

The catalytic activity of copper nanoparticles on aminomodified silica support in the flow azide-alkyne cycloaddition reaction using macrocyclic substrates

© **Albina T. Nurmukhametova, Roman N. Belov, Vladimir A. Burilov,*⁺ and Igor S. Antipin**
*Department of Organic Chemistry. A.M. Butlerov Chemical Institute. Kazan Federal University.
Kremlyovskaya St., 18. Kazan, 420008. Russia. Phone: +7 (843) 233-73-44. E-mail: ultrav@bk.ru*

*Supervising author; ⁺Corresponding author

Keywords: Modified silica, azide-alkyne cycloaddition reaction, heterogeneous catalysis, copper nanoparticles, flow chemistry.

Abstract

Using the chemical reduction method, a copper-containing catalyst on an amino-modified silica was obtained. The structure and composition of the catalyst were characterized by low-temperature nitrogen adsorption and inductively coupled plasma mass spectrometry. It was found that the modification of silica with amino groups and copper nanoparticles leads to a significant change in textural characteristics: nanoparticles and the modifier fill the pores in the size range of 5-10 nm. Obtained catalyst showed good activity in the flow cycloaddition of azides and alkynes of various nature. The comparative activity of azides and alkynes was analyzed. It has been established that among the azides studied (benzyl azide, *p*-nitrobenzylazide, *p*-methoxybenzylazide, 2-azidoethylacetate and 1-azidodecane), alkyl and aryl azides with electron-withdrawing groups were most active due to an increase in the electrophilicity of the terminal nitrogen atom of the azide group. Among the studied acetylenes (phenylacetylene, hexin-1, trimethylsilylacetylene and propargyl alcohol), propargyl alcohol was the most and trimethylsilylacetylene was the less active. Increased activity of propargyl alcohol may be due to a donor hydroxyl group capable of coordinating with copper; reduced activity of trimethylsilylacetylene can be resulted from steric hindrances. *p*-*tert*-Butyl and *p*-*H*-calix[4]arens were also used in the reaction. Full conversion of macrocycles was achieved after 3 consecutive reaction cycles. The resulting triazoles were isolated and characterized by a complex of physical methods. Thus, It has been demonstrated that carrying out the reaction in a flow by maintaining stable and fully reproducible reaction parameters makes it possible to quickly evaluate the relative reactivity of molecules.

References

- [1] R. Huisgen. 1,3-Dipolar Cycloadditions. Past and Future. *Angew. Chem. Int. Ed. Engl.* **2013**. Vol.2. Iss.10. P.565-598. DOI: 10.1002/anie.196305651
- [2] C.W. Tornøe, C. Christensen, M. Meldal. Peptidotriazoles on Solid Phase: [1,2,3]-Triazoles by Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of Terminal Alkynes to Azides. *J. Org. Chem.* **2002**. Vol.67. Iss.9. P.3057-3062. DOI: 10.1021/jo011148j
- [3] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective “Ligation” of Azides and Terminal Alkynes. *Angew. Chem. Int. Ed.* **2002**. Vol.41. P.2596-2599. DOI: 10.1002/1521-3773(20020715)41:14<2596::AID-ANIE2596>3.0.CO;2-4
- [4] C. Wang, D. Ikhlef, S. Kahlal, J.-Y. Saillard, D. Astruc. Metal-catalyzed azide-alkyne “click” reactions: Mechanistic overview and recent trends. *Coord. Chem. Rev.* **2016**. Vol.316. P.1-20. DOI: 10.1016/j.ccr.2016.02.010
- [5] J.E. Hein, V.V. Fokin. Copper-catalyzed azide-alkyne cycloaddition (CuAAC) and beyond: new reactivity of copper(I) acetylides. *Chem. Soc. Rev.* **2010**. Vol.39. Iss.4. P.1302-1315. DOI: 10.1039/B904091A
- [6] X.-P. He, Y.-L. Zeng, Y. Zang, J. Li, R.A. Field, G.-R. Chen. Carbohydrate CuAAC click chemistry for therapy and diagnosis. *Carbohydr. Res.* **2016**. Vol.429. P.1-22. DOI: 10.1016/j.carres.2016.03.022.
- [7] A.Y. Mitrofanov, A.V. Murashkina, I. Martín-García, F. Alonso, I.P. Beletskaya. Formation of C–C, C–S and C–N bonds catalysed by supported copper nanoparticles. *Catal. Sci. Technol.* **2017**. Vol.7. Iss.19. P.4401-4412. DOI: 10.1039/C7CY01343D
- [8] M.B. Gawande, A. Goswami, F.-X. Felpin, T. Asefa, X. Huang, R. Silva, X. Zou, R. Zboril, R.S. Varma. Cu and Cu-Based Nanoparticles: Synthesis and Applications in Catalysis. *Chem. Rev.* **2016**. Vol.116. P.3722-3811. DOI: 10.1021/acs.chemrev.5b00482

- [9] M. Dixit, M. Mishra, P.A. Joshi, D.O. Shah. Study on the catalytic properties of silica supported copper catalysts. *Procedia Engineering*. **2013**. Vol.51. P.467-472. DOI: 10.1016/j.proeng.2013.01.066
- [10] S. Ogasawara, Y. Hayashi. Multistep Continuous-Flow Synthesis of (–)-Oseltamivir. *Synthesis*. **2017**. Vol.49. Iss.2. P.424-472. DOI: 10.1055/s-2016-0036-1588899
- [11] V.A. Burilov, A.N. Nurmukhametova, R.N. Belov, D.A. Mironova, V.V. Vorob'ev, Y.N. Osin, I.S. Antipin. New copper-containing catalysts based on modified amorphous silica and their use in flow azide-alkyne cycloaddition. *Russ. Chem. Bull.* **2018**. Vol.67. No.3. P.461-468. (russian)
- [12] W. Xu, J.J. Vittal, R.J. Puddephatt. Propargyl calix[4]arenes and their complexes with silver(I) and gold(I). *Can. J. Chem.* **1996**. Vol.74. Iss.5. P.766-774. DOI: 10.1139/v96-084
- [13] S.W. Kwok, J.R. Fotsing, R.J. Fraser, V.O. Rodionov, V.V. Fokin. Transition-Metal-Free Catalytic Synthesis of 1,5-Diaryl-1,2,3-triazoles. *Org. Lett.* **2010**. Vol.12. Iss.19. P.4217-4219. DOI: 10.1021/ol101568d
- [14] M.S. Alam, R. Kajlki, H. Hanatani, X. Kong, F. Ozoe, Y. Matsui, F. Matsumura, Y. Ozoe. Synthesis and Structure-Activity Relationships of 1-Phenyl-1H-1,2,3-triazoles as Selective Insect GABA Receptor Antagonists. *J. Agric. Food Chem.* **2006**. Vol.54. Iss.4. P.1361-1372. DOI: 10.1021/jf052773i
- [15] A.W. Gann, J.W. Amoroso, V.J. Einck, W.P. Rice, J.J. Chambers, N.A. Schnarr. A Photoinduced, Benzyne Click Reaction. *Org. Lett.* **2014**. Vol.16. Iss.7. P.2003-2005. DOI: 10.1021/ol500389t
- [16] D. Dou, G. He, Y. Li, Z. Lai, L. Wei, K.R. Alliston, G.H. Lushington, D.M. Eichhorn, W.C. Groutas. Utilization of the 1,2,3,5-thiatriazolidin-3-one 1,1-dioxide scaffold in the design of potential inhibitors of human neutrophil proteinase 3. *Bioorg. Med. Chem.* **2010**. Vol.18. Iss.3. P.1093-1102. DOI: 10.1016/j.bmc.2009.12.057
- [17] M. Swetha, P.V. Ramana, S.G. Shirodkar. Simple and Efficient Method for the Synthesis of Azides in Water-THF Solvent System. *Org. Prep. Proced. Int.* **2011**. Vol.43. Iss.4. P.348-353. DOI: 10.1080/00304948.2011.594002
- [18] W.L.F. Armarego, C.L. Chai. Purification of Laboratory Chemicals. *New York: Elsevier*. **2009**. P.743.
- [19] M.B. Plutschack, B. Pieber, K. Gilmore, P.H. Seeberger. The Hitchhiker's Guide to Flow Chemistry. *Chem. Rev.* **2017**. Vol.117. Iss.18. P.11796-11893. DOI: 10.1021/acs.chemrev.7b00183
- [20] P.L. Golas, N.V. Tsarevsky, K. Matyjaszewski. Structure-Reactivity Correlation in "Click" Chemistry: Substituent Effect on Azide Reactivity. *Macromol. Rapid Commun.* **2008**. Vol.29. Iss.12. P.1167-1171. DOI: 10.1002/marc.200800118
- [21] J.E. Hein, V.V. Fokin. Copper-catalyzed azide-alkyne cycloaddition (CuAAC) and beyond: new reactivity of copper(I) acetylides. *Chem. Soc. Rev.* **2010**. Vol.39. Iss.4. P.1302-1315. DOI: 10.1039/B904091A
- [22] X. Zhang, P. Liu, L. Zhu. Structural Determinants of Alkyne Reactivity in Copper-Catalyzed Azide-Alkyne Cycloadditions. *Molecules*. **2016**. Vol.21. Iss.12. P.1697-1714. DOI: 10.3390/molecules21121697
- [23] D. De, T.K. Pal, S. Neogi, S. Senthilkumar, D. Das, S.S. Gupta, P.K. Bharadwaj. A Versatile Cu^{II} Metal-Organic Framework Exhibiting High Gas Storage Capacity with Selectivity for CO₂: Conversion of CO₂ to Cyclic Carbonate and Other Catalytic Abilities. *Chem. Eur. J.* **2016**. Vol.22. Iss.10. P.3387-3396. DOI: 10.1002/chem.201504747
- [24] V.A. Burilov, R.R. Ibragimova, B.H. Gafiatullin, S.E. Solovieva, I.S. Antipin. The microwave synthesis of bifunctional derivatives of *p*-tert-butylthiacalix[4]arene containing alkyl and bromoalkyl moieties. *Butlerov Communications*. **2016**. Vol.47. No.8. P.23-28. DOI: 10.37952/ROI-jbc-01/16-47-8-23
- [25] A.A. Muravev, F.B. Galieva, S.E. Solovieva, I.S. Antipin. Synthesis and structure of calix[4]arene with alkyne substituents on the lower rim. *Butlerov Communications*. **2017**. Vol.52. No.12. P.82-86. DOI: 10.37952/ROI-jbc-01/17-52-12-82