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Article

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Pd-Catalyzed approach for assembling 9-arylacridines via a cascade tandem reaction of 2-(arylamino)benzonitrile with arylboronic acids in water

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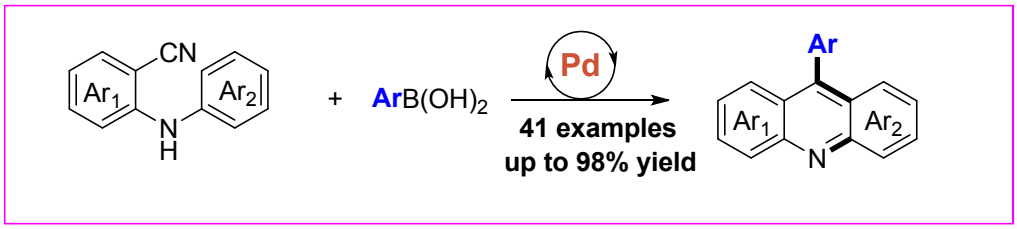


ABSTRACT: A novel palladium-catalyzed protocol for the synthesis of 9-arylacridines via tandem reaction of 2-(arylamino)benzonitrile with arylboronic acids in water has been developed with good functional group tolerance. The present synthetic route could be readily scaled up to gram quantity without difficulty. This methodology was further extended to the synthesis of a 4'-OH derivative which showed estrogenic biological activity. Preliminary mechanistic experiments showed that this transformation involves a nucleophilic addition of aryl pallidium species to the nitrile to generate an aryl ketone intermediate followed by an intramolecular Friedel-Crafts acylation and dehydration to acridines.

INTRODUCTION

Acridines are an important class of heteroaromatic compounds[1] which exhibit versatile biological properties,[2] such as antimalarial,[2b] anticancer[2c] and antileukaemia.[2d] Acridines analogues have also been used as effective organocatalyst for photocatalytic oxygenation of anthracenes and olefins[3a] and hydroetherification of alkenols.[3b] In addition, 9-methylacridines and other acridine-containing analogues have been applied to new fluorescent probes and organic light-emitting diodes.[4] Consequently, the development of methods for the preparation of acridines is of importance to medicinal chemistry and represents a worthwhile goal of organic synthesis.

Many elegant general synthetic approaches have been developed. The earliest acridine synthesis was achieved by Brenthsen in 1878 by heating a diaryl amine and a carboxylic acid under $ZnCl_2$ at elevated temperatures.[5] Inspired by this work, many modifications have been discovered. Azides were nicely applied as the sole nitrogen source in building acridine skeleton. Ellman and co-workers developed a Rh-catalyzed formal [3+3] annulation of aromatic azides and imines to provide acridine derivatives in reasonable yields.[6a] Wang and Jiang reported a nitrogen–iodine exchange protocol of diaryliodonium salts with sodium azide salt for general construction of acridines.[6b] Transient directing group promoted C(sp^2)–H functionalization of benzaldehydes for the construction of acridines have also been achieved. Park and Kim disclosed the transient directing group assisted Rh(III)-catalyzed C−H functionalization cyclization between benzaldehydes and

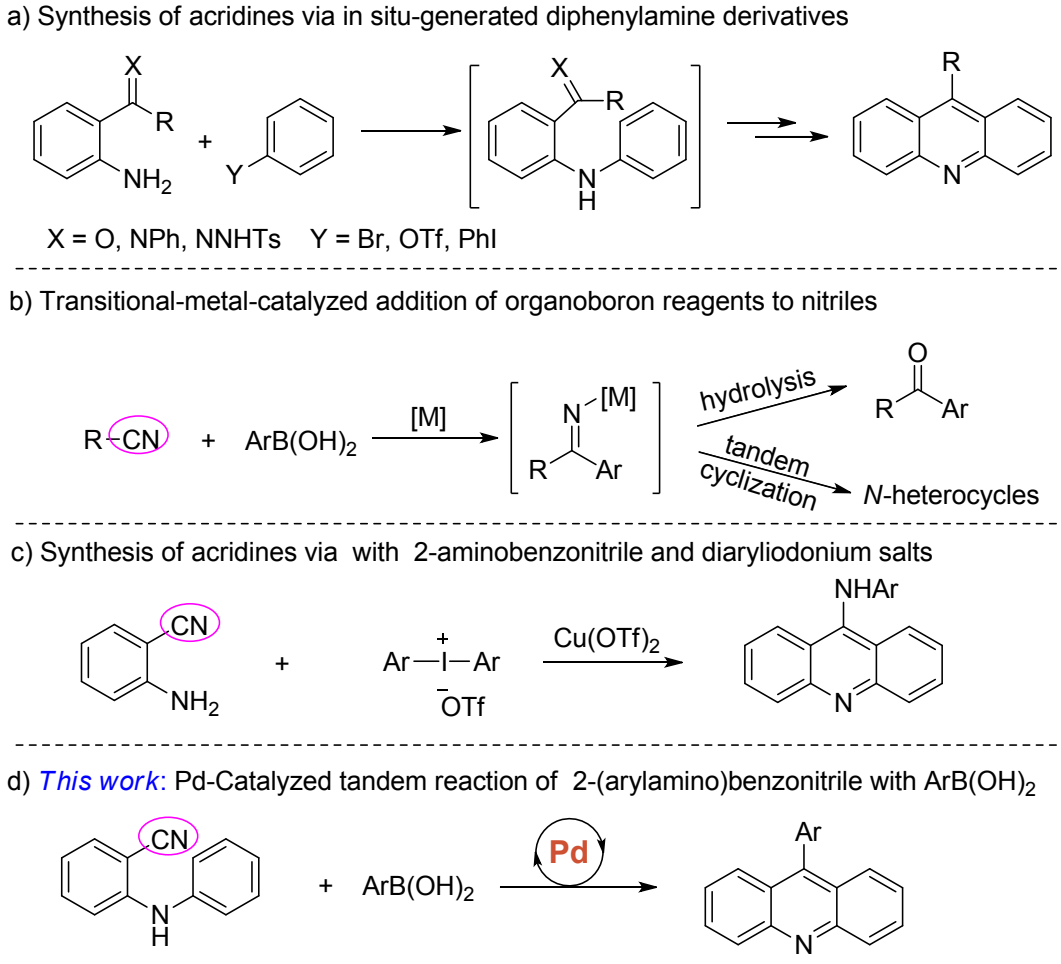
anthranils.[7a] Cheng demonstrated an efficient procedure to access acridine analogues starting from aromatic aldehydes and aryl nitrosos enabled by *in situ* formation and removal of an imino transient directing group.[7b] Catalytic dehydrogenation reaction of partially saturated *N*-heterocycles to acridines is also realized in contemporary science.[8] The most well-developed general methods for the construction of acridines were inter-and intramolecular cyclizations with various *in situ*-generated diphenylamine derivatives as the substrates (Scheme 1a).[9]

Transition-metal-catalyzed transformation of nitriles serves as a powerful strategy to build carbon–carbon and carbon–heteroatom bonds for organic chemistry research.[10] To date, a number of catalytic protocols for the carbometallization of nitriles with organoboron reagents to ketones and nitrogen-containing compounds such as quinolone, isoquinoline, quinazoline and indole have been realized (Scheme 1b).[11] Compared to the nucleophilic addition of organometallic reagents such as organolithium or organomagnesium to nitriles, organoboron reagents are highly regarded due to their advantages of stability to air and moisture as well as good functional group tolerance.[12] However, transition-metal-catalyzed carbometallization of nitriles with organoboron to acridines have not been realized to date. Chen reported efficient tandem reaction to construct acridines derivatives with readily available 2-aminobenzonitrile and diaryliodonium salts (Scheme 1c).[13] From the viewpoint of diverse synthesis concerns, development of environmentally friendly shortcuts for accessing acridine from easily available nitriles remains a demanding goal.

Additionally, water as a reaction medium for green chemistry has recently attracted

considerable attention in organic synthesis due to its environmental acceptability, abundance, safety and low cost, and would thus be highly advantageous alternatives to organic solvents from both economical and ecological standpoints.[14] Inspired by hereinbefore work, as a part of our research program aimed at palladium-catalyzed synthesis of *N*-containing heterocycles with organoboron reagents and nitriles,[15] we envisioned that carbopalladation of 2-aminobenzonitrile derivatives would afford 2-aminoaryl ketones easily, which might further prompt an intramolecular tandem arylation/Friedel-Crafts procedure with the aid of lewis acid and/or acid medium, providing the desire acridines skeletons (Scheme 1d).

Scheme 1. Acridines synthesis strategies

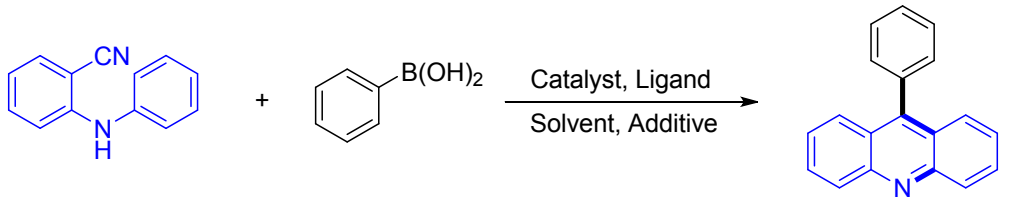


RESULTS AND DISCUSSION

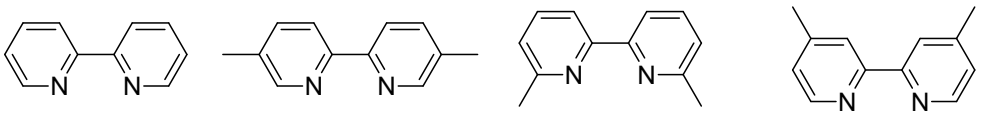
At the outset of our study, 2-(phenylamino)benzonitrile (**1a**) and phenylboronic acid (**2a**)were chosen as the model reaction to optimize the reaction conditions. The reaction in the presence of $Pd(OAc)_2$ (10 mol%), 2,2'-bipyridine (**L1**) (20 mol%) and D-camphorsulfonic acid (D-CSA) (5 equiv) was performed in toluene (2mL) at 100 ^oC for 24 h under air atmosphere, affording the target structure 9-phenylacridine (**3a**) in 54% yield (Table 1, entry 1). A survey of the solvent effect revealed that water was optimal to give a best 84% yield, and the use of toluene, *N*,*N*-Dimethylformamide (DMF) and MeOH led to lower yields (Table 1, entries 1-4). Among the various acid additives we screened, methanesulfonic acid (CH_3SO_3H) and trifluoromethanesulfonic acid (CF_3SO_3H) were most effective, affording **3a** in the highest yield of 93% (Table 1, entries 5-8). A variety of Pd(II) salts are reactive, with $Pd(OAc)_2$ being the optimal choice (Table 1, entries 9-11). It was worth noting that the reaction did not work when Pd(0) such as $Pd(PPh_3)_4$ was employed as catalyst (Table 1, entry 12). Other bidentate nitrogen ligands, such as 5,5'-dimethyl-2,2'-bipyridine (**L2**) and 6,6'-dimethyl-2,2'-bipyridine (**L3**) and 4,4'-dimethyl-2,2'- bipyridine (**L4**) affected the tandem reaction adversely due to the steric effect or electronic effect (Table 1, entries 13-15). The yield decreased to 61% when the temperature was 80 ^oC. No significantly improvement of yield was achieved by elevating reaction temperature to 120 ^oC (Table 1, entries 16-17). Shorten the reaction time to 12 h led to a lower yield of the desire product (Table 1, entry 18). To

our delight, the isolated yield of **3a** remained when catalyst loading was 5 mol% (Table 1, entry 19). The transformation efficiency of acridines decreased to some extent either lower the amount of phenylboronic acid (**2a**) or CH_3SO_3H (Table 1, entry 20). The reactants remained unreacted when the Pd catalyst was absent (Table 1, entry 21). Only trace amount of **3a** was detected when the ligand was omitted from the reaction medium (Table 1, entry 22). The reaction could not work well when the methanesulfonic acid was absent (Table 1, entry 23). Therefore, the optimal reaction conditions can be summarized as follows: 0.5 mmol 2-(phenylamino)benzonitrile and 0.75 mmol phenylboronic acid in water (2 mL) with $Pd(OAc)_2$ catalyst (5 mol %), CH_3SO_3H (5 equiv), 2,2'-bipyridine (10 mol%), at 100 °C for 24 h under air atmosphere.

Table 1. Optimization of reaction conditions[a]



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



L1 **L2** **L3** **L4**

Entry	Pd Source	Ligand	Additive	Solvent	Temp(^{o}C)	Time(h)	Yield(%)
1	$Pd(OAc)_2$	**L1**	D-CSA	toluene	100	24	54
2	$Pd(OAc)_2$	**L1**	D-CSA	DMF	100	24	64
3	$Pd(OAc)_2$	**L1**	D-CSA	MeOH	100	24	76
4	$Pd(OAc)_2$	**L1**	D-CSA	H_2O	100	24	84
5	$Pd(OAc)_2$	**L1**	CH_3CO_2H	H_2O	100	24	13
6	$Pd(OAc)_2$	**L1**	CF_3CO_2H	H_2O	100	24	82
7	$Pd(OAc)_2$	**L1**	CF_3SO_3H	H_2O	100	24	93
8	$Pd(OAc)_2$	**L1**	CH_3SO_3H	H_2O	100	24	93
9	$Pd(acac)_2$	**L1**	CH_3SO_3H	H_2O	100	24	81
10	$Pd(CF_3CO_2)_2$	**L1**	CH_3SO_3H	H_2O	100	24	75
11	$PdCl_2$	**L1**	CH_3SO_3H	H_2O	100	24	75
12	$Pd(PPh_3)_4$	**L1**	CH_3SO_3H	H_2O	100	24	trace
13	$Pd(OAc)_2$	**L2**	CH_3SO_3H	H_2O	100	24	81
14	$Pd(OAc)_2$	**L3**	CH_3SO_3H	H_2O	100	24	<10
15	$Pd(OAc)_2$	**L4**	CH_3SO_3H	H_2O	100	24	73
16	$Pd(OAc)_2$	**L1**	CH_3SO_3H	H_2O	80	24	61
17	$Pd(OAc)_2$	**L1**	CH_3SO_3H	H_2O	120	24	92
18	$Pd(OAc)_2$	**L1**	CH_3SO_3H	H_2O	100	12	85
19	**$Pd(OAc)_2$**	**L1**	**CH_3SO_3H**	**H_2O**	**100**	**24**	**92**[b](70)[c]
20	$Pd(OAc)_2$	**L1**	CH_3SO_3H	H_2O	100	24	68[d](76)[e]
21	-	**L1**	CH_3SO_3H	H_2O	100	24	NR
22	$Pd(OAc)_2$	**-**	CH_3SO_3H	H_2O	100	24	trace
23	$Pd(OAc)_2$	**L1**	-	H_2O	100	24	trace

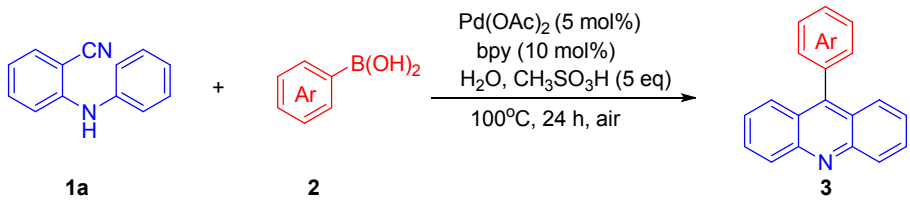
[a] Conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), Pd Source (10 mol %), Ligand (20 mol %), Solvent (2.0 mL), additive (5 equiv), 100 ^{o}C, 24 h, air, isolated yields, [b] Pd Source (5 mol %), Ligand (10 mol %). [c] Pd Source (3 mol %), Ligand (10 mol %). [d] 3 equiv of CH_3SO_3H was used. [e] 1.2 equiv of **2a** was used.

With these optimized conditions in hand, we subsequently explored the substrate scope and limitations of this palladium-catalyzed addition/cyclization of organoboron to 2-(phenylamino)benzonitrile derivatives for the construction of acridines. First, the variation of the arylboronic acids was investigated (Table 2). The results showed that

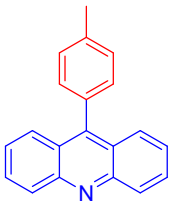
the steric effect of the substituent had an obvious impact on the reaction under the standard conditions. For example, treatment of **1a** with *para*- and *meta*-tolylboronic acids provided 88% and 86% yields of **3b** and **3c**, respectively, while the *ortho*-tolylboronic acid afforded the desired product **3d** with a diminished yield of 51%. 3,5-Dimethyl phenylboronic acid afforded the desire **3e** in comparable 84% yield while bulky (2-isopropylphenyl)boronic acid only afforded the desired acridine **3f** in 37% yield. 2,4,6-Trimethyl phenylboronic acid were unsuitable in this transformation. The electronic properties of the substituents on the phenyl ring of the arylboronic acids affected the reaction to some extent. In general, the substrates bearing a moderate electron-withdrawing substituent provided a slightly higher yield than those of substrates with electron-donating groups. For example, (4-isopropylphenyl)boronic acid and (4-(tert-butyl)phenyl)boronic acid provided the corresponding acridines **3h** and **3i** in 88 and 89% yield, while arylboronic acids bearing methoxy substituents at 4-positions can only provide the corresponding product **3j** in 56% yield, with **1j** recovered in 30% yield. To our delight, the method tolerates the entire range of halogen substituents, affording the desired products **3k**-**3s** in 62-98% yield, which makes this method particularly appealing, enabling further access to more complex compounds in combination with cross-coupling transformations. However, arylboronic acids bearing strong electron-withdrawing groups decreased the reactivity. For examples, (4-(trifluoromethyl)phenyl)boronic acid was converted to **3t** in 63% yield, accompanied by the formation of uncyclized ketone (2-(phenylamino)phenyl)(4-(trifluoromethyl)phenyl)methanone **3t-1** in 32%

yield, and 4-nitrophenyl)boronic acid was inefficient substrate under current conditions. Additionally, naphthalen-2-ylboronic acid was also successfully transformed to target acridine **3v** in 86% yield. However, when thiophen-3-ylboronic acid was subjected to the reaction condition, the desired product **3w** was obtained in only 29% yield. Unfortunately, (4-hydroxyphenyl)boronic acid and (4-(methoxycarbonyl)phenyl)boronic acid did not undergo any detectable conversion to afford the desired acridine products **3x** and **3y**, with 2-(phenylamino)benzonitrile recovered. The acridine **3z** was obtained in only 10% yield when the (4-formylphenyl)boronic acid was used in the reaction. At last, other organo boronic acids such as methylboronic acid and (*E*)-styrylboronic acid were also tried in this reaction respectively, but the desired acridines **3za** and **3zb** were not obtained.

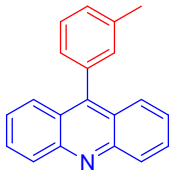
Table 2. The scope of arylboronic acids [a]



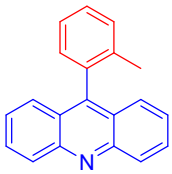
1a **2** **3**



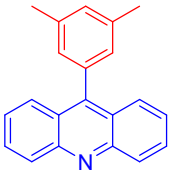
3b, 88%



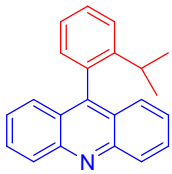
3c, 86%



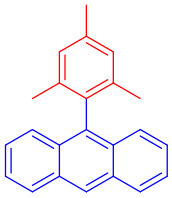
3d, 51%



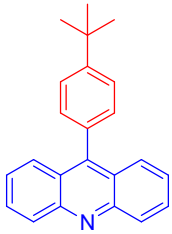
3e, 84%



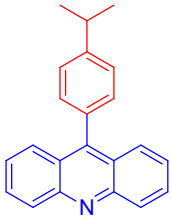
3f, 37%



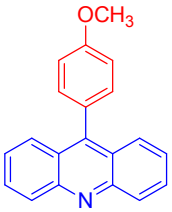
3g, ND



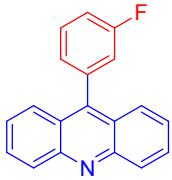
3h, 88%



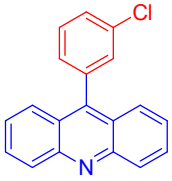
3i, 89%



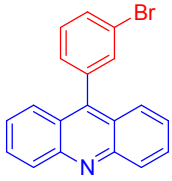
3j, 56%



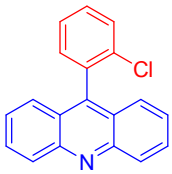
3k, 96%



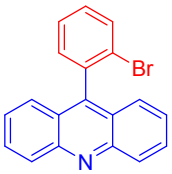
3l, 76% (98%)[b]



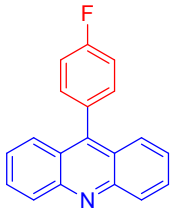
3m, 56% (90%)[b]



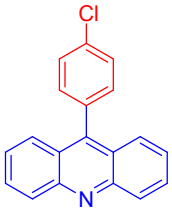
3n, 37% (76%)[b]



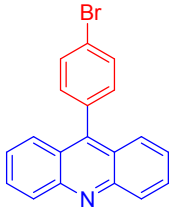
3o, 62%[b]



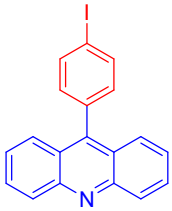
3p, 94%



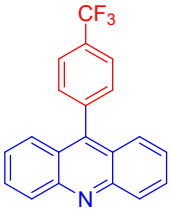
3q, 92%



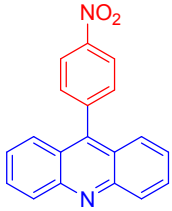
3r, 60% (94%)[b]



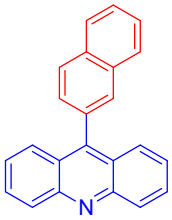
3s, 92%



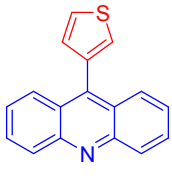
3t, 62%



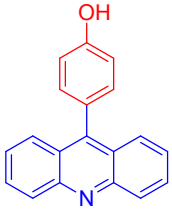
3u, ND



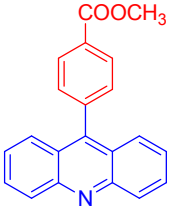
3v, 86%



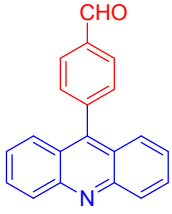
3w, 29%



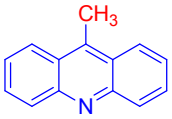
3x, 0%



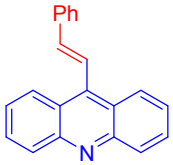
3y, 0%



3z, 10%



3za, 0%

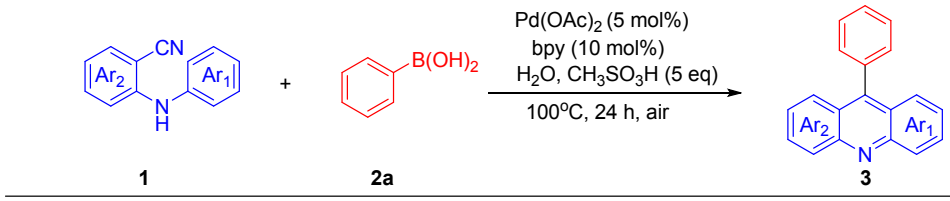


3zb, 0%

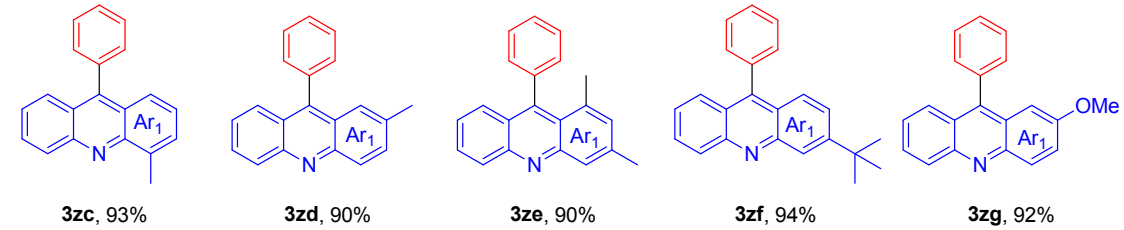
[a] Reaction conditions: **1a** (0.5 mmol), **2** (0.75 mmol), $Pd(OAc)_2$ (5 mol%), bpy (10 mol%), H_2O (2.0 mL), CH_3SO_3H (5 equiv), 100 °C, 24 h, air, isolated yield. [b] CF_3SO_3H was used instead of CH_3SO_3H.

Encouraged by these results, we next set out to investigate the reaction of various substituted 2-(phenylamino)benzonitriles with phenylboronic acid under our optimal conditions (Table 3). The influence of substitutions on the aniline ring Ar_1 was first investigated. The electronic effect of the substituents affected the yields of this transformation to some extent. For example, when substrates bearing an *ortho*-, *para*-methyl, 2, 4-dimethyl, 4-tertiary butyl and 4-methoxyl on the Ar_1 ring were examined, **3zc-3zg** were obtained in 90-94% yield, respectively. Electron-withdrawing groups, such as fluoro, chloro, bromo on the Ar_1 ring at the *para*-position, were well tolerated in this transformation, affording the desired 9-phenylacridines **3zh-3zj** in a lower yield, ranging from 81 to 86%. Naphthyl-containing compound such as **1zk** do not interfere with the palladium-catalyzed addition/cyclization progress, afforded the acridine **3zk** in 85% yield. We next examined the influence of substitutions on the aryl nitriles ring Ar_2. Substrates bearing a methyl and chloro group attaching to the Ar_2 ring were evaluated, affording **3zl-3zo** in 88-94% yield respectively. However, the yield was decreased dramatically when 2-(phenylamino)nicotinonitrile (**1zp**) was used as the substrate.

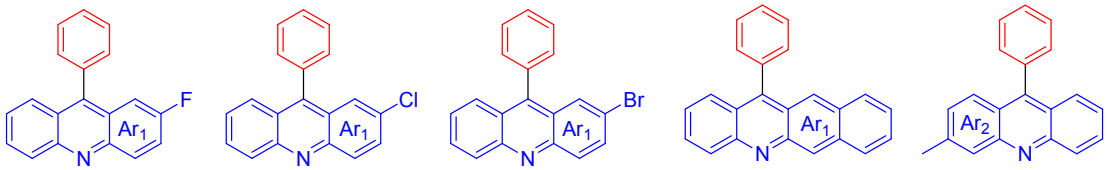
Table 3. The scope of 2-(phenylamino)benzonitriles. [a]



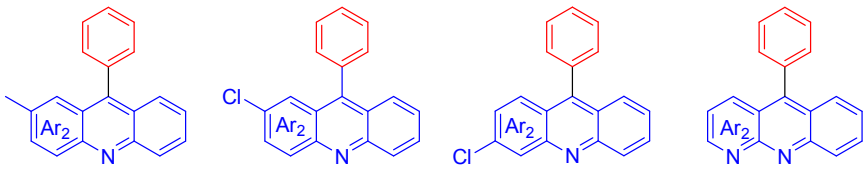
1 **2a** **3**



3zc, 93% **3zd**, 90% **3ze**, 90% **3zf**, 94% **3zg**, 92%



3zh, 81% **3zi**, 84% **3zj**, 86% **3zk**, 85% **3zl**, 93%

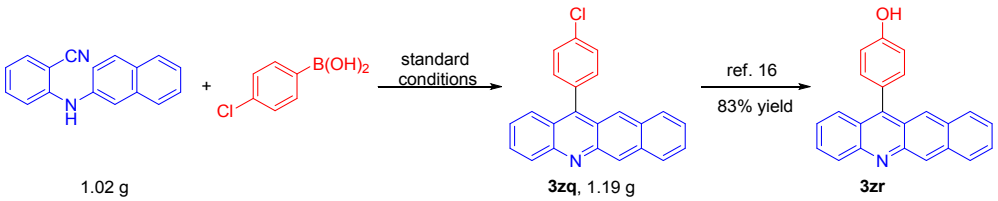


3zm, 88% **3zn**, 94% **3zo**, 88% **3zp**, 19%

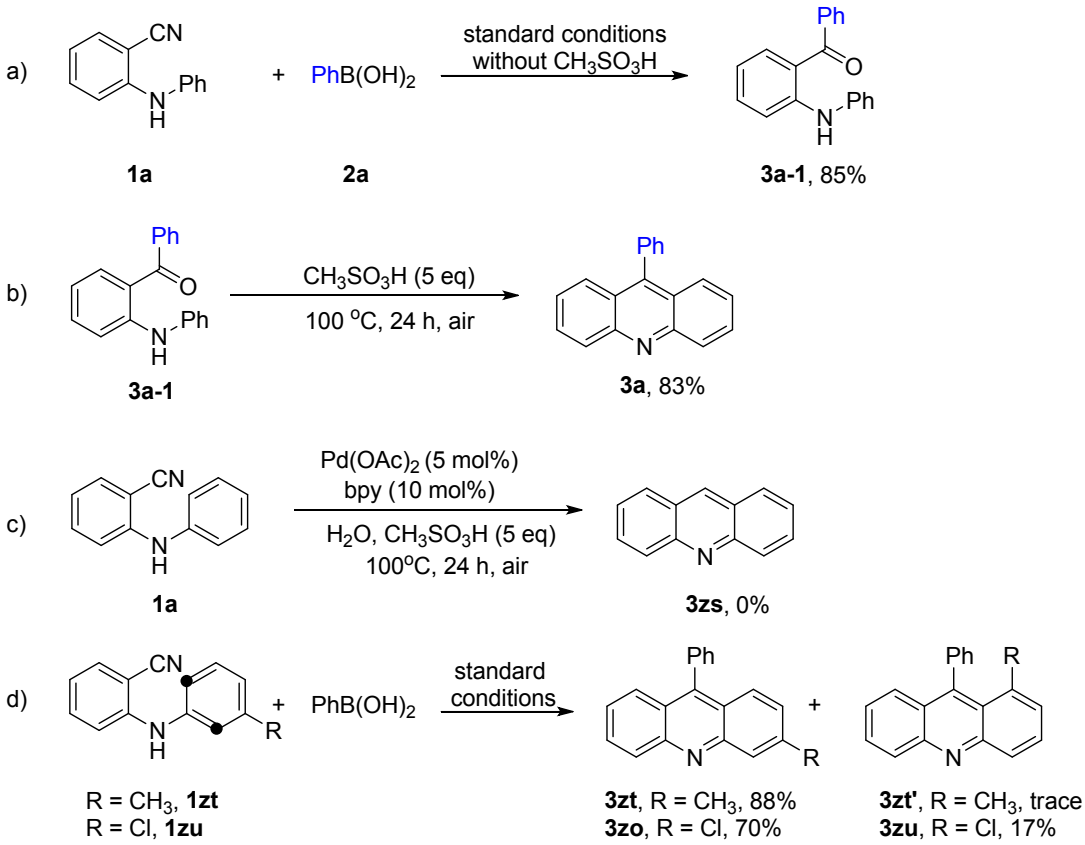
[a] Reaction conditions: **1** (0.5 mmol), **2** (0.75 mmol), $Pd(OAc)_2$ (5 mol%), bpy (10 mol%), H_2O (2.0 mL), CH_3SO_3H (5 equiv), 100 °C, 24 h, air, isolated yield.

The efficiency of this catalytic system was further demonstrated by running the transformation on a laboratory preparative scale. For example, the tandem reaction of 2-(naphthalen-2-ylamino)benzonitrile with (4-chlorophenyl)boronic acid was performed on a gram scale (4.19 mmol), and **3zq** was obtained in 84% isolated yield (Scheme 2). Furthermore, the utility of this methodology was further applied to the synthesis of 4-(benzo[*b*]acridin-12-yl)phenol (**3zr**), which showed estrogenic biological activity.[16]

Scheme 2 Gram-scale synthesis of 3zq and subsequent hydroxylation



Scheme 3 Control experiments

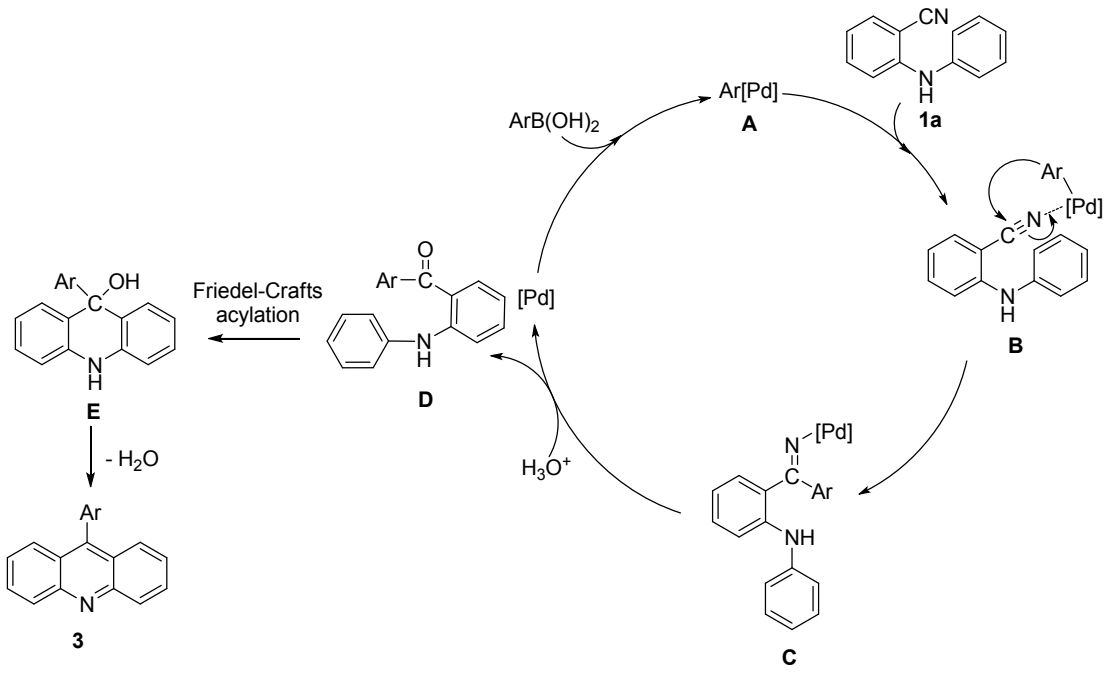


To gain some insight into the mechanism of this palladium-catalyzed addition/cyclization process, a set of control experiments were conducted. First, phenyl(2-(phenylamino)phenyl)methanone (**3a-1**) was obtained in 85% yield when the model reaction was performed without methanesulfonic acid (Scheme 3a), indicating that the ketone **3a-1** might be an intermediate in the current transformation. Furthermore, the reaction of **3a-1** under methanesulfonic acid condition could afford cyclized acridine **3a** in 83% yield (Scheme 3b), indicating the reaction may involve a Friedel-Crafts procedure. These results showed that the palladium catalyst is essential

for the formation of intermediate **3a-1**, and the acid is crucial for further Friedel-Crafts cyclization. Furthermore, the 2-(phenylamino)benzonitrile **1a** remained unchanged under the standard conditions in the absence of phenyl boronic acid with no simple acridine **3zs** formed (Scheme 3c), indicating that the palladium-aryl species which generated from the transmetalation process derived from the Pd(II) catalyst and arylboronic acid is essential to the transformation. To further prove the reaction mechanism may involve intramolecular Friedel-Crafts procedure, meta-substituted starting materials (**1zt** and **1zu**) were investigated (Scheme 3d). These two reactions showed interesting regioselectivities and led to a mixture of products, i.e., **3zt** and **3zt'** as well as **3zo** and **3zu**, in total yields of 88% and 87%, respectively. These results show that cyclization favors the higher electron density carbon of the Ar_1 ring for the formation of acridines, which is consistent with the rules of Friedel-Crafts acylation.

On the basis of the above mentioned results and relevant reports in the literature, a plausible mechanism for this palladium-catalyzed addition/cyclization reaction is shown in Scheme 4. First, palladium-aryl species **A** is generated from the transmetalation process derived from the Pd(II) catalyst and arylboronic acid. Thereafter, functionalized nitrile **1a** coordinated to Pd[Ar] to afford the intermediate **B**, which undergoes an intramolecular insertion of the cyano group to yield the corresponding ketimine palladium complex **C**. The ketone intermediate **D** will be formed after the hydrolysis, accompanied by the regeneration of the Pd(II) species. The ketone intermediate **D** undergoes Friedel-Crafts acylation to afford **E**, which is followed by intramolecular dehydration to yield the desired product **3**.

Scheme 4 Proposed mechanism.



CONCLUSIONS

In summary, we have developed a new approach for the synthesis of 9-arylacridines by the Pd-catalyzed tandem reaction of 2-(arylamino)benzonitrile with arylboronic acids in water. This protocol provides an alternative synthetic pathway to access arylacridines compared with classical condensation reaction of diphenylamine derivatives. Moreover, this methodology was further extended to the synthesis of a 4'-OH derivative which shows estrogenic biological activity. Further efforts to extend this catalytic system to the preparation of other useful heterocyclic compounds are currently underway in our laboratories.

EXPERIMENTAL SECTION

General Methods. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz spectrometer (^{1}H at 500 MHz, ^{13}C at 125 MHz), using $CDCl_3$ and d_6-DMSO as the solvent at room temperature. Chemical shifts are given δ relative to TMS, and the coupling constants J are given in hertz. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. 2-Aminobenzonitriles derivatives were synthesized according to the literature.[17a] Column chromatography was performed using EM silica gel 60 (300−400 mesh).

General procedure for the synthesis of 9-arylacridines.

In a 25 mL Schlenk reaction tube, 2-aminobenzonitrile **1** (0.5 mmol), arylboronic acid **2** (0.75 mmol, 1.5 equiv.), Pd $(OAc)_2$ (0.025 mmol, 5 mol%), 2,2'-bipyridyl (0.05 mmol, 10 mol%) and methylsulphonic acid/ trifluoromethanesulfonic acid (2.5 mmol, 5.0 equiv) were dissolved in H_2O (2.0 mL). The heterogeneous reaction mixture was then heated at 100 °C (oil bath) with vigorous stirring for 24 hours. After the reaction equilibrium, the mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (1 × 10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The filtrate was concentrated in vacuo and purified by a silica gel packed flash chromatography column with hexane/ethyl acetate (20:1) as the eluent to afford the desired products **3**.

2-((3,5-Dimethylphenyl)amino)benzonitrile (**1ze**): White solid (270.8 mg, 61%). MP: 100-101 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.47 (m, 1H), 7.37-7.34 (m, 1H), 7.21-7.19

(m, 1H), 6.84-6.80 (m, 3H), 6.78 (s, 1H), 6.24 (brs, 1H), 2.31 (s, 6H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) 147.7, 139.9, 139.5, 134.0, 133.1, 126.2, 119.7, 119.1, 117.7, 114.5, 98.4, 21.5. HRMS calcd for $C_{15}H_{15}N_2^+$ $[M + H]^+$: 223.1230, found 223.1228. IR (cm^{-1}) 3313, 2220, 1600, 1504, 1453 ,1320, 1288, 1176, 859, 818, 752, 571, 538, 509, 480.

2-((3-(tert-Butyl)phenyl)amino)benzonitrile (**1zf**): White solid (295.0 mg, 59%). MP: 119-120 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.38-7.28 (m, 2H), 7.19-7.17 (m, 3H), 7.05-7.03 (m, 1H), 6.84-6.80 (m, 1H), 6.34 (brs, 1H), 1.33 (s, 9H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) 153.3, 147.8, 139.7, 134.0, 133.1, 129.3, 121.6, 119.1, 119.0, 118.9, 117.8, 114.1, 98.3, 34.9, 31.4. HRMS calcd for $C_{17}H_{19}N_2^+$ $[M + H]^+$: 251.1543, found 251.1546. IR (cm^{-1}) 3315, 2959, 2227, 1603, 1574, 1454, 1296, 747, 704, 498, 491.

2-(Naphthalen-2-ylamino)benzonitrile (**1zk**): White solid (278.2 mg, 57%). MP: 117-118 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86-7.81 (m, 2H), 7.75-7.73 (m, 1H), 7.60 (s, 1H), 7.55-7.53 (m, 1H), 7.50-7.46 (m, 1H), 7.44-7.38 (m, 2H), 7.34-7.29 (m, 2H), 6.90-6.87 (m, 1H), 6.53 (brs, 1H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) 147.3, 137.6, 134.3, 134.1, 133.3, 130.8, 129.7, 127.9, 127.2, 126.9, 125.2, 122.0, 119.7, 117.7, 117.6, 114.6, 99.0. HRMS calcd for $C_{17}H_{13}N_2^+$ $[M + H]^+$: 245.1073, found 245.1080. IR (cm^{-1}) 3312, 3050, 2220, 1600, 1503, 1453, 1288, 1048, 817, 752, 572, 480.

4-Methyl-2-(phenylamino)benzonitrile (**1zl**): White solid (212.2 mg, 51%). MP:

122-123 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.35 (m, 3H), 7.20-7.12 (m, 3H), 7.01 (s, 1H), 6.68-6.66 (m, 1H), 6.27 (brs,1H), 2.29 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 147.4, 145.2, 140.2, 132.9, 129.7, 124.2, 121.9, 120.7, 118.0, 114.7, 96.0, 22.3. HRMS calcd for $C_{14}H_{13}N_2^+$ [M + H]$^+$: 209.1073, found 209.1075. IR (cm^{-1}) 3304, 2960, 2223, 1597, 1569, 1494, 1286, 804, 743, 693, 523, 480.

5-Methyl-2-(phenylamino)benzonitrile (**1zm**): White solid (237.1 mg, 57%). MP: 88-89 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.31 (m, 3H), 7.21-7.14 (m, 4H), 7.10-7.07 (m, 1H), 6.21 (brs, 1H), 2.27 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 145.0, 140.8, 135.0, 132.9, 129.7, 129.4, 123.7, 121.0, 117.8, 115.2, 99.2, 20.3. HRMS calcd for $C_{14}H_{13}N_2^+$ [M + H]$^+$: 209.1073, found 209.1075. IR (cm^{-1}) 3342, 2924, 2213, 1597, 1575, 1482, 1312, 815, 745, 696, 492, 488.

4-Chloro-2-(phenylamino)benzonitrile (**1zn**): White solid (264.5 mg, 58%). MP: 114-115 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.39 (m, 3H), 7.22-7.20 (m, 3H), 7.11-7.10 (m, 1H), 6.80 (dd, J = 8.3 Hz, J = 1.9 Hz, 1H), 6.40 (brs, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): 148.8, 140.8, 139.0, 134.0, 130.0, 125.5, 123.0, 119.5, 117.0, 113.8, 96.6. HRMS calcd for $C_{13}H_{10}ClN_2^+$ [M + H]$^+$: 229.0527, found 229.0529. IR (cm^{-1}) 3315, 3031, 2228, 1870, 1491, 1425, 1178, 1074, 930, 852, 798, 736, 518, 502, 471, 424.

2-(m-Tolylamino)benzonitrile (**1zt**): White solid (253.8 mg, 61%). MP: 88-89 °C.

Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.39-7.35 (m, 1H), 7.28-7.20 (m, 1H), 7.22-7.20 (m, 1H), 7.02-7.01 (m, 2H), 6.97-6.95 (m, 1H), 6.86-6.82 (m, 1H), 6.33 (brs, 1H), 2.36 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 147.6, 140.0, 139.8, 134.0, 133.1, 129.5, 125.2, 122.6, 119.2, 119.0, 117.7, 114.4, 98.6, 21.8. HRMS calcd for $C_{14}H_{13}N_2^+$ [M + H]$^+$: 209.1073, found 209.1075. IR (cm^{-1}) 3381, 2216, 1586, 1472, 1318, 1295, 1162, 787, 755, 691, 563, 407.

2-((3-Chlorophenyl)amino)benzonitrile (**1zv**): White solid (264.5 mg, 58%). MP: 114-115 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 40/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.52 (m, 1H), 7.45-7.41 (m, 1H), 7.30-7.24 (m, 2H), 7.20-7.19 (m, 1H), 7.09-7.04 (m, 2H), 6.94-6.89 (m, 1H), 6.31 (brs, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 146.4, 141.7, 135.4, 134.1, 133.3, 130.8, 124.1, 121.0, 120.5, 119.2, 117.4, 115.3, 99.9. HRMS calcd for $C_{13}H_{10}ClN_2^+$ [M + H]$^+$: 229.0527, found 229.0529. IR (cm^{-1}) 3325, 2221, 1590, 1571, 1416, 1323, 1184, 1093, 921, 879, 751, 699, 491.

9-Phenylacridine (**3a**): Yellow solid (118.6 mg, 93%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* =8.8 Hz, 2H), 7.80-7.76 (m, 2H), 7.72-7.70 (m, 2H), 7.61-7.58 (m, 3H), 7.46-7.41 (m, 4H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.9, 147.2, 136.0, 130.5, 129.9, 129.7, 128.5, 128.4, 126.9, 125.6, 125.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

Phenyl(2-(phenylamino)phenyl)methanone (**3a-1**): Yellow oil (116.0 mg, 85%).

Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.14 (brs, 1H), 7.73-7.71 (m, 2H), 7.58-7.55 (m, 2H), 7.51-7.47 (m, 2H), 7.40-7.30 (m, 6H) 7.13-7.09 (m, 1H) ,6.74-6.70 (m, 1H) ; ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 199.3, 148.2, 140.7, 140.0, 135.1, 134.4, 131.5, 129.6, 129.5, 128.3, 123.7, 122.4, 119.9, 116.7, 114.8. HRMS calcd for $C_{19}H_{16}NO^{+}$ $[M + H]^{+}$: 274.1227, found 274.1229. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(p-Tolyl)acridine (**3b**): Yellow solid (118.4 mg, 88%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29（d, *J* = 8.7 Hz, 2H）, 7.79-7.74 (m, 4H), 7.44-7.32 (m, 4H), 7.34-7.32 (m, 2H), 2.53 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) 148.8, 147.9, 138.4, 133.0, 130.5, 130.2, 129.6, 129.3, 127.1, 125.7, 125.5, 21.5. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(m-Tolyl)acridine (**3c**): Yellow solid (115.7 mg, 86%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.8 Hz, 2H), 7.80-7.72 (m, 4H), 7.51-7.48 (m, 1H), 7.45-7.38 (m, 3H), 7.25-7.23 (m, 2H), 2.48 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.7, 148.0, 138.3, 136.0, 131.2, 130.3, 129.5, 129.3, 128.5, 127.7, 127.2, 125.7 ,125.4, 21.6. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(o-Tolyl)acridine (**3d**): Yellow solid (68.6 mg, 51%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d,

J = 8.8 Hz, 2H), 7.80-7.76 (m, 2H), 7.55-7.53 (m, 2H), 7.49-7.38 (m, 5H), 7.25-7.23 (m, 1H), 1.88 (s, 3H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 149.0, 147.3, 137.1, 135.7, 130.4, 130.4, 130.2, 129.8, 128.8, 126.7, 126.0, 125.9, 125.3, 19.9. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(3,5-Dimethylphenyl)acridine (**3e**): Yellow solid (118.9 mg, 84%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* =8.6 Hz, 2H), 7.77-7.74 (m, 4H), 7.43-7.40 (m, 2H), 7.20 (s, 1H), 7.05 (s, 2H), 2.43 (s, 6H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.9, 148.0, 138.1, 136.0, 130.1, 130.0, 129.7, 128.3, 127.2, 125.6, 125.4, 21.5. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(2-Isopropylphenyl)acridine (**3f**): Yellow solid (54.9 mg, 37%). MP: 185-186°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35-8.34 (m, 2H), 7.81-7.78 (m, 2H), 7.59-7.56 (m, 4H), 7.44-7.37 (m, 3H), 7.18-7.16 (m, 1H), 2.30-2.25 (m, 1H), 0.99-0.98 (m, 6H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.0, 135.2, 134.8, 134.2, 130.9, 130.6, 130.3, 129.3, 129.2, 127.1, 126.0, 125.9, 125.9, 30.8, 24.2. HRMS calcd for $C_{22}H_{20}N^+$ $[M + H]^+$: 298.1590, found 298.1592. IR (cm^{-1}) 3060, 2963, 1929, 1668, 1629, 1557, 1541, 1345, 1010, 957, 767, 751, 652, 619, 421.

9-(4-(tert-Butyl)phenyl)acridine (**3h**): Yellow solid (136.8 mg, 88%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30-8.28 (m, 2H), 7.79-7.76 (m, 4H), 7.62-7.60 (m, 2H), 7.44-7.41 (m, 2H), 7.39-7.37 (m, 2H), 1.43 (s, 9H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 151.5,

148.9, 147.8, 133.0, 130.4, 130.1, 129.7, 127.2, 125.6, 125.5, 125.4, 35.0, 31.6. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Isopropylphenyl)acridine (**3i**): Yellow solid (132.2 mg, 89%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.3 Hz, 2H), 7.79-7.75 (m, 4H), 7.47-7.40 (m, 4H), 7.37-7.35 (m, 2H), 3.10-3.07 (m, 1H), 1.40 (d, J = 6.9 Hz, 6H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 149.2, 148.9, 147.8, 133.3, 130.6, 130.1, 129.7, 127.2, 126.6, 125.6, 125.5, 34.2, 24.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Methoxyphenyl)acridine (**3j**): Yellow solid (79.8 mg, 56%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.9 Hz, 2H), 7.77-7.76 (m, 4H), 7.43-7.40 (m, 2H), 7.37-7.36 (m, 2H), 7.13 (d, J = 8.3 Hz, 2H), 3.94 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 159.9, 149.1, 147.3, 131.9, 130.0, 129.8, 128.2, 127.1, 125.7, 125.6, 114.1, 55.6. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(3-Fluorophenyl)acridine (**3k**): Yellow solid (131.0 mg, 96%). MP: 160-161 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 2H), 7.82-7.78 (m, 2H), 7.69 (d, J = 8.5 Hz, 2H),7.61-7.56 (m, 1H), 7.48-7.44 (m, 2H), 7.32-7.29 (m, 1H), 7.24-7.23 (m, 1H), 7.20-7.17 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) 163.0 (C-F, $^{1}J_{C\text{-}F}$=248 Hz),

148.6, 138.2, 130.5, 130.4 (C-F, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 130.3, 126.6, 126.3 (C-F, $^{4}J_{C\text{-}F}$ = 3.06 Hz), 126.4, 125.1, 117.8 (C-F, $^{2}J_{C\text{-}F}$ =21.9 Hz), 115.7 (C-F, $^{2}J_{C\text{-}F}$ = 20.8 Hz). HRMS calcd for $C_{19}H_{12}FNNa^{+}$ $[M + Na]^{+}$: 296.0852, found 296.0822. IR (cm^{-1}) 3038, 1610, 1494, 1432, 1359, 1228, 1151, 978, 865, 783, 748, 707, 595, 531, 443.

9-(3-Chlorophenyl)acridine (**3l**): Yellow solid (141.6 mg, 98%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.8 Hz, 2H),7.81-7.77 (m, 2H), 7.67 (d, *J* = 8.7 Hz, 2H), 7.59-7.55 (m, 2H),7.53-7.44 (m, 3H), 7.35-7.33 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.8, 138.0, 134.8, 130.6, 130.3, 130.0, 129.8, 128.8, 128.8, 126.6, 126.2, 125.1. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(3-Bromophenyl)acridine (**3m**): Yellow solid (149.9 mg, 90%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.8 Hz, 2H), 7.81-7.77 (m, 2H), 7.74-7.72 (m, 1H), 7.68-7.66 (d, *J* = 8.4 Hz, 2H), 7.62-7.61 (m, 1H), 7.51-7.42 (m, 3H), 7.40-7.38 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.7, 145.5, 138.3, 133.4, 131.7, 130.3, 130.2, 129.8, 129.3, 126.6, 125.1, 122.9. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(2-Chlorophenyl)acridine (**3n**): Yellow solid (109.8 mg, 76%). MP: 233-234 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 7.81-7.77 (m, 2H), 7.61-7.65 (m, 1H), 7.56-7.43 (m, 6H), 7.36-7.34 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.9,

144.3, 135.1, 134.3, 132.2, 130.2, 130.2, 130.1, 130.0, 127.0, 126.4, 126.2, 125.1. HRMS calcd for $C_{19}H_{13}ClN^+$ [M + H]$^+$: 290.0731, found 290.0737. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(2-Bromophenyl)acridine (**3o**): Yellow solid (100.0 mg, 62%). MP: 234-235 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 2H), 7.85 (d, J = 7.2 Hz, 1H), 7.81-7.77 (m, 2H), 7.55-7.51 (m, 3H), 7.47-7.43 (m, 3H), 7.34 (dd, J = 1.6 Hz, J = 7.5 Hz, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) 148.9, 145.8, 137.3, 133.2, 132.1, 130.3, 130.2, 129.9, 127.6, 126.4, 126.2, 124.9, 124.2. HRMS calcd for $C_{19}H_{13}BrN^+$ [M + H]$^+$: 334.0226, found 334.0330. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Fluorophenyl)acridine (**3p**): Yellow solid (128.3 mg, 94%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.7 Hz, 2H), 7.80-7.77 (m, 2H), 7.68 (d, J = 8.6 Hz, 2H), 7.46-7.41 (m, 4H), 7.33-7.30 (m, 2H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 163.0 (C-F, $^1J_{C\text{-}F}$ = 247.9 Hz), 149.0, 146.1, 132.3 (C-F, $^3J_{C\text{-}F}$ = 8.1 Hz), 132.0 (C-F, $^4J_{C\text{-}F}$ = 3.4 Hz), 131.1, 129.9, 126.7, 126.0, 125.4, 115.8 (C-F, $^2J_{C\text{-}F}$ = 21.5 Hz). Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Chlorophenyl)acridine (**3q**): Yellow solid (132.9 mg, 92%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.7 Hz, 2H), 7.80-7.76 (m, 2H), 7.67 (d, J = 8.4 Hz, 2H),

7.61-7.58 (m, 2H), 7.47-7.42 (m, 2H), 7.40-7.37 (m, 2H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.9, 145.8, 134.8, 134.6, 132.0, 130.1, 129.9, 129.0, 126.6, 126.0, 125.1. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Bromophenyl)acridine (**3r**): Yellow solid (156.5 mg, 94%). MP: 244-245 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.8 Hz, 2H), 7.80-7.74 (m, 4H), 7.67 (d, J = 8.7 Hz, 2H), 7.46-7.42 (m, 2H), 7.32 (d, J = 8.2 Hz, 2H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.8, 145.9, 135.0, 132.3, 131.9, 130.3, 129.8, 126.6, 126.1, 125.1, 123.0. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(4-Iodophenyl)acridine (**3s**): Yellow solid (175.3 mg, 92%). MP: 238-239 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J= 8.8 Hz, 2H), 7.98-7.97 (m, 2H), 7.82-7.79 (m, 2H), 7.70-7.69 (m, 2H), 7.49-7.46 (m, 2H), 7.19-7.18 (m, 2H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 137.9, 135.2, 132.3, 131.2, 131.1, 128.7, 126.7, 126.4, 125.0, 95.0. HRMS calcd for $C_{19}H_{13}IN^{+}$ $[M + H]^{+}$: 382.0087, found 382.0088. IR (cm^{-1}) 2928, 2250, 1722, 1551, 1263, 1054, 1027, 1006, 752, 705, 490.

9-(4-(Trifluoromethyl)phenyl)acridine (**3t**): Yellow solid (100.1 mg, 62%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 7.82-7.78 (m, 2H), 7.62-7.58 (m, 4H), 7.48-7.44 (m, 2H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) 148.8, 145.5,

140.1, 131.1 (C-F, $^{2}J_{C\text{-}F}$ = 32.2 Hz), 131.9, 130.3, 129.9, 126.3 (C-F, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 125.7 (C-F, $^{3}J_{C\text{-}F}$ = 5.4 Hz), 125.0, 124.3 (C-F, $^{1}J_{C\text{-}F}$ = 272.3 Hz), 121.0. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

(2-(Phenylamino)phenyl)(4-(trifluoromethyl)phenyl)methanone (**3t-1**): Yellow oli (54.6 mg, 32%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (brs, 1H), 7.80-7.74 (m, 4H), 7.46-7.44 (m, 1H), 7.41-7.36 (m, 4H), 7.32-7.30 (m, 2H), 7.16-7.12 (m, 1H), 6.72-6.68 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) 198.0, 148.9, 143.3, 140.2, 135.1, 135.0, 132.9 (C-F, $^{2}J_{C\text{-}F}$ = 32.8 Hz), 129.6, 129.5, 125.4 (C-F, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 124.2, 123.9 (C-F, $^{1}J_{C\text{-}F}$ = 272.7 Hz), 122.9, 118.8, 116.7, 114.8. HRMS calcd for $C_{20}H_{15}F_3NO^+$ [M + H]$^+$: 342.1100, found 342.1108.

9-(Naphthalen-2-yl)acridine (**3v**): Yellow solid (131.2 mg, 86%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 8.3 Hz, 1H), 8.03-8.01 (m, 1H), 7.95-7.91 (m, 2H), 7.81-7.73 (m, 4H), 7.64-7.61 (m, 2H), 7.56 (d, J = 8.4 Hz, 1H), 7.43-7.40 (m, 2H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.9, 147.4, 133.6, 133.3, 133.2, 130.2, 129.9, 129.8, 128.4, 128.3, 128.3, 128.1, 127.1, 127.0, 126.9, 125.9, 125.5. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

9-(thiophen-3-yl)acridine (**3w**): Yellow solid (37.8 mg, 29%). MP: 182-183°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.80-7.76 (m, 2H), 7.63-7.61 (m, 1H), 7.48-7.44 (m, 3H), 7.27 (dd, *J* = 4.9 Hz, *J* = 1.1 Hz, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 148.9, 142.8, 135.9, 130.3, 130.2, 129.8, 126.8, 126.2, 126.0, 125.9, 125.8. HRMS calcd for $C_{17}H_{12}NS^+$ $[M + H]^+$: 262.0685, found 262.0688. IR (cm^{-1}) 3037, 2928, 1723, 1600, 1551, 1514, 1459, 1422, 1273, 1181,1030, 762, 751, 704, 491, 477, 438.

4-(acridin-9-yl)benzaldehyde (**3z**): Yellow solid (14.2 mg, 10%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 10.21 (brs, 1H), 8.30 (d, *J* = 8.9 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 7.81-7.77 (m, 1H), 7.65-7.59 (m, 4H), 7.47-7.43 (m, 2H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 191.9, 148.8, 145.5, 142.7, 136.4, 131.4, 130.3, 130.0, 129.9, 126.3, 124.7, 121.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

4-Methyl-9-phenylacridine (**3zc**): Yellow solid (125.1 mg, 93%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.8 Hz, 1H), 7.77-7.73 (m, 1H), 7.69-7.66 (m, 1H), 7.62-7.54 (m, 5H), 7.45-7.41 (m, 3H), 7.33-7.29 (m, 1H), 3.01 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 148.5, 148.2, 147.0, 137.5, 136.7, 130.6, 130.4, 129.5, 129.3, 128.5, 128.3, 126.8, 125.6, 125.5, 125.2, 125.1, 125.0, 18.8. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

2-Methyl-9-phenylacridine (**3zd**): Yellow solid (121.0 mg, 90%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500

MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.8 Hz, 1H), 8.19 (d, *J* = 8.9 Hz, 1H), 7.74-7.70 (m, 1H),7.67-7.64 (d, *J* = 8.7 Hz, 1H), 7.61-7.56 (m, 4H), 7.43-7.36 (m, 4H), 2.43 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 148.4, 147.9, 146.1, 136.3, 135.5, 132.9, 130.6, 129.7, 129.5, 128.5, 128.3, 126.8, 125.6, 125.4, 125.2, 124.8, 22.1. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

1,3-Dimethyl-9-phenylacridine (**3ze**): Yellow solid (127.3 mg, 90%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 1H), 7.94 (s, 1H), 7.72-7.68 (m, 1H), 7.53-7.51 (m, 3H), 7.43-7.41 (m, 1H), 7.37-7.32 (m, 3H), 7.08 (s, 1H), 2.52 (s, 3H), 1.99 (s, 3H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 150.5, 147.9, 147.0, 140.0, 139.9, 135.8, 132.0, 130.3, 129.7, 129.1, 128.1, 128.0, 127.5, 127.2, 126.3, 125.1, 123.1, 24.8, 21.8. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

3-(tert-Butyl)-9-phenylacridine (**3zf**): Yellow solid (146.2 mg, 94%). MP: 150-151 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.7 Hz, 1H), 8.22-8.21 (m, 1H), 7.77-7.73 (m, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.59-7.56 (m, 3H), 7.54-7.51 (m, 1H), 7.44-7.37 (m, 3H), 1.46 (s, 9H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 153.3, 149.3, 149.0, 146.8, 136.2, 130.6, 129.9, 129.5, 128.5, 128.4, 126.9, 126.5, 125.4, 125.3, 125.1, 124.2, 123.6, 35.4, 31.0. HRMS calcd for $C_{23}H_{22}N^+$ $[M + H]^+$: 312.1747, found 312.1760. IR (cm^{-1}) 3051, 2966, 1612, 1542, 1416, 1351, 1264, 1071, 1013, 957, 821, 737, 736, 640, 612, 564, 491, 433, 407.

2-Methoxy-9-phenylacridine (**3zg**): Yellow solid (131.1 mg, 92%). MP: 153-154 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 8.7 Hz, 1H), 8.16 (d, J = 9.4 Hz, 1H), 7.69-7.65 (m, 1H), 7.62-7.53 (m, 4H), 7.45-7.34 (m, 4H), 6.80-6.79 (m,1H), 3.69 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 157.0, 147.3, 146.1, 144.7, 136.4, 131.3, 130.4, 129.7, 128.8, 128.7, 128.3, 126.4, 126.0, 125.8, 125.5, 125.0, 102.1, 55.3. HRMS calcd for $C_{20}H_{16}NO^+$ $[M + H]^+$: 286.1227, found 286.1228. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

2-Fluoro-9-phenylacridine (**3zh**): Yellow solid (110.6 mg, 81%). MP: 192-193°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.91 (m, 2H), 7.44-7.40 (m, 1H), 7.35 (d, J = 8.7 Hz, 1H), 7.29-7.21 (m, 4H), 7.12-7.08 (m, 3H), 6.96-6.93 (m, 1H), ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 159.8 (C-F, $^{1}J_{C\text{-}F}$ = 248.9 Hz), 148.5 (C-F, $^{4}J_{C\text{-}F}$ = 2.1 Hz), 146.6 (C-F, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 146.4, 135.8, 132.6 (C-F, $^{3}J_{C\text{-}F}$ = 9.1 Hz), 130.4, 129.9, 128.8, 128.7, 126.5 (C-F, $^{2}J_{C\text{-}F}$ = 32.8 Hz, 125.5 (C-F, $^{3}J_{C\text{-}F}$ = 9.5 Hz), 125.4, 121.8 (C-F, $^{3}J_{C\text{-}F}$ = 9.5 Hz), 108.9, 108.7. HRMS calcd for $C_{19}H_{12}FNNa^+$ $[M + Na]^+$: 296.0852, found 296.0822. IR (cm^{-1}) 3062, 2923, 1635, 1451, 1156, 999, 861, 753, 600, 580, 490.

2-Chloro-9-phenylacridine (**3zi**): Yellow solid (121.4 mg, 84%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (dd, J = 8.8 Hz, J = 18.5 Hz, 2H), 7.80-7.76 (m, 1H), 7.69-7.66 (m, 3H), 7.64-7.54 (m, 3H), 7.46-7.41 (m, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.8, 147.0, 146.0, 146.8, 135.4, 131.7, 131.4, 131.3, 130.5, 129.7, 128.8, 128.8,

127.0, 126.4, 125.6, 125.6, 125.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

2-Bromo-9-phenylacridine (**3zj**): Yellow solid (143.2 mg, 86%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* =8.8 Hz, 1H), 8.15 (d, *J* = 9.2 Hz, 1H), 7.85-7.84 (m, 1H), 7.81-7.76 (m, 2H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.64-7.60 (m, 3H), 7.45-7.41 (m, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 148.9, 147.1, 146.7, 135.3, 133.7, 131.4, 130.5, 129.7, 128.9, 128.8, 128.7, 128.6, 127.0, 126.4, 126.1, 125.5, 120.1. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

12-Phenylbenzo[*b*]*acridine* (**3zk**): Yellow solid (129.6 mg, 85%). MP: 204-205 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.6 Hz, 1H), 8.07-8.05 (m, 1H), 7.95-7.93 (m, 1H), 7.83-7.78 (m, 2H), 7.68-7.61 (m, 4H), 7.49-7.40 (m, 5H), 7.17-7.13 (m, 1H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 150.1, 147.1, 146.7, 140.0, 133.3, 133.0, 130.7, 130.0, 129.8, 129.6, 129.1, 128.9, 128.7, 128.6, 127.1, 127.0, 126.0, 126.9, 126.4, 126,1, 122,3. HRMS calcd for $C_{23}H_{16}N^{+}$ $[M + H]^{+}$: 306.1277, found 306.1279. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

3-Methyl-9-phenylacridine (**3zl**): Yellow solid (129.5 mg, 93%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* =8.7 Hz, 1H), 8.05 (s, 1H), 7.76-7.72 (m, 1H), 7.69-7.67 (m, 1H), 7.61-7.56 (m, 4H), 7.43-7.36 (m, 3H), 7.25-7.23 (m, 1H), 2.59 (s, 3H);

$^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 149.3, 149.0, 146.9, 140.4, 136.2, 130.5, 129.9, 129.6, 128.6, 128.5, 128.4, 128.1, 126.9, 126.6, 125.3, 124.9, 123.6, 22.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

2-Methyl-9-phenylacridine (**3zm**): Yellow solid (118.4 mg, 88%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 8.8 Hz, 1H), 8.19 (d, J = 8.9 Hz, 1H), 7.74-7.70 (m, 1H), 7.67-7.64 (d, J = 8.7 Hz, 1H), 7.61-7.56 (m, 4H), 7.43-7.36 (m, 4H), 2.43 (s, 3H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.4, 147.9, 146.1, 136.3, 135.5, 132.9, 130.6, 129.7, 129.5, 128.5, 128.3, 126.8, 125.6, 125.4, 125.2, 124.8, 22.1. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

2-Chloro-9-phenylacridine (**3zn**): Yellow solid (135.8 mg, 94%). MP: 148-149°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (dd, J = 8.8 Hz, J = 18.5 Hz, 2H), 7.80-7.76 (m, 1H), 7.69-7.66 (m, 3H), 7.64-7.54 (m, 3H), 7.46-7.41 (m, 3H); $^{13}C\{^{1}H\}$NMR (125 MHz, $CDCl_3$) δ 148.8, 147.0, 146.0, 146.8, 135.4, 131.7, 131.4, 130.5, 129.7, 128.8, 128.8, 127.0, 126.4, 125.6, 125.6, 125.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

3-Chloro-9-phenylacridine (**3zo**): Yellow solid (127.2 mg, 88%). MP: 192-193°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 2.2 Hz, 1H), 8.25-8.23 (m, 1H), 7.80-7.76 (m, 1H), 7.70-7.58 (m, 5H), 7.45-7.41 (m, 3H), 7.36-7.33 (m, 1H); $^{13}C\{^{1}H\}$NMR (125 MHz,

$CDCl_3$) δ 149.5, 148.9, 147.7, 136.3, 135.6, 130.7, 130.5, 129.7, 128.7, 128.7, 128.5, 128.2, 127.1, 126.1, 125.3, 123.7. HRMS calcd for $C_{19}H_{13}ClN^+$ $[M + H]^+$: 290.0731, found 290.0753. IR (cm^{-1}) 3057, 1631, 1472, 1433, 1343, 1271, 1226, 1165, 1026, 866, 824, 756, 749, 601, 472.

5-Phenylbenzo[b][1,8]naphthyridine (**3zp**): Yellow solid (24.3 mg, 19%). MP: 182-183°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 9.26-9.25 (m, 1H), 8.41 (d, J = 8.3 Hz, 1H), 8.11-8.03 (m, 1H), 7.84-7.80 (m, 1H), 7.75-7.73 (m, 1H), 7.63-7.60 (m, 3H), 7.50-7.46 (m, 1H), 7.44-7.42 (m, 2H), 7.37-7.34 (m, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 155.8, 154.3, 150.6, 149.7, 136.4, 135.0, 131.1, 130.6, 130.5, 128.9, 128.8, 126.8, 126.6, 125.7, 121.1, 120.0. HRMS calcd for $C_{18}H_{13}N_2^+$ $[M + H]^+$: 257.1073, found 256.1081. IR (cm^{-1}) 3037, 2928, 1723, 1600, 1551, 1514, 1459, 1422, 1273, 1181, 1030, 762, 751, 704, 491, 477, 438.

12-(4-Chlorophenyl)benzo[b]acridine (**3zq**): Yellow solid (1.19 g, 85%). MP: 143-144 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.3 Hz, 1H), 8.06-8.03 (m, 1H), 7.95-7.93 (m, 1H), 7.85-7.79 (m, 2H), 7.66-7.64 (m, 2H), 7.58-7.48 (m, 4H), 7.38-7.30 (m, 2H), 7.24-7.20 (m, 1H); $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$) δ 150.1, 147.2, 144.8, 138.4, 134.6, 133.0, 132.9, 131.0, 130.3, 130.0, 129.8, 129.2, 129.1, 129.0, 128.4, 127.2, 126.6, 126.5, 126.4, 126.2, 122.1. HRMS calcd for $C_{19}H_{13}ClN^+$ $[M + H]^+$: 340.0888, found 340.0888. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

4-(Benzo[b]acridin-12-yl)phenol (**3zr**): White solid (133.2 mg, 83%). MP: 143-144 °C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.94 (brs, 1H), 8.24-8.22 (m, 1H), 8.10-8.07 (m, 1H), 7.98-7.95 (m, 2H), 7.89-7.85 (m, 1H), 7.64-7.53 (m, 4H), 7.27-7.20 (m, 3H), 7.10-7.08 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 157.6, 149.5, 146.8, 146.5, 132.9, 132.5, 130.2, 130.1, 129.9, 129.3, 129.1, 128.9, 128.7, 127.9, 127.2, 126.7, 126.6, 126.3, 126.2, 121.7, 116.7. HRMS calcd for $C_{23}H_{16}NO^{+}$ $[M + H]^{+}$: 322.1227, found 322.1227. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

3-Methyl-9-phenylacridine (**3zt**): Yellow solid (129.5 mg, 93%). Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J =8.7 Hz, 1H), 8.05 (s, 1H), 7.76-7.72 (m, 1H), 7.69-7.67 (m, 1H), 7.61-7.56 (m, 4H), 7.43-7.36 (m, 3H), 7.25-7.23 (m, 1H), 2.59 (s, 3H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ 149.3, 149.0, 146.9, 140.4, 136.2, 130.5, 129.9, 129.6, 128.6, 128.5, 128.4, 128.1, 126.9, 126.6, 125.3, 124.9, 123.6, 22.2. Spectroscopic data for the title compound were consistent with those reported in the literature.[17]

1-Chloro-9-phenylacridine (**3zu**): Yellow solid (24.6 mg, 17%). MP: 182-183°C. Column chromatography on silica gel (Eluent: hexane/ethyl acetate, 20/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 8.7 Hz, 2H), 7.79-7.75 (m, 1H), 7.65-7.61 (m, 1H), 7.55-7.48 (m, 5H), 7.42-7.38 (m, 1H), 7.37-7.34 (m, 2H); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$) δ 149.8, 148.4, 147.2, 138.2, 131.3, 130.8, 130.3, 130.1, 129.3, 129.2, 129.0,

128.2, 127.8, 127.5, 127.0, 126.4, 122.4. HRMS calcd for $C_{19}H_{13}ClN^+$ $[M + H]^+$: 290.0731, found 290.0753. IR (cm^{-1}) 3055, 2923, 1926, 1513, 1472, 1440, 1122, 750, 705, 490, 468, 427.

ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra for all products. This material is available free of charge on the ACS Publications website.

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Notes

The authors declare no competing financial interest.

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