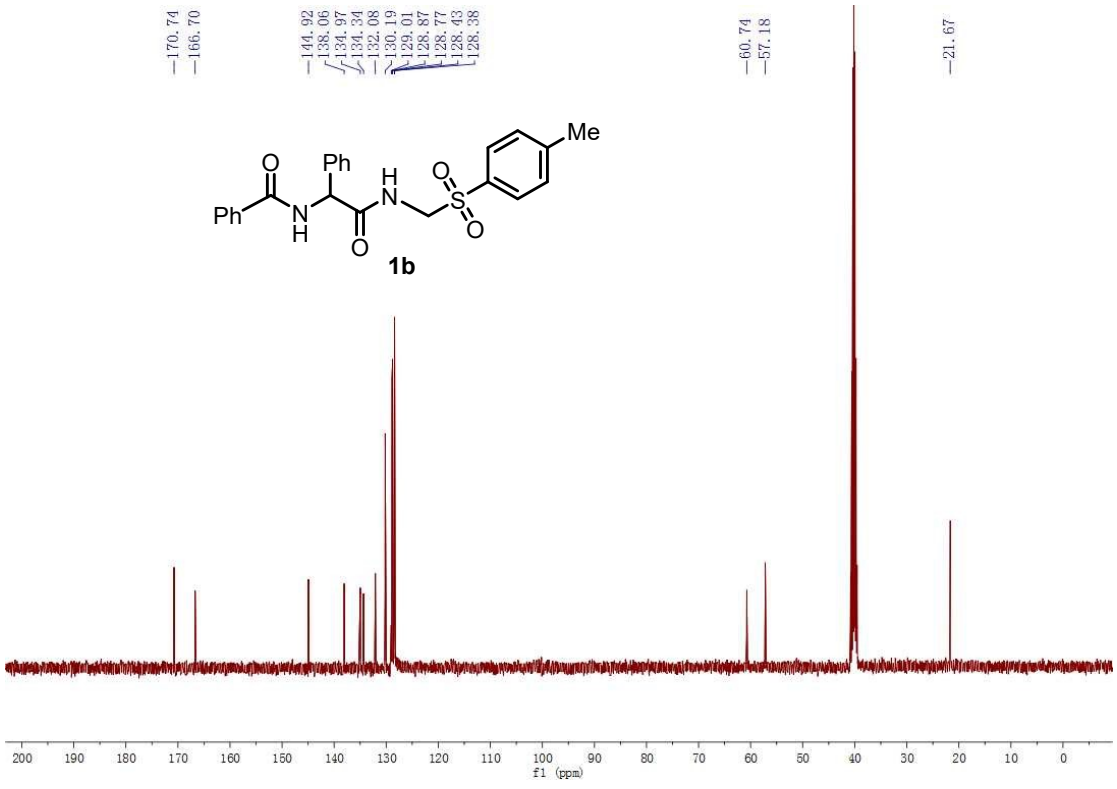

$^{13}$C NMR spectra of compound **1a** (101 MHz, DMSO-$d_6$)



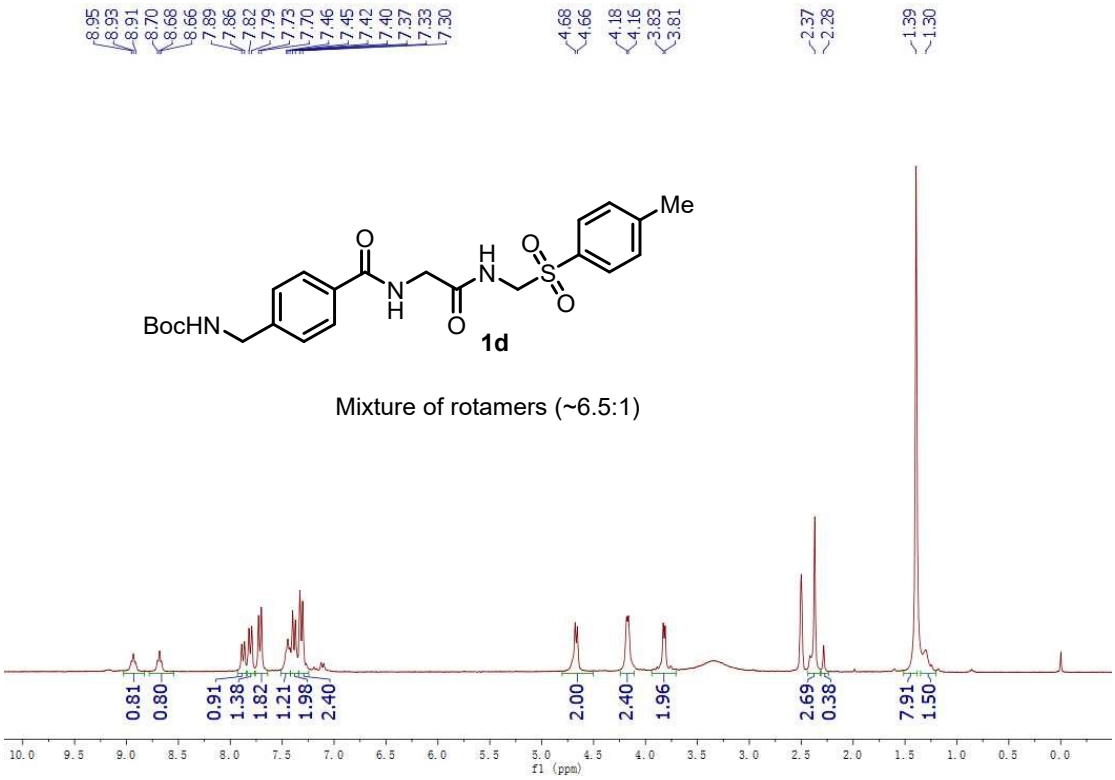
$^{1}$H spectra of compound **1b** (400 MHz, DMSO-$d_6$)



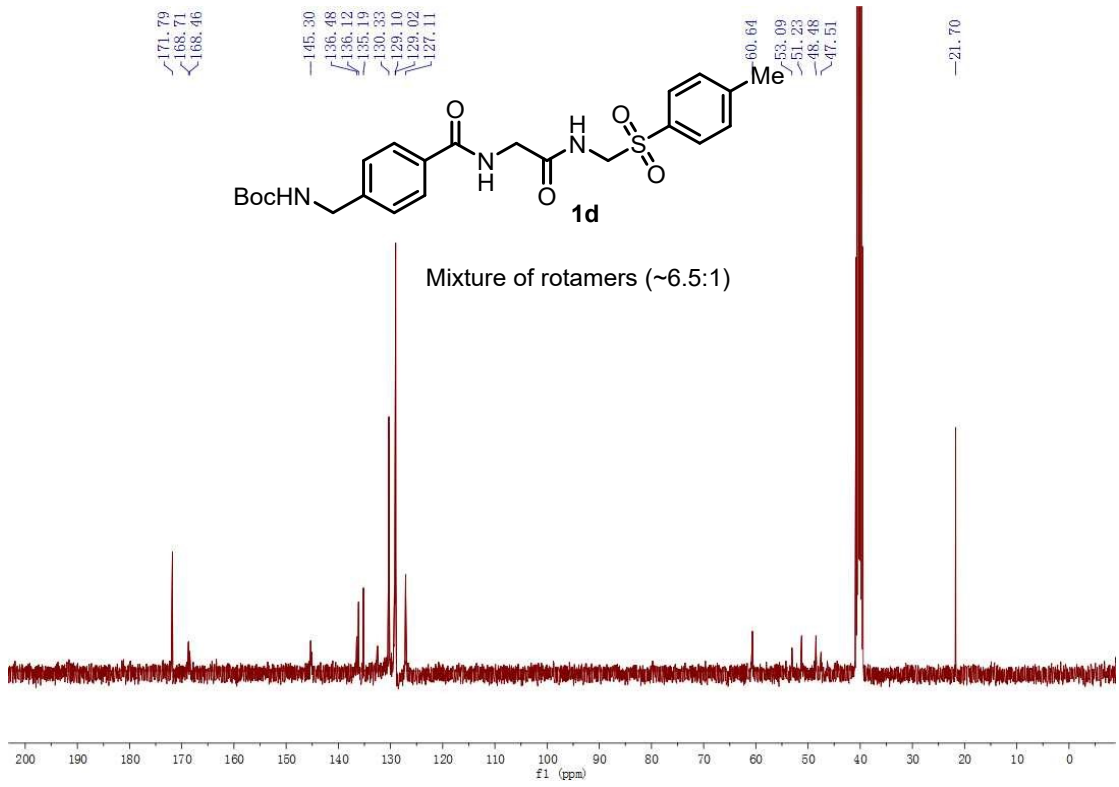

$^{13}$C NMR spectra of compound **1b** (101 MHz, DMSO-$d_6$)



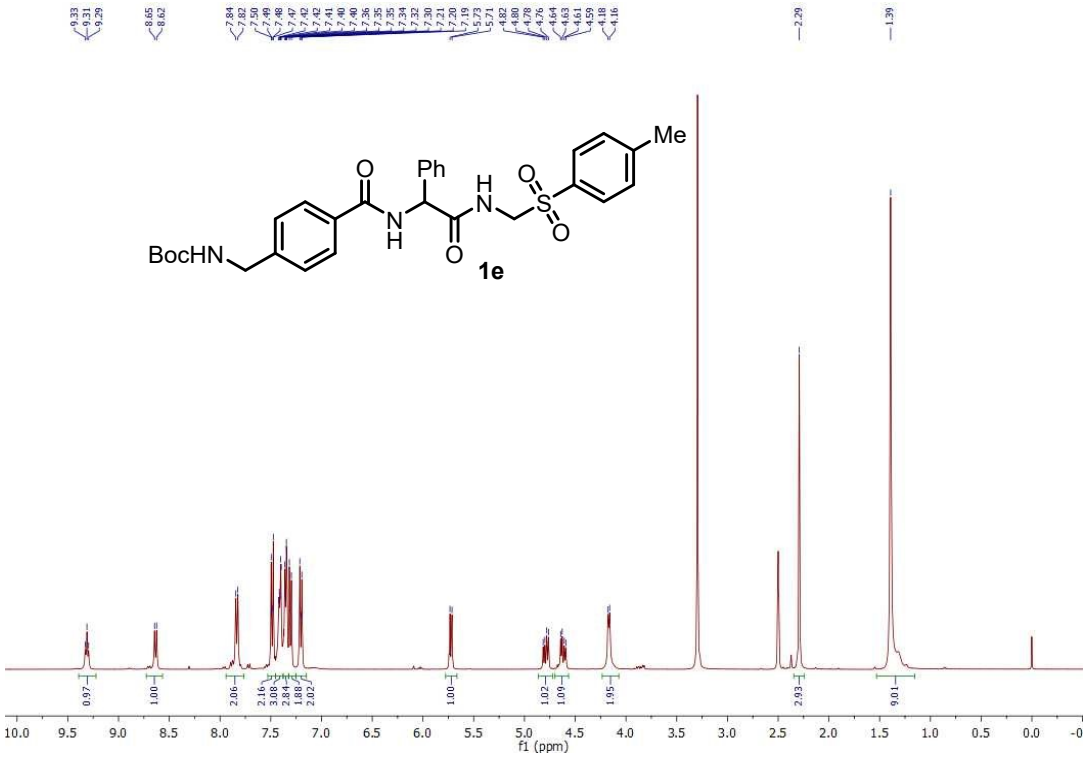
$^{1}$H spectra of compound **1d** (300 MHz, DMSO-$d_6$)



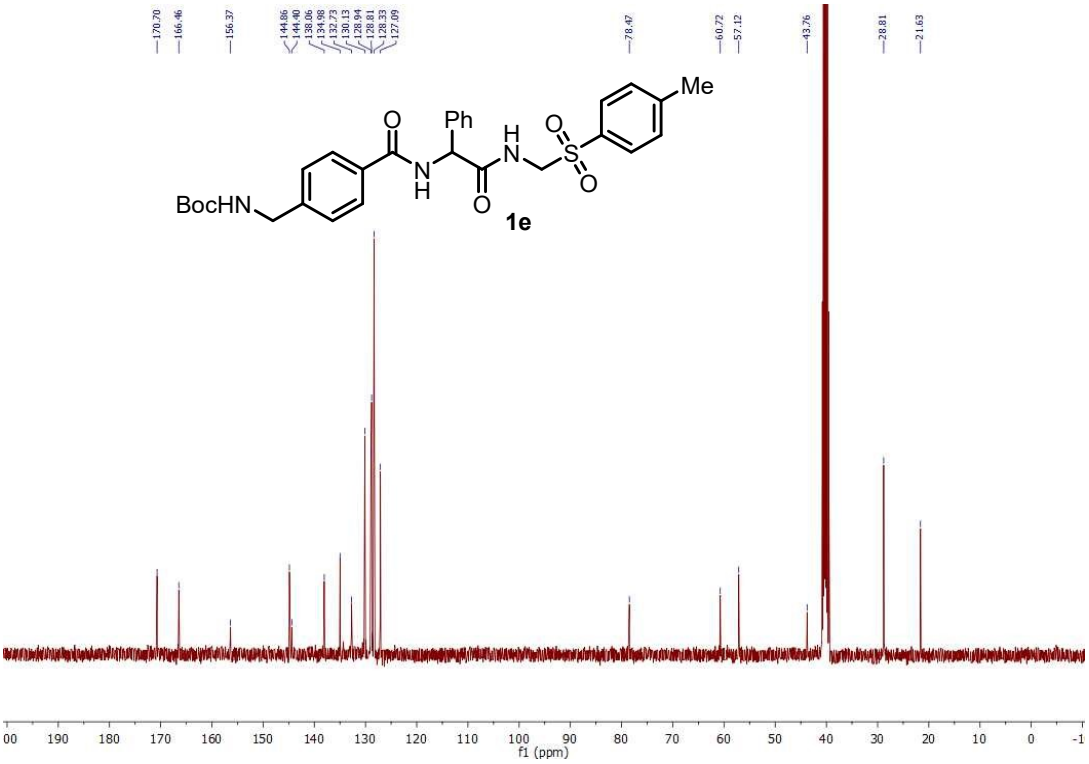

$^{13}$C NMR spectra of compound **1d** (101 MHz, DMSO-$d_6$)



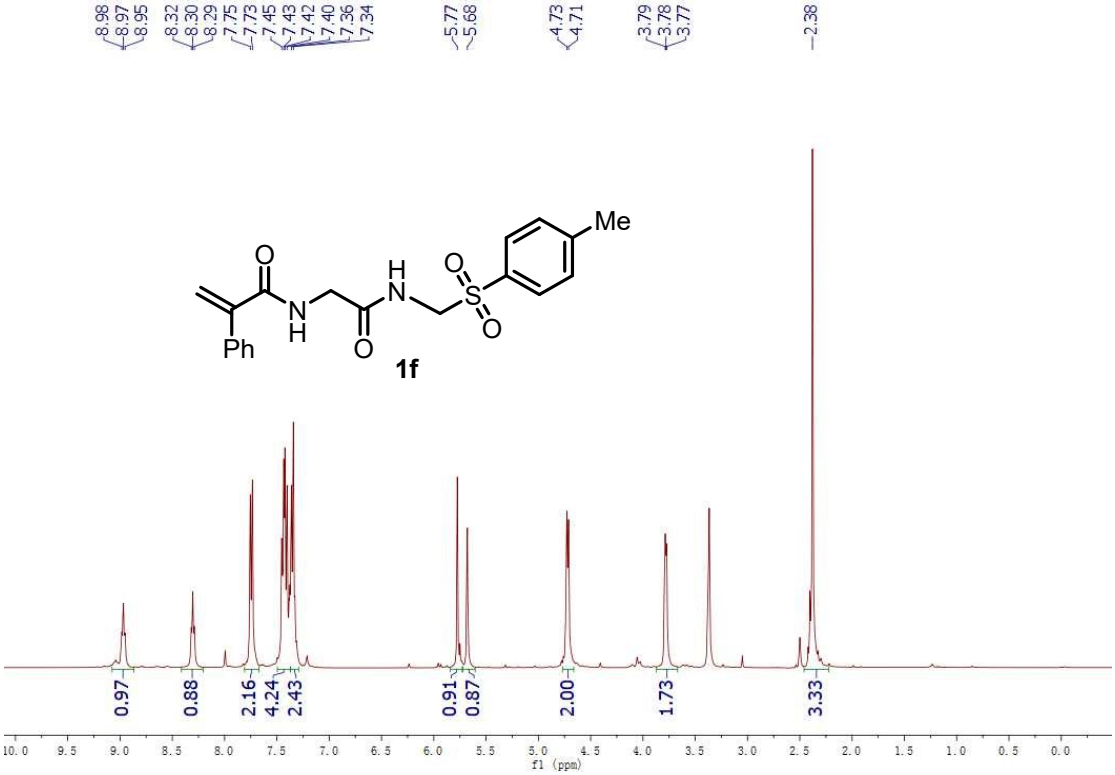
$^{1}$H spectra of compound **1e** (400 MHz, DMSO-$d_6$)



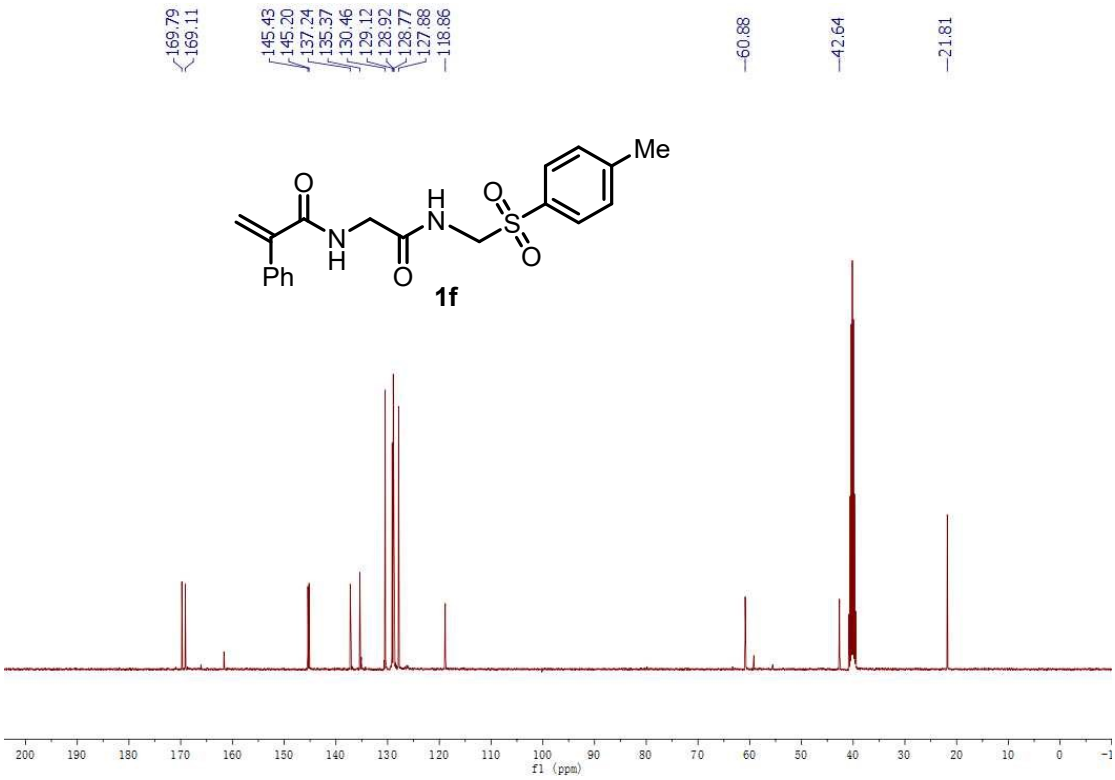

$^{13}$C NMR spectra of compound **1e** (101 MHz, DMSO-$d_6$)



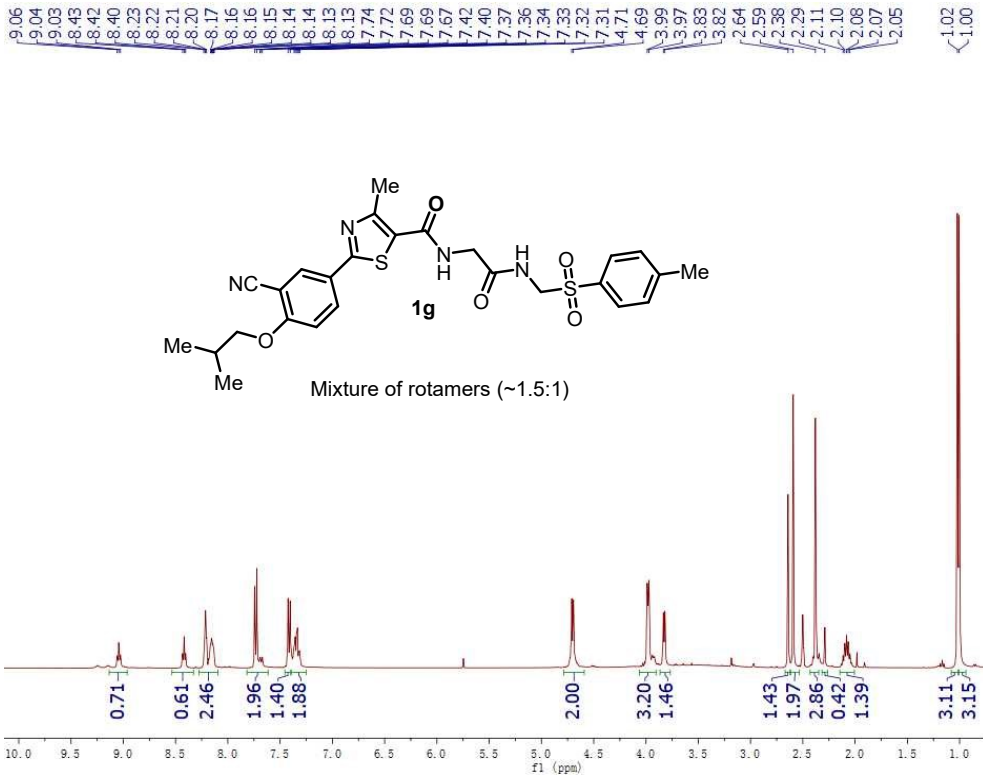
$^{1}$H spectra of compound **1f** (400 MHz, DMSO-$d_6$)



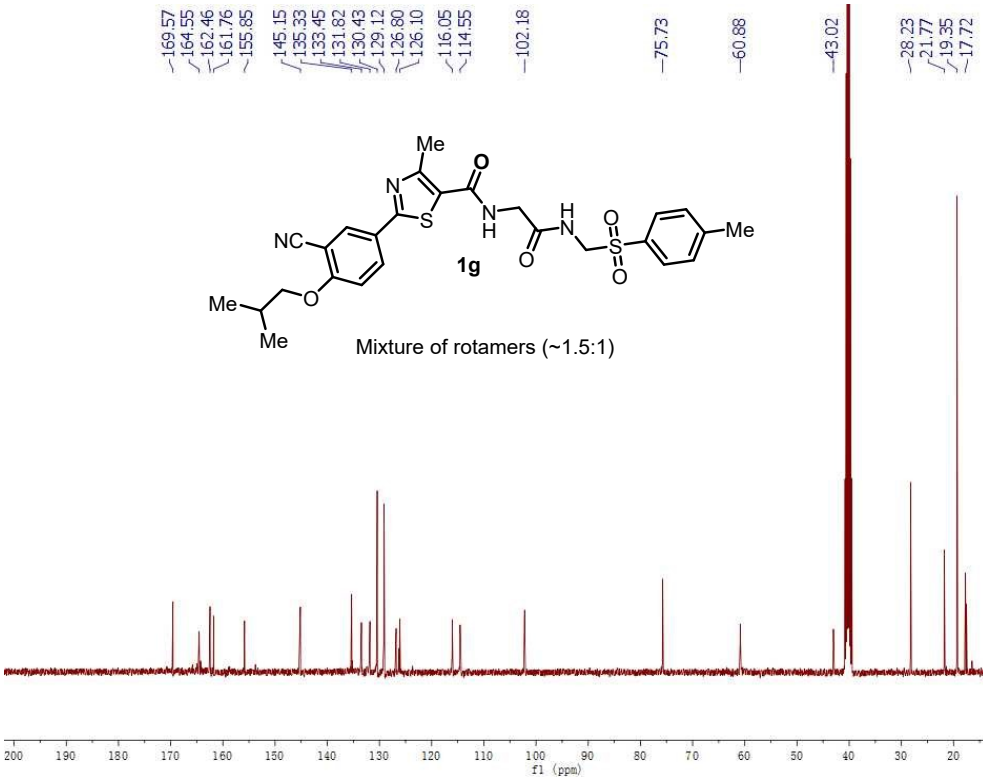

$^{13}$C NMR spectra of compound **1f** (101 MHz, DMSO-$d_6$)



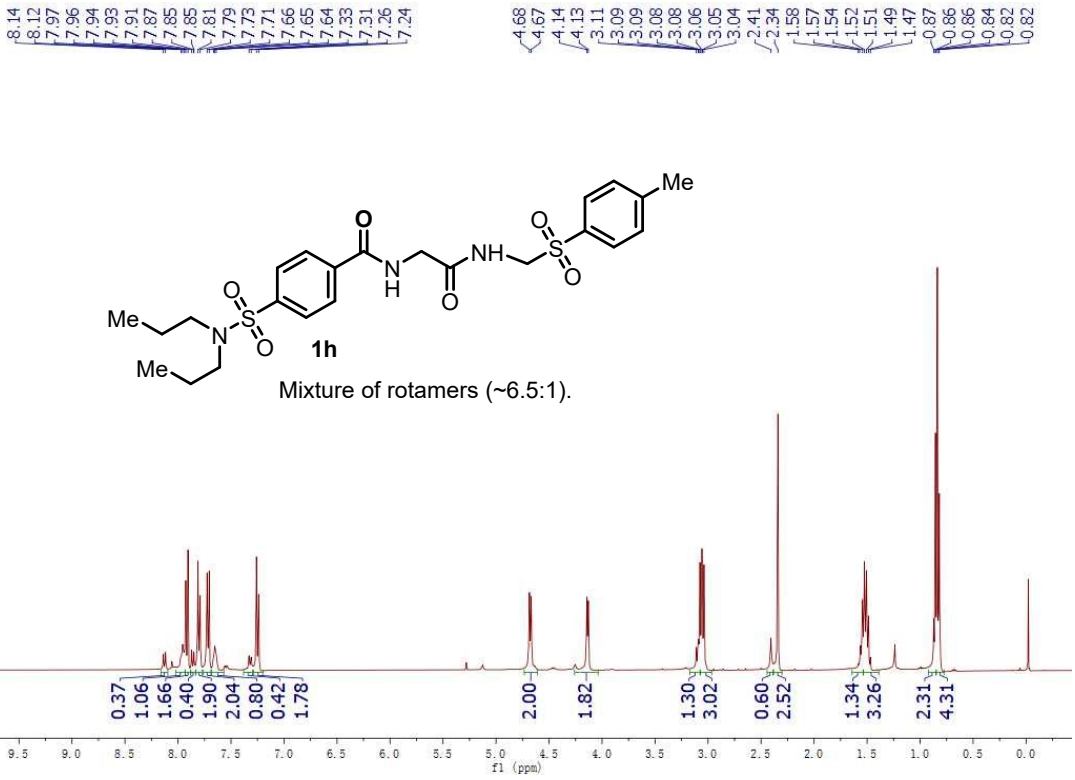
$^{1}$H spectra of compound **1g** (400 MHz, DMSO-$d_6$)



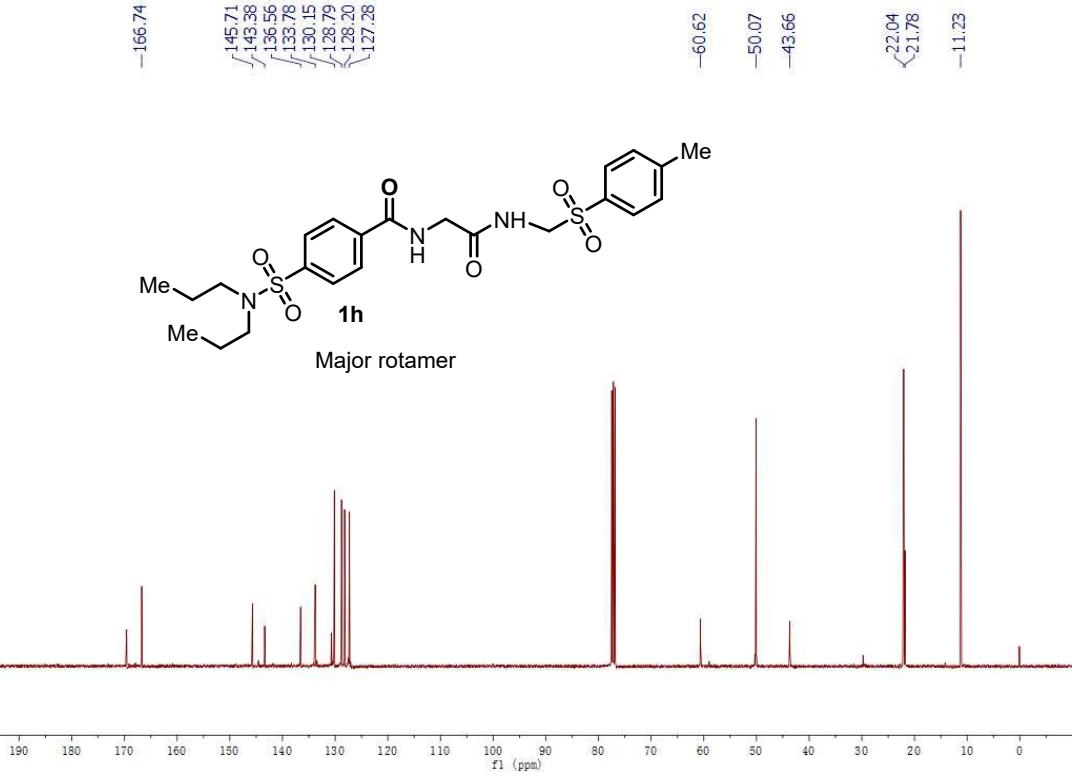

$^{13}$C NMR spectra of compound **1g** (101 MHz, DMSO-$d_6$)



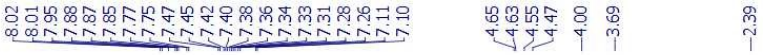
$^{1}$H spectra of compound **1h** (400 MHz, $CDCl_3$)

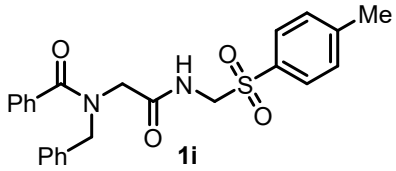



$^{13}$C NMR spectra of compound **1h** (101 MHz, $CDCl_3$)



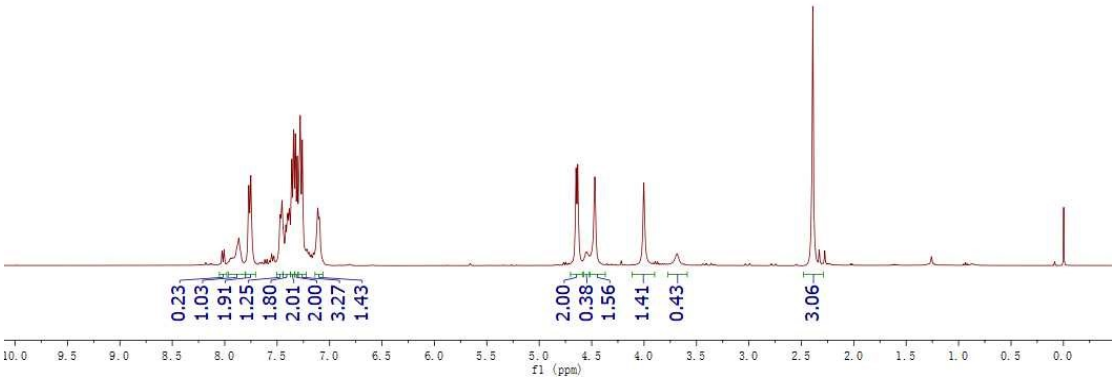
$^{1}$H spectra of compound **1i** (400 MHz, $CDCl_3$)



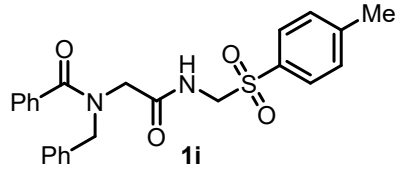




**1i**

Mixture of rotamers (~5.7:1)

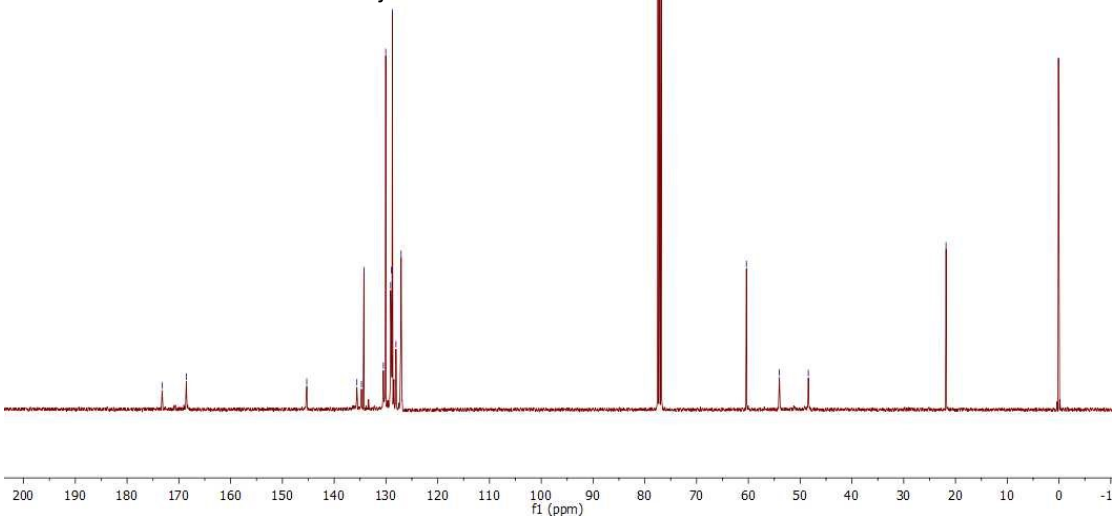



$^{13}$C NMR spectra of compound **1i** (101 MHz, $CDCl_3$)

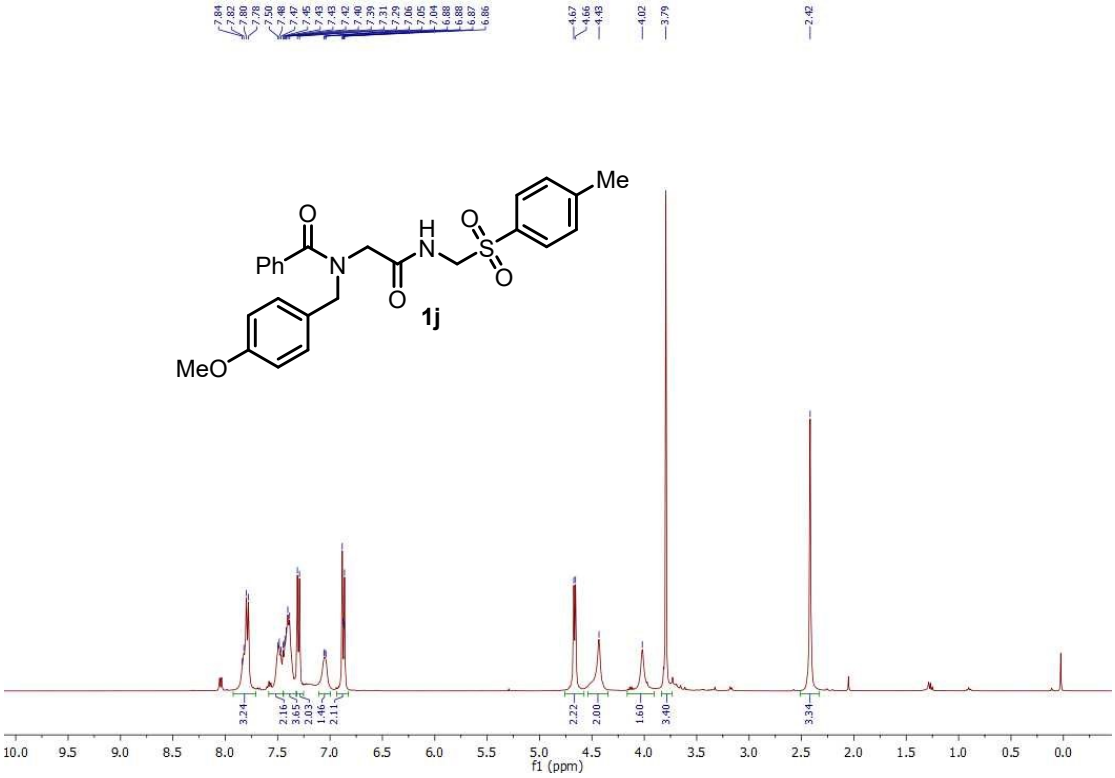




**1i**

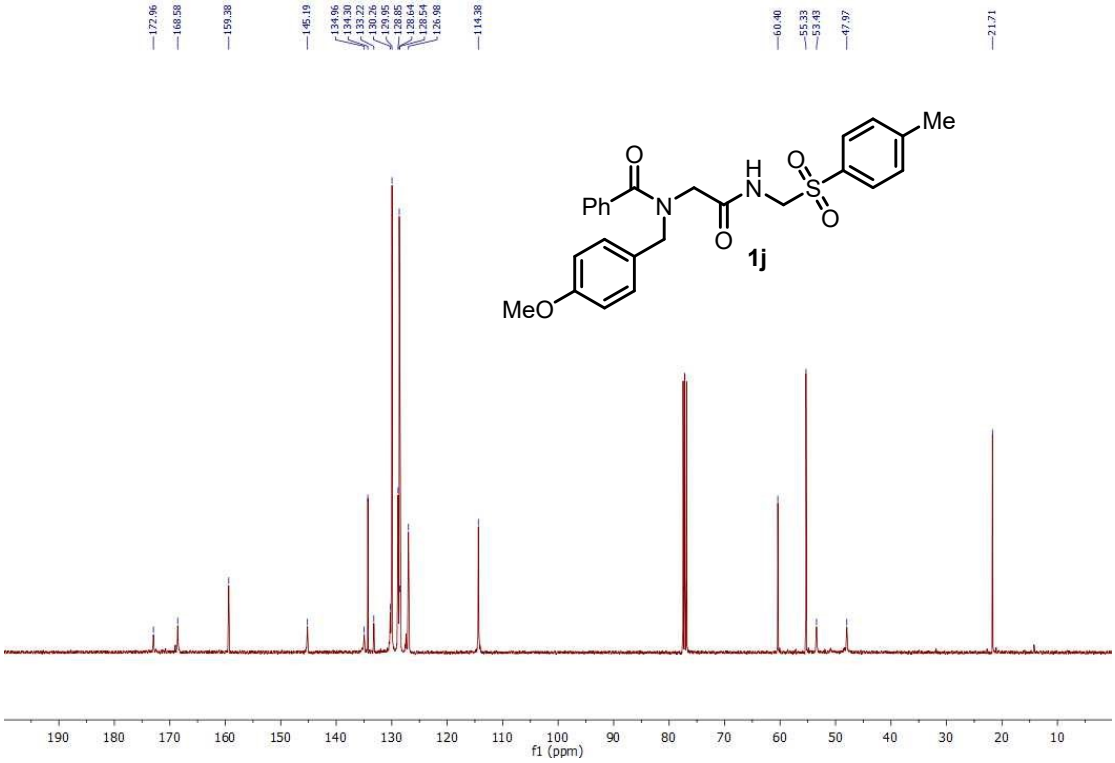
Major rotamer



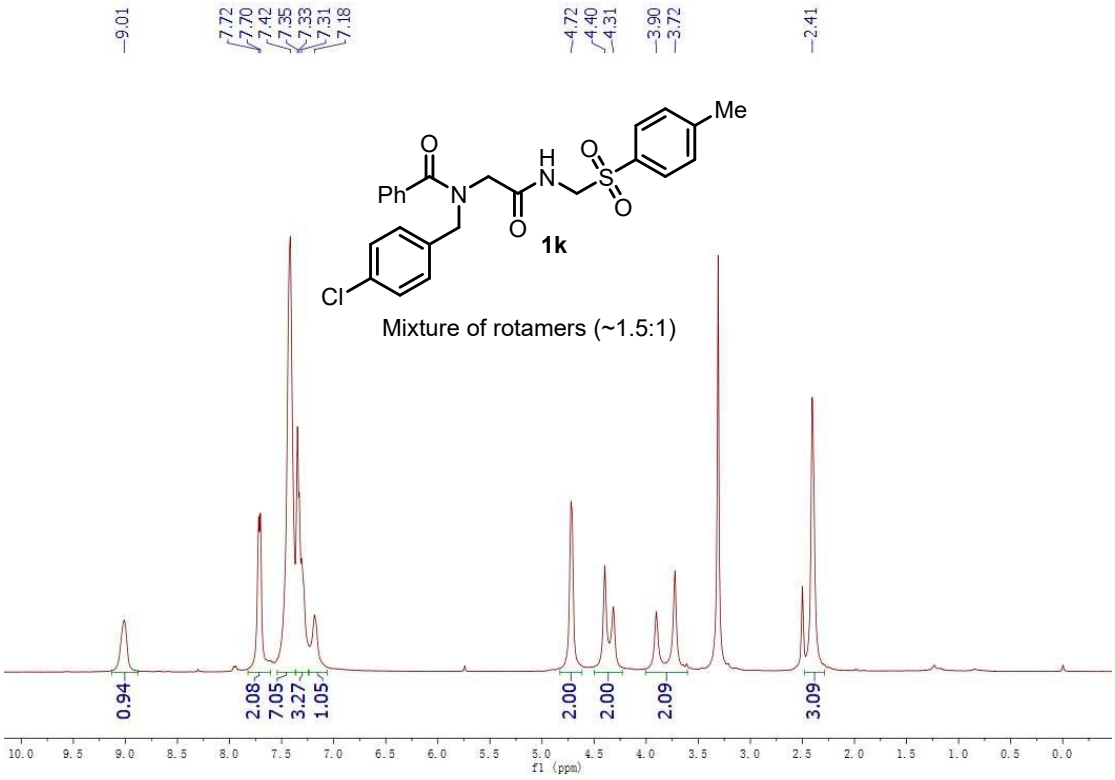
$^{1}$H spectra of compound **1j** (400 MHz, $CDCl_3$)



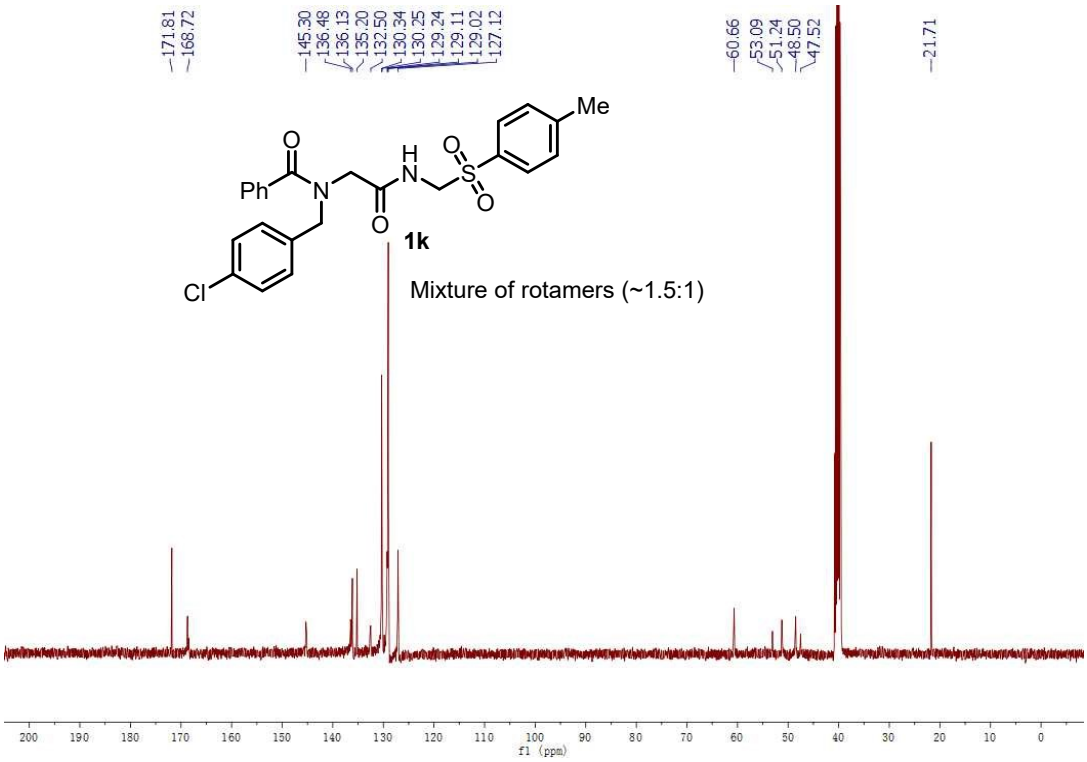

$^{13}$C NMR spectra of compound **1j** (101 MHz, $CDCl_3$)



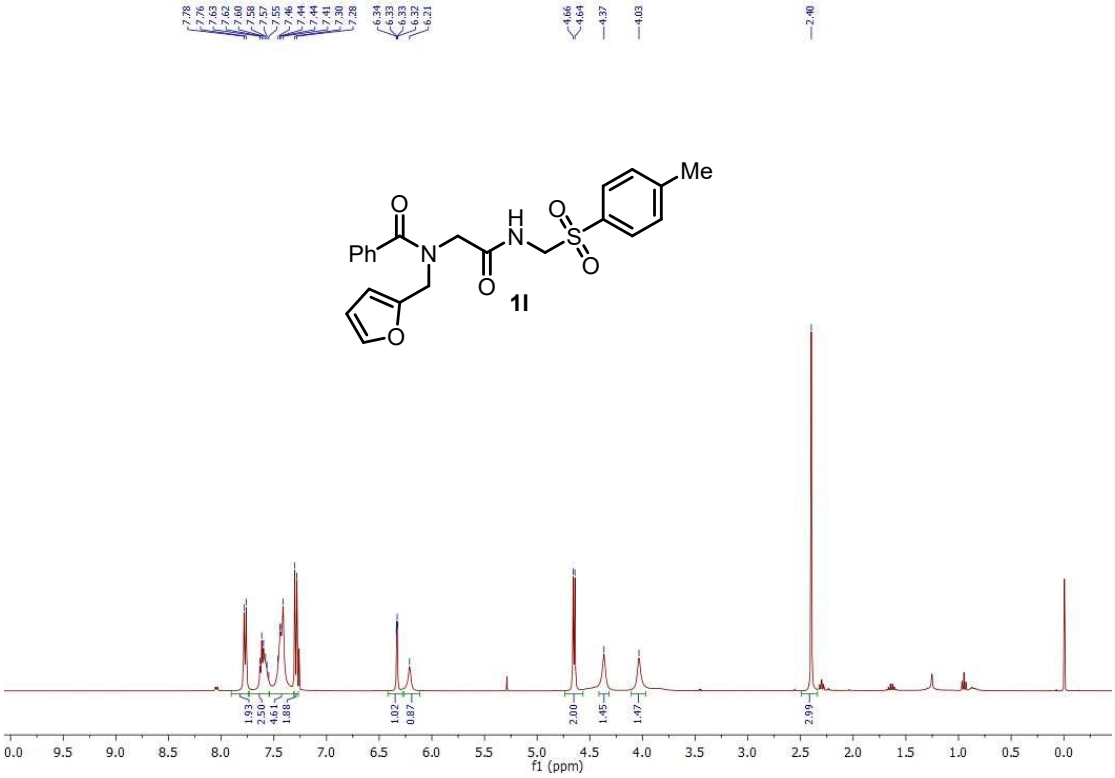
$^{1}$H spectra of compound **1k** (400 MHz, DMSO-$d_6$)



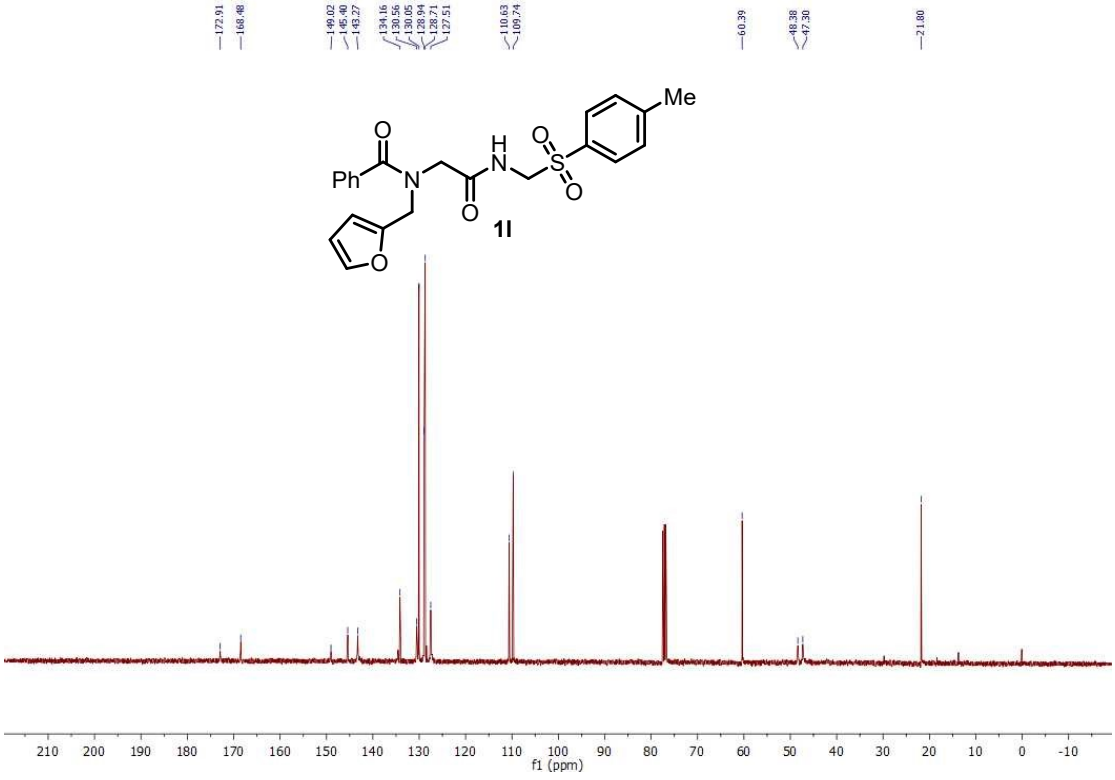

$^{13}$C NMR spectra of compound **1k** (101 MHz, DMSO-$d_6$)



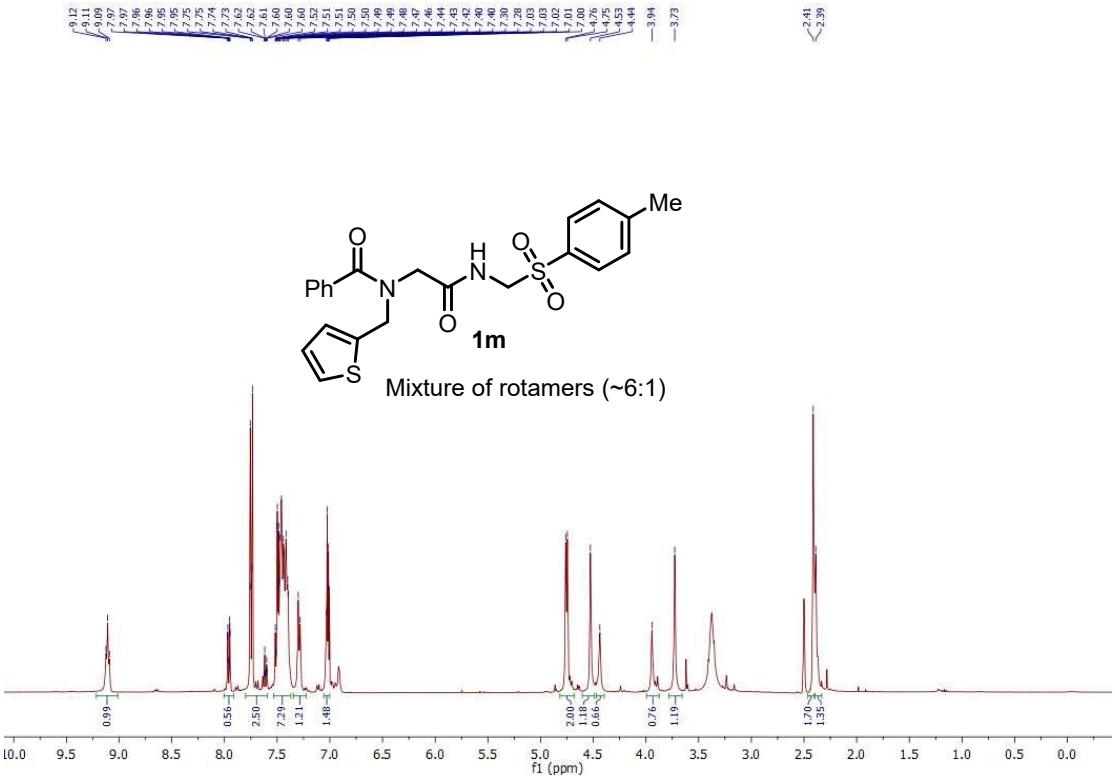
$^{1}$H spectra of compound **1l** (400 MHz, $CDCl_3$)



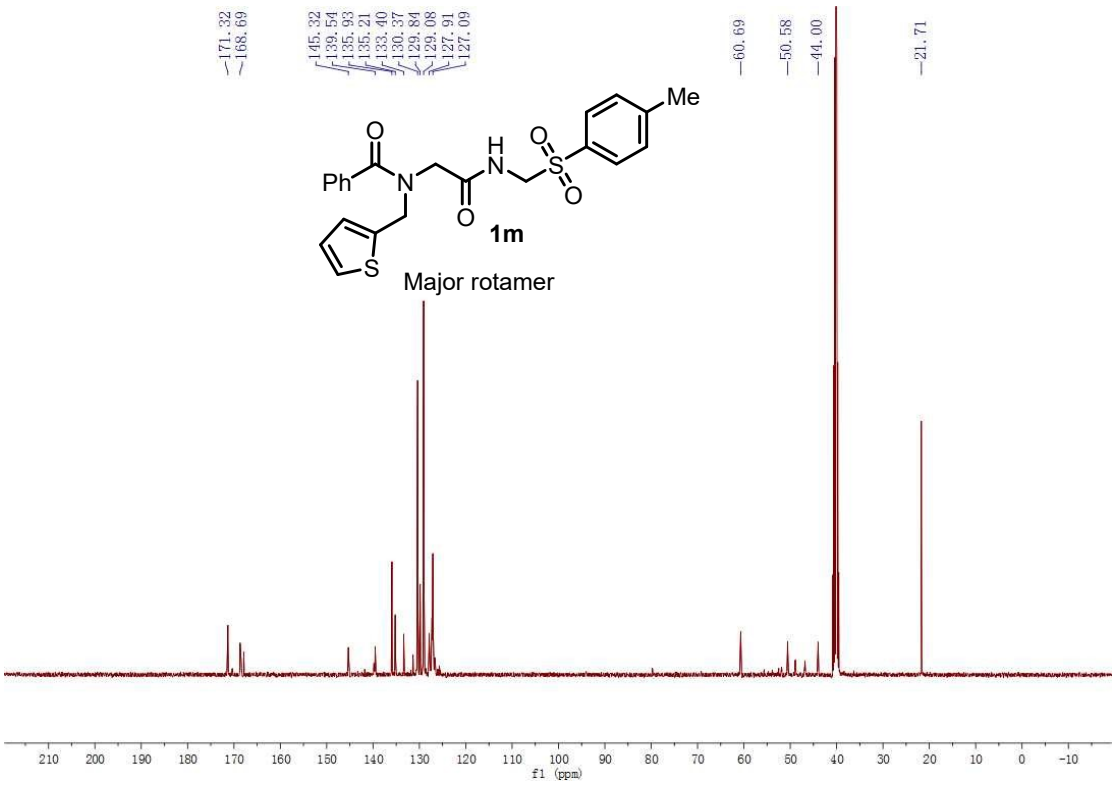

$^{13}$C NMR spectra of compound **1l** (101 MHz, $CDCl_3$)



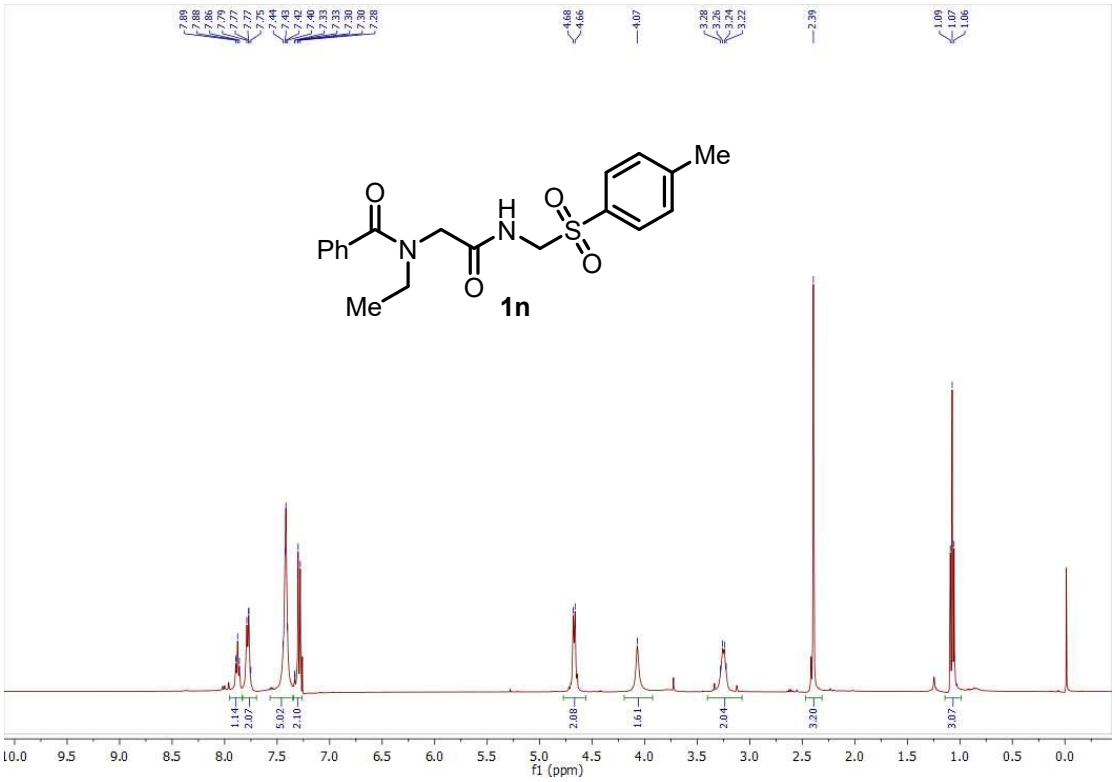
$^{1}$H spectra of compound **1m** (400 MHz, DMSO-$d_6$)



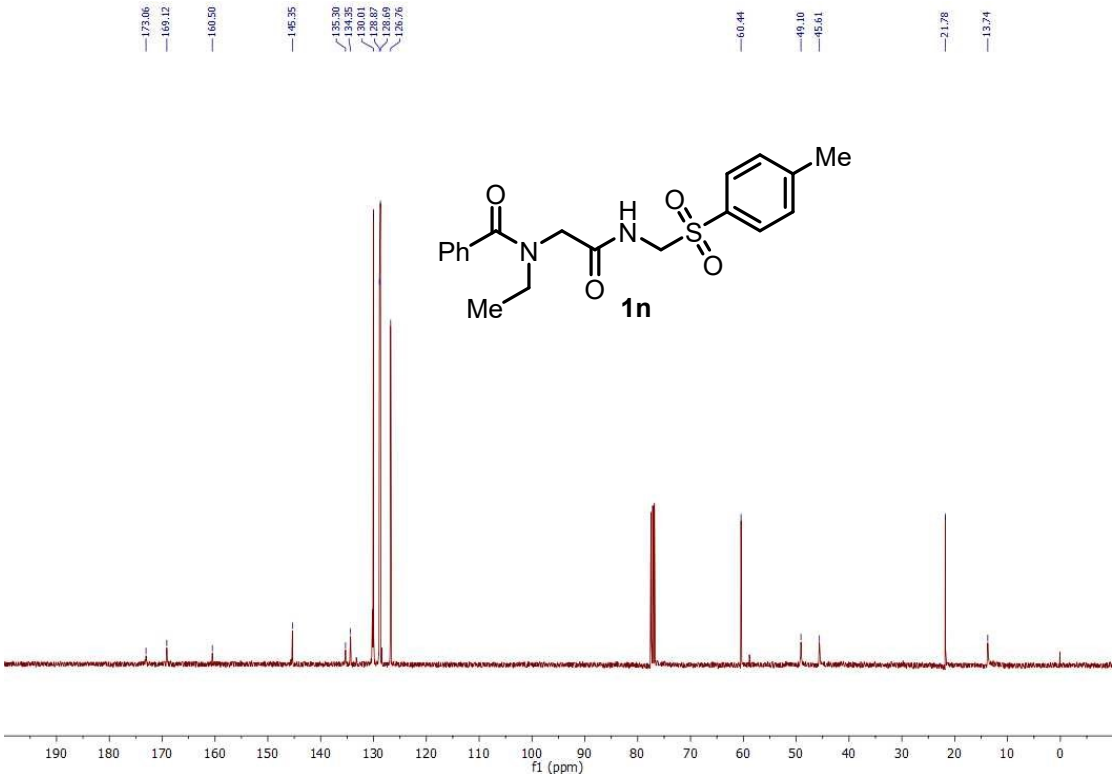

$^{13}$C NMR spectra of compound **1m** (101 MHz, DMSO-$d_6$)



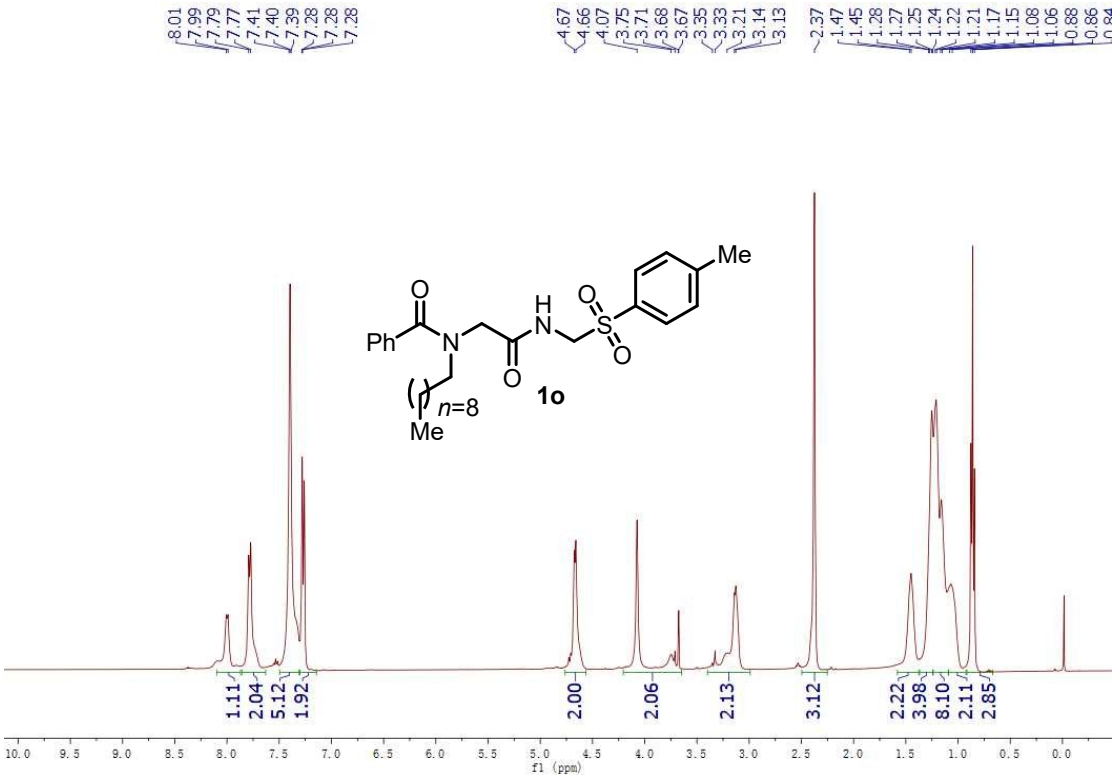
$^{1}$H spectra of compound **1n** (400 MHz, $CDCl_3$)



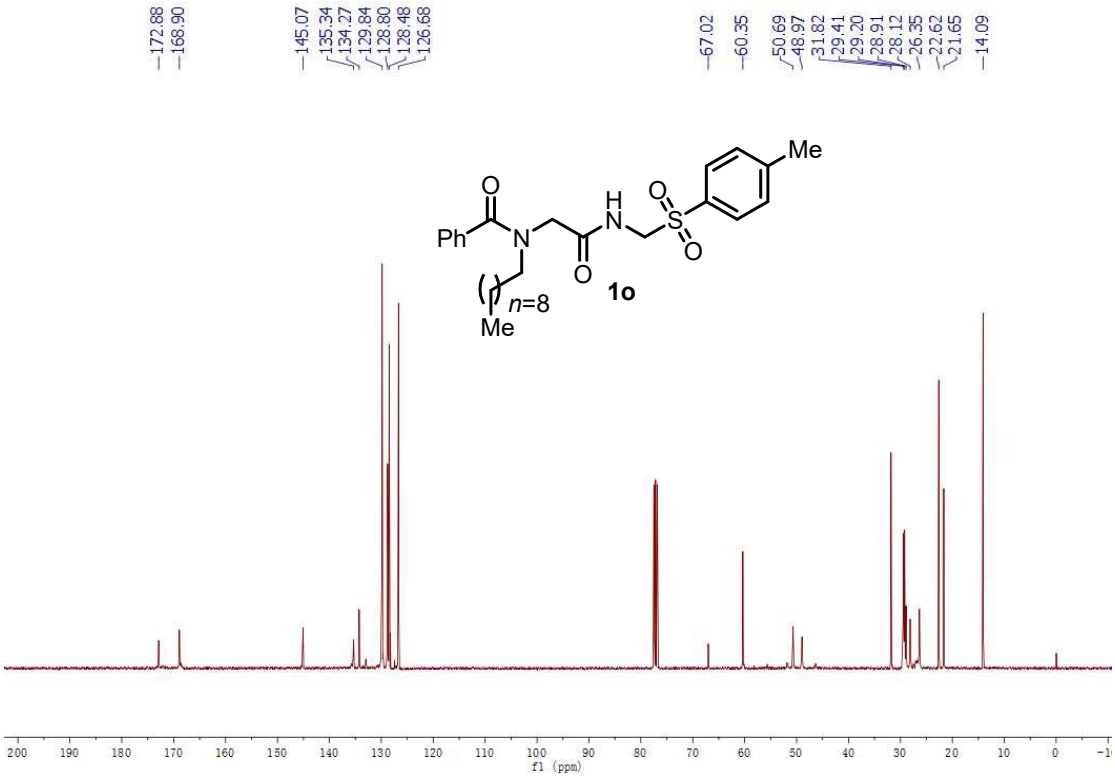

$^{13}$C NMR spectra of compound **1n** (101 MHz, $CDCl_3$)



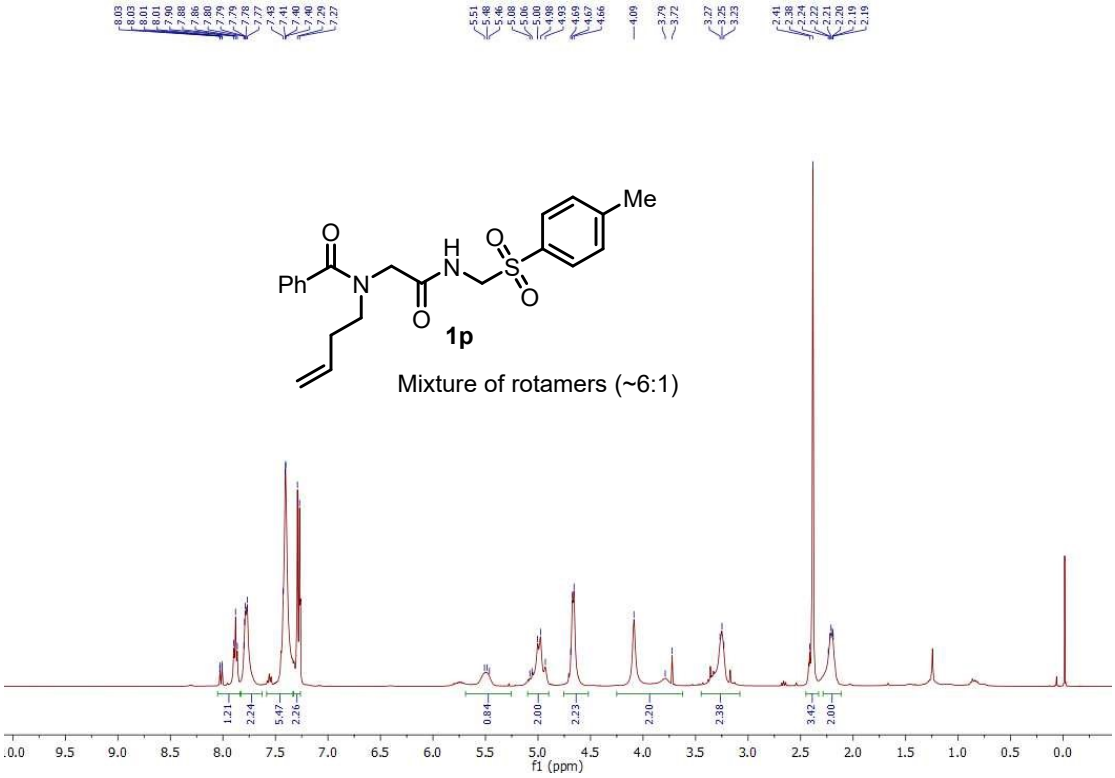
$^{1}$H spectra of compound **1o** (400 MHz, $CDCl_3$)



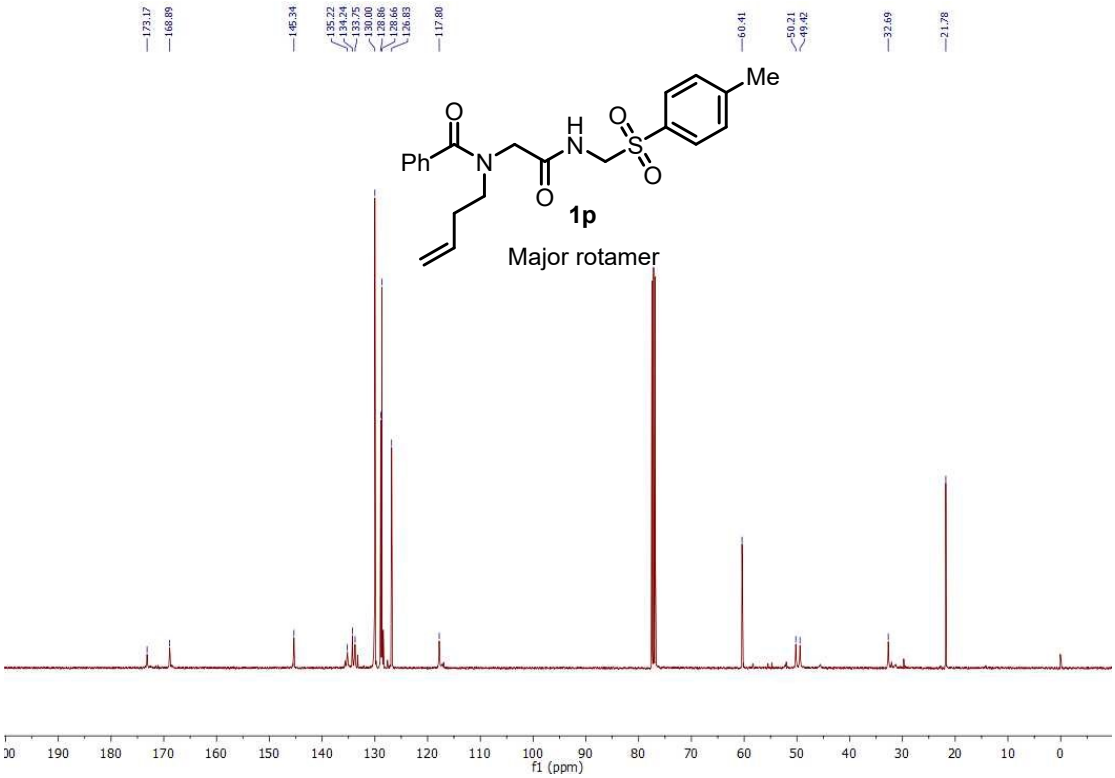

$^{13}$C NMR spectra of compound **1o** (101 MHz, $CDCl_3$)



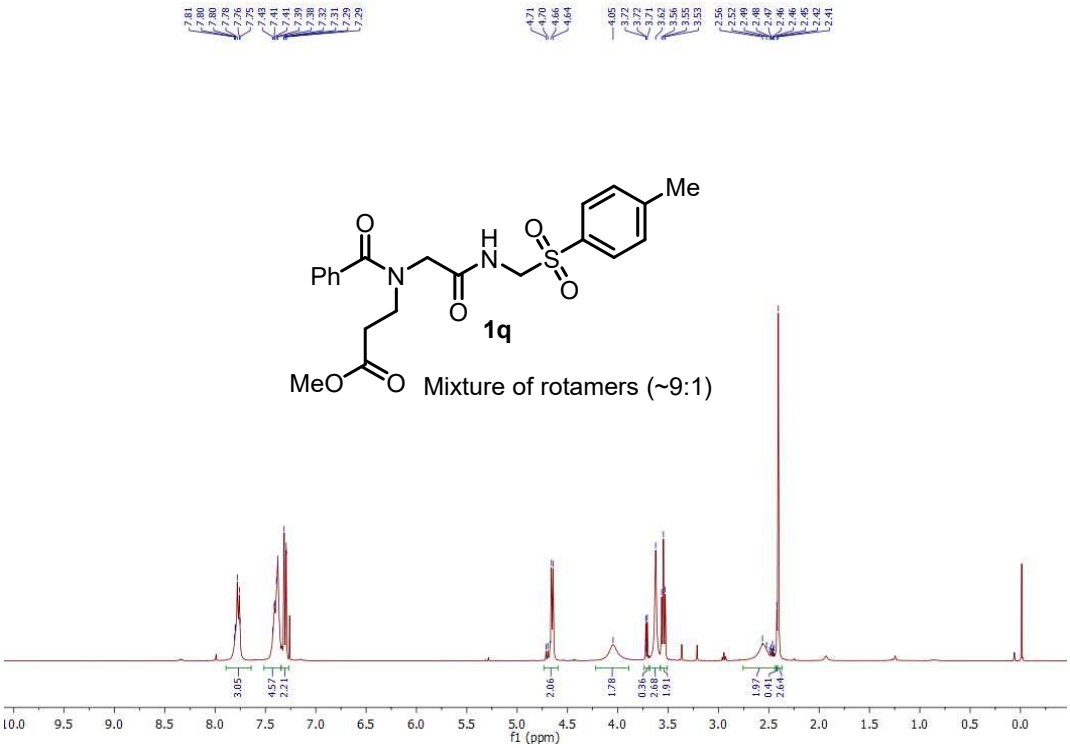
$^{1}$H spectra of compound **1p** (400 MHz, $CDCl_3$)



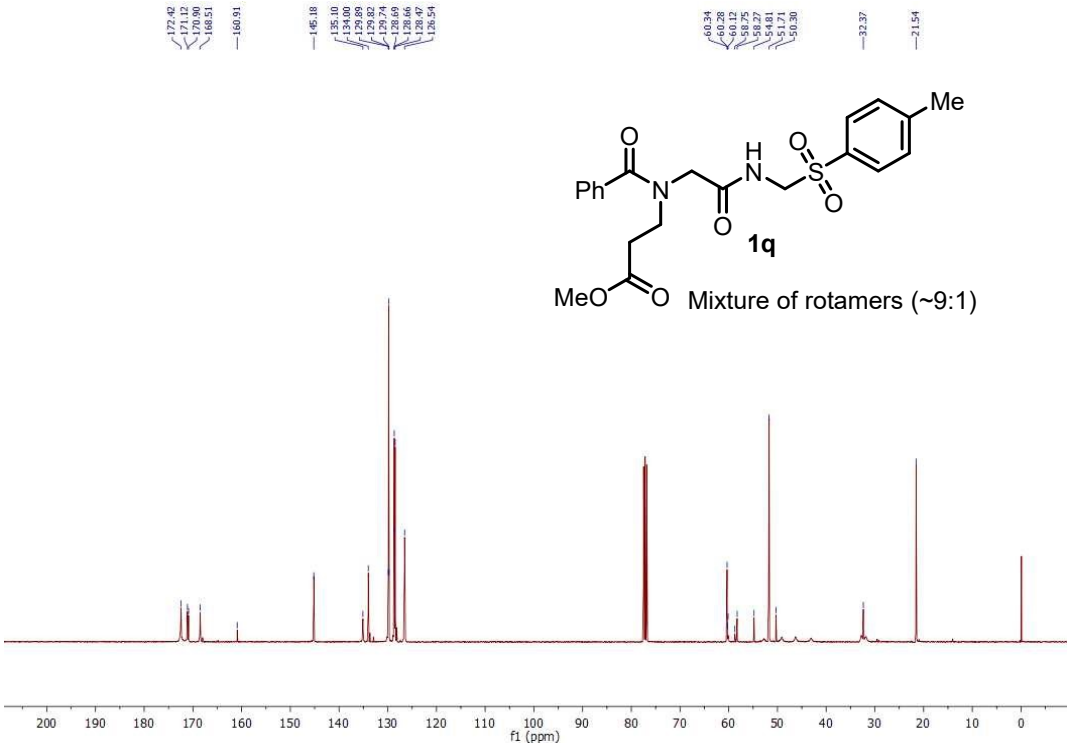

$^{13}$C NMR spectra of compound **1p** (101 MHz, $CDCl_3$)



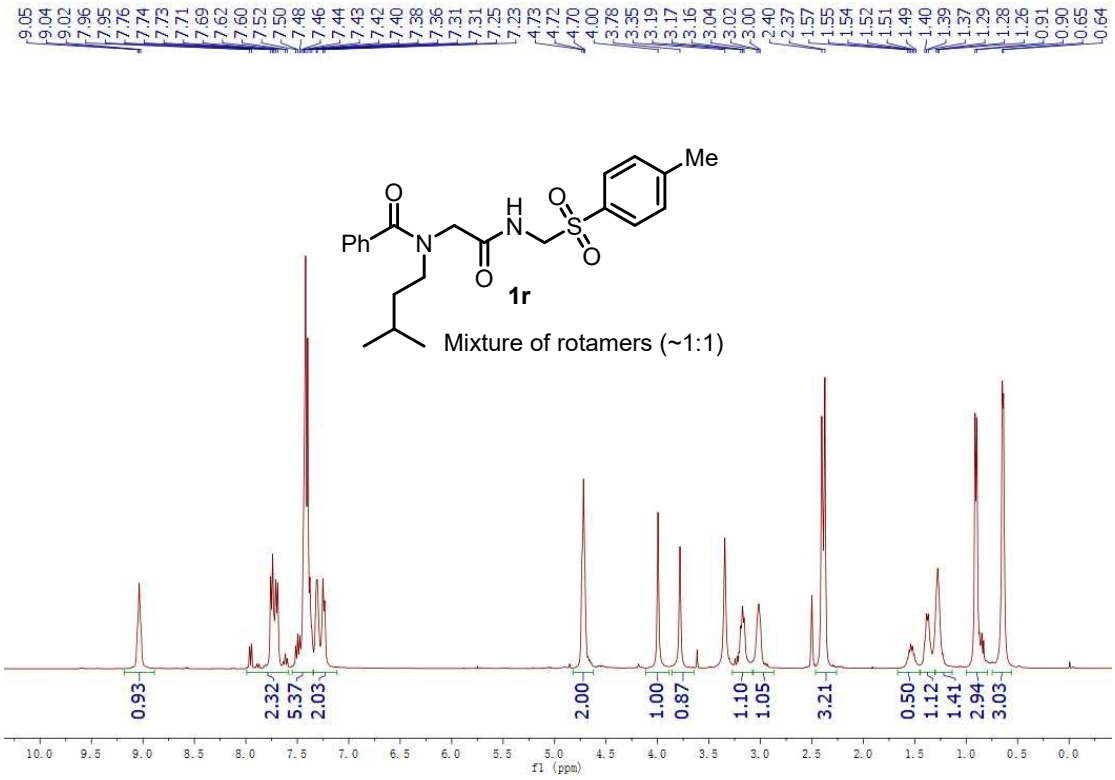
$^{1}$H spectra of compound **1q** (400 MHz, $CDCl_3$)



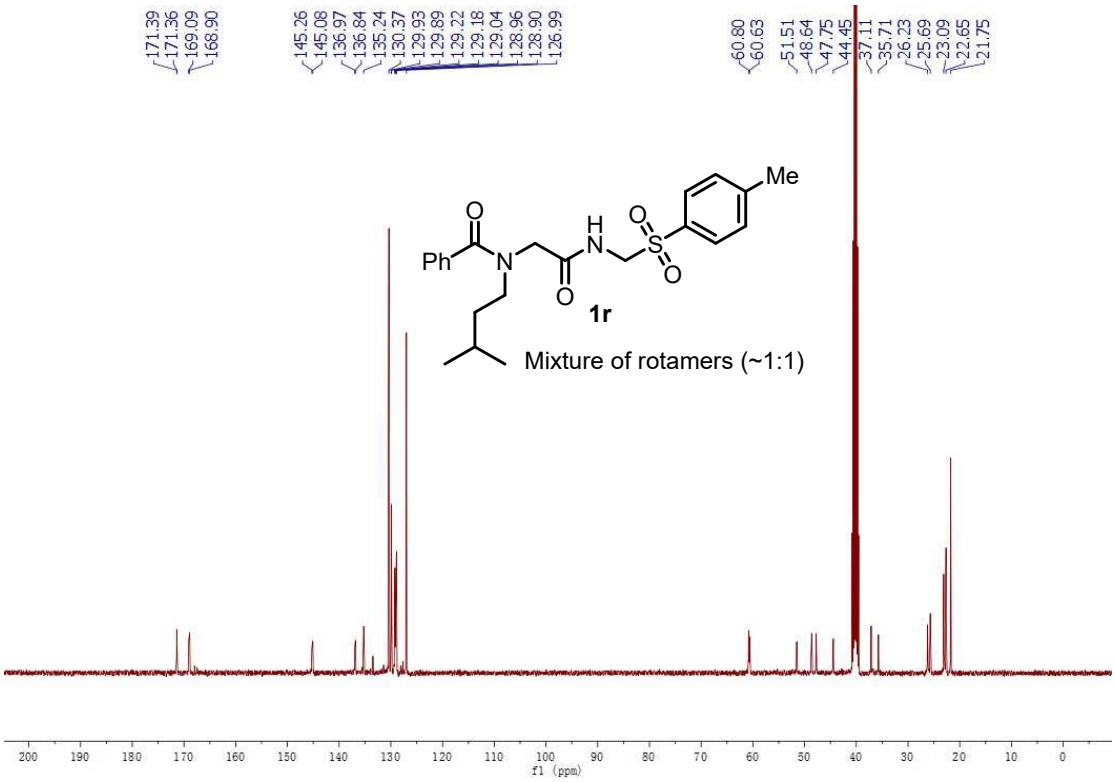

$^{13}$C NMR spectra of compound **1q** (101 MHz, $CDCl_3$)



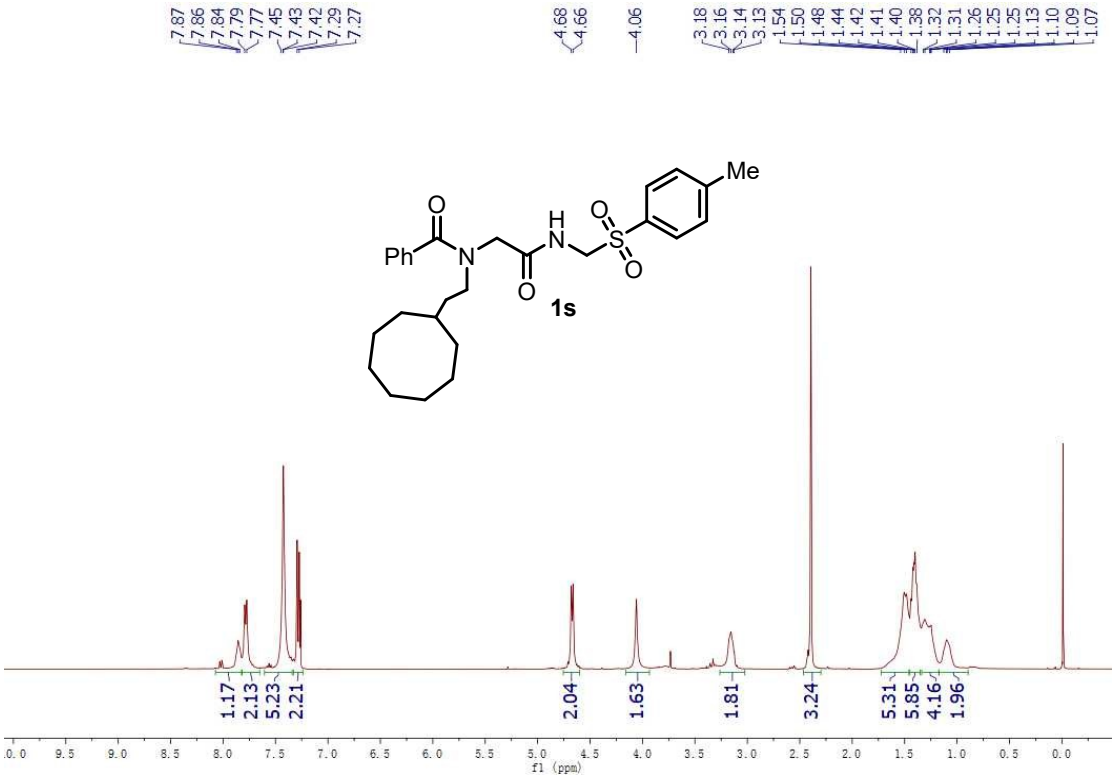
$^{1}$H spectra of compound **1r** (400 MHz, DMSO-$d_6$)



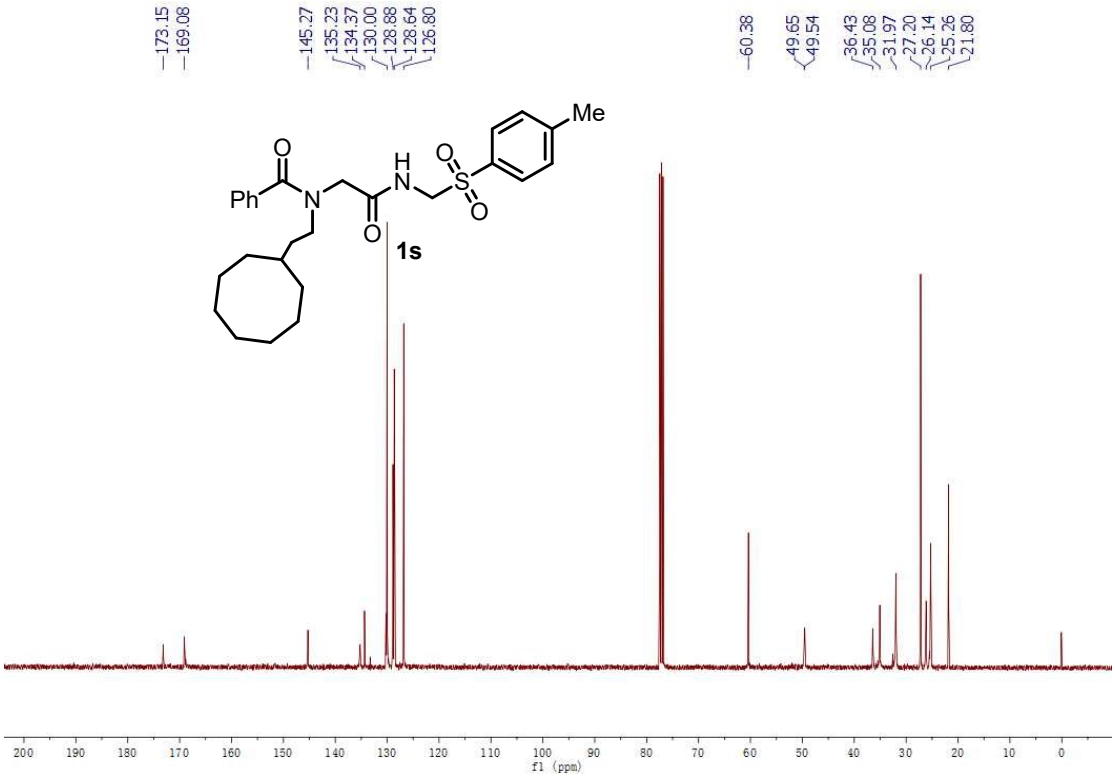

$^{13}$C NMR spectra of compound **1r** (101 MHz, DMSO-$d_6$)



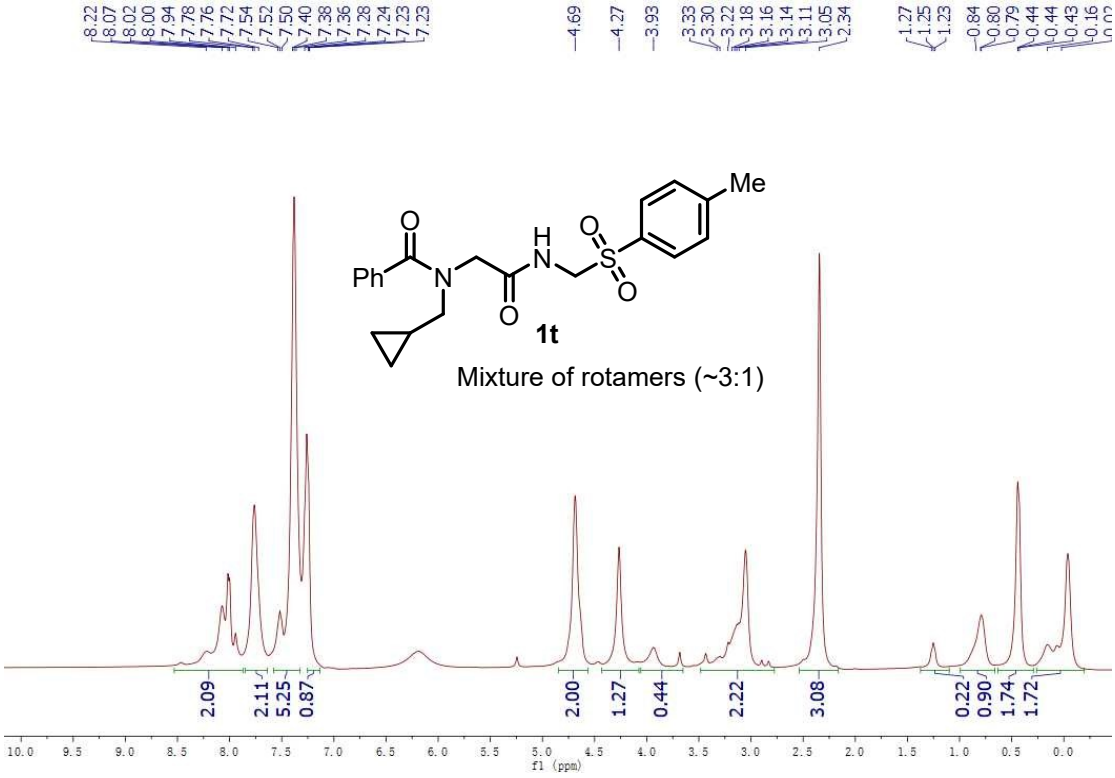
$^{1}$H spectra of compound **1s** (400 MHz, $CDCl_3$)



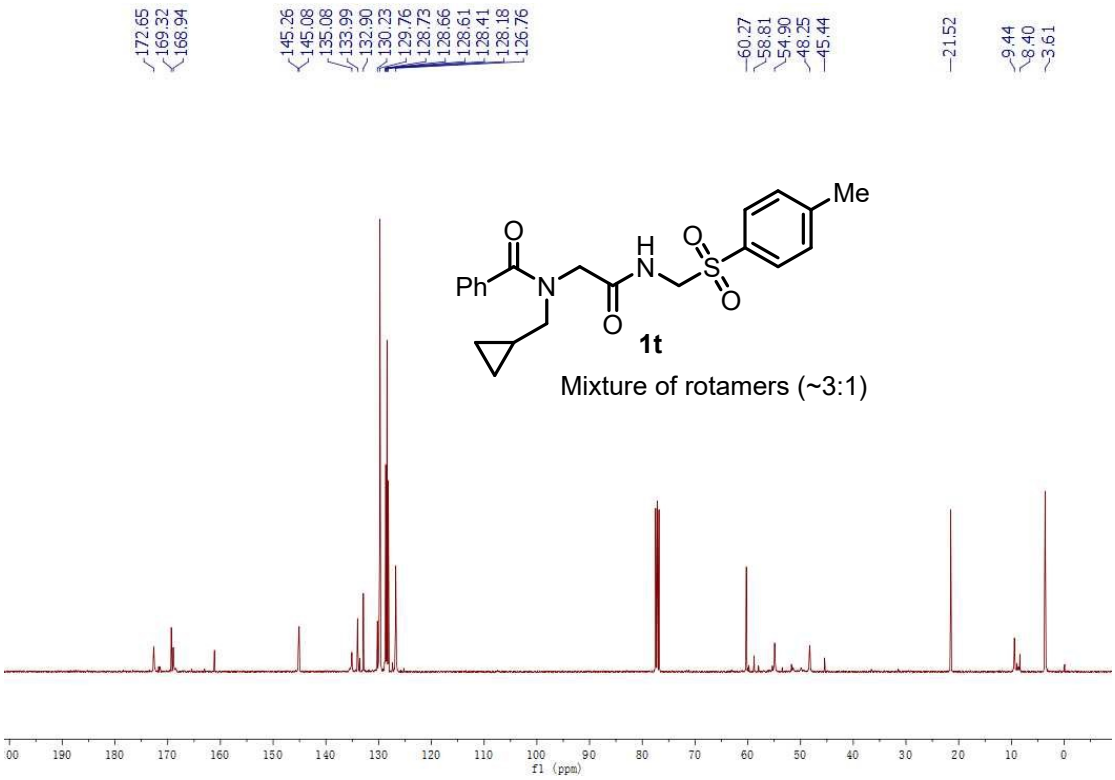

$^{13}$C NMR spectra of compound **1s** (101 MHz, $CDCl_3$)



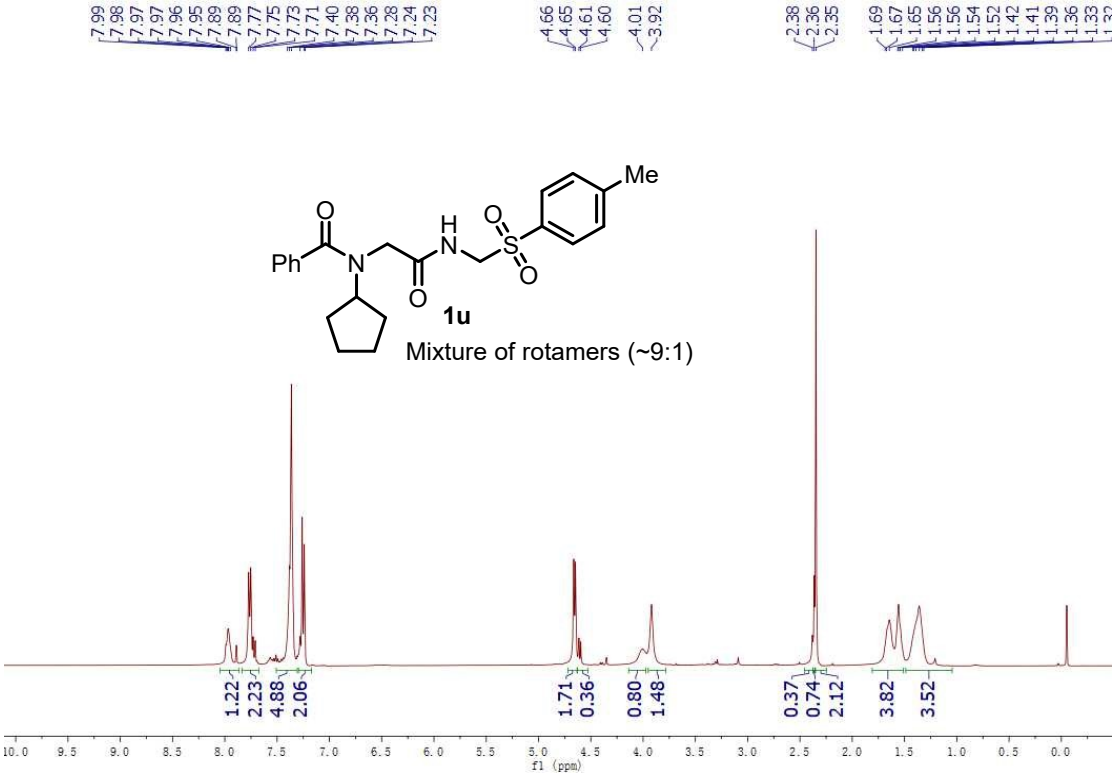
$^{1}$H spectra of compound **1t** (400 MHz, $CDCl_3$)



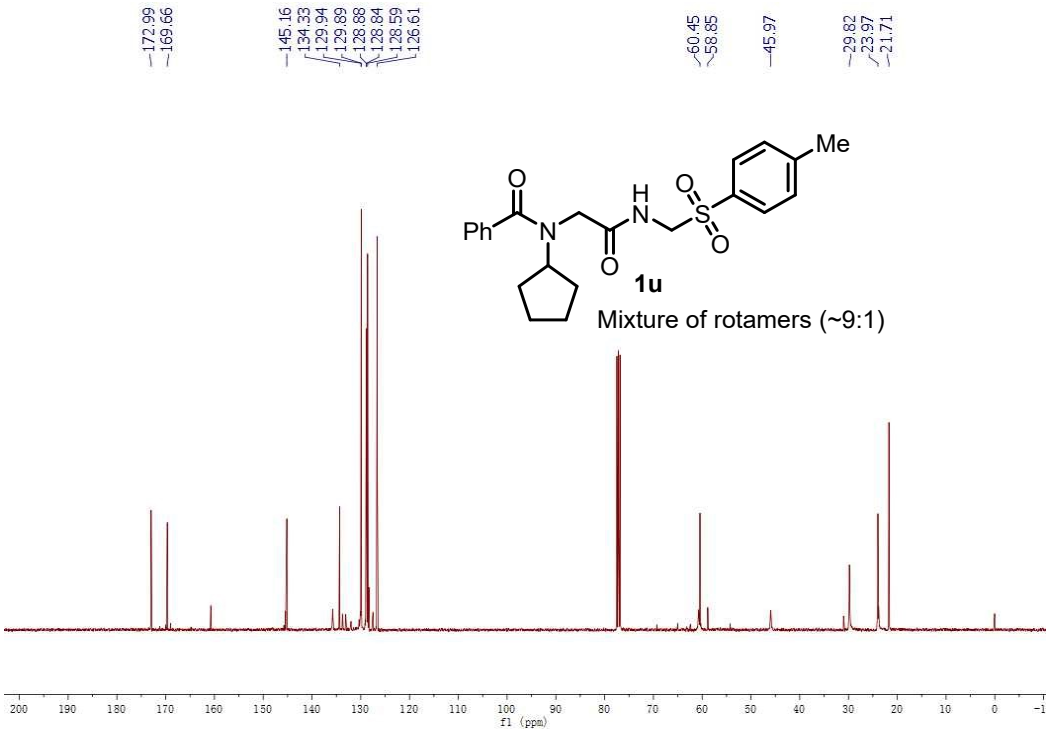

$^{13}$C NMR spectra of compound **1t** (101 MHz, $CDCl_3$)



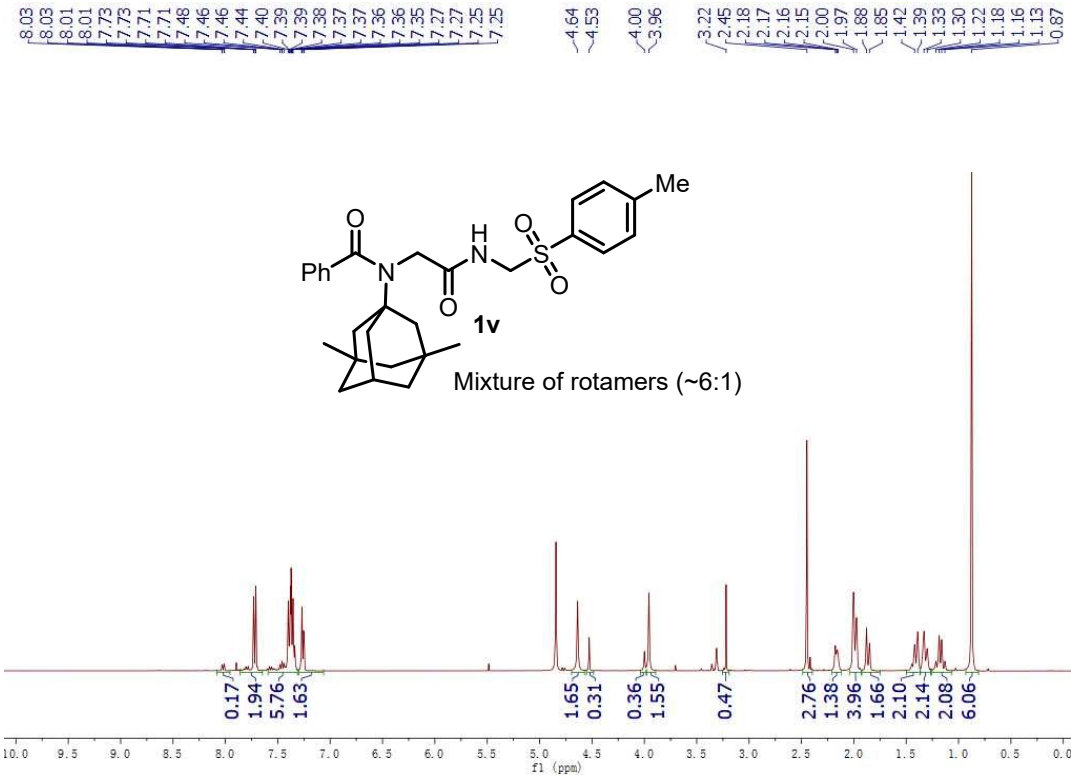
$^{1}$H spectra of compound **1u** (400 MHz, $CDCl_3$)



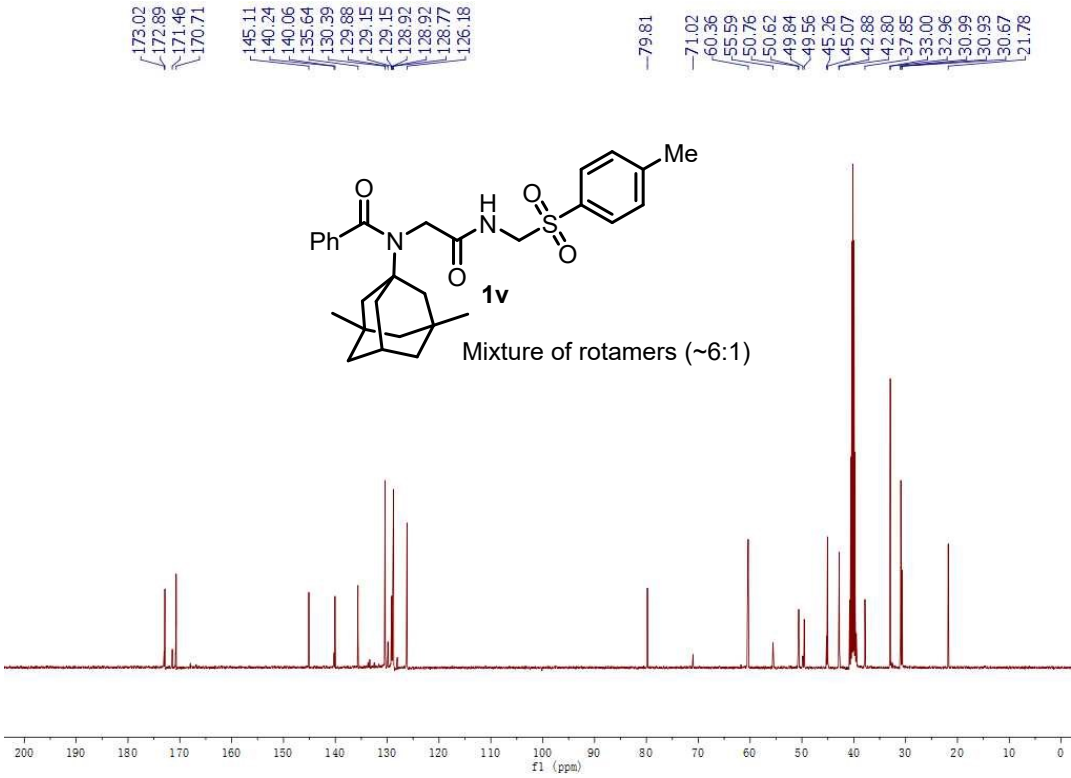

$^{13}$C NMR spectra of compound **1u** (101 MHz, $CDCl_3$)



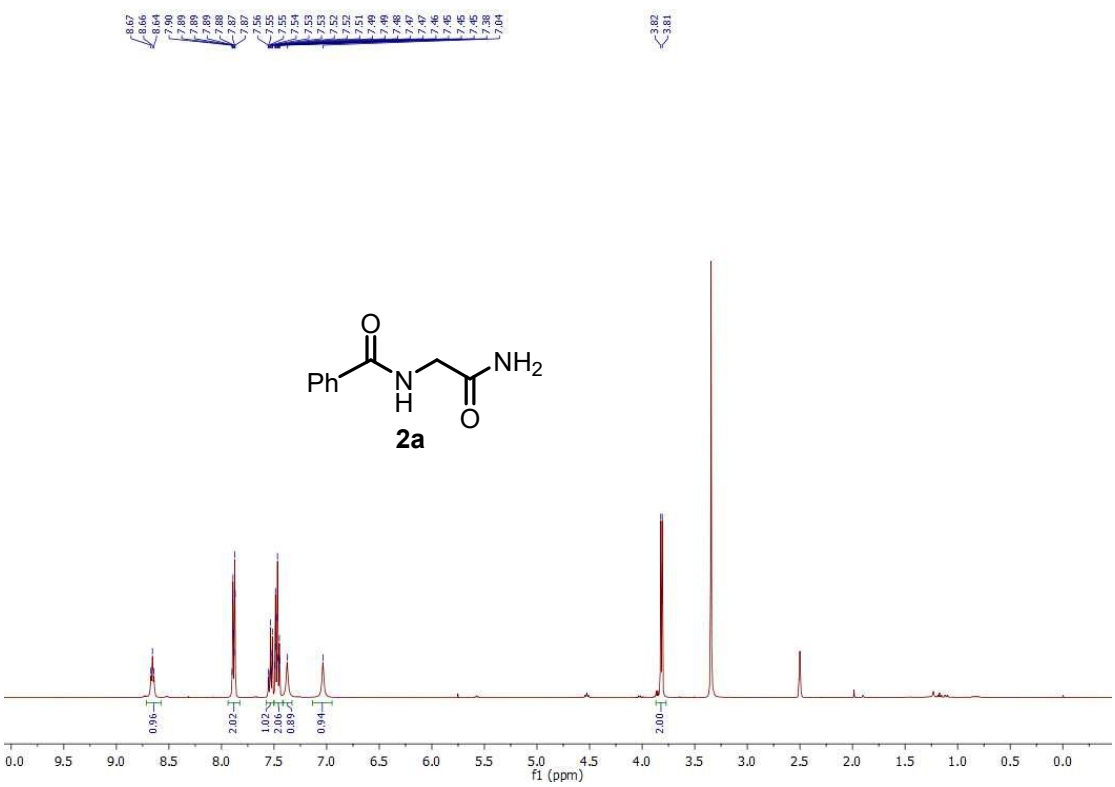
$^{1}$H spectra of compound **1v** (400 MHz, MeOH-$d_4$)



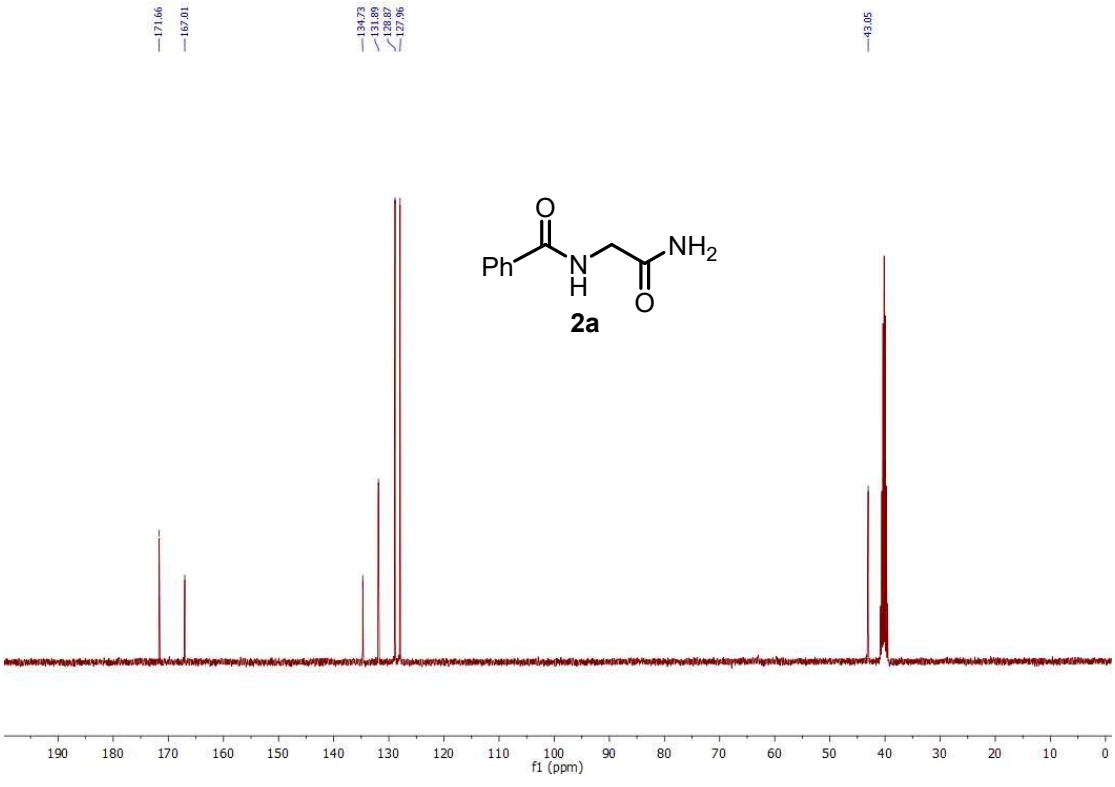

$^{13}$C NMR spectra of compound **1v** (101 MHz, DMSO-$d_6$)



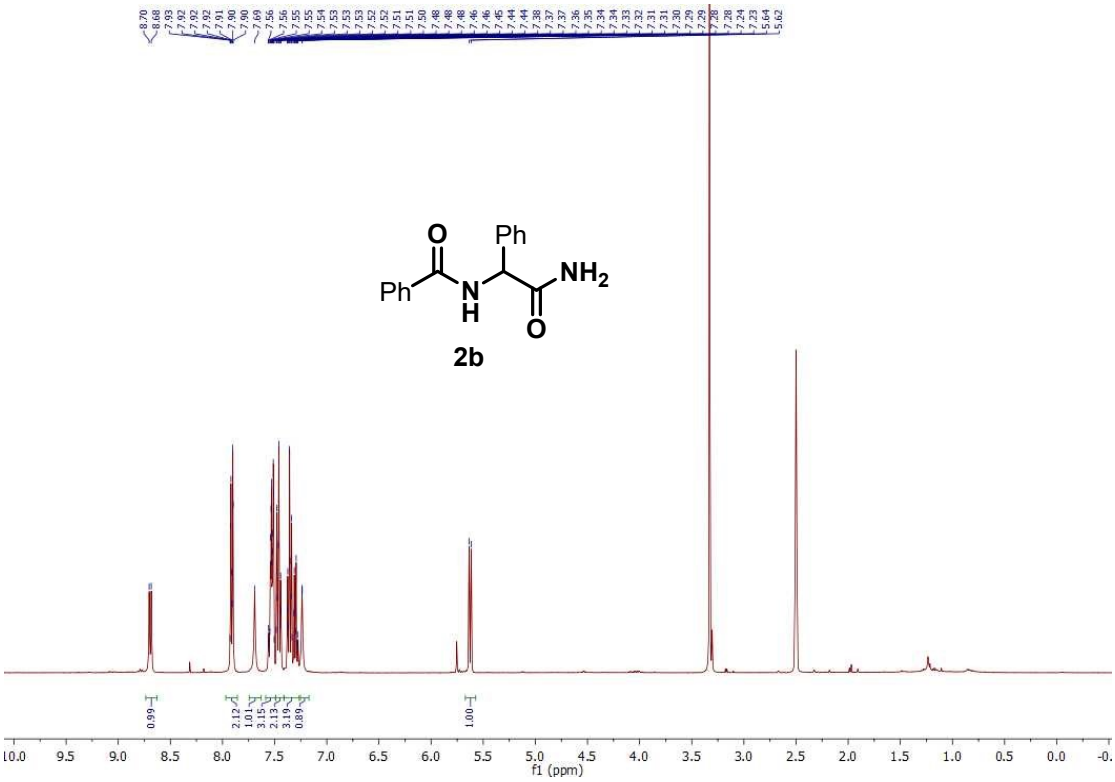
$^{1}$H spectra of compound **2a** (400 MHz, DMSO-$d_6$)



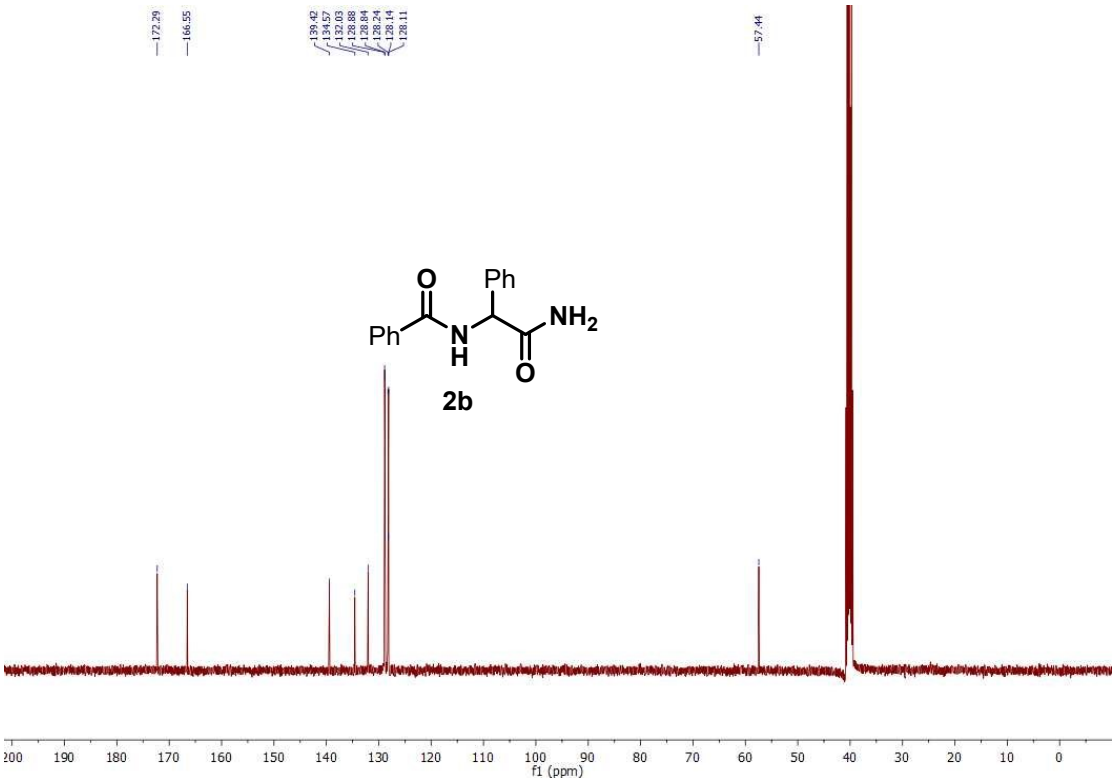

$^{13}$C NMR spectra of compound **2a** (101 MHz, DMSO-$d_6$)



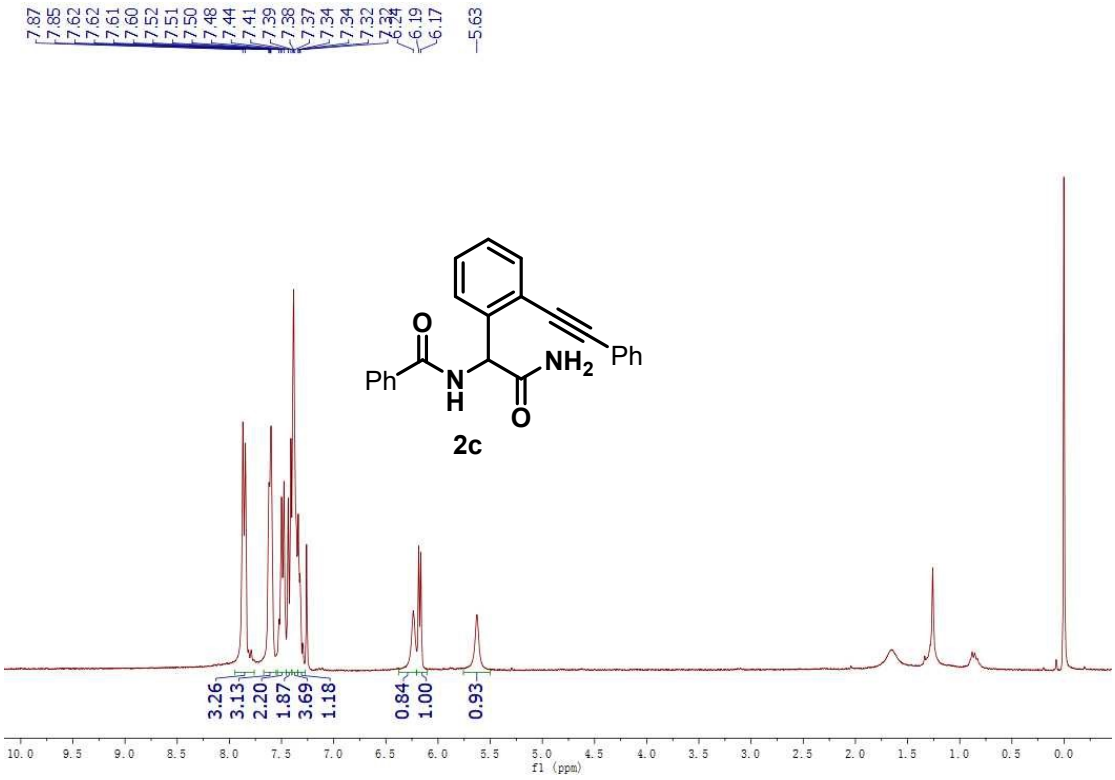
$^{1}$H spectra of compound **2b** (400 MHz, DMSO-$d_6$)



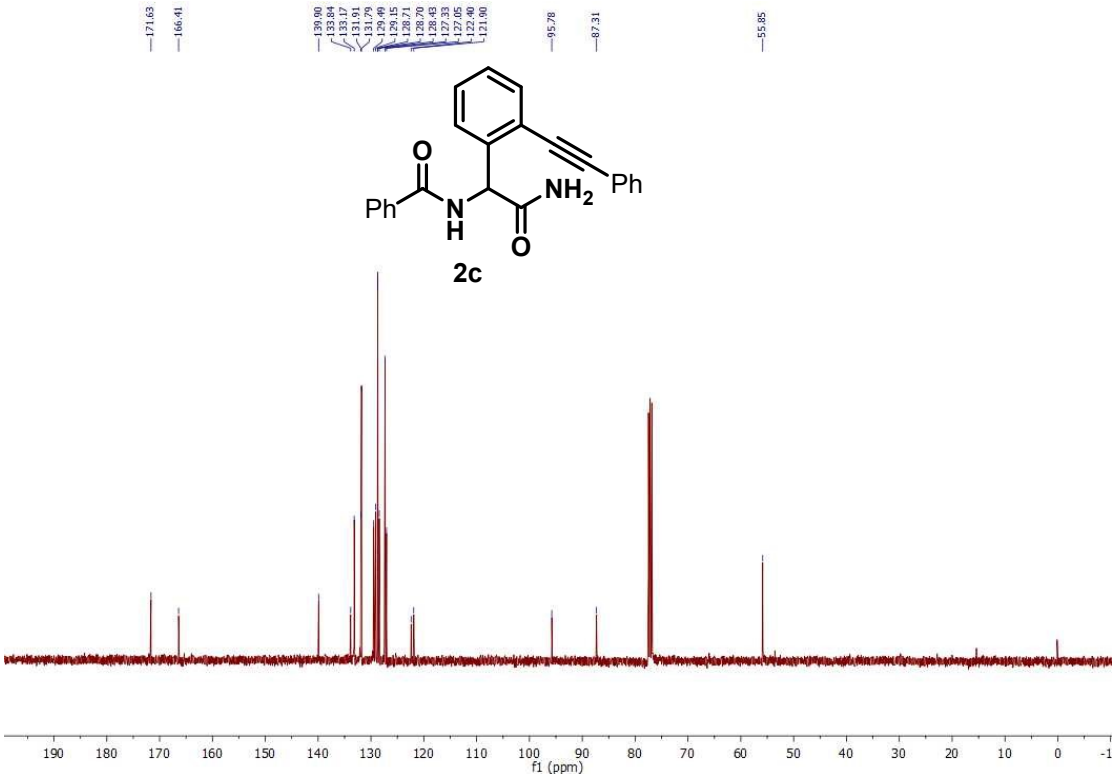

$^{13}$C NMR spectra of compound **2b** (101 MHz, DMSO-$d_6$)



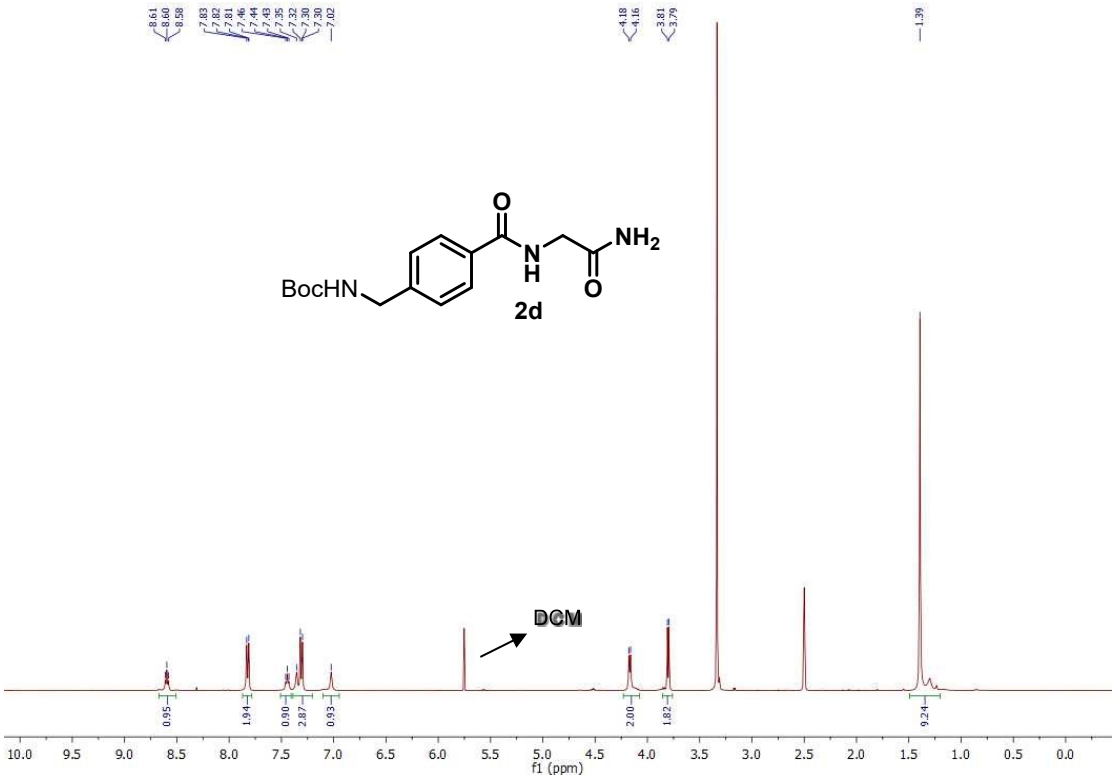
$^{1}$H spectra of compound **2c** (300 MHz, $CDCl_3$)



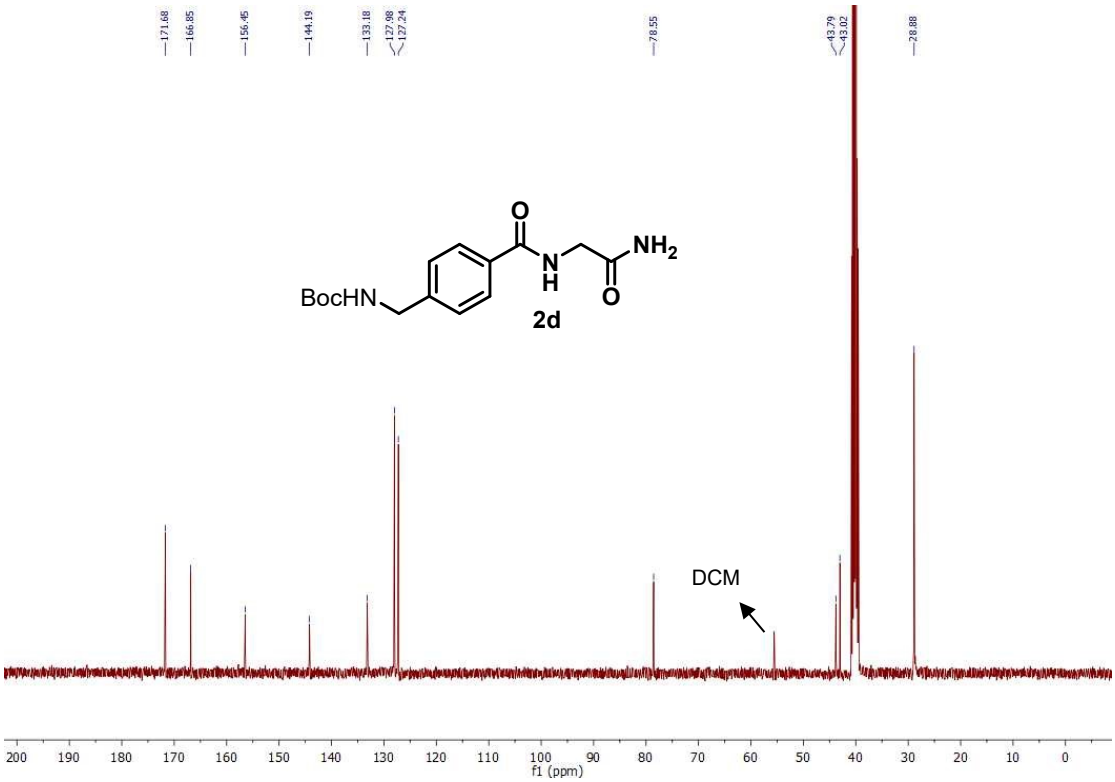

$^{13}$C NMR spectra of compound **2c** (101 MHz, $CDCl_3$)



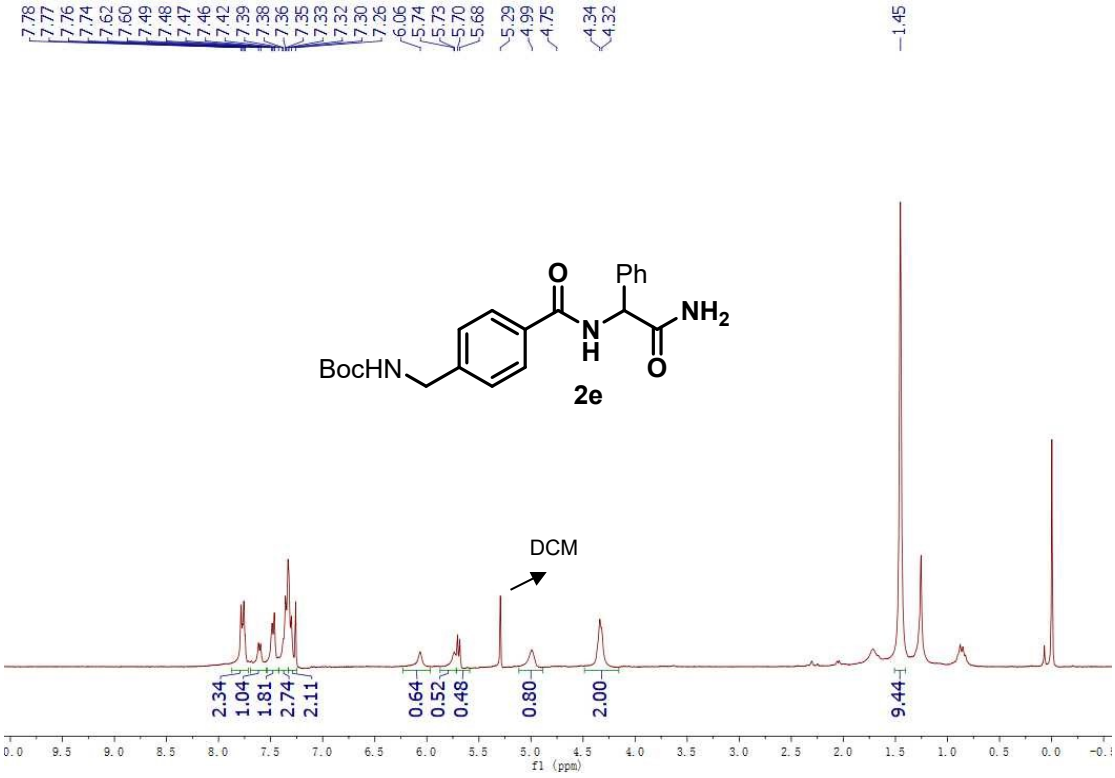
$^{1}$H spectra of compound **2d** (400 MHz, DMSO-$d_6$)



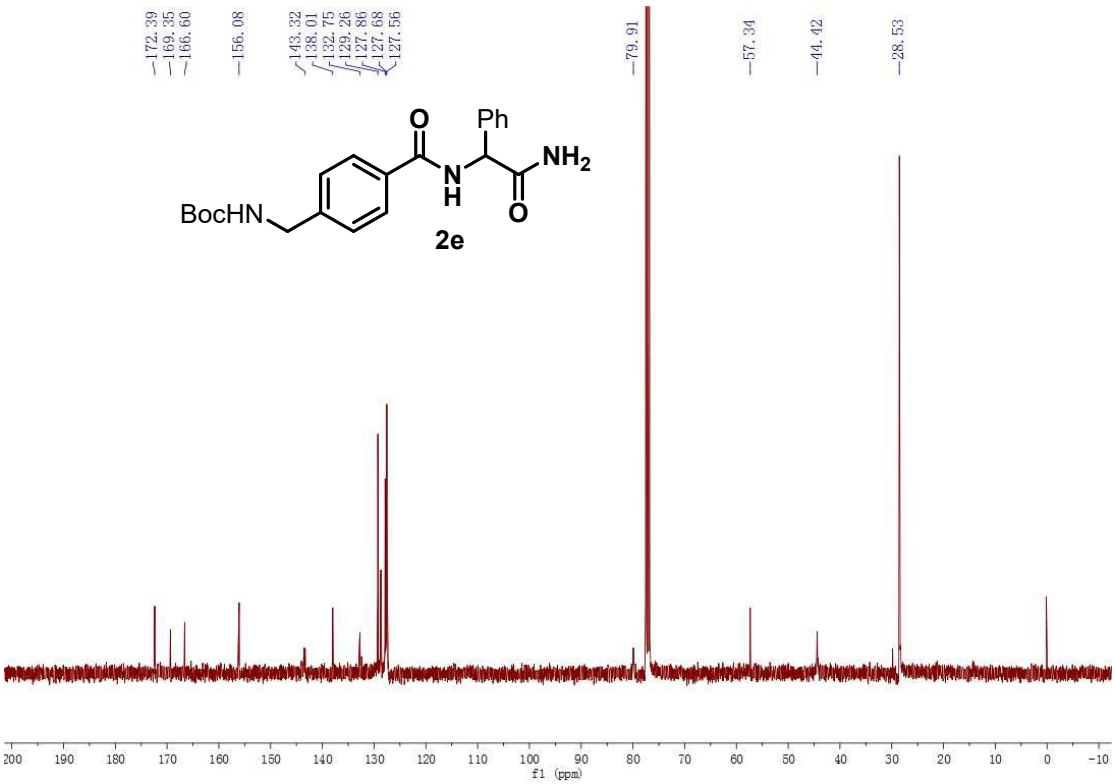

$^{13}$C NMR spectra of compound **2d** (101 MHz, DMSO-$d_6$)



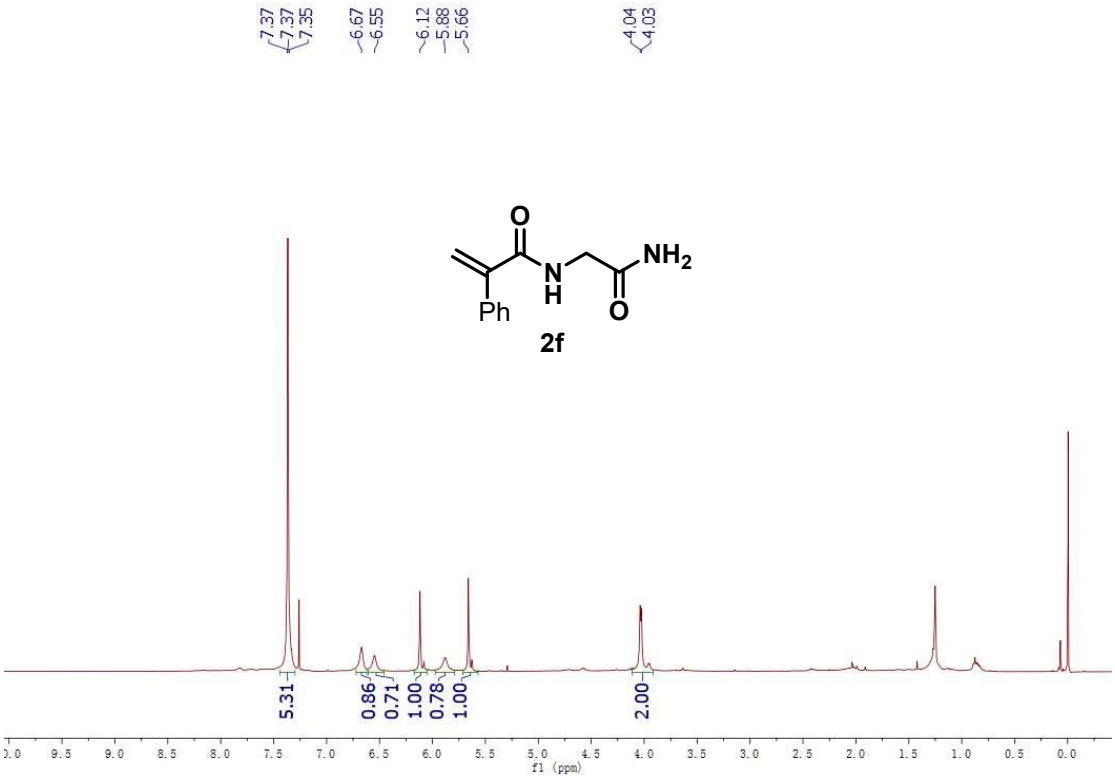
$^{1}$H spectra of compound **2e** (300 MHz, $CDCl_3$)



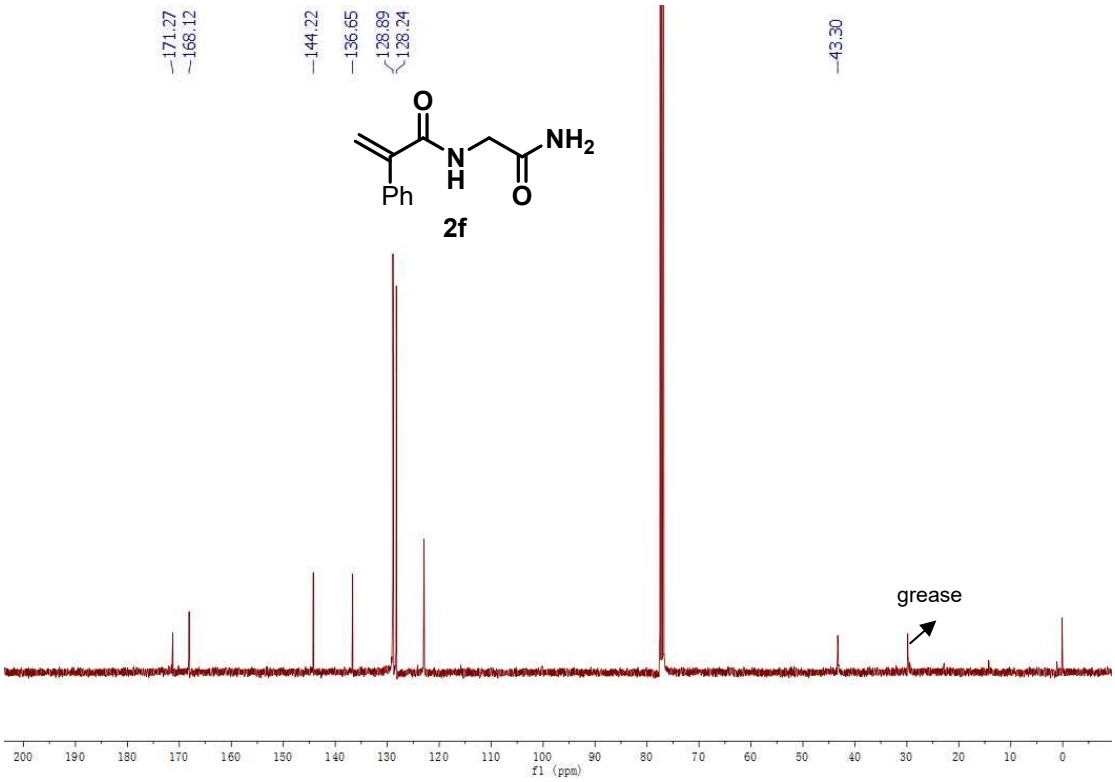

$^{13}$C NMR spectra of compound **2e** (101 MHz, $CDCl_3$)



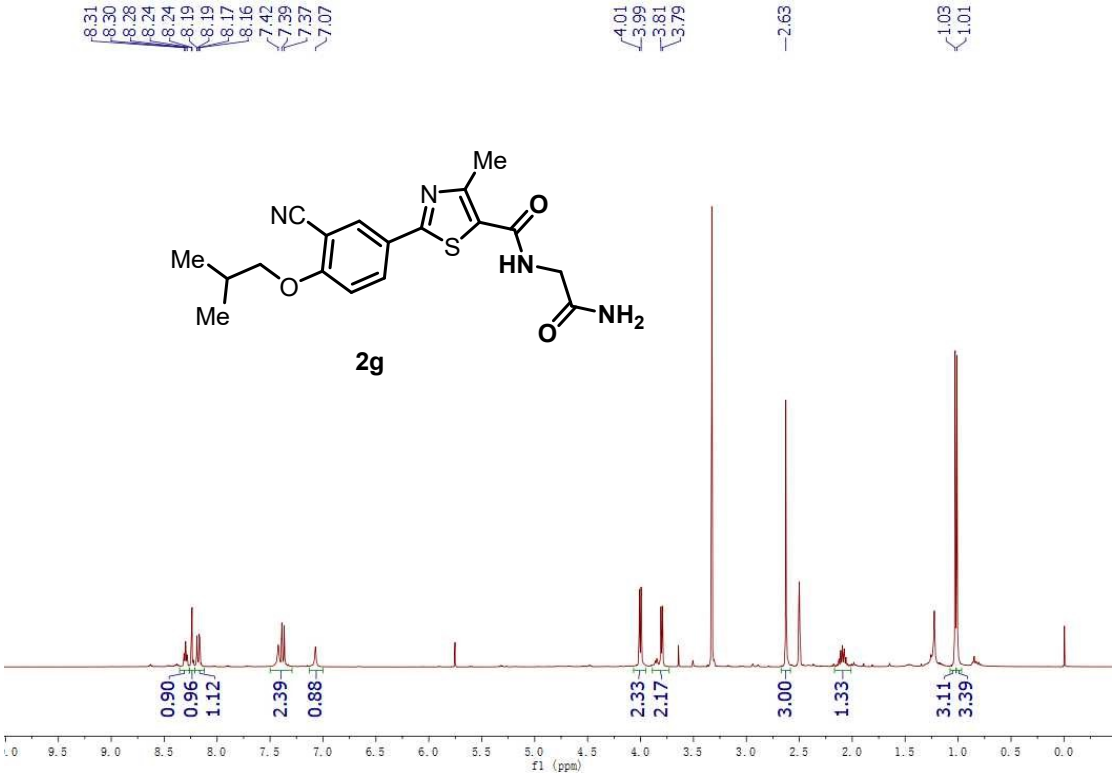
$^{1}$H spectra of compound **2f** (400 MHz, $CDCl_3$)



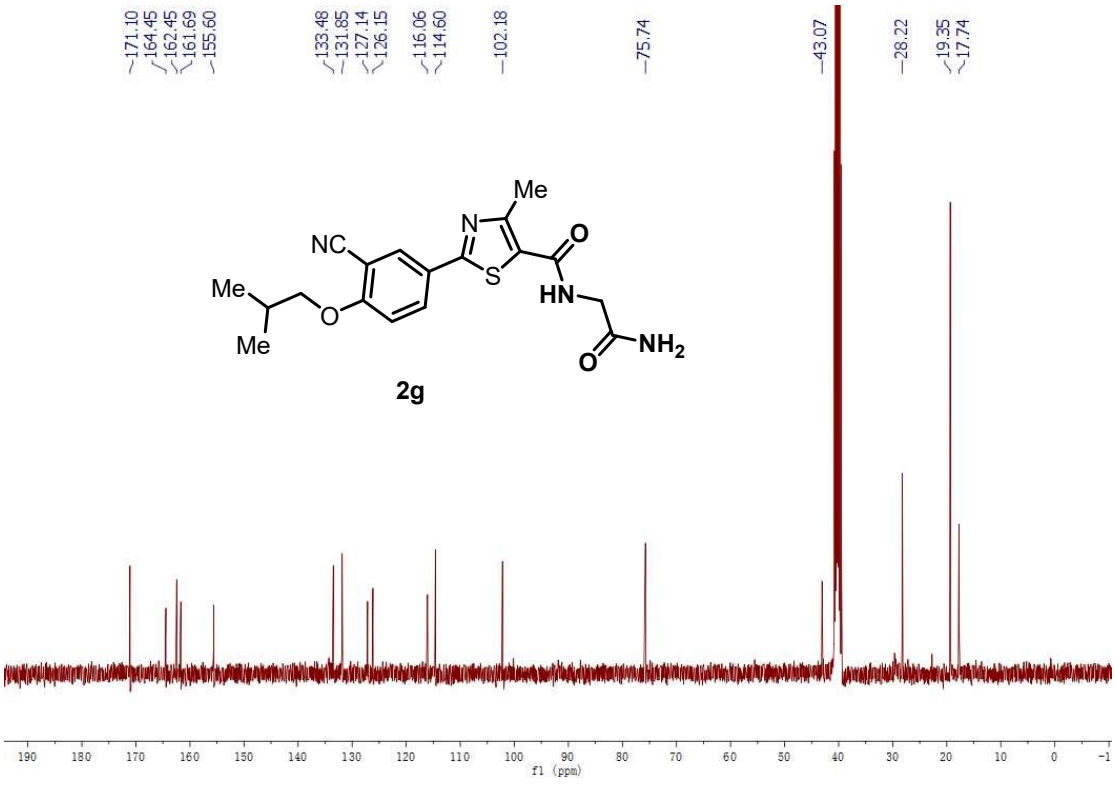

$^{13}$C NMR spectra of compound **2f** (101 MHz, $CDCl_3$)



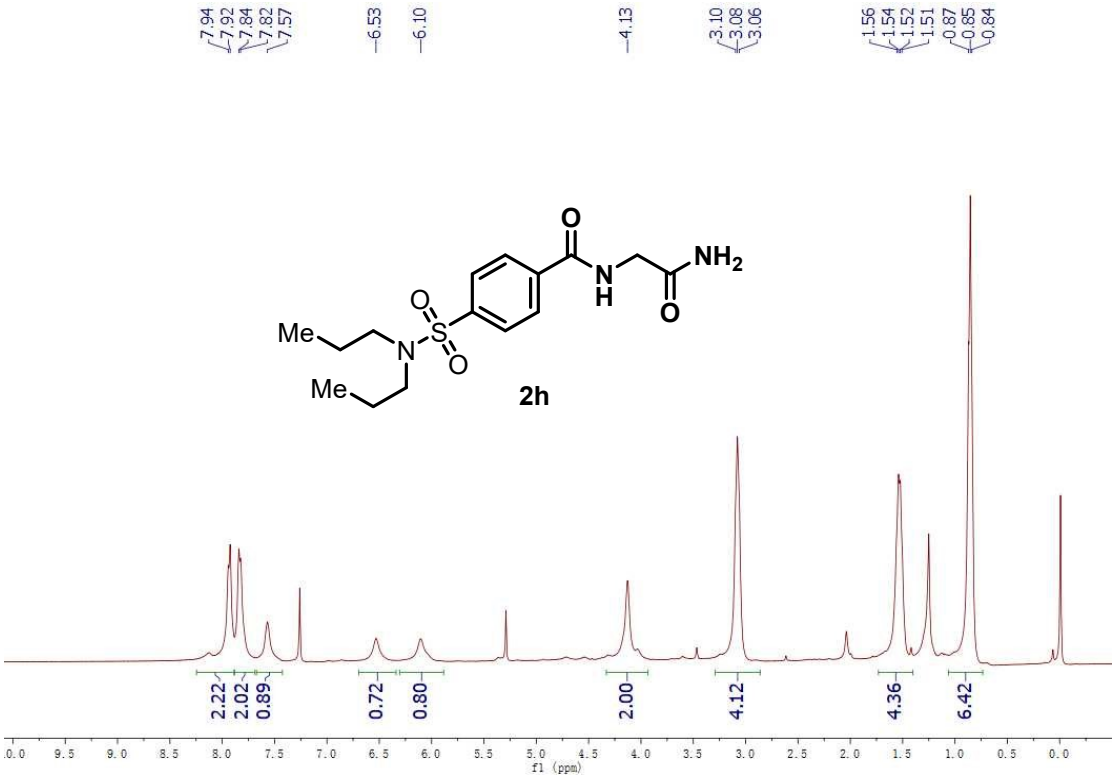
$^{1}$H spectra of compound **2g** (400 MHz, DMSO-$d_6$)



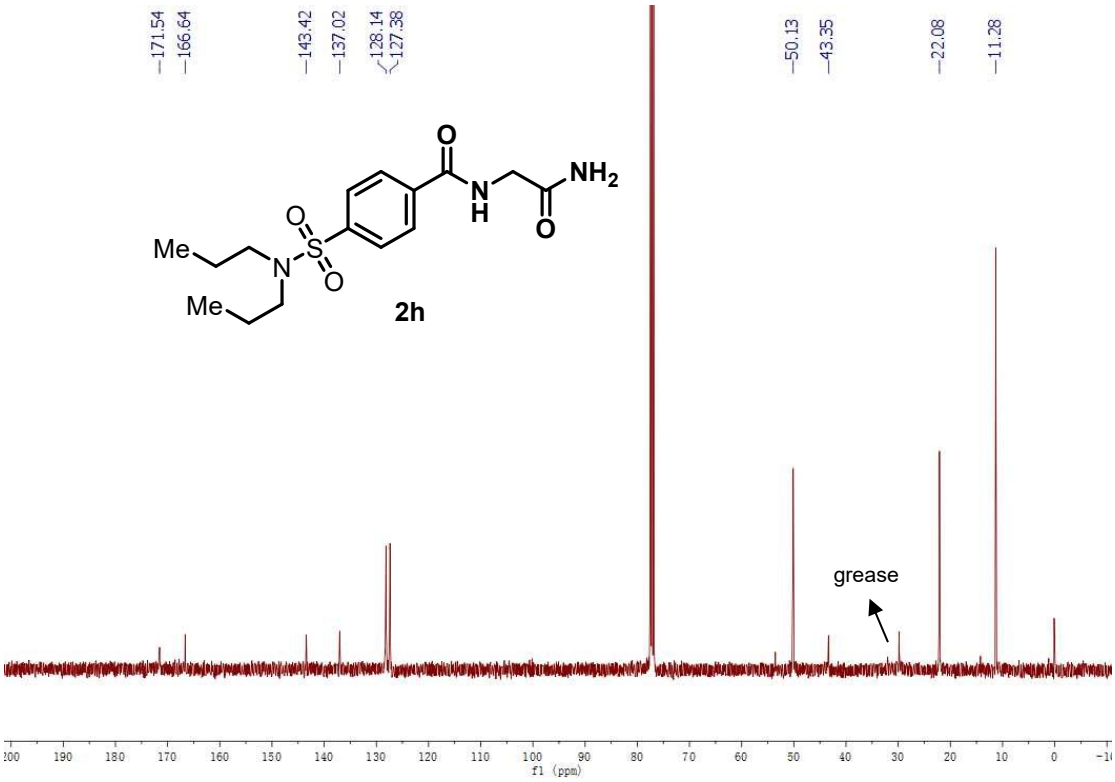

$^{13}$C NMR spectra of compound **2g** (101 MHz, DMSO-$d_6$)



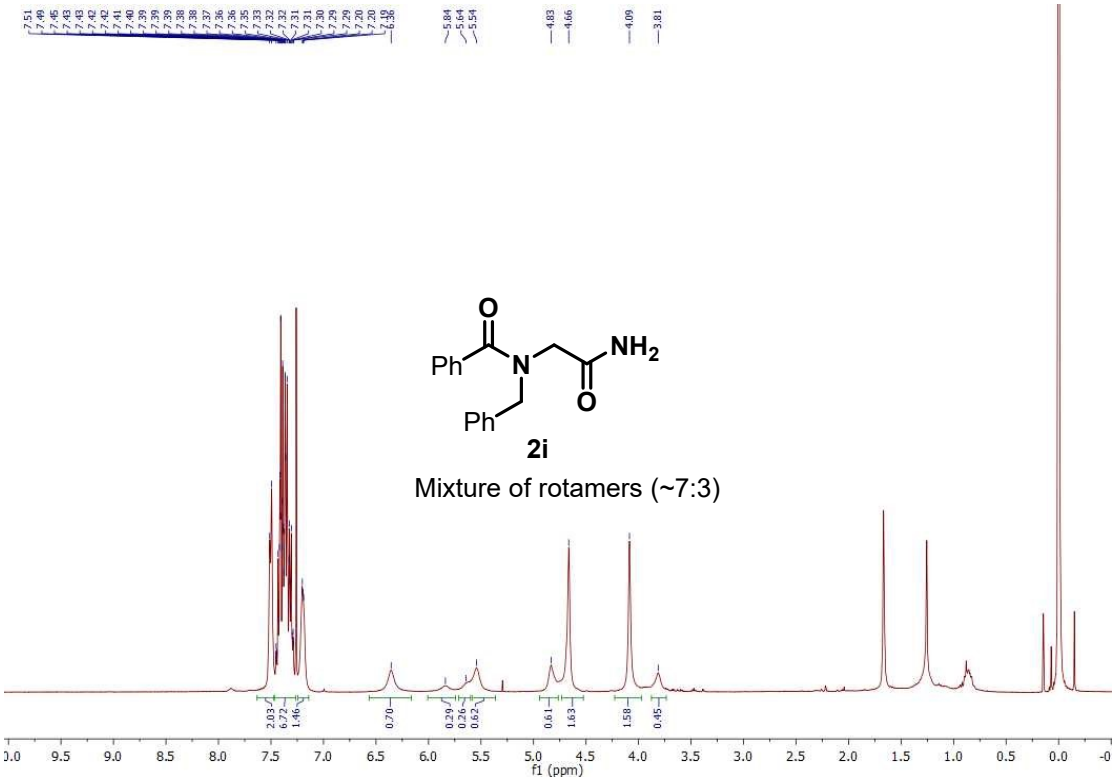
$^{1}$H spectra of compound **2h** (400 MHz, $CDCl_3$)



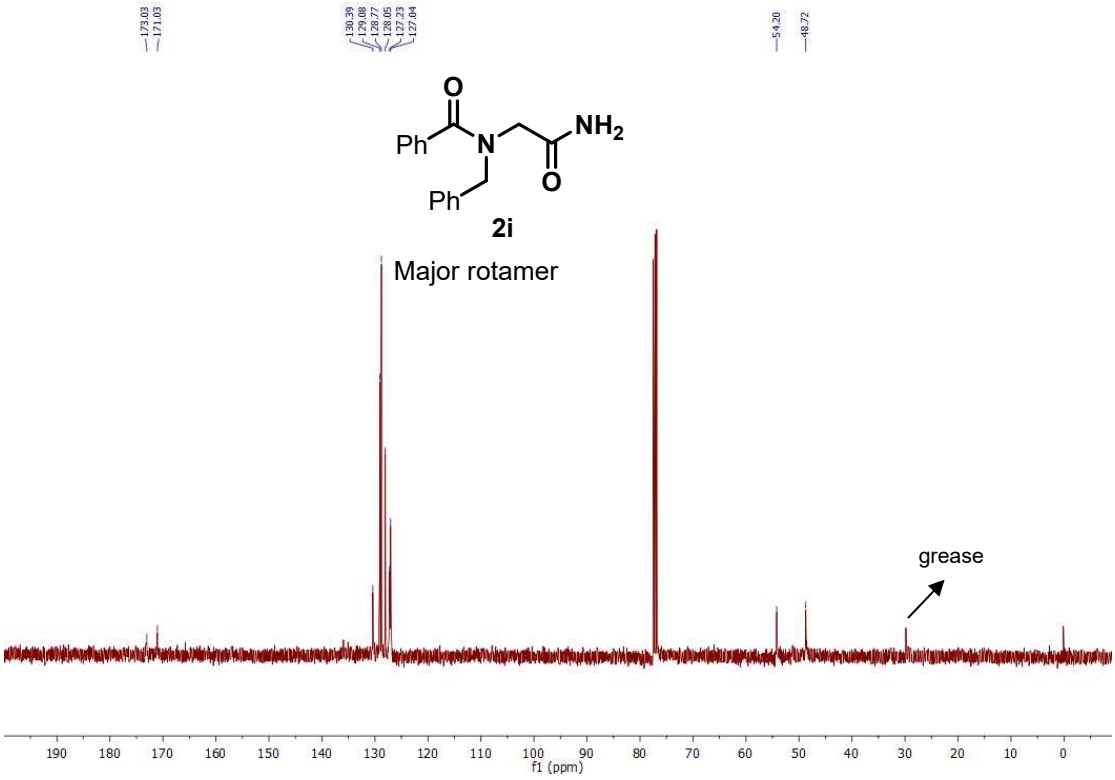

$^{13}$C NMR spectra of compound **2h** (101 MHz, $CDCl_3$)



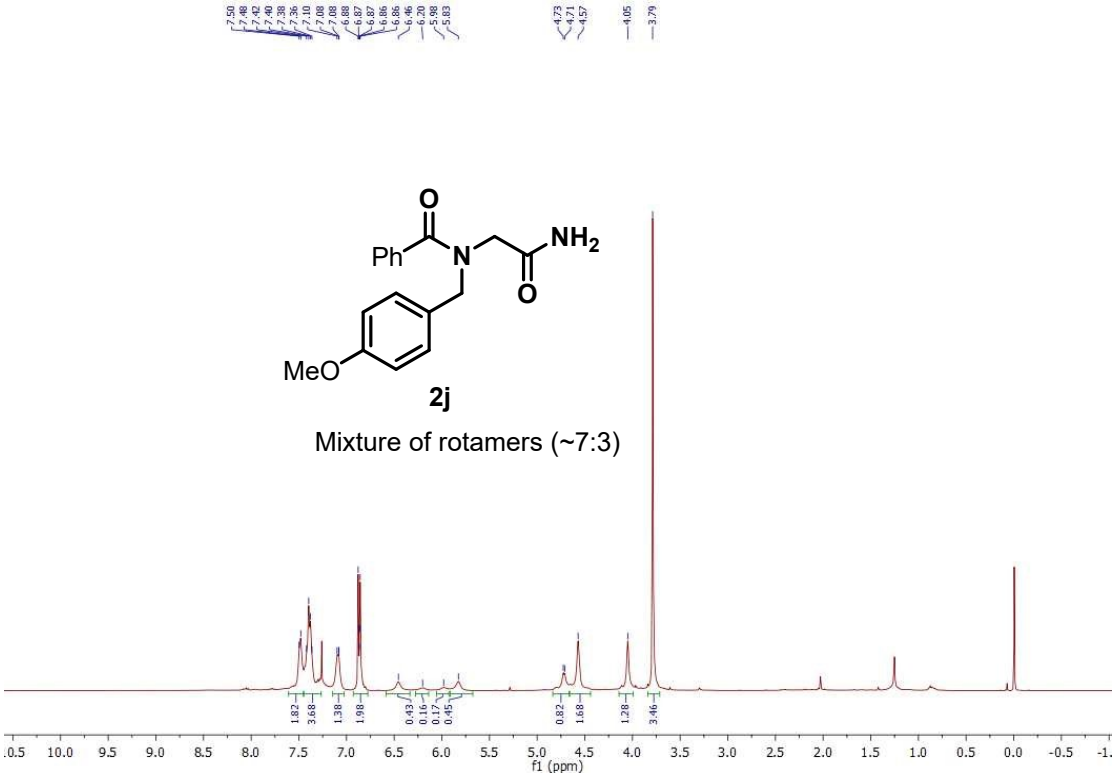
$^{1}$H spectra of compound **2i** (400 MHz, $CDCl_3$)



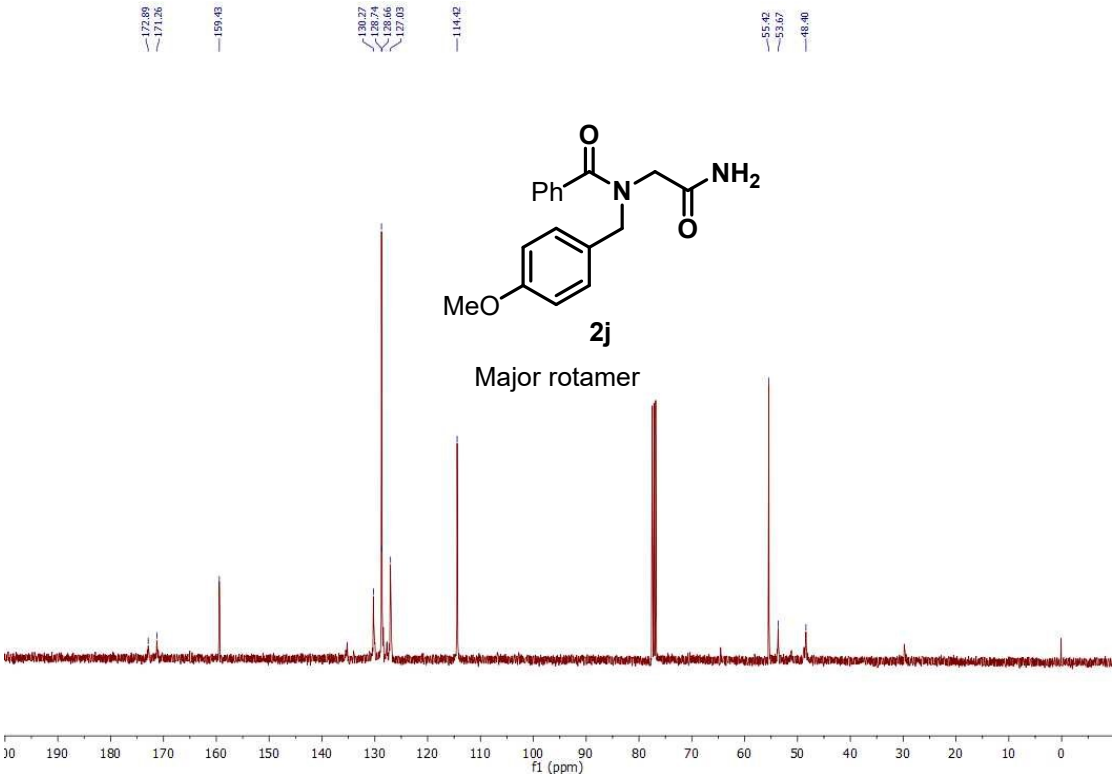

$^{13}$C NMR spectra of compound **2i** (101 MHz, $CDCl_3$)



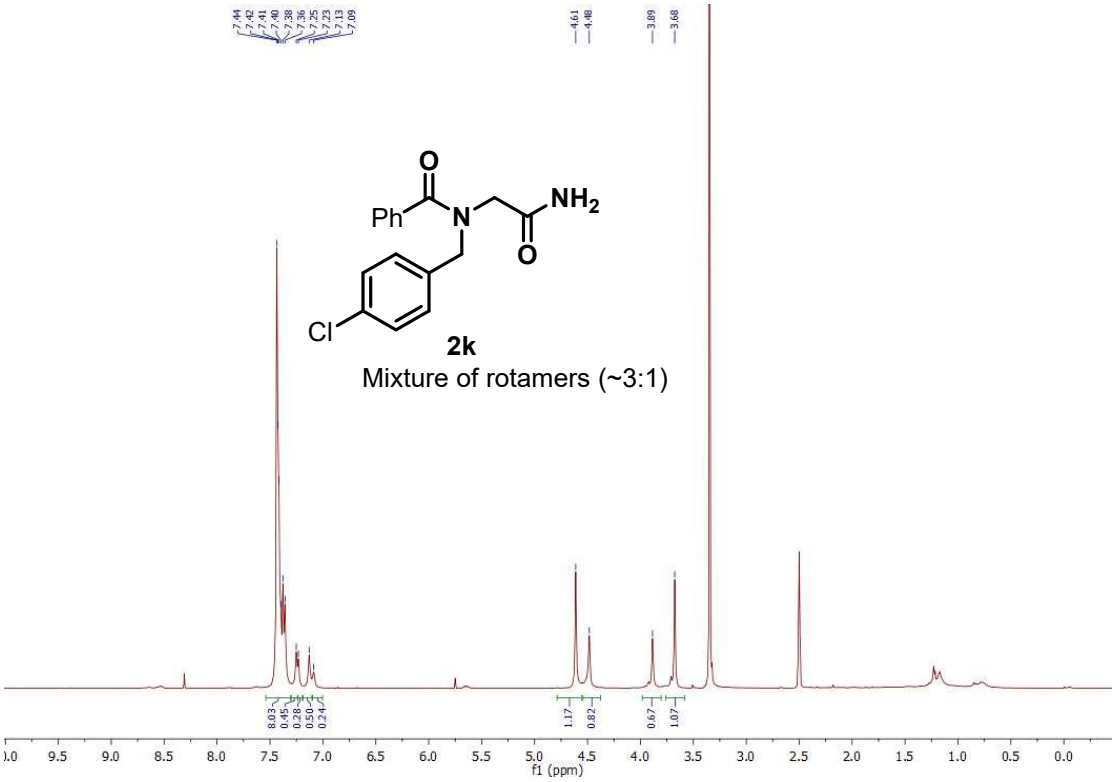
$^{1}$H spectra of compound **2j** (400 MHz, $CDCl_3$)



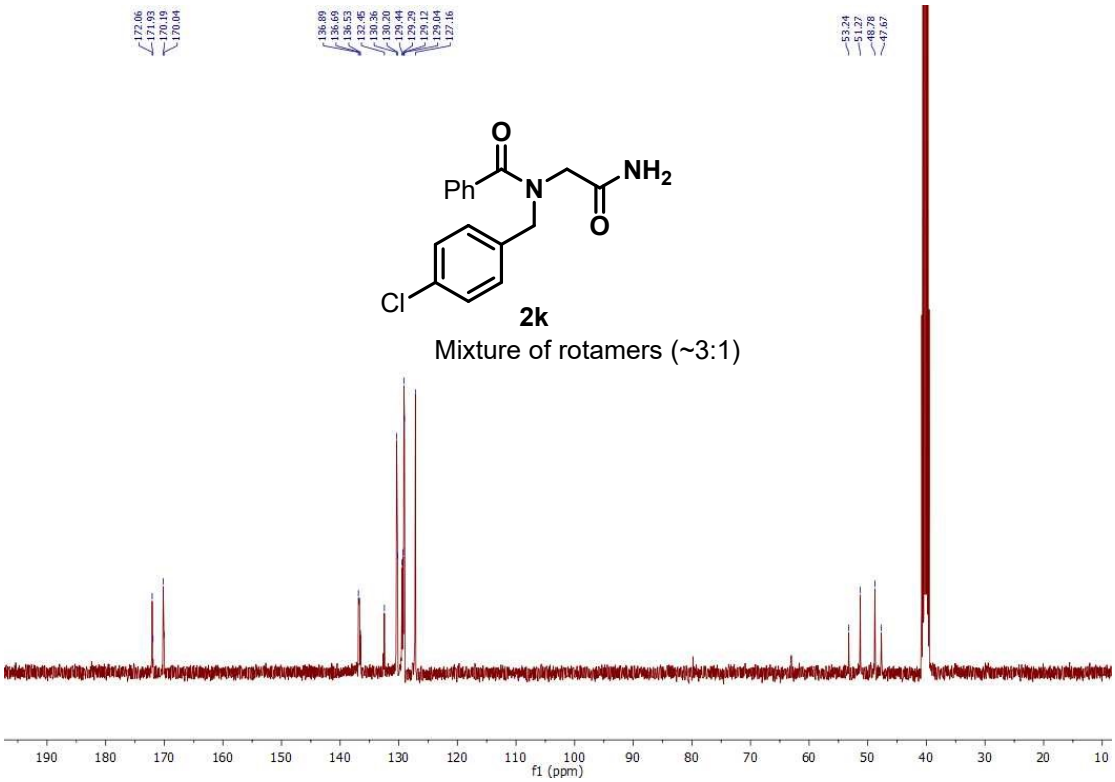

$^{13}$C NMR spectra of compound **2j** (101 MHz, $CDCl_3$)



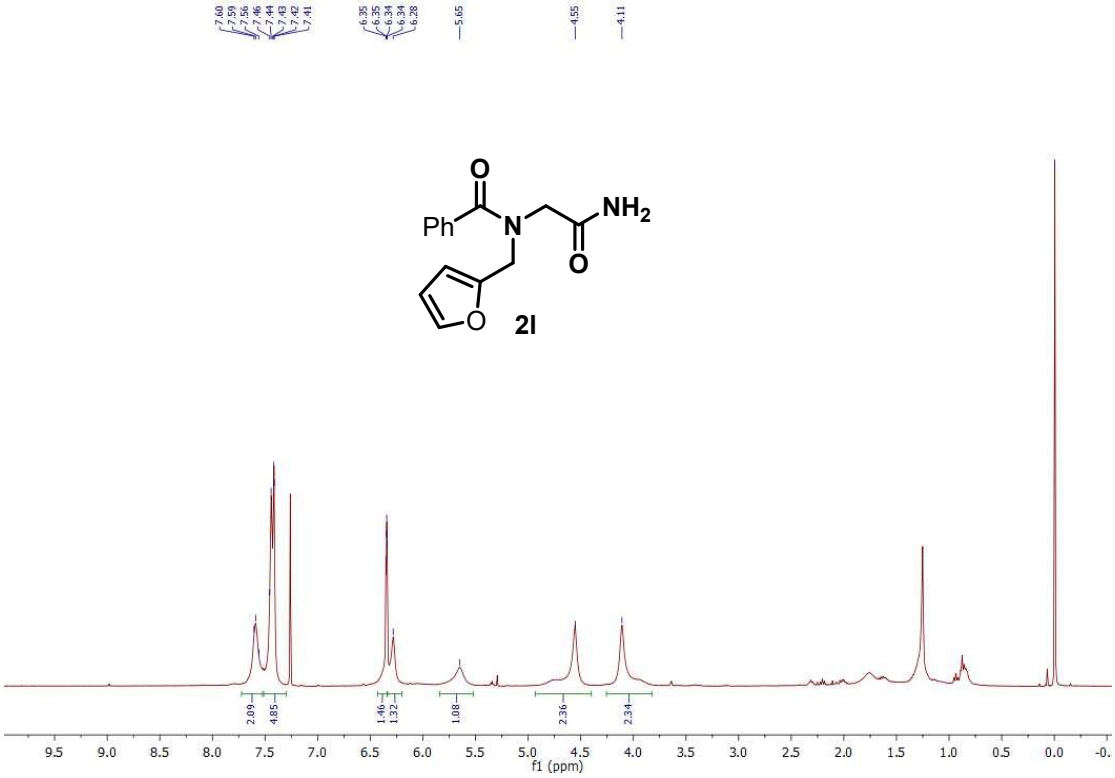
$^{1}$H spectra of compound **2k** (400 MHz, DMSO-$d_6$)



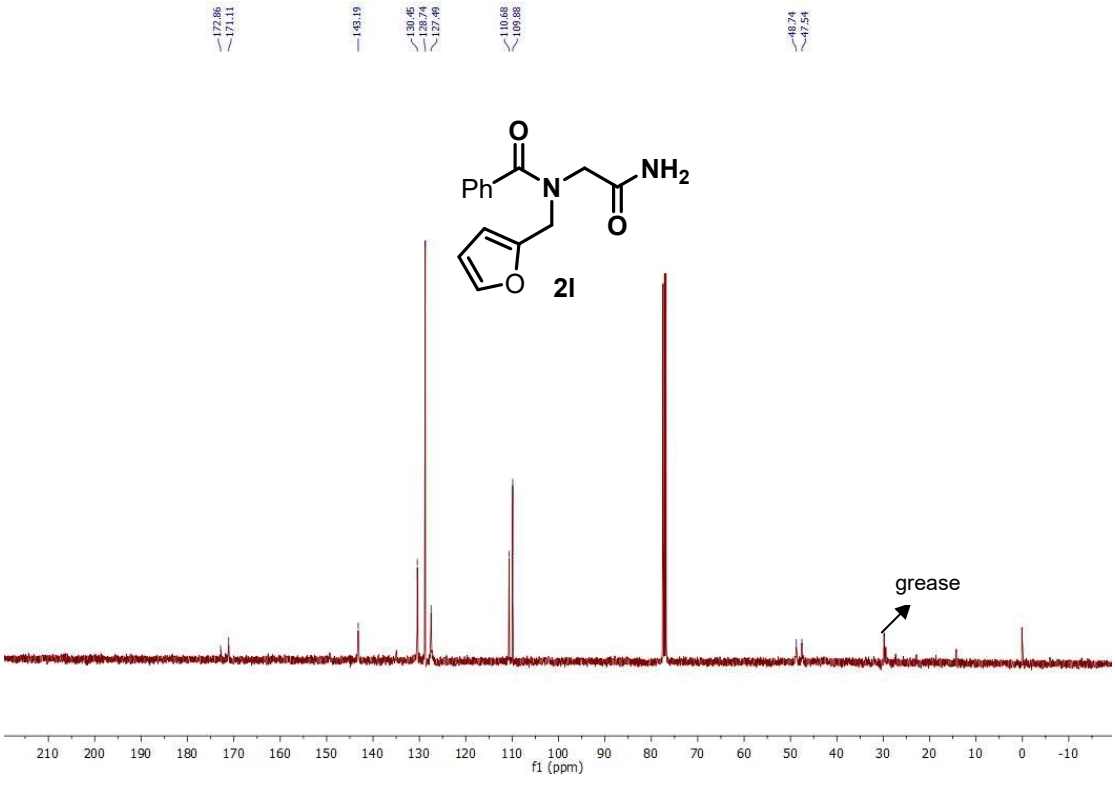

$^{13}$C NMR spectra of compound **2k** (101 MHz, DMSO-$d_6$)



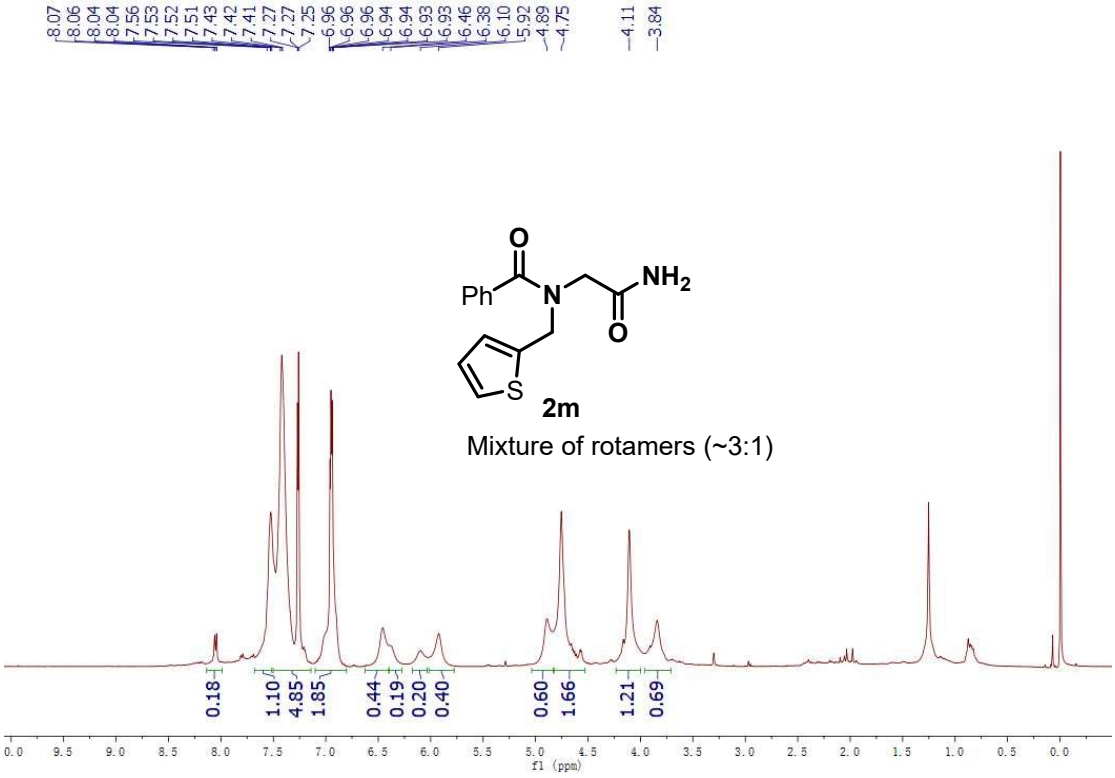
$^{1}$H spectra of compound **2l** (400 MHz, $CDCl_3$)



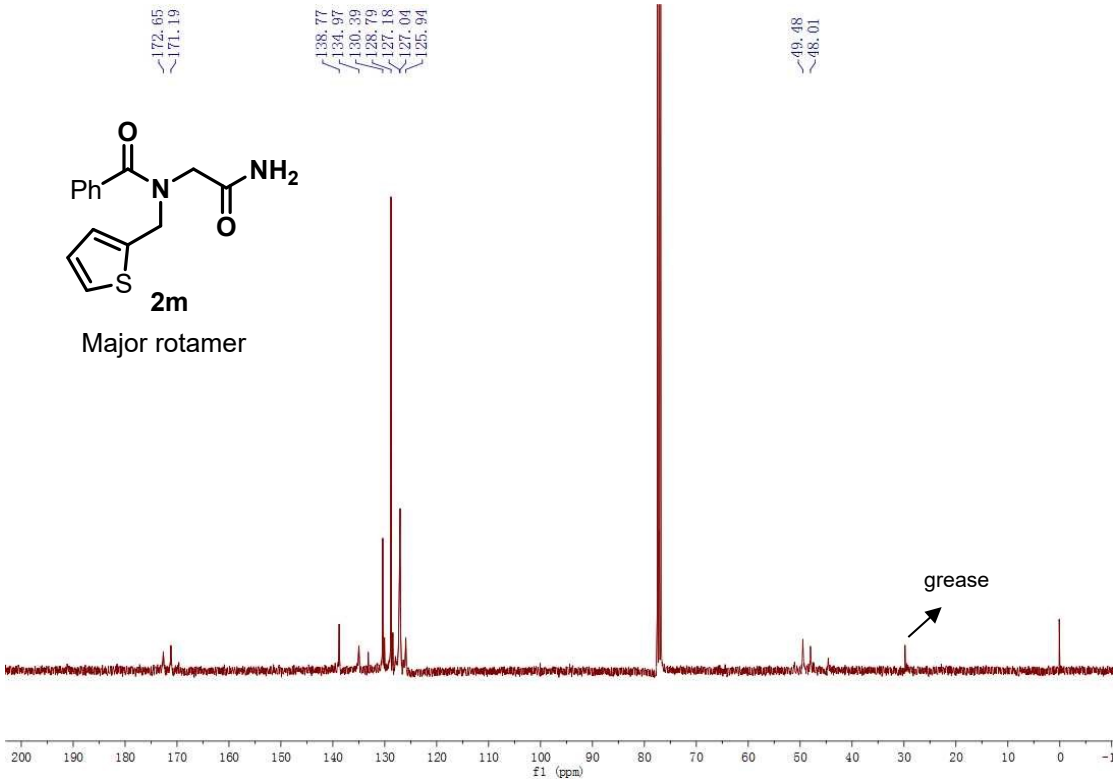

$^{13}$C NMR spectra of compound **2l** (101 MHz, $CDCl_3$)



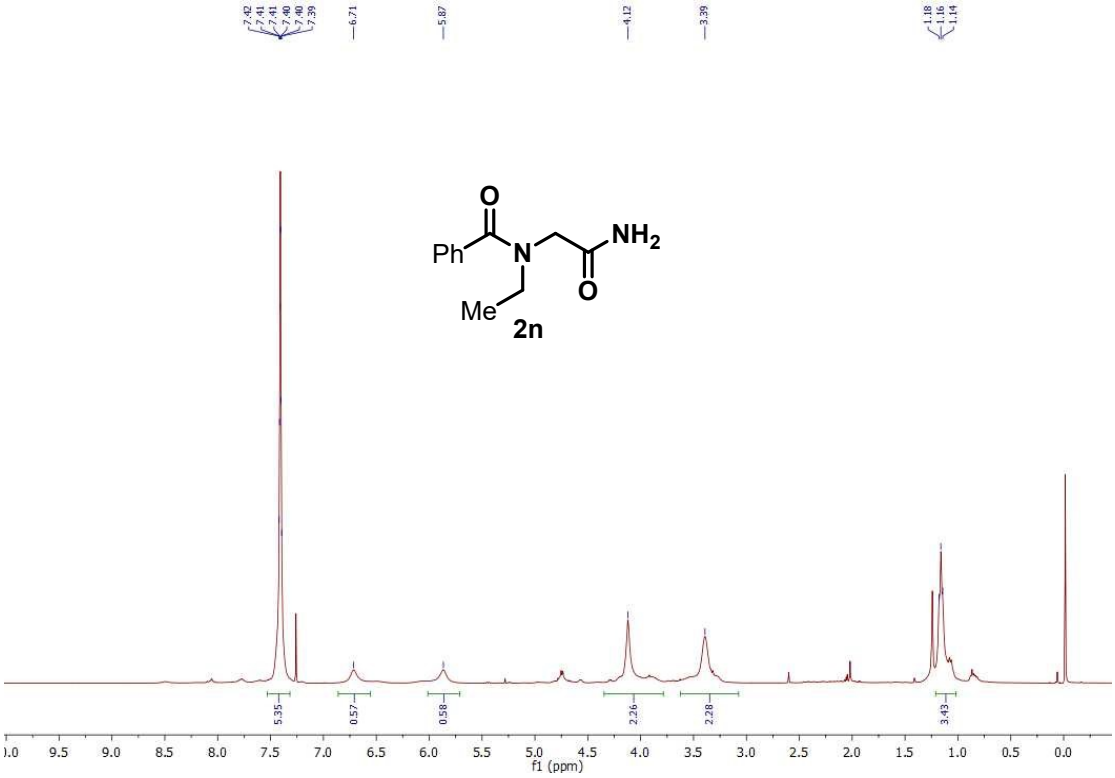
$^{1}$H spectra of compound **2m** (400 MHz, $CDCl_3$)



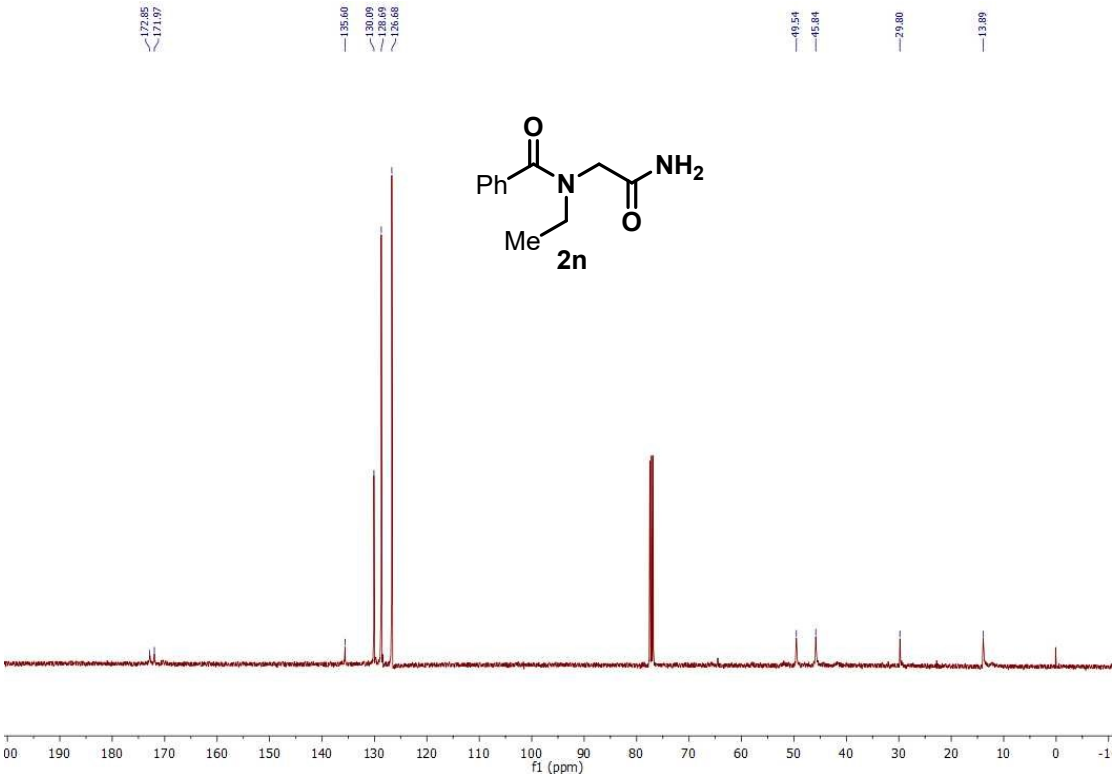

$^{13}$C NMR spectra of compound **2m** (101 MHz, $CDCl_3$)



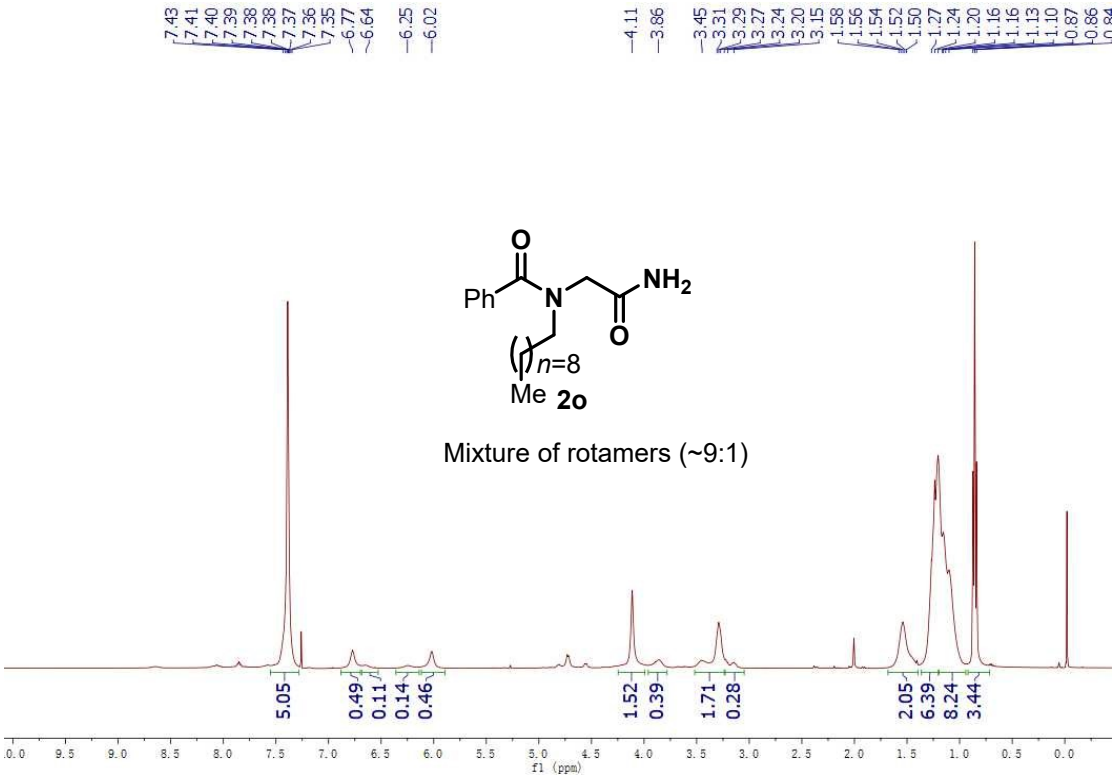
$^{1}$H spectra of compound **2n** (400 MHz, $CDCl_3$)



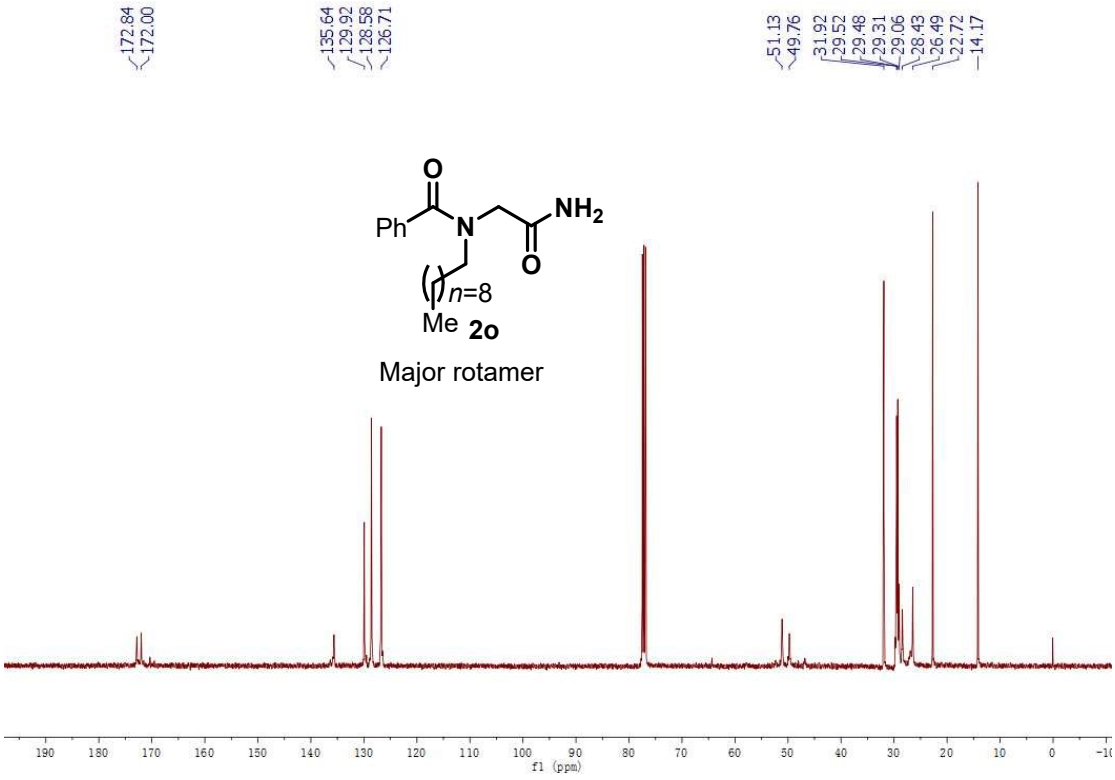

$^{13}$C NMR spectra of compound **2n** (101 MHz, $CDCl_3$)



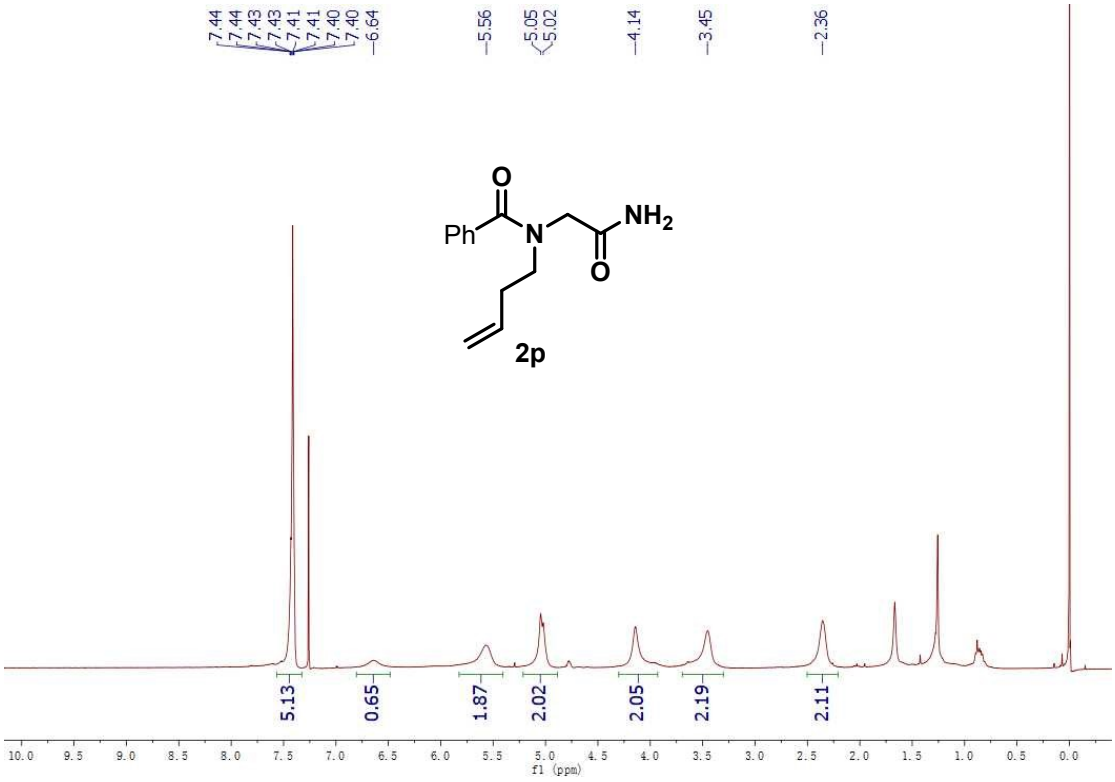
$^{1}$H spectra of compound **2o** (400 MHz, $CDCl_3$)



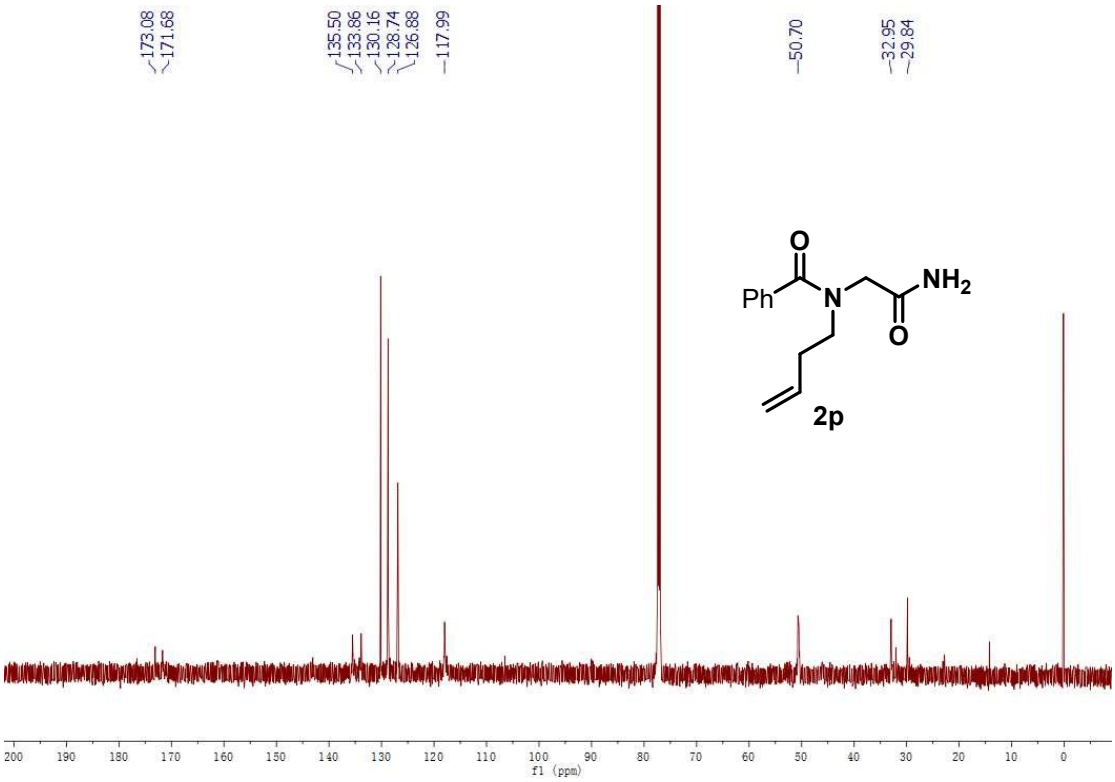

$^{13}$C NMR spectra of compound **2o** (101 MHz, $CDCl_3$)



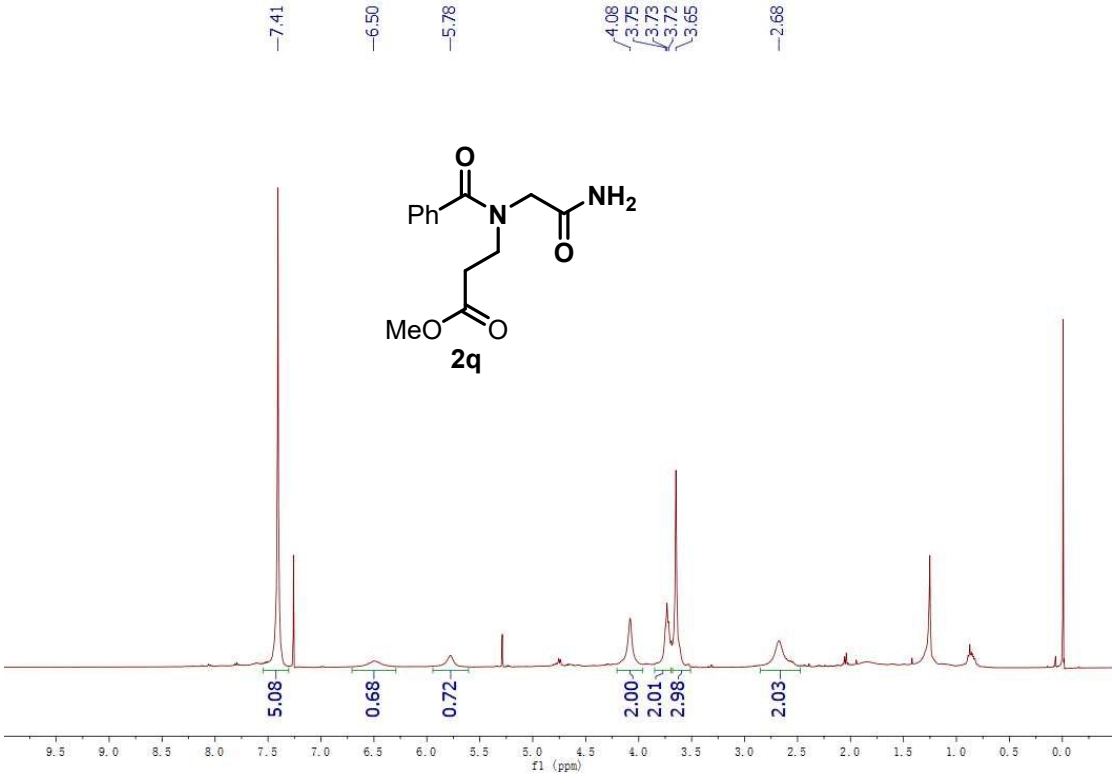
$^{1}$H spectra of compound **2p** (400 MHz, $CDCl_3$)



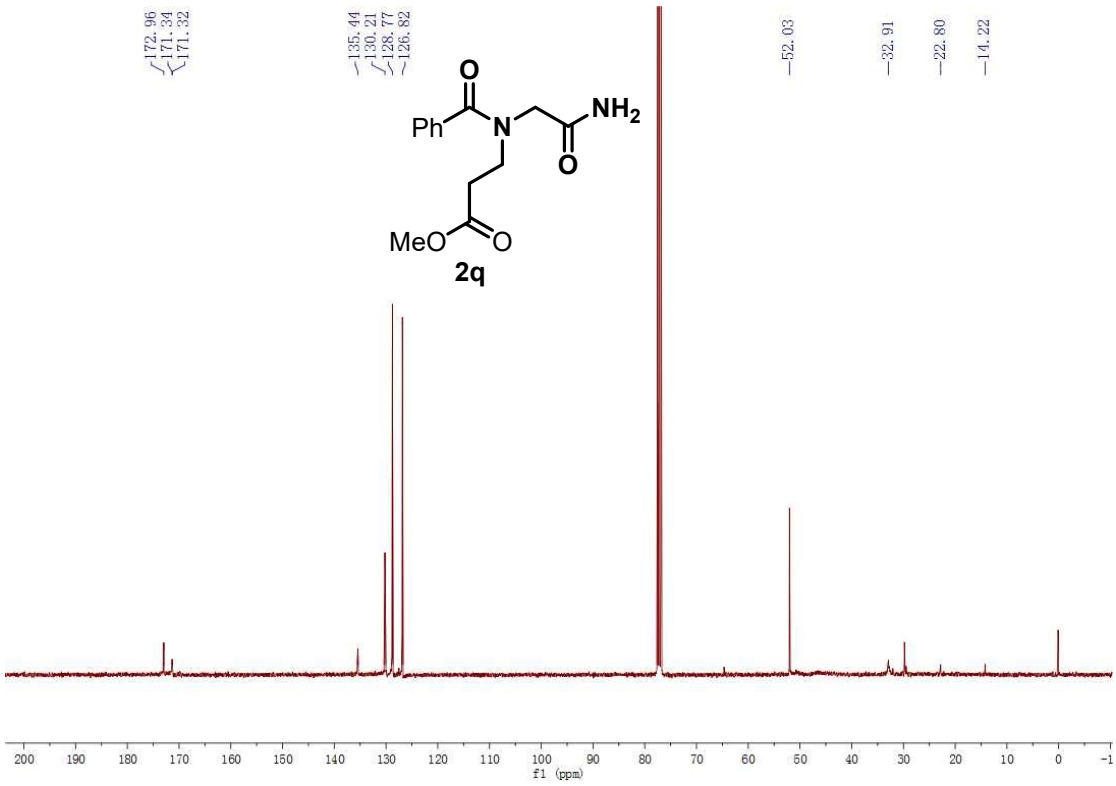

$^{13}$C NMR spectra of compound **2p** (151 MHz, $CDCl_3$)



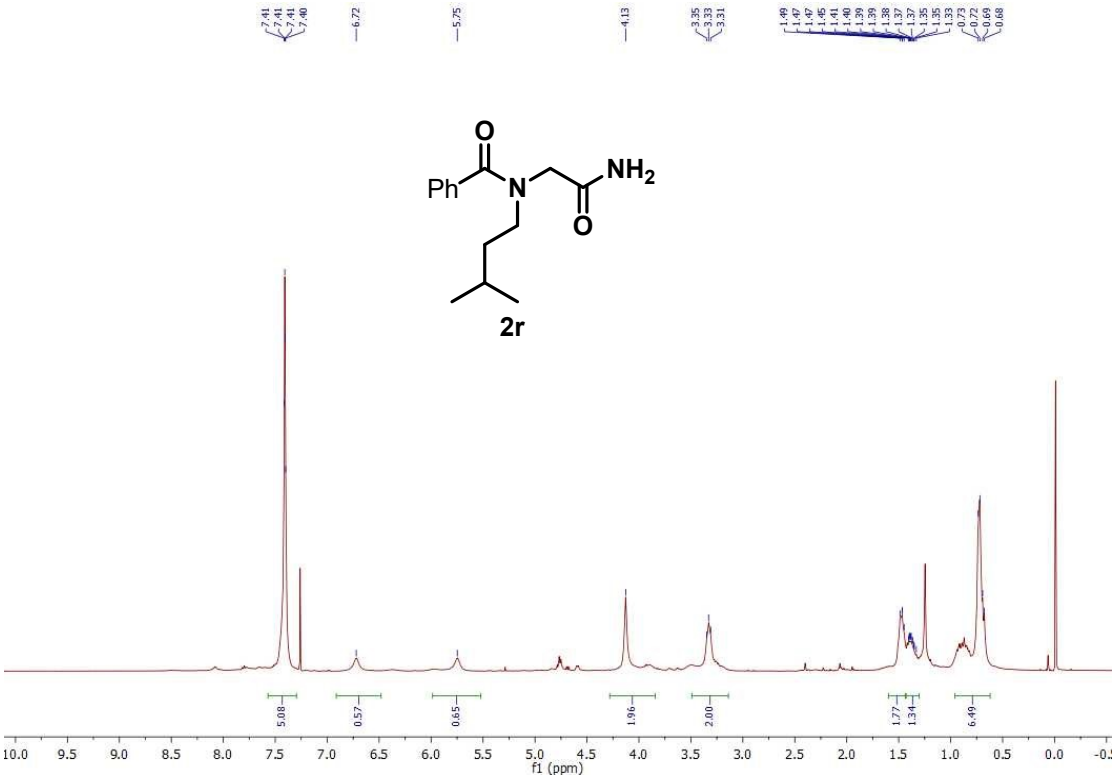
$^{1}$H spectra of compound **2q** (400 MHz, $CDCl_3$)



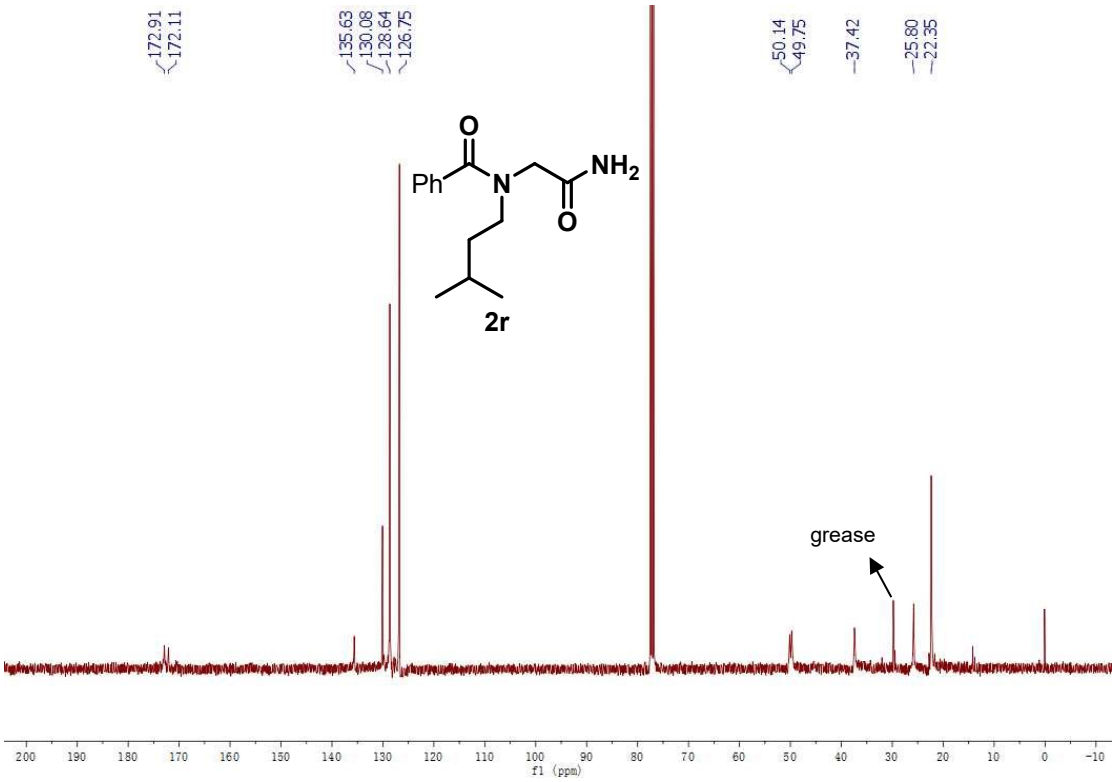

$^{13}$C NMR spectra of compound **2q** (101 MHz, $CDCl_3$)



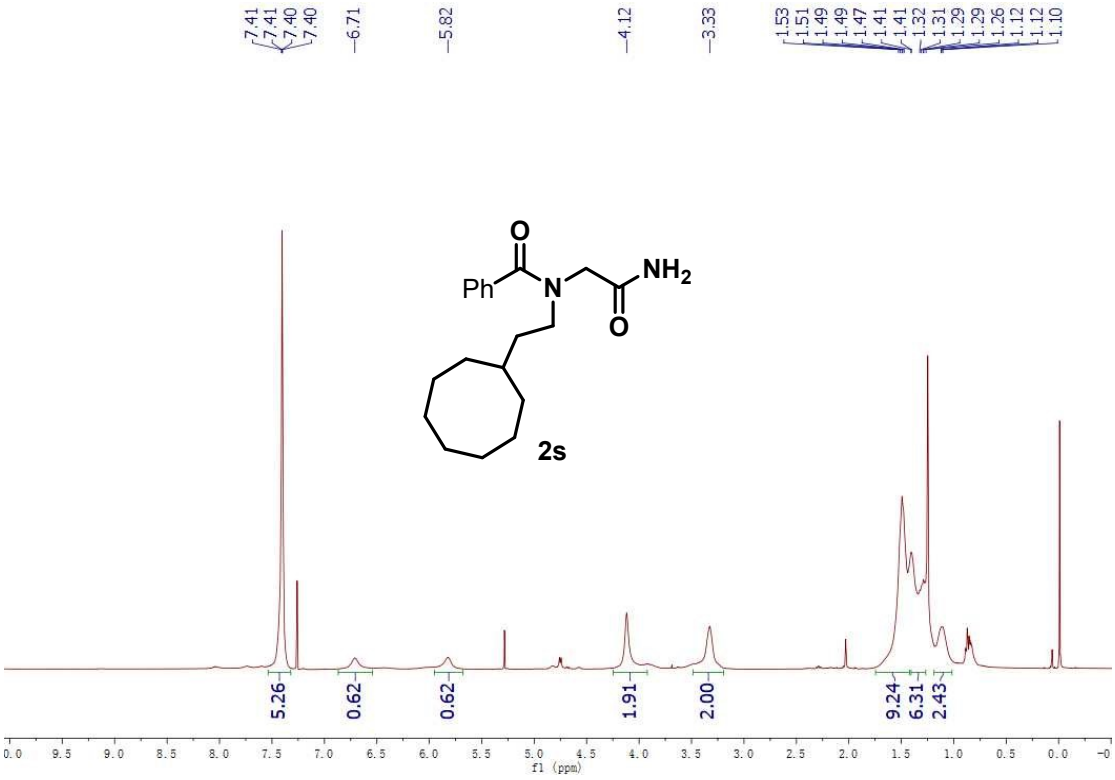
$^{1}$H spectra of compound **2r** (400 MHz, $CDCl_3$)



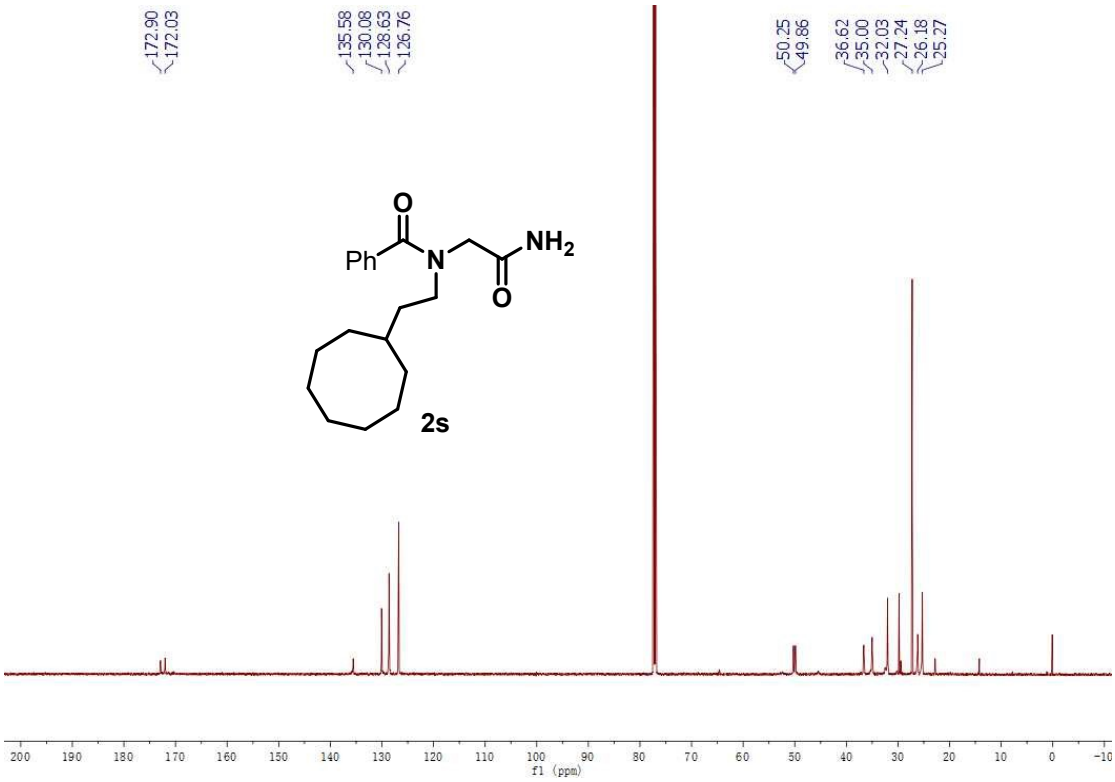

$^{13}$C NMR spectra of compound **2r** (101 MHz, $CDCl_3$)



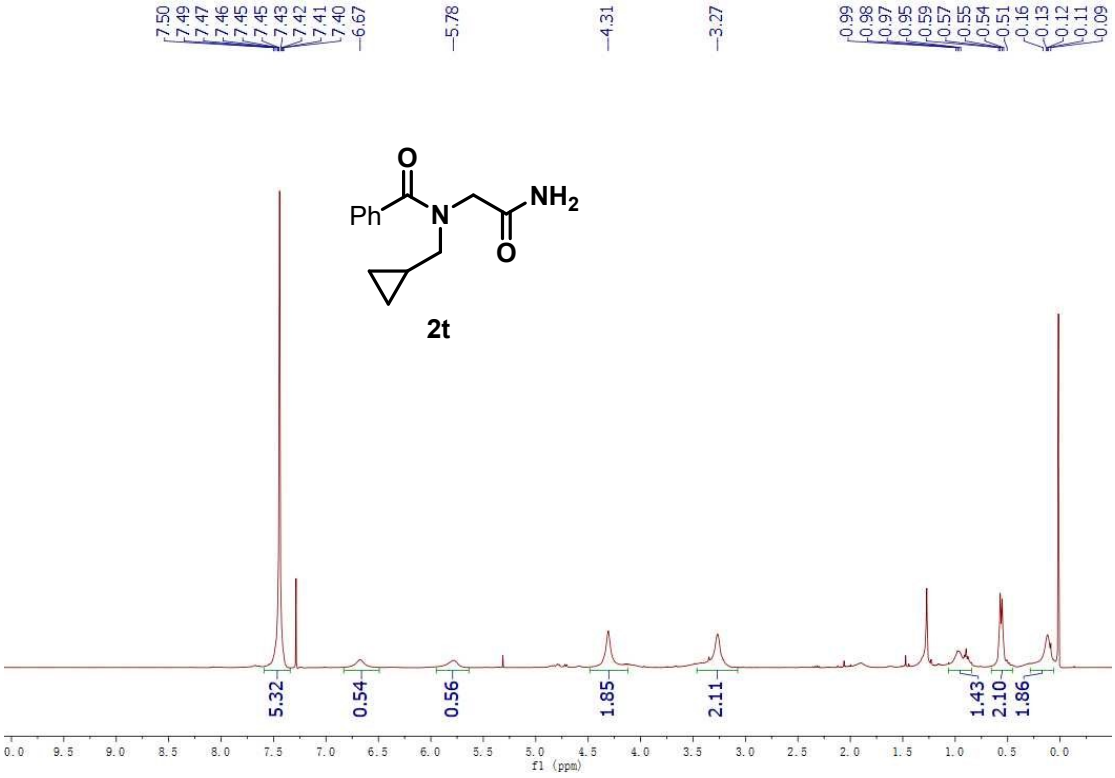
$^{1}$H spectra of compound **2s** (400 MHz, $CDCl_3$)



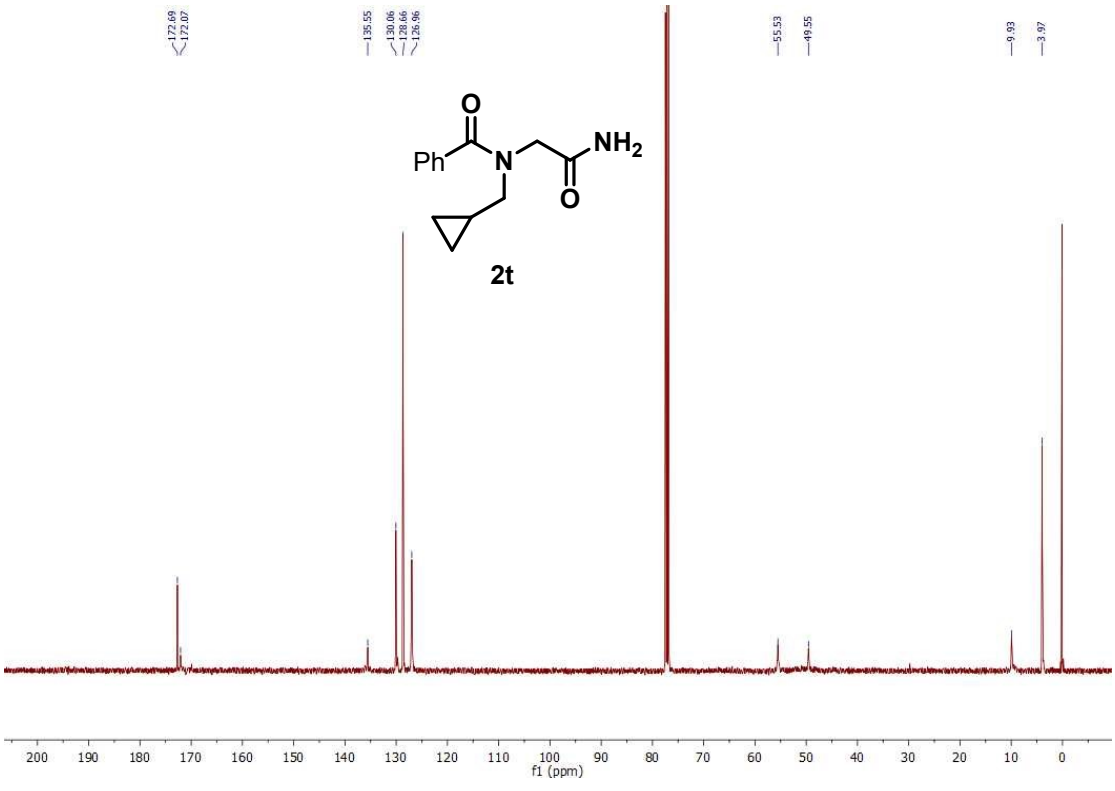

$^{13}$C NMR spectra of compound **2s** (151 MHz, $CDCl_3$)



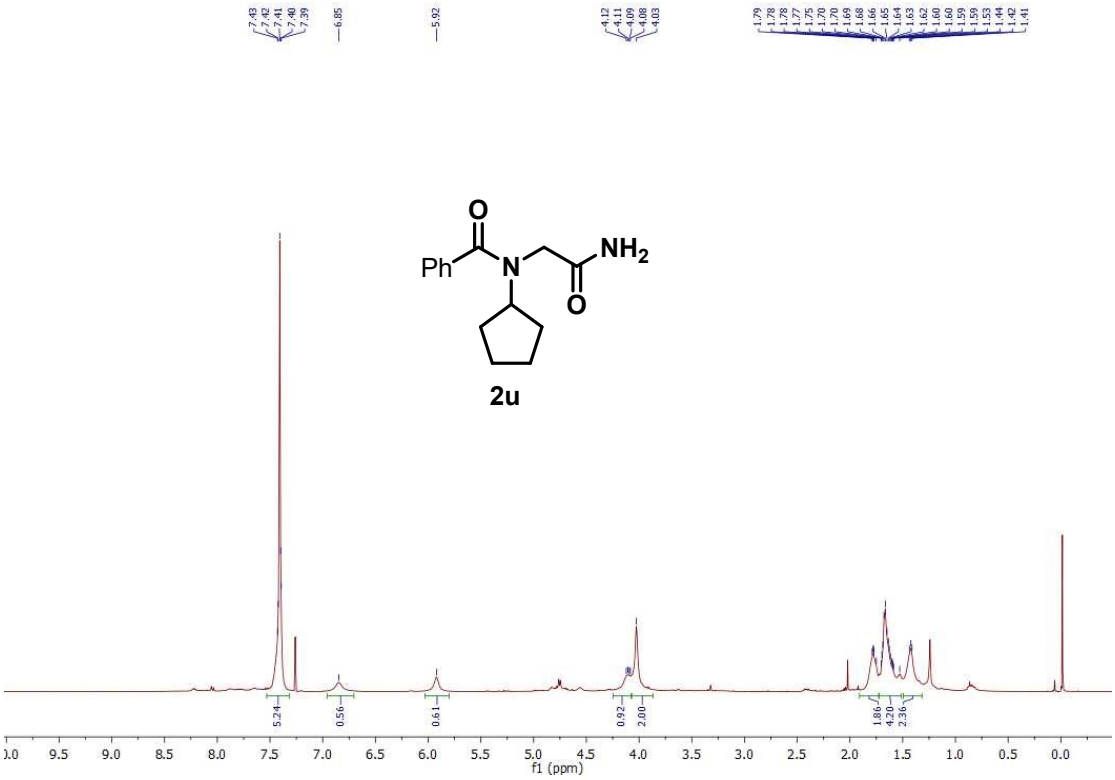
$^{1}$H spectra of compound **2t** (400 MHz, $CDCl_3$)



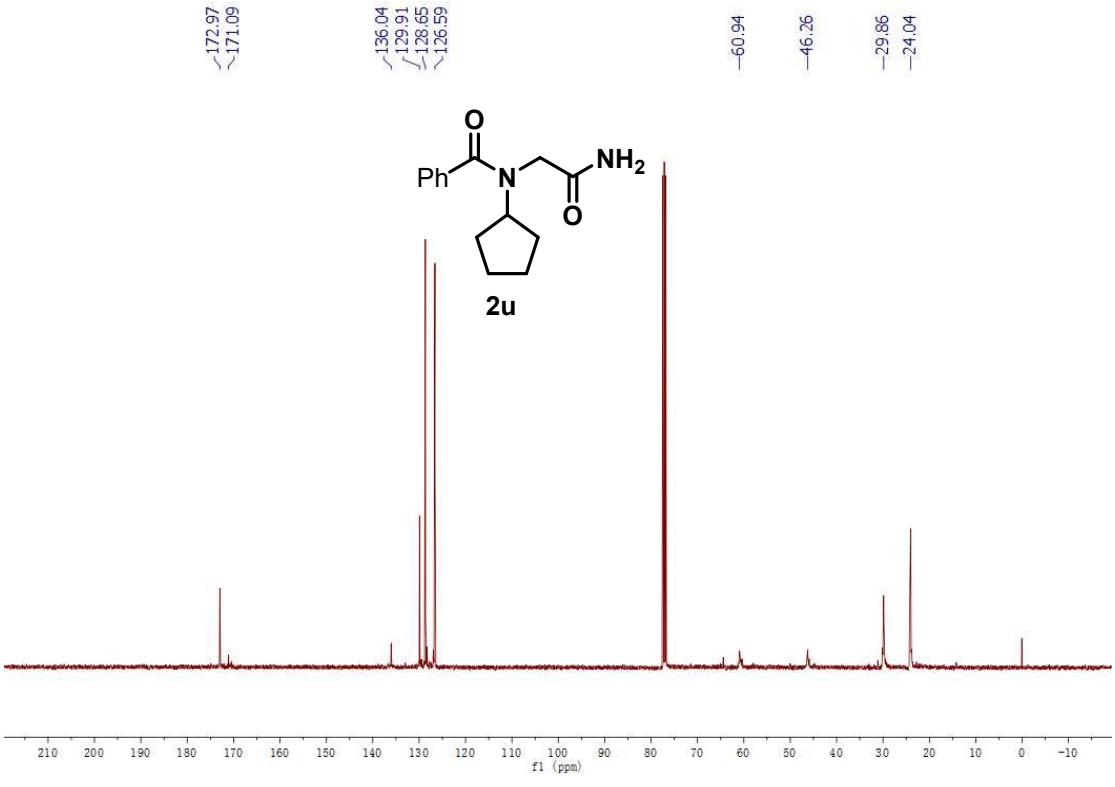

$^{13}$C NMR spectra of compound **2t** (101 MHz, $CDCl_3$)



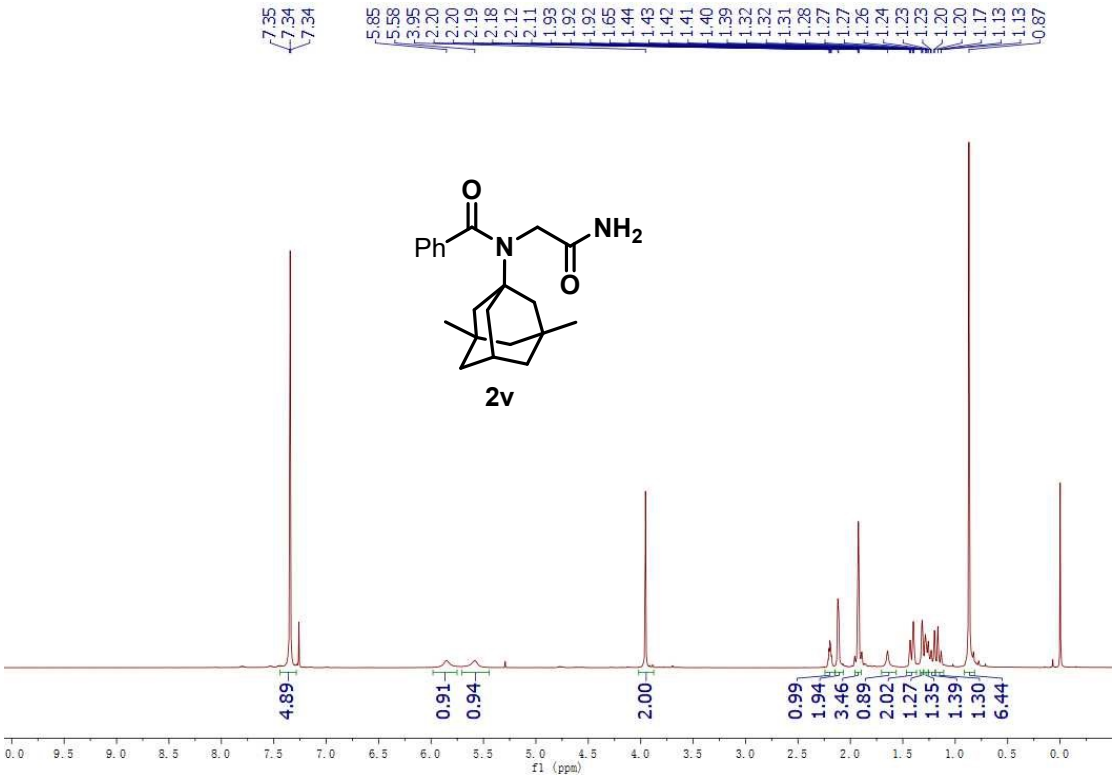
$^{1}$H spectra of compound **2u** (400 MHz, $CDCl_3$)



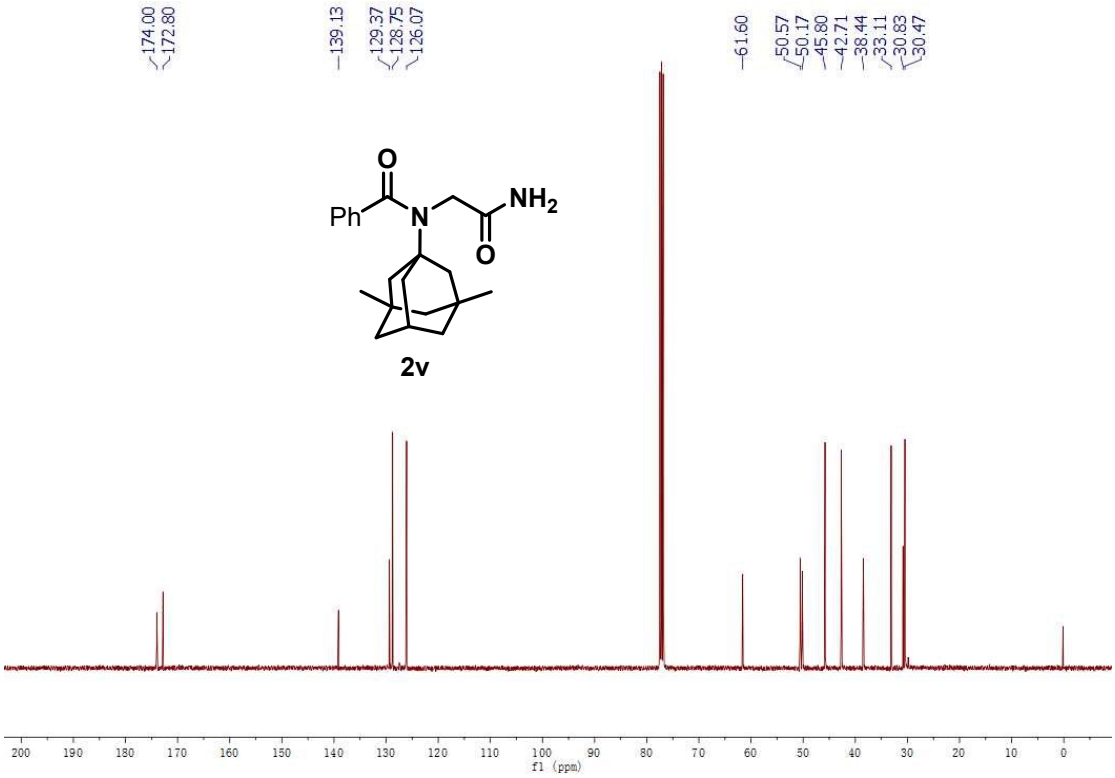

$^{13}$C NMR spectra of compound **2u** (101 MHz, $CDCl_3$)



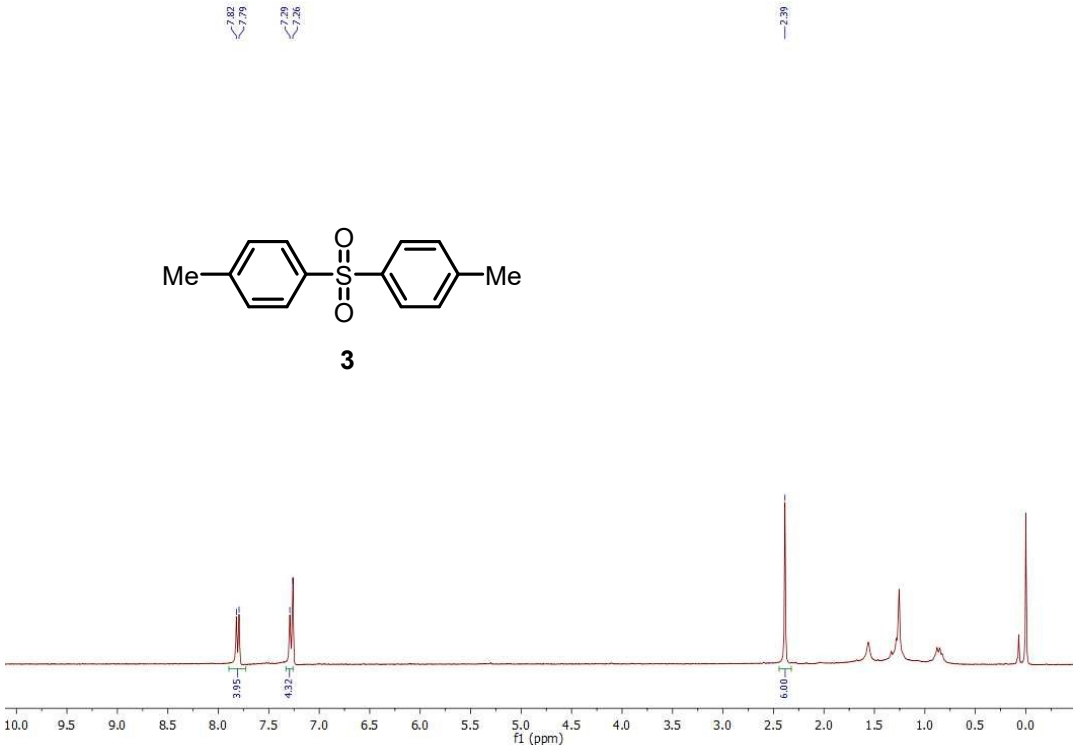
$^{1}$H spectra of compound **2v** (400 MHz, $CDCl_3$)




$^{13}$C NMR spectra of compound **2v** (101 MHz, $CDCl_3$)



$^{1}H$ spectra of compound **3** (300 MHz, $CDCl_3$)




$^{13}C$ spectra of compound **3** (101 MHz, $CDCl_3$)