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Novel and efficient synthesis of substituted quinoline-1-oxides and the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) with the aid of stannous chloride

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ABSTRACT

A novel and efficient approach to the synthesis of substituted quinoline-1-oxides and the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) was developed. The reaction has fancy selectivity when 3-(2-nitrophenyl)acrylonitriles were treated with the aid of $SnCl_2$ reagent under the same conditions. When R is −CN or −COOR′ the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) were obtained. Whereas, when R is H or aryl another series of substituted quinoline-1-oxides were formed. The products have been screened for their anticancer activities.

1. Introduction

Quinoline-*N*-oxide is an important class of quinoline derivatives. The quinoline-*N*-oxide core unit has been found in drugs exerting microsomal Na, K-ATPase activity,[1] protein kinase inhibition and anticancer,[2] antiviral[3] or antimalarian activities.[4,5] They have also relevant applications as spin traps in biological studies,[6] and are efficient in age-related diseases,[7] due to both in vitro and in vivo[8] stability of resulting nitroxide radicals.

Metal complexes have a massive impact on medicine. They are attractive candidates for the design of new anticancer agents. Cisplatin, carboplatin and oxaloplatin were the first clinically used antitumour drugs. Some diorganotin(IV) complexes were found to have even better activity than cisplatin, which made them suitable candidates for possible clinical use.[9]

The importance of quinoline-*N*-oxides has stimulated the development of a number of approaches for the synthesis of the quinoline-*N*-oxide ring system. Kim et al. have reported the synthesis of 3-substituted-4-hydroxyquinoline-*N*-oxides from the Baylis–Hillman adducts of *o*-nitrobenzaldehydes.[10,11] Makosza et al. have synthesized substituted quinoline-*N*-oxides and 3,4-dihydroquinoline-*N*-oxides via reductive cyclization of alkylidene *o*-nitroarylacetonitriles[12] and 2-phenyl-2-(*o*-nitrobenzyl)-alkanenitriles,[13] respectively. Recently Lamaty et al. have synthesized a novel pyrrolo[3,2-*c*]quinoline-*N*-oxide by aza-Baylis–Hillman adduct of *o*-nitrobenzaldehyde.[14] Moreover, quinoline-*N*-oxides can also be prepared using molecular sieve[15] or urea hydrogen peroxide[16] as catalysts. However, these methods suffer from some disadvantages, such as drastic conditions, unsatisfactory yields, long-reaction time, complex manipulation and inaccessible starting materials. Therefore, the development of more efficient methods for preparing this kind of compounds with milder reaction conditions and improved yields is highly desired.

In recent years, our interest has been focused on the synthesis of heterocyclic compounds using $SnCl_2$ as reductive reagent.[17–22] We have previously reported the synthesis of 1-hydroxy-quinazolinones[17] via the reaction of 2-nitrobenzamides with ketones induced by $SnCl_2$. As our earlier works goes, herein, we report a novel and convenient protocol for the synthesis of substituted quinolin-1-oxides using 3-(2-nitrophenyl)acrylonitriles as starting materials induced by $SnCl_2$.

2. Results and discussion

In a preliminary study, 2-(2-nitrobenzylidene)malononitrile **1a** was chosen as starting material for synthesis of 2-amino-3-cyanoquinoline-1-oxide (Scheme 1). We proceeded this reaction in EtOH at reflux in the presence of 3 equiv of $SnCl_2\cdot 2H_2O$. To our surprise, the expected product 2-amino-3-cyanoquinoline-1-oxide was not detected, while an unidentified product was obtained. Later, the unidentified product was identified to be the complex compound **2a** by their ^1H NMR and HRMS spectra. So a protocol for the synthesis of the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) was developed. The reaction conditions were optimized by testing several parameters. The results were summarized in Table 1.

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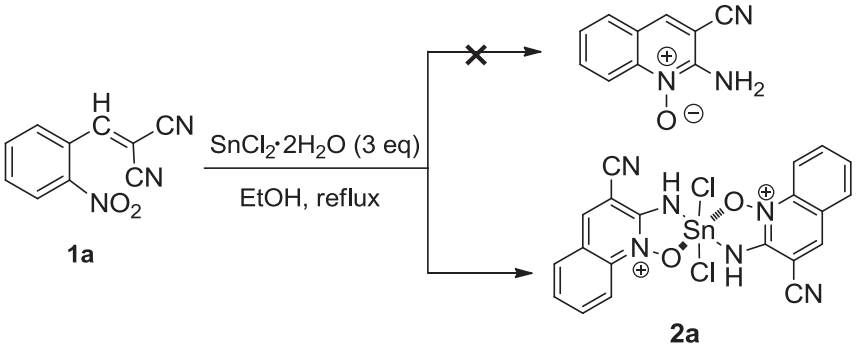


Scheme 1. The synthesis of the compound **2a**.

Table 1
Optimization for the synthesis of **2a**

Entry	Reductive reagent	Ratio[a]	Temperature (°C)	Solvent	Time (h)	Yield[b] (%)
1	$SnCl_2·2H_2O$	1:3	rt	EtOH	3	34
2	$SnCl_2·2H_2O$	1:3	40	EtOH	2	54
3	$SnCl_2·2H_2O$	1:3	60	EtOH	2	87
4	$SnCl_2·2H_2O$	1:3	Reflux	EtOH	2	88
5	$SnCl_2·2H_2O$	1:3	60	THF	2	61
6	$SnCl_2·2H_2O$	1:3	60	$CHCl_3$	2	56
7	$SnCl_2·2H_2O$	1:3	60	DMF	2	23
8	$SnCl_2·2H_2O$	1:1	60	EtOH	4	25
9	$SnCl_2·2H_2O$	1:2	60	EtOH	4	40
10	$SnCl_2·2H_2O$	1:4	60	EtOH	2	83
11	Zn+HOAc	1:3	60	EtOH	2	80[c]

[a] Ratio of **1a** and $SnCl_2·2H_2O$ system.
[b] Isolated yield.
[c] The yield of 2-amino-3-cyanoquinoline.

As shown in Table 1, we briefly examined the effect of different temperatures, different solvents and ratio of **1a**:$SnCl_2·2H_2O$. The results showed that at 60 °C the reaction proceeded smoothly in high yield. In order to further evaluate the influence of the ratio of **1a**/$SnCl_2·2H_2O$, the reaction was carried out in ethanol using a 1:1 to 1:4 ratio of **1a**/$SnCl_2·2H_2O$ (Table 1, entries 8, 9, 3, 10), leading to **2a** in 25%, 40%, 87% and 83% yields, respectively. We concluded the best ratio of **1a**:$SnCl_2·2H_2O$ was 1:3. Moreover, other organic solvents were further investigated as shown in Table 1 (entries 5–7), we concluded that ethanol was the best solvent for this reaction. It is indicated that the reductive agent is very important for the synthesis of **2a**. When compound **2a** was reduced by Zn in HOAc, only 2-amino-3-cyanoquinoline was obtained (Table 1, entry 11).

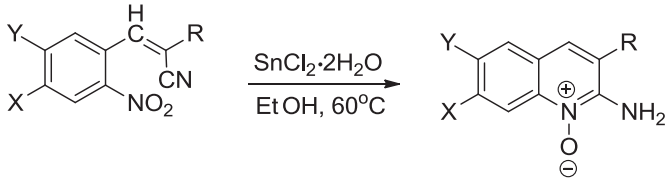
With the optimized conditions in hand, we then performed a more detailed examination of the substrates. We found that when R was CN or COOR′, the desired products SnL_2Cl_2 (L=2-aminoquinoline-*N*-oxides) were obtained (Scheme 2). The results were summarized in Table 2.

As shown in Table 2, it can be seen that this protocol can be applied to 3-(2-nitrophenyl)-acrylonitriles **1** with either electron-withdrawing groups (such as halide groups) or electron-donating groups (such as alkyl groups) under the same conditions to give moderate to good yields.

Table 2
Synthesis of the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) **2**

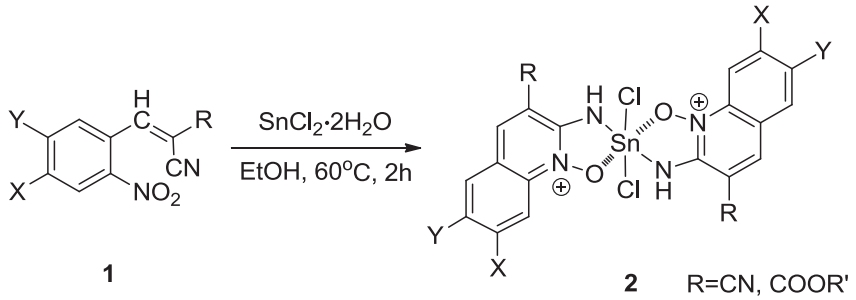
Entry	Products	X	Y	R	Isolated yield (%)
1	**2a**	H	H	CN	87
2	**2b**	H	H	$COOCH(CH_3)_2$	83
3	**2c**	H	Cl	$COOCH_3$	85
4	**2d**	H	H	$COOC_2H_5$	84
5	**2e**	H	Cl	$COOC_2H_5$	77
6	**2f**	H	Cl	$COOCH(CH_3)_2$	80
7	**2g**	H	Cl	CN	72
8	**2h**	OCH_2O		$COOC_2H_5$	79

However, to our surprise the complex compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) were not obtained when R was aryl or H groups. Instead we obtained a series of novel compounds, which were identified as quinoline-1-oxides **2** (Scheme 3, Table 3).



Scheme 3. The synthesis of quinoline-1-oxides **3**.

Similarly, 3-(2-nitrophenyl)acrylonitriles **1** containing electron-donating and electron-withdrawing substituents were reacted well under the same conditions. Therefore, we can conclude that the electronic nature of the substituents has no significant effect on this reaction.



Scheme 2. The synthesis of SnL_2Cl_2 (L=2-aminoquinoline-1-oxides) **2**.

Table 3
Synthesis of the quinoline-1-oxides **3**

Entry	Products	X	Y	R	Isolated yield (%)
1	**3a**	H	H	4-ClC_6H_4	70
2	**3b**	H	H	C_6H_5	80
3	**3c**	H	Cl	4-ClC_6H_4	83
4	**3d**	CH_3O	CH_3O	C_6H_5	84
5	**3e**	CH_3O	CH_3O	4-ClC_6H_4	76
6	**3f**	CH_3O	CH_3O	4-BrC_6H_4	70
7	**3g**	OCH_2O		C_6H_5	71
8	**3h**	H H		H	74

All the products were characterized by IR, ^{1}H NMR and HRMS spectra. The structure of **2e** was further confirmed by X-ray diffraction analysis.[23] The molecular structure of the product **2e** is shown in Fig. 1.

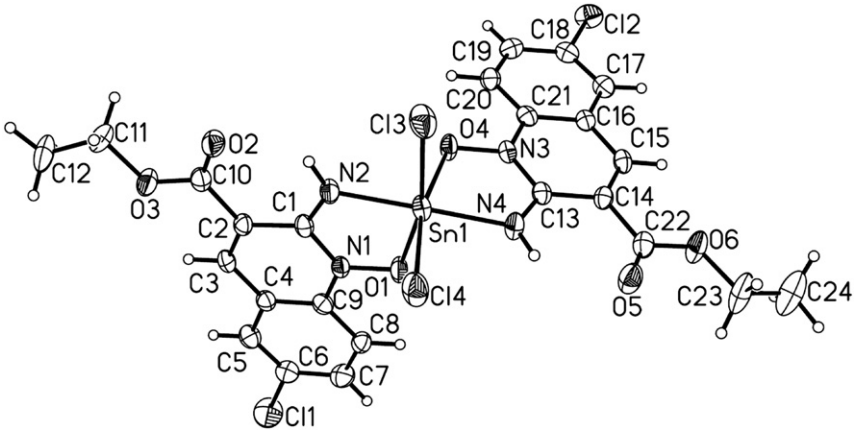


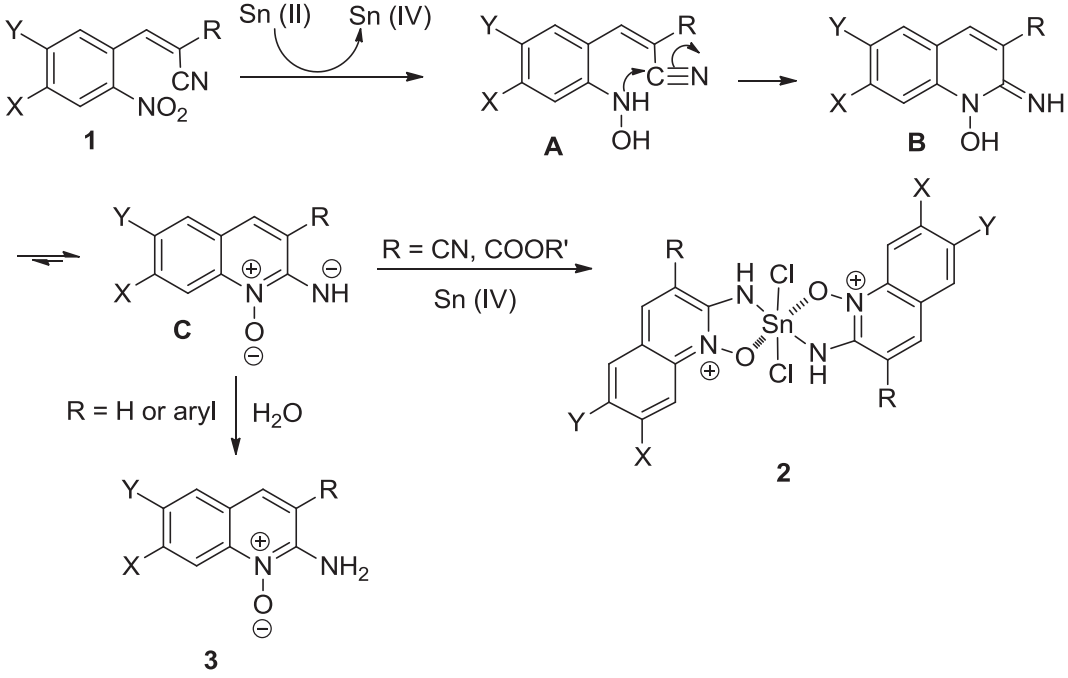
Fig. 1. Molecular structure of product **2e**.

Although the detailed mechanism of the above reaction has not been clarified yet, the formation of 2-aminoquinoline-1-oxide derivatives **2** or **3** can be explained by a possible mechanism presented in Scheme 4. In the initial step, 3-(2-nitrophenyl)acrylonitrile derivatives **1** were reduced by tin(II) chloride to corresponding hydroxylamine compounds **A** and Sn(II) was oxidated to Sn(IV). The hydroxylamine compounds **A** then reacted with cyano group by intramolecular cyclization to give the intermediate **B**. Another intermediate **C** was formed by tautomerization of intermediate **B**. When R=H or aryl, the intermediate **C** was not stable and reacted with water to give the products **3**. When R=CN or COOR′, the intermediate **C** was stable and coordinated with Sn(IV) to give the complex compounds **2**.

Finally, the synthetic compounds were screened for anticancer activity by the sulforhodamine B (SRB) method. The cells used in this study were human liver cancer cell line $HepG_2$. The results of the prescreening are listed in Table 4. It could be seen that only some products (e.g., **2f**, **3c** and **3d**) had weak anticancer activity.

3. Conclusion

In summary, we have described a novel and efficient method for the synthesis of highly functionalized quinolin-1-oxides and complex



Scheme 4. Proposed reaction mechanism.

Table 4
Survival rate of compounds **2** and **3** in 30 μm on $HepG_2$ cells

Compound	Survival rate	Compound	Survival rate
2a	1.005822	**3a**	0.911343
2b	1.262193	**3b**	0.961391
2c	0.947602	**3c**	0.780358
2d	0.994587	**3d**	0.773887
2e	1.098769	**3e**	0.947469
2f	0.607987	**3f**	0.870194
2g	1.007865	**3g**	0.966882
2h	0.936878	**3h**	1.112676

compounds SnL_2Cl_2 (L=2-aminoquinoline-1-oxides). Our protocol is characterized by (i) faster reaction times (1–2 h) and moderate to high yields, (ii) handy manipulation (only one pot) and (iii) isolation of products via simple recrystallization to give higher purities.

4. Experimental section

4.1. General

Commercial solvents and reagents were used as received. Melting points are uncorrected. IR spectra were recorded on Varian F-1000 spectrometer in KBr with absorptions in cm^{-1}. ^1H NMR was determined on Varian-400 MHz or Varian-300 MHz spectrometer in DMSO-d_6 solution. *J* values are in hertz. Chemical shifts are expressed in parts per million downfield from internal standard TMS. HRMS data were obtained using microma GCT-TOF instrument. X-ray crystallographic analysis was performed with a Rigaku Mercury CCD/AFC diffractometer.

4.2. General procedure for the synthesis of 2 and 3 is represented as follows

A solution of 3-(2-nitrophenyl)acrylonitrile derivatives **1** (1 mmol) and $SnCl_2{\cdot}2H_2O$ (3 mmol) in EtOH (5 mL) was stirred at 60 °C for 1–2 h. After this period, the TLC analysis of the mixture showed the reaction to be completed. The mixture was quenched with 3% HCl (10 mL) and filtered and the crude product was purified by recrystallization from 95% ethanol and DMF.

*4.2.1. Compound **2a**.* White solid; mp: >300 °C. IR (KBr) *ν*: 3309, 3046, 2235, 1619, 1602, 1577, 1529, 1453, 1343, 1287, 1230, 1212, 1042, 942, 873, 761, 619 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.54 (t, *J*=7.6 Hz, 2H, ArH), 7.92 (t, *J*=8.0 Hz, 2H, ArH), 7.98–8.02 (m, 4H, ArH), 8.91 (s, 2H, ArH), 9.25 (s, 2H, 2× NH). HRMS found: *m*/*z* 557.9428 (M^+), calcd for $C_{20}H_{12}N_6O_2{}^{35}Cl_2Sn$: M, 557.9421.

*4.2.2. Compound **2b**.* White solid; mp: 226–227 °C; IR (KBr) *ν*: 3343, 2983, 2934, 1701, 1621, 1603, 1576, 1528, 1457, 1364, 1301, 1221, 1184, 1100, 1036, 788, 759, 625 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 1.45 (d, *J*=6.4 Hz, 12H, 4× CH_3), 5.28–5.35 (m, 2H, 2× CH), 7.54 (t, *J*=7.6 Hz, 2H, ArH), 7.90 (t, *J*=8.0 Hz, 2H, ArH), 7.99 (d, *J*=8.4 Hz, 2H, ArH), 8.21 (d, *J*=8.0 Hz, 2H, ArH), 8.84 (s, 2H, 2× NH), 8.96 (s, 2H, ArH). HRMS found: *m*/*z* 680.0251 (M^+), calcd for $C_{26}H_{26}N_4O_6{}^{35}Cl_2Sn$: M, 680.0251.

*4.2.3. Compound **2c**.* White solid; mp: >300 °C; IR (KBr) *ν*: 3337, 3057, 2954, 1708, 1615, 1599, 1570, 1522, 1438, 1364, 1288, 1206, 1183, 1035, 836, 786, 633 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 4.03 (s, 6H, 2× CH_3), 7.89 (d, *J*=8.4 Hz, 2H, ArH), 7.97 (d, *J*=8.4 Hz, 2H, ArH), 8.35 (s, 2H, ArH), 8.81 (s, 2H, 2× NH), 8.96 (s, 2H, ArH). HRMS found: *m*/*z* 691.8848 (M^+), calcd for $C_{22}H_{16}N_4O_6{}^{35}Cl_4Sn$: M, 691.8846.

*4.2.4. Compound **2d**.* White solid; mp: 297–299 °C; IR (KBr) *ν*: 3334, 3088, 3056, 2993, 2908, 1699, 1619, 1575, 1524, 1456, 1368, 1303, 1220, 1039, 787, 764, 625 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 1.45 (t, *J*=7.6 Hz, 6H, 2× CH_3), 4.47–4.53 (m, 4H, 2× CH_2), 7.54 (t, *J*=7.2 Hz, 2H, ArH), 7.90 (t, *J*=8.0 Hz, 2H, ArH), 7.99 (d, *J*=8.4 Hz, 2H, ArH), 8.21 (d, *J*=8.4 Hz, 2H, ArH), 8.80 (s, 2H, 2× NH), 8.99 (s, 2H, ArH). HRMS found: *m*/*z* 651.9941 (M^+), calcd for $C_{24}H_{22}N_4O_6{}^{35}Cl_2Sn$: M, 651.9938.

*4.2.5. Compound **2e**.* White solid; mp: 274–276 °C; IR (KBr) *ν*: 3344, 3048, 2964, 2937, 1708, 1672, 1616, 1599, 1519, 1418, 1368, 1286, 1182, 1083, 1036, 821, 786, 694 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 1.43 (t, *J*=7.2 Hz, 6H, 2× CH_3), 4.49 (dd, J_1=14 Hz, J_2=6.8 Hz, 4H, 2× CH_2), 7.88 (d, *J*=9.2 Hz, 2H, ArH), 7.97 (d, *J*=8.4 Hz, 2H, ArH), 8.35 (s, 2H, ArH), 8.84 (s, 2H, 2× NH), 8.95 (s, 2H, ArH). HRMS found: *m*/*z* 719.9167 (M^+), calcd for $C_{24}H_{20}N_4O_6{}^{35}Cl_4Sn$: M, 719.9159.

*4.2.6. Compound **2f**.* White solid; mp: 207–210 °C; IR (KBr) *ν*: 3341, 3058, 2982, 1707, 1618, 1570, 1522, 1418, 1365, 1283, 1206, 1150, 1030, 938, 787, 626 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 1.44 (d, *J*=6.0 Hz, 12H, 4× CH_3), 5.28–5.34 (m, 2H, 2× CH), 7.88 (d, *J*=9.2 Hz, 2H, ArH), 7.97 (d, *J*=8.8 Hz, 2H, ArH), 8.37 (s, 2H, ArH), 8.87 (s, 2H, 2× NH), 8.93 (s, 2H, ArH). HRMS found: *m*/*z* 747.9477 (M^+), calcd for $C_{26}H_{24}N_4O_6{}^{35}Cl_4Sn$: M, 747.9472.

*4.2.7. Compound **2g**.* White solid; mp: >300 °C; IR (KBr) *ν*: 3304, 3041, 2928, 2854, 2236, 1666, 1617, 1602, 1575, 1526, 1416, 1365, 1210, 1036, 944, 836, 652 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.90–7.99 (m, 4H, ArH), 8.12 (s, 2H, ArH), 8.82 (s, 2H, ArH), 9.45 (s, 2H, 2× NH). HRMS found: *m*/*z* 625.8646 (M^+), calcd for $C_{20}H_{10}N_6O_2{}^{35}Cl_4Sn$: M, 625.8641.

*4.2.8. Compound **2h**.* White solid; mp: 262–264 °C; IR (KBr): *ν* 3344, 3130, 3058, 2981, 2907, 1699, 1623, 1597, 1535, 1438, 1373, 1250, 1217, 1034, 991, 938, 785, 629 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 1.38 (t, *J*=7.2 Hz, 6H, 2× CH_3), 4.39–4.46 (m, 4H, 2× CH_2), 6.23 (s, 4H, 2× OCH_2O), 7.34 (s, 2H, 2× NH), 7.61 (s, 2H, ArH), 8.56 (s, 2H, ArH), 8.74 (s, 2H, ArH). HRMS found: *m*/*z* 739.9767 (M^+), calcd for $C_{26}H_{22}N_4O_{10}{}^{35}Cl_2Sn$: M, 739.9735.

*4.2.9. 2-Amino-3-(4-chlorophenyl)quinoline-1-oxide (**3a**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3418, 3068, 3045, 1715, 1621, 1580, 1516, 1481, 1453, 1358, 1183, 1094, 903, 836, 754, 632 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 6.22 (s, 1H, NH), 7.26 (s, 1H, ArH), 7.39 (t, *J*=5.7 Hz, 1H, ArH), 7.54 (d, *J*=8.8 Hz, 2H, ArH), 7.57 (d, *J*=8.4 Hz, 2H, ArH), 7.66–7.68 (m, 1H, ArH), 7.70–7.73 (m, 2H, ArH+NH), 8.22 (d, *J*=6.3 Hz, 1H, ArH). HRMS found: *m*/*z* 270.0563 (M^+), calcd for $C_{15}H_{11}N_2O^{35}Cl$: M, 270.0560.

*4.2.10. 2-Amino-3-phenylquinoline-1-oxide (**3b**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3423, 3050, 2928, 1670, 1621, 1515, 1482, 1358, 1211, 1189, 1154, 1006, 915, 775, 759, 661, 630 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 7.47 (t, *J*=7.5 Hz, 1H, ArH), 7.54–7.62 (m, 5H, ArH), 7.74–7.85 (m, 2H, ArH), 7.95–8.02 (m, 2H, ArH), 8.07–8.11 (m, 2H, NH_2). HRMS found: *m*/*z* 236.0960 (M^+), calcd for $C_{15}H_{12}N_2O$: M, 236.0950.

*4.2.11. 2-Amino-6-chloro-3-(4-chlorophenyl)quinoline-1-oxide (**3c**).* White solid; mp: 241–243 °C; IR (KBr) *ν*: 3416, 3046, 2928, 2854, 1675, 1510, 1418, 1211, 1182, 1089, 923, 836, 730, 634 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 7.57–7.65 (m, 4H, ArH), 7.74–7.83 (m, 2H, ArH), 7.92–7.98 (m, 2H, NH_2), 8.01–8.05 (m, 2H, ArH). HRMS found: *m*/*z* 304.0178 (M^+), calcd for $C_{15}H_{10}N_2O^{35}Cl_2$: M, 304.0170.

*4.2.12. 2-Amino-6,7-dimethoxy-3-phenylquinoline-1-oxide (**3d**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3418, 3049, 2999, 2831, 1669, 1611, 1515, 1446, 1409, 1267, 1163, 986, 828, 715, 688 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 3.84 (s, 3H, CH_3O), 3.89 (s, 3H,

CH_3O), 7.27 (s, 1H, ArH), 7.44 (s, 2H, ArH), 7.52–7.60 (m, 5H, ArH), 7.93–7.97 (m, 2H, NH_2). HRMS found: *m*/*z* 296.1158 (M^+), calcd for $C_{17}H_{16}N_2O_3$: M, 296.1161.

*4.2.13. 2-Amino-3-(4-chlorophenyl)-6,7-dimethoxyquinoline-1-oxide (**3e**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3429, 3406, 3006, 2968, 2933, 1677, 1608, 1515, 1409, 1271, 1164, 1094, 986, 833, 769, 659 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 3.84 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 7.27 (s, 1H, ArH), 7.43 (s, 1H, ArH), 7.62 (dd, J_1=8.4 Hz, J_2=17.1 Hz, 5H, ArH), 7.95 (s, 2H, NH_2). HRMS found: *m*/*z* 330.0771 (M^+), calcd for $C_{17}H_{15}N_2O_3{}^{35}Cl$: M, 330.0771.

*4.2.14. 2-Amino-3-(4-bromophenyl)-6,7-dimethoxyquinoline-1-oxide (**3f**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3421, 3401, 3043, 2927, 1677, 1607, 1516, 1459, 1409, 1269, 1164, 1084, 985, 832, 767, 651 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 3.84 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 7.27 (s, 1H, ArH), 7.43 (s, 1H, ArH), 7.53 (d, *J*=8.1 Hz, 2H, ArH), 7.74–7.83 (m, 3H, ArH), 7.94 (s, 2H, NH_2). HRMS found: *m*/*z* 374.0272 (M^+), calcd for $C_{17}H_{15}N_2O_3{}^{79}Br$: M, 374.0266.

*4.2.15. 6-Amino-7-phenyl-[1,3]dioxo[4,5-g]quinoline-5-oxide (**3g**).* White solid; mp: >300 °C; IR (KBr) *ν*: 3416, 3405, 3056, 2910, 1676, 1628, 1522, 1479, 1445, 1256, 1208, 1118, 1038, 943, 834, 753, 671 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 6.21 (s, 2H, OCH_2O), 7.41–7.42 (m, 2H, ArH), 7.53–7.56 (m, 1H, ArH), 7.60–7.62 (m, 5H, ArH), 7.95 (s, 2H, NH_2). HRMS found: *m*/*z* 280.0849 (M^+), calcd for $C_{16}H_{12}N_2O_3$: M, 280.0848.

*4.2.16. 2-Aminoquinoline-1-oxide (**3h**).* White solid; mp: >300 °C. IR (KBr) *ν*: 3428, 3359, 3318, 1633, 1525, 1389, 1210, 1053, 812, 754 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ_H 7.30–7.31 (m, 1H, ArH), 7.40–7.41 (m, 1H, ArH), 7.69–7.72 (m, 1H, ArH), 7.90–7.91 (m, 3H, ArH+NH_2), 8.04–8.06 (m, 1H, ArH), 9.04 (t, *J*=4.5 MHz, 1H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 156.8, 144.9, 141.5, 139.8, 137.6, 134.4, 129.6, 120.3, 119.4. HRMS found: *m*/*z* 161.0716 $(M+H)^+$, calcd for $C_9H_9N_2O$: M+H, 161.0715.

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Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.07.049.

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23. Crystallographic data for the structures of **2e** has been deposited at the Cambridge Crystallographic Data Centre, deposit number is CCDC-837216. Copies of available material can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).