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Full Paper





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

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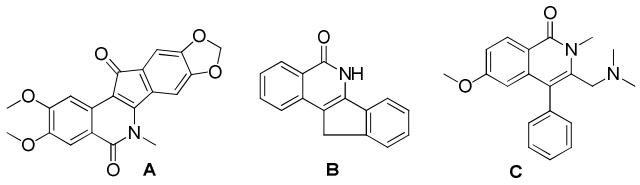
**The intramolecular coupling of amides and ketones was achieved in the presence of KO*t*-Bu/DMF. The reaction provided a variety of isoquinolinones in good yields. A reaction mechanism of radical addition and subsequent E2-elimination is proposed.**

## 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

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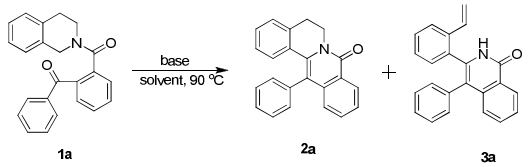
on this side reaction. The loading of KO*t*-Bu was examined and the results are summarized in Table 1. While the loading of KO*t*-Bu was decreased, the generation of **3a** was inhibited (Table 1, entries 1-5). The best yield of **2a** was obtained with 1.2 equivalents of KO*t*-Bu (Table 1, entry 3). 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]



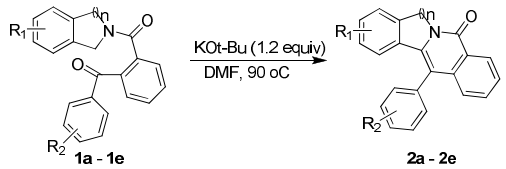

1a 2a 3a

| 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]



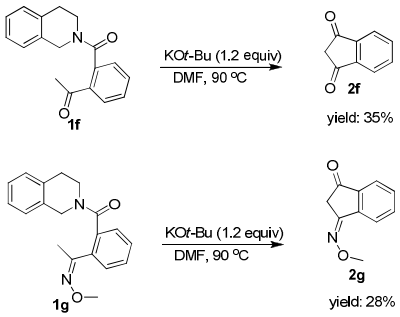

1a - 1e 2a - 2e

| 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

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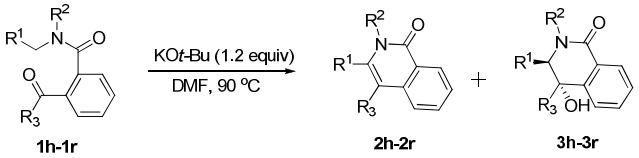
with *trans*-4-hydroxy-dihydroisoquinolinones **3h-3r** were obtained in good yields. The *N*-substitution with methyl, ethyl, isopropyl and benzyl are tolerated well. The substrates with electron-donating groups (**1l**, **1m**) obviously favor the formation of *trans*-4-hydroxy-dihydroisoquinolinones (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]



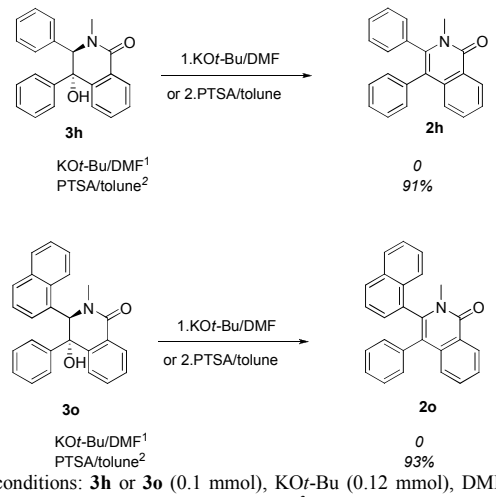

**1h-1r** **2h-2r** **3h-3r**

| 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.

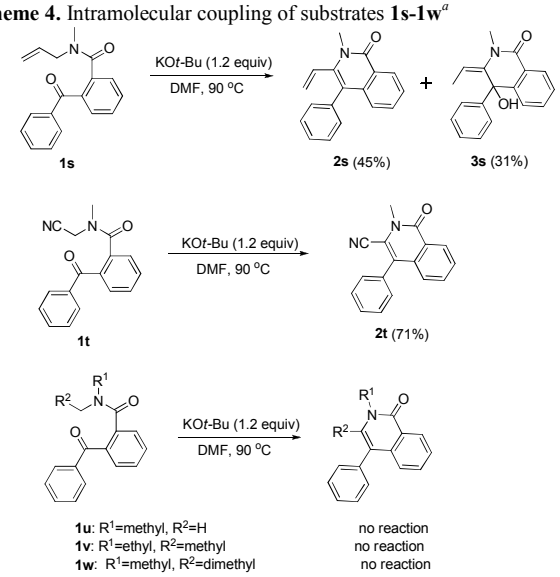
The reaction of allyl amine derived amide **1s** provided 3-vinylisoquinolinone **2s** and 4-hydroxy-3-ethylidene-dihydroisoquinolinone **3s** (Scheme 4). The reaction of α-cyano methylamine derived amide **1t** provided product **2t** in a good yield. Dialkyl amine derived amides **1u**, **1v** and **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**




[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

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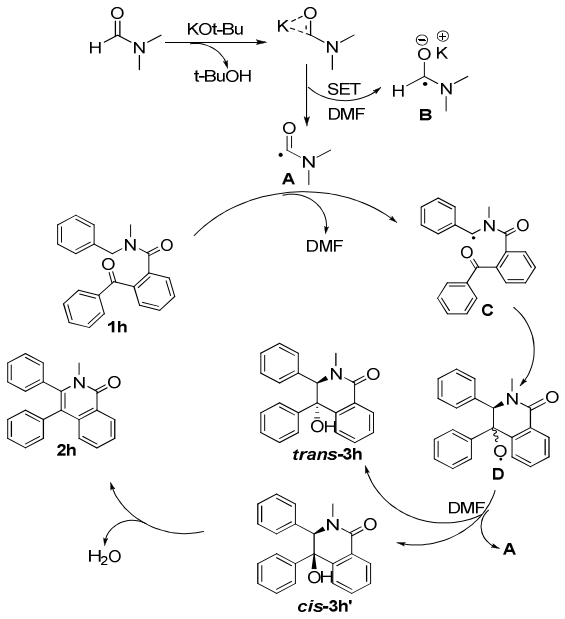
hydroxyl group and the hydrogen. In the case of tetrahydroisoquinoline derived amides **1a**-**1e**, the fused ring structures may result in the stereoselective formation of *cis*-isomers. The subsequent dehydration leads to the isoquinolinone products **2a**-**2e** exclusively.

**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**

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**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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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)$\nu$/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) $\nu$/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.

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**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**

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(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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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) $\nu$/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

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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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