无金属和氧化剂温和条件下碱促进的烯胺酮碳-碳双键断裂 合成 NH_2 -结构脒类化合物

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摘要 报道了室温条件下烯胺酮和磺酰叠氮通过碳-碳双键断裂合成 *N*-磺酰基脒类化合物的方法。反应在 1,8-二氮杂双环[5.4.0]十一碳-7-烯(DBU)存在下进行, 无需使用任何金属和氧化剂, 具有良好的底物适用性。烯胺酮上的 ^{15}N 同位素标记实验证实, 磺酰叠氮仅作为产物中的磺酰胺片段供体, 同时, 该实验也有力地支持反应机理涉及关键的 1,2,3-三唑啉中间体的原位形成以及环分解。

关键词 烯胺酮; 碳-碳双键断裂; 无金属; 无氧化剂; 脒

Base-Promoted, Metal- and Oxidant-Free C=C Bond Cleavage in Enaminones for Ambient Synthesis of NH_2 -Amidines

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Abstract The C=C double bond cleavage of NH_2 -functionalized enaminones has been realized at room temperature to provide various *N*-sulfonyl amidines by reacting with sulfonyl azides. The reactions take place with good substrate tolerance in the presence of 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) without any metal or oxidant reagent. The ^{15}N -labelling experiment on enaminone indicates that the sulfonyl azide component donates solely the sulfonamide fragment, and the reaction mechanism involving a key decomposition of the *in situ* generated 1,2,3-triazoline intermediate is convincingly supported.

Keywords Enaminone; C=C bond cleavage; Metal-free; Oxidant-free; Amidines

1 Introduction

Effectively scissoring carbon-carbon bond represents one of the most important tools in current organic synthesis because of the ubiquitous presence of carbon-carbon bond in both saturated and unsaturated forms in nature.^[1] The past decades have witnessed spectacular advances in synthetic organic reactions based on the key functionalization or activation of carbon-carbon bonds. Among the numerous known donors of reactive carbon-carbon bond,^[2] the enaminones have been identified as a class of promising substrates in the designation of practical organic reactions by cleaving the C=C double bond in recent years.^[3] As typical stable enamine species, the C=C double bonds in enaminones have been found to be capable of decomposing via the formation and reorganization of 1,2-dioxetane^[4]/1,2-oxathietane intermediate,^[5] free radical-based

bond cleavage via DMF release,^[6] ring opening and reconstruction of cyclopropane intermediate resulting from carbene cycloaddition,^[7] and Pd-catalyzed tandem enamine hydrolysis and decarbonylation.^[8]

On the other hand, as a typical transformation, the cycloaddition of the *in situ* formed unstable enamine intermediate and azide has been found as highly important route to cleave the carbon-carbon bond via the decomposition of the resulted triazoline ring, which provides effective accesses to amidines.^[9] Accordingly, the employment of stable enamines such as enaminones has also received concerns in the development of synthetic method toward amidine scaffolds. Early in 1963, Fusco and co-workers^[10] have observed the formation of *N*-sulfonyl amidines in the reactions of aryl stabilized *N,N*-disubstituted α -aminostyrene with tosyl azide. Later efforts in similar reactions, unexceptionally, can be used only for the synthesis of

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N-sulfonyl amidines featured with *N,N*-disubstituted substructure because only *N,N*-disubstituted α -aminostyrenes are the tolerable enamine substrates.^[11] Clearly, such synthetic methods suffer from rigid restriction in the synthesis of amidine products with diversified amino functionalization, thus reflects the urgent requirement in developing new synthetic approaches allowing the synthesis of other amino group, such as free NH_2 -functionalized amidines.

Over past decade, an array of different tactics have been devised for the synthesis amidines. For instance, the condensation of amines with amide acetals or *in situ* activated amides,^[12] the decomposition of *in situ* generated 1,2,3-triazoline ring given by copper-catalyzed alkyne-azide dipolar cycloaddition,^[13] the activation of terminal alkynes,^[14] catalytic $\text{C}=\text{N}$ bond formation from the thioamide $\text{C}=\text{S}$ bond^[15] *etc* have been disclosed as useful methods. Amazingly, regardless the availability of these important synthetic routes,^[16] most of them are limited in the synthesis of *N,N*-disubstituted or *N*-substituted amidines. Only rather a few transition-metal-catalyzed protocols, on the contrary, can be used for the synthesis of amidines bearing free NH_2 -group.^[9c,17] The synthesis of NH_2 -free amidines under transition-metal-free conditions, however, has not yet been realized. In combination of the urgent requirement to find transition-metal-free NH_2 -amidine synthesis and the highly versatile application of enaminone platform synthons in the synthesis of diversified organic products,^[18] we thought that NH_2 -functionalized enaminones might be used as proper precursors to achieve such expected synthesis. Herein, we report the first metal-free method for the synthesis of NH_2 -featured *N*-sulfonyl amidines via the reactions of NH_2 -functionalized enaminones and sulfonyl azides, which significantly expands the frontiers of enaminones in the synthesis of structurally diverse amidines and sulfonylated scaffolds.^[19]

2 Results and discussion

Originally, the readily available enaminone **1a** and tosyl azide **2a** were selected as substrates to probe practical reaction conditions. As presented in Table 1, by stirring in DMF at room temperature, the reaction of the two substrates in the presence of *t*-BuONa gave the target amidine product **3a** with 21% yield, and **3a** was not observed without using any additive (Entries 1, 2, Table 1). Following these results, a series of different base additives, including organic and inorganic ones, were then screened. Based on the in hand data, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was identified as amongst the best additive by assisting the formation of **3a** with 46% yield (Entries 3~7, Table 1). Heightening the reaction temperature led to inferior result (Entry 8, Table 1). Later on, this reaction was conducted independently in different media such as water, MeCN, toluene, EtOH, dimethyl sulfoxide (DMSO) and tetrahydrofuran (THF) (Entries 9~14, Table 1). However, DMF was yet the best medium. In further study, prolonging the reaction time to 12 h was found to improve

the yield of the target product (Entries 15~16, Table 1). On the other hand, increasing the amount of tosyl azide **2a** could also help in enhancing the product yield (Entries 17, 18, Table 1). Finally, when the loading of DBU was increased to 5 equiv., the target product was obtained with 91% yield (Entries 19, 20, Table 1).

Table 1 Optimization on reaction conditions^a

Entry	Additive	Solvent	Yield ^b /%
1	<i>t</i> -BuONa	DMF	21
2	—	DMF	0
3	NaHCO_3	DMF	20
4	NaOH	DMF	19
5	DBU	DMF	46
6	DMAP	DMF	17
7	2,6-Lutidine	DMF	12
8 ^c	DBU	DMF	26
9	DBU	H_2O	38
10	DBU	MeCN	35
11	DBU	Toluene	38
12	DBU	EtOH	37
13	DBU	DMSO	34
14	DBU	THF	28
15 ^d	DBU	DMF	61
16 ^e	DBU	DMF	48
17 ^{d,f}	DBU	DMF	52
18 ^{d,g}	DBU	DMF	67
19 ^{d,g,h}	DBU	DMF	81
20 ^{d,g,i}	DBU	DMF	91

^a General conditions: **1a** (0.2 mmol), **2a** (0.5 mmol), additive (0.4 mmol) in 2 mL of solvent, stirred at r.t. for 6 h. ^b Yield of isolated product based on **1a**.

^c Reaction at 60 °C. ^d Stirred for 12 h. ^e Stirred for 24 h. ^f With 0.3 mmol of **2a**.

^g With 1.0 mmol of **2a**. ^h With 0.8 mmol of DBU. ⁱ With 1.0 mmol of DBU.

With the optimized reaction conditions, the application scope of this $\text{C}=\text{C}$ bond cleavage reaction in the synthesis of NH_2 -functionalized *N*-sulfonyl amidines was systematically investigated (Table 2). Firstly, the enaminone **1a** was employed to react with a plethora of aryl sulfonyl azides, respectively. As expected, the reaction displayed broad tolerance to the aryl substructure. Azides functionalized with phenyl containing electron donating (**3a**~**3b**) and withdrawing (**3c**~**3d**) group in the *para*-position, the phenyls with *ortho*- and *meta*-substituent (**3e**~**3g**) and polysubstituted phenyl (**3h**), as well as naphthyl/heteroaryl (**3i**~**3j**) were all transformed into the target products with good to excellent yields. On the other hand, enaminones **1** with alkyl (**3k**~**3n**), alkoxy (**3o**~**3p**), halogen (**3q**) substituted β -phenyl also participated the reaction to provide the products with satisfactory results. Furthermore, equivalent enaminones featured with heteroaryl (**3r**) and fuse aryl (**3s**) were also practical substrates. Finally, employing methyl sulfonyl azide to react with enaminone **1a** did not provide the expected amidine product under the standard

conditions.

Table 2 Scope on the enaminone-based synthesis of *N*-sulfonyl amidines^{a,b}

^a General conditions: **1** (0.2 mmol), **2** (1.0 mmol), DBU (1.0 mmol) in DMF (2 mL), stirred at r.t. for 12 h. ^b Yield of isolated products based on **1**.

Encouraged by the successful synthesis of the diverse amidine products, the gram scale reaction for the synthesis of **3a** was then performed. We were delighted to find that authentically practical result was provided by the scale-up synthesis with up to 78% yield of **3a** (Eq. 1).

Later on, for the sake of probing the reaction mechanism, several control experiments were then designed and conducted. First, the model reaction for **3a** synthesis was conducted in the presence of free radical scavenger 2,2,6,6-Tetramethylpiperidinoxy (TEMPO) and 2,6-di-*t*-butyl-*p*-cresol (BHT), respectively. Both scavengers, however, exhibited no inhibition effect to the reaction even at the loading of 4 equiv. (Eqs. 2, 3), suggesting against the formation of any free radical intermediate in the reaction. In addition, the reaction of ¹⁵N-labelled enaminone and tosyl azide **2a** gave ¹⁵N-labelled product ¹⁵N-**3a**, confirming that the amino group in the enaminone substrate was retained during the reaction process (Eq. 4).

On the basis of the results obtained in hand, a plausible mechanism for the reaction is proposed. As outlined in Scheme 1, initially, the enaminone and sulfonyl azide couples provide 1,2,3-triazoline intermediate **4** via the well documented dipolar cycloaddition. The possible transformation of this intermediate to 1,2,3-triazole **7** by eliminating ammonium can be inhibited by the presence of DBU. Instead, the other transformation route of ring decomposition providing amidine **5** and the diazoketone **6** is favored under the present reaction conditions. The tautomerization of **5** then yields the final amidine products **3**.

Scheme 1 Proposed reaction mechanism

3 Conclusions

In conclusion, by employing NH₂-functionalized enaminone esters as the C=C bond donors, we have successfully established the first metal-free protocol toward the synthesis of free NH₂-featured *N*-sulfonyl amidines by cleaving C=C double bond. Besides the metal-free operation, the ambient reaction conditions as well as the practical scale-up synthesis constitute also notable advantages of this work.

4 Experimental section

4.1 General experimental information

All experiments were carried out under air atmosphere. Enaminones **1**^[20] and tosyl azides **2** (except the commercially available **2a**)^[21] were synthesized following literature processes. All other chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. ¹H NMR and ¹³C NMR spectra were recorded in 400 MHz apparatus and the

frequencies for ^1H NMR and ^{13}C NMR test are 400 MHz and 100 MHz, respectively. The chemical shifts were reported with TMS as internal standard. Melting points were tested in an X-4A instrument without correcting temperature and the HRMS were obtained under ESI model in a mass spectrometer equipped with TOF analyzer.

4.2 General procedure for the synthesis of amidines 3

To a 25 mL round-bottom flask were added enaminone **1** (0.2 mmol), sulfonyl azide **2** (1.0 mmol), DBU (1.0 mmol) and DMF (2.0 mL). Then the mixture was stirred at the room temperature for 12 h (TLC). Upon completion, 5 mL of water was added, and the resulting mixture was extracted with ethyl acetate (8 mL $\times$ 3). The organic phases were combined and washed with small amount of water for three times. After drying with anhydrous Na_2SO_4 , the solid was filtered and the solvent in the acquired solution was removed under reduced pressure. The resulting residue was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether/ethyl acetate ($V:V=5:1$ or $3:1$).

N-Tosylbenzimidamide (**3a**):^[22] 49.8 mg, 91% yield. White solid, m.p. 153~155 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.30 (s, 1H), 7.86 (d, $J=8.4$ Hz, 2H), 7.78 (d, $J=7.6$ Hz, 2H), 7.49 (t, $J=7.4$ Hz, 1H), 7.37 (t, $J=7.8$ Hz, 2H), 7.26 (d, $J=8.0$ Hz, 2H), 6.68 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.8, 143.0, 139.3, 133.3, 132.7, 129.4, 128.7, 127.4, 126.4, 21.5.

N-(4-Methoxyphenylsulfonyl)benzimidamide (**3b**): 49.0 mg, 84% yield. White solid, m.p. 109~111 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.26 (s, 1H), 7.90 (d, $J=8.8$ Hz, 2H), 7.78 (d, $J=7.6$ Hz, 2H), 7.48 (t, $J=7.4$ Hz, 1H), 7.36 (t, $J=7.4$ Hz, 2H), 6.92 (d, $J=8.8$ Hz, 2H), 6.88 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.7, 134.1, 133.3, 132.7, 128.7, 128.5, 128.5, 127.5, 114.0, 55.6; ESI-HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 291.0798, found 291.0799.

N-(4-Chlorophenylsulfonyl)benzimidamide (**3c**): 46.1 mg, 78% yield. White solid, m.p. 98~100 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.29 (s, 1H), 7.90 (d, $J=8.8$ Hz, 2H), 7.78 (d, $J=7.6$ Hz, 2H), 7.51 (t, $J=7.4$ Hz, 1H), 7.46~7.35 (m, 4 H), 6.80 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.2, 140.6, 138.7, 133.0, 132.9, 129.1, 128.8, 127.9, 127.5; ESI-HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 295.0303, found 295.0304.

N-(4-Bromophenylsulfonyl)benzimidamide (**3d**): 49.9 mg, 74% yield. White solid, m.p. 102~103 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.29 (s, 1H), 7.83 (d, $J=8.4$ Hz, 2H), 7.77 (d, $J=7.2$ Hz, 2H), 7.59 (d, $J=8.4$ Hz, 2H), 7.52 (t, $J=7.4$ Hz, 1H), 7.39 (t, $J=7.6$ Hz, 2H), 6.85 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.3, 141.2, 133.0, 132.9, 132.1, 128.8, 128.0, 127.5, 127.2; ESI-HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{BrN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 338.9797, found 338.9798.

N-(*o*-Tolylsulfonyl)benzimidamide (**3e**): 40.0 mg, 73% yield. White solid, m.p. 68~70 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.25 (s, 1H), 8.06 (d, $J=8.0$ Hz, 1H), 7.79 (d,

$J=7.2$ Hz, 2H), 7.50 (t, $J=7.4$ Hz, 1H), 7.45~7.35 (m, 3H), 7.29 (d, $J=7.2$ Hz, 2H), 6.63 (s, 1H), 2.75 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.8, 140.2, 137.6, 133.3, 132.7, 132.4, 132.3, 128.8, 127.7, 127.4, 125.8, 20.4; ESI-HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 275.0849, found 275.0852.

N-(2-Chlorophenylsulfonyl)benzimidamide (**3f**): 38.4 mg, 65% yield. White solid, m.p. 91~92 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.43 (s, 1H), 8.20 (dd, $J=7.8$, 1.4 Hz, 1H), 7.79 (d, $J=7.2$ Hz, 2H), 7.56~7.43 (m, 3H), 7.39 (d, $J=7.6$ Hz, 3H), 6.73 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 164.1, 139.4, 133.3, 133.2, 132.8, 132.6, 131.6, 129.7, 128.8, 127.5, 126.9; ESI-HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 295.0303, found 295.0305.

N-(3-Chlorophenylsulfonyl)benzimidamide (**3g**): 41.3 mg, 70% yield. White solid, m.p. 79~80 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.33 (s, 1H), 7.97 (s, 1H), 7.88 (d, $J=7.2$ Hz, 1H), 7.80 (d, $J=7.2$ Hz, 2H), 7.60~7.47 (m, 2H), 7.43 (t, $J=7.4$ Hz, 3H), 6.64 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.3, 143.8, 134.9, 133.1, 132.9, 132.5, 130.2, 128.9, 127.5, 126.6, 124.6; ESI-HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 295.0303, found 295.0302.

N-(Mesitylsulfonyl)benzimidamide (**3h**): 49.3 mg, 82% yield. White solid, m.p. 90~92 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.17 (s, 1H), 7.76 (d, $J=7.6$ Hz, 2H), 7.49 (t, $J=7.4$ Hz, 1H), 7.39 (t, $J=7.6$ Hz, 2H), 6.92 (s, 2H), 6.40 (s, 1H), 2.71 (s, 6 H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 161.8, 141.6, 138.7, 136.4, 133.6, 132.5, 131.6, 128.8, 127.3, 22.7, 20.9; ESI-HRMS calcd for $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 303.1162, found 303.1166.

N-(Naphthalen-2-ylsulfonyl)benzimidamide (**3i**): 49.7 mg, 80% yield. White solid, m.p. 103~105 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.52 (s, 1H), 8.38 (s, 1H), 7.97 (d, $J=8.4$ Hz, 1H), 7.90 (t, $J=8.4$ Hz, 2H), 7.85 (d, $J=8.0$ Hz, 1H), 7.68 (d, $J=8.0$ Hz, 2H), 7.61~7.51 (m, 2H), 7.13 (d, $J=8.0$ Hz, 2H), 6.74 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 163.1, 143.7, 139.1, 134.7, 132.1, 130.2, 129.4, 129.3, 129.1, 128.5, 127.8, 127.5, 127.3, 127.1, 122.4, 21.5; ESI-HRMS calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 311.0849, found 311.0850.

N-(Quinolin-8-ylsulfonyl)benzimidamide (**3j**): 45.2 mg, 73% yield. White solid, m.p. 107~109 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ : 9.18 (s, 1H), 8.98 (s, 1H), 8.77 (s, 1H), 8.55~8.42 (m, 2H), 8.26 (d, $J=8.0$ Hz, 1H), 7.91~7.71 (m, 3H), 7.70~7.60 (m, 1H), 7.58~7.49 (m, 1H), 7.48~7.38 (m, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ : 164.0, 151.4, 144.0, 139.6, 137.3, 134.3, 133.7, 132.6, 130.4, 129.0, 128.9, 128.2, 126.1, 122.7; ESI-HRMS calcd for $\text{C}_{16}\text{H}_{14}\text{N}_3\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 312.0801, found 312.0803.

4-Methyl-*N*-tosylbenzimidamide (**3k**): 50.7 mg, 88% yield. White solid, m.p. 167~168 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.27 (s, 1H), 7.86 (d, $J=8.0$ Hz, 2H), 7.68 (d, $J=8.0$ Hz, 2H), 7.26 (d, $J=8.0$ Hz, 2H), 7.18 (d, $J=8.0$ Hz, 2H), 6.53 (s, 1H), 2.39 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 162.7, 143.5, 142.9, 139.5, 130.4, 129.4, 129.3, 127.4, 126.4, 21.5; ESI-HRMS calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 289.1005, found 289.1008.

N-(4-Chlorophenylsulfonyl)-4-methylbenzimidamide (**3l**): 46.0 mg, 75% yield. White solid, m.p. 151~152 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.27 (s, 1H), 7.90 (d, *J*=8.4 Hz, 2H), 7.68 (d, *J*=8.4 Hz, 2H), 7.43 (d, *J*=8.8 Hz, 2H), 7.19 (d, *J*=8.0 Hz, 2H), 6.69 (s, 1H), 2.37 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 163.2, 143.9, 140.8, 138.6, 130.0, 129.5, 129.0, 127.9, 127.5, 21.5; ESI-HRMS calcd for C₁₄H₁₄ClN₂O₂S [M+H]⁺ 309.0459, found 309.0460.

4-Methyl-*N*-(naphthalen-2-ylsulfonyl)benzimidamide (**3m**): 50.6 mg, 78% yield. White solid, m.p. 160~162 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.52 (s, 1H), 8.38 (s, 1H), 7.97 (d, *J*=8.4 Hz, 1H), 7.90 (t, *J*=8.4 Hz, 2H), 7.85 (d, *J*=8.0 Hz, 1H), 7.68 (d, *J*=8.0 Hz, 2H), 7.61~7.49 (m, 2H), 7.13 (d, *J*=8.0 Hz, 2H), 6.74 (s, 1H), 2.30 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 163.1, 143.7, 139.1, 134.7, 132.1, 130.2, 129.4, 129.3, 129.1, 128.5, 127.8, 127.5, 127.3, 127.1, 122.4, 21.5; ESI-HRMS calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, found 325.1006.

4-Methyl-*N*-(quinolin-8-ylsulfonyl)benzimidamide (**3n**): 45.0 mg, 69% yield. White solid, m.p. 164~166 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.22 (s, 1H), 8.05 (d, *J*=2.8 Hz, 1H), 7.84 (s, 1H), 7.62~7.50 (m, 2H), 7.34 (d, *J*=8.0 Hz, 1H), 6.88~6.78 (m, 3H), 6.73 (q, *J*=4.0 Hz, 1H), 6.32 (d, *J*=8.0 Hz, 2H), 1.40 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ: 163.8, 151.4, 144.0, 143.0, 139.7, 137.2, 133.6, 131.4, 130.3, 129.4, 129.0, 128.3, 126.1, 122.7, 21.4; ESI-HRMS calcd for C₁₇H₁₆N₃O₂S [M+H]⁺ 326.0958, found 326.0961.

4-Methoxy-*N*-tosylbenzimidamide (**3o**): 48.8 mg, 80% yield. White solid, m.p. 164~166 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.24 (s, 1H), 7.86 (d, *J*=8.0 Hz, 2H), 7.77 (d, *J*=8.8 Hz, 2H), 7.26 (d, *J*=8.0 Hz, 2H), 6.87 (d, *J*=9.2 Hz, 2H), 6.54 (s, 1H), 3.82 (s, 3H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 163.4, 162.2, 142.8, 139.6, 129.4, 129.3, 126.4, 125.2, 114.0, 55.5, 21.5; ESI-HRMS calcd for C₁₅H₁₇N₂O₃S [M+H]⁺ 305.0954, found 305.0958.

N-(4-Chlorophenylsulfonyl)-4-methoxybenzimidamide (**3p**): 46.6 mg, 72% yield. White solid, m.p. 72~74 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.23 (s, 1H), 7.90 (d, *J*=8.4 Hz, 2H), 7.77 (d, *J*=8.8 Hz, 2H), 7.43 (d, *J*=8.4 Hz, 2H), 6.87 (d, *J*=8.8 Hz, 2H), 6.69 (s, 1H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 163.5, 162.7, 141.0, 138.5, 129.5, 129.0, 127.9, 124.8, 114.1, 55.5; ESI-HRMS calcd for C₁₄H₁₄ClN₂O₃S [M+H]⁺ 325.0408, found 325.0409.

4-Chloro-*N*-tosylbenzimidamide (**3q**): 47.5 mg, 77% yield. White solid, m.p. 108~109 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.30 (s, 1H), 7.85 (d, *J*=8.4 Hz, 2H), 7.72 (d, *J*=8.4 Hz, 2H), 7.34 (d, *J*=8.8 Hz, 2H), 7.28 (d, *J*=10.0 Hz, 2H), 6.67 (s, 1H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 161.7, 143.3, 139.1, 131.6, 129.7, 129.5, 129.0, 128.9, 126.4, 21.5; ESI-HRMS calcd for C₁₄H₁₄ClN₂O₂S [M+H]⁺ 309.0459, found 309.0456.

N-Tosylfuran-2-carboximidamide (**3r**): 38.0 mg, 72% yield. White solid, m.p. 145~146 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.19 (s, 1H), 7.85 (d, *J*=8.0 Hz, 2H), 7.51 (s, 1H), 7.26 (d, *J*=8.0 Hz, 2H), 7.22 (d, *J*=3.2 Hz,

1H), 6.73 (s, 1H), 6.53~6.45 (m, 1H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 153.2, 146.5, 146.0, 143.0, 139.3, 129.4, 126.4, 116.9, 113.0, 21.5; ESI-HRMS calcd for C₁₂H₁₃N₂O₃S [M+H]⁺ 265.0641, found 265.0642.

N-Tosyl-2-naphthimidamide (**3s**): 55.0 mg, 85% yield. White solid, m.p. 181~183 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.21 (s, 1H), 8.52 (s, 1H), 8.32 (s, 1H), 8.04 (d, *J*=7.6 Hz, 1H), 8.02~7.96 (m, 2H), 7.93~7.87 (m, 3H), 7.69~7.57 (m, 2H), 7.38 (d, *J*=8.0 Hz, 2H), 2.37 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ: 163.1, 142.9, 140.2, 135.1, 132.4, 131.1, 129.9, 129.5, 129.2, 128.7, 128.5, 128.1, 127.4, 126.6, 124.6, 21.4; ESI-HRMS calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, found 325.1007.

Supporting Information The ¹H NMR and ¹³C NMR spectra of all products, the HRMS spectrum of ¹⁵N-**3a**. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn/>.

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