JOC The Journal of Organic Chemistry

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Copper-Catalyzed Azide–Alkyne Cycloaddition Reaction in Water Using Cyclodextrin as a Phase Transfer Catalyst

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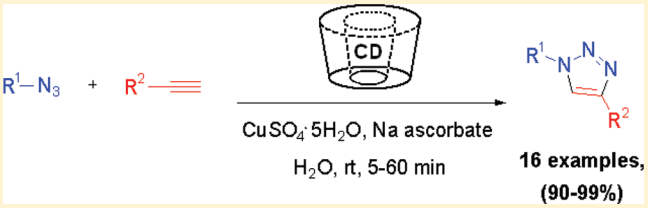
Supporting Information

ABSTRACT: 1,4-Disubstituted-1,2,3-triazoles were obtained in excellent yields from azides and terminal alkynes in H_2O in the presence of catalytic amount of β-cyclodextrin as a phase transfer catalyst. Also, a one-pot CuAAC reaction was carried out successfully, affording 1,4-disubstituted-1,2,3-triazoles in good to high yields starting from an alkyl bromide, sodium azide, and terminal alkyne.



Copper-catalyzed azide–alkyne 1,3-dipolar cycloaddition (CuAAC) reactions to form 1,4-disubstituted-1,2,3-triazoles are relatively well established and applications of these reactions are found in various fields of chemistry.[1]

In CuAAC reactions, a mixture of water and water-miscible organic solvents such as DMSO, THF, and ^{t}BuOH has been traditionally used as solvent system.[2] In general, water is the ideal solvent, which is eco-friendly, nontoxic, cheap and abundant. From this point of view, CuAAC reactions in water using these simple and classical systems without organic solvent are meaningful and valuable. However, examples of the reactions using water only as solvent have been developed rarely.[3]

Cyclodextrins are cyclic oligosaccharides of D(+)-glucopyranosyl units linked by α-1,4-glycosidic bonds and consist of a hydrophilic outer surface and a hydrophobic central cavity.[4]

Cyclodextrins can include water-insoluble organic materials into the cavity in aqueous solution because of these features. Thus, complexation with cyclodextrin is well-known as an effective method for enhancing dissolution properties of poorly soluble organic materials.[4a,5] By using these properties, cyclodextrins and cyclodextrin derivatives have been used as a phase transfer catalyst in organic synthesis.[6] To the best of our knowledge, however, CuAAC reactions catalyzed by cyclodextrin are not reported.

Here, we report CuAAC reaction in water using β-cyclodextrin(CD) as an efficient phase transfer catalyst.

First of all, to ensure cyclodextrin effects on this CuAAC reaction, we carried out this reaction to obtain triazole product **3aa** from benzyl azide **1a** with phenyl acetylene **2a** in water as shown in Table 1.

At first, azide **1a** was reacted with alkyne **2a** in the absence of cyclodextrin in water at room temperature. After 1 h, the desired adduct **3aa** was just obtained in 40.5% yield, and the reaction was almost completed after 5.5 h (entries 1, 2). However, when it was run in the presence of β-cyclodextrin (10 mol %), **3aa** was obtained in 100% conversion yield just 10 min later. (entry 3). This result shows that β-cyclodextrin obviously plays a critical role as an effective phase transfer catalyst for CuAAC reaction in water.[7] Moreover, both α-cyclodextrin and γ-cyclodextrin also gave desired product **3aa** in only 10 min (entries 4, 5). Through these experiments, we found that all α-, β-, and γ-cyclodextrin worked well equally in this system. Among them, we chose β-cyclodextrin, which is the cheapest[8] and used in various application fields.[4] However, when we used 10 mol % of β-cyclodextrin, the conversion to triazole was very quick, but the isolated yield was lower than the expected yields (78%). We tried to find the reason of the loss of product yields. Finally, we found that **3aa** inserted into β-cyclodextrin in the aqueous media and formed a water-soluble inclusion complex. In order to get **3aa** in high yield, we reduced the amount of β-cyclodextrin from 10 to 2.5 mol % (entry 6). The conversion to **3aa** was finished in 15 min, and the isolated yield was 96%. When we used 1 mol % of β-cyclodextrin, this reaction was accomplished in 30 min, and the isolated yield was 97% (entry 7). From these experiments, amount of β-cyclodextrin could be reduced to 1 mol % without loss of yields. Though both 2.5 and 1 mol % work well, we decided to use 2.5 mol % of β-cyclodextrin in view of optimal reaction time and yields.

To understand the role of phase transfer catalyst of β-cyclodextrin, we used an NMR technique. NMR is the most powerful tool for the inclusion of guest molecules into the hydrophobic cyclodextrin cavity in solution.[9] Particularly, chemical shift variations of host or guest molecules could provide evidence for the formation of inclusion or not. The formation of the inclusion complex results in upfield shift changes in the H-3 and H-5 protons, which are directed toward the interior of the cyclodextrin, whereas the H-1, H-2, and H-4 protons, which are directed on the exterior of the cyclodextrin, are relatively unaffected.[10]

The proton chemical shifts for β-cyclodextrin in the absence and the presence of benzyl azide or phenyl acetylene are shown in Figure 1. In the presence of benzyl azide or phenyl acetylene, all protons of β-cyclodextrin are shielded. It was evidence that there existed an interaction between guest molecules and β-

Received: January 11, 2012
Published: March 26, 2012

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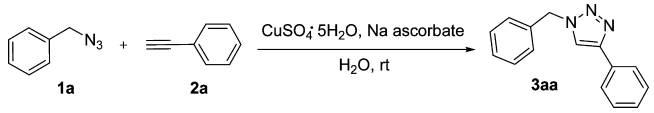
dx.doi.org/10.1021/jo3000095 | J. Org. Chem. 2012, 77, 4117–4122

Table 1. Cyclodextrin Effects on Cu-Catalyzed [2 + 3] Cycloaddition of Azide 1a with Alkyne 2a



entry	additive (mol %)	reaction time	conversion (%)[a]
1		1 h	40.5
2		5.5 h	99.5
3[b]	β-CD (10)	10 min	100
4	α-CD (10)	10 min	100
5	γ-CD (10)	10 min	100
6[c]	β-CD (2.5)	10 min	93.3
7[d]	β-CD (1)	10 min	82.2

[a]Conversion yield was monitored by ^{1}H NMR. [b]Isolated yield was 78%. [c]The conversion to triazole **3aa** was completed after 15 min. After workup, isolated yield was 96%. [d]The conversion to **3aa** was finished after 30 min. After workup, isolated yield was 97%.

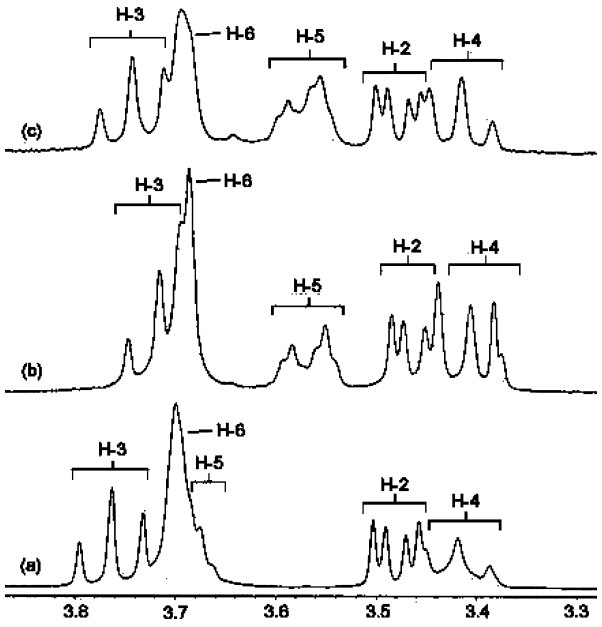


Figure 1. Part of ^{1}H NMR spectra (300 MHz, D_2O) showing β-CD protons: (a) β-CD only, (b) β-CD/phenyl acetylene mixture, and (c) β-CD/benzyl azide mixture.

cyclodextrin, with a partial or complete inclusion. As can be seen in Figure 1 and Table 2, the downfield variation of β-cyclodextrin in the presence of benzyl azide or phenyl acetylene was apparently largest in H-5 proton, which is located inside the cavity at the narrow side. From these observations, we could find that guest molecules such as benzyl azide or phenyl acetylene are included deep in the cavity of β-cyclodextrin.

Table 2. ^{1}H NMR Chemical Shifts for β-Cyclodextrin (CD) in the Absence and the Presence of Benzyl Azide (1a) or Phenyl Acetylene (2a)

β-CD proton	δ (free)	δ (β-CD/ **1a**)	Δδ[a]	δ (β-CD/ **2a**)	Δδ[a]
H-1	4.934	4.897	−0.037	4.881	−0.053
H-2	3.481	3.484	−0.003	3.465	−0.016
H-3	3.764	3.749	−0.015	3.718	−0.046
H-4	3.418	3.421	−0.003	3.397	−0.021
H-5	3.676	3.577	−0.099	3.569	−0.107
H-6	3.701	3.700	−0.001	3.688	−0.013

[a]$\Delta\delta = \delta_{(complex)} - \delta_{(free)}$

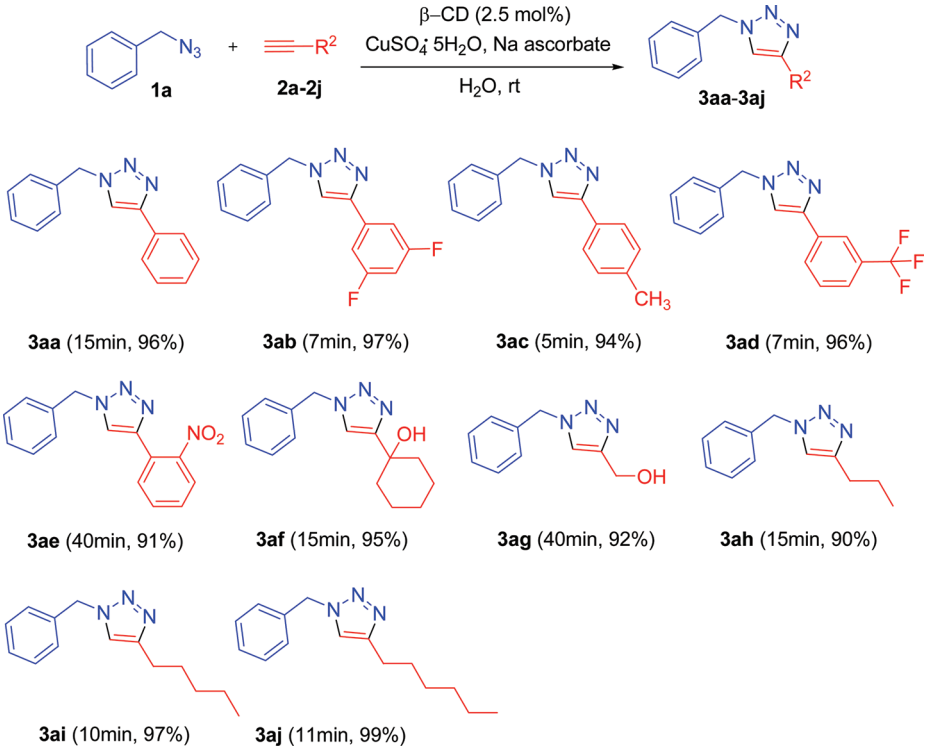
Using optimal conditions, these reactions were carried out in the presence of copper sulfate pentahydrate, sodium ascorbate, and β-cyclodextrin in H_2O at room temperature to generate the desired compounds **3aa**−**3aj** as listed in Scheme 1. As expected, aromatic acetylenes (**2a**−**2d**) reacted readily to form the desired triazole products in excellent yields (94−97%) within 15 min, while 2-nitrophenyl acetylene **2e** reacted somewhat slower because of its low solubility in water. However, the product was still obtained in 91% yields. In addition to aromatic acetylenes, cycloaliphatic acetylene **2f** also worked well. But, in the case of propargyl alcohol **2g**, the reaction proceeded slower. It may be due to its high polarity, which interferes with inclusion of **2g** into β-cyclodextrin. In the case of aliphatic alkynes, which are known for their low reactivity,[11] the reactions gave **3ah**, **3ai**, and **3aj** in quantitative yields after 10−15 min only.

To demonstrate the scope and the generality of CuAAC reaction, we applied several azides **1b**−**1e** to this reaction system. The results are summarized in Scheme 2. Reactions of phenethyl azide **1b** with alkynes such as aromatic alkyne **2a**, cyclohexyl alkyne **2f**, or aliphatic alkyne **2j** afforded excellent yields of 1,4-disubstituted-1,2,3-tetrazoles (**4ba**, **4bf**, and **4bj**), respectively. 3-Phenylpropyl azide **1c** also reacted readily to give the desired triazole product **4ca** in 93% yields within 20 min. Bulky azide **1d**, which has poor solubility in water, reacted with **2a** to provide the corresponding product **4da** in 60 min completely. Interestingly, reaction of **1d** with aliphatic alkyne **2j** afforded the desired triazole product **4dj** within 30 min under the same reaction conditions. Unfortunately, no CuAAC reaction of octyl azide **1e** with **2a** using β-cyclodextrin in water proceed at all.

Next, a one-pot process[3a,c,12] involving the formation of the organic azide in situ from the corresponding bromide with sodium azide was carried out as shown in Scheme 3. Under the above-mentioned reaction conditions, benzyl bromide **1f** was converted into the triazole **3aa** in 98% yield within 25 min. In the case of **1g**, the reaction proceeded slowly because of low solubility in H_2O. Thus, when increasing the reaction temperature to 60 °C, the corresponding product **5ga** could be acquired completely after 180 min.[13] In the case of allyl bromide **1h**, the desired product **5ha** was obtained along with byproduct **5h′a**. As results, 1,4-disubstituted-1,2,3-triazoles could be obtained directly from several bromides. Moreover, it is remarkable that in this process, bromides play roles of

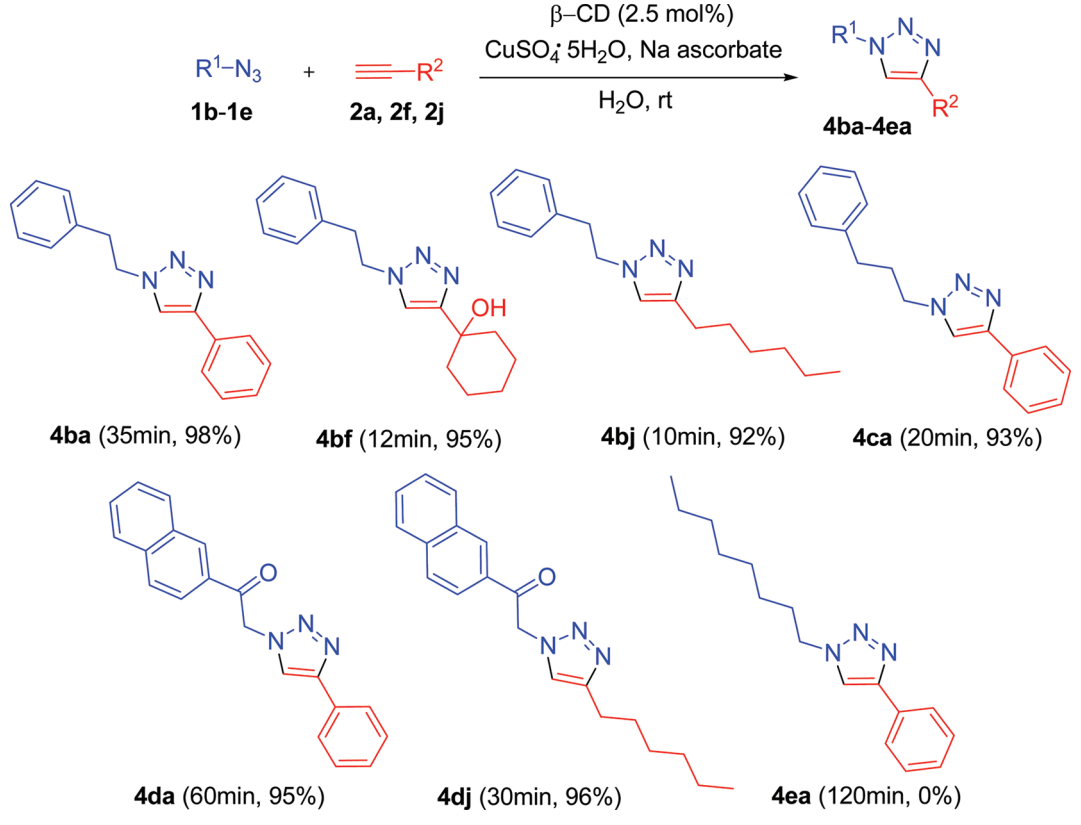
dx.doi.org/10.1021/jo3000095 | J. Org. Chem. 2012, 77, 4117−4122

Scheme 1. Results of the CuAAC Reaction of 1a with Various Alkynes 2a–2j Using β-Cyclodextrin (CD) in Water[a]



[a]All reactions were carried out using azide **1a** (0.75 mmol), alkynes **2a–2j** (1.05 equiv), $CuSO_4 \cdot 5H_2O$ (5 mol %), Na ascorbate (15 mol %), and β-cyclodextrin (2.5 mol %) in H_2O (1 mL) at room temp. Reported yields are for the isolated products.

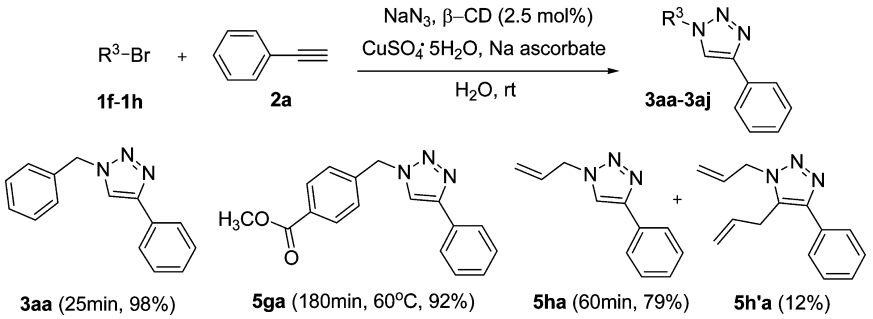
Scheme 2. Results of the CuAAC Reaction of Alkynes (2a, 2f, or 2j) with Various Azides 1b–1e Using β-Cyclodextrin in Water[a]



[a]All reactions were carried out using azide **1b–1e** (0.75 mmol), alkynes **2a**, **2f**, **2j** (1.05 equiv), $CuSO_4 \cdot 5H_2O$ (5 mol %), Na ascorbate (15 mol %), and β-cyclodextrin (2.5 mol %) in H_2O (1 mL) at room temp. Reported yields are for the isolated products.

dx.doi.org/10.1021/jo3000095 | J. Org. Chem. 2012, 77, 4117–4122

Scheme 3. One-Pot Synthesis of Triazoles from Bromides 1f−1h[a]



[a]All reactions were carried out using bromides **1f−1h** (0.75 mmol), alkynes **2a** (1.05 equiv), NaN_3 (1.1 equiv), $CuSO_4{\cdot}5H_2O$ (5 mol %), Na ascorbate (15 mol %), and β-cyclodextrin (2.5 mol %) in H_2O (1 mL) at room temperature, except for **1g** (60 °C). Reported yields are for the isolated products.

synthetic equivalents of hazarous organic azides, which are well-known to be difficult to manipulate and store.

In summary, we found that by using 2.5 mol % of β-cyclodextrin as a phase transfer catalyst, the CuAAC reactions of azides with various alkynes were performed well in water and provided the desired 1,4-disubstituted-1,2,3-triazoles in excellent yields within a few minutes. Moreover, one-pot cycloaddition process from bromide substrates, by treatment with sodium azide, was demonstrated. These reactions, which were carried out in the presence of β-cyclodextrin in water, are very useful both from an economic and an environmental point of view and also for the practical convenience of not handling flammable anhydrous organic solvents, toxic and expensive reagents.

EXPERIMENTAL SECTION

Typical Procedure for CuAAC at Room Temperature. In a vial fitted with a screw cap, benzyl azide **1a** (100 mg, 0.75 mmol) and phenyl acetylene **2a** (83 mg, 1.05 equiv) were added to a mixture of copper(II) sulfate pentahydrate (9.4 mg, 0.05 equiv), sodium ascorbate (23 mg, 0.15 equiv), and β-cyclodextrin (22 mg, 0.025 equiv) dissolved in H_2O (1 mL) at room temperature. The reaction mixture was stirred for 15 min at room temperature. The resulting mixture was poured into CH_2Cl_2 (3 mL) and H_2O (3 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 mL) three times. The combined organic layer was concentrated in vacuo. The residue was purified by short column chromatography on silica gel (70−230 mesh) eluted with hexane/EtOAc (3/1) to give 169 mg of **3aa** (96%).

Typical Procedure for CuAAC Using Benzyl Bromide Derivatives. In a vial fitted with a screw cap, benzyl bromide **1d** (129 mg, 0.75 mmol) and phenyl acetylene **2a** (83 mg, 1.05 equiv) were added to a mixture of sodium azide (54 mg, 1.1 equiv), copper(II) sulfate pentahydrate (9.4 mg, 0.05 equiv), sodium ascorbate (23 mg, 0.15 equiv), and β-cyclodextrin (22 mg, 0.025 equiv) dissolved in H_2O (1 mL) at room temperature. The reaction mixture was stirred for 25 min at room temperature. The resulting mixture was poured into CH_2Cl_2 (3 mL) and H_2O (3 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 mL) three times. The combined organic layer was concentrated in vacuo. The residue was purified by short column chromatography on silica gel (70−230 mesh) eluted with hexane/EtOAc (3/1) to give 173 mg of **3aa** (98%).

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole[3a] (3aa). Ivory needles (96%): mp = 131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 9 Hz, 2H), 7.63 (s, 1H), 7.40−7.23 (m, 7H), 5.56 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 134.5, 130.4, 129.0, 128.7, 128.0, 127.9, 125.6, 119.4, 54.2.

1-Benzyl-4-(3,5-difluorophenyl)-1*H*-1,2,3-triazole (3ab). Tan needles (97%): mp = 130−133 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30−8.22 (m, 1H), 7.79 (d, *J* = 3.6 Hz, 1H), 7.39−7.27 (m, 2H), 7.30−7.23 (m, 3H), 7.00−6.94 (dt, *J* = 7.8 Hz, 2.4 Hz, 1H), 6.88−6.81 (m, 1H) 5.58 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9 (d, *J* = 11.7 Hz), 160.6 (d, *J* = 11.7 Hz), 157.3 (d, *J* = 11.4 Hz), 140.8, 134.5, 129.0, 128.7, 128.6, 127.9, 122.0 (d, *J* = 12.2 Hz), 114.9 (d, *J* = 11.6 Hz), 111.7 (d, *J* = 3.37 Hz), 103.9 (t, *J* = 25.3 Hz), 54.2; IR (KBr, cm^{-1}) 3165, 3061, 1623, 1601, 1558, 1493, 1462, 1454, 1433, 1413, 1366, 1279, 1265, 1246, 1120, 1186, 1141, 1104, 1070, 1049, 982, 964, 951, 856, 813, 779, 725, 694; HRMS calcd for $C_{15}H_{11}F_2N_3$ 271.0921, found 271.0923.

1-Benzyl-4-*p*-tolyl-1*H*-1,2,3-triazole[14] (3ac). Ivory needles (94%): mp = 154−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.66 (d, *J* = 7.8 Hz, 2H), 7.61 (s, 1H), 7.36−7.34 (m, 3H), 7.30−7.27 (m, 2H), 7.20−7.18 (d, *J* = 7.5 Hz, 2H), 5.55 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 137.8, 134.9, 129.3, 129.0, 128.6, 127.9, 127.6, 125.4, 119.1, 54.2, 21.3.

1-Benzyl-4-(3-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (3ad). Ivory amorphous solid (96%): mp = 70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01−7.96 (m, 2H), 7.72 (s, 1H), 7.55−7.46 (m, 2H), 7.39−7.32 (m, 2H), 7.30−7.27 (m, 2H), 5.57 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 134.3, 131.8, 131.3−131.2 (m), 130.8, 130.3, 129.1 (d, *J* = 7.12 Hz), 128.7 (d, *J* = 6.82 Hz), 128.0, 125.7, 124.6 (q, *J* = 3.75 Hz), 122.3 (q, *J* = 3.97 Hz), 119.9, 54.4; IR (KBr, cm^{-1}) 3137, 3117, 3090, 3035, 2990, 1622, 1607, 1498, 1456, 1432, 1355, 1315, 1234, 1226, 1191, 1165, 1122, 1097, 1068, 1051, 1030, 998, 989, 898, 892, 816, 797, 770, 725, 699, 691; HRMS calcd for $C_{16}H_{12}F_3N_3$ 303.0983, found 303.0991.

1-Benzyl-4-(2-nitrophenyl)-1*H*-1,2,3-triazole[15] (3ae). Pale-brown needles (91%): mp = 109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.70 (s, 1H), 7.62 (t, *J* = 6.3 Hz, 1H), 7.46 (t, *J* = 6.6 Hz, 1H), 7.38−7.33 (m, 2H), 7.29−7.26 (m, 2H), 5.57 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 142.3, 135.4, 134.2, 132.4, 130.9, 129.1, 128.8, 128.7, 127.9, 124.5, 123.9, 122.8, 54.3.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)cyclohexanol[3c] (3af). Yellowish green needles (95%): mp = 123−125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.22 (m, 6H), 5.46 (s, 2H), 2.79 (brs, -OH), 1.93−1.18 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 134.5, 128.9, 128.5, 127.9, 119.5, 69.4, 54.1, 38.0, 25.1, 21.9.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methanol[16] (3ag). Yellowish green needles (92%): mp = 77 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (brs, 1H), 7.27−7.12 (m, 5H), 5.37 (s, 2H), 4.63 (brs, 2H), 4.18 (brs, −OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 134.3, 128.9, 128.5, 127.9, 122.6, 55.9, 54.2.

1-Benzyl-4-propyl-1*H*-1,2,3-triazole[17] (3ah). Pale yellow needles (90%): mp = 29 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.32 (m, 3H), 7.24−7.21 (m, 2H), 7.17 (s, 1H), 5.48 (s, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.69−1.62 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 134.8, 128.9, 128.5, 127.8, 120.5, 54.0, 27.8, 22.7, 13.9.

dx.doi.org/10.1021/jo3000095 | J. Org. Chem. 2012, 77, 4117−4122

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole[17] (3ai). Yellowish green needles (97%): mp = 42 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.31 (m, 3H), 7.25−7.21 (m, 2H), 7.17 (s, 1H), 5.47 (s, 2H), 2.67 (t, J = 7.5 Hz, 2H), 1.63−1.57 (m, 2H), 1.33−1.28 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 134.7, 128.6, 128.2, 127.5, 120.4, 53.7, 31.2, 28.9, 25.5, 22.2, 13.9.

1-Benzyl-4-hexyl-1*H*-1,2,3-triazole[17] (3aj). Yellowish green needles (99%): mp = 55−56 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.24 (m, 3H), 7.21−7.17 (m, 3H), 5.44 (s, 2H), 2.65 (t, J = 7.8 Hz, 2H), 1.63−1.56 (m, 2H), 1.33−1.26 (m, 6H), 0.84 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 134.8, 128.5, 128.3, 127.7, 120.4, 53.8, 31.5, 29.3, 28.8, 25.7, 22.5, 14.0.

1-Phenethyl-4-phenyl-1*H*-1,2,3-triazole[18] (4ba). White amorphous solid (98%): mp = 140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 7.2 Hz, 2H), 7.44 (s, 1H), 7.40−7.35 (m, 2H), 7.31−7.23 (m, 4H), 7.11 (d, J = 6.2 Hz, 2H), 4.61 (t, J = 7.5 Hz, 2H), 3.23 (t, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.3, 136. 9, 130.5, 128.7, 128.7, 128.6, 127.9, 127.0, 125.5, 119.8, 51.7, 36.8.

1-(1-Phenethyl-1*H*-1,2,3-triazol-4-yl)cyclohexanol (4bf). Ivory needles (95%): mp = 109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−7.04 (m, 6H), 4.55 (t, J = 7.2 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 2.46 (brs, OH), 1.93−1.70 (m, 6H), 1.59−1.32 (m, 4H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 136.9, 128.6, 128.6, 126.9, 120.0, 69.5, 51.7, 38.2, 36.9, 25.4, 22.1; IR (KBr, cm^{-1}) 3315, 3138, 3038, 2950, 2929, 2855, 1500, 1456, 1405, 1336, 1263, 1211, 1182, 1164, 1152, 1132, 1079, 1065, 1049, 1032, 995, 975, 907, 850, 816, 755, 735, 701, 670; HRMS calcd for $C_{16}H_{21}N_3O$ 271.1685, found 271.1643.

4-Hexyl-1-phenethyl-1*H*-1,2,3-triazole[19] (4bj). White amorphous solid (92%): mp = 40 °C; ^{1}H NMR (300 M Hz, $CDCl_3$) δ 7.21−7.12 (m, 3H), 6.984 (d, J = 6.6 Hz, 2H), 6.90 (s, 1H), 4.44 (t, J = 6.9 Hz, 2H), 3.09 (t, J = 6.9 Hz, 2H), 2.57 (t, J = 7.8 Hz, 2H), 1.53−1.49 (m, 2H), 1.20−1.19 (m, 6H), 0.81−0.77 (m, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 137.0, 128.5, 128.5, 126.8, 120.8, 51.4, 36.8, 31.5, 29.4, 28.8, 25.6, 22.6, 14.1.

4-Phenyl-1-(3-phenylpropyl)-1*H*-1,2,3-triazole[20] (4ca). Ivory needles (93%): mp = 81−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$), 7.81 (d, J = 7.8 Hz, 2H), 7.69 (s, 1H), 7.41 (t, J = 7.2 Hz, 2H), 7.31−7.26 (m, 3H), 7.22−7.16 (m, 3H), 4.39 (t, J = 6.9 Hz, 2H), 2.69 (t, J = 7.8 Hz, 2H), 2.30 (quintet, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 139.9, 130.4, 128.7, 128.4, 128.3, 128.0, 126.2, 125.5, 119.4, 49.5, 32.5, 31.7.

1-(Naphthalene-6-yl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-ethanone[21] (4da). Ivory needles (95%): mp = 183−185 °C; ^{1}H NMR (300 MHz, $CDCl_3$), 8.56 (s, 1H), 8.02−7.85 (m, 7H), 7.66−7.60 (m, 2H), 7.43 (t, J = 7.2 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 6.03 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.0, 148.1, 136.0, 132.2, 131.1, 130.4, 130.2, 129.7, 129.3, 129.2, 128.7, 128.1, 127.9, 127.3, 125.7, 123.2, 121.4, 55.5.

2-(4-Hexyl-1*H*-1,2,3-triazol-1-yl)-1-(naphthalene-6-yl)-ethanone (4dj). Pale yellow needles (96%): mp = 110 °C; ^{1}H NMR (300 MHz, $CDCl_3$), 8.51 (s, 1H), 7.99−7.87 (m, 2H), 7.82−7.78 (m, 2H), 7.68−7.53 (m, 2H), 7.47 (s, 1H), 5.93 (s, 2H), 2.77 (t, J = 7.5 Hz, 2H), 1.71 (quintet, J = 6.9 Hz, 2H), 1.35−1.29 (m, 6H), 0.88 (t, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.3, 148.7, 135.9, 132.2, 131.2, 130.1, 129.6, 129.2, 129.0, 127.8, 127.2, 123.1, 122.3, 55.4, 31.6, 29.4, 29.0, 25.8, 22.6, 14.2; IR (KBr, cm^{-1}) 3120, 3061, 2951, 2932, 2858, 1695, 1625, 1595, 1470, 1436, 1363, 1340, 1271, 1261, 1217, 1178, 1128, 1067, 1030, 861, 819, 759, 746; HRMS calcd for $C_{20}H_{23}N_3O$ 321.1841, found 321.1873.

Methyl-4-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)benzoate (5ga). White needles (92%): mp = 167−169 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.02 (d, J = 9.0 Hz, 2H), 7.78 (d, J = 6.6 Hz, 2H), 7.67 (s, 1H), 7.41−7.31 (m, 5H), 5.63 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 148.4, 139.4, 130.5, 130.3, 130.0, 128.7, 128.2, 127.8, 127.7, 125.6, 119.5, 53.8, 52.3; IR (KBr, cm^{-1}) 3109, 3083, 3058, 2953, 1714, 1614, 1485, 1465, 1442, 1418, 1357, 1317, 1281, 1224, 1195, 1114, 1078, 1049, 1021, 839, 801, 771, 746, 713, 696; HRMS calcd for $C_{17}H_{15}N_3O_2$ 293.1164, found 293.1173.

1-Allyl-4-phenyl-1*H*-1,2,3-triazole[22] (5ha). White needles (79%): mp = 56−58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.69−7.65 (d, J = 10.2 Hz, 2H), 7.63 (s, 1H), 7.26 (t, J = 6.9 Hz, 2H), 7.19−7.14 (m, 1H), 5.95−5.82 (m, 1H), 5.20 (d, J = 9.0 Hz, 2H), 5.14 (s, 1H), 4.84 (d, J = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 131.0, 130.3, 128.5, 128.4, 127.8, 126.9, 125.4, 119.8, 119.4, 52.6.

1,5-Diallyl-4-phenyl-1*H*-1,2,3-triazole[23] (5h′a). Yellow liquid (12%): ^{1}H NMR (300 MHz, $CDCl_3$) 7.61−7.56 (m, 2H), 7.37−7.32 (m, 2H), 7.29−7.26 (m, 1H), 5.98−5.81 (m, 1H), 5.23−5.03 (m, 3H), 4.92−4.86 (m, 2H), 3.52−3.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 132.4, 131.6, 131.2, 130.1, 128.6, 127.7, 127.0, 118.6, 117.7, 50.7, 27.0.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(8) The cost of 25 g of β-cyclodextrin is $56.2 from Sigma-Aldrich, whereas 1 g of α-cyclodextrin costs $24.5, and 1 g of γ-cyclodextrin costs $257.

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