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INDIUM-MEDIATED REDUCTIVE CYCLIZATION OF 2-NITROCHALCONES TO QUINOLINES

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Abstract - The reductive cyclization of 2-nitrochalcones using indium in an aqueous alcohol solution containing ammonium chloride produced the corresp onding quinolines in reasonable yields.

INTRODUCTION

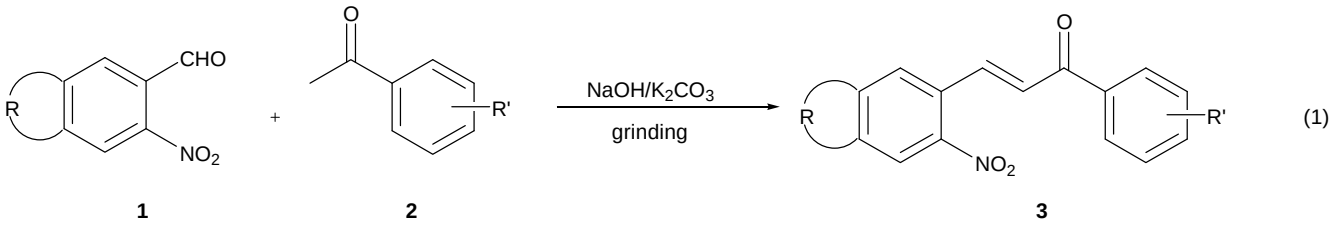
Since Rieke reported the first use of indium in organic synthesis in 1975,[1] the use of indium for organic synthesis has developed widely because of its low ionic potential and aqueous condition.[2,3] In particular, indium-mediated reactions in aqueous media have been focused on synthetic applications because of environmental issues and the ease of reactions, eliminating the need for inflammable anhydrous organic solvents and an inert atmosphere.[4] Recently, indium has been extensively applied to various reductive reactions including the reduction of imines, iminium salts, conjugate alkenes, nitro compounds, and azides.[2]

Of special interest to us was the possibility of utilizing an indium-promoted reaction for the preparation of nitrogen containing 6-membered heterocyclic compounds as an extension of our previous study on the reductive cyclization reaction of 2-nitroarenes.[5] As transformations of 2-nitroarenes into 5-membered heterocycles, such as 2,1-benzisoxazoles, benzimidazoles, and benzotriazoles were successful with metal-mediated reductive conditions, cyclization to 6-membered heterocycles can be done if the reaction condition is properly controlled. Quinolines are known to exhibit a variety of biologically active compounds such as antiasthmatic, anti-inflammatory, and antimalarial compounds.[6] Consequently,

various methods for the synthesis of quinolines are known,[7] but the use of environmentally favorable indium metal for the reductive cyclizations of *o*-nitrochalcones to quinolines has not been tried much. Thus, we have examined the utilization of indium metal for the preparation of 6-membered heterocycles, quinolines, in a continuous effort to achieve indium-mediated heterocyclization reactions. The results, reported herein, demonstrate indium-mediated reductive cyclization, which is a simple and efficient chemical method for the preparation of quinolines from 2-nitrochalcones.

RESULTS AND DISCUSSION

Starting substrates, *i.e.*, 2-nitrochalcones, were obtained easily *via* modified Claisen-Schmidt reactions; treatment of 2-nitrobenzaldehyde (**1**) with acetophenone derivatives (**2**) in the presence of a NaOH- and K_2CO_3-mixed catalyst under solvent-free conditions using the grinding method[8] that produced the desired 2-nitrochalcone derivatives (**3**) in moderate to good yields (43-73%, Eq. 1).



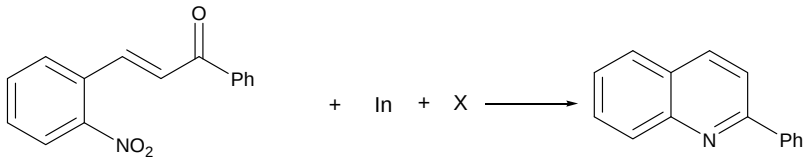
1 **2** **3** (1)

R = H, R' = H (73%), *p*-OMe (52%), *p*-Me (48%), *p*-F (61%), *p*-Cl (49%), *p*-Br (51%), *m*-OMe (62%), *m*-F (66%), *m*-Cl (68%), *m*-Br (56%), *o*-Me (68%), *o*-F (68%), *o*-Cl (65%), *o*-Br (61%),
R = -OCH_2O-, R' = H (43%)

With 2-nitrochalcone, **3a** as a standard substrate, various reaction conditions were attempted to find out the optimum condition for the reductive intramolecular cyclization reaction of 2-nitrochalcone. The representative results are summarized in Table 1. Reactions of 2-nitrochalcone in the presence of indium in THF produced a low yield of a desired product, 2-phenylquinoline (**4a**) (Table 1, Entry 1). We also tried the reaction in the presence of 2-bromo-2-nitropropane (BNP)/indium in an MeOH solution at room temperature, which were the conditions used for the synthesis of 2,1-benzisoxazoles,[5d] but there was no significant improvement (Entry 2). The addition of acetic acid, $InCl_3$, or I_2 in place of BNP did not help appreciably and produced but a low yield of the desired 2-phenylquinoline (Table 1, Entries 3-6). The reductive reaction of 2-nitrochalcone in the presence of indium/iodine in THF or indium/$InCl_3$ in MeOH produced a considerable amount of 2-benzoylindole[9] in addition to quinoline (Entries 5, 6), which probably came from the low reduction ability of the indium/iodine system. On the other hand, the reaction of 2-nitrochalcone with indium at room temperature in aqueous alcohol containing ammonium chloride

gave better results for the desired 2-phenylquinoline (**4a**) than any other reactions we tried. Moreover, by increasing the reaction temperature to the reflux, the yield of the cyclized 2-phenylquinoline product considerably improved (Table 1, Entry 8). Even though reductive cyclizations using $TiCl_4$/Zn have been reported recently and have been claimed as simple and mild reactions,[10] the use of indium/ MeOH/sat-aq. NH_4Cl is significantly superior to the use of zinc, as our indium condition is very easy to handle and environmentally favorable.

Table 1. Selected control experiments for reductive intramolecular cyclization reactions



3a **4a**

Entry	Molar ratio **3** : In : X	X	Solvent	Temp. (^oC)	Time (hrs)	Yield (%)[b]
1	1 : 5: 0	-	THF	reflux	24	9[c]
2	1 : 5 : 2	BNP	MeOH	rt	24	20[c]
3	1 : 5 : 5	AcOH	MeOH	rt	24	19[c]
4	1: 5: 10	AcOH	MeOH	50	24	18[c]
5	1: 5: 1.0	$InCl_3$	MeOH	50	24	17[d]
6	1: 5: 0.8	I_2	THF	reflux	24	10[c,d]
7	1: 5: 0	-	MeOH/sat-aq. NH_4Cl (v/v=3:1)	rt	24	31[c]
8	1: 5: 0	-	MeOH/sat-aq. NH_4Cl (v/v=3:1)	reflux	5	73[e]

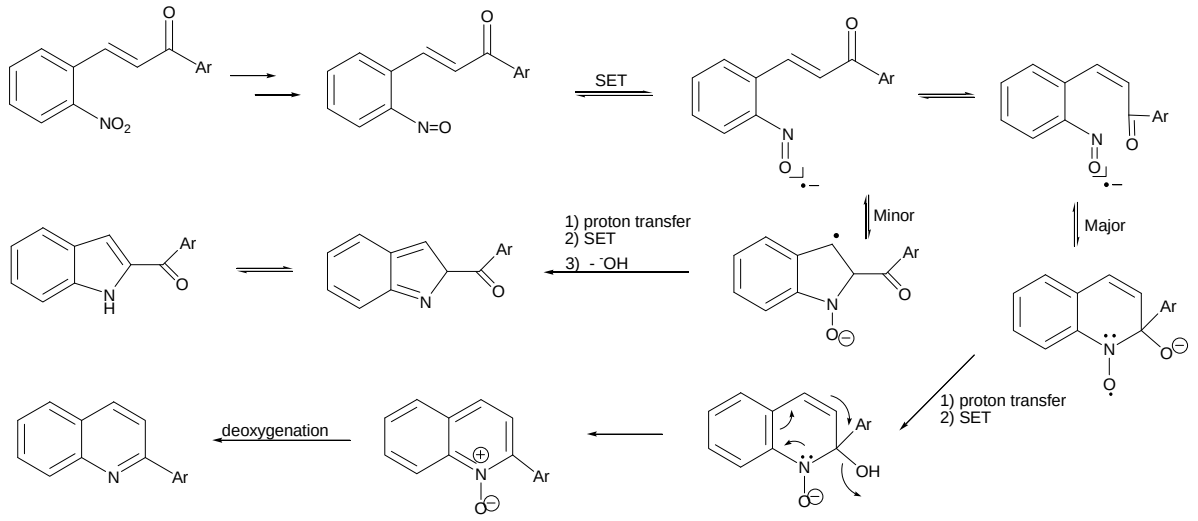
[a]All reactions were carried out with 0.5 mmol of 2-nitrochalcone. [b]Isolated yield. [c]Starting substrate was recovered mostly. [d]2-Benzoylindole (~10%) was observed. [e]Traces of benzoylindole and 2-nitrosochalcone were detected on GS-MS without starting substrate left.

To test the utilization of the alcohol/sat-aq. NH_4Cl/indium conditions for quinoline synthesis, we examined the reductive intramolecular cyclization reactions of 2-nitrochalcone derivatives under optimized conditions, *i.e.,* MeOH/sat-aq. NH_4Cl (v/v = 3:1) at reflux. Fifteen compounds were examined and the results are summarized in Table 2. In most cases, moderate to good yields of 2-arylquinoline derivatives were obtained easily independent of the position and the character of the substituent of the aromatic ring. The reductive intramolecular cyclization reactions of 2`-bromo-2-nitrochalcones or 4`-bromo-2-nitrochalcones (Entries 10, 14) produced a debrominated product, 2-phenylquinoline, trace of up to ~4% observed with GC-MS analysis, which is a strong evidence of radical intermediacy. Moreover, the formation of 2-aroylindole (trace – 10%) was detected with GC-MS analysis in addition to the corresponding 2-arylquinoline formation for most of the reductive reactions of 2-nitrochalcones, which were the evidence of radical intermediate also

.

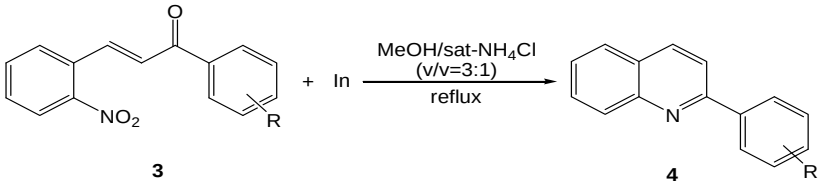
For mechanistic purposes, some inhibition experiments were carried out. In the presence of 10 mol% of *m*-dinitrobenzene, the reductive cyclization reaction of **2a** was retarded effectively. Whereas the normal reaction of **2a** showed 58% (1 h), 85% (2.5 h), and 100% (5 h) conversion, the reaction of **2a** in the presence of 10 mol% of *m*-dinitrobenzene showed only 20% (1 h) and 45% (2.5 h) conversion. Moreover, 2-phenylquinoline *N*-oxide and indole were observed with the GC-MS analysis of the mixture of a normal 2.5-h reaction, which explain well the reaction path. Apparently, electron transfer processes are involved during the reductive cyclization reaction. Compared to nitrobenzene (-0.45 V, -0.93 V, Pt cathode, 1.0 M $LiClO_4$ in MeOH, Ag/AgCl, 50 mV/s), 2-nitrochalcone (-0.78 V, Pt cathode, 1.0 M $LiClO_4$ in MeOH/DMSO (v/v=3:2), Ag/AgCl, 50 mV/s) had a lower reduction potential. Thus, electron transfer from indium to 2-nitrochalcone may lead easily to the formation of a radical anion species that changes to a nitroso intermediate through consequent proton transfer, dehydroxylation, and electron transfer reaction. Since the nitroso is a better electron-accepting group than the nitro functional group, the nitroso intermediate is immediately transformed into a nitroso radical anion intermediate, which may trigger the reductive cyclization, *i.e.,* the attack by the nitrogen anion of the carbonyl group to form the six-membered ring (Scheme 1). *Cis-trans* isomerization of the olefinic site of the substrate for the proper orientation of the ring formation may occur when the radical anion is formed. 2-Aroylindole is also possible if the radical site of the nitroso anion attacks the α-position of the carbonyl group to form the benzylic radical.

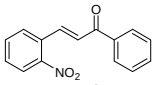
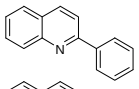
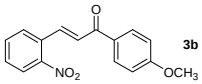
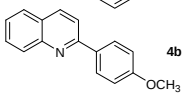
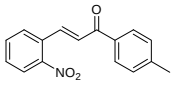
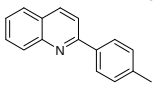
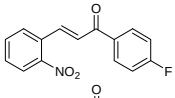
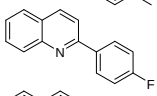
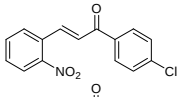
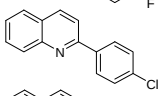
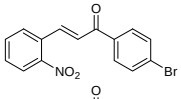
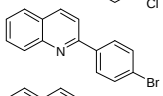
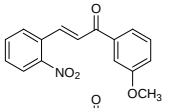
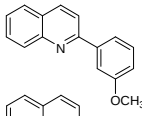
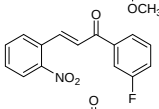
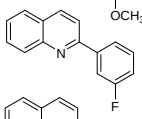
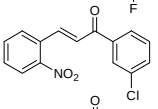
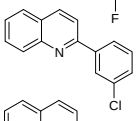
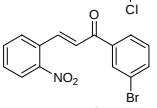
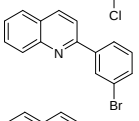
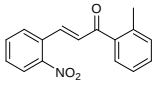
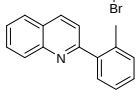
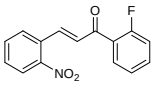
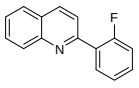
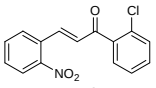
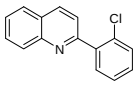
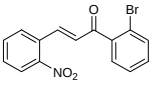
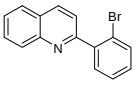
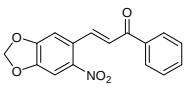
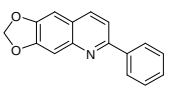
Scheme 1



In summary, we established a new synthetic method of producing 2-arylquinolines from the intramolecular reductive reactions of 2-nitrochalcone using indium powders in aqueous methanol containing ammonium chloride.

Table 2. Reactions of 2-nitrochalcones (1 equiv.) with In (5 equiv.) in MeOH/sat-aq. NH_4Cl (v/v = 3:1) at reflux.[a]



entry	substrate	reaction time (hrs)	product	isolated yield (%)
1	 **3a**	5	 **4a**	73[b]
2	 **3b**	2.5	 **4b**	65
3	 **3c**	4	 **4c**	70
4	 **3d**	4.5	 **4d**	64
5	 **3e**	2	 **4e**	69
6	 **3f**	2	 **4f**	42
7	 **3g**	4	 **4g**	61
8	 **3h**	3	 **4h**	81
9	 **3i**	3.5	 **4i**	66
10	 **3j**	2.5	 **4j**	60[b,c]
11	 **3k**	3.5	 **4k**	72[b]
12	 **3l**	3	 **4l**	62[b]
13	 **3m**	4.5	 **4m**	61[d]
14	 **3n**	6.5	 **4n**	44[b,c]
15	 **3o**	4	 **4o**	40[e]

[a]All reactions were carried out with 0.5 mmol of 2-nitrochalcone and its derivatives. [b]1 ~3% of 2-aroylindole was observed on GC-MS analysis. [c]Debrominated product was observed on GC-MS analysis. [c]~10% of 2-aroylindole was observed on GC-MS analysis.[d]12% of corresponding 2-benzoylindole was observed on GC-MS analysis.

EXPERIMENTAL

1. General considerations

Chemical reagents were purchased mostly from Alfa Aesar and used without further purification in most cases. Solvents were purchased and dried usibg a standard method. ^{1}H NMR spectra were recorded on a 300 MHz Bruker or a 400 MHz Jeol instrument and ^{13}C NMR spectra were recorded on a 75 MHz Bruker or a 100 MHz Jeol instrument. Chemical shifts were in ppm from tetramethylsilane (TMS). GC/MS was recorded on a Shimadzu QP2010 mass spectrometer. IR spectra were recorded on a Perkin-Elmer FT-IR 1730 infrared spectra photometer. Melting points were determined by capillary method and were uncorrected.

All the major products were isolated by flash column chromatography on silica gel (100-200 mesh, ZCX-II) with eluents of mixed solvents (petroleum ether and ethyl acetate).

2. Typical procedure for the reductive cyclization reaction

To a solution of the 2-nitrochalcone derivatives (0.5 mmol) in MeOH (3 mL) was added saturated aq. NH_4Cl solution (1 mL) and indium powder (2.5 mmol). The mixture was stirred at reflux under a nitrogen atmosphere. When the starting material disappeared (typically after 2 - 6.5 h), the reaction stopped and cooled down. The reaction mixture was diluted with water (30 mL), filtered through Celite, and washed with AcOEt (3 × 10 mL). The pH of the aqueous filtrate was adjusted to 9 with an aq. NaOH (4 M), and was extracted with AcOEt (3 × 20 mL). Combined organic layers (80 mL) were dried over $MgSO_4$ and concentrated. The residue was purified by flash silica gel column chromatography to yield the desired product.

2-Phenylquinoline (4a)： light brown solid; mp 79-81 ^{o}C (lit.,[11] mp 83 ^{o}C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.40-7.60 (m, 4H), 7.75 (t, J = 8.4 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 8.17-8.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 119.0, 126.3, 127.2, 127.5, 127.6, 128.9, 129.3, 129.7, 129.8, 136.8; 139.7, 148.3, 157.4；IR (KBr) 1596, 1554, 1507, 1490 cm^{-1}; GC-MS m/z (rel. intensity) 205 (100, M^+), 176 (9), 102 (29), 88 (1), 76 (1).

2-(4-Methoxyphenyl)quinoline (4b) : white solid; mp 122-124 ^{o}C (lit.,[11] mp 122-123 ^{o}C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.91(s, 3H), 7.07 (d, J = 8.7 Hz, 2H), 7.52 (t, J = 7.8 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.81-7.88 (m, 2H), 8.14-8.23 (m, including J = 8.7 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 55.4, 114.2, 118.5, 125.9, 126.9, 127.4, 128.9, 129.6, 129.9, 132.3, 136.6, 148.3, 156.9, 160.8; IR (KBr) 1602, 1519, 1499, 1431, 1251 cm^{-1}; GC-MS m/z (rel. intensity) 235 (100, M^+), 220 (32), 204 (6), 191 (35), 128 (6), 102 (6), 75 (6).

2-(4-Methylphenyl)quinoline (4c) : white solid; mp 80-82 ^{o}C (lit.,[11] mp 81-82 ^{o}C); ^{1}H NMR (300

MHz, $CDCl_3$): δ (ppm) 2.46 (s, 3H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.82-7.90 (m, 2H), 8.11 (d, *J* = 7.8 Hz, 2H), 8.17 - 8.23 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.3, 118.8, 126.1, 127.1, 127.4, 129.6, 129.7, 136.6, 137.0, 139.4, 148.3, 157.3; IR (KBr) 1596, 1553, 1492, 1431 cm^{-1}; GC-MS m/z (rel. intensity) 219 (100, M^+), 204 (23), 109 (23), 75 (1).

2-(4-Fluorophenyl)quinoline (4d) : white solid; mp 91-93 °C (lit.,[12] mp 92-93 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.23 (t, *J* = 8.7 Hz, 2H), 7.52-7.58 (m, 1H), 7.72-7.79 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 8.14-8.24 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 115.7 (d, J_{C-F} = 21.8 Hz) 118.6, 126.3, 127.1, 127.5, 129.4 (d, J_{C-F} = 8.3 Hz) , 129.7, 129.8, 135.8 (d, J_{C-F} = 3.0 Hz), 136.9, 148.2, 156.2, 163.8 (d, J_{C-F} = 247.5 Hz); IR (KBr) 1597, 1569, 1496, 1432 cm^{-1}; GC-MS m/z (rel. intensity) 223 (100, M^+), 202 (6), 111 (24), 75 (12).

2-(4-Chlorophenyl)quinoline (4e) : white solid; mp 112-113 °C (lit.,[13] mp 112 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.45 – 7.58 (m, including *J* = 8.4 Hz, 3H), 7.72-7.84 (m, 3H), 8.10 - 8.23 (m, including *J* = 8.4 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 118.5, 126.5, 127.2, 127.5, 128.8, 129.0, 129.7, 129.9, 135.5, 137.0, 138.0, 148.2, 156.0; IR (KBr) 1593, 1554, 1486, 1430 cm^{-1}; GC-MS m/z (rel. intensity) 239 (100, M^+), 204(74), 176 (1), 102 (40), 88 (1), 76 (2).

2-(4-Bromophenyl)quinoline (4f) : white solid; mp 121-123 °C (lit.,[13] mp 123-124 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.53 – 7.59 (m, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.73 – 7.79 (m, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 8.07 (d, *J* = 8.5 Hz, 2H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 118.5, 124.0, 126.5, 127.2, 127.5, 129.1, 129.7, 129.9, 132.0, 137.0, 138.5, 148.3, 156.0; IR (KBr) 1594, 1550, 1485, 1429 cm^{-1}; GC-MS m/z (rel. intensity) 285 (66, M^+), 204(100), 176 (18), 102 (78), 88 (24), 75 (29).

2-(3-Methoxyphenyl)quinoline (4g)[14] **:** light yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.95 (s, 3H), 7.05 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.43 - 7.60 (m, 2H); 7.70 - 7.80 (m, 2H), 7.82 (s, 1H), 7.84-7.89 (m, 2H), 8.19 - 8.24 (m, including *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 55.4, 112.8, 115.4, 119.1, 120.0, 126.3, 127.3, 127.5, 129.7, 129.8, 129.9, 136.8, 141.2, 148.3, 157.1, 160.2; IR (KBr) 1605, 1520, 1449, 1374, 1243, 1047 cm^{-1}; GC-MS m/z (rel. intensity) 235 (76, M^+), 234 (100), 220 (32), 204 (58), 191 (17), 128 (17), 102 (15), 75 (7).

2-(3-Fluorophenyl)quinoline (4h)[15] **:** white solid; mp 44-47 °C ; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.15 – 7.21 (m, 1H), 7.46-7.59 (m, 2H), 7.73 – 7.79 (m, 1H), 7.84 (d, *J* =8.5 Hz, 2H), 7.94 (d, *J* = 7.5 Hz, 2H), 8.20 (d, *J* = 8.3 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 114.5 (d, J_{C-F} = 22.5 Hz), 116.2 (d, J_{C-F} = 21.0 Hz), 118.7, 123.1 (d, J_{C-F} = 2.3 Hz), 126.6, 127.4, 127.5, 129.8, 129.9, 130.3 (d, J_{C-F} = 8.3 Hz), 137.0, 142.0 (d, J_{C-F} = 7.5 Hz), 148.2, 155.8, 163.4 (d, J_{C-F} = 244.5 Hz); IR (KBr) 1597, 1555, 1507, 1447, 1266 cm^{-1}; GC-MS m/z (rel. intensity) 223 (100, M^+), 202 (6), 111 (18), 88 (7),

75 (12).

2-(3-Chlorophenyl)quinoline (4i) : light yellow solid; mp 64-66 °C (lit.,[10] mp 59-61 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.43-7.50 (m, 2H), 7.52 – 7.62 (m, 1H), 7.73 – 7.80 (m, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 8.02-8.07 (m, 1H), 8.17 - 8.26 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 118.7, 125.6, 126.6, 127.4, 127.5, 127.7, 129.3, 129.8, 129.9, 130.0, 135.0, 137.0, 141.4, 148.2, 155.7; IR (KBr) 1594, 1552, 1505, 1426 cm^{-1}; GC-MS m/z (rel. intensity) 239 (100, M^+), 204(94), 176 (13), 102 (41), 88 (15), 75 (21).

2-(3-Bromophenyl)quinoline (4j) : white solid; mp 69-73 °C (lit.,[16] mp 74.5-76 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.40 (t, *J* = 7.8 Hz, 1H), 7.52-7.62 (m, 2H), 7.70-7.859 (m, 3H), 8.08 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 8.38 (dd, *J* = 1.8, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 118.6, 123.2, 126.1, 126.7, 127.3, 127.5, 129.8, 129.9, 130.3, 130.6, 132.2, 137.0, 141.7, 148.2, 155.6; IR (KBr) 1592, 1545, 1503, 1426 cm^{-1}; GC-MS m/z (rel. intensity) 285 (51, M^+), 204(100), 176 (15), 102 (53), 88 (15), 75 (22).

2-(2-Methylphenyl)quinoline (4k)[12] **:** viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.44 (s, 3H), 7.30 – 7.43 (m, 3H), 7.50-7.62 (m, 3H), 7.74 – 7.80 (m, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 8.24 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 20.3, 122.4, 126.0, 126.4, 126.8, 127.5, 128.5, 129.6, 129.7, 130.9, 136.0, 136.1, 140.7, 147.9, 160.3; IR (KBr) 1592, 1552, 1501, 1431, 1378, cm^{-1}; GC-MS m/z (rel. intensity) 219 (40, M^+), 218 (100), 204 (23), 109 (25), 75 (1).

2-(2-Fluorophenyl)quinoline (4l) : white solid; mp 65-67 °C (lit.,[17] bp 127-129 °C at 0.02 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.19 – 7.27 (m, 1H), 7.31 – 7.37 (m, 1H), 7.42-7.47 (m, 1H), 7.50 – 7.65 (m, 1H), 7.70 – 7.80 (m, 1H), 7.81 – 7.95 (m, 2H), 8.13 (t, *J* = 7.5 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 116.2 (d, $J_{C\text{-}F}$ = 22.5 Hz), 122.5 (d, $J_{C\text{-}F}$ = 7.5 Hz), 124.7 (d, $J_{C\text{-}F}$ = 3.0 Hz), 126.6, 127.2, 127.5, 128.0 (d, $J_{C\text{-}F}$ = 12.0 Hz), 129.6, 129.8, 130.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 131.6 (d, $J_{C\text{-}F}$ = 2.3 Hz), 136.1, 148.4, 154.1, 160.8 (d, $J_{C\text{-}F}$ = 248.3 Hz); IR (KBr) 1604, 1567, 1495, 1452 cm^{-1}; GC-MS m/z (rel. intensity) 223 (100, M^+), 202 (1), 111 (12), 88 (1), 75 (12); HRMS (EI) calcd for $C_{15}H_{10}FN$ 223.0798, found 223.0794.

2-(2-Chlorophenyl)quinoline (4m) : light yellow solid; mp 74-78 °C (lit.,[17] mp 79.5-80 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.42 (br, 2H), 7.52 – 7.63 (m, 2H), 7.68-7.82 (m, 3H), 7.89 (d, *J* = 7. 8 Hz, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 122.8, 126.8, 127.2, 127.6, 129.7, 129.8, 129.9, 130.1, 131.7, 132.4, 135.7, 139.7, 148.1, 157.4; IR (KBr) 1598, 1555, 1504, 1434 cm^{-1}; GC-MS m/z (rel. intensity) 239 (44, M^+), 204 (100), 176 (12), 102 (29), 88 (12), 75 (15).

2-(2-Bromophenyl)quinoline (4n) : white solid; mp 69-71 °C (lit.,[17] mp 72-73 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.38 (m, 1H), 7.47 (dd, *J* = 7.5, 7.2 Hz, 1H), 7.57-7.80 (m, 5H), 7.89 (d, *J* = 8.4 Hz, 1H), 8.22 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 121.9, 122.7, 126.8, 127.1, 127.6,

127.7, 129.7, 130.0, 131.6, 133.3, 135.7, 141.7, 148.0, 158.7; IR (KBr) 1598, 1556, 1504, 1431 cm^{-1}; GC-MS m/z (rel. intensity) 285 (29, M^+), 204 (100), 176 (19), 102 (52), 88 (15), 75 (17).

6,7-Methylenedioxy-2-phenylquinoline (4o) : light yellow solid; mp 116-118 °C (lit.,[18] mp 144-146 °C); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.06 (s, 2H), 7.02 (s, 1H), 7.39 – 7.50 (m, 4H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 8.08 – 8.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 101.6, 102.5, 106.2, 117.1, 124.1, 127.2, 128.7, 128.8, 135.4, 139.8, 146.5, 147.7, 150.8, 155.2; IR (KBr) 1615, 1515, 1465, 1225 cm^{-1}; GC-MS m/z (rel. intensity) 249 (100, M^+), 220 (4), 190 (33), 163 (9), 95 (13), 76 (1); HRMS (EI) calcd for $C_{16}H_{11}NO_2$ 249.0790, found 249.0794.

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