## Supporting Information

**Synthesis of Isoquinolones via Rh-Catalyzed C–H Activation of Substituted Benzamides Using Air as the Sole Oxidant in Water**

*Nitinkumar Satyadev Upadhyay, Vijaykumar H. Thorat, Ryota Sato, Annamalai Pratheepkumar, Chuang, Shih-Ching* and *Chien–Hong Cheng*

Department of Chemistry, National Tsing Hua University, Hsinchu 30013, Taiwan  
chcheng@mx.nthu.edu.tw

### Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental Section</td>
<td>S-2</td>
</tr>
<tr>
<td>Synthesis of Compound 1a-\textit{d}</td>
<td>S-3</td>
</tr>
<tr>
<td>Synthesis of Compound 1a-\textit{ds}</td>
<td>S-4</td>
</tr>
<tr>
<td>Reversible D/H exchange</td>
<td>S-5</td>
</tr>
<tr>
<td>Intermolecular Kinetic Isotope Effect</td>
<td>S-7</td>
</tr>
<tr>
<td>Intramolecular Kinetic Isotope Effect</td>
<td>S-9</td>
</tr>
<tr>
<td>Gram-scale Synthesis of Isoquinolones</td>
<td>S-10</td>
</tr>
<tr>
<td>Evaluation of Green metrics of the process</td>
<td>S-10</td>
</tr>
<tr>
<td>$^1$H and $^{13}$C NMR and IR Data</td>
<td>S-14</td>
</tr>
<tr>
<td>References</td>
<td>S-26</td>
</tr>
<tr>
<td>$^1$H and $^{13}$C NMR Spectra</td>
<td>S-27</td>
</tr>
<tr>
<td>ORTEP Diagram and X-ray Data</td>
<td>S-58</td>
</tr>
</tbody>
</table>
General. All reactions were conducted under a nitrogen atmosphere on a dual-manifold Schlenk line unless otherwise mentioned and in oven-dried glass wares. All solvents were dried according to known methods and distilled prior to use \(^1\). \([\text{Cp*Rh(CH}_3\text{CN)}_3\text{][BF}_4]_2\) was prepared from \(\text{RhCl}_3\cdot x\text{H}_2\text{O}\) following a literature procedure.\(^2\) Other reagents were commercially available and used as purchased.

General Procedure for the Synthesis of Isoquinolones by Rhodium-Catalyzed C–H Activation.

To a screw-capped glass tube containing \([\text{Cp*Rh(CH}_3\text{CN)}_3\text{][BF}_4]_2\) (4.0 mol %), \(\text{K}_2\text{CO}_3\) (0.20 mmol), \(N\)-alkyl benzamide 1 (0.40 mmol), and acetylene 2 (0.50 mmol) was added water (2.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h. After completion, the reaction mixture was cooled and extracted with E.A. (ethyl acetate, 3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over \(\text{MgSO}_4\). The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by a silica gel column using hexane/ethyl acetate (90/10) as eluent to yield the desired pure product 3.

The spectral data and a copy of \(^1\)H and \(^13\)C NMR spectra for all compounds 3 are listed below (p. S26)

Synthesis of 2-deuteriobromobenzene.\(^4\)

\[
\begin{array}{c}
\text{Br} \\
1) \text{i-PrMgCl} / 78 ^\circ\text{C} \\
2) \text{CD}_3\text{OD}
\end{array}
\rightarrow
\begin{array}{c}
\text{D} \\
\text{Br}
\end{array}
\]

To a stirred solution of 1-bromo-2-iodobenzene (5.00 g, 17.7 mmol) in a mixture of THF and \(\text{Et}_2\text{O}\) (120 mL, 1:1) at -78 °C was added dropwise isopropyl magnesium chloride (2 M in \(\text{Et}_2\text{O}\), 10.6 mL, 21.2 mmol). The mixture was stirred at that temperature for 2 h and then, \(\text{CD}_3\text{OD}\) (2.2 mL, 53.0 mmol) was added. The solution was slowly warmed to room temperature, then an aq. HCl (10%, 100 mL) solution was added and the resulting mixture was stirred for 30 min at room temperature. The aqueous layer was extracted with \(\text{Et}_2\text{O}\) (3 x 30 mL). The combined organic phase was dried over \(\text{MgSO}_4\), filtered and the solvents were removed under reduced pressure. The pure 2-deuteriobromobenzene was obtained by distillation.
**Synthesis of 2-deuteriobenzoic acid.**

To a stirred solution of 2-deuteriobromobenzene (1.00 g, 6.32 mmol) in dry THF (20 mL) was added a solution of \( n \)-BuLi in \( n \)-hexane (3.0 mL, 2.5M, 7.59 mmol) dropwise at -78 °C for 30 min. The mixture was stirred at the same temperature for 30 min, and then CO\(_2\) was bubbled through the mixture at -78 °C for 30 min. The mixture was allowed to warm to ambient temperature, quenched with H\(_2\)O (20 mL), acidified to pH = 1 with 1M HCl, and extracted with EtOAc (2 × 30 mL). The combined organic phase was dried over MgSO\(_4\), filtered and the solvents were removed in vacuum to give product 2-deuteriobenzoic acid (550 mg, 70 %).

**Synthesis of \( N \)-methyl-2-deuteriobenzamide 1a-d.**

To the solution of the 2-deuteriobenzoic acid (550 mg, 4.47 mmol) in dry E.A. (20 mL) at 0 °C under N\(_2\) were added dropwise oxalyl chloride (372 mg, 6.70 mmol) and a catalytic amount of dry DMF (2 drops). The reaction was allowed to stir at room temperature for 5 h. The solvent was then removed under reduced pressure to afford the corresponding crude deuterated acid chloride. Methyl amine hydrochloride (450 mg, 5.36 mmol) was added to a biphasic mixture of K\(_2\)CO\(_3\) (1.23 g, 8.92 mmol) in a 2:1 mixture of EtOAc (30 mL) and H\(_2\)O (15 mL). The resulting solution was cooled to 0°C followed by dropwise addition of the unpurified deuterated acid chloride dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at room temperature for 10 h. Afterwards the phases were extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over MgSO\(_4\), filtered and evaporated under reduced pressure to give the desired product without any further purification. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.75-7.72 (m, 1 H), 7.40-7.36 (m, 1 H), 7.31-7.27 (m, 2 H), 7.19 (br, 1 H, NH), 2.88 (d, 3 H). HRMS (FAB+) calcd for C\(_8\)H\(_8\)DNO 136.074, found 136.073.
Synthesis of N-methyl-2,3,4,5,6-pentadeuteriobenzamide 1a-d.\(^4\)

\(\text{N-methyl-2,3,4,5,6-pentadeuteriobenzamide was prepared from 2,3,4,5,6-pentadeuteriobenzene using the same procedure as the synthesis of } \text{N-methyl-2-deuteriobenzamide, } ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta \text{ 6.18 (s, 1 H, NH), 2.99 (d, 3 H).}\)
Reversible D/H exchange:

\[
\begin{align*}
\text{D/H} & \quad \text{D} \\
\text{D/H} & \quad \text{D} \\
\text{D/H} & \quad \text{D} \\
\text{N} & \quad \text{O} \\
\text{Me} & \quad \text{N} \\
\text{D} & \quad \text{O} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\text{D} & \quad \text{D} \\
\end{align*}
\]

93% H

(1)

To a sealed tube containing \([\text{Cp*Rh(MeCN)}_3][\text{BF}_4]_2\) (4 mol%), \(\text{K}_2\text{CO}_3\) (0.20 mmol), \(N\)-methyl-2,3,4,5,6-pentadeueriobenzamide \(\text{1a-d}_5\) (0.40 mmol) was added water (2.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h, when the reaction was complete, the mixture was cooled and the reaction mixture was extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over \(\text{MgSO}_4\). The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to yield \(\text{1a'}-\text{d}_5\).

The D/H incorporation in \(\text{1a'}-\text{d}_5\) was determined by \(^1\text{H}-\text{NMR spectroscopy.}\)
Rh-Catalyzed Isoquinolones from 1a-d₅:

A sealed tube containing [Cp*Rh(CH₃CN)₃](BF₄)₂ (4.0 mol %), K₂CO₃ (0.20 mmol), N-methyl-2,3,4,5,6-pentadeueriobenzamide 1a-d₅ (0.40 mmol), diphenyl acetylene 2a (0.50 mmol) then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air in filled a balloon for 16 h, when the reaction was complete, the mixture was cooled and the reaction mixture was diluted and extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over MgSO₄. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to yield 3aa-d₄. The ortho deuterium content 92% was determined by ¹H-NMR spectroscopy.
$^1$H NMR (400 MHz, CDCl$_3$) spectra of compound 3aa-d$_4$.

Intermolecular Kinetic Isotope Effect

A sealed tube containing $[\text{Cp}^*\text{Rh(CH}_3\text{CN)_3}](\text{BF}_4)_2$ (4.0 mol %), K$_2$CO$_3$ (0.20 mmol), N-methyl benzamide 1a (0.20 mmol), N-methyl-2,3,4,5,6-pentadeueriobenzamide 1a-d$_5$ (0.20 mmol), diphenyl acetylene 2a (0.50 mmol) then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 30 min, then the mixture was cooled and the reaction mixture was diluted and extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over MgSO$_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to afford a
mixture of products 3aa and 3aa-d₄ in 26% yield. The ratio of two compounds was determined by ¹H NMR integration to give intermolecular kinetic isotopic effect (KIE) $k_H/k_D = 2.5$

¹H NMR (400 MHz, CDCl₃) spectra of compound

Parallel Experiment:
A sealed tube containing [Cp*Rh(CH₃CN)₃](BF₄)₂ (4.0 mol %), K₂CO₃ (0.20 mmol), N-methyl benzamide 1a (0.40 mmol), diphenyl acetylene 2 (0.50 mmol) was sealed with a septum, then water (2.0 mL) was added to the system via syringe and similarly in another sealed tube N-methyl-2,3,4,5,6-pentadeueriobenzamide 1a-d₅ (0.40 mmol) was added instated of N-methyl benzamide 1a (0.40 mmol), both tubes were allowed to stir at 110 °C under one atmosphere of air filled a balloon for 30 min, then the mixtures were cooled and both reaction mixtures were extracted with E.A. (3 x 10 mL). The combined organic layer was washed with brine (10 mL) and dried over MgSO₄. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane/E.A.: 90/10) to afford a mixture of products 3aa and 3aa-d₄ in 27% yield. The ratio of two compounds was determined by ¹H NMR integration to give intermolecular kinetic
isotopic effect (KIE) \( k_H/k_D = 1.3 \)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) crude spectra of compound 3aa and 3aa-d\(_4\).

Intramolecular Kinetic Isotope Effect

\[
\begin{align*}
\text{[Cp*Rh(MeCN)}_3[BF_4]_2 (4 \text{ mol\%}) &\xrightarrow{K_2CO_3 (0.20 \text{ mmol})} \text{O}_2, \text{H}_2\text{O, 110 °C, 30 min} \\
\frac{k_H}{k_D} = 3.7
\end{align*}
\]

A sealed tube containing \([\text{Cp*Rh(CH}_3\text{CN)}_3][\text{BF}_4]_2\) (4.0 mol %), \(\text{K}_2\text{CO}_3\) (0.20 mmol), \(\text{N}\)-methyl benzamide [D\(_1\)]-1a (0.40 mmol), diphenyl acetylene 2 (0.50 mmol) was sealed with a septum, then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled a balloon for 30 min, then the mixture was cooled and the reaction mixture was extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over MgSO\(_4\). The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to afford a mixture of products 3aa and 3aa-d\(_1\) in 26%
yield. The ratio of two compounds was determined by $^1$H NMR integration to give intermolecular kinetic isotopic effect (KIE) $k_H/k_D = 3.7$

$^1$H NMR (400 MHz, CDCl$_3$) spectra of compound 3aa and 3aa-d.

Gram-scale Synthesis of Isoquinolones via Rhodium-Catalyzed C–H Activation.

To a screw-capped glass tube containing [Cp*Rh(CH$_3$CN)$_3$][BF$_4$]$_2$ (4.0 mol %), K$_2$CO$_3$ (4.4 mmol), N-alkyl benzamide 1a (1g, 7.4 mmol), and acetylene 2 (1.32g, 7.4 mmol) was added water (20.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 20 h. After completion, the reaction solution was cooled to room temperature, the precipitate was collected and was washed with H$_2$O (3 x 20 mL) and dried in vacuum to give the crude product which was further purified by a silica gel column using hexane/ethyl acetate (90/10) as eluent to yield the desired pure product 3 in 86 % (1.99 g).

Evaluation of Green metrics of the process.
Atom economy defined as “how much of the reactants remain in the final desired product”

\[
\text{Atom economy (AE)} = \frac{\text{Molecular mass of desired product}}{\text{Molecular mass of all reactants}} \times 100
\]

Reaction mass efficiency (RME) defined as “the percentage of the mass of the reactants that remain in the product”

\[
\text{Reaction mass efficiency (RME)} = \frac{\text{mass of desired product}}{\text{mass of all reactants}} \times 100
\]

**Evaluation of Green metrics for the current methodology.**

Reaction scheme

Chemical Formula: C₈H₉NO
Molecular Weight: 135.1632

Chemical Formula: C₁₄H₁₀
Molecular Weight: 178.2292

**Product Yield: 86%**

Total = 135.16 + 178.23 = 313.39

<table>
<thead>
<tr>
<th>Reactant</th>
<th>Chemical Formula</th>
<th>Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactant 1</td>
<td>N-methylbenzamide ((1g))</td>
<td>C₈H₉NO</td>
</tr>
<tr>
<td>Reactant 2</td>
<td>1,2-diphenylethyne ((1.32g))</td>
<td>C₁₄H₁₀</td>
</tr>
<tr>
<td>Base</td>
<td>Potassium Carbonate ((0.51g))</td>
<td></td>
</tr>
<tr>
<td>Solvent</td>
<td>H₂O</td>
<td></td>
</tr>
<tr>
<td>Auxiliary</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>2-methyl-3,4-diphenylisoquinolin-1(2H)-one ((3aa))</td>
<td>C₂₂H₁₇NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>FW 135.16</td>
<td></td>
</tr>
<tr>
<td>FW 178.22</td>
<td></td>
</tr>
<tr>
<td>FW 138.20</td>
<td></td>
</tr>
<tr>
<td>FW 311.37</td>
<td></td>
</tr>
</tbody>
</table>
Product yield = 86%

E-factor = \( \frac{1g + 1.32g + 20g + 0.51g - 1.99g}{1.99g} \) = 10.47 kg waste/1 kg product

Atom economy = \( \frac{311}{313} \times 100 \) = 99.4%

Atom efficiency = \( 86 \times \frac{99.4}{100} \) = 85.5%

Carbon efficiency = \( \frac{22}{8 + 14} \times 100 \) = 100%

Reaction mass efficiency = \( \frac{1.99g}{1g + 1.32g} \times 100 \) = 85.8%
Evaluation of Green metrics for the reported methodology \(^6\).

**Reaction scheme**

\[
\text{N-methylbenzamide (1g)} + \text{1,2-diphenylethyne (1.32g)} \rightarrow \text{Product (1.56g)}
\]

**Chemical Formula:** C\(_{22}\)H\(_{17}\)NO  
**Molecular Weight:** 311.3765

**Product Yield:** 68%

---

<table>
<thead>
<tr>
<th>Reactant 1</th>
<th>N-methylbenzamide (1g)</th>
<th>1g</th>
<th>0.0074 mol</th>
<th>FW 135.16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactant 2</td>
<td>1,2-diphenylethyne (1.32g)</td>
<td>1.32g</td>
<td>0.0074 mol</td>
<td>FW 178.22</td>
</tr>
<tr>
<td>Oxidant</td>
<td>Cu(OAc)(_2).H(_2)O</td>
<td>2.95g</td>
<td>0.0148 mol</td>
<td>FW 199.65</td>
</tr>
<tr>
<td>Solvent</td>
<td>t-amyl alcohol</td>
<td>40.25 g (50 mL)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Auxiliary</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Product</td>
<td>2-methyl-3,4-diphenylisoquinolin-1(2H)-one</td>
<td>1.56g</td>
<td>0.005 mol</td>
<td>FW 311.37</td>
</tr>
</tbody>
</table>

**Product yield:** 68%

- **E-factor** = \(\frac{1g + 1.32g + 40.25g + 2.95g - 1.56g}{1.56g}\) = 28.18 kg waste/1 kg product
- **Atom economy** = \(\frac{311}{313}\) X 100 = 99.4%
- **Atom efficiency** = \(68 \times (99.4/100)\) = 67.6%
- **Carbon efficiency** = \(\frac{22}{8 + 14}\) X 100 = 100%
- **Reaction mass efficiency** = \(\frac{1.56g}{1g + 1.32g}\) X 100 = 67.2%
To a screw-capped glass tube containing [Cp*Rh(CH$_3$CN)$_3$](BF$_4$)$_2$ (4.0 mol %), K$_2$CO$_3$ (0.20 mmol), primary benzamide 1t (0.40 mmol), and diphenylacetylene 2a (1.50 mmol) was added water (3.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h. After completion, the reaction mixture was cooled and extracted with ethyl acetate, (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over MgSO$_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by a silica gel column using hexane/ethyl acetate (80/20) as eluent to yield the desired pure product 3ta.

The spectral data and a copy of $^1$H and $^{13}$C NMR spectra for all compounds 3ta are listed below (p. S56)

2-Methyl-3,4-diphenylisoquinolin-1(2H)-one (3aa)

![Structure of 2-Methyl-3,4-diphenylisoquinolin-1(2H)-one (3aa)](image)

White solid, m.p. 245-248 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.55 (d, $J = 9.2$ Hz 1 H), 7.52-7.45 (m, 2 H), 7.23-7.09 (m, 9 H), 7.05-7.03 (m, 2 H), 3.34 (s, 3 H) ; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.7 (C), 141.2 (C), 137.1 (C), 136.4 (C), 135.0 (C), 131.9 (CH), 131.5 (2CH), 129.9 (2CH), 128.1 (3CH), 127.8 (2CH), 127.7 (CH), 126.7 (CH), 126.5 (CH), 125.3 (CH), 124.9 (C), 118.8 (C), 34.3 (CH$_3$);

HRMS (ESI) cal. for C$_{22}$H$_{17}$NO 311.1310, found 311.1310; IR (KBr): 2923, 1648, 1604, 1550, 1425, 1030, 925, 698 cm$^{-1}$

2-Ethyl-3,4-diphenylisoquinolin-1(2H)-one (3ba)

![Structure of 2-Ethyl-3,4-diphenylisoquinolin-1(2H)-one (3ba)](image)

Yellow solid, m.p. 246-248 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.55-8.53 (m, 1 H), 7.51-7.45 (m, 2 H), 7.23-7.09 (m, 9 H), 7.04-7.02 (m, 2 H), 3.96-3.90 (q, 2 H), 1.15 (t, $J = 14.0$ Hz 3 H) ; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 160.0 (C), 141.0 (C), 137.1 (C), 136.5 (C), 134.7 (C), 131.9 (CH), 131.5 (2 CH), 130.1 (2 CH), 128.1 (CH), 127.8 (2 CH), 127.8 (2 CH), 127.7 (CH), 126.7 (CH), 126.5 (CH), 125.3 (CH), 37.5 (CH$_3$), 14.0 (CH$_2$), 13.8 (CH$_3$).
(CH), 125.2 (C), 119.0 (C), 41.3 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI) cal. for C$_{23}$H$_{19}$NO 325.1467, found 325.1467; IR (KBr): 2923, 1645, 1548, 1427, 1080, 925, 771, 698 cm$^{-1}$

**2,3,4-Triphenylisoquinolin-1(2H)-one (3ca)**

![2,3,4-Triphenylisoquinolin-1(2H)-one (3ca)](image)

White solid, m.p. 167-170 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.56 (d, $J = 8.0$ Hz 1 H), 7.59-7.49 (m, 2 H), 7.25-7.08 (m, 11 H), 6.87 (s, 5 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.6 (C), 141.0 (C), 139.4 (C), 137.6 (C), 136.3 (C), 134.7 (CH), 132.5 (CH), 131.6 (2 CH), 131.0 (2 CH), 129.5 (2 CH), 128.5 (2 CH), 128.2 (CH), 127.9 (2 CH), 127.5 (CH), 127.2 (CH), 127.0 (2 CH), 126.8 (CH), 125.5 (2 CH), 118.8 (C); HRMS (ESI) cal. for C$_{27}$H$_{19}$NO 373.1467, found 373.1466; IR (KBr): 2923, 1648, 1604, 1550, 1425, 1030, 925, 698 cm$^{-1}$

**2-Benzyl-3,4-diphenylisoquinolin-1(2H)-one (3da)**

![2-Benzyl-3,4-diphenylisoquinolin-1(2H)-one (3da)](image)

Yellow solid, m.p. 167-170 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.61-8.59 (m 1 H), 7.56-7.19 (m, 2 H), 7.17-7.09 (m, 8 H), 7.06-7.02 (m, 4 H), 6.89-6.82 (m, 4 H), 5.20 (s, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.6 (C), 141.3 (C), 137.7 (C), 137.3 (C), 136.4 (C), 134.3 (C), 132.2 (CH), 131.4 (2 CH), 130.4 (2 CH), 128.2 (CH), 128.1 (2 CH), 128.0 (CH), 127.8 (CH), 127.5 (2 CH), 126.9 (2 CH), 126.8 (2 CH), 126.7 (CH), 126.7 (CH), 125.4 (CH), 125.1 (C), 119.4 (C), 49.0 (CH$_2$)

HRMS (ESI) cal. for C$_{28}$H$_{21}$NO 387.1623, found 387.1620; IR (KBr): 2854, 1645, 1604, 1548, 1427, 1080, 925, 771, 698 cm$^{-1}$

**2-(4-Methoxyphenyl)-3,4-diphenylisoquinolin-1(2H)-one (3ea)**

![2-(4-Methoxyphenyl)-3,4-diphenylisoquinolin-1(2H)-one (3ea)](image)

Yellow solid, m.p. 219-221 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.59-8.56 (m, 1 H), 7.57-7.47 (m, 2 H), 7.26-7.11 (m, 6 H), 7.04-6.90 (m, 2 H), 6.90 (m, 5 H), 6.74-6.70 (m, 2 H), 3.66 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$
162.7 (C), 158.3 (C), 141.2 (C), 137.4 (C), 136.2 (C), 134.7 (C), 132.3 (CH), 132.0 (C), 131.4 (2 CH), 130.8 (2 CH), 130.2 (2 CH), 128.1 (CH), 127.8 (2 CH), 127.0 (2 CH), 127.0 (2 CH), 126.6 (CH), 125.4 (CH), 125.3 (CH), 118.5 (C), 113.7 (CH), 55.1 (CH$_3$); **HRMS (ESI)** cal. for C$_{28}$H$_{21}$NO$_2$ 403.1572, found 403.1572; IR (KBr): 2923, 1655, 1604, 1508, 1323, 1229, 1030, 771 cm$^{-1}$

### 2,6-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3fa)

![Structure of 2,6-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3fa)](structure.png)

White solid, m.p. 263-265 °C; **$^1$H NMR** (400 MHz, CDCl$_3$): δ 8.44 (d, $J = 8.0$ Hz 1 H), 7.31-7.29 (d, $J = 8.0$ Hz 1 H), 7.21-7.02 (m, 10 H), 6.90 (s, 1 H), 3.32 (s, 3 H), 2.32 (s, 3 H); **$^{13}$C NMR** (100 MHz, CDCl$_3$): δ 162.6 (C), 142.4 (C), 141.2 (C), 137.1 (C), 136.5 (C), 135.1 (C), 131.4 (2 CH), 131.3 (2 CH), 129.8 (2 CH), 128.1 (2CH), 128.0 (CH), 127.8 (CH), 126.6 (CH), 126.4 (CH), 124.9 (CH), 122.7 (C), 118.6 (C), 34.1 (CH$_3$), 21.8 (CH$_3$); **HRMS** (ESI) cal. for C$_{23}$H$_{19}$NO; found 325.1469; IR (KBr): 2931, 1645, 1604, 1548, 1425, 1080, 925, 830, 771, 698 cm$^{-1}$

### 6-Methoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ga)

![Structure of 6-Methoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ga)](structure.png)

Yellow solid, m.p. 220-223 °C, **$^1$H NMR** (400 MHz, CDCl$_3$): δ 8.47 (d, $J = 8.8$ Hz 1 H), 7.22-7.23 (m, 10 H), 6.50-6.49 (m, 1 H), 3.65 (s, 3 H), 3.30 (s, 3 H); **$^{13}$C NMR** (100 MHz, CDCl$_3$): δ 162.5 (C), 162.3 (C), 141.8 (C), 139.1 (C), 136.4 (C), 135.1 (C), 131.4 (2 CH), 129.9 (2 CH), 129.8 (2 CH), 128.1 (2 CH), 127.8 (2 CH), 126.7 (CH), 118.9 (C), 118.5 (C), 115.4 (CH), 106.9 (CH), 55.1 (CH$_3$), 34.0 (CH$_3$); **HRMS** (ESI) cal for C$_{23}$H$_{19}$NO$_2$ 341.1416, found 341.1414; IR (KBr): 2931, 1645, 1604, 1548, 1425, 1080, 925, 830, 771, 698 cm$^{-1}$

### 6-Chloro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ha)

![Structure of 6-Chloro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ha)](structure.png)

Yellow solid, m.p. 220-223 °C, **$^1$H NMR** (400 MHz, CDCl$_3$): δ 8.47 (d, $J = 8.8$ Hz 1 H), 7.22-7.23 (m, 10 H), 6.50-6.49 (m, 1 H), 3.65 (s, 3 H), 3.30 (s, 3 H); **$^{13}$C NMR** (100 MHz, CDCl$_3$): δ 162.5 (C), 162.3 (C), 141.8 (C), 139.1 (C), 136.4 (C), 135.1 (C), 131.4 (2 CH), 129.9 (2 CH), 129.8 (2 CH), 128.1 (2 CH), 127.8 (2 CH), 126.7 (CH), 118.9 (C), 118.5 (C), 115.4 (CH), 106.9 (CH), 55.1 (CH$_3$), 34.0 (CH$_3$); **HRMS** (ESI) cal for C$_{23}$H$_{19}$NO$_2$ 341.1416, found 341.1414; IR (KBr): 2931, 1645, 1604, 1548, 1427, 1030, 1080, 925, 813, 771, 698 cm$^{-1}$
Yellow solid, m.p. 267-270 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.46 (d, $J = 8.4$ Hz 1 H), 7.41-7.38 (m, 1 H), 7.23-7.08 (m, 9 H), 7.03-7.01 (m, 2 H), 3.31 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.1 (C), 142.6 (C), 138.6 (C), 138.4 (C), 135.6 (C), 134.7 (C), 131.3 (2 CH), 129.6 (3 CH), 128.3 (CH), 128.2 (2 CH), 128.1 (2 CH), 127.0 (2 CH), 124.6 (CH), 123.2 (C), 117.9 (C), 34.3 (CH); HRMS (ESI) cal. for C$_{22}$H$_{16}$ClNO 345.0920, found 345.0918; IR (KBr): 2923, 2854, 1651, 1614, 1548, 1427, 1002, 875, 833, 782 cm$^{-1}$

2-Methyl-3,4-diphenyl-6-(trifluoromethyl)isoquinolin-1(2H)-one (3ia)

White solid, m.p. 175-178 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.66 (d, $J = 8.4$ Hz 1 H), 7.67-7.65 (m,1 H), 7.42 (s, 1 H), 7.26-7.14 (m, 7 H), 7.12-7.09 (m, 2 H), 7.04-7.02 (m, 2 H), 3.35 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 161.9 (C), 142.9 (C), 137.2 (C), 135.4 (C), 134.5 (C), 133.6 (CH, $J_{C-F} = 321$ Hz), 131.3 (2 CH), 129.7 (2 CH), 129.0 (CH), 128.5 (CH), 128.3 (3 CH), 128.2 (2 CH), 127.3 (CH), 126.9 (C), 125.1 (C), 122.5 (C, $J_{C-F} = 222$ Hz), 123.2 (CH), 118.6 (C), 34.5 (CH); HRMS (ESI) cal. for C$_{23}$H$_{16}$F$_3$NO 379.1184, found 379.1183; IR (KBr): 2854, 1645, 1604, 1548, 1427, 1313, 1008, 785, 740 cm$^{-1}$

6-(Tert-butyl)-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ja)

White solid, m.p. 135-138 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.48 (d, $J = 8.0$ Hz 1 H), 7.56 (dd, $J = 8.0$ Hz 1 H), 7.22-7.08 (m, 12 H), 3.32 (s, 3 H), 1.20 (t, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.5 (C), 155.3 (C), 141.0 (C), 136.9 (C), 136.4 (C), 135.1 (C), 131.4 (2 CH), 129.9 (2 CH), 128.0 (2 CH), 128.0 (CH), 127.7 (2 CH), 127.5 (CH), 126.6 (CH), 124.6 (CH), 122.6 (C), 121.2 (CH), 119.1 (C), 35.0 (C), 34.1 (CH$_3$), 30.9 (3 CH$_3$); HRMS (ESI) cal. for C$_{25}$H$_{25}$NO 367.1936, found 367.1934; IR (KBr): 2960.20, 1654.00, 1588.20, 1480.03, 1080.20, 925.40, 760.30, 698.30 cm$^{-1}$

2,8-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3ka)
Yellow solid, m.p. 220-224 °C; **\textbf{1H NMR}** (400 MHz, CDCl$_3$): \(\delta\) 7.31-7.29 (m, 1 H), 7.23-7.18 (m, 9 H), 7.16-7.08 (m, 2 H), 7.04-6.95 (m, 1 H), 3.28 (s, 3 H), 3.02 (s, 3 H); **\textbf{13C NMR}** (100 MHz, CDCl$_3$): \(\delta\) 163.4 (C), 141.5 (C), 141.1 (C), 138.8 (C), 137.1 (C), 135.2 (C), 131.5 (2 CH), 131.1 (CH), 129.7 (3 CH), 128.0 (2 CH), 127.9 (2 CH), 127.8 (CH), 126.6 (CH), 123.6 (CH), 123.4 (CH), 118.7 (C), 34.2 (CH$_3$), 24.3 (CH$_3$); **HRMS** (ESI) cal. for C$_{23}$H$_{19}$NO$_3$ 325.1467, found 325.1467; IR (KBr): 2854, 1645, 1499, 1497, 1145, 948, 771, 730 cm$^{-1}$

**8-Fluoro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3la)**

White solid, m.p. 228-230 °C; **\textbf{1H NMR}** (400 MHz, CDCl$_3$): \(\delta\) 7.40-7.35 (m, 1 H), 7.23-7.00 (m, 11 H), 6.88 (d, \(J = 8.0\) Hz 1 H), 3.27 (s, 3 H); **\textbf{13C NMR}** (100 MHz, CDCl$_3$): \(\delta\) 161.8 (C, \(J_{\text{C-F}} = 381\) Hz ), 161.1 (C), 142.5 (C), 139.7 (C), 136.3 (C), 134.7 (C), 132.5 (CH, \(J_{\text{C-F}} = 10\) Hz), 131.4 (2 CH), 129.5 (2 CH), 128.2 (CH), 128.1 (2 CH), 127.9 (2 CH), 126.8 (CH), 121.2 (CH, \(J_{\text{C-F}} = 4\) Hz), 117.0 (C), 114.1 (C, \(J_{\text{C-F}} = 4\) Hz), 113.2 (CH, \(J_{\text{C-F}} = 21\) Hz), 34.0 (CH$_3$); **HRMS** (ESI) cal. for C$_{22}$H$_{16}$FNO 329.1216, found 329.1216; IR (KBr): 2923, 1651, 1611, 1483, 1417, 1134, 1048, 925, 781 cm$^{-1}$

**8-Chloro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ma)**

White solid, m.p. 220-222 °C; **\textbf{1H NMR}** (400 MHz, CDCl$_3$): \(\delta\) 7.48-7.47 (m, 1 H), 7.46-7.29 (m, 1 H), 7.22-7.00 (m, 11 H), 3.29 (s, 3 H); **\textbf{13C NMR}** (100 MHz, CDCl$_3$): \(\delta\) 160.8(C), 142.3 (C), 140.1 (C), 136.4 (C), 135.2 (C), 134.6 (C), 131.4 (2 CH), 131.3 (2 CH), 129.6 (2 CH), 129.4 (2 CH), 128.1 (CH), 127.9 (CH), 126.8 (CH), 124.5 (CH), 121.2 (C), 117.9 (C), 34.46 (CH$_3$); **HRMS** (ESI) cal. for C$_{22}$H$_{16}$ClNO 345.0920, found 345.0919; IR (KBr): 2931, 1649, 1597, 1443, 1417, 1380, 1070, 935, 861, 784 cm$^{-1}$

**7,8-Dimethoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3na)**
White solid, m.p. 221-223 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.20-7.09 (m, 7 H), 7.08-7.05 (m, 2 H), 7.01-6.99 (m, 2 H), 6.85-6.83 (d, \(J = 8.4\) Hz 1 H), 4.02 (s, 3 H), 3.87 (s, 3 H), 3.26 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 160.7 (C), 151.4 (C), 149.2 (C), 139.5 (C), 136.9 (C), 135.1 (C), 132.8 (C), 131.5 (2 CH), 129.9 (2 CH), 128.0 (2 CH), 127.9 (CH), 127.8 (2 CH), 126.6 (CH), 121.6 (CH), 119.8 (C), 118.1 (CH), 117.8 (C), 61.5 (OCH\(_3\)), 56.6 (CH\(_3\)), 34.2 (CH\(_3\)), 55.1 (CH\(_3\)); HRMS (ESI) cal. for C\(_{24}\)H\(_{21}\)NO\(_3\) 371.1521, found 371.1520; IR (KBr): 2954, 1647, 1610, 1483, 1427, 1070, 1001, 771 cm\(^{-1}\)

6-Methyl-4,5-diphenylthieno[2,3-c]pyridin-7(6H)-one (3oa)

Yellow solid, m.p. 242-243 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.59 (d, \(J = 8.0\) Hz 1 H), 7.26-7.23 (m, 3 H), 7.17-7.09 (m, 5 H), 7.05-7.03 (m, 2 H), 6.88 (d, \(J = 5.2\) Hz 1 H), 3.37 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 158.8 (C), 145.5 (C), 142.3 (C), 136.8 (C), 134.6 (C), 132.7 (CH), 130.6 (CH), 130.1 (CH), 128.8 (CH), 128.4 (CH), 128.3 (C), 127.8 (CH), 126.7 (CH), 124.7 (CH), 117.7 (C), 34.2 (CH\(_3\)); HRMS (ESI) cal. for C\(_{20}\)H\(_{15}\)NOS 317.0874, found 317.0872; IR (KBr): 2923, 1640, 1577, 1490, 1440, 780, 698 cm\(^{-1}\)

5-Fluoro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3pa)

Yellow solid, m.p. 244-246 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 8.39 (d, \(J = 8.0\) Hz 1 H), 7.45-7.39 (m, 1 H), 7.23-7.17 (m, 4 H), 7.11-7.02 (m, 7 H), 3.20 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): δ 161.6 (C), 158.1 (C, \(J_{C-F} = 253\) Hz), 142.6 (C), 138.3 (2 C), 134.6 (C), 130.6 (CH, \(J_{C-F} = 3\) Hz), 129.8 (2 CH), 128.2 (CH), 128.1 (2 CH), 127.1 (3 CH), 126.3 (CH), 125.9 (C, \(J_{C-F} = 9\) Hz), 124.0 (CH \(J_{C-F} = 4\) Hz), 119.0 (CH), 118.7 (CH), 114.6 (C), 34.5 (CH\(_3\)); HRMS (ESI) cal. for C\(_{22}\)H\(_{16}\)FNO 329.1216, found 329.1215; IR (KBr): 2954, 1651, 1611, 1548, 1416, 1002, 833, 782 cm\(^{-1}\)
2,7-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3qa)

White solid, m.p. 232-234 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta 8.35 (s, 1\ H), 7.34-7.32 (m, 1\ H), 7.24-7.02 (m, 11\ H), 3.33 (s, 3\ H), 2.47 (s, 3\ H)\); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta 162.6 (C), 140.2 (C), 136.6 (2\ C), 135.1 (C), 134.8 (C), 133.4 (CH), 131.4 (2\ CH), 130.0 (CH), 128.1 (3\ CH), 127.8 (2\ CH), 127.3 (2\ CH), 126.6 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 34.3 (CH\textsubscript{3}), 21.3 (CH\textsubscript{3});\) HRMS (ESI) cal. for C\textsubscript{23}H\textsubscript{19}NO\textsubscript{3} 325.1467, found 325.1467; IR (KBr): 2923, 1645, 1499, 1340, 1142, 948, 770, 730 cm\textsuperscript{-1}

6,7-Dimethoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ra)

White solid, m.p. 240-242 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta 7.90 (s, 1\ H), 7.18-7.00 (m, 10\ H), 6.40 (s, 1\ H), 4.00 (s, 3\ H), 3.64 (s, 3\ H), 3.32 (s, 3\ H);\) \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta 161.9 (C), 153.0 (C), 149.0 (C), 139.8 (C), 136.6 (C), 135.1 (C), 132.5 (2\ CH), 131.3 (2\ CH), 130.0 (2\ CH), 128.0 (2\ CH), 128.0 (2\ CH), 127.8 (CH), 126.7 (CH), 118.9 (CH), 118.4 (CH), 107.6 (C), 105.5 (C), 55.6 (OCH\textsubscript{3}), 55.1 (OCH\textsubscript{3}), 34.3 (CH\textsubscript{3});\) HRMS (ESI) cal. for C\textsubscript{24}H\textsubscript{21}NO\textsubscript{3} 371.1521, found 371.1520; IR (KBr): 2954, 1645, 1604, 1483, 1415, 1230, 1143, 1072, 1001, 856, 781 cm\textsuperscript{-1}

7-Methyl-8,9-diphenyl-[1,3]dioxolo[4,5-f]isoquinolin-6(7H)-one (3sa)

White solid, m.p. 248-250 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta 8.21 (d, J = 8.4\ Hz 1\ H), 7.21-7.16 (M, 3\ H), 7.07-7.00 (m, 8\ H), 5.70 (s, 2\ H), 3.26 (s, 3\ H);\) \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta 162.0 (C), 150.5 (C), 142.0 (C), 141.8 (C), 137.4 (C), 134.8 (C), 131.2 (2\ CH), 129.9 (2\ CH), 128.0 (2\ CH), 126.9 (2\ CH), 126.4 (CH), 123.6 (CH), 121.6 (C), 120.3 (C), 114.5 (C), 108.9 (CH), 101.4 (CH\textsubscript{2}), 34.1 (CH\textsubscript{3});\) HRMS (ESI) cal. for C\textsubscript{23}H\textsubscript{17}NO\textsubscript{3} 355.1208, found 355.1206; IR (KBr): 2931, 1720, 1634, 1248, 1227, 1180, 925, 771, 705 cm\textsuperscript{-1}
2-Methyl-3,4-di-p-tolylisoquinolin-1(2H)-one (3ab)

Yellow solid, m.p. 197-198 °C; \textit{\textsuperscript{1}H NMR} (400 MHz, CDCl\textsubscript{3}):
\[\delta 8.53 \text{ (d, } J = 7.2 \text{ Hz, } 1 \text{ H}), 7.80-7.43 \text{ (m, } 2 \text{ H}), 7.14 \text{ (d, } J = 7.6 \text{ Hz, } 1 \text{ H}), 7.03-6.91 \text{ (m, } 8 \text{ H}), 3.13 \text{ (s, } 3 \text{ H}), 2.26 \text{ (s, } 3 \text{ H}); \textit{\textsuperscript{13}C NMR} (100 MHz, CDCl\textsubscript{3}):
\[\delta 162.8 \text{ (C), 141.3 (C), 137.8 (C), 137.4 (C), 136.1 (C), 133.5 (C), 132.2 (2 CH), 131.8 (2 CH), 131.3 (2 CH), 129.7 (2 CH), 128.8 (CH), 128.6 (CH), 127.7 (CH), 126.4 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 34.2 (CH\textsubscript{3}), 21.2 (CH\textsubscript{3}), 21.1 (CH\textsubscript{3}); \textit{HRMS} (ESI) cal. for C\textsubscript{24}H\textsubscript{21}NO 339.1623, found 339.1621; IR (KBr): 2854, 1640, 1592, 1480, 1411, 1080, 817, 773 cm\textsuperscript{-1}.}

3,4-Bis(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one (3ac)

Yellow solid, m.p. 161-162 °C; \textit{\textsuperscript{1}H NMR} (400 MHz, CDCl\textsubscript{3}):
\[\delta 8.52 \text{ (d, } J = 7.6 \text{ Hz, } 1 \text{ H}), 7.51-7.42 \text{ (m, } 2 \text{ H}), 7.16 \text{ (d, } J = 8.0 \text{ Hz, } 1 \text{ H}), 7.01 \text{ (dd, } J = 7.6 \text{ Hz, } 2 \text{ H}), 6.99 \text{ (dd, } J = 7.6 \text{ Hz, } 2 \text{ H}), 6.75-6.71 \text{ (m, } 4 \text{ H)}, \ 3.73 \text{ (s, } 6 \text{ H}), 3.32 \text{ (s, } 3 \text{ H}); \textit{\textsuperscript{13}C NMR} (100 MHz, CDCl\textsubscript{3}):
\[\delta 162.7 \text{ (C), 159.0 (C), 158.1 (C), 141.2 (C), 137.5 (C), 132.4 (2 CH), 131.8 (CH), 131.0 (2 CH), 128.8 (C), 127.7 (CH), 127.5 (C), 126.3 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 113.5 (2 CH), 113.3 (2 CH), 55.0 (OCH\textsubscript{3}), 55.0 (OCH\textsubscript{3}), 34.2 (CH\textsubscript{3}); \textit{HRMS} (ESI) cal. for C\textsubscript{24}H\textsubscript{21}NO 371.1521, found 371.1518; IR (KBr): 2923, 1730, 1644, 1548, 1427, 1180, 925, 862, 731 cm\textsuperscript{-1}.}

2-Methyl-3,4-bis(4-(trifluoromethyl)phenyl)isoquinolin-1(2H)-one (3ad)

\[\text{2-Me-3,4-bis(4-(CF\textsubscript{3})\textsuperscript{3})-I-1(2H)-one (3ad)}\]
White solid, m.p. 198-200 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.56-8.54 (m, 1 H), 7.57-7.46 (m, 8 H), 7.27-7.25 (m, 2 H), 7.19-7.17 (m, 2 H), 7.05-7.03 (m, 1 H), 3.31 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.4 (C), 139.9 (2 C), 138.1 (C), 136.3 (C), 132.4 (CH), 131.8 (2 CH), 130.8 (C, \(J_{C-F} = 32\) Hz), 130.3 (2 CH), 129.1 (C, \(J_{C-F} = 32\) Hz), 129.0 (C), 128.1 (CH), 127.3 (CH), 125.5 (CH), 125.2 (CH), 125.1 (CH), 125.0 (CH), 122.3 (C, \(J_{C-F} = 35\) Hz), 117.7 (C), 34.3 (CH\(_3\)); HRMS (ESI) cal. for C\(_{24}\)H\(_{15}\)F\(_6\)NO 447.1058, found 447.1057; IR (KBr): 2923, 2399, 1639, 1604, 1548, 1447, 1080, 817, 771, 728 cm\(^{-1}\)

3,4-Bis(4-bromophenyl)-2-methylisoquinolin-1(2H)-one (3ae)

White solid, m.p. 202-204 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.53 (d, \(J = 8.4\) Hz 1 H), 7.39(dd, \(J = 16.8\) Hz 2 H), 7.39-7.33 (m, 4 H), 7.09-7.06 (m, 1 H), 6.99 (dd, \(J = 8.4\) Hz 2 H), 6.92 (d, \(J = 8.4\) Hz 2 H), 3.30 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.5 (C), 140.1 (C), 136.6 (C), 135.1 (C), 133.6 (C), 133.0 (2 CH), 132.2 (CH), 131.7 (2 CH), 131.4 (4 CH), 127.9 (CH), 127.0 (CH), 125.0 (CH), 124.9 (C), 122.8 (C), 121.3 (C), 117.8 (2 C), 34.3 (CH\(_3\)); HRMS (ESI) cal. for C\(_{22}\)H\(_{15}\)Br\(_2\)NO 468.9520, found 468.9519; IR (KBr): 2954, 1640, 1604, 1548, 1427, 1159, 1054, 771, 730 cm\(^{-1}\)

3,4-Bis(4-fluorophenyl)-2-methylisoquinolin-1(2H)-one (3af)

White solid, m.p. 173-175 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.54 (d, \(J = 8.0\) Hz 1 H), 7.55-7.47 (m, 2 H), 7.11-7.06 (m, 3 H), 7.01-6.87 (m, 6 H), 3.30 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.6 (C), 162.2 (C, \(J_{C-F} = 248\) Hz), 161.6 (C, \(J_{C-F} = 246\) Hz), 140.4 (C), 136.9 (C), 133.0 (2 CH, \(J_{C-F} = 8\) Hz), 132.2 (C), 132.1 (CH), 131.7 (2 CH, \(J_{C-F} = 8\) Hz), 130.9 (C), 127.9 (CH), 126.8 (CH), 125.1 (CH), 124.4 (C), 118.1 (C), 115.6 (CH), 115.4 (CH), 115.2 (CH), 115.0 (CH), 34.2 (CH\(_3\)); HRMS (ESI) cal. for C\(_{22}\)H\(_{15}\)F\(_2\)NO 347.1122, found 347.1121; IR (KBr): 2928,
1640, 1604, 1508, 1482, 1080, 817, 771, 728 cm⁻¹

2-Methyl-3,4-di(thiophen-2-yl)isoquinolin-1(2H)-one (3ag)

Brown solid, m.p. 228-230 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.51 (d, \(J = 7.6\) Hz 1 H), 7.57-7.50 (m, 2 H), 7.36-7.31 (m, 2 H), 7.25-7.24 (m, 1 H), 6.94-6.91 (m, 3 H), 6.83-6.82 (m, 1 H), 3.31 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.6 (C), 137.1 (C), 136.9 (C), 136.2 (C), 134.9 (C), 132.3 (CH), 130.1 (CH), 129.7 (CH), 127.7 (2 CH), 127.3 (CH), 126.6 (CH), 126.5 (2 CH), 125.4 (CH), 125.1 (C), 114.2 (C), 34.2 (CH\(_3\)); HRMS (ESI) cal. for C\(_{18}\)H\(_{13}\)NOS\(_2\) 323.0439, found 323.0441; IR (KBr): 2957, 1640, 1604,1548,1470, 780, 760, 700 cm⁻¹

2-Methyl-3,4-dipropylisoquinolin-1(2H)-one (3ah)

Yellow solid, m.p. 60-62 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.44 (d, \(J = 8.0\) Hz 1 H), 7.60-7.59 (m, 2 H), 7.41-7.36 (m, 1 H), 3.60 (s, 3 H), 2.71-2.64 (m, 4 H), 1.64-1.53 (m, 4 H), 1.08-1.01 (m, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.9 (C), 139.8 (C), 136.4 (C), 131.8 (C), 128.2 (C), 125.5 (2 CH), 124.7 (CH), 122.5 (2 CH), 113.8 (4 CH), 31.7 (CH), 31.2 (CH), 29.76 (CH), 23.60 (C), 22.5 (C), 14.3 (C), 14.1 (CH\(_3\)); HRMS (ESI) cal. for C\(_{16}\)H\(_{21}\)NO 243.1623, found 243.1622; IR (KBr): 2931, 1645, 1547, 1457, 1057, 898, 740 cm⁻¹

4-Ethyl-2-methyl-3-phenylisoquinolin-1(2H)-one (3ai)

Yellow solid, m.p. 130-132 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.52-8.50 (m, 1 H), 7.84-7.65 (m, 2 H), 7.52-7.44 (m, 4 H), 7.28-7.24 (m, 2 H), 3.21 (s, 3 H), 2.40 (q, 2 H), 1.05 (t, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 162.5 (C), 140.1 (C), 136.0 (C), 135.6 (C), 132.1 (CH), 129.1 (CH), 129.0 (2 CH), 128.7 (CH), 128.4
(CH), 127.7 (CH), 126.3 (CH), 125.7 (C), 123.1 (CH), 116.7 (C), 34.11 (CH), 22.6 (CH₂), 14.8 (CH₃); HRMS (ESI) cal. for C₁₈H₁₇NO 263.1310, found 263.1310; IR (KBr): 3010, 1641, 1485, 1409, 1186, 1007, 840, 787, 704 cm⁻¹

4-Butyl-3-(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one (3aj)

White semi-solid, ¹H NMR (400 MHz, CDCl₃): δ 8.51-8.49 (m, 1 H), 7.67-7.61 (m, 2 H), 7.47-7.42 (m, 1 H), 7.16-7.14 (m, 2 H), 7.00-6.96 (m, 2 H), 3.84 (s, 3 H), 3.20 (s, 3 H), 2.39-2.35 (m, 2 H), 1.42-1.37 (m, 2 H), 1.20-1.16 (m, 2 H), 0.77-0.73 (m, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 162.4 (C), 159.6 (C), 140.0 (C), 136.2 (C), 131.8 (CH), 130.3 (2 CH), 128.1 (CH), 127.7 (C), 126.1 (CH), 123.1 (CH), 115.9 (C), 114.1 (2 CH), 113.9 (C), 55.22 (OCH₃), 33.96 (CH₃), 32.49 (CH₃), 28.1 (CH₂), 22.7 (CH₂), 13.7 (CH₂); HRMS (ESI) cal. for C₂₁H₂₃NO 321.1729, found 321.1729; IR (KBr): 2957, 1642, 1611, 1518, 1411, 1180, 840, 771, 700 cm⁻¹

Ethyl 2-methyl-1-oxo-3-phenyl-1,2-dihydroisoquinoline-4-carboxylate (3ak)

White solid, m.p. 167-170 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.49 (d, J = 7.6 Hz 1 H), 7.67-7.65 (m, 2 H), 7.53-7.49 (m, 1 H), 7.47-7.44 (m, 3 H), 7.36-7.33 (m, 2 H), 3.94 (q, 2 H), 3.30 (s, 3 H), 0.84 (t, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 166.9 (C), 162.5 (C), 143.5 (C), 134.3 (C), 133.4 (C), 132.7 (CH), 129.3 (CH), 129.0 (2 CH), 128.6 (2 CH), 128.0 (CH), 127.2 (CH), 124.5 (C), 123.9 (CH), 112.5 (C), 61.0 (CH₂), 34.0 (CH₃), 13.4 (CH₃); HRMS (ESI) cal. for C₁₉H₁₇NO₃ 307.1208, found 307.1208; IR (KBr): 2923, 1730, 1644, 1284, 1247, 1193, 761, 705 cm⁻¹

3-((Dimethylamino)methyl)-6-methoxy-2-methyl-4-phenylisoquinolin-1(2H)-one (3fj)

S-24
White solid, m.p. 167-170 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.40 (d, $J = 8.8$ Hz 1 H), 7.46-7.40 (m, 3 H), 7.19-7.02 (m, 2 H), 7.01 (d, $J = 8.0$ Hz, 1 H), 6.28 (s, 1 H), 3.81 (s, 3 H), 3.64 (m, 3 H), 3.24 (d, 2 H), 1.23 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.8 (C), 162.2 (C), 139.0 (C), 137.2 (C), 136.9 (C), 131.6 (2 CH), 129.9 (CH), 128.5 (2 CH), 127.6 (CH), 119.7 (C), 118.9 (C), 115.1 (CH), 107.3 (CH), 57.8 (OCH$_3$), 55.1 (CH$_2$), 44.6 (2 CH$_3$), 31.1 (CH$_2$); HRMS (ESI) cal. for C$_{20}$H$_{22}$N$_2$O$_2$ 322.1681, found 322.1682; IR (KBr): 2954, 1730.00, 1644.60, 1284.02, 1247.03, 1193.10, 761.80, 705.00 cm$^{-1}$

5,6,13-Triphenyl-8H-isoquinolinol[3,2-a]isoquinolin-8-one (3ta)

Yellow solid, m.p. 165-167 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.24 (d, $J = 8.0$ Hz 1 H), 7.61-7.47 (m, 6 H), 7.42 (t, $J = 16.0$ Hz, 1 H), 7.33 (dd, $J = 8.0$ Hz 1 H), 7.27-7.06 (m, 13 H), 6.86 (t, $J = 16.0$ Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 162.2 (C), 138.6 (C), 137.1 (2 C), 136.3 (C), 136.2 (C), 133.8 (C), 133.1 (C), 132.3 (CH), 132.2 (2 CH), 131.5 (2 CH), 129.7 (2 CH), 129.0 (CH), 128.9 (2 CH), 128.5 (CH), 128.1 (CH), 127.9 (2 CH), 127.6 (C), 127.4 (CH), 127.1 (2 CH), 126.9 (CH), 126.8 (CH), 126.7 (C), 126.4 (CH), 126.3 (CH), 125.8 (C), 125.6 (CH), 125.5 (CH), 116.9 (C); HRMS (ESI) cal. for C$_{35}$H$_{23}$NO 473.1780, found 473.1778; IR (KBr): 2923, 1644, 1538, 1180, 925, 862, 701 cm$^{-1}$

References

$^1$H and $^{13}$C NMR spectra of compound 3aa.
$^1$H and $^{13}$C NMR spectra of compound 3ba.

$^1$H and $^{13}$C NMR spectra of compound 3ca.
$^1$H and $^{13}$C NMR spectra of compound 3da.
$^{1}H$ and $^{13}C$ NMR spectra of compound 3ea.
$^1$H and $^{13}$C NMR spectra of compound 3fa.
$^1$H and $^{13}$C NMR spectra of compound 3ga.
\(^1\)H and \(^{13}\)C NMR spectra of compound 3ha.
$^1$H and $^{13}$C NMR spectra of compound 3ia.
$^1$H and $^{13}$C NMR spectra of compound 3ja
$^1$H and $^{13}$C NMR spectra of compound 3ka.
$^1$H and $^{13}$C NMR spectra of compound 3la
$^1$H and $^{13}$C NMR spectra of compound 3ma.
$^1$H and $^{13}$C NMR spectra of compound 3na
$^1$H and $^{13}$C NMR spectra of compound 30a
$^1$H and $^{13}$C NMR spectra of compound 3pa.
\(^1\)H and \(^{13}\)C NMR spectra of compound 3qa.
$^1$H and $^{13}$C NMR spectra of compound 3ra.
$^1$H and $^{13}$C NMR spectra of compound 3sa
$^{1}$H and $^{13}$C NMR spectra of compound 3ab.
$^1$H and $^{13}$C NMR spectra of compound 3ac.
$^1$H and $^{13}$C NMR spectra of compound 3ad.
$^1$H and $^{13}$C NMR spectra of compound 3ae.
$^1$H and $^{13}$C NMR spectra of compound 3af.
$^1$H and $^{13}$C NMR spectra of compound 3ag.
$^1$H and $^{13}$C NMR spectra of compound 3ah.
$^1$H and $^{13}$C NMR spectra of compound 3ai.
$^1$H and $^{13}$C NMR spectra of compound 3aj
$^1$H and $^{13}$C NMR spectra of compound 3ak
$^1$H and $^{13}$C NMR spectra of compound 3fl.

$^1$H and $^{13}$C NMR spectra of compound 3ta.
ORTEP diagram of compound 3aa
Table 1. Crystal data and structure refinement for mo_150714lt_0m (3aa).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>mo_150714lt_0m</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C22 H17 N O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>311.36</td>
</tr>
<tr>
<td>Temperature</td>
<td>100(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P -1</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 9.3178(12) Å, b = 9.5222(12) Å, c = 10.9385(14) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>789.02(18) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.311 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.080 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>328</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.20 x 0.20 x 0.15 mm³</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.102 to 26.485°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11&lt;=h&lt;=8, -11&lt;=k&lt;=11, -13&lt;=l&lt;=13</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>12357</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>3208 [R(int) = 0.0214]</td>
</tr>
<tr>
<td>Completeness to theta = 25.242°</td>
<td>99.3 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9485 and 0.8621</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3208 / 0 / 218</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.043</td>
</tr>
</tbody>
</table>
Final R indices [I>2sigma(I)]
R indices (all data)
Extinction coefficient
Largest diff. peak and hole

R1 = 0.0354, wR2 = 0.0897
R1 = 0.0422, wR2 = 0.0944
n/a
0.277 and -0.191 e.Å^{-3}

ORTEP diagram of compound 3ak

Table 2. Crystal data and structure refinement for mo_160743_0m_a (3ak).

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>mo_160743_0m_a</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C19 H17 N O3</td>
</tr>
<tr>
<td>Formula weight</td>
<td>307.33</td>
</tr>
<tr>
<td>Temperature</td>
<td>296(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P 21/c</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 9.4992(7) Å</td>
</tr>
<tr>
<td></td>
<td>b = 12.0176(9) Å</td>
</tr>
<tr>
<td></td>
<td>c = 14.7148(11) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>1600.6(2) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.275 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.087 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>648</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.22 x 0.18 x 0.16 mm³</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.232 to 26.457°.</td>
</tr>
</tbody>
</table>
Index ranges -11<=h<=11, -14<=k<=15, -18<=l<=18
Reflections collected 13301
Independent reflections 3284 [R(int) = 0.0487]
Completeness to theta = 25.242° 99.8 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.9485 and 0.8834
Refinement method Full-matrix least-squares on F²
Data / restraints / parameters 3284 / 0 / 210
Goodness-of-fit on F² 1.030
Final R indices [I>2sigma(I)] R1 = 0.0588, wR2 = 0.1424
R indices (all data) R1 = 0.1079, wR2 = 0.1690
Extinction coefficient n/a
Largest diff. peak and hole 0.309 and -0.329 e.Å⁻³

ORTEP diagram of compound 3f1

Table 3.  Crystal data and structure refinement for 160602LT_0M (3f1).
Identification code 160602lt_0m
Empirical formula C20 H22 N2 O2
Formula weight 322.39
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Monoclinic
Space group P 21/n
Unit cell dimensions a=10.0712(6) Å
                b = 9.0247(5) Å
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>$1706.90(16) , \text{Å}^3$</td>
</tr>
<tr>
<td>$Z$</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>$1.255 , \text{Mg/m}^3$</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.082 mm$^{-1}$</td>
</tr>
<tr>
<td>$F(000)$</td>
<td>688</td>
</tr>
<tr>
<td>Crystal size</td>
<td>$0.20 \times 0.18 \times 0.18 , \text{mm}^3$</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.169 to 26.406°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>$-12 \leq h \leq 12, -11 \leq k \leq 11, -23 \leq l \leq 23$</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>14501</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>3493 [R(int) = 0.0362]</td>
</tr>
<tr>
<td>Completeness to theta = 25.242°</td>
<td>99.8%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9485 and 0.8976</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on $F^2$</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3493 / 0 / 221</td>
</tr>
<tr>
<td>Goodness-of-fit on $F^2$</td>
<td>1.076</td>
</tr>
<tr>
<td>Final R indices [$I&gt;2\sigma(I)$]</td>
<td>$R_1 = 0.0424$, $wR_2 = 0.1059$</td>
</tr>
<tr>
<td>$R$ indices (all data)</td>
<td>$R_1 = 0.0539$, $wR_2 = 0.1133$</td>
</tr>
<tr>
<td>Extinction coefficient</td>
<td>n/a</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.325 and -0.327 e.Å$^{-3}$</td>
</tr>
</tbody>
</table>