JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

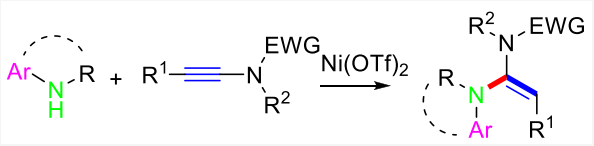
Nickel-Catalyzed Regioselective Hydroamination of Ynamides with Secondary Amines

Xiao-Di Nie, Xiao-Li Han, Jian-Ting Sun, Chang-Mei Si,* Bang-Guo Wei,* and Guo-Qiang Lin

Cite This: J. Org. Chem. 2021, 86, 3433−3443 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: The first $Ni(OTf)_2$-catalyzed hydroamination of ynamides **2** was developed by reacting with secondary amines (**1** and **4**). This protocol features excellent regioselectivity, a broad substrate scope of secondary aryl amines, and good functional group tolerance for ynamides. Using this method, a variety of substituted ethene-1,1-diamine compounds were prepared in moderate to excellent yields with high regioselectivities.



INTRODUCTION

The development of efficient synthetic methodologies has always been important and attractive to organic chemists,[1] due to their potential use in syntheses of natural products and pharmaceutical drugs.[2] In particular, hydroamination has attracted significant interest because of its utilization in the preparation of heterocyclic compounds,[3] including depsipeptides,[4] pharmaceuticals,[5] and important natural products.[6] Although hydroamination usually involves the challenging formation of enamine-containing heterocyclic compounds, the reaction process can overcome the intriguing selectivity of inter/intramolecular nucleophilic attack and demonstrate exceptional ability to activate π-conjugated systems. In the past few decades, numerous precious metals, lanthanides, and alkaline earth metals have been widely used to catalyze hydroamination of alkynes.[7] Moreover, base-mediated hydroamination reactions have also been reported in recent years.[8] However, the application of cheap metal Lewis acid remains to be explored for the catalysis of the hydroamination process.

Hydroamination of alkynes mostly used indole or substituted indoles as amine partners (Figure 1a),[8b,c,9] and this strategy was further developed to a cascade process to form some valuable heterocyclic skeletons (Figure 1b).[10] Another important type of hydroamination is the reaction of alkynes with amides, leading to an isoquinolin-1(2*H*)-one framework (Figure 1c).[11] Very recently, Esteruelas and co-workers established Ruthenium-catalyzed oxidative amidation of terminal alkynes with primary and secondary amines to afford the corresponding amides (Figure 1d).[7c]

Ynamides, known as nitrogen-substituted alkynes with an electron-withdrawing group at the nitrogen atom, have undoubtedly become one of the most popular synthons due to their high reactivity and high regio- and stereoselectivity.[12] In the past decade, ynamides were successfully applied in the syntheses of many important versatile skeletons, including functional indoles,[13] quinolines,[14] pyridines,[15] pyrroles,[16] oxazoles,[17] benzofurans,[18] carbolines,[19] amidines,[20] and

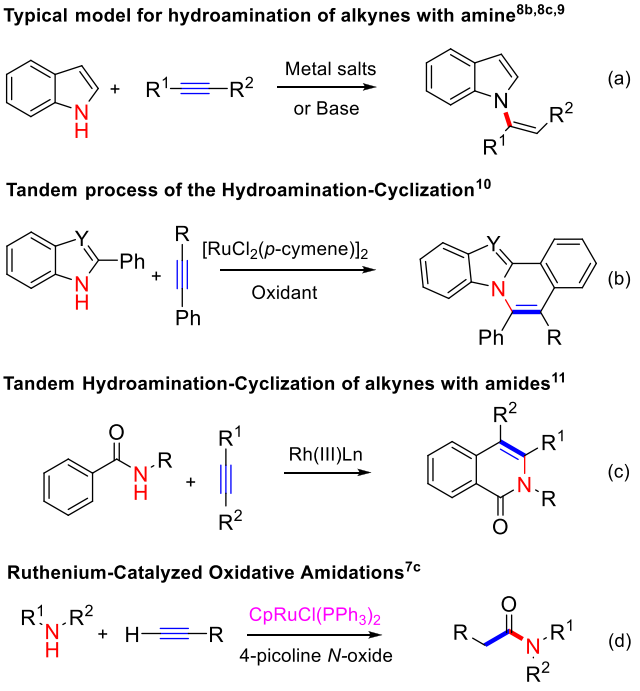


Figure 1. Hydroamination of amines with alkynes.

enamides.[21] In addition, ynamide was studied for the hydroamination reaction, in which noble metal Au was used to catalyze the addition of primary amines to ynamides to

Received: November 24, 2020
Published: February 3, 2021

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

afford enamines (Figure 2a).[22] Later on, transition-metal-free hydroamination was developed, and indole substrates could

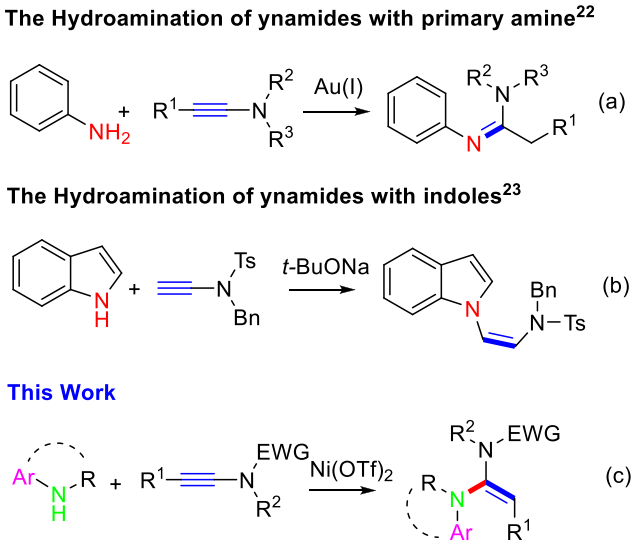


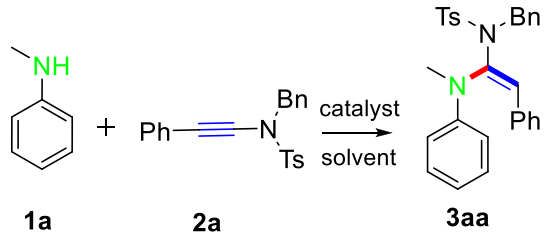
Figure 2. Hydroamination of amines with ynamides.

undergo the addition to ynamides, producing (*Z*)-*N*-(2-aminovinyl)-sulfonamide with excellent regioselectivity (Figure 2b).[23] To our best knowledge, such hydroamination with secondary amines other than indole and its analogues has not been reported. On the basis of our continuous efforts in Lewis acid-catalyzed chemical transformations of ynamides,[24] we envisioned the addition of amines to ynamides could occur under Lewis acid conditions. Herein we present our work on the first $Ni(OTf)_2$-catalyzed regioselective hydroamination of secondary amines with ynamides (Figure 2c).

RESULTS AND DISCUSSION

Our investigation started with the reaction of *N*-methylaniline **1a** with ynamide **2a**. First, various inorganic bases including Na_2CO_3, K_3PO_4,[25] NaO^{t}Bu,[23] and KOH[8b,c] failed to promote the reaction (Table 1, entries 1−4). Then $AuCl_3$ and $PPh_3AuCl/AgSbF_6$[24b] were examined, and both reactions were messy (Table 1, entries 5 and 6). Fortunately, $[Ph_3C][B(C_6F_5)_4]$[26] could lead to the desired product **3aa** in 56% yield with moderate regioselectivity (*E*/*Z* = 10:1, Table 1, entry 7). $BF_3{\cdot}Et_2O$[24e] and TMSOTf[24a] could effectively improve the regioselectivity (*E*/*Z* > 20:1), but the yields were still unsatisfactory (Table 1, entries 8 and 9). Next, a variety of Lewis acids, including a catalytic amount of $Sc(OTf)_3$, $Cu(OTf)_2$,[24b] $Er(OTf)_3$, and $La(OTf)_3$, were examined. Although most of them could maintain or enhance *E*/*Z* selectivities, they failed to improve the yields of the desired product **3aa**, and $La(OTf)_3$ could not catalyze this reaction at all (Table 1, entries 10−13). Fortunately, $Ni(OTf)_2$ could effectively catalyze this hydroamination reaction, and the desired product **3aa** was obtained in 92% yield with excellent regioselectivity (*E*/*Z* > 20:1, Table 1, entry 14). It is worth noting that other nickel salts, $NiBr_2$, $Ni(acac)_2$, and $(Ph_3P)_2NiCl_2$, could not catalyze this reaction (Table 1, entries 15−17). The evaluation of reaction temperatures and solvents led to the best outcome when the reaction was conducted in toluene at 80 °C (Table 1, entries 18−23). Although the reaction could work in a halogenated solvent like

Table 1. Optimization of Reaction Conditions



entry[a]	catalyst	solvent	yield (%)[b]	*E*/*Z*[c]
1[d]	Na_2CO_3	DMF	NR	
2[d]	K_3PO_4	DMF	NR	
3[d]	NaO^{t}Bu	DMF	NR	
4[d]	KOH	DMF	NR	
5	$AuCl_3$	toluene	complex	
6	$PPh_3AuCl/AgSbF_6$	toluene	complex	
7	$[Ph_3C][B(C_6F_5)_4]$	toluene	56	10:1
8	$BF_3{\cdot}Et_2O$	toluene	58	>20:1
9	TMSOTf	toluene	46	>20:1
10	$Sc(OTf)_3$	toluene	66	10:1
11	$Cu(OTf)_2$	toluene	53	>20:1
12	$Er(OTf)_3$	toluene	45	>20:1
13	$La(OTf)_3$	toluene	trace	
14	$Ni(OTf)_2$	toluene	92	>20:1
15	$NiBr_2$	toluene	NR	
16	$Ni(acac)_2$	toluene	NR	
17	$(Ph_3P)_2NiCl_2$	toluene	NR	
18[e]	$Ni(OTf)_2$	toluene	43	>20:1
19[f]	$Ni(OTf)_2$	toluene	91	>20:1
20[e]	$Ni(OTf)_2$	THF	NR	
21	$Ni(OTf)_2$	DCE	68	>20:1
22	$Ni(OTf)_2$	DMF	NR	
23	$Ni(OTf)_2$	MeCN	NR	
24[g]	$Ni(OTf)_2$	toluene	86	>20:1

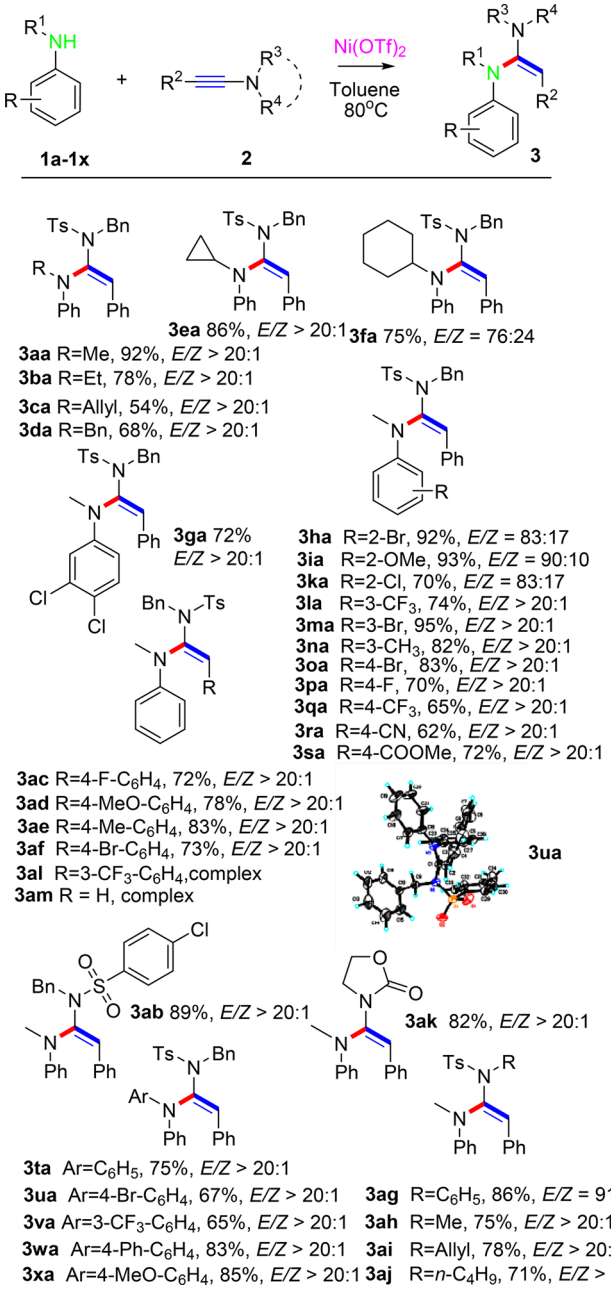
[a]The reactions were performed with **1a** (0.4 mmol), **2a** (0.6 mmol), and the catalyst (0.04 mmol) in dry solvent (2 mL) at 80 °C for 15 min to 1 h. [b]Isolated yield. NR = no reaction. [c]*E*/*Z* was determined by ^{1}H NMR and HPLC. [d]0.8 mmol of the base was used. [e]The reaction temperature was 60 °C. [f]The reaction temperature was 110 °C. [g]The reaction was performed with **1a** (2.8 mmol), **2a** (4.2 mmol), and $Ni(OTf)_2$ (0.28 mmol) in anhydrous toluene (14 mL) at 80 °C for 1h.

DCE, the yield was reduced. Polar solvents, such as THF, DMF, and MeCN, were unsuitable for this hydroamination reaction. Notably, a gram-scale reaction was performed under optimal reaction conditions, and the desired product **3aa** was obtained in 86% yield with excellent regioselectivity (*E*/*Z* > 20:1, Table 1, entry 24).

Next, we turned to investigate the scope and limitation of such hydroamination of secondary amines **1a**−**1x** with ynamides **2** (Scheme 1). First, the reactions of TsNBn-type ynamides with *N*-substituted (alkyl, allyl, and benzyl) anilines **1a**−**1f** were surveyed under the optimized conditions, and the results were summarized in Scheme 1. *N*-Methyl- and *N*-ethyl-substituted anilines **1a** and **1b** could smoothly react with ynamide **2a**, producing the desired products **3aa**−**3ba** in excellent yields with high regioselectivities. *N*-Allyl and *N*-benzyl-substituted anilines could give corresponding products **3ca** and **3da** in moderate yields, together with excellent regioselectivities. Larger substitutions like *N*-cyclopropyl and *N*-cyclohexyl groups were also tolerated, albeit with a slight

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

Scheme 1. Reactions of Secondary Amines with Ynamides[a,b,c]

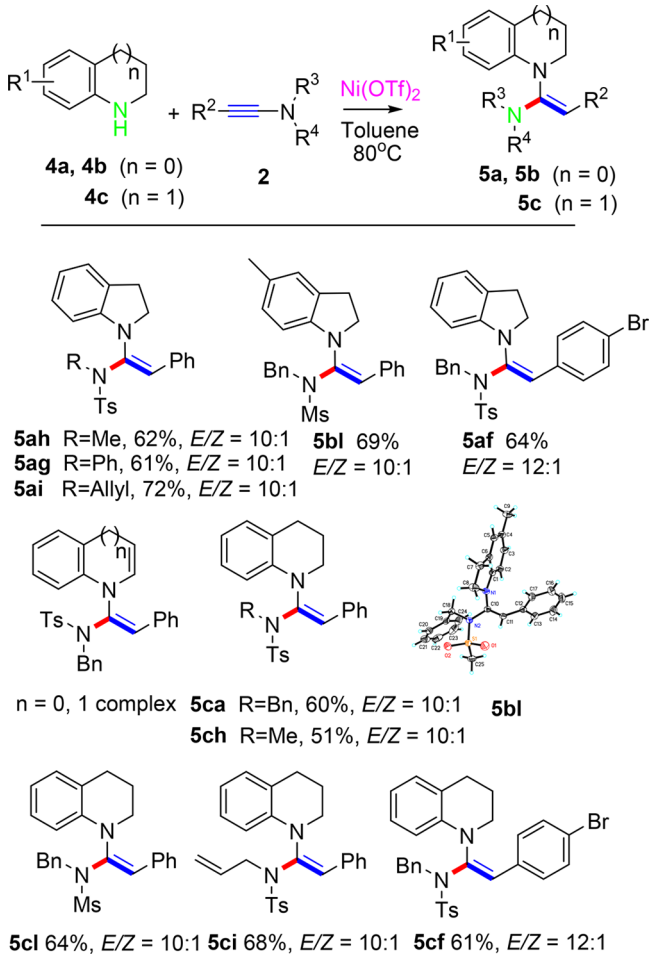


[a]The reaction was performed with **1** (0.4 mmol), **2** (0.6 mmol), and $Ni(OTf)_2$ (0.04 mmol) in anhydrous toluene (2 mL) for 15 min to 1 h at 80 °C. [b]Isolated yield. [c]*E*/*Z* was determined by ^1H NMR and HPLC.

decrease in regioselectivity for **3fa**. Then, various substitutions at the phenyl ring of *N*-methylaniline were investigated under the optimized conditions. The results showed that all these substituted *N*-methyl anilines **1g**−**1s** could react with ynamide **2a**, affording the desired products **3ga**−**3sa** in excellent regioselectivities. The *para*-electron-withdrawing substitutions (**1p**−**1s**) generally led to slightly decreased yields. Diarylamines **1t**−**1x** were also examined, and the desired products **3ta**−**3xa** were produced in moderate yields with excellent regioselectivities. Finally, different substituted ynamides **2c**−**2j** were evaluated, and the desired products **3ac**−**3aj** were obtained in moderate yields with excellent regioselectivities. The reaction of *N*-methylaniline **1a** with the ynamide containing *m*-trifluoromethyl **2l** is complex. We also tried the reaction of *N*-Methylaniline **1a** and ynamides containing terminal alkyne **2m**, but the result was complex. In addition, the replacement of the Ts group in ynamides with *p*-chlorobenzenesulfonyl or oxazolidin-2-one also gave positive results under the optimized conditions, and the desired products **3ab** and **3ak** were obtained in moderate yields with satisfactory regioselectivities. It is worth noting that non-aromatic secondary amines such as *N*-methylpentane-1-amine and pyrrolidine were not suitable for this hydroamination reaction. The chemical structures of **3aa**−**3ak**, **3ba**−**3xa** were unambiguously confirmed by the result of X-ray crystallographic analysis of compound **3ua** (see the Supporting Information).

Next, we turned our attention to investigate the hydroamination of bicyclic secondary amines **4** with ynamides **2** (Scheme 2). When indolines **4a** and **4b** were applied, the desired products **5ah** and **5bl** were obtained in moderate yields with 10:1 *E*/*Z* selectivities (Scheme 2). Other ynamides **2g**, **2i**, and **2f** also led to similar results. Notably, both 1*H*-indole and

Scheme 2. Reactions of Indolines and Tetrahydroquinoline with Ynamides[a,b,c]



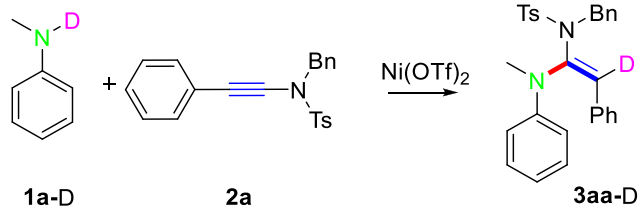
[a]The reaction was performed with **4** (0.4 mmol), **2** (0.6 mmol), and $Ni(OTf)_2$ (0.04 mmol) in anhydrous toluene (2 mL) for 15 min to 1 h at 80 °C. [b]Isolated yield. [c]*E*/*Z* was determined by ^1H NMR and HPLC.

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

1,4-dihydroquinoline failed to obtain the desired products due to the complex reaction system. When tetrahydroquinoline **4c** was used, the desired **5ca**−**5cf** were obtained in moderate yields and mostly with 10:1 *E*/*Z* selectivities. We think that steric hindrance and ring tension of bicyclic secondary amines have a significant effect on stereoselectivity. According to the experimental X-ray crystallographic analysis of compound **5bl**, the chemical structures of **5ah**−**5cf** were unambiguously determined (see the Supporting Information).

To verify this process, **2a** was subjected to the standard reaction conditions with deuterated *N*-methylaniline **1a-D**,[27] and the desired isotope-substituted product **3aa-D** was isolated (Scheme 3). This showed that the proton for hydroamination came from secondary amines (see the Supporting Information).

Scheme 3. Deuterium Labeling Experiment[a]



[a]The reaction was performed with **1a-D** (0.4 mmol), **2a** (0.6 mmol), and $Ni(OTf)_2$ (0.04 mmol) in anhydrous toluene (2 mL) for 1 h at 80 °C, 26% for **3aa-D**, 66% for **3aa**, *E*/*Z* > 20:1.

As shown in Figure 3, a plausible mechanism was proposed for this $Ni(OTf)_2$-catalyzed transformation based on the above

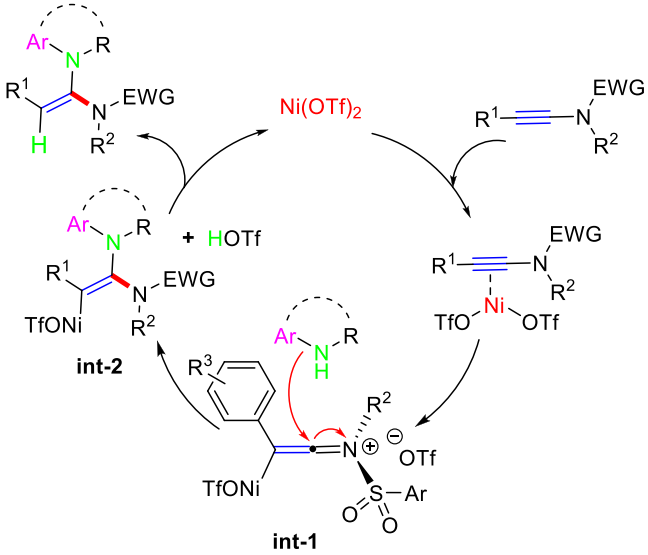


Figure 3. Proposed reaction mechanism.

experimental results and the known ynamide chemistry.[12,24] In brief, the activation of the alkyne bond in **2** led to a vinyl Ni(II) intermediate **int-1**, which was further attacked by secondary amines from the less steric side to give **int-2**. The subsequent protonation could readily afford the desired product, along with the release of $Ni(OTf)_2$ into the catalytic cycle.

CONCLUSIONS

In summary, a new method for the hydroamination of ynamides **2** with secondary amines (**1** and **4**) has been developed through the catalysis of Lewis acid $Ni(OTf)_2$. This facile and convenient process could afford substituted ethene-1,1-diamine compounds **3aa**−**3ak**, **3ba**−**3xa**, and **5ah**−**5cf** in moderate to excellent yields with high regioselectivities.

EXPERIMENTAL SECTION

General. Toluene was dried with calcium chloride and distilled. THF was treated with sodium metal. All reactions were monitored by thin-layer chromatography (TLC). IR spectra were recorded using film on a Fourier transform infrared spectrometer. NMR spectra were tested at 400 or 600 MHz, and chemical shifts are reported in δ (ppm) referenced to the appropriate residual solvent peaks unless otherwise noted. HRMS were measured on an LTQ-Orbitrap-XL apparatus. The heat source was an oil bath. The secondary amines **1a**−**1x** and **4a**−**4c**, conventional solvents, and reagents are commercially available.

General Procedure for the Synthesis of Ynamides ***2***.[24e,28] A solution of an amide (2 mmol), K_3PO_4 (4 mmol), $CuSO_4{\cdot}5H_2O$ (0.2 mmol), and 1,10-phenanthroline (0.4 mmol) in dry toluene was added 1-bromoalkyne (2.2 mmol in toluene) under a nitrogen atmosphere. The reaction was stirred at 75 °C for 24 h. The heat source was an oil bath. The reaction mixture was cooled to room temperature, diluted with EtOAc, and filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The crude products were purified by using column chromatography on silica gel to afford the desired ynamide.

General Procedure for the Synthesis of 3 and 5. To a solution of $Ni(OTf)_2$ (0.04 mmol) and ynamides **2** (0.6 mmol) in anhydrous toluene (2 mL) under a N_2 atmosphere was added secondary amines **1** or **4** (0.4 mmol) at 80 °C. The heat source was an oil bath. After stirring for 15 min to 1 h, the reaction was quenched by aqueous $NaHCO_3$ and then extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure, and the residue was purified by using column chromatography on silica gel to give the desired products **3** or **5**.

Procedure for Synthesis of 3aa (Gram Scale). To a solution of $Ni(OTf)_2$ (0.28 mmol, 100 mg) and ynamide **2a** (4.2 mmol, 1.5 g) in anhydrous toluene (14 mL) under a N_2 atmosphere was added secondary amine **1a** (2.8 mmol, 0.30 mL) at 80 °C. The heat source was an oil bath. After stirring for 1 h, the reaction was quenched by aqueous $NaHCO_3$, extracted with EtOAc (20 mL × 3), and washed with brine. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure, and the residue was purified by using column chromatography on silica gel to give the desired products **3aa** (1.13 g, 86%, *E*/*Z* > 20:1, PE/EA = 15:1)

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)benzenesulfonamide (**3aa**):* colorless oil (172 mg, 92%, PE/EA = 15:1); IR (film) ν_{max} 3449, 2925, 1634, 1496, 1346, 1161, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.77−7.72 (m, 2H), 7.44−7.40 (m, 2H), 7.32−7.27 (m, 3H), 7.23−7.20 (m, 2H), 7.13−7.09 (m, 2H), 7.07−7.03 (m, 1H), 7.01−6.96 (m, 4H), 6.71−6.66 (m, 1H), 6.64−6.59 (m, 2H), 6.03 (s, 1H), 4.61−4.56 (m, 2H), 2.59 (s, 3H), 2.43 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.6, 143.8, 129.7, 128.2, 128.1, 128.0, 127.4, 127.1, 119.1, 116.1, 115.4, 51.2, 36.4, 21.0 ppm; HRMS (ESI-Orbitrap) *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{29}N_2O_2S^+$ 469.1944, found 469.1947.

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)benzenesulfonamide (**3aa-D**).* To a solution of $Ni(OTf)_2$ (0.04 mmol) and ynamide **2a** (0.6 mmol) in anhydrous toluene (2 mL) under a N_2 atmosphere was added secondary amine **1a-D** (0.4 mmol) at 80 °C. After stirring for 1 h, the reaction mixture was quenched with aqueous $NaHCO_3$ and extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine. Dried, filtered, and concentrated, the residue was purified by flash

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

chromatography on silica gel to give the desired product **3aa-D** (28% D): colorless oil (48 mg, 26%, PE/EA = 15:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76−7.70 (m, 2H), 7.43−7.39 (m, 2H), 7.31−7.25 (m, 3H), 7.22−7.18 (m, 2H), 7.13−7.07 (m, 2H), 7.07−7.01 (m, 1H), 7.00−6.94 (m, 4H), 6.69−6.66 (m, 1H), 6.63−6.57 (m, 2H), 6.01 (s, 0.72H), 4.60−4.56 (m, 2H), 2.57 (s, 3H), 2.42 (s, 3H) ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}DN_2O_2SNa^+$ 492.1827, found 492.1812.

*(E)-N-Benzyl-N-(1-(ethyl(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ba**):* colorless oil (150 mg, 78%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2090, 1597, 1480, 1136, 696 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.32−7.26 (m, 3H), 7.25−7.21 (m, 2H), 7.07−7.02 (m, 2H), 7.02−6.96 (m, 3H), 6.94−6.88 (m, 2H), 6.63−6.53 (m, 3H), 6.02 (s, 1H), 4.65−4.55 (m, 2H), 3.27−3.15 (m, 2H), 2.43 (s, 3H), 0.80 (t, J = 7.0 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.0, 143.9, 136.6, 136.2, 135.2, 134.1, 129.8, 128.4, 128.3, 128.3, 127.8, 127.6, 127.5, 127.4, 126.6, 119.0, 117.5, 115.4, 51.2, 42.5, 21.0, 12.9 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{30}N_2O_2SNa^+$ 505.1920, found 505.1925.

*(E)-N-(1-(Allyl(phenyl)amino)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide (**3ca**):* colorless oil (107 mg, 54%, PE/EA = 15:1); IR (film) ν_{max} 3372, 2084, 1637, 1495, 1347, 1160, 749, 695 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.31−7.26(m, 3H), 7.25−7.21 (m, 2H), 7.07−7.00 (m, 3H), 6.97−6.88 (m, 4H), 6.66−6.57 (m, 3H), 5.96 (s, 1H), 5.50−5.38 (m, 1H), 5.12 (dd, J = 17.4, 1.4 Hz, 1H), 5.02 (dd, J = 10.4, 1.2 Hz, 1H), 4.65−4.56 (m, 2H), 3.79 (d, J = 6.0 Hz, 2H), 2.43 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.1, 143.9, 136.4, 136.1, 135.9, 134.5, 134.1, 129.8, 128.4, 128.3, 128.2, 127.8, 127.6, 127.5, 126.7, 119.4, 117.5, 117.1, 116.2, 51.5, 51.0, 21.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{31}H_{30}N_2O_2SNa^+$ 517.1920, found 517.1923.

*(E)-N-Benzyl-N-(1-(benzyl(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3da**):* colorless oil (148 mg, 68%, PE/EA = 10:1); IR (film) ν_{max} 3442, 2089, 1631, 1495, 1347, 1159, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.25−7.21 (m, 5H), 7.19−7.17 (m, 2H), 7.16−7.13 (m, 5H), 7.01−6.97 (m, 3H), 6.96−6.92 (m, 2H), 6.92−6.88 (m, 2H), 6.69 (d, J = 8.0 Hz, 2H), 6.63 (dd, J = 8.0, 7.6 Hz, 1H), 5.97 (s, 1H), 4.65−4.62 (m, 2H), 4.54−4.51 (m, 2H), 2.39 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 145.2, 143.9, 139.1, 137.1, 136.6, 136.5, 134.0, 129.6, 129.0, 128.8, 128.6, 128.5, 128.4, 128.2, 127.8, 127.5, 127.0, 126.9, 120.2, 117.8, 116.9, 52.8, 52.3, 21.7 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{35}H_{32}N_2O_2SNa^+$ 567.2077, found 567.2077.

*(E)-N-Benzyl-N-(1-(cyclopropyl(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ea**).* colorless oil (170 mg, 86%, PE/EA = 15:1); IR (film) ν_{max} 3443, 2089, 1639, 1480, 1159, 694 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.18−7.14 (m, 5H), 7.13−7.08 (m, 2H), 7.07−7.01 (m, 5H), 6.83 (d, J = 7.6 Hz, 2H), 6.78−6.72 (m, 1H), 6.40 (s, 1H), 4.59−4.51 (m, 2H), 2.40 (s, 3H), 2.36−2.31 (m, 1H), 0.56−0.48 (m, 2H), 0.36−0.29 (m, 2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.6, 143.7, 136.7, 136.7, 134.3, 134.3, 129.6, 128.5, 128.3, 128.0, 127.7, 127.5, 127.2, 127.0, 120.9, 119.6, 115.4, 50.6, 30.1, 21.0, 8.8 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{31}H_{30}N_2O_2SNa^+$ 517.1920, found 517.1921.

*(E)-N-Benzyl-N-(1-(cyclohexyl(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3fa**):* colorless oil (161 mg, 75%, PE/EA = 15:1). E/Z = 76:24 in a mixture. The major peak in HPLC report (Supporting Information) is the stereochemistry of E: IR (film) ν_{max} 3418, 2083, 1633, 1346, 1160, 697 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 8.4 Hz, 2H, major), 7.57 (d, J = 8.0 Hz, 0.6H, minor), 7.43 (d, J = 8.0 Hz, 2H, major), 7.36−7.34 (m, 0.6H, minor), 7.34−7.28 (m, 5H, major), 7.25−7.22 (m, 1.5H, minor), 7.19−7.18 (m, 0.3H, minor), 7.18−7.16 (m, 1H, major), 7.13−7.07 (m, 1.2H, minor), 7.05−6.99 (m, 4H, major), 6.99−6.96 (m, 1.2H, minor), 6.95−6.93 (m, 0.3H, minor), 6.92−6.81 (m, 4H, major), 6.67−6.60 (m, 1H, major), 5.79 (s, 1H, major), 5.39 (s, 0.3H, minor), 4.62−4.58 (m, 2H, major), 3.49−3.40 (m, 1H, major), 3.05−2.99 (m, 0.3H, minor), 2.42 (s, 3H, major), 2.38 (s, 0.9H, minor), 1.58−1.45 (m, 4H, major), 1.44−1.41 (m, 1.2H, minor), 1.38−1.33 (m, 2H, major), 1.32−1.28 (m, 0.6H, minor), 1.13−1.07 (m, 0.9H, minor), 1.00−0.90 (m, 3H, major), 0.82−0.78 (m, 0.3H, minor), 0.77−0.67 (m, 1H, major) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 145.0 (minor), 143.8 (major), 143.7 (major), 143.6 (minor), 142.1 (minor), 138.3 (major),137.6 (minor), 137.0 (major), 136.2 (major), 136.1 (minor), 135.5 (minor), 135.0 (major), 130.0 (minor), 129.7 (major), 129.5 (minor), 128.7 (minor), 128.4 (major), 128.2 (minor), 128.1 (major), 127.9 (major), 127.7 (minor), 127.5 (major), 127.4 (major), 127.3 (minor), 127.1 (minor), 126.1 (major), 126.7, 124.6, 121.7 (major), 121.0 (minor), 57.6 (major), 57.1 (minor), 51.9 (minor), 51.4 (major), 30.8 (major), 25.9 (major), 25.7 (minor),, 25.2 (minor), 25.0 (major), 21.0 (major), 20.9 (minor) ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{34}H_{36}N_2O_2SNa^+$ 559.2390, found 559.2395.

*(E)-N-Benzyl-N-(1-((3,4-dichlorophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ga**):* colorless oil (154 mg, 72%, PE/EA = 15:1); IR (film) ν_{max} 3287, 2092, 1635, 1480, 1348, 1161, 697 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.31−7.26 (m, 3H), 7.24−7.21 (m, 2H), 7.16−7.09 (m, 3H), 7.08−7.06 (m, 1H), 6.90 (d, J = 7.2 Hz, 2H), 6.57 (d, J = 2.8 Hz, 1H), 6.45 (dd, J = 8.8, 2.8 Hz, 1H), 6.08 (s, 1H), 4.70−4.65 (m, 2H), 2.62 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.6, 144.0, 136.3, 136.2, 136.1, 133.9, 130.8, 129.8, 129.7, 128.3, 127.7, 127.3, 127.2, 127.2, 120.1, 117.7, 116.4, 115.0, 51.8, 35.9, 21.1 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{26}Cl_2N_2O_2SNa^+$ 559.0984, found 559.0985.

*(E)-N-Benzyl-N-(1-((2-bromophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ha**):* colorless oil (201 mg, 92%, PE/EA = 15:1), E/Z = 83:17 in a mixture. The major peak in HPLC report (Supporting Information) is the stereochemistry of E: IR (film) ν_{max} 3396, 2082, 1638, 1476, 1347, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.66 (m, 0.4H, minor), 7.65−7.62 (m, 2H, major), 7.49−7.46 (m, 1H, minor), 7.40−7.37 (m, 1H, minor), 7.32−7.27 (m, 5H, major), 7.25−7.21 (m, 5H, major), 7.20−7.19 (m, 2H, major), 7.18−7.17 (m, 0.4H, minor), 7.15−7.14 (m, 0.2H, minor), 7.12−7.07 (m, 2H, major), 6.95−6.89 (m, 1H, major), 6.83−6.80 (m, 0.4H, minor), 5.66 (s, 0.2H, minor), 5.35 (s, 1H, major), 4.63−4.61 (m, 2H, major), 3.09 (s, 3H, major), 2.90 (s, 0.6H, minor), 2.49 (s, 3H, major), 2.41 (s, 0.6H, minor) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 145.7 (minor), 145.3 (major), 143.8 (major), 143.4 (minor), 140.9 (major), 139.8 (minor), 137.4 (minor), 136.6 (major), 136.3 (minor), 135.7 (minor), 135.5 (major), 135.5 (major), 134.0 (minor), 134.0 (major), 130.5 (major), 129.7 (minor), 129.3 (major), 129.3 (minor), 129.0 (minor), 128.7 (major), 128.5 (major), 128.4 (minor), 128.2 (major), 128.2 (minor), 128.1 (major), 127.8 (major), 127.6 (minor), 127.5 (major), 126.2 (major), 125.7 (minor), 125.6 (major), 121.7 (minor), 119.7 (major), 112.2 (major), 111.9 (minor), 54.1 (major), 51.1 (minor), 40.5 (major), 40.0 (minor), 21.7 (major), 21.6 (minor) ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}BrN_2O_2SNa^+$ 569.0869, found 569.0869.

*(E)-N-Benzyl-N-(1-((2-methoxyphenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ia**):* colorless oil (185 mg, 93%, PE/EA = 15:1), E/Z = 90:10 in a mixture. The major peak in HPLC report (Supporting Information) is the stereochemistry of E: IR (film) ν_{max} 3395, 2957, 2076, 1627, 1499, 1346, 1161, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H, major), 7.39−7.34 (m, 0.2H, minor), 7.27−7.24 (m, 0.5H, minor), 7.22−7.19 (m, 5H, major), 7.19−7.16 (m, 2H, major), 7.15−7.14 (m, 0.2H, minor), 7.14−7.06 (m, 5H, major), 7.06−7.04 (m, 0.5H, minor), 7.04−7.00 (m, 1H, major), 7.00−6.99 (m, 0.1H, minor), 6.99−6.98 (m, 0.1H, minor), 6.96−6.93 (m, 1H, major), 6.93−6.90 (m, 0.1H, minor), 6.90−6.87 (m, 0.1H, minor), 6.81−6.76 (m, 1H, major), 6.66 (dd, J = 8.0, 1.2 Hz, 1H, major), 5.47 (s, 0.1H, minor), 5.43 (s, 1H, major), 4.55−4.52 (m, 2H, major), 3.81 (s, 0.3H, minor), 3.57 (s, 3H, major), 2.87 (s, 3H, major), 2.69 (s, 0.3H, minor), 2.41 (s, 3H, major), 2.33 (s, 0.3H, minor) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.3 (minor), 153.1 (major), 143.5 (major), 143.0

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

(minor), 141.5 (major), 141.5 (minor), 137.9 (minor), 137.7 (major), 137.3 (minor), 136.8 (major), 136.3 (major), 136.0 (minor), 135.0 (major), 130.6 (minor), 129.2 (major), 129.1 (minor), 128.4 (major), 128.4 (major), 128.2 (major), 128.1 (minor), 128.1 (minor), 128.0 (minor), 127.8 (major), 127.8 (major), 127.2 (major), 126.9 (minor), 126.1 (minor), 125.6 (major), 125.5 (minor), 125.3 (major), 124.5 (major), 121.4 (minor), 120.9 (major), 112.1 (minor), 111.4 (major), 110.5 (major), 110.3 (minor), 55.5 (minor), 54.9 (major), 52.6 (major), 52.0 (minor), 39.9 (major), 39.0 (minor), 22.7 (minor), 21.7 (major) ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{30}N_2O_3SNa^+$ 521.1869, found 521.1868.

*(E)-N-Benzyl-N-(1-((2-chlorophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ka**):* colorless oil (140 mg, 70%, PE/EA = 15:1). E/Z = 83:17 in a mixture. The major peak in HPLC report (Supporting Information) is the stereochemistry of E: IR (film) ν_{max} 3442, 2090, 1629, 1480, 1348, 1162, 698 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68−7.62 (m, 2H, major), 7.48−7.45 (m, 0.4H, minor), 7.44−7.41 (m, 2H, major), 7.41−7.39 (m, 0.4H, minor), 7.37−7.29 (m, 1H, minor), 7.29−7.21 (m, 5H, major), 7.19−7.17 (m, 1H, minor), 7.16−7.12 (m, 5H, major), 7.07−7.05 (m, 0.6H, minor), 7.05−7.00 (m, 3H, major), 6.99−6.94 (m, 1H, major), 6.92−6.90 (m, 0.2H, minor), 5.46 (s, 0.2H, minor), 5.33 (s, 1H, major), 4.57−4.50 (m, 2H, major), 2.87 (s, 3H, major), 2.57 (s, 0.6H, minor), 2.43 (s, 3H, major), 2.36 (s, 0.6H, minor) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.0 (major), 143.8 (minor), 143.4 (minor), 143.3 (major), 140.2 (major), 139.5 (minor), 136.9 (major), 135.7 (minor), 135.3 (minor), 134.8 (major),134.5 (major), 130.6 (minor), 130.4 (major), 130.2 (minor), 130.0 (major), 129.5 (major), 128.5 (minor), 128.4 (minor), 128.2 (minor), 128.0 (major), 127.9 (major), 127.7 (major), 127.6 (minor), 127.5 (major), 127.5 (major), 127.3 (minor), 127.2 (minor), 127.1 (major), 126.1 (major), 126.0 (minor), 125.7 (minor), 124.8 (major),111.9 (major), 110.9 (minor), 53.1 (major), 50.7 (minor), 26.3 (minor), 21.1 (major) ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}ClN_2O_2SNa^+$ 525.1374, found 525.1378.

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(3-(trifluoromethyl)phenyl)-amino)-2-phenylvinyl)benzenesulfonamide (**3la**):* colorless oil (159 mg, 74%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2083, 1636, 1339, 1162, 663 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 2H), 7.27−7.23 (m, 5H), 7.22−7.18 (m, 2H), 7.06−6.98 (m, 4H), 6.90−6.85 (m, 3H), 6.72−6.64 (m, 2H), 6.00 (s, 1H), 4.67−4.63 (m, 2H), 2.72 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.4, 137.2, 136.3, 134.5, 131.0 (C−F, $^1J_{C-F}$ = 31.0 Hz), 129.7, 129.0, 128.6, 128.3, 128.0, 127.8, 127.6, 127.2, 124.2 (C−F, $^2J_{C-F}$ = 271.0 Hz), 118.6, 117.8, 115.9 (C−F, $^3J_{C-F}$ = 3.0 Hz), 112.0 (C−F, $^2J_{C-F}$ = 3.0 Hz), 52.7, 36.5, 21.7 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −60.9 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{27}F_3N_2O_2SNa^+$ 559.1638, found 559.1635.

*(E)-N-Benzyl-N-(1-((3-bromophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ma**):* colorless oil (207 mg, 95%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2924, 2105, 1635, 1481, 1347, 698 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.31−7.25 (m, 3H), 7.24−7.19 (m, 2H), 7.14−7.08 (m, 2H), 7.07−7.01 (m, 1H), 6.96−6.91 (m, 2H), 6.90−6.84 (m, 1H), 6.80−6.75 (m, 1H),6.68−6.64 (m, 1H), 6.52 (dd, J = 8.4, 1.6 Hz, 1H), 6.06 (s, 1H), 4.71−4.58 (m, 2H), 2.60 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 146.1, 143.9, 136.4, 136.3, 136.2, 134.1, 129.9, 129.8, 128.2, 128.1, 127.6, 127.3, 127.1, 127.0, 121.8, 121.5, 117.6, 117.4, 113.9, 51.6, 36.0, 21.1 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}BrN_2O_2SNa^+$ 569.0869, found 569.0871.

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(m-tolyl)amino)-2-phenylvinyl)benzenesulfonamide (**3na**):* colorless oil (158 mg, 82%, PE/EA = 15:1); IR (film) ν_{max} 3652, 3341, 2105, 1493, 1346, 1160, 697 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.33−7.25 (m, 3H), 7.19−7.16 (m, 2H), 7.14−7.09 (m, 2H), 7.05−7.01 (m, 1H), 6.98−6.94 (m, 2H), 6.90−6.85 (m, 1H), 6.50 (d, J = 7.6 Hz, 1H), 6.44−6.33 (m, 2H), 5.99 (s, 1H), 4.60−4.51 (m, 2H), 2.58 (s, 3H), 2.41 (s, 3H), 2.05 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 153.4, 144.6, 143.8, 137.5, 137.4, 136.5, 136.5, 134.6, 129.7, 128.3, 128.2, 128.1, 127.9, 127.4, 127.1, 126.6, 120.2, 116.1, 112.6, 51.1, 36.6, 21.2, 21.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{30}N_2O_2SNa^+$ 505.1920, found 505.1921.

*(E)-N-Benzyl-N-(1-((4-bromophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3oa**):* colorless oil (181 mg, 83%, PE/EA = 15:1); IR (film) ν_{max} 3419, 2102, 1635, 1491, 1161, 698 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.30−7.25 (m, 3H), 7.24−7.21 (m, 2H), 7.14−7.05 (m, 5H), 6.05−6.90 (m, 2H), 6.48 (dd, J = 7.2, 2.0 Hz, 2H), 6.04 (s, 1H), 4.66−4.58 (m, 2H), 2.57 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 144.0, 143.9, 136.7, 136.3, 136.3, 134.2, 130.8, 129.8, 128.2, 128.2, 128.1, 127.5, 127.3, 127.1, 126.9, 117.1, 116.8, 110.5, 51.6, 36.1, 21.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}BrN_2O_2SNa^+$ 569.0869, found 569.0867.

*(E)-N-Benzyl-N-(1-((4-fluorophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3pa**):* colorless oil (136 mg, 70%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2084, 1633, 1508, 1346, 1161, 665 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.32−7.25 (m, 3H), 7.24−7.20 (m, 2H), 7.14−7.07 (m, 2H), 7.05−6.99 (m, 1H), 6.93 (d, J = 7.2 Hz, 2H), 6.83−6.74 (m, 2H), 6.62−6.54 (m, 2H), 5.97 (s, 1H), 4.65−4.57 (m, 2H), 2.58 (s, 3H), 2.41 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 156.0 (C−F, $^1J_{C-F}$ = 234.7 Hz), 143.8, 141.2, 137.5, 136.4 (C−F, $^4J_{C-F}$ = 4.1 Hz), 134.4, 129.7, 128.2, 128.1, 127.5, 127.4, 127.1, 126.6, 117.0 (C−F, $^3J_{C-F}$ = 7.5 Hz), 115.6, 114.7 (C−F, $^2J_{C-F}$ = 22.1 Hz), 51.5, 36.6, 21.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −125.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{29}H_{27}FN_2O_2SNa^+$ 509.1670, found 509.1672.

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(4-(trifluoromethyl)phenyl)-amino)-2-phenylvinyl)benzenesulfonamide (**3qa**):* colorless oil (139 mg, 65%, PE/EA = 15:1); IR (film) ν_{max} 3561, 2084, 1634, 1495, 1352, 1161, 665 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.31−7.24 (m, 5H), 7.24−7.20 (m, 2H), 7.15−7.04 (m, 3H), 6.94 (d, J = 7.6 Hz, 2H), 6.63 (d, J = 8.4 Hz, 2H), 6.16 (s, 1H), 4.72−4.65 (m, 2H), 2.66 (s, 3H), 2.40 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 147.7, 143.9, 136.3 (C−F, $^3J_{C-F}$ = 2.0 Hz), 133.9, 129.7, 128.7, 128.2, 128.2, 127.5, 127.3, 127.2, 127.1, 125.4 (C−F, $^3J_{C-F}$ = 2.0 Hz), 124.7 (C−F, $^2J_{C-F}$ = 268.9 Hz), 118.8 (C−F, $^1J_{C-F}$ = 31.9 Hz), 118.1, 114.5, 51.9, 36.1, 20.9 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −59.7 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{27}F_3N_2O_2SNa^+$ 559.1638, found 559.1639.

*(E)-N-Benzyl-N-(1-((4-cyanophenyl)(methyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ra**):* colorless oil (122 mg, 62%, PE/EA = 15:1); IR (film) ν_{max} 3350, 2215, 1644, 1346, 1161, 699 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.33−7.27 (m, 5H), 7.25−7.21 (m, 2H), 7.14−7.05 (m, 3H), 6.94−6.87 (m, 2H), 6.57 (d, J = 9.2 Hz, 2H), 6.19 (s, 1H), 4.72−4.64 (m, 2H), 2.65 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 148.2, 144.0, 136.1, 136.1, 135.5, 133.7, 132.5, 129.9, 128.4, 128.3, 128.3, 127.7, 127.3, 127.3, 119.6, 118.9, 114.8, 99.7, 51.8, 35.7, 21.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{30}H_{27}N_3O_2SNa^+$ 516.1716, found 516.1717.

*Methyl-(E)-4-((1-((N-benzyl-4-methylphenyl)sulfonamido)-2-phenylvinyl)(methyl)amino)benzoate (**3sa**):* colorless oil (151 mg, 72%, PE/EA = 8:1); IR (film) ν_{max} 3442, 2084, 1637, 1433, 1278, 664 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.30−7.24 (m, 5H), 7.11−7.06 (m, 2H), 7.05−7.01 (m, 1H), 6.95−6.90 (m, 2H), 6.55 (d, J = 9.2 Hz, 2H), 6.17 (s, 1H), 4.73−4.61 (m, 2H), 3.72 (s, 3H), 2.66 (s, 3H), 2.40 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 165.9, 148.7, 143.9, 136.3, 136.2, 136.0, 129.9, 129.8, 128.3, 128.2, 128.2, 127.6, 127.3, 127.2, 127.2, 119.4, 118.4, 114.1, 51.7, 51.4, 35.8, 21.0 ppm; HRMS (ESI-Orbitrap) m/z [M + Na]$^+$ calcd for $C_{31}H_{30}N_2O_4SNa^+$ 549.1819, found 549.1822.

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

*(E)-N-Benzyl-N-(1-(diphenylamino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ta**):* white solid (159 mg, 75%, PE/EA = 10:1); mp 127−128 °C; IR (film) ν_{max} 3321, 2959, 1739, 1689, 1525, 1367, 1179, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.35−7.32 (m, 3H), 7.32−7.27 (m, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.13−7.09 (m, 2H), 7.08−7.02 (m, 5H), 7.02−6.97 (m, 2H), 6.95−6.89 (m, 2H), 6.87−6.82 (m, 4H), 6.27 (s, 1H), 4.63−4.58 (m, 2H), 2.48 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.1, 143.7, 137.0, 136.9, 136.1, 134.3, 129.4, 128.8, 128.6, 128.4, 128.3, 127.6, 127.6, 127.5, 126.6, 123.2, 123.1, 117.1, 51.5, 21.6 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{34}H_{30}N_2O_2SNa^+$ 553.1920, found 553.1920.

*(E)-N-Benzyl-N-(1-((4-bromophenyl)(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3ua**):* white solid (163 mg, 67%, PE/EA = 15:1); mp 121−122 °C; IR (film) ν_{max} 3448, 2089, 1636, 1487, 990, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.31−7.26 (m, 3H), 7.21−7.16 (m, 2H), 7.11−7.08 (m, 3H), 7.08−7.04 (m, 3H), 7.03−6.94 (m, 4H), 6.79 (d, J = 8.0 Hz, 2H), 6.55 (d, J = 9.2 Hz, 2H), 6.18 (s, 1H), 4.55−4.48 (m, 2H), 2.42 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 143.8, 143.1, 142.8, 136.5, 136.0, 134.9, 133.5, 131.3, 129.7, 129.0, 128.3, 128.0, 127.7, 127.6, 127.5, 127.0, 126.9, 123.8, 123.7, 123.0, 117.5, 114.3, 51.2, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{34}H_{29}BrN_2O_2SNa^+$ 631.1025, found 631.1024.

*(E)-N-Benzyl-4-methyl-N-(2-phenyl-1-(phenyl(3-(trifluoromethyl)phenyl)amino)vinyl)benzenesulfonamide (**3va**):* white solid (155 mg, 65%, PE/EA = 15:1); mp 119−120 °C; IR (film) ν_{max} 3417, 2106, 1632, 1493, 1333, 1162, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.28−7.23 (m, 5H), 7.18−7.12 (m, 3H), 7.09−7.03 (m, 2H), 7.02−6.96 (m, 5H), 6.95−6.92 (m, 2H), 6.66 (d, J = 8.4 Hz, 1H), 6.63−6.59 (m, 1H), 6.17 (s, 1H), 4.57−4.44 (m, 2H), 2.42 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.9, 144.0, 142.0, 136.1, 135.9, 135.0, 133.5, 129.8, 129.5, 129.3, 129.1 (C−F, $^1J_{C-F}$ = 31.4 Hz), 128.3, 128.0, 127.7, 127.6, 126.9, 125.2, 124.6, 123.8, 123.7 (C−F, $^2J_{C-F}$ = 271.1 Hz), 117.8 (C−F, $^3J_{C-F}$ = 3.8 Hz), 117.5, 116.7 (C−F, $^3J_{C-F}$ = 3.8 Hz), 51.2, 21.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −56.9 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{35}H_{29}F_3N_2O_2SNa^+$ 621.1794, found 621.1795.

*(E)-N-(1-([1,1′-Biphenyl]-4-yl(phenyl)amino)-2-phenylvinyl)-N-benzyl-4-methylbenzenesulfonamide (**3wa**):* colorless oil (201 mg, 83%, PE/EA = 15:1); IR (film) ν_{max} 3425, 2920, 2082, 1632, 1488, 1160, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.4 Hz, 2H), 7.49−7.44 (m, 2H), 7.41−7.35 (m, 2H), 7.31−7.27 (m, 3H), 7.27−7.23 (m, 3H), 7.23−7.19 (m, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.08−7.05 (m, 2H), 7.04−6.99 (m, 2H), 6.98−6.87 (m, 4H), 6.85−6.79 (m, 4H), 6.24 (s, 1H), 4.60−4.55 (m, 2H), 2.38 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.1, 143.8, 143.5, 140.6, 137.0, 137.0, 136.0, 135.9, 134.3, 129.5, 128.9, 128.8, 128.7, 128.5, 128.3, 127.7, 127.6, 127.4, 127.0, 126.8, 126.7, 123.4, 123.3, 117.6, 51.7, 21.6 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{40}H_{34}N_2O_2SNa^+$ 629.2233, found 629.2231.

*(E)-N-Benzyl-N-(1-((4-methoxyphenyl)(phenyl)amino)-2-phenylvinyl)-4-methylbenzenesulfonamide (**3xa**):* colorless oil (190 mg, 85%, PE/EA = 15:1); IR (film) ν_{max} 3396, 3063, 2047, 1630, 1348, 747 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.54 (d, J = 8.0 Hz, 2H), 7.35−7.26 (m, 5H), 7.23−7.17(m, 2H), 7.09−7.03 (m, 2H), 7.02−6.92 (m, 3H), 6.90−6.80 (m, 4H), 6.74−6.63 (m, 3H), 6.47 (d, J = 7.6 Hz, 2H), 6.08 (s, 1H), 4.56−4.45 (m, 2H), 3.72 (s, 3H), 2.41 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 156.3, 144.7, 143.7, 136.7, 136.1, 135.6, 135.3, 133.8, 129.6, 128.3, 128.3, 127.9, 127.6, 127.6, 127.4, 127.0, 126.6, 125.9, 121.3, 119.9, 116.6, 114.4, 55.2, 51.0, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{35}H_{32}N_2O_3SNa^+$ 583.2026, found 583.2026.

*(E)-N-Benzyl-4-chloro-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)benzenesulfonamide (**3ab**):* white solid (174 mg, 89%, PE/EA = 15:1); mp 116−117 °C; IR (film) ν_{max} 3442, 2090, 1634, 1496, 1350, 1162, 695 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.81 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.33−7.27 (m, 3H), 7.26−7.22 (m, 2H), 7.13−7.09 (m, 2H), 7.06−6.94 (m, 5H), 6.72−6.65 (m, 1H), 6.59 (d, J = 8.0 Hz, 2H), 6.02 (s, 1H), 4.72−4.61 (m, 2H), 2.61 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.6, 138.2, 138.1, 137.4, 136.3, 134.3, 129.4, 129.3, 129.1, 129.0, 128.5, 128.3, 128.1, 127.6, 127.4, 127.1, 126.8, 126.3, 119.4, 116.4, 115.4, 51.8, 36.7 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{28}H_{25}ClN_2O_2SNa^+$ 511.1218, found 511.1217.

*(E)-N-Benzyl-N-(2-(4-fluorophenyl)-1-(methyl(phenyl)amino)-vinyl)-4-methylbenzenesulfonamide (**3ac**):* white solid (140 mg, 72%, PE/EA = 15:1); mp 113−114 °C; IR (film) ν_{max} 3442, 2922, 2104, 1632, 1347, 1160, 698 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.31−7.25 (m, 3H), 7.22−7.17 (m, 2H), 7.01−6.97 (m, 3H), 6.96−6.89 (m, 3H), 6.71−6.63 (m, 1H), 6.57 (d, J = 8.0 Hz, 2H), 6.01 (s, 1H), 4.60−4.52 (m, 2H), 2.57 (s, 3H), 2.42 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 160.7 (C−F, $^1J_{C-F}$ = 242.9 Hz), 144.6, 143.8, 137.0, 136.5, 136.4, 131.0 (C−F, $^4J_{C-F}$ = 3.0 Hz), 129.8, 129.0 (C−F, $^3J_{C-F}$ = 8.0 Hz), 128.4, 128.2, 128.1, 127.5, 127.4, 119.4, 115.4, 115.0 (C−F, $^2J_{C-F}$ = 21.2 Hz), 114.9, 51.1, 36.1, 21.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.9 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{29}H_{27}FN_2O_2SNa^+$ 509.1670, found 509.1671.

*(E)-N-Benzyl-N-(2-(4-methoxyphenyl)-1-(methyl(phenyl)amino)-vinyl)-4-methylbenzenesulfonamide (**3ad**):* yellow oil (155 mg, 78%, PE/EA = 15:1); IR (film) ν_{max} 3441, 2090, 1637, 1245, 1025, 990, 663 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.31−7.24 (m, 3H), 7.21−7.16 (m, 2H), 7.02−6.95 (m, 2H), 6.93 (d, J = 8.8 Hz, 2H), 6.72−6.65 (m, 3H), 6.58 (d, J = 8.0 Hz, 2H), 6.01 (s, 1H), 4.58−4.51 (m, 2H), 3.64 (s, 3H), 2.59 (s, 3H), 2.41 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 158.1, 144.7, 143.7, 136.6, 135.5, 135.1, 129.7, 128.6, 128.4, 128.2, 128.0, 127.4, 126.8, 118.9, 116.9, 114.9, 113.7 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{30}H_{30}N_2O_3SNa^+$ 521.1869, found 521.1872.

*(E)-N-Benzyl-4-methyl-N-(1-(methyl(phenyl)amino)-2-(p-tolyl)-vinyl)benzenesulfonamide (**3ae**):* white solid (160 mg, 83%, PE/EA = 15:1); mp 105−106 °C; IR (film) ν_{max} 3374, 1633, 1510, 1347, 1161, 748, 698 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.4 Hz, 2H), 7.42−7.38 (m, 2H), 7.29−7.25 (m, 3H), 7.20−7.16 (m, 2H), 7.00−6.96 (m, 2H), 6.94−6.90 (m, 2H), 6.88−6.84 (m, 2H), 6.67 (dd, J = 7.6, 6.8 Hz, 2H), 6.58 (d, J = 8.0 Hz, 2H), 5.99 (s, 1H), 4.57−4.53 (m, 2H), 2.57 (s, 3H), 2.42 (s, 3H), 2.16 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.7, 143.8, 136.6, 136.5, 136.3, 136.0, 131.5, 129.7, 128.8, 128.4, 128.2, 128.0, 127.4, 127.4, 127.1, 119.1, 116.6, 115.1, 51.1, 36.2, 21.0, 20.7 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{30}H_{30}N_2O_2SNa^+$ 505.1920, found 505.1923.

*(E)-N-Benzyl-N-(2-(4-bromophenyl)-1-(methyl(phenyl)amino)-vinyl)-4-methylbenzenesulfonamide (**3af**):* white solid (159 mg, 73%, PE/EA = 15:1); mp 96−97 °C; IR (film) ν_{max} 3442, 2085, 1633, 1495, 1090, 593 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.29−7.25 (m, 5H), 7.21−7.19 (m, 2H), 6.98 (dd, J = 8.4, 7.2 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.72−6.65 (m, 1H), 6.59 (d, J = 8.0 Hz, 2H), 5.97 (s, 1H), 4.59−4.52 (m, 2H), 2.57 (s, 3H), 2.41 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.5, 143.9, 137.9, 136.4, 136.2, 133.9, 131.0, 129.8, 129.0, 128.5, 128.2, 128.1, 127.5, 127.4, 119.6, 119.2, 115.7, 114.3, 51.3, 36.3, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{29}H_{27}BrN_2O_2SNa^+$ 569.0869, found 569.0873.

*(E)-4-Methyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)-N-phenylbenzenesulfonamide (**3ag**):* colorless oil (156 mg, 86%, PE/EA = 15:1), E/Z = 91:9 in a mixture. The major peak in the HPLC report (Supporting Information) is the stereochemistry of E: IR (film) ν_{max} 3367, 2922, 2091, 1642, 1354, 1206, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.53 (d, J = 8.4 Hz, 2H, major), 7.48−7.46 (m, 0.12H, minor), 7.43−7.39 (m, 2H, major), 7.36−7.35 (m, 0.12H, minor), 7.32−7.28 (m, 3H, major), 7.27−7.26 (m, 0.18H, minor), 7.24−7.23 (m, 0.12H, minor), 7.20 (d, J = 7.6 Hz, 2H, major), 7.18−7.17 (m, 0.18H, minor), 7.16−7.09 (m, 5H, major), 7.09−7.07 (m, 0.3H, minor), 7.06−7.00 (m, 2H, major), 6.95−6.89 (m, 0.12H, minor), 6.78−6.71 (m, 3H, major), 6.13 (s, 1H, major), 5.93 (s, 0.06H,

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

minor), 2.70 (s, 3H, major), 2.59 (s, 0.18H, minor), 2.40 (s, 3H, major), 2.34 (s, 0.18H, minor) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 154.3 (minor), 145.0 (major), 144.5 (major), 139.6 (major), 138.3 (major), 136.9 (major), 134.8 (major), 130.3 (major), 130.1 (minor), 129.8 (major), 129.3 (major), 129.0 (major), 128.9 (major), 128.1 (major), 127.9 (minor), 127.7 (major), 127.5 (major), 126.6 (minor), 124.0 (minor), 119.9 (major), 119.1 (major), 115.7 (major), 115.5 (major), 38.3 (major), 26.8 (minor), 21.5 (major) ppm; HRMS (ESI-Orbitrap) m/z $[M + H]^+$ calcd for $C_{29}H_{27}FN_2O_2SNa^+$, 509.1669, found 509.1672; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{28}H_{26}N_2O_2SNa^+$ 477.1607, found 477.1609.

*(E)-N,4-Dimethyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)-benzenesulfonamide (**3ah**):* colorless oil (117 mg, 75%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2090, 1635, 1349, 1164, 666 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.59 (d, J = 8.4 Hz, 2H), 7.37(d, J = 8.0 Hz, 2H), 7.22−7.14 (m, 4H), 7.13−7.05 (m, 3H), 6.81−6.77 (m, 2H), 6.77−6.75 (m, 1H), 5.67 (s, 1H), 3.04 (s, 3H), 2.94 (s, 3H), 2.40 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 145.1, 143.6, 140.8, 134.6, 129.6, 128.7, 128.3, 127.2, 127.0, 126.8, 119.1, 115.3, 114.9, 37.8, 37.5, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{23}H_{24}N_2O_2SNa^+$ 415.1451, found 415.1450.

*(E)-N-Allyl-4-methyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)benzenesulfonamide (**3ai**):* colorless oil (130 mg, 78%, PE/EA = 15:1); IR (film) ν_{max} 3443, 2082, 1635, 1347, 1161, 695 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.18−7.13 (m, 2H), 7.12−7.03 (m, 5H), 6.82 (d, J = 8.0 Hz, 2H), 6.76−6.69 (m, 1H), 5.95 (s, 1H), 5.87−5.72 (m, 1H), 5.22−5.11 (m, 2H), 4.01 (d, J = 6.0 Hz, 2H), 2.85 (s, 3H), 2.39 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.8, 143.6, 137.8, 136.5, 134.4, 133.7, 129.6, 128.5, 128.2, 127.3, 127.1, 126.7, 119.3, 118.4, 116.1, 115.4, 50.7, 36.9, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{25}H_{26}N_2O_2SNa^+$ 441.1607, found 441.1609.

*(E)-N-butyl-4-Methyl-N-(1-(methyl(phenyl)amino)-2-phenylvinyl)benzenesulfonamide (**3aj**).* colorless oil (123 mg, 71%, PE/EA = 15:1); IR (film) ν_{max} 3442, 2995, 2089, 1769, 1635, 1376, 1056, 628 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.18−7.13 (m, 2H), 7.12−7.04 (m, 5H), 6.83 (d, J = 7.6 Hz, 2H), 6.75−6.67 (m, 1H), 5.95 (s, 1H), 3.28 (dd, J = 8.2, 7.4 Hz, 2H), 2.87 (s, 3H), 2.41 (s, 3H), 1.57−1.45 (m, 2H), 1.23−1.14 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.8, 143.7, 137.2, 136.5, 134.5, 129.7, 128.6, 128.2, 127.4, 127.2, 126.8, 119.3, 116.1, 115.3, 47.5, 36.6, 30.5, 21.0, 19.3, 13.5 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}N_2O_2SNa^+$ 457.1920, found 457.1921.

*(E)-3-(1-(Methyl(phenyl)amino)-2-phenylvinyl)oxazolidin-2-one (**3ak**):* white solid (158 mg, 82%, PE/EA = 4:1); mp 98−99 °C; IR (film) ν_{max} 3562, 2083, 1754, 1645, 1448, 1211, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.29−7.25 (m, 5H), 7.23−7.22 (m, 1H), 7.18−7.12 (m, 1H), 6.86−6.81 (m, 2H), 6.82−6.79 (m, 1H), 6.20 (s, 1H), 4.25−4.19 (m, 2H), 3.66−3.58 (m, 2H), 3.03 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 155.4, 145.0, 136.1, 134.5, 129.2, 128.5, 127.1, 126.8, 119.0, 113.9, 113.8, 61.6, 44.2, 37.5 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{18}H_{18}N_2O_2Na^+$ 317.1261, found 317.1256.

*(E)-N-(1-(Indolin-1-yl)-2-phenylvinyl)-N,4-dimethylbenzenesulfonamide (**5ah**):* white solid (100 mg, 62%, E/Z = 10:1, PE/EA = 15:1); mp 98−99 °C; IR (film) ν_{max} 3443, 2089, 1632, 1484, 1156, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.19−7.14 (m, 2H), 7.12−7.04 (m, 4H), 6.91−6.85 (m, 1H), 6.74−6.67 (m, 1H), 6.22 (d, J = 7.6 Hz, 1H), 5.45 (s, 1H), 3.76 (dd, J = 9.0, 8.2 Hz, 2H), 3.11 (dd, J = 9.0, 8.2 Hz, 2H), 3.07 (s, 3H), 2.44 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.5, 143.8, 136.8, 135.2, 130.6, 129.5, 128.3, 128.1, 128.0, 127.0, 126.4, 124.7, 119.5, 113.1, 110.7, 50.5, 37.8, 28.5, 21.7 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{24}H_{24}N_2O_2SNa^+$ 427.1451, found 427.1453.

*(E)-N-(1-(Indolin-1-yl)-2-phenylvinyl)-4-methyl-N-phenylbenzenesulfonamide (**5ag**):* colorless oil (140 mg, 61%, E/Z = 10:1, PE/EA = 15:1); IR (film) ν_{max} 3442, 2083, 1635, 1485, 1165, 695 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.54 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.32−7.29 (m, 4H), 7.28−7.25 (m, 1H), 7.21−7.17 (m, 2H), 7.11−7.07 (m, 3H), 6.96 (d, J = 7.2 Hz, 1H), 6.78 (dd, J = 7.8, 7.0 Hz, 1H), 6.59−6.53 (m, 1H), 6.21 (d, J = 8.0 Hz, 1H), 5.92 (s, 1H), 3.61 (dd, J = 9.0, 8.2 Hz, 2H), 2.82 (dd, J = 9.0, 8.2 Hz, 2H), 2.42 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.6, 144.1, 138.5, 136.7, 134.5, 134.4, 130.0, 129.9, 129.0, 128.2, 127.9, 127.8, 127.7, 127.4, 126.5, 126.4, 124.4, 119.2, 114.0, 109.7, 50.1, 27.4, 21.1 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{29}H_{26}N_2O_2SNa^+$ 489.1607, found 489.1609.

*(E)-N-Allyl-N-(1-(indolin-1-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (**5ai**):* colorless oil (124 mg, 72%, E/Z = 10:1, PE/EA = 15:1); IR (film) ν_{max} 3456, 2923, 2109, 1633, 1484, 1398, 748 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.18−7.11 (m, 2H), 7.09−6.99 (m, 4H), 6.80−6.73 (m, 1H), 6.64−6.57 (m, 1H), 6.04 (d, J = 8.0 Hz, 1H), 5.87−5.72 (m, 1H), 5.61 (s, 1H), 5.15−5.05 (m, 2H), 3.99 (d, J = 6.4 Hz, 2H), 3.62 (dd, J = 9.4, 8.4 Hz, 2H), 3.03 (dd, J = 9.0, 8.2 Hz, 2H), 2.43 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.6, 143.8, 136.0, 134.6, 132.8, 130.0, 129.7, 128.1, 127.7, 127.4, 126.4, 126.3, 124.5, 119.3, 118.9, 115.1, 109.5, 51.5, 49.3, 27.4, 21.1 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{26}H_{26}N_2O_2SNa^+$ 453.1607, found 453.1604.

*(E)-N-Benzyl-N-(1-(5-methylindolin-1-yl)-2-phenylvinyl)-methanesulfonamide (**5bl**):* white solid (115 mg, 69%, E/Z = 10:1, PE/EA = 15:1); mp 129−130 °C.IR (film) ν_{max} 3443, 2085, 1632, 1493, 1339, 1149, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 5H), 7.19−7.13 (m, 2H), 7.12−7.02 (m, 3H), 6.95−6.89 (m, 1H), 6.68 (dd, J = 8.0, 0.4 Hz, 1H), 6.13 (d, J = 8.0 Hz, 1H), 5.77 (s, 1H), 4.52−4.48 (m, 2H), 3.67 (dd, J = 9.0, 8.2 Hz, 2H), 3.04 (dd, J = 9.0, 8.2 Hz, 2H), 2.91 (s, 3H), 2.21 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 142.6, 135.9, 135.0, 134.1, 130.5, 129.3, 129.1, 128.7, 128.2, 127.4, 126.4, 125.6, 113.5, 110.3, 52.1, 50.5, 42.0, 28.1, 20.8 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{25}H_{26}N_2O_2SNa^+$ 441.1607, found 441.1606.

*(E)-N-Benzyl-N-(2-(4-bromophenyl)-1-(indolin-1-yl)vinyl)-4-methylbenzenesulfonamide (**5af**):* colorless oil (143 mg, 64%, E/Z = 12:1, PE/EA = 15:1); IR (film) ν_{max} 3443, 2089, 1631, 1485, 1161, 702 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.73 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.31−7.29 (m, 1H), 7.28−7.25 (m, 4H), 7.21−7.17 (m, 2H), 7.04 (d, J = 7.2 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 6.72 (dd, J = 8.0, 7.2 Hz, 1H), 6.58 (dd, J = 7.8, 7.0 Hz, 1H), 5.75 (d, J = 8.0 Hz, 1H), 5.63 (s, 1H), 4.56−4.52 (m, 2H), 3.31−3.26 (m, 2H), 2.91 (dd, J = 8.8, 8.0 Hz, 2H), 2.45 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 144.4, 136.4, 136.1, 134.5, 134.0, 131.5, 130.6, 130.3, 130.0, 129.5, 128.7, 128.3, 128.0, 126.7, 125.0, 119.6, 119.3, 113.9, 110.0, 53.0, 49.5, 27.7, 21.6 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{30}H_{27}BrN_2O_2SNa^+$ 581.0869, found 581.0872.

*(E)-N-Benzyl-N-(1-(3,4-dihydroquinolin-1(2H)-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (**5ca**):* white solid (118 mg, 60%, E/Z = 10:1, PE/EA = 15:1); mp 137−138 °C; IR (film) ν_{max} 3519, 2083, 1632, 1493, 1159, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.26−7.22 (m, 4H), 7.22−7.19 (m, 3H), 7.13−7.03 (m, 5H), 6.92 (d, J = 7.6 Hz, 1H), 6.75−6.69 (m, 1H), 6.65−6.58 (m, 1H), 6.48 (dd, J = 8.2, 0.6 Hz, 1H), 6.03 (s, 1H), 4.66−4.58 (m, 2H), 3.17−3.03 (m, 2H), 2.66 (dd, J = 6.8, 6.0 Hz, 2H), 2.42 (s, 3H), 1.77−1.70 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.7, 140.6, 137.7, 137.2, 136.9, 135.2, 129.5, 129.2, 128.5, 128.4, 128.2, 128.1, 127.8, 127.6, 126.8, 126.7, 124.5, 119.2, 117.2, 116.1, 51.6, 47.8, 27.7, 21.9, 21.7 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{31}H_{30}N_2O_2SNa^+$ 517.1920, found 517.1923.

*(E)-N-(1-(3,4-Dihydroquinolin-1(2H)-yl)-2-phenylvinyl)-N,4-dimethylbenzenesulfonamide (**5ch**):* white solid (85 mg, 51%, E/Z = 10:1, PE/EA = 15:1); mp 123−124 °C; IR (film) ν_{max} 3442, 2939, 2091, 1631, 1493, 1172, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.4 Hz, 2H), 7.22−7.18 (m, 3H), 7.17−7.13 (m, 3H), 7.12−7.07 (m, 1H), 6.99−6.92 (m, 2H), 6.74−6.68 (m, 1H), 6.63 (dd, J = 8.4, 0.8 Hz, 1H), 5.73 (s, 1H), 3.34 (dd, J = 6.2, 5.4 Hz, 2H),

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

3.09 (s, 3H), 2.74 (dd, J = 6.8, 6.0 Hz, 2H), 2.40 (s, 3H), 2.06−1.85 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.6, 141.0, 140.4, 135.7, 135.3, 129.4, 129.3, 128.4, 127.6, 127.5, 126.9, 126.6, 124.9, 119.2, 116.2, 115.7, 48.9, 37.8, 27.6, 21.9, 21.6 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{25}H_{26}N_2O_2SNa^+$ 441.1607, found 441.1609.

*(E)-N-Benzyl-N-(1-(3,4-dihydroquinolin-1(2H)-yl)-2-phenylvinyl)-methanesulfonamide (**5cl**):* white solid (107 mg, 64%, E/Z = 10:1, PE/EA = 15:1); mp 122−123 °C; IR (film) ν_{max} 3442, 2084, 1633, 1493, 1339, 1148, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.38 (m, 2H), 7.37−7.29 (m, 3H), 7.20−7.15 (m, 4H), 7.12−7.07 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 7.00−6.94 (m, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.76−6.70 (m, 1H), 6.01 (s, 1H), 4.65−4.55 (m, 2H), 3.34−3.22 (m, 2H), 2.79−2.76 (m, 2H), 2.76 (s, 3H), 1.96−1.82 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.9, 138.4, 136.7, 135.0, 129.5, 128.8, 128.6, 128.4, 128.0, 127.7, 127.0, 126.9, 124.8, 119.7, 117.0, 116.3, 51.9, 48.6, 42.1, 27.5, 22.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{25}H_{26}N_2O_2SNa^+$ 441.1607, found 441.1608.

*(E)-N-Allyl-N-(1-(3,4-dihydroquinolin-1(2H)-yl)-2-phenylvinyl)-4-methylbenzenesulfonamide (**5ci**):* white solid (121 mg, 68%, E/Z = 10:1, PE/EA = 15:1); mp 101−102 °C; IR (film) ν_{max} 3442, 2089, 1634, 1493, 1346, 1160, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.16−7.11 (m, 4H), 7.10−7.03 (m, 1H), 6.95 (d, J = 7.2 Hz, 1H), 6.88−6.82 (m, 1H), 6.76−6.72 (m, 1H), 6.69−6.62 (m, 1H), 6.00 (s, 1H), 5.91−5.79 (m, 1H), 5.15 (dd, J = 7.6, 1.2 Hz, 1H), 5.13−5.09 (m, 1H), 4.05 (d, J = 6.0 Hz, 2H), 3.28 (dd, J = 6.2, 5.4 Hz, 2H), 2.72 (d, J = 6.8, 6.0 Hz, 2H), 2.41 (s, 3H), 1.94−1.82 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.7, 140.8, 137.5, 137.4, 135.1, 133.8, 129.5, 129.2, 128.3, 127.9, 127.8, 126.9, 126.6, 124.3, 119.2, 118.3, 117.2, 116.2, 50.9, 48.1, 27.6, 21.9, 21.6 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{27}H_{28}N_2O_2SNa^+$ 467.1764, found 467.1766.

*(E)-N-Benzyl-N-(2-(4-bromophenyl)-1-(3,4-dihydroquinolin-1(2H)-yl)vinyl)-4-methylbenzenesulfonamide (**5cf**):* white solid (140 mg, 61%, E/Z = 12:1, PE/EA = 15:1); mp 107−108 °C; IR (film) ν_{max} 3418, 2088, 1631, 1491, 1128, 701 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.74 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 7.27−7.23 (m, 3H), 7.21−7.16 (m, 2H), 6.96 (d, J = 8.4 Hz, 2H), 6.93−6.87 (m, 1H), 6.66−6.59 (m, 1H), 6.58−6.53 (m, 1H), 6.34 (dd, J = 8.0, 0.8 Hz, 1H), 5.99 (s, 1H), 4.70−4.49 (m, 2H), 2.92 (dd, J = 6.0, 5.2 Hz, 2H), 2.61 (dd, J = 6.6, 5.8 Hz, 2H), 2.41 (s, 3H), 1.67−1.60 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 143.9, 139.7, 136.8, 136.5, 136.3, 134.0, 131.0, 129.7, 129.1, 129.0, 128.2, 128.0, 127.5, 127.4, 126.0, 124.2, 119.3, 118.9, 115.1, 50.9, 46.8, 26.7, 21.0 ppm; HRMS (ESI-Orbitrap) m/z $[M + Na]^+$ calcd for $C_{31}H_{29}BrN_2O_2SNa^+$ 595.1025, found 595.1025.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02807.

NMR spectra for all compounds, HPLC reports, and structural data (PDF)

Accession Codes

CCDC 2041436, 2041437 contain 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.

■ AUTHOR INFORMATION

Corresponding Authors

Chang-Mei Si − *School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, Shanghai 201203, China*; Email: sicm@fudan.edu.cn

Bang-Guo Wei − *School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, Shanghai 201203, China*; orcid.org/0000-0003-3470-6741; Email: bgwei1974@fudan.edu.cn

Authors

Xiao-Di Nie − *School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, Shanghai 201203, China*

Xiao-Li Han − *School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, Shanghai 201203, China*

Jian-Ting Sun − *School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, Shanghai 201203, China*

Guo-Qiang Lin − *Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c02807

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (21772027 to B.-G.W. and 21702032 to C.-M.S.) for financial support. The authors also thank Dr. Han-Qing Dong (Arvinas, Inc.) for helpful suggestions.

■ REFERENCES

(1) For selected reviews, see: (a) Wu, X.-F.; Anbarasan, P.; Neumann, H.; Beller, M. From Noble Metal to Nobel Prize: Palladium-Catalyzed Coupling Reactions as Key Methods in Organic Synthesis. *Angew. Chem., Int. Ed.* **2010**, *49*, 9047−9050. (b) de Barros, S. D. T.; Senra, J. D.; Lachter, E. R.; Malta, L. F. B. Metal-catalyzed cross-coupling reactions with supported nanoparticles: Recent developments and future directions. *Catal. Rev.: Sci. Eng.* **2016**, *58*, 439−496. (c) Ruiz-Castillo, P.; Buchwald, S. L. Applications of Palladium-Catalyzed C−N Cross-Coupling Reactions. *Chem. Rev.* **2016**, *116*, 12564−12649. (d) Choi, J.; Fu, G. C. Transition metal−catalyzed alkyl-alkyl bond formation: Another dimension in cross-coupling chemistry. *Science* **2017**, *356*, eaaf7230. (e) Bauer, I.; Knölker, H.-J. Iron Catalysis in Organic Synthesis. *Chem. Rev.* **2015**, *115*, 3170−3387.

(2) (a) Magano, J.; Dunetz, J. R. Large-Scale Applications of Transition Metal-Catalyzed Couplings for the Synthesis of Pharmaceuticals. *Chem. Rev.* **2011**, *111*, 2177−2250. (b) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *C-H* Bond Functionalization: Emerging Synthetic Tools for Natural Products and Pharmaceuticals. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960−9009.

(3) For selected examples, see: (a) Tashrifi, Z.; Mohammadi Khanaposhtani, M.; Biglar, M.; Larijani, B.; Mahdavi, M. Recent Advances in Alkyne Hydroamination as a Powerful Tool for the Construction of *C−N* Bonds. *Asian J. Org. Chem.* **2020**, *9*, 969−991. (b) Ganley, J. M.; Murray, P. R. D.; Knowles, R. R. Photocatalytic Generation of Aminium Radical Cations for *C−N* Bond Formation. *ACS Catal.* **2020**, *10*, 11712−11738. (c) Colonna, P.; Bezzenine, S.; Gil, R.; Hannedouche, J. Alkene Hydroamination via Earth-Abundant Transition Metal (Iron, Cobalt, Copper and Zinc) Catalysis: A Mechanistic Overview. *Adv. Synth. Catal.* **2020**, *362*, 1550−1563.

(d) Korch, K. M.; Watson, D. A. Cross-Coupling of Heteroatomic Electrophiles. *Chem. Rev.* **2019**, *119*, 8192−8228. (e) Khan, I.; Zaib, S.; Ibrar, A. New frontiers in the transition-metal-free synthesis of heterocycles from alkynoates: an overview and current status. *Org. Chem. Front.* **2020**, *7*, 3734. (f) Hua, T.-B.; Xiao, C.; Yang, Q.-Q.; Chen, J.-R. Recent advances in asymmetric synthesis of 2-substituted indoline derivatives. *Chin. Chem. Lett.* **2020**, *31*, 311−323.

(4) (a) Sarojini, V.; Cameron, A. J.; Varnava, K. G.; Denny, W. A.; Sanjayan, G. Cyclic Tetrapeptides from Nature and Design: A Review of Synthetic Methodologies, Structure, and Function. *Chem. Rev.* **2019**, *119*, 10318−10359. (b) Shanbhag, G. V.; Kumbar, S. M.; Halligudi, S. B. Chemoselective synthesis of *β*-amino acid derivatives by hydroamination of activated olefins using AlSBA-15 catalyst prepared by post-synthetic treatment. *J. Mol. Catal. A: Chem.* **2008**, *284*, 16−23.

(5) (a) Meanwell, N. A. Improving Drug Candidates by Design: A Focus on Physicochemical Properties As a Means of Improving Compound Disposition and Safety. *Chem. Res. Toxicol.* **2011**, *24*, 1420−1456. (b) Trivella, Daniela B. B.; Pereira, Alban R.; Stein, Martin L.; Kasai, Y.; Byrum, T.; Valeriote, Frederick A.; Tantillo, Dean J.; Groll, M.; Gerwick, William H.; Moore, Bradley S. Enzyme Inhibition by Hydroamination: Design and Mechanism of a Hybrid Carmaphycin-Syringolin Enone Proteasome Inhibitor. *Chem. Biol.* **2014**, *21*, 782−791.

(6) (a) Reich, D.; Trowbridge, A.; Gaunt, M. J. Rapid Syntheses of (−)-FR901483 and (+)-TAN1251C Enabled by Complexity-Generating Photocatalytic Olefin Hydroaminoalkylation. *Angew. Chem., Int. Ed.* **2020**, *59*, 2256−2261. (b) Berthold, D.; Geissler, A. G. A.; Giofré, S.; Breit, B. Rhodium-Catalyzed Asymmetric Intramolecular Hydroamination of Allenes. *Angew. Chem., Int. Ed.* **2019**, *58*, 9994−9997. (c) Tian, G.; Song, L.; Li, Z.; Robeyns, K.; Van Meervelt, L.; Van der Eycken, E. V. A Gold(I)-Catalyzed Hydroamination/Cycloisomerization Cascade: Concise Synthesis of (±)-seco-Antofine and (±)-Septicine. *Org. Lett.* **2020**, *22*, 8441.

(7) For selected examples of metal-catalyzed hydroamination, see: (a) Lee, W.-C. C.; Wang, W.; Li, J. J. Copper(II)-Mediated ortho-Selective C(sp^2)−H Tandem Alkynylation/Annulation and ortho-Hydroxylation of Anilides with 2-Aminophenyl-1H-pyrazole as a Directing Group. *J. Org. Chem.* **2018**, *83*, 2382−2388. (b) Shaikh, M. M.; Patel, A. P.; Patel, S. P.; Chikhalia, K. H. Synthesis, in vitro COX-1/COX-2 inhibition testing and molecular docking study of novel 1,4-benzoxazine derivatives. *New J. Chem.* **2019**, *43*, 10305−10317. (c) Álvarez-Pérez, A.; Esteruelas, M. A.; Izquierdo, S.; Varela, J. A.; Saá, C. Ruthenium-Catalyzed Oxidative Amidation of Alkynes to Amides. *Org. Lett.* **2019**, *21*, 5346−5350. (d) Thavaselvan, S.; Parthasarathy, K. Nickel-Catalyzed Cyclization Strategy for the Synthesis of Pyrroloquinolines, Indoloquinolines, and Indoloisoquinolines. *Org. Lett.* **2020**, *22*, 3810−3814.

(8) For selected examples of base-mediated hydroamination, see: (a) Patel, M.; Saunthwal, R. K.; Verma, A. K. Base-Mediated Hydroamination of Alkynes. *Acc. Chem. Res.* **2017**, *50*, 240−254. (b) Joshi, M.; Patel, M.; Tiwari, R.; Verma, A. K. Base-Mediated Selective Synthesis of Diversely Substituted *N*-Heterocyclic Enamines and Enaminones by the Hydroamination of Alkynes. *J. Org. Chem.* **2012**, *77*, 5633−5645. (c) Verma, A. K.; Patel, M.; Joshi, M.; Likhar, P. R.; Tiwari, R. K.; Parang, K. Base-Mediated Chemo- and Stereoselective Addition of 5-Aminoindole/Tryptamine and Histamines onto Alkynes. *J. Org. Chem.* **2014**, *79*, 172−186. (d) Kozell, V.; Rahmani, F.; Piermatti, O.; Lanari, D.; Vaccaro, L. A stereoselective organic base-catalyzed protocol for hydroamination of alkynes under solvent-free conditions. *Mol. Catal.* **2018**, *455*, 188−191.

(9) For selected examples of hydroamination of alkynes with amine, see: (a) Verma, A. K.; Joshi, M.; Singh, V. P. Base-Mediated Regio- and Stereoselective Intermolecular Addition of Alkynes to *N*-Heterocycles. *Org. Lett.* **2011**, *13*, 1630−1633. (b) Patel, M.; Saunthwal, R. K.; Verma, A. K. Base-Mediated Deuteration of Organic Molecules: A Mechanistic Insight. *ACS Omega.* **2018**, *3*, 10612−10623. (c) Sevov, C. S.; Zhou, J.; Hartwig, J. F. Iridium-Catalyzed, Intermolecular Hydroamination of Unactivated Alkenes with Indoles. *J. Am. Chem. Soc.* **2014**, *136*, 3200−3207. (d) Hojo, R.; Short, S.; Jha, M. Synthesis of 1,2-Fused Tricyclic Indoles via Cu-/Base-Mediated Hydroamination of Alkynes. *J. Org. Chem.* **2019**, *84*, 16095−16104.

(10) Kavitha, N.; Sukumar, G.; Kumar, V. P.; Mainkar, P. S.; Chandrasekhar, S. Ruthenium-catalyzed benzimidazoisoquinoline synthesis via oxidative coupling of 2-arylbenzimidazoles with alkynes. *Tetrahedron Lett.* **2013**, *54*, 4198−4201.

(11) Hyster, T. K.; Rovis, T. Rhodium-Catalyzed Oxidative Cycloaddition of Benzamides and Alkynes via C−H/N−H Activation. *J. Am. Chem. Soc.* **2010**, *132*, 10565−10569.

(12) For selected reviews, see: (a) Zhou, B.; Tan, T.-D.; Zhu, X.-Q.; Shang, M.; Ye, L.-W. Reversal of Regioselectivity in Ynamide Chemistry. *ACS Catal.* **2019**, *9*, 6393−6406. (b) Peng, Z.; Zhang, Z.; Zeng, X.; Tu, Y.; Zhao, J. Regio- and Stereoselective Hydrophosphorylation of Ynamides: A Facile Approach to (*Z*)-*β*-Phosphor-Enamides. *Adv. Synth. Catal.* **2019**, *361*, 4489−4494. (c) Dodd, R. H.; Cariou, K. Ketenimines Generated from Ynamides: Versatile Building Blocks for Nitrogen-Containing Scaffolds. *Chem. - Eur. J.* **2018**, *24*, 2297−2304. (d) Wang, X.-N.; Yeom, H.-S.; Fang, L.-C.; He, S.; Ma, Z.-X.; Kedrowski, B. L.; Hsung, R. P. Ynamides in Ring Forming Transformations. *Acc. Chem. Res.* **2014**, *47*, 560−578. (e) Evano, G.; Coste, A.; Jouvin, K. Ynamides: Versatile Tools in Organic Synthesis. *Angew. Chem., Int. Ed.* **2010**, *49*, 2840−2859. (f) DeKorver, K. A.; Li, H.; Lohse, A. G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. Ynamides: A Modern Functional Group for the New Millennium. *Chem. Rev.* **2010**, *110*, 5064−5106.

(13) For selected examples, see: (a) Li, L.; Chen, X.-M.; Wang, Z.-S.; Zhou, B.; Liu, X.; Lu, X.; Ye, L.-W. Reversal of Regioselectivity in Catalytic Arene-Ynamide Cyclization: Direct Synthesis of Valuable Azepino[4,5-b] indoles and *β*-Carbolines and DFT Calculations. *ACS Catal.* **2017**, *7*, 4004−4010. (b) Frischmuth, A.; Knochel, P. Preparation of Functionalized Indoles and Azaindoles by the Intramolecular Copper-Mediated Carbomagnesiation of Ynamides. *Angew. Chem., Int. Ed.* **2013**, *52*, 10084−10088.

(14) For selected examples, see: (a) Vanjari, R.; Dutta, S.; Gogoi, M. P.; Gandon, V.; Sahoo, A. K. Gold-Catalyzed syn-1,2-Difunctionalization of Ynamides via Nitrile Activation. *Org. Lett.* **2018**, *20*, 8077−8081. (b) Jin, H.; Tian, B.; Song, X.; Xie, J.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Gold-Catalyzed Synthesis of Quinolines from Propargyl Silyl Ethers and Anthranils through the Umpolung of a Gold Carbene Carbon. *Angew. Chem., Int. Ed.* **2016**, *55*, 12688−12692. (c) Wezeman, T.; Zhong, S.; Nieger, M.; Bräse, S. Synthesis of Highly Functionalized 4-Aminoquinolines. *Angew. Chem., Int. Ed.* **2016**, *55*, 3823−3827.

(15) For selected examples, see: (a) Gati, W.; Rammah, M. M.; Rammah, M. B.; Couty, F.; Evano, G. De Novo Synthesis of 1,4-Dihydropyridines and Pyridines. *J. Am. Chem. Soc.* **2012**, *134*, 9078−9081. (b) Garcia, P.; Evanno, Y.; George, P.; Sevrin, M.; Ricci, G.; Malacria, M.; Aubert, C.; Gandon, V. Regioselective Cobalt-Catalyzed Formation of Bicyclic 3- and 4-Aminopyridines. *Org. Lett.* **2011**, *13*, 2030−2033.

(16) For selected examples, see: (a) Prabagar, B.; Mallick, R. K.; Prasad, R.; Gandon, V.; Sahoo, A. K. Umpolung Reactivity of Ynamides: An Unconventional [1,3]-Sulfonyl and [1,5]-Sulfinyl Migration Cascade. *Angew. Chem., Int. Ed.* **2019**, *58*, 2365−2370. (b) Dutta, S.; Mallick, R. K.; Prasad, R.; Gandon, V.; Sahoo, A. K. Alkyne Versus Ynamide Reactivity: Regioselective Radical Cyclization of Yne-Ynamides. *Angew. Chem., Int. Ed.* **2019**, *58*, 2289−2294. (c) Zhou, A.-H.; He, Q.; Shu, C.; Yu, Y.-F.; Liu, S.; Zhao, T.; Zhang, W.; Lu, X.; Ye, L.-W. Atom-economic generation of gold carbenes: gold-catalyzed formal [3 + 2] cycloaddition between ynamides and isoxazoles. *Chem. Sci.* **2015**, *6*, 1265−1271.

(17) For selected examples, see: Davies, P. W.; Cremonesi, A.; Dumitrescu, L. Intermolecular and Selective Synthesis of 2,4,5-Trisubstituted Oxazoles by a Gold-Catalyzed Formal [3 + 2] Cycloaddition. *Angew. Chem., Int. Ed.* **2011**, *50*, 8931−8935.

(18) For selected examples, see: (a) Kong, Y.; Jiang, K.; Cao, J.; Fu, L.; Yu, L.; Lai, G.; Cui, Y.; Hu, Z.; Wang, G. Synthesis of 3-Alkyl- or

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443

3-Allenyl-2-amidobenzofurans via Electrophilic Cyclization of *o*-Anisole-Substituted Ynamides with Carbocations. *Org. Lett.* **2013**, *15*, 422−425. (b) Oppenheimer, J.; Johnson, W. L.; Tracey, M. R.; Hsung, R. P.; Yao, P.-Y.; Liu, R.; Zhao, K. A Rhodium(I)-Catalyzed Demethylation−Cyclization of *o*-Anisole-Substituted Ynamides in the Synthesis of Chiral 2-Amido Benzofurans. *Org. Lett.* **2007**, *9*, 2361−2364.

(19) For selected examples, see: Cao, J.; Xu, Y.; Kong, Y.; Cui, Y.; Hu, Z.; Wang, G.; Deng, Y.; Lai, G. Synthesis of *δ*-Carbolines via a Pd-Catalyzed Sequential Reaction from 2-Iodoanilines and *N*-Tosyl-enynamines. *Org. Lett.* **2012**, *14*, 38−41.

(20) For selected examples, see: Shindoh, N.; Takemoto, Y.; Takasu, K. Atropisomerism of *α,β*-Unsaturated Amidines: Stereoselective Synthesis by Catalytic Cascade Reaction and Optical Resolution. *Chem. - Eur. J.* **2009**, *15*, 7026−7030.

(21) For selected examples, see: (a) Dutta, S.; Yang, S.; Vanjari, R.; Mallick, R. K.; Gandon, V.; Sahoo, A. K. Keteniminium-Driven Umpolung Difunctionalization of Ynamides. *Angew. Chem., Int. Ed.* **2020**, *59*, 10785−10790. (b) Xu, S.; Liu, J.; Hu, D.; Bi, X. Metal-free hydroacyloxylation and hydration reactions of ynamides: synthesis of *α*-acyloxyenamides and *N*-acylsulfonamides. *Green Chem.* **2015**, *17*, 184−187. (c) Yang, Y.; Wang, L.; Zhang, F.; Zhu, G. Preparation of (*Z*)-*α,β*-Disubstituted Enamides via Palladium-Catalyzed Addition of Boronic Acids to Ynamides. *J. Org. Chem.* **2014**, *79*, 9319−9324. (d) Mulder, J. A.; Kurtz, K. C. M.; Hsung, R. P.; Coverdale, H.; Frederick, M. O.; Shen, L.; Zificsak, C. A. Highly Stereoselective Synthesis of Novel *α*-Haloenamides via a Mild and Efficient Hydrohalogenation of Ynamides. *Org. Lett.* **2003**, *5*, 1547−1550.

(22) Kramer, S.; Dooleweerdt, K.; Lindhardt, A. T.; Rottländer, M.; Skrydstrup, T. Highly Regioselective Au(I)-Catalyzed Hydroamination of Ynamides and Propiolic Acid Derivatives with Anilines. *Org. Lett.* **2009**, *11*, 4208−4211.

(23) Hentz, A.; Retailleau, P.; Gandon, V.; Cariou, K.; Dodd, R. H. Transition-Metal-Free Tunable Chemoselective *N* Functionalization of Indoles with Ynamides. *Angew. Chem., Int. Ed.* **2014**, *53*, 8333−8337.

(24) For selected examples of our recent efforts in the study of ynamides, see: (a) Han, X.-L.; Nie, X.-D.; Chen, Z.-D.; Si, C.-M.; Wei, B.-G.; Lin, G.-Q. Synthesis of a 3,4-Dihydro-1,3-oxazin-2-ones Skeleton via an Intermolecular [4 + 2] Process of *N*-Acyliminium Ions with Ynamides/Terminal Alkynes. *J. Org. Chem.* **2020**, *85*, 13567−13578. (b) Han, P.; Mao, Z.-Y.; Li, M.; Si, C.-M.; Wei, B.-G.; Lin, G.-Q. Synthesis of Amide Enol Carbamates and Carbonates through $Cu(OTf)_2$-Catalyzed Reactions of Ynamides with *t*-Butyl Carbamates/Carbonates. *J. Org. Chem.* **2020**, *85*, 4740−4752. (c) Zhang, Y.-X.; Chen, L.-Y.; Sun, J.-T.; Si, C.-M.; Wei, B.-G. Gold-Catalyzed Addition−*N*-Boc Cleavage−Cyclization of *N,O*-Acetal with Ynamides for Construction of 6-(*tert*-Butyldimethylsilyl)-oxy-tetrahydropyrrolo[1,2-c][1,3]oxazin-1-ones. *J. Org. Chem.* **2020**, *85*, 12603−12613. (d) Liu, Y.-W.; Mao, Z.-Y.; Nie, X.-D.; Si, C.-M.; Wei, B.-G.; Lin, G.-Q. Approach to Tertiary-Type *β*-Hydroxyl Carboxamides Through $Sc(OTf)_3$-Catalyzed Addition of Ynamides and Ketones. *J. Org. Chem.* **2019**, *84*, 16254−16261. (e) Han, P.; Mao, Z.-Y.; Si, C.-M.; Zhou, Z.; Wei, B.-G.; Lin, G.-Q. Stereoselective Synthesis of Pyrido- and Pyrrolo[1,2-c][1,3]oxazin-1-ones via a Nucleophilic Addition-Cyclization Process of *N,O*-Acetal with Ynamides. *J. Org. Chem.* **2019**, *84*, 914−923.

(25) Nayak, S.; Ghosh, N.; Sahoo, A. K. Access to Cyclobutene-Fused Azepines through Au-Catalyzed Cycloisomerization of Stable Alkyne Tethered Ketene *N,N*-Acetals. *Org. Lett.* **2014**, *16*, 2996−2999.

(26) Zhu, W.; Sun, Q.; Wang, Y.; Yuan, D.; Yao, Y. Chemo- and Regioselective Hydroarylation of Alkenes with Aromatic Amines Catalyzed by $[Ph_3C][B(C_6F_5)_4]$. *Org. Lett.* **2018**, *20*, 3101−3104.

(27) Yang, H.; Zhang, L.; Jiao, L. *N*-Methylanilines as Simple and Efficient Promoters for Radical-Type Cross-Coupling Reactions of Aryl Iodides. *Chem. - Eur. J.* **2017**, *23*, 65−69.

(28) Mallick, R. K.; Prabagar, B.; Sahoo, A. K. Regioselective Synthesis of 2,4,5-Trisubstituted Oxazoles and Ketene Aminals via Hydroamidation and Iodo-Imidation of Ynamides. *J. Org. Chem.* **2017**, *82*, 10583−10594.

https://dx.doi.org/10.1021/acs.joc.0c02807
J. Org. Chem. 2021, 86, 3433−3443