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TEMPO-catalyzed decarboxylation reactions for the synthesis of 1,2-unsubstituted indolizines

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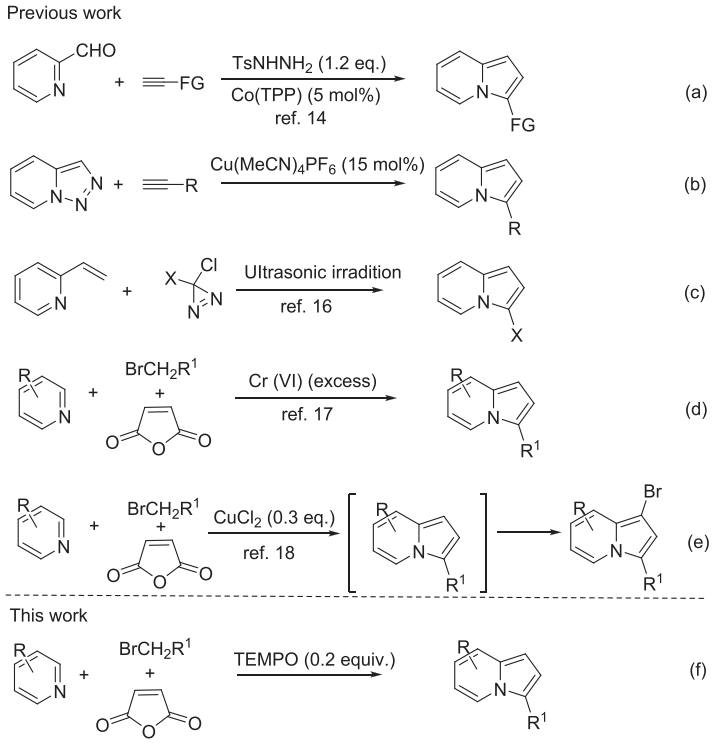
Abstract

An efficient synthesis of 1,2-unsubstituted indolizines was developed via 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)–catalyzed decarboxylation reaction. A series of target products were successfully prepared with the tolerance of a variety of functional groups. This protocol features advantages such as easily available substrates, broad substituent scope, and eco-friendly conditions.

1 | INTRODUCTION

Indolizines are basic structural motifs in many biologically active molecules [1–3] and have exhibited significant biological activities [4–8] and fluorescence properties .[9–11] Consequently, there are great demands for the synthesis of indolizines with different substitution patterns .[12,13]

As a class of important indolizine derivatives, 1,2-unsubstituted indolizines also drew much effort for their syntheses. [14–17] The existing synthetic protocols to these compounds mainly include Co(II)-catalyzed denitrogenative transannulation reaction of picolinaldehyde with alkynes (Scheme 1a) [14]; Cu(I)-catalyzed transannulation reaction of pyridotriazoles with terminal alkynes (Scheme 1b) [15]; cyclization of 2-vinylpyridine with chlorocarbenes (Scheme 1c) [16]; and Cr(VI)-promoted oxidative decarboxylation reaction of pyridines, bromides and maleic anhydride (Scheme 1d) .[17] Among these synthetic routes, oxidative decarboxylation reaction is very attractive because of its easily available substrates and high yields. However, this reaction generally proceeds with excess amount of metal oxidant, which leads to environmental pollution. Besides, 1,2-unsubstituted indolizines are likely to undergo C–H



SCHEME 1 Synthesis of indolizines

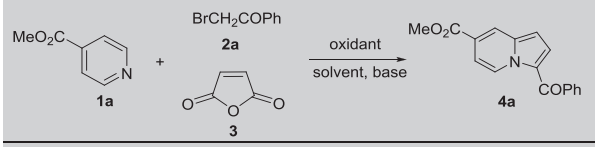
functionalization under transition metal–catalyzed conditions (Scheme 1e). [18] Hence, we wish to find new reaction conditions to assemble 1,2-unsubstituted indolizines via oxidative decarboxylation reaction, especially under metal-free conditions.

In the past decade, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) has been developed to be an efficient oxidant in many organic reactions. [19–23] Recently, we also reported a TEMPO-promoted reaction of pyridines, methyl ketones, and alkenoic esters to prepare multisubstituted indolizines. [24] However, to the best of our knowledge, TEMPO has rarely been applied to oxidative decarboxylation reaction. [25] Herein, we described a TEMPO-catalyzed three-component reaction for the synthesis of 1,2-unsubstituted indolizines (Scheme 1f).

2 | RESULTS AND DISCUSSION

To begin our work, we employed methyl isonicotinate **1a**, bromoketone **2a**, and maleic anhydride **3** as the model reactants. Solvent effect was first investigated by heating **1a** (1.5 mmol), **2a** (0.5 mmol), **3** (0.5 mmol), and TEMPO (0.25 mmol) with different solvents. It is found that acetonitrile provided the highest yields (Table 1, entries 1-6). With acetonitrile as the solvent, we then screened different oxidants including TBHP, DTBP, $K_2S_2O_8$, and $PhI(OAc)_2$ but found no oxidant that performs better than TEMPO (Table 1, entries 7-10). Further research showed the loading of TEMPO could be reduced to 0.2 equiv in the air (Table 1, entry 11-12). Therefore, the

TABLE 1 Optimization of reaction conditions[a,b]



Entry	Solvent	Oxidant, equiv	*T*, °C	Yield, %[a]
1	DMF	TEMPO (0.5)	90	76
2	Dioxane	TEMPO (0.5)	90	53
3	Benzene	TEMPO (0.5)	Reflux	32
4	Toluene	TEMPO (0.5)	90	30
5	CH_3CN	TEMPO (0.5)	Reflux	82
6	THF	TEMPO (0.5)	Reflux	27
7	CH_3CN	TBHP (0.5)	Reflux	36
8	CH_3CN	DTBP (0.5)	Reflux	28
9	CH_3CN	$K_2S_2O_8$ (0.5)	Reflux	23
10	CH_3CN	$PhI(OAc)_2$ (0.5)	Reflux	21
11	CH_3CN	TEMPO (0.2)	Reflux	82
12	CH_3CN	TEMPO (0.1)	Reflux	63

Note. Conditions: **1a** (1.5 mmol), **2a** (0.5 mmol), **3a** (0.5 mmol), and oxidant, heating in solvent for 6 h.

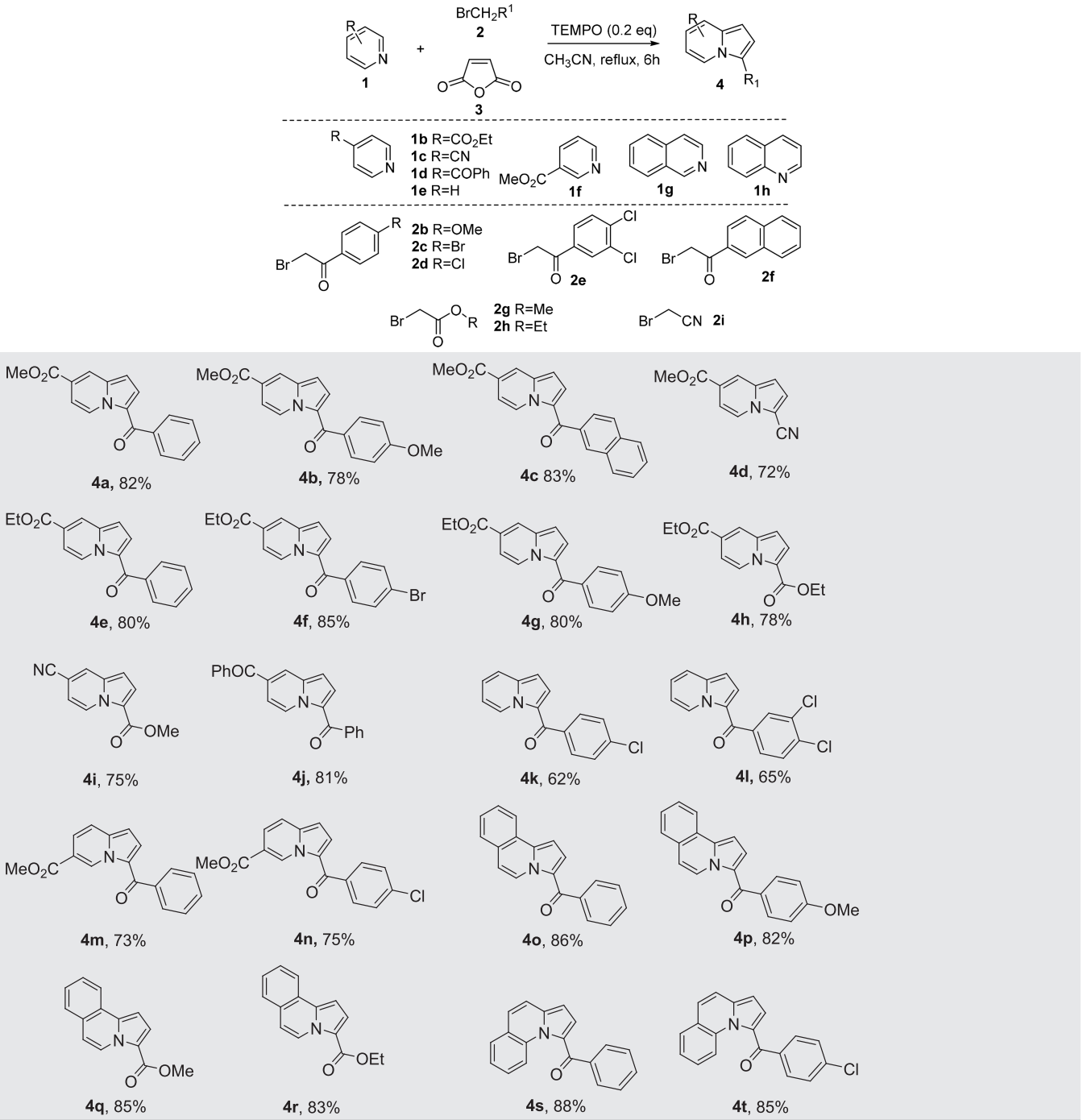
Abbreviations: DMF, dimethylformamide; THF, tetrahydrofuran.

[a]Isolated yields.

optimal conditions were refluxing the mixture of **1a** (1.5 mmol), **2a** (0.5 mmol), **3** (0.5 mmol), and TEMPO (0.1 mmol) in acetonitrile in a round bottle for 6 hours.

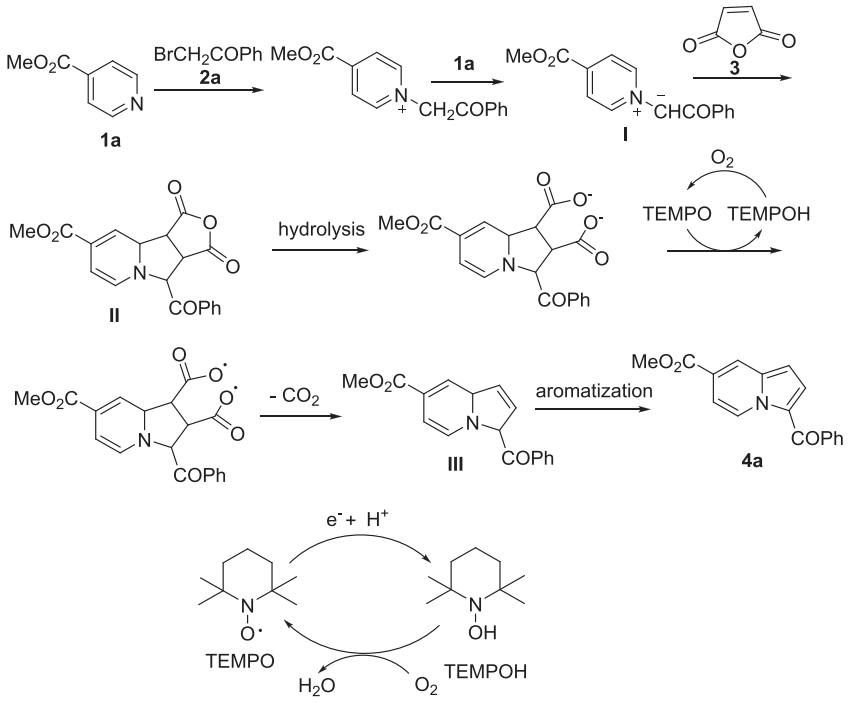
With the optimal condition in hand, we then turned our attention to expand the reactant scope (Table 2). Initially, we focused on the kind of bromides and used different bromides **2** to react with isonicotinate (**1a** or **1b**) and maleic anhydride **3**. It showed that bromoketone (**2b**, **2c**, **2f**), bromonitrile (**2i**), and bromoester (**2 h**) all performed well, giving 1,2-unsubstituted indolizines **4a**-**4h** in 72% to 85% yields. Then we investigated the scope of pyridine derivatives **1**. By employing 4-cyanopyridines **1c** and 4-acylpyridine **1d** as the starting materials, we obtained products **4i**-**4j** in good yields.

TABLE 2 Synthesis of indolizines **4**[a,b]



Note. Conditions: **1** (1.5 mmol), **2** (0.5 mmol), **3** (0.5 mmol), and TEMPO (0.1 mmol), refluxing in acetonitrile (10 mL) for 6 h.

[a]Isolated yields.



SCHEME 2 Plausible reaction mechanism

When pyridine **1e** without substituent was used in this reaction, we isolated product **4k** and **4l** in moderate yields. Furthermore, high regioselectivity was observed when methyl nicotinate **1f** was used as substrate, and products **4m**-**4n** were formed in 73% and 75% yields, respectively. Besides, annulated pyridines **1g** and **1h** afforded the target products **4o**-**4t** in 82% to 88% yields under the optimal condition. All the products were characterized by NMR and high-resolution mass spectrometry (HRMS), and the data of the known compounds were in accordance with our previous report. [17]

On the basis of these experimental results, a plausible mechanism was suggested, as shown as Scheme 2. Initially, the reaction of **1a** and **2a** formed intermediate **I**, which underwent cycloaddition with maleic anhydride **3**, leading to intermediate **II**. Subsequently, **II** was converted to **III** via a hydrolysis, TEMPO oxidation [26], and decarboxylation cascade. Finally, the desired product **4a** was given from intermediate **III** by aromatization. In the reaction process, TEMPO was regenerated from TEMPOH by the oxidation of molecular oxygen in the air [24,27–30], and TEMPO could be used in catalytic amount.

3 | CONCLUSIONS

In conclusion, an efficient synthetic protocol was developed to assemble 1,2-unsubstituted indolizines under metal-free conditions. This TEMPO-mediated reaction uses only catalytic amount of TEMPO with molecular oxygen as the terminal oxidant. Various functional groups could be well tolerated under this mild reaction condition. This work represents a valuable example of TEMPO-catalyzed decarboxylation reaction.

4 | EXPERIMENTAL

4.1 | General

Melting points are uncorrected. ^{1}H NMR spectra were measured at 400 MHz with $CDCl_3$ as solvent. The chemical shifts (δ) are reported in parts per million relative to the residual deuterated solvent signal, and coupling constants (*J*) are given in hertz. ^{13}C NMR spectra were measured at 100 MHz with $CDCl_3$ as solvent.

4.2 | General procedure for the preparation of 4

The mixture of pyridines **1** (1.5 mmol), acyl bromides **2** (0.5 mmol), maleic anhydride **3** (0.5 mmol), and TEMPO (0.1 mmol) was refluxed in acetonitrile (10 ml) for 6 hours in a round bottle. After the reaction was completed, the solvent was removed under reduced pressure, and the residue was separated by flash chromatography on a silica gel column with ethyl acetate/petroleum as eluent to give the products **4**.

4.2.1 | Methyl 3-benzoylindolizine-7-carboxylate (4a)

Yield: 82%. Yellow solid, mp 132-134°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97 (s, 3H), 6.76 (d, J = 4.4 Hz, 1H), 7.40 (d, J = 4.4 Hz, 1H), 7.45-7.57 (m, 4H), 7.81 (dd, J = 8.4, 1.6 Hz, 2H), 8.32 (d, J = 0.8 Hz, 1H), 9.89 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.4, 165.7, 140.3, 137.8, 131.4, 129.1, 128.3, 127.9, 126.9, 124.9, 124.1, 121.6, 112.5, 106.0, 52.5. HRMS (electrospray ionization [ESI]) m/z calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0974, found 280.0975.

4.2.2 | Methyl 3-(4-methoxybenzoyl) indolizine-7-carboxylate (4b)

Yield: 78%. Yellow solid, mp 148-150°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H), 3.97 (s, 3H), 6.76 (d, J = 4.4 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 7.40-7.43 (m, 2H), 7.82-7.85 (m, 2H), 8.30 (s, 1H), 9.81 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.3, 165.7, 162.4, 137.4, 132.6, 131.2, 127.7, 126.2, 124.4, 121.6, 113.6, 112.2, 105.6, 55.4, 52.4. HRMS (ESI) m/z calcd for $C_{18}H_{16}NO_4$ $[M + H]^+$ 310.1079, found 310.1085.

4.2.3 | Methyl 3-(2-naphthoyl)indolizine-7-carboxylate (4c)

Yield: 83%. Yellow solid, mp 160-162°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (s, 3H), 6.79 (d, J = 4.4 Hz, 1H), 7.46-7.49 (m, 2H), 7.56-7.60 (m, 2H), 7.91-7.97 (m, 4H), 8.32 (d, J = 9.2 Hz, 2H), 9.92 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.2, 165.6, 137.8, 137.4, 134.7, 132.4, 129.9, 129.1, 128.2, 127.9, 127.8, 127.7, 127.0, 126.7, 125.6, 124.8, 124.2, 121.6, 112.5, 106.0, 52.5. HRMS (ESI) m/z calcd for $C_{21}H_{16}NO_3$ $[M + H]^+$ 330.1130, found 330.1132.

4.2.4 | Methyl 3-cyanoindolizine-7-carboxylate (4d)

Yield: 72%. White solid, mp 153-155°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.96 (s, 3H), 6.74 (d, J = 4.4 Hz, 1H), 7.37 (d, J = 4.8 Hz, 1H), 7.39 (dd, J = 7.2, 1.6 Hz, 1H), 8.26-8.28 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 135.0, 124.7, 123.4, 123.3, 122.7, 112.2, 105.4, 52.6. HRMS (ESI) m/z calcd for $C_{11}H_9N_2O_2$ $[M + H]^+$ 201.0664, found 201.0678.

4.2.5 | Ethyl 3-benzoylindolizine-7-carboxylate (4e)

Yield: 80%. Yellow solid, mp 128-130°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (t, J = 7.2 Hz, 3H), 4.43 (q, J = 7.2 Hz, 2H), 6.76 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 4.8 Hz, 1H), 7.47-7.57 (m, 4H), 7.82 (d, J = 7.2 Hz, 2H), 8.33 (s, 1H), 9.89 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.7, 165.5, 140.6, 138.2, 131.7, 129.4, 128.7, 128.3, 127.3, 125.6, 124.4, 121.9, 112.9, 106.2, 61.9, 14.8. HRMS (ESI) m/z calcd for $C_{18}H_{16}NO_3$ $[M + H]^+$ 294.1130, found 294.1128.

4.2.6 | Ethyl 3-(4-bromobenzoyl) indolizine-7-carboxylate (4f)

Yield: 85%. Yellow solid, mp 154-155°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (t, J = 7.2 Hz, 3H), 4.43 (q, J = 7.2 Hz, 2H), 6.77 (d, J = 4.8 Hz, 1H), 7.36 (d, J = 4.8 Hz, 1H), 7.48 (dd, J = 7.2, 1.6 Hz, 1H), 7.63-7.71 (m, 4H), 8.32 (s, 1H), 9.86 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.9, 165.1, 139.0, 138.2, 131.6, 130.6, 127.9, 126.7, 126.1, 125.6, 123.7, 121.5, 112.8, 106.1, 100.0, 61.6, 14.4. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{15}BrNO_3$ $[M + H]^+$ 372.0235, found 372.0241.

4.2.7 | Ethyl 3-(4-methoxybenzoyl) indolizine-7-carboxylate (4g)

Yield: 80%. Yellow solid, mp 112-114°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (t, J = 7.2 Hz, 3H), 3.90 (s, 3H), 4.42 (q, J = 7.2 Hz, 2H), 6.75 (d, J = 4.8 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 7.40-7.44 (m, 2H), 7.84 (d, J = 8.8 Hz, 2H), 8.31 (s, 1H), 9.81 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.3, 165.2, 162.4, 137.5, 132.7, 131.3, 127.7, 126.3, 124.8, 124.1, 121.5, 113.6, 112.2, 105.6, 61.4, 55.5, 14.3. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{18}NO_4$ $[M + H]^+$ 324.1236, found 324.1241.

4.2.8 | Diethyl indolizine-3,7-dicarboxylate (4h)

Yield: 78%. White solid, mp 63-65°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39-1.44 (m, 6H), 4.37-4.43 (m, 4H), 6.71 (d, J = 4.4 Hz, 1H), 7.34 (dd, J = 7.6, 2.0 Hz, 1H), 7.55 (d, J = 4.8 Hz, 1H), 8.26 (s, 1H), 9.39 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 161.2, 136.5, 126.5, 122.9, 122.2, 121.9, 116.3, 111.5, 105.1, 61.3, 60.2, 14.5, 14.3. HRMS (ESI) m/z calcd for $C_{14}H_{16}NO_4$ $[M + H]^+$ 262.1079, found 262.1078.

4.2.9 | Methyl 7-cyanoindolizine-3-carboxylate (4i)

Yield: 75%. White solid, mp 135-137°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.94 (s, 3H), 6.75 (d, J = 4.8 Hz, 1H), 6.88 (dd, J = 7.2, 1.6 Hz, 1H), 7.59 (d, J = 4.4 Hz, 1H), 7.90 (d, J = 1.2 Hz, 1H), 9.45 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 135.3, 127.5, 125.4, 122.8, 118.1, 112.2, 105.4, 104.0, 51.6. HRMS (ESI) m/z $[M + H]^+$ calcd for. $C_{11}H_9N_2O_2$ $[M + H]^+$ 201.0664, found 201.0668.

4.2.10 | Indolizine-3,7-diylbis(phenylmethanone) (4j)

Yield: 81%. Yellow solid, mp 143-145°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.77 (d, J = 4.8 Hz, 1H), 7.42 (dd, J = 7.2, 2.0 Hz, 2H), 7.49-7.64 (m, 6H), 7.82-7.85 (m, 4H), 8.02 (s, 1H), 9.94 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3, 185.4, 140.1, 137.4, 137.1, 132.6, 131.7, 131.4, 129.8, 129.0, 128.5, 128.3, 128.1, 127.0, 124.1, 122.6, 113.1, 106.4. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{16}NO_2$ $[M + H]^+$ 326.1181, found 326.1193.

4.2.11 | (4-Chlorophenyl)(indolizin-3-yl) methanone (4k)

Yield: 62%. Yellow solid, mp 121-122°C (lit.[17] 123-125°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (d, J = 4.8 Hz, 1H), 6.97 (td, J = 7.2, 0.8 Hz, 1H), 7.21 (td, J = 7.6, 1.2 Hz, 1H), 7.30 (d, J = 4.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 9.94 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 139.7, 139.1, 137.0, 130.3, 128.8, 128.4, 126.6, 124.6, 122.3, 118.7, 114.0, 102.8.

4.2.12 | (3,4-Dichlorophenyl)(indolizin-3-yl)methanone (4l)

Yield: 65%. Yellow solid, mp 157-159°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.56 (d, J = 4.4 Hz, 1H), 6.98 (td, J = 7.2, 1.2 Hz, 1H), 7.23 (dd, J = 8.4, 0.8 Hz, 1H), 7.31 (d, J = 4.8 Hz, 1H), 7.55-7.65 (m, 3H), 7.89 (d, J = 2.0 Hz, 1H), 9.93 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.2, 140.6, 135.1, 132.7, 130.9, 130.3, 128.9, 128.1, 126.7, 125.1, 118.8, 114.3, 103.3. HRMS (ESI) m/z calcd for $C_{15}H_{10}Cl_2NO$ $[M + H]^+$ 290.0139, found 290.0139.

4.2.13 | Methyl 3-benzoylindolizine-6-carboxylate (4m)

Yield: 73%. Yellow solid, mp 118-120°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97 (s, 3H), 6.59 (d, J = 4.4 Hz, 1H), 7.45-7.52 (m, 3H), 7.55-7.59 (m, 2H), 7.72 (d, J = 9.2 Hz, 1H), 7.81-7.83 (m, 2H), 10.62 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 165.8, 140.1, 139.6, 132.7, 131.3, 129.0, 128.7, 128.3, 123.5, 123.4, 118.1, 117.5, 112.5, 104.3, 103.2, 52.4. HRMS (ESI) m/z calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0974, found 280.0980.

4.2.14 | Methyl 3-(4-chlorobenzoyl) indolizine-6-carboxylate (4n)

Yield: 75%. Yellow solid, mp 162-164°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97 (s, 3H), 6.60 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 4.8 Hz, 1H), 7.48 (d, J = 8.8 Hz, 2H), 7.59 (dd, J = 9.2, 0.4 Hz, 1H), 7.72-7.78 (m, 3H), 10.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3, 165.7, 139.8, 138.5, 137.5, 132.6, 130.4, 130.3, 128.6, 128.5, 123.7, 118.1, 117.7, 103.4, 52.4. HRMS (ESI) m/z calcd for $C_{17}H_{13}ClNO_3$ $[M + H]^+$ 314.0584, found 314.0597.

4.2.15 | Phenyl (pyrrolo[2,1-*a*]isoquinolin-3-yl)methanone (4o)

Yield: 86%. Yellow solid, mp 140-141°C (lit.[17] 140-142°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, J = 4.4 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 4.4 Hz, 1H), 7.48-7.58 (m, 5H), 7.73 (dd, J = 7.2, 1.6 Hz, 1H), 7.84-7.86 (m, 2H), 8.16-8.19 (m, 1H), 9.61 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.4, 140.6, 136.9, 131.1, 129.1, 128.9, 128.2, 128.0, 127.7, 126.9, 126.0, 125.8, 124.6, 123.6, 113.4, 101.9.

4.2.16 | (4-Methoxyphenyl)(pyrrolo[2,1-*a*] isoquinolin-3-yl)methanone (4p)

Yield: 82%. Yellow solid, mp 185-186°C (lit.[17] 187-189°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H), 6.99 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 4.4 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 4.4 Hz, 1H), 7.53-7.56 (m, 2H), 7.70 (dd, J = 8.4, 1.6 Hz, 1H), 7.86 (d, J = 8.4 Hz, 2H), 8.16 (d, J = 7.2 Hz, 1H), 9.53 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.4, 162.2, 136.6, 133.1, 131.3, 128.8, 127.8, 127.6, 126.9, 125.8, 125.2, 124.8, 123.5, 113.5, 113.1, 101.6, 55.4.

4.2.17 | Methyl pyrrolo[2,1-*a*]isoquinoline-3-carboxylate (4q)

Yield: 85%. White solid, mp 110-112°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92 (s, 3H), 6.99-7.02 (m, 2H), 7.48-7.54 (m, 3H), 7.66 (dd, J = 7.6, 1.2 Hz, 1H), 8.11 (dd, J = 8.0, 0.8 Hz, 1H), 9.21 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 135.4, 127.8, 127.6, 127.3, 126.8, 125.1, 124.9, 123.1, 120.6, 116.2, 112.7, 101.1, 51.2. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{12}NO_2$ 226.0868, found 226.0877.

4.2.18 | Ethyl pyrrolo[2,1-*a*]isoquinoline-3-carboxylate (4r)

Yield: 83%. White solid, mp 94-96°C (lit.[17] 95-97°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, J = 7.2 Hz, 3H), 4.39 (q, J = 7.2 Hz, 2H), 6.99-7.01 (m, 2H), 7.48-7.53 (m, 3H), 7.66 (d, J = 7.6 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 9.22 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 135.4, 127.8, 127.6, 127.3, 126.8, 125.1, 124.9, 123.1, 120.5, 116.6, 112.6, 101.0, 60.0, 14.6.

4.2.19 | Phenyl (pyrrolo[1,2-*a*]quinolin-1-yl)methanone (4s)

Yield: 88%. Yellow solid, mp 93-95°C (lit.[17] 93-95°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (d, J = 4.4 Hz, 1H), 7.20 (d, J = 4.4 Hz, 1H), 7.39-7.43 (m, 3H), 7.49-7.54 (m, 3H), 7.61 (t, J = 7.6 Hz, 1H), 7.72 (dd, J = 8.0, 1.2 Hz, 1H), 8.06 (dd, J = 8.0, 1.2 Hz, 2H), 8.17 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.3, 139.5, 139.4, 133.7, 132.2, 130.1, 128.9, 128.6, 128.5, 128.2, 128.0, 125.7, 125.0, 124.7, 120.1, 117.9, 104.1.

4.2.20 | (4-Chlorophenyl)(pyrrolo[1,2-*a*]quinolin-1-yl)methanone (4t)

Yield: 85%. Yellow solid, mp 108-110°C (lit.[17] 110-112°C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (d, J = 4.4 Hz, 1H), 7.18 (d, J = 4.4 Hz, 1H), 7.41-7.43 (m, 3H), 7.48-7.53 (m, 3H), 7.72 (dd, J = 8.0, 1.6 Hz, 1H), 8.00 (dd, J = 6.8, 2.0 Hz, 2H), 8.14 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.8, 139.7, 138.5, 137.9, 133.7, 131.4, 128.9, 128.7, 128.5, 128.1, 128.0, 126.0, 125.0, 124.8, 120.0, 117.8, 104.3.

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