Cuprous oxide on charcoal-catalyzed ligand-free synthesis of 1,4-disubstituted 1,2,3-triazoles *via* click chemistry

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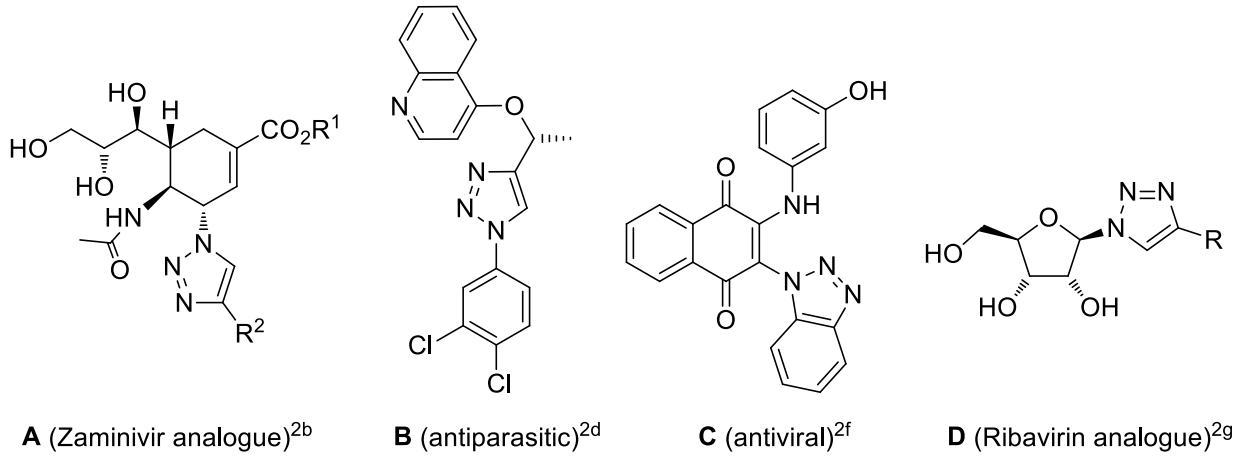
Abstract

Cuprous oxide on charcoal (Cu_2O/C), the preparation of which is described for the first time, catalyzes the formation of 1,4-disubstituted 1,2,3-triazoles from organic azides and terminal alkynes in good to excellent yields (69-94%). These disubstituted triazoles can be equally efficiently generated in a one-pot process from alkyl bromides, sodium azide, and terminal acetylenes in 50% aqueous isopropanol containing a suspension of the catalyst. This obviates the necessity to isolate potentially explosive organic azides.

Keywords: 1,3-Dipolar cycloaddition, click chemistry, Cu_2O/C, triazoles

Introduction

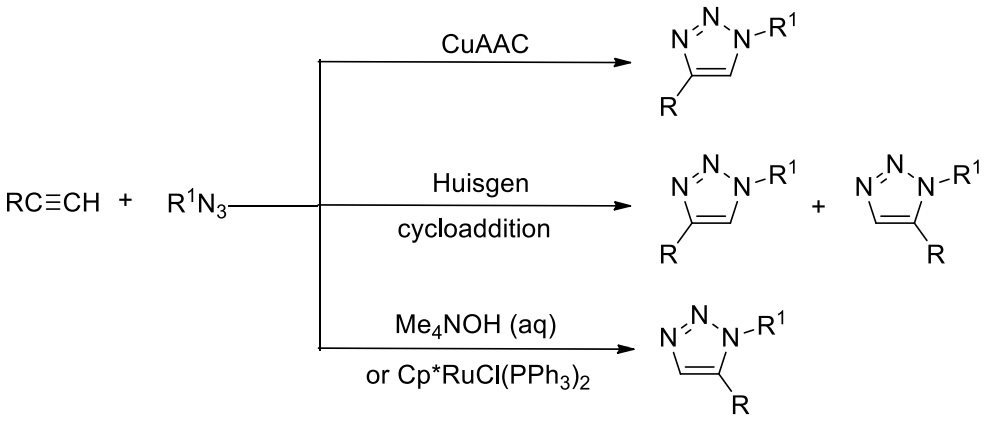
Recent advances in the Huisgen 1,3-dipolar cycloaddition reaction have led to a renewed interest in its applications to the synthesis of 1,2,3-triazoles.[1] Small molecules containing the triazole functionality have been shown to exhibit a range of biological functions, including antitumor, antibacterial, antiparasitic and antiviral activity (Figure 1).[2]



A (Zaminivir analogue)[2b] **B** (antiparasitic)[2d] **C** (antiviral)[2f] **D** (Ribavirin analogue)[2g]

Figure 1. Representative examples of biologically active 1,2,3-triazoles.

Historically, 1,2,3-triazoles have been prepared *via* the Huisgen 1,3-dipolar cycloaddition reaction of azides and alkynes.[1a,3] This reaction sometimes requires relatively high temperatures and long reaction times. The main disadvantage of this methodology is that regioisomeric mixtures of the 1,4- and 1,5-disubstituted 1,2,3-triazoles are often formed. Recently, Fokin and coworkers developed new methodology for the preparation of 1,5-dialkyl 1,2,3-triazoles in high yields from aryl azides and terminal alkynes in the presence of catalytic tetramethylammonium hydroxide or Cp*RuCl(PPh_3)$_2$.[4] In addition, Sharpless[1c] and Meldal[1e] have found that catalytic copper(I) dramatically accelerates the reaction resulting in the highly regioselective formation of 1,4-disubstituted triazoles. This powerful, highly reliable, and selective reaction meets the set of stringent criteria required in click chemistry as defined by Sharpless *et al*.[1b] Thus, the copper(I)-catalysed process is the preferred methodology for effecting this reaction (See Scheme 1). The sources of copper(I) include: a) copper(I) salts, normally in the presence of a base and/or a ligand, b) *in-situ* reduction of copper(II) salts (e.g., copper sulfate with sodium ascorbate) and c) disproportionation of copper(0) and copper(II), generally limited to special applications.[5] For instance, reactions performed in some of the commonly used solvents (e.g. water-alcohol solvent mixtures) can be problematic, especially for insoluble reagents or very soluble products, thus reducing the application scope. Another aspect to consider is the reaction time, which, in general, is relatively long, requiring 12-24 h for completion. The addition of some copper complexes[6] or ligands[5,7] was found to enhance the reaction rate. New and interesting advances in the title reaction involve heterogeneous catalysis. Thus copper(I) on charcoal, in the presence of triethylamine, was shown to be an efficient heterogeneous catalyst for the title reaction, the reaction times being reduced to 10-120 min.[8] Copper(I) on zeolite was also recently found to catalyze the cycloaddition reaction from halides or tosylates, sodium azide, and alkynes.[9]



Scheme 1

Recently, increasing attention has been devoted to the use of copper nanoparticles (CuNPs), as substitutes for bulk copper metal, in order to reduce both the catalyst loading and the reaction time.[10] Also the use of CuNPs has shown a general beneficial effect in the cycloaddition of alkynes and azides. Furthermore, easy-to-prepare and versatile heterogeneous copper catalysts that can efficiently promote the multicomponent 1,3-dipolar cycloaddition of organic azides and alkynes in water are welcome. Herein we describe the virtues of Cu_2O on charcoal (Cu_2O/C) as a simple, inexpensive, general, and efficient heterogeneous catalyst for use in click chemistry.

Results and Discussion

(a) Preparation of catalyst

The copper catalyst immobilized on charcoal (Aldrich, Graphite 99.999%, 325 mesh) was readily prepared in a two-step procedure. 1) Preparation of graphite. A high energy mill Spex 8000D, D2 tool steel and hardened steel balls were used. 50 balls of 1.04 g each, and 1.0 g of graphite (99.999%, 325 mesh) were introduced into the vial. Graphite was milled for 40 minutes under a static air atmosphere. 2) Impregnation of charcoal with Cu_2O particles was done using $CuSO_4 \cdot 5H_2O$ as the copper source. $CuSO_4 \cdot 5H_2O$ (0.3062 g) was dissolved in 5.68 mL of deionized water and 1.0 g of milled graphite was added to this solution. The volumetric flask (50 mL) containing this mixture was placed in an ultrasonic bath for 1 h. Finally, the resulting suspension was filtered and dried in an oven for 4 h at 110°C, to obtain nanoparticle-size Cu_2O/C.[11] The cuprous oxide on charcoal catalyst was characterized by its X-ray diffraction pattern (XRD). The copper content in the catalyst (0.89 wt%), was determined by flame atomic absorption spectrophotometry (in 2% nitric acid). Analysis by SEM images revealed the presence of agglomerates of around up to 5 μm, Figure 2a. Each of these agglomerates is formed of platelets with sizes of up to around 200 nm, as can be seen in the dark field transmission electron microscopy image shown in Figure 3a. Each platelet is formed by nanocrystals with

sizes below around 10 nm. The backscattered electron image confirmed the presence of Cu_2O sizes of up to around 1 μm (see Figure 4).

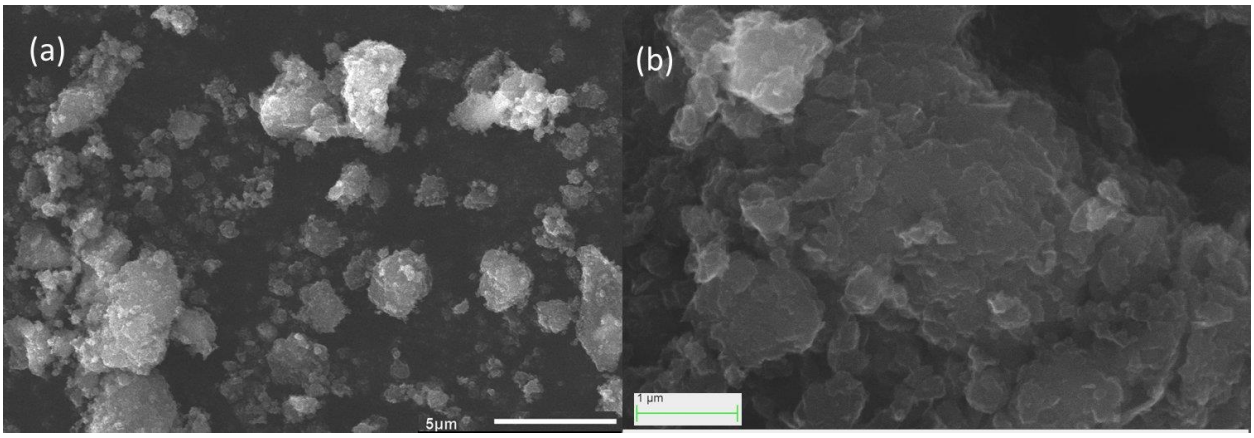


Figure 2. Secondary electron SEM images of graphite milled for 40 minutes.

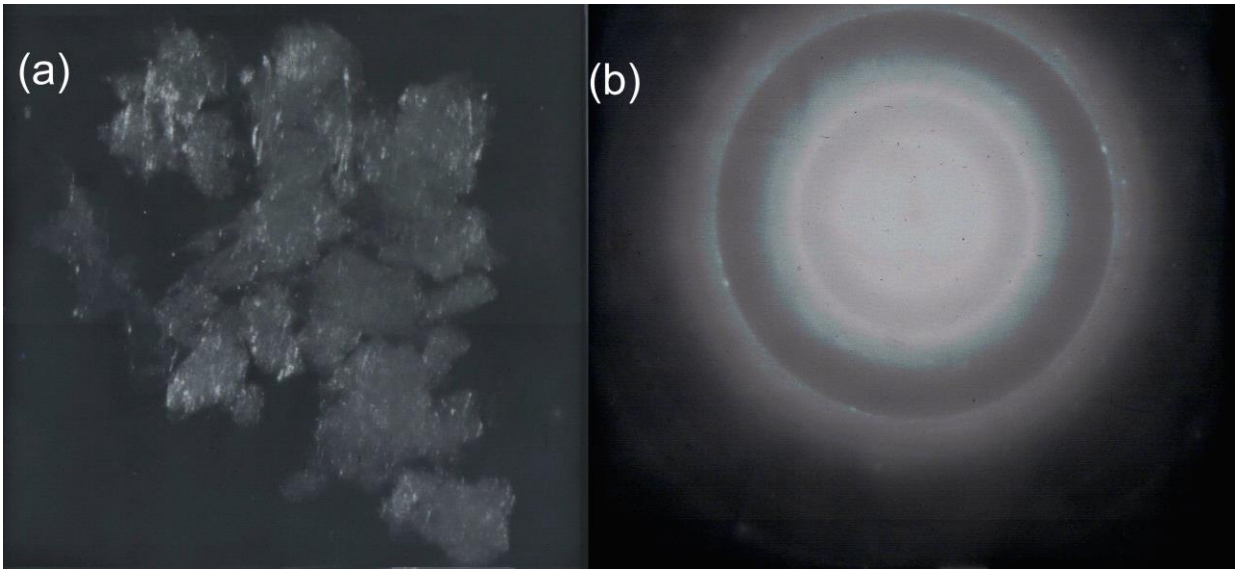


Figure 3. (a) Dark field TEM image of milled graphite, and (b) the corresponding selected area electron diffraction pattern.

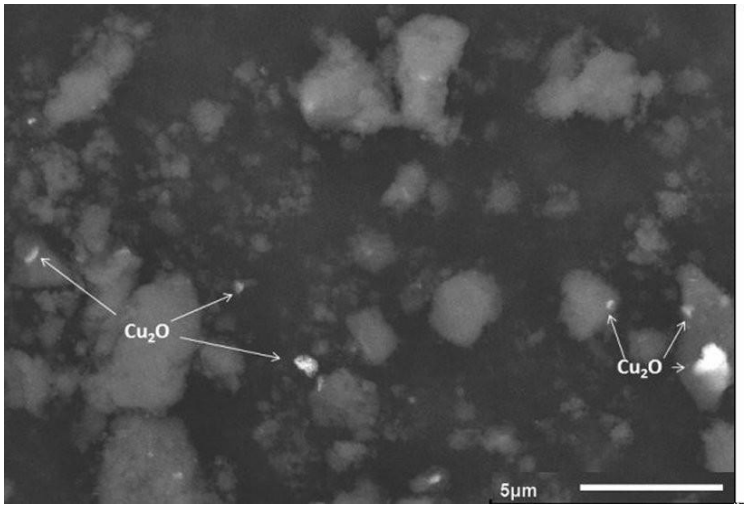


Figure 4. Backscattered electrons SEM image of milled graphite, after treatment with a $CuSO_4$ solution in an ultrasonic bath. Bright particles correspond to Cu_2O.

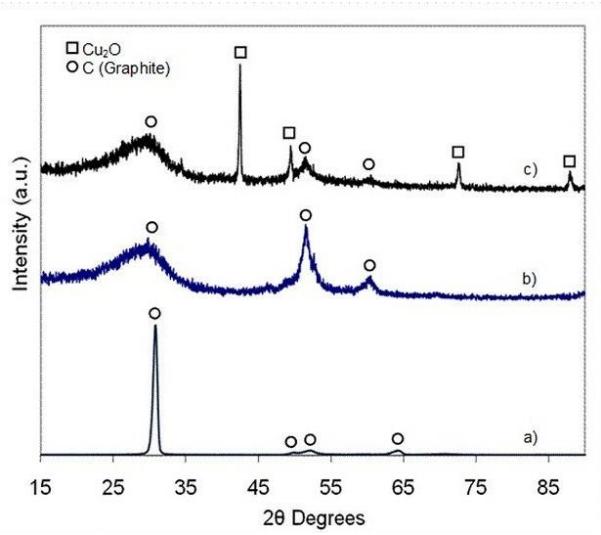


Figure 5. X-ray diffraction patterns of a) unmilled graphite, b) graphite milled for 40 minutes, and c) milled graphite, after treatment with a $CuSO_4$ solution in an ultrasonic bath. The formation of Cu_2O can be observed.

Figure 5 shows the X-ray diffraction patterns of a) unmilled graphite, b) milled graphite and c) milled graphite after treatment with a $CuSO_4$ solution followed by ultrasonication. The patterns shown in a) and b) correspond with the card JCPDS 23-64, for graphite. The peak broadening in Figure 5b is due to crystallite size under 100 nm,[12] in agreement with the nanoparticles shown in Figure 5a. The most noticeable peak broadening was produced in the direction perpendicular to (002) planes, as could be expected for weak bonding between basal planes in graphite. Figure 5c shows that the Cu_2O (JCPDS 1-1142) was formed after

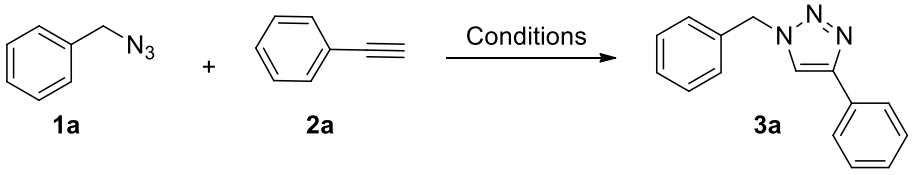
ultrasonication of an aqueous $CuSO_4$ solution containing suspended graphite (after drying at 120ºC overnight). Assuming catalysis by Cu(I), reduction by charcoal could account for the observed activity as described by Lipshutz.[8a]

(b) Application of the Cu_2O/C catalyst for the preparation of 1,5-disubstituted 1,2,3-triazoles

The selected area electron-diffraction pattern of the copper is in agreement with the presence of Cu_2O.[13] It is worthy of note that Cu_2O very recently has been found to catalyze the 1,3-dipolar cycloaddition of azides and terminal alkynes.[14] The reaction of benzyl azide (**1a**) with phenyl acetylene (**2a**) was chosen as a model system (Table 1). Initially, we attempted to adopt a previously reported reaction protocol [PS-EPG-terpyridine copper(I) complex/H_2O/40ºC][15] to synthesize the targeted product **3a**, but to our surprise, **3a** was not formed. Modification of the procedure reported by Chowdhury[16] with increased catalyst loading and manipulation of various parameters (Table 1) including different solvent systems did, however, provide **3a**. It was found that the solvent system plays a very important role in terms of reaction rate, isolated yields, and regioselectivity with the 50% aqueous isopropanol mixture being especially efficacious (Table 1, entry 6). In addition, examination of the effect of various bases showed that triethylamine was the preferred one (Table 1). The TON and the turnover frequency (TOF) of the catalyst reached 1957.32 and 13.5 h^{-1}, respectively; these are, as far as we know, one of the higher TON and TOF obtained for heterogeneous catalysts.[8a,17]

With the optimized conditions (Table 1, entry 6) in hand, the scope of the reaction was explored by reacting various azido compounds (**1a-f**) with terminal alkynes (**2a-e**). The results are summarized in Table 2. All products were characterized by spectral and analytical data (see Experimental Section). The molecular structures of triazoles **3c**, **3l**, **3p** and **3v** were confirmed unambiguously by single-crystal X-ray analyses (see Figure 6).[18] It is obvious that a wide variety of aryl, benzyl, and alkyl azides possessing different functional groups reacted successfully.

Table 1. 1,3-Dipolar Huisgen cycloaddition reaction of benzyl azide and phenylacetylene under various conditions



1a + **2a** → **3a**

Entry	Conditions	Yield (%)[a]
1	Charcoal, (no Cu_2O), r.t., 2 h	0
2	H_2O, with 5% Catalyst, r.t., 2 h	0
3	Acetonitrile, 5% Catalyst, Et_3N, r.t., 1 h	78[b]
4	Acetonitrile, 5% Catalyst, Et_3N, r.t., 24 h	79
5	Acetonitrile, 10% Catalyst, Et_3N, r.t., 1 h	81

Table 1. Continued

Entry	Conditions	Yield (%)[a]
6	H_2O:Isopropanol, 5% Catalyst, Et_3N, r.t., 2 h	82
7	H_2O:Isopropanol, 10% Catalyst, Et_3N, r.t., 2 h	83
9	H_2O:Isopropanol, 15% Catalyst, Et_3N, r.t., 2 h	77
10	H_2O:Isopropanol, 20% Catalyst, Et_3N, r.t., 2 h	85
11	H_2O:Isopropanol, 5% Catalyst, K_2CO_3, r.t., 24 h	64
12	H_2O:Isopropanol, 10% Catalyst, K_2CO_3, r.t., 24 h	57
13	H_2O:Isopropanol, 15% Catalyst, K_2CO_3, r.t., 24 h	66
14	H_2O:Isopropanol, 20% Catalyst, K_2CO_3, r.t., 24 h	65
15	H_2O:Isopropanol, 5% Catalyst, 2,6-lutidine, r.t., 24 h	0[c]

[a] Chromatographically isolated yield of pure product. [b] The catalyst was not recovered. [c] No product formation was observed despite increasing the amount of 2,6-lutidine and catalyst.

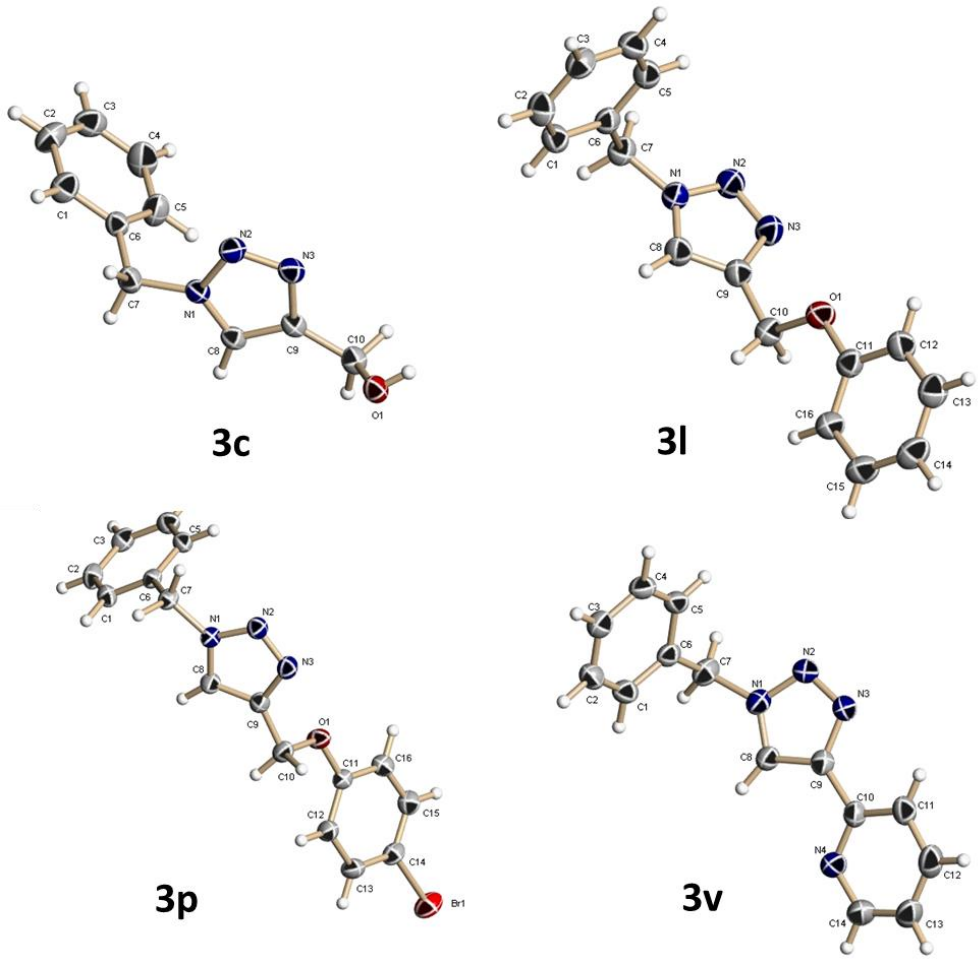


Figure 6. X-Ray structures of **3c**, **3l**, **3p** and **3v.**

Table 2. Click reactions catalyzed by Cu_2O/C[a]

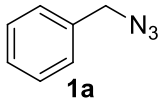
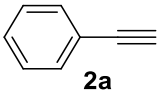
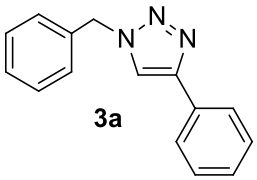
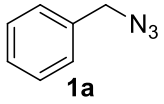
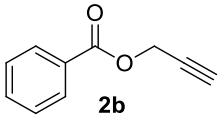
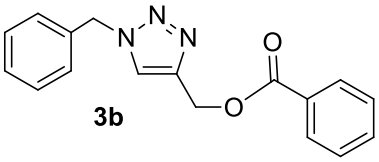
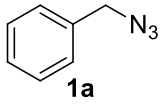
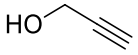
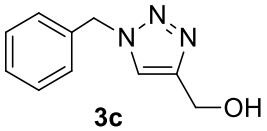
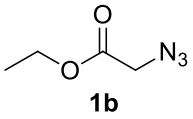
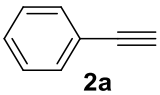
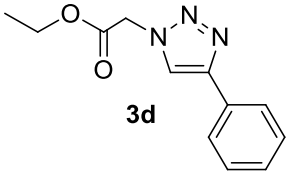
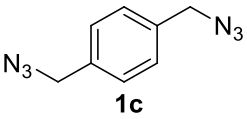
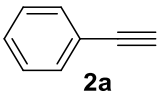
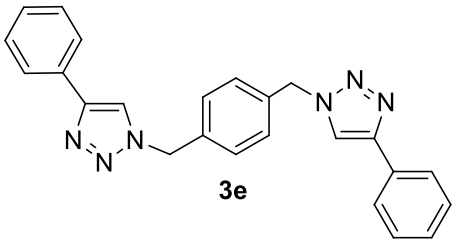
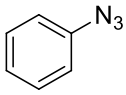
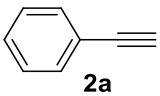
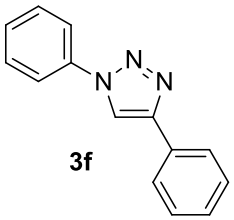
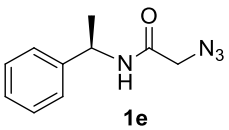
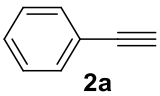
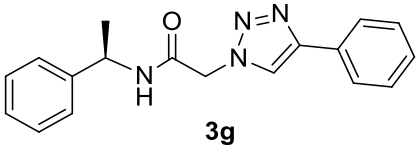
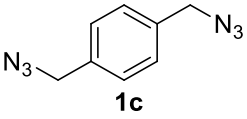
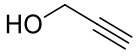
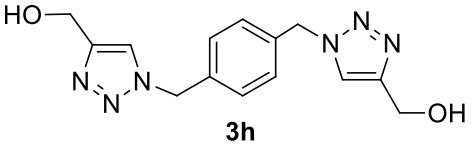
Entry	Azide	Alkyne	Triazole	Yield (%)[b]
1	 **1a**	 **2a**	 **3a**	82
2	 **1a**	 **2b**	 **3b**	84
3	 **1a**	 **2c**	 **3c**	69
4	 **1b**	 **2a**	 **3d**	77
5	 **1c**	 **2a**	 **3e**	79
6	 **1d**	 **2a**	 **3f**	84
7	 **1e**	 **2a**	 **3g**	89
8	 **1c**	 **2c**	 **3h**	76

Table 2. Continued

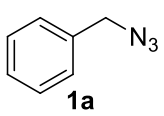
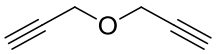
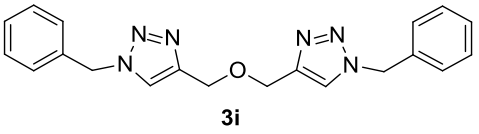
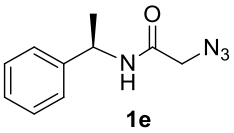
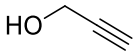
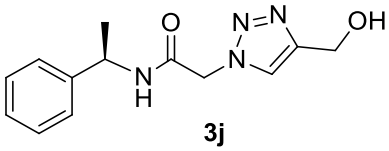
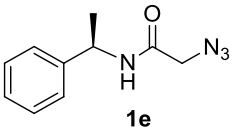
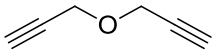
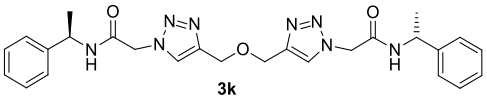
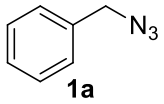
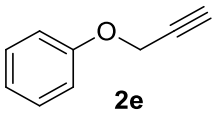
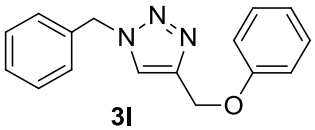
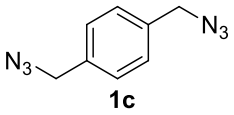
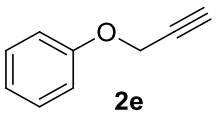
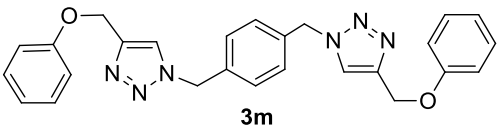
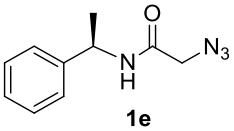
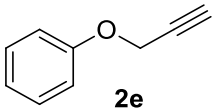
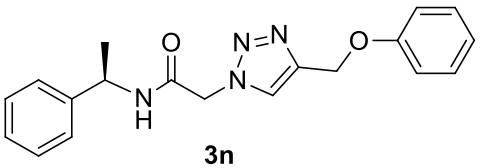
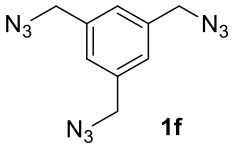
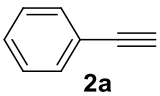
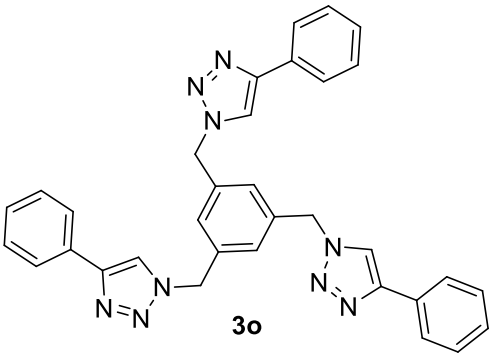
Entry	Azide	Alkyne	Triazole	Yield (%)[b]
9	 1a	 2d	 3i	94
10	 1e	 2c	 3j	79
11	 1e	 2d	 3k	83
12	 1a	 2e	 3l	83
13	 1c	 2e	 3m	71
14	 1e	 2e	 3n	77
15	 1f	 2a	 3o	79

Table 2. Continued

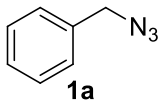
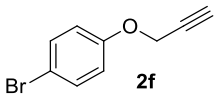
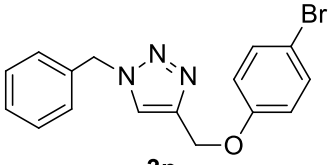
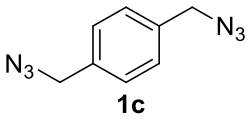
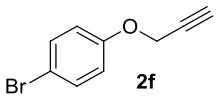
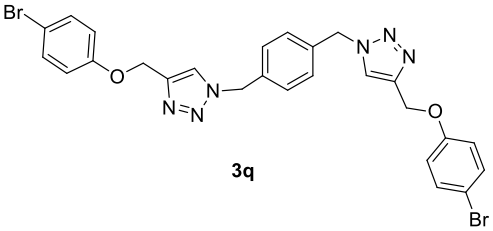
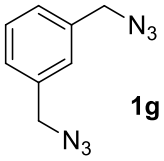
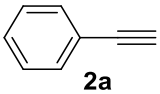
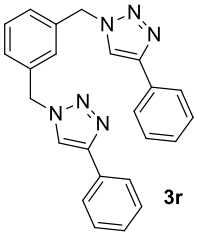
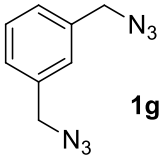
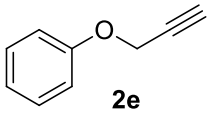
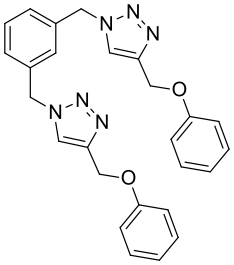
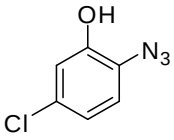
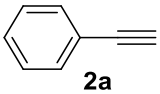
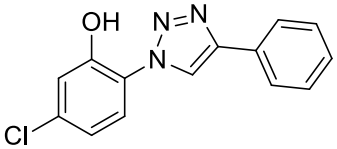
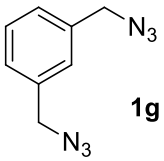
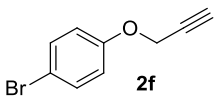
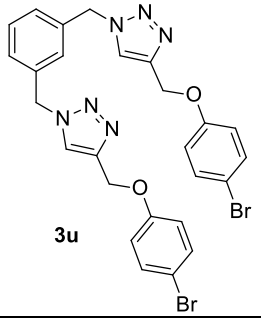
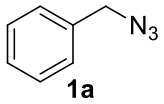
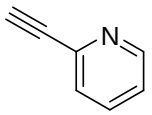
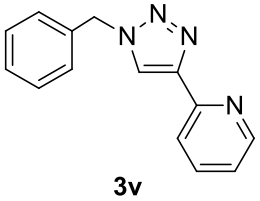
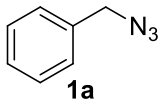
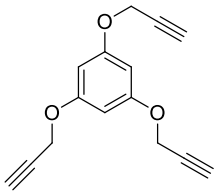
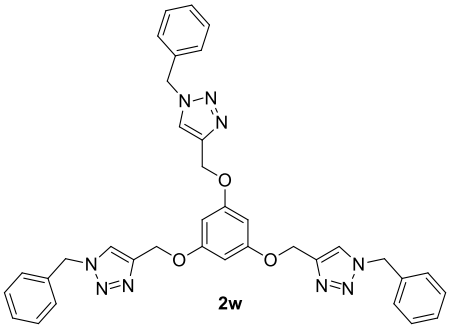
Entry	Azide	Alkyne	Triazole	Yield (%)[b]
16	 **1a**	 **2f**	 **3p**	80
17	 **1c**	 **2f**	 **3q**	87
18	 **1g**	 **2a**	 **3r**	79
19	 **1g**	 **2e**	 **3s**	80
20	 **1h**	 **2a**	 **3t**	80
21	 **1g**	 **2f**	 **3u**	90

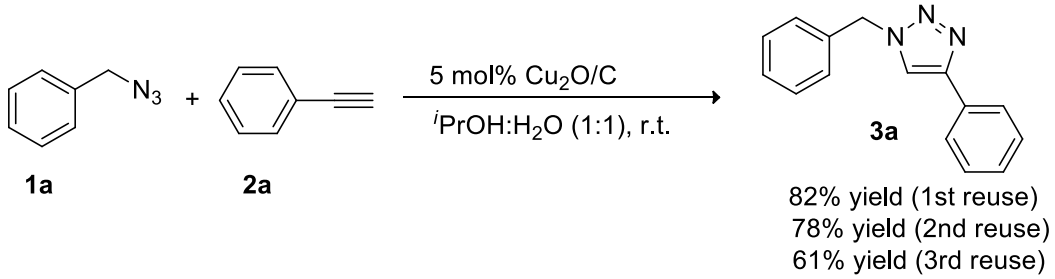
Table 2. Continued

Entry	Azide	Alkyne	Triazole	Yield (%)[b]
22	 **1a**	 **2g**	 **3v**	78
23	 **1a**	 **2h**	 **2w**	79

[a]Reaction was performed using 1 mL of H_2O and 1 mL of Isopropanol at room temperature with 5 mol**%** Cu_2O/C and 1.1 mL of Et_3N. [b]Product was further purified by silica gel chromatography.

(c) Catalyst durability

Numerous control experiments indicated not only that the Cu_2O/C on charcoal is essential for catalysis, but that it is also quite robust. For example, the recyclability of Cu_2O/C was examined for the click reaction of benzyl azide (**1a**) with phenylacetylene (**2a**). Thus after the first reaction, which give 82% of 1-benzyl-4-phenyl-1*H*-1,2,3-triazole (**3a**), the catalyst was recovered by simple filtration, washed with water, dried under vacuum, and reused three times under similar reaction conditions to give **3a** in 78% and 61% yields (Scheme 2).



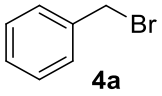
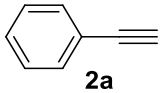
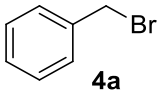
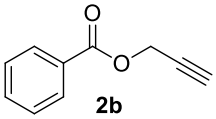
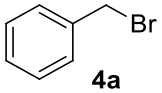
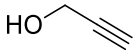
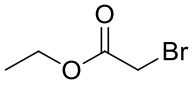
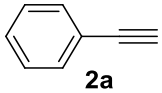
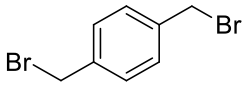
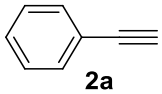
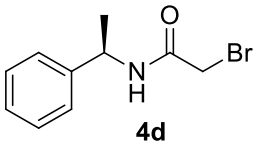
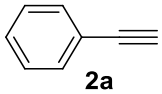
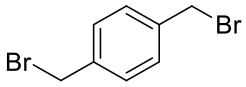
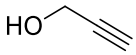
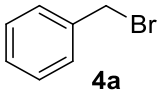
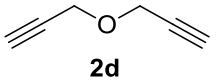
Scheme 2

(d) One pot procedure

In an attempt to circumvent the risk of working with potentially explosive organic azides, we investigated the possibility of carrying out the click reaction without having to isolate the azides.

It is known that 1,4-disubstituted 1,2,3-triazoles can be prepared efficiently in a two step one-pot procedure, in a CuI-zeolite-catalyzed synthesis of triazoles from halides or tosylates, sodium azide, and alkynes at 90ºC.[9a] Benzyl bromide and phenylacetylene were selected as model compounds to find the appropriate conditions for the desired one-pot process. Various reaction conditions were examined including the amount of Cu_2O/C, the reaction temperature, and different solvent systems. Once again 50% aqueous isopropanol clearly stood out as the solvent system of choice providing a fast reaction rate at 80ºC (reflux), high yield, and selectivity (see Table 3). The scope of the reaction was explored by reacting sodium azide, benzyl bromide or alkyl bromides (**4a-d**) with terminal alkynes (**2a-d**). The results are summarized in Table 3.

Table 3. One-pot Cu_2O/C synthesis of 1,4-disubstituted triazoles from halides and related compounds [a]

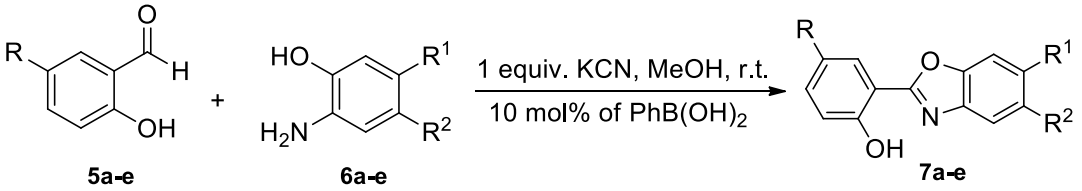
Entry	Halide	Alkyne	Triazole	Yield (%)[b]
1	 **4a**	 **2a**	**3a**	84
2	 **4a**	 **2b**	**3b**	83
3	 **4a**	 **2c**	**3c**	80
4	 **4b**	 **2a**	**3d**	71
5	 **4c**	 **2a**	**3e**	79
5	 **4d**	 **2a**	**3g**	77
6	 **4c**	 **2c**	**3h**	71
7	 **4a**	 **2d**	**3i**	75

[a] Run at 2 equiv of sodium azide, 1 mL of H_2O and 1 mL of isopropanol at 80ºC with 5 mol **%** Cu_2O/C and 4 equiv. of Et_3N for 2 h.

[b] Product was further purified by silica gel chromatography.

(e) Application to other systems

The synthesis of **7a-e** was carried out following recently described methodology.[19] This procedure involves the condensation of salicylaldehyde derivatives with 2-aminophenols in the presence of phenylboronic and catalytic potassium cyanide to give the 2-(2-hydroxyphenyl)benzoxazole derivatives (**7a-e**). (Scheme 3)



	R	R^1	R^2	Yield (%)
a	-H	$-CH_3$	-H	81
b	-H	-Cl	-H	57
c	-H	$-NO_2$	-Cl	69
d	-Br	-H	$-CH_3$	70
e	-Br	-H	-H	56

Scheme 3

The 2-(2-hydroxyphenyl)benzoxazole derivatives (**7a-e**) were subsequently alkylated with propargyl bromide in the presence of potassium carbonate to afford the corresponding benzoxazole derivatives **8a-e**. These compounds, without purification, were reacted with benzyl azide, under the conditions described above to give the 1,2,3-triazole derivatives **9a-e**. (Scheme 4). The structure of the 1,2,3-triazole derivatives **9a-e** was unequivocally established by the usual spectroscopic means, as well as by X-ray crystal structure for compound **9d** (Figure 7, vide infra).[20]

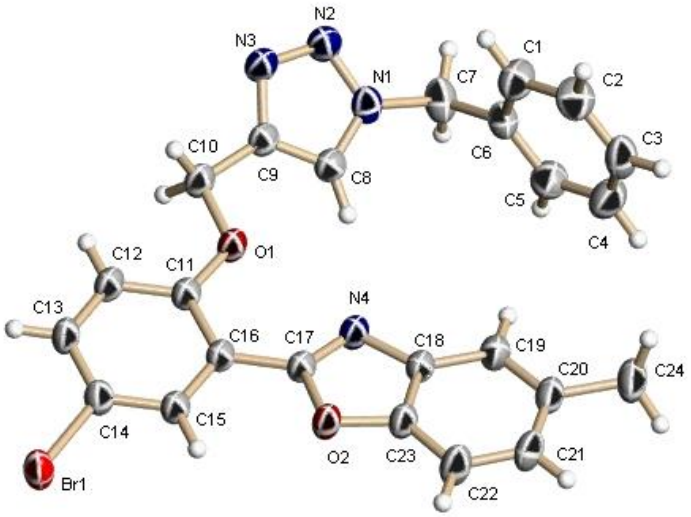
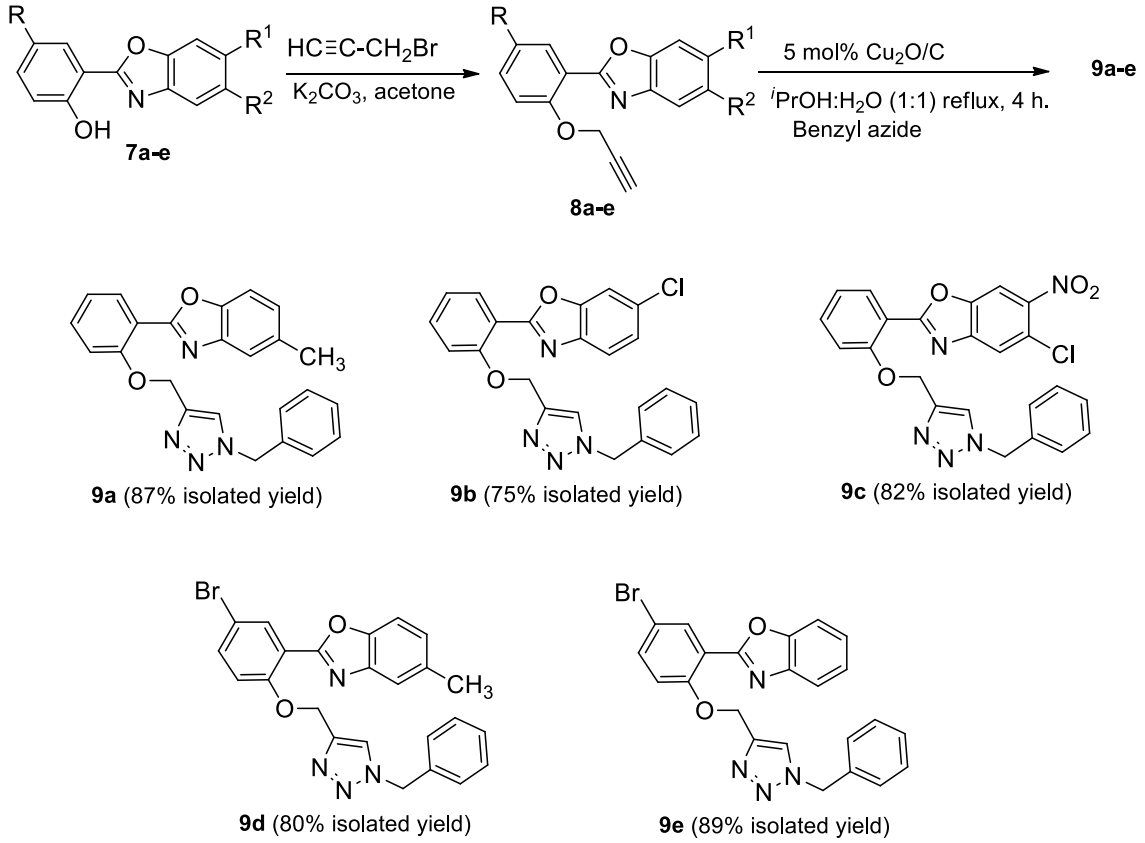


Figure 7. X-Ray structure of **9d.**



Scheme 4

The mechanism of these reactions proceeds similarly to previous reports.[8a-b,21,22]

Conclusions

We describe in this paper a facile preparation of a new supported catalyst (Cu_2O/C) for Copper-Catalyzed Alkyne-Azide Cycloaddition. This material was found to efficiently catalyze the formation of several 1,4-disubstituted 1,2,3-triazoles from organic azides and various terminal alkynes. In addition, a multicomponent, one-pot protocol for the synthesis of 1,4-disubstituted 1,2,3-triazoles from alkyl azides was devised. Considering the good triazole yields, the operational ease with which these reactions can be carried out, and the inexpensive chemicals involved, we believe this protocol will be of great benefit to medicinal and synthetic organic chemistry.

Experimental Section

General. TLC was performed on Merck-DC-F_{254} plates, detection was made by shining UV light. Flash column chromatography was performed using Merck silica gel (230-240 mesh).

Melting points were measured in open capillary tubes on a Büchi Melting Point B-540 apparatus and have not been corrected. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL Eclipse+400 (400 MHz, 100 MHz)) and a Varian VNMRS 400 (400 and 100 MHz) spectrometers. Chemical shifts (δ) are indicated in ppm downfield from internal TMS used as reference; the coupling constants (*J*) are given in Hz. IR spectra were measured on a Perkin Elmer GX FT-IR. Elemental analyses were performed on a Perkin-Elmer Series II CHNS/O Analyzer 2400.

General procedure for the preparation of 1,2,3-triazoles

In a 10 mL round-bottomed flask fitted with a magnetic stirring bar was placed 1.0 equiv. of azide 1 and 1.0 equiv. of terminal alkyne 2 in 2 mL of [H_2O:^{i}PrOH (1:1)], further was added Cu_2O/C (5% w/w) and 1.1 mL of Et_3N (for 100 mg of alkyl azide). The reaction mixture was warmed to 80 °C and monitored by TLC until total conversion of the starting material. The crude reaction mixture was filtered through a filter paper, washed and extracted with EtOAc or CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with 15 mL of saturated aq. NH_4Cl, dried over anhydrous sodium sulfate, and evaporated under reduced pressure in vacuum. The crude reaction mixture was purified by column chromatography or crystallization to afford **3a-w**.

General procedure for the one-pot direct synthesis of 1,2,3-triazoles

In a 10 mL round-bottomed flask fitted with a magnetic stirring bar was placed 1.0 equiv. of alkyl halide **4**, 2 equiv. of sodium azide in 2 mL of [H_2O:^{i}PrOH (1:1)], 1.0 equiv. of terminal alkyne 2, Cu_2O/C (5% w/w) and 1.1 mL of Et_3N (for 0.734 mmol of alkyl halide). The reaction mixture was warmed to 80 °C and monitored by TLC until total conversion of the starting material. The crude reaction mixture was filtered through a filter paper, washed and extracted with EtOAc or CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with 15 mL of saturated aq. NH_4Cl, dried over anhydrous sodium sulfate, and evaporated under reduced pressure in vacuum. The crude reaction mixture was purified by column chromatography or crystallization to afford **3a-e** and **3g-i**.

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (3a).[7a,8a,8d,9a,15,23,24] The general procedure was followed using 0.1 g (0.734 mmol) of benzyl azide (**1a**), 0.81 mL (0.734 mmol) of phenylacetylene, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.139 g (82%) of **3a** as a white solid. Purification was performed by crystallization using (ethyl acetate/diethyl ether). Mp 131-133 °C (lit.[23a] mp: 130-132°C; lit.[8c] mp: 129-129.5°C).

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl benzoate (3b). The general procedure was followed using 0.10 g (0.734 mmol) of benzyl azide (**1a**), 0.10 mL (0.734 mmol) of propargyl benzoate, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.180 g (84%) of **3b** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 106-109 °C; IR (film) ν_{max}/cm^{-1}: 3070, 1722, 1603, 1453, 1275, 1111, 1052, 956, 713; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 7.94 (m, 2H), 7.54 (s, 1H), 7.45 (m, 1H), 7.35-7.19 (m, 7H,), 5.44 (s, 2H), 5.36 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 166.4, 143.3, 134.3, 133.2, 129.8, 129.6, 129.1,

128.8, 128.3, 128.1, 123.8, 58.0, 54.2 Anal. Calcd for $C_{17}H_{15}N_3O_2$ C, 69.61; H, 5.15; N, 14.33. Found: C, 69.98; H, 4.86; N, 13.96%.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methanol (3c).[8c,18a,25] The general procedure was followed using 0.10 g (0.734 mmol) of benzyl azide (**1a**), 0.16 mL (1.1 mmol) of propargyl alcohol, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.096 g (69%) of **3c** as a white solid. The solid residue was purified by crystallization using (hexane/diethyl ether). Mp 77-79°C (lit.[8c] mp: 78-78.5 °C.

Ethyl 2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)acetate (**3d**).[8d,10,23a,24a] The general procedure was followed using 0.10 g (0.825 mmol) of ethyl azidoacetate (**1b**), 0.09 mL (0.825 mmol) of phenylacetylene, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.150 g (77%) of **3d** as a white solid. The solid residue was purified by crystallization using (hexane/diethyl ether). Mp 94-96 °C (lit.[23a] mp: 93-95 °C; lit.[10] mp: 94-95 °C).

1,4-Bis[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]benzene (3e). The general procedure was followed using 0.10 g (0.531 mmol) of 1,4-bis(azidomethyl)benzene (**1c**), 0.116 mL (1.06 mmol) of phenylacetylene, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.280 g (79%) of **3e** as a yellow solid. The solid residue was purified by flash chromatography using (ethyl acetate / hexane). Mp 253-255 °C; IR (film) ν_{max}/cm^{-1}: 3098, 2924, 1470, 1363, 772, 482; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8,61 (s, 2H), 7.80 (m, 4H), 7.41-7.29 (m, 10H), 5.61 (s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 147.1, 136.4, 131.0, 129.3, 128.8, 128.3, 125.6, 122.1, 53.1. Anal. Calcd for $C_{24}H_{20}N_6$ C, 73.45; H, 5.14; N, 21.41. Found: C, 73.25; H, 4.98; N, 21.32%.

1,4-diphenyl-1*H*-1,2,3-triazole (3f).[10a, 23a, 23b, 23d, 24a] The general procedure was followed using 0.515 g (4.3 mmol) of phenyl azide (**1d**), 0.47 mL (4.3 mmol) of phenylacetylene, 5 mg of Cu_2O/C and 5.6 mL of Et_3N to give 0.767 g (84%) of **3f** as a yellow solid. The solid residue was purified by crystallization using (dichloromethane/diethyl ether). Mp 183-185 °C (lit.[23a] mp: 183-184°C).

(*R*)-2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-*N*-(1-phenylethyl)acetamide (3g). The general procedure was followed using 0.480 g (2.35 mmol) of (*R*)-2-azido-*N*-(1-phenylethyl)acetamide (**1e**), 0.258 mL (2.35 mmol) of phenylacetylene, 25 mg of Cu_2O/C and 5.3 mL of Et_3N to give 0.640 g (89%) of **3g** as a white solid. The solid residue was purified by crystallization using (hexane/diethyl ether). Mp 244-245 °C; IR (film) ν_{max}/cm^{-1}: 3275, 3095, 1658, 1561, 750, 688 ; ^{1}H NMR (DMSO-d_6, 400 MHz) δ/ppm: 8.86 (d, 1H, J 6.4 Hz), 8.47 (s, 1H), 7.81 (m, 2H), 7.41-7.20 (m, 8H), 5.15 (s, 2H), 4.90 (m, 1H), 1.36 (d, 3H, *J* 6.8 Hz). ^{13}C NMR (DMSO-d_6, 100 MHz) δ/ppm: 164.8, 146.4, 144.4, 131.1, 129.3, 128.8, 128.3, 127.3, 126.4, 125.5, 123.4, 52.1, 48.8, 22.8. Anal. Calcd for $C_{18}H_{18}N_4O$ C, 70.57; H, 5.92; N, 18.29. Found: C, 70.31; H, 5.69; N, 18.65%.

[1,1-[1,4-phenylenebis(methylene)]bis(1*H*-1,2,3-triazol-4,1-diyl)]dimethanol (3h). The general procedure was followed using 0.10 g (0.531 mmol) of 1,4-bis(azidomethyl)benzene (**1c**), 0.065 mL (1.06 mmol) of propargyl alcohol, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.767 g (84%) of **3h** as a yellow solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 71-74 °C; IR (film) ν_{max}/cm^{-1}: 3163, 2928, 1652, 1467, 1258, 1041, 860, 766; ^{1}H NMR (DMSO-d_6, 400 MHz) δ/ppm: 7.98 (s, 2H), 7.37 (s, 4H), 5.54 (s, 4H), 5.15

(m, 2H), 4.44 (m, 4H). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 148.8, 135.9, 129.2, 123.3, 55.4, 53.6. Anal. Calcd for $C_{14}H_{16}N_6O_2$ C, 55.99; H, 5.36; N, 27.98. Found: C, 55.71; H, 4.99; N, 27.72%.

4,4-[Oxybis(methylene)]bis(1-benzyl-1*H*-1,2,3-triazole) (3i).[7a] The general procedure was followed using 0.10 g (0.367 mmol) of benzyl azide (**1a**), 0.047 mL (1.06 mmol) of propargyl ether, 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.248 g (94%) of **3i** as a yellow solid. The solid residue was purified by crystallization using (dichloromethane/diethyl ether). Mp 124-126 °C; IR (film) ν_{max}/cm^{-1}: 3141, 2937, 2869, 1606 ,1457, 1223, 1129, 1055, 728 ; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.13 (s, 2H), 7.34-7.24 (m, 10H), 5.54 (s, 4H), 4.50 (s, 4H),. ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 144.3, 136.5, 129.1, 128.5, 128.3, 124.6, 63.1, 53.1. Anal. Calcd for $C_{20}H_{20}N_6O$ C, 66.65; H, 5.59; N, 23.32. Found: C, 66.40; H, 5.40; N, 22.99%.

(*R*)-2-[4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]-*N*-(1-phenylethyl)acetamide (3j). The general procedure was followed using 0.20 g (0.979 mmol) of (*R*)-2-azido-*N*-(1-phenylethyl)acetamide (**1e**), 0.058 mL (1.06 mmol) of propargyl alcohol, 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.189 g (79%) of **3j** as a yellow solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 92-94 °C; IR (film) ν_{max}/cm^{-1}: 2934, 1670, 1562, 1252, 1041, 702 ; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.78 (m, 1H), 7.85 (s, 1H), 7.30-7.20 (m, 5H), 5.07 (s, 2H), 4.88 (m, 1H), 4.45 (d, 2H, *J* 5.6 Hz), 1.33 (d, 3H, *J* 7.2 Hz). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 164.9, 148.0, 144.4, 128.8, 127.3, 126.4, 124.6, 55.4, 51.9, 48.7, 22.8. Anal. Calcd for $C_{13}H_{16}N_4O_2$ C, 59.99; H, 6.20; N, 21.52. Found C, 60.22; H, 6.64; N, 21.71%.

2,2-[4,4-[Oxybis(methylene)bis(1*H*-1,2,3-triazole-4,1-diyl)]]bis-*N*-[(*R*)-1-phenylethyl]acetamide (3k). The general procedure was followed using 0.210 g (1.02 mmol) of (*R*)-2-azido-*N*-(1-phenylethyl)acetamide (**1e**), 0.048 mL (1.06 mmol) of propargyl ether, 10 mg of Cu_2O/C and 2.3 mL of Et_3N to give 0.603 g (83%) of **3k** as a yellow solid. The solid residue was purified by flash chromatography using ethyl acetate/hexane. Mp 182-184 °C; IR (film) ν_{max}/cm^{-1}: 3300, 2976, 2681, 2499, 1669, 1565, 1059, 701 ; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.96 (m, 2H), 8.01 (s, 2H), 7.29-7.18 (m, 10H), 5.13 (s, 4H), 4.87 (m, 2H), 4.51 (s, 4H), 1.34 (d, 6H, *J* 6.8 Hz). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 164.9, 144.5, 143.7, 128.5, 127.5, 126.4, 126.1, 62.9, 51.9, 48.8, 22.9.

1-Benzyl-4-(phenoxymethyl)-1*H*-1,2,3-triazole (3l).[1c,8d,15,23b,25] The general procedure was followed using 0.10 g (0.734 mmol) of benzyl azide (**1a**), 0.097 g (0.734 mmol) of (prop-2-yn-1-yloxy)benzene (**2e**), 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.161 g (83%) of **3l** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 126-128 °C; IR (film) ν_{max}/cm^{-1}: 3134, 1599, 1495, 1224, 1007, 756; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.51 (s, 1H), 7.35-7.23 (m, 7H,), 6.95-6.93 (m, 3H), 5.47 (s, 2H), 5.15 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 158.1, 144.6, 134.3, 129.5, 129.2, 128.8, 128.1, 122.6, 121.3, 114.7, 61.9, 59.3. Anal. Calcd for $C_{16}H_{15}N_3O$ C, 72.43; H, 5.70; N, 15.84. Found: C, 72.48; H, 5.62; N, 15.98%.

1,4-Bis[[4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl]methyl]benzene (3m). The general procedure was followed using 0.15 g (0.797 mmol) of 1,4-bis(azidomethyl)benzene (**1c**), 0.240 g (1.59

mmol) of (prop-2-yn-1-yloxy)benzene (**2e**), 7.5 mg of Cu_2O/C and 1.65 mL of Et_3N to give 0.255 g (71%) of **3m** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 192-194 °C; IR (film) ν_{max}/cm^{-1}: 3145, 1595, 1433, 1212, 1006, 758 ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.53 (s, 2H), 7.27-7.23 (m, 8H), 6.94-6.92 (m, 6H), 5.50 (s, 4H), 5.17 (s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 158.1, 144.8, 135.2, 129.6, 128.8, 122.7, 121.3, 114.7, 61.9, 53.7. Anal. Calcd for $C_{26}H_{24}N_6O_2$ C, 69.01; H, 5.35; N, 18.57. Found: C, 69.07; H, 5.16; N, 18.44%.

(*R*)-2-[4-(Phenoxymethyl)-1*H*-1,2,3-triazol-1-yl]-*N*-(1-phenylethyl)acetamide (3n). The general procedure was followed using 0.200 g (0.797 mmol) of (*R*)-2-azido-*N*-(1-phenylethyl)acetamide (**1e**), 0.130 g (0.980 mmol) of (prop-2-yn-1-yloxy)benzene (**2e**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.253 g (77%) of **3n** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/diethyl ether). Mp 132-135 °C; IR (film) ν_{max}/cm^{-1}: 3287, 3063, 1669, 1599, 1551, 1494, 1240, 1032, 754; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.76 (s, 1H), 7.29-7.18 (m, 7H), 6.97-6.93 (m, 3H), 5.14 (s, 2H), 5.03 (m, 1H), 4.94 (m, 2H), 1.40 (d, 3H, *J* 7.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 164.1, 158.0, 144.6, 142.3, 129.6, 128.7, 127.5, 126.1, 124.6, 121.4, 114.7, 61.8, 52.8, 49.6, 21.7. Anal. Calcd for $C_{19}H_{20}N_4O_2$ C, 67.84; H, 5.99; N, 16.66. Found: C, 67.67; H 5.35; N, 16.78%.

1,3,5-Tris[(4-phenyl-1*H*-1,2,3-triazol-yl)methyl]benzene (3o).[7a,24] The general procedure was followed using 0.10 g (1.23 mmol) of 1,2,3-tris(azidomethyl)benzene (**1f**), 0.134 mL (1.23 mmol) of phenylacetylene (**2a**), 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.120 g (79%) of **3n** as a white solid. The solid residue was purified by flash chromatography using (ethyl acetate/hexane). Mp 221-223 °C; IR (film) ν_{max}/cm^{-1}: 3076, 2938, 1430, 1353, 762 ; ^{1}H NMR (DMSO-d_6, 400 MHz) δ/ppm: 8.56 (s, 3H), 7.76 (d, 6H, *J* 7.3 Hz), 7.37 (t, 6H, J 7.3 Hz), 7.29 (m, 9H), 5.61 (s , 6H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ/ppm: 147.2, 137.8, 131.2, 129.4, 128.5, 127.8, 125.7, 122.0, 53.1.

1-Benzyl-4-[(4-bromophenoxy)methyl]-1*H*-1,2,3-triazole (3p). The general procedure was followed using 0.20 g (1.46 mmol) of benzyl azide (**1a**), 0.308 g (1.46 mmol) of 1-bromo-4-(pro-2-yn-1-yloxy)benzene (**2f**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.402 g (80%) of **3p** as a white solid. The solid residue was purified by crystallization using (acetone/diethyl ether). Mp 132-134 °C; IR (film) ν_{max}/cm^{-1}: 3139, 1623, 1585, 1489, 1227, 995, 619 ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.44 (s, 1H), 7.30-7.23 (m, 5H,), 7.19-7.15 (m, 2H), 6.76 (d, 2H, *J* 8.8 Hz), 5.12 (s, 2H), 5.03 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 157.2, 144.1, 134.3, 132.3, 129.1, 128.8, 128.1, 127.7, 122.7, 116.5, 113.4, 62.1, 54.2 Anal. Calcd for $C_{16}H_{14}BrN_3O$ C, 55.83; H, 4.10; N, 12.21. Found: C, 55.84; H, 4.03; N, 11.88% HRMS (ESI) Calcd for $C_{16}H_{14}BrN_3O$ [$(M+H)^+$] 344.0399; Found 344.0393.

1,4-Bis[[4-[(4-bromophenoxy)methyl]-1*H*-1,2,3-triazol-4-yl]methyl]benzene (3q). The general procedure was followed using 0.20 g (1.06 mmol) of 1,4-bis(azidomethyl)benzene (**1c**), 0.45 g (2.12 mmol) of 1-bromo-4-(pro-2-yn-1-yloxy)benzene (**2f**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.564 g (87%) of **3q** as a yellow solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp 177-179°C; IR (film) ν_{max}/cm^{-1}: 3074, 1590,

1489, 1238, 1040, 814, 619 ; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.23 (s, 2H), 7.40 (d, 4H, *J* 8.8 Hz), 7.27 (s, 4H), 6.95 (d, 4H, *J* 9.2 Hz), 5.55 (s, 4H), 5.07 (s, 4H). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 157.7, 143.1, 136.4, 132.6, 128.8, 125.2, 117.5, 112.7, 61.7, 52.8 Anal. Calcd for $C_{26}H_{22}Br_2N_6O_2$ C, 51.17; H, 3.63; N, 13.77. Found: C, 51.02; H, 3.60; N, 13.50%. HRMS (ESI) Calcd for $C_{26}H_{22}Br_2N_6O_2$ [(M+H)$^+$] 609.0250; Found 609.0244.

1,3-Bis[(4-benzyl-1*H*-1,2,3-triazol-yl)methyl]benzene (3r). The general procedure was followed using 0.50 g (2.65 mmol) of 1,3-bis(azidomethyl)benzene (**1g**), 0.58 mL (5.31 mmol) of phenylacetylene (**2a**), 25 mg of Cu_2O/C and 5.5 mL of Et_3N to give 0.821 g (79%) of **3r** as a white solid. The solid residue was purified by crystallization using ethyl acetate. Mp 162-164°C; IR (film) ν_{max}/cm^{-1}: 3130, 2919, 1609, 1432, 1221, 1074, 764 ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.77 (dd, 4H, *J* 1.2 Hz, *J* 8.0 Hz), 7.68 (s, 2H,), 7.40-7.37(m, 4H), 7.32-7.24 (m,6H), 5.54 (s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 148.3, 135.9, 130.2, 130.0, 128.8, 128.3, 128.2, 127.3, 125.7, 119.6, 53.8 Anal. Calcd for $C_{24}H_{20}N_6$ C, 73.45; H, 5.14; N, 21.41 Found: C, 73.02; H, 5.16; N, 21.59%. HRMS (ESI) Calcd for $C_{24}H_{20}N_6$, [(M+H)$^+$] 393.1828 ; Found 393.1826.

1,3-Bis[[(4-phenoxymethyl)-1*H*-1,2,3-triazol-1-yl]methyl]benzene (3s). The general procedure was followed using 0.39 g (2.07 mmol) of 1,3-bis(azidomethyl)benzene (**1g**), 0.540 g (4.14 mmol) of (prop-2-yn-1-yloxy)benzene (**2e**), 19 mg of Cu_2O/C and 4.3 mL of Et_3N to give 0.739 g (80%) of **3s** as a white solid. The solid residue was purified by crystallization using ethyl acetate. Mp 115-117°C; IR (film) ν_{max}/cm^{-1}: 3140, 2924, 1601, 1498, 1247, 1030, 756; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 7.54 (s, 2H), 7.34 (t, 1H, *J* 7.6 Hz), 7.27-7.15 (m, 6H,), 7.13 (m, 1H) 6.95-6.92 (m, 6H), 5.47 (s, 4H), 5.15 (s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 158.1, 144.8, 135.6, 130.0, 129.5, 128.3, 127.5, 122.8, 121.3, 114.7, 61.9, 53.7 Anal. Calcd for $C_{26}H_{24}N_6O_2$ C, 69.01; H, 5.35; N, 18.57. Found: C, 68.70; H, 5.32; N, 18.43%. HRMS (ESI) Calcd for $C_{26}H_{24}N_6O_2$ [(M+H)$^+$] 453.2040; Found 453.2034.

5-Chloro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)phenol (3t). The general procedure was followed using 0.375 g (2.22 mmol) of 2-azido-5-chlorophenol (**1h**), 0.244 mL (2.22 mmol) of phenylacetylene (**2a**), 19 mg of Cu_2O/C and 4.12 mL of Et_3N to give 0.480 g (80%) of **3t** as a white solid. The solid residue was purified by flash chromatography using (ethyl acetate/hexane). Mp 276-278 °C; IR (film) ν_{max}/cm^{-1}: 3452, 2919, 2850, 1601, 1438, 1235, 1060, 757; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.93 (s, 1H), 7.95(d, 2H, *J* 6.8), 7.67 (d, 1H, *J* 8 Hz), 7.48 (m, 2H), 6.37 (m, 1H), 7.20 (d, 1H, *J* 2 Hz), 7.09 (dd, 1H, *J* 2.4 Hz, *J* 8.4 Hz). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz) δ/ppm: 151.7, 146.7, 134.5, 130.8, 129.4, 128.5, 127.3, 125.7, 124.2, 123.5, 119.7, 117.1. Anal. Calcd for $C_{14}H_{10}ClN_3O$ C, 61.89; H, 3.71; N, 15.47. Found: C, 61.50; H, 3.66; N, 14.89%. HRMS (ESI) Calcd for $C_{14}H_{10}ClN_3O$ [(M+H)$^+$] 272.0591; Found 272.0584.

1,3-Bis[[4-[(4-bromophenoxy)methyl]-1*H*-1,2,3-triazol-1-yl]methyl]benzene (3u). The general procedure was followed using 0.20 g (1.06 mmol) of 1,3-bis(azidomethyl)benzene (**1g**), 0.45 mL (1.14 mmol) of 1-bromo-4-(prop-2-yn-1-yloxy)benzene (**2f**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.580 g (90%) of **3u** as a brown solid. The solid residue was purified by crystallization using dichloromethane. Mp 166-168 °C; IR (film) ν_{max}/cm^{-1}: 3153, 1592, 1489, 1253, 1044, 825; ^{1}H NMR (DMSO-*d*$_6$, 400 MHz) δ/ppm: 8.25 (s, 2H), 7.42 (d, 4H, *J* 9.2 Hz),

7.35 (t, 1H, *J* 7.6 Hz), 7.30 (m, 1H), 7.22 (dd, 2H, *J* 1.6 Hz, *J* 7.6 Hz), 6.97 (d, 4H, *J* 9.2 Hz), 5.57 (s, 4H), 5.09 (s, 4H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ/ppm: 157.7, 143.1, 137.0, 132.5, 129.8, 128.2, 128.0, 125.3, 117.5, 112.7, 61.7, 53.0. Anal. Calcd for $C_{26}H_{22}Br_2N_6O_2$ C, 51.17; H, 3.63; N, 13.77. Found: C, 51.13; H, 3.46; N, 13.01%. HRMS (ESI) Calcd for $C_{26}H_{22}$ $Br_2N_6O_2$ [$(M+H)^+$] 609.0250; Found 609.0239.

2-(1-Benzyl-1*H*-1,2,3-triazol-1-yl)pyridine (3v). The general procedure was followed using 0.10 g (0.734 mmol) of benzyl azide (**1a**), 0.073 mL (0.734 mmol) of 2-ethynylpyridine (**2g**), 5 mg of Cu_2O/C and 1.1 mL of Et_3N to give 0.130 g (78%) of **3v** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp 118-120 °C; IR (film) ν_{max}/cm^{-1}: 3106, 1595, 1421, 1224, 1045, 786, 727 ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ/ppm: 8.50 (m, 1H), 8.14 (dd, 1H, *J* 1.2 Hz, *J* 8.4 Hz), 8.02 (s,1H), 7.37 (td, 1H, *J* 2.4 Hz, *J* 8.4 Hz), 7.35-7.29 (m, 5H), 7.18-7.16 (m, 1H), 5.55 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ/ppm: 150.2, 149.3, 148.7, 136.9, 134.3, 129.1, 128.8, 128.3, 122.8, 121.9, 120.2, 54.3. Anal. Calcd for $C_{14}H_{12}N_4$ C, 71.17; H, 5.12; N, 23.71. Found: C, 70.93; H, 5.13; N, 23.78%. HRMS (ESI) Calcd for $C_{14}H_{12}N_4$ [$(M+H)^+$] 237.1141; Found 237.1136.

1,3,5-Tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyloxy]benzene (3w). The general procedure was followed using 0.20 g (1.46 mmol) of benzyl azide (**1a**), 0.117 g (0.489 mmol) of 1,3,5-tris(prop-2-ynyloxy)benzene (**2h**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.130 g (78%) of **3w** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp 144-146°C; IR (film) ν_{max}/cm^{-1}: 3141, 1610, 1457, 1153, 1051, 804, 720 ; ^{1}H NMR (DMSO-d_6, 400 MHz) δ/ppm: 8.24 (s, 3H), 7.33-7.26 (m, 15H), 6.27 (s,3H), 7.57 (s, 6H), 5.03 (s, 6H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ/ppm: 160.2, 143.3, 136.4, 129.2, 128.6, 128.4, 125.2, 94.9, 61.5, 53.3. Anal. Calcd for $C_{36}H_{33}N_9O_3$ C, 67.59; H, 5.20; N, 19.71. Found: C, 67.36; H, 5.07 N, 19.62%. HRMS (ESI) Calcd for $C_{36}H_{33}N_9O_3$ [$(M+H)^+$], 640.2785; Found 640.2778.

2-[2-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl]-5-methylbenzoxazole (9a). The general procedure was followed using 0.1 g (0.73 mmol) of benzyl azide (**1a**), 0.20 g (0.76 mmol) of 5-methyl-2-(2-prop-2-yn-1-yloxy)phenyl)benzoxazole (**8a**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.26 g (87%) of **9a** as a white solid. The solid residue was purified by flash chromatography using (ethyl acetate/hexane). Mp. 179-180^{o}C. IR (film) ν_{max}/cm^{-1}: 3412, 2346, 1585, 1603, 133.2, 2918; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.04 (dd, *J* 2.0 Hz, *J* 7.6 Hz, 1H, 2H), 7.74 (s, 1H), 7.40 (ddd, *J* 2.0 Hz, *J* 7.6 Hz, *J* 8.4 Hz, 1H), 7.32 (m, 1H), 7.30 (m, 3H), 7.21 (m, 2H), 7.40 (d, *J* 8.4 Hz, 1H), 7.10 (d, *J* 8.0 Hz, 1H), 7.03 (m, 2H), 5.46 (s, 2H), 5.32 (s, 2H), 2.41 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ/ppm: 161.6, 156.9, 148.6, 145.2, 142.2, 134.6, 134.0, 132.7, 131.2, 129.2, 128.8, 128.1, 126.1, 122.8, 121.5, 119.8, 116.9, 114.0, 109.7, 63.9, 54.3, 21.5. Anal. Calcd for $C_{24}H_{20}N_4O_2$ C, 72.71; H, 5.08; N, 14.13. Found: C, 72.43; H, 5.09; N, 14.16%.

2-[2-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxyl]phenyl]-6-chlorobenzoxazole (9b). The general procedure was followed using 0.10 g (0.73 mmol) of benzyl azide (**1a**), 0.20 g (0.73 mmol) of 6-

chloro-2-(2-prop-2-yn-1-yloxy)phenyl)benzoxazole (**8b**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.22 g (75%) of **9b** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp. 171-172ºC. IR (film) ν_{max}/cm^{-1}: 763, 3453, 2346, 1452, 1598, 133.2, 2920; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.07 (dd, *J* 1.7 Hz, *J* 7.8 Hz, 1H), 7.74 (s, 1H), 7.47 (ddd, *J* 1.7 Hz, *J* 7.3 Hz, 1H), 7.47 (d, *J* 8.4 Hz, 1H), 7.39 (d, *J* 1.8 Hz, 1H), 7.36 (m, 3H), 7.27 (m, 3H), 7.17 (dd, *J* 0.7 Hz, *J* 8.4 Hz, 1H), 7.09 (td, *J* 1.0 Hz, *J* 7.7 Hz, 1H), 5.53 (s, 2H), 5.37 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ppm: 162.2, 157.0, 150.5, 144.9, 140.7, 134.4, 133.2, 131.3, 130.5, 129.2, 128.9, 128.2, 125.0, 122.7, 121.5, 120.4, 116.2, 113.9, 110.9, 63.8, 54.3. Anal. Calcd for $C_{23}H_{17}ClN_4O_2$ C, 66.27; H, 4.11; N, 13.44. Found: C, 66.25; H, 4.02; N, 13.47%.

2-[2-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl]-5-chloro-6-nitrobenzoxazole (9c). The general procedure was followed using 0.08 g (0.61 mmol) of benzyl azide (**1a**), 0.20 g (0.61 mmol) of 5-chloro-6-nitro-2-(2-prop-2-ynyloxy)phenyl)benzoxazole (**8c**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.23 g (82%) of **9c** as a yellow solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp. 188-189ºC.^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.07 (dd, *J* 2.0 Hz, *J* 8.0 Hz, 1H), 7.89 (s, 1H), 7.67 (s, 1H), 7.60 (s, 1H), 7.5 (ddd, *J* 1.6 Hz, *J* 7.2 Hz, *J* 8.8 Hz, 1H), 7.34-7.31 (m, 3H), 7.23 (dd, *J* 2.8 Hz, *J* 7.6 Hz, 2H), 7.18 (d, *J* 7.6 Hz, 1H), 7.07 (td, *J* 1.0 Hz, *J* 7.6 Hz, *J* 8.4 Hz, 1H), 5.50 (s, 1H), 5.33 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ppm: 166.5, 157.6, 147.7, 145.8, 144.4, 134.5, 134.3, 131.7, 129.3, 129.1, 128.2, 123.4, 122.6, 122.0, 121.6, 114.9, 113.9, 108.4, 63.6, 54.4. Anal. Calcd for $C_{23}H_{16}ClN_5O_4$; C, 59.81; H, 3.49; N, 15.16. Found: C, 59.58; H, 3.29; N, 14.88%.

2-[2-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]-5-bromophenyl]-5-methylbenzoxazole (9d). The general procedure was followed using 0.079 g (0.58 mmol) of benzyl azide (**1a**), 0.20 g (0.58 mmol) of 2-(5-bromo-2-(prop-2-ynyloxy)phenyl)-5-methylbenzoxazole (**8d**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.22 g (80%) of **9d** as a white solid The solid residue was purified by flash chromatography using (ethyl acetate/hexane). Mp. 193-195ºC. IR (film) ν_{max}/cm^{-1}: 757, 3440, 2345, 1594, 1592, 1033, 2919.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.16 (s, 1H), 7.71 (s, 1H), 7.46 (d, *J* 8 Hz, 1H), 7.34-7.30 (m, 4H), 7.14-7.21 (m, 3H), 7.05 (d, *J* 8 Hz, 1H), 7.01 (d, *J* 8 Hz, 1H), 5.46 (s, 2H), 5.29 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ/ppm: 160.0, 155.8, 148.5, 144.5, 141.9, 135.1, 134.4, 134.3, 133.5, 129.2, 128.8, 128.1, 126.5, 122.8, 119.9, 118.6, 115.8, 113.7, 109.7, 64.0, 54.31, 21.5. Anal. Calcd for $C_{24}H_{19}BrN_4O_2$; C, 60.64; H, 4.04; N, 11.79. Found: C, 60.66; H, 3.64; N, 11.56%.

2-[2-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyloxy]-5-bromophenyl]benzoxazole (9e). The general procedure was followed using 0.09 g (0.66 mmol) of benzyl azide (**1a**), 0.200 g (0.61 mmol) of 2-(5-bromo-2-(prop-2-yn-1-yloxy)phenyl)benzoxazole (**8e**), 10 mg of Cu_2O/C and 2.2 mL of Et_3N to give 0.25 g (89%) of **9e** as a white solid. The solid residue was purified by crystallization using (ethyl acetate/hexane). Mp. 179-180ºC. IR (film) ν_{max}/cm^{-1}: IR (film) ν_{max}/cm^{-1}: 739, 3440, 2341, 1541, 1613, 1033, 2926; ^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 8.18 (d, *J* 2.0 Hz, 1H), 7.70 (s, 1H), 7.56 (ddd, *J* 0.6 Hz, *J* 3.0 Hz, *J* 7.5 Hz, 1H), 7.48 (dd, *J* 2.5 Hz, *J* 8.8 Hz, 1H), 7.27 (m, 6H), 7.20 (m, 2H), 7.03 (d, *J* 8.9 Hz, 1H), 5.46 (s, 2H), 5.30 (s, 2H). ^{13}C

NMR (100 MHz, $CDCl_3$) δ/ppm: 160.0, 156.0, 150.3, 144.5, 141.7, 135.3, 134.4, 133.6, 129.2, 128.9, 128.2, 125.4, 124.5, 122.9, 120.1, 118.5, 116.0, 113.8, 110.4, 64.0, 54.3. Anal. Calcd for $C_{23}H_{17}BrN_4O_2$; C, 59.88; H, 3.71; N, 12.15. Found: C, 59.86; H, 3.78; N, 11.98%.

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References

1. (a) Huisgen, R. *1,3-Dipolar Cycloaddition Chemistry;* Padwa, A., Ed.; Wiley: New York, 1984.
(b) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004-2021. http://dx.doi.org/10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.3.CO;2-X
(c) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596-2599. http://dx.doi.org/10.1002/1521-3773(20020715)41:14<2596::AID-ANIE2596>3.0.CO;2-4
(d) Kelly, A. R.; Wei, J.; Kesavan, S.; Marié, J.–C.; Windmon, N.; Young, D. W.; Marcaurelle, L. A. *Org. Lett.* **2009**, *11*, 2257-2260. http://dx.doi.org/10.1021/ol900562u; PMid:19473044 PMCid:2702139.
(e) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057- 3064. http://dx.doi.org/10.1021/jo011148j
2. (a) Lewis, W. G.; Green, L. G.; Grynszpan, F.; Radiæ, Z.; Carlier, P. R.; Taylor, P.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 1053-1057.
(b) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278-308. http://dx.doi.org/10.1002/med.20107; PMid:17763363.
(c) Lee, T.; Cho, M.; Ko, S.-Y.; Youn, H.-J.; Baek, D. J.; Cho, W.-J.; Kang, C.-Y.; Kim, S. *J. Med. Chem.* **2007**, *50*, 585-589. http://dx.doi.org/10.1021/jm061243q; PMid:17266209.
(d) Maurya, S. K.; Gollapalli, D. R.; Kirubakaran, S.; Zhang, M.; Johnson, C. R.; Benjamin, N. N.; Hedstrom, L.; Cuny, G. D. *J. Med. Chem.* **2009**, *52*, 4623-4630. http://dx.doi.org/10.1021/jm900410u; PMid:19624136 PMCid:2810100.
(e) Kold, H. C.; Sharpless, K. B. *Drug Discovery Today* **2003**, *8*, 1128-1137.

(f) Puig-Basagoiti, F.; Qing, M.; Dong, H.; Zhang, B.; Zou, G.; Yuan, Z.; Shi, P.-Y. *Antiviral Res.* **2009**, *83*, 71-79.
http://dx.doi.org/10.1016/j.antiviral.2009.03.005; PMid:19501258 PMCid:3214651.
(g) Guezguez, R.; Bougrin, K.; Akri, K. E.; Benhida, R. *Tetrahedron Lett.* **2006**, *47*, 4807-4811.
http://dx.doi.org/10.1016/j.tetlet.2006.05.050

3. (a) Huisgen, R.; Knorr, R.; Moebius, L.; Szeimies, G. *Chem. Ber.* **1965**, *98*, 4014-4021.
http://dx.doi.org/10.1002/cber.19650981228
(b) Huisgen, R. *Pure Appl. Chem.* **1989**, *61*, 613-628.
http://dx.doi.org/10.1351/pac198961040613
4. (a) Kwok, A. W.; Fotsing, J. R.; Fraser, R. J.; Rodionov, V. O.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4217-4219.
(b) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, L. D.; Sharples, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.* **2005**, *127*, 15998- 15999.
http://dx.doi.org/10.1021/ja054114s; PMid:16287266.
5. For recent reviews, see: (a) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 54-68.
(b) Moses, H. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249-1262.
http://dx.doi.org/10.1039/b613014n; PMid:17619685.
(c) Melda, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952-3015.
http://dx.doi.org/10.1021/cr0783479; PMid:18698735.
6. (a) Diez-González, S.; Correa, A.; Cavallo, L.; Nolan, S. P. *Chem, Eur. J.* **2006**, *12*, 7558-7564.
http://dx.doi.org/10.1002/chem.200600961; PMid:16969776.
(b) Broggi, J.; Díez-González, S.; Petersen, J. L.; Berteina-Raboin, S.; Nolan, S. P.; Agrofolio, L. A. *Synthesis* **2008**, 141-148.
7. (a) Chan, T. R.; Hilgraf, R.; Sharpless, K. B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 2853-2855. PMid:15330631.
(b) Gerard, B.; Ryan, J.; Beeler, A. B.; Porco, J. A. Jr. *Tetrahedron* **2006**, *62*, 6405-6411.
http://dx.doi.org/10.1016/j.tet.2006.04.025
8. (a) Lipshutz, B. H.; Taft, B. R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 8235-8238.
(b) Lipshutz, B. Frieman, B. A.; Tomaso, A. E. Jr. *Angew. Chem., Int. Ed.* **2006**, *45*, 1259-1264.
http://dx.doi.org/10.1002/anie.200503149; PMid:16425315.
(c) Sharghi, H.; Khalifeh, R.; Doroodmand, M. M. *Adv. Synth. Catal.* **2009**, *351*, 207-212.
(d) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Adv. Synth. Catal.* **2010**, *352*, 3208-3214.
http://dx.doi.org/10.1002/adsc.201000637
(e) Lee, C.-T.; Hung, S.; Lipshutz, B. H. *Adv. Synth. Catal.* **2009**, *351*, 3139-3142.
http://dx.doi.org/10.1002/adsc.200900604
(f) Fuch, M.; Goessler, W.; Pilger, C.; Kappe, C. O. *Adv. Synth. Catal.* **2010**, *352*, 323-228.

(g) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Org. Biomol. Chem.* **2011**, 9, 6385-6395. http://dx.doi.org/10.1039/c1ob05735a; PMid:21789331.

9. (a) Bénéteau, V.; Olmos, A.; Boningari, T.; Sommer, J.; Pale, P. *Tetrahedron Lett.* **2010**, *51*, 3673-3677.
(b) Alix, A.; Chassaing, S.; Pale, P.; Sommer, J. *Tetrahedron* **2008**, *64*, 8922-8929. http://dx.doi.org/10.1016/j.tet.2008.06.086
10. (a) Alonso, F., Moglie, Y.; Radivoy, G.; Yus, M. *Tetrahedron Lett.* **2009**, *50*, 2358-2362. http://dx.doi.org/10.1016/j.tetlet.2009.02.220
(b) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Eur. J. Org. Chem.* **2010**, 1875-1884. http://dx.doi.org/10.1016/j.tetlet.2005.02.127
(c) Durán-Pachón, L; van Maarseveen, J. H.; Rothenberg, G. *Adv. Synth. Catal*. **2005**, *347*, 811-815.
(d) Orgueira, H. A.; Fokas, D.; Isome, Y.; Chan, P. C.-M.; Baldino, C. M. *Tetrahedron Lett*. **2005**, *46*, 2911-2914. http://dx.doi.org/10.1016/j.tetlet.2005.02.127
(e) García-Muñoz, A.; González, J, Trujillo-Reyes, J.; Morales-Luckie, R. A.; Sánchez-Mendieta, V.; González, C.; Fuentes, A.; Cuevas-Yañez, E. *Lett. Org. Chem*. **2012**, *9*, 160-164.
(f) Kantam, M. L.; Jaya, V. S.; Sreedhar, B.; Mohan Rao, M. M.; Choudary, B. M. *J. Mol. Catal. A: Chemical* **2006**, *256*, 273-277. http://dx.doi.org/10.1016/j.molcata.2006.04.054
11. (a) Song, S.; Rao, R.; Yang, H.; Zhang, A. *J. Phys. Chem. C*, **2010**, *114*, 13998-14003.
(b) Orel, Z. C.; Anzlovar, A.; Drazic, G.; Zigon, M. *Crystal Growth & Design*, **2007**, *7*, 453-458. http://dx.doi.org/10.1021/cg060615t
(c) Liu, H.; Miao, W.; Yang, S.; Zhang, Z.; Chen, J. *Crystal Growth & Design*, **2009**, *9*, 1733-1740. http://dx.doi.org/10.1021/cg800703n
12. Klug, H. P.; Alexander, L. E. *X-Ray Diffraction Procedures for Polycrystalline and Amorphous Materials*, John Wiley and Sons, 1974, pp. 643.
13. De Jongh, P. E.; Vanmaekelbergh, D.; Kelly, J. *Chem. Commun.* **1999**, 1069-1070. http://dx.doi.org/10.1039/a901232j
14. Shao, C.; Zhu, R.; Luo, S.; Zhang, Q.; Wang, X.; Hu, Y. *Tetrahedron Lett.* **2011**, *52*, 3782-3785. http://dx.doi.org/10.1016/j.tetlet.2011.05.061
15. Suzuka, T.; Ooshiro, K.; Kina, K. *Heterocycles* **2010**, *81*, 601-610. http://dx.doi.org/10.3987/COM-09-11872
16. Chowdhury, C.; Sasmal, A. K.; Dutta, P. K. *Tetrahedron Lett.* **2009**, *50*, 2678-2681. http://dx.doi.org/10.1016/j.tetlet.2009.03.120

17. (a)Yamaguchi, K.; Oishi, T.; Katayama, T.; Mizuno, N. *Chem. Eur. J.* **2009**, *15*, 10464-10472.
(b) Jin, T.; Yan, M.; Menggenbateer; Minato, T. Bao, M.; Yamamoto, Y. *Adv. Synth. Catal.* **2011**, *353*, 3095-3100.
http://dx.doi.org/10.1002/adsc.201100760
(c) Megia-Fernández, A.; Ortega-Muñoz, M.; López-Jaramillo, J.; Hernández-Mateo, F.; Santoyo-Gonzaleza, F. *Adv. Synth. Catal*. **2010**, *352*, 3306-3320.
(d) Duran-Panchón, L.; van Maarseven, J. H.; Rothenberg, G. *Adv. Synth. Catal*. **2005**, *347*, 811-815.
(e) Park, I. S.; Kwon, M. S.; Kim, Y.; Lee, J. S.; Park, J. *Org. Lett*. **2008**, *10*, 497-500.
http://dx.doi.org/10.1021/ol702790w; PMid:18181635.
(f) Rejander Reddy, K.; Rajgopal, K.; Kantam, M. L. *Catal. Lett*. **2007**, *114*, 36-40.
(g) Chassaing, S.; Kummarraja, M.; Sido, A. S. S.; Pale, P.; Sommer, J. *Org. Lett*, **2007**, 9, 883-886.
http://dx.doi.org/10.1021/ol0631152; PMid:17286410.
(h) Chassaing, S.; Sido, A. S. S.; Alix, A.; Kumarraja, M.; Pale, P.; Sommer, J. *Chem. Eur. J.* **2008**, *14*, 6713-6721.
http://dx.doi.org/10.1002/chem.200800479; PMid:18576412.
(i) Namitharan, K.; Kumarraja, M.; Pitchumani, K. *Chem. Eur. J*. **2009**, *15*, 2755-2758.
(j) Katayama, K.; Kamata, K.; Yamaguchi, K.; Mizumo, N. *ChemSusChem* **2009**, *2*, 59-62.
http://dx.doi.org/10.1002/cssc.200800202; PMid:19132695.
18. Crystallographic data (excluding structure factors) for the structures in this paper has been deposited with the Cambridge Crystallographic Data Centre as a Supplementary Publication Numbers, CCDC 887985 No. for **3c**, CCDC 887987 No. for **3l**, CCDC 887986 No. for **3p** and CCDC 887989 No. for **3v** Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
19. López-Ruiz, H.; Briseño-Ortega, H.; Rojas-Lima, S.; Santillan, R.; Farfán, N. *Tetrahedron Lett*. **2011**, *52*, 4308-4312.
http://dx.doi.org/10.1016/j.tetlet.2011.06.039
20. Crystallographic data (excluding structure factors) for the structures in this paper has been deposited with the Cambridge Crystallographic Data Centre as a Supplementary Publication Numbers, CCDC 887990 No. for **9d**.
21. Wang, Y.; Liu, J.; Xia, C. *Adv. Synth. Catal.* **2011**, *353*, 1534-1542.
http://dx.doi.org/10.1002/adsc.201000868
22. Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302-1315.
http://dx.doi.org/10.1039/b904091a; PMid:20309487 PMCid:3073167.
23. (a) Shao, C.; Wang, X.; Xu, J.; Zhao, J.; Zhang, Q.; Hu, Y. *J. Org. Chem*. **2010**, *75*, 7002-7005.

(b) Jlalia, I.; Elamari, H.; Meganem, F.; Herscovici, J.; Girard, C. *Tetrahedron Lett*. **2008**, *49*, 6756-6758.
http://dx.doi.org/10.1016/j.tetlet.2008.09.031
(c) Li, P.; Wang, L.; Zhang, Y. *Tetrahedron* **2008**, *64*, 10825-10830.
http://dx.doi.org/10.1016/j.tet.2008.09.021
(d) Díez-González, S.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2008**, *47*, 8881-8884.

24. (a) Feldman, A.; Colasson, B. Fokin, V. V. *Org. Lett.* **2004**, *6*, 3897-3899.
http://dx.doi.org/10.1021/ol048859z; PMid:15496058.
(b) López-Ruiz, H.; Cortés-Hernández, M.; Rojas-Lima, S.; Höpfl, H. *J. Mex. Chem. Soc.* **2011**, *55*, 168-175.
25. Orgueira, H. A.; Fokas, D.; Isome, Y.; Chan, P.; Baldino, C. *Tetrahedron Lett*. **2005**, *46*, 2911-2914.
http://dx.doi.org/10.1016/j.tetlet.2005.02.127

