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A novel synthesis of acridones via iron(II)-catalyzed intramolecular acylation of *N*-phenylanthranilic acids

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Dedicated to Professor Hans-Günther (Hagga) Schmalz in celebration of his outstanding career and on the occasion of his retirement

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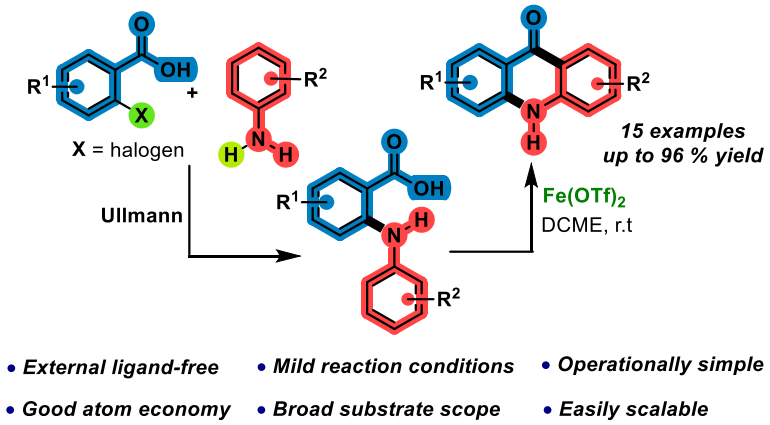
Abstract

A practical and efficient strategy for the synthesis of *N*–H acridones via intramolecular Friedel–Crafts-type cyclization of *N*-phenylanthranilic acids is reported. The reaction proceeds under mild, ligand-free conditions using a cooperative catalytic system comprising $Fe(OTf)_2$ and dichloromethyl methyl ether (DCME). This methodology features a broad substrate scope, providing functionalized acridones with high regioselectivity, very good to excellent yields, and high atom economy. The synthetic utility of the transformation is further demonstrated by the gram-scale preparation of a bioactive acridone with established antiviral activity.



Keywords: Synthesis, Acridones, Intramolecular acylation, Iron catalysis, DCME

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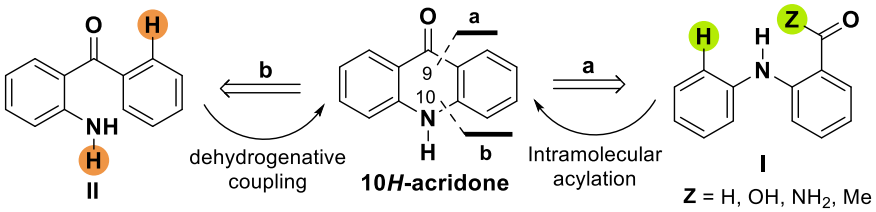
Introduction

Acridones are aromatic heterocyclic compounds derived from acridine, with a core structure based on 9(10*H*)-acridone. Their fused tricyclic framework is found in a wide range of natural and synthetic products, many of which demonstrate a wide biomedical potential due to their diverse mechanisms of action.[1] Numerous studies have documented their activity as antitumor, antiviral, antimicrobial, and anti-inflammatory agents.[2] Additionally, acridones serve as valuable building blocks in the development of organic semiconductors,[3,4] dyes, and fluorescent labels.[4-9] Due to their rigid framework and nitrogen donor atom, acridones are also attractive candidates as potential ligands or catalysts.[10,11] Consequently, significant efforts have been devoted to advancing new methods for their synthesis.

The basic 10*H*-acridin-9-one structure reveals that its precursors are of aromatic origin, and under appropriate reaction conditions, aromatic nucleophilic substitution followed by cyclization is feasible. Scheme 1 outlines the traditional retrosynthetic strategies to access the acridone framework, in which the C-C (**a**) and C-N (**b**) disconnections leading to the diarylamine (**I**) and 2-aminobenzophenone (**II**) precursors, respectively.



Scheme 1. Retrosynthetic analysis of access to the 10*H*-acridone scaffold.

In 2012, Deng et al. reported a methodology for intramolecular cyclization via copper-promoted C–H amination in oxidative media, resulting in C–N bond formation from 2-aminobenzophenones (path b).[12] Interestingly, Zhang's group developed a Cu(II)-mediated cascade reaction involving 2-aminoacetophenones (**II**) and arylboronic acids, which proceeds through the concurrent rearrangement of isatin intermediates (path a).[13] Zou introduced a metal-free alternative employing *t*-BuO$^-$K$^+$/DMSO and air as a coupling promoter system (path b).[14]

In 2013, Yang described the synthesis of acridones using Sc(OTf)$_3$ as a promoter for the intramolecular closure of 2-aminobenzaldehydes via C–H activation (path a).[15] Subsequently, Deng and Fu developed an alternative strategy using CuI under an oxygen atmosphere, starting from acetophenone as the precursor (path a).[16,17] More recently, our research group introduced a novel approach for the direct synthesis of acridones based on a palladium-catalyzed domino reaction. This strategy involves a tandem Buchwald–Hartwig amination followed by an arylative coupling reaction through cleavage of an aldehyde C–H bond, using commercially available 2-aminobenzaldehydes and 1,2-dihaloarenes as starting materials, all under ligand-free conditions (path a).[18] Additional synthetic routes to acridones have also been reported in related studies.

In recent years, numerous modern strategies have emerged to construct acridone scaffolds through C–H activation, oxidative coupling, or metal-free protocols. For example, Zhou and Dong reported an Ir(III)-catalyzed annulation of 2-phenyloxazoles with anthranils under atom-economical conditions via C–H amination.[19] Guo et al. developed a Pd-catalyzed oxidative carbonylation of diarylamines using Cr(CO)$_6$ as a carbon monoxide surrogate, enabling the preparation of acridones with broad functional group tolerance.[20] Askarzadeh and co-workers recently introduced a metal-free intramolecular Friedel–Crafts-type acylation of

phenylboronic acids under mild, green conditions.[21] Moreover, a recent comprehensive review by Yadav et al. highlights the biomedical relevance of acridone-based derivatives, particularly emphasizing their potential as anticancer agents and the structure–activity relationships governing their bioactivity.[22] These studies underscore the ongoing interest in developing efficient and sustainable acridone syntheses.

Despite the diversity of methods available for constructing the acridone framework, the cyclodehydration of *N*-phenylanthranilic acids remains the most straightforward and conceptually simple synthetic route (path a).[23-27]

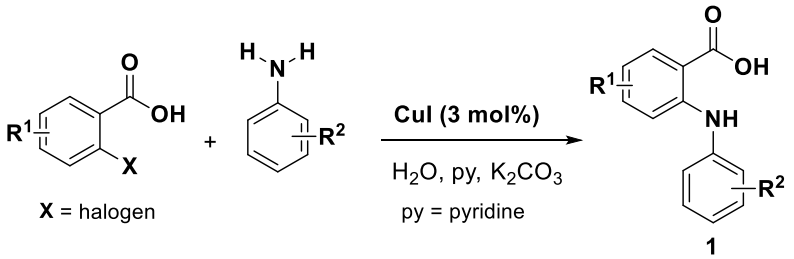
Although numerous synthetic strategies have been explored for the generation of acridone derivatives, most of these methods present several drawbacks, including high reaction temperatures, the use of strong acids, low yields, the high cost of metals, and sensitivity to air and humidity. Consequently, there is a need to develop a complementary reaction that can be conducted under mild and straightforward conditions.

Recent interest in using Fe^{+2}/Fe^{+3} salts as substitutes for noble transition metals in homogeneous catalysis has emerged, offering efficient alternatives that are highly abundant, low in toxicity, cost-effective, and environmentally friendly.[28-30]

The current study presents an alternative synthetic route for 10*H*-acridones synthesis under more efficient, greener, and eco-friendly conditions. This approach also relies on the intramolecular *ortho*-acylation of *N*-phenylanthranilic acids, employing $Fe(OTf)_2$ and DCME as the catalytic system, under mild and straightforward reaction conditions.

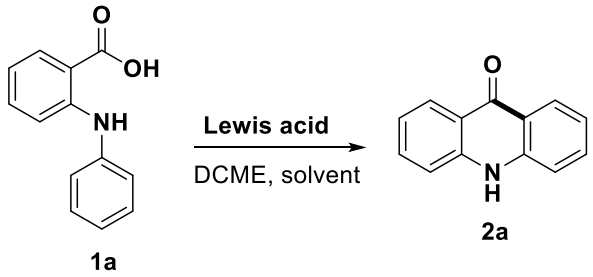
Results and Discussion

For several years, our research group has focused on the development of new sustainable methodologies for the synthesis of fused tricyclic heterocycles, such as xanthones,[18,31] acridones,[32] dibenzo[b,e]oxepinones,[33] and carbazoles.[34] Building on our previous experience, we initiated our studies by focusing on the synthesis of acridones, employing commercially available *N*-phenylanthranilic acid (**1a**) as a model substrate to optimize the reaction conditions. Some of the precursors **1** were obtained from commercial sources, while the remaining substrates were synthesized via modified Ullmann condensation protocols (see Supporting Information for experimental details). The reactions were carried out using CuI as the catalyst, water as the solvent, and a combination of K_2CO_3 and pyridine as cocatalysts, as depicted in Scheme 2.[35]



Scheme 2. Synthesis of *N*-phenylanthranilic acids *via* Ullmann coupling.

Table 1. Optimization of the reaction conditions[a]



1a **2a**

Entry	Lewis acid (mol%)	DCME (equiv)	Time (h)	Solvent	Yield (%)[b]
1	--	1.0	12	DCM	NR[d]
2	$SnCl_4$ (6)	1.0	12	DCM	12
3	$SnCl_2$ (6)	1.0	12	DCM	16
4	$AlCl_3$ (6)	1.0	12	DCM	9
5	$CuCl_2$ (6)	1.0	12	DCM	NR[c]
6	$ZnCl_2$ (6)	1.0	12	DCM	8
7	$FeBr_3$ (6)	1.0	12	DCM	trace
8	$FeCl_3$ (6)	1.0	12	DCM	trace
9	$FeCl_2$ (6)	1.0	12	DCM	45
10	$Zn(OTf)_2$ (6)	1.0	12	DCM	21
11	$Cu(OTf)_2$ (6)	1.0	12	DCM	35
12	$Fe(OTf)_2$ (6)	1.0	12	DCM	84
13	$Fe(OTf)_2$ (6)	1.0	12	DCM	84[d]
14	$Fe(OTf)_2$ (6)	--	12	DCM	NR[c]
15	$Fe(OTf)_2$ (6)	0.5	12	DCM	43
16	$Fe(OTf)_2$ (6)	1.5	12	DCM	72
17	$Fe(OTf)_2$ (8)	1.0	12	DCM	70
18	$Fe(OTf)_2$ (4)	1.0	12	DCM	91
19	$Fe(OTf)_2$ (3)	1.0	12	DCM	79
20	$Fe(OTf)_2$ (4)	1.0	12	Xylene	63
21	$Fe(OTf)_2$ (4)	1.0	12	Toluene	59
22	$Fe(OTf)_2$ (4)	1.0	12	DCE	67
23	$Fe(OTf)_2$ (4)	1.0	6	DCM	91
24	$Fe(OTf)_2$ (4)	1.0	3	DCM	90
25	$Fe(OTf)_2$ (4)	1.0	1.5	DCM	78

[a]Standard reactions conditions: substrate **1a** (1 mmol), dichloromethyl methyl ether (DCME), in solvent (0.1 M) at room temperature, under argon atmosphere for 12 h. [b] Isolated yield. [c] NR: no reaction. [d] Reaction was conducted in DCM at reflux.

In light of our group's previous findings,[33] we initiated our investigation into acridone synthesis through the intramolecular cyclization of **1a** (1 mmol) using various commercially available Lewis acids in the presence of 1 equiv (1 mmol) of DCME at room temperature for 12 h. A control experiment was first conducted in the absence of a catalyst, which resulted in the recovery of unreacted starting material **1a** (Table 1, entry 1). The results show that the use of tin salts led to yields of less than 20% (Table 1, entries 2 and 3). Likewise, no reaction progress was detected when using $CuCl_2$ (Table 1, entry 5), while the use of $AlCl_3$ and $ZnCl_2$ resulted in very low acridone formation (Table 1, entries 4 and 6). Among the iron halide-derived catalysts evaluated, $FeCl_2$ gave acridone **2a** in a 45% yield (Table 1, entry 9), whereas the use of $FeBr_3$ or $FeCl_3$ resulted in only traces of the desired acridone (Table 1, entries 7 and 8). As a result of their potential catalytic activity in the Friedel-Crafts reaction, a series of commercially available metal triflates were evaluated.[36,37] The use of $Zn(OTf)_2$ led to the formation of **2a** in 21% yield, whereas $Cu(OTf)_2$ generated the acridone scaffold in 35% yield (Table 1, entry 11). Gratifyingly, an increase in the formation of **2a** (84%) was obtained by combining 6 mol% of $Fe(OTf)_2$ and 1 equiv of DCME (Table 1, entry 12).

Considering the results summarized in Table 1, we selected $Fe(OTf)_2$ as the most efficient Lewis acid catalyst for the desired transformation under standard reaction conditions. Control experiments were performed to demonstrate the necessity of the coexistence of the $Fe(OTf)_2$ catalyst and the promoter Cl_2CHOCH_3. No differences in yield were observed when $Fe(OTf)_2$ (6 mol %) and DCME (1 equiv) were tested in DCM under reflux for 12 h (Table 1, entry 13). A longer reaction time also did not allow for an improvement in the conversion of precursor **1a** to acridone **2a**. Interestingly, the experimental results showed that the presence of DCME is crucial for the success of the reaction (Table 1, entry 14). Reducing the amount of DCME to 0.5 equiv led to a pronounced decrease of the acridone **2a** (Table 1, entry 15). An increase in the amount of DCME from 1.0 to 1.5 equiv did not improve the yield of **2a** (Table 1, entry 16).

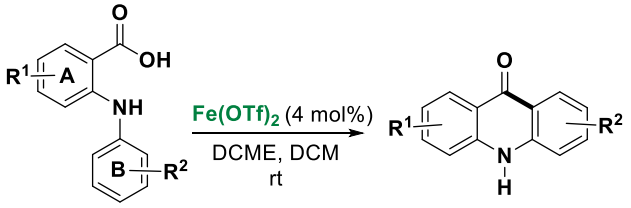
With the amount of DCME equivalents optimized, the reaction efficiency was assessed based on the yield of **2a** using different $Fe(OTf)_2$ loadings, as shown in Table 1. When iron(II) triflate loadings greater than 6 mol % were used, no significant changes in reaction efficiency were observed (Table 1, entry 17). To our delight, we found that the reaction proceeded with a significant increase in the yield of **2a** (91%) using a catalyst loading of 4 mol % (Table1, entry 18). The attempt to reduce the catalyst loading to 3 mol % led to a decrease in yield of **2a** (Table 1, entry 19).

To evaluate the influence of the solvent on the reaction course, different solvents were tested. Among those studied, dichloromethane (Table 1, entry 17) proved to be the most efficient compared to toluene, xylene, and 1,2-dichloroethane (Table 1, entries 20–22) at room temperature. Additionally, the formation of **2a** was evaluated at different reaction times under the optimized amounts of DCME and $Fe(OTf)_2$. In this case, we were able to isolate acridone **2a** in 91% yield after just 6 h of reaction (Table 1, entry 23). Based on this result, we explored the progress of the process at even shorter times, observing a 90% yield after 3 h of reaction (Table 1, entry 24). A further reduction in time did not improve the efficiency of the reaction in terms of yield (Table 1, entry 25). The combined results of these studies established that the use of 6 mol % $Fe(OTf)_2$ as an environmentally benign catalyst, in combination with 1.0 equiv. of DCME in dichloromethane at room temperature, served as optimal conditions for the direct intramolecular acylation of **1a**, affording the desired acridone **2a** in just 3 h.

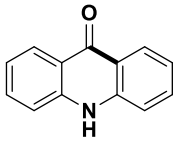
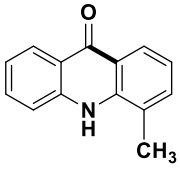
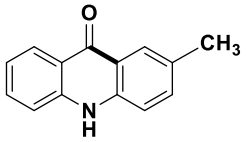
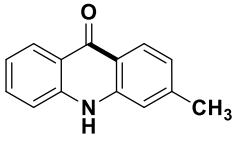
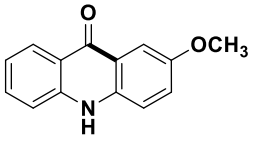
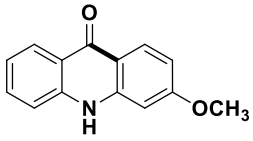
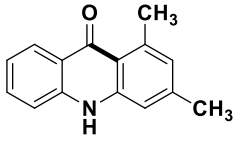
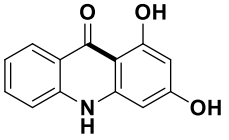
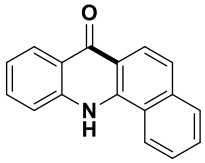
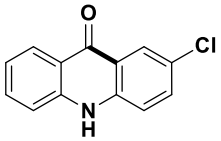
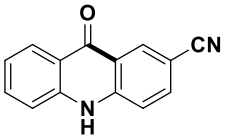
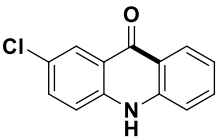
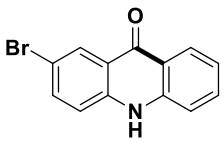
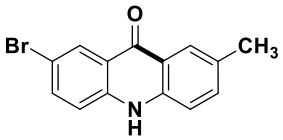
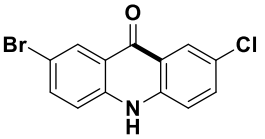
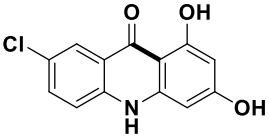
With the optimized reaction conditions in hand, we began to evaluate the scope of different *N*-phenylanthranilic acids, as summarized in Table 2. The present protocol accommodates a variety of functional groups in substrates **1** (phenyl, nitrile, bromo, chlorine, alkoxy, alkyl, and a free phenolic hydroxyl group), resulting in a small library of 10*H*-acridones **2a–2o** with very good to excellent yields. *N*-Phenylanthranilic acids bearing electron-donating substituents (alkyl, phenyl, hydroxyl and alkoxy) on the aromatic ring B were

tolerated in the intramolecular acylation reaction, yielding to the desired 10*H*-acridones **2a-2i** in excellent yields. Slightly lower yields were observed for *N*-phenylanthranilic acids with electron-deficient groups on the aromatic B ring (**2j** and **2k**). However, the incorporation of halogenated substituents on the aromatic ring A (**2j** and **2l**) resulted in a decrease in yield. The intramolecular acylation reaction of *N*-phenylanthranilic acids **1m** and **1n** under optimized conditions afforded the disubstituted acridones **2m** and **2n** in good to very good yields. This new approach was also applied to the synthesis of the antiviral 10*H*-acridone **2o**[38,39] from 5-chloro-2-((3,5-dihydroxyphenyl)amino)benzoic acid (**1o**) in very good yield (82%).

Table 2. Scope synthesis for the synthesis of acridones[a]



1a-1o **2a-2o**

			
2a 94 % (90 %)	**2b** 95 % (91 %)	**2c** 99 % (96 %)	**2d** 91 % (87 %)
			
2e 95 % (90 %)	**2f** 92 % (88 %)	**2g** 97 % (92 %)	**2h** 93 % (89 %)
			
2i 90 % (87 %)	**2j** 85 % (82 %)	**2k** 87 % (83 %)	**2j** 75 % (71 %)
			
2l 77 % (73 %)	**2m** 81 % (77 %)	**2n** 73 % (70 %)	**2o** 85 % (82 %)

[a] Reaction conditions: *N*-phenylanthranilics **1** (1 mmol), $Fe(OTf)_2$ (4 mol %), DCME (1 equiv), DCM (0.1 M), at rt for 3 h. Quantified by GC-MS analysis using internal standard method. Isolated yield after purification (in parentheses).

Intramolecular Friedel–Crafts acylation exhibited complete *para* regioselectivity for substrates bearing a meta substituent on the aniline ring (**2d** and **2f**). This outcome is likely governed primarily by steric factors: although the *ortho* and *para* positions are electronically comparable, the formation of the *ortho* isomer would require the acyl intermediate to approach a peri-substituted site, resulting in significant steric hindrance. In contrast, the *para* position remains more accessible and thus energetically favored. These observations are consistent with previous reports on similar systems, where steric repulsion was found to be the dominant factor influencing regioselectivity.[40] The exclusive formation of the *para* product in our case reinforces this mechanistic rationale.

A comparative analysis between our method and commonly employed strategies for intramolecular *ortho*-acylation reveals that 10*H*-acridones are obtained with significantly higher efficiency using our simple and reliable protocol (Table 3). Traditional approaches typically require harsh conditions, such as concentrated H_2SO_4[27] (Table 3, entry 1), polyphosphoric acid (Table 3, entry 2)[41], Eaton's reagent (Table 3, entry 3)[42], or $BF_3{\cdot}Et_2O$ (Table 3, entry 4).[43] In contrast, our protocol (Table 3, entry 5) operates under milder conditions, avoids the use of excess catalysts, long reaction times, elevated temperatures, and minimizes waste generation during quenching—factors that often compromise selectivity and scalability in conventional methods.

Moreover, our approach employs simple, readily available precursors without the need for preactivation. It also exhibits broader functional group tolerance across both aromatic rings of the *N*-phenylanthranilic acid derivatives. The use of an environmentally benign catalyst and the operational simplicity of the protocol further underscore its suitability for scale-up and practical application.

Table 3. Comparison of selected methods for 10*H*-acridone synthesis from *N*-phenylanthranilic acids

Entry	Reaction conditions	Time (h)	Yield (%)[a]
1	H_2SO_4 concd, 100 °C	4-6	55-60
2	Polyphosphoric acid (exc.), 100 °C	2-4	58-70
3	Eaton's reagent, 80 °C	5-10	72-78
4	$BF_3{\cdot}Et_2O$, 60 °C	3-4	78-83
5	$Fe(OTf)_2$ (4 mol %) / DCME (1 equiv) / DCM, rt	3	70-96

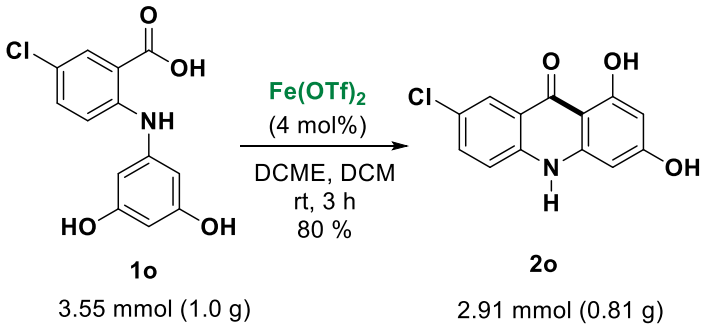
[a] Isolated yield.

Notably, under the applied reaction conditions, no byproducts were detected, as determined by GC-MS analysis of the crude reaction mixtures. The workup and isolation procedure involved the addition of water to the reaction mixture, followed by successive extractions with DCM and subsequent washing with saturated aqueous $NaHCO_3$. The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was then purified by column chromatography on silica gel 60. Structural elucidation of all synthesized 10*H*-acridones was confirmed by spectroscopic data, as detailed in the Experimental Section.

Attempts to reuse the Fe(II) catalyst under identical reaction conditions resulted in significantly diminished activity, likely due to oxidation or structural degradation of the catalyst during work-up. Optimization of reuse conditions is currently under investigation.

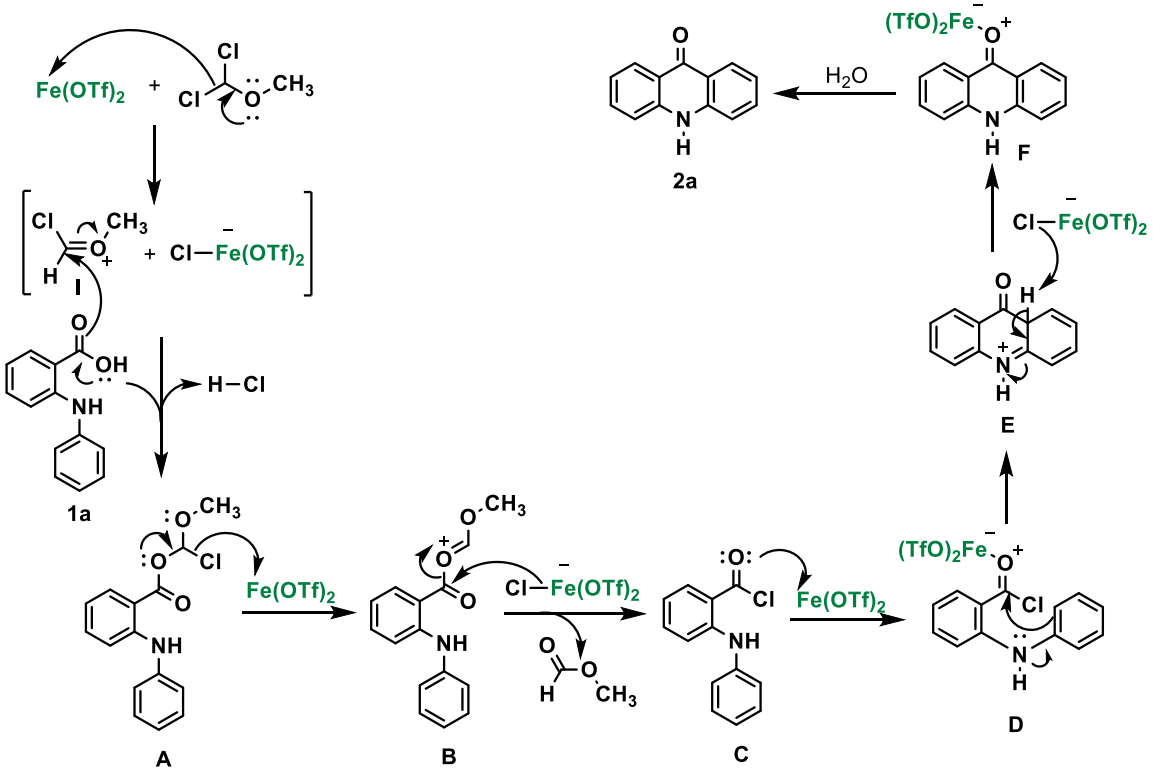
In order to evaluate the scalability and synthetic application of our optimized protocol, a gram-scale reaction of the bioactive acridone **2o** was carried out starting from 1.0 g of 5-chloro-2-((3,5-dihydroxyphenyl)amino)benzoic acid (**1o**). The scale-up reaction was performed under the same optimized

conditions, demonstrating the robustness of the method. After 3 h at room temperature, the reaction afforded the bioactive acridone **2o** in an 80% yield, highlighting the efficiency and reproducibility of the process at a larger scale (Scheme 3). These results suggest that the optimized protocol is suitable for larger-scale applications and could be potentially adapted for the synthesis of other bioactive acridones.



Scheme 3. Gram-scale synthesis of acridone **2o** using the $Fe(OTf)_2$/DCME catalytic system.

While the precise reaction mechanism remains under investigation, a plausible pathway is proposed based on precedents from related transformations (Scheme 4).[44,45] The proposed initial step involves the deoxygenative chlorination of substrate **1a**, leading to the formation of the acid chloride intermediate **C**. This transformation likely proceeds *via* the *in situ* generation of a reactive chloromethylating species **I**, formed from dichloromethyl methyl ether in the presence of $Fe(OTf)_2$. Intermediate **I** then reacts with **1a** to yield compound **A**, which, upon activation by a Lewis acid, leads to the formation of oxocarbenium species **B**. Nucleophilic attack by a chloride ion on **B** affords the dehydroxy-chlorinated product **C**.



Scheme 4. Proposed mechanism for the cyclization of *N*-phenylanthranilic acid promoted by $Fe(OTf)_2$/DCME.

Subsequently, an intramolecular Friedel–Crafts cyclization is triggered by the coordination of $Fe(OTf)_2$ to the carbonyl oxygen of intermediate **C**, thereby activating the carbonyl group toward electrophilic attack and facilitating the formation of the cyclized intermediate **D**. This step is followed by a proton abstraction—most likely mediated by the triflate counterion—from intermediate **E**, which restores aromaticity in the newly formed ring system, leading to intermediate **F**. Finally, hydrolysis of **F** furnishes the acridone base **2a**.

Conclusions

In summary, we have developed a new and complementary methodology for the efficient synthesis of a small library of 10*H*-acridones starting from readily accessible *N*-phenylanthranilic acids. This transformation, mediated by a cooperative $Fe(OTf)_2/Cl_2CHOCH_3$ system under mild conditions, proceeds rapidly in just 3 h and tolerates a broad range of substrates, including neutral, electron-rich, and electron-deficient derivatives, providing excellent yields ranging from very good to excellent. Compared to traditional Friedel–Crafts-based approaches, this protocol offers significant improvements in terms of generality and functional group compatibility, enabling the construction of fused tricyclic dibenzo-4-pyridone scaffolds—structures of increasing interest in drug discovery and materials science.

To further demonstrate the robustness and practical utility of the methodology, we successfully carried out a gram-scale synthesis of the bioactive acridone **2o** from precursor **1o**, using commercially available and inexpensive starting materials such as 5-aminobenzene-1,3-diol and 2-bromo-5-chlorobenzoic acid. The reaction afforded the desired product in excellent yield, confirming the scalability and reproducibility of the process under the optimized conditions.

Owing to its operational simplicity, low cost, scalability, and high atom economy under mild conditions, this synthetic strategy holds significant potential for broad application in synthetic chemistry. Its versatility makes it particularly promising in the fields of medicinal chemistry and drug discovery, where the rapid and efficient generation of complex bioactive molecules is essential. Additionally, the methodology could be easily adapted for the synthesis of other bioactive acridones or related heterocyclic compounds, thus opening new possibilities for the development of therapeutic acridone-based agents.

Experimental Section

General. Reagents were obtained commercially and used without further purification. Solvents were technical grade and distilled prior to use. Catalysts were purchased as analytical reagent grade. Reactions were monitored by thin-layer chromatography on silica gel plates (60F-254) visualized under UV light and/or using 5% phosphomolybdic acid in ethanol. All ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$, or DMSO-d_6 on a Bruker Advance ARX-300 spectrophotometer. Chemical shifts (δ) are reported in parts per million (ppm) from tetramethylsilane (TMS) using the residual solvent resonance. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad signal. IR spectra were recorded on a Nicolet Nexus 470/670/870 FT-IR spectrometer at room temperature. Melting points were determined using a Büchi 510 apparatus and are not corrected. Mass spectra (EI) were obtained at 70 eV on a Hewlett Packard HP-5890 GC-MS instrument equipped with a HP-5972 selective mass detector. The purity of volatile compounds and the chromatographic analyses (GC) were determined with a GC Shimadzu (GC-14B) with a flame ionization detector equipped with a HP-5MS column (30 m × 0.25 mm × 0.25

μm) using nitrogen as carrier gas. High resolution mass spectra were recorded on Thermo Fisher LTQ Orbitrap XL, (for EI). Flash column chromatography was performed using Macherey Nagel MN Silica 60M (0.040-0.063 mm / 230-240 mesh ASTM). Substrates **1a-1f**, **1i-1j,** and **1l** were obtained from commercially available sources.

General procedure for the synthesis of acridin-9(10*H*)-ones. Functionalized *N*-phenylanthranilic acids (1.0 mmol), $Fe(OTf)_2$ (14 mg, 0.04 mmol, 0.04 equiv), dichloromethyl methyl ether (91 μL, 1 mmol, 1.0 equiv), and CH_2Cl_2 (10 mL) were added to a Schlenk tube under argon. The resulting solution was stirred at room temperature until the completion of the reaction. The progress of the reaction was monitored by TLC and GC-MS, and the reaction was quenched by the addition of water. The mixture was extracted with DCM, washed with aqueous saturated $NaHCO_3$ and then the combined organic layers were dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using silica gel 60 or recrystallized in isoamyl alcohol.

Acridin-9(10*H*)-one (2a). Prepared from *N*-phenylanthranilic acid (**1a**); purified by recrystallization from isoamyl alcohol; yellow solid (175 mg, 90%); mp > 300 °C (lit.[17] 344-346 °C). IR (solid, KBr, νmax, cm^{-1}): 3439, 3099, 2993, 2949, 1636, 1598, 1557, 1531, 1473, 1347, 752, 673. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.22-7.24 (2H, m), 7.42 (2H, dd*, J* 7.5 Hz), 7.75-7-73 (2H, m), 8.24 (2H, dd, *J* 7.5 Hz), 11.75 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 117.3 120.5, 121.1, 126.0, 133.6, 140.9, 176.8. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_9NO$: 195.0684; found: 195.0686. The spectral data were in accordance with those reported in the literature.[46]

4-Methylacridin-9(10*H*)-one (2b). Prepared from 2-(*o*-tolylamino)benzoic acid (**1b**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); yellow solid (190 mg, 91%); mp > 300 °C (lit.[17] 345 °C). IR (solid, KBr, νmax, cm^{-1}): 3444, 3285, 1623, 1619, 1576, 1529, 1463, 1348, 753, 684. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.59 (3H, s, CH_3), 7.15 (1H, d, *J* 7.9 Hz), 7.24 (1H, td, *J* 7.9 Hz), 7.60 (1H, d, *J* 7.9 Hz), 7.75-7.77 (1H, m), 7.93 (1H, d, *J* 8.0 Hz), 8.12 (1H, d, *J* 8.0 Hz), 8.20 (1H, dd, *J* 7.9 Hz), 10.60 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 17.8, 118.3, 120.7, 121.8, 122.1, 124.2, 125.9, 126.6, 133.4, 134.2, 139.4, 141.4, 175.4. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0845. The spectral data were in accordance with those reported in the literature.[46a]

2-Methylacridin-9(10*H*)-one (2c). Prepared from 2-(*p*-tolylamino)benzoic acid (**1c**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); yellow solid (200 mg, 96%); mp > 300 °C (lit.[17] 335 °C). IR (solid, KBr, νmax, cm^{-1}): 3438, 2991, 1656, 1601, 1567, 1526, 1477, 1352, 1264, 1212, 1159, 815, 753. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.43 (3H, s, CH_3), 7.20-7,22 (1H, m), 7.43 (1H, d, *J* 7.9 Hz), 7.53-7.58 (2H, m), 7.71 (1H, t, *J* 7.9 Hz), 8.01 (1H, s), 8.21 (1H, dd, *J* 7.9 Hz), 11.73 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 21.2, 117.9, 120.4, 120.8, 125.2, 126.0, 130.0, 133.2, 134.8, 139.5, 141.3, 177.0. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0837. The spectral data were in accordance with those reported in the literature.[46]

3-Methylacridin-9(10*H*)-one (2d). Prepared from 2-(*m*-tolylamino)benzoic acid (**1d**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); yellow solid (182 mg, 87%); mp > 300 °C (lit.[17] 334 °C). IR (solid, KBr, νmax, cm^{-1}): 3424, 3027, 2979, 1639, 1588, 1152, 754. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.47 (3H, s, CH_3), 7.06 (1H, d, *J* 8.3 Hz), 7.17-7.23 (1H, m), 7.27 (1H, s), 7.50 (1H, d, *J* 7.9 Hz), 7.67-7.69 (1H, m), 8.08 (1H, s), 8.19 (1H, dd, *J* 7.9 Hz), 11.58 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 22.1, 117.0, 117.7, 119.1, 121.1, 121.4, 123.4, 126.5, 126.6, 133.7, 141.4, 141.6, 144.3, 177.0. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0850. The spectral data were in accordance with those reported in the literature.[13]

2-Methoxyacridin-9(10*H*)-one (2e). Prepared from 2-((4-methoxyphenyl)amino)benzoic acid (**1e**); purified by recrystallization from isoamyl alcohol; yellow solid (202 mg, 90%); mp 280-282 °C (lit.[17] 272 °C). IR (solid, KBr,

νmax, cm^{-1}): 3437, 1688, 1599, 1571, 1531, 1494, 1477, 1230, 1156, 1035, 754. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 3.86 (3H, s, OCH_3), 7.22-7.25 (1H, m), 7.40-7.47 (1H, m), 7.54 (1H, d, *J* 2.8 Hz), 7.58 (1H, d, *J* 2.8 Hz), 7.63 (1H, d, *J* 2.8 Hz), 7.70-7.76 (1H, m), 8.23 (1H, dd, *J* 7.9 Hz), 11.77 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 60.6, 110.3, 122.4, 123.9, 124.5, 125.9, 126.4, 129.6, 131.2, 138.3, 140.9, 145.7, 159.2, 181.3. HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NO_2$: 225.0790; found: 225.0792. The spectral data were in accordance with those reported in the literature.[46]

3-Methoxyacridin-9(10*H*)-one (2f). Prepared from 2-((3-methoxyphenyl)amino)benzoic acid (**1f**); purified by recrystallization from isoamyl alcohol; yellow solid (198 mg, 88%); mp 259-261 °C (lit.[14] 260-262 °C). IR (solid, KBr, νmax, cm^{-1}): 3435, 2952, 1629, 1155, 1032, 756. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 3.91 (3H, s, OCH_3), 6.87-6.80 (2H, m), 7.21-7.25 (1H, m), 7.50 (1H, dd, *J* 7.9 Hz), 7.70 (1H, d, *J* 7.9 Hz), 8.13-8.19 (2H, m), 11.59 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 55.9, 98.4, 111.9, 115.5, 117.5, 121.1, 121.4, 126.4, 128.5, 133.5, 141.4, 143.3, 163.8, 176.3. HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NO_2$: 225.0790; found: 225.0785. The spectral data were in accordance with those reported in the literature.[14]

1,3-Dimethylacridin-9(10*H*)-one (2g).

Prepared from 2-((3,5-dimethylphenyl)amino)benzoic acid (**1g**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); yellow solid (200 mg, 92%); mp > 300 °C (lit.[17] 303-306 °C). IR (solid, KBr, νmax, cm^{-1}): 3420, 3037, 2975, 1628, 1588, 1150, 755. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.38 (3H, s, CH_3), 2.56 (3H, s, CH_3), 7.21-7.27 (1H, m), 7.09 (1H, s) 7.15 (1H, td, *J* 7.9 Hz and *J* 1.0 Hz), 7.88-7.91 (2H, m), 8.12 (1H, dd, *J* 7.9 Hz), 10.48 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 17.6, 20.4, 118.0, 119.9, 120.7, 120.9, 123.0, 124.9, 125.8, 129.6, 132.9, 135.5, 137.7, 140.1, 175.2. HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{13}NO$: 223.0780; found: 223.0777. The spectral data were in accordance with those reported in the literature.[47]

1,3-Dihydroxyacridin-9(10*H*)-one (2h). Prepared from 2-((3,5-dihydroxyphenyl)amino)benzoic acid (**1h**); purified by recrystallization from isoamyl alcohol; orange solid (202 mg, 89%); mp > 300 °C (lit.[48] 344-346 °C). IR (solid, KBr, νmax, cm^{-1}): 3440, 3165, 3076, 1645, 1609, 1458, 1183, 827. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.04 (1H, d, *J* 2.2 Hz), 6.31 (1H, d, *J* 2.2 Hz), 7.22-7.27 (1H, m), 7.46-7.40 (1H, m), 7.63-7.69 (1H, m), 8.16 (1H, dd, *J* 7.9 Hz), 10.49 (1H, s, NH), 11.77 (1H, s, OH), 14.72 (1H, s, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 91.3, 96.1, 104.3, 117.8, 119.8, 122.1, 126.0, 134.6, 141.7, 144.3, 164.7, 165.3, 180.4. HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_9NO_3$: 227.0194; found: 227.0189. The spectral data were in accordance with those reported in the literature.[48]

Benzo[*c*]acridin-7(12*H*)-one (2i). Prepared from 2-(naphthalen-1-ylamino)benzoic acid (**1i**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 95:5); yellow solid (213 mg, 87%); mp >300 °C (lit.[49] 365-366 °C). IR (solid, KBr, νmax, cm^{-1}): 3432, 3038, 1664, 1598, 1443, 1322, 752, 673. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 6.87 (1H, d, *J* 7.9 Hz), 7.38 (1H, s, NH), 7.55-7.64 (3H, m), 7.65-7.68 (1H, m), 7.78-7.80 (1H, m), 7.99 (1H, d, *J* 7.9 Hz), 8.22 (1H, d, *J* 8.4 Hz), 8.27 (1H, d, *J* 8.4 Hz), 8.63 (1H, d, *J* 7.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 117.2, 121.5, 122.3, 122.8, 123.1, 124.5, 124.8, 126.2, 127.6, 128.3, 128.7, 133.4, 136.5, 144.1, 145.9, 177.7. HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{11}NO$: 245.0841; found: 245.0846. The spectral data were in accordance with those reported in the literature.[50]

2-Chloroacridin-9(10*H*)-one (2j). Prepared from 2-((4-chlorophenyl)amino)benzoic acid (**1j**); purified by column chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); pale yellow solid (187 mg, 82%); mp > 300 °C (lit.[17] 329 °C). IR (solid, KBr, νmax, cm^{-1}): 3432, 2918, 1629, 1600, 1024, 824. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.29 (1H, t, *J* 7.9 Hz), 7.55-7.61 (2H, m), 7.74-7.78 (2H, m), 8.15 (1H, d, *J* 2.5 Hz), 8.23 (1H, d, *J* 7.9 Hz), 11.92 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 118.0, 120.3, 120.8, 121.7, 121.9,

125.2, 125.9, 126.5, 133.9, 134.3, 139.9, 141.3, 176.2. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_8ClNO$: 229.0294; found: 229.0297. The spectral data were in accordance with those reported in the literature.[46]

The acridone derivative **2j** was also synthesized from 5-chloro-2-(phenylamino)benzoic acid (**1j´**) to give a yellow solid (162 mg, 71%).

9-Oxo-9,10-dihydroacridine-2-carbonitrile (2k). Prepared from 2-((4-cyanophenyl)amino)benzoic acid (**1k**); purified by chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 80:20); yellow solid (183 mg, 83%); mp > 300 °C (lit.[17] mp > 300 °C). IR (solid, KBr, νmax, cm^{-1}): 3435, 2221, 1630, 1602, 1155, 1032. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.37 (1H, m), 7.60-7.68 (2H, m), 7.85 (1H, t, *J* 7.9 Hz), 8.06 (1H, d, *J* 7.9 Hz), 8.24 (1H, d, *J* 7.9 Hz), 8.52 (1H, s), 12.44 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 103.1, 118.0, 119.1, 119.2, 120.1, 121.1, 122.6, 126.3, 132.3, 134.6, 135.2, 140.8, 143.3, 176.0. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_8N_2O$: 220.0637; found: 220.0640. The spectral data were in accordance with those reported in the literature.[17]

2-Bromoacridin-9(10*H*)-one (2l). Prepared from 5-bromo-2-(phenylamino)benzoic acid (**1l**); purified by chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 90:10); pale yellow solid (200 mg, 73%); mp > 300 °C (lit.[17] mp > 300 °C). IR (solid, KBr, νmax, cm^{-1}): 3426, 2946, 1628, 1555, 1470, 1273, 1024, 822, 755, 688. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.24-7.31 (1H, m), 7.50-7.56 (2H, m), 7.75-8.01 (2H, m), 8.25-8.30 (2H, m), 11.52 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 113.4, 118.1, 120.5, 120.5, 120.8, 122.0, 122.2, 126.5, 128.4, 134.4, 140.2, 141.2, 176.1. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_8BrNO$: 274.1003; found: 274.1009. The spectral data were in accordance with those reported in the literature.[51]

2-Bromo-7-methylacridin-9(10*H*)-one (2m). Prepared from 5-bromo-2-(*p*-tolylamino)benzoic acid (**1m**); purified by chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 90:10); light yellow solid (221 mg, 77%); mp > 300 °C (lit.[17] mp > 300 °C). IR (solid, KBr, νmax, cm^{-1}): 3420, 2948, 1634, 1560, 1470, 1279, 1024, 822, 755, 680. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.39 (3H, s, CH_3), 7.42-7.48 (2H, m), 7.56 (1H, d, *J* 8.5 Hz and *J* 1.7 Hz), 7.80 (1H, dd, *J* 8.5 Hz and *J* 1.7 Hz), 7.98 (1H, s), 8.25 (1H, d, *J* 1.7 Hz), 11.83 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 21.1, 113.4, 118.1, 120.5, 120.8, 122.2, 125.6, 128.5, 131.3, 135.9, 136.3, 139.4, 140.2, 176.0. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{10}BrNO$: 287.0034; found: 287.0039. The spectral data were in accordance with those reported in the literature.[17]

2-Bromo-7-chloroacridin-9(10*H*)-one (2n). Prepared from 5-bromo-2-((4-chlorophenyl)amino)benzoic acid (**1n**); purified by chromatography on silica gel with petroleum ether/ethyl acetate (PE/EtOAc 50:50); light yellow solid (214 mg, 70%); mp > 300 °C (lit.[17] m.p > 300 °C). IR (solid, KBr, νmax, cm^{-1}): 3430, 2915, 1633, 1600, 1024, 829. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.57 (1H d, *J* 8.9 Hz), 7.63 (1H, d, *J* 8.9 Hz), 7.83 (1H, dd, *J* 9.0 Hz and *J* 2.4 Hz), 7.93 (1H, dd, *J* 8.9 Hz and *J* 2.3 Hz), 8.18 (1H, d, *J* 2.4 Hz), 8.32 (1H, d, *J* 2.2 Hz), 12.13 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 114.3, 120.7, 120.9, 121.8, 122.2, 125.4, 126.6, 128.6, 134.5, 137.0, 140.0, 140.3, 175.3. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_7BrClNO$: 306.9364; found: 306.9367. The spectral data were in accordance with those reported in the literature.[17]

7-Chloro-1,3-dihydroxyacridin-9(10*H*)-one (2o). Prepared from 5-chloro-2-((3,5-dihydroxyphenyl)amino)benzoic acid (**1o**); purified by recrystallization from isoamyl alcohol; yellow solid (214 mg, 82%); mp > 300 °C (lit.[38] mp > 300 °C). IR (solid, KBr, νmax, cm^{-1}): 3450, 3300, 3200, 1660, 1600, 1540, 1470, 1024, 820. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.32 (1H, d, *J* 2 Hz), 6.48 (1H, d, *J* 2 Hz), 7.34 (1H, d, *J* 9 Hz), 7.41 (1H, dd, *J* 2 and 9 Hz), 8.18 (1H, d, *J* 2 Hz), 8.51 (1H, s, 3-OH), 10.49 (1H, s, NH), 13.98 (1H, s, 1-OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 90.4, 95.5, 102.5, 118.1, 120.9, 123.3, 131.3, 133.3, 139.5, 144.4, 164.0, 164.4, 180.9. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_8ClNO_3$: 261.0056; found: 261.0051. The spectral data were in accordance with those reported in the literature.[38]

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Supplementary Material

Spectroscopic data of synthesized compounds are available in the Supplementary material file associated with this manuscript.

References

1. Kumar, R.; Sharma, S.; Prasad, D. *Chapter 3 - Acridones: A Relatively Lesser Explored Heterocycle for Multifactorial Diseases. In Key Heterocycle Cores for Designing Multitargeting Molecules*, Silakari, O. Elsevier: 2018; pp 53-132. https://doi.org/10.1016/B978-0-08-102083-8.00003-0
2. Oyedele, A. S.; Bogan, D. N.; Okoro, C. O. *Biorg. Med. Chem.* **2020**, *28*, 115426. https://doi.org/10.1016/j.bmc.2020.115426
3. Miglbauer, E.; Demitri, N.; Himmelsbach, M.; Monkowius, U.; Sariciftci, N. S.; Głowacki, E. D.; Oppelt, K. T. *ChemistrySelect* **2016**, *1*, 6349. https://doi.org/10.1002/slct.201601682
4. Hamzehpoor, E.; Ruchlin, C.; Tao, Y.; RamosSanchez, J. E.; Titi, H. M.; Cosa, G.; Perepichka, D. F. J. *Phys. Chem. Lett.* **2021**, *12*, 6431. https://doi.org/10.1021/acs.jpclett.1c01552
5. Gao, H.; Zhang, G. *Eur. J. Org. Chem.* **2020**, 5455. https://doi.org/10.1002/ejoc.202000871
6. Pereira, R. C.; Pontinha, A. D. R.; Pineiro, M.; Seixas de Melo, J. S. *Dyes Pigm.* **2019**, *166*, 203. https://doi.org/10.1016/j.dyepig.2019.03.028
7. Chan, Y. C.; Li, C. Y.; Lai, C. W.; Wu, M. W.; Tseng, H. J.; Chang, C. C. *Appl. Sci.* **2020**, *10*, 8708. https://doi.org/10.3390/app10238708
8. Singh, P.; Kumar, A.; Kaur, S.; Singh, A.; Gupta, M.; Kaur, G. *Med. Chem. Commun.* **2016**, *7*, 632. https://doi.org/10.1039/C5MD00534E
9. Faller, T.; Hutton, K.; Okafo, G.; Gribble, A.; Camilleri, P.; Games, D. E. *Chem. Commun.* **1997**, 1529. https://doi.org/10.1039/A701787A
10. Ye, X.; Plessow, P. N.; Brinks, M. K.; Schelwies, M.; Schaub, T.; Rominger, F.; Paciello, R.; Limbach, M.; Hofmann, P. *J. Am. Chem. Soc.* **2014**, *136*, 5923. https://doi.org/10.1021/ja409368a
11. Graham, L. A.; Suryadi, J.; West, T. K.; Kucera, G. L.; Bierbach, U. *J. Med. Chem.* **2012**, *55*, 7817. https://doi.org/10.1021/jm300879k
12. Zhou, W.; Liu, Y.; Yang, Y.; Deng, G. J. *Chem. Commun.* **2012**, *48*, 10678.

https://doi.org/10.1039/C2CC35425J
13. Wu, H.; Zhang, Z.; Liu, Q.; Liu, T.; Ma, N.; Zhang, G. *Org. Lett.* **2018**, *20*, 2897. https://doi.org/10.1021/acs.orglett.8b00957
14. Wei, W. T.; Sheng, J. F.; Miao, H.; Luo, X.; Song, X. H.; Yan, M.; Zou, Y. *Adv. Synth. Catal.* **2018**, *360*, 2101. https://doi.org/10.1002/adsc.201701579
15. Li, X. A.; Wang, H. L.; Yang, S. D. *Org. Lett.* **2013**, *15*, 1794. https://doi.org/10.1021/ol400371h
16. Zhou, W.; Yang, Y.; Liu, Y.; Deng, G. J. *Green Chem.* **2013**, *15*, 76. https://doi.org/10.1039/C2GC36502B
17. Yu, J.; Yang, H.; Jiang, Y.; Fu, H. *Chem. Eur. J.* **2013**, *19*, 4271. https://doi.org/10.1002/chem.201204169
18. Steingruber, H. S.; Mendioroz, P.; Castro, M. J.; Volpe, M. A.; Gerbino, D. C. *Synthesis* **2023**, *55*(04): 692. https://doi.org/10.1055/s-0042-1751371
19. Zhou, H-Y.; Dong, L. *Org. Biomol. Chem*. **2024**, *22*, 4036. https://doi.org/10.1039/D4OB00377B
20. Guo, W.; Wu, W.; Huang, J.; Zhang, C.; Wang, H.; Zhou, H.; Hu, W. *Asian J. Org. Chem*. **2024**, *13*, e202300584. https://doi.org/10.1002/ajoc.202300584
21. Askarzadeh, M.; Moazzam, A.; Sayahi, M. H.; Fouladvand, A.; Adib, M.; Mahdavi, M. *Tetrahedron Lett*. **2023**, *123*, 154532. https://doi.org/10.1016/j.tetlet.2023.154532
22. Yadav, T. T.; Murahari, M.; Peters, G. J.; Mayur, Y. C. *Eur. J. Med. Chem*. **2022**, *239*, 114527. https://doi.org/10.1016/j.ejmech.2022.114527
23. Parveen, M.; Aslam, A.; Nami, S. A.; Malla, A. M.; Alam, M.; Lee, D. U.; Rehman, S.; Silva, P. S.; Silva, M. R. *J. Photochem. Photobiol. B.* **2016**, *161*, 304. https://doi.org/10.1016/j.jphotobiol.2016.05.028
24. Nishio, R.; Wessely, S.; Sugiura, M.; Kobayashi, S. *J. Comb. Chem.* **2006**, *8*, 459. https://doi.org/10.1021/cc060011+
25. Goodell, J. R.; Madhok, A. A.; Hiasa, H.; Ferguson, D. M. *Bioorg. Med. Chem.* **2006**, *14*, 5467. https://doi.org/10.1016/j.bmc.2006.04.044
26. Pal, C.; Kundu, M. K.; Bandyopadhyay, U.; Adhikari, S. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 3563. https://doi.org/10.1016/j.bmcl.2011.04.127
27. Allen, C. F. H.; Mckee, G. H. W. *Org. Syn.* **1943**, *2*, 15. https://doi.org/10.15227/orgsyn.019.0006
28. Bolm, C.; Legros, J. ; Le Paih, J. ; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. https://doi.org/10.1021/cr040664h
29. Bauer, I.; Knölker, H.-J. *Chem. Rev.* **2015**, *115*, 3170. https://doi.org/10.1021/cr500425u
30. Fürstner, A. *ACS Cent. Sci.* **2016**, *2*, 778. https://doi.org/10.1021/acscentsci.6b00272
31. Menéndez, C.; Nador, F.; Radivoy, G.; Gerbino, D. C. *Org. Lett.* **2014**, *16*, 2846. https://doi.org/10.1021/ol500964e
32. Steingruber, H. S.; Mendioroz, P.; Diez, A. S.; Gerbino, D. C. *Synthesis* **2020**, *52*, 619. https://doi.org/10.1055/s-0039-1691069

33. Scoccia, J.; Castro, M. J.; Faraoni, M. A.; Bouzat, C.; Martín, V. S.; Gerbino, D. C. *Tetrahedron* **2017**, *73*, 2913. https://doi.org/10.1016/j.tet.2017.03.085
34. Steingruber, H. S.; Mendioroz, P.; Volpe, M. A.; Gerbino, D. C. *Synthesis* **2021**, *53*, 4048. https://doi.org/10.1055/s-0037-1610778
35. Pellón, R. F., Mamposo, T., Carrasco, R., Rodés, L. *Synth. Commun.* **1996**, *26*, 3877. https://doi.org/10.1080/00397919608003805
36. Li, J.; Jin, C.; Su, W. K. *Heterocycles* **2010**, *81*, 2555. https://doi.org/10.1002/chin.201113148
37. Ross, J.; Xiao, J. L. *Green Chem.* **2002**, *4*, 129. https://doi.org/10.1039/B109847K
38. Bastow, K. F.; Itoigawa, M.; Furukawa, H.; Kashiwada, Y.; Bori, I. D.; Ballas, L. M.; Lee, K. H. *Bioorg. Med. Chem.* **1994**, 2, 1403. https://doi.org/10.1016/S0166-3542(00)00068-1
39. Akanitapichat, P.; Lowden, C. T.; Bastow, K. F. *Antivir. Res.* **2000**, 45, 123. https://doi.org/10.1016/S0166-3542(00)00068-1
40. Olah, G. A.; Kobayashi, S. *J. Am. Chem. Soc*. **1971**, *93*, 6964. https://doi.org/10.1021/ja00754a045
41. Dodean, R. A.; Kancharla, P.; Li, Y.; Melendez, V.; Read, L.; Bane, C. E.; Vesely, B.; Kreishman-Deitrick, M.; Black, C.; Li, Q.; Sciotti, R. J.; Olmeda, R.; Luong, T. L.; Gaona, H.; Potter, B.; Sousa, J.; Marcsisin, S.; Caridha, D.; Xie, L.; Vuong, C.; Zeng, Q.; Zhang, J.; Zhang, P.; Lin, H.; Butler, K.; Roncal, N.; Gaynor-Ohnstad, L.; Leed, S. E.; Nolan, C.; Huezo, S. J.; Rasmussen, S. A.; Stephens, M. T.; Tan, J. C.; Cooper, R. A.; Smilkstein, M. J.; Pou, S.; Winter, R. W.; Riscoe, M. K.; Kelly, J. X. *J. Med. Chem*., **2019**, *62*, 3475. https://doi.org/10.1021/acs.jmedchem.8b01961
42. Speight, L. C.; Muthusamy, A. K.; Goldberg, J. M.; Warner, J. B.; Wissner, R. F.; Willi, T. S.; Woodman, B. F.; Mehl, R. A.; Petersson, E. J. *J. Am. Chem. Soc*., **2013**, *135*, 18806. https://doi.org/10.1021/ja403247j
43. Zhang, E. ; Zhang, X. ; Wei, W. ; Wang, D. ; Cai, Y. ; Xu, T. ; Yan, M. ; Zou, Y. *RSC Adv*., **2015**, *5*, 5288. https://doi.org/10.1039/C4RA12479K
44. Polat, E.; Cakici, M. *Eur. J. Org. Chem.* **2022**, e202201106. https://doi.org/10.1002/ejoc.202201106
45. Kancharla, P.; Dodean, R. A.; Li, Y.; Kelly, J. X. *RSC Adv.* **2019**, *9*(72), 42284. https://doi.org/10.1039/C9RA09478D
46. Wen, J.; Tang, S.; Zhang, F.; Shi, R.; Lei, A. *Org. Lett.* **2017**, *19*, 94. https://doi.org/10.1021/acs.orglett.6b03356
47. Murahari, M.; Kharkar, P. S.; Lonikar, N. ; Mayur, Y. C. *Eur. J. Med. Chem.* **2017**, *130*, 154. https://doi.org/10.1016/j.ejmech.2017.02.022
48. Mandal, T.; Karmakar, S.; Kapat, A.; Dash, J. *ACS omega* **2021**, *6*(41), 27062. https://doi.org/10.1021/acsomega.1c03629
49. Knapp, W. Über neuartige Ringsysteme III. **1937**, *70* (1), 251. https://doi.org/10.1007/BF01755669
50. Xiong, Z.; Zhang, X.; Li, Y.; Peng, X.; Guo, J.; Xie, F.; Jiang, C.; Lin, B.; Liu, Y.; Cheng, M. *Org. Biomol. Chem.* **2018**, *16*, 7361. https://doi.org/10.1039/C8OB01684D

51. Orlov, V. Y.; Ganzha, V. V.; Kotov, A. D.; Sokolov, V. G. *Russ. J. Org. Chem.* **2007**, *43,* 1502. https://doi.org/10.1134/S1070428007100168