Synthesis Y. Feng et al. Paper

Highly Efficient Synthesis of *N*-Sulfonylamidines via Silver-Catalyzed or Metal-Free Thermally Promoted Denitrogenative Amination of *N*-Sulfonyl-1,2,3-triazoles

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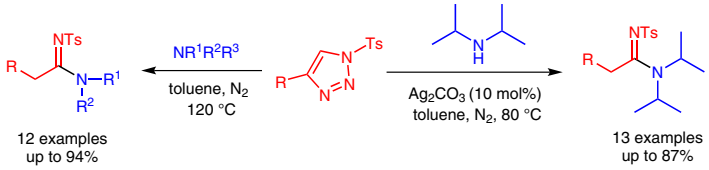


Received: 21.09.2016
Accepted after revision: 27.10.2016
Published online: 28.11.2016
DOI: 10.1055/s-0036-1588103; Art ID: ss-2016-h0659-op

Abstract A highly efficient synthesis of *N*-sulfonylamidines from *N*-sulfonyl-1,2,3-triazoles and amines is reported. This transformation undergoes silver-catalyzed or metal-free thermally promoted denitrogenation of *N*-sulfonyl-1,2,3-triazoles to afford *N*-sulfonylketenimine intermediates and subsequent nucleophilic addition with amines. The amine plays dual roles as base and nucleophile.

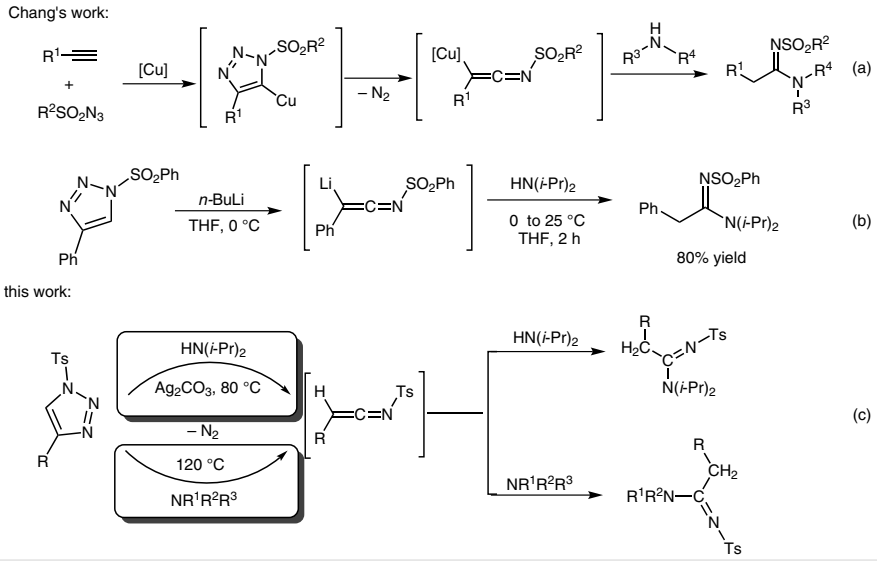
Key words amination, denitrogenation, *N*-sulfonylamidines, *N*-sulfonyl-1,2,3-triazoles, nucleophilic addition

N-Sulfonylamidines are gaining increasing attention in the field of synthetic and medicinal chemistry due to their unique structure and fascinating chemical properties. They are not only the essential part of a wide range of natural products and biologically active molecules,[1] but also serve as useful intermediates for the synthesis of a variety of heterocyclic compounds and efficient coordinating ligands.[2]

A variety of methods are known for the synthesis of *N*-sulfonylamidines.[3] With the requirement of more efficient synthesis of *N*-sulfonylamidine derivatives, a pioneering copper-catalyzed three-component coupling of a terminal alkyne, sulfonyl azide, and secondary amine to construct *N*-sulfonylamidine was reported by Chang et al. (Scheme 1, a).[4] This reaction has received much attention due to the tolerance of various functional groups. Subsequently, Chang and several other groups applied this strategy to synthesize amidines and its derivatives,[5] poly(*N*-sulfonylamidine)s[6] and aminonaphthoquinone-sulfonylamidine conjugates.[1d] Mechanistically, the formation of *N*-sulfonylamidine takes place by the nucleophilic attack of amine to the in situ generated *N*-sulfonylketenimine intermediate. However, the attempts of Chang et al. to prepare *N*-sulfonylamidines using *N*-sulfonyltriazoles as starting materials were unsuccessful due to the stability of *N*-sulfonyltriazole under their employed conditions. It is well known that the relatively stable metalated ketenimine can be formed when *N*-sulfonyltriazole is treated with a strong base, such as *n*-BuLi at low temperature.[7] The only example of *N*-sulfonylamidine formation from metalated ketenimine, lithiated ketenimine, and diisopropylamine was reported by Chang et al. (Scheme 1, b).[5c] However, the use of strong base limits the scope of *N*-sulfonyltriazoles. Recently, Li et al. reported the synthesis of *N*-sulfonylamidines from *N*-sulfonyl-1,2,3-triazoles and nitrosobenzene derivatives under rhodium-catalyzed conditions via α-imino rhodium carbene intermediates.[8]

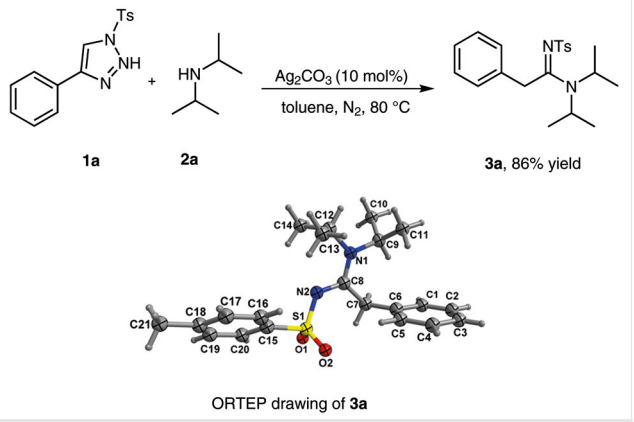
Inspired by Chang's and Li's work and interested in developing a new route to *N*-sulfonylamidines, we envisioned that *N*-sulfonyltriazoles may serve as the precursors of *N*-sulfonylketenimines under appropriate reaction condition, followed by the nucleophilic addition of amines to the in situ generated *N*-sulfonylketenimines to form *N*-sulfonylamidines. Herein, we report a highly efficient method for the synthesis of *N*-sulfonylamidines via silver-catalyzed or metal-free thermally promoted denitrogenative amination of *N*-sulfonyl-1,2,3-triazoles (Scheme 1, c).

Initially, our exploratory studies commenced with 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**), which was prepared from the copper-catalyzed ethynylbenzene/4-methylbenzenesulfonyl azide cycloaddition[9] and diisopropylamine (**2a**). Based on our continuous endeavor in developing silver-catalyzed organic reaction,[10] **1a** was reacted with 1.5 equivalents of **2a** in the presence of 10 mol% $AgNO_3$ relative to **1a** using toluene as solvent at 80 °C for 12 hours under



Scheme 1 Synthesis of *N*-sulfonylamidines via *N*-sulfonylketenimine intermediates

nitrogen atmosphere. To our delight, the *N*-sulfonylamidine, *N*,*N*-diisopropyl-2-phenyl-*N*′-tosylacetimidamide (**3a**), was obtained in 52% yield. The structure of **3a** was unambiguously confirmed by the X-ray single crystal diffraction (Scheme 2)[11] and spectral and analytical data. This prompted us to undertake further investigation, and it was finally found that the reaction of **1a** with **2a** in toluene in the presence of 10 mol% Ag_2CO_3 relative to **1a** under nitrogen atmosphere could afford **3a** in 86% yield (Scheme 2).



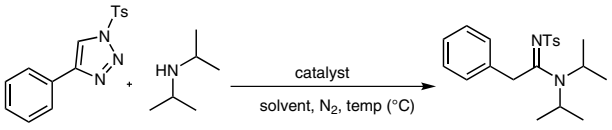
Scheme 2 Silver-catalyzed synthesis of **3a** from **1a** and **2a**

To evaluate the catalytic efficiency of Ag_2CO_3, The reaction of **1a** with **2a** was investigated under different reaction conditions including catalysts, reaction temperatures, and solvents. The results are summarized in Table 1. It is noticeable that several catalysts, namely, AgOTf, $AgNO_3$, Ag_2O, CuI, CuOAc, $Pd(PPh_3)_4$, $Pd(OAc)_2$, K_2CO_3, and Li_2CO_3 were tried, but only silver salt was found to be effective in this reaction (Table 1 entries 1–4). Among the Ag salts screened, Ag_2CO_3 was the best catalyst in term of the yield. $Pd(PPh_3)_4$ and $Pd(OAc)_2$ were found to be poor catalysts for this reaction (entries 11, 12). In contrast, with CuI, CuOAc, K_2CO_3, and Li_2CO_3, respectively, as catalyst under similar conditions, the reaction of **1a** with **2a** gave no expected product (entries 7–10). When the loading of Ag_2CO_3 was decreased to 5 mol%, the yield of product decreased to 15% (entry 5). The control experiment in the absence of Ag_2CO_3 was also carried out and no expected product was detected (entry 6).

The effects of reaction temperatures and different solvents on the reaction of **1a** with **2a** using 10 mol% Ag_2CO_3 as catalyst were also studied. When the reaction was performed at room temperature and 40 °C, respectively, no expected product was obtained (Table 1, entries 13, 14). Upon further raising the reaction temperature to 120 °C, the desired product was isolated in 43% yield (entry 15). The cause of low yield at 120 °C is probably due to the low boiling point of diisopropylamine. Different solvents were surveyed to ascertain the effect of the reaction medium on the yield. Among the solvents studied, the reaction worked most effectively in toluene. Inferior results were observed when the reaction was performed in other solvents, such as DCE, 1,4-dioxane, DMSO, and EtOH (entries 16–19).

After determining the optimized reaction conditions, we investigated the scope of the reaction for many different *N*-sulfonyltriazoles. As shown in Table 2, a variety of the *N*-sulfonyltriazoles with various substituents at the C4 position can be subjected to this silver-catalyzed denitrogenative amination reaction, giving the corresponding products in moderate to excellent yields. Aside from these common electron-rich and -deficient (hetero)aryl and alkyl groups (Table 2, entries 1–8, 10, 12), several highly reactive functional groups, including alkenyl, and cyclopropyl moieties

Table 1 Optimization of Reaction Conditions[a]



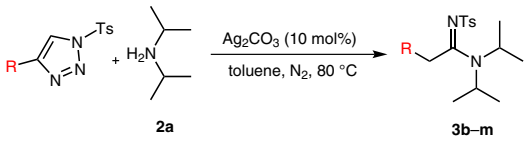
1a **2a** **3a**

Entry	Catalyst (mol%)	Temp (°C)	Solvent	Yield (%)[b]
1	$AgNO_3$ (10)	80	toluene	52
2	AgOTf (10)	80	toluene	46
3	Ag_2O (10)	80	toluene	73
4	Ag_2CO_3 (10)	80	toluene	86
5	Ag_2CO_3 (5)	80	toluene	15
6	–	80	toluene	N.D.
7	K_2CO_3 (10)	80	toluene	N.D.
8	Li_2CO_3 (10)	80	toluene	N.D.
9	CuI (10)	80	toluene	N.D.
10	CuOAc (10)	80	toluene	N.D.
11	$Pd(PPh_3)_4$ (10)	80	toluene	42
12	$Pd(OAc)_2$ (10)	80	toluene	37
13	Ag_2CO_3 (10)	r.t.	toluene	N.D.
14	Ag_2CO_3 (10)	40	toluene	N.D.
15	Ag_2CO_3 (10)	120	toluene	43
16	Ag_2CO_3 (10)	80	DCE	23
17	Ag_2CO_3 (10)	80	1,4-dioxane	71
18	Ag_2CO_3 (10)	80	DMSO	6
19	Ag_2CO_3 (10)	80	EtOH	trace

[a] Reaction conditions: The mixture of 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**; 0.5 mmol), *i*-Pr_2NH (0.75 mmol), and the catalyst in toluene (1 mL) was stirred for 12 h under N_2 atmosphere.
[b] Isolated yield; N.D. = not detected.

(entries 9, 11), were found to be well tolerated. However, when we attempted to further broaden the scope of amines, this transformation was unsuccessful. For example, with *N*-methylaniline (**2b**) instead of **2a**, the expected *N*-sulfonylamidine was not obtained and desulfonylated triazole was generated via the nucleophilic substitution reaction. We speculate that a competitive reaction between the ring opening of *N*-sulfonyltriazole and the nucleophilic substitution reaction could be in existence, and the weak basicity of **2b** relative to **2a** could cause the nucleophilic substitution reaction. Although the reaction mechanism is not completely understood at present, the synergistic effect of Ag_2CO_3 and diisopropylamine probably promote the ring-opening of *N*-sulfonyltriazole and accelerate the loss of nitrogen to form the *N*-sulfonylketenimine intermediate followed by the nucleophilic addition of diisopropylamine to the in situ generated *N*-sulfonylketenimine affording *N*,*N*-diisopropyl-*N*-sulfonylamidine (Scheme 1, c). The diisopropylamine could play dual roles as base and nucleophile. These postulates need to be demonstrated through further experimental results.

Table 2 Silver-Catalyzed Synthesis of *N*,*N*-Diisopropyl-*N*-sulfonylamidines



2a **3b–m**

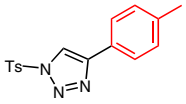
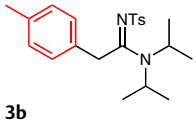
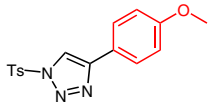
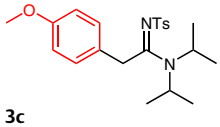
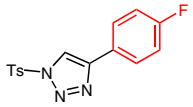
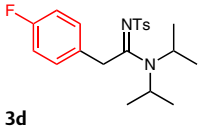
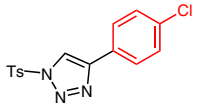
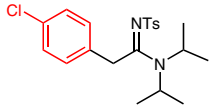
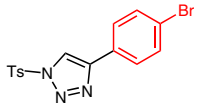
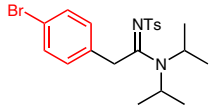
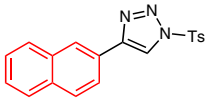
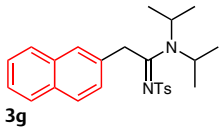
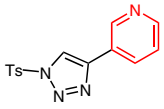
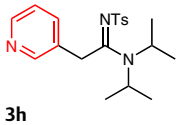
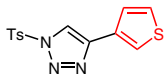
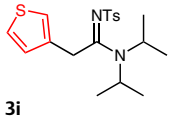
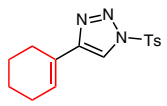
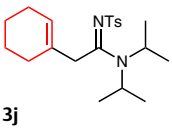
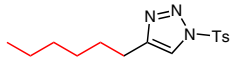
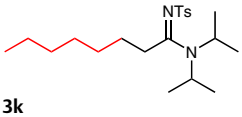
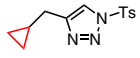
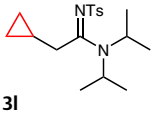
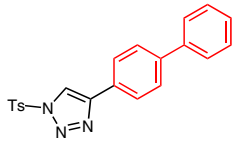
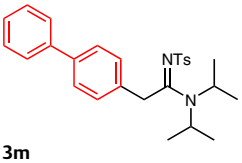
Entry	*N*-Sulfonyltriazole	Product	Yield (%)[a]
1		 **3b**	85
2		 **3c**	87
3		 **3d**	77
4		 **3e**	76
5		 **3f**	76
6		 **3g**	79
7		 **3h**	82
8		 **3i**	75

Table 3 (continued)

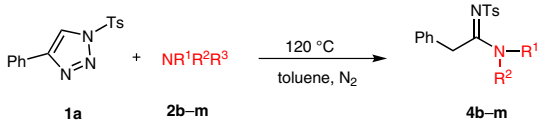
Entry	*N*-Sulfonyltriazole	Product	Yield (%)[a]
9		 **3j**	61
10		 **3k**	83
11		 **3l**	51
12		 **3m**	86

[a] Isolated yield.

For broadening the scope of amines, we further optimized the reaction conditions based on the above conditions. In order to suppress the nucleophilic substitution reaction and promote the ring-opening of *N*-sulfonyltriazole to form the corresponding *N*-sulfonylketenimine intermediate, the reaction temperature was raised to 120 °C. The formation of *N*-sulfonylketenimine intermediates from *N*-sulfonyl-1,2,3-triazoles under thermal conditions has been demonstrated by Shi and co-workers.[12] To our delight, the *N*-sulfonylamidine, *N*-methyl-*N*,2-diphenyl-*N*′-tosylacetimidamide (**4b**), was obtained in 92% yield. To our surprise, **4b** was also obtained in the same yield in the absence of Ag_2CO_3 (Table 3, entry 1). With the further optimized conditions in hand, an array of amines including primary, secondary, and tertiary amines were screened in the absence of Ag_2CO_3 at 120 °C using toluene as solvent. As shown in Table 3, a range of *N*-sulfonylamindines was generated in excellent yield. However, we found that desulfonylated triazole was generated again when **1a** was reacted with aniline. This result implies that the steric hindrance effect of the amine needs to be considered for the formation of *N*-sulfonylketenimine intermediate; the bulky amines are in favor of *N*-sulfonylketenimine formation under thermal conditions.

In conclusion, we have developed a highly efficient method to construct *N*-sulfonylamidines. This transformation undergoes silver-catalyzed or metal-free thermally promoted denitrogenation of *N*-sulfonyl-1,2,3-triazoles to afford *N*-sulfonylketenimine intermediates and subsequent nucleophilic addition with amines. To the best of our knowledge, *N*-sulfonyl-1,2,3-triazoles as precursors of *N*-sulfonylketenimines have been little investigated and the use of *N*-sulfonyl-1,2,3-triazoles as starting material for the synthesis of *N*-sulfonylamidines is underdeveloped so far. Additional studies directed at better understanding the mechanism of this process and at further exploring its utility are currently underway and will be reported in due course.

Table 3 Metal-Free Thermally Promoted Synthesis of *N*-Sulfonylamidines



1a **2b–m** **4b–m**

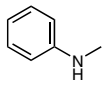
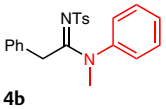
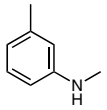
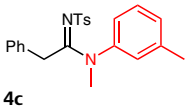
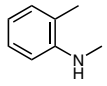
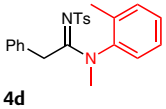
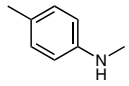
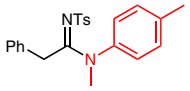
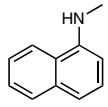
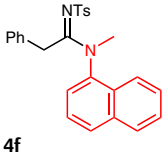
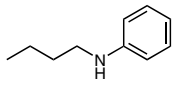
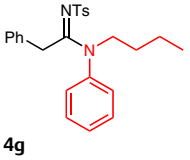
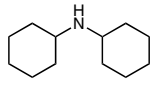
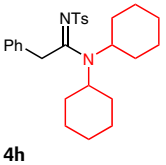
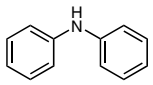
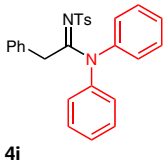
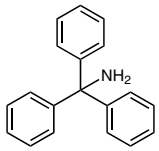
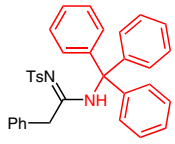
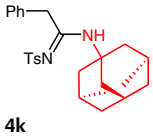
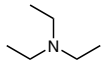
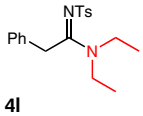
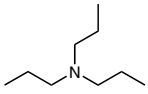
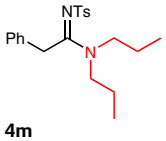
Entry	Amine	Product	Yield (%)[a]
1		 **4b**	92
2		 **4c**	89
3		 **4d**	92
4		 **4e**	93
5		 **4f**	94
6		 **4g**	93
7		 **4h**	89

Table 3 (continued)

Entry	Amine	Product	Yield (%)[a]
8		 **4i**	90
9		 **4j**	94
10		 **4k**	90
11		 **4l**	90
12		 **4m**	89

[a] Isolated yield.

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded at 25 °C on a Varian 500 MHz or 400 MHz and ^{13}C NMR spectra were recorded at 25 °C on a Varian 125 MHz, respectively, using TMS as internal standard. Mass spectra were recorded on Bruker AutoflexIII Smartbeam MS-spectrometer. High-resolution mass spectra (HRMS) were recorded on Bruck microTof by using ESI method.

Silver-Catalyzed Denitrogenative Amination of *N*-Sulfonyl-1,2,3-triazoles 1a–m with Diisopropylamine; *N*,*N*-Diisopropyl-2-phenyl-*N*′-tosylacetimidamide (3a); Typical Procedure

A mixture of *i*-Pr_2NH (76 mg, 0.75 mmol), 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**; 150 mg, 0.5 mmol) and Ag_2CO_3 (13.8 mg, 0.05 mmol) in toluene (1 mL) was stirred at 80 °C under N_2 for 12 h until the substrates had disappeared. The reaction was quenched with H_2O. The reaction mixture was filtered to remove insoluble substance and the filterate was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were concentrated in vacuo and the residue was purified by flash chromatography on silica gel to give **3a** as a white solid; yield: 160 mg (86%); mp 147.5–148.5 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.5 Hz, 6 H), 1.39 (d, *J* = 6.5 Hz, 6 H), 2.34 (s, 3 H), 3.44–3.48 (m, 1 H), 3.96–4.02 (m, 1 H), 4.41 (s, 2 H), 7.11–7.31 (m, 7 H), 7.81 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (125MHz, $CDCl_3$): δ = 19.8, 21.4, 38.7, 48.0, 50.4, 126.2, 126.7, 128.0, 128.8, 129.0, 134.9, 141.5, 141.5, 163.4.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{29}N_2O_2S$ [M + H]$^+$: 373.1951; found: 373.1950.

N,*N*-Diisopropyl-2-(*p*-tolyl)-*N*′-tosylacetimidamide (3b)

White solid; yield: 164 mg (85%); mp 165–166 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.5 Hz, 6 H), 1.39 (d, *J* = 6.5 Hz, 6 H), 2.30 (s, 3 H), 2.39 (s, 3 H), 3.41–3.45 (m, 1 H), 3.97–4.02 (m, 1 H), 4.35 (s, 2 H), 7.02–7.11 (m, 4 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.82 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.8, 19.8, 21.0, 21.4, 38.3, 47.9, 50.3, 126.1, 127.7, 128.9, 129.4, 131.7, 136.2, 141.4, 163.6.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{29}N_2O_2S$ [M + H]$^+$: 387.2107; found: 387.2111.

N,*N*-Diisopropyl-2-(4-methoxyphenyl)-*N*′-tosylacetimidamide (3c)

White solid; yield: 175 mg (87%); mp 111–112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.4 Hz, 6 H), 1.38 (d, *J* = 6.8 Hz, 6 H), 2.39 (s, 3 H), 3.41–3.45 (m, 1 H), 3.78 (s, 3 H), 3.99–4.05 (m, 1 H), 4.32 (s, 2 H), 6.82 (d, *J* = 8.4 Hz, 2 H), 7.12 (d, *J* = 8.4 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.83 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.75, 19.82, 21.4, 37.9, 47.9, 50.3, 55.2, 114.2, 126.1, 126.8, 129.0, 129.0, 141.5, 158.3, 163.7.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{29}N_2O_3S$ [M + H]$^+$: 402.5511; found: 402.5513.

2-(4-Fluorophenyl)-*N*,*N*-diisopropyl-*N*′-tosylacetimidamide (3d)

White solid; yield: 150 mg (77%); mp 150–151 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 8.0 Hz, 6 H), 1.37 (d, *J* = 8.5 Hz, 6 H), 2.40 (s, 3 H), 3.43–3.46 (m, 1 H), 3.93–4.00 (m, 1 H), 4.37 (s, 2 H), 6.97–7.01 (m, 2 H), 7.18–7.21 (m, 2 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.82 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 19.8, 21.4, 37.9, 48.0, 50.3, 115.5, 115.7, 126.1, 129.0, 129.48, 129.54, 141.3, 141.6, 160.6, 162.6, 163.0.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{26}FN_2O_2S$ [M + H]$^+$: 390.5111; found: 390.5113.

2-(4-Chlorophenyl)-*N*,*N*-diisopropyl-*N*′-tosylacetimidamide (3e)

White solid; yield: 155 mg (76%); mp 155–156 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.0 Hz, 6 H), 1.38 (d, *J* = 6.5 Hz, 6 H), 2.40 (s, 3 H), 3.43–3.49 (m, 1 H), 3.93–3.95 (m, 1 H), 4.37 (s, 2 H), 7.15 (d, *J* = 7.5 Hz, 2 H), 7.22–7.27 (m, 4 H), 7.81 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 19.9, 21.4, 38.0, 48.1, 50.4, 126.1, 128.9, 129.0, 129.3, 132.6, 133.4, 141.2, 141.7, 162.7.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{26}ClN_2O_2S$ [M + H]$^+$: 406.9712; found: 406.9716.

2-(4-Bromophenyl)-*N*,*N*-diisopropyl-*N*′-tosylacetimidamide (3f)

White solid; yield: 171 mg (76%); mp 154–155 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.5 Hz, 6 H), 1.38 (d, *J* = 6.5 Hz, 6 H), 2.40 (s, 3 H), 3.42–3.49 (m, 1 H), 3.91–3.96 (m, 1 H), 4.36 (s, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 7.80 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 19.9, 21.4, 38.0, 48.1, 50.4, 120.7, 126.1, 129.0, 129.6, 131.9, 133.9, 141.2, 141.7, 162.6.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{26}BrN_2O_2S$ [M + H]$^+$: 451.4221; found: 451.4225.

N,N-Diisopropyl-2-(naphthalen-2-yl)-N′-tosylacetimidamide (3g)

White solid; yield: 167 mg (79%); mp 160–161 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.5 Hz, 6 H), 0.86 (d, *J* = 7.0 Hz, 6 H) 2.28 (s, 3 H), 3.45–3.51 (m, 1 H), 4.05–4.09 (m, 1 H), 4.56 (s, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 1 H), 7.43–7.47 (m, 3 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.76–7.82 (m, 4 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.9, 21.3, 38.3, 48.1, 50.4, 125.7, 126.1, 126.1, 126.2, 126.3, 127.5, 127.6, 128.5, 128.9, 132.1, 132.2, 133.4, 141.3, 141.6, 163.4.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{29}N_2O_2S$ [M + H]$^+$: 422.5812; found: 422.5815.

N,N-Diisopropyl-2-(pyridin-3-yl)-N′-tosylacetimidamide (3h)

Yellow solid; yield: 153 mg (82%); mp 146.6–147.7 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 7.5 Hz, 6 H), 1.38 (d, *J* = 7.5 Hz, 6 H), 2.40 (s, 3 H), 3.45–3.49 (m, 1 H), 3.90–3.96 (m, 1 H), 4.42 (s, 1 H), 7.24–7.28 (m, 3 H), 7.66 (d, *J* = 7.5 Hz, 1 H), 7.82 (d, *J* = 7.5 Hz, 2 H), 8.46 (s, 1 H), 8.50 (d, *J* = 4.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 19.9, 21.4, 36.0, 48.2, 50.4, 123.7, 126.1, 129.1, 130.8, 135.5, 141.1, 141.8, 148.3, 149.2, 162.0.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{26}N_3O_2S$ [M + H]$^+$: 373.5114; found: 373.5118.

N,N-Diisopropyl-2-(thiophen-3-yl)-N′-tosylacetimidamide (3i)

White solid; yield: 147 mg (75%); mp 149.1–150.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 6.8 Hz, 6 H), 1.37 (d, *J* = 6.8 Hz, 6 H), 2.39 (s, 3 H), 3.46–3.50 (m, 1 H), 4.13–4.16 (m, 1 H), 4.53 (s, 2 H), 6.87 (s, 1 H), 6.89–6.91 (m, 1 H), 7.16 (d, *J* = 4.8 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.81 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 20.0, 21.4, 32.9, 48.2, 50.5, 124.4, 126.2, 127.0, 129.0, 136.1, 141.3, 141.6, 162.0.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{25}N_2O_2S_2$ [M + H]$^+$: 378.5521; found: 378.5525.

2-(Cyclohex-1-en-1-yl)-N,N-diisopropyl-N′-tosylacetimidamide (3j)

White solid; yield: 115 mg (61%); mp 98–99 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (d, *J* = 6.5 Hz, 6 H), 1.40 (d, *J* = 6.5 Hz, 6 H), 1.47–1.51 (m, 2 H), 1.54–1.59 (m, 2 H), 1.84–1.90 (m, 2 H), 1.91–1.97 (m, 2 H), 2.38 (s, 3 H), 3.47–3.53 (m, 1 H), 3.57 (s, 2 H), 3.93–3.95 (m, 1 H), 5.21 (t, *J* = 5.5 Hz, 1 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 7.78 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 20.0, 20.2, 21.4, 21.9, 22.6, 25.1, 28.5, 39.7, 48.0, 50.2, 123.3, 126.2, 128.9, 131.1, 141.3, 141.6, 163.8.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{31}N_2O_2S$ [M + H]$^+$: 484.1141, found: 484.1145.

N,N-Diisopropyl-N′-tosyloctanimidamide (3k)

White solid; yield: 158 mg (83%); mp 113–114 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.91 (m, 3 H), 1.24 (d, *J* = 6.5 Hz, 6 H), 1.26–1.30 (m, 6 H), 1.31 (d, *J* = 6.5 Hz, 6 H), 1.38–1.42 (m, 2 H), 1.57–1.63 (m, 2 H), 2.40 (s, 3 H), 2.86–2.89 (m, 2 H), 3.47–3.52 (m, 1 H), 4.00–4.06 (m, 1 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.82 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.1, 20.0, 20.7, 21.4, 22.6, 27.3, 28.8, 29.8, 31.7, 32.8, 47.8, 49.8, 126.0, 129.0, 141.3, 141.9.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{35}N_2O_2S$ [M + H]$^+$: 376.5614; found: 376.5618.

2-Cyclopropyl-N,N-diisopropyl-N′-tosylacetimidamide (3l)

White solid; yield: 86 mg (51%); mp 94–95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.51–0.55 (m, 2 H), 0.56–0.61 (m, 2 H), 0.91–0.96 (m, 1 H), 1.24 (d, *J* = 6.4 Hz, 6 H), 1.32 (d, *J* = 6.8 Hz, 6 H), 2.39 (s, 3 H), 2.99 (d, *J* = 6.4 Hz, 2 H), 3.48–3.53 (m, 1 H), 4.20–4.25 (m, 1 H), 7.24 (d, *J* = 8.0 Hz, 2 H) 7.80 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 5.2, 8.6, 20.0, 20.6, 21.4, 35.6, 47.8, 50.3, 126.0, 128.9, 141.3, 141.8, 165.2.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{27}N_2O_2S$ [M + H]$^+$: 336.4902; found: 336.4908.

2-([1,1′-Biphenyl]-4-yl)-N,N-diisopropyl-N′-tosylacetimidamide (3m)

White solid; yield: 193 mg (86%); mp 157–159 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 5.0 Hz, 6 H), 1.41 (d, *J* = 6.0 Hz, 6 H), 2.38 (s, 3 H), 3.45–3.50 (m, 1 H), 4.02–4.06 (m, 1 H), 4.45 (s, 2 H), 7.22–7.25 (m, 4 H), 7.32–7.36 (m, 1 H), 7.41–7.45 (m, 2 H), 7.53 (d, *J* = 7.0 Hz, 2 H), 7.57 (d, *J* = 6.5 Hz, 2 H), 7.84 (d, *J* = 6.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.8, 19.9, 21.4, 38.3, 48.0, 50.4, 126.2, 126.9, 127.3, 127.4, 128.3, 128.7, 129.0, 133.9, 139.5, 140.5, 141.4, 141.6, 163.3.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{31}N_2O_2S$ [M + H]$^+$: 448.6217; found: 448.6221.

Metal-Free Thermally Promoted Denitrogenative Amination of 4-Phenyl-1-tosyl-1*H*-1,2,3-triazole (1a) with Various Amines; N,N-Dicyclohexyl-2-phenyl-N′-tosylacetimidamide (4h); Typical Procedure

A mixture of 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**; 150 mg, 0.5 mmol) and dicyclohexylamine (0.75 mmol) in toluene (1 mL) was stirred under N_2 atmosphere for 12 h at 120 °C until the substrates had disappeared. The reaction was quenched with H_2O and the mixture was extracted by CH_2Cl_2 (3 × 20 mL). The combined organic layers were concentrated in vacuo and the residue was purified by flash chromatography on silica gel to give **4h** as a white solid; yield: 201 mg (89%); mp 157–158 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87–0.94 (m, 4 H), 1.08–1.15 (m, 4 H), 1.27–1.36 (m, 4 H), 1.49–1.53 (m, 2 H), 1.57–1.65 (m, 2 H), 1.66–1.72 (m, 2 H), 2.41 (s, 3 H), 2.58–2.63 (m, 2 H), 2.92–2.96 (m, 1 H), 3.54–3.59 (m, 1 H), 4.40 (s, 2 H), 7.19–7.30 (m, 8 H), 7.86 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.4, 24.9, 25.2, 25.5, 26.3, 28.5, 30.2, 39.4, 58.6, 59.3, 126.2, 126.7, 128.2, 128.7, 128.9, 135.3, 141.5, 141.6, 163.6.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{35}N_2O_2S$ [M + H]$^+$: 452.6511; found: 452.6515.

N-Methyl-N,2-diphenyl-N′-tosylacetimidamide (4b)

White solid; yield: 174 mg (92%); mp 131.5–133.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.32 (s, 3 H), 4.24 (s, 2 H), 6.76–6.81 (m, 4 H), 7.03–7.09 (m, 3 H), 7.19–7.28 (m, 5 H), 7.87 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.4, 37.6, 41.1, 126.3, 126.4, 127.2, 128.1, 128.3, 129.0, 129.4, 134.6, 141.0, 142.0, 142.5, 144.6, 166.3.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{21}N_2O_2S$ [M + H]$^+$: 378.4912; found: 378.4915.

***N*-Methyl-2-phenyl-*N*-(*m*-tolyl)-*N*′-tosylacetimidamide (4c)**

White solid; yield: 175 mg (89%); mp 120–121 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3 H), 2.41 (s, 3 H), 3.31 (s, 3 H), 4.22 (s, 2 H), 6.49 (s, 1 H), 6.67 (d, *J* = 7.5 Hz, 1 H), 6.78 (d, *J* = 6.0 Hz, 2 H), 7.06–7.14 (m, 5 H), 7.22–7.28 (m, 2 H), 7.88 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.0, 21.4, 37.8, 41.0, 124.0, 126.3, 126.4, 128.1, 128.4, 129.1, 129.2, 134.9, 139.6, 141.1, 142.0, 142.4, 166.4.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_2O_2S$ [M + H]$^+$: 392.5113; found: 392.5115.

***N*-Methyl-2-phenyl-*N*-(*o*-tolyl)-*N*′-tosylacetimidamide (4d)**

White solid; yield: 180 mg (92%); mp 122–123 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.67 (s, 3 H), 2.42 (s, 3 H), 3.22 (s, 3 H), 4.11 (d, *J* = 15.0 Hz, 1 H), 4.25 (d, *J* = 15.0 Hz, 1 H), 6.75 (d, *J* = 7.0 Hz, 2 H), 6.83 (d, *J* = 8.0 Hz, 1 H), 7.06–7.11 (m, 5 H), 7.21–7.28 (m, 3 H), 7.91 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 16.7, 21.4, 37.7, 39.8, 126.4, 126.6, 127.0, 127.8, 128.1, 128.9, 129.0, 129.1, 131.4, 133.9, 135.9, 141.15, 141.21, 142.0, 166.5.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_2O_2S$ [M + H]$^+$: 392.5122; found: 392.5125.

***N*-Methyl-2-phenyl-*N*-(*p*-tolyl)-*N*′-tosylacetimidamide (4e)**

White solid; yield: 182 mg (93%); mp 121–122 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.30 (s, 3 H), 2.40 (s, 3 H), 3.31 (s, 3 H), 4.23 (s, 2 H), 6.69 (d, *J* = 8.0 Hz, 2 H), 6.79 (d, *J* = 6.5 Hz, 2 H), 7.00 (d, *J* = 8.0 Hz, 2 H), 7.06–7.11 (m, 3 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.85 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.0, 21.4, 37.5, 41.1, 126.3, 126.4, 126.8, 128.1, 128.3, 129.0, 130.0, 134.7, 138.4, 140.0, 141.0, 141.9, 166.4.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_2O_2S$ [M + H]$^+$: 392.5123; found: 392.5126.

***N*-Methyl-*N*-(naphthalen-1-yl)-2-phenyl-*N*′-tosylacetimidamide (4f)**

White solid; yield: 201 mg (94%); mp 157–158 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 3.42 (s, 3 H), 3.82 (d, *J* = 15.0 Hz, 1 H), 4.43 (d, *J* = 15.0 Hz, 1 H), 6.62 (d, *J* = 7.5 Hz, 2 H), 6.89–6.95 (m, 4 H), 7.24 (d, *J* = 7.5 Hz, 1 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.38–7.41 (m, 2 H), 7.45–7.47 (m, 1 H), 7.80–7.85 (m, 2 H), 7.94 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.5, 37.9, 40.8, 121.7, 125.2, 125.8, 126.3, 126.4, 126.6, 127.6, 128.0, 128.3, 128.4, 129.1, 129.2, 129.4, 134.3, 134.6, 138.5, 141.1, 142.1, 167.3.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{23}N_2O_2S$ [M + H]$^+$: 428.5506; found: 428.5510.

***N*-Butyl-*N*,2-diphenyl-*N*′-tosylacetimidamide (4g)**

White solid; yield: 196 mg (93%); mp 158–159 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.77–0.80 (t, *J* = 7.5 Hz, 3 H), 1.18–1.22 (m, 2 H), 1.45–1.50 (m, 2 H), 2.38 (s, 3 H), 3.70 (t, *J* = 7.5 Hz, 2 H), 4.17 (s, 2 H), 6.70–6.78 (m, 4 H), 7.03–7.07 (m, 3 H), 7.17 (t, *J* = 7.5 Hz, 2 H), 7.23–7.25 (m, 3 H), 7.84 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 13.6, 19.9, 21.4, 28.7, 38.0, 52.7, 126.3, 126.3, 128.1, 128.1, 128.3, 129.0, 129.3, 134.8, 141.2, 141.2, 141.9, 165.7.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{27}N_2O_2S$ [M + H]$^+$: 420.5710; found: 420.5713.

***N*,*N*,2-Triphenyl-*N*′-tosylacetimidamide (4i)**

White solid; yield: 198 mg (90%); mp 185–186 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 4.46 (s, 2 H), 6.92–6.93 (m, 4 H), 7.14–7.16 (m, 6 H), 7.20–7.29 (m, 7 H), 7.60 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.4, 38.4, 126.2, 126.6, 127.0, 128.4, 128.5, 128.9, 129.2, 134.6, 140.5, 141.4, 142.0, 166.9.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{23}N_2O_2S$ [M + H]$^+$: 440.5613; found: 440.5617.

2-Phenyl-*N*′-tosyl-*N*-tritylacetimidamide (4j)

White solid; yield: 249 mg (94%); mp 145–146 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 4.40 (s, 2 H), 6.36 (s, 1 H), 6.90–6.96 (m, 6 H), 7.02 (d, *J* = 8.0 Hz, 2 H), 7.10–7.18 (m, 11 H), 7.29–7.37 (m, 3 H), 7.39–7.42 (m, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.4, 40.8, 71.8, 126.1, 127.0, 127.7, 127.8, 127.9, 128.3, 128.47, 128.51, 128.6, 129.0, 129.6, 130.1, 133.4, 140.1, 141.5, 143.2, 163.8.

HRMS (ESI): *m*/*z* calcd for $C_{34}H_{29}N_2O_2S$ [M + H]$^+$: 530.6817; found: 5320.6821.

***N*-[(3s,5s,7s)-Adamantan-1-yl]-2-phenyl-*N*′-tosylacetimidamide (4k)**

White solid; yield: 190 mg (90%); mp 145–146 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.52–1.61 (m, 6 H), 1.86 (d, *J* = 2.5 Hz, 6 H), 1.99 (s, 3 H), 2.42 (s, 3 H), 4.25 (s, 2 H), 4.88 (s, 1 H), 7.20 (d, *J* = 7.0 Hz, 2 H), 7.27 (d, *J* = 8.5 Hz, 2 H), 7.28–7.38 (m, 3 H), 7.86 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.5, 29.2, 36.1, 40.5, 40.6, 54.0, 126.1, 128.0, 129.1, 129.3, 130.0, 133.5, 141.1, 141.8, 164.6.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{29}N_2O_2S$ [M+ H]$^+$: 422.5812; found: 422.5816.

***N*,*N*-Diethyl-2-phenyl-*N*′-tosylacetimidamide (4l)**

White solid; yield: 155 mg (90%); mp 116–117 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 8.5 Hz, 3 H), 1.15 (t, *J* = 8.5 Hz, 3 H), 2.36 (s, 3 H), 3.20 (q, *J* = 8.5 Hz, 2 H), 3.50 (q, *J* = 8.5 Hz, 2 H), 4.38 (s, 2 H), 7.11 (d, *J* = 8.5 Hz, 2 H), 7.16–7.19 (m, 2 H), 7.21–7.25 (m, 2 H), 7.75 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 11.9, 13.4, 21.4, 36.5, 43.2, 43.3, 126.2, 126.7, 127.8, 128.8, 128.9, 134.3, 141.2, 141.6, 164.5.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{23}N_2O_2S$ [M + H]$^+$: 344.4712; found: 344.4715.

2-Phenyl-*N*,*N*-dipropyl-*N*′-tosylacetimidamide (4m)

White solid; yield: 166 mg (89%); mp 118–119 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75 (t, *J* = 7.0 Hz, 3 H), 0.85 (t, *J* = 7.0 Hz, 3 H), 1.34–1.40 (m, 2 H), 1.58–1.66 (m, 2 H), 2.37 (s, 3 H), 3.08 (t, *J* = 7.5 Hz, 2 H), 3.39 (t, *J* = 7.5 Hz, 2 H), 4.39 (s, 2 H), 7.09–7.27 (m, 7 H), 7.77 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 11.0, 11.4, 20.0, 21.4, 21.7, 36.8, 50.6, 50.8, 126.1, 126.7, 127.9, 128.8, 128.9, 134.4, 141.3, 141.6, 164.8.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{27}N_2O_2S$ $[M + H]^+$: 372.5220; found: 372.5224.

Acknowledgment

This work was supported by the NSFC (21522202, 21372038), the Ministry of Education of the People's Republic of China (NCET-13-0714), the Jilin Provincial Research Foundation for Basic Research (20140519008JH), and Fundamental Research Funds for the Central Universities (2412015BJ005).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588103.

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(11) Crystallographic data for **3a**: space group *P*-1, *a* = 8.2090(6) Å, *b* = 11.2709(9) Å, *c* = 12.4772(10) Å, *α* = 114.679(1)°, *β* = 100.637(1)°, *γ* = 97.570(1)°, *V* = 1002.38(14) Å^3, *T* = 293 K,

Z = 2. CCDC 1491766 contains the supplementary crystallographic data for compound **3a** reported in this paper. These da can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

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