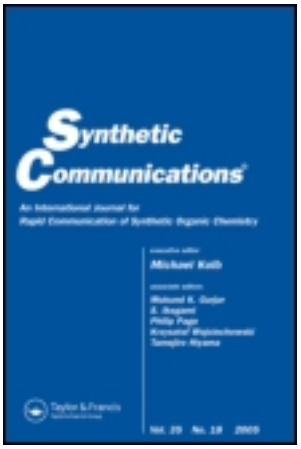

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Polymer-Supported Azide and Copper(I): Green Reusable Reagent and Catalyst for Click Cyclization

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POLYMER-SUPPORTED AZIDE AND COPPER(I): GREEN REUSABLE REAGENT AND CATALYST FOR CLICK CYCLIZATION

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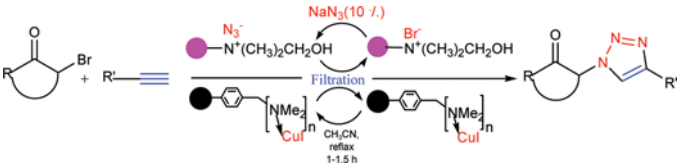
GRAPHICAL ABSTRACT



Abstract *In this work, polymer-supported copper(I) iodide catalyst and macroporous polymer-supported azide reagent were used to simplify the synthesis of 1,4-disubstituted-1H-1,2,3-triazoles from α-bromo ketones/amides/esters following green chemistry principles. This new one-pot protocol facilitates the workup of the reaction and provides the products in short times and excellent yields. Heterogeneous catalyst and reagent can be reused at least for five runs without significant yield decreases.*

Keywords Alkynes; α-bromo ketones; 1,3-dipolar cycloaddition; green chemistry; heterogeneous catalysis

INTRODUCTION

According to one of the basic principles of green chemistry, catalytic or recyclable reagents are superior to stoichiometric reagents.[1] Polymer-supported reagents are increasingly being used in the synthesis and purification of many organic reactions.[2,3] They possess advantages such as reaction monitoring as well as increased safety, more than ever when the unsupported reagents are toxic or dangerous, as they can be easily removed from reaction media and recycled.[4,5] In addition, employing an excess amount of reagent is permissible without the need for additional purification.

Sodium azide is an essential reagent, and copper(I) is a wonderful catalyst for 1,3-dipolar cycloaddition between organic azides and terminal alkynes, which is best known as the click reaction.[6–8] This cycloaddition has been applied in various ways

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in drug discovery, chemical biology, and medicinal chemistry,[9–12] as well as material science and solid-phase organic synthesis.[13–16] However, sodium azide and copper salts are highly toxic compounds. Sodium azide is a potent toxin, has a similar toxicity as the cyanide ion ($LD_{50} = 27$ mg/kg for rats), and can be absorbed through the skin mucous membranes. Regardless of toxicity, copper(I) iodide salt suffers from thermodynamic instability and the formation of undesired alkyne-alkyne coupling products, which are sometimes observed in its presence.[17,18] On the other hand, these homogeneous processes possess one or more disadvantages such as difficulty separating the product from the reaction medium. These homogenous catalysts are generally unrecyclable and have poor regioselectivity and long reaction times.

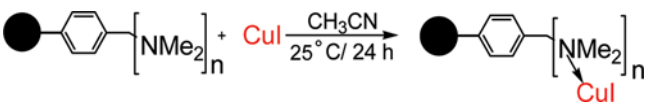
Nevertheless, nitrogen- or phosphorus-based ligands have been shown to protect the metal center from oxidation and disproportionation while enhancing its catalytic activity.[19–21] Recently, heterogeneous copper(I) catalysts based on silica,[22–24] montmorillonite,[25] zeolites,[26–28] and Cu on charcoal[29,30] have been developed. There are also some reports about using of polymer-supported CuI as recoverable catalyst for this cyclization.[31–33] These catalysts possess increased advantages over their homogeneous counterparts. However, to the best of our knowledge, there is no report for one-pot multicomponent synthesis of 1,4-disubstituted 1,2,3-triazoles that utilize polymer-supported azide, which can significantly reduce the toxicity and environmental impacts of this reagent.

In contination of our recent work that reported directly prepared phenacyl azides from styrenes for click synthesis of 1,4-disubstituted triazole,[34] herein we report a new, facile, and green protocol for one-pot multicomponent click synthesis of 1,4-disubstituted-1H-1,2,3-triazoles from α-bromo ketones, amides, and esters using polymer-supported azide and CuI.

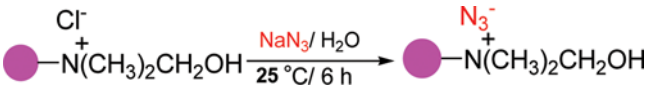
RESULTS AND DISCUSSION

The preparation procedures followed to obtain polymer-supported Cu(I) iodide catalyst and polymer-supported azide reagent are outlined in Schemes 1 and 2. These consist of building up suitable heterogeneous polymer-supported copper(I) iodide catalyst (Scheme 1) and macroporous polymer-supported azide nucleophile (Scheme 2) structures on the surface of commercially available amberlyst A-21 (mesh 20–50) and amberlite IRA-910Cl (mesh 16–50). Preparation of heterogeneous copper(I) iodide catalyst and polymer-supported azide reagent by these procedures is facile and straightforward.

To optimize the reaction conditions, phenyl acetylene and phenacyl bromide for the synthesis of 1-phenyl-2-(4-phenyl-1-H-1,2,3-triazol-1yl)-1-ethanone (Table 1, entry 1b) were selected as the test substrates, and acetonitrile, methylene chloride, ethanol, and water were selected as solvents. Unfortunately we did not get any result



Scheme 1. Preparation of amberlyst-supported CuI (A-21CuI). (Figure is provided in color online.)



Scheme 2. Preparation of amberlite-supported azide (IRA-910N_3). (Figure is provided in color online.)

at room temperature with various amounts of heterogeneous catalyst and reagent with each of the solvents, so the reaction was done at reflux conditions.

From Table 2, it can be seen that acetonitrile, A-21CuI (60 mg, 10%), and IRA-910N_3 (1 g) are optimized conditions for multicomponent click cyclization. The results were evaluated qualitatively through thin-layer chromatography (TLC) (Table 1). The best conditions employ 1:1:1.5:0.1 mol ratios of phenyl acetylene, phenacyl bromide, IRA-910N_3, and A-21CuI at reflux conditions using acetonitrile as solvent.

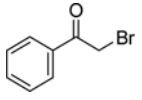
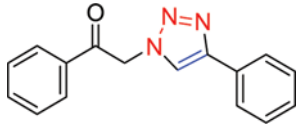
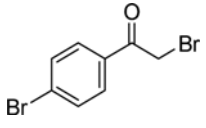
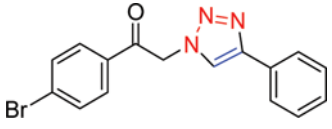
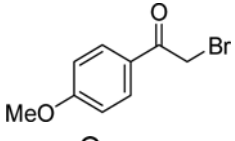
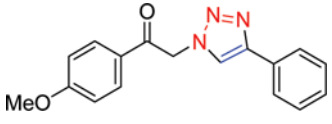
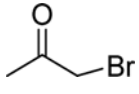
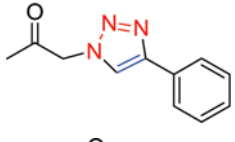
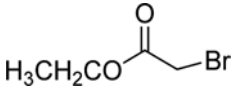
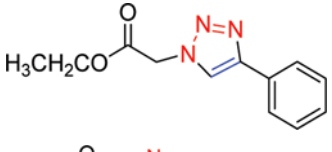
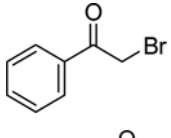
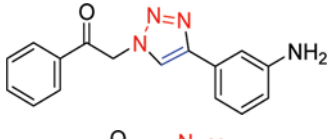
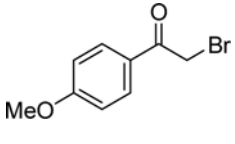
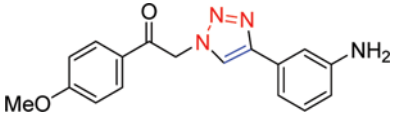
Using these optimized conditions, the reaction of various terminal alkynes and α-bromo ketones, amides, or esters was explored (Scheme 3). All the products were easily isolated with straightforward filtration and evaporation of solvent. A simple purification technique is one of the key characteristics of click reactions.[7] The solid products were easily recrystallized in hot ethanol. In some cases, the solid product was dissolved in a minimum amount of ethyl acetate and n-hexane was added dropwise to give pure product crystals (Table 1, entries 2, 13, and 14).

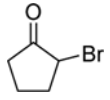
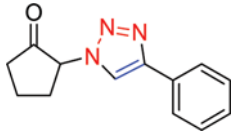
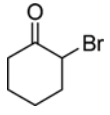
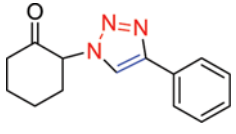
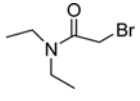
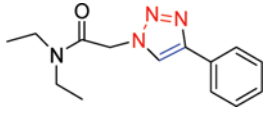
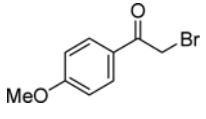
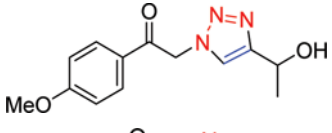
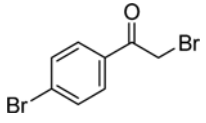
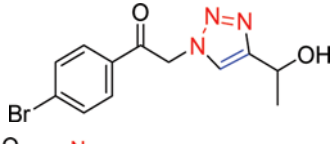
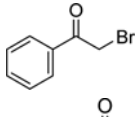
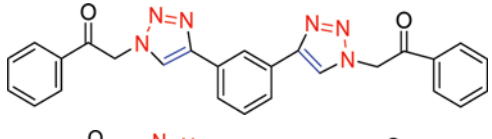
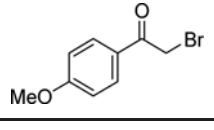
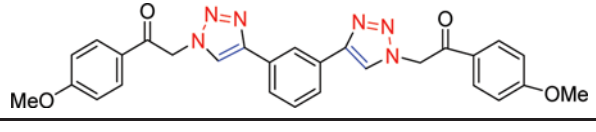
Click condensations were confirmed by the appearance of a singlet in the region of 8–8.5 ppm in ^{1}H NMR spectra, which corresponds to the hydrogen on the 5-position of triazole ring and confirms the regioselective synthesis of 1,4-disubstituted triazole regioisomers.[34] Because α-azido ketones are often unstable in heat and light, their in situ preparation is a great alternative to their use and handling. α-Azido ketones were prepared in situ and subjected to multicomponent click cyclization with various terminal alkynes.

The using of 1,3-diethynylbenzene in click cyclizations led to the synthesis of some interesting symmetrical bis-triazoles (Table 1, entries 13 and 14 and Scheme 4). α-Bromo amides and α-bromo esters were also subjected to click cyclization with terminal alkynes to give the corresponding 1,4-disubstituted-1H-1,2,3-triazloes in good yields (Table 1, entries 5 and 10 and Scheme 5).

It is also noteworthy that resins do not suffer from extensive mechanical degradation after running. When using a heterogeneous catalyst, the key point is the deactivation and recyclability of the catalyst. Polymer-supported CuI can be reused for up to five runs without reloading. Polymer-supported azide nucleophile can be loaded several times. To exhibit the reusability of the polymer-supported azide and CuI, click cyclization of phenyl acetylene and phenacyl bromide was chosen as a model. After reaction completion, the resin mixture was washed with distilled water and then subjected to aqueous NaN_3 solution to reload IRA-910N_3. This process was repeated five times and no appreciable yield decrease was observed (Table 3 and Fig. 1). The copper content of the amberlyst–CuI catalyst was measured with atomic absorption spectroscopy after five runs (copper content was calculated to be 1.25 mmol per gram of polymeric catalyst). The difference between the copper content of the fresh catalyst and the used catalyst (fifth run) is only 5%, which indicates the low leaching amount of copper iodide catalyst into the reaction mixture.

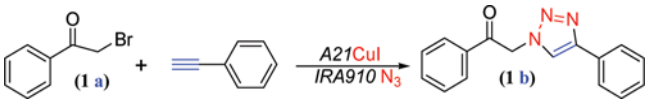
Table 1. Synthesis of 1,4-disubstituted-1H-1,2,3-triazoles using polymer-supported reagent and catalyst

Entry	α-Bromo ketone/amide/ester (a)	Product (b)	Melting point (°C)	Time (h)	Yield (%)[a]
1			136	1	89
2			145	1	90
3			142	1	86
4			138	1.45	79
5			112	1.30	85
6			146	1.30	87
7			163	1	89

8			147	1.30	90
9			148	1.45	92
10			140	1.30	80
11			118	1.20	78
12			108	1.20	85
13			More than 300	1.30	90
14			More than 300	1.30	86

[a]Yields refer to isolated and pure products.

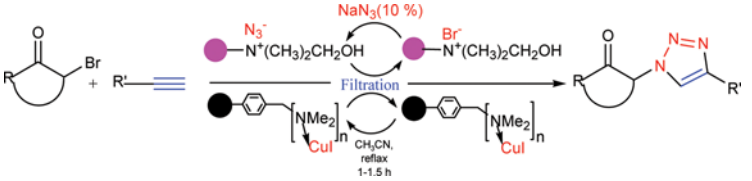
Table 2. effect of solvent on the polymer-supported CuI/N_3-mediated 1,4-disubstituted-1H-1,2,3-triazole synthesis



Entry	Solvent	IRA-910N_3 (g)	A-21CuI (mg)	Time (h)	Yield (%)[a]
1	CH_3OH	1	60	2	45
2	H_2O	1	60	2	40
3	CH_2Cl_2	1	60	2	65
4	CH_3CN	1	60	1	89

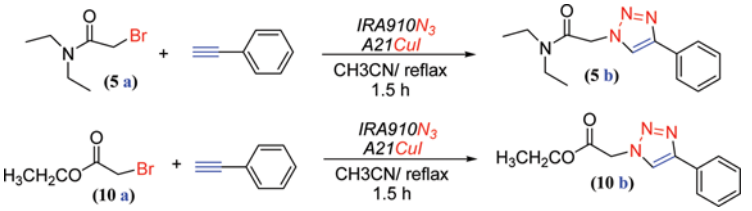
[a]Yields refer to pure and separated products.

To evaluate the catalytic property and reusability of other polymer-supported Cu(I) salts, amberlyst-supported CuCl and CuBr were prepared according to the procedure applied for CuI and used for the same reaction. All the three catalysts gave good yields from the first up to the third runs, but the yields decreased in the



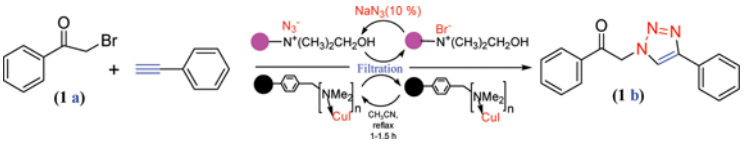
Scheme 3. Multicomponent synthesis of 1,4-disubstituted-1H-1,2,3-triazoles using recoverable polymer-supported azide and CuI. (Figure is provided in color online.)

Scheme 4. Synthesis of symmetrical substituted bis-triazoles using phenacyl bromides and 1,3-diethynyl-benzene. (Figure is provided in color online.)



Scheme 5. Click cyclization of α-bromo amides and α-bromo esters using polymer-supported azide and CuI. (Figure is provided in color online.)

Table 3. Recyclability and reusability of polymer-supported azide and CuI



Entry	Loading	Yield (%)[a]
1	1	89
2	2	90
3	3	84
4	4	82
5	5	78

[a]Yields refer to isolated and pure products.

fourth and fifth runs using amberlyst-supported CuCl and CuBr (Fig. 1). We relate these observations to the greater oxidation tendency of CuCl and CuBr in the aqueous medium, which made CuI the best choice to support on amberlyst for our purposes.

In conclusion, we have developed a simple, benign, and multicomponent regioselective synthesis of biologically significant 1,4-disubstituted-1H-1,2,3-triazoles with short times and good yields under polymer-supported catalyst and reagent conditions. The protocol is applicable to a wide range of α-halo ketones/amides/esters, and acetylenic compounds and allows the assembly of a diverse set of 1,4-disubstituted-1H-1,2,3-triazoles. The final reaction product can be simply filtered and separated without the need for a further chromatographic step. In addition, the spent polymeric reagent can be regenerated and reused several times without appreciable loss capacity and efficiency. Using of A-21 CuI as catalyst protects the metal center from oxidation and disproportionation while enhancing its catalytic activity and makes it a reusable catalyst. Minimal waste generation of this "user-friendly" process should be beneficial for industrial applications.

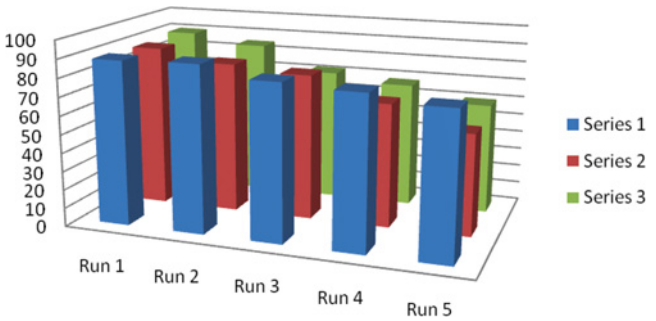


Figure 1. Reusability of polymer-supported copper(I) catalysts: Series 1, CuI; series 2, CuCl; and series 3, CuBr. (Figure is provided in color online.)

EXPERIMENTAL

All of the triazole derivatives were prepared by our procedure; their spectroscopic and physical data were compared with those of authentic samples. NMR spectra were recorded in dimethylsulfoxide (DMSO-d_6) or $CDCl_3$ on a Bruker Advanced DPX 500- and 400-MHz instrument spectrometers using tetramethylsilane (TMS) as internal standard. Infrared (IR) spectra were recorded on a BOMEMMB-Series 1998 Fourier transform (FT)–IR spectrometer.

Preparation of Polymer-Supported Azide Reagent (IRA-910N_3)

Amberlite IRA-910N_3 was easily prepared from its corresponding chloride form via ion exchange using 10% NaN_3 aqueous solution. Two g of amberlite IRA-910 chloride (mesh 16–50) were stirred for 6 h in the corresponding solution (100 mL of 10% NaN_3 aqueous solution), filtered off, washed several times with water, and stirred for an additional 5 min. It was then decanted, washed several times with water until the supernatant liquid gave a negative azide test with ferric nitrate, and dried under vacuum at 50 °C.

The exchange capacity of the resin was determined by passing 1 N sodium chloride solution (50 mL) through the resin (0.3 g) packed in a column. The amount of sodium salt of the nucleophile in the eluent was then titrated with 0.01 normal hydrochloric acid using methyl orange as indicator. The exchange capacity of polymer-supported nucleophile was calculated to be 1.5 mmol/g of N_3^-.

Preparation of the Supported Catalyst (*A-21*CuI)

Dry amberlyst A-21 (1.0 g, 4.8 mmol amine; mesh 20–50) was added to a solution of copper(I) iodide (381 mg, 2.00 mmol) in acetonitrile (20 ml) and gently shaken on an orbital stirrer for 24 h. The solvent was filtered, and the resin washed with CH_3CN (2×20 mL) and CH_2Cl_2 (2×20 mL) and dried under vacuum at 40 °C over night. The weight increase was 0.31 g (1.63 mmol CuI), which gave a polymer loading of 1.24 mmol $CuI \cdot g^{-1}$. Elemental analysis gave a copper content of 8.32%, indicative of a loading of 1.32 mmol $CuI \cdot g^{-1}$.

The same procedure was used for the preparation of amberlyst-supported CuCl (A-21CuCl; loading 1.27 mmol $CuCl \cdot g^{-1}$) and amberlyst-supported CuBr (A-21CuBr; loading 1.15 mmol $CuBr \cdot g^{-1}$).

Typical Procedure for Multicomponent Synthesis of 1-Phenyl-2-(4-phenyl-1-h-1,2,3-triazol-1yl)-1-ethanone (1b)

2-Bromo-1-phenyl-1-ethanone (1 mmol) and phenyl acetylene (1 mmol) were placed together in a round-bottom flask containing 10 mL of acetonitrile. Amberlyst A-21 CuI (60 mg, loading 1.35 mmol/g) and amberlite IRA-910N_3(1 g, loading: 1.5 meq/g) were added at once to the mixture. The suspension was magnetically stirred under reflux conditions. After completion of the reaction (1 h) as followed by TLC (n-hexane–ethyl acetate; 4:1), the resins were filtered and washed with

acetonitrile (2×5 mL). The filtrates were evaporated to dryness, and then the solid residue was recrystallized in hot ethanol to give pure product crystals.

REUSING POLYMER-SUPPORTED CATALYST AND REAGENT

The filtered mixture of resins was washed with 25 mL of distillated water and stirred for 6 h in the corresponding solution (50 mL of 10% NaN_3 aqueous solution) and dried under vacuum at 50 °C before next run.

1-Phenyl-2-(4-phenyl-1-H-1,2,3-triazol-1yl)-1-ethanone (1b)

Mp 136 °C.[34] IR (KBr): 1697 (CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): $\delta = 8.53$(s, 1 H, CHN), 8.11 (d, 2H, $J = 8.15$ Hz), 7.88 (d, 2H, $J = 8.15$ Hz), 7.77–7.74 (m, 1 H), 7.63 (t, 2H, $J = 7.7$ Hz), 7.47 (t, 2H, $J = 7.7$ Hz), 7.37–7.34 (m, 1 H), 6.27 (s, 2 H, CH_2CO). ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 195$ (CO), 152.4, 139, 138.2, 134.5, 133.5, 133.2, 132.7, 132.5, 130.1, 126.4, 59.9. HRMS (EI) m/z found: 263.3 (calculated for $C_{16}H_{13}N_3O$, M^+, requires: 263.3). Elem. anal. found: C, 73.00%; H, 4.86%; N, 16.03% (calculated for $C_{16}H_{13}N_3O$: C, 72.92%; H, 4.94%; N, 15.95%).

1-(4-Bromophenyl)-2-(4-phenyl-1H-1,2,3-triazole-1-yl)-1-ethanone (2b)

Mp 145 °C.[34] IR (KBr): 1702 (CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): $\delta = 8.53$(s, 1H), 8.04 (d, 2H $J = 8.2$ Hz), 7.88–7.86 (m, 2H), 7.71–7.68 (m, 1H), 7.61–7.57 (m, 2H), 7.46–7.42 (m, 2H), 7.31–7.38 (m, 1H), 6.08 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): $\delta = 192.1$ (CO), 146.7, 133.6, 132.6, 131.2, 130.7, 129.4, 129.0, 128.4, 125.6, 123.5, 56.5. HRMS (EI) m/z found 341.2 (calculated for $C_{16}H_{12}BrN_3O$, M^+, requires: 342.2). Elem. Anal. Found: C, 55.93%; H, 3.45%; N, 12.35% (calculated for $C_{16}H_{12}BrN_3O$: C, 56.11%; H, 3.51%; N, 12.27%).

1-(4-Methoxyphenyl)-2-(4-phenyl-1-H-1,2,3-triazol-1yl)-1-ethanone (3b)

Mp 142 °C.[34] IR (KBr): 1697 (CO) cm^{-1}. ^1H-NMR (500 MHz, DMSO-d_6): $\delta = 8.52$ (s, 1H, CHN), 8.08 (d, 2H, $J = 8.4$ Hz), 7.88 (d, $J = 8.4$ Hz, 2H), 7.47 (t, 2H, $J = 7.6$ Hz), 7.35 (t, 1H, $J = 7$ Hz), 7.14 (d, 2H, $J = 8.5$ Hz), 6.19 (s; 2H, CH_2CO), 3.9 (s, 3H, CH_3O). ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 194.95$ (CO), 162.12, 141.9, 134.5, 131.66, 131.51, 129.82, 128.71, 126, 123.96, 115.13, 56.58, 56.49. HRMS (EI) m/z found 295.3 (calculated for $C_{17}H_{15}N_3O_2$, M^+, requires: 294.3). Elem. anal. found: C, 69.57%; H, 5.06%; N, 14.33% (calculated for $C_{17}H_{15}N_3O_2$: C, 69.61%; H, 5.15%; N, 14.33%).

1-(4-Phenyl-1H-1,2,3-triazole-1-yl)acetone (4b)

Mp 138 °C.[35] IR (KBr): 1729 (CO) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.88$–7.87 (m, 3H), 7.46 (t, 2H, $J = 7.50$ *Hz*), 7.40–7.36 (m, 1H), 2.30 (s, 3H),

5.28 (s, 2H)), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 199.61$, 148.64, 130.77, 129.30, 128.74, 126.22, 121.55, 58.96, 27.66. HRMS (EI) m/z found: 201.2 (calculated for $C_{11}H_{11}N_3O$, M^+. requires: 201.2). Elem. anal. found: C, 66.56%; H, 5.57%; N, 20.49% (calculated for $C_{11}H_{11}N_3O$: C, 65.66%; H, 5.51%; N, 20.88%).

Ethyl 2-(4-Phenyl-1H-1,2,3-triazol-1-yl)acetate (5b)

Mp 112 °C. IR (KBr): 1755 (CO) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.9$ (s, 1H, CHN), 7.88 (d, 2H, $J = 8.4$ *Hz*), 7.46 (t, 2H, $J = 7.5$ Hz), 7.37 (t, 1H, $J = 7.4$ Hz), 5.23 (s, 2H, CH_2CO), 4.30 (q, 2H (CH_2), $J = 7.1$ Hz,), 1.33 (t, 3H (CH3)) $J = 7.1$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.7$ (CO), 148.6, 130.82, 129.26, 128.7, 126.24, 121.4, 62.9, 51.38, 14.5. HRMS (EI) m/z found: 231.3 (calculated for $C_{12}H_{13}N_3O_2$, M^+ requires: 231.3). Elem. anal. found: C, 62.67%; H, 5.30%; N, 18.06% (calculated for $C_{12}H_{13}N_3O_2$: C, 62.33%; H, 5.67%; N, 18.17%).

2-[4-(3-Aminophenyl)-1H-1,2,3-triazol-1yl]-1-phenyl-1-ethanone (6b)

Mp 146 °C.[34] IR (KBr): 3420 and 3338 (NH_2), 1701 (CO) cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.35 ppm (s, 1H), 8.11 (d, 2H, J = 7.46 Hz), 7.75 (t, 1H, J = 7 Hz,), 7.62 (t, 2H, J = 7.32 Hz), 7.15 (s, 1H), 7.9 (t, 1H, J = 7.6 Hz), 6.98 (d, 1H, J = 7.5 Hz,), 6.56 (d, 1H, J = 7.5 Hz), 6.22 (s, 2H), 5.22 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 193.1$ (CO), 149.9, 147.85, 135.13, 135.02, 132.09, 130.27, 129.88, 129.8, 123.46, 114.48, 113.9, 111.38, 56.78.

2-[4-(3-Aminophenyl)-1H-1,2,3-triazol-1yl]-1-(4-methoxyphenyl)-1-ethanone (7b)

Mp 163 °C.[34] IR (KBr): 3424 and 3332 (NH_2), 1695 (CO) cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 8.34$ ppm (1H, s), 8.08 (d, 2H, J = 8.9), 7.14 (d, 3H, J = 8.9,), 7.13 (s, 1H), 7.09 (t, 1H, J = 7.74), 6.97–6.95 (m, 1H), 6.55–6.53 (m, 1H), 6.14 (s, 2H), 5.18 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 191.3$, 164.8, 149.9, 147.78, 132.12, 131.48, 130.24, 127.89, 123.48, 115.12, 114.42, 113.85, 111.34, 56.57, 56.40.

2-(4-Phenyl-1H-1,2,3-triazol-1-yl)-1-cyclopentanone (8b)

Mp 147 °C.[35] IR (KBr): 1755 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.89$ (s, 1H), 7.84 (d, 2H, $J = 7.48$ Hz), 7.40–7.44 (m, 2H), 7.35–7.31 (m, 1H), 4.96 (dd, 1H, $J_1 = 11.4$ Hz and $J_2 = 8.44$ Hz), 2.86–2.79 (m, 1H), 2.65–2.42 (m, 3H), 2.36–2.29 (m, 1H), 2.12–2.01 (m, 1H).

1-(Cyclohexan-1-on-2-yl))-4-phenyl-1H-1,2,3-triazole (9b)

Mp 148 °C.[35] TR (KBr): 1719 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.86$–7.84 (m, 3H), 7.44–7.41 (m, 2H), 7.35–7.31 (m, 1H), 5.47 (dd, $J_1 = 13.14$ Hz, $J_2 = 5.68$ Hz, 1H), 2.72–2.52 (m, 3H), 2.29–2.20 (m, 2H), 2.14–2.12 (m, 1H), 2.01–1.81 (m, 2H). HRMS: calcd for $C_{14}H_{15}N_3O$ 241.2884, found 241.1719.

2-[4-(1-Hydroxyethyl)-1H-1,2,3-triazole-1-yl)]-1-(4-methoxyphenyl)-1-ethanone (11b)

IR (KBr): 3503 (OH), 1694 (CO) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.07$ (d, 2H, $j = 8.74$ Hz), 7.87 (s, 1H), 7.13 (d, 2H, $J = 8.75$ Hz), 6.07 (s, 2H), 5.28 (s, 1H), 4.89–4.86 (m, 1H), 3.89 (s, 3H), 1.45 (d, 3H, $j = 8.75$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 191.38$, 164.74, 153.37, 131.42, 127.95, 123.86, 115.08, 62.54, 56.56, 56.18, 24.70.

2-(4-{3-[1-(2-Oxo-2-phenylethyl)1H-1,2,3-triazol-4-yl]phenyl}-1H-1,2,3-triazol-1-yl)-1-phenyl-1-ethanone (13b)

Mp $\geq 300\,^{\circ}C$. IR (KBr): 1696 (CO) cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): $\delta = 8.64$ ppm (s, 2H, $2 \times$ CHN), 8.43 (s, 1H), 8.12 (d, 4H, $J = 8.3$ Hz), 7.88 (d, 1H, $J = 1.6$ Hz), 7.86 (d, 1H, $J = 1.6$ Hz), 7.76 (t, 2H, $J = 7.7$ Hz), 7.6 (t, 4H, $J = 8.3$ Hz), 7.58 (t, 1H, $J = 7.7$ Hz), 6.29 (s, 2H, CH_2O), 6.28 (s, 2H, CH_2CO). ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 193$(CO), 146.97, 135.17, 135, 132.29, 130.55, 129.9, 129.1, 125.5, 124.26, 122.7, 56.91.

1-(4-Methoxyphenyl)-2-[4-(3-{1-[2-(4-methoxyphenyl)-2-oxoethyl]-1H-1,2,3-triazol-4-yl}phenyl)-1H-1,2,3-triazol-1yl]-1-ethanone (14b)

IR (KBr): 1697 (CO) cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): $\delta = 8.5$ ppm (s, 2H), 8.41 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 4H), 7.90 (d, 4H, $J = 8.4$ Hz), 7.78 (t, 2H, $J = 7.6$ Hz), 7.59 (t, 1H, $J = 7.6$ Hz), 7.15 (d, 2H, $J = 8.5$ Hz), 6.19 ppm (s, 4H), 3.85 (s, 6H). ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 194.9$ (CO), 163.1, 141.9, 133.2, 131.66, 129.82, 128.4, 126, 123.96, 115.2, 56.58, 56.49.

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