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Water-Promoted Regiospecific Azidolysis and Copper-Catalyzed Azide−Alkyne Cycloaddition: One-Pot Synthesis of 3-Hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-triazol-1-yl)methyl]indolin-2-ones

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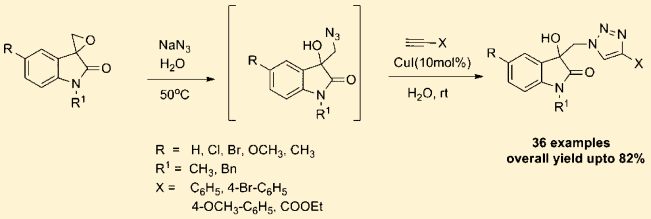
Supporting Information

ABSTRACT: An efficient, eco-friendly, base free, one-pot, sequential protocol was developed for epoxide azidolysis and copper-catalyzed azide−alkyne cycloaddition using water as the solvent for the synthesis of 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-triazol-1-yl)methyl]indolin-2-ones. The optimized reaction conditions have been generalized in the case of aromatic as well as aliphatic alkyne partners to afford good yields and high regioselectivity.



INTRODUCTION

3-Substituted indolin-2-ones such as convolutamydines, diazonamide A, leptosin D, 3-hydroxyglucoisatisin, witindolinone C, TMC-95, celogentin K, and dioxibrassinine as well as several other biologically active compounds are widely found in nature and have demonstrated diverse biological properties.[1] Few natural products containing the 3-hydroxyoxindole scaffold are illustrated in Figure 1. The activity of these molecules mainly resides in the substitution at the C-3 quaternary center. Kumar et al. established the antimalarial, antitubercular, and antiprotozoal activity of 1*H*-1,2,3-triazole tethered with oxindole.[1d−f] Copper-catalyzed azide−alkyne cycloaddition (CuAAC) and Huisgen cycloaddition are two of the most important methods for the formation of 1,4-disubstituted 1,2,3-triazoles[2] with high efficiency, regioselectivity, and excellent atom economy. These molecules exhibit interesting biological properties[3] and have found numerous applications in various fields like bioconjugation,[4] dendrimer synthesis,[5] surface science,[6] combinatorial organic synthesis,[7] as well as material science.[8]

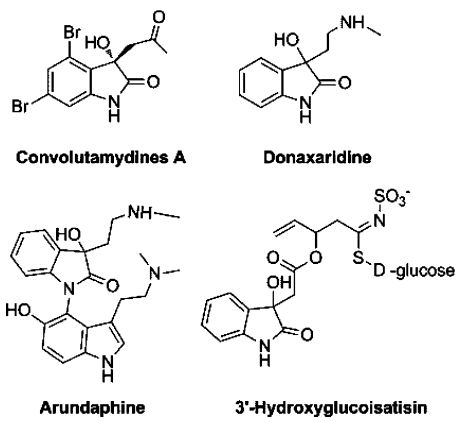


Figure 1. Natural products containing a 3-hydroxyoxindole scaffold.

Examination of the literature provides various synthetic modifications employing different metals such as Zn,[9] Ni,[10] Ag,[11] Ru,[12] Ir,[13] and ligands[14] to protect the metal center from disproportionation and oxidation, different copper salts on solid supports,[15] and even without the use of copper.[16] Recently, transition-metal nanoparticles were found to serve as efficient catalysts for the synthesis of this privileged scaffold.[17] Furthermore, one-pot multicomponent reactions have proven their utility for regioselective triazole synthesis.[18]

Despite the wide applicability, the available methods have limitations such as presynthesis of the metal complex, long reaction time, moderate yields, use of air- and moisture-sensitive reagents or catalysts, and lack of cost effectiveness, which provide sufficient scope for the development of better conditions. In continuation of our investigations on 3-substituted indolin-2-ones,[19,20] efforts were mainly focused on the development of an ecofriendly one-pot sequential protocol for epoxide azidolysis and copper-catalyzed cycloaddition reaction using water as the reaction medium. The developed protocol afforded 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-

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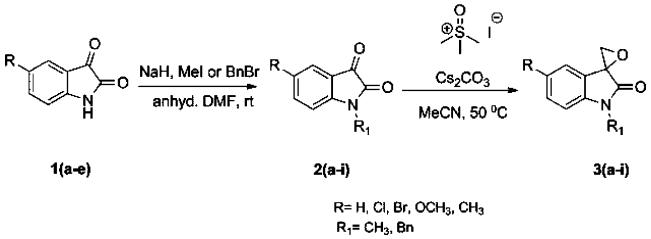
triazol-1-yl)methyl]indolin-2-ones with excellent yields and regioselectivity in a short span of time.

RESULTS AND DISCUSSION

The required oxirane derivatives were prepared as illustrated in Scheme 1. *N*-Alkyl derivatives were synthesized by treating

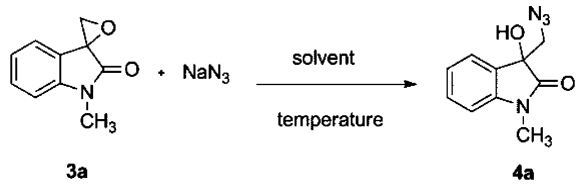
Scheme 1. Synthesis of 3-Epoxyindolin-2-ones



isatins with NaH and then reacting them with methyl iodide or benzyl bromide in dry DMF at room temperature. Construction of the epoxy ring at the C-3 position of isatin derivatives was realized by a Corey–Chakovsky reaction using trimethylsulfoxonium iodide and cesium carbonate in acetonitrile solvent at 50 °C to afford a good yield of 3-epoxyindolin-2-ones.

Based on our previous work on water-promoted epoxide aminolysis,[21] we decided to apply a similar strategy for the synthesis of the azide partner required for azide–alkyne cycloaddition reaction. For a detailed investigation, a model reaction was performed with 1-methylspiro[indoline-3,2′-oxiran]-2-one (**3a**) and sodium azide in different solvents at room temperature, as illustrated in Scheme 2. Solvents like

Scheme 2. Azidolysis of the 3-Epoxyindolin-2-one



cyclohexane, toluene, DMF, DMSO, DCM, 1,4-dioxane, and THF did not afford the product (Table 1), while an improvement was observed with polar solvents. We envisaged that this may be due to the better solubility of the sodium azide in polar medium, which serves as a nucleophile for opening of the oxirane ring.

To evaluate our assumption, we used water as the reaction medium, which afforded 65% of the desired product at room temperature, indicating an enhancement in the reaction rate. Even then the reaction was slow, consuming 12 h for completion. A separate study demonstrated a drastic rate enhancement at 50 °C, attaining completion in 0.75 h to afford 92% yield with a regiospecific oxirane ring opening from the less hindered end. A further increase in temperature did not improve the yield of the reaction. From the above observation, we inferred that reacting 1.0 equiv of 1-methylspiro[indoline-3,2′-oxiran]-2-one and 1.2 equiv of sodium azide in water at 50 °C would be the most suitable conditions for the reaction. The synthesized 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one was used in the copper-catalyzed azide–alkyne cycloaddition reaction. To investigate the reaction in detail, a model reaction

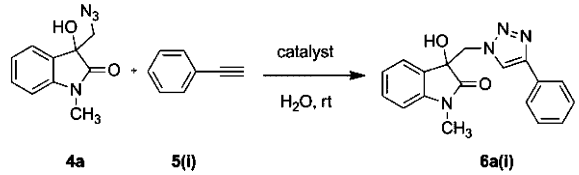
Table 1. Effect of Solvents on Azidolysis of the Oxirane Ring[a]

entry	solvent	time (h)	yield[b] (%)
1	cyclohexane	8	
2	toluene	8	
3	DMF	8	
4	DMSO	8	
5	DCM	8	
6	1,4-dioxane	8	
7	THF	8	
8	EtOH	4	42
9	EtOH[c]	2	60
10	H_2O	12	65
11	H_2O[c]	0.75	92
12	H_2O[d]	0.75	93
13	H_2O[e]	0.75	92

[a]Reaction conditions: 1-methylspiro[indolin-3,2′-oxiran]-2-one (1.0 equiv), sodium azide (1.2 equiv), 30 °C. [b]Isolated yield. [c]Temperature: 50 °C. [d]Temperature: 70 °C. [e]Temperature: 90 °C.

of phenylacetylene **5(i)** and 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one (**4a**) was performed in the presence of different copper salts using water as solvent at room temperature (Scheme 3).

Scheme 3. Catalytic Azide–Alkyne Cycloaddition Reaction



From the different copper salts employed, it was inferred that CuI provided maximum yields of the product, in a short reaction time, at an optimum catalyst concentration of 10 mol % compared with CuCl and CuBr, which provided inferior results (Table 2).

Table 2. Effect of Different Copper Salts on Azide–Alkyne Cycloaddition Reaction[a]

entry	catalyst (10 mol %)	time (h)	yield[b] (%)
1	CuBr	4.5	82
2	$Cu(OAc)_2$	4.0	84
3	CuCl(I)	3.0	87
4	CuCl(II)	3.5	78
5	CuO	5.0	68
6	CuI	0.5	90

[a]Reaction condition: 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one (1.0 equiv), phenylacetylene (1.2 equiv), water (3 mL), 30 °C. [b]Isolated yield.

The effect of the solvent, as a reaction variable was also evaluated. In the case of nonpolar solvents like cyclohexane and toluene, the reaction afforded unsatisfactory results compared to aprotic solvents like THF, DCM, acetonitrile, and chloroform (Table 3). Protic polar solvents like EtOH and ^{t}BuOH afforded better yields. However, water was found to significantly enhance the reaction rate to afford the best yields of the desired product in 0.5 h.

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Table 3. Effect of Solvent on Copper-Catalyzed Azide–Alkyne Cycloaddition Reaction[a]

entry	solvent	time (h)	yield[b] (%)
1	toluene	5	46
2	cyclohexane	5	52
3	chloroform	5	65
4	THF	5	72
5	DCM	5	67
6	acetonitrile	5	78
7	EtOH	5	80
8	^{t}BuOH	5	82
9	H_2O	0.5	90

[a]Reaction condition: 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one (1.0 equiv), phenylacetylene (1.2 equiv), CuI (0.1 equiv), 30 °C. [b]Isolated yield.

To evaluate the prospect of both reactions sequentially, azidolysis of the oxirane ring and copper-catalyzed cycloaddition reaction were performed in one pot without isolating the intermediate 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one derivative. A model reaction employing 1.0 equiv of 1-methylspiro[indolin-3,2′-oxiran]-2-one (**3a**) and 1.2 equiv of sodium azide in water as solvent was heated at 50 °C for 0.75 h. The completion of the azidolysis was monitored by TLC analysis. Thereafter, the reaction temperature was allowed to attain room temperature and to this reaction mixture was added 0.1 equiv of CuI and 1.2 equiv of phenylacetylene **5(i)** without isolating the 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one (**4a**).

The reaction mixture was then allowed to stir at room temperature for another 0.5 h. The progress of the reaction was followed by TLC analysis. To our satisfaction, the reaction afforded the desired 3-hydroxy-1-methyl-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one **6a(i)** with 82% yield (Table 4, entry 1). The scope of the optimized one-pot protocol was further extended to different 3-epoxyindolin-2-ones and phenylacetylene derivatives bearing both electron-withdrawing and -donating groups. The reaction afforded the desired 1,4-disubstituted 1,2,3-triazole derivatives (Scheme 4) in good to excellent yields (Table 4). The optimized conditions were further extended to alkyne variants such as ethyl propiolate and 3-epoxyindolin-2-ones (Scheme 5) and found to afford the products in reasonably good yields (Table 5). To account for the regioselective formation of 1,4-disubstituted 1,2,3-triazole by azidolysis and azide–alkyne cycloaddition reaction, we propose a plausible mechanism (Figure 2).

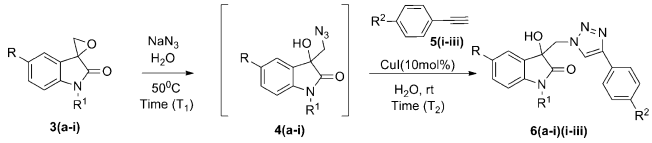
In the azidolysis reaction, water can be envisioned to activate the reactant by hydrogen bonding, thereby enhancing the electrophilicity of the oxirane ring to overcome the energy barrier to facilitate a nucleophilic attack by the azide. The azide would attack the least hindered end of the oxirane ring to provide high regioselectivity for the reaction. Further, in the azide–alkyne cycloaddition reaction also, water would activate the substrate to form intermediate I, which coordinates with the copper salt to afford intermediate II. Thereafter, the alkyne coordinates to copper via a π-complex and subsequently generates the intermediate III. The terminal nitrogen N1 attacks the alkyne via a six-membered cyclic transition state to form the intermediate IV. Finally, a reductive elimination yields the intermediate V, which affords the desired 1,4-disubstituted 1,2,3-triazole, regenerating the copper catalyst for another catalytic cycle.

Table 4. Generalization of Optimized Conditions for One-Pot Epoxide Azidolysis and Azide–Alkyne Cycloaddition Reaction[a]

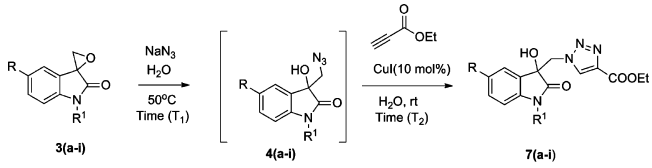
entry	R	R_1	R_2	time (T_1/T_2)(h)	product	yield[b] (%)
1	H	Me	H	0.75/0.5	**6a(i)**	82
2	H	Me	Br	0.75/1.5	**6a(ii)**	76
3	H	Me	OMe	0.75/1.0	**6a(iii)**	79
4	H	Bn	H	1.5/1.0	**6b(i)**	78
5	H	Bn	Br	1.5/2.0	**6b(ii)**	72
6	H	Bn	OMe	1.5/1.5	**6b(iii)**	76
7	Cl	Me	H	1.5/1.5	**6c(i)**	77
8	Cl	Me	Br	1.5/2.0	**6c(ii)**	75
9	Cl	Me	OMe	1.5/1.5	**6c(iii)**	78
10	Cl	Bn	H	2.5/1.5	**6d(i)**	76
11	Cl	Bn	Br	2.5/2.0	**6d(ii)**	70
12	Cl	Bn	OMe	2.5/1.5	**6d(iii)**	73
13	Br	Me	H	1.5/1.5	**6e(i)**	80
14	Br	Me	Br	1.5/2.0	**6e(ii)**	76
15	Br	Me	OMe	1.5/1.5	**6e(iii)**	78
16	Br	Bn	H	3.0/1.5	**6f(i)**	76
17	Br	Bn	Br	3.0/2.5	**6f(ii)**	72
18	Br	Bn	OMe	3.0/1.5	**6f(iii)**	69
19	OMe	Me	H	1.5/1.0	**6g(i)**	78
20	OMe	Me	Br	1.5/1.5	**6g(ii)**	73
21	OMe	Me	OMe	1.5/1.0	**6g(iii)**	75
22	Me	Me	H	2.5/1.0	**6h(i)**	75
23	Me	Me	Br	2.5/1.5	**6h(ii)**	72
24	Me	Me	OMe	2.5/1.0	**6h(iii)**	74
25	Me	Bn	H	3.0/1.5	**6i(i)**	78
26	Me	Bn	Br	3.0/2.0	**6i(ii)**	73
27	Me	Bn	OMe	3.0/1.5	**6i(iii)**	75

[a]Reaction conditions: 3-epoxyindolin-2-one (1.0 equiv), sodium azide (1.2 equiv), phenylacetylene (1.2 equiv), CuI (0.1 equiv), 30 °C. [b]Overall isolated yield, T_1 = time for epoxide azidolysis, T_2 = time for CuAAC reaction.

Scheme 4. One-Pot Azidolysis and Cycloaddition Reactions with Arylacetylenes



Scheme 5. One-Pot Azidolysis and Cycloaddition Reactions with Alkynes



To conclude, an eco-friendly, one-pot sequential protocol was developed for epoxide azidolysis and copper-catalyzed azide–alkyne cycloaddition using water as the reaction medium. The developed protocol demonstrated regioselectivity in both azidolysis of oxirane derivatives and CuAAC reactions where opening of the oxirane ring from the less substituted end followed by regioselective formation of 1,4-disubstituted 1,2,3-triazole was observed. The optimized reaction conditions were extended to obtain 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-

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Table 5. Generalization of Optimized Conditions of One-Pot Azidolysis and Azide−Alkyne Cycloaddition Reactions[a]

entry	R	R_1	time (T_1/T_2)(h)	product	yield[b](%)
1	H	Me	0.75/1.0	**7a**	78
2	H	Bn	1.5/2.5	**7b**	72
3	Cl	Me	1.5/1.5	**7c**	76
4	Cl	Bn	2.5/3.0	**7d**	68
5	Br	Me	1.5/1.5	**7e**	73
6	Br	Bn	3.0/4.0	**7f**	66
7	OMe	Me	1.5/1.5	**7g**	76
8	Me	Me	2.5/1.5	**7h**	74
9	Me	Bn	3.0/2.5	**7i**	69

[a]Reaction conditions: 3-epoxyindolin-2-one (1.0 equiv), sodium azide (1.2 equiv), ethyl propiolate (1.2 equiv), CuI (0.1 equiv), 30 °C. [b]Overall isolated yield, T_1 = time for epoxide azidolysis, T_2 = time for CuAAC reaction.

triazol-1-yl)methyl]indolin-2-one derivatives with good to excellent yields. The present method has advantages over previously reported methods such as an environmentally benign protocol, catalytic use of readily available and inexpensive CuI, simplicity of the reaction conditions, base free, and short reaction times with high regioselectivity.

EXPERIMENTAL SECTION

The ^{1}H NMR and ^{13}C NMR spectra were recorded in deuteriated solvent ($CDCl_3$/DMSO) using TMS as the internal standard. The chemical shifts (δ) are given in ppm relative to residual signal of the solvents. Coupling constants are given in hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, double doublet; brs, broad singlet signal. HRMS spectra were recorded on a Bruker Maxix TOF spectrometer. Melting points were recorded and uncorrected. All of the starting materials [isatin, 5-chloro isatin, 5-bromo isatin, 5-methoxy isatin, 5-methyl isatin], benzyl bromide, methyl iodide, trimethylsulfoxonium iodide, phenylacetylene, 4-bromophenylacetylene, 4-methoxyphenylacetylene, ethylpropiolate, copper iodide, and cesium−carbonate were purchased from commercial sources and used as such without further purification.

Typical Procedure for Spiro[indoline-3,2′-oxiran]-2-one Formation. A mixture of trimethylsulfoxonium iodide (1.0 mmol) and cesium carbonate (2.0 mmol) in dry acetonitrile was stirred at 50 °C for 1 h under nitrogen atmosphere to generate the sulfur ylide. To this was added a solution of isatin (1.0 mmol) in dry acetonitrile (5 mL) dropwise over 10 min. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was filtered through a Celite bed, and the filtrate was evaporated to dryness. The crude product thus obtained was purified by column chromatography on silica gel (60−120 mesh) using a EtOAc/hexane (05:95) mixture as the eluent to afford the pure product.

*1-Methylspiro[indolin-3,2′-oxiran]-2-one (**3a**):* pale yellow solid; mp 84−86 °C; yield 0.13 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.37 (m, 1H), 7.13−7.07 (m, 2H), 6.93 (d, 1H, J = 7.8 Hz), 3.59

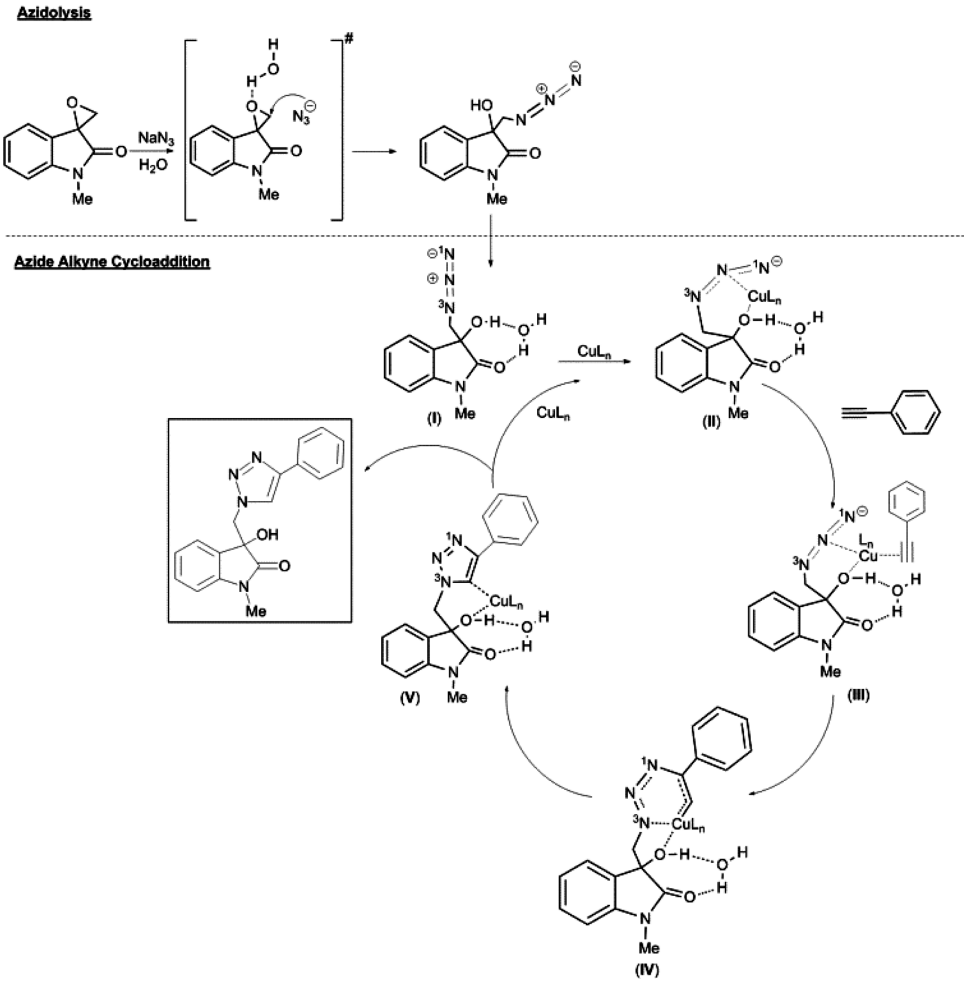

Figure 2. Plausible mechanism.

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(d, 1H, J = 6.7 Hz), 3.44 (d, 1H, J = 6.7 Hz), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.8, 145.1, 130.4, 122.9, 122.7, 122.1, 108.8, 56.4, 54.1, 26.6; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{10}H_9NNaO_2$ 198.0531, found 198.0527.

*1-Benzylspiro[indolin-3,2′-oxiran]-2-one (**3b**):* pale orange solid; mp 114−116 °C; yield 0.19 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.26 (m, 6H), 7.15−7.13 (m, 1H), 7.08−7.04 (m, 1H), 6.84 (d, 1H, J = 7.9 Hz), 4.98 (q, 2H, J = 11.4, 15.7 Hz), 3.67 (d, 1H, J = 6.7 Hz), 3.50 (d, 1H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 144.3, 135.4, 130.4, 128.9, 127.9, 127.4, 123.0, 122.7, 122.2, 109.9, 56.4, 56.3, 44.3; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{13}NNaO_2$ 274.0844, found 274.0840.

*5-Chloro-1-methylspiro[indolin-3,2′-oxiran]-2-one (**3c**):* pale yellow solid; mp 163−165 °C; yield 0.16 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40−7.37 (m, 1H), 7.11 (d, 1H, J = 2.1 Hz), 6.87 (d, 1H, J = 8.3 Hz), 3.62 (d, 1H, J = 6.7 Hz), 3.45 (d, 1H, J = 6.7 Hz), 3.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 143.6, 130.3, 128.5, 124.5, 122.6, 109.8, 56.2, 54.2, 26.8; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{10}H_8ClNNaO_2$ 232.0141, found 232.0134.

*1-Benzyl-5-chlorospiro[indolin-3,2′-oxiran]-2-one (**3d**):* brownish solid; mp 144−148 °C; yield 0.20 g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.31 (m, 5H), 7.26−7.24 (m, 1H), 7.12 (d, 1H, J = 2.1 Hz), 6.74 (d, 1H, J = 8.4 Hz), 4.98 (q, 2H, J = 5.7, 15.7 Hz), 3.69 (d, 1H, J = 6.7 Hz), 3.49 (d, 1H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 142.7, 134.9, 130.2, 129.0, 128.6, 128.0, 127.4, 124.5, 122.7, 110.9, 56.2, 54.5, 44.4; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{12}ClNNaO_2$ 308.0454, found 308.0446.

*5-Bromo-1-methylspiro[indolin-3,2′-oxiran]-2-one (**3e**):* brownish solid; mp 167−169 °C; yield 0.19 g, 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55−7.52 (m, 1H), 7.29−7.24 (m, 1H), 6.83 (d, 1H, J = 8.3 Hz), 3.61 (d, 1H, J = 6.6 Hz), 3.45 (d, 1H, J = 6.7 Hz), 3.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 144.1, 133.2, 125.4, 124.8, 115.6, 110.3, 56.0, 54.2, 26.8; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{10}H_8BrNNaO_2$ 275.9636, found 275.9623.

*1-Benzyl-5-bromospiro[indolin-3,2′-oxiran]-2-one (**3f**):* reddish solid; mp 150−152 °C; yield 0.23 g, 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.28 (m, 6H), 7.25 (d, 1H, J = 1.9 Hz), 6.70 (d, 1H, J = 8.3 Hz), 4.98 (q, 2H, J = 4.8, 15.7 Hz), 3.68 (d, 1H, J = 6.7 Hz), 3.49 (d, 1H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 143.2, 134.8, 133.1, 129.0, 128.0, 127.4, 125.5, 124.9, 115.7, 111.4, 56.0, 54.5, 44.4; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{12}BrNNaO_2$ 351.9949, found 351.9918.

*5-Methoxy-1-methylspiro[indolin-3,2′-oxiran]-2-one (**3g**):* brownish solid; mp 144−146 °C; yield 0.14 g, 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.93 (dd, 1H, J = 2.5, 6.0 Hz), 6.85 (d, 1H, J = 8.5), 6.74 (d, 1H, J = 2.5 Hz), 3.81 (s, 3H), 3.60 (d, 1H, J = 6.7 Hz), 3.43 (d, 1H, J = 6.7 Hz), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.5, 156.3, 138.4, 124.0, 115.1, 109.4, 109.1, 56.7, 55.9, 54.2, 26.7; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{11}H_{11}NNaO_3$ 228.0637, found 228.0638.

*1,5-Dimethylspiro[indolin-3,2′-oxiran]-2-one (**3h**):* brownish solid; mp 118−120 °C; yield 0.13 g, 68%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, 1H, J = 0.9 Hz), 6.95−6.94 (m, 1H), 6.83 (d, 1H, J = 7.9 Hz), 3.59 (d, 1H, J = 6.7 Hz), 3.43 (d, 1H, J = 6.7 Hz), 3.28 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 142.7, 132.6, 130.6, 122.8, 122.7, 108.6, 56.5, 54.0, 26.7, 21.0; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{11}H_{11}NNaO_2$ 212.0687, found 212.0681.

*1-Benzyl-5-methylspiro[indolin-3,2′-oxiran]-2-one (**3i**):* white solid; mp 148−150 °C; yield 0.17 g, 65%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.28 (m, 5H), 7.09−7.07 (m, 1H), 6.96 (s, 1H), 6.72 (d, 1H, J = 8.0 Hz), 4.97 (q, 2H, J = 7.9, 15.6 Hz), 3.67 (d, 1H, J = 6.7 Hz), 3.48 (d, 1H, J = 6.7 Hz), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 141.9, 135.4, 132.6, 130.6, 128.8, 127.8, 127.4, 122.9, 122.7, 109.7, 56.4, 54.2, 44.3, 20.9; ESI-HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{15}NNaO_2$ 288.1000, found 288.0993.

Typical Procedure for Synthesis of 3-Hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-triazol-1-yl)methyl]indolin-2-one Derivatives. A mixture of oxindole oxirane (1.0 mmol) and sodium azide (1.2 mmol) was stirred in water at 50 °C. The progress of reaction was monitored by TLC. After complete consumption of oxirane, the reaction mixture was cooled to room temperature, and to this were added CuI (10 mol %) and phenyl acetylene/ethylpropiolate (1.2 mmol). After completion, the reaction mixture was washed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, washed with brine, and evaporated under reduced pressure to dryness. The crude product thus obtained was purified by column chromatography on activated silica gel (60−120 mesh) using dichloromethane/methanol (99:01) solvent mixture as the eluent to afford the pure product.

*3-Hydroxy-1-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-indolin-2-one [**6a(i)**]:* white solid; mp 156−158 °C; yield 0.26 g, 82%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (s, 1H), 7.86−7.84 (m, 2H), 7.46−7.43 (m, 2H), 7.38−7.33 (m, 2H), 7.04−7.02 (m, 1H), 6.85−6.78 (m, 2H), 4.83 (d, 1H, J = 14.2 Hz), 4.74 (d, 1H, J = 14.2 Hz), 4.04 (brs, 1H), 3.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 147.7, 143.0, 130.8, 130.3, 128.9, 128.3, 126.7, 125.8, 124.6, 123.8, 121.5, 108.9, 75.2, 55.4, 26.5; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{17}N_4O_2$ 321.1352, found 321.1338.

*3-((4-(4-Bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1-methylindolin-2-one [**6a(ii)**]:* white solid; mp 167−169 °C; yield 0.30 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (s, 1H), 7.75−7.71 (m, 2H), 7.59−7.56 (m, 2H), 7.39−7.35(m, 1H), 7.08−7.04 (m, 1H), 6.87−6.80 (m, 2H), 4.81 (d, 1H, J = 14.2 Hz), 4.75 (d, 1H, J = 14.2 Hz), 3.60 (brs, 1H), 3.22 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.5, 145.2, 143.7, 132.3, 130.3, 128.6, 127.6, 124.7, 123.5, 122.8, 121.3, 109.2, 74.7, 55.0, 26.5; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{16}BrN_4O_2$ 399.0457, found 399.0445.

*3-Hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)-methyl)-1-methylindolin-2-one [**6a(iii)**]:* yellow solid; mp 186−188 °C; yield 0.28 g, 79%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.76 (d, 2H, J = 8.7 Hz), 7.36−7.28 (m, 1H), 7.04−7.01 (m, 1H), 6.97 (d, 2H, J = 8.7 Hz), 6.84−6.78 (m, 2H), 4.80 (d, 1H, J = 14.1 Hz), 4.71 (d, 1H, J = 14.2 Hz), 4.18 (brs, 1H), 3.86 (s, 3H), 3.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.4, 159.7, 147.5, 143.0, 130.7, 127.1, 126.8, 124.6, 123.7, 123.0, 120.7, 114.2, 108.9, 75.2, 55.3, 55.3, 26.5; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{19}N_4O_3$ 351.1457, found 351.1450.

*1-Benzyl-3-hydroxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-indolin-2-one [**6b(i)**]:* white solid; mp 169−171 °C; yield 0.31 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.83 (d, 2H, J = 7.4 Hz), 7.46−7.35 (m, 3H), 7.26−7.22 (m, 6H), 7.03 (t, 1H, J = 7.6 Hz), 6.91 (d, 1H, J = 7.4 Hz), 6.73 (d, 1H, J = 7.9 Hz), 5.00 (d, 1H, J = 15.6 Hz), 4.92 (d, 1H, J = 14.0 Hz), 4.80 (t, 2H, J = 15.6 Hz), 3.59 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.7, 146.3, 142.9, 136.3, 131.0, 130.3, 129.4, 129.0, 128.6, 128.4, 127.8, 127.5, 125.6, 125.1, 123.0, 109.9, 75.0, 54.8, 43.2; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{24}H_{21}N_4O_2$ 397.1665, found 397.1659.

*1-Benzyl-3-((4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxyindolin-2-one [**6b(ii)**]:* white solid; mp 172−174 °C; yield 0.34 g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.94 (s, 1H), 7.70−7.67 (m, 2H), 7.57−7.54 (m, 2H), 7.27−7.18 (m, 6H), 7.06−7.02 (m, 1H), 6.92−6.90 (m, 1H), 6.73 (d, 1H, J = 7.9 Hz), 5.00 (d, 1H, J = 15.7 Hz), 4.90 (d, 1H, J = 14.1 Hz), 4.80 (q, 2H, J = 9.4, 15.7 Hz), 3.74 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.3, 146.7, 142.4, 134.7, 132.0, 130.9, 129.2, 129.0, 128.0, 127.3, 127.1, 126.6, 124.7, 123.8, 122.2, 121.4, 110.1, 75.2, 55.3, 44.1; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{24}H_{20}BrN_4O_2$ 475.0770, found 475.0756.

*1-Benzyl-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)indolin-2-one [**6b(iii)**]:* yellow solid; mp 138−140 °C; yield 0.32 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (s, 1H), 7.75 (d, 2H, J = 8.8 Hz), 7.27−7.18 (m, 6H), 7.04−6.96 (m, 3H), 6.90 (d, 1H, J = 6.9 Hz), 6.71 (d, 1H, J = 7.9 Hz), 5.00 (d, 1H, J = 15.9 Hz), 4.90 (d, 1H, J = 14.1 Hz), 4.79 (q, 2H, J = 2.0, 13.6 Hz), 3.92 (brs, 1H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.3, 159.7, 142.4, 134.8, 130.8, 129.0, 127.9, 127.1, 126.7, 124.7, 123.8, 123.0, 120.5, 114.2, 110.0, 93.3, 75.2, 55.4, 55.2, 44.1; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{25}H_{23}N_4O_3$ 427.1770, found 427.1763.

*5-Chloro-3-hydroxy-1-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl indolin-2-one [**6c(i)**]:* white solid; mp 226−228 °C; yield 0.27 g, 77%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92 (s, 1H), 7.86−7.84 (m, 2H), 7.47−7.44 (m, 2H), 7.39−7.33 (m, 2H), 6.92 (d, 1H, J = 2.0

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Hz), 6.77 (d, 1H, J = 8.4 Hz), 4.81 (d, 1H, J = 14.1 Hz), 4.75 (d, 1H, J = 14.1 Hz), 3.66 (brs, 1H), 3.20 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.2, 146.3, 142.7, 130.8, 130.5, 130.1, 129.4, 128.4, 126.9, 125.6, 125.0, 123.1, 110.8, 74.9, 54.5, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{16}ClN_4O_2$, 355.0962, found 355.0956.

*3-((4-(4-Bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-5-chloro-3-hydroxy-1-methylindolin-2-one [**6c(ii)**]:* white solid; mp 218−220 °C; yield 0.32 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (m, 1H), 7.87−7.83 (m, 2H), 7.50−7.34 (m, 3H), 7.06−7.04 (m, 1H), 6.86−6.81 (m, 1H), 4.81−4.76 (m, 2H), 3.18 (s, 3H), 3.11 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 179.9, 150.0, 147.4, 137.1, 135.4, 135.0, 134.8, 132.4, 131.6, 129.7, 128.3, 126.1, 115.5, 79.6, 59.4, 31.4; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{15}BrClN_4O_2$ 433.0067, found 433.0064.

*5-Chloro-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-methylindolin-2-one [**6c(iii)**]:* white solid; mp 198−200 °C; yield 0.30 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (s, 1H), 7.75 (d, 2H, J = 8.8 Hz), 7.34−7.31 (m, 1H), 6.97 (d, 2H, J = 8.8 Hz), 6.92 (d, 1H, J = 2.0 Hz), 6.75 (d, 1H, J = 8.4 Hz), 4.79 (d, 1H, J = 14.2 Hz), 4.73 (d, 1H, J = 14.2 Hz), 3.86 (s, 3H), 3.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.7, 159.8, 147.7, 141.6, 130.7, 129.2, 128.4, 127.1, 125.2, 122.9, 120.6, 114.3, 109.9, 75.1, 60.4, 55.1, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{18}ClN_4O_3$ 385.1067, found 385.1062.

*1-Benzyl-5-chloro-3-hydroxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl)indolin-2-one [**6d(i)**]:* white solid; mp 177−179 °C; yield 0.33 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (s, 1H), 7.82−7.80 (m, 2H), 7.46−7.42 (m, 2H), 7.39−7.35 (m, 1H), 7.24−7.19 (m, 4H), 7.15−7.13 (m, 2H), 7.02 (d, 1H, J = 2.1 Hz), 6.61 (d, 1H, J = 8.4 Hz), 4.97 (d, 1H, J = 15.7 Hz), 4.87 (q, 2H, J = 11.2, 14.1 Hz), 4.73 (d, 1H, J = 15.7 Hz), 4.02 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.0, 147.8, 140.9, 134.2, 130.7, 130.1, 129.3, 129.0, 128.9, 128.4, 128.3, 128.1, 127.0, 125.8, 125.3, 121.2, 111.1, 75.2, 55.0, 44.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{24}H_{20}ClN_4O_2$ 431.1275, found 431.1270.

*1-Benzyl-3-((4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-5-chloro-3-hydroxyindolin-2-one [**6d(ii)**]:* white solid; mp 196−198 °C; yield 0.36 g, 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (s, 1H), 7.68−7.66 (m, 2H), 7.56−7.54 (m, 2H), 7.35−7.32 (m, 1H), 7.25−7.21 (m, 3H), 7.14−7.12 (m, 2H), 7.02 (d, 1H, J = 2.0 Hz), 6.64−6.60 (m, 1H), 4.96 (d, 1H, J = 15.7 Hz), 4.86 (q, 2H, J = 4.1, 14.1 Hz), 4.71 (d, 1H, J = 15.7 Hz), 4.27 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.1, 146.8, 140.8, 134.2, 132.0, 130.7, 129.3, 129.0, 128.4, 128.1, 127.3, 127.0, 125.3, 124.1, 122.3, 121.4, 111.1, 75.2, 55.1, 44.2; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{24}H_{19}BrClN_4O_2$ 509.0380, found 509.0373.

*1-Benzyl-5-chloro-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)indolin-2-one [**6d(iii)**]:* white solid; mp 198−200 °C; yield 0.34 g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (s, 1H), 7.75−7.73 (m, 2H), 7.32−7.31 (m, 1H), 7.25−7.21 (m, 3H), 7.16−7.15 (m, 2H), 7.02 (d, 1H, J = 2.0 Hz), 6.97 (d, 2H, J = 8.8 Hz), 6.61 (d, 1H, J = 8.4 Hz), 4.97 (d, 1H, J = 15.7 Hz), 4.85 (q, 2H, J = 14.0, 16.1 Hz), 4.74 (d, 1H, J = 15.7 Hz), 3.87 (s, 3H), 3.86 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.3, 159.5, 146.3, 142.2, 135.9, 132.9, 131.1, 129.0, 128.1, 127.8, 127.4, 127.0, 123.5, 122.1, 114.8, 114.8, 111.9, 75.0, 55.6, 55.3, 43.2; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{25}H_{22}ClN_4O_3$ 461.1380, found 461.1371.

*5-Bromo-3-hydroxy-1-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl)indolin-2-one [**6e(i)**]:* white solid; mp 238−240 °C; yield 0.32 g, 80%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (m, 1H), 7.87−7.83 (m, 2H), 7.50−7.34 (m, 4H), 7.06−7.04 (m, 1H), 6.86−6.81 (m, 1H), 4.81−4.76 (m, 2H), 3.18 (s, 3H), 3.11 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.1, 146.3, 143.1, 132.9, 131.0, 129.4, 128.4, 127.7, 125.6, 123.2, 114.5, 111.3, 110.0, 74.8, 54.6, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{16}BrN_4O_2$ 399.0457, found 399.0448.

*5-Bromo-3-((4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1-methylindolin-2-one [**6e(ii)**]:* white solid; mp 224−226 °C; yield 0.36 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00−7.94 (m, 1H), 7.74−7.70 (m, 2H), 7.58−7.54 (m, 2H), 7.51−7.49 (m, 1H), 7.07−7.06 (m, 1H), 6.73 (d, 1H, J = 8.3 Hz), 4.82−4.73 (m, 2H), 3.86 (brs, 1H), 3.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 146.6, 140.6, 133.5, 132.0, 131.0, 129.4, 127.3, 126.7, 125.3, 122.1, 121.6, 108.7, 75.2, 55.4, 21.1; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{15}Br_2N_4O_2$ 476.9562, found 476.9550.

*5-Bromo-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-methylindolin-2-one [**6e(iii)**]:* yellow solid; mp 166−168 °C; yield 0.33 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (s, 1H), 7.77−7.72 (m, 2H), 7.48−7.64 (m, 1H), 7.06 (d, 1H, J = 1.9 Hz), 6.98−6.94 (m, 2H), 6.69 (d, 1H, J = 8.3 Hz), 4.80−4.72 (m, 2H), 4.31 (brs, 1H), 3.86 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.8, 159.7, 147.6, 142.1, 133.5, 128.8, 128.0, 127.1, 122.8, 120.7, 116.3, 114.3, 110.4, 75.1, 55.4, 55.1, 29.7; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{18}BrN_4O_3$ 429.0562, found 429.0556.

*1-Benzyl-5-bromo-3-hydroxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl)indolin-2-one [**6f(i)**]:* white solid; mp 182−184 °C; yield 0.36 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (s, 1H), 7.82 (d, 2H, J = 7.2 Hz), 7.46−7.32 (m, 5H), 7.24−7.14 (m, 5H), 6.56 (d, 1H, J = 8.4 Hz), 4.96 (d, 1H, J = 15.7 Hz), 4.87 (q, 2H, J = 4.1, 14.1 Hz), 4.73 (d, 1H, J = 15.7 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.3, 146.4, 142.2, 135.7, 133.0, 131.0, 130.8, 129.4, 129.0, 128.5, 128.1, 127.8, 127.4, 125.6, 123.0, 114.9, 111.9, 75.0, 54.3, 43.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{24}H_{20}BrN_4O_2$ 475.0770, found 475.0768.

*1-Benzyl-5-bromo-3-((4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)-methyl)-3-hydroxyindolin-2-one [**6f(ii)**]:* white solid; mp 198−200 °C; yield 0.40 g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (s, 1H), 7.68 (d, 2H, J = 8.5 Hz), 7.57−7.55 (m, 2H), 7.36 (dd, 1H, J = 1.9, 2.0 Hz), 7.24−7.23 (m, 3H), 7.17−7.12 (m, 3H), 6.57 (d, 1H, J = 8.4 Hz), 4.96 (d, 1H, J = 15.8 Hz), 4.86 (q, 2H, J = 4.6, 14.1 Hz), 4.72 (d, 1H, J = 15.7 Hz), 4.04 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.8, 141.4, 134.2, 133.7, 132.0, 129.0, 128.6, 128.1, 128.0, 127.4, 127.0, 124.1, 122.3, 121.4, 116.5, 111.6, 75.1, 55.1, 44.2; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{24}H_{19}Br_2N_4O_2$ 552.9875, found 552.9874.

*1-Benzyl-5-bromo-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)indolin-2-one [**6f(iii)**]:* white solid; mp 206−208 °C; yield 0.35 g, 69%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78−7.73 (m, 2H), 7.37−7.32 (m, 2H), 7.25−7.23 (m, 3H), 7.17−7.15 (m, 2H), 6.98 (d, 2H, J = 8.7 Hz), 6.56 (d, 1H, J = 8.4 Hz), 4.97 (d, 1H, J = 15.7 Hz), 4.85 (q, 2H, J = 14.1, 15.6 Hz), 4.74 (d, 1H, J = 15.7 Hz), 3.87 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 176.1, 160.3, 147.1, 143.0, 136.6, 133.7, 131.9, 129.8, 128.9, 128.6, 128.2, 127.8, 124.3, 122.9, 115.6, 115.6, 112.7, 75.8, 56.4, 55.1, 44.1; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{25}H_{22}BrN_4O_3$ 505.0875, found 505.0870.

*3-Hydroxy-5-methoxy-1-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)indolin-2-one [**6g(i)**]:* yellow solid; mp 198−200 °C; yield 0.27 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (s, 1H), 7.86−7.84 (m, 2H), 7.47−7.43 (m, 2H), 7.38−7.35 (m, 1H), 6.87 (dd, 1H, J = 2.6,Hz), 6.75 (d, 1H, J = 8.5 Hz), 6.36 (d, 1H, J = 2.5 Hz), 4.82(d, 1H, J = 14.2 Hz), 4.73 (d, 1H, J = 14.2 Hz), 3.97 (brs, 1H), 3.67 (s, 3H), 3.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.9, 156.6, 136.2, 130.3, 128.9, 128.3, 127.7, 125.8, 121.5, 115.8, 111.1, 109.6, 75.5, 55.7, 55.4, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{19}N_4O_3$ 351.1457, found 351.1445.

*3-((4-(4-Bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxy-5-methoxy-1-methylindolin-2-one [**6g(ii)**]:* white solid; mp 204−206 °C; yield 0.31 g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (s, 1H), 7.70 (d, 2H, J = 8.4 Hz), 7.54 (d, 2H, J = 8.4 Hz), 6.86 (dd, 1H, J = 2.4 Hz), 6.74 (d, 1H, J = 8.5 Hz), 6.39 (d, 1H, J = 2.4 Hz), 4.78 (d, 1H, J = 14.2 Hz), 4.73 (d, 1H, J = 14.2 Hz), 4.33 (brs, 1H), 3.67 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.9, 156.6, 146.7, 136.1, 132.0, 129.3, 127.7, 127.3, 122.2, 121.6, 115.7, 111.2, 109.6, 75.4, 55.8, 55.5, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{18}BrN_4O_3$ 429.0562, found 429.0551.

*3-Hydroxy-5-methoxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-1-methylindolin-2-one [**6g(iii)**]:* yellow solid; mp 168−170 °C; yield 0.28 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (s, 1H), 7.76−7.74 (m, 2H), 6.97−6.94 (m, 2H), 6.84 (dd, 1H, J = 2.5, 2.6 Hz), 6.72 (d, 1H, J = 8.5 Hz), 6.36 (d, 1H, J = 2.5 Hz), 4.80 (d, 1H, J = 14.2 Hz), 4.70 (d, 1H, J = 14.2 Hz), 4.48 (brs, 1H), 3.86 (s, 3H), 3.68 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 159.6, 156.6, 147.6, 136.1, 127.9, 127.1, 123.0, 120.8, 115.7,

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114.2, 111.1, 109.5, 75.6, 55.7, 55.4, 55.3, 26.6; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{20}H_{21}N_4O_4$ 381.1563, found 381.1550.

*3-Hydroxy-1,5-dimethyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl)indolin-2-one [**6h(i)**]:* yellow solid; mp 196−198 °C; yield 0.25 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, 1H, J = 3.1 Hz), 7.86−7.84 (m, 2H), 7.46−7.42 (m, 2H), 7.38−7.33 (m, 1H), 7.14−7.12 (m, 1H), 6.72 (d, 1H, J = 8.0 Hz), 6.66−6.64 (m, 1H), 4.79 (d, 1H, J = 2.8 Hz), 4.74 (d, 1H, J = 13.0 Hz), 3.17 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.4, 147.6, 140.6, 133.4, 130.9, 130.5, 128.8, 128.2, 126.8, 125.8, 125.4, 121.5, 108.6, 75.4, 55.3, 26.5, 21.1; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{19}N_4O_2$ 335.1508, found 335.1503.

*3-((4-(4-Bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1,5-dimethylindolin-2-one [**6h(ii)**]:* yellow solid; mp 208−210 °C; yield 0.30 g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.01 (s, 1H), 7.73−7.70 (m, 2H), 7.57−7.54 (m, 2H), 7.17−7.14 (m, 1H), 6.74−6.68 (m, 2H), 4.78 (d, 1H, J = 14.2 Hz), 4.74 (d, 1H, J = 14.2 Hz), 4.00 (brs, 1H), 3.17 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 146.6, 140.6, 133.5, 132.0, 131.0, 129.4, 127.3, 126.7, 125.3, 122.1, 121.6, 108.7, 75.2, 55.4, 26.5, 21.1; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{18}BrN_4O_2$ 413.0613, found 413.0607.

*3-Hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)-methyl)-1,5-dimethylindolin-2-one [**6h(iii)**]:* brownish solid; mp 204−206 °C; yield 0.27 g, 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (s, 1H), 7.79−7.77 (m, 2H), 7.32−7.31 (m, 1H), 7.15 (d, 1H, J = 7.8 Hz), 6.99−6.97 (m, 2H), 6.73 (d, 1H, J = 7.9 Hz), 4.78−4.74 (m, 2H), 3.87 (s, 3H), 3.19 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 140.7, 133.5, 131.0, 127.1, 126.7, 125.4, 124.1, 123.1, 120.6, 115.9, 114.3, 108.7, 75.3, 55.4, 31.6, 26.5, 21.1; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{20}H_{21}N_4O_3$ 365.1614, found 365.1608.

*1-Benzyl-3-hydroxy-5-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)-methyl) indolin-2-one [**6i(i)**]:* white solid; mp 148−151 °C; yield 0.32 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, 1H, J = 2.8 Hz), 7.80 (d, 2H, J = 7.9 Hz), 7.44−7.38 (m, 2H), 7.37−7.31 (m, 1H), 7.21−7.09 (m, 5H), 7.07−7.00 (m, 1H), 6.80 (s, 1H), 6.57 (d, 1H, J = 8.0 Hz), 4.96−4.82 (m, 3H), 4.70 (d, 1H, J = 15.6 Hz), 3.12 (brs, 1H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.6, 147.7, 139.9, 134.8, 133.5, 130.9, 130.3, 128.9, 128.8, 128.7, 128.2, 127.8, 127.0, 126.8, 125.8, 125.5, 121.4, 75.5, 55.2, 44.1, 21.0; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{25}H_{23}N_4O_2$ 411.1821, found 411.1813.

*1-Benzyl-3-((4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)methyl)-3-hydroxy-5-methylindolin-2-one [**6i(ii)**]:* white solid; mp 208−210 °C; yield 0.36 g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.66 (d, 2H, J = 8.5 Hz), 7.55−7.53 (m, 2H), 7.23−7.14 (m, 5H), 7.03 (d, 1H, J = 8.8 Hz), 6.80 (s, 1H), 6.59 (d, 1H, J = 8.0 Hz), 4.96 (d, 1H, J = 15.6 Hz), 4.86−4.85 (m, 2H), 4.71 (d, 1H, J = 15.6 Hz), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.5, 146.7, 139.9, 134.8, 133.6, 132.0, 131.0, 129.3, 128.9, 127.9, 127.3, 127.0, 126.7, 125.4, 122.1, 121.5, 109.8, 75.3, 55.3, 44.1, 21.0; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{25}H_{22}BrN_4O_2$ 489.0926, found 489.0916.

*1-Benzyl-3-hydroxy-3-((4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methyl)-5-methylindolin-2-one [**6i(iii)**]:* brown solid; mp 228−230 °C; yield 0.33 g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (s, 1H), 7.74 (d, 2H, J = 8.8 Hz), 7.32−7.29 (m, 1H), 7.25−7.16 (m, 5H), 7.03−6.96 (m, 2H), 6.79 (s, 1H), 6.58 (d, 1H, J = 8.0 Hz), 4.97 (d, 1H, J = 15.6 Hz), 4.85 (q, 2H, J = 14.0 Hz), 4.74 (d, 1H, J = 15.7 Hz), 3.87 (s, 3H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.4, 147.6, 139.9, 134.8, 133.5, 131.0, 128.9, 128.9, 127.8, 127.2, 127.1, 126.7, 125.4, 123.1, 120.5, 114.2, 109.8, 75.4, 55.4, 55.2, 44.1, 29.7; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{26}H_{25}N_4O_3$ 441.1927, found 441.1916.

*Ethyl 1-((3-hydroxy-1-methyl-2-oxoindolin-3-yl)methyl)-1H-1,2,3-triazole-4-carboxylate (**7a**):* yellow solid; mp 200−202 °C; yield 0.25 g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.40 (s, 1H), 7.38−7.34 (m, 1H), 7.05−7.02 (m, 1H), 6.86 (d, 1H, J = 7.8 Hz), 6.69 (d, 1H, J = 7.3 Hz), 4.80 (d, 1H, J = 14.1 Hz), 4.75 (d, 2H, J = 14.1 Hz), 4.43 (q, 2H, J = 7.1 Hz), 4.37 (brs, 1H), 3.20 (s, 3H), 1.42 (t, 3H, J = 7.2, 14.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 160.8, 142.9, 140.2, 130.9, 129.4, 126.4, 124.5, 123.9, 109.1, 74.8, 61.5, 55.4, 26.6, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{17}N_4O_4$ 317.1250, found 317.1238.

*Ethyl 1-((1-benzyl-3-hydroxy-2-oxoindolin-3-yl)methyl)-1H-1,2,3-triazole-4-carboxylate (**7b**):* yellow solid; mp 138−140 °C; yield 0.28 g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (s, 1H), 7.34−7.28 (m, 3H), 7.28−7.22 (m, 3H), 7.04−7.00 (m, 1H), 6.77−6.73 (m, 2H), 4.98 (d, 1H, J = 15.6 Hz), 4.85−4.78 (m, 3H), 4.44 (q, 2H, J = 7.2 Hz), 3.69 (brs, 1H), 1.43 (t, 3H, J = 7.1, 14.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.0, 160.7, 142.2, 140.3, 134.7, 131.0, 129.3, 129.0, 128.0, 127.2, 126.2, 124.6, 123.9, 110.1, 74.9, 61.5, 55.5, 44.2, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{21}N_4O_4$ 393.1563, found 393.1550.

*Ethyl 1-((5-chloro-3-hydroxy-1-methyl-2-oxoindolin-3-yl)-methyl)-1H-1,2,3-triazole-4-carboxylate (**7c**):* white solid; mp 208−210 °C; yield 0.27 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.34 (s, 1H), 7.36−7.33 (m, 1H), 6.88 (d, 1H, J = 2.1 Hz), 6.79 (d, 1H, J = 8.4 Hz), 4.79 (s, 2H), 4.43 (q, 2H, J = 7.1 Hz), 3.19 (s, 3H), 1.43 (t, 3H, J = 7.2, 14.3 Hz); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 179.7, 165.4, 147.4, 143.5, 135.6, 135.1, 134.9, 131.6, 129.7, 115.6, 79.3, 65.8, 59.2, 31.4, 19.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{16}ClN_4O_4$ 351.0860, found 351.0847.

*Ethyl 1-((1-benzyl-5-chloro-3-hydroxy-2-oxoindolin-3-yl)methyl)-1H-1,2,3-triazole-4-carboxylate (**7d**):* yellow solid; mp 120−122 °C; yield 0.29 g, 68%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.30 (s, 1H), 7.33−7.31 (m, 3H), 7.24−7.17 (m, 3H), 6.92 (d, 1H, J = 2.0 Hz), 6.67−6.62 (m, 1H), 4.94 (d, 1H, J = 15.6 Hz), 4.85−4.75 (m, 3H), 4.44 (q, 2H, J = 7.1, 14.2 Hz), 4.06 (brs, 1H), 1.44 (t, 3H, J = 2.9, 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.7, 160.6, 140.7, 140.3, 134.2, 130.9, 129.4, 129.3, 129.1, 128.2, 128.0, 127.1, 125.2, 124.1, 74.9, 61.5, 55.2, 44.3, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{20}ClN_4O_4$ 427.1173, found 427.1163.

*Ethyl 1-((5-bromo-3-hydroxy-1-methyl-2-oxoindolin-3-yl)-methyl)-1H-1,2,3-triazole-4-carboxylate (**7e**):* white solid; mp 196−198 °C; yield 0.29 g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.32 (s, 1H), 7.50−7.48 (m, 1H), 7.06−7.03 (m, 1H), 6.74−6.70 (m, 1H), 4.80 (d, 2H, J = 13.9 Hz), 4.42 (q, 2H, J = 7.1, 14.2 Hz), 4.23 (brs, 1H), 3.18 (s, 3H), 1.43 (t, 3H, J = 2.6, 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.6, 160.6, 142.0, 140.2, 133.8, 129.4, 128.4, 127.8, 116.5, 110.5, 74.8, 61.5, 55.2, 26.7, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{16}BrN_4O_4$ 395.0355, found 395.0346.

*Ethyl 1-((1-benzyl-5-bromo-3-hydroxy-2-oxoindolin-3-yl)-methyl)-1H-1,2,3-triazole-4-carboxylate (**7f**):* yellow solid; mp 124−126 °C; yield 0.31 g, 66%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.30 (s, 1H), 7.38−7.29 (m, 4H), 7.18−7.16 (m, 2H), 7.08 (d, 1H, J = 1.9 Hz), 6.60 (d, 1H, J = 8.4 Hz), 4.92 (d, 1H, J = 15.7 Hz), 4.85 (s, 2H), 4.75 (d, 1H, J = 15.7 Hz), 4.42 (q, 2H, J = 7.1, 14.2 Hz), 4.29 (brs, 1H), 1.42 (t, 3H, J = 7.2, 13.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.7, 160.6, 141.2, 140.3, 134.2, 133.7, 129.3, 129.1, 128.5, 128.2, 127.9, 127.1, 116.6, 111.6, 74.9, 61.5, 55.2, 44.2, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{20}BrN_4O_4$ 471.0668, found 471.0664.

*Ethyl 1-((3-hydroxy-5-methoxy-1-methyl-2-oxoindolin-3-yl)-methyl)-1H-1,2,3-triazole-4-carboxylate (**7g**):* yellow solid; mp 176−178 °C; yield 0.26 g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.39 (s, 1H), 6.86 (dd, 1H, J = 2.5, 6.0 Hz), 6.76 (d, 1H, J = 8.6 Hz), 6.36 (d, 1H, J = 2.5 Hz), 4.80 (d, 1H, J = 14.2 Hz), 4.75 (d, 1H, J = 14.1 Hz), 4.42 (q, 2H, J = 7.1, 14.2 Hz), 4.36 (brs, 1H), 3.70 (s, 3H), 3.18 (s, 3H), 1.42 (t, 3H, J = 3.4, 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.0, 160.7, 156.7, 140.2, 136.0, 129.4, 127.6, 115.6, 111.4, 109.7, 75.2, 61.4, 55.8, 55.5, 26.6, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{19}N_4O_5$ 347.1355, found 347.1354.

*Ethyl 1-((3-hydroxy-1,5-dimethyl-2-oxoindolin-3-yl)methyl)-1H-1,2,3-triazole-4-carboxylate (**7h**):* white solid; mp 168−170 °C; yield 0.24 g, 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (s, 1H), 7.16 (d, 1H, J = 7.9 Hz), 6.75 (d, 1H, J = 8.0 Hz), 6.63 (d, 1H, J = 10.8 Hz), 4.77 (s, 2H), 4.45 (q, 2H, J = 7.2, 14.3 Hz), 3.72 (brs, 1H), 3.20 (s, 3H), 2.28 (s, 3H), 1.44 (t, 3H, J = 4.6, 8.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.9, 151.8, 140.5, 133.7, 131.2, 126.3, 125.2, 124.1, 115.9, 108.8, 74.9, 61.4, 55.5, 29.7, 26.6, 14.3; ESI-HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{19}N_4O_4$ 331.1406, found 331.1402.

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Ethyl 1-((1-benzyl-3-hydroxy-5-methyl-2-oxoindolin-3-yl)-methyl)-1H-1,2,3-triazole-4-carboxylate (7i): brown solid; mp 96–98 °C; yield 0.28 g, 69%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (s, 1H), 7.33–7.29 (m, 2H), 7.27–7.18 (m, 3H), 7.03 (d, 1H, J = 7.8 Hz), 6.65–6.61 (m, 2H), 4.93 (d, 1H, J = 15.6 Hz), 4.83 (s, 2H), 4.75 (d, 1H, J = 15.6 Hz), 4.42 (q, 2H, J = 7.0, 14.1 Hz), 4.19 (brs, 1H), 2.24 (s, 3H), 1.42 (t, 3H, J = 7.1, 13.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.2, 160.7, 140.2, 139.7, 134.8, 133.7, 131.1, 129.4, 129.0, 127.9, 127.2, 126.4, 125.3, 109.9, 75.1, 61.4, 55.4, 44.1, 21.0, 14.3; ESI-HRMS (m/z) $[M + H]^+$ calcd for $C_{22}H_{23}N_4O_4$ 407.1719, found 407.1712.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01819.

^{1}H NMR, ^{13}C NMR, and HRMS spectra (PDF)

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Notes

The authors declare no competing financial interest.

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