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Synthesis of α,β-Unsaturated Amidines through Gold-Catalyzed Intermolecular Reaction of Azides with Ynamides

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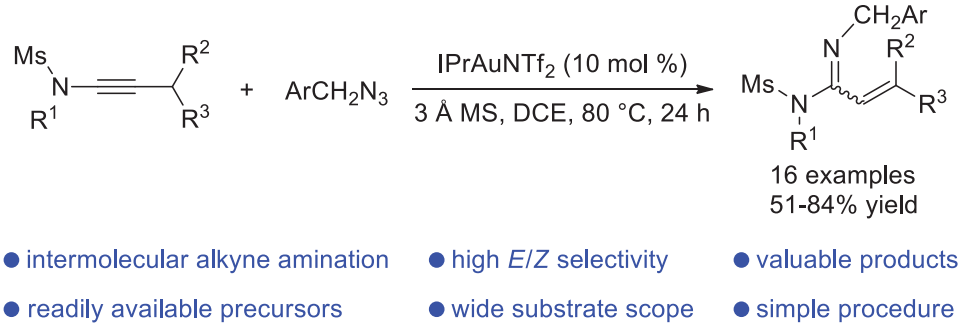


ABSTRACT: A concise and flexible synthesis of α,β-unsaturated amidines via gold-catalyzed intermolecular ynamide amination/carbene 1,2-shift between ynamides and benzylic azides has been developed. Under mild reaction conditions, various α,β-unsaturated amidines were obtained in mostly good yields, thus providing an efficient and atom-economic way for the construction of valuable α,β-unsaturated amidines.

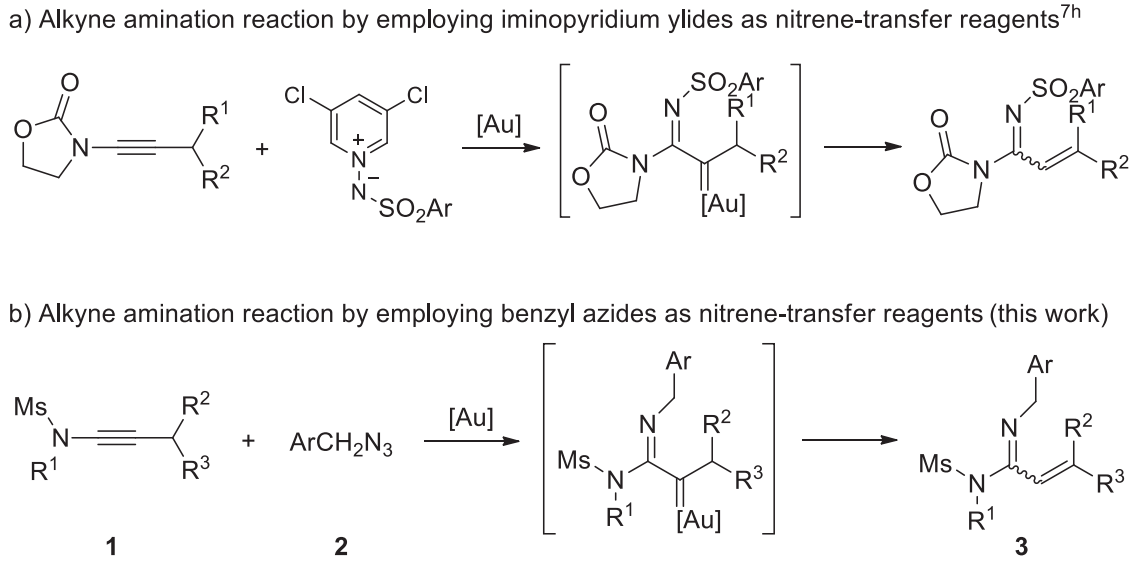
Introduction

α,β-Unsaturated amidines are important structural motifs found in a variety of pharmacologically active molecules,[1] and they are also widely employed as versatile building blocks in organic synthesis, especially as pivotal intermediates for the construction of valuable amidines.[2] It is surprising, however, that only a few preparative methods have been reported to date.[3] Consequently, the development of novel methods for the preparation of α,β-unsaturated amidines is highly desirable, especially those based on assembling structures directly from readily available and easily diversified precursors.

Recently, the generation of α-imino gold carbenes[4] through gold-catalyzed alkyne amination has gained significant attention, as this chemistry offers easy access to an incredible variety of useful complex nitrogen-containing molecules.[5-7] Compared with intramolecular alkyne amination,[6] the intermolecular approach offers much more flexibility, and therefore it is more synthetically useful.[7] For examples, Zhang and co-workers demonstrated an elegant protocol for the gold-catalyzed intermolecular alkyne amination for the synthesis of α,β-unsaturated amidines by employing iminopyridium ylides as nitrene-transfer reagents (Scheme 1a).[7g] In our recent study on the ynamide chemistry,[8,9] we first disclosed that benzyl azides could serve as efficient nitrene transfer reagents to react with ynamides for the intermolecular generation of α-imino gold carbenes, thus leading to the efficient synthesis of versatile 2-aminoindoles and 3-amino-β-carbolines.[10a] Importantly, this protocol provides a strategically novel, atom-economic route to the generation of α-imino gold carbenes. On the basis of this work, we further developed the relevant gold-catalyzed intermolecular ynamide amination initiated aza-Nazarov cyclization[10b,11] and C−H functionalization,[10c] which afforded highly functionalized 2-aminopyrroles

and 2-aza-1,3-butadienes, respectively. Herein, we would like to communicate a gold-catalyzed intermolecular alkyne amination/carbene 1,2-shift by employing benzyl azides as nitrene-transfer reagents, allowing the efficient synthesis of various α,β-unsaturated amidines under mild reaction conditions, particularly in an atom- and step- economic manner (Scheme 1b).

Scheme 1. Synthesis of α,β-Unsaturated Amidines through Gold-Catalyzed Intermolecular Alkyne Amination Reaction.

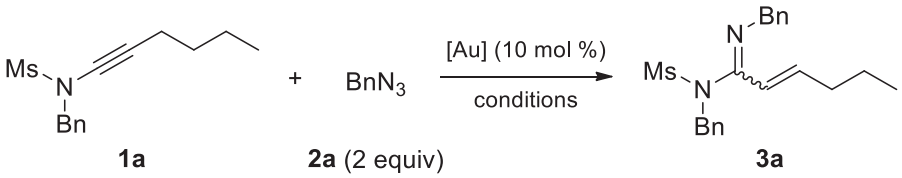


Results and Discussion

At the outset, ynamide **1a** and benzyl azide **2a** were chosen as the model substrates for our initial study and some of the results are listed in Table 1. To our delight, it was found that the reaction of ynamide **1a** and benzyl azide **2a** in the presence of $IPrAuNTf_2$ and 3 Å MS in DCE under 80 °C could afford the desired α,β-unsaturated amidine **3a** in 49% yield with good E/Z selectivity (Table 1, entry 1). Then, the screening of various gold catalysts bearing different ligands showed that $Ph_3PAuNTf_2$ and $XPhosAuNTf_2$ were not effective in promoting this reaction, while $Cy\text{-}JohnPhosAuNTf_2$ and $BrettPhosAuNTf_2$ could hardly work for the reaction (Table 1, entries 2-5). Notably molecular sieves were found to be indispensible for the reaction as confirmed by the control experiment (Table 1, entry 6), and 3 Å MS was found to be superior to 4 Å MS and 5 Å MS (entry 1 vs entries 7-8). Notably, other solvents such as toluene and PhCl failed to produce the desired product (Table 1, entries 9-10).

Increasing the equivalents of **2a** could enhance the reaction (Table 1, entries 11-12), and the reaction with 4 equivalents of **2a** gave a yield of 81% (Table 1, entry 12). Further investigation revealed that the reaction also proceeded at lower temperature, but resulting in a slightly decreased yield (Table 1, entry 13).

Table 1. Optimization of Reaction Conditions[a]



1a **2a** (2 equiv) **3a**

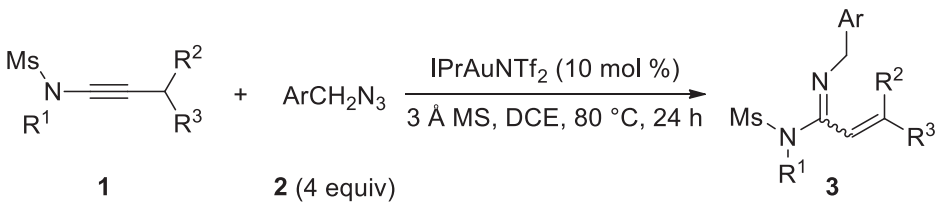
entry	gold catalyst	conditions	yield (%)[b]
1	$IPrAuNTf_2$	3 Å MS, DCE, 80 °C, 24 h	49
2	$Ph_3PAuNTf_2$	3 Å MS, DCE, 80 °C, 24 h	6
3	Cy-JohnPhosAuNTf_2	3 Å MS, DCE, 80 °C, 24 h	<2
4	$XPhosAuNTf_2$	3 Å MS, DCE, 80 °C, 24 h	8
5	$BrettPhosAuNTf_2$	3 Å MS, DCE, 80 °C, 24 h	<2
6	$IPrAuNTf_2$	DCE, 80 °C, 24 h	13
7	$IPrAuNTf_2$	4 Å MS, DCE, 80 °C, 24 h	41
8	$IPrAuNTf_2$	5 Å MS, DCE, 80 °C, 24 h	24
9	$IPrAuNTf_2$	3 Å MS, toluene, 80 °C, 24 h	<2
10	$IPrAuNTf_2$	3 Å MS, PhCl, 80 °C, 24 h	<2
11[c]	$IPrAuNTf_2$	3 Å MS, DCE, 80 °C, 24 h	64
12[d]	**$IPrAuNTf_2$**	**3 Å MS, DCE, 80 °C, 24 h**	**81**
13[d]	$IPrAuNTf_2$	3 Å MS, DCE, 60 °C, 36 h	74

[a]Reaction conditions: [**1a**] = 0.05 M; DCE: 1, 2-dichloroethane; *E*/*Z* = 8/1. [b]Estimated by ^1H NMR using diethyl phthalate as internal reference. [c]3 equiv of **2a** was used. [d]4 equiv of **2a** was used.

With the optimized reaction conditions in hand (Table 1, entry 12), we set out to probe the scope of this novel transformation and the results are summarized in Table 2. Besides ynamide **1a**, the reaction also worked for methyl and cyclopropyl ynamides, affording the desired α,β-unsaturated amidines **3** in

good yields (Table 2, entries 2, 15-16). Then benzyl azides with different groups at the benzene ring were also examined, and the desired products **3c**–**h** could be formed in 66-84% yields (Table 2, entries 3-8). Besides, the variation of alkyl groups on the triple bond was also possible, and the reaction proceeded well for ynamides with different linear, branched, and cyclic alkyl groups, leading to the corresponding products **3i–l** in good yields (Table 2, entries 9-12). In addition, various functional groups including OBoc and OAc were found to be well tolerated under this reaction (Table 2, entries 13-14). Of note, a longer reaction time was needed in some cases (Table 2, entries 2, 10, 13-16). Finally, it should be mentioned that high E/Z selectivity was achieved in all cases, which is better than observed in Zhang's protocol[7g] and our previous result in the relevant alkyne oxidation reaction.[12] While the exact reason for the observed high E/Z selectivity here remains unclear, we suspect that it should be attributed to thermodynamic factors, and further studies on theoretical calculations to elucidate it will be pursued. Thus, this protocol provides a highly convenient and atom-economic route for the construction of synthetically useful α,β-unsaturated amidines, which may find practical applications in organic synthesis.[2,3]

Table 2. Reaction Scope Study[a]



1 **2** (4 equiv) **3**

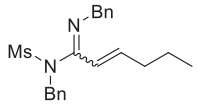
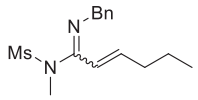
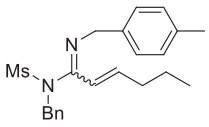
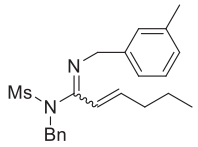
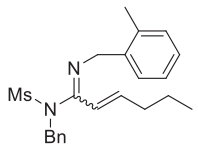
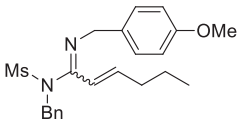
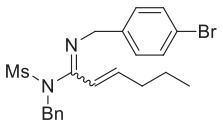
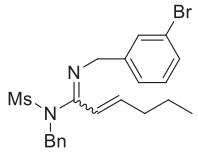
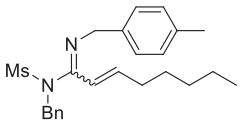
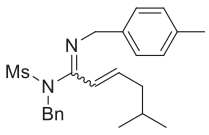
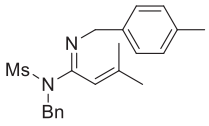
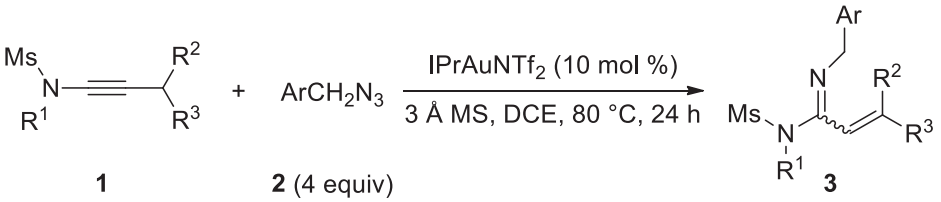
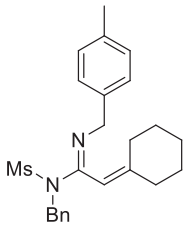
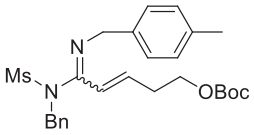
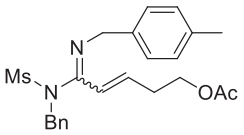
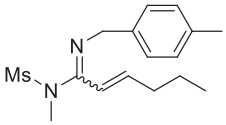
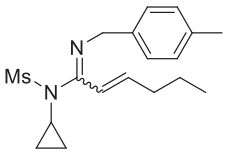
entry	product	3	*E*/*Z*[b]	yield (%)[c]
1		**3a**	8/1	76
2[d]		**3b**	9/1	69
3		**3c**	7/1	83
4		**3d**	>10/1	76
5		**3e**	>10/1	66
6		**3f**	5/1	84
7		**3g**	5/1	71
8		**3h**	>10/1	67
9		**3i**	>10/1	65
10[d]		**3j**	>10/1	74
11		**3k**	-	75

Table 2. (Continued)



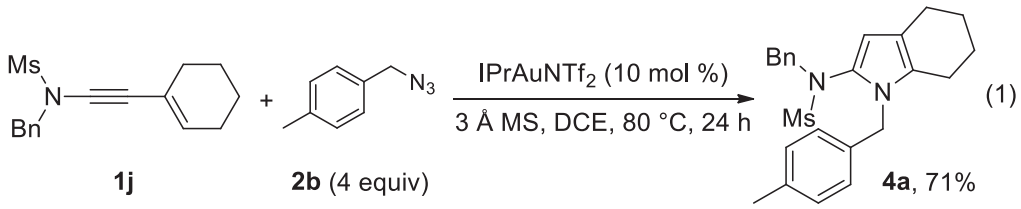
1 **2** (4 equiv) **3**

entry	product	3	*E*/*Z*[b]	yield (%)[c]
12		**3l**	-	78
13[d]		**3m**	9/1	72
14[d]		**3n**	9/1	51
15[d]		**3o**	>10/1	62
16[d]		**3p**	5/1	75

[a]Reactions run in vials; [**1**] = 0.05 M. [b]Determined by ^{1}H NMR integration of the crude mixture. [c]Isolated yield. [d]Time = 30 h.

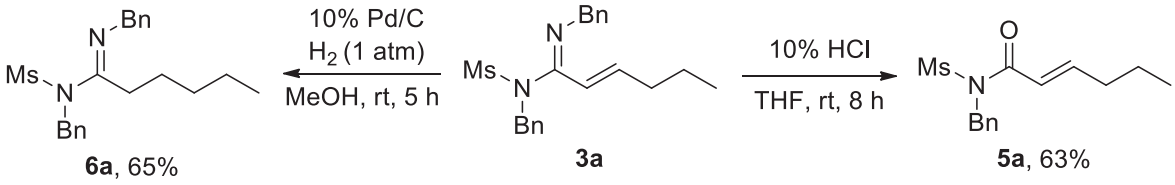
We then considered the possibility of extending the reaction to the conjugated N-sulfonyl ynamide. However, as depicted in eq 1, only 2-aminopyrrole **4a** formation was observed under the above optimized reaction conditions presumably via a gold-catalyzed tandem ynamide amination/aza-Nazarov cyclization.[10b] Of note, this is distinctively different from the relevant ynamide oxidation reaction, where the corresponding α,β,γ,δ-unsaturated N-sulfonyl imide was formed.[12] In addition, it should be

mentioned that other types of azides such as alkyl azides and phenyl azides were not effective substrates for this reaction (<10% ^{1}H NMR yield), which is in accordance with our previous work.[10]



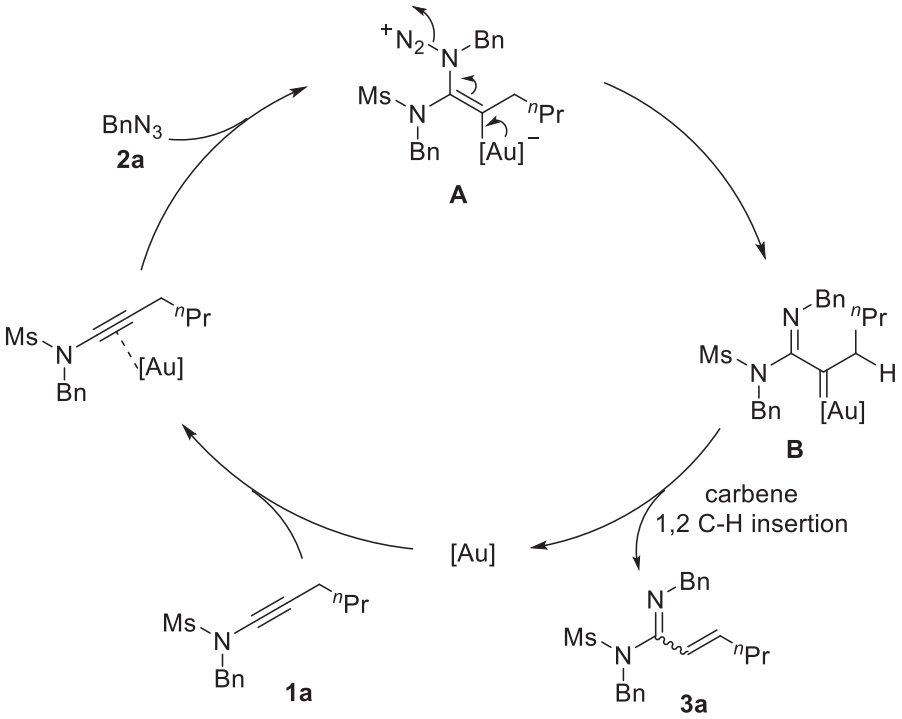
These α,β-unsaturated amidines are potentially useful in organic synthesis,[2] as depicted in Scheme 2. For α,β-unsaturated amidine **3a**, it could be readily converted into the corresponding α,β-unsaturated amide **5a** and amidine **6a** in in 63% and 65%yield, respectively.[3a]

Scheme 2. Synthetic Applications



Based on the above experimental observations and our previous results,[10] the catalytic pathway for the formation of **3** is considered to proceed as illustrated in Scheme 3. Taking substrates **1a** and **2a** for example, similarly, the transformation possibly starts with the nucleophilic attack of benzyl azide **2a** to the Au-ligated alkyne of ynamide **1a** to give the vinyl gold intermediate **A**, which is further transformed into the α-imino gold carbene intermediate **B**. Subsequent carbene 1,2-shift is expected to generate the desired product **3a**.[13]

Scheme 3. Plausible Reaction Mechanism



Conclusion

In summary, we have developed an efficient, flexible, and viable alternative strategy for the preparation of synthetically useful α,β-unsaturated amidines through gold-catalyzed intermolecular ynamide amination/carbene 1,2-shift of ynamides with azides. Compared to the previously reported protocol, this strategy provides an atom- and step- economic way for the construction of functionalized α,β-unsaturated amidines. Other notable features of this method include widespread availability of the substrates, compatibility with broad functional groups, simple procedure and mild reaction conditions. Further synthetic applications of this chemistry are in progress in our laboratory.

Experimental Section

General Information. Ethyl acetate (ACS grade), hexanes (ACS grade) and anhydrous 1,2-dichloroethane (ACS grade) were obtained commercially and used without further purification. Methylene chloride, tetrahydrofuran and diethyl ether were purified according to standard methods unless otherwise noted. Commercially available reagents were used without further purification. High-resolution mass spectra were obtained using electrospray ionization using an ICR analyzer (ESI-MS).

^{1}H NMR spectra were recorded in chloroform-d_3. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data are being reported as (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, brs = broad singlet, coupling constant(s) in Hz, integration).

^{13}C NMR spectra were recorded in chloroform-d_3. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard.

Representative Synthetic Procedures for the Preparation of Ynamides 1.[14] Alkynyl bromide (1.1 mmol) was added to a stirred solution of amide (1.0 mmol), K_2CO_3 (2.0 mmol, 276.4 mg), $CuSO_4 \cdot 5H_2O$ (0.1 mmol, 25.0 mg), 1,10-phenthroline (0.2 mmol, 36.0 mg) and toluene (2 mL) under air, and the resulting mixture was stirred at 80 °C for 8-32 h. The suspension was filtered, and the residue was washed with diethyl ether (3 × 10 mL). The purification of products was achieved by flash chromatography (eluent: hexanes/ethyl acetate = 10/1) to afford the desired ynamide **1**.

*N-benzyl-N-(hex-1-yn-1-yl)methanesulfonamide (**1a**).* Pale yellow oil (201.4mg, 75%). This compound is known and the spectroscopic data match those reported.[10c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.31 (m, 5H), 4.56 (s, 2H), 2.86 (s, 3H), 2.26 (t, J = 6.8 Hz, 2H), 1.53 – 1.41 (m, 2H), 1.40 – 1.26 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 128.9, 128.6, 128.5, 72.9, 71.3, 55.6, 38.2, 30.8, 21.8, 18.1, 13.5.

*N-(hex-1-yn-1-yl)-N-methylmethanesulfonamide (**1b**).* Pale yellow oil (147.4 mg, 78%). This compound is known and the spectroscopic data match those reported.[7c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 3H), 3.03 (s, 3H), 2.28 (t, *J* = 6.8 Hz, 2H), 1.52 – 1.31 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 74.1, 68.9, 39.0, 35.6, 30.8, 21.7, 17.8, 13.4.

*N-benzyl-N-(oct-1-yn-1-yl)methanesulfonamide (**1c**).* Pale yellow oil (237.3 mg, 81%). This compound is known and the spectroscopic data match those reported.[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 5H), 4.46 (s, 2H), 2.76 (s, 3H), 2.15 (t, *J* = 6.8 Hz, 2H), 1.42 – 1.31 (m, 2H), 1.26 – 1.10

(m, 6H), 0.76 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 128.7, 128.5, 128.3, 72.8, 71.1, 55.4, 38.0, 31.1, 28.6, 28.2, 22.4, 18.2, 13.9.

*N-benzyl-N-(5-methylhex-1-yn-1-yl)methanesulfonamide (**1d**)*. Pale yellow oil (203.7 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.33 (m, 5H), 4.56 (s, 2H), 2.86 (s, 3H), 2.26 (t, J = 7.2 Hz, 2H), 1.62 – 1.52 (m, 1H), 1.38 – 1.32 (m, 2H), 0.86 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.7, 128.8, 128.6, 128.4, 77.3, 71.3, 55.5, 38.1, 37.6, 27.0, 22.0, 16.4; IR (neat): 2956, 2931, 2252, 1358, 1163, 583, 514; HRESIMS Calcd for $[C_{15}H_{21}NNaO_2S]^+$ (M + Na^+) 302.1185, found 302.1189.

*N-benzyl-N-(3-methylbut-1-yn-1-yl)methanesulfonamide (**1e**)*. Pale yellow oil (165.8 mg, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 4.55 (s, 2H), 2.85 (s, 3H), 2.69 – 2.56 (m, 1H), 1.13 (d, J = 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 128.9, 128.5, 128.4, 76.6, 72.5, 55.6, 38.0, 23.0, 20.3; IR (neat): 2967, 2918, 2251, 1356, 1163, 582, 513; HRESIMS Calcd for $[C_{13}H_{17}NNaO_2S]^+$ (M + Na^+) 274.0872, found 274.0870.

*N-benzyl-N-(cyclohexylethynyl)methanesulfonamide (**1f**)*. Pale yellow oil (218.3 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 5H), 4.56 (s, 2H), 2.85 (s, 3H), 2.52 – 2.42 (m, 1H), 1.79 – 1.68 (m, 2H), 1.67 – 1.56 (m, 2H), 1.52 – 1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 129.0, 128.6, 128.5, 75.4, 73.3, 55.6, 38.1, 32.7, 28.7, 25.8, 24.6; IR (neat): 2929, 2852, 2247, 1358, 1163, 585, 514; HRESIMS Calcd for $[C_{16}H_{21}NNaO_2S]^+$ (M + Na^+) 314.1185, found 314.1188.

*5-(N-benzylmethylsulfonamido)pent-4-yn-1-yl tert-butyl carbonate (**1g**)*. Pale yellow oil (121.1 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.29 (m, 5H), 4.55 (s, 2H), 4.06 (t, J = 6.4 Hz, 2H), 2.87 (s, 2H), 2.37 (t, J = 7.2 Hz, 2H), 1.84 – 1.75 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 134.5, 128.6, 128.5, 128.3, 81.7, 73.5, 69.6, 65.2, 55.3, 38.1, 27.8, 27.5, 14.9; IR (neat): 2979, 2933, 2255, 1740 (s), 1359, 1163, 583, 515; HRESIMS Calcd for $[C_{18}H_{25}NNaO_5S]^+$ (M + Na^+) 390.1346, found 390.1347.

*5-(N-benzylmethylsulfonamido)pent-4-yn-1-yl acetate (**1h**).* Pale yellow oil (108.2 mg, 35%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 5H), 4.56 (s, 2H), 4.07 (t, *J* = 6.4 Hz, 2H), 2.88 (s, 3H), 2.35 (t, *J* = 7.0 Hz, 2H), 2.03 (s, 3H), 1.81 – 1.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 134.5, 128.7, 128.5, 128.4, 73.5, 69.7, 62.7, 55.3, 38.2, 27.7, 20.7, 15.0; IR (neat): 2925, 2254, 1738 (s), 1357, 1162, 582, 514; HRESIMS Calcd for $[C_{15}H_{19}NNaO_4S]^+$ (M + Na^+) 332.0927, found 332.0929.

*N-cyclopropyl-N-(hex-1-yn-1-yl)methanesulfonamide (**1i**).* Pale yellow oil (118.4 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (s, 3H), 3.00 – 2.91 (m, 1H), 2.29 (t, *J* = 6.8 Hz, 2H), 1.55 – 1.34 (m, 4H), 0.97 – 0.79 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.5, 70.8, 36.6, 32.6, 30.9, 21.8, 18.0, 13.5, 6.2; IR (neat): 2958, 2933, 2252, 1360, 1167, 758, 514; HRESIMS Calcd for $[C_{10}H_{17}NNaO_2S]^+$ (M + Na^+) 238.0872, found 238.0874.

*N-benzyl- N-(cyclohex-1-en-1-ylethynyl)methanesulfonamide (**1j**).* Pale yellow oil (216.8 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.32 (m, 5H), 6.03 – 5.99 (m, 1H), 4.60 (s, 2H), 2.85 (s, 3H), 2.10 – 2.03 (m, 4H), 1.65 – 1.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 134.3, 128.8, 128.6, 128.4, 119.5, 79.4, 72.9, 55.6, 38.3, 29.2, 25.5, 22.1, 21.3; IR (neat): 2930, 2859, 2228, 1359, 1163, 703, 514; HRESIMS Calcd for $[C_{16}H_{19}NNaO_2S]^+$ (M + Na^+) 312.1029, found 312.1026.

General Procedure of the Synthesis of α,β-Unsaturated Amidine 3 from Ynamide 1. A solution of ynamide **1** (0.2 mmol) and benzyl azide **2** (0.8 mmol) in dry DCE (4 mL) was added into the mixture of $IPrAuNTf_2$ (17.3 mg, 0.02 mmol) and 3 Å MS (40 mg) in 10 mL Schlenk flask under N_2 at room temperature. The reaction mixture was stirred at 80 °C and the progress of the reaction was monitored by TLC. The reaction typically took 24 h. Upon completion, the mixture was then diluted with DCM, filtered, concentrated and the residue was purified by chromatography on silicagel (eluent: hexanes/ethyl acetate = 10/1) to afford the desired α,β-unsaturated amidine **3**.

(1E,2E)-N,N'-dibenzyl-N-(methylsulfonyl)hex-2-enimidamide ***(3a)***. Pale yellow oil (56.4 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 10H), 6.46 (dt, J = 15.5, 7.0 Hz, 1H), 6.11 (dt, J = 15.4, 1.5

Hz, 1H), 4.72 (s, 2H), 4.65 (s, 2H), 2.99 (s, 3H), 2.16 – 2.08 (m, 2H), 1.42 – 1.32 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 146.5, 139.5, 135.9, 129.1, 128.4, 127.8, 127.4, 126.7, 119.5, 54.0, 52.6, 39.9, 34.7, 21.5, 13.6; IR (neat): 3030, 2959, 2931, 1650 (s), 1613, 1344, 1152, 964, 699, 516; HRESIMS Calcd for $[C_{21}H_{26}N_2NaO_2S]^+$ ($M^+ Na^+$) 393.1607, found 393.1608.

(1E,2E)-N'-benzyl-N-methyl-N-(methylsulfonyl)hex-2-enimidamide ***(3b)***. Pale yellow oil (40.6 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.22 (m, 5H), 6.64 (dt, J = 15.3, 7.0 Hz, 1H), 6.17 (dt, J = 15.4, 1.4 Hz, 1H), 4.66 (s, 2H), 3.12 (s, 3H), 3.11 (s, 3H), 2.29 – 2.19 (m, 2H), 1.56 – 1.47 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 146.2, 139.6, 128.4, 127.3, 126.8, 118.6, 53.8, 38.0, 36.3, 34.8, 21.6, 13.7; IR (neat): 3028, 2960, 2930, 1650 (s), 1615, 1343, 1148, 966, 699, 517; HRESIMS Calcd for $[C_{15}H_{22}N_2NaO_2S]^+$ ($M + Na^+$) 317.1294, found 317.1299.

(1E,2E)-N-benzyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3c)***. Pale yellow oil (63.7 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 5H), 7.24 – 7.12 (m, 4H), 6.50 – 6.40 (m, 1H), 6.14 – 6.07 (m, 1H), 4.71 (s, 2H), 4.60 (s, 2H), 2.98 (s, 3H), 2.34 (s, 3H), 2.15 – 2.07 (m, 2H), 1.43 – 1.32 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 146.4, 136.5, 136.3, 136.0, 129.2, 129.1, 128.4, 127.8, 127.4, 119.6, 53.8, 52.7, 39.9, 34.7, 21.5, 21.1, 13.6; IR (neat): 3030, 2959, 2929, 1647 (s), 1613, 1344, 1153, 965, 700, 516; HRESIMS Calcd for $[C_{22}H_{28}N_2NaO_2S]^+$ ($M + Na^+$) 407.1764, found 407.1772.

(1E,2E)-N-benzyl-N'-(3-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3d)***. Pale yellow oil (58.4 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.18 (m, 7H), 7.11 – 7.03 (m, 2H), 6.45 (dt, J = 15.4, 7.0 Hz, 1H), 6.12 (dt, J = 15.4, 1.5 Hz, 1H), 4.72 (s, 2H), 4.62 (s, 2H), 2.99 (s, 3H), 2.35 (s, 3H), 2.16 – 2.08 (m, 2H), 1.43 – 1.31 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 146.5, 139.5, 138.0, 135.9, 129.2, 128.4, 128.3, 128.2, 127.8, 127.5, 124.5, 119.5, 54.0, 52.6, 39.9, 34.7, 21.5, 21.4, 13.6; IR (neat): 3030, 2959, 2929, 1647 (s), 1609, 1343, 1153, 965, 699, 516; HRESIMS Calcd for $[C_{22}H_{28}N_2NaO_2S]^+$ ($M + Na^+$) 407.1764, found 407.1771.

(1E,2E)-N-benzyl-N'-(2-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3e)***. Pale yellow oil (50.7 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.25 (m, 5H), 7.23 – 7.14 (m, 4H), 6.46 (dt, J = 15.5, 7.1 Hz, 1H), 6.12 (dt, J = 15.4, 1.5 Hz, 1H), 4.71 (s, 2H), 4.59 (s, 2H), 2.98 (s, 3H), 2.29 (s, 3H), 2.16 –2.08 (m, 2H), 1.44 – 1.33 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 146.4, 137.6, 135.9, 135.8, 130.1, 129.2, 128.4, 127.8, 127.6, 126.8, 126.0, 119.5, 52.6, 52.1, 40.0, 34.7, 21.5, 19.2, 13.6; IR (neat): 3030, 2959, 2929, 1646 (s), 1605, 1343, 1152, 964, 700, 516; HRESIMS Calcd for $[C_{22}H_{28}N_2NaO_2S]^+$ (M + Na^+) 407.1764, found 407.1768.

(1E,2E)-N-benzyl-N'-(4-methoxybenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3f)***. Pale yellow oil (67.2 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 5H), 7.20 – 7.14 (m, 2H), 6.90 – 6.84 (m, 2H), 6.46 (dt, J = 15.5, 7.0 Hz, 1H), 6.11 (dt, J = 15.5, 1.5 Hz, 1H), 4.71 (s, 2H), 4.59 (s, 2H), 3.80 (s, 3H), 2.98 (s, 3H), 2.15 – 2.08 (m, 2H), 1.44 – 1.32 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 156.5, 146.3, 136.0, 131.7, 129.2, 128.5, 128.4, 127.8, 119.6, 113.8, 55.3, 53.5, 52.6, 39.9, 34.7, 21.5, 13.6; IR (neat): 3031, 2959, 2931, 1647 (s), 1611, 1342, 1152, 964, 703, 516; HRESIMS Calcd for $[C_{22}H_{28}N_2NaO_3S]^+$ (M + Na^+) 423.1713, found 423.1715.

(1E,2E)-N-benzyl-N'-(4-bromobenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3g)***. Pale yellow oil (63.6 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.31 – 7.24 (m, 5H), 7.15 – 7.10 (m, 2H), 6.46 (dt, J = 15.5, 7.0 Hz, 1H), 6.07 (dt, J = 15.5, 1.5 Hz, 1H), 4.73 (s, 2H), 4.58 (s, 2H), 2.98 (s, 3H), 2.16 –2.08 (m, 2H), 1.44 – 1.33 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 146.7, 138.7, 135.9, 131.5, 129.2, 129.1, 128.5, 127.9, 120.5, 119.5, 53.4, 52.5, 40.3, 34.7, 21.5, 13.6; IR (neat): 3031, 2959, 2929, 1647 (s), 1613, 1343, 1153, 966, 700, 517; HRESIMS Calcd for $[C_{21}H_{25}BrN_2NaO_2S]^+$ (M + Na^+) 471.0712, found 471.0719.

(1E,2E)-N-benzyl-N'-(3-bromobenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3h)***. Pale yellow oil (59.2 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.42 (m, 1H), 7.41 – 7.36 (m, 1H), 7.34 – 7.24 (m, 5H), 7.21 – 7.17 (m, 2H), 6.47 (dt, J = 15.5, 7.1 Hz, 1H), 6.07 (dt, J = 15.4, 1.5 Hz, 1H), 4.74 (s, 2H), 4.60 (s, 2H), 2.99 (s, 3H), 2.18 – 2.10 (m, 2H), 1.44 – 1.34 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 157.1, 146.8, 142.0, 135.8, 130.5, 130.0, 129.8, 129.0, 128.5, 127.9, 126.0, 122.5, 119.4, 53.3, 52.5, 40.3, 34.7, 21.5, 13.6; IR (neat): 3031, 2959, 2929, 1647 (s), 1613, 1343, 1152, 964, 700, 517; HRESIMS Calcd for $[C_{21}H_{25}BrN_2NaO_2S]^+$ (M + Na^+) 471.0712, found 471.0718.

(1E,2E)-N-benzyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)oct-2-enimidamide ***(3i)***. Pale yellow oil (53.6 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 5H), 7.14 (s, 4H), 6.46 (dt, J = 15.4, 7.0 Hz, 1H), 6.10 (dt, J = 15.4, 1.6 Hz, 1H), 4.71 (s, 2H), 4.61 (s, 2H), 2.98 (s, 3H), 2.35 (s, 3H), 2.17 – 2.07 (m, 2H), 1.39 – 1.13 (m, 6H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 146.8, 136.5, 136.3, 136.0, 129.2, 129.1, 128.4, 127.8, 127.4, 119.4, 53.8, 52.7, 39.8, 32.7, 31.2, 28.0, 22.4, 21.1, 13.9; IR (neat): 3030, 2956, 2927, 1646(s), 1613, 1344, 1153, 962, 700, 516; HRESIMS Calcd for $[C_{24}H_{32}N_2NaO_2S]^+$ (M + Na^+) 435.2077, found 435.2081.

(1E,2E)-N-benzyl-5-methyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3j)***. Pale yellow oil (58.9 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 5H), 7.14 (s, 4H), 6.46 (dt, J = 15.2, 7.5 Hz, 1H), 6.11 (dt, J = 15.3, 1.4 Hz, 1H), 4.71 (s, 2H), 4.61 (s, 2H), 2.98 (s, 3H), 2.35 (s, 3H), 2.05 – 1.99 (m, 2H), 1.68 – 1.57 (m, 1H), 0.82 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 145.6, 136.4, 136.3, 135.9, 129.2, 129.1, 128.4, 127.8, 127.4, 120.5, 53.7, 52.7, 42.0, 39.5, 27.9, 22.3, 21.1; IR (neat): 3030, 2955, 2926, 1646 (s), 1612, 1344, 1153, 965, 700, 518; HRESIMS Calcd for $[C_{23}H_{30}N_2NaO_2S]^+$ (M + Na^+) 421.1920, found 421.1918.

(E)-N-benzyl-3-methyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)but-2-enimidamide ***(3k)***. Pale yellow oil (55.5 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 5H), 7.18 – 7.08 (m, 4H), 5.60 (s, 1H), 4.90 (s, 2H), 4.47 (s, 2H), 3.10 (s, 3H), 2.32 (s, 3H), 1.83 (d, J = 1.2 Hz, 3H), 1.61 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 144.5, 137.5, 137.2, 135.9, 128.9, 128.5, 128.0, 127.4, 127.2, 116.4, 54.1, 50.0, 43.4, 25.0, 21.0, 20.3; IR (neat): 3030, 2920, 1638 (s), 1341, 1152, 960, 701, 515; HRESIMS Calcd for $[C_{21}H_{26}N_2NaO_2S]^+$ (M + Na^+) 393.1607, found 393.1608.

(E)-N-benzyl-2-cyclohexylidene-N'-(4-methylbenzyl)-N-(methylsulfonyl)acetimidamide ***(3l)***. Pale yellow oil (64.0 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 5H), 7.19 – 7.08 (m, 4H), 5.49 (s, 1H), 4.93 (s, 2H), 4.49 (s, 2H), 3.12 (s, 3H), 2.32 (s, 3H), 2.18 (t, J = 5.6 Hz, 2H), 2.05 (t, J = 6.4 Hz, 2H), 1.63 – 1.39 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 151.5, 137.6, 137.3, 135.9, 128.9, 128.5, 127.8, 127.4, 127.2, 112.9, 54.4, 50.1, 43.4, 36.1, 30.9, 28.1, 26.8, 25.9, 21.0; IR (neat): 3030, 2929, 2855, 1638 (s), 1342, 1153, 960, 701, 516; HRESIMS Calcd for $[C_{24}H_{30}N_2NaO_2S]^+$ (M + Na^+) 433.1920, found 433.1923.

(3E,5E)-5-(N-benzylmethylsulfonamido)-5-((4-methylbenzyl)imino)pent-3-en-1-yl tert-butyl carbonate ***(3m)***. Pale yellow oil (70.0 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 5H), 7.13 (s, 4H), 6.36 (dt, J = 15.5, 6.9 Hz, 1H), 6.19 (dt, J = 15.6, 1.5 Hz, 1H), 4.72 (s, 2H), 4.60 (s, 2H), 4.03 (t, J = 6.4 Hz, 2H), 2.99 (s, 3H), 2.53 – 2.46 (m, 2H), 2.34 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 153.3, 140.4, 136.4, 136.3, 135.9, 129.2, 129.1, 128.5, 127.9, 127.3, 121.9, 82.2, 64.9, 53.9, 52.5, 40.3, 31.9, 27.7, 21.1; IR (neat): 2977, 2926, 1740 (s), 1650, 1615, 1343, 1154, 963, 701, 516; RESIMS Calcd for $[C_{26}H_{34}N_2NaO_5S]^+$ (M + Na^+) 509.2081, found 509.2091.

(3E,5E)-5-(N-benzylmethylsulfonamido)-5-((4-methylbenzyl)imino)pent-3-en-1-yl acetate ***(3n)***. Pale yellow oil (43.7 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 5H), 7.13 (s, 4H), 6.37 (dt, J = 15.5, 6.9 Hz, 1H), 6.19 (dt, J = 15.5, 1.5 Hz, 1H), 4.71 (s, 2H), 4.61 (s, 2H), 4.03 (t, J = 5.2 Hz, 2H), 2.99 (s, 3H), 2.49 – 2.42 (m, 2H), 2.35 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 156.1, 141.0, 136.4, 136.2, 135.8, 129.2, 129.1, 128.4, 127.9, 127.3, 121.8, 62.5, 53.9, 52.6, 39.8, 31.9, 21.1, 20.9; IR (neat): 3024, 2924, 2854, 1738 (s), 1650, 1614, 1341, 1152, 963, 700, 515; HRESIMS Calcd for $[C_{23}H_{28}N_2NaO_4S]^+$ (M + Na^+) 451.1662, found 451.1668.

(1E,2E)-N-methyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3o)***. Pale yellow oil (44.4 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 7.16 – 7.12 (m, 2H), 6.63 (dt, J = 15.4, 7.0 Hz, 1H), 6.17 (dt, J = 15.4, 1.5 Hz, 1H), 4.61 (s, 2H), 3.10 (s, 6H), 2.34 (s, 3H), 2.27 – 2.19 (m, 2H), 1.56 – 1.46 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.5, 146.1, 136.6,

136.4, 129.1, 127.3, 118.6, 53.6, 38.0, 36.3, 34.8, 21.6, 21.1, 13.7; IR (neat): 2958, 2925, 1649 (s), 1615, 1342, 1148, 967, 771, 518; HRESIMS Calcd for $[C_{16}H_{24}N_2NaO_2S]^+$ (M + Na^+) 331.1451, found 331.1453.

(1E,2E)-N-cyclopropyl-N'-(4-methylbenzyl)-N-(methylsulfonyl)hex-2-enimidamide ***(3p)***. Pale yellow oil (50.1 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.11 (m, 4H), 6.60 (dt, J = 15.2, 7.0 Hz, 1H), 6.31 (dt, J = 15.1, 1.5 Hz, 1H), 4.65 (s, 2H), 3.13 (s, 3H), 2.92 – 2.85 (m, 1H), 2.34 (s, 3H), 2.26 – 2.17 (m, 2H), 1.56 – 1.44 (m, 2H), 0.93 (t, J = 7.6 Hz, 3H), 0.84 – 0.74 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 146.5, 136.4, 136.3, 129.1, 127.3, 120.3, 53.6, 38.4, 34.7, 30.4, 21.6, 21.1, 13.7, 7.0; IR (neat): 3016, 2959, 2928, 1647 (s), 1613, 1344, 1156, 966, 760, 522; HRESIMS Calcd for $[C_{18}H_{26}N_2NaO_2S]^+$ (M + Na^+) 357.1607, found 357.1608.

N-benzyl-N-(1-(4-methylbenzyl)-4,5,6,7-tetrahydro-1H-indol-2-yl)methanesulfonamide ***(4a)***. Pale yellow oil (50.8 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 5H), 7.01 (d, J = 8.0 Hz, 2H), 6.71 (d, J = 8.0 Hz, 2H), 5.74 (s, 1H), 5.09 (s, 1H), 4.76 (s, 1H), 4.53 (s, 1H), 4.13 (s, 1H), 2.77 (s, 3H), 2.50 – 2.43 (t, J = 6.4 Hz, 2H), 2.28 (s, 3H), 2.27 – 2.10 (m, 2H), 1.77 – 1.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.8, 135.5, 129.7, 129.1, 128.4, 128.1, 127.8, 126.2, 125.2, 116.0, 104.9, 56.4, 45.7, 37.9, 23.4, 23.1, 22.9, 22.2, 21.0; IR (neat): 2926, 2852, 1340, 1154, 913, 748, 700; HRESIMS Calcd for $[C_{24}H_{28}N_2NaO_2S]^+$ (M + Na^+) 431.1764, found 431.1765.

(E)-N-benzyl-N-(methylsulfonyl)hex-2-enamide ***(5a)***. Compound **5a** (0.2 mmol scale) was prepared according to the known procedures.[3a] Pale yellow oil (35.5 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 4H), 7.31 – 7.26 (m, 1H), 7.14 (dt, J = 15.2, 7.2 Hz, 1H), 6.49 (dt, J = 15.2, 1.6 Hz, 1H), 5.05 (s, 2H), 3.14 (s, 3H), 2.23 – 2.17 (m, 2H), 1.51 – 1.42 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 152.4, 136.5, 128.8, 127.9, 127.6, 120.7, 48.9, 43.1, 34.7, 21.2, 13.6; IR (neat): 2924, 2848, 1681 (s), 1632, 1536, 1495, 1453, 1353, 1179, 1159, 962, 700; HRESIMS Calcd for $[C_{14}H_{19}NNaO_3S]^+$ (M + Na^+) 304.0978, found 304.0981.

(E)-N,N'-dibenzyl-N-(methylsulfonyl)hexanimidamide ***(6a)***. Compound **6a** (0.2 mmol scale) was prepared according to the known procedures.[3a] Pale yellow oil (48.4 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 10H), 4.80 (s, 2H), 4.57 (s, 2H), 3.05 (s, 3H), 2.45 (t, J = 8.0 Hz, 2H), 1.33 – 1.28 (m, 2H), 1.18 – 1.11 (m, 4H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 139.6, 136.7, 128.7, 128.5, 128.4, 127.7, 127.4, 126.8, 53.8, 51.1, 40.3, 31.5, 30.6, 25.2, 22.2, 13.8; IR (neat): 2925, 2855, 1652, 1558. 1496, 1455, 1341, 1150, 1076, 1027, 961, 698, 517; HRESIMS Calcd for $[C_{21}H_{28}N_2NaO_2S]^+$ (M + Na^+) 395.1764, found 395.1765.

ASSOCIATED CONTENT

Supporting Information Available. ^{1}H and ^{13}C NMR spectra for all described compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected examples, see: (a) Le, D. D.; Cortesi, A. T.; Myers, S. A.; Burlingame, A. L.; Fujimori, D. G. J. Am. Chem. Soc. **2013**, 135, 2879. (b) Smith, N. D.; Govek, S. P.; Kahraman, M.; Julien, J. D.; Nagasawa, J. Y.; Douglas, K. L.; Bonnefous, C.; Lai, A. G. PCT Int. Appl. WO 2013142266A1, **2013**. (c) Otogouro, K.; Iwatsuki, M.; Ishiyama, A.; Namatame, M.; Nishihara-Tukashima, A.; Shibahara, S.; Kondo, S.; Yamada, H.; Ōmura, S. J. Antibiot. **2010**, 63, 381. (d) Chalifour, R. J.; Kong, X.; Wu, X.; Lu, W. PCT Int. Appl. WO 2003017994A1, **2003**. (e) Saluste, C. G.; Whitby, R. J.; Furber, M. Angew. Chem., Int. Ed. **2000**, 39, 4156. (f) Vicini, P.; Zani, F. Farmaco **1997**, 52, 21. (g) Greenhill, J. V.; Lue, P. Prog. Med. Chem. **1993**, 30, 203.

(2) For a review, see: (a) Rauws, T. R. M.; Maes, B. U. W. Chem. Soc. Rev. **2012**, 41, 2463. For recent selected examples, see: (b) Chang, S.-Y.; Bae, S. J.; Lee, M. Y.; Baek, S.-H.; Chang, S.; Kim, S. H. Bioorg. Med. Chem. Lett. **2011**, 21,727. (c) Lee, M. Y.; Kim, M. H.; Kim, J.; Kim, S. H.; Kim, B. T.; Jeong, I. H.; Chang, S.; Kim, S. H.; Chang, S. Bioorg. Med. Chem. Lett. **2010**, 20, 541. (d) Shindoh, N.; Takemoto, Y.; Takasu, K. Chem. - Eur. J. **2009**, 15, 7026. (e) Calas, M.; Ouattara, M.; Piquet, G.; Ziora, Z.; Bordat, Y.; Ancelin, M. L.; Escale, R.; Vial, H. J. Med. Chem. **2007**, 50, 6307. (f) Thominiaux, C.; de Bruin, B.; Bramoulle, Y.; Hinnen, F.; Demphel, S.; Valette, H.; Bottlaender, M.; Besret, L.; Kassiou, M.; Dolle, F. Appl. Radiat. Isot. **2006**, 64, 348.

(3) For recent examples, see: (a) Singh, R. R.; Liu, R.-S. Adv. Synth. Catal. **2016**, 358, 1421. (b) Wang, J.; Lu, P.; Wang, Y. Org. Chem. Front. **2015**, 2, 1346. (c) Chauhan, D. P.; Varma, S. J.; Vijeta, A.; Banerjee, P.; Talukdar, P. Chem.Commun. **2014**, 50, 323. (d) Yao, B.; Shen, C.; Liang, Z.; Zhang, Y. J. Org. Chem. **2014**, 79, 936. (e) Yan, X.; Liao, J.; Lu, Y.; Liu, J.; Zeng, Y.; Cai, Q. Org. Lett. **2013**, 15, 2478. (f) Shindoh, N.; Kitaura, K.; Takemoto, Y.; Takasu, K. J. Am. Chem. Soc. **2011**, 133, 8470. (g) Tetala, K.; Whiteby, R. J.; Light, M. E.; Hurtshouse, M. B. Tetrahedron Lett. **2004**, 45, 6991.

(4) For recent selected reviews on gold carbene chemistry, see: (a) Asiri, A. M.; Hashmi, A. S. K. Chem. Soc. Rev. **2016**, 45, 4471. (b) Zheng, Z.; Wang, Z.; Wang, Y.; Zhang, L. Chem. Soc. Rev. **2016**, 45, 4448. (c) Pflästerer, D.; Hashmi, A. S. K. Chem. Soc. Rev. **2016**, 45, 1331. (d) Liu, L.; Zhang, J.

Chem. Soc. Rev. **2016**, 45, 506. (e) Qian, D.; Zhang, J. Chem. Soc. Rev. **2015**, 44, 677. (f) Wang, Y.; Muratore, M. E.; Echavarren, A. E. Chem. - Eur. J. **2015**, 21, 7332. (g) Wei, F.; Song, C.; Ma, Y.; Zhou, L.; Tung, C.-H.; Xu, Z. Sci. Bull. **2015**, 60, 1479. (h) Yeom, H.-S.; Shin, S. Acc. Chem. Res. **2014**, 47, 966. (i) Zhang, L. Acc. Chem. Res. **2014**, 47, 877. (j) Hashmi, A. S. K. Acc. Chem. Res. **2014**, 47, 864.

(5) For a review, see: Davies, P. W.; Garzón, M. Asian J. Org. Chem. **2015**, 4, 694.

(6) For selected examples on the intramolecular generation of α-imino gold carbenes, see: (a) Li, N.; Lian, X.-L.; Li, Y.-H.; Wang, T.-Y.; Han, Z.-Y.; Zhang, L.; Gong, L.-Z. Org. Lett. **2016**, 18, 4178. (b) Pan, Y.; Chen, G.-W.; Shen, C.-H.; He, W.; Ye, L.-W. Org. Chem. Front. **2016**, 3, 491. (c) Prechter, A.; Henrion, G.; Faudot dit Bel, P.; Gagosz, F. Angew. Chem., Int. Ed. **2014**, 53, 4959. (d) Tokimizu, Y.; Oishi, S.; Fujii, N.; Ohno, H. Org. Lett. **2014**, 16, 3138. (e) Yan, Z.-Y.; Xiao, Y.; Zhang, L. Angew. Chem., Int. Ed. **2012**, 51, 8624. (f) Lu, B.; Luo, Y.; Liu, L.; Ye, L.; Wang, Y.; Zhang, L. Angew. Chem., Int. Ed. **2011**, 50, 8358. (g) Wetzel, A.; Gagosz, F. Angew. Chem., Int. Ed. **2011**, 50, 7354. (h) Gorin, D. J.; Davis, N. R.; Toste, F. D. J. Am. Chem. Soc. **2005**, 127, 11260.

(7) For selected examples on the intermolecular generation of α-imino gold carbenes, see: (a) Jin, H.; Tian, B.; Song, X.; Xie, J.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Angew. Chem., Int. Ed. **2016**, 55, 12688. (b) Jin, H.; Huang, L.; Xie, J.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Angew. Chem., Int. Ed. **2016**, 55, 794. (c) Zhu, L.; Yu, Y.; Mao, Z.; Huang, X. Org. Lett. **2015**, 17, 30. (d) Pawar, S. K.; Sahani, R. L.; Liu, R.-S. Chem. - Eur. J. **2015**, 21, 10843. (e) Chatzopoulou, E.; Davies, P. W. Chem. Commun. **2013**, 49, 8617. (f) Davies, P. W.; Cremonesi, A.; Dumitrescu, L. Angew. Chem., Int. Ed. **2011**, 50, 8931. (g) Li, C.; Zhang, L. Org. Lett. **2011**, 13, 1738.

(8) For recent reviews on ynamide reactivity, see: (a) Evano, G.; Theunissen, C.; Lecomte, M. Aldrichimica Acta **2015**, 48, 59. (b) Wang, X.-N.; Yeom, H.-S.; Fang, L.-C.; He, S.; Ma, Z.-X.; Kedrowski, B. L.; Hsung, R. P. Acc. Chem. Res. **2014**, 47, 560. (c) DeKorver, K. A.; Li, H.; Lohse, A.

G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. Chem. Rev. **2010**, 110, 5064. (d) Evano, G.; Coste, A.; Jouvin, K. Angew. Chem., Int. Ed. **2010**, 49, 2840.

(9) (a) Zhou, B.; Li, L.; Zhu, X.-Q.; Yan, J.-Z.; Guo, Y.-L.; Ye, L.-W. Angew. Chem., Int. Ed. **2017**, 56, 4015. (b) Shen, W.-B.; Xiao, X.-Y.; Sun, Q.; Zhou, B.; Zhu, X.-Q.; Yan, J.-Z.; Lu, X.; Ye, L.-W. Angew. Chem., Int. Ed. **2017**, 56, 605. (c) Li, L.; Zhou, B.; Wang, Y.-H.; Shu, C.; Pan, Y.-F.; Lu, X.; Ye, L.-W. Angew. Chem., Int. Ed. **2015**, 54, 8245. (d) Zhou, A.-H.; He, Q.; Shu, C.; Yu, Y.-F.; Liu, S.; Zhao, T.; Zhang, W.; Lu, X.; Ye, L.-W. Chem. Sci. **2015**, 6, 1265. (e) Li, L.; Shu, C.; Zhou, B.; Yu, Y.-F.; Xiao, X.-Y.; Ye, L.-W. Chem. Sci. **2014**, 5, 4057.

(10) (a) Shu, C.; Wang, Y.-H.; Zhou, B.; Li, X.-L.; Ping, Y.-F.; Lu, X.; Ye, L.-W. J. Am. Chem. Soc. **2015**, 137, 9567. (b) Shu, C.; Wang, Y.-H.; Shen, C.-H.; Ruan, P.-P.; Lu, X.; Ye, L.-W. Org. Lett. **2016**, 18, 3254. (c) Shu, C.; Shen, C.-H.; Wang, Y.-H.; Li, L.; Li, T.; Lu, X.; Ye, L.-W. Org. Lett. **2016**, 18, 4630.

(11) Hashmi, A. S. K.; Pankajakshan, S.; Rudolph, M.; Enns, E.; Bander, T.; Rominger, F.; Frey, W. Adv. Synth. Catal. **2009**, 351, 2855.

(12) Pan, F.; Shu, C.; Ping, Y.-F.; Pan, Y.-F.; Ruan, P.-P.; Fei, Q.-R.; Ye, L.-W. J. Org. Chem. **2015**, 80, 10009.

(13) For other expamles of such a Wagner-Meerwein 1,2-shift in gold catalysis, see: (a) Lauterbach, T.; Higuchi, T.; Hussong, M. W.; Rudolph, M.; Rominger, F.; Mashima, K.; Hashmi, A. S. K. Adv. Synth. Catal. **2015**, 357, 775. (b) Wang, T.; Shi, S.; Hansmann, M. M.; Rettenmeier, E.; Rudolph, M.; Hashmi, A. S. K. Angew. Chem., Int. Ed. **2014**, 53, 3715. (c) Wang, T.; Huang, L.; Shi, S.; Rudolph, M.; Hashmi, A. S. K. Chem. - Eur. J. **2014**, 20, 14868. (d) Wang, T.; Shi, S.; Rudolph, M.; Hashmi, A. S. K. Adv. Synth. Catal. **2014**, 356, 2337. (e) Lauterbach, T.; Ganschow, M.; W. Hussong, M.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Adv. Synth. Catal. **2014**, 356, 680. (f) Nösel, P.; dos Santos Comprido, L. N.; Lauterbach, T.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. J. Am. Chem. Soc. **2013**, 135,

15662. (g) Lauterbach, T.; Gatzweiler, S.; Nösel, P.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Adv. Synth. Catal. **2013**, 355, 2481. (h) Yao, X.; Wang, T.; Zhang, X.; Wang, P.; Zhang, B.; Wei, J.; Zhang, Z. Adv. Synth. Catal. **2016**, 358, 1534. (i) Wang, J.; Yao, X.; Wang, T.; Han, J.; Zhang, J.; Zhang, X.; Wang, P.; Zhang, Z. Org. Lett. **2015**, 17, 5124. (j) dos Santos Comprido, L. N.; Klein, J. E. M. N.; Knizia, G.; Kästner, J.; Hashmi, A. S. K. Chem. - Eur. J. **2016**, 22, 2892. (k) Nunes dos Santos Comprido, L.; Klein, J. E. M. N.; Knizia, G.; Kästner, J.; Hashmi, A. S. K. Angew. Chem., Int. Ed. **2015**, 54, 10336.

(14) Zhang, Y.; Hsung, R. P.; Tracey, M. R.; Kurtz, K. C. M.; Vera, E. L. Org. Lett. **2004**, 6, 1151.

(15) Yao, B.-B.; Liang, Z.-J.; Niu, T.-M.; Zhang, Y.-H. J. Org. Chem. **2009**, 74, 4630.