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Full Paper

An expedite synthesis of isoquinolinones by intramolecular coupling of amides and ketones

Wen-Tao Wei, Yu Liu, Lin-Miao Ye, Rong-Hui Lei, Xue-Jing Zhang and Ming Yan*

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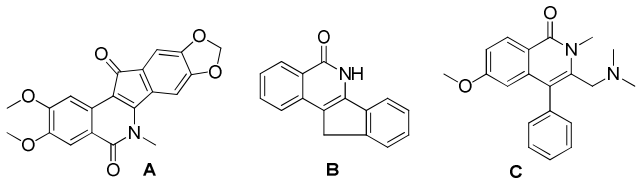
The intramolecular coupling of amides and ketones was achieved in the presence of KO*t*-Bu/DMF. The reaction provided a variety of isoquinolinones in good yields. A reaction mechanism of radical addition and subsequent E2-elimination is proposed.

Introduction

Isoquinolinones are important structural motif in natural products and drugs.[1] For example (Scheme 1), compound **A** is a lead molecule for the development of inhibitors of topoisomerase I.[2a] Tetracyclic indeno[1,2-c]-isoquinolinone **B** showed attractive inhibition activity against poly(ADP-ribose) polymerase-1.[2b] The compound **C** is a potassium channel inhibitor and is potentially useful for the treatment of cardiac diseases.[2c] The synthesis of isoquinolinones has been receiving the great attenations.[3-4] The typical methods include base-promoted condensation of 2-(bromomethyl)benzonitrile,[5] the rearrangement of 2-(2-benzofurnanyl)-benzonitriles,[6] double metalation of arylbenzamides,[7] the cyclization of 2-chlorobenzonitriles and β-ketoesters,[8] Ugi and Heck reactions.[9] Among the numerous methods, the transition metal catalyzed cyclizations of aryl amides and alkynes are most popular.[10] To the best of our knowledge, the synthesis of isoquinolinones through intramolecular radical coupling of benzamides and ketones has never been reported. Recently, we found that KO*t*-Bu/DMF can promote the generation of α-aminoalkyl radicals from tertiary amines. The consequent radical additions to alkenes and ketones are highly efficient for the synthesis of α-alkyl amines and nitrogen heterocycles.[11-12] We also found that KO*t*-Bu/DMF promotes the intra- and inter- molecular addition of tetrahydroisoquinoline derived amides to styrenes.[13] The experiment data suggested that the generation of α-amidoalkyl radical intermediates in the reaction. We speculate the α-amidoalkyl radicals are also reactive with ketones. Such a reaction can provide a new strategy for the synthesis of isoquinolinones and other nitrogen heterocycles. Herein, we report the intramolecular coupling of amides and ketones in the presence of KO*t*-Bu/DMF. The reaction provided a series of isoquinolinones in good yields.



Scheme 1. Representative examples of biologically active isoquinolinones.

Results and discussion

Tetrahydroisoquinoline derived amides **1a-1e** were readily prepared from tetrahydroisoquinolines and 2-benzoyl benzoic aids through the dehydration in the presence of EDCI. The other substrates **1f-1r** were prepared from the substituted benzylamines via the same procedure (see the supporting information for the details). Initially, **1a** was treated in DMF with 3.0 equivalents of KO*t*-Bu at 90 °C. The expected product **2a** was obtained in low yield. Instead, the ring-opening product **3a** was obtained in moderate yield. Compound **3a** was obviously generated from **2a** by a base-promoted C-N cleavage.[13-14] The concentration of KO*t*-Bu probably exerts significant effect

Institute of Drug Synthesis and Pharmaceutical Process, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, China. E-mail: yanming@mail.sysu.edu.cn; Fax/Tel: + 86-20-39943049

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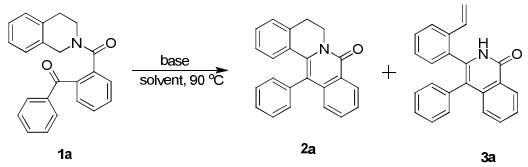
on this side reaction. The loading of KO*t*-Bu was examined and the results are summarized in Table 1. While the loading of KO*t*-Bu was decreased, the generation of **3a** was inhibited (Table 1, entries 1-5). The best yield of **2a** was obtained with 1.2 equivalents of KO*t*-Bu (Table 1, entry 3). The influence of reaction temperature was also explored. Inferior yields were obtained at 120 °C and 60 °C respectively (Table 1, entries 6-7).

Other bases were examined and the results are listed in Table 1. NaO*t*-Bu, LiO*t*-Bu, KOMe, NaOMe also promoted the reaction, but the yields were lower (Table 1, entries 8-13). KOH, NaOH gave poor yields of **2a**. $CsCO_3$ and Et_3N were inefficient. The effect of reaction solvents was also investigated. *N,N*-Dimethylacetamide (DMA) is applicable, however lower yield was obtained (Table 1, entry 14). The reaction in DMSO provided **3a** exclusively (Table 1, entry 15). Other solvents such as toluene, acetonitrile, dioxin, *t*-BuOH, and THF are incompatible with the reaction. The radical scavenger *p*-benzoquinone, oxygen and DPPH inhibited the reaction significantly (Table 1, entries 16,17 and 19), however TEMPO showed slight effect on the yield (Table 1, entry 18).

Table 1. The optimization of reaction conditions[a]



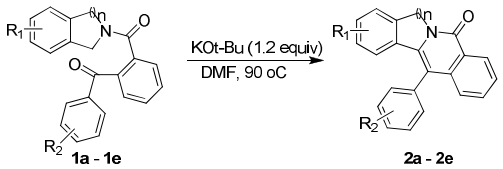
1a 2a 3a

Entry	Base (equiv.)	Solvent	Time (h)	Yield (%)[b] 2a	Yield(%)[b] 3a
1	KO*t*-Bu (3.0)	DMF	1	30	62
2	KO*t*-Bu (2.0)	DMF	1	52	39
3	KO*t*-Bu (1.2)	DMF	1	81	12
4	KO*t*-Bu (1.0)	DMF	1	69	16
5	KO*t*-Bu (0.5)	DMF	1	59	6
6[c]	KO*t*-Bu (1.2)	DMF	1	69	24
7[d]	KO*t*-Bu (1.2)	DMF	1.5	44	28
8	LiO*t*-Bu (1.2)	DMF	1	31	37
9	NaO*t*-Bu(1.2)	DMF	1	50	22
10	KOMe (1.2)	DMF	1	63	15
11	NaOMe (1.2)	DMF	1	72	6
12	KOH (1.2)	DMF	1	15	-
13	NaOH (1.2)	DMF	1	9	-
14	KO*t*-Bu (1.2)	DMA	1	56	6
15	KO*t*-Bu (1.2)	DMSO	1	-	37
16[e]	KO*t*-Bu (1.2)	DMF	1	35	-
17[f]	KO*t*-Bu (1.2)	DMF	1	-	-
18[g]	KO*t*-Bu (1.2)	DMF	1	70	-
19[h]	KO*t*-Bu (1.2)	DMF	1	-	-

[a] Reaction conditions: **1a** (0.1 mmol), base, solvent (1 mL), at 90 °C under an argon atmosphere. [b] Isolated yields. [c] Reaction was carried out at 120 °C. [d] Reaction was carried out at 60 °C. [e] Reaction was carried out under an oxygen atmosphere. [f] *p*-Benzoquinone (0.12 mmol) was added. [g] TEMPO (0.12 mmol) was added. [h] DPPH (0.12 mmol) was added.

The reaction was extended to a number of tetrahydroisoquinoline derived amides and the results are summarized in Table 2. The reaction of 4-methylphenyl ketone **1b** and 4-chlorolphenyl ketone **1c** provided the expected products in good yields (Table 2, entries 3-4). Tetrahydroisoquinoline derivative **1d** with 6,7-dimethoxy substitution gave product **2d** in a good yield (Table 2, entry 4). The isoindoline derived amide **1e** was also examined. The product **2e** was obtained in a moderate yield (Table 2, entry 5).

Table 2. Intramolecular coupling of benzamides **1a-1e**[a]



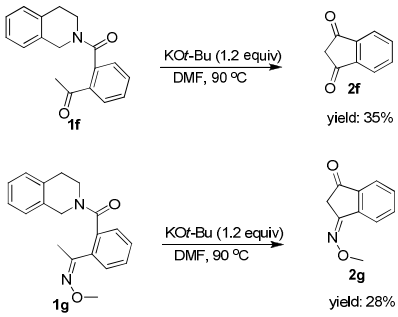
1a - 1e 2a - 2e

Entry	1	R^1	R^2	n	Product yield[b] (%)
1	**1a**	H	H	2	**2a** /81
2	**1b**	H	4-Me	2	**2b** /82
3	**1c**	H	4-Cl	2	**2c** /85
4	**1d**	3,4-$(MeO)_2$	H	2	**2d** /82
5	**1e**	H	H	1	**2e** /68

[a] Reaction conditions: **1a-1e** (0.2 mmol), KO*t*-Bu (0.24 mmol), DMF (2.0 mL), at 90 °C under an argon atmosphere, 1 h. [b] Isolated yields.

The reaction of acetophenone derivative **1f** and its oxime **1g** did not give the expected products (Scheme 2). Instead the intramolecular condensation and the cleavage of the amide bond led to **2f** and **2g** in low yields. The results indicated the ketones with α-H are not compatible with the reaction.

Scheme 2. Intramolecular condensation of acetophenone derivative **1f** and its oxime **1g**[a]

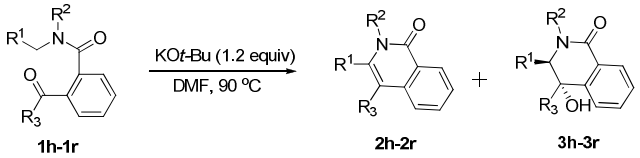


[a] Reaction conditions: **1f** and **1g** (0.2 mmol), KO*t*-Bu (0.24 mmol), DMF (2.0 mL), at 90 °C under an argon atmosphere, 1 h.

The reaction is further extended to arylmethylamine derived amides **1h-1r** and the results are summaried in Table 3. The expected isoquinolinones **2h-2r**, together

with *trans*-4-hydroxy-dihydroisoquinolinones **3h-3r** were obtained in good yields. The *N*-substitution with methyl, ethyl, isopropyl and benzyl are tolerated well. The substrates with electron-donating groups (**1l**, **1m**) obviously favor the formation of *trans*-4-hydroxy-dihydroisoquinolinones (Table 3, entries 5-6). On the other hand, the substrate **1q** with electron-withdrawing group (cyano group) gave the dehydration product **2q** excusively (Table 3, entry 10). The steric hindrance of the substrate also exerts siginificant effect on the ratio of the dehydration product and *trans*-4-hydroxy-dihydroisoquinolinone. The substrates **1o** and **1p** with naphthyl and 2-chloro-phenyl provided higher ratios of *trans*-4-hydroxy-dihydroisoquinolinones than the substrate **1h** (Table 3, entries 8-9 vs 1). The substrate **1r** with thiophenyl group was also examined in the reaction, the expected products **2r** and **3r** were obtained in good yield (Table 3, entry 11). The control experiments with **3h** and **3o** demonstrated that the dehydration did not occur in the presence of KO*t*-Bu/DMF. However the treatment of **3h** and **3o** with *p*-toluenesulfonic acid (PTSA) in toluene gave **2h** and **2o** in good yields (Scheme 3).

Table 3. Intramolecular coupling of arylmethylamine derived substrates **1h-1r**[a]



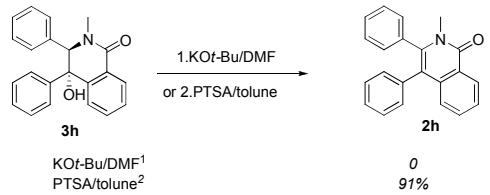
1h-1r **2h-2r** **3h-3r**

Entry	1	R^1	R^2	R^3	Product yield[b] (%)	
1	**1h**	ph	Me	ph	**2h** /37	**3h** /45
2	**1i**	ph	Et	ph	**2i** /36	**3i** /57
3	**1j**	ph	*i*-pr	ph	**2j** /39	**3j** /46
4	**1k**	ph	Bn	ph	**2k** /42	**3k** /44
5	**1l**	4-MeO-C_6H_4	Me	ph	**2l** /15	**3l** /66
6	**1m**	4-Me-C_6H_4	Me	ph	**2m** /28	**3m** /64
7	**1n**	ph	Me	4-Cl-C_4H_6	**2n** /36	**3n** /47
8	**1o**	2-naphthyl	Me	ph	**2o** /26	**3o** /69
9	**1p**	2-Cl-C_6H_4	Me	ph	**2p** /20	**3p** /45
10	**1q**	4-CN-C_6H_4	Me	ph	**2q** /67	-
11	**1r**	ph	Me	2-thiophenyl	**2r** /34	**3r** /47

[a] Reaction conditions: **1h-1r** (0.2 mmol), KO*t*-Bu (0.24 mmol), DMF (2.0 mL), at 90 °C under an argon atmosphere, 3 h. [b] Isolated yields.

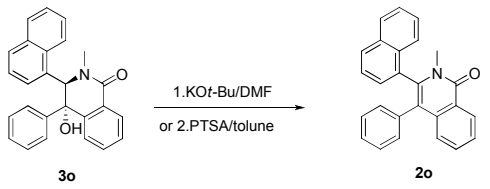
The reaction of allyl amine derived amide **1s** provided 3-vinylisoquinolinone **2s** and 4-hydroxy-3-ethylidene-dihydroisoquinolinone **3s** (Scheme 4). The reaction of α-cyano methylamine derived amide **1t** provided product **2t** in a good yield. Dialkyl amine derived amides **1u**, **1v** and **1w** are unreactive under the present reaction conditions. The activation of amides with α-aryl, allyl or cyano groups seems to be necessary for the reaction. Since these substitutents are capable of stabilizing the neighboring alkyl radicals, the results are in good accordance to α-amidoalkyl radical reaction pathway.

Scheme 3. The dehydration of **3h** and **3o**



3h **2h**

KO*t*-Bu/DMF[1] *0*
PTSA/tolune[2] *91%*

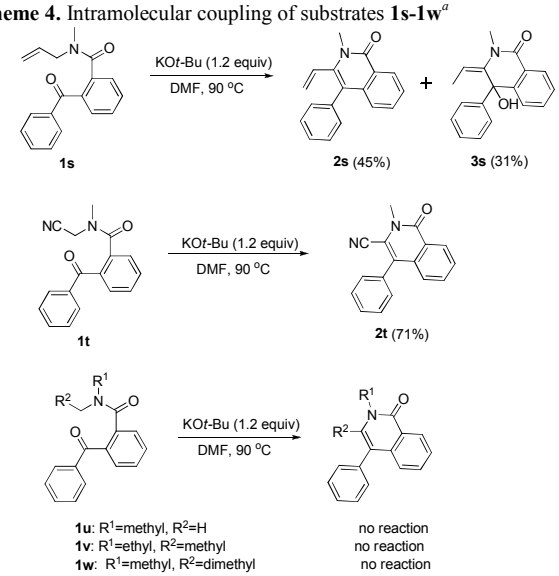


3o **2o**

KO*t*-Bu/DMF[1] *0*
PTSA/tolune[2] *93%*

[1]Reaction conditions: **3h** or **3o** (0.1 mmol), KO*t*-Bu (0.12 mmol), DMF (1.0 mL), at 90 °C under an argon atmosphere, 15 h. [2]Reaction conditions: **3h** or **3o** (0.1 mmol), PTSA (0.12 mmol), tolune (1.0 mL), at 90 °C under an argon atmosphere, 2 h.

Scheme 4. Intramolecular coupling of substrates **1s-1w**[a]

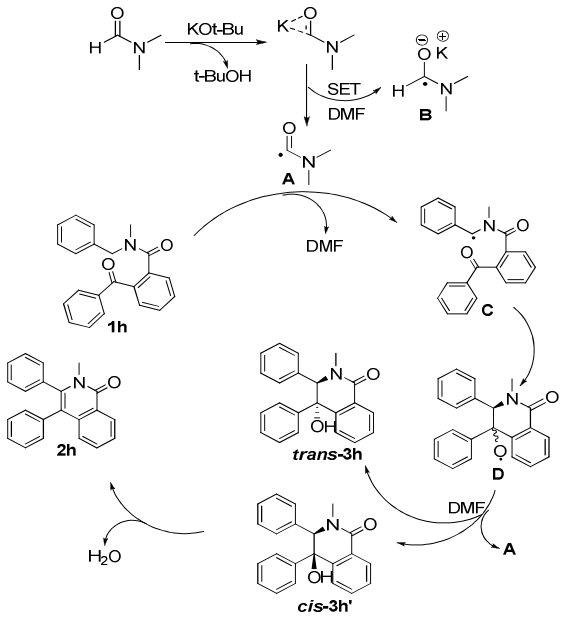


[a]Reaction conditions: **1s-1w** (0.2 mmol), KO*t*-Bu (0.24 mmol), DMF (2.0 mL), at 90 °C under an argon atmosphere, 3 h.

A tentative reaction mechanism is suggested (Scheme 5).[11] The carbamoyl radical **A** generated in KO*t*-Bu/DMF abstracts a hydrogen from **1h**. The resulted radical intermediate **C** adds to the carbonyl group. The radical intermediate **D** gets a hydrogen from DMF to generate *cis* and *trans*-**4**-hydroxy-dihydroisoquinolinone. The *cis*-isomer **3h′** undergoes a base-promoted E2-elimination to give the product **2h**. The *trans*-isomer **3h** is resistant to E2-elimination due to the unfavorable arrangement of the

hydroxyl group and the hydrogen. In the case of tetrahydroisoquinoline derived amides **1a**-**1e**, the fused ring structures may result in the stereoselective formation of *cis*-isomers. The subsequent dehydration leads to the isoquinolinone products **2a**-**2e** exclusively.

Scheme 5. Tentative reaction mechanism



Conclusion

In summary, we have developed an intramolecular coupling of amides and ketones in the presence of KO*t*-Bu/DMF. The reaction is applicable for tetrahydroisoquinoline and arylmethylamine derived amides. A series of multi-substituted isoquinolinones were prepared in good yields. A radical addition and subsequent E2-elimination reaction mechanism is suggested. The method represents a new strategy for the synthesis of isoquinolinones.

Experimental

Representative experiment procedure

A solution of (2-benzoylphenyl)(3,4-dihydroisoquinolin-2(1H)-yl)methanone **1a** (68.4 mg, 0.2 mmol), KO*t*-Bu (27.0 mg, 0.24 mmol) in DMF (2 mL) was stirred at 90 °C under an argon atmosphere. After the completion of the reaction as shown by TLC, the solvent was removed under vacuum. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether = 1:3) to give **2a** as a white solid (52.3 mg, yield: 81%).

12-phenyl-5,6-dihydroisoquino[3,2-a]isoquinolin-8-one (2a).

The product was obtained following the general procedure. Yield: 81%. White solid. Mp 208–209 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 7.8 Hz, 1H), 7.56-7.47 (m, 2H), 7.44 – 7.35 (m, 3H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 4.3 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.12 (t, *J* = 6.8 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.79 (t, *J* = 7.1 Hz, 1H), 4.37 (t, *J* = 5.6 Hz, 2H), 2.98 (t, *J* = 5.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.72, 138.41, 137.77, 137.36, 134.73, 131.98, 131.03, 130.46, 128.97, 128.31, 127.81, 127.57, 126.96, 126.70, 125.58, 124.89, 117.84, 41.53, 29.70. **IR** (KBr) *v*/cm^{-1}: 2932, 1638, 1588, 1482, 1345, 1158, 925, 704, 699. **HRMS** (ESI) calculated for $C_{23}H_{18}NO$ $(M+H)^+$: 324.1383, found : 324.1375.

12-p-tolyl-5,6-dihydroisoquino[3,2-a]isoquinolin-8-one (2b).

The product was obtained following the general procedure. Yield: 82%. White solid. Mp 198–199 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 7.8 Hz, 1H), 7.54-7.45 (m, 2H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.20 (t, *J* = 9.3 Hz, 3H), 7.17 – 7.09 (m, 3H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.81 (t, *J* = 7.6 Hz, 1H), 4.35 (t, *J* = 5.6 Hz, 2H), 2.96 (t, *J* = 5.6 Hz, 2H), 2.42 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.71, 138.34, 137.56, 137.24, 134.62, 131.92, 131.78, 131.06, 130.59, 129.71, 128.23, 127.77, 126.93, 126.64, 125.67, 125.61, 124.88, 117.82, 41.56, 29.70, 21.35. **IR** (KBr) *v*/cm^{-1}: 2933, 1639, 1589, 1484, 1347, 1158, 926, 699, 708. **HRMS** (ESI) calculated for $C_{24}H_{20}NO$ $(M+H)^+$: 338.1539, found : 338.1532.

12-(4-chlorophenyl)-5,6-dihydroisoquino[3,2-a]isoquinolin-8-one (2c)

The product was obtained following the general procedure. Yield: 85%. White solid. Mp 205–206 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 7.6 Hz, 1H), 7.62 – 7.47 (m, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.23 – 7.12 (m, 4H), 6.89 – 6.77 (m, 2H), 4.35 (t, *J* = 5.6 Hz, 2H), 2.98 (t, *J* = 5.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.66, 138.51, 137.05, 136.29, 135.02, 133.61, 133.37, 132.14, 130.97, 130.14, 129.29, 128.57, 127.95, 127.14, 126.87, 125.80, 125.21, 124.87, 116.46, 41.54, 29.65. **IR** (KBr) *v*/cm^{-1}: 2882, 1643, 1484, 1343, 1266, 1158, 1091, 1017, 856, 763, 699, 523, 463. **HRMS** (ESI) calculated for $C_{23}H_{17}NOCl$ $(M+H)^+$: 358.0993, found : 358.0990.

2,3-dimethoxy-12-phenyl-5,6-dihydroisoquino[3,2-a]isoquinolin-8-one (2d)

The product was obtained following the general procedure. Yield: 82%. White solid. Mp 213-214 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.48-7.44 (m, 3H), 7.39 (d, *J* = 7.0 Hz, 1H), 7.31-7.26 (m, 3H), 6.68 (s, 1H), 6.46 (s, 1H), 4.37 (t, *J* = 5.6 Hz, 2H), 3.88 (s, 3H), 3.17 (s, 3H), 2.92 (t, *J* = 5.6 Hz, 2H). **^{13}C**

NMR (100 MHz, $CDCl_3$) δ 161.75, 148.89, 146.29, 138.47, 137.48, 134.72, 132.02, 131.95, 131.53, 129.26, 127.80, 127.46, 126.35, 125.25, 124.52, 122.30, 116.35, 114.32, 109.56, 55.81, 55.31, 41.45, 29.07. **IR** (KBr) ν/cm^{-1}: 3000, 2932, 2834, 1635, 1604, 1512, 1462, 1342, 1229, 1165, 1095, 928, 876, 778, 695, 504. **HRMS** (ESI) calculated for $C_{25}H_{22}NO_3$ $(M+H)^+$: 384.1594, found : 384.1586.

12-phenylisoindolo[2,1-b]isoquinolin-5(7H)-one (2e)

The product was obtained following the general procedure. Yield: 68%. White solid. Mp 256–258 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (d, J = 7.2 Hz, 1H), 7.62 – 7.51 (m, 6H), 7.45 – 7.39 (m, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.24 (d, J =8.0 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 5.27 (s, 2H). **^{13}C NMR** (100MHz, $CDCl_3$) δ 160.77, 138.78, 138.43, 138.10, 135.25, 134.42, 132.00, 131.11, 129.45, 129.24, 128.44, 127.92, 127.28, 126.24, 125.21, 124.18, 124.05, 123.08, 114.52, 51.83. **IR** (KBr, thin film) ν/cm^{-1}: 2868, 1766, 1651, 1621, 1477, 1341, 1311, 761, 696, 552. **HRMS** (ESI) calculated for $C_{22}H_{16}NO$ $(M+H)^+$: 310.1226, found : 310.1219.

1H-indene-1,3(2H)-dione (2f)

The product was obtained following the general procedure. Yield: 35%. Purple solid. Mp 131-132 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00-7.98 (m, 2H), 7.86-7.84 (m, 2H), 3.25 (s, 2H). **^{13}C NMR** (100 MHz, CDCl3) δ 197.39, 143.37, 135.58, 123.20, 45.04. **IR** (KBr, thin film) ν/cm^{-1}: 2868, 1716, 1651, 1341, 761, 696, 552. **HRMS** (ESI) calculated for $C_9H_5O_2$ $(M-H)^-$: 145.0295, found : 145.0297.

(E)-3-(methoxyimino)-2,3-dihydro-1H-inden-1-one (2g).

The product was obtained following the general procedure. Yield: 28%. Brown solid. Mp 85-87 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 4.05 (s, 3H), 3.36 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.98, 152.17, 144.85, 138.43, 135.21, 130.87, 123.55, 121.90, 62.63, 37.47. **IR** (KBr, thin film) ν/cm^{-1}:1680, 1492, 1380, 1110, 933, 827, 568. **HRMS** (ESI) calculated for $C_{10}H_8NO_2$ $(M-H)^-$: 174.0561, found : 174.0566.

2-methyl-3,4-diphenylisoquinolin-1(2H)-one (2h)

The product was obtained following the general procedure. Yield: 37%. White solid. Mp 233–234 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, J = 7.2 Hz, 1H), 7.59 – 7.40 (m, 2H), 7.28 – 7.09 (m, 9H), 7.06 (d, J = 6.4 Hz, 2H), 3.36 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.77, 141.26, 137.19, 136.49, 135.08, 132.03, 131.54, 129.95, 128.20, 127.92, 127.84, 126.80, 126.61, 125.36, 124.94, 118.91, 34.35. **IR** (KBr, thin film) ν/cm^{-1}: 2881, 1640, 1513, 1463, 1343, 1267, 1159, 830, 760, 698, 589, 520. **HRMS** (ESI) calcd. for $C_{22}H_{18}NO$ $(M+H)^+$: 312.1383, found: 312.1377.

2-ethyl-3,4-diphenylisoquinolin-1(2H)-one (2i)

The product was obtained following the general procedure. Yield: 36%. White solid. Mp 216–217 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.57 (d, J = 7.2 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.23-7.12 (m, 9H), 7.06 (d, J = 8.0 Hz, 2H), 3.95 (q, J = 7.0 Hz, 2H), 1.17 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.07, 141.11, 137.20, 136.62, 134.82, 132.01, 131.54, 130.21, 128.19, 127.92, 127.87, 127.80, 126.74, 126.55, 125.35, 125.23, 119.11, 41.38, 14.15. **IR** (KBr, thin film) ν/cm^{-1}: 2886, 1645, 1533, 1467, 1353, 1277, 1157, 835, 767, 692, 589. **HRMS** (ESI) calculated for $C_{23}H_{20}NO$ $(M+H)^+$: 326.1539, found : 326.1531.

2-isopropyl-3,4-diphenylisoquinolin-1(2H)-one (2j)

The product was obtained following the general procedure. Yield: 39%. White solid. Mp 243–244 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.52 (d, J = 7.2 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.22-7.18 (m, 3H), 7.16 (d, J = 1.6 Hz, 1H), 7.15-7.12 (m, 4H), 7.07 (dd, J = 7.5, 1.4 Hz, 1H), 7.04 (d, J = 1.7 Hz, 1H), 7.02 (t, J = 1.6 Hz, 1H), 4.10 (dt, J = 13.5, 6.8 Hz, 1H), 1.58 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.66, 141.76, 136.98, 135.77, 131.88, 131.52, 129.70, 128.09, 128.05, 127.83, 127.48, 126.62, 126.49, 126.44, 125.20, 119.04, 53.57, 19.47. **IR** (KBr, thin film) ν/cm^{-1}: 2882, 1640, 1531, 1465, 1350, 1271, 1156, 825, 767, 692, 520. **HRMS** (ESI) calcd. for $C_{24}H_{22}NO$ $(M+H)^+$: 340.1696, found: 340.1988.

2-benzyl-3,4-diphenylisoquinolin-1(2H)-one (2k)

The product was obtained following the general procedure. Yield: 42%. White solid. Mp 162–163 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (d, J = 7.2 Hz, 1H), 7.58-7.48 (m, 2H), 7.20 – 7.09 (m, 8H), 7.09 – 7.00 (m, 4H), 6.89 (d, J = 7.1 Hz, 4H), 5.21 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.73, 141.35, 137.78, 137.40, 136.44, 134.36, 132.31, 131.52, 130.48, 128.28, 128.20, 128.14, 127.88, 127.61, 126.96, 126.88, 126.80, 126.75, 125.51, 125.20, 119.48, 49.14. **IR** (KBr, thin film)ν/cm^{-1}: 2881, 1643, 1531, 1485, 1467, 1353, 1266, 1157, 856, 767, 698, 529. **HRMS** (ESI) calculated for $C_{28}H_{22}NO$ $(M+H)^+$: 388.1702, found : 388.1696.

3-(4-methoxyphenyl)-2-methyl-4-phenylisoquinolin-1(2H)-one (2l)

The product was obtained following the general procedure. Yield: 15%. White solid. Mp 204–205 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (d, J = 7.2 Hz, 1H), 7.50 – 7.38 (m, 2H), 7.17 – 7.06 (m, 4H), 7.00-6.95 (m, 4H), 6.68 (d, J = 8.7 Hz, 2H), 3.67 (s, 3H), 3.29 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.83, 158.15, 140.11, 136.18, 135.72, 130.95, 130.50, 130.16, 126.95, 126.79, 126.42, 125.70, 125.48, 124.30, 123.89, 118.16, 112.58, 54.12, 33.27. **IR** (KBr, thin film) ν/cm^{-1}: 2883, 1644, 1513, 1251, 778, 740, 705, 694, 543. **HRMS** (ESI) calcd. for $C_{23}H_{20}NO_2$ $(M+H)^+$: 342.1489, found: 342.1477.

2-methyl-4-phenyl-3-p-tolylisoquinolin-1(2H)-one (2m)

The product was obtained following the general procedure. Yield: 28%. White solid. Mp 210–211 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 7.6 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.23-7.14 (m, 4H), 7.10 – 6.97 (m, 6H), 3.35 (s, 3H), 2.27 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.83, 141.39, 137.97, 137.24, 136.67, 132.14, 131.96, 131.54, 129.78, 128.89, 127.92, 127.81, 126.72, 126.50, 125.32, 124.89, 118.90, 34.31, 21.23. **IR** (KBr, thin film) *ν*/cm^{-1}: 2883, 1640, 1514, 1466, 1346, 1264, 1157, 1072, 830, 769, 619, 514. **HRMS** (ESI) calcd. for $C_{23}H_{20}NO$ $(M+H)^+$: 326.1539, found: 326.1527.

4-(4-chlorophenyl)-2-methyl-3-phenylisoquinolin-1(2H)-one (2n)

The product was obtained following the general procedure. Yield: 36%. White solid. Mp 207–208 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 7.6 Hz, 1H), 7.58 – 7.47 (m, 2H), 7.28-7.26 (m, 4H), 7.17 (d, *J* = 2.0 Hz, 1H), 7.14-7.10 (m, 3H), 7.00 (d, *J* = 8.4 Hz, 2H), 3.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.69, 141.52, 136.87, 135.04, 134.82, 132.87, 132.83, 132.17, 129.81, 128.46, 128.41, 128.25, 127.97, 126.77, 125.02, 124.96, 117.57, 34.32. **IR** (KBr, thin film) *ν*/cm^{-1}: 2884, 1643, 1517, 1458, 1380, 1363, 1266, 1158, 1091, 1015, 1039, 856, 760, 698, 589, 520. **HRMS** (ESI) calcd. for $C_{22}H_{17}NOCl$ $(M+H)^+$: 346.0993, found: 346.0985.

2-methyl-3-(naphthalen-1-yl)-4-phenylisoquinolin-1(2H)-one (2o)

The product was obtained following the general procedure. Yield: 26%. White solid. Mp 228–229 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 7.2 Hz, 1H), 7.83 – 7.78 (m, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.67-7.65 (m, 1H), 7.58 – 7.53 (m, 2H), 7.50 – 7.44 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.25-7.23 (m, 2H), 7.21 – 7.16 (m, 2H), 7.06 – 7.00 (m, 1H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 3.23 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.81, 139.57, 137.32, 136.39, 133.13, 132.43, 132.10, 132.08, 131.32, 129.90, 129.04, 128.65, 128.48, 127.93, 127.84, 127.59, 127.07, 126.87, 126.78, 126.22, 125.47, 125.15, 125.02, 124.92, 119.86, 33.41. **IR** (KBr, thin film) *ν*/cm^{-1}: 2881, 1644, 1513, 1454, 1334, 1267, 1159, 1028, 830, 741, 690, 587. **HRMS** (ESI) calcd. for $C_{26}H_{20}NO$ $(M+H)^+$: 362.1539, found: 362.1524.

3-(2-chlorophenyl)-2-methyl-4-phenylisoquinolin-1(2H)-one (2p)

The product was obtained following the general procedure. Yield: 20%. White solid. Mp 179 - 181 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.60 – 7.47 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.22 – 7.13 (m, 6H), 7.13 – 7.09 (m, 2H), 3.36 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.58, 138.44, 137.12, 136.13, 134.32, 134.26, 132.05, 131.94, 131.17, 130.13, 130.11, 129.41, 128.34, 127.92, 127.72, 127.22, 126.90, 126.77, 125.49, 125.25, 119.16, 32.94. **IR** (KBr, thin film) *ν*/cm^{-1}: 2885, 1641, 1517, 1458, 1382, 1361, 1256, 1148, 1091, 1037, 846, 761, 696, 585. **HRMS** (ESI) calcd. for $C_{22}H_{17}NOCl$ (M+H)+: 346.0093, found: 346.0987.

4-(2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinolin-3-yl)benzonitrile (2q)

The product was obtained following the general procedure. Yield: 67%. White solid. Mp 244–246 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 – 8.46 (m, 1H), 7.56 – 7.51 (m, 4H), 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 3H), 7.18 – 7.14 (m, 1H), 7.07 – 6.99 (m, 2H), 3.34 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.52, 139.68, 139.10, 136.81, 135.62, 132.34, 132.06, 131.37, 130.91, 128.31, 127.93, 127.40, 127.26, 125.55, 125.13, 119.32, 118.12, 112.29, 34.45. **IR** (KBr, thin film) *ν*/cm^{-1}: 2889, 1655, 1543, 1470, 1356, 1279, 1167, 845, 767, 696, 589. **HRMS** (ESI) calculated for $C_{23}H_{17}N_2O$ $(M+H)^+$: 337.1335, found : 337.1341.

2-methyl-3-phenyl-4-(thiophen-2-yl)isoquinolin-1(2H)-one (2r)

The product was obtained following the general procedure. Yield: 34%. White solid. Mp 238–240 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.53-7.48 (m, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.22 – 7.17 (m, 3H), 6.87 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.76 (dd, *J* = 3.5, 1.2 Hz, 1H), 3.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.76, 143.58, 137.67, 137.30, 134.99, 132.31, 129.70, 129.62, 128.51, 128.29, 127.76, 126.83, 126.51, 126.44, 125.19, 124.71, 111.06, 34.49. **IR** (KBr, thin film) *ν*/cm^{-1}: 2889, 1672, 1523, 1473, 1333, 1287, 1179, 835, 761, 698, 589, 523. **HRMS** (ESI) calcd. for $C_{20}H_{16}NOS$ $(M+H)^+$: 318.0947, found: 318.0957.

2-methyl-4-phenyl-3-vinylisoquinolin-1(2H)-one (2s)

The product was obtained following the general procedure. Yield: 45%. White solid. Mp 189–191 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.34 (m, 5H), 7.26 – 7.19 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.38 (dd, *J* = 17.8, 11.5 Hz, 1H), 5.40 (dd, *J* = 11.5, 1.3 Hz, 1H), 5.16 (dd, *J* = 17.8, 1.3 Hz, 1H), 3.67 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.62, 138.54, 137.18, 137.00, 131.91, 131.55, 130.29, 128.42, 127.76, 127.28, 126.53, 125.46, 124.63, 124.06, 118.23, 33.25. **IR** (KBr, thin film) *ν*/cm^{-1}: 2930, 1635, 1431, 1244, 1128, 1015, 967, 878, 743, 564. **HRMS** (ESI) calcd. for $C_{18}H_{16}NO$ $(M+H)^+$: 262.1226, found: 262.1223.

2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carbonitrile (2t)

The product was obtained following the general procedure. Yield: 71%. White solid. Mp 271–274 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 – 8.51 (m, 1H), 7.69 – 7.61 (m, 2H), 7.56-7.54 (m, 3H), 7.45 – 7.39 (m, 2H), 7.36 – 7.30 (m, 1H), 3.85 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.01, 134.91, 133.23, 132.81, 130.52, 130.32, 130.03, 129.42, 129.03, 128.34, 127.42, 126.78, 115.37, 113.24, 34.42. **IR** (KBr, thin film) *ν*/cm^{-1}: 3430, 3060, 2921, 2223, 1656, 1589, 1494, 1328, 1129, 1021, 783, 696, 567, 457. **HRMS**

(ESI) calcd. for $C_{17}H_{13}N_2O$ $(M+H)^+$: 261.1022, found: 261.1019.

4-phenyl-3-(2-vinylphenyl)isoquinolin-1(2H)-one (3a)

The product was obtained following the general procedure. Yield: 12%. Yellow solid. Mp 189–191 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 9.0 Hz, 1H), 8.45 (s, 1H), 7.64 – 7.57 (m, 1H), 7.56 – 7.46 (m, 2H), 7.35 (d, *J*= 8.0 Hz, 1H), 7.28-7.19 (m, 5H), 7.15 – 7.03 (m, 3H), 6.75-6.68 (m, 1H), 5.68 (d, *J* = 17.4 Hz, 1H), 5.26 (d, *J* = 11.0 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.28, 138.43, 136.48, 136.42, 135.31, 133.95, 133.30, 132.66, 130.79, 129.20, 128.06, 127.63, 127.44, 127.21, 126.69, 125.57, 125.41, 125.30, 118.37, 116.54. **IR** (KBr) *v*/cm^{-1}: 2848, 1653, 1479, 1345, 1152, 1031, 909, 776, 664, 581. **HRMS** (ESI) calculated for $C_{23}H_{18}NO$ $(M+H)^+$: 324.1383, found : 324.1370.

4-hydroxy-2-methyl-3,4-diphenyl-3,4-dihydroisoquinolin-1(2H) -one (3h)

The product was obtained following the general procedure. Yield: 45%. White solid. Mp 180–180 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30-8.20 (m, 1H), 7.52-7.50 (m, 2H), 7.45 – 7.37 (m, 1H), 7.31-7.28 (m, 8H), 7.17-7.14 (m, 2H), 4.73 (s, 1H), 2.87 (s, 3H). **^{13}C NMR** (100 MHz, CDCl3) δ 164.09, 144.84, 140.71, 134.71, 132.90, 128.96, 128.91, 128.89, 128.66, 128.60, 128.41, 128.02, 127.53, 126.06, 125.39, 75.03, 74.50, 34.47. **IR** (KBr, thin film) *v*/cm^{-1}: 3342, 2848, 1638, 1575, 1490, 1385, 1302, 1263, 1242, 1068,700, 614, 542. **HRMS** (ESI) calcd. for $C_{22}H_{20}NO_2$ $(M+H)^+$: 330.1489, found: 330.1476.

2-ethyl-4-hydroxy-3,4-diphenyl-3,4-dihydroisoquinolin-1(2H)-one (3i)

The product was obtained following the general procedure. Yield: 57%. White solid. Mp 204–205 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 – 8.20 (m, 1H), 7.57 – 7.46 (m, 2H), 7.43 – 7.36 (m, 1H), 7.33 – 7.24 (m, 8H), 7.19-7.17 (m, 2H), 4.70 (s, 1H), 3.92 (dq, J = 14.3, 7.2 Hz, 1H), 2.65 (dq, J = 14.2, 7.1 Hz, 1H), 2.09 (s, 1H), 0.59 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.49, 144.59, 140.22, 135.31, 132.87, 129.34, 129.09, 128.85, 128.76, 128.64, 128.26, 128.04, 127.39, 126.33, 125.31, 75.50, 72.20, 41.21, 11.79. **IR** (KBr, thin film) *v*/cm^{-1}: 3343, 2849, 1638, 1577, 1492, 1385, 1305, 1263, 1068, 773, 616, 544 . **HRMS** (ESI) calcd. for $C_{23}H_{22}NO_2$ $(M+H)^+$: 344.1645, found: 344.1636.

4-hydroxy-2-isopropyl-3,4-diphenyl-3,4-dihydroisoquinolin-1(2H)-one (3j)

The product was obtained following the general procedure. Yield: 46%. White solid. Mp 174–175 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 – 8.22 (m, 1H), 7.57 – 7.44 (m, 2H), 7.38 – 7.34 (m, 1H), 7.29 (s, 4H), 7.27 – 7.22 (m, 4H), 7.22 – 7.16 (m, 2H), 4.86 (dt, *J* = 13.7, 6.8 Hz, 1H), 4.72 (s, 1H), 2.06 (s, 1H), 0.67 (d, *J* = 6.9 Hz, 3H), 0.44 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.50, 144.22, 139.71, 137.00, 132.85, 130.17, 128.97, 128.69, 128.66, 128.49, 128.26, 128.08, 127.54, 126.63, 125.17, 76.04, 67.03, 45.24, 20.06, 18.76. **IR** (KBr, thin film) *v*/cm^{-1}: 3346, 2848, 1648, 1565, 1498, 1375, 1302, 1263, 1068, 730, 614, 540. **HRMS** (ESI) calcd. for $C_{24}H_{24}NO_2$ $(M+H)^+$: 358.1802, found: 358.1791.

2-benzyl-4-hydroxy-3,4-diphenyl-3,4-dihydroisoquinolin-1(2H)-one (3k)

The product was obtained following the general procedure. Yield: 44%. White solid. Mp 184–185 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.39 – 8.26 (m, 1H), 7.61 – 7.47 (m, 2H), 7.44 – 7.37 (m, 1H), 7.32 – 7.26 (m, 3H), 7.22-7.20 (m, 1H), 7.16-7.06 (m, 5H), 7.04 – 6.99 (m, 2H), 6.93 (t, *J* = 5.6 Hz, 2H), 6.60 (d, *J* = 7.4 Hz, 2H), 5.53 (d, *J* = 14.9 Hz, 1H), 4.64 (s, 1H), 3.41 (d, *J* = 14.9 Hz, 1H), 2.00 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.06, 144.34, 140.21, 135.71, 134.69, 133.12, 129.17, 128.99, 128.92, 128.73, 128.29, 128.22, 127.96, 127.71, 126.92, 126.44, 125.49, 75.32, 70.54, 48.45. **IR** (KBr, thin film) *v*/cm^{-1}: 3343, 2848, 1639, 1575, 1492, 1385, 1305, 1263, 1242, 1068, 981, 730, 654, 542. **HRMS** (ESI) calcd. for $C_{28}H_{24}NO_2$ $(M+H)^+$: 406.1802, found: 406.1787.

4-hydroxy-3-(4-methoxyphenyl)-2-methyl-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one (3l)

The product was obtained following the general procedure. Yield: 66%. White solid. Mp 179–180 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.1, 2.0 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.45 – 7.42 (m, 1H), 7.33 – 7.27 (m, 5H), 7.06 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.67 (s, 1H), 3.76 (s, 3H), 2.86 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.01, 160.08, 144.82, 140.83, 132.87, 130.08, 128.69, 128.55, 128.38, 127.96, 127.47, 126.29, 126.07, 125.48, 114.32, 75.00, 74.01, 55.27, 34.38. **IR** (KBr, thin film) *v*/cm^{-1}: 3373, 2945, 1630, 1574, 1514, 1397, 1247, 1179, 1068, 1037, 835, 737, 697, 530. **HRMS** (ESI) calcd. for $C_{23}H_{22}NO_3$ $(M+H)^+$: 360.1594, found: 360.1584.

4-hydroxy-2-methyl-4-phenyl-3-p-tolyl-3,4-dihydroisoquinolin-1(2H)-one (3m)

The product was obtained following the general procedure. Yield: 64%. White solid. Mp 209–210 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 – 8.20 (m, 1H), 7.53 – 7.45 (m, 2H), 7.46 – 7.40 (m, 1H), 7.34 – 7.25 (m, 5H), 7.10 - 7.02 (m, 4H), 4.69 (s, 1H), 2.85 (s, 3H), 2.29 (s, 3H), 2.09 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.09, 144.89, 140.80, 138.92, 132.83, 131.52, 129.62, 128.79, 128.71, 128.52, 128.37, 127.96, 127.47, 126.10, 125.43, 74.98, 74.28, 34.43, 21.04. **IR** (KBr, thin film) *v*/cm^{-1}: 3343, 2848, 1639, 1575, 1490, 1385, 1302, 1263, 1068, 742, 614, 542. **HRMS** (ESI) calcd. for $C_{23}H_{22}NO_2$ $(M+H)^+$: 344.1645, found: 344.1630.

4-(4-chlorophenyl)-4-hydroxy-2-methyl-3-phenyl-3,4-dihydroisoquinolin-1(2H)-one (3n)

The product was obtained following the general procedure. Yield: 47%. White solid. Mp 224–225 °C. **^{1}H NMR** (400

MHz, $CDCl_3$) δ 8.35 – 8.18 (m, 1H), 7.56 – 7.49 (m, 2H), 7.43 – 7.38 (m, 1H), 7.31 – 7.25 (m, 7H), 7.14 (dd, *J* = 7.5, 1.9 Hz, 2H), 4.64 (s, 1H), 2.88 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.94, 143.35, 140.31, 134.34, 133.95, 133.07, 129.15, 129.01, 128.88, 128.84, 128.52, 127.68, 127.58, 125.29, 74.63, 74.55, 34.52. **IR** (KBr, thin film) *v*/cm^{-1}: 3379, 2921, 1631, 1578, 1490, 1398, 1255, 1070, 1014, 848, 760, 694, 534, 471; **HRMS** (ESI) calcd. for $C_{22}H_{19}NO_2Cl$ $(M+H)^+$: 364.1099, found: 364.1090.

4-hydroxy-2-methyl-3-(naphthalen-1-yl)-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one (3o)

The product was obtained following the general procedure. Yield: 69%. White solid. Mp 216–217 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.6 Hz, 1H), 8.34 (d, *J* = 6.7 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.54-7.50 (m, 4H), 7.40 (t, *J* = 7.3 Hz, 3H), 7.35 (d, *J* = 7.1 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 5.78 (s, 1H), 2.86 (s, 3H), 1.94 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.43, 145.47, 140.74, 133.91, 133.61, 132.95, 130.75, 129.56, 129.03, 128.65, 128.61, 128.03, 127.44, 126.80, 126.04, 125.81, 125.52, 125.41, 125.35, 123.72, 76.04, 68.94, 34.68. **IR** (KBr, thin film) *v*/cm^{-1}: 3345, 2858, 1639, 1577, 1492, 1477, 1396, 1304, 1254, 1067, 774, 640, 544; **HRMS** (ESI) calcd. for $C_{26}H_{22}NO_2$ $(M+H)^+$: 380.1645, found: 380.1629.

3-(2-chlorophenyl)-4-hydroxy-2-methyl-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one (3p)

The product was obtained following the general procedure. Yield: 45%. White solid. Mp 241–243 °C.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 – 8.16 (m, 1H), 7.54–7.51 (m, 2H), 7.45 – 7.37 (m, 1H), 7.33 – 7.27 (m, 5H), 7.27 – 7.25 (m, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 4.73 (s, 1H), 2.86 (s, 3H), 2.09 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.94, 143.32, 140.27, 134.34, 133.91, 133.07, 129.15, 129.01, 128.88, 128.84, 128.62, 128.52, 127.68, 127.58, 125.29, 74.66, 74.55, 34.52. **IR** (KBr, thin film) *v*/cm^{-1}: 3375, 2920, 1641, 1575, 1493, 1398, 1256, 1070, 1016, 848, 765, 694, 534, 470; **HRMS** (ESI) calcd. for $C_{22}H_{19}NO_2Cl$ $(M+H)^+$: 364.1099, found: 364.1096.

4-hydroxy-2-methyl-3-phenyl-4-(thiophen-2-yl)-3,4-dihydroisoquinolin-1(2H)-one (3r)

The product was obtained following the general procedure. Yield: 47%. White solid. Mp 199–201 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 – 8.12 (m, 1H), 7.44 – 7.38 (m, 2H), 7.33 – 7.29 (m, 1H), 7.25 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.7 Hz, 2H), 6.72 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.60 (d, *J* = 7.3 Hz, 2H), 5.83 (dd, *J* = 3.5, 0.8 Hz, 1H), 5.01 (s, 1H), 4.69 (s, 1H), 2.97 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.34, 144.09, 139.64, 135.95, 132.33, 129.35, 128.71, 128.47, 128.20, 128.00, 127.40, 127.23, 126.43, 125.09, 76.41, 76.29, 34.64. **IR** (KBr, thin film) *v*/cm^{-1}: 3345, 2841, 1639, 1578, 1494, 1385, 1302, 1273, 1242, 1069,700, 614, 542. **HRMS** (ESI) calcd. for $C_{20}H_{18}NO_2S$ $(M+H)^+$: 336.1053, found: 336.1069.

3-ethylidene-4-hydroxy-2-methyl-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one (3s)

The product was obtained following the general procedure. Yield: 31%. Yellow solid. Mp 186–188 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.20 (m, 3H), 7.16 – 7.07 (m, 2H), 5.86 (q, *J* = 7.3 Hz, 1H), 3.09 (s, 3H), 2.71 (s, 1H), 1.78 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.05, 144.47, 143.05, 142.71, 132.41, 131.54, 128.47, 128.31, 128.29, 128.00, 126.28, 123.88, 109.46, 77.23, 36.03, 13.26. **IR** (KBr, thin film) *v*/cm^{-1}: 3369, 2930, 1635, 1451, 1367, 1246, 1129, 1016, 967, 872, 743, 554. **HRMS** (ESI) calcd. for $C_{18}H_{18}NO_2$$(M+H)^+$: 280.1332, found: 280.1329.

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