One-pot three component synthesis of 5-allyl-1,2,3-triazoles using copper(i) acetylides†

Parigi Raghavendar Reddy, Lianji Cui and Jae-Sang Ryu †*

One-pot three-component reactions using copper(i) acetylide, azide, allyl iodide, and NaOH have been developed. The reactions proceed smoothly at room temperature to afford 5-allyl-1,2,3-triazoles, which can be further transformed into a variety of 1,2,3-triazole-fused bi/tricyclic scaffolds. This method offers the most efficient, convenient, and practical route towards useful polycyclic scaffolds in moderate to excellent yields.

Introduction

1,2,3-Triazoles† are very important heterocycles in chemistry and biology. Synthetic molecules containing a 1,2,3-triazole scaffold exhibit diverse biological activities, which have drawn the attention of medicinal chemists in the drug discovery field. Currently, there are several 1,2,3-triazole-containing medicines on the market, and the number of potential pharmaceuticals based on these scaffolds keeps increasing. Beyond the drug market, 1,2,3-triazoles are utilized in a variety of areas including bioconjugation, polymer and materials science, and related areas including supramolecular chemistry, DNA labeling and oligonucleotide synthesis. Such wide applications of 1,2,3-triazoles are due to their facile synthesis through Cu(i)-catalyzed azide–alkyne cycloaddition (CuAAC), so-called ‘click chemistry’. Since it was first introduced by Sharpless and co-workers, CuAAC has been rapidly adopted as a universal coupling process. However, in terms of substrate scope, CuAAC is restricted to terminal alkynes, leading to 1,4-disubstituted 1,2,3-triazoles, and the one-pot synthetic methods for the fully substituted 1,2,3-triazoles are still relatively few.

In one-pot three-component reactions used to obtain 5-halo 1,2,3-triazoles, an electrophile X+ (X = Cl, Br, and I) is added into the CuAAC reaction to trap X+ with an in situ generated 5-copper(i) 1,2,3-triazole intermediate A (Scheme 1). However, the result is usually the formation of a mixture of the desired 5-substituted 1,2,3-triazole 3 and the byproduct 1,4-disubstituted 1,2,3-triazole 4, which is generated from a competitive protonation of the 5-copper(i) 1,2,3-triazole intermediate A. This competitive protonation is accelerated by a proton source, provided from the terminal alkyne substrate in the normal CuAAC. Therefore, this problem cannot be avoided in the presence of terminal alkyne substrates or protic polar solvents. Recently, this drawback was smartly overcome by using copper(i) acetylde instead of a terminal alkyne in the halogena tion and acylation, by Y. Hu’s group.

Copper(i) acetylides are highly crystalline polymeric complexes, [RC≡CCu]z. They are stable to air, water, acid/base and heat so they can be kept on the shelf for several months without the quality deteriorating. In the absence of exogenous ligands or additives, copper(i) phenylacetylide, PhC≡CCu, is not effective under typical CuAAC conditions; it did not undergo a cycloaddition with azide and did not provide a 1,2,3-triazole product. However, when it was combined with both azide and acyl chloride, it quickly provided 5-acyl-1,2,3-triazoles. The presence of acyl chloride accelerated the cycloaddition of copper(i) phenylacetylide and azide. This intriguing result motivated us to investigate one-pot three-component reactions using copper(i) phenylacetylide. We are particularly interested in 5-allyl-1,2,3-triazoles as precursors for the development of new anticancer agents. However, efficient

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† Electronic supplementary information (ESI) available: Copies of 1H and 13C NMR spectra for 3a–z and 6a–z. See DOI: 10.1039/c7ra12889d
methods for the synthesis of 5-allyl-1,2,3-triazoles are rare.\textsuperscript{10a,b} Interestingly, copper(i) acetylides have never been used directly as a substrate for the synthesis of 5-allyl-1,2,3-triazoles, although it is known to be a key intermediate. Herein, we report one-pot three-component reactions for the synthesis of 5-allyl-1,2,3-triazoles from copper(i) acetylides.

\section*{Results and discussion}

To assess the feasibility of the tandem CuAAC–allylation reaction, we started to investigate one-pot three component reactions in the presence of copper(i) phenylacetylide (1a), 4-cyanobenzyl azide (2a), allyl iodide, and base (Table 1). In preliminary screening of reaction conditions, we obtained the desired product 5-allyl-1,2,3-triazole 3a and a byproduct enyne 5a with 47\% and 42\% yield respectively after 4 h at room temperature when 1.5 equivalents of cyanobenzyl azide (2a), 3 equivalents of allyl iodide, and 2 equivalents of Et\textsubscript{3}N were employed (entry 1). The yield of the desired product 3a increased to 60\% and the yield of the byproduct enyne 5a decreased to 36\% when the amount of allyl iodide increased to 4 equivalents (entry 2). The use of Et\textsubscript{3}N appeared to decompose the stable polymeric complex with the structure $[\text{PhCCu}]_n$ into a lower polymeric or a more reactive monomeric structure. 

As soon as Et\textsubscript{3}N was added, the heterogeneous reaction mixture became clear and rapidly yielded both an undesired byproduct as well as the desired product. However, replacing Et\textsubscript{3}N with pyridine, quinine, or inorganic bases such as Na\textsubscript{2}CO\textsubscript{3}, K\textsubscript{2}CO\textsubscript{3}, Na\textsubscript{2}CO\textsubscript{3}, NaOH, or KOH did not change the heterogeneity of the reaction. The copper(i) phenylacetylide (1a) remained suspended in CH\textsubscript{2}Cl\textsubscript{2}, which not only slowed reaction progress but also significantly reduced byproduct formation. The reaction using quinine increased the yield of desired product 3a up to 74\%, but interestingly 2\% of a protonated byproduct 4a was isolated instead of the allyl alkyne byproduct 5a (entry 3). The reaction using pyridine did not significantly increase the yield compared to the reaction of Et\textsubscript{3}N. However, the formation of byproducts 4a and 5a was not observed (entry 4). Similarly, the reactions using inorganic bases also generated 5-allyl-1,2,3-triazole 3a as a sole product (entries 5–11). Hydroxide bases (KOH, NaOH; entries 10 and 11) are better than carbonate bases [Na\textsubscript{2}CO\textsubscript{3}, K\textsubscript{2}CO\textsubscript{3}, Cs\textsubscript{2}CO\textsubscript{3}; entries 7–9] in terms of yield. Among bases used, the best result was obtained with NaOH (84\%, entry 10). It appears the use of base is essential for the reaction. Without a base, 5-allyl-1,2,3-triazole 3a was isolated with only a moderate yield (52\%, entry 12). The role of NaOH is not clear, and it is still under investigation. It is also noteworthy that the byproduct 1,4-disubstituted 1,2,3-triazole 4a, which is generated from a competitive protonation of 5-copper(i) 1,2,3-triazole intermediate $A$, was not detected in reactions using copper(i) phenylacetylide (1a) with the exception of quinine.

Next, we investigated the solvent effect on the yield of Cu(i)-catalyzed azide–alkyne cycloaddition–allylation reactions of copper(i) acetylides in the presence of NaOH. The reactions were effective in various solvents including CH\textsubscript{2}Cl\textsubscript{2}, dioxane, THF, toluene, and CH\textsubscript{3}CN (entries 13–16). Considering yield of the product, toluene (entry 15) was the best solvent for the reaction. On the basis of Table 1, we chose NaOH as a base and the relatively nonpolar solvent, toluene, for further study.

Once we had established optimal reaction conditions, we examined the scope of one-pot three-component reactions (Table 2). We applied the copper(i) acetylidyte system to various azides in toluene at room temperature. All reactions using copper(i) acetylides in Table 2 smoothly furnished 5-allyl-1,4-disubstituted 1,2,3-triazoles 3b–u and a trace amount of enyne byproduct 5b–u at room temperature. As anticipated, the 1,4-disubstituted 1,2,3-triazoles 4, which are unavoidable in the typical CuAAC reactions, were not detected. First, we explored the reaction scope with benzyl azides. The reaction yields were independent of the electronic nature of azides. Substrates 2c–e bearing electron-donating substituents and substrates 2f–h bearing electron- withdrawing substituents underwent the one-pot three-component reactions very smoothly, and provided the corresponding 5-allyl-1,4-disubstituted 1,2,3-triazoles 3c–h at room temperature, in good to excellent yields (85–97\%). The reaction scope was not limited to only benzyl azides, but was

\begin{table}[h]
\begin{center}
\begin{tabular}{lllll}
Entry & Base & Solvent & Time (h) & Yield\textsuperscript{b} (\%) \\
\hline
1\textsuperscript{a} & Et\textsubscript{3}N & CH\textsubscript{2}Cl\textsubscript{2} & 4 & 47 & 0 & 42 \\
2 & Et\textsubscript{3}N & CH\textsubscript{2}Cl\textsubscript{2} & 4 & 60 & 0 & 36 \\
3 & Quinine & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 74 & 2 & 0 \\
4 & Pyridine & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 63 & 0 & 0 \\
5 & Na\textsubscript{2}CO\textsubscript{3} & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 47 & 0 & 0 \\
6 & K\textsubscript{2}CO\textsubscript{3} & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 45 & 0 & 0 \\
7 & Na\textsubscript{2}CO\textsubscript{3} & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 62 & 0 & 0 \\
8 & K\textsubscript{2}CO\textsubscript{3} & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 71 & 0 & 0 \\
9 & Cs\textsubscript{2}CO\textsubscript{3} & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 67 & 0 & 0 \\
10 & NaOH & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 84 & 0 & 0 \\
11 & KOH & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 83 & 0 & 0 \\
12 & — & CH\textsubscript{2}Cl\textsubscript{2} & 24 & 52 & 0 & 0 \\
13 & NaOH & Dioxane & 24 & 89 & 0 & 0 \\
14 & NaOH & THF & 24 & 85 & 0 & 0 \\
15 & NaOH & Toluene & 24 & 94 & 0 & 0 \\
16 & NaOH & CH\textsubscript{3}CN & 24 & 68 & 0 & 0 \\
\hline
\end{tabular}
\end{center}
\caption{Optimization of reaction conditions\textsuperscript{a}}
\end{table}

\textsuperscript{a} Reaction conditions: 1a (65.8 mg, 400 \textmu mol), 2a (94.9 mg, 600 \textmu mol), base (800 \textmu mol), allyl iodide (146 \textmu L, 1.60 mmol), solvent (1 mL). All reactions were carried out under Ar.\textsuperscript{b} Isolated yields.\textsuperscript{c} 1.20 mmol of allyl iodide was used.
Table 2 Cu(I)-catalyzed azide–alkyne cycloaddition–allylation reactions under optimized conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Yield of 3a</th>
<th>Yield of 6a</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>3a (80%)</td>
<td>6a (79%)</td>
</tr>
<tr>
<td>2</td>
<td>3b (75%)</td>
<td>6b (87%)</td>
</tr>
<tr>
<td>3</td>
<td>3c (65%)</td>
<td>6c (92%)</td>
</tr>
<tr>
<td>4</td>
<td>3d (53%)</td>
<td>6d (70%)</td>
</tr>
<tr>
<td>5</td>
<td>3e (75%)</td>
<td>6e (70%)</td>
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</table>

| Reaction conditions: 1a (65.8 mg, 400 μmol), 2 (600 μmol), NaOH (32.0 mg, 800 μmol), allyl iodide (146 μL, 1.60 mmol), toluene (1 mL). All reactions were carried out under Ar. | a Reaction conditions: 1a (65.8 mg, 400 μmol), 2 (600 μmol), NaOH (32.0 mg, 800 μmol), allyl iodide (146 μL, 1.60 mmol), toluene (1 mL). All reactions were carried out under Ar. |
| --- | --- | --- |
| 3h (65%, 24 h) | 3i (65%, 24 h) | 3k (65%, 24 h) |
| 3j (65%, 24 h) | 3l (65%, 24 h) | 3m (70%, 48 h) |
| 3n (54%, 48 h) | 3o (57%, 48 h) | 3p (75%, 48 h) |
| 3q (90%, 24 h) | 3r (86%, 24 h) | 3s (73%, 24 h) |

Table 3 Synthesis of fused 1,2,3-triazoles using Cu(I)-catalyzed azide–alkyne cycloaddition–allylation reactions and ring closing metathesis.

also compatible with aryl azides 2i–k and aliphatic azide 2l. In addition, a variety of copper(i) arylacetylides were also tested. Regardless of the electronic influence of substituents on copper(i) arylacetylides, desired products 3m–p were obtained in moderate to good yields (54–75%). It is worth noting that this method is not limited to the use of simple allyl iodide. Other various substituted allyl iodides could be used for one-pot three-component reactions, and produced the corresponding 5-allyl-1,4-disubstituted 1,2,3-triazoles 3q–t with yields in the range of 53–90%. Delightfully, the reaction scope was also expandable to copper(i) alkylacetylide, which afforded 4-alkyl 1,2,3-triazole 3u.

Finally, we studied further transformations of 5-allyl-1,4-disubstituted 1,2,3-triazoles into various fused polyheterocycles in order to demonstrate the synthetic utility of the 5-allyl-1,4-disubstituted 1,2,3-triazoles as versatile building blocks (Table 3). The alkene-tethered 5-allyl-1,2,3-triazoles 3v–x were synthesized based on Cu(i)-catalyzed azide-alkyne cycloaddition–allylation reactions of copper(i) acetylide in good yields...
Formations were also applicable to substrates bearing styrene (entries 4 and 5, 70–3z proceeds smoothly to a copper(I) 1,2,3-triazole intermediate. The byproduct 1,4-disubstituted 1,2,3-triazole Cu(I)-intermediate contracts to the Cu(I)-1,2,3-triazole intermediate, which is readily trapped by allyl iodide to yield the desired 5-allyl-1,4-disubstituted 1,2,3-triazole (entries 4 and 5, 70–92%).

On the basis of previous mechanistic studies and our own observation, we speculate that Cu(1) acetylide coordinates with the azide to form the intermediate I-1 and following cyclization leads to the metallocycle intermediate I-2. The 6-membered Cu(I)-intermediate contracts to the Cu(I)-1,2,3-triazole intermediate I-3, which is readily trapped by allyl iodide to yield the desired 5-allyl-1,4-disubstituted 1,2,3-triazole 3 (Scheme 2).

Scheme 2 Plausible mechanism of Cu(1)-mediated one-pot three component synthesis of 5-allyl-1,2,3-triazoles.

Conclusions

In conclusion, we have developed a novel one-pot three component reaction method for the synthesis of 5-allyl-1,4-disubstituted 1,2,3-triazoles from copper(I) acetylides. The 5-allyl-1,4-disubstituted 1,2,3-triazoles were produced via a 1,3-dipolar cycloaddition followed by in situ trapping of the C(sp²)-Cu intermediate. The byproduct 1,4-disubstituted 1,2,3-triazole 4, which is generated from a competitive protonation of 5-copper(I) 1,2,3-triazole intermediate A, was not isolated. The present method was successfully applied to achieve production of synthetically useful heterocycles. This domino reaction is characterized by mild conditions and no protonated byproduct formation, and allows for the efficient construction of functionalized fused polycyclic 1,2,3-triazoles.

Experimental

General All reactions were performed in oven-dried glassware fitted with glass stoppers under positive pressure of Ar with magnetic stirring, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless-steel cannula. TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with cerium ammonium molybdenate (CAM), potassium permanganate (KMnO₄) or p-anisaldehyde. Flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. Reagents were purchased from commercial suppliers, and used without further purification unless otherwise noted. Solvents were distilled from proper drying agents (CaH₂ or Na wire) under Ar atmosphere at 760 mmHg. NMR spectra were recorded at 24 °C. Chemical shifts are expressed in ppm relative to TMS (1H, 0 ppm), CDCl₃ (1H, 7.26 ppm; 13C, 77.2 ppm), and C₆H₅F (19F, –113.15 ppm); coupling constants are expressed in Hz. High resolution mass spectra (HRMS) were obtained by electrospray ionization (ESI, TOF) or electron ionization (EI, magnetic sector). Infrared spectra were recorded with peaks reported in cm⁻¹.

General procedure for the Cu(I)-catalyzed azide–alkyne cycloaddition–allylation reactions

Copper(I) acetylide (400 μmol) was placed in a 25 mL one-arm roundbottom flask. A solution of azide (600 μmol) in anhydrous toluene (1 mL), allyl iodide (268 mg, 1.60 mmol) and NaOH (32.0 mg, 800 μmol) were sequentially added to the reaction mixture. The resulting suspension was stirred at room temperature for 24 h or 48 h as indicated in Table 1. The mixture was filtered and washed with CH₂Cl₂ (20 mL). To scavenge Cu, polymer-bound ethylenediaminetriacetic acid acetamide (3.0–4.0 mmol g⁻¹, 200 mg) was added to the filtrate, and stirred for 2 h. The polymer was filtered off and the filtrate was concentrated by rotary evaporation. Purification of crude residue by column chromatography yielded 3a-z. The reaction of 3y was carried out for 3 days at room temperature.

4-(5-Allyl-4-phenyl-1H-1,2,3-triazol-1-yl)methylbenzonitrile (3a). TLC: Rᵢ 0.25 (2:1 hexane/EtOAc). White solid (113 mg, 94%). Mp = 113–115 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.68–7.63 (m, 4H), 7.45–7.41 (m, 2H), 7.38–7.34 (m, 1H), 7.28 (d, J = 8.4 Hz, 2H), 5.83 (m, 1H), 5.57 (s, 2H), 5.15 (dd, J = 10.4 Hz, 1.2 Hz, 1H), 4.88 (dd, J = 16.8 Hz, 1.2 Hz, 1H), 1.35 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 146.2, 140.3, 132.9, 131.1, 131.0, 130.4, 128.9, 128.3, 128.0, 127.3, 118.3, 118.2, 112.6, 51.4, 27.1. HRMS (ESI) m/z calculated for C₁₉H₁₇N₄ [M + H⁺] 301.1448, found 301.1451. IR (KBr film): ν 3061, 2229, 1639, 1506, 920, 800, 777, 699 cm⁻¹.

5-Allyl-1-benzyl-4-phenyl-1H-1,2,3-triazole (3b). TLC: Rᵢ 0.52 (2:1 hexane/EtOAc). Pale yellow liquid (97.9 mg, 89%). ¹H NMR (400 MHz, CDCl₃): δ 7.70–7.67 (m, 2H), 7.44–7.40 (m, 2H), 7.36–7.30 (m, 4H), 7.20–7.18 (m, 2H), 5.83 (m, 1H), 5.54 (s, 2H), 5.15 (dm, J = 12.0 Hz, 1H), 4.92 (dm, J = 15.2 Hz, 1H), 3.45 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 146.0, 135.1, 132.4, 131.5, 130.4, 129.1, 128.8, 128.5, 128.0, 127.3, 117.9, 52.1, 27.1. HRMS (ESI) m/z calculated for C₁₅H₁₃N₃ [M + H⁺] 276.1495, found 276.1501. IR (KBr film): ν 3063, 3033, 1639, 1608, 1496, 918, 800, 764 cm⁻¹.

5-Allyl-1-(4-methylbenzyl)-4-phenyl-1H-1,2,3-triazole (3c). TLC: Rᵢ 0.55 (2:1 hexane/EtOAc). White solid (97.9 mg, 85%). Mp = 42–44 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.69–7.66 (m, 2H), 7.44–7.39 (m, 2H), 7.36–7.31 (m, 1H), 7.14 (d, J = 8.0 Hz,
2H), 7.09 (d, J = 8.0 Hz, 2H), 5.84 (m, 1H), 5.49 (s, 2H), 5.17 (dq, J = 10.4 Hz, 2.0 Hz, 1H), 4.93 (dq, J = 17.2 Hz, 2.0 Hz, 1H), 3.45 (m, 2H), 2.33 (s, 3H). 1H NMR (400 MHz, CDCl3): δ 146.0, 138.3, 132.5, 131.1, 131.5, 130.4, 129.8, 128.8, 128.0, 127.3, 117.9, 52.0, 27.2, 21.3. HRMS (ESI) m/z calculated for C14H13NO3 [M + H]+ 280.0969, found 280.0971. 15C NMR (100 MHz, CDCl3): δ 184.0, 160.8, 156.1, 142.3, 136.7, 132.7, 131.1, 130.1, 128.9, 128.3, 128.2, 127.3, 123.4, 118.2, 51.1, 27.1. HRMS (ESI) m/z calculated for C18H14N2O3 [M + H]+ 321.1346, found 321.1348. 13C NMR (100 MHz, CDCl3): δ 145.4, 140.1, 134.1, 133.4, 131.4, 131.1, 130.1, 129.8, 128.1, 127.3, 125.5, 118.2, 27.7, 21.4. HRMS (ESI) m/z calculated for C18H14N2O3 [M + H]+ 276.1495, found 276.1501. IR (KBr film): ν 3091, 1517, 992, 934, 710 cm−1.

5-Allyl-4-phenyl-1-(p-tolyl)-1H-1,2,3-triazole (3i). TLC: Rf 0.72 (2 : 1 hexane/EtOAc). White solid (98.3 mg, 89%). Mp = 106–108 °C. 1H NMR (400 MHz, CDCl3): δ 7.82 (d, J = 8.4 Hz, 2H), 7.48–4.37 (m, 5H), 7.33 (d, J = 8.4 Hz, 2H), 5.91 (m, 1H), 5.19 (d, J = 9.6 Hz, 1H), 4.93 (d, J = 17.2 Hz, 1H), 3.57 (d, J = 4.0 Hz, 2H), 2.45 (s, 3H). 13C NMR (100 MHz, CDCl3): δ 145.4, 140.1, 134.1, 133.4, 131.4, 131.1, 130.1, 129.8, 128.1, 127.3, 125.5, 118.2, 27.7, 21.4. HRMS (ESI) m/z calculated for C18H14N2O3 [M + H]+ 276.1495, found 276.1501. IR (KBr film): ν 3091, 1517, 992, 934, 710 cm−1.
128.5, 127.6 (d, J<sub>C-F</sub> = 3.1 Hz), 127.4, 118.0, 115.8 (d, J<sub>C-F</sub> = 20.9 Hz), 52.2, 27.1. 19F NMR (376 MHz, CDCl<sub>3</sub>): δ −110.9. HRMS (ESI) m/z calculated for C<sub>12</sub>H<sub>9</sub>F<sub>2</sub>N<sub>2</sub> [M + H]<sup>+</sup> 352.1808, found 352.1807. IR (KBr film): ν 3058, 3032, 1954, 1628 cm<sup>−1</sup>.

1-Benzyl-3-(methylbut-2-en-1-yl)-4-phenyl-1H-1,2,3-triazole (3s). TLC: R<sub>r</sub> 0.37 (2 : 1 hexane/EtOAc). Pale white solid (89.0 mg, 73%). Mp = 86–88 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.67 (d, J = 7.2 Hz, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.38–7.28 (m, 4H), 7.16 (d, J = 6.4 Hz, 2H), 5.54 (s, 2H), 4.93 (m, 1H), 3.41 (d, J = 6.4 Hz, 2H), 1.65 (d, J = 1.6 Hz, 3H), 1.62 (d, J = 0.8 Hz, 3H). 13C NMR (100 MHz, CDCl<sub>3</sub>): δ 145.1, 135.2, 131.5, 132.6, 131.6, 131.6, 129.8, 126.1, 127.7, 127.4, 127.0, 118.5, 52.0, 25.5, 22.3, 18.1. HRMS (ESI) m/z calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub> [M + H]<sup>+</sup> 340.1808, found 340.1811. IR (KBr film): ν 3025, 1654, 1602, 1494, 1249, 968, 728, 708 cm<sup>−1</sup>.

1-Benzyl-3-cinnamyl-4-phenyl-1H-1,2,3-triazole (3t). TLC: R<sub>r</sub> 0.51 (2 : 1 hexane/EtOAc). White solid (74.5 mg, 53%). Mp = 100–102 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.72 (d, J = 7.2 Hz, 2H), 7.43 (t, J = 7.2 Hz, 2H), 7.38–7.26 (m, 6H), 7.25–7.18 (m, 5H), 6.51 (d, J = 16.0 Hz, 1H), 6.12 (d, J = 16.0, 5.2 Hz, 1H), 5.58 (s, 2H), 3.61 (dd, J = 5.2, 1.2 Hz, 2H). 13C NMR (100 MHz, CDCl<sub>3</sub>): δ 145.9, 136.3, 135.0, 132.5, 131.3, 130.5, 129.0, 128.7, 128.6, 128.3, 129.9, 127.8, 127.3, 127.2, 126.2, 123.6, 52.2, 26.3. HRMS (ESI) m/z calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub> [M + H]<sup>+</sup> 352.1808, found 352.1812. IR (KBr film): ν 3082, 3025, 1955, 1654, 727 cm<sup>−1</sup>.

1-Allyl-3-benzyl-4-phenyl-1H-1,2,3-triazole (3u). TLC: R<sub>r</sub> 0.54 (2 : 1 hexane/EtOAc). Colorless oil (87.2 mg, 77%). 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.36–7.27 (m, 3H), 7.12 (d, J = 8.0 Hz, 2H), 7.52–5.5 (m, 1H), 5.46 (s, 2H), 5.07 (d, J = 10.4 Hz, 1H, 16.8 Hz, 16, 1H), 1.68 (dd, J = 7.2 Hz, 2H), 1.62 (dd, J = 5.2, 1.2 Hz, 2H). 13C NMR (100 MHz, CDCl<sub>3</sub>): δ 148.8, 141.6, 133.3, 130.4, 128.6, 127.8, 127.2, 116.7, 50.6, 30.9, 28.9, 28.2, 25.9, 24.2, 22.0, 13.8. HRMS (ESI) m/z calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub> [M + H]<sup>+</sup> 340.2124, found 340.2127. IR (KBr film): ν 3065, 3033, 2928, 1640, 1456, 992, 729 cm<sup>−1</sup>.

1-Allyl-3-(but-3-en-1-yl)-4-phenyl-1H-1,2,3-triazole (3v). TLC: R<sub>r</sub> 0.55 (2 : 1 hexane/EtOAc). Pale yellow liquid (76.8 mg, 80%). 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.67 (d, J = 6.8 Hz, 2H), 7.42 (t, J = 6.8 Hz, 2H), 7.33 (tt, J = 6.8 Hz, 1H, 1H), 5.97 (m, 1H), 5.78 (m, 1H), 5.21 (dq, J = 10.0 Hz, 0.8 Hz, 1H), 5.14–5.08 (m, 2H), 4.94 (d, J = 17.2 Hz, 0.8 Hz, 1H), 4.29 (t, J = 7.2 Hz, 2H), 3.58 (m, 2H), 2.70 (q, J = 7.2 Hz, 2H). 13C NMR (100 MHz, CDCl<sub>3</sub>): δ 145.3, 133.5, 132.8, 131.6, 128.8, 127.9, 127.3, 118.2, 117.9, 47.5, 34.4, 27.2. HRMS (ESI) m/z calculated for C<sub>24</sub>H<sub>22</sub>N<sub>3</sub> [M + H]<sup>+</sup> 340.1495, found 340.1502. IR (KBr film): ν 3080, 1640, 1495, 918, 766, 699 cm<sup>−1</sup>.

1-Allyl-3-(pent-4-en-1-yl)-4-phenyl-1H-1,2,3-triazole (3w). TLC: R<sub>r</sub> 0.70 (2 : 1 hexane/EtOAc). Pale yellow liquid (77.7 mg, 77%). 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.67 (d, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.33 (tt, J = 7.2 Hz, 1H), 5.95 (m, 1H), 5.79 (m, 1H), 5.20 (d, J = 10.0 Hz, 1H), 5.07 (d, J = 10.0 Hz, 1H), 5.03 (d, J = 17.2 Hz, 1H), 4.95 (d, J = 17.2 Hz, 1H), 4.23 (t, J = 7.2 Hz, 2H), 3.57 (m, 2H), 2.14 (q, J = 7.2 Hz, 2H), 2.04 (quin, J = 7.2 Hz, 2H). 13C NMR (100 MHz, CDCl<sub>3</sub>): δ 145.3, 136.8, 132.8, 131.6, 130.0, 128.7, 127.8, 127.2, 117.8, 116.1, 47.4, 30.7, 29.1, 27.1. HRMS (ESI) m/z calculated for C<sub>26</sub>H<sub>22</sub>N<sub>3</sub> [M + H]<sup>+</sup> 354.1652, found 354.1660. IR (KBr film): ν 3079, 2979, 1640, 1495, 916, 765, 700 cm<sup>−1</sup>.
5-Allyl-1-(hex-5-en-1-yl)-4-phenyl-1H-1,2,3-triazole (3x). TLC: Rf 0.65 (2 : 1 hexane/EtOAc). Pale yellow liquid (60.9 mg, 53%).

1H NMR (400 MHz, CDCl3): δ 7.83 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 5.81 (m, 1H), 5.80 (m, 1H), 5.67 (dd, J = 17.2 Hz, 0.8 Hz, 1H), 5.48 (dd, J = 12.0 Hz, 0.8 Hz, 1H), 5.37 (d, J = 10.4 Hz, 1H), 4.88 (d, J = 17.2 Hz, 1H), 3.41 (m, 1H).

13C NMR (100 MHz, CDCl3): δ 146.0, 136.7, 133.4, 132.3, 132.1, 131.4, 130.7, 128.9, 128.6, 128.4, 128.0, 127.5, 127.3, 126.8, 118.2, 117.8, 49.8, 27.1. HRMS (ESI) m/z calculated for C25H20N3 [M + H]+ 388.1495, found 388.1494.

Experimental procedure for ring closing metathesis

Synthesis of 3-phenyl-7,8-dihydro-4H-[1,2,3]triazolo[1,5-a]azepine (6y). The diene 3w (53.5 mg, 200 μmol) was dissolved in anhydrous CH2Cl2 (6 mL). A solution of Grubbs’ 1st generation catalyst (8.2 mg, 10.0 μmol) in anhydrous CH2Cl2 (3.3 mL) was added to the reaction mixture via a cannula. The reaction mixture was stirred at room temperature for 2 h. Upon completion of the reaction, the solvent was removed in vacuo. The residue was purified by column chromatography to afford 6w as a white solid (31.0 mg, 65%) and a dimer 6x as colorless liquid (8.0 mg, 8%). 6x: TLC: Rf 0.2 (2 : 1 hexane/ EtOAc). Mp = 250–255 °C. 1H NMR (400 MHz, CDCl3): δ 7.68 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (t, J = 7.6 Hz, 1H), 5.81 (m, 1H), 5.66 (m, 1H), 4.51 (t, J = 6.0 Hz, 2H), 3.61 (d, J = 7.6 Hz, 2H). 13C NMR (100 MHz, CDCl3): δ 145.2, 131.7, 131.5, 131.0, 128.9, 128.0, 127.6, 126.3, 45.8, 25.9, 25.1, 23.0, 21.9. HRMS (ESI) m/z calculated for C33H34N3 [M + H]+ 420.1495, found 420.1498. IR (KBr film): ν 2959, 2932, 1491, 733, 720, 697 cm⁻¹.

Synthesis of 3-phenyl-4,7,8,9-tetrahydro-[1,2,3]triazolo[1,5-a]azocine (6w). The diene 3w (50.7 mg, 200 μmol) was dissolved in anhydrous CH2Cl2 (6 mL). A solution of Grubbs’ 1st generation catalyst (8.2 mg, 10.0 μmol) in anhydrous CH2Cl2 (3.3 mL) was added to the reaction mixture via a cannula. The reaction mixture was stirred at room temperature for overnight, and was brought to reflux for 6 h. Upon completion of the reaction, the solvent was removed in vacuo. The residue was purified by column chromatography to afford 6w as pale yellow liquid (39.0 mg, 87%). TLC: Rf 0.35 (2 : 1 hexane/ EtOAc). 1H NMR (400 MHz, CDCl3): δ 7.61 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 5.79–5.67 (m, 2H), 4.53 (t, J = 5.2 Hz, 2H), 3.64 (d, J = 4.8 Hz, 2H). 13C NMR (100 MHz, CDCl3): δ 144.4, 132.9, 131.7, 128.8, 127.4, 127.1, 147.2, 27.2, 24.4, 23.1. HRMS (ESI) m/z calculated for C19H18N3 [M + H]+ 226.1339, found 226.1336. IR (KBr film): ν 2929, 1656, 1247, 733, 698 cm⁻¹.

Synthesis of (E)-3-phenyl-7,8,9,10-tetrahydro-4H-[1,2,3]triazolo[1,5-a]azoline (6x) and (E)-1,10-bis(5-allyl-1-phenyl-1H-1,2,3-triazol-1-yl)dec-5-ene (6z). The diene 3x (53.5 mg, 200 μmol) was dissolved in anhydrous CH2Cl2 (6 mL). A solution of Grubbs’ 1st generation catalyst (8.2 mg, 10.0 μmol) in anhydrous CH2Cl2 (3.3 mL) was added to the reaction mixture via a cannula. The reaction mixture was brought to reflux for 8 h. Upon completion of the reaction, the solvent was removed in vacuo. The residue was purified by column chromatography to afford 6x as a white solid (31.0 mg, 65%) and a dimer 6y as colorless liquid (8.0 mg, 8%). 6y: TLC: Rf 0.37 (6 : 1 hexane/ EtOAc). Mp = 292–295 °C. 1H NMR (400 MHz, CDCl3): δ 7.67 (d, J = 7.2 Hz, 4H), 7.42 (t, J = 7.2 Hz, 4H), 7.34 (t, J = 7.2 Hz, 2H), 6.00–5.91 (m, 2H), 3.59–3.55 (m, 4H), 2.01 (quin, J = 6.4 Hz, 2H), 1.67–1.61 (m, 2H). 

13C NMR (100 MHz, CDCl3): δ 145.2, 131.7, 131.5, 131.0, 128.9, 128.0, 127.6, 126.3, 45.8, 25.9, 25.1, 23.0, 21.9. HRMS (ESI) m/z calculated for C33H34N3 [M + H]+ 420.1495, found 420.1498. IR (KBr film): ν 2959, 2932, 1491, 733, 720, 697 cm⁻¹.
EtOAc). Mp = 96–98 °C. 1H NMR (400 MHz, CDCl₃): δ 8.15 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.50–7.41 (m, 4H), 7.41–7.36 (m, 2H), 6.65 (d, J = 10.4 Hz, 1H), 6.18 (m, 1H), 3.51 (d, J = 6.4 Hz, 2H). 13C NMR (100 MHz, CDCl₃): δ 142.2, 135.0, 134.9, 130.9, 130.8, 130.2, 129.0, 128.8, 128.7, 128.2, 128.1, 127.9, 127.6, 124.0, 21.2. HRMS (ESI) m/z calculated for C₁₇H₁₄N₃ [M + H]+ 260.1182, found 260.1179. IR (KBr film): ν 2919, 1700, 1600, 1491, 992, 772, 699 cm⁻¹.

**Synthesis of (Z)-3-phenyl-1,11-dihydrobenzo[f][1,2,3]triazolo[1,5-a]azocine (6z).** The diene 3z (47.0 mg, 150 μmol) was dissolved in anhydrous CH₂Cl₂ (6 mL). A solution of Hoveyda-Grubbs’s 2nd generation catalyst (5.0 mg, 7.9 μmol) in anhydrous CH₂Cl₂ (3.3 mL) was added to the reaction mixture via a cannula. The reaction mixture was stirred at room temperature for 4 h. Upon completion of the reaction, the solvent was removed in vacuo. The residue was purified by column chromatography to afford 6z as a pale green solid (29.5 mg, 72%). TLC: Rₖ 0.27 (6 : 1 hexane/EtOAc). Mp = 159–161 °C. 1H NMR (400 MHz, CDCl₃): δ 7.75–7.54 (m, 3H), 7.45–7.38 (m, 3H), 3.73–3.75 (m, 2H), 7.30 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 10.4 Hz, 1H), 6.03 (dt, J = 10.4 Hz, 7.6 Hz, 1H), 5.49 (s, 2H), 3.30 (d, J = 8.0 Hz, 2H). 13C NMR (100 MHz, CDCl₃): δ 144.8, 139.2, 134.0, 131.5, 131.3, 130.9, 129.3, 128.8, 128.7, 128.6, 128.2, 128.0, 127.7, 126.2, 53.4, 22.6. HRMS (ESI) m/z calculated for C₁₇H₁₄N₃ [M + H]+ 274.1339, found 274.1336. IR (KBr film): ν 3025, 2360, 1494, 995, 754, 735, 699 cm⁻¹.

**Conflicts of interest**

There are no conflicts to declare.

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