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Transition metal- and catalyst-free one-pot green method for the synthesis of *N*-sulfonyl amidines *via* direct reaction of sulfonyl azides with amines†

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In this report, a green synthesis of *N*-sulfonyl amidines *via* the direct reaction of tertiary or secondary amines with sulfonyl azides is described. Transition metal- and catalyst-free conditions were used for the synthesis of biologically important *N*-sulfonyl amidines. Further studies showed that the reaction proceeded *via in situ* aerobic oxidation of amines under reflux conditions.

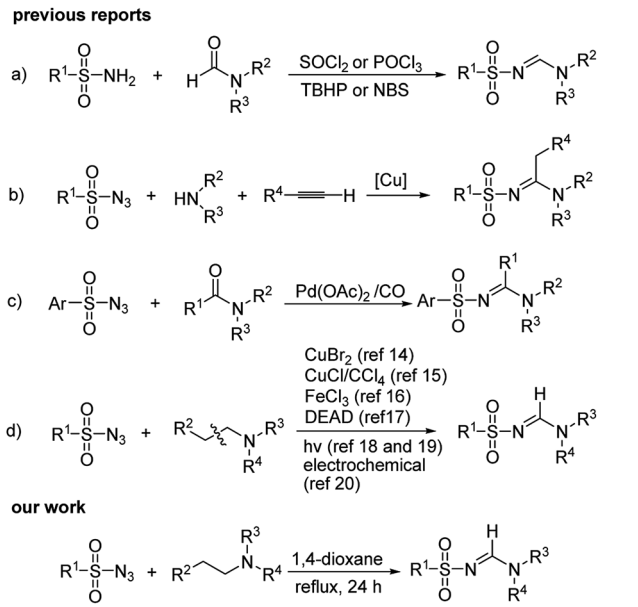
Introduction

Amidines with N–C=N bonds are known compounds in nature with an important role in pharmaceuticals and strong coordination affinity toward metal ions.[1–4] Among the amidine compounds, *N*-sulfonyl amidines are of interest as they are effective in medicinal chemistry and synthesis of synthetic intermediates for drugs.[5–12] A number of *N*-sulfonyl amidines with medicinal and biochemical applications are shown in Scheme 1. These compounds are bioactive pharmacophores with inhibitors of dopamine transporter,[6] anti tumour,[7] anti-bone resorptive agent[8] and anti-proliferative[9] properties (Fig. 1).

In the past years, various methods have been developed for the synthesis of *N*-sulfonyl amidines.[13–21] These include: (a) condensation of amides with sulfonylamides,[13,14] (b) Cu-catalyzed three-component coupling reactions of sulfonyl azides, alkynes and secondary amines,[15] (c) Pd-catalyzed carbonylation/coupling of sulfonylazides and substituted amides,[16] and (d) cross-coupling reaction of sulfonyl azides with tertiary amines[17–21] (Scheme 1). Among them, cross-coupling of sulfonyl azides with tertiary amines has attracted much more attention. The key intermediate is enamine generated by oxidative dehydrogenation of amines in the presence of $CuBr_2$,[17] $CuCl/CCl_4$,[18] or $FeCl_3$.[19] On the other hand, Li and co-workers reported the cascade reaction of tertiary amines with sulfonyl azides in the presence of DEAD (diethyl azodicarboxylate) for the preparation of *N*-sulfonyl amidines.[20]

Recently, photocatalyzed cross-coupling of arylsulfonyl azides with tertiary amines in the presence of eosin Y and acridinium salts have been reported by Zeng *et al.*[21] and Pan *et al.*[22] respectively. An electrochemical synthesis of *N*-sulfonyl amidines from aliphatic amines and sulfonyl azides has been reported by Wang, Du and Zah.[23] Syntheses of *N*-sulfonyl amidines based on the reaction between the sulfonyl azides and amines require harsh reaction conditions and stoichiometric or catalytic amounts of transition metal catalysts. Therefore, the development of an efficient, green, and novel method for the synthesis of *N*-sulfonyl amidines is thus highly desirable.

Recently we have reported catalyst-free synthesis of alkylaminophenols *via* Petasis-type reaction[24] and decarboxylative P–C coupling reaction of amino acids.[25] In continuation of our efforts in developing new green synthetic methods, herein we



Scheme 1 Previously reported works and our work.

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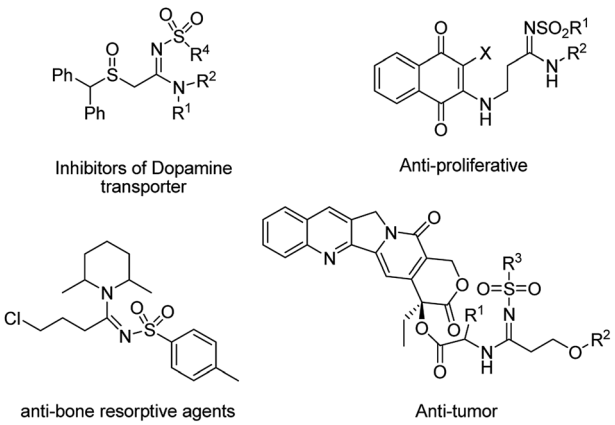


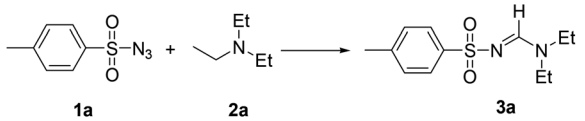
Fig. 1 Structures of biological active *N*-sulfonyl amidines.

report an efficient, practical, and high yielding catalyst-free synthesis of *N*-sulfonylamidines *via* the direct reaction of tertiary or secondary amines with sulfonyl azides.

Results and discussion

The cascade reaction of *p*-tosylazide (**1a**) with triethyl amine (**2a**) was chosen as the model reaction and screening results listed in Table 1. Initially, no reaction was observed when DMSO was used as a solvent at room temperature for 24 h (entry 1). Upon heating the reaction mixture, the compound **3a** was obtained in 35% yield after 24 h at reflux condition (entry 2). The results for the reactions conducted in various solvents showed that using 1,4-dioxane as a solvent, the compound **3a** was obtained in 66% isolated yield (entries 3–8). When the reaction was conducted with 2 eq. of the amine **2a**, the compound **3a** was obtained in 71% yield (entry 10). No reaction was observed when the reaction conducted under Ar or N_2 atmosphere at reflux for 24 h (entry 11). With 2 : 1 ratio of azide to amine, the compound **3a** was obtained in 25% yield (entry 12). The reaction afforded **3a** in good yield at a reflux condition (entries 13–16). When the reaction was conducted in the presence of TEMPO (1 eq.), the compound **3a** was obtained in 68% yield (entry 17). The reaction afforded **3a** in 71% yield (same aerobic condition) in the presence of dioxygen at reflux condition (entry 18).

Table 1 Screening of various reaction condition for the preparation of compound **3a**



Entry	Solvent (2 mL)	T (°C)	Ratio of 1a 2a	Time (h)	Yield[a] (%)
1	DMSO	rt	1 : 1	24	—[b]
2	DMSO	110	1 : 1	24	35
3	$CHCl_3$	Reflux	1 : 1	24	55
4	THF	Reflux	1 : 1	24	51
5	Toluene	Reflux	1 : 1	24	62
6	EtOH	Reflux	1 : 1	24	40
7	CH_3CN	Reflux	1 : 1	24	61
8	1,4-Dioxane	Reflux	1 : 1	24	66
9	1,4-Dioxane	Reflux	1 : 1.5	24	69
10	1,4-Dioxane	Reflux	1 : 2	24	71
11	1,4-Dioxane	Reflux	1 : 2	24	—[c]
12	1,4-Dioxane	Reflux	2 : 1	24	25
13	1,4-Dioxane	rt	1 : 2	48	—[b]
14	1,4-Dioxane	60	1 : 2	48	—[b]
15	1,4-Dioxane	80	1 : 2	48	54
16	1,4-Dioxane	Reflux	1 : 2	48	71
17	1,4-Dioxane	Reflux	1 : 2	24	68[d]
18	1,4-Dioxane	Reflux	1 : 2	24	71[e]

[a] Yields refers to the isolated pure products after short column chromatography. [b] No reaction. [c] Reaction under Ar or N_2. [d] Reaction in the presence of TEMPO (1 equiv.). [e] Reaction in the presence of dioxygen.

This result showed that the reaction mixture has no any radical intermediate under reaction condition. Therefore, further optimization on the amount of *p*-tosylazide (**1a**) and triethyl amine showed that treatment of azide **1a** with 2 equiv. of triethyl amine for 24 h produced *p*-tosylamidine **3a** in 71% yield (entries 9–18).

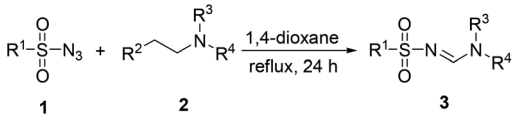
Under the optimized conditions, a wide range of sulfonyl azides were employed in the cascade reaction with tertiary amines for the synthesis of *N*-sulfonylamidines in good to modest yields as shown in Table 2. The arylsulfonyl azides bearing electron-donating and electron-withdrawing groups reacted with triethylamine to afford the corresponding *N*-sulfonylamidines in moderate to good yields (**3a–3e**). The steric hindrance did not apply considerable influence on the reaction. 2,4,6-Trimethyl-benzenesulfonyl azide reacted smoothly with triethyl amine **2a** and the corresponding *N*-sulfonylamidines **3e** was obtained in 70% yield.

The aliphatic sulfonyl azides, camphorsulfonyl azide and methylsulfonyl azide, afforded the corresponding *N*-sulfonylamidines **3f** and **3g** in 63% and 71% isolated yields respectively. Furthermore, the reaction of arylsulfonyl azides with tri-propyl and tributyl amines afforded corresponding *N*-sulfonylamidines (**3h–3l**) in moderate to good yield (entries 8–12). Tertiary amines with different alkyl groups, *N*,*N*-diisopropylethylamine and *N*,*N*-diethyl aniline, were also investigated and the corresponding *N*-sulfonylamidines were obtained for each tertiary amine in good yields (entries 13–16). The cascade reaction of DABCO as a cyclic tertiary amine with *p*-methylphenylsulfonyl azide gave a mixture of unknown products (entry 17).

Interestingly, the corresponding sulfonamide **4** was obtained in 46% yield with using triethanol amine (Scheme 2). This experiment showed the product was obtained by the conversion of triethanol amine to its secondary amine followed by a nucleophilic substitution under optimized reaction condition.

In other attempt, a one-pot three component reaction of sulfonyl chloride **5a** with sodium azide (2 equiv.) and triethyl amine (2 equiv.) for the synthesis of *N*-sulfonylamidines was examined. The compound **3a** was obtained in 78% yield in 1,4-dioxane at reflux for 24 h (Scheme 3).

Table 2 The reaction of sulfonyl azides with tertiary amines for the preparation of *N*-sulfonylamidines



1 2 3

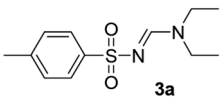
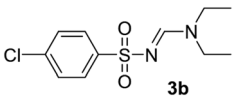
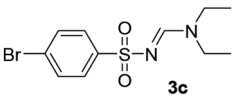
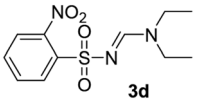
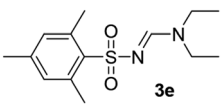
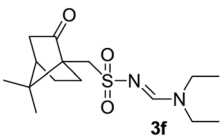
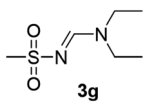
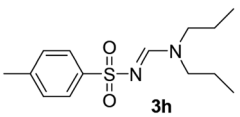
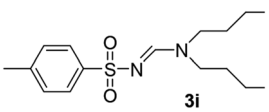
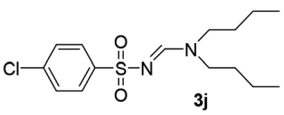
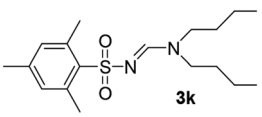
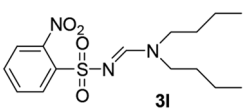
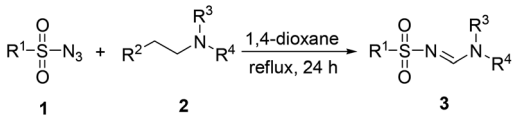
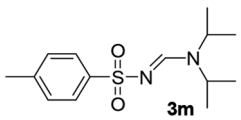
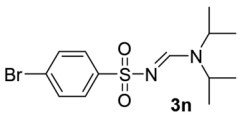
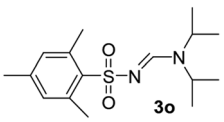
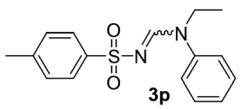
Entry	R^1	R^2	R^3	R^4	Product **3**	Yield[a] (%)
1	*p*-MeC_6H_4–	H	Et	Et	 **3a**	71
2	*p*-ClC_6H_4–	H	Et	Et	 **3b**	77
3	*p*-BrC_6H_4–	H	Et	Et	 **3c**	68
4	*o*-$NO_2C_6H_4$–	H	Et	Et	 **3d**	54
5	2,4,6-$Me_3C_6H_2$–	H	Et	Et	 **3e**	70
6	Camphoryl	H	Et	Et	 **3f**	63
7	Me–	H	Et	Et	 **3g**	71
8	*p*-MeC_6H_4–	Me	*n*-Pr	*n*-Pr	 **3h**	69
9	*p*-MeC_6H_4–	Et	*n*-Bu	*n*-Bu	 **3i**	58
10	*p*-ClC_6H_4–	Et	*n*-Bu	*n*-Bu	 **3j**	50
11	2,4,6-$Me_3C_6H_2$–	Et	*n*-Bu	*n*-Bu	 **3k**	46
12	*o*-$NO_2C_6H_4$–	Et	*n*-Bu	*n*-Bu	 **3l**	42

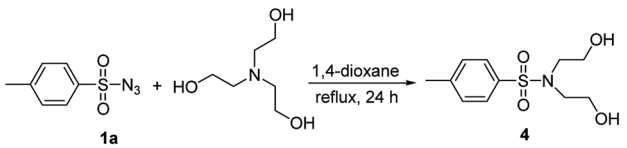
Table 2 (*Contd.*)



1 2 3

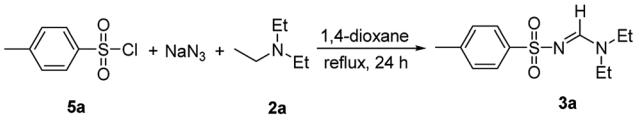
Entry	R^1	R^2	R^3	R^4	Product **3**	Yield[a] (%)
13	*p*-MeC_6H_4–	H	i-Pr	i-Pr	 **3m**	73
14	*p*-BrC_6H_4–	H	i-Pr	i-Pr	 **3n**	66
15	2,4,6-$Me_3C_6H_2$–	H	i-Pr	i-Pr	 **3o**	66
16	*p*-MeC_6H_4–	H	Et	Ph	 **3p**	48[b]
17	*p*-MeC_6H_4–	—	—	—	—	—[c]

[a] Yields refers to the isolated pure products after short column chromatography. [b] Mixture of *E* and *Z* configurations. [c] Mixture of unknown compounds in the presence DABCO.



1a 4

Scheme 2 Reaction of **1a** with triethanol amine in 1,4-dioxane.



5a 2a 3a

Scheme 3 One pot reaction of **5a** with triethylamine and sodium azide in 1,4-dioxane.

In order to find the activity of secondary amines, diethylamine **6a** was attempted to be employed in the reaction with sulfonyl azide **1a** in dioxane at reflux for 24 h. Interestingly, the compound **3a** was obtained in 83% yield as found for the triethylamine. A series of sulfonyl azides were used to react with secondary amines **6** to provide the same products as found for the tertiary amines (Table 3) with moderate to good yields.

According to the literature reports and control experiments (Table 1, entries 10 and 16), a proposed mechanism was outlined in Scheme 4. Initially, the cascade reaction was started *via* aerobic oxidation–dehydration of C–H bond adjacent to nitrogen atom of tertiary amines. Then, the formed enamine **I** was reacted with sulfonyl azide **1** to yield the unstable cyclic compound **II**. Finally *N*-sulfonylamidine **3** was obtained by a retro cycloaddition of the compound **II**. With secondary amines, the reaction proceeded by the enamine **I** formation *via* a known conversion of diethylamine to enamine **I** (Scheme 4).[14]

Conclusion

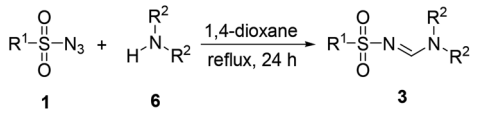
In summary, we report a green synthesis of *N*-sulfonyl amidines *via* the direct reaction of tertiary or secondary amines with sulfonyl azides. Under transition metal- and catalyst-free condition, aromatic and aliphatic *N*-sulfonyl azides could be converted into *N*-sulfonyl amidines in modest to good yields. The reported method is easy to handle, readily available starting materials, air and moisture insensitive reagents, and a simple method compared with previously reported methods.

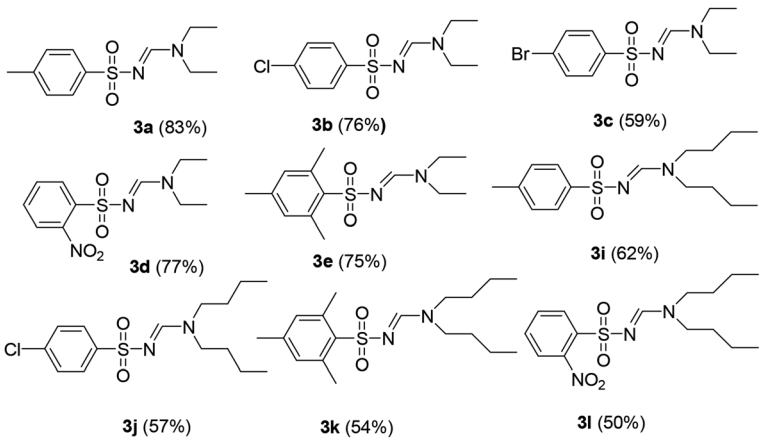
Experimental section

General

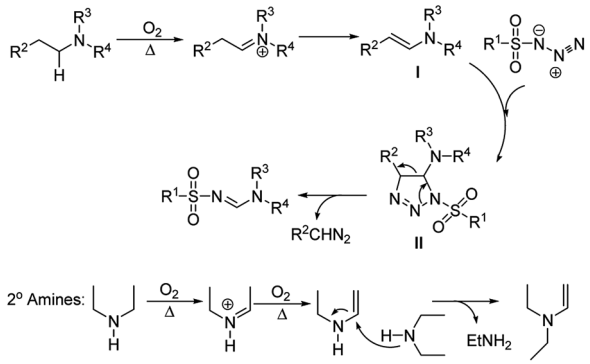
NMR spectra were obtained on a 400 and 250 MHz NMR Spectrometer (^{1}H NMR: 400 and 250 MHz and ^{13}C NMR: 100 and 63 MHz). HRMS measurements were obtained on an ESI-

Table 3 The reaction of sulfonyl azides with secondary amines for the synthesis of *N*-sulfonylamidines[a]





[a] Yields refers to the isolated pure products after short column chromatography.



Scheme 4 Proposed mechanism for the synthesis of compound **3**.

TOF-Ms machine. Analytical TLC was carried out with plates pre-coated with silica gel 60 F_{254} (0.25 mm thick). Column chromatography was performed either with silica gel 60 (70–230 mesh) in common glass columns. All solvents were distillated before use.

General procedure for the synthesis of *N*-sulfonyl amidines from sulfonyl azides

Sulfonyl azide (1 mmol) was added to a solution of amine (2 mmol) in 1,4-dioxane (2 mL). The mixture was stirred for 24 h at reflux (oil bath at 110 °C) without using any inert gas under air. Water (5 mL) was added to the reaction mixture and the mixture was washed with ethyl acetate (3 × 5 mL) and dried over sodium sulfate. The solvent was evaporated and the crude product was purified by a short column chromatography with *n*-hexane–EtOAc (7 : 3) to give compound **3** as the yellow viscous oil or white solid (the reaction was also examined with 5 mmol of sulfonyl azide of **1a** with triethyl amine and a similar yield of **3a** was obtained).

(*E*)-*N*′-((4-Methylphenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3a)[17]

Yellow oil (198 mg, 78% direct method from sulfonyl chloride); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 7.79 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 3.50 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.1, 142.3, 139.7, 129.3, 126.4, 47.1, 40.9, 21.5, 14.5, 12.1; HRMS (ESI): calcd for $C_{12}H_{19}N_2O_2S$ $[M + H]^+$: 255.1167, found: 255.1151.

(*E*)-*N*′-((4-Chlorophenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3b)[17]

Yellow oil (211 mg, 77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (s, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H), 3.49 (q, J = 7.2 Hz, 2H), 3.41 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.1, 141.2, 138.0, 128.9, 127.9, 47.2, 41.1, 14.5, 12.1.

(*E*)-*N*′-((4-Bromophenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3c)[22]

Light yellow solid (216 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (s, 1H), 7.76 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 3.48 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.3 Hz, 2H), 1.27 (t, J = 7.2 Hz, 3H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.2, 141.7, 131.9, 128.0, 126.5, 47.2, 41.1, 14.5, 12.1.

(*E*)-*N*′-((2-Nitrophenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3d)[17]

Yellow oil (154 mg, 54%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.31 (d, J = 8.3 Hz, 1H), 8.13 (s, 1H), 7.75–7.64 (m, 3H), 3.45–3.55 (m, 4H), 1.36 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 159.9, 147.7, 135.4, 132.7, 132.4, 130.7, 124.0, 47.4, 41.3, 14.4, 12.1.

(*E*)-*N*′-((2,4,6-Trimethylphenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3e)[26]

White solid (199 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (s, 1H), 6.94 (s, 2H), 3.48 (q, J = 7.2 Hz, 2H), 3.38 (q, J = 7.3 Hz, 2H), 2.71 (s, 6H), 2.31 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 157.4, 141.1, 138.4, 136.6, 131.4, 46.8, 40.8, 23.0, 20.9, 14.6, 12.1.

(*E*)-*N*′-(((7,7-Dimethylbicyclo[2.2.1]hept-2-en-1-yl)methyl)sulfonyl)-*N*,*N*-diethylformimidamide (3f)[22]

Colorless viscous oil (192 mg, 61%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 3.51–3.31 (m, 4H), 3.02–2.88 (m, 1H), 2.59 (ddd, J = 14.8, 11.4, 4.0 Hz, 1H), 2.40–2.19 (m, 1H), 2.09–1.94 (m, 2H), 1.86 (d, J = 18.3 Hz, 1H), 1.69 (ddd, J = 13.9, 9.2, 4.5 Hz, 1H), 1.44–1.29 (m, 2H), 1.29–1.02 (m, 9H), 0.82 (d, J = 3.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 215.3, 158.7, 58.5, 50.6, 48.0, 46.9, 42.7, 42.6, 40.7, 27.0, 24.7, 19.9, 19.7, 14.5, 12.0.

(*E*)-*N*′-(Methanesufonyl)-*N*,*N*-diethylformimidamide (3g)[19]

Colorless viscous oil (126 mg, 71%); ^{1}H NMR (250 MHz, chloroform-*d*) δ: 8.05 (s, 1H), 3.47 (q, J = 7.2 Hz, 2H), 3.37 (q, J = 7.3 Hz, 2H), 2.94 (s, 3H), 1.29–1.22 (m, 3H), 1.22–1.14 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.1, 44.0, 39.0, 37.8, 11.5, 9.0.

(*E*)-*N*′-((4-Methylphenyl)sulfonyl)-*N*,*N*-dipropylformimidamide (3h)[17]

Yellow viscous oil (195 mg, 69%); ^{1}H NMR (250 MHz, chloroform-*d*) δ 8.13 (s, 1H), 7.73 (d, J = 7.9 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 3.33 (t, J = 7.8 Hz, 2H), 3.24 (t, J = 7.3 Hz, 2H), 2.37 (s, 3H), 1.58 (dd, J = 14.6, 7.3 Hz, 4H), 0.86 (dt, J = 14.1, 7.4 Hz, 6H);^{13}C{^{1}H} NMR (63 MHz, $CDCl_3$) δ: 155.9, 139.2, 136.8, 126.3, 123.3, 51.3, 44.8, 18.9, 18.5, 16.9, 8.2, 7.9.

(*E*)-*N*′-((4-Methylphenyl)sulfonyl)-*N*,*N*-dibutylformimidamide (3i)[17]

Yellow oil (171 mg, 55%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (s, 1H), 7.77 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 3.42 (t, J = 7.4, 2H), 3.31 (t, J = 7.4 Hz, 2H), 2.42 (s, 3H), 1.62–1.50 (m, 4H), 1.25–1.35 (m, 4H), 0.96 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.7, 142.2, 139.8, 129.2, 126.3, 52.3, 46.0, 30.7, 28.7, 21.5, 20.0, 19.7, 13.7, 13.6.

(*E*)-*N*′-((4-Chlorophenyl)sulfonyl)-*N*,*N*-dibutylformimidamide (3j)[17]

Yellow oil (165 mg, 50%); ^{1}H NMR (400 MHz, $CDCl_3$); δ: 8.14 (s, 1H), 7.82 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H), 3.41 (t, J = 7.6 Hz, 2H), 3.32 (t, J = 7.4 Hz, 2H), 1.63–1.49 (m, 4H), 1.33–1.24 (m, 4H), 0.95 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.8, 141.3, 137.9, 128.9, 127.8, 52.4, 46.1, 30.7, 28.7, 19.9, 19.6, 13.7, 13.6.

(*E*)-*N*′-((2,4,6-Trimethylphenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3k)[26]

White solid (157 mg, 46%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (s, 1H), 6.93 (s, 2H), 3.39 (t, J = 7.2 Hz, 2H), 3.29 (t, J = 7.4 Hz, 2H), 2.70 (s, 6H), 2.31 (s, 3H), 1.61–1.51 (m, 4H), 1.35–1.29 (m, 4H), 0.96 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 157.9, 141.0, 138.3, 136.6, 131.4, 52.2, 46.1, 30.8, 28.7, 23.0, 20.9, 20.1, 19.6, 13.7, 13.6.

(*E*)-*N*′-((2-Nitrophenyl)sulfonyl)-*N*,*N*-diethylformimidamide (3l)[17]

Yellow oil (143 mg, 42%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29–8.26 (m, 1H), 8.11 (s, 1H), 7.73–7.64 (m, 3H), 3.40 (m, 4H), 1.70–1.62 (m, 2H), 1.58–1.51 (m, 2H), 1.40–1.27 (m, 4H), 0.98 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 160.3, 147.7, 135.4, 132.7, 132.0, 130.7, 124.0, 52.7, 46.2, 30.6, 28.6, 19.8, 19.6, 13.6.

(*E*)-*N*′-((4-Methylphenyl)sulfonyl)-*N*,*N*-diisopropylformimidamide (3m)[17]

Yellow oil (206 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26 (s, 1H), 7.76 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 4.53 (p, J = 6.8 Hz, 1H), 3.70 (p, J = 6.8 Hz, 1H), 2.41 (s, 3H), 1.32 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 156.4, 142.1, 139.9, 129.3, 126.2, 48.6, 47.9, 23.6, 21.5, 19.6.

(*E*)-*N*′-((4-Bromophenyl)sulfonyl)-*N*,*N*-diisopropylformimidamide (3n)[21]

White solid (228 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.6 Hz, 2H), 4.54 (hept, J = 6.8 Hz, 1H), 3.73 (hept, J = 6.8 Hz, 1H), 1.35 (d, J = 6.8 Hz, 6H), 1.25 (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 156.4, 141.9, 131.9, 127.9, 126.3, 48.8, 48.1, 23.6, 19.6.

(*E*)-*N*′-((2,4,6-Trimethylphenyl)sulfonyl)-*N*,*N*-diisopropyl formimidamide (3o)[21]

White solid (205 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 6.93 (s, 2H), 4.53 (sep, J = 6.9 Hz, 1H), 3.69 (sep, J = 6.8 Hz, 1H), 2.69 (s, 6H), 2.30 (s, 3H), 1.33 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 155.7, 141.0, 138.3, 136.6, 131.4, 48.2, 47.7, 23.7, 22.9, 20.9, 19.7.

(*E*)-*N*′′-((*p*-Methylphenyl)sulfonyl)-*N*-ethyl-*N*′-phenylformimidamide (3p)[26]

White solid (139 mg, 46%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.48 (s, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.50–7.43 (m, 2H), 7.40–7.37 (m, 1H), 7.34–7.30 (m, 2H), 7.26–7.18 (m, 2H), 4.00 (q, J = 7.2 Hz, 2H), 2.45 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.1, 142.7, 141.9, 139.1, 129.9, 129.4, 127.7, 126.6, 123.6, 44.1, 21.5, 12.4.

***N*,*N*-Bis(hydroxymethyl)-4methylbenzenesulfonamide (4)[27]**

Colorless oil (143 mg, 46%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.12 (s, 2H), 3.88 (t, J = 4.9 Hz, 4H), 3.28 (t, J = 4.8 Hz, 4H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 143.8, 135.2, 129.9, 127.3, 62.3, 53.0, 21.5.

Conflicts of interest

There are no conflicts to declare.

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