JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

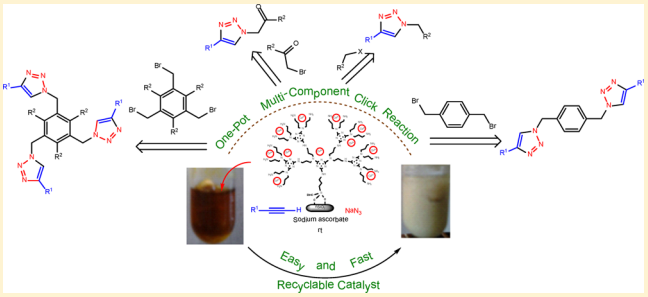
Copper Immobilized on Nanosilica Triazine Dendrimer (Cu(II)-TD@nSiO$_2$)-Catalyzed Regioselective Synthesis of 1,4-Disubstituted 1,2,3-Triazoles and Bis- and Tris-Triazoles via a One-Pot Multicomponent Click Reaction

Mahboobeh Nasr-Esfahani, Iraj Mohammadpoor-Baltork,* Ahmad R. Khosropour,* Majid Moghadam, Valiollah Mirkhani, Shahram Tangestaninejad, and Hadi Amiri Rudbari

Department of Chemistry, Catalysis Division, University of Isfahan, Isfahan 81746-73441, Iran

Supporting Information

ABSTRACT: An efficient, atom-economical, and regioselective synthesis of a wide range of 1,4-disubstituted 1,2,3-triazoles in excellent yields has been achieved via a one-pot three-component reaction of alkynes and sodium azide with organic halides or α-bromo ketones catalyzed by Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature. This catalytic system also showed excellent activity in the synthesis of bis- and tris-1,4-substituted 1,2,3-triazoles. Moreover, the catalyst could be recycled and reused for seven cycles without any loss in its catalytic activity.



Click chemistry, which has been applied for the copper-catalyzed alkyne−azide cycloaddition (CuAAC) to give 1,2,3-triazoles, has emerged as a prominent organic transformation.[1] On the other hand, the development of new synthetic protocols has attracted the interest of chemists because of the significance of these heterocycles in the fields of bioconjugation,[2] pharmaceutical science,[3] dendrimers,[4] and materials science.[5] For instance, some 1,2,3-triazoles exhibit crucial biological activities such as anti-HIV,[6] antibacterial,[7] and antiallergic[8] properties. One of the most widely used methods for the synthesis of 1,2,3-triazoles is Huisgen [3 + 2] cycloaddition of organic azides and terminal alkynes in the presence of copper catalysts.[9] In the first report of this reaction, the active Cu(I) species were directly formed from Cu(I) salts in the presence of ligands.[1a,10] However, because of the instability of Cu(I) salts, usually Cu(I) is prepared in situ via reduction of Cu(II) with ascorbate[11] or by comproportionation of Cu metal and Cu(II) salts.[12] By the way, because of the explosive property and difficulty of handling some of the low-molecular-weight azides, various procedures for the preparation of 1,4-disubstituted 1,2,3-triazoles through the in situ generation of organic azides have been developed.[13] In comparison with alkyl- or benzyl-substituted 1,2,3-triazoles, little attention has been paid to the synthesis of β-keto-1,2,3-triazoles, and only a few reports are available dealing with the synthesis of these compounds from α-bromo or α-azido ketones.[14]

Very recently, we reported Cu(II)-TD@nSiO$_2$ (Figure 1) as a recyclable catalyst for the synthesis of benzimidazoles, benzothiazoles, bis(benzimidazole)s, and bis(benzothiazole)s.[15] In continuation of our research on the application of this

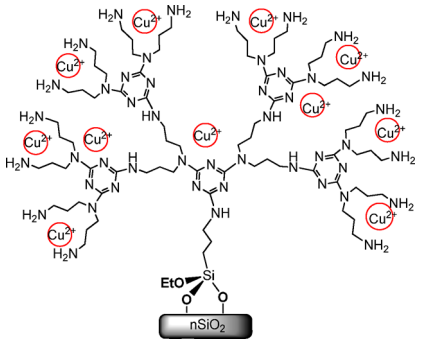


Figure 1. Structure of copper immobilized on nanosilica triazine dendrimer (Cu(II)-TD@nSiO$_2$).

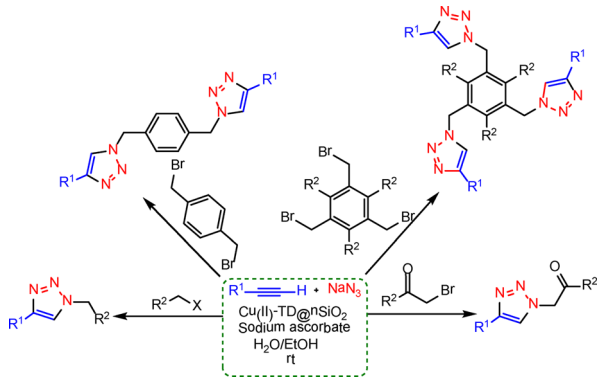
catalyst, herein we describe a convenient and efficient one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles and bis- and tris-triazoles catalyzed by Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature (Scheme 1).

The Cu(II)-TD@nSiO$_2$ catalyst was prepared according to our previously reported procedure.[15] Briefly, the reaction of aminopropylated nanosilica (AP-nSiO$_2$) with cyanuric chloride (CC) and then with bis(3-aminopropyl)amine was carried out in the presence of diisopropylethylamine (DIPEA) in a stepwise manner to afford the second generation of nanosilica-supported dendrimer (G2 or TD@nSiO$_2$). The resulting dendrimer with NH$_2$ groups on its periphery was used suitably for encapsulation of Cu(II). The encapsulation was carried out

Received: October 1, 2013

 © XXXX American Chemical Society dx.doi.org/10.1021/jo402170n | J. Org. Chem. XXXX, XXX, XXX−XXX

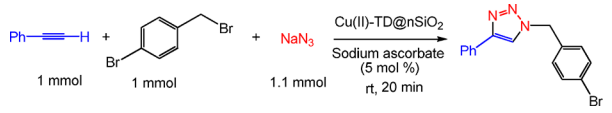
Scheme 1. Synthesis of 1,2,3-Triazoles and Bis- and Tris-Triazoles Catalyzed by Cu(II)-TD@nSiO$_2$/Sodium Ascorbate



by the reaction of G2 with $CuCl_2{\cdot}2H_2O$ to afford Cu(II)-TD@nSiO$_2$. The synthesized catalyst was characterized by several instrumental methods.[15] Thermogravimetric analysis (TGA) indicated that the total amount of organic moieties on nanosilica was about 0.76 mmol/g. The copper content of Cu(II)-TD@nSiO$_2$ was found to be 0.34 mmol of Cu(II) per gram of the catalyst as measured by ICP-OES analysis. The morphology of the catalyst surface, studied by field emission scanning electron microscopy (FE-SEM), showed that the Cu(II)-TD@nSiO$_2$ particles are spherical. Energy-dispersive X-ray (EDX) results obtained from SEM analysis of Cu(II)-TD@nSiO$_2$ revealed that Cu(II) particles had been introduced into the nanosilica-supported dendrimer. A transmission electron microscopy (TEM) image of Cu(II)-TD@nSiO$_2$ revealed dark-colored regions or black spots and colorless parts that correspond to the copper species and nanosilica, respectively. The size distribution histogram demonstrated that the average diameter of the matrix was about 20−30 nm.

Initially, for screening experiments, the three-component reaction between phenylacetylene (1 mmol), 4-bromobenzyl bromide (1 mmol), and sodium azide (1.1 mmol) was chosen as a model reaction (Table 1). The model reaction was first carried out in the absence of sodium ascorbate and catalyst, and no product was formed under these conditions (Table 1, entry 1). In the presence of Cu(II)-TD@nSiO$_2$ (0.3 mol %, 10 mg) without sodium ascorbate, the desired product was obtained in 45% yield (Table 1, entry 2). Then, the same reaction was performed in the presence of Cu(II)-TD@nSiO$_2$ (0.3 mol %, 10 mg) and sodium ascorbate (5 mol %, 10 mg) in different single and mixed solvents at room temperature (Table 1, entries 3−12). As can be seen, the maximum yields were obtained in both H_2O/MeOH (2:1) and H_2O/EtOH (2:1) mixed solvent systems (Table 1, entries 11 and 12). However, H_2O/EtOH (Table 1, entry 12) was preferred because of safety problems. Next, we examined the catalyst loading (0.1−0.4 mol %), and 0.3 mol % was found to be the optimum catalyst loading for completion of this reaction (Table 1, entries 12−15). When a catalyst loading of 0.4 mol % was used, the yield of the product was still 99%, but the reaction rate increased, so that the reaction was complete within 17 min (Table 1, entry 15). The model reaction was also carried out in the presence of a 0.3 mol % loading of conventional copper salts such as CuI, CuCl, $CuCl_2{\cdot}2H_2O$/sodium ascorbate, and $CuSO_4{\cdot}5H_2O$/sodium ascorbate (Table 1, entries 16−19). Under these

Table 1. Screening of the Experimental Conditions for the Synthesis of 3aa



entry	mol % [Cu][a]	solvent	yield (%)[b]
1[c]	–	H_2O/MeOH (2:1)	–
2[c]	0.3	H_2O/MeOH (2:1)	45
3	0.3	CH_3CN	10
4	0.3	DMF	10
5	0.3	EtOAC	10
6	0.3	H_2O	55
7	0.3	MeOH	30
8	0.3	EtOH	35
9	0.3	H_2O/MeOH (1:1)	80
10	0.3	H_2O/EtOH (1:1)	85
11	0.3	H_2O/MeOH (2:1)	98
12	0.3	H_2O/EtOH (2:1)	99
13	0.1	H_2O/EtOH (2:1)	65
14	0.2	H_2O/EtOH (2:1)	85
15[d]	0.4	H_2O/EtOH (2:1)	99
16	CuI, 0.3	H_2O/EtOH (2:1)	32
17	CuCl, 0.3	H_2O/EtOH (2:1)	45
18[e]	$CuCl_2{\cdot}2H_2O$, 0.3	H_2O/EtOH (2:1)	68
19[e]	$CuSO_4{\cdot}5H_2O$, 0.3	H_2O/EtOH (2:1)	40

[a]Unless otherwise noted, [Cu] = Cu(II)-TD@nSiO$_2$ containing 0. 34 mmol of Cu(II) per gram of catalyst as determined by ICP-OES analysis. [b]Isolated yields. [c]Without sodium ascorbate at rt. [d]The reaction was complete after 17 min. [e]With sodium ascorbate.

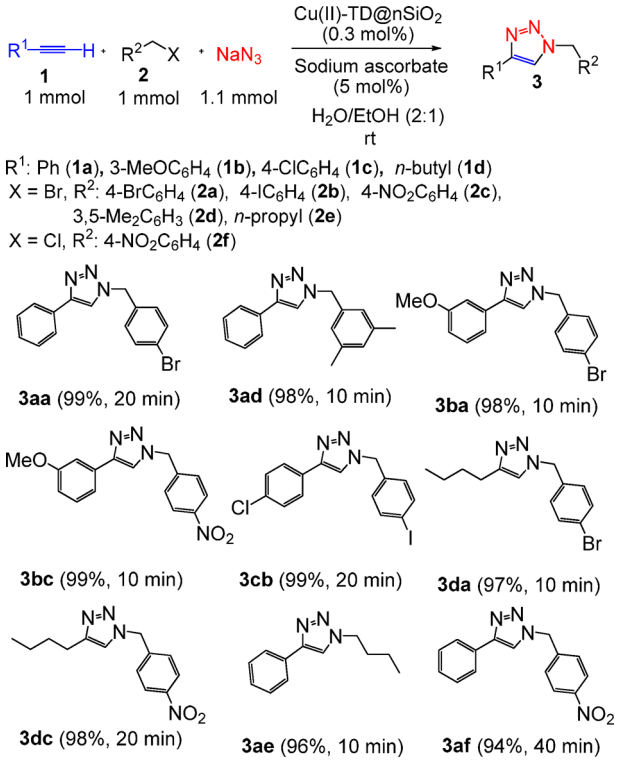
conditions, the desired product was obtained in lower yields (32−68%) compared with that using Cu(II)-TD@nSiO$_2$.

Under the optimized reaction conditions, the efficiency of this protocol for the synthesis of various 1,4-disubstituted 1,2,3-triazoles was studied, and the results are summarized in Scheme 2. Aryl acetylenes such as phenylacetylene (**1a**), 3-methoxyphenylacetylene (**1b**), and 4-chlorophenylacetylene (**1c**) as well as alkyl acetylenes such as 1-hexyne (**1d**) reacted rapidly and smoothly with benzyl bromides **2a−d** and sodium azide in the presence of Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature to afford the corresponding 1,4-disubstituted 1,2,3-triazoles **3aa−dc** in excellent yields (97−99%). Under the same conditions, the reactions of **1a** with butyl bromide (**2e**) and 4-nitrobenzyl chloride (**2f**) proceeded efficiently to provide the desired 1,4-disubstituted 1,2,3-triazoles **3ae** and **3af** in 96% and 94% yield, respectively. It is noteworthy that the reactions were completed within 10−40 min at room temperature, and the products were obtained in excellent yields with high purity and excellent regioselectivity, in which only 1,4-regioisomeric products were formed.

Encouraged by the excellent results obtained with alkyl/benzyl halides, we then examined the activity of this catalytic system for the preparation of 1,4-disubstituted 1,2,3-triazoles using α-bromo ketones. As shown in Scheme 3, various α-bromo ketones **4a−i** having different functionalities on the aromatic ring reacted smoothly with terminal alkynes **1a**, **1b**, **1d**, and **1e** and sodium azide in the presence of Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature to give the corresponding β-keto-1,2,3-triazoles **5aa−ei** in 88−99% yield within 10−30 min. The heterocyclic α-bromo ketone 2-bromo-1-(furan-2-yl)ethanone (**4j**) also participated well in this

dx.doi.org/10.1021/jo402170n | J. Org. Chem. XXXX, XXX, XXX−XXX

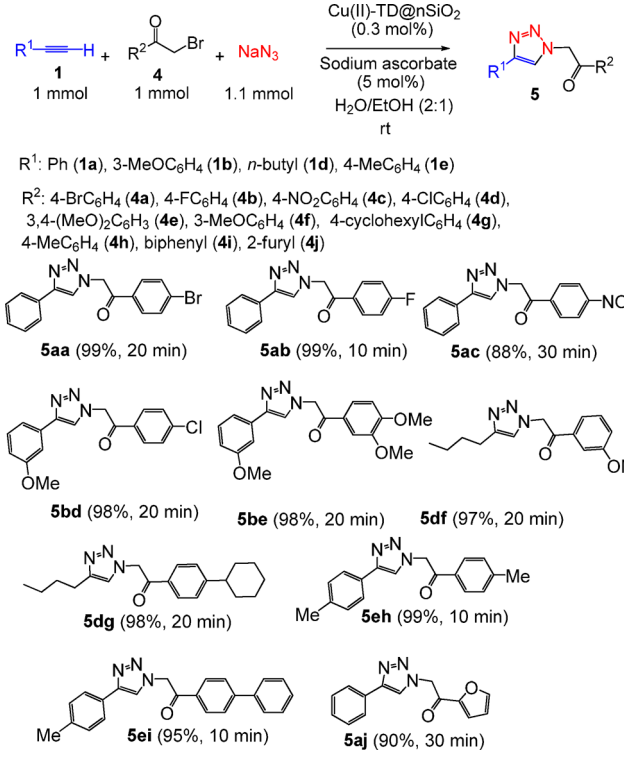
Scheme 2. Cu(II)-TD@nSiO$_2$-Catalyzed Three-Component Synthesis of 1,4-Disubstituted 1,2,3-Triazoles from Alkyl/Benzyl Halides[a]



R^1: Ph (**1a**), 3-MeOC$_6$H$_4$ (**1b**), 4-ClC$_6$H$_4$ (**1c**), *n*-butyl (**1d**)
X = Br, R^2: 4-BrC$_6$H$_4$ (**2a**), 4-IC$_6$H$_4$ (**2b**), 4-NO$_2$C$_6$H$_4$ (**2c**), 3,5-Me$_2$C$_6$H$_3$ (**2d**), *n*-propyl (**2e**)
X = Cl, R^2: 4-NO$_2$C$_6$H$_4$ (**2f**)

[a]Isolated yields are shown.

Scheme 3. Cu(II)-TD@nSiO$_2$-Catalyzed Three-Component Synthesis of 1,4-Disubstituted 1,2,3-Triazoles from α-Bromo Ketones[a]



R^1: Ph (**1a**), 3-MeOC$_6$H$_4$ (**1b**), *n*-butyl (**1d**), 4-MeC$_6$H$_4$ (**1e**)

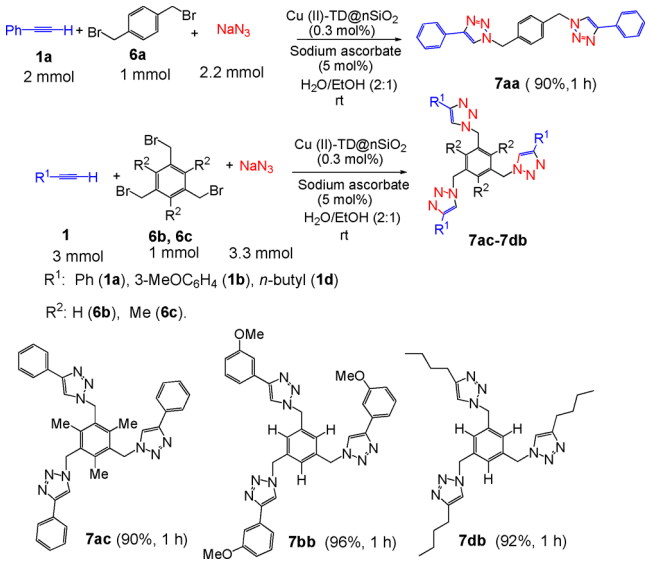
R^2: 4-BrC$_6$H$_4$ (**4a**), 4-FC$_6$H$_4$ (**4b**), 4-NO$_2$C$_6$H$_4$ (**4c**), 4-ClC$_6$H$_4$ (**4d**), 3,4-(MeO)$_2$C$_6$H$_3$ (**4e**), 3-MeOC$_6$H$_4$ (**4f**), 4-cyclohexylC$_6$H$_4$ (**4g**), 4-MeC$_6$H$_4$ (**4h**), biphenyl (**4i**), 2-furyl (**4j**)

[a]Isolated yields are shown.

reaction under similar conditions to provide the desired product **5aj** in 90% yield after 30 min.

To further widen the applicability of the present methodology and because of the various applications of bis- and tris-triazoles in the field of organic semiconductors,[16] as precursors of ionic liquids,[17] and as ligands in chemistry,[18] their synthesis was also examined. As shown in Scheme 4, the reactions of 1,4-bis(bromomethyl)benzene (**6a**), 1,3,5-tris(bromomethyl)-benzene (**6b**), and 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene (**6c**) with terminal alkynes **1a**, **1b**, and **1d** and sodium azide proceeded efficiently in the presence of Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature, and the corresponding bis- and tris-triazoles **7aa**–**db** were obtained in 90–96% yield within 1 h. It is noteworthy that the synthesis of bis- and tris-triazoles through such a one-pot multicomponent reaction has not been previously reported. This method also offers several advantages such as high product yields, short reaction times, mild reaction conditions, excellent regioselectivity, cleaner reaction profiles, and operational simplicity. Therefore, this synthetic methodology can be considered as a useful practical achievement in the preparation of these important heterocyclic compounds.

Scheme 4. Cu(II)-TD@nSiO$_2$ Catalyzed Synthesis of Bis- and Tris-Triazoles[a]



R^1: Ph (**1a**), 3-MeOC$_6$H$_4$ (**1b**), *n*-butyl (**1d**)
R^2: H (**6b**), Me (**6c**).

[a]Isolated yields are shown.

Table 2. Reusability of the Cu(II)-TD@nSiO$_2$ Catalyst in the Synthesis of 3aa[a]

run	1	2	3	4	5	6	7	8
yield (%)[b]	99	99	97	98	97	96	95	95

[a]Reaction conditions: phenylacetylene (1 mmol), 4-bromobenzyl bromide (1 mmol), sodium azide (1.1 mmol), Cu(II)-TD@nSiO$_2$ (0.3 mol %, 10 mg), sodium ascorbate (5 mol %, 10 mg), rt, 20 min. [b]Isolated yields.

dx.doi.org/10.1021/jo402170n | J. Org. Chem. XXXX, XXX, XXX–XXX

filtration, dried, and used for subsequent runs. The experimental results indicated that the catalyst can be reused at least seven times without considerable loss of activity and product yield (95−99%). Furthermore, the leaching of copper from the Cu(II)-TD@nSiO$_2$ catalyst was measured by ICP-OES, and it was found that only very limited leaching of copper (less than 0.1 ppm) occurred during the reaction. This clearly revealed that the catalyst is stable under the reaction conditions and can be recovered and reused.

The structure of the products was identified by IR, MS, and ^{1}H and ^{13}C NMR spectra and elemental analysis. Furthermore, the structure of **3ad** was confirmed by X-ray crystallographic analysis (Figure 2; CCDC 948081).

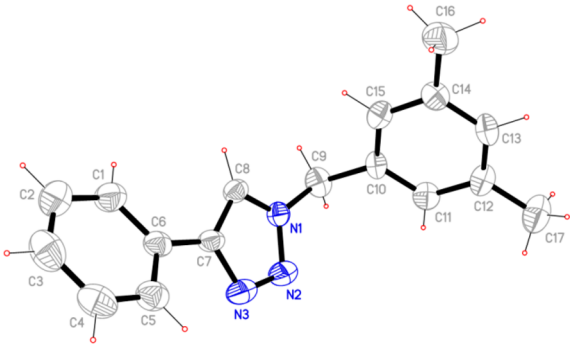


Figure 2. X-ray crystal structure of **3ad**.

In conclusion, we have demonstrated a novel and efficient strategy for the regioselective synthesis of a variety of 1,4-disubstituted 1,2,3-triazoles via a one-pot three-component reaction of terminal alkynes, organic halides or α-bromo ketones, and sodium azide in the presence of catalytic amounts of Cu(II)-TD@nSiO$_2$/sodium ascorbate at room temperature. Also, this catalytic system exhibited excellent activity in the synthesis of bis- and tris-triazoles. The noteworthy features of the present method are excellent regioselectivity, short reaction times, excellent yields, very mild reaction conditions, operational simplicity, avoidance of isolation and handling of potentially unstable small organic azides, stability and reusability of the catalyst, and use of a green solvent system, making it a useful and attractive process for the synthesis of 1,4-disubstituted 1,2,3-triazoles and bis- and tris-triazoles in a single-step operation.

EXPERIMENTAL SECTION

Melting points were determined with a Stuart Scientific SMP2 apparatus. FT-IR spectra were recorded on a Nicolet Impact 400D instrument in the range of 400−4000 cm^{-1}. ^{1}H and ^{13}C NMR spectra (400 and 100 MHz) were recorded on a Bruker Avance 400 spectrometer using $CDCl_3$ as the solvent. Mass spectra were recorded on a Micromass Platform II spectrometer in EI mode at 70 eV. Elemental analysis was done on a LECO CHNS-932 analyzer. The α-bromo ketones were prepared as described previously.[19]

General Procedure for the One-Pot Synthesis of 1,4-Disubstituted 1,2,3-Triazoles from Alkyl/Benzyl Halides Catalyzed by Cu(II)-TD@nSiO$_2$ (Scheme 2). A mixture of sodium ascorbate (5 mol %, 10 mg) and Cu(II)-TD@nSiO$_2$ (0.3 mol %, 10 mg) in 3 mL of H$_2$O/EtOH (2:1) was stirred for 1 min. Then the alkyne (1 mmol), the alkyl/benzyl halide (1 mmol), and sodium azide (1.1 mmol) were added, and the mixture was stirred at room temperature for 10−40 min, during which the desired 1,4-disubstituted 1,2,3-triazole precipitated out. After completion of the reaction (as monitored by TLC, eluting with *n*-hexane/ethyl acetate, 2:1), the mixture was diluted with water and EtOAc and filtered. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over MgSO$_4$ and evaporated to afford the pure 1,4-disubstituted 1,2,3-triazole in most cases. If necessary, the product was purified by recrystallization from *n*-hexane/EtOAc.

General Procedure for the One-Pot Synthesis of 1,4-Disubstituted 1,2,3-Triazoles from α-Bromo Ketones Catalyzed by Cu(II)-TD@nSiO$_2$ (Scheme 3). A mixture of sodium ascorbate (5 mol %, 10 mg) and Cu(II)-TD@nSiO$_2$ (0.3 mol %, 10 mg) in 3 mL of H$_2$O/EtOH (2:1) was stirred for 1 min. Then the alkyne (1 mmol), the α-bromo ketone (1 mmol), and sodium azide (1.1 mmol) were added, and the resulting mixture was stirred at room temperature for 10−30 min. The progress of the reaction was monitored by TLC (eluting with *n*-hexane/ethyl acetate, 1:1). After completion of the reaction, the mixture was diluted with water and EtOAc and filtered. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over MgSO$_4$ and evaporated to afford the pure triazole in most cases. If necessary, the product was purified by recrystallization from *n*-hexane/EtOAc.

General Procedure for the One-Pot Synthesis of Bis- and Tris-Triazoles Catalyzed by Cu(II)-TD@nSiO$_2$ (Scheme 4). A mixture of sodium ascorbate (5 mol %, 20−30 mg) and Cu(II)-TD@nSiO$_2$ (0.3 mol %, 20−30 mg) in 4−6 mL of H$_2$O/EtOH (2:1) was stirred for 1 min. Then 1,4-bis(bromomethyl)benzene, 1,3,5-tris(bromomethyl)benzene, or 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene (1 mmol), the alkyne (2−3 mmol), and sodium azide (2.2−3.3 mmol) were added, and the resulting mixture was stirred at room temperature for 1 h. The progress of the reaction was monitored by TLC (eluting with *n*-hexane/ethyl acetate, 1:1). The workup was performed as in the general procedure for one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles, and the pure product was obtained by recrystallization of the crude product from *n*-hexane/EtOAc.

1-(4-Bromobenzyl)-4-phenyl-1*H*-1,2,3-triazole (Scheme 2, 3aa).[9i] Yield: 99% (310 mg). Mp: 148−150 °C. IR (KBr): ν_{max} = 3109, 3082, 1579, 1485, 1220, 1076, 764, 689, 484 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 7.6 Hz, 2H), 7.77 (s, 1H), 7.52 (d, J = 7.6 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.6 Hz, 2H), 5.54 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.7, 132.4, 130.4, 129.7, 128.9, 128.3, 125.7, 123.0, 119.4, 53.6. MS: m/z (%) 315.99 ([M + 1]$^+$, 15.59), 314.98 ([M]$^+$, 60.39), 286.00 (65.88), 206.17 (78.82), 168.91 (100.00), 130.14 (47.84), 115.83 (100.00), 102.21 (98.04), 89.51 (100.00), 77.11 (70.20), 63.09 (100.00), 43.21 (19.51). Anal. Calcd for $C_{15}H_{12}N_3Br$: C, 57.34; H, 3.85, N, 13.37. Found: C, 57.14; H, 3.89; N, 13.29.

1-(3,5-Dimethylbenzyl)-4-phenyl-1*H*-1,2,3-triazole (Scheme 2, 3ad). Yield: 98% (257 mg). Mp: 114−115 °C. IR (KBr): ν_{max} = 3082, 3028, 1609, 1461, 1347, 1215, 1082, 857, 763, 515 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.4 Hz, 2H), 7.68 (s, 1H), 7.44 (t, J = 7.2 Hz, 2H), 7.35 (tt, ^1J = 7.6 Hz, ^2J = 1.6 Hz, 1H), 7.02 (s, 1H), 6.94 (s, 2H), 5.52 (s, 2H), 2.35 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 138.9, 134.5, 130.7, 130.4, 128.8, 128.1, 125.9, 125.7, 119.5, 54.2, 21.2. MS: m/z (%) 265.18 ([M + 2]$^+$, 3.37), 263.17 ([M]$^+$, 72.35), 220.15 (77.42), 193.19 (32.72), 158.18 (23.27), 132.14 (70.05), 119.12 (93.55), 116.09 (100.00), 91.08 (80.18), 77.10 (76.50), 55.15 (46.08), 43.18 (49.77). Anal. Calcd for $C_{17}H_{17}N_3$: C, 77.54; H, 6.51; N, 15.96. Found: C, 77.37; H, 6.55; N, 15.89.

1-(4-Bromobenzyl)-4-(3-methoxyphenyl)-1*H*-1,2,3-triazole (Scheme 2, 3ba). Yield: 98% (337 mg). Mp: 82−84 °C. IR (KBr): ν_{max} = 3113, 3077, 2936, 1616, 1583, 1450, 1222, 1041, 784 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.44 (s, 1H), 7.34 (d, J = 6.0 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 6.91−6.88 (m, 1H), 5.55 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 148.3, 133.7, 132.4, 131.7, 129.9, 129.7, 123.0, 119.6, 118.1, 114.4, 110.7, 55.4, 53.6. MS: m/z (%) 344.06 ([M]$^+$, 16.73), 314.27 (11.80), 171.06 (62.68), 146.16 (100.00), 119.16 (23.24), 90.17 (78.17), 76.15 (70.42), 63.16 (71.83), 55.20 (31.69), 43.22 (56.34). Anal. Calcd for $C_{16}H_{14}BrN_3O$: C, 55.83; H, 4.10; N, 12.21. Found: C, 55.69; H, 4.13; N, 12.14.

dx.doi.org/10.1021/jo402170n | J. Org. Chem. XXXX, XXX, XXX−XXX

4-(3-Methoxyphenyl)-1-(4-nitrobenzyl)-1*H*-1,2,3-triazole (Scheme 2, 3bc). Yield: 99% (306 mg). Mp: 136−138 °C. IR (KBr): ν_{max} = 3113, 3086, 1616, 1583, 1521, 1487, 1348, 1168, 1043, 837, 780, 568 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 8.8 Hz, 2H), 7.76 (s, 1H), 7.47 (d, J = 8.4 Hz, 3H), 7.36 (d, J = 7.2 Hz, 2H), 6.92−6.89 (m, 1H), 5.71 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 148.6, 148.1, 141.7, 131.4, 129.9, 128.6, 124.4, 119.9, 118.1, 114.5, 110.9, 55.4, 53.2. MS: m/z (%) 311.08 ($[M + 1]^+$, 34.51), 310.07 ($[M]^+$, 74.90), 281.10 (59.61), 251.13 (41.57), 235.17 (48.24), 165.17 (36.47), 145.90 (100.00), 119.14 (66.67), 90.11 (71.37), 77.14 (55.29), 51.13 (59.22), 43.20 (22.90). Anal. Calcd for $C_{16}H_{14}N_4O_3$: C, 61.93; H, 4.55; N, 18.06. Found: C, 61.84; H, 4.60; N, 17.99.

4-(4-Chlorophenyl)-1-(4-iodobenzyl)-1*H*-1,2,3-triazole (Scheme 2, 3cb). Yield: 99% (390 mg). Mp: 90−92 °C. IR (KBr): ν_{max} = 3126, 3084, 2923, 1605, 1565, 1455, 1095, 812, 728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.6 Hz, 4H), 7.60 (s, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.07 (t, J = 8.0 Hz, 1H), 5.44 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 136.9, 130.9, 130.7, 129.1, 127.3, 127.0, 124.4, 119.5, 119.4, 53.4. MS: m/z (%) 397.85 ($[M + 2]^+$, 0.53), 395.83 ($[M]^+$, 1.57), 394.82 (8.73), 253.01 (10.88), 240.03 (72.16), 216.89 (79.61), 204.06 (33.73), 178.03 (55.69), 149.85 (100.00), 135.94 (68.63), 89.98 (100.00), 76.99 (91.37), 52.03 (69.41). Anal. Calcd for $C_{15}H_{11}ClIN_3$: C, 45.54; H, 2.80; N, 10.62. Found: C, 45.68; H, 2.76; N, 10.73.

1-(4-Bromobenzyl)-4-butyl-1*H*-1,2,3-triazole (Scheme 2, 3da).[9i] Yield: 97% (285 mg). Mp: 64−65 °C. IR (KBr): ν_{max} = 3109, 2931, 1591, 1489, 1213, 1051, 847, 772, 490 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (dt, ^1J = 7.6 Hz, ^2J = 2.0 Hz, 2H), 7.20 (s, 1H), 7.15 (d, J = 8.4 Hz, 2H), 5.46 (s, 2H), 2.73 (t, J = 8.0 Hz, 2H), 1.68 (quin, J = 7.6 Hz, 2H), 1.42 (sex, J = 7.6 Hz, 2H), 0.95 (t, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 134.1, 132.2, 129.6, 122.7, 120.4, 53.3, 31.5, 29.7, 22.3, 13.8. MS: m/z (%) 295.05 ($[M + 1]^+$, 4.68), 294.07 ($[M]^+$, 2.21), 253.05 (41.57), 171.03 (89.80), 168.94 (100.00), 143.15 (25.10), 115.19 (26.27), 91.17 (44.71), 89.12 (75.29), 69.20 (51.76), 55.20 (41.96), 43.22 (47.84). Anal. Calcd for $C_{13}H_{16}BrN_3$: C, 53.07; H, 5.48; N, 14.28. Found: C, 52.94; H, 5.53; N, 14.19.

4-Butyl-1-(4-nitrobenzyl)-1*H*-1,2,3-triazole (Scheme 2, 3dc).[9i] Yield: 98% (254 mg). Mp: 60−61 °C. IR (KBr): ν_{max} = 3115, 3063, 2924, 1606, 1518, 1351, 1217, 1051, 859, 712, 478 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.26 (dt, ^1J = 8.4 Hz, ^2J = 2.4 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 7.28 (s, 1H), 5.66 (s, 2H), 2.76 (t, J = 8.0 Hz, 2H), 1.70 (quin, J = 7.6 Hz, 2H), 1.44 (sex, J = 8.0 Hz, 2H), 0.96 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.5, 148.0, 142.2, 128.4, 124.2, 120.8, 52.9, 31.4, 25.4, 22.3, 13.8. MS: m/z (%) 262.18 ($[M + 2]^+$, 5.10), 260.14 ($[M]^+$, 15.69), 217.06 (75.69), 203.03 (49.02), 188.99 (82.75), 143.08 (40.39), 135.81 (100.00), 121.01 (80.00), 115.05 (25.49), 105.84 (100.00), 91.02 (62.75), 77.60 (100.00), 55.02 (94.51), 41.00 (100.00). Anal. Calcd for $C_{13}H_{16}N_4O_2$: C, 59.99; H, 6.20; N, 21.52. Found: C, 59.85; H, 6.24; N, 21.41.

1-Butyl-4-phenyl-1*H*-1,2,3-triazole (Scheme 2, 3ae).[9j] Yield: 96% (193 mg). Mp: 42−44 °C. IR (KBr): ν_{max} = 3085, 2956, 1609, 1463, 1217, 1077, 761, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, ^1J = 8.4 Hz, ^2J = 2.0 Hz, 2H), 7.80 (s, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.37 (tt, ^1J = 7.6 Hz, ^2J = 1.2 Hz, 1H), 4.44 (t, J = 7.2 Hz, 2H), 1.99 (quin, J = 7.6 Hz, 2H), 1.46 (sex, J = 7.2 Hz, 2H), 1.01 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 130.8, 128.8, 128.1, 125.7, 119.4, 50.1, 32.3, 19.7, 13.5. MS: m/z (%) 202.09 ($[M + 1]^+$, 3.17), 201.10 ($[M]^+$, 8.93), 145.10 (13.10), 130.08 (20.44), 102.09 (33.53), 90.11 (24.40), 77.14 (24.40), 63.12 (29.56), 41.19 (100.00). Anal. Calcd for $C_{12}H_{15}N_3$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.51; H, 7.56; N, 20.77.

1-(4-Nitrobenzyl)-4-phenyl-1*H*-1,2,3-triazole (Scheme 2, 3af).[9g] Yield: 94% (263 mg). Mp: 154−155 °C. IR (KBr): ν_{max} = 3127, 3080, 1605, 1518, 1349, 1077, 859, 763, 511 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (dt, ^1J = 8.4 Hz, ^2J = 2.0 Hz, 2H), 7.74 (dt, ^1J = 8.0 Hz, ^2J = 2.0 Hz, 2H), 7.68 (s, 1H), 7.36−7.32 (m, 4H), 7.28 (tt, ^1J = 8.0 Hz, ^2J = 1.6 Hz, 1H), 5.63 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 130.1, 128.9, 128.6, 128.5, 125.8, 124.4, 119.6, 53.2. MS: m/z (%) 281.14 ($[M + 1]^+$, 7.11), 280.14 ($[M]^+$, 37.62), 251.16 (30.48), 205.19 (51.43), 178.20 (22.38), 136.17 (41.90), 121.16 (63.33), 116.13 (100.00), 106.17 (59.05), 102.15 (63.81), 91.18 (34.29), 78.17 (73.33), 63.16 (68.10), 51.20 (55.24), 43.26 (21.31). Anal. Calcd for $C_{15}H_{12}N_4O_2$: C, 64.28; H, 4.32; N, 19.99. Found: C, 64.42; H, 4.36; N, 19.90.

1-(4-Bromophenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-ethanone (Scheme 3, 5aa).[14d] Yield: 99% (338 mg). Mp: 178−180 °C. IR (KBr): ν_{max} = 3142, 2936, 1709, 1582, 1229, 847, 762, 562 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.92 (t, J = 7.6 Hz, 4H), 7.73 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 5.88 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5, 148.3, 132.6, 130.4, 130.2, 129.6, 128.9, 128.3, 125.8, 121.4, 55.4. MS: m/z (%) 343.00 ($[M + 1]^+$, 0.51), 341.98 ($[M]^+$, 1.42), 340.98 (0.61), 314.01 (0.38), 286.04 (1.01), 182.99 (19.48), 154.98 (20.29), 130.09 (48.70), 116.08 (18.83), 102.08 (100.00), 76.07 (85.71), 41.15 (13.80). Anal. Calcd for $C_{16}H_{12}BrN_3O$: C, 56.16; H, 3.53; N, 12.28. Found: C, 56.02; H, 3.56; N, 12.39.

1-(4-Fluorophenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-ethanone (Scheme 3, 5ab).[14e] Yield: 99% (278 mg). Mp: 174−176 °C. IR (KBr): ν_{max} = 3152, 2979, 1695, 1597, 1232, 835, 767 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (dd, ^1J = 7.2 Hz, ^2J = 2.0 Hz, 2H), 7.94 (s, 1H), 7.86 (dt, ^1J = 7.6 Hz, ^2J = 1.6 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (tt, ^1J = 7.2 Hz, ^2J = 1.2 Hz, 1H), 7.24 (td, ^1J = 7.2 Hz, ^2J = 2.0 Hz, 2H), 5.86 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.8, 167.9 (d, $^1J_{CF}$ = 257 Hz), 148.3 (d, $^4J_{CF}$ = 5 Hz), 131.1 (d, $^3J_{CF}$ = 9 Hz), 130.4, 129.2, 128.9, 128.4, 128.3, 125.8, 121.4, 116.6 (d, $^2J_{CF}$ = 22 Hz), 55.4. Anal. Calcd for $C_{16}H_{12}FN_3O$: C, 68.32; H, 4.30; N, 14.94. Found: C, 68.15; H, 4.35; N, 14.84.

1-(4-Nitrophenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-ethanone (Scheme 3, 5ac).[14e] Yield: 88% (271 mg). Mp: 184−186 °C. IR (KBr): ν_{max} = 3139, 2968, 1693, 1599, 1213, 835, 752 cm^{-1}. ^1H NMR (400 Hz, $CDCl_3$): δ 8.28 (d, J = 8.0 Hz, 2H), 7.99 (d, J = 8.0 Hz, 2H), 7.54 (s, 1H), 7.50−7.53 (m, 2H), 7.42 (d, J = 6.8 Hz, 2H), 6.77 (s, 1H), 5.48 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8, 167.9, 131.9, 130.1, 130.0, 129.0, 128.9, 128.8, 128.7, 127.9, 127.8, 53.4. Anal. Calcd for $C_{16}H_{12}N_4O_3$: C, 62.33; H, 3.92; N, 18.17. Found: C, 62.19; H, 3.96; N, 18.05.

1-(4-Chlorophenyl)-2-(4-(3-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)ethanone (Scheme 3, 5bd). Yield: 98% (320 mg). Mp: 131−132 °C. IR (KBr): ν_{max} = 3141, 2924, 1692, 1590, 1470, 1343, 1245, 992, 818, 569 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.8 Hz, 2H), 7.95 (s, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.47 (s, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 6.91 (dd, ^1J = 8.0 Hz, ^2J = 2.0 Hz, 1H), 5.86 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2, 160.0, 141.4, 132.2, 131.6, 129.9, 129.6, 129.59, 121.6, 118.2, 114.5, 110.8, 55.39, 55.37. MS: m/z (%) 329.07 ($[M + 2]^+$, 1.75), 327.01 ($[M]^+$, 5.51), 270.08 (4.78), 183.00 (2.51), 160.10 (76.42), 139.00 (93.40), 111.03 (100.00), 89.04 (97.64), 75.04 (98.11), 50.10 (85.38), 43.17 (30.66). Anal. Calcd for $C_{17}H_{14}ClN_3O_2$: C, 62.30; H, 4.31; N, 12.82. Found: C, 62.15; H, 4.33; N, 12.74.

1-(3,4-Dimethoxyphenyl)-2-(4-(3-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)ethanone (Scheme 3, 5be). Yield: 98% (346 mg). Mp: 136−138 °C. IR (KBr): ν_{max} = 3135, 2969, 1695, 1590, 1516, 1462, 1270, 1131, 1015, 854, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.66 (dd, ^1J = 8.4 Hz, ^2J = 1.6 Hz, 1H), 7.53 (d, J = 1.6 Hz, 1H), 7.48 (s, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.90 (dd, ^1J = 8.0 Hz, ^2J = 2.0 Hz, 1H), 5.85 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.8, 160.0, 154.5, 149.5, 148.1, 131.8, 129.9, 127.1, 123.0, 121.6, 118.2, 114.4, 110.7, 110.3, 110.1, 56.2, 56.1, 55.4, 55.1. MS: m/z (%) 353.15 ($[M]^+$, 3.77), 342.12 (0.74), 296.16 (1.33), 266.14 (2.14), 165.10 (100.00), 151.11 (49.71), 135.10 (22.70), 107.07 (35.34), 89.08 (61.78), 51.12 (59.20), 43.17 (29.89). Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.39; H, 5.49; N, 11.78.

2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)-1-(3-methoxyphenyl)-ethanone (Scheme 3, 5df). Yield: 97% (264 mg). Mp: 72−74 °C. IR (KBr): ν_{max} = 3059, 2931, 1701, 1596, 1560, 1458, 1343, 1263,

dx.doi.org/10.1021/jo402170n | J. Org. Chem. XXXX, XXX, XXX−XXX

1167, 1024, 868, 790 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (dt, ^1J = 8.4 Hz, ^2J = 0.8 Hz, 1H), 7.51 (t, J = 2.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.21 (dd, ^1J = 8.0 Hz, ^2J = 2.4 Hz, 1H), 5.80 (s, 2H), 3.87 (s, 3H), 2.79 (t, J = 8.4 Hz, 2H), 1.73 (quin, J = 7.2 Hz, 2H), 1.46 (sex, J = 7.2 Hz, 2H), 0.97 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 160.1, 148.8, 135.3, 130.2, 122.4, 121.0, 120.6, 112.4, 55.5, 55.4, 31.5, 25.4, 22.3, 13.8. MS: m/z (%) 273.16 ($[M]^+$, 1.15), 244.15 (3.80), 174.07 (10.69), 149.04 (61.18), 136.03 (37.65), 120.92 (90.98), 109.98 (100.00), 90.97 (97.25), 76.99 (98.83), 63.98 (90.98), 55.01 (86.27), 43.06 (84.31). Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.78; H, 7.07; N, 15.29.

2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)-1-(4-cyclohexylphenyl)-ethanone (Scheme 3, 5dg). Yield: 98% (318 mg). Mp: 144−146 °C. IR (KBr): ν_{max} = 3142, 2927, 1696, 1604, 1567, 1453, 1236, 994, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.6 Hz, 2H), 7.45 (s, 1H), 7.38 (d, J = 8.0 Hz, 2H), 5.79 (s, 2H), 2.79 (t, J = 8.4 Hz, 2H), 2.62 (t, J = 7.6 Hz, 1H), 1.89 (d, J = 6.0 Hz, 4H), 1.74 (quin, J = 8.4 Hz, 2H), 1.50−1.37 (m, 6H), 1.32−1.23 (m, 2H), 0.91 (t, J = 8.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 155.5, 148.8, 131.9, 128.4, 127.6, 122.4, 55.2, 44.8, 34.0, 31.5, 26.6, 26.0, 25.4, 22.3, 13.9. MS: m/z (%) 325.21 ($[M]^+$, 0.43), 296.22 (1.25), 214.19 (1.42), 187.10 (49.34), 115.1 (17.35), 110.13 (65.46), 91.09 (43.09), 67.11 (28.95), 55.14 (31.91), 41.18 (100.00). Anal. Calcd for $C_{20}H_{27}N_3O$: C, 73.81; H, 8.36; N, 12.91. Found: C, 73.69; H, 8.41; N, 12.82.

1-*p*-Tolyl-2-(4-*p*-tolyl-1*H*-1,2,3-triazol-1-yl)ethanone (Scheme 3, 5eb).[14b] Yield: 98% (388 mg). Mp: 164−166 °C. IR (KBr): ν_{max} = 3109, 2919, 1698, 1604, 1570, 1460, 1343, 1233, 814, 731, 567 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.0 Hz, 2H), 7.92 (s, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 5.88 (s, 2H), 2.48 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 145.8, 138.0, 131.5, 129.9, 129.5, 128.3, 127.8, 125.7, 121.1, 55.4, 21.9, 21.3. MS: m/z (%) 292.07 ($[M]^+$, 0.84), 291.08 (4.15), 262.14 (2.21), 234.15 (6.64), 144.11 (70.35), 133.10 (38.94), 119.07 (93.81), 105.10 (73.89), 91.05 (100.00), 77.10 (72.57), 51.11 (71.24), 41.16 (45.13). Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.35; H, 5.94; N, 14.33.

1-(Biphenyl-4-yl)-2-(4-*p*-tolyl-1*H*-1,2,3-triazol-1-yl)ethanone (Scheme 3, 5ei). Yield: 95% (335 mg). Mp: 102−103 °C. IR (KBr): ν_{max} = 3030, 2922, 1698, 1602, 1403, 1559, 1231, 995, 819, 761 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 8.0 Hz, 2H), 7.86 (s, 1H), 7.70 (d, J = 8.0 Hz, 4H), 7.58 (dd, ^1J = 7.2 Hz, ^2J = 1.6 Hz, 3H), 7.44−7.36 (m, 4H), 5.85 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 147.3, 139.3, 138.1, 132.6, 129.5, 129.1, 128.9, 128.8, 128.7, 127.8, 127.3, 126.2, 125.8, 121.1, 55.5, 21.3. MS: m/z (%) 353.18 ($[M]^+$, 0.26), 181.11 (24.02), 152.10 (36.61), 115.11 (35.04), 91.08 (25.89), 77.11 (29.13), 57.14 (60.63), 43.19 (100.00). Anal. Calcd for $C_{23}H_{19}N_3O$: C, 78.16; H, 5.42; N, 11.89. Found: C, 78.25; H, 5.45; N, 11.79.

1-(Furan-2-yl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethanone (Scheme 3, 5aj). Yield: 90% (227 mg). Mp: 121−123 °C. IR (KBr): ν_{max} = 3071, 2925, 1736, 1585, 1461, 1377, 1262, 1094, 821, 518 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.90 (dd, ^1J = 7.6 Hz, ^2J = 1.2 Hz, 2H), 7.72 (d, J = 0.8 Hz, 1H), 7.47−7.43 (m, 2H), 7.42 (d, J = 3.6 Hz, 1H), 7.39 (tt, ^1J = 7.2 Hz, ^2J = 1.2 Hz, 1H), 6.68 (dd, ^1J = 3.6 Hz, ^2J = 1.2 Hz, 1H), 5.77 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4, 147.7, 130.5, 128.8, 128.2, 126.2, 125.8, 121.3, 119.2, 113.2, 54.9. MS: m/z (%) 253.08 ($[M]^+$, 1.82), 168.10 (4.94), 130.06 (15.38), 102.06 (51.28), 95.03 (100.00), 89.07 (14.23), 77.10 (28.72), 63.10 (19.63), 51.14 (19.36). Anal. Calcd for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.24; H, 4.40; N, 16.47.

1,4-Bis((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)benzene (Scheme 4, 7aa). Yield: 90% (352 mg). Mp: 248−250 °C. IR (KBr): ν_{max} = 3056, 2956, 2922, 1726, 1606, 1581, 1461, 1263, 1114, 752, 689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, ^1J = 7.2 Hz, ^2J = 1.6 Hz, 2H), 7.35−7.29 (m, 4H), 7.24 (d, J = 7.2 Hz, 2H), 7.12 (d, J = 7.2 Hz, 4H), 6.90 (d, J = 7.6 Hz, 2H), 6.70 (d, J = 8.0 Hz, 2H), 5.31 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.0, 128.9, 128.8, 128.4, 128.3, 125.8, 125.7, 119.4, 53.5. MS: m/z (%) 393.28 ($[M + 1]^+$, 1.67), 392.27 ($[M]^+$, 1.45), 378.08 (1.70), 252.57 (2.59), 163.10 (16.70), 116.03 (35.15), 91.10 (25.31), 77.11 (21.76), 57.12 (45.19), 43.19 (100.00). Anal. Calcd for $C_{24}H_{20}N_6$: C, 73.45; H, 5.14; N, 21.41. Found: C, 73.19; H, 5.18; N, 21.34.

1,1′,1″-(2,4,6-Trimethylbenzene-1,3,5-triyl)tris(methylene)-tris(4-phenyl-1*H*-1,2,3-triazole) (Scheme 4, 7ac). Yield: 90% (531 mg). Mp: 185−187 °C. IR (KBr): ν_{max} = 3133, 2924, 1612, 1562, 1476, 1339, 1150, 763 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.6 Hz, 6H), 731 (t, J = 7.2 Hz, 6H), 7.27 (s, 3H), 7.24 (dt, ^1J = 8.4 Hz, ^2J = 0.8 Hz, 3H), 5.58 (s, 6H), 2.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 131.7, 128.8, 128.2, 125.7, 118.6, 48.7, 20.2. Anal. Calcd for $C_{36}H_{33}N_9$: C, 73.07; H, 5.62; N, 21.30. Found: C, 72.88; H, 5.68; N, 21.24.

1,3,5-Tris((4-(3-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-methyl)benzene (Scheme 4, 7bb). Yield: 96% (613 mg). Mp: 211−213 °C. IR (KBr): ν_{max} = 3130, 2937, 1605, 1588, 1557, 1485, 1243, 1042, 847, 783, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 3H), 7.33 (s, 3H), 7.21 (d, J = 7.2 Hz, 6H), 7.12 (s, 3H), 6.80 (d, J = 6.8 Hz, 3H), 5.42 (s, 6H), 3.75 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 137.0, 131.5, 130.0, 127.5, 118.1, 114.5, 110.7, 55.4, 53.4. Anal. Calcd for $C_{36}H_{33}N_9O_3$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.34; H, 5.26; N, 19.60.

1,3,5-Tris((4-butyl-1*H*-1,2,3-triazol-1-yl)methyl)benzene (Scheme 4, 7db). Yield: 92% (450 mg). Mp: 141−143 °C. IR (KBr): ν_{max} = 3127, 3074, 2929, 1610, 1550, 1460, 1349, 1050, 826, 777 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.21 (s, 3H), 7.08 (s, 3H), 5.41 (s, 6H), 2.70 (t, J = 7.6 Hz, 6H), 1.65 (quin, J = 7.2 Hz, 6H), 1.40 (sex, J = 7.2 Hz, 6H), 0.93 (t, J = 7.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 137.1, 127.2, 120.8, 53.1, 31.4, 25.3, 22.5, 13.8. MS: m/z (%) 489.16 ($[M]^+$, 0.28), 461.09 (3.22), 366.11 (1.51), 211.10 (4.75), 126.05 (10.69), 117.04 (25.49), 91.03 (17.94), 55.10 (24.02), 41.15 (100.00). Anal. Calcd for $C_{27}H_{39}N_9$: C, 66.23; H, 8.03; N, 25.74. Found: C, 65.98; H, 8.10; N, 25.62.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Crystallographic data in CIF format and copies of ^1H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: imbaltork@sci.ui.ac.ir.

*E-mail: arkhosropour@sci.ui.ac.ir.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors are grateful to the Research Council of the University of Isfahan for financial support of this work.

■ REFERENCES

(1) (a) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057−3064. (b) Sommer, S.; Weikart, N. D.; Brockmeyer, A.; Janning, P.; Mootz, H. D. *Angew. Chem., Int. Ed.* **2011**, *50*, 9888−9892. (c) Lallana, E.; Riguera, R.; Fernandez-Megia, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8794−8804. (d) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952−3015.

(2) (a) Lutz, J. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2182−2184. (b) Lutz, J. F.; Borner, H. G. *Prog. Polym. Sci.* **2008**, *33*, 1−39. (c) Brennan, J. L.; Hatzakis, N. S.; Tshikhudo, T. R.; Dirvianskyte, N.; Razumas, V.; Patkar, S.; Vind, J.; Svendsen, A.; Nolte, R. J. M.; Rowan, A. E.; Brust, M. *Bioconjugate Chem.* **2006**, *17*, 1373−1375. (d) Gupta, S. S.; Kuzelka, J.; Singh, P.; Lewis, W. G.; Manchester, M.; Finn, M. G. *Bioconjugate Chem.* **2005**, *16*, 1572−1579. (e) Pacini, A.; Caricato, M.; Ferrari, S.; Capsoni, D.; de Ilarduya, A. M.; Muñoz-Guerra, S.; Pasini, D. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 4790−4799.

(3) (a) Whiting, M.; Muldoon, J.; Lin, Y.-C.; Silverman, S. M.; Lindstrom, W.; Olson, A. J.; Kolb, H. C.; Finn, M. G.; Sharpless, K. B.; Elder, J. H.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 1435−1439. (b) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278−308. (c) Sharpless, K. B.; Manetsch, R. *Expert Opin. Drug Discovery* **2006**, *1*, 525−538.
(4) (a) Liang, L.; Astruc, D. *Coord. Chem. Rev.* **2011**, *255*, 2933−2945. (b) Voit, B. *New J. Chem.* **2007**, *31*, 1139−1151.
(5) (a) Nandivada, H.; Jiang, X.; Lahann, J. *Adv. Mater.* **2007**, *19*, 2197−2208. (b) Caricato, M.; Olmo, A.; Gargiulli, C.; Gattuso, G.; Pasini, D. *Tetrahedron* **2012**, *68*, 7861−7866. (c) Pasini, D. *Molecules* **2013**, *18*, 9512−9530. (d) Wong, C.-H.; Zimmerman, S. C. *Chem. Commun.* **2013**, *49*, 1679−1695.
(6) (a) Ouellet, M.; Mercier, S.; Pelletier, I.; Bounou, S.; Roy, J.; Hirabayashi, J.; Sato, S.; Tremblay, M. J. *J. Immunol.* **2005**, *174*, 4120−4126. (b) Velazquez, S.; Alvarez, R.; Perez, C.; Gago, F.; De Clercq, E.; Balzarini, J.; Camarasa, M. J. *Antiviral Chem. Chemother.* **1998**, *9*, 481−489.
(7) Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A.; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenco, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953−970.
(8) Buckle, D. R.; Rockell, C. J. M.; Smith, H.; Spicer, B. A. *J. Med. Chem.* **1986**, *29*, 2262−2267.
(9) (a) van Berkel, S. S.; Brauch, S.; Gabriel, L.; Henze, M.; Stark, S.; Vasilev, D.; Wessjohann, L. A.; Abbas, M.; Westermann, B. *Angew. Chem., Int. Ed.* **2012**, *51*, 5343−5346. (b) Whittaker, M. R.; Urbani, C. N.; Monteiro, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 11360−11361. (c) Lallana, E.; Riguera, R.; Fernandez-Megia, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8794−8804. (d) Clavé, G.; Campidelli, S. *Chem. Sci.* **2011**, *2*, 1887−1896. (e) Yamada, Y. M. A.; Sarkar, S. M.; Uozumi, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9285−9290. (f) Jin, T.; Yan, M.; Menggenbateer; Minato, T.; Bao, M.; Yamamoto, Y. *Adv. Synth. Catal.* **2011**, *353*, 3095−3100. (g) Shao, C.; Cheng, G.; Su, D.; Xu, J.; Wang, X.; Hu, Y. *Adv. Synth. Catal.* **2010**, *352*, 1587−1593. (h) Yamaguchi, K.; Oishi, T.; Katayama, T.; Mizuno, N. *Chem.—Eur. J.* **2009**, *15*, 10464−10472. (i) Cook, T. L.; Walker, J. A.; Mack, J. *Green Chem.* **2013**, *15*, 617−619. (j) Zsombor, G.; Zoltan, N. *Dalton Trans.* **2010**, *39*, 726−729.
(10) Rostovtsev, H. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596−2599.
(11) (a) Feldman, A. K.; Colasson, B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 3897−3899. (b) Campbell-Verduyn, L. S.; Mirfeizi, L.; Dierckx, R. A.; Elsinga, P. H.; Feringa, B. L. *Chem. Commun.* **2009**, 2139−2141.
(12) (a) Wang, Q.; Chan, T. R.; Hilgraf, R.; Fokin, V. V.; Sharpless, K. B.; Finn, M. G. *J. Am. Chem. Soc.* **2003**, *125*, 3192−3193. (b) Himo, F.; Lovell, T.; Hilgraf, R.; Rostovtsev, V. V.; Noodleman, L.; Sharpless, K. B.; Fokin, V. V. *J. Am. Chem. Soc.* **2005**, *127*, 210−216.
(13) (a) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297−368. (b) Kumaravel, K.; Vasuki, G. *Curr. Org. Chem.* **2009**, *13*, 1820−1841. (c) Jiang, B.; Rajale, T.; Wever, W.; Tu, S.-J.; Li, G. *Chem.—Asian J.* **2010**, *5*, 2318−2335. (d) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Adv. Synth. Catal.* **2010**, *352*, 3208−3214.
(14) (a) Reddy, P. S.; Sreedhar, B. *Synthesis* **2009**, 4203−4207. (b) Kumar, D.; Patel, G.; Reddy, V. B. *Synlett* **2009**, 399−402. (c) Kumar, D.; Reddy, V. B.; Varma, R. S. *Tetrahedron Lett.* **2009**, *50*, 2065−2068. (d) Keshavarz, M.; Badri, R. *Mol. Diversity* **2011**, *15*, 957−962. (e) Kónya, K.; Fekete, S.; Ábrahám, A.; Patonay, T. *Mol. Diversity* **2012**, *16*, 91−102.
(15) Nasr-Esfahani, M.; Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.; Mirkhani, V.; Tangestaninejad, S. *J. Mol. Catal. A: Chem.* **2013**, *379*, 243−254.
(16) Beltrán, E.; Serrano, J. L.; Sierra, T.; Giménez, R. *Org. Lett.* **2010**, *12*, 1404−1407.
(17) (a) Choi, J. W.; Cho, B.-K. *Soft Matter* **2011**, *7*, 4045−4049. (b) Marcos, M.; Martín-Rapún, R.; Omenat, A.; Barberá, J.; Serrano, J. L. *Chem. Mater.* **2006**, *18*, 1206−1212. (c) Aizpurua, J. M.; Sagartzazu-Aizpurua, M.; Azcune, I.; Miranda, J. I.; Monasterio, Z.; García-Lecina, E.; Fratila, R. M. *Synthesis* **2011**, 2737−2742.
(18) (a) Schweinfurth, D.; Pattacini, R.; Strobel, S.; Sarkar, B. *Dalton Trans.* **2009**, 9291−9297. (b) Yan, W.; Ye, X.; Akhmedov, N. G.; Petersen, J. L.; Shi, X. *Org. Lett.* **2012**, *14*, 2358−2361. (c) Zhao, P.; Li, N.; Salmon, L.; Liu, N.; Ruiz, J.; Astruc, D. *Chem. Commun.* **2013**, *49*, 3218−3220.
(19) King, L. C.; Ostrum, G. K. *J. Org. Chem.* **1964**, *29*, 3459−3461.

dx.doi.org/10.1021/jo402170n | *J. Org. Chem.* XXXX, XXX, XXX−XXX