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Base-Promoted Stereoselective Hydrogenation of Ynamides with Sulfonyl Hydrazide to Give *Z*-Enamides

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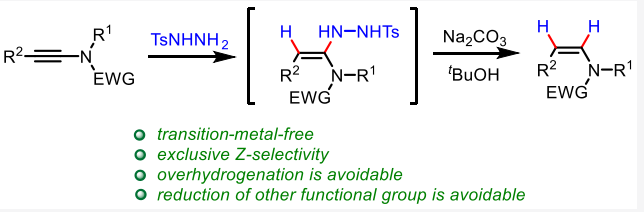
ABSTRACT: A base-mediated semihydrogenation of ynamides using *p*-toluenesulfonyl hydrazide as an inexpensive and easy-to-handle hydrogen donor is reported. This transition-metal-free protocol avoids overhydrogenation and reduction of other functional groups, generating the thermodynamically unfavorable *Z*-enamides exclusively.



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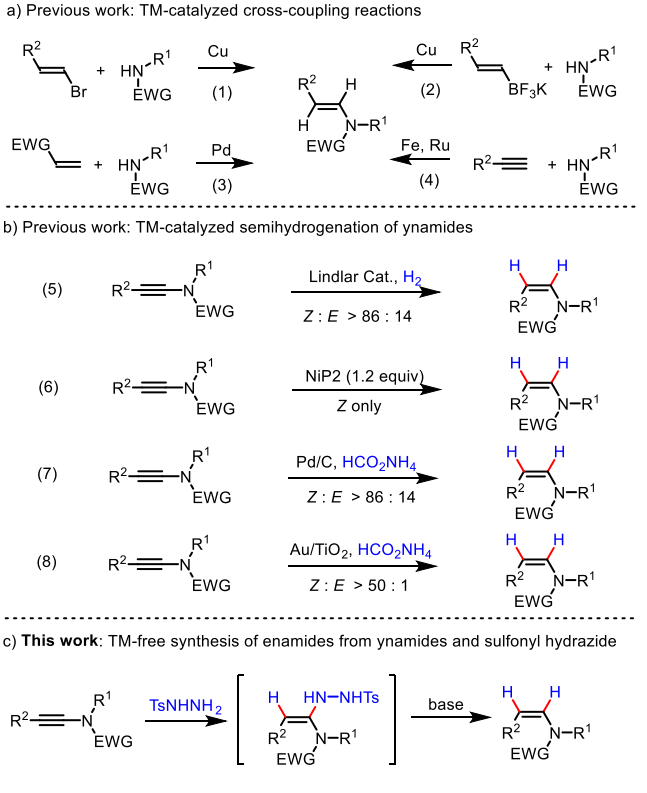
INTRODUCTION

Enamides are versatile motifs that have been widely found in biologically active natural products.[1] In addition, they also serve as valuable building blocks in organic synthesis.[2] Traditional approaches to these motifs are mainly through the condensation reactions of carbonyl compounds with amides, in which relatively harsh conditions were usually required.[3] In the past decades, the transition metal (TM)-catalyzed cross-coupling reactions have emerged as powerful strategies to access enamide moieties. These strategies include (1) the Ullmann-type reaction of alkenyl bromides with amides (Scheme 1a, route 1);[4] (2) the Chan−Lam-type reaction between alkenyltrifluoroborate salts and amides (Scheme 1a, route 2);[5] (3) the oxidative cross-coupling between electron-deficient alkenes with amides (Scheme 1a, route 3);[6] and (4) the addition of N−H bonds of amides to alkynes (Scheme 1a, route 4).[7] However, the above-mentioned protocols commonly gave the thermodynamically favorable *E*-enamides as the major isomers.

The TM-catalyzed semihydrogenation of alkynes is one of the most commonly used methods to obtain *Z*-olefins.[8] In 2006, Hsung and co-workers documented the synthesis of *Z*-enamides from ynamides[9] using a Lindlar catalyst (Scheme 1b, route 5).[10] Miesch reported that the semihydrogenation of ynamides using 1.2 equiv of NiP2 could give *Z*-enamides exclusively (Scheme 1b, route 6).[11] Recently, Pd/HCO_2NH_4 and Au/HCO_2NH_4 catalytic systems have been developed for the semihydrogenation of ynamides to give *Z*-enamides with high stereoselectivity by Swamy's and Xu's groups, respectively (Scheme 1b, routes 7 and 8).[12] However, these methods also possess several disadvantages such as the requirement of noble metal catalysts, overhydrogenation, reduction of other functional groups, and the formation of non-negligible *E*-isomers in some cases.[13] Thus, the development of TM-free and stereoselective hydrogenation of ynamides is highly desirable. Herein, we report a base-promoted hydrogenation of ynamides

Scheme 1. Synthesis of Enamides



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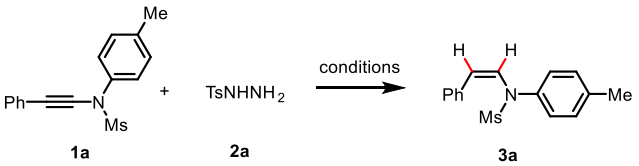
using inexpensive and easy-to-handle sulfonyl hydrazide as the hydrogenating source to deliver *Z*-enamides with exclusive stereoselectivily (Scheme 1c).

RESULTS AND DISCUSSION

We initially studied the stereoselective semihydrogenation reaction by investigating the model reaction of ynamide **1a** (0.1 mmol), *p*-toluenesulfonyl hydrazide **2a** (2 equiv), and K_2CO_3 (2 equiv) in DMF (1 mL) at 100 °C under a nitrogen atmosphere for 12 h. To our delight, the desired product **3a** was acquired in 50% yield (Table 1, entry 1). Then we

Table 1. Optimization of the Reaction Conditions[a]



1a **2a** **3a**

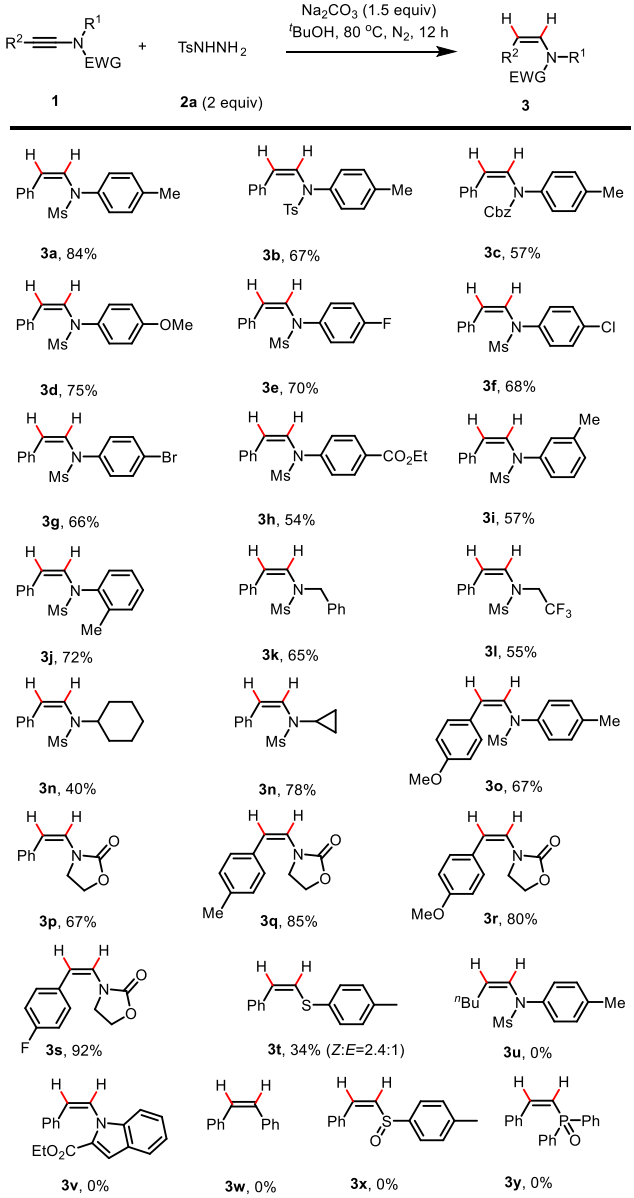
entry	solvent	base	yield (%)[b]
1	DMF	K_2CO_3	50
2	DMSO	K_2CO_3	68
3	*tert*-butanol	K_2CO_3	68
4	acetonitrile	K_2CO_3	44
5	toluene	K_2CO_3	36
6	DCE	K_2CO_3	trace
7	dioxane	K_2CO_3	30
8	*tert*-butanol	KOH	53
9	*tert*-butanol	K_3PO_4	45
10	*tert*-butanol	Li_2CO_3	trace
11	*tert*-butanol	Cs_2CO_3	trace
12	*tert*-butanol	Na_2CO_3	74
13	*tert*-butanol		12
14[c]	*tert*-butanol	Na_2CO_3	78
15[d]	*tert*-butanol	Na_2CO_3	66
16[e]	*tert*-butanol	Na_2CO_3	84
17[f]	***tert*-butanol**	**Na_2CO_3**	85 (84)
18[g]	*tert*-butanol	Na_2CO_3	76

[a]**1a** (0.1 mmol), **2a** (0.2 mmol), solvent (1 mL), base (2.0 equiv) at 100 °C for 12 h, under N_2. [b]The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard. Isolated yield is shown in parentheses. [c]At 80 °C. [d]**2a** (1.5 equiv). [e]**2a** (2.5 equiv). [f]Na_2CO_3 (1.5 equiv). [g]Na_2CO_3 (1.0 equiv).

screened a range of solvents under the above conditions. It can be observed that the yields increased obviously to 68% in both DMSO and *tert*-butanol, probably because polar solvents favored this transformation (entries 2 and 3). No expected product was observed or the yields dropped slightly with 1,2 dichloroethane, toluene, 1,4-dioxane, and acetonitrile as the solvents (entries 4−7). Next, we surveyed the influence of bases on the reactivity of this reaction using *tert*-butanol as solvent. When K_2CO_3 was replaced with KOH and K_3PO_4, the yield dropped clearly to 53% and 45%, separately (entries 8 and 9). When Li_2CO_3 and Cs_2CO_3 were used, a trace of **3a** was discovered (entries 10 and 11). It is noteworthy that the yield improved slightly to 74% when Na_2CO_3 was used (entry 12). However, only a 12% yield of **3a** was formed in the absence of Na_2CO_3 (entry 13). The screening of the reaction temperature showed that the yield of **3a** was increased slightly at 80 °C (entry 14). We further investigated the loading of **2a** and Na_2CO_3, and the optimized reaction conditions were obtained as follows: **1a** (0.1 mmol), **2a** (2 equiv), and Na_2CO_3 (1.5 equiv) in *tert*-butanol (1 mL) at 80 °C under a nitrogen atmosphere for 12 h (entry 17).

With the optimal conditions in hand, we investigated the scope and limitations of this semihydrogenation reaction (Scheme 2). In addition to the Ms-protected ynamide **1a**, Ts- and Cbz-protected ynamides smoothly convert to the corresponding *Z*-enamides in good yields (**3b**, **3c**). It should be noted that the Cbz− group could not survive under Pd/H_2 hydrogenation reaction conditions. Ynamides with an electron-donating (**3d**) and electron-withdrawing group (**3h**) on *N*-arenes were both well compatible. Halogens (F−, Cl−, and Br−) were also tolerated to give the desired products in 66−70% yields (**3e**−**g**). It is gratifying that the introduction of *N*-alkyl groups did not cause significant effects, good yields were generally observed, and the stereoselectivity remains the same

Scheme 2. Scope of Ynamides[a]



[a]Reaction conditions: **1** (0.1 mmol), **2a** (0.2 mmol), *tert*-butanol (1 mL), Na_2CO_3 (1.5 equiv), 80 °C, 12 h, under N_2.

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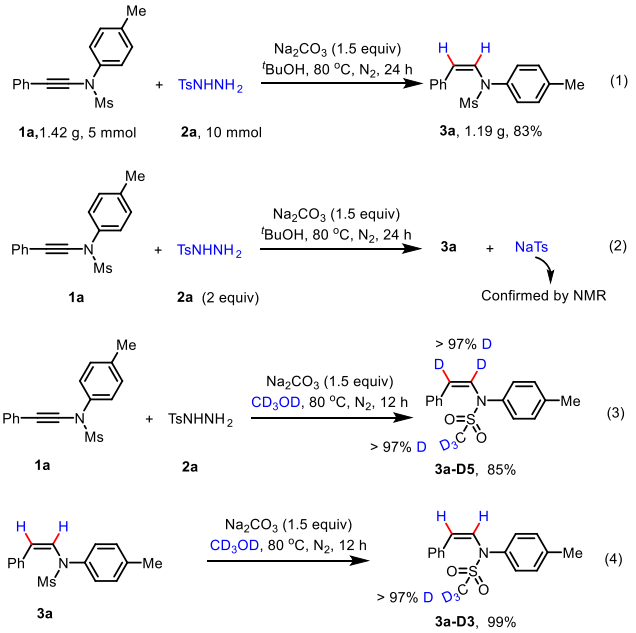
(**3k**−**n**). In the further course of the evaluation of the substrate scope, we noticed that a variety of *N*-alkynyl oxazolidin-2-ones were suitable substrates to give the corrsponding (*Z*)-3-styryloxazolidin-2-ones in good to excellent yields (**3p**−**s**). It should be noted that exclusive *Z*-isomers were formed in all cases of the aforementioned semihydrogenation reactions, as indicated by the X-ray structures of **3s**. We also evaluated the semihydrogenation reaction of (phenylethynyl)(*p*-tolyl)-sulfane, and low yield and poor stereoselectivity (*Z*/*E* = 2.4:1) were observed (**3t**). However, alkyl alkyne (**3u**), indole-based ynamide (**3v**), and 1,2-diphenylethyne (**3w**) failed to deliver the reduction products. In addition, sulfinyl alkyne completely decomposed under the reaction conditions (**3x**). No reaction occurred when phosphoryl alkyne (**3y**) was subjected to the reaction system, probably because phosphoryl alkyne is a poor electrophilic Michael acceptor that is unlikely to be attacked by hydrazide.

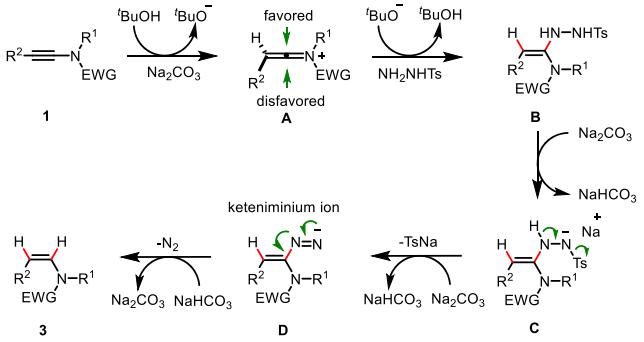
To verify the generality of this reaction, we applied the reaction system in a gram-scale synthesis of **3a**, which was obtained in 83% yield (eq 1). It is worth mentioning that the



generation of sodium 4-methylbenzenesulfinate (NaTs) was confirmed by ^{1}H and ^{13}C{1H} NMR (eq 2). To further explore the mechanism of the reaction, we conducted the deuteration experiments. The ynamide **1a** was subjected to the standard reaction conditions using CD_3OD as a solvent, leading to H/D exchange occurring at the alkenyl position of the corresponding product (eq 3). In addition, the incorporation of deuterium at the alkenyl position did not occur when **3a** was subjected to the deuteration conditions in the obsence of *p*-toluenesulfonyl hydrazide (eq 4). Meawhile, full deuterium incorporation on the Ms group of the above-mentioned expriments was observed.

According to the above experiments, we propose a mechanism as outlined in Scheme 3. First, keteniminium ionic species **A** is formed under basic conditions from ynamide **1**.[9] Then the nucleophilic addition of *p*-toluenesulfonyl hydrazide to **A**, which is highly regio- and stereoselective, occurred at the sterically less hindered face to give intermediate **B**. Subsquently, N anion **C** is generated through

Scheme 3. Proposed Reaction Pathway



deprotonation of **B**. Finally, the sequential release of a TsNa and a N_2 from **B** leads to the desired *Z*-enamide **3**.

CONCLUSIONS

In summary, we have discovered a transition-metal-free semihydrogenation reaction of ynamides using *p*-toluenesulfonyl hydrazide as an inexpensive and commercially available hydrogen donor. A broad range of *Z*-enamides were synthesized in moderate to excellent yields with exclusive stereoselectivity. This eco-friendly protocol proceeded under transition-metal-free conditions using alcohol as solvents, avoiding overhydrogenation and reduction of other functional groups.

EXPERIMENTAL SECTION

General Information. All commercially available solvents were of analytical grade and used as received.The other commercial chemicals were used without further purification. All reactions were performed under an inert atmosphere of nitrogen in flame-dried glassware, unless otherwise stated. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. Preparative TLC was performed on 1.0 mm silica gel. ^{1}H NMR spectra were recorded on a Bruker Avance III instrument (500 MHz). ^{13}C NMR spectra were recorded on a Bruker Avance III instrument (126 MHz) and were fully decoupled by broad band proton decoupling. High-resolution mass spectra (HRMS) were recorded on an Agilent 1290 Mass spectrometer using ESI-TOF (electrospray ionization time-of-flight). Crystal structure and data were recorded on an Agilent Gemini E diffractometer. NMR spectra were recorded in $CDCl_3$. ^{1}H NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in hertz (Hz). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

Typical Procedure for the Synthesis of Ynamide 1a.[14] To a dried flask were added *N*-(*p*-tolyl)methanesulfonamide (0.906 g, 5.0 mmol), bromoalkyne (1.08 g, 6.0 mmol), $CuSO_4{\cdot}5H_2O$ (0.125 g, 0.5 mmol), 1,10-phenanthroline (0.18 g, 1.0 mmol), K_2CO_3 (1.38 g, 10.0 mmol), and toluene (30 mL). The flask was charged with nitrogen, and the solution was heated at 80 °C in oil bath for 12 h. After completion, the crude reaction mixture was cooled to room temperature, filtered through Celite, and concentrated. Purification of the crude residue using silica gel flash column chromatography gave **1a** as yellow solid (0.989 g, 69%).

General Procedure 3. A dried 10 mL Schlenk tube was charged with ynamide **1** (0.1 mmol, 1 equiv), 4-methylbenzenesulfonohydrazide (37.2 mg, 0.2 mmol, 2.0 equiv), Na_2CO_3 (15.9 mg, 0.15 mmol, 1.5 equiv), and *tert*-butanol (1 mL) under a nitrogen atmosphere. The reaction mixture was heated to 80 °C on a heating plate for 12 h with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate,

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and filtered through a pad of Celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate:hexane to give the corresponding products **3**.

*(Z)-N-Styryl-N-(p-tolyl)methanesulfonamide (**3a**).* (24.1 mg, 84%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow solid; mp 92−93 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.14−7.09 (m, 4H), 7.04−6.97 (m, 3H), 6.91−6.86 (m, 2H), 6.59 (d, *J* = 9.0 Hz, 1H), 6.04 (d, *J* = 9.0 Hz, 1H), 2.83 (s, 3H), 2.14 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 137.1, 136.4, 133.8, 129.4, 128.9, 127.6, 127.1, 126.7, 126.3, 121.7, 36.7, 20.8; IR (ATR) ν 2926 (m) 1614 (w) 813 (m) 764 (m) 700 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2S$ 288.1053; found 288.1052.

*(Z)-4-Methyl-N-styryl-N-(p-tolyl)benzenesulfonamide (**3b**).* (25.2 mg, 67%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 110−111 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.48−7.44 (m, 2H), 7.22 (td, *J* = 5.9 Hz, 2.8 Hz, 4H), 7.09−7.02 (m, 3H), 6.91−6.84 (m, 4H), 6.53 (d, *J* = 9.1 Hz, 1H), 6.03 (d, *J* = 9.0 Hz, 1H), 2.40 (s, 3H), 2.18 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 143.9, 136.9 (d, *J* = 9.1 Hz), 134.0 (d, *J* = 14.9 Hz), 129.4, 129.0, 127.9, 127.5, 127.4, 127.0, 126.7, 122.0, 21.5, 20.9; IR (ATR) ν 2921 (m) 1598 (w) 812 (m) 768 (m) 703 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{22}H_{21}NO_2S$ 364.1366, found 364.1367.

*Benzyl (Z)-Styryl(p-tolyl)carbamate (**3c**).* (19.7 mg, 57%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a colorless oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.31−7.27 (m, 3H), 7.20 (dd, *J* = 7.3 Hz, 2.3 Hz, 2H), 7.14−7.05 (m, 7H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.59−6.45 (m, 1H), 6.11 (d, *J* = 9.1 Hz, 1H), 5.08 (s, 2H), 2.22 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 154.3, 137.5, 136.0, 135.5, 134.9, 129.0, 128.3 (d, *J* = 11.5 Hz), 128.0, 127.8, 127.3, 127.0, 125.5 (d, *J* = 14.0 Hz), 67.8, 20.8; IR (ATR) ν 2922 (m) 2852 (m) 1709 (s) 1643 (w) 816 (m) 762 (m) 694 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{23}H_{22}NO_2$ 344.1645, found 344.1643.

*(Z)-N-(4-Methoxyphenyl)-N-styrylmethanesulfonamide (**3d**).* (22.7 mg, 75%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow solid; mp 88−89 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.16 (ddd, *J* = 13.0 Hz, 7.3 Hz, 1.9 Hz, 4H), 7.10−7.02 (m, 3H), 6.69 (d, *J* = 9.2 Hz, 1H), 6.67−6.63 (m, 2H), 6.06 (d, *J* = 9.1 Hz, 1H), 3.69 (s, 3H), 2.90 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 158.5, 133.8, 131.4, 128.8, 128.6, 127.5, 127.0, 126.5, 120.2, 114.0, 55.3, 36.5; IR (ATR) v 2935 (m) 2839 (m) 1608 (w) 823 (m) 766 (m) 699 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_3S$ 304.1002, found 304.1003.

*(Z)-N-(4-Fluorophenyl)-N-styrylmethanesulfonamide (**3e**).* (20.2 mg, 70%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow solid; mp 90−91 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.25−7.22 (m, 2H), 7.12−7.05 (m, 5H), 6.84−6.80 (m, 2H), 6.70 (d, *J* = 9.1 Hz, 1H), 6.10 (d, *J* = 9.1 Hz, 1H), 2.92 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 161.3 (d, *J* = 247.9 Hz), 134.7 (d, *J* = 3.2 Hz), 133.6, 129.0 (d, *J* = 8.7 Hz), 128.7, 127.6, 127.2, 126.3, 120.6, 115.7 (d, *J* = 23.0 Hz), 36.9; IR (ATR) ν 2927 (m) 1605 (w) 1321 (s) 830 (m) 759 (m) 700 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{15}FNO_2S$ 292.0802, found 292.0802.

*(Z)-N-(4-Chlorophenyl)-N-styrylmethanesulfonamide (**3f**).* (21.1 mg, 68%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.23−7.20 (m, 2H), 7.16−7.07 (m, 7H), 6.66 (d, *J* = 9.0 Hz, 1H), 6.15 (d, *J* = 9.0 Hz, 1H), 2.93 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 137.5, 133.6, 132.8, 128.9 (d, *J* = 25.5 Hz), 127.9 (d, *J* = 25.6 Hz), 127.5, 125.9, 122.0, 37.1, 29.7; IR (ATR) ν 2926 (m) 1639 (w) 826 (m) 770 (m) 732 (s) 699 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{15}ClNO_2S$ 308.0507, found 308.0506.

*(Z)-N-(4-Bromophenyl)-N-styrylmethanesulfonamide (**3g**).* (23.4 mg, 66%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow solid; mp 125−126 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.28−7.26 (m, 2H), 7.16−7.14 (m, 3H), 7.14−7.04 (m, 4H), 6.65 (d, *J* = 9.0 Hz, 1H), 6.16 (d, *J* = 9.0 Hz, 1H), 2.93 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 138.1, 133.5, 132.0, 128.8, 128.2, 127.8, 127.5, 125.8, 122.3 (d, *J* = 2.0 Hz), 120.7, 37.2; IR (ATR) ν 2925 (m) 2853 (m) 1590 (w) 823 (m) 759 (m) 700 (m) 535 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{15}BrNO_2S$ 352.0001, found 352.0002.

*Ethyl (Z)-4-(N-Styrylmethylsulfonamido)benzoate (**3h**).* (9.1 mg, 54%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.87−7.84 (m, 2H), 7.41−7.38 (m, 2H), 7.21−7.18 (m, 2H), 7.12−7.05 (m, 3H), 6.65 (d, *J* = 8.9 Hz, 1H), 6.26 (d, *J* = 8.8 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 165.7, 143.2, 133.3, 130.3, 128.7, 128.4, 127.9, 127.8, 125.3, 125.2, 124.3, 61.1, 37.6, 14.3; IR (ATR) ν 2925 (m) 2852 (m) 1712 (s) 1604 (m) 855 (m) 768 (m) 696 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{18}H_{20}NO_4S$ 346.1108, found 346.1107.

*(Z)-N-Styryl-N-(m-tolyl)methanesulfonamide (**3i**).* (16.1 mg, 57%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.18−7.15 (m, 2H), 7.11−7.04 (m, 5H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.89−6.86 (m, 1H), 6.67 (d, *J* = 9.1 Hz, 1H), 6.11 (d, *J* = 9.1 Hz, 1H), 2.92 (s, 3H), 2.19 (d, *J* = 0.8 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 140.3, 136.0, 130.6, 130.3, 129.7, 129.0, 128.6, 126.8, 126.4, 125.4, 111.8, 39.4, 21.3; IR (ATR) ν 2925 (m) 2854 (m) 1608 (w) 780 (m) 762 (m) 692 (s) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2S$ 288.1053, found 288.1051.

*(Z)-N-Styryl-N-(o-tolyl)methanesulfonamide (**3j**).* (21.1 mg, 72%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.05 (dd, *J* = 7.8 Hz, 1.3, 1H), 6.96−6.91 (m, 5H), 6.89 (dd, *J* = 7.3 Hz, 1.9 Hz, 1H), 6.84−6.80 (m, 2H), 6.79 (d, *J* = 9.9 Hz, 1H), 5.93 (d, *J* = 9.8 Hz, 1H), 3.01 (s, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 137.5, 136.5, 134.1, 131.2, 129.4, 128.3, 127.1, 126.3, 126.2 (d, *J* = 6.4 Hz), 115.1, 38.5, 19.0; IR (ATR) ν 2928 (m) 1585 (w) 1495 (m) 734 (m) 700 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2$ 288.1053, found 288.1050.

*(Z)-N-Benzyl-N-styrylmethanesulfonamide (**3k**).* (19.4 mg, 65%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow solid; mp 65−66 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.44−7.40 (m, 2H), 7.36−7.32 (m, 2H), 7.30−7.23 (m, 4H), 7.20−7.17 (m, 2H), 6.19 (d, *J* = 8.7 Hz, 1H), 6.13 (d, *J* = 8.7 Hz, 1H), 4.52 (s, 2H), 2.81 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 135.7, 134.4, 128.9, 128.7, 128.4, 128.1, 127.9, 125.5, 125.0, 52.3, 39.1; IR (ATR) ν 2926 (m) 1701 (w) 1455 (m) 733 (m) 696 (m); HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{16}H_{18}NO_2S$ 288.1053, found 288.1053.

*(Z)-N-Styryl-N-(2,2,2-trifluoroethyl)methanesulfonamide (**3l**).* (15.3 mg, 55%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 65−66 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.48−7.44 (m, 2H), 7.41−7.37 (m, 2H), 7.35−7.31 (m, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.18 (d, *J* = 8.4 Hz, 1H), 3.93 (q, *J* = 8.6 Hz, 2H), 3.03 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 133.5, 128.9, 128.8, 128.6, 128.1, 124.0, 124.0 (q, *J* = 281.4 Hz), 48.8 (q, *J* = 34.4 Hz), 39.4; IR (ATR) ν 2926 (m) 1643 (w) 1342 (s) 724 (m) 690 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{11}H_{13}F_3NO_2S$ 280.0614, found 280.0613.

*(Z)-N-Cyclohexyl-N-styrylmethanesulfonamide (**3m**).* (11.0 mg, 40%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 88−89 °C.

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^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.75−7.71 (m, 2H), 7.35−7.28 (m, 3H), 6.54 (d, *J* = 8.3 Hz, 1H), 5.94 (d, *J* = 8.4 Hz, 1H), 3.94−3.88 (m, 1H), 2.85 (s, 3H), 1.92−1.88 (m, 2H), 1.75 (dt, *J* = 14.4 Hz, 3.3 Hz, 2H), 1.58 (d, *J* = 7.5 Hz, 3H), 1.50−1.43 (m, 2H), 1.31 (dt, *J* = 13.4 Hz, 3.6 Hz, 1H), 1.01 (dt, *J* = 13.1 Hz, 3.7 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 135.2, 134.1, 129.7, 128.7, 128.3, 122.1, 60.2, 39.1, 30.7, 25.8, 25.2; IR (ATR) ν 2928 (s) 2853 (m) 1667 (w) 765 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{22}NO_2S$ 280.1366, found 280.1364.

*(Z)-N-Cyclopropyl-N-styrylmethanesulfonamide (**3n**).* (18.9 mg, 78%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 100−101 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.45−7.42 (m, 2H), 7.31−7.24 (m, 3H), 6.25 (d, *J* = 8.6 Hz, 1H), 6.04 (d, *J* = 8.7 Hz, 1H), 2.97 (s, 3H), 2.53 (tt, *J* = 7.0 Hz, 3.6 Hz, 1H), 0.77−0.73 (m, 2H), 0.60−0.56 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 135.1, 129.0, 128.1, 127.8, 125.5 (d, *J* = 5.5 Hz), 37.7, 31.2, 8.2; IR (ATR) ν 2923 (w) 1640 (w) 761 (m) 693 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{12}H_{16}NO_2S$ 238.0896, found 238.0895.

*(Z)-N-(4-Methoxystyryl)-N-(p-tolyl)methanesulfonamide (**3o**).* (24.5 mg, 67%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.28−7.23 (m, 5H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.70−6.65 (m, 2H), 6.51 (d, *J* = 8.7 Hz, 1H), 6.12 (d, *J* = 8.7 Hz, 1H), 3.74 (d, *J* = 1.2 Hz, 3H), 2.90 (d, *J* = 1.2 Hz, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 158.9, 137.0 (d, *J* = 6.2 Hz), 130.5, 129.6, 126.3 (d, *J* = 24.8 Hz), 124.3, 123.9, 113.3, 55.2, 36.5, 20.9; IR (ATR) ν 2927 (m) 1607 (w) 816 (m) 731 (m) 700 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{17}H_{20}NO_3S$ 318.1158, found 318.1159.

*(Z)-3-Styryloxazolidin-2-one (**3p**).* (12.9 mg, 67%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a colorless oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.32 (dd, *J* = 8.1 Hz, 6.7 Hz, 2H), 7.27−7.20 (m, 3H), 6.66 (d, *J* = 9.8 Hz, 1H), 5.99 (d, *J* = 9.7 Hz, 1H), 4.28−4.24 (m, 2H), 3.39−3.35 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 157.2, 135.5, 129.2, 127.9, 127.1, 124.2, 112.8, 62.6, 45.0; IR (ATR) ν 2921 (m) 1746 (s) 1599 (w) 756 (m) 698 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{11}H_{12}NO_2$ 190.0863, found 190.0862.

*(Z)-3-(4-Methylstyryl)oxazolidin-2-one (**3q**).* (17.5 mg, 85%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 72−73 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.14−7.09 (m, 4H), 6.62 (d, *J* = 9.7 Hz, 1H), 5.96 (d, *J* = 9.6 Hz, 1H), 4.28−4.24 (m, 2H), 3.41−3.37 (m, 2H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 157.2, 136.9, 132.4, 129.1, 128.6, 123.8, 113.1, 62.6, 44.9, 21.1; IR (ATR) ν 2920 (m) 1747 (s) 1608 (w) 817 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{12}H_{14}NO_2$ 204.1019, found 204.1020.

*(Z)-3-(4-Methoxystyryl)oxazolidin-2-one (**3r**).* (17.5 mg, 80%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 90−91 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.16−7.12 (m, 2H), 6.88−6.83 (m, 2H), 6.58 (d, *J* = 9.6 Hz, 1H), 5.95 (d, *J* = 9.6 Hz, 1H), 4.29−4.25 (m, 2H), 3.81 (s, 3H), 3.42−3.37 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 158.6, 157.3, 130.3, 127.7, 123.6, 113.4, 113.1, 62.6, 55.2, 44.9; IR (ATR) ν 2924 (m) 1751 (s) 1654 (w) 831 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{12}H_{14}NO_3$ 220.0968, found 220.0967.

*(Z)-3-(4-Fluorostyryl)oxazolidin-2-one (**3s**).* (19.0 mg, 92%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a white solid; mp 72−73 °C.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.22−7.17 (m, 2H), 7.05−6.99 (m, 2H), 6.65 (d, *J* = 9.7 Hz, 1H), 5.94 (d, *J* = 9.7 Hz, 1H), 4.31−4.26 (m, 2H), 3.38−3.34 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 161.8 (d, *J* = 247.1 Hz), 157.1, 131.4 (d, *J* = 3.4 Hz), 130.8 (d, *J* = 8.0 Hz), 124.5, 114.9 (d, *J* = 21.5 Hz), 111.7, 62.6, 44.9; IR (ATR) ν 2920 (m) 1744 (s) 1601 (w) 833 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{11}H_{11}FNO_2$ 208.0768, found 208.0770.

*(Z)-Styryl(p-tolyl)sulfane (**3t**).* (*Z*:*E* = 2.4:1) (7.2 mg, 34%) was prepared from the typical procedure (ethyl acetate:hexane = 1:20) as a yellow oil.

^{1}H NMR (500 MHz, Chloroform-*d*) δ = 7.55−7.50 (m, 2H), 7.41−7.20 (m, 5H), 7.16 (d, *J* = 7.8 Hz, 2H), 6.54 (d, *J* = 10.7 Hz, 1H), 6.46 (d, *J* = 10.8 Hz, 1H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ = 137.3, 136.7, 131.1, 130.6, 130.5, 129.9, 128.6, 127.4, 125.9, 124.4, 21.1; IR (ATR) ν 2922 (m) 2853 (m) 1596 (m) 804 (s) 740 (m) 688 (m) HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{15}S$ 227.0889, found 227.0884.

Gram-Scale Synthesis of 3a. A dried 100 mL Schlenk tube was charged with *N*-(phenylethynyl)-*N*-(*p*-tolyl)methanesulfonamide **1a** (1.43 g, 5.0 mmol, 1 equiv), 4-methylbenzenesulfonohydrazide (1.8664 g, 10 mmol, 2.0 equiv), Na_2CO_3 (0.7957 g, 7.5 mmol, 1.5 equiv), and *tert*-butanol (50 mL). In a nitrogen atmosphere, the reaction mixture was heated to 80 °C in an oil bath for 24 h under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of Celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by chromatography with ethyl acetate:petroleum ether = 1:20 to give the corresponding products **3a** (1.19 g, 83%) as a yellow oil.

Confirmation of Sodium 4-Methylbenzenesulfinate. A dried 10 mL Schlenk tube was charged with ynamide **1a** (0.2 mmol, 1 equiv), 4-methylbenzenesulfonohydrazide (74.4 mg, 0.4 mmol, 2.0 equiv), Na_2CO_3 (31.8 mg, 0.3 mmol, 1.5 equiv), and *tert*-butanol (2 mL) under a nitrogen atmosphere. The reaction mixture was heated to 80 °C on a heating plate for 12 h with vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with H_2O (10 mL), and extracted with DCM (3 × 10 mL). The aqueous phase was concentrated under vacuum to give the crude NaTs.

^{1}H NMR (500 MHz, D_2O) δ = 7.42−7.38 (m, 1H), 7.19 (d, *J* = 7.9, 1H), 2.22 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz, D_2O) δ = 150.5, 141.1, 129.6, 123.5, 20.5.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01085.

General experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra of new compounds (PDF)

Accession Codes

CCDC 2081409 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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