One-pot multicomponent click synthesis of some novel 1,4-disubstituted-1H-1,2,3-triazoles from alkenes

Mosadegh Keshavarz

Department of Gas and Petroleum, Yasouj University, Gachsaran, Iran

Abstract

A facile and one-pot multicomponent synthesis of novel 1,4-disubstituted-1*H*-1,2,3-triazoles from alkenes at room temperature is reported. At the first step, in the presence of I_2/NaN_3 reagents, various alkenes were converted to the corresponding azido iodides and in the next step, the reaction of these compounds with phenylacetylene in the presence of catalytic amount of sodium ascorbate/ $CuSO_4$ afforded regioselective synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles in short times and at good to high yields.

Keywords: Click chemistry; styrene; regioselective; sodium azide; triazole; azido iodination.

Introduction

Copper-catalyzed azide-alkyne cycloaddition (CuAAC) which is best known as the click reaction is a widely utilized, reliable, and straightforward way to make covalent connections between building blocks containing various functional groups [1]. This cycloaddition has been applied in various ways in drug discovery, chemical biology, and medicinal chemistry as well as material science and solid phase organic synthesis [2-4]. Although organic azides are generally stable against most reaction conditions such as water and oxygen [5], isolation or purification of lower organic azides or polyazides can be problematic. Therefore, a procedure that avoids the isolation of organic azides is desirable. To keep away from the isolation of azide partner and in searching for step-economic synthesis, one-pot CuAAC with in situ generated organic azide from alkyl or aryl halides [6-9], α-

haloketones [10-12], tosylates [13], boronic acids [14], epoxides [15,16], secondary alcohols [17], glucals [18], unprotected monosaccharides [19], benzylic acetates [20] and aromatic amines [21] have been reported. One-Pot synthesis of 1,4-disubstituted 1,2,3-triazoles from aldehydes and amines has also been explored [22]. However, to the best of my knowledge, there is no report for one-pot preparation of 1,4-disubstituted 1,2,3-triazoles from alkenes. In recent years, we have investigated various ways to improve click reaction of organic azide and terminal alkynes for the preparation of diversity kinds of 1,4-disubstituted-1*H*-1,2,3-triazoles. For example, nano-CuI supported on polymeric support such as poly(4-vinyl pyridine) [23,24] and polyaniline [25] have been reported as reusable nanocatalytic systems for click synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles. Macroporous polymer supported azide and nanocopper (I)

*Corresponding author: Mosadegh Keshavarz

Tel: +98 (99) 04240422, Fax: +98 (99) 04240422
E-mail: chem.mosadegh@gmail.com

were also used to facilitate the workup of the click reaction and provided the products in short times and at high yields [26,27]. Next, we used $[Cu(Im^{12})_2]CuCl_2$ ionic liquid as a versatile, homogeneous, and recyclable catalyst for the Huisgen preparation of 1,4-disubstituted 1,2,3-triazoles in various organic and inorganic solvents [28], especially in [bmim]BF$_4$ [29]. Finally, we have reported a facile and one-pot synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from terminal alkynes and phenacyl azides prepared from styrenes by CAN oxidant and sodium azide. By this procedure, α-azido ketones were directly prepared in situ from various substituted styrenes using the oxidant cerium ammoniumnitrate and sodium azide [30]. Herein, with reference to our above-mentioned works, a one-pot synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from azideo iodides and terminal alkynes in which azideo iodide precursors are directly prepared in situ from various alkenes is reported. Considering the diversity of commercially available alkenes and the lack of any report on this procedure encouraged us to find a facile and straightforward way for the synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from alkenes. Such chemistry should not only circumvent the isolation of azide intermediates, hence saving time, reagents, and solvents, but also broaden the scope and application of the CuAAC.

Experimental

General

All of the 1,2,3-triazoles derivatives were prepared by our procedure. NMR spectra were recorded in DMSO-d$_6$ or CDCl$_3$ on Bruker AVANCE DPX 400 MHz instrument spectrometers using TMS as internal standard. IR spectra were recorded on a BOMEMMB-Series 1998 FT-IR spectrometer. Elemental analyses (C, H, and N) were performed with a Heraeus CHN-O-Rapid analyzer.

General procedure for synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles (2a-2m)

Alkene (1.2 mmol) was added to a stirred solution of molecular iodine (2 mmol) and sodium azide(3 mmol) in a mixture of solvents involve $CH_3OH/H_2O/PEG400$ (3:2:2 V/V), and allowed to stir at room temperature for 0.5-1.5 h (table 1). On completion of azido iodination reaction as was indicated by TLC, and confirmed by IR spectroscopy, sodium ascorbate 10% (0.2g in 5 mL of H_2O) was added to the mixture. After the brown solution became colorless, phenylacetylene (1 mmol) and CuSO$_4$ (0.05 g) were added and the mixture was stirred for another 0.5 h. After completion of click cyclization as indicated by TLC, the reaction mixture was diluted with water (10 mL) and the organic phase was extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous sodium sulfate, filtrated and distilled using rotary vacuum evaporator. The solid residue was recrystallized with ethanol/water (1:2 v/v) and dried in vacuum over night to give pure 1,4-disubstituted-1*H*-1,2,3-triazoles(table 1, entries 1-11).

Spectral data

2a) *1-(2-iodo-1-phenylethyl)-4-phenyl-1H-1,2,3-triazole*: white powder, 0.29 g M.p: 148-148.5°C,^{1}H NMR(400 MHz, DMSO-d$_6$): δ 8.88 (1H, s), 8.91-8.60(2H, d, *j=7.5 Hz*), 7.51-7.33(8H, m), 6.10-6.06(1H, dd, *j$_1$=10.7 Hz, j$_2$=5.14 Hz*), 4.25-4.20(1H, t, *j=10.7 Hz*), 4.10-4.02(1H, dd, *j$_1$=10.7 Hz, j$_2$=5.14 Hz*). ^{13}C NMR(100 MHz, DMSO-d$_6$): δ 146.97, 138.59, 130.95,

129.46, 129.39, 129.28, 128.52, 127.31, 125.56, 121.02, 66.20, 7.26. Anal. calcd. For $C_{16}H_{14}IN_3$: C, 51.22; H, 3.76; N, 11.20. Found: C, 51.20; H, 3.73; N, 11.22.

2b) *1-[2-(iodo-1-(4-methylphenyl)ethyl]-4-phenyl-1H-1,2,3-triazole*: white to yellow powder, 0.31 g, M.p.142-143°C, ^{1}H NMR(400 MHz, DMSO-d$_6$) δ 8.6(1H, s), 7.78-7.76(2H, d, j=8 Hz), 7.46-7.42(4H, m), 7.34-7.32(1H, m), 7.15-7.13(2H, d, j=8 Hz), 5.80-5.76(1H, dd, j_1=8.3 Hz, j_2=6.2 Hz), 4.28-4.23(1H, t; j_1=9.9 Hz), 3.90-3.86(1H, dd, j_1=8.3 Hz, j_2=6.2 Hz). ^{13}C NMR(100 MHz, CDCl$_3$) δ 139.8, 139.5, 134, 130.14, 129.9, 129.5, 129.2, 128.85, 128.47, 128.31, 126.82, 125.74, 67.2, 21.18, 5.02. Anal. calcd. For $C_{17}H_{16}IN_3$: C, 52.46; H, 4.14; N, 10.80. Found: C, 52.48; H, 4.12; N, 10.83.

2c) *1-[2-(iodo-1-(4-methoxyphenyl)ethyl]-4-phenyl-1H-1,2,3-triazole*: white powder, 0.33 g, M.p. 146-148°C; ^{1}H NMR(400 MHz, DMSO-d$_6$) δ 8.83(1H, s), 7.85-7.83(2H, d, j=8.35 Hz), 7.47-7.43(4H, m), 7.36-7.32(1H, t, j=7.3 Hz), 6.96-6.94(2H, d, j=8.35 Hz), 6.02-5.98(1H, dd, j_1=10.6 Hz, j_2=5.3 Hz), 4.20-4.15(1H, t, j=10.6 Hz), 4.052-4.012(1H, dd, j_1=10.6 Hz, j_2=5.3 Hz), 3.74(3H, s). ^{13}C NMR(100 MHz, CDCl$_3$): δ 140.2, 138.5, 134.2, 130.14, 129.8, 129.5, 129, 128.8, 128.4, 128.3, 126.72, 125.74, 77.2, 25.18, 8.10. Anal. calcd. For $C_{17}H_{16}IN_3O$: C, 50.39; H, 3.98; N, 10.37. Found: C, 50.31; H, 3.97; N, 10.40.

2d) *1-[1-(4-bromophenyl)-2-iodoethyl]-4-phenyl-1H-1,2,3-triazole*: white to yellow powder, 0.30 g, M.p. 137-139°C; ^{1}H NMR(400 MHz, CDCl$_3$) δ 7.84-7.82(2H, d, j=7.8 Hz), 7.77(1H, s), 7.57-7.55(2H, d, j=7.8 Hz), 7.45-7.42(2H, t, j=7.3 Hz), 7.38-7-28(3H, m), 5.77-5.73(1H, t; j=8.3 Hz), 4.24-4.19(1H, t, j=9.8 Hz), 3.88-3.84(1H, dd, j_1=8.3 Hz, j_2=6 Hz). ^{13}C

NMR(100 MHz, CDCl$_3$): δ 135.96, 132.51, 129.83, 129.22, 128.92, 128.65, 128.58, 125.89, 123.7, 119.8, 66.6, 4.37. Anal. calcd. For $C_{16}H_{13}BrIN_3$: C, 42.32; H, 2.89; N, 9.25. Found: C, 42.31; H, 2.91; N, 9.21.

2e) *1-{4-[2-iodo-1-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl]phenyl}-1-ethanone*: white powder, 0.35 g, M.p. 139-141°C; ^{1}H NMR(400 MHz, DMSO-d$_6$) δ 8.80(1H, s), 7.84-7.82(2H, d, j=8.3 Hz), 7.45-7..41(2H, d, j=7.8 Hz), 7.43-7.40(2H, t, j=7.2 Hz), 6.94-6.92(2H, d, j=8.3 Hz), 5.98-5.96(1H, dd, j_1=10.7 Hz, j_2=5.6 Hz), 4.18-4.13(1H, t, j=10.7 Hz), 4.04-4.00(1H, dd, j_1=10.7 Hz, j_2=5.6 Hz), 2.45(3H, s). ^{13}C NMR(100 MHz, CDCl$_3$): δ 195.1, 141., 138, 133.5, 130.2, 129.7, 129.4, 129, 128.7, 128.2, 128., 126.5, 125.4, 57.2, 26.2, 7.4. Anal. calcd. For $C_{18}H_{16}IN_3O$: C, 51.81; H, 3.87; N, 10.07. Found: C, 51.77; H, 3.90; N, 10.05.

2f) *1-(2-iodo-1-methyl-1-phenylethyl)-4-phenyl-1H-1,2,3-triazole*: white to yellow powder, 0.34 g, M.p. 133-135°C; ^{1}H NMR(400 MHz, CDCl$_3$) δ 7.89-7.88(3H, m), 7.44-7.48(3H, m), 7.47-7.44(3H, m), 7.41-7.36(3H, m), 7.16-7.13(2H, m), 4.43-4.40(1H, d, j=10.7 Hz), 4.09-4.06(1H, d, j=10.7 Hz), 2,27(3H, s). ^{13}C NMR(100 MHz, CDCl$_3$): δ 140.9, 130.6, 129, 128.9, 128.77, 128.48, 128.38, 127.89, 125.97, 125,44, 51.48, 28.59, 15.22. Anal. calcd. For $C_{17}H_{16}IN_3$: C, 52.46; H, 4.14; N, 10.80. Found: C, 52.42; H, 4.10; N, 10.83.

2g) *1-[1-(4-chloroophenyl)-2-iodoethyl]-4-phenyl-1H-1,2,3-triazole*: white powder, 0.35 g, M.p. 131-133°C; ^{1}H NMR(400 MHz, CDCl$_3$) δ 7.82-7.80(2H, d, j=7.8 Hz), 7.77(1H, s), 7.57-7.55(2H, d, j=7.8 Hz), 7.44-7.41(2H, t, j=7.3 Hz), 7.38-7-28(3H, m), 5.76-5.72(1H, dd, j_1=10.5 Hz, j_2=5.2 Hz), 4.24-4.19(1H, t, j=10.5 Hz), 3.86-3.82(dd, 1H, j_1=10.5 Hz,

j_2=5.2 Hz). ^{13}C NMR(100 MHz, CDCl$_3$): δ 135.8, 132.2, 129.5, 129.22, 128.90, 128.50, 128.48, 125.89, 123.8, 120, 67, 4.50. Anal. calcd. For C$_{16}$H$_{13}$ClIN$_3$: C, 46.91; H, 3.20; N, 10.26. Found: C, 46.94; H, 3.22; N, 10.25.

2h) *1-(1-benzyl-2-iodoethyl)-4-phenyl-1H-1,2,3-triazole*: white powder, 0.35 g, M.p. 125-127 ° C; ^{1}H NMR(500 MHz, CDCl$_3$) δ 7.85-7.83(d, 2H, j=6 Hz), 7.63(1H, s), 7.47-7.44(2H, t, *j*=6 Hz), 7.39-7.36(1H, t, *j*=5.8 Hz), 7.32-7.27(3H, m), 7.12-7.11(2H, d, *j*=6 Hz), 4.84-4.81(1H, m), 3.75-3.80(2H, m), 3.45-3.44(2H, d, *j*=5.8 Hz). ^{13}C NMR(100 MHz, CDCl$_3$): δ 140.12, 138.4, 129.5, 128.8, 128, 127.9, 127.2 126.8, 125.26, 113.5, 57.7, 29.8, 6.9. Anal. calcd. For C$_{17}$H$_{16}$IN$_3$: C, 52.46; H, 4.14; N, 10.80. Found: C, 52.45; H, 4.17; N, 10.79.

2i) *1-[1-(3,4-dimethoxybenzyl)-2-iodoethyl]-4-phenyl-1-H-1,2,3-triazole*: white powder, 0.31 g, M.p. 128-130 ˚C; ^{1}H NMR(400 MHz, DMSO-d$_6$) δ 8.6 (1H, s), 7.81-7.79(2H, d, *j*=7.2 Hz), 7.46-7.42(2H, t, *j*=7.5 Hz), 7.34-7.31(1H, t, *j*=7.2 Hz), 6.77-6.75(1H, d, *j*=8.1 Hz), 6.65-6.64(1H, m,), 6.58-6.57(1H, m), 5.05-4.95(1H, m), 3.85-3.82(1H, dd, j_1=7.3 Hz, j_2=3.8 Hz), 3.76-3.71(1H, dd, j_1=10 Hz, j_2=9 Hz), 3.65(3H, s), 3.60(3H, s), 3.31-3.27(1H, dd, j_1=7.2 Hz, j_2=3.8Hz), 3.19-3.14(1H, dd, j_1=10.5 Hz, j_2=9.4Hz). Anal. calcd. For C$_{19}$H$_{20}$IN$_3$O$_2$: C, 50.79; H, 4.49; N, 9.35. Found: C, 50.76; H, 4.52; N, 9.31.

2j) *1-(3-iodo-tetrahydro-2H-2-pyranyl)-4-phenyl-1H-1,2,3-triazole*: white powder, 0.35 g, M.p. 136-138 ˚C; ^{1}H NMR(400 MHz, DMSO-d$_6$) δ 8.4(1H, s), 7.89-7.87(2H, d, *j*=8 Hz), 7.65-7.61(2H, t, *j*=7.7 HZ), 7.49-7.45(1H, m), 6.35-6.33(1H, m, CHO), 4.43-4.40(1H, CHI), 3.89-3.79(1H, m, CH$_2$O), 3.75-3.62(1H, m, CH$_2$O), 2.45–

2.35(1H, m), 2.11-1.90(1H, m) 1.59–1.72(2H, m), ^{13}C NMR (100MHz, DMSO-d$_6$): 148.5, 130.3, 129.6, 129.3, 128.7, 127.5, 103.5, 67.2, 32.4, 24.9. Anal. calcd. For C$_{13}$H$_{14}$IN$_3$O: C, 43.96; H, 3.97; N, 11.83. Found: C, 43.95; H, 3.94; N, 11.87.

2k) *1-(3-iodo-tetrahydro-2-furanyl)-4-phenyl-1H-1,2,3-triazole*: white powder, 0.34 g, M.p. 134-136 ° C; ^{1}H NMR (400 MHz, DMSO-d$_6$): 8.53(1H, s), 7.84-7.82(2H, d, *j*=8.3 Hz), 7.58-7.54(2H, t, *j*=7.9 HZ), 7.51-7.47(1H, m), 6.21–6.17 (1H, m, CHO), 4.38–4.20 (3H, m, CH$_2$O, CHI), 2.60–2.47 (1H, m, CH$_2$), 2.28-2.18(1H, m, CH2), ^{13}C NMR (100 MHz, DMSO-d$_6$): 148.5, 131.1, 129.5, 129.3, 128.7, 127.6, 104.1, 67.4, 36.5, 27.0. Anal. calcd. For C$_{12}$H$_{12}$IN$_3$O: C, 42.25; H, 3.55; N, 12.32. Found: C, 42.28; H, 3.52; N, 12.35.

Results and discussion

One-step transformation of an alkene to the corresponding azideo iodide is easily possible with using of sodium azide and molecular iodine reagents in a mixture of solvents include CH$_3$OH/H$_2$O (3:2: v/v) [31]. We found that the addition of PEG 400 to this mixture can reduce the reaction times and also increase the yields since PEG works as solvent as well as phase transfer catalyst. At the first step, we began with styrene derivatives precursors and styrene was selected as model. Molecular iodine (2 mmol) and sodium azide (3 mmol) were dissolved in a mixture of CH$_3$OH/H$_2$O/PEG 400 (3:2:2 v/v), then styrene (1 mmol) was added to the mixture at room temperature. The azido iodination of styrene was completed after 45 min as reaction progress was checked by TLC and identified by IR spectroscopy with characteristics signals at about 2100-

2115 cm^{-1} for C-N$_3$ and 800-850 cm^{-1} for C-I bond, Scheme 1.

X= H, Me, OMe, Br, MeCO
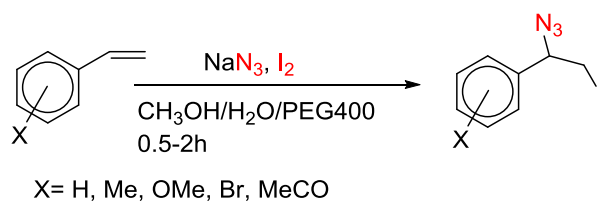
**Scheme 1.** Preparation of azido iodides from styrenes

At the first attempt for click cyclization of the prepared azido iodide, it was found that the extra amount of molecular iodine should be removed from reaction medium because the addition of phenylacetylene and copper(I) iodide to the reaction mixture did not lead to click cyclization. The reason of failed cyclization is that the alkynyl group of phenylacetylene underwent the addition reaction with extra amounts of molecular iodine in the same way as styrene before click cyclization. Consequently, at the second attempt, it was tried to remove the additional molecular iodine. After completion of azido iodination, aqua solution of sodium thiosulfate (Na$_2$S$_2$O$_3$ 5%) was added drop-wise until the dark brown mixture became colorless. The addition of phenylacetylene and CuI to the colorless mixture led to cyclization after 40 min but the product yield was very low. Working on the challenge to remove the additional amount of molecular iodine, it was found that sodium ascorbate is capable to reduce the molecular iodine quickly. Consequently, an experiment was followed in which after the azido iodination reaction an aqua solution of sodium ascorbate 10% was added drop-wise until the mixture became colorless; then CuSO$_4$ and phenylacetylene were added. Fortunately, these conditions led to click cyclization after 30 min at high yield, Scheme 2. The ^{1}H NMR spectrum of 2a (Table 1) exhibited a characteristic singlet at δ 8.88 for triazolyl C$_5$–H which is consistent with the disappearance of the azide signal in the IR spectrum. This characteristic singlet appeared in all the products and confirmed the regioselective synthesis of 1,4-disubstituted-1H-1,2,3-triazole regioisomers. It is worth noting that the chemical shift of triazolyl C$_5$–H depends on the ^{1}H-NMR solvent. Using CDCl$_3$ as solvent, this hydrogen appeared in 7.7-7.9 ppm and with DMSO_d$_6$, appeared in lower fields (8.3-8.9 ppm) probably because of the interaction between this acidic hydrogen and nonbonding electrons of oxygen from solvent. With a variety of substituted styrenes in hand, various azido iodides were prepared according to the aforementioned procedure and afterward were in situ subjected to click cyclization with phenylacetylene in the presence of sodium ascorbate and copper sulfate to afford desired 1,4-disubstituted-1*H*-1,2,3-triazole compounds, Scheme 2 and Table 1. It is noteworthy that sodium ascorbate was not only used as a reducer for Cu(II) but also for molecular iodine.

The phase transfer catalytic properties of PEG work in a similar fashion to those of crown ethers and these properties significantly reduced click cyclization times in comparison with other solvents. A simple technique was used for purification of the products.

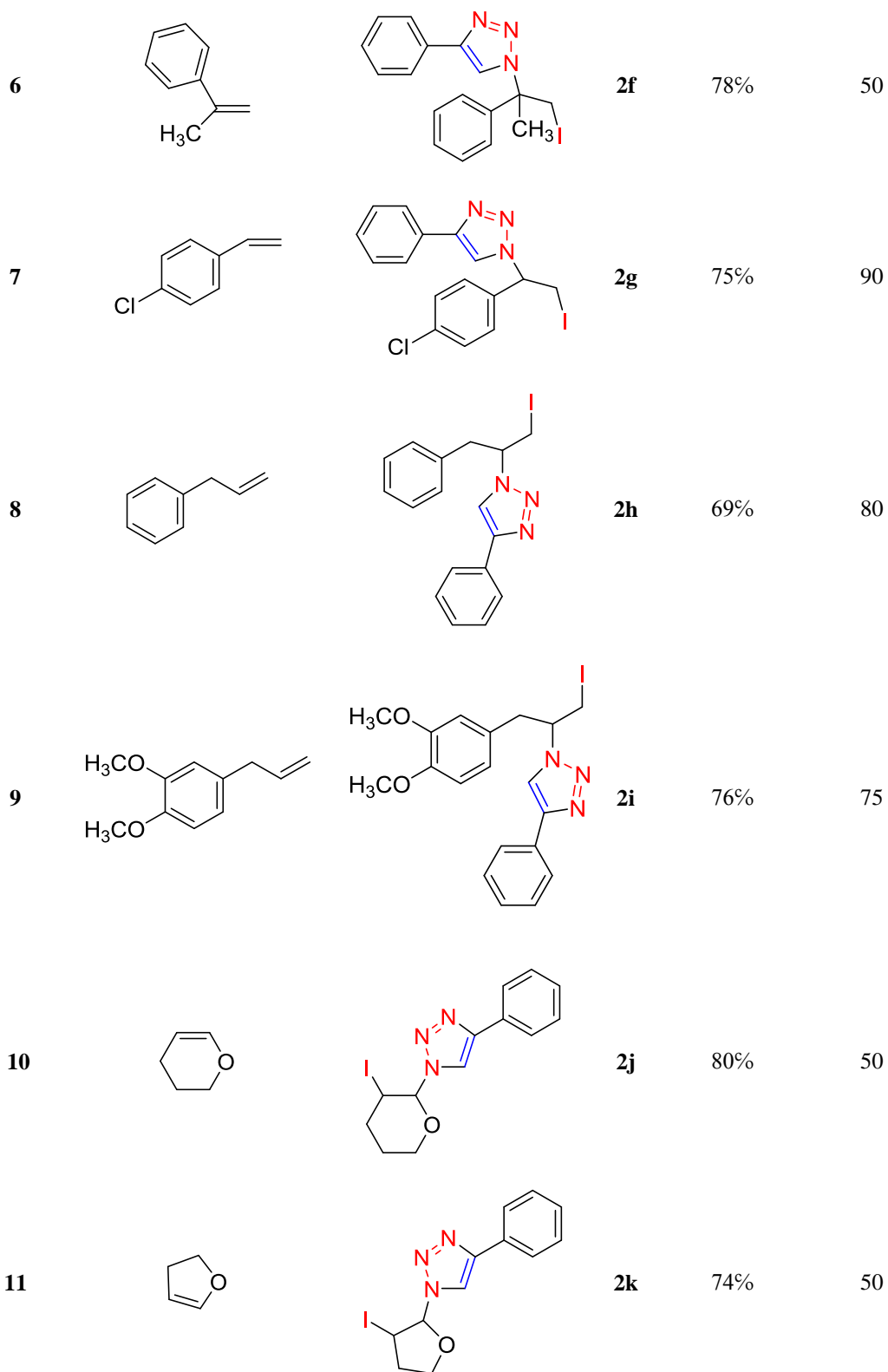The solid products were dissolved in minimum amount of alcohol and water was added drop-wise to give the pure product crystals (CH$_3$OH/H$_2$O, 1:2 v/v).
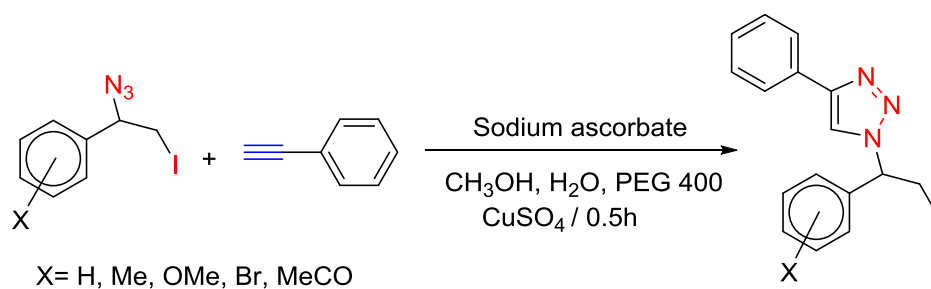
Scheme 2. Synthesis of 1,4-disubstituted triazoles from azido iodide

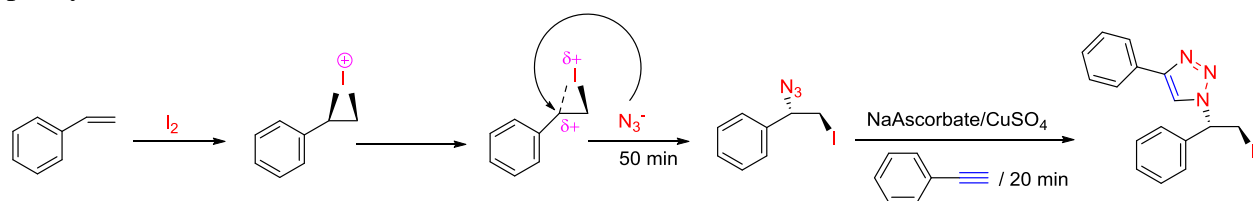**Table 1.** Synthesis of 1,4-disubstituted 1,2,3-triazoles from azido iodide

Entry	Alkene	1,2,3-triazole (2a-2m)		Yield[a] (%)	Time(min)
1			2a	75	70
2			2b	78%	65
3			2c	70%	50
4			2d	80%	75
5			2e	73%	70

6		**2f**	78%	50
7		**2g**	75%	90
8		**2h**	69%	80
9		**2i**	76%	75
10		**2j**	80%	50
11		**2k**	74%	50

[a]Yields of pure and isolated products

On the base of 1H-NMR spectra, in all the cases, azide anion attacked region specifically on the benzylic position of substituted styrenes (Table 1, Entries 1-7). In the cases of allylbenzene and 4-allyl-1,2-dimethoxybenzene, (Table 1, Entries 8 and 9), azide anion attacked only on more favorable secondary carbon of iodonium bridges and led to 1-(1-benzyl-2-iodoethyl)-4-phenyl-1H-1,2,3-triazole (2h) and 1-[1-(3,4-dimethoxybenzyl)-2-iodoethyl]-4-phenyl-1*H*-1,2,3-triazole (2i),

respectively. The proposed mechanism for typical synthesis of 1-(2-iodo-1-phenylethyl)-4-phenyl-1*H*-1,2,3-triazole from styrene is shown in Scheme 3. In the presence of molecular iodine, the iodonium bridge is obtained; attacking of azide anion on the more favorable benzylic position converts it to an azido iodide moiety which consecutively, in the presence of in situ prepared Cu(I), reacts with terminal alkyne to produce 1,4-disubstituted-1*H*-1,2,3-triazole.

Scheme 3. proposed mechanism for I$_2$/N$_3$ mediated 1,4-disubstituted-1*H*-1,2,3-triazole synthesis

From Table 1, for 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran (Entries 12 and 13), it can be seen that regiospecific attack of azide anion on the preferred carbons next to the ring

oxygens has occurred and in the following step, click cyclization has led to corresponding products. These observations are consistent with proposed mechanism, Scheme 4.
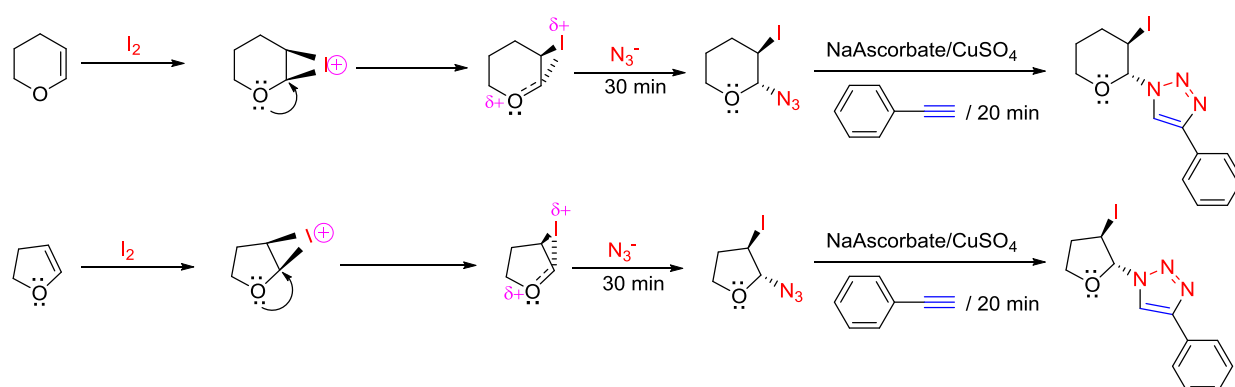
Scheme 4. Synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran

Conclusion

A one-pot multicomponent approach to the synthesis of some novel 1,4-disubstituted-1*H*-triazoles from alkenes at room temperature is reported. This method significantly reduces cyclization times, requires a simple purification technique and affords products quickly in high yields.

Supplementary material

Selected IR, ^{1}HNMR and ^{13}CNMR spectra of synthesized triazole products can be found in supplementary material.

References

[1] C.D. Hein, X.M. Liu, D. Wang, *Pharm. Res.,* **2008**, *25*, 2216–2230.

[2] A.D. Moorhouse, S. Haider, M. Gunaratnam, D. Munnur, S. Neidle, J.E. Moses, *Mol. BioSyst.,* **2008**, *4*,629–642.

[3] A.D. Moorhouse, J.E. Moses, *Chem. Med. Chem.,* **2008**, *3*, 715-723..

[4] M.V. Gil, M.J. Arevalo, O. Lopez, *Synthesis,* **2007**, *11*, 1589–1620.

[5] E.F.V. Scriven, K. Turnbull, *Chem. Rev*., **198**8, *88*, 297-300.

[6] A.K. Feldman, B. Colasson, V.V. Fokin, *Org. Lett.,* **2004**, *6*, 3897-3900.

[7] P. Appukkuttan, W. Dehaen, V.V. Fokin, E. Van der Eycken, *Org. Lett.,* **2004**, *6*, 4223-4225.

[8] J.A. Demaray, J.E. Thuener, M.N. Dawson, S.J. Sucheck, *Bioorg. Med. Chem. Lett.,* **2008**, *18*, 4868-4872.

[9] K.A. Dururgkar, R.G. Gonnade, C.V. Ramana, *Tetrahedron*, **2009**, *65*, 3974-3978.

[10] K. Odlo, E.A. Høydahl, T.V. Hansen, *Tetrahedron Lett.,* **2007**, *48*, 2097-3001.

[11] V.S. Sudhir, R.B.N. Baig, S. Chandrasekaran, *Eur. J. Org. Chem*., **2008**, 2423-2427.

[12] D. Kumar, *et al., Synlett*, **2009**, *3*, 399-402.

[13] D. Kumar, V.B. Reddy, R.S. Varma, *Tetrahedron Lett*., **2009**, *50*, 2065-2068.

[14] C.Z. Tao, X. Cui, J. Li, A.X. Liu, L. Liu, Q.X. Guo, *Tetrahedron Lett*., **2007**, *48*, 3525-3528.

[15] J.S. Yadav, B.V.S. Reddy, G.M. Reddy, D.N. Chary, *Tetrahedron Lett*., **2007**, *48*, 8773-8775.

[16] G. Kumaraswamy, K. Ankamma, A. Pitchaiah, *J. Org. Chem*., **2007**, *72*, 9822-98.26.

[17] B. Sreedhar, P.S. Reddy, V.R. Krishna, *Tetrahedron Lett*., **2007**, *48*, 5831-58-34.

[18] J.S. Yadav, B.V.S. Reddy, D.N. Chary, C.H.S. Reddy, *Tetrahedron Lett*., **2008**, *49*, 2649-2652.

[19] S. Chittaboina, F. Xie, Q. Wang, *Tetrahedron Lett.,* **2005**, *46*, 2331-2334.

[20] S. Fukuzawa, E. Shimizu, S. Kikuchi, *Synlett*, **2007**, *15*, 2436-2438.

[21] N.M. Smith, M.J. Greaves, R. Jewell, M.W.D. Perry, M.J. Stocks, J.P. Stonehouse, *Synlett*, **2009**, *9*, 1391-1394.

[22] S. Maisonneuve, J. Xie, *Synlett*, **2009**, *18*, 2977-2981.

[23] J. Albadi, M. Keshavarz, F. Shirini, M. Vafaie-nezhad, *Catal. Commun.,* **201**2, *27*, 17-20.

[24] J. Albadi, M. Keshavarz, M. Abedini, M. Vafaie-nezhad, *Chin.Chem. Lett*., **2012**, *23*, 797-800.

[25] S. Saadat, S. Nazari, M. Afshari, M. Keshavarz, *Orient. J. Chem*., **2015**, *31*, 1005-1012.

[26] M. Keshavarz, N. Iravani, A. Ghaedi, A. Zarei Ahmady, M. Vafaei-Nezhad, S. Karimi, *SpringerPlus*., **2013**, *2*, 64-70.

[27] J. Albadi, M. Keshavarz, *Synthetic. Commun*., **2013**, *43*, 2119-2030.

[28] A. Zarei Ahmady, F. Heidarizadeh, M. Keshavarz, *Synthetic. commun*., **2013**, *43*, 2100-2109.

[29] M. Keshavarz, B. Karami, A. Zarei Ahmady, A. Ghaedi, H. Vafaei, *C.R. Chimie*. **2014**, *17*, 570-576.

[30] M. Keshavarz, R. Badri, *Mol. Divers*., **2011**, *15*, 957-962.

[31] A.O. Terent'ev, et al. *Synthetic. Commun*., **2008**, *38*, 3797-3809.