Manganese(III) Acetate Mediated Oxidative Radical Cyclizations of *N*-(2-Alkenylaryl)-Substituted Enamines

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Received: 01.09.2013; Accepted after revision: 25.10.2013

Abstract: A method has been developed for the synthesis of highly functionalized quinolines from readily available *N*-(2-alkenylaryl)-substituted enamines via a 6-*exo*-*trig* radical cyclization of an imine radical. Several useful functional groups including morpholinocarbonyl, benzoyl, and cyano, are compatible with the reaction conditions. Under the Mn(II)/Co(II)/O_2 redox system, these *N*-(2-alkenylaryl)enamines were also converted into the corresponding quinolines effectively. This strategy was further applied to related 1,4-naphthoquinone derivatives, and benzo[*b*]acridine-6,11-diones were formed in good yields.

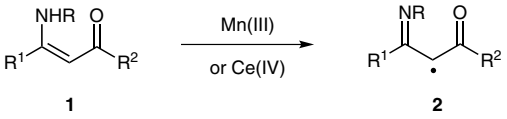
Key words: manganese(III) acetate, oxidative, free radical, enamines, quinolines

Addition reactions of carbon-centered radicals to alkenes are versatile tools for the formation of carbon–carbon bonds, and many new methods that use radical reactions in organic synthesis have been developed.[1,2] During the last three decades, metal salt mediated oxidative free radical reactions have been extensively explored, and they have become increasingly important in the synthesis of useful and complex molecules. Among these, manganese(III) acetate and cerium(IV) ammonium nitrate (CAN) have been used most efficiently.[2–5]

Quinolines and their derivatives are known to possess a wide range of biological activity and they have pharmacological properties that includes antimalarial,[6] antibacterial,[7] anti-inflammatory,[8] anticancer,[9] anti-asthmatic,[10] anti-alzheimer,[11] and anti-HIV.[12] As a result of the remarkable importance of this class of heterocyclic compound, a large number of methodologies have been developed for the syntheses of functionalized quinolines, such as Skraup, Doebner–von Miller, Friedländer, and Combes synthesis.[13] However, most of these methods require high temperatures or harsh reaction conditions, they give the products in low yields, and they have problems associated with the low stability of carbonyl reagents. Some of these drawbacks have been overcome by the use of more efficient methods such as modified Friedländer strategies[14] and transition-metal-catalyzed reactions.[15] The development of mild and simple approaches to quinoline derivatives represents a challenge in organic and medical chemistry.

SYNTHESIS 2014, 46, 0175–0182
Advanced online publication: 28.11.2013
DOI: 10.1055/s-0033-1338561; Art ID: SS-2013-F0596-OP

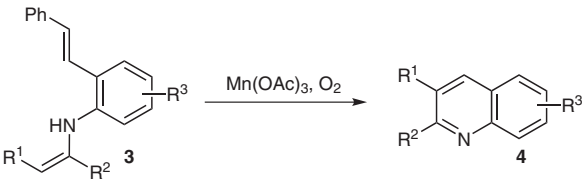
Imine radicals **2** can be generated effectively by the oxidation of enamines **1** with metal salts (Scheme 1) and they undergo efficient addition to C=C bonds.[16] We describe here a more effective method for the synthesis of highly functionalized quinolines via the manganese(III)-mediated oxidative radical cyclization reaction of enamines.



1 **2**

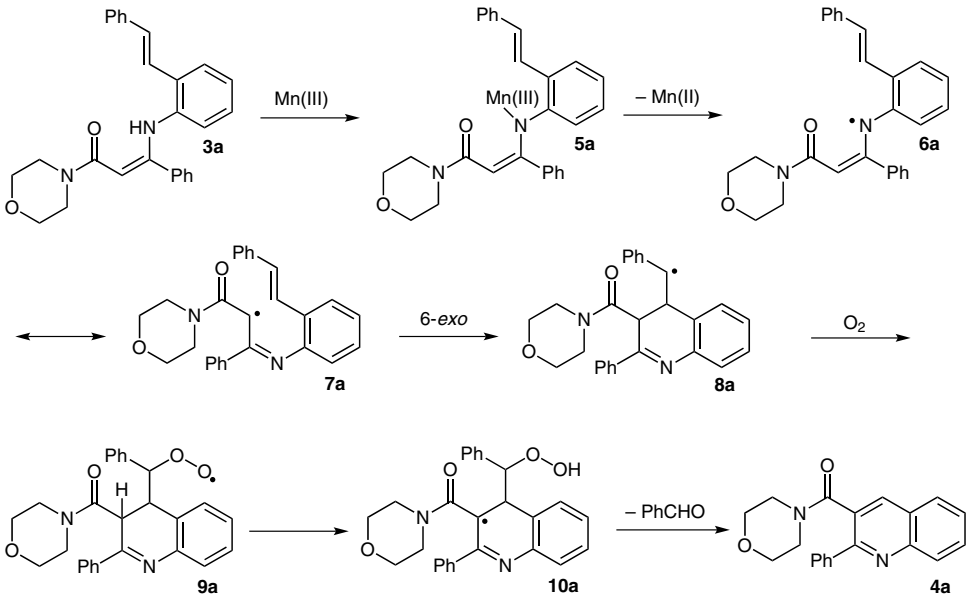
Scheme 1

Our studies commenced with the readily available *N*-(2-alkenylaryl)enamine carboxamide **3a**, which was prepared by the condensation of 1-morpholino-3-phenylpropane-1,3-dione with (*E*)-2-(2-phenylethenyl)phenylamine (see Supporting Information). With enamine **3a** in hand, we examined the radical reaction of **3a** with manganese(III) acetate under various reaction conditions (Scheme 2, Table 1). When the reaction of **3a** and manganese(III) acetate (4 equiv) was carried out in acetic acid at room temperature under air for one hour, the target cyclization product **4a** was obtained in 58% yield (entry 1). It is noteworthy that under an oxygen atmosphere instead of air the yield improved to 78% (entry 2). When a catalytic amount (0.3 equiv) of manganese(III) acetate was used, it resulted mainly in the decomposition of **3a** and a prolonged reaction time was required; the desired product **4a** was formed in 14% yield after stirring at room temperature for five hours (entry 3). Under a nitrogen atmosphere, the reaction was slow with an unsatisfactory yield (25%), confirming the necessity for molecular oxygen in this reaction (entry 4). In an attempt to investigate the range of solvents compatible with this reaction, the reaction between **3a** and manganese(III) acetate was next performed in various solvents. In acetonitrile, **4a** was obtained in good yield (80%), however, the reaction was sluggish and required one hour at 80 °C to go to completion (entry 5).



3 **4**

Scheme 2



Scheme 3

In 2,2,2-trifluoroethanol, formic acid, and chloroform, the desired product **4a** was produced in much lower yields (entries 6–8).

Table 1 Optimization of Reaction Conditions with *N*-(2-Alkenylaryl)enamine **3a**

Entry	Solvent	Atmosphere	Temp (°C)	Time (h)	Yield[a] (%) of **4a**
1	AcOH	air	r.t.	1	58
2	AcOH	O_2	r.t.	0.5	78
3	AcOH	O_2	r.t.	5	14[b]
4	AcOH	N_2	r.t.	1.5	25
5	MeCN	O_2	80	1	80
6	CF_3CH_2OH	O_2	80	1	56
7	HCO_2H	O_2	r.t.	0.5	26
8	$CHCl_3$	O_2	80	1	18

[a] Yield of isolated product.
[b] $Mn(OAc)_3$ (0.3 equiv) was used.

Since dioxygen plays an important role in this reaction, a plausible reaction mechanism for the formation of **4a** is proposed (Scheme 3). Initiation occurs with the chelation of manganese(III) acetate by the enamine nitrogen of **3a** to produce Mn(III) complex **5a**. Subsequently, homolytic cleavage of Mn(III) complex **5a** takes place to generate imine radical **7a** and manganese(II) acetate. This resulting radical intermediate **7a** undergoes a 6-*exo*-*trig* cyclization to give radical **8a**, which is then trapped by oxygen to give peroxy radical intermediate **9a**. Finally, hydroperoxide **10a**, formed by intramolecular hydrogen atom abstraction in **9a**, undergoes fragmentation to produce quinoline **4a** and benzaldehyde.[17a]

Using the optimal reaction conditions (Table 1, entry 2), we explored the scope and limitations of this newly developed manganese(III)/oxygen/acetic acid method (Table 2, entries 1–14, method A). By varying substituents R^1 of enamines **3**, it was shown that several useful functional groups, including morpholinocarbonyl, cyano, and benzoyl, were tolerated under the reaction conditions and the expected quinolines **4** were formed effectively. To our delight, when R^2 was an alkyl substituent, the desired oxidative cyclization products **4l–n** were also obtained in acceptable yields (entries 12–14). Substrates bearing different functional groups (R^3) on the aniline moiety in the substrate, including 4-methyl, 2,4-dimethyl, 4,5-dimethyl, and 4-chloro, all worked well in moderate to good yields.

A carbon radical is produced by the Mn(II)/Co(II)/oxygen redox system and it undergoes efficient addition to a C=C bond.[18] In this reaction, Mn(II) can be continuously reoxidized to Mn(III) by the action of a Co(III)–dioxygen complex generated in situ from Co(II) and oxygen and a catalytic amount of Mn(II) is used. Environmental concerns have encourage the development of greener reaction conditions. We have continued to study the radical cyclization of reaction of *N*-(2-alkenylaryl)-substituted enamines **3** under the Mn(II)/Co(II)/O_2 redox system.

When *N*-(2-alkenylaryl)enamine carboxamide **3a** was treated with manganese(II) acetate (0.3 equiv) and cobalt(II) acetate (1 equiv) in acetic acid at 80 °C under an oxygen atmosphere (method B), the target cyclization product **4a** was obtained in 74% yield (Table 2, entry 15).

By increasing the amount cobalt (II) acetate (1.5 equiv), the yield can be improved to 84% (entry 16). Analogous results were obtained with other enamines **3** (entries 17–26). In all cases, quinolines **4** were produced in a better reaction yield than those performed with manganese(III) acetate (method A).

Stimulated by the structural analogy of 2-(arylamino)-1,4-naphthoquinones with enamino carbonyl compounds, the manganese(III)-mediated radical cyclizations of 2-[(2-alkenylaryl)amino]-1,4-naphthoquinones **11** could be envisioned to occur (Scheme 4). These 2-[(2-alkenylaryl)amino]-1,4-naphthoquinones **11** were readily available from the copper(II) acetate catalyzed addition of (*E*)-2-(2-phenylethenyl)phenylamine to 1,4-naphthoquinone (see Supporting Information). Indeed, when the reaction of 2-[(2-alkenylaryl)amino]-1,4-naphthoquinone **11a** and manganese(III) acetate (Method A) was carried out in acetic acid at room temperature under an oxygen atmosphere for nine hours, the target cyclization product **12a** was obtained in 26% (Table 3, entry 2). The yield can be improved to 86% by using formic acid as solvent instead of acetic acid and reaction time was shorten to 30 minutes (entry 5). Performing the reaction in acetonitrile with

Table 2 Reactions of *N*-(Alk-2-enylaryl)enamines **3**

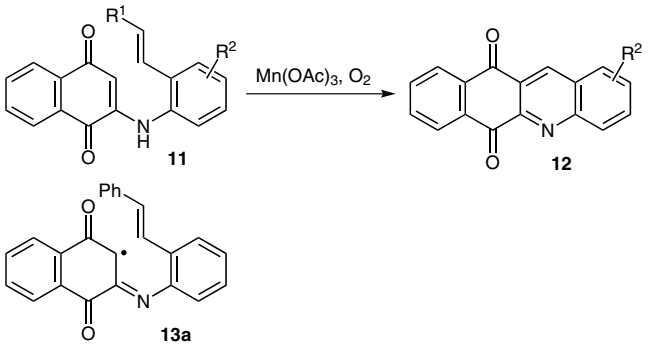
Entry	**3**	R^1	R^2	R^3	Method[a]	Product	Yield[b] (%)
1	**3a**	$CO[N(CH_2CH_2)_2O]$	Ph	H	A	**4a**	78
2	**3b**	$CO[N(CH_2CH_2)_2O]$	Ph	4-Me	A	**4b**	80
3	**3c**	$CO[N(CH_2CH_2)_2O]$	Ph	2,4-Me_2	A	**4c**	78
4	**3d**	$CO[N(CH_2CH_2)_2O]$	Ph	4,5-Me_2	A	**4d**	77
5	**3e**	$CO[N(CH_2CH_2)_2O]$	Ph	4-Cl	A	**4e**	81
6	**3f**	COPh	Ph	H	A	**4f**	80
7	**3g**	COPh	Ph	4-Me	A	**4g**	75
8	**3h**	COPh	Ph	4-Cl	A	**4h**	78
9	**3i**	CN	Ph	H	A	**4i**	78
10	**3j**	CN	Ph	4-Me	A	**4j**	83
11	**3k**	CN	Ph	4-Cl	A	**4k**	82
12	**3l**	COPh	Me	H	A	**4l**	64
13	**3m**	COPh	Me	4-Me	A	**4m**	75
14	**3n**	COPh	Me	4-Cl	A	**4n**	57
15	**3a**	$CO[N(CH_2CH_2)_2O]$	Ph	H	B[c]	**4a**	74
16	**3a**	$CO[N(CH_2CH_2)_2O]$	Ph	H	B	**4a**	84
17	**3b**	$CO[N(CH_2CH_2)_2O]$	Ph	4-Me	B	**4b**	90
18	**3c**	$CO[N(CH_2CH_2)_2O]$	Ph	2,4-Me_2	B	**4c**	89
19	**3d**	$CO[N(CH_2CH_2)_2O]$	Ph	4,5-Me_2	B	**4d**	86
20	**3e**	$CO[N(CH_2CH_2)_2O]$	Ph	4-Cl	B	**4e**	86
21	**3f**	COPh	Ph	H	B	**4f**	87
22	**3g**	COPh	Ph	4-Me	B	**4g**	86
23	**3h**	COPh	Ph	4-Cl	B	**4h**	85
24	**3i**	CN	Ph	H	B	**4i**	87
25	**3j**	CN	Ph	4-Me	B	**4j**	85
26	**3k**	CN	Ph	4-Cl	B	**3k**	92

[a] Method A: $Mn(OAc)_3$ (4 equiv), AcOH, r.t., O_2 atmosphere; Method B: $Mn(OAc)_2$ (0.3 equiv), $Co(OAc)_2$ (1.5 equiv), AcOH (5 mL), 80 °C, O_2 atmosphere.
[b] Yield of isolated product.
[c] $Co(OAc)_2$ (1 equiv) was used.

Table 3 Optimization of Reaction Conditions with 2-(2-Alkenylarylamino)-1,4-naphthoquinone **11a**

Entry	Solvent	Atmosphere	Temp (°C)	Time (h)	Yield[a] (%) of **12a**
1	AcOH	air	45	3	24
2	AcOH	O_2	r.t.	9	26
3	AcOH	O_2	45	1	29
4	HCO_2H	O_2	45	0.5	82
5	HCO_2H	O_2	r.t.	0.5	86
6	MeCN	air	80	2	0[b]

[a] Yield of isolated product.
[b] Starting **9a** (88%) was recovered.



Scheme 4

heating at 80 °C for two hours resulted in the recovery of starting **11a** (88%) only, and the desired **12a** was not formed (entry 6). Benzo[*b*]acridine-6,11-dione (**12a**) was formed by the radical cyclization of an imine radical[19] **13a** via a similar reaction route to that shown in Scheme 3. As listed in Table 4, a variety of 2-[(2-alkenylaryl)amino]-1,4-naphthoquinones **11** were evaluated to explore the scope of this oxidative radical cyclization reaction under the Mn(III)/oxygen/formic acid conditions. The results demonstrated that the electronic properties of arylic substituents (R^1) at the terminal of C=C bond affected the reaction to some extent; electron-donating groups, such as methyl or methoxy group, gave **12a** in 91–93% yield (entries 5 and 6), but electron-withdrawing groups, such as chloro or cyano group, gave **12a** in lower yields (entries 7 and 8). However, regardless of R^2 on the aniline moiety, electron-donating or electron-withdrawing, the oxidative cyclization products **11b–d** were obtained in good yields (entries 2–4). The radical cyclization of reaction of **11** was also conducted using the Mn(II)/Co(II)/O_2 redox system. As shown in Table 4 (entries 9–12), benzo[*b*]acridine-6,11-diones **12** were also formed effectively by this Mn(II)/Co(II)/O_2 method.

In conclusion, the syntheses of highly functionalized quinolines and benzo[*b*]acridine-6,11-diones are described. Imine radicals **7** can be produced by the manganese(III) acetate oxidation of *N*-(2-alkenylaryl)enamines and undergo a 6-*exo*-*trig* cyclization onto the C=C bond efficiently. This reaction provides a synthetically useful method for the synthesis of 2,3-disubstituted quinolines. A variety of functional groups, including cyano, morpholinocarbonyl, and benzoyl, are compatible with the reaction conditions. The traditional harshly basic or acidic conditions can be avoided. Under Mn(II)/Co(II)/O_2 redox system, these *N*-(2-alkenylaryl)enamines were also converted into the corresponding quinolines effectively. This strategy was further applied for related 1,4-naphthoqui-

Table 4 Reactions of 2-(2-Alkenylarylamino)-1,4-naphthoquinones **11**

Entry	Substrate	R^1	R^2	Method	Product	Yield[b] (%)
1	**11a**	Ph	H	A	**12a**	86
2	**11b**	Ph	4-Me	A	**12b**	90
3	**11c**	Ph	2,4-Me_2	A	**12c**	91
4	**11d**	Ph	4-Cl	A	**12d**	90
5	**11e**	4-MeC_6H_4	H	A	**12a**	91
6	**11f**	4-$MeOC_6H_4$	H	A	**12a**	93[17b]
7	**11g**	4-ClC_6H_4	H	A	**12a**	82
8	**11h**	4-NCC_6H_4	H	B	**12a**	80[17c]
9	**11a**	Ph	H	B	**12a**	75
10	**11b**	Ph	4-Me	B	**12b**	78
11	**11c**	Ph	2,4-Me_2	B	**12c**	75
12	**11d**	Ph	4-Cl	B	**12d**	75

[a] Method A: $Mn(OAc)_3$ (4 equiv), HCO_2H, r.t., O_2 atmosphere; Method B: $Mn(OAc)_2$ (0.3 equiv), $Co(OAc)_2$ (1.5 equiv), AcOH (5 mL), 80 °C, O_2 atmosphere.
[b] Yield of isolated product.

none derivatives, and benzo[*b*]acridine-6,11-diones were formed in good yields.

Melting points are uncorrected. IR spectra were taken with a Hitachi 260-30 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer with TMS as internal reference. The multiplicity of the ^{13}C NMR signals was determined by DEPT 135 experiments. Elemental analyses were performed with a Heraeus CHN-Rapid Analyzer. Mass spectra were recorded on a Jeol JMS-SX 102A mass spectrometer. Analytical TLC was performed with precoated silica gel 60 F-254 plates (0.25-mm thick) from EM Laboratories and visualized by UV. The reaction mixture was purified by column chromatography over EM Laboratories silica gel (70–230 mesh).

3-(Morpholinocarbonyl)-2-phenylquinoline (4a); Typical Procedure

Method A: A mixture of **3a** (103 mg, 0.25 mmol) and $Mn(OAc)_3{\cdot}2H_2O$ (274 mg, 1.02 mmol) in AcOH (5 mL) was stirred at r.t. for 30 min under an O_2 atmosphere (1 atm). The mixture was then diluted with EtOAc (100 mL), washed with sat. aq sodium bisulfite (3 × 50 mL), sat. aq $NaHCO_3$ (3 × 50 mL), and water (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20 g, EtOAc–hexane, 1:3) followed by crystallization ($CHCl_3$–hexane) to give **4a** (62 mg, 78%).

Method B: A mixture of **3a** (103 mg, 0.25 mmol), $Mn(OAc)_2{\cdot}4H_2O$ (18 mg, 0.07 mmol), and $Co(OAc)_2{\cdot}4H_2O$ (93 mg, 0.37 mmol) in AcOH (5 mL) was heated at 80 °C for 5 min under an O_2 atmosphere (1 atm). The mixture was then diluted with EtOAc (100 mL), washed with sat. aq sodium bisulfite (3 × 50 mL), sat. aq $NaHCO_3$ (3 × 50 mL), and water (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20 g, EtOAc–hexane, 1:3) followed by crystallization ($CHCl_3$–hexane) to give **4a** (67 mg, 84%).

Colorless crystals; mp 149–150 °C.

IR (KBr): 2860, 1635, 1440, 1110, 775 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 2.71 (ddd, *J* = 13.3, 5.1, 3.2 Hz, 1 H, CH), 2.96 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.26 (ddd, *J* = 11.4, 5.1, 3.2 Hz, 1 H, CH), 3.33 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 3.53 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.64 (ddd, *J* = 11.4, 5.1, 3.2 Hz, 1 H, CH), 3.78 (ddd, *J* = 13.3, 5.1, 3.2 Hz, 1 H, CH), 7.46–7.55 (m, 3 H, H_{Ar}), 7.60 (t, *J* = 7.7 Hz, 1 H, H_{Ar}), 7.79 (t, *J* = 7.7 Hz, 1 H, H_{Ar}), 7.84–7.91 (m, 3 H, H_{Ar}), 8.19 (d, *J* = 8.5 Hz, 1 H, H_{Ar}), 8.28 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 42.0 (t), 46.8 (t), 65.6 (t), 65.9 (t), 126.3 (s), 127.2 (d), 127.6 (d), 128.6 (2 d), 128.8 (s), 129.0 (2 d), 129.5 (2 d), 130.7 (d), 136.5 (d), 139.2 (s), 148.1 (s), 155.0 (s), 168.5 (s).

Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.38; H, 5.74; N, 8.75.

6-Methyl-3-(morpholinocarbonyl)-2-phenylquinoline (4b)

Colorless needles; yield: 64 mg (80%) (method A), 73 mg (90%) (method B); mp 138–139 °C.

IR (KBr): 2860, 1620, 1435, 1110, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 2.57 (s, 3 H, CH_3), 2.71 (ddd, *J* = 13.3, 5.0, 3.2 Hz, 1 H, CH), 2.95 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.25 (ddd, *J* = 11.4, 5.0, 3.2 Hz, 1 H, CH), 3.32 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 3.52 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.64 (ddd, *J* = 11.4, 5.0, 3.2 Hz, 1 H, CH), 3.79 (ddd, *J* = 13.3, 5.0, 3.2 Hz, 1 H, CH), 7.45–7.54 (m, 3 H, H_{Ar}), 7.60–7.65 (m, 1 H, H_{Ar}), 7.63 (s, 1 H, H_{Ar}), 7.81–7.89 (m, 2 H, H_{Ar}), 8.07 (d, *J* = 9.3 Hz, 1 H, H_{Ar}), 8.18 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.6 (q), 42.0 (t), 46.8 (t), 65.7 (t), 65.9 (t), 126.32 (s), 126.36 (d), 128.6 (2 d), 128.8 (s), 129.0 (2 d), 129.2 (d), 129.3 (d), 133.1 (d), 135.8 (d), 137.3 (s), 139.3 (s), 146.7 (s), 154.1 (s), 168.7 (s).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.94; H, 6.13; N, 8.43.

6,8-Dimethyl-3-(morpholinocarbonyl)-2-phenylquinoline (4c)

Colorless needles; yield: 93 mg (78%) (method A), 72 mg (89%) (method B); mp 190–191 °C.

IR (KBr): 2855, 1615, 1110, 775, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (ddd, *J* = 11.3, 8.0, 3.2 Hz, 1 H, CH), 2.51 (s, 3 H, CH_3), 2.68 (ddd, *J* = 13.2, 5.0, 3.2 Hz, 1 H, CH), 2.82 (s, 3 H, CH_3), 2.92 (ddd, *J* = 13.2, 8.0, 3.2 Hz, 1 H, CH), 3.22 (ddd, *J* = 11.3, 5.0, 3.2 Hz, 1 H, CH), 3.36 (ddd, *J* = 11.3, 8.0, 3.2 Hz, 1 H, CH), 3.54 (ddd, *J* = 13.2, 8.0, 3.2 Hz, 1 H, CH), 3.64 (ddd, *J* = 11.3, 5.0, 3.2 Hz, 1 H, CH), 3.80 (ddd, *J* = 13.2, 5.0, 3.2 Hz, 1 H, CH), 7.44–7.53 (m, 5 H, H_{Ar}), 7.88–7.96 (m, 2 H, H_{Ar}), 8.14 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.7 (q), 21.6 (q), 42.0 (t), 46.9 (t), 65.7 (t), 66.0 (t), 124.3 (d), 126.4 (s), 128.3 (s), 128.6 (2 d), 129.3 (3 d), 133.1 (d), 136.1 (d), 137.0 (s), 137.2 (s), 139.7 (s), 145.8 (s), 152.6 (s), 169.2 (s).

Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.33; H, 6.40; N, 7.98.

6,7-Dimethyl-3-(morpholinocarbonyl)-2-phenylquinoline (4d)

Colorless crystals; yield: 67 mg (77%) (method A), 70 mg (86%) (method B); mp 141–142 °C.

IR (KBr): 2860, 1625, 1440, 1110, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43–2.54 (m, 1 H, CH), 2.47 (s, 3 H, CH_3), 2.50 (s, 3 H, CH_3), 2.70 (ddd, *J* = 13.3, 5.1, 3.2 Hz, 1 H, CH), 2.94 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.24 (ddd, *J* = 11.5, 5.1, 3.2 Hz, 1 H, CH), 3.32 (ddd, *J* = 11.5, 8.0, 3.2 Hz, 1 H, CH), 3.51 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.62 (ddd, *J* = 11.5, 5.1, 3.2 Hz, 1 H, CH), 3.78 (ddd, *J* = 13.3, 5.1, 3.2 Hz, 1 H, CH), 7.44–7.53 (m, 3 H, H_{Ar}), 7.60 (s, 1 H, H_{Ar}), 7.82–7.87 (m, 2 H, H_{Ar}), 7.95 (s, 1 H, H_{Ar}), 8.15 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.1 (q), 20.6 (q), 42.0 (t), 46.9 (t), 65.8 (t), 66.0 (t), 125.0 (s), 126.8 (d), 128.0 (s), 128.6 (2 d), 128.9 (d), 129.1 (2 d), 129.3 (d), 135.5 (d), 137.5 (s), 139.5 (s), 141.4 (s), 147.4 (s), 154.1 (s), 169.0 (s).

Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.34; H, 6.41; N, 8.05.

6-Chloro-3-(morpholinocarbonyl)-2-phenylquinoline (4e)

Colorless crystals; yield: 97 mg (81%) (method A), 70 mg (86%) (method B); mp 166–167 °C.

IR (KBr): 2860, 1620, 1460, 1115, 940 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 2.69 (ddd, *J* = 13.3, 5.0, 3.2 Hz, 1 H, CH), 2.95 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.26 (ddd, *J* = 11.4, 5.0, 3.2 Hz, 1 H, CH), 3.33 (ddd, *J* = 11.4, 8.0, 3.2 Hz, 1 H, CH), 3.53 (ddd, *J* = 13.3, 8.0, 3.2 Hz, 1 H, CH), 3.65 (ddd, *J* = 11.4, 5.0, 3.2 Hz, 1 H, CH), 3.78 (ddd, *J* = 13.3, 5.0, 3.2 Hz, 1 H, CH), 7.47–7.56 (m, 3 H, H_{Ar}), 7.72 (dd, *J* = 9.0, 2.4 Hz, 1 H, H_{Ar}), 7.82–7.89 (m, 3 H, H_{Ar}), 8.12 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 8.19 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 42.0 (t), 46.8 (t), 65.6 (t), 65.9 (t), 126.2 (d), 126.9 (s), 128.7 (2 d), 129.0 (2 d), 129.70 (d), 129.75 (s), 131.1 (d), 131.7 (d), 133.0 (s), 135.5 (d), 138.8 (s), 146.4 (s), 155.2 (s), 168.1 (s).

Anal. Calcd for $C_{20}H_{17}ClN_2O_2$: C, 68.09; H, 4.86; N, 7.94. Found: C, 67.96; H, 4.93; N, 7.87.

(Phenyl)(2-phenylquinolin-3-yl)methanone (4f)
White needles; yield: 93 mg (80%) (method A), 66 mg (87%) (method B); mp 133–134 °C.

IR (KBr): 1655, 1595, 1270, 775, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.31 (m, 3 H, H_{Ar}), 7.33 (t, *J* = 7.6 Hz, 2 H, H_{Ar}), 7.48 (t, *J* = 7.8 Hz, 1 H, H_{Ar}), 7.60–7.66 (m, 3 H, H_{Ar}), 7.72 (d, *J* = 7.6 Hz, 2 H, H_{Ar}), 7.84 (t, *J* = 7.8 Hz, 1 H, H_{Ar}), 7.92 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 8.25 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 8.35 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 125.8 (s), 127.3 (d), 128.1 (d), 128.4 (4 d), 128.8 (d), 129.3 (2 d), 129.7 (d), 130.0 (2 d), 131.2 (d), 132.8 (s), 133.3 (d), 137.0 (s), 137.6 (d), 139.7 (s), 148.3 (s), 157.5 (s), 196.9 (s).

Anal. Calcd for $C_{22}H_{15}NO$: C, 85.41; H, 4.89; N, 4.53. Found: C, 85.21; H, 5.01; N, 4.60.

(6-Methyl-2-phenylquinolin-3-yl)(phenyl)methanone (4g)
White needles; yield: 88 mg (75%) (method A), 68 mg (86%) (method B); mp 148–149 °C.

IR (KBr): 1660, 1445, 1270, 890, 735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, CH_3), 7.22–7.30 (m, 3 H, H_{Ar}), 7.32 (t, *J* = 7.6 Hz, 2 H, H_{Ar}), 7.47 (t, *J* = 7.6 Hz, 1 H, H_{Ar}), 7.58–7.63 (m, 2 H, H_{Ar}), 7.65–7.69 (m, 2 H, H_{Ar}), 7.71 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 8.14 (d, *J* = 9.2 Hz, 1 H, H_{Ar}), 8.25 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.6 (q), 125.8 (s), 126.8 (d), 128.3 (4 d), 128.6 (d), 129.2 (2 d), 129.3 (d), 129.9 (2 d), 132.7 (s), 133.2 (d), 133.5 (d), 136.9 (d), 137.1 (s), 137.3 (s), 139.8 (s), 147.0 (s), 156.5 (s), 197.1 (s).

Anal. Calcd for $C_{23}H_{17}NO$: C, 85.42; H, 5.30; N, 4.33. Found: C, 85.27; H, 5.33; N, 4.29.

(6-Chloro-2-phenylquinolin-3-yl)(phenyl)methanone (4h)
White needles; yield: 64 mg (78%) (method A), 68 mg (85%) (method B); mp 161–162 °C.

IR (KBr): 1665, 1475, 1270, 885, 720 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.31 (m, 3 H, H_{Ar}), 7.34 (t, *J* = 7.5 Hz, 2 H, H_{Ar}), 7.49 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.58–7.64 (m, 2 H, H_{Ar}), 7.70 (d, *J* = 7.5 Hz, 2 H, H_{Ar}), 7.76 (dd, *J* = 9.0, 2.3 Hz, 1 H, H_{Ar}), 7.89 (d, *J* = 2.3 Hz, 1 H, H_{Ar}), 8.18 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 8.24 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 126.4 (s), 126.6 (d), 128.4 (4 d), 129.0 (d), 129.2 (2 d), 129.9 (2 d), 131.2 (d), 132.1 (d), 133.0 (s), 133.5 (d), 133.6 (s), 136.5 (d), 136.7 (s), 139.3 (s), 146.7 (s), 157.6 (s), 196.5 (s).

Anal. Calcd for $C_{22}H_{14}ClNO$: C, 76.86; H, 4.10; N, 4.07. Found: C, 76.77; H, 4.15; N, 4.03.

3-Cyano-2-phenylquinoline (4i)
White needles; yield: 57 mg (78%) (method A), 63 mg (87%) (method B); mp 195–196 °C.

IR (KBr): 2220, 1555, 1375, 755, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.61 (m, 3 H, H_{Ar}), 7.67 (t, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.90 (t, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.91 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.97–8.04 (m, 2 H, H_{Ar}), 8.21 (d, *J* = 7.9 Hz, 1 H, H_{Ar}), 8.67 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 105.6 (s), 117.9 (s), 125.0 (s), 127.7 (d), 128.1 (d), 128.7 (2 d), 129.1 (2 d), 129.9 (d), 130.1 (d), 133.0 (d), 137.6 (s), 144.2 (d), 148.7 (s), 158.0 (s).

Anal. Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.38; H, 4.38; N, 12.16.

3-Cyano-6-methyl-2-phenylquinoline (4j)
Colorless needles; yield: 61 mg (83%) (method A), 63 mg (85%) (method B); mp 172–173 °C.

IR (KBr): 2220, 1590, 1380, 830, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.59 (s, 3 H, CH_3), 7.50–7.62 (m, 3 H, H_{Ar}), 7.66 (s, 1 H, H_{Ar}), 7.72 (dd, *J* = 8.6, 1.9 Hz, 1 H, H_{Ar}), 7.96–8.03 (m, 2 H, H_{Ar}), 8.10 (d, *J* = 8.6 Hz, 1 H, H_{Ar}), 8.57 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.6 (q), 105.4 (s), 118.1 (s), 125.0 (s), 126.4 (d), 128.6 (2 d), 129.0 (2 d), 129.5 (d), 129.9 (d), 135.3 (d), 137.7 (s), 138.3 (s), 143.4 (d), 147.3 (s), 157.1 (s).

Anal. Calcd for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47. Found: C, 83.58; H, 4.97; N, 11.47.

6-Chloro-3-cyano-2-phenylquinoline (4k)
White needles; yield: 60 mg (82%) (method A), 70 mg (92%) (method B); mp 197–198 °C.

IR (KBr): 2220, 1550, 1475, 925, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.61 (m, 3 H, H_{Ar}), 7.82 (dd, *J* = 9.0, 2.2 Hz, 1 H, H_{Ar}), 7.90 (d, *J* = 2.2 Hz, 1 H, H_{Ar}), 7.96–8.03 (m, 2 H, H_{Ar}), 8.15 (d, *J* = 9.0 Hz, 1 H, H_{Ar}), 8.58 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 106.6 (s), 117.5 (s), 125.5 (s), 126.2 (d), 128.8 (2 d), 129.1 (2 d), 130.3 (d), 131.5 (d), 133.9 (d), 134.1 (s), 137.3 (s), 143.1 (d), 147.1 (s), 158.2 (s).

Anal. Calcd for $C_{16}H_9ClN_2$: C, 72.60; H, 3.43; N, 10.58. Found: C, 72.36; H, 3.46; N, 10.53.

(2-Methylquinolin-3-yl)(phenyl)methanone (4l)
Pale yellow oil; yield: 47 mg (64%) (method A).

IR (KBr): 1660, 1595, 1240, 880, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.75 (s, 3 H, CH_3), 7.51 (t, *J* = 7.6 Hz, 2 H, H_{Ar}), 7.56 (t, *J* = 7.8 Hz, 1 H, H_{Ar}), 7.65 (t, *J* = 7.6 Hz, 1 H, H_{Ar}), 7.76–7.83 (m, 1 H, H_{Ar}), 7.80 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 7.85 (d, *J* = 7.6 Hz, 2 H, H_{Ar}), 8.09 (d, *J* = 7.8 Hz, 1 H, H_{Ar}), 8.13 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.2 (q), 125.3 (s), 126.6 (d), 128.1 (d), 128.7 (3 d), 130.1 (2 d), 131.0 (d), 132.2 (s), 133.7 (d), 136.7 (d), 137.3 (s), 148.0 (s), 156.6 (s), 196.7 (s).

HMRS (EI): *m/z* $[M]^+$ calcd for $C_{17}H_{13}NO$: 247.0997; found: 247.0992.

(2,6-Dimethylquinolin-3-yl)(phenyl)methanone (4m)
Colorless needles; yield: 84 mg (75%) (method A); mp 68–69 °C.

IR (KBr): 1660, 1595, 1245, 830, 730 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.54 (s, 3 H, CH_3), 2.72 (s, 3 H, CH_3), 7.50 (t, *J* = 7.7 Hz, 2 H, H_{Ar}), 7.56 (s, 1 H, H_{Ar}), 7.62 (dd, *J* = 8.7, 1.9 Hz, 1 H, H_{Ar}), 7.64 (t, *J* = 7.7 Hz, 1 H, H_{Ar}), 7.84 (d, *J* = 7.7 Hz, 2 H, H_{Ar}), 7.98 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 8.04 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.5 (q), 24.1 (q), 125.3 (s), 126.9 (d), 128.3 (d), 128.7 (2 d), 130.1 (2 d), 132.1 (s), 133.3 (d), 133.6 (d), 136.2 (d), 136.6 (s), 137.4 (s), 146.7 (s), 155.6 (s), 196.9 (s).

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.59; H, 5.79; N, 5.32.

(6-Chloro-2-methylquinolin-3-yl)(phenyl)methanone (4n)
Colorless needles; yield: 64 mg (57%) (method A); mp 121–122 °C.

IR (KBr): 1660, 1595, 1275, 835, 725 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.72 (s, 3 H, CH_3), 7.51 (t, *J* = 7.7 Hz, 2 H, H_{Ar}), 7.65 (t, *J* = 7.7 Hz, 1 H, H_{Ar}), 7.71 (dd, *J* = 8.9, 2.3 Hz, 1 H, H_{Ar}), 7.78 (d, *J* = 2.3 Hz, 1 H, H_{Ar}), 7.83 (d, *J* = 7.7 Hz, 2 H, H_{Ar}), 8.02 (d, *J* = 8.9 Hz, 1 H, H_{Ar}), 8.02 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 24.2 (q), 125.9 (s), 126.6 (d), 128.8 (2 d), 130.1 (2 d), 130.3 (d), 131.8 (d), 132.3 (s), 133.1 (s), 133.9 (d), 135.4 (d), 136.9 (s), 146.4 (s), 156.9 (s), 196.3 (s).

Anal. Calcd for $C_{17}H_{12}ClNO$: C, 72.47; H, 4.29; N, 4.97. Found: C, 72.34; H, 4.35; N, 4.95.

Benzo[*b*]acridine-6,11-dione (12a); Typical Procedure

Method A: A mixture of **11a** (107 mg, 0.30 mmol) and $Mn(OAc)_3{\cdot}2H_2O$ (381 mg, 1.42 mmol) in HCO_2H (7 mL) was heated at r.t. for 30 min under an O_2 atmosphere (1 atm). The mixture was then diluted with EtOAc (100 mL), washed with sat. aq sodium bisulfite (3 × 50 mL), sat. aq $NaHCO_3$ (3 × 50 mL), and water (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20 g, CH_2Cl_2–hexane, 1:1) followed by crystallization ($CHCl_3$–hexane) to give **12a** (64 mg, 86%).

Method B: A mixture of **11a** (150 mg, 0.43 mmol), $Mn(OAc)_2{\cdot}4H_2O$ (34 mg, 0.13 mmol), and $Co(OAc)_2{\cdot}4H_2O$ (160 mg, 0.64 mmol) in AcOH (8 mL) was stirred at 80 °C for 5.5 h under an O_2 atmosphere (1 atm). The mixture was then diluted with EtOAc (100 mL), washed with sat. aq sodium bisulfite (3 × 50 mL), sat. aq $NaHCO_3$ (3 × 50 mL), and water (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 20 g, CH_2Cl_2–hexane, 1:1) followed by crystallization ($CHCl_3$–hexane) to give **12a** (83 mg, 75%).

Pale yellow needles; mp 310–311 °C.

IR (KBr): 1690, 1670, 1580, 1275, 975 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (t, *J* = 8.0 Hz, 1 H, H_{Ar}), 7.86–7.92 (m, 2 H, H_{Ar}), 7.97 (td, *J* = 8.0, 1.3 Hz, 1 H, H_{Ar}), 8.12 (d, *J* = 8.0 Hz, 1 H, H_{Ar}), 8.39–8.44 (m, 1 H, H_{Ar}), 8.48–8.54 (m, 1 H, H_{Ar}), 8.51 (d, *J* = 8.0 Hz, 1 H, H_{Ar}), 9.23 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 127.4 (s), 127.5 (d), 128.3 (d), 129.0 (s), 129.6 (d), 129.8 (d), 131.6 (d), 133.2 (d), 133.6 (s), 134.5 (s), 134.69 (d), 134.74 (d), 138.0 (d), 147.8 (s), 150.2 (s), 181.7 (s), 182.4 (s).

Anal. Calcd for $C_{17}H_9NO_2$: C, 78.76; H, 3.50; N, 5.40. Found: C, 78.66; H, 3.42; N, 5.40.

3-Methylbenzo[*b*]acridine-6,11-dione (12b)

Pale yellow needles; yield: 91 mg (90%) (method A), 86 mg (78%) (method B); mp 284–285 °C.

IR (KBr): 1695, 1665, 1575, 1275, 975 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.62 (s, 3 H, CH_3), 7.77 (dd, *J* = 8.7, 1.6 Hz, 1 H, H_{Ar}), 7.83–7.90 (m, 2 H, H_{Ar}), 7.84 (s, 1 H, H_{Ar}), 8.37 (d, *J* = 8.7 Hz, 1 H, H_{Ar}), 8.37–8.41 (m, 1 H, H_{Ar}), 8.46–8.51 (m, 1 H, H_{Ar}), 9.09 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.8 (q), 127.4 (d s), 128.2 (2 d), 129.1 (s), 131.2 (d), 133.6 (s), 134.4 (s), 134.5 (d), 134.6 (d), 135.7 (d), 136.9 (d), 140.4 (s), 147.1 (s), 148.8 (s), 181.7 (s), 182.5 (s).

Anal. Calcd for $C_{18}H_{11}NO_2$: C, 79.11; H, 4.06; N, 5.13. Found: C, 78.90; H, 4.12; N, 5.07.

1,3-Dimethylbenzo[*b*]acridine-6,11-dione (12c)

Pale yellow needles; yield: 104 mg (91%) (method A), 82 mg (76%) (method B); mp 285–286 °C.

IR (KBr): 1685, 1665, 1575, 1275, 975 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, CH_3), 2.95 (s, 3 H, CH_3), 7.62 (s, 1 H, H_{Ar}), 7.67 (s, 1 H, H_{Ar}), 7.82–7.89 (m, 2 H, H_{Ar}), 8.36–8.42 (m, 1 H, H_{Ar}), 8.45–8.49 (m, 1 H, H_{Ar}), 9.03 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.0 (q), 21.9 (q), 126.2 (d), 127.3 (s), 127.4 (d), 128.1 (d), 129.3 (s), 133.7 (s), 134.4 (d), 134.6 (d), 134.7 (s), 135.8 (d), 137.0 (d), 139.6 (s), 140.2 (s), 146.1 (s), 148.1 (s), 181.8 (s), 182.9 (s).

Anal. Calcd for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56; N, 4.88. Found: C, 79.19; H, 4.53; N, 4.63.

3-Chlorobenzo[*b*]acridine-6,11-dione (12d)

Pale yellow needles; yield: 102 mg (90%) (method A), 85 mg (75%) (method B); mp 332–333 °C.

IR (KBr): 1690, 1665, 1580, 1280, 980 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.93 (m, 3 H, H_{Ar}), 8.10 (d, *J* = 2.2 Hz, 1 H, H_{Ar}), 8.39–8.43 (m, 1 H, H_{Ar}), 8.45 (d, *J* = 9.1 Hz, 1 H, H_{Ar}), 8.48–8.53 (m, 1 H, H_{Ar}), 9.14 (s, 1 H, H_{Ar}).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 127.6 (d), 127.97 (d), 128.01 (s), 128.4 (d), 129.6 (s), 133.1 (d), 133.5 (s), 134.3 (d), 134.4 (s), 134.9 (d), 135.0 (d), 136.1 (s), 137.0 (d), 147.9 (s), 148.6 (s), 181.4 (s), 182.1 (s).

Anal. Calcd for $C_{17}H_8ClNO_2$: C, 69.52; H, 2.75; N, 4.77. Found: C, 69.37; H, 2.77; N, 4.74.

Acknowledgment

We are grateful to the National Science Council of ROC for financial support (Grant No. NSC-100-2113-M-006-009-MY2).

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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