



**A theophylline based copper N-heterocyclic carbene complex: synthesis and activity studies in green media**

Journal:	<i>RSC Advances</i>
Manuscript ID	RA-COM-03-2016-006682.R1
Article Type:	Communication
Date Submitted by the Author:	25-Apr-2016
Complete List of Authors:	Szadkowska, Anna; University of Warsaw, Department of Chemistry Staszko, Sebastian; Military University of Technology, them. Jaroslaw Dabrowski, Faculty of Advanced Technologies and Chemistry; University of Warsaw, Department of Chemistry Zaorska, Ewelina; University of Warsaw, Department of Chemistry Pawłowski, Robert; Warsaw University of Technology, Faculty of Chemistry; University of Warsaw, Department of Chemistry
Subject area & keyword:	Catalysis < Organic



Journal Name

## COMMUNICATION

# A theophylline based copper *N*-heterocyclic carbene complex: synthesis and activity studies in green media

Received 00th January 20xx,  
Accepted 00th January 20xx

Anna Szadkowska,<sup>\*a</sup> Sebastian Staszko,<sup>a,b</sup> Ewelina Zaorska,<sup>a</sup> and Robert Pawłowski<sup>a,c</sup>

DOI: 10.1039/x0xx00000x

www.rsc.org/

**The synthesis of easy accessible theophylline-derived copper complex with additional ammonium functionalization has been developed. This xanthine-based metal compound turned out as an active initiator of alkyne-azide cycloaddition reaction (CuAAC) and Glaser homo-coupling reaction in aqueous media at room temperature.**

## Introduction

Copper catalysts are widely used in many commercial chemical processes.<sup>1</sup> Thus, modifications and improvements in activity and selectivity of copper initiators may affect in significant way the sustainability of chemical transformations. Especially, copper(I) complexes bearing NHC ligands have been disclosed as active catalysts for several transformations including various type of cycloadditions<sup>2</sup> and homo- and hetero-coupling reactions.<sup>3</sup> In addition, current research trends have demonstrated a renewal of chemistry of carbon-carbon triple bond, where copper on first oxidation state plays a crucial role.<sup>4</sup>

A good example of the reaction promoted by catalytic amounts of copper(I) complexes using alkynes as starting materials is the Huisgen 1,3-dipolar cycloaddition.<sup>5</sup> This synthetic approach based on the reaction between alkyne and azide proved to be a straightforward method leading to valuable triazole ring.<sup>6</sup> The heterocyclic core of 1,2,3-triazole became the subject of considerable interest due to its utility in organic chemistry and presented biological properties by some of its derivatives.<sup>7</sup> It's also worth to mention that, copper catalysts favour the formation of 1,4-disubstituted 1,2,3-triazoles as only isomers. Lately, most of studies on 1,3-dipolar

cycloaddition have explored activity of various modified copper(I) complexes containing NHC ligands.<sup>8</sup> In general, these modern copper initiators bearing NHC moiety possess very good stability and can be used even in high-temperature conditions.

Another representative reaction for the construction of complex molecules, which employs terminal alkynes is oxidative homo-coupling termed as Glaser-type coupling.<sup>9</sup> This synthetic strategy involves dimerization of two terminal alkynes in the presence of oxygen and catalytic amount of copper active species in order to give 1,3-diynes. The unique structure as well as good stability and reactivity of homo-coupled products make them precious scaffolds in organic synthesis, supramolecular chemistry and material science.<sup>10</sup> Despite a great number of examples in the literature showing the use of copper salts and copper complexes in Glaser-type coupling, only very few of them relate to copper compounds having NHC ligands.<sup>11</sup> Thus, we considered this gap in the synthesis of 1,3-diynes promoted by NHC copper complexes under aqueous conditions as worth to expand.

In recent decade, various transformations promoted by new generation of water-soluble NHC copper catalysts in aqueous media and biomass-derived solvents have been intensively studied.<sup>12</sup> Attaching ionic groups or strong polar substituents to NHC ligands is a typical method to solubilize metal complexes in green media.<sup>13</sup> The presence of various functionalizations of NHCs ligands such as: carboxylate,<sup>14</sup> ester,<sup>15</sup> sulfonate<sup>16</sup> and ammonium<sup>17</sup> increase water solubility. Apart from well-known procedures for the preparation of such NHC precursors, there are also available natural products, which contain NHC building blocks and may exhibit similar properties compared to synthetic analogues.<sup>18</sup> To date, several examples of water-soluble transition metal complexes containing natural heterocyclic core, such as carbohydrates and alkaloids derivatives have been presented in literature.<sup>19</sup> However, these scientific reports were rather limited to the description of antimicrobial activity and cytotoxicity of new metal complexes.<sup>19,20</sup> According to our knowledge, synthesis

<sup>a</sup> Department of Chemistry, University of Warsaw, Pasteura 1, 02-093 Warsaw, Poland. E-mail: szadkowska.anna@gmail.com.

<sup>b</sup> Faculty of Advanced Technologies and Chemistry, Military University of Technology, them. Jaroslaw Dabrowski, gen. Sylwester Kaliski 2, 00-908 Warsaw 49, Poland.

<sup>c</sup> Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland.

† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization of compounds. See DOI: 10.1039/x0xx00000x

and catalytic activity of NHC copper complexes based on natural products have been studied very little up to now.<sup>21</sup>

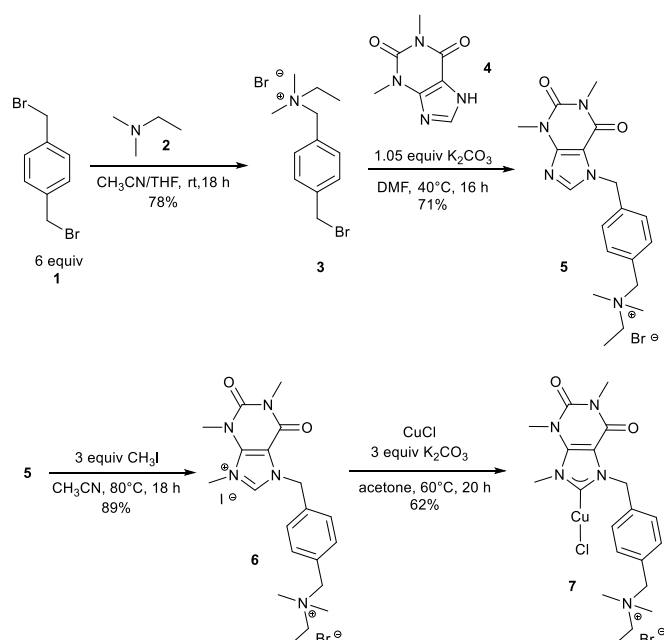
In this context, our intention was to prepare copper catalytic system based on a naturally occurring molecule with additional ammonium functionalization to increase the aqueous solubility of the NHC metal complex. We also intended to investigate potential activity of novel copper compound in CuAAC transformation and in Glaser-type homo-coupling in aqueous media. As part of our studies, the recovery and the reuse of a new presumed copper catalyst in selected reactions were investigated.

## Results and discussion

With the goal to enhance solubility in water of novel copper complex, we have planned the synthetic route utilizing theophylline as a basic scaffold. Theophylline as caffeine or theobromine is a alkaloid closely related to nucleobases of DNA or RNA, which widely occurs in nature, in the cacao tree.<sup>22</sup> Another valuable feature of theophylline as a NHC precursor is a suitable structure for synthetic application. As will be shown, one of the nitrogen atom of this compound can be easily deprotonated *via* substitution reaction.

The starting point of our four-steps synthesis was the preparation of ammonium moiety. Further experiments showed that employment of this type of functionalization in the structure of metal complex can vitally improve the hydrophilicity of whole molecule.<sup>23</sup> As depicted in **Scheme 1**, the ammonium scaffold has been obtained in one step.

Scheme 1. Synthesis of water soluble copper complex **7**



The reaction between commercially available reagents: an excess of  $\alpha,\alpha$ -dibromo-*p*-xylene **1** and *N,N*-dimethylethylamine **2** in the mixture of  $\text{CH}_3\text{CN}/\text{THF}$  at room temperature led to the

formation of water-soluble quaternary ammonium salt **3** in 78% yield. With required water-soluble moiety **3** in hand, we proceeded with the synthesis of the planned NHC copper complex. Thus, the compound **3** was linked to the theophylline **4** using alkylation conditions affording the precursor **5** in 71% yield. Subsequently, the resulting product **5** was methylated with 3 equivalents of methyl iodide in  $\text{CH}_3\text{CN}$  at  $80^\circ\text{C}$  to afford the desired water-soluble NHC salt **6** in high yield (89%). Finally, the treatment of compound **6** with copper(I) chloride and an excess of  $\text{K}_2\text{CO}_3$  in dry acetone under reflux conditions gave a new copper complex **7** with good yield (67%). The last step of the presented synthesis required the purification of crude mixture by filtration through Celite and the precipitation of the copper compound **7** from mixture of solvents: dichloromethane/*n*-pentane. Obtained white-off powder of the copper complex **7** was characterized by standard spectroscopic methods. However, several attempts to obtain single crystals suitable for X-Ray analysis measurements were ineffective.

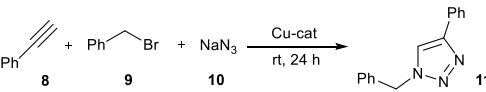
Before starting the study on activity of complex **7**, we also checked the solubility of this compound in water. The theophylline which plays a role of NHC core is generally slightly soluble in water (8.3 mg/mL),<sup>24</sup> but the addition of a quaternary ammonium group has increased the solubility to 15.5 mg/mL.

In order to examine the activity assay of the theophylline copper complex **7**, two different reactions were selected and tested. At first, to illustrate the applicability of novel copper complex **7** in three component click reaction, we initially carried out the model reaction between phenylacetylene **8**, benzyl bromide **9** and  $\text{NaN}_3$  **10** in various solvents (**Table 1**, entries 1-7). The results were summarized in **Table 1**.

It was interesting to notice that this type of 1,3-dipolar cycloaddition reaction proceeded well in various green solvents including: water, CPME and glycerol (**Table 1**, entries: 1-3, 73-87%) as well as in MeOH (**Table 1**, entry 4, 75%) after 24 hours. As shown in **Table 1**, we observed also some exceptions for transformations carried out in traditional solvents such as: DCM, toluene and DMSO. The use of these solvents provided definitely lower yields (**Table 1**, entries 5-7, up to 35%). As the survey of solvents revealed that the best medium for three component click reaction catalysed by new copper complex **7** is water, we were interested in whether it was possible to reduce the catalyst loading of this catalytic reaction. To determine optimal conditions, we conducted three experiments with reduced amount of complex **7** (**Table 1**, entries 8-10, 2.5 mol% to 0.5 mol%). The catalytic amount of 1 mol%, was found to be optimal for the studied reaction (**Table 1**, entry 9) to obtain the product **11** with 88% yield. Further decreasing of catalyst loading to 0.5 mol% led to lower yield 69% (**Table 1**, entry 10). Moreover, no product was detected in the absence of theophylline based complex **7** (**Table 1**, entry 11), showing that the presence of copper compound is essential for this reaction. Finally, we also proceeded the benchmark reaction with CuI (**Table 1**, entry 12). We found, that under optimized conditions, compound **11** was obtained only with 21% yield using CuI. This result

revealed the advantage of new copper complex **7** over traditional copper catalytic system. To compare the activity of water-soluble theophylline-based complex **7** and well-known NHC copper complexes, we enriched **Table 1** (entries 13-14) with results provided by Nolan and co-workers.<sup>12c</sup> The traditional NHC copper complexes such as: SIMesCuCl and IMesCuCl showed diverse reactivity (65-93%), depending on used nature of NHC ligand. Furthermore, authors applied complexes in higher loading (5 mol%) and in the mixture of solvents: H<sub>2</sub>O/*t*-BuOH.

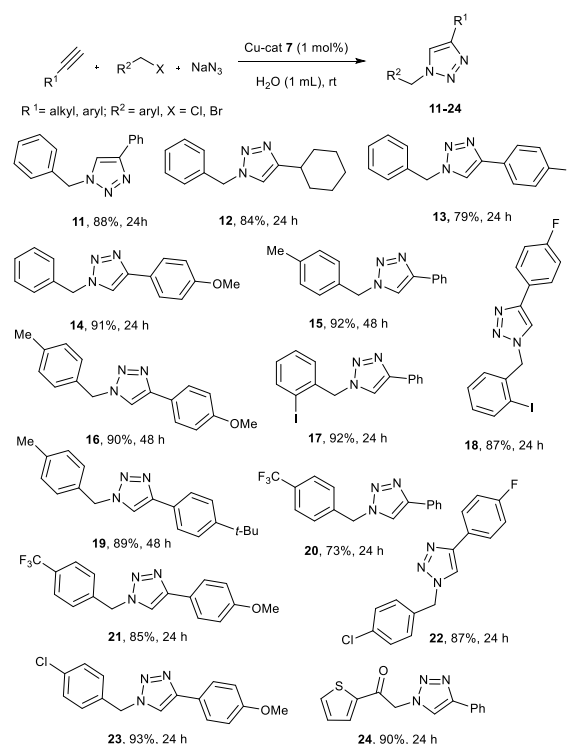
Table 1. Optimization of CuAAC reaction conditions. Reaction conditions: phenylacetylene **8** (1.1 mmol), benzyl bromide (1.0 mmol), sodium azide (1.1 mmol), 1 mL of solvent, 24 h. <sup>a</sup>Isolated yields, n. d. not determined.

				
Entry	Cu-cat	(mol%)	Solvent (1 mL)	Yield (%) <sup>a</sup>
1	<b>7</b>	5	water	87
2	<b>7</b>	5	CPME	73
3	<b>7</b>	5	glycerol	82
4	<b>7</b>	5	MeOH	75
5	<b>7</b>	5	DCM	35
6	<b>7</b>	5	toluene	trace
7	<b>7</b>	5	DMSO	trace
8	<b>7</b>	2.5	water	86
9	<b>7</b>	1	water	88
10	<b>7</b>	0.5	water	69
11	—	—	water	n.d.
12	CuI	5	water	21
13	SIMesCuCl	5	water/ <i>t</i> -BuOH (3 mL)	93
14	IMesCuCl	5	water/ <i>t</i> -BuOH (3 mL)	65

With the optimized conditions in hands, we surveyed the reaction scope using different substituted benzyl halides and alkynes in water (**Scheme 2**).

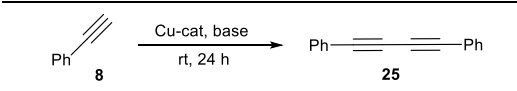
The reactions employing aliphatic and aromatic terminal alkynes with various substituents proceeded smoothly and a series of 1,4-substituted triazoles (**Scheme 2**, examples: **11-24**) were afforded in very good yields (73-93%). In general, no clear trend was observed between steric or electronic factors of substrates and the formation of 1,4-substituted triazoles. However, in most cases substrates with electron-rich substituents (**Scheme 2**, examples: **14**, **15**, **16**, **19** and **23**) worked more efficiently toward CuAAC transformation, affording appropriate 1,4-triazoles with higher yields (89-93%). It should be also noted that the presence of the electron-rich methyl group in benzyl bromide have caused the prolongation of the CuAAC reaction time from 24 hours to 48 hours (**Scheme 2**, examples: **15**, **16** and **19**). Interestingly, theophylline based complex **7** turned out as a tolerant and an active catalyst of the tricky *S*-bearing triazole (**Scheme 2**, example **24**).

Scheme 2. Catalytic activity of theophylline-based copper complex (**7**) in three component CuAAC reaction. Reaction conditions: benzyl halide (1.0 mmol), NaN<sub>3</sub> (1.1 mmol), alkyne (1.1 mmol), Cu cat. **7** (1 mol%), H<sub>2</sub>O (1 mL), rt, 24 h.



Continuing the exploration of catalytic performance of new copper complex **7** in aqueous media, we then conducted model transformation of Glaser-type homo-coupling. To optimize the reaction conditions, phenylacetylene **8** was selected as a substrate. The benchmark reaction was performed in water at room temperature (**Table 2**).

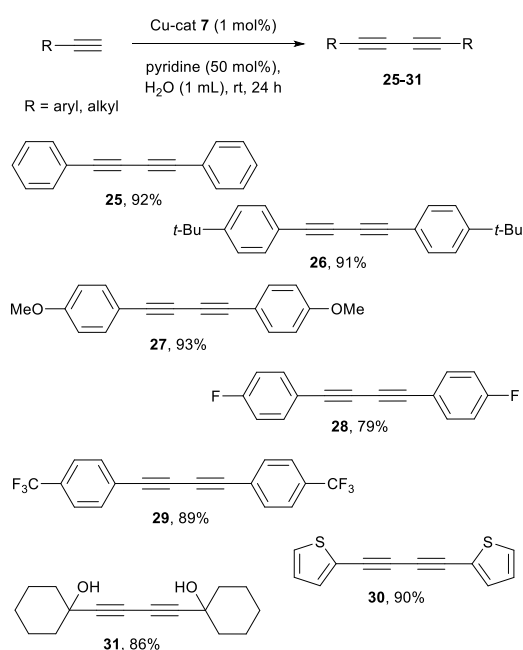
Table 2. Optimization of Glaser homo-coupling reaction conditions. Reaction conditions: phenylacetylene **8** (1.0 mmol), base, 1 mL of solvent, rt, 24 h. <sup>a</sup>Isolated yields, n. d. not determined.

					
Entry	Cu-cat	(mol%)	Solvent (1 mL)	Base	Yield (%) <sup>a</sup>
1	<b>7</b>	5	water	—	n.d.
2	<b>7</b>	5	water	Et <sub>3</sub> N (50 mol%)	79
3	<b>7</b>	5	CPME	Et <sub>3</sub> N (50 mol%)	56
4	<b>7</b>	5	glycerol	Et <sub>3</sub> N (50 mol%)	78
5	<b>7</b>	5	water	pyridine (50 mol%)	91
6	<b>7</b>	5	water	( <i>i</i> -Pr) <sub>2</sub> EtN (50 mol%)	55
7	<b>7</b>	2.5	water	pyridine (50 mol%)	92
8	<b>7</b>	1	water	pyridine (50 mol%)	92
9	<b>7</b>	0.5	water	pyridine (50 mol%)	84
10	<b>7</b>	1	water	pyridine (25 mol%)	77
11	—	—	water	pyridine (50 mol%)	n.d.
12	CuI	5	water	pyridine (50 mol%)	15

The preliminary experiment indicated that product **25** was not detected in 24 hours in the absence of any base (Table 2, entry 1). Thus, next trials were performed with the addition of 50 mol% of Et<sub>3</sub>N in various green media including: water, CPME and glycerol (Table 2, entries 2-4). The results of these three experiments showed that the combination of Et<sub>3</sub>N with water improved the efficiency of the formation of **25** (Table 2, entry 2, 79%). While studying other compounds with basic character, it turned out that better reactivity was obtained using pyridine (Table 2, entries: 5-6). In order to improve the reaction efficiency by reducing the catalyst's loading and the amount of the base, we continued evaluation studies. A decrease in the catalyst loading to 2.5 mol% and 1 mol%, allowed to afford the product **25** in 92% yield (Table 2, entries: 7-8). Further reduction of loading of copper complex **7** to 0.5 mol% diminished yield of the expected 1,3-diyne **25** to 84% (Table 2, entry 9). Next, the amount of base was under investigation (Table 2, entry 10). It turned out, that no improvements in the yield was observed, when the loading of pyridine was reduced to 25 mol% (Table 2, entry 10, 77%). Considering the key role of copper compounds in the model reaction, another two experiments were carried out (Table 2, entries 11-12). Performing the Glaser homo-coupling reaction without any copper compounds or using standard catalytic systems such as CuI didn't improve yields of 1,3-diyne **25**.

Based on the presented survey, the optimal conditions for Glaser-type homo-coupling were proposed as follows: 1 mol% of catalyst combined with 50 mol% of pyridine and the use of water as a solvent (Table 2). Having demonstrated methodology of Glaser-type homo-coupling reaction, we next focused on the scope using copper complex **7**. To our delight, new catalyst **7** promoted the reaction of alkynes bearing a variety of functional groups (Scheme 3).

Scheme 3. Catalytic activity of theophylline-based copper complex **7** in Glaser-type cross-coupling reaction. Reaction conditions: alkyne (1.0 mmol), pyridine (50 mol%), Cu cat. **7** (1.0 mol%), H<sub>2</sub>O (1.0 mL), rt, 24 h.



The results showed that 1,3-diynes containing electron-donating and electron-withdrawing substituents and as well as heterocyclic moiety were formed with very high yields using complex **7** (Scheme 3, examples **25-30**, 79-93%). In addition, also aliphatic terminal alkyne with hydroxyl group was selectively coupled to afford internal 1,3-diyne **31** with 86% yield (Scheme 3). Based on conducted experiments, the advantage of merging water and new catalytic system **7** was the facile isolation of desired 1,3-diynes.

At the present time, the common practice in metal catalysed reactions in green media, is the probe of recycling of the obtained catalyst.<sup>25</sup> To demonstrate the catalytic efficiency of copper complex **7**, we carried out both examined transformations: CuAAC reaction and Glaser-type homo-coupling reaction once more to investigate the possible recovery of initiator **7** from the previous run. The reuse test was executed in 1 mL of water, using 1 mol% of catalyst **7** and in case of Glaser-type transformation with 50 mol% of pyridine. After the completion of each reaction, monitoring by with TLC plate, Et<sub>2</sub>O was added to the flask and using the extraction step, product was set apart from the reaction mixture. The aqueous phase with the catalyst **7** was reused for the next course. Observed recyclability for both reactions was disclosed on Figure 1.

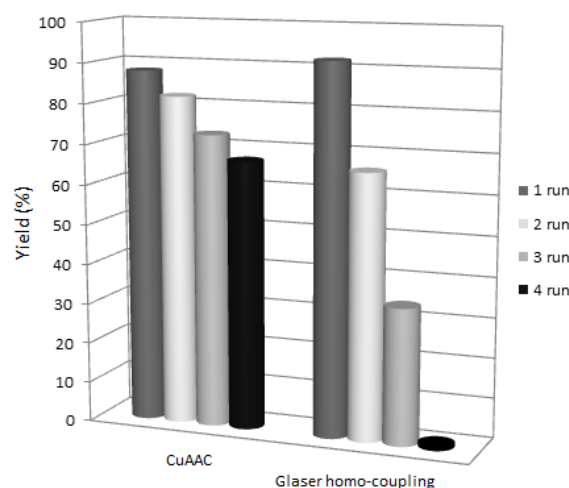


Figure 1. The recyclability test of complex **7**

In case of CuAAC transformation, the copper complex **7** was applied to the reaction four times, giving 67% of isolated product **11** in the fourth run. A significant decrease in the recovery of initiator **7** was observed for Glaser-type homo-coupling. In each run, the product **25** was obtained with lower yield, giving in the third time only 34% of the desired compound **25**. In the fourth run, the product **25** was not detected. This outcome might be a consequence of the deactivation of the copper initiator **7** under Glaser reaction conditions after longer time of use.

## Conclusions

In summary, the synthesis of easy accessible novel water-soluble copper complex containing theophylline moiety has been presented. The catalyst bearing ammonium functionalization displayed high activity in three component click reaction and in Glaser homo-coupling reaction under mild conditions. A broad range of 1,4-substituted triazoles and 1,3-diynes have been formed by the incorporation of 1 mol% of new simple copper complex at room temperature in water. Presented catalytic system is a good example of sustainable approach due to its ability to be recycle up to fourth times in water in three component click reaction. In case of Glaser homo-coupling reaction, the novel initiator allows to obtain the expected homo-dimer only three times, however in each run with diminished yield. Further investigations into the utility of this new water-soluble copper complex bearing theophylline moiety in other catalytic reactions are in progress.

## Acknowledgments

‡ Authors gratefully acknowledge financial support from the National Science Centre (DEC-2012/07/D/ST5/02260). R.P. thanks Warsaw Consortium of Academic Chemistry for KNOW scholarship. The study was carried out at the Biological and Chemical Research Centre, University of Warsaw, established within the project co-financed by European Union from the European Regional Development Fund under the Operational Programme Innovative Economy, 2007–2013.

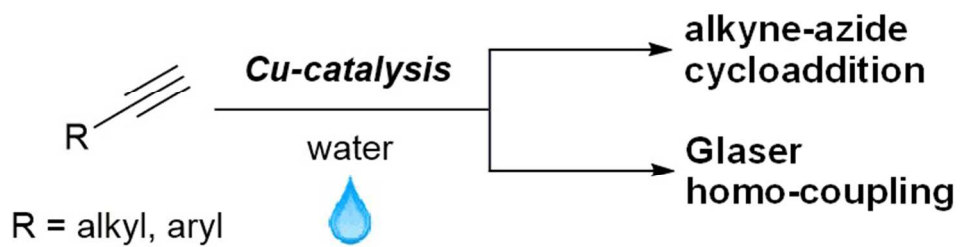
## Notes and references

- 1 a) N. Krause, ed. *Modern Organocopper Chemistry*. Wiley-VCH, Weinheim, 2002. b) A. Lauria, R. Delisi, F. Mingoia, A. Terenzi, A. Martorana, G. Barone and A. M. Almerico, *Eur. J. Org. Chem.*, 2014, 3289. c) N. Jagerovic, C. Gómez de la Oliva, P. Goya, A. Dordal and R. Cuberes, *Eur. Pat. Appl.*, 2006, 0380290. d) <http://www.copper.org>.
- 2 a) R. Huisgen, *1,3-Dipolar Cycloaddition Chemistry*, Wiley, New York, 1984, pp. 1-176. b) P. K. Fraser and S. Woodward, *Tetrahedron Lett.*, 2001, **42**, 2747. c) S. Díez-González and S. P. Nolan, *Synlett*, 2007, 2158. d) M. Michalak, M. Stodulski, S. Stecko, M. Woźnica, O. Staszewska-Krajewska, P. Kalicki, B. Furman, J. Frelek and M. Chmielewski, *Tetrahedron*, 2012, **68**, 10806.
- 3 a) V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2596. b) J. D. Egbert, C. S. J. Cazin and S. P. Nolan, *Catal. Sci. Technol.*, 2013, **3**, 912.
- 4 a) G. Evano, C. Theunissen and A. Pradal, *Nat. Prod. Rep.*, 2013, **30**, 1467. X.-X. Guo, D.-W. Gu, Z. Wu and W. Zhang, *Chem. Rev.*, 2015, **115**, 1622. b) M. Xu, C. Kuang, Z. Wang, Q. Yang, Y. Jiang, *Synthesis*, 2011, 223. c) P. Aschwanden and E. M. Carreira, *Acetylene Chemistry*, Wiley, Weinheim, 2005.
- 5 a) R. Huisgen, *Pure Appl. Chem.*, 1989, **61**, 613. b) R. Huisgen, G. Szeimies, L. Möbius, *Chem. Ber.*, 1967, **100**, 2494.
- 6 a) R. Alvarez, S. Velazquez, A. San-Felix, S. Aquaro, E. De Clercq, C. F. Perno, A. Karlsson, J. Balzarini, M. J. Camarasa, *J. Med. Chem.*, 1994, **37**, 4185. b) W.-Q. Fan, A. R. Katritzky in *Comprehensive heterocyclic chemistry II*; A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Eds.; Elsevier Science: Oxford, 1996; Vol. 4, pp. 1.
- 7 a) Z.-J. Zheng, D. Wand, Z. Xu and L.-W. Xu, *Beilstein J. Org. Chem.*, 2015, **11**, 2557; b) K. A. Kalesh, H. Shi, J. Ge and S. Q. Yao, *Org. Biomol. Chem.*, 2010, **8**, 174; c) A. D. Moorhouse and J. E. Moses, *ChemMedChem*, 2008, **3**, 715; d) G. C. Tron, T. P. Piralí, R. A. Billington, P. L. Canonico, G. Sorba and A. Genazzani, *Med. Res. Rev.*, 2008, **28**, 278.
- 8 a) J. García-Álvarez, J. Díez and J. Gimeno, *Green Chem.*, 2010, **12**, 2127. b) D. Wang, N. Li, M. Zhao, W. Shi, C. Ma and B. Chen, *Green Chem.*, 2010, **12**, 2120. c) S. Díez-González, A. Correa, L. Cavallo and S. P. Nolan, *Chem.-Eur. J.*, 2006, **12**, 7558. d) S. Díez-González, E. C. Escudero-Adán, J. Benet-Buchholz, E. D. Stevens, A. M. Z. Slawin and S. P. Nolan, *Dalton Trans.*, 2010, **39**, 7595. e) B. Liu, C. Chen, Y. Zhang, X. Liu and W. Chen, *Organometallics* 2013, **32**, 5451. f) B. Lander and O. Navarro, *Eur. J. Inorg. Chem.*, 2012, 2980.
- 9 a) C. Glaser, *Ann. Chem. Pharm.*, 1870, **154**, 137. b) P. Siemsen, R. C. Livingston and F. Diederich, *Angew. Chem., Int. Ed.*, 2000, **39**, 2632.
- 10 K. S. Sindhu and G. Anilkumar, *RSC Adv.*, 2014, **4**, 27867.
- 11 W. Shi and A. Lei, *Tetrahedron Lett.*, 2014, **55**, 2763.
- 12 a) J. García-Álvarez, J. Díez and J. Gimeno, *Green Chem.*, 2010, **12**, 2127. b) C. Vidal and J. García-Álvarez, *Green Chem.*, 2014, **16**, 3515. c) D. Wang, N. Li, M. Zhao, W. Shi, C. Ma and B. Chen, *Green Chem.*, 2010, **12**, 2120. d) S. Díez-González, A. Correa, L. Cavallo and S. P. Nolan, *Chem.-Eur. J.*, 2006, **12**, 7558.
- 13 a) H. Diaz-Velázquez, Y. Ruiz-García, M. Vandichel, A. Madder and F. Verpoort, *Org. Biomol. Chem.*, 2014, **12**, 9350. b) S. Díez-González, *Catal. Sci. Technol.*, 2011, **1**, 166. c) S. Díez-González, E. D. Stevens and S. P. Nolan, *Chem. Commun.*, 2008, 4747. d) L. A. Schaper, S. J. Hock, W. A. Herrmann and F. E. Kühn, *Angew. Chem., Int. Ed.*, 2013, **52**, 270.
- 14 a) L. R. Moore, S. M. Cooks, M. S. Anderson, H.-J. Schanz, S. T. Griffin, R. D. Rogers, M. C. Kirk, K. H. Shaughnessy, *Organometallics* 2006, **25**, 5151. b) L. Li, J. Wang, C. Zhou, R. Wang, M. Hong, *Green Chem.*, 2011, **13**, 2071.
- 15 W. A. Herrmann, L. J. Gooßen and M. Spegler, *J. Organomet. Chem.*, 1997, **547**, 357.
- 16 a) W. A. Herrmann, M. Elison, J. Fischer, C. Köcher and K. Öfele, U. S. Patent 5,728, **839**, 1998. b) D.-Q. Xu, J. Wu, S.-P. Luo, J.-X. Zhang, J.-Y. Wu, X.-H. Du and Z.-Y. Xu, *Green Chem.*, 2009, **11**, 1239. c) F. Godoy, C. Segarra, M. Poyatos and E. Peris, *Organometallics* 2011, **30**, 684. d) A. Azua, S. Sanz and E. Peris, *Chem.-Eur. J.*, 2011, **17**, 3963.
- 17 a) S. L. Balof, S. J. P. Pool, N. J. Berger, E. J. E. J. Valente, A. M. Shiller, H.-J. Schanz, *Dalton Trans.*, 2008, 5791. c) W. Wang, J. Wu, C. Xia, F. Li, *Green Chem.*, 2011, **13**, 3440.
- 18 a) B. Gyurcsik and L. Nagy, *Coord. Chem. Rev.*, 2000, **203**, 81. b) J. Schütz and W. A. Herrmann, *J. Organomet. Chem.*, 2004, **689**, 2995. c) B. K. Keitz and R. H. Grubbs, *Organometallics* 2010, **29**, 403.
- 19 a) F. Tewes, A. Schlecker, K. Harms and F. Glorius, *J. Organometal. Chem.*, 2007, **692**, 4593. b) C.-C. Yang, P.-S. Lin, F.-C. Liu, I. J. B. Lin, G.-H. Lee and S.-M. Peng, *Organometallics*, 2010, **29**, 5959. c) M. J. Pazner, A. Deeraksa, A. Smith, B. D. Wright, K. M. Hinid, A. Kascatan-Nebioglu, A. G. Torres, B. M. Judy, C. E. Hovis, J. K. Hillard, R. J. Mallet, E. Cope, D. M. Estes, C. L. Cannon, J. G. Leid and W. J. Youngs, *Eur. J. Inorg. Chem.*, 2009, **13**, 1739. d) H. A. Mohamed, B. R. M. Lake, T. Laing, R. M. Phillips and C. E. Willans, *Dalton Trans.*, 2015, 7563. e) B. Bertrand, L. Stefan, M. Pirrotta, D. Monchaud, E. Bodio, P. Richard, P. Le Gendre, E. Warmerdam, M. H. de Jager, G. M. M. Groothuis, M. Picquet and A. Casini, *Inorg. Chem.*, 2014, **53**, 2296.

## COMMUNICATION

Journal Name

- 20 M. J. Pazner, K. M. Hindi, B. D. Wright, J. B. Taylor, D. S. Han, W. J. Youngs and C. L. Cannon, *Dalton Trans.*, 2009, 7308.
- 21 V. B. Purohit, S. C. Karad, K. H. Patel and D. K. Raval, *RSC Adv.*, 2014, **4**, 46002.
- 22 a) H. Ashihara, H. Sano and A. Crozier, *Phytochemistry*, 2008, **69**, 841. b) E. Martínez-Pinilla, A. Oñatibia-Astibia and R. Franco, *Front. Pharmacol.*, 2015, **6**, 1.
- 23 a) K. H. Shaughnessy, *Chem. Rev.*, 2009, **109**, 643. b) D. Rix, F. Căișo, I. Laurent, Ł. Gulajski, K. Grela and M. Mauduit, *Chem. Commun.*, 2007, 3771.
- 24 [http://www.chemicalbook.com/ChemicalProductProperty\\_EN\\_CB4285388.htm](http://www.chemicalbook.com/ChemicalProductProperty_EN_CB4285388.htm)
- a) G. Centi and S. Perathoner, *Catalysis Today*, 2003, **77**, 287. b) J. L. Tucker, *Org. Process Res. Dev.*, 2006, **10**, 315.



70x17mm (300 x 300 DPI)