Micellar Promoted Multi-Component Synthesis of 1,2,3-Triazoles in Water at Room Temperature

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Reagents and Materials.

General

1H NMR were recorded at 298 K, unless otherwise stated, on a Bruker AVANCE 300 spectrometer operating at 300.15 MHz. δ values in ppm are relative to SiMe₄. GC analysis were performed on HP SERIES II 5890 equipped with a HPS column (30 m, i. D. 0.25 m, film 0.25 μm) using He as gas carrier and FID. GC-MS analyses were performed on a GC Trace GC 2000 equipped with a HP5-MS column (30 m, i.D. 0.25 mm, film 0.25 μm) using He gas carrier and coupled with a quadrupole MS Thermo Finnigan Trace MS with Full Scan method.

Solvents and reactants were used as received; otherwise they were purified as reported in the literature. TLC analysis were performed on TLC Polygram ® Sil G/UV254 of 0.25 mm thickness and flash-chromatography separations were performed on silica gel Merk 60, 230-400 mesh.

Substrates and surfactants

All the organic bromides, aliphatic and aromatic terminal alkynes, surfactants and Cu(I) catalyst [Cu(IMes)Cl] 1 (IMes 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) are all commercially available products (Aldrich) and were used as received without any further purification. All the triazoles products were identified by GC-MS and 1H-NMR analysis.

Catalytic Studies

Catalytic multicomponent reaction between alkyl bromides with sodium azide and alkyne mediated by [Cu(IMes)Cl] 1

General procedure for the multicomponent triazole synthesis in water: in a vial equipped with a screw capped septum and magnetic bar the alkyl bromide (0.25 mmol), the alkyne (0.37 mmol) and sodium azide (0.37 mmol) were dissolved in water (1 mL) with the aid of the proper amount of surfactant (180 mM). The reaction mixture was stirred at 750 rpm at room temperature for 1h. A methanol solution of the catalyst 1 (0.0025 mmol) was added to this solution and the vial was stirred at room temperature for 15, 30 minutes, 1h or 2h as a function of the substrates considered. Subsequently, 2 mL of AcOEt or Et₂O were added to the vial, the mixture was stirred for 10' and the organic phase was separated and concentrated under vacuum. 1H NMR and GC-MS analysis were employed to determine product yield.

Scheme S1. Structure of the correct triazole product 4 and of the dimeric atropoisomeric by-product 3,3'-dibenzyl-5,5'-di-n-hexyl-3H,3'H-4,4'-bis-1,2,3-triazole observed in the multi-component reaction when carried out with catalyst 1 present since the beginning of the reaction.
1-benzyl-4-hexyl-1,2,3-triazole

$^1$H NMR 300 MHz δ (ppm), 7.35 (m, 3H), 7.25 (m, 2H), 7.17 (s, 1H), 5.49 (s, 2H), 2.68 (t, $J = 7.7$ Hz, 2H), 1.63 (q, $J = 7.4$ Hz, 2H), 1.29 (m, 4H), 0.85 (t, $J = 6.7$ Hz, 3H).

1-benzyl-4-octil-1,2,3-triazole

$^1$H NMR 300 MHz δ (ppm), 7.41-7.32 (m, 3H), 7.27-7.24 (m, 2H), 7.17 (s, 1H), 5.49 (s, 2H), 2.68 (t, $J = 7.7$ Hz, 2H), 1.62 (dd, $J = 14.3$, 7.0 Hz, 2H), 1.27 (m, 10 H), 0.87 (t, $J = 6.8$ Hz, 3H).
1-benzyl-4-tridecyl-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm), 7.43 – 7.28 (m, 3H), 7.23 (m, 2H), 7.17 (s, 1H), 5.49 (s, 2H), 2.72 – 2.62 (m, 2H), 1.71 – 1.57 (m, 2H) 1.26 (m, 20 H), 0.88 (t, $J = 6.6$ Hz, 3H).

1-benzyl-4-phenyl-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm), 7.40–7.10 (m, 10 H), 7.02 (s, 1H), 5.47 (s, 2H), 2.72 – 2.62 (m, 2H), 1.71 – 1.57 (m, 2H)
1-benzyl-1H-[1,2,3]triazolo-4-ylmethyl)-malonate dimethyl ester

$^1$H NMR 300 MHz $\delta$ (ppm), 7.41 – 7.15 (m, 6H), 5.48 (s, 2H), 3.89 (t, $J = 7.5$ Hz, 1H), 3.69 (s, 6H), 3.29 (d, $J = 7.5$ Hz, 2H).

1-benzyl-4-phenyl-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm), 7.81-7.83 (d, 2H); 7.69 (s, 1H), 7.29-7.42 (m, 8H), 5.60 (s, 2H).
1-benzyl-4-p-tolyl-1,2,3-triazole

$^{1}H$ NMR 300 MHz δ (ppm), 7.69 (d, $J = 8.0$ Hz, 2H), 7.62 (s, 1H), 7.43 – 7.28 (m, 5H), 7.21 (d, $J = 8.0$ Hz, 2H), 5.57 (s, 2H), 2.33 (s, 3H).

1-benzyl-4-(4-(tert-butyl)phenyl)-1,2,3-triazole

$^{1}H$ NMR 300 MHz δ (ppm), 7.69 (d, $J = 7.8$ Hz, 2H), 7.63 (s, 1H), 7.42 – 7.20 (m, 7H), 5.51 (s, 2H), 1.32 (s, 9H).
1-(3-bromobenzyl)-4-hexyl-1,2,3-triazole

$^1$H NMR 300 MHz δ (ppm), 7.50 - 7.15 (m, 5H), 5.46 (s, 2H), 2.69 (t, $J = 7.7$ Hz, 2H), 1.76 – 1.55 (m, 2H), 1.43 – 1.17 (m, 6H), 0.87 (t, $J = 6.6$ Hz, 3H).

1-(4-bromobenzyl)-4-hexyl-1,2,3-triazole

$^1$H NMR 300 MHz δ (ppm), 7.50 - 7.15 (m, 5H), 5.44 (s, 2H), 2.68 (t, $J = 7.7$ Hz, 2H), 1.62 (bs, 2H), 1.29 (M 6H), 0.85 (T, $J = 6.8$ Hz, 3H)
1-benzyl-4-(m-tolyl)-1H-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm) 7.69 – 7.53 (m, 3H), 7.65 (s, 1H), 7.27 – 7.08 (m, 6H), 5.57 (s, 2H), 2.38 (s, 3H).

1-benzyl-4-(4-methoxyphenyl)-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm) 7.72 (d, $J = 8.5$ Hz, 2H), 7.57 (s, 1H), 7.46 – 7.27 (m, 5H), 6.93 (d, $J = 8.5$ Hz, 2H), 5.56 (s, 2H), 3.83 (s, 3H).
1-allyl-4-hexyl-1,2,3-triazole

\[ \text{H NMR 300 MHz } \delta \text{ (ppm), 7.26 (s, 1H), 6.00 (ddt, } J = 16.3, 10.3, 6.1 \text{ Hz, 1H), 5.30 (m, 2H), 4.93 (dd, } J = 6.1, 1.1 \text{ Hz, 1H), 2.70 (t, } J = 7.7 \text{ Hz, 2H), 1.65 (dt, } J = 15.2, 7.5 \text{ Hz, 2H), 1.30 (m, 6H), 0.87 (t, } J = 6.5 \text{ Hz, 3H).} \]
1-allyl-4-tridecyl-1,2,3-triazole

\(^\text{1}H\) NMR 300 MHz (ppm), 7.26 (s, 1H), 6.00 (ddt, \(J = 16.7, 10.8, 6.0\) Hz, 1H), 5.36 – 5.20 (m, 2H), 4.92 (dd, \(J = 6.1, 1.0\) Hz, 2H), 2.69 (t, \(J = 7.7\) Hz, 2H), 1.63 (m, 2H), 1.24 (s, 20H), 0.86 (t, \(J = 6.5\) Hz, 3H)

1-allyl-4-phenethyl-1,2,3-triazole

\(^\text{1}H\) NMR 300 MHz (ppm), 7.32 – 7.15 (m, 5H), 7.13 (s, 1H), 5.97 (ddt, \(J = 16.3, 10.2, 6.0\) Hz, 1H), 5.26 (ddd, \(J = 17.9, 13.6, 1.1\) Hz, 2H), 4.91 (dt, \(J = 6.0, 1.1\) Hz, 2H), 3.09 – 2.94 (m, 4H).
Dimethyl-2-((1-allyl-1H-1,2,3-triazole-4-yl)methyl)malonate

\[ \text{H NMR 300 MHz } \delta \text{ (ppm), } 7.37 \text{ (s, 1H), 5.98 (ddt, } J = 16.3, 10.3, 6.1 \text{ Hz, 1H), 5.41 – 5.19 (m, 2H), 4.91 (d, } J = 6.1 \text{ Hz, 2H), 3.89 (t, } J = 7.4 \text{ Hz, 1H), 3.72 (s, 6H), 3.30 (d, } J = 7.4 \text{ Hz, 2H).} \]

1-Allyl-4-phenyl-1,2,3-triazole

\[ \text{H NMR 300 MHz } \delta \text{ (ppm), } 7.76 \text{ (s, 1H), 7.52 – 7.46 (m, 2H), 7.36 – 7.29 (m, 3H), 6.06 (ddd, } J = 16.4, 10.4, 5.8 \text{ Hz, 1H), 5.41 – 5.30 (m, 2H), 5.03 (d, } J = 6.1 \text{ Hz, 2H).} \]
4-(p-tolyl)-1-allyl-1,2,3-triazole

\[ \text{H NMR 300 MHz } \delta (\text{ppm}), 7.72 (d, J = 8.2 \text{ Hz}, 2H), 7.71 (s, 1H), 7.23 (d, J = 8.2 \text{ Hz}, 2H), 6.06 (ddt, J = 16.6, 10.4, 6.1 \text{ Hz}, 1H), 5.41 – 5.29 (m, 2H), 5.01 (d, J = 6.1 \text{ Hz}, 2H), 2.37 (d, J = 4.2 \text{ Hz}, 2H). \]

4-(t-butyl-phenyl)-1-allyl-1,2,3-triazole

\[ \text{H NMR 300 MHz } \delta (\text{ppm}), 7.76 (d, J = 8.3 \text{ Hz}, 2H), 7.73 (s, 1H), 7.30 - 7.40 (m, 2H), 6.06 (ddt, J = 16.4, 10.3, 6.1 \text{ Hz}, 1H), 5.33 (m, 2H), 5.01 (d, J = 6.1 \text{ Hz}, 1H), 1.35 (s, 9H). \]
1-allyl-4-(4-methoxyphenyl)-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm) 7.74 (d, $J = 8.9$ Hz, 2H), 7.67 (s, 1H), 6.95 (d, $J = 8.9$ Hz, 2H), 6.14 – 5.95 (m, 1H), 5.42 – 5.28 (m, 2H), 5.00 (dt, $J = 6.1$, 1.4 Hz, 1H), 3.83 (s, 3H).

1-allyl-4-(m-tolyl)-1,2,3-triazole

$^1$H NMR 300 MHz $\delta$ (ppm) 7.72 – 7.53 (m, 2H), 7.34 – 7.09 (m, 2H), 6.14 – 5.94 (m, 1H), 5.42 – 5.25 (m, 2H), 5.05 – 4.93 (m, 2H), 2.39 (s, 3H).