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SUPPORTING INFORMATION (*SI*)

Exposure to Air Boosts CuAAC Reactions Catalyzed by PEG-stabilized Cu Nanoparticles

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1. General data

All solvents and chemicals were used as purchased, unless otherwise noted.

- UV-vis. absorption spectra were measured with a Perkin-Elmer Lambda 19 UV-vis. spectrometer.
- NMR spectra were recorded at 25 °C with a Bruker AC 400, or 300 (400 or 300 MHz). All the chemical shifts are reported in parts per million (δ, ppm) with reference to Me4Si for the ^{1}H NMR spectra.
- Transmission Electron Microscopy (TEM) images and High-resolution TEM (HRTEM) images were recorded with the JEOL JEM-2100F.
- X-ray photoelectron spectra (XPS):

System: SPECS SAGE HR, X-Ray source: Mg Kα non-monochromatic, operated at 12.5 kV and 250 W. Take off angle 90°, at ~10-8 Torr. Pass energy for survey spectra 30 eV, 15 eV for narrow scans. Analysis: spectra are calibrated to CC carbon 285 eV. Analysis consisted of Shirley background subtraction. Peaks are fitted with symmetrical Gaussian-Lorentizan (GL) line shapes. Sample is dispersed on silica substrate and evaporated prior to measurement.

- Flash column chromatography was performed using silica gel (300-400 mesh).
- Elemental analyses were recorded on a PAR 273 potentiostat under nitrogen atmosphere.

2. Details of the synthesis

Tetrahydrofuran (THF), acetonitrile (CH_3CN) and dichloromethane (CH_2Cl_2) were refluxed and freshly distilled, Milli-Q water was degassed by N_2 for 10 min to remove O_2 before use.

2.1 Sodium naphthalenide

Sodium naphthalenide was synthesized according to previous report.[S1] Sodium metal (1.1 equiv) was dissolved in a solution of naphthalene (100 mg, 0.78 mmol) in THF (20 mL), the mixture was stirred for 12 h under N_2 atmosphere in a standard Schlenk flask, providing sodium-naphthalenide with green colour.

2.2 Cu(0)NP-PEG, Cu(0)NP-PEG-1 and Cu(I)NP-PEG nanoparticles

$CuSO_4 \cdot 5H_2O$ (2 mg, 8×10^{-3} mmol) were dissolved in 20 mL CH_3CN under nitrogen in a standard Schlenk flask and stirred for 3h at 80°C. The mixture was cooled down to room temperature, and PEG-2000 (43 mg, 2.15×10^{-2} mmol) was added. Thereafter, the fresh sodium-naphthalenide solution was injected in excess into the Schlenk flask, the color of the solution changed from colorless to grey. Crude Cu nanoparticles were dried under vacuum, then extracted using CH_2Cl_2 and degassed H_2O under N_2. The aqueous phase was removed, and the CH_2Cl_2 phase was dried under vacuum. Extraction using degassed H_2O was continued, and CH_2Cl_2 was added under N_2. This operation was repeated 3 times. Then pure aqueous Cu nanoparticles are acquired (denoted as Cu(0)NP-PEG). Crude Cu nanoparticles without purification were dissolved in degassed water (equal volume ratio) to destroy the excess of sodium-naphthalenide). The resulting CuNPs are denoted Cu(0)NP-PEG-1 and the fresh Cu(0)NP-PEG exposed to air 30 min are denoted Cu(I)NP-PEG.

2.3 Preparation of the supported catalyst Cu(I)NP-PEG@SBA-15

The Cu(I)NP-PEG and SBA-15 (pore size 8 nm) with mol ratio 1:300 were dispersed in degassed H_2O and ultra-sonic processed for 1 h, and stirring was conducted for 3 h. The system was kept overnight without stirring under N_2. Thereafter, the CuNPs were centrifugated with washing by deionezed water 3 times and dried at 50°C. The ICP content is 0.06 wt%.

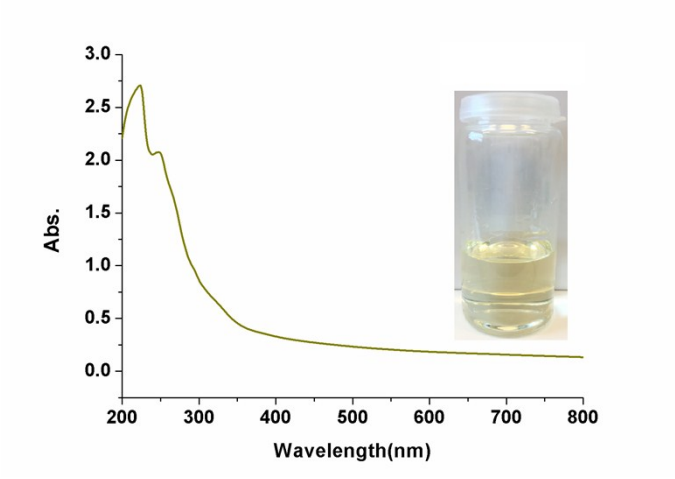


Figure S1. UV-vis. spectrum of pure Cu(0)NP-PEG nanoparticles.

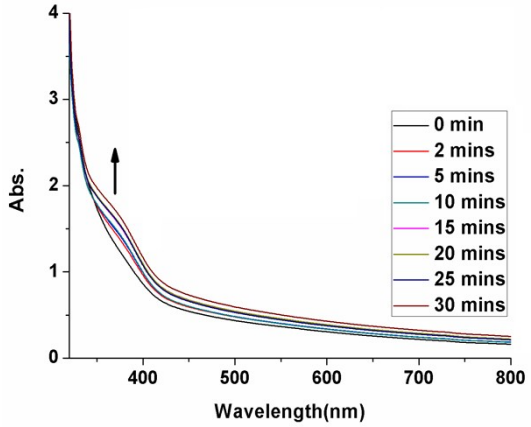


Figure S2. UV-vis. spectrum of the conversion from Cu(0)NP-PEG to Cu(I)NP-PEG in air.

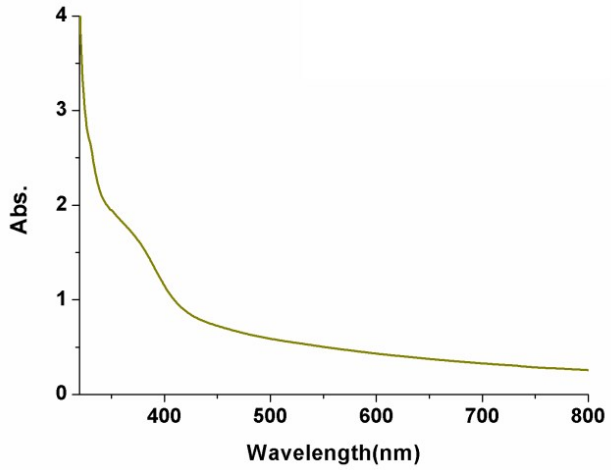


Figure S3. UV-vis. spectrum of Cu(0)NP-PEG exposed in air for 1 day leading to (Cu(I)NP-PEG).

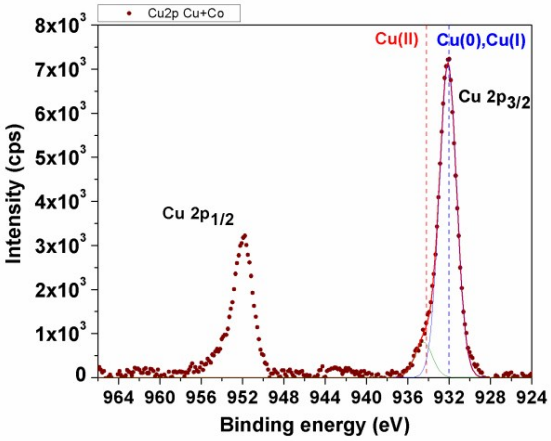


Figure S4. X-ray photoelectron spectroscopy of Cu(I)NP-PEG.

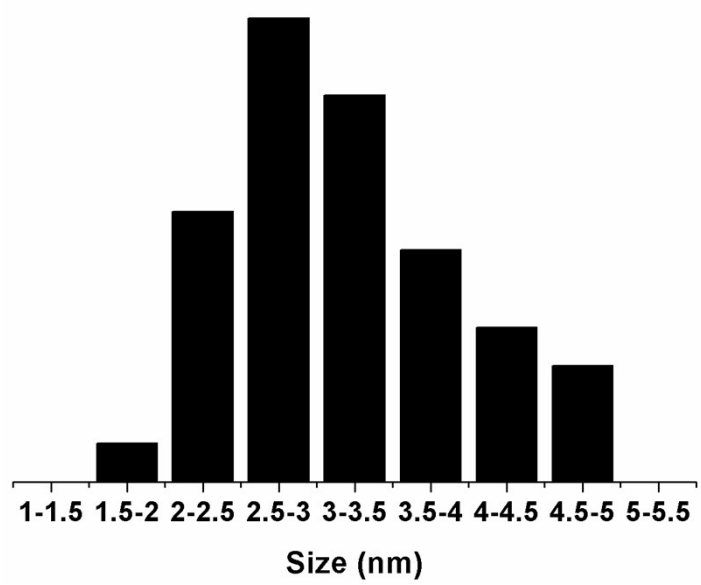


Figure S5. Histogram of Cu(I)NP-PEG nanoparticles.

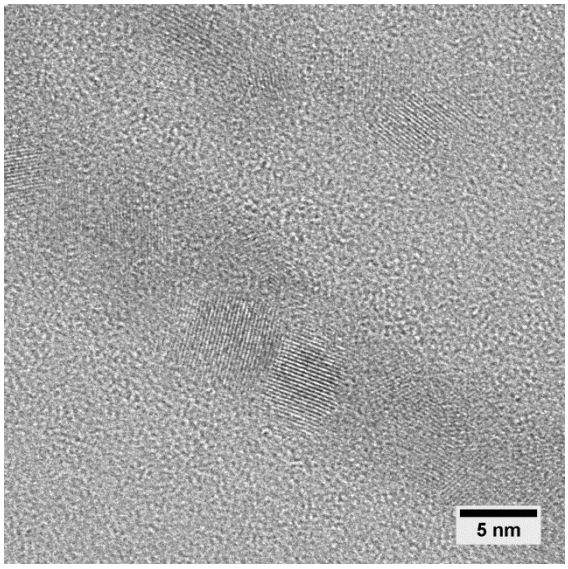


Figure S6. HRTEM of the Cu(I)NP-PEG catalyst.

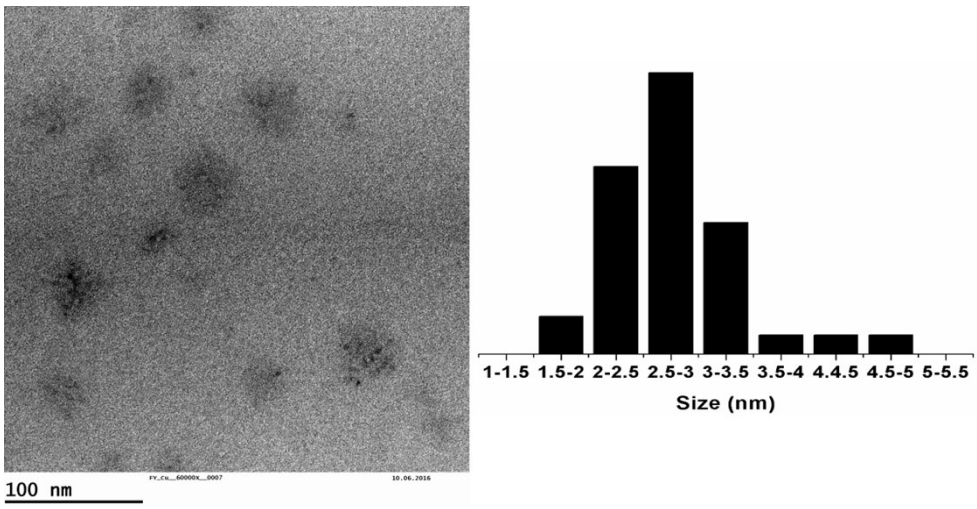


Figure S7. TEM image (left) and histogram (right) of Cu(I)NP-PEG-1 nanoparticles (without purification).

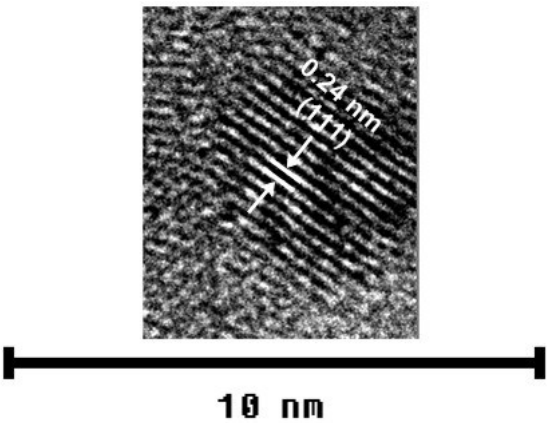


Figure S8. HRTEM of Cu(I)NP-PEG nanoparticle (0.4 nm)

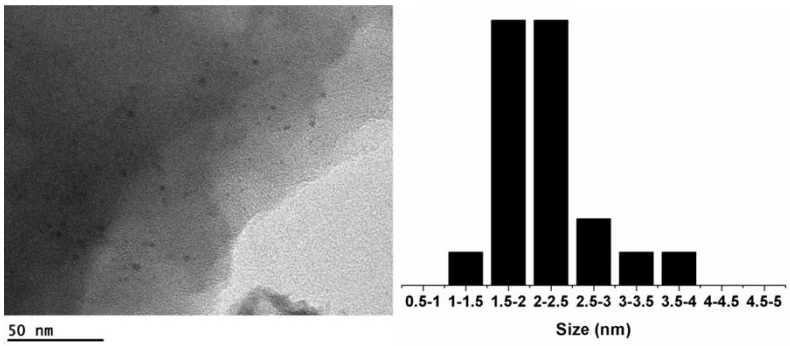
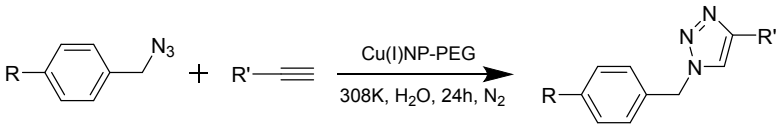


Figure S9. TEM image (left) and histogram (right) of the catalyst Cu(I)NP-PEG@SBA-15.

3. General procedure for the azide-alkyne cycloaddition reaction catalyzed by Cu(I)NP-PEG.

A glass vessel equipped with a magnetic stir bar was charged with 0.5 mmol of benzyl azide and 0.505 mmol of phenylacetylene under N_2. The catalyst was added into the vessel under N_2, and deionezed water was added in order to obtain a given volume of aqueous solution (2 mL). The reaction mixture was then stirred for 24 h at 35 °C under N_2. After the reaction, the final product was extracted from water with CH_2Cl_2 (3 x 15 mL). The organic layer was dried over Na_2SO_4 and filtered, and the solvent was removed under vacuum to give the 1-benzyl-4-phenyl-1H-[1,2,3] triazole. The purity of the crude product was checked by ^{1}H NMR in order to calculate the conversion. In parallel, the reaction was checked using TLC. The product was then purified by silica chromatography when necessary.

Table S1. Substrates for the CuAAC reactions between various azides and alkynes using the catalyst Cu(I)NP-PEG.[a]



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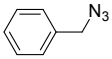
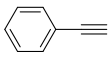
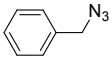
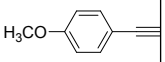
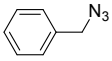
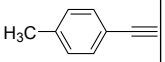
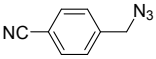
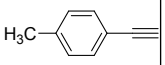
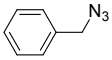
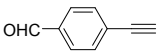
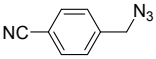
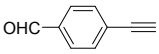
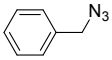
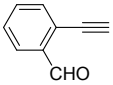
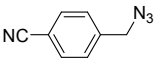
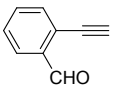
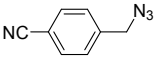
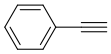
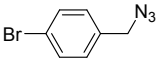
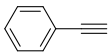
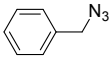
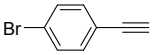
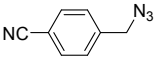
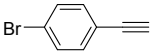
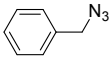
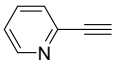
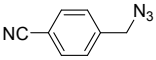
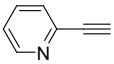
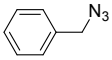
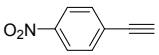
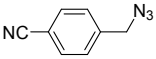
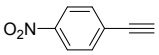
1	100 (in air)			95 (80)
2	200			92
3	200			93
4	200			82
5	200			90
6	200			85
7	200			95
8	200			75
9	200			86
10	200			92
11	200			81
12	200			90
13	200			84
14	200			95
15	200			87
16	200			93

[a] Reaction conditions: 0.5 mmol of azide, 0.505 mmol of alkyne, 2 mL H_2O, 35°C, 24 h, under N_2. [b] Amount of catalyst used in the catalyzed CuAAC reduction. [c] Isolated yield.

4. Procedure for the "click"functionalization of biomedical compounds

Taking the synthesis of (1-benzyl-1H-[1,2,3]triazol-4-yl)- cyclohexylmethanol (compound **2**) as the example:

A glass vessel equipped with a magnetic stirring bar was charged with 1-ethynylcyclohexanol (0.505 mmol,) and 0.5 mmol of benzyl azide under N_2 atmosphere. The Cu(I)NP-PEG@SBA-15 catalyst (1000 ppm) was added into the vessel under N_2, and deionized water and *tert*-butanol (1:1) were added in order to obtain 2 mL as the total volume. The reaction mixture was stirred during 24 h at 35 °C, the white solid formed. After the reaction, *tert*-butanol was removed under vacuum and the final product was extracted from water with CH_2Cl_2 (3 x 15 mL). The organic layer was dried over Na_2SO_4 and filtrated, the solvent was removed in vacuo and washed twice with Et_2O to yield the pure product.

5. Recycling of the Cu(I)NP-PEG@SBA-15 catalyst

The catalyst Cu(I)NP-PEG@SBA-15 was well dispersed in water and insoluble in CH_2Cl_2. After the CuAAC reaction, extraction of the "click" products by water and CH_2Cl_2 was conducted several times, then the aqueous solution was centrifugated with washing by deionized water 3 times, and the white solid was directly used for the next catalytic run.

Table S2. Recycling results of CuAAC reactions between benzyl azide and phenylacetylene using 300 ppm of Cu(I)NP-PEG@SBA-15 (ICP content: 0.06 wt%).

Catalytic runs	1st	2nd	3rd	4th	5th
Yield (%)	97	95	90	92	89

6. Characterization of the click products by ^{1}H NMR spectroscopy

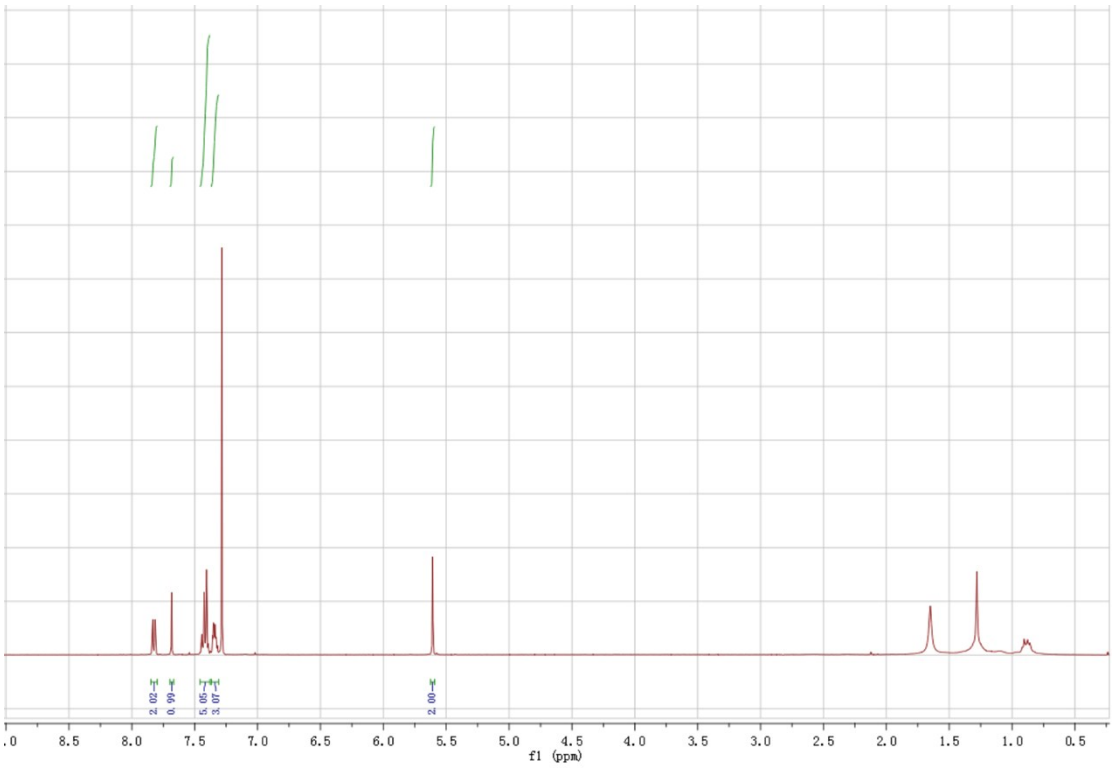


Figure S10. ^{1}H NMR spectrum of 1-benzyl-4-phenyl-1H-[1,2,3]triazole.[S2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.68 (s, 1H), 7.46 – 7.38 (m, 5H), 7.37 – 7.31 (m, 3H), 5.61 (s, 2H).

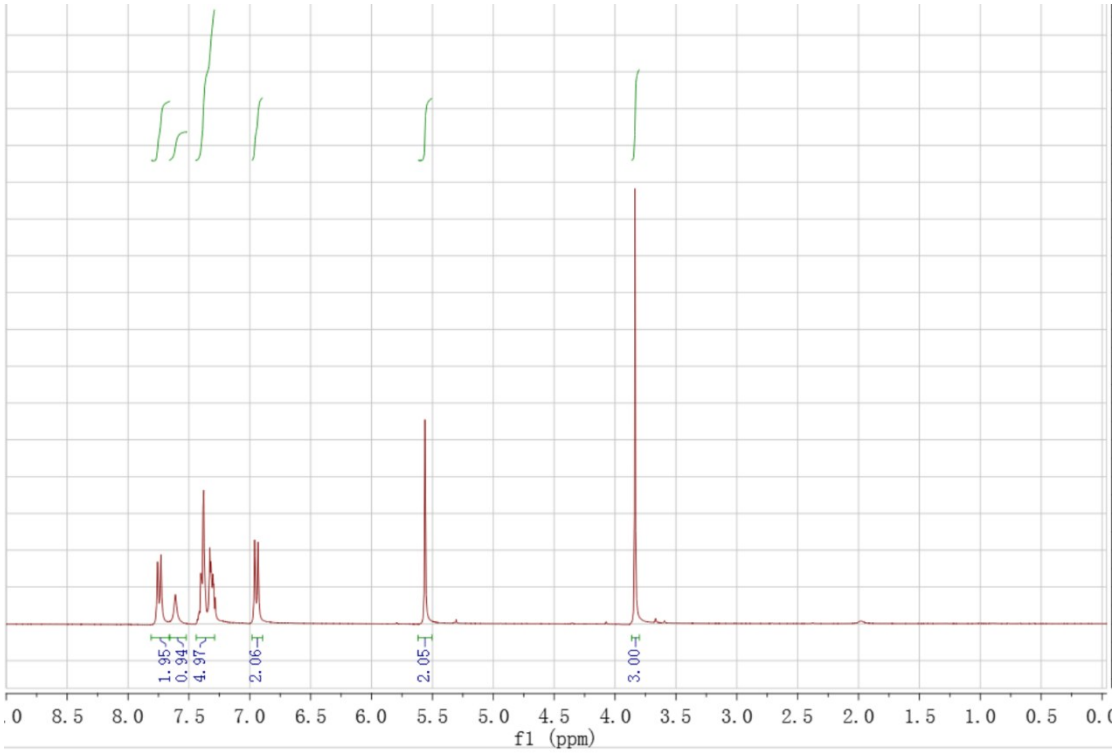


Figure S11. ^{1}H NMR spectrum of 1-benzyl-4-(4-methoxyphenyl)-1H-1, 2,3- triazole.[S3]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (t, *J* = 15.3 Hz, 2H), 7.61 (s, 1H), 7.44 – 7.29 (m, 5H), 6.95 (d, *J* = 8.6 Hz, 2H), 5.56 (s, 2H), 3.84 (s, 3H).

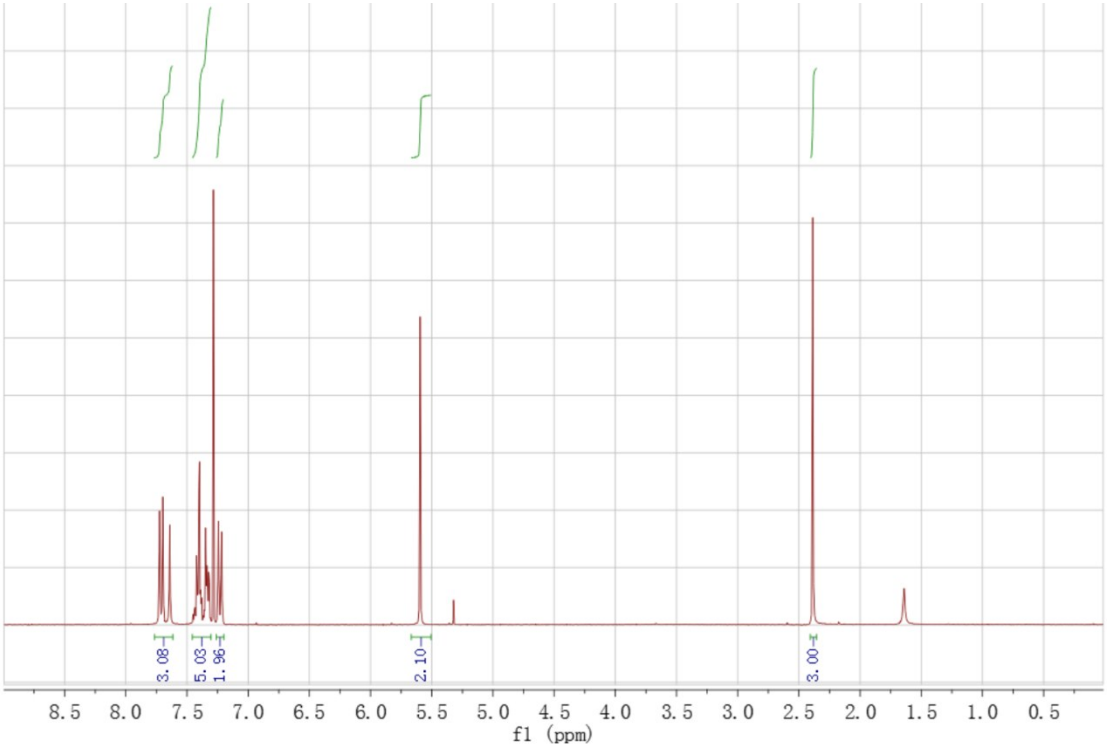


Figure S12. ^{1}H NMR spectrum of 1-benzyl-4-(p-tolyl)-1H-1,2,3-triazole.[S3]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 – 7.62 (m, 3H), 7.46 – 7.30 (m, 5H), 7.23 (d, *J* = 7.9 Hz, 2H), 5.60 (s, 2H), 2.39 (s, 3H).

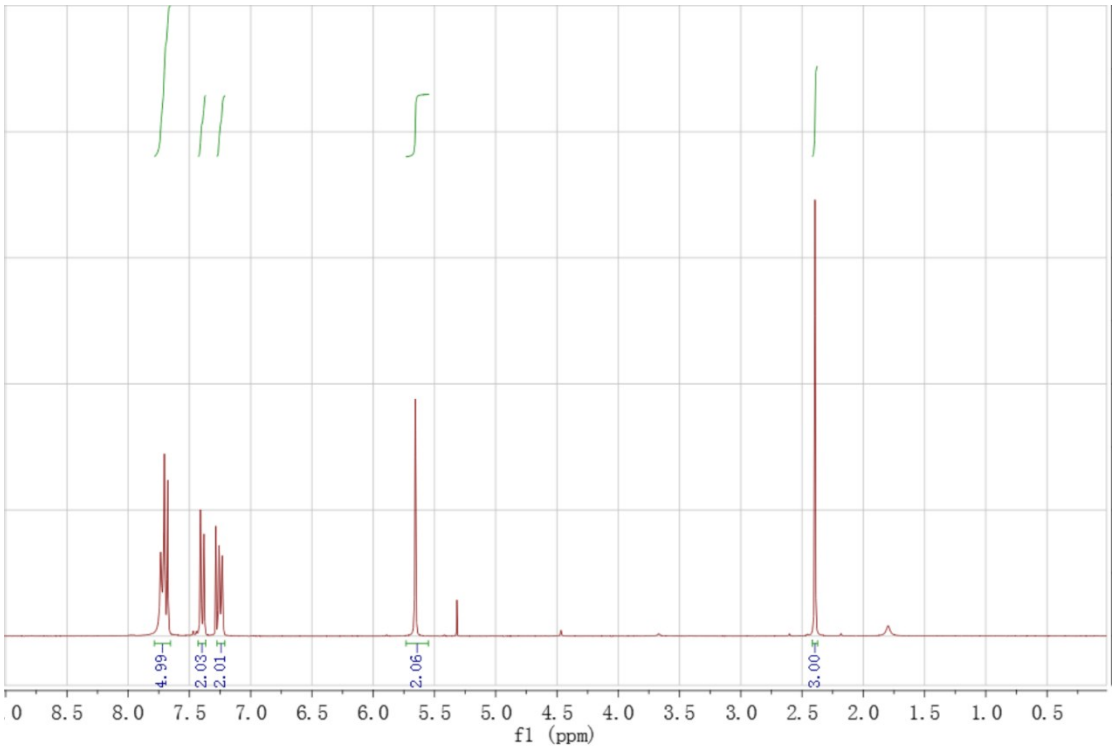


Figure S13. ^{1}H NMR spectrum of 4 -((4-(p-tolyl)-1H-1,2,3-triazol-1-yl) methyl) benzonitrile.[S4]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 12.0, 5.4 Hz, 5H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 5.66 (s, 2H), 2.39 (s, 3H).

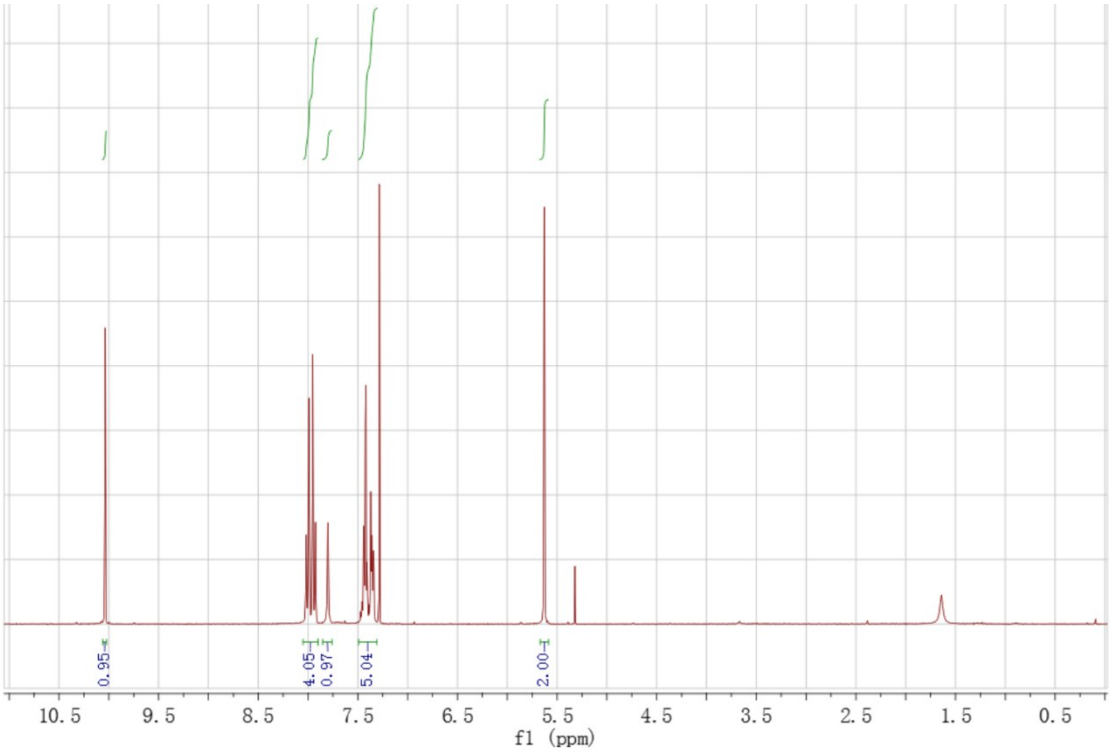


Figure S14. ^{1}H NMR spectrum of 4-(1-benzyl-1H-1,2,3-triazol-4-yl) benzaldehyde.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.97 (q, *J* = 8.4 Hz, 4H), 7.80 (s, 1H), 7.49 – 7.31 (m, 5H), 5.63 (s, 2H).

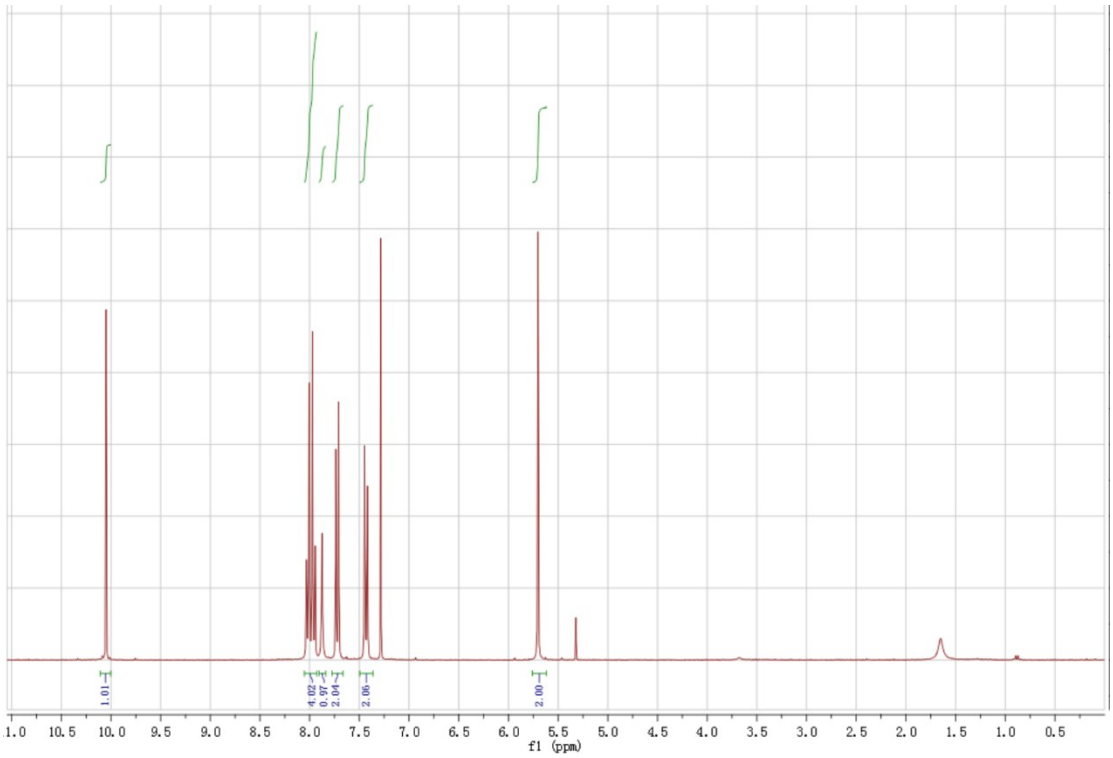


Figure S15. ^{1}H NMR spectrum of 4-((4-(4-formylphenyl)-1H-1,2,3- triazol-1-yl) methyl) benzonitrile.

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.99 (q, *J* = 8.4 Hz, 4H), 7.88 (s, 1H), 7.78 – 7.66 (m, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 5.70 (s, 2H).

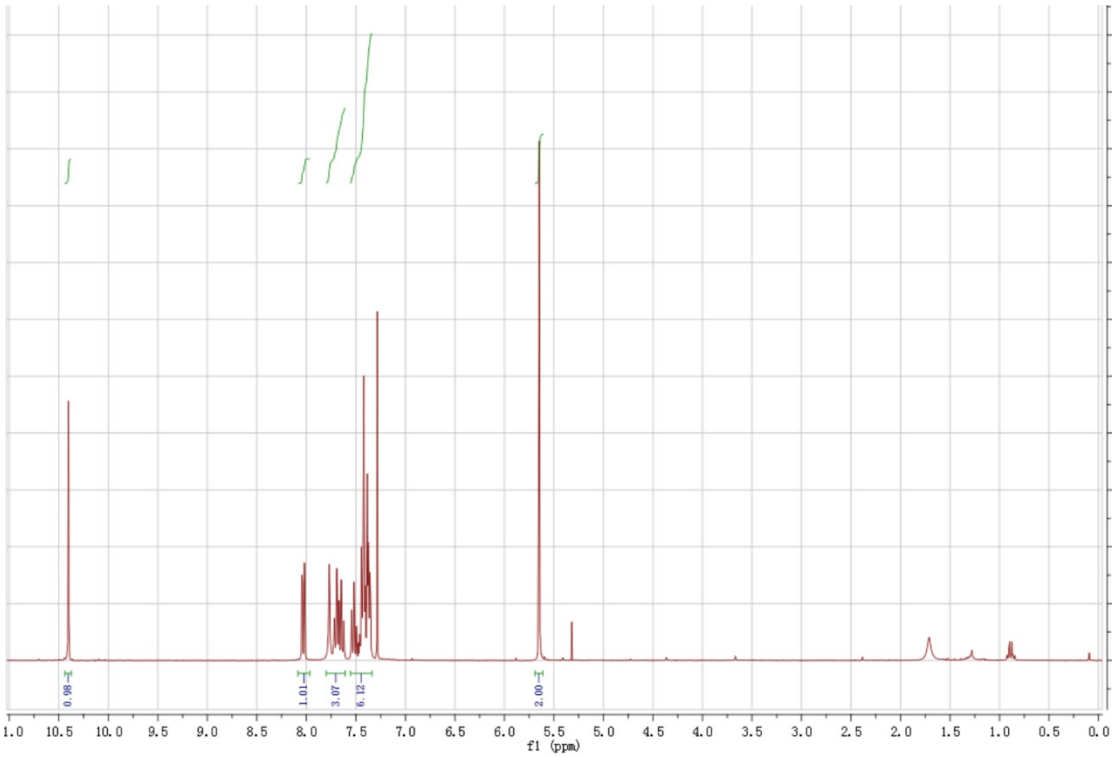


Figure S16. ^{1}H NMR spectrum of 2-(1-benzyl-1H-1,2,3-triazol-4-yl) benzaldehyde.[S5]

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.40 (d, *J* = 0.6 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.80 – 7.61 (m, 3H), 7.56 – 7.34 (m, 6H), 5.65 (s, 2H).

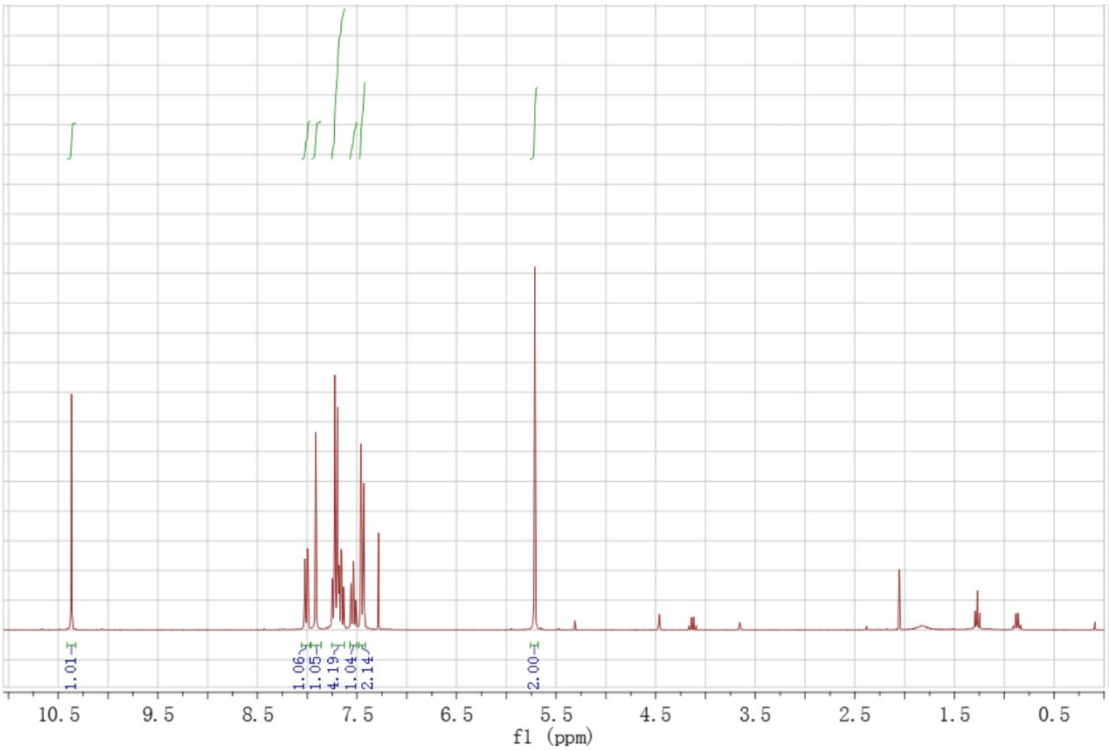


Figure S17. ^{1}H NMR spectrum of 4-((4-(2-formylphenyl)-1H-1,2,3- triazol-1-yl) methyl) benzonitrile.

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.37 (d, *J* = 0.5 Hz, 1H), 8.00 (dt, *J* = 7.7, 3.8 Hz, 1H), 7.91 (s, 1H), 7.75 – 7.63 (m, 4H), 7.57 – 7.50 (m, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 5.71 (s, 2H).

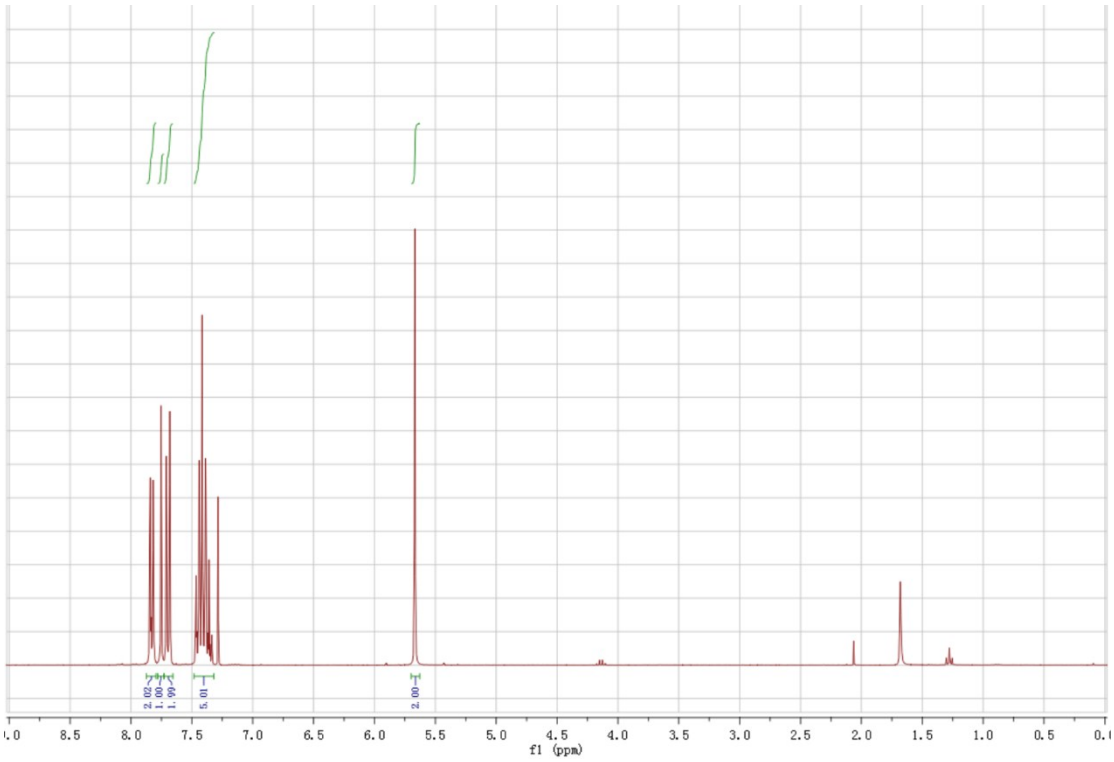


Figure S18. ^{1}H NMR spectrum of 4-((4-phenyl-1H-1,2,3-triazol-1-yl) methyl) benzonitrile.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.79 (m, 2H), 7.75 (s, 1H), 7.73 – 7.66 (m, 2H), 7.48 – 7.32 (m, 5H), 5.67 (s, 2H).

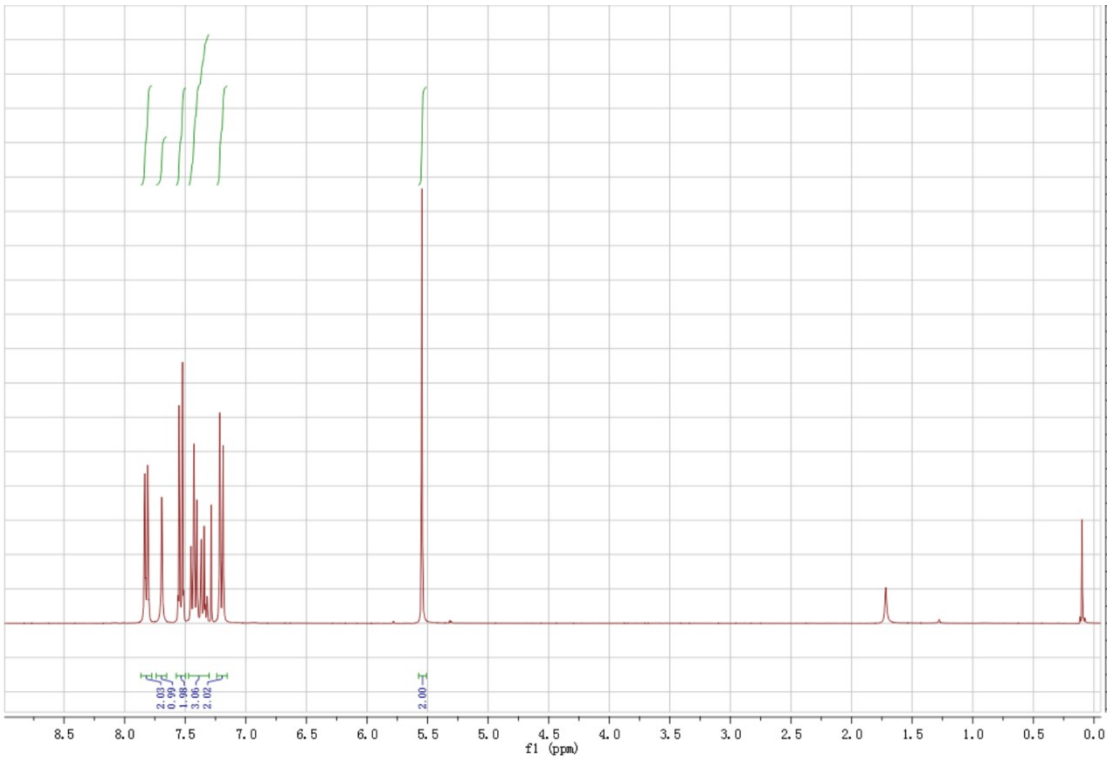


Figure S19. ^{1}H NMR spectrum of 1-(4-bromobenzyl)-4- phenyl-1H-1,2,3- triazole.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.77 (m, 2H), 7.69 (s, 1H), 7.57 – 7.50 (m, 2H), 7.47 – 7.30 (m, 3H), 7.24 – 7.15 (m, 2H), 5.55 (s, 2H).

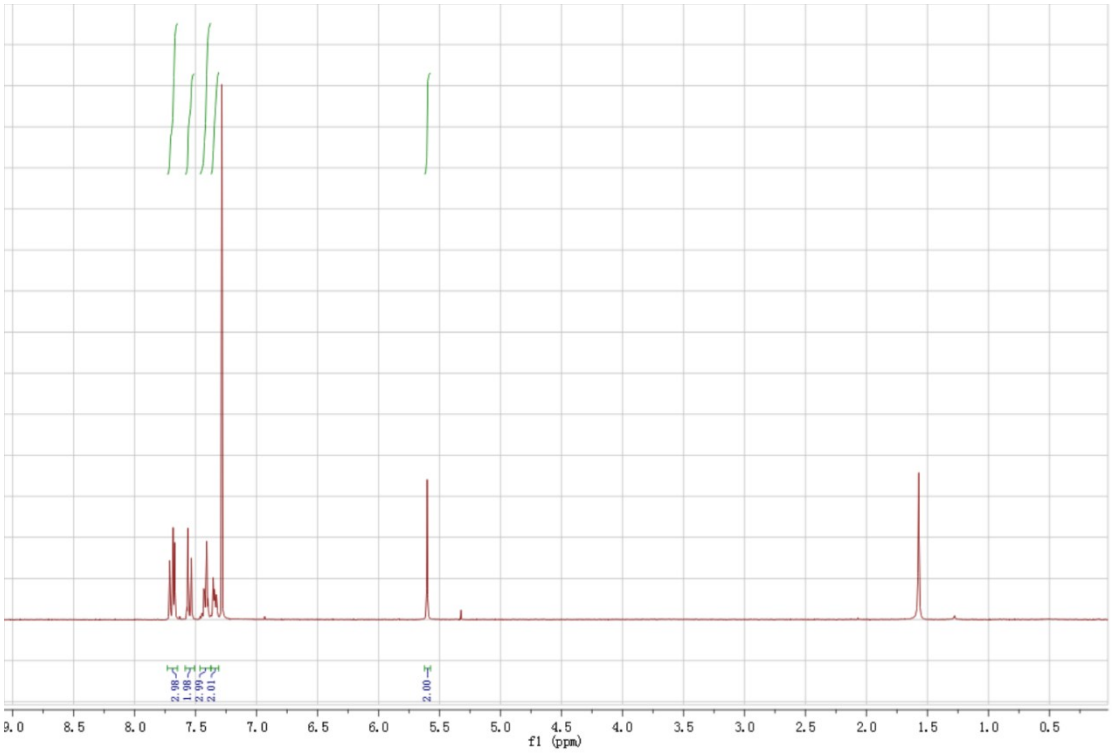


Figure S20. ^{1}H NMR spectrum of 1-benzyl-4- (4-bromophenyl)-1H -1,2,3- triazole.[S3]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (dt, *J* = 10.4, 3.0 Hz, 3H), 7.58 – 7.51 (m, 2H), 7.46 – 7.38 (m, 3H), 7.37 – 7.31 (m, 2H), 5.60 (s, 2H).

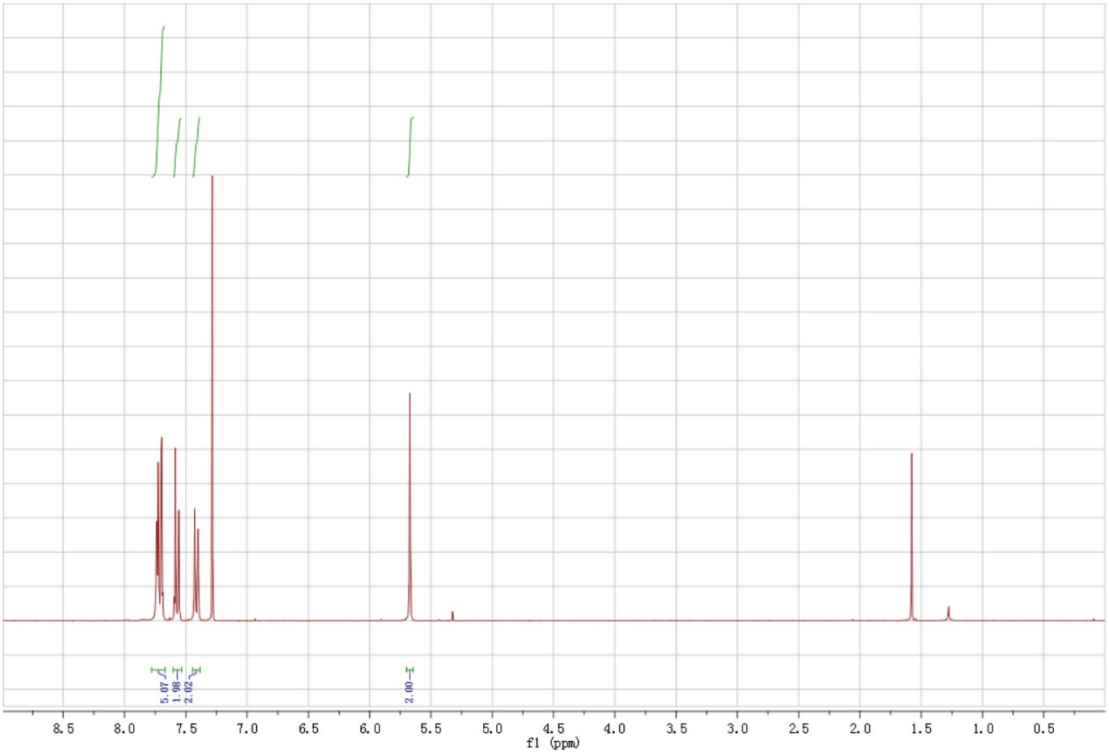


Figure S21. ^{1}H NMR spectrum of 4-((4-(4-bromophenyl)-1H-1,2,3- triazol-1-yl) methyl) benzonitrile.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.67 (m, 5H), 7.60 – 7.53 (m, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 5.67 (s, 2H).

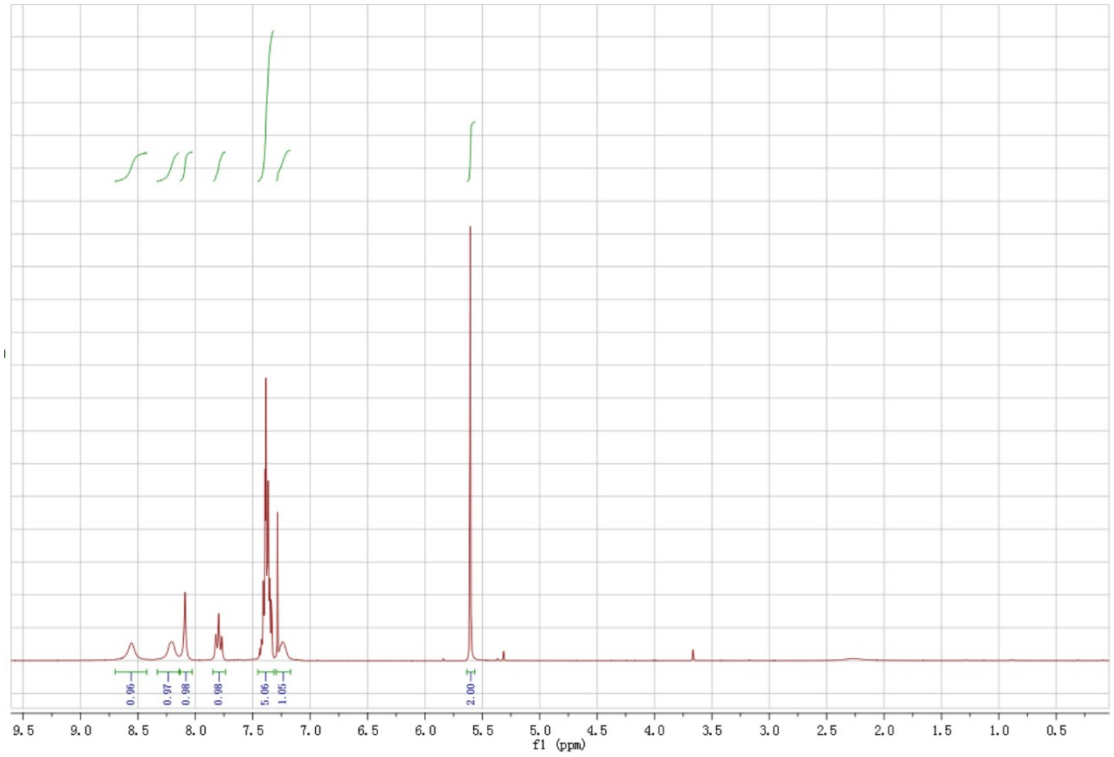


Figure S22. ^{1}H NMR spectrum of 2-(1-benzyl-1H-1,2,3-triazol-4-yl) pyridine.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 (s, 1H), 8.09 (s, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.46 – 7.31 (m, 5H), 7.26 (d, *J* = 13.1 Hz, 1H), 5.60 (s, 2H).

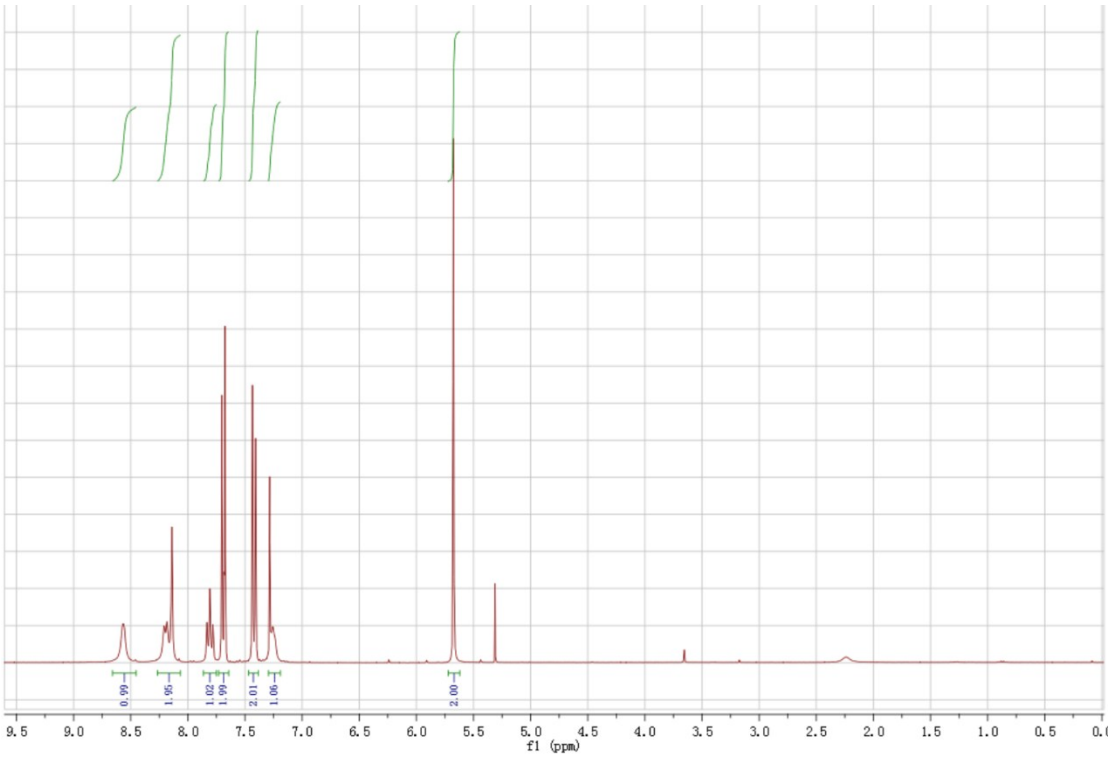


Figure S23. ^{1}H NMR spectrum of 4-((4-(pyridin-2-yl)-1H-1,2,3- triazol-1-yl) methyl) benzonitrile.[S6]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, *J* = 32.5 Hz, 1H), 8.27 – 8.06 (m, 2H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 7.7 Hz, 1H), 5.68 (s, 2H).

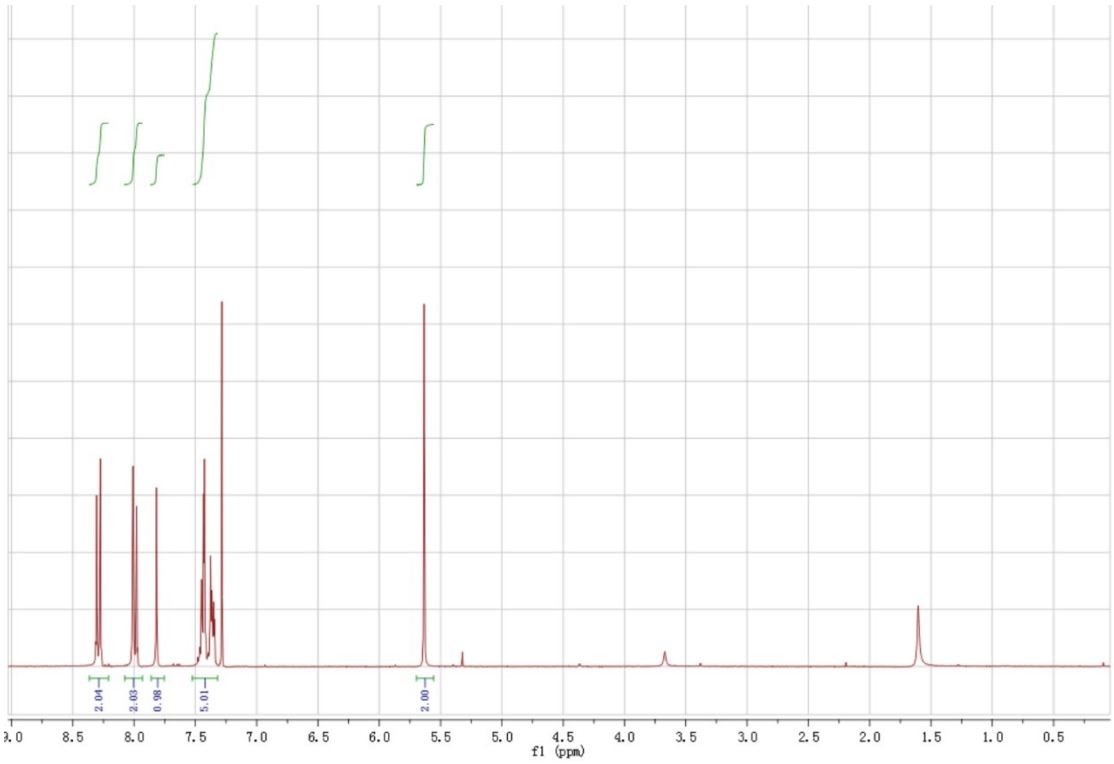


Figure S24. ^{1}H NMR spectrum of 1-benzyl-4-(4-nitrophenyl)-1H-1,2,3- triazole.[S7]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 – 8.21 (m, 2H), 8.08 – 7.93 (m, 2H), 7.82 (s, 1H), 7.52 – 7.32 (m, 5H), 5.63 (s, 2H).

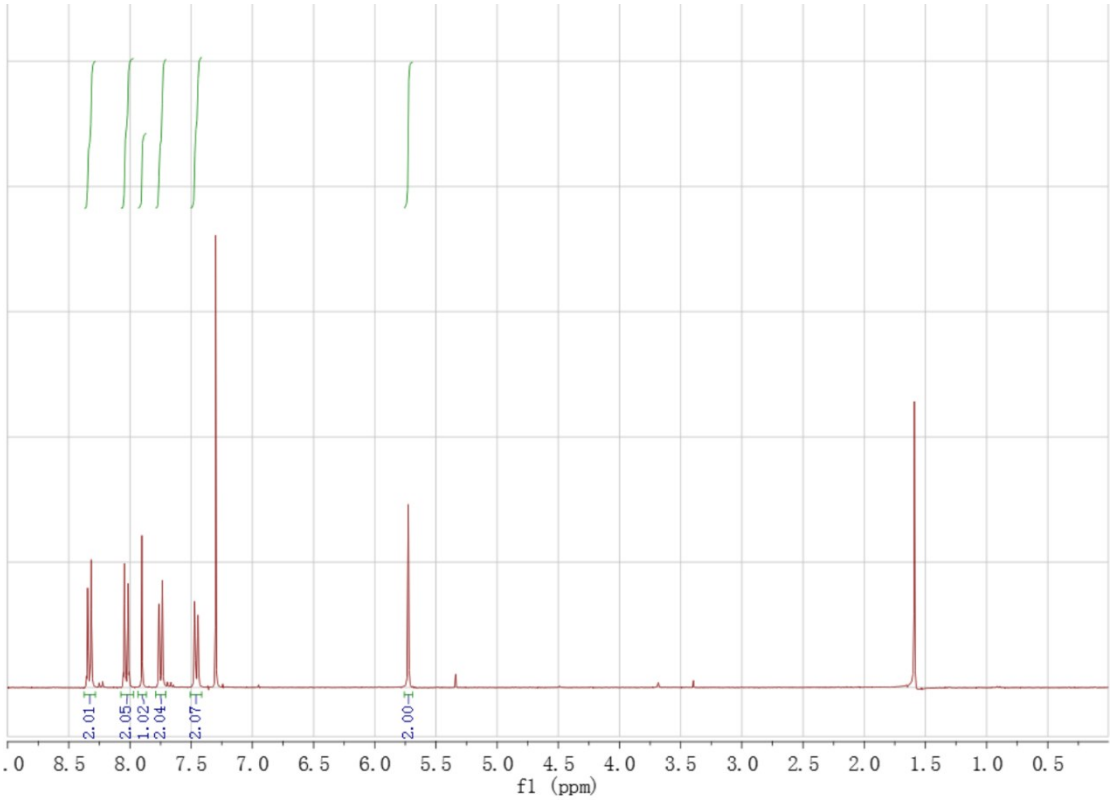


Figure S25. ^{1}H NMR spectrum of 4-((4-(4-nitrophenyl)-1H-1,2,3- triazol-1-yl) methyl) benzonitrile.[S7]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 – 8.28 (m, 2H), 8.07 – 7.97 (m, 2H), 7.90 (s, 1H), 7.79 – 7.71 (m, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 5.73 (s, 2H).

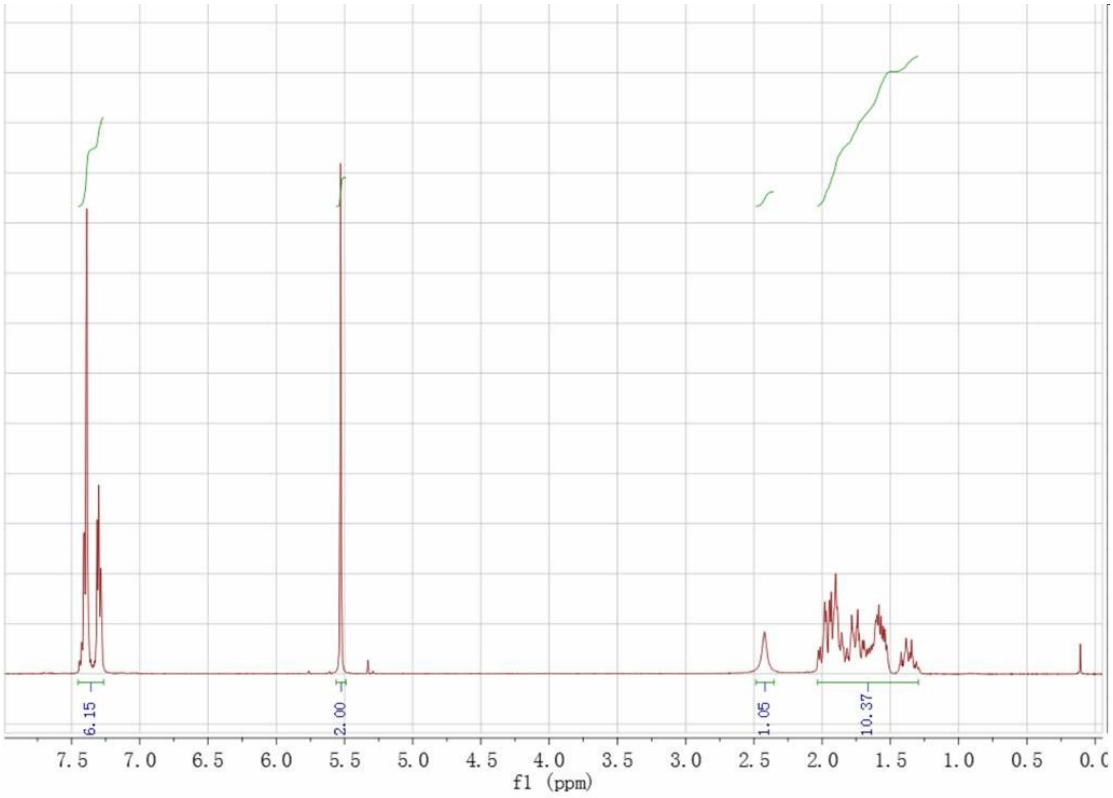


Figure S26. ^{1}H NMR spectrum of (1-benzyl-1H-[1,2,3]triazol-4-yl)- cyclohexylmethanol.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.26 (m, 6H), 5.53 (s, 2H), 2.42 (s, 1H), 2.03 – 1.30 (m, 10H).

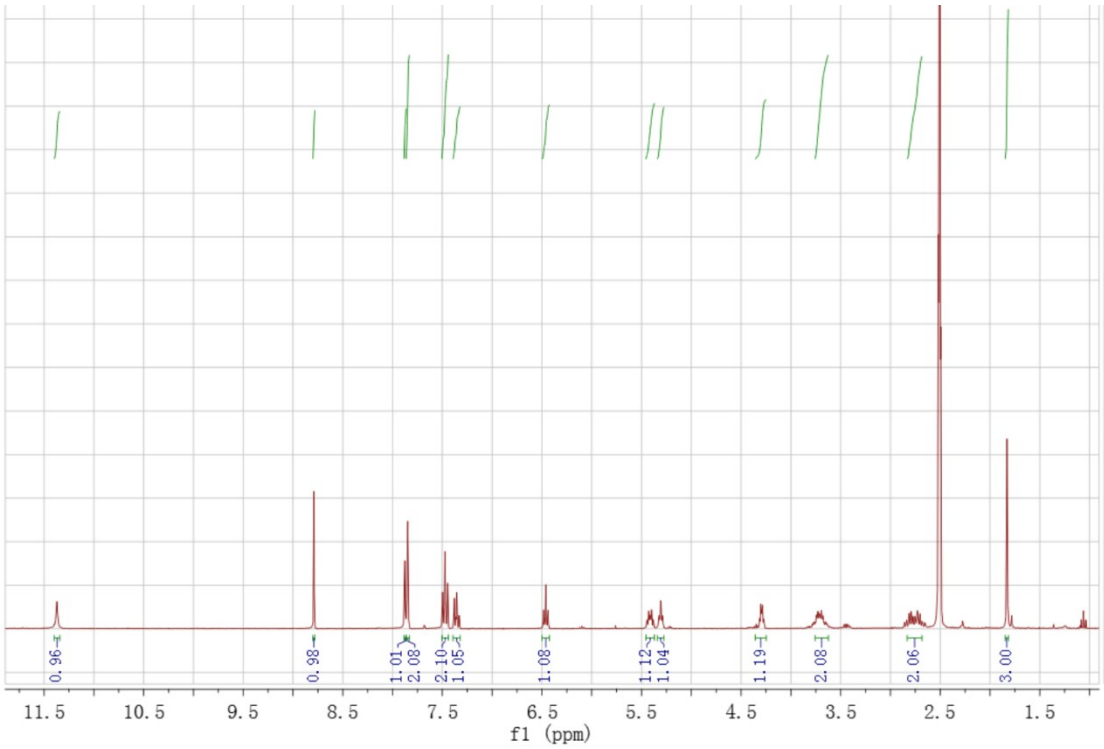


Figure S27. ^{1}H NMR spectrum of compound 4.[S8]

^{1}H NMR (300 MHz, DMSO) δ 11.37 (s, 1H), 8.79 (s, 1H), 7.86 (dt, *J* = 7.4, 1.3 Hz, 3H), 7.54 – 7.42 (m, 2H), 7.42 – 7.29 (m, 1H), 6.46 (t, *J* = 6.6 Hz, 1H), 5.41 (dt, *J* = 8.7, 5.6 Hz, 1H), 5.35 – 5.19 (m, 1H), 4.29 (dd, *J* = 9.0, 3.5 Hz, 1H), 3.79 – 3.61 (m, 2H), 2.75 (tdd, *J* = 14.1, 11.3, 6.7 Hz, 2H), 1.83 (d, *J* = 1.1 Hz, 3H).

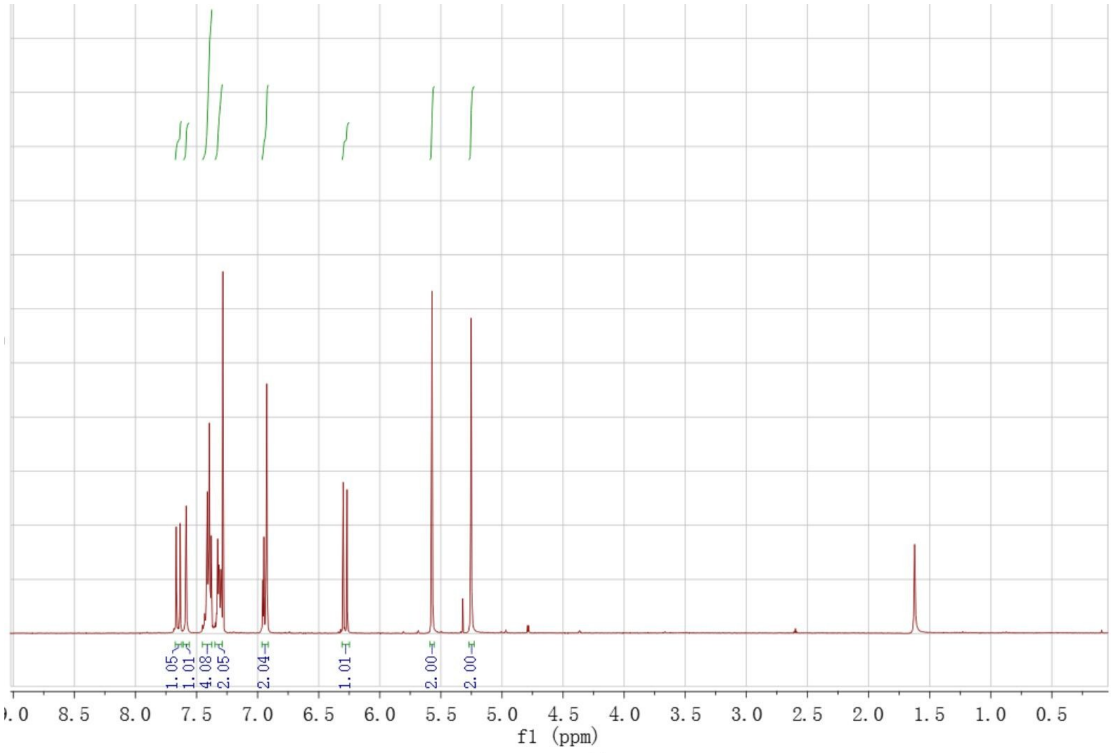


Figure S28. ^{1}H NMR spectrum of compound 6.[S2]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 – 7.62 (m, 1H), 7.58 (s, 1H), 7.41 (dtd, *J* = 6.5, 4.7, 1.9 Hz, 4H), 7.35 – 7.29 (m, 2H), 6.94 (dd, *J* = 7.5, 2.1 Hz, 2H), 6.31 – 6.25 (m, 1H), 5.57 (s, 2H), 5.25 (s, 2H).

7. References

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