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PhI(OAc)$_2$-Mediated Intramolecular Oxidative Aryl-Aldehyde Csp^2–Csp^2 Bond Formation: Metal-Free Synthesis of Acridone Derivatives

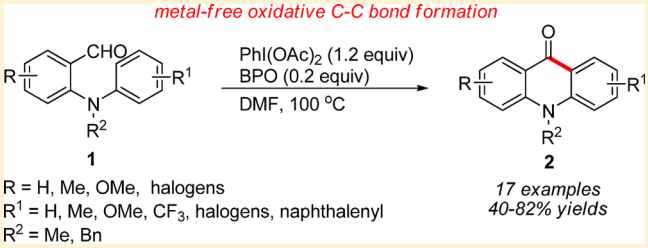
Zisheng Zheng,[†] Longyang Dian,[†] Yucheng Yuan,[†] Daisy Zhang-Negrerie,[†] Yunfei Du,*[,†,‡] and Kang Zhao*[,†]

[†]Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China

[‡]Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300072, China

Supporting Information

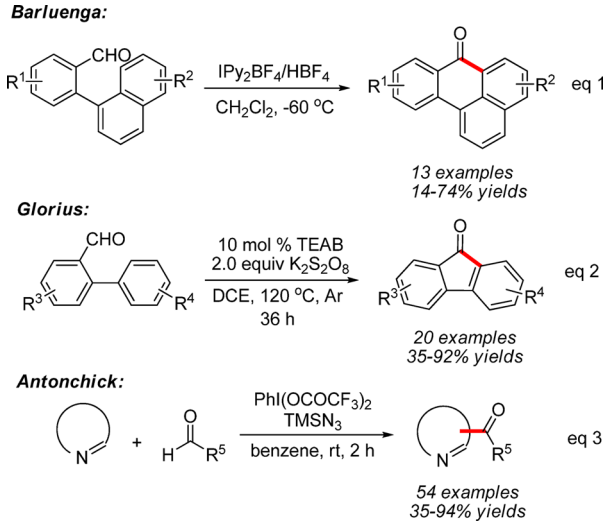
ABSTRACT: A metal-free protocol for direct aryl-aldehyde Csp^2–Csp^2 bond formation via a PhI(OAc)$_2$-mediated intramolecular cross-dehydrogenative coupling (CDC) of various 2-(*N*-arylamino)aldehydes was developed. The novel methodology requires no need of preactivation of the aldehyde group, is applicable to a large variety of functionalized substrates, and most of all provides a convenient approach to the construction of biologically important acridone derivatives.



INTRODUCTION

During the past decade, C–H activation has gained considerable attention in constructing C–C bonds in organic chemistry.[1] One of the recent advancement is the emergence of cross-dehydrogenative coupling (CDC), which has proven to be an even more powerful and atom-economic approach to C–C bond formation.[2] Among them, CDC between an aromatic C–H bonds and aldehyde C–H bonds has offered an economic approach to produce cyclic[3]/diaryl ketones[4] and other heterocycles, including indoline-2,3-diones,[5] xanthones,[3c,6] and acridones.[7] For examples, Cheng and co-workers pioneered in developing a Pd-catalyzed cross-coupling of 2-arylpyridines, using dioxygen as oxidant, with benzaldehydes to give aromatic ketones.[4a] Li and co-workers reported a solvent-free oxidative coupling of 2-arylpridines with aliphatic aldehydes by TBHP in the presence of Pd as a catalyst.[4b] Later on, other transition metal-catalyzed coupling reactions involving substrates with different directing groups for the direct C–H bond acylation were described.[4c−f,5,6] However, one drawback persisting throughout the reported transformations was the requirement of a transition metal as catalyst,[3c,4a−f,5−7] until less than a decade ago when metal-free strategies started being explored.[3a,b,4g] In 2006, Barluenga reported the synthesis of cyclic ketones by the reaction of direct intramolecular arylation of aldehydes with IPy$_2$BF$_4$/HBF$_4$ (Scheme 1, eq 1).[3a] In 2013, Glorius described the synthesis of fluorenones via quaternary ammonium salt-promoted intramolecular dehydrogenative arylation of aldehydes by dual C–H functionalization employing potassium persulfate ($K_2S_2O_8$) as oxidant (Scheme 1, eq 2).[3b] In the meantime, Antonchick reported a CDC of heterocycles with aldehydes utilizing hypervalent iodine reagent (PhI(OCOCF$_3$)$_2$) as oxidant and trimethylsilyl azide (TMSN$_3$) as additive (Scheme 1, eq 3).[4g]

Scheme 1. Reported Metal-Free Transformations of Aldehydes to Form Arylated Ketones



In 2013, Yang reported Sc(OTf)$_3$-catalyzed dehydrogenative cyclization of 2-(*N*-methyl-*N*-phenylamino)benzaldehydes **1** in forming an active intermediate, *N*-methyl-aridin-9-ol, which is then quickly oxidized in situ to afford acridones **2** (Scheme 2).[7] However, there are still some limitations with this transition metal-catalyzed annulation, such as exclusion of moisture, and heavy metal residue in drug development. It is notable that metal-free approaches to the constructions of acridone derivatives via intramolecular aryl-aldehyde Csp^2–Csp^2 formation

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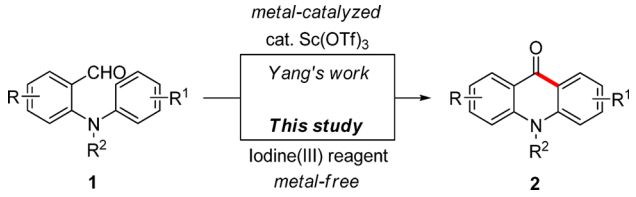
Scheme 2. Reported and Designed Routes for the Formation of 2 via CDC Reactions

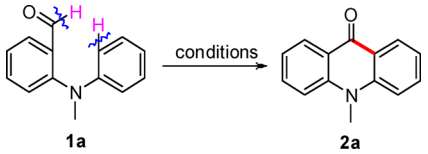


have never been reported. Herein, we disclose the result of such an approach, with $PhI(OAc)_2$ as oxidant, which has resulted in a convenient assemblage of the biologically important acridone[7−11] **2** skeletons.

RESULTS AND DISCUSSION

We applied Antonchick's condition[4g] in our initial study on the readily available substrate, 2-(methyl(phenyl)amino)benzaldehyde[7] **1a** (Table 1, entry 1), prepared via Ullmann condensation of benzoic acid and aniline, followed by *N*-functionalization, LAH-reduction and subsequent IBX-oxidation; however, no desired product was detected. Subsequent studies showed that Glorius' conditions[3b] only provided a very poor yield of only 5% of the acridone product **2a**. To our delight, by switching the oxidant to $PhI(OAc)_2$, **2a** was furnished in a much improved yield of 43% (an overall yield of 20% due to a 47% conversion of the starting material) (Table 1, entry 2). On the other hand, other types of hypervalent iodine oxidants, such as PhIO (iodosobenzene), IBX (2-iodoxybenzoic acid), or DMP (Dess−Martin periodinane), led to either sluggish reactions or no conversion even though under the same conditions. An attempt to improve the reactive efficiency by having the reactive iodine(III) species generated in situ via oxidation of aryl iodide with peracetic acid was proven to be unsuccessful.[12] Among the solvents tested, DMF (Table 1, entry 3) was shown to be the most effective in comparison to MeCN, EtOAc, toluene, and $CHCl_3$ etc. (results are not shown). Protic solvents, e.g., alcohols such as MeOH, trifluoroethanol (TFE), and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), or acids such as AcOH, and trifluoroacetic acid (TFA), led to no desired product (not shown). Further study indicated that the reaction performance was improved by increasing the dosage of the oxidant (Table 1, entries 3−4), though the yield was still fairly low due to incomplete conversion of the substrate. The conversion rate was not improved either by employing Chang's protocol,[13] which might be due to the low thermo-stability of the hypervalent iodine reagents at the reaction temperature.[12,14] A slightly improved yield was obtained after lowering the reaction temperature to 100 °C and extending the reaction time to 24 h (Table 1, entries 5−6). Various additives, including $BF_3{\cdot}Et_2O$,[15a] TfOH,[15b] Ac_2O, TEA,[15c] NaOH,[15d] Na_2CO_3,[15e] Na_2SO_4,[7] $Cu(OTf)_2$,[15f] TBAI,[15g] and 4 Å MS were tested out, among which Na_2SO_4 was proven to be the most effective (Table 1, entry 7; others were not shown), even though the actual cause of this difference was still unknown.[7] A paper by Caddick et al. in 2010 which discussed the involvement of a radical initiator to facilitate an aldehyde auto-oxidation as the method for C−H functionalization,[16] inspired us to employ their strategy to our reaction. The overall yields were indeed dramatically improved, with either benzoyl peroxide (BPO) (Table 1, entry 8) or azobis(isobutyronitrile) (AIBN) (Table 1, entry 9) added as additive, mainly due to the much improved conversion rate of the starting material to almost completion. On the other hand, without the oxidant $PhI(OAc)_2$, even with excess of BPO in the reaction mixture, almost no conversion of the starting substrate occurred, even after 24 h of heating (Table 1, entry 10). Further minute improvement of the yield was observed with a decreased amount of the oxidant as well as that of the additive (Table 1, entries 8, 11−12). The yield

Table 1. Optimization of Reaction Conditions[a]



entry	oxidant (equiv)	solvent	additive (equiv)	temperature (°C)	time (h)	conc. (mol/L)	yield[b] (%)
1	$PhI(OCOCF_3)_2$ (2)	benzene	NaN_3 (2)	rt	2	0.13	n.d.
2	$PhI(OAc)_2$ (1.5)	DCE	–	80	12	0.1	20 (43)
3	$PhI(OAc)_2$ (1.5)	DMF	–	80	12	0.1	30 (61)
4	$PhI(OAc)_2$ (3)	DMF	–	80	12	0.1	40 (67)
5[c]	$PhI(OAc)_2$ (3)	DMF	–	140	4	0.1	36 (70)
6	$PhI(OAc)_2$ (3)	DMF	–	100	24	0.1	51 (73)
7[c,e]	$PhI(OAc)_2$ (3)	DMF	Na_2SO_4 (0.5)	100	24	0.1	54 (75)
8	$PhI(OAc)_2$ (3)	DMF	BPO (1)	100	24	0.1	77
9	$PhI(OAc)_2$ (3)	DMF	AIBN (1)	100	24	0.1	73
10	–	DMF	BPO (3)	100	24	0.1	5
11	$PhI(OAc)_2$ (1.2)	DMF	BPO (1)	100	24	0.1	81
12	***$PhI(OAc)_2$ (1.2)***	***DMF***	***BPO (0.2)***	***100***	***24***	***0.1***	***81***
13[d]	$PhI(OAc)_2$ (1.2)	DMF	BPO (0.2)	100	24	0.1	70 (78)
14[e]	$PhI(OAc)_2$ (1.2)	DMF	BPO (0.2)	100	24	0.1	64 (75)
15	$PhI(OAc)_2$ (1.2)	DMF	BPO (0.2)	100	24	0.2	72
16	$PhI(OAc)_2$ (1.2)	DMF	BPO (0.2)	100	24	0.05	76

[a]Reaction conditions: **1a** (0.5 mmol), oxidant and additive in solvent, under air, unless otherwise stated. [b]Isolated yields. [c]Reaction performed in a sealed tube. [d]Under O_2 atmosphere. [e]Under N_2 atmosphere. rt = room temperature, n.d. = not detected, BPO = benzoyl peroxide. Values in parentheses indicate yields based on converted starting material.

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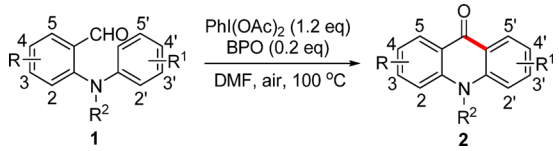
slightly decreased if the reaction was conducted under oxygen or nitrogen atmosphere (Table 1, entries 13−14). However, either more concentrated or diluted the reaction mixture negatively affected the yield (Table 1, entries 12, 15−16).

With the optimized reaction conditions established (Table 1, entry 12), the scope of the newly discovered oxidative aryl-aldehyde Csp^2−Csp^2 bond formation reaction was investigated (Table 2). It was found that both electron-withdrawing

Table 2. Oxidative Dehydrogenative Cyclization of Aldehyde Substrates 1 to Acridone Derivatives 2[a]



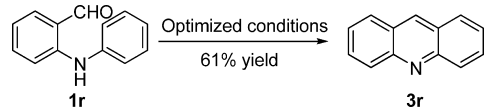
1 2

entry	product no.	R	R^1	R^2	time (h)	yield (%)[b]
1	**2a**	H	H	Me	24	81
2	**2b**	H	3′-CF_3	Me	>72	60(66)
3	**2c**	H	3′-Br	Me	48	70
4	**2d**	H	4′-F	Me	36	58
5	**2e**	H	4′-Cl	Me	48	60
6	**2f**	H	4′-Br	Me	24	80
7	**2g**	H	4′-OMe	Me	48	52
8	**2h**	H	4′-Me	Me	24	75
9	**2i**	H	2′-Me	Me	>72	60(73)
10	**2j**	H	naphthalenyl	Me	60	49
11	**2k**	3-Cl	H	Me	24	55
12	**2l**	4-F	H	Me	24	57
13	**2m**	4-OMe	H	Me	36	49
14	**2n**	4-Me	H	Me	24	82
15	**2o**	3-Cl	4′-Br	Me	12	63
16	**2p**	4-Me	4′-Me	Me	24	40
17	**2q**	H	H	Bn	12	74

[a]Reaction conditions: **1** (0.5 mmol), $PhI(OAc)_2$ (0.6 mmol) and BPO (0.1 mmol) in DMF (5.0 mL, c = 0.1 M) at 100 °C, under air. [b]Isolated yields. Values in parentheses indicate yields based on recovered starting material.

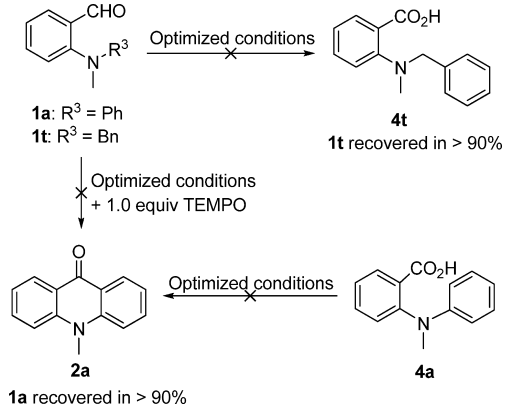
(**2b**−**f**) and electron-donating (**2g**−**i**) R^1 groups were tolerated. Reactions of substrates **1b** and **1i** were sluggish and the starting material was not consumed completely, probably due to the strong electron-withdrawing effect of the trifluoromethyl group in the former and the *ortho* position of the substituent in the latter which blocked 50% of the bonding spot. The *para*-methoxy substituted substrate **1g** provided a relatively lower yield under the identical condition.[17] It is worth noting that 2-(methyl(naphthalen-1-yl)- amino)benzaldehyde **1j** also afforded the cyclized product, albeit with prolonged reaction time and a lower yield. However, *meta*-nitro substituted substrate **1s** did not afford any cyclized product (not shown in Table 2). The substitution effect of R group on the aryl ring with the formyl group attached was then examined. It was found that both electron-withdrawing (**2k** and **2l**) and electron-donating substituents (**2m** and **2n**) were well tolerated, with methyl group giving the highest yield, methoxy the lowest,[17] and the halogens in between. With electron-withdrawing group substituted on both aryl rings, substrate **1o** successfully cyclized into the corresponding acridone product **2o** in 63% yield. However, when the electron-withdrawing group was replaced with the electron-donating group, i.e., methyl group, the desired acridone product **2p** was obtained in a decreased 40% yield (Table 2, entry 16). Finally, the substitution effect of R^2 group, the benzyl protected diarylamine substrate **1q** likewise afforded the corresponding product (**2q**) in very good yield. However, as for the diarylamine substrate **1r**, dehydration was occurred to furnish the acridine product **3r** in 61% yield (Scheme 3).[18]

Scheme 3. Dehydration of 2-Phenylaminobenzaldehyde 1r to Afford Acridine 3r under the Optimized Conditions



1r 3r

Scheme 4. Investigation of the Mechanistic Pathway for the Dehydrogenative Cyclization



To explore the reaction mechanism, control experiments were conducted under the optimized conditions (Scheme 4). The reaction of 2-(benzyl(methyl)amino)benzaldehyde **1t** with $PhI(OAc)_2$/BPO gave no corresponding acid product **4t**. Meanwhile, when 2-(methyl(phenyl)amino)benzoic acid **4a** was subjected to the optimized reaction conditions, it did not generate the cyclized acridone product **2a**. These two experimental facts demonstrated that the cyclization did not undergo the oxidation, followed by classical Friedel−Crafts reaction, but they suggested the involvement of an acyl radical. Additional support rose from the results of running the reaction in the presence of a radical scavenger TEMPO,[3b,c] which showed complete inhibition of the conversion.[19]

A mechanism entailing a radical pathway has been proposed for this cyclization reaction (Scheme 5). Initiation occurs at the heating of BPO with the formation of benzoyloxy radical **A**, which may react with iodosobenzene diacetate **B** to generate radical **C**[4g,20] along with $PhCO_2OAc$. H-abstraction by radical **C** of the −CHO hydrogen then takes place and generates acyl radical **D**[21] which subsequent breaks a π-bond and generates the cyclohexadienyl radical **E**.[3b,c,22] Finally, a second H-abstraction takes place by radical **B** of the hydrogen connected to the sp^3-carbon, through which aromaticity is regained, leading to the final product **2**. Alternatively, single electron oxidation of radical **E** by **B** or radical **C** gives cation **F**, which is deprotonated by the formed acetate anion to give the cyclized product **2**.[3b] The proposed mechanism depicts the important roles of the catalytic amount of BPO as a radical initiator as well as the stoichiometric amount of $PhI(OAc)_2$,[23] both of which are in total agreement with our experimental observations.

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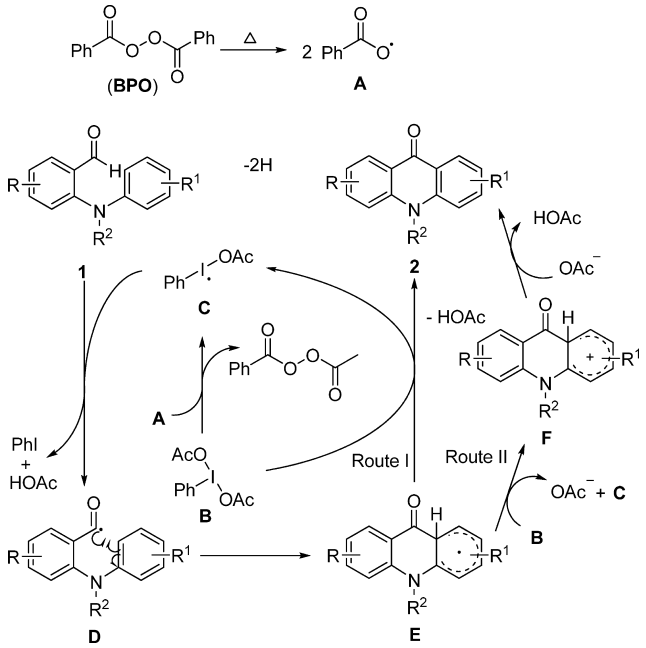
Scheme 5. Proposed Mechanism for the Dehydrogenative Cyclization

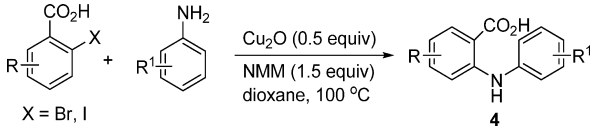


In summary, we have developed an intramolecular cross-dehydrogenative coupling (CDC) reaction of various 2-(*N*-arylamino)aldehydes via $PhI(OAc)_2$-promoted oxidative coupling between an aldehyde sp^2-carbon and an aromatic sp^2-carbon. This reaction tolerates various functional groups and proceeds efficiently to synthesize acridone derivatives with no additional base required. The reaction serves as a complement to classical Friedel–Crafts approaches and therefore expands the area in direct acylation reaction of aldehydes. Moreover, this is the first report on an oxidative C–C bond formation promoted by a combination of a radical initiator (BPO) and a hypervalent iodine(III) reagent.

EXPERIMENTAL SECTION

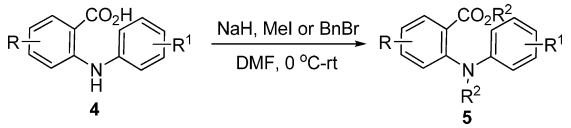
I. General Information. All reactions were conducted without precaution of air, and mixtures were stirred magnetically. ^1H and ^{13}C NMR spectra were recorded on a 600 MHz spectrometer at 25 °C. Chemical shift values are given in parts per million and referred to the internal standard, TMS (tetramethylsilane). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets; br s, broad singlet. The coupling constants (*J*) are reported in hertz. High-resolution mass spectrometry (HRMS) was conducted on a Q-TOF micro-spectrometer. Melting points were determined with a national micro-melting point apparatus without corrections. Reagents and solvents were purchased as reagent grade and were used without further purification. Flash column chromatography was performed over silica gel 200–300 mesh, and the eluent was a mixture of ethyl acetate and petroleum ether.

II. General Synthesis of the Substrate 1. *a. Preparation of Substituted N-Arylanthranilic Acid 4.*[24]



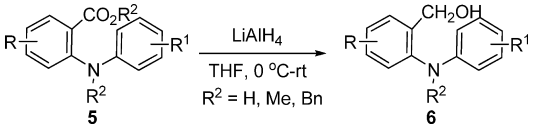
Substituted 2-halobenzoic acid (30 mmol), substituted aniline (36 mmol), *N*-methylmorpholine (45 mmol), and cuprous oxide (15 mmol) were heated to reflux in dioxane (75 mL) under nitrogen for 3 h. The reaction mixture was allowed to cool, and 200 mL of 1 N NaOH (aq.) was then added. The resulting mixture was extracted with DCM (100 mL), and the aqueous phase was acidified with 3 N HCl (aq.) to pH = 2. The precipitate was collected and dried in air overnight, which was used in the next step without further purification. (Note: *N*-phenylanthranilic acid **4r** (R = R^1 = H) was directly reduced into its corresponding alcohol **6r** using $LiAlH_4$, followed by oxidation to afford adehyde **1r** over three steps.)

b. Preparation of Substituted 2-Arylaminobenzoate 5.[7]



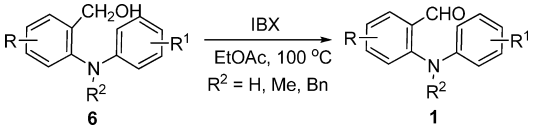
To a solution of substituted *N*-arylanthranilic acid **4** (15 mmol) in DMF (30 mL) was added NaH (60% in mineral oil, 45 mmol) portionwise, with cooling in an ice–water bath. The solution was stirred for 30 min, followed by the addition of methyl iodide/benzyl bromide (45 mmol). The resulting mixture was stirred at room temperature until TLC indicated the total consumption of the acid substrate **4**. The reaction mixture was poured into water (300 mL) and extracted with EtOAc (2 × 100 mL). The organic layer was separated, washed with water (150 mL) and brine (150 mL), and then dried over anhydrous Na_2SO_4. The solvent was evaporated, and the residue was purified through column chromatography on silica gel (EtOAc/Petroleum ether as eluent) to afford desired ester **5**, which was used in the next reduction step.

c. Reduction of Substituted 2-Arylaminobenzoate 5.[7]



A solution of *N*-phenylanthranilic acid **4r** (10 mmol) or substituted 2-arylaminobenzoate **5** (10 mmol) in anhydrous THF (40 mL) was added dropwise at 0 °C to a stirred solution of $LiAlH_4$ (15 mmol) in THF (10 mL). The resulting mixture was stirred at room temperature until TLC indicated the total consumption of the substrate **4r** or **5**. EtOAc (15 mL) and then water (10 mL) were added cautiously to the solution. After filtration and removal of the solvent, the residue was extracted with EtOAc (20 mL), and the organic phase was dried over anhydrous Na_2SO_4. The solvent was then evaporated to give the corresponding alcohol **6** as oil, which was used in the next oxidation step without further purification.

d. Preparation of the Aldehyde Substrate 1.[7]



To a suspension of IBX (12.5 mmol) in EtOAc (50 mL) was added a solution of alcohol **6** (5 mmol) in EtOAc (50 mL). The reaction mixture was heated at 100 °C for 3 h, cooled and filtered; the filtered solid was washed with EtOAc (2 × 5 mL). The combined filtrate and washings were evaporated under reduced pressure and purified by column chromatography on silica gel, eluting with petroleum ether, to give the desired aldehyde **1**. The aldehyde substrates **1** thus obtained were characterized as follows:

*2-(Methyl(phenyl)amino)benzaldehyde (**1a**).*[25] Following the general procedure, using 2-iodobenzoic acid and aniline as starting materials, **1a** was isolated as a yellow solid. Yield: 0.95 g, 41% (over four steps), mp 42–43 °C (lit.[26] 39.5–40.5 °C); ^1H NMR (600 MHz, $CDCl_3$) δ 10.14 (s, 1H), 7.94 (dd, 1H, *J* = 7.8, 1.8 Hz), 7.62 (td, 1H, *J* = 7.8, 1.8 Hz), 7.33 (t, 1H, *J* = 7.5 Hz), 7.25 (d, 1H, *J* = 8.4 Hz), 7.21–7.18 (m, 2H), 6.81 (t, 1H, *J* = 7.5 Hz), 6.72 (d, 2H, *J* = 7.8 Hz), 3.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.3, 152.0, 150.1, 135.8, 132.8, 129.3, 129.0, 127.7, 126.0, 119.1, 115.1, 41.6.

*2-(Methyl(3-(trifluoromethyl)phenyl)amino)benzaldehyde (**1b**).* Following the general procedure, using 2-iodobenzoic acid and 3-(trifluoromethyl)aniline as starting materials, **1b** was isolated as a yellow liquid. Yield: 1.10 g, 33% (over four steps); ^1H NMR (600 MHz,

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$CDCl_3$) δ 10.12 (s, 1H), 7.99 (d, 1H, J = 7.2 Hz), 7.69 (t, 1H, J = 7.5 Hz), 7.43 (t, 1H, J = 7.5 Hz), 7.28−7.25(m, 2H), 7.04 (d, 1H, J = 7.8 Hz), 6.94 (s, 1H), 6.79 (d, 1H, J = 8.4 Hz), 3.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.8, 150.7, 149.9, 136.3, 133.0, 131.6 (q, J = 31.5 Hz), 129.7, 129.5, 128.5, 127.2, 126.9, 124.2 (q, J = 271.5 Hz), 117.6, 115.1 (q, J = 3.5 Hz), 110.3 (q, J = 3.5 Hz), 41.4; HRMS (ESI) calcd for $C_{15}H_{12}F_3NNaO^+$ [M + Na^+] 302.0763, found 302.0760.

*2-((3-Bromophenyl)(methyl)amino)benzaldehyde (**1c**).* Following the general procedure, using 2-iodobenzoic acid and 3-bromoaniline as starting materials, **1c** was isolated as a yellow liquid. Yield: 1.23 g, 39% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.11 (s, 1H), 7.97 (d, 1H, J = 7.8 Hz), 7.67 (t, 1H, J = 7.5 Hz), 7.41 (t, 1H, J = 7.5 Hz), 7.26 (d, 1H, J = 7.8 Hz), 7.03 (t, 1H, J = 8.1 Hz), 6.92 (d, 1H, J = 7.8 Hz), 6.84 (s, 1H), 6.56 (dd, 1H, J = 8.4, 2.1 Hz), 3.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.9, 151.0, 150.9, 136.2, 133.0, 130.5, 129.3, 128.4, 127.0, 123.4, 121.6, 117.1, 113.2, 41.4; HRMS (ESI) calcd for $C_{14}H_{12}BrNNaO^+$ [M + Na^+] 311.9994, found 311.9998.

*2-((4-Fluorophenyl)(methyl)amino)benzaldehyde (**1d**).* Following the general procedure, using 2-iodobenzoic acid and 4-fluoroaniline as starting materials, **1d** was isolated as a yellow liquid. Yield: 1.01 g, 40% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.16 (s, 1H), 7.92 (d, 1H, J = 7.8 Hz), 7.62 (t, 1H, J = 7.8 Hz), 7.31 (t, 1H, J = 7.5 Hz), 7.23 (d, 1H, J = 7.8 Hz), 6.92 (t, 2H, J = 9.3 Hz), 6.72−6.70 (m, 2H), 3.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.2, 156.9 (d, J = 238.5 Hz), 152.3 146.8, 135.8, 132.1, 129.2, 126.8, 125.7, 117.2 (d, J = 7.5 Hz), 115.8 (d, J = 22.5 Hz), 42.2; HRMS (ESI) calcd for $C_{14}H_{12}FNNaO^+$ [M + Na^+] 252.0795, found 252.0796.

*2-((4-Chlorophenyl)(methyl)amino)benzaldehyde (**1e**).* Following the general procedure, using 2-iodobenzoic acid and 4-chloroaniline as starting materials, **1e** was isolated as a yellow solid. Yield: 1.04 g, 44% (over four steps), mp 58−59 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.12 (s, 1H), 7.95 (dd, 1H, J = 7.8, 1.8 Hz), 7.62 (td, 1H, J = 7.5, 2.1 Hz), 7.37 (t, 1H, J = 7.5 Hz), 7.25 (d, 1H, J = 7.8 Hz), 7.14 (d, 2H, J = 9.0 Hz), 6.63 (d, 2H, J = 9.0 Hz), 3.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.0, 151.4, 148.6, 136.0, 132.7, 129.3, 129.1, 127.9, 126.5, 124.0, 116.1, 41.7; HRMS (ESI) calcd for $C_{14}H_{12}{}^{35}ClNNaO^+$ [M + Na^+] 268.0500, found 268.0499.

*2-((4-Bromophenyl)(methyl)amino)benzaldehyde (**1f**).*[7] Following the general procedure, using 2-iodobenzoic acid and 4-bromoaniline as starting materials, **1f** was isolated as a light yellow solid. Yield: 1.29 g, 42% (over four steps), mp 85−86 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.11 (s, 1H), 7.95 (dd, 1H, J = 7.5, 0.9 Hz), 7.65 (t, 1H, J = 7.5 Hz), 7.38 (t, 1H, J = 7.5 Hz), 7.28 (d, 2H, J = 9.0 Hz), 7.25 (d, 1H, J = 8.4 Hz), 6.58 (d, 2H, J = 8.4 Hz), 3.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.0, 151.3, 149.0, 136.1, 132.8, 132.0, 129.3, 128.0, 126.6, 116.4, 111.2, 41.6.

*2-((4-Methoxyphenyl)(methyl)amino)benzaldehyde (**1g**).* Following the general procedure, using 2-iodobenzoic acid and 4-methoxyaniline as starting materials, **1g** was isolated as a red liquid. Yield: 1.11 g, 45% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.17 (s, 1H), 7.86 (dd, 1H, J = 7.8, 1.2 Hz), 7.57 (td, 1H, J = 7.8, 1.5 Hz), 7.22 (t, 1H, J = 7.2 Hz), 7.20 (d, 1H, J = 8.4 Hz), 6.79 (s, 4H), 3.76 (s, 3H), 3.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.4, 153.9, 152.9, 145.0, 135.4, 131.1, 129.0, 125.2, 124.4, 118.9, 114.8, 55.6, 42.5; HRMS (ESI) calcd for $C_{15}H_{15}NNaO_2^+$ [M + Na^+] 264.0995, found 264.0999.

*2-(Methyl(p-tolyl)amino)benzaldehyde (**1h**).*[7] Following the general procedure, using 2-iodobenzoic acid and 4-methylaniline as starting materials, **1h** was isolated as a yellow solid. Yield: 1.01 g, 42% (over four steps), mp 39−40 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.15 (s, 1H), 7.91 (d, 1H, J = 7.8 Hz), 7.60 (t, 1H, J = 8.4 Hz), 7.28 (t, 1H, J = 7.5 Hz), 7.23 (d, 1H, J = 7.8 Hz), 7.02 (d, 2H, J = 8.4 Hz), 6.68 (d, 2H, J = 8.4 Hz), 3.34 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.5, 152.5, 148.2, 135.7, 132.2, 129.9, 129.0, 128.9, 126.8, 125.4, 116.1, 41.9, 20.5.

*2-(Methyl(o-tolyl)amino)benzaldehyde (**1i**).* Following the general procedure, using 2-iodobenzoic acid and 2-methylaniline as starting materials, **1i** was isolated as a light yellow solid. Yield: 1.00 g, 39% (over four steps), mp 87−88 °C; ^{1}H NMR (600 MHz,$CDCl_3$) δ 10.02 (s, 1H), 7.75 (s, 1H), 7.46 (s, 1H), 7.20−6.97 (6H), 3.25 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.7, 153.5, 150.8, 134.7, 133.2, 132.0, 129.9, 127.5, 127.4, 125.1, 124.6, 121.6, 119.9, 43.1, 18.5; HRMS (ESI) calcd for $C_{15}H_{15}NNaO^+$ [M + Na^+] 248.1046, found 248.1050.

*2-(Methyl(naphthalen-1-yl)amino)benzaldehyde (**1j**).* Following the general procedure, using 2-iodobenzoic acid and naphthalen-1-amine as starting materials, **1j** was isolated as a yellow solid. Yield: 1.05 g, 36% (over four steps), mp 84−85 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.19 (d, 1H, J = 7.8 Hz), 7.85 (d, 1H, J = 7.2 Hz), 7.76 (d, 1H, J = 6.6 Hz), 7.62 (d, 1H, J = 8.4 Hz), 7.52−7.48 (m, 3H), 7.31 (t, 1H, J = 7.8 Hz), 7.15 (d, 1H, J = 8.4 Hz), 7.06 (t, 1H, J = 7.5 Hz), 6.99 (d, 1H, J = 7.2 Hz), 3.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.9, 154.0, 150.0, 135.3, 134.8, 129.6, 129.0, 128.9, 127.6, 126.8, 126.5, 126.1, 125.7, 123.1, 122.2, 121.9, 119.7, 43.4; HRMS (ESI) calcd for $C_{18}H_{15}NNaO^+$ [M + Na^+] 284.1046, found 284.1047.

*4-Chloro-2-(methyl(phenyl)amino)benzaldehyde (**1k**).*[7] Following the general procedure, using 2-bromo-4-chlorobenzoic acid and aniline as starting materials, **1k** was isolated as a yellow liquid. Yield: 1.03 g, 38% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.84 (d, 1H, J = 8.4 Hz), 7.24−7.21 (m, 4H), 6.88 (t, 1H, J = 7.2 Hz), 6.80 (d, 2H, J = 7.8 Hz), 3.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.0, 152.9, 149.9, 141.6, 130.4, 129.5, 126.9, 125.9, 120.4, 116.5, 41.8 (one carbon peak was missing due to overlapping).

*2-(Methyl(naphthalen-1-yl)amino)benzaldehyde (**1l**).*[7] Following the general procedure, using 2-bromo-5-fluorobenzoic acid and aniline as starting materials, **1l** was isolated as a orange solid. Yield: 0.99 g, 39% (over four steps), mp 55−56 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.08 (d, 1H, J = 3.0 Hz), 7.61 (dd, 1H, J = 7.8, 3.3 Hz), 7.34 (td, 1H, J = 8.1, 3.0 Hz), 7.25 (dd, 1H, J = 8.7, 4.5 Hz), 7.21 (t, 2H, J = 8.1 Hz), 6.82 (t, 1H, J = 7.2 Hz), 6.68 (d, 2H, J = 8.4 Hz), 3.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.3, 160.6 (d, J = 247.5 Hz), 149.9, 148.1 (d, J = 3.0 Hz), 134.7 (d, J = 7.5 Hz), 130.3 (d, J = 7.5 Hz), 129.4, 123.2 (d, J = 22.5 Hz), 119.1, 114.7, 114.7 (d, J = 22.5 Hz), 41.6.

*5-Methoxy-2-(methyl(phenyl)amino)benzaldehyde (**1m**).*[7] Following the general procedure, using 2-bromo-5-methoxybenzoic acid and aniline as starting materials, **1m** was isolated as a orange solid. Yield: 1.06 g, 40% (over four steps), mp 58−59 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.43 (d, 1H, J = 3.0 Hz), 7.24−7.16 (m, 4H), 6.78 (t, 1H, J = 7.2 Hz), 6.65 (d, 2H, J = 8.4 Hz), 3.87 (s, 3H), 3.31 (s, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ 191.5, 158.0, 150.2, 145.4, 134.2, 130.1, 129.2, 123.9, 118.3 114.0, 110.5, 55.8, 41.5.

*5-Methyl-2-(methyl(phenyl)amino)benzaldehyde (**1n**).*[7] Following the general procedure, using 2-bromo-5-methylbenzoic acid and aniline as starting materials, **1n** was isolated as a yellow liquid. Yield: 1.02 g, 43% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.12 (s, 1H), 7.76 (s, 1H), 7.45 (d, 1H, J = 7.8 Hz), 7.19 (t, 2H, J = 7.8 Hz), 7.15 (d, 1H, J = 8.4 Hz), 6.79 (t, 1H, J = 7.5 Hz), 6.69 (d, 2H, J = 8.4 Hz), 3.33 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.7, 150.1, 149.6, 136.9, 136.3, 132.7, 129.2, 128.9, 128.1, 118.7, 114.6, 41.5, 21.0.

*2-((4-Bromophenyl)(methyl)amino)-4-chlorobenzaldehyde (**1o**).* Following the general procedure, using 2-bromo-4-chlorobenzoic acid and 4-bromoaniline as starting materials, **1o** was isolated as a light yellow oil. Yield: 0.91 g, 28% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.86 (d, 1H, J = 8.4 Hz), 7.31 (d, 3H, J = 8.4 Hz), 7.23 (s, 1H), 6.63 (d, 2H, J = 9.0 Hz), 3.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.4, 152.2, 148.7, 141.7, 132.3, 130.7, 130.7, 127.4, 126.6, 117.5, 112.5, 41.7; HRMS (ESI) calcd for $C_{14}H_{11}{}^{79}Br^{35}ClNNaO^+$ [M + Na^+] 345.9605, found 345.9600.

*5-Methyl-2-(methyl(p-tolyl)amino)benzaldehyde (**1p**).* Following the general procedure, using 2-bromo-5-methylbenzaldehyde and 4-methylaniline as starting materials, **1p** was isolated as a light yellow oil. Yield: 0.72 g, 30% (over four steps); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.12 (s, 1H), 7.73 (s, 1H), 7.41 (d, 1H, J = 7.8 Hz), 7.13−7.11 (m, 1H), 6.99 (d, 2H, J = 6.6 Hz), 6.63−6.62 (m, 2H), 3.30 (s, 3H), 2.39 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.6, 150.1, 148.3, 136.6, 135.7, 132.4, 129.8, 128.9, 128.3, 127.4, 115.4, 41.7, 20.9, 20.4; HRMS (ESI) calcd for $C_{16}H_{17}NNaO^+$ [M + Na^+] 262.1202, found 262.1205.

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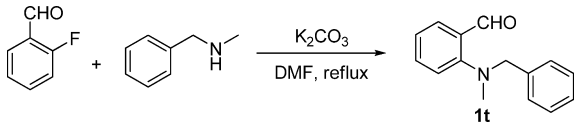
*2-(Benzyl(phenyl)amino)benzaldehyde (**1q**).*[27] Following the general procedure, using 2-iodobenzoic acid and aniline as starting materials, **1q** was isolated as a light yellow solid. Yield: 1.23 g, 44% (over four steps), mp 107−108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.13 (s, 1H), 7.92 (d, 1H, J = 8.4 Hz), 7.61 (t, 1H, J = 8.4 Hz), 7.36−7.28 (m, 6H), 7.24−7.22 (m, 1H), 7.16 (t, 2H, J = 7.8 Hz), 6.80 (t, 1H, J = 7.5 Hz), 6.74 (d, 2H, J = 8.4 Hz), 5.00 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.1, 150.6, 150.0, 138.1, 135.9, 132.9, 129.4, 129.4, 128.7, 128.4, 127.3, 127.2, 126.2, 119.4, 115.7, 57.7.

*2-(Phenylamino)benzaldehyde (**1r**).*[28] Following the general procedure, using 2-iodobenzoic acid and aniline as starting materials, **1r** was isolated as a yellow solid. Yield: 0.89 g, 56% (over three steps), mp 71−72 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.02 (s, 1H), 9.87 (s, 1H), 7.53 (d, 1H, J = 7.8 Hz), 7.36−7.32 (m, 3H), 7.26 (d, 2H, J = 7.8 Hz), 7.22 (d, 1H, J = 8.4 Hz), 7.13 (t, 1H, J = 7.5 Hz), 6.80 (t, 1H, J = 7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.3, 147.8, 139.7, 136.7, 135.6, 129.5, 124.4, 123.2, 119.4, 117.2, 112.9.

*2-(Methyl(3-nitrophenyl)amino)benzaldehyde (**1s**).* Following the general procedure, using 2-iodobenzoic acid and 3-nitroaniline as starting materials, **1s** was isolated as a orange solid. Yield: 1.07 g, 33% (over four steps), mp 83−84 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.00 (d, 1H, J = 7.8 Hz), 7.73 (t, 1H, J = 7.8 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.52 (s, 1H), 7.49 (t, 1H, J = 7.5 Hz), 7.32−7.28 (m, 2H), 6.91 (dd, 1H, J = 8.4, 2.4 Hz), 3.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.4, 150.4, 149.7, 149.3, 136.4, 133.0, 130.1, 129.8, 128.8, 127.7, 119.8, 113.0, 107.8, 41.4; HRMS (ESI) calcd for $C_{14}H_{12}N_2NaO_3^+$ [M + Na$^+$] 279.0740, found 279.0739.

*e. Preparation of the Aldehyde Substrate **1t**.*[29]

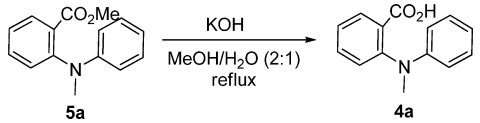


1t

To a solution of 2-fluorobenzaldehyde (1.24 g, 10 mmol) and potassium carbonate (1.59 g, 11.5 mmol) in DMF (10 mL) was added *N*-methyl-*N*-benzylamine (1.39 g, 11.5 mmol). The resulting reaction mixture was heated under reflux for 4 h. The reaction mixture was subsequently allowed to cool to room temperature, diluted with water (50 mL), and extracted with EtOAc (2 × 40 mL). The combined organic layers were washed with brine (50 mL) and subsequently dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica, eluting with petroleum ether, to afford the product **1t**.

*2-(Benzyl(methyl)amino)benzaldehyde (**1t**).*[29] Isolated as a light yellow liquid. Yield: 1.58 g, 70%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.39 (s, 1H), 7.82 (dd, 1H, J = 7.5, 1.5 Hz), 7.48 (td, 1H, J = 8.4, 1.5 Hz), 7.32 (t, 2H, J = 7.5 Hz), 7.28−7.25 (m, 3H), 7.10 (d, 1H, J = 8.4 Hz), 7.06 (t, 1H, J = 7.5 Hz), 4.33 (s, 2H), 2,81 (s, 3H).

III. Preparation of the Acid Substrate 4a.[30]

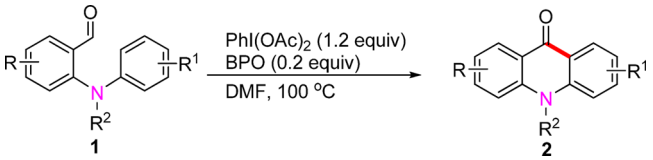


5a 4a

To a solution of methyl 2-(methyl(phenyl)amino)benzoate (0.72 g, 3 mmol) in MeOH/H_2O (15 mL, v:v = 2:1) was added KOH (0.34 g, 6 mmol). The resulting mixture was heated under reflux until TLC indicated the total consumption of substrate. The reaction mixture was subsequently allowed to cool to room temperature. The solvent was removed under vacuum. The residue was diluted with water (10 mL), and acidified with 3 N HCl (aq.) to pH = 2. The precipitate was collected and dried under reduced pressure to afford the desired acid **4a**.

*2-(Methyl(phenyl)amino)benzoic acid (**4a**).*[30] Isolated as a yellow solid. Yield: 0.63 g, 93%, mp 101−102 °C (lit.[30] 103−104 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 14.22 (s, 1H), 8.36 (dd, 1H, J = 8.4, 1.2 Hz), 7.58 (td, 1H, J = 8.1, 1.2 Hz), 7.45 (t, 1H, J = 7.5 Hz), 7.29 (t, 2H, J = 7.8 Hz), 7.12 (d, 1H, J = 7.8 Hz), 7.06 (t, 1H, J = 7.2 Hz), 6.92 (d, 2H, J = 8.4 Hz), 3.22 (s, 3H).

IV. Preparation of the Acridone Derivatives 2 and 3.



1 2

To a solution of aldehyde **1** (0.5 mmol) in DMF (5 mL) was added PIDA (0.6 mmol) and BPO (0.2 mmol). The resulting mixture was heated to 100 °C with vigorous stirring and maintained at the same temperature until TLC indicated the total consumption of the aldehyde substrate **1**. The reaction mixture was cooled to room temperature, diluted with water (25 mL) and then extracted with EtOAc (2 × 20 mL). The organic layers were combined, saturated with brine (20 mL), and dried over anhydrous Na_2SO_4. The solvent was then evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel, eluting with EtOAc and petroleum ether, to give the product **2**. The acridone derivatives **2** thus obtained were characterized as follows:

*10-Methylacridin-9(10H)-one (**2a**).*[7] Following the general procedure, **2a** was isolated as a light yellow solid. Yield: 85 mg, 81%, mp 203−204 °C (lit.[7] 202−203 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (dd, 2H, J = 7.8, 1.2 Hz), 7.73−7.71 (m, 2H), 7.52 (d, 2H, J = 9.0 Hz), 7.29 (t, 2H, J = 7.5 Hz), 3.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.0, 142.4, 133.7, 127.6, 122.4, 121.1, 114.7, 33.5.

*10-Methyl-3-(trifluoromethyl)acridin-9(10H)-one (**2b**).*[10h] Following the general procedure, **2b** was isolated as a light yellow solid. Yield: 83 mg, 60%, mp 195−196 °C (lit.[10h] 169−170 °C); ^{1}H NMR (600 MHz, d^6-DMSO) δ 8.49 (d, 1H, J = 8.4 Hz), 8.33 (dd, 1H, J = 7.8, 1.2 Hz), 8.13 (s, 1H), 7.91−7.85 (m, 2H), 7.59 (d, 1H, J = 7.8 Hz), 7.40−7.37 (m, 1H), 3.99 (s, 3H); ^{13}C NMR (150 MHz, d^6-DMSO) δ 176.1, 142.5, 142.0, 134.6, 133.3 (q, J = 31.5 Hz), 128.2, 126.5, 123.9 (q, J = 271.5 Hz), 123.4, 121.9, 121.9, 116.6 (q, J = 3.0 Hz), 116.5, 113.8 (q, J = 4.0 Hz), 34.1.

*3-Bromo-10-methylacridin-9(10H)-one (**2c**).*[10h] Following the general procedure, **2c** was isolated as a light brown solid. Yield: 101 mg, 70%, mp 177−178 °C (lit.[10h] 178−180 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, 1H, J = 7.8 Hz), 8.29 (d, 1H, J = 7.8 Hz), 7.65 (t, 1H, J = 7.5 Hz), 7.55 (s, 1H), 7.38 (d, 1H, J = 8.4 Hz), 7.30 (d, 1H, J = 7.8 Hz), 7.24 (t, 1H, J = 7.2 Hz), 3.73 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 143.0, 142.2, 134.0, 129.2, 128.9, 127.5, 124.6, 122.4, 121.7, 121.0, 117.7, 114.9, 33.7.

*2-Fluoro-10-methylacridin-9(10H)-one (**2d/l**).*[7] Following the general procedure, **2d** was isolated as a light yellow solid. Yield: 66 mg, 58%. **2l** was isolated as a light yellow solid. Yield: 65 mg, 57%, mp 185−186 °C (lit.[7] 179−180 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, 1H, J = 7.8 Hz), 8.04 (dd, 1H, J = 8.4, 2.4 Hz), 7.63 (t, 1H, J = 7.5 Hz), 7.38−7.31 (m, 3H), 7.20 (t, 1H, J = 7.2 Hz), 3.75 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 157.4 (d, J = 241.5 Hz), 142.1, 138.9, 133.9, 127.4, 123.1 (d, J = 6.0 Hz), 122.0 (d, J = 24.0 Hz), 121.5, 121.3, 116.9 (d, J = 7.5 Hz), 114.7, 111.7 (d, J = 21.0 Hz), 33.8.

*2-Chloro-10-methylacridin-9(10H)-one (**2e**).*[7] Following the general procedure, **2e** was isolated as a light brown solid. Yield: 73 mg, 60%, mp 176−177 °C (lit.[7] 175−176 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, 1H, J = 7.8 Hz), 8.41 (d, 1H, J = 2.4 Hz), 7.69 (t, 1H, J = 7.8 Hz), 7.55 (dd, 1H, J = 9.0, 2.4 Hz), 7.45 (d, 1H, J = 9.0 Hz), 7.38 (d, 1H, J = 9.0 Hz), 7.26 (t, 1H, J = 7.2 Hz), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.9, 142.3, 140.8, 134.1, 133.7, 127.7, 127.1, 126.7, 123.1, 122.2, 121.6, 116.6, 114.9, 33.8.

*2-Bromo-10-methylacridin-9(10H)-one (**2f**).*[7] Following the general procedure, **2f** was isolated as a light brown solid. Yield: 115 mg, 80%, mp 199−200 °C (lit.[7] 194−195 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, 1H, J = 1.8 Hz), 8.39 (d, 1H, J = 7.8 Hz), 7.65 (t, 1H, J = 7.5 Hz), 7.61 (dd, 1H, J = 9.0, 1.8 Hz), 7.39 (d, 1H, J = 8.4 Hz), 7.25−7.20 (m, 2H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 142.1, 141.0, 136.3, 134.1, 129.7, 127.5, 123.4, 122.2, 121.6, 116.8, 114.9, 114.5, 33.7.

*2-Methoxy-10-methylacridin-9(10H)-one (**2g/m**).*[7] Following the general procedure, **2g** was isolated as a light yellow solid. Yield: 62 mg,

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52%. **2m** was isolated as a light yellow solid. Yield: 59 mg, 49%, mp 141−142 °C (lit.[7] 141−142 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, 1H, J = 7.8 Hz), 7.91 (s, 1H), 7.66 (t, 1H, J = 7.5 Hz), 7.43 (t, 2H, J = 9.0 Hz), 7.31 (d, 1H, J = 9.0 Hz), 7.24 (t, 1H, J = 7.5 Hz), 3.92 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 154.3, 142.0, 137.3, 133.5, 127.6, 124.4, 123.0, 121.6, 120.9, 116.5, 114.6, 106.5, 55.8, 33.7.

*2,10-Dimethylacridin-9(10H)-one (**2h/n**).*[7] Following the general procedure, **2h** was isolated as a light yellow solid. Yield: 79 mg, 71%. **2n** was isolated as a light yellow solid. Yield: 91 mg, 82%, mp 151−152 °C (lit.[7] 150−151 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (d, 1H, J = 7.8 Hz), 8.29 (s, 1H), 7.65 (t, 1H, J = 7.5 Hz), 7.47 (d, 1H, J = 7.8 Hz), 7.42 (d, 1H, J = 9.0 Hz), 7.34 (d, 1H, J = 9.0 Hz), 7.23 (t, 1H, J = 7.2 Hz), 3.78 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.0, 142.3, 140.5, 135.2, 133.6, 130.8, 127.6, 126.9, 122.2, 122.2, 120.9, 114.8, 114.7, 33.5, 20.6.

*4,10-Dimethylacridin-9(10H)-one (**2i**).*[7] Following the general procedure, **2i** was isolated as a light brown solid. Yield: 67 mg, 60%, mp 85−86 °C (lit.[7] 86−87 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (dd, 1H, J = 7.8, 1.2 Hz), 7.32 (d, 1H, J = 7.8 Hz), 7.66 (t, 1H, J = 8.4 Hz), 7.48 (d, 1H, J = 7.2 Hz), 7.42 (d, 1H, J = 8.4 Hz), 7.23 (t, 1H, J = 7.2 Hz), 7.18 (t, 1H, J = 7.2 Hz), 3.85 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.1, 146.4, 145.5, 137.4, 133.7, 127.0, 126.4, 125.1, 125.1, 123.0, 122.1, 121.4, 116.5, 42.8, 23.1.

*12-Methylbenzo[c]acridin-7(12H)-one (**2j**).*[7] Following the general procedure, **2j** was isolated as a light brown solid. Yield: 63 mg, 49%, mp 173−174 °C (lit.[7] 141−142 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, 1H, J = 7.8 Hz), 8.40 (d, 1H, J = 8.4 Hz), 8.21 (d, 1H, J = 8.4 Hz), 7.86 (d, 1H, J = 7.8 Hz), 7.69 (t, 1H, J = 7.5 Hz), 7.60−7.55 (m, 3H), 7.49 (t, 1H, J = 7.5 Hz), 7.30 (t, 1H, J = 7.5 Hz), 4.07 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.7, 145.5, 144.0, 137.3, 133.3, 128.8, 128.2, 127.3, 126.8, 124.8, 124.6, 123.9, 123.2, 122.5, 122.4, 121.4, 117.3, 44.8.

*3-Chloro-10-methylacridin-9(10H)-one (**2k**).*[7] Following the general procedure, **2k** was isolated as a light yellow solid. Yield: 67 mg, 55%, mp 175−176 °C (lit.[7] 155−156 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, 1H, J = 7.2 Hz), 8.43 (d, 1H, J = 8.4 Hz), 7.69 (t, 1H, J = 7.8 Hz), 7.45 (d, 1H, J = 9.6 Hz), 7.28 (t, 1H, J = 6.6 Hz), 7.20 (d, 1H, J = 9.0 Hz), 3.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.3, 143.1, 142.4, 140.2, 134.1, 129.4, 127.7, 122.5, 121.9, 121.8, 120.8, 114.9, 114.7, 33.8.

*2-Bromo-6-chloro-10-methylacridin-9(10H)-one (**2o**).* Following the general procedure, **2o** was isolated as a light yellow solid. Yield: 102 mg, 63%, mp >250 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, 1H, J = 2.4 Hz), 8.44 (d, 1H, J = 8.4 Hz), 7.69 (dd, 1H, J = 9.0, 2.4 Hz), 7.50 (s, 1H), 7.38 (d, 1H, J = 9.6 Hz), 7.26−7.24 (m, 1H), 3.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.1, 143.1, 141.3, 140.7, 136.8, 130.2, 129.5, 123.9, 122.4, 120.9, 116.9, 115.2, 114.8, 34.0; HRMS (ESI) calcd for $C_{14}H_9BrClNNaO^+$ [M + Na^+] 343.9448, found 343.9447.

*2,7,10-Trimethylacridin-9(10H)-one (**2p**).* Following the general procedure, **2p** was isolated as a light yellow solid. Yield: 47 mg, 40%, mp 183−185 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (s, 2H), 7.51 (d, 2H, J = 8.4 Hz), 7.39 (d, 2H, J = 8.4 Hz), 3.84 (s, 3H), 2.46 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.9, 140.6, 135.0, 130.5, 127.1, 122.3, 114.6, 33.5, 20.6; HRMS (ESI) calcd for $C_{16}H_{15}NNaO^+$ [M + Na^+] 260.1046, found 260.1042.

*10-Benzylacridin-9(10H)-one (**2q**).*[10h] Following the general procedure, **2q** was isolated as a light yellow solid. Yield: 105 mg, 74%, mp 184−185 °C (lit.[10h] 178−181 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 (d, 2H, J = 7.8 Hz), 7.60 (t, 2H, J = 7.5 Hz), 7.36−7.26 (m, 7H), 7.19 (d, 2H, J = 7.2 Hz), 5.57 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.3, 142.5, 135.5, 134.1, 129.3, 127.8, 127.7, 125.7, 122.5, 121.7, 115.3, 50.8.

*Acridine (**3r**).*[9m] Following the general procedure, **3r** was isolated as a light yellow solid. Yield: 59 mg, 61%, mp 105−106 °C (lit.[9m] 105−108 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (d, 1H, J = 5.4 Hz), 8.24 (d, 2H, J = 8.4 Hz), 7.99−7.97 (m, 2H), 7.78 (t, 2H, J = 7.5 Hz), 7.52 (t, 2H, J = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.0, 136.2, 130.4, 129.4, 128.3, 126.6, 125.7; ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.0, 136.2, 130.4, 129.4, 128.3, 126.6, 125.7.

■ ASSOCIATED CONTENT

Supporting Information

Spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: duyunfeier@tju.edu.cn.

*E-mail: kangzhao@tju.edu.cn.

Notes

The authors declare no competing financial interest.

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