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I_2催化下通过2-氨基吡啶和*N*-对甲苯磺酰腙氧化偶联反应合成1,2,4-三唑[4,3-*a*]吡啶

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摘要 报道了一种利用*N*-对甲苯磺酰腙和2-氨基吡啶为原料，通过S—N/C—N键裂解和新的C—N键形成，高效合成1,2,4-三唑[4,3-*a*]吡啶类化合物的新路线. 该方法以I_2为催化剂，是一种简单、通用且高效的方法，适应于不同取代基的各类底物，并能以较好的产率得到目标化合物.

关键词 过氧化氢叔丁醇; 2-氨基吡啶; *N*-对甲苯磺酰腙; 环化; 1,2,4-三唑[4,3-*a*]吡啶

Synthesis of 1,2,4-Triazolo[4,3-*a*]pyridines by I_2-Catalyzed Oxidative Coupling of 2-Aminopyridines with *N*-Tosylhydrazones

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Abstract An efficient synthesis of 1,2,4-triazolo[4,3-*a*]pyridines from *N*-tosylhydrazones and 2-aminopyridines via S—N/C—N bond cleavage and new C—N bond formation has been developed. The procedure, using I_2 as the catalyst, is a simple, general, and efficient protocol, which could be applied to various substrates in moderate to good yields.

Keywords *tert*-butyl hydroperoxide (TBHP); 2-aminopyridine; *N*-tosylhydrazone; cyclization; 1,2,4-triazolo[4,3-*a*]pyridine

1 Introduction

As an essential part of ubiquitous fused heterocyclic motifs which can be found in many natural products and pharmaceutically active compounds, triazolopyridines have wide applications in the medicinal chemistry regarding their significant and remarkable biological activities, such as anti-inflammatory, antihypertensive, antiviral, antipsychotic, anticancer, and antibacterial.[1-2] Among large kinds of triazolopyridine derivatives, the 1,2,4-triazolo[4,3-*a*]-pyridine scaffold is widely contained in a range of compounds with diverse pharmaceutical properties, such as against p38a mitogen activated protein kinase, antipsychotic activity in mice, and regulating proinflammatory mediators.[3] Owing to their important applications, the synthesis of the 1,2,4-triazolo[4,3-*a*]pyridines has attracted great attention over the past decades. Traditional methods for the synthesis of triazolopyridines are typically classified into cyclodehydration of acylated 2-hydrazinopyridines, tandem/one-pot reaction of 2-hydrazinopyridines with carboxylic acids/aldehydes/alkenes, oxidative cyclization of 2-pyridylhydrazones, metal-catalyzed direct C—H (hetero)-arylation of preformed 1,2,4-triazolo[4,3-*a*]pyridines and tetrabutylammoniumfluoride (TBAF) mediated cyclization reaction of 2-hydrazinopyridines with isothiocyanates.[4-5] In the above numerous methods, many of these reactions require high temperature, multistep synthesis, dangerous reagents, microwave irradiation and even larger amount of oxidants which may cause environmental issues. Thus, it is highly sought after to develop an efficient, eco-friendly and straightforward strategy to synthesize 1,2,4-triazolo[4,3-*a*]pyridines.

In recent years, molecular iodine or iodine-containing compounds have been considered as an important and effective catalyst to carry out various organic reactions.[6-7] In

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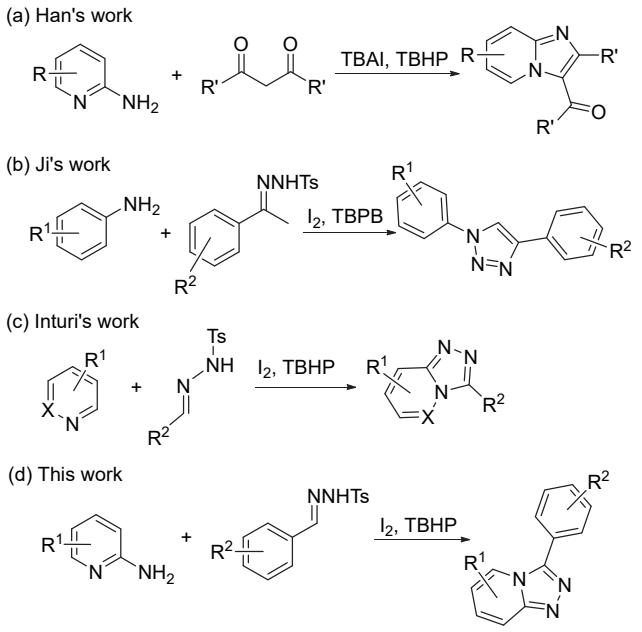
2011, Han and co-workers[8] reported the tetrabutylammonium iodide (TBAI) catalyzed direct oxidative C—N coupling reaction using *tert*-butyl hydroperoxide (TBHP) as the terminal oxidant (Scheme 1, a). Ji's group[9] developed an efficient I_2/*tert*-butyl peroxybenzoate (TBPB) mediated oxidative reaction for the synthesis of 1,2,3-triazoles (Scheme 1, b). More recently, Inturi *et al.*[10] reported I_2-TBHP catalyzed synthesis of 4,3-fused 1,2,4-triazoles from *N*-tosylhydrazones and aromatic *N*-heterocycles via intermolecular formal 1,3-dipolar cycloaddition (Scheme 1, c). Encouraged by graceful strategies above, we demonstrated an efficient synthesis of 1,2,4-triazolo[4,3-*a*]pyridines from *N*-tosylhydrazones and 2-aminopyridines. In this strategy, S—N/C—N bond was cleaved and new C—N bond was formed (Scheme 1, d).

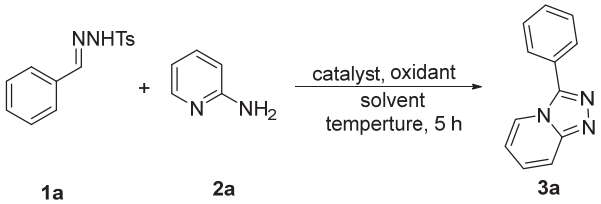


Scheme 1 Synthesis of diverse structural motifs by metal-free strategies

2 Results and discussion

For the initial studies, the reaction was carried out by treating *N*-tosylhydrazone (**1a**) and 2-aminopyridine (**2a**) with I_2 (20 mol%) in the presence of TBHP (2.0 equiv.) and 1,4-dioxane (2 mL) at 80 ℃ for 5 h. To our delight, the desired triazopyridine **3a** was obtained in 74% yield. In order to accelerate the reaction rate and improve the yield, different catalysts, oxidants, solvents and reaction temperature, as well as the amount of reactants were further tested (Table 1). In this preliminary experiment, other iodine-containing catalysts such as *N*-iodo-succininide (NIS), tetrabutylammonium iodide (TBAI), PhI, KI and iodobenzene diacetate (PIDA) were used, and the reaction proceeded less efficiently (Table 1, Entries 2～6). Next, the yield of desired product **3a** could not be improved when the reaction was screened at other oxidants (Table 1, Entries 7～10). The influences of other solvents like *N*,*N*′-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), toluene, PhCl, 1,2-dichloroethane (DCE) and CH_3CN were also examined (Table 1, Entries 11～17). Among different solvents, it was found that 1,4-dioxane was the most suitable solvent for this reaction. Based on the above studied results, the reaction temperature was conducted. It was found that the desired product **3a** was obtained with a lower yield at lower temperature, and the product **3a** was not detected at a higher reaction temperature (Table 1, Entries 19 and 20). Finally, further experiments manifested that the amount of I_2, TBHP, *N*-tosylhydrazone and 2-aminopyridine displayed crucial reactivity for the reaction (Table 1, Entries 18, 21～24). Thus, the optimized conditions for the reaction was established: **1a** (0.22 mmol), **2a** (0.2 mmol), I_2 (5 mol%), TBHP (2.0 equiv.), and 1,4-dioxane (2 mL) at 80 ℃ for 5 h.

Table 1 Optimization of the reaction conditions[a]



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

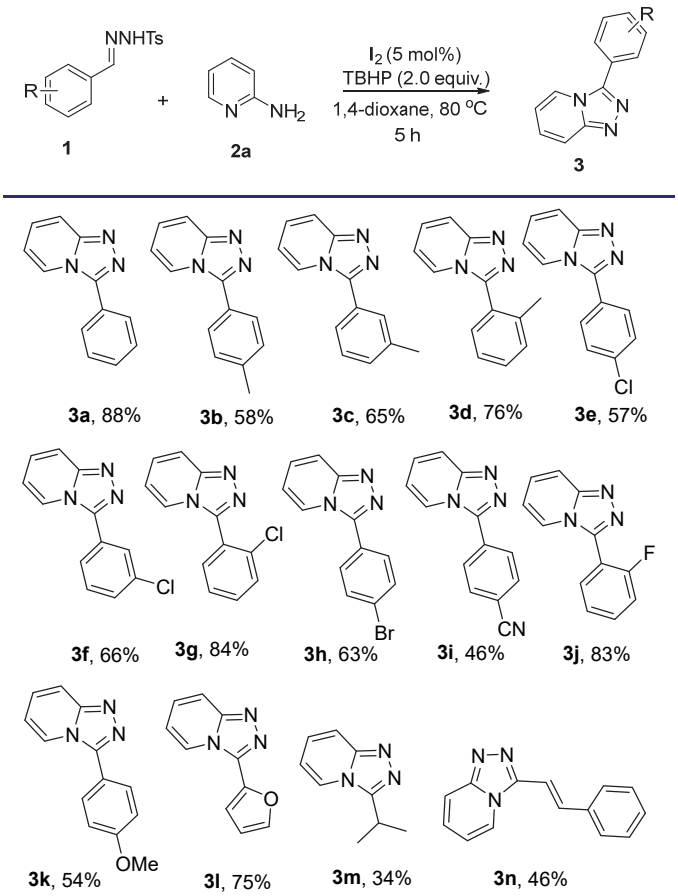
Entry	Catalyst	Oxidant	Solvent	Yield[b]/%
1	I_2	TBHP	1,4-Dioxane	74
2	NIS	TBHP	1,4-Dioxane	Trace
3	TBAI	TBHP	1,4-Dioxane	37
4	PhI	TBHP	1,4-Dioxane	Nd
5	KI	TBHP	1,4-Dioxane	64
6	PIDA	TBHP	1,4-Dioxane	Nd
7	I_2	$K_2S_2O_4$	1,4-Dioxane	Nd
8	I_2	O_2	1,4-Dioxane	Trace
9	I_2	DDQ	1,4-Dioxane	Nd
10	I_2	DTBP	1,4-Dioxane	49
11	I_2	TBHP	DMF	Nd
12	I_2	TBHP	DMSO	Nd
13	I_2	TBHP	DMA	Nd
14	I_2	TBHP	Toluene	Trace
15	I_2	TBHP	PhCl	39
16	I_2	TBHP	DCE	30
17	I_2	TBHP	CH_3CN	46
18[c]	I_2	TBHP	1,4-Dioxane	76
19[c,d]	I_2	TBHP	1,4-Dioxane	30
20[c,e]	I_2	TBHP	1,4-Dioxane	Trace
21[c,f]	I_2	TBHP	1,4-Dioxane	20
22[c,g]	I_2	TBHP	1,4-Dioxane	Nd
23[c,h]	I_2	TBHP	1,4-Dioxane	67
24[c,i]	**I_2**	**TBHP**	**1,4-Dioxane**	**88**

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), catalyst (20 mol%), oxidant (2 equiv.) in solvent (2 mL) under air at 80 ℃ for 5 h. [b] Isolated yields. [c] I_2 (5 mol%). [d] At 60 ℃. [e] At 100 ℃. [f] TBHP (1 equiv.). [g] TBHP (4 equiv.). [h] **1a**∶**2a**=1∶1.1. [i] **1a**∶**2a**=1.1∶1.

With the optimized reaction conditions in hand, we sought to explore the scope of substrate and generality of this reaction. First, the substituent effects of *N*-tosylhydrazones on the reaction were investigated (Table 2).

N-Tosylhydrazones with electron-neutral or electron-donating groups on aryl rings such as methyl and methoxyl all afforded the desired products in good yields. *N*-Tosylhydrazones with electron-withdrawing substituents, such as chloro, fluoro, bromo and even cyano-group, were well tolerated and gave the corresponding products in 46%～83% yields. However, the yield of the desired product by reaction with *N*-tosyl-hydrazone substituted by strong electron withdrawing group (CN) is lower than that of *N*-tosyl-hydrazone substituted by other groups (Cl, F, Br). Based on the yields, it was found that different positions of the aryl ring affect the efficiency weakly (**3b**, **3c**, **3d**). To our delight, a heterocyclic *N*-tosylhydrazone with the furan (**1l**) was also tolerated and afforded the desired 3-(furan-2-yl)[1,2,4]-triazolo[4,3-*a*]pyridine (**3l**) in 75% yield. In addition, *N*-tosylhydrazones derived from aliphatic aldehydes (**1m**) and cinnamaldehyde (**1n**) also underwent the desired reaction to give the corresponding products (**3m**, **3n**) in moderate yields.

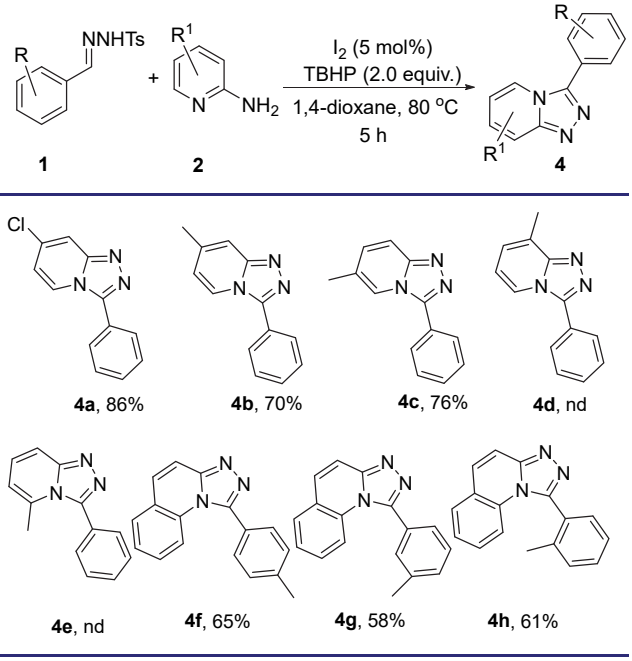
Table 2 Reactions of **2a** with *N*-tosylhydrazones[a]



[a] Reaction conditions: **1** (0.22 mmol), **2a** (0.2 mmol), I_2 (5 mol%), TBHP (2 equiv.) in 1,4-dioxane (2 mL) under air at 80 ℃ for 5 h.

Subsequently, the feasibility of different 2-aminopyridines was investigated, and the results are summarized in Table 3. 2-Aminopyridines bearing halogen substituents such as Cl, also reacted well with *N*-tosylhydrazone to give the triazolopyridines derivatives (**4a**). Substrates with methyl substituents at the 4- and 5- position afforded the corresponding products with excellent yields (**4b**, **4c**). However, substrates with methyl substituents at the 3- and 6-position did not accrue under the present reaction condition which may be due to the steric hindrance effect (**4d**, **4e**). To our delight, reacting 2-aminoquinoline with different *N*-tosylhydrazones gave the desired products (**4f**, **4g**, **4h**) with good yields, possibly because of a favourable electronic influence in quinoline over methyl (**4d**, **4e**).

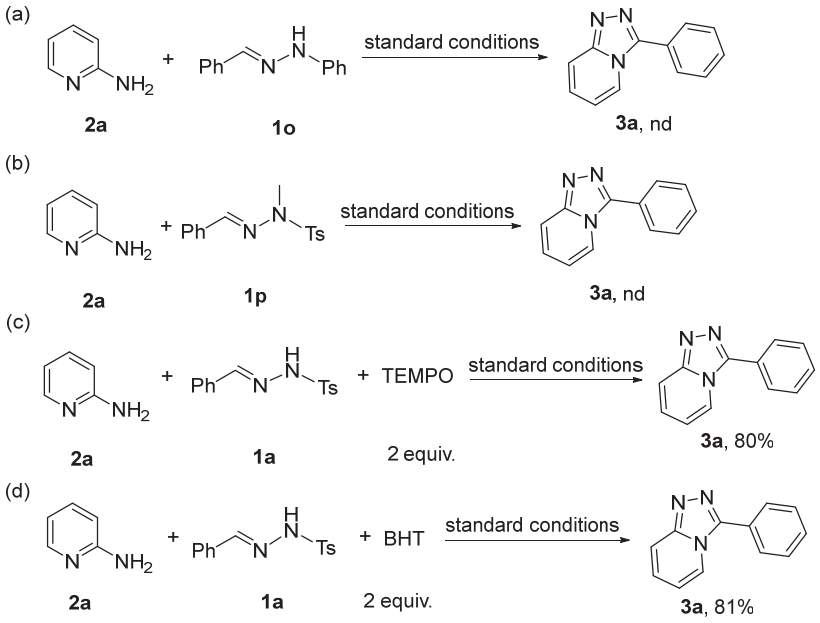
Table 3 Reactions of **2** with *N*-tosylhydrazones[a]



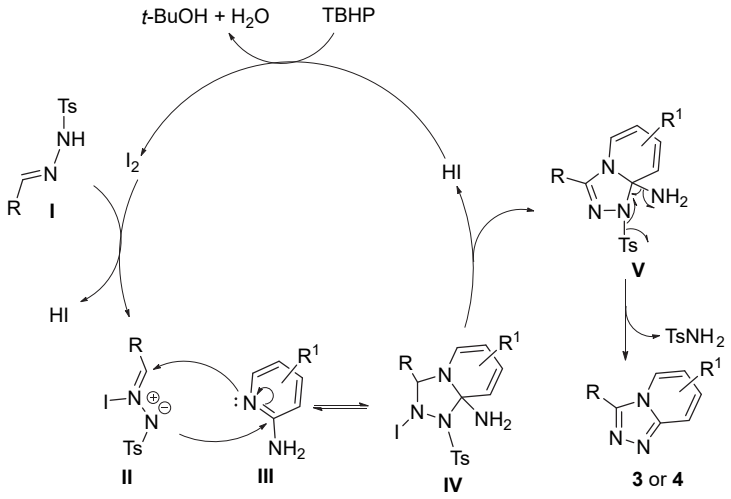
[a] Reaction conditions: **1** (0.22 mmol), **2** (0.2 mmol), I_2 (5 mol%), TBHP (2 equiv.) in 1,4-dioxane (2 mL) under air at 80 ℃ for 5 h.

To understand the reaction mechanism, various experiments were performed (Scheme 2). Firstly, the reaction of **2a** with the bisarylhydrazone (**1o**) did not afford the desired product **3a** (Scheme 2, a). Additionally, when the reaction between *N*-methyl tosylhydrazone (**1p**) and 2-aminopyridine (**2a**) were conducted under the optimized reaction conditions, the corresponding product **3a** was also not found (Scheme 2, b). Finally, when 2 equiv. of radical scavenger (TEMPO or BHT) was added to the reaction system under the optimized reaction conditions, the yield of the desired product **3a** did not change significantly (Scheme 2, c and d).

On the basis of the above results and previous studies,[7a,8-10] a tentative mechanism for the I_2/TBHP mediated oxidative formal [3＋2] cycloaddition toward 1,2,4-triazolo[4,3-*a*]pyridines is proposed (Scheme 3). In the first step, the *N*-tosylhydrazones **I** is converted to an iodosubstituted dipolar complex **II** by elimination of HI in the presence of I_2.[9] Next, the unidirectional intermolecular formal [3＋2]-cycloaddition between the highly reactive species **II** and dipolarophile **III** leads to generation of the fused cycloadduct **IV**.[10] Then intermediate **IV** would form an triazoline in termediate **V** through reductive elimination of HI. At last, to regain the aromaticity, the Ts and the fused



Scheme 2 Control experiments



Scheme 3 Proposed mechanism

ring NH_2 have been triggered off automatically affording the fused triazoles **VI** in excellent yields. Meanwhile, the eliminated HI would be oxidized to I_2 in the presence of TBHP, which completed the catalytic cycle.

3 Conclusions

In conclusion, an efficient method to access 1,2,4-triazolo[4,3-*a*]pyridines via TBHP/I_2-mediated cyclization of *N*-tosylhydrazones with 2-aminopyridines has been developed. This protocol involves the functionalization of the C(sp^2)−H bond, the formation of C—N bonds, and the cleavage of S—N and C—N in one manipulation. This approach affords a generality, high efficiency and useful strategy for the synthesis of 1,2,4-triazolo[4,3-*a*]pyridines with advantages including cheap catalysts, mild conditions and ready availability of the starting materials.

4 Experimental section

4.1 General remarks

^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz in $CDCl_3$ on a superconducting Fourier Nuclear Magnetic Resonance Spectrometer (300 MHz, Agilent, USA). All chemical shifts are given with reference to tetramethylsilane (TMS) as an internal standard. The high-resolution mass spectra (HRMS) were recorded on a liquid chromatography-tandem time of flight mass spectrometry (1260LC-6530TOF, Agilent, USA) using electrospray ionization (ESI). Products were purified by flash chromtogrgraphy on 200～300 mesh silica gel. Unless otherwise noted, commercially reagents were used without

further purification.

4.2 General procedure for the synthesis of **3** and **4**

A sealed reaction tube was charged with 2-aminopyridines (0.2 mmol), *N*-tosylhydrazones (0.22 mmol), I_2 (5 mol%) and TBHP (2.0 equiv.) in 1,4-dioxane (2 mL). The mixture was stirred at 80 ℃ for 5 h under air atmosphere. After that, the solvent was removed under vacuum, and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (V ∶ V = 1 ∶ 1) to afford products **3** and **4**.

3-Phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (**3a**): White solid. m.p. 176～178 ℃ (lit.[10] 175～176 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.29 (d, J=6.8 Hz, 1H), 8.01～7.74 (m, 3H), 7.71～7.47 (m, 3H), 7.35～7.24 (m, 1H), 6.88 (t, J=6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.4, 146.6, 130.1, 129.2, 128.1, 127.0, 126.5, 122.5, 116.6, 114.1.

3-(*p*-Tolyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3b**): Yellow solid. m.p. 158～161 ℃ (lit.[3c] 157 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.27 (d, J=7.0 Hz, 1H), 7.79 (d, J=9.3 Hz, 1H), 7.71 (d, J=8.0 Hz, 2H), 7.38 (d, J=7.9 Hz, 2H), 7.27 (dd, J=9.3, 6.6 Hz, 1H), 6.86 (t, J=6.8 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.3, 146.7, 140.3, 129.8, 127.9, 126.9, 123.5, 122.6, 116.5, 113.9, 21.4.

3-(*m*-Tolyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3c**): Pale yellow solid. m.p. 62～64 ℃ (lit.[4f] 52～53 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.30 (dd, J=7.0, 1.0 Hz, 1H), 7.86～7.74 (m, 1H), 7.72～7.54 (m, 2H), 7.45 (t, J=7.6 Hz, 1H), 7.40～7.21 (m, 2H), 6.95～6.84 (m, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.2, 146.6, 139.0, 130.7, 128.9, 128.7, 127.0, 126.1, 124.7, 122.5, 116.3, 114.0, 21.2.

3-(*o*-Tolyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3d**): White solid. m.p. 138～141 ℃ (lit.[3c] 132～135 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.87～7.75 (m, 2H), 7.51～7.39 (m, 3H), 7.39～7.26 (m, 2H), 6.84 (t, J=7.0 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.7, 146.2, 138.4, 130.9, 130.4, 130.1, 127.0, 126.1, 125.4, 122.6, 116.4, 113.9, 19.7.

3-(4-Chlorophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3e**): Pale yellow solid. m.p. 194～196 ℃ (lit.[5c] 198～199 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.28 (d, J=7.0 Hz, 1H), 7.85～7.76 (m, 3H), 7.55 (d, J=8.4 Hz, 2H), 7.32 (dd, J=9.5, 6.2 Hz, 1H), 6.93 (t, J=6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.3, 145.4, 136.0, 129.3, 129.1, 127.1, 124.8, 122.3, 116.4, 114.4.

3-(3-Chlorophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3f**): Pale yellow solid. m.p. 152～155 ℃ (lit.[4f] 159～161 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.31 (d, J=7.0 Hz, 1H), 7.78 (dd, J=30.5, 6.6 Hz, 3H), 7.59～7.44 (m, 2H), 7.33 (dd, J=8.9, 6.8 Hz, 1H), 6.95 (t, J=6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.5, 145.2, 135.1, 130.5, 130.1, 128.1, 128.0, 127.3, 125.9, 122.3, 116.6, 114.6.

3-(2-Chlorophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3g**): Pale yellow solid. m.p. 126～128 ℃ (lit.[5c] 125～127 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.83 (dd, J=11.7, 8.2 Hz, 2H), 7.68 (dd, J=7.3, 1.4 Hz, 1H), 7.62～7.44 (m, 3H), 7.38～7.30 (m, 1H), 6.90 (t, J=6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.05, 144.78, 133.86, 133.07, 131.89, 129.98, 127.32, 125.67, 123.36, 116.27, 113.76.

3-(4-Bromophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3h**): Pale yellow solid. m.p. 178～181 ℃ (lit.[4f] 198～200 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.27 (d, J=7.1 Hz, 1H), 7.82 (d, J=9.3 Hz, 1H), 7.72 (s, 4H), 7.32 (dd, J=9.2, 7.1, 1H), 6.93 (t, J=6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.5, 145.6, 132.4, 129.4, 127.2, 125.4, 124.4, 122.3, 116.7, 114.5.

4-([1,2,4]Triazolo[4,3-*a*]pyridin-3-yl)benzonitrile (**3i**): Pale yellow solid. m.p. 256～258 ℃ (lit.[5c] 258～260 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.33 (d, J=6.9 Hz, 1H), 8.07～8.00 (m, 2H), 7.95～7.85 (m, 3H), 7.42～7.33 (m, 1H), 6.99 (t, J=6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.0, 145.0, 133.0, 131.0, 128.4, 127.7, 122.2, 118.0, 117.10, 115.1, 113.6.

3-(2-Fluorophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3j**): Pale yellow solid. m.p. 99～102 ℃ (lit.[4d] 108～109 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.02～7.94 (m, 1H), 7.84 (ddd, J=5.1, 2.2, 1.1 Hz, 2H), 7.59 (ddd, J=4.5, 1.8, 1.0 Hz, 1H), 7.43～7.28 (m, 3H), 6.98～6.88 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.2, 157.9, 150.4, 142.7, 132.4 (d, J=8.3 Hz), 132.1 (d, J=2.7 Hz), 127.3, 125.0 (d, J=3.4 Hz), 116.2 (d, J=6.3 Hz), 116.0, 113.9.

3-(4-Methoxyphenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3k**): Pale yellow solid. m.p. 126～129 ℃ (lit.[5c] 123～125 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.24 (d, J=7.1 Hz, 1H), 7.85～7.73 (m, 3H), 7.30～7.26 (m, 1H), 7.13～7.07 (m, 2H), 6.85 (t, J=6.8 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.0, 141.0, 131.5, 129.7, 126.8, 122.6, 118.8, 116.8, 114.7, 114.0, 55.4.

3-(Furan-2-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (**3l**): Brown solid. m.p. 83～86 ℃ (lit.[4d] 92～94 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.73 (d, J=7.0 Hz, 1H), 7.80 (d, J=9.3 Hz, 1H), 7.67 (d, J=1.2 Hz, 1H), 7.35～7.22 (m, 2H), 6.94 (t, J=6.7 Hz, 1H), 6.64 (dd, J=3.4, 1.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.7, 143.4, 142.6, 139.33, 127.3, 124.0, 116.2, 114.4, 111.9, 110.8.

3-Isopropyl-[1,2,4]triazolo[4,3-*a*]pyridine (**3m**):[12] Brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.94 (d, J=7.0 Hz, 1H), 7.76 (d, J=9.3 Hz, 1H), 7.24 (ddd, J=9.3, 6.8, 1.0 Hz, 1H), 6.85 (t, J=6.7 Hz, 1H), 3.39 (dt, J=13.8, 6.9 Hz, 1H), 1.54 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.1, 150.1, 126.5, 121.9, 116.7, 113.4, 25.1, 20.1.

(*E*)-3-Styryl-[1,2,4]triazolo[4,3-*a*]pyridine (**3n**): Pale yellow solid. m.p. 185～187 ℃ (lit.[4d] 185～187 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.17 (d, J=6.8 Hz, 1H), 7.89 (d, J=16.2 Hz, 1H), 7.77 (d, J=9.2 Hz, 1H), 7.59 (d, J=7.1 Hz, 2H), 7.48～7.31 (m, 3H), 7.30～7.21 (m, 1H), 7.16 (d, J=16.2 Hz, 1H), 6.92 (t, J=6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.3, 145.3, 135. 9, 135.4, 129.3, 129.1, 127.2, 127.1, 122.2, 117.0, 114.4, 109.5.

7-Chloro-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (**4a**): Pale yellow solid. m.p. 185～187 ℃ (lit.[5c] 187～189 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.24 (d, J=7.2 Hz, 1H), 7.81～7.75 (m, 3H), 7.62～7.51 (m, 3H), 6.85 (d, J=7.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 133.7, 130.4, 129.3,

128.0, 125.9, 123.0, 116.0, 115.0.

7-Methyl-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (**4b**): Pale yellow solid. m.p. 125～127 ℃ (lit.[12] 126～128 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.75 (d, J=8.3 Hz, 2H), 7.52～7.48 (m, 2H), 7.38 (dd, J=15.0, 7.6 Hz, 4H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.6, 145.6 134.3, 131.5, 129.7, 129.6, 128.8, 128.6, 128.4, 128.2, 21.7.

6-Methyl-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (**4c**): Pale yellow solid. m.p. 150～153 ℃ (lit.[4f] 155～156 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04 (s, 1H), 7.85～7.78 (m, 2H), 7.71 (d, J=9.4 Hz, 1H), 7.61～7.50 (m, 3H), 7.13 (d, J=9.4 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.8, 146.1, 130.4, 129.9, 129.1, 128.0, 126.7, 124.0, 119.4, 115.7, 18.1.

1-(*p*-Tolyl)-[1,2,4]triazolo[4,3-*a*]quinolone (**4f**): Pale yellow solid. m.p. 145～148 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.62 (d, J=7.7 Hz, 1H), 7.53 (d, J=9.5 Hz, 1H), 7.42 (t, J=8.1 Hz, 4H), 7.33～7.12 (m, 4H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.7, 149.1, 140.6, 131.8, 130.8, 129.7, 129.2, 128.8, 127.6, 126.3, 126.0, 124.4, 116.6, 114.9, 21.5; HRMS (ESI) calcd for $C_{17}H_{14}N_3$ $(M+H)^+$ 260.1182, found 260.1179.

1-(*m*-Tolyl)-[1,2,4]triazolo[4,3-*a*]quinolone (**4g**): Pale yellow solid. m.p. 133～136 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.80 (dd, J=7.8, 1.3 Hz, 1H), 7.68 (d, J=9.4 Hz, 1H), 7.57 (dd, J=7.7, 4.6 Hz, 2H), 7.53 (d, J=6.2 Hz, 1H), 7.47 (dt, J=9.3, 4.6 Hz, 4H), 7.40～7.32 (m, 1H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 138.9, 131.8, 131.2, 130.4, 129.7, 129.2, 128.8, 126.8, 126.0, 124.5, 116.7, 114.9, 21.4; HRMS (ESI) calcd for $C_{17}H_{14}N_3$ $(M+H)^+$ 260.1182, found 260.1180.

1-(*o*-Tolyl)-[1,2,4]triazolo[4,3-*a*]quinolone (**4h**): Pale yellow solid. m.p. 142～145 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.80 (d, J=7.6 Hz, 1H), 7.71 (d, J=9.5 Hz, 1H), 7.65～7.49 (m, 3H), 7.45 (t, J=8.3 Hz, 3H), 7.31 (dd, J=7.1, 1.3 Hz, 1H), 7.26 (t, J=6.6 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.46, 148.20, 138.47, 131.85, 130.82, 130.60, 129.69, 129.36, 129.22, 129.17, 126.54, 126.08, 124.33, 115.52, 114.98, 19.57; HRMS (ESI) calcd for $C_{17}H_{14}N_3$ $(M+H)^+$ 260.1182, found 260.1185.

Supporting Information ^{1}H NMR and ^{13}C NMR spectra of compounds **3** and **4**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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(Zhao, C.)

