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Metal Free C–C Coupling of an Allenyl Sulfone with Picolyl Amides to Access Vinyl Sulfones via Pyridine-Initiated *In-Situ* Generation of Sulfinate Anion

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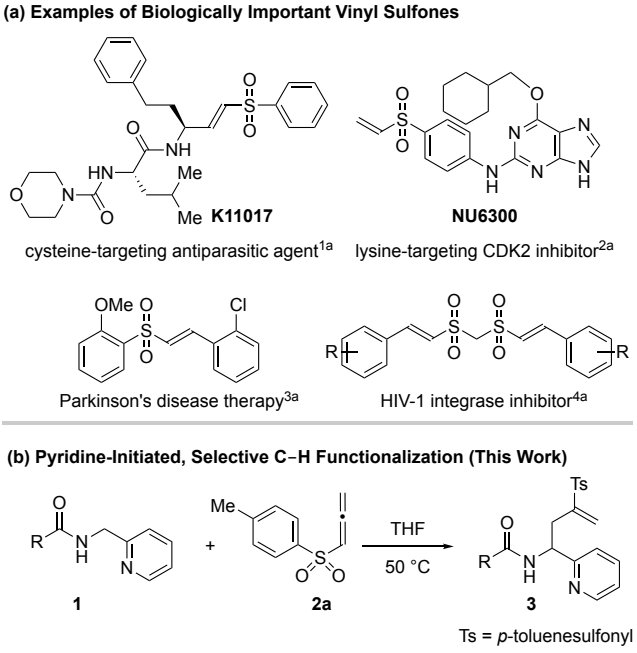
ABSTRACT: Vinyl sulfones are privileged motifs known for their biological activity and synthetic utility. Synthetic transformations to efficiently access high-value compounds with these motifs are desired and sought after. Herein, a new procedure is described to form vinyl sulfone-containing compounds by selective functionalization of the C(sp^3)–H bond adjacent to the pyridine ring of pharmacologically prevalent picolyl amides with an allenyl sulfone, 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene. The reaction conditions are mild with no metal catalyst or additives required and displays good functional group tolerance. Mechanistic studies for this unusual transformation suggest that the reaction operates via a rare pyridine-initiated and *p*-toluenesulfinate anion-mediated activation of the allenyl sulfone analogous to phosphine-triggered reactions.

Introduction

Vinyl sulfones occur in a number of compounds widely known for their therapeutic value, functioning as: cysteine-[1] and lysine-[2] targeting covalent inhibitors; neuroprotective agents for potential treatment of Parkinson's disease;[3] HIV-1 integrase inhibitors;[4] and more[5] (Scheme 1a). In addition, the vinyl sulfone moiety has synthetic utility as a Michael acceptor,[6] a building block for cycloaddition reactions[7] and other organic transformations.[8] There are efficient methods to synthesize vinyl sulfones, e.g., oxidation of vinyl sulfides, olefination reactions of carbonyl compounds, addition of sulfonyl radicals to alkenes and alkynes, and use of organometallic reagents such as palladium or zirconium.[9] However, the practical utility of these methods is often limited by the requirement of prefunctionalized starting materials, harsh reaction conditions, and low regio- and stereoselectivity.[10] Because of the importance of vinyl sulfones, new synthetic methodologies continue to be highly desired.[10,11]

This work was inspired by our mechanistic studies to understand the Ni-catalyzed oxidative annulation reaction of aromatic amides and alkynes,[12,13,14] and a number of C–H metalation/allene insertion reactions.[15] We postulated that replacement of the alkyne with an allenyl sulfone[16] would afford access to vinyl sulfones. However, to our surprise the reaction of 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene (**2a**) with picolyl amide **1a** (R = Ph) afforded vinyl sulfone **3a** (R = Ph), in the absence of the nickel catalyst (Scheme 1b).[17] Herein, we describe a novel metal-free selective C(sp^3)–H functionalization[18,19] of picolyl amides with allenic sulfone **2a** as an efficient and mild method to install vinyl sulfone groups to rapidly access covalent inhibitors.[2c,20] The reaction mechanism of this transformation operates via a rare pyridine-initiated generation of a *p*-toluenesulfinate anion mediated process analogous to phosphine-triggered reactions.[21]

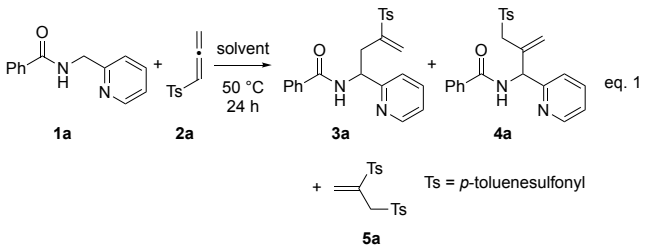
Scheme 1. Vinyl Sulfones: Biological Properties and their Synthetic Preparation Using Allenyl Sulfone.



Results and Discussion

Our initial goals of this investigation were to determine whether allenyl sulfones could be inserted selectively into the C(sp^2)–H bond of aromatic amides with nickel catalysis and a pyridine directing group. In order to test this hypothesis, 2-picolyl amide **1a** (0.19 mmol) was reacted with 3 equiv of **2a** using 10 mol% $Ni(OTf)_2$ at 120 °C which afforded two products in a 75:25 ratio (entry 1, Table 1). Interestingly, structural confirmation revealed sulfones **3a** and **4a**, products arising from functionalization of a C(sp^3)–H bond instead of the anticipated C(sp^2)–H bond of the aryl ring. The structure of **3a** was established by X-ray crystallography, see Supporting Information (SI). Additionally, disulfone 4,4'-(prop-2-ene-1,2-diyldisulfonyl)bis(methylbenzene) (**5a**) was isolated in 10% yield calculated based upon allenyl sulfone equivalents (eq 1).

Repeating this reaction in the absence of the Ni(II) catalyst gave the same products **3a** and **4a** in an identical ratio with a slightly higher yield (entry 2), evidence that **3a** and **4a** are resulting from a metal-free reaction mechanism.



eq. 1

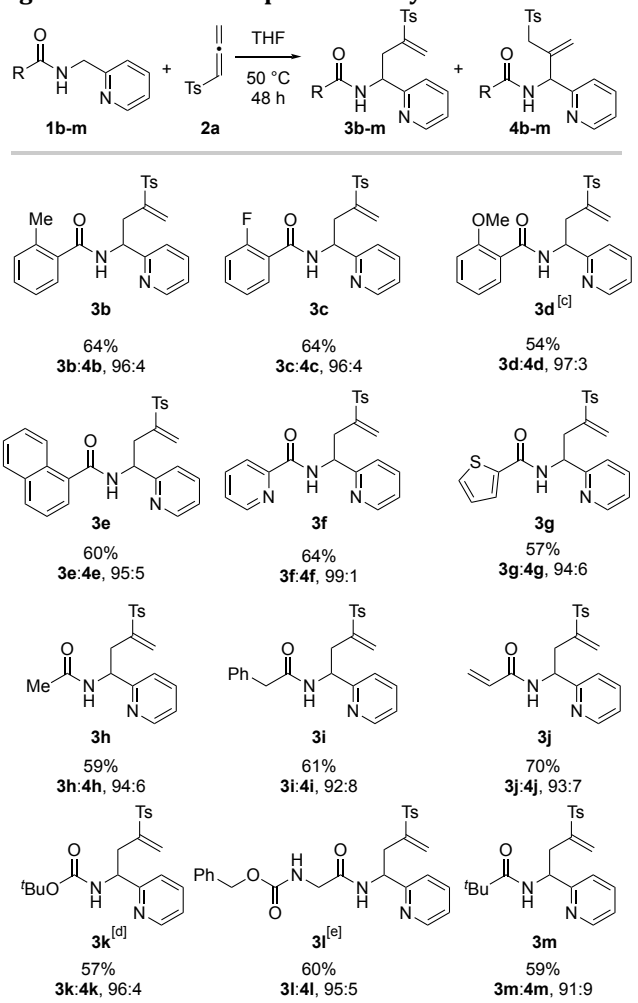
Table 1. Optimizing the Reaction of 2-Picolyl Amide 1a with Allenyl Sulfone 2a[a]

entry	**2a** (equiv)	solvent (dielectric constant, ε)[22]	yield (%)	selectivity (**3a**:**4a**)
1[b]	3.0	toluene (2)	64	75:25
2[c]	3.0	toluene (2)	67	75:25
3	2.0	toluene (2)	64	94:6
4	2.0	DMSO (47)	15[d]	–
5	2.0	CH_3CN (36)	68	67:33
6	2.0	EtOH (25)	53[e]	63:37
7	2.0	THF (8)	67	98:2
8	1.5	THF (8)	56[f]	98:2
9[g]	2.0	THF (8)	0	–
10[h]	2.0	THF (8)	0	–
11[i]	2.0	THF (8)	0	–

[a]Reaction conditions: 0.19 mmol of **1a** (1.0 equiv), **2a**, in solvent (1 mL, 0.19 M) at 50 °C for 24 h. [b]10 mol% $Ni(OTf)_2$, 120 °C, stirred for 1 h. [c]120 °C, stirred for 1 h. [d]NMR yield. [e]9% recovered **1a**. Attempts to separate **3a** and **4a** by HPLC using a C18 column were not successful. [f]17% recovered **1a**. [g]2 equiv NaTs. [h]NaTs (1.0 equiv) and stirred for 2 h. [i]0.07 mmol of **1a** (1.0 equiv), **2a**, NaTs (0.1 equiv) in THF (0.37 mL, 0.19 M) at 50 °C.

In order to increase selectivity for vinyl sulfone **3a**, a number of reaction parameters, e.g., temperature, allenyl sulfone equivalents, and solvents with different dielectric constants were examined. On reducing the reaction temperature to 50 °C with 2 equivalents of **2a**, the yield was unaffected but the **3a**:**4a** ratio improved to 94:6 (entry 3). However, performing this reaction at lower temperature required a longer reaction time (24 h) as evidenced by the slower disappearance of the ^{1}H NMR resonance of the C(sp^3)–H $_{bond}$ of **1a**. We next screened solvents to examine solvent effects on the yield and selectivity. Switching to a polar solvent DMSO (ε = 47) resulted in a 15% yield of **3a** with complete consumption of **2a** by ^{1}H NMR (entry 4). DMSO contributed to the decomposition of the allenyl sulfone presumably via a nucleophilic attack on the electron deficient *sp* hybridized carbon of the allene.[23] Acetonitrile (ε = 36) slightly improved the product yield but gave lower selectivity (entry 5). Ethanol (ε = 25), a protic solvent, gave a 53% yield of **3a**:**4a** with 9% recovered starting material **1a** after 24 h and afforded the lowest product selectivity (**3a**:**4a**, 63:37) (entry 6). Finally, switching to THF (ε = 8) as solvent gave the same yield with higher selectivity (**3a**:**4a**, 98:2) than toluene (compare entries 2 and 7). Lowering the equivalents of **2a** to 1.5 gave a 56% yield with a **3a**:**4a** ratio of 98:2 and 17% recovered **1a** after column chromatography (entry 8). Finally, sodium *p*-toluenesulfinate was included as an additive because we predict it is generated *in situ*, thereby activating **2a** (vide infra). However, this resulted in complete decomposition of **2a** (entries 9, 10 and 11). For optimized reactions conditions, we selected THF as the solvent with 2 equivalents of **2a** and a reaction temperature of 50 °C.

Figure 1. Substrate Scope of 2-Picolyl Amide with 2a[a,b,f]

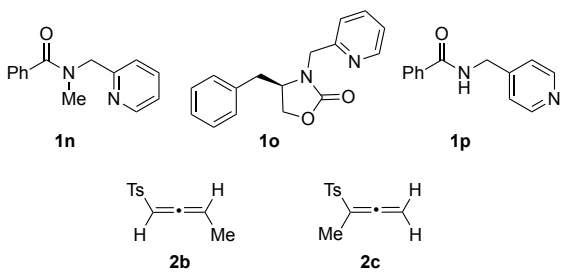


[a]Reaction conditions: 0.2 mmol of **1b-m** (1.0 equiv), **2a** (2 equiv) in THF (1 mL, 0.2 M) at 50 °C. [b]Yield and selectivity are average of two identical runs on 0.2 mmol scale of 2-picolyl amide. [c]Yield (BRSM) 66%. [d]Second run was stirred for 72 h. [e]Stirred for 24 h; experiment was carried out four times and in one run product selectivity was 85:15 (see supporting information (SI)); yield is average of four runs and selectivity is average of three runs excluding the run with

85:15 product ratio; [f]Modified protocol was employed for 2-picolyl amide solids and oils (see SI).

We next investigated the substrate scope of the reaction with 2-picolyl amides **1b-m** (Figure 1). Both aryl and alkyl picolyl amides were tested by varying the R group on **1** to examine the functional group tolerance. The *ortho*-methyl and fluoro substituted aryl amides **1b** and **1c** gave **3b** and **3c** in 64% yield. The *ortho*-methoxy substituted aryl amide **1d** gave **3d** in a lower yield of 54% (66% based upon recovered **1d**). The reaction was also affected with a bulky naphthamide **1e** affording **3e** in 60% yield. Pyridine and thiophene picolyl amides **1f** and **1g** afford **3f** and **3g** with similar yields and excellent product selectivity. Feasibility studies of alkyl and benzyl picolyl amides were carried out using **1h** and **1i** having α-acidic protons. In both cases, the reaction was selective for the C(sp^3)–H bond next to the pyridine ring to afford the vinyl sulfone products **3h** and **3i** in good yields and selectivities. Acrylamide **1j** reacted to form the vinyl sulfone **3j**:**4j** in 70% yield with a 93:7 ratio. Picolyl amides containing a number of commonly used protecting groups were then examined. Boc-, Cbz- and pivaloyl-protected amides **1k**, **1l**, and **1m** gave the vinyl sulfone products, **3k**, **3l**, and **3m**, respectively with comparable yields and selectivities, providing ready access to amino functionalized building blocks.

Figure 2. Unreactive Substrates: Picolyl Amides and Allenyl Sulfones

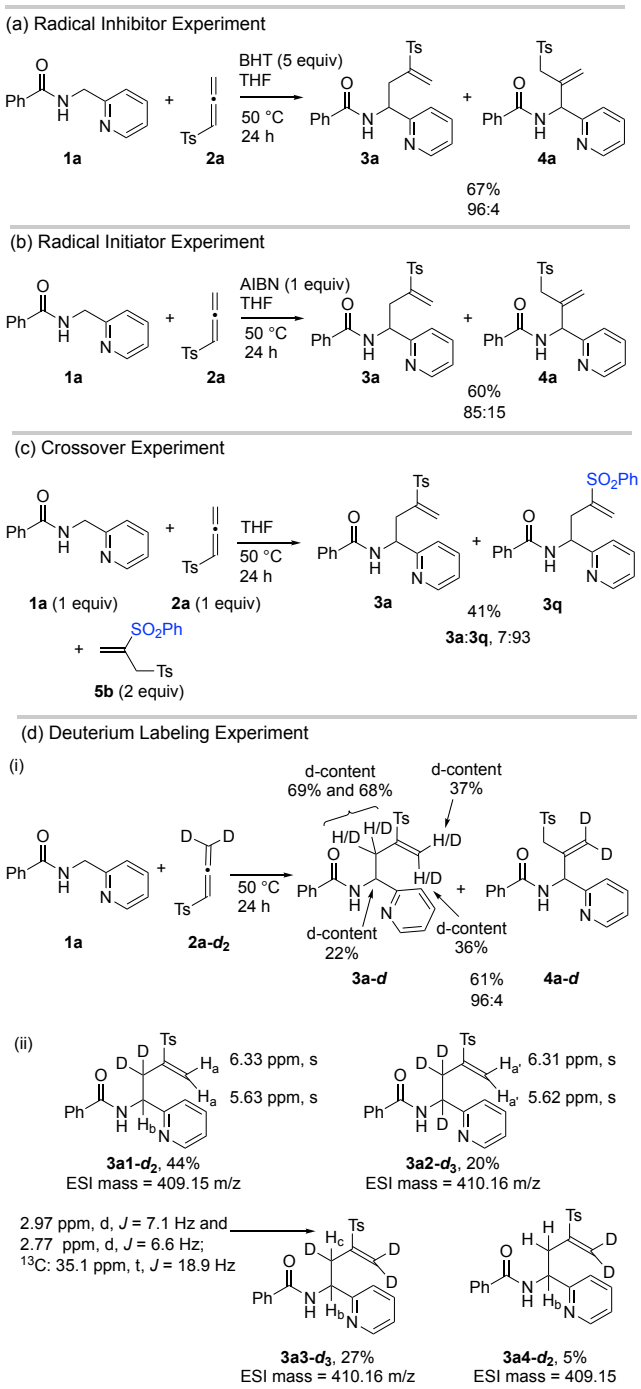


Tertiary picolyl amide **1n** and carbamate **1o** were subjected to the optimized reactions conditions (Figure 2). However, unreacted **1n** or **1o** and **2a** remained after 24 h based on ^{1}H NMR of the crude reaction mixture. ^{1}H NMR signals of disulfone **5a** were observed as well. 4-Picolyl amide **1p** reacted giving uncharacterizable products along with disulfone **5a**. Repeating this reaction at room temperature also resulted in decomposition of **1p** and formation of disulfone **5a**. These results suggest that **2a** is activated for picolyl amides **1n**, **1o**, and **1p** to generate *p*-toluenesulfinate anion to form disulfone **5a**, but C–H functionalization does not occur due to steric hindrance imposed by the tertiary amide or carbamate (vide infra).

To determine the reaction scope of the allenyl sulfone, 1,3- and 1,1-disubstituted allenyl sulfones **2b** and **2c** were reacted with **1a** (1 equiv) at 50 °C. In the case of 1,3-disubstituted allenyl sulfone **2b**, ^{1}H NMR of the crude reaction mixture showed unreacted **1a** and disappearance of signals corresponding to **2b** with no evidence of formation of any disulfone intermediate. We attribute the lability of **2b** to isomerization(s) affording uncharacterizable compounds. The 1,1-disubstituted allenyl sulfone (**2c**) was unreactive under the reaction conditions with **1a** at 50 °C with unreacted **1a**, **2c** observed and no formation of disulfone based on ^{1}H NMR of the crude reaction mixture.

Studies to Understand the Mechanism for Vinyl Sulfone Formation

Scheme 2. Experimental Studies of Reaction Mechanism



A number of experiments were carried out to understand how the vinyl sulfones are formed. The proposed mechanism is a challenging arrow-pushing exercise, which is supported by experimental observations (vide infra). First, because **2a** was prepared using $AgSbF_6$, inductively coupled plasma mass spectrometry (ICP-MS) analysis was carried out to determine whether trace silver contaminants were

present in **2a**. A silver concentration of 4.5±0.4 μg/L was found in 10 mg sample of **2a**, which suggests that the formation of the vinyl sulfones is not catalyzed by trace Ag from the allene.[24] To account for the mass balance in the reaction of **1c** with **2a**, the silica gel in the chromatography column was flushed several times with ethyl acetate and acetone. The total mass of the isolated fractions accounted for the initial mass of the starting materials ^{1}H NMR analysis of the baseline materials showed uncharacterizable resonances with large signals mostly in the aromatic region of the spectrum. The reaction of **1a** with **2a** in the presence of radical scavenger BHT (5 equiv) afforded **3a**:**4a** in the same yield and product selectivity (compare entry 7, Table 1 with Scheme 2a). Similarly, reaction of **1a** with **2a** in the presence of AIBN, a radical initiator, afforded only a slight decrease in selectivity (Scheme 2b). In order to test the role of disulfone **5** in the reaction mechanism, a crossover experiment was designed using **5b** having a phenyl sulfonyl group (blue). Reaction of **1a** with **2a** in the presence of **5b** gave a 41% yield of **3q:3a** in a 93:7 ratio with the major product having a vinyl phenyl sulfonyl group (Scheme 2c). Finally, the reaction of **1a** with only **5b** in the presence of potassium carbonate gave recovered starting materials (see SI).[25,20d] This experiment suggests that the allenyl sulfone **2a** is required in the reaction mechanism.

To further probe the reaction mechanism, deuterium labeling experiments were carried out where **2a-*d*$_2$** was reacted with **1a** (Scheme 2d). Comparison of the ^{1}H NMR spectra of **3a** and **3a-*d*** shows ~68.5% d-content at the allylic C–H protons and ~36.5% at the alkenyl C–H protons. The ^{1}H NMR is complicated showing at least five different deuterated compounds for **3a-d** and **4a-d**. Compounds **3a1-*d*$_2$** and **3a2-*d*$_3$** were formed in a 2:1 ratio and the structures are supported by alkenyl resonances (6.33 and 5.63 ppm) and (6.31 and 5.62 ppm), respectively. The total percentages of these compounds in the deuterated product mixture is determined by comparison of the integrated ratio of the alkenyl resonances H_a or $H_{a'}$ to a pyridinyl resonance at 8.54 ppm. The structural assignment of **3a3-*d*$_3$** is supported by resonances at 2.97 and 2.77 ppm. H_c shows a vicinal splitting with H_b only; the geminal splitting present in **3a4-*d*$_2$** is present in 5% of the product mixture. A low intensity multiplet splitting pattern in the ^{13}C NMR signal at 35.1 ppm corresponding to the deuterated allylic carbons in the compound mixture **3a-*d*** is also observed. Mass spectrometric analysis shows ESI masses of 409.15 and 410.16 m/z, providing support for trideuterated products **3a2-*d*$_3$** and **3a3-*d*$_3$** alongside di-deuterated products **3a1-*d*$_2$** and **3a4-*d*$_2$**.

To determine if allyl sulfone **4a** was interconverting to vinyl sulfone **3a**, **1a** and **2a** were reacted in the presence of **3a** and **4a** (59:41 ratio) at 50 °C in THF (SI). ^{1}H NMR of the crude residue showed a 78:22 ratio of **3a**:**4a** after 24 h; a ratio that is consistent with **1a** and **2a** reacting to form **3a**:**4a** in a 98:2 ratio together with the initial ratio of **3a**:**4a** (59:41). In a separate experiment, the reaction of **1a** and **2a** was performed in an NMR tube at 50 °C in toluene-d_8 and monitored every hour by ^{1}H NMR for 25.5 h. Analysis of these spectra showed a steady increase for the signals of **3a** that correlated with a decrease of **1a**. Signals for **4a** were not observed in these spectra due to low abundance. Together, these two experiments confirm that **4a** does not interconvert to **3a** during the course of the reaction.

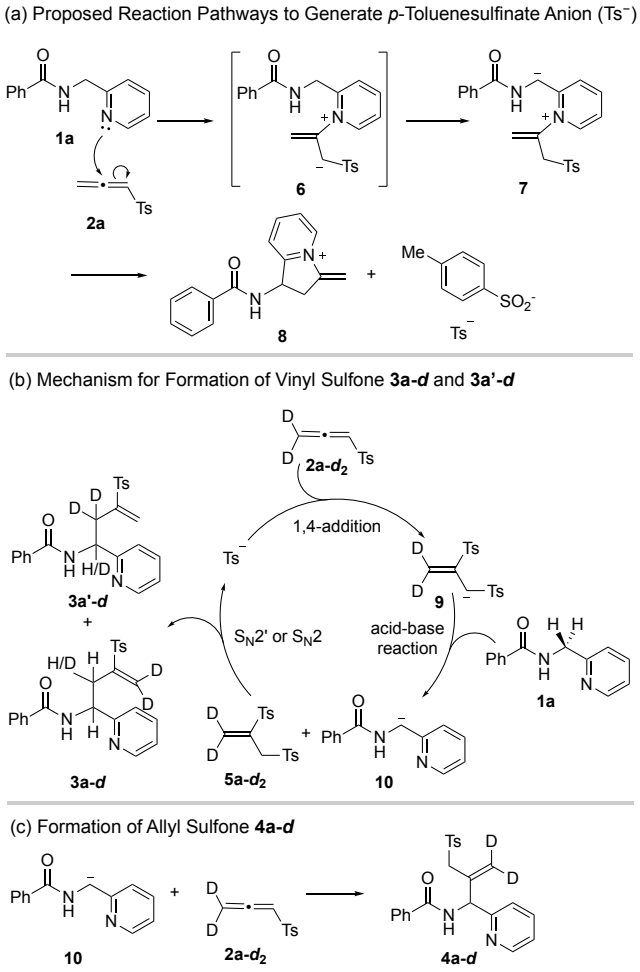
Based on the experimental results above, the following reaction mechanism involving a *p*-toluenesulfinate anion is proposed (Scheme 3). Nucleophilic attack of the pyridinyl nitrogen of **1a** to the central carbon of allene **2a-*d*$_2$** affords zwitterion **6**, which may react via several possible reaction pathways (see SI for alternative mechanisms). One mechanism involves protonation of the newly generated α-sulfonyl carbanion of **6** followed by deprotonation of the C(sp^3)–H bond to form **7** that undergoes an addition-elimination reaction to give the *p*-toluenesulfinate anion (Ts^-) and an unstable five-membered pyridinium species **8** (Scheme 3a). DFT calculations suggest that formation of **8** from **7** is facile (see SI for details).

To establish the role of the *intramolecular* pyridinyl group of picolyl amide in the proposed mechanism, *N*-benzylbenzamide (not shown) was reacted with **2a** (2 equiv) and pyridine (1 equiv), which gave complete decomposition of **2a** and unreacted *N*-benzylbenzamide. Repeating this reaction with less pyridine (0.2 equiv) gave the same result but with formation of **5a** (~17% based on 2 equiv of **2a**) as determined by ^{1}H NMR of the crude reaction mixture. These two experiments suggest that pyridine may activate the allenic sulfone **2a** leading to disulfone **5a**, via a *p*-toluenesulfinate anion and increase the acidity of the C(sp^3)–H bond in the amide. These conclusions are supported by DFT calculations discussed in the next section.

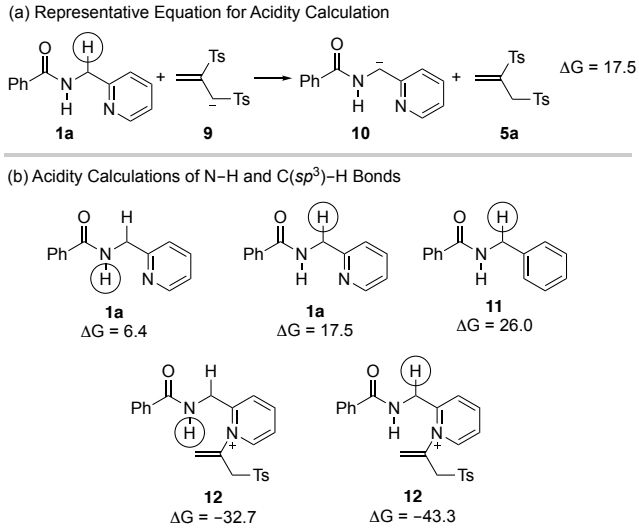
After *in situ* formation of trace tosyl (Ts) anion, formation of vinyl sulfones **3a-*d*** and **3a'-d** is proposed to occur via the 1,4-addition of the Ts anion to the allenyl sulfone **2a-*d*$_2$** to give disulfone carbanion **9** (Scheme 3b). This carbanion abstracts a proton from the C(sp^3)–H bond adjacent to the pyridine group to yield disulfone **5a-*d*$_2$** and picolyl amide anion **10**. Our hypothesis for anion formation from deprotonation at the C(sp^3)–H instead of the amide hydrogen is provide below. The picolyl amide anion **10** reacts with **5a-*d*$_2$** by an S_N2' mechanism to afford vinyl sulfone **3a'-*d***, or more specifically **3a1-*d*$_2$** and **3a2-*d*$_3$** in agreement with deuterium labeling experiment shown in Scheme 2. On the other hand, an S_N2 reaction between **10** and **5a-*d*$_2$** affords **3a-*d*,** i.e., **3a3-*d*$_3$** and **3a4-*d*$_2$**.

The mechanism for formation of allyl sulfone **4a-*d*** involves direct addition of the anion **10** to the central carbon of allenyl sulfone **2a-*d*$_2$** (Scheme 3c). This addition mechanism is supported by the higher ratios of allyl sulfone **4a** observed when elevated temperatures and higher equivalents of **2a** were used (Table 1, compare entries 2 and 3). This C–H bond deprotonation is promoted at higher temperatures and the higher concentration of **2a** favors formation of allyl sulfone product. The solvent polarity also impacts the proportion of vinyl sulfone to allyl sulfone where the allyl sulfone is afforded in increasing quantities in solvents with higher dielectric constants (compare entries 5 and 7, Table 1).

Scheme 3. Proposed Reaction Mechanisms for Formation of Vinyl Sulfone and Allyl Sulfone



Scheme 4. Relative Acidity of N–H versus C(sp^3)–H bonds from DFT Calculations[a]



[a]All ΔG values are reported in kcal/mol. Calculations were performed at M06-2X/6-311+G(d,p)/SMD(toluene)//B3LYP-D3/6-31G(d) level of theory.

The proposed mechanism requires deprotonation at the C(sp^3)–H bond of **1a**. To understand why this occurs in the presence of the more acidic amide N–H, relative acidity calculations were performed using DFT. As expected, deprotonation with **9** of the amide N–H bond of **1a** is thermodynamically favored over deprotonation of the C(sp^3)–H ($\Delta\Delta G$ = 11.1 kcal/mol) (Scheme 4). Although, formation of anion **10** is thermodynamically disfavored, low concentrations may be present in the reaction mixture. Calculations reveal that the acidity of the C(sp^3)–H bond of **1a** is increased dramatically when the *N*-pyridinyl group is bonded to the allenyl sulfone (Scheme 4b). In this case, the C(sp^3)–H bond of the pyridinium ion **12** is more acidic than the amide N–H bond ($\Delta\Delta G$ = 10.6 kcal/mol). Furthermore, because the reaction of **1a** and disulfone **5b** failed in the absence of allene **2a**, even with added K_2CO_3, we propose that formation of the intermediate pyridinium ion **12** is required for C–H deprotonation. We note that the relative acidity of benzylic C(sp^3)–H bond of *N*-benzylbenzamide **11** shows the C(sp^3)–H bond as much less acidic than **1a** ($\Delta\Delta G$ = 8.5 kcal/mol), likely why no reaction was observed between **11** and allenyl sulfone **2a** even in the presence of pyridine (vide supra).

Conclusions

In summary, we have developed a protocol to form vinyl sulfones via selective C(sp^3)–H functionalization of pharmacologically prevalent picolyl amide with 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene. We expect this procedure will be useful for installing the vinyl sulfone warhead on picolyl amides in covalent inhibitor design. Furthermore, studies suggest that the reaction mechanism operates via a rare pyridine-initiated activation of an allenyl sulfone to form *p*-toluenesulfinate anion *in situ*, which in turn functions catalytically to afford vinyl sulfones.

Experimental Section

General Methods. Unless otherwise indicated, all reactions were performed in flame-dried glassware under an inert atmosphere of dry nitrogen and stirred with Teflon-coated magnetic stir bars. All commercially available compounds were purchased and used as received unless otherwise specified. The solvents tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were purified by passing through alumina using the Sol-Tek ST-002 solvent purification system. Toluene and acetonitrile (CH_3CN) were distilled from calcium hydride prior to use. Deuterated chloroform ($CDCl_3$) was stored over 3 Å molecular sieves. Nitrogen gas was purchased from Matheson Tri Gas.

Purification of compounds by flash column chromatography was performed using silica gel (40-63 μm particle size, 60 Å pore size). TLC analyses were performed on silica gel F254 glass-backed plates (250 μm thickness). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, 500 or 600 MHz spectrometers. Spectra were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.16 ppm, ^{13}C). Chemical shifts (δ) are reported in ppm and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet) and br (broad).

Coupling constants, *J*, are reported in hertz (Hz). All NMR spectra were obtained at room temperature. IR spectra were obtained using PerkinElmer Spectrum Two FT-IR spectrometer.

Atmospheric Solids Analysis Probe (ASAP) mass spectroscopy was performed on a Micromass Q-TOF API-US high resolution mass spectrometer, while Electrospray Ionization (ESI) mass spectroscopy was performed on a Thermo Scientific Q Exactive high resolution mass spectrometer. All melting points are uncorrected. Product metal concentrations were measured on a Perkin/Elmer NExION 300x Inductively Coupled Mass Spectrometer after digestion in sub-boil distilled concentrated nitric acid.

General Procedure A: Conversion of Aryl Carboxylic Acids to Aryl 2-Picolyl Amides. The synthesis of aryl 2-picolyl amide was performed using a modified literature procedure.[13] A flame-dried, 2-necked, round-bottomed flask equipped with a stir bar, rubber septum, and nitrogen inlet adaptor was charged with carboxylic acid (1.0 equiv), dichloromethane (0.5 M), and *N,N*-dimethylformamide (0.05 equiv). The flask was placed in an ice/water bath. Oxalyl chloride (1.1 equiv) was added dropwise via syringe over 5 min. After 5 min, the reaction mixture was allowed to warm to rt by removal of ice/water bath and maintained for 2-4 h. The reaction progress was monitored by TLC and ^{1}H NMR and judged complete upon disappearance of the aryl carboxylic acid. The flask was placed in an ice/water bath. 2-Picolylamine (1.1 equiv) was added dropwise via syringe, the reaction mixture was allowed to warm to rt and vigorously stirred overnight. Sat'd aq sodium bicarbonate was added, the reaction mixture was transferred to a separatory funnel and diluted with dichloromethane. The aqueous layer was separated and the organic layer was washed with water, dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography.

General Procedure B: Conversion of Alkyl Carboxylic Acids to Alkyl 2-Picolyl Amides. The synthesis of alkyl 2-picolyl amide was performed using a modified literature procedure.[13] A flame-dried, 2-necked round-bottomed flask equipped with a stir bar, rubber septum, and nitrogen inlet adaptor was charged with carboxylic acid (1.0 equiv), dichloromethane (0.5 M), and N,N-dimethylformamide (0.05 equiv). The flask was placed in an ice/water bath. Oxalyl chloride (1.1 equiv) was added dropwise via syringe over 5 min. After 5 min, the reaction mixture was allowed to warm to rt by removal of ice/water bath and maintained for 2-4 h. The reaction was monitored by TLC and ^{1}H NMR and judged complete upon disappearance of the alkyl carboxylic acid. The flask was placed in an ice/water bath. 2-Picolylamine (1.1 equiv) was added dropwise via syringe, the reaction mixture was allowed to warm to rt and vigorously stirred overnight. Sat'd aq sodium hydroxide was added, the reaction mixture was transferred to a separatory funnel and diluted with dichloromethane. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2x) and the combined organic layers were dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography.

General Procedure C: Reaction of 2-Picolyl Amide (solid) with 1-methyl-4-(propa-1,2-dien-1-yl-sulfonyl) benzene. An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with 2-picolyl amide (solid) and 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl) benzene in air. The tube was sealed with a cap (ChemGlass, CG-4910-15, TFE septum). The septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated for 1-2 sec and filled with nitrogen (3x). THF was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The reaction progress was monitored by ^{1}H NMR and judged complete upon disappearance of the picolyl amide. This was accomplished by removal an aliquot via syringe, transfer to an NMR tube, and diluting with $CDCl_3$. Upon completion, the reaction mixture was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography.

General Procedure D: Reaction of 2-Picolyl Amide (liquid) with 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl) benzene. An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with 2-picolyl amide (liquid), THF, and 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene open to air. The tube was sealed with a cap (ChemGlass, CG-4910-15, TFE septum). The septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated for 1-2 sec and filled with nitrogen (3x). The cap and septum are wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The reaction progress was monitored by ^{1}H NMR for 48-72 h. The reaction mixture was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography.

Compound Synthesis and Characterization: Synthesis of Picolyl Amides.

N-(pyridin-2-ylmethyl)benzamide (**1a**). Follows General Procedure A. Benzoic acid (1.0 g, 8.2 mmol), CH_2Cl_2 (16 mL), *N,N*-dimethylformamide (0.03 mL, 0.4 mmol), oxalyl chloride (0.77 mL, 9.0 mmol), 2-picolylamine (0.92 mL, 9.0 mmol). The crude product was purified by silica gel flash chromatography (40-100% ethyl acetate/hexane) to yield the title compound as a white solid (1.6 g, 94%). Spectral data matched that previously reported for compound **1a**:[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ8.56 (d, J = 4.8 Hz, 1 H), 7.87 (dd, J = 7.7, 1.5 Hz, 2 H), 7.70-7.65 (m, 2 H), 7.50 (ddd, J = 7.4, 7.1, 1.2 Hz, 1 H), 7.44 (dd, J = 7.8, 7.3 Hz, 2 H), 7.33 (d, J = 7.8 Hz, 1 H), 7.21 (dd, J = 7.1, 5.0 Hz, 1 H), 4.76 (d, J = 5.0, Hz, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.5, 156.3, 149.1, 137.0, 134.5, 131.6, 128.7 (2 C), 127.2 (2 C), 122.6, 122.3, 44.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2O$ 213.1022; Found 213.1020; TLC R_f = 0.23 (100% ethyl acetate), visualized with UV.

2-methyl-N-(pyridin-2-yl-methyl)benzamide (**1b**). Follows General Procedure A. 2-Methylbenzoic acid (300 mg, 2.2 mmol), CH_2Cl_2 (4 mL), *N, N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.21 mL, 2.5 mmol), 2-picolylamine (0.25 mL, 2.5 mmol). The crude product was purified by silica gel flash chromatography (10-100% ethyl acetate/hexane) to yield the title compound as an orange solid (353 mg, 71%). Spectral data matched that previously reported for compound **1b**:[27] FID (HO-02-206); ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.53 (d, J = 4.7 Hz, 1 H), 7.71 (dt, J = 7.7, 1.8 Hz, 1 H), 7.47 (d, J = 7.7 Hz, 1 H), 7.36 (d, J = 7.9 Hz, 1 H), 7.31 (dd, J = 7.1, 1.3 Hz, 1 H), 7.24-7.20 (m, 3 H), 7.14 (br, 1 H), 4.76 (d, J = 4.9 Hz, 2 H), 2.48 (s, 3 H), spectrum contains small amounts of ethyl acetate; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.2, 156.3, 149.0, 137.2, 136.4, 136.3, 131.2, 130.1, 127.2, 125.9, 122.6, 122.4, 44.7, 20.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1179; Found 227.1181; TLC R_f = 0.31 (100% ethyl acetate), visualized with UV.

2-fluoro-N-(pyridin-2-ylmethyl)benzamide (**1c**). Follows General Procedure A. 2-Fluorobenzoic acid (350 mg, 2.5 mmol), CH_2Cl_2 (5 mL), *N, N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.24 mL, 2.8 mmol), 2-picolylamine (0.29 mL, 2.8 mmol). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a white solid (481 mg, 84%). Spectral data matched that previously reported for compound **1c**:[26] ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.6 Hz, 1 H), 8.13 (dt, J = 7.8, 1.8 Hz, 1 H), 7.98 (s, 1 H), 7.68 (dt, J = 7.7, 1.7 Hz, 1 H), 7.50-7.45 (m, 1 H), 7.34 (d, J = 7.8 Hz, 1 H), 7.28-7.24 (m, 1 H), 7.21 (dd, J = 7.0, 5.0 Hz, 1 H), 7.14 (dd, J = 11.3, 8.4 Hz, 1 H), 4.81 (d, J = 4.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.5 (d, J = 2.9 Hz), 161.0 (d, J = 248.2 Hz), 156.4, 149.3, 136.9, 133.4 (d, J = 9.2 Hz), 132.2 (d, J = 2.1 Hz), 124.8 (d, J = 3.4 Hz), 122.5, 122.1, 121.2 (d, J = 11.5 Hz), 116.2 (d, J = 24.6 Hz), 45.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}N_2OF$ 231.0928; Found 231.0928; TLC R_f = 0.41 (100% ethyl acetate), visualized with UV.

2-methoxy-N-(pyridin-2-yl-methyl)benzamide (**1d**). Follows General Procedure A. 2-Methoxybenzoic acid (350 mg, 2.3 mmol), CH_2Cl_2 (4.6 mL), *N, N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.22 mL, 2.6 mmol), 2-picolylamine (0.27 mL, 2.6 mmol). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a pale green oil (445 mg, 80%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1 H), 8.58 (d, J = 4.5 Hz, 1 H), 8.25 (dd, J = 7.8, 1.8 Hz, 1 H), 7.66 (dt, J = 7.7, 1.7 Hz, 1 H), 7.45 (dt, J = 8.1, 1.8 Hz, 1 H), 7.36 (d, J = 7.8 Hz, 1 H), 7.19 (dd, J = 6.9, 5.1 Hz, 1 H), 7.08 (t, J = 7.4 Hz, 1 H), 6.99 (d, J = 8.3 Hz, 1 H), 4.81 (d, J = 5.2 Hz, 2 H), 4.00 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.5, 157.9, 157.6, 149.3, 136.8, 132.9, 132.5, 122.3, 122.2, 121.6, 121.4, 111.5, 56.1, 45.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2$ 243.1128; Found 243.1124; TLC R_f = 0.28 (100% ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)-1-naphthamide (**1e**). Follows General Procedure A. 1-Naphthoic acid (300 mg, 1.7 mmol), CH_2Cl_2 (4 mL), *N,N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.17 mL, 2.0 mmol), 2-picolylamine (0.20 mL, 2.0 mmol). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a pale yellow solid (353 mg, 77%). Spectral data matched that previously reported for compound **1e**:[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.7 Hz, 1 H), 8.40 (dd, J = 8.6, 1.4 Hz, 1 H), 7.93 (d, J = 8.3 Hz, 1 H), 7.87 (dd, J = 8.4, 2.0 Hz, 1 H), 7.73-7.69 (m, 2 H), 7.48 (dd, J = 8.2, 7.1 Hz, 1 H), 7.57-7.51 (m, 2 H), 7.38 (d, J = 7.8 Hz, 1 H), 7.36 (br, 1 H), 7.22 (dd, J = 7.0, 5.3 Hz, 1 H), 4.87 (d, J = 4.8 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.7, 156.2, 149.2, 137.0, 134.5, 133.9, 130.8, 130.4, 128.4, 127.2, 126.5, 125.7, 125.4, 124.9, 122.6, 122.3, 45.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}N_2O$ 263.1179; Found 263.1176; TLC R_f = 0.30 (100% ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)picolinamide (**1f**). Follows General Procedure A. Picolinic acid (300 mg, 2.4 mmol), CH_2Cl_2 (5 mL), *N, N*-dimethylformamide (0.01 mL, 0.12 mmol), oxalyl chloride (0.24 mL, 2.8 mmol), 2-picolylamine (0.28 mL, 2.8 mmol). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a pale yellow solid (355 mg, 68%). Spectral data matched that previously reported for compound **1f**:[29] ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1 H), 8.61-8.58 (m, 2 H), 8.22 (d, J = 7.8 Hz, 1 H), 7.85 (dt, J = 7.7, 1.7 Hz, 1 H), 7.66 (dt, J = 7.7, 1.8 Hz, 1 H), 7.43 (ddd, J = 7.6, 4.8, 1.2 Hz, 1 H), 7.34 (d, J = 7.8 Hz, 1 H), 7.20 (dd, J = 7.0, 4.9 Hz, 1 H), 4.80 (d, J = 5.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.6, 157.1, 150.0, 149.5, 148.4, 137.4, 136.9, 126.3, 122.5, 122.4, 122.0, 44.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}N_3O$ 214.0975; Found 214.0973; TLC R_f = 0.30 (100% ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)thiophene-2-carboxamide (**1g**). Follows General Procedure A. Thiophene-2-carboxylic acid (300 mg, 2.3 mmol), CH_2Cl_2 (5 mL), *N, N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.23 mL, 2.6 mmol), 2-picolylamine (0.27 mL, 2.6 mmol). The crude product was purified by silica gel flash chromatography (0-100% ethyl acetate/hexane) to yield the title compound as a white solid (331 mg, 65%). Spectral data matched that previously reported for compound **1g**:[27] ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 4.8 Hz, 1 H), 7.69 (dt, J = 7.7, 1.8 Hz, 1 H), 7.60 (dd, J = 3.7, 1.0 Hz, 1 H), 7.48 (dd, J = 5.0, 1.0 Hz, 1 H), 7.42 (br, 1 H), 7.32 (d, J = 7.8 Hz, 1 H), 7.22 (dd, J = 7.7, 5.0 Hz, 1 H), 7.09 (dd, J = 5.0, 3.8 Hz, 1 H), 4.74 (d, J = 4.8 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0, 156.2, 149.2, 139.1, 137.0, 130.1, 128.3, 127.7, 122.6, 122.4, 44.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_2OS$ 219.0587; Found 219.0588; TLC R_f = 0.28 (100% ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)acetamide (**1h**). Follows General Procedure B. Acetic acid (250 mg, 4.2 mmol), CH_2Cl_2 (8 mL), *N,N*-dimethylformamide (0.02 mL, 0.2 mmol), oxalyl chloride (0.40 mL, 4.7 mmol), 2-picolylamine (0.48 mL, 4.7 mmol). The crude product was purified by silica gel flash chromatography (0-100% acetone/ethyl acetate) to yield the title compound as a pale-yellow oil which solidified as a brown solid in the freezer (420 mg, 67%). Spectral data matched that previously reported for compound **1h**:[30] ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J = 4.6 Hz, 1 H), 7.66 (dt, J = 7.7, 1.7 Hz, 1 H), 7.26-7.25 (m, 1 H), 7.20 (dd, J = 7.1, 5.1 Hz, 1 H), 6.73 (br, 1 H), 4.56 (d, J = 4.8 Hz, 2 H), 2.08 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.3, 156.4, 149.1, 136.9, 122.5, 122.3, 44.7, 23.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_8H_{11}N_2O$ 151.0866; Found 151.0863; TLC R_f = 0.29 (100% acetone), visualized with UV.

2-phenyl-N-(pyridin-2-ylmethyl)acetamide (**1i**). Follows General Procedure A. 2-Phenylacetic acid (350 mg, 2.6 mmol), CH_2Cl_2 (5 mL), *N, N*-dimethylformamide (0.01 mL, 0.13 mmol), oxalyl chloride (0.25 mL, 2.9 mmol), 2-picolylamine (0.30 mL, 2.9 mmol). The crude product was purified by silica gel flash chromatography (0-100% ethyl acetate/hexane) to yield the title compound as a white solid (484 mg, 83%). Spectral data matched that previously reported for compound **1i:**[31] ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.7 Hz, 1 H), 7.63 (dt, J = 7.7, 1.7 Hz, 1 H), 7.37-7.29

(m, 5 H), 7.20 (d, *J* = 7.8 Hz, 1 H), 7.16 (dd, *J* = 7.2, 5.0 Hz, 1 H), 6.66 (s, 1 H), 4.53 (d, *J* = 5.1 Hz, 2 H), 3.65 (s, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.1, 156.5, 149.1, 136.8, 135.0, 129.6 (2 C), 129.1 (2 C), 127.4, 122.4, 122.1, 44.7, 43.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1179; Found 227.1174; TLC R_f = 0.17 (100% ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)acrylamide (**1j**). Follows General Procedure B. Acrylic acid (315 mg, 4.4 mmol), CH_2Cl_2 (9 mL), *N,N*-dimethylformamide (0.02 mL, 0.2 mmol), oxalyl chloride (0.42 mL, 4.9 mmol), 2-picolylamine (0.51 mL, 4.9 mmol). The crude product was purified by silica gel flash chromatography (0-100% acetone/ethyl acetate) to yield the title compound as a white solid (460 mg, 65%). Spectral data matched that previously reported for compound **1j**:[32] ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.7 Hz, 1 H), 7.67 (dt, *J* = 7.7, 1.8 Hz, 1 H), 7.29 (d, *J* = 7.8 Hz, 1 H), 7.21 (dd, *J* = 7.0, 5.0 Hz, 1 H), 6.9 (s, 1 H), 6.34 (dd, *J* = 17.0, 1.6 Hz, 1 H), 6.22 (dd, *J* = 17.0, 10.1 Hz, 1 H), 5.68 (dd, *J* = 10.1, 1.6 Hz, 1 H), 4.65 (d, *J* = 4.9 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.7, 156.2, 149.1, 137.0, 130.9, 126.7, 122.6, 122.3, 44.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_9H_{11}N_2O$ 163.0871; Found 163.0874; TLC R_f = 0.54 (100% acetone), visualized with UV.

tert-butyl (pyridin-2-ylmethyl)carbamate (**1k**). *tert*-butyl (pyridin-2-ylmethyl)carbamate was synthesized using a modified literature procedure.[33] To a 50 mL, 2-necked flame-dried round-bottomed flask equipped with stir bar, rubber septum, and nitrogen inlet, di-*tert*-butyl dicarbonate (250 mg, 1.15 mmol) and 2-picolylamine (0.12 mL, 1.15 mmol) were added. The reaction mixture was stirred at 80 °C for 15 min. The crude product was purified by silica gel flash chromatography (20-100% diethyl ether /hexane) to yield the title compound as a clear oil (230 mg, 96%). Spectral data matched that previously reported for compound **1k**:[33] ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.5 Hz, 1 H), 7.65 (dt, *J* = 7.7, 1.7 Hz, 1 H), 7.26 (d, *J* = 7.8 Hz, 1 H), 7.17 (dd, *J* = 7.0, 5.0 Hz, 1 H), 5.57 (s, 1 H), 4.44 (d, *J* = 5.3 Hz, 2 H), 1.46 (s, 9 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.6, 156.1, 149.2, 136.8, 123.3, 121.8, 79.6, 45.9, 28.5 (3 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{17}N_2O_2$ 209.1285; Found 209.1283; TLC R_f = 0.61 (100% ethyl acetate), visualized with UV.

benzyl(2-oxo-2-((pyridin-2-ylmethyl)amino)ethyl) carbamate (**1l**). Follows General Procedure B. ((benzyloxy)carbonyl)glycine (350 mg, 1.7 mmol), CH_2Cl_2 (3 mL), *N,N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.16 mL, 1.9 mmol), 2-picolylamine (0.19 mL, 1.9 mmol). The crude product was purified by silica gel flash chromatography (50-100% ethyl acetate/hexane followed by 20-70% acetone/ethyl acetate) to yield the title compound as a white solid (127 mg, 25%). Spectral data matched that previously reported for compound **1l**:[34] ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.6 Hz, 1 H), 7.66 (dt, *J* = 7.6, 1.4 Hz, 1 H), 7.41-7.29 (m, 5 H), 7.26-7.19 (m, 3 H), 5.47 (br, 1 H), 5.14 (s, 2 H), 4.58 (d, *J* = 4.8 Hz, 2 H), 3.98 (d, *J* = 5.5 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.0, 156.7, 156.0, 149.2, 137.0, 136.3, 128.7 (2 C), 128.3, 128.2 (2 C), 122.6, 122.2, 67.3, 44.6, 44.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}N_3O_3$ 300.1343; Found 300.1358; TLC R_f = 0.31 (50% acetone/ethyl acetate), visualized with UV.

N-(pyridin-2-ylmethyl)pivalamide (**1m**). Follows General Procedure B. Pivalic acid (300 mg, 2.9 mmol), CH_2Cl_2 (6 mL), *N, N*-dimethylformamide (0.01 mL, 0.1 mmol), oxalyl chloride (0.28 mL, 3.3 mmol), 2-picolylamine (0.34 mL, 3.3 mmol). The crude product was purified by silica gel flash chromatography (0-100% ethyl acetate/hexane) to yield the title compound as a white solid (491 mg, 87%). Spectral data matched that previously reported for compound **1m**:[35] ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.7 Hz, 1 H), 7.66 (dt, *J* = 7.7, 1.8 Hz, 1 H), 7.24 (d, *J* = 7.9 Hz, 1 H), 7.19 (dd, *J* = 7.1, 5.0 Hz, 1 H), 7.01 (br s, 1 H), 4.54 (d, *J* = 4.7 Hz, 2 H), 1.26 (s, 9 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.7, 156.8, 149.2, 136.8, 122.4, 122.2, 44.6, 38.9, 27.8 (3 C); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{17}N_2O$ 193.1335; Found 193.1327; TLC R_f = 0.21 (100% ethyl acetate), visualized with UV.

N-methyl-N-(pyridin-2-ylmethyl)benzamide (**1n**). Follows General Procedure A. Benzoic acid (400 mg, 23.3 mmol), CH_2Cl_2 (6 mL), *N, N*-dimethylformamide (0.013 mL, 0.16 mmol), oxalyl chloride (0.31 mL, 3.6 mmol), 2-[(Methylamino)methyl]pyridine (0.44 mL, 3.6 mmol). The crude product was purified by silica gel flash chromatography (30-100% ethyl acetate/hexane) to yield the title compound as a slightly pale-yellow oil (573 mg, 77%). Spectral data matched that previously reported for compound **1n**:[36] ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.5 Hz, 1 H), 7.70 (dt, *J* = 7.7, 1.8 Hz, 1 H), 7.48-7.47 (m, 2 H), 7.42-7.34 (m, 4 H), 7.21(dd, *J* = 7.0, 5.0 Hz, 1 H), 4.88 (s, 1 H), 4.61 (s, 1 H), 3.09 (s, 1.5 H), 3.00* (s, 1.5 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.6, 171.7*, 157.3, 156.8*, 149.9, 149.4*, 137.0, 136.1, 129.7, 128.5, 127.2, 126.9, 122.5, 122.3, 121.0, 57.0, 53.1*, 38.0, 33.7* ppm, * Second isomer was distinguishable; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1179; Found 227.1177; TLC R_f = 0.41 (100% ethyl acetate), visualized with UV.

(R)-4-benzyl-3-(pyridin-2-ylmethyl)oxazolidin-2-one (**1o**): The synthesis of (*R*)-4-benzyl-3-(pyridin-2-ylmethyl)oxazolidin-2-one was performed using a modified literature procedure.[37] A flame-dried, 3-necked 50 mL round-bottomed flask equipped with a stir bar, rubber septa, and nitrogen inlet adaptor was charged with (*R*)-4-benzyloxazolidin-2-one (425 mg, 2.4 mmol) and THF (8 mL). The flask was placed in a dry ice/acetone bath at −78 °C. n-BuLi (1.5 mL, 2.4 mmol) was added dropwise via syringe over 5 min. The reaction was maintained for 15 min. 2-(Bromomethyl)pyridine hydrobromide (300 mg, 1.2 mmol) was added by temporary removal of the septum and stirred for 3 h at −78 °C. The dry ice/acetone bath was removed and stirred at rt for 22 h. The reaction mixture was diluted with dichloromethane and washed with 10% sodium hydroxide solution. The aqueous layer was extracted with dichloromethane and the organic layer was combined, dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (30-100% ethyl acetate/hexane) to yield the title compound as a colorless oil (313 mg, 98%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 1 H), 7.69 (dt, *J* = 7.7, 1.8 Hz, 1 H), 7.33 (d, *J* = 7.8 Hz, 1 H), 7.30-7.21 (m, 4 H), 7.08 (d, *J* = 6.8 Hz, 2 H), 4.84 (d, *J* = 15.6 Hz, 1 H), 4.41 (d, *J* = 15.6 Hz, 1 H), 4.20-4.13 (m, 1 H), 4.06-3.99 (m, 2 H), 3.23 (dd, *J* = 13.4, 3.8 Hz, 1 H), 2.66-2.60 (m, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 156.3, 149.6, 137.1, 135.7, 129.2 (2 C), 129.0 (2 C), 127.3, 122.9, 122.7, 67.3, 56.5, 48.2, 38.4 ppm ; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_2$ 269.1285; Found

269.1282; TLC R_f = 0.41 (100% ethyl acetate), visualized with UV.

N-(pyridin-4-ylmethyl)benzamide (**1p**): The synthesis of *N*-(pyridin-4-ylmethyl)benzamide was performed using a modified literature procedure.[38] A flame-dried, 2-necked 25-mL, round-bottomed flask equipped with a stir bar, rubber septum, and a nitrogen inlet adaptor was charged with benzoic acid (300 mg, 2.5 mmol), dichloromethane (5 mL), and *N,N*-dimethylformamide (0.01 mL, 0.12 mmol). The flask was placed in an ice/water bath. Oxalyl chloride (0.42 mL, 4.9 mmol) was added dropwise via syringe. After 30 min, the reaction mixture was allowed to warm to rt by removal of ice/water bath and maintained for 5 h. The reaction progress was monitored by TLC and judged complete upon disappearance of the benzoic acid. Excess oxalyl chloride was removed using high vacuum. The flask was placed in an ice/water bath. Pyridin-4-ylmethanamine (0.50 mL, 4.9 mmol) and triethylamine (0.68 mL, 4.9 mmol) in dichloromethane was added dropwise via syringe, the reaction mixture was allowed to warm to rt and vigorously stirred for 24 h. Sat'd aq sodium bicarbonate was added, the reaction mixture was transferred to a separatory funnel and diluted with dichloromethane. The aqueous layer was separated and organic layer was washed with water, dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (20-100% ethyl acetate/hexane and then 5% methanol/ethyl acetate) to yield the title compound as a pale yellow solid (300 mg, 58%). Spectral data matched that previously reported for compound **1p**:[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54-8.52 (m, 2 H), 7.82 (dd, *J* = 7.1, 1.4 Hz, 2 H), 7.53 (dt, *J* = 7.4, 1.9 Hz, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 7.23 (d, *J* = 5.9 Hz, 2 H), 6.86 (br s, 1 H), 4.64 (d, *J* = 6.1 Hz, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.8, 150.2 (2 C), 147.6, 134.0, 132.0, 128.8 (2 C), 127.2 (2 C), 122.4 (2 C), 42.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2O$ 213.1022; Found 213.1021; TLC R_f = 0.16 (100% ethyl acetate), visualized with UV.

N-benzylbenzamide (**11**): The synthesis of *N*-benzylbenzamide was performed using a modified literature procedure.[38] A flame-dried, 2-necked, 15-mL, round-bottomed flask equipped with a stir bar, rubber septum, and nitrogen inlet adaptor was charged with benzoic acid (300 mg, 2.5 mmol), dichloromethane (5 mL), and *N,N*-dimethylformamide (0.01 mL, 0.12 mmol). The flask was placed in an ice/water bath. Oxalyl chloride (0.42 mL, 4.9 mmol) was added dropwise via syringe. After 30 min, the reaction mixture was allowed to warm to rt by removal of ice/water bath and maintained for 8 h. The reaction progress was monitored by TLC and judged complete upon disappearance of the benzoic acid. Excess oxalyl chloride was removed using high vacuum. The flask was placed in an ice/water bath. Benzyl amine (0.54 mL, 4.9 mmol) and triethylamine (0.68 mL, 4.9 mmol) in dichloromethane was added dropwise via syringe, the reaction mixture was allowed to warm to rt and vigorously stirred for 24 h. Sat'd aq sodium bicarbonate was added, the reaction mixture was transferred to a separatory funnel and diluted with dichloromethane. The aqueous layer was separated and organic layer was washed with water, dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (10-40% ethyl acetate/hexane) to yield the title compound as a white solid (429 mg, 83%). Spectral data matched that previously reported for compound **11**:[40] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.69 (m, 2 H), 7.42-7.16 (m, 8 H), 6.38 (br, 1 H), 4.56-4.54 (m, 2 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.5, 138.4, 134.6, 131.7, 128.9 (2 C), 128.7 (2 C), 128.1 (2 C), 127.8, 127.1 (2 C), 44.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}NO$ 212.1070; Found 212.1059; TLC R_f = 0.30 (30% ethyl acetate/hexane), visualized with UV.

Prop-2-yn-1-yl 4-methylbenzenesulfinate (**13**): The synthesis of prop-2-yn-1-yl 4-methylbenzenesulfinate was performed using a modified literature procedure.[41] A flame-dried, 250-mL, 3-necked, round-bottomed flask equipped with stir bar, rubber septum, nitrogen inlet adaptor and addition funnel was charged with tosyl chloride (3.00 g, 15.7 mmol) and dichloromethane (39 mL). Triethylamine (2.4 mL, 17.3 mmol) was added via syringe. The flask was placed in an ice/water bath (10-15 °C). An oven-dried beaker was charged with triphenylphosphine (4.12 g, 15.7 mmol), dichloromethane (39 mL) and propargyl alcohol (0.91 mL, 15.7 mmol) and the beaker was swirled to form a uniform solution and the contents transferred to the addition funnel. The solution of triphenylphosphine, dichloromethane and propargyl alcohol was added dropwise via the addition funnel over 10 min while maintaining the temperature of the ice/water bath at 10-15 ° C. The reaction progress was monitored by TLC. After 3 h the reaction mixture was transferred to a 600 mL beaker and 20% Et_2O/hexane solution was added to produce a white precipitate. Removal of this precipitate was accomplished by filtering the mixture through a pad of silica gel under reduced pressure (water aspirator) and rinsed with ether. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-15% ethyl acetate/hexane) to yield the title compound as a clear oil (2.35 g, 77%). Spectral data matched that previously reported for compound **13**:[42] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2 H), 7.35 (d, *J* = 7.9 Hz, 2 H), 4.60 (dd, *J* = 15.5, 2.4 Hz, 1 H), 4.28 (dd, *J* = 15.5, 2.4 Hz, 1 H), 2.49 (t, *J* = 2.4 Hz, 1 H), 2.43 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.4, 141.2, 130.0 (2 C), 125.5 (2 C), 77.8, 76.2, 51.6, 21.7; TLC R_f = 0.30 (10% ethyl acetate/hexane), visualized with UV.

1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene (**2a**): The synthesis of 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl) benzene was performed using a modified literature procedure.[41] A flame-dried, 100-mL, 3-necked, round-bottomed flask equipped with a stir bar was charged with silver hexafluoroantimonate(V) (83 mg, 0.24 mmol) in a glovebox. The flask was equipped with an addition funnel and septa, then removed from the glovebox and placed under an atmosphere of nitrogen using an inlet adaptor. The addition funnel was charged with a solution of prop-2-yn-1-yl 4-methylbenzenesulfinate (2.35 g, 12.1 mmol) in dichloromethane (24 mL) and added dropwise into the reaction flask over 10 min. The reaction progress was monitored by TLC. After 2 h, the reaction mixture was vacuum filtered (water aspirator) through a pad of silica gel with Et_2O. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-30% ethyl acetate/hexane) to yield the title compound as white crystals (2.22 g, 94%). Spectral data matched that previously reported for compound **2a**:[43]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 8.0 Hz, 2 H), 6.23 (t, J = 6.4 Hz, 1 H), 5.43 (d, J = 6.4 Hz, 2 H), 2.45 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 209.4, 144.7, 138.5, 130.0 (2 C), 127.8 (2 C), 101.4, 84.2, 21.8; HRMS (ASAP) m/z: [M + H]$^+$ Calcd for $C_{10}H_{11}O_2S$ 195.0480; Found 195.0491; TLC R_f = 0.25 (20% ethyl acetate/hexane), visualized with UV.

prop-2-yn-1,1-d2-1-ol (**14**): The synthesis of prop-2-yn-1,1-*d2*-1-ol was performed using a modified literature procedure. [44] A flame-dried, 100-mL, 2-necked, round-bottomed flask equipped with stir bar and rubber septa was charged with lithium aluminum deuteride, $LiAlD_4$ (642 mg, 15.3 mmol) by temporary removal of a septum. Et_2O (26 mL) was added via syringe and reaction flask was placed in an ethanol bath (−70 °C, temperature maintained using cryo cool). Ethyl propiolate (2.07 mL, 20.4 mmol) dissolved in Et_2O (13 mL) was added to the flask via syringe pump (25 mL/h) over a period of 30 min. During the addition, the bath temperature was maintained between −70 to −60 °C. Upon completion of addition, the bath temperature was increased to −45 °C. The reaction progress was monitored by TLC. After maintaining the reaction overnight at -45 °C, complete consumption of starting material was observed. Water (0.7 mL), 15% sodium hydroxide solution (0.7 g NaOH in 4.7 ml water) and water (2 mL) were added affording an off-white precipitate. The reaction mixture was gravity filtered and the precipitate rinsed with Et_2O. The filtrate was dried over magnesium sulfate, gravity filtered, and distilled at atmospheric pressure to remove Et_2O. The bulk of this residue, a slightly pale-yellow oil, was transferred to vial 1. The flask was rinsed with a small quantity of ether and transferred to vial 2. Vial 2 was further concentrated using rotary evaporation and a bath temperature of 10 °C. Vial 1 (445 mg, contains **14**:Et_2O:EtOH in a ratio of 1:0.8:0.2 for ~200 mg of **14**); vial 2 (114 mg, contains **14**:Et_2O:EtOH in a ratio of 1:0.11:0.08 for ~95 mg of **14**) in an overall yield of 25%. Spectral data matched that previously reported for compound **14**:[45] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 1 H), 2.11 (br s, 1 H), sample contains diethyl ether and ethanol ^{1}H NMR resonances; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 82.1, 73.9, 50.4 (quint, J = 22.6 Hz) ppm. Diethyl ether resonances at 66.0, 15.3 ppm, ethanol resonances at 58.6, 18.4; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_3H_3D_2O$ 59.04604; Found 59.04601; TLC R_f = 0.32 (30% ethyl acetate/hexane), visualized with $KMnO_4$.

Prop-2-yn-1-yl-1,1-d2 4-methylbenzenesulfinate (**15**): The synthesis of prop-2-yn-1-yl-1,1-*d2* 4-methylbenzenesulfinate was performed using a modified literature procedure.[41] A flame-dried 50-mL, 2-necked round-bottomed flask equipped with stir bar, rubber septum and nitrogen inlet adaptor was charged with tosyl chloride (985 mg, 5.2 mmol) and dichloromethane (13 mL). Triethylamine (0.82 mL, 5.9 mmol) was added via syringe. The reaction flask was placed in an ice/water bath (10-20 °C). An oven-dried conical flask was charged with triphenylphosphine (1355 mg, 5.2 mmol), dichloromethane (9 mL) and prop-2-yn-1,1-*d2*-1-ol (**14**:Et_2O:EtOH; 1:0.8:0.2, ~200 mg, 3.44 mmol). This solution was added dropwise to the flask at 10-20 °C. The reaction was monitored by TLC and ^{1}H NMR. After 2.5 h, ^{1}H NMR showed complete consumption of prop-2-yn-1,1-*d2*-1-ol. The reaction mixture was transferred to a beaker and 20% Et_2O/hexane solution was added to produce a white precipitate. Removal of this precipitate was accomplished by filtering the mixture through a pad of silica gel under reduced pressure (water aspirator) and the precipitate was rinsed with ether. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-20% ethyl acetate/hexane) to yield the title compound as a slightly pale-yellow oil (701 mg) which also contains side-product ethyl 4-methylbenzenesulfinate in a ratio of title compound: side-product of 85:15. The title compound and the side-product were characterized as a mixture: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.2 Hz, 2 H), 7.35 (d, J = 7.9 Hz, 2 H), 2.48 (s, 1 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 143.3, 141.1, 129.9 (2 C), 125.4 (2 C), 77.6, 76.2, 51.0 (quint, J = 23.2 Hz, 1 C), 21.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{10}H_9D_2O_2S$ 197.05998; Found 197.05955; TLC R_f = 0.19 (15% ethyl acetate/hexane), visualized with UV.

ethyl 4-methylbenzenesulfinate (**16**): FID (HO-03-55); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.2 Hz, 2 H), 7.37-7.31 (m, 2 H), 4.10 (dq, J = 9.9, 7.1 Hz, 1 H), 3.72 (dq, J = 10.0, 7.1 Hz 1 H), 2.42, 1.27 (t, J = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 142.7, 141.9, 129.7 (2 C), 125.3 (2 C), 60.8, 21.6, 15.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_9H_{13}O_2S$ 185.0631; Found 185.0627; TLC R_f = 0.19 (15% ethyl acetate/hexane), visualized with UV.

1-methyl-4-((propa-1,2-dien-1-yl-3,3-d2)sulfonyl)benzene (**2a-*d*$_2$**): The synthesis of 1-methyl-4-((propa-1,2-dien-1-yl-3,3-*d2*)sulfonyl)benzene was performed using a modified literature procedure.[41] A flame-dried 10-mL, single-necked, round-bottomed flask equipped with stir bar and rubber septum was charged with silver hexafluoroantimonate(V) (3.5 mg, 0.01 mmol) in glovebox. The flask was removed from the glovebox and placed under N_2. A solution of prop-2-yn-1-yl-1,1-*d2* 4-methylbenzenesulfinate (100.9 mg, 0.51 mmol) in dichloromethane (1 mL) was added dropwise via syringe to the flask over 5 min. The reaction progress was monitored by TLC. After 3 h, the reaction mixture was vacuum filtered (water aspirator) through a pad of silica gel in a fritted funnel using diethyl ether as an eluent. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (5-30% ethyl acetate/hexane) to yield the title compound as white solid (71 mg, 70%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2 H), 7.34 (d, J = 8.0 Hz, 2 H), 6.24 (s, 1 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 209.4, 144.8, 138.4, 130.0 (2 C), 127.8 (2 C), 101.5, 83.9 (quint, J = 26.2 Hz, 1 C), 21.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{10}H_9D_2O_2S$ 197.05998; Found 197.05939; TLC R_f = 0.28 (20% ethyl acetate/hexane), visualized with UV.

But-3-yn-2-yl 4-methylbenzenesulfinate (**17**): The synthesis of but-3-yn-2-yl 4-methylbenzenesulfinate was performed using a modified literature procedure.[41] A flame-dried 50-mL, 3-necked, round-bottomed flask equipped with stir bar, rubber septa and nitrogen inlet adaptor was charged with tosyl chloride (1.00 g, 5.3 mmol) and dichloromethane (13 mL). Triethylamine (0.8 mL, 5.8 mmol) was added via syringe. The flask was placed in an ice/water bath (10-15 ° C). An oven-dried beaker was charged with triphenylphosphine (1.38 g, 5.3 mmol), dichloromethane (13 mL) and 3-butyn-2-ol (0.4 mL, 5.3 mmol) and the beaker was swirled to form a uniform solution. The solution was added dropwise via syringe over 15 min while maintaining the temperature of the ice/water bath at 10-15 ° C. The reaction was monitored by TLC. After 3 h, the reaction mixture

was transferred to a beaker and a 20% Et_2O/hexane solution was added affording a white precipitate. Removal of this precipitate was accomplished by filtering the mixture through a pad of silica gel under reduced pressure (water aspirator) and the precipitate was rinsed with ether. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-20% ethyl acetate/hexane) to yield the title compound as a 1:1 mixture of diastereomers as a clear, slightly pale yellow oil (0.94 g, 86%). The spectral data matched that previously reported for compound **17**:[41] ^{1}H NMR (400 MHz, $CDCl_3$) characterized as 1:1 mixture of diastereomers, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.9 Hz, 2 H), 7.34 (d, J = 8.0 Hz, 1 H), 7.32* (d, J = 8.0 Hz, 1 H), 5.05-4.96 (m, 1 H), 2.64* (d, J = 1.8 Hz, 0.5 H), 2.42 (s, 3 H), 2.39 (d, J = 1.9 Hz, 0.5 H), 1.59 (d, J = 6.7 Hz, 1.5 H), 1.53* (d, J = 6.7 Hz, 1.5 H), *second diastereomer distinguishable; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.1, 141.8, 142.4*, 129.84, 129.76, 125.6, 125.2, 82.4, 82.1*, 75.2*, 74.6, 64.0*, 62.1, 23.9, 23.1*, 21.7; TLC R_f = 0.25 (10% ethyl acetate/hexane), visualized with UV.

1-(buta-1,2-dien-1-ylsulfonyl)-4-methylbenzene (**2b**): The synthesis of 1-(buta-1,2-dien-1-ylsulfonyl)-4-methylbenzene was performed using a modified literature procedure.[41] A flame-dried, 15-mL, single-necked, round-bottomed flask equipped with stir bar and rubber septum was charged with silver hexafluoroantimonate(V) (31 mg, 0.09 mmol) in a glovebox. The round-bottomed flask was removed the glovebox and placed under nitrogen. A solution of but-3-yn-2-yl 4-methylbenzenesulfinate (0.93 g, 4.5 mmol) in dichloromethane (9 mL) was added dropwise via the syringe to the flask over 5 min. The reaction progress was monitored by TLC. After 4 h, the reaction mixture was vacuum filtered (water aspirator) through a pad of silica gel with Et_2O as the eluent. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-30% ethyl acetate/hexane) to yield the title compound as clear oil that crystallized slowly over time in the freezer (0.80 g, 86%). The spectral data matched that previously reported for compound **2b**:[41] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.2 Hz, 2 H), 7.33 (d, J = 8.2 Hz, 2 H), 6.14 (dq, J = 7.5, 3.0 Hz, 1 H), 5.80 (quint, J = 7.4 Hz, 1 H), 2.44 (s, 3 H), 1.78 (dd, J = 7.4, 3.0 Hz, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.2, 144.5, 138.6, 129.9 (2 C), 127.7 (2 C), 100.8, 96.1, 21.8, 13.1; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{11}H_{13}O_2S$ 209.0631; Found 209.0627; TLC R_f = 0.29 (20% ethyl acetate/hexane), visualized with UV.

But-2-yn-1-yl 4-methylbenzenesulfinate (**18**): The synthesis of but-2-yn-1-yl 4-methylbenzenesulfinate was performed using a modified literature procedure.[41] A flame-dried, 50-mL, 3-necked, round-bottomed flask equipped with stir bar, rubber septa and nitrogen inlet adaptor was charged with tosyl chloride (1.00 g, 5.3 mmol). Dichloromethane (13 mL) and triethylamine (0.8 mL, 5.8 mmol) were added via syringe. The flask was placed in an ice/water bath (10-15 °C). An oven-dried beaker was charged with triphenylphosphine (1.38 g, 5.3 mmol), dichloromethane (13 mL) and but-2-yn-1-ol (0.39 mL, 5.3 mmol) and the beaker was swirled to form a uniform solution. This solution was added dropwise to the flask via syringe over 20 min at 10-15 °C. The reaction progress was monitored by TLC. After 5.5 h, the reaction mixture was transferred to a beaker and 20% Et_2O/hexane solution was added affording a white precipitate. This suspension was vacuum filtered (water aspirator) through a pad of silica gel in a fritted funnel using diethyl ether as an eluent. The filtrate was collected and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (0-20% ethyl acetate/hexane) to yield the title compound as a pale-yellow oil (0.80 g, 73%). The spectral data matched that previously reported for compound **18**:[46] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2 Hz, 2 H), 7.34 (d, J = 7.9 Hz, 2 H), 4.58 (qd, J = 15.0, 2.4 Hz, 1 H), 4.27 (dq, J = 14.9, 2.4 Hz, 1 H), 2.43 (s, 3 H), 1.82 (t, J = 2.4 Hz, 3 H), spectrum contains impurities at δ 7.46, 7.23, 7.22, 7.20, 7.14, 2.38, 1.58-1.57; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.1, 141.6, 129.9 (2 C), 125.5 (2 C), 84.9, 73.3, 52.8, 21.7, 3.8; TLC R_f = 0.34 (10% ethyl acetate/hexane), visualized with UV.

1-(buta-2,3-dien-2-ylsulfonyl)-4-methylbenzene (**2c**): The synthesis of 1-(buta-2,3-dien-2-ylsulfonyl)-4-methylbenzene was performed using a modified literature procedure.[41] A flame-dried, 15-mL, single-necked, round-bottomed flask equipped with stir bar and rubber septum was charged with silver hexafluoroantimonate(V) (26 mg, 0.08 mmol) in a glovebox. The flask was removed from the glovebox and placed under nitrogen. A solution of but-2-yn-1-yl 4-methylbenzenesulfinate (0.79 g, 3.8 mmol) in dichloromethane (8 mL) was added dropwise via the syringe to the flask over 5 min. The reaction was monitored by TLC. After 4 h, the reaction mixture was vacuum filtered (water aspirator) through a pad of silica gel with Et_2O as the eluent. The filtrate was collected and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (0-30% ethyl acetate/hexane) to yield the title compound as white crystals (0.63 g, 80%). The spectral data matched that previously reported for compound **2c**.[46] Chromatographic separation afforded *p*-tolyl 4-methylbenzenesulfinate (white crystals) as a side-product (64 mg, 7%) also a known compound.[47] **2c**: FID (HO-02-137); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 2 H), 7.33 (d, J = 8.0 Hz, 2 H), 5.29 (q, J = 3.1 Hz, 2 H), 2.44 (s, 3 H), 1.93 (t, J = 3.1 Hz, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 208.0, 144.6, 137.0, 129.8 (2 C), 128.3 (2 C), 108.5, 82.9, 21.8, 13.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{11}H_{13}O_2S$ 209.0631; Found 209.0628; TLC R_f = 0.30 (20% ethyl acetate/hexane), visualized with UV.

p-tolyl 4-methylbenzenesulfinate (**19**): FID (HO-02-137); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.3 Hz, 2 H), 7.32-7.28 (m, 4 H), 7.20 (d, J = 8.0 Hz, 2 H), 2.48 (s, 3 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.7, 142.2, 140.7, 136.6 (2 C), 130.3 (2 C), 129.5 (2 C), 127.8 (2 C), 124.8, 21.8, 21.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{14}H_{15}O_2S$ 247.0787; Found 247.0785; TLC R_f = 0.55 (20% ethyl acetate/hexane), visualized with UV.

4,4'-(prop-2-ene-1,2-diyldisulfonyl)bis(methylbenzene) (**5a**): The byproduct disulfone, 4,4'-(prop-2-ene-1,2-diyldisulfonyl)bis(methylbenzene) (**5a**) obtained in the reaction of picolyl amide and allenyl sulfone was previously characterized:[20d,48] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.59 (m, 4 H), 7.28 (dd, J = 8.3, 2.3 Hz, 4 H), 6.64 (d, J = 0.8 Hz, 1 H), 6.50 (d, J = 1.0 Hz, 1 H), 4.03 (d, J = 0.7 Hz, 2 H), 2.44 (d, J = 1.9 Hz, 6 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 145.5, 145.3, 139.9, 135.0, 134.9, 130.6, 130.1 (2 C), 130.0 (2 C), 128.7 (2 C), 128.6 (2 C), 54.3, 21.88, 21.85; HRMS (ESI) m/z: [M + H]$^+$

Calcd for $C_{17}H_{19}O_4S_2$ 351.0719; Found 351.0717; TLC R_f = 0.58 (50% ethyl acetate/hexane), visualized with UV.

1-methyl-4-((2-(phenylsulfonyl)allyl)sulfonyl)benzene (**5b**): The synthesis of 1-methyl-4-((2-(phenylsulfonyl)allyl)sulfonyl)benzene was performed using a modified literature procedure.[20d] A flame-dried, 15-mL, single-necked, round-bottomed flask equipped with stir bar and rubber septum was charged with allenyl sulfone, 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene (100 mg, 0.52 mmol), thiophenol (0.06 mL, 0.6 mmol), triethylamine (0.01 mL, 0.05 mmol) and methanol (2 mL) at rt. After 30 min, the reaction was concentrated under reduced pressure. The residue was dissolved in dichloromethane (5 mL) and *meta*-chloroperoxybenzoic acid (300 mg, 1.6 mmol) was added in one portion to the flask at rt. After 1 h, the reaction was not complete as evidenced by TLC; however, the reaction mixture was diluted with dichloromethane, washed with $NaHSO_3$ solution, sat'd $NaHCO_3$ solution, dried over magnesium sulfate, vacuum filtered with water aspirator, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (0-50% ethyl acetate/hexane) to yield the title compound as a white solid (124 mg, 71%). The spectral data matched that previously reported for compound **5b**:[20d] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.2, 1.4 Hz, 2 H), 7.66-7.60 (m, 3 H), 7.50 (t, J = 7.9 Hz, 2 H), 7.28 (d, J = 8.1 Hz, 2 H), 6.68 (d, J = 1.0 Hz, 1 H), 6.52 (d, J = 1.1 Hz, 1 H), 4.04 (d, J = 0.9 Hz, 2 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 145.5, 139.8, 138.0, 135.0, 134.1, 131.2, 130.1 (2 C), 129.5 (2 C), 128.7 (2 C), 128.6 (2 C), 54.3, 21.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{17}O_4S_2$ 337.0563; Found 337.0560; TLC R_f = 0.52 (50% ethyl acetate/hexane), visualized with UV.

(Table 1, entry 7): *N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)benzamide* (**3a**). Follows general procedure C. **1a** (40 mg, 0.19 mmol), **2a** (74 mg, 0.38 mmol), THF (1 mL). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a red-brown solid (51.7 mg, 67%, 98:2). The product selectivity was measured after chromatography using the ^{1}H NMR integration ratios. The title compound **3a** was characterized as a 98:2 mixture of **3a**:**4a** (Table 1, entry 7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.7 Hz, 1 H), 7.86 (d, J = 8.1 Hz, 2 H), 7.80 (d, J = 8.1 Hz, 2 H), 7.68 (br d, J = 7.4 Hz, 1 H), 7.64 (dt, J = 7.7, 1.6 Hz, 1 H), 7.52-7.42 (m, 3 H), 7.33 (d, J = 8.1 Hz, 2 H), 7.28 (d, J = 8.0 Hz, 1 H), 7.21-7.17 (m, 1 H), 6.34 (s, 1 H), 5.64 (s, 1 H), 5.53 (q, J = 7.4 Hz, 1 H), 3.00 (dd, J = 15.2, 7.7 Hz, 1 H), 2.79 (dd, J = 15.2, 6.4 Hz, 1 H), 2.43 (s, 3 H), spectrum contains ethyl acetate resonances at 4.2, 2.1 and 1.3; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.9, 158.7, 149.5, 146.7, 144.9, 136.9, 135.3, 134.2, 131.8, 130.1 (2 C), 128.74 (2 C), 128.69 (2 C), 127.3 (2 C), 126.7, 122.9, 122.5, 53.9, 35.6, 21.8; IR (cm^{-1}) 3346, 2923, 1644, 1522, 1485, 1435, 1288, 1132, 1080, 712; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{23}H_{23}N_2O_3S$ 407.1424; Found 407.1408; mp 56-60 °C; TLC R_f = 0.19 (50% ethyl acetate/hexane), visualized with UV.

(Table 1, entry 6): *N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)benzamide* (**4a**): Follows general procedure C. **1a** (40 mg, 0.19 mmol), **2a** (74 mg, 0.38 mmol), THF (1 mL). The crude product was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound (minor product) red-brown solid (46.2 mg, 53%, 63:37). The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Compound **4a** was characterized as a mixture of **3a**:**4a** (Table 1, entry 6): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 4.6 Hz, 1 H), 8.24 (d, J = 7.1 Hz, 1 H), 7.91 (d, J = 7.4 Hz, 2 H), 7.69 (t, J = 7.7 Hz, 1 H), 7.23-7.21 (m, 1 H), 6.03 (d, J = 7.3 Hz, 1 H), 5.37 (s, 1 H), 5.16 (s, 1 H), 4.07 (d, J = 14.1 Hz, 1 H), 3.75 (d, J = 14.1 Hz, 1 H), 2.38 (3 H) ppm. Note: ^{1}H NMR resonances are those distinguishable from **3a**; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 166.7, 157.4, 149.2, 144.9, 137.1, 136.2, 135.2, 134.0, 131.7, 129.8 (2 C), 128.6 (4 C), 127.3 (2 C), 124.2, 123.1, 123.0, 59.8, 58.3, 21.7; IR (cm^{-1}) 3362, 2926, 1653, 1594, 1518, 1480, 1294, 1142, 1081, 909, 724; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{23}H_{23}N_2O_3S$ 407.1424; Found 407.1400; TLC R_f = 0.63 (100% ethyl acetate/hexane), visualized with UV.

2-methyl-N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)benzamide (**3b**). Follows general procedure C. **1b** (45.3 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as a light-orange solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (55 mg, 65%, 96:4); Run 2 (52.6 mg, 63%, 96:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.6 Hz, 1 H), 7.81 (d, J = 8.3 Hz, 2 H), 7.65 (dt, J = 7.7, 1.8 Hz, 1 H), 7.36 (d, J = 7.7 Hz, 1 H), 7.33-7.28 (m, 4 H), 7.21-7.17 (m, 3 H), 7.03 (d, J = 7.9 Hz, 1 H), 6.36 (s, 1 H), 5.68 (br s, 1 H), 5.56 (q, J = 7.5 Hz, 1 H), 2.97 (ddd, J = 15.4, 7.6, 0.9 Hz, 1 H), 2.77 (dd, J = 15.2, 6.9 Hz, 1 H), 2.42 (s, 3 H), 2.39 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 158.4, 149.6, 146.8, 144.9, 136.9, 136.4, 136.0, 135.3, 131.2, 130.1, 130.1 (2 C), 128.8 (2 C), 127.0, 126.2, 125.9, 123.0, 122.8, 53.2, 36.0, 21.8, 20.1; IR (cm^{-1}) 3338, 2982, 1647, 1592, 1506, 1436, 1289, 1133, 1081, 733; HRMS (ESI) m/z: [M − H]$^-$ Calcd for $C_{24}H_{23}N_2O_3S$ 421.1424; Found 421.1412; mp 76-82 ° C; TLC R_f = 0.24 (50% ethyl acetate/hexane), visualized with UV.

2-methyl-N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)benzamide (**4b**) ^{1}H NMR resonances distinguishable at: δ 6.07, 5.34, 5.16, 3.76.

2-fluoro-N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)benzamide (**3c**). Follows general procedure C. **1c** (46.1 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-60% ethyl acetate/hexane) to yield the title compound as a pale-yellow solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (54.5 mg, 64%, 95:5); Run 2 (54.1 mg, 64%, 97:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 4.7 Hz, 1 H), 8.03 (dt, J = 7.9, 1.5 Hz, 1 H), 7.86-7.84 (m, 1 H), 7.81 (d, J = 8.2 Hz, 2 H), 7.63 (dt, J = 7.6, 1.4 Hz, 1 H), 7.48-7.42 (m, 1 H), 7.31 (d, J = 8.2 Hz, 2 H), 7.27-7.24 (m, 2 H), 7.22-7.17 (m, 1 H), 7.11 (dd, J = 11.8, 8.3 Hz, 1 H), 6.33 (s, 1 H), 5.61 (s, 1 H), 5.63-5.57 (m, 1 H), 2.99 (dd, J = 15.1, 7.2 Hz, 1 H), 2.80 (dd, J = 15.2, 7.4 Hz, 1 H), 2.41 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.9 (d, J = 3.1 Hz), 160.8 (d, J = 248.4 Hz), 158.2, 149.6, 146.6, 144.8, 136.8, 135.4, 133.4 (d, J = 9.3 Hz), 132.0 (d, J = 1.9 Hz), 130.1 (2 C), 128.7 (2 C), 126.5, 124.8 (d, J = 3.1 Hz), 122.9 (2 C), 121.2 (d, J = 11.5 Hz), 116.2 (d, J = 24.4 Hz), 53.5, 36.1, 21.8; IR (cm^{-1}) 3344, 2926, 1634, 1591, 1522, 1480, 1313, 1291, 1133, 731; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{23}H_{22}N_2O_3SF$ 425.1330; Found 425.1338; mp 85-92 °C; TLC R_f = 0.29 (50% ethyl acetate/hexane), visualized with UV.

2-fluoro-N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)benzamide (**4c**) ^{1}H NMR resonances distinguishable at: δ 8.58, 6.09, 5.41, 5.23, 4.04, 3.73.

2-methoxy-N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)benzamide (**3d**). Follows general procedure D. **1d** (49 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as a red-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (49.6 mg, 56%, 96:4; 2-picolyl amide **1d** recovered 7.3 mg; yield based on recovered starting material 66%); Run 2 (45.9 mg, 52%, 97:3; 2-picolyl amide **1d** recovered 10.1 mg; yield based on recovered starting material 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, J = 7.5 Hz, 1 H), 8.55 (dd, J = 4.8, 0.8 Hz, 1 H), 8.14 (dd, J = 7.8, 1.8 Hz, 1 H), 7.79 (d, J = 8.3 Hz, 2 H), 7.61 (dt, J = 7.7, 1.8 Hz, 1 H), 7.44 (dt, J = 7.8, 1.8 Hz, 1 H), 7.31-7.26 (m, 3 H), 7.17 (ddd, J = 7.5, 4.9, 1.0 Hz, 1 H), 7.05 (dt, J = 7.7, 0.9 Hz, 1 H), 6.96 (d, J = 8.2 Hz, 1 H), 6.34 (s, 1 H), 5.70 (s, 1 H), 5.57 (q, J = 7.4 Hz, 1 H), 3.96 (s, 3 H), 3.02 (dd, J = 15.5, 7.7 Hz, 1 H), 2.81 (dd, J = 15.5, 6.9 Hz, 1 H), 2.41 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.9, 159.1, 157.9, 149.6, 147.0, 144.6, 136.8, 135.7, 133.0, 132.3, 130.0 (2 C), 128.7 (2 C), 125.9, 122.8, 122.7, 121.5, 121.3, 111.5, 56.1, 53.5, 35.6, 21.8; IR (cm^{-1}) 3370, 2925, 1647, 1596, 1517, 1482, 1290, 1134, 1081, 731; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{25}N_2O_4S$ 437.1530; Found 437.1517; mp 49-56 ° C; TLC R_f = 0.27 (100% ethyl acetate/hexane), visualized with UV.

2-methoxy-N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)benzamide (**4d**) ^{1}H NMR resonances distinguishable at: δ 6.10, 5.41.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)-1-naphthamide (**3e**). Follows general procedure C. **1e** (52.5 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as a light-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (52.8 mg, 58%, 94:6); Run 2 (56.7 mg, 62%, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 4.1 Hz, 1 H), 8.29-8.26 (m, 1 H), 7.92 (d, J = 8.2 Hz, 1 H), 7.87-7.82 (m, 3 H), 7.67 (dt, J = 7.7, 1.7 Hz, 1 H), 7.62 (dd, J = 7.0, 1.0 Hz, 1 H), 7.54-7.49 (m, 2 H), 7.45 (dd, J = 7.2, 8.2 Hz, 1 H), 7.34 (d, J = 7.8 Hz, 1 H), 7.31-7.29 (m, 3 H), 7.21 (ddd, J = 7.8, 4.8, 0.9 Hz, 1 H), 6.39 (s, 1 H), 5.72 (s, 1 H), 5.69 (q, J = 7.6 Hz, 1 H), 3.04 (dd, J = 15.2, 7.6 Hz, 1 H), 2.83 (dd, J = 15.3, 6.8 Hz, 1 H), 2.40 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.0, 158.4, 149.6, 146.8, 144.9, 136.9, 135.3, 134.1, 133.9, 131.0, 130.4, 130.1 (2 C), 128.8 (2 C), 128.4, 127.2, 126.5, 126.4, 125.6, 125.3, 124.9, 123.0, 122.9, 53.4, 36.2, 21.8; IR (cm^{-1}) 3330, 2927, 1651, 1592, 1515, 1291, 1134, 1082, 782, 732; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{27}H_{25}N_2O_3S$ 457.1580; Found 457.1602; mp 105-114 ° C; TLC R_f = 0.26 (50% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)-1-naphthamide (**4e**) ^{1}H NMR resonances distinguishable at: δ 6.20, 5.38, 5.19, 4.16, 3.81 ppm.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)picolinamide (**3f**). Follows general procedure C. **1f** (42.6 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The crude product was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as an orange solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios of the purified fractions. Run 1 (54 mg, 66%, 99:1); Run 2 (49.7 mg, 61%, 98:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, J = 8.5 Hz, 1 H), 8.57-8.56 (m, 2 H), 8.15 (d, J = 7.8 Hz, 1 H), 7.85-7.79 (m, 3 H), 7.61 (dt, J = 7.6, 1.8 Hz, 1 H), 7.41 (ddd, J = 7.7, 4.8, 1.1 Hz, 1 H), 7.31 (d, J = 8.0 Hz, 2 H), 7.26-7.24 (m, 1 H), 7.18 (ddd, J = 7.7, 4.8, 0.9 Hz, 1 H), 6.32 (s, 1 H), 5.66 (s, 1 H), 5.54 (q, J = 7.4 Hz, 1 H), 2.99 (dd, J = 15.4, 7.5 Hz, 1 H), 2.88 (dd, J = 15.4, 7.2 Hz, 1 H), 2.42 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 158.6, 149.8, 148.4, 146.7, 144.7, 137.4, 136.8, 135.6, 130.0 (2 C), 128.7 (2 C), 126.4, 126.2, 122.9 (2 C), 122.4, 52.8, 35.9, 21.8; IR (cm^{-1}) 3366, 2923, 1669, 1591, 1506, 1432, 1289, 1132, 1081, 731; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{22}H_{22}N_3O_3S$ 408.1376; Found 408.1390; mp 64-75 ° C; TLC R_f = 0.66 (100% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)picolinamide (**4f**) ^{1}H NMR resonances distinguishable at: δ 6.08, 5.37, 5.20, 4.04, 3.75 ppm.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)thiophene-2-carboxamide (**3g**). Follows general procedure C. **1g** (43.7 mg, 0.2 mmol), 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene (78 mg, 0.4 mmol), THF (1 mL). The crude product was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as a light-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (47.7 mg, 58%, 94:6); Run 2 (46.1 mg, 56%, 94:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.7 Hz, 1 H), 7.80 (d, J = 8.2 Hz, 2 H), 7.66-7.62 (m, 3 H), 7.48 (dd, J = 5.0, 0.9 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.29 (d, J = 7.8 Hz, 1 H), 7.19 (dd, J = 7.5, 5.3 Hz, 1 H), 7.08 (dd, J = 4.9, 3.8 Hz, 1 H), 6.33 (s, 1 H), 5.62 (s, 1 H), 5.46 (q, J = 7.4 Hz, 1 H), 2.98 (dd, J = 15.1, 7.8 Hz, 1 H), 2.77 (dd, J = 15.2, 6.3 Hz, 1 H), 2.43 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.6, 158.6, 149.5, 146.5, 145.0, 139.0, 137.0, 135.2, 130.5, 130.2 (2 C), 128.7 (2 C), 128.4, 127.8, 127.0, 122.9, 122.5, 54.1, 35.4, 21.8; IR (cm^{-1}) 3344, 2923, 1635, 1592, 1533, 1508, 1438, 1289, 1136, 1081, 730; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{21}H_{21}N_2O_3S_2$ 413.0988; Found 413.1008; mp 90-98 °C; TLC R_f = 0.19 (50% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)thiophene-2-carboxamide (**4g**) ^{1}H NMR resonances distinguishable at: δ 8.58, 8.15, 5.98, 5.38, 4.09, 3.75.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)acetamide (**3h**). Follows general procedure C. **1h** (30.0 mg, 0.2 mmol), 1-methyl-4-(propa-1,2-dien-1-ylsulfonyl)benzene (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (50-100% ethyl acetate/hexane then 10-40% acetone/ethyl acetate) to yield the title compound as a red-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (41.4 mg, 60%, 94:6); Run 2 (39.1 mg, 57%, 94:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 4.6 Hz, 1 H), 7.78 (d, J = 8.2 Hz, 2 H), 7.61 (dt, J = 7.7, 1.6 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.21-7.16 (m, 2 H), 6.80 (d, J = 7.0 Hz, 1 H), 6.30 (s, 1 H), 5.55 (s, 1 H), 5.31 (q, J = 7.4 Hz, 1 H), 2.85 (dd, J = 15.1, 7.4 Hz, 1 H), 2.65 (dd, J = 15.1, 6.9 Hz, 1 H), 2.43 (s, 3 H), 1.98 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.8, 158.5, 149.5, 146.7, 144.9, 136.8, 135.3, 130.1 (2 C), 128.7 (2 C), 126.4, 122.9, 122.8, 53.2, 35.7, 23.4, 21.8; IR (cm^{-1}) 3283, 3056, 1655, 1593, 1531, 1435, 1289, 1135, 1081, 728; HRMS (ESI)

m/z: [M + H]$^+$ Calcd for $C_{18}H_{21}N_2O_3S$ 345.1267; Found 345.1290; mp 117-122 °C; TLC R_f = 0.17 (100% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)acetamide (**4h**) ^{1}H NMR resonances distinguishable at: δ 8.53, 7.67, 5.22, 5.06, 5.83, 4.00, 3.67 ppm.

2-phenyl-N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl) acetamide (**3i**). Follows general procedure C. **1i** (45.3 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-70% ethyl acetate/hexane) to yield the title compound as a light-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (52.5 mg, 62%, 92:8); Run 2 (50 mg, 59%, 92:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 4.2 Hz, 1 H), 7.75 (d, J = 8.2 Hz, 2 H), 7.57 (dt, J = 7.7, 1.8 Hz, 1 H), 7.35-7.24 (m, 7 H), 7.16-7.11 (m, 2 H), 6.77 (d, J = 7.6 Hz, 1 H), 6.23 (s, 1 H), 5.46 (s, 1 H), 5.30 (q, J = 7.4 Hz, 1 H), 3.57-3.54 (m, 2 H), 2.79 (dd, J = 15.2, 7.5 Hz, 1 H), 2.62 (dd, J = 15.1, 6.8 Hz, 1 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.6, 158.4, 149.4, 146.5, 144.8, 136.8, 135.4, 135.0, 130.1 (2 C), 129.4 (2 C), 129.0 (2 C), 128.7 (2 C), 127.3, 126.4, 122.8, 122.6, 53.1, 44.0, 35.6, 21.8; IR (cm^{-1}) 3294, 2924, 1639, 1594, 1537, 1433, 1302, 1134, 1082, 735; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{25}N_2O_3S$ 421.1580; Found 421.1571; mp 109-114 °C; TLC R_f = 0.33 (70% ethyl acetate/hexane), visualized with UV.

2-phenyl-N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl) acetamide (**4i**) ^{1}H NMR resonances distinguishable at: δ 8.46, 7.64, 5.82, 5.15, 5.00, 3.93.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)acrylamide (**3j**). Follows general procedure C. **1j** (32.5 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a red brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (49.9 mg, 70%, 94:6); Run 2 (49.3 mg, 69%, 92:8). FID (HO-03-48); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 4.6 Hz, 1 H), 7.78 (dd, J = 8.0, 0.9 Hz, 2 H), 7.62 (t, J = 7.6 Hz, 1 H), 7.34 (d, J = 7.8 Hz, 2 H), 7.22 (d, J = 7.8 Hz, 1 H), 7.19-7.16 (m, 1 H), 7.00 (br s, 1 H), 6.31-6.26 (m, 2 H), 6.13 (dd, J = 17.0, 10.2 Hz, 1 H), 5.64 (d, J = 10.2 Hz, 1 H), 5.58 (s, 1 H), 5.39 (q, J = 7.4 Hz, 1 H), 2.90 (dd, J = 15.2, 7.6 Hz, 1 H), 2.70 (dd, J = 15.2, 6.8 Hz, 1 H), 2.43 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.1, 158.4, 149.5, 146.6, 144.9, 136.9, 135.3, 130.9, 130.1 (2 C), 128.7 (2 C), 126.8, 126.6, 122.9, 122.7, 53.3, 35.5, 21.8; IR (cm^{-1}) 3284, 2925, 1660, 1593, 1527, 1436, 1291, 1134, 1081, 729; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{19}H_{21}N_2O_3S$ 357.1267; Found 357.1249; mp 43-49 °C; TLC R_f = 0.31 (100% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl)acrylamide (**4j**) ^{1}H NMR resonances distinguishable at: δ 5.91, 5.27, 4.04, 3.70.

tert-butyl (1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl) carbamate (**3k**). Follows general procedure D. **1k** (41.7 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-70% diethyl ether/hexane) to yield the title compound as a pale-yellow solid contaminated with **1k**. The yield was calculated using mole ratios from ^{1}H NMR integration ratios. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. For characterization purposes, a second purification was performed using silica gel flash chromatography (20-70% ethyl acetate/hexane). Run 1 (44.3 mg, 55%, 96:4, 48 h); Run 2 (47.5 mg, 59%, 96:4, 72 h). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 4.4 Hz, 1 H), 7.77 (d, J = 8.0 Hz, 2 H), 7.61 (dt, J = 7.7, 1.6 Hz, 1 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.19 (d, J = 7.8 Hz, 1 H), 7.16 (dd, J = 7.5, 5.5 Hz, 1 H), 6.30 (s, 1 H), 5.67-5.59 (m, 2 H), 5.03 (q, J = 7.6 Hz, 1 H), 2.80-2.67 (m, 2 H) 2.44 (s, 3 H), 1.41 (s, 9 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 155.3, 149.5, 146.9, 144.7, 136.8, 135.5, 130.0 (2 C), 128.7 (2 C), 125.9, 122.7, 122.4, 79.7, 54.3, 36.1, 28.5 (3 C), 21.8; IR (cm^{-1}) 3374, 2978, 1706, 1594, 1572, 1494, 1437, 1366, 1313, 1302, 1164, 1144, 731; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{21}H_{27}N_2O_4S$ 403.1686; Found 403.1678; mp 106-110 °C; TLC R_f = 0.37 (50% ethyl acetate/hexane), visualized with UV. *tert-butyl (1-(pyridin-2-yl)-2-(tosylmethyl)allyl)carbamate* (**4k**) ^{1}H NMR resonances distinguishable at: δ 6.70, 5.98 ppm.

Benzyl (2-oxo-2-((1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)amino)ethyl)carbamate (**3l**). Follows general procedure C. **1l** (44.9 mg, 0.15 mmol), **2a** (58.3 mg, 0.30 mmol), THF (0.8 mL). The residue was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a light-brown solid. The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. Run 1 (44.2 mg, 60%, 85:15); Run 2 (41.4 mg, 56%, 94:6). Run 3: Follows general procedure C. **1l** (10 mg, 0.033 mmol), **2a** (13 mg, 0.067 mmol), THF (0.18 mL). The residue was purified by silica gel flash chromatography (50-100% ethyl acetate/hexane) to yield the title compound as a light-brown solid (10.6 mg, 64%, 95:5). The product selectivity was measured after chromatography using ^{1}H NMR integration ratios.

Benzyl (2-oxo-2-((1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)amino)ethyl)carbamate (**3l**). Follows general procedure C. **1l** (7 mg, 0.024 mmol), **2a** (9 mg, 0.047 mmol), THF (0.15 mL). The residue was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a light-brown solid (7.0 mg, 58%, 96:4). The product selectivity was measured after chromatography using ^{1}H NMR integration ratios. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.6 Hz, 1 H), 7.77 (d, J = 8.0 Hz, 2 H), 7.61 (t, J = 7.1 Hz, 1 H), 7.33-7.26 (m, 8 H), 7.21-7.15 (m, 2 H), 6.26 (s, 1 H), 5.52-5.50 (m, 2 H), 5.34 (q, J = 7.2 Hz, 1 H), 5.12 (s, 2 H), 3.89 (s, 2 H), 2.82 (dd, J = 15.0, 7.4 Hz, 1 H), 2.70 (dd, J = 14.5, 6.3 Hz, 1 H), 2.43 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.6, 158.1, 156.6, 149.4, 146.4, 144.9, 136.9, 136.4, 135.2, 130.1 (2 C), 128.7 (2 C), 128.6 (3 C), 128.3, 128.2, 126.8, 122.9, 122.6, 67.2, 53.3, 44.6, 35.6, 21.8; IR (cm^{-1}) 3319, 3059, 2927, 1719, 1667, 1594, 1512, 1438, 1290, 1135, 1081, 729; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{28}N_3O_5S$ 494.1744; Found 494.1734; mp 66-72 °C; TLC R_f = 0.56 (100% ethyl acetate/hexane), visualized with UV.

benzyl (2-oxo-2-((1-(pyridin-2-yl)-2-(tosylmethyl)allyl)-amino)ethyl)carbamate (**4l**) ^{1}H NMR resonances distinguishable at: δ 8.52, 7.68, 5.83, 5.00, 3.65.

N-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl)pivalamide (**3m**). Follows general procedure C. **1m** (38.5 mg, 0.2 mmol), **2a** (78 mg, 0.4 mmol), THF (1 mL). The residue was purified by silica gel flash chromatography (20-100% ethyl acetate/hexane) to yield the title compound as a pale-yellow solid. The product selectivity was measured after chromatography using NMR integration ratios. Run 1 (46.3 mg, 60%, 92:8); Run 2 (44.8 mg, 58%, 90:10). ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.50 (d, J = 4.0 Hz, 1 H), 7.76 (d, J = 8.0 Hz, 2 H), 7.60 (t, J = 7.0 Hz, 1 H), 7.33 (d, J = 7.8 Hz, 2 H), 7.18-7.15 (m, 2 H), 7.04 (d, J = 6.9 Hz, 1 H), 6.32 (s, 1 H), 5.63 (s, 1 H), 5.32-5.25 (m, 1 H), 2.85 (dd, J = 15.2, 7.9 Hz, 1 H), 2.67 (dd, J = 15.2, 6.3 Hz, 1 H), 2.43 (s, 3 H), 1.20 (s, 9 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.4, 159.1, 149.5, 146.9, 144.8, 136.8, 135.5, 130.1 (2 C), 128.6 (2 C), 126.3, 122.7, 122.3, 53.3, 38.9, 35.4, 27.6 (3 C), 21.7; IR (cm^{-1}) 3388, 2963, 1658, 1593, 1571, 1497, 1399, 1312, 1301, 1290, 1134, 1082, 731; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{27}N_2O_3S$ 387.1737; Found 387.1759; mp 41-47 °C; TLC R_f = 0.26 (50% ethyl acetate/hexane), visualized with UV. *N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl) pivalamide* (**4m**) ^1H NMR resonances distinguishable at: δ 5.79, 5.08, 4.00, 3.69, 1.25 ppm.

Radical Inhibitor Experiment (Scheme 2a)

An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with **1a** (40 mg, 0.19 mmol), **2a** (74 mg, 0.38 mmol) and butylated hydroxytoluene (BHT, 208 mg, 0.94 mmol) in air. The tube was sealed with a cap (ChemGlass, CG-4910-15, TFE septum). The septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated and filled with nitrogen (3x). THF (1 mL) was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). After 24 h, the reaction mixture was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography (20-70% ethyl acetate/hexane) to yield **3a**:**4a** as a red brown solid (51.6 mg, 67%, 96:4). The product selectivity was measured after chromatography using ^1H NMR integration ratios.

Radical Initiator Experiment (Scheme 2b)

An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with **1a** (40 mg, 0.19 mmol) and **2a** (74 mg, 0.38 mmol). The screw-top tube was transferred into glovebox and charged with azobisisobutyronitrile (AIBN, 31 mg, 0.19 mmol). The tube was sealed with a cap (ChemGlass, CG-4910-15, TFE septum) and removed the glovebox. The septum of the cap was pierced with a needle connected to a Schlenk line and THF (1 mL) was added via syringe into the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). After 24 h, the reaction was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography (20-70% ethyl acetate/hexane) to yield **3a**:**4a** as a red brown solid (45.8 mg, 60%, 85:15). Starting material **1a** was recovered (7.1 mg, 18%). The product selectivity was measured after chromatography using ^1H NMR integration ratios.

Crossover Experiment (Scheme 2c)

An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with **1a** (15 mg, 0.07 mmol), **2a** (13.7 mg, 0.07 mmol), and **5b** (47.6 mg, 0.14 mmol). The tube was sealed with a cap (ChemGlass, CG-4910-15, TFE septum). The septum of the cap was pierced with a needle connected to a Schlenk line and THF (0.37 mL) was added via syringe into the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). After 24 h, the reaction was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography (20-80% ethyl acetate/hexane) to yield mixed fractions of *N*-(3-(phenylsulfonyl)-1-(pyridin-2-yl)but-3-en-1-yl)benzamide (**3q**) and **3a** as a light brown solid (11.3 mg, 41%, 93:7). The product selectivity was measured after chromatography using ^1H NMR integration ratios. ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.2 Hz, 1 H), 7.93 (dd, J = 7.3, 1.4 Hz, 2 H), 7.85 (dd, J = 7.1, 1.5 Hz, 2 H), 7.67-7.61 (m, 3 H), 7.56-7.48 (m, 3 H), 7.43 (dt, J = 7.0, 1.2 Hz, 2 H), 7.27 (m, 1 H), 7.19 (ddd, J = 7.5, 4.9, 0.9 Hz, 1 H), 6.37 (s, 1 H), 5.68 (s, 1 H), 5.53 (q, J = 7.4 Hz, 1 H), 3.00 (dd, J = 15.2, 7.7 Hz, 1 H), 2.80 (dd, J = 15.2, 6.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.9, 158.6, 149.5, 146.4, 138.3, 137.0, 134.1, 133.9, 131.8, 129.5 (2 C), 128.7 (4 C), 127.3 (2 C), 127.2, 123.0, 122.6, 53.8, 35.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}N_2O_3S$ 393.1267; Found 393.1260; TLC R_f = 0.33 (70% ethyl acetate/hexane), visualized with UV. **5a** was isolated in ~57% yield based on **2a** as the limiting reagent. **5b** and **2a** were recovered in 61% and 48%, respectively.

Deuterium Labeling Experiment (Scheme 2d)

Run 1: An oven-dried, 8-mL, screw-top tube equipped with a magnetic stir bar was charged with **1a** (30 mg, 0.14 mmol) and **2d** (55.5 mg, 0.28 mmol) in air. The tube was sealed with a cap and the septum of the cap pierced with a needle connected to a Schlenk line and the tube evacuated and filled with nitrogen (3x). THF (0.74 mL) was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The reaction mixture was stirred for 24 h. It was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. The crude residue was purified by silica gel flash column chromatography (20-90% ethyl acetate/hexane) to yield *N*-(1-(pyridin-2-yl)-3-tosylbut-3-en-1-yl-2,2-d2)benzamide (**3a-D**) and *N*-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl-3,3-d2)benzamide (**4a-D**) as a red brown solid (35.2 mg, 61%, 96:4). The product selectivity was measured after chromatography using ^1H NMR integration ratios. ^1H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, J = 4.4 Hz, 1 H), 7.86 (d, J = 7.7 Hz, 2 H), 7.80 (d, J = 8.2 Hz, 2 H), 7.70 (br d, J = 6.9 Hz, 1 H), 7.63 (dt, J = 7.6, 1.4 Hz, 1 H), 7.51-7.48 (m, 1 H), 7.45-7.42 (m, 2 H), 7.32 (d, J = 8.1 Hz, 2 H), 7.28 (d, J = 7.7 Hz, 1 H), 7.18 (dd, J = 7.3, 5.2 Hz, 1 H), 6.33 (s, 0.42 H), 6.31 (s, 0.19 H), 5.63 (s, 0.42 H), 5.62 (s, 0.20 H), 5.53-5.51 (m, 0.75 H), 2.99 (dd, J = 18.0, 6.9 Hz, 0.04 H), 2.97 (d, J = 7.1 Hz, 0.26 H), 2.78 (dd, J = 16.7, 6.6 Hz, 0.05 H), 2.77 (d, J = 6.6 Hz, 0.26 H), 2.42 (s, 3 H); ^2D NMR (600 MHz, $CHCl_3$) δ 6.37 (0.29 D), 5.68-5.51 (0.48 D), 2.98-2.78 (1.40 D); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 166.9, 158.7, 149.5, 146.6-146.5 (m, 1 C), 144.9, 136.9, 135.3, 134.1, 131.7, 130.1 (2 C), 128.70 (2 C), 128.67 (2 C), 127.3 (2 C), 126.7, 122.8, 122.5, 53.8 (d, J = 5.6 Hz, 1 C), 35.3-34.9 (m, 1 C), 21.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}D_2N_2O_3S$ 409.1549; Found 409.1531; TLC R_f = 0.31 (70% ethyl acetate/hexane), visualized with UV. *N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl-3,3-d2)benzamide* ^1H NMR resonances distinguishable at: δ 8.23, 7.92, 6.03, 3.75 ppm.

Run 2: Followed the procedure used in Run 1: **1a** (15 mg, 0.07 mmol), **2d** (28 mg, 0.14 mmol),THF (0.37 mL) The crude residue was purified by silica gel flash column chromatography (20-100% ethyl acetate/hexane) to yield **3a-D**

and **4a-D** as a red brown solid (18.7 mg, 65%, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.4 Hz, 1 H), 7.86 (d, J = 7.4 Hz, 2 H), 7.80 (d, J = 8.2 Hz, 2 H), 7.72 (d, J = 7.1 Hz, 1 H), 7.64 (dt, J = 7.8, 1.4 Hz, 1 H), 7.52-7.41 (m, 3 H), 7.33-7.28 (m, 3 H), 7.19 (dd, J = 7.0, 5.2 Hz, 1 H), 6.33 (s, 0.40 H), 6.32 (s, 0.21 H), 5.64 (s, 0.40 H), 5.63 (s, 0.22 H), 5.54-5.51 (m, 0.75 H), 2.99 (dd, J = 15.1, 7.8 Hz, 0.02 H), 2.98 (d, J = 7.3 Hz, 0.25 H), 2.80 (dd, J = 13.8, 6.4 Hz, 0.04 H), 2.78 (d, J = 6.2 Hz, 0.26 H), 2.42 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.9, 158.7, 149.4, 146.5, 144.9, 137.1, 135.3, 134.1, 131.7, 130.1 (2 C), 128.71 (2 C), 128.67 (2 C), 127.3 (2 C), 126.8, 122.9, 122.6, 53.9, 53.8, 35.2 (t, d, J = 18.9 Hz, 1 C), 21.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}D_2N_2O_3S$ 409.1549; Found 409.1529; TLC R_f = 0.33 (70% ethyl acetate/hexane), visualized with UV.

N-(1-(pyridin-2-yl)-2-(tosylmethyl)allyl-3,3-d2)benzamide ^{1}H NMR resonances at 8.23, 6.03, 5.37, 5.16, 4.08, 3.75 ppm.

Reaction of N-benzylbenzamide and 2a, with and without Pyridine as an Additive

Run 1: An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with *N*-benzylbenzamide (5 mg, 0.02 mmol) and **2a** (9.2 mg, 0.05 mmol) in air. The tube was sealed with a cap and the septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated and filled with nitrogen (3x). Toluene (0.2 mL) was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The reaction mixture was stirred for 24 h. It was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. ^{1}H NMR of the crude residue showed unreacted *N*-benzylbenzamide and **2a** and byproduct **5a** was not observed.

Run 2, followed a modified procedure used in Run 1: *N*-benzylbenzamide (5 mg, 0.02 mmol), **2a** (9.2 mg, 0.05 mmol), pyridine (2 μL, 0.02 mmol), and toluene (0.2 mL). ^{1}H NMR of the crude residue shows unreacted *N*-benzylbenzamide. Allene **2a** and byproduct **5a** were not observed.

Run 3, followed a modified procedure used in Run 1: *N*-benzylbenzamide (5 mg, 0.02 mmol), and **2a** (9.2 mg, 0.05 mmol), pyridine (0.15 mL of 0.031 M solution in toluene, 0.005 mmol), toluene (0.05 mL). ^{1}H NMR of the crude residue shows unreacted *N*-benzylbenzamide, near complete consumption of **2a** (~82% allenyl sulfone consumed) and some **5a** byproduct (~17% based on 2 equiv of allenyl sulfone **2a**).

Run 4, followed a modified procedure used in Run 1: *N*-benzylbenzamide (20 mg, 0.09 mmol), **2a** (37 mg, 0.19 mmol), pyridine (0.38 mL of 0.012 M solution in toluene, 0.005 mmol), and toluene (0.41 mL). ^{1}H NMR of the crude residue showed unreacted *N*-benzylbenzamide and **2a** and byproduct **5a** was not observed.

Probing for conversion of Allyl Sulfone 4a to Vinyl Sulfone 3a.

Experiment 1a: Follows general procedure C. **1a** (80 mg, 0.38 mmol), **2a** (146 mg, 0.75 mmol), EtOH (2 mL). The crude product was purified by silica gel flash chromatography (30-70% ethyl acetate/hexane) to yield **3a**:**4a** as a red brown solid (106.5 mg, 70%, 59:41). The product selectivity was measured after chromatography using ^{1}H NMR integration ratios of the collected fractions.

Experiment 1b: An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with **1a** (20 mg, 0.09 mmol), **2a** (37 mg, 0.19 mmol) and **3a**:**4a** (38.3 mg, 0.09 mmol, 59:41) in air. The tube was sealed with a cap and the septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated and filled with nitrogen (3x). THF (0.5 mL) was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The mixture was stirred for 24 h, diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. ^{1}H NMR of the crude residue showed **3a**:**4a** in a 78:22 ratio.

Experiment 2: A flame-dried, 20-mL scintillation via was charged with **1a** (5 mg, 0.02 mmol) and **2a** (9.2 mg, 0.05 mmol) in air. Toluene-d8 (0.5 mL) was added via syringe. The solution was transferred into an oven-dried NMR tube and the tube was sealed with a septum. The septum was pierced with a needle connected to a Schlenk line and the tube evacuated and filled (3x) with nitrogen. The cap was wrapped with parafilm and the tube was inserted in a 600 MHz NMR probe preheated to 50 °C. The tube was maintained in the probe for 25.5 h and 24 spectra were collected. At no point during the course of the reaction was the minor product, allyl sulfone **4a** signal observed with each spectrum showing only **3a**.

Reaction of Picolyl Amide 1a with Disulfone 5b

Experiment 1: An oven-dried, 8-mL screw-top tube equipped with a magnetic stir bar was charged with **1a** (10 mg, 0.05 mmol), **5b** (16 mg, 0.05 mmol) and potassium carbonate (13 mg, 0.09 mmol) in air. The tube was sealed with a cap and the septum of the cap was pierced with a needle connected to a Schlenk line and the tube evacuated and filled with nitrogen (3x). Acetonitrile (0.5 mL) was added via syringe to the reaction tube. The cap was wrapped with parafilm and the tube was lowered into a preheated oil bath (50 °C). The reaction mixture was stirred for 24 h. It was diluted with dichloromethane, transferred into a 20-mL scintillation vial and concentrated under reduced pressure using rotary evaporation. ^{1}H NMR of the crude residue shows unreacted **1a** and decomposition of **5b**.

Experiment 2: followed the procedure used in Experiment 1: **1a** (10 mg, 0.05 mmol), **5b** (16 mg, 0.05 mmol) and potassium carbonate (6.5 mg, 0.05 mmol), and acetonitrile (0.5 mL). ^{1}H NMR of the crude residue shows unreacted **1a** and almost complete disappearance of **5b.**

ASSOCIATED CONTENT

Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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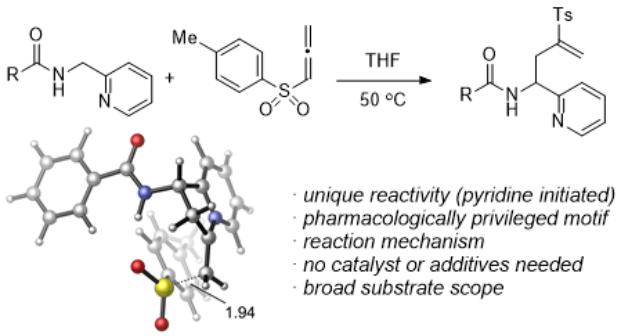

- *unique reactivity (pyridine initiated)*
- *pharmacologically privileged motif*
- *reaction mechanism*
- *no catalyst or additives needed*
- *broad substrate scope*