# Isoindolone synthesis via palladium-catalysed intramolecular amination of benzylic C–H bonds

**Ming Zhang[a]***

[a]*College of Chemistry and Key Laboratory of Functional Small Organic Molecules, Ministry of Education, Jiangxi Normal University (Yaohu campus), 99 Ziyangdadao, Nanchang, Jiangxi 330022, P.R. China.*

A new method for the construction of isoindolones is presented in this paper. Four 7-methyl-2-(8-quinolinyl)-2,3-dihydro-1*H*-isoindol-1-ones were synthesised from 2,6-dimethyl-*N*-(8-quinolinyl)benzamides *via* intramolecular direct amination of benzylic C–H bonds. This approach provides a convenient method affording structurally new isoindolones for medicinal chemistry research.

**Keywords:** amination, coupling, lactam, palladium, cyclisation

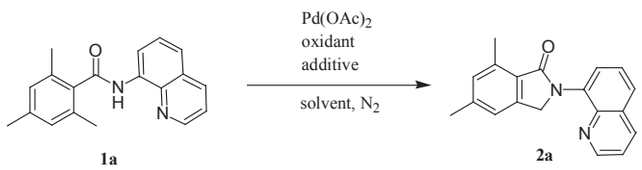
Construction of heterocyclic scaffolds *via* $sp^3$ C–H functionalisation has witnessed great progress in recent years,[1–4] this strategy provides straightforward and efficient methods for synthesis of various heterocyclic compounds. The direct coupling of a $sp^3$ C–H bond with a heteroatom is a challenge in this research area. In 2006, pioneering work in this field was reported by Chang's group.[5] Formation of aryl lactones was achieved by coupling of a $sp^3$ C–H bond and a pendant oxygen function.[5,6] 4*H*-3,1-Benzoxazines and oxazoles were also synthesised *via* coupling of a $sp^3$ C–H bond with the oxygen atom of an amide group.[7,8] In 2009, Glorius's group reported coupling of a $sp^3$ C–H bond with a nitrogen atom leading to indolines from anilines.[9] In 2011, a picolinamide directed coupling of a $sp^3$ C–H bond with a N–H bond was used to form four-, five- and six-membered heterocycles.[10,11] An N-substituted isoindolone is the intermediate of a mGluR2 positive allosteric modulator of an indicator of schizophrenia. In the literature,[12] three steps were needed to construct the isoindolone scaffold from 4-bromo-2,6-dimethylbenzoic acid in 33% overall yield. We now report that the isoindolone scaffold can be constructed in a two-step procedure from the same starting material in 75% overall yield (Scheme 1). This approach will provide structurally diverse compounds for medicinal chemistry research. Here we describe the synthesis of isoindolones *via* intramolecular coupling of a benzylic C–H bond with an amide N–H bond.

## Results and discussion

It was found that *N*-(8-quinolinyl)-2,4,6-trimethylbenzamide **1a** could be cyclised to afford 5,7-dimethyl-2-(8-quinolinyl)-2,3-dihydro-1*H*-isoindol-1-one **2a** in 73% yield *via* benzylic C–H-amide N–H coupling (Table 1), using $Pd(OAc)_2$ (5 mol%) as a catalyst and $PhI(OAc)_2$ (2.5 equiv.) as an oxidant. An acidic additive is essential in this cyclisation, and of those tested, HOAc gave the best result.

With the optimised reaction conditions in hand, the scope of substrate variation was explored (Table 2). It was observed that *N*-(8-quinolinyl)- and 2,6-dimethylbenzoyl were essential moieties in the substrates for cyclisation and gave the products in 57–88% yield. The substrates **1c** and **1d** containing fluorine and

**Table 1** Optimisation of the reaction conditions for the coupling[a]



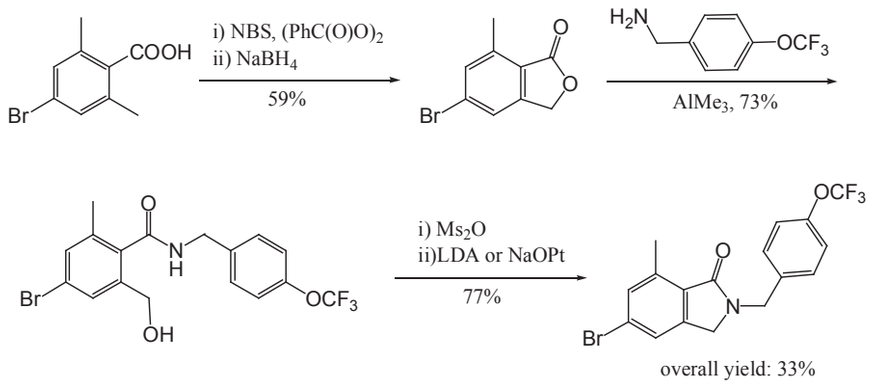

**1a** **2a**

| Entry | $Pd(OAc)_2$/ mol% | Oxidant (equiv.) | Additive /5 equiv. | Solvent | T/°C | Reaction time/h | Yield/%[b] |
|---|---|---|---|---|---|---|---|
| 1 | 10 | AgOAc (3) | – | DCE | 70 | 24 | 0 |
| 2 | 10 | $PhI(OAc)_2$ (2.5) | – | DCE | 70 | 24 | 0 |
| 3 | 10 | $Cu(OAc)_2$ (3) | – | DCE | 70 | 24 | 0 |
| 4 | 10 | Selectfluor (3) | – | DCE | 70 | 24 | 0 |
| 5 | 10 | $Na_2S_2O_8$ (6) | – | DCE | 70 | 24 | 0 |
| 6 | 10 | $Na_2S_2O_8$ (3) | HOAc | DCE | 70 | 24 | 0 |
| 7 | 10 | $Na_2S_2O_8$ (3) | TFA | DCE | 70 | 24 | 0 |
| 8 | 10 | $Na_2S_2O_8$ (3) | $CF_3SO_3H$ | DCE | 70 | 24 | 0 |
| 9 | 10 | $Na_2S_2O_8$ (3) | $K_2CO_3$ (3) | DCE | 70 | 24 | 0 |
| 10 | 10 | $PhI(OAc)_2$ (2.5) | HOAc | Mesitylene | 140 | 24 | 31 |
| 11 | 10 | $PhI(OAc)_2$ (2.5) | HOAc | DCE | 70 | 72 | 26 |
| 12 | 5 | $PhI(OAc)_2$ (2.5) | TFA | Toluene | 100 | 24 | trace |
| 13 | 5 | $PhI(OAc)_2$ (2.5) | HOAc | Toluene | 100 | 24 | 43 |
| 14 | 5 | $PhI(OAc)_2$ (2.5) | $^tBuCOOH$ | Toluene | 100 | 24 | 34 |
| 15 | 5 | $PhI(OAc)_2$ (2.5) | $CF_3SO_3H$ | Toluene | 100 | 24 | 0 |
| 16 | 5 | $PhI(OAc)_2$ (2.5) | HOAc | Mesitylene | 120 | 24 | 73 |

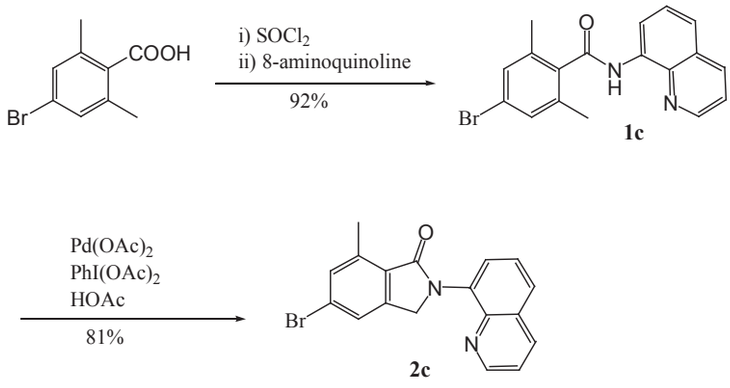
[a]Reaction conditions: **1a** (0.29 mmol), $Pd(OAc)_2$, oxidant, additive, solvent (2 mL), heat.
[b]Isolated yield.

* Correspondent. E-mail: zmchem@163.com

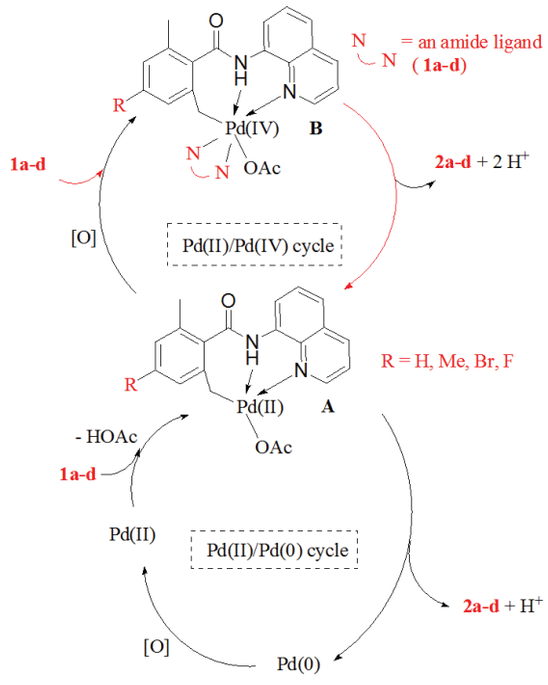
1) Literature procedure[12] :




2) This work:

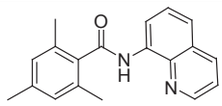
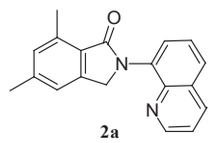
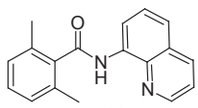
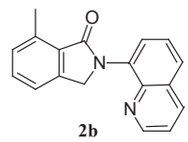
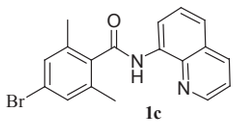
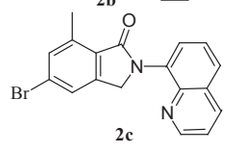
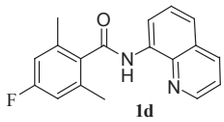
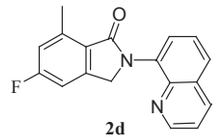
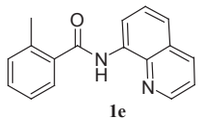
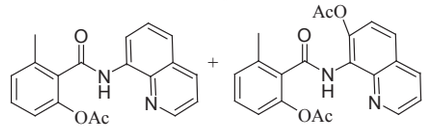
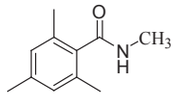
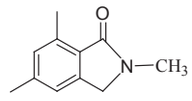



**Scheme 1** Two routes to isoindolones.




**Scheme 2** A possible mechanism.

**Table 2** Cyclisation studies[a]

| Entry | Substrate | Product | Yield/% |
|---|---|---|---|
| 1 |  **1a** |  **2a** | 73 |
| 2 |  **1b** |  **2b** | 57 |
| 3 |  **1c** |  **2c** | 81 |
| 4 |  **1d** |  **2d** | 88 |
| 5 |  **1e** |  **2e-1** **2e-2** | 10+ 14 |
| 6 |  **1f** |  | 0 |

[a]Reaction conditions: **1** (0.29 mmol), $Pd(OAc)_2$ (5 mol%), $PhI(OAc)_2$ (2.5 equiv.), HOAc (5 equiv), Mesitylene (2 mL), 120 °C, 24 h.

bromine substituents gave higher yields (81 and 88% respectively) than those from **1a** and **1b**. There are not obvious electronic effects on the cyclisation yields. When 2-methyl-*N*-(8-quinolinyl) benzamide **1e** was tested both mono- and di-acetoxylated products were isolated, and no cyclisation product was obtained. The substrate **1f** without an *N*-(8-quinolinyl) function was tested under the reaction conditions, but no cyclisation occurred.

A possible mechanism involves[2,8,12,13] benzylic C–H activation of **1a–d**, directed by the bidentate 8-aminoquinoline system, to produce intermediate **A**, then reductive elimination gives the product **2a–d** and Pd(0). Oxidation of Pd(0) to Pd(II) completes the Pd(II)–Pd(0) catalytic cycle. A Pd(II)–Pd(IV) catalytic cycle is also possible. Thus, intermediate **A** is oxidised to the Pd(IV) species **B**, then reductive elimination gives the product **2a–d** and Pd(II) so completing the catalytic cycle (Scheme 2).

In summary, a method for the construction of isoindolones from 2,6-dimethyl-*N*-(8-quinolinyl)benzamides is described. This approach involves the directed amination of benzylic C–H bonds *via* the bidentate 8-aminoquinoline system. Four desired compounds were synthesised in 57–88% yields. The present synthetic route for the construction of isoindolones is new, straightforward and helpful for medicinal chemistry research.

## Experimental

All reactions were performed under an atmosphere of nitrogen. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker Avance 400 spectrometer with TMS as the internal standard and $CDCl_3$ as solvent. $^{19}$F NMR spectra were determined on a Bruker Avance 500 spectrometer. MS were recorded on an Agilent Technologies 5973 N spectrometer. High-resolution mass spectra (HRMS) were obtained on a Waters Micromass GCT Premier spectrometer.

*N-(8-Quinolinyl)benzamides (***1a–e***); general procedure*

A solution of 8-aminoquinoline (0.3950 g, 2.74 mmol) and $Et_3N$ (0.42 mL, 3 mmol) in $CH_2Cl_2$ (5 mL) was cooled to 0 °C, then an acyl chloride (2.74 mmol) was added (the acyl chloride was prepared by reaction of the appropriate carboxylic acid with $SOCl_2$). After addition, the reaction mixture was warmed to room temperature and stirred for 24 h. The reaction mixture was washed with water (1 mL), brine (1.5 mL × 3), and dried over $Na_2SO_4$. The solvent was removed and the product was obtained by recrystallisation or flash chromatography.

N-*(8-Quinolinyl)-2,4,6-trimethylbenzamide* (**1a**): Yield: 0.66 g (87%); pale brown crystals; m.p. 142–144 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, Me), 2.40 (s, 6H, 2Me), 6.94 (s, 2H, ArH), 7.44–7.47 (q, $J$=4 Hz, 1H, ArH), 7.56–7.63 (m, 2H, ArH), 8.19 (app. d, $J_{app.}$=8.4 Hz, 1H, ArH), 8.74 (t, $J$=2.4 Hz, 1H, ArH), 8.99 (app. d, $J_{app.}$=7.6 Hz, 1H, ArH), 9.95 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ=19.44, 21.18, 116.81, 121.64, 121.86, 127.48, 128.01, 128.42, 134.43, 134.53, 135.33, 136.49, 138.38, 138.77, 148.16, 169.17. HRMS (EI): *m/z* [$M^+$] calcd for $C_{19}H_{18}N_2O$: 290.1419; found: 290.1422.

*2,6-Dimethyl*-N-*(8-quinolinyl)benzamide* (**1b**): Yield: 0.67 g (89%); colourless crystals; m.p. 153–159 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 6H, 2Me), 7.11 (app. d, $J_{app.}$=7.6 Hz, 2H, ArH), 7.23 (app. d, $J_{app.}$=7.6 Hz, 1H, ArH), 7.45 (dd, $J$=4.4, 10 Hz, 1H, ArH), 7.58–7.62 (m, 2H, ArH), 8.18 (app. d, $J_{app.}$=8.4 Hz, 1H, ArH), 8.74 (app. d, $J_{app.}$=2.8 Hz, 1H, ArH), 8.98 (app. d, $J_{app.}$=7.2 Hz, 1H, ArH), 9.93 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.46, 16.81, 121.67, 121.94, 127.44, 127.73, 128.05, 128.99, 134.46, 134.59, 136.35, 138.08, 138.59, 148.30, 168.89. HRMS (EI): *m/z* [$M^+$] calcd For $C_{18}H_{16}N_2O$: 276.1263; found 276.1265.

*4-Bromo-2,6-dimethyl*-N-*(8-quinolinyl)benzamide* (**1c**): Yield: 0.89 g (92%); colourless crystals; m.p. 155–156 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 6H, 2Me), 7.28 (s, 2H, ArH), 7.45–7.47 (m, 1H, ArH), 7.57–7.61 (m, 2H, ArH), 8.18 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 8.74 (d, $J$ = 2 Hz, 1H, ArH), 8.94 (app. d, $J_{app.}$ = 6.8 Hz, 1H, ArH), 9.90 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.28, 116.84, 121.74, 122.15, 122.87, 127.40, 128.04, 130.59, 134.19, 136.38, 136.82, 136.94, 138.53, 148.39, 167.85. HRMS (EI): *m/z* [M$^+$] calcd for $C_{18}H_{15}{}^{79}BrN_2O$: 354.0368; found: 354.0366.

*2,6-Dimethyl-4-fluoro*-N-*(8-quinolinyl)benzamide* (**1d**): Yield: 0.73 g (91%); colourless crystals; m.p. 136–138 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 6H, 2Me), 6.81 (app. d, $J_{app}$ = 9.2 Hz, 2H, ArH), 7.46 (q, $J$ = 4 Hz, 1H, ArH), 7.57–7.62 (m, 2H, ArH), 8.19 (app. d, $J_{app}$ = 8.4 Hz, 1H, ArH), 8.75 (app. d, $J_{app}$ = 4 Hz, 1H, ArH), 8.96 (app. d, $J_{app}$ = 7.2 Hz, 1H, ArH), 9.90 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.61, 114.33 (d, $^2J_{F–C}$ = 21.1 Hz), 116.82, 121.72, 122.08, 127.41, 128.05, 134.29, 136.39, 137.40, 137.49, 138.55, 148.37, 161.33 (d, $^1J_{F–C}$ = 246.4 Hz), 168.10. $^{19}$F NMR (470 MHz, $CDCl_3$): δ –112.37. HRMS (EI): *m/z* [M$^+$] calcd for $C_{18}H_{15}FN_2O$: 294.1168; found: 294.1172.

*2-Methyl*-N-*(8-quinolinyl)benzamide* (**1e**): Yield: 0.67 g (93%); pale brown crystals; m.p. 114–115 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.61 (s, 3H, Me), 7.33 (t, $J$ = 7.6 Hz, 2H, ArH), 7.42 (t, $J$ = 7.2 Hz, 1H, ArH), 7.47 (q, $J$ = 4.4 Hz, 1H, ArH), 7.56–7.64 (m, 2H, ArH), 7.69 (app. d, $J_{app.}$ = 7.2 Hz, 1H, ArH), 8.79 (m, 1H, ArH), 8.95 (app. d, $J_{app.}$ = 7.2 Hz, 1H, ArH), 10.24 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 20.27, 116.72, 121.70, 121.85, 126.04, 127.33, 127.53, 128.05, 130.38, 131.40, 134.68, 136.60, 136.73, 138.39, 138.47, 148.21, 168.30. HRMS (EI): *m/z* [M$^+$] calcd for $C_{17}H_{14}N_2O$: 262.1106; found: 262.1107.

N,*2,4,6,-Tetramethylbenzamide* (**1f**): A solution of $CH_3NH_2$ (13.6 g, 438 mmol) in ethanol (28 mL) was cooled to 0 °C, then 2,4,6-trimethylbenzoyl chloride (4 g, 21.9 mmol) was added. After the addition, the reaction mixture was warmed to room temperature, and stirred for 24 h. The solvent was removed, the residue was extracted with ethyl acetate (60 mL), the organic layer was washed with water (3 mL), brine (3 mL × 3), dried over $Na_2SO_4$, concentrated and cooled. The white crystals that precipitated were collected by filtration. Yield: 0.44 g (91%); white crystals; m.p. 154–156 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 9H, 3Me), 2.99 (d, $J$ = 4.8 Hz, 3H, Me), 5.69 (s, 1H, NH), 6.83 (s, 2H, ArH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.11, 21.07, 26.41, 128.13, 134.16, 134.88, 138.40, 171.40. HRMS (EI): *m/z* [M$^+$] calcd for $C_{11}H_{15}NO$: 177.1154; found: 177.1151.

*Substituted 7-methyl-2-(8-quinolinyl)-2,3-dihydro-1H-isoindol-1-ones; general procedure*

Amide **1** (0.29 mmol), $Pd(OAc)_2$ (0.0033 g, 5 mol%), $PhI(OAc)_2$ (0.2335 g, 2.5 equiv.), HOAc (0.083 mL, 5 equiv.) and mesitylene (1 mL) were added to a tube, then the reaction mixture was heated under an $N_2$ atmosphere at 120 °C for 24 h. After cooling to room temperature, $Et_3N$ (1.2 mL, 30 equiv.) was added to the reaction mixture. The mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography to give the corresponding product.

*5,7-Dimethyl-2-(8-quinolinyl)-2,3-dihydro-1*H-*isoindol-1-one* (**2a**): Pale yellow solid; m.p. 166–168 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.45(s, 3H, Me), 2.75 (s, 3H, Me), 5.18 (s, 2H, $CH_2$), 7.07 (s, 1H, ArH), 7.14 (s, 1H, ArH), 7.41–7.44 (m, 1H, ArH), 7.63 (t, $J$ = 8 Hz, 1H, ArH), 7.82 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.91 (app. d, $J_{app.}$ = 7.2 Hz, 1H, ArH), 8.21 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 8.88–8.89 (m. 1H, ArH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 17.34, 21.77, 53.08, 120.66, 121.33, 126.45, 127.13, 127.30, 128.94, 129.48, 130.90, 135.84, 136.50, 137.98, 141.86, 143.53, 144.37, 149.89, 169.72. HRMS (EI): *m/z* [M$^+$] calcd for $C_{19}H_{16}N_2O$: 288.1263; found: 288.1264.

*7-Methyl-2-(8-quinolinyl)-2,3-dihydro-1*H-*isoindol-1-one* (**2b**): Colourless solid; m.p. 169–170 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.80(s, 3H, Me), 5.24 (s, 2H, $CH_2$), 7.25 (m, 1H, ArH), 7.34 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.43–7.49 (m, 2H, ArH), 7.64 (app. d, $J_{app.}$ = 7.6 Hz, 1H, ArH), 7.83 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.92 (app. d, $J_{app.}$ = 7.6 Hz, 1H, ArH), 8.22 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 8.89 (t, $J$ = 2 Hz. 1H, ArH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 17.41, 53.21, 120.11, 121.35, 126.39, 127.39, 128.89, 129.49, 129.63, 129.86, 131.27, 135.78, 136.34, 138.38, 143.07, 144.51, 150.01, 169.63. HRMS (EI): *m/z* [M$^+$] calcd for $C_{18}H_{14}N_2O$: 274.1106; found: 274.1105.

*5-Bromo-7-methyl-2-(8-quinolinyl)-2,3-dihydro-1*H-*isoindol-1-one* (**2c**): Pale yellow solid; m.p. 245–246 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.76(s, 3H, Me), 5.21 (s, 2H, $CH_2$), 7.42–7.45 (m, 2H, ArH), 7.49 (s, 1H, ArH), 7.63 (t, $J$ = 8 Hz, 1H, ArH), 7.83 (app. d, $J_{app.}$ = 8.4 Hz, 1H, ArH), 7.90 (app. d, $J_{app.}$ = 7.2 Hz, 1H, ArH), 8.22 (m, 1H, ArH), 8.87 (m, 1H, ArH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 17.16, 52.73, 121.44, 123.45, 125.85, 126.38, 127.60, 128.70, 128.84, 129.48, 132.95, 135.31, 136.38, 140.23, 144.35, 144.81, 150.07, 168.75. HRMS (EI): *m/z* [M$^+$] calcd for $C_{18}H_{13}{}^{79}BrN_2O$: 352.0211; found: 352.0214.

*5-Fluoro-7-methyl-2-(8-quinolinyl)-2,3-dihydro-1*H-*isoindol-1-one* (**2d**): Colourless solid; m.p. 178–179 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.78(s, 3H, Me), 5.22 (s, 2H, $CH_2$), 6.96–7.03 (m, 2H, ArH), 7.43 (q, $J$ = 4 Hz, 1H, ArH), 7.63 (t, $J$ = 8 Hz, 1H, ArH), 7.83 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.91 (app. d, $J_{app.}$ = 7.6 Hz, 1H, ArH), 8.21 (app. d, $J_{app.}$ = 8.4 Hz, 1H, ArH), 8.88 (app. d, $J_{app.}$ = 4 Hz. 1H, ArH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 17.43, 52.98 (d, $^4J_{F–C}$ = 2.8 Hz), 107.24 (d, $^2J_{F–C}$ = 23.5 Hz), 117.09 (d, $^2J_{F–C}$ = 22.3 Hz), 121.41, 125.76, 126.37, 127.52, 128.83, 129.48, 135.43, 136.40, 141.13 (d, $^3J_{F–C}$ = 9.5 Hz), 144.38, 145.44 (d, $^3J_{F–C}$ = 10.7 Hz), 150.03, 163.54, 168.67 (d, $^1J_{F–C}$ = 264 Hz). $^{19}$F NMR (470 MHz, $CDCl_3$): δ–108.168. HRMS (EI): *m/z* [M$^+$] calcd for $C_{18}H_{13}FN_2O$: 292.1012; found: 292.1010.

*2-Acetoxy-6-methyl*-N-*(8-quinolinyl)benzamide* (**2e-1**): **1e** was used as substrate according to the procedure for the synthesis of isoindolones. The reaction residue was subjected to silica gel column chromatography, **2e-1** was obtained firstly with PE-EtOAc (7:1) as the eluent, subsequently **2e-2** was obtained with PE-EtOAc (3:1) as the eluent.

**2e-1**: Pale yellow solid; m.p. 44–45 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3H, Me), 2.50(s, 3H, OCOMe), 7.05 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.19 (app. d, $J_{app.}$ = 7.6 Hz, 1H, ArH), 7.38 (t, $J$ = 7.6 Hz, 1H, ArH), 7.46 (q, $J$ = 4 Hz, 1H, ArH), 7.57–7.61 (m, 2H, ArH), 8.19 (app. d, $J_{app.}$ = 8.4 Hz, 1H, ArH), 8.78 (app. d, $J_{app.}$ = 4 Hz. 1H, ArH), 8.93 (app. d, $J_{app.}$ = 6.8 Hz, 1H, ArH), 10.04 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.60, 20.86, 116.95, 120.33, 121.77, 122.17, 127.42, 128.01, 128.28, 130.13, 130.68, 134.26, 136.41, 137.59, 138.42, 147.46, 148.42, 164.90, 169.63. MS: *m/z* (%) = 320 (M$^+$, 94), 177 (3.25), 171 (1.54), 149 (100), 144 (26.72), 135 (24.43). HRMS (EI): *m/z* [M$^+$] calcd for $C_{19}H_{16}N_2O_3$: 320.1161; found: 320.1164.

*2-Acetoxy-6-methyl*-N-*(7-acetoxy-8-quinolinyl)benzamide* (**2e-2**): Orange solid; m.p. 57–58 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H, Me), 2.48(s, 6H, 2 OCOMe), 7.05 (app. d, $J_{app.}$ = 8 Hz, 1H, ArH), 7.19 (app. d, $J_{app.}$ = 7.2 Hz, 1H, ArH), 7.36 (m, 2H, ArH), 7.50 (q, $J$ = 4.4 Hz, 1H, ArH), 8.19 (app. d, $J_{app.}$ = 8.4 Hz, 1H, ArH), 8.81 (app. d, $J_{app.}$ = 4.4 Hz. 1H, ArH), 8.95 (app. d, $J_{app.}$ = 8.4 Hz, 1H, ArH), 9.94 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.56, 20.91, 20.95, 116.25, 119.31, 120.33, 121.99, 128.27, 128.31, 130.18, 130.36, 130.62, 132.60, 137.55, 138.79, 140.99, 147.44, 148.85, 164.80, 169.63, 169.67. MS: *m/z* (%) = 378 (M$^+$, 16.03), 336 (23.36), 202 (11.05), 177 (18.2), 160 (63.71), 149 (14.41), 135 (100). HRMS (EI): *m/z* [M$^+$] calcd for $C_{21}H_{18}N_2O_5$: 378.1216; found: 378.1213.

## Electronic Supplementary Information

The $^1$H and $^{13}$C NMR spectra for the compounds described are available as electronic supplementary information available from: stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data

This work was financially supported by the National Natural Science Foundation of China (No. 21262017 ) and a research project (GJJ10390) from Jiangxi Provincial Department of Education, P.R. China.

*Received 4 July 2013; accepted 30 July 2013*
*Paper 1302039 doi: 10.3184/174751913X13801883437178*
*Published online: 7 October 2013*

## References

1 T.-S. Mei, L. Kou, S. Ma, K.M. Engle and J.-Q. Yu, *Synthesis*, 2012, **44**, 1778.
2 R. Jazzar, J. Hitee, A. Renaudat, J. Safack-Kreutzer and O. Baudoin, *Chem. Eur. J.,* 2010, **16**, 2654.
3 M. Zhang, A.-Q. Zhang and Y. Peng, *J. Organomet. Chem.,* 2013, **723**, 224.
4 T.W. Lyons and M.S. Sanford, *Chem. Rev.,* 2010, **110**, 1147.
5 J.M. Lee and S. Chang, *Tetrahedron Lett.,* 2006, **47**, 1375.
6 P. Novak, A. Correa, J. Gallardo-Donaire and R. Martin, *Angew. Chem. Int. Ed.,* 2011, **50**, 12236.
7 Y. Li, Z. Li, T. Xiong, Q. Zhang and X. Zhang, *Org. Lett.,* 2012, **14**, 3522.
8 P. Hu, Q. Wang, Y. Yan, S. Zhang, B. Zhang and Z. Wang, *Org. Biomol. Chem.*, 2013, **11**, 4304.
9 J. Neumann, S. Rakshit, T. Droge and F. Glorius, *Angew. Chem. Int. Ed.,* 2009, **48**, 6892.
10 G. He, Y. Zhao, S. Zhang, C. Lu and G. Chen, *J. Am. Chem. Soc.,* 2012, **134**, 3.
11 E.T. Nadres and O. Daugulis, *J. Am. Chem. Soc.,* 2012, **134**, 7.
12 M. Ball, A. Boyd, G. Churchill, M. Cuthbert, M. Drew, M. Fielding, G. Ford, L. Frodsham, M. Golden, K. Leslie, S. Lyons, B. McKeever-Abbas, A. Stark, P. Tomlin, S. Gottsching, A. Hajar, J. Jiang, J. Lo and B. Suchozak, *Org. Process Res. Dev.,* 2012, **16**, 741.
13 E.J. Yoo, S. Ma, T.-S. Mei, K.S. L. Chan and J.-Q. Yu, *J. Am. Chem. Soc*., 2011, **133**, 7652.
14 G.-W. Wang, T.-T. Yuan and D.D. Li, *Angew. Chem. Int. Ed.,* 2011, **50**, 1380.