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# Silver-Catalyzed Cascade Reaction of Tosylmethyl Isocyanide (TosMIC) with Propargylic Alcohols to (*E*)-Vinyl Sulfones: Dual Roles of TosMIC

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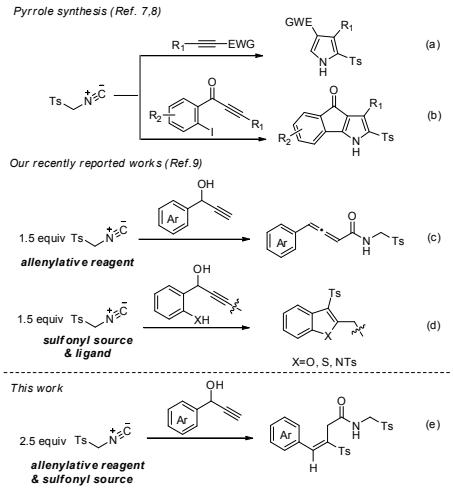
An unprecedented silver-catalyzed cascade reaction of tosylmethyl isocyanide (TosMIC) with propargylic alcohols for the efficient synthesis of (*E*)-vinyl sulfones has been developed where TosMIC plays a dual role as both the reactant in the allenylation of propargylic alcohols and the sulfonyl source.

## Introduction

Since the introduction of tosylmethyl isocyanide (TosMIC) by van Leusen,[1] this reagent has been of immense use in organic chemistry.[2] Its broad synthetic application emanates from its isocyano group, acidic α-carbon atom and sulfonyl group acting as both a sulfonyl leaving group and the aid to the enhanced acidity of the α-carbon. Extensive investigations of reactions of TosMIC with various substrates containing unsaturated bonds such as C=O, C=N, and C=C, etc. that offer a large variety of heterocyclic chemical structures (for example, oxazoles,[3] imidazoles,[4] pyrroles[5] and indoles[6]), have been reported. However, in contrast to the reaction of TosMIC with various substrates containing the aforementioned unsaturated bonds, reports relating to reactions of TosMIC with substrates containing C≡C are relatively underdeveloped. To the best our knowledge, there are six known reports of reactions of TosMIC with substrates containing C≡C; the reaction between acetylenic esters and TosMIC to afford the corresponding pyrroles (Scheme 1, a)[7] and the tandem reactions of TosMIC with 1-(2-Iodoary)-2-yn-1-ones to synthesize 4-oxo-indeno[1,2-*b*]pyrroles(Scheme 1, b).[8] Recently, we realized that TosMIC can react with propargylic alcohols in a peculiar manner where TosMIC acted as allenylative reagent or dual roles, that is, as sulfonyl source and ligand (Scheme 1, c and d).[9] As part of our ongoing interest in TosMIC chemistry, especially on the area of its reaction with propargylic alcohols, we herein report an unprecedented silver-catalyzed cascade reaction of TosMIC with propargylic alcohols to access (*E*)-vinyl sulfones (Scheme 1, e). Mechanistic investigations have shown that TosMIC plays a duel role as the reactant in the allenylation of propargylic alcohols and the sulfonyl source. So far, this is the first example where TosMIC has acted as allenylative reagent and sulfonyl source in a cascade reaction.




Scheme 1. The reaction of TosMIC with various substrates containing C≡C

## Results and discussion

Initially, the reaction of 1-phenylprop-2-yn-1-ol **1a** with TosMIC **2b** was repeated according to our reported procedure.9a When we increased the TosMIC from 1.5 equiv to 2.5 equiv on a 10 mol% $Ag_2CO_3$ as catalyst in 1,4-dioxane at 80 °C for 1 h, the expected product, 4-phenyl-N-(tosylmethyl)buta-2,3-dienamide, was not obtained. After workup and purification, a differently new product characterized as vinyl sulfone **3a**, (*E*)-4-phenyl-3-tosyl-N-(tosylmethyl)but-3-enamide from its spectral and analytical data, was obtained in 61% yield (Scheme 2). The *E*-configuration of product **3a** was verified by its 2D-NOESY spectrum. This reaction represents a new route to vinyl sulfones.

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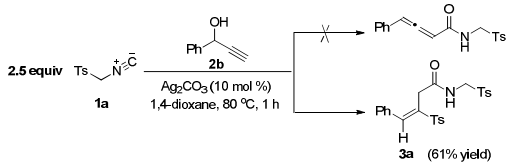
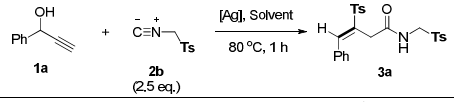
† Electronic supplementary information (ESI) available: Experimental procedure, $^1H$ and $^{13}C$ NMR spectra for all compounds. CCDC 946538. For ESI and crystallographic data in CIF or other electronic format. See DOI: 10.1039/x0xx00000x




Scheme 2. The reaction of 2.5 equiv of TosMIC with 1-phenylprop-2-yn-1-ol

The importance of vinyl sulfones in the pharmaceutical industry[10] as well as in the diverse fields of organic synthesis[11] encourages us to carry out an extensive optimization of the reaction conditions. As shown in table 1, a series of solvents including 1,4-dioxane, $CH_2Cl_2$, DMF and toluene were examined in the presence of 10 mol% $Ag_2CO_3$ at 80 °C for 1 h. Although the reaction proceeded smoothly in these solvents, 1,4-dioxane provided a peerless result (Table 1, entries 1-4). Various silver salts such as AgF, AgOAc and $AgNO_3$ were also evaluated (Table 1, entries 5-7). Among these salts, AgOAc was most effective and $AgNO_3$ was ineffective. To our delight, when the amount of AgOAc was increased from 10 mol% to 20 mol%, a significant increase in the yield (Table 1, entry 8) was realized. In a control experiment, the necessity of a silver catalyst was demonstrated (Table 1, entry 9). Conditions listed in entry 8, being optimal were therefore selected for further investigations

Table 1. Condition screening

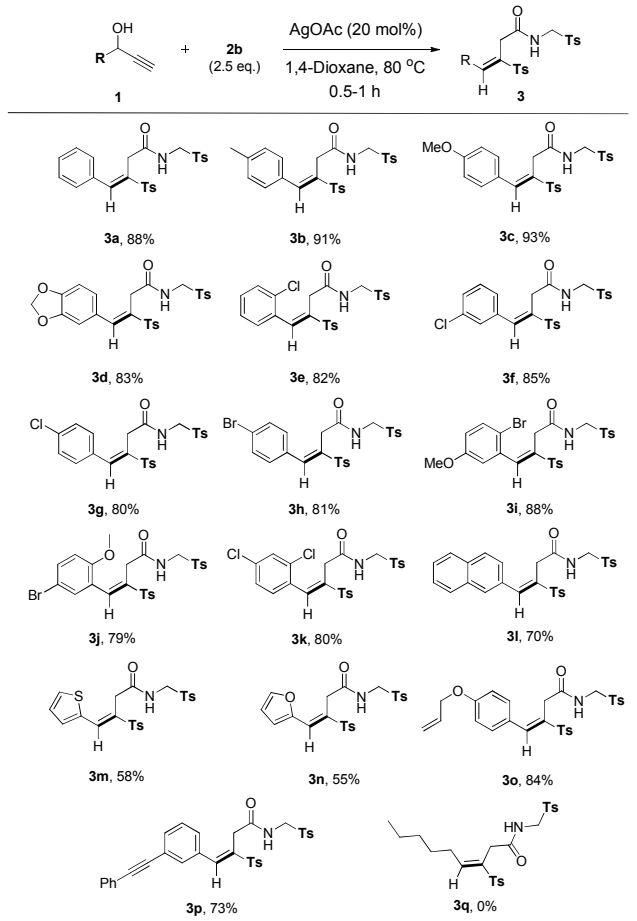



| Entry | [Ag] | Amount (mol%) | Solvent | Yield **3a** (%)[a] |
|---|---|---|---|---|
| 1 | $Ag_2CO_3$ | 10 | $CH_2Cl_2$ | 60 |
| 2 | $Ag_2CO_3$ | 10 | DMF | 58 |
| 3 | $Ag_2CO_3$ | 10 | Toluene | 59 |
| 4 | $Ag_2CO_3$ | 10 | 1,4-Dioxane | 61 |
| 5 | $AgNO_3$ | 10 | 1,4-Dioxane | 0 |
| 6 | AgF | 10 | 1,4-Dioxane | 55 |
| 7 | AgOAc | 10 | 1,4-Dioxane | 65 |
| **8** | **AgOAc** | **20** | **1,4-Dioxane** | **88** |
| 9 | -- | -- | 1,4-Dioxane | 0 |

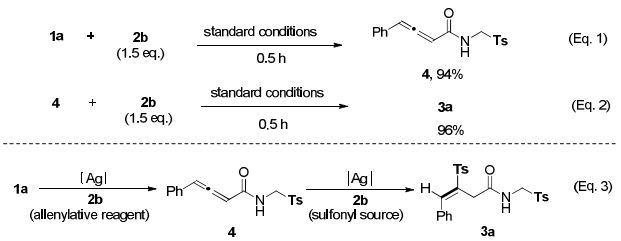
[a] Isolated yields of the product **3a**

With the optimized conditions in hand (Table 1, entry 8), the substrate scope of propargylic alcohols that could be used in this cascade reaction was investigated (Table 2). A range of substrates bearing various R groups including (hetero)aryl, fused aryl (**1b**−**1p**) were converted into the corresponding vinyl sulfones (**3b**−**3p**) in synthetically useful yields under the optimized conditions. Moreover, wide variation of the substituents on the benzene ring including electron-donating (e.g., RO and Me) and -withdrawing groups (e.g., Br and Cl) allowed the formation of diversely high functionalized vinyl sulfones (**3b**−**3k**) in moderate to excellent yields. It is worth mentioning that several interesting functional groups on the phenyl ring, such as allyloxy or phenylethynyl group, were well tolerated under the optimized reaction condition (**3o** and **3p**), which might provide an opportunity for further functionalization. However, when the R group was alkyl, the cascade reaction was unsuccessful (**3q**).

Table 2. Substrate Scope

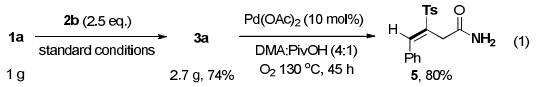



Subsequently, we turned our attention to the reaction mechanism. To better understand the reaction routes, the following experimental investigations were carried out. As shown in scheme 3. Firstly, when the reaction of **1a** with 1.5 equiv of **2b** under the optimized conditions for 0.5 h was terminated, the intermediate **4**, 4-phenyl-*N*-(tosylmethyl)buta-2,3-dienamide, was obtained in 94% yield [Scheme 3. Eq. (1)]. Next, the intermediate **4** further reacted with 1.5 equiv of **2b** under the optimized reaction for 0.5 h to afford **3a** in 96% yield [Scheme 3. Eq. (2)], in which TosMIC might decompose to formaldehyde and a Ts group, probably accompanied by the generation of a cyanide ion ($CN^-$).[9b,12] Based on the above results and related precedents,[9,12] a plausible reaction pathway was proposed [Scheme 3. Eq. (3)]. The cascade reaction started with the reaction of propargylic alcohol **1a** with TosMIC **2b** to yield the intermediate **4** by allenylation of the former in which TosMIC acted as the allenylative reagent. Next, the stereodefined sulfonylation of **4** took place with the TosMIC as sulfonyl source, thus affording vinyl sulfone **3a**.



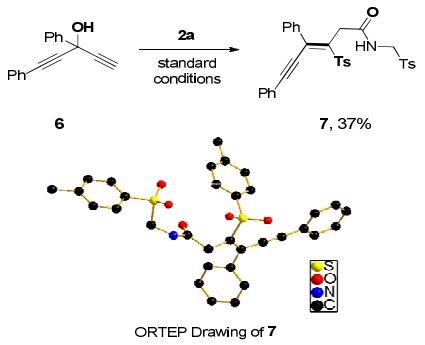

Scheme 3. Mechanistic investigations

To investigate the synthetic potential of this method, the reaction of propargylic alcohol **1a** with TosMIC **2b** was carried out on a gram scale. To our delight, the corresponding vinyl sulfone **3a** was obtained in 74% yield. Furthermore, good conversion of **3a** into (*E*)-4-phenyl-3-tosylbut-3-enamide **5** was achieved under palladium-catalyzed condition [Eq. (1)].




1 g 2.7 g, 74%

To expand the scope of this methodology further, propargylic alcohols **6**, 1,3-diphenylpenta-1,4-diyn-3-ol, was prepared by a two-step synthesis. Ethynylbenzene was first subjected to reaction with benzoyl chloride to synthesize the 1,3-diphenylprop-2-yn-1-one under the palladium-catalyzed condition,[13] followed by reaction with ethynylmagnesium bromide to afford the target product **6**. Under the optimized conditions, the product **7**, (*Z*)-4,6-diphenyl-3-tosyl-*N*-(tosylmethyl)hex-3-en-5-ynamide, was obtained in 37% yield (Scheme 4). The structure of product **7** was unambiguously established by XRD analysis (CCDC 946538).




Scheme 4. Synthesis of (*Z*)-4,6-diphenyl-3-tosyl-*N*-(tosylmethyl)hex-3-en-5-ynamide

## Conclusion

In conclusion, we have conceived an unprecedented cascade reaction of tosylmethyl isocyanide (TosMIC) with propargylic alcohols affording the corresponding (*E*)-vinyl sulfones in synthetically useful yields. TosMIC plays a dual role, that is, as the reactant in the allenylation of propargylic alcohols and the sulfonyl source. To the best our knowledge, TosMIC as allenylative reagent and sulfonyl source in a cascade reaction has not been reported to date. This result opens up a new aspect of synthetic utility of TosMIC and expands TosMIC chemistry.

## Experimental section

### General information

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. **$^1$H NMR** and **$^{13}$C NMR** spectra were recorded at 25 ºC on a Varian 500 MHz and 125 MHz, respectively, and TMS was used as internal standard. Mass spectra were recorded on BRUKER AutoflexIII Smartbeam MS-spectrometer. High resolution mass spectra (**HRMS**) were recorded on Bruck microTof by using ESI method.

### General procedure for synthesis

**General procedure for the synthesis of compounds 3a–p** (with **3a** as an example). To a mixture of 1-phenylprop-2-yn-1-ol (**1a**) (66 mg, 0.5 mmol) and AgOAc (16.7 mg, 0.1 mmol) in 1,4-dioxane (0.5 mL), 1-isocyanomethanesulfonyl-4-methyl-benzene (**2b**) (244 mg, 1.25 mmol ) which was dissolved in 2.0 mL 1,4-dioxane and added in 10 minutes at 80 °C. The reaction mixture was then stirred for 0.5 h-1 h until substrate 1a had been consumed as indicated by TLC. The resulting mixture was concentrated and taken up by dichloromethane. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product with flash column chromatography (silica gel; petroleum ether: ethyl acetate = 3: 1) gave **3a** in 88% yield as a white solid.

**Synthesis of compound 5.** To a mixture of (*E*)-4-phenyl-3-tosyl-*N*-(tosylmethyl)but-3-enamide (**3a**) (242 mg, 0.5 mmol) in 2.5 mL of N,N-dimethylformamide: pivalic acid (4:1) at 130 oC with oxygen balloon, $Pd(OAc)_2$ (11.3 mg, 0.05 mmol) was added. The reaction mixture was then stirred for 45 h until substrate **3a** had been consumed as indicated by TLC. The resulting mixture was concentrated and taken up by dichloromethane. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product with flash column chromatography (silica gel; petroleum ether: ethyl acetate = 1: 1) gave **5** in 80% yield as a white solid.

**Synthesis of compound 7.** To a mixture of 1,3-diphenylpenta-1,4-diyn-3-ol (**6**) (116 mg, 0.5 mmol) and AgOAc (16.7 mg, 0.1 mmol) in 1,4-dioxane (0.5 mL), 1-isocyanomethanesulfonyl-4-methyl -benzene (**2b**) (244 mg, 1.25 mmol) which was dissolved in 2.0 mL 1,4-dioxane and added in 10 minutes at 80 °C. The reaction mixture was then stirred for 0.5 h-1 h until substrate 1a had been consumed as indicated by TLC. The resulting mixture was concentrated and taken up by dichloromethane. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product with flash column chromatography (silica gel; petroleum ether: ethyl acetate = 3: 1) gave **7** in 37% yield as a white solid.

**(*E*)-4-phenyl-3-tosyl-N-(tosylmethyl)but-3-enamide (3a).** White solid, m.p. 157-158 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ

2.21 (s, 3H), 2.43 (s, 3H), 3.24 (s, 2H), 4.70 (d, *J* = 6.5 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.37-7.45 (m, 5H); 7.74 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 1H), 8.02 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.1, 60.3, 128.3, 128. 8, 129.0, 129.9, 130.2, 130.4, 130.8, 132.0, 133.1,133.7, 134.8, 142.5, 145.16, 145.21, 167.7; **HRMS** (ESI) m/z calculated for $C_{25}H_{26}NO_5S_2$ $[M+H]^+$: 484.1141, found: 484.1145.

**(*E*)-4-(p-tolyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3b).** White solid, m.p. 161-162 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.38 (s, 3H), 2.44 (s, 3H), 3.21 (s, 2H), 4.68 (d, *J* = 6.5 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 4H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.91 (s, 1H), 8.00 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.7, 35.2, 60.3, 128.2, 128.8, 129.3, 129.7, 129.9, 130.1, 130.6, 131.7, 133.7; 134.9, 141.5, 142.5, 145.08, 145.10, 167.8; **HRMS** (ESI) m/z calculated for $C_{26}H_{28}NO_5S_2$ $[M+H]^+$: 498.1403, found: 498.1408.

**(*E*)-4-(4-methoxyphenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3c).** White solid, m.p. 165-166 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.42 (s, 3H), 3.20 (s, 2H), 3.83 (s, 3H), 4.67 (d, *J* = 6.5 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.87 (s, 1H), 8.06 (t, *J* = 7.0Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.2, 55.4, 60.3, 114.4, 124.7, 128.1, 128.8, 129.75, 129.81, 130.1, 132.6, 133.7, 135.1, 142.0, 144.95, 145.04, 161.7, 168.0; **HRMS** (ESI) m/z calculated for $C_{26}H_{28}NO_6S_2$ $[M+H]^+$: 514.1353, found: 514.1352.

**(*E*)-4-(benzo[*d*][1,3]dioxol-5-yl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3d)**. White solid, m.p. 133-134 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.43 (s, 3H), 3.20 (s, 2H), 4.67 (d, *J* = 6.5 Hz, 2H), 6.01 (s, 2H), 6.82 (d, *J* = 8.5 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.73-7.76 (m, 4H), 7.82 (s, 1H), 8.00 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.0, 60.3, 101.8, 108.7, 109.8, 126.2, 126.7, 128.1, 128.8, 129.8, 130.1, 130.6, 133.7, 135.0, 142.1, 145.0, 145.1, 148.2, 149.9, 167.8; **HRMS** (ESI) m/z calculated for $C_{26}H_{26}NO_7S_2$ $[M+H]^+$: 528.1145, found: 528.1148.

**(*E*)-4-(2-chlorophenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3e).** White solid, m.p. 180-181 °C; **$^1$H NMR** (500 MHz, CDCl3) δ 2.29 (s, 3H), 2.45 (s, 3H), 3.10 (s, 2H), 4.69 (d, *J* = 6.5 Hz, 2H), 7.25-7.30 (m, 5H), 7.33-7.38 (m, 3H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.5 Hz, 2H), 7.87 (t, *J* = 6.5 Hz, 1H), 8.17 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.6, 21.7, 34.9, 60.4, 127.1, 128.4, 128.9, 129.6, 130.2, 130.5, 131.3, 133.8, 134.5, 134.8, 136.3, 140.1, 145.3, 145.3, 167.7; **HRMS** (ESI) m/z calculated for $C_{25}H_{25}ClNO_5S_2$ $[M+H]^+$: 518.0867, found: 518.0870.

**(*E*)-4-(3-chlorophenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3f).** White solid, m.p. 159-160 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.45 (s, 3H), 3.20 (s, 2H), 4.70 (d, *J* = 6.5 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.31-7.35 (m, 2H), 7.36-7.41 (m, 3H), 7.42 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.84 (s, 1H), 7.99 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 34.9, 60.3, 128.0, 128.3, 128.8, 129.8, 130.0, 130.05, 130.13, 130.2, 130.5, 133.7, 133.8, 134.6, 134.8, 135.1, 140.8, 145.2,145.4, 167.4; **HRMS** (ESI) m/z calculated for $C_{25}H_{25}ClNO_5S_2$ $[M+H]^+$: 518.0950, found: 518.0954.

**(*E*)-4-(4-chlorophenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3g)**. White solid, m.p. 189-190 °C; $^1$H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3H), 2.44 (s, 3H), 3.20 (s, 2H), 4.68 (d, *J* = 6.5 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.34-7.40 (m, 6H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.86 (s, 1H), 7.99 (t, *J* = 6.0 Hz,1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.7, 35.1, 60.3, 128.3, 128.8, 129.2, 129.9, 130.2, 130.5, 133.8, 131.7, 133.76, 133.79, 134.6, 137.0, 141.0, 145.2, 145.4, 167.6; **HRMS** (ESI) m/z calculated for $C_{25}H_{25}ClNO_5S_2$ $[M+H]^+$: 518.0977, found: 518.0980.

**(*E*)-4-(4-bromophenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3h).** White solid, m.p. 185-186 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.42 (s, 3H), 3.21 (s, 2H), 4.67 (d, *J* = 6.5 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0Hz, 2H), 7.84 (s, 1H), 7.99 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.0, 60.3, 125.3, 128.3, 128.8, 129.9, 130.2, 131.0, 131.7, 132.2, 133.7; 134.1, 134.6, 141.0, 145.2, 145.3, 167.5; **HRMS** (ESI) m/z calculated for $C_{25}H_{24}BrNaNO_5S_2$ $[M+Na]^+$: 586.0148, found: 586.0145.

**(*E*)-4-(2-bromo-4-methoxyphenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3i).** White solid, m.p.174-175 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.29 (s, 3H), 2.43 (s, 3H), 3.13 (s, 2H), 3.71 (s, 3H), 4.70 (d, *J* = 6.5 Hz, 2H), 6.80-6.82 (m, 1H), 6.94 (s, 1H), 7.26 (d, *J* = 8.0, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 8.04 (t, *J* = 6.5 Hz, 1H), 8.10 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.0, 56.0, 60.5, 114.7, 114.9, 118.9， 128.4, 128.8, 130.0, 130.1, 132.8, 133.3; 133.8, 134.8, 136.1, 142.6, 145.27, 145.32, 159.0, 167.8; **HRMS** (ESI) m/z calculated for $C_{26}H_{26}BrNO_6S_2$ $[M+H]^+$: 594.0463. found: 594.0461.

**(*E*)-4-(5-bromo-2-methoxyphenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3j).** White solid, m.p. 169-170 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.20 (s, 3H), 2.43 (s, 3H), 3.10 (s, 2H), 3.88 (s, 3H), 4.66 (d, *J* = 6.5 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.47 (dd, *J* = 2.5 Hz, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.84 (t, *J* = 6.5 Hz, 1H), 8.14 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 100 MHz) δ 21.5, 21.7, 34.9, 56.0, 60.3, 112.3, 112.9, 123.0, 128.3, 128.9, 129.9, 130.1, 132.4, 133.5, 134.4, 135.0, 137.4, 145.1, 145.2, 156.9, 167.3; **HRMS** (ESI) m/z calculated for $C_{26}H_{27}BrNO_5S_2$ $[M+H]^+$: 592.0463, found: 592.0465.

**(*E*)-4-(2,4-dichlorophenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3k)**. White solid, 195-196 °C; **$^1$H NMR** (500 MHz,

$CDCl_3$) δ 2.32 (s, 3H), 2.45 (s, 3H), 3.10 (s, 2H), 4.70 (d, *J* = 6.5 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.27-7.32 (m, 4H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.45 (s, 1H), 7.79-7.81 (m, 4H), 7.89 (t, *J* = 6.5 Hz, 1H), 8.08 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.6, 21.7, 35.0, 60.3, 127.6, 128.4, 128.9, 129.0, 129.6, 130.0, 130.3, 131.4, 133.8, 134.6, 135.3, 136.9, 138.9, 145.4, 145.5, 167.6; **HRMS** (ESI) m/z calculated for $C_{25}H_{24}Cl_2NO_5S_2$ $[M+H]^+$: 552.0467, found: 552.0470.

**(*E*)-4-(naphthalen-1-yl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3l).** White solid, m.p. 196-197 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 1.90 (s, 3H), 2.45 (s, 3H), 3.30 (s, 2H), 4.73 (d, *J* = 6.5 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.50-7.57 (m, 3H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.81-7.85 (m, 5H), 7.93 (s, 1H), 8.09 (s, 1H), 8.11 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.2, 21.7, 35.4, 60.3, 126.7, 126.9, 127.5, 128.0, 128.3, 128.6, 129.1, 129.4, 129.8, 130.2, 131.4, 132.9, 133.1, 133.7, 133.9, 134.8, 142.5, 145.1, 145.3, 167.9; **HRMS** (ESI) m/z calculated for $C_{29}H_{28}NO_5S_2$ $[M+H]^+$: 534.1389, found: 534.1387.

**(*E*)-4-(thiophen-2-yl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3m).** White solid, m.p. 177-178 °C; **$^1$H NMR** (500 MHz, CDCl3) δ 2.29 (s, 3H), 2.44 (s, 3H), 3.29 (s, 2H), 4.64 (d, *J* = 6.5 Hz, 2H), 7.13-7.17 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.46 (d, J = 3.5 Hz, 1H), 7.56 (d, *J* = 5.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.75-7.80 (m, 3H), 8.03 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.6, 35.3, 60.3, 128.2, 128.6, 128.8, 129.4, 129.7, 130.2, 131.7, 133.7, 133.8, 133.9, 134.8, 135.2, 145.0, 145.2, 166.9; **HRMS** (ESI) m/z calculated for $C_{23}H_{23}NNaO_5S_3$ $[M+Na]^+$: 512.0631, found: 512.0635.

**(*E*)-4-(furan-2-yl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3n)**. White solid, m.p. 141-142 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.43 (s, 3H), 3.36 (s, 2H), 4.61 (d, *J* = 7.0 Hz, 2H), 6.50 -6.52 (m, 1H), 6.88 (d, *J* = 3.5 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 6.5 Hz, 1H), 7.56 (s, 1H), 7.67-7.69 (m, 3H), 7.74 (d, *J* = 8.5 Hz, 2H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.6, 21.7, 35.2, 60.3, 112.8, 118.7, 128.0, 128.2, 128.7, 129.1, 129.8, 130.1, 133.8, 134.9, 145.0, 145.1, 146.3, 148.4, 167.3; **HRMS** (ESI) m/z calculated for $C_{23}H_{24}NO_6S_2$ $[M+H]^+$: 474.1040, found: 474.1044.

**(*E*)-4-(4-(allyloxy)phenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3o).** White solid, m.p. 165-166 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.36 (s, 3H), 3.13 (s, 2H), 4.90 (d, *J* = 5.0 Hz, 2H), 4.61 (d, *J* = 7.0 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H), 5.32 (d, *J* = 17.0 Hz, 1H), 5.92-6.00 (m, 1H), 6.84 (d, *J* = 9.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.80 (s, 1H), 8.00 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 100 MHz) δ 21.5, 21.6, 35.2, 60.3, 68.8, 115.1, 118.2, 124.8, 128.1, 128.8, 129.8, 129. 9, 130.1, 132.4, 132.6, 133.7, 135.1, 142.0, 144.9,145.1, 160.7, 168.0; **HRMS** (ESI) m/z calculated for $C_{28}H_{30}NO_6S_2$ $[M+H]^+$: 540.1515, found: 540.1520.

**(*E*)-4-(3-(phenylethynyl)phenyl)-3-tosyl-*N*-(tosylmethyl)but-3-enamide (3p).** White solid, m.p. 149-150 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.44 (s, 3H), 3.24 (s, 2H), 4.70 (d, *J* = 6.5 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.36-7.42 (m, 7H), 7.53-7.57 (m, 4H), 7.74 (d, J = 8.5 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.89 (s, 1H), 7.96 (t, *J* = 6.5 Hz, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.5, 21.6, 35.0, 60.4, 88.1, 90.7, 122.7, 124.2, 128.3, 128.4, 128.6, 128.8, 129.1, 129.2, 129.9, 130.2, 131.7, 132.4, 133.3, 133.6, 133.8,134.6, 134.8, 141.6, 145.2, 145.3, 167.5; **HRMS** (ESI) m/z calculated for $C_{33}H_{30}NO_5S_2$ $[M+H]^+$: 584.1567, found: 584.1567.

**(*E*)-4-phenyl-3-tosylbut-3-enamide (5)**. White solid, m.p. 193-194 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.33 (s, 2H), 5.45 (s, 1H), 6.90 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.42-7.47 (m, 3H), 7.59-7.63 (m, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.99 (s, 1H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.7, 35.3, 128.3, 129.1, 130.1, 130.3, 130.7, 132.3, 134.0, 135.0, 142.0, 145.1, 170.3; **HRMS** (ESI) m/z calculated for $C_{17}H_{18}NO_3S$ $[M+H]^+$: 518.0950, found: 518.0954.

**(*Z*)-4,6-diphenyl-3-tosyl-*N*-(tosylmethyl)hex-3-en-5-ynamide (7)**. White solid, m.p. 215-216 °C; **$^1$H NMR** (500 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.38 (s, 3H), 3.48 (s, 2H), 4.75 (d, *J* = 6.5 Hz, 2H), 7.00 (t, *J* = 6.5 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.33-7.42 (m, 10H), 7.84–7.88 (m, 4H); **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ 21.65, 21.70, 31.0, 37.9, 60.5, 86.9, 106.3, 121.9, 128.2, 128.41, 128.43, 128.5, 129.0, 129.2, 129.4, 129.7, 130.1, 131.7, 136.9, 137.0, 137.1, 141.0, 144.3, 145.2, 168.6; **HRMS** (ESI) m/z calculated for $C_{33}H_{29}NO_5S_2$ $[M+H]^+$: 518.0950, found: 518.0954.

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