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Full Paper

Alkyne–Azide Cycloaddition

Magnetically Recoverable Cu^0/Fe_3O_4-Catalysed One-Pot Tandem Synthesis of Sulfur-Containing Triazoles from Alkynes and Azide: DMSO Acts as an Alkylating Agent

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Abstract: An efficient one-pot tandem nano Cu^0/Fe_3O_4-catalysed synthesis of sulfur-containing triazoles from alkynes and azide has been developed. In this newly developed method, the readily available TMS-azide and dimethyl sulfoxide act as nitrogen and sulfur sources, respectively. The catalyst was magnetically recovered and reused six times without any significant loss of activity.

Introduction

1,2,3-Triazoles and their derivatives are some of the most well-known five-membered nitrogen-containing heterocycles by virtue of their frequent appearance in a large number of biologically and pharmaceutically relevant molecules, agrochemicals, and functional materials.[1] The fact that several of these molecules have been found to show different potent biological activities, such as anti-HIV,[2] anticancer,[3] antimicrobial,[4] and b3-adrenergic receptor agonist[5] activities, has aroused substantial interest among medicinal chemists. In the recent past, sulfur-containing triazoles in particular have also gained huge momentum, due to their presence in a wide variety of therapeutically interesting drug candidates, such as mPGES-1 and anti-inflammatory agents.[6] Despite their being an integral part of life-saving drugs, surprisingly, the synthesis of sulfur-containing triazoles remains rather underexplored.[7] The methods available in the literature have various disadvantages, such as harsh reaction conditions, expensive starting materials, long reaction times, and laborious and complex work-up procedures. Furthermore, the recovery and reusability of the catalyst is probably one of the great challenges associated with these methods. Therefore, the development of a new catalytic system to overcome these shortcomings and fulfil the criteria of a mild, efficient, and environmentally benign protocol for the synthesis of substituted triazoles would be highly desirable.

In recent years, heterogeneous catalysts, particularly magnetite-supported copper nanoparticles, are increasingly being used for various functional-group transformations in organic reactions.[8] Such catalysts have high thermal and mechanical stability along with a high surface area to increase the number of catalytic active sites.[9] Furthermore, their unique paramagnetic nature and inherent insolubility in most reaction solvents allows them to be simply and efficiently separated from reaction mixtures using an external magnet, in an economical, practical, and environmentally benign way.[10] Recently, our group have prepared Cu^0/Al_2O_3 and magnetically separable Cu^0/Fe_3O_4 nanocatalysts, and successfully demonstrated their catalytic activities in alkyne–isocyanide cycloaddition reactions to give synthetically challenging 2,4-disubstitiuted pyrroles and 2,3,4 trisubstitiuted pyrroles, respectively.[11,12] In a continuation of this research programme, we report in this paper our new findings on the synthesis of sulfur-containing triazoles from terminal alkynes and azide in the presence of a magnetically separable and reusable nano Cu^0/Fe_3O_4 catalyst (Figure 1).

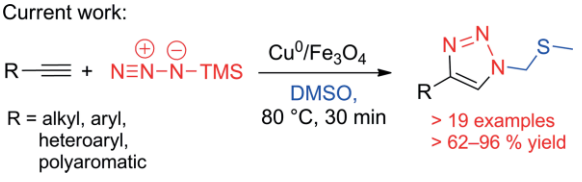

Figure 1. Cu^0/Fe_3O_4-catalysed alkyne–azide click reaction.

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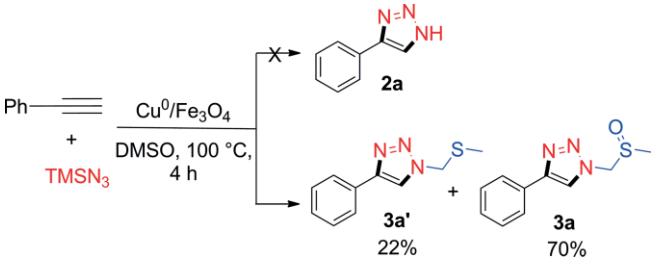
Results and Discussion

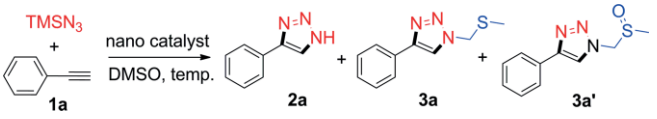
We chose phenylacetylene (**1a**) and $TMSN_3$ (TMS = trimethylsilyl) as model substrates to start our study. When a mixture of phenylacetylene (**1a**; 1.0 mmol), $TMSN_3$ (1.10 mmol), and freshly prepared Cu^0/Fe_3O_4 (90 mg) in DMSO (2.0 mL) was heated at 100 °C for 4 h under a nitrogen atmosphere, the corresponding sulfur-containing 1,2,3-triazole (i.e., **3a**) was obtained in 70 % yield, along with partially oxidised product **3a′** in 22 % yield (Scheme 1). It is worth noting that under these catalytic conditions, the expected 4-phenyl-1*H*-1,2,3-triazole (**2a**) was not detected, even in a trace amount. At this stage, the structure of the unexpected product (i.e., **3a**) was well characterised using all spectroscopic techniques, and the ultimate structural proof of **3a** was obtained by single-crystal X-ray diffraction analysis (Figure 2). Since this reaction represents an efficient and mild route to pharmaceutically valuable sulfur-containing triazoles, we systematically carried out an extensive optimisation of the reaction conditions (Table 1).



Scheme 1. Cu^0/Fe_3O_4-catalysed unexpected formation of **3a** from phenylacetylene (**1a**) and $TMSN_3$ in DMSO at 100 °C under nitrogen.

In order to minimise the formation of the undesired product (i.e., **3a′**), we initially decreased the catalyst loading (to 60 from 90 mg). However, under these conditions, **3a** and **3a′** were obtained in 75 and 15 % yields, respectively (Table 1, entry 2). Further decreasing the catalyst loading (to 30 mg) did not help much, and **3a** and **3a′** were produced in a similar ratio (Table 1, entry 3). Increasing the reaction temperature was also found to be less effective, and produced a poor yield of the desired product (i.e., **3a**; Table 1, entry 4). However, when the reaction temperature was decreased to 80 °C, the desired product (i.e., **3a**) was obtained in 76 % yield, along with **3a′** in in 20 % yield (Table 1, entry 5). Further decreasing the temperature (60 °C) produced **3a** and **3a′** in lower yields (Table 1 entry 6). In contrast, when the reaction time was decreased to 2 h from 4 h, we surprisingly obtained the desired product (i.e., **3a**) in 85 % yield, along with **3a′** in 10 % yield (Table 1, entry 7). Further decreasing the reaction time (1 h) gave **3a′** in 90 % yield, along with a trace amount of the undesired **3a′** (Table 1, entry 8). To our delight, when the reaction was quenched after 0.5 h, the desired product (i.e., **3a**) was obtained as the sole product in 96 % yield (Table 1, entry 9).

Table 1. Optimisation of the reaction conditions.[a]



Entry	Catalyst (mg)	*T* [°C]	Time [h]	Isolated yield [%][d]		
				2a	**3a**	**3a′**
1	Cu^0/Fe_3O_4 (90)	100	4	n.o.	70	22
2	Cu^0/Fe_3O_4 (60)	100	4	n.o.	75	15
3	Cu^0/Fe_3O_4 (30)	100	4	n.o.	75	15
4	Cu^0/Fe_3O_4 (30)	120	4	n.o.	65	27
5	Cu^0/Fe_3O_4 (30)	80	4	n.o.	76	20
6	Cu^0/Fe_3O_4 (30)	60	4	n.o.	53	20
7	Cu^0/Fe_3O_4 (30)	80	2	n.o.	85	10
8	Cu^0/Fe_3O_4 (30)	80	1	n.o.	90	trace
9	Cu^0/Fe_3O_4 (30)	80	0.5	n.o.	96	n.o.
10	Cu^0/Fe_2O_3 (30)	80	0.5	10	65	n.o.
11	Cu^0/Al_2O_3 (30)	80	0.5	70	n.o.	n.o.
12	Cu^0/(rGO) (30)	80	0.5	58	10	n.o.
13	Cu^0/polymer(30)	80	0.5	67	8	n.o.
14	Cu^0/Fe_3O_4 (30)	80	0.5	86	no	n.o.[b]
15	Cu^0/Fe_3O_4 (30)	80	0.5	n.o.	61	n.o.[c]

[a] Reaction was carried out using phenylacetylene (**1a**; 1.0 mmol), $TMSN_3$ (1.10 mmol) and Cu^0/Fe_3O_4 (30 mg) in DMSO (2.0 mL) at 80 °C for 0.5 h under nitrogen. [b] NaN_3 was used as an azide source. [c] DPPA (diphenylphosphoryl azide) was used as an azide source. [d] Isolated yields; n.o.: not obtained.

We screened various copper nanocatalysts for this reaction, including Cu^0/Fe_2O_3, Cu^0/Al_2O_3, Cu^0/graphene oxide, and Cu^0/

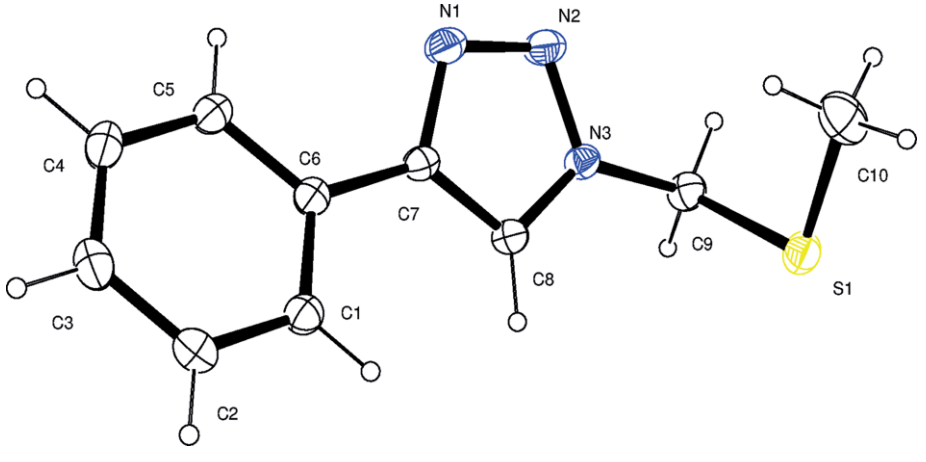
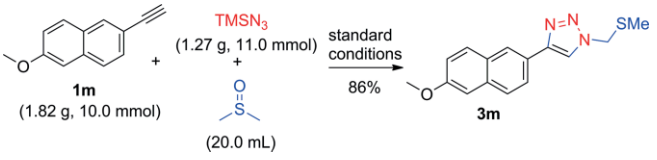


Figure 2. ORTEP diagram of **3a** with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30 % probability level, and hydrogen atoms are shown as small spheres of arbitrary radius.[14]

polymer. Most of them were found to be less efficient, and produced undesired product **2a** in very high yields, except for Cu^0/Fe_2O_3, which gave the desired product (i.e., **3a**) in 65 % yield (Table 1 entries 10–13). The bimetallic nature of the Cu/iron-oxide catalyst could be responsible for the formation of unexpected sulfur-containing triazole **3a** under these catalytic conditions.[13] It is also important to note that, the reaction was completely shut down when NaN_3 was used as the source of azide (Table 1 entry 14). However, a 61 % yield of the desired product (i.e., **3a**) was obtained when DPPA (diphenylphosphoryl azide) was used as the azide source (Table 1, entry 15).

Having optimised the reaction conditions (Table 1 entry 9), we evaluated the substrate scope of this reaction with respect to various alkyl/aryl alkynes. The results are summarised in Table 2. We were pleased to see that various aromatic alkynes bearing both electron-donating and -withdrawing groups underwent the azide–alkyne cycloaddition to give the corresponding sulfur-containing triazole products in good yields (62–96 %). A wide range of arylacetylenes bearing alkyl (methyl, ethyl, propyl, *tert*-butyl and pentyl; **1b**–**1f**), alkoxy (**1g**–**1h**), and trifluoromethyl (**1i**) groups gave the corresponding sulfur-containing triazoles (i.e., **3b**–**3l**) in very high yields. It is important to note that the presence of bulky groups such as isopropyl (**1f**) and *tert*-butyl (**1g**) on the phenyl ring did not affect the outcome of the reaction, and excellent yields of the desired products were obtained. *m*-Trifluoromethylphenylacetylene (**1i**) reacted with $TMSN_3$ under the optimised reaction conditions to give the corresponding product (i.e., **3i**) in 91 % yield. Various heteroaromatic alkynes, including thienyl (**1j**), 2-pyridyl (**1k**), and pyrrole (**1l**) derivatives, reacted smoothly with $TMSN_3$ to give the corresponding sulfur-containing triazoles (i.e., **3j–3l**) in very good yields. Furthermore, various polycyclic aromatic alkynes, including 6-methoxy-2-ethynylnaphthalene (**1m**), 9-ethynylphenanthrene (**1n**), and pyrene (**1o**), reacted effectively with $TMSN_3$ under the optimised reaction conditions, and gave comparable yields of the desired products (i.e., **3m**–**3o**). Notably, aliphatic alkynes **1p**–**1s** were also found to be suitable substrates for this reaction, although lower yields of the corresponding triazoles (i.e., **3p**–**3s**) was obtained.

To demonstrate the synthetic utility of our strategy, a gram-scale synthesis of **3m** was carried out under the standard conditions. Pleasingly, sulfur-containing triazole **3m** was obtained in a satisfactory yield (86 %) when the reaction was carried out on a 10.0 mmol scale (Scheme 2). This result indicates that there is also potential for industrial application.



Scheme 2. Synthesis of **3m** on a gram scale.

Next, we investigated the recovery and reusability of the catalyst. After completion of the reaction, the stirring was stopped, and the catalyst was separated magnetically. The recovered catalyst was washed thoroughly with diethyl ether, and dried at 120 °C for 12 h. A new reaction was then carried out with fresh reactants, under the optimised reaction conditions. We found that Cu^0/Fe_3O_4 could be reused in up to six consecutive catalytic runs without any significant change in activity (Figure 3).

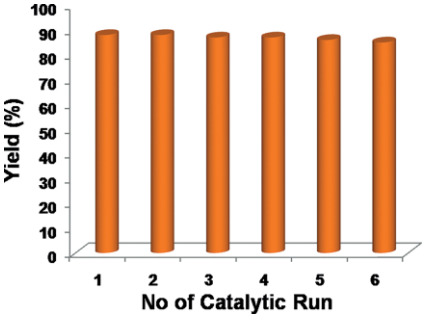
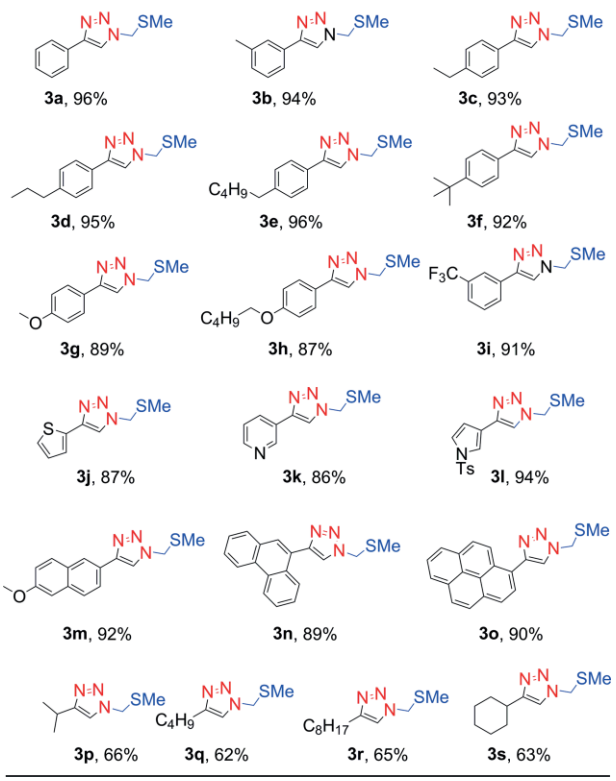


Figure 3. Recycling of the Cu^0/Fe_3O_4 catalyst for the preparation of sulfur-containing trazoles. Reaction conditions: **1a** (1.0 mmol), $TMSN_3$ (1.0 mmol), cat. (Cu 8 wt.-%, 30 mg), DMSO (2.0 mmol), 80 °C, 0.5 h.

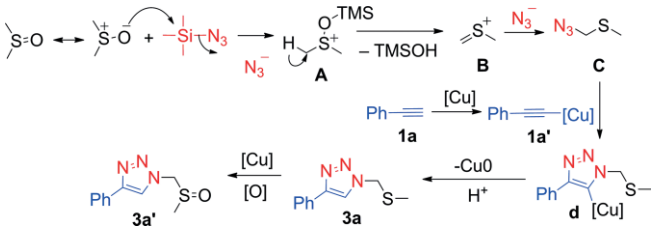
Based on our findings and on literature reports,[7c,15] a plausible mechanism for the synthesis of sulfur-containing triazoles from alkynes and $TMSN_3$ is shown in Scheme 3. Initially, the oxygen of the polarised DMSO attacks $TMSN_3$, leading to the formation of intermediate **A** along with release of azide ion. Intermediate **A** loses a proton to give thionium ion **B**, which undergoes nucleophilic substitution with azide ion to give intermediate **C**. Intermediate **C** then undergoes a click reaction

Table 2. Substrate scope.[a]



[a] Reaction conditions: Phenylacetylene (**1a**; 1.0 mmol), $TMSN_3$ (1.10 mmol), Cu^0/Fe_3O_4 (30 mg), DMSO (2.0 mL), at 80 °C for 0.5 h under nitrogen.

with copper acetylide (**1a'**) to produce intermediate **D**, and this finally loses Cu to give the desired product (i.e., **3a**).



Scheme 3. Proposed reaction mechanism.

Conclusions

In summary, we have developed an efficient method to access medicinally important sulfur-containing triazoles from alkynes and azide in the presence of magnetically separable copper nanocatalyst (Cu^0/Fe_3O_4). The reaction is compatible with various alkynes, including aromatic, aliphatic, heteroaromatic, and polyaromatic examples, and as a result, a series of 19 sulfur-containing triazoles was prepared. Considering, the ready availability of the starting materials, the broad substrate scope, the operational simplicity, and the highly functionalised nature of the reaction products, this method provides an attractive and convenient protocol for the synthesis of sulfur-containing triazoles.

Experimental Section

General Remarks: The reagents, chemicals, and solvents were either purchased from commercial suppliers or prepared and purified by standard techniques. Column chromatography was carried out using silica gel 100–200 mesh. Infrared spectra were recorded using an FTIR spectrophotometer, and values are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded with 300 and 500 MHz NMR instruments, using tetramethylsilane as an internal standard. High-resolution mass spectra (ESI-HRMS) were recorded with an ESI-QTOF mass spectrometer. X-ray powder diffraction (XRD) data were collected with a Simens/D-5000 diffractometer using Cu-K_α radiation. XPS spectra were recorded with a Kratos AXIS 165 apparatus with a dual anode (Mg and Al) using the Mg-K_α anode. The pressure in the spectrometer was about 10^{-9} Torr. The particle size and external morphology of the samples were observed with a JEOL JEM-2100 high-resolution transmission electron microscope (HRTEM). Auger electron spectroscopic (AES) analysis was carried out at a base pressure of 10^{-10} Torr, within a kinetic energy range of 110–700 eV (beam voltage of 3 kV, eV/step 1 eV, time/step 50 ms). X-ray absorption spectra were recorded using a Rigaku spectrometer with a rotating anode X-ray generator (Ru-200B, Rigaku, Japan).

General Experimental Procedure for the Synthesis of Sulfur-Containing Triazoles 3a–3s: Freshly prepared Cu^0/Fe_3O_4 was added to a mixture of alkyne **1a–1s** (1.0 mmol) and $TMSN_3$ (1.10 mmol) in DMSO (2.0 mL), and the reaction mixture was heated at 70 °C for 30 min under a nitrogen atmosphere. Stirring was then stopped, and the mixture was allowed to cool to room temperature. The catalyst was separated using an external magnet, and water (5.0 mL) was added to the reaction mixture. The aqueous layer was further washed with ethyl acetate (3 × 10 mL). The organic layer was washed with brine (10.0 mL), and dried with anhydrous sodium sulfate. The solvent was then removed under reduced pressure. The residue was purified by column chromatography using 100–200 mesh silica gel to give sulfur-containing triazole **3a–3s**.

1-[(Methylthio)methyl]-4-phenyl-1*H*-1,2,3-triazole (3a): White solid (96 %), m.p. 75 –77 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1 H), 7.86–7.83 (m, 2 H), 7.46–7.42 (m, 2 H), 7.38–7.32 (m, 1 H), 5.38 (s, 2 H), 2.17 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 128.91, 128.38, 125.77, 118.88, 52.75, 14.84 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{10}H_{12}N_3S$ $[M + H]^+$ 206.07464; found 206.07472.

1-[(Methylthio)methyl]-4-(*m*-tolyl)-1*H*-1,2,3-triazole (3b): Sticky white solid (94 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.70 (s, 1 H), 7.62 (d, J = 7.7 Hz, 1 H), 7.32 (t, J = 7.6 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 5.37 (s, 2 H), 2.41 (s, 3 H), 2.16 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.82, 138.61, 129.16, 128.80, 126.46, 122.88, 118.87, 77.31, 77.06, 76.80, 52.74, 21.46, 14.82 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{11}H_{14}N_3S$ $[M + H]^+$ 220.09029; found 220.09035.

4-(4-Ethylphenyl)-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3c): White solid (93 %), m.p. 72–75 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.96 (s, 1 H), 7.76 (d, J = 8.2 Hz, 2 H), 7.32 (d, J = 8.2 Hz, 2 H), 2.68 (q, J = 7.6 Hz, 2 H), 2.15 (s, 3 H), 1.26 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.64, 128.39, 127.80, 125.77, 77.30, 77.05, 76.79, 52.70, 28.71, 15.53, 14.81 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{12}H_{16}N_3S$ $[M + H]^+$ 234.10594; found 234.10586.

1-[(Methylthio)methyl]-4-(4-propylphenyl)-1*H*-1,2,3-triazole (3d): White solid (95 %), m.p. 62–64 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1 H), 7.75 (d, J = 8.0 Hz, 2 H), 7.25 (d, J = 8.0 Hz, 2 H), 5.37 (s, 2 H), 2.61 (t, J = 7.6 Hz, 2 H), 2.15 (s, 3 H), 1.67 (dq, J = 14.7, 7.4 Hz, 2 H), 0.95 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.09, 129.02, 127.80, 125.86, 125.70, 52.78, 37.85, 24.49, 14.84, 13.81 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{13}H_{18}N_3S$ $[M + H]^+$ 248.12159; found 248.12181.

1-[(Methylthio)methyl]-4-(4-pentylphenyl)-1*H*-1,2,3-triazole (3e): White solid (96 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1 H), 7.75 (d, J = 8.1 Hz, 2 H), 7.29 (d, J = 8.1 Hz, 2 H), 5.37 (s, 2 H), 2.64 (t, J = 7.3 Hz, 2 H), 2.16 (s, 3 H), 1.64 (dt, J = 15.0, 7.5 Hz, 2 H), 1.38–1.22 (m, 4 H), 0.90 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.35, 128.95, 127.76, 125.69, 118.56, 52.70, 35.75, 31.49, 31.10, 22.57, 14.79, 14.06 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{15}H_{22}N_3S$ $[M + H]^+$ 276.15289; found 276.15293.

4-[4-(*tert*-Butyl)phenyl]-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3f): White solid (92 %), m.p. 80–82 °C ^1H NMR (500 MHz, $CDCl_3$): δ = 7.96 (s, 1 H), 7.78 (d, J = 8.2 Hz, 2 H), 7.46 (d, J = 8.1 Hz, 2 H), 5.37 (s, 2 H), 2.15 (s, 3 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.50, 127.50, 125.80, 125.49, 118.05, 52.68, 34.71, 31.30, 14.77 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{14}H_{20}N_3S$ $[M + H]^+$ 262.13724; found 262.13742.

4-(4-Methoxyphenyl)-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3g): White solid (89 %), m.p. 98–100 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.78 (d, J = 8.8 Hz, 2 H), 6.97 (d, J = 8.8 Hz, 2 H), 5.36 (s, 2 H), 3.85 (s, 3 H), 2.16 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.74, 131.87, 127.06, 123.08, 114.29, 55.35, 52.68, 14.80 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{11}H_{14}N_3OS$ $[M + H]^+$ 236.08521; found 236.08525.

1-[(Methylthio)methyl]-4-[4-(pentyloxy)phenyl]-1*H*-1,2,3-triazole (3h): White solid (87 %), m.p. 80–82 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.76 (d, J = 8.0 Hz, 2 H), 6.96 (d, J = 8.1 Hz, 2 H), 5.36 (s, 2 H), 3.99 (t, J = 6.6 Hz, 3 H), 2.16 (s, 3 H), 1.82–1.77 (m, 2 H), 1.50–1.43 (m, 2 H), 1.41–1.37 (m, 2 H), 0.94 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.36, 130.94, 128.87,

127.03, 122.93, 114.89, 68.13, 52.79, 28.98, 28.23, 22.50, 14.83, 14.06 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{15}H_{22}N_3OS$ [M + H]$^+$ 292.14781; found 292.14801.

1-[(Methylthio)methyl]-4-[3-(trifluoromethyl)phenyl]-1*H*-1,2,3-triazole (3i): White gummy solid (91 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (s, 1 H), 7.77 (d, *J* = 7.9 Hz, 1 H), 7.72–7.62 (m, 2 H), 7.50 (dd, *J* = 7.8, 6.9 Hz, 2 H), 5.40 (s, 2 H), 2.16 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.03, 132.05, 131.67, 128.43, 126.20, 126.14, 122.36, 122.31, 52.79, 14.75 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{11}H_{11}N_3S$ [M + H]$^+$ 274.06203; found 274.06215.

1-[(Methylthio)methyl]-4-(thiophen-2-yl)-1*H*-1,2,3-triazole (3j): White solid (87 %), m.p. 100–102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.73 (dd, *J* = 2.8, 0.9 Hz, 1 H), 7.53–7.47 (m, 1 H), 7.42 (dd, *J* = 5.0, 3.0 Hz, 1 H), 5.39 (s, 2 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.87, 131.62, 126.44, 125.77, 121.36, 118.63, 52.69, 14.78 ppm. HRMS (ESI, Orbitrap): calcd. for $C_8H_{10}N_3S_2$ [M + H]$^+$ 212.03107; found 212.03127.

3-{1-[(Methylthio)methyl]-1*H*-1,2,3-triazol-4-yl}pyridine (3k): White solid (86 %), m.p. 70–72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, *J* = 3.9 Hz, 1 H), 8.54 (s, 1 H), 8.24 (d, *J* = 7.9 Hz, 1 H), 7.86 (t, *J* = 7.7 Hz, 1 H), 7.38–7.27 (m, 1 H), 5.41 (s, 2 H), 2.19 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = δ = 148.52, 137.89, 123.20, 122.11, 120.68, 53.02, 15.01 ppm. HRMS (ESI, Orbitrap): calcd. for $C_9H_{11}N_4S$ [M + H]$^+$ 207.06989; found 207.06101.

1-[(Methylthio)methyl]-4-(1-tosyl-1*H*-pyrrol-3-yl)-1*H*-1,2,3-triazole (3l): White solid (94 %), m.p. 76–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (s, 1 H), 7.45 (dd, *J* = 3.3, 1.8 Hz, 1 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.16 (d, *J* = 8.1 Hz, 2 H), 6.67 (dd, *J* = 3.4, 1.8 Hz, 1 H), 6.37 (t, *J* = 3.4 Hz, 1 H), 5.38 (s, 2 H), 2.34 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.18, 139.11, 135.33, 129.85, 127.12, 126.93, 124.83, 124.75, 123.55, 117.33, 112.49, 52.82, 21.62, 14.97 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{15}H_{17}N_4O_2S_2$ [M + H]$^+$ 349.07874; found 349.08001.

4-(6-Methoxynaphthalen-2-yl)-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3m): White solid (92 %), m.p. 125–127 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (s, 1 H), 8.07 (s, 1 H), 7.91 (d, *J* = 8.5 Hz, 1 H), 7.80 (dd, *J* = 8.6, 4.4 Hz, 2 H), 7.20–7.14 (m, 2 H), 5.41 (s, 2 H), 3.94 (s, 3 H), 2.19 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.03, 148.91, 134.48, 129.75, 128.99, 127.44, 125.61, 124.45, 124.36, 119.38, 118.80, 105.84, 77.32, 77.07, 76.81, 55.37, 52.78, 14.87 ppm. HRMS (ESI, Orbitrap): calcd. for $C_9H_{11}N_4S$ [M + H]$^+$ 207.06989; found 207.06989.

1-[(Methylthio)methyl]-4-(phenanthren-9-yl)-1*H*-1,2,3-triazole (3n): White solid (89 %), m.p. 135–137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 7.9 Hz, 1 H), 8.72 (d, *J* = 8.2 Hz, 1 H), 8.39 (dd, *J* = 8.2, 1.0 Hz, 1 H), 8.10 (s, 1 H), 8.03 (s, 1 H), 7.93 (dd, *J* = 7.8, 1.1 Hz, 1 H), 7.73–7.67 (m, 2 H), 7.66–7.60 (m, 2 H), 5.49 (s, 2 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.30, 130.77, 130.50, 130.07, 128.94, 128.55, 127.24, 127.01, 126.96, 126.79, 126.57, 126.09, 123.08, 122.61, 122.17, 52.91, 15.11 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{18}H_{16}N_3S$ [M + H]$^+$ 306.10594; found 306.10518.

1-[(Methylthio)methyl]-4-(pyren-1-yl)-1*H*-1,2,3-triazole (3o): White solid (90 %), m.p. 163–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 9.3 Hz, 1 H), 8.29–8.24 (m, 2 H), 8.22 (s, 1 H), 8.21–8.18 (m, 2 H), 8.14 (d, *J* = 9.3 Hz, 1 H), 8.10–8.07 (m, 2 H), 8.03 (t, *J* = 7.6 Hz, 1 H), 5.51 (s, 2 H), 2.28 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.46, 130.91, 128.87, 128.61, 128.31, 127.96, 127.39, 127.19, 126.15, 125.50, 125.23, 124.90, 124.68, 122.20, 52.93, 15.13 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{20}H_{16}N_3S$ [M + H]$^+$ 330.10594; found 330.10594.

4-Isopropyl-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3p): White gummy solid (66 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (s, 1 H), 5.30 (s, 2 H), 3.14 (dq, *J* = 20.6, 7.0 Hz, 2 H), 2.13 (s, 3 H), 1.34 (d, *J* = 6.9 Hz, 3 H), 1.32 (d, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.72, 52.56, 25.94, 22.51, 22.48, 14.88 ppm. HRMS (ESI, Orbitrap): calcd. for $C_7H_{14}N_3S$ [M + H]$^+$ 172.09029; found 172.09041.

4-Butyl-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3q): Sticky solid (62 %). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (s, 1 H), 5.28 (s, 2 H), 2.72 (t, *J* = 7.1 Hz, 2 H), 2.10 (s, 3 H), 1.68–1.62 (m, 2 H), 1.36–1.28 (m, 2 H), 0.87 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.30, 119.95, 52.33, 31.78, 29.30, 29.26, 29.19, 29.15, 25.68, 22.60, 14.71, 14.05 ppm. HRMS (ESI, Orbitrap): calcd. for $C_8H_{16}N_3S$ [M + H]$^+$ 186.10594; found 186.10602.

1-[(Methylthio)methyl]-4-octyl-1*H*-1,2,3-triazole (3r): White solid (65 %), m.p. 68–70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (s, 1 H), 5.28 (s, 2 H), 2.71 (t, *J* = 7.0 Hz, 2 H), 2.11 (s, 3 H), 1.71–1.64 (m, 2 H), 1.38–1.22 (m, 10 H), 0.87 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.30, 119.95, 52.33, 31.78, 29.30, 29.26, 29.19, 29.15, 25.68, 22.60, 14.71, 14.05 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{12}H_{24}N_3S$ [M + H]$^+$ 242.16854; found 242.16868.

4-Cyclohexyl-1-[(methylthio)methyl]-1*H*-1,2,3-triazole (3s): White solid (63 %), m.p. 82–84 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47 (s, 1 H), 5.29 (s, 2 H), 2.79 (tt, *J* = 7.5, 3.7 Hz, 1 H), 2.12 (s, 3 H), 2.10–2.02 (m, 2 H), 1.84–1.77 (m, 2 H), 1.77–1.69 (m, 2 H), 1.44–1.36 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.70, 118.70, 52.48, 35.32, 32.97, 32.85, 32.02, 26.11, 26.02, 14.83 ppm. HRMS (ESI, Orbitrap): calcd. for $C_{12}H_{24}N_3S$ [M + H]$^+$ 242.16854; found 242.16868.

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[14] For X-ray data and an ORTEP depiction of compound **3a**, please see the Supporting Information. CCDC 1478158 (for **3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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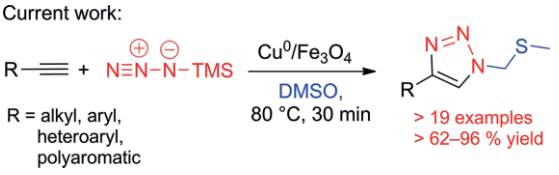

An efficient one-pot tandem nano Cu^0/Fe_3O_4-catalysed synthesis of sulfur-containing triazoles from alkynes and azide has been developed. TMS-Azide and dimethyl sulfoxide act as the nitrogen and sulfur sources, respectively. The catalyst can be recovered magnetically and reused six times without any significant loss of activity.

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