Supporting Information

Catalyst-free N^1-Regioselective Aza-Michael Addition of Vinyl Ketones with 1,2,3-Triazole Derivatives

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Supporting Information

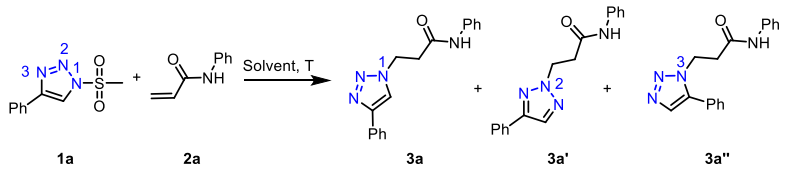
1. General experimental information

Unless otherwise noted, all chemicals were purchased form chemical companies and were used without further purification. All reactions and manipulations were carried out under an air atmosphere, in a 4 mL sealed vial equipped with a stir bar, ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded using a Brucker 400 MHz spectrometer in $CDCl_3$. Tetramethylsilane (TMS) served as an internal standard ($\delta = 0$) for ^{1}H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, qd = quartet of doublets, m = multiplet). High-resolution mass spectrometry (**HRMS**) was performed on IonSpec FT-ICR or Waters Micromass Q-TOF micro Synapt High-Definition Mass Spectrometer. Mass spectra were recorded on the HP-5989 instrument by ESI methods. The X-ray diffraction analysis was performed using a Bruker Smart-1000 X-ray diffractometer.

Supporting Information

2. Optimization of the reaction conditions.

Table S1 Condition filtering



entry	n(**1a**): n(**2a**)	solvent	T/℃	yield[b] (%)	regioselectivity[c] N^1:(N^2+N^3)
1	1:2	DCE	rt	15	16:1
2	1:2	DCE	30	35	16:1
3	**1:2**	**DCE**	**50**	**80**	**16:1**
4	1:2	DCE	70	80	16:1
5	1:2	MeOH	50	35	15:1
6	1:2	CH_3CN	50	53	>20:1
7	1:2	DMF	50	trace	-
8	1:2	THF	50	20	15:1
9	1:2	PhMe	50	41	7:1
10	1:1.5	DCE	50	70	16:1
11	1:1.2	DCE	50	56	16:1
12	1:1	DCE	50	44	16:1

[a] Unless otherwise noted, all the reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol) in solvent (2.0 mL) were reacted at the specified reaction temperature for 6h. [b] Isolated yield. [c] determined by LC/MS. DCE =1,2-Dichloroethane. DMF = *N, N*-Dimethylformamide.

Supporting Information

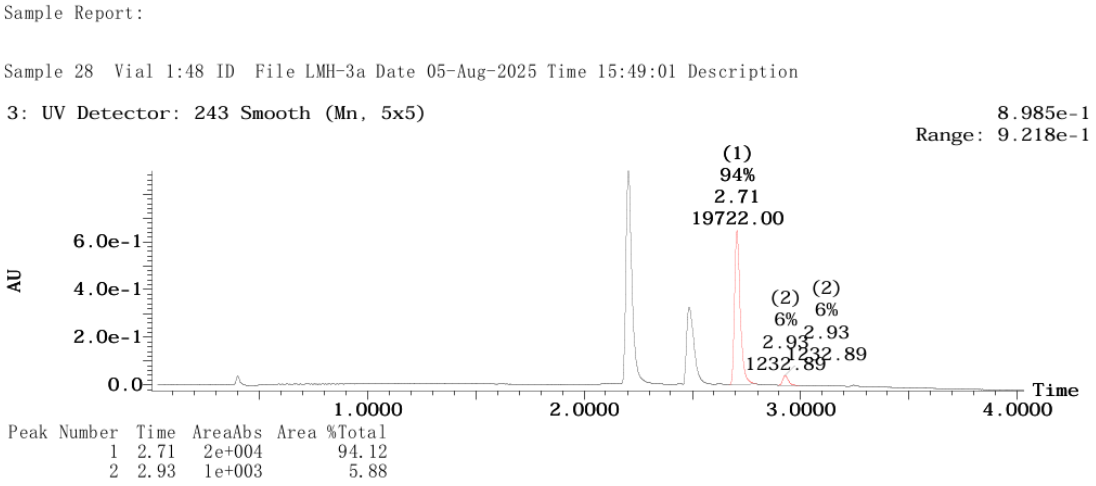


Figure S1. The LC-MS report of **entry 3** (N^1:N^2=16:1)

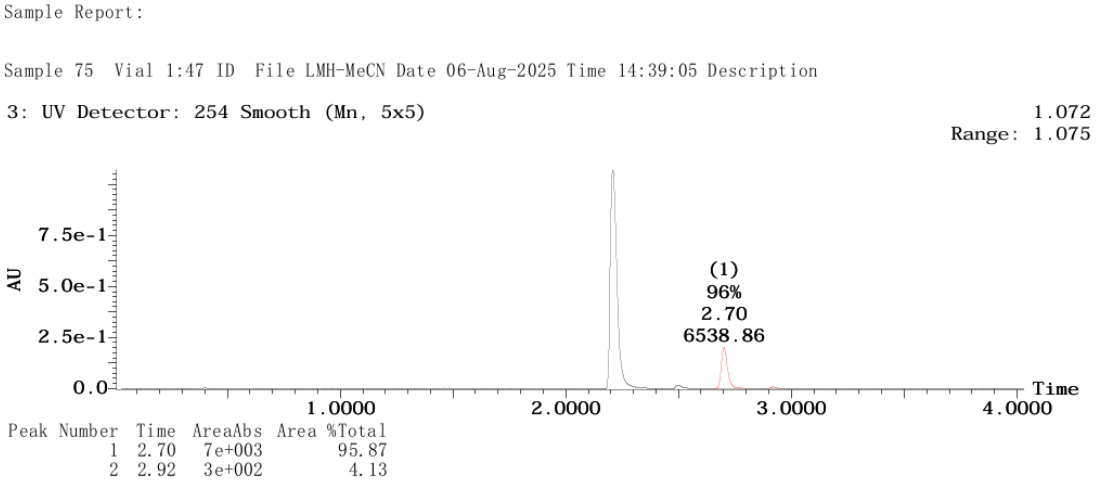


Figure S2. The LC-MS report of **entry 6** (N^1:N^2>20:1)

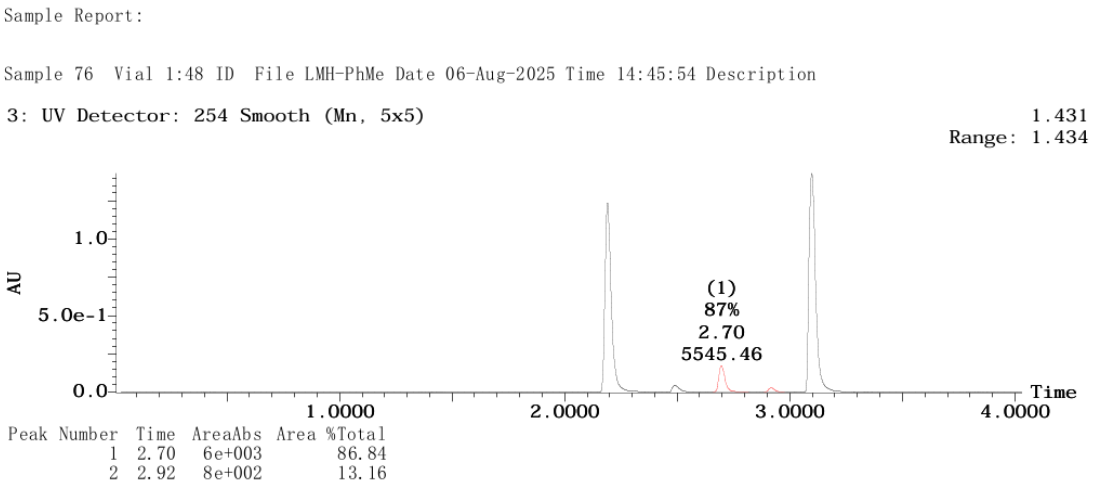


Figure S3. The LC-MS report of **entry 9** (N^1:N^2=7:1)

3. ^{1}H NMR spectra of *N*-alkylation products with different positional substitutions

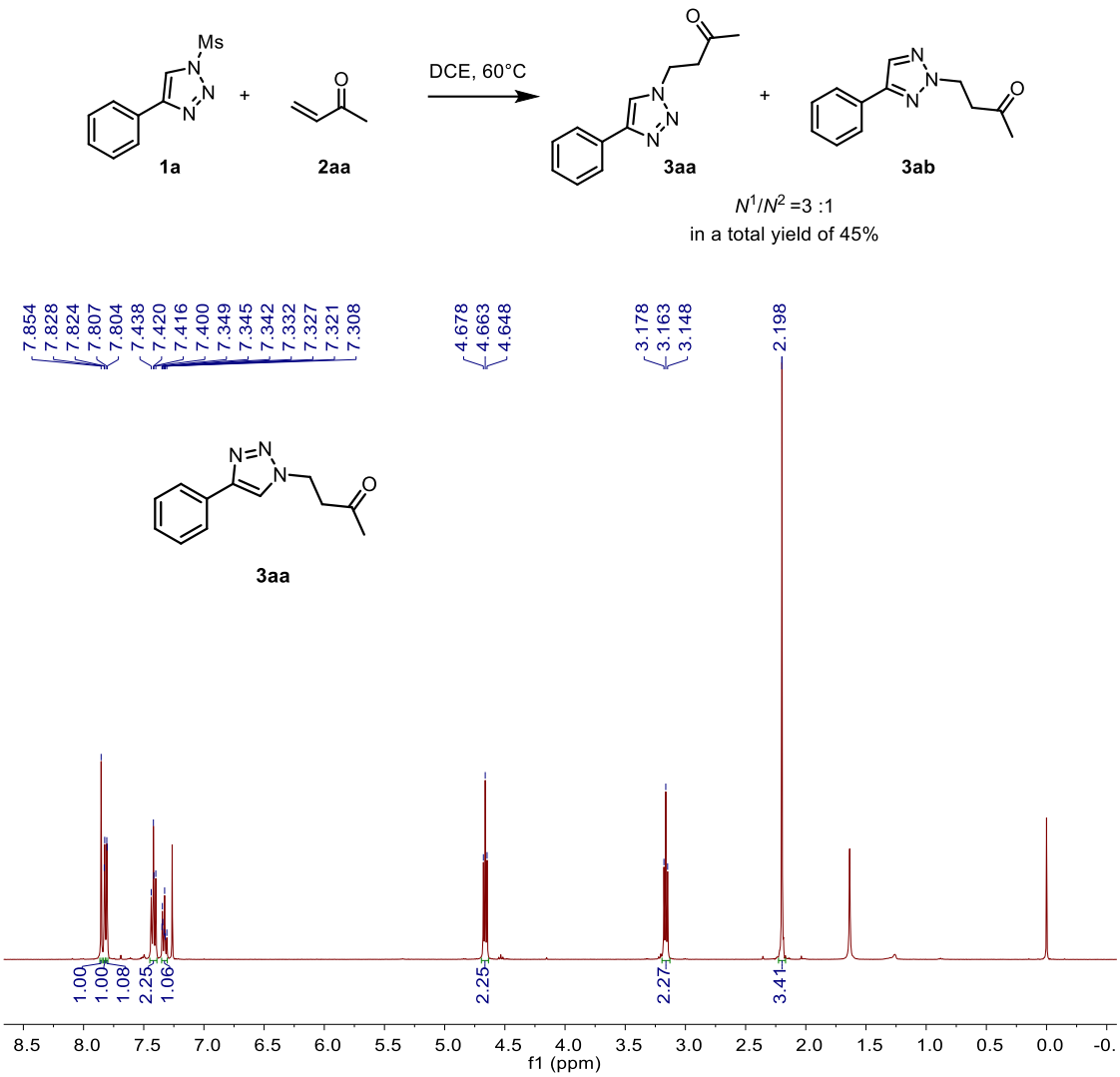


Figure S4. Reaction process and ^{1}H NMR of N^1-alkylation products

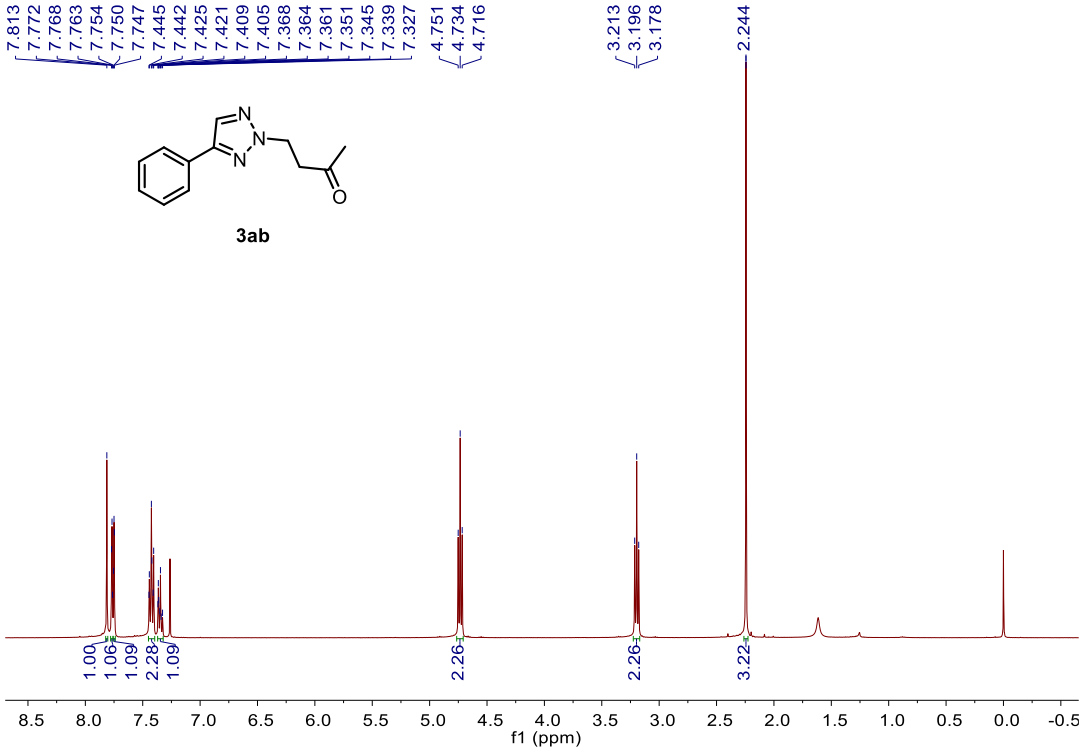


Figure S5. ^{1}H NMR of N^{2}-alkylation products

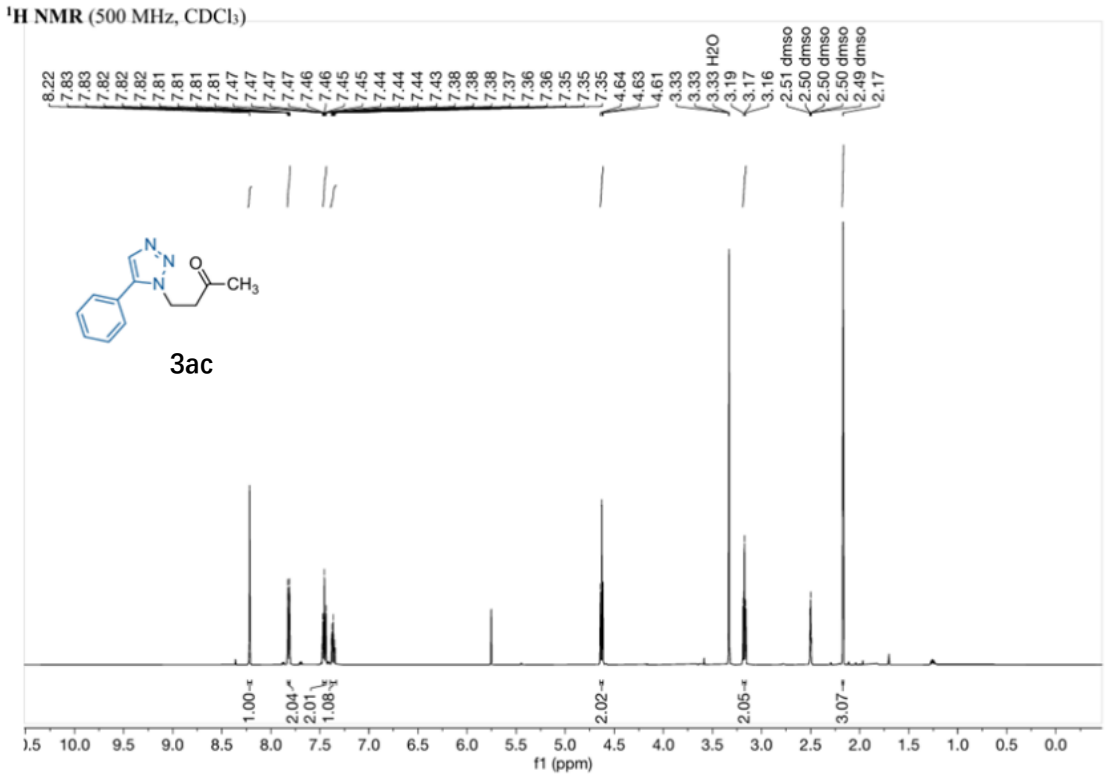


Figure S6. ^{1}H NMR of N^{3}-alkylation products **3ac** [3]

4. General Procedure for Synthesis of 1*H*-1,2,3-triazoles 1 and Olefins 2.

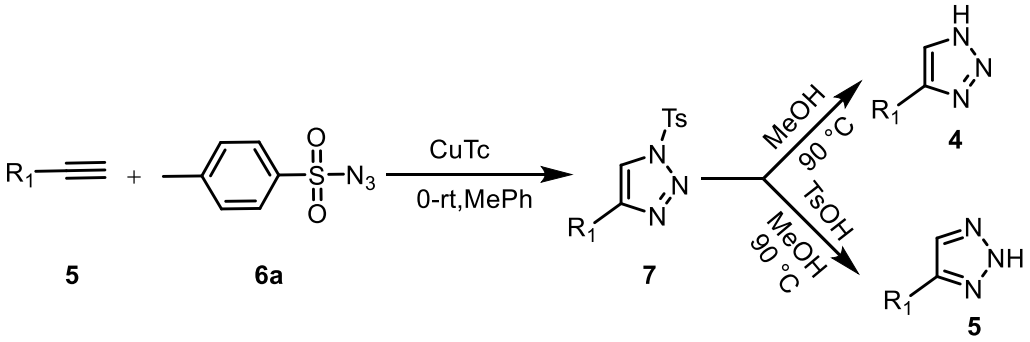


Figure S7. Preparation of common 1*H*-1,2,3-triazoles and 2*H*-1,2,3-triazoles

sulfonyl-1,2,3-triazoles **1** were prepared from the corresponding alkynes and sulfonyl azides according to previously reported synthetic procedures. [1]

Attention! Sulfonyl azides are potentially explosive materials and must be handled with caution! Due to the potential danger of methane sulfonyl azide, we strongly recommend to avoid isolating this compound in large quantities. [2]

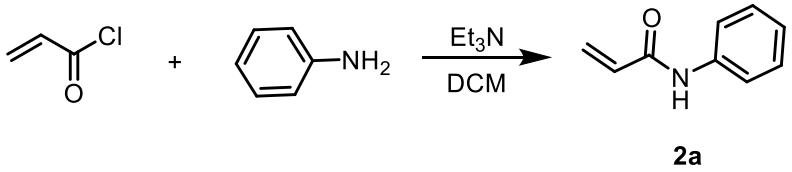


Figure S8. Synthesis of raw material *N*-phenylacrylamide

Aniline (10 mmol) and triethylamine (20 mmol) were dissolved in DCM, acryloyl chloride (20mmol) was added slowly at 0 ℃, and the reaction was completed after stirring at room temperature for 2 h. The product was purified by column chromatography using PE: EA=14:1-12:1 to obtain **2a** of product.

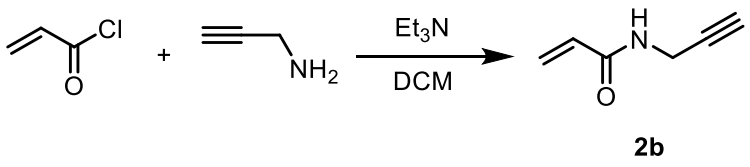


Figure S9. Synthesis of raw material *N*-(prop-2-yn-1-yl) acrylamide

Amino alkynes (1.0 mmol) and triethylamine (2.0 mmol) were dissolved in dichloromethane, acryloyl chloride (1.0 mmol) was added slowly at 0 °C, and the

reaction was completed after stirring for 1h at room temperature, and the target product **2b** was obtained by recrystallization.

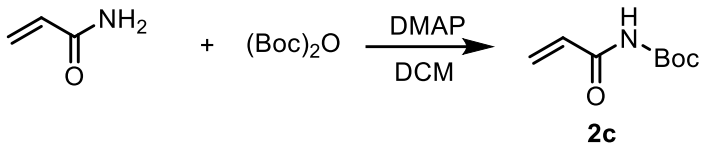


Figure S10. Synthesis of raw material tert-butyl acryloylcarbamate

Acrylamide (8.0 mmol) and DMAP (0.4 mmol) were dissolved in dichloromethane, Boc anhydride (12.8 mmol) was added at 0 °C, and the reaction was stirred at room temperature for 2h. After completion of the reaction, the target product **2c** was recrystallized.

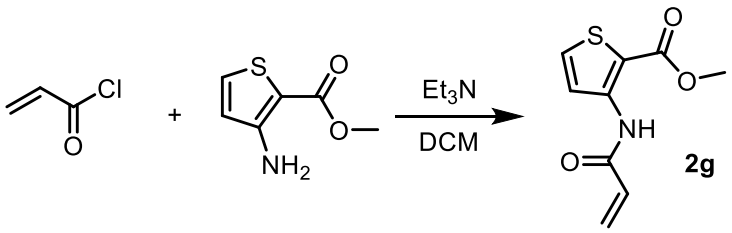


Figure S11. Synthesis of raw material methyl 3-acrylamidothiophene-2-carboxylate

Methyl 3-aminothiophene-2-carboxylate (5.0 mmol) and triethylamine (10 mmol) were dissolved in dichloromethane, acryloyl chloride (5.0 mmol) was added at 0 ℃, and the reaction was stirred at room temperature for 6h. After the reaction was completed, the target product **2g** was purified by column chromatography with PE: EA=13:1-10:1.

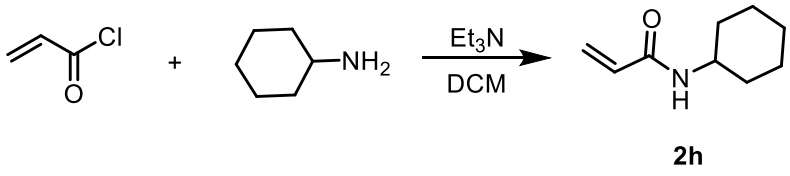


Figure S12. Synthesis of raw material *N*-cyclohexylacrylamide

Cyclohexanamine (10 mmol) and triethylamine (20 mmol) were dissolved in DCM, acryloyl chloride (20 mmol) was added slowly at 0 °C, and the reaction was completed after stirring at room temperature for 8h, and the product was purified by column

chromatography using PE: EA=10:1-7:1 to obtain the product **2h**.

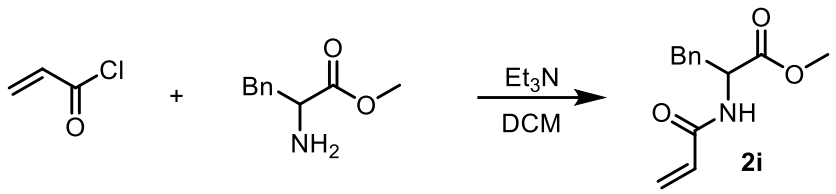


Figure S13. Synthesis of raw material methyl acryloylphenylalaninate

methyl phenylalaninate (5.0 mmol) and triethylamine (10 mmol) were dissolved in dichloromethane, acryloyl chloride (5.0 mmol) was added at 0 °C, and the reaction was stirred at room temperature for 3h. After completion of the reaction, the target product was purified by column chromatography with PE: EA=15:1-12:1 to obtain the target product **2i**.

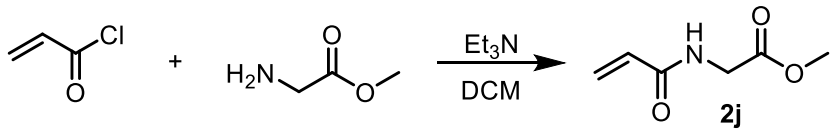


Figure S14. Synthesis of raw material methyl acryloylglycinate

Methyl glycinate (5.0 mmol) and triethylamine (10 mmol) were dissolved in dichloromethane, acryloyl chloride (5.0 mmol) was added at 0 °C, and the reaction was stirred at room temperature for 3h. After completion of the reaction, the target product **2j** was recrystallized.

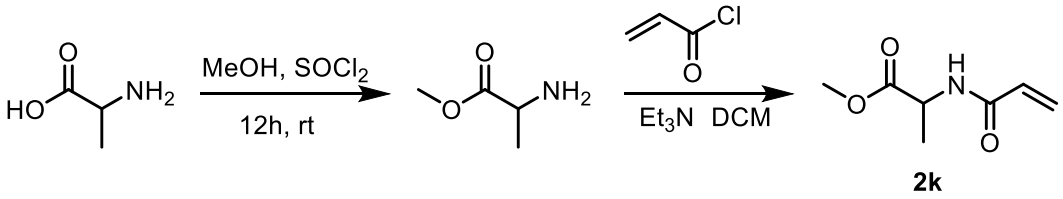


Figure S15. Synthesis of raw material methyl acryloylalaninate

Dissolve alanine (20 mmol) with dissolved in methanol (40 mL), add dichlorosulfoxide (4.0 mL) at 0 ℃, stir the reaction at room temperature overnight, after the completion of the reaction will be recrystallized and purified dissolved in dichloromethane and add triethylamine (40 mmol), add acryloyl chloride (20 mmol) at 0 ℃ stirring the reaction for 4h, after the completion of the reaction was recrystallized

to obtain the product **2k**.

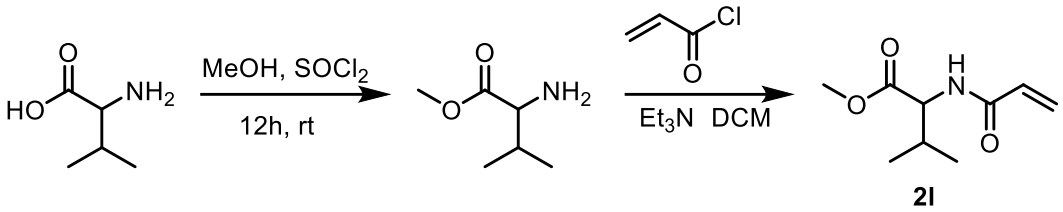


Figure S16. Synthesis of raw material methyl acryloylvalinate

The valine (20 mmol) was dissolved in methanol (40 mL), dichlorosulfoxide (4.0 mL) was added at 0 ℃, and the reaction was stirred at room temperature overnight, after the reaction was completed, it was recrystallized and purified and dissolved in dichloromethane and triethylamine (40 mmol) was added, acryloyl chloride (20 mmol) was added at 0℃ and the reaction was stirred for 6h, and after the reaction was completed, it was recrystallized to obtain the product **2l**.

5. Experimental procedures

General procedures for products **3**:

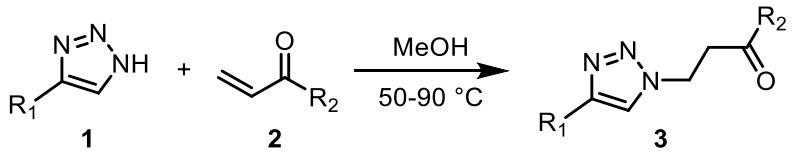


Figure S17. Reaction Main Synthesis Methods

1*H*-1,2,3-triazole **1** (0.2 mmol) and 2 ml of methanol were added to a 5.0 ml sealed thermostatic vial fitted with a stirrer. Alkenone **2** (0.24 mmol) was then added. Upon completion of the reaction, the petroleum ether/ethyl acetate (3:1-2:1) mixture was purified by column chromatography to give the product in high yield and purity **3**.

6. NEOSY two-dimensional nuclear magnetic resonance (2DNR) of 3i

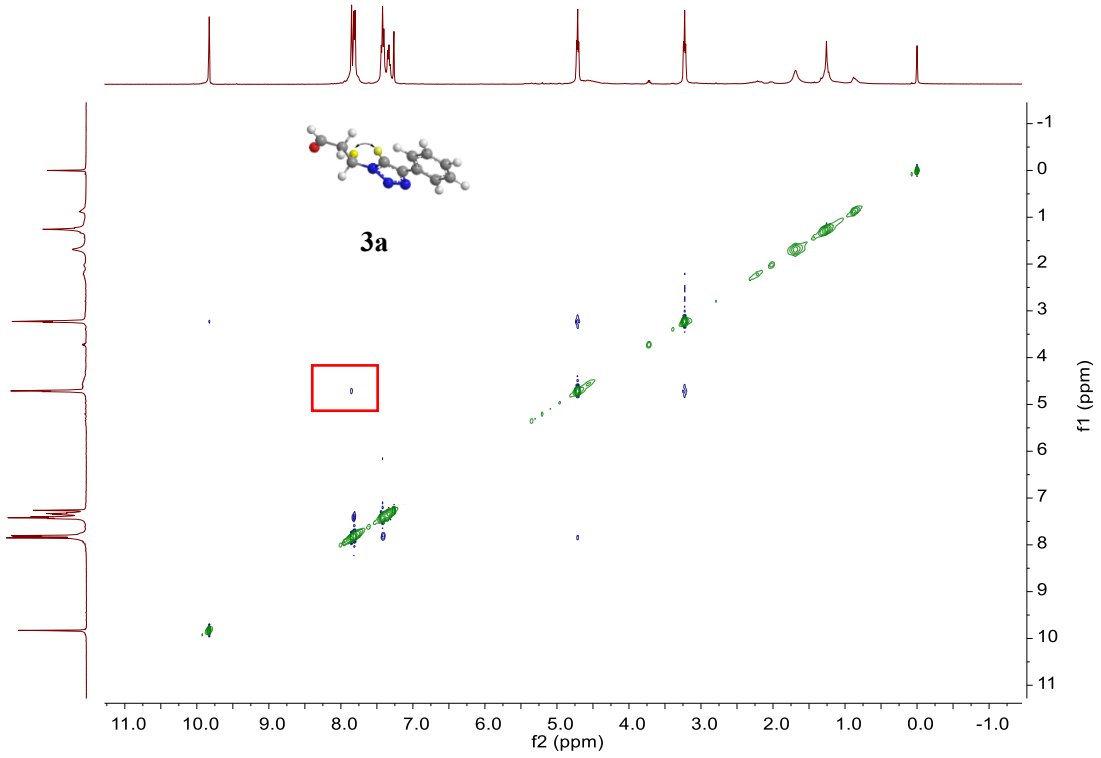
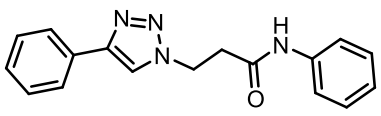


Figure S18. Synthesis of raw material

The structural assignment of compound **3i** was corroborated by 2D NMR NOESY analysis. A distinct through-space correlation was observed between the protons on the 1,2,3-triazole ring and the methylene protons at the N1 position of the triazole moiety (Figure S18). This NOESY interaction unambiguously confirms the formation of the N^1-alkylation product as the predominant regioisomer in this reaction.

7. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR data of compounds

N-phenyl-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propenamide (3a)

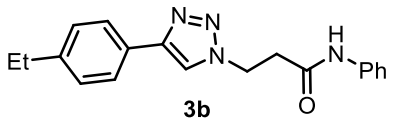


3a

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL DCE were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 7h at 50 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford

product **3a** in 80% yield as a white solid. m. p. 198–199 ℃.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.34 (s, 1H), 7.92 (s, 1H), 7.77 (d, *J* = 7.7 Hz, 2H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.35 – 7.23 (m, 3H), 7.09 (t, *J* = 7.3 Hz, 1H), 4.79 (t, *J* = 6.0 Hz, 2H), 3.09 (t, *J* = 6.1 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 167.8, 137.5, 131.0, 130.3, 129.0, 128.9, 128.3, 125.8, 124.7, 121.3, 120.2, 46.1, 37.4. **HRMS**(ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{17}N_4O$ 293.1394. Found: 293.1391.

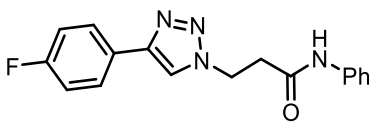
3-(4-(4-ethylphenyl)-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3b)



3b

In a 5 mL sealed vial equipped with a stir bar, 4-(4-ethylphenyl)-1*H*-1,2,3-triazole **1b** (0.2 mmol, 34.6 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 6h at 50 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3b** in 86% yield as a white solid. m. p. 127–128 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 8.49 (s, 1H), 7.74 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 7.9 Hz, 2H), 7.33 – 7.24 (m, 4H), 7.04 (t, *J* = 7.4 Hz, 1H), 4.70 (t, *J* = 6.6 Hz, 2H), 3.05 (t, *J* = 6.7 Hz, 2H), 2.61 (q, *J* = 7.6 Hz, 2H), 1.18 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.6, 146.7, 143.9, 139.3, 129.2, 128.7, 128.6, 125.6, 123.8, 121.8, 119.6, 46.2, 36.8, 28.4, 16.0.

3-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3c)

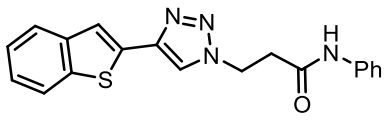


3c

In a 5 mL sealed vial equipped with a stir bar, 4-(4-fluorophenyl)-1*H*-1,2,3-triazole **1c** (0.2 mmol, 32.6 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 6h at 55 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3c** in 73% yield as a white solid. m. p. 134–135 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.09 (s, 1H), 8.55 (s, 1H), 7.93 – 7.83 (m, 2H), 7.56 (d, *J* = 7.3 Hz, 1H), 7.31 – 7.26 (m, 4H), 7.04 (t, *J* = 7.4 Hz, 1H), 4.70 (t, *J* =

6.7 Hz, 2H), 3.04 (t, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.5, 162.2 (d, *J* = 242.9 Hz), 145.7, 139.4, 129.2, 127.8 (d, *J* = 3.1 Hz), 127.6 (d, *J* = 8.3 Hz), 123.8, 122.2, 119.6, 116.3 (d, *J* = 21.7 Hz), 46.2, 36.7. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -114.18 (m).

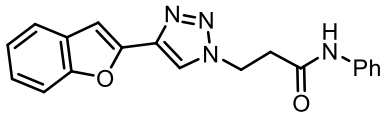
3-(4-(benzo[*b*]thiophen-2-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3d)



3d

In a 5 mL sealed vial equipped with a stir bar, 4-(benzo[*b*]thiophen-2-yl)-1*H*-1,2,3-triazole **1d** (0.2 mmol, 40 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 7h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (3:1) as eluent to afford product **3a** in 70% yield as a white solid. m. p. 167–168 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.63 (s, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.24 (m, 5H), 7.04 (t, *J* = 7.2 Hz, 1H), 4.78 (t, *J* = 6.6 Hz, 2H), 3.09 (t, *J* = 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.5, 154.4, 148.7, 139.3, 138.8, 129.2, 128.8, 125.1, 123.83, 123.81, 123.3, 121.7, 119.6, 111.6, 102.7, 46.4, 36.6.

3-(4-(benzofuran-2-yl)-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3e)

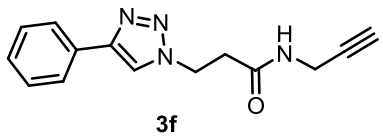


3e

In a 5 mL sealed vial equipped with a stir bar, 4-(benzofuran-2-yl)-1*H*-1,2,3-triazole **1e** (0.2 mmol, 37 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (3:1) as eluent to afford product **3e** in 51% yield as a white solid. m. p. 153–154 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.61 (s, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.26 (m, 5H), 7.04 (t, *J* = 7.3 Hz, 1H), 4.76 (t, *J* = 6.6 Hz, 2H), 3.07 (t, *J* = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 168.5, 154.4, 148.6, 139.3, 138.8, 134.4,

129.2, 128.7, 125.1, 123.9, 123.3, 121.8, 119.6, 111.6, 102.8, 46.4, 36.6.

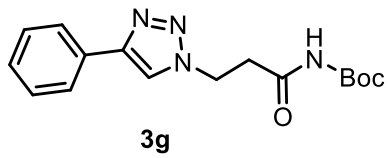
1-(ethynylamino)-4-(4-phenyl-1*H*-1,2,3-triazol-1-yl) butan-2-one (3f)



3f

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the 1-(ethynylamino) but-3-en-2-one **2b** (0.24 mmol, 26 mg) were added to the mixture. The vial was capped and stirred for within 6h at 55 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (5:1) as eluent to afford product **3f** in 75% yield as a white solid. m. p. 160–161℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.87 (s, 1H), 7.80 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 6.44 (s, 1H), 4.74 (t, J = 6.1 Hz, 2H), 4.01 (d, J = 5.2 Hz, 2H), 2.90 (t, J = 6.1 Hz, 2H), 2.14 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 169.2, 147.7, 130.4, 128.9, 128.2, 125.7, 121.1, 79.1, 71.7, 46.1, 36.3, 29.3. **HRMS**(ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{14}N_4NaO$ 277.1060. Found: 277.1081.

tert-butyl (3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoyl) carbamate (3g)

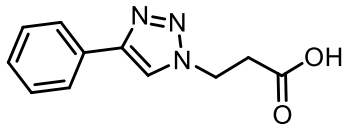


3g

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the tert-butyl acryloylcarbamate **2c** (0.24 mmol, 41 mg) and DBU (0.4 mmol, 68 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (3:1) as eluent to afford product **3g** in 73% yield as a white solid. m. p. 119–120 ℃.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (s, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.49 (s, 1H), 7.41 (t, J = 7.5 Hz, 3H), 7.32 (t, J = 7.4 Hz, 1H), 4.76 (t, J = 6.1 Hz, 2H), 3.45 (t, J = 6.0 Hz, 2H), 1.47 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.6, 150.2, 147.6, 130.6, 128.8, 128.1, 125.7, 121.0, 83.3, 44.8, 36.8, 28.0. **HRMS**(ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{23}N_4O_3$

331.1699. Found: 331.1689.

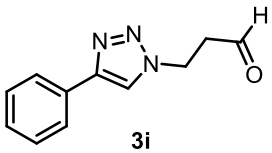
3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoic acid (3h)



3h

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the acrylic acid **2d** (0.24 mmol, 17 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (2:1) as eluent to afford product **3h** in 72% yield as a white solid. m. p. 175–176 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.55 (s, 1H), 8.57 (s, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 4.61 (t, J = 6.7 Hz, 2H), 2.97 (t, J = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 172.3, 146.6, 131.2, 129.4, 128.3, 125.6, 122.1, 46.0, 34.4. **HRMS**(ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{11}N_3NaO_2$ 240.0743. Found: 240.0747.

3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanal (3i)

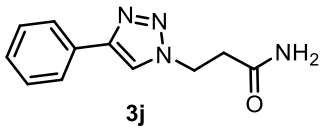


3i

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the acrylaldehyde **2e** (0.24 mmol, 14 mg) were added to the mixture. The vial was capped and stirred for within 6h at 50 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3i** in total 78% yield (N^1: N^2 = 2:1) as a white solid. m. p. 112–113 ℃.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.83 (s, 1H), 7.86 (s, 1H), 7.81 (d, J = 7.7 Hz, 2H), 7.42 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 4.72 (t, J = 6.1 Hz, 2H), 3.23 (t, J = 6.1 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 198.4, 147.8, 130.4, 128.9, 128.2, 125.7, 120.8, 43.6, 43.1. **HRMS**(ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{12}N_3O_2$ 230.0921,

Found: 230.0929.

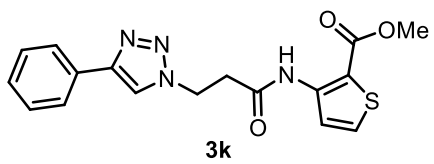
3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propenamide (3j)



3j

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 44 mg) and 2 mL methanol were added. Then the acrylamide **2f** (0.24 mmol, 17 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (2:1) as eluent to afford product **3j** in 69% yield as a white solid. m. p. 168–169 ℃. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.83 (d, J = 7.8 Hz, 2H), 7.45 (t, J = 7.7 Hz, 3H), 7.33 (t, J = 7.3 Hz, 1H), 6.98 (s, 1H), 4.59 (t, J = 6.8 Hz, 2H), 2.76 (t, J = 6.8 Hz, 2H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 171.5, 146.5, 131.3, 129.4, 128.3, 125.6, 122.1, 46.4, 35.6. **HRMS**(ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{12}N_4NaO$ 239.0903. Found: 239.0924.

methyl 3-(3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanamido) thiophene-2-carboxylate (3k)

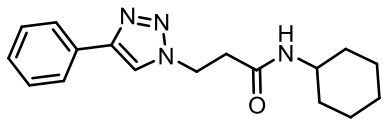


3k

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the methyl 3-acrylamidothiophene-2-carboxylate **2g** (0.24 mmol, 50 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (2:1) as eluent to afford product **3k** in 45% yield as a white solid. m. p. 118–119 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 10.24 (s, 1H), 8.07 (d, J = 5.4 Hz, 1H), 7.91 (s, 1H), 7.81 (d, J = 7.5 Hz, 2H), 7.47 (d, J = 5.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 4.83 (t, J = 6.1 Hz, 2H), 3.87 (s, 3H), 3.15 (t, J = 6.1 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 166.9, 164.7, 147.7, 143.9, 131.8, 130.6, 128.8, 128.1, 125.8, 122.2,

120.9, 110.8, 52.1, 45.5, 37.2. **HRMS**(ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}N_4O_3S$ 371.1170, Found: 371.1153.

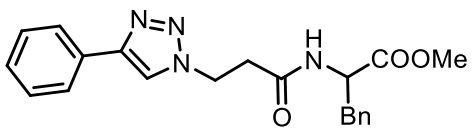
1-cyclohexyl-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propan-1-one (3l)



3l

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the 1-cyclohexylprop-2-en-1-one **2h** (0.24 mmol,33 mg) were added to the mixture. The vial was capped and stirred for within 10h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (15:1) as eluent to afford product **3l** in 78% yield as a white solid. m. p. 166–167 ℃.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.90 (s, 1H), 7.78 (d, J = 6.7 Hz, 2H), 7.44 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 6.37 (s, 1H), 4.70 (s, 2H), 3.71 (d, J = 6.6 Hz, 1H), 2.81 (s, 2H), 1.80 (d, J = 10.0 Hz, 2H), 1.59 (dd, J = 28.7, 9.9 Hz, 3H), 1.28 (d, J = 12.4 Hz, 2H), 1.14 – 0.95 (m, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 168.4, 147.5, 130.5, 128.9, 128.2, 125.7, 121.2, 48.6, 46.5, 36.8, 32.9, 25.4, 24.8. **HRMS**(ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}N_4$ NaO 321.1686. Found: 321.1699.

methyl (3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoyl) phenylalaninate (3m)

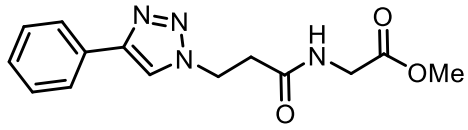


3m

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the methyl acryloylphenylalaninate **2i** (0.24 mmol, 56 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3m** in 71% yield as a white solid. m. p. 106–107 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.85 (s, 1H), 7.81 (d, J = 7.7 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 7.23 – 7.11 (m, 3H), 6.98 (d, J = 7.2 Hz, 2H), 6.37 (s, 1H), 4.83 (q, J = 6.4 Hz, 1H), 4.67 (q, J = 5.8 Hz, 2H), 3.67 (s,

3H), 3.12 – 2.96 (m, 2H), 2.84 (t, *J* = 6.1 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ* 171.7, 169.1, 147.6, 135.6, 130.6, 129.1, 128.8, 128.6, 128.1, 127.2, 125.7, 121.0, 53.4, 52.4, 45.8, 37.7, 36.2. **HRMS**(ESI) m/z: [M+Na] $^{+}$ Calcd for $C_{21}H_{22}N_4NaO_3$ 401.1584. Found: 401.1577.

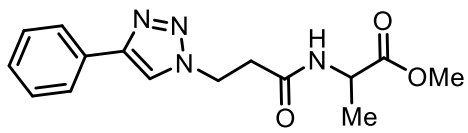
methyl (3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoyl) glycinate (3n)



3n

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the methyl acryloylglycinate **2j** (0.24 mmol, 34 mg) were added to the mixture. The vial was capped and stirred for within 8h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3n** in 67% yield as a white solid. m. p. 137–138 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) *δ* 7.92 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.1 Hz, 1H), 6.97 (s, 1H), 4.72 (t, *J* = 5.9 Hz, 2H), 3.99 (d, *J* = 5.3 Hz, 2H), 3.69 (s, 3H), 2.93 (t, *J* = 5.9 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ* 170.0, 167.0, 147.6, 130.5, 128.8, 128.2, 125.7, 121.2, 52.4, 46.1, 41.3, 36.1. **HRMS**(ESI) m/z: [M+Na] $^{+}$ Calcd for $C_{14}H_{17}N_4O_3$ 289.1292. Found: 289.1287.

methyl (3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoyl) alaninate (3o)

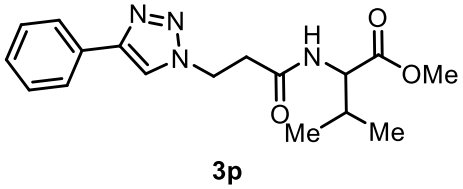


3o

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the methyl acryloylalaninate **2k** (0.24 mmol, 37 mg) were added to the mixture. The vial was capped and stirred for within 6h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (5:1) as eluent to afford product **3o** in 75% yield as a white solid. m. p. 142–143 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) *δ* 7.91 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 7.4 Hz, 1H), 6.81 (s, 1H),

4.72 (t, *J* = 6.2 Hz, 2H), 4.62 – 4.35 (m, 1H), 3.68 (s, 3H), 2.89 (t, *J* = 6.2 Hz, 2H), 1.34 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ* 173.1, 169.2, 147.6, 130.5, 128.8, 128.1, 125.7, 121.1, 52.5, 48.3, 46.1, 36.3, 17.9. **HRMS**(ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{19}N_4O_3$ 303.1449. Found: 303.1441.

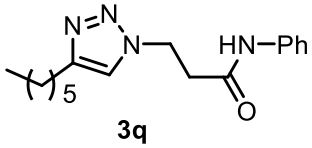
methyl (3-(4-phenyl-1*H*-1,2,3-triazol-1-yl) propanoyl) valinate (3p)



3p

In a 5 mL sealed vial equipped with a stir bar, 4-phenyl-1*H*-1,2,3-triazole **1a** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the methyl acryloylvalinate **2l** (0.24 mmol, 45 mg) were added to the mixture. The vial was capped and stirred for within 120 min at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3p** in 73% yield as a white solid. m. p. 126–127 ℃.**^{1}H NMR** (400 MHz, Chloroform-*d*) *δ* 7.87 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 6.25 (s, 1H), 4.80 – 4.67 (m, 2H), 4.51 (dd, *J* = 8.6, 5.1 Hz, 1H), 3.69 (s, 3H), 3.05 – 2.79 (m, 2H), 2.15 – 2.00 (m, 1H), 0.82 (t, *J* = 6.1 Hz, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ* 172.1, 169.4, 130.5, 128.8, 128.1, 125.7, 121.0, 57.4, 52.3, 46.1, 36.6, 31.1, 18.8, 17.7. **HRMS**(ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}N_4NaO_3$ 353.1584. Found: 353.1597.

3-(4-hexyl-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3q)

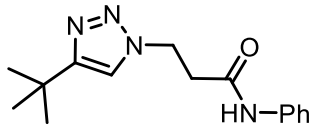


3q

In a 5 mL sealed vial equipped with a stir bar, 4-hexyl-1*H*-1,2,3-triazole **1f** (0.2 mmol, 30 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 8h at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (3:1) as eluent to afford product **3q** in 69% yield as a white solid. m. p. 143–144 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) *δ* 7.88 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.38 (s, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 4.77 (t, *J* = 6.6 Hz, 2H), 3.03 (d, *J* = 6.5 Hz, 2H), 2.66 (t, *J* = 7.8 Hz, 2H), 1.64 (d,

J = 7.2 Hz, 2H), 1.36 – 1.28 (m, 6H), 0.90 – 0.85 (m, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 168.0, 149.2, 137.7, 132.8, 129.0, 124.5, 119.8, 50.4, 37.2, 31.5, 29.3, 28.9, 25.5, 22.6, 14.1. **HRMS**(ESI) m/z: [M+Na] $^+$ Calcd for $C_{17}H_{24}N_4NaO$ 323.1842, Found: 323.1865.

3-(4-(tert-butyl)-1*H*-1,2,3-triazol-1-yl)-*N*-phenylpropanamide (3r)



3r

In a 5 mL sealed vial equipped with a stir bar, 4-(tert-butyl)-1*H*-1,2,3-triazole **1g** (0.2 mmol, 25 mg) and 2 mL methanol were added. Then the *N*-phenylacrylamide **2a** (0.4 mmol, 59 mg) were added to the mixture. The vial was capped and stirred for within 120 min at 60 ℃. After the completion of the reaction, the mixture was purified by column chromatography using Petroleum ether/ethyl acetate mixture (4:1) as eluent to afford product **3r** in 78% yield as a white solid. m. p. 158–159 ℃. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.39 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.38 (s, 1H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 4.69 (t, *J* = 6.3 Hz, 2H), 3.00 (t, *J* = 6.3 Hz, 2H), 1.30 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 168.1, 157.6, 137.8, 129.5, 128.9, 124.5, 120.3, 120.2, 46.0, 37.5, 30.8, 30.4. **HRMS**(ESI) m/z: [M+Na] $^+$ Calcd for $C_{17}H_{24}N_4NaO$ 295.1529, Found: 295.1538.

8. ^{1}H, ^{19}F and ^{13}C NMR Spectra

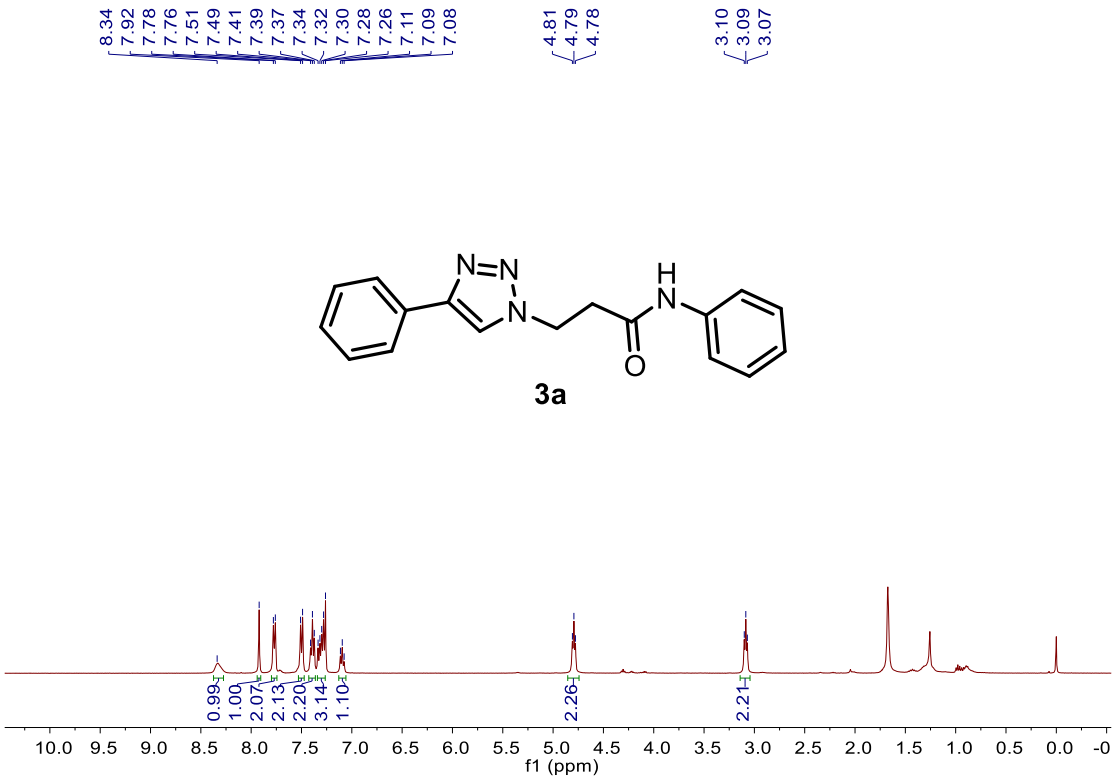


Figure S19. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum for **3a**

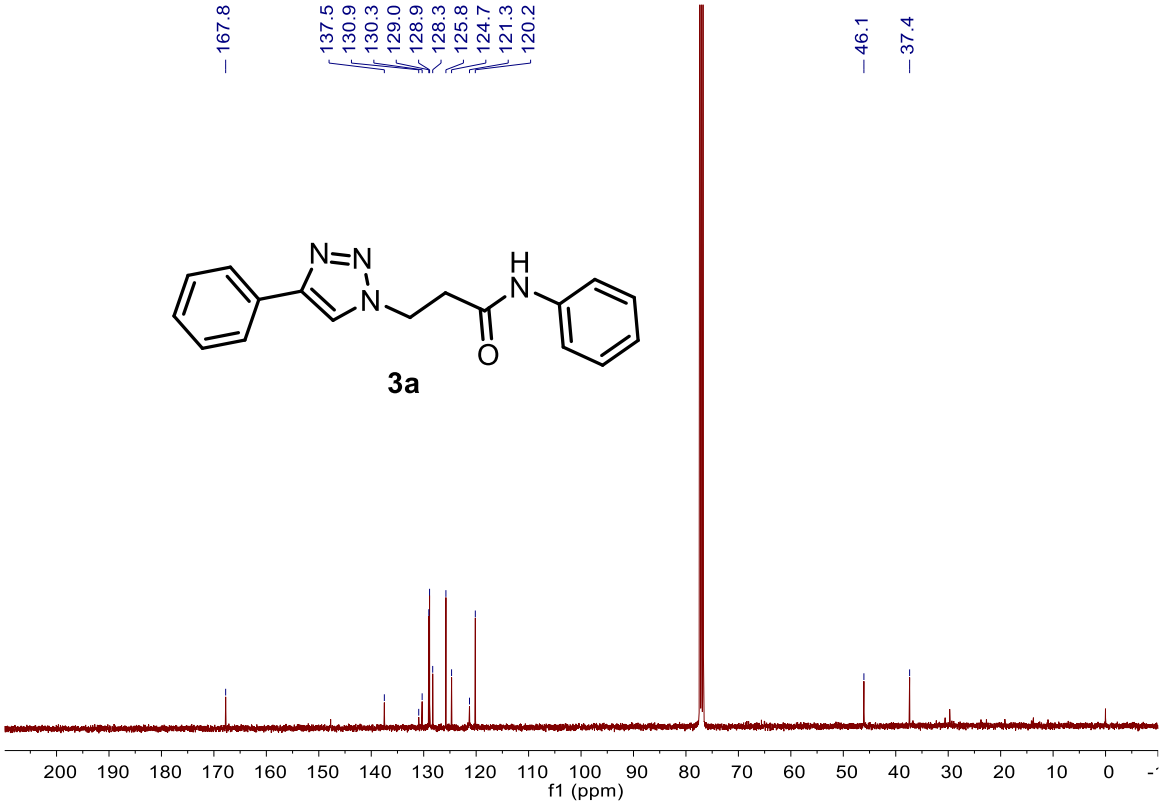


Figure S20.^{13}C NMR (100 MHz, Chloroform-*d*) spectrum for **3a**

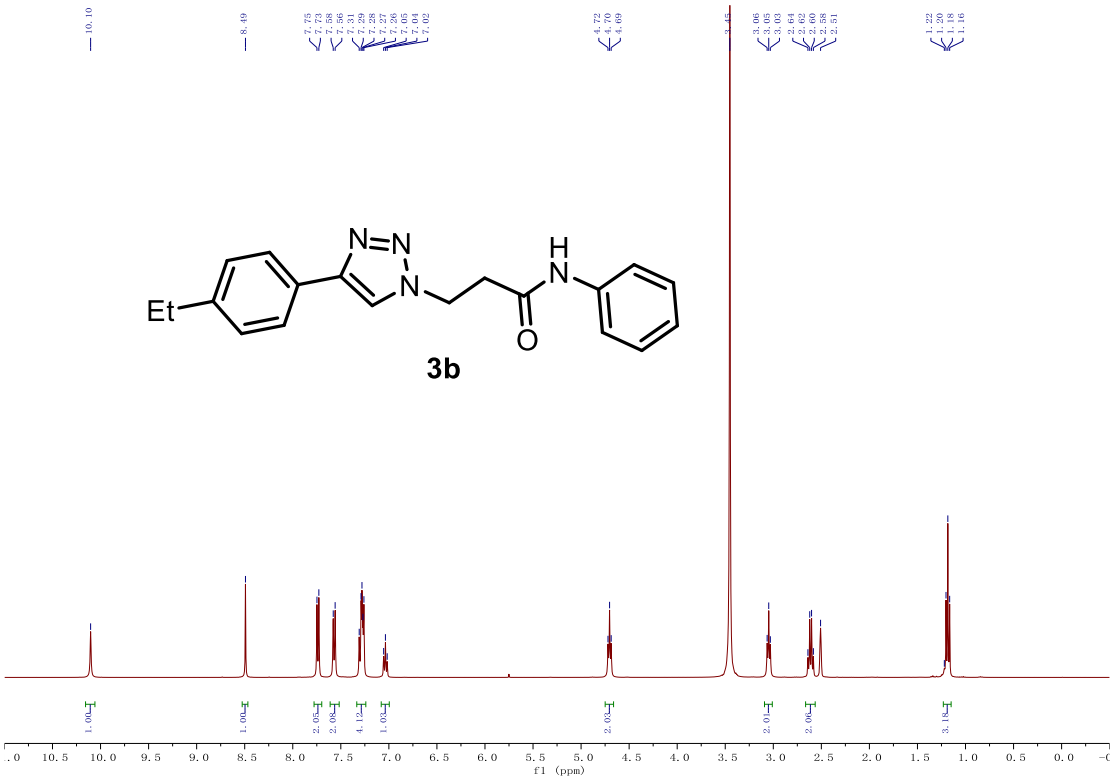


Figure S21.[1]H NMR (400 MHz, DMSO-d_6) spectrum for **3b**

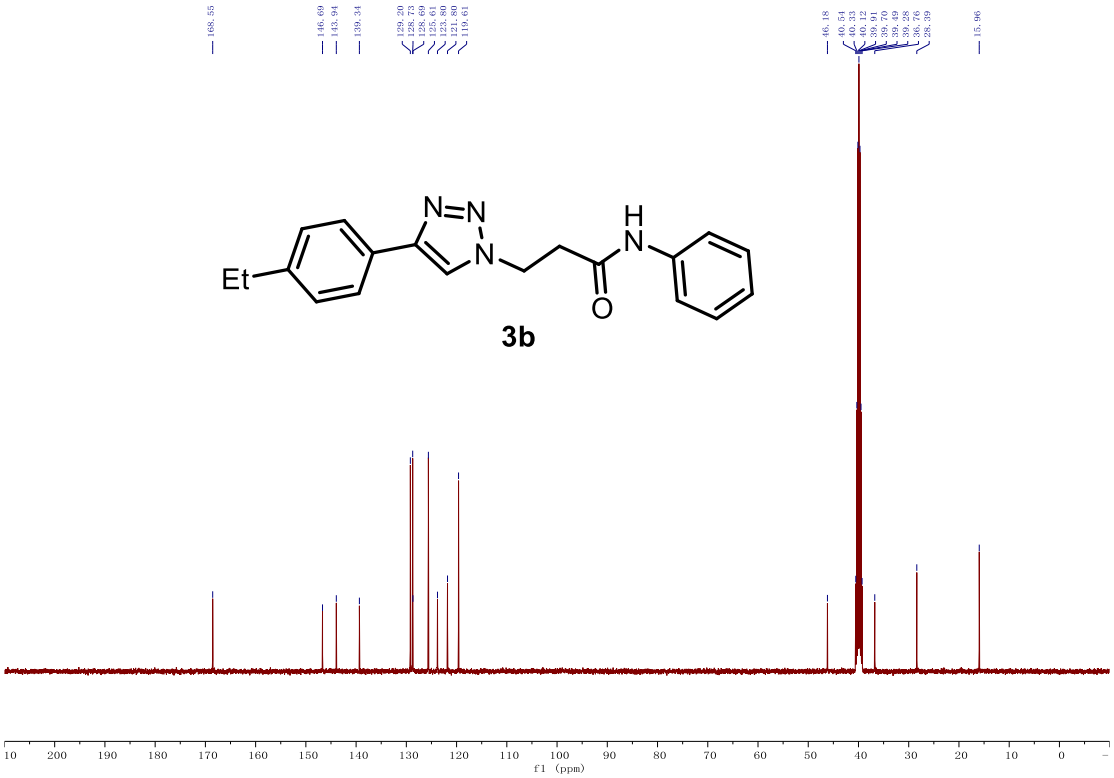


Figure S22.[13]C NMR (100 MHz, DMSO-d_6) spectrum for **3b**

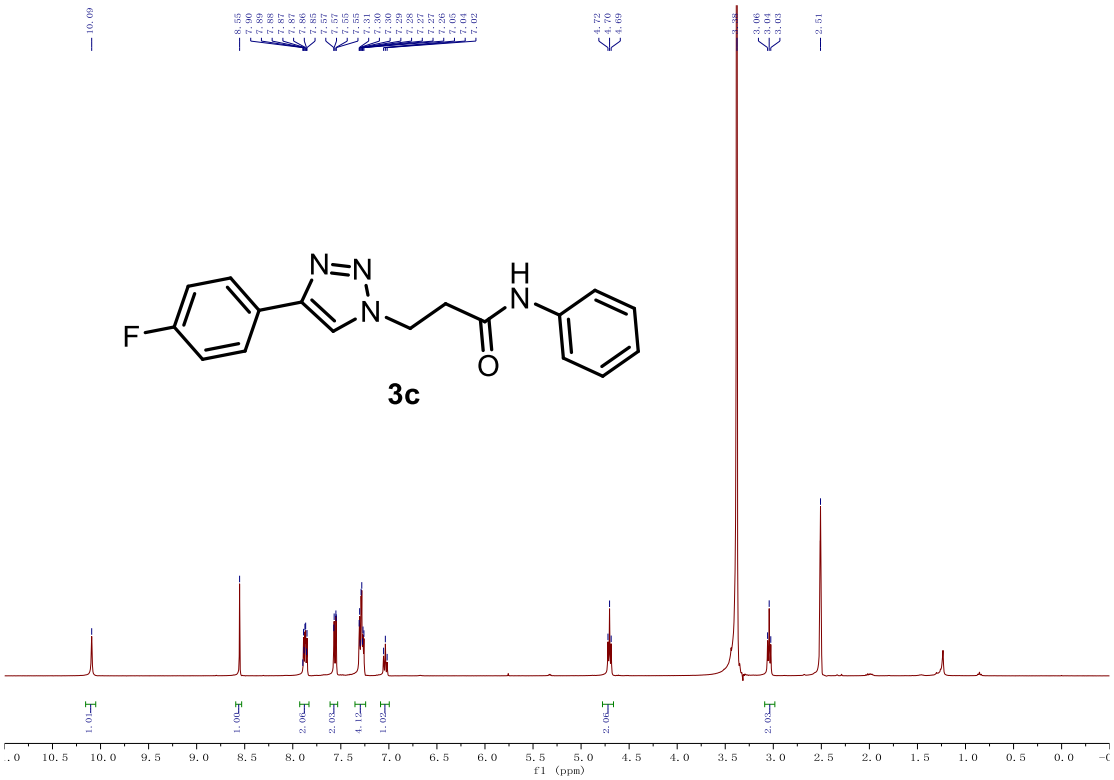


Figure S23.[1]H NMR (400 MHz, DMSO-*d*$_6$) spectrum for **3c**

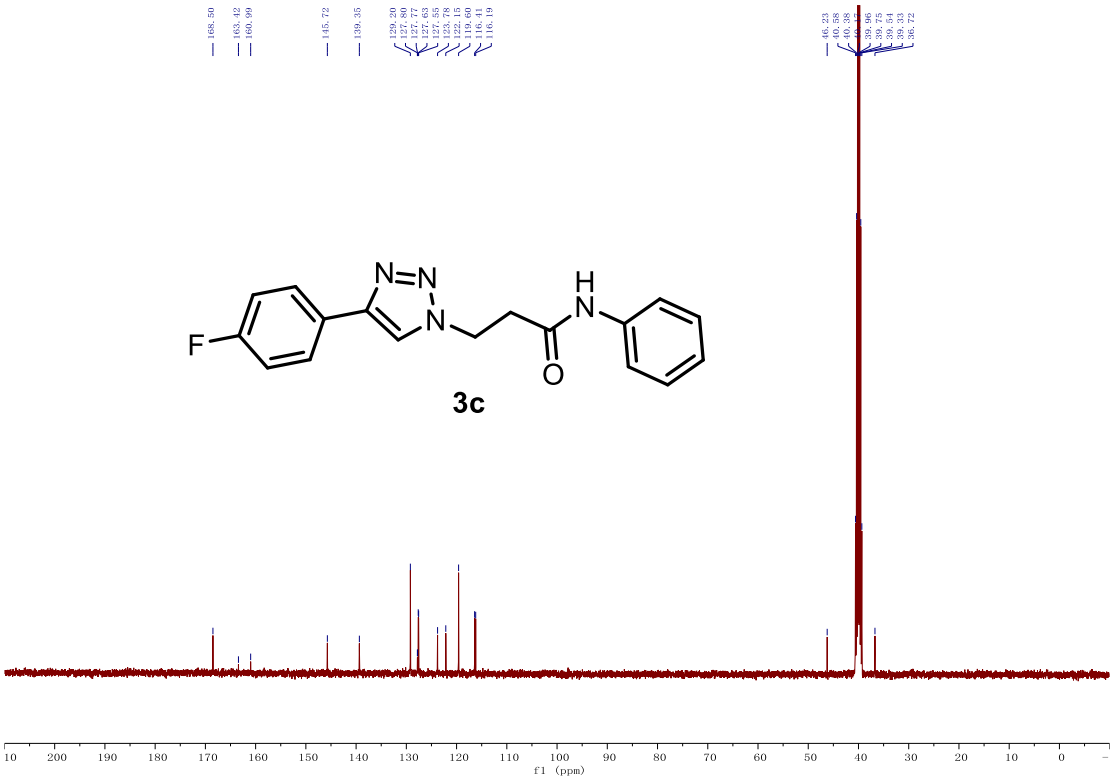


Figure S24.[13]C NMR (100 MHz, DMSO-*d*$_6$) spectrum for **3c**

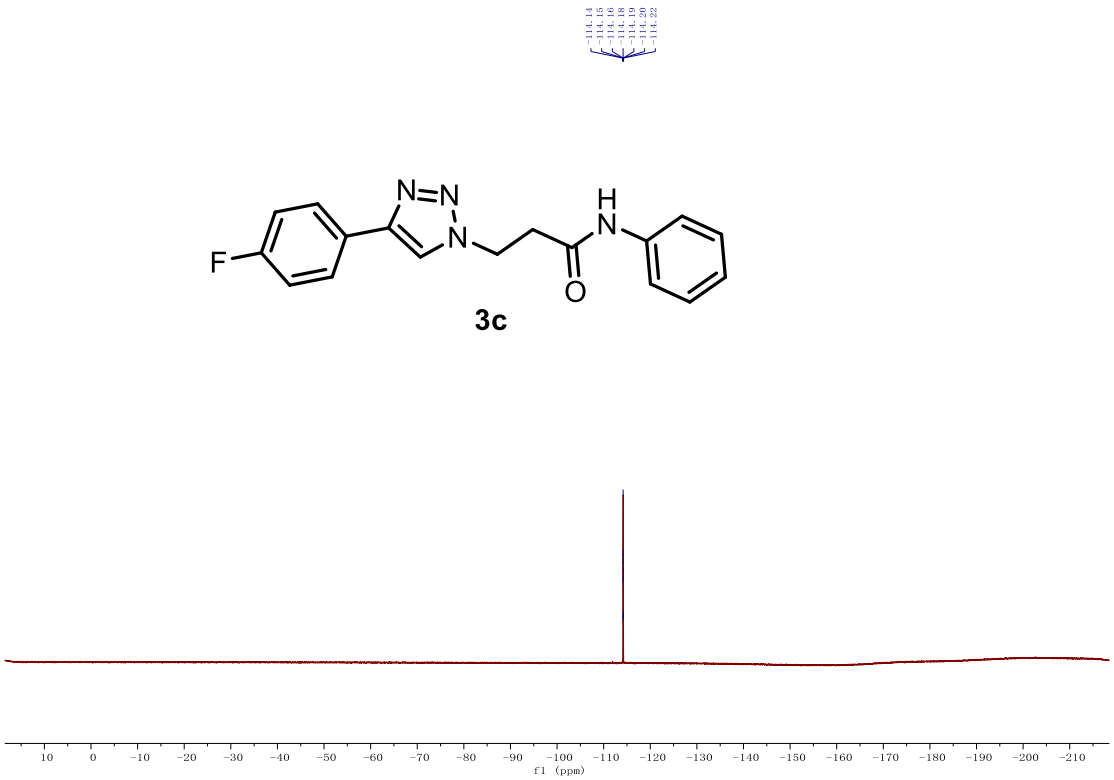


Figure S25.^{19}F NMR (376 MHz, DMSO-d_6) spectrum for **3c**

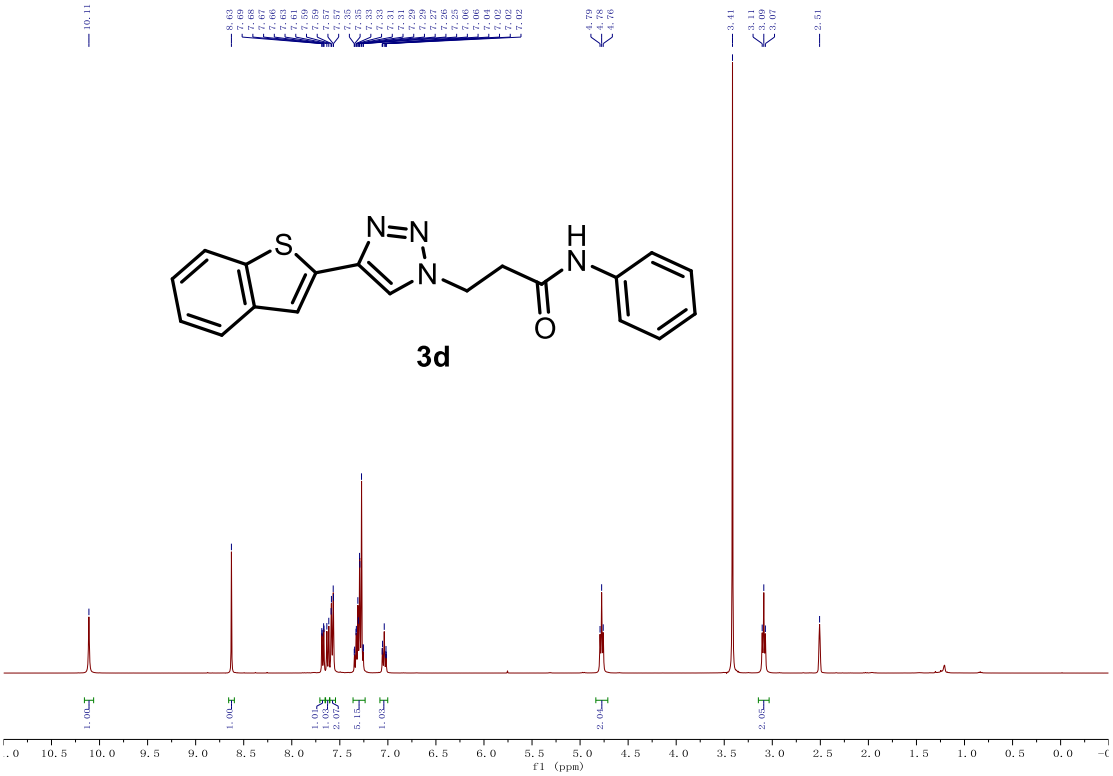


Figure S26.[1]H NMR (400 MHz, DMSO-d_6) spectrum for **3d**

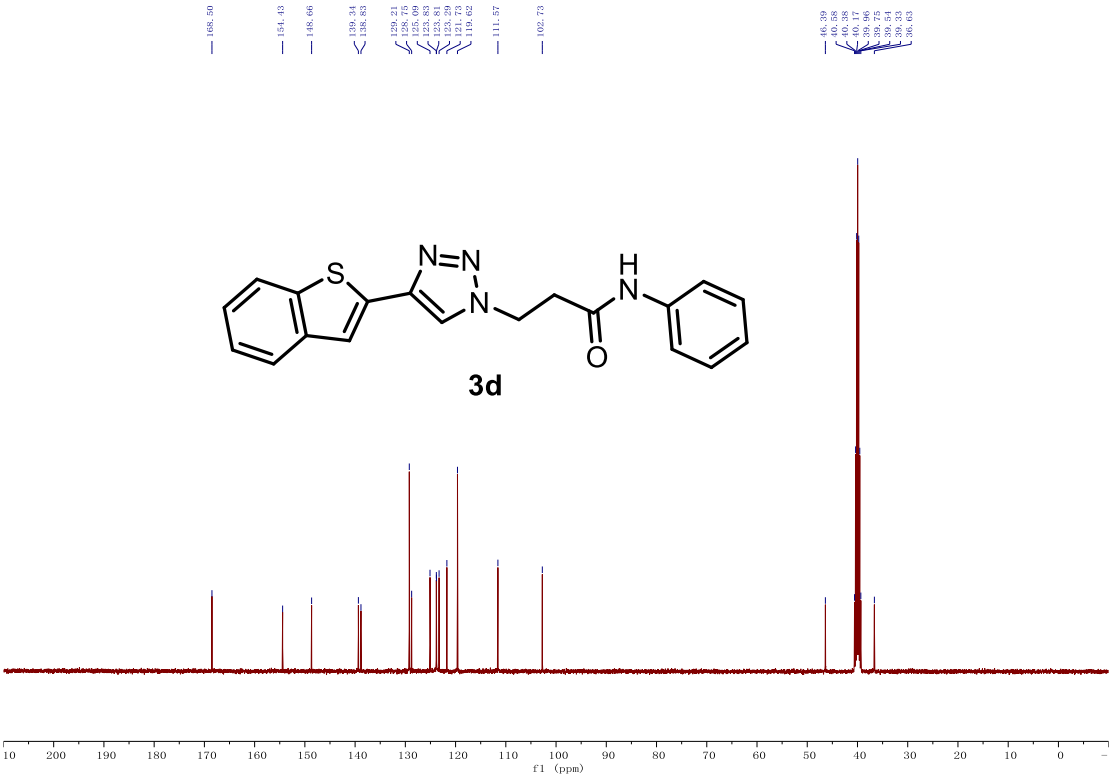


Figure S27.[13]C NMR (100 MHz, DMSO-d_6) spectrum for **3d**

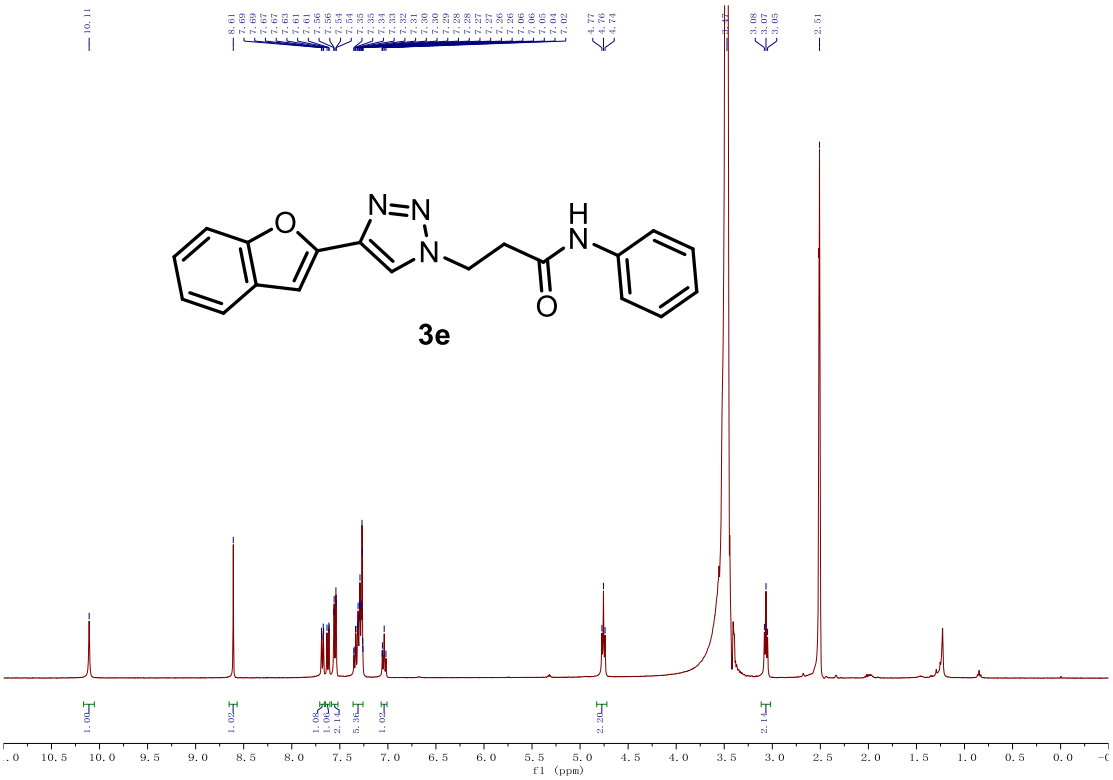


Figure S28.[1]H NMR (400 MHz, DMSO-d_6) spectrum for **3e**

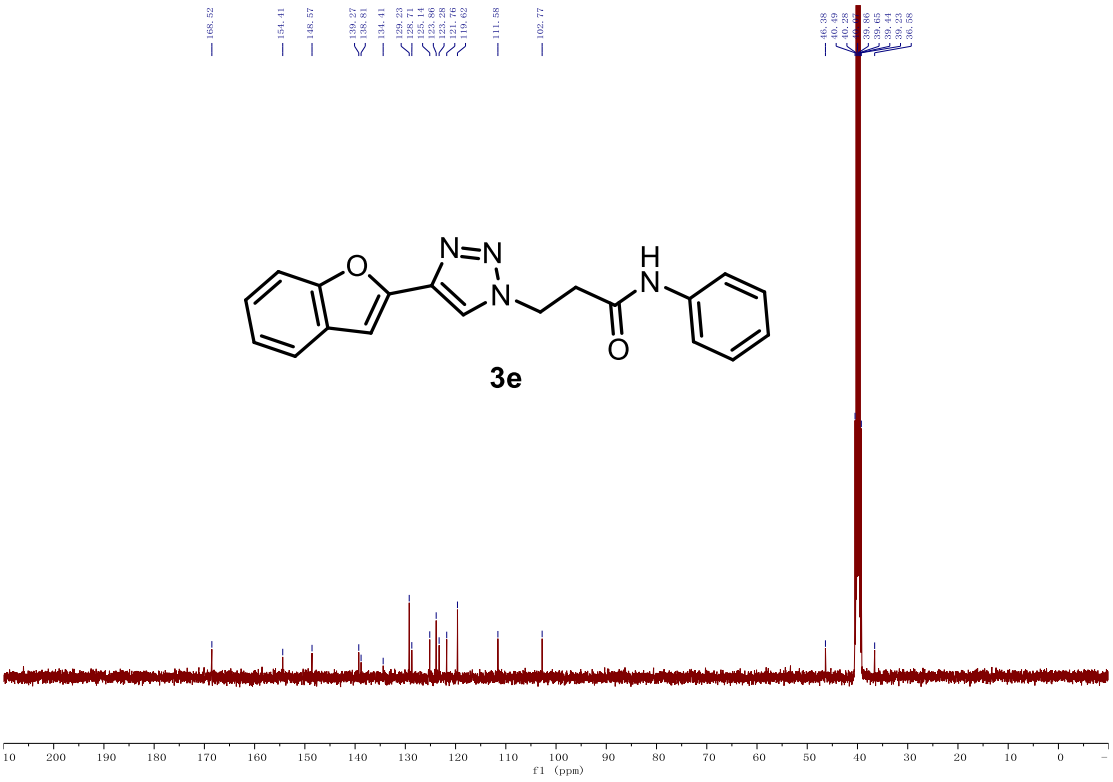


Figure S29.[13]C NMR (100 MHz, DMSO-d_6) spectrum for **3e**

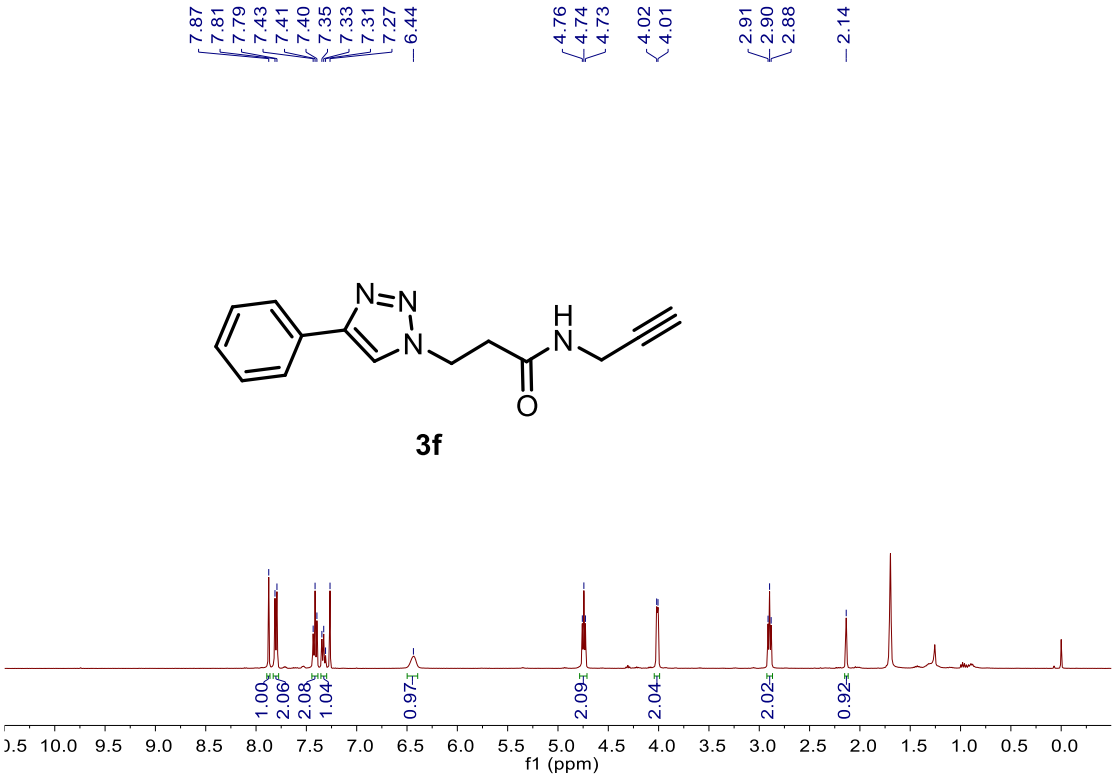


Figure S30.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3f**

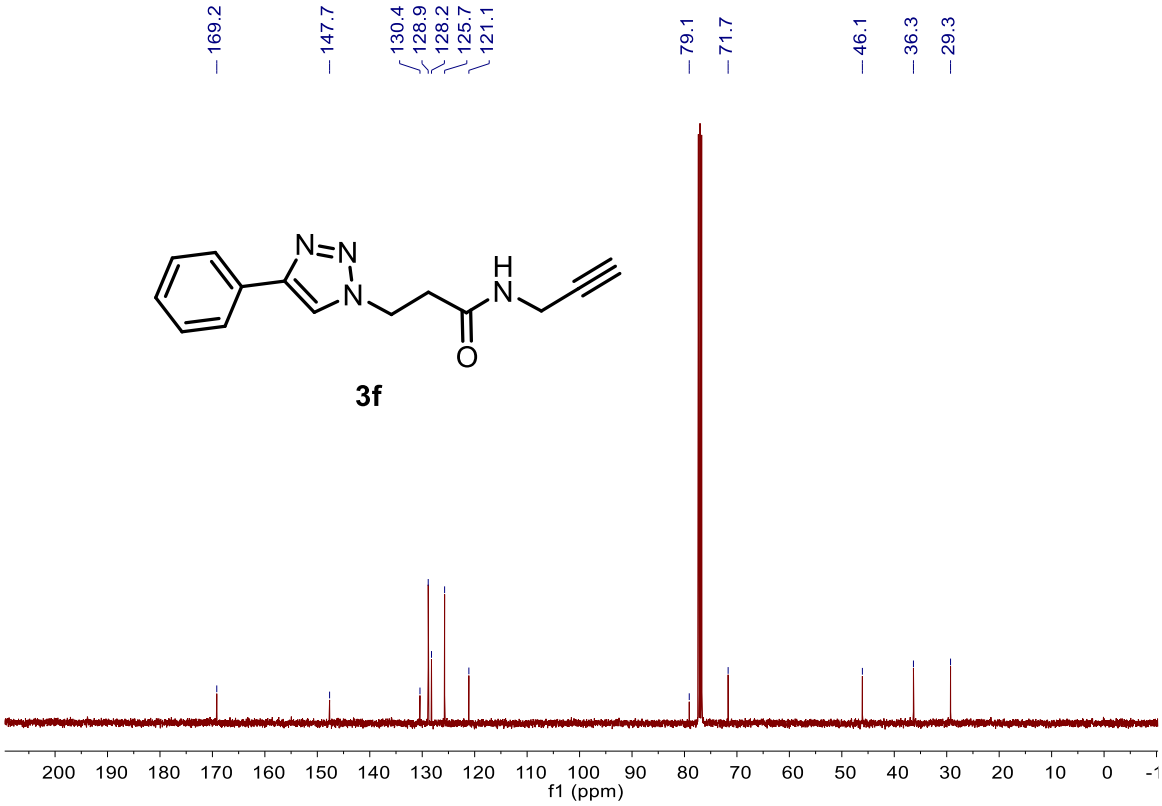


Figure S31.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3f**

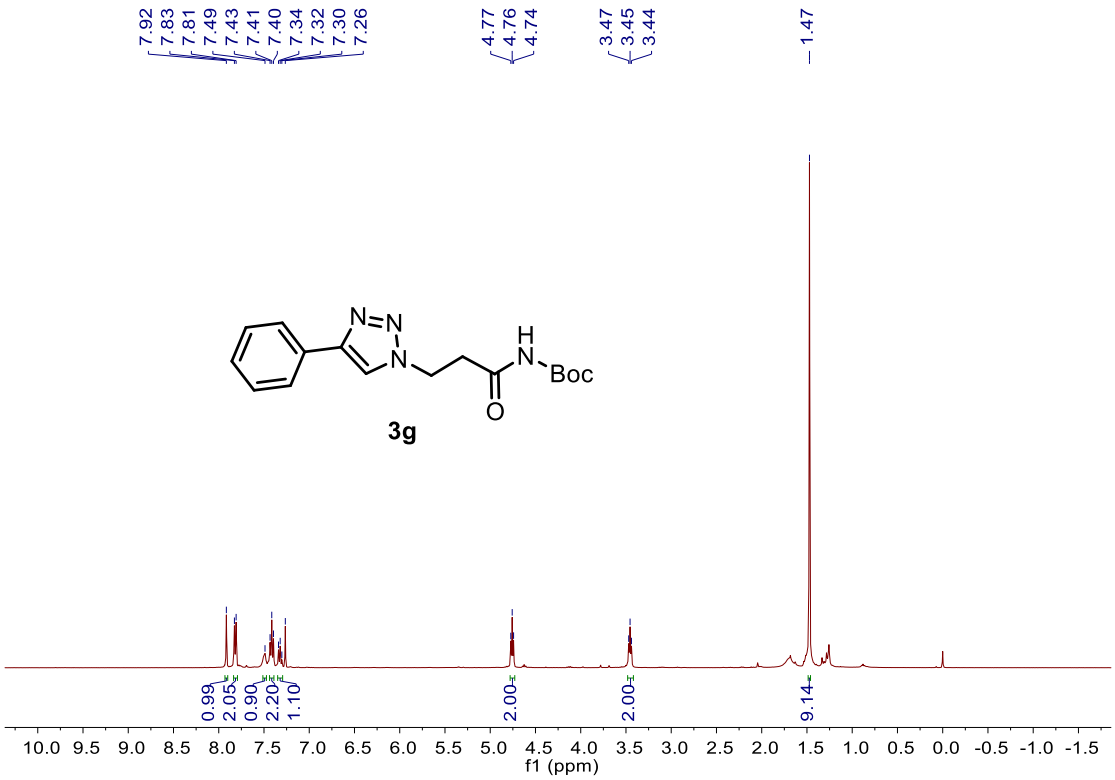


Figure S32.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3g**

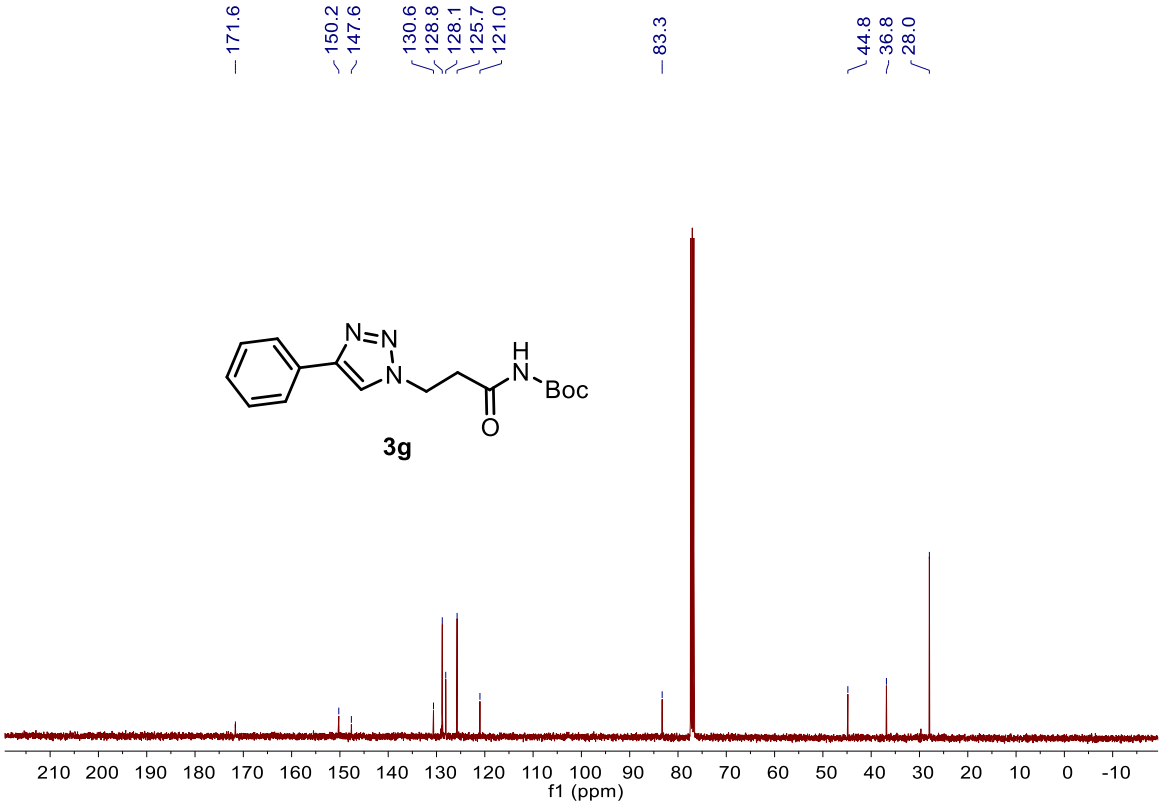


Figure S33.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3g**

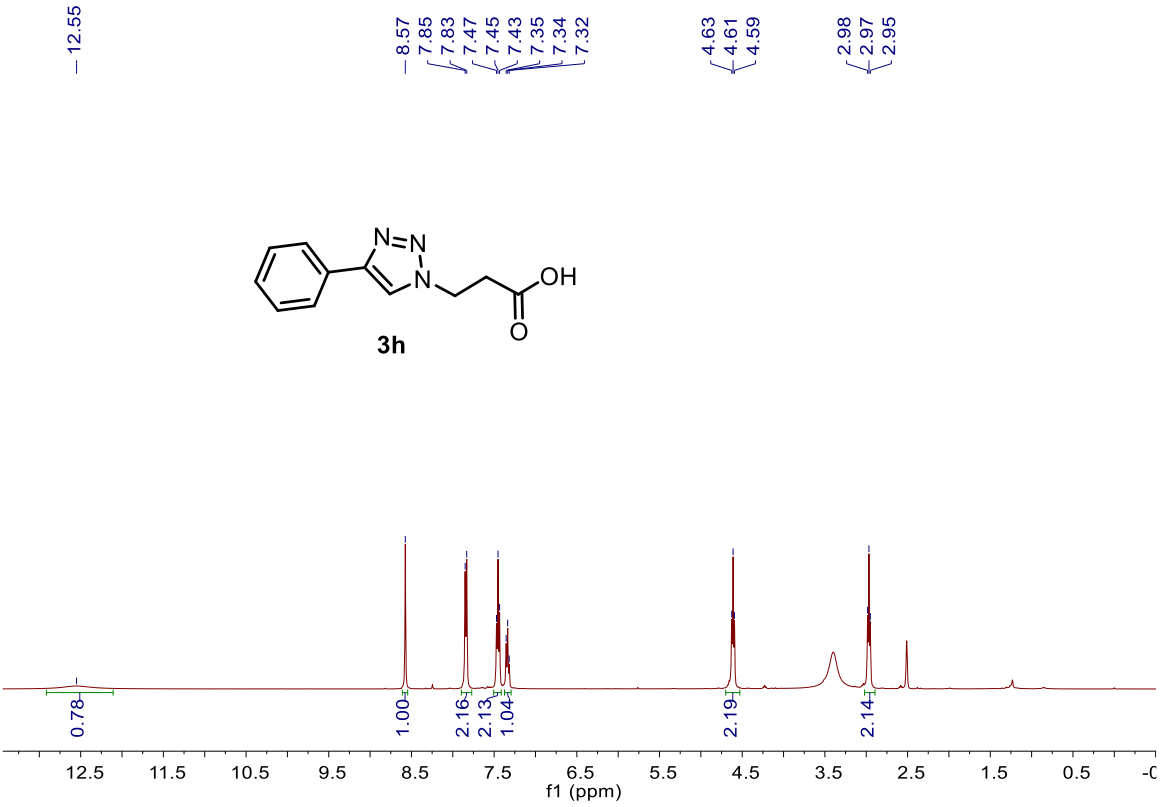


Figure S34.[1]H NMR (400 MHz, DMSO-d_6) spectrum for **3h**

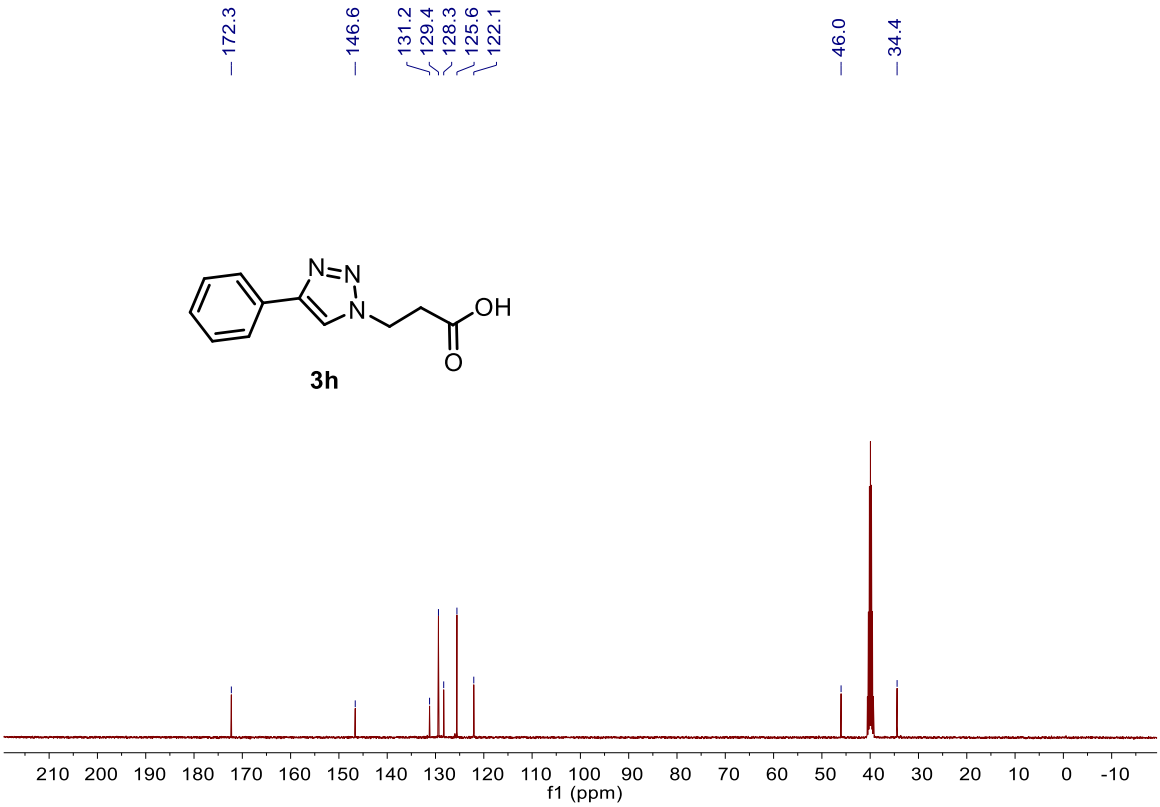


Figure S35.[13]C NMR (100 MHz, DMSO-d_6) spectrum for **3h**

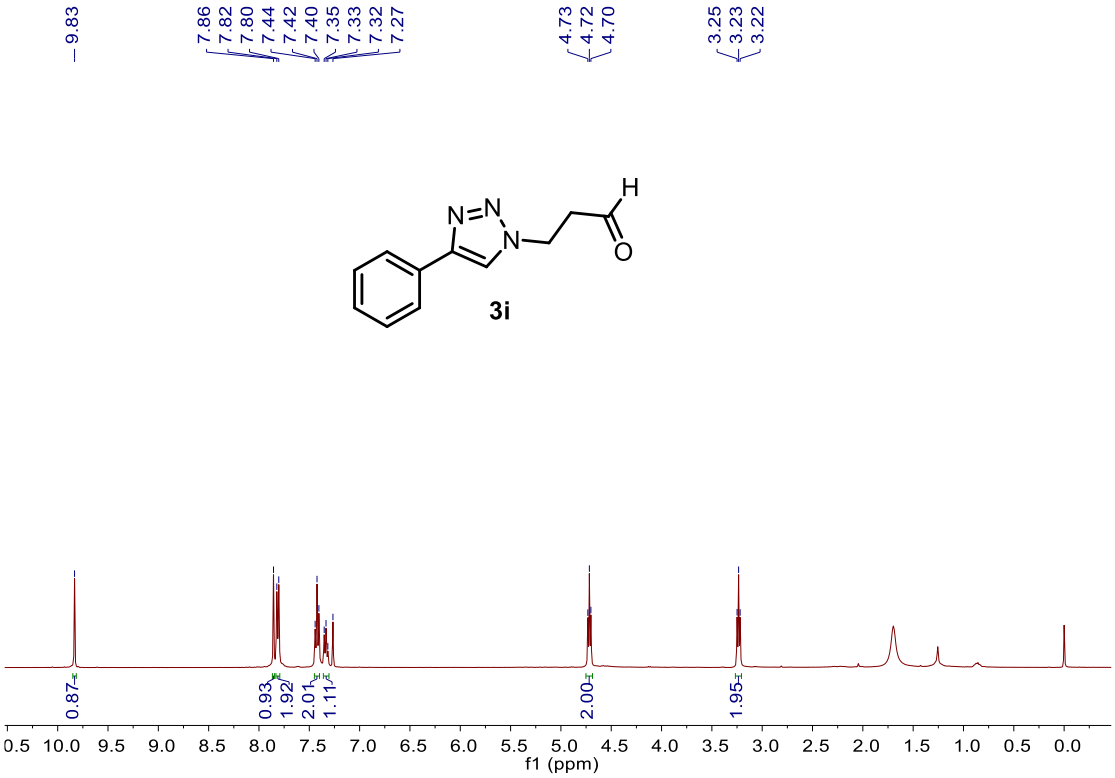


Figure S36.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3i**

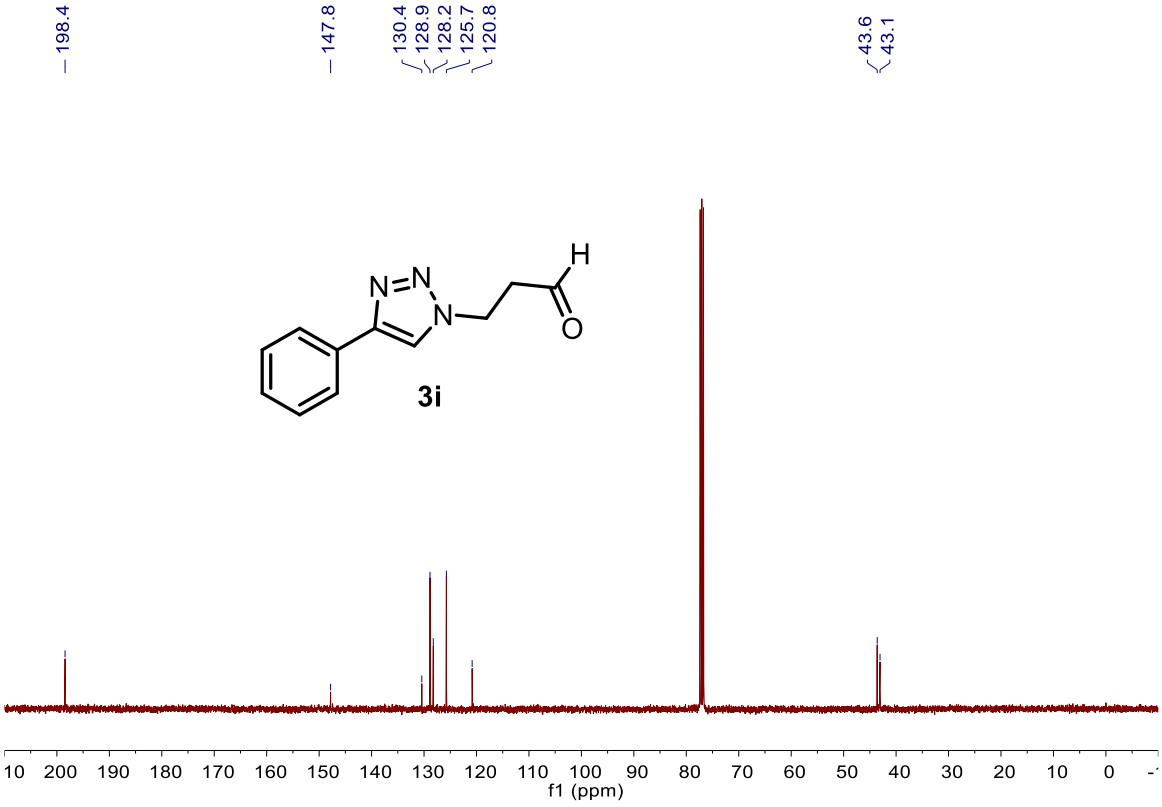


Figure S37.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3i**

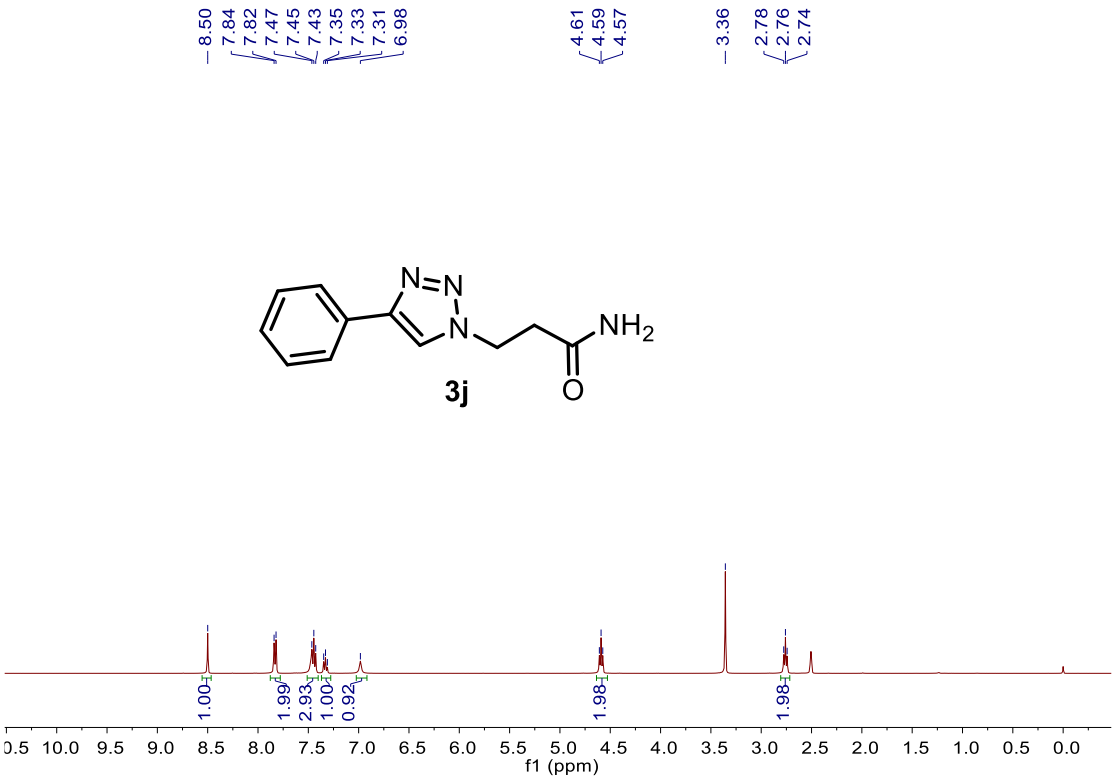


Figure S38.[1]H NMR (400 MHz, DMSO-d_6) spectrum for **3j**

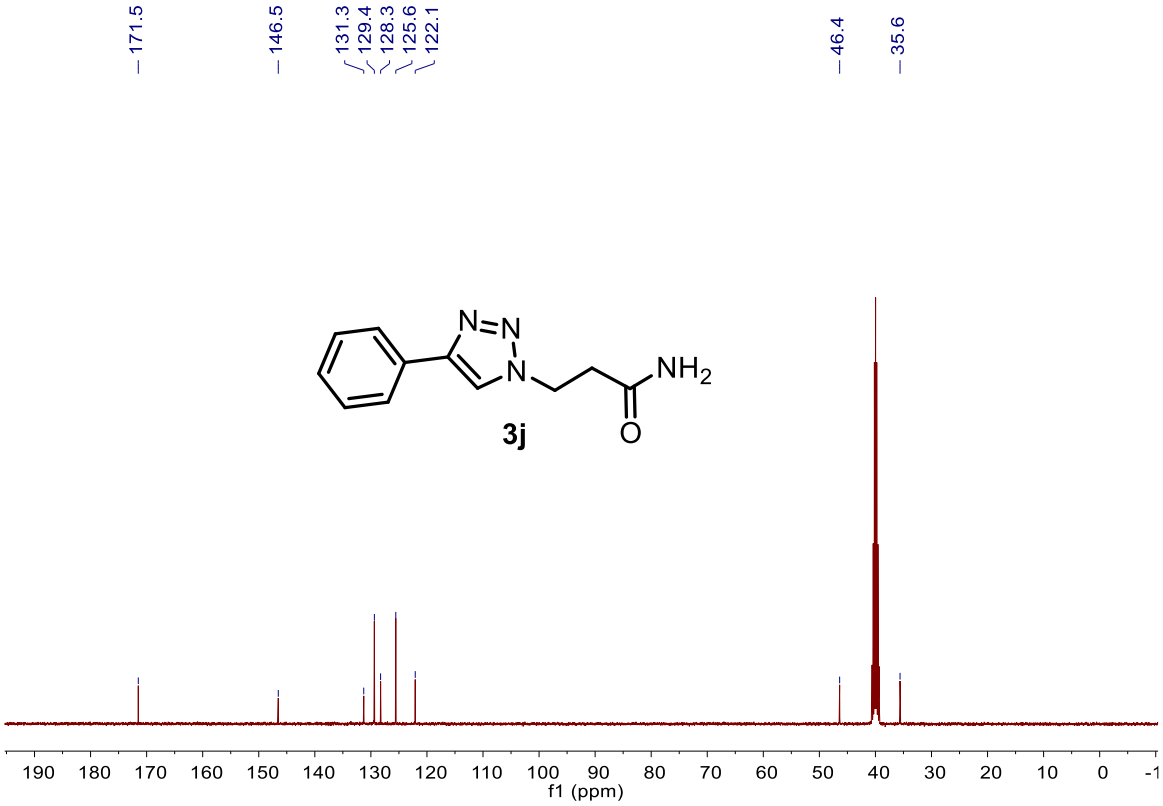


Figure S39.[13]C NMR (100 MHz, DMSO-d_6) spectrum for **3j**

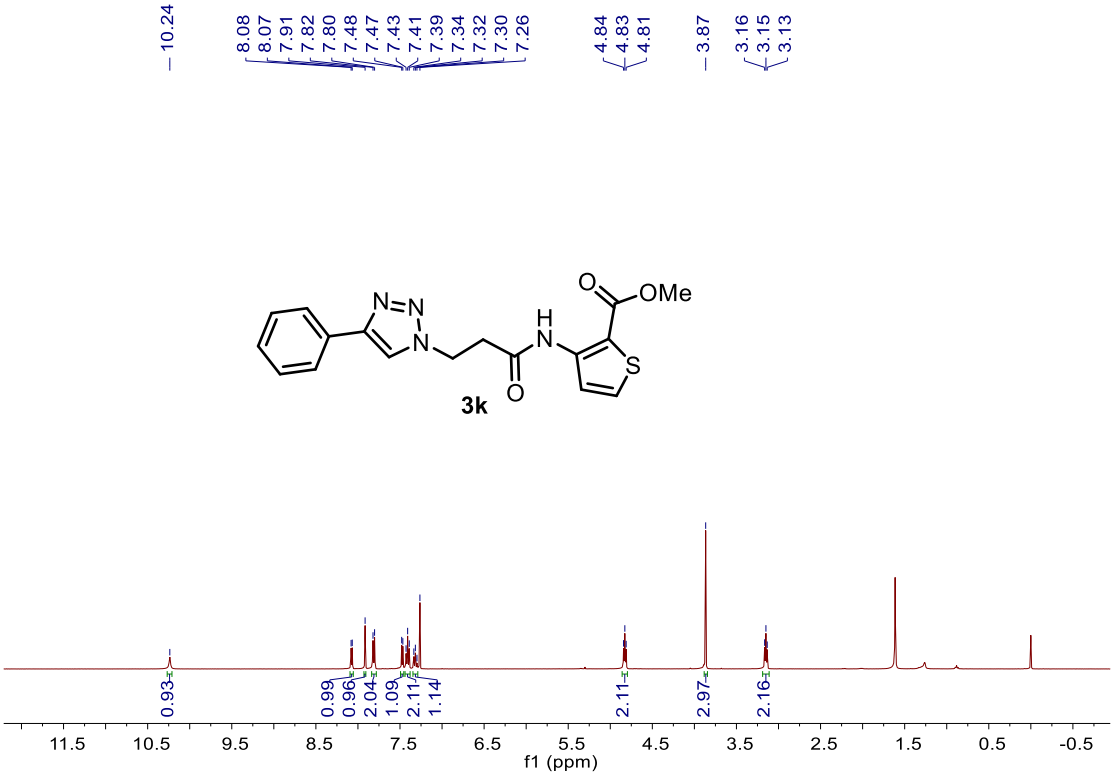


Figure S40.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3k**

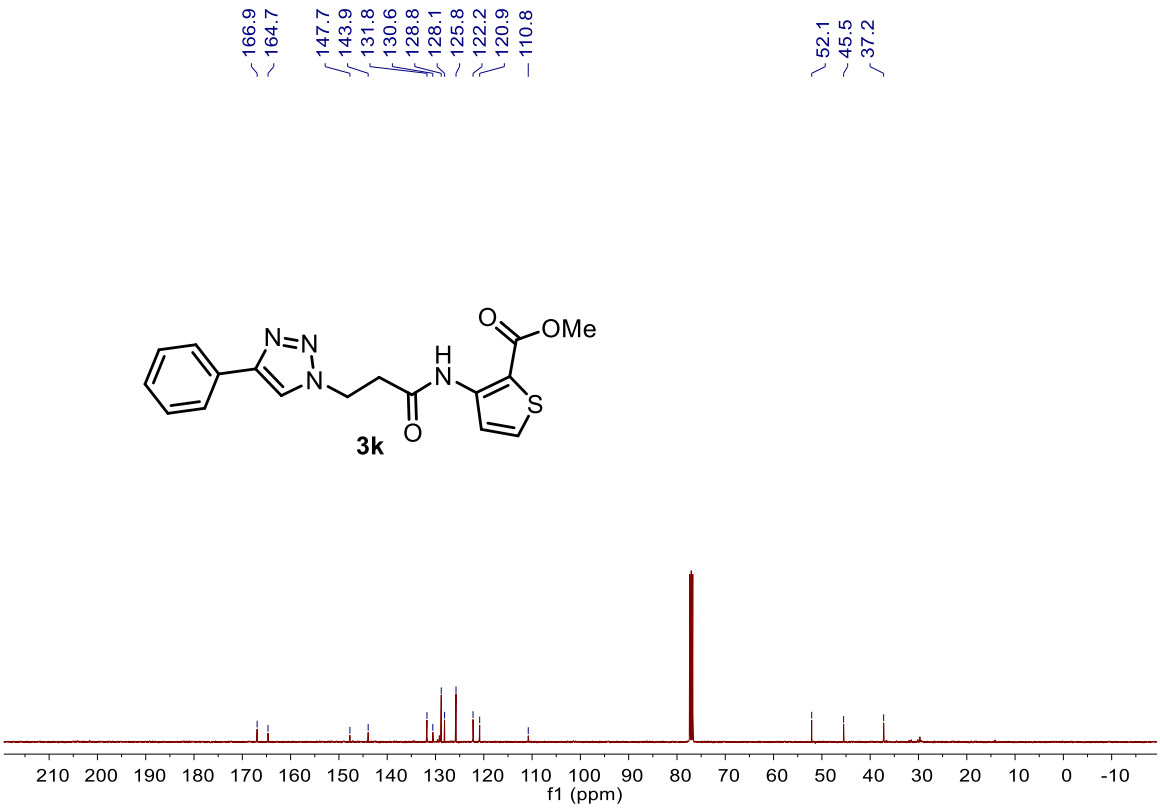


Figure S41.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3k**

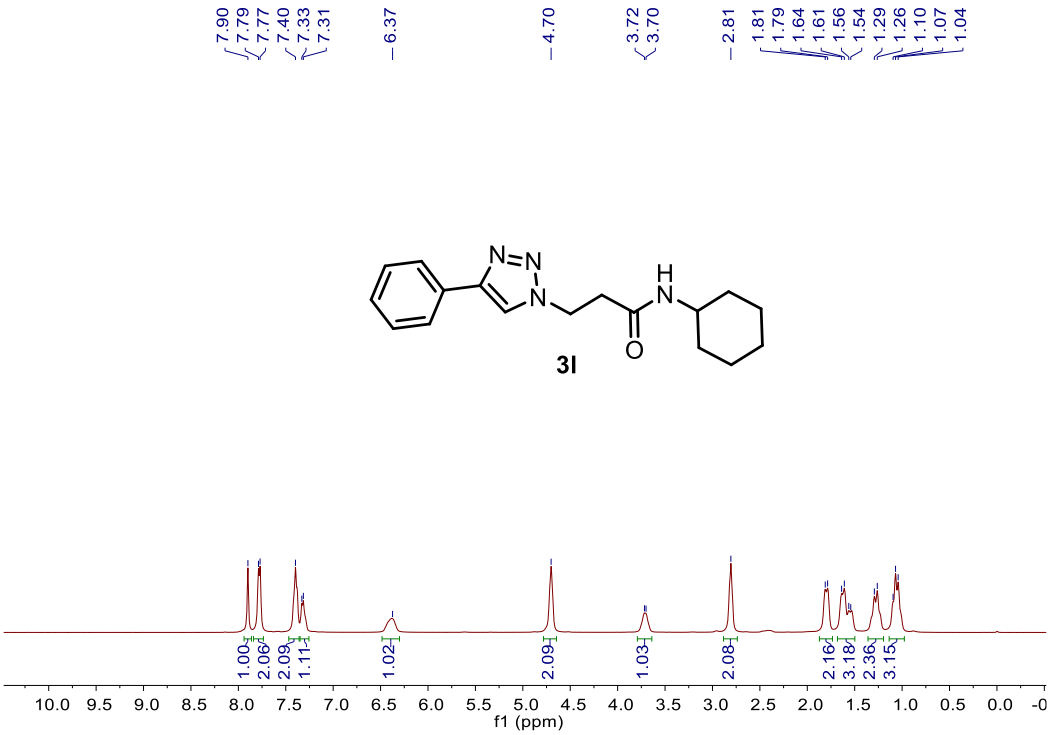


Figure S42.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3l**

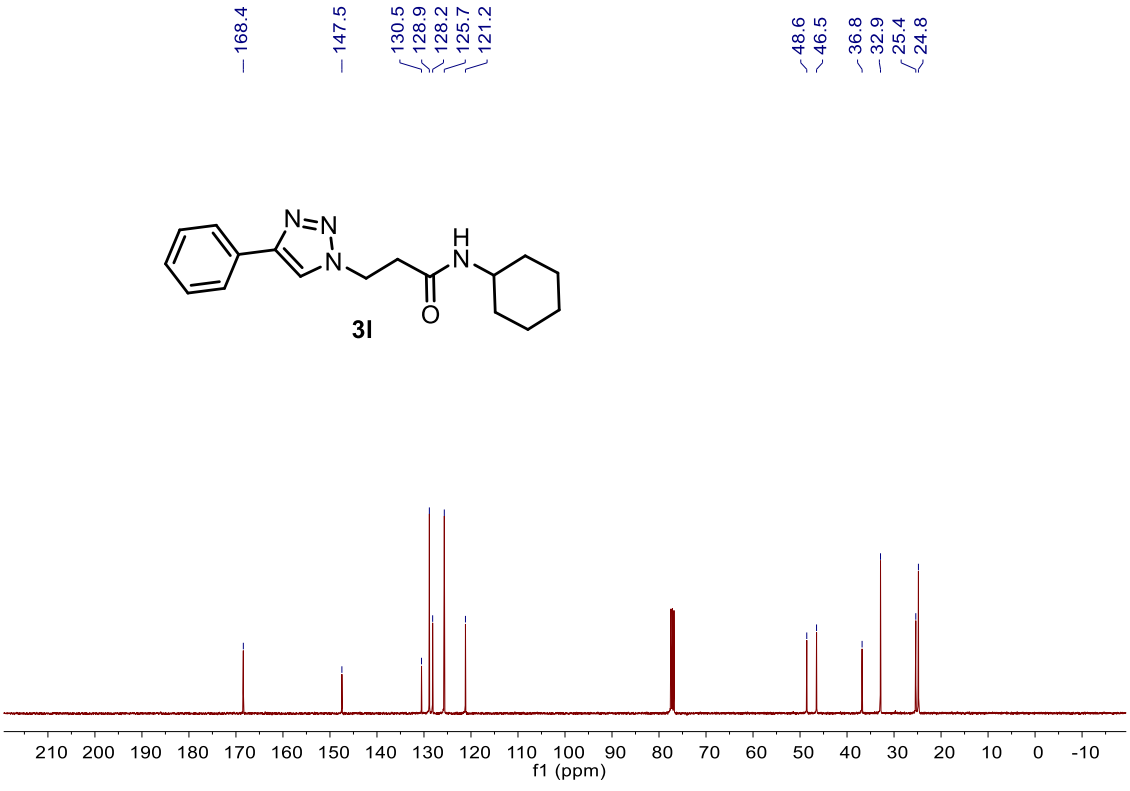


Figure S43.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3l**

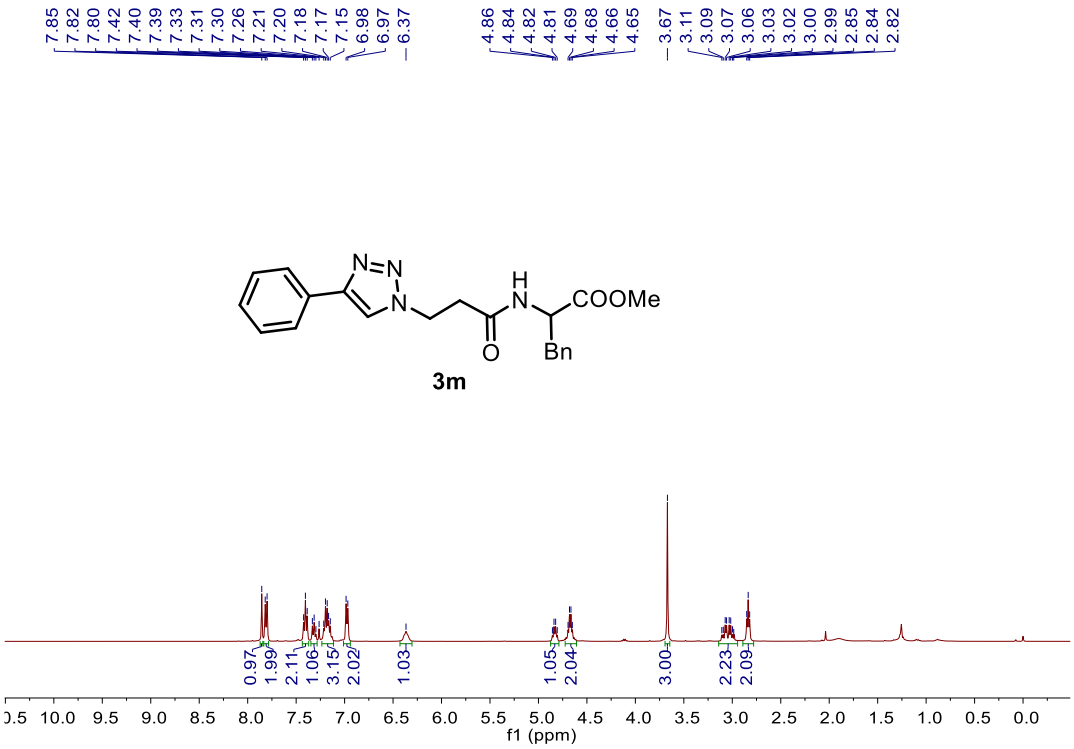


Figure S44.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3m**

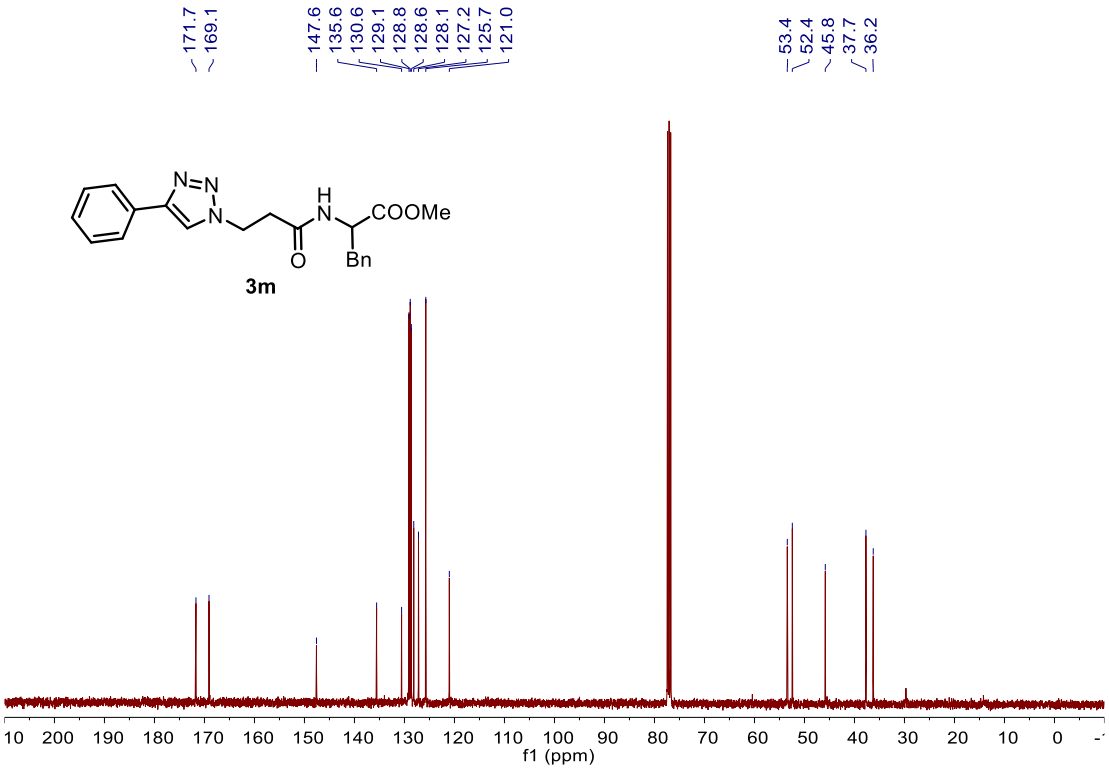


Figure S45.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3m**

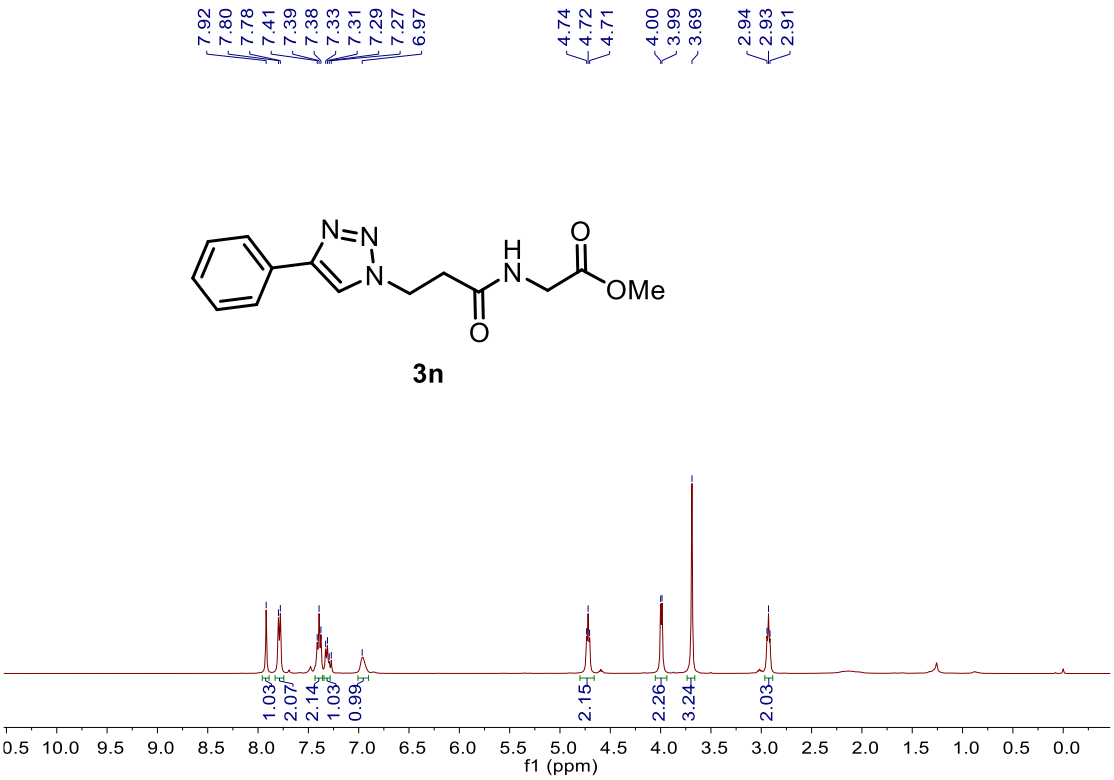


Figure S46.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3n**

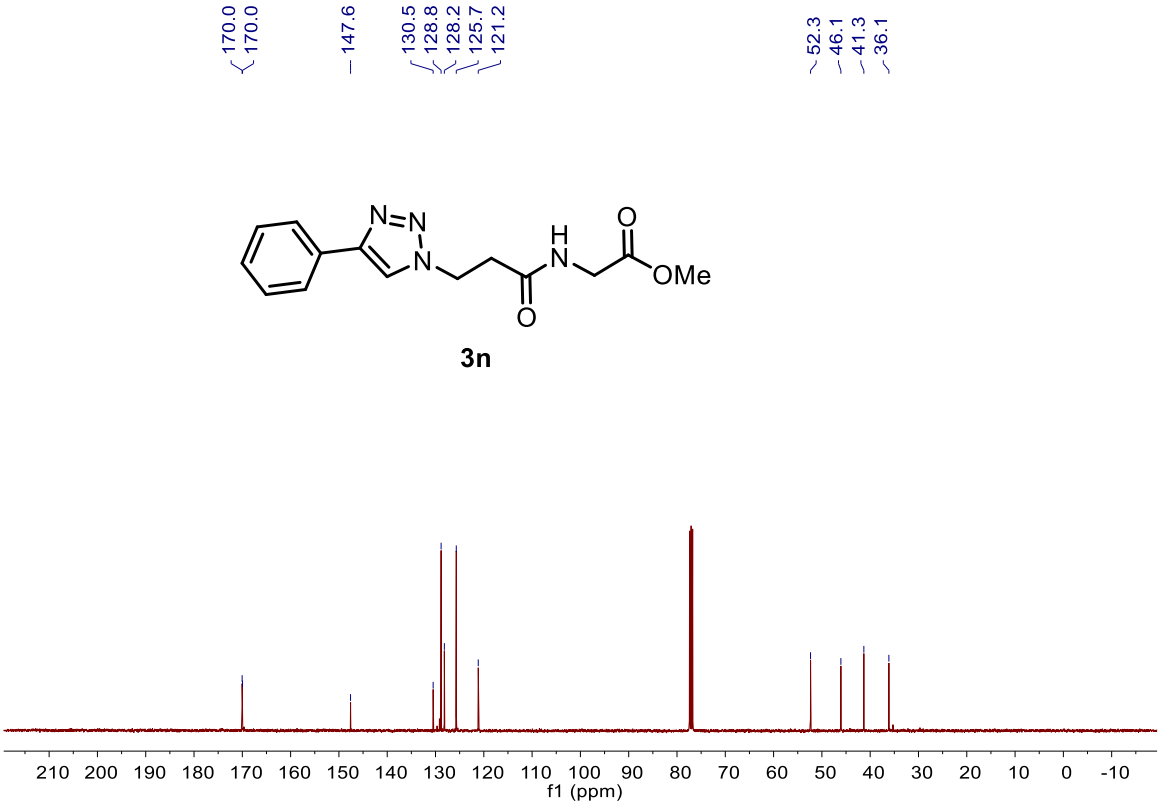


Figure S47.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3n**

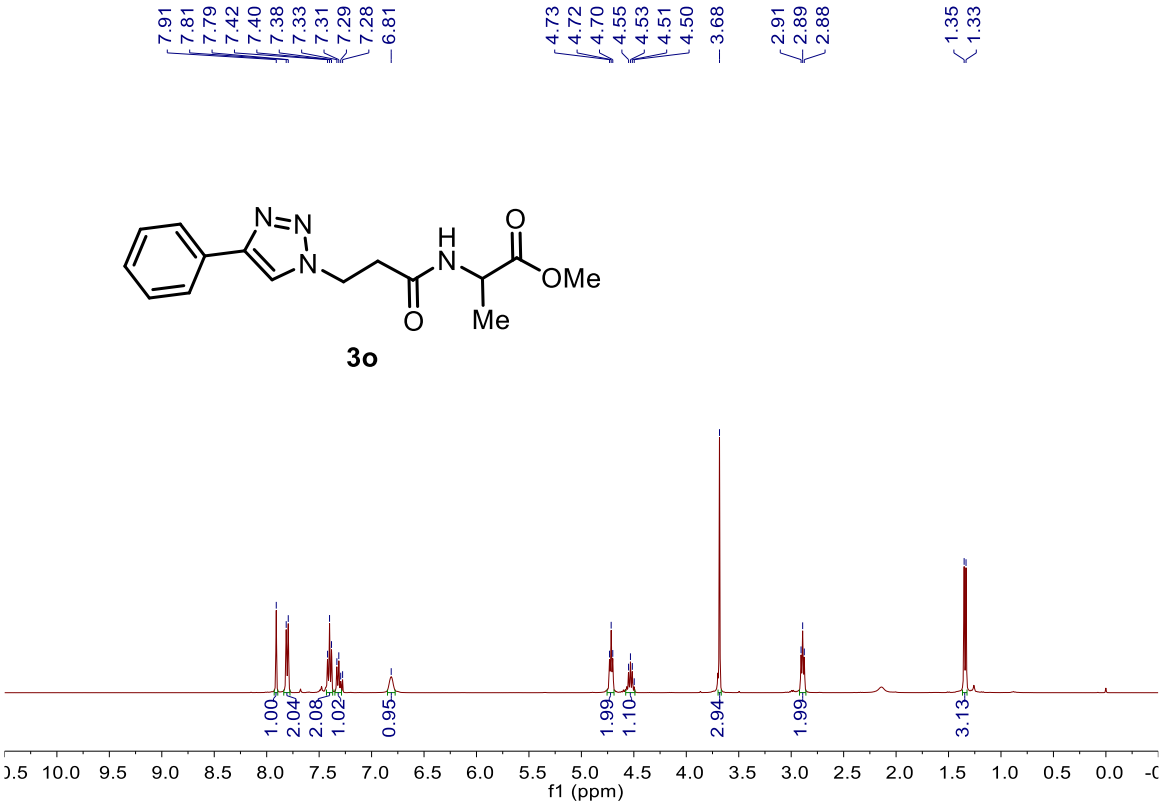


Figure S48.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3o**

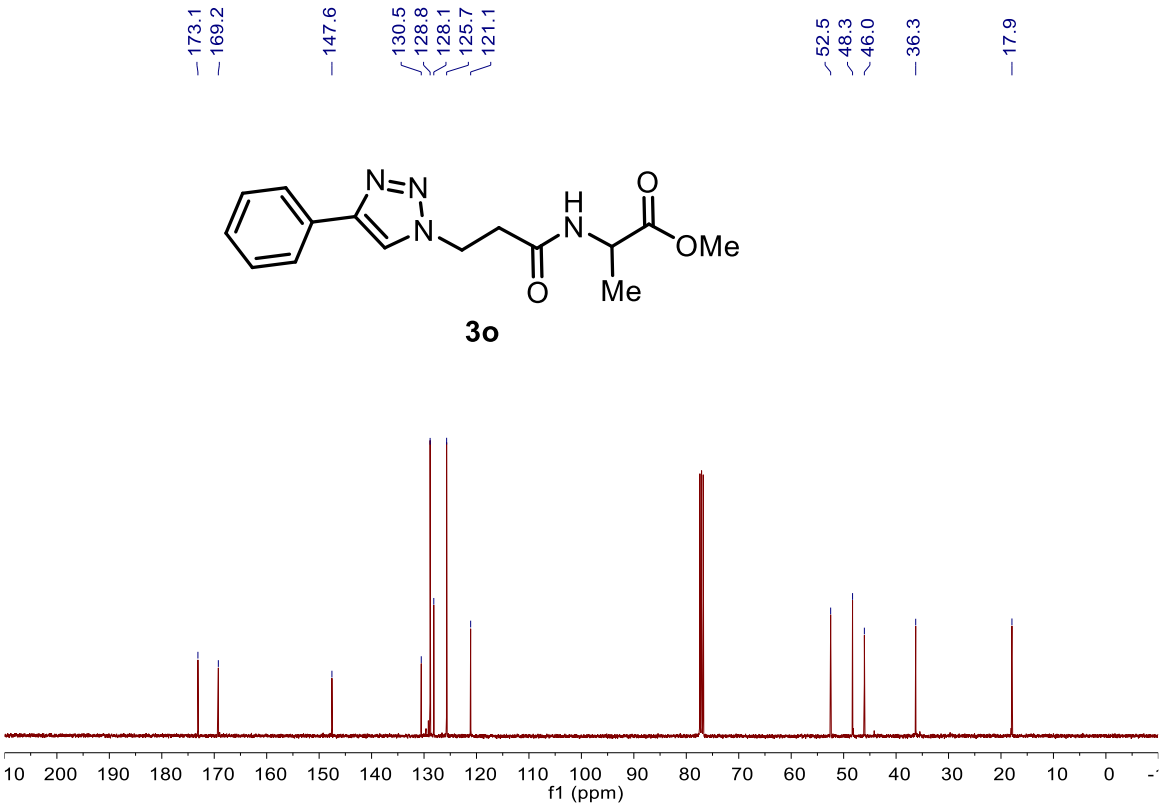


Figure S49.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3o**

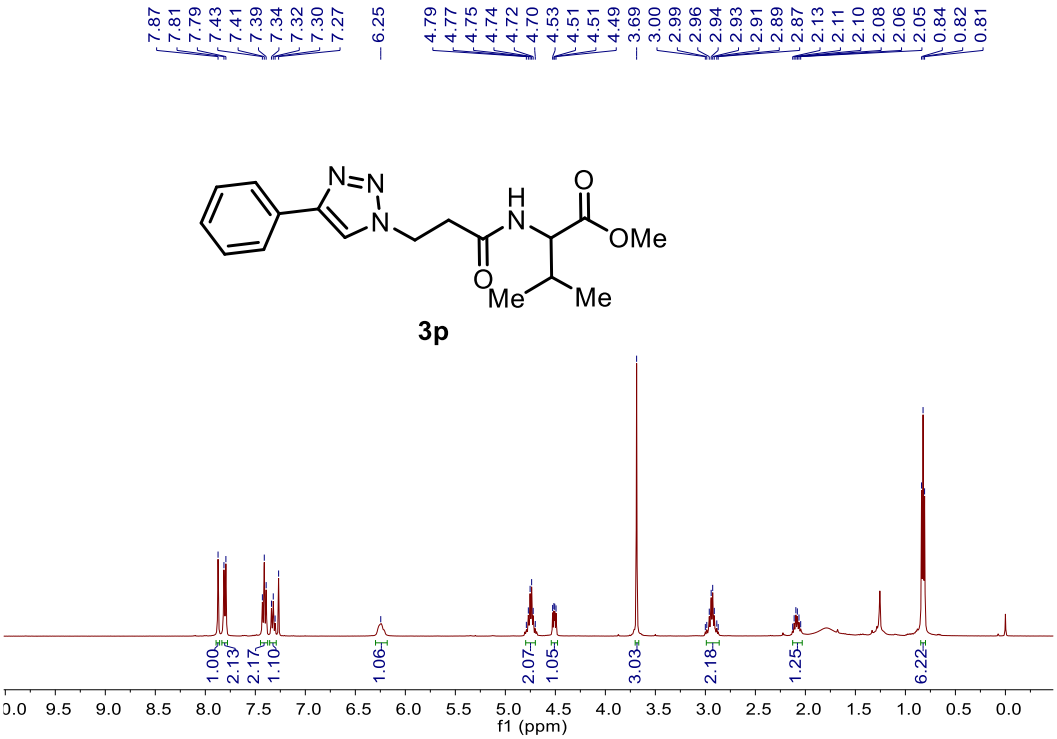


Figure S50.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3p**

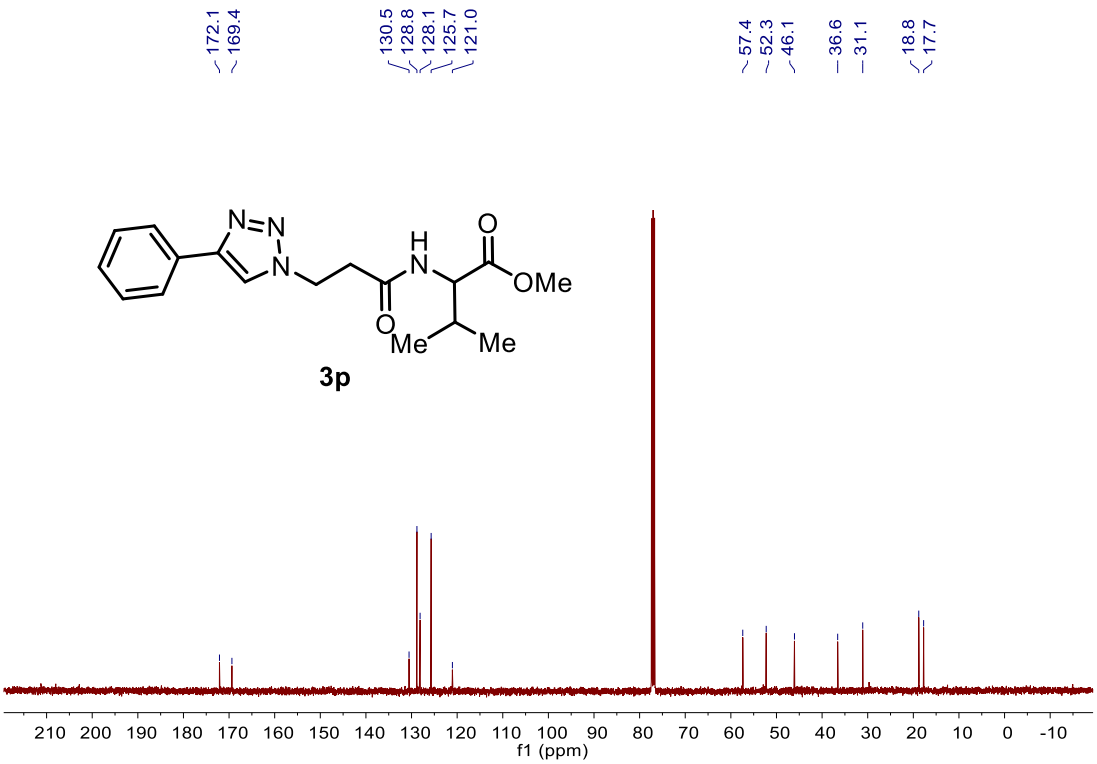


Figure S51.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3p**

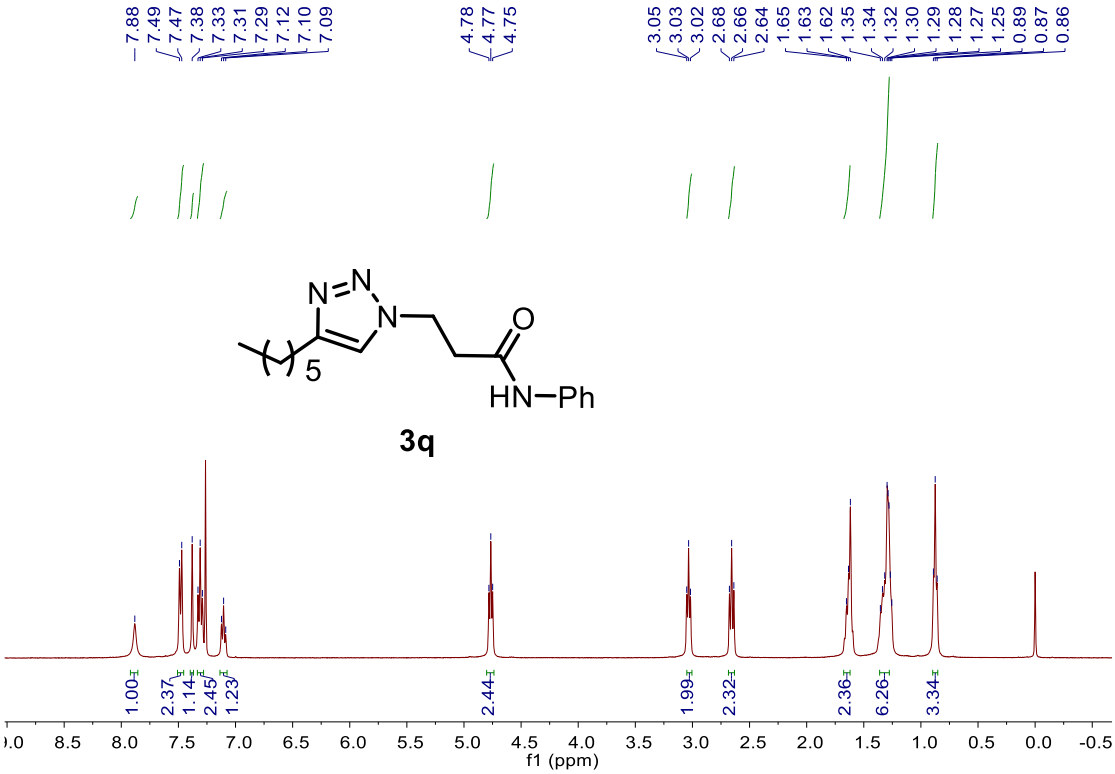


Figure S52.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3q**

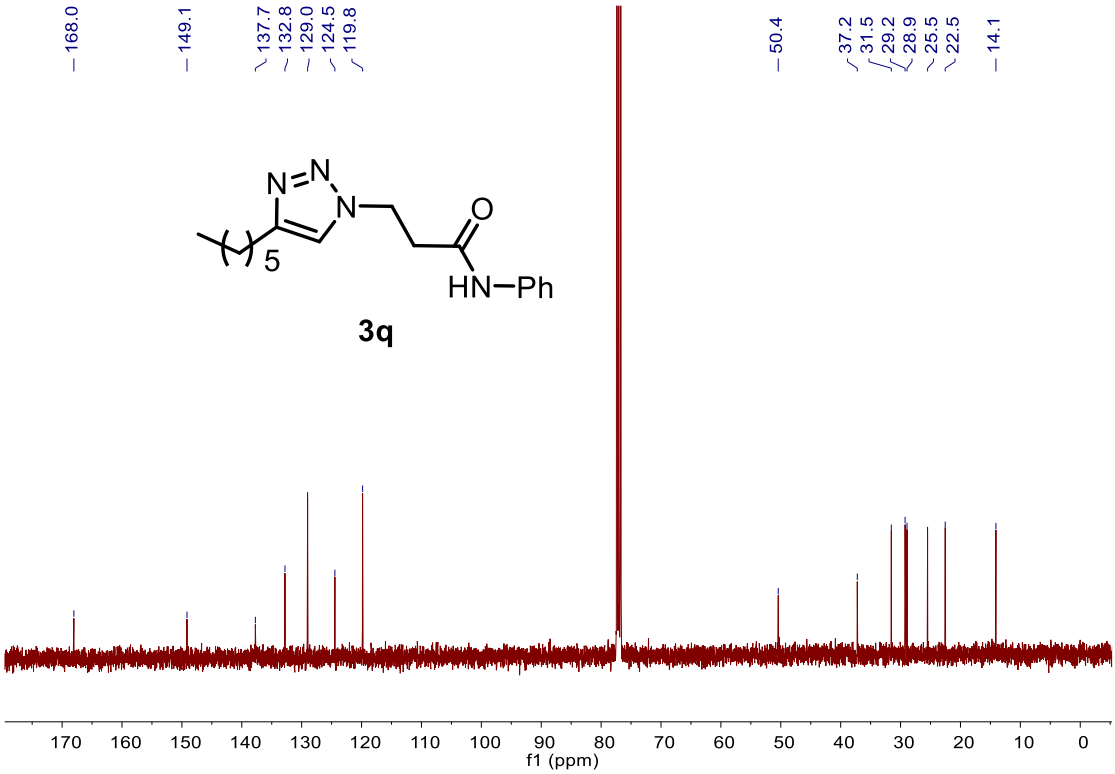


Figure S53.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3q**

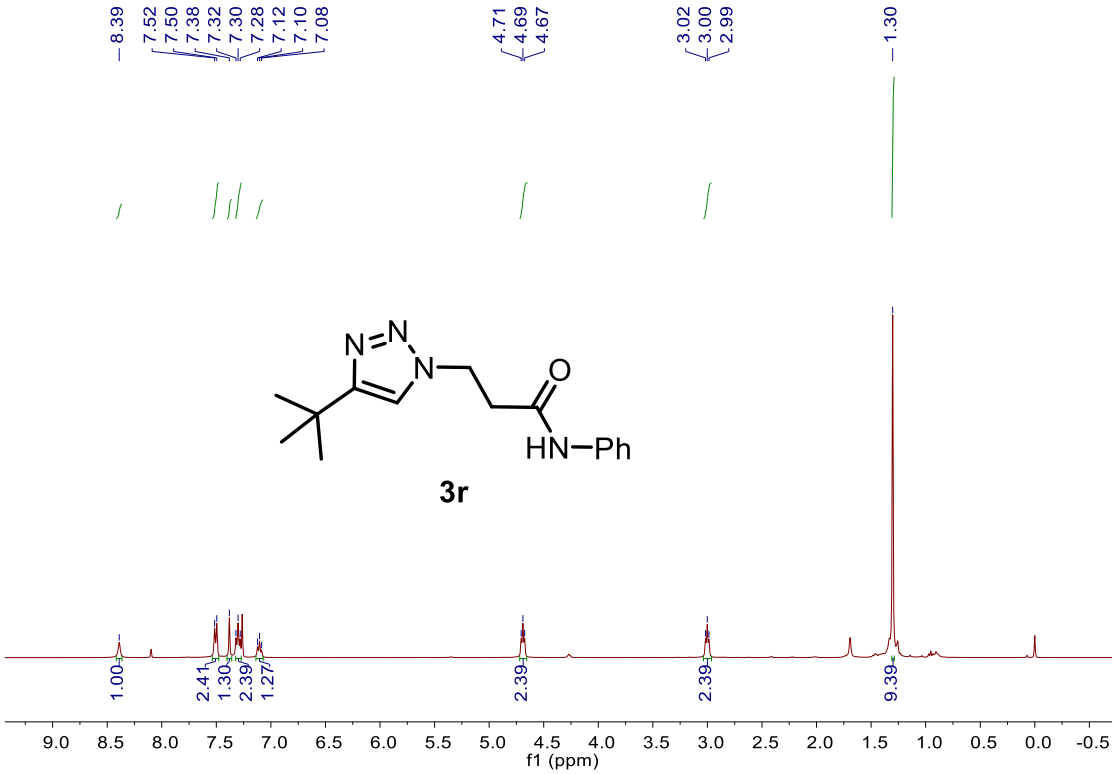


Figure S54.[1]H NMR (400 MHz, Chloroform-*d*) spectrum for **3r**

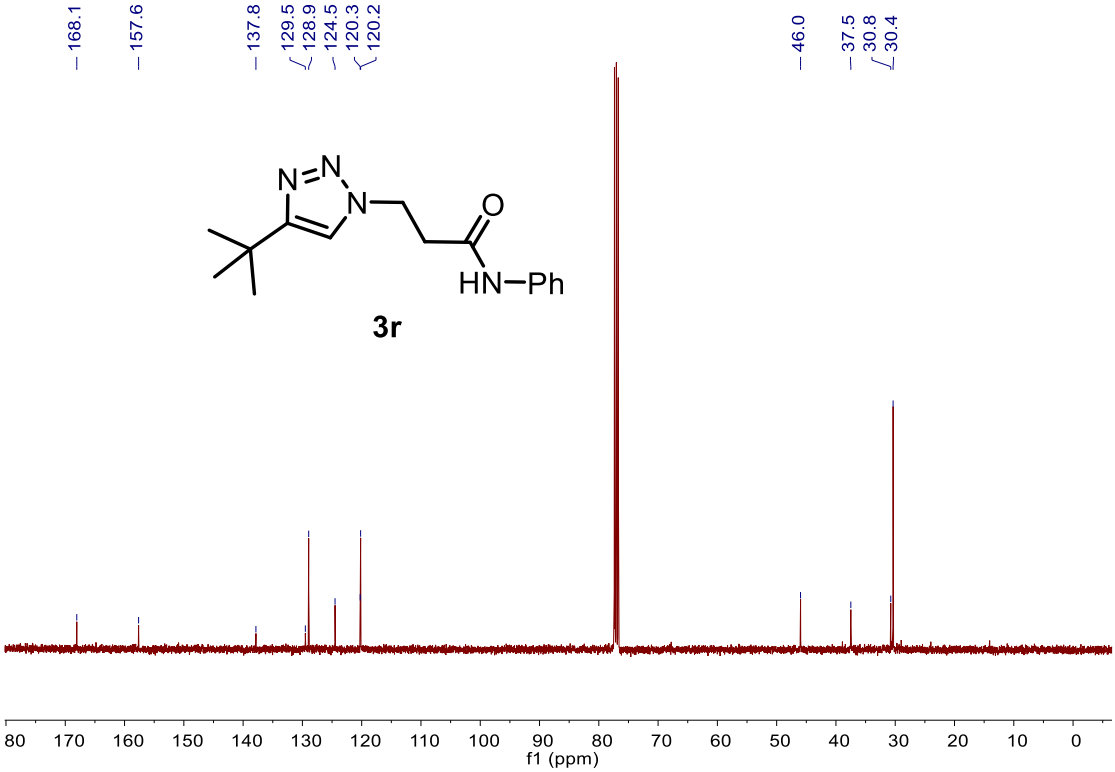


Figure S55.[13]C NMR (100 MHz, Chloroform-*d*) spectrum for **3r**

Supporting Information

9. References

[1] Garlets, Z. J.; Davies, H. M. L., Harnessing the β-Silicon Effect for Regioselective and Stereoselective Rhodium (II)-Catalyzed C–H Functionalization by Donor/Acceptor Carbenes Derived from 1-Sulfonyl-1,2,3-triazoles. *Org. Lett.* **2018**, *20*, 2168–2171.

[2] Kwok, S. W.; Zhang, L.; Grimster, N. P.; Fokin, V. V., Catalytic Asymmetric Transannulation of NH-1,2,3-Triazoles with Olefins. *Angew. Chem. Int. Ed*. **2014**, *53*, 3452–3456.

[3] Treitler, D. S.; Leung, S., How Dangerous Is Too Dangerous? A Perspective on Azide Chemistry. *J. Org. Chem.* **2022,** *87*, 11293-11295.