Dendritic Copper Catalysts for Homogeneous Click Chemistry in Water

Category

Polymer-Supported
Synthesis

Key words

dendrimers

Huisgen
cycloaddition

click chemistry

copper catalysis

SYNFACT
of the month

conditions A: dendrimer **1** (1 mol%), [hexabenzyltren-Cu]Br **3** (0.1 mol%), H₂O, 25 °C, 3 h
 conditions B: catalyst **1-Cu^I** (4–50 ppm Cu^I), H₂O, 30 °C, 24 h
 conditions C: catalyst **1-Cu^I** (4–50 ppm Cu^I), H₂O, 35 °C, 24 h

Selected examples:

2a R¹ = H, R² = Ph
 conditions A: 91% yield
 conditions B: 99% yield (4 ppm Cu^I)

2b R¹ = H, R² = TMS
 conditions A: 89% yield
 conditions C: 81% yield (20 ppm Cu^I)

2c R¹ = Me, R² = Ph
 conditions A: 90% yield
 conditions B: 89% yield (20 ppm Cu^I)

2d R¹ = CN, R² = Ph
 conditions A: 90% yield
 conditions B: 90% yield (50 ppm Cu^I)

2e R¹ = Br, R² = Ph
 conditions A: 96% yield
 conditions C: 89% yield (50 ppm Cu^I)

Significance: The dendrimer **1** consists of water/organic compatible 27 triethyleneglycol (TEG) termini and a hydrophobic core (for the preparation of **1**, see: *Chem. Commun.* **2013**, 49, 8169). [Hexabenzyltren-Cu]Br **3** and **1** promote the click reaction of benzyl azides and phenyl acetylenes in water to give the corresponding triazoles in 89–96% yield. The catalyst **1-Cu^I** (4–200 ppm Cu^I), prepared from CuSO₄·5H₂O and NaAsc, also catalyzed the click reaction in 81–99% yield.

Comment: The TEG termini render the dendrimer **1** water-soluble, and the hydrophobic core allows solubilization of the hydrophobic compound **3** and the substrates in water. The interaction between **1** and **3** was shown by selective ¹H NMR shifts and a NOESY spectrum. The micelle nanoreactor **1** was recycled ten times (10th reuse: **2a**, 91% yield). The click reaction was performed with 1 ppm **1-Cu^I** to give **2a** in 50% yield, whose turnover number (TON) and turnover frequency (TOF) were 510000 and 21200 h^{−1}, respectively.

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