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Acid-Promoted Redox-Annulation toward 1,2-Disubstituted-5,6-dihydropyrrolo[2,1-α]isoquinolines: Synthesis of the Lamellarin Core

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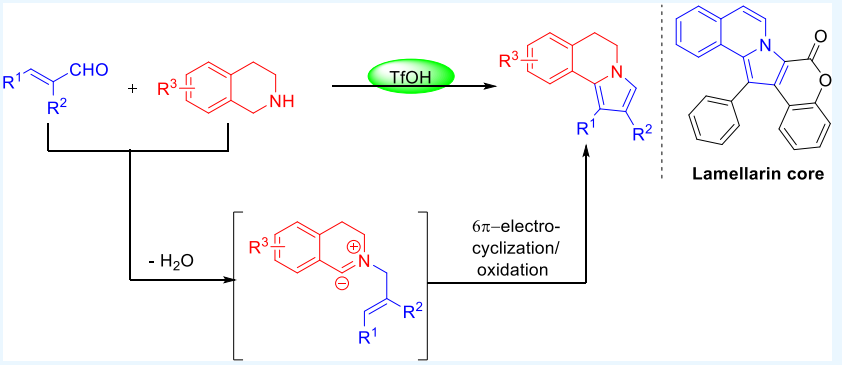

ABSTRACT: An efficient synthesis of a variety of 1,2-disubstituted-5,6-dihydropyrrolo[2,1-α]isoquinoline derivatives via an acid-promoted cyclization reaction between 1,2,3,4-tetrahydroisoquinoline (THIQ) and substituted α,β-unsaturated aldehyde derivatives is reported. This cycloaddition allows access to structurally diverse multisubstituted dihydropyrrolo[2,1-α]isoquinolines in moderate to good yields, which was the core scaffold of marine natural alkaloid lamellarins.

INTRODUCTION

Pyrroles are prominent structural motifs in numerous biologically active substances,[1,2] especially pyrrolo[2,1-α]-isoquinoline and its derivatives, which have a variety of pharmacological properties.[3−5] For example, pyrroloisoquinoline alkaloid crispine A, which has emerged as natural products' target of interest isolated in 2002 from the antitumor active extract of Carduus crispus (Figure 1), due to reports of its cytotoxic activity and similarity to known congeners, has been shown to exhibit antidepressant-like activity.[6−13] The marine natural alkaloid lamellarins, bearing a pyrrolo[2,1-α]-isoquinoline core, were found to have a wide spectrum of pharmacological activities.[14−19] For example, lamellarin I exhibited direct inhibition of P-glycoprotein-mediated drug efflux at noncytotoxic doses to reverse multidrug resistance;[20,21] lamellarin D showed potent antitumor activity to be an inhibitor of human topoisomerase I.[22−25] Also, lamellarin K and L have been investigated for their immunomodulatory effects in the micromolar range,[26,27] and lamellarin α-20-sulfate was expected to be a drug candidate for the inhibition of HIV integrase at noncytotoxic concentrations.[28,29]

The novel structure of the lamellarin as well as their pharmacological potential led to a tremendous interest in these compounds. The lamellarin alkaloids were first isolated by Faulkner and co-workers from the prosobranch mollusc Lamellaria sp.[30] To better understand these attractive compounds, various efficient synthetic methods have been developed.[31−39] These processes mostly entail 1,3-dipolar cycloaddition to construct the core scaffold pyrrolo[2,1-α]isoquinoline (Scheme 1). In 2007, Porco's group developed an efficient synthesis of lamellarin products involving Ag(I)-catalyzed domino cycloisomerization/dipolar cycloaddition of readily available alkynyl *N*-benzylidene glycinates via azomethine ylides as a key intermediate (Scheme 1, eq. 1).[40] Zhen and Wang reported an azodicarboxylate (DEAD)-promoted oxidative [3+2] cycloaddition/aromatization tandem reaction for the construction of pyrrolo[2,1-α]isoquinolines (eq. 21).[41] Wu and co-workers demonstrated an intermolecular [3+2] cycloaddition for the directed synthesis of pyrrolo[2,1-α]isoquinolines core from 1,2,3,4-tetrahydroisoquinoline (THIQ), phenylglyoxal monohydrate, and (*E*)-(2-nitrovinyl)-benzene (eq. 31).[42]

However, efficient approaches for synthesizing pyrrolo[2,1-α]isoquinoline are still rare in the literature. Thus, exploiting more new synthetic strategies is still a pressing task to realize the potential applications of biologically active lamellarin

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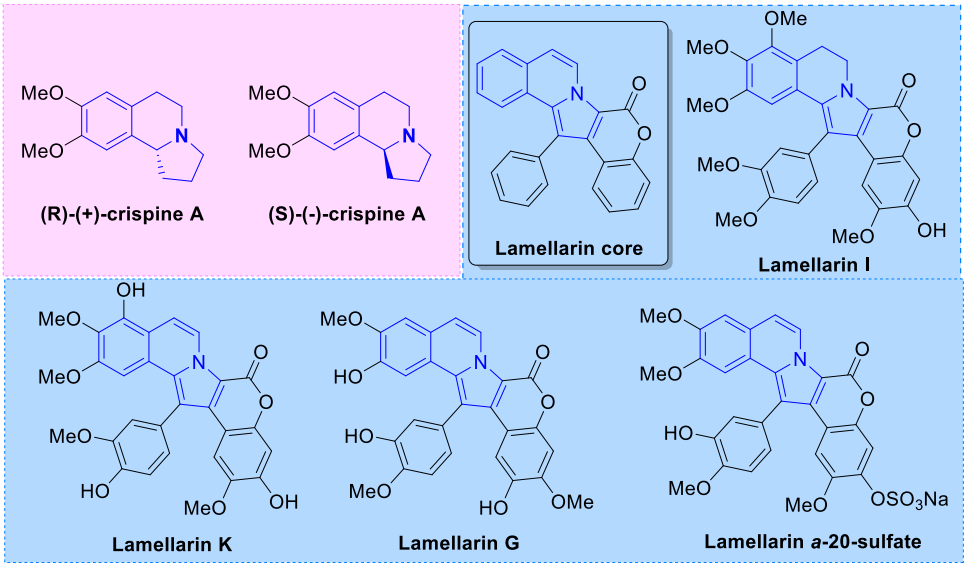
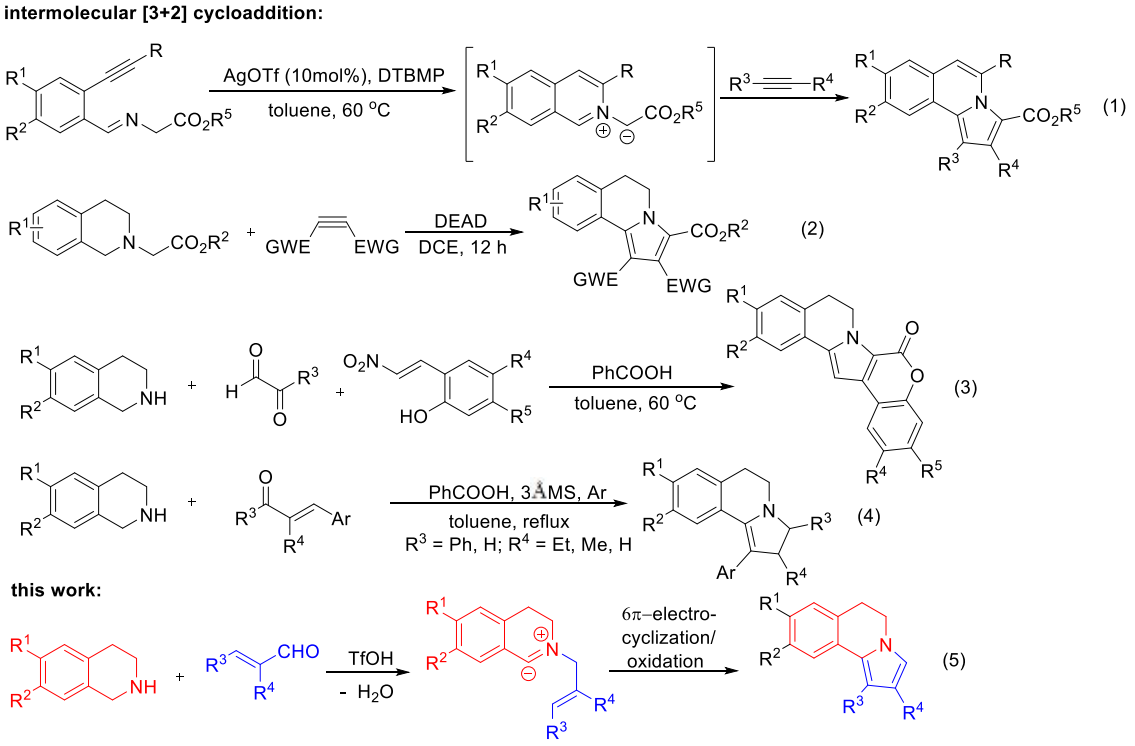


Figure 1. Representative examples of pyrroloisoquinoline.

Scheme 1. Synthetic Strategies of Pyrroloisoquinoline



alkaloids. Recently, Seidel developed a strategy for the rapid formation of fused tricyclic ring systems via redox-neutral annulations of cyclic amines (e.g., pyrrolidine and THIQ) with aldehydes and ketones (eq. 41).[43−47] Previously, we developed a concise and general strategy for the construction of quinazolinones by a direct cyclization reaction between anthranils and cyclic amines in the absence of a transition-metal catalyst without the use of an additional initiator/oxidant.[48] To continue the synthesis of heterocycle-fused quinazolinones, we herein develop an efficient one-pot acid-promoted redox-annulation of cascade C−C and C−N coupling for the synthesis of 1,2-disubstituted-5,6-dihydropyrrolo[2,1-α]isoquinoline using THIQ and α, β-unsaturated aldehydes as the starting materials (Scheme 1, eq. 5). A similar reaction was reported by the Seidel group in 2015,[45] different from our covering work; the substrates and reaction conditions used were different and the products they obtained were dihydropyrrole derivatives, and further oxidation (TEMPO, air) was required to obtain aromatized products (eq. 41).

RESULTS AND DISCUSSION

Initially, (*E*)-2,3-diphenylacrylaldehyde **1a** (0.5 mmol) was reacted with 1,2,3,4-tetrahydroisoquinoline (THIQ) **2a** (1 mmol, 2 equiv) in the presence of TFA (trifluoroacetic acid, 2 equiv) at 80 °C under air in PhMe (2 mL), and the desired

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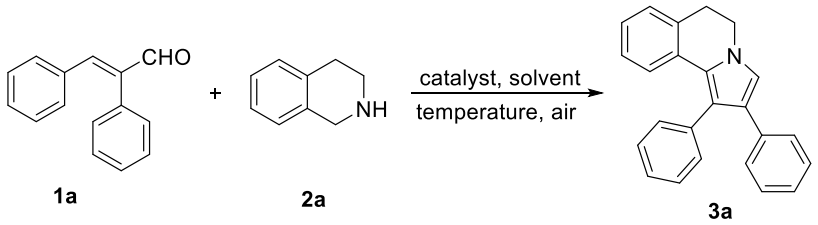
Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

entry	additive	time (h)	solvent	temperature (°C)	yield (%)[b]
1	TFA	5	PhMe	80	8
2	TFA	5	PhMe	100	65
3	TFA	5	PhMe	130	81
4	TFA	5	PhMe	150	76
5	PhCOOH	5	PhMe	130	83
6	AcOH	5	PhMe	130	89
7	**TfOH**	**5**	**PhMe**	**130**	**90**
8	CuCl2	5	PhMe	130	7
9	AuBr3	5	PhMe	130	68
10		5	PhMe	130	74
11	TfOH	5	DCE	130	88
12	TfOH	5	MeOH	130	
13	TfOH	5	DMSO	130	3
14	TfOH	5	1,4-dioxane	130	trace
15	TfOH	5	DMF	130	trace
16	TfOH	5	MeCN	130	10
17	TfOH	12	PhMe	130	81
18	TfOH	5	PhMe	150	67

[a]Reaction condition: **1a** (0.5 mmol), **2a** (1 mmol), and additive (2 equiv) in solvent (2 mL) were stirred at a temperature under air for 5−12 h. [b]Isolated yield.

product 1,2-diphenyl-5,6-dihydropyrrolo[2,1-*a*]isoquinoline **3a** was obtained in 8% yield in 5 h (Table 1, entry 1). Then, the screening of reaction temperature was carried out (entries 2−4). To our delight, an increase in the temperature to 130 °C resulted in a high yield of 81%. Higher temperatures could result in solvent loss and product decomposition. A variety of acid additives and Lewis acids, such as PhCOOH, AcOH, TfOH (trifluoromethanesulfonic acid), $CuCl_2$, and $AuBr_3$, were examined to investigate their effects on the reaction. Among the various additives tested, we were pleased to find that TfOH was the most effective one for the reaction with a best yield of up to 90%, and the reaction gave the target compound in 74% yield in the absence of an acid additive (entries 5−10). Encouraged by this result, various solvents, including DCE, MeOH, DMSO, 1,4-dioxane, DMF, and MeCN, were screened for the reaction, but toluene was indicated from the results to be the best choice for this reaction; other solvents gave lower yields (entries 11−16). Extending the reaction time and increasing the reaction temperature did not improve the reaction yield either (entries 17−18, Table 1). Therefore, 2 equiv of TfOH in toluene at 130 °C for 5 h were found to be the optimal conditions for the synthesis of 1,2-diphenyl-5,6-dihydropyrrolo[2,1-*a*]-isoquinoline (Scheme 2).

With the optimized reaction conditions in hand, we proceeded to investigate the substrate scope of the reaction using a variety of substituted (*E*)-2,3-diphenylacrylaldehyde derivatives **1**. Notably, the (*E*)-2,3-diphenylacrylaldehyde derivatives **1** with both electron-withdrawing and electron-donating substituents on the R^2 aromatic moiety were tolerated under the optimized reaction conditions to furnish the desired products **3b**−**3k** in moderate to good yields. Halogen-substituted substrates (4-Br, 3-Br) reacted smoothly to afford the corresponding products in 55−80% yields. The phenyl ring R^2 bearing electron-donating (−CH_3, −OMe) and electron-withdrawing groups (−Br, −CF_3) reacted smoothly to afford the desired products **3b**−**3g** in 55−88% yields. As expected, substitution at the *meta* position of arenes R^2 gives products **3f** and **3g** smoothly in 55 and 57% yields, respectively. Moreover, the arene ring was not limited to benzene; the polycyclic-substituted derivatives also worked well and afforded products **3i** and **3j** in 72 and 76% yields, respectively. Remarkably, the pyrene-substituted substrate reacted as anticipated to give the corresponding product **3k** in 53% yield. Satisfactory yields were observed with electron-donating (−CH_3, −OMe) groups attached to the benzene ring R^1 (92%, 94%; **3l**, **3m**). Prompted by the results achieved above, the scope of cinnamic aldehyde derivatives **1** was further investigated. As expected, derivatives **1** with electron-donating (−CH_3) and electron-withdrawing (−Br) groups at the aryl *para* position both reacted well to provide the corresponding products **3n**−**3p** in 45−58% yields. The molecular structure of **3o** was unambiguously confirmed using X-ray crystallography (CCDC 2078071, for detail, see the Supporting Information). Moreover, (*E*)-2-methyl-3-phenylacrylaldehyde also worked well and afforded products **3q** in 43% yield.

Next, we turned our attention to investigating the scope and limitations of the reaction with various THIQs. The results are summarized in Scheme 3. Notably, the THIQ derivatives **2** with both electron-withdrawing and electron-donating substituents on the aromatic moiety were tolerated under the optimized reaction conditions to furnish the desired products

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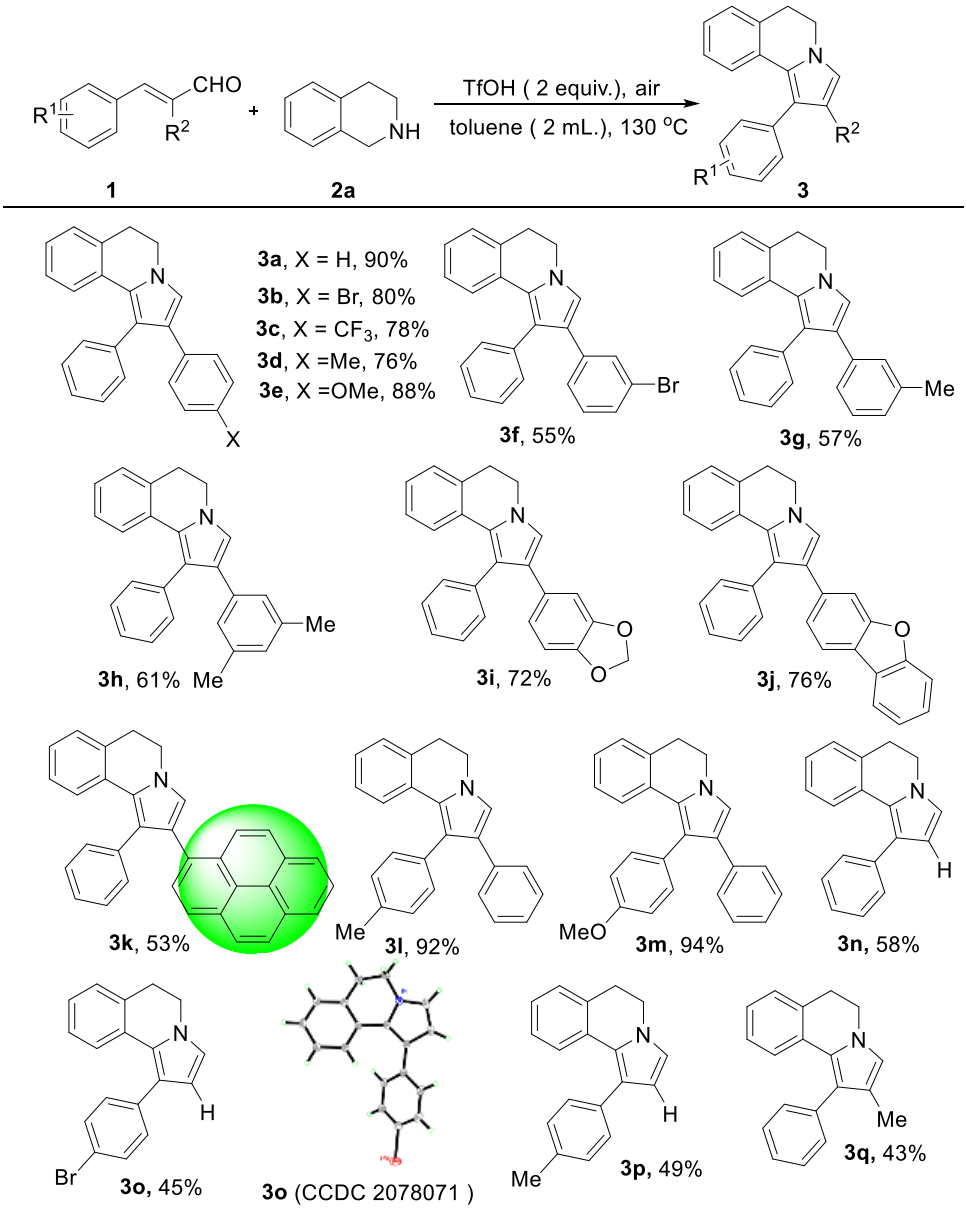
Scheme 2. Substrate Scope of Unsaturated Aldehydes[a,b]



[a]Reaction condition: **1** (0.5 mmol), **2a** (1 mmol), and TfOH (2 equiv) in toluene (2 mL) were stirred at 130 °C under air for 5 h. [b]Isolated yield.

4a−**4e** in moderate to good yields. Halogen-substituted substrates (6-Br, 7-Br) reacted smoothly to afford the corresponding products in 70 and 72% yields, respectively. Furthermore, to demonstrate the synthetic utility of this protocol developed, the product **3i** was treated with *N*-bromosuccinimide (NBS) in THF at 25 °C for 30 min to give the brominated compound **5** in 90% yield. Suzuki coupling of the brominated product **5** with phenylboronic acid afforded the lamellarin-like compound **6** in good yield (Scheme 4).[49] The formyl group was introduced by the Vilsmeier−Haack reaction with DMF/$POCl_3$ to give the derivative **7** in 62% yield, which could transform to lamellarin in few steps.[50] Finally, the pyrrolo[2,1-α]isoquinoline derivative **3a** was modified with methyl acrylate with the $Pd(OAc)_2$/AgOAc system through oxidative Heck coupling to give the corresponding product **8** in 76% yield.[51]

To study the mechanism of this strategy, some control experiments were carried out (Scheme 5). When Ar was employed as the reaction atmosphere, the yield of the desired product was reduced to 5%, which indicates that air is essential for the formation of the final product. The unoxidized product **3a′** was found using GCMS in the blank reaction (without TfOH) in 1 h and was converted into the oxidized target product **3a** with the passage of time. However, when the acid was added into the reaction, the unoxidized product **3a′** was not detected in 1 h, indicating that the acid promoted the formation of the target product (GCMS and NMR spectra attached to the Supporting Information).

On the basis of the above control experimental results, a reasonable mechanism of the reaction was proposed (Figure 2). The reaction is most likely initiated by addition of THIQ **2** to α,β-unsaturated aldehydes **1**; subsequent elimination of water could occur with the assistance of TfOH, yielding iminium **B**, which resonated from intermediate **A**. Electrocyclization of intermediate **B** leads to the formation of

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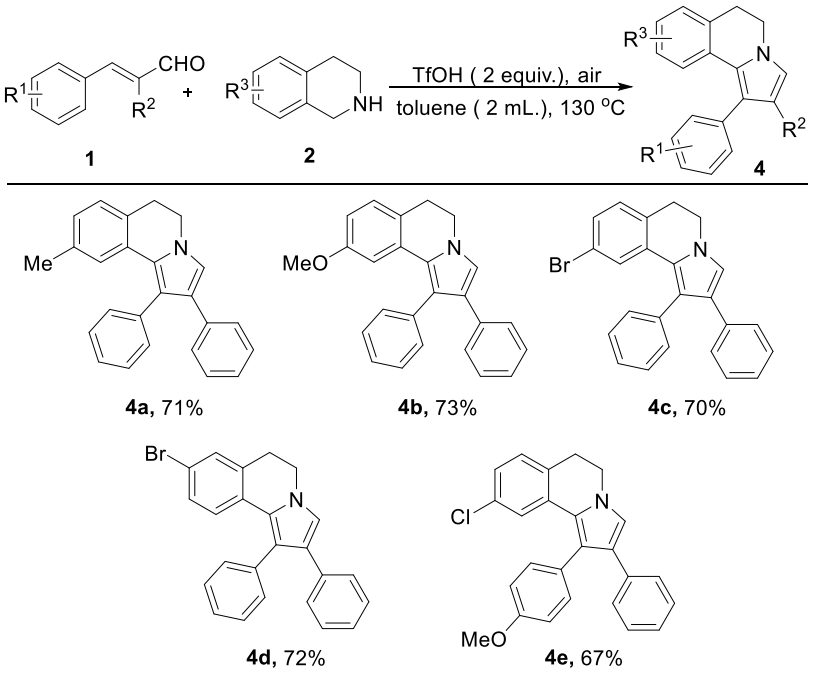
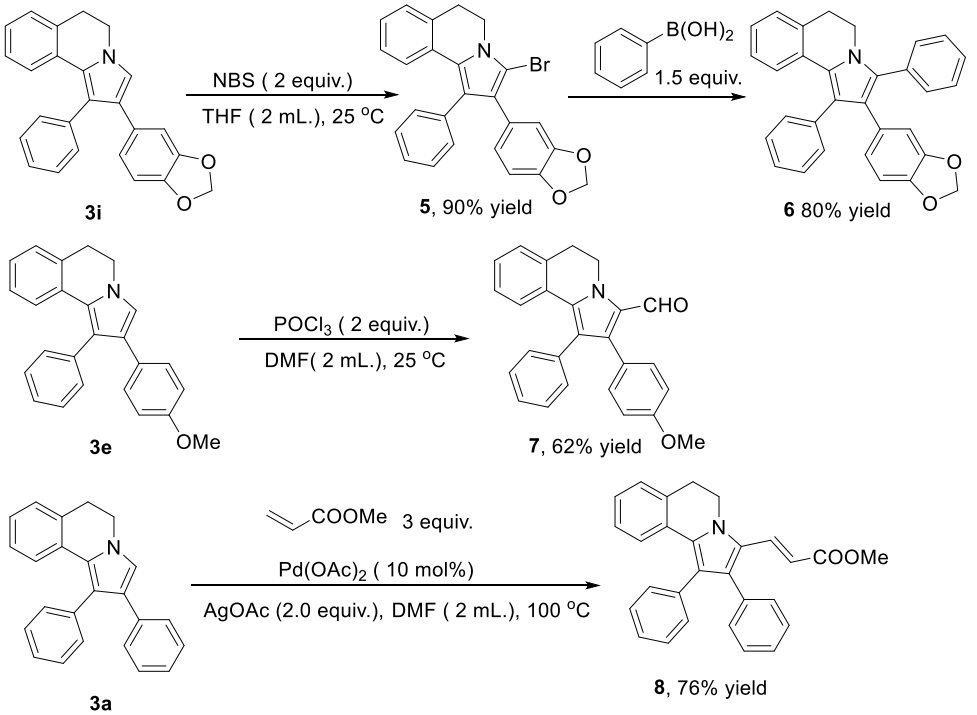
Scheme 3. Substrate Scope of THIQs[a,b]



[a]Reaction condition: **1** (0.5 mmol), **2** (1 mmol), and TfOH (2 equiv) in toluene (2 mL) were stirred at 130 °C under air for 5 h. [b]Isolated yield.

Scheme 4. Product Application



compound **C**. Finally, air oxidative aromatization as key step for this process, affords the final product **3**.

In conclusion, we have developed a facile and efficient approach for the synthesis of the 1,2-disubstituted-5,6-dihydropyrrolo[2,1-α]isoquinoline derivative by a direct cyclization reaction between THIQ and substituted α,β-unsaturated aldehydes. Applying this electrocyclization reaction, an easy synthesis of lamellarin core, which is an important class of marine natural alkaloids, has been accomplished without a multistep process under simple reaction conditions. Further synthetic applications and mechanism of this strategy are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all commercially available reagents were used without further purification. Solvents and reagents were purchased from commercial sources and used without further purification.

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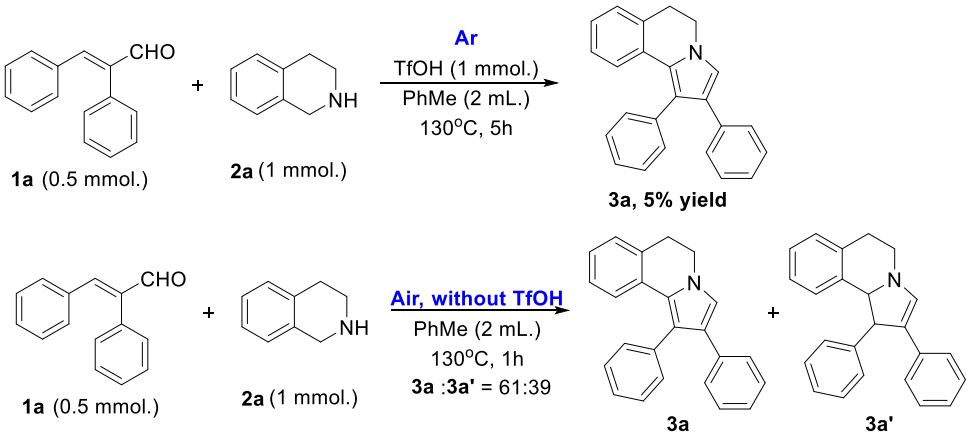
Scheme 5. Control Experiment



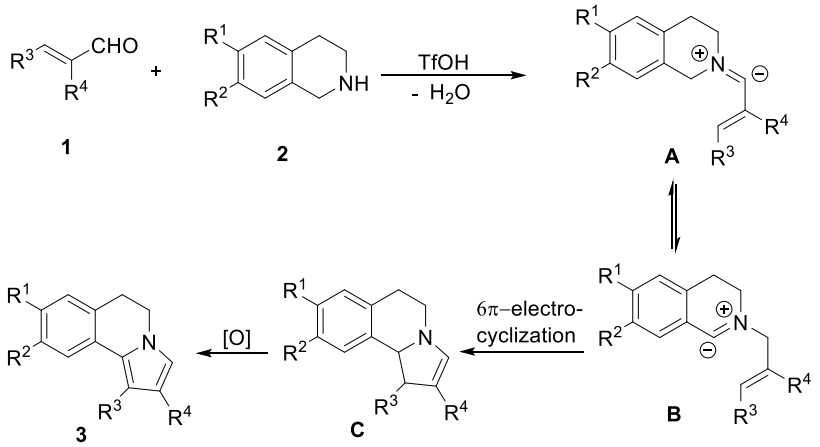


Figure 2. Proposed reaction mechanism.

Flash column chromatography was performed using silica gel (200−300 mesh). Analytical thin-layer chromatography was performed using glass plates precoated with 200−300 mesh silica gel impregnated with a fluorescent indicator (254 nm). NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on Bruker NMR-300 (300 MHz) and NMR-400 (400 MHz) spectrometers with TMS as an internal reference. HRMS was performed on an Agilent 6540 Q-TOF mass spectrometer (ESI). IR spectra were recorded on a Thermo Fisher IS50 FT-IR spectrometer. X-ray crystallographic data were collected using a SMART APEX II X-ray diffractometer. THIQ derivatives were prepared according to the previously reported literature procedures.[16]

General Procedure for the Preparation of ***1****.* Starting materials **1** were prepared according to the previously reported literature procedures.[19] **1b, 1f, 1g,** and **1i−1k** are unknown compounds.

General Procedure for the Target Products ***3*** *and* ***4****.* In a 25 mL Shrek tube were added compound **1** (0.5 mmol), 1,2,3,4-tetrahydroisoquinoline derivatives **2** (1.0 mmol), TfOH (1.0 mmol), and 2.0 mL of toluene. The mixture was stirred under air at 130 °C for 5 h. After the complete conversion of the substrates (monitored by TLC), the reaction mixture was concentrated, and the residue was purified using silica gel column chromatography to give the desired product. The obtained product was analyzed by ^{1}H NMR, ^{13}C NMR, and HRMS.

*(E)-2-(4-Bromophenyl)-3-phenylacrylaldehyde (****1b****).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1b** as a yellow solid (1.07 g, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.40 (s, 1H), 7.32 (t, J = 7.1 Hz, 1H), 7.28−7.18 (m, 4H), 7.08 (d, J = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 150.6, 140.4, 133.5, 132.0, 131.9, 131.1, 130.6, 130.4, 128.5, 122.5, 99.8. MS (m/z): 285.9.

*(E)-2-(3-Bromophenyl)-3-phenylacrylaldehyde (****1f****).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1f** as a yellow solid (1.09 g, 76% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.51 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.40 (s, 1H), 7.36 (t, J = 1.8 Hz, 1H), 7.33−7.17 (m, 6H), 7.12 (dt, J = 7.6, 1.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.1, 150.8, 140.1, 135.3, 133.4, 132.1, 131.3, 130.6, 130.5, 130.3, 128.6, 128.0, 122.7. MS (m/z): 285.9.

*(E)-3-Phenyl-2-(m-tolyl)acrylaldehyde (****1g****).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1g** as a white solid (0.81 g, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.34 (s, 1H), 7.31−7.15 (m, 7H), 7.04−6.92 (m, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 149.9, 141.7, 138.3, 133.9, 133.1, 130.6, 130.0, 129.6, 128.9, 128.6, 128.3, 126.1, 21.3. MS (m/z): 222.1.

*(E)-2-(Benzo[d][1,3]dioxol-5-yl)-3-phenylacrylaldehyde (****1i****).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1i** as a white solid (0.97 g, 77% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.32 (s,

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1H), 7.26 (q, J = 7.4, 6.2 Hz, 5H), 6.83 (d, J = 7.7 Hz, 1H), 6.65 (d, J = 8.1 Hz, 2H), 5.95 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 150.1, 147.8, 147.4, 141.0, 133.8, 130.5, 130.0, 128.3, 126.4, 122.8, 109.5, 108.7, 101.0. MS (m/z): 252.1.

*(E)-2-(Dibenzo[b,d]furan-4-yl)-3-phenylacrylaldehyde (**1j**).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1j** as a yellow solid (1.07 g, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.05−7.89 (m, 2H), 7.65 (s, 1H), 7.39 (d, J = 7.5 Hz, 3H), 7.33−7.24 (m, 2H), 7.23−7.15 (m, 3H), 7.11 (t, J = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 155.9, 153.5, 151.4, 136.4, 133.9, 130.4, 130.3, 128.4, 128.0, 127.2, 124.7, 123.9, 123.1, 122.7, 120.9, 120.5, 117.9, 111.7. MS (m/z): 298.1.

*(E)-3-Phenyl-2-(pyren-4-yl)acrylaldehyde (**1k**).* Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **1k** as a yellow solid (1.10 g, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.17 (dd, J = 17.2, 7.7 Hz, 2H), 8.11−8.03 (m, 3H), 7.94 (dd, J = 8.4, 5.0 Hz, 2H), 7.81 (d, J = 9.2 Hz, 1H), 7.74 (d, J = 5.7 Hz, 2H), 7.13−7.05 (m, 1H), 6.95 (d, J = 5.1 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 151.4, 140.7, 133.7, 131.4, 131.1, 130.9, 130.7, 130.4, 128.8, 128.8, 128.4, 128.0, 127.7, 127.3, 127.0, 126.0, 125.3, 125.2, 124.9, 124.7, 124.2. MS (m/z): 334.1.

3a: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3a** as a yellow solid (144 mg, 90%). mp: 52−53 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 4.7 Hz, 5H), 7.14 (d, J = 7.4 Hz, 3H), 7.10 (d, J = 7.1 Hz, 3H), 7.01 (td, J = 7.3, 1.6 Hz, 1H), 6.98−6.88 (m, 2H), 6.84 (s, 1H), 4.07 (t, J = 6.4 Hz, 2H), 3.08 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 136.5, 131.7, 130.9, 129.5, 129.0, 128.4, 127.9, 127.8, 126.5, 126.4, 125.8, 125.3, 124.1, 123.8, 120.0, 118.4, 113.4, 55.0, 44.4, 30.0. IR (KBr): ν = 3054, 2922, 1601, 1534, 1467, 1395, 1330, 1165, 766, 751, 700. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{20}N$ 322.1590; found 322.1587.

3b: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3b** as a yellow solid (160 mg, 80%). mp: 168−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.23 (m, 7H), 7.16 (d, J = 7.4 Hz, 1H), 7.03 (td, J = 7.0, 2.1 Hz, 1H), 6.95 (d, J = 8.7 Hz, 4H), 6.84 (s, 1H), 4.09 (t, J = 6.4 Hz, 2H), 3.10 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 134.4, 131.7, 131.0, 130.8, 129.4, 129.3, 128.6, 127.9, 126.6, 126.6, 126.3, 125.6, 123.9, 123.3, 120.0, 119.1, 118.9, 44.5, 30.0. IR (KBr): ν = 3045, 2916, 1604, 1529, 1469, 1405, 1167, 1020, 828, 768, 700. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}BrN$ 400.0695; found 400.0692.

3c: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3c** as a light green solid (155 mg, 78%). mp: 128−129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.27 (m, 7H), 7.18 (d, J = 7.8 Hz, 3H), 7.08−7.01 (m, 1H), 6.93 (d, J = 8.6 Hz, 3H), 4.12 (t, J = 6.4 Hz, 2H), 3.12 (t, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.1, 131.8, 130.8, 129.2, 128.7, 127.9, 127.7, 126.8, 126.7, 126.5, 125.7, 124.9, 124.9, 124.0, 123.1, 120.2, 119.4, 44.6, 29.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.18. IR (KBr): ν = 3058, 2940, 1615, 1605, 1459, 1324, 1160, 1119, 1064, 845, 773, 748, 697. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{19}F_3N$ 390.1464; found 390.1462.

3d: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3d** as a yellow solid (127 mg, 76%). mp: 140−141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 4.6 Hz, 5H), 7.15 (d, J = 7.4 Hz, 1H), 7.03−6.88 (m, 7H), 6.83 (s, 1H), 4.07 (t, J = 6.4 Hz, 2H), 3.09 (t, J = 6.4 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 134.7, 132.4, 131.7, 130.9, 129.5, 128.7, 128.4, 127.8, 126.5, 126.4, 126.0, 125.3, 124.4, 123.9, 120.1, 118.7, 44.5, 30.0, 21.0. IR (KBr): ν = 3022, 2891, 1603, 1540, 1396, 1329, 1157, 822, 771, 764, 754. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}N$ 336.1747; found 336.1746.

3e: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3e** as a white solid (154 mg, 88%). mp: 133−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 4.3 Hz, 5H), 7.13 (d, J = 7.4 Hz, 1H), 7.05−6.87 (m, 5H), 6.77 (s, 1H), 6.70 (d, J = 8.7 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.71 (s, 3H), 3.06 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 136.7, 131.9, 131.0, 129.7, 129.2, 128.6, 128.1, 128.0, 126.7, 126.5, 126.0, 125.5, 124.3, 124.0, 120.2, 118.6, 113.6, 55.2, 44.6, 30.2. IR (KBr): ν = 3001, 2956, 1602, 1556, 1501, 1468, 1398, 1242, 1032, 833, 763. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}NO$ 352.1696; found 352.1693.

3f: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3f** as a white solid (110 mg, 55%). mp: 116−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 6H), 7.19 (dd, J = 13.4, 7.6 Hz, 2H), 7.04 (td, J = 7.1, 2.1 Hz, 1H), 7.00−6.90 (m, 4H), 6.88 (s, 1H), 4.11 (t, J = 6.5 Hz, 2H), 3.11 (t, J = 6.4 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 136.0, 131.7, 130.8, 130.6, 129.4, 129.3, 128.6, 128.1, 127.9, 126.7, 126.6, 126.4, 126.3, 125.6, 124.0, 123.0, 122.0, 120.2, 119.1, 44.6, 30.0. IR (KBr): ν = 3038, 2923, 1602, 1592, 1467, 1328, 1163, 1017, 782, 771, 703, 656. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}BrN$ 400.0695; found 400.0692.

3g: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3g** as a yellow solid (95 mg, 57%). mp: 52−53 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H), 7.15 (d, J = 8.1 Hz, 1H), 7.06−6.95 (m, 4H), 6.92 (dd, J = 7.4, 5.0 Hz, 2H), 6.86 (d, J = 5.1 Hz, 2H), 4.08 (t, J = 6.4 Hz, 2H), 3.09 (t, J = 6.4 Hz, 2H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 136.5, 135.3, 131.7, 130.9, 129.5, 128.7, 128.4, 127.8, 127.8, 126.6, 126.4, 126.0, 126.0, 125.4, 125.1, 124.5, 123.9, 120.2, 118.9, 44.5, 30.0, 21.4. IR (KBr): ν = 3022, 2919, 1603, 1466, 765, 742. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}N$ 336.1747; found 336.1745.

3h: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3h** as a white solid (106 mg, 61%). mp: 59−60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.23 (m, 5H), 7.14 (d, J = 7.4 Hz, 1H), 6.99 (d, J = 9.3 Hz, 2H), 6.92 (d, J = 8.0 Hz, 1H), 6.84 (s, 1H), 6.73 (d, J = 9.9 Hz, 3H), 4.07 (t, J = 6.4 Hz, 2H), 3.08 (t, J = 6.4 Hz, 2H), 2.15 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.1, 136.6, 135.1, 131.7, 130.9, 129.5, 128.3, 127.8, 126.9, 126.5, 126.3, 125.9, 125.9, 125.3, 124.6, 123.9, 120.3, 118.9, 44.4, 30.0, 21.2. IR (KBr): ν = 3022, 2915, 1601, 1466, 1371, 1160, 848, 763, 702, 639. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{26}H_{24}N$ 350.1903; found 350.1902.

3i: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3i** as a white solid (131 mg, 72%). mp: 61−62 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 5H), 7.14 (d, J = 7.4 Hz, 1H), 7.00 (t, J = 8.0 Hz, 1H), 6.91 (dd, J = 14.2, 6.9 Hz, 2H), 6.76 (s, 1H), 6.59 (d, J = 12.0 Hz, 3H), 5.83 (s, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.06 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1, 145.3, 136.3, 131.7, 130.8, 129.5, 129.4, 128.5, 127.8, 126.5, 126.5, 125.9, 125.4, 124.2, 123.8, 121.2, 120.0, 118.6, 108.6, 107.9, 100.5, 44.4, 29.9. IR (KBr): ν = 2882, 1603, 1534, 1483, 1038, 811, 766, 701.

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HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{20}NO_2$ 366.1489; found 366.1486.

3j: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3j** as a white solid (156 mg, 76%). mp: 93−94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 1.2 Hz, 1H), 7.68 (dd, J = 7.6, 1.3 Hz, 1H), 7.54 (d, J = 8.2 Hz, 1H), 7.44−7.34 (m, 4H), 7.33−7.22 (m, 4H), 7.16 (d, J = 7.5 Hz, 1H), 7.08−6.89 (m, 5H), 4.18 (t, J = 6.4 Hz, 2H), 3.12 (t, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 153.2, 136.3, 131.5, 130.4, 129.1, 128.1, 127.5, 127.1, 126.4, 126.3, 126.2, 125.7, 125.1, 124.2, 123.7, 123.7, 122.1, 122.0, 121.1, 120.5, 120.1, 119.8, 117.3, 117.1, 111.2, 44.4, 29.7. IR (KBr): ν = 3055, 1603, 1532, 1167, 764, 752, 701. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{30}H_{22}NO$ 412.1696; found 412.1693.

3k: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3k** as a light green solid (118 mg, 53%). mp: 125−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 9.2 Hz, 1H), 8.05 (t, J = 7.2 Hz, 2H), 7.98−7.85 (m, 5H), 7.66 (d, J = 7.9 Hz, 1H), 7.23−7.11 (m, 4H), 7.05 (d, J = 5.9 Hz, 4H), 7.00−6.93 (m, 1H), 6.86 (s, 1H), 4.06 (t, J = 6.4 Hz, 2H), 3.08 (t, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 131.8, 131.3, 131.3, 131.0, 130.5, 129.7, 129.6, 129.5, 129.2, 128.1, 127.9, 127.4, 126.7, 126.6, 126.6, 126.1, 126.0, 125.6, 125.5, 125.5, 124.8, 124.5, 124.3, 124.2, 124.1, 123.0, 122.3, 121.3, 44.6, 30.0. IR (KBr): ν = 3038, 1602, 1458, 1166, 847, 765, 754, 700. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{34}H_{24}N$ 446.1903; found 446.1905.

3l: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3l** as a white solid (154 mg, 92%). mp: 59−60 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.07 (m, 10H), 7.04−6.97 (m, 2H), 6.96−6.88 (m, 1H), 6.83 (s, 1H), 4.06 (t, J = 6.5 Hz, 2H), 3.07 (t, J = 6.4 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.9, 135.6, 133.3, 131.7, 130.7, 129.6, 129.3, 128.0, 127.9, 127.8, 126.6, 126.1, 125.4, 125.2, 124.5, 124.0, 120.2, 118.9, 44.5, 30.1, 21.3. IR (KBr): ν = 3051, 2921, 1601, 1534, 1469, 1108, 1031, 766, 697, 593. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}N$ 336.1747; found 336.1748.

3m: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3m** as a white solid (164 mg, 94%). mp: 61−62 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.07 (m, 8H), 7.05−6.92 (m, 3H), 6.87 (d, J = 8.7 Hz, 2H), 6.84 (s, 1H), 4.07 (dd, J = 7.0, 5.9 Hz, 2H), 3.82 (s, 3H), 3.08 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 135.6, 131.9, 131.7, 129.7, 128.7, 128.0, 127.9, 127.9, 126.6, 126.1, 125.4, 125.2, 124.6, 123.9, 119.8, 118.9, 114.0, 55.1, 44.5, 30.0. IR (KBr): ν = 3059, 2931, 1601, 1534, 1173, 1032, 835, 765, 740, 698. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}NO$ 352.1696; found 352.1693.

3n: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3n** as a yellow oil (71 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 6.9 Hz, 2H), 7.28 (t, J = 7.8 Hz, 3H), 7.18 (t, J = 7.3 Hz, 1H), 7.12−7.07 (m, 1H), 6.94 (dtd, J = 22.9, 7.5, 1.4 Hz, 2H), 6.63 (d, J = 2.7 Hz, 1H), 6.16 (d, J = 1.9 Hz, 1H), 3.97 (t, J = 6.4 Hz, 2H), 3.00 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 131.9, 129.0, 128.4, 127.9, 126.6, 126.1, 125.6, 124.0, 122.5, 120.3, 110.5, 44.7, 30.2. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{16}N$ 246.1277; found 246.1276.

3o: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3o** as a red solid (73 mg, 45%). mp: 111−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.19 (d, J = 7.4 Hz, 1H), 7.04 (dtd, J = 20.4, 7.4, 1.5 Hz, 2H), 6.71 (d, J = 2.7 Hz, 1H), 6.20 (d, J = 2.7 Hz, 1H), 4.05 (t, J = 6.4 Hz, 2H), 3.08 (t, J = 6.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.6, 131.9, 131.4, 130.5, 129.4, 128.0, 126.6, 125.8, 123.8, 121.0, 120.4, 119.8, 110.2, 44.6, 30.1. IR (KBr): ν = 3043, 2944, 1653, 1493, 1069, 1010, 836, 825, 764, 742. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{15}BrN$ 324.0382; found 324.0380.

3p: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3p** as a yellow solid (63 mg, 49%). mp: 144−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.27 (m, 3H), 7.09 (d, J = 7.8 Hz, 3H), 6.94 (dtd, J = 19.0, 7.4, 1.5 Hz, 2H), 6.63 (s, 1H), 6.14 (s, 1H), 3.97 (t, J = 6.4 Hz, 2H), 3.00 (t, J = 6.4 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.3, 134.3, 131.5, 129.5, 128.8, 128.5, 127.6, 126.2, 125.1, 123.6, 122.1, 119.8, 110.1, 44.3, 29.9, 20.9. IR (KBr): ν = 3019, 2938, 2914, 2360, 2341, 1510, 1491, 1330, 825, 763, 738, 699, 668. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}N$ 260.1434; found 260.1434.

3q: Column chromatography on silica gel (EA/PE = 1:50) afforded the title product **3q** as a colorless oil (55 mg, 43%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, J = 6.5 Hz, 5H), 7.16−7.12 (m, 1H), 7.04−6.87 (m, 3H), 6.54 (d, J = 1.0 Hz, 1H), 4.01 (t, J = 6.5 Hz, 2H), 3.06 (t, J = 6.5 Hz, 2H), 2.00 (d, J = 0.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9, 131.6, 130.4, 129.7, 128.4, 127.9, 126.5, 126.2, 125.2, 125.1, 123.6, 121.9, 118.7, 118.4, 44.2, 30.1, 10.5. IR (KBr): ν = 3011, 2928, 1513, 1481, 1340, 834, 767, 738, 697. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}N$ 260.1434; found 260.1431.

4a: Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **4a** as a green solid (119 mg, 71% yield). mp: 70−71 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.26 (m, 5H), 7.17−7.07 (m, 5H), 7.03 (d, J = 7.7 Hz, 1H), 6.82 (d, J = 4.3 Hz, 2H), 6.74 (s, 1H), 4.04 (dd, J = 7.0, 5.9 Hz, 2H), 3.03 (t, J = 6.4 Hz, 2H), 2.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 135.9, 135.5, 130.9, 129.3, 128.8, 128.4, 128.0, 127.9, 127.7, 126.4, 126.2, 126.2, 125.2, 124.7, 124.3, 120.1, 118.9, 44.6, 29.6, 21.2. IR (KBr): ν = 3022, 2921, 2868, 1598, 1497, 1449, 1330, 1262, 813, 766, 741, 719, 699. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}N$ 336.1747; found 336.1747.

4b: Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **4b** as a yellow solid (128 mg, 73% yield). mp: 63−64 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 7.20−7.08 (m, 5H), 7.05 (d, J = 8.3 Hz, 1H), 6.88 (s, 1H), 6.58 (dd, J = 8.3, 2.7 Hz, 1H), 6.51 (d, J = 2.7 Hz, 1H), 4.08 (t, J = 6.5 Hz, 2H), 3.33 (s, 3H), 3.04 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 136.6, 135.4, 131.1, 130.3, 128.7, 128.5, 128.0, 127.9, 126.6, 126.3, 125.3, 124.3, 123.8, 120.3, 119.0, 112.6, 108.0, 54.6, 44.8, 29.1. IR (KBr): ν = 3000, 2957, 1604, 1555, 1508, 1394, 1031, 830, 766, 701. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}NO$ 352.1696; found 352.1696.

4c: Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **4c** as a white solid (139 mg, 70% yield). mp: 146−147 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.27 (m, 5H), 7.21−7.07 (m, 6H), 7.02 (dd, J = 5.0, 3.0 Hz, 2H), 6.88 (s, 1H), 4.09 (t, J = 6.5 Hz, 2H), 3.05 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 135.1, 131.4, 130.7, 130.4, 129.4, 128.7, 128.1, 128.0, 128.0, 126.9, 126.6, 125.5, 124.8, 124.7, 121.2, 120.4, 119.5, 44.3, 29.5. IR (KBr): ν = 3050, 2951, 2873, 1728, 1598, 1549, 1497, 1480, 789, 728.

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HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}BrN$ 400.0695; found 400.0693.

4d: Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **4d** as a white solid (133 mg, 67% yield). mp: 110−111 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 6H), 7.21−7.07 (m, 5H), 7.04 (dd, J = 8.5, 2.1 Hz, 1H), 6.88 (s, 1H), 6.79 (d, J = 8.5 Hz, 1H), 4.10 (t, J = 6.5 Hz, 2H), 3.09 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.1, 135.2, 133.8, 130.8, 130.7, 129.7, 128.6, 128.5, 128.0, 128.0, 126.7, 125.5, 125.4, 125.3, 124.8, 120.7, 119.3, 118.7, 44.3, 29.8. IR (KBr): ν = 3056, 2954, 2868, 1726, 1592, 1544, 1456, 782, 726, 685. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}BrN$ 400.0695; found 400.0696.

4e: Column chromatography on silica gel (EA/PE = 1:20) afforded the title product **4e** as a yellow solid (119 mg, 67% yield). mp: 65−66 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.03 (m, 8H), 7.02−6.93 (m, 2H), 6.95−6.84 (m, 3H), 4.08 (t, J = 6.5 Hz, 2H), 3.84 (s, 3H), 3.06 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 135.3, 132.3, 131.7, 131.2, 129.9, 129.0, 128.0, 127.9, 127.9, 125.4, 125.1, 125.0, 124.8, 123.6, 120.7, 119.4, 114.1, 55.2, 44.4, 29.5. IR (KBr): ν = 3063, 2918, 1593, 1559, 1176, 1150, 1061, 1018, 839, 794, 772, 729. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{21}ClNO$ 386.1306; found 386.1306.

5: To a 10 mL round-bottomed flask were added dry THF (2 mL) and NBS (2 equiv), **3i** (0.09 mmol) was added at 25 °C, and the mixture was stirred overnight. Then, the solvent was evaporated under a vacuum. The crude product was purified using flash column chromatography on silica gel (EA/PE = 1:20) to afford the title product **5** as a white solid (0.09 mmol scale, 36 mg, 90% yield). mp: 57−58 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19−7.08 (m, 6H), 6.99−6.92 (m, 1H), 6.85 (t, J = 6.6 Hz, 2H), 6.58 (s, 2H), 6.55−6.49 (m, 1H), 5.80 (s, 2H), 4.05 (dd, J = 7.1, 5.9 Hz, 2H), 3.02 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 144.9, 134.5, 130.8, 129.7, 128.0, 127.4, 126.8, 126.7, 125.7, 125.6, 124.9, 123.1, 122.9, 122.9, 120.9, 109.8, 106.8, 101.7, 99.7, 42.2, 28.6. IR (KBr): ν = 2888, 1601, 1481, 1388, 1034, 934, 811, 773, 707. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{19}BrNO_2$ 444.0594; found 444.0597.

6: A solution of 5 (0.08 mmol), K_2CO_3 (2 equiv), $Pd(PPh_3)_4$ (20 mol %), and phenylboronic acid (1.5 equiv) were added to a 10 mL Schlenk tube under a N_2 atmosphere. Anhydrous THF (15 mL) was added, and the mixture was heated to 70 °C for 12 h. After the mixture was cooled down to room temperature, it was filtered through a short plug of silica (EA/PE = 1:20), and the volatiles were removed in vacuo and afforded the title product 6 as a white solid (0.081 mmol scale, 28 mg, 80% yield). mp: 57−58 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22−7.15 (m, 3H), 7.11 (ddd, J = 7.7, 2.9, 1.8 Hz, 3H), 7.00−6.93 (m, 1H), 6.89−6.82 (m, 2H), 6.63−6.50 (m, 3H), 5.82 (s, 2H), 4.14−4.01 (m, 2H), 3.04 (t, J = 6.5 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 144.9, 134.5, 130.8, 129.7, 128.0, 127.4, 126.8, 126.7, 125.7, 125.6, 124.9, 123.1, 122.9, 122.9, 120.9, 109.8, 106.8, 101.7, 99.7, 42.2, 28.6. IR (KBr): ν = 2879, 1602, 1478, 1383, 1319, 1234, 1213, 1037, 935, 760, 698. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{31}H_{24}NO_2$ 442.1802; found 442.1804.

7: Under a N_2 atmosphere, to a 25 mL round-bottomed flask were added dry DMF (1 mL) and $POCl_3$ (2 equiv), 3e (0.19 mmol) dissolved in dry DMF (1 mL) was added slowly below 35 °C, and the mixture was stirred for 35 min. Then, the solvent was evaporated under a vacuum. The crude product was purified using flash column chromatography on silica gel (EA/PE= 1:50) to afford the desired product 7 as a white solid (44 mg, 62% yield). mp: 193−194 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.26 (dd, J = 9.1, 3.4 Hz, 4H), 7.20−7.13 (m, 3H), 7.07 (d, J = 8.7 Hz, 2H), 7.02−6.93 (m, 2H), 6.78 (d, J = 8.7 Hz, 2H), 4.81−4.69 (m, 2H), 3.77 (s, 3H), 3.12 (t, J = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.0, 158.8, 138.5, 134.5, 134.2, 133.1, 132.0, 130.8, 128.4, 127.9, 127.9, 127.5, 126.9, 126.7, 126.6, 126.1, 124.4, 122.7, 113.3, 55.1, 42.0, 29.3. IR (KBr): ν = 2836, 1640, 1531, 1416, 1402, 1208, 1031, 847, 762, 745. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{26}H_{22}NO_2$ 380.1645; found 380.1642.

8: To a 25 mL round-bottomed flask were added **3a** (0.12 mmol), AgOAc (2 equiv), $Pd(OAc)_2$ (10 mol %), methyl acrylate (3 equiv), and DMF (2 mL). The resulting mixture was stirred at 100 °C for 4 h. Then, the solvent was evaporated under a vacuum. The crude product was purified using flash column chromatography on silica gel (EA/PE = 1:20) and afforded the title product **8** as a yellow solid (37 mg, 76% yield). mp: 200−201 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 16.1 Hz, 1H), 7.26−7.20 (m, 7H), 7.18−7.06 (m, 5H), 6.95 (d, J = 3.8 Hz, 2H), 5.79 (d, J = 16.1 Hz, 1H), 4.28 (t, J = 6.5 Hz, 2H), 3.72 (s, 3H), 3.16 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 144.9, 134.5, 130.8, 129.7, 128.0, 127.4, 126.8, 126.7, 125.7, 125.6, 124.9, 123.1, 122.9, 122.9, 120.9, 109.8, 106.8, 101.7, 99.7, 42.2, 28.6. IR (KBr): ν = 2945, 1702, 1615, 1133, 761, 696. HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{28}H_{24}NO_2$ 406.1802; found 406.1800.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c01941.

Experimental procedures and spectral data for all new compounds (PDF)

Crystallographic data (CIF)

Accession Codes

CCDC 2078071 contains the supplementary crystallographic data for this article. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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