Efficient Synthesis and Antibacterial Activities of Some Novel 1,2,3-Triazoles Prepared from Propargylic Alcohols and Benzyl Azides

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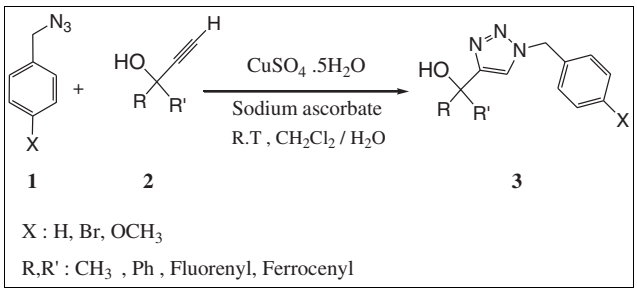
Received September 3, 2011
DOI 10.1002/jhet.1680
Published online 17 March 2014 in Wiley Online Library (wileyonlinelibrary.com).



A simple and effective procedure for regioselective preparation of 1,2,3-triazoles from benzyl azides and propargylic alcohols is described using $CuSO_4.5H_2O$ and sodium ascorbate. To screen the antibacterial activity of some newly synthesized triazole derivatives, minimum inhibitory concentration of **3d** and **3k** was evaluated against gram positive *Staphylococcus aureus* and *Bacillus subtilis* and gram negative *Escherichia coli* and *Pseudomonas aeruginosa*.

J. Heterocyclic Chem., **51**, 1298 (2014).

INTRODUCTION

N-Heterocyclic compounds such as 1,2,3-triazoles have shown important biological activities, and there are numerous examples in the literature including anti-HIV activity [1,2], antibacterial activity [3], antiallergic activity [4], and selective β_3 adrenergic receptor agonism [5]. 1,2,3-Triazoles have also a range of important applications in industries such as dyes, corrosion inhibition, photostabilizers, photographic materials, and agrochemicals [6].

Several different methods have been described for synthesis of 1,2,3-triazoles including the intramolecular cyclization of bishydrazones or mixed hydrazones and miscellaneous oxidations, as well as the 1,3-dipolar cycloaddition of azides to alkynes [6–8]. Huisgen's dipolar cycloaddition of organic azides and alkynes is the most direct route to 1,2,3-triazoles [9]. However, because of the high activation energy (ca. 24–26 kcal/mol), these cycloadditions are often very slow even at elevated temperature (80–120°C for 12–24 h) and produce mixtures of regioisomers. Recently, copper catalysts have been reported for the construction of 1,2,3-triazoles. The 'click' chemistry reported by Sharpless group described that the Cu(I)-catalyzed cycloaddition can be conducted at room temperature and results in 1,4-disubstituted triazoles in high regioselectivity [10].

Although several different methods have been described for synthesis of 1,2,3-triazoles from azides and a wide variety of alkynes [11], only few articles have reported the use of propargylic alcohols (especially tertiary propargylic alcohols) for synthesis of triazoles. Therefore, we wish here to report the synthesis of some new 1,2,3-triazoles by 1,3-dipolar cycloaddition between azides and propargylic alcohols in the presence of $CuSO_4.5H_2O$ and sodium ascorbate at room temperature (Scheme 1). The antibacterial activity of some novel triazoles (**3d** and **3k**) will be also reported.

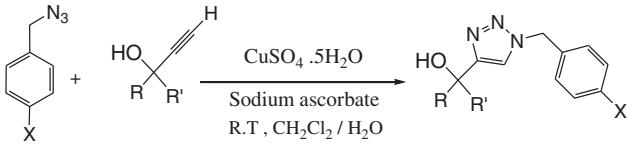
RESULTS AND DISCUSSION

Initially, propargylic alcohols were easily synthesized by treating trimethylsilyl acetylide with the ketones in dry ether at −10°C. Desilylation of corresponding propargyl alcohols with K_2CO_3 in THF and methanol gave desired products in good yields (Scheme 2).

There are a number of methods for the formation of azides from halides [12]. We prepared azides from the reaction between benzyl halides and NaN_3 in DMSO at room temperature [13].

To find the best conditions for the reaction of propargylic alcohols and azides, the reaction of 1,1-diphenylprop-2-yn-1-ol and benzyl azide was chosen as model reaction. Different solvents and catalysts were screened, and the results are summarized in Table 1. When 1,1-diphenylprop-2-yn-1-ol (**2a**) and benzyl azide were treated with $CuSO_4.5H_2O$ and sodium ascorbate at room temperature in different solvents

Scheme 1



1 **2** **3**

X : H, Br, OCH_3

R,R' : CH_3 , Ph , Fluorenyl, Ferrocenyl

(Table 1, entries 1–5), the best result was achieved in CH_2Cl_2/H_2O (1:1), and (1-benzyl-1H-1,2,3-triazol-4-yl) diphenyl methanol (**3a**) was obtained in 95% yield after 5 h (Table 1, entry 5).

We have also examined the reactivity of some other catalysts such as $Cu(NO_3)_2.3H_2O$, $CuCl_2.2H_2O$, and $Cu(OAc)_2.H_2O$ for the preparation of triazole **3a**. The results show that these catalysts are not efficient to improve the yield of product, and therefore, $CuSO_4.5H_2O$ appeared to be the most efficient catalyst. When **1a** was treated with **2a** without copper catalyst, no change took place (Table 1, entry 9), implying that Cu catalyst is essential in this reaction.

To show the generality of this method, a variety of propargylic alcohols and benzyl azides was treated with $CuSO_4.5H_2O$ (15 mol%) and sodium ascorbate (45 mol%) in CH_2Cl_2/H_2O (1/1) at room temperature, and results are presented in Table 2.

As can be seen from Table 2, 1,1-diphenylprop-2-yn-1-ol reacted with benzyl azide and 4-methoxybenzyl azide under optimum reaction conditions to give the corresponding triazoles in good yields (Table 2, entries 1 and 2). Electron-withdrawing group on the aromatic ring in propargylic alcohols did not have significant effects on the yields of the reactions (Table 2, entries 3 and 4). Propargylic alcohols with fluorenyl and ferrocenyl moieties also gave high yields of the new triazole products (Table 2, entries 5–8). When aliphatic propargylic alcohol such as 2-methylbut-3-yn-2-ol and 1-ethynylcyclohexanol reacted with benzyl azide, 4-methoxybenzyl azide, and 4-bromobenzyl azide under the same reaction conditions, very good yields of the triazole products were obtained (Table 2, entries 9–14). It is interesting to mention that all reactions were regioselective and gave only expected 1,4-disubstituted triazoles in good yields.

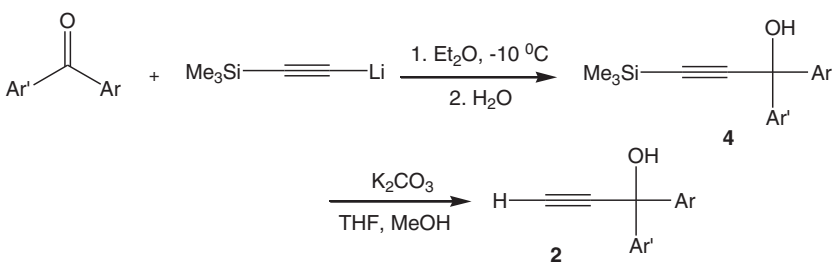
To screen the antibacterial activity of newly synthesized triazole derivatives, minimum inhibitory concentration (MIC) was evaluated against gram positive *Staphylococcus aureus* and *Bacillus subtilis* and gram negative *Escherichia coli* and *Pseudomonas aeruginosa*. In addition, the finding towards inhibition of microorganisms was correlated with a standard antibiotic tetracycline (Table 3). The results revealed that the triazole **3k** inhibited growth of bacteria at low concentration of 150 μg/mL, whereas the growth inhibitory effects of the compound **3d** on all bacteria were shown at high concentration of 250 μg/mL (Table 3). However, the MIC values for both triazole compounds against bacteria were high as compared with the standard antibiotic tetracycline; these results suggest that the compound **3k** exhibited good antibacterial activities and can be further developed for application as effective antimicrobial agent.

In conclusion, we have developed a simple and efficient method for the [3 + 2]-cycloaddition of terminal propargylic alcohols with benzyl azides by $CuSO_4.5H_2O$ and sodium ascorbate. The most of 1,4-disubstituted-[1,2,3]-triazole derivatives are novel compounds and were obtained in high yields under mild conditions. The MIC of **3d** and **3k** were evaluated against gram positive *S. aureus* and *B. subtilis* and gram negative *E. coli* and *P. aeruginosa*, and the results show that the compound **3k** exhibited good antibacterial activities.

EXPERIMENTAL

General. All commercial chemicals were purchased from Fluka and Merck and were used without further purification. Tetracycline was purchased from Sigma-Aldrich (Germany), Bacto trypto from Quelab (Montreal, Canada) and Yeast extract from Merck. All the bacteria were purchased from PTTC (Persian Type Culture Collection) and ATTC (American Type Culture Collection). Melting points were determined with a Stuart Scientific SMP1 and Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Bruker Vector

Scheme 2



Ar, Ar'= Ph, Fluorenyl, Ferrocenyl

Table 1

The solvent and catalyst optimization of reaction **1a** and **2a** to form **3a**.[a]

1a **2a** **3a**

Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	$CuSO_4.5H_2O$	DMSO	24	40
2	$CuSO_4.5H_2O$	DMF	24	40
3	$CuSO_4.5H_2O$	CH_3CN	24	trace
4	$CuSO_4.5H_2O$	EtOAc/H_2O (1:1)	24	50
5	$CuSO_4.5H_2O$	CH_2Cl_2/H_2O (1:1)	5	95
6	$Cu(NO_3)_2.3H_2O$	CH_2Cl_2/H_2O (1:1)	5	90
7	$CuCl_2.2H_2O$	CH_2Cl_2/H_2O (1:1)	5	90
8	$Cu(OAc)_2.H_2O$	CH_2Cl_2/H_2O (1:1)	5	85
9	—	CH_2Cl_2/H_2O (1:1)	24	—

[a]A mixture of **1a**, **2a**, sodium ascorbate, and 15 mol% $CuSO_4.5H_2O$ was stirred at room temperature.
[b]Yields of isolated pure product **3a**.

22 FT-IR spectrometer using potassium bromide pellets. The 1H-NMR and 13C-NMR spectra were recorded on a Bruker Avance III 400 MHz and Bruker Avance DRX 500 MHz spectrometer in CDCl3. CHN analyses were obtained from a CHN Elemental Analyzer LECO 600. The progress of the reactions was checked by TLC chromatography on Merck silica-gel 60 F-254 plates. Silica gel (70-230 mesh) was used for column chromatography.

General procedure for the preparation of benzyl azide (1) [11a]. To a solution of NaN_3 (0.065 g, 1 mmol) in dry DMSO (2 mL) was added benzyl halide (1 mmol). The reaction mixture was stirred at room temperature for 5 h. After completion of the reaction, dichloromethane (30 mL) and water (30 mL) were added to the reaction mixture, and the mixture was transferred into a separatory funnel. Organic layer was washed with water (30 mL), dried over anhydrous Na_2SO_4 and concentrated by a rotary evaporator.

Benzyl azide (1a). Yield 98%, IR (KBr, υ cm^{-1}): 2850, 2100, 1720; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (s, 2H), 7.28–7.39 ppm (m, 5H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.74, 128.21, 128.28, 128.81, 135.38.

4-Methoxybenzyl azide (1b). Yield 80%, IR (KBr, υ cm^{-1}): 2850, 2100, 1600; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 3H), 4.29 (s, 2H), 6.95 (d, J = 8.8 Hz, 2H), 7.28 ppm (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.39, 55.28, 114.22, 127.43, 129.78, 159.67.

4-Bromobenzyl azide (1c). Yield 98%, IR (KBr, υ cm^{-1}): 2830, 2100, 1500; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30 (s, 2H), 7.19 (d, J = 6.4 Hz, 2H), 7.51 ppm (d, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.06, 122.31, 129.82, 131.98, 134.41.

General procedure for the preparation of trimethylsilylethynyl alcohol (4). To a stirred solution of trimethylsilylacetylene (2.5 mL, 26 mmol) in dry ether (25 mL) was added a solution of *n*-BuLi 1.5 M (16 mL, 24 mmol) during 0.5 h at −10°C under argon. Stirring was continued 1 h at the same temperature. The resulting trimethylsilyl acetylide solution was added dropwise at −10°C under argon to a stirred solution of ketone (22 mmol) in dry ether. Then, the solution allowed warm up to room temperature. After completion of the reaction as monitored by TLC, water (30 mL) was added to the reaction mixture and then extracted with ether (2 × 30 mL). The organic layer was dried over anhydrous sodium sulfate. After filtration, the solution concentrated under reduced pressure, and the residue recrystallized from *n*-hexane-dichloromethane to yield 9-(trimethylsililethynyl) alcohol.

1-(4-Chlorophenyl)-3-(trimethylsilyl)-1-phenylprop-2-yn-1-ol. Yield 85%, pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.38 (s, 9H), 3.31 (s, 1H), 7.34–7.45 (m, 5H), 7.63–7.72 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.02, 74.31, 92.50, 107.57, 126.09, 127.64, 128.00, 128.44, 128.47, 133.57, 143.58, 144.56. *Anal*. Calcd for $C_{18}H_{19}ClOSi$: C, 68.66; H, 6.08; found: C, 68.32; H, 5.90.

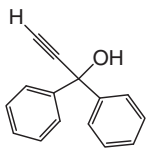
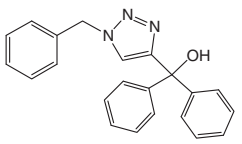
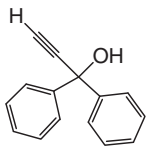
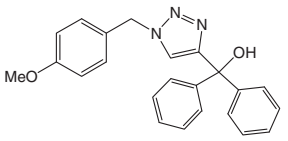
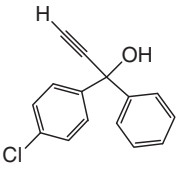
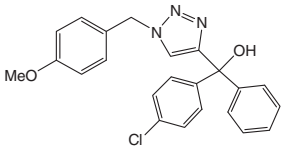
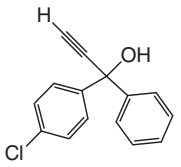
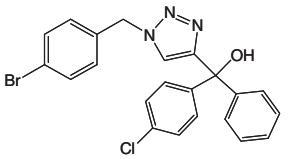
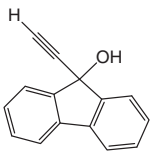
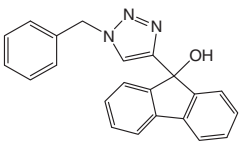
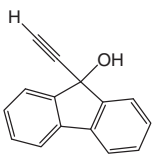
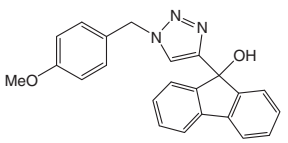
9-(2-Trimethylsilylethynyl)-flouren-9-ol. Yield 80%, mp 120–122°C [14]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.17 (s, 9H), 2.50 (s, 1H), 7.32–7.41 (m, 4H), 7.60 (d, J = 7.2 Hz, 2H), 7.69 ppm (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −0.16, 75.05, 88.34, 104.82, 120.14, 124.33, 128.55, 129.63, 139.19, 147.06.

1-Ferrocenyl-3-(trimethylsilyl)-1-phenylprop-2-yn-1-ol. Yield 82%, mp 119–121°C [15]; IR (KBr, υ cm^{-1}): 3565, 2321, 1500, 1420, 1250; ^{1}H NMR (500 MHz $CDCl_3$): δ (ppm) = 0.31 (s, 9H), 3.07 (s, 1H), 4.15 (br.s, 1H), 4.21 (br.s, 1H), 4.30 (s, 5H), 4.34 (br. s, 1H), 4.39 (br.s, 1H), 7.23 (t, J = 7.4 Hz, 1H), 7.29 (t, J = 7.5 Hz, 2H), 7.62 ppm (d, J = 7.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 0.09, 65.10, 68.28, 68.50, 69.08, 71.7, 89.41, 96.84, 125.62, 127.59, 128.01, 143.90.

General procedure for the preparation of propargylic alcohols (2). Trimethylsilylethynyl alcohols (12 mmol) was reacted with K_2CO_3 (72 mmol) in MeOH (45 mL) and THF (45 mL). After completion of the reaction, the solvent was evaporated. The solid was dissolved in water–ethyl acetate

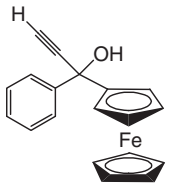
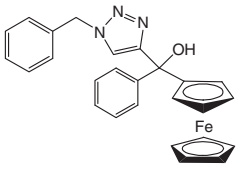
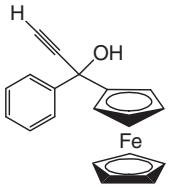
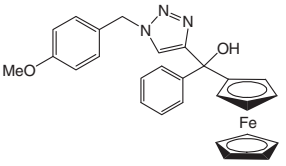
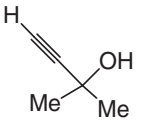
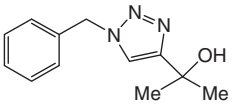
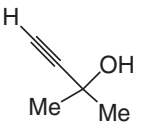
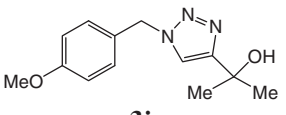
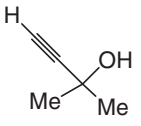
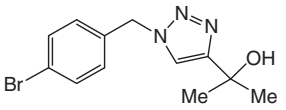
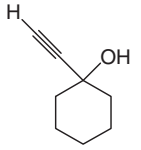
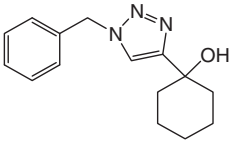
Table 2

Preparation of 1,2,3-triazoles from benzyl azides and propargyl alcohols.

Entry	Azide	Alkynol	1,2,3-Triazole	Time (h)	Yield (%)[a]
1	$PhCH_2N_3$ **1a**	 **2a**	 **3a**	5	95
2	4-MeO$PhCH_2N_3$ **1b**	 **2a**	 **3b**	5	97
3	4-MeO$PhCH_2N_3$ **1b**	 **2b**	 **3c**	5	90
4	4-Br$PhCH_2N_3$ **1c**	 **2b**	 **3d**	3	83
5	$PhCH_2N_3$ **1a**	 **2c**	 **3e**	6	85
6	4-MeO$PhCH_2N_3$ **1b**	 **2c**	 **3f**	3	95

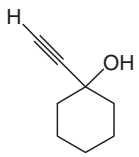
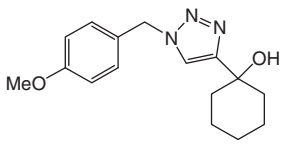
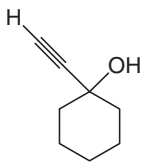
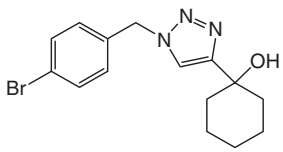
(*Continued*)

Table 2
(Continued)

Entry	Azide	Alkynol	1,2,3-Triazole	Time (h)	Yield (%)[a]
7	$PhCH_2N_3$ **1a**	 **2d**	 **3g**	6	75
8	4-$MeOPhCH_2N_3$ **1b**	 **2d**	 **3h**	4	90
9	$PhCH_2N_3$ **1a**	 **2e**	 **3i**	3	80
10	4-$MeOPhCH_2N_3$ **1b**	 **2e**	 **3j**	3	85
11	4-$BrPhCH_2N_3$ **1c**	 **2e**	 **3k**	3	88
12	$PhCH_2N_3$ **1a**	 **2f**	 **3l**	2	90

(*Continued*)

Table 2
(Continued)

Entry	Azide	Alkynol	1,2,3-Triazole	Time (h)	Yield (%)[a]
13	4-MeOPhCH$_2$N$_3$ **1b**	 **2f**	 **3m**	2	94
14	4-BrPhCH$_2$N$_3$ **1c**	 **2f**	 **3n**	2	95

[a]All of the products were identified by NMR, IR and elemental analysis.
[b]Yields refer to isolated products.

(100 mL). After separation of organic layer, the solvent was evaporated to give a solid, which recrystallized from *n*-hexane-dichloromethane to obtain propargylic alcohols **2**.

1-(4-Chlorophenyl)-1-phenylprop-2-yn-1-ol (2b). Yield 75%, pale yellow oil [16]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92 (s, 1H), 3.12(s, 1H), 7.30–7.40 (m, 5H), 7.55–7.63 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 73.85, 75.92, 85.96, 125.93, 127.51, 128.12, 128.44, 128.46, 133.75, 143.05, 144.05.

9-Ethynyl-9-flourenol (2c). Yield 83%, mp 107–109°C [17]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 1H), 2.60 (s, 1H), 7.38 (dt, J = 9.3, 1.5 Hz, 2H), 7.44 (dt, J = 9.2, 1.6 Hz, 2H), 7.64 (dd, J = 8.8, 0.8 Hz, 2H), 7.73 ppm (dd, J = 8.8, 0.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.41, 74.59, 83.85, 120.28, 124.27, 128.66, 129.89, 139.13, 146.60.

1-Ferrocenyl-1-phenylprop-2-yn-1-ol (2d). Yield 78%, mp 91–93°C [15a]; IR (KBr, υ cm^{-1}): 3520, 3250, 2350, 1518, 1350, 1100; ^{1}H NMR (500 MHz $CDCl_3$): δ 2.81 (s, 1H), 3.19 (s, 1H), 4.18 (br.s, 1H), 4.26 (br.s, 1H), 4.32 (m, 6H), 4.48 (br. s, 1H), 7.26–7.32 (m, 3H), 7.62 ppm (*pseudo* br.s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 65.18, 68.35, 68.55, 69.11, 71.24, 86.87, 96.67, 125.55, 127.74, 128.10, 143.83. *Anal*. Calcd for $C_{19}H_{16}FeO$: C, 72.18; H, 5.10; found: C, 72.30; H, 5.15.

Table 3

Minimum inhibitory concentration of the compounds **3d** and **3k**.

	Minimum inhibitory concentration (μg/mL)		
Strain	Compound **3d**	Compound **3k**	Tetracycline
E. coli	250	200	25
P. aeruginosa	250	150	50
S. aureus	250	150	10
B. subtilis	250	150	25

General procedure for preparation of triazoles (3). To a solution of azide (1 mmol) in CH_2Cl_2/H_2O (5 mL) were added propargylic alcohol (1 mmol), sodium ascorbate (0.090 g, 45 mol %) and $CuSO_4.5H_2O$ (0.038 g, 15 mol%). The reaction mixture was stirred at room temperature. After completion of the reaction as monitored by TLC, dichloromethane (15 mL) and water (15 mL) were added, and the reaction mixture was transferred into a separatory funnel. Organic layer was washed with water (30 mL) and saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by recrystallization by using a mixture of *n*-hexane and dichloromethane.

(1-Benzyl-1H-1,2,3-triazol-4-yl)diphenylmethanol (3a). Yield 95%, mp 135–136°C [18]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84(s, 1H), 5.51(s, 2H), 7.09 (s, 1H), 7.25–7.39 ppm (m, 15H); ^{13}C NMR (100 MHz, CDCl3): δ 54.17, 65.33, 122.41, 127.19, 127.53, 127.89, 128.05, 128.75, 129.13, 134.55, 145.63, 158.44.

(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)diphenylmethanol (3b). Yield 97%, mp 134–135°C; IR (KBr, υ cm^{-1}): 3410, 3140, 3060, 2930, 2810, 1560, 1350, 750; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82(s, 3H), 5.43(s, 2H), 6.90 (d, J = 8.8 Hz, 2H), 7.07 (s, 1H), 7.21(d, J = 8.8 Hz, 2H), 7.27–7.35 ppm (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.74, 55.34, 62.87, 114.49, 122.23, 126.52, 127.50, 128.03, 129.50, 132.66, 145.68, 154.44, 159.90. *Anal*. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31; found: C, 74.23; H, 5.73; N, 11.27.

(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)(4-chlorophenyl) (phenyl)methanol (3c). Yield 90%, mp 116–118°C; IR (KBr, υ cm^{-1}): 3394, 2950, 2837, 1514, 1257, 823,765; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 4.02 (s,1H), 5.42 (s, 2H), 6.90 (d J = 8.4 Hz, 2H), 7.06 (s, 1H), 7.21 (d J = 8.4 Hz, 2H), 7.27–7.29 ppm (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.79, 55.35, 76.34, 114.50, 122.17, 126.39, 127.10, 127.72, 128.16, 128.30, 128.71, 129.55, 133.37, 144.29, 145.25, 154.02, 159.92. *Anal*. Calcd for $C_{23}H_{20}ClN_3O_2$: C, 68.06; H, 4.97; N, 10.35; found: C, 68.02; H, 4.83; N, 10.18.

(1-(4-Bromobenzyl)-1H-1,2,3-triazol-4-yl)(4-chlorophenyl) (phenyl) methanol (3d). Yield 83%, mp 123–125°C; IR (KBr, υ cm^{-1}): 3422, 3155, 3060, 1609, 1591, 814, 762; ^1H NMR (400 MHz, $CDCl_3$): δ 4.54 (s, 1H), 5.38 (s, 2H), 7.08 (d J = 8.4 Hz, 2H), 7.11 (s, 1H), 7.22–7.30 (m, 9H), 7.47 ppm (d J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.44, 60.48, 122.57, 122.94, 127.11, 127.74, 128.16, 128.18, 128.74, 129.59, 132.31, 133.36, 133.52, 144.28, 145.23, 154.30. *Anal*. Calcd for $C_{22}H_{17}BrCl\ N_3O_2$: C, 58.11; H, 3.77; N, 9.24; found: C, 58.28; H, 3.66; N, 9.05.

9-(1-Benzyl-1H-1,2,3-triazol-4-yl)-9H-fluoren-9-ol (3e). Yield 85%, mp 140–141°C; IR (KBr, υ cm^{-1}): 3520, 3130, 3090, 2890, 1485, 750; ^1H NMR (400 MHz, $CDCl_3$): δ 3.65 (s, 1H), 5.44 (s, 2H), 7.15 (s, 1H), 7.21–7.66 ppm (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.15, 63.86, 120.19, 120.45, 124.88, 128.06, 128.36, 128.73, 129.09, 129.46, 134.39, 139.58, 147.83, 150.82. *Anal*. Calcd for $C_{22}H_{17}N_3O$: C, 77.86; H, 5.05; N, 12.38; found: C, 77.42; H, 5.09; N, 12.08.

9-(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)-9H-fluoren-9-ol (3f). Yield 95%, mp 109–111°C; IR (KBr, υ cm^{-1}): 3312, 3145, 3065, 2839, 1614, 1453, 755; ^1H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 5.27 (s, 2H), 6.79 (d, J = 9.2 Hz, 2H), 7.10 (d, J = 9.2 Hz, 2H), 7.15 (s, 1H), 7.25 (dt, J = 7.6, 1.2 Hz, 2H), 7.34 (dt, J = 7.6, 1.2 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.60 ppm (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.58, 55.28, 78.59, 114.37, 120.15, 120.48, 124.96, 126.46, 128.31, 129.36, 129.65, 139.56, 148.00, 150.81, 159.73. *Anal*. Calcd for $C_{23}H_{19}N_3O_2$: C, 74.71; H, 5.18; N, 11.37; found: C, 74.32; H, 5.22; N, 11.29.

(1-Benzyl)-1H-1,2,3-triazol-4-yl)(phenyl)(ferrocenyl)methanol (3g). Yield 75%, mp 115–116°C; IR (KBr, υ cm^{-1}): 3498, 3150, 3060, 2800, 1480, 1295, 790; ^1H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 1H), 4.13–4.25 (m, 9H), 5.50 (d, J = 14.8 Hz, 1H), 5.53 (d, J = 14.8 Hz, 1H), 7.22–7.45 ppm (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.43, 66.66, 68.22, 68.28, 68.64, 73.23, 121.15, 126.24, 127.17, 127.77, 127.84, 128.71, 129.13, 134.87, 145.29, 155.06. *Anal*. Calcd for $C_{26}H_{23}FeN_3O$: C, 69.50; H, 5.16; N, 9.35; found: C, 69.23; H, 5.01; N, 9.15.

(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)(phenyl)(ferrocenyl) methanol (3h). Yield 90%, mp 141–142°C; IR (KBr, υ cm^{-1}): 3490, 2850, 1630, 1250, 499; ^1H NMR (400 MHz, $CDCl_3$): δ 3.62 (s, 1H), 3.81 (s, 3H), 4.13–4.34 (m, 9H), 5.40 (d, J = 15.2 Hz, 1H), 5.44 (d, J = 15.2 Hz, 1H), 6.90 (d, J = 8.4 Hz, 2H), 7.18–7.30 (m, 6H), 7.46 ppm (d, J = 8.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 53.62, 55.37, 67.87, 69.22, 69.66, 69.84, 73.14, 114.49, 120.85, 126.25, 126.80, 127.17, 127.79, 129.44, 145.01, 154.70, 159.86. *Anal*. Calcd for $C_{27}H_{25}FeN_3O_2$: C, 67.65; H, 5.26; N, 8.77; found: C, 67.28; H, 5.17; N, 8.55.

2-(1-Benzyl-1H-1,2,3-triazol-4-yl)propan-2-ol (3i) [19]. Yield 80%, mp 78–80°C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.62 (s, 6H), 2.75 (s, 1H), 5.50 (s, 2H), 7.27–7.39 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.44, 54.21, 68.45, 119.13, 128.17, 128.77, 29.13, 134.56, 156.16.

2-(1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (3j). Yield 85%, mp 86–88°C [19]; ^1H NMR (400 MHz, $CDCl_3$): δ 1.59 (s, 6H), 2.87 (s, 1H), 3.79 (s, 3H), 5.41 (s, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.43, 53.66, 55.34, 68.44, 114.44, 118.92, 126.58, 129.76, 156.00, 159.87.

2-(1-(4-Bromobenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (3k). Yield 88%, mp 115–117°C; IR (KBr, υ (cm^{-1}): 3200, 2917, 2787, 2287, 1014, 954; ^1H NMR (400 MHz, $CDCl_3$): δ 1.57 (s, 6H), 3.43 (s, 1H), 5.39 (s, 2H), 7.10 (d, J = 7.6 Hz, 2H), 7.39 (s, 1H), 7.44 ppm (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.45, 53.33, 68.41, 119.31, 122.79, 129.75, 132.20, 133.71, 156.33. *Anal*. Calcd for $C_{12}H_{14}BrN_3O$: C, 48.67; H, 4.76; N, 14.19; found: C, 48.68; H, 4.81; N, 14.18.

1-(1-Benzyl-1H-1,2,3-triazol-4-yl)cyclohexanol (3l). Yield 90%, mp 114–116°C; IR (KBr, υ cm^{-1}): 3350, 2830, 2760, 1450, 715, 220; ^1H NMR (400 MHz, $CDCl_3$): δ 1.31–1.94 (m, 10H), 2.70 (s, 1H), 5.48 (s, 2H), 7.25–7.38 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.35, 38.08, 40.89, 54.13, 69.47, 119.63, 128.10, 128.69, 129.09, 134.68, 156.14. Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33; found: C, 69.65; H, 7.62; N, 16.68.

1-(1-(4-Methoxybenzyl-1H-1,2,3-triazol-4-yl)cyclohexanol (3m). Yield 94%, mp 83–85°C; IR (KBr, υ cm^{-1}): 3420, 3210, 2890, 2784, 1509, 1210, 870; ^1H NMR (400 MHz, $CDCl_3$): δ 1.50–1.97 (m, 10H), 2.55 (s, 1H), 3.80 (s, 3H), 5.42 (s, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.94, 25.35, 38.08, 53.69, 55.33, 69.49, 114.45, 119.33, 126.61, 129.72, 155.96, 159.88. *Anal.* Calcd for $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62; found: C, 66.70; H, 7.62; N, 14.56.

1-(1-(4-Bromobenzyl-1H-1,2,3-triazol-4-yl)cyclohexanol (3n). Yield 95%, mp 128–130°C; IR (KBr, υ cm^{-1}): 3382, 3123, 2928, 2854, 1344, 1144, 890; ^1H NMR (400 MHz, $CDCl_3$): δ 1.53–1.96 (m, 10H), 2.00 (s, 1H), 5.47 (s, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.38 (s, 1H), 7.52 ppm (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.93, 25.32, 38.12, 53.47, 69.58, 119.47, 122.91, 129.73, 132.30, 133.68, 156.42. *Anal.* Calcd for $C_{15}H_{18}BrN_3O$: C, 53.58; H, 5.40; N, 12.50; found: C, 53.54; H, 5.49; N, 12.46.

Antibacterial assay. The *in vitro* biocidal screening, antibacterial activities of the synthesized triazoles assayed onto LB medium contained: Bacto™ Tryptone, 10.0 g/L; yeast extract, 5.0 g/L; NaCl, 5.0 g/L; and glucose, 1.0 g/L [20]. The medium was dispensed into universal bottles and sterilized at 121°C for 15 min. The synthesized triazoles were dissolved into DMSO and filter sterilized using a 0.22 μm Ministart (Sartorius). The sterile synthesized stock solutions were added into LB medium to give a final concentration of 1–300 μg/mL as required [21]. The antibacterial activities of the triazoles compounds were compared with known antibiotic tetracycline at the same concentration.

Minimum inhibitory concentrations of the compounds were assayed using a standard method against some bacteria including *E. coli* PTCC 1330, *P. aeruginosa* PTCC 1074, *S. aureus* ATCC 35923 and *B. subtilis* PTCC 1023. Late exponential phase of the bacteria was prepared by inoculating 1% (v/v) of the cultures into the fresh LB medium and incubating on an orbital shaker at 37°C and 100 rpm overnight. Before using the cultures, they were standardized with a final cell density of approximately 10^8 cfu/mL. A 1% (v/v) inoculums of each culture was inoculated into the LB medium containing different concentration of the synthesized compounds and incubated on the orbital shaker at 37°C and 100 rpm. The compound sensitivity of the strains was assayed for positive or negative growth after 24–48 h.

Acknowledgment. We are thankful to the Research Council of University of Mazandaran for the support of this work.

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