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Synthesis of 3-Azabicyclo[m.2.0] Ring Systems via Copper-Catalyzed Cascade Reaction of Diazo Compounds with 1,n-Allenynes

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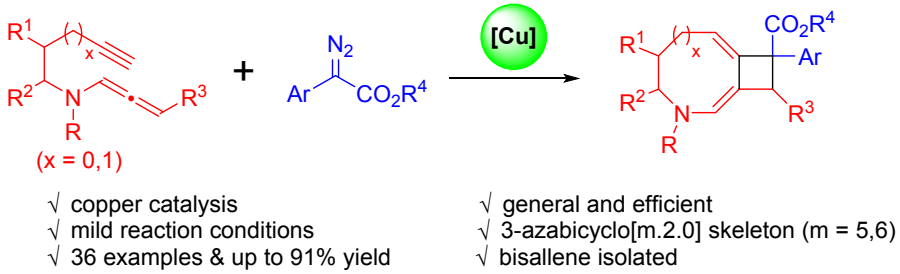
ABSTRACT GRAPHIC



ABSTRACT

A copper-catalyzed cascade reaction of diazo compounds with 1,n-allenynes (n = 6,7) was reported, which provides an efficient access to various functionalized 3-azabicyclo[m.2.0] frameworks (m = 5,6) in moderate to excellent yields under mild reaction conditions. The reaction proceeds through intermolecular cross-coupling to form bisallene intermediates followed by subsequent intramolecular [2+2] cycloaddition.

INTRODUCTION

Four-membered carbocycles are widely found in natural products and other biologically active compounds.[1] In particular, cyclobutane-fused frameworks are found in several natural products (Figure 1). For example, Cytosporolide A–C, caryophyllene-derived meroterpenoids with a cyclobutane motif, were isolated from cultures of the fungus *Cytospora* sp. and showed significant antimicrobial activity against the Gram-positive bacteria *Staphylococcus aureus* and *Streptococcus pneumoniae*.[2] Tripartilactam, a structurally unprecedented cyclobutane-bearing tricyclic lactam metabolite from a *Streptomyces* sp. in a dung beetle's brood ball, was evaluated as a Na^+/K^+ ATPase inhibitor.[3] Paesslerins A–B, novel cyclobutane-containing tricyclic sesquiterpenoids isolated from the soft coral *Alcyonium paessleri*, showed moderate cytotoxicity against human tumor cell lines.[4] Psiguadial B, a novel sesquiterpenoid-diphenylmethane meroterpenoid isolated from the leaves of *Psidium guajava*, exhibited potent antiproliferative activity against human hepatoma cells.[5] Flueggedine**,** isolated from the twigs and leaves of *Flueggeavirosa*, was an interesting axisymmetric [2+2] cycloaddition indolizidine alkaloid dimer.[6] As such, the development of methodologies for the synthesis of these cyclobutane-fused structures is of significant interest.

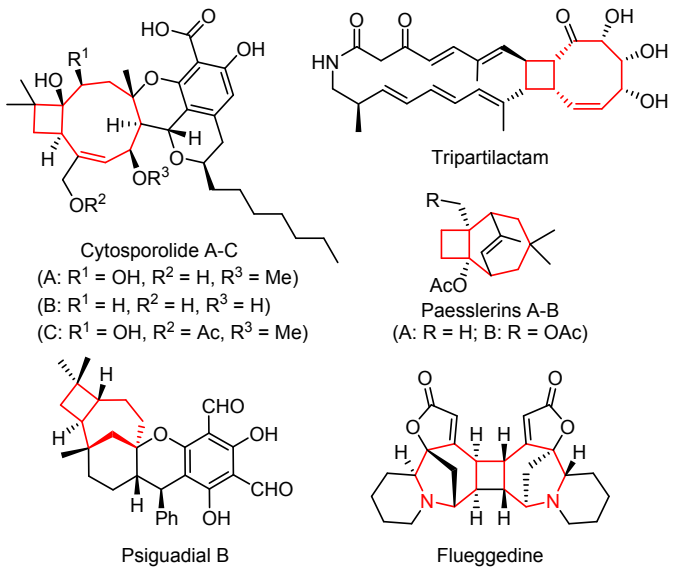
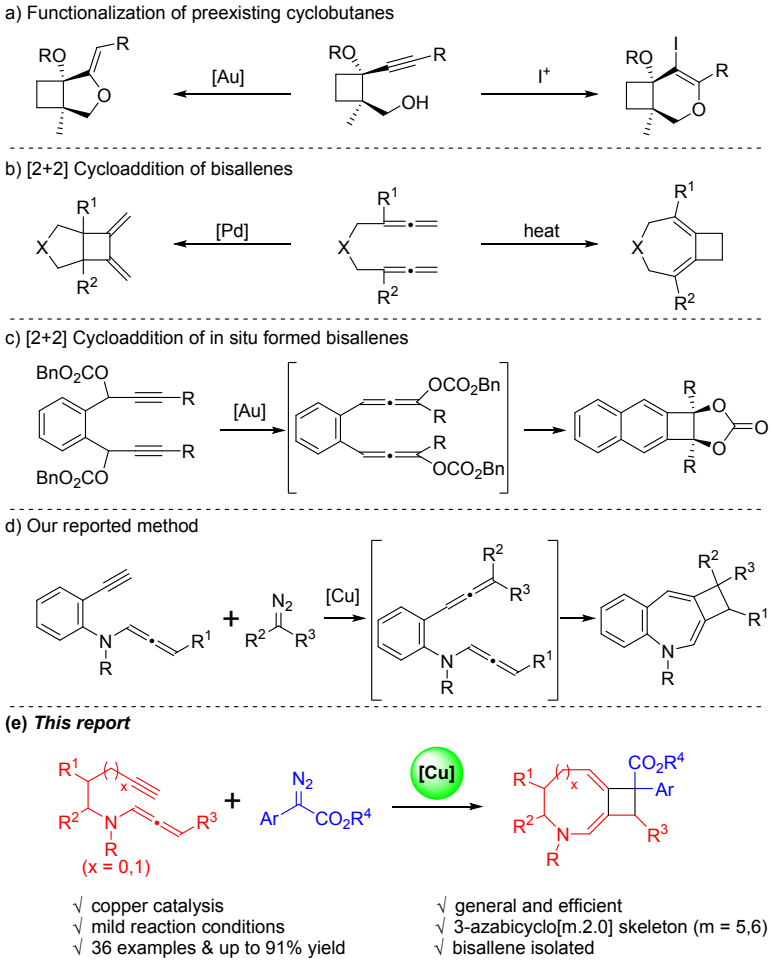


Figure 1. Selected Natural Products.

Recently, Vaquero and co-workers reported regiodivergent electrophilic cyclizations of alkynylcyclobutanes bearing an appended hydroxyl group for the synthesis of cyclobutane-fused O-heterocycles (Scheme 1a).[7-8] Compared with the efficient yet limited methods through functionalization of preexisting cyclobutanes, the intramolecular [2+2] cycloaddition of bisallenes has been found to be a more efficient alternative for the construction of cyclobutane-fused bicyclic systems.[9] For example, in 2006, Ma and co-workers realized two different [2+2] cycloaddition pathways of 1,5-bisallenes, providing two types of cyclobutane-fused bicyclic products (Scheme 1b).[9b] However, such strategies are limited presumably due to the high instability of bisallenes and difficulty of their synthesis. The complementary method has been well established by in situ bisallene formation from diyne precursors via intramolecular rearrangement.[10] For example, in 2013, Liu and co-workers discovered a novel gold-catalyzed cascade cyclization of diynes for the synthesis of naphtho[*b*]cyclobutenes, in which the generation of bisallenes via double 3,3-rearrangement of diyne precursors was considered to be the key step (Scheme 1c).[10a] Recently, our group reported a novel copper-catalyzed cascade reaction of diazo compounds with 1,6-allenynes bearing an aromatic linker for the synthesis of 3-azabicyclo[5.2.0] ring systems, which proceeds through intermolecular cross-coupling to form bisallene intermediates followed by subsequent intramolecular [2+2] cycloaddition (Scheme 1d).[11] Despite these advances, general and efficient strategies for the rapid assembly of cyclobutane-fused bicyclic scaffolds still remain scarce. Based on the former reports and our continuous interests in diazo chemistry,[12] we describe herein a novel and general copper-catalyzed cascade reaction of diazo compounds with benzo-free 1,n-allenynes under mild reaction conditions for the rapid assembly of cyclobutane-fused bicyclo[m.2.0] ring systems, which would be potentially useful in the total synthesis of natural products and attractive for drug development in medicinal chemistry (Scheme 1e).

Scheme 1. Synthesis of Cyclobutane-Fused Bicyclic Structures.

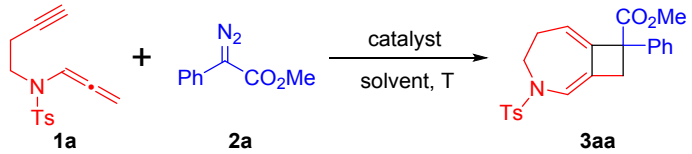


RESULTS AND DISCUSSIONS

We first utilized benzo-free 1,6-allenyne **1a** and phenyl diazoacetate **2a** as model substrates to optimize the reaction conditions (Table 1). Both the catalyst and the reaction medium were crucial for the reaction. When the reaction was performed in methylene dichloride (CH_2Cl_2) at room temperature without catalyst, the reaction did not happen (entry 1). Different copper catalysts were then tested. Gratifyingly, CuCl gave desired product **3aa** in 45% yield, while CuBr afforded product in 27% yield and CuI did not catalyze the reaction at all (entries 2–4). The low efficiency was due to the diazo homo-coupling reaction and the incomsumption of allenyne substrate. When $Cu(PPh_3)_3Br$ was employed, the yield was increased to 83% (entry 5). It is worth noting that the catalytic activity of CuBr is quite different with our previous report.[11] Other copper catalysts and metal catalysts[13] showed no catalytic activity for the reaction (entries 6–9). These results indicate that both the solubility and ligand type of

copper catalysts have significant impact on the reaction. Next, various solvents were screened. CH_2Cl_2 was better than the alternative 1,2-dichloroethane (DCE), whereas other solvents[14] such as acetonitrile (MeCN) and tetrahydrofuran (THF) were not suitable for the reaction (entries 10–12). The reaction did not happen at 0 °C, and led to a lower yield at 60 °C due to product decomposition (entries 13–14). Notebly, the adding method of phenyl diazoacetate **2a** was detrimental to the reaction. When the reaction was conducted in a one-pot manner without a syringe pump, almost no product was obtained (entry 15). Bases did not improve the reaction outcome (entries 16–17).

Table 1. Optimization of Reaction Conditions[a]

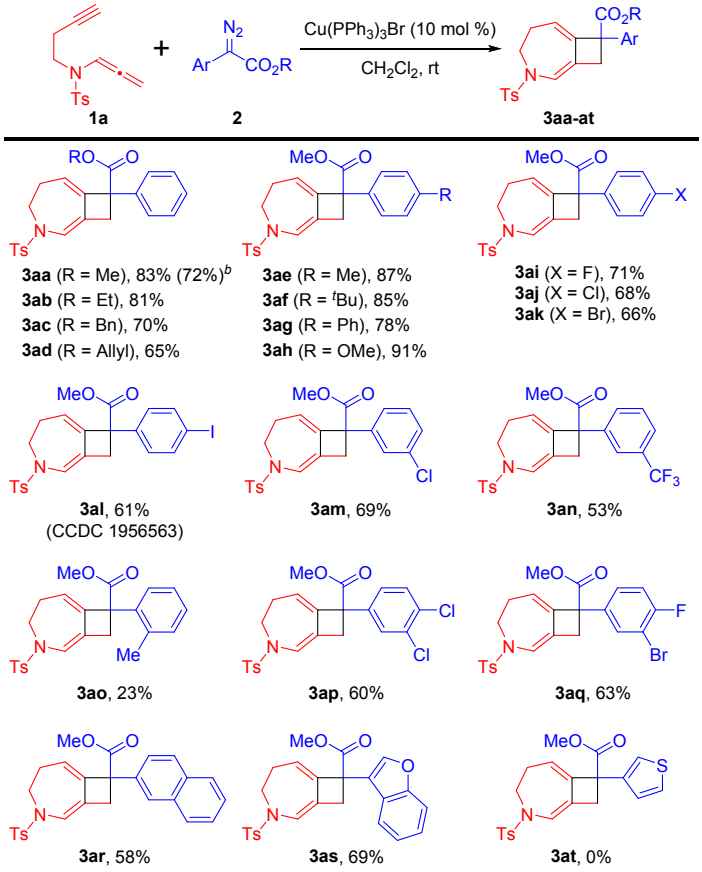


entry	catalyst	solvent	yield (%)
1	-	CH_2Cl_2	-
2	CuCl	CH_2Cl_2	45
3	CuBr	CH_2Cl_2	27
4	CuI	CH_2Cl_2	-
5	$Cu(PPh_3)_3Br$	CH_2Cl_2	83
6	$Cu(1,10\text{-}Phen)(PPh_3)Br$	CH_2Cl_2	-
7	CuOTf	CH_2Cl_2	-
8	$Cu(tfacac)_2$	CH_2Cl_2	-
9	IPrCuOTf	CH_2Cl_2	-
10	$Cu(PPh_3)_3Br$	DCE	32
11	$Cu(PPh_3)_3Br$	MeCN	-
12	$Cu(PPh_3)_3Br$	THF	<10
13[b]	$Cu(PPh_3)_3Br$	CH_2Cl_2	-
14[c]	$Cu(PPh_3)_3Br$	CH_2Cl_2	46
15[d]	$Cu(PPh_3)_3Br$	CH_2Cl_2	<10
16[e]	$Cu(PPh_3)_3Br$	CH_2Cl_2	37
17[f]	$Cu(PPh_3)_3Br$	CH_2Cl_2	-

[a]Reaction conditions: **2a** (0.4 mmol) in solvent (1.0 mL) was injected into a solution of **1a** (0.2 mmol) and catalyst (10 mol %) in solvent (1.0 mL) via a syringe pump within 2 h, and the reaction was continued at rt for another 12 h. [b]At 0 °C. [c]At 60 °C. [d]Without a syringe pump. [e]Et_3N (0.2 mmol) was added. [f]Cs_2CO_3 (0.2 mmol) was added. (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene. Tf = trifluoromethanesulfonyl. tfacac = trifluoroacetoacetyl.

With the established optimal reaction conditions, we investigated the scope of diazo compounds for the synthesis of 3-azabicyclo[5.2.0] products (Scheme 2). Diazo compounds with various ester groups, such as methyl, ethyl, benzyl or even active allyl group, were all tolerated for the reaction and gave the corresponding products in good yields (**3aa**–**ad**). Aryl diazoacetates bearing electron-donating or electron-withdrawing substituents at the aryl moiety were all found to be suitable for the reaction, providing the desired products in moderate to excellent yields (**3ae**–**ao**). Both the position and electronic properties of substituents have significant influence on the reaction. Additionally, disubstituted aryl diazoacetates, 2-naphthyl substituted diazoacetate, and benzofuran-derived diazoacetate were also amenable to the reaction (**3ap**–**as**). Thiophene-derived diazoacetate was not suitable for the reaction, presumably due to the sulfur deactivation of copper-containing catalyst. Gram-scale synthesis gave product **3aa** in 72% yield under standard reaction conditions. Unfortunately, diazo compounds of acceptor-H type and acceptor-acceptor type were not suitable for this reaction. The structure of **3al** was confirmed by X-ray diffraction analysis.[15]

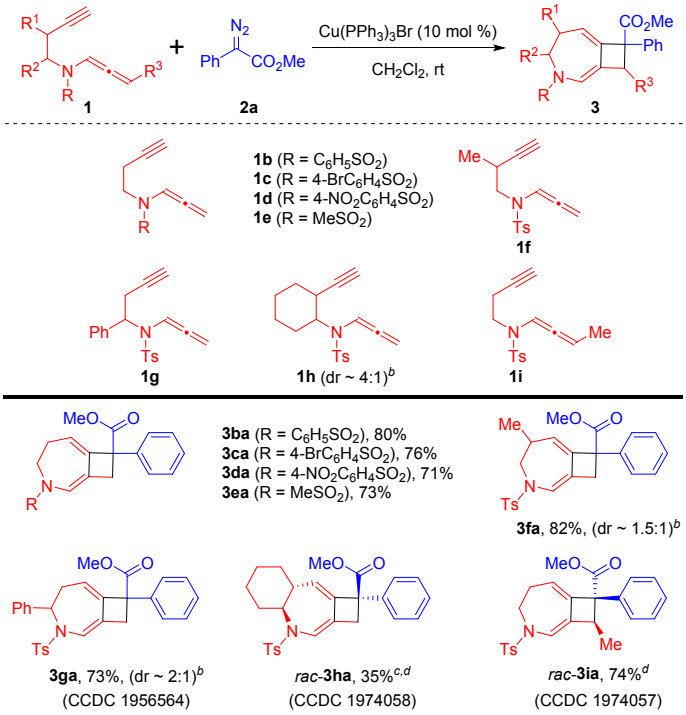
Scheme 2. Scope of Diazo Substrates[a]



[a]Reaction conditions: **2** (0.4 mmol) in CH_2Cl_2 (1.0 mL) was injected into a solution of **1a** (0.2 mmol) and $Cu(PPh_3)_3Br$ (10 mol %) in CH_2Cl_2 (1.0 mL) via a syringe pump within 2 h, and the reaction was continued at rt for another 12 h. [b]Yield of 5.0 mmol scale in parentheses.

For the scope of 1,6-allenynes (Scheme 3), the reaction tolerated different sulfonyl substituents at the R position, furnishing the corresponding products in good yields (**3ba**–**ea**). Unfortunately, no desired product obtained when R is acetyl group. Then, the reaction of phenyl diazoacetate **2a** with 1,6-allenynes bearing methyl (R^1) or phenyl (R^2) substituent on the aliphatic linker afforded the desired products as mixtures of two inseparable regioisomers (**3fa**–**ga**). Furthermore, cyclohexane-derived 1,6-allenyne **1h** was also tested and product **3ha** was isolated in 35% yield. Gratifyingly, 1,6-allenyne **1i** (R^3 = Me) was well suitable for the reaction, leading to the desired product **3ia** in 74% yield. The relative stereochemistry of **3ha** and **3ia** as well as the structure of **3ga** were determined by X-ray diffraction analysis.[15]

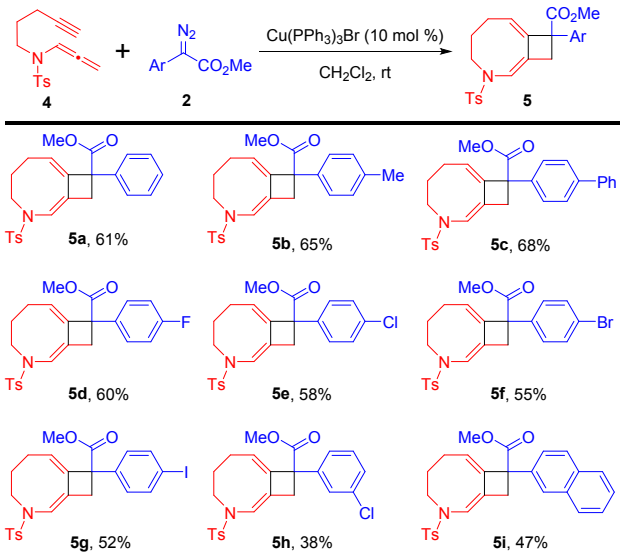
Scheme 3. Scope of 1,6-Allenyne Substrates[a]



[a]Reaction conditions: **2a** (0.4 mmol) in CH_2Cl_2 (1.0 mL) was injected into a solution of **1** (0.2 mmol) and $Cu(PPh_3)_3Br$ (10 mol %) in CH_2Cl_2 (1.0 mL) via a syringe pump within 2 h, and the reaction was continued at rt for another 12 h. [b]Dr values were determined by ^1H NMR analysis. [c]Yield of flash chromotography followed by recrystallization. [d]One diastereomer was obtained.

In addition to 1,6-allenynes, 1,7-allenyne **4** was also evaluated for the reaction and the expected 3-azabicyclo[6.2.0] product **5a** was obtained in 61% yield under the optimized reaction conditions (Scheme 4). The reactions of 1,7-allenyne **4** with various substituted aryl diazoacetates all proceeded well and afforded the desired 3-azabicyclo[6.2.0] products in moderate to good yields (**5b**–**h**). Notably, bulky 2-naphthyl substituted diazoacetate was also suitable for the reaction and gave product **5i** in 47% yield.

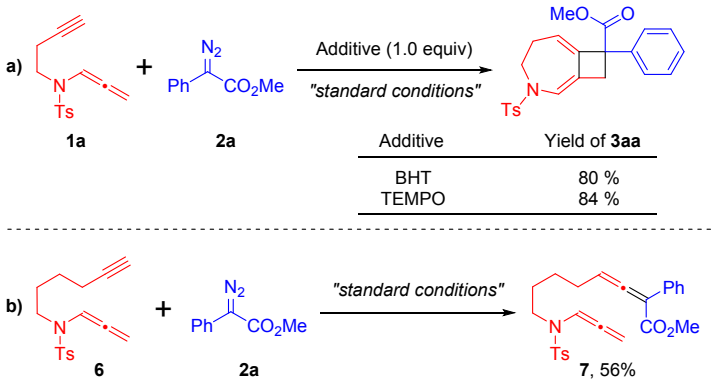
Scheme 4. Scope of Diazo Substrates with 1,7-Allenyne[a]



[a]Reaction conditions: **2** (0.4 mmol) in CH_2Cl_2 (1.0 mL) was injected into a solution of **4** (0.2 mmol) and $Cu(PPh_3)_3Br$ (10 mol %) in CH_2Cl_2 (1.0 mL) via a syringe pump within 2 h, and the reaction was continued at rt for another 12 h.

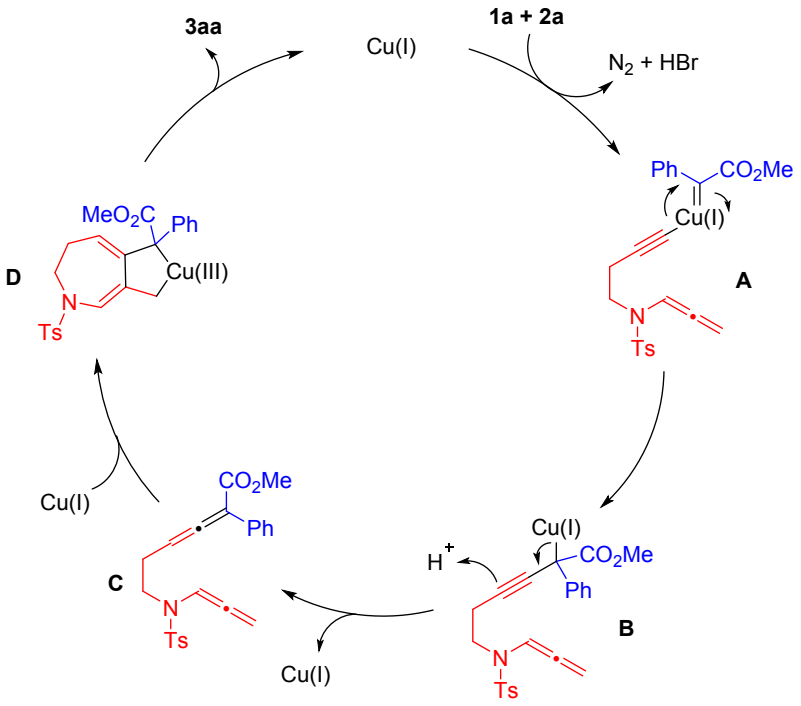
Control experiments were conducted to understand the cycloaddition process (Scheme 5). The reaction went smoothly to give the desired product **3aa** in good yield when a radical inhibitor BHT or TEMPO was present, which showed that the reaction did not proceed via a radical mechanism (Scheme 5a). When 1,8-allenyne **6** with longer aliphatic chain was subjected to the reaction, only the cross-coupling bisallene **7** was isolated in 56% yield, which indicated that the reaction may involve a bisallene intermediate. Unfortunately, efforts for transformations of product **3aa**, such as reduction of double bond or thermal rearrangement, all failed.

Scheme 5. Control Experiments.



Based on our previous report and related investigations,[9c,12,16] a plausible mechanism has been proposed in Scheme 6. The whole sequence is initiated by the formation of copper-carbene intermediate **A** from the reaction of 1,6-allenyne **1a** with phenyl diazoacetate **2a** in the presence of copper catalyst, which is followed by migratory insertion of the carbenic carbon to the alkynyl group to generate intermediate **B.** Protonation of intermediate **B** afforded bisallene intermediate **C**. The regioselective coordination of bisallene intermediate **C** to copper species followed by C-C bond formation would produce the cupracyclopentane intermediate **D**, which would undergo quick reductive elimination to give product **3aa**.

Scheme 6. Proposed Reaction Mechanism.



CONCLUSION

In summary, we have developed a general and efficient strategy for the synthesis of various functionalized 3-azabicyclo[5.2.0] and 3-azabicyclo[6.2.0] frameworks via copper-catalyzed tandem cross-coupling/[2+2] cycloaddition reaction of diazo compounds with benzo-free 1,n-allenynes. This

protocol features mild reaction condition, moderate to excellent yields, and broad substrate scope. Further applications of this method are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in oven-dried glassware. All solvents for reactions were analytical grade and purified/dried according to standard procedures. Solvents for flash chromatography were technical grade and distilled before use. All commercially available compounds were used without further purification. 10-Channels syringe pump (model: LSP10-1B) of Longer Precision Pump Co., Ltd. was used for slow injection. Thin layer chromatography (TLC) was carried out using precoated silica gel plates (0.25 mm, F254) and visualization was accomplished under UV light (254 nm). Flash chromatography was performed using silica gel (200–300 mesh). Melting points were obtained uncorrected from an SGW X-4B melting point apparatus. ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded in $CDCl_3$ on a Bruker Ascend™ 500 spectrometer (500 MHz), chemical shifts are reported in ppm with the solvent signals as reference, and coupling constants (*J*) are given in Hertz. The peak information is described as: s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiplet). All high-resolution mass spectra (HRMS) were obtained on a Thermo Scientific™ Q Exactive™ UHMR (Ultra-High Mass Range) Hybrid Quadrupole-Orbitrap™ mass spectrometer.

Safety Note. Handling of diazo compounds should only be done in a well-ventilated fume cupboard using an additional blast shield.

Synthesis of $Cu(PPh_3)_3Br$ Catalyst. Copper catalyst $Cu(PPh_3)_3Br$ used in this reaction was synthesized according to reported method.[17]

Synthesis of Diazo Substrates. The aryldiazoacetates **2a**–**t** were prepared according to well-documented literature procedures.[18]

General Procedure for the Synthesis of 1,n-Allenyne Substrates 1, 4 and 6 (GP-A). The corresponding aminoalkynes (1.0 equiv) and K_2CO_3 (5.0 equiv) were added into acetone (0.5 M). Then, propargyl bromide (2.5 equiv) was added in one portion. The reaction mixture was stirred at 60 ^{o}C in an

oil bath under an N_2 balloon. After the reaction was completed (monitored by TLC), the resulting mixture was cooled down to rt, filtered via a short pad of celite and washed once with acetone. The combined organic phase was concentrated under reduced pressure to obtain the propargylated crude product, which was dissolved in THF (0.33 M). The mixture was cooled down to 0 ºC in an ice-bath and ^{t}BuOK (30 mol %) was added in portions. Then, the reaction was warmed to rt and stirred until completed (monitored by TLC). The resulting mixture was filtered via a short pad of celite and washed with CH_2Cl_2. The combined organic phase was concentrated and the residue was purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc) to afford the pure 1,n-allenyne substrates.

N-(but-3-yn-1-yl)-4-methyl-N-(propa-1,2-dien-1-yl)benzenesulfonamide (1a): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[19] following GP-A, and obtained as white solid in 60% yield (1568.0 mg, 10 mmol scale); **mp:** 59–60 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.84 (t, *J* = 6.2 Hz, 1H), 5.36 (d, *J* = 6.2 Hz, 2H), 3.42–3.15 (m, 2H), 2.47–2.42 (m, 5H), 1.98 (t, *J* = 2.7 Hz, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 200.8, 144.1, 135.3, 130.0, 127.2, 100.0, 88.4, 80.5, 70.2, 45.1, 21.7, 18.4; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{14}H_{15}NO_2SNa$ 284.0716; Found 284.0716.

N-(but-3-yn-1-yl)-N-(propa-1,2-dien-1-yl)benzenesulfonamide (1b): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[19] following GP-A, and obtained as colorless oil in 71% yield (878.0 mg, 5 mmol scale); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.84–7.80 (m, 2H), 7.64–7.59 (m, 1H), 7.57–7.52 (m, 2H), 6.84 (t, *J* = 6.3 Hz, 1H), 5.36 (d, *J* = 6.3 Hz, 2H), 3.35–3.30 (m, 2H), 2.48–2.43 (m, 2H), 1.99 (t, *J* = 2.7 Hz, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 200.8, 138.2, 133.2, 129.3, 127.1, 99.8, 88.5, 80.4, 70.2, 45.1, 18.4; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. For $C_{13}H_{13}NO_2SNa$ 270.0559; Found 270.0556.

4-Bromo-N-(but-3-yn-1-yl)-N-(propa-1,2-dien-1-yl)benzenesulfonamide (1c): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[19] following GP-A, and obtained as white solid in 74% yield (1207.0 mg, 5 mmol scale); **mp:** 66–68 °C; **^{1}H NMR (500 MHz,**

$CDCl_3$): δ 7.68 (s, 4H), 6.80 (t, *J* = 6.2 Hz, 1H), 5.38 (d, *J* = 6.2 Hz, 2H), 3.33–3.28 (m, 2H), 2.49–2.44 (m, 2H), 2.00 (t, *J* = 2.7 Hz, 1H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 200.9, 137.2, 132.7, 128.7, 128.3, 99.6, 88.7, 80.3, 70.4, 45.2, 18.5; **HRMS** (ESI) *m/z*: $[M + H]^+$ Calcd. for $C_{13}H_{13}BrNO_2S$ 325.9845; Found 325.9841.

N-(but-3-yn-1-yl)-4-nitro-N-(propa-1,2-dien-1-yl)benzenesulfonamide (1d): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[19] following GP-A, and obtained as white solid in 38% yield (555.0 mg, 5 mmol scale); **mp:** 79–81 °C; **^1H NMR (500 MHz, $CDCl_3$):** δ 8.42–8.37 (m, 2H), 8.04–7.99 (m, 2H), 6.81 (t, *J* = 6.2 Hz, 1H), 5.41 (d, *J* = 6.2 Hz, 2H), 3.37–3.33 (m, 2H), 2.52–2.47 (m, 2H), 2.01 (t, *J* = 2.7 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 201.0, 150.4, 143.8, 128.5, 124.7, 99.3, 89.1, 79.9, 70.6, 45.4, 18.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{13}H_{12}N_2O_4SNa$ 315.0410; Found 315.0408.

N-(but-3-yn-1-yl)-N-(propa-1,2-dien-1-yl)methanesulfonamide (1e): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[19] following GP-A, and obtained as white solid in 66% yield (611.2 mg, 5 mmol scale); **mp:** 73–75 °C; **^1H NMR (500 MHz, $CDCl_3$):** δ 6.69 (t, *J* = 6.3 Hz, 1H), 5.46 (d, *J* = 6.3 Hz, 2H), 3.51 (t, *J* = 7.4 Hz, 2H), 2.95 (s, 3H), 2.51 (td, *J* = 7.6, 2.7 Hz, 2H), 2.03 (t, *J* = 2.7 Hz, 1H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 200.5, 99.5, 88.6, 80.5, 70.5, 45.3, 38.5, 18.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_8H_{11}NO_2SNa$ 208.0403; Found 208.0402.

4-Methyl-N-(2-methylbut-3-yn-1-yl)-N-(propa-1,2-dien-1-yl)benzenesulfonamide (1f): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[20] following GP-A, and obtained as colorless oil in 69% yield (950.0 mg, 5 mmol scale); **^1H NMR (500 MHz, $CDCl_3$):** δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.54 (t, *J* = 6.4 Hz, 1H), 5.24 (d, *J* = 6.4 Hz, 2H), 4.37–4.28 (m, 1H), 2.55–2.47 (m, 1H), 2.45–2.37 (m, 4H), 1.94 (d, *J* = 5.3 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 203.9, 143.8, 137.2, 129.8, 127.3, 94.7, 85.6, 80.9, 70.6, 53.9, 24.2, 21.7, 17.1; **HRMS** (ESI) *m/z*: $[M + H]^+$ Calcd. for $C_{15}H_{18}NO_2S$ 276.1053; Found 276.1048.

4-Methyl-N-(1-phenylbut-3-yn-1-yl)-N-(propa-1,2-dien-1-yl) benzenesulfonamide (1g): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[20] following GP-

A, and obtained as colorless oil in 57% yield (961.6 mg, 5 mmol scale); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.65–7.61 (m, 2H), 7.32–7.21 (m, 7H), 6.35 (t, *J* = 6.3 Hz, 1H), 5.44 (dd, *J* = 8.6, 6.6 Hz, 1H), 5.09 (dd, *J* = 10.5, 6.3 Hz, 1H), 5.02 (dd, *J* = 10.5, 6.3 Hz, 1H), 3.05 (ddd, *J* = 17.0, 8.7, 2.7 Hz, 1H), 2.74 (ddd, *J* = 17.0, 6.6, 2.7 Hz, 1H), 2.41 (s, 3H), 1.92 (t, *J* = 2.7 Hz, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 204.6, 143.7, 137.2, 136.9, 129.6, 128.3, 128.1, 127.9, 127.4, 95.6, 85.7, 80.7, 71.3, 60.1, 22.2, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{20}H_{19}NO_2SNa$ 360.1029; Found: 360.1024.

N-(2-ethynylcyclohexyl)-4-methyl-N-(propa-1,2-dien-1-yl) benzenesulfonamide (1h): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[20] following GP-A, and obtained as white solid in 86% yield (1356.0 mg; 5 mmol scale; mixture of two inseparable diasteroisomers; dr ~ 4:1); **mp:** 63–66 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.85–7.75 (m, 2H), 7.31–7.25 (m, 2H), 6.45 (t, *J* = 6.3 Hz, 1H), 5.24–5.17 (m, 2H), 3.98–3.72 (m, 1H), 2.83–2.44 (m, 1H), 2.43–2.40 (m, 3H), 1.85–1.78 (m, 1H), 1.75–1.60 (m, 4H), 1.54–1.01 (m, 4H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 205.1, 144.0, 143.4, 137.8, 136.4, 129.5, 129.4, 127.9, 127.6, 85.0, 84.93, 84.88, 69.9, 69.8, 62.6, 62.5, 33.6, 33.3, 33.0, 32.7, 31.0, 30.2, 25.5, 25.0, 24.9, 24.6, 21.7, 21.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{18}H_{21}NO_2SNa$ 338.1185; Found 338.1178.

N-(but-3-yn-1-yl)-N-(buta-1,2-dien-1-yl)-4-methylbenzenesulfonamide (1i): The title compound was synthesized from the corresponding 1-bromo-2-butyne and aminoalkyne[19] following GP-A, and obtained as colorless oil in 47% yield (647.2 mg, 5 mmol scale); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.73–7.66 (m, 2H), 7.35–7.29 (m, 2H), 6.71 (dq, *J* = 5.6, 2.7 Hz, 1H), 5.71 (qd, *J* = 7.0, 5.9 Hz, 1H), 3.34–3.22 (m, 2H), 2.45–2.40 (m, 5H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.71 (dd, *J* = 7.0, 2.8 Hz, 3H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 195.6, 143.9, 135.4, 129.8, 127.2, 99.5, 99.0, 80.7, 70.1, 45.1, 21.6, 18.1, 16.0; **HRMS** (ESI) *m/z*: $[M + H]^+$ Calcd. for $C_{15}H_{18}NO_2S$ 276.1053; Found 276.1054.

4-Methyl-N-(pent-4-yn-1-yl)-N-(propa-1,2-dien-1-yl)benzenesulfonamide (4): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[21] following GP-A, and obtained as white solid in 44% yield (1212.0 mg, 10 mmol scale); **mp:** 97–99 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.82 (t, *J* = 6.2 Hz, 1H), 5.31 (d, *J* = 6.2

Hz, 2H), 3.20 (t, *J* = 7.0 Hz, 2H), 2.43 (s, 3H), 2.23 (td, *J* = 7.2, 2.6 Hz, 2H), 1.94 (t, *J* = 2.7 Hz, 1H), 1.82–1.74 (m, 2H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 201.4, 143.9, 135.4, 129.9, 127.3, 100.3, 88.0, 83.5, 68.9, 45.7, 27.0, 21.7, 15.9; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{15}H_{17}NO_2SNa$ 298.0872; Found: 298.0868.

N-(hex-5-yn-1-yl)-4-methyl-N-(propa-1,2-dien-1-yl)benzenesulfonamide (6): The title compound was synthesized from the corresponding 3-bromopropyne and aminoalkyne[21] following GP-A, and obtained as colorless oil in 23% yield (665.6 mg, 10 mmol scale); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.70–7.66 (m, 2H), 7.33–7.29 (m, 2H), 6.82 (t, *J* = 6.2 Hz, 1H), 5.30 (d, *J* = 6.2 Hz, 2H), 3.12 (t, *J* = 7.0 Hz, 2H), 2.43 (s, 3H), 2.20 (td, *J* = 7.0, 2.7 Hz, 2H), 1.94 (t, *J* = 2.7 Hz, 1H), 1.70–1.63 (m, 2H), 1.58–1.52 (m, 2H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 201.5, 143.8, 135.4, 129.8, 127.2, 100.1, 87.7, 84.1, 68.7, 46.0, 26.8, 25.3, 21.6, 18.1; **HRMS** (ESI) *m/z*: $[M + H]^+$ Calcd. for $C_{16}H_{20}NO_2S$ 290.1209; Found 290.1203.

General Procedure for the Synthesis of Compounds 3, 5 and 7 (GP-B).

A solution of aryl diazoacetate (0.4 mmol, 2.0 equiv) in CH_2Cl_2 (1.0 mL) was injected into a solution of 1,n-allenyne (0.2 mmol, 1.0 equiv) and $Cu(PPh_3)_3Br$ (18.6 mg, 0.02 mmol, 10 mol %) in CH_2Cl_2 (1.0 mL) via a syringe pump over 2 h at rt. Then the resulting solution was continued at rt for 12 h. The mixture was concentrated under reduced pressure and purified by flash column chromatography (eluent: hexanes/EtOAc) on silica gel to afford the corresponding 3-azabicyclo[m.2.0] products **3** and **5** or the bisallene product **7**.

Methyl 8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6 diene-8-carboxylate (3aa): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 83% yield (68.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.34–7.23 (m, 7H), 6.58 (s, 1H), 5.96 (t, *J* = 4.9 Hz, 1H), 3.86–3.34 (m, 6H), 2.87 (dd, *J* = 14.8, 2.1 Hz, 1H), 2.51–2.29 (m, 5H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.5, 144.0, 141.3, 140.9, 136.2, 130.0, 128.6, 127.3, 127.1, 126.3, 125.7, 122.7, 121.0, 57.2, 52.8, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{23}H_{23}NO_4SNa$ 432.1240; Found 432.1238.

Ethyl 8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ab): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 81% yield (68.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.33–7.22 (m, 7H), 6.58 (s, 1H), 5.96 (t, *J* = 4.9 Hz, 1H), 4.18–4.04 (m, 2H), 3.81–3.30 (m, 3H), 2.87 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.52–2.27 (m, 5H), 1.15 (t, *J* = 7.1 Hz, 3H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.9, 143.9, 141.4, 141.0, 136.2, 130.0, 128.5, 127.2, 127.1, 126.3, 125.6, 122.5, 121.2, 61.4, 57.2, 46.9, 38.4, 32.6, 21.7, 14.1; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1388.

Benzyl 8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ac): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 70% yield (68.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.63 (m, 2H), 7.32–7.21 (m, 10H), 7.17–7.10 (m, 2H), 6.58 (s, 1H), 5.93 (t, *J* = 4.9 Hz, 1H), 5.14–5.05 (m, 2H), 4.00–3.20 (m, 3H), 2.90 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.47–2.25 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.6, 143.9, 141.1, 140.7, 136.2, 135.9, 130.0, 128.52, 128.47, 128.1, 127.7, 127.3, 127.1, 126.4, 125.8, 122.6, 121.0, 66.9, 57.3, 46.9, 38.4, 32.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{29}H_{27}NO_4SNa$ 508.1553; Found 508.1549.

Allyl 8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ad): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 65% yield (56.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.64 (m, 2H), 7.35–7.22 (m, 7H), 6.59 (s, 1H), 5.99 (t, *J* = 4.9 Hz, 1H), 5.84–5.75 (m, 1H), 5.15–5.09 (m, 2H), 4.60–4.51 (m, 2H), 4.10–3.15 (m, 3H), 2.90 (dd, *J* = 14.9, 1.9 Hz, 1H), 2.49–2.30 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.6, 143.9, 141.2, 140.9, 136.2, 132.0, 130.0, 128.5, 127.3, 127.1, 126.3, 125.8, 122.6, 121.0, 117.8, 65.7, 57.2, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{25}NO_4SNa$ 458.1397; Found 458.1388.

Methyl 8-(p-tolyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ae): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc =

7:1) on silica gel and obtained as colorless oil in 87% yield (73.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.57 (s, 1H), 5.94 (t, *J* = 4.9 Hz, 1H), 3.82–3.22 (m, 6H), 2.85 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.50–2.26 (m, 8H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.6, 143.9, 141.1, 138.3, 137.0, 136.2, 130.0, 129.3, 127.1, 126.2, 125.6, 122.6, 121.0, 56.9, 52.7, 46.9, 38.5, 32.6, 21.7, 21.2; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1388.

Methyl 8-(4-(tert-butyl)phenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3af): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 85% yield (79.2 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.63 (m, 2H), 7.34–7.27 (m, 4H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.57 (s, 1H), 5.95 (t, *J* = 4.9 Hz, 1H), 3.95–3.35 (s, 6H), 2.88 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.48–2.31 (m, 5H), 1.30 (s, 9H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.7, 150.1, 143.9, 141.2, 138.2, 136.3, 130.0, 127.1, 126.0, 125.54, 125.51, 122.5, 121.1, 56.9, 52.7, 47.0, 38.5, 34.6, 32.7, 31.4, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{27}H_{32}NO_4S$ 488.1866; Found 488.1861.

Methyl 8-([1,1'-biphenyl]-4-yl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ag): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 78% yield (75.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.59–7.51 (m, 4H), 7.46–7.28 (m, 7H), 6.60 (s, 1H), 6.00 (t, *J* = 4.9 Hz, 1H), 3.98–3.39 (m, 6H), 2.92 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.52–2.34 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.5, 144.0, 141.0, 140.7, 140.30, 140.28, 136.3, 130.0, 128.9, 127.5, 127.4, 127.19, 127.15, 126.8, 125.7, 122.8, 120.9, 57.0, 52.8, 47.0, 38.6, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{29}H_{27}NO_4SNa$ 508.1553; Found 508.1550.

Methyl 8-(4-methoxyphenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ah): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 91% yield (80.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* =

8.8 Hz, 2H), 6.57 (s, 1H), 5.95 (t, *J* = 4.9 Hz, 1H), 3.84–3.62 (m, 9H), 2.85 (dd, *J* = 14.8, 2.0 Hz, 1H), 2.48–2.30 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.7, 158.8, 143.9, 141.2, 136.2, 133.4, 130.0, 127.5, 127.1, 125.5, 122.6, 121.0, 113.9, 56.5, 55.4, 52.7, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_5SNa$ 462.1346; Found 462.1339.

Methyl 8-(4-fluorophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ai): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 71% yield (60.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.32–7.24 (m, 4H), 7.02–6.96 (m, 2H), 6.59 (s, 1H), 5.95 (t, *J* = 4.9 Hz, 1H), 3.77–3.28 (m, 6H), 2.84 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.52–2.27 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.3, 162.0 (d, *J* = 246.3 Hz), 144.0, 140.9, 137.0 (d, *J* = 3.6 Hz), 136.2, 130.0, 128.1 (d, *J* = 8.1 Hz), 127.1, 125.7, 122.9, 120.6, 115.4 (d, *J* = 21.3 Hz), 56.6, 52.8, 46.9, 38.6, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{23}H_{22}FNO_4SNa$ 450.1146; Found 450.1136.

Methyl 8-(4-chlorophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3aj): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as white solid in 68% yield (60.4 mg); **mp:** 144 –147 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.63 (m, 2H), 7.32–7.21 (m, 6H), 6.59 (s, 1H), 5.94 (t, *J* = 4.8 Hz, 1H), 3.87–3.34 (m, 6H), 2.83 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.53–2.28 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.1, 144.0, 140.7, 139.8, 136.2, 133.2, 130.1, 128.7, 127.9, 127.1, 125.8, 123.0, 120.5, 56.7, 52.9, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{23}H_{22}ClNO_4SNa$ 466.0850; Found 466.0848.

Methyl 8-(4-bromophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ak): The title compound was prepared via following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as white solid in 66% yield (64.5 mg); **mp:** 153–155 °C**; ^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.62 (m, 2H), 7.46–7.39 (m, 2H), 7.33–7.27 (m, 2H), 7.21–7.14 (m, 2H), 6.59 (s, 1H), 5.93 (t, *J* = 4.8 Hz, 1H), 3.85–3.30 (m, 6H), 2.83 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.54–2.28 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.0, 144.0, 140.6, 140.3, 136.2, 131.7,

130.1, 128.2, 127.1, 125.8, 123.0, 121.3, 120.4, 56.8, 52.9, 46.9, 38.5, 32.7, 21.8; **HRMS** (ESI) *m/z*: [M + Na]$^+$ Calcd. for $C_{23}H_{22}BrNO_4SNa$ 510.0345; Found 510.0337.

Methyl 8-(4-iodophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3al): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as white solid in 61% yield (65.3 mg); **mp:** 145–148 ^oC**; ^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.60 (m, 4H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 2H), 6.59 (s, 1H), 5.93 (t, *J* = 4.9 Hz, 1H), 3.85–3.34 (m, 6H), 2.82 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.51–2.29 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.0, 144.0, 141.0, 140.6, 137.7, 136.2, 130.0, 128.5, 127.1, 125.8, 123.0, 120.4, 92.9, 56.8, 52.9, 46.9, 38.4, 32.7, 21.8; **HRMS** (ESI) *m/z*: [M + Na]$^+$ Calcd. for $C_{23}H_{22}INO_4SNa$ 558.0206; Found 558.0195.

Methyl 8-(3-chlorophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3am): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 69% yield (61.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.64 (m, 2H), 7.33–7.22 (m, 5H), 7.21–7.13 (m, 1H), 6.60 (s, 1H), 5.95 (t, *J* = 4.9 Hz, 1H), 3.90–3.35 (m, 6H), 2.84 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.48–2.32 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.9, 144.1, 143.2, 140.3, 136.2, 134.5, 130.1, 129.9, 127.5, 127.1, 126.6, 126.0, 124.7, 123.1, 120.5, 56.9, 52.9, 46.9, 38.5, 32.6, 21.7; **HRMS** (ESI) *m/z*: [M + Na]$^+$ Calcd. for $C_{23}H_{22}ClNO_4SNa$ 466.0850; Found 466.0842.

Methyl 3-tosyl-8-(3-(trifluoromethyl)phenyl)-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3an): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 53% yield (50.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.64 (m, 2H), 7.56–7.47 (m, 3H), 7.47–7.41 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.62 (s, 1H), 5.97 (t, *J* = 4.8 Hz, 1H), 3.85–3.25 (m, 6H), 2.87 (dd, *J* = 14.8, 2.0 Hz, 1H), 2.47–2.33 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.8, 144.1, 142.2, 140.3, 136.1, 130.9 (q, *J* = 32.3 Hz), 130.1, 130.0, 129.2, 127.1, 126.0, 124.3 (q, *J* = 3.6 Hz), 124.1 (q, *J* = 272.5 Hz), 123.2, 123.1 (q, *J* = 4.5

Hz), 120.2, 57.0, 53.0, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{22}F_3NO_4SNa$ 500.1114; Found 500.1108.

Methyl 8-(o-tolyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ao): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 10:1 to 7:1) on silica gel and obtained as colorless oil in 23% yield (19.4 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.64 (m, 2H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.22–7.11 (m, 3H), 6.61 (s, 1H), 5.86 (t, *J* = 4.8 Hz, 1H), 4.00–3.45 (m, 6H), 2.63 (dd, *J* = 14.5, 2.0 Hz, 1H), 2.54–2.32 (m, 5H), 2.12 (s, 3H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.4, 144.0, 140.4, 138.8, 136.3, 136.1, 131.3, 130.0, 127.5, 127.2, 126.5, 126.0, 125.7, 123.3, 120.8, 57.4, 52.9, 46.9, 37.3, 32.6, 21.7, 19.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1388.

Methyl 8-(3,4-dichlorophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ap): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 60% yield (57.4 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.40–7.35 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.13 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.61 (s, 1H), 5.93 (t, *J* = 4.9 Hz, 1H), 3.84–3.53 (m, 6H), 2.82 (dd, *J* = 15.0, 1.9 Hz, 1H), 2.49–2.33 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.6, 144.1, 141.4, 140.2, 136.1, 132.7, 131.5, 130.6, 130.1, 128.5, 127.1, 126.0, 123.3, 120.0, 56.5, 53.0, 46.9, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + H]^+$ Calcd. for $C_{23}H_{22}Cl_2NO_4S$ 478.0641; Found 478.0641.

Methyl 8-(3-bromo-4-fluorophenyl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3aq): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 63% yield (63.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.50–7.44 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.24–7.18 (m, 1H), 7.08–7.03 (m, 1H), 6.61 (s, 1H), 5.94 (t, *J* = 4.9 Hz, 1H), 3.80–3.32 (m, 6H), 2.82 (dd, *J* = 14.9, 1.8 Hz, 1H), 2.51–2.31 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.8, 158.3 (d, *J* = 247.3 Hz), 144.1, 140.4, 138.6 (d, *J* = 3.7 Hz), 136.1, 131.5, 130.1, 127.2 (d, *J* = 7.3 Hz), 127.1, 126.0, 123.3,

120.1, 116.5 (d, J = 22.7 Hz), 109.2 (d, J = 21.2 Hz), 56.3, 53.0, 46.9, 38.6, 32.7, 21.8; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{23}H_{21}FBrNO_4SNa$ 528.0251; Found 528.0247.

Methyl 8-(naphthalen-2-yl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ar): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 58% yield (53.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.82–7.76 (m, 3H), 7.74 (s, 1H), 7.69–7.64 (m, 2H), 7.49–7.43 (m, 2H), 7.41–7.37 (m, 1H), 7.28 (d, J = 8.0 Hz, 2H), 6.62 (s, 1H), 6.05 (t, J = 4.8 Hz, 1H), 4.00–3.30 (m, 6H), 2.95 (dd, J = 14.8, 2.0 Hz, 1H), 2.56–2.35 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.4, 143.9, 140.8, 138.5, 136.3, 133.2, 132.6, 130.0, 128.6, 128.1, 127.7, 127.1, 126.4, 126.2, 125.9, 124.8, 124.6, 122.9, 120.9, 57.4, 52.8, 47.0, 38.5, 32.7, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{27}H_{25}NO_4SNa$ 482.1397; Found 482.1391.

Methyl 8-(benzofuran-3-yl)-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3as): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 69% yield (62.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.66 (m, 2H), 7.49–7.40 (m, 3H), 7.33–7.28 (m, 3H), 7.22–7.18 (m, 1H), 6.65 (s, 1H), 5.92 (t, J = 4.8 Hz, 1H), 3.84–3.28 (m, 6H), 2.93 (dd, J = 14.8, 1.9 Hz, 1H), 2.46–2.31 (m, 5H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.7, 155.9, 144.1, 142.2, 140.7, 136.2, 130.1, 127.2, 126.1, 124.7, 124.5, 123.4, 122.9, 121.3, 121.1, 120.3, 111.9, 52.9, 50.1, 46.9, 36.9, 32.5, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{23}NO_5SNa$ 472.1189; Found 472.1184.

Methyl 8-phenyl-3-(phenylsulfonyl)-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ba): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 80% yield (63.2 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.80–7.76 (m, 2H), 7.61–7.57 (m, 1H), 7.53–7.48 (m, 2H), 7.33–7.23 (m, 5H), 6.59 (s, 1H), 5.96 (t, J = 4.8 Hz, 1H), 3.92–3.45 (m, 6H), 2.88 (dd, J = 14.9, 1.9 Hz, 1H), 2.53–2.28 (m, 2H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.4, 141.2, 140.8, 139.2, 133.1, 129.4, 128.6, 127.3, 127.1,

126.3, 125.8, 122.5, 121.3, 57.2, 52.8, 47.0, 38.5, 32.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{22}H_{21}NO_4SNa$ 418.1084; Found 418.1078.

Methyl 3-((4-bromophenyl)sulfonyl)-8-phenyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ca): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 76% yield (72.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.64 (s, 4H), 7.35–7.24 (m, 5H), 6.54 (s, 1H), 5.98 (t, *J* = 4.8 Hz, 1H), 3.90–3.35 (m, 6H), 2.88 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.52–2.29 (m, 2H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.3, 141.0, 140.8, 138.3, 132.7, 128.64, 128.57, 128.1, 127.4, 126.3, 126.1, 122.3, 122.2, 57.2, 52.8, 47.0, 38.5, 32.5; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{22}H_{20}BrNO_4SNa$ 496.0189; Found 496.0186.

Methyl 3-((4-nitrophenyl)sulfonyl)-8-phenyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3da): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 71% yield (62.5 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.36–8.32 (m, 2H), 7.98–7.95 (m, 2H), 7.33–7.24 (m, 5H), 6.55 (s, 1H), 6.00 (t, *J* = 4.7 Hz, 1H), 3.84–3.49 (m, 6H), 2.91 (dd, *J* = 15.1, 1.9 Hz, 1H), 2.51–2.31 (m, 2H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.2, 150.2, 144.9, 140.79, 140.76, 128.7, 128.3, 127.5, 126.5, 126.2, 124.7, 123.6, 121.6, 57.2, 52.8, 47.2, 38.5, 32.5; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{22}H_{20}N_2O_6SNa$ 463.0934; Found 463.0928.

Methyl 3-(methylsulfonyl)-8-phenyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ea): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as colorless oil in 73% yield (48.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40–7.32 (m, 4H), 7.30–7.25 (m, 1H), 6.41 (s, 1H), 6.12 (t, *J* = 4.8 Hz, 1H), 3.94–3.56 (m, 6H), 2.96–2.88 (m, 4H), 2.79–2.60 (m, 2H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.5, 141.2, 141.1, 128.7, 127.4, 126.4, 125.9, 122.2, 121.6, 57.3, 52.9, 46.7, 39.9, 38.4, 33.6; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{19}NO_4SNa$ 356.0927; Found 356.0923.

Methyl 5-methyl-8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3fa): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc =

7:1) on silica gel and obtained as colorless oil in 82% yield (69.4 mg; mixture of two inseparable regioisomers; dr ~ 1.5:1); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68–7.62 (m, 2H), 7.40–7.23 (m, 7H), 6.57–6.46 (m, 1H), 5.88–5.78 (m, 1H), 4.61–4.51 (m, 1H), 3.81–3.73 (m, 1H), 3.68–3.63 (m, 3H), 2.96–2.88 (m, 1H), 2.45–2.34 (m, 4H), 2.11–1.94 (m, 1H), 0.96–0.86 (m, 3H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.6, 173.5, 143.90, 143.85, 141.84, 141.77, 141.2, 141.1, 136.1, 135.9, 130.0, 129.9, 128.7, 128.5, 127.30, 127.25, 126.41, 126.38, 122.2, 121.9, 121.7, 120.1, 119.0, 118.9, 57.1, 57.0, 52.8, 52.7, 50.2, 49.5, 38.9, 38.6, 36.8, 36.6, 21.7, 17.1, 17.0; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1389.

Methyl 4,8-diphenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ga): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as white solid in 73% yield (70.9 mg; mixture of two inseparable regioisomers; dr ~ 2:1); **mp:** 172–175 °C**; ^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.74–7.66 (m, 2H), 7.36–7.15 (m, 8H), 7.10–6.96 (m, 2H), 6.82–6.58 (m, 1H), 6.51–6.47 (m, 1H), 5.97–5.67 (m, 2H), 3.68–3.39 (m, 4H), 3.30–3.07 (m, 1H), 2.86–2.39 (m, 5H), 2.21–1.95 (m, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.5, 172.9, 144.2, 144.0, 142.63, 142.58, 141.5, 141.0, 139.0, 138.6, 136.1, 135.6, 130.2, 130.0, 128.50, 128.45, 128.4, 127.9, 127.6, 127.4, 127.3, 127.0, 126.9, 126.8, 126.7, 126.4, 126.3, 125.8, 123.7, 123.0, 122.9, 121.5, 119.8, 119.7, 58.2, 57.2, 57.0, 56.9, 52.53, 52.49, 39.4, 38.6, 34.2, 33.7, 21.8; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{29}H_{27}NO_4SNa$ 508.1553; Found 508.1552.

Methyl 1-phenyl-4-tosyl-2,4,4a,5,6,7,8,8a-octahydro-1H-benzo[b]cyclobuta[e]azepine-1-carboxylate (3ha): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel to obtain a mixture of four inseparable regioisomers, which was further recrystallized in hexanes/EtOAc to obtain one major regioisomer as white solid in 35% yield (32.4 mg); **mp:** 177–179 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.65–7.59 (m, 2H), 7.32–7.24 (m, 3H), 7.17–7.07 (m, 4H), 6.40–6.36 (m, 1H), 5.60–5.58 (m, 1H), 3.75 (dd, *J* = 15.1, 2.4 Hz, 1H), 3.64 (s, 3H), 3.04–2.97 (m, 1H), 2.87 (dd, *J* = 15.1, 1.6 Hz, 1H), 2.63–2.55 (m, 1H), 2.38 (s, 3H), 2.33–2.22 (m, 1H), 2.06–1.92 (m, 2H), 1.84–1.76 (m, 1H), 1.65–1.58 (m, 1H), 1.28–1.16 (m,

1H), 1.08–0.95 (m, 2H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.5, 143.1, 140.3, 139.4, 137.6, 132.3, 129.7, 129.5, 128.5, 127.24, 127.15, 126.5, 125.8, 67.4, 57.8, 52.7, 45.4, 38.2, 34.9, 32.7, 26.7, 24.8, 21.8; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{27}H_{29}NO_4SNa$ 486.1710; Found 486.1705.

Methyl 9-methyl-8-phenyl-3-tosyl-3-azabicyclo[5.2.0]nona-1,6-diene-8-carboxylate (3ia): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 7:1) on silica gel and obtained as white solid in 74% yield (62.7 mg; one regioisomer); **mp**: 166–168 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.66 (m, 2H), 7.34–7.26 (m, 5H), 7.09 (d, *J* = 7.0 Hz, 2H), 6.59 (s, 1H), 5.86 (t, *J* = 4.8 Hz, 1H), 3.98–3.92 (m, 1H), 3.84–3.44 (m, 5H), 2.51–2.28 (m, 5H), 0.70 (d, *J* = 7.1 Hz, 3H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 174.1, 143.9, 138.9, 137.5, 136.4, 130.0, 128.6, 128.4, 127.5, 127.3, 127.2, 126.4, 122.1, 62.0, 52.7, 47.1, 41.9, 32.5, 21.8, 16.2; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1391.

Methyl (1Z,7E)-9-phenyl-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5a): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 61% yield (51.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.65 (m, 2H), 7.37–7.23 (m, 7H), 6.28 (s, 1H), 5.73 (t, *J* = 6.6 Hz, 1H), 3.90–3.82 (m, 1H), 3.76–3.68 (m, 1H), 3.65 (s, 3H), 3.61 (dd, *J* = 14.0, 1.9 Hz, 1H), 2.71 (dd, *J* = 14.0, 1.7 Hz, 1H), 2.42 (s, 3H), 2.33–2.24 (m, 1H), 2.19–2.09 (m, 1H), 1.83–1.72 (m, 1H), 1.62–1.52 (m, 1H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.4, 143.9, 141.07, 141.06, 136.2, 130.0, 128.7, 127.3, 127.1, 126.7, 122.3, 121.4, 118.2, 57.7, 52.6, 48.0, 38.8, 25.3, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{25}NO_4SNa$ 446.1397; Found 446.1389.

Methyl (1Z,7E)-9-(p-tolyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5b): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 65% yield (57.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.27 (s, 1H), 5.72 (t, *J* = 6.7 Hz, 1H), 3.89–3.81 (m, 1H), 3.75–3.68 (m, 1H), 3.64 (s, 3H), 3.59 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.68 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.42 (s, 3H), 2.34–2.24 (m, 4H), 2.17–2.09

(m, 1H), 1.82–1.72 (m, 1H), 1.60–1.52 (m, 1H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.6, 143.9, 141.3, 138.1, 137.1, 136.2, 130.0, 129.4, 127.1, 126.6, 122.1, 121.4, 118.4, 57.4, 52.6, 48.0, 38.8, 25.2, 22.6, 21.7, 21.2; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{27}NO_4SNa$ 460.1553; Found 460.1547.

Methyl (1Z,7E)-9-([1,1'-biphenyl]-4-yl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5c): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 68% yield (68.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.70–7.66 (m, 2H), 7.58–7.52 (m, 4H), 7.45–7.40 (m, 4H), 7.36–7.32 (m, 1H), 7.31–7.28 (m, 2H), 6.31 (s, 1H), 5.77 (t, *J* = 6.5 Hz, 1H), 3.91–3.84 (m, 1H), 3.78–3.70 (m, 1H), 3.68 (s, 3H), 3.64 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.75 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.41 (s, 3H), 2.35–2.26 (m, 1H), 2.20–2.12 (m, 1H), 1.84–1.74 (m, 1H), 1.64–1.55 (m, 1H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.4, 143.9, 141.1, 140.7, 140.3, 140.1, 136.2, 130.0, 128.9, 127.5, 127.4, 127.2, 127.1, 122.3, 121.5, 118.2, 57.5, 52.7, 48.0, 38.8, 25.4, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{30}H_{29}NO_4SNa$ 522.1710; Found 522.1702.

Methyl (1Z,7E)-9-(4-fluorophenyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5d): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 60% yield (53.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.70–7.65 (m, 2H), 7.35–7.27 (m, 4H), 7.03–6.96 (m, 2H), 6.30 (s, 1H), 5.72 (t, *J* = 6.6 Hz, 1H), 3.89–3.83 (m, 1H), 3.74–3.64 (m, 4H), 3.60 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.67 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.42 (s, 3H), 2.33–2.24 (m, 1H), 2.19–2.10 (m, 1H), 1.82–1.73 (m, 1H), 1.62–1.53 (m, 1H); **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.2, 162.0 (d, *J* = 246.2 Hz), 143.9, 141.0, 136.8 (d, *J* = 3.4 Hz), 136.1, 130.0, 128.5 (d, *J* = 7.5 Hz), 127.1, 122.3, 121.6, 117.8, 115.5 (d, *J* = 21.2 Hz), 57.0, 52.7, 47.9, 38.8, 25.4, 22.5, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{24}FNO_4SNa$ 464.1302; Found 464.1298.

Methyl (1Z,7E)-9-(4-chlorophenyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5e): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 58% yield (53.0 mg); **^{1}H**

NMR (500 MHz, $CDCl_3$): δ 7.69–7.65 (m, 2H), 7.32–7.25 (m, 6H), 6.30 (s, 1H), 5.71 (t, *J* = 6.6 Hz, 1H), 3.89–3.82 (m, 1H), 3.71–3.63 (m, 4H), 3.60 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.66 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.42 (s, 3H), 2.33–2.25 (m, 1H), 2.19–2.10 (m, 1H), 1.82–1.73 (m, 1H), 1.62–1.53 (m, 1H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 173.0, 144.0, 140.7, 139.6, 136.1, 133.2, 130.0, 128.8, 128.2, 127.1, 122.4, 121.6, 117.6, 57.2, 52.8, 47.9, 38.8, 25.4, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{24}ClNO_4SNa$ 480.1007; Found 480.0999.

Methyl (1Z,7E)-9-(4-bromophenyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5f): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 55% yield (55.3 mg); **^1H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.65 (m, 2H), 7.45–7.42 (m, 2H), 7.31–7.28 (m, 2H), 7.24–7.20 (m, 2H), 6.30 (s, 1H), 5.70 (t, *J* = 6.6 Hz, 1H), 3.88–3.82 (m, 1H), 3.70–3.63 (s, 4H), 3.60 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.66 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.42 (s, 3H), 2.33–2.25 (m, 1H), 2.19–2.10 (m, 1H), 1.82–1.73 (m, 1H), 1.63–1.53 (m, 1H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 172.9, 144.0, 140.7, 140.2, 136.1, 131.8, 130.0, 128.6, 127.1, 122.5, 121.7, 121.3, 117.6, 57.2, 52.8, 47.9, 38.7, 25.4, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{24}BrNO_4SNa$ 524.0502; Found 524.0490.

Methyl (1Z,7E)-9-(4-iodophenyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5g): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 52% yield (57.0 mg); **^1H NMR (500 MHz, $CDCl_3$):** δ 7.70–7.61 (m, 4H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.12–7.07 (m, 2H), 6.29 (s, 1H), 5.69 (t, *J* = 6.6 Hz, 1H), 3.88–3.81 (m, 1H), 3.72–3.62 (m, 4H), 3.60 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.65 (dd, *J* = 13.9, 1.8 Hz, 1H), 2.43 (s, 3H), 2.33–2.25 (m, 1H), 2.19–2.09 (m, 1H), 1.82–1.73 (m, 1H), 1.62–1.53 (m, 1H); **$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):** δ 172.9, 144.0, 140.9, 140.6, 137.7, 136.1, 130.0, 128.9, 127.1, 122.4, 121.7, 117.6, 92.9, 57.3, 52.8, 47.9, 38.7, 25.4, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{24}INO_4SNa$ 572.0363; Found 572.0358.

Methyl (1Z,7E)-9-(3-chlorophenyl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5h): The title compound was prepared following GP-B, purified by flash column chromatography

(hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 38% yield (34.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.66 (m, 2H), 7.33–7.28 (m, 3H), 7.26–7.20 (m, 3H), 6.30 (s, 1H), 5.72 (t, *J* = 6.4 Hz, 1H), 3.89–3.83 (m, 1H), 3.71–3.64 (m, 4H), 3.61 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.68 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.42 (s, 3H), 2.34–2.25 (m, 1H), 2.20–2.11 (m, 1H), 1.82–1.72 (m, 1H), 1.64–1.56 (m, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 172.9, 144.0, 143.2, 140.4, 136.1, 134.5, 130.0, 129.9, 127.6, 127.1, 127.0, 125.0, 122.7, 121.7, 117.5, 57.4, 52.8, 47.9, 38.8, 25.5, 22.6, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{24}H_{24}ClNO_4SNa$ 480.1007; Found 480.1003.

Methyl (1Z,7E)-9-(naphthalen-2-yl)-3-tosyl-3-azabicyclo[6.2.0]deca-1,7-diene-9-carboxylate (5i): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as colorless oil in 47% yield (44.5 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.83–7.77 (m, 4H), 7.69–7.64 (m, 2H), 7.50–7.40 (m, 3H), 7.29–7.25 (m, 2H), 6.30 (s, 1H), 5.82 (t, *J* = 6.6 Hz, 1H), 3.91–3.84 (m, 1H), 3.78–3.64 (m, 5H), 2.79 (dd, *J* = 14.0, 1.8 Hz, 1H), 2.42–2.30 (m, 4H), 2.24–2.16 (m, 1H), 1.87–1.78 (m, 1H), 1.68–1.59 (m, 1H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 173.4, 143.9, 141.0, 138.4, 136.1, 133.2, 132.6, 130.0, 128.6, 128.1, 127.7, 127.1, 126.4, 126.2, 125.3, 125.0, 122.4, 121.6, 118.1, 57.9, 52.7, 48.0, 38.7, 25.5, 22.8, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{28}H_{27}NO_4SNa$ 496.1553; Found 496.1550.

Methyl 8-((4-methyl-N-(propa-1,2-dien-1-yl)phenyl)sulfonamido)-2-phenylocta-2,3-dienoate (7): The title compound was prepared following GP-B, purified by flash column chromatography (hexanes/EtOAc = 15:1 to 7:1) on silica gel and obtained as light-yellow oil in 56% yield (49.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.66 (m, 2H), 7.50–7.46 (m, 2H), 7.37–7.28 (m, 5H), 6.81 (t, *J* = 6.2 Hz, 1H), 5.79 (t, *J* = 7.0 Hz, 1H), 5.26 (d, *J* = 6.3 Hz, 2H), 3.81 (s, 3H), 3.09 (t, *J* = 7.0 Hz, 2H), 2.42 (s, 3H), 2.26–2.20 (m, 2H), 1.67–1.59 (m, 2H), 1.58–1.50 (m, 2H); **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 211.7, 201.5, 167.0, 143.8, 135.4, 133.0, 129.9, 128.5, 128.4, 127.7, 127.3, 103.3, 100.3, 96.0, 87.7, 52.4, 46.3, 27.8, 27.5, 25.8, 21.7; **HRMS** (ESI) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{27}NO_4SNa$ 460.1553; Found 460.1546.

Gram-Scale Synthesis. A solution of phenyl diazoacetate **2a** (1761.8 mg, 10.0 mmol, 2.0 equiv) in CH_2Cl_2 (25.0 mL) was added dropwise into a solution of allenyne **1a** (1306.5 mg, 5.0 mmol, 1.0 equiv) and $Cu(PPh_3)_3Br$ (465.2 mg, 0.5 mmol, 10 mol %) in CH_2Cl_2 (25.0 mL) via a constant pressure dropping funnel over 2 h at rt under N_2. Then the resulting mixture was continued at rt for 12 h (monitored by TLC). The mixture was concentrated under reduced pressure and purified by flash column chromatography (eluent: hexanes/EtOAc = 7:1) on silica gel to afford the corresponding product **3aa** in 72% yield (1474.2 mg).

Radical Inhibition Experiments. A solution of phenyl diazoacetate **2a** (70.5 mg, 0.4 mmol, 2.0 equiv) in CH_2Cl_2 (1.0 mL) was injected into a solution of allenyne **1a** (52.3 mg, 0.2 mmol, 1.0 equiv), $Cu(PPh_3)_3Br$ (18.6 mg, 0.02 mmol, 10 mol %) and additive (BHT 44.1 mg or TEMPO 31.2 mg, 0.2 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) via a syringe pump over 2 h at rt. Then the resulting mixture was continued at rt for 12 h (monitored by TLC). The solution was concentrated under reduced pressure and purified by flash column chromatography (eluent: hexanes/EtOAc = 7:1) on silica gel to afford the corresponding product **3aa** in 80% yield (BHT, 65.5 mg) or 84% yield (TEMPO, 68.8 mg).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

Figures of copies of ^1H and ^{13}C NMR spectra and single crystal X-ray structures (PDF)

Crystal data for **3al**, **3ga**, **3ha**, **3ia** (CIF)

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Notes

The authors declare no competing financial interest.

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14. Other solvents including *n*-hexane, toluene, xylenes, 1,4-dioxane, diethyl ether, ethyl acetate, acetone, *N*,*N*-dimethylformamide, dimethyl sulfoxide, and methanol were tested.

15. CCDC 1956563 (**3al**), CCDC 1956564 (**3ga**), CCDC 1974058 (**3ha**), and CCDC 1974057 (**3ia**) contain the supplementary crystallographic data for this paper, which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

16. For the mechanistic proposal involving the migratory insertion of copper-carbene intermediate **A** to intermediate **B** for the bisallene intermediate **C** formation, see: (a) Zhou, L.; Shi, Y.; Xiao, Q.; Liu, Y.; Ye, F.; Zhang, Y.; Wang, J. CuBr-Catalyzed Coupling of *N*-Tosylhydrazones and Terminal Alkynes: Synthesis of Benzofurans and Indoles. *Org. Lett.* **2011**, *13*, 968–971. (b) Liu, K.; Zhu, C.; Min, J.; Peng, S.; Xu, G.; Sun, J. Stereodivergent Synthesis of N-Heterocycles by Catalyst-Controlled, Activity-Directed Tandem Annulation of Diazo Compounds with Amino Alkynes. *Angew. Chem. Int. Ed.* **2015**, *54*, 12962–12967. (c) Chu, W.-D.; Zhang, L.; Zhang, Z.; Zhou, Q.; Mo, F.; Zhang, Y.; Wang, J. Enantioselective Synthesis of Trisubstituted Allenes via Cu(I)-Catalyzed Coupling of Diazoalkanes with Terminal Alkynes. *J. Am. Chem. Soc.* **2016**, *138*, 14558−14561. (d) Hossain, M. L.; Wang, J. Cu(I)-Catalyzed Cross-Coupling of Diazo Compounds with Terminal Alkynes: An Efficient Access to Allenes. *Chem. Rec.* **2018**, *18*, 1548–1559. For the mechanistic proposal involving a cupracycle intermediate for the intramolecular [2+2]

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