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A facile and regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles using click chemistry

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ABSTRACT

The reaction of α-tosyloxy ketones, sodium azide, and terminal alkynes in presence of copper(I) in aqueous polyethylene glycol afforded regioselectively 1,4-disubstituted 1,2,3-triazoles in good yield at ambient temperature. The one-pot exclusive formation of 1,4-disubstituted 1,2,3-triazoles involves in situ formation of α-azido ketones, followed by cycloaddition reaction with terminal alkyne. The generality of this one-pot method was demonstrated by synthesizing an array of diverse 1,4-disubstituted 1,2,3-triazoles.

Five-membered nitrogen heterocycles play an important role in biological systems. Among these, the 1,2,3-triazole heterocycles are reported to have several biological activities, including anti-HIV,[1] antiallergic,[2] antifungal,[3] and antimicrobial.[4] 1,2,3-Triazoles are useful building blocks in chemistry, and are stable to moisture, oxygen, light, and also metabolism in the body. Moreover, these moieties can be tuned to form powerful pharmacophores[5] and also play an important role in bio-conjugation. The lack of well-deserved attention to these molecules in the past was, in part, due to the paucity of direct synthetic methods. Several methods are reported for the synthesis of 1,2,3-triazoles in the literature, including the 1,3-dipolar cycloaddition of azides to alkynes, organolanthanide-based synthesis from nitriles and diazocompounds, and cycloaddition of nitroethenes with trimethylsilyl azide.[6] Some reports[7] have discussed the synthesis of these molecules on solid supports, while others include addition of bromomagnesium acetylides to azides, and reactions of sodium phenylacetylide and sodium alkoxide with tosyl azides.[8] The cycloaddition of azides with alkynes is typically carried out under refluxing conditions, but labile molecules may not survive these conditions. Synthesis of substituted 1,2,3-triazoles by the direct alkylation of 1,2,3-triazoles is generally not preferred because of poor regioselectivity.

Multicomponent reactions (MCRs) have attracted significant attention for being powerful tools for producing diverse array of compounds.[9a] These reactions constitute an especially attractive synthetic strategy since they provide easy and rapid access to large libraries of organic compounds with diverse substitution patterns.

In order to meet the stringent environmental regulations, it has become highly desirable to conduct organic reactions in benign medium, which offers many potential advantages and benefits in terms of safety, efficiency, cost, and selectivity. In the recent past, water has become the solvent of choice to perform many organic transformations, this being one of the most abundant, cheapest, and greener solvents.[9b,c] Polyethylene glycol (PEG) is used extensively for a variety of purposes, ranging from additives in pharmaceutical industry to various medical purposes.[10] The enhanced solubility of organic compounds in PEG renders this as a versatile solvent as well as a phase-transfer catalyst in organic synthesis.[11] The water-soluble and eco-friendly PEG can also be considered a co-solvent in water which leads to changes in its physicochemical properties.[12]

Recently, the conception of click chemistry by Sharpless and his co-workers is hailed for its regioselectivity and the ease of its protocol mimicking the nature's way of synthesis. Click chemistry has been explored as a newer approach for the synthesis of drug-like molecules that can accelerate the drug discovery process by utilizing a few practical and reliable reactions.[13] This is very much evident from the ever growing amount of work reported in the literature.[14,15]

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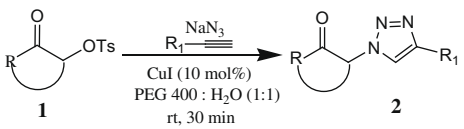
α-Tosyloxy ketones, ideal substitutes for the lachrymatory α-haloketones, are easily accessible starting materials for a variety of organic transformations and in the construction of diverse heterocyclic compounds. These useful intermediates can be easily prepared from enolizable ketones using Koser's reagent, [hydroxy(tosyloxy)iodo]benzene.[16]

We report a facile and benign synthesis of 1,4-disubstituted 1,2,3-triazoles involving the three-component, one-pot condensation of α-tosyloxy ketones, sodium azide, and terminal acetylenes using the copper(I)-catalyzed 'click' azide-alkyne cycloaddition reaction in aqueous PEG 400 (Scheme 1).

Though the 'click' azide-alkyne cycloaddition reaction is reported in a wide variety of organic solvents, including THF,[17] *t*-BuOH/H_2O,[6a] DMSO/H_2O,[18] MeCN,[19] and 1,4-dioxane/H_2O,[6b] we focused our attention to investigate the reaction in environmentally benign solvents. Our initial attempts in aqueous medium failed to yield any product. Encouraged by our recent success with benign aqueous PEG 400, we turned our attention to the PEG 400.[20] The reaction of α-tosyloxy ketone, sodium azide, and phenylacetylene in presence of copper iodide (10 mol %) in PEG 400 afforded good results, but the reaction took 24 h to complete (Table 1, entry 1). Attributing this sluggish reaction to the high viscosity of the PEG 400, we zeroed in on the aqueous PEG 400 system. Several combinations of this solvent system were studied and finally optimized results were obtained using PEG 400/H_2O (1:1, v/v). The reaction time with this aqueous PEG 400 system was as low as 30 min when compared to 12–24 h with *t*-BuOH/H_2O (1:1, v/v). We expect that this prodigious behavior is due to the phase-transfer catalytic nature of PEG. One-pot reaction of α-tosyloxyacetophenone, sodium azide, and phenylacetylene in presence of copper iodide (10 mol %) in aqueous PEG 400 at room temperature afforded pure 4-phenyl-1-(2-phenylethan-2-on-1-yl)-1*H*-1,2,3-triazole **2a** in 82% yield. The IR spectra of **2a** exhibited a strong band at about 1695 cm^{-1} indicating the presence of ketonic functionality. Its ^1H NMR displayed a characteristic singlet at δ 8.19 for triazolyl C_5–H. High resolution mass spectra of this compound show the molecular ion peak at *m/z* 263.2415 which is in agreement with the calculated value, *m/z* 263.2939.

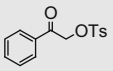
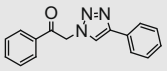
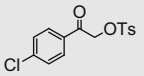
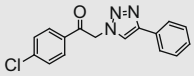
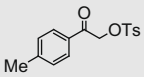
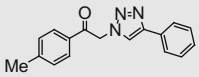
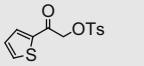
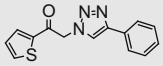
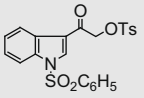
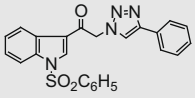
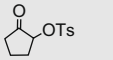
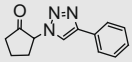
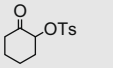
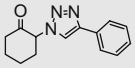
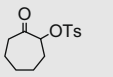
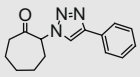
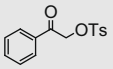
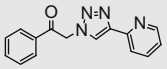
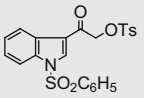
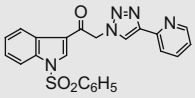
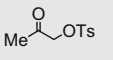
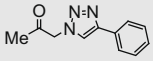
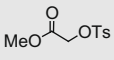
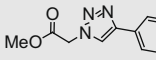
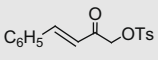
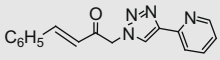
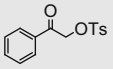
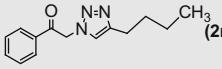
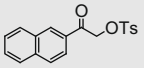
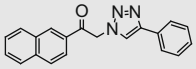
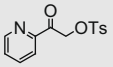
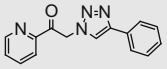
Under optimized conditions, syntheses of a variety of 1,4-disubstituted 1,2,3-triazoles **2b–p** were undertaken using various α-tosyloxy ketones and acetylenic compounds (Table 1).[21] Aromatic, heterocyclic, and aliphatic terminal alkynes underwent three-component condensation smoothly to afford a wide range of 1,4-disubstituted 1,2,3-triazoles. The rich variety in the α-tosyloxy ketones also demonstrates the functional group tolerance of the reaction. The α-tosylate-substituted ester reacted smoothly to produce 1,4-disubstituted 1,2,3-triazole with 10 mol % of copper(I) (Entry 12, Table 1). Also, the tosylate of α,β-unsaturated ketone afforded 1,4-disubstituted 1,2,3-triazole in good yield (Table 1, entry 13). The moderate to good yields of the products show the viability of the reaction at higher scales. All the products were isolated by simple filtration of the reaction mixture after dilution with water. Analytically pure products were obtained by percolating the crude products through a bed of silica gel. Finally, it was found that catalyst and aqueous PEG could be recycled for three times successively without loss of activity and product yields (Table 1, entry 1).

α-Azido ketones are often unstable to heat and light; therefore, in situ formation of these compounds is advantageous to handle



Scheme 1. Regioselective synthesis of 1,2,3-triazoles.

Table 1
Synthesis of 1,4-disubstituted 1,2,3-triazoles **2**

Entry	α-Tosyloxy ketone (**1**)	1,2,3-Triazole (**2a–p**)	Yield[a] (%)
1		 **(2a)**	82
2		 **(2b)**	79
3		 **(2c)**	81
4		 **(2d)**	80
5		 **(2e)**	85
6		 **(2f)**	81
7		 **(2g)**	83
8		 **(2h)**	77
9		 **(2i)**	78
10		 **(2j)**	83
11		 **(2k)**	86
12		 **(2l)**	74
13		 **(2m)**	76
14		 **(2n)**	82
15		 **(2o)**	79
16		 **(2p)**	75

[a] Yields of pure and isolated products.

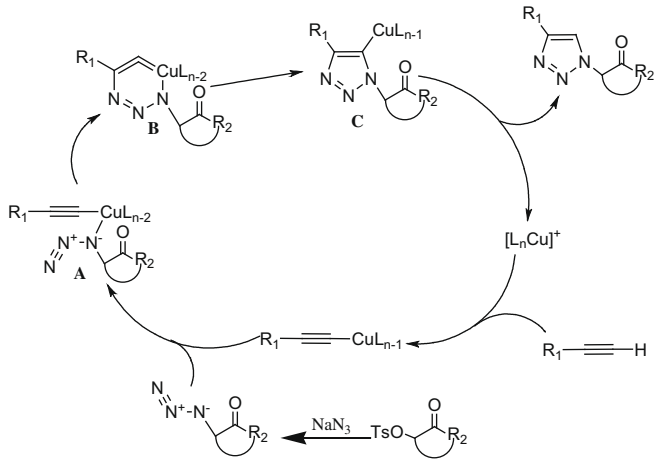


Figure 1. Mechanistic pathway for the formation of 1,2,3-triazoles.

them safely. Initial formation of the α-azido ketone intermediate was unambiguously confirmed by reacting equimolar quantities of α-tosyloxy ketone and sodium azide in aqueous PEG 400. After the formation of α-azido ketone, as indicated by TLC and IR (2100 cm^{-1}), phenylacetylene was added to the reaction mixture. The products of this reaction and the one-pot condensation reaction (Table 1, entry 1) were found to be identical.

The step-wise mechanism[22] involves the initial formation of the α-azido ketone from the reaction of α-tosyloxy ketone with sodium azide. The copper(I) quickly forms an acetylide with the terminal alkyne, which in turn forms adduct **A** with α-azido ketone.

Subsequent intramolecular cyclization of **A** produces another cyclic adduct **B** which rearranges to copper-containing 1,2,3-triazole **C**. Finally, the protonation of **C** leads to 1,2,3-triazole **2** and catalyst regeneration (Fig. 1).

In conclusion, we have developed a simple, benign, and one-pot regioselective synthesis of biologically significant 1,4-disubstituted-1*H*-1,2,3-triazoles in good yields under catalytic conditions. The protocol is applicable to a wide range of α-tosyloxy ketones and acetylenic compounds, and allows the assembly of a diverse set of 1,4-disubstituted-1*H*-1,2,3-triazoles. The use of copper(I) as a reusable catalyst in aqueous PEG makes this method facile, cost effective, and eco-friendly.

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References and notes

1. Alvarez, R.; Velazquez, S.; San, F.; Aquaro, S.; De, C.; Perno, C. F.; Karlsson, A.; Balzarini, J.; Camarasa, M. J. *J. Med. Chem.* **1994**, *37*, 4185.
2. Buckle, D. R.; Rockell, C. J. M.; Smith, H.; Spicer, B. A. *J. Med. Chem.* **1986**, *29*, 2262.
3. (a) Vicentini, C. B.; Brandolini, V.; Guarneri, M.; Giori, P. *Farmaco* **1992**, *47*, 1021; (b) Joan, C. F. T.; Elizabeth, H.; Beatrice, M.; Daniel, P. B. *Antimicrob. Agents Chemother.* **1998**, *42*, 313.
4. 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.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953.
5. Bourne, Y.; Kolb, H. C.; Radić, Z.; Sharpless, K. B.; Taylor, P.; Marchot, P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 1449.
6. (a) Kristin, O.; Edmund, A. H.; Trond, V. H. *Tetrahedron Lett.* **2007**, *48*, 2097; (b) Dong, Y.; Na, F.; Zenglu, L.; Ying, L.; Baohua, C. *Synlett* **2007**, 278; (c) William, J. E.; Elizabeth, M.; Timothy, M. C.; Joseph, W. Z.; Antonio, G. D.; Arnold, L. R. *J. Am. Chem. Soc.* **2008**, *130*, 16; (d) David, A.; Francesco, F.; Oriana, P.; Ferdinando, P.; Ennio, Z.; Luigi, V. *J. Org. Chem.* **2005**, *70*, 6526.
7. Yongnian, G.; Yulin, L. *Org. Lett.* **2006**, *8*, 3283.
8. (a) Antoni, K.; Valery, V. F.; Sharpless, K. B. *Org. Lett.* **2004**, *6*, 1237; (b) Boyer, J. H.; Mack, C. H.; Goebel, N.; Morgan, L. R. *J. Org. Chem.* **1958**, *23*, 1051.
9. (a) Zhu, J.; Bienayme, H. *Multicomponent Reactions*, 1st Ed.; Wiley-VCH: Weinheim, 2005; (b) Polshettiwar, V.; Varma, R. S. *Chem. Soc. Rev.* **2008**, *37*, 1546; (c) Polshettiwar, V.; Varma, R. S. *Acc. Chem. Res.* **2008**, *41*, 629.
10. (a) Eunsook, C.; Hyesun, G.; Inkoo, C. *Int. J. Pharm.* **2008**, *349*, 101; (b) Tatsuhiro, I.; Xin, Y. W.; Taro, S.; Kosuke, N.; Hiroshi, K. *J. Controlled Release* **2007**, *122*, 349; (c) Pengzhan, Y.; Chunyang, Z.; Jing, C.; Guifeng, Z.; Yongdong, L.; Xiaoyan, S.; Guicai, Z.; Zhiguo, S. *Bioorg. Med. Chem.* **2007**, *15*, 5396.
11. Vladimir, V. K.; Diego, R. M. A.; Arnold, R. R. B. *Tetrahedron Lett.* **2008**, *49*, 3097.
12. Ji, C.; Scott, K. S.; Jonathan, G. H.; Robin, D. R. *Green Chem.* **2005**, *7*, 64.
13. (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004; (b) Kolb, H. C.; Sharpless, K. B. *Drug. Discovery Today* **2003**, *8*, 1128.
14. (a) Christopher, D. S.; Ian, R. B.; Steve, L.; John, J. H.; Stephen, C. S.; Steven, V. L. *Org. Biomol. Chem.* **2007**, *5*, 1559; (b) Basak, A.; Chandra, R. P.; Ghosh, S. C. *Synlett* **2007**, 1585; (c) Hao, C.; Janet, L. T.; Suzanne, R. A. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1979.
15. Maria, V. G.; Maria, J. A.; Oscar, L. *Synthesis* **2007**, 1589.
16. Gerald, F. K.; Attila, G. R.; Alexander, N. K.; Louis, R.; Richard, H. W. *J. Org. Chem.* **1982**, *47*, 2487.
17. Alexandru, G.; Erick, C. Y.; Joachim, H.; Willi, B.; Narasaiah, B.; Oliver, R. *Synlett* **2006**, 2767.
18. Karol, K. *Synlett* **2005**, 943.
19. Stan, G.; Brian, H. M.; Peter, J. L. M. Q.; Harlof, C. P. F. R.; Roel, W. W.; Richard, H. B.; Floris, L. V. D.; Floris, P. J. T. R. *Synthesis* **2006**, *18*, 3146.
20. (a) Kumar, D.; Reddy, V. B.; Mishra, B. G.; Rana, R. K.; Mallikarjuna, N. N.; Varma, R. S. *Tetrahedron* **2007**, *63*, 3093; (b) Kumar, D.; Patel, G.; Mishra, B. G.; Varma, R. S. *Tetrahedron Lett.* **2008**, *49*, 6974.
21. *General procedure for the synthesis of 1,4-disubstituted-1H-1,2,3-triazoles* (**2a–p**): To a stirred solution of α-tosyloxy ketone (1 mmol), sodium azide (1 mmol) in aqueous PEG 400 (2 ml, 1:1, v/v), phenyl acetylene (1 mmol), 10 mol % of copper iodide were added and allowed to stir at room temperature for 30 min. The reaction mixture appeared turbid. On completion of the reaction as was indicated by the TLC, the reaction mixture was diluted with water and filtered at the pump to collect the product or extracted with ethyl acetate (3 × 2 ml). The organic layer was dried over anhydrous sodium sulfate and distilled using rotary vacuum evaporator to afford pure 1,4-disubstituted-1*H*-1,2,3-triazoles (Table 1, entries 1–16). *4-Phenyl-1-(2-phenylethan-2-on-1-yl)-1H-1,2,3-triazole* (**2a**): ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.19 (s, 1H), 8.08–8.06 (m, 2H), 7.88–7.86 (m, 2H), 7.71–7.68 (m, 1H), 7.61–7.57 (m, 2H), 7.46–7.42 (m, 2H), 7.31–7.38 (m, 1H), 6.08 (s, 2H). HRMS: calcd for $C_{16}H_{13}N_3O$ 263.2939, found 263.2415. IR (cm^{-1}): 1695.
1-(2-(4-Chlorophenyl)-ethan-2-on-1-yl)-4-phenyl-1H-1,2,3-triazole (**2b**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97–7.93 (m, 3H), 7.85 (d, *J* = 8.48 Hz, 2H), 7.51 (d, *J* = 8.60 Hz, 2H), 7.45–7.41 (m, 2H), 7.37–7.33 (m, 1H), 5.85 (s, 2H). HRMS: calcd for $C_{16}H_{12}ClN_3O$ 297.7389, found 297.2148. IR (cm^{-1}): 1685.
1-(2-(4-Methylphenyl)-ethan-2-on-1-yl)-4-phenyl-1H-1,2,3-triazole (**2c**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.85 (m, 3H), 7.79 (d, *J* = 7.32 Hz, 2H), 7.39–7.35 (m, 2H), 7.29–7.27 (m, 3H), 5.81 (s, 2H), 2.38 (s, 3H). HRMS: calcd for $C_{17}H_{15}N_3O$ 277.3205, found 277.3172. IR (cm^{-1}): 1690.
4-Phenyl-1-(2-(thiophen-2-yl)-ethan-2-on-1-yl)-1H-1,2,3-triazole (**2d**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.82–7.79 (m, 3H), 7.74–7.73 (m, 1H), 7.39–7.35 (m, 2H), 7.30–7.26 (m, 1H), 7.17–7.15 (m, 1H), 5.73 (s, 2H). HRMS: calcd for $C_{14}H_{11}N_3OS$ 269.3216, found 269.1185. IR (cm^{-1}): 1665.
4-Phenyl-1-(2-[1-(phenylsulfonyl)-1H-indol-3-yl]-ethan-2-on-1-yl)-1H-1,2,3-triazole (**2e**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (s, 1H), 8.18 (d, *J* = 7.48 Hz, 1H), 7.89–7.87 (m, 4H), 7.77 (d, *J* = 7.28 Hz, 2H), 7.52–7.48 (m, 1H), 7.40–7.24 (m, 7H), 5.70 (s, 2H). HRMS: calcd for $C_{24}H_{18}N_4O_3S$ 442.4897, found 442.3253. IR (cm^{-1}): 1680.
1-(Cyclopentan-1-on-2-yl)-4-phenyl-1H-1,2,3-triazole (**2f**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.84 (d, *J* = 7.48 Hz, 2H), 7.40–7.44 (m, 2H), 7.35–7.31 (m, 1H), 4.96 (dd, *J* = 11.46 Hz and *J* = 8.44 Hz, 1H), 2.86–2.79 (m, 1H), 2.65–2.42 (m, 3H), 2.36–2.29 (m, 1H), 2.12–2.01 (m, 1H). HRMS: calcd for $C_{13}H_{13}N_3O$ 227.2618, found 227.1572. IR (cm^{-1}): 1720.
1-(Cyclohexan-1-on-2-yl))-4-phenyl-1H-1,2,3-triazole (**2g**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86–7.84 (m, 3H), 7.44–7.41 (m, 2H), 7.35–7.31 (m, 1H), 5.47 (dd, *J* = 13.14 Hz and 5.68 Hz, 1H), 2.72–2.52 (m, 3H), 2.29–2.20 (m, 2H), 2.14–2.12 (m, 1H), 2.01–1.81 (m, 2H). HRMS: calcd for $C_{14}H_{15}N_3O$ 241.2884, found 241.1719. IR (cm^{-1}): 1715.
1-(Cycloheptan-1-on-2-yl)-4-phenyl-1H-1,2,3-triazole (**2 h**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.84–7.90 (m, 2H), 7.49–7.32 (m, 3H), 5.77–5.69 (m, 1H), 2.88–2.55 (m, 2H), 2.40–1.70 (m, 8H). HRMS: calcd for $C_{15}H_{17}N_3O$ 255.3149, found 255.1032. IR (cm^{-1}): 1710.
4-(2-Pyridyl)-1-(2-phenyl ethan-2-on-1-yl)-1H-1,2,3-triazole (**2i**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64–8.59 (m, 1H), 8.30 (s, 1H), 8.25–8.19 (m, 1H), 8.01–8.10 (m, 2H), 7.87–7.52 (m, 4H), 7.30–7.22 (m, 1H), 5.94 (s, 2H). +EMS (turbo spray): calcd for $C_{15}H_{12}N_4O$ 264.2819, found: 265.2. IR (cm^{-1}): 1690.
4-(2-Pyridyl)-1-(2-[1-(phenylsulfonyl)-1H-indol-3-yl]-ethan-2-on-1-yl)-1H-1,2,3-triazole (**2j**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, J = 4.28 Hz, 1H), 8.40–8.36 (m, 2H), 8.27 (d, *J* = 7.44 Hz, 1H), 8.21 (d, *J* = 7.96 Hz, 1H), 7.99–7.97 (m, 3H), 7.83–7.79 (m, 1H), 7.63–7.59 (m, 1H), 7.52–7.48 (m, 2H), 7.45–7.35 (m, 2H), 7.27–7.24 (m, 1H), 5.79 (s, 2H). +EMS (turbo spray): calcd for $C_{23}H_{17}N_5O_3S$ 443.4778, found 443.9. IR (cm^{-1}): 1680.
4-Phenyl-1-(propan-2-on-1-yl)-1H-1,2,3-triazole (**2k**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84–7.83 (m, 3H), 7.46–7.42 (m, 2H), 7.37–7.33 (m, 1H), 5.26 (s,

2H), 2.29 (s, 3H). HRMS: calcd for $C_{11}H_{11}N_3O$ 201.2245, found 201.1501. IR (cm^{-1}): 1720.

4-Phenyl-1-(2-methoxyethan-2-on-1-yl)-1H-1,2,3-triazole (**2l**): ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.86–7.83 (m, 2H), 7.45–7.41 (m, 2H), 7.37–7.31 (m, 1H), 5.22 (s, 2H), 3.82 (s, 3H). +EMS (turbo spray): calcd for $C_{11}H_{11}N_3O_2$ 217.2239, found: 217.9. IR (cm^{-1}): 1740.

4-Phenyl-1-(2-(2-phenylethene-1-yl)-ethan-2-on-1-yl)-1H-1,2,3-triazole (**2m**): ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.88–7.86 (m, 2H), 7.79 (d, J = 16.4 Hz, 1H), 7.59–7.56 (m, 2H), 7.46–7.40 (m, 5H), 7.37–7.33 (m, 1H), 6.79 (d, J = 16.0 Hz, 1H), 5.51 (s, 2H). +EMS (turbo spray): calcd for $C_{18}H_{15}N_3O$ 289.3312, found: 290.0. IR (cm^{-1}): 1660.

4-Butyl-1-(2-phenyl ethan-2-on-1-yl)-1H-1,2,3-triazole (**2n**): ^1H NMR (400 MHz, $CDCl_3$): δ 8.02–7.99 (m, 2H), 7.69–7.65 (m, 1H), 7.56–7.52 (m, 2H), 7.45 (s, 1H), 5.82 (s, 2H), 2.77 (t, J = 7.60 Hz, 2H), 1.70 (pentet, J = 7.60 Hz, 2H), 1.410 (sextet, J = 7.60 Hz, 2H), 0.945 (t, J = 7.60 Hz, 3H). +EMS: calcd for $C_{14}H_{17}N_3O$ 243.1, found 244.1 $(M+H)^+$. IR (cm^{-1}): 1697.

1-((Naphthalen-3-yl)-ethan-2-on-1-yl)-(4-phenyl)-1H-1,2,3-triazole (**2o**): ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.06–7.87 (m, 7H), 7.70–7.60 (m, 2H), 7.46–7.42 (m, 2H), 7.36–7.33 (m, 1H), 6.04 (s, 2H). +EMS: calcd for $C_{20}H_{15}N_3O$ 313.1, found 314.2 $(M+H)^+$. IR (cm^{-1}): 1703.

(4-Phenyl)-1-((pyridin-2-yl)-ethan-2-on-1-yl)-1H-1,2,3-triazole (**2p**): ^1H NMR (400 MHz, $CDCl_3$): δ 8.77–8.75 (m, 1H), 8.13–8.11 (m, 1H), 7.95–7.88 (m, 5H), 7.62–7.59 (m, 1H), 7.47–7.43 (m, 2H), 7.38–7.33 (m, 1H), 6.20 (s, 2H). +EMS: calcd for $C_{15}H_{12}N_4O$ 264.1, found 265.1 $(M+H)^+$. IR (cm^{-1}): 1722.

22. (a) Wang, Q.; Chittaboina, S.; Barnhill, H. N. *Lett. Org. Chem.* **2005**, *2*, 293; (b) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596; (c) Himo, F.; Lovell, T.; Hilgraf, R.; Rostovtsev, V. V.; Noodleman, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **2005**, *127*, 210.