

## PAPER

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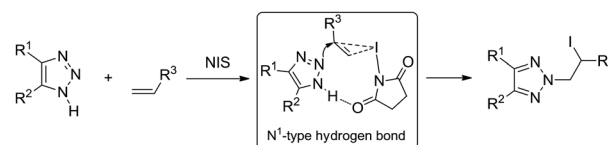
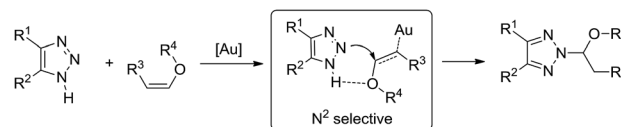
# N<sup>2</sup>-selective alkylation of NH-1,2,3-triazoles with vinyl ethers *via* gold catalysis†

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A new method was developed to synthesize N<sup>2</sup>-alkyl-substituted 1,2,3-triazoles *via* gold catalyzed alkylation of vinyl ethers with mono- and unsubstituted NH-1,2,3-triazoles and benzotriazole. A hydrogen bond between the oxygen atom of the vinyl ethers, activated *via* the gold catalyst, and the NH-1,2,3-triazoles was supposed to be generated, which selectively gave the N<sup>2</sup>-alkylation products.

## Introduction

Substituted 1,2,3-triazoles are among the most important N-heterocyclic compounds and display a broad spectrum of applications in the areas of medicinal chemistry, agrochemicals, and materials science.<sup>1</sup> 1,2,3-Triazoles containing heterocyclic compounds serve as intermediates for the synthesis of biologically active compounds.<sup>2</sup> Both thermal and Cu(I)/Ru(II)-catalyzed condensations of alkynes and azides provide an excellent approach to N<sup>1</sup>-substituted triazoles.<sup>3</sup> However, the synthesis of N<sup>2</sup>-substituted triazoles remains a challenge.<sup>4,5</sup> A particularly interesting subset of these compounds are N<sup>2</sup>-alkyl-1,2,3-triazoles, which possess a broad spectrum of antiherpetic, antiarrhythmic and antiviral activities.<sup>6</sup> Ideally, the most direct route to N<sup>2</sup>-alkyl-1,2,3-triazoles involves nucleophilic substitution of alkylating reactants with NH-1,2,3-triazoles, however, a mixture of the isomeric products is often produced.<sup>7</sup> Recently, the N<sup>2</sup>-selective alkylation reactions of alkyl halides with 1,2,3-triazoles have been achieved by incorporating C-4- and C-5-substituents on the heteroarenes, of which the synthetic utility was thus restricted by the substrate's steric requirements. Another route to the N<sup>2</sup>-alkyl-1,2,3-triazoles, addition of 1-sulfonyl-1,2,3-triazoles to olefins or vinyl ethers catalyzed by TSOH or gold catalyst, was reported by Chen and our group.<sup>8</sup> Very recently, Chen and co-workers reported the highly N<sup>2</sup>-selective alkylation reactions of NH-1,2,3-triazoles with olefins mediated by NIS,<sup>9</sup> in which the favored N<sup>1</sup>-type intermolecular hydrogen bonding connection during the transition state provides the coupling adduct with a high N<sup>2</sup>-selectivity (Scheme 1a). Based on our previous report of gold catalyzed N<sup>2</sup> alkylation of 1-sulfonyl-1,2,3-triazoles with vinyl ethers,<sup>8b</sup> we hope to extend this reaction involving the use of NH-1,2,3-triazoles as nucleophiles, in which the hydrogen bond

(a) chen group : NIS mediated N<sup>2</sup> alkylation of NH-1,2,3-triazoles with olefins(b) this work : gold catalyzed N<sup>2</sup> alkylation of NH-1,2,3-triazoles with vinyl ethersScheme 1 N<sup>2</sup> alkylation of NH-1,2,3-triazoles.

between the oxygen atom of vinyl ethers activated *via* gold catalyst with NH-1,2,3-triazoles produces N<sup>2</sup>-alkyl-1,2,3-triazoles (Scheme 1b).

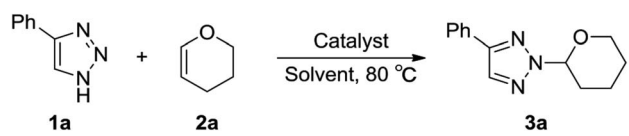
## Results and discussion

Based on our previous results with respect to the N<sup>2</sup>-selective gold-catalyzed alkylation of 1-sulfonyl-1,2,3-triazoles,<sup>8b</sup> we began our studies by exploring the reaction between NH-1,2,3-triazole (**1a**) and vinyl ether (**2a**). The optimization results are summarized in Table 1. To our delight, the desired N<sup>2</sup>-alkyl-1,2,3-triazole **3a** was obtained in 95% yield in the presence of Ph<sub>3</sub>PAuCl (5 mol%)/AgNTf<sub>2</sub> (5 mol%) in 1,2-dichloroethane (DCE) at 80 °C, without a N<sup>1</sup>-coupling adduct (Table 1, entry 1). In order to optimize the reaction conditions, different silver salts were screened, of which Ph<sub>3</sub>PAuCl/AgNTf<sub>2</sub> was found to be the best silver combination (Table 1, entries 2 and 3). The catalyst ligands were then evaluated. The N-heterocyclic carbene ligand IPrAuCl showed moderate activity, while the phosphine ligand JohnphosAuCl was not favored in this transformation, affording **3a** in only 30% yield (Table 1, entries 4 and 5). Further solvent optimization identified DCE to be the best

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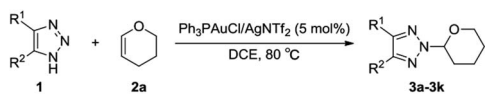
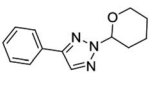
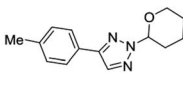
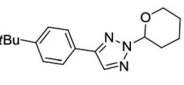
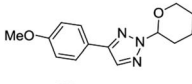
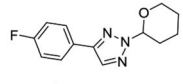
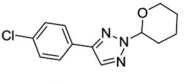
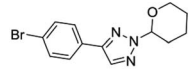
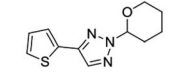
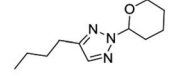

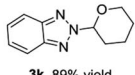
† Electronic supplementary information (ESI) available. See DOI: 10.1039/c8ra04790a

Table 1 Condition optimization for the reaction of **1a** with **2a**<sup>a</sup>

				
Entry	Cat. (mol%)	Solvent	Time (h)	Yield <sup>b</sup> (%)
1	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	DCE	6	95
2	Ph <sub>3</sub> PAuCl/AgOTf (5)	DCE	6	81
3	Ph <sub>3</sub> PAuCl/AgSbF <sub>6</sub> (5)	DCE	6	75
4	IPrAuCl/AgNTf <sub>2</sub> (5)	DCE	6	79
5	JohnphosAuCl/AgNTf <sub>2</sub> (5)	DCE	6	30
6	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	DCM	6	34
7	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	CHCl <sub>3</sub>	6	24
8	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	CH <sub>3</sub> CN	6	60
9	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	Toluene	6	71
10 <sup>c</sup>	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	DCE	22	69
11 <sup>d</sup>	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (5)	DCE	24	65
12	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> (2)	DCE	24	72
13 <sup>e</sup>	Ph <sub>3</sub> PAuCl (5)	DCE	24	NR
14 <sup>e</sup>	AgNTf <sub>2</sub> (5)	DCE	24	NR

<sup>a</sup> Unless noted, all reactions were carried out at the 0.1 mmol scale in 3 mL solvent with the addition of 5 mol% catalyst (**1a/2a** = 1/3) at 80 °C, NR = no reaction. <sup>b</sup> Isolated yield. <sup>c</sup> 100 mg 4 Å MS was added. <sup>d</sup> 2 Equiv. **2a** was added. <sup>e</sup> No consumption of starting material **1a** was seen after 24 h.

Table 2 Variation of the NH-1,2,3-triazoles **1**<sup>a,b</sup>

		
 <b>3a</b> , 95% yield	 <b>3b</b> , 80% yield	 <b>3c</b> , 80% yield
 <b>3d</b> , 87% yield	 <b>3e</b> , 56% yield	 <b>3f</b> , 64% yield
 <b>3g</b> , 76% yield	 <b>3h</b> , 77% yield	 <b>3i</b> , 72% yield
 <b>3j</b> , 61% yield	 <b>3k</b> , 89% yield	

<sup>a</sup> Unless noted, all reactions were carried out at the 0.1 mmol scale in 3 mL solvent with the addition of 5 mol% catalyst (**1/2a** = 1/3) at 80 °C. <sup>b</sup> Isolated yield.

reaction medium (Table 1, entries 6–9). The addition of 4 Å molecular sieves resulted in a decreased conversion into **3a** in 69% yield after 22 hours (Table 1, entry 10), due to the possible gold catalyst poisons contained in molecular sieves.<sup>10</sup> Variation of the number of equivalents of **2a** from 3.0 to 2.0 lowered the

conversion of **3a** to 65% (Table 1, entry 11), which indicates that the excess of vinyl ether probably is necessary due to the high tendency of vinyl ethers to undergo cationic polymerization initiated by gold(I).<sup>11</sup> Decreasing the catalyst loading to 2 mol% led to reduced reaction yield of 72% (Table 1, entry 12). In the control experiments, employing Ph<sub>3</sub>PAuCl and AgNTf<sub>2</sub> separately gave none of the desired product (Table 1, entries 12 and 13) even after 24 hours.

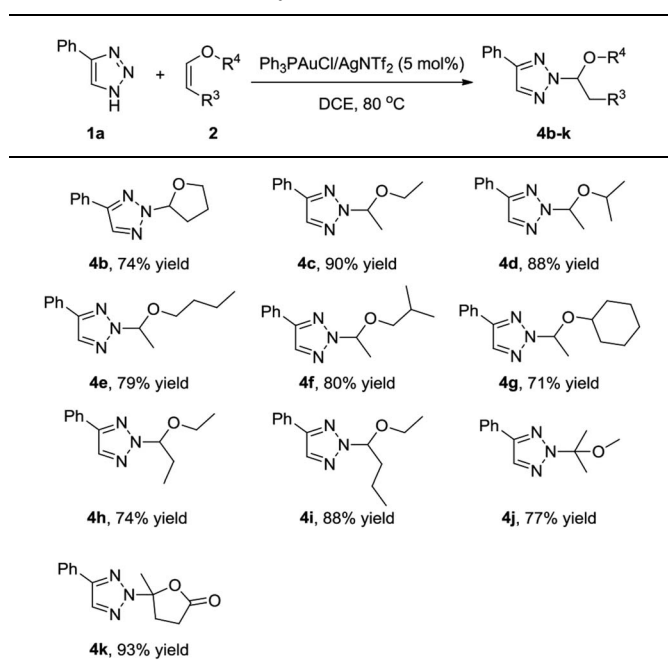
With the optimized reaction conditions in hand, we examined the scope of this transformation by synthesizing a series N<sup>2</sup>-alkyl-1,2,3-triazoles. As shown in Table 2, various NH-1,2,3-triazoles were explored by using vinyl ether **2a** as the reactants. First, various 4-aryl substituted NH-1,2,3-triazoles were explored. The NH-1,2,3-triazoles containing electron-donating functional groups, such as methyl, *t*-butyl, and methoxy, at the *para* position of the aromatic ring gave comparably good yields (80–87%) of the desired N<sup>2</sup>-alkyl-1,2,3-triazoles. However, 4-halogen phenyl substituted NH-1,2,3-triazoles gave the corresponding products in moderate yields, in which the more electron deficient triazole rings reduced their nucleophilicities. The reaction of 2-thienyl substituted NH-1,2,3-triazoles went smoothly, affording **3h** in 77% yield. Moreover, 4-alkyl substituted NH-1,2,3-triazoles **1i** and unsubstituted NH-1,2,3-triazole **1j** could also provide the corresponding N<sup>2</sup>-alkyl-substituted 1,2,3-triazoles **3i** and **3j** in moderate yields. Benzo-triazole **1k** was also tested, giving **3k** in 89% yield.

We next set out to explore the scope of vinyl ethers **2** in the presence of 4-phenyl substituted 1,2,3-triazole **1a** (Table 3). First, cyclic vinyl ether 2,3-dihydrofuran **2b** worked very well, giving **4b** in 74% yield. Next, we investigated the linear vinyl ether's reactions. We found that mono-substituted and 1,2-disubstituted linear vinyl ether could be employed in this reaction and gave the desired products in good yields. Moreover, 1,1-disubstituted vinyl ether **2j** could also provide the desired N<sup>2</sup>-alkyl-1,2,3-triazole **4j** in 77% yield. This reaction was also efficient with alpha-angelica lactone, giving **4k** in 93% yield.

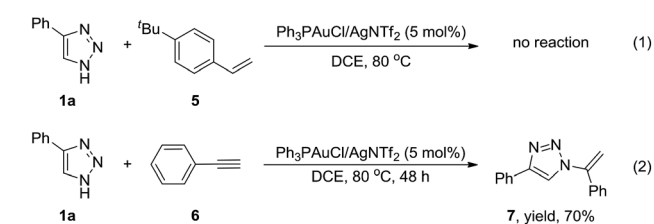
In order to understand the mechanism for the regioselective synthesis of N<sup>2</sup>-alkyl-1,2,3-triazoles, we performed two control experiments. First, we replaced vinyl ether with 4-*tert*-butylstyrene in the model reaction, no product was obtained. This may be due to the lower complexation of olefin with gold (Scheme 2(1)). Then, we performed this reaction in the presence of phenylacetylene, N<sup>1</sup>-vinyl substituted 1,2,3-triazole **7** was obtained in 70% yield, which was in accordance with our previous report (Scheme 2(2)).<sup>12</sup> The two control experiments suggested that the N<sup>2</sup>-regioselectivity may be induced by the substrate vinyl ethers in this reaction.

Based on our experimental results and precedents in the literature, a proposed catalytic cycle for the N<sup>2</sup>-selective alkylation is presented in Scheme 3. Initial complexation of gold could occur *via* pathway A<sup>8a</sup> or B.<sup>13</sup> Pathway A shows a one-step process involving the nucleophilic attack of the internal nitrogen of the NH-1,2,3-triazole **1a** on Au(I)-coordinated vinyl ether **2a** through the hydrogen bond interaction to form the alkyl gold intermediate. This subsequently undergoes protodemetalation<sup>14</sup> giving the N<sup>2</sup>-alkyl-1,2,3-triazole **3a**. Pathway B shows a two-step process invoking a triazole–Au complex, which then activated vinyl ether

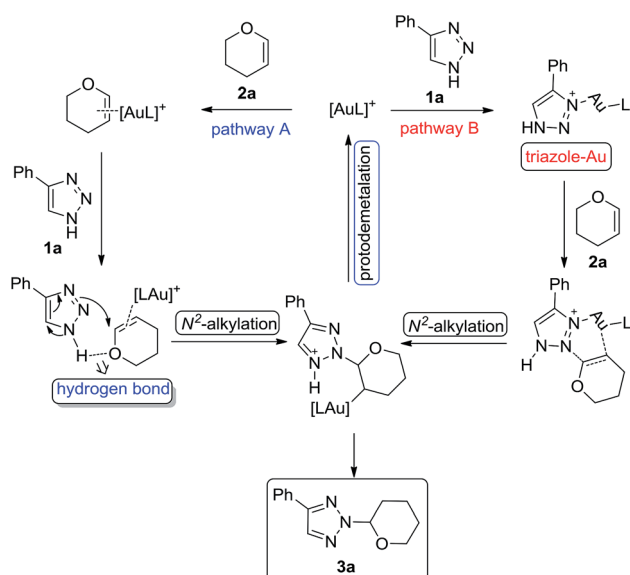


Table 3 Variation of the vinyl ethers 2<sup>a,b</sup>

<sup>a</sup> Unless noted, all reactions were carried out at the 0.1 mmol scale in 3 mL solvent with the addition of 5 mol% catalyst (1a/2 = 1/3) at 80 °C. <sup>b</sup> Isolated yield.



Scheme 2 Control experiments.

Scheme 3 Proposed catalytic cycle for the N<sup>2</sup>-selective alkylation.

and subsequently undergoes N<sup>2</sup>-selective alkylation with the internal nitrogen of the NH-1,2,3-triazole **1a** to give the alkyl gold intermediate. This subsequently undergoes protodemetalation<sup>14</sup> giving the N<sup>2</sup>-alkyl-1,2,3-triazole **3a**. However, pathway B might be unfavorable because the N<sup>2</sup>-vinyl substituted 1,2,3-triazole could not be observed in our control experiment (Scheme 2(2)).

## Conclusions

In summary, we have developed a new method to synthesis N<sup>2</sup>-alkyl-1,2,3-triazoles through gold catalyzed alkylation of vinyl ethers with NH-1,2,3-triazoles. The reaction is facile, high yielding and regioselective. The regioselectivity may be induced by the hydrogen bond between the oxygen atom of vinyl ethers with NH-1,2,3-triazole. The potential utilization and extension of this interesting synthetic methodology are currently underway.

## Experimental

### General methods

All reactions were performed using Schlenk-tubes, septa, and syringes under nitrogen atmosphere. Commercial reagents were used as supplied or purified by standard techniques where necessary. Column chromatography was performed using 200–300 mesh silica with the proper solvent system according to TLC analysis using KMnO<sub>4</sub> stain and UV light to visualize the reaction components. Unless otherwise noted, nuclear magnetic resonance spectra were recorded on a Agilent 400 MHz spectrometer using CDCl<sub>3</sub> with TMS as internal reference at room temperature. NMR data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and bs = broad singlet), coupling constant in Hz and integration. Chemical shifts for <sup>13</sup>C NMR spectra were recorded in parts per million from tetramethylsilane using the central peak of deuteriochloroform (77.0 ppm) as the internal standard. Melting points were determined on a WRS-1B digital melting point instrument. IR spectra were obtained on Nicoletisso FTIR using KBr disks. HR-MS spectral were determined on a Bruker Daltonics Bio TOF mass spectrometer. NH-1,2,3-triazoles **1a–1m** were prepared according to the published methods.<sup>14</sup> Vinyl ethers were obtained commercially and used without further purification.

### General procedure for synthesis of compound **3a**

To a Schlenk tube charged with nitrogen was added Ph<sub>3</sub>PAuCl/AgNTf<sub>2</sub> (5 mol%) in dry DCE (3 mL). After three minutes, NH-1,2,3-triazole **1a** (0.1 mmol), vinyl ether **2a** (0.3 mmol) were added to the reaction. Then the reaction mixture was stirred at 80 °C for 6 h until complete consumption of starting material as monitored by TLC. Concentration of the reaction mixture *in vacuo* followed by purification through flash chromatography on silica gel column (hexane/EtOAc = 30/1) afforded N<sup>2</sup>-alkyl-substituted 1,2,3-triazole **3a**.

**4-Phenyl-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3a).** The spectroscopic data are in accordance with those reported.<sup>5b</sup>



Yield: 21.8 mg (95%); yellow oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3475, 2951, 1611, 1391, 1063  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92 (s, 1H), 7.82 (d,  $J$  = 7.7 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.35 (t,  $J$  = 6.9 Hz, 1H), 5.75 (d,  $J$  = 8.8 Hz, 1H), 4.08 (d,  $J$  = 11.3 Hz, 1H), 3.77 (t,  $J$  = 10.4 Hz, 1H), 2.52–2.45 (m, 1H), 2.15–2.10 (m, 2H), 1.74–1.72 (m, 2H), 1.69–1.63 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.1, 131.5, 130.1, 128.8, 128.5, 126.1, 89.1, 67.5, 29.4, 24.7, 21.8.

**2-(Tetrahydro-2H-pyran-2-yl)-4-(*p*-tolyl)-2H-1,2,3-triazole (3b).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 19.4 mg (80%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3466, 2955, 1645, 1398, 1070  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.89 (s, 1H), 7.71 (d,  $J$  = 8.0 Hz, 2H), 7.23 (d,  $J$  = 7.9 Hz, 2H), 5.73 (dd,  $J$  = 9.3, 2.4 Hz, 1H), 4.08 (d,  $J$  = 11.4 Hz, 1H), 3.80–3.73 (m, 1H), 2.54–2.44 (m, 1H), 2.38 (s, 3H), 2.17–2.08 (m, 2H), 1.78–1.72 (m, 2H), 1.68–1.62 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.2, 138.5, 131.4, 129.5, 127.2, 125.9, 89.1, 77.3, 29.4, 24.8, 21.9, 21.3.

**4-(4-(*tert*-Butyl)phenyl)-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3c).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 22.8 mg (80%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3470, 2970, 1644, 1490, 1092  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.88 (s, 1H), 7.74 (d,  $J$  = 8.4 Hz, 2H), 7.44 (d,  $J$  = 8.3 Hz, 2H), 5.77–5.70 (m, 1H), 4.06 (d,  $J$  = 11.4 Hz, 1H), 3.76 (t,  $J$  = 9.7 Hz, 1H), 2.51–2.43 (m, 1H), 2.14–2.08 (m, 2H), 1.75–1.71 (m, 2H), 1.67–1.62 (m, 1H), 1.33 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  151.7, 148.1, 131.5, 127.3, 125.9, 125.7, 89.1, 67.5, 34.7, 31.3, 29.4, 24.8, 21.9.

**4-(4-Methoxyphenyl)-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3d).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 22.6 mg (87%); yellow oil liquid;  $R_f$  = 0.10 (hexane–EtOAc, 10 : 1). IR (neat): 3467, 2954, 1631, 1396, 1058  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.83 (s, 1H), 7.73 (d,  $J$  = 8.5 Hz, 2H), 6.94 (d,  $J$  = 8.7 Hz, 2H), 5.71 (dd,  $J$  = 9.5, 2.6 Hz, 1H), 4.06 (d,  $J$  = 11.5 Hz, 1H), 3.83 (s, 3H), 3.74 (t,  $J$  = 11.2, 1H), 2.50–2.43 (m, 1H), 2.14–2.07 (m, 2H), 1.75–1.70 (m, 2H), 1.68–1.63 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  159.9, 148.0, 131.1, 127.4, 122.8, 114.2, 89.1, 67.5, 55.3, 29.4, 24.8, 21.9.

**4-(4-Fluorophenyl)-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3e).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 13.8 mg (56%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3477, 2959, 1617, 1397, 1094  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.86 (s, 1H), 7.80–7.75 (m, 2H), 7.10 (t,  $J$  = 8.6 Hz, 2H), 5.72 (dd,  $J$  = 9.1, 2.0 Hz, 1H), 4.06 (d,  $J$  = 11.4 Hz, 1H), 3.75 (t,  $J$  = 10.7 Hz, 1H), 2.49–2.42 (m, 1H), 2.13–2.07 (m, 2H), 1.74–1.71 (m, 2H), 1.68–1.63 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  162.9 (d,  $J$  = 246.5 Hz), 147.3, 131.3, 127.9 (d,  $J$  = 8.2 Hz), 126.4, 115.8 (d,  $J$  = 21.6 Hz), 89.2, 67.5, 29.4, 24.8, 21.9.

**4-(4-Chlorophenyl)-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3f).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 16.8 mg (64%); yellow oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3475, 2971, 1645, 1393, 1093  $\text{cm}^{-1}$ .  $^1\text{H}$

NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.90 (s, 1H), 7.76 (d,  $J$  = 8.3 Hz, 2H), 7.40 (d,  $J$  = 8.2 Hz, 2H), 5.77–5.72 (m, 1H), 4.08 (d,  $J$  = 11.8 Hz, 1H), 3.79 (d,  $J$  = 9.9 Hz, 1H), 2.51–2.43 (m, 1H), 2.16–2.09 (m, 2H), 1.77–1.72 (m, 2H), 1.69–1.66 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.1, 134.4, 131.5, 129.0, 128.7, 127.3, 89.2, 67.5, 29.4, 24.8, 21.8.

**4-(4-Bromophenyl)-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3g).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 17.7 mg (76%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3470, 2948, 1645, 1387, 1066  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.93 (s, 1H), 7.72 (d,  $J$  = 8.4 Hz, 2H), 7.58 (d,  $J$  = 8.3 Hz, 2H), 5.79–5.74 (m, 1H), 4.10 (d,  $J$  = 11.7 Hz, 1H), 3.79 (d,  $J$  = 9.9 Hz, 1H), 2.53–2.45 (m, 1H), 2.18–2.12 (m, 2H), 1.78–1.71 (m, 2H), 1.72–1.67 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.1, 131.9, 131.5, 129.1, 127.6, 122.6, 89.2, 67.5, 29.4, 24.8, 21.8.

**2-(Tetrahydro-2H-pyran-2-yl)-4-(thiophen-2-yl)-2H-1,2,3-triazole (3h).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 18.1 mg (77%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3470, 2951, 1648, 1392, 1075  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.80 (s, 1H), 7.64 (d,  $J$  = 1.4 Hz, 1H), 7.47 (d,  $J$  = 5.0 Hz, 1H), 7.39–7.34 (m, 1H), 5.71 (dd,  $J$  = 9.0, 1.9 Hz, 1H), 4.06 (d,  $J$  = 11.4 Hz, 1H), 3.74 (t,  $J$  = 10.6 Hz, 1H), 2.49–2.42 (m, 1H), 2.13–2.06 (m, 2H), 1.74–1.72 (m, 2H), 1.69–1.63 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  144.3, 131.7, 131.5, 126.4, 126.0, 122.0, 89.1, 67.5, 29.4, 24.8, 21.9.

**4-Butyl-2-(tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3i).** Yield: 15.1 mg (72%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3464, 2931, 1658, 1266, 1092  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36 (s, 1H), 5.55 (dd,  $J$  = 9.5, 1.6 Hz, 1H), 3.98 (d,  $J$  = 11.6 Hz, 1H), 3.65 (t,  $J$  = 10.7 Hz, 1H), 2.62 (t,  $J$  = 7.8 Hz, 2H), 2.33 (dd,  $J$  = 20.2, 9.8 Hz, 1H), 2.00 (t,  $J$  = 14.0 Hz, 2H), 1.68–1.52 (m, 5H), 1.31 (dd,  $J$  = 14.9, 7.4 Hz, 2H), 0.86 (t,  $J$  = 7.3 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.3, 133.2, 88.8, 67.6, 31.2, 29.4, 25.2, 24.8, 22.3, 22.1, 13.8. HRMS (ESI):  $m/z$  [ $M$  +  $H$ ]<sup>+</sup> calcd for  $\text{C}_{11}\text{H}_{20}\text{N}_3\text{O}^+$ : 210.1601; found: 210.1599.

**2-(Tetrahydro-2H-pyran-2-yl)-2H-1,2,3-triazole (3j).** Yield: 9.3 mg (61%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3454, 2954, 1661, 1358, 1095  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.68 (s, 2H), 5.73 (d,  $J$  = 9.1 Hz, 1H), 4.04 (d,  $J$  = 11.5 Hz, 1H), 3.77–3.71 (m, 1H), 2.48–2.39 (m, 1H), 2.09–2.06 (m, 2H), 1.73–1.65 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.6, 88.9, 67.4, 29.4, 24.7, 21.8. HRMS (ESI):  $m/z$  [ $M$  +  $H$ ]<sup>+</sup> calcd for  $\text{C}_7\text{H}_{12}\text{N}_3\text{O}^+$ : 154.0975; found: 154.0968.

**2-(Tetrahydro-2H-pyran-2-yl)-2H-benzo[d][1,2,3]triazole (3k).** Yield: 18.1 mg (89%); colorless oil liquid;  $R_f$  = 0.10 (hexane–EtOAc, 10 : 1). IR (neat): 3467, 2940, 1664, 1274, 1086  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.07 (d,  $J$  = 8.4 Hz, 1H), 7.74 (d,  $J$  = 8.3 Hz, 1H), 7.49 (t,  $J$  = 7.6 Hz, 1H), 7.38 (t,  $J$  = 7.7 Hz, 1H), 6.04 (dd,  $J$  = 8.2, 2.7 Hz, 1H), 3.95 (dd,  $J$  = 11.7, 4.6 Hz, 1H), 3.83–3.75 (m, 1H), 2.68–2.57 (m, 1H), 2.23–2.19 (m, 1H), 1.90–1.71 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  127.4, 124.1, 119.9, 111.1, 85.6, 66.8, 29.3, 24.9, 21.6. HRMS (ESI):  $m/z$  [ $M$  +  $H$ ]<sup>+</sup> calcd for  $\text{C}_{11}\text{H}_{14}\text{N}_3\text{O}^+$ : 204.1131; found: 204.1130.

**4-Phenyl-2-(tetrahydrofuran-2-yl)-2H-1,2,3-triazole (4b).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>





Yield: 15.9 mg (74%); colorless oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3474, 2979, 1645, 1381, 1074  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.97 (s, 1H), 7.89 (d,  $J$  = 7.4 Hz, 2H), 7.52 (t,  $J$  = 7.6 Hz, 2H), 7.45 (t,  $J$  = 7.3 Hz, 1H), 6.43 (dd,  $J$  = 6.7, 2.3 Hz, 1H), 4.30 (dd,  $J$  = 14.1, 7.6 Hz, 1H), 4.16 (dd,  $J$  = 14.0, 7.7 Hz, 1H), 2.83–2.76 (m, 1H), 2.59–2.48 (m, 2H), 2.25–2.16 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.0, 131.4, 130.3, 128.8, 128.5, 126.0, 92.3, 69.6, 31.4, 24.5.

**2-(1-Ethoxyethyl)-4-phenyl-2H-1,2,3-triazole (4c).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 19.5 mg (90%); colorless oil liquid;  $R_f$  = 0.40 (hexane–EtOAc, 10 : 1). IR (neat): 3466, 3001, 1650, 1357, 1125  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.07 (s, 1H), 7.98 (d,  $J$  = 7.1 Hz, 2H), 7.59 (t,  $J$  = 7.4 Hz, 2H), 7.51 (t,  $J$  = 7.4 Hz, 1H), 5.96 (q,  $J$  = 6.0 Hz, 1H), 3.75–3.68 (m, 1H), 3.58–3.50 (m, 1H), 2.00 (d,  $J$  = 6.0 Hz, 3H), 1.32 (t,  $J$  = 7.0 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.8, 131.3, 130.3, 128.8, 128.5, 126.0, 89.5, 64.6, 20.9, 14.7.

**2-(1-Isopropoxyethyl)-4-phenyl-2H-1,2,3-triazole (4d).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 20.3 mg (88%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3473, 2972, 1649, 1375, 1118  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.02 (s, 1H), 7.95 (d,  $J$  = 7.1 Hz, 2H), 7.55 (t,  $J$  = 7.5 Hz, 2H), 7.47 (t,  $J$  = 7.4 Hz, 1H), 6.03 (q,  $J$  = 6.0 Hz, 1H), 3.87–3.77 (m, 1H), 1.94 (d,  $J$  = 6.0 Hz, 3H), 1.36 (d,  $J$  = 6.1 Hz, 3H), 1.07 (d,  $J$  = 6.2 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.7, 131.2, 130.3, 128.8, 128.5, 126.0, 87.4, 70.4, 22.7, 21.4, 21.3.

**2-(1-Butoxyethyl)-4-phenyl-2H-1,2,3-triazole (4e).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 19.4 mg (79%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3475, 2956, 1634, 1381, 1129  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.89 (s, 1H), 7.81 (d,  $J$  = 7.1 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.34 (t,  $J$  = 7.3 Hz, 1H), 5.77 (q,  $J$  = 6.0 Hz, 1H), 3.49 (dt,  $J$  = 9.2, 6.7 Hz, 1H), 3.31 (dt,  $J$  = 9.4, 6.6 Hz, 1H), 1.82 (d,  $J$  = 6.0 Hz, 3H), 1.53–1.45 (m, 2H), 1.33–1.24 (m, 2H), 0.83 (t,  $J$  = 7.4 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.8, 131.2, 130.3, 128.8, 128.5, 126.0, 89.7, 68.9, 31.2, 20.8, 19.1, 13.7.

**2-(1-Isobutoxyethyl)-4-phenyl-2H-1,2,3-triazole (4f).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 19.6 mg (80%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3468, 2959, 1648, 1381, 1126  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.89 (s, 1H), 7.81 (d,  $J$  = 7.1 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.34 (t,  $J$  = 7.4 Hz, 1H), 5.76 (q,  $J$  = 6.0 Hz, 1H), 3.26 (dd,  $J$  = 9.2, 6.9 Hz, 1H), 3.08 (dd,  $J$  = 9.2, 6.6 Hz, 1H), 1.82 (d,  $J$  = 6.0 Hz, 3H), 1.78 (dd,  $J$  = 13.4, 6.7 Hz, 1H), 0.85 (d,  $J$  = 6.7 Hz, 3H), 0.80 (d,  $J$  = 6.7 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.7, 131.2, 130.4, 128.8, 128.5, 126.0, 89.9, 75.8, 28.2, 20.8, 19.2, 19.1.

**2-(1-(Cyclohexyloxy)ethyl)-4-phenyl-2H-1,2,3-triazole (4g).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 19.3 mg (71%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3465, 2948, 1644, 1383, 1102  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.88 (s, 1H), 7.81 (d,  $J$  = 7.1 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.34 (t,  $J$  = 7.4 Hz, 1H), 5.93 (q,  $J$  = 6.0 Hz, 1H), 3.40–3.34 (m, 1H), 2.00–1.98 (m, 1H), 1.80 (d,  $J$  = 6.0 Hz, 3H), 1.71–1.70 (m, 1H), 1.63–1.56 (m, 1H), 1.48–1.33 (m, 3H), 1.23–1.10 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.7, 131.1, 130.4, 128.8, 128.5, 126.0, 87.2, 76.2, 32.7, 31.4, 25.5, 24.0, 23.9, 21.4.

**2-(1-Ethoxypropyl)-4-phenyl-2H-1,2,3-triazole (4h).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 17.1 mg (74%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3465, 2963, 1650, 1381, 1107  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.90 (s, 1H), 7.82 (d,  $J$  = 7.1 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.34 (t,  $J$  = 7.4 Hz, 1H), 5.52 (t,  $J$  = 6.7 Hz, 1H), 3.57–3.50 (m, 1H), 3.43–3.36 (m, 1H), 2.21 (p,  $J$  = 7.4 Hz, 2H), 1.15 (t,  $J$  = 7.0 Hz, 3H), 0.88 (t,  $J$  = 7.5 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.9, 131.3, 130.3, 128.8, 128.5, 126.0, 94.5, 64.7, 28.0, 14.7, 9.0.

**2-(1-Ethoxybutyl)-4-phenyl-2H-1,2,3-triazole (4i).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 21.6 mg (88%); colorless oil liquid;  $R_f$  = 0.50 (hexane–EtOAc, 10 : 1). IR (neat): 3469, 2962, 1647, 1381, 1112  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.89 (s, 1H), 7.81 (d,  $J$  = 7.2 Hz, 2H), 7.42 (t,  $J$  = 7.4 Hz, 2H), 7.34 (t,  $J$  = 7.3 Hz, 1H), 5.60 (t,  $J$  = 6.7 Hz, 1H), 3.57–3.49 (m, 1H), 3.43–3.35 (m, 1H), 2.19–2.147 (m, 2H), 1.45–1.35 (m, 1H), 1.28–1.21 (m, 1H), 1.15 (t,  $J$  = 7.0 Hz, 3H), 0.93 (t,  $J$  = 7.4 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.8, 131.3, 130.3, 128.8, 128.5, 126.0, 93.0, 64.7, 36.7, 18.0, 14.7, 13.5.

**2-(2-Ethoxypropan-2-yl)-4-phenyl-2H-1,2,3-triazole (4j).** Yield: 16.7 mg (77%); colorless oil liquid;  $R_f$  = 0.30 (hexane–EtOAc, 10 : 1). IR (neat): 3442, 2940, 1661, 1384, 1072  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92 (s, 1H), 7.84 (d,  $J$  = 7.2 Hz, 2H), 7.44 (t,  $J$  = 7.5 Hz, 2H), 7.37 (d,  $J$  = 7.4 Hz, 1H), 3.10 (s, 3H), 1.98 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.5, 131.0, 128.8, 128.4, 126.0, 93.0, 50.8, 25.7. HRMS (ESI):  $m/z$  [ $M + H$ ]<sup>+</sup> calcd for  $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}^+$ : 218.1288; found: 218.1289.

**5-Methyl-5-(4-phenyl-2H-1,2,3-triazol-2-yl)dihydrofuran-2(3H)-one (4k).** The spectroscopic data are in accordance with those reported.<sup>8b</sup>

Yield: 22.6 mg (93%); yellow oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3465, 2978, 1740, 1635, 1380  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz, DMSO):  $\delta$  8.43 (s, 1H), 7.87 (d,  $J$  = 7.2 Hz, 2H), 7.46 (t,  $J$  = 7.4 Hz, 2H), 7.39 (t,  $J$  = 7.3 Hz, 1H), 3.09–2.96 (m, 2H), 2.84–2.75 (m, 1H), 2.68–2.60 (m, 1H), 2.14 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz, DMSO):  $\delta$  176.0, 148.4, 133.2, 129.8, 129.5, 129.4, 126.4, 97.9, 33.7, 29.2, 25.1.

**4-Phenyl-1-(1-phenylvinyl)-1H-1,2,3-triazole (7).** The spectroscopic data are in accordance with those reported.<sup>12</sup>

Yield: 17.2 mg (70%); yellow oil liquid;  $R_f$  = 0.20 (hexane–EtOAc, 10 : 1). IR (neat): 3038, 2934, 1496, 1459, 756  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.99–7.97 (m, 2H), 7.93 (s, 1H), 7.60–7.45 (m, 8H), 6.00 (d,  $J$  = 1.0 Hz, 1H), 5.69 (d,  $J$  = 0.9 Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  147.6, 143.0, 134.6, 130.2, 129.9, 128.9, 128.8, 128.3, 127.4, 125.8, 119.8, 109.4.

## Conflicts of interest

There are no conflicts to declare.

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