molecules

MDPI

Article

Copper-Catalyzed One-Pot Synthesis of *N*-Sulfonyl Amidines from Sulfonyl Hydrazine, Terminal Alkynes and Sulfonyl Azides

Yu Zhao [1,†], Zitong Zhou [1,†], Man Chen [1] and Weiguang Yang [1,2,*]

1 The Marine Biomedical Research Institute, Guangdong Medical University, Zhanjiang 524023, China; gdmuzy@163.com (Y.Z.); zzt15766229745@163.com (Z.Z.); chenman66@126.com (M.C.)
2 The Marine Biomedical Research Institute of Guangdong Zhanjiang, Zhanjiang 524023, China
* Correspondence: 09ywg@163.com
† These authors contributed equally to this work.

Abstract: *N*-Sulfonyl amidines are developed from a Cu-catalyzed three-component reaction from sulfonyl hydrazines, terminal alkynes and sulfonyl azides in toluene at room temperature. Particularly, the intermediate *N*-sulfonylketenimines was generated via a CuAAC/ring-opening procedure and took a nucleophilic addition with the weak nucleophile sulfonyl hydrazines. In addition, the stability of the product was tested by a HNMR spectrometer.

Keywords: amidines; multicomponent reactions; CuAAC/ring-opening; *N*-sulfonylketenimines; nucleophilic addition

Citation: Zhao, Y.; Zhou, Z.; Chen, M.; Yang, W. Copper-Catalyzed One-Pot Synthesis of *N*-Sulfonyl Amidines from Sulfonyl Hydrazine, Terminal Alkynes and Sulfonyl Azides. *Molecules* **2021**, *26*, 3700. https://doi.org/10.3390/molecules26123700

Academic Editors: Joice Thomas, Nithya Joseph and Dmitry Eremin

Received: 25 May 2021
Accepted: 14 June 2021
Published: 17 June 2021

1. Introduction

Amidine derivatives are important privileged scaffolds in medicinal chemistry [1–3], synthetic chemistry [4] and an important pharmacophore in drug discovery [5,6]. One subset of such compounds is *N*-sulfonyl amidine derivatives that show a prolific set of biological activities, including antifungal (I) [7], anticancer (II) [8], antiresorptive (III and IV) [9–11], antiproliferative (V) [12], dopamine transporter inhibitors (VI) [13] (Figure 1), etc. [14,15]. Therefore, the establishment of robust synthetic approaches for the preparation of *N*-sulfonyl amidines and their functionalizations is highly required.

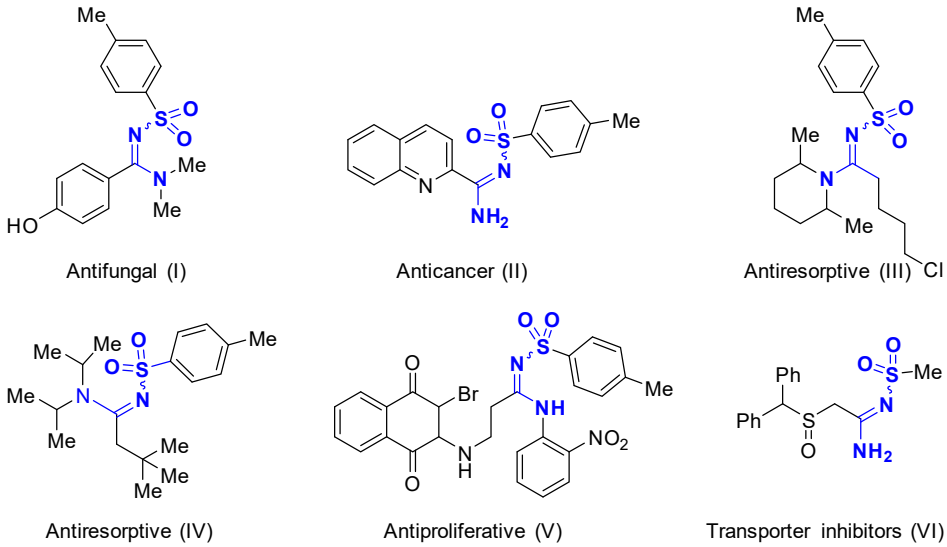
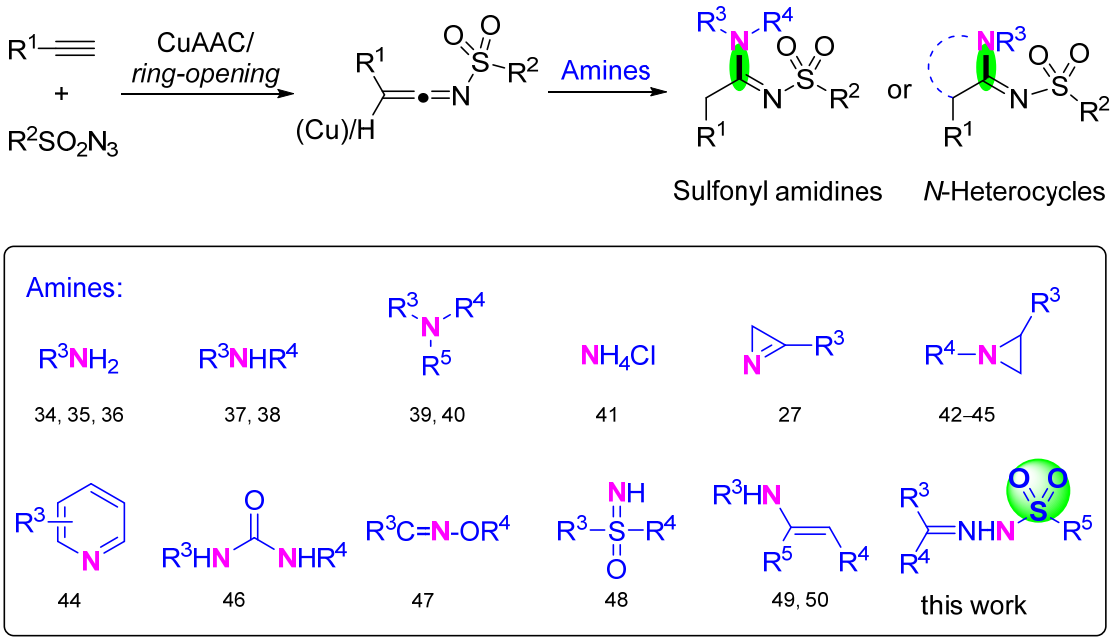


Figure 1. Part of the sulfonyl amidine drug candidates.

Classical types of reactions have focused on the preparation of *N*-sulfonyl amidines involved in the reaction of cyclic thioamides and thioacetamide derivatives with sulfonyl azides [14,16–18], the phosphite-mediated Beckmann-like coupling of oximes and *p*-toluenesulfonyl azide [19], sulfonamide derivatives condensation with DMF–DMA [20], the sulfonamide reaction with formamide [21] and the sulfonyl ynamide rearrangement [22]. The most efficient method is the Cu-catalyzed multicomponent reaction of terminal alkynes, sulfonyl azides and amines, which has been applied to synthesize numerous oxygen-containing and nitrogen-containing heterocyclic compounds [23–31]. The ketenimine intermediate generated by Cu-catalyzed alkynes and sulfonyl azides [31–33] could take a nucleophilic addition reaction with most amines, as show in Scheme 1, including aliphatic primary amines [34–36], aliphatic secondary amines [37,38], aliphatic tertiary amines [39,40], quaternary amine salts [41], imines [27], nitrogenous heterocyclic compounds [42–45], urea derivatives [46], oximes [47], sulfoximines [48] and enyl amine [49,50]. However, to our knowledge, there are few previous works that used the weak nucleophile sulfonyl hydrazines for this method. Herein, the Cu-catalyzed one-pot synthesis of *N*-sulfonyl amidines from sulfonyl hydrazine, terminal alkynes and sulfonyl azides was reported.



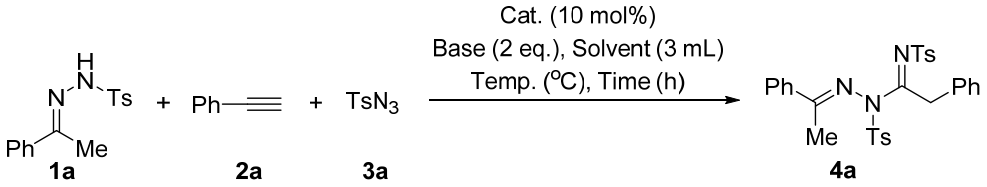
Scheme 1. Copper-catalyzed tandem reactions of the terminal alkynes, sulfonyl azides and amines.

2. Results

We began our investigation by examining the synthesis of 4-methyl-*N*-(2-phenyl-1-(2-(1-phenylethylidene)-1-tosylhydrazinyl) ethylidene)benzenesulfonamide **4a** via 4-methyl-*N*′-(1-phenylethylidene)benzenesulfonohydrazide **1a**, ethynylbenzene **2a** and *p*-tosyl azide **3a**. The reaction was carried out in the presence of CuI and Et_3N in CH_2Cl_2 at room temperature for 1 h, and **4a** was isolated in a 78% yield (Table 1, entry 1). Based on this finding, the reaction conditions were screened. First, several catalysts were screened, and most Cu-catalysts exhibited a high catalytic reactivity in this reaction, whether Cu^I-catalysts or Cu^{II}-catalysts (Table 1, entries 2–6). Other catalysts such as AgTFA failed to produce the desired product (Table 1, entries 7). Then, the effects of different bases were evaluated, and the screening results revealed that the use of Et_3N achieved a superior result compared to DMAP, DIPEA, pyridine and the other bases (Table 1, entries 8–12). Finally, the solvents were screened, and a lower or comparable yield was obtained when $CHCl_3$, DCE, MeCN, THF, DMSO and DMF were used as solvents, while toluene gave **4a** the highest yield of 84% (Table 1, entry 13–19). Encouraged by this promising result, we tracked the reaction

by TLC and found that it could be completed in less than an hour at room temperature (Table 1, entry 20–23).

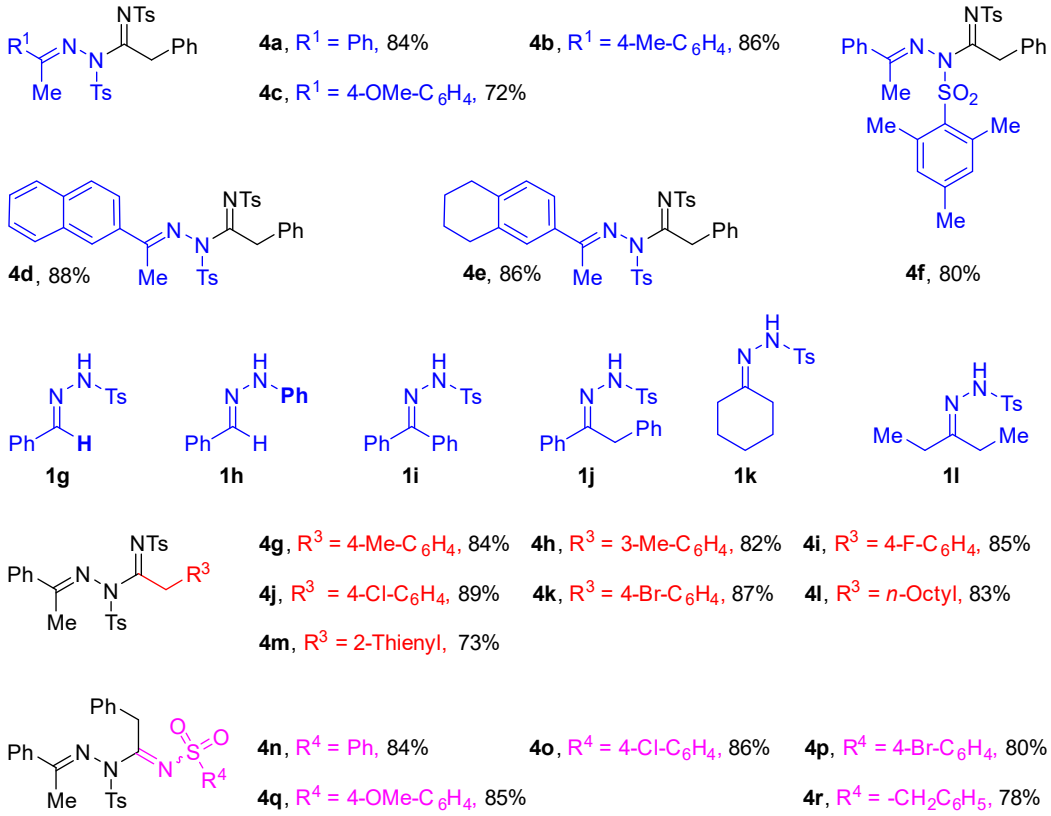
Table 1. Optimization of the catalytic conditions [a].



Entry	Cat. (10 mol%)	Base (10 mol%)	Solvent (10 mol%)	Temp. (°C)	Time (h)	Yield (%) [b]
entry 1	CuI	Et_3N	CH_2Cl_2	rt	1.0	78
entry 2	CuBr	Et_3N	CH_2Cl_2	rt	1.0	76
entry 3	CuCl	Et_3N	CH_2Cl_2	rt	1.0	72
entry 4	$CuBr_2$	Et_3N	CH_2Cl_2	rt	1.0	64
entry 5	$Cu(OAc)_2$	Et_3N	CH_2Cl_2	rt	1.0	52
entry 6	$Cu(OTf)_2$	Et_3N	CH_2Cl_2	rt	1.0	21
entry 7	AgTFA	Et_3N	CH_2Cl_2	rt	1.0	0
entry 8	CuI	DMAP	CH_2Cl_2	rt	1.0	26
entry 9	CuI	DIPEA	CH_2Cl_2	rt	1.0	75
entry 10	CuI	Pyridine	CH_2Cl_2	rt	1.0	32
entry 11	CuI	^{t}-BuONa	CH_2Cl_2	rt	1.0	10
entry 12	CuI	K_2CO_3	CH_2Cl_2	rt	1.0	8
entry 13	CuI	Et_3N	$CHCl_3$	rt	1.0	76
entry 14	CuI	Et_3N	DCE	rt	1.0	75
entry 15	CuI	Et_3N	Toluene	rt	1.0	84
entry 16	CuI	Et_3N	MeCN	rt	1.0	52
entry 17	CuI	Et_3N	THF	rt	1.0	80
entry 18	CuI	Et_3N	DMSO	rt	1.0	10
entry 19	CuI	Et_3N	DMF	rt	1.0	6
entry 20	CuI	Et_3N	Toluene	40	1.0	75
entry 21	CuI	Et_3N	Toluene	rt	0.5	80
entry 22	CuI	Et_3N	Toluene	rt	2.0	84
entry 23	CuI	Et_3N	Toluene	rt	3.0	84

[a] Reaction conditions: To **1a** (0.5 mmol), Cat. 10 mol%, base 1.2 eq. in the solvent (3 mL) was added **2a** (1.2 eq.) and **3a** (1.2 eq.), stirred at specified temperatures and times. [b] Isolated yields.

With the optimized reaction conditions obtained, the substrate diversity with the sulfonyl hydrazines **1** was tested first. As shown in Scheme 2, the R^1 electron effects of the substituents **1** had slight influences. For example, substrates bearing 4-OMe-C_6H_4, 4–Me-C_6H_4, 2-naphthyl and 2-tetra-hydronaphthalyl were examined, and the 72–88% yields of **4a**–**4e** were isolated. The R^2 of substrates **1** bearing the 2,4,6-trimethylphenyl group also can obtain **4f** in a good yield of 80%. However, when changing the substrates **1** to other sulfonyl hydrazines, such as **1g**–**1k**, it could not obtain the desired products and give decomposed or complex compounds. Next, the scopes and limitations of terminal alkynes **2** and sulfonyl azides **3** were examined. An aryl-substituted, aliphatic or 2-thienyl terminal alkynes and aryl-substituted or aliphatic sulfonyl azides can smoothly obtain the corresponding products **4g**–**4m** with yields of 73–89% and **4n**–**4q** with yields of 78–86%, in which both the substituents led to high yields and were influenced slightly.



Scheme 2. The synthesis of products **4a**–**4r.**

The structure of **4a** was confirmed by X-ray crystallography (Figure 2, CCDC deposition number 2075031).

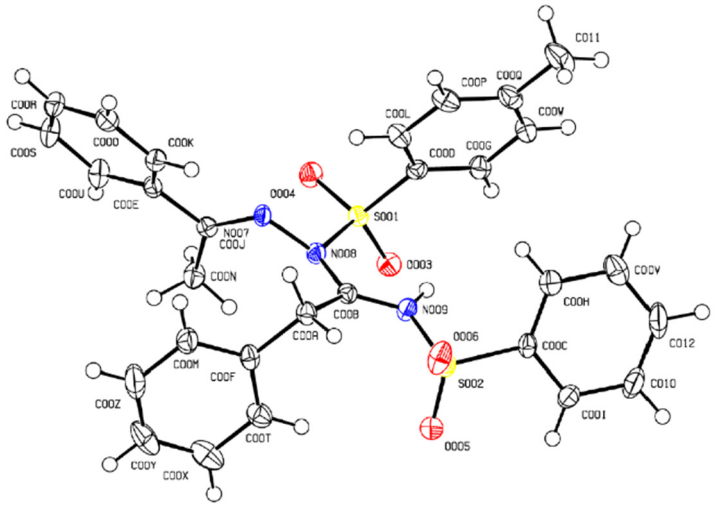


Figure 2. X-ray crystal structure of compound **4a**.

Curiously, we found that the separated products in the solvent were unstable and would decompose. Thus, the stability of product **4a** was tested by a HNMR spectrometer. As shown in Figure 3, the products dissolved in DMSO were relatively stable in the first four days, and the decomposition complex could be observed starting from the fifth day; then, the concentration of byproducts became thicker day by day. After a month, the system was relatively stable, and the decomposition was slow. Therefore, it is recommended that products **4a**–**4q** should be dried and stored at a low temperature.

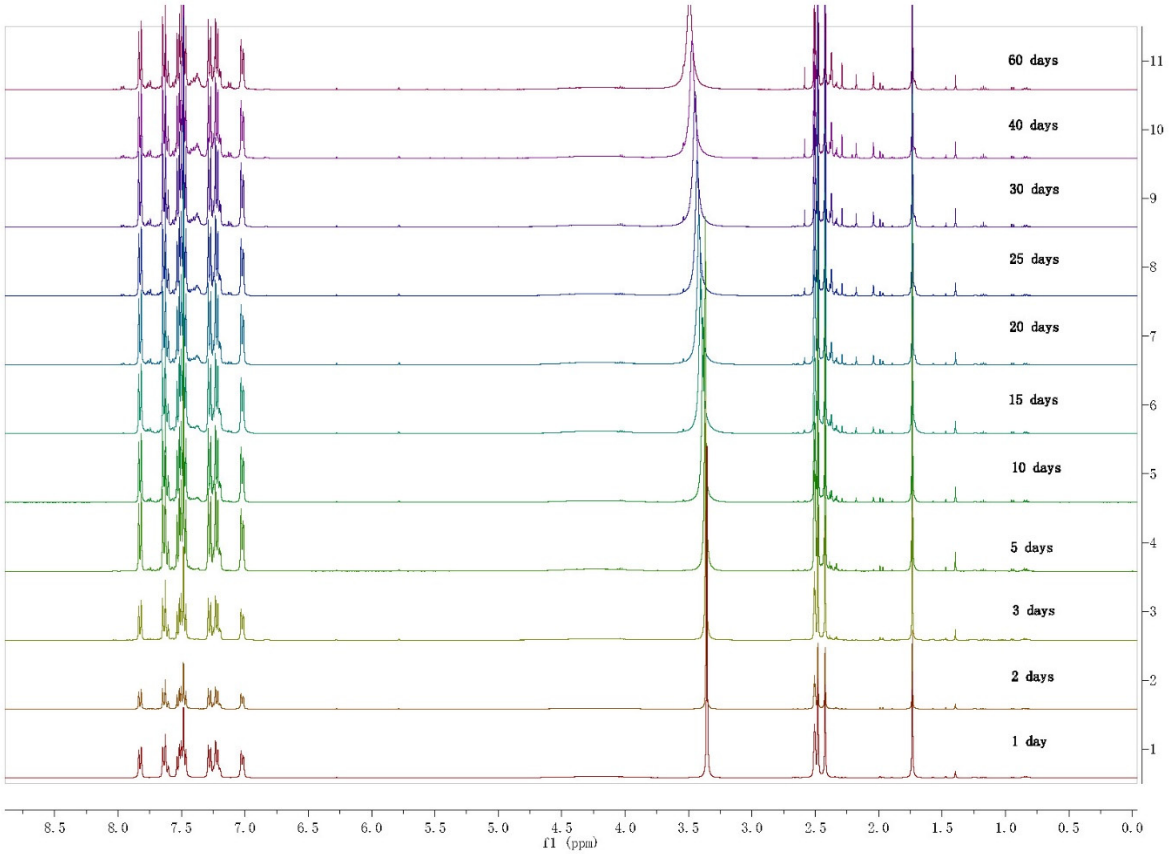


Figure 3. The stability of product **4a** tested by a HNMR spectrometer.

3. Experimental

3.1. General Information

All melting points were determined on a Yanaco melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Nicolet FT-IR 5DX spectrometer. All spectra of ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a 400 MHz Bruker spectrometer using DMSO-d_6 or $CDCl_3$ as the solvent, with tetramethylsilane (TMS) as the internal standard, at room temperature. Chemical shifts are given in δ relative to TMS, and the coupling constants *J* are given in Hz. HRMS were obtained on a Bruker micrOTOF-Q II spectrometer. All commercially available reagents were purchased from Sigma-Aldrich, Acros, Aladdin, TCI, Alfa, Innochem in China and were used without further purification. All reactions were carried out in dried reaction tube (25 mL). The original ^{1}H and ^{13}C NMR spectra are available in supplementary material.

3.2. Compound Characterizations and Preparations

4-methyl-*N*-((*E*)-2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-osylhydrazineyl) ethylidene) benzenesulfonamide (**4a)**. 4-methyl-*N*′-(1-phenylethylidene) benzenesulfonohydrazide (**1a**) (0.114 mg, 0.50 mmol) was mixed with CuI (9.5 mg, 0.05 mmol) in 1-mL toluene. Then, ethynylbenzene (**2a**) (76.5 mg, 0.75 mmol), TsN_3 (147.8 mg, 0.75 mmol) and TEA (101 mg, 1.0 mmol) were mixed in toluene (2 mL). After stirring at room temperature for 1 h and concentrated under reduced pressure, the mix was purified a flash chromatography (petroleum ether/ethyl acetate: 7:1) to give product **4a** as a white solid, mp 143–144 °C. IR (KBr) ν 3063, 1564, 1492, 1442, 1309, 1145, 1082 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, J = 8.0 Hz, 2H), 7.62 (t, J = 8.0 Hz, 3H), 7.53–7.46 (m, 6H), 7.28–7.21 (m, 5H), 7.01 (d, J = 6.8 Hz, 2H), 4.14 (s, 2H), 2.48 (s, 3H), 2.42 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.7, 165.2, 145.6, 143.6, 138.6, 135.0, 134.0, 133.1, 132.4, 129.7 (2C), 129.6 (2C), 128.9 (2C),

128.8 (2C), 128.6, 128.5 (2C), 127.8 (2C), 127.2, 126.5 (3C), 21.3 (3C), 17.7; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{29}N_3O_4S_2$, $[M + H]^+$ 560.1672; found 560.1675.

The products **4b**–**4q** were prepared by a similar procedure.

4-methyl-*N*-((*E*)-2-phenyl-1-(2-((*E*)-1-(*p*-tolyl)ethylidene)-1-tosylhydrazineyl) ethylidene) benzenesulfonamide (**4b**). White solid, mp 153–155 °C. IR (KBr) ν 3062, 1594, 1568, 1307, 1172, 1147, 1084 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.8 Hz, 4H), 7.31 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.24–7.19 (m, 3H), 7.00 (d, J = 6.8 Hz, 2H), 4.19 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 2.39 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.3, 165.3, 145.5, 143.5, 142.6, 138.6, 134.0, 133.1, 132.3, 129.7 (2C), 129.6 (2C), 129.3 (2C), 128.9 (2C), 128.6 (2C), 128.5 (2C), 127.8 (2C), 127.1, 126.5 (3C), 21.2 (3C), 17.7; HRMS (ESI-TOF) (m/z). Calcd for $C_{31}H_{31}N_3O_4S_2$, $[M + H]^+$ 574.1829; found 574.1831.

N-((*E*)-1-(2-((*E*)-1-(4-methoxyphenyl)ethylidene)-1-tosylhydrazineyl)-2-phenylethylidene)-4-methylbenzenesulfonamide (**4c**). White solid, mp 141–143 °C. IR (KBr) ν 3063, 1590, 1494, 1289, 1173, 1141, 1085 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.81 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.8 Hz, 4H), 7.27 (d, J = 8.0 Hz, 2H), 7.23–7.18 (m, 3H), 7.05–6.99 (m, 4H), 4.49 (s, 2H), 3.85 (s, 3H), 2.47 (s, 3H), 2.42 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 165.3, 162.6, 145.5, 143.5, 138.7, 134.0, 133.1, 132.3, 129.7 (2C), 129.6 (2C), 129.5 (2C), 128.9 (2C), 128.6, 128.5 (2C), 127.3, 127.1, 126.5 (3C), 114.1, 55.6, 21.2 (3C), 17.2; HRMS (ESI-TOF) (m/z). Calcd for $C_{31}H_{31}N_3O_5S_2$, $[M + H]^+$ 590.1778; found 590.1782.

4-methyl-*N*-((*E*)-1-(2-((*E*)-1-(naphthalen-2-yl)ethylidene)-1-tosylhydrazineyl)-2-phenylethylidene)benzenesulfonamide (**4d)**. White solid, mp 172–173 °C. IR (KBr) ν 3056, 1590, 1574, 1494, 1359, 1305, 1144, 1084 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.02 (t, J = 7.2 Hz, 3H), 7.68–7.61 (m, 4H), 7.53–7.46 (m, 4H), 7.29 (d, J = 8.0 Hz, 2H), 7.25–7.17 (m, 3H), 7.02 (d, = 7.2, 2H), 4.34 (s, 2H), 2.48 (s, 3H), 2.43 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.3, 165.3, 145.6, 143.6, 138.6, 134.7, 134.0, 133.1, 132.4 (2C), 129.6 (2C), 129.4 (2C), 129.3 (2C), 128.9 (2C), 128.6, 128.5 (2C), 128.3, 128.2, 127.7, 127.2, 127.0, 126.5 (3C), 123.7, 21.2 (3C), 17.6; HRMS (ESI-TOF) (m/z). Calcd for $C_{34}H_{31}N_3O_4S_2$, $[M + H]^+$ 610.1829; found 610.1832.

4-methyl-*N*-((*E*)-2-phenyl-1-(2-((*E*)-1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylidene)-1-tosylhydrazineyl)ethylidene)benzenesulfonamide (4e). White solid, mp 173–174 °C. IR (KBr) ν 3062, 3030, 1590, 1494, 1370, 1176, 1145, 1083 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.61 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 6.4 Hz, 5H), 7.28–7.16 (m, 6H), 6.99 (d, J = 8.0, 2H), 4.02 (s, 2H), 2.78 (s, 4H), 2.47 (s, 3H), 2.42 (s, 3H), 1.76 (s, 4H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.6, 165.3, 145.6, 143.6, 141.8, 138.6, 137.2, 134.0, 133.1, 132.4, 129.7 (2C), 129.6 (2C), 129.3, 128.9 (2C), 128.7 (2C), 128.6 (2C), 128.4, 127.2, 126.5 (2C), 124.9, 28.9 (2C), 22.6, 22.5, 21.3, 21.2, 17.6 (2C); HRMS (ESI-TOF) (m/z). Calcd for $C_{34}H_{35}N_3O_4S_2$, $[M + H]^+$ 614.2142; found 614.2145.

N-(1-(1-(mesitylsulfonyl)-2-((*E*)-1-phenylethylidene)hydrazineyl)-2-phenylethylidene)-4-methylbenzenesulfonamide (**4f**). White solid, mp 181–183 °C. IR (KBr) ν 3062, 1600, 1551, 1354, 1304, 1141, 1088 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.77 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.2 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.34–7.17 (m, 7H), 7.03 (d, J = 7.2 Hz, 2H), 6.93 (s, 2H), 4.58 (s, 2H), 2.43 (s, 6H), 2.34 (s, 3H), 2.32 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.3, 164.7, 143.9, 143.2, 140.3, 138.5, 135.0, 133.1, 132.4, 132.3, 132.0, 131.9, 129.4 (2C), 128.8, 128.7 (2C), 128.5 (2C), 127.9, 127.7 (2C), 127.1 (2C), 126.3 (2C), 21.8 (2C), 21.0 (2C), 20.7, 18.5; HRMS (ESI-TOF) (m/z). Calcd for $C_{32}H_{33}N_3O_4S_2$, $[M + H]^+$ 590.1985; found 590.1988.

4-methyl-*N*-((E)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl)-2-(*p*-tolyl)ethylidene) benzenesulfonamide (**4g**). White solid, mp 159–160 °C. IR (KBr) ν 3062, 2920, 1596, 1566, 1367, 1174, 1142, 1085 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.83 (d, J = 7.6 Hz, 2H), 7.61

(d, *J* = 8.0 Hz, 3H), 7.54–7.45 (m, 6H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 7.6 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 4.19 (s, 2H), 2.47 (s, 3H), 2.41 (s, 3H), 2.26 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.7, 165.4, 145.5, 143.5, 143.2, 138.6, 136.4, 135.1, 134.0, 132.3, 130.0, 129.6 (2C), 129.5 (2C), 129.1 (2C), 128.8 (2C), 128.5 (2C), 127.8 (2C), 126.5 (3C), 21.2 (2C), 20.7 (2C), 17.8; HRMS (ESI-TOF) (m/z). Calcd for $C_{31}H_{31}N_3O_4S_2$, $[M + H]^+$ 574.1829; found 574.1832.

4-methyl-*N*-((*E*)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl)-2-(*m*-tolyl)ethylidene) benzenesulfonamide (**4h**). White solid, mp 146–148 °C. IR (KBr) ν 3062, 2920, 1598, 1569, 1489, 1359, 1367, 1294, 1142, 1087 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 3H), 7.53–7.45 (m, 6H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.66 (s, 1H), 4.21 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 1.99 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.6, 165.2, 145.6, 138.6, 137.7, 134.9, 134.0, 133.0, 132.4, 130.5 (2C), 129.6 (2C), 129.5 (2C), 128.7 (2C), 128.5 (2C), 127.8 (2C), 127.6, 126.5 (3C), 125.7, 21.2 (3C), 20.7, 17.6; HRMS (ESI-TOF) (m/z). Calcd for $C_{31}H_{31}N_3O_4S_2$, $[M + H]^+$ 574.1829; found574.1830.

N-((*E*)-2-(4-fluorophenyl)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene)-4-methylbenzenesulfonamide (**4i**). White solid, mp 157–159 °C. IR (KBr) ν 3062, 1595, 1564, 1375, 1308, 1190, 1083 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 3H), 7.54–7.45 (m, 6H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.09–7.05 (m, 4H), 4.20 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.5, 165.0, 161.2 (d, *J* = 256.7 Hz), 145.7, 143.6, 138.5, 135.0, 133.9, 132.4, 130.7 (2C), 129.7 (2C), 129.6 (2C), 129.2 (d, *J* = 3.1 Hz), 128.8 (2C), 128.5 (2C), 127.8 (2C), 126.5 (3C), 115.5 (d, *J* = 21.8 Hz), 21.1 (2C), 21.1 (d, *J* = 7.7 Hz), 17.9; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{28}FN_3O_4S_2$, $[M + H]^+$ 578.1578; found 578.1581.

N-((*E*)-2-(4-chlorophenyl)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene)-4-methylbenzenesulfonamide (**4j**). White solid, mp 153–155 °C. IR (KBr) ν 3064, 1593, 1562, 1444, 1345, 1272, 1122, 1081 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 3H), 7.53–7.45 (m, 6H), 7.30–7.27 (m, 4H), 7.02 (d, *J* = 8.8 Hz, 2H), 4.24 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.5, 164.8, 145.7, 143.7, 138.4, 135.0, 133.8, 132.4, 132.1, 132.0, 130.6 (2C), 129.7 (2C), 129.6 (2C), 128.8 (2C), 128.5 (2C), 127.8 (2C), 126.5 (3C), 38.0, 21.1 (2C), 21.1, 18.0; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{28}ClN_3O_4S_2$, $[M + H]^+$ 594.1283; found 594.1285.

N-((*E*)-2-(4-bromophenyl)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene)-4-methylbenzenesulfonamide (**4k**). White solid, mp 158–160 °C. IR (KBr) ν 3062, 1592, 1560, 1486 1369, 1282, 1142, 1082 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 (d, *J* = 7.2 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 3H), 7.53–7.41 (m, 8H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 4.21 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.4, 164.7, 145.7, 143.6, 138.4, 135.0, 133.8, 132.5, 132.4, 131.5, 132.0, 130.8 (2C), 129.7 (2C), 129.6 (2C), 128.8 (2C), 128.5 (2C), 127.8 (2C), 126.5 (3C), 120.3, 21.1 (2C), 18.0; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{28}BrN_3O_4S_2$, $[M + H]^+$ 638.0778; found 638.0779.

4-methyl-*N*-((*E*)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl)octylidene) benzenesulfonamide (**4l**). White solid, mp 103–105 °C. IR (KBr) ν 3063, 2864, 1595, 1338, 1264, 1155, 1076 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.57–7.53 (m, 6H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.75 (d, *J* = 7.6 Hz, 2H), 2.56 (s, 3H), 2.44 (s, 3H), 2.40 (s, 3H), 1.39 (s, 2H), 1.17–1.08 (m, 8H), 0.75 (t, *J* = 6.8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 167.9, 145.6, 143.3, 138.9, 135.4, 134.1, 132.4, 129.7 (2C), 129.6 (2C), 128.9 (2C), 128.4 (2C), 127.8 (2C), 126.3 (2C), 32.5, 30.9, 28.8, 27.8, 24.9, 21.9, 21.3, 21.1, 18.7, 13.9; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{37}N_3O_4S_2$, $[M + H]^+$ 568.2298; found 568.2231.

4-methyl-*N*-((*E*)-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl)-2-(thiophen-2-yl) ethylidene)benzenesulfonamide (**4m**). Yellow solid, mp 67–69 °C. IR (KBr) ν 3062, 2927, 2866, 1590, 1369, 1307, 1153, 1087 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (t, *J* = 6.8 Hz,

4H), 7.65 (d, *J* = 9.2 Hz, 3H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 3H), 6.86–6.82 (m, 2H), 4.58 (s, 2H), 2.50 (s, 3H), 2.41 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.3, 163.9, 145.4, 143.4, 139.2, 135.8, 134.4, 134.2, 132.2, 129.4 (2C), 129.3 (2C), 129.2 (2C), 128.8 (2C), 128.1, 127.9 (2C), 127.1 (2C), 127.0, 125.4, 33.8, 21.9, 21.8, 18.2; HRMS (ESI-TOF) (m/z). Calcd for $C_{28}H_{27}N_3O_4S_3$, $[M + H]^+$ 565.1237; found 565.1239.

N-(2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl)ethylidene) benzenesulfonamide (**4n**). White solid, mp 149–151 °C. IR (KBr) ν 3062, 1589, 1561, 1494, 1365, 1282, 1140, 1085 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 6.8 Hz, 3H), 7.70–7.60 (m, 3H), 7.53–7.46 (m, 4H), 7.27–7.20 (m, 5H), 7.02 (d, *J* = 6.8 Hz, 2H), 4.23 (s, 2H), 2.41 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.7, 165.7, 145.6, 141.3, 135.0, 133.9, 133.1, 133.0, 132.4, 129.6, 129.3 (2C), 128.9 (2C), 128.8 (2C), 128.6 (2C), 128.5 (2C), 127.8 (2C), 127.2, 126.4 (3C), 21.2 (2C), 17.7; HRMS (ESI-TOF) (m/z). Calcd for $C_{29}H_{27}N_3O_4S_2$, $[M + H]^+$ 546.1516; found 546.1519.

4-chloro-*N*-(2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene) benzenesulfonamide (**4o**). White solid, mp 141–143 °C. IR (KBr) ν 3067, 1592, 1554, 1493, 1341, 1308, 1146, 1081 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.75 (t, *J* = 9.6 Hz, 4H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 4H), 7.29–7.20 (m, 5H), 7.02 (t, *J* = 6.8 Hz, 2H), 4.15 (s, 2H), 2.42 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.8, 165.5, 145.7, 140.2, 138.0, 135.0, 134.0, 133.0, 132.4, 129.6 (2C), 129.4 (3C), 128.8, 128.7 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 127.8 (2C), 127.2, 21.2 (2C), 17.8; HRMS (ESI-TOF) (m/z). Calcd for $C_{29}H_{26}ClN_3O_4S_2$, $[M + H]^+$ 580.1126; found 580.1128.

4-bromo-*N*-(2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene) benzenesulfonamide (**4p**). White solid, mp 139–140 °C. IR (KBr) ν 3066, 1594, 1554, 1493, 1374, 1309, 1145, 1083 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.83 (t, *J* = 7.6 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.53–7.49 (m, 4H), 7.29–7.20 (m, 5H), 7.01 (t, *J* = 7.2 Hz, 2H), 4.23 (s, 2H), 2.42 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.8, 165.5, 145.7, 140.6, 135.0, 134.0, 133.0, 132.4 (3C), 129.6 (2C), 128.8 (4C), 128.7 (2C), 128.4 (3C), 128.3 (2C), 127.2 (2C), 127.0, 21.2 (2C), 17.8; HRMS (ESI-TOF) (m/z). Calcd for $C_{29}H_{26}BrN_3O_4S_2$, $[M + H]^+$ 624.0621; found 624.0622.

4-methoxy-*N*-(2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene) benzenesulfonamide (**4q**). White solid, mp 143–145 °C. IR (KBr) ν 3010, 1592, 1561, 1492, 1367, 1296, 1144, 1082 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, *J* = 7.6 Hz, 2H), 7.69 (t, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 4H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.24–7.17 (m, 5H), 7.01 (d, *J* = 6.8 Hz, 2H), 4.24 (s, 2H), 3.92 (s, 3H), 2.42 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.0, 165.4, 163.1, 146.0, 135.5, 134.4, 133.6, 132.7, 130.0, 129.3 (2C), 129.2 (3C), 129.1 (4C), 129.0 (2C), 128.9 (2C), 128.2 (2C), 127.5, 114.8, 56.3, 21.7 (2C), 18.1; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{29}N_3O_5S_2$, $[M + H]^+$ 576.1622; found 576.1621.

1-phenyl-*N*-(2-phenyl-1-(2-((*E*)-1-phenylethylidene)-1-tosylhydrazineyl) ethylidene) methanesulfonamide (**4r**). White solid, mp 125–127 °C. IR (KBr) ν 3063, 2972, 1590, 1576, 1493, 1365, 1293, 1173, 1086 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85–7.79 (m, 4H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.56–7.50 (m, 4H), 7.21 (t, *J* = 6.8 Hz, 3H), 7.01 (d, *J* = 7.2 Hz, 2H), 4.18 (s, 2H), 3.04(t, *J* = 7.6 Hz, 2H), 2.46 (s, 3H), 1.75 (s, 3H), 1.69 (s, 2H), 1.02 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.5, 165.5, 145.7, 135.1, 134.6, 133.1, 132.3, 129.9 (3C), 128.9 (2C), 128.8 (3C), 128.6 (2C), 128.3 (3C), 127.8 (3C), 127.1, 56.0 (2C), 21.2, 17.6, 16.8, 12.6; HRMS (ESI-TOF) (m/z). Calcd for $C_{30}H_{29}N_3O_4S_2$, $[M + H]^+$ 560.1672; found 560.1676.

4. Conclusions

We developed an effective copper-catalyzed three-component one-pot synthesis of *N*-sulfonyl amidines from terminal alkynes, sulfonyl azides and weak nucleophilic sulfonyl hydrazine. The synthetic pathway extended the applications of the CuAAC/ring-opening

reaction, and we expect that this methodology and *N*-sulfonyl amidines products could be applied to organic synthesis.

Supplementary Materials: The following are available online, The original ^{1}H and ^{13}C NMR spectra are available in supplementary material.

Author Contributions: Conceptualization, methodology and supervision W.Y.; experiment, Y.Z., Z.Z. and M.C.; spectroscopic characterization Y.Z. and Z.Z. and writing—review and editing, Y.Z., Z.Z., M.C. and W.Y. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the Applied and Basic Research Fund of Guangdong Province (2019A1515110918), the Medical Scientific Research Foundation of Guangdong Province (A2020202 and A2021037), the Science and Technology Planning Program of Zhanjiang (2019A01018) for support and the funds provided, in 2019, for the PhD-level researchers of Guangdong Medical University.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data is contained within the article.

Conflicts of Interest: The authors declare no conflict of interest.

Sample Availability: Samples of the compounds **4a**–**4r** are available from the authors.

References

1. Cheng, L.; Chen, S.; Wu, W.; Kuo, Z.C.; Wei, Z.; Meng, S.; Chen, C.; Zhang, C.; He, Y. Gastric cancer in young patients: A separate entity with aggressive features and poor prognosis. *J. Cancer Res. Clin. Oncol.* **2020**, *146*, 2937–2947. [CrossRef]
2. Greenhill, J.V.; Lue, P. Amidines and guanidines in medicinal chemistry. *Prog. Med. Chem.* **1993**, *30*, 203–326. [PubMed]
3. Adiche, C.; Hamadouche, M.; Abed, D.E. Facile synthesis of sulfonyl amidines by 1,3-dipolar cycloaddition between 1-morpholinocycloalkenes and sulfonyl azides without catalyst. *Heterocycles* **2016**, *92*, 1614–1628.
4. Boyd, G.V. Reactions and Synthetic Uses of Amidines. In *The Chemistry of Amidines and Imidates*; Patai, S., Ed.; John Wiley & Sons: Hoboken, NJ, USA, 1991; pp. 67–424.
5. Edwards, P.D.; Albert, J.S.; Sylvester, M.; Aharony, D.; Andisik, D.; Callaghan, O.; Campbell, J.B.; Carr, R.A.; Chessari, G.; Congreve, M.; et al. Application of fragment-based lead generation to the discovery of novel, cyclic amidine beta-secretase inhibitors with nanomolar potency, cellular activity, and high ligand efficiency. *J. Med. Chem.* **2007**, *50*, 5912–5925. [CrossRef] [PubMed]
6. Peterlin-Masic, L.; Kikelj, D. Arginine mimetics. *Tetrahedron* **2001**, *57*, 7073–7105. [CrossRef]
7. Iwakawa, T.; Tamura, H.; Masuko, M.; Murabayashi, A.; Hayase, Y. Synthesis and rice-blast control activity of sulfonylamidines. *J. Pesticide Sci.* **1992**, *17*, 131–135. [CrossRef]
8. Gobis, K.; Foks, H.; Sławiński, J.; Sikorski, A.; Trzybiński, D.; Augustynowicz-Kopeć, E.; Napiórkowska, A.; Bojanowski, K. Synthesis, structure, and biological activity of novel heterocyclic sulfonyl-carboximidamides. *Monatsh. Chem.* **2013**, *144*, 647–658. [CrossRef]
9. Chang, S.Y.; Bae, S.J.; Lee, M.Y.; Baek, S.H.; Chang, S.; Kim, S.H. Chemical affinity matrix-based identification of prohibitin as a binding protein to anti-resorptive sulfonyl amidine compounds. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 727–729. [CrossRef] [PubMed]
10. Kim, M.H.; Park, M.; Song, J.S.; Park, S.J.; Kim, S.H. Anti-resorptive activity and pharmacokinetic study of N^1,N^1-diisopropyl-N^2-(diphenylphosphoryl)-2-(4-nitrophenyl)acetamidine. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4263–4266. [CrossRef]
11. Lee, M.Y.; Kim, M.H.; Kim, J.; Kim, S.H.; Kim, B.T.; Jeong, I.H.; Chang, S.; Kim, S.H.; Chang, S.Y. Synthesis and SAR of sulfonyl- and phosphoryl amidine compounds as anti-resorptive agents. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 541–545. [CrossRef] [PubMed]
12. Suja, T.D.; Divya, K.V.L.; Naik, L.V.; Kumar, A.R.; Kamal, A. Copper-catalyzed three-component synthesis of aminonaphthoquinone-sulfonylamidine conjugates and in vitro evaluation of their antiproliferative activity. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 2072–2076. [CrossRef] [PubMed]
13. Beryozkina, T.; Bakulev, V.; Dianova, L.; Berseneva, V.; Slepukhin, P.; Leban, J.; Kalaba, P.; Aher, N.Y.; Ilic, M.; Sitte, H.H.; et al. Organometallic routes to novel steroids containing heterocyclic c-17 side-chains. *Synthesis* **2016**, *48*, 48–56.
14. Filimonov, V.O.; Dianova, L.N.; Galata, K.A.; Beryozkina, T.V.; Novikov, M.S.; Berseneva, V.S.; Eltsov, O.S.; Lebedev, A.T.; Slepukhin, P.A.; Bakulev, V.A. Switchable synthesis of 4,5-functionalized 1,2,3-thiadiazoles and 1,2,3-triazoles from 2-cyanothioacetamides under diazo group transfer conditions. *J. Org. Chem.* **2017**, *82*, 4056–4071. [CrossRef] [PubMed]
15. Song, Z.-L.; Chen, H.-L.; Wang, Y.-H.; Goto, M.; Gao, W.-J.; Cheng, P.-L.; Morris-Natschke, S.L.; Liu, Y.-Q.; Zhu, G.-X.; Wang, M.-J.; et al. Design and synthesis of novel PEG-conjugated 20(S)-camptothecin sulfonylamidine derivatives with potent in vitro antitumor activity via Cu-catalyzed three-component reaction. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 2690–2693. [CrossRef] [PubMed]
16. Ilkin, V.; Berseneva, V.; Beryozkina, T.; Glukhareva, T.; Dianova, L.; Dehaen, W.; Seliverstova, E.; Bakulev, V. Gastric cancer in young patients: A separate entity with aggressive features and poor prognosis. *J. Org. Chem.* **2020**, *16*, 2937–2947.

17. Filimonov, V.O.; Dianova, L.N.; Beryozkina, T.V.; Mazur, D.; Beliaev, N.A.; Volkova, N.N.; Ilkin, V.G.; Dehaen, W.; Lebedev, A.T.; Bakulev, V.A. Water/Alkali-catalyzed reactions of azides with 2-cyanothioacetamides. eco-friendly synthesis of monocyclic and bicyclic 1,2,3-thiadiazole-4-carbimidamides and 5-amino-1,2,3-triazole-4-carbothioamides. *J. Org. Chem.* **2019**, *84*, 13430–13446. [CrossRef]
18. Aswad, M.; Chiba, J.; Takenori, T.; Hatanaka, Y. Evaluation of dipole moment and electrophilicity on the nature of click-type coupling reaction between thioamide and sulfonyl azide. *Tetrahedron Lett.* **2016**, *57*, 1313–1316. [CrossRef]
19. Fleury, L.M.; Wilson, E.E.; Vogt, M.; Fan, T.J.; Oliver, A.G.; Ashfeld, B.L. Amine-free approach toward *N*-toluenesulfonyl amidine construction: A phosphite-mediated Beckmann-like coupling of oximes and *p*-toluenesulfonyl azide. *Angew. Chem.* **2013**, *52*, 11589–11593. [CrossRef]
20. Chandna, N.; Chandak, N.; Kumar, P.; Kapoor, J.K.; Sharma, P.K. Metal- and solvent-free synthesis of *N*-sulfonylformamidines. *Green Chem.* **2013**, *15*, 2294–2301. [CrossRef]
21. Chen, S.; Xu, Y.; Wan, X. Direct condensation of sulfonamide and formamide: NaI-catalyzed synthesis of *N*-sulfonyl formamidine using TBHP as oxidant. *Org. Lett.* **2011**, *13*, 6152–6155. [CrossRef] [PubMed]
22. DeKorver, K.A.; Johnson, W.L.; Zhang, Y.; Hsung, R.P.; Dai, H.; Deng, J.; Lohse, A.G.; Zhang, Y.-S. N-allyl-N-sulfonyl ynamides as synthetic precursors to amidines and vinylogous amidines. An unexpected *N*-to-C 1,3-sulfonyl shift in nitrile synthesis. *J. Org. Chem.* **2011**, *76*, 5092–5103. [CrossRef]
23. Kim, S.H.; Park, S.H.; Choi, J.H.; Chang, S. Sulfonyl and phosphoryl azides: Going further beyond the click realm of alkyl and aryl azides. *Chem. Asian. J.* **2011**, *6*, 2618–2634. [CrossRef] [PubMed]
24. Xu, L.; Zhou, T.; Liao, M.; Hu, R.; Tang, B.Z. Multicomponent polymerizations of alkynes, sulfonyl azides, and 2-hydroxybenzonitrile/2-aminobenzonitrile toward multifunctional iminocoumarin/quinoline-containing poly(n-sulfonylimine)s. *ACS Macro. Lett.* **2019**, *8*, 101–106. [CrossRef]
25. Yang, W.; Huang, D.; Zeng, X.; Zhang, J.; Wang, X.; Hu, Y. *N*-Sulfonyl acetylketenimine as a highly reactive intermediate for synthesis of *N*-Aroylsulfonamides. *Tetrahedron* **2019**, *75*, 381–386. [CrossRef]
26. Yang, W.; Huang, D.; Zeng, X.; Luo, D.; Wang, X.; Hu, Y. *N*-Sulfonyl acetylketenimine as a highly reactive intermediate for the synthesis of *N*-sulfonyl amidines. *Chem. Commun.* **2018**, *54*, 8222–8225. [CrossRef] [PubMed]
27. Nallagangula, M.; Namitharan, K. Copper-catalyzed sulfonyl azide-alkyne cycloaddition reactions: Simultaneous generation and trapping of copper-triazoles and -ketenimines for the synthesis of triazolopyrimidines. *Org. Lett.* **2017**, *19*, 3536–3539. [CrossRef]
28. Reichart, B.; Cruz, G.G.D.L.; Zangger, K.; Kappe, C.O.; Glasnov, T. Copper/Nafion-catalyzed hydroarylation process involving ketenimine intermediates: A novel and synthetic approach to 4-sulfonamidoquinoline-2-ones and derivatives thereof. *Adv. Synth. Catal.* **2016**, *358*, 50–55. [CrossRef]
29. Kumar, R.; Thorat, S.H.; Reddy, M.S. Cu-Catalyzed iminative hydroolefination of unactivated alkynes en route to 4-imino-tetrahydropyridines and 4-aminopyridines. *Chem. Commun.* **2016**, *52*, 13475–13478. [CrossRef] [PubMed]
30. Ramanathan, D.; Pitchumani, K. Copper(I)-Y Zeolite-catalyzed regio- and stereoselective [2 + 2 + 2] cyclotrimerization cascade: An atom- and step-economical synthesis of pyrimido [1,6-a]quinolone. *J. Org. Chem.* **2015**, *80*, 10299–10308. [CrossRef] [PubMed]
31. Xing, Y.; Cheng, B.; Wang, J.; Lu, P.; Wang, Y. Copper-catalyzed three-component synthesis of 3-aminopyrazoles and 4-iminopyrimidines via β-alkynyl-*N*-sulfonyl ketenimine intermediates. *Org. Lett.* **2014**, *16*, 4814–4817. [CrossRef]
32. Yoo, E.J.; Ahlquist, M.; Bae, I.; Sharpless, K.B.; Fokin, V.V.; Chang, S. Mechanistic studies on the Cu-catalyzed three-component reactions of sulfonyl azides, 1-alkynes and amines, alcohols, or water: Dichotomy via a common pathway. *J. Org. Chem.* **2008**, *73*, 5520–5528. [CrossRef] [PubMed]
33. Hwang, S.J.; Cho, S.H.; Chang, S. Comparison of phenolic compounds of rhubarbs in the section deserticola with Rheum palmatum by HPLC-DAD-ESI-MSn. *Pure Appl. Chem.* **2008**, *80*, 873–879. [CrossRef]
34. Sedaghat, A.; Nematpour, M.; Bayanati, M.; Tabatabai, S.A. Synthesis of functionalized quinoline derivatives via intramolecular C–H activation reactions of *N*-sulfonylamidines and isocyanides. *Monatsh. Chem.* **2020**, *151*, 1591–1596. [CrossRef]
35. Kumar, Y.K.; Kumar, G.R.; Reddy, T.J.; Sridhar, B.; Reddy, M.S. Synthesis of 3-Sulfonylamino Quinolines from 1-(2-Aminophenyl) Propargyl Alcohols through a Ag(I)-Catalyzed hydroamination, (2 + 3) cycloaddition, and an unusual strain-driven ring expansion. *Org. Lett.* **2015**, *17*, 2226–2229. [CrossRef] [PubMed]
36. Tang, H.L.; Shu, M.M.; Dong, B.X.; Gu, H.T.; Liang, R.; Bai, Q.X.; Yang, L.; Zhang, T.; Gao, G.X.; Chen, X.Q. Influence of CD117 expression on response of multiple myeloma patients to chemotherapy. *Zhongguo Shi Yan Xue Ye Xue Za Zhi* **2015**, *23*, 1346–1351. [PubMed]
37. Ghorai, S.; Lee, D. Selectivity for alkynyl or allenyl imidamides and imidates in copper-catalyzed reactions of terminal 1,3-diynes and azides. *Org. Lett.* **2021**, *23*, 697–701. [CrossRef] [PubMed]
38. Kim, J.Y.; Kim, S.H.; Chang, S. Highly efficient synthesis of α-amino amidines from ynamides by the Cu-catalyzed three-component coupling reactions. *Tetrahedron Lett.* **2008**, *49*, 1745–1749. [CrossRef]
39. Chauhan, D.P.; Varma, S.J.; Vijeta, A.; Banerjee, P.; Talukdar, P. A 1,3-amino group migration route to form acrylamidines. *Chem. Commun.* **2014**, *50*, 323–325. [CrossRef] [PubMed]
40. Yavari, I.; Ahmadian, S.; Ghazanfarpur-Darjani, M.; Solgi, Y. Formation of *N*-sulfonylamidines by copper-catalyzed coupling of sulfonyl azides, terminal alkynes, and trialkylamines. *Tetrahedron Lett.* **2011**, *52*, 668–670. [CrossRef]
41. Kim, J.; Lee, S.Y.; Lee, J.; Do, Y.; Chang, S. Synthetic utility of ammonium salts in a Cu-catalyzed three-component reaction as a facile coupling partner. *J. Org. Chem.* **2008**, *73*, 9454–9457. [CrossRef]

42. Cui, S.L.; Wang, J.; Wang, Y.J. Copper-catalyzed multicomponent reaction: Facile access to functionalized 5-arylidene-2-imino-3-pyrrolines. *Org. Lett.* **2007**, *9*, 5023–5025. [CrossRef] [PubMed]
43. Li, S.; Zou, S.; Wu, J. An efficient approach for the construction of benzazepine and benzoxepine derivatives. *Chem. Asian J.* **2012**, *7*, 2882–2887. [CrossRef] [PubMed]
44. Massaro, N.P.; Chatterji, A.; Sharma, I. Three-component approach to pyridine-stabilized ketenimines for the synthesis of diverse heterocycles. *J. Org. Chem.* **2019**, *84*, 13676–13685. [CrossRef] [PubMed]
45. Chen, J.L.; Namirembe, S.; Lauchert, L.T.; Tsougranis, G.H.; Isaacs, A.K. Cu(I)-catalyzed synthesis of *N*-tosyl-4-iminoquinolizines. *Tetrahedron Lett.* **2015**, *56*, 4105–4108. [CrossRef]
46. Tong, T.; Wu, X.; Li, E.; Kang, H.; Wang, X.; Lv, X. One-pot synthesis of 4-sulfonyliminotetrahydropyrimidin-2-one derivatives through a copper-catalyzed tandem reaction. *J. Org. Chem.* **2018**, *83*, 15533–15540. [CrossRef] [PubMed]
47. Zhang, D.; Nakamura, I.; Terada, M. Copper-catalyzed cascade transformation of o-propargylic oximes with sulfonyl azides to α,β-unsaturated *N*-acylamidines. *Org. Lett.* **2014**, *16*, 5184–5187. [CrossRef] [PubMed]
48. Choi, W.; Kim, J.; Ryu, T.; Kim, K.B.; Lee, P.H. Synthesis of *N*-Imidoyl and *N*-oxoimidoyl sulfoximines from 1-alkynes, *N*-sulfonyl azides, and sulfoximines. *Org. Lett.* **2015**, *17*, 3330–3333. [CrossRef] [PubMed]
49. Ramanathan, D.; Pitchumani, K. Copper(I)-catalyzed one-pot synthesis of highly functionalized pyrrolidines from sulfonyl azides, alkynes, and dimethyl 2-(phenylamino)maleate. *Eur. J. Org. Chem.* **2015**, 463–467. [CrossRef]
50. Zhou, F.; Liu, X.; Zhang, N.; Liang, Y.; Zhang, R.; Xin, X.; Dong, D. Copper-catalyzed three-component reaction: Solvent-controlled regioselective synthesis of 4-amino- and 6-amino-2-iminopyridines. *Org. Lett.* **2013**, *15*, 5786–5789. [CrossRef] [PubMed]