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One-Pot Base-Mediated Synthesis of Functionalized Aza-Fused Polycyclic Quinoline Derivatives

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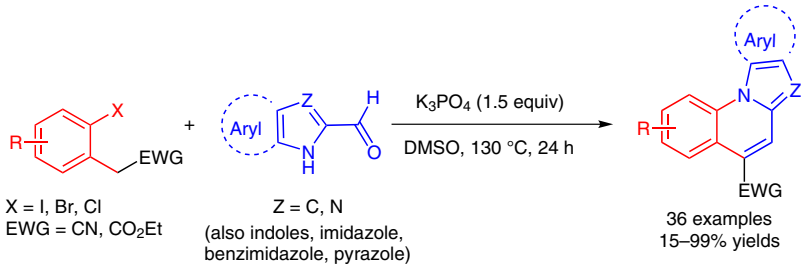

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Abstract A new one-pot protocol has been developed for the facile and efficient synthesis of aza-fused polycyclic quinolines (e.g., pyrrolo[1,2-*a*]quinolines) by the base-catalyzed reaction of 2-formylpyrroles and 2-halophenylacetonitriles. This reaction proceeded under transition metal-free conditions and showed high functional group tolerance, with the desired products being formed in good yields.

Key words one-pot, base-catalyzed, transition metal free, aza-fused polycyclic quinolones, pyrrolo[1,2-*a*]quinolines

Aza-fused polycyclic quinoline ring systems can be found in several natural products and synthetic heterocyclic compounds, and compounds belonging to this structural class have been reported to exhibit a wide range of biological activities.[1] For example, pyrrolo[1,2-*a*]quinoline derivatives possess a broad range of medicinal properties, including antimicrobial (**A**),[2] antileukemic (**B**),[3] antibacterial (**C**),[4] and human recombinant NK1 receptor ligand (**D**)[5] activities (Figure 1). Furthermore, imidazo[1,2-*a*]quinoline derivatives have been shown to play important roles as topoisomerase II inhibitors and inducers of strong G2/M cell cycle arrest (**E**),[6] as well as being used as clinical antiallergic reagents (**F**).[7]

Since Roberts and Gates[8] reported the first synthesis of pyrrolo[1,2-*a*]quinoline derivatives via the thermal and acid-catalyzed cyclization of 1-(2-quinoly1)propane-2,3-diol, several other synthetic methods have been developed for the construction of these interesting compounds. For instance, Zamola et al.[6] described the synthesis of benzimidazo[1,2-*a*]quinolines via a photochemical dehydrocyclization reaction, whereas Klumpp[9] reported the development of a superelectrophilic cyclization method for the construction of aza-polycyclic aromatic compounds. Several other synthetic protocols have also been developed to provide access to aza-fused quinolines using transition-metal catalysts,[10] such as palladium, platinum, and gold. Furthermore, copper-catalyzed Ullmann-type coupling have been explored extensively in recent years and widely used for the formation of diversified heterocyclic compounds.[11] For example, Ding[12] reported the synthesis of benzimidazo[1,2-*a*]quinolines following this strategy. However, the use of these methods has been limited by their requirement for expensive catalysts and ligands, multistep syntheses, or the generation of waste products.

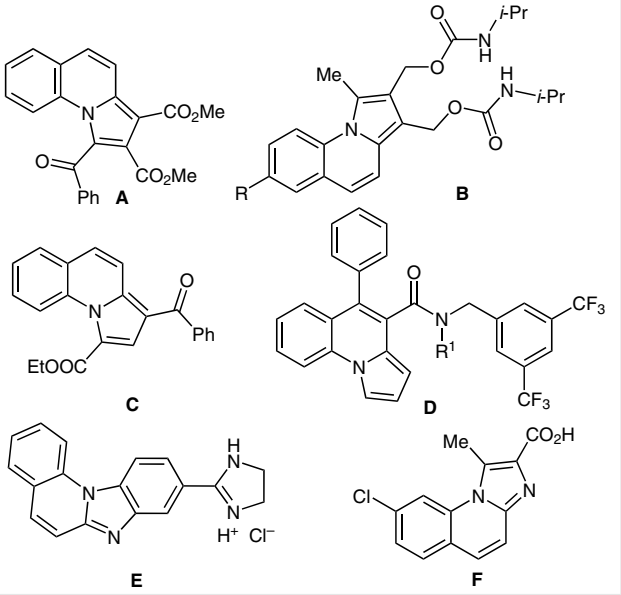
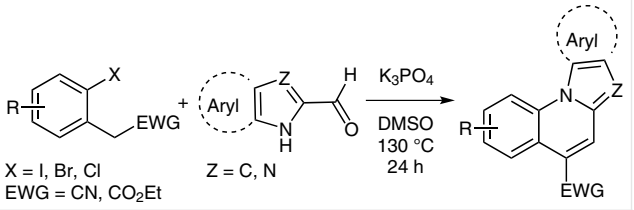


Figure 1 Some important aza-fused polycyclic quinoline derivatives

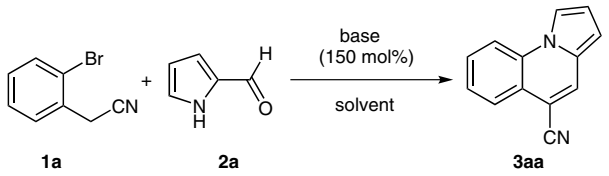
Significant progress has recently been made in the development of metal-free transformations for the formation of C–N bonds.[13] For example, the groups of Yus[14] and Ramón [15] have developed new methods for the arylation of different aromatic heterocycles under strongly basic conditions without the need for a transition metal catalyst. Furthermore, Heo et al.[16] recently reported the transition-metal-free synthesis of a series of dibenzo[*b*,*f*]oxepine-10-carbonitrile derivatives via the formation of an intramolecular C–O bond between 2-halobenzaldehydes and (2-hydroxyphenyl)acetonitriles in the presence of Cs_2CO_3. Herein, we report the development of a one-pot, base-mediated process for the synthesis of pyrrolo[1,2-*a*]quinolines from 2-formylpyrrole derivatives and various 2-halophenylacetonitriles (Scheme 1).



Scheme 1 Reaction of 2-formylpyrroles with 2-halophenylacetonitriles to give pyrrolo[1,2-*a*]quinolines

The reaction between 2-bromophenylacetonitrile (**1a**) and 1*H*-pyrrole-2-carbaldehyde (**2a**) was selected as a model reaction to identify the optimum conditions for the transformation. All of the optimization reactions were carried out in DMSO at 130 °C using a variety of different bases, and the results are shown in Table 1. The use of strong bases such as KOH and NaOH failed to provide any of the desired product (Table 1, entries 1 and 2). Pleasingly, the use of potassium *tert*-butoxide afforded the desired product **3aa**, albeit in a low yield of 13% (entry 3). The yield of the **3aa** was improved dramatically to 68% when Cs_2CO_3 (150 mol%) was used as the base in DMSO at 130 °C (entry 4). The use of potassium phosphate led to a further increase in the yield of **3aa** to 86% (entry 6). Attempts to increase the amount of potassium phosphate added to the reaction, however, were unsuccessful, with the yield of **3aa** being reduced to 70% (entry 7). A significant reduction in the yield of **3aa** was also observed when the reaction was conducted in the presence of a stoichiometric amount of potassium phosphate (entry 8). Moreover, further reducing the charge of potassium phosphate to 50 mol% resulted in a yield of <10% after an extended reaction time of one day at 130 °C (entry 9). Several other solvents were also screened against this reaction, including THF, DMF, toluene, and 1,4-dioxane, but they failed to provide better yields than DMSO (entries 10–14). Decreasing the temperature to 110 °C also led to a decrease in the yield of **3aa** to 72% (entry 15). Furthermore, increasing the temperature failed to provide any improvement in the yield of the product (entry 16). A further increase in the amount of 1*H*-pyrrole-2-carbaldehyde to 1 mmol provided the expected product in 84% yield (entry 17). Finally, the reaction failed in the presence of air (entry 18).

Table 1 Optimization of the Reaction Conditions[a]



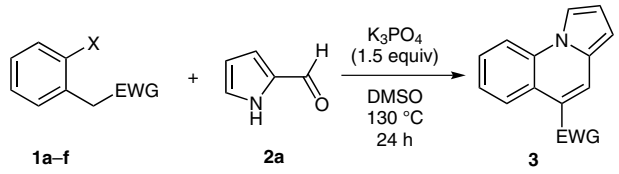
1a **2a** **3aa**

Entry	Solvent	Base	Temp (°C)	Time (h)	Yield (%)[b]
1	DMSO	NaOH	130	24	0
2	DMSO	KOH	130	24	0
3	DMSO	KO*t*-Bu	130	24	13
4	DMSO	Cs_2CO_3	130	24	68
5	DMSO	K_2CO_3	130	24	64
6	**DMSO**	**K_3PO_4**	**130**	**24**	**86**
7	DMSO	K_3PO_4	130	24	70[c]
8	DMSO	K_3PO_4	130	24	43[d]
9	DMSO	K_3PO_4	130	24	<10[e]
10	THF	K_3PO_4	130	24	27
11	DMF	K_3PO_4	130	24	34
12	toluene	K_3PO_4	130	24	36
13	1,4-dioxane	K_3PO_4	130	24	<5
14	MeCN	K_3PO_4	130	24	55
15	DMSO	K_3PO_4	110	24	72
16	DMSO	K_3PO_4	140	24	85
17	DMSO	K_3PO_4	130	24	84[f]
18	DMSO	K_3PO_4	130	24	0[g]

[a] Reaction conditions: 2-bromophenylacetonitrile (**1a**; 0.2 mmol), 1*H*-pyrrole-2-carbaldehyde (**2a**; 0.2 mmol), and base (0.3 mmol) in solvent (2.0 mL) under a N_2 atmosphere, for 24 h at the specified reaction temperature.
[b] Isolated yields after column chromatography.
[c] Reaction with 200 mol% of base.
[d] Reaction with 100 mol% of base.
[e] Reaction with 50 mol% of base.
[f] The reaction was carried out with **1a** (1 mmol), **2a** (1 mmol), and base (1.5 mmol) in solvent (5 mL).
[g] Reaction under air.

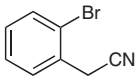
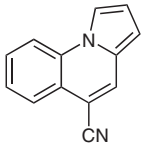
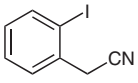
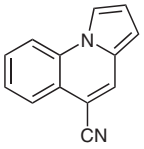
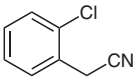
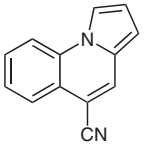
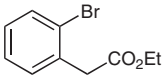
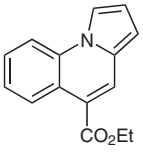
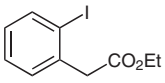
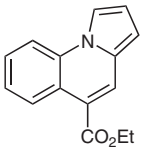
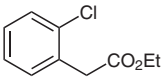
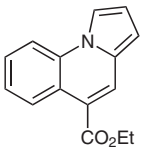
It should be noted that some metal elements are present as impurities in the K_3PO_4. This minor amount of transition-metal elements might be the real catalyst, as it was previously demonstrated for the copper cases.[14] So as to remove the possibility of the existence of trace transition-metal elements in the commercially available K_3PO_4 that would possibly affect our investigation results, high-purity K_3PO_4 (99.99% from Aldrich) was applied in the reaction instead of K_3PO_4 (99.6% from Shanghai), providing almost the

Table 2 Investigation on the Scope of 2-Halophenylacetonitriles or 2-Halophenylacetates for the Formation of Pyrrolo[1,2-*a*]quinolines[a]



1a–f **2a** **3**

X = I, Br, Cl
EWG = CN, CO_2Et

Entry	Substrate	Product	Yield (%)[b]
1	**1a** 	**3aa** 	86
2	**1b** 	**3aa** 	65
3	**1c** 	**3aa** 	70
4	**1d** 	**3da** 	34
5	**1e** 	**3da** 	25[c]
6	**1f** 	**3da** 	19[c]

[a] Reaction conditions: 1*H*-pyrrole-2-carbaldehyde (**2a**; 0.2 mmol), 2-halophenylacetonitrile or 2-halophenylacetate **1a–f** (0.2 mmol), and K_3PO_4 (0.3 mmol) in DMSO (2.0 mL) under a N_2 atmosphere, for 24 h at 130 °C.
[b] Isolated yield.
[c] Reaction time 48 h and at 150 °C.

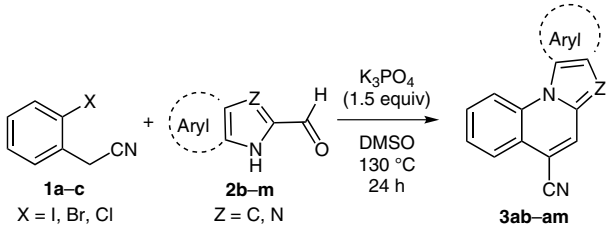
same results. Therefore, we are confident that the possible impurities are not responsible for the reaction depicted in this process.

With the optimized conditions in hand, the scope of reaction was investigated using a variety of 2-halophenylacetonitriles and ethyl 2-halophenylacetates. As shown in Table 2, when the reaction was carried out with 2-halophenylacetonitriles **1a–c**, only the pyrrolo[1,2-*a*]quinoline-5-carbonitrile (**3aa**) was obtained (Table 2, entries 1–3). Ethyl 2-(2-bromophenyl)acetate (**1d**) also reacted smoothly under the optimized conditions to give ethyl pyrrolo[1,2-*a*]quinoline-5-carboxylate (**3da**) (entry 4). However, when the protocol was applied to ethyl 2-(2-iodophenyl)acetate (**1e**) and ethyl 2-(2-chlorophenyl)acetate (**1f**), longer reaction times were required and the product **3da** was formed in low yields (entries 5, 6).

The scope of the formylpyrrole compounds was also investigated, and the results are shown in Table 3. Substituents were found to be well tolerated at the 3-, 4-, and 5-positions of the pyrrole ring, with the corresponding products **3ab**,**ac** being formed in good yields (Table 3, entries 1–6). Pleasingly, almost all of the 2-formylindole compounds evaluated bearing electron-withdrawing or electron-donating groups reacted smoothly with the 2-halophenylacetonitriles to provide the desired products in excellent or moderate yields (entries 7–18). 1*H*-Indole-2-carbaldehyde (**2d**) afforded the desired product **3ad** in 84% yield (entry 8), and 5-chloro-1*H*-indole-2-carbaldehyde (**2e**) and 5-bromo-1*H*-indole-2-carbaldehyde (**2f**) gave **3ae** and **3af** in yields of 90 and 93%, respectively (entries 11 and 14). It is noteworthy that the 2-formyldiazole components **2h**,**i** reacted with several 2-halophenylacetonitriles **1a–c** to give the corresponding imidazo[1,2-*a*]quinoline derivatives **3ah**,**ai** in modest yields (30–48%), albeit under drastic conditions (24 h, 150 °C) (entries 19–24). Furthermore, 5-methyl-1*H*-benzo[*d*]imidazole-2-carbaldehyde (**2j**) participated in the cyclization reaction to give a mixture of the two isomers 9-methylbenzo[4,5]imidazo[1,2-*a*]quinoline-5-carbonitrile (**3aj**) and 10-methylbenzo[4,5]imidazo[1,2-*a*]quinoline-5-carbonitrile (**3aj'**) in a combined yield of 32% (1.1:1 ratio by ^1H NMR analysis) (entry 26). Unfortunately, 5-nitro-1*H*-benzo[*d*]imidazole-2-carbaldehyde (**2k**) and 5-nitro-1*H*-indole-2-carbaldehyde (**2l**) failed to provide any of the desired products under the optimized reaction conditions (entries 28–33). Notably, the annulation of formylimidazole (**2m**) with **1a** also worked well to provide the desired product **3am** in 67% yield (entry 35).

Lastly, we wondered about the most likely mechanism for this reaction and it was initially suspected that an aryne intermediate was involved in this transformation.[13b] 2-(3-Bromophenyl)acetonitrile (**1g**) and 1*H*-pyrrole-2-carbaldehyde (**2a**) were selected as substrates to evaluate the likelihood of this reaction pathway, with the expectation that pyrrolo[1,2-*a*]quinoline-5-carbonitrile (**3aa**) would be isolated as the product[13c,17] (Scheme 2). However, as shown in Scheme 2, none of the desired product was formed in this experiment.

Table 3 Investigation on the Scope of the Heterocyclic Substrates[a]



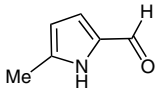
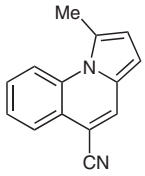
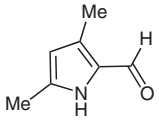
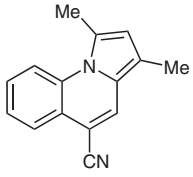
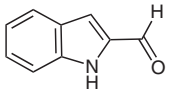
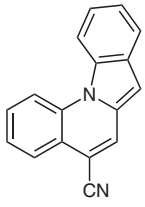
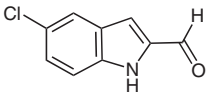
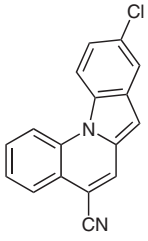
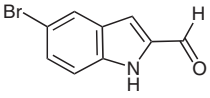
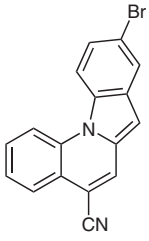
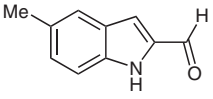
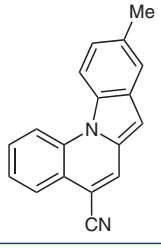
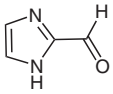
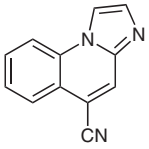
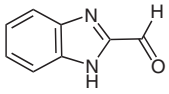
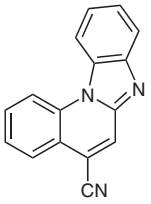
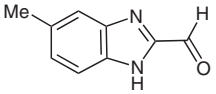
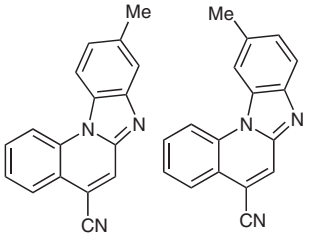
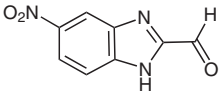
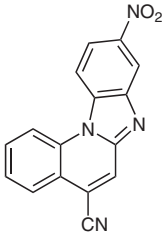
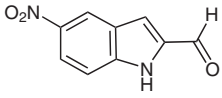
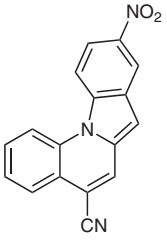
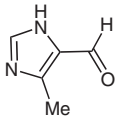
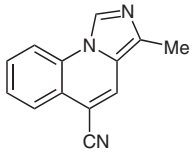
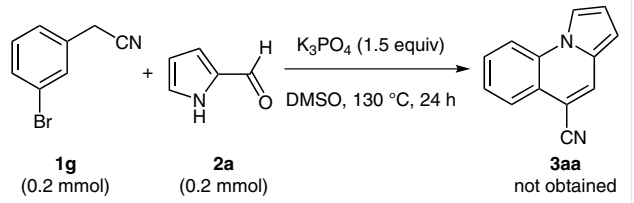
Entry	Heterocyclic substrate		X	Product		Yield (%)[b]
1 2 3	**2b**		I Br Cl	**3ab**		72 93 81
4 5 6	**2c**		I Br Cl	**3ac**		79 98 82
7 8 9	**2d**		I Br Cl	**3ad**		73 84 69
10 11 12	**2e**		I Br Cl	**3ae**		57 90 61
13 14 15	**2f**		I Br Cl	**3af**		70 93 76
16 17 18	**2g**		I Br Cl	**3ag**		62 99 70

Table 3 (continued)

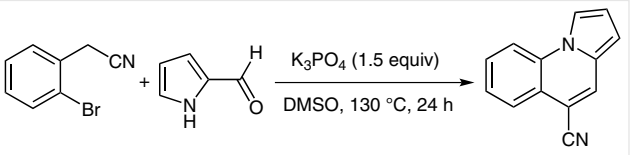
Entry	Heterocyclic substrate	X	Product	Yield (%)[b]
19 20 21	**2h** 	I Br Cl	**3ah** 	30[c] 48[c] 35[c]
22 23 24	**2i** 	I Br Cl	**3ai** 	33[c] 41[c] 34[c]
25 26 27	**2j** 	I Br Cl	**3aj** + **3aj′**  1.1:1	21[c] 32[c] 15[c]
28 29 30	**2k** 	I Br Cl	**3ak** 	0[d] 0[d] 0[d]
31 32 33	**2l** 	I Br Cl	**3al** 	0[d] 0[d] 0[d]
34 35 36	**2m** 	I Br Cl	**3am** 	57 67 61

[a] Reaction conditions: Compounds **1a**–**c** (0.2 mmol), **2b**–**m** (0.2 mmol), and K_3PO_4 (0.3 mmol) in DMSO (2.0 mL) under a N_2 atmosphere for 24 h at 130 °C.
[b] Isolated yield after flash chromatography.
[c] Reaction time 24 h and at 150 °C.
[d] Reaction time 48 h and at 150 °C.



Scheme 2 Synthesis of pyrrolo[1,2-*a*]quinoline-5-carbonitrile (**3aa**)

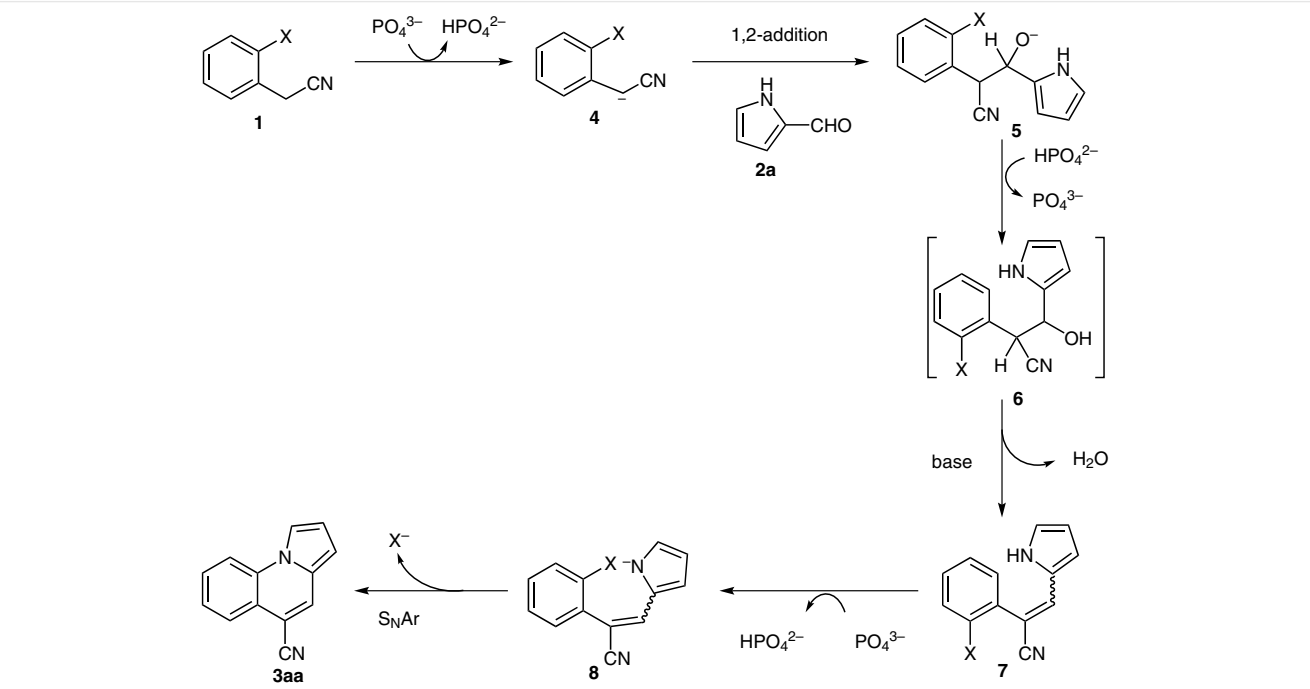
This result indicated that aryne intermediates do not play a central role in the current annulation reaction, and it was therefore assumed that this reaction pathway involved the formation of short-lived radical intermediates.[13c] With this in mind, several experiments were designed to evaluate the potential role of radical species in the reaction. As shown in Scheme 3, the presence of radical scavenger,[18] such as TEMPO or hydroquinone (HQ), had no impact on the reaction, with the desired product **3aa** being formed in good yields. This observation therefore indicated that radical intermediates were not involved in this cascade reaction.



no radical scavenger	86%
TEMPO (0.5 equiv)	86%
TEMPO (2.0 equiv)	86%
hydroquinone (2.0 equi)	86%

Scheme 3 Radical trapping experiments

Based on these results, we have proposed a base-mediated reaction mechanism[19] for the one-pot formation of **3aa**, which is shown in Scheme 4. The reaction of **1** with **2a** would yield compound **5** via a base-catalyzed 1,2-addition between the nitrile and the aldehyde. Then, an intramolecular dehydration reaction of compound **6** would give compound **7**. Finally, compound **7** would then undergo an intramolecular S_NAr reaction to afford the product pyrrolo[1,2-*a*]quinoline-5-carbonitrile (**3aa**).



Scheme 4 A proposed base-promoted mechanism

In summary, we have developed a simple and effective method for the synthesis of aza-fused polycyclic quinolines under mild reaction conditions. A variety of pyrrolo[1,2-*a*]quinoline derivatives were synthesized from 2-formylpyrroles and 2-halophenylacetonitriles (or 2-halophenylacetates) in moderate to excellent yields. The method worked well for all of the 2-bromo-, 2-iodo-, and 2-chloroarylacetonitriles tested and showed great functional group compatibility. This study therefore provides a base-catalyzed process for the synthesis of pyrrolo[1,2-*a*]quinolines and other quinoline derivatives from readily accessible starting materials and should find numerous applications in the synthesis of biologically and medicinally relevant compounds.

All starting materials and solvents were either purchased from commercial sources and used as received (compounds **1a**–**c**, **1g**, **2b**, **2c**, **2h**, and **2m**) and were purified according to standard procedures or prepared according to literature procedures (compounds **1d**–**f**, **2d**–**g**,**i**–**l**; see the Supporting Information). ^{1}H NMR spectra were recorded at 300 MHz on a Bruker Avance 300 spectrometer with TMS as the internal standard and $CDCl_3$ or DMSO-d_6 as the solvent. ^{13}C NMR spectra were recorded at 75 MHz on a Bruker Avance 300 spectrometer with TMS as the internal standard and $CDCl_3$ or DMSO-d_6 as the solvent. HRMS was obtained with a Finnigan MAT 95 spectrometer (ESI).

Pyrrolo[1,2-*a*]quinoline-5-carbonitrile (3aa); Typical Procedure

A flask was equipped with a magnetic stir bar and charged with 1*H*-pyrrole-2-carbaldehyde (**2a**; 19.0 mg, 0.2 mmol, 1.0 equiv), 2-bromophenylacetonitrile (**1a**; 39.2 mg, 0.2 mmol, 1.0 equiv), and K_3PO_4 (63.6 mg, 0.3 mmol, 1.5 equiv). The flask was evacuated and filled with N_2, and then anhydrous DMSO (2.0 mL) was introduced via a syringe. The flask was heated in a 130 °C oil bath for 24 h, at which time TLC analysis [petroleum ether (bp 60–90 °C)–EtOAc, 10:1] indicated complete consumption of **2a** and **1a**. The reaction mixture was cooled to r.t. and added to a sat. solution of NaCl (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and filtered. The filtrate was concentrated, and the residue was purified by column chromatography on SiO_2 [petroleum ether (bp 60–90 °C)–EtOAc, 10:1 to 30:1] to give **3aa**; yield: 32.9 mg (86%); tan yellow solid; mp 155.6–156.3 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.51 (s, 1 H), 7.95 (d, *J* = 8.1 Hz, 1 H), 8.25 (s, 1 H), 7.86 (d, *J* = 6.3 Hz, 1 H), 7.72–7.67 (m, 1 H), 7.56–7.51 (m, 1 H), 6.94 (d, *J* = 10.0 Hz, 2 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 131.9, 131.4, 129.6, 128.6, 128.0, 125.4, 125.1, 119.4, 117.4, 117.3, 115.5, 114.7, 109.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_9N_2$: 193.0766; found: 193.0773.

1-Methylpyrrolo[1,2-*a*]quinoline-5-carbonitrile (3ab)

Yield: 38.2 mg (93%); fluorescent yellow solid; mp 154.2–155.7 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.6 Hz, 1 H), 7.96 (d, *J* = 7.8 Hz, 1 H), 7.69 (s, 1 H), 7.53–7.48 (m, 1 H), 7.43–7.38 (m, 1 H), 6.72 (d, *J* = 3.9 Hz, 1 H), 6.62 (d, *J* = 3.8 Hz, 1 H), 2.95 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.7, 130.5, 129.7, 127.9, 126.1, 124.2, 121.7, 117.9, 116.5, 115.0, 107.9, 102.7, 98.6, 18.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{11}N_2$: 207.0863; found: 207.0870.

1,3-Dimethylpyrrolo[1,2-*a*]quinoline-5-carbonitrile (3ac)

Yield: 43.0 mg (98%); fluorescent yellow solid; mp 168.1–168.6 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 9.0 Hz, 1 H), 7.85 (d, *J* = 9.0 Hz, 1 H), 7.58 (s, 1 H), 7.45–7.40 (m, 1 H), 7.36–7.26 (m, 1 H), 6.42 (s, 1 H), 2.84 (s, 3 H), 2.31 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.7, 129.6, 127.6, 127.5, 125.9, 125.5, 121.8, 121.7, 118.4, 117.9, 117.7, 115.9, 96.5, 18.2, 10.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}N_2$: 221.1014; found: 221.1019.

Indolo[1,2-*a*]quinoline-5-carbonitrile (3ad)

Yield: 40.5 mg (84%); fluorescent yellow solid; mp 193.7–194.6 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, *J* = 8.5 Hz, 1 H), 8.47 (d, *J* = 8.6 Hz, 1 H), 8.06 (d, *J* = 7.4 Hz, 1 H), 7.93 (d, *J* = 8.3 Hz, 2 H), 7.75–7.71 (m, 1 H), 7.57–7.52 (m, 1 H), 7.49–7.42 (m, 2 H), 7.10 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.5, 133.2, 131.9, 131.7, 130.2, 128.6, 126.9, 124.3, 123.8, 122.8, 122.3, 119.1, 116.9, 115.6, 114.3, 104.5, 102.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{11}N_2$: 243.0826; found: 243.0834.

9-Chloroindolo[1,2-*a*]quinoline-5-carbonitrile (3ae)

Yield: 49.5 mg (90%); fluorescent yellow solid; mp 208.5–209.6 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.6 Hz, 1 H), 8.39 (d, *J* = 9.2 Hz, 1 H), 8.08 (d, *J* = 7.5 Hz, 1 H), 7.90 (d, *J* = 5.3 Hz, 2 H), 7.75 (s, 1 H), 7.52–7.47 (m, 2 H), 7.04 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.2, 135.7, 135.6, 134.9, 131.9, 130.6, 128.3, 127.2, 124.5, 124.1, 119.6, 116.9, 116.6, 114.3, 114.0, 105.6, 101.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{10}ClN_2$: 277.0542; found: 277.0553.

9-Bromoindolo[1,2-*a*]quinoline-5-carbonitrile (3af)

Yield: 59.2 mg (93%); fluorescent yellow solid; mp 205.6–207.1 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.66 (d, *J* = 24.4 Hz, 2 H), 8.43 (s, 1 H), 8.18 (s, 1 H), 7.92 (s, 1 H), 7.81 (s, 1 H), 7.58 (s, 2 H), 7.24 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 134.9, 133.9, 131.6, 131.1, 131.0, 129.2, 126.5, 126.1, 124.5, 124.1, 119.4, 116.7, 116.6, 116.2, 115.3, 105.3, 102.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{10}BrN_2$: 320.9941; found: 320.9949.

9-Methylindolo[1,2-*a*]quinoline-5-carbonitrile (3ag)

Yield: 50.8 mg (99%); fluorescent yellow solid; mp 199.4–201.1 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.73 (d, *J* = 8.46 Hz, 1 H), 8.55 (d, *J* = 8.82 Hz, 1 H), 8.39 (s, 1 H), 7.91 (d, *J* = 7.65 Hz, 1 H), 7.83–7.77 (m, 1 H), 7.74 (s, 1 H), 7.57–7.52 (m, 1 H), 7.37 (d, *J* = 8.64 Hz, 1 H), 7.18 (s, 1 H), 2.51 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 135.2, 133.0, 131.9, 131.6, 130.8, 129.8, 129.5, 126.2, 125.9, 124.0, 121.4, 119.4, 116.9, 116.1, 114.6, 103.9, 102.5, 21.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{13}N_2$: 257.1053; found: 257.1062.

Imidazo[1,2-*a*]quinoline-5-carbonitrile (3ah)

Yield: 18.7 mg (48%); tan solid; mp 182.3–183.6 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22–8.19 (m, 2 H), 8.10 (s, 1 H), 8.01 (d, *J* = 4.9 Hz, 1 H), 7.86 (s, 1 H), 7.81–7.78 (m, 1 H), 7.66–7.63 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 135.2, 130.5, 127.3, 127.2, 126.2, 125.0, 121.7, 120.0, 115.6, 113.1, 108.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_8N_3$: 194.0618; found: 194.0625.

Benzo[4,5]imidazo[1,2-*a*]quinoline-5-carbonitrile (3ai)

Yield: 19.9 mg (41%); tan solid; mp 251.7–252.8 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.68 (d, *J* = 8.6 Hz, 1 H), 8.47–8.43 (m, 1 H), 8.28 (d, *J* = 7.8 Hz, 1 H), 8.16 (s, 1 H), 8.14–8.11 (m, 1 H), 7.95–7.89 (m, 1 H), 7.69–7.63 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.3, 145.2, 135.4, 131.4, 130.9, 127.6, 127.6, 126.0, 125.5, 125.3, 124.7, 121.7, 120.0, 115.7, 114.3, 113.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{10}N_3$: 244.0815; found: 244.0823.

9-Methylbenzo[4,5]imidazo[1,2-*a*]quinoline-5-carbonitrile (3aj) and 10-Methylbenzo[4,5]imidazo[1,2-*a*]quinoline-5-carbonitrile (3aj')

Yield: 16.2 mg (32%); tan oil; 1.1:1 mixture of inseparable isomers (ratio by ^{1}H NMR analysis).

Major Isomer 3aj

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (m, 1 H), 8.32–8.23 (m, 2 H), 8.14 (s, 1 H), 7.89 (d, *J* = 7.5 Hz, 1 H), 7.67–7.65 (m, 1 H), 7.45 (m, 1 H), 7.26 (m, 1 H), 2.62 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.3, 145.5, 131.3, 131.2, 127.5, 127.4, 126.5, 126.1, 125.9, 125.2, 125.1, 121.1, 115.8, 115.7, 114.0, 113.8, 21.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{12}N_3$: 258.1046; found: 258.1052.

3-Methylimidazo[1,5-*a*]quinoline-5-carbonitrile (3am)

Yield: 27.9 mg (67%); tan solid; mp 191.3–192.0 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.20 (s, 1 H), 8.45 (s, 1 H), 8.41 (d, *J* = 8.3 Hz, 1 H), 7.85 (d, *J* = 7.9 Hz, 1 H), 7.76–7.71 (m, 1 H), 7.63–7.58 (m, 1 H), 2.56 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 137.1, 131.0, 130.2, 127.2, 127.2, 126.7, 125.6, 122.9, 119.9, 117.1, 116.0, 99.7, 12.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}N_3$: 208.0831; found: 208.0840.

Ethyl Pyrrolo[1,2-*a*]quinoline-5-carboxylate (3da)

Yield: 16.1 mg (34%); light yellow solid; mp 186.5–188.4 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.94 (d, *J* = 8.2 Hz, 1 H), 8.24 (s, 1 H), 7.97–7.91 (m, 2 H), 7.57–7.52 (m, 1 H), 7.44–7.39 (m, 1 H), 6.84 (d, *J* = 20.3 Hz, 2 H), 4.47–4.40 (m, 2 H), 1.47–1.33 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 139.4, 137.8, 131.4, 130.6, 128.4, 127.6, 125.2, 123.4, 114.1, 112.6, 111.8, 100.9, 60.9, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{14}NO_2$: 240.0973; found: 240.0982.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1380506.

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