Supplementary Information

for

Transition-Metal-Free Synthesis of 4-Amino Isoquinolin-1(2H)-ones via Tandem Reaction of Arynes and Oxazoles

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S1
1 General information

Unless otherwise indicated, all reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring bar. All other chemicals were obtained from commercial supplies and used as received without any further purification. Column chromatograph was performed with silica gel (200~300 mesh) and analytical TLC on silica gel 60-F254. $^1$H, $^{13}$C, $^{19}$F NMR and NOE spectra were recorded on a Bruker AVANCE III spectrometer (400 MHz, 100 MHz and 376 MHz, respectively), Chemical shifts are reported parts per million (ppm) referenced to CDCl$_3$ (δ 7.26 ppm), tetramethylsilane (TMS, δ 0.00 ppm) for $^1$H, $^{13}$C and $^{19}$F NMR. High-resolution mass spectra (HRMS) were obtained on a Q Exactive mass spectrometry and an LTQ Orbitrap XL mass spectrometry equipped with an APCI and ESI source from Thermo Scientific. X-Ray diffraction study for product 3ah was carried out on Bruker D8 VENTURE photon II diffractometer with Iµs 3.0 microfocus X-ray source using APEX III program.

2 Experimental section

2.1 General procedure for synthesis of substrates 1a-1g, 1j-1q, 1s and 1u:

Substrates were prepared according to the known literature. [1, 2] To a 150 mL round-bottom flask was added amino acid (10 mmol), dioxane/H$_2$O (v/v=2:1, 30 mL), NaOH (0.4 g, 10 mmol) and then cooled in an ice-bath. Subsequently, (Boc)$_2$O (3.27 g, 15 mmol) and NaHCO$_3$ (0.84 g, 10 mmol) were added to the reaction mixture which was reacted overnight at room temperature and monitored by TLC. After completion of the reaction, the solvent was evaporated to a half of the volume. The residue was diluted with EtOAc (40 mL), cooled in an ice-bath and acidified to pH=2-3 with 1.0 M HCl successively. The solution was layered, then the aqueous phase was extracted with EtOAc (2×20 mL). The combined organic phase was washed with 1.0 M HCl (20 mL), saturated NaHCO$_3$ (20 mL) and brine (20 mL) successively. The solution was concentrated under vacuum to give N-Boc-amino acid as colourless oil which was used for the next step without further purification.

To a solution of N-Boc-amino acid in anhydrous THF (30 mL) was added Et$_3$N (1.2 equiv) and cooled to -30 °C, at this time, ethyl chloroformate (1.1 equiv) was added dropwise. After reacting for 30 min, Et$_3$NH (2.0 equiv) was added and the solution was stirred at this temperature for additional 15 min. Subsequently, the reaction mixture was warmed to room temperature naturally and continued to stir until the reaction was completed (detected by TLC, about 2 h). The reaction mixture was quenched with H$_2$O (30 mL) and extracted with ethyl acetate (2×20 mL). The combined organic phase was washed with 1.0 M HCl (20 mL), saturated NaHCO$_3$ (20 mL) and brine (20 mL) successively. The organic phase was then dried and concentrated under vacuum to afford corresponding amide which was used for the next step without further purification.
The obtained amide (1.0 equiv) was treated with trifluoroacetic acid (13 equiv) in DCM (1.0 M) at room temperature for 1 h. After removal of the solvent and excess trifluoroacetic acid, the residue was re-dissolved in DCM (20 mL) and washed with saturated NaHCO₃ (30 mL). The aqueous layer was extracted with DCM (2×30 mL), and the combined organic layer was washed with brine, dried over anhydrous Na₂SO₄ and concentrated under vacuum to get unprotected amide. This unprotected amide was dissolved in 20 mL of anhydrous DCM and cooled to 0 °C. To the solution was added acetic formic anhydride (3.0 equiv) and the reaction was stirred at this temperature for 15 min at 0 °C. Then, the reaction was warmed to room temperature and stirred for an additional 1 h until the complete consumption of starting material. The reaction was subsequently quenched with ice-water and extracted with DCM (3×10 mL). The combined organic phase was washed with cold water (2×20 mL), saturated NaHCO₃ (3×20 mL), and brine (20 mL). The organic phase was dried over anhydrous Na₂SO₄, then concentrated under vacuum to give the corresponding formamide in quantitative yield. The crude formamide was used in the next step without further purification.

To a solution of formamide in dry THF (30 mL) was added Et₃N (5.0 equiv), then cooled it to -30 °C, at this time, POCl₃ (1.1 equiv) was added dropwise. The reaction mixture was reacted at this temperature for 2 h (monitored by TLC). Then, saturated aq. Na₂CO₃ (20 mL) was added and the reaction was warmed to room temperature. After separation of the reaction solution, the aqueous layer was extracted with ethyl acetate (2×20 mL), then the combined organic layer was washed with brine, dried and concentrated. The residue was dissolved in ethyl acetate (10 ml) and added silica gel for continued stirring overnight. Evaporation of the solvent under vacuum, followed by purification through flash chromatography on silica gel (200-300 mesh, PE/EtAc v/v=1:1), the desired 4, 5-disubstituted oxazole was obtained.

2.2 General procedure for synthesis of substrates 1h or 1i:[3, 4]

To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added the methyl isocyanoacetate (0.454 mL, 5 mmol, 1.0 equiv) and diethylamine (0.567 mL, 5.5 mmol, 1.1 equiv). Then, the reaction mixture was stirred at room temperature for overnight. The reaction mixture was further purified by silica gel flash chromatography (200-300 mesh, PE/EtAc v/v=2:1) to give the desired isocyanoacetamide.

To a solution of isocyanoacetamide (282 mg, 2 mmol, 1 equiv) in dry DMSO (10 mL) was added Cs₂CO₃ (978 mg, 3.0 mmol, 1.5 equiv). The mixture was stirred at room temperature for 10 min under an nitrogen atmosphere. Fluoroarene (2 mmol, 1 equiv) was added and stirring was continued at room temperature for 15 h. Then, the reaction was quenched with water and diluted with AcOEt (30 mL). After separation
of the reaction mixture, the aqueous phase was extracted with AcOEt (3×30 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue was re-dissolved in AcOEt (10 mL) and added silica gel for continued stirring overnight. Evaporation of the solvent under vacuum, followed by purification through flash chromatography on silica gel (200-300 mesh, PE/EA v/v=3:1) to obtain pure oxazole compound 1h or 1i.

2.3 General procedure for synthesis of substrates 1r or 1t:[5,6]

Acetic formic anhydride (3.0 equiv) was added dropwise to a solution of amino acid (1.0 equiv) in formic acid (20 mL) at 0 °C. After the addition was completed, the reaction mixture was stirred at room temperature for an additional 1 h. Ice-water (20 mL) was added and the mixture was concentrated under vacuum to give the white crystalline N-formyl amino acid. Subsequently, to a solution of N-formyl amino acid (1.0 equiv) and morpholine (1.2 equiv) in CH₂Cl₂ (50 mL) was added Et₃N (1.2 equiv), HOBt (1.2 equiv) and EDCl (1.2 equiv) successively, and then the reaction mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with aqueous NH₄Cl solution (30 mL) and extracted with CH₂Cl₂ (2×30 mL). The organic phase was washed with brine and dried over anhydrous Na₂SO₄. Evaporation of solvent under vacuum to afford the crude product which was further purified by flash chromatography on silica gel (200-300 mesh, PE/EA v/v=1:1) to give the pure amide.

To a solution of formamide in dry THF (30 mL) was added Et₃N (5.0 equiv) and cooled to -30 °C, at this time, POCl₃ (1.1 equiv) was added dropwise. The reaction mixture was stirred at this temperature for 2 h (monitored by TLC). Then, saturated aq. Na₂CO₃ (20 mL) was added and the reaction was warmed to room temperature. The aqueous layer was extracted with ethyl acetate (2×20 mL) and the combined organic layer was washed with brine, dried and concentrated. The residue was dissolved in ethyl acetate (10 mL) and added silica gel for continued stirring overnight. Evaporation of the solvent under vacuum, followed by purification through flash chromatography on silica gel (200-300 mesh, PE/EA v/v=1:1), the desired 1r or 1t was obtained.

2.4 General procedure for synthesis of products:

To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added KF (58.1 mg, 0.6 mmol, 3.0 equiv) and 18-Crown-6 (158.6 mg, 0.6 mmol, 3.0 equiv). Then the tube was evacuated under vacuum and charged with N₂ (1 atm, 3
times). The reaction mixture was dissolved in anhydrous THF (2.0 mL) under protection of N₂ atmosphere and subsequently cooled the reaction mixture to 0 or -20 °C with stirring. At this moment, aryne precursor 2 (0.3 mmol, 1.5 equiv) and oxazole 1 (0.2 mmol, 1.0 equiv) was successively added in the stirring solution under protection of N₂ atmosphere. The mixture was reacted at 0 or -20 °C until completion of the reaction which was detected by TLC. The reaction mixture was then diluted with 40 mL dichloromethane and washed with saturated K₂SO₄ aqueous solution (3×10 mL). The residue was successively dried with anhydrous Na₂SO₄, filtered and evaporated of solvent to give the crude product. The crude product was purified by column chromatography on silica gel (200-300 mesh, PE/EA v/v=5:1–2:1) to afford the corresponding isoquinolin-1(2H)-one.

2.5 Procedure for derivatization reaction:

2.5.1 Procedure for synthesis of 4-6:[7]

To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added 3aa (58.4 mg, 0.2 mmol, 1.0 equiv). Then the tube was evacuated under vacuum and charged with N₂ (1 atm, 3 times). Cooled the reaction mixture to 0 °C, at this moment, DMF (2.0 mL) and NaH (16.0 mg, 0.4 mmol, 2.0 equiv) was added under N₂ atmosphere. After stirring for 30 min at 0 °C, the halide (0.4 mmol, 2.0 equiv) was added to the stirring solution, and then the reaction mixture was further reacted at room temperature. When complete consumption of 3aa which was monitored by TLC, the reaction mixture was quenched with brine (10 mL) and extracted with ethyl acetate (2×20 mL). The combined organic phase was washed with brine (20 mL) and water, dried over anhydrous Na₂SO₄ and concentrated under vacuum to give the crude product. The crude product was purified by column chromatography on silica gel (200-300 mesh, PE/EA v/v=15:1) to afford the corresponding derivative product.

2.5.2 Procedure for synthesis of 7-9:[8]

To a 50 mL Schlenk sealed tube was added 3aa (58.4 mg, 0.2 mmol, 1.0 equiv), bromide (0.3 mmol, 1.5 equiv), Cs₂CO₃ (97.7 mg, 0.3 mmol, 1.5 equiv) and DMF (1 mL). The reaction was heated to 50 °C in an oil bath for 3 h. Then, the reaction mixture was allowed to cool to ambient temperature, and diluted with EtOAc (2 x 10 mL) and washed over anhydrous Na₂SO₄, evaporation of solvent giving the crude product which was further purified by flash column chromatography on silica gel (200-300 mesh, PE/EA=5:1) to give the desired N-substituted products.

2.5.3 Procedure for synthesis of 10 and 11:[9, 10]

To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added 3aa (58.4 mg, 0.2 mmol, 1.0 equiv), anhydrous acetonitrile (2.0 mL), and POCl₃ (65 μL, 0.7 mmol). The reaction mixture was reflux for 2 h, then cooled to 0 °C, diluted with dichloromethane (5 mL), and quenched with a dropwise addition of sat. aq. NaHCO₃ (5 mL). The biphasic mixture was stirred vigorously and allowed to warm to room temperature. After 1 h, the layers were separated and the aqueous fraction was extracted with DCM (2×10 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (10 mL), brine (10 mL), dried over Na₂SO₄, and concentrated to yield crude product. The crude product was purified by column chromatography on silica gel (200-300 mesh, PE/EA v/v=15:1) to afford the pure product 10.
To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added the 10 (62.1 mg, 0.2 mmol, 1 equiv). Then the tube was evacuated under vacuum and charged with N₂ (1 atm, 3 times). Then, Pd(dppf)Cl₂ (7.4 mg, 0.01 mmol, 5.0 mol%), TMEDA (0.051 mL, 0.34 mmol, 1.7 equiv) and NaBH₄ (12.9 mg, 0.34 mmol, 1.7 equiv) were introduced in sequence. The mixture was stirred at room temperature under N₂ atmosphere until the full consumption of 10. The residue was quenched with brine and extracted with ethyl acetate. The organic phase was separated, then dried over Na₂SO₄. The solvent was evaporated to give the crude product which was purified by flash column chromatography on silica gel (200-300 mesh, PE/EA v/v=20:1) to afford the corresponding product in excellent yields.

2.5.4 Procedure for synthesis of 12-14:\(^\text{[11]}\)

To a solution of 3aa (87.6 mg, 0.3 mmol, 1.0 equiv) in anhydrous DCM (1 mL) was added pyridine (0.036 mL, 0.45 mmol, 1.5 equiv) and cooled to 0 °C, then Tf₂O (0.056 mL, 0.33 mmol, 1.1 equiv) was added dropwise. After 30 min, the reaction mixture was warmed to room temperature and continued for stirring until the reaction was completed (detected by TLC). The reaction mixture was diluted with water (10 mL) and extracted with DCM (2×10 mL). The combined organic layer was dried over Na₂SO₄ and concentrated under vacuum to obtain crude product, which was further purified by silica gel flash chromatography on silica gel (200-300 mesh, PE/EA v/v=50:1) to give product 12.

Under N₂ atmosphere, to a 25 mL Schlenk sealed tube was charged with 12 (84.9 mg, 0.2 mmol, 1 equiv), PhB(OH)₂ (26.8 mg, 0.22 mmol, 1.1 equiv), Pd(PPh₃)₄ (9.2 mg, 4 mol%), Cs₂CO₃ (91.2 mg, 0.28 mmol, 1.4 equiv) and dry 1,4-dioxane (2.0 mL). The mixture was reacted at 85 °C in oil bath overnight under nitrogen atmosphere. After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was then diluted with water (10 mL) and extracted with DCM (2×10 mL), and the combined organic layers was dried over Na₂SO₄ and concentrated under vacuum to obtain crude product, which was further purified by silica gel flash chromatography on silica gel (200-300 mesh, PE/EA v/v=40:1) to give product 13.

To a 25 mL Schlenk sealed tube was charged with 3fa (74.5 mg, 0.2 mmol, 1 equiv), trimethylsilylacetylene (0.059 mL, 0.4 mmol, 2.0 equiv), PdCl₂(PPh₃)₂ (28.1 mg, 0.04 mmol, 20 mol%), CuI (7.6 mg, 0.04 mmol, 20 mol%), DIPEA (0.070 mL, 0.4 mmol, 2.0 equiv) and dry DMF (2 mL). The mixture was reacted at 80 °C in oil bath overnight under nitrogen atmosphere. After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was dilution with water (10 mL) and extracted with DCM (2×10 mL). The organic layer was then dried and concentrated under vacuum to obtain crude product, which was further purified by silica gel flash chromatography on silica gel (PE/EA v/v=5:1) to give product 14.

2.5.5 Procedure for one-pot synthesis of 4:

To an oven-dried 50 mL Schlenk sealed tube equipped with a magnetic stir bar was added KF (58.1 mg, 0.6 mmol, 3.0 equiv) and 18-Crown-6 (158.6 mg, 0.6 mmol, 3.0 equiv). Then the tube was evacuated under vacuum and charged with nitrogen (1 atm, 3 times). The reaction mixture was dissolved in anhydrous THF (2.0 mL) under protection of N₂ atmosphere and subsequently cooled the reaction mixture to -20 °C with stirring. At this moment, aryne precursor 2a (89.4 mg, 0.3 mmol, 1.5 equiv) and
oxazole 1a (43.2 mg, 0.2 mmol, 1.0 equiv) was added in the stirring solution under protection of N₂ atmosphere. The mixture was reacted at -20 °C until completion of the reaction which was detected by TLC, then warming the reaction to 0 °C and NaH (16.0 mg, 0.4 mmol, 2.0 equiv) was added. After further stirring for 30 min, methyl iodide (25 μL, 0.4 mmol, 2.0 equiv) was added, and the solution was stirred at room temperature. When complete consumption of intermediate 3aa which was monitored by TLC, the reaction mixture was quenched with brine (10 mL) and then extracted with EA (2×20 mL). The combined organic phase was washed with brine (20 mL) and H₂O (20 mL) respectively, then dried over anhydrous Na₂SO₄. After evaporation of solvent, the crude product was obtained which was subsequently purified by column chromatography on silica gel (200-300 mesh, PE/EA v/v=15:1) to afford the product 4 in 80% isolated yield.

2.5.6 Gram-scale preparation of 3aa:

To an oven-dried 250 mL three-necked flask with a magnetic stir bar was added KF (1.046 g, 18 mmol, 3.0 equiv) and 18-Crown-6 (4.758 g, 18 mmol, 3.0 equiv). Then the tube was evacuated under vacuum and charged with N₂ (1 atm, 3 times). The reaction mixture was dissolved in anhydrous THF (60.0 mL) under protection of N₂ atmosphere and subsequently cooled the reaction mixture to -20 °C with stirring. At this moment, aryne precursor 2a (2.682 g, 9.0 mmol, 1.5 equiv) and oxazole 1a (1.296 g, 6.0 mmol, 1.0 equiv) was successively added to the stirring solution under protection of N₂ atmosphere. The mixture was reacted at -20 °C until completion of the reaction which was detected by TLC. The reaction mixture was then diluted with 100 mL dichloromethane and washed with saturated K₂SO₄ aqueous solution (3×40 mL). The residue was successively dried with anhydrous Na₂SO₄, filtered and evaporated of solvent to give the crude product. The crude product was purified by column chromatography on silica gel (200-300 mesh, PE/EA v/v=5:1–2:1) to afford the 3aa in 1.49 g and 85% isolated yields.

2.6 Preparing single-crystal of 3ah and 3ai’ and relating crystal data:

Suitable single crystal for product 3ah and 3ai’ were obtained by slow volatilization of the mixed solution (THF:n-hexane (v/v=1:3) as solvent) in a test tube for 5 days.
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<tr>
<td>Empirical formula</td>
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<tr>
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<tr>
<td>R indices (all data)</td>
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<td>Largest diff. peak and hole</td>
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</tr>
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The CCDC number of product 3ah is 2098712.

Figure S2 Crystal structure of 3ai' at 30% probability level.

Table S2 Crystal data and structure refinement for 3ai'.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{23}H_{22}N_{2}O</td>
</tr>
</tbody>
</table>
Formula weight 342.42  
Temperature 173.0 K  
Wavelength 0.71073 Å  
Crystal system Triclinic  
Space group P-1  
Unit cell dimensions  
\[ a = 9.4001(5) \text{ Å}, \quad \alpha = 94.508(2)^\circ. \]  
\[ b = 9.5785(5) \text{ Å}, \quad \beta = 94.426(2)^\circ. \]  
\[ c = 10.6816(5) \text{ Å}, \quad \gamma = 110.611(2)^\circ. \]  
Volume 891.73(8) Å³  
Z 2  
Density (calculated) 1.275 Mg/m³  
Absorption coefficient 0.078 mm⁻¹  
F(000) 364  
Crystal size 0.19 x 0.17 x 0.16 mm³  
Theta range for data collection 2.286 to 26.741°.  
Index ranges -11<=h<=11, -12<=k<=12, -13<=l<=13  
Reflections collected 11292  
Independent reflections 3783 [R(int) = 0.0294]  
Completeness to theta = 25.242° 99.8%  
Absorption correction Semi-empirical from equivalents  
Max. and min. transmission 0.7454 and 0.6706  
Refinement method Full-matrix least-squares on F²  
Data / restraints / parameters 3783 / 0 / 237  
Goodness-of-fit on F² 1.032  
Final R indices [I>2sigma(I)]  
\[ R_1 = 0.0456, \quad wR_2 = 0.1213 \]  
R indices (all data)  
\[ R_1 = 0.0573, \quad wR_2 = 0.1324 \]  
Extinction coefficient n/a  
Largest diff. peak and hole 0.275 and -0.189 e.Å⁻³  

The CCDC number of product 3ai' is 2132074.

### 2.7 Characterization of substrates and products:

#### 2.7.1 Characterization of substrates:

\( \text{N, N-diethyl-4-phenyl-4, 5-dihydrooxazol-5-amine (1a):} \ ¹\text{H NMR (400 MHz, CDCl₃)} \delta 8.09-8.01 (m, 2H), 7.70 (s, 1H), 7.43-7.33 (m, 2H), 7.28-7.22 (m, 1H), 3.10 (q, J = 7.2 Hz, 4H), 1.06 (t, J = 7.2 Hz, 6H). \ ¹³\text{C NMR (100 MHz, CDCl₃)} \delta 150.5, 146.8, 132.0, 128.3, 126.9, 126.5, 125.9, 47.4, 13.0. \)

\( \text{N, N-diethyl-4-(p-tolyl)-4, 5-dihydrooxazol-5-amine (1b):} \ ¹\text{H NMR (400 MHz, CDCl₃)} \delta 7.95 (d, J = 8.4 Hz, 2H), 7.68 (s, 1H), 7.19 (d, J = 8.0 Hz, 2H), 3.07 (q, J =
$N, N$-diethyl-4-(4-methoxyphenyl)-4, 5-dihydrooxazol-5-amine (1c): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07-7.93 (m, 2H), 7.70 (s, 1H), 7.11-7.02 (m, 2H), 3.82 (s, 3H), 3.07 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.9, 149.9, 146.8, 136.6, 129.1, 129.0, 126.8, 125.8, 47.5, 21.2, 13.0.

$N, N$-diethyl-4-(4-fluorophenyl)-4, 5-dihydrooxazol-5-amine (1d): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.08-8.01 (m, 2H), 7.70 (s, 1H), 7.11-7.02 (m, 2H), 3.07 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H). 13C NMR (100 MHz, CDCl$_3$) $\delta$ 161.9 (d, $J = 244.4$ Hz), 150.1 (d, $J = 1.8$ Hz), 147.0, 128.1 (d, $J = 7.8$ Hz), 126.2, 155.2 (d, $J = 2.1$ Hz), 47.6, 12.9.

$N, N$-diethyl-4-(4-chlorophenyl)-4, 5-dihydrooxazol-5-amine (1e): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03-7.95 (m, 2H), 7.70 (s, 1H), 7.39-7.31 (m, 2H), 3.09 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.6, 146.9, 132.6, 130.5, 128.5, 127.2, 125.8, 47.5, 13.0.

$N, N$-diethyl-4-(4-bromophenyl)-4, 5-dihydrooxazol-5-amine (1f): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.99-7.87 (m, 2H), 7.70 (s, 1H), 7.55-7.46 (m, 2H), 3.09 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.6, 146.9, 131.4, 130.9, 127.5, 125.8, 47.5, 12.9.

$N, N$-diethyl-4-(2-fluorophenyl)-4, 5-dihydrooxazol-5-amine (1g): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.65-7.58 (m, 2H), 7.30-7.23 (m, 1H), 7.19-7.13 (m, 1H), 7.13-7.05 (m, 1H), 3.09 (q, $J = 7.2$ Hz, 4H), 1.03 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.9 (d, $J = 247.9$ Hz), 152.1, 144.9, 130.7 (d, $J = 3.3$ Hz), 128.9 (d, $J = 8.0$ Hz), 123.8 (d, $J = 3.6$ Hz), 120.8 (d, $J = 13.9$ Hz), 116.8 (d, $J = 1.5$ Hz), 115.8 (d, $J = 21.9$ Hz), 45.8, 13.2. 19F NMR (376 MHz, CDCl$_3$) $\delta$ -112.9.

$N, N$-diethyl-4-(2-nitrophenyl)oxazol-5-amine (1h): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J = 8.0$ Hz, 1H), 7.67 (d, $J = 7.2$ Hz, 1H), 7.61 (s, 1H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.45-7.36 (m, 1H), 3.07 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H).

$N, N$-diethyl-4-(4-methoxy-2-nitrophenyl)oxazol-5-amine (1i): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.60 (s, 1H), 7.57 (d, $J = 8.8$ Hz, 1H), 7.33 (d, $J = 2.8$ Hz, 1H), 7.11 (dd, $J = 8.8, 2.8$ Hz, 1H), 3.88 (s, 3H), 3.03 (q, $J = 7.2$ Hz, 4H), 1.02 (t, $J = 7.2$ Hz, 6H).

$N, N$-diethyl-4-(naphthalen-1-yl)-4, 5-dihydrooxazol-5-amine (1j): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80-7.72 (m, 1H), 7.68 (d, $J = 8.8$ Hz, 1H), 7.53 (d, $J = 7.2$ Hz, 1H), 7.47-7.38 (m, 1H), 7.25 (s, 1H), 7.23 (s, 1H), 7.19 (d, $J = 7.2$ Hz, 4H), 1.01 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.2, 144.1, 133.8, 132.2, 130.2, 128.2, 128.1, 127.8, 126.2, 125.9, 125.7, 125.1, 119.5, 45.7, 13.2.
N, N-diethyl-4-(thiophen-3-yl)-4, 5-dihydrooxazol-5-amine (1k): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.73 (dd, $J = 2.8, 1.2$ Hz, 1H), 7.71-7.66 (m, 2H), 7.32 (dd, $J = 5.2, 3.2$ Hz, 1H), 3.08 (q, $J = 7.2$ Hz, 4H), 1.04 (t, $J = 7.2$ Hz, 6H).

4-benzyl-N, N-diethyl-4, 5-dihydrooxazol-5-amine (1l): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.61 (s, 1H), 7.30-7.24 (m, 4H), 7.23-7.13 (m, 1H), 3.79 (s, 2H), 2.98 (q, $J = 7.2$ Hz, 4H), 0.99 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 150.6, 147.2, 139.5, 128.7, 128.3, 128.3, 126.1, 48.1, 31.6, 13.3.

N, N-diethyl-4-isobutyl-4, 5-dihydrooxazol-5-amine (1m): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.62 (s, 1H), 2.96 (q, $J = 7.2$ Hz, 4H), 2.29 (d, $J = 7.2$ Hz, 2H), 2.11-1.99 (m, 1H), 0.99 (t, $J = 7.2$ Hz, 6H), 0.92 (d, $J = 6.8$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 150.5, 146.9, 129.0, 48.1, 34.1, 27.6, 22.4, 13.1.

N-isopropyl-N-methyl-4-phenyl-4, 5-dihydrooxazol-5-amine (1n): $^1$H NMR (400 MHz, CDCl$_3$) δ 8.06-7.93 (m, 2H), 7.66 (s, 1H), 7.38 (t, $J = 7.6$ Hz, 2H), 7.27-7.20 (m, 1H), 3.40-3.26 (m, 1H), 2.74 (s, 3H), 1.13 (d, $J = 6.4$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.7, 146.4, 132.1, 128.3, 126.9, 125.9, 124.9, 54.0, 35.6, 20.1.

N-butyl-N-methyl-4-phenyl-4, 5-dihydrooxazol-5-amine (1o): $^1$H NMR (400 MHz, CDCl$_3$) δ 8.00-7.90 (m, 2H), 7.63 (s, 1H), 7.42-7.34 (m, 2H), 7.26-7.20 (m, 1H), 3.01 (t, $J = 7.2$ Hz, 2H), 2.77 (s, 3H), 1.53-1.41 (m, 2H), 1.34-1.20 (m, 2H), 0.85 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 152.2, 145.8, 132.0, 128.3, 126.8, 126.0, 123.3, 54.5, 40.4, 29.7, 20.2, 13.9.

N, N-diallyl-4-phenyl-4, 5-dihydrooxazol-5-amine (1p): $^1$H NMR (400 MHz, CDCl$_3$) δ 8.03-7.94 (m, 2H), 7.65 (s, 1H), 7.39 (t, $J = 8.0$ Hz, 2H), 7.29-7.22 (m, 1H), 5.91-5.77 (m, 2H), 5.22-5.08 (m, 4H), 3.70-3.64 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.0, 146.4, 133.9, 131.8, 128.4, 127.0, 126.0, 125.1, 118.4, 55.2.

N, N-dibenzyl-4-phenyl-4, 5-dihydrooxazol-5-amine (1q): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.91-7.84 (m, 2H), 7.61 (s, 1H), 7.42-7.36 (m, 2H), 7.29-7.20 (m, 11H), 4.18 (s, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.0, 146.0, 136.9, 131.7, 128.8, 128.4, 128.3, 127.6, 127.0, 126.1, 124.5, 56.0.

4-phenyl-5-(pyrrolidin-1-yl)-4, 5-dihydrooxazole (1r): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.75-7.62 (m, 2H), 7.52 (s, 1H), 7.42-7.31 (m, 2H), 7.24-7.14 (m, 1H), 3.30-3.20 (m, 4H), 1.98-1.87 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 150.7, 143.4, 132.7, 128.1, 126.6, 126.1, 118.3, 50.2, 25.4.

4-phenyl-5-(piperidin-1-yl)-4, 5-dihydrooxazole (1s): $^1$H NMR (400 MHz, CDCl$_3$) δ 8.02-7.88 (m, 2H), 7.62 (s, 1H), 7.43-7.35 (m, 2H), 7.27-7.20 (m, 1H), 3.05 (t, $J = 5.2$ Hz, 4H), 1.76-1.67 (m, 4H), 1.65-1.55 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 152.7, 145.5, 132.1, 128.4, 126.6, 125.7, 122.0, 51.3, 25.9, 23.9.

4-(4-phenyl-4, 5-dihydrooxazol-5-yl)morpholine (1t): $^1$H NMR (400 MHz, CDCl$_3$) δ 7.98-7.92 (m, 2H), 7.65 (s, 1H), 7.44-7.37 (m, 2H), 7.29-7.23 (m, 1H), 7.13 (s, 1H), 3.84-3.63 (m, 4H), 1.97-1.74 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.0, 146.4, 133.9, 131.8, 128.4, 127.0, 126.0, 125.1, 118.4, 55.2.
3.85 (t, J = 4.8 Hz, 4H), 3.11 (t, J = 4.8 Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.2, 146.0, 131.6, 128.5, 127.1, 125.9, 123.3, 66.9, 50.3.

4-phenyl-5-(4-phenylpiperazin-1-yl)-4,5-dihydrooxazole (1u): $^1$H NMR (400 MHz, CDCl$_3$) δ 8.04-7.93 (m, 2H), 7.66 (s, 1H), 7.44-7.36 (m, 2H), 7.33-7.25 (m, 3H), 6.98 (d, J = 8.0 Hz, 2H), 6.95-6.86 (m, 1H), 3.38-3.32 (m, 4H), 3.32-3.25 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.4, 151.3, 146.0, 131.7, 129.2, 128.5, 127.0, 125.9, 123.1, 120.3, 116.6, 50.2, 49.6.

2.7.2 Characterization of products:

4-(diethylamino)-3-phenylisoquinolin-1(2H)-one (3aa): white solid (54.3 mg, 93% yield, TLC (PE/EA, 2:1): R$_f$ = 0.23). mp 160-161 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.42 (dd, J = 8.0, 0.8 Hz, 1H), 8.29 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.74-7.68 (m, 1H), 7.52-7.48 (m, 1H), 7.48-7.43 (m, 5H), 3.00-2.80 (m, 4H), 0.94 (t, J = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.1, 140.5, 138.1, 135.3, 132.3, 129.1, 129.0, 128.3, 127.8, 126.4, 125.8, 125.0, 124.4, 48.4, 14.3. HRMS (ESI) m/z: (M-H) - calcd for C$_{19}$H$_{20}$N$_2$O 291.1503; Found 291.1499.

IR (KBr, thin film): 2970, 2844, 1657, 1607, 1545, 1490, 1459, 1376, 1245, 1117, 858, 781, 700, 577 cm$^{-1}$.

4-(diethylamino)-3-(p-tolyl)isoquinolin-1(2H)-one (3ba): white solid (51.0 mg, 84% yield, TLC (PE/EA, 5:1): R$_f$ = 0.14). mp 164-165 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.41 (dd, J = 8.0, 1.2 Hz, 2H), 8.00 (d, J = 8.4 Hz, 1H), 7.74-7.66 (m, 1H), 7.53-7.45 (m, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.27 (s, 2H), 3.00-2.79 (m, 4H), 2.43 (s, 3H), 0.95 (t, J = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 162.2, 140.6, 138.8, 138.2, 132.3, 132.2, 128.9, 127.7, 126.2, 125.7, 124.8, 124.3, 48.3, 21.4, 14.3. HRMS (ESI) m/z: (M-H) - calcd for C$_{20}$H$_{22}$N$_2$O 305.1659; Found 305.1655.

IR (KBr, thin film): 3154, 2970, 1642, 1508, 1470, 1348, 1218, 1113, 1025, 895, 785, 529 cm$^{-1}$.

4-(diethylamino)-3-(4-methoxyphenyl)isoquinolin-1(2H)-one (3ca): white solid (56.4 mg, 88% yield, TLC (PE/EA, 3:1): R$_f$ = 0.20). mp 159-160 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.53 (s, 1H), 8.40 (d, J = 7.6 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.74-7.66 (m, 1H), 7.52-7.45 (m, 1H), 7.44-7.37 (m, 2H), 7.02-6.96 (m, 2H), 3.88 (s, 3H), 3.00-2.82 (m, 4H), 0.95 (t, J = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 161.2, 159.0, 139.6, 137.0, 131.1, 129.4, 126.7, 126.5, 125.1, 124.6, 123.8, 128.9, 127.7, 126.2, 125.7, 124.8, 124.3, 48.3, 21.4, 13.3. HRMS (ESI) m/z: (M-H) - calcd for C$_{20}$H$_{22}$N$_2$O 321.1608; Found 321.1603.

IR (KBr, thin film): 2970, 2850, 1641, 1512, 1465, 1346, 1247, 1176, 1035, 833, 777, 626 cm$^{-1}$.

4-(diethylamino)-3-(4-fluorophenyl)isoquinolin-1(2H)-one (3da): white solid (49.7 mg, 80% yield, TLC (PE/EA, 5:1): R$_f$ = 0.16). mp 182-183 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 9.64 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.74-7.66 (m, 1H), 7.56-7.43 (m, 3H), 7.22-7.12 (m, 2H), 3.04-2.82 (m, 4H), 0.93 (t, J = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.0 (d, J = 247.1 Hz), 162.6, 140.3, 132.2, 131.3 (d, J = 8.0 Hz), 131.1 (d, J = 3.4 Hz), 127.8, 126.4, 125.8, 125.2, 124.3, 115.1 (d, J = 21.5 Hz), 48.4, 14.3. $^{19}$F NMR (376 MHz, CDCl$_3$) δ -112.2. HRMS (ESI) m/z: (M-H)$^-$ calcd for C$_{19}$H$_{19}$FN$_2$O 309.1409; Found 309.1403. IR (KBr, thin film): 2971, 1651, 1610, 1508, 1383, 1317, 1219, 1157, 841, 771, 628, 527 cm$^{-1}$.
3-(4-chlorophenyl)-4-(diethylamino)isoquinolin-1(2H)-one (3ea): white solid (52.7 mg, 81% yield, TLC (PE/EA, 5:1): Rf = 0.15). mp 164-165 °C. 
1H NMR (400 MHz, CDCl3) δ 9.37 (s, 1H), 8.37 (dd, J = 8.0, 0.8 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.73-7.06 (m, 1H), 7.53-7.48 (m, 1H), 7.45 (s, 4H), 3.03-2.88 (m, 4H), 0.93 (t, J = 7.2 Hz, 6H). 
13C NMR (100 MHz, CDCl3) δ 162.6, 140.1, 137.5, 134.8, 133.5, 132.3, 130.8, 128.3, 127.9, 126.5, 125.9, 125.2, 124.3, 48.4, 14.3. HRMS (ESI) m/z: (M+H)+ calcd for C19H19ClN2O 368.1605; Found 368.1609. IR (KBr, thin film): 3441, 3155, 2968, 2831, 1650, 1525, 1348, 1309, 1159, 1068, 864, 773, 586 cm−1.

3-(4-bromophenyl)-4-(diethylamino)isoquinolin-1(2H)-one (3fa): white solid (57.5 mg, 78% yield, TLC (PE/EA, 5:1): Rf = 0.15). mp 175-176 °C. 
400 MHz, CDCl3) δ 9.11 (s, 1H), 8.41-8.35 (m, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.74-7.67 (m, 1H), 7.64-7.58 (m, 2H), 7.54-7.48 (m, 1H), 7.42-7.34 (m, 2H), 3.04-2.86 (m, 4H), 0.93 (t, J = 7.2 Hz, 6H). 
13C NMR (100 MHz, CDCl3) δ 162.6, 140.1, 137.5, 134.9, 133.9, 132.3, 131.1, 127.9, 126.5, 125.9, 125.2, 124.3, 123.1, 48.4, 14.3. HRMS (ESI) m/z: (M-H)- calcd for C19H19BrN2O 369.0608; Found 369.0600. IR (KBr, thin film): 3161, 1974, 1645, 1485, 1463, 1348, 1309, 1159, 1068, 864, 773, 586 cm−1.

4-(diethylamino)-3-(2-fluorophenyl)isoquinolin-1(2H)-one (3ga): white solid (57.5 mg, 93% yield, TLC (PE/EA, 2:1): Rf = 0.25). mp 190-191 °C. 
1H NMR (400 MHz, CDCl3) δ 8.78 (s, 1H), 8.39 (dd, J = 8.0, 0.8 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.74-7.67 (m, 1H), 7.55-7.43 (m, 2H), 7.40 (td, J = 7.6, 2.0 Hz, 1H), 7.28-7.15 (m, 2H), 2.99-2.83 (m, 4H), 0.94 (t, J = 7.2 Hz, 6H). 
13C NMR (100 MHz, CDCl3) δ 162.0, 160.1 (d, J = 247.0 Hz), 140.0, 132.7, 132.2, 131.8 (d, J = 2.7 Hz), 131.2 (d, J = 8.0 Hz), 127.9, 126.8, 126.7, 126.2, 124.5, 123.8 (d, J = 3.6 Hz), 122.9 (d, J = 15.4 Hz), 115.9 (d, J = 21.5 Hz), 48.3, 14.4. 19F NMR (376 MHz, CDCl3) δ -112.4. HRMS (ESI) m/z: (M+H)+ calcd for C19H18FN2O 311.1554; Found 311.1551. IR (KBr, thin film): 3307, 2949, 1945, 1654, 1450, 1345, 1320, 1221, 1108, 1070, 779, 587 cm−1.

4-(diethylamino)-3-(2-nitrophenyl)isoquinolin-1(2H)-one (3ha): yellow solid (32.1 mg, 95% yield, TLC (PE/EA, 1:1): Rf = 0.11). mp 256-257 °C. 
1H NMR (400 MHz, d6-DMSO) δ 11.43 (s, 1H), 8.28 (t, J = 8.0 Hz, 2H), 7.91-7.82 (m, 2H), 7.76 (t, J = 7.6 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 3.02-2.83 (m, 2H), 2.83-2.71 (m, 1H), 2.71-2.57 (m, 1H), 0.84 (t, J = 7.2 Hz, 3H), 0.70 (t, J = 7.2 Hz, 3H). 
13C NMR (100 MHz, d6-DMSO) δ 161.4, 148.0, 139.5, 137.4, 134.3, 134.0, 132.7, 130.9, 130.4, 128.0, 126.9, 126.7, 125.0, 124.5, 124.2, 49.1, 48.0, 15.2, 15.1. HRMS (ESI) m/z: (M+H)+ calcd for C19H18N4O4S 338.1499; Found 338.1503. IR (KBr, thin film): 3438, 3158, 2977, 2923, 2855, 1647, 1605, 1525, 1468, 1352, 781, 703 cm−1.

4-(diethylamino)-3-(4-methoxy-2-nitrophenyl)isoquinolin-1(2H)-one (3ia): yellow solid (86.1 mg, 84% yield, TLC (PE/EA, 1:1): Rf = 0.12). mp 245-246 °C. 
1H NMR (400 MHz, CDCl3) δ 9.55 (s, 1H), 8.33 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 2.4 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.29-7.21 (m, 1H), 3.97 (s, 3H), 2.96-2.64 (m, 4H), 0.87 (s, 6H). 
13C NMR (100 MHz, CDCl3) δ 162.4, 160.4, 148.9, 139.8, 135.2, 133.9, 132.1, 127.9, 126.4, 126.1, 124.3, 122.1, 119.3, 109.6, 56.0, 48.4, 14.7. HRMS (ESI) m/z: (M+H)+ calcd for C20H17N4O5 368.1605; Found 368.1609. IR (KBr, thin film): 3441, 3155, 2968, 2831, 1650, 1525, 1346, 1304, 1233, 1031, 778, 718 cm−1.
4-(diethylamino)-3-(naphthalen-1-yl)isoquinolin-1(2H)-one (3ja): white solid (57.9 mg, 85% yield, TLC (PE/EA, 2:1): R_f = 0.33). mp 196-197 °C. 
^1^H NMR (400 MHz, CDCl_3) δ 8.43 (dd, J = 8.0, 0.8 Hz, 1H), 8.30 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.91-7.77 (m, 2H), 7.70-7.48 (m, 4H), 7.48-7.42 (m, 1H), 3.07-2.86 (m, 2H), 2.62-2.38 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H), 0.67 (t, J = 6.8 Hz, 3H). 

13C NMR (100 MHz, CDCl_3) δ 161.6, 140.6, 136.2, 133.6, 132.4, 132.0, 131.7, 129.8, 128.5, 128.2, 127.7, 127.3, 126.8, 126.4, 125.9, 125.3, 124.8, 124.6, 49.6, 47.1, 14.8, 14.6. HRMS (ESI) m/z: (M+H)^+ calcd for C_{23}H_{23}N_2O 343.1805; Found 343.1800.

IR (KBr, thin film): 2974, 1643, 1557, 1466, 1348, 1224, 1187, 1089, 1019, 776, 575 cm^{-1}.

4-(diethylamino)-3-(thiophen-3-yl)isoquinolin-1(2H)-one (3ka): white solid (21.8 mg, 46% yield, TLC (PE/EA, 2:1): R_f = 0.32). mp 126-127 °C. 
^1^H NMR (400 MHz, CDCl_3) δ 8.98 (s, 1H), 8.41 (dd, J = 8.0, 1.2 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.72-7.64 (m, 2H), 7.52-7.46 (m, 1H), 7.46-7.39 (m, 2H), 3.17-2.95 (m, 4H), 0.97 (t, J = 7.2 Hz, 6H). 

13C NMR (100 MHz, CDCl_3) δ 162.3, 140.3, 135.0, 134.0, 132.2, 128.1, 127.9, 126.2, 125.6, 125.4, 125.3, 124.3, 124.2, 48.3, 14.1. HRMS (ESI) m/z: (M+Na)^+ calcd for C_{17}H_{18}N_2OSNa 321.1032; Found 321.1032. 

IR (KBr, thin film): 3302, 2969, 2919, 1742, 1472, 1386, 1304, 1140, 1082, 1054, 717, 652, 549 cm^{-1}.

3-benzyl-4-(diethylamino)isoquinolin-1(2H)-one (3la): white solid (27.0 mg, 46% yield, TLC (PE/EA, 2:1): R_f = 0.39). mp 114-115 °C. 
^1^H NMR (400 MHz, CDCl_3) δ 8.30 (dd, J = 8.0, 1.2 Hz, 2H), 7.82 (d, J = 8.4 Hz, 1H), 7.69-7.63 (m, 1H), 7.47-7.41 (m, 1H), 7.36-7.29 (m, 2H), 7.29-7.26 (m, 1H), 4.19 (s, 2H), 3.25 (q, J = 7.2 Hz, 4H), 1.09 (t, J = 7.2 Hz, 6H). 

13C NMR (100 MHz, CDCl_3) δ 162.3, 139.2, 138.7, 137.0, 132.1, 129.1, 129.0, 128.2, 127.1, 126.0, 125.7, 124.6, 123.8, 49.2, 35.5, 15.2. HRMS (ESI) m/z: (M+H)^+ calcd for C_{20}H_{23}N_2O 307.1805; Found 307.1805.

IR (KBr, thin film): 2970, 2925, 1651, 1553, 1467, 1344, 1238, 1135, 1028, 774, 713, 520 cm^{-1}.

4-(diethylamino)-3-isobutylisoquinolin-1(2H)-one (3ma): white solid (30.1 mg, 56% yield, TLC (PE/EA, 2:1): R_f = 0.39). mp 91-92 °C. 
^1^H NMR (400 MHz, CDCl_3) δ 10.40 (s, 1H), 8.40 (dd, J = 8.0, 1.2 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.67-7.60 (m, 1H), 7.46-7.39 (m, 1H), 3.27-3.05 (m, 4H), 2.71 (d, J = 8.0 Hz, 2H), 2.26-2.21 (m, 1H), 1.09-0.98 (m, 12H). 

13C NMR (100 MHz, CDCl_3) δ 162.9, 140.5, 139.9, 131.9, 127.9, 125.5, 125.3, 124.9, 49.0, 38.2, 29.7, 27.7, 22.5, 15.1. HRMS (ESI) m/z: (M+H)^+ calcd for C_{17}H_{25}N_2O 273.1961; Found 273.1962. IR (KBr, thin film): 3202, 2969, 2919, 1742, 1472, 1386, 1304, 1140, 1082, 1054, 717, 652, 549 cm^{-1}.

4-(isopropyl(methyl)amino)-3-phenylisoquinolin-1(2H)-one (3na): white solid (56.9 mg, 92% yield, TLC (PE/EA, 3:1): R_f = 0.22). mp 142-143 °C. 
^1^H NMR (400 MHz, CDCl_3) δ 8.55 (s, 1H), 8.42 (dd, J = 8.0, 1.2 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.75-7.67 (m, 1H), 7.55-7.40 (m, 6H), 3.15-3.03 (m, 1H), 2.83 (s, 3H), 0.93-0.76 (m, 6H). 

13C NMR (100 MHz, CDCl_3) δ 162.9, 140.5, 139.9, 131.9, 127.9, 125.5, 125.3, 123.9, 49.0, 38.2, 29.7, 27.7, 22.5, 15.1. HRMS (ESI) m/z: (M+H)^+ calcd for C_{19}H_{21}N_2O 293.1650; Found 293.1652. IR (KBr, thin film): 3202, 2969, 2919, 1742, 1472, 1386, 1304, 1140, 1082, 1054, 717, 652, 549 cm^{-1}.
4-(butyl(methylamino))-3-phenylisoquinolin-1(2H)-one (3oa): white solid (58.4 mg, 95% yield, TLC (PE/EA, 3:1): Rf = 0.22). mp 152-153 °C. 1H NMR (400 MHz, CDCl3) δ 8.55 (s, 1H), 8.41 (dd, J = 8.0, 0.8 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.78-7.86 (m, 1H), 7.58-7.38 (m, 6H), 2.78 (s, 3H), 2.64 (q, J = 7.6 Hz, 2H), 1.32-1.22 (m, 2H), 1.15-1.03 (m, 2H), 0.74 (t, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ 162.0, 139.2, 136.8, 135.3, 132.4, 129.0, 128.9, 128.5, 127.9, 127.2, 126.4, 125.9, 124.0, 55.8, 42.9, 30.9, 20.2, 13.9. HRMS (ESI) m/z: (M+H)+ calcd for C20H21N2O 305.1646; Found 305.1805. IR (KBr, thin film): 3163, 2948, 1641, 1467, 1348, 1272, 1186, 1033, 912, 786, 759, 568 cm⁻¹.

4-(diallylamino)-3-phenylisoquinolin-1(2H)-one (3ra): white solid (51.2 mg, 81% yield, TLC (PE/EA, 2:1): Rf = 0.37). mp 97-98 °C. 1H NMR (400 MHz, CDCl3) δ 8.60 (s, 1H), 8.41 (dd, J = 8.0, 0.8 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.76-7.70 (m, 1H), 7.55-7.43 (m, 6H), 5.76-5.62 (m, 2H), 5.02-4.98 (m, 1H), 4.98-4.92 (m, 3H), 3.58-3.39 (m, 4H); 13C NMR (100 MHz, CDCl3) δ 163.2, 140.7, 139.3, 137.2, 136.1, 133.4, 130.3, 130.1, 129.3, 128.9, 127.4, 126.7, 126.1, 124.9, 117.6, 58.1. HRMS (ESI) m/z: (M+H)+ calcd for C20H21N2O 305.1648; Found 317.1649. IR (KBr, thin film): 3007, 2845, 1645, 1466, 1412, 1341, 1208, 1171, 1025, 917, 775, 567 cm⁻¹.

4-(dibenzylaminio)-3-phenylisoquinolin-1(2H)-one (3qa): white solid (67.8 mg, 82% yield, TLC (PE/EA, 5:1): Rf = 0.12). mp 226-227 °C. 1H NMR (400 MHz, CDCl3) δ 8.56 (s, 1H), 8.45 (dd, J = 8.0, 1.6 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.83-7.75 (m, 1H), 7.58-7.51 (m, 1H), 7.48-7.37 (m, 1H), 7.36-7.28 (m, 2H), 7.26-7.15 (m, 6H), 7.10-6.96 (m, 4H), 6.95-6.84 (m, 2H), 4.1 (dd, J = 30.8, 14.0 Hz, 4H); 13C NMR (100 MHz, CDCl3) δ 161.7, 138.5, 138.5, 137.8, 135.0, 132.6, 129.2, 129.1, 128.8, 128.4, 128.3, 128.2, 127.1, 126.6, 125.9, 124.5, 124.2, 57.6; HRMS (ESI) m/z: (M+H)+ calcd for C20H21N2O 417.1961; Found 417.1962. IR (KBr, thin film): 3030, 2843, 1656, 1608, 1494, 1447, 1349, 1264, 1192, 1081, 762, 698 cm⁻¹.

3-phenyl-4-(pyrrolidin-1-yl)isoquinolin-1(2H)-one (3ra): white solid (51.9 mg, 90% yield, TLC (PE/EA, 2:1): Rf = 0.31). mp 183-184 °C. 1H NMR (400 MHz, CDCl3) δ 8.71 (s, 1H), 8.44 (d, J = 8.0 Hz, 1H), 7.77-7.67 (m, 2H), 7.54-7.42 (m, 6H), 3.07 (t, J = 6.4 Hz, 4H), 1.91-1.82 (m, 4H). 13C NMR (100 MHz, CDCl3) δ 162.4, 138.6, 138.4, 134.8, 132.2, 128.8, 128.6, 128.3, 128.2, 126.0, 123.3, 122.9, 51.5, 26.1. HRMS (ESI) m/z: (M-H)− calcd for C19H18N3O 289.1346; Found 289.1342. IR (KBr, thin film): 2963, 1648, 1611, 1471, 1348, 1265, 1148, 1032, 942, 781, 694, 558 cm⁻¹.

3-phenyl-4-(piperidin-1-yl)isoquinolin-1(2H)-one (3sa): white solid (55.9 mg, 92% yield, TLC (PE/EA, 2:1): Rf = 0.29). mp 251-252 °C. 1H NMR (400 MHz, CDCl3) δ 8.32 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.77-7.68 (m, 1H), 7.64-7.35 (m, 6H), 3.13-2.87 (m, 2H), 2.58-2.34 (m, 2H), 1.74-1.56 (m, 3H), 1.54-1.36 (m, 2H), 1.30-1.13 (m, 1H). 13C NMR (100 MHz, CDCl3) δ 161.9, 138.9, 135.4, 135.3, 132.4, 129.3, 128.1, 128.1, 127.8, 126.5, 125.7, 123.7, 53.2, 27.0, 24.2; HRMS (ESI) m/z: (M+H)+ calcd for C20H21N3O 305.1648; Found 305.1646. IR (KBr, thin film): 2937, 1654, 1553, 1469, 1346, 1270, 1211, 1118, 911, 777, 756, 599 cm⁻¹.

4-morpholino-3-phenylisoquinolin-1(2H)-one (3ta): white solid (57.0 mg, 90% yield, TLC (PE/EA, 1:1): Rf = 0.20). mp 248-249 °C. 1H NMR (400 MHz, CDCl3) δ 8.43 (d, J = 7.6 Hz, 1H), 8.32 (s, 1H), 8.06 (dd, J = 8.4, 0.8 Hz, 1H), 7.76 (t, J =
IR (KBr, thin film): 2964, 2851, 1654, 1616, 1492, 1361, 1227, 1179, 883, 849, 765, 523 cm⁻¹.

Found 327.1309.

7.6 Hz, 1H), 7.58-7.47 (m, 4H), 7.47-7.39 (m, 2H), 3.80-3.61 (m, 4H), 2.93 (d, J = 12.4 Hz, 2H), 2.77-2.65 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 138.3, 136.2, 134.8, 132.7, 129.5, 129.2, 128.7, 128.0, 126.8, 126.4, 123.3, 67.8, 52.1. HRMS (ESI) m/z: (M+H)⁺ calec for C₁₀H₁₆N₂O₃ 307.1441; Found 307.1443. IR (KBr, thin film): 3440, 3154, 2950, 2851, 1647, 1557, 1449, 1269, 1200, 1105, 778, 564 cm⁻¹.

3-phenyl-4-(4-phenylpiperazin-1-yl)isoquinolin-1(2H)-one (3ua): white solid (17.8 mg, 20% yield, TLC (PE/EA, 1:1): Rₜ = 0.24). mp 245-246 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.48-8.37 (m, 2H), 8.08 (d, J = 8.0 Hz, 1H), 7.78-7.70 (m, 1H), 7.57-7.43 (m, 6H), 7.29-7.21 (m, 2H), 6.94-6.83 (m, 3H), 3.29 (d, J = 11.2 Hz, 2H), 3.20-3.01 (m, 4H), 2.81 (t, J = 9.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 161.6, 151.6, 138.4, 135.7, 134.9, 132.8, 129.5, 129.1, 128.8, 128.0, 126.9, 126.6, 125.6, 125.7, 123.5, 120.0, 116.3, 51.9, 50.4. HRMS (ESI) m/z: (M+H)⁺ calec for C₂₅H₂₁F₂N₄O 382.1914; Found 382.1913. IR (KBr, thin film): 3058, 2920, 1730, 1648, 1606, 1497, 1449, 1371, 124, 952, 757, 528 cm⁻¹.

4-(diethylamino)-6, 7-dimethyl-3-phenylisoquinolin-1(2H)-one (3ab): white solid (52.7 mg, 83% yield, TLC (PE/EA, 2:1): Rₜ = 0.21). mp 244-245 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, 1H), 8.14 (s, 1H), 7.73 (s, 1H), 7.47-7.42 (m, 5H), 3.01-2.80 (m, 4H), 2.44 (s, 3H), 2.41 (s, 3H), 0.93 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.9, 142.2, 138.5, 137.1, 135.9, 135.6, 129.0, 128.8, 128.3, 128.0, 124.8, 124.7, 123.9, 48.4, 48.2, 19.7, 14.3. HRMS (ESI) m/z: (M+H)⁺ calec for C₂₂H₂₅N₂O 319.18159; Found 319.18094. IR (KBr, thin film): 2970, 2914, 2859, 1651, 1616, 1494, 1470, 1379, 1232, 1191, 1130, 1021, 773, 553 cm⁻¹.

4-(diethylamino)-6, 7-dimethoxy-3-phenylisoquinolin-1(2H)-one (3ac): white solid (49.3 mg, 70% yield, TLC (PE/EA, 1:1): Rₜ = 0.25). mp 130-131 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.98 (s, 1H), 7.75 (s, 1H), 7.54-7.39 (m, 6H), 4.03 (d, J = 1.2 Hz, 6H), 2.99-2.72 (m, 4H), 0.97 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 160.9, 153.0, 148.5, 136.1, 135.8, 134.8, 128.7, 128.4, 127.8, 124.3, 118.9, 107.1, 104.5, 55.7, 55.0, 47.9, 14.1. HRMS (ESI) m/z: (M+H)⁺ calec for C₂₃H₂₄N₂O 353.1860; Found 353.1859. IR (KBr, thin film): 2926, 2848, 1650, 1509, 1491, 1434, 1381, 1271, 1147, 1032, 878, 849, 765, 523 cm⁻¹.

4-(diethylamino)-6, 7-difluoro-3-phenylisoquinolin-1(2H)-one (3ad): white solid (39.4 mg, 60% yield, TLC (PE/EA, 2:1): Rₜ = 0.40). mp 221-222 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.98 (s, 1H), 8.10 (dd, J = 10.4, 8.0 Hz, 1H), 7.82 (dd, J = 12.0, 7.6 Hz, 1H), 7.52-7.41 (m, 5H), 2.95-2.64 (m, 4H), 0.95 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 138.5 (d, J = 53.5 Hz), 134.3, 132.1, 129.2, 128.7, 128.6, 128.3, 128.1, 126.2, 123.9, 115.3 (d, J = 20.4 Hz), 112.1 (d, J = 19.4 Hz), 48.0, 14.0. HRMS (ESI) m/z: (M+H)⁺ calec for C₁₀H₁₆F₂N₂O 327.1314; Found 327.1309. IR (KBr, thin film): 2964, 2851, 1654, 1616, 1492, 1463, 1361, 1227, 1179, 883, 772, 542 cm⁻¹.

4-(diethylamino)-3-phenyl-2, 6, 7, 8-tetrahydro-1H-cyclopenta[ gjisosquinolines 1-one (3ae): white solid (49.8 mg, 76% yield, TLC (PE/EA, 2:1): Rₜ = 0.21). mp 228-229 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.36 (s, 1H), 8.25 (s, 1H), 7.81 (s, 1H), 7.51-7.40 (m, 5H), 3.06 (q, J = 7.2 Hz, 4H), 3.01-2.83 (m, 4H), 2.21-2.11 (m, 2H), 0.93 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 162.1, 150.1, 143.7, 139.3, 136.9, 135.6, 129.1, 128.8, 128.3, 125.2, 124.5, 122.9, 119.5, 48.4, 33.4, 32.5, 25.7, 14.3. HRMS (ESI) m/z: (M+H)⁺ calec for...
C_{22}H_{24}N_{2}O 331.1816; Found 331.1810. IR (KBr, thin film): 2971, 2914, 2834, 1617, 1492, 1463, 1361, 1227, 1179, 883, 772, 542 cm\(^{-1}\).

8-(diethylamino)-7-phenyl-[1, 3]dioxolo[4, 5-g]isoquinolin-5(6H)-one (3af): white solid (51 mg, 76% yield, TLC (PE/EA, 2:1): \(R_f = 0.24\)). mp 265-266 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.84 (s, 1H), 7.71 (s, 1H), 7.51-7.38 (m, 6H), 6.09 (s, 2H), 2.95-2.69 (m, 4H), 0.93 (t, \(J = 7.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 161.3, 152.5, 147.7, 138.8, 137.1, 135.4, 129.3, 129.3, 128.2, 125.2, 121.4, 105.8, 103.1, 101.7, 48.3, 14.3. HRMS (ESI) m/z: (M-H\(^{-}\)) calcd for C_{20}H_{19}N_{2}O 335.1401; Found 335.1396. IR (KBr, thin film): 2970, 2835, 1641, 1463, 1379, 1257, 1120, 1029, 935, 877, 744, 507 cm\(^{-1}\).

4-(diethylamino)-5, 8-dimethyl-3-phenylisoquinolin-1(2H)-one (3ag): white solid (41.01 mg, 64% yield, TLC (PE/EA, 5:1): \(R_f = 0.36\)). mp 159-160 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.68 (s, 1H), 7.47-7.38 (m, 5H), 7.25 (s, 1H), 7.03 (d, \(J = 7.6\) Hz, 1H), 2.75-2.57 (m, 8H), 2.57-2.45 (m, 2H), 0.86 (t, \(J = 7.2\) Hz, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 164.0, 142.8, 140.1, 137.0, 136.8, 136.0, 133.2, 130.0, 129.4, 129.3, 128.7, 125.4, 123.5, 48.8, 24.4, 24.8, 24.17, 13.11. HRMS (ESI) m/z: (M-H\(^{-}\)) calcd for C_{21}H_{25}N_{2}O 343.1805; Found 343.1802. IR

4-(diethylamino)-3-phenylbenzo[g]isoquinolin-1(2H)-one (3ah): white solid (57.53 mg, 84% yield, TLC (PE/EA, 5:1): \(R_f = 0.25\)). mp 252-253 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.04 (s, 1H), 8.45 (s, 1H), 8.13-8.04 (m, 2H), 8.00 (d, \(J = 8.4\) Hz, 1H), 7.64-7.58 (m, 5H), 7.56-7.45 (m, 6H), 7.30-2.88 (m, 4H), 1.00 (t, \(J = 7.2\) Hz, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.5, 136.4, 135.9, 135.6, 135.4, 131.5, 129.3, 129.2, 129.0, 128.9, 128.5, 128.3, 128.1, 126.0, 124.8, 124.3, 123.3, 48.4, 14.4. HRMS (ESI) m/z: (M-H\(^{-}\)) calcd for C_{22}H_{23}N_{2}O 341.1659; Found 341.1653. IR (KBr, thin film): 2968, 1655, 1624, 1486, 1446, 1361, 1200, 1123, 959, 892, 776, 537 cm\(^{-1}\).

1-(diethylamino)-2-phenylbenzo[f]isoquinolin-4(3H)-one (3ai): fluorescent green solid (13.7 mg, 46% yield, TLC (PE/EA, 5:1): \(R_f = 0.11\)). mp 245-246 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.18 (s, 1H), 9.94 (d, \(J = 8.0\) Hz, 1H), 8.17 (d, \(J = 9.2\) Hz, 1H), 8.06 (d, \(J = 8.8\) Hz, 1H), 7.90 (d, \(J = 7.2\) Hz, 1H), 7.68-7.54 (m, 7H), 3.05-2.83 (m, 4H), 0.97 (t, \(J = 7.2\) Hz, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 163.7, 143.7, 141.2, 135.6, 134.1, 132.8, 130.0, 129.6, 129.0, 128.6, 128.5, 128.2, 126.9, 125.9, 123.1, 119.5, 49.4, 14.9. HRMS (ESI) m/z: (M-H\(^{-}\)) calcd for C_{23}H_{22}N_{2}O 343.1805; Found 343.1800. IR (KBr, thin film): 2968, 2926, 1633, 1548, 1446, 1246, 1191, 1097, 918, 833, 761, 510 cm\(^{-1}\).

4-(diethylamino)-3-phenylbenzo[h]isoquinolin-1(2H)-one (3ai′): fluorescent green solid (13.5 mg, 20% yield, TLC (PE/EA, 5:1): \(R_f = 0.28\)). mp 222-223 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.07 (d, \(J = 8.8\) Hz, 1H), 9.42 (s, 1H), 8.38 (d, \(J = 8.8\) Hz, 1H), 7.91 (dd, \(J = 8.0, 1.2\) Hz, 1H), 7.85 (d, \(J = 8.8\) Hz, 1H), 7.67-7.60 (m, 1H), 7.59-7.44 (m, 6H), 2.97-2.85 (m, 2H), 2.74-2.63 (m, 2H), 0.96 (t, \(J = 7.2\) Hz, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 161.6, 141.2, 138.7, 136.5, 135.5, 130.5, 129.3, 128.8, 128.8, 128.5, 128.4, 128.3, 127.9, 125.7, 124.8, 123.9, 123.7, 48.2, 12.8. HRMS (ESI) m/z: (M-H\(^{-}\)) calcd for C_{23}H_{22}N_{2}O 343.1805; Found 343.1802. IR (KBr, thin film): 2929, 1740, 1635, 1541, 1485, 1379, 1245, 1107, 917, 840, 762, 584 cm\(^{-1}\).

4-(diethylamino)-5-methyl-3-phenylisoquinolin-1(2H)-one (3aj): white solid (31.4 mg, 51% yield, TLC (PE/EA, 2:1): \(R_f = 0.68\)). mp 166-167 °C. \(^1\)H NMR (400
HRMS (ESI) m/z: (M+H)+ calcd for C_{20}H_{23}N_{2}O_{3} 307.1805; Found 307.1801. IR (KBr, thin film): 2973, 2847, 1642, 1564, 1465, 1379, 1257, 1120, 1029, 935, 877, 744, 507 cm\(^{-1}\).

2.7.3 Characterization of derivatization products:

4-(diethylamino)-8-methyl-3-phenylisoquinolin-1(2H)-one (3aj\(^{+}\)): white solid (24.8 mg, 42% yield, TLC (PE/EA, 2:1): R\(_{f}\) = 0.49). mp 197-198 \(^{\circ}\)C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.56-8.42 (m, 1H), 7.99 (d, \(J = 8.4\) Hz, 1H), 7.70-7.63 (m, 1H), 7.53-7.42 (m, 4H), 7.33-7.27 (m, 2H), 3.21 (s, 3H), 2.85-2.66 (m, 4H), 0.89 (t, \(J = 7.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.3, 142.5, 139.2, 135.1, 131.7, 129.6, 128.6, 128.3, 128.0, 126.5, 126.3, 125.4, 124.1, 48.4, 33.8, 14.5. HRMS (ESI) m/z: (M+H\(^{+}\)) calcd for C\(_{20}\)H\(_{23}\)N\(_{2}\)O\(_{3}\) 371.1424; Found 371.1424.

4-(diethylamino)-3-phenylisoquinolin-1-yl methanesulfonate (5): white solid (39.8 mg, 68% yield, TLC (PE/EA, 5:1): R\(_{f}\) = 0.56). mp 86-87 \(^{\circ}\)C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.25 (d, \(J = 8.0\) Hz, 1H), 8.00 (d, \(J = 7.6\) Hz, 1H), 7.52-7.45 (m, 4H), 7.32-7.27 (m, 2H), 3.21 (s, 3H), 2.83-2.66 (m, 4H), 0.89 (t, \(J = 7.2\) Hz, 6H). \(^{13}\)C NMR (100 Hz, CDCl\(_3\)) \(\delta\) 162.3, 142.5, 139.2, 135.1, 131.7, 129.6, 128.6, 128.3, 128.0, 126.5, 126.3, 124.1, 48.4, 33.8, 14.5. HRMS (ESI) m/z: (M+H\(^{+}\)) calcd for C\(_{20}\)H\(_{23}\)N\(_{2}\)O\(_{3}\) 371.1424; Found 371.1424. IR (KBr, thin film): 3058, 3025, 2975, 2838, 1614, 1585, 1448, 1261, 1183, 892, 813, 573 cm\(^{-1}\).

4-(diethylamino)-3-phenylisoquinolin-1-yl 4-methylbenzenesulfonate (6): white solid (58.0 mg, 65% yield, TLC (PE/EA, 5:1): R\(_{f}\) = 0.62). mp 89-90 \(^{\circ}\)C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.27 (d, \(J = 8.4\) Hz, 1H), 8.20 (d, \(J = 8.0\) Hz, 1H), 7.99 (d, \(J = 8.0\) Hz, 2H), 7.73 (t, \(J = 7.6\) Hz, 1H), 7.62 (t, \(J = 7.2\) Hz, 1H), 7.48-7.34 (m, 5H), 7.24 (d, \(J = 8.0\) Hz, 2H), 3.02 (q, \(J = 6.8\) Hz, 4H), 2.42 (s, 3H), 0.97 (t, \(J = 7.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 150.0, 146.8, 144.8, 140.7, 139.8, 138.3, 134.7, 130.6, 129.4, 129.3, 127.6, 127.5, 125.4, 124.2, 120.6, 48.0, 21.7, 14.3. HRMS (ESI) m/z: (M+H\(^{+}\)) calcd for C\(_{24}\)H\(_{25}\)N\(_{2}\)O\(_{3}\)S 447.1737; Found 447.1739. IR (KBr, thin film): 3065, 2968, 2858, 1590, 1450, 1374, 1340, 1192, 1048, 892, 774, 541 cm\(^{-1}\).

2-benzyl-4-(diethylamino)-3-phenylisoquinolin-1(2H)-one (7): colorless oily liquid (56.1 mg, 74% yield, TLC (PE/EA, 10:1): R\(_{f}\) = 0.33). \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.54 (d, \(J = 8.0\) Hz, 1H), 8.03 (d, \(J = 8.4\) Hz, 1H), 7.69 (t, \(J = 7.2\) Hz, 1H), 7.52 (t, \(J = 7.6\) Hz, 1H), 7.36 (t, \(J = 7.6\) Hz, 1H), 7.28 (t, \(J = 7.6\) Hz, 2H), 7.20-7.09 (m, 3H), 7.04 (d, \(J = 7.2\) Hz, 2H), 6.81 (t, \(J = 3.2\) Hz, 2H), 5.08 (s, 2H), 2.85-2.55 (m, 4H), 0.88 (t, \(J = 7.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 162.3, 142.4, 139.4, 137.9, 134.1, 132.0, 130.2, 128.6, 128.3, 128.2, 127.6, 126.8, 126.7, 125.7, 124.3, 48.6, 48.4, 14.5. HRMS (ESI) m/z: (M+H\(^{+}\)) calcd for C\(_{26}\)H\(_{27}\)N\(_{2}\)O\(_{3}\)S 383.2118;
Found 383.2119. IR (KBr, thin film): 3422, 3065, 2967, 2923, 1654, 1578, 1340, 1212, 1096, 776 cm⁻¹.

2-allyl-4-(diethylamino)-3-phenylisoquinolin-1(2H)-one (9): yellow solid (49.7 mg, 75% yield, TLC (PE/EA, 5:1): Rf = 0.23). mp 71-72 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.49 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 7.2 Hz, 2H), 7.68 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.47-7.37 (m, 3H), 7.35-7.27 (m, 2H), 5.83-5.70 (m, 1H), 4.15 (d, J = 10.4 Hz, 1H), 4.78 (d, J = 17.2 Hz, 1H), 4.37 (d, J = 4.8 Hz, 2H), 2.85-2.63 (m, 4H), 0.90 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 161.7, 142.3, 139.4, 134.3, 133.2, 131.9, 130.1, 128.7, 128.2, 127.7, 126.5, 126.5, 124.6, 116.3, 77.4, 77.1, 76.78, 48.4, 47.8, 14.3. HRMS (ESI) m/z: (M+H)⁺ calea for C₁₁H₁₄ClN₂ 333.1961; Found 333.1963. IR (KBr, thin film): 2806, 2794, 1777, 1661, 1588, 1571, 1464, 1342, 1209, 778 cm⁻¹.

chboro-N, N-diethyl-3-phenylisoquinolin-4-amine (10): white solid (60.5 mg, 97% yield, TLC (PE/EA, 5:1): Rf = 0.78). mp 64-65 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.31 (t, J = 8.4 Hz, 2H), 7.79-7.72 (m, 1H), 7.68-7.63 (m, 1H), 7.60-7.55 (m, 2H), 7.47-7.41 (m, 2H), 7.41-7.35 (m, 2H), 2.99 (q, J = 7.2 Hz, 4H), 0.99 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 149.9, 146.1, 140.3, 139.9, 139.0, 130.5, 129.3, 128.0, 127.8, 127.8, 126.9, 126.7, 125.0, 48.0, 14.3. HRMS (ESI) m/z: (M+H)⁺ calea for C₁₀H₁₂ClN₂ 311.1310; Found 311.1313. IR (KBr, thin film): 2964, 2828, 1607, 1556, 1442, 1382, 1259, 1174, 1056, 856, 767, 606 cm⁻¹.

N, N-diethyl-3-phenylisoquinolin-4-amine (11): yellow solid (50.7 mg, 92% yield, TLC (PE/EA, 20:1): Rf = 0.13). mp 91-92 °C. ¹H NMR (400 MHz, CDCl₃) δ 9.11 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.2 Hz, 1H), 7.62-7.53 (m, 3H), 7.45 (t, J = 7.2 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 3.02 (q, J = 7.2 Hz, 4H), 0.99 (t, J = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 151.0, 148.4, 141.8, 138.9, 130.0, 129.7, 127.9, 127.7, 127.4, 126.7, 124.4, 48.0, 14.3. HRMS (ESI) m/z: (M+H)⁺ calea for C₁₀H₁₂N₂ 277.1699; Found 277.1703. IR (KBr, thin film): 3420, 3051, 2965, 2834, 1623, 1554, 1498, 1349, 1239, 1188, 1069, 769 cm⁻¹.

4-(diethylamino)-3-phenylisoquinolin-1-yl trifluoromethanesulfonate (12): yellow solid (117.9 mg, 93% yield, TLC (PE/EA, 50:1): Rf = 0.56). mp 91-92 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.28 (d, J = 8.8 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.72-7.63 (m, 3H), 7.49-7.36 (m, 3H), 3.09 (q, J = 7.2 Hz, 4H), 1.02 (t, J = 7.2 Hz, 3H), 1.51 (m, 2H, 1H), 1.39 (s, 1H), 1.35 (s, 1H), 1.29 (s, 1H), 1.27 (s, 1H), 1.25 (s, 1H), 1.22 (s, 1H), 1.19 (s, 1H), 0.97 (t, J = 17.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 147.1, 145.9, 140.2, 139.1, 138.2, 130.1, 128.3, 127.3, 127.0, 126.9, 124.0, 122.2, 119.0, 117.7 (q, J = 319.0 Hz), 46.94, 13.22; HRMS (ESI) m/z: (M+H)⁺ calea for C₁₀H₁₂F₃N₂O₇S 425.1141; Found 425.1144. IR (KBr, thin film): 2982, 2935, 2837, 1626, 1590, 1415, 1337, 1248, 1212, 1141, 1040, 888, 775 cm⁻¹.

N, N-diethyl-1, 3-diphenylisoquinolin-4-amine (13): yellow solid (38.5 mg, 55% yield, TLC (PE/EA, 40:1): Rf = 0.34). mp 98-99 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.36 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 7.77-7.60 (m, 5H),...
7.46 (dt, \( J = 24.4 \), 7.2 Hz, 6H), 7.35 (t, \( J = 7.2 \) Hz, 1H), 3.05 (q, \( J = 7.2 \) Hz, 4H), 1.04 (t, \( J = 7.2 \) Hz, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 156.4, 150.1, 141.9, 139.9, 138.4, 138.1, 130.2, 129.5, 129.3, 128.2, 127.8, 127.3, 127.0, 126.4, 124.7, 48.1, 14.5. HRMS (ESI) m/z: (M+H)\(^+\) calcd for C\(_{25}\)H\(_{25}\)N\(_2\) 353.2012; Found 353.2015. IR (KBr, thin film): 3054, 3021, 2968, 2923, 2858, 1614, 1548, 1498, 1388, 1254, 1028, 778 cm\(^{-1}\).

4-(diethylamino)-3-(4-((trimethylsilyl)ethynyl)phenyl)isoquinolin-1(2H)-one (14): yellow solid (46.32 mg, 60% yield, TLC (PE/EA, 2:1): \( R_f = 0.49 \). mp 254-255 °C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.50 (s, 1H), 8.36 (d, \( J = 8.0 \) Hz, 1H), 7.95 (s, 1H), 7.75-7.65 (m, 1H), 7.57 (d, \( J = 8.0 \) Hz, 2H), 7.53-7.40 (m, 3H), 3.10-2.81 (m, 4H), 0.93 (t, \( J = 6.8 \) Hz, 6H), 0.29 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 162.2, 140.1, 137.6, 135.2, 132.4, 131.9, 129.1, 128.0, 126.7, 125.9, 125.2, 124.4, 123.8, 104.5, 95.9, 48.5, 14.3, 0.0. HRMS (ESI) m/z: (M+H)\(^+\) calcd for C\(_{24}\)H\(_{29}\)N\(_2\)OSi 389.2049; Found 389.2052. IR (KBr, thin film): 3679, 3164, 2971, 2923, 2852, 2149, 1647, 1605, 1445, 1251, 867, 840 cm\(^{-1}\).

### 2.8 Reference


3 Copies of NMR spectra of substrates and products

3.1 Copies of NMR spectra of substrates:

1a

$^1H$ NMR (400 MHz, CDCl$_3$)

$^1C$ NMR (100 MHz, CDCl$_3$)
1b

$^1$H NMR (400 MHz, CDCl$_3$)

1.08  0.88  1.99

f1 (ppm)

$^{13}$C NMR (100 MHz, CDCl$_3$)

148.32

77.44  77.12

f1 (ppm)
$^1$H NMR (600 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
\[1^1HNMR\ (\text{DMSO-}d_6)\]

\[1^1\text{C NMR} \ (\text{DMSO-}d_6)\]
$^1$H NMR (400 MHz, CDCl$_3$)

S30
In

$^1H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

S34
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl3)

$^1$H NMR (400 MHz, CDCl3)
$^1\text{H NMR} (600\text{ MHz}, \text{CDCl}_3)$

$^{13}\text{C NMR} (150\text{ MHz}, \text{CDCl}_3)$
$^{1}$H NMR (400 MHz, CDC$_3$)

$^{13}$C NMR (100 MHz, CDC$_3$)
3.2 Copies of NMR spectra of products:

3aa

$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
3ma

$^1$H NMR (400 MHz, CDCl$_3$)

$^1$C NMR (100 MHz, CDCl$_3$)
3na

$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
30a

$^1$H NMR (400 MHz, CDCl$_3$)

$^13$C NMR (100 MHz, CDCl$_3$)
3pa

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)

S57
3ra

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
3ab

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)

S63
3ac

$^1$H NMR (400 MHz, CDCl$_3$)

$^1$C NMR (100 MHz, CDCl$_3$)

S64
$3ai'$

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
The regioselectivity was determined by NOE experiment. For 3aj, NOE correlation was observed between methyl-H in the 5th position and methyl-H of diethylin.
3.3 Copies of NMR spectra of derivatization products:

\begin{align*}
\text{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3})}
\end{align*}
$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)