Water-Mediated C-H Activation of Arenes with Secure Carbene Precursors: the Reaction and its Application

Ruifang Nie,† Ruizhi Lai,† Songyang Lv, Yingying Xu, Li Guo, Qiantao Wang* and Yong Wu*

Sichuan Engineering Laboratory for Plant-Sourced Drug and Research Center for Drug Industrial Technology, Key Laboratory of Drug-Targeting and Drug Delivery System of the Education Ministry
West China School of Pharmacy, Sichuan University
Chengdu, 610041 (China).

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1. General Information

Unless otherwise noted, all reactions were carried out in reaction vessels in sealed tubes. Reactions were carried out without any precautions to extrude moisture or air unless otherwise noted. Solvents used were of analytical purity. All reactions were monitored by thin-layer chromatography (TLC) and were visualized using UV light. Product purification was done using silica gel column chromatography. Thin layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2mm), while column chromatography characterization was performed with silica gel (100-200mesh). $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded with tetramethylsilane (TMS, $\delta = 0.00$ ppm) as the internal standard. $^1$H NMR spectra were recorded at 400 or 600 MHz (Varian), $^{13}$C NMR spectra were recorded at 100 or 150 MHz (Varian) and $^{19}$F NMR spectra were recorded at 376 MHz (Varian). Chemical shifts are reported in ppm downfield from CDCl$_3$ ($\delta = 7.26$ ppm) or DMSO-$d_6$ ($\delta = 2.54$ ppm) for $^1$H NMR and chemical shifts for $^{13}$C NMR spectra are reported in ppm relative to the central CDCl$_3$ ($\delta = 77.0$ ppm) or DMSO-$d_6$ ($\delta = 39.6$ ppm). Coupling constants were given in Hz. HRMS spectra were recorded on a Waters Q-TOF Premier. Melting points were measured with YRT-3 melting point apparatus (Shantou Keyi Instrument & Equipment Co., Ltd., Shantou, China). Commercial reagents were from Best-reagent (Homepage: http://www.best-reagent.com) or Astatech Chemical Technology Co, Ltd. (Homepage: http://www.astabio-chem.com). All reagents were used without further purification.

2. Preparation of sulfoxonium ylides$^{[1]}$

To a stirred solution of potassium tert-butoxide (1.0 g, 9.1 mmol) in THF (10 mL) was added trimethylsulfoxonium iodide (1.5 g, 6.9 mmol) at room temperature. The resulting mixture was refluxed for 2 h. Then the reaction mixture was cooled to 0 °C, followed by addition of acylchlorides (2.3 mmol) in THF (2 mL). The reaction was allowed to room temperature and stirred for 3 h. After the solvent was evaporated, water (20 mL) and ethyl acetate (20 mL) were added to the residual crude product. The aqueous layer was separated and washed with ethylacetate (3 × 20 mL) and the organic layers were combined. The organic solution was dried over anhydrous Na$_2$SO$_4$, and evaporated under vacuum. The residue was purified by column chromatography on silica gel to afford the sulfoxonium ylide.

3. Optimization of the reaction conditions (Table S1)

Table S1. Reaction optimization$^{[a]}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent$^{[b]}$</th>
<th>Yield$^{[d]}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Cp*RhCl$_2$]$_2$/AgSbF$_6$</td>
<td>[BMIM]BF$_4$</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>[Cp*RhCl$_2$]$_2$/AgSbF$_6$</td>
<td>[BMIM]NTf$_2$</td>
<td>53%</td>
</tr>
<tr>
<td>3</td>
<td>[Cp*RhCl$_2$]$_2$/AgSbF$_6$</td>
<td>[BTMG]PF$_6$</td>
<td>62%</td>
</tr>
</tbody>
</table>
4. General procedures for the acylmethylation (3a as an example)

\[
\begin{align*}
\text{1a} & \quad \text{2a} & \quad \text{3a} \\
\text{N} & \quad \text{O} & \quad \text{O} \\
\end{align*}
\]

A mixture of 2-phenylpyridines 1a (0.2 mmol), dimethyloxosulfonium benzyolmethylide 2a (0.4 mmol), [Cp*Rh(OAc)\(_2\)] (0.05 mmol) were weighed in a Schlenk tube equipped with a stir bar. Water (1.5 mL) was added and the mixture was stirred at 100 °C for 6 h under air. After completion, the reaction mixture was extracted with dichloromethane. The organic phase was evaporated under reduced pressure. The oily residue was purified by chromatography on a silica gel column (eluent: PE/EA = 50/1) and product 3a was obtained with a 86% yield.

5. General procedure for C-H activation/annulation of sulfoximines and sulfoxonium ylides (5c as an example)

\[
\begin{align*}
\text{4c} & \quad \text{2c} & \quad \text{5c} \\
\text{R} & \quad \text{R} & \quad \text{R} \\
\end{align*}
\]

A mixture of the S-phenyl-S-methylsulfoximines 4c (0.2 mmol), dimethyloxosulfonium tertbutyloxylide 2c (0.4 mmol), [Cp*Rh(OAc)\(_2\)] (0.05 mmol) were weighted in a Schlenk tube equipped with a stir bar. Water (1.5 mL) was added and the mixture was stirred at 100 °C for 24 h under air. After completion, the reaction mixture was extracted with dichloromethane. The organic phase was evaporated under reduced pressure. The oily residue was purified by chromatography on a silica gel column (eluent: PE/EA = 50/1) and product 5c was obtained with a 91% yield.
6. General procedure for C-H activation/annulation of benzylamines and sulfoxonium ylides (7a as an example)

\[
\begin{align*}
\text{6a} & \quad + \quad \text{2b} + [\text{Cp*RhOAc}_2] \quad \xrightarrow{\text{H}_2\text{O}, 100^\circ\text{C}, 24\ h} \quad \text{7a}
\end{align*}
\]

A mixture of benzylamine 6a (0.2 mmol), dimethyloxosulfonium 2,6-dimethoxyl-1-benzoylemethylide 2b (0.4 mmol), [Cp*Rh(OAc)] (0.05 mmol) were weighted in a Schlenk tube equipped with a stir bar. Water (1.5 mL) was added and the mixture was stirred at 100 °C for 24 h under air. After completion, the reaction mixture was extracted with dichloromethane. The organic phase was evaporated under reduced pressure. The oily residue was purified by chromatography on a silica gel column (eluent: PE/EA = 20/1) and product 7a was obtained with a 81% yield.

7. A large scale of the reactions (7a as an example)

\[
\begin{align*}
\text{6a} & \quad + \quad \text{2b} + [\text{Cp*RhOAc}_2] \quad \xrightarrow{\text{H}_2\text{O}, 100^\circ\text{C}, 24\ h} \quad \text{7a}
\end{align*}
\]

A mixture of benzylamine 6a (5 mmol), dimethyloxosulfonium 2,6-dimethoxyl-1-benzoylemethylide 2b (10 mmol), [Cp*Rh(OAc)] (0.15 mmol) were weighted in a Schlenk tube equipped with a stir bar. Water (25 mL) was added and the mixture was stirred at 100 °C for 24 h under air. After completion, the reaction mixture was extracted with dichloromethane. The organic phase was evaporated under reduced pressure. The oily residue was purified by chromatography on a silica gel column (eluent: PE/EA = 20/1) and product 7a was obtained with a 75% yield.

8. The synthesis of natural products

**Synthesis of decumbenine B**

(1) To a 75 ml tube was added benzo[d][1,3]dioxol-5-ylmethanamine B (907.2 mg, 6 mmol), sulfonium ylide C (721 mg, 3 mmol), [Cp*Rh(OAc)] 5 mol% (100 mg, 5 mol%) in H\text{2O} (15 mL). The tube was sealed and stirred at 100 °C for 24 h. Afterwards, the reaction mixture was extracted with dichloromethane. After extraction and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel (PE/EtOAc) to get yellow solid (compound A) in 30% yield. (264 mg).
(2) To a 75 ml oven-dried tube was added ZnBr$_2$ (0.045 mmol, 10 mg), RuCl$_3$·xH$_2$O (0.09 mmol, 22.8 mg), THF (5.0 mL), compound A (0.9 mmol, 264 mg), paraformaldehyde (4.5 mmol, 135.5 mg) and ZnMe$_2$ (3.2 mmol, 1.0 M in toluene, 3.2 mL) sequentially under argon. The tube was sealed and stirred at 60 °C for 24 h. After completion, the reaction mixture was diluted with saturated aq. NH$_4$Cl (30 mL) and extracted with ethylacetate (3 x 30 mL). Then the organic layer was dried with anhydrous sodium sulfate, concentrated in vacuo and purified by silica gel column chromatography (5:1 PE/DCM to 200:1 DCM/MeOH) to provide decumbenine B (198 mg, 68%).

Synthesis of Palmatine

(3) To a 75 ml tube was added (2,3-dimethoxyphenyl)methanamine (1 g, 6 mmol), sulfonium ylide E (768.9 mg, 3 mmol), [Cp*Rh(OAc)$_2$] 5 mol% (100 mg, 5 mol%) in H$_2$O (15 mL). The tube was sealed and stirred at 100 °C for 24 h. Afterwards, the reaction mixture was extracted with dichloromethane. After extraction and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel (PE/EtOAc) to get yellow solid (compound F) in 37% yield.

(4) A mixture of compound F (361 mg, 1.1mmol), 5-Diazo-2,2-dimethyl-1,3-dioxane-4,6-dione (224.6mg, 1.32 mmol) and [Cp*IrCl$_2$]$_2$ (43.8 mg, 5 mol %) was added in one-pot and stirred in MeOH (5 mL) at 100 °C for 2 h. The mixture was cooled to room temperature, filtered through a pad of Celite, and concentrated under reduced pressure. The residue was then purified by flash column chromatography to give compound G in 42% yield.

(5) Under Ar, compound G (183.6 mg) was suspended in dry THF. LiAlH$_4$ (2eq) in THF was added to the mixture dropwise at 0 °C, the mixture was stirred for half an hour and then diluted with EtOAc, and quenched with water. aq. NaOH (4M) was added and the mixture was stirred at room temperature for half an hour and then filtered through a plug of celite. After extraction and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel to get yellow solid.

(6) Then this yellow solid was dissolved in SOCl$_2$ and stirred at room temperature for 1h. The reaction mixture was concentrated under reduced pressure, and water was added. After extraction with EtOAc for 4 times, the oil layer was discarded and the aqueous layer was extracted with DCM. Then the combined organic layer was dried with anhydrous sodium sulfate and concentrated in vacuo to provide Palmatine (129.2 mg).
9. Mechanistic study

On the basis of the previously reported examples of the rhodium-catalyzed C-H activation with sulfoxonium ylides, the mechanism of acylmethylation and 1,2-benzothiazines formation was widely recognized.\[1,2\] However, benzylamines as C-H activation substrates had two possible paths according to previous related studies.\[3,4\] In order to gain the insight into the reaction mechanism, some experiments for the mechanistic study was conducted. First, using α-phenylbenzenemethanimine 9 with sulfoxonium ylide 2b under the standard reaction conditions was carried out (Scheme S1). α-Phenylbenzenemethanimine 9 was hydrolyzed completely, only affording diphenylmethanone 10 with a 85% yield (Scheme S2, \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.84 – 7.77 (m, 4H), 7.59 (td, \(J = 7.2, 1.4\) Hz, 2H), 7.53 – 7.43 (m, 4H)). This result indicated that aryl imine is extremely sensitive in water, and aryl amine is more likely as a directing group rather than imine.

\[
\begin{align*}
\text{NH} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{N}
\end{align*}
\]

Scheme S1. The reaction of α-phenylbenzenemethanimine

\[\text{α-phenylbenzenemethanimine 9} + \text{2b} \rightarrow \text{diphenylmethanone 10, 85%}\]

\[\text{H}_2\text{O, 100 °C 24 h} + \text{10, 85%} \]

Then, we used 6m with [Cp*Rh(OAc)\(_2\)] to obtained the intermediate I (Scheme S3). Unfortunately, we failed to isolated the intermediate I after trying our best. Therefore, the \(^1\)H NMR spectrum of the reaction mixture was confirmed (Scheme S4). The characteristic peaks showed that the intermediate I is possibly a amine complex, which stability is inferior to the imine complex.

\[
\begin{align*}
\text{NH} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{N}
\end{align*}
\]

Scheme S2. The \(^1\)H NMR Spectra of diphenylmethanone
Scheme S3. The intermediate I formation

The mixture was then recovered for the next reaction with sulfoxonium ylide 2b. The reaction still performed well affording the desired product 7m successfully (Scheme S5).

Scheme S5. The reaction of intermediate I with sulfoxonium ylide 2b

To further probe the pathway of this protocol, the reaction of benzylamine 6a and dimethyloxosulfonium 2,6-dimethoxy-1-benzoylmethylide 2b was carried out under Ar (Scheme S6).

Scheme S6. The key experiment for the mechanistic study

The reaction proceeded successfully affording the desired product 7a with a 80% yield. This result indicated that benzylamine 6a may occur C-H activation directly without an amine oxidation to imine. According to the relevant research,[3b] the extrusion of H₂ was also detected by phosphomolybdic acid/PdCl₂ testing paper (Scheme S7). Based on the results above, the possible mechanism for this protocol was more likely to be as shown in Scheme S8.
Schem S7. The test paper changing as the reaction proceeding

Scheme S8. The possible mechanism

10. Reference

11. Characterization data for the products

1-phenyl-2-(2-(pyridin-2-yl)phenyl)ethan-1-one (3a)

Yield 88% (48.0 mg). Yellow solid, m.p. 95-96 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.39 \text{ (d, } J = 4.2 \text{ Hz, } 1\text{H}), 7.90 \text{ (d, } J = 7.4 \text{ Hz, } 2\text{H}), 7.69 \text{ (td, } J = 7.8, 1.6 \text{ Hz, } 1\text{H}), 7.56 - 7.36 \text{ (m, } 7\text{H}), 7.35 - 7.30 \text{ (m, } 1\text{H}), 7.16 - 7.10 \text{ (m, } 1\text{H}), 4.53 \text{ (s, } 2\text{H}); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 197.8, 159.4, 148.6, 139.9, 137.1, 136.7, 133.4, 132.7, 131.9, 129.8, 128.6, 128.5 \text{ (2C), 128.3 (2C), 127.3, 123.8, 121.8, 43.6. HRMS (ESI): } m/z \text{ calculated for C}_{19}\text{H}_{15}\text{NO}^+: 274.1226, \text{ found: 274.1224.}

2-(3-methyl-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3b)

Yield 76% (43.7 mg). Yellow solid, m.p. 99-100 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.64 \text{ (d, } J = 4.4 \text{ Hz, } 1\text{H}), 7.76 \text{ (d, } J = 7.6 \text{ Hz, } 2\text{H}), 7.63 \text{ (td, } J = 7.6, 2.0 \text{ Hz, } 1\text{H}), 7.47 \text{ (t, } J = 7.2 \text{ Hz, } 1\text{H}), 7.35 \text{ (t, } J = 7.6 \text{ Hz, } 2\text{H}), 7.28 - 7.14 \text{ (m, } 4\text{H}), 7.11 \text{ (d, } J = 7.4 \text{ Hz, } 1\text{H}), 4.07 \text{ (s, } 2\text{H}), 2.07 \text{ (s, } 3\text{H}); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 198.1, 159.1, 149.4, 140.3, 136.7, 136.4, 136.2, 133.2, 132.9, 129.0, 128.5 \text{ (2C), 128.3, 128.2 (2C), 128.1, 125.3, 122.0, 43.4, 20.4. HRMS (ESI): } m/z \text{ calculated for C}_{20}\text{H}_{17}\text{NO}^+: 288.1383, \text{ found: 288.1381.}

2-(4-methyl-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3c)

Yield 80% (46.0 mg). Yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.42 \text{ (d, } J = 4.2 \text{ Hz, } 1\text{H}), 7.89 \text{ (d, } J = 7.4 \text{ Hz, } 2\text{H}), 7.68 \text{ (td, } J = 7.8, 1.7 \text{ Hz, } 1\text{H}), 7.52 \text{ (t, } J = 7.4 \text{ Hz, } 1\text{H}), 7.47 - 7.37 \text{ (m, } 3\text{H}), 7.32 \text{ (s, } 1\text{H}), 7.21 \text{ (s, } 2\text{H}), 4.47 \text{ (s, } 2\text{H}), 2.40 \text{ (s, } 3\text{H); } \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 198.2, 159.5, 148.6, 139.7, 137.1, 136.9, 136.7, 133.2, 132.9, 129.4, 128.4 (2C), 128.3 (2C), 123.9, 121.8, 43.1, 21.1. HRMS (ESI): } m/z \text{ calculated for C}_{20}\text{H}_{17}\text{NO}^+: 288.1383, \text{ found: 288.1381.}

2-phenyl-2-(2-(pyridin-2-yl)-4-(trifluoromethyl)phenyl)ethan-1-one (3d)

Yield 79% (53.9 mg). Yellow solid, m.p. 74-75 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta 8.48 – 8.38 \text{ (m, } 1\text{H}), 7.92 – 7.84 \text{ (m, } 2\text{H}), 7.75 \text{ (td, } J = 7.8, 1.8 \text{ Hz, } 1\text{H}), 7.69 \text{ (d, } J = 1.8 \text{ Hz, } 1\text{H}), 7.65 \text{ (dd, } J = 8.0, 1.8 \text{ Hz, } 1\text{H}), 7.58 – 7.51 \text{ (m, } 1\text{H}), 7.51 – 7.39 \text{ (m, } 4\text{H}), 7.21 \text{ (ddd, } J = 7.6, 5.0, 1.2 \text{ Hz, } 1\text{H}), 4.56 \text{ (s, } 2\text{H); } \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 198.3, 159.5, 148.6, 139.7, 137.1, 136.9, 136.7, 132.7, 131.6, 130.6, 130.2, 129.4, 128.4 (2C), 128.3 (2C), 123.9, 121.8, 43.1, 21.1. HRMS (ESI): } m/z \text{ calculated for C}_{20}\text{H}_{14}\text{F}_{3}\text{NOH}^+: 342.1100, \text{ found: 342.1102.}

2-(5-methoxy-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3e)

Yield 85% (51.6 mg). Yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.33 \text{ (d, } J = 4.2 \text{ Hz, } 1\text{H}), 7.90 \text{ (d, } J = 7.4 \text{ Hz, } 2\text{H}), 7.66 \text{ (td, } J = 7.7, 1.9 \text{ Hz, } 1\text{H}), 7.53 \text{ (t, } J = 7.4 \text{ Hz, } 1\text{H}), 7.43 \text{ (q, } J = 8.4, 7.3 \text{ Hz, } 4\text{H}), 7.12 – 7.05 \text{ (m, } 1\text{H}), 6.92 \text{ (dd, } J = 8.5, 2.7 \text{ Hz, } 1\text{H}), 6.86 \text{ (d, } J = 2.4 \text{ Hz, } 1\text{H}), 4.52 \text{ (s, } 2\text{H), 3.84 \text{ (s, } 3\text{H); } \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 197.8, 159.7, 148.4, 137.1, 136.7, 134.2, 132.7, 131.1, 130.0, 128.4 \text{ (2C), 128.3 (2C), 123.6, 121.3, 117.3, 112.7, 55.3, 43.9. HRMS (ESI): } m/z \text{ calculated for C}_{20}\text{H}_{17}\text{NO}^+: 304.1332, \text{ found: 304.1334.}
2-(5-methyl-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3f)

Yield 86% (49.4 mg). Yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36 (d, $J$ = 4.0 Hz, 1H), 7.90 (d, $J$ = 7.4 Hz, 2H), 7.72 – 7.62 (m, 1H), 7.53 (t, $J$ = 7.4 Hz, 1H), 7.48 – 7.34 (m, 4H), 7.19 (d, $J$ = 7.8 Hz, 1H), 7.16 – 7.05 (m, 2H), 4.50 (s, 2H), 2.39 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 198.0, 159.4, 148.4, 138.4, 137.2, 136.9, 136.6, 133.1, 132.6, 129.7, 128.4 (2C), 128.3, 128.2 (2C), 128.0, 123.7, 121.5, 43.5, 21.2. HRMS (ESI): m/z calculated for C$_{20}$H$_{17}$NOH$: 288.1383, found: 288.1381.

2-(5-chloro-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3g)

Yield 86% (52.9 mg). Yellow solid, m.p. 55-56 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36 (d, $J$ = 4.8 Hz, 1H), 7.88 (d, $J$ = 7.8 Hz, 2H), 7.70 (td, $J$ = 7.8, 2.0 Hz, 1H), 7.54 (t, $J$ = 7.4 Hz, 1H), 7.48 – 7.39 (m, 4H), 7.38 – 7.31 (m, 2H), 7.14 (dd, $J$ = 7.6, 4.8 Hz, 1H), 4.51 (s, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 197.0, 158.0, 148.3, 137.2, 136.8, 135.3, 132.9, 131.9, 131.0, 130.1, 128.5 (2C), 128.4, 128.1 (2C), 127.5, 123.9, 122.2, 43.3. HRMS (ESI): m/z calculated for C$_{19}$H$_{14}$ClNOH$: 308.0837, found: 308.0835.

2-(5-nitro-2-(pyridin-2-yl)phenyl)-1-phenylethan-1-one (3h)

Yield 56% (35.7 mg). Yellow solid, m.p. 111-112 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.38 (d, $J$ = 4.2 Hz, 1H), 8.31 – 8.15 (m, 2H), 7.90 (d, $J$ = 7.6 Hz, 2H), 7.75 (t, $J$ = 7.6 Hz, 1H), 7.67 (d, $J$ = 8.4 Hz, 1H), 7.57 (t, $J$ = 7.2 Hz, 1H), 7.47 (dt, $J$ = 15.0, 7.6 Hz, 3H), 7.24 – 7.14 (m, 1H), 4.65 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.4, 157.3, 148.9, 147.6, 146.0, 137.1, 136.6, 135.6, 133.2, 130.7, 128.7 (2C), 128.1 (2C), 127.2, 124.0, 122.9, 122.3, 43.5. HRMS (ESI): m/z calculated for C$_{19}$H$_{14}$N$_2$O$_3$H$: 319.1077, found: 319.1075.

1-phenyl-2-(3-(pyridin-2-yl)naphthalen-2-yl)ethan-1-one (3i)

Yield 94% (60.8 mg). Brown solid, m.p. 98-99 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.42 (d, $J$ = 4.4 Hz, 1H), 7.97 (s, 1H), 7.94 – 7.86 (m, 3H), 7.86 – 7.78 (m, 2H), 7.74 (t, $J$ = 7.8 Hz, 1H), 7.60 (d, $J$ = 7.8 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.46 – 7.36 (m, 2H), 7.20 – 7.11 (m, 1H), 4.72 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 197.9, 159.5, 148.4, 147.6, 146.0, 137.1, 136.6, 135.6, 133.2, 130.7, 128.7 (2C), 128.1 (2C), 127.2, 124.0, 122.9, 122.3, 43.5. HRMS (ESI): m/z calculated for C$_{23}$H$_{17}$NO$: 324.1388, found: 324.1387.

1-phenyl-2-(2-(pyridin-2-yl)thiophen-3-yl)ethan-1-one (3j)

Yield 77% (43.0 mg). Yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.45 (q, $J$ = 1.7 Hz, 1H), 8.04 (d, $J$ = 7.3 Hz, 2H), 7.65 (td, $J$ = 7.7, 1.9 Hz, 1H), 7.54 (t, $J$ = 7.8 Hz, 2H), 7.46 (d, $J$ = 7.8 Hz, 2H), 7.33 (d, $J$ = 5.1 Hz, 1H), 7.16 – 7.06 (m, 1H), 7.02 (d, $J$ = 5.1 Hz, 1H), 4.75 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 197.7, 153.1, 149.1, 138.1, 137.1, 136.9, 133.2, 132.9, 131.7, 128.6 (2C), 128.5 (2C), 125.3, 122.1, 121.6, 39.8. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$NOS$: 280.0791, found: 280.0792.

1-phenyl-2-(5-(pyridin-2-yl)benzo[d][1,3]dioxol-4-yl)ethan-1-one (3k)
Yield 77% (48.9 mg). Yellow solid, m.p. 100-101 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.33 (d, \(J = 4.2\) Hz, 1H), 7.94 (d, \(J = 7.6\) Hz, 2H), 7.65 (t, \(J = 7.5\) Hz, 1H), 7.55 (t, \(J = 7.4\) Hz, 1H), 7.44 (t, \(J = 7.8\) Hz, 3H), 7.09 (dd, \(J = 7.6, 4.8\) Hz, 1H), 7.04 (d, \(J = 8.2\) Hz, 1H), 6.85 (d, \(J = 8.0\) Hz, 1H), 6.01 (s, 2H), 4.53 (s, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 196.6, 158.6, 148.2, 147.6, 137.0, 136.9, 133.3, 132.7, 130.1, 128.4 (2C), 128.1 (2C), 123.6, 123.5, 121.5, 115.6, 107.1, 101.3, 37.1. HRMS (ESI): m/z calculated for C\(_{20}\)H\(_{15}\)NO\(_3\)H\(^+\):381.1125, found: 381.1123.

1-phenyl-2-(1-(pyridin-2-yl)-1H-indol-2-yl)ethan-1-one (3l)
Yield 54% (33.7 mg). Amorphous light yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.37 (dd, \(J = 5.2, 1.8\) Hz, 1H), 7.91 (d, \(J = 7.6\) Hz, 2H), 7.84 – 7.51 (m, 3H), 7.46 – 7.40 (m, 3H), 7.20 – 7.13 (m, 3H), 6.57 (s, 1H), 4.69 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 196.1, 151.4, 149.2, 138.4, 136.9, 136.7, 133.9, 133.0, 128.7, 128.5 (2C), 128.3 (2C), 122.3, 121.6, 120.9, 120.5, 120.2, 110.3, 106.0, 38.4. HRMS (ESI): m/z calculated for C\(_{21}\)H\(_{16}\)N\(_2\)OH+:313.1335, found: 313.1332.

1-phenyl-2-(2-(pyrimidin-2-yl)phenyl)ethan-1-one (3m)
Yield 78% (42.8 mg). Yellow solid, m.p. 115-116 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.51 (d, \(J = 4.8\) Hz, 2H), 8.30 – 8.22 (m, 1H), 8.02 (d, \(J = 7.4\) Hz, 2H), 7.57 (t, \(J = 7.4\) Hz, 1H), 7.51 – 7.43 (m, 4H), 7.38 – 7.33 (m, 1H), 7.04 (t, \(J = 4.8\) Hz, 1H), 4.69 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 165.7, 156.5, 137.7, 136.6, 135.0, 133.4, 132.9, 132.4, 130.9, 130.2, 130.1, 128.5 (2C), 128.1 (2C), 127.4, 118.6, 45.1. HRMS (ESI): m/z calculated for C\(_{18}\)H\(_{14}\)N\(_2\)OH+:275.1179, found: 275.1182.

2-(2-(1H-pyrazol-1-yl)phenyl)-1-phenylethan-1-one (3n)
Yield 55% (28.9 mg). Yellow solid, m.p. 72-73 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.88 (d, \(J = 7.6\) Hz, 2H), 7.61 (d, \(J = 2.0\) Hz, 1H), 7.54 (t, \(J = 7.4\) Hz, 1H), 7.51 – 7.33 (m, 6H), 6.34 (s, 1H), 4.40 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 197.1, 140.6, 140.0, 136.6, 133.1, 132.1, 131.0, 130.9, 128.6 (2C), 128.1 (2C), 127.4, 118.6, 45.1. HRMS (ESI): m/z calculated for C\(_{17}\)H\(_{14}\)N\(_2\)OH+:263.1179, found: 263.1182.

2-(2-(isoquinolin-3-yl)phenyl)-1-phenylethan-1-one (3o)
Yield 52% (33.6 mg). Yellow wax. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.11 (s, 1H), 7.93 (d, \(J = 8.2\) Hz, 1H), 7.73 (td, \(J = 7.7, 1.8\) Hz, 1H), 7.37 (m, 2H), 7.31 – 7.64 (m, 1H), 7.59 (td, \(J = 4.3, 2.1\) Hz, 2H), 7.50 – 7.45 (m, 1H), 7.44 – 7.32 (m, 5H), 4.55 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 198.1, 153.1, 151.4, 137.1, 136.5, 133.6, 132.6, 131.7, 130.6, 130.3, 130.1, 128.4, 128.4 (2C), 128.3 (2C), 127.5, 127.2, 126.8, 120.3, 43.6. HRMS (ESI): m/z calculated for C\(_{23}\)H\(_{17}\)NOH+:324.1383, found: 324.1382.

3,3-dimethyl-1-(2-(pyridin-2-yl)phenyl)butan-2-one (3p)
Yield 31% (15.2 mg). Colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.62 (d, \(J = 4.4\) Hz, 1H), 7.73 (td, \(J = 7.7, 1.8\) Hz, 1H), 7.43 – 7.37 (m, 2H), 7.37 – 7.33 (m,
2H), 7.24 – 7.17 (m, 2H), 4.12 (s, 2H), 1.04 (s, 9H). 13C NMR (100 MHz, CDCl3) δ 212.0, 159.1, 147.5, 139.5, 135.6, 132.3, 130.6, 128.7, 127.3, 126.0, 123.2, 120.7, 43.2, 40.5, 25.6 (3C). HRMS (ESI): m/z calculated for C17H19NOH+: 254.1539, found: 254.1542.

1-((3r,5r,7r)-adamantan-1-yl)-2-(2-(pyridin-2-yl)phenyl)ethan-1-one (3q)

Yield 85% (56.3 mg). Colorless oil. 1H NMR (400 MHz, CDCl3) δ 8.63 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.72 (td, J = 7.7, 1.9 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.36 – 7.32 (m, 2H), 7.22 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.19 – 7.14 (m, 1H), 4.05 (s, 2H), 1.98 (s, 3H), 1.72 – 1.67 (m, 9H), 1.66 – 1.60 (m, 3H). 13C NMR (100 MHz, CDCl3) δ 212.7, 160.0, 148.5, 140.4, 136.7, 133.4, 131.7, 129.8, 128.4, 126.9, 124.3, 121.8, 41.2, 38.7, 38.4 (3C), 36.5 (3C), 28.0 (3C). HRMS (ESI): m/z calculated for C23H25NOH+: 332.2009, found: 332.2011.

1-methyl-3-phenylbenzo[e][1,2]thiazine 1-oxide (5a)

Yield 35% (17.9 mg). Yellow solid, m.p. 94-95 °C. 1H NMR (400 MHz, CDCl3) δ 7.95 (d, J = 7.2 Hz, 2H), 7.80 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.44 – 7.34 (m, 5H), 6.68 (s, 1H), 3.62 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 147.1, 138.5, 136.7, 132.6, 128.9, 128.3 (2C), 127.2 (2C), 126.5, 126.3, 117.9, 96.2, 45.1, 36.3, 21.3 (2C). HRMS (ESI): m/z calculated for C15H13NOSH+: 256.0791, found: 256.0795.

3-isopropyl-1-methylbenzo[e][1,2]thiazine 1-oxide (5b)

Yield 90% (39.8 mg). White solid, m.p. 85-86 °C. 1H NMR (400 MHz, CDCl3) δ 7.70 (d, J = 8.1 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 5.95 (s, 1H), 3.48 (s, 3H), 2.60 (q, J = 6.8 Hz, 1H), 1.23 (s, 3H), 1.21 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 157.5, 136.9, 132.4, 126.4, 125.6, 123.3, 117.9, 96.2, 45.1, 36.3, 21.3 (2C). HRMS (ESI): m/z calculated for C12H15NOSH+: 222.0947, found: 222.0949.

3-(tert-butyl)-1-methylbenzo[e][1,2]thiazine 1-oxide (5c)

Yield 91% (42.4 mg). Yellow oil. 1H NMR (400 MHz, CDCl3) δ 7.71 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.37 – 7.23 (m, 2H), 6.06 (s, 1H), 3.47 (s, 3H), 1.27 (s, 9H); 13C NMR (100 MHz, CDCl3) δ 159.8, 137.0, 132.3, 126.8, 125.7, 123.2, 117.7, 95.2, 45.1, 37.3, 28.9 (3C). HRMS (ESI): m/z calculated for C13H17NOSH+: 236.1104, found: 236.1108.

3-(tert-butyl)-6-methoxy-1-methylbenzo[e][1,2]thiazine 1-oxide (5d)

Yield 91% (45.4 mg). White solid, m.p. 98-99 °C. 1H NMR (400 MHz, CDCl3) δ 7.60 (d, J = 8.1 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.31 – 7.23 (m, 2H), 6.06 (s, 1H), 3.47 (s, 3H), 1.27 (s, 9H); 13C NMR (100 MHz, CDCl3) δ 159.8, 142.8, 137.0, 132.3, 126.8, 125.7, 123.2, 117.7, 95.2, 45.1, 37.3, 28.9 (3C), 21.7. HRMS (ESI): m/z calculated for C14H19NOSH+: 250.1260, found: 250.1262.

3-(tert-butyl)-6-methoxy-1-methylbenzo[e][1,2]thiazine 1-oxide (5e)

Yield 89% (47.2 mg). White solid, m.p. 109-110 °C. 1H NMR (400 MHz, CDCl3) δ 7.63 (d, J = 8.8 Hz, 1H), 6.88 (dd, J = 8.8, 2.4 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 5.98 (s, 1H), 3.43 (s, 3H), 2.39 (s, 3H), 1.26 (s, 9H); 13C NMR (100 MHz, CDCl3) δ 159.7, 142.8, 137.2, 127.1, 126.4, 123.2, 115.3, 94.9, 45.2, 37.2, 28.9 (3C), 21.7. HRMS (ESI): m/z calculated for C14H19NOSH+: 250.1260, found: 250.1262.
$J = 2.3$ Hz, 1H), 5.96 (s, 1H), 3.86 (s, 3H), 3.41 (s, 3H), 1.26 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.6, 160.7, 139.8, 125.5, 115.2, 110.9, 107.6, 95.0, 55.6, 45.9, 37.4, 29.0 (3C). HRMS (ESI): $m/z$ calculated for C$_{14}$H$_{16}$NO$_2$SH$: 266.1209$, found: 266.1206.

3-(tert-butyl)-6-fluoro-1-methylbenzo[e][1,2]thiazine 1-oxide (5f)

Yield 70% (35.5 mg). Light yellow solid, m.p. 95-96 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.72 (dd, $J = 8.8$, 5.4 Hz, 1H), 7.03 (td, $J = 8.4$, 2.5 Hz, 1H), 6.92 (dd, $J = 10.0$, 2.5 Hz, 1H), 6.00 (s, 1H), 3.45 (s, 3H), 1.26 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 166.0, 163.4, 161.5, 140.2, 114.3, 114.1, 113.9, 111.6, 111.4, 94.9, 45.5, 37.4, 28.8 (3C).

19F NMR (376 MHz, CDCl$_3$) δ -105.9. HRMS (ESI): $m/z$ calculated for C$_{13}$H$_{16}$FNOSH$: 254.1009$, found: 254.1011.

3-(tert-butyl)-8-methoxy-1-methylbenzo[e][1,2]thiazine 1-oxide (5g)

Yield 85% (45.1 mg). White solid, m.p. 155-156 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42 (t, $J = 8.1$ Hz, 1H), 6.89 (d, $J = 8.0$ Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.04 (s, 1H), 4.01 (s, 3H), 3.66 (s, 3H), 1.27 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 160.0, 155.7, 139.1, 132.8, 119.5, 107.9, 106.2, 94.8, 56.2, 48.2, 37.2, 29.0(3C). HRMS (ESI): $m/z$ calculated for C$_{14}$H$_{18}$NO$_2$SH$: 266.1209$, found: 266.1206.

3-(tert-butyl)-1-isopropylbenzo[e][1,2]thiazine 1-oxide (5h)

Yield 30% (15.8 mg). Light Yellow solid, m.p. 60-61 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 (d, $J = 7.9$ Hz, 1H), 7.45 (t, $J = 7.5$ Hz, 1H), 7.33 – 7.13 (m, 2H), 5.88 (s, 1H), 3.71 (hept, $J = 7.1$, 6.2 Hz, 1H), 1.47 (d, $J = 6.4$ Hz, 3H), 1.26 (s, 9H), 1.07 (d, $J = 6.3$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 161.1, 139.3, 132.5, 126.5, 125.3, 124.3, 113.5, 93.8, 58.0, 37.7, 29.0(3C). HRMS (ESI): $m/z$ calculated for C$_{15}$H$_{21}$NOSH$: 264.1417$, found: 264.1414.

3-(tert-butyl)-1-phenylbenzo[e][1,2]thiazine 1-oxide (5i)

Yield 91% (54.1 mg). Yellow solid, m.p. 87 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.98 – 7.85 (m, 2H), 7.64 – 7.51 (m, 3H), 7.41 (ddd, $J = 8.2$, 7.0, 1.3 Hz, 1H), 7.32 – 7.13 (m, 2H), 7.15 (ddd, $J = 8.1$, 6.9, 1.2 Hz, 1H), 6.19 (s, 1H), 1.34 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.8, 141.1, 136.7, 133.1, 131.7, 129.1 (2C), 128.9 (2C), 125.7, 124.8, 118.7, 95.0, 37.6, 29.0 (3C). HRMS (ESI): $m/z$ calculated for C$_{18}$H$_{19}$NOSH$: 298.1260$, found: 298.1264.

1-benzyl-3-(tert-butyl) benzo[e][1,2]thiazine 1-oxide (5j)

Yield 62% (38.6 mg). Amorphous yellow solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.58 (d, $J = 7.9$ Hz, 1H), 7.41 (t, $J = 7.5$ Hz, 1H), 7.26 – 7.18 (m, 2H), 7.16 (t, $J = 7.4$ Hz, 2H), 7.09 (d, $J = 7.5$ Hz, 3H), 5.72 (s, 1H), 4.76 – 4.50 (m, 2H), 1.21 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 160.6, 139.1, 132.7, 131.2 (2C), 128.5, 128.4, 128.2 (2C), 126.4, 125.2, 124.9, 114.3, 94.2, 64.1, 37.5, 29.0 (3C). HRMS (ESI): $m/z$ calculated for C$_{19}$H$_{21}$NOSH$: 312.1417$, found: 312.1414.

3-(2,6-dimethoxyphenyl)isoquinoline (7a)

Yield 81% (43.0 mg). White solid, m.p. 148 °C. $^1$H NMR (400 MHz, CDCl$_3$)
δ 9.39 (s, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.71 (s, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 8.4 Hz, 1H), 6.69 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 157.3 (2C), 150.8, 146.4, 135.2, 129.0, 128.6, 126.5, 126.4, 125.9, 125.7, 121.4, 117.9, 103.1 (2C), 54.9 (2C). HRMS (ESI): m/z calculated for C₁₇H₁₅NO₂⁺: 266.1176, found: 266.1171.

3-(2,6-dimethoxyphenyl)-8-methylisoquinoline (7b)

Yield 80% (44.7 mg). White solid, m.p.: 158-160 °C. 1H NMR (400 MHz, CDCl₃) δ 9.59 (s, 1H), 7.69 (s, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.35 (m, 2H), 6.69 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H), 2.81 (s, 3H); 13C NMR (150 MHz, CDCl₃) δ 158.3 (2C), 148.8, 147.3, 136.6, 135.3, 129.9, 129.6, 127.6, 126.4, 125.1, 119.1, 104.21 (2C), 56.0 (2C), 18.5. HRMS (ESI): m/z calculated for C₁₈H₁₇NO₂⁺: 280.1332, found: 280.1336.

3-(2,6-dimethoxyphenyl)-8-fluoroisoquinoline (7c)

Yield 40% (22.7 mg). Light yellow solid, m.p. 68-69 °C. 1H NMR (400 MHz, CDCl₃) δ 9.65 (s, 1H), 7.71 (s, 1H), 7.60 (t, J = 4.0 Hz, 2H), 7.35 (t, J = 8.4 Hz, 1H), 7.24 – 7.16 (m, 1H), 6.69 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 158.3 (d, J = 256.9 Hz), 157.2 (2C), 147.6, 144.6 (d, J = 4.6 Hz), 136.6 (d, J = 3.6 Hz), 129.4 (d, J = 8.5 Hz), 128.8, 121.6 (d, J = 4.5 Hz), 120.8 (d, J = 2.8 Hz), 117.6, 116.9 (d, J = 15.9 Hz), 109.6 (d, J = 19.1 Hz), 103.1 (2C), 54.9 (2C). 19F NMR (376 MHz, CDCl₃) δ -123.3. HRMS (ESI): m/z calculated for C₁₇H₁₄FNO₂⁺: 284.1081, found: 284.1062.

3-(2,6-dimethoxyphenyl)-8-(trifluoromethyl)isoquinoline (7d)

Yield 89% (59.3 mg). Yellow solid, m.p. 101-102 °C. 1H NMR (400 MHz, CDCl₃) δ 9.46 (s, 1H), 8.12 (d, J = 12.0 Hz, 2H), 7.80 (s, 1H), 7.75 (dd, J = 8.4, 1.2 Hz, 1H), 7.37 (t, J = 8.4 Hz, 1H), 6.70 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 157.2 (2C), 150.8, 148.1, 134.2, 130.6 (q, J = 32.6 Hz), 129.0, 127.7, 127.0, 124.2, 123.2, 123.2 (q, J = 4.5 Hz), 122.0, 121.6 (d, J = 1.3 Hz), 117.3, 103.1 (2C), 54.9 (2C). 19F NMR (376 MHz, CDCl₃) δ -62.90. HRMS (ESI): m/z calculated for C₁₈H₁₄FNO₂⁺: 334.1049, found: 334.1046.

3-(2,6-dimethoxyphenyl)-7-methylisoquinoline (7e)

Yield 67% (37.4 mg). Light yellow solid, m.p. 98-99 °C. 1H NMR (400 MHz, CDCl₃) δ 9.29 (s, 1H), 7.75 (s, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.66 (s, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 8.4 Hz, 1H), 6.68 (d, J = 8.4 Hz, 2H), 3.72 (s, 6H), 2.55 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 158.3 (2C), 150.8, 146.7, 136.7, 134.6, 132.3, 129.5, 127.6, 126.5, 126.2, 122.1, 119.2, 104.2 (2C), 56.0 (2C), 21.8. HRMS (ESI): m/z calculated for C₁₈H₁₇NO₂⁺: 280.1332, found: 280.1334.

3-(2,6-dimethoxyphenyl)-7-methylisoquinoline (7f)

Yield 56% (31.3 mg). Brown oil. 1H NMR (400 MHz, CDCl₃) δ 9.31 (s, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 9.7 Hz, 2H), 7.42 (d, J = 8.4, 1.2 Hz, 1H), 7.34 (t, J = 8.4 Hz, 1H), 6.68 (d, J = 8.4 Hz, 2H), 3.73 (s, 6H), 2.54 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 157.3 (2C), 150.3, 146.3, 139.4, 135.6, 128.5, 128.2, 126.3, 124.8, 124.6, 120.9, 118.0, 103.1 (2C), 54.9 (2C).
54.9 (2C), 21.1. HRMS (ESI): m/z calculated for C_{18}H_{17}NO_2H^+: 280.1332, found: 280.1333.

3-(2,6-dimethoxyphenyl)-6-methoxyisoquinoline (7g)

Yield 43% (25.4 mg). Amorphous yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.25 (s, 1H), 7.89 (d, \(J = 9.0\) Hz, 1H), 7.60 (s, 1H), 7.34 (t, \(J = 8.4\) Hz, 1H), 7.22 (dd, \(J = 9.0, 2.4\) Hz, 1H), 7.07 (d, \(J = 2.4\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.94 (s, 3H), 3.73 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.9 (2C), 157.3, 156.3, 149.7, 146.5, 137.3, 128.6, 128.3, 122.2, 120.8, 119.2, 103.2, 103.1 (2C), 55.0 (2C). HRMS (ESI): m/z calculated for C_{18}H_{17}NO_2H^+: 296.1281, found: 296.1277.

3-(2,6-dimethoxyphenyl)-6-fluoroisoquinoline (7h)

Yield 30% (17.0 mg). Amorphous yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.38 (s, 1H), 8.03 (dd, \(J = 8.0, 4.0\) Hz, 1H), 7.68 (s, 1H), 7.43 (dd, \(J = 8.0, 4.0\) Hz, 1H), 7.36 (t, \(J = 8.4\) Hz, 1H), 6.69 (d, \(J = 8.4\) Hz, 2H), 3.74 (s, 6H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.3 (d, \(J = 253.0\) Hz), 157.2 (2C), 150.3, 147.0, 136.8 (d, \(J = 10.7\) Hz), 129.7 (d, \(J = 10.7\) Hz), 117.2, 116.6 (d, \(J = 25.9\) Hz), 109.0 (d, \(J = 20.9\) Hz), 103.1 (2C), 54.9 (2C). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -106.8. HRMS (ESI): m/z calculated for C_{17}H_{14}FNO_2H^+: 284.1081, found: 284.1067.

6-chloro-3-(2,6-dimethoxyphenyl)isoquinoline (7i)

Yield 40% (24.0 mg). Light yellow solid, m.p.: 97-98 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.34 (s, 1H), 7.93 (d, \(J = 8.7\) Hz, 1H), 7.81 (d, \(J = 2\) Hz, 1H), 7.62 (s, 1H), 7.52 (dd, \(J = 8.7, 2\) Hz, 1H), 7.35 (t, \(J = 8.4\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.73 (s, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.2 (2C), 150.5, 147.6, 135.9, 135.2, 128.8, 128.2, 127.0, 124.5, 120.5, 117.5, 103.1 (2C), 54.9 (2C). HRMS (ESI): m/z calculated for C_{17}H_{14}ClNO_2H^+: 300.0786, found: 300.0788.

6-bromo-3-(2,6-dimethoxyphenyl)isoquinoline (7j)

Yield 71% (48.9 mg). White solid, m.p. 68-69 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.34 (s, 1H), 7.99 (d, \(J = 1.6\) Hz, 1H), 7.86 (d, \(J = 8.8\) Hz, 1H), 7.65 (dd, \(J = 8.8, 1.6\) Hz, 1H), 7.61 (s, 1H), 7.35 (t, \(J = 8.4\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.73 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 158.2 (2C), 151.7, 148.7, 137.3, 130.5, 129.9 129.2, 128.8, 128.2, 124.5, 120.5, 118.5, 104.2 (2C), 56.0 (2C). HRMS (ESI): m/z calculated for C_{17}H_{14}BrNO_2H^+: 344.0279, found: 344.0281.

3-(2,6-dimethoxyphenyl)-6-(trifluoromethyl)isoquinoline (7k)

Yield 89% (24.0 mg). White solid, m.p. 98-99 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.73 (s, 1H), 8.00 (d, \(J = 8.4\) Hz, 1H), 7.91 (s, 1H), 7.81 (d, \(J = 8.4\) Hz, 1H), 7.78 (s, 1H), 7.68 (t, \(J = 7.8\) Hz, 1H), 7.37 (t, \(J = 8.4\) Hz, 1H), 6.70 (d, \(J = 8.4\) Hz, 2H), 3.74 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.2 (2C), 151.7, 148.7, 137.3, 130.5, 129.9 129.2, 128.9, 125.7, 124.9, 121.5, 118.5, 104.2 (2C), 56.0 (2C). HRMS (ESI): m/z calculated for C_{18}H_{14}F_3NO_2H^+: 334.1049, found: 334.1052.
3-(2,6-dimethoxyphenyl)-5-methoxyisoquinoline (7l)

Yield 74% (43.7 mg). Yellow solid, m.p. 138-139 °C. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 9.33 (s, 1H), 8.06 (s, 1H), 7.56 (d, \(J = 8.2\) Hz, 1H), 7.48 (t, \(J = 8.0\) Hz, 1H), 7.33 (t, \(J = 8.4\) Hz, 1H), 6.96 (d, \(J = 7.6\) Hz, 1H), 6.67 (d, \(J = 8.4\) Hz, 2H), 3.97 (s, 3H), 3.72 (s, 6H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta 157.3 (2C), 157.2, 149.2, 144.3, 131.0, 128.5, 127.5, 127.2, 122.4, 121.3, 117.8, 103.6, 103.1 (2C), 54.9 (2C), 54.4. HRMS (ESI): \(m/z\) calculated for C\(_{18}\)H\(_{17}\)NO\(_3\)H+: 296.1281, found: 296.1279.

3-(2,6-dimethoxyphenyl)benzo[h]isoquinoline (7m)

Yield 73% (46.0 mg). White solid, m.p. 202-203 °C. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 10.16 (s, 1H), 8.81 (d, \(J = 8.2\) Hz, 1H), 7.89 (d, \(J = 8.8\) Hz, 2H), 7.77 (s, 1H), 7.75 – 7.59 (m, 3H), 7.37 (t, \(J = 8.4\) Hz, 1H), 6.71 (d, \(J = 8.4\) Hz, 2H), 3.75 (s, 6H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta 157.3 (2C), 148.6, 145.1, 135.2, 131.1, 130.3, 128.7, 127.5, 126.7, 126.1, 124.2, 122.6, 122.3, 121.0, 117.8, 103.2 (2C), 55.0 (2C). HRMS (ESI): \(m/z\) calculated for C\(_{21}\)H\(_{17}\)NO\(_2\)H+: 316.1332, found: 316.1331.

5-(2,6-dimethoxyphenyl)thieno[2,3-c]pyridine (7n)

Yield 30% (43.7 mg). Yellow solid, m.p. 170-171 °C. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 9.28 (s, 1H), 7.75 (s, 1H), 7.71 (d, \(J = 5.4\) Hz, 1H), 7.40 – 7.31 (m, 2H), 6.68 (d, \(J = 8.3\) Hz, 2H), 3.73 (s, 6H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta 158.2, 147.5, 145.4, 144.0, 134.8, 131.8, 129.6, 123.2, 120.1, 118.9, 104.1 (2C), 56.0 (2C). HRMS (ESI): \(m/z\) calculated for C\(_{15}\)H\(_{13}\)NO\(_2\)SH+: 272.0740, found: 272.0742.

3-(2,6-dimethoxyphenyl)-1-methylisoquinoline (7o)

Yield 95% (53.1 mg). White solid, m.p. 196-197 °C. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 8.13 (d, \(J = 8.4\) Hz, 1H), 7.80 (d, \(J = 8.0\) Hz, 1H), 7.63 (t, \(J = 7.2\) Hz, 1H), 7.55 (t, \(J = 7.2\) Hz, 2H), 7.33 (t, \(J = 8.4\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.72 (s, 6H), 3.03 (s, 3H); \(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta 158.4 (2C), 158.0, 146.5, 136.4, 129.6, 129.4, 127.4, 126.6, 126.3, 125.6, 120.9, 119.5, 104.4 (2C), 56.0 (2C), 22.5. HRMS (ESI): \(m/z\) calculated for C\(_{18}\)H\(_{17}\)NO\(_2\)H+: 280.1332, found: 280.1335.

3-(2,6-dimethoxyphenyl)-1-phenylisoquinoline (7p)

Yield 95% (64.9 mg). White solid, m.p. 142-143 °C. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 8.11 (d, \(J = 8.4\) Hz, 1H), 7.89 (d, \(J = 8.2\) Hz, 1H), 7.76 (d, \(J = 7.6\) Hz, 2H), 7.72 (s, 1H), 7.68 – 7.62 (m, 1H), 7.56 – 7.43 (m, 4H), 7.32 (t, \(J = 8.4\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.77 (s, 6H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta 160.0 (2C), 158.5, 146.9, 139.9, 137.3, 130.3 (2C), 129.6, 129.5, 128.3, 128.2 (2C), 127.5, 127.2, 126.8, 125.6, 121.8, 104.5 (2C), 56.1 (2C). HRMS (ESI): \(m/z\) calculated for C\(_{23}\)H\(_{19}\)NO\(_2\)H+: 342.1489, found: 342.1487.

1-methyl-3-phenylisoquinoline (8a)

Yield 56% (24.6 mg). Yellow wax. \(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta 8.14 (t, \(J = 6.8\) Hz, 3H), 7.92 (s, 1H), 7.86 (d, \(J = 8.2\) Hz, 1H), 7.67 (t, \(J = 7.4\) Hz, 1H), 7.46 (s, 1H), 7.36 (d, \(J = 7.6\) Hz, 1H), 3.96 (s, 3H), 3.72 (s, 3H). HRMS (ESI): \(m/z\) calculated for C\(_{19}\)H\(_{15}\)NOH+: 273.1174, found: 273.1173.
7.57 (t, $J = 7.6$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 2H), 7.41 (t, $J = 7.4$ Hz, 1H), 3.05 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.5, 148.9, 138.7, 135.7, 129.0, 127.7 (2C), 127.3, 126.6, 126.0 (2C), 125.8, 125.5, 124.6, 114.3, 21.6. HRMS (ESI): m/z calculated for C$_{19}$H$_{13}$N$: 220.1121, found: 220.1122.

1-methyl-3-($o$-tolyl)isoquinoline (8b)

Yield 68% (24.6 mg). Yellow wax. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J = 8.4$ Hz, 1H), 7.91 – 7.81 (m, 2H), 7.74 – 7.66 (m, 2H), 7.62 (t, $J = 7.6$ Hz, 1H), 7.54 – 7.44 (m, 1H), 7.42 – 7.28 (m, 2H), 3.04 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.0, 152.5, 140.8, 136.4, 136.2, 130.8, 130.1, 130.0, 128.0, 127.4, 126.9, 126.1, 125.9, 125.7, 118.8, 22.5, 20.5. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$NH$: 234.1283, found: 234.1282.

3-(2-chlorophenyl)-1-methylisoquinoline (8c)

Yield 66% (33.5 mg). Yellow wax. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J = 8.4$ Hz, 1H), 7.91 – 7.81 (m, 2H), 7.74 – 7.66 (m, 2H), 7.62 (t, $J = 7.6$ Hz, 1H), 7.54 – 7.44 (m, 1H), 7.42 – 7.28 (m, 2H), 3.04 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.4, 148.0, 138.5, 134.9, 131.5, 130.9, 129.1, 128.1, 126.6, 126.2, 125.9, 125.4, 124.6, 118.9, 21.4. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$ClNH$: 254.0731, found: 254.0729.

3-(3-chlorophenyl)-1-methylisoquinoline (8d)

Yield 52% (26.4 mg). Yellow wax. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.22 – 8.08 (m, 2H), 8.01 (d, $J = 7.8$ Hz, 1H), 7.92 (s, 1H), 7.87 (d, $J = 8.2$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.60 (t, $J = 7.6$ Hz, 1H), 7.47 – 7.32 (m, 2H), 3.05 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 158.8, 148.3, 141.5, 136.6, 134.8, 130.3, 129.9, 128.3, 127.7, 127.1, 126.8, 125.7, 125.0, 115.6, 29.7. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$ClNH$: 254.0731, found: 254.0733.

3-(3-methoxyphenyl)-1-methylisoquinoline (8e)

Yield 57% (28.4 mg). Yellow solid, m.p. 66-67 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 (d, $J = 8.4$ Hz, 1H), 7.91 (s, 1H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.74 (s, 1H), 7.68 (dd, $J = 17.4$, 7.6 Hz, 2H), 7.57 (ddd, $J = 8.2$, 6.8, 1.2 Hz, 1H), 7.41 (t, $J = 8.0$ Hz, 1H), 6.96 (dd, $J = 8.4$, 2.8 Hz, 1H), 3.93 (s, 3H), 3.04 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.0, 157.5, 148.7, 140.3, 135.7, 129.0, 128.6, 126.6, 125.8, 125.6, 124.6, 118.7, 114.4, 113.2, 111.3, 54.3, 21.6. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$NOH$: 250.1226, found: 250.1228.

1-methyl-3-($p$-tolyl)isoquinoline (8f)

Yield 49% (22.9 mg). Yellow oil. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.11 (d, $J = 8.4$ Hz, 1H), 8.05 (d, $J = 7.8$ Hz, 2H), 7.89 (s, 1H), 7.84 (d, $J = 8.2$ Hz, 1H), 7.65 (t, $J = 7.4$ Hz, 1H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.31 (d, $J = 7.8$ Hz, 2H), 3.04 (s, 3H), 2.43 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 157.4, 149.0, 137.1, 136.0, 135.8, 128.9, 128.4 (2C), 126.5, 125.8 (2C), 125.5, 125.4, 124.6, 113.7, 21.6, 20.2. HRMS (ESI): m/z calculated for C$_{17}$H$_{15}$NH$: 234.1277, found: 234.1279.

3-(3,5-dimethylphenyl)-1-methylisoquinoline (8g)
Yield 46% (22.8 mg). White solid, m.p. 92-93 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.13 (dd, J = 8.4, 1.0 Hz, 1H), 7.91 (s, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.76 (s, 2H), 7.67 (dd, J = 8.2, 6.8, 1.2 Hz, 1H), 7.56 (ddd, J = 8.2, 6.8, 1.2 Hz, 1H), 7.05 (s, 1H), 3.06 (s, 3H), 2.44 (s, 6H). ¹³C NMR (150 MHz, CDCl₃) δ 158.4, 150.3, 139.6, 138.2 (2C), 136.8, 130.0, 130.0, 127.6, 126.6, 126.5, 125.6, 124.8 (2C), 115.3, 29.7, 21.5 (2C). HRMS (ESI): m/z calculated for C₁₈H₁₇N⁺: 248.1434, found: 248.1432.

1-methyl-3-(naphthalen-2-yl)isoquinoline(8h)

Yield 75% (40.4 mg). Brown solid, m.p. 98-99 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.68 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.08 (s, 1H), 7.98 – 7.84 (m, 2H), 7.70 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.55 – 7.45 (m, 2H), 3.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.7, 148.6, 135.8, 135.8, 132.7, 132.4, 129.2, 127.7, 127.3, 126.7, 126.6, 125.9, 125.6, 125.2, 125.1, 124.7, 123.8, 114.6, 21.6. HRMS (ESI): m/z calculated for C₂₀H₁₅N⁺: 270.1277, found: 270.1278.

3-(furan-2-yl)-1-methylisoquinoline (8i)

Yield 33% (13.8 mg). Yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, J = 8.2 Hz, 1H), 7.88 (s, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.65 (ddd, J = 8.2, 6.8, 1.2 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.13 (d, J = 3.6 Hz, 1H), 6.55 (dd, J = 3.4, 1.8 Hz, 1H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.9, 153.2, 141.9, 141.1, 135.5, 129.3, 126.6, 125.7, 125.6, 124.7, 112.0, 110.9, 107.1, 21.5. HRMS (ESI): m/z calculated for C₁₄H₁₁NO⁺: 210.0915, found: 210.0913.

3-(tert-butyl)isoquinoline (8j)

Yield 32% (11.9 mg). Yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (s, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.69 – 7.58 (m, 2H), 7.53 (t, J = 7.6 Hz, 1H), 1.47 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 161.8, 150.4, 135.5, 129.1, 126.3, 125.8, 125.5, 125.4, 113.2, 36.0, 29.2 (3C). HRMS (ESI): m/z calculated for C₁₃H₁₅N⁺: 186.1277, found: 186.1272.

3-((3r,5r,7r)-adamantan-1-yl)isoquinoline (8k)

Yield 46% (24.2 mg). Yellow solid, m.p. 63-64 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (s, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.67 (ddd, J = 8.2, 6.8, 1.2 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.13 (d, J = 3.6 Hz, 1H), 6.55 (dd, J = 3.4, 1.8 Hz, 1H), 3.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.7, 150.5, 135.6, 129.0, 126.3, 125.9, 125.6, 125.3, 113.4, 40.9 (3C), 37.2, 35.9 (3C), 27.8 (3C). HRMS (ESI): m/z calculated for C₁₉H₂₁N⁺: 264.1747, found: 264.1751.

8-(benzo[d][1,3]dioxol-5-yl)-[1,3]dioxolo[4,5-f]isoquinoline (A)

8-(benzo[d][1,3]dioxol-5-yl)-[1,3]dioxolo[4,5-f]isoquinoline (A)
Decumbenine B

Total yield 68% (44.0 mg). White solid, m.p. 224-225 °C. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 9.29 (s, 1H), 7.87 (s, 1H), 7.81 (d, \(J = 8.6\) Hz, 1H), 7.50 (d, \(J = 8.5\) Hz, 1H), 7.20 (d, \(J = 8.1\) Hz, 1H), 6.97 (d, \(J = 8.0\) Hz, 1H), 6.32 (s, 2H), 6.12 (s, 2H), 5.54 (t, \(J = 5.7\) Hz, 1H), 4.42 (d, \(J = 5.5\) Hz, 2H); \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) 152.1, 151.1, 147.2, 147.1, 146.6, 139.9, 134.5, 124.0, 123.2, 121.6, 121.3, 112.0, 111.1, 111.1, 107.6, 102.6, 101.3, 55.2. HRMS (ESI): \(m/z\) calculated for C\(_{18}\)H\(_{13}\)NO\(_5\)Na\(^+\): 346.0686; found: 346.0688.

3-(3,4-dimethoxyphenyl)-7,8-dimethoxyisoquinoline (F)

Yield 37% (24.1 mg). Yellow solid, m.p. 122-123 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.60 (s, 1H), 7.93 (s, 1H), 7.76 (d, \(J = 2.0\) Hz, 1H), 7.66-7.58 (m, 2H), 7.50 (d, \(J = 9.2\) Hz, 1H), 6.99 (d, \(J = 8.4\) Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 4.02 (s, 3H), 3.95 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 149.5, 149.3, 149.1, 148.6, 147.0, 144.0, 132.7, 132.4, 122.9, 122.9, 120.5, 119.1, 115.2, 111.3, 109.9, 61.8, 57.1, 56.0, 56.0. HRMS (ESI): \(m/z\) calculated for C\(_{19}\)H\(_{19}\)NO\(_4\)H\(^+\): 326.1387, found: 326.1372.

methyl 2-(2-(7,8-dimethoxyisoquinolin-3-yl)-4,5-dimethoxyphenyl)acetate (G)

Yield 35% (27.8 mg). Yellow oil. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 9.37 (s, 1H), 7.90 (s, 1H), 7.76 (s, 2H), 7.14 (s, 1H), 3.99 (d, \(J = 5.9\) Hz, 6H), 3.82 (d, \(J = 5.1\) Hz, 6H), 3.80 (s, 2H), 3.48 (s, 3H). \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) 172.3, 151.0, 149.0, 148.8, 148.1, 145.8, 143.2, 133.0, 132.1, 125.7, 123.5, 122.3, 121.3, 119.3, 115.8, 114.0, 61.7, 57.3, 56.2, 56.2, 51.8, 38.9. HRMS (ESI): \(m/z\) calculated for C\(_{22}\)H\(_{23}\)NO\(_6\)H\(^+\): 398.1598, found: 398.1599.

Palmatine

Yellow solid, m.p. 173-174 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.19 (s, 1H), 8.73 (s, 1H), 8.00 (d, \(J = 8.6\) Hz, 1H), 7.69 (d, \(J = 8.5\) Hz, 1H), 7.46 (s, 1H), 6.72 (s, 1H), 5.24 - 5.15 (m, 2H), 4.25 (s, 3H), 4.08 (s, 3H), 4.02 (s, 3H), 3.95 (s, 3H), 3.29 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 152.1, 150.3, 149.4, 146.0, 144.6, 137.8, 133.7, 128.1, 125.9, 123.8, 121.9, 120.3, 118.9, 110.7, 108.7, 62.6, 57.2, 57.0, 56.3, 29.8, 27.3. HRMS (ESI): \(m/z\) calculated for C\(_{21}\)H\(_{22}\)NO\(_4\)\(^{+}\) [M-Cl\(^-\)]: 352.1543, found: 352.1540.
12. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR Spectra of Products