

Self-assembled nanospheres as a reaction vessel to facilitate dinuclear Cu(I) catalyzed cyclization reactions

Sergio Gonell¹, Xavier Caumes¹, Nicole Orth², Ivana Ivanović-Burmazović² and Joost N. H. Reek¹

¹Homogeneous, Supramolecular and Bio-Inspired Catalysis, Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, Amsterdam 1098XH, The Netherlands.

²Lehrstuhl für Bioanorganische Chemie, Department Chemie und Pharmazie, Friedrich-Alexander-Universität Erlangen, Egerlandstrasse 3, Erlangen 91058, Germany.
x.caumes@uva.nl

The mechanism of the copper(I)-catalyzed cycloisomerization of alkynoic acids has been elucidated by means of a detailed mechanistic study including NMR, HRMS and kinetic following. Reaction kinetics show a higher order in copper, indicating the formation of a bis-Cu intermediate as the key rate determining step of the reaction. This intermediate was further identified during catalysis by cold spray ionization mass spectrometry analysis of the reaction mixture. Based on the mechanistic findings, a supramolecular approach was developed to pre-organize the copper catalysts in a nanosphere and facilitate the formation of the bis-Cu intermediate.

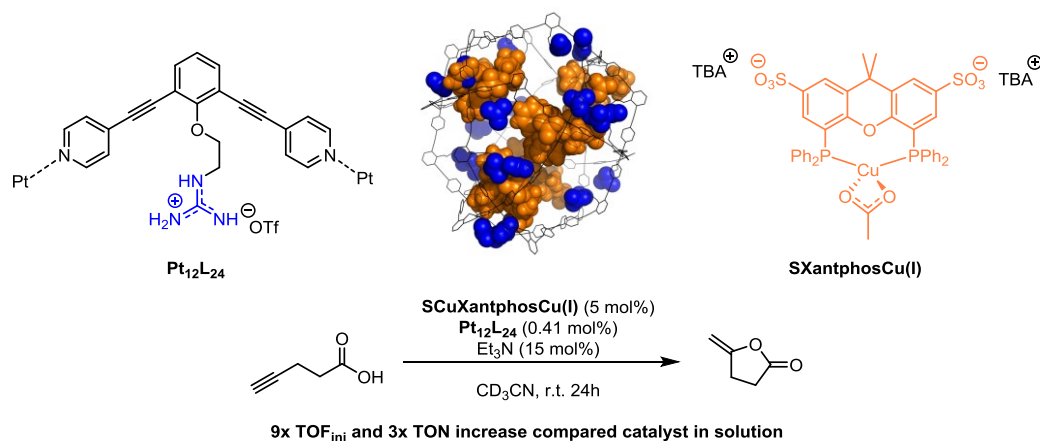


Figure 1: Top) Encapsulation of SXantphosCu(I) and guanidinium nanosphere, bottom) Reaction condition for the cyclization of 4-pentynoic acid.

Using our previously published strategy with endo-functionalisation of a nanosphere with guanidinium groups and the use of a sulfonated ligand,¹ close proximity between copper catalyst can be obtained inside the nanosphere. As anticipated, this high local concentration of copper catalyst lead to higher reaction rates as the bi-metallic pathway is favored and lead to important increase of the TOF and TON compared to the free catalyst in solution.

1. Wang, Q.-Q.; Gonell, S.; Leenders, S. H. A. M.; Dürr, M.; Ivanović-Burmazović, I.; Reek, J. N. H. *Nat. Chem.* **2016**, 8 (3), 225.