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Syntheses of *N*-sulfonyl-*N,N*-disubstituted amidines via a three-component free-radical coupling reaction of tertiary amines and arenesulfonyl azides with terminal alkynes

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A facile and efficient synthesis of *N*-sulfonyl-*N,N*-disubstituted amidines has been achieved via a CuI-catalyzed three-component free-radical coupling reaction of tertiary amines and arenesulfonyl azides with terminal alkynes in the presence of azodiisobutyronitrile (AIBN). The reaction mechanism of this reaction has also been studied.

free radical, multicomponent reaction, sulfonyl azide, terminal alkyne

1 Introduction

Multicomponent reactions (MCRs) offer an efficient and straightforward route for the generation of complexity and diversity in a single operation, and have found wide applications in combinational chemistry and drug discovery [1]. Among various MCRs recently developed [2–5], the CuI-catalyzed MCRs of sulfonyl azides and alkynes with a third component, like amines, water, alcohol, imines, salicylaldehyde, aziridine or nitroolefin have attracted increasing research interests lately [6–15]. For example, Chang's [16–27] and Wang's [28–33] groups have applied these CuI-catalyzed MCRs on terminal alkynes respectively for the efficient generation of *N*-sulfonylamidines, amides, *N*-sulfonylazetidin-2-imines, iminocoumarins, 5-arylidene-2-imino-3-pyrrolines, and γ-nitro imidates. Our group has also applied this reaction for the efficient generation of benzoxazoline-amidines and 4-arylsulfonylimino-4,5-dihydrofurans by reacting sulfonyl azides and alkynes with Schiff bases or β-ketoesters [34, 35].

Amidines widely exist in natural products [36], possess various interesting chemical properties, and have been widely used in medical and synthetic chemistry [37]. For example, as the building blocks for the synthesis of iminopeptides [38, 39], antitumor and antibiotic compounds [40], the traditional synthetic methods for amidines are mainly based on the functional group transformation from some precursors such as azidolactams [41], isonitriles [42], or aldoximes [43]. Chang has improved the synthesis by developing a tandem nucleophilic addition reaction of sulfonyl azides and alkynes with primary or secondary amines [16] and has applied it for the efficient synthesis of sulfonyl amidine derivatives. On the other hand, no tertiary amine has been used for the synthesis of sulfonyl amidine derivatives [44–46]. Herein we report a facile synthesis of *N*-sulfonyl-*N,N*-disubstituted amidines via a MCR free radical coupling of tertiary amines and arenesulfonyl azides with terminal alkynes (Scheme 1).

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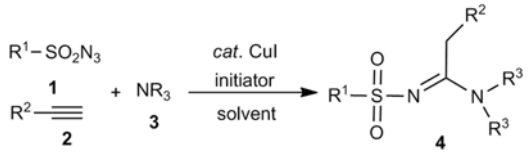
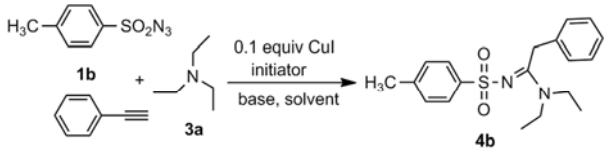


Scheme 1 Synthsis of *N*-sulfonylamidine derivatives **4**. Reaction conditions: CuI (0.1 equiv), AIBN (2.0 equiv), **3** (3 equiv, slow addition), 80 °C, 8 h.

2 Results and discussion

The optimized reaction conditions for the MCR of arenesulfonyl azides **1b** and alkynes **2a** with tertiary amines **3a** were obtained by varying the reaction conditions, including the base, the solvent, the temperature, and the free radical's initiator, as summarized in Table 1. Triethylamine (TEA) as base gave the best result (Table 1, entry 6). Tetrahydrofuran (THF) as solvent afforded good yield (Table 1, entries 1–4). The decrease of reaction time led to the great decrease of the yield with 8 h as the optimized reaction time (Table 1, entry 8). In addition, the free radical's initiator played an important role in this reaction. No reaction was observed without a free radical's initiator (Table 1, entry 18). In comparison with diethyl azodicarboxylate (DEAD), AIBN gave a better result (Table 1, entries 5 and 14). Thus the optimized reaction condition was set at THF, TEA, AIBN, 80 °C and 8 h. Under this condition, the desired *N,N*-diethyl-2-phenyl-*N′*-tosylacet amidine **4b** was obtained in 82% yield (Table 1, entry 6). The chemical structure of compound **4b** [47] was confirmed by X-ray analysis result as shown in Figure 1.

Table 1 Optimization of the reaction conditions for the CuI-catalyzed three-component reactions of arenesulfonyl azide **1b** and alkyne **2a** with tertiary amine **3a**



Entry	Base	Solvent	Temp. (°C)	Time (h)	Initiator	Yield (%)[a)]
1	TEA	THF	80	8	AIBN	73
2	TEA	DMF	80	12	AIBN	54
3	TEA	CH_3CN	80	8	AIBN	61
4	TEA	CH_2Cl_2	80	8	AIBN	62
5	TEA	THF	rt	8	AIBN	70
6	TEA[b)]	THF	80	8	AIBN	82
7	TEA[b)]	THF	40	8	AIBN	56
8	TEA[b)]	THF	80	4	AIBN	59
9	TEA[b)]	THF	rt	8	DEAD	72
10	K_3PO_4/TEA	THF	80	8	DEAD	65
11	Pyridine	THF	rt	8	DEAD	0
12	TEA	THF	0–5	8	DEAD	42
13	TEA	THF	50	8	DEAD	60
14	TEA	THF	rt	8	DEAD	51
15	K_3PO_4/TEA	THF	rt	8	AIBN	24
16	Pyridine	THF	80	8	AIBN	0
17	K_2CO_3/TEA	THF	80	10	AIBN	72
18	TEA	THF	80	8	–	0

a) Reaction conditions: *p*-tolysulfonyl azide (1.1 mmol), phenylacetylene (1.0 mmol), AIBN or DEAD (2.0 mmol), CuI (0.1 mmol), and TEA (3.0 mmol), N_2 atmosphere. b) 2.0 mmol.

To test the versatility of this reaction, the optimized reaction condition was further applied for the reaction of other arenesulfonyl azides **1** and terminal alkynes **2** with tertiary amines **3** as summarized in Table 2. Both alkyl and aryl alkynes can be used for this reaction, but alkyl alkynes generally give relatively high yields. The presence of either electron-withdrawing (–Cl) or electron-donating groups ($-CH_3$) on arenesulfonyl azides **1** provides high yields (Table 2, entries 1, 2, 6). Long-chain containing tertiary alkylamines **3** generally give better yields of the desired products (Table 2, entries 1, 8, 14).

To study the reaction mechanism, *N,N*-dimethyl-1-phenylmethanamine **3d** was used to substitute the alkylamine for this reaction, from which a mixture of compounds **4** and **5** was obtained (Table 3). The NMR yield analysis shows that the yield of compounds **4** and **5** were obtained with a ratio close to the theoretical ratio 1:2 for this reaction. The decrease of the yield of compound **4** in this case was attributed to the electron withdrawing effect of the phenyl substituent.

The ESI-MS analysis results (Scheme 2) of the reaction mixture indicated the formation of 2,2-dimethylhexanenitrile and methacrylonitrile when tributylamine was used. On the other hand, the usage of *N,N*-dimethyl-1-phenylmethanamine **3d** gave a mixture of two nitrile compounds (pivalonitrile and 2,2-dimethyl-3-phenyl propanenitrile).

On the basis of these experimental results, we proposed a three component free radical coupling reaction mechanism for this reaction as shown in Scheme 3. According to Chang [16–27] and Wang [28–33], arenesulfonyl azide **1** can react with the alkyne **2** to form the ketenimine species **B** in the

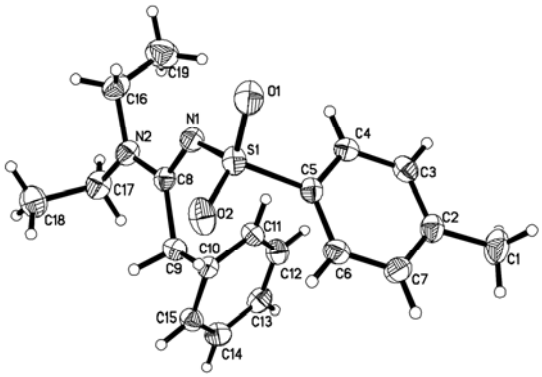
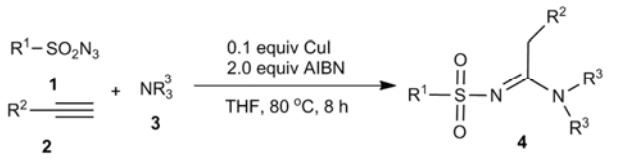


Figure 1 X-ray crystal structure of compound **4b**.

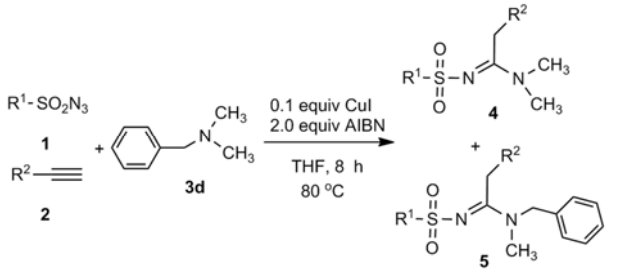
Table 2 CuI-catalyzed three-component coupling reactions for the generation of *N*-sulfonyl-*N,N*-disubstituted amidines **4**



Entry	R^1	R^2	R^3	Yield (%) [a]	
1	C_6H_5 (**1a**)	C_6H_5 (**2a**)	C_2H_5 (**3a**)	**4a**	80
2	*p*-MeC_6H_4 (**1b**)	**2a**	**3a**	**4b**	82
3	**1b**	CH_2CH_2OTBS (**2b**)	**3a**	**4c**	79
4	**1a**	*n*-C_5H_{11} (**2c**)	**3a**	**4d**	82
5	**1b**	**2c**	**3a**	**4e**	85
6	*p*-ClC_6H_4 (**1c**)	**2c**	**3a**	**4f**	81
7	**1a**	**2a**	*n*-C_4H_9 (**3b**)	**4g**	82
8	**1b**	**2a**	**3b**	**4h**	84
9	**1c**	**2a**	**3b**	**4i**	79
10	**1a**	**2c**	**3b**	**4j**	83
11	**1b**	**2c**	**3b**	**4k**	86
12	**1c**	**2c**	**3b**	**4l**	82
13	**1a**	**2a**	*n*-C_9H_{19} (**3c**)	**4m**	83
14	**1b**	**2a**	**3c**	**4n**	84
15	**1a**	**2c**	**3c**	**4o**	83
16	**1b**	**2c**	**3c**	**4p**	86
17	**1c**	**2c**	**3c**	**4q**	85
18	**1b**	*p*-MeC_6H_4 (**2d**)	**3b**	**4r**	83
19	**1a**	**2d**	**3a**	**4s**	81

a) Reaction conditions: arenesulfonyl azide (1.1 mmol), phenylacetylene (1.0 mmol), AIBN (2.0 mmol), CuI (0.1 mmol), and tertiary amine (3.0 mmol), N_2 atmosphere, 80 °C, 8 h.

Table 3 Using *N,N*-dimethyl-1-phenylmethanamine **3d** as a substrate for the synthesis of *N*-sulfonylamidines **4** and **5**



Entry	R^1	R^2	Yield (%) [a]			
			4		**5**	
1	C_6H_5 (**1a**)	C_6H_5 (**2a**)	**4t**	31	**5t**	35
2	*p*-MeC_6H_4 (**1b**)	**2a**	**4u**	34	**5u**	36

a) Isolated yield.

presence of CuI. Meanwhile, AIBN releases nitrogen under heat condition to form the free radical **C**, which attacks TEA (**3**) to generate a free radical **D** and methacrylonitrile with the release of hydrogen radical. Subsequently, the hydrogen radical and the free radical **D** attack the intermediate **B** to generate the target *N*-sulfonylamidine derivatives **4**.

There are possibly two competitive reaction routes for the formation of compound **4** (Scheme 4): the reaction between the intermediate **B** and hydrogen radical and the one between **B** and the free radical **D**. Therefore, a quantum chemical calculation has been performed. With DFT method implemented in Gaussian 09 package [48] under B3LYP/6-31+g** level, the reactants, products, possible intermediates and transition state geometries along the proposed reaction routes are optimized, and the reaction potential energy profiles are plotted in Figure 2. In the first step of pathway **I**, the reaction between hydrogen radical and intermediate **B** to form intermediate **E** is exothermic. The energy released from this step is large enough for the subsequent step reaction (2.4 kcal/mol). In contrast, the first step in pathway **II** is endothermic, and requires about 9.6 kcal/mol energy. Thus, pathway **I** is dominant in the formation of compound **4**.

3 Conclusions

In conclusion, we have developed a new general approach for the convenient synthesis of *N*-sulfonyl-*N,N*-disubstituted amidines, based on a CuI-catalyzed multicomponent free-radical coupling reaction of arenesulfonyl azides and terminal alkynes with tertiary amines. The reaction mechanism has been studied. The usage of tertiary amine is our synthetic approach as a complementary to Chang's strategy, might find applications for the efficient synthesis of various *N*-sulfonylamidine derivatives.

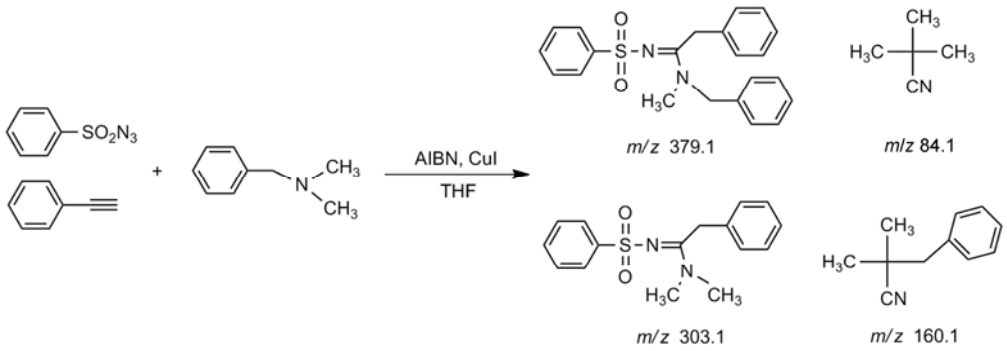
4 Experimental section

General

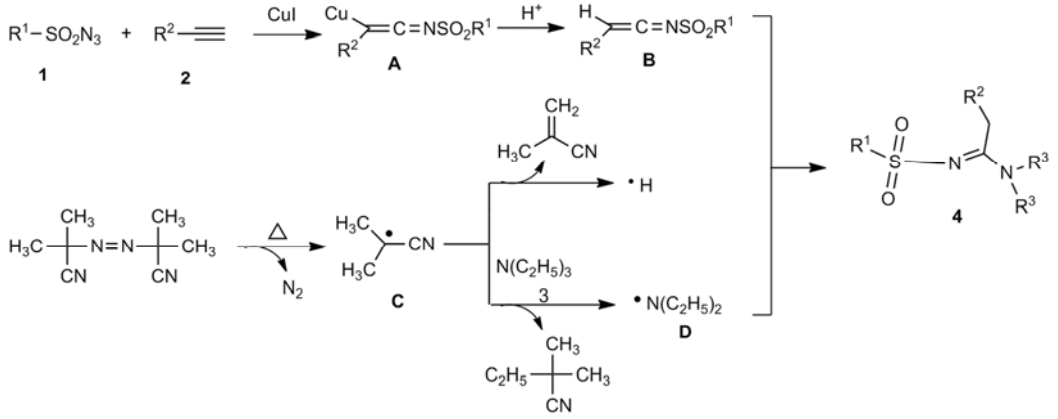
All reactions were carried out using standard Schlenk techniques. Et_3N, CH_2Cl_2 and CH_3CN were distilled from CaH_2, THF and toluene were distilled from sodium/benzophenone. ^1H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ with TMS as internal standard. Chemical shifts are reported in ppm relative to the ^1H and ^{13}C residue signals of the deuterated solvent. IR spectra were taken with KBr plates. Mass spectra were obtained with a mass spectrometer. Only characteristic fragments containing the isotopes of highest abundance are listed. Melting points were measured with melting point apparatus. Single crystal X-ray diffraction data were collected in diffractiometers. High-resolution mass spectrometry (HRMS) was obtained using electron spray ionization (ESI) mass spectrometry.

General procedure for the synthesis of N-sulfonyl-N,N-disubstituted amidines

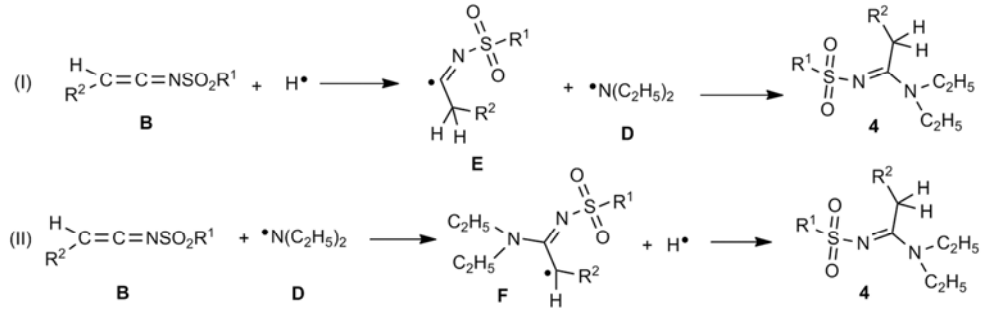
To a stirred mixture of CuI (19.1 mg, 0.1 mmol), AIBN (328 mg, 2 mmol), *p*-toluenesulfonyl azide (236 mg, 1.2 mmol), phenylacetylene (102 mg, 1 mmol) in anhydrous



Scheme 2 The ESI-MS analysis results for the reaction of benzenesulfonyl azide and phenylacetylene with *N,N*-dimethyl-1-phenylmethanamine **3d**.



Scheme 3 The reaction pathway for the formation of *N*-sulfonylamidine derivatives **4**.



Scheme 4 The two reaction routes for the generation of compound **4**.

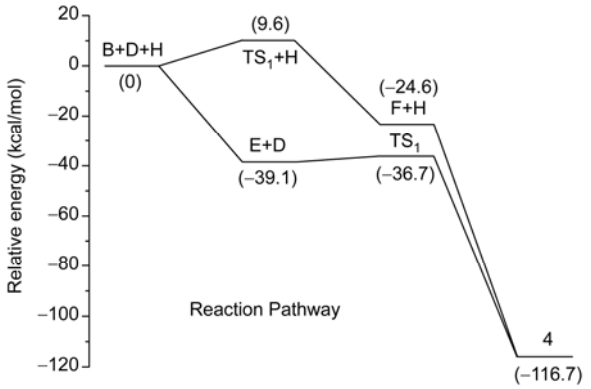


Figure 2 Calculated relative energies of the two reaction pathways in the formation of compound **4**.

THF (5 mL) was slowly added TEA (303 mg, 3.0 mmol) via syringe under a N_2 atmosphere. Slowly raise the reaction temperature to 80 °C and let the reaction mixture stirring for 8 h. Solvent was removed under vacuum. The residue was washed with water, and extracted with CH_2Cl_2 (3 × 10 mL). Organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (200–300 mesh) with ethyl acetate and petroleum ether (*v*/*v* = 1:8–1:10) as eluting solvent to give the desired product **4** and **5**.

*N,N-diethyl-2-phenyl-N′-(phenylsulfonyl)acetamidine (**4a**) [49]*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 7.5 Hz, 2H,

$SO_2C_6\mathbf{H_5}$), 7.36–7.44 (m, 3H, $SO_2C_6\mathbf{H_5}$), 7.19–7.26 (m, 3H, $CH_2C_6\mathbf{H_5}$), 7.11 (d, J = 7.5 Hz, 2H, $CH_2C_6\mathbf{H_5}$), 4.39 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.51 (q, J = 7.2 Hz, 2H, $C\mathbf{H_2}CH_3$), 3.21 (q, J = 6.9 Hz, 2H, $C\mathbf{H_2}CH_3$), 1.16 (t, J = 7.2 Hz, 3H, $CH_2C\mathbf{H_3}$), 0.96 (t, J = 7.2 Hz, 3H, $CH_2C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 144.0, 134.3, 133.4, 131.2, 129.4, 128.9, 128.4, 127.8, 126.8, 126.2, 43.3, 36.6, 29.7, 13.4, 11.8 ppm; IR (KBr) ν 3062, 3030, 2978, 2937, 1716, 1627, 1585, 1550, 1477, 1456, 1436, 1382, 1361, 1274, 1217, 1141, 1091, 1078, 1024, 979, 923, 896, 819, 794, 763, 721, 690, 669, 613, 569, 538, 509 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}N_2O_2S$ ([M+H]$^+$) 331.1480, found 331.1474.

*N,N-diethyl-2-phenyl-N′-tosylacetamidine (**4b**) [49]*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.16–7.26 (m, 5H, $CH_2C_6\mathbf{H_5}$), 7.10 (d, J = 7.2 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 4.38 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.50 (t, J = 7.2 Hz, 2H, $C\mathbf{H_2}CH_3$), 3.21 (t, J = 7.2 Hz, 3H, $CH_2C\mathbf{H_3}$), 2.36 (s, 3H, $C\mathbf{H_3}C_6H_4$), 1.16 (t, J = 6.9 Hz, 3H, $CH_2C\mathbf{H_3}$), 0.93 (t, J = 6.9 Hz, 3H, $CH_2C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 141.4, 134.2, 130.6, 130.2, 130.0, 128.9, 128.8, 128.1, 126.4, 126.2, 49.0, 48.4, 36.9, 30.6, 28.9, 13.7, 13.6 ppm; IR (KBr) ν: 3060, 3028, 2991, 2951, 1716, 1627, 1585, 1477, 1456, 1436, 1385, 1361, 1274, 1217, 1141, 1091, 1078, 1024, 979, 923, 896, 819, 794, 763, 721, 690, 669, 613, 585, 545 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{24}N_2O_2S$ ([M+H]$^+$) 345.1636, found 345.1631.

*4-(tert-Butyldimethylsilyloxy)-N,N-diethyl-N′-tosylbutanamidine (**4c**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ7.81 (d, J = 8.1 Hz, 2H, $C_6\mathbf{H_4}$), 7.25 (d, J = 7.8 Hz, 2H, $C_6\mathbf{H_4}$), 3.67 (t, J = 5.4 Hz, 2H, $C\mathbf{H_2}CH_2CH_2$OTBS), 3.39–3.46 (m, 4H, $\mathbf{CH_2}CH_3$), 2.97 (t, J = 7.8 Hz, 2H, $CH_2CH_2C\mathbf{H_2}$OTBS), 2.39 (s, 3H, $C\mathbf{H_3}C_6H_4$), 1.87–1.96 (m, 2H, $CH_2C\mathbf{H_2}CH_2$OTBS), 1.61 (t, J = 7.6 Hz, 2H, $C\mathbf{H_2}CH_3$), 1.20 (t, J = 7.5 Hz, 3H, $CH_2C\mathbf{H_3}$), 1.10 (t, J = 7.2 Hz, 3H, $CH_2C\mathbf{H_3}$), 0.89 (s, 9H, $SiC_4\mathbf{H_9}$), 0.05 (s, 6H, $Si(C\mathbf{H_3})_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 141.5, 129.0, 126.0, 62.0, 43.1, 42.8, 30.7, 27.5, 25.7, 21.4, 18.1, 14.2, 12.0, -5.4 ppm; IR (KBr) ν: 3062, 3028, 2961, 2930, 2865, 1649, 1535, 1485, 1435, 1384, 1279, 1253, 1145, 1087, 1078, 969, 898, 851, 776, 735, 685, 658, 585, 505 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{38}N_2O_3SSi$ ([M+H]$^+$) 427.2451, found 427.2459.

*N,N-diethyl-N′-(phenylsulfonyl)nonanamidine (**4d**) [50]*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.90 (m, 3H, $C_6\mathbf{H_5}$), 7.37–7.41 (m, 2H, $C_6\mathbf{H_5}$), 3.39 (q, J = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_3$), 3.30 (q, J = 6.9 Hz, 2H, $NC\mathbf{H_2}CH_3$), 2.80 (t, J = 7.8 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 1.52–1.60 (m, 2H, $CH_2C\mathbf{H_2}C_4H_9$), 1.32–1.37 (m, 2H, $C_2H_4C\mathbf{H_2}C_3H_7$), 1.19–1.25 (m, 2H, $C_3H_6C\mathbf{H_2}C_2H_5$), 1.15–1.17 (m, 2H, $C_4H_8C\mathbf{H_2}CH_3$), 1.02–1.07 (m, 6H, $NCH_2C\mathbf{H_3}$), 0.84 (t, J = 6.3 Hz, 3H, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 144.6, 134.1, 131.1, 128.4, 125.9, 64.3, 62.8, 43.2, 31.2, 31.0, 29.5, 27.4, 22.5, 14.2, 14.0, 12.1 ppm; IR (KBr) ν: 3062, 3030, 2958, 2930, 2865, 1649, 1535, 1485, 1435, 1384, 1279, 1253, 1145, 1087, 1024, 969, 896, 851, 776, 735, 686, 658, 589, 545 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{28}N_2O_2S$ ([M+H]$^+$) 325.1950, found 325.1961.

*N,N-diethyl-N′-tosylnonanamidine (**4e**) [50]*

^{1}H NMR (300 MHz, $CDCl_3$) δ7.82 (d, J = 7.8 Hz, 2H, $C_6\mathbf{H_4}$), 7.24 (d, J = 7.5 Hz, 2H, $C_6\mathbf{H_4}$), 3.44 (q, J = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_3$), 3.34 (q, J = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_3$), 2.84 (t, J = 7.2 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 2.39 (s, 3H, $C\mathbf{H_3}C_6H_4$), 1.41–1.60 (m, 2H, $CH_2C\mathbf{H_2}C_4H_9$), 1.29–1.39 (m, 2H, $C_2H_4C\mathbf{H_2}C_3H_7$), 1.23–1.25 (m, 2H, $C_3H_6C\mathbf{H_2}C_2H_5$), 1.13–1.23 (m, 2H, $C_4H_8C\mathbf{H_2}CH_3$), 1.08–1.13 (m, 6H, $NCH_2C\mathbf{H_3}$), 0.88 (t, J = 6.3 Hz, 3H, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.9, 143.1, 141.9, 141.4, 128.9, 126.2, 48.8, 48.3, 31.4, 31.0, 27.6, 21.8, 19.9, 13.5 ppm; IR (KBr) ν: 3062, 3028, 2956, 2872, 2858, 1708, 1596, 1541, 1465, 1431, 1369, 1274, 1165, 1147, 1087, 1024, 968, 896, 845, 812, 763, 709, 673, 596, 578, 545 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{30}N_2O_2S$ ([M+H]$^+$) 339.2106, found 339.2107.

*N′-(4-chlorophenylsulfonyl)-N,N-diethylheptanamidine (**4f**) [50]*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 (d, J = 8.1 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.38 (d, J = 8.7 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 3.38 (q, J = 7.5 Hz, 2H, $NC\mathbf{H_2}CH_3$), 3.31(q, J = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_3$), 2.80 (t, J = 7.8 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 1.28–1.69 (m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 1.20 (t, J = 6.6 Hz, 3H, $NCH_2C\mathbf{H_3}$), 1.06 (t, J = 7.2 Hz, 3H, $NCH_2C\mathbf{H_3}$), 0.85 (t, J = 7.2 Hz, 3H, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.7, 143.1, 137.2, 129.7, 129.0, 128.6, 127.5, 123.8, 121.4, 44.0, 43.3, 39.1, 36.1, 31.1, 30.2, 29.5, 28.2, 27.4, 25.6, 25.1, 24.1, 23.3, 22.7, 22.4, 19.8, 14.1, 13.9, 12.0 ppm; IR (KBr) ν: 3091, 3062, 2956, 2933, 2872, 2237, 2017, 1722, 1583, 1548, 1477, 1436, 1386,1359, 1269, 1217, 1145, 1089, 1012, 974, 925, 893, 829, 786, 754, 707, 644, 590, 578, 543, 482 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{27}ClN_2O_2S$ ([M+H]$^+$) 359.1560, found 359.1554.

*N,N-dibutyl-2-phenyl-N′-(phenylsulfonyl)acetamidine (**4g**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.2 Hz, 2H, $SO_2C_6\mathbf{H_5}$), 7.36–7.44 (m, 3H, $SO_2C_6\mathbf{H_5}$), 7.13–7.28 (m, 5H, $CH_2C_6\mathbf{H_5}$), 4.39 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.40 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.11 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 1.11–1.71 (m, 8H, $NCH_2C_2\mathbf{H_4}CH_3$), 0.77–0.86 (m, 6H, $NC_3H_6C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.7, 144.2, 134.5, 131.2, 128.9, 128.3, 127.9, 126.8, 126.1, 48.8, 36.9, 30.4, 28.6, 20.1, 13.6 ppm; IR (KBr) ν: 3062, 3028, 2958, 2931, 2872, 2231, 1585, 1544, 1467, 1431, 1373, 1276, 1195, 1143, 1087, 1024, 952, 904, 848, 756, 729, 690, 624, 586, 534, 518 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{30}N_2O_2S$

([M+H]$^+$) 387.2106, found 387.2107.

*N,N-dibutyl-2-phenyl-N′-tosylacetamidine (**4h**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.23 (d, J = 6.9 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.15–7.18 (m, 5H, $CH_2C_6\mathbf{H_5}$), 4.38 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.39 (t, J = 6.6 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.09 (t, J = 6.9 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 2.35 (s, 3H, $SO_2C_6H_4C\mathbf{H_3}$), 1.50–1.55 (m, 4H, $NC_2H_4C\mathbf{H_2}CH_3$), 1.11–1.25 (m, 4H, $NCH_2C\mathbf{H_2}C_2H_5$), 0.78–0.86 (m, 6H, $NC_3H_6C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.6, 141.6, 141.4, 134.5, 128.9, 128.8, 127.9, 126.7, 126.1, 49.0, 48.8, 36.8, 30.4, 28.7, 21.4, 20.2, 19.9, 13.7, 13.6 ppm; IR (KBr) v:3061, 3026, 2954, 2929, 2872, 1574, 1552, 1473, 1471, 1371, 1276, 1261, 1199, 1182, 1136, 1083, 1018, 950, 912, 856, 813, 727, 692, 655, 596, 549,501 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{32}N_2O_2S$ ([M+H]$^+$) 401.2263, found 401.2261.

*N,N-dibutyl-N′-(4-chlorophenylsulfonyl)-2-phenylacetamidine (**4i**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (d, J = 8.1 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.33 (d, J = 8.7 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.09–7.28 (m, 5H, $CH_2C_6\mathbf{H_5}$), 4.36 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.39 (t, J = 7.8 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.11 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 1.10–1.68 (m, 8H, $NCH_2C_2\mathbf{H_4}CH_3$), 0.78–0.87 (m, 6H, $NC_3H_6C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.8, 142.7, 137.4, 134.1, 128.9, 128.5, 127.8, 127.7, 126.9, 49.1, 48.9, 36.8, 30.5, 28.6, 20.2, 19.8, 13.7, 13.5 ppm; IR (KBr) v: 3064, 3028, 2956, 2872, 1552, 1465, 1452, 1373, 1276, 1257, 1199, 1134, 1087, 1010, 974, 950, 904, 862, 823, 758, 719, 655, 590, 528, 491, 453 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{29}ClN_2O_2S$ ([M+H]$^+$) 421.1716, found 421.1706.

*N,N-dibutyl-N′-(phenylsulfonyl)heptanamidine (**4j**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.5 Hz, 2H, $C_6\mathbf{H_5}$), 7.87 (d, J = 7.8 Hz, 1H, $C_6\mathbf{H_5}$), 7.37–7.39 (m, 2H, $C_6\mathbf{H_5}$), 3.29 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.20 (t, J = 7.8 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 2.80 (t, J = 5.4 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 1.39–1.61 (m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 1.06–1.27 (m, 8H, $NCH_2C_2\mathbf{H_4}CH_3$), 0.75–0.92 (m, 9H, $NC_3H_6C\mathbf{H_3}$, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.8, 144.6, 131.1, 128.3, 125.9, 53.5, 48.8, 48.7, 47.5, 45.6, 31.2, 31.1, 29.9, 29.5, 28.9, 28.5, 27.3, 26.2, 22.5, 20.7, 20.2, 20.1, 20.0, 14.0, 13.7, 9.6 ppm; IR (KBr) v: 3062, 3028, 2958, 2931, 2872, 1645, 1544, 1479, 1465, 1431, 1375, 1276, 1193, 1145, 1087, 997, 896, 852, 754, 729, 690, 669, 626, 586, 530 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{36}N_2O_2S$ ([M+H]$^+$) 381.2575 found 381.2571.

*N,N-dibutyl-N′-tosylheptanamidine (**4k**) [50]*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.78 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_5}$), 7.20 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_5}$), 3.33 (t, J = 6.9 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.21 (t, J = 6.6 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 2.82 (t, J = 7.5 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 2.36 (s, 3H, $SO_2C_6H_5C\mathbf{H_3}$), 1.44–1.59 (m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 1.20–1.27 (m, 8H, $NCH_2C_2\mathbf{H_4}CH_3$), 0.78–0.93 (m, 9H, $NC_3H_6C\mathbf{H_3}$, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.8, 141.9, 141.4, 129.4, 129.1, 129.0, 128.9, 127.2, 126.0, 48.8, 31.0, 29.6, 28.9, 27.4, 22.5, 21.4, 20.1, 14.0, 13.7 ppm; IR (KBr) v: 3062, 3030, 2956, 2872, 2858, 1708, 1598, 1541, 1465, 1431, 1355, 1325, 1274, 1165, 1145, 1087, 1018, 968, 896, 852, 812, 763, 709, 673, 596, 578, 547 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{38}N_2O_2S$ ([M+H]$^+$) 395.2732, found 395.2724.

*N,N-dibutyl-N′-(4-chlorophenylsulfonyl)heptanamidine (**4l**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81 (d, J = 8.1 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.36 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 3.29 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 3.21 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_3H_7$), 2.80 (t, J = 8.4 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 2.24–2.39 (m, 4H, $NCH_2C\mathbf{H_2}C_2H_5$), 1.21–1.28 (m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 0.84–0.89 (m, 9H, $NC_3H_6C\mathbf{H_3}$, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.9, 143.2, 137.2, 128.5, 127.5, 53.6, 48.9, 48.7, 41.7, 31.2, 29.5, 28.7, 28.0, 27.4, 26.6, 25.1, 22.5, 20.7, 20.0, 15.6, 14.0, 13.7 ppm; IR (KBr) v: 3062,3028, 2958, 2931, 2872, 2233, 2019, 1635, 1544, 1475, 1431, 1379, 1286, 1271, 1193, 1170, 1145, 1087, 1012, 947, 896, 852, 827,756, 731, 707, 655, 626, 588, 555, 530, 482 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{35}ClN_2O_2S$ ([M+H]$^+$) 415.2186, found 415.2186.

*N,N-dinonyl-2-phenyl-N′-(phenylsulfonyl)acetamidine (**4m**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88 (d, J = 8.1 Hz, 2H, $SO_2C_6\mathbf{H_5}$), 7.37–7.40 (m, 3H, $SO_2C_6\mathbf{H_5}$), 7.14–7.24 (m, 5H, $CH_2C_6\mathbf{H_5}$), 4.38 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.38 (t, J = 6.7 Hz, 2H, $C\mathbf{H_2}C_8H_{17}$), 3.08 (t, J = 6.8 Hz, 2H, $C\mathbf{H_2}C_8H_{17}$), 1.18–1.49 (m, 28H, $CH_2C_7\mathbf{H_{14}}CH_3$), 0.78–0.87 (m, 6H, $CH_2C_7H_{14}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.7, 144.2, 134.5, 131.2, 128.8, 128.6, 128.3, 127.9, 126.8, 126.2, 126.1, 53.3, 49.3, 49.1, 36.9, 31.9, 31.6, 29.6, 29.4, 29.1, 28.4, 27.4, 26.9, 26.6, 25.7, 22.6, 14.1 ppm; IR (KBr) v: 3062, 3028, 2926, 2854, 2235, 1672, 1606, 1585, 1548, 1467, 1454, 1431, 1375, 1278, 1145, 1089, 1024, 999, 952, 902, 846, 754, 727, 690, 626, 586, 557 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{50}N_2O_2S$ ([M+H]$^+$) 527.3671, found 527.3672.

*N,N-dinonyl-2-phenyl-N′-tosylacetamidine (**4n**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.13–7.23 (m, 7H, $SO_2C_6\mathbf{H_4}$, $CH_2C_6\mathbf{H_5}$), 4.36 (s, 2H, $C\mathbf{H_2}C_6H_5$), 3.37 (t, J = 6.7 Hz, 2H, $\mathbf{CH_2}C_7H_{14}CH_3$), 3.07 (t, J = 6.8 Hz, 2H, $C\mathbf{H_2}C_7H_{14}CH_3$), 2.34 (s, 3H, $SO_2C_6H_4C\mathbf{H_3}$), 1.18–1.51 (m, 28H, $CH_2C_7\mathbf{H_{14}}CH_3$), 0.78–0.86 (m, 6H, $CH_2C_7H_{14}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.6, 141.5, 141.4, 134.5, 128.9, 128.8, 127.9, 126.7, 126.1, 49.2, 49.0, 36.8, 31.7, 31.6, 29.5, 29.2, 28.4, 26.9, 26.6, 22.6, 21.3, 14.1 ppm; IR (KBr) v:3030, 2954, 2926, 2854, 1716, 1608, 1548, 1489, 1465, 1456, 1377, 1346, 1298, 1282, 1147, 1089, 1020, 950, 883, 850, 813,

761, 723, 707, 677, 597, 580, 553 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{52}N_2O_2S$ ($[M+H]^+$) 541.3828, found 541.3827.

*N,N-dinonyl-N′-(phenylsulfonyl)heptanamidine (**4o**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.90 (d, J = 7.6 Hz, 2H, $C_6\mathbf{H_5}$), 7.40–7.43 (m, 3H, $C_6\mathbf{H_5}$), 3.31 (t, J = 7.2 Hz, 2H, $NC\mathbf{H_2}C_8H_{17}$), 3.21 (t, J = 7.2 Hz, 2H, $NC\mathbf{H_2}C_8H_{17}$), 2.83 (t, J = 7.8 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 1.61–1.73 (m, 14H, $CH_2C_7\mathbf{H_{14}}CH_3$), 1.45–1.61 (m, 14H, $CH_2C_7\mathbf{H_{14}}CH_3$), 1.39–1.44 (m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 1.16 (t, J = 7.3 Hz, 3H, $C_5H_{10}C\mathbf{H_3}$), 0.87 (t, J = 7.3 Hz, 6H, $C_8H_{16}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.8, 144.6, 131.1, 128.3, 125.9, 121.4, 49.1, 49.0, 39.3, 31.8, 31.7, 31.2, 29.6, 29.2, 28.9, 27.3, 26.9, 26.8, 23.4, 22.6, 22.4, 14.1 ppm; IR (KBr) ν: 3064, 2926, 2854, 2241, 2019, 1544, 1463, 1379, 1278, 1228, 1147, 1089, 1024, 850, 754, 729, 690, 628, 590, 565 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{56}N_2O_2S$ ($[M+H]^+$) 521.4140 found 521.4132.

*N,N-dinonyl-N′-tosylheptanamidine (**4p**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.69 (d, J = 7.2 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.13 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 3.24 (t, J = 7.8 Hz, 2H, $C\mathbf{H_2}C_7H_{14}CH_3$), 3.14 (t, J = 7.5 Hz, 2H, $C\mathbf{H_2}C_7H_{14}CH_3$), 2.73 (t, J = 8.1 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 2.34 (s, 3H, $SO_2C_6H_4\,C\mathbf{H_3}$), 1.42–1.61 (m, 28H, $NCH_2C_7\mathbf{H_{14}}CH_3$), 1.09–1.17(m, 8H, $CH_2C_4\mathbf{H_8}CH_3$), 0.73–0.79 (m, 9H, $NC_8H_{16}C\mathbf{H_3}$, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.6, 141.9, 141.3, 130.3, 130.1, 129.4, 129.1, 128.8, 128.3, 125.8, 121.4, 120.3, 118.9, 67.9, 48.9, 48.7, 39.2, 31.6, 31.1, 30.8, 29.4, 28.9, 27.2, 26.6, 24.9, 23.0, 22.4, 21.2, 13.8 ppm; IR (KBr) *ν*:3028, 2954, 2854, 2239, 1681, 1598, 1544, 1463, 1379, 1274, 1145, 1112, 1041, 1012, 898, 850, 813, 721, 707, 688, 590, 553, 482 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{58}N_2O_2S$ ($[M+H]^+$) 535.4297, found 535.4303.

*N′-(4-chlorophenylsulfonyl)-N,N-dinonylheptanamidine (**4q**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81 (d, J = 8.4 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.34 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 3.26 (t, J = 7.5 Hz, 2H, $C\mathbf{H_2}C_7H_{14}CH_3$), 3.19 (t, J = 7.5 Hz, 2H, $NC\mathbf{H_2}C_7H_{14}CH_3$), 2.79 (t, J = 8.4 Hz, 2H, $C\mathbf{H_2}C_5H_{11}$), 2.34–2.36 (m, J = 8.6 Hz, 2H, $CH_2C\mathbf{H_2}C_4H_9$), 1.12–1.62 (m, 34H, $NCH_2C_7\mathbf{H_{14}}CH_3$, $C_2H_4C_3\mathbf{H_6}CH_3$), 0.79–0.84 (m, 9H, $NCH_2C_7H_{14}C\mathbf{H_3}$, $C_5H_{10}C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.8, 143.3, 137.2, 128.5, 127.5, 53.9, 49.4, 49.0, 31.8, 31.7, 31.2, 29.5, 29.3, 29.1, 28.9, 27.5, 27.4, 26.8, 26.7, 26.4, 22.6, 22.4, 14.0 ppm; IR (KBr) *ν*:3088, 3057, 2954, 2926, 2852, 1573, 1544, 1467, 1435, 1375, 1286, 1259, 1143, 1087, 1012, 985, 898, 854, 829, 792, 756, 723, 707, 678, 657, 572, 538, 513, 480 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{55}ClN_2O_2S$ ($[M+H]^+$) 555.3751, found 555.3740.

*N,N-dibutyl-2-p-tolyl-N′-tosylacetamidine (**4r**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.71 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.66 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.43 (d, J = 8.1 Hz, 2H, $CH_2C_6\mathbf{H_4}$), 7.25 (d, J = 7.8 Hz, 2H, $CH_2C_6\mathbf{H_4}$), 3.07 (t, J = 7.2 Hz, 2H, $C\mathbf{H_2}C_6H_4$), 2.40 (s, 4H, $NC\mathbf{H_2}C_3H_7$), 2.36 (s, 3H, $SO_2C_6H_4C\mathbf{H_3}$), 2.32 (s, 3H, $CH_2C_6H_4C\mathbf{H_3}$), 1.21–1.50 (m, 8H, $NCH_2C_2\mathbf{H_4}CH_3$), 0.86–0.90 (m, 6H, $C_3H_6C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.4, 144.6, 142.9, 136.7, 130.3, 129.4, 127.7, 126.9, 125.8, 124.4, 120.6, 117.0, 48.1, 30.8, 29.7, 29.2, 24.6, 21.4, 21.2, 19.9, 13.6 ppm; IR (KBr) *ν*: 3051, 3028, 2958, 2929, 2872, 1716, 1670, 1635, 1597, 1512, 1490, 1458, 1379, 1330, 1261, 1159, 1145, 1089, 1016, 921, 813, 754, 704, 655, 584, 569, 549, 522, 509 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{34}N_2O_2S$ ($[M+H]^+$) 415.2419, found 415.2415.

*N,N-diethyl-N′-(phenylsulfonyl)-2-p-tolylacetamidine (**4s**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.09 (d, J = 6.9 Hz, 2H, $SO_2C_6\mathbf{H_5}$), 7.67–7.90 (m, 3H, $SO_2C_6\mathbf{H_5}$), 7.47 (d, J = 8.1 Hz, 2H, $CH_2C_6\mathbf{H_4}CH_3$), 7.23 (d, J = 6.9 Hz, 2H, $CH_2C_6\mathbf{H_4}CH_3$), 2.62 (s, 2H, $C\mathbf{H_2}C_6H_4CH_3$), 2.34 (s, 3H, $CH_2C_6H_4C\mathbf{H_3}$), 2.28 (q, J = 5.4 Hz, 4H, $NC\mathbf{H_2}CH_3$), 2.23 (t, J = 7.2 Hz, 6H, $NCH_2C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.7, 148.1, 135.3, 133.8, 132.7, 129.7, 129.6, 129.4, 128.9, 126.0, 125.8, 41.9, 39.2, 31.8, 29.3, 22.6, 14.0 ppm; IR (KBr) *ν*: 3060, 3028, 2991, 2951, 1716, 1627, 1585, 1477, 1456, 1436, 1385, 1361, 1274, 1217, 1141, 1091, 1078, 1024, 979, 923, 896, 819, 794, 763, 721, 690, 669, 613, 585, 545 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{24}N_2O_2S$ ($[M+H]^+$) 345.1592, found 345.1576.

*N,N-dimethyl-2-phenyl-N′-(phenylsulfonyl)acetamidine (**4t**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.44 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.11–7.24 (m, 8H, $SO_2C_6\mathbf{H_4}$, $CH_2C_6\mathbf{H_5}$), 2.41 (s, 2H, $C\mathbf{H_2}C_6H_5$), 2.36 (s, 6H, $NC\mathbf{H_3}$), ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.7, 144.6, 142.1, 140.3, 136.5, 130.2, 129.4, 127.6, 124.6, 63.2, 40.5, 21.7 ppm; IR (KBr) *ν*: 3065, 3032, 2956, 2916, 2358, 1928, 1890, 1749, 1635, 1589, 1489, 1398, 1377, 1323, 1300, 1290, 1209, 1161, 1139, 1105, 1076, 1035, 1012, 815, 806, 704, 651, 584, 520, 505, 484 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{18}N_2O_2S$ ($[M+H]^+$) 303.1167, found 303.1143.

*N,N-dimethyl-2-phenyl-N′-tosylacetamidine (**4u**) [51]*

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.63 (d, J = 7.8 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.40 (d, J = 7.5 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.25–7.32 (m, 5H, $CH_2C_6\mathbf{H_5}$), 2.65 (s, 8H, $C\mathbf{H_2}C_6H_5$, $NC\mathbf{H_3}$), 2.41 (s, 3H, $C\mathbf{H_3}C_6H_4SO_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 164.7, 144.6, 142.1, 140.2, 136.4, 130.2, 129.4, 128.7, 127.6, 124.5, 63.1, 40.6, 21.7, 21.5 ppm; IR (KBr) *ν*: 3065, 3032, 2956, 2916, 2358, 1928, 1890, 1749, 1635, 1589, 1489, 1398, 1377, 1323, 1300, 1290, 1209, 1161, 1139, 1105, 1076, 1035, 1012, 815, 806, 704, 651, 584, 520, 505, 484 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_2S$ ($[M+H]^+$) 317.1324, found 317.1642.

*N-benzyl-N-methyl-2-phenyl-N′-(phenylsulfonyl)acetamidine (**5t**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 7.2 Hz, 2H,

$SO_2C_6\mathbf{H_5}$), 7.25–7.33 (m, 3H, $SO_2C_6\mathbf{H_5}$), 7.16–7.21 (m, 5H, $NCH_2C_6\mathbf{H_5}$), 7.04–7.11 (m, 5H, $CH_2C_6\mathbf{H_5}$), 5.12 (s, 2H, $NC\mathbf{H_2}C_6H_5$), 3.96 (s, 2H, $C\mathbf{H_2}C_6H_5$), 2.53 (s, 3H, $C\mathbf{H_3}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.2, 143.0, 136.8, 131.2, 130.7, 130.4, 129.6, 129.1, 128.3, 127.9, 126.6, 126.1, 61.6, 42.9, 42.0 ppm; IR (KBr) *v*: 3462, 3061, 3030, 2927, 2756, 2235, 1732, 1714, 1556, 1479, 1444, 1386, 1338, 1265, 1136, 1076, 1022, 999, 954, 842, 775, 742, 690, 648, 584, 532, 472 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{22}N_2O_2S$ ([M+H]$^+$) 379.1480, found 379.1471.

*N-benzyl-N-methyl-2-phenyl-N′-tosylacetamidine (**5u**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 6.9 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.81 (d, *J* = 6.9 Hz, 2H, $SO_2C_6\mathbf{H_4}$), 7.41–7.46 (m, 5H, $CH_2C_6\mathbf{H_5}$), 7.26–7.37 (m, 5H, $NCH_2C_6\mathbf{H_5}$), 3.54 (s, 2H, $NC\mathbf{H_2}C_6H_5$), 2.31 (s, 6H, $NC\mathbf{H_3}$, $C\mathbf{H_3}SO_2C_6H_4$), 2.01 (s, 2H, $C\mathbf{H_2}C_6H_5$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 146.3, 141.8, 137.6, 131.2, 130.8, 130.4, 130.0, 129.4, 128.7, 128.6, 124.4, 121.4, 114.1, 39.3, 23.4, 21.8, 21.5 ppm; IR (KBr) *v*: 3566, 2956, 2924, 2848, 2343, 2322, 1749, 1716, 1674, 1647, 1558, 1506, 1489, 1456, 1394, 1377, 1024, 893, 858, 763, 696, 669, 648, 586, 518 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}N_2O_2S$ ([M+H]$^+$) 393.1636, found 393.1625.

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1 Tuch A, Wallé S. In *Handbook of Combinatorial Chemistry*, Nicolaou KC, Hanko R, Hartwig W. Eds. Wiley-VCH, Weinheim, Germany, 2002,Vol. 2, Chapter 23
2 Wasilke JC, Obrey SJ , Baker RT, Bazan GC. Concurrent tandem catalysis. *Chem Rev*, 2005, 105: 1001–1020
3 von Wangelin AJ, Neumann H, Gördes D, Klaus S, Strübing D, Beller M. Multicomponent coupling reactions for organic synthesis: chemoselective reactions with amide-aldehyde mixtures. *Chem Eur J*, 2003, 9: 4286–4294
4 Tejedor D, García TF. Chemo-differentiating ABB′ multicomponent reactions. Privileged building blocks. *Chem Soc Rev*, 2007, 36: 484–491
5 Ramón DJ, Yus M. Asymmetric multicomponent reactions (AMCRs): The new frontier. *Angew Chem Int Ed*, 2005, 44: 1602–1634
6 Zhang L, Malinakova HC. Copper-catalyzed multicomponent cascade process for the synthesis of hexahydro-1*H*-isoindolones. *J Org Chem*, 2007, 72: 1484–1487
7 Huang BS, Yao XQ, Li CJ. Diastereoselective synthesis of α-oxyamines via gold-, silver- and copper-catalyzed, three-component couplings of α-oxyaldehydes, alkynes, and amines in water. A*dv Synth Catal*, 2006, 348: 1528–1532
8 Gheorghe A, Matsuno A, Reiser O. Expedient immobilization of TEMPO by copper-catalyzed azide-alkyne [3+2]-cycloaddition onto polystyrene resin. *Adv Synth Catal*, 2006, 348: 1016–1020
9 Pirali T, Tron GC, Zhu JP. One-pot synthesis of macrocycles by a tandem three-component reaction and intramolecular [3+2] cycloaddition. *Org Lett*, 2006, 8: 4145–4148
10 Margathe J, Shipman M, Smith SC. Solid-phase, multicomponent reactions of methyleneaziridines: Synthesis of 1,3-disubstituted propanones. *Org Lett*, 2005, 7: 4987–4990
11 Black DA, Arndtsen BA. Copper-catalyzed coupling of imines, acid chlorides, and alkynes: A multicomponent route to propargylamides. *Org Lett*, 2004, 6: 1107–1110
12 Cuny G, Bois-choussy M, Zhu JP. Palladium- and copper-catalyzed synthesis of medium- and large-sized ring-fused dihydroazaphenanthrenes and 1,4-benzodiazepine-2,5-diones. Control of reaction pathway by metal-switching. *J Am Chem Soc*, 2004, 126: 14475–14484
13 Shi L, Tu YQ, Wang M, Zhang FM, Fan CA. Microwave-promoted three-component coupling of aldehyde, alkyne, and amine via C–H activation catalyzed by copper in water. *Org Lett*, 2004, 6: 1001–1003
14 Kamijo S, Jin T, Huo ZB, Yamamoto Y. A one-pot procedure for the regiocontrolled synthesis of allyltriazoles via the Pd-Cu bimetallic catalyzed three-component coupling reaction of nonactivated terminal alkynes, allyl carbonate, and trimethylsilyl azide. *J Org Chem*, 2004, 69: 2386–2393
15 Gommermann N, Koradin C, Polborn K, Knochel P. Enantioselective, copper(I)-catalyzed three-component reaction for the preparation of propargylamines. *Angew Chem Int Ed*, 2003, 42: 5763–5766
16 Bae I, Han H, Chang S. Highly efficient one pot synthesis of *N*-sulfonylamidines by Cu-catalyzed three-component coupling of sulfonyl azide, alkyne, and amine. *J Am Chem Soc*, 2005, 127: 2038–2039
17 Cho SH, Yoo EJ, Bae I, Chang S. Copper-catalyzed hydrative amide synthesis with terminal alkyne, sulfonyl azide, and water. *J Am Chem Soc*, 2005, 127: 16046–16047
18 Chang S, Lee M, Jung DY, Yoo EJ, Cho SH, Han SK. Catalytic one-pot synthesis of cyclic amidines by virtue of tandem reactions involving intramolecular hydroamination under mild conditions. *J Am Chem Soc*, 2006, 128: 12366–12367
19 Yoo EJ, Bae I, Cho SH, Han H, Chang S. A facile access to *N*-sulfonylimidates and their synthetic utility for the transformation to amidines and amides. *Org Lett*, 2006, 8: 1347–1350
20 Cho SH, Chang S. Rate-accelerated nonconventional amide synthesis in water: A practical catalytic aldol-surrogate reaction. *Angew Chem Int Ed*, 2007, 46: 1897–1900
21 Yoo EJ, Chang S. A new route to indolines by the Cu-catalyzed cyclization reaction of 2-ethynylanilines with sulfonyl azides. *Org Lett*, 2008, 10: 1163–1166
22 Cho SH, Chang S. Room temperature copper-catalyzed 2-functionalization of pyrrole rings by a three-component coupling reaction. *Angew Chem Int Ed*, 2008, 47: 2836–2839
23 Yoo EJ, Ahlquist M, Bae I, Sharpless KB, Fokin VV, 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
24 Kim J, Lee 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
25 Yoo EJ, Park SH, Lee SH, Chang S. A new entry of copper-catalyzed four-component reaction: Facile access to α-aryl β-hydroxy imidates. *Org Lett*, 2009, 11: 1155–1158
26 Husmann R, Na YS, Bolm C, Chang S. Copper catalyzed one-pot synthesis of α-functionalized imidates. *Chem Commun*, 2010, 46: 5494–5496
27 Yoo EJ, Chang S. Copper-catalyzed multicomponent reactions: Securing a catalytic route to ketenimine intermediates and their reactivities. *Curr Org Chem*, 2009, 13: 1766–1776
28 Cui SL, Lin XF, Wang YG. Novel and efficient synthesis of iminocoumarins via copper-catalyzed multicomponent reaction. *Org Lett*, 2006, 8: 4517–4520
29 Cui SL, Wang J, Wang YG. Copper-catalyzed multicomponent reaction: Facile access to functionalized 5-arylidene-2-imino-3-pyrrolines. *Org Lett*, 2007, 9: 5023–5025
30 Cui SL, Wang J, Wang YG. Efficient synthesis of 2-imino-1,2-dihydroquinolines and 2-imino-thiochromenes *via* copper-catalyzed domino reaction. *Tetrahetron*, 2008, 64: 487–492
31 She J, Jiang Z, Wang YG. One-pot synthesis of functionalized benzimidazoles and 1*H*-pyrimidines via cascade reactions of *o*-aminoanilines or naphthalene-1,8-diamine with alkynes and *p*-tolylsulfonyl azide. *Synlett*, 2009, 12: 2023–2027
32 Lu W, Song WZ, Hong D, Lu P, Wang YG. Copper-catalyzed one-pot synthesis of 2-alkylidene-1,2,3,4-tetrahydropyrimidines. *Adv*

Synth Catal, 2009, 351: 1768–1772
33 Song WZ, Lu W, Wang J, Lu P, Wang YG. A facile route to γ-nitro imidates via four-component reaction of alkynes with sulfonyl azides, alcohols, and nitroolefins. *J Org Chem*, 2010, 75: 3481–3483
34 Shang YJ, He XW, Hu JS, Wu JW, Zhang M, Yu SY, Zhang QQ. Copper-catalyzed efficient multicomponent reaction: Synthesis of benzoxazoline-amidine derivatives. *Adv Synth Catal*, 2009, 351: 2709–2713
35 Shang YJ, Ju K, He XW, Hu JS, Yu SY, Zhang M, Liao KS, Wang LF, Zhang P. Copper-catalyzed multicomponent reaction: Synthesis of 4-arylsulfonylimino-4,5-dihydrofuran derivatives. *J Org Chem*, 2010, 75: 5743–5745
36 Goto T, Isobe M, Coviello DA, Kishi Y, Inoue S. Cypridina bioluminescence-VII : The bioluminescence of cypridina luciferin analogs. *Tetrahedron*, 1973, 29: 2035–2039
37 Greenhill JV, Lue P. Amidines and guanidines in medicinal chemistry. *Prog Med Chem*, 1993, 30: 203–326
38 Yamada T, Suegane K, Kuwata S, Watanabe H. Studies of unusual amino acids and their peptides. VII. The syntheses and the reactions of iminopeptides. *Bull Chem Soc Jpn*, 1977, 50: 1088–1093
39 Yamada T, Takashima K, Miyazawa T, Kuwata S, Watanabe H. Studies of unusual amino acids and their peptides. IX. The synthetic study of bottromycins B_1 and B_2. *Bull Chem Soc Jpn*, 1978, 51: 878–883
40 Umezawa H, Takita T, Sugiura Y, Otsuka M, Kobayashi S, Ohno M. DNA-bleomycin interaction: Nucleotide sequence-specific binding and cleavage of DNA by bleomycin. *Tetrahedron*, 1984, 40: 501–509
41 Kumagai N, Matsunaga S, Shibasaki M. An efficient synthesis of bicyclic amidines by intramolecular cyclization. *Angew Chem Int Ed*, 2004, 43: 478–482
42 Lange UEW, Schäfer B, Baucke D, Buschmann E, Mack H. A new mild method for the synthesis of amidines. *Tetrahedron Lett*, 1999, 40: 7067–7070
43 Takuwa T, Minowa T, Onishi JY, Mukaiyama T. Facile one-pot syntheses of amidines and enamines from oximes via beckmann rearrangement using trifluoromethanesulfonic anhydride. *Bull Chem Soc Jpn*, 2004, 77: 1717–1725
44 Xu X, Li X, Ma L, Ye N, Weng B. An unexpected diethyl azodicarboxylate-promoted dehydrogenation of tertiaryamine and tandem reaction with sulfonyl azide. *J Am Chem Soc*, 2008, 130: 14048–14049
45 Liu N, Tang B, Chen Y, He L. Catalyzed imidation of tertiary amines by simple copper salts. *Eur J Org Chem*, 2009, 13: 2059–2062
46 Y 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
47 Crystallographic data for **4b**: space group $P1$, a = 8.5576(7) Å, b = 12.6617(10) Å, c = 8.7146(7) Å, α = 90°, β = 105.0090(10)°, γ = 90°, V = 912.05(13) Å^3, T = 293(2) K, Z = 2. Crystallographic data for compound **4b** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-740915. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/conts/retrieving.html
48 Frisch MJ, Trucks GW, Schlegel HB. Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT, 2009
49 Kuehne ME, Sheeran PJ. Reactions of ynamines. *J Org Chem*, 1968, 33: 4406–4413
50 Iwakawa T, Tamura H, Masuko M, Akira M, Hayase Y. Synthesis and rice-blast control activity of sulfonylamidines. *J Pesticide Sci*, 1992, 17: 131–135
51 Gotthardt H, Lohr T, Brauerb DJ. Neue reaktionen von schwefeldiimiden mit elektronenreichen und elektronenarmen alkinen. *Chem Ber*, 1987, 120: 751–760