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腐殖酸作用下 Strecker 反应快速高效合成 α-氨基腈

席 敏 段 超 迟 捷 付 甜 苏小龙 王宏社*
(宝鸡文理学院化学化工学院 陕西省植物化学重点实验室 陕西宝鸡 721013)

摘要 以腐殖酸为催化剂, 在室温无溶剂条件下, 通过醛(酮)、胺和三甲基硅氰(TMSCN)的一锅三组分 Strecker 反应, 绿色高效合成了 α-氨基腈. 该法具有产率高、无需金属催化剂、反应时间短、反应条件温和、操作简便以及催化剂绿色并可重复使用等优点.

关键词 Strecker 反应; 腐殖酸; 羰基化合物; 胺; α-氨基腈

An Efficient and Rapid Synthesis of α-Aminonitriles via Strecker Reaction Catalyzed by Humic Acid

Xi, Min Duan, Chao Chi, Jie Fu, Tian Su, Xiaolong Wang, Hongshe*
(*Shaanxi Key Laboratory for Phytochemistry*, *Department of Chemistry and Chemical Engineering*, *Baoji University of Arts and Sciences*, *Baoji*, *Shaanxi 721013*)

Abstract An efficient one pot three-component Strecker reaction for the green synthesis of α-aminonitriles from carbonyl compounds, amines and trimethylsilyl cyanide (TMSCN) in the presence of a catalytic amount of humic acid catalyst under solvent-free conditions at room temperature has been developed. This methodology has advantages of high yield, no need for metal catalysts, short reaction time, mild reaction conditions, simple operation, green and reusable catalyst.

Keywords Strecker reaction; humic acid; carbonyl compound; amine; α-aminonitrile

α-Aminonitriles are very important intermediates in the preparation of amino acids, 1,2-diamines and a variety of nitrogen containing heterocycles, such as imidazoles or thiadiazoles.[1] Numerous methods describing the preparation of α-aminonitriles have been reported in the literature, such as the oxidative cyanation of secondary or tertiary amines and anodic oxidative cyanation of tertiary amines.[2] The Strecker reaction is one of the most straightforward and efficient methods for the synthesis of α-aminonitriles. Moreover, the asymmetric Strecker reaction is one of the most powerful strategies for the synthesis of chiral α-amino acids, and great endeavors have been devoted to this area and a number of successful protocols have been disclosed.[3] The classical Strecker reaction is generally carried out with hydrogen cyanide (HCN) or potassium cyanide (KCN) in aqueous solution. The drawback is the high toxicity of HCN and KCN and thus limits the scope of this valuable reaction. To overcome this limitation, several modifications of the Strecker reaction have been reported. These modifications use alternative cyanide sources, such as diethyl phosphorocyanidated [$(OEt)_2P(O)CN$],[4] diethyl aluminum cyanide (Et_2AlCN),[5] tributyltin cyanide (Bu_3SnCN),[6] trimethylsilyl cyanide (TMSCN), potassium hexacyanoferrate(II) ($K_4[Fe(CN)_6]$),[7] acetyl cyanide (MeCOCN),[8] acetone cyanohydrin [$(CH_3)_2C(OH)CN$][9] and ethyl cyanoformate [EtOC(O)CN][10] under various reaction conditions. Among these cyanide agents, TMSCN has proven to be relatively safe, easy to handle, highly soluble in organic solvents, and more effective as a cyanide anion source for the nucleophilic addition of imines under mild conditions compared to other cyanating reagents. In recent years, numerous methods have been developed for the synthesis of α-aminonitriles via Strecker reaction using TMSCN as a cyanide source catalyzed by various catalysts, such as MnO-doped Fe_3O_4 NPs,[11] SiO_2,[12] Fe_3O_4@SiO_2 core-shell MNPs,[13] natural halloysite nanotubes,[14] mandelic acid,[15] Fe_3O_4,[16] $CeCl_3$,[17] MCM-41,[18] I_2,[19] polymer,[20] g-C_3N_4-anchored sulfonic acid,[21] ionic liquids,[22] ZnO,[23] Cd-Fe_2O_4@SiO_2@ZrO_2/SO_4^{2-}/Cu/Ni,[24] CMK-5-SO_3H,[25] Fe_3O_4@SiO_2-APTES-TFA,[26] S_mI_3,[27] Fe_3O_4@SiO_2-NH_2-

* Corresponding author. E-mail: hongshewang@126.com
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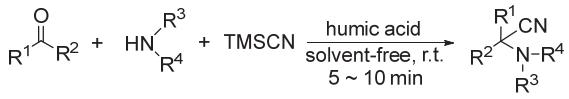
GA,[28] metal organic framework (MOFs)[29] and covalent organic frameworks (COFs).[30] Although each of the above methods has its own merit, most of these methods are associated with certain disadvantages including the use of commercially unavailable metal catalysts, organic solvents, low yields and long reaction times. Therefore, there is a need for an efficient method for the synthesis of *α*-aminonitriles.

Nowadays, one pot multicomponent reactions (MCRs) have received much attention for the synthesis of diverse compounds and contribute to sustainability by simplifying the synthetic route. MCRs combine three or more starting reagents at a time in the same pot to create the target molecule, since there is no need of separating intermediate, which help reduce the energy consumption, solvent waste and reaction time and thus have the advantages of synthetic efficiency, simplicity, atom economy.[31]

Humic acid as a high-molecular weight polymer is insoluble in water and organic solvents. It is a non-toxic, inexpensive and easily available organocatalyst. Organocatalysts are relatively nontoxic, stable to air and water, easily handled, eco-friendly, and readily separable from crude reaction mixture, which makes them a fantastic tool for organic synthesis in pharmaceutical industries and academia. Furthermore, they are inexpensive in comparison to transition metal catalysts and have wide substrate scope too.[32] There are only a few reports in which catalytic activity of humic acid has been described.[33] In view of the efforts toward development of the potential of humic acid as a catalyst, herein, we report a highly efficient, one pot, three-component protocol for the synthesis of *α*-aminonitriles from carbonyl compounds, amines and TMSCN in the presence of a catalytic amount of a recyclable, environmentally friendly and inexpensive humic acid catalyst under solvent-free conditions at room temperature (Scheme 1).



Scheme 1 Humic acid catalyzed one pot three-component synthesis of *α*-aminonitriles

1 Results and Discussion

In order to establish optimum conditions for the synthesis of *α*-aminonitriles in the presence of humic acid, the effect of the amount of catalyst (Table 1) and solvent (Table 2) was examined in the reaction of benzaldehyde, aniline and TMSCN. As for the amount of the catalyst used, it was found that 0.1 g of humic acid is sufficient to promote reaction efficiently (Table 1, Entry 6). The reaction did not proceed with no catalyst in 5 min (Table 1, Entry 1). Decreasing the amount of catalyst resulted in lower yields under the same conditions (Table 1, Entries 2～5). An increase in the amount of catalyst did not show any significant effect on yields (Table 1, Entries 7 and 8). The use of solvents was found to be detrimental to the catalytic efficiency of humic acid. The use of water and organic solvents such as *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), tetrahydrofuran (THF), ethanol, dichloromethane, and toluene resulted in lower yields (Table 2, Entries 1～7). The best result was obtained when the reaction was carried out under solvent-free conditions (Table 2, Entry 8). Solvent-free conditions were found to be conducive to the reaction. The reason is probably that the micro-environment and the higher concentration of reactants in the absence of solvent led to more favourable kinetics than in solution resulting in improved efficiency.[34] Recently, because of the growing concern about the influence of the organic solvent on the environment as well as on the human body, organic reactions under solvent-free conditions have received much attention in view of green methodologies.

Table 1 Effect of catalyst loading on the synthesis of 2-phenyl-2-(phenylamino)acetonitrile[a]

Entry	Catalyst loading/g	Yield[b]/%
1	None	0
2	0.02	63
3	0.04	78
4	0.06	83
5	0.08	91
6	**0.10**	**98**
7	0.12	98
8	0.15	98

[a] Reaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), TMSCN (1.2 mmol), catalyst humic acid at room temperature for 5 min under solvent-free conditions. [b] Isolated yields.

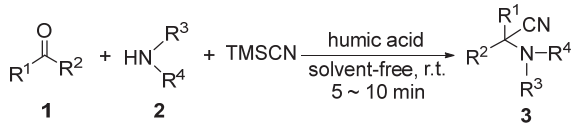
Table 2 Effect of solvent on the synthesis of 2-phenyl-2-(phenylamino)acetonitrile[a]

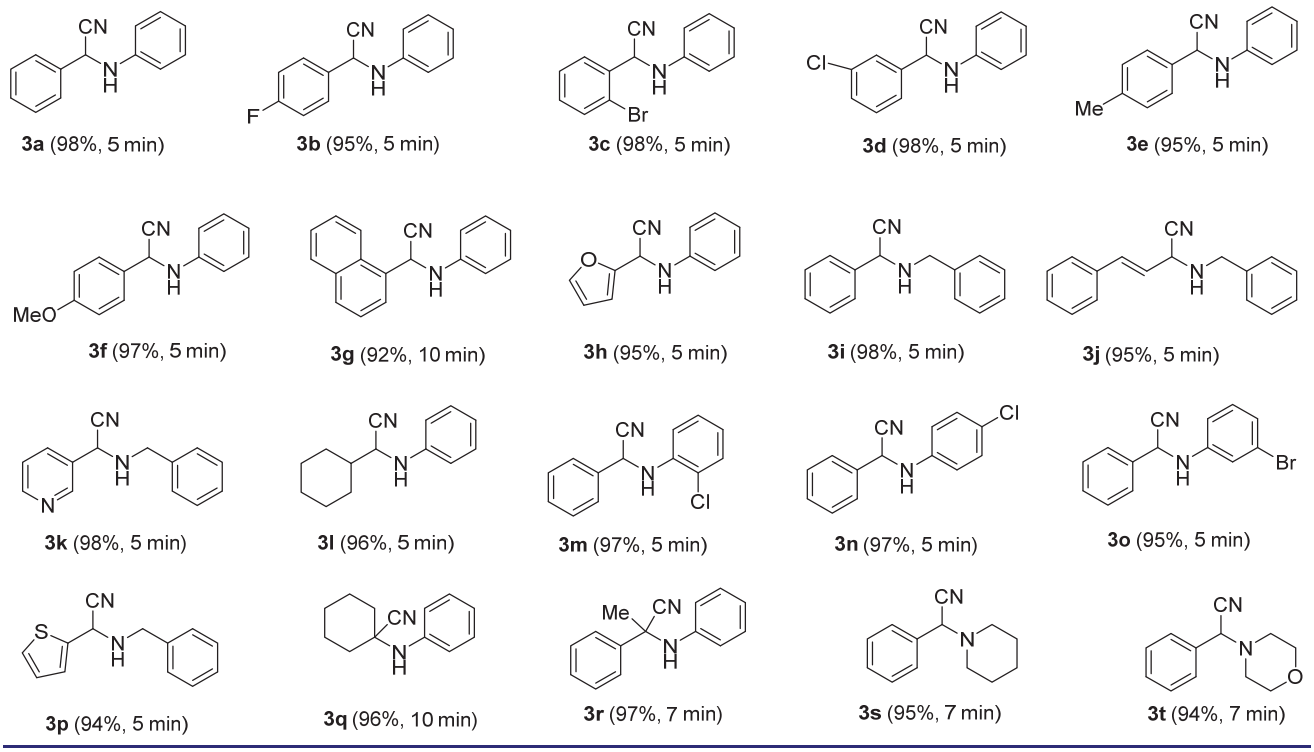
Entry	Solvent	Yield[b]/%
1	Water	89
2	DMF	78
3	DMSO	71
4	THF	88
5	Ethanol	83
6	Toluene	69
7	Dichloromethane	64
8	**Solvent-free**	**98**

[a] Reaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), TMSCN (1.2 mmol), humic acid (0.1 g) at room temperature for 5 min. [b] Isolated yields.

To show the efficiency and applicability of the method, the reaction of various carbonyl compounds, amines, and TMSCN in the presence of humic acid under solvent-free conditions at room temperature was investigated. As shown in Table 3, the reaction proceeded equally well irrespective of the nature of the carbonyl compounds (aliphatic, aromatic, heteroaromatic) or amines (aliphatic, heterocyclic, and aromatic) to afford the corresponding products in excellent yields (92%～98%) in short reaction time (5～10 min). The catalytic system worked well with acid sensitive heteroaromatic aldehyde (Table 3, **3h** and **3p**), *α*,*β*-unsaturated

Table 3 Synthesis of α-aminonitriles catalyzed by humic acid[a,b]





[a] Reaction conditions: carbonyl compounds (1 mmol), amines (1 mmol), TMSCN (1.2 mmol), humic acid (0.1 g) at room temperature under solvent-free conditions. [b] Isolated yields.

aldehyde (Table 3, **3j**). Aromatic primary amines, benzyl amine, heterocyclic amines such as piperidine and morpholine (Table 3, **3s** and **3t**) could effectively undergo Strecker reaction with carbonyl compounds and TMSCN to give the corresponding products in excellent yields. For 1-naphthaldehyde (Table 3, **3g**), relatively slower reaction rate was observed. Aliphatic and aromatic ketones such as cyclohexanone and acetophenone (Table 3, **3q** and **3r**) also afforded the desired products in high yields. However, the reaction of electron-rich 4-methoxyacetophenone with electron-poor 4-nitroaniline and TMSCN was found to be unreactive under the optimized conditions, and no product formation was observed. Also, the attempts to facilitate the Strecker reaction by raising the reaction temperature and increasing the amount of the catalyst remained unsuccessful. The reason is that the reaction of ketone containing electron-donating group and amine containing electron-withdrawing group in the aromatic rings inhibits the nucleophilic attack of the amine on the carbonyl group of the ketone to produce the corresponding imine.

Furthermore, the present route to α-aminonitriles was successfully applied to a large scale of reaction. For instance, the reaction of benzaldehyde (10.6 g, 0.1 mol), aniline (9.3 g, 0.1 mol) and TMSCN (11.9 g, 0.12 mol) promoted by humic acid (10 g) provided the desired product 2-phenyl-2-(phenylamino)acetonitrile (**3a**) in 97% yield.

The reusability of the catalyst is one of the most important benefits and makes it useful for commercial applications. Thus, the reusability of the catalyst humic acid was investigated. The catalyst was easily reused by filtration after completion of the reaction. The recycled catalyst has been examined in the next run. Five consecutive experiments in the synthesis of **3a** were performed to demonstrate the stability and reusability of humic acid catalyst. It was also noteworthy that the humic acid catalyst was successfully recycled without any significant loss of activity under the optimized reaction conditions (Table 4).

Table 4 Reusability of the catalyst humic acid[a]

Run	Yield[b]/%
1	98
2	98
3	98
4	98
5	97

[a] Reaction conditions: benzaldehyde ((1 mmol), aniline ((1 mmol), TMSCN (1.2 mmol), humic acid (0.1 g) at room temperature for 5 min under solvent-free conditions. [b] Isolated yields.

In comparison with other catalysts reported in the literature for the synthesis of **3a**, humic acid shows more catalytic

activity than most of the other catalysts in terms of higher yield and shorter reaction time (Table 5). In addition, humic acid is a commercially available catalyst.

Humic acid is an acidic catalyst owing to the presence of abundant carboxyl and phenolic hydroxyl groups in the structure of it. A plausible mechanism may follow a two-step pathway. In the first step, humic acid acts as a protic acid to facilitate formation of the corresponding imine from the condensation of amine and carbonyl compound. In the subsequent step, the imine is further activated due to the presence of humic acid, to form a more electrophilic C=N intermediate. As a result, an attack of TMSCN to the imine carbon can take place and thus the corresponding *α*-aminonitriles is formed via hydrolysis in water. The active site on the humic acid represented as COOH is considered in the mechanism (Scheme 2).

2 Conclusions

In summary, humic acid catalyst has been demonstrated to be an efficient, mild, safe and recoverable catalyst for one pot synthesis of *α*-aminonitriles in high yields under solvent-free conditions at room temperature. This environmentally friendly method to synthesize *α*-aminonitriles holds promising potential for future applications in both academic and industrial research.

3 Experimental section

3.1 General information

Humic acid and other chemicals were all purchased from Aladdin Reagent Company and used as received unless mentioned otherwise. Melting points were determined on an XT4A electrothermal apparatus equipped with a microscope and are uncorrected. NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$. High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer.

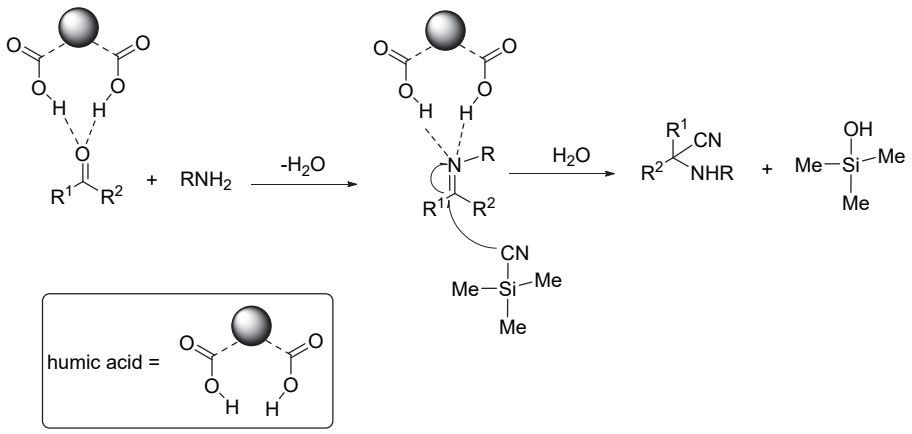
3.2 General procedure for the synthesis of *α*-aminonitriles

A mixture of carbonyl compound (1 mmol), amine (1 mmol), TMSCN (1.2 mmol) and humic acid (0.1 g) was stirred at room temperature. The completion of the reaction was monitored by thin layer chromatography (TLC). After completion of the reaction, ethyl acetate (15 mL) was added and the reaction mixture was then filtered to separate out the catalyst, which is not soluble in ethyl acetate. The catalyst filtered was washed with ethanol and reused. The filtrate was collected, the solvent was removed under reduced pressure and the product was purified by column chromatography over silica gel with hexane-ethyl acetate (V∶V=7∶1) as eluent to afford the pure product. All the products

Table 5 Comparison of various catalysts used in the synthesis of **3a** from benzaldehyde, aniline and TMSCN

Entry	Conditions	Yield/%	Reference
1[a]	Mitsunobu's reagent (100 mol%), solvent-free, r.t., 20 min	98	[35]
2	Fe_3O_4 (10 mol%), solvent-free, r.t., 20 min	95	[16]
3	$TiCl_3$•$4H_2O$ (1 mol%), solvent-free, r.t., 15 min	94	[36]
4	SO_4^{2-}/ZrO_2 (0.1 g/mmol), THF, r.t., 90 min	93	[37]
5[a]	I_2 (10 mol%), CH_3CN, r.t., 1 h	94	[19]
6	Fe_3O_4@SiO_2 core-shell MNP (1 mg/mmol), solvent-free, 50 ℃, 30 min	87	[13]
7	Fe_3O_4@cellulose-OSO_3H (0.04 g/mmol), EtOH, r.t., 15 min	87	[38]
8	Cd(II)-MOF (3 mol%), solvent-free, r.t., 6 h	91	[29f]
9	SmI_3 (10 mol%), THF, r.t., 30 min	98	[27]
10[a]	Humic acid (0.1 g/mmol), solvent-free, r.t., 5 min	98	This work

[a] Commercially available metal-free catalyst.



Scheme 2 Plausible mechanism for the synthesis of *α*-aminonitriles catalyzed by humic acid

are known compounds and the spectral data and melting points were in agreement with those reported in the literature.

2-Phenyl-2-(phenylamino)acetonitrile (**3a**): Brown solid. m.p. 77～79 ℃ (lit.[22] 78～80 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63～7.56 (m, 2H), 7.52～7.43 (m, 3H), 7.30～7.26 (m, 2H), 6.94～6.86 (m, 1H), 6.83～6.77 (m, 2H), 5.46 (s, 1H), 4.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.83, 134.16, 129.73, 129.75, 129.53, 127.44, 120.46, 118.36, 114.38, 50.49; HRMS calcd for $C_{14}H_{13}N_2$ $[M+H]^+$ 209.1079, found 209.1075.

2-(4-Fluorophenyl)-2-(phenylamino)acetonitrile (**3b**):[16] White solid. m.p. 98～100 ℃ (lit.[16] 98～100 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45～7.43 (m, 2H), 7.16～7.14 (m, 2H), 7.03～6.96 (m, 2H), 6.82～6.77 (m, 1H), 6.65 (d, J=7.8 Hz, 2H), 5.27～5.29 (m, 1H), 4.05 (d, J=8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.23, 162.25, 144.45, 129.68, 129.19, 120.55, 118.04, 116.47, 114.24, 49.65; HRMS calcd for $C_{14}H_{12}FN_2$ $[M+H]^+$ 227.0985, found 227.0981.

2-(2-Bromophenyl)-2-(phenylamino)acetonitrile (**3c**):[27] White solid. m.p. 77～79 ℃ (lit.[27] 76～78 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J=7.7 Hz, 1H), 7.55 (d, J=8.0 Hz, 1H), 7.28 (t, J=7.6 Hz, 1H), 7.17～7.15 (m, 3H), 6.83～6.77 (m, 1H), 6.65 (d, J=8.1 Hz, 2H), 5.58 (s, 1H), 3.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.66, 133.82, 133.41, 131.21, 129.59, 129.28, 128.46, 123.62, 120.46, 117.90, 114.33, 50.48; HRMS calcd for $C_{14}H_{12}BrN_2$ $[M+H]^+$ 287.0184, found 287.0188.

2-(3-Chlorophenyl)-2-(phenylamino)acetonitrile (**3d**): Brown solid. m.p. 73～75 ℃ (lit.[13] 74～76 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (s, 1H), 7.36 (d, J=7.8 Hz, 1H), 7.33～7.20 (m, 2H), 7.13 (t, J=7.6 Hz, 2H), 6.83 (t, J=7.6 Hz, 1H), 6.66 (d, J=7.6 Hz, 2H), 5.27 (s, 1H), 4.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.37, 135.83, 135.36, 130.64, 129.83, 129.66, 127.48, 125.41, 120.63, 117.74, 114.34, 49.72; HRMS calcd for $C_{14}H_{12}ClN_2$ $[M+H]^+$ 243.0689, found 243.0686.

2-(Phenylamino)-2-(*p*-tolyl)acetonitrile (**3e**): White solid. m.p. 75～76 ℃ (lit.[19] 76～78 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, J=7.8 Hz, 2H), 7.15～7.10 (m, 4H), 6.82～6.74 (m, 1H), 6.63 (d, J=7.8 Hz, 2H), 5.23 (s, 1H), 3.91 (s, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.75, 139.61, 131.06, 130.04, 129.63, 127.25, 120.26, 118.45, 114.17, 50.04, 21.36; HRMS calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1235, found 223.1230.

2-(4-Methoxyphenyl)-2-(phenylamino)acetonitrile (**3f**): Yellow solid. m.p. 75～76 ℃ (lit.[20] 74～75 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, J=8.6 Hz, 2H), 7.27～7.23 (m, 2H), 6.95 (d, J=8.6 Hz, 2H), 6.93～6.85 (m, 1H), 6.74 (d, J=8.6 Hz, 2H), 5.34～5.31 (m, 1H), 4.03～3.96 (m, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.44, 144.77, 129.64, 128.77, 125.91, 120.11, 118.54, 114.63, 114.12, 55.49, 49.55; HRMS calcd for $C_{15}H_{15}N_2O$ $[M+H]^+$ 239.1184, found 239.1178.

2-(Naphthalen-1-yl)-2-(phenylamino)acetonitrile (**3g**): White solid. m.p. 83～85 ℃ (lit.[23] 82～84 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75～7.70 (m, 4H), 7.41～7.34 (m, 3H), 7.17 (t, J=7.6 Hz, 2H), 6.76 (t, J=7.6 Hz, 1H), 6.63 (d, J=8.2 Hz, 2H), 5.77 (d, J=8.2 Hz, 1H), 3.95 (d, J=7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 1144.86, 134.09, 130.81, 130.25, 129.81, 129.25, 129.07, 127.53, 126.72, 126.40, 125.37, 122.95, 120.24, 118.46, 113.77, 48.37; HRMS calcd for $C_{18}H_{15}N_2$ $[M+H]^+$ 259.1235, found 259.1230.

2-(Furan-2-yl)-2-(phenylamino)acetonitrile (**3h**): Brown solid. m.p. 62～64 ℃ (lit.[17] 63～65 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (s, 1H), 7.24～7.17 (m, 2H), 6.86～6.85 (m, 1H), 6.73 (d, J=7.8 Hz, 2H), 6.51 (d, J=3.6 Hz, 1H), 6.36～6.33 (m, 1H), 5.41 (s, 1H), 4.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.07, 144.13, 129.67, 120.70, 116.68, 114.61, 114.48, 111.11, 109.82, 44.38; HRMS calcd for $C_{12}H_{11}N_2O$ $[M+H]^+$ 199.0871, found 199.0875.

2-(Benzylamino)-2-phenylacetonitrile (**3i**):[22] Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, J=7.9 Hz, 2H), 7.43～7.41 (m, 4H), 7.37～7.33 (m, 3H), 7.31～7.27 (m, 1H), 4.74 (s, 1H), 4.06 (d, J=13.6 Hz, 1H), 3.95 (d, J=13.6 Hz, 1H), 1.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.21, 134.83, 129.17, 129.02, 128.71, 128.54, 127.76, 127.49, 118.84, 53.51, 51.38; HRMS calcd for $C_{14}H_{15}N_2$ $[M+H]^+$ 223.1333, found 223.1338.

2-(Benzylamino)-4-phenylbut-3-enenitrile (**3j**):[14] Yellow solid. m.p. 116～118 ℃ (lit.[14] 116～118 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44～7.31 (m, 10H), 6.95 (d, J=16.6, 1H), 6.24 (d, J=16.6 Hz, 1H), 4.43 (d, J=5.8 Hz, 1H), 4.07 (d, J=12.8 Hz, 1H), 3.90 (d, J=12.8 Hz, 1H) 1.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.29, 135.42, 134.35, 128.91, 128.85, 128.67, 128.23, 127.85, 127.08, 122.53, 118.38, 51.44, 51.35; HRMS calcd for $C_{17}H_{17}N_2$ $[M+H]^+$ 249.3265, found 249.3269.

2-(Benzylamino)-2-(pyridin-3-yl)acetonitrile (**3k**):[16] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (d, J=2.6 Hz, 1H), 8.62 (d, J=4.8 Hz, 1H), 7.85 (d, J=8.0 Hz, 1H), 7.44～7.35 (m, 2H), 7.35～7.31 (m, 3H), 7.29～7.24 (m, 1H), 4.76 (s, 1H), 4.03 (d, J=13.0 Hz, 1H), 3.92 (d, J=13.0 Hz, 1H), 2.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.49, 148.82, 137.74, 135.08, 130.72, 128.83, 128.56, 127.96, 123.73, 117.84, 51.55, 51.34; HRMS calcd for $C_{14}H_{14}N_3$ $[M+H]^+$ 224.2826, found 224.2822.

2-Cyclohexyl-2-(phenylamino)acetonitrile (**3l**):[37] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.17 (t, J=7.5 Hz, 2H), 6.76 (t, J=7.6 Hz, 1H), 6.64 (d, J=7.6 Hz, 2H), 3.95 (d, J=6.8 Hz, 1H), 3.63 (s, 1H), 1.90～1.84 (m, 2H), 1.73～1.61 (m, 4H), 1.26～1.08 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.31, 129.59, 119.90, 119.01, 114.09, 51.82, 40.78, 29.73, 29.03, 26.01, 25.69, 25.58; HRMS calcd for $C_{14}H_{19}N_2$ $[M+H]^+$ 215.1548, found 215.1543.

2-((2-Chlorophenyl)amino)-2-phenylacetonitrile (**3m**):[36] Brown solid. m.p. 82～84 ℃ (lit.[36] 81～83 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, J=7.6 Hz, 2H), 7.34 (d, J=6.8 Hz, 3H), 7.24 (d, J=7.6 Hz, 1H), 7.13 (t, J=7.8 Hz, 1H), 6.77～6.72 (m, 2H), 5.34 (d, J=7.8 Hz, 1H), 4.66 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.79, 133.43, 129.81, 129.73, 129.49, 128.11, 127.18, 120.49,

120.32, 117.77, 112.79, 49.73; HRMS calcd for $C_{14}H_{12}ClN_2$ $[M+H]^+$ 243.0689, found 243.0683.

2-((4-Chlorophenyl)amino)-2-phenylacetonitrile (**3n**): Brown solid. m.p. 69～71 ℃ (lit.[26] 70～72 ℃); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45～7.43 (m, 2H), 7.35 (d, J=4.2 Hz, 3H), 7.11 (d, J=8.4 Hz, 2H), 6.58 (d, J=8.5 Hz, 2H), 5.27 (d, J=7.3 Hz, 1H), 4.08 (d, J=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.28, 133.61, 129.69, 129.58, 129.51, 127.29, 125.14, 118.11, 115.48, 50.31; HRMS calcd for $C_{14}H_{12}ClN_2$ $[M+H]^+$ 243.0689, found 243.0686.

2-((3-Bromophenyl)amino)-2-phenylacetonitrile (**3o**): White solid. m.p. 112～114 ℃ (lit.[23] 111～113 ℃); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.59～7.57 (m, 2H), 7.48～7.45 (m, 3H), 7.13～7.12 (m, 1H), 7.04 (d, J=7.9 Hz, 1H), 6.91～6.90 (m, 1H), 6.71～6.67 (m, 1H), 5.38 (d, J=8.0 Hz, 1H), 4.17 (d, J=7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.03, 133.51, 131.02, 129.79, 129.53, 127.28, 123.50, 123.21, 117.88, 117.13, 112.69, 50.01; HRMS calcd for $C_{14}H_{12}BrN_2$ $[M+H]^+$ 287.0184, found 287.0190.

2-(Benzylamino)-2-(thiophen-2-yl)acetonitrile (**3p**):[22] Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46～7.21 (m, 7H), 7.03 (dd, J=5.3 Hz, J=3.6 Hz, 1H), 4.96 (d, J=1.6 Hz, 1H), 4.06 (d, J=12.8 Hz, 1H), 3.98 (d, J=12.8 Hz, 1H), 2.11 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.29, 137.91, 128.83, 128.48, 127.83, 127.02, 126.88, 126.53, 118.18, 51.07, 49.39; HRMS calcd for $C_{13}H_{13}N_2S$ $[M+H]^+$ 229.3243, found 229.3248.

1-(Phenylamino)cyclohexanecarbonitrile (**3q**):[17] Brown oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.25～1.36 (m, 6H), 1.60～1.81 (m, 2H), 2.31～2.40 (m, 2H), 3.25 (brs, 1H), 6.90～6.93 (m, 3H), 7.25～7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.52, 129.25, 121.15, 120.63, 117.61, 54.41, 36.67, 24.91, 22.23; HRMS calcd for $C_{13}H_{17}N_2$ $[M+H]^+$ 201.2861, found 201.2865.

2-Phenyl-2-(phenylamino)propanenitrile (**3r**):[21] Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.95 (s, 3H), 4.34 (brs, 1H), 6.56 (d, J=6.8 Hz, 2H), 6.82 (t, J=7.6 Hz, 1H), 7.14 (t, J=7.6 Hz, 2H), 7.39～7.43 (m, 3H), 7.61～7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.45, 139.88, 129.26, 129.04, 128.61, 124.89, 120.72, 119.99, 115.77, 57.13, 33.41; HRMS calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.2916, found 223.2911.

2-Phenyl-2-(piperidin-1-yl)acetonitrile (**3s**):[26] Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.56～7.52 (m, 2H), 7.41～7.30 (m, 3H), 4.80 (s, 1H), 2.64～2.47 (m, 4H), 1.63～1.38 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.73, 128.85, 128.87, 127.98, 115.78, 63.19, 51.11, 25.94, 24.16; HRMS calcd for $C_{13}H_{17}N_2$ $[M+H]^+$ 201.1446, found 201.1449.

2-Morpholino-2-phenylacetonitrile (**3t**):[20] White solid. m.p. 71～72 ℃ (lit.[20] 72～73 ℃); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53～7.50 (m, 2H), 7.41～7.36 (m, 3H), 4.80 (s, 1H), 3.75～3.67 (m, 4H), 2.74～2.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 132.83, 129.34, 129.17, 128.08, 115.52, 66.64, 62.76, 50.38; HRMS calcd for $C_{12}H_{15}N_2O$ $[M+H]^+$ 203.1186, found 203.1183.

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

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(Zhao, C.)

