JOC The Journal of Organic Chemistry
Article
pubs.acs.org/joc

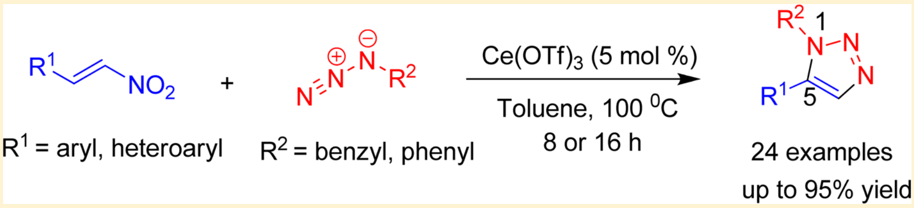
Ce(OTf)$_3$-Catalyzed [3 + 2] Cycloaddition of Azides with Nitroolefins: Regioselective Synthesis of 1,5-Disubstituted 1,2,3-Triazoles

Ying-Chun Wang,[†,‡,§] Yu-Yang Xie,[†,§] Hong-En Qu,[†] Heng-Shan Wang,*[,†] Ying-Ming Pan,*[,†] and Fu-Ping Huang[†]

[†]Key Laboratory for the Chemistry and Molecular Engineering of Medicinal Resources (Ministry of Education of China), School of Chemistry & Chemical Engineering of Guangxi Normal University, Guilin 541004, People's Republic of China

[‡]College of Chemistry and Chemical Engineering, Jishou University, Jishou 416000, People's Republic of China

Supporting Information



ABSTRACT: The first example of rare earth metal-catalyzed [3 + 2] cycloaddition of organic azides with nitroolefins and subsequent elimination reaction is described. In the presence of a catalytic amount of Ce(OTf)$_3$, both benzyl and phenyl azides react with a broad range of aryl nitroolefins containing a range of functionalities selectively producing 1,5-disubstituted 1,2,3-triazoles in good to excellent yields.

INTRODUCTION

The 1,2,3-triazole nucleus represents a significant class of biologically active nitrogen compounds that exhibit a number of important biological properties, such as antibacterial, anticancer, antivirus, and antituberculosis.[1] In recent years, more and more 1,2,3-triazole compounds are frequently employed as candidates or clinical drugs for the therapy of various types of diseases. Moreover, 1,2,3-triazoles have found industrial applications as dyes, agrochemicals, corrosion inhibitors, and photostabilizers.[2] Therefore, the building up of a 1,2,3-triazole moiety invokes ever growing synthetic efforts. The conventional route to 1,2,3-triazole is the Huisgen dipolar cycloaddition of alkynes with organic azides.[3] However, because of the high activation energy, these cycloadditions generally require elevated temperatures and long reaction times and usually afford a mixture of the 1,4- and 1,5-regioisomers. Catalyzed Huisgen cycloaddition of azides and terminal alkynes by complexes of Cu(I) (CuAAC) represents an extremely powerful method for the rapid assembly of 1,2,3-triazoles;[4] nevertheless, the CuAAC process works only with terminal alkynes and produces 1,4-disubstituted 1,2,3-triazoles exclusively. Although the ruthenium (RuAAC)-catalyzed process provides ready access to the complementary 1,5-regioisomers of 1,2,3-triazoles, all the reactions require the use of expensive ruthenium complexes as catalysts.[5] In contrast, there are as yet few satisfactory catalytic systems for the regioselective formation of 1,5-disubstituted 1,2,3-triazoles. On the other hand, although numerous of alternative successful examples have been reported in the literature for the preparation of 1,2,3-triazoles,[6] less attention has been paid to investigate [3 + 2] cycloaddition reactions of azides with nitroolefins, because, in the absence of catalysts, these cycloaddition reactions tend to be extremely sluggish and may take weeks, or even months, at room temperature or elevated temperatures to get only partial completion (Scheme 1a; refs 7a and 7b).[7] Amantini et al. reported in 2005 that TBAF could promote addition of azides to nitroethenes, delivering the corresponding 1*H*-1,2,3-triazoles in good yields under solvent-free conditions; nevertheless, the reaction is limited to particularly activated, electron-deficient nitroolefins (2-aryl-1-cyano- or 2-aryl-1-carbethoxy-1-nitroethenes) and TMSN$_3$ (Scheme 1a; ref 8).[8] For these reasons, the general, efficient, and highly regioselective protocol for the synthesis of 1,2,3-triazoles from simple olefins has emerged as an attractive and challenging goal.

Recently, the use of rare earth metal-catalyzed reactions has emerged as a versatile tool for developing syntheses due to their numerous advantages, namely, their relatively high efficiency, water compatibility, mild reaction conditions, and eco-friendly catalytic reactions.[9] Herein, we report that 1,5-disubstituted 1,2,3-triazoles can be obtained by a Ce(OTf)$_3$-catalyzed [3 + 2] cycloaddition of azides with nitroolefins (Scheme 1b), thereby providing a new synthetic method for 1,5-disubstituted 1,2,3-triazole formation. To the best of our knowledge, this is the first time that a rare earth metal catalyst has been described for [3 + 2] cycloadditions of azides with electron-deficient olefins.

Received: February 22, 2014

dx.doi.org/10.1021/jo5004339 | *J. Org. Chem.* XXXX, XXX, XXX−XXX

Scheme 1. Comparison of Previous Study and Our Work

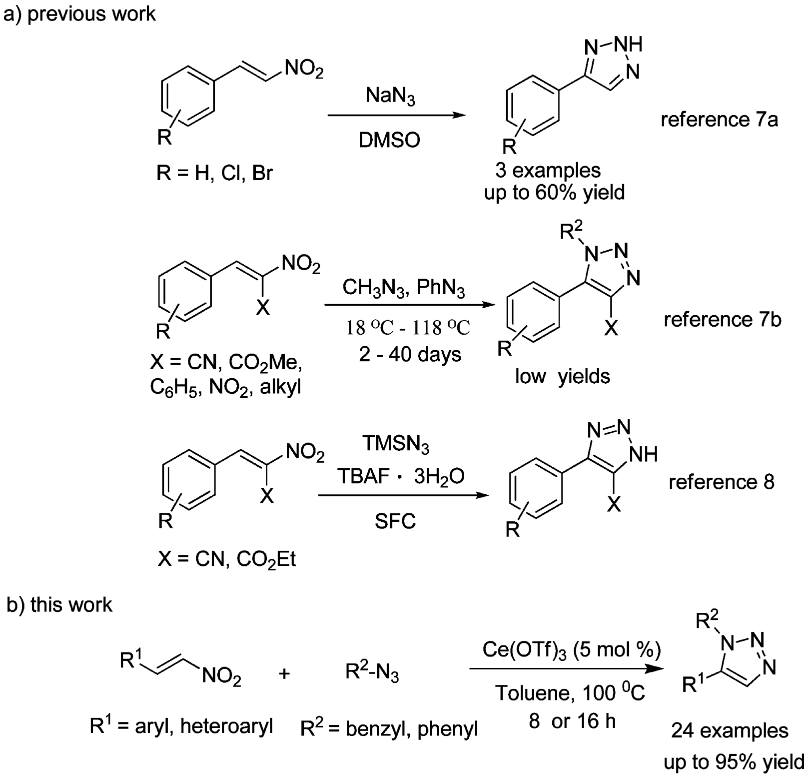
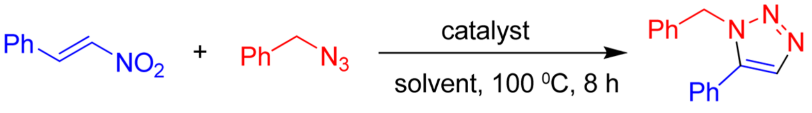


Table 1. Optimization of Reaction Conditions[a]

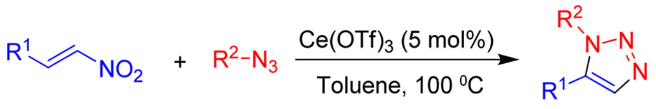


1a **2a**

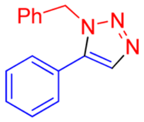
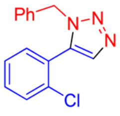
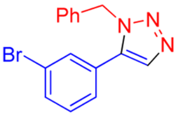
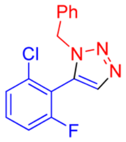
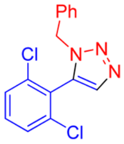
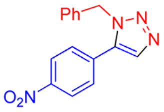
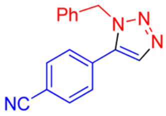
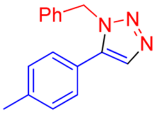
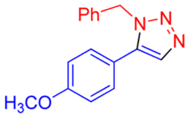
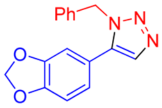
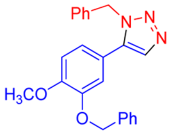
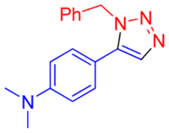
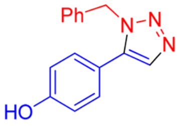
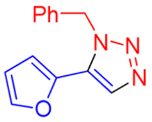
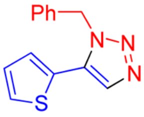
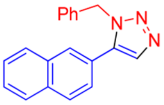
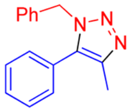
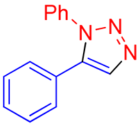
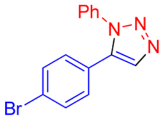
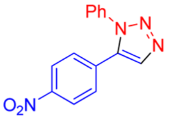
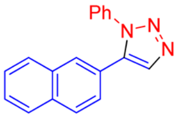
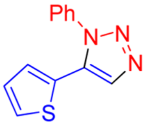
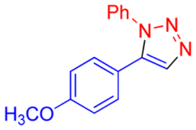
entry	catalyst	solvent	yield of **2a** (%)[b]
1[c]	none	toluene	32
2	$In(OTf)_3$ (5 mol %)	toluene	18
3	$Cu(OTf)_2$ (5 mol %)	toluene	21
4	$Bi(OTf)_3$ (5 mol %)	toluene	16
5	AgOTf (5 mol %)	toluene	0
6	$Zn(OTf)_2$ (5 mol %)	toluene	24
7	$Y(OTf)_3$ (5 mol %)	toluene	30
8	$Sc(OTf)_3$ (5 mol %)	toluene	trace
9	$[Rh(COD)Cl]_2$ (5 mol %)	toluene	trace
10	$PdCl_2(dppf)_2$ (5 mol %)	toluene	trace
11[d]	**$Ce(OTf)_3$ (5 mol %)**	**toluene**	**85**
12	$Sm(OTf)_3$ (5 mol %)	toluene	76
13	$Er(OTf)_3$ (5 mol %)	toluene	73
14	$Pr(OTf)_3$ (5 mol %)	toluene	70
15	$Yb(OTf)_3$ (5 mol %)	toluene	74
16	$Ce(OTf)_3$ (10 mol %)	toluene	86
17	$Ce(OTf)_3$ (1 mol %)	toluene	60
18[e]	$Ce(OTf)_3$ (5 mol %)	DCE	0
19	$Ce(OTf)_3$ (5 mol %)	DMF	trace
20	$Ce(OTf)_3$ (5 mol %)	DMSO	0
21	$Ce(OTf)_3$ (5 mol %)	PhCl	32

[a] Carried out with 0.5 mmol of **1a** and 0.6 mmol of benzyl azide in the presence of catalyst in solvent (2 mL) at 100 °C for 8 h (except for entry 1). [b] Isolated yield of pure product based on **1a**. [c] Carried out with 0.5 mmol of **1a** and 0.6 mmol of benzyl azide in toluene (2 mL) at 100 °C for 3 days. [d] The reaction of **1a** was also performed on a 20 mmol scale, and **2a** was isolated in 78% yield. [e] Reaction proceeded under reflux.

Table 2. Substrate Scope for the Reaction of Nitroolefins 1 and Azides[a,b]



1 **2**

 **2a** 85%	 **2b** 89%	 **2c** 90%
 **2d** 88%	 **2e** 95%	 **2f** 88%
 **2g** 90%	 **2h** 88%	 **2i** 80%
 **2j** 75%	 **2k** 76%	 **2l** 71%
 **2m** 70%	 **2n** 68%	 **2o** 84%
 **2p** 86%	 **2q** 82%	 **2r** 78%
 **2s** 68%	 **2t** 80%	 **2u** 75%
 **2v** 70%	 **2w** 67%	 **2x** 45%

[a] Reaction conditions: 0.5 mmol of **1** and 0.6 mmol of azide in the presence of $Ce(OTf)_3$ (5 mol %) in 2 mL of toluene at 100 °C for 8 or 16 h.
[b] Isolated yield of pure product based on **1**.

■ RESULTS AND DISCUSSION

We initiated our research on the model reaction of benzyl azide with nitrostyrene **1a** under different reaction conditions (Table 1). 1,5-Disubstituted 1,2,3-triazole (**2a**) was obtained in 85% isolated yield upon treatment of a 1:1.2 mixture of **1a** and benzyl azide with 5 mol % $Ce(OTf)_3$ in toluene at 100 °C for 8 h (Table 1, entry 11). Without any catalysts, nitrosytrene **1a** reacted with benzyl azide in toluene at 100 °C to give **2a** in a low yield (32%) after a long reaction time (3 days) (Table 1, entry 1). Other common Lewis acids were not effective for this conversion (Table 1, entries 2−7), and only a trace of desired product was detected with $Sc(OTf)_3$, $[Rh(COD)Cl]_2$, and $PdCl_2(dppf)_2$ as the catalysts (Table 1, entries 8−10). Among the different rare earth metal catalysts, it was found that $Ce(OTf)_3$ was the most effective (Table 1, entry 11 vs entries 12−15). Increasing the amount of catalyst to 10 mol % did not improve the yield (Table 1, entry 16), whereas, when the amount of catalyst was decreased to 1 mol %, only a 60% yield of **2a** was obtained (Table 1, entry 17). Additionally, toluene appeared to be the best choice among common solvents, such as DCE, DMF, DMSO, and PhCl (Table 1, entries 11 and 18−21).

Using our optimized experimental conditions, the scope of the $Ce(OTf)_3$-catalyzed formation of 1,5-disubstituted 1,2,3-triazoles was examined. First, various arylnitroolefins were investigated in reactions with benzyl azide (Table 2). Nitroolefins bearing electron-withdrawing substituents on the aryl ring facilitated the cycloaddition with excellent yields (**2b**−**2h**), and electron-rich aryl nitroolefins also proceeded smoothly with good yields (**2i**−**2n**). Generally, high yields were obtained with nitroolefins bearing a heterocyclic (**2o** and **2p**) and naphthyl (**2q**). Notably, several sensitive functionalities, such as nitriles (**2h**), alkoxy (**2j**, **2k**, **2l**, **2x**), hydroxyl (**2n**), and nitro (**2f**, **2g**, **2u**), were unaffected under the present reaction conditions, and the reaction also tolerated ortho substitution in the aromatic ring (**2b**, **2d**, **2e**, **2g**). The crystallization of compound **2n** from ethanol gave a single crystal suitable for X-ray analysis. Figure 1 illustrates the molecular structure of the 1,5-disubstituted 1,2,3-triazole **2n**. To our delight, 1,4,5-trisubstituted 1,2,3-triazole **2r** was obtained in 78% yield upon cycloaddition of 1-phenyl-2-nitropropene with benzyl azide. In addition, the phenyl azide substrates were further investigated, and the results indicated that both benzyl and phenyl azides reacted successfully, whereas, with phenyl azides, the yields were somewhat lower and a prolonged reaction time (16 h) was needed (**2s**−**2x**). The chemoselectivity of the reaction was also noteworthy. For all the aryl nitroolefins tested, 1,5-disubstituted 1,2,3-triazole **2** was observed as the sole product.

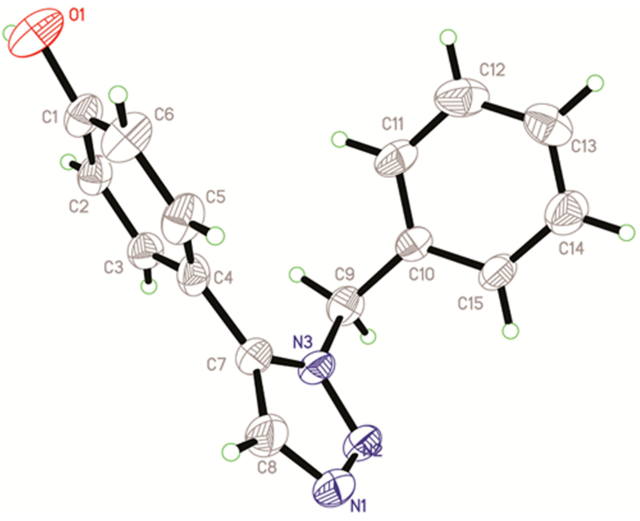


Figure 1. X-ray crystal structure of 1,5-disubstituted 1,2,3-triazole **2n**.

The scope of the reaction with respect to other electron-deficient olefins, such as chalcone, cinnamonitrile, ethyl cinnamate, and cinnamic aldehyde, was next investigated, and satisfyingly, under the present reaction conditions, the [3 + 2] cycloaddition reactions of chalcones with benzyl azide were completed in a shorter time (5 h) and 1,4,5-trisubstituted 1,2,3-triazoles **3a**−**3c** were isolated in excellent yields (85, 92, and 82%, respectively) (Scheme 2). The structure of **3b** was confirmed by X-ray diffraction analysis (Figure 2). Unfortunately, when cinnamonitrile, ethyl cinnamate, and cinnamic aldehyde were used as substrates, respectively, only trace amounts of the corresponding 1,4,5-trisubstituted 1,2,3-triazoles were obtained.

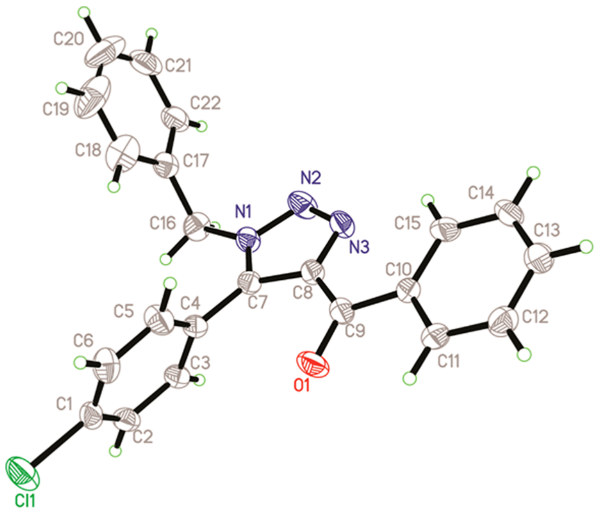
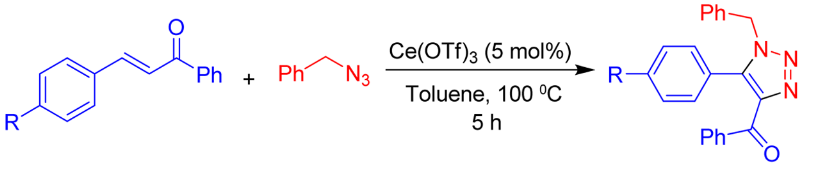


Figure 2. X-ray crystal structure of 1,4,5-trisubstituted 1,2,3-triazole **3b**.

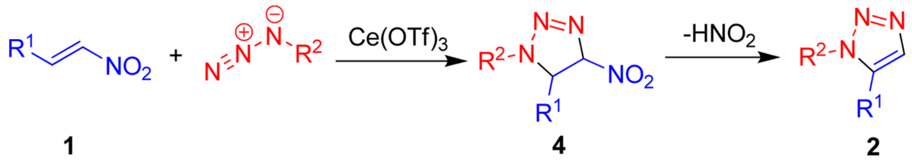
A plausible mechanism for this $Ce(OTf)_3$-catalyzed [3 + 2] cycloaddition reaction is outlined in Scheme 3. As described previously,[7b,8] the first step of the reaction is the regioselective 1,3-dipolar cycloaddition of azide with nitroolefin **1** to form the triazoline intermediate **4**. Probably rare earth metal complexes

Scheme 2. Synthesis of 1,4,5-Trisubstituted 1,2,3-Triazoles 3 from Chalcone



3a: R = H 85%
3b: R = Cl 92%
3c: R = OCH_3 82%

Scheme 3. A Plausible Reaction Mechanism



accelerated the reaction by increasing the electrophilicity of the nitroolefin through coordination. The second step is the elimination of HNO_2 of the intermediate **4** leading to 1,5-disubstituted 1,2,3-triazoles **2**.

■ CONCLUSIONS

We have disclosed the first rare earth metal-catalyzed [3 + 2] cycloaddition of organic azides with nitroolefins to yield 1,5-disubstituted 1,2,3-triazoles with good to excellent yields. Easily available starting materials, experimentally convenient catalytic process, as well as less expensive catalyst were the advantages of the present procedure. Furthermore, this catalytic process did not require dried glassware and an inert atmposphere. Further study to explore the rare earth metal-catalyzed reactions of azides with olefins to construct the biologically active molecules is ongoing in our laboratory.

■ EXPERIMENTAL SECTTION

General Experimental Procedure for Synthesis of 1,5-Disubstituted 1,2,3-Triazoles 2. A mixture of nitroolefin (1.0 equiv, 0.5 mmol), azide (1.2 equiv, 0.6 mmol), $Ce(OTf)_3$ (0.05 equiv, 0.025 mmol), and 2 mL of toluene was refluxed at 100 °C for 8 or 16 h. The progress of the reaction was monitored by thin-layer chromatography. The mixture was then cooled and evaporated under reduced pressure. The target product **2** was purified by column chromatography on silica gel using a mixture of ethyl acetate and petroleum ether.

1-Benzyl-5-phenyl-1H-1,2,3-triazole[5g] ***(2a)***. White solid (100 mg, 85%); mp 72–74 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.47–7.34 (m, 3H), 7.34–7.27 (m, 5H), 7.11–7.03 (m, 2H), 5.55 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 135.5, 133.3, 129.5, 128.9, 128.9, 128.8, 128.1, 127.1, 126.9, 51.8 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{14}N_3$, 236.1188; found, 236.1185.

1-Benzyl-5-(2-chlorophenyl)-1H-1,2,3-triazole ***(2b)***. White solid (120 mg, 89%); mp 58–60 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.49 (dd, J = 8.1, 1.0 Hz, 1H), 7.41–7.38 (m, 1H), 7.28–7.16 (m, 4H), 7.01 (dd, J = 7.6, 1.6 Hz, 1H), 6.95 (dd, J = 7.5, 1.7 Hz, 2H), 5.44 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 134.8, 134.4, 134.3, 132.0, 131.2, 129.9, 128.6, 128.2, 127.7, 126.9, 126.4, 52.5 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{13}ClN_3$, 270.0798; found 270.0781.

1-Benzyl-5-(3-bromophenyl)-1H-1,2,3-triazole ***(2c)***. Yellow solid (140 mg, 90%); mp 68–70 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.35–7.24 (m, 2H), 7.24–7.15 (m, 3H), 7.02–6.91 (m, 3H), 5.43 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 134.7, 134.3, 133.1, 132.1, 131.3, 128.6, 128.4, 128.2, 127.8, 127.4, 124.3, 52.5 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_3Br$, 314.0293, 316.0272; found 314.0275, 316.0255.

1-Benzyl-5-(2-chloro-6-fluorophenyl)-1H-1,2,3-triazole ***(2d)***. White solid (126 mg, 88%); mp 62–65 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.37–7.31 (m, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.20–7.09 (m, 3H), 6.99 (m, 1H), 6.92–6.89 (m, 2H), 5.42 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4 (d, $^1J_{CF}$ = 250.1 Hz), 135.6 (d, $^4J_{CF}$ = 3 Hz), 135.5, 134.1, 132.2 (d, $^3J_{CF}$ = 9.4 Hz), 128.6, 128.6, 128.3, 127.6, 125.6 (d, $^4J_{CF}$ = 3.6 Hz), 115.3 (d, $^2J_{CF}$ = 18.6 Hz), 114.3 (d, $^2J_{CF}$ = 21.7 Hz), 52.9 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{12}ClFN_3$, 288.0704; found 288.0694.

1-Benzyl-5-(2,6-dichlorophenyl)-1H-1,2,3-triazole ***(2e)***. Yellow solid (144 mg, 95%); mp 118–120 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.34–7.32 (m, 3H), 7.22–7.14 (m, 3H), 6.97–6.94 (m, 2H), 5.40 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 134.9, 133.9, 131.7, 128.9, 128.6, 128.3, 128.2, 128.1, 125.9, 52.9 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{12}Cl_2N_3$, 304.0408; found 304.0387.

1-Benzyl-5-(4-nitrophenyl)-1H-1,2,3-triazole[5g] ***(2f)***. Yellow solid (123 mg, 88%); mp 96–99 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.7 Hz, 2H), 7.83 (s, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.31–7.28 (m, 3H), 7.10–7.01 (m, 2H), 5.60 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 134.8, 134.1, 131.1, 129.7, 129.1, 128.6, 127.6, 126.9, 124.1, 52.4 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_4O_2$, 281.1039; found 281.1018.

1-Benzyl-5-(2-nitrophenyl)-1H-1,2,3-triazole[10] ***(2g)***. Yellow solid (126 mg, 90%); mp 149–151 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15–8.07 (m, 1H), 7.68–7.61 (m, 2H), 7.56–7.52 (m, 1H), 7.24–7.16 (m, 5H), 7.02 (dd, J = 7.6, 1.3 Hz, 1H), 5.41 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 134.2, 133.9, 133.3, 133.2, 133.1, 131.1, 128.7, 128.4, 127.8, 124.9, 122.1, 52.8 ppm; HRMS (APCI-ion trap) m/z $[M + H]^+$ calcd for $C_{15}H_{13}N_4O_2$, 281.1039; found 281.1019.

4-(1-Benzyl-1H-1,2,3-triazol-5-yl)benzonitrile ***(2h)***. Yellow solid (114 mg, 88%); mp 84–86 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.73–7.65 (m, 2H), 7.39–7.34 (m, 2H), 7.32–7.25 (m, 3H), 7.08–6.98 (m, 2H), 5.57 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 134.9, 133.909, 132.7, 131.5, 129.4, 129.1, 128.5, 126.9, 117.9, 113.4, 52.3 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{16}H_{13}N_4$, 261.1140; found 261.1132.

1-Benzyl-5-(4-methylphenyl)-1H-1,2,3-triazole[6d] ***(2i)***. Colorless oil (100 mg, 80%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.29–7.26 (m, 3H), 7.22 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 7.09–7.07(m, 2H), 5.53 (s, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 138.2, 135.7, 133.1, 129.6, 128.8, 128.8, 128.1, 127.1, 123.9, 51.7, 21.3 ppm; HRMS (APCI-ion trap) m/z $[M + H]^+$ calcd for $C_{16}H_{16}N_3$, 250.1344; found 250.1328.

1-Benzyl-5-(4-methoxyphenyl)-1H-1,2,3-triazole[6d] ***(2j)***. Pale yellow oil (99 mg, 75%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.30–7.27 (m, 3H), 7.17–7.14 (m, 2H), 7.09–7.07 (m, 2H), 6.94–6.90 (m, 2H), 5.53 (s, 2H), 3.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 137.9, 135.7, 133.1, 130.3, 128.8, 128.1, 127.1, 118.9, 114.4, 55.4, 51.7 ppm; HRMS (APCI-ion trap) m/z $[M + H]^+$ calcd for $C_{16}H_{16}N_3O$, 266.1293; found 266.1279.

5-(1,3-Benzodioxol-5-yl)-1-benzyl-1H-1,2,3-triazole ***(2k)***. Yellow oil (106 mg, 76%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.34–7.25 (m, 3H), 7.12–7.05 (m, 2H), 6.83 (d, J = 8.0 Hz, 1H), 6.75–6.66 (m, 2H), 6.01 (s, 2H), 5.53 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 148.1, 137.9, 135.5, 133.2, 128.9, 128.2, 127.1, 123.0, 120.2, 109.1, 108.8, 101.6, 51.7 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{16}H_{14}N_3O_2$, 280.1086; found 280.1071.

1-Benzyl-5-[3-(benzyloxy)-4-methoxyphenyl]-1H-1,2,3-triazole ***(2l)***. Yellow oil (131 mg, 71%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.44–7.26 (m, 8H), 7.11–7.04 (m, 2H), 6.90 (d, J = 8.3 Hz, 1H), 6.76 (dd, J = 8.2, 2.0 Hz, 1H), 6.62 (d, J = 1.9 Hz, 1H), 5.52 (s, 2H), 5.18 (s, 2H), 3.65 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 149.1, 138.1, 136.5, 135.9, 133.1, 128.9, 128.7, 128.1, 128.1, 127.3, 126.9, 121.6, 119.6, 113.8, 112.3, 70.9, 55.8, 51.7 ppm; HRMS (ESI-ion trap) m/z $[M + H]^+$ calcd for $C_{23}H_{22}N_3O_2$, 372.1712; found 372.1688.

4-(1-Benzyl-1H-1,2,3-triazol-5-yl)-N,N-dimethylamine ***(2m)***. Red solid (97 mg, 70%); mp 132–134 °C (lit.[11] 132 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.34–7.25 (m, 3H), 7.13–7.10 (m, 4H), 6.71–6.67 (m, 2H), 5.54 (s, 2H), 3.00 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 138.7, 136.0, 132.6, 129.7, 128.8, 127.9, 127.1, 113.7, 112.1, 51.5, 40.2 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{17}H_{19}N_4$, 279.1610; found 279.1592.

4-(1-Benzyl-1H-1,2,3-triazol-5-yl)phenol ***(2n)***. Yellow solid (85 mg, 68%); mp 179−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.41−7.23 (m, 4H), 7.12−7.09 (m, 3H), 6.97−6.83 (m, 2H), 5.53 (s, 2H), 5.30 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 138.3, 135.5, 132.8, 130.4, 128.8, 128.2, 127.2, 118.4, 116.1, 51.8 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{15}H_{14}N_3O$, 252.1137; found 252.1117.

1-Benzyl-5-(2-furyl)-1H-1,2,3-triazole ***(2o)***. Yellow solid (95 mg, 84%); mp 79−81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.43 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.34−7.25 (m, 3H), 7.13−7.05 (m, 3H), 7.01 (dd, *J* = 3.6, 1.2 Hz, 1H), 5.65 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 141.3, 135.1, 132.4, 129.1, 128.9, 128.2, 127.1, 111.8, 110.4, 52.8 ppm; HRMS (APCI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{13}H_{12}N_3O$, 226.0980; found 226.0967.

1-Benzyl-5-(2-thienyl)-1H-1,2,3-triazole ***(2p)***. Yellow solid (104 mg, 86%); mp 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.44 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.34−7.26 (m, 3H), 7.13−7.05 (m, 3H), 7.02 (dd, *J* = 3.6, 1.2 Hz, 1H), 5.66 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 133.9, 131.8, 128.9, 128.5, 128.2, 128.1, 127.9, 126.9, 126.6, 51.9 ppm; HRMS (APCI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{13}H_{12}N_3S$, 242.0752; found 242.0739.

1-Benzyl-5-(2-naphthyl)-1H-1,2,3-triazole[11] ***(2q)***. Yellow oil (117 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.49 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.42−7.38 (m, 1H), 7.28−7.16 (m, 4H), 7.01 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.95−6.93 (m, 2H), 5.44 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 135.6, 133.5, 133.3, 132.9, 128.9, 128.8, 128.6, 128.2, 128.2, 127.8, 127.3, 127.2, 127.0, 125.9, 124.1, 52.0 ppm; HRMS (APCI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{19}H_{16}N_3$, 286.1344; found 286.1331.

4-Benzyl-4-methyl-5-phenyl-1H-1,2,3-triazole ***(2r)***. Colorless oil (97 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.39 (m, 3H), 7.25−7.23 (m, 3H), 7.18−7.09 (m, 2H), 7.07−6.96 (m, 2H), 5.43 (s, 2H), 2.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 135.6, 134.6, 129.5, 129.2, 128.9, 128.7, 128.0, 127.4, 127.3, 52.0, 10.67 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{16}H_{16}N_3$, 250.1344; found 250.1325.

1,5-Diphenyl-1H-1,2,3-triazole ***(2s)***. White solid (74 mg, 68%); mp 112−113 °C (lit.[6c] 113−114 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.47−7.41 (m, 3H), 7.40−7.32 (m, 5H), 7.24−7.21 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 136.6, 133.4, 129.4, 129.2, 128.9, 128.6, 126.8, 125.2 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}N_3$, 222.1031; found 222.1018.

5-(4-Bromophenyl)-1-phenyl-1H-1,2,3-triazole ***(2t)***. Yellow solid (119 mg, 80%); mp 149−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.51−7.41 (m, 5H), 7.38−7.32 (m, 2H), 7.12−7.06 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 133.4, 132.8, 132.2, 130.0, 129.5, 129.5, 125.7, 125.2, 123.7 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{14}H_{11}BrN_3$, 300.0136, 302.0116; found 300.0121, 302.0099.

5-(4-Nitrophenyl)-1-phenyl-1H-1,2,3-triazole ***(2u)***. Yellow solid (100 mg, 75%); mp 143−144 °C (lit.[12] 144−145 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.18 (m, 2H), 7.99 (s, 1H), 7.53−7.46 (m, 3H), 7.44−7.39 (m, 2H), 7.38−7.32 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 135.9, 134.2, 133.0, 129.9, 129.8, 129.3, 125.3, 124.5, 124.2 ppm; HRMS (APCI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{14}H_{11}N_4O_2$, 267.0882; found 267.0864.

5-(2-Naphthyl)-1-phenyl-1H-1,2,3-triazole ***(2v)***. Yellow oil (95 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.84−7.75 (m, 4H), 7.56−7.48 (m, 2H), 7.48−7.35 (m, 5H), 7.22 (dd, *J* = 8.5, 1.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 136.7, 133.7, 133.2, 133.0, 129.4, 129.2, 128.6, 128.3, 128.2, 127.8, 127.2, 126.9, 125.6, 125.2, 124.1 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{18}H_{14}N_3$, 272.1188; found 272.1184.

1-Phenyl-5-(2-thienyl)-1H-1,2,3-triazole[6d] ***(2w)***. Brown oil (76 mg, 67%);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.57−7.49 (m, 3H), 7.48−7.41 (m, 2H), 7.36 (d, *J* = 5.1 Hz, 1H), 7.01−6.98 (m, 1H), 6.94 (d, *J* = 3.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 133.0, 132.5, 130.0, 129.4, 128.1, 127.7, 127.7, 127.1, 126.1 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{12}H_{10}N_3S$, 228.0595; found 228.0581.

Methyl 4-(1-Phenyl-1H-1,2,3-triazol-5-yl)phenyl Ether[6d] ***(2x)***. Yellow oil (56 mg, 45%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.46−7.35 (m, 5H), 7.17−7.12 (m, 2H), 6.88−6.84 (m, 2H), 3.81 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 137.6, 136.7, 133.0, 130.0, 129.4, 129.2, 125.2, 118.9, 114.3, 55.3 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{15}H_{14}N_3O$, 252.1137; found 252.1119.

(1-Benzyl-5-phenyl-1H-1,2,3-triazol-4-yl)(phenyl)methanone ***(3a)***. Colorless oil (144 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34−8.23 (m, 2H), 7.59−7.54 (m, 1H), 7.50−7.41 (m, 5H), 7.30−7.24 (m, 5H), 7.08−7.04 (m, 2H), 5.47 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.4, 143.8, 141.8, 137.1, 134.7, 133.0, 130.7, 130.1, 129.8, 128.9, 128.7, 128.5, 128.2, 127.7, 126.4, 52.1 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{22}H_{18}N_3O$, 340.1450; found 340.1439.

(1-Benzyl-5-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)(phenyl)methanone ***(3b)***. White solid (171 mg, 92%); mp 130−132 °C (lit.[13] 129−131 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38−8.28 (m, 2H), 7.54−7.49 (m, 2H), 7.47−7.43 (m, 2H), 7.37−7.28 (m, 6H), 7.12−7.08 (m, 2H), 5.49 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.2, 140.8, 137.0, 136.4, 134.5, 133.2, 131.2, 131.0, 130.7, 129.4, 129.0, 129.0, 128.6, 128.3, 127.6, 52.2 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{22}H_{17}ClN_3O$, 374.1060; found 374.1052.

(1-Benzyl-5-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)(phenyl)methanone ***(3c)***. Yellow oil (151 mg, 82%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30−8.26 (m, 2H), 7.61−7.52 (m, 1H), 7.49−7.45 (m, 2H), 7.31−7.28 (m, 3H), 7.23−7.20 (m, 2H), 7.12−7.09 (m, 2H), 6.99−6.94 (m, 2H), 5.48 (s, 2H), 3.85 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.5, 160.9, 143.6, 141.8, 137.3, 134.9, 133.0, 131.3, 130.7, 128.9, 128.4, 128.2, 127.6, 118.2, 114.2, 55.4, 51.9 ppm; HRMS (ESI-ion trap) *m/z* [M + H]$^+$ calcd for $C_{23}H_{20}N_3O_2$, 370.1556; found 370.1544.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental methods; ^{1}H and ^{13}C NMR spectra of compounds **2a−2x** and **3a−3c**; high-resolution mass spectra of compounds **2a−2x** and **3a−3c**; and X-ray crystallographic files (CIF) for **2n** and **3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: whengshan@163.com. Phone: +86-773-5846279. Fax: +86-773-5803930 (H.-S.W.).
*E-mail: panym2013@hotmail.com (Y.-M.P.).

Author Contributions

[§]Y.-C.W. and Y.-Y.X. contributed equally to this work.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the project 973 (2011CB512005), Ministry of Education of China (IRT1225), the National Natural Science Foundation of China (21362002, 41206077, and 81260472), the Guangxi Natural Science Foundation of China (2012GXNSFAA053027 and 2011GXNSFD018010), and the Bagui Scholar Program of Guangxi for financial support.

■ REFERENCES

(1) (a) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278. (b) Thirumurugan, P.; Matosiuk, D.; Jozwiak, K. *Chem. Rev.* **2013**, *113*, 4905.

(2) (a) For general reviews on chemistry and applications of 1,2,3-triazoles: Fan, W.-Q.; Katritzky, A. R. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Elsevier Science: Oxford, U.K., 1996; Vol. *4*, pp 1−126. (b) Morgan, N. H. *Eur. Pat. Appl.* EP 437979 A2 19910742, 1991.

(3) Himo, F.; Lovell, T.; Hilgraf, R.; Rostovtsev, V. V.; Noodleman, L.; Sharpless, K. B.; Fokin, V. V. *J. Am. Chem. Soc.* **2005**, *127*, 210.

(4) For selected examples, see: (a) Golas, P. L.; Matyjaszewski, K. *Chem. Rev.* **2010**, *39*, 1338. (b) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302. (c) Liang, L.; Astruc, D. *Chem. Rev.* **2011**, *255*, 2933.

(5) (a) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.* **2005**, *127*, 15998. (b) Tam, A.; Arnold, U.; Soellner, M. B.; Raines, R. T. *J. Am. Chem. Soc.* **2007**, *129*, 12670. (c) Majireck, M. M.; Weinreb, S. M. *J. Org. Chem.* **2006**, *71*, 8680. (d) Rasmussen, L. K.; Boren, B. C.; Fokin, V. V. *Org. Lett.* **2007**, *9*, 5337. (e) Boren, B. C.; Narayan, S.; Rasmussen, L. K.; Zhang, L.; Zhao, H.; Lin, Z.; Jia, G.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 8923. (f) Johansson, J. R.; Lincoln, P.; Norden, B.; Kann, N. *J. Org. Chem.* **2011**, *76*, 2355. (g) Wang, D.; Salmon, L.; Ruiz, J.; Astruc, D. *Chem. Commun.* **2013**, *49*, 6956.

(6) For selected examples, see: (a) Lewis, W. G.; Green, L. G.; Grynszpan, F.; Radié, Z.; Carlier, P. R.; Taylor, P.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 1053. (b) Krasinski, A.; Fokin, V. V.; Sharpless, K. B. *Org. Lett.* **2004**, *6*, 1237. (c) Kwok, S. W.; Fotsing, J. R.; Fraser, R. J.; Rodionov, V. O.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4217. (d) Hong, L.; Lin, W.; Zhang, F.; Liu, R.; Zhou, X. *Chem. Commun.* **2013**, *49*, 5589.

(7) (a) Zefirov, N. S.; Chapovskaya, N. K.; Kolesnikov, V. V. *Chem. Commun.* **1971**, 1001. (b) Piet, J. C.; Le H, G.; Cailleux, P.; Benhaoua, H.; Carrie, R. *Bull. Soc. Chim. Belg.* **1996**, *105*, 33.

(8) Amantini, D.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Zunino, E.; Vaccaro, L. *J. Org. Chem.* **2005**, *70*, 6526.

(9) For selected examples, see: (a) Guan, B.-T.; Hou, Z. *J. Am. Chem. Soc.* **2011**, *133*, 18086. (b) Atesin, A. C.; Ray, N. A.; P Stair, C.; Marks, T. J. *J. Am. Chem. Soc.* **2012**, *134*, 14682. (c) Szostak, M.; Procter, D. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 9238. (d) Hatanaka, M.; Morokuma, K. *J. Am. Chem. Soc.* **2013**, *135*, 13972.

(10) McIntosh, M. L.; Johnston, R. C.; Pattawong, O.; Ashburn, B. O.; Naffziger, M. R.; P; Cheong, Ha-Y.; Carter, R. G. *J. Org. Chem.* **2012**, *77*, 1101.

(11) Chuprakov, S. N.; Chernyak, N.; Dudnik, A. S.; Gevorgyan, V. *Org. Lett.* **2007**, *9*, 2333.

(12) Kadaba, P. K.; Edelstein, S. B. *J. Org. Chem.* **1990**, *55*, 5891.

(13) Singh, N.; Pandey, S. K.; Tripathi, R. P. *Carbohydr. Res.* **2010**, *345*, 1641.