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Cu-Catalyzed Conversion of Propargyl Acetates to *E*-α,β-Unsaturated Amides via Ketenimine Formation with Sulfonyl Azides

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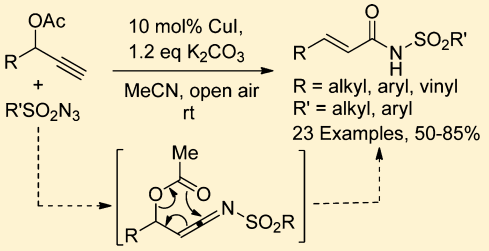
Supporting Information

ABSTRACT: The reaction between readily accessible propargyl acetates and sulfonyl azides in the presence of CuI catalyst yields *trans*-α,β-unsaturated *N*-tosylamides via *N*-sulfonyl ketenimine formation followed by a probable 1,3-OAc migration ([3,3]-sigmatropic rearrangement). The reaction is very general, allowing all kinds of substitution, including alkyl, aryl (electron-donating, -withdrawing, and -neutral), heteroaryl, and vinyl groups, on the C-terminal of acrylamide. Also, the method affords the products at ambient temperature with excellent diastereoselectivity in moderate to good yields.



The *E*-α,β-unsaturated amide subunit is found in a large number of natural products[1] and synthetic compounds of biological and pharmaceutical interest.[2] Inspite of its wide occurrence and usefulness, the synthetic viability developed to date is very limited.[3] Especially, the synthesis of 1° or 2° amides is underdeveloped because of the presence of an acidic hydrogen (N−H) in the corresponding starting materials, which does not comfortably bear with basic conditions as in the case of the conventional aldol condensation, Wittig, and Horner−Wadsworth−Emmons reactions that are used for the synthesis of their ester counterparts (i.e., α,β-unsaturated esters). Condensation of amines with presynthesized α,β-unsaturated acids (using the Perkin reaction) is one of the few practical approaches available. Many of the methods reported to date suffer from multiple steps, harsh conditions, limited substitution tolerance, poor diastereoselectivity, etc. We herein report a highly convenient method for the synthesis of alkyl/vinyl/aryl/heteroaryl-substituted *N*-sulfonyl *E*-α,β-unsaturated primary amides from readily available propargyl alcohols/acetates and sulfonyl azides at ambient temperature under affordable conditions. This method merits further attention in light of the widespread importance of the sulfonamide moiety in the design of pharmaceuticals.[4] Over 30 drugs containing *N*-arylsulfonamides are in clinical use as antibacterials, non-nucleotide reverse transcriptase inhibitors, antitumor agents, and HIV-1 protease inhibitors.[4]

A recent breakthrough in the synthesis of ketenimines via a copper-catalyzed azide−alkyne cycloaddition (CuAAC)[5] has opened a new pathway for the synthesis of diverse nitrogen-containing cyclic and acyclic motifs of biological and pharmaceutical interest. Chang,[5] Wang,[6] and others[7] have reported a number of elegant novel methods that involve trapping of ketenimines obtained by this route. Most of them have used amines, alcohols, and water as external nucleophiles. Very few methods use internal nucleophiles to trap the ketenimines successfully.[7a−c] Most recently, during the preparation of our manuscript, Talukdar and co-workers reported a 1,3-migration of a substituted amino group onto a ketenimine generated in situ for the synthesis of acrylamidines.[7b] Along the same lines, and in continuation of our interest in alkyne functionalization chemistry,[8] we herein report a practical method for the synthesis of *N*-sulfonyl *E*-α,β-unsaturated amides from readily available propargyl acetates (Scheme 1, eq 2).

Initially, we envisioned that the hydroxyl function of the propargyl alcohol would attack (four-membered) on its in situ-generated ketenimine, leading to double-bond isomerization to afford the corresponding α,β-unsaturated amide. Cho and Chang[5d] used propargyl alcohols for a similar reaction in the presence of water as a ready external nucleophile to obtain β-hydroxyamides (Scheme 1, eq 1). We wanted to pursue the reaction in the absence of water to make the internal hydroxyl group the only available nucleophile. To test the feasibility of this transformation, the model substrate **1a** and TsN_3 were selected.

The initial reaction was performed in the presence of 10 mol % copper(I) iodide using K_2CO_3 as the base in acetonitrile at room temperature. To our delight, the expected α,β-unsaturated amide **3a** was formed and was isolated in 32% yield (Table 1, entry 1) after 24 h of reaction at room temperature. The structure of **3a** was confirmed by NMR (the coupling constant of the olefinic protons in the ^{1}H NMR spectrum was J = 15.8 Hz) and by comparison to literature data.[9] Changing the catalyst or solvent (entries 2 and 3) led only to decreases in the yield along with increased decomposition. Neither the starting material nor any significant byproducts were observed. We presume that the strain

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Scheme 1. Synthesis of Amides from Propargyl Alcohols/Acetates

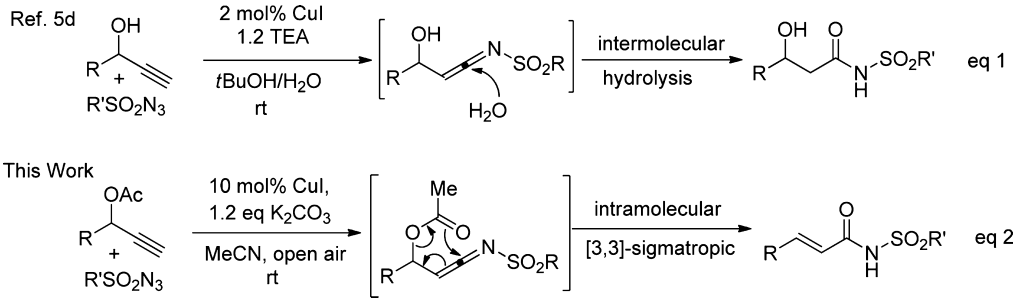
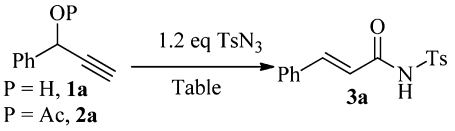


Table 1. Optimization Studies[a]



entry	substrate	catalyst	solvent	base	time (h)	yield (%)[b]
1	**1a**	CuI	MeCN	K_2CO_3	24	32
2	**1a**	CuI	DCE	K_2CO_3	24	15
3	**1a**	CuBr	MeCN	K_2CO_3	24	25
4	**2a**	**CuI**	**MeCN**	**K_2CO_3**	**12**	**78**
5	**2a**	CuI	Toluene	K_2CO_3	12	35
6	**2a**	CuI	THF	K_2CO_3	12	50
7	**2a**	CuI	MeCN	TEA	12	10
8	**2a**	CuI	MeCN	DIPEA	12	12
9	**2a**	CuI	MeCN	Cs_2CO_3	12	50
10	**2a**	CuCl	MeCN	K_2CO_3	12	52
11	**2a**	CuBr	MeCN	K_2CO_3	12	62

[a]Reaction conditions: TsN_3 (1.2 mmol), **1a**/**2a** (1.0 mmol), base (1.2 mmol), copper(I) salt (0.1 mmol), solvent (10 mL), rt, open air. [b]Isolated yields.

associated with the formation of the four-membered transition state involved in the 1,3-OH migration process in the sensitive ketenimine might have slowed down the formation of the end product and thereby led to sidewise decomposition. We envisaged that the exchange of the hydroxyl group with an acetoxy group would create a spatially closer nucleophile, in the form of the carbonyl of the acetyl group, that could decrease the activation energy for the migration process and would lead to the product in good yield. As anticipated, upon treatment with 10 mol % CuI and 1.2 equiv of K_2CO_3 in MeCN, **2a**[10] and tosyl azide produced **3a** at ambient temperature in 78% yield (entry 4). Organic bases (TEA or DIPEA) gave poorer yields of product compared with inorganic bases (K_2CO_3 or Cs_2CO_3), as is evident from entries 7 and 8. MeCN was found to be a better choice of solvent than toluene (entry 5) or THF (entry 6).

Next, a range of substrates[10] with variation in the substitution (aryl, heteroaryl, alkyl, and vinyl) of both the propargyl acetate and the sulfonyl azide were subjected to the cascade reaction to validate its generality. As is evident from Table 2, all of them were applicable in the cascade process, providing the acrylamide derivatives **3** in yields of 50−85%. Initially, various aryl-substituted propargyl acetates were screened. Unsubstituted and methyl-substituted substrates gave the corresponding products **3a**−**c** in consistently good yields (70−78%). All halogen groups (bromo, chloro, and fluoro) at various positions of the phenyl ring survived well in the reaction to produce **3d**−**k** in yields of 71−85%. Electron-rich phenyl substrates **2n** and **2o** furnished products with better yields (78−80%) compared with their electron-poor counterparts **2l** and **2m** (60−65%). The steric properties of the aryl ring did not appear to significantly affect the yield or the stereoselectivity, as *ortho*-functionalized aryl substrates **2d**, **2h**, **2j**, **2l**, and **2o** performed equally well in the reaction sequence. Variation in the substitution on the sulfonyl azide moiety (i.e., using benzenesulfonyl azide and methanesulfonyl azide rather than toluenesulfonyl azide) also afforded the corresponding products **3p** and **3q** in good yields (63−70%). The cascade was then tested for the synthesis of heteroaryl-substituted acrylamides **3r** and **3s**, which were obtained in 60% and 62% yield, respectively. Of particular note is the observation that the cinnamyl-substituted propargyl acetate **2t** also reacted smoothly to afford the conjugated dienamide **3t** as a single diastereomer in 70% yield. Next, to find out that whether conjugation was responsible for the exclusive formation of the *trans* product and to expand the reaction generality, we conducted the reaction on alkyl-substituted substrates. Pleasingly, the alkyl-substituted acrylamides **3u**, **3v** and **3w** were obtained with excellent stereoselection, although in moderate yields of 50−65%.

A plausible mechanism for the exclusive formation of (*E*)-acrylamides is depicted in Figure 1. As described in several papers recently by Chang[5], Wang,[6] and others,[7] CuAAC of terminal alkynes generates *N*-sulfonyl ketenimines via triazole formation followed by N_2 expulsion. In the present case, intermediate **B** (formed via **A**) probably undergoes a [3,3]-sigmatropic rearrangement (1,3-acetyl migration) to afford the *trans* adduct **D**, hydrolysis of which gives the corresponding amide **3**. The six-membered transition state **C** formed during the migration might position the hydrogen atoms in axial positions to minimize the steric hindrance and therefore yield the (*E*)-acrylamide selectively.

In conclusion, we have described an efficient route for the preparation of *trans*-α,β-unsaturated *N*-tosylamides by a copper-catalyzed reaction of propargyl acetates with sulfonyl azides that proceeds through a cascade of CuAAC, ketenimine formation, and a probable [3,3]-sigmatropic rearrangement (1,3-acyl migration).

EXPERIMENTAL SECTION

General Information. All of the reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300 or 400 MHz spectrometer for ^1H and 75 or 100 MHz for ^{13}C. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$/DMSO-d_6 for ^1H and ^{13}C NMR spectroscopy, respectively. Multiplicities are reported as follows: singlet (s), doublet (d), broad singlet (bs), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS was performed using QToF mass spectrometer. Column chromatography was performed with silica gel (100−200 mesh) as the stationary phase.

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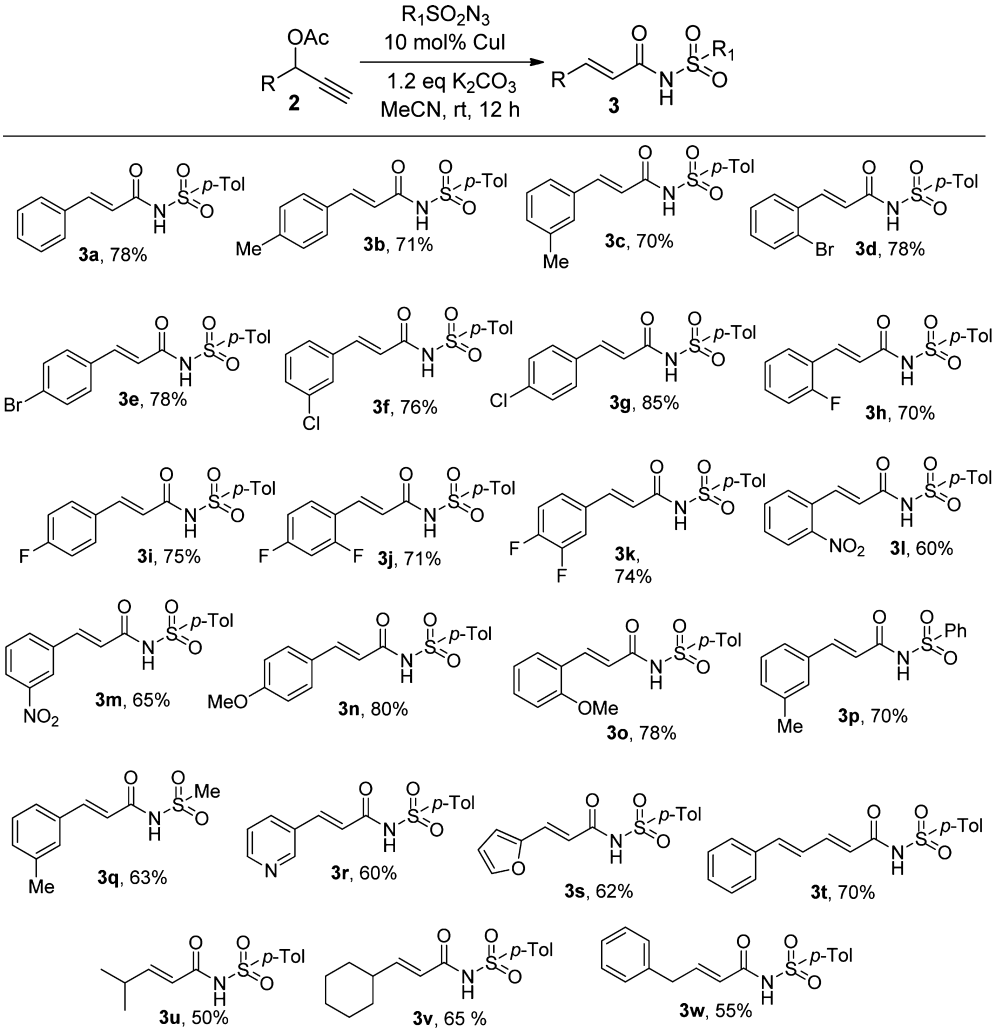
Table 2. Copper(I)-Catalyzed Synthesis of Amides 3 from Propargyl Acetates 2[a,b]



[a]Reaction conditions: Sulfonyl azide (1.2 mmol), **2** (1.0 mmol), base (2.0 mmol), CuI (0.1 mmol), MeCN (10 mL, 0.1 M solution), rt, open air. [b]Isolated yields are shown.

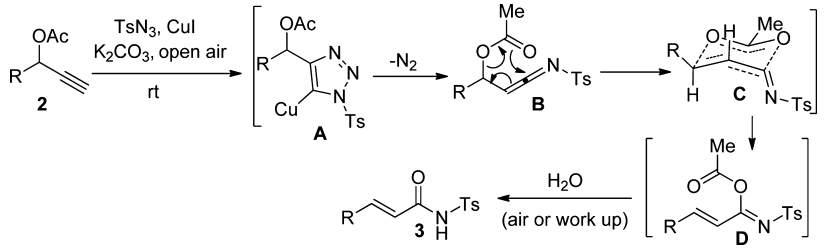


Figure 1. Plausible mechanism for the formation of (*E*)-acrylamides **3** from propargyl acetates **2**.

All of the reactions were monitored by TLC. The purity and characterization of compounds were further established by HRMS.

General Procedure for the Synthesis of 3 from 2[10] Using the Synthesis of 3a as an Example. To the substrate **2a**[10] (174 mg, 1 mmol) dissolved in acetonitrile (10 mL) was added tosyl azide (236 mg, 1.2 mmol), copper iodide (19 mg, 0.1 mmol), and K_2CO_3 (165 mg, 1.2 mmol). The mixture was stirred at room temperature for 12 h. Water (5 mL) and then brine solution (5 mL) were added, and the reaction mixture was extracted with ethyl acetate (3 × 10 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. The crude solid product was washed with cold diethyl ether (2 × 3 mL) to remove some soluble impurities/byproducts, and the remaining insoluble crude material was purified by column chromatography (silica gel, 15−30% EtOAc in hexanes) to get the pure product **3** (270 mg, 78% yield).

*N-4-Toluenesulfonyl-(E)-3-phenylprop-2-enamide (**3a**).*[9] 78% yield (270 mg); white solid; mp 130−132 °C; R_f = 0.40 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.26 (bs, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.59−7.54 (m, 3H), 7.45−7.42 (m, 5H), 6.61 (d, J = 15.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.8, 144.7, 144.3, 136.9, 134.3, 131.1, 130.1, 129.5, 128.6, 128.1, 119.4, 21.5; IR ν (cm^{-1}) 3425, 2926, 1628, 1450, 1215, 867; HRMS (ESI-TOF) calcd for $C_{16}H_{16}NO_3S$ $[M + H]^+$ 302.0851, found 302.0847.

*N-4-Toluenesulfonyl-(E)-3-(4-methylphenyl)prop-2-enamide (**3b**).*[9] 71% yield (238 mg); white solid; mp 172−174 °C; R_f = 0.40 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.17

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(bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 15.8 Hz, 1H), 7.47−7.43 (m, 4H), 7.24 (d, J = 8.3 Hz, 2H), 6.55 (d, J = 15.8 Hz, 1H), 2.40 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 144.7, 144.3, 141.2, 137.0, 131.6, 130.1, 129.9, 128.6, 128.1, 118.2, 21.5, 21.4; IR ν (cm^{-1}) 3423, 3021, 1627, 1408, 1215, 759; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3S$ [M + H]$^+$ 316.1007, found 316.1005.

N-4-Toluenesulfonyl-(E)-3-(3-methylphenyl)prop-2-enamide (**3c**). 70% yield (235 mg); white solid; mp 140−142 °C; R_f = 0.40 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.19 (bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 15.8 Hz, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.37−7.36 (m, 2H), 7.32 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 7.4 Hz, 1H), 6.58 (d, J = 15.8 Hz, 1H), 2.40 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 144.7, 144.4, 138.8, 136.9, 134.2, 131.8, 130, 129.4, 129.2, 128.1, 125.7, 119.2, 21.5, 21.2; IR ν (cm^{-1}) 3426, 2925, 1626, 1445, 1216, 859; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3S$ [M + H]$^+$ 316.1007, found 316.1005.

N-4-Toluenesulfonyl-(E)-3-(2-bromophenyl)prop-2-enamide (**3d**). 78% yield (233 mg); white solid; mp 172−174 °C; R_f = 0.30 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.37 (bs, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.77 (d, J = 15.7 Hz, 1H), 7.71 (dd, J = 7.9, 1.2 Hz, 1H), 7.67 (dd, J = 7.9, 1.6 Hz, 1H), 7.48−7.44 (m, 3H), 7.39−7.35 (m, 1H), 6.61 (d, J = 15.7 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.4, 144.9, 141.7, 136.8, 133.8, 133.8, 132.7, 130.1, 128.9,128.5, 128.2, 125.1, 122.6, 21.6; IR ν (cm^{-1}) 3432, 3019, 1627, 1467, 1215, 757; HRMS (ESI-TOF) calcd for $C_{16}H_{15}BrNO_3S$ [M + H]$^+$ 379.9956, found 379.9954.

N-4-Toluenesulfonyl-(E)-3-(4-bromophenyl)prop-2-enamide (**3e**).[9] 78% yield (233 mg); white solid; mp 219−221 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.28 (bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 7.56−7.51 (m, 3H), 7.44 (d, J = 8.3 Hz, 2H), 6.61 (d, J = 15.8 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.7, 144.8, 142.9, 136.9, 133.6, 132.5, 130.5, 130.0, 128.1, 124.5, 120.2, 21.5; IR ν (cm^{-1}) 3432, 3019, 1629, 1415, 1215, 849; HRMS (ESI-TOF) calcd for $C_{16}H_{15}BrNO_3S$ [M + H]$^+$ 379.9956, found 379.9954.

N-4-Toluenesulfonyl-(E)-3-(3-chlorophenyl)prop-2-enamide (**3f**). 76% yield (245 mg); white solid; mp 146−148 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.29 (bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.65 (s, 1H), 7.57−7.53 (m, 2H), 7.51−7.43 (m, 4H), 6.64 (d, J = 15.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.6, 144.8, 142.6, 136.9, 136.6, 134.2, 131.3, 130.6, 130.0, 128.4, 128.2, 126.9, 121.1, 21.5; IR ν (cm^{-1}) 3433, 3019, 1631, 1415, 1215, 850; HRMS (ESI-TOF) calcd for $C_{16}H_{15}ClNO_3S$ [M + H]$^+$ 336.0461, found 336.0454.

(N-4-Toluenesulfonyl-(E)-3-(4-chlorophenyl)prop-2-enamide (**3g**).[9] 85% yield (274 mg); white solid; mp 204−206 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.25 (bs, 1H), 7.86 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 15.9 Hz, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 6.60 (d, J = 15.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.7, 144.8, 142.8, 136.9, 135.6, 133.2, 130.3, 130.0, 129.6, 128.2, 120.2, 21.5; IR ν (cm^{-1}) 3430, 3021, 1628, 1413, 1215, 759; HRMS (ESI-TOF) calcd for $C_{16}H_{15}ClNO_3S$ [M + H]$^+$ 336.0461, found 336.0454.

N-4-Toluenesulfonyl-(E)-3-(2-fluorophenyl)prop-2-enamide (**3h**). 70% yield (233 mg); yellow solid; mp 165−167 °C; R_f = 0.30 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.33 (bs, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.67−7.63 (m, 1H), 7.59 (d, J = 16.0 Hz, 1H), 7.51−7.48 (m, 1H), 7.45 (d, J = 8.3 Hz, 2H), 7.32−7.26 (m, 2H), 6.72 (d, J = 16.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.7, 161.1 (d, J = 250 Hz), 144.8, 136.8 (d, J = 21 Hz), 133.0 (d, J = 8 Hz), 130.4, 130.0, 128.2, 125.6, 122.3, 122.1 (d, J = 11 Hz), 121.9, 116.6 (d, J = 21 Hz), 21.5; IR ν (cm^{-1}) 3395, 3022, 1628, 1417, 1216, 759; HRMS (ESI-TOF) calcd for $C_{16}H_{15}FNO_3S$ [M + H]$^+$ 320.0757, found 320.0757.

N-4-Toluenesulfonyl-(E)-3-(4-fluorophenyl)prop-2-enamide (**3i**).[9] 75% yield (250 mg); yellow solid; mp 190−192 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.25 (bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.66−7.63 (m, 2H), 7.57 (d, J = 15.9 Hz, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.30−7.26 (m, 2H), 6.55 (d, J = 15.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.8 (d, J = 247 Hz), 163.8, 144.7, 143, 136.9, 131.0, 130.9 (d, J = 8 Hz), 128.1, 119.3,116.5 (d, J = 22 Hz), 21.5; IR ν (cm^{-1}) 3430, 3023, 1631, 1406, 1216, 760; HRMS (ESI-TOF) calcd for $C_{16}H_{15}FNO_3S$ [M + H]$^+$ 320.0757, found 320.0757.

N-4-Toluenesulfonyl-(E)-3-(2,4-difluorophenyl)prop-2-enamide (**3j**). 71% yield (228 mg); white solid; mp 161−163 °C; R_f = 0.25 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.31 (bs, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.76−7.70 (m, 1H), 7.54 (d, J = 16.0 Hz, 1H), 7.45 (d, J = 8.2 Hz, 2H), 7.40−7.34 (m, 1H), 7.21−7.16 (m, 1H), 6.68 (d, J = 16.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.7, 163.5 (dd, J = 225, 13 Hz), 161.4 (dd, J = 228, 13 Hz), 144.8, 136.9, 135.9, 132.1 (dd, J = 4, 2 Hz), 130.0, 128.2, 121.9 (d, J = 7 Hz), 118.9 (dd, J = 12, 3 Hz), 113.0 (dd, J = 22, 3 Hz), 105.3 (t, J = 26 Hz), 21.5; IR ν (cm^{-1}) 3396, 3022, 1622, 1429, 1215, 857; HRMS (ESI-TOF) calcd for $C_{16}H_{14}F_2NO_3S$ [M + H]$^+$ 338.0662, found 338.0662.

N-4-Toluenesulfonyl-(E)-3-(3,4-difluorophenyl)prop-2-enamide (**3k**). 74% yield (237 mg); white solid; mp 178−180 °C; R_f = 0.25 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.27 (bs, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.72−7.66 (m, 1H), 7.56−7.43 (m, 5H), 6.57 (d, J = 15.9 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.6, 151.0 (dd, J = 249, 13 Hz) 150.0 (dd, J = 245, 13 Hz), 144.8, 141.9, 136.9, 132.2 (dd, J = 6, 4 Hz), 130.0, 128.1, 125.9 (d, J = 3 Hz), 120.9, 118.6 (d, J = 17 Hz), 117.4 (d, J = 18 Hz), 21.5; IR ν (cm^{-1}) 3423, 3021, 1632, 1427, 1215, 759; HRMS (ESI-TOF) calcd for $C_{16}H_{14}F_2NO_3S$ [M + H]$^+$ 338.0662, found 338.0662.

N-4-Toluenesulfonyl-(E)-3-(2-nitrophenyl)prop-2-enamide (**3l**).[9] 60% yield (190 mg); yellow solid; mp 211−213 °C; R_f = 0.15 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.44 (bs, 1H), 8.09 (dd, J = 8.1, 0.9 Hz, 1H), 7.89−7.79 (m, 4H), 7.74−7.67 (m, 2H), 7.46 (d, J = 8.1 Hz, 2H), 6.55 (d, J = 15.7 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.4, 148.7, 144.9, 141.7, 136.8, 136.2, 134.6, 131.1, 130.0, 128.2, 125.2, 122.9, 122.4, 21.5; IR ν (cm^{-1}) 3433, 3019, 1633, 1404, 1215, 757; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_5S$ [M + H]$^+$ 347.0702, found 347.0706.

N-4-Toluenesulfonyl-(E)-3-(3-nitrophenyl)prop-2-enamide (**3m**). 65% yield (205 mg); yellow solid; mp 189−191 °C; R_f = 0.15 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.34 (bs, 1H), 8.42 (s, 1H), 8.26 (dd, J = 8.2, 1.5 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.75−7.68 (m, 2H), 7.45 (d, J = 8.3 Hz, 2H), 6.77 (d, J = 15.9 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 166.1, 148.7, 144.9, 139.6, 136.8, 134.6, 131.5, 130.1, 129.9, 129.5, 128.2, 125.3, 123.9, 21.6; IR ν (cm^{-1}) 3428, 3021, 1631, 1405, 1216, 760; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_5S$ [M + H]$^+$ 347.0702, found 347.0706.

N-4-Toluenesulfonyl-(E)-3-(4-methoxyphenyl)prop-2-enamide (**3n**).[9] 80% yield (260 mg); white solid; mp 198−200 °C; R_f = 0.25 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.10 (bs, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.54−7.49 (m, 3H), 7.44 (d, J = 8.2 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.46 (d, J = 15.8 Hz, 1H), 3.79 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 164.1, 161.8, 144.6, 144.1, 137.1, 130.5, 129.9, 128.1, 126.9, 116.6, 115.0, 55.8, 21.5; IR ν (cm^{-1}) 3427, 3021, 1631, 1409, 1215, 759; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_4S$ [M + H]$^+$ 332.0957, found 332.0961.

N-4-Toluenesulfonyl-(E)-3-(2-methoxyphenyl)prop-2-enamide (**3o**). 78% yield (253 mg); white solid; mp 168−170 °C; R_f = 0.25 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.18 (bs, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 15.9 Hz, 1H), 7.51−7.39 (m, 4H), 7.09 (d, J = 8.2 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.71 (d, J = 15.9 Hz, 1H), 3.85 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 164.3, 158.7, 144.7, 139.5, 137.1, 132.7, 130.0, 129.6, 128.1, 122.6, 121.2, 119.8, 112.3, 56.1, 21.5; IR ν (cm^{-1}) 3427, 3021, 1625, 1411, 1215, 759; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_4S$ [M + H]$^+$ 332.0957, found 332.0961.

N-Phenylsulfonyl-(E)-3-(3-methylphenyl)prop-2-enamide (**3p**). 70% yield (224 mg); white solid; mp 124−126 °C; R_f = 0.40 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.28 (bs, 1H), 7.99−7.97 (m, 2H), 7.75−7.71 (m, 1H), 7.67−7.63 (m, 2H), 7.53 (d, J = 15.8 Hz, 1H), 7.38−7.36 (m, 2H), 7.32 (t, J = 7.4 Hz, 1H),

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7.23 (d, J = 7.4 Hz, 1H), 6.61 (d, J = 15.8 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 144.5, 139.8, 138.8, 134.2, 134.1, 131.9, 129.6, 129.4, 129.2, 128.1, 125.7, 119.1, 21.3; IR ν (cm^{-1}) 3424, 3021, 1627, 1412, 1282, 856; HRMS (ESI-TOF) calcd for $C_{16}H_{16}NO_3S$ [M + H]$^+$ 302.0851, found 302.0848.

*N-Methylsulfonyl-(E)-3-(3-methylphenyl)prop-2-enamide (**3q**).* 63% yield (160 mg); white solid; mp 138−140 °C; R_f = 0.40 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 11.87 (bs, 1H), 7.65 (d, J = 15.9 Hz, 1H), 7.43−7.41 (m, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 7.5 Hz, 1H), 6.66 (d, J = 15.9 Hz, 1H), 3.33 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 164.9, 144.3, 138.8, 134.3, 131.8, 129.5, 129.2, 125.8, 119.4, 41.7, 21.3; IR ν (cm^{-1}) 3424, 3022, 1627, 1405, 1215, 759; HRMS (ESI-TOF) calcd for $C_{11}H_{14}NO_3S$ [M + H]$^+$ 240.0694, found 240.0688.

*N-4-Toluenesulfonyl-(E)-3-(3-pyridyl)prop-2-enamide (**3r**).* 60% yield (207 mg); yellow solid; mp 217−219 °C; R_f = 0.1 (SiO_2, 40% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.32 (bs, 1H), 8.77 (s, 1H), 8.60 (s, 1H), 7.99 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 15.9 Hz, 1H), 7.48−7.44 (m, 3H), 6.70 (d, J = 15.9 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.5, 151.6, 150.1, 144.8, 140.9, 136.9, 134.9, 130.2, 130.0, 128.2, 124.6, 121.4, 21.5; IR ν (cm^{-1}) 3429, 3021, 1630, 1408, 1215, 759; HRMS (ESI-TOF) calcd for $C_{15}H_{15}N_2O_3S$ [M + H]$^+$ 303.0803, found 303.0800.

*N-4-Toluenesulfonyl-(E)-3-(2-furyl)prop-2-enamide (**3s**).* 62% yield (220 mg); yellow solid; mp 114−116 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.19 (bs, 1H), 7.86−7.84 (m, 3H), 7.44 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 15.5 Hz, 1H), 6.91 (d, J = 3.4 Hz, 1H), 6.63 (dd, J = 3.4, 1.8 Hz, 1H), 6.36 (d, J = 15.5 Hz, 1H) 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.7, 150.6, 146.7, 144.7, 136.9, 130.9, 130.0, 128.1, 117.4, 115.9, 113.3, 21.5; IR ν (cm^{-1}) 3426, 3021, 1632, 1409, 1215, 760; HRMS (ESI-TOF) calcd for $C_{14}H_{14}NO_4S$ [M + H]$^+$ 292.0644, found 292.0639.

*N-4-Toluenesulfonyl-(2E,4E)-5-phenylpent-2,4-dienamide (**3t**).* 70% yield (224 mg); yellow solid; mp 225−227 °C; R_f = 0.30 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.17 (bs, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.3 Hz, 2H), 7.41−7.30 (m, 4H), 7.09−7.08 (m, 2H), 6.14 (d, J = 15.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 144.9, 144.7, 141.9, 137.1, 136.2, 130.0, 129.7, 129.3, 128.1, 127.9, 126.6, 122.0, 21.5; IR ν (cm^{-1}) 3428, 3021, 1625, 1405, 1282, 759; HRMS (ESI-TOF) calcd for $C_{18}H_{18}NO_3S$ [M + H]$^+$ 328.1007, found 328.1005.

*N-4-Toluenesulfonyl-(E)-4-methylpent-2-enamide (**3u**).* 50% yield (191 mg); white solid; mp 120−122 °C; R_f = 0.25 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.13 (bs, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 6.88 (dd, J = 15.5, 6.5 Hz, 1H), 5.98 (dd, J = 15.5, 1.4 Hz, 1H), 2.62−2.60 (m, 1H), 2.49 (s, 3H), 1.06 (d, J = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, DMSO) δ 163.8, 155.5, 144.6, 137.0, 129.9, 128.1, 119.6, 30.7, 21.5, 21.3; IR ν (cm^{-1}) 3022, 2964, 1640, 1415, 1216; HRMS (ESI-TOF) calcd for $C_{13}H_{18}NO_3S$ [M + H]$^+$ 268.1007, found 268.1006.

*N-4-Toluenesulfonyl-(E)-3-cyclohexylprop-2-enamide (**3v**).* 60% yield (224 mg); white solid; mp 132−134 °C; R_f = 0.35 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.02 (bs, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 6.75 (dd, J = 15.6, 6.7 Hz, 1H), 5.87 (dd, J = 15.6, 1.3 Hz, 1H), 2.39 (s, 3H), 2.13−2.06 (m, 1H), 1.68−1.59 (m, 5H), 1.26−1.02 (m, 5H); ^{13}C NMR (100 MHz, DMSO) δ 163.8, 154.3, 144.6, 137.0, 129.9, 128.1, 119.9, 31.5, 25.8, 25.5, 21.5; IR ν (cm^{-1}) 3401, 3022, 1640, 1415, 1216, 668; HRMS (ESI-TOF) calcd for $C_{16}H_{22}NO_3S$ [M + H]$^+$ 308.1320, found 308.1312.

*N-4-Toluenesulfonyl-(E)-4-phenylbut-2-enamide (**3w**).* 60% yield (189 mg); white solid; mp 139−140 °C; R_f = 0.3 (SiO_2, 30% EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO) δ 12.06 (bs, 1H), 7.80 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 7.31 (t, J = 7.1 Hz, 2H), 7.23 (t, J = 7.3 Hz, 1H), 7.17 (d, J = 7.1 Hz, 2H), 6.96−6.89 (m, 1H), 5.89 (d, J = 15.4 Hz, 1H), 3.49 (d, J = 6.6 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.5, 148.2, 144.6, 138.2, 137.0, 129.9, 129.2, 129.1, 128.1, 126.9, 122.9, 37.9, 21.5; IR ν (cm^{-1}) 3421, 3022, 1663, 1403, 1263, 760; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3S$ [M + H]$^+$ 316.1007, found 316.1000.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR and mass spectra for the products **3a**−**w**. 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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