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DBU-Promoted Cyclization of *ortho*-(3-Hydroxy-1-alkynyl)benzamide: Synthesis of *trans*-3,4-Dihydroisoquinolin-1(2*H*)-ones and (*E*)-4-(1-Alkenyl)isoquinolin-1(2*H*)-ones

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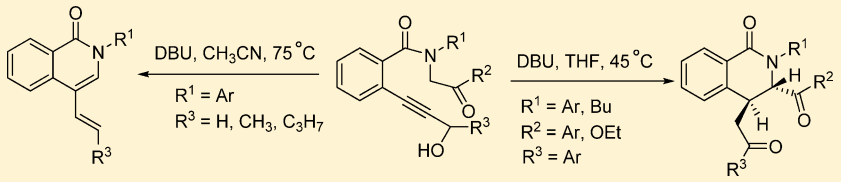
Supporting Information



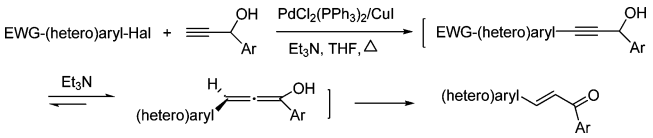
ABSTRACT: DBU-promoted cyclization of *ortho*-(3-hydroxy-1-alkynyl)benzamide is presented, providing an efficient method for the synthesis of *trans*-3,4-dihydroisoquinolin-1(2*H*)-ones and (*E*)-4-(1-alkenyl)isoquinolin-1(2*H*)-ones under mild conditions.

Dihydroisoquinolin-1(2*H*)-ones are an important class of heterocycles due to their applications as bioactive compounds and synthetic intermediates in organic synthesis.[1−9] However, there are only a few approaches about their synthesis. The main known approach of dihydroisoquinolin-1(2*H*)-one derivatives was the condensation of homophthalic anhydride with imines and involves the acid- or base-catalyzed or thermal conditions that often produce a *cis*-isomer or a mixture of *cis*- and *trans*-isomers, favoring the *cis*-isomer.[10−17] Afterward, $BF_3{\cdot}Et_2O$,[18] trimethyl orthoformate,[19] and $TiCl_4$[20] have been employed for the preparation of thermodynamically more stable *trans*-isomers using homophthalic anhydride reacted with imines. Recently, Murakami has reported a nickel-catalyzed denitrogenative annulation reactions of 2,3-benzotriazin-4(3*H*)-ones with 1,3-dienes and alkenes to give dihydroisoquinolin-1(2*H*)-ones.[21] Although these methods are effective for the synthesis of some dihydroisoquinolin-1(2*H*)-one derivatives, development of new and efficient methodologies for the stereoselective synthesis of dihydroisoquinolin-1(2*H*)-one derivatives with different substituent groups from simple, readily available starting materials remains an important research theme in organic chemistry.

Combining two or more reactions into one sequential reaction, which usually involves a series of inter- or intramolecular processes wherein the product of one reaction is programmed to be the substrate for the next, represents an elegant and efficient way to access novel and complex molecules from simple, readily available starting materials.[22−27] Recently, Müller et al. have reported a Pd-catalyzed coupling and base-induced propargyl alcohol−enone isomerization providing an efficient synthesis of α,β-unsaturated ketones[28,29] (Scheme 1), which could be further transformed to some interesting heterocycles in a one-pot fashion.[30−34]

In these reactions, the aryl propargyl alcohols with an electron-withdrawing group were used as an efficient potential

Scheme 1



synthon of α,β-unsaturated ketones through propargyl alcohol−enone isomerization. We envision that this kind of aryl propargyl alcohol might be used as an efficient structure unit in the construction of dihydroisoquinolin-1(2*H*)-ones (Figure 1). This new subsequent intramolecular cyclization

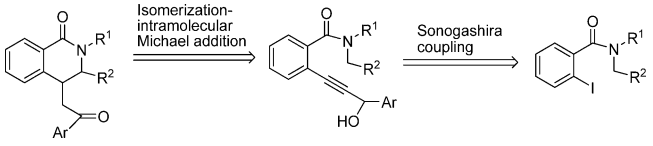


Figure 1. Synthetic strategy.

approach may yield the thermodynamically more stable *anti*-dihydroisoquinolin-1(2*H*)-ones with different substituent groups.

As a first attempt, we chose 2-(3-hydroxy-3-phenyl-1-propynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenyl-benzamide (**1a**) as the starting material, which could be easily prepared via a Sonogashira reaction with 2-iodo-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide and 1-phenyl-2-propyn-1-ol (Scheme 2).

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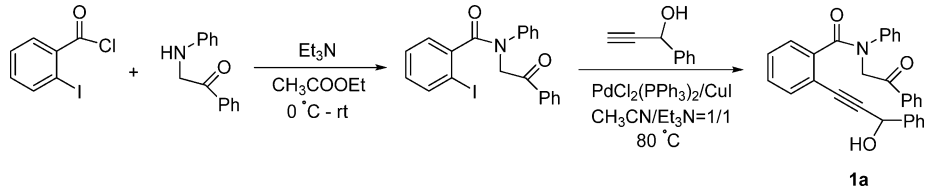
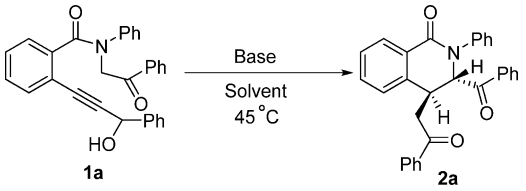
Scheme 2



On the basis of the previous investigation, we initiated our study by testing the reaction of **1a** in the presence of various bases and solvents (Table 1). Triethylamine could not promote

Table 1. Base and Solvent Effect[a]



entry	base	solvent	time (h)	yield (%)[b]
1	Et_3N	THF	48	0
2	NaH	THF	1	55
3	DBU	THF	16	85
4	DBU	THF	12	78[c]
5	DBU	C_2H_5OH	44	35[d]
6	DBU	CH_3CN	17	70
7	DBU	DMF	17	50
8	DBU	Toluene	27	75

[a]Substrate **1a** (0.2 mmol) and base (2 equiv) in solvent (2 mL) under atmosphere. [b]Isolated yield based on **1a**. [c]The reaction temperature was 60 °C. [d]27% of **1a** was recovered.

the reaction. A strong base could trigger the expected reaction and give *anti*-dihydroisoquinolin-1(2*H*)-one (**3a**) as the product (entries 2−3, Table 1). The stereochemistry was established on the coupling constant[35] between protons H-3 and H-4 and was further confirmed by a NOESY experiment (**2a**, Figure 2). A more competitive yield was obtained using

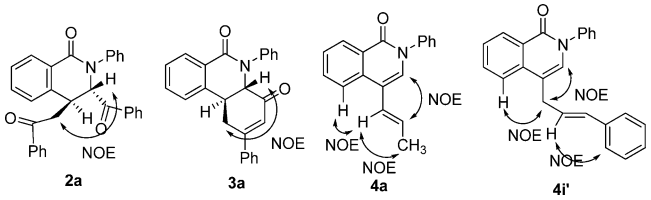


Figure 2. NOE experiment of **2a**, **3a**, **4a**, and **4i'**.

DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) as the base (entry 3, Table 1). Further examination of solvent choice showed that THF was the suitable reaction medium for this reaction (entries 3−7, Table 1).

With the optimized reaction conditions in hand (Table 1, entry 3), we further tried other aryl propargyl alcohols in the reaction (Table 2). From the results in Table 2, we could see that the reaction could proceed smoothly to afford *anti*-dihydroisoquinolin-1(2*H*)-ones in moderate to good yields under mild conditions. The reaction also exhibited an excellent stereoselectivity. When **1j** was used as the substrate, a tricycle product **3a** was obtained. NOESY experiment also demonstrated the *anti*-configuration (**3a**, Figure 2). We think that its formation may be through an *anti*-dihydroisoquinolin-1(2*H*)-one intermediate (Scheme 3).

To determine the scope of this transformation, we next examined the reaction of 2-(3-hydroxy-1-pentynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide **1k**, which has a methyl (alkyl substituent) in alkyne unit. When using the above reaction conditions, no reaction occurred. Then we further screened the reaction conditions. Luckily, when we choose CH_3CN as solvent at elevated temperature (75 °C), a dihydroisoquinolin-1(2*H*)-one compound **4a** with an (*E*)-propenyl substituent was obtained in a yield of 70%. The stereochemistry was established on the basis of ^{1}H NMR (the coupling constant for the vinyl protons) and NOESY experiment (**4a**, Figure 2). Then we further examined the scope of the reaction, and the results were summarized in Table 3. Alkyl substitutes such as hydrogen, methyl, propyl, and benzyl were all effective for this reaction, and the corresponding dihydroisoquinolin-1(2*H*)-ones were obtained in moderate yields.

On the basis of the above results and previous investigations, a possible mechanism for the DBU-promoted cyclization of *ortho*-(3-hydroxy-1-alkynyl)benzamide is shown in Scheme 4. When the substrate has an aryl group (R^3 = aryl), an initial base-induced propargyl alcohol−enone isomerization provided the intermediate **A**. Subsequently, the intramolecular attack at the less sterically hindered side and capture of a hydrogen cation afforded **2**. While the substrate has an alkyl group (R^3 = alkyl), the above isomerization did not occur. At elevated temperature, an initial base-induced 6-exo-dig afforded the intermediate **B**, which could rearrange to **C**. Subsequent elimination a hydroxyl and concurrence attack to the intramolecular carbonyl through the six-membered ring transition state provided intermediate **D**. Finally, leaving a benzoic acid anion[36] and capture of a hydrogen cation afforded the product **4**.

These *trans*-3,4-dihydroisoquinolin-1(2*H*)-ones bearing 1,5-dicarbonyl functional groups and isoquinolin-1(2*H*)-ones with an alkenyl functional group may be converted to other interesting and useful structural units in organic synthesis.[37−40] We treated **2a** with NH_4OAc in CH_3COOH to access 2,4,5-triphenylbenzo[*c*]-[1,7]naphthyridin-6(5*H*)-one (**5a**) in moderate yield (Scheme 5).

In summary, we have developed an efficient method for the synthesis of *trans*-3,4-dihydroisoquinolin-1(2*H*)-ones and (*E*)-4-(1-alkeny)lisoquinolin-1(2*H*)-ones in moderate to good yields under mild conditions. Further studies into the scope and synthetic applications of this transformation are being carried out in our laboratory.

EXPERIMENTAL SECTION

General Procedures. All ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ or DMSO-d_6 and recorded on a 500 MHz (125 MHz for ^{13}C) spectrometer with TMS as the internal standard. Chemical shifts are expressed in ppm and *J*-values are given in Hz. High-resolution mass spectroscopy (HRMS) was carried out in electrospray mode. Solvents were distilled before use.

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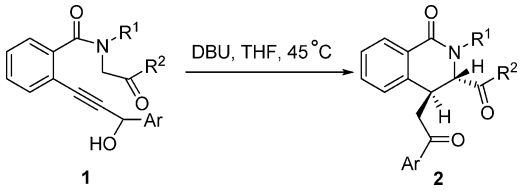
Table 2. Synthesis of *anti*-Dihydroisoquinolin-1(2*H*)-ones 2

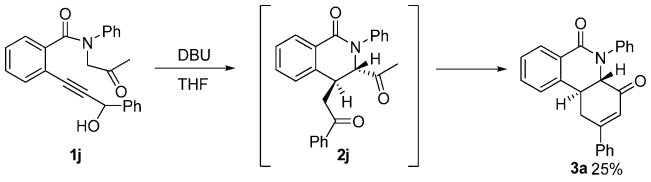


1 2

entry	$R^1/R^2/Ar$	time (h)	product	yield (%)[a]
1	$C_6H_5/C_6H_5/C_6H_5$, **1a**	16	**2a**	85
2[b]	$C_6H_5/C_6H_5/p$-ClC_6H_4, **1b**	11	**2b**	78
3	$C_6H_5/C_6H_5/m$-BrC_6H_4, **1c**	16	**2c**	67
4	p-$CH_3C_6H_4/C_6H_5/C_6H_5$, **1d**	16	**2d**	75
5	p-$CH_3C_6H_4/C_6H_5/p$-$CH_3C_6H_4$, **1e**	16	**2e**	72
6	p-$CH_3C_6H_4/p$-ClC_6H_4/p-$CH_3C_6H_4$, **1f**	16	**2f**	67
7	p-$ClC_6H_4/C_6H_5/p$-$CH_3C_6H_4$, **1g**	16	**2g**	80
8	C_6H_5/OEt/C_6H_5, **1h**	16	**2h**	79 (97:3)[c]
9	Bu/OEt/C_6H_5, **1i**	17	**2i**	58 (96:4)[c]

[a]Isolated yield based on **1**. [b]The reaction temperature was 0 °C. [c]The ratio of *trans*/*cis* was determined by ^{1}H NMR analysis

Scheme 3



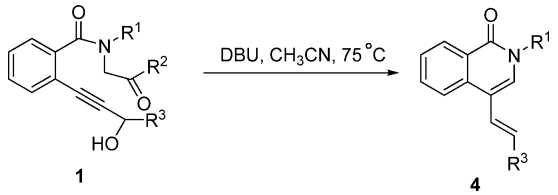
Typical Procedure for Synthesis of 1. To a solution of 2-iodo-*N*-phenylbenzamide (0.3 mmol) and substituted 2-propyn-1-ol (1.2 equiv) in CH_3CN (1 mL) were added CuI (2.9 mg. 0.015 mmol) and $PdCl_2(PPh_3)_2$ (10.5 mg, 0.015 mmol), and Et_3N (1 mL) was then added under a N_2 atmosphere at room temperature. Then, the reaction mixture was warmed to 80 °C and stirred until the reaction was completed (monitored by TLC). After evaporation of reaction solvent, saturated aqueous NH_4Cl was added, extracted with ethyl acetate, and dried over anhydrous $MgSO_4$. After evaporation of ethyl acetate, chromatography on silica gel (eluent: EtOAc/petroleum ether = 3/1) afforded **1** (for **1b**, **1c**, **1n**, **1q**, **1r**, 30% catalyst was loaded and run at rt).

2-(3-Hydroxy-3-phenyl-1-propynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1a). Yellow solid (118 mg, 88%): mp 110–112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 7.3 Hz, 2H), 7.68 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.34–7.30 (m, 4H), 7.21–7.19 (m, 1H), 7.15–7.07 (m, 5H), 5.78 (d, J = 5.0 Hz,1H), 5.33 (d, J = 17.3 Hz, 1H), 5.28 (d, J = 17.3 Hz, 1H), 4.56 (d, J = 5.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 170.2, 142.6, 141.0, 139.5, 134.9, 133.9, 131.8, 128.9, 128.8, 128.5, 128.2, 128.1, 128.0, 127.8, 127.5, 127.1, 126.9, 120.5, 93.7, 84.1, 64.9, 56.4; HRMS-ESI $[M + Na]^+$ Calcd for $C_{30}H_{23}NNaO_3$ 468.1576, found 468.1585.

2-[3-(4-Chlorophenyl)-3-hydroxy-1-propynyl]-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1b). Yellow solid (82 mg, 57%): mp 149–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.4 Hz, 2H), 7.62–7.58 (m, 3H), 7.46 (t, J = 7.7 Hz, 2H), 7.34–7.29 (m, 5H), 7.18–7.07 (m, 6H), 5.73 (d, J = 4.0 Hz, 1H), 5.36 (d, J = 17.3 Hz, 1H), 5.23 (d, J = 17.3 Hz, 1H), 4.76 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3, 170.1, 142.6, 139.7, 139.6, 134.9, 134.0, 133.8, 131.8, 129.0, 128.8, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 127.0, 120.5, 93.2, 84.4, 64.3, 56.4; HRMS-ESI $[M + Na]^+$ Calcd for $C_{30}H_{22}ClNNaO_3$ 502.1186, found 502.1170.

2-[3-(3-Bromophenyl)-3-hydroxy-1-propynyl]-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1c). Yellow solid (25 mg, 16%): mp 74–76 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 2H), 7.87 (s, 1H), 7.61 (t, J = 6.8 Hz, 2H), 7.49–7.44 (m, 3H), 7.33–7.31 (m, 3H), 7.25 (t, J = 7.9 Hz, 1H), 7.22–7.09 (m, 6H), 5.74 (s, 1H), 5.37 (d, J = 17.4 Hz, 1H), 5.30 (d, J = 17.4 Hz, 1H); 4.87 (br, 1H);

Table 3. Synthesis of Dihydroisoquinolin-1(2*H*)-ones 4



1 4

entry	$R^1/R^2/R^3$	time (h)	product	yield (%)[a]
1	$C_6H_5/C_6H_5/CH_3$, **1k**	24	**4a**	70
2	p-$CH_3C_6H_4/C_6H_5/CH_3$, **1l**	24	**4b**	69
3	p-$ClC_6H_4/C_6H_5/CH_3$, **1m**	16	**4c**	78
4	o-$ClC_6H_4/C_6H_5/CH_3$, **1n**	22	**4d**	86
5	C_6H_5/C_6H_5/H, **1o**	28	**4e**	42
6	$C_6H_5/C_6H_5/n$-C_3H_7, **1p**	16	**4f**	64
7	p-$CH_3C_6H_4/C_6H_5/n$-C_3H_7, **1q**	24	**4g**	55
8	p-$ClC_6H_4/C_6H_5/n$-C_3H_7,**1r**	16	**4h**	66
9	$C_6H_5/C_6H_5/CH_2C_6H_5$, **1s**	24	**4i**/**4i′**	50 (16:34)[b]

[a]Isolated yield based on **1**. [b]Determined by isolation.

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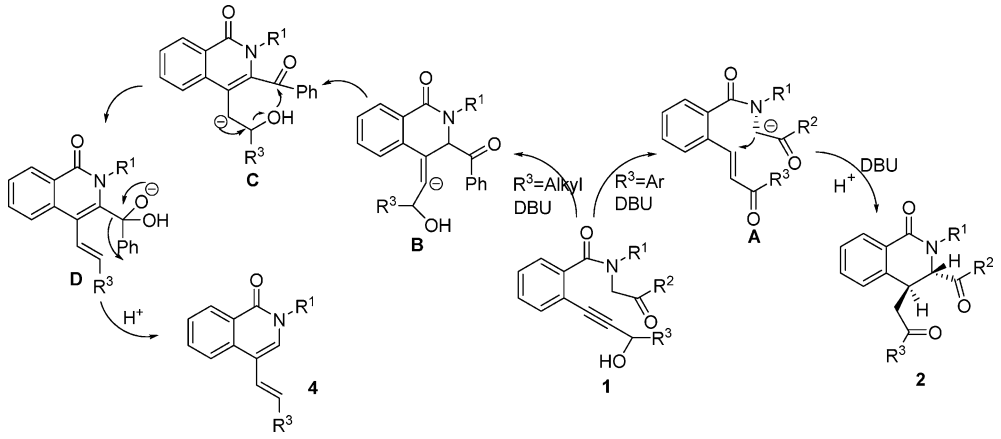
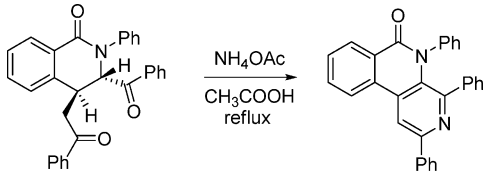
Scheme 4



Scheme 5



^{13}C NMR (125 MHz, $CDCl_3$) δ 194.3, 170.2, 143.3, 142.6, 139.6, 134.9, 134.0, 131.8, 131.1, 130.1, 130.0, 129.0, 128.8, 128.5, 128.2, 128.0, 127.9, 127.6, 127.1, 125.6, 122.5, 120.4, 93.0, 84.5, 64.2, 56.4; HRMS-ESI [M + Na]$^+$ Calcd for $C_{30}H_{22}BrNNaO_3$ 546.0681, found 546.0655.

2-(3-Hydroxy-3-phenyl-1-propynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-(*p*-tolyl)benzamide (1d). Yellow solid (113 mg, 82%): mp 70–72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 7.4 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.4 Hz, 2H), 7.31–7.25 (m, 2H), 7.22–7.20 (m, 1H), 7.17 (d, J = 8.2 Hz, 2H), 7.12–7.09 (m, 2H), 6.89 (d, J = 8.2 Hz, 2H), 5.75 (d, J = 4.0 Hz, 1H), 5.28 (d, J = 17.3 Hz, 1H), 5.22 (d, J = 17.3 Hz, 1H), 4.70 (br, 1H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.2, 170.2, 141.1, 140.0, 139.7, 137.2, 135.0, 133.8, 131.7, 129.5, 128.7, 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 127.1, 126.9, 120.4, 93.6, 84.1, 64.9, 56.4, 20.9; HRMS-ESI [M + Na]$^+$ Calcd for $C_{31}H_{25}NNaO_3$ 482.1732, found 482.1720.

2-[3-Hydroxy-3-(*p*-tolyl)prop-1-ynyl]-*N*-(2-oxo-2-phenylethyl)-*N*-(*p*-tolyl)benzamide (1e). Yellow solid (118 mg, 83%): mp 144–146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.4 Hz, 2H), 7.56–7.54 (m, 3H), 7.42 (t, J = 7.8 Hz, 2H), 7.28–7.25 (m, 1H), 7.22–7.20 (m, 1H), 7.18 (d, J = 8.1 Hz, 4H), 7.13–7.09 (m, 2H), 6.89 (d, J = 8.1 Hz, 2H), 5.72 (s, 1H), 5.29 (d, J = 17.4 Hz, 1H), 5.21 (d, J = 17.4 Hz, 1H), 4.59 (br, 1H), 2.34 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 170.2, 140.0, 139.7, 138.2, 137.7, 137.2, 135.0, 133.7, 131.7, 129.4, 129.1, 128.7, 128.3, 128.1, 127.7, 127.1, 126.9, 120.5, 93.8, 83.9, 64.7, 56.4, 21.1, 20.9; HRMS-ESI [M + Na]$^+$ Calcd for $C_{32}H_{27}NNaO_3$ 496.1889, found 496.1875.

***N*-[2-(4-Chlorophenyl)-2-oxoethyl]-2-[3-hydroxy-3-(*p*-tolyl)-1-propynyl]-*N*-(*p*-tolyl)benzamide (1f).** Yellow solid (108 mg, 71%): mp 67–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H), 7.32–7.28 (m, 1H), 7.24–7.19 (m, 5H), 7.17–7.13 (m, 2H), 6.93 (d, J = 8.2 Hz, 2H), 5.72 (d, J = 5.0 Hz, 1H), 5.29 (d, J = 17.3 Hz, 1H), 5.17 (d, J = 17.3 Hz, 1H), 4.46 (br, 1H), 2.37 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.1, 170.2, 140.3, 139.9, 139.6, 138.1, 137.8, 137.3, 133.4, 131.8, 129.5, 129.2, 129.1, 128.4, 127.8, 127.7, 127.1, 126.9, 120.5, 93.8, 84.0, 64.8, 56.3, 21.2, 20.9; HRMS-ESI [M + Na]$^+$ Calcd for $C_{32}H_{26}ClNNaO_3$ 530.1499, found 530.1473.

***N*-(4-Chlorophenyl)-2-[3-hydroxy-3-(*p*-tolyl)-1-propynyl]-*N*-(2-oxo-2-phenylethyl)benzamide (1g).** Yellow solid (107 mg, 72%): mp 69–71 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.30–7.28 (m, 1H), 7.24–7.15 (m, 7H), 7.06 (d, J = 8.6 Hz, 2H), 5.71 (d, J = 3.6 Hz, 1H), 5.27 (d, J = 17.4 Hz, 1H), 5.20 (d, J = 17.4 Hz, 1H), 4.40 (br, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 170.0, 141.1, 139.2, 138.1, 137.9, 134.8, 134.0, 133.1, 131.9, 129.4, 129.2, 129.0, 128.8, 128.7, 128.1, 128.0, 127.1, 126.8, 120.4, 94.0, 83.8, 64.7, 56.2, 21.2; HRMS-ESI [M + Na]$^+$ Calcd for $C_{31}H_{24}ClNNaO_3$ 516.1342, found 516.1322.

Ethyl 2-[2-(3-Hydroxy-3-phenyl-1-propynyl)-*N*-phenylbenzamido]acetate (1h). Yellow gum (103 mg, 83%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 7.29–7.25 (m, 3H), 7.18–7.09 (m, 6H), 5.72 (s, 1H), 4.60 (d, J = 17.1 Hz, 1H), 4.54 (d, J = 17.1 Hz, 1H), 4.31 (br, 1H), 4.24–4.14 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 169.5, 142.3, 141.0, 139.3, 131.7, 128.9, 128.5, 128.1, 127.8, 127.5, 127.0, 126.9, 120.4, 93.6, 83.9, 64.8, 61.7, 51.5, 14.0; HRMS-ESI [M + Na]$^+$ Calcd for $C_{26}H_{23}NNaO_4$ 436.1525, found 436.1511.

Ethyl 2-[*N*-Butyl-2-(3-hydroxy-3-phenyl-1-propynyl)-benzamido]acetate (1i). Yellow solid (91 mg, 77%): mp 140–142 °C; ^{1}H NMR (500 MHz, DMSO, 80 °C) δ 7.54–7.20 (m, 9H), 5.82 (s, 1H), 5.60 (s, 1H), 4.19–3.90 (m, 4H), 3.42 (s, 1H), 1.52–1.24 (m, 5H), 1.11–1.03 (m, 2H), 0.91–0.88 (m, 1H), 0.65 (t, J = 7.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 168.5, 141.6, 138.9, 131.6, 131.4, 128.4, 128.1, 127.7, 127.1, 126.2, 126.0, 125.9, 119.0, 94.3, 81.6, 62.8, 60.3, 60.0. 49.9, 48.9, 46.5, 45.6, 29.4, 28.4, 19.2, 18.6, 13.6, 13.4, 13.0, 12.6; HRMS-ESI [M + Na]$^+$ Calcd for $C_{24}H_{27}NNaO_4$ 416.1838, found 416.1818.

2-(3-Hydroxy-3-phenyl-1-propynyl)-*N*-(2-oxopropyl)-*N*-phenylbenzamide (1j). Yellow gum (92 mg, 80%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 7.29–7.28 (m, 1H), 7.21–7.07 (m, 8H), 5.75 (s, 1H), 4.64 (d, J = 17.6 Hz, 1H), 4.60 (d, J = 17.6 Hz, 1H), 4.45 (br, 1H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 169.9, 142.4, 141.0, 139.2, 131.8, 128.9, 128.5, 128.0, 127.8, 127.7, 127.4, 127.1, 126.8, 120.4, 93.6, 83.9, 64.8, 59.5, 27.5; HRMS-ESI [M + Na]$^+$ Calcd for $C_{25}H_{21}NNaO_3$ 406.1419, found 406.1405.

2-(3-Hydroxy-1-butynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1k). Yellow solid (101 mg, 88%): mp 150–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.8 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.36 (d, J = 7.6 Hz, 2H), 7.28–7.27 (m, 1H), 7.20–7.07 (m, 6H), 5.36 (s, 2H), 4.85 (q, J = 6.5 Hz, 1H), 4.27 (br, 1H), 1.60 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 170.1, 142.6, 139.4, 134.9, 133.8, 131.6, 128.8, 128.7, 128.4, 128.1, 127.9, 127.5, 127.4, 127.1, 120.8, 95.9, 81.5, 58.6, 56.3, 23.9; HRMS-ESI [M + H]$^+$ Calcd for $C_{25}H_{22}NO_3$ 384.1600, found 384.1601.

2-(3-Hydroxy-1-butynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-(*p*-tolyl)benzamide (1l). Yellow solid (104 mg, 87%): mp 65–67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.29–7.28 (m, 1H), 7.23

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(d, J = 8.3 Hz, 2H), 7.20−7.10 (m, 3H), 6.95 (d, J = 8.2 Hz, 2H), 5.34 (d, J = 17.4 Hz, 1H), 5.31 (d, J = 17.4 Hz, 1H), 4.85 (q, J = 6.5 Hz, 1H), 4.17 (br, 1H), 2.20 (s, 3H), 1.60 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 170.3, 140.1, 139.7, 137.3, 135.0, 133.8, 131.6, 129.5, 128.8, 128.3, 128.1, 127.6, 127.5, 127.0, 120.7, 95.8, 81.6, 58.6, 56.4, 24.0, 20.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{26}H_{24}NO_3$ 398.1756, found 398.1741.

***N*-(4-Chlorophenyl)-2-(3-hydroxy-1-butynyl)-*N*-(2-oxo-2-phenylethyl)benzamide (1m).** Yellow solid (104 mg, 83%): mp 139−141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 8.7 Hz, 3H), 7.21−7.11 (m, 5H), 5.32 (s, 2H), 4.82 (q, J = 6.6 Hz, 1H), 4.14 (br, 1H), 1.58 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.9, 170.1, 141.2, 139.1, 134.8, 134.0, 133.2, 131.8, 129.3, 129.0, 128.8, 128.7, 128.1, 127.7, 127.0, 120.7, 96.1, 81.4, 58.6, 56.3, 23.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{25}H_{21}ClNO_3$ 418.1210, found 418.1202.

***N*-(2-Chlorophenyl)-2-(3-hydroxy-1-butynyl)-*N*-(2-oxo-2-phenylethyl)benzamide (1n).** Yellow solid (114 mg, 91%): mp 73−75 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03−8.00 (m, 2H), 7.93−7.89 (m, 1H), 7.62 (t, J = 7.3 Hz, 1H), 7.51−7.48 (m, 2H), 7.35−7.31 (m, 2H), 7.20−7.05 (m, 5H), 6.08 (d, J = 4.1 Hz, 0.5H), 6.05 (d, J = 4.1 Hz, 0.5H), 4.93−4.85 (m, 1H), 4.54−4.49 (m, 1.5H), 4.30 (d, J = 6.8 Hz, 0.5H), 1.65 (d, J = 6.6 Hz, 1.5H), 1.60 (d, J = 6.6 Hz, 1.5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.2, 194.1, 170.2, 170.1, 139.6, 139.4, 139.3, 134.8, 134.0, 132.2, 132.1, 132.0, 131.6, 131.4, 129.7, 129.6, 128.9, 128.8, 128.7, 128.2, 128.1, 127.7, 127.6, 124.8, 124.7, 121.0, 96.4, 96.3, 81.7, 81.4, 58.9, 58.5, 54.4, 24.3,23.5; HRMS-ESI $[M + H]^+$ Calcd for $C_{25}H_{21}ClNO_3$ 418.1210, found 418.1204.

2-(3-Hydroxy-1-propynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1o). Yellow solid (85 mg, 77%): mp 151−153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 7.7 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.34 (d, J = 7.7 Hz, 2H), 7.29−7.27 (m, 1H), 7.22−7.08 (m, 6H), 5.36 (s, 2H), 4.57 (s, 2H), 3.96 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 170.2, 142.6, 139.5, 134.9, 133.9, 131.6, 128.9, 128.8, 128.5, 128.1, 127.8, 127.6, 127.4, 127.1, 120.7, 92.3, 83.2, 56.4, 51.6; HRMS-ESI $[M + H]^+$ Calcd for $C_{24}H_{20}NO_3$ 370.1443, found 370.1449.

2-(3-Hydroxy-1-hexynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1p). Yellow gum (38 mg, 31%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 7.7 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.36 (d, J = 7.7 Hz, 2H), 7.29 (d, J = 7.7 Hz, 1H), 7.20−7.09 (m, 6H), 5.36 (d, J = 17.6 Hz, 1H), 5.34 (d, J = 17.6 Hz, 1H), 4.71 (t, J = 6.5 Hz, 1H), 4.07 (br, 1H), 1.91−1.81 (m, 2H), 1.65−1.57 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 170.1, 142.7, 139.4, 134.9, 133.9, 131.7, 128.9, 128.8, 128.4, 128.1, 127.9, 127.5, 127.4, 127.1, 120.9, 95.2, 82.4, 62.6, 56.3, 39.7, 18.5, 13.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{27}H_{26}NO_3$ 412.1913, found 412.1905.

2-(3-Hydroxy-1-hexynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-(*p*-tolyl)benzamide (1q). Yellow solid (60 mg, 47%): mp 110−112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.30−7.28 (m, 1H), 7.23 (d, J = 8.3 Hz, 2H), 7.20−7.09 (m, 3H), 6.95 (d, J = 8.2 Hz, 2H), 5.33 (d, J = 17.5 Hz, 1H), 5.31 (d, J = 17.5 Hz, 1H), 4.71 (t, J = 6.6 Hz, 1H), 4.08 (br, 1H), 2.20 (s, 3H), 1.90−1.82 (m, 2H), 1.65−1.57 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 170.3, 140.1, 139.6, 137.3, 135.0, 133.8, 131.7, 129.5, 128.8, 128.3, 128.1, 127.7, 127.5, 127.0, 120.8, 95.1, 82.5, 62.6, 56.4, 39.7, 20.9, 18.5, 13.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{28}H_{28}NO_3$ 426.2069, found 426.2056.

***N*-(4-Chlorophenyl)-2-(3-hydroxy-1-hexynyl)-*N*-(2-oxo-2-phenylethyl)benzamide (1r).** Yellow gum (112 mg, 84%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.2 Hz, 3H), 7.21−7.12 (m, 5H), 5.32 (s, 2H), 4.68 (t, J = 6.4 Hz, 1H), 4.02 (br, 1H), 1.89−1.78 (m, 2H), 1.63−1.55 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.9, 170.0, 141.2, 139.1, 134.8, 134.0, 133.2, 131.9, 129.3, 129.1, 128.8, 128.7, 128.1, 127.7, 127.0, 120.8, 95.4, 82.3, 62.5, 56.3, 39.7, 18.5, 13.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{27}H_{25}ClNO_3$ 446.1523, found 446.1518.

2-(3-Hydroxy-4-phenyl-1-butynyl)-*N*-(2-oxo-2-phenylethyl)-*N*-phenylbenzamide (1s). Yellow gum (83 mg, 60%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.40 (d, J = 7.4 Hz, 2H), 7.35−7.32 (m, 4H), 7.27−7.20 (m, 3H), 7.17−7.08 (m, 5H), 5.35 (d, J = 17.6 Hz, 1H), 5.33 (d, J = 17.6 Hz, 1H), 4.91 (t, J = 6.5 Hz, 1H), 4.24 (br, 1H), 3.24−3.16 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0, 170.0, 142.6, 139.3, 137.2, 134.9, 133.8, 131.7, 129.8, 128.8, 128.7, 128.4, 128.2, 128.1, 127.8, 127.6, 127.3, 127.1, 126.5, 120.7, 94.4, 83.3, 63.8, 56.3, 43.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{31}H_{26}NO_3$ 460.1913, found 460.1920.

Typical Procedure for Synthesis of 2. To a solution of *ortho*-(3-hydroxyalkynyl)benzamide (0.2 mmol) in THF (2 mL) was added DBU (2 equiv) at room temperature. Then the reaction mixture was warmed to 45 °C and stirred until the reaction was completed (monitored by TLC). After evaporation of reaction solvent, chromatography on silica gel (eluent: EtOAc/petroleum ether = 3/1) afforded **2** (for **2b** run at 0 °C).

***trans*-3-Benzoyl-4-(2-oxo-2-phenylethyl)-2-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2a).** White solid (76 mg, 85%): mp 223−225 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32−8.28 (m, 3H), 8.07−8.05 (m, 2H), 7.67−7.62 (m, 2H), 7.56−7.52 (m, 4H), 7.45−7.39 (m, 2H), 7.33−7.20 (m, 5H), 7.03−7.01 (m, 1H), 5.83 (d, J = 1.4 Hz, 1H), 4.16−4.03 (m, 2H), 3.39 (dd, J_1 = 18.1 Hz, J_2 = 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 195.7, 164.9, 142.5, 137.4, 136.3, 134.0, 133.8, 132.5, 129.5, 129.2, 129.0, 128.9, 128.2, 128.1, 127.0, 126.8, 126.6, 68.3, 44.0, 37.8; HRMS-ESI $[M + H]^+$ Calcd for $C_{30}H_{24}NO_3$ 446.1756, found 446.1748.

***trans*-3-Benzoyl-4-[2-(4-chlorophenyl)-2-oxoethyl]-2-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2b).** White solid (75 mg, 78%): mp 209−211 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29−8.27 (m, 3H), 7.99 (d, J = 8.6 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.50 (d, J = 8.6 Hz, 2H), 7.45−7.39 (m, 2H), 7.33−7.30 (m, 2H), 7.24−7.20 (m, 3H), 7.01−6.99 (m, 1H), 5.79 (s 1H), 4.15−3.98 (m, 2H), 3.35 (dd, J_1 = 18.4 Hz, J_2 = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 195.6, 164.8, 142.5, 140.6, 137.2, 134.5, 134.0, 133.8, 132.5, 129.5, 129.3, 129.2, 129.1, 129.0, 128.9, 128.3, 127.1, 126.7, 126.5, 68.2, 43.9, 37.7; HRMS-ESI $[M + H]^+$ Calcd for $C_{30}H_{23}ClNO_3$ 480.1366, found 480.1348.

***trans*-3-Benzoyl-4-[2-(3-bromophenyl)-2-oxoethyl]-2-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2c).** White solid (70 mg, 67%): mp 221−223 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29−8.27 (m, 3H), 8.20 (t, J = 1.7 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.79−7.77 (m, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.5 Hz, 2H), 7.46−7.39 (m, 3H), 7.32 (t, J = 7.4 Hz, 2H), 7.25−7.21 (m, 3H), 7.02−7.00 (m, 1H), 5.78 (d, J = 1.4 Hz, 1H), 4.12−3.98 (m, 2H), 3.35 (dd, J_1 = 18.4 Hz, J_2 = 2.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 195.6, 164.8, 142.4, 137.9, 137.1, 136.8, 134.0, 133.8, 132.5, 131.2, 130.5, 129.5, 129.3, 129.1, 128.9, 128.3, 127.0, 126.6, 126.5, 123.4, 68.2, 44.0, 37.6; HRMS-ESI $[M + H]^+$ Calcd for $C_{30}H_{23}BrNO_3$ 524.0861, found 524.0842.

***trans*-3-Benzoyl-4-(2-oxo-2-phenylethyl)-2-(*p*-tolyl)-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2d).** White solid (69 mg, 75%): mp 249−251 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30−8.28 (m, 3H), 8.05 (d, J = 7.6 Hz, 2H), 7.67−7.61 (m, 2H), 7.55−7.52 (m, 4H), 7.42−7.38 (m, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 7.02−7.00 (m, 1H), 5.78 (d, J = 1.1 Hz, 1H), 4.15−4.02 (m, 2H), 3.38 (dd, J_1 = 17.9 Hz, J_2 = 2.4 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 195.8, 164.9, 140.0, 137.4, 136.8, 136.3, 134.0, 133.9, 132.4, 129.8, 129.6, 129.1, 129.0, 128.9, 128.8, 128.2, 128.1, 126.6, 126.5, 68.4, 44.0, 37.7, 21.0; HRMS-ESI $[M + H]^+$ Calcd for $C_{31}H_{26}NO_3$ 460.1913, found 460.1902.

***trans*-3-Benzoyl-4-[2-oxo-2-(*p*-tolyl)ethyl]-2-(*p*-tolyl)-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2e).** White solid (68 mg, 72%): mp 209−211 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30−8.27 (m, 3H), 7.95 (d, J = 8.2 Hz, 2H), 7.62 (t, J = 7.3 Hz, 1H), 7.54 (t, J = 7.5 Hz, 2H), 7.42−7.39 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 7.01−7.00 (m, 1H), 5.77 (d, J = 1.3 Hz, 1H), 4.12−4.00 (m, 2H), 3.33 (dd, J_1 = 18.1 Hz, J_2 = 2.5 Hz, 1H), 2.46 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

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197.8, 195.8, 165.0, 145.0, 139.9, 137.5, 136.8, 133.8, 132.3, 129.8, 129.6, 129.1, 128.9, 128.8, 128.3, 128.1, 126.6, 126.5, 68.4, 43.8, 37.7, 21.7, 21.0; HRMS-ESI $[M + H]^+$ Calcd for $C_{32}H_{28}NO_3$ 474.2069, found 474.2062.

***trans*-3-(4-Chlorobenzoyl)-4-[2-oxo-2-(*p*-tolyl)ethyl]-2-(*p*-tolyl)-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2f).** White solid (68 mg, 67%): mp 199−201 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29−8.26 (m, 3H), 7.95 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 7.43−7.40 (m, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.10 (s, 4H), 7.02−7.00 (m, 1H), 5.73 (s, 1H), 4.08−4.02 (m, 2H), 3.36−3.30 (m, 1H), 2.47 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 194.9, 164.9, 145.1, 140.5, 139.9, 137.3, 136.9, 133.7, 132.5, 132.2, 130.6, 129.9, 129.7, 129.5, 129.2, 128.9, 128.3, 128.2, 126.6, 126.5, 68.4, 43.8, 37.7, 21.7, 21.0; HRMS-ESI $[M + H]^+$ Calcd for $C_{32}H_{27}ClNO_3$ 508.1679, found 508.1658.

***trans*-3-Benzoyl-2-(4-chlorophenyl)-4-[2-oxo-2-(*p*-tolyl)-ethyl]-3,4-dihydroisoquinolin-1(2*H*)-one (*trans*-2g).** White solid (79 mg, 80%): mp 219−221 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29−8.25 (m, 3H), 7.95 (d, J = 8.1 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.44−7.39 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.02−7.01 (m, 1H), 5.79 (d, J = 1.0 Hz, 1H), 4.13−3.94 (m, 2H), 3.35 (dd, J_1 = 18.3 Hz, J_2 = 2.8 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 195.6, 164.9, 145.2, 141.0, 137.5, 134.1, 133.7, 133.6, 132.6, 129.7, 129.3, 129.2, 129.1, 129.0, 128.9, 128.3, 128.2, 126.6, 68.3, 43.7, 37.8, 21.7; HRMS-ESI $[M + H]^+$ Calcd for $C_{31}H_{25}ClNO_3$ 494.1523, found 494.1507.

***trans*-Ethyl 1-Oxo-4-(2-oxo-2-phenylethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (*trans*-2h).** White gum (65 mg, 79%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, J_1 = 7.7 Hz, J_2 = 0.7 Hz, 1H), 7.96−7.94 (m, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.49−7.25 (m, 10H), 4.82 (d, J = 1.8 Hz, 1H), 4.25−4.22 (m, 1H), 4.14−4.09 (m, 2H), 3.70 (dd, J_1 = 17.9 Hz, J_2 = 9.2 Hz, 1H), 3.43 (dd, J_1 = 17.9 Hz, J_2 = 4.7 Hz, 1H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 170.5, 163.9, 142.2, 138.7, 136.4, 133.7, 132.6, 129.2, 129.0, 128.8, 128.2, 128.1, 127.1, 126.6, 65.8, 61.9, 43.0, 37.4, 14.0; HRMS-ESI $[M + H]^+$ Calcd for $C_{26}H_{24}NO_4$ 414.1705, found 414.1685.

***trans*-Ethyl 2-Butyl-1-oxo-4-(2-oxo-2-phenylethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (*trans*-2i).** White gum (46 mg, 58%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 7.7 Hz, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.47−7.35 (m, 4H), 7.20 (d, J = 7.3 Hz, 1H), 4.42 (d, J = 1.3 Hz, 1H), 4.17−4.07 (m, 4H), 3.48 (dd, J_1 = 18.0 Hz, J_2 = 9.8 Hz, 1H), 3.19 (dd, J_1 = 18.0 Hz, J_2 = 4.2 Hz, 1H), 2.95−2.90 (m, 1H), 1.43−1.39 (m, 2H), 1.31−1.26 (m, 2H), 1.11 (t, J = 7.2 Hz, 3H), 0.76 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 170.6, 164.2, 138.5, 136.4, 133.6, 132.2, 128.8, 128.5, 128.0, 127.9, 126.9, 61.8, 61.7, 46.8, 42.7, 36.6, 30.0, 20.2, 14.0, 13.6; HRMS-ESI $[M + H]^+$ Calcd for $C_{24}H_{28}NO_4$ 394.2018, found 394.2001.

***trans*-2,5-Diphenyl-1,4a,5,10b-tetrahydrophenanthridine-4,6-dione (*trans*-3a).** White solid (19 mg, 25%): mp 223−225 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 1H), 7.60−7.56 (m, 4H), 7.49−7.37 (m, 7H), 7.30 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 6.40 (d, J = 2.6 Hz, 1H), 4.74 (d, J = 4.9 Hz, 1H), 4.33 (s, 1H), 3.70 (d, J = 18.3 Hz, 1H), 3.44 (d, J = 18.3 Hz 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 163.2, 155.9, 142.4, 137.9, 136.7, 132.3, 130.7, 130.6, 129.7, 129.0, 128.9, 127.9, 126.8, 126.7, 126.1, 125.6, 123.3, 67.9, 39.1, 30.1; HRMS-ESI $[M + H]^+$ Calcd for $C_{25}H_{20}NO_2$ 366.1494, found 366.1488.

Typical Procedure for Synthesis of 4. To a solution of *ortho*-(3-hydroxyalkynyl)benzamide (0.2 mmol) in CH_3CN (2 mL) was added DBU (5 equiv) at room temperature. Then the reaction mixture was warmed to 75 °C and stirred until the reaction was completed (monitored by TLC). After evaporation of reaction solvent, chromatography on silica gel (eluent: EtOAc/petroleum ether = 2/1) afforded **4**.

***(E)*-2-Phenyl-4-(1-propenyl)isoquinolin-1(2*H*)-one (4a).** White solid (37 mg, 70%): mp 121−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (dd, J_1 = 8.0 Hz, J_2 = 0.6 Hz, 1H), 7.79−7.72 (m, 2H), 7.57−7.42 (m, 6H), 7.24 (s, 1H), 6.63 (d, J = 15.3 Hz, 1H), 6.03 (dq, J_1 = 15.3 Hz, J_2 = 6.6 Hz, 1H), 1.93 (dd, J_1 = 6.6 Hz, J_2 = 1.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 141.4, 136.2, 132.4, 129.3, 128.8, 128.7, 128.1, 127.1, 126.9, 126.0, 124.3, 123.2, 116.3, 18.5; HRMS-ESI $[M + H]^+$ Calcd for $C_{18}H_{16}NO$ 262.1232, found 262.1231.

***(E)*-4-(1-Propenyl)-2-(*p*-tolyl)isoquinolin-1(2*H*)-one (4b).** Yellow solid (38 mg, 69%): mp 119−121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 7.78−7.70 (m, 2H), 7.56−7.53 (m, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.22 (s, 1H), 6.63 (d, J = 15.3 Hz, 1H), 6.02 (dq, J_1 = 15.3 Hz, J_2 = 6.6 Hz, 1H), 2.44 (s, 3H), 1.92 (dd, J_1 = 6.6 Hz, J_2 = 1.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 138.9, 138.0, 136.2, 132.3, 129.8, 129.0, 128.7, 128.0, 127.0, 126.6, 126.0, 124.4, 123.1, 116.1, 21.1, 18.5; HRMS-ESI $[M + H]^+$ Calcd for $C_{19}H_{18}NO$ 276.1388, found 276.1381.

***(E)*-2-(4-Chlorophenyl)-4-(1-propenyl)isoquinolin-1(2*H*)-one (4c).** White solid (46 mg, 78%): mp 129−131 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 7.6 Hz, 1H), 7.78−7.72 (m, 2H), 7.56 (dt, J_1 = 7.5 Hz, J_2 = 1.3 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 7.18 (s, 1H), 6.62 (d, J = 15.3 Hz, 1H), 6.03 (dq, J_1 = 15.3 Hz, J_2 = 6.6 Hz, 1H), 1.93 (dd, J_1 = 6.6 Hz, J_2 = 1.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 139.8, 136.1, 133.9, 132.6, 129.4, 128.7, 128.4, 128.3, 128.2, 127.3, 125.9, 124.2, 123.3, 116.7, 18.5; HRMS-ESI $[M + H]^+$ Calcd for $C_{18}H_{15}ClNO$ 296.0842, found 296.0838.

***(E)*-2-(2-Chlorophenyl)-4-(1-propenyl)isoquinolin-1(2*H*)-one (4d).** White solid (51 mg, 86%): mp 130−132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 7.80−7.72 (m, 2H), 7.60−7.54 (m, 2H), 7.46−7.41 (m, 3H), 7.05 (s, 1H), 6.63 (d, J = 15.3 Hz, 1H), 6.03 (dq, J_1 = 15.3 Hz, J_2 = 6.6 Hz, 1H), 1.92 (dd, J_1 = 6.6 Hz, J_2 = 1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 138.8, 136.4, 132.6, 132.2, 130.5, 130.0, 129.7, 128.7, 128.4, 128.3, 127.9, 127.1, 125.9, 124.2, 123.4, 116.5, 18.5; HRMS-ESI $[M + H]^+$ Calcd for $C_{18}H_{15}ClNO$ 296.0842, found 296.0831.

2-Phenyl-4-vinylisoquinolin-1(2*H*)-one (4e). Yellow solid (21 mg, 42%): mp 89−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 7.8 Hz, 1H), 7.79−7.73 (m, 2H), 7.59−7.52 (m, 3H), 7.49−7.43 (m, 3H), 7.34 (s, 1H), 6.99 (dd, J_1 = 17.3 Hz, J_2 = 10.8 Hz, 1H), 5.59 (dd, J_1 = 17.3 Hz, J_2 = 1.1 Hz, 1H), 5.35 (dd, J_1 = 10.8 Hz, J_2 = 1.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 141.3, 135.8, 132.6, 130.8, 129.3, 128.8, 128.2, 127.2, 126.9, 126.0, 123.0, 116.2, 116.0; HRMS-ESI $[M + H]^+$ Calcd for $C_{17}H_{14}NO$ 248.1075, found 248.1069.

***(E)*-4-(1-Pentenyl)-2-phenylisoquinolin-1(2*H*)-one (4f).** Yellow solid (37 mg, 64%): mp 89−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 7.79−7.72 (m, 2H), 7.58−7.43 (m, 6H), 7.25 (s, 1H), 6.62 (d, J = 15.4 Hz, 1H), 6.02 (dt, J_1 = 15.4 Hz, J_2 = 6.9 Hz, 1H), 2.24 (dq, J_1 = 6.9 Hz, J_2 = 1.3 Hz, 2H), 1.57−1.50 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 141.4, 136.2, 133.4, 132.4, 129.3, 128.7, 128.1, 127.1, 126.9, 126.0, 123.2, 116.3, 35.1, 22.5, 13.7; HRMS-ESI $[M + H]^+$ Calcd for $C_{20}H_{20}NO$ 290.1545, found 290.1538.

***(E)*-4-(1-Pentenyl)-2-(*p*-tolyl)isoquinolin-1(2*H*)-one (4g).** Yellow solid (33 mg, 55%): mp 88−90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 7.78−7.71 (m, 2H), 7.55 (dt, J_1 = 7.5 Hz, J_2 = 1.1 Hz, 1H), 7.35 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.23 (s, 1H), 6.62 (d, J = 15.4 Hz, 1H), 6.00 (dt, J_1 = 15.4 Hz, J_2 = 6.9 Hz, 1H), 2.44 (s, 3H), 2.24 (dq, J_1 = 6.9 Hz, J_2 = 1.2 Hz, 2H), 1.56−1.49 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 138.9, 138.0, 136.2, 133.3, 132.3, 129.9, 129.0, 128.7, 127.0, 126.6, 126.0 123.3, 123.1, 116.1, 35.1, 22.5, 21.1, 13.7; HRMS-ESI $[M + H]^+$ Calcd for $C_{21}H_{22}NO$ 304.1701, found 304.1699.

***(E)*-2-(4-Chlorophenyl)-4-(1-pentenyl)isoquinolin-1(2*H*)-one (4h).** White solid (43 mg, 66%): mp 99−101 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 7.8 Hz, 1H), 7.78−7.72 (m, 2H), 7.56 (t, J = 7.0 Hz, 1H), 7.49 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.19 (s, 1H), 6.60 (d, J = 15.4 Hz, 1H), 6.02 (dt, J_1 = 15.4 Hz, J_2 = 6.9 Hz, 1H), 2.24 (dq, J_1 = 7.0 Hz, J_2 = 1.2 Hz, 2H), 1.57−1.50 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 139.8, 136.2, 133.9, 133.7, 132.6, 129.4, 128.7, 128.3, 128.2, 127.3, 125.9, 123.3, 123.1, 116.7, 35.1, 22.5, 13.7; HRMS-ESI $[M + H]^+$ Calcd for $C_{20}H_{19}ClNO$ 324.1155, found 324.1145.

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(*E*)-2-Phenyl-4-(3-phenyl-1-propenyl)isoquinolin-1(2*H*)-one (4i). Yellow solid (11 mg, 16%): mp 158−160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 7.78−7.73 (m, 2H), 7.58−7.42 (m, 6H), 7.34 (t, J = 7.4 Hz, 2H), 7.28−7.24 (m, 4H), 6.70 (d, J = 15.3 Hz, 1H), 6.18 (dt, J_1 = 15.3 Hz, J_2 = 6.8 Hz, 1H), 3.60 (d, J = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 141.4, 139.8, 136.1, 132.4, 131.6, 129.2, 129.0, 128.7, 128.6, 128.5, 128.1, 127.1, 126.9, 126.3, 126.1, 124.4, 123.1, 115.7, 39.4; HRMS-ESI $[M + H]^+$ Calcd for $C_{24}H_{20}NO$ 338.1545, found 338.1532.

4-Cinnamyl-2-phenylisoquinolin-1(2*H*)-one (4i′). Yellow solid (23 mg, 34%): mp 169−171 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J = 8.0 Hz, 1H), 7.77−7.72 (m, 2H), 7.58−7.41 (m, 6H), 7.36 (d, J = 7.4 Hz, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.11 (s, 1H), 6.55 (d, J = 15.9 Hz, 1H), 6.41 (dt, J_1 = 15.9 Hz, J_2 = 6.4 Hz, 1H), 3.65 (d, J = 6.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 141.4, 137.1, 136.7, 132.5, 132.2, 130.5, 129.3, 128.8, 128.5, 128.0, 127.4, 127.3, 127.1, 126.9, 126.7, 126.2, 123.2, 114.5, 32.9; HRMS-ESI $[M + H]^+$ Calcd for $C_{24}H_{20}NO$ 338.1545, found 338.1528.

Typical Procedure for Synthesis of 5a. To a solution of *trans*-3-benzoyl-4-(2-oxo-2-phenylethyl)-2-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one **2a** (80 mg, 0.18 mmol) in CH_3COOH (2 mL) was added NH_4OAc (40 equiv) at room temperature. Then the reaction mixture was refluxed for 48 h. After it cooled, saturated aqueous NaCl was added, extracted with ethyl acetate, and dried over anhydrous $MgSO_4$. After evaporation of solvent, chromatography on silica gel (eluent: EtOAc/petroleum ether = 3/1) afforded **5a** in 60% yield.

2,4,5-Triphenylbenzo[*c*][1,7]naphthyridin-6(5*H*)-one (5a). White solid (46 mg, 60%): mp 260−262 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, J_1 = 7.9 Hz, J_2 = 0.9 Hz, 1H), 8.53 (d, J = 8.1 Hz, 1H), 8.49 (s, 1H), 8.17−8.16 (m, 2H), 7.93 (t, J = 7.3 Hz, 1H), 7.78 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.44 (t, J = 7.3 Hz, 1H), 7.18−7.02 (m, 8H), 6.97−6.96 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 151.1, 150.6, 141.0, 140.2, 138.6, 133.3, 132.7, 132.3, 130.4, 129.5, 129.3, 129.2, 128.8, 128.7, 128.2, 127.6, 127.5, 127.4, 127.0, 126.8, 122.6, 110.4; HRMS-ESI $[M + H]^+$ Calcd for $C_{30}H_{21}N_2O$ 425.1654, found 425.1653.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR and NOESY spectra of selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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