

Supporting Information

Rh(III)-Catalyzed Three-Component Cascade Annulation to Produce *N*-oxopropyl Chain of Isoquinolone Derivatives

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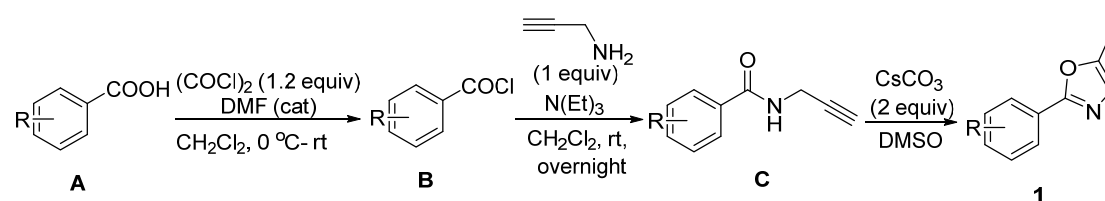
1. General Information

All reactions were carried out in high-pressure reaction tube. Column chromatography was performed with silica gel (200–300 mesh). High-resolution mass spectra (HRMS) were obtained with a Waters-Q-TOF-Premier (ESI). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz and 100MHz instrument. Spectra were reported relative to Me_4Si (δ 0.0 ppm), CDCl_3 (δ 7.26 ppm). ^{13}C NMR were reported relative to CDCl_3 (δ 77.16 ppm). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Compounds were characterized by ^1H NMR, ^{13}C NMR, ^{19}F NMR and HRMS.

2. Material

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Solvents were dried over sodium (for THF and ether) by refluxing for overnight and freshly distilled prior to use. Unless otherwise noted, all methanol was obtained from commercial suppliers and used without further purification. Methanol was dried and distilled from magnesium powder under nitrogen atmosphere. 2,5-diphenyloxazole,^[1] 5-(*tert*-butyl)-2-phenyloxazole,^[1] 2-phenyl-5-(*p*-tolyl)oxazole,^[2] 5-(4-methoxyphenyl)-2-phenyloxazole^[2], 2-phenyl-5-(*m*-tolyl)oxazole,^[2] 5-(3-methoxyphenyl)-2-phenyloxazole^[2] were all prepared following literature procedures.

Preparation of 2-aryloxazoline

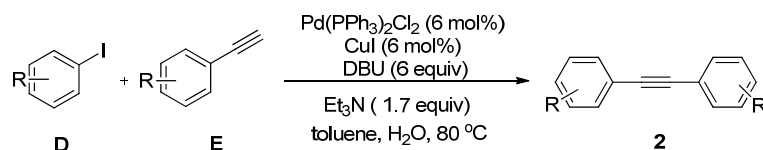


A 100 mL oven-dried round bottom flask with a stir bar was purged with argon and charged with benzoic acid **A** (5 mmol) in anhydrous CH_2Cl_2 (15 mL), which was added DMF (3 drop) at 0 °C and $(\text{COCl})_2$ (1.2 equiv) was subsequently added dropwise by syringe. After 15 min, the reaction mixture was allowed to warm to room temperature overnight. After removal of the volatiles under vacuum, the crude product **B** was used directly without any further purification.^[3]

To a solution of the propargylic amine (5.0 mmol) in anhydrous CH_2Cl_2 (15 mL) at 0 °C, Et_3N (1.5 equiv) and DMAP (2 mol%) were added, and the acid chloride (1.0 equiv) was added dropwise at 0 °C. After 15 min, the mixture was stirred overnight at room temperature overnight. After the reaction was completed, the mixture was quenched with water and extracted with CH_2Cl_2 (3×20 mL), the combined organic layer was washed with brine and then the combined organic layers were dried (MgSO_4), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether/ethyl acetate = 3/1, v/v) afforded the product **C**.^[4]

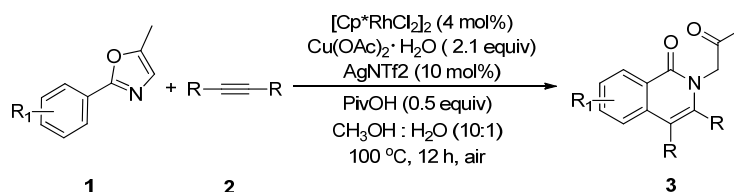
A mixture of propargylamides **C**, Cs_2CO_3 (2 equiv), DMSO (10 mL), was heated at 100 °C for 2 h and cooled to room temperature. The mixture was quenched with water and extracted with EtOAc (3×20 mL), the combined organic layer was washed with brine and then the combined organic layers were dried (MgSO_4), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether/ethyl acetate = 10/1, v/v) afforded the product **1**.^[5]

Preparation of diphenylacetylene derivatives



To a solution of the Pd(PPh₃)₂Cl₂ (6 mol%), CuI (6 mol%), DBU (6 equiv), Et₃N (1.7 equiv) in toluene (30 mL) and H₂O (0.4 equiv), iodide derivatives **D** (6 mmol, 1 equiv) and alkyne derivatives **E** (1.1 equiv) were added and stirred at 80 °C for 18 h. The mixture was quenched with water and extracted with EtOAc (3 × 20 mL), the combined organic layer was washed with brine and then the combined organic layers were dried (MgSO₄), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether) afforded the product **2**.^[6]

3. General Procedure for the Synthesis of Isoquinolone Derivatives



A mixture of 2-phenyloxazole **1** (0.05 mmol), acetylene derivatives **2** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂·H₂O (2.1 equiv), AgNTf₂ (10 mol%) and PivOH (0.5 equiv) were added to an oven dried high pressure tube under air atmosphere. MeOH (0.5 mL) and H₂O (50 μL) were then added by syringe. The reaction mixture was stirred at 100 °C for 12 h. After removal of the volatiles under vacuum, the crude product was purified by column chromatography on silica gel afforded the pure product **3**.

4. Optimization of the Reaction Conditions

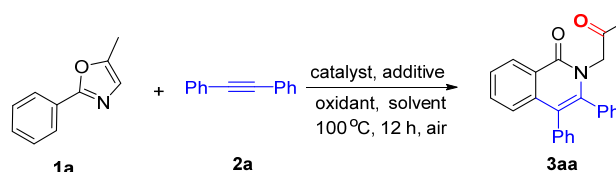


Table S1. The effect of catalysts on the reaction^a

Entry	Catalyst	Oxidant	Solvent	Yield ^b /%
1	[RhCl(C ₂ H ₄) ₂] ₂	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	ND
2	[Rh(OAc) ₂] ₂	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	ND
3	[Rh(COD)Cl] ₂	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	ND
4	[Rh(COD) ₂ BF ₄]	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	ND
5	Cp*Rh(OAc) ₂ ·H ₂ O	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	18

6	Cp*Rh(CH ₃ CN) ₃ (SbF ₆) ₂	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	44
7	[Cp*RhCl ₂] ₂	Cu(OAc) ₂ ·H ₂ O	CH ₃ OH	57

^aReaction conditions: **1a** (0.05 mmol), **2a** (2.0 equiv), Catalyst (5 mol%), Cu(OAc)₂·H₂O (2.1 equiv), AgNTf₂ (20 mol%), CH₃OH (0.5 mL), 100 °C, 12 h under air. ^bIsolated yields.

Table S2. The effect of oxidants and additives on the reaction^a

Entry	Oxidant	Additive	Yield ^b /%
1	Cu(acac) ₂	AgNTf ₂	ND
2	Cu(OTf) ₂	AgNTf ₂	ND
3	AgCO ₃	AgNTf ₂	ND
4	AgOAc	AgNTf ₂	ND
5	Cu(OAc) ₂	AgNTf ₂	Trace
6	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂	57
7	Cu(OAc) ₂ ·H ₂ O	AgSbF ₆	52
8	Cu(OAc) ₂ ·H ₂ O	AgOTf	14
9	Cu(OAc) ₂ ·H ₂ O	AgSO ₃ CH ₃	40
10	Cu(OAc) ₂ ·H ₂ O	AgBF ₄	51
11	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /H ₂ O	65
12	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PhSO ₃ H/H ₂ O	ND
13	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /AcOH/H ₂ O	42
14	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PhCOOH/H ₂ O	65
15	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /TFA/H ₂ O	40
16	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PhOCH ₂ COOH/H ₂ O	64
17	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /1-AdCOOH/H ₂ O	66
18	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PivOH/H ₂ O	74
19 ^c	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PivOH/H ₂ O	53
20 ^d	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /PivOH/H ₂ O	52
21	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /K ₃ PO ₄ /H ₂ O	67
22	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /Na ₂ CO ₃ /H ₂ O	40
23	Cu(OAc) ₂ ·H ₂ O	AgNTf ₂ /NaHCO ₃ /H ₂ O	54

^aReaction conditions: **1a** (0.05 mmol), **2a** (2.0 equiv), [Cp*RhCl₂]₂ (5 mol%), Oxidant (2.1 equiv), silver salt (20 mol%)/Additive (1 equiv)/ H₂O (50 μL), CH₃OH (0.5 mL), 100 °C, 12 h under air. ^bIsolated yields. ^c80 °C. ^d120 °C.

Table S3. The effect of solvents on the reaction^a

Entry	Solvent	Yield ^b /%
1	THF	56
2	DCE	41
3	CH ₃ CN	57
4	Toluene	Trace
5	1,4-Dioxane	42
6	EtOH	64

7	H ₂ O	ND
8 ^c	CH ₃ OH	60
9	CH ₃ OH	74
10 ^d	CH ₃ OH	46

^aReaction conditions: **1a** (0.05 mmol), **2a** (2.0 equiv), [Cp*RhCl₂]₂ (5 mol%), Cu(OAc)₂·H₂O (2.1 equiv), AgNTf₂ (20 mol%), PivOH (1 equiv), Solvent (0.5 mL), H₂O (50 μL), 100 °C, 12 h under air. ^bIsolated yields. ^c30 μL H₂O. ^d70 μL H₂O.

Table S4. The effect of equivalent on the reaction^a

Entry	2a /equiv	Catalyst/mol%	Oxidant/equiv	AgNTf ₂ /mol%	PivOH/equiv	Yield ^b /%
1	2	[Cp*RhCl ₂] ₂ /2	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	70
2	2	[Cp*RhCl ₂] ₂ /3	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	72
3	2	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	80
4	2	[Cp*RhCl ₂] ₂ /5	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	74
5	1.2	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	75
6	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	82
7	1.8	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1	80
8	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/1.5	AgNTf ₂ /20	PivOH/1	62
9	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.5	AgNTf ₂ /20	PivOH/1	66
10	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/1.5	75
11	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /20	PivOH/0.5	82
12	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /30	PivOH/0.5	73
13	1.5	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /10	PivOH/0.5	86

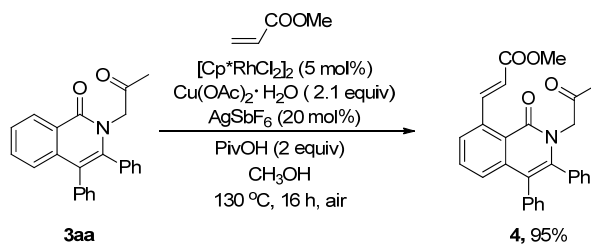
^aReaction conditions: **1a** (0.05 mmol), **2a** (x equiv), [Cp*RhCl₂]₂ (x mol%), Cu(OAc)₂·H₂O (x equiv), AgNTf₂ (x mol%), PivOH (x equiv), CH₃OH (0.5 mL), 50 μL H₂O, 100 °C, 12 h under air. ^bIsolated yields.

Table S5. The effect of methanol on the reaction^a

Entry	Catalyst/mol%	Oxidant/equiv	AgNTf ₂ /mol%	Solvent	Yield ^b /%
1	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ ·H ₂ O/2.1	AgNTf ₂ /10	MeOH	40
2	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ /2.1	AgNTf ₂ /10	MeOH	9
3	[Cp*RhCl ₂] ₂ /4	Cu(OAc) ₂ /2.1	AgNTf ₂ /10	MeOH ^c	33%

^aReaction conditions: **1a** (0.05 mmol), **2a** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Oxidant (2.1 equiv), AgNTf₂ (10mol%), treated anhydrous CH₃OH (0.5 mL), 100 °C, 12 h under air. ^bIsolated yields. ^cuntreated MeOH.

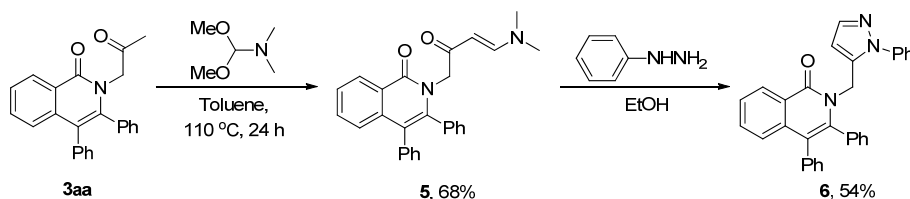
5. Synthetic Applications



Synthesis of 4

A mixture of **3aa** (0.05 mmol), methyl acrylate (3 equiv), [Cp*RhCl₂]₂ (5 mol%), Cu(OAc)₂·H₂O (2.1 equiv), AgSbF₆ (20 mol%) and PivOH (2 equiv) were added to an oven dried high pressure tube under air atmosphere. MeOH (0.5 mL) was then added by syringe. The reaction mixture was stirred at 130 °C for 16 h. After removal of the solvent, the crude product was separated by column chromatography (petroleum ether/ethyl acetate = 4/1, v/v) to afford the product **4** as a white solid (95% yield). Melting point: 178.3 – 181.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 9.04 (d, *J* = 15.8 Hz, 1H), 7.53 – 7.42 (m, 2H), 7.21–7.13 (m, 7H), 7.11–7.04 (m, 4H), 6.17 (d, *J* = 15.9 Hz, 1H), 4.61 (s, 2H), 3.81 (s, 3H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 167.3, 162.1, 147.8, 141.4, 139.1, 138.5, 136.5, 134.4, 132.0, 131.6, 129.9, 128.7, 128.3, 128.2, 127.4, 127.3, 127.1, 122.5, 119.7, 118.9, 55.7, 51.8, 27.4. HRMS (ESI): *m/z* calcd for C₂₈H₂₃O₄NNa [M+Na]⁺ : 460.1525, found: 460.1527.

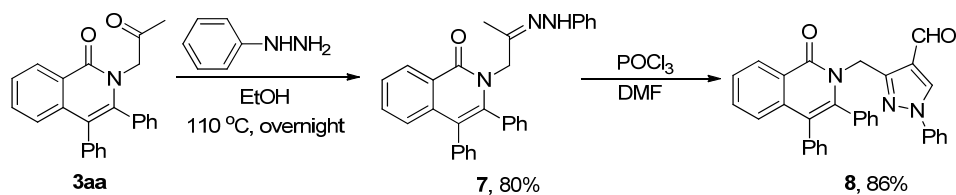
Synthesis of 6



To a stirred solution of **3aa** (0.05 mmol, 1.0 equiv) in toluene (0.5 mL), 1,1-dimethoxy-N,N-dimethylmethanamine (3 equiv) was added, and the mixture was stirred at 110 °C. After completion of the reaction (monitored by TLC), The reaction mixture was allowed to cool to room temperature. The resulting solid was filtered off, washed with toluene, the crude product **5** was used directly without any further purification.^[7]

A mixture of **5** (0.04 mmol) and phenylhydrazine (0.05 mL) in ethanol (0.5 mL) was refluxed at 110 °C overnight. After removal of the solvent, the crude product was separated by column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1, v/v) to afford the pure product **6** as a white solid (54% yield).^[8] Melting point: 162.1 – 163.3 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.61 (d, *J* = 5.6 Hz, 1H), 7.79 (d, *J* = 2.4 Hz, 1H), 7.64 – 7.46 (m, 4H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.26 – 7.11 (m, 10H), 7.11 – 7.05 (m, 2H), 6.37 (d, *J* = 2.4 Hz, 1H), 5.24 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 162.6, 150.9, 141.6, 140.2, 137.6, 136.7, 134.5, 132.4, 131.7, 130.8, 129.4, 128.4, 128.2, 128.0, 127.8, 127.3, 126.9, 126.7, 126.2, 125.6, 125.3, 119.4, 118.9, 107.3, 44.3. HRMS (ESI): *m/z* calcd for C₃₁H₂₃ON₃Na [M+Na]⁺ : 476.1739, found: 476.1736.

Synthesis of 8

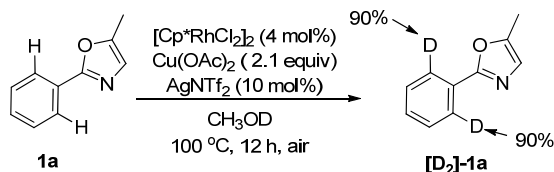


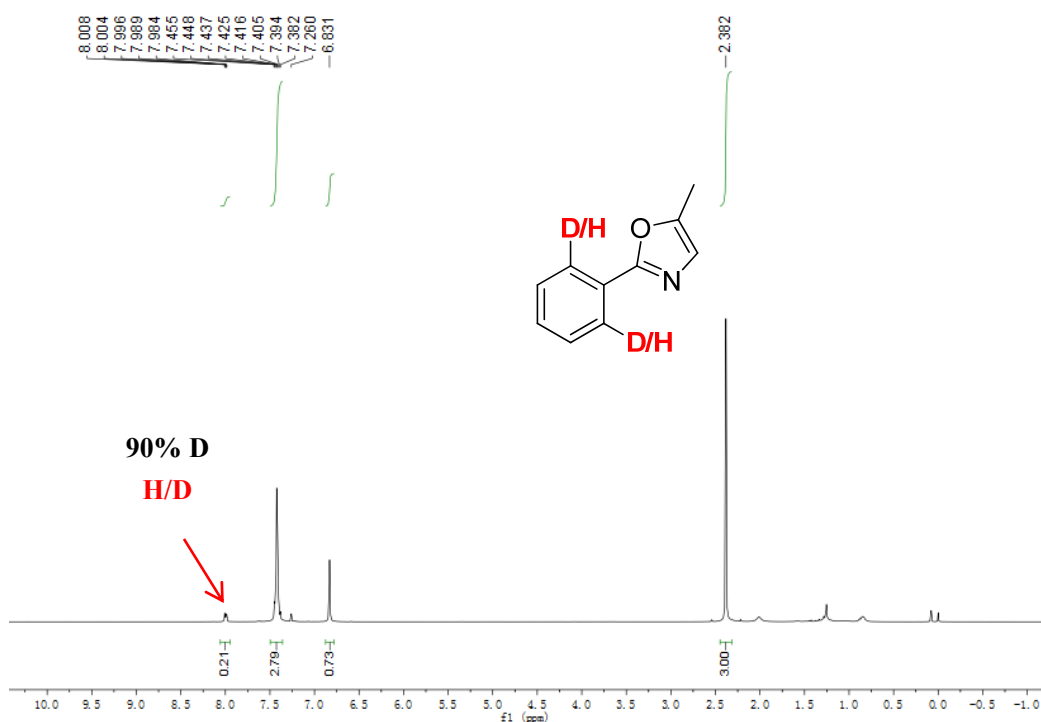
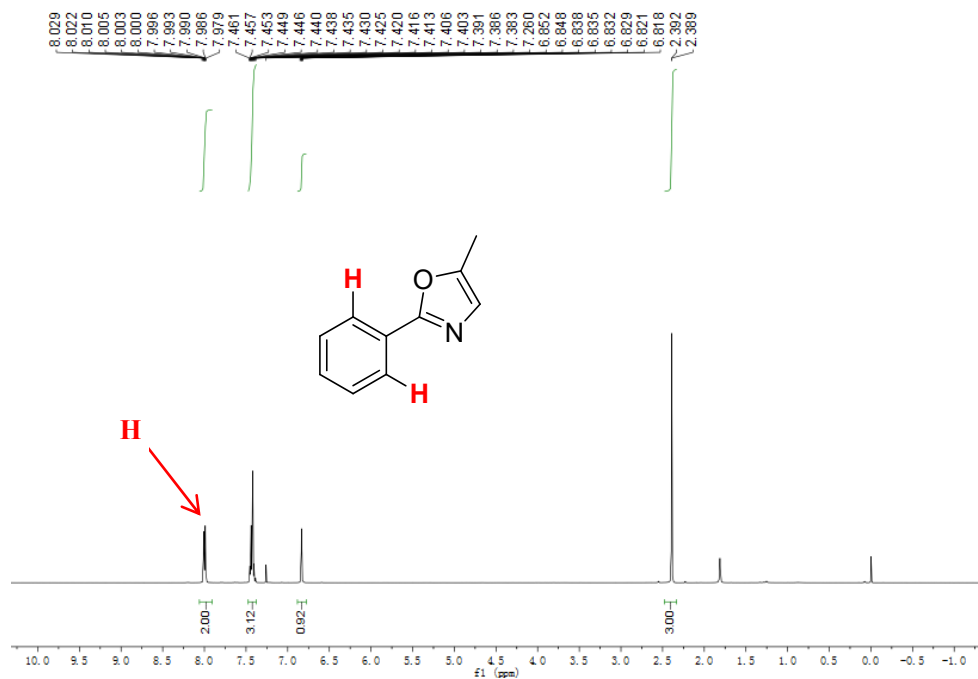
A mixture of **3aa** (0.1 mmol), AcOH (3drop) and phenylhydrazine (0.05 mL) in ethanol (0.5 mL) was refluxed at 110 °C overnight. The reaction mixture was refluxed overnight, and allowed to cool at room temperature. The solid product formed was collected by filtration and recrystallized from ethanol to afford the product **7**.

POCl₃ (0.1 mol) was added dropwise to DMF (2 mL) at 0 °C. After 1 h, a solution of **7** (0.05 mol) in DMF (1 mL) was added dropwise at 0 °C. The mixture was stirred at 0 °C for 1 h and at 80 °C for 1 h, then cooled to room temperature and 100 g ice was added. The solid product formed was collected by filtration to give the crude product, the crude product was separated by column chromatography on silica gel (petroleum ether/ethyl acetate =2/1, v/v) afforded the pure products **8** as a white solid (86% yield).^[9] Melting point: 201.1 – 203.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 9.85 (s, 1H), 8.56 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.29 (s, 1H), 7.63 – 7.47 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.23 – 7.06 (m, 11H), 5.47 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 184.0, 162.5, 151.5, 141.5, 139.1, 137.7, 136.7, 134.8, 132.4, 131.9, 131.7, 130.5, 129.7, 128.4, 128.3, 128.0, 127.9, 127.7, 126.9, 126.7, 125.6, 125.2, 122.5, 119.6, 119.3, 43.5. HRMS (ESI): *m/z* calcd for C₃₂H₂₃O₂N₃Na [M+Na]⁺ : 504.1688, found: 504.1690.

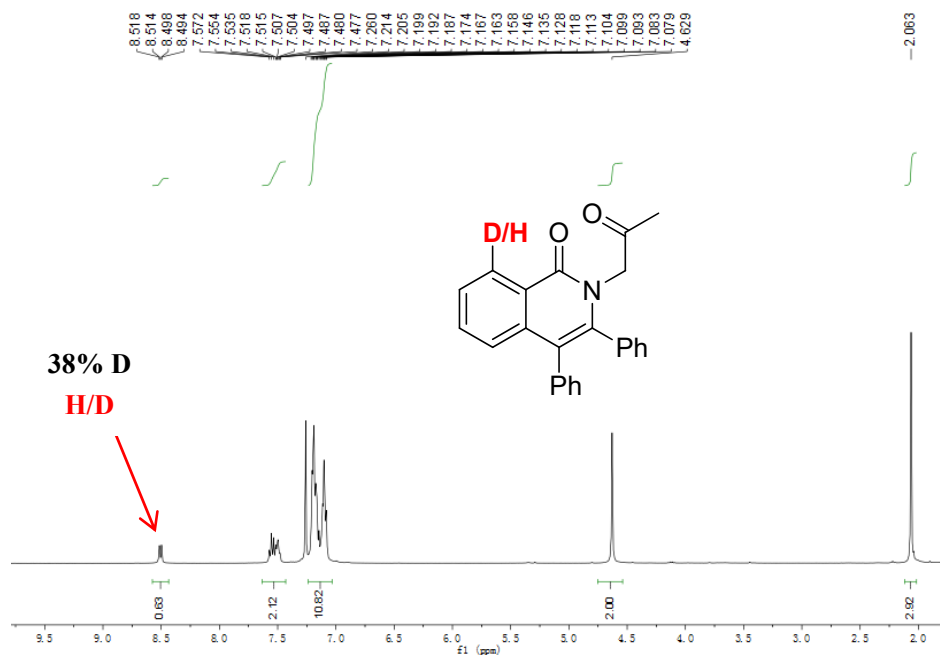
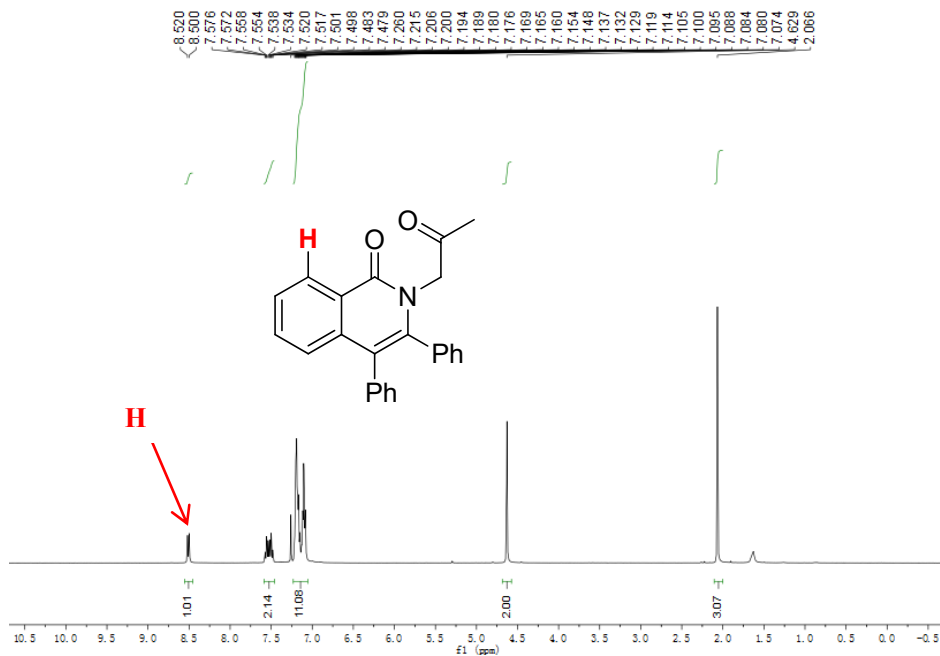
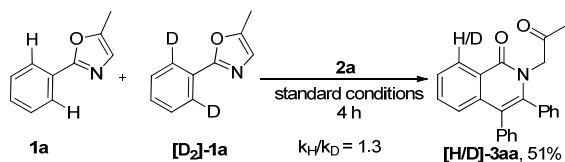
6. Mechanism Study

Deuterium-labeling experiments were carried out to study the mechanism of this reaction. **1a** (0.2 mmol), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂ (2.1 equiv), AgNTf₂ (10 mol%) were stirred in CH₃OD (1 mL) under air atmosphere at 100 °C for 12 h. After completion, the crude product was separated by column chromatography (petroleum ether/ethyl acetate =10/1, v/v) to afford the product **1a**+**[D₂]-1a**. The deuterium rate (90%) was obtained from ¹H NMR. Deuterium was observed at both *ortho*-positions, which indicated the possibility of the reaction pathway via *ortho* C–H activation.

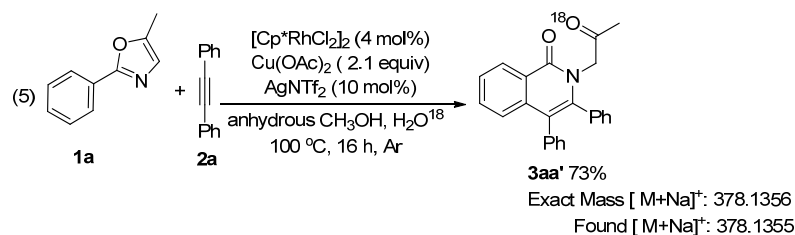




In addition, the kinetic isotope effect (KIE) study was conducted. **1a** (0.05 mmol), [**D**₂]-**1a** (0.05 mmol, 90% D), and diphenylacetylene **2a** (3 equiv) were stirred at 100 °C for 4 h under standard conditions. After completion, the reaction mixture was purified by flash chromatography eluting with ethyl acetate and petroleum ether (1:3) to give **3aa** + [**D**]-**3aa**. The ratio of two products was determined by ¹H NMR integration method to give kinetic isotopic effect (KIE) $k_H/k_D = 1.3$, thus indicating that the first C-H bond cleavage might be not involved in the product determining step.



¹⁸O labeling experiments were carried out to study the mechanism of this reaction. **1a** (0.05 mmol), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂ (2.1 equiv), AgNTf₂ (10 mol%) were stirred in treated anhydrous CH₃OH (0.5 mL) under Ar atmosphere at 100 °C for 16 h. After completion, the crude product was separated by column chromatography (petroleum ether/ethyl acetate =10/1, v/v) to afford the product **3aa'**.

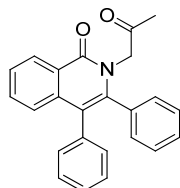


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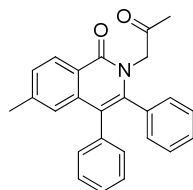
8. Characterization Data and NMR Spectra of isoquinolone derivatives

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



The general procedure was applied to **1a** (0.05 mmol), **2a** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3aa** as a white solid (86% yield). Melting point: 183.6 – 184.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.51 (d, *J* = 7.9 Hz, 1H), 7.53 (m, 2H), 7.23 – 7.05 (m, 11H), 4.63 (s, 2H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.9, 162.3, 140.6, 137.6, 136.4, 134.7, 132.6, 131.6, 130.1, 128.7, 128.3, 128.1, 128.0, 127.0, 126.9, 125.7, 124.8, 119.2, 55.7, 27.4. HRMS (ESI): *m/z* calcd for C₂₄H₁₉O₂NNa [M+Na]⁺: 376.1313, found: 376.1315.

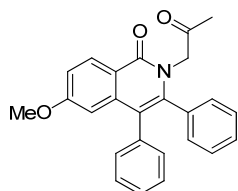
6-methyl-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2H)-one (**3ba**)



The general procedure was applied to **1b** (0.05 mmol), **2a** (1.2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH

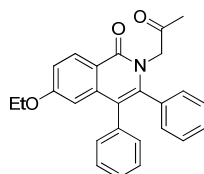
(0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ba** as a white solid (75% yield). Melting point: 185.5 – 187.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.39 (d, *J* = 8.2 Hz, 1H), 7.32 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.24 – 7.14 (m, 6H), 7.13 – 7.05 (m, 4H), 6.94 (s, 1H), 4.61 (s, 2H), 2.35 (s, 3H), 2.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.1, 162.3, 143.2, 140.7, 137.7, 136.6, 134.8, 131.6, 130.2, 128.6, 128.5, 128.3, 128.1, 128.0, 126.9, 125.3, 122.7, 119.1, 55.6, 27.4, 22.2. HRMS (ESI): *m/z* calcd for C₂₅H₂₁O₂NNa [M+Na]⁺ : 390.1470, found: 390.1474.

6-methoxy-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ca**)



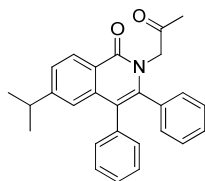
The general procedure was applied to **1c** (0.05 mmol), **2a** (1.5 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ca** as a white solid (93% yield). Melting point: 180.1 – 181.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.42 (d, *J* = 8.9 Hz, 1H), 7.23 – 7.12 (m, 6H), 7.12 – 7.04 (m, 5H), 6.52 (d, *J* = 2.5 Hz, 1H), 4.59 (s, 2H), 3.69 (s, 3H), 2.05 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.1, 163.0, 161.9, 141.3, 139.8, 136.4, 134.8, 131.5, 130.2, 130.0, 128.6, 128.3, 128.1, 127.0, 118.9, 118.8, 115.7, 107.4, 55.5, 55.4 (d, *J* = 8.1 Hz), 27.4. HRMS (ESI): *m/z* calcd for C₂₅H₂₁O₃NNa [M+Na]⁺ : 406.1419, found: 406.1420.

6-ethoxy-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3da**)



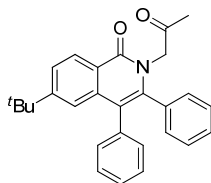
The general procedure was applied to **1d** (0.05 mmol), **2a** (1.2 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3da** as a white solid (82% yield). Melting point: 195.9 – 198.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.41 (d, *J* = 8.9 Hz, 1H), 7.22 – 7.11 (m, 6H), 7.10 – 7.00(m, 5H), 6.51 (s, 1H), 4.59 (s, 2H), 3.90 (q, *J* = 7.0 Hz, 2H), 2.04 (s, 3H), 1.32 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.4, 161.9, 141.2, 139.7, 136.5, 134.8, 131.5, 130.1, 130.0, 128.5, 128.2, 128.0, 126.9, 118.9, 118.6, 115.9, 108.1, 63.6, 55.4, 27.3, 14.6. HRMS (ESI): *m/z* calcd for C₂₆H₂₃O₃NNa [M+Na]⁺ : 420.1576, found: 420.1578.

6-isopropyl-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ea**)



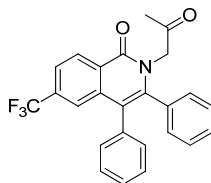
The general procedure was applied to **1e** (0.05 mmol), **2a** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ea** as a white solid (83% yield). Melting point: 158.8 – 160.1 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.44 (d, *J* = 8.3 Hz, 1H), 7.40 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.22 – 7.14 (m, 6H), 7.13 – 7.06 (m, 4H), 6.99 (s, 1H), 4.61 (s, 2H), 2.88 (m, 1H), 2.05 (s, 3H), 1.17 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.2, 153.9, 140.6, 137.8, 136.5, 134.8, 131.6, 130.2, 128.6, 128.3, 128.2, 128.0, 126.9, 125.6, 123.1, 123.0, 119.3, 55.6, 34.6, 27.4, 23.8. HRMS (ESI): *m/z* calcd for C₂₇H₂₅O₂NNa [M+Na]⁺ : 418.1783, found: 418.1780.

6-(*tert*-butyl)-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3fa**)



The general procedure was applied to **1f** (0.05 mmol), **2a** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3fa** as a white solid (73% yield). Melting point: 167.2 – 169.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.43 (d, *J* = 8.5 Hz, 1H), 7.57 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.24 – 7.13 (m, 7H), 7.13 – 7.07 (m, 4H), 4.61 (s, 2H), 2.06 (s, 3H), 1.22 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.2, 156.1, 140.5, 137.5, 136.5, 134.9, 131.6, 130.2, 128.6, 128.3, 128.0, 127.8, 126.9, 125.0, 122.6, 121.7, 119.5, 55.6, 35.4, 31.1, 27.4. HRMS (ESI): *m/z* calcd for C₂₈H₂₇O₂NNa [M+Na]⁺ : 432.1939, found: 432.1934.

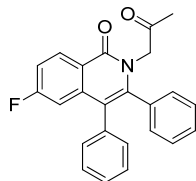
2-(2-oxopropyl)-3,4-diphenyl-6-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3ga**)



The general procedure was applied to **1g** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ga** as a white solid (74% yield). Melting point: 163.9 – 165.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.61 (d, *J* = 8.4 Hz, 1H), 7.69 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.45 (s, 1H), 7.25 – 7.16 (m, 6H), 7.13 – 7.03 (m, 4H), 4.65 (s, 2H), 2.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.4, 161.5, 142.3, 137.7, 135.3, 134.2, 134.1 (q, *J* = 32.3 Hz),

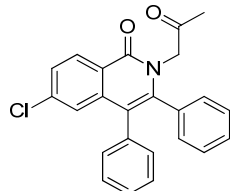
131.4, 129.9, 129.2, 129.0, 128.5, 128.4, 127.5, 126.9, 123.8 (q, $J = 271.2$ Hz), 122.9 (d, $J = 11.3$ Hz), 122.9 (d, $J = 3.8$ Hz), 118.9, 55.8, 27.4. ^{19}F NMR (376 MHz, CDCl_3): $\delta = -63.00$. HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{18}\text{F}_3\text{O}_2\text{NNa}$ $[\text{M}+\text{Na}]^+$: 444.1187, found: 444.1189.

6-fluoro-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ha**)



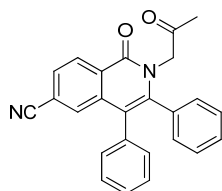
The general procedure was applied to **1h** (0.05 mmol), **2a** (1.5 equiv), $[\text{Cp}^*\text{RhCl}_2]_2$ (4 mol%), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (2.1 equiv), AgNTf_2 (10 mol%), PivOH (0.5 equiv) and H_2O (50 μL) in MeOH (0.5 mL) at 100 $^\circ\text{C}$ for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ha** as a white solid (35% yield). Melting point: 169.8 – 171.1 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3): $\delta = 8.51$ (dd, $J = 8.9, 5.9$ Hz, 1H), 7.24 – 7.16 (m, 7H), 7.12 – 7.06 (m, 4H), 6.80 (dd, $J = 10.4, 2.5$ Hz, 1H), 4.61 (s, 2H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 201.8, 165.6$ (d, $J = 250.5$ Hz), 161.6, 142.0, 140.2 (d, $J = 9.9$ Hz), 135.9, 134.4, 131.4, 131.3 (d, $J = 9.9$ Hz), 129.9, 128.9, 128.4, 128.3, 127.3, 121.5 (d, $J = 1.7$ Hz), 118.7 (d, $J = 3.3$ Hz), 115.5 (d, $J = 23.5$ Hz), 110.8 (d, $J = 23.2$ Hz), 55.6, 27.4. ^{19}F NMR (376 MHz, CDCl_3): $\delta = -105.39$. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{19}\text{O}_2\text{NF}$ $[\text{M}+\text{H}]^+$: 372.1400, found: 372.1404.

6-chloro-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ia**)



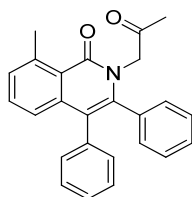
The general procedure was applied to **1i** (0.05 mmol), **2a** (1.5 equiv), $[\text{Cp}^*\text{RhCl}_2]_2$ (4 mol%), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (2.1 equiv), AgNTf_2 (10 mol%), PivOH (0.5 equiv) and H_2O (50 μL) in MeOH (0.5 mL) at 100 $^\circ\text{C}$ for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ia** as a white solid (41 % yield). Melting point: 175.1 – 177.1 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3): $\delta = 8.43$ (d, $J = 8.6$ Hz, 1H), 7.44 (dd, $J = 8.6, 2.0$ Hz, 1H), 7.24 – 7.15 (m, 6H), 7.14 (d, $J = 2.0$ Hz, 1H), 7.12 – 7.04 (m, 4H), 4.61 (s, 2H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 201.6, 161.7, 142.1, 139.3, 139.0, 135.7, 134.4, 131.5, 129.9, 128.9, 128.4, 128.3, 127.5, 127.3, 125.0, 123.2, 118.4, 55.7, 27.4$. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{19}\text{ClO}_2\text{N}$ $[\text{M}+\text{H}]^+$: 388.1104, found: 388.1104.

1-oxo-2-(2-oxopropyl)-3,4-diphenyl-1,2-dihydroisoquinoline-6-carbonitrile (**3ja**)



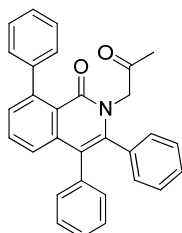
The general procedure was applied to **1j** (0.05 mmol), **2a** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ja** as a white solid (51 % yield). Melting point: 131.5 – 133.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.58 (d, *J* = 8.3 Hz, 1H), 7.68 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.50 (d, *J* = 1.5 Hz, 1H), 7.25 – 7.17 (m, 6H), 7.13 – 7.02 (m, 4H), 4.64 (s, 2H), 2.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.2, 161.3, 142.9, 137.8, 135.0, 133.9, 131.4, 130.7, 129.8, 129.3, 129.1, 128.6, 128.5, 127.7, 127.1, 118.4, 118.3, 116.1, 55.8, 27.4. HRMS (ESI): *m/z* calcd for C₂₅H₁₉O₂N₂ [M+H]⁺ : 379.1447, found: 379.1446.

8-methyl-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ka**)



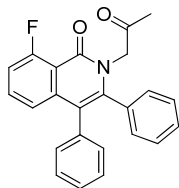
The general procedure was applied to **1k** (0.05 mmol), **2a** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3ka** as a white solid (51% yield). Melting point: 140.1 – 141.1 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.36 (t, *J* = 7.7 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.22 – 7.12 (m, 6H), 7.12 – 7.04 (m, 4H), 6.99 (d, *J* = 8.1 Hz, 1H), 4.57 (s, 2H), 2.97 (s, 3H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.3, 162.9, 142.0, 140.7, 139.4, 137.1, 134.9, 131.7, 130.1, 130.0, 128.5, 128.3, 128.0, 126.9, 124.1, 123.5, 119.1, 55.7, 27.4, 24.4. HRMS (ESI): *m/z* calcd for C₂₅H₂₁O₂NNa [M+Na]⁺ : 390.1470, found: 390.1469.

2-(2-oxopropyl)-3,4,8-triphenylisoquinolin-1(2*H*)-one (**3la**)



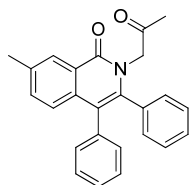
The general procedure was applied to **1l** (0.05 mmol), **2a** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3la** as a white solid (21% yield). Melting point: 221.5 – 224.1 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.55 – 7.47 (m, 1H), 7.44 – 7.33 (m, 5H), 7.29 – 7.25 (m, 1H), 7.25 – 7.11 (m, 9H), 7.11 – 7.06 (m, 2H), 4.56 (s, 2H), 1.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 161.4, 144.7, 143.9, 141.2, 139.2, 137.0, 134.9, 131.8, 131.2, 130.6, 130.0, 128.6, 128.5, 128.3, 128.1, 127.5, 127.0, 126.6, 125.6, 122.1, 118.8, 55.4, 27.2. HRMS (ESI): *m/z* calcd for C₃₀H₂₃O₂NNa [M+Na]⁺ : 452.1626, found: 452.1629.

8-fluoro-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ma**)



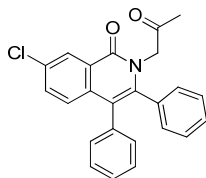
The general procedure was applied to **1m** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3ma** as a white solid (50% yield). Melting point: 191.9 – 192.5 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.44 (td, *J* = 8.1, 4.9 Hz, 1H), 7.24 – 7.12 (m, 6H), 7.12 – 7.03 (m, 5H), 6.91 (d, *J* = 8.2 Hz, 1H), 4.55 (s, 2H), 2.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 162.7 (d, *J* = 262.7 Hz), 159.4 (d, *J* = 4.7 Hz), 142.1, 140.4, 136.3, 134.4, 133.2 (d, *J* = 10 Hz), 131.5, 129.8, 128.8, 128.3, 128.1, 127.1, 121.6 (d, *J* = 4.4 Hz), 118.3 (d, *J* = 2.5 Hz), 114.0 (d, *J* = 4.9 Hz), 113.6 (d, *J* = 21.6 Hz), 55.4, 27.5. ¹⁹F NMR (376 MHz, CDCl₃): δ = -110.67. HRMS (ESI): *m/z* calcd for C₂₄H₁₉O₂FNH [M+H]⁺ : 372.1400, found: 372.1396.

7-methyl-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2H)-one (**3na**)



The general procedure was applied to **1n** (0.05 mmol), **2a** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3na** as a white solid (84% yield). Melting point: 138.8 – 140.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.31 (s, 1H), 7.35 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.22 – 7.11 (m, 6H), 7.08 (m, 5H), 4.62 (s, 2H), 2.47 (s, 3H), 2.04 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.9, 162.1, 139.6, 136.8, 136.4, 135.2, 134.6, 133.9, 131.4, 130.1, 128.5, 128.2, 127.9, 127.5, 126.8, 125.5, 124.6, 119.0, 55.5, 27.3, 21.4. HRMS (ESI): *m/z* calcd for C₂₅H₂₁O₂NNa [M+Na]⁺ : 390.1470, found: 390.1470.

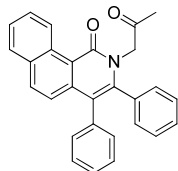
7-chloro-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2H)-one (**3oa**)



The general procedure was applied to **1o** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3oa** as a white solid (49% yield). Melting point: 157.8 – 159.5 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.46 (d, *J* = 2.3 Hz, 1H), 7.47 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.18 (m, 6H), 7.14 – 7.04 (m, 5H), 4.62 (s, 2H), 2.05 (s, 3H); ¹³C NMR (100 MHz,

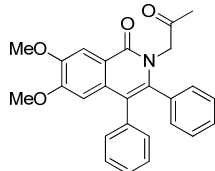
CDCl₃): δ = 201.6, 161.3, 141.0, 136.0, 135.9, 134.3, 133.0, 132.9, 131.5, 130.0, 128.8, 128.4, 128.2, 127.5, 127.4, 127.2, 125.9, 118.7, 55.7, 27.4. HRMS (ESI): m/z calcd for C₂₄H₁₈O₂CINNa [M+Na]⁺ : 410.0924, found: 410.0925.

2-(2-oxopropyl)-3,4-diphenylbenzo[*h*]isoquinolin-1(2*H*)-one (**3pa**)



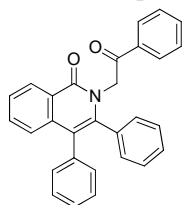
The general procedure was applied to **1p** (0.05 mmol), **2a** (1.5 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μ L) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3pa** as a white solid (66% yield). Melting point: 161.3 – 162.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 10.23 (d, J = 8.7 Hz, 1H), 7.89 (t, J = 9.2 Hz, 2H), 7.74 (t, J = 7.1 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.25 – 7.17 (m, 7H), 7.17 – 7.11 (m, 4H), 4.73 (s, 2H), 2.16 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.4, 142.6, 139.0, 137.0, 134.9, 133.9, 132.3, 132.0, 131.9, 129.9, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 127.1, 126.6, 123.6, 119.5, 118.4, 56.3, 27.6. HRMS (ESI): m/z calcd for C₂₈H₂₁O₂NNa [M+Na]⁺ : 426.1470, found: 426.1470.

6,7-dimethoxy-2-(2-oxopropyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3qa**)



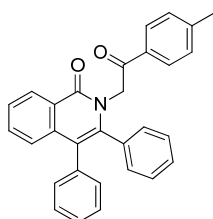
The general procedure was applied to **1q** (0.05 mmol), **2a** (1.5 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μ L) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3qa** as a white solid (50% yield). Melting point: 252.2 – 253.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.88 (s, 1H), 7.22 – 7.13 (m, 6H), 7.13 – 7.06 (m, 4H), 6.52 (s, 1H), 4.61 (s, 2H), 4.01 (s, 3H), 3.69 (s, 3H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.1, 161.5, 153.6, 149.3, 139.4, 136.7, 134.8, 133.2, 131.5, 130.3, 128.6, 128.3, 128.1, 127.0, 118.9, 118.8, 107.9, 106.0, 56.3 (d, J = 2.6 Hz), 55.9 (d, J = 2.3 Hz), 55.8, 27.5. HRMS (ESI): m/z calcd for C₂₆H₂₄O₄N [M+H]⁺ : 414.1705, found: 414.1699.

2-(2-oxo-2-phenylethyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ra**)



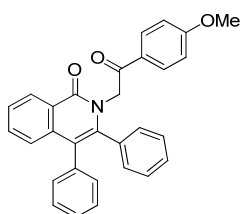
The general procedure was applied to **1r** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3ra** as a white solid (62% yield). Melting point: 224.3 – 225.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.54 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 2H), 7.60 – 7.47 (m, 3H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.07 (m, 11H), 5.27 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 193.6, 162.4, 141.0, 137.7, 136.5, 135.2, 134.7, 133.6, 132.5, 131.6, 130.1, 128.7, 128.6, 128.3, 128.1, 128.0, 128.0, 126.9, 126.8, 125.6, 124.9, 119.2, 52.6. HRMS (ESI): *m/z* calcd for C₂₉H₂₁O₂NNa [M+Na]⁺ : 438.1470, found: 438.1472.

2-(2-oxo-2-phenylethyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3sa**)



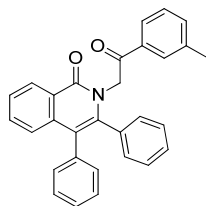
The general procedure was applied to **1s** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3sa** as a white solid (29% yield). Melting point: 239.3 – 241.5 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.53 (d, *J* = 8, 1H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.60 – 7.47 (m, 2H), 7.23 – 7.08 (m, 13H), 5.24 (s, 2H), 2.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): 193.2, 162.5, 144.5, 141.0, 137.7, 136.6, 134.8, 132.8, 132.5, 131.7, 130.2, 129.4, 128.6, 128.3, 128.2, 128.1, 128.1, 127.0, 126.8, 125.7, 125.0, 119.2, 52.5, 21.8. HRMS (ESI): *m/z* calcd for C₃₀H₂₃O₂NNa [M+Na]⁺ : 452.1626, found: 452.1627.

2-(2-(4-methoxyphenyl)-2-oxoethyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ta**)



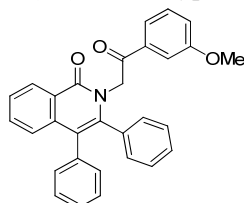
The general procedure was applied to **1t** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3ta** as a white solid (42% yield). Melting point: 247.5 – 248.7 °C ; ¹H NMR (400 MHz, CDCl₃): δ = 8.53 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.53 (dt, *J* = 26.0, 7.3 Hz, 2H), 7.23 – 7.08 (m, 11H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.23 (s, 2H), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 192.0, 163.9, 162.5, 141.1, 137.7, 136.6, 134.8, 132.5, 131.7, 130.3, 130.2, 128.6, 128.3, 128.2, 128.1, 127.0, 126.8, 125.7, 125.0, 119.2, 113.9, 55.6, 52.3. HRMS (ESI): *m/z* calcd for C₃₀H₂₃O₃NNa [M+Na]⁺ : 468.1576, found: 468.1576.

2-(2-oxo-2-phenylethyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3ua**)



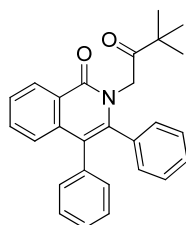
The general procedure was applied to **1u** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3ua** as a white solid (20% yield). Melting point: 219.1 – 222.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.53 (d, *J* = 7.5 Hz, 1H), 7.67 – 7.46 (m, 4H), 7.32 (dd, *J* = 22.5, 7.6 Hz, 2H), 7.24 – 7.09 (m, 11H), 5.24 (s, 2H), 2.36 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 193.9, 162.4, 141.1, 138.6, 137.7, 136.6, 135.3, 134.8, 134.4, 132.5, 131.7, 130.2, 128.6, 128.6, 128.3, 128.2, 128.1, 127.0, 126.8, 125.7, 125.2, 125.0, 119.3, 52.7, 21.4. HRMS (ESI): *m/z* calcd for C₃₀H₂₃O₂NNa [M+Na]⁺ : 452.1626, found: 452.1624.

2-(2-(3-methoxyphenyl)-2-oxoethyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3va**)



The general procedure was applied to **1v** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **3va** as a white solid (27% yield). Melting point: 262.7 – 265.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.53 (d, *J* = 7.9 Hz, 1H), 7.61 – 7.47 (m, 2H), 7.35 (dt, *J* = 5.9, 1.7 Hz, 2H), 7.30 (t, *J* = 8.1 Hz, 1H), 7.25 – 7.05 (m, 12H), 5.24 (s, 2H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 193.5, 162.4, 159.9, 141.0, 137.7, 136.6, 134.7, 132.6, 131.7, 130.2, 129.8, 128.7, 128.3, 128.2, 128.1, 127.0, 126.9, 125.7, 124.9, 120.5, 120.2, 119.3, 112.3, 55.6, 52.8. HRMS (ESI): *m/z* calcd for C₃₀H₂₃O₃NNa [M+Na]⁺ : 468.1576, found: 468.1576.

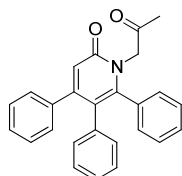
2-(3,3-dimethyl-2-oxobutyl)-3,4-diphenylisoquinolin-1(2*H*)-one (**3wa**)



The general procedure was applied to **1w** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv), and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3wa** as a white solid (60% yield). Melting point:

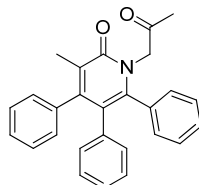
226.9 – 229.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.51 (d, *J* = 6.4 Hz, 1H), 7.50 (dt, *J* = 21.9, 6.4 Hz, 2H), 7.23 – 7.03 (m, 11H), 4.89 (s, 2H), 1.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 208.5, 162.3, 140.8, 137.6, 136.5, 134.7, 132.4, 131.6, 130.2, 128.6, 128.1, 128.0, 126.9, 126.7, 125.6, 124.9, 119.1, 51.1, 43.2, 26.4. HRMS (ESI): *m/z* calcd for C₂₇H₂₅O₂NNa [M+Na]⁺ : 418.1783, found: 418.1783.

1-(2-oxopropyl)-4,5,6-triphenylpyridin-2(1*H*)-one (**3xa**)



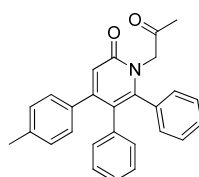
The general procedure was applied to **1x** (0.05 mmol), **2a** (1.5 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3xa** as a white solid (26% yield). Melting point: 160.7 – 161.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.24 – 7.17 (m, 3H), 7.17 – 7.10 (m, 3H), 7.10 – 6.99 (m, 4H), 6.95 – 6.81 (m, 3H), 6.77 – 6.66 (m, 3H), 4.61 (s, 2H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.4, 161.9, 154.2, 147.3, 138.8, 136.7, 134.4, 131.7, 129.7, 128.9, 128.4, 127.8, 127.4, 126.3, 120.8, 119.0, 55.7, 27.6. HRMS (ESI): *m/z* calcd for C₂₆H₂₁O₂NNa [M+Na]⁺ : 402.1470, found: 402.1465.

3-methyl-1-(2-oxopropyl)-4,5,6-triphenylpyridin-2(1*H*)-one (**3ya**)



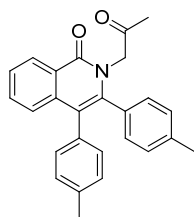
The general procedure was applied to **1y** (0.05 mmol), **2a** (1.5 equiv), [Cp**Rh*Cl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3ya** as a white solid (48% yield). Melting point: 188.3 – 193.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.23 – 7.04 (m, 8H), 6.98 – 6.93 (m, 2H), 6.83 – 6.74 (m, 3H), 6.73 – 6.64 (m, 2H), 4.59 (s, 2H), 2.12 (s, 3H), 2.00 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.7, 162.4, 150.8, 143.6, 138.4, 137.3, 134.5, 131.6, 129.9, 128.9, 128.7, 128.3, 127.7, 127.0, 126.9, 125.8, 125.6, 121.5, 56.2, 27.7, 15.0. HRMS (ESI): *m/z* calcd for C₂₇H₂₃O₂NNa [M+Na]⁺ : 416.1626, found: 416.1624.

1-(2-oxopropyl)-5,6-diphenyl-4-(*p*-tolyl)pyridin-2(1*H*)-one (**3za**)



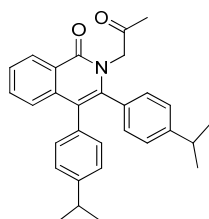
The general procedure was applied to **1z** (0.05 mmol), **2a** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3za** as a white solid (47% yield). Melting point: 162.3 – 163.9 °C; ¹H NMR (400 MHz, CDCl₃): δ = 7.23 – 7.15 (m, 3H), 7.11 – 7.04 (m, 2H), 6.94 (s, 4H), 6.92 – 6.86 (m, 3H), 6.78 – 6.72 (m, 2H), 6.70 (s, 1H), 4.60 (s, 2H), 2.24 (s, 3H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.5, 162.0, 154.1, 147.3, 137.7, 136.8, 135.8, 134.5, 131.7, 129.7, 128.9, 128.6, 128.4, 127.4, 126.2, 120.9, 118.9, 55.7, 27.6, 21.3. HRMS (ESI): *m/z* calcd for C₂₇H₂₃O₂NNa [M+Na]⁺ : 416.1626, found: 416.1626.

2-(2-oxopropyl)-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (**3ab**)



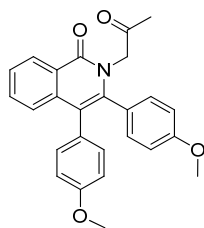
The general procedure was applied to **1a** (0.05 mmol), **2b** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ab** as a white solid (75% yield). Melting point: 145.1 – 148.3 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.49 (d, *J* = 6.4 Hz, 1H), 7.50 (dt, *J* = 21.1, 7.0 Hz, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.03 – 6.95 (m, 8H), 4.61 (s, 2H), 2.27 (d, *J* = 2.9 Hz, 6H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.4, 140.7, 138.4, 137.9, 136.4, 133.4, 132.4, 131.8, 131.4, 129.9, 129.0, 128.8, 127.9, 126.7, 125.7, 124.8, 119.2, 55.7, 27.4, 21.4 (d, *J* = 1.9 Hz), 21.3 (d, *J* = 1.7 Hz). HRMS (ESI): *m/z* calcd for C₂₆H₂₄O₂N [M+H]⁺ : 382.1807, found: 382.1813.

3,4-bis(4-isopropylphenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3ac**)



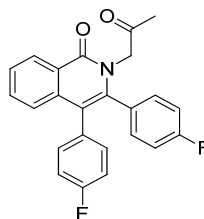
The general procedure was applied to **1a** (0.05 mmol), **2c** (1.5 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ac** as a white solid (63% yield). Melting point: 132 – 137 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.51 (d, *J* = 6.4 Hz, 1H), 7.59 – 7.45 (m, 2H), 7.28 (s, 1H), 7.07 – 6.95 (m, 8H), 4.68 (s, 2H), 2.88 – 2.74 (m, 2H), 2.09 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 12H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.1, 162.3, 149.2, 147.3, 140.9, 137.8, 133.7, 132.4, 132.1, 131.4, 130.1, 127.9, 126.7, 126.1, 125.9, 125.8, 124.7, 119.4, 55.7, 33.9, 33.8, 27.5, 24.0, 23.8. HRMS (ESI): *m/z* calcd for C₃₀H₃₂O₂N [M+H]⁺ : 438.2433, found: 438.2428.

3,4-bis(4-methoxyphenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3ad**)



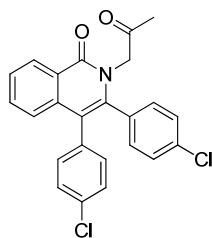
The general procedure was applied to **1a** (0.05 mmol), **2d** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ad** as a white solid (76% yield). Melting point: 204.7 – 206.5 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.48 (d, *J* = 6.4, 1H), 7.58 – 7.42 (m, 2H), 7.19 (d, *J* = 9.2 Hz, 1H), 7.04 – 6.95 (m, 4H), 6.80 – 6.67 (m, 4H), 4.63 (s, 2H), 3.74 (d, *J* = 4.4 Hz, 6H), 2.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.1, 162.4, 159.4, 158.3, 140.7, 138.0, 132.6, 132.5, 131.3, 128.8, 128.0, 127.2, 126.7, 125.7, 124.8, 119.2, 113.7, 113.5, 55.7, 55.3 (d, *J* = 2.7), 55.2 (d, *J* = 2.6), 27.5. HRMS (ESI): *m/z* calcd for C₂₆H₂₃O₄NNa [M+Na]⁺: 436.1525, found: 436.1530.

3,4-bis(4-fluorophenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3ae**)



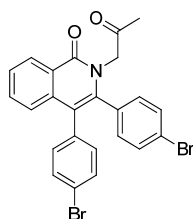
The general procedure was applied to **1a** (0.05 mmol), **2e** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ae** as a white solid (71% yield). Melting point: 172.5 – 173.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.48 (d, *J* = 7.5 Hz, 1H), 7.53 (dt, *J* = 24.6, 7.4 Hz, 2H), 7.18 – 6.98 (m, 5H), 6.90 (t, *J* = 8.5 Hz, 4H), 4.61 (s, 2H), 2.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 162.5 (d, *J* = 248.3 Hz), 162.1, 161.8 (d, *J* = 245.2 Hz), 139.9, 137.4, 133.1 (d, *J* = 7.9 Hz), 132.7, 132.2 (d, *J* = 3.4 Hz), 132.0 (d, *J* = 8.1 Hz), 130.5 (d, *J* = 3.7 Hz), 128.1, 127.1, 125.4, 124.9, 118.5, 115.6 (d, *J* = 21.5 Hz), 115.3 (d, *J* = 21.4 Hz), 55.5, 27.5. ¹⁹F NMR (376 MHz, CDCl₃): δ = -111.32, -114.74. HRMS (ESI): *m/z* calcd for C₂₄H₁₇O₂F₂NNa [M+Na]⁺: 412.1125, found: 412.1127.

3,4-bis(4-chlorophenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3af**)



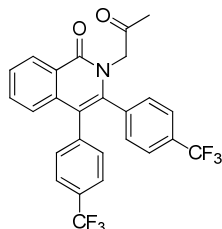
The general procedure was applied to **1a** (0.05 mmol), **2f** (1.2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3af** as a white solid (58% yield). Melting point: 197.3 – 200.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.48 (d, *J* = 6.4 Hz, 1H), 7.61 – 7.47 (m, 2H), 7.20 (d, *J* = 7.5 Hz, 4H), 7.11 (d, *J* = 7.3 Hz, 1H), 7.03 (dd, *J* = 14.2, 8.4 Hz, 4H), 4.59 (s, 2H), 2.10 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 162.1, 139.6, 137.1, 135.1, 134.6, 133.3, 132.8, 131.4, 128.9, 128.6, 128.2, 127.3, 125.4, 124.9, 118.2, 55.6, 27.6. HRMS (ESI): *m/z* calcd for C₂₄H₁₇Cl₂O₂NNa [M+Na]⁺: 444.0534, found: 444.0528.

3,4-bis(4-bromophenyl)-2-(2-oxopropyl)isoquinolin-1(2H)-one (**3ag**)



The general procedure was applied to **1a** (0.05 mmol), **2g** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ag** as a white solid (62% yield). Melting point: 219.3 – 220.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.48 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.47 (m, 2H), 7.36 (dd, *J* = 8.4, 2.6 Hz, 4H), 7.11 (d, *J* = 8.7 Hz, 1H), 6.97 (dd, *J* = 12.8, 8.4 Hz, 4H), 4.58 (s, 2H), 2.10 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 162.1, 139.6, 137.0, 135.1, 133.2, 133.1, 132.8, 131.8, 131.6, 131.6, 128.1, 127.3, 125.4, 124.9, 123.4, 121.6, 118.1, 55.6, 27.6. HRMS (ESI): *m/z* calcd for C₂₄H₁₇O₂NBr₂Na [M+Na]⁺: 531.9524, found: 531.9526.

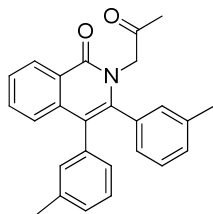
2-(2-oxopropyl)-3,4-bis(4-(trifluoromethyl)phenyl)isoquinolin-1(2H)-one (**3ah**)



The general procedure was applied to **1a** (0.05 mmol), **2h** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ah** as a white solid (39% yield). Melting point:

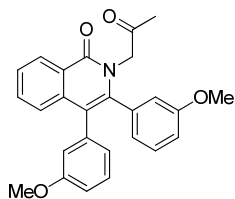
210.7 – 213.1 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.49 (d, *J* = 7.8 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.50 – 7.44 (m, 4H), 7.22 (dd, *J* = 19.7, 8.1 Hz, 4H), 7.05 (d, *J* = 8.4 Hz, 1H), 4.55 (s, 2H), 2.09 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.7, 162.1, 139.9, 139.4, 137.8, 136.8, 133.1, 131.9, 131.3 (d, *J* = 33.0 Hz), 130.6, 129.7 (d, *J* = 32.4 Hz), 129.6, 128.3, 127.7, 125.6 (d, *J* = 10.7 Hz), 125.6 (d, *J* = 3.7 Hz), 125.4 (d, *J* = 11 Hz), 125.4 (d, *J* = 3.9 Hz), 125.0, 124.0 (q, *J* = 271.0 Hz), 123.6 (q, *J* = 271.0 Hz), 118.2, 55.6, 27.6. ¹⁹F NMR (376 MHz, CDCl₃): δ = -62.72, -62.99. HRMS (ESI): *m/z* calcd for C₂₆H₁₇O₂F₆NNa [M+Na]⁺ :512.1061, found:512.1060.

2-(2-oxopropyl)-3,4-di-*m*-tolylisoquinolin-1(2*H*)-one (**3ai**)



The general procedure was applied to **1a** (0.05 mmol), **2i** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ai** as a white solid (75% yield). Melting point: 152.9 – 154.4 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.50 (d, *J* = 7.5 Hz, 1H), 7.51 (dt, *J* = 25.2, 7.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.12 – 7.04 (m, 2H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.98 – 6.86 (m, 5H), 4.70 – 4.53 (m, 2H), 2.22 (s, 6H), 2.07 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.9, 162.3, 140.7, 137.9 (d, *J* = 7.2 Hz), 137.7, 137.4 (d, *J* = 6.9 Hz), 136.3, 134.6, 132.5, 132.3 (d, *J* = 6.5 Hz), 130.7 (d, *J* = 7.2 Hz), 129.3 (d, *J* = 2.1 Hz), 128.6, 128.1 (d, *J* = 7.7 Hz), 128.0, 127.8 (d, *J* = 6 Hz), 127.7 (d, *J* = 1.5 Hz), 127.1 (d, *J* = 3.6 Hz), 126.8, 125.7, 124.8, 119.2, 55.7, 27.4, 21.4 (d, *J* = 1.1 Hz), 21.3 (d, *J* = 2.4 Hz). HRMS (ESI): *m/z* calcd for C₂₆H₂₃O₂NNa [M+Na]⁺ : 404.1626, found: 404.1630.

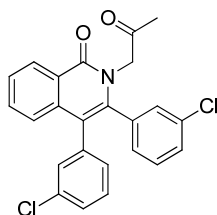
3,4-bis(3-methoxyphenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3aj**)



The general procedure was applied to **1a** (0.05 mmol), **2j** (1.2 equiv), [Cp**RhCl*₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3aj** as a white solid (78% yield). Melting point: 174.2 – 175.6 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.49 (d, *J* = 7.9 Hz, 1H), 7.60 – 7.45 (m, 2H), 7.22 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.12 (qd, *J* = 8.1, 2.1 Hz, 2H), 6.81 – 6.67 (m, 5H), 6.63 (s, 1H), 4.73 – 4.53 (m, 2H), 3.68 (d, *J* = 3.8 Hz, 3H), 3.65 (d, *J* = 2.6 Hz, 3H), 2.10 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0 (d, *J* = 1.5 Hz), 202.0, 162.3, 159.3 (d, *J* = 6.2 Hz), 140.3, 137.7 (d, *J* = 2.1 Hz), 137.5 (d, *J* = 2.1 Hz), 135.8 (d, *J* = 2.4 Hz), 132.6, 129.5 (d, *J* = 9.5 Hz), 129.0 (d, *J* = 7.4 Hz), 128.0, 126.9, 125.7, 124.8, 124.1 (d, *J* = 8.8 Hz), 122.4 (d, *J* = 12.2 Hz), 118.9, 116.9 (d,

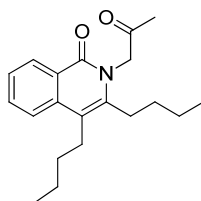
$J = 7.2$ Hz), 115.3 (d, $J = 14.6$ Hz), 114.9, 113.0, 55.7 (d, $J = 2.7$ Hz), 55.4, 55.3, 27.5. HRMS (ESI): m/z calcd for $C_{26}H_{24}O_4N$ $[M+H]^+$: 414.1705, found: 414.1704.

3,4-bis(3-chlorophenyl)-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3ak**)



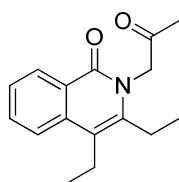
The general procedure was applied to **1a** (0.05 mmol), **2k** (1.2 equiv), $[Cp^*RhCl_2]_2$ (4 mol%), $Cu(OAc)_2 \cdot H_2O$ (2.1 equiv), $AgNTf_2$ (10 mol%), $PivOH$ (0.5 equiv) and H_2O (50 μ L) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ak** as a white solid (37% yield). Melting point: 154.1 – 155.9 °C; 1H NMR (400 MHz, $CDCl_3$): $\delta = 8.49$ (d, $J = 7.9$ Hz, 1H), 7.70 – 7.46 (m, 2H), 7.25 – 7.08 (m, 7H), 7.08 – 6.94 (m, 2H), 4.80 – 4.46 (m, 2H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.7$ (d, $J = 1.8$ Hz), 162.1, 139.4, 137.9 (d, $J = 2.0$ Hz), 136.9, 135.9, 134.5 (d, $J = 14.9$ Hz), 134.1 (d, $J = 13$ Hz), 132.9, 131.5 (d, $J = 10.3$ Hz), 130.0 (d, $J = 8.9$ Hz), 129.8, 129.6 (d, $J = 8.6$ Hz), 129.3, 128.3 (d, $J = 8$ Hz), 128.2, 127.6, 127.4, 125.5, 124.9, 118.1, 55.6, 27.5. HRMS (ESI): m/z calcd for $C_{24}H_{17}O_2NCl_2Na$ $[M+Na]^+$: 444.0534, found: 444.0534.

3,4-dibutyl-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3al**)



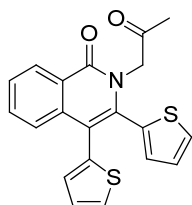
The general procedure was applied to **1a** (0.05 mmol), **2l** (1.2 equiv), $[Cp^*RhCl_2]_2$ (4 mol%), $Cu(OAc)_2 \cdot H_2O$ (2.1 equiv), $AgNTf_2$ (10 mol%), $PivOH$ (0.5 equiv) and H_2O (50 μ L) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3al** as a white solid (81% yield). Melting point: 107.6 – 110.3 °C; 1H NMR (400 MHz, $CDCl_3$): $\delta = 8.40$ (d, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 3.8$ Hz, 2H), 7.46 – 7.39 (m, 1H), 4.91 (s, 2H), 2.72 (t, $J = 7.2$ Hz, 2H), 2.54 (t, $J = 7.2$ Hz, 2H), 2.28 (s, 3H), 1.52 (m, 8H), 1.03 – 0.93 (q, $J = 6.8$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 202.8$, 162.7, 139.0, 137.0, 132.5, 128.5, 126.0, 124.7, 122.9, 114.5, 53.9, 32.6, 31.5, 29.7, 27.6, 27.6 (d, $J = 1.6$ Hz), 23.2, 23.0, 14.1, 13.8. HRMS (ESI): m/z calcd for $C_{20}H_{27}O_2NNa$ $[M+Na]^+$: 336.1939, found: 336.1938.

3,4-diethyl-2-(2-oxopropyl)isoquinolin-1(2*H*)-one (**3am**)



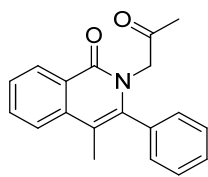
The general procedure was applied to **1a** (0.05 mmol), **2m** (2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (3 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3am** as a white solid (95% yield). Melting point: 105.3 – 106.8 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.40 (d, *J* = 7.5 Hz, 1H), 7.73 – 7.61 (m, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 4.92 (s, 2H), 2.78 (q, *J* = 7.5 Hz, 2H), 2.61 (q, *J* = 7.6 Hz, 2H), 2.29 (s, 3H), 1.22 (dt, *J* = 12.2, 7.5 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.7, 162.7, 139.9, 136.8, 132.6, 128.5, 126.0, 124.8, 122.8, 115.4, 53.7, 27.6, 22.9, 20.8, 14.9, 13.8. HRMS (ESI): *m/z* calcd for C₁₆H₁₉O₂NNa [M+Na]⁺ : 280.1313, found: 280.1314.

2-(2-oxopropyl)-3,4-di(thiophen-2-yl)isoquinolin-1(2*H*)-one (**3an**)



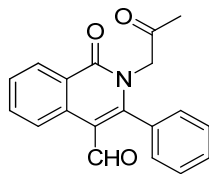
The general procedure was applied to **1a** (0.05 mmol), **2n** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3an** as a white solid (52% yield). Melting point: 164.3 – 167.9 °C; ¹H NMR (400 MHz, CDCl₃): 8.47 (d, *J* = 6.4 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.31 (t, *J* = 2.8 Hz, 1H), 7.28 – 7.23 (m, 1H), 6.96 – 6.87 (m, 3H), 6.85 (d, *J* = 2.9 Hz, 1H), 4.72 (s, 2H), 2.13 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.8, 162.2, 137.5, 136.8, 135.6, 134.4, 132.9, 130.9, 130.2, 129.9, 128.4, 128.0, 127.7, 126.9, 126.7, 126.6, 125.8, 125.1, 114.8, 55.8, 27.4. HRMS (ESI): *m/z* calcd for C₂₀H₁₅O₂NS₂Na [M+Na]⁺ : 388.0442, found: 388.0445.

4-methyl-2-(2-oxopropyl)-3-phenylisoquinolin-1(2*H*)-one (**3ao**)



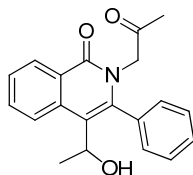
The general procedure was applied to **1a** (0.05 mmol), **2o** (1.5 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 10 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ao** as a white solid (91% yield). Melting point: 153.2 – 154.1 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.48 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.55 – 7.49 (m, 1H), 7.47 – 7.43 (m, 3H), 7.25 – 7.20 (m, 2H), 4.54 (s, 2H), 2.01 (d, *J* = 2.2 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 162.2, 139.5, 137.5, 135.4, 132.7, 129.9, 129.6, 129.2, 129.1, 128.3, 126.7, 125.2, 123.5, 115.4, 110.8, 55.6, 27.3, 14.9. HRMS (ESI): *m/z* calcd for C₁₉H₁₇O₂NNa [M+Na]⁺ : 314.1157, found: 314.1158.

1-oxo-2-(2-oxopropyl)-3-phenyl-1,2-dihydroisoquinoline-4-carbaldehyde (**3ap**)



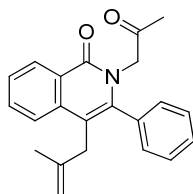
The general procedure was applied to **1a** (0.05 mmol), **2p** (1.2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ap** as a white solid (64% yield). Melting point: 188.5 – 190.7 °C; ¹H NMR (400 MHz, CDCl₃): δ = 9.44 (s, 1H), 9.18 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.63 – 7.46 (m, 4H), 7.34 (d, *J* = 7.3 Hz, 2H), 4.58 (s, 2H), 2.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 200.7, 191.3, 162.1, 156.6, 134.2, 133.4, 131.4, 130.5, 129.5, 129.2, 128.0, 127.9, 125.6, 124.3, 113.8, 55.0, 27.4. HRMS (ESI): *m/z* calcd for C₁₉H₁₅O₃NNa [M+Na]⁺ : 328.0950, found: 328.0948.

4-(1-hydroxyethyl)-2-(2-oxopropyl)-3-phenylisoquinolin-1(2H)-one (**3aq**)



The general procedure was applied to **1a** (0.05 mmol), **2q** (1.2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3aq** as a white solid (60% yield). Melting point: 167.9 – 169.2 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.55 (d, *J* = 8.4 Hz, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.52 – 7.37 (m, 4H), 7.13 (d, *J* = 6.6 Hz, 2H), 4.64 (q, *J* = 6.7 Hz, 1H), 4.49 – 4.22 (m, 2H), 2.38 (s, 1H), 1.94 (s, 3H), 1.54 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 201.9, 162.1, 139.6, 135.1, 134.5, 132.1, 129.5, 129.4, 129.1, 128.7, 128.5, 126.8, 126.5, 126.0, 117.8, 68.5, 55.3, 27.3, 22.7. HRMS (ESI): *m/z* calcd for C₂₀H₁₉O₃NNa [M+Na]⁺ : 344.1263, found: 344.1263.

4-(2-methylallyl)-2-(2-oxopropyl)-3-phenylisoquinolin-1(2H)-one (**3ar**)



The general procedure was applied to **1a** (0.05 mmol), **2r** (1.2 equiv), [Cp*RhCl₂]₂ (4 mol%), Cu(OAc)₂•H₂O (2.1 equiv), AgNTf₂ (10 mol%), PivOH (0.5 equiv) and H₂O (50 μL) in MeOH (0.5 mL) at 100 °C for 12 h under air. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3ar** as a white solid (88% yield). Melting point: 153.2 – 154.9 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.47 (d, *J* = 6.8 Hz, 1H), 7.66 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.46 – 7.39 (m, 3H),

7.26 – 7.22 (m, 2H), 4.80-4.75 (m, 1H), 4.55 (s, 2H), 4.51 (s, 1H), 3.04 (s, 2H), 2.02 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 201.9, 162.3, 144.0, 140.9, 137.1, 134.9, 132.5, 129.3, 129.1, 128.9, 128.3, 126.7, 125.3, 124.4, 112.9, 111.8, 55.7, 36.8, 27.3, 23.4. HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{21}\text{O}_2\text{NNa}$ $[\text{M}+\text{Na}]^+$: 354.1470, found: 354.1474.

9. ^1H , ^{13}C and ^{19}F NMR spectra

