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SYNTHESIS OF NOVEL FLUORESCENT BICYCLIC AMIDINES AND EVALUATION OF THEIR PHOTOPHYSICAL PROPERTIES

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This article is dedicated to Professor Dr. Somsak Ruchirawat on his 80th birthday.

Abstract – A metal-free process for the synthesis of novel bicyclic amidines was developed. The key conversions involved a cascade of double intramolecular cyclization of Michael adducts under a mild condition to provide 39 analogs in up to 93% yield. Photophysical properties of the representatives, a parent molecule and its free base form were studied on different solvents. From the results, a free base form exhibited strong fluorescent emission wavelength in up to 491 nm and large Stoke shift in up to 140 nm, offering positive information for their future development.

INTRODUCTION

Amidines are a ubiquitous class of organic compounds containing two nitrogen analogs of carboxylic derivatives.[1] They have been found as structural motifs or sub-units both in natural and synthetic molecules, such as callyimine A from the marine sponge metabolite,[2] a macrocyclic peptide with antibiotic activity bottromycin A2 from *Streptomyces bottropensis*,[3] a synthetic drug Diminazene (known as Azidin, Berenil, or Pirocide) for treatment of trypanosoniasis,[4] and a well-known organic base DBU (Figure 1).

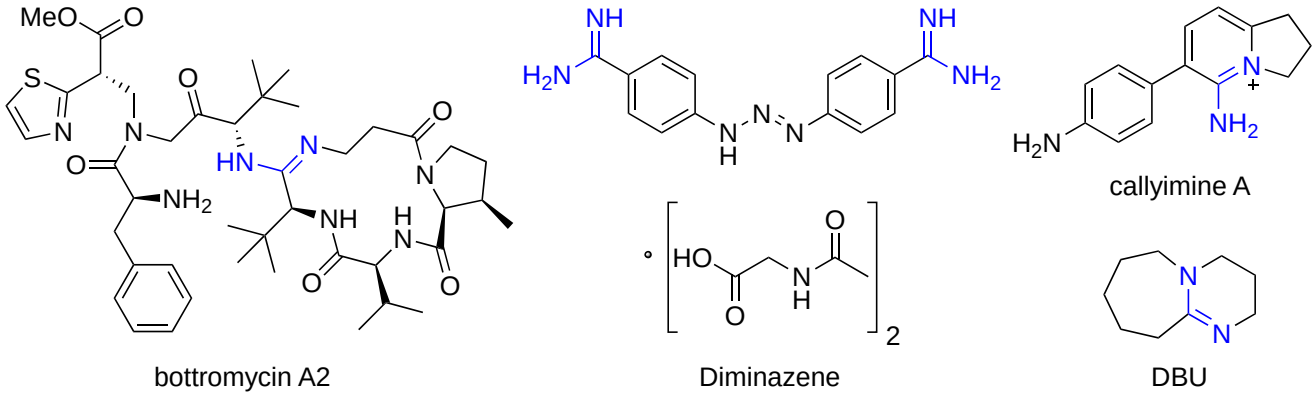
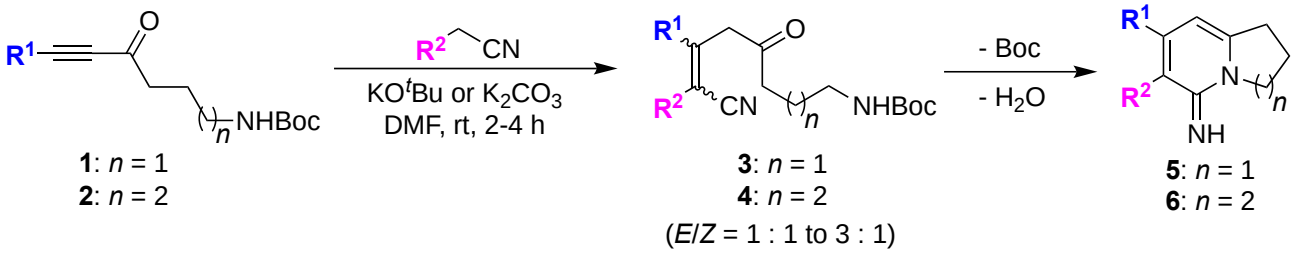


Figure 1. Examples of naturally occurring, and synthetic amidines

Their unique chemical diversity under different pH conditions depends on the substituents on the sp^2-amidinyl carbon. These make them become versatile structural motifs that could be utilized for several purposes, including a building block in organic synthesis, catalyst design, material science, medicinal chemistry, and drug discovery.[5] Therefore, numerous methods for the synthesis of amidines have been established.[1,6] In general, either nitrile or amide was employed as a starting material to generate a reactive intermediate bearing a high inductive effect leaving group to increase reactivity of the electrophilic carbon for the subsequent nucleophile substitution. The well-known Pinner reaction and modified process usually require an anhydrous condition of hydrogen chloride in alcohol for converting nitrile to the corresponding imidate salt as a reactive intermediate.[7] Several metal complex catalysts such as Yb, Al, and Ni, have been reported for the alternative direct addition of amine to nitrile. Other starting materials such as carbodiimide, aldoxime, oxadiazolone, benzotriazole, aminopyrazole, and isothiocyanate were also employed under various conditions to afford amidines scaffolds.[6]

Previously, our group reported a one-pot, metal-free approach using the intramolecular, two-fold sequential cyclization of Michael adducts **3** for the synthesis of 3,4-disubstituted, bicyclic 2-pyridones and expanded this concept to access bicyclic 2-pyridones with chiral centers.[8] In general, the mild and practical process for the synthesis of molecules having various functionalities is vital for further utilization in the fields of medicine and materials science. Therefore, inspired by our successful development and previous report of the photophysical *properties* of cyclic *amidine* fluorophores,[9] herein we employed our previous key-step reaction and further searched for a more practical way for the preparation of bicyclic amidines. In addition, we also investigated photophysical properties of novel amidines for essential information and development in the future (Scheme 1).



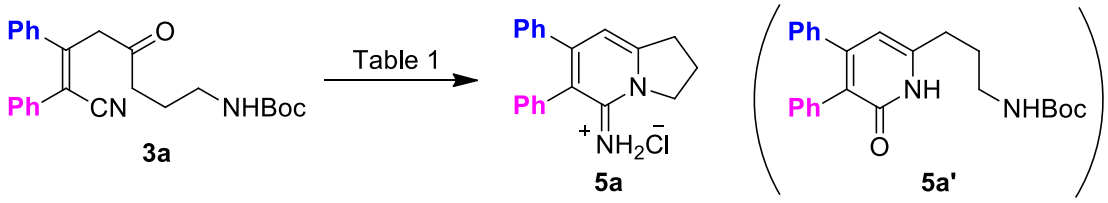
Scheme 1. Our synthetic approach to bicyclic amidines

RESULTS AND DISCUSSION

Optimization condition for a one-pot, double cyclization to amidine 5a

In our previously reported method, we found that the 1,4-addition of arylacetonitrile to internal ynones **1** or **2** was successful using KO^{t}Bu or K_2CO_3 in DMF, to afford Michael adducts **3 or 4** in good yields. We initially employed **3a** (R^1 = R^2 = Ph, n = 1) for further optimization both in stepwise and one-pot procedures to **5a** (Table 1). According to our previous condition, after removal of Boc group in **3a** using the *in situ* generation of HCl from TMSCl in MeOH, the volatile materials were removed *in vacuo* and the resulting mixture was further treated with SiO_2 in CH_2Cl_2 to furnish the amidine **5a** in 85–91% yield (Table 1, entry 1). When the double cyclization of **deBoc-3a** was examined under base condition using K_2CO_3 in MeOH at room temperature or refluxing (Table 1, entries 2 and 3), the reaction smoothly proceeded to the corresponding free base form of amidine **5a**. Due to an impractical method for a small scale purification of a target compound and an intermediate **deBoc-3a**, products were isolated in lower isolated yields, compared to a standard condition in entry 1. Treating the reaction of **deBoc-3a** in toluene using a pressurized tube at 150 °C for 1 h, **5a** was obtained in a moderate yield (Table 1, entry 4). To implement a one-pot methodology, a solution of **3a** was reacted in a pressurized tube in the presence of acidic alcohol at temperatures of 60 and 100 °C. However, the improved chemical yields were not observed (Table 1, entries 5 and 6). Based on the screening results, the double cyclization occurred under thermal weak acid conditions at high temperatures, and the desired product **5a** could be easily purified in acid form. Removal of the *N*-Boc group using water at elevated temperatures has been previously reported. Unfortunately, unlike the previous results using 2-pyrones as a starting material, the reaction of **3a** in aqueous alcohols at 100 °C gave **5a** in trace amount, detected by ^{1}H NMR, and the intramolecular cyclization between ketone and cyanide groups gave 2-pyridone **5a'** as a major product (Table 1, entries 7 and 8).

Table 1. Optimization conditions for the stepwise and one-pot transformation of **3a** to **5a**[a]



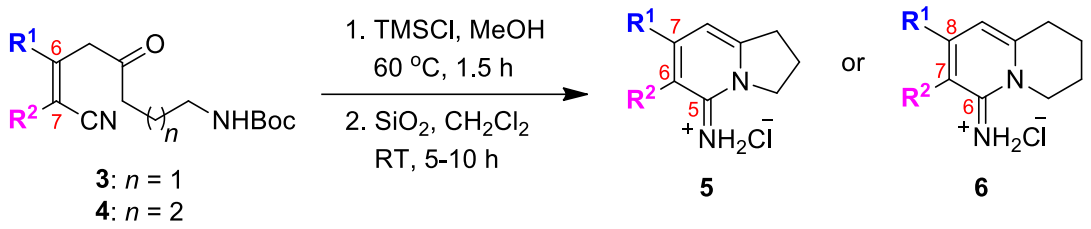
Entry	Condition		Yield of **5a** (%)[b]
	Step 1:	Step 2:	
1	TMSCl, MeOH, 60 °C, 1.5 h	SiO_2, CH_2Cl_2, rt, 5–10 h	85–91
2		K_2CO_3, MeOH, rt, 3 h	35[c]
3		K_2CO_3, MeOH, 60 °C, 1 h	24[c]
4		toluene, 150 °C, 1 h	41
5	TMSCl, MeOH, 60 °C, 3 h		0[d]
6	TMSCl, EtOH, 100 °C, 3 h		33
7	50% EtOH in water, 100 °C, 3 h		trace[e]
8	50% TFE in water, 100 °C, 3 h		trace[e]

[a] Reaction was performed in a conventional round-bottom flask (entries 1-3) or a pressurized tube (entries 4-8) using **3a** (0.1 mmol) in the indicated solvents. [b] Isolated yield using SiO_2 chromatography. [c] **5a** was isolated as a free base form. [d] None of product **5a** was observed, only intermediate **deBoc-3a** was detected by ^{1}H NMR. [e] **5a** was detected in trace amounts, by ^{1}H NMR, while 2-pyridone **5a'** was a major product.

Scope of Substrates

Based on the stability of amidines, we employed our previous standard method (Table 1, entry 1) for the synthesis of amidines. A variety of key starting materials, Michael adducts, with variation at $C_{6/7}$ were prepared according to our previous experiment, see the SI. The isolated yields of amidines **5** and **6** are shown in Scheme 2. In general, amidines could be prepared using optimization conditions in good to excellent yields (75–93%). Except for Michael adduct **3v** from 3,4,5-trimethoxyphenylacetonitrile, an intermediated open-ring was isolated as a stable compound in 52% yield, while the desired amidine **5v** was synthesized in low yield (28%). Fortunately, through prolonged heating in ethanol at 150 °C for 12 h, **3v** was transformed to the target with a better chemical conversion and a moderate isolated yield (62%).

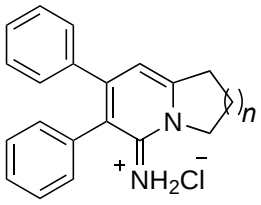
Scheme 2. Scope of reactions using substrates with variations at the $C_{6/7}$ and ring sizes[a]



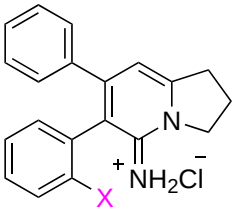
3: *n* = 1
4: *n* = 2

5

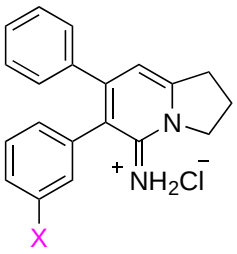
6



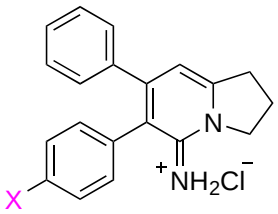
5a: *n* = 1 (91%)
6a: *n* = 2 (89%)



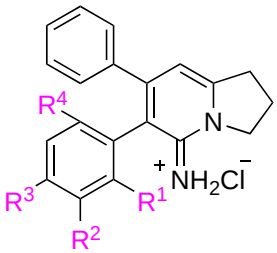
5b: X = Cl (83%)
5c: X = Br (85%)
5d: X = I (78%)
5e: X = Me (79%)
5f: X = CF_3 (80%)
5g: X = OMe (82%)



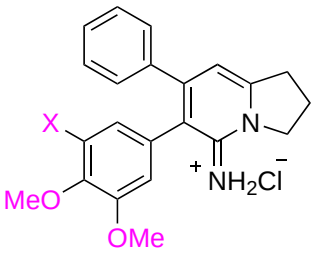
5h: X = Cl (86%)
5i: X = Br (85%)
5j: X = Me (78%)
5k: X = OMe (83%)



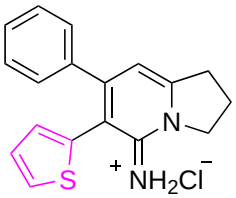
5l: X = Cl, *n* = 1 (85%)
5m: X = Br, *n* = 1 (82%)
5n: X = Me, *n* = 1 (75%)
5o: X = OMe, *n* = 1 (82%)
5p: X = NO_2, *n* = 1 (79%)
5q: X = NH_2.HCl, *n* = 1 (71%)
6b: X = NO_2, *n* = 2 (75%)



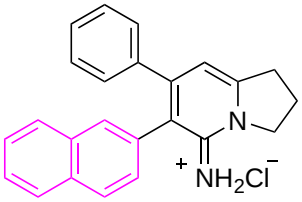
5r: R^1 = R^3 = Cl, R^2 = H (89%)
5s: R^2 = R^3 = Cl, R^1 = R^2 = H (87%)
5t: R^1 = R^4 = Cl, R^2 = R^3 = H (80%)



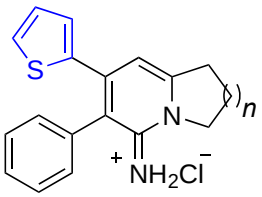
5u: X = H (81%)
5v: X = OMe (62%)[b]



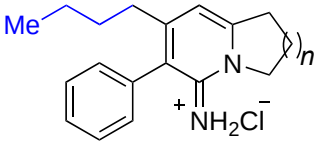
5w (75%)



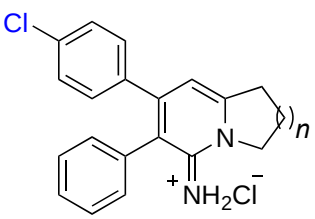
5x (93%)



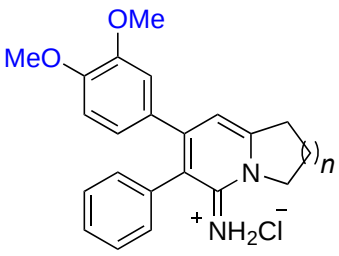
5y: *n* = 1 (76%)
6c: *n* = 2 (79%)



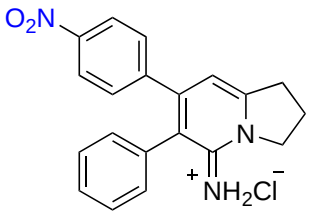
5z: *n* = 1 (77%)
6d: *n* = 2 (78%)



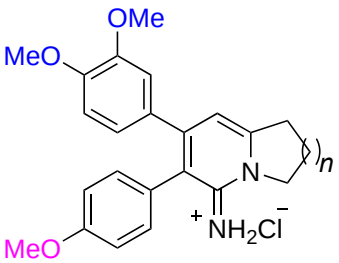
5α: *n* = 1 (83%)
6e: *n* = 2 (85%)



5β: *n* = 1 (82%)
6f: *n* = 2 (83%)



5χ (79%)



5δ: *n* = 1 (79%)
6g: *n* = 2 (77%)

[a] Reaction was performed in a conventional round-bottom flask using **3** or **4** (0.25 mmol). [b] Using a pressurized tube at 150 °C.

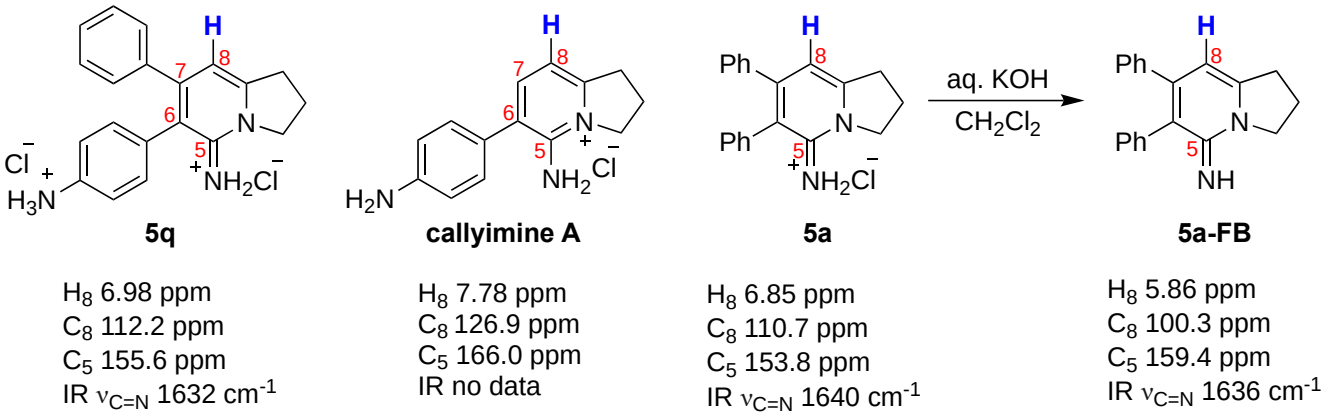
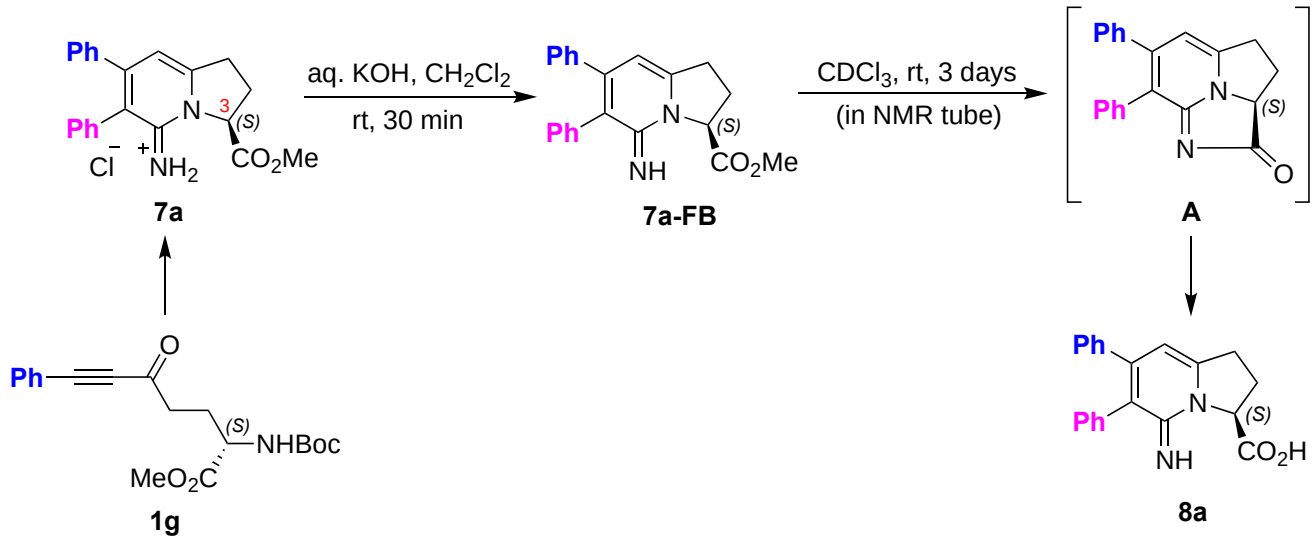


Figure 2. Spectral data of synthetic amidines **5a**, **5a-FB**, and **5q** and naturally occurring callyimine A

Comparison of NMR and IR data between our synthetic compound **5q** and a naturally occurring callyimine A isolated from the marine sponge metabolite, the chemical shift of H_8, C_8, and C_5, as well as the infrared absorption of C=N of these compounds, were differentiable (Figure 2). Thus, the analytical data revealed that the amidine moiety of **5q** is in a form of imine group, while callyimine A presents in a form of amino group. In a separated experiment, **5a** was treated with aq. KOH in CH_2Cl_2 for 30 min, the isolated free base form **5a-FB** showed different data in NMR and IR, compared to **5a** (Figure 2). Interestingly, a solution of **5a-FB** in CH_2Cl_2 under 365 nm UV lamp showed an intense bright yellow.



Scheme 3. Transformation of **7a-FB** to **8a** via the intramolecular lactamization

We also synthesized amidine-based peptidomimetic having chiral moiety at C_3 position from the corresponding internal ynone **1g** (Scheme 3). We found that a free base form **7a-FB** was unstable in a solution, and it was smoothly transformed to **8a** via the intramolecular nucleophilic addition between imine and ester to intermediate A, and completely converted to **8a** after several days at room temperature.

Photophysical properties of 5a and 5a-FB

The parent amidine of **5a** and its free base **5a-FB** as the representatives were measured for their photophysical properties and the results are summarized in Table 2.

Table 2. Absorption and emission properties of amidines **5a** and its free base **5a-FB** in different solvents[a]

Solvent	Solvent polarity (E_T^N)[b]	Compounds	$^{max}\lambda_{Abs}$ (nm)	$^{max}\lambda_{Em}$ (nm)	ε ($M^{-1}cm^{-1}$)	Stokes shift (nm, cm^{-1})
1,4-dioxane	0.164	**5a**	328	420	7357	92, 6678
		5a-FB	364	490	4070	126, 7064
THF	0.207	**5a**	327[c]	424	3958	97, 6996
		5a-FB	371	490	4100	119, 6546
EtOAc	0.228	**5a**	325[c]	422	1224	97, 7072
		5a-FB	344	484	3280	140, 8409
CH_2Cl_2	0.321	**5a**	322	419	7550	97, 7190
		5a-FB	364	485	4060	121, 6854
MeCN	0.461	**5a**	315	413	8320	98, 7533
		5a-FB	364	491	2860	127, 7106
MeOH	0.762	**5a**	317	417	6970	100, 7565
		5a-FB	317	415	7870	98, 7449
1% TFA in MeCN	-	**5a**	315	415	8210	100, 7650
		5a-FB	315	415	7990	100, 7650

[a] Measurement at concentrations 10^{-4} M for absorption spectra and 10^{-6} M for emission spectra. [b] See reference 10. [c] at concentrations 10^{-5} M.

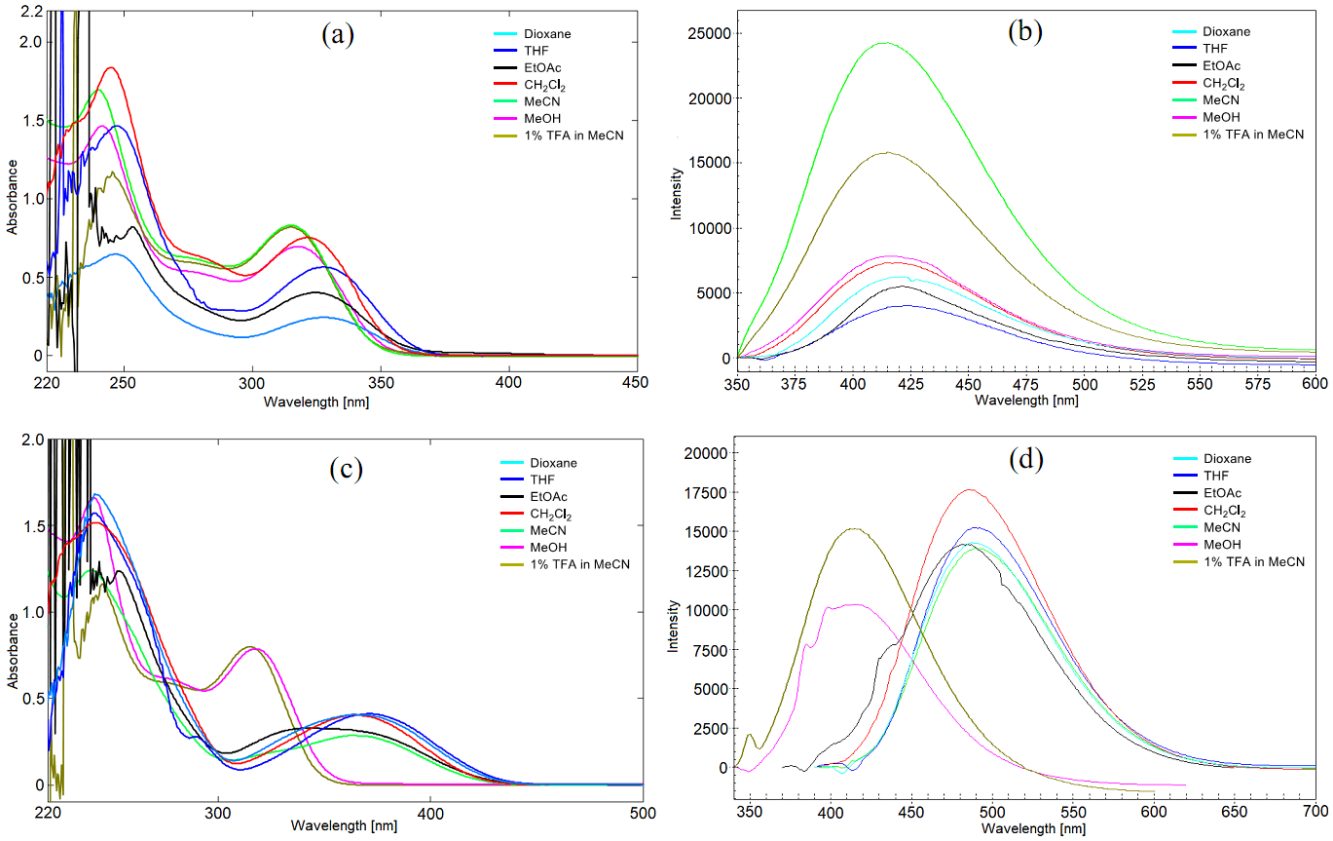


Figure 3. (a) absorption spectra and (b) emission spectra of **5a**, (c) absorption spectra and (d) emission spectra of **5a-FB**, in different solvents

Absorption and emission spectra of **5a** and **5a-FB** in different solvents, including 1,4-dioxane, THF, EtOAc, CH_2Cl_2, MeCN, and MeOH are compared (Figure 3). Interestingly, **5a** and **5a-FB** exhibited different wavelengths in each solvent. In the case of **5a**, the maximum absorption and emission wavelengths are in the range 315 to 328 nm, and 413 to 424 nm, respectively. While, free base **5a-FB** exhibited broad absorptions and emission wavelengths from 317 to 371 nm, and 415 to 491 nm, respectively. In general, both **5a** and **5a-FB** showed absorption spectra with maximum wavelengths independent of the solvent polarity because the molecule in the ground and excited states are in the same local environments. Specifically, the maximum absorption wavelength of **5a-FB** was substantially shifted, compared to **5a**, because the ground state conformation is stabilized via π-conjugation between amidine and aromatic moieties and also via charge transfer from the lone electron pair at imino nitrogen (lp(*N*)) to π*-orbital of the aromatic fragment. Following the Franck-Condon principle energy diagram of electronic transitions between the ground and excited states, the molecule has a significant dipole moment in the excited state than in the ground state. Thus, polar solvents could stabilize the excited state having lower energy. Accordingly, when the solvent polarity increases, this effect becomes substantial and results in emission at lower energy or longer wavelength.[11] However, compounds **5a** and **5a-FB** did not

significantly display sensitivity to solvent polarity. The emission maxima of **5a-FB** in different solvents were longer wavelengths than **5a**. In general, all coefficient values of **5a** in explored solvents are higher than that of **5a-FB**, except for THF, EtOAc, and MeOH. **5a** showed strong absorption with a high extinction coefficient (ε) of 8320 $M^{-1}cm^{-1}$ in MeCN. Based on the absorption and emission wavelengths in Table 2, **5a** and **5a-FB** showed remarkable large Stokes shifts in the range 92 to 140 nm. In general, the Stokes shift values of **5a-FB** are higher than that of **5a** and show a slight change in different solvents. Emission wavelengths of **5a-FB** exhibited broad differences in each solvent up to 491 nm with Stoke shift 127 nm in MeCN. In aprotic solvents, broader bathochromic shifts of **5a-FB** were observed, while a narrow shift was detected in a polar protic solvent of MeOH. The Stokes shift of **5a-FB** decreased with the growth of the solvent polarity. A strong acid such as TFA was also added to MeCN, aiming to evaluate the effect of acid on the Stokes shift. Compared with **5a-FB** in MeCN, when **5a-FB** was exposed to a solution of 1% TFA in MeCN, a solution color changed from yellow to colorless, and a hypsochromic shift was observed. This result indicated the rapid transformation of a free base form to a salt form. These could be supposed that **5a-FB** was stabilized mainly by the amidine-aromatic π-conjugation and the lp(*N*)–π* interaction, thus, the protonation of the imino nitrogen with 1% TFA in MeCN inhibited this evidence. Furthermore, the excited state may be quenched through hydrogen bonding of MeOH to an amidine group. These resulted in the hypsochromic shift by 76 nm, giving spectra similar to **5a**. In contrast, **5a** without the free lone pair electrons did not affect both maxima wavelengths.

CONCLUSION

In conclusion, we have developed a facile and metal-free process for the synthesis of bicyclic amidines, and successfully applied for the preparation of 39 amidines in yields 62–93%. The representative amidines **5a** and its free base **5a-FB** were measured for photophysical properties on different solvents environments. From the results, amidine in a free base form showed stronger fluorescence emission in up to 491 nm in MeCN, which belongs to the blue region of the visible light spectrum, and large Stokes shift in up to 140 nm in EtOAc. Treatment of a MeCN solution of **5a-FB** with TFA generated salts form, resulting in a change in color from yellow to colorless. From the results, the photophysical properties of a free base form indicated positive implications in their application in the nearest future.

EXPERIMENTAL

General Information:

Unless otherwise noted, all commercial-grade reagents were ordered from Sigma Aldrich, Fluka, Merck, and TCI. These chemicals were used without further purification. Anhydrous solvents were purified by a solvent purification system. Thin layer chromatography (TLC) was carried out on alumina plates precoated with 0.25 mm of silica gel 60 F_{254}. Column chromatography was performed on 230-400 mesh silica gel or Sephadex^{TM} LH-20 from GE healthcare. The NMR spectra were performed with Bruker Biospin AG instrument. ^{1}H NMR spectra were recorded on a 300 MHz NMR spectrometer. Chemical shifts (δ values) for ^{1}H NMR spectra are reported in parts per million (ppm) downfield from tetramethyl-silane (δ = 0.00 ppm) as an internal reference, and the coupling constants (*J* values) are in *Hz*. ^{13}C spectra were recorded on a 75 MHz NMR spectrometer with complete proton decoupling. Infrared (IR) spectra were obtained using Perkin Elmer Spectrum One FT-IR spectrometer with the universal attenuated total reflectance (UATR) technique and are reported in wavenumbers (cm^{-1}). High-resolution mass spectrometry (HRMS) was performed using the Bruker Micro TOF-LC mass spectrometer. Optical rotations were recorded on a Jasco P-1020 digital polarimeter. Melting points (mp) were determined with Stuart Scientific SMP3 melting point apparatus and are reported without correction. The UV-Vis absorption spectra were measured by a Shimadzu UV-1700 PharmaSpec spectrophotometer. The emission spectra were recorded using Photon Technology International spectrofluorometer with PTI FeliX32 fluorescence analysis solfware. Absorption and emission spectra were measurement using analytical grade solvents with concentrations 10^{-4} and 10^{-6} M at room temperature in 10 mm quartz cuvettes.

General procedure for the synthesis of amidines 5-7.

In a round-bottomed flask, a solution of the Michael adduct **3** or **4** (0.25 mmol) prepared according to literature, see the SI, in MeOH (3 mL) was added trimethylchlorosilane (TMSCl, 0.1 mL, 0.79 mmol, 3.2 equiv) and the mixture was heated at 60 °C for 1.5 h. Then, the volatile organic materials were removed under reduced pressure to afford the corresponding **deBoc-3** or **deBoc-4**. Next, the resulting deBoc-compound was dissolved in CH_2Cl_2 (5 mL) and added into a suspension of silica gel (3 g) in CH_2Cl_2 (5 mL). The reaction was stirred at room temperature for 5-10 h. After that, the solid was filtered out through a paper pad and the pad was successively washed with a solvent mixture of 10% MeOH in CH_2Cl_2. The combined filtrate was concentrated under reduced pressure. The obtained solid was purified by column chromatography on silica gel using CH_2Cl_2 and an increasing proportion of MeOH as eluents

to afford **5**, **6**, or **7**. In addition, amidine **5q** was further purified on Sephadex^{TM} LH-20 using CH_2Cl_2 and MeOH as eluents.

6,7-Diphenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5a). A white solid, mp 228.2–230.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.33 (m, 3H), 7.26–7.17 (m, 3H), 7.12–7.12 (m, 4H), 6.45 (s, 1H), 4.92 (t, J = 7.4 Hz, 2H), 3.34 (t, J = 7.7 Hz, 2H), 2.53 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.85, 151.91, 150.72, 136.73, 131.52, 130.13, 129.61, 129.17, 128.85, 128.48, 128.21, 121.97, 110.74, 54.89, 31.27, 21.57; IR (UATR) ν_{max} 3336, 1640, 1561, 1516, 1507, 1479, 1440, 1395, 1238, 1158, 1071, 1011, 848, 769, 723, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{19}N_2$ $(M+H)^+$ 287.1543, found 287.1545.

6,7-Diphenyl-2,3-dihydroindolizin-5(1*H*)-imine (5a-FB). A yellow solid, mp 201.7–203.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.68 (m, 10H), 5.86 (s, 1H), 4.12 (t, J = 7.1 Hz, 2H), 3.03 (t, J = 7.7 Hz, 2H), 2.23 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.45, 148.18, 145.86, 140.15, 136.29, 130.95, 128.63, 128.60, 127.68, 127.19, 127.05, 125.04, 100.27, 49.87, 31.30, 21.33; IR (UATR) ν_{max} 3327, 1636, 1558, 1520, 1443, 1382, 1239, 1173, 1071, 1014, 903, 767, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{19}N_2$ $(M+H)^+$ 287.1543, found 287.1541.

6-(2-Chlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5b). A pale yellow solid, mp 238.7–240.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.18 (m, 6H), 7.13–7.03 (m, 3H), 6.85 (s, 1H), 5.00 (dt, J = 14.0, 7.7 Hz, 1H), 4.87 (dt, J = 14.0, 7.7 Hz, 1H), 3.37 (t, J = 7.7 Hz, 2H), 2.55 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.93, 151.48, 136.61, 134.65, 132.32, 131.23, 130.53, 129.26, 128.37, 128.07, 127.96, 119.62, 110.46, 55.21, 31.41, 21.63; IR (UATR) ν_{max} 3344, 3132, 1641, 1565, 1508, 1467, 1432, 1397, 1236, 1160, 1064, 1032, 848, 767, 731, 701 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}Cl_1N_2$ $(M+H)^+$ 321.1153, found 321.1157.

6-(2-Bromophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5c). A yellow solid, mp 241.0–243.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 7.7 Hz, 1H), 7.35–7.14 (m, 5H), 7.16–7.04 (m, 3H), 6.85 (s, 1H), 4.98 (dt, J = 13.0, 7.3 Hz, 1H), 4.86 (dt, J = 13.0, 7.3 Hz, 1H), 3.38 (t, J = 7.7 Hz, 2H), 2.55 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.58, 151.44, 151.28, 136.55, 133.73, 132.56, 132.49, 131.27, 129.24, 128.64, 128.33, 128.05, 124.87, 121.26, 110.47, 55.14, 31.40, 21.60; IR (UATR) ν_{max} 3335, 3056, 1640, 1564, 1507, 1460, 1439, 1396, 1235, 1160, 1073, 1008, 850, 767, 727, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}N_2Br_1$ $(M+H)^+$ 365.0648, found 365.0646.

6-(2-Iodophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5d). A yellow solid, mp 218.2–220.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (dd, J = 7.6, 1.2 Hz, 1H), 7.37 (td, J = 8.5, 1.0 Hz, 1H), 7.30–7.20 (m, 3H), 7.15 (dd, J = 7.6, 1.2 Hz, 2H), 7.09 (d, J =7.6 Hz, 2H), 6.84 (s, 1H), 5.02 (dt, J = 13.4, 7.5 Hz, 1H), 4.87 (dt, J = 13.4, 7.5 Hz, 1H), 3.38 (t, J = 7.9 Hz, 2H), 2.55 (quint, J = 7.7 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.13, 151.43, 151.10, 140.17, 136.46, 136.40, 131.98, 131.00, 129.35, 129.19, 128.25, 128.23, 124.09, 110.59, 100.86, 55.09, 31.41, 21.56; IR (UATR) ν_{max} 3352, 3111, 1641, 1564, 1508, 1460, 1439, 1396, 1235, 1160, 1073, 1008, 850, 767, 727, 701 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}I_1N_2$ $(M+H)^+$ 413.0509, found 413.0513.

7-Phenyl-6-(*o*-tolyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5e). A yellow solid, mp 231.3–233.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.16 (m, 6H), 7.10–7.00 (m, 3H), 6.86 (s, 1H), 4.93 (t, J = 7.2 Hz, 2H), 3.37 (t, J = 7.7 Hz, 2H), 2.63–2.47 (m, 2H), 1.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.81, 151.84, 150.74, 137.07, 136.72, 131.36, 130.70, 130.47, 129.85, 129.18, 128.30, 128.20, 127.10, 121.46, 110.40, 55.13, 31.30, 21.67, 19.32; IR (UATR) ν_{max} 3340, 3061, 1639, 1562, 1505, 1479, 1439, 1395, 1238, 1224, 1159, 1071, 1012, 849, 767, 730, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{21}N_2$ $(M+H)^+$ 301.1699, found 301.1699.

7-Phenyl-6-(2-(trifluoromethyl)phenyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5f). A yellow solid, mp 251.7–255.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.56 (t, J = 7.7 Hz, 1H), 7.36 (d, J = 7.5 Hz, 1H), 7.26–7.18 (m, 2H), 7.06 (dd, J = 8.3, 1.6 Hz, 2H), 6.84 (s, 1H), 5.05 (dt, J = 13.4, 7.5 Hz, 1H), 4.82 (dt, J = 13.4, 7.5 Hz, 1H), 3.37 (t, J = 7.7 Hz, 2H), 2.55 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.57, 151.80, 151.47, 136.42, 133.48, 132.84, 130.30, 130.16, 129.75, 129.39, 129.36, 129.18, 128.35, 128.26, 127.99, 127.92, 127.86, 127.79, 124.82, 121.19, 119.08, 110.70, 55.28, 31.37, 21.57; IR (UATR) ν_{max} 3333, 3090, 1641, 1566, 1509, 1482, 1441, 1396, 1313, 1267, 1235, 1167, 1122, 1064, 1033, 847, 774, 767, 721, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{18}F_3N_2$ $(M+H)^+$ 355.1417, found 355.1418.

6-(2-Methoxyphenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5g). A pale yellow solid, mp 265.0–268.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.30 (m, 1H), 7.26–7.16 (m, 3H), 7.06 (dd, J = 8.1, 1.4 Hz, 2H), 6.95–6.86 (m, 3H), 6.83 (s, 1H), 4.92 (dt, J = 13.3, 7.4 Hz, 1H), 4.83 (dt, J = 13.3, 7.4 Hz, 1H), 3.35 (t, J = 7.7 Hz, 2H), 2.52 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.85, 154.56, 151.68, 150.37, 137.21, 131.37, 131.21, 128.74, 127.97, 127.74, 121.37, 119.89, 119.03, 111.37, 110.34, 55.26, 54.65, 31.15, 21.50; IR (UATR) ν_{max} 3361, 3154, 1642, 1563, 1483, 1437, 1397, 1277, 1250, 1161, 1119, 1020, 766, 702 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{21}N_2O_1$ $(M+H)^+$ 317.1648, found 317.1648.

6-(3-Chlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5h). A pale yellow solid, mp 201.7–203.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 5H), 7.12 (s, 1H), 7.09–6.99 (m, 3H), 6.90 (s, 1H), 4.88 (t, J = 7.4 Hz, 2H), 3.41 (t, J = 7.7 Hz, 2H), 2.54 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.09, 151.33, 136.12, 135.14, 133.27, 130.77, 129.91, 129.18, 128.87, 128.38, 128.20, 128.16, 120.12, 110.73, 54.79, 31.19, 21.33; IR (UATR) ν_{max} 3307, 3055, 1640, 1564, 1469, 1438, 1392,

1238, 1080, 1032, 884, 781, 700 cm^{-1}; HRMS (ESI^+) calcd for $C_{20}H_{18}Cl_1N_2$ $(M+H)^+$ 321.1153, found 321.1152.

6-(3-Bromophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5i). A pale yellow solid, mp 232.7–236.1 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.1 Hz, 1H), 7.32–7.21 (m, 5H), 7.08–7.00 (m, 3H), 6.85 (s, 1H), 4.93 (t, J = 7.7 Hz, 2H), 3.37 (t, J = 7.7 Hz, 2H), 2.54 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.06, 151.54, 151.34, 136.26, 133.66, 132.82, 132.02, 130.98, 129.01, 128.81, 128.27, 128.14, 123.03, 120.03, 110.70, 54.62, 31.24, 21.32; IR (UATR) ν_{max} 3302, 3056, 1642, 1563, 1470, 1439, 1392, 1237, 1073, 997, 884, 779, 732, 700 cm^{-1}; HRMS (ESI^+) calcd for $C_{20}H_{18}Br_1N_2$ $(M+H)^+$ 365.0648, found 365.0648.

7-Phenyl-6-(*m*-tolyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5j). A pale yellow solid, mp 233.7–235.9 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.18 (m, 4H), 7.15 (d, J = 7.7 Hz, 1H), 7.06 (dd, J = 8.1, 1.4 Hz, 2H), 6.92 (s, 1H), 6.84 (s, 1H), 6.82 (d, J = 7.7 Hz, 1H), 4.90 (t, J = 7.2, 2.7 Hz, 2H), 3.34 (t, J = 7.7 Hz, 2H), 2.53 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.63, 152.16, 150.41, 139.67, 136.89, 131.43, 130.46, 130.08, 129.64, 128.96, 128.57, 128.30, 127.24, 122.35, 110.63, 55.10, 31.29, 21.71, 21.28; IR (UATR) ν_{max} 3349, 3053, 1641, 1561, 1439, 1393, 1249, 1183, 1072, 1039, 844, 782, 763, 700 cm^{-1}; HRMS (ESI^+) calcd for $C_{21}H_{21}N_2$ $(M+H)^+$ 301.1699, found 301.1699.

6-(3-Methoxyphenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5k). A yellow solid, mp 201.7–203.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.20 (m, 4H), 7.08 (dd, J = 8.1, 1.8 Hz, 2H), 6.87 (dd, J = 8.4, 1.8 Hz, 1H), 6.83 (s, 1H), 6.67 (d, J = 7.6 Hz, 1H), 6.57 (dd, J = 2.2, 1.7 Hz, 1H), 4.93 (t, J = 7.5 Hz, 2H), 3.32 (t, J = 7.7 Hz, 2H), 2.52 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.45, 153.76, 152.09, 150.63, 136.88, 132.76, 130.93, 129.05, 128.48, 128.38, 122.24, 115.82, 114.85, 110.65, 55.28, 55.16, 31.33, 21.69; IR (UATR) ν_{max} 3379, 2931, 1640, 1588, 1493, 1456, 1380, 1260, 1231, 1135, 1039, 824, 765, 736, 702 cm^{-1}; HRMS (ESI^+) calcd for $C_{21}H_{21}N_2O_1$ $(M+H)^+$ 317.1648, found 317.1650.

6-(4-Chlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5l). A pale yellow solid, mp 241.0–243.8 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, J = 8.5 Hz, 2H), 7.30–7.21 (m, 3H), 7.08–7.00 (m, 4H), 6.84 (s, 1H), 3.93 (t, J = 7.4 Hz, 2H), 3.35 (t, J = 7.7 Hz, 2H), 2.53 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.30, 151.87, 151.22, 136.55, 135.53, 131.67, 130.03, 129.12, 128.48, 128.46, 120.86, 110.85, 55.25, 31.39, 21.64; IR (UATR) ν_{max} 3313, 3051, 1640, 1560, 1480, 1439, 1391, 1239, 1090, 1009, 833, 763, 724, 699 cm^{-1}; HRMS (ESI^+) calcd for $C_{20}H_{18}Cl_1N_2$ $(M+H)^+$ 321.1153, found 321.1152.

6-(4-Bromophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5m). A yellow solid, mp 253.0–255.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.32–7.22 (m, 3H), 7.03 (dd, J =

8.2, 1.7 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.84 (s, 1H), 4.95 (t, *J* = 7.4 Hz, 2H), 3.34 (t, *J* = 7.7 Hz, 2H), 2.53 (quint, *J* = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.95, 151.37, 151.32, 136.43, 132.58, 131.87, 130.52, 128.73, 128.29, 128.16, 123.16, 120.37, 110.76, 54.57, 31.23, 21.32; IR (UATR) ν_{max} 3284, 3053, 1642, 1566, 1479, 1439, 1388, 1239, 1072, 1008, 829, 762, 731 722, 699 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}Br_1N_2$ $(M+H)^+$ 365.0648, found 365.0651.

7-Phenyl-6-(*p*-tolyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5n). A yellow solid, mp 225.0–228.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.18 (m, 3H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.05 (dd, *J* = 8.1, 1.7 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 2H), 6.84 (s, 1H), 4.86 (t, *J* = 7.4 Hz, 2H), 3.34 (t, *J* = 7.7 Hz, 2H), 2.52 (quint, *J* = 7.7 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.72, 152.10, 150.48, 139.23, 136.93, 130.32, 129.94 128.80, 128.53, 128.40, 128.23, 122.10, 110.73, 54.86, 31.25, 21.60, 21.12; IR (UATR) ν_{max} 3438, 3053, 1641, 1562, 1484, 1439, 1393, 1249, 1183, 1072, 1039, 844, 782, 763, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{21}N_2$ $(M+H)^+$ 301.1699, found 301.1700.

6-(4-Methoxyphenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5o). A yellow solid, mp 248.7–251.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.18 (m, 3H), 7.10–7.03 (m, 2H), 7.00 (d *J* = 8.1 Hz, 2H), 6.88 (s, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 4.86 (t, *J* = 7.2 Hz, 2H), 3.38 (t, *J* = 7.4 Hz, 2H), 2.52 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.55, 153.57, 151.79, 150.25, 136.58, 131.08, 128.44, 128.20, 127.92, 122.97, 121.33, 114.75, 110.57, 54.92, 54.54, 30.96, 21.58; IR (UATR) ν_{max} 3370, 3056, 1640, 1561, 1484, 1439, 1393, 1272, 1239, 1071, 1032, 1010, 822, 763, 726, 699 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{21}N_2O_1$ $(M+H)^+$ 317.1648, found 317.1647.

6-(4-Nitrophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5p). A brown solid, mp 271.0–275.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.20–7.05 (m, 3H), 7.00–6.88 (m 2H), 6.78 (s, 1H), 4.72 (t, *J* = 7.2 Hz, 2H), 3.30 (t, *J* = 7.7 Hz, 2H), 2.44 (quint, *J* = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.41, 152.04, 151.11, 147.57, 138.72, 136.19, 131.88, 129.01, 128.34, 128.26, 124.43, 119.67, 110.75, 54.86, 31.36, 21.34; IR (UATR) ν_{max} 3327, 1636, 1557, 1516, 1239, 1014, 768, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}N_3O_2$ $(M+H)^+$ 332.1394, found 332.1390.

6-(4-Aminophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5q). A white solid, mp 235.0–238.0 °C; ^{1}H NMR (300 MHz, MeOH-d4) δ 7.28–7.11 (m, 5H), 6.98 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 4.40 (t, *J* = 7.4 Hz, 2H), 3.39 (t, *J* = 7.8 Hz, 2H), 2.49 (quint, *J* = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.64, 153.82, 152.28, 149.96, 139.35, 132.44, 129.98, 129.56, 129.21, 123.68, 121.70, 116.70, 112.15, 54.26, 32.12, 22.36; IR (UATR) ν_{max} 3326, 1632, 1563, 1483, 1438, 1393, 1287, 1240, 1180, 1070, 1031, 838, 787, 764, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{20}N_3$ $(M+H)^+$ 302.1652, found 302.1651.

6-(2,4-Dichlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5r). A pale yellow solid, mp 261.2–264.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.33–7.21 (m, 4H), 7.11–7.03 (m, 3H), 6.86 (s, 1H), 4.97 (dt, J = 13.0, 7.8 Hz, 1H), 4.85 (dt, J = 13.0, 7.8 Hz, 1H), 3.40 (t, J = 7.7 Hz, 2H), 2.24 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.25, 151.99, 151.17, 136.58, 136.34, 135.44, 133.23, 130.34, 129.35, 129.08, 128.46, 127.80, 118.32, 110.56, 55.15, 31.43, 21.54; IR (UATR) ν_{max} 3328, 3058, 1641, 1564, 1509, 1467, 1440, 1398, 1378, 1256, 1222, 1159, 1143, 1101, 1075, 1010, 865, 809, 787, 764, 727, 699 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{17}Cl_2N_2$ $(M+H)^+$ 355.0763, found 355.0761.

6-(3,4-Dichlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5s). A pale yellow solid, mp 271.7–274.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, J = 8.2 Hz, 1H), 7.34–7.25 (m, 3H), 7.23 (d, J = 2.0 Hz, 1H), 7.04 (dd, J = 8.2, 1.8 Hz, 2H), 6.95 (dd, J = 8.2, 2.0 Hz, 1H), 6.84 (s, 1H), 4.92 (t, J = 7.7 Hz, 2H), 3.36 (t, J = 7.7 Hz, 2H), 2.54 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.42, 151.74, 151.31, 136.06, 133.63, 133.51, 131.90, 131.54, 129.73, 129.08, 128.39, 128.21, 119.24, 110.82, 54.99, 31.31, 21.40; IR (UATR) ν_{max} 3291, 3056, 1643, 1563, 1467, 1375, 1236, 1133, 1031, 885, 815, 763, 700 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{17}Cl_2N_2$ $(M+H)^+$ 355.0763, found 355.0766.

6-(2,6-Dichlorophenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5t). A pale yellow solid, mp 230.7–236.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.14 (m, 8H), 6.85 (s, 1H), 4.93 (t, J = 7.3 Hz, 2H), 3.40 (t, J = 7.7 Hz, 2H), 2.56 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.75, 152.107, 150.60, 136.37, 136.17, 131.86, 129.59, 129.51, 128.85, 128.31, 127.30, 117.10, 110.42, 55.24, 31.42, 21.52; IR (UATR) ν_{max} 3296, 3053, 1642, 1563, 1430, 1396, 1238, 1193, 1158, 1123, 1030, 845, 773, 730, 699 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{17}Cl_2N_2$ $(M+H)^+$ 355.0763, found 355.0764.

6-(3,4-Dimethoxyphenyl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5u). A pale yellow solid, mp 282.5–286.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.20 (m, 3H), 7.10–7.03 (m, 2H), 6.86 (d, J =7.8 Hz, 1H), 6.83 (s, 1H), 6.73 (d, J =7.8 Hz, 1H), 6.43 (s, 1H), 4.92 (t, J = 6.6 Hz, 2H), 3.87 (s, 3H), 3.64 (s, 3H), 3.33 (t, J = 7.5 Hz, 2H), 2.60–2.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.82, 152.29, 150.42, 149.86, 149.63, 137.09, 128.90, 128.42, 128.38, 123.52, 122.68, 122.01, 113.13, 111.93, 110.64, 55.89, 55.85, 55.11, 31.29, 21.71; IR (UATR) ν_{max} 3380, 2959, 1638, 1602, 1553, 1520, 1464, 1422, 1321, 1263, 1141, 1020, 857, 814, 768, 706 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{22}H_{23}N_2O_2$ $(M+H)^+$ 347.1754, found 2347.1755.

7-Phenyl-6-(3,4,5-trimethoxyphenyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5v). A pale yellow solid, mp 201.7–203.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–7.22 (m, 3H), 7.09 (dd, J = 8.0, 1.4 Hz, 2H), 6.84 (s, 1H), 6.26 (s, 2H), 4.91 (t, J = 7.4 Hz, 2H), 3.34 (t, J = 7.7 Hz, 2H), 2.53 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.18, 153.82, 152.03, 150.63, 138.63, 136.92, 129.06,

128.43, 128.26, 126.58, 122.10, 110.59, 107.26, 60.93, 56.16, 55.06, 31.31, 21.69; IR (UATR) ν_{max} 3368, 1642, 1583, 1487, 1464, 1414, 1343, 1271, 1240, 1172, 1122, 1001, 932, 845, 765, 731, 704 cm^{-1}; HRMS (ESI^+) calcd for $C_{23}H_{25}N_2O_3$ $(M+H)^+$ 377.1860, found 377.1861.

7-Phenyl-6-(thiophen-2-yl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5w). A dark brown solid, mp 221.7–225.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J = 5.0, 1.1 Hz, 1H), 7.34–7.22 (m, 3H), 7.18–7.11 (dd, J = 8.1, 1.3 Hz, 2H), 7.08–7.00 (m, 2H), 6.83 (s, 1H), 4.93 (t, J = 7.4 Hz, 2H), 3.35 (t, J = 7.7 Hz, 2H), 2.52 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.48, 152.15, 151.61, 136.54, 131.35, 130.19, 128.99, 128.11, 127.90, 127.67, 114.53, 110.47, 54.99, 31.25, 21.39; IR (UATR) ν_{max} 3336, 3057, 1639, 1565, 1533, 1439, 1395, 1237, 1072, 974, 846, 762, 703 cm^{-1}; HRMS (ESI^+) calcd for $C_{18}H_{17}N_2S_1$ $(M+H)^+$ 293.1107, found 293.1104.

6-(Naphthalen-2-yl)-7-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5x). A white solid, mp 282.0–286.2 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85–7.71 (m, 3H), 7.67 (s, 1H), 7.58–7.48 (m, 2H), 7.17 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 7.23–7.02 (m, 2H), 6.87 (s, 1H), 4.96 (t, J = 7.4 Hz, 2H), 3.35 (t, J = 7.7 Hz, 2H), 2.54 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.02, 152.19, 150.77, 136.78, 133.17, 132.90, 129.83, 129.77, 128.97, 128.89, 128.57, 128.38, 127.95, 127.76, 127.30, 126.94, 126.91, 121.98, 110.84, 55.20, 31.35, 21.69; IR (UATR) ν_{max} 3436, 3052, 1641, 1561, 1489, 1439, 1396, 1271, 1218, 1191, 1071, 1031, 948, 862, 821, 730, 697 cm^{-1}; HRMS (ESI^+) calcd for $C_{24}H_{21}N_2$ $(M+H)^+$ 337.1699, found 337.1705.

6-Phenyl-7-(thiophen-3-yl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5y). A brown solid, mp 228.5–231.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.43 (m, 3H), 7.20–7.13 (m, 3H), 7.06 (dd, J = 2.9, 1.3 Hz, 1H), 6.93 (s, 1H), 6.70 (dd, J = 5.0, 1.3 Hz, 1H), 4.90 (t, J = 7.4 Hz, 2H), 3.33 (t, J = 7.7 Hz, 2H), 2.51 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.00, 150.72, 147.59, 136.84, 132.01, 130.05, 129.84, 129.60, 127.54, 127.35, 126.00, 120.76, 109.89, 54.87, 31.22, 21.56; IR (UATR) ν_{max} 3366, 3088, 2924, 1641, 1566, 1441, 1429, 1361, 1230, 1074, 1017, 849, 800, 769, 703 cm^{-1}; HRMS (ESI^+) calcd for $C_{18}H_{17}N_2S$ $(M+H)^+$ 293.1107, found 293.1104.

7-Butyl-6-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5z). A yellow solid, mp 201.0–203.8 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60–7.45 (m, 3H), 7.20–7.10 (m, 2H), 6.71 (s, 1H), 4.82 (t, J = 7.4 Hz, 2H), 3.28 (t, J = 7.7 Hz, 2H), 2.46 (quint, J = 7.7 Hz, 2H), 2.34 (t, J = 7.7 Hz, 2H), 1.50–1.36 (m, 2H), 1.27–1.13 (m, 2H), 0.77 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.61, 151.70, 150.24, 131.36, 130.02, 129.65, 129.58, 122.83, 109.92, 54.73, 33.26, 31.70, 31.08, 22.21, 21.62, 13.45; IR (UATR) ν_{max} 3340, 3058, 2957, 2927, 1643, 1573, 1485, 1443, 1395, 1248, 1074, 1033, 849, 763, 705 cm^{-1}; HRMS (ESI^+) calcd for $C_{18}H_{23}N_2$ $(M+H)^+$ 267.1856, found 267.1856.

7-(4-Chlorophenyl)-6-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5α). A pale yellow solid, mp 260.7–264.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.35 (m, 3H); 7.20 (d, J = 8.6 Hz, 2H), 7.12–7.05 (m, 2H), 6.98 (d, J = 8.6 Hz, 2H), 6.83 (s, 1H), 4.91 (t, J = 7.4 Hz, 2H), 3.37 (t, J = 7.7 Hz, 2H), 2.53 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.33, 151.67, 151.18, 135.10, 134.85, 131.22, 130.00, 129.81, 129.58, 129.12, 128.32, 121.68, 110.40, 54.66, 31.22, 21.36; IR (UATR) ν_{max} 3348, 3059, 1642, 1558, 1495, 1443, 1394, 1238, 1090, 1013, 902, 829, 759, 703 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}Cl_1N_2$ $(M+H)^+$ 321.1153, found 321.1154.

7-(3,4-Dimethoxyphenyl)-6-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5β). A yellow solid, mp 201.7–203.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.37 (m, 3H), 7.12 (d, J = 7.7 Hz, 1H), 7.11 (dd, J = 6.8, 1.8 Hz, 1H), 6.87 (s, 1H), 6.79 (d, J = 8.7 Hz, 1H), 6.78 (d, J = 8.7 Hz, 1H), 6.40 (d, J =1.4 Hz, 1H), 4.92 (t, J = 7.4 Hz, 2H), 3.33 (t, J = 7.7 Hz, 2H), 2.51 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.29, 152.10, 150.56, 149.82, 148.37, 132.24, 130.23, 130.00, 129.34, 128.94, 121.89, 121.38, 112.28, 110.85, 110.51, 55.80, 55.62, 55.10, 31.34, 21.71; IR (UATR) ν_{max} 3444, 3048, 1640, 1600, 1559, 1518, 1464, 1439, 1417, 1386, 1326, 1260, 1222, 1178, 1141, 1108, 1021, 862, 813, 725, 703 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{22}H_{23}N_2O_2$ $(M+H)^+$ 347.1754, found 347.1752.

7-(4-Nitrophenyl)-6-phenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5χ). A brown solid, mp 270.7–273.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.9 Hz, 2H), 7.43–7.37 (m, 3H), 7.27 (d, J = 8.9 Hz, 2H), 7.13–7.06 (m, 2H), 6.83 (s, 1H), 4.97 (t, J = 7.4 Hz, 2H), 3.39 (t, J = 7.7 Hz, 2H), 2.56 (quint, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.15, 151.66, 151.31, 147.67, 143.21, 130.63, 130.05, 129.99, 129.87, 129.64, 123.49, 122.61, 109.93, 55.47, 31.48, 21.66; IR (UATR) ν_{max} 3336, 3059, 2924, 1643, 1601, 1567, 1516, 1480, 1444, 1396, 1346, 1239, 1159, 1107, 1013, 850, 703 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{20}H_{18}N_3O_2$ $(M+H)^+$ 332.1394, found 332.1393.

7-(3,4-Dimethoxyphenyl)-6-(4-methoxyphenyl)-2,3-dihydroindolizin-5(1*H*)-iminium chloride (5δ). A yellow solid, mp 287.1–290.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 6.89 (s, 1H), 6.78 (d, J = 0.8 Hz, 2H), 6.45 (s, 1H), 4.87 (t, J = 7.2 Hz, 2H), 3.85 (s, 3H), 3.81 (s, 3H), 3.55 (s, 3H), 3.36 (t, J = 7.7 Hz, 2H), 2.57–2.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.86, 153.19, 152.02, 150.23, 149.42, 148.09, 131.29, 128.97, 123.72, 121.70, 120.88, 115.17, 112.00, 110.63, 110.45, 55.60, 55.43, 55.18, 54.71, 31.12, 21.51; IR (UATR) ν_{max} 3373, 3077, 1640, 1608, 1560, 1518, 1486, 1464, 1418, 1385, 1246, 1177, 1140, 1020, 838, 814, 765, 729, 699 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{23}H_{25}N_2O_3$ $(M+H)^+$ 377.1860, found 377.1862.

7,8-Diphenyl-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6a). A white solid, mp 230.5–233.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.00 (m, 3H), 7.25–7.15 (m, 3H), 7.10–7.00 (m, 4H), 6.73 (s, 1H), 4.58 (t, J = 6.3 Hz, 2H), 3.08 (t, J = 6.5 Hz, 2H), 2.25 (quint, J = 6.2 Hz, 2H), 2.00–1.90 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.49, 152.24, 147.21, 136.42, 131.82, 130.24, 129.82, 129.40, 128.99, 128.52, 128.31, 122.44, 115.22, 50.07, 29.41, 22.09, 17.57; IR (UATR) ν_{max} 3433, 3056, 2956, 1638, 1552, 1519, 1463, 1443, 1422, 1321, 1261, 1175, 1140, 1019, 930, 855, 812, 787, 767, 729, 704 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{21}N_2$ $(M+H)^+$ 301.1699, found 301.1703.

7-(4-Nitrophenyl)-8-phenyl-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6b). A brown solid, mp 275.7–279.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.25–7.07 (m, 3H), 7.00–6.90 (m, 3H), 6.73 (s, 1H), 4.42 (br m, 2H), 3.08 (t, J = 6.1 Hz, 2H), 2.25–2.10 (m, 2H), 2.00–1.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.25, 152.67, 148.69, 147.59, 138.79, 135.55, 131.77, 129.02, 128.29, 128.12, 124.43, 119.71, 115.32, 49.60 29.21, 21.67, 17.08; IR (UATR) ν_{max} 3338, 3065, 2927, 1642, 1603, 1565, 1514, 1482, 1445, 1392, 1347, 1242, 1160, 1107, 1015, 851, 702 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{21}H_{20}N_3O_2$ $(M+H)^+$ 346.1550, found 346.1555.

7-Phenyl-8-(thiophen-3-yl)-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6c). A brown solid, mp 201.7–203.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.42 (m, 3H), 7.20–7.12 (m, 4H), 7.00 (s, 1H), 6.71 (dd, J = 4.8, 1.5 Hz, 1H), 4.48 (t, J = 6.3 Hz, 2H), 3.15 (t, J = 6.6 Hz, 2H), 2.23 (quint, J = 6.3 Hz, 2H), 1.94 (quint, J = 6.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.88, 147.08, 145.71, 136.07, 132.07, 129.82, 129.60, 129.34, 127.55, 127.05, 125.67, 120.43, 114.33, 49.29, 28.92, 21.61, 17.12; IR (UATR) ν_{max} 3445, 3038, 2944, 1642, 1562, 1521, 1467, 1443, 1320, 1283, 1259, 1147, 1094, 1015, 877, 849, 815, 799, 778, 727, 703 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{19}N_2S_1$ $(M+H)^+$ 307.1263, found 307.1266.

8-Butyl-7-phenyl-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6d). A pale yellow solid, mp 208.3– 211.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59–7.49 (m, 3H), 7.18 (d, J = 7.9 Hz, 1H), 7.17 (d, J = 7.4 Hz, 1H), 6.67 (s, 1H), 4.43 (t, J = 6.3 Hz, 2H), 3.07 (t, J = 6.5 Hz, 2H), 2.30 (t, J = 7.7 Hz, 2H), 2.21 (quint, J = 6.3 Hz, 2H), 1.92 (quint, J = 6.4 Hz, 2H), 1.48–1.35 (m, 2H), 1.18 (sext, J = 7.3 Hz, 2H), 0.76 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.78, 153.26, 146.55, 131.25, 129.64, 129.20, 122.63, 114.50, 49.02, 32.48, 31.13, 28.79, 21.82, 21.59, 17.11, 13.07; IR (UATR) ν_{max} 3433, 3146, 2956, 2870, 1640, 1568, 1505, 1485, 1443, 1265, 1175, 1090, 1013, 853, 787, 758, 706 cm^{-1}; HRMS (ESI$^+$) calcd for $C_{19}H_{24}N_2$ $(M+H)^+$ 281.2012, found 281.2012.

8-(4-Chlorophenyl)-7-phenyl-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6e). A pale yellow solid, mp 231.7–233.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.36 (m, 3H), 7.20 (d, J = 8.6 Hz, 2H), 7.13–7.05 (m, 2H), 6.99 (d, J = 8.6 Hz, 2H), 6.71 (s, 1H), 4.58 (t, J = 6.3 Hz, 2H), 3.10 (t, J = 6.5 Hz, 2H), 2.27 (quint, J = 6.3 Hz, 2H), 1.97 (quint, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.91, 150.64, 147.54, 134.84, 134.46, 131.30, 129.85, 129.66, 129.60, 129.16, 128.23, 121.81, 114.84, 49.58, 29.04, 21.64, 17.10; IR (UATR) ν_{max} 3434, 3057, 2952, 1639, 1577, 1553, 1504, 1480, 1443, 1395, 1325, 1253,

1161, 1090, 1014, 887, 832, 787, 752, 705 cm^{-1}; HRMS (ESI^+) calcd for $C_{21}H_{20}Cl_1N_2$ $(M+H)^+$ 335.1310, found 335.1308.

8-(3,4-Dimethoxyphenyl)-7-phenyl-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6f). A pale yellow solid, mp 285.7–289.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45–7.36 (m, 3H), 7.16–7.12 (m, 2H), 6.85 (s, 1H), 6.81 (d, J = 8.7 Hz, 1H), 6.76 (d, J = 8.7 Hz, 1H), 6.40 (d, J = 1.8 Hz, 1H), 4.51 (t, J = 6.3 Hz, 2H), 3.014 (t, J = 6.5 Hz, 2H), 2.25 (quint, J = 6.3 Hz, 2H), 1.96 (quint, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.84, 151.33, 149.39, 147.91, 147.03, 132.23, 129.99, 129.67, 128.96, 128.12, 121.64, 121.03, 114.95, 111.88, 110.52, 55.47, 55.28, 49.38, 29.06, 21.73, 17.22; IR (UATR) ν_{max} 3433, 3056, 2956, 1638, 1552, 1519, 1463, 1443, 1422, 1321, 1260, 1175, 1140, 1019, 855, 813, 787, 767, 729, 704 cm^{-1}; HRMS (ESI^+) calcd for $C_{23}H_{25}N_2O_2$ $(M+H)^+$ 361.1911, found 361.1913.

8-(3,4-Dimethoxyphenyl)-7-(4-methoxyphenyl)-3,4-dihydro-1*H*-quinolizin-6(2*H*)-iminium chloride (6g). A pale yellow solid, mp 290.7–295.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.75 (s, 2H), 6.43 (s, 1H), 6.35 (s, 1H), 4.25 (t, J = 6.3 Hz, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.54 (s, 3H), 2.95 (t, J = 6.5 Hz, 2H), 2.13 (quint, J = 6.1 Hz, 2H), 1.90 (quint, J = 6.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.05, 157.45, 148.49, 147.78, 147.65, 145.58, 131.38, 129.88, 125.98, 122.06, 121.12, 114.54, 111.92, 110.27, 110.18, 55.33, 55.16, 54.86, 46.78, 28.94, 22.04, 17.73; IR (UATR) ν_{max} 3326, 2938, 1623, 1552, 1520, 1464, 1418, 1321, 1287, 1244, 1175, 1138, 1023, 838, 794, 765, 733 cm^{-1}; HRMS (ESI^+) calcd for $C_{24}H_{27}N_2O_3$ $(M+H)^+$ 391.2016, found 391.2015.

(*S*)-3-(Methoxycarbonyl)-6,7-diphenyl-2,3-dihydroindolizin-5(1*H*)-iminium chloride (7a). A white solid, mp 235.1–237.5 °C; $[\alpha]_D^{26}$ – 134 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.32 (m, 3H), 7.27–7.14 (m, 4H), 7.10–7.02 (m, 3H), 6.90 (dd, J = 8.4, 1.9 Hz, 1H), 6.84 (s, 1H), 3.95 (s, 3H), 3.26 (dd, J = 8.9, 5.9 Hz, 2H), 2.88–2.72 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.20, 154.38, 152.84, 150.14, 136.62, 131.37, 130.25, 130.19, 129.73, 129.64, 129.33, 129.05, 128.53, 128.28, 122.74, 110.83, 66.97, 53.85, 29.67, 27.31; IR (UATR) ν_{max} 3395, 3042, 1743, 1652, 1608, 1567, 1509, 1482, 1443, 1432, 1402, 1336, 1266, 1208, 1068, 1047, 1009, 986, 853, 810, 781, 769, 757, 730, 702, 668 cm^{-1}; HRMS (ESI^+) calcd for $C_{22}H_{21}N_2O_2$ $(M+H)^+$ 345.1598, found 345.1594.

(*S*)-5-Imino-6,7-diphenyl-1,2,3,5-tetrahydroindolizine-3-carboxylic acid (8a). A white solid, mp 265.1–269.9 °C; $[\alpha]_D^{26}$ – 155 (c 1.0, MeOH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.00 (m, 10H), 6.74 (s, 1H), 5.56 (d, J = 9.0 Hz, 1H), 3.47 (ddd, J = 17.0, 11.5, 9.0 Hz, 1H), 3.10 (dd, J = 17.0, 8.4 Hz, 1H), 2.88 (dd, J = 12.4, 8.4 Hz, 1H), 2.65–2.48 (m, 1H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.98, 152.98, 152.68, 151.29, 137.39, 132.29, 130.89, 130.13, 129.55, 129.25, 128.83, 128.61, 128.52, 128.12, 122.08, 110.23, 69.40, 30.50, 28.16; IR (UATR) ν_{max} 3335, 3177, 3059, 1616, 1563, 1507, 1481, 1442, 1372, 1285, 1239,

1220, 1159, 1072, 1011, 849, 816, 772, 732, 700 cm^{-1}; HRMS (ESI^+) calcd for $C_{21}H_{19}N_2O_2$ $(M+H)^+$ 331.1441, found 331.1442.

General procedure for photophysical properties measurements

Absorption spectra of **5a** and **5a-FB** were measurement in analytical grade solvents, including 1,4-dioxane, THF, EtOAc, CH_2Cl_2, MeCN, and MeOH with concentrations 10^{-4} M at room temperature in 10 mm quartz cuvettes. Emission spectra were recorded at concentrations 10^{-6} M.

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SUPPORTING INFORMATION

Supplementary (synthesis of the starting azides, HPLC chromatograms, IR, ^1H and ^{13}C NMR, MS spectra, etc.) data associated with this article can be found, in the online version, at URL: https://www.heterocycles.jp/newlibrary/downloads/PDFsi/27295/105/1.

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