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One-Pot Synthesis of Pyrrolo[3,4-*a*]indolizine-1,3-diones through [3+2] Cycloaddition-Oxidation Reaction Catalyzed by Cu^{II} Salt and O_2 as the Oxidant

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An efficient one-pot synthesis of pyrrolo[3,4-*a*]indolizine-1,3-diones has been developed from maleimides, pyridines, and acyl bromides through a [3+2] cyclization–oxidation reaction catalyzed by Cu^{II} salt under O_2 atmosphere. The advantage of this method is the use of molecular oxygen as the oxidant, in the presence of a catalytic amount of hydrated copper(II) chloride, to accomplish the reaction with broad substrate scope and excellent yields.

Introduction

Indolizines, as an important class of N-heterocycles, have received much attention in recent years.[1] These molecules have found various pharmaceutical applications as anti-tuberculosis agents,[2] PLA2 inhibitors,[3] histamine H3 receptor antagonists,[4] 5-HT3 receptor antagonists,[5] MPtpA/MPtpB phosphatases inhibitors[6] and 15-lipoxygenase inhibitors.[7] They are playing an increasingly important role in developing new pharmaceuticals for the treatment of human diseases such as cancer,[8] cardiovascular disease[9] and HIV infections.[10] It is also known that the maleimide skeleton is an important core unit. Current studies have shown that maleimide is a potent inhibitor of topoisomerase II in vitro and in vivo, and that substituted maleimides have strong antifungal activity.[11] In addition, polycyclic N-heterocycles are ubiquitous in a variety of natural products and biologically-active molecules,[12] and they have been assigned as privileged structures in drug development because N-heterocyclic moieties often exhibit improved solubility and can facilitate salt formation, both of which are important for oral absorption and bioavailability.[13]

Therefore, we tried to synthesize pyrrolo[3,4-*a*]indolizine-1,3-diones to combine the maleimide and indolizine frameworks, with the aim of exploring the potential biological activity of this class of compounds.

To the best of our knowledge, only isolated examples of pyrrolo[3,4-*a*]indolizine-1,3-dione syntheses have been reported by using the reaction of pyridinium salts with maleimides followed by oxidation with a stoichiometric amount of oxidant such as tetrakispyridinecobalt(II) dichromate[14] or *t*BuOOH.[15] The shortcoming of these methods are the limited substrate scope and a requirement for a stoichiometric amount of oxidant, which is not economical or environmentally friendly, and complicates the work-up. Copper(II) salt is a particularly attractive oxidant because, under appropriate conditions and with suitable substrates, oxidation reactions can be carried out with catalytic amounts of Cu by using ambient air or O_2 as the stoichiometric oxidant.[16] In continuation of our ongoing research interest in the synthesis of indolizine derivatives,[14b,17] and with the aim of developing general and practical synthetic methods for polycyclic N-heterocycles, we report the high-yielding one-pot synthesis of pyrrolo[3,4-*a*]indolizine-1,3-diones from maleimides, pyridines, and acyl bromides through a [3+2] cyclization-oxidation reaction catalyzed by Cu^{II} salt by using molecular oxygen as the oxidant.

Results and Discussion

Initially, *N*-phenylmaleimide (**1a**; 2.0 mmol) was subjected to the copper(II)-promoted reaction with pyridine (**2a**; 6.0 mmol) and acyl bromide **3a** (2.0 mmol) in CH_3CN at reflux temperatures by using hydrated copper(II) chloride (20 mol-%) as the catalyst under 1 atm O_2 (Table 1). By heating to reflux for 24 h, product **4a** was obtained in 71% yield. On the basis of this result, we began to optimize the

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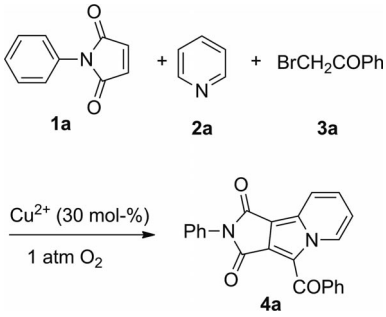
reaction conditions. In screening the catalysts, hydrated copper(II) chloride proved to be the most promising (Table 1, Entries 5–7). Relative to copper(II) chloride, copper(II) bromide provided a similar yield but more by-products (Table 1, Entry 6). When copper(II) acetate was used as the catalyst, it led to a slightly lower yield (Table 1, Entry 7). The effect of the amount of the catalyst was also examined and it was found that 30 mol-% of hydrated copper(II) chloride gave the best result with 91% product yield (Table 1, Entries 1–5). Solvent screening showed that acetonitrile offered optimal selectivity (Table 1, Entries 3 and 8–10). Finally, a significant decrease of the reaction yield was observed when the reaction temperature was decreased (Table 1, Entry 11 and 12). In this reaction, an excess of pyridine was necessary for the deprotonation step and HBr trapping. Decreasing the amount of pyridine led to a decreased yield. As the oxidant, oxygen is more efficient than ambient air. When the reaction was carried out in air, an increased amount of copper(II) salt was necessary to obtain the product in high yield. In contrast, when the reaction was carried out under an Ar atmosphere in the presence of 30% copper(II) salt, only trace amounts of product were formed. However, by using a stoichiometric amount of Cu^{II} salt, the reaction proceeds smoothly under an Ar atmosphere to give the product in a yield similar to that when using a catalytic amount of Cu^{II} salt under 1 atm oxygen. Therefore, the optimal reaction condition are heating the reactants in CH_3CN to reflux with 30 mol-% of hydrated copper(II) chloride as catalyst under 1 atm O_2.

Table 1. Optimization of the reaction conditions.[a]

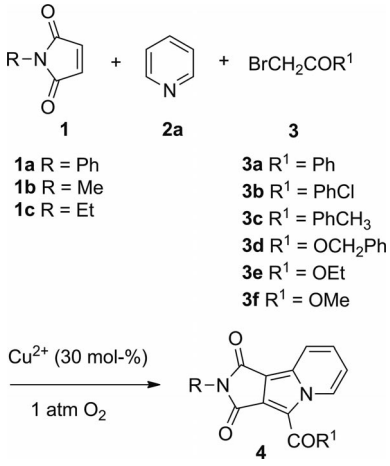


Entry	Solvent	Catalyst	Temp. [°C]	Yield [%][c]
1	CH_3CN	$CuCl_2$ (20 mol-%)	reflux	71
2	CH_3CN	$CuCl_2$ (25 mol-%)	reflux	80
3	CH_3CN	$CuCl_2$ (30 mol-%)	reflux	91
4	CH_3CN	$CuCl_2$ (35 mol-%)	reflux	91
5	CH_3CN	none	reflux	0[b]
6	CH_3CN	$CuBr_2$ (30 mol-%)	reflux	87
7	CH_3CN	$Cu(OAc)_2$ (30 mol-%)	reflux	80
8	C_6H_6	$CuCl_2$ (30 mol-%)	reflux	72
9	C_2H_5OH	$CuCl_2$ (30 mol-%)	reflux	67
10	DMF	$CuCl_2$ (30 mol-%)	reflux	85
11	CH_3CN	$CuCl_2$ (30 mol-%)	60	62
12	CH_3CN	$CuCl_2$ (30 mol-%)	r.t.	0

[a] Reagents and conditions: pyridine (6.0 mmol), acyl bromide (2.0 mmol), maleimide (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol), heated to reflux in solvent for 24 h under 1 atm O_2. [b] Without copper salt, no product **4a** was formed and the reaction system was complicated with many byproducts. [c] Isolated yields.

With the optimized reaction conditions in hand, we then investigated the substrate scope for the copper-catalyzed reactions. First, a variety of acyl bromides **3** was treated with *N*-phenylmaleimide (**1a**) and pyridine (**2a**) under the optimized reaction conditions. Both phenacyl bromides **3a**–**3c** and 2-bromoacetates **3d** and **3e** produced corresponding products **4a**–**4e** smoothly in good to excellent yields (Table 2, Entries 1–5). The results demonstrated that various acyl bromides showed similar reactivity and took part in the reaction efficiently to yield the final products. Meanwhile, the reactivity of *N*-methylmaleimide (**1b**), and *N*-ethylmaleimide (**1c**) were also studied. It was found that **1b** and **1c** under the optimized conditions also reacted smoothly to give **4f**–**4o** in slightly higher yields than *N*-phenylmaleimide (Table 2, Entries 6–15). All these pyrrolo[3,4-*a*]indolizine-1,3-diones were previously unknown and have been fully characterized by analytical and spectroscopic (IR, NMR, and HRMS) data. Moreover, the structure of **4j** was further established by X-ray crystallography (Figure 1). These results showed that this reaction provides a general and convenient high-yielding synthesis of pyrrolo[3,4-*a*]indolizine-1,3-diones derivatives.

Table 2. Reaction scope with various maleimides and acyl bromides.[a]



Entry	**1**, R	**3**, R^1	Product	Yield [%][b]
1	Ph	Ph	**4a**	91
2	Ph	C_6H_4Cl-*p*	**4b**	95
3	Ph	C_6H_4Me-*p*	**4c**	93
4	Ph	OCH_2Ph	**4d**	92
5	Ph	OEt	**4e**	88
6	Me	Ph	**4f**	93
7	Me	C_6H_4Cl-*p*	**4g**	97
8	Me	OCH_2Ph	**4h**	95
9	Me	OEt	**4i**	88
10	Me	OMe	**4j**	85
11	Et	Ph	**4k**	92
12	Et	C_6H_4Cl-*p*	**4l**	95
13	Et	OCH_2Ph	**4m**	96
14	Et	OEt	**4n**	89
15	Et	OMe	**4o**	86

[a] Reagents and conditions: pyridine (6.0 mmol), acyl bromide (2.0 mmol), maleimide (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol), reflux in acetonitrile for 24 h under 1 atm O_2. [b] Isolated yields.

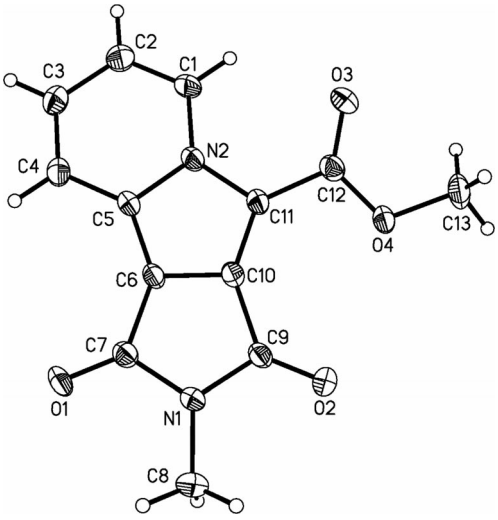
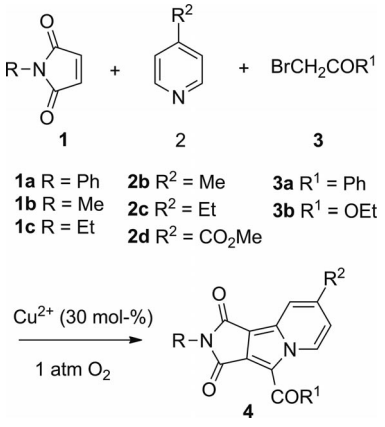


Figure 1. ORTEP drawing of **4j**.

To further extend the utility of this tandem reaction, we investigated the reactions of 4-substituted pyridines **2b**, **2c**, and **2d** in place of pyridine (Table 3). It was found that the properties of the substituents on pyridine have little effect on the reaction. Pyridines with either electron-donating groups, such as **2b** or **2c**, or with electron-withdrawing group, such as **2d**, reacted equally well with maleimide **1** and acyl bromide **3** to give corresponding products **4p**–**4w** in high yields.

Table 3. Reaction scope with 4-substituted pyridines.[a]

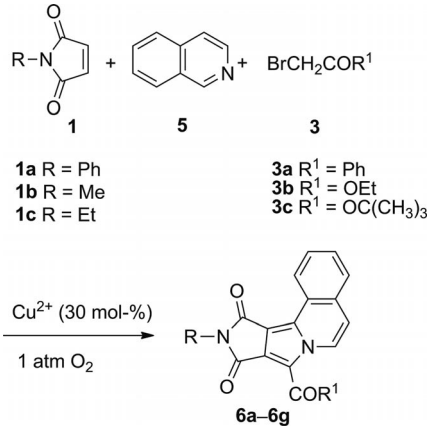


Entry	**1**	**2**	**3**	Product	Yield [%][b]
1	**a**	**b**	**a**	**4p**	90
2	**a**	**b**	**b**	**4q**	85
3	**b**	**b**	**a**	**4r**	93
4	**c**	**b**	**a**	**4s**	92
5	**a**	**c**	**a**	**4t**	91
6	**a**	**c**	**b**	**4u**	87
7	**a**	**d**	**a**	**4v**	88
8	**a**	**d**	**b**	**4w**	83

[a] Reagents and conditions: 4-substituted pyridine (6.0 mmol), acyl bromide (2.0 mmol), maleimide (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol), at reflux temperatures in acetonitrile for 24 h under 1 atm O_2. [b] Isolated yields.

For the synthesis of further annulated indolizine derivatives, we also investigated the reactions of isoquinoline **5** with maleimides and acyl bromide. When *N*-phenylmaleimide (**1a**; 2.0 mmol) was heated with isoquinoline (**5**; 6.0 mmol), phenacyl bromide (**3a**; 2.0 mmol), and hydrated copper chloride (0.6 mmol) in acetonitrile at reflux temperatures for 24 h, corresponding product **6a** was obtained in 92% yield. It was further found that the reaction of **5** with 2-bromoacetate **3b** or **3c** and *N*-phenylmaleimide (**1a**) also led to corresponding annulated benzo[*f*]pyrrolo[3,4-*a*]-indolizine-1,3-dione derivatives **6b** and **6c** in high yields. Meanwhile, when *N*-methylmaleimide or *N*-ethylmaleimide was used as the substrate to react with isoquinoline and acyl bromides, desired products **6d**–**6g** were generated in excellent yields (Table 4).

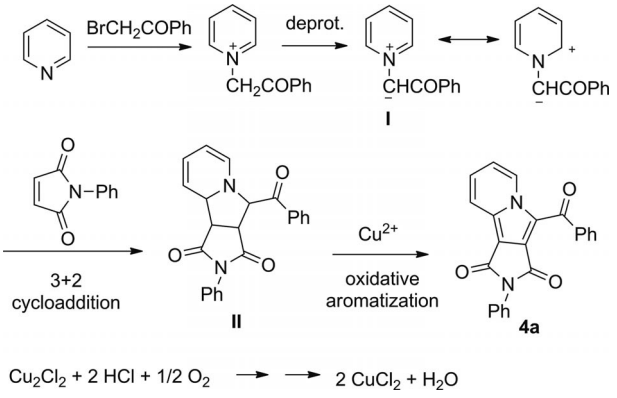
Table 4. Reaction scope with isoquinoline.[a]



Entry	**1**, R	**3**, R^1	Product	Yield [%][b]
1	Ph	Ph	**6a**	92
2	Ph	OEt	**6b**	87
3	Ph	$OC(CH_3)_3$	**6c**	89
4	Me	Ph	**6d**	95
5	Me	$OC(CH_3)_3$	**6e**	91
6	Et	Ph	**6f**	93
7	Et	$OC(CH_3)_3$	**6g**	90

[a] Reagents and conditions: isoquinoline (6.0 mmol), acyl bromide (2.0 mmol), maleimide (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol), reflux in acetonitrile for 24 h under 1 atm O_2. [b] Isolated yields.

A possible mechanism for this reaction is suggested in Scheme 1. First, deprotonation of the pyridinium salt formed by the reaction of pyridine with acyl bromide yields pyridinium ylide **I**. Subsequent [3+2] cycloaddition reaction of **I** with *N*-phenylmaleimide affords **II**,[18] which on oxidative aromatization catalyzed by Cu^{2+} furnishes product **4a**. The copper(II) salt can be regenerated through oxidation by oxygen. It is worth noting that copper(II) salt in this reaction acts as an oxidation catalyst and also catalyzes the cycloaddition reaction step owing to its Lewis acid character.[15]



Scheme 1. Proposed mechanism of the formation for **4a**.

Conclusions

We have described a general and efficient method for the synthesis of pyrrolo[3,4-*a*]indolizine-1,3-diones and their further-annulated derivatives in one-pot, copper(II)-catalyzed three-component reaction of maleimides, pyridines, and acyl bromides. The most attractive features of this procedure are the broad reaction scope and the use of molecular oxygen as the oxidant in place of a stoichiometric amount of oxidants through catalysis by hydrated copper(II) chloride. The pyrrolo[3,4-*a*]indolizine-1,3-diones prepared are currently being subjected to biological evaluation.

Experimental Section

General Procedure for the Preparation of Benzo[*f*]pyrrolo[3,4-*a*]-indolizine-1,3-diones 4: Pyridine **1** (6.0 mmol), acyl bromide **2** (2.0 mmol), maleimide **3** (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol) were mixed in CH_3CN (15 mL) and heated to reflux for 24 h under an oxygen atmosphere. The reaction mixture was then allowed to cool to room temperature. After evaporation of the solvent under vacuum, the mixture was purified by column chromatography on silica gel to afford pure product **4**.

9-Benzoyl-2-phenyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4a): Yellow solid, m.p. 223–224 °C. IR (KBr): 1765, 1718, 1622, 1578, 1512, 1501, 1334, 1299, 1219, 1169, 1087, 872, 751, 685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16 (td, J = 7.2, 1.2 Hz, 1 H), 7.30–7.34 (m, 3 H), 7.42 (t, J = 9.0 Hz, 2 H), 7.48–7.55 (m, 3 H), 7.62 (t, J = 7.6 Hz, 1 H), 7.87 (d, J = 7.2 Hz, 2 H), 8.02 (d, J = 9.2 Hz, 1 H), 9.65 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 162.4, 162.0, 138.8, 133.1, 132.6, 132.2, 130.1, 130.0, 129.5, 128.9, 128.7, 128.4, 127.8, 127.0, 118.9, 117.7, 116.6 ppm. HRMS (ESI): calcd. for $C_{23}H_{14}N_2NaO_3$ $[M + Na]^+$ 389.0902; found 389.0903.

9-(4-Chlorobenzoyl)-2-phenyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4b): Yellow solid, m.p. 287–289 °C. IR (KBr): 1715, 1682, 1645, 1621, 1592, 1556, 1425, 1323, 1296, 1219, 1176, 1092, 853, 762, 747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.20 (t, J = 6.8 Hz, 1 H), 7.38 (t, J = 7.2 Hz, 3 H), 7.48 (t, J = 7.6 Hz, 4 H), 7.57 (t, J = 8.0 Hz, 1 H), 7.85 (d, J = 8.4 Hz, 2 H), 8.06 (d, J = 8.4 Hz, 1 H), 9.66 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.0, 162.6, 162.2, 141.0, 139.3, 137.1, 133.2, 132.1, 130.9, 129.4, 129.0, 128.7, 127.8, 126.9, 119.3, 117.5, 116.9, 109.5 ppm. HRMS (ESI): calcd. for $C_{23}H_{13}ClN_2NaO_3$ $[M + Na]^+$ 423.0512; found 423.0510.

9-(4-Methylbenzoyl)-2-phenyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4c): Yellow solid, m.p. 229–230 °C. IR (KBr): 1763, 1716, 1623, 1604, 1557, 1501, 1451, 1357, 1331, 1297, 1171, 1060, 875, 747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 7.14 (t, J = 7.2 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 2 H), 7.34 (d, J = 7.6 Hz, 3 H), 7.43 (t, J = 8.0 Hz, 2 H), 7.50 (t, J = 8.0 Hz, 1 H), 7.82 (d, J = 8.0 Hz, 2 H), 8.01 (d, J = 8.8 Hz, 1 H), 957 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.2, 162.7, 162.2, 144.1, 135.9, 132.4, 132.2, 130.0, 129.9, 129.6, 129.1, 128.9, 128.5, 127.7, 127.0, 118.8, 117.9, 116.4, 110.3, 21.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{16}N_2NaO_3$ $[M + Na]^+$ 403.1059; found 403.1056.

Benzyl 1,3-Dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4d): Yellow solid, m.p. 218–220 °C. IR (KBr): 1772, 1711, 1684, 1645, 1541, 1515, 1499, 1338, 1222, 1152, 1091, 1065, 811, 749, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.51 (s, 2 H), 7.09 (td, J = 7.2, 1.2 Hz, 1 H), 7.29–7.33 (m, 1 H), 7.38–7.46 (m, 6 H), 7.50 (td, J = 7.6, 1.6 Hz, 2 H), 7.60 (d, J = 7.2 Hz, 2 H), 7.95 (d, J = 9.2 Hz, 1 H), 9.63 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 162.0, 159.9, 135.7, 132.4, 132.1, 129.9, 129.4, 129.0, 128.6, 128.3, 128.2, 127.9, 127.6, 127.2, 118.9, 116.2, 110.5, 110.1, 66.8 ppm. HRMS (ESI): calcd. for $C_{24}H_{16}N_2NaO_4$ $[M + Na]^+$ 419.1008; found 419.1003.

Ethyl 1,3-Dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4e): Yellow solid, m.p. 195–197 °C. IR (KBr): 1765, 1711, 1690, 1541, 1503, 1399, 1363, 1334, 1225, 1168, 1094, 1039, 930, 793, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.50 (t, J = 7.2 Hz, 3 H), 4.48 (d, J = 7.2 Hz, 2 H), 7.10 (t, J = 6.8 Hz, 1 H), 7.39–7.46 (m, 4 H), 7.50 (t, J = 7.6 Hz, 2 H), 7.96 (d, J = 8.8 Hz, 1 H), 9.63 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 162.1, 160.1, 132.5, 131.9, 129.7, 129.3, 129.0, 127.8, 127.4, 127.2, 118.9, 116.0, 110.5, 110.3, 61.5, 14.3 ppm. HRMS (ESI): calcd. for $C_{19}H_{14}N_2NaO_4$ $[M + Na]^+$ 357.0851; found 357.0840.

9-Benzoyl-2-methyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4f): Yellow solid, m.p. 254–256 °C. IR (KBr): 1756, 1715, 1651, 1621, 1500, 1377, 1353, 1333, 1170, 1144, 898, 842, 789, 732, 665 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.03 (s, 3 H), 7.11 (t, J = 6.8 Hz, 1 H), 7.46–7.55 (m, 3 H), 7.68 (td, J = 7.2, 0.8 Hz, 1 H), 7.83 (d, J = 6.8 Hz, 2 H), 7.94 (d, J = 8.8 Hz, 1 H), 9.61 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 163.8, 163.2, 139.0, 132.9, 132.1, 131.0, 130.0, 129.5, 128.5, 128.3, 118.6, 116.2, 111.1, 24.2 ppm. HRMS (ESI): calcd. for $C_{18}H_{12}N_2NaO_3$ $[M + Na]^+$ 327.0746; found 327.0740.

9-(4-Chlorobenzoyl)-2-methyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4g): Yellow solid, m.p. 277–279 °C. IR (KBr): 1754, 1716, 1652, 1615, 1590, 1500, 1456, 1356, 1331, 1172, 1091, 838, 743, 685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.06 (s, 3 H), 7.14 (t, J = 7.2 Hz, 1 H), 7.46–7.53 (m, 3 H), 7.80 (d, J = 8.4 Hz, 2 H), 7.96 (d, J = 8.8 Hz, 1 H), 9.60 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.1, 163.7, 163.3, 139.4, 137.1, 132.3, 131.6, 131.0, 130.9, 130.0, 128.9, 128.7, 118.7, 117.0, 116.4, 24.3 ppm. HRMS (ESI): calcd. for $C_{18}H_{11}ClN_2NaO_3$ $[M + Na]^+$ 361.0356; found 361.0359.

Benzyl 2-Methyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4h): Yellow solid, m.p. 157–159 °C. IR (KBr): 1756, 1704, 1682, 1647, 1533, 1517, 1434, 1355, 1240, 1218, 1116, 1068, 989, 885, 752, 710 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.15 (s, 3 H), 5.50 (s, 2 H), 7.03 (td, J = 7.2, 1.2 Hz, 1 H), 7.34–7.43 (m, 4 H), 7.62 (d, J = 7.2 Hz, 2 H), 7.86 (d, J = 7.2 Hz, 1 H), 956 (d, J

= 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 163.2, 160.0, 135.7, 131.6, 130.6, 129.3, 128.6, 128.3, 128.2, 128.1, 127.3, 118.7, 115.7, 66.8, 24.3 ppm. HRMS (ESI): calcd. for $C_{19}H_{14}N_2NaO_4$ $[M + Na]^+$ 357.0851; found 357.0853.

Ethyl 2-Methyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4i): Yellow solid, m.p. 200–202 °C. IR (KBr): 1765, 1717, 1650, 1541, 1502, 1424, 1379, 1348, 1235, 1166, 1091, 1021, 804, 755, 734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (t, J = 7.2 Hz, 3 H), 3.14 (s, 3 H), 4.49 (qd, J = 7.2, 2.0 Hz, 2 H), 7.03 (t, J = 6.4 Hz, 1 H), 7.37 (t, J = 7.2 Hz, 1 H), 7.86 (d, J = 9.2 Hz, 1 H), 9.55 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 163.3, 160.1, 131.5, 130.3, 129.2, 127.1, 118.6, 115.6, 110.6, 110.1, 61.4, 24.2, 14.3 ppm. HRMS (ESI): calcd. for $C_{14}H_{12}N_2NaO_4$ $[M + Na]^+$ 295.0695; found 295.0697.

Methyl 2-Methyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4j): Yellow solid, m.p. 231–233 °C. IR (KBr): 1762, 1693, 1641, 1545, 1512, 1428, 1339, 1242, 1221, 1166, 1064, 998, 762, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (s, 3 H), 4.04 (s, 3 H), 7.06 (d, J = 6.4 Hz, 1 H), 7.39 (t, J = 8.0 Hz, 1 H), 7.88 (d, J = 8.8 Hz, 1 H), 9.56 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 163.3, 160.5, 131.5, 130.1, 129.1, 127.2, 118.7, 115.7, 110.7, 109.6, 52.2, 24.2 ppm. HRMS (ESI): calcd. for $C_{13}H_{10}N_2NaO_4$ $[M + Na]^+$ 281.0528; found 281.0522.

CCDC-909367 (for **4j**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

9-Benzoyl-2-ethyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4k): Yellow solid, m.p. 205–207 °C. IR (KBr): 1756, 1713, 1625, 1510, 1341, 1225, 1183, 1014, 878, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.2 Hz, 3 H), 3.60 (q, J = 7.2 Hz, 2 H), 7.12 (t, J = 6.4 Hz, 1 H), 7.48–7.57 (m, 3 H), 7.70 (t, J = 7.2 Hz, 1 H), 7.86 (d, J = 6.8 Hz, 2 H), 7.96 (d, J = 8.4 Hz, 1 H), 9.64 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 163.7, 162.9, 138.9, 132.9, 132.1, 131.0, 130.2, 130.0, 129.5, 128.5, 128.4, 128.3, 118.6, 117.3, 116.2, 111.2, 33.0, 14.1 ppm. HRMS (ESI): calcd. for $C_{19}H_{14}N_2NaO_3$ $[M + Na]^+$ 341.0902; found 341.0907.

9-(4-Chlorobenzoyl)-2-ethyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4l): Yellow solid, m.p. 230–232 °C. IR (KBr): 1752, 1712, 1622, 1592, 1534, 1509, 1401, 1342, 1299, 1224, 1149, 1088, 1063, 880, 757 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, J = 7.2 Hz, 3 H), 3.60 (q, J = 7.2 Hz, 2 H), 7.11 (td, J = 7.2, 0.8 Hz, 1 H), 7.47–7.50 (m, 3 H), 7.80 (d, J = 8.4 Hz, 2 H), 7.95 (d, J = 8.8 Hz, 1 H), 9.59 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.1, 163.5, 163.0, 139.4, 137.1, 132.3. 131.0, 130.9, 130.0, 128.6, 128.5, 118.6, 116.9, 116.3, 111.4, 33.1, 14.1 ppm. HRMS (ESI): calcd. for $C_{19}H_{13}ClN_2NaO_3$ $[M + Na]^+$ 375.0512; found 375.0508.

Benzyl 2-Ethyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4m): Yellow solid, m.p. 178–180 °C. IR (KBr): 1759, 1702, 1688, 1640, 1542, 1513, 1348, 1256, 1217, 1142, 1019, 951, 756 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 3 H), 3.70 (q, J = 7.2 Hz, 2 H), 5.50 (s, 2 H), 7.00 (td, J = 7.2, 1.2 Hz, 1 H), 7.33–7.42 (m, 4 H), 7.62 (d, J = 7.2 Hz, 2 H), 7.85 (d, J = 8.8 Hz, 1 H), 9.55 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 162.9, 159.9, 135.7, 131.6, 130.6, 129.3, 128.6, 128.5, 128.3, 128.2, 128.1, 127.2, 127.0, 118.6, 115.7, 66.7, 33.1, 14.2 ppm. HRMS (ESI): calcd. for $C_{20}H_{16}N_2NaO_4$ $[M + Na]^+$ 371.1008; found 371.1006.

Ethyl 2-Ethyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4n): Yellow solid, m.p. 195–197 °C. IR (KBr): 1756, 1709, 1644, 1541, 1513, 1347, 1335, 1229, 1159, 1038, 1019, 760,744 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 3 H), 1.52 (t, J = 7.2 Hz, 3 H), 3.70 (q, J = 7.2 Hz, 2 H), 4.48 (q, J = 7.2 Hz, 2 H), 7.03 (t, J = 6.8 Hz, 1 H), 7.38 (t, J = 6.8 Hz, 1 H), 7.87 (d, J = 8.8 Hz, 1 H), 9.56 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 163.1, 160.1, 131.5, 130.4, 129.2, 127.1, 118.7, 115.6, 110.7, 110.0, 61.4, 33.0, 14.3, 14.2 ppm. HRMS (ESI): calcd. for $C_{15}H_{14}N_2NaO_4$ $[M + Na]^+$ 309.0851; found 309.0853.

Methyl 2-Ethyl-1,3-dioxo-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-9-carboxylate (4o): Yellow solid, m.p. 210–212 °C. IR (KBr): 1756, 1707, 1646, 1542, 1514, 1438, 1347, 1232, 1156, 1028, 808, 758, 744 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.2 Hz, 3 H), 3.71 (d, J = 7.2 Hz, 2 H), 4.06 (s, 3 H), 7.06 (t, J = 7.2 Hz, 1 H), 7.40 (t, J = 76 Hz, 1 H), 7.89 (d, J = 8.8 Hz, 1 H), 9.58 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 163.2, 160.5, 131.6, 130.5, 129.2, 127.2, 118.7, 115.7, 110.8, 109.5, 52.3. 33.1, 14.2 ppm. HRMS (ESI): calcd. for $C_{14}H_{12}N_2NaO_4$ $[M + Na]^+$ 295.0695; found 295.0698.

4-Benzoyl-8-methyl-2-phenyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4p): Yellow solid, m.p. 243–245 °C. IR (KBr): 1757, 1716, 1651, 1620, 1599, 1501, 1420, 1354, 1334, 1299, 1222, 1170, 1089, 843, 791, 733 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54 (s, 3 H), 7.01 (d, J = 7.2 Hz, 1 H), 7.33 (t, J = 8.0 Hz, 3 H), 7.44 (t, J = 8.0 Hz, 2 H), 7.50 (t, J = 7.6 Hz, 2 H), 7.63 (t, J = 7.2 Hz, 1 H), 7.82 (s, 1 H), 7.88 (d, J = 7.2 Hz, 2 H), 9.55 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.5, 162.7, 162.1, 140.8, 138.9, 133.1, 132.9, 132.3, 130.3, 129.5, 128.9, 128.3, 127.7, 127.0, 119.2, 117.5, 117.4, 109.4, 21.5 ppm. HRMS (ESI): calcd. for $C_{24}H_{16}N_2NaO_3$ $[M + Na]^+$ 403.1059; found 403.1061.

Ethyl 8-Methyl-1,3-dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]-indolizine-4-carboxylate (4q): Yellow solid, m.p. 228–229 °C. IR (KBr): 1766, 1710, 1690, 1545, 1450, 1399, 1361, 1332, 1220, 1088, 1042, 804, 755 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 (t, J = 7.2 Hz, 3 H), 2.49 (s, 3 H), 4.47 (q, J = 7.2 Hz, 2 H), 6.93 (dd, J = 7.2, 1.5 Hz, 1 H), 7.38–7.43 (m, 3 H), 7.49 (t, J = 7.6 Hz, 2 H), 7.74 (s, 1 H), 9.50 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 162.3, 160.2, 139.3, 132.6, 132.4, 129.8, 129.0, 128.6, 127.7, 127.2, 127.1, 118.6, 117.5, 61.4, 21.4, 14.3 ppm. HRMS (ESI): calcd. for $C_{20}H_{16}N_2NaO_4$ $[M + Na]^+$ 371.1008; found 371.1009.

4-Benzoyl-2,8-dimethyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4r): Yellow solid, m.p. 214–216 °C. IR (KBr): 1751, 1714, 1650, 1626, 1527, 1515, 1427, 1373, 1359, 1300, 1220, 1159, 1059, 973, 842, 746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H), 3.01 (s, 3 H), 6.94 (dd, J = 7.2, 1.2 Hz, 1 H), 7.51 (t, J = 8.0 Hz, 2 H), 7.66 (t, J = 7.6 Hz, 1 H), 7.71 (s, 1 H), 7.81 (dd, J = 8.4, 1.2 Hz, 2 H), 9.51 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.5, 164.0, 163.3, 140.5, 139.1, 132.7, 132.6, 131.2, 129.4, 129.3, 128.3, 118.8, 117.2, 117.0, 110.0, 24.2, 21.5 ppm. HRMS (ESI): calcd. for $C_{19}H_{14}N_2NaO_3$ $[M + Na]^+$ 341.0902; found 341.0905.

4-Benzoyl-2-ethyl-8-methyl-1*H*-pyrrolo[3,4-*a*]in-dolizine-1,3(2*H*)-dione (4s): Yellow solid, m.p. 232–234 °C. IR (KBr): 1752, 1709, 1649, 1624, 1559, 1509, 1418, 1341, 1262, 1226, 1097, 1022, 801, 695, 663 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, J = 7.2 Hz, 3 H), 2.50 (s, 3 H), 3.56 (q, J = 7.2 Hz, 2 H), 6.93 (dd, J = 7.2, 1.6 Hz, 1 H), 7.51 (t, J = 7.6 Hz, 2 H), 7.65 (d, J = 7.2 Hz, 1 H), 7.72 (s, 1 H), 7.82 (d, J = 8.0 Hz, 2 H), 9.52 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 163.8, 163.0, 140.4, 139.1, 132.8, 132.6, 129.4, 129.3, 128.2, 118.8, 117.2, 33.0,

21.5, 14.1 ppm. HRMS (ESI): calcd. for $C_{20}H_{16}N_2NaO_3$ 355.1059; found 355.1063.

4-Benzoyl-8-ethyl-2-phenyl-1*H*-pyrrolo[3,4-*a*]indolizine-1,3(2*H*)-dione (4t): Yellow solid, m.p. 199–200 °C. IR (KBr): 1762, 1715, 1652, 1611, 1531, 1499, 1423, 1351, 1261, 1225, 1170, 1087, 1053, 879, 808, 730 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.6 Hz, 3 H), 2.75 (d, J = 7.6 Hz, 2 H), 6.95 (dd, J = 7.6, 1.5 Hz, 1 H), 7.25 (d, J = 8.4 Hz, 3 H), 7.34 (t, J = 7.6 Hz, 2 H), 7.40 (t, J = 7.6 Hz, 2 H), 7.53 (t, J = 7.6 Hz, 1 H), 7.73 (s, 1 H), 7.79 (dd, J = 8.0, 1.2 Hz, 2 H), 9.49 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.5, 162.8, 162.1, 146.7, 138.9, 133.2, 132.9, 132.3, 130.3, 129.6, 129.5, 129.4, 128.9, 128.8, 128.4, 128.3, 127.7, 127.0, 126.9, 118.2, 117.4, 116.1, 109.6, 28.6, 14.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{18}N_2NaO_3$ [M + Na]$^+$ 417.1215; found 417.1210.

Ethyl 8-Ethyl-1,3-dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]-indolizine-4-carboxylate (4u): Yellow solid, m.p. 205–207 °C. IR (KBr): 1762, 1709, 1541, 1500, 1359, 1248, 1215, 1167, 1116, 1049, 962, 810, 747, 682, 619 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.2 Hz, 3 H), 1.53 (t, J = 7.2 Hz, 3 H), 2.80 (q, J = 7.2, Hz, 2 H), 4.50 (q, J = 7.2 Hz, 2 H), 6.98 (d, J = 7.2 Hz, 1 H), 7.40–7.45 (m, 3 H), 7.50–7.54 (m, 2 H), 7.76 (s, 1 H), 9.54 (d, J = 7.2 Hz,1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 162.9, 160.2, 132.6, 129.0, 128.9, 128.8, 127.7, 127.2, 127.1, 126.2, 124.5, 121.1, 117.7, 116.1, 113.2, 61.4, 28.5, 14.3, 14.1 ppm. HRMS (ESI): calcd. for $C_{21}H_{18}N_2NaO_4$ [M + Na]$^+$ 385.1164; found 385.1168.

Methyl 4-Benzoyl-1,3-dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-8-carboxylate (4v): Yellow solid, m.p. 229–230 °C. IR (KBr): 1761, 1720, 1630, 1597, 1518, 1503, 1459, 1403, 1371, 1288, 1249, 1150, 1086, 976, 895, 749 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.03 (s, 3 H), 7.34 (t, J = 7.6 Hz, 3 H), 7.44 (t, J = 7.6 Hz, 2 H), 7.51 (t, J = 7.6 Hz, 2 H), 7.63–7.68 (m, 2 H), 7.89 (d, J = 8.0 Hz, 2 H), 8.71 (s, 1 H), 9.59 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 164.5, 162.1, 161.6, 138.2, 133.5, 132.0, 130.9, 130.5, 129.6, 129.4, 129.2, 129.0, 128.9, 128.5, 127.9, 126.9, 121.0, 118.8, 115.3, 113.6, 53.1 ppm. HRMS (ESI): calcd. for $C_{25}H_{16}N_2NaO_5$ [M + Na]$^+$ 447.0957; found 447.0960.

4-Ethyl 8-Methyl 1,3-Dioxo-2-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*a*]indolizine-4,8-dicarboxylate (4w): Yellow solid, m.p. 212–214 °C. IR (KBr): 1770, 1724, 1693, 1597, 1519, 1499, 1458, 1377, 1345, 1291, 1159, 1085, 1026, 895, 830, 753, 692, 617 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.50 (t, J = 7.2 Hz, 3 H), 4.00 (s, 3 H), 4.51 (q, J = 7.2 Hz, 2 H), 7.40–7.43 (m, 3 H), 7.51 (t, J = 8.0 Hz, 2 H), 7.62 (dd, J = 7.6, 2.0 Hz, 1 H), 8.64 (s, 1 H), 9.64 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 162.2, 161.6, 159.8, 132.2, 130.4, 130.2, 129.1, 128.8, 128.7, 128.1, 128.0, 127.1, 121.0, 114.9, 113.5, 111.9, 61.9, 53.0, 14.2 ppm. HRMS (ESI): calcd. for $C_{21}H_{16}N_2NaO_6$ [M + Na]$^+$ 415.0906; found 415.0912.

General Procedure for the Preparation of Benzo[*f*]pyrrolo[3,4-*a*]-indolizine-1,3-diones 6: Isoquinoline **5** (6.0 mmol), acyl bromide **2** (2.0 mmol), maleimide **3** (2.0 mmol), and hydrated copper(II) chloride (0.6 mmol) were mixed in CH_3CN (15 mL) and heated to reflux for 24 h under an oxygen atmosphere. The reaction mixture was then allowed to cool to room temperature. After evaporation of the solvent under vacuum, the mixture was purified by column chromatography on silica gel to afford pure product **6**.

8-Benzoyl-10-phenylpyrrolo[3′,4′:3,4]pyrrolo[2,1-*a*]isoquinoline-9,11-dione (6a): Yellow solid, m.p. 293–295 °C. IR (KBr): 1760, 1713, 1611, 1532, 1498, 1403, 1339, 1154, 1094, 803, 755, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.42 (m, 4 H), 7.47 (t, J = 7.6 Hz, 2 H), 7.54 (t, J = 7.6 Hz, 2 H), 7.67 (t, J = 7.6 Hz, 1 H), 7.78–7.86 (m, 3 H), 7.97 (d, J = 7.2 Hz, 2 H), 9.19 (d, J = 7.6 Hz, 1 H), 9.40 (dd, J = 7.6, 0.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.8, 180.4, 178.2, 142.8, 141.4, 138.5, 138.4, 130.7, 129.8, 129.2, 128.9, 128.5, 127.8, 127.0, 126.8, 125.4, 125.0, 124.5, 116.7, 112.3 ppm. HRMS (ESI): calcd. for $C_{27}H_{16}N_2NaO_3$ [M + Na]$^+$ 439.1059; found 439.1051.

Ethyl 9,11-Dioxo-10-phenyl-10,11-dihydro-9*H*-pyrrolo[3′,4′:3,4]-pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (6b): White solid, m.p. 247–249 °C. IR (KBr): 1763, 1709, 1603, 1541, 1500, 1361, 1247, 1050, 809, 747, 674 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.52 (t, J = 7.2 Hz, 3 H), 4.51 (q, J = 7.2 Hz, 2 H), 7.29 (d, J = 7.6 Hz, 1 H), 7.41 (t, J = 7.2 Hz, 1 H), 7.46–7.52 (m, 4 H), 7.70–7.79 (m, 3 H), 9.29 (dd, J = 7.2, 1.6 Hz, 1 H), 9.37 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 161.8, 160.0, 132.6, 131.6, 131.0, 130.4, 129.3, 129.1, 129.0, 127.9, 127.8, 127.4, 127.2, 126.7, 124.9, 123.9, 116.4, 112.6, 112.5, 61.7, 14.3 ppm. HRMS (ESI): calcd. for $C_{23}H_{16}N_2NaO_4$ 407.1008; found 407.1011.

***tert*-Butyl 9,11-Dioxo-10-phenyl-10,11-dihydro-9*H*-pyrrolo[3′,4′:3,4-]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (6c):** White solid, m.p. 235–237 °C. IR (KBr): 1765, 1710, 1542, 1499, 1456, 1420, 1394, 1366, 1247, 1217, 1161, 1115, 1093, 1047, 963, 891, 841, 803, 733, 692, 652, 622 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 9 H), 7.34–7.47 (m, 6 H), 7.62–7.71 (m, 3 H), 9.23 (d, J = 7.6 Hz, 1 H), 9.30 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 161.8, 159.4, 132.7, 131.3, 130.2, 129.2, 129.0, 128.9, 127.9, 127.5, 127.4, 127.3, 126.6, 125.0, 124.0, 116.1, 114.0, 112.4, 83.6, 28.4 ppm. HRMS (ESI): calcd. for $C_{25}H_{20}N_2NaO_4$ 435.1321; found 435.1319.

8-Benzoyl-10-methylpyrrolo[3′,4′:3,4]pyrrolo[2,1-*a*]isoquinoline-9,11-dione (6d): Yellow solid, m.p. 258–260 °C. IR (KBr): 1749, 1704, 1630, 1531, 1449, 1341, 1283, 1014, 941, 805 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.01 (s, 3 H), 7.19 (s, 1 H), 7.46 (t, J = 7.6 Hz, 2 H), 7.60–7.70 (m, 4 H), 7.82 (dd, J = 8.0, 1.2 Hz, 2 H), 9.03 (d, J = 7.6 Hz, 1 H), 9.16 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.7, 164.0, 162.9, 138.7, 133.3, 131.8, 130.8, 130.5, 129.7, 129.0, 128.9, 128.4, 127.6, 126.6, 126.5, 125.3, 123.7, 119.2, 116.2, 113.1, 24.5 ppm. HRMS (ESI): calcd. for $C_{22}H_{14}N_2NaO_3$ 377.0902; found 377.0905.

***tert*-Butyl 10-Methyl-9,11-dioxo-10,11-dihydro-9*H*-pyrrolo[3′,4′:3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (6e):** White solid, m.p. 217–219 °C. IR (KBr): 1763, 1703, 1543, 1461, 1428, 1363, 1350, 1253, 1150, 1131, 979, 801 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.65 (s, 9 H), 3.12 (s, 3 H), 7.10 (d, J = 7.6 Hz, 1 H), 7.61–7.64 (m, 3 H), 9.11 (d, J = 8.0 Hz, 1 H), 9.19 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 163.1, 159.3, 130.7, 130.0, 129.0, 128.8, 127.9, 127.2, 126.5, 124.9, 123.8, 115.6, 113.5, 112.7, 83.3, 28.4, 24.4 ppm. HRMS (ESI): calcd. for $C_{20}H_{18}N_2NaO_4$ 373.1164; found 373.1169.

8-Benzoyl-10-ethylpyrrolo[3′,4′:3,4]pyrrolo[2,1-*a*]isoquinoline-9,11-dione (6f): Yellow solid, m.p. 229–230 °C. IR (KBr): 1748, 1707, 1629, 1532, 1452, 1341, 1237, 1014, 941, 805, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, J = 7.2 Hz, 3 H), 3.58 (q, J = 7.2 Hz, 2 H), 7.20 (d, J = 7.6 Hz, 1 H), 7.47 (t, J = 8.0 Hz, 2 H), 7.62–7.70 (m, 4 H), 7.84 (dd, J = 7.2, 1.2 Hz, 2 H), 9.06 (d, J = 7.6 Hz, 1 H), 9.20 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.8, 163.8, 162.7, 138.7, 133.3, 131.9, 130.5, 129.8, 129.0, 128.9, 128.4, 128.3, 127.6, 126.7, 125.4, 123.8, 119.2, 116.2, 113.3, 33.3, 14.1 ppm. HRMS (ESI): calcd. for $C_{23}H_{16}N_2NaO_3$ 391.1059; found 391.1053.

***tert*-Butyl 10-Ethyl-9,11-dioxo-10,11-dihydro-9*H*-pyrrolo[3′,4′:3,4]-pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (6g):** White solid, m.p. 183–

184 °C. IR (KBr): 1761, 1704, 1546, 1457, 1367, 1347, 1246, 1129, 1045, 1018, 808, 745 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.2 Hz, 3 H), 1.65 (s, 9 H), 3.68 (q, J = 7.2 Hz, 2 H), 7.11 (d, J = 7.6 Hz, 1 H), 7.61–7.65 (m, 3 H), 9.13 (d, J = 7.6 Hz, 1 H), 9.21 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 162.7, 159.3, 129.9, 129.0, 128.7, 127.2, 126.4, 124.9, 123.8, 115.5, 113.4, 112.8, 83.3, 33.2, 28.4, 14.2 ppm. HRMS (ESI): calcd. for $C_{21}H_{20}N_2NaO_4$ 387.1321; found 387.1317.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra.

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