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Water Promoted Regiospecific Azidolysis and Copper Catalysed 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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Key words: *Regioselectivity, water, click chemistry, 1,2,3-triazole.*

ABSTRACT: An efficient, eco-friendly, base free, one-pot, sequential protocol was developed for epoxide azidolysis and copper catalysed azide-alkyne cycloaddition using water as the solvent for the synthesis of 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1H-1,2,3-triazol-1-yl)methyl]indolin-2-ones. The optimised reaction condition has been generalised in the case of aromatic as well as aliphatic alkyne partner affording 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 3-hydroxy oxindole scaffold are illustrated in **Figure 1**. The activity of these molecules mainly resides in the substitution at the C-3 quaternary centre. Kumar *et. al.* established the antimalarial, antitubercular and anti-protozoal activity of 1*H*-1,2,3-triazole tethered with oxindole.[1d-f] Copper-catalyzed azide–alkyne cycloaddition (CuAAC) or Huisgen cycloaddition is one 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 in material science.[8]

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 centre 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 proved their utility for regioselective triazole synthesis.[18]

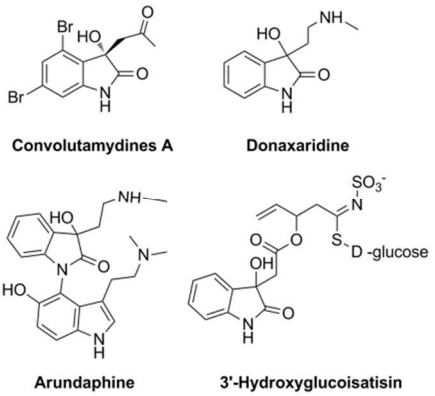


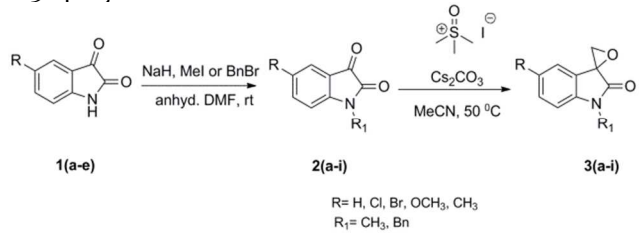
Figure 1. Natural products containing 3-hydroxy oxindole scaffold.

Despite the wide applicability, the available methods have limitations such as pre-synthesis of metal complex, long reaction time, moderate yields, use of air and moisture sensitive reagents or catalysts, 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 eco-friendly one-pot sequential protocol for epoxide azidolysis and copper catalysed cycloaddition reaction using water as the reaction medium. The developed protocol afforded 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1H-1,2,3-triazol-1-yl)methyl]indolin-2-ones with excellent yields and regioselectivity in a short span of time.

Results and Discussion

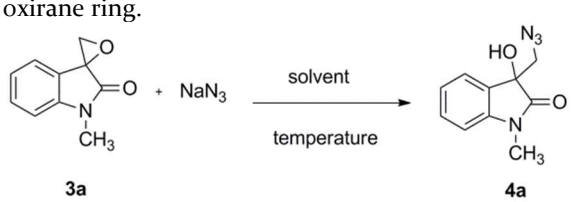
The required oxirane derivatives were prepared as illustrated in **Scheme 1**. *N*-alkyl derivatives were synthesized

by treating isatins with NaH and then reacting with methyl iodide or benzyl bromide, in dry DMF at room temperature. Construction of epoxy ring at C-3 position of isatin derivatives were realised by Corey-Chakovsky reaction using trimethylsulfoxonium iodide and cesium carbonate in acetonitrile solvent at 50 °C to afford good yield of 3-epoxy-indolin-2-ones.



Scheme 1. Synthesis of 3-epoxy-indolin-2-ones.

Based on our earlier 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 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.



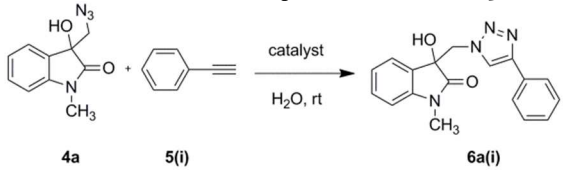
Scheme 2. Azidolysis of the 3-epoxy-indolin-2-one.

Table 1. Effect of solvents on azidolysis of 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 condition: 1-methylspiro[indolin-3,2'-oxiran]-2-one (1.0 equiv.), sodium azide (1.2 equiv.), temp. 30°C; [b]isolated yield; [c]temp. 50°C; [d]temp. 70°C; [e]temp. 90°C.

To evaluate our assumption, we tried 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 50ºC attaining completion in 0.75 h affording 92% yield with a regiospecific oxirane ring opening from the less hindered end. Further increase in temperature did not improve the yield of the reaction. From the above observation, we inferred that reacting 1.0 equivalent of 1-methylspiro[indoline-3,2'-oxiran]-2-one and 1.2 equivalent of sodium azide in water at 50ºC would be the most suitable condition for the reaction. The synthesized 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one were used in copper catalysed azide-alkyne cycloaddition reaction. To investigate the reaction in detail, a model reaction 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 (10mol%)	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), temp. 30°C; [b]isolated yield.

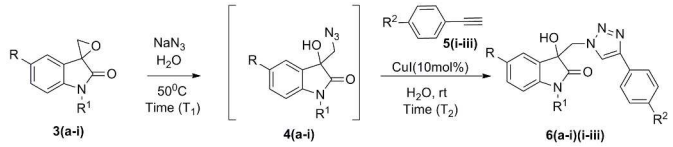
The effect of the solvent, as a reaction variable was also evaluated. In the case of non-polar solvents like cyclohexane and toluene, the reaction afforded unsatisfactory results compared to aprotic solvents like THF, DCM, acetonitrile and chloroform (Table 3). Protic polar solvents like EtOH and ^{t}BuOH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

Table 3. Effect of solvent on copper catalysed 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.), temp. 30°C; [b]isolated yield.

To evaluate the prospect of both the reactions sequentially, azidolysis of oxirane ring and copper catalysed 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 equivalent of 1-methylspiro[indolin-3,2'-oxiran]-2-one **3a** and 1.2 equivalent of sodium azide in water as solvent was heated at 50ºC 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 equivalent of CuI and 1.2 equivalent of phenylacetylene **5(i)** without isolating the 3-(azidomethyl)-3-hydroxy-1-methylindolin-2-one **4a**.



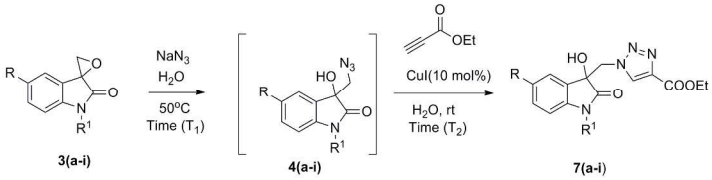
Scheme 4. One-pot azidolysis and cycloaddition reactions with aryl acetylenes.

Table 4. Generalisation of optimised condition 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 condition: 3-epoxy-indolin-2-one (1.0 equiv.), sodium azide (1.2 equiv.), phenylacetylene (1.2 equiv.), CuI (0.1 equiv.), temp. 30°C, [b]overall isolated yield, T_1 = time for epoxide azidolysis, T_2 = time for CuAAC reaction.

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-epoxy-indolin-2-ones and phenylacetylene derivatives bearing both electron withdrawing and donating groups. The reaction afforded 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 ethylpropiolate and 3-epoxy-indolin-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**).



Scheme 5. One-pot azidolysis and cycloaddition reactions with alkynes.

Table 5. Generalisation of optimised conditions of one pot azidolysis and azide-alkyne cycloaddition reaction[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 condition: 3-epoxy-indolin-2-one (1.0 equiv.), sodium azide (1.2 equiv.), ethylpropiolate (1.2 equiv.), CuI (0.1 equiv.), temp. 30°C, [b]overall isolated yield, T_1 = time for epoxide azidolysis, T_2 = time for CuAAC reaction.

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 providing high regioselectivity for the reaction. Further in the azide-alkyne cycloaddition reaction also water would activate the substrate to form the intermediate I which coordinates with the copper salt to afford the intermediate II. Thereafter the alkyne coordinates to copper via a π-complex, and subsequently generates the intermediate III. The terminal nitrogen N_1 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.

To conclude, an eco-friendly one-pot sequential protocol was developed for epoxide azidolysis and copper catalysed 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 condition was extended to obtain 3-hydroxy-1-alkyl-3-[(4-aryl/alkyl-1*H*-1,2,3-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 environmental benign protocol, catalytic use of readily available and inexpensive CuI, simplicity of the reaction condition, base free and short reaction time with high regioselectivity.

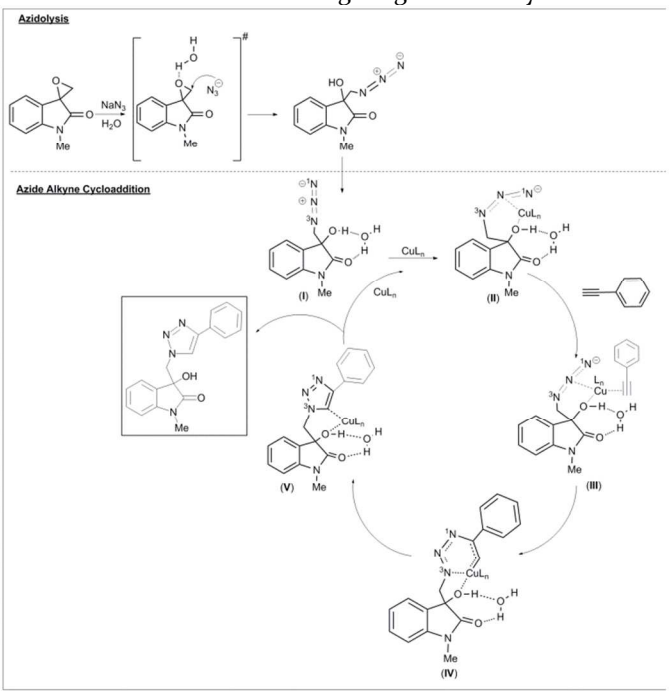


Figure 2. Plausible mechanism.

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 Hz. 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 Bruker Maxix TOF spectrometer. Melting points were recorded and uncorrected. All the starting materials [isatin, 5-chloro isatin, 5-bromo isatin, 5-methoxy isatin, 5-methyl isatin], benzyl bromide, methyl iodide, trimethylsulphoxonium iodide, phenylacetylene, 4-bromo phenylacetylene, 4-methoxyphenylacetylene, ethylpropiolate, copper-iodide, 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 sulphur ylide. To this, a solution of isatin (1.0 mmol) in dry acetonitrile (5 mL) was added 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 (60–120mesh) using 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: 0.13g, 78%; 1H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.37 (m, 1H), 7.13-7.07 (m, 2H), 6.93 (d, 1H, J = 7.8Hz), 3.59 (d, 1H, J = 6.7Hz), 3.44 (d, 1H, J = 6.7Hz), 3.28 (s, 3H); 13C NMR ($CDCl_3$, 100MHz) 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: 0.19g, 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* = 7.9Hz), 4.98 (q, 2H, *J* = 11.4, 15.7Hz), 3.67 (d, 1H, *J* = 6.7Hz), 3.50 (d, 1H, *J* = 6.7Hz); ^{13}C NMR ($CDCl_3$, 100MHz) *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: 0.16g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.40-7.37 (m, 1H), 7.11 (d, 1H, *J* = 2.1Hz), 6.87 (d, 1H, *J* = 8.3Hz), 3.62 (d, 1H, *J* = 6.7Hz), 3.45 (d, 1H, *J* = 6.7Hz), 3.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) *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: 0.20g, 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* = 2.1Hz), 6.74 (d, 1H, *J* = 8.4Hz), 4.98 (q, 2H, *J* = 5.7, 15.7Hz), 3.69 (d, 1H, *J* = 6.7Hz), 3.49 (d, 1H, *J* = 6.7Hz); ^{13}C NMR ($CDCl_3$, 100MHz) *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: 0.19g, 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* = 8.3Hz), 3.61 (d, 1H, *J* = 6.6Hz), 3.45 (d, 1H, *J* = 6.7Hz), 3.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) *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: 0.23g, 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 7.41-7.28 (m, 6H), 7.25 (d, 1H, *J* =

1.9Hz), 6.70 (d, 1H, *J* = 8.3Hz), 4.98 (q, 2H, *J* = 4.8, 15.7Hz), 3.68 (d, 1H, *J* = 6.7Hz), 3.49 (d, 1H, *J* = 6.7Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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: 0.14g, 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.93 (dd, 1H, *J* = 2.5, 6.0Hz), 6.85 (d, 1H, *J* = 8.5), 6.74 (d, 1H, *J* = 2.5Hz), 3.81 (s, 3H), 3.60 (d, 1H, *J* = 6.7Hz), 3.43 (d, 1H, *J* = 6.7Hz), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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: 0.13g, 68%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, 1H, *J* = 0.9Hz), 6.95-6.94 (m, 1H), 6.83 (d, 1H, *J* = 7.9Hz), 3.59 (d, 1H, *J* = 6.7Hz), 3.43 (d, 1H, *J* = 6.7Hz), 3.28 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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: 0.17g, 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* = 8.0Hz), 4.97 (q, 2H, *J* = 7.9, 15.6Hz), 3.67 (d, 1H, *J* = 6.7Hz), 3.48 (d, 1H, *J* = 6.7Hz), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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) were stirred in water at 50°C. The progress of reaction was monitored by TLC. After complete consumption of oxirane, reaction mixture was cooled to room temperature and to this CuI (10 mol%) and phenyl acetylene/ethylpropiolate (1.2 mmol) were added. After completion, the reaction mixture was washed with water and extracted with ethyl acetate(3x20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and 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-1*H*-1,2,3-triazol-1-yl)methyl)indolin-2-one [6a(i)]

White solid; mp 156-158°C; Yield: 0.26g, 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* = 14.2Hz), 4.74 (d, 1H, *J* = 14.2Hz), 4.04 (brs, 1H), 3.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1-methyl indolin-2-one [6a(ii)]

White solid; mp 167-169°C; Yield: 0.30g, 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* = 14.2Hz), 4.75 (d, 1H, *J* = 14.2Hz), 3.60 (brs, 1H), 3.22 (s, 3H); ^{13}C NMR (DMSO-d_6, 100MHz) 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: 0.28g, 79%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.76 (d, 2H, *J* = 8.7Hz), 7.36-7.28 (m, 1H), 7.04-7.01 (m, 1H), 6.97 (d, 2H, *J* = 8.7Hz), 6.84-6.78 (m, 2H), 4.80 (d, 1H, *J* = 14.1Hz), 4.71 (d, 1H, *J* = 14.2Hz), 4.18 (brs, 1H), 3.86 (s, 3H), 3.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl)indolin-2-one [6b(i)]

White solid; mp 169-171°C; Yield: 0.31g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.83 (d, 2H, *J* = 7.4Hz), 7.46-7.35 (m, 3H), 7.26-7.22 (m, 6H), 7.03 (t, 1H, *J* = 7.6Hz), 6.91 (d, 1H, *J* = 7.4Hz), 6.73 (d, 1H, *J* = 7.9Hz), 5.00 (d, 1H, *J* = 15.6Hz), 4.92 (d, 1H, *J* = 14.0Hz), 4.80 (t, 2H, *J* = 15.6Hz), 3.59 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxyindolin-2-one [6b(ii)]

White solid; mp 172-174°C; Yield: 0.34g, 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* = 7.9Hz), 5.00 (d, 1H, *J* = 15.7Hz), 4.90 (d, 1H, *J* = 14.1Hz), 4.80 (q, 2H, *J* = 9.4, 15.7Hz), 3.74 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)indolin-2-one [6b(iii)]

Yellow solid; mp 138-140°C; Yield: 0.32g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (s, 1H), 7.75 (d, 2H, *J* = 8.8Hz), 7.27-7.18 (m, 6H), 7.04-6.96 (m, 3H), 6.90 (d, 1H, *J* = 6.9Hz), 6.71 (d, 1H, *J* = 7.9Hz), 5.00 (d, 1H, *J* = 15.9Hz), 4.90 (d, 1H, *J* = 14.1Hz), 4.79 (q, 2H, *J* = 2.0, 13.6Hz), 3.92 (brs, 1H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6c(i)]

White solid; mp 226-228°C; Yield: 0.27g, 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 = 2.0Hz), 6.77 (d, 1H, J = 8.4Hz), 4.81 (d, 1H, J = 14.1Hz), 4.75 (d, 1H, J = 14.1Hz), 3.66 (brs, 1H), 3.20 (s, 3H); ^{13}C NMR (DMSO-d_6, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-5-chloro-3-hydroxy-1-methylindolin-2-one [6c(ii)]

White solid; mp 218-220°C; Yield: 0.32g, 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, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl) -1-methylindolin-2-one [6c(iii)]

White solid; mp 198-200°C; Yield: 0.30g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (s, 1H), 7.75 (d, 2H, J = 8.8Hz), 7.34-7.31 (m, 1H), 6.97 (d, 2H, J = 8.8Hz), 6.92 (d, 1H, J = 2.0Hz), 6.75 (d, 1H, J = 8.4Hz), 4.79 (d, 1H, J = 14.2Hz), 4.73 (d, 1H, J = 14.2Hz), 3.86 (s, 3H), 3.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6d(i)]

White solid; mp 177-179°C; Yield: 0.33g, 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 = 2.1Hz), 6.61 (d, 1H, J = 8.4Hz), 4.97 (d, 1H, J = 15.7Hz), 4.87 (q, 2H, J = 11.2, 14.1Hz), 4.73 (d, 1H, J = 15.7Hz), 4.02 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-5-chloro-3-hydroxyindolin-2-one [6d(ii)]

White solid; mp 196-198°C; Yield: 0.36g, 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 = 2.0Hz), 6.64-6.60 (m, 1H), 4.96 (d, 1H, J = 15.7Hz), 4.86 (q, 2H, J = 4.1, 14.1Hz), 4.71 (d, 1H, J = 15.7Hz), 4.27 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)indolin-2-one [6d(iii)]

White solid; mp 198-200°C; Yield: 0.34g, 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 = 2.0Hz), 6.97 (d, 2H, J = 8.8Hz), 6.61 (d, 1H, J = 8.4Hz), 4.97 (d, 1H, J = 15.7Hz), 4.85 (q, 2H, J = 14.0, 16.1Hz), 4.74 (d, 1H, J = 15.7Hz), 3.87 (s, 3H), 3.86 (brs, 1H); ^{13}C NMR (DMSO-d_6, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6e(i)]

White solid; mp 238-240°C; Yield: 0.32g, 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, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1-methylindolin-2-one [6e(ii)]

White solid; mp 224-226°C; Yield: 0.36g, 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 = 8.3Hz), 4.82-4.73 (m, 2H), 3.86 (brs, 1H), 3.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl) -1-methylindolin-2-one [6e(iii)]

Yellow solid; mp 166-168°C; Yield: 0.33g, 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 = 1.9Hz), 6.98-6.94 (m, 2H), 6.69 (d, 1H, J = 8.3Hz), 4.80-4.72 (m, 2H), 4.31 (brs, 1H), 3.86 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6f(i)]

White solid; mp 182-184°C; Yield: 0.36g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (s, 1H), 7.82 (d, 2H, J = 7.2Hz), 7.46-7.32 (m, 5H), 7.24-7.14 (m, 5H), 6.56 (d, 1H, J = 8.4Hz), 4.96 (d, 1H, J = 15.7Hz), 4.87 (q, 2H, J = 4.1, 14.1Hz), 4.73 (d, 1H, J = 15.7Hz); ^{13}C NMR (DMSO-d_6, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxyindolin-2-one [6f(ii)]

White solid; mp 198-200°C; Yield: 0.40g, 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (s, 1H), 7.68 (d, 2H, J = 8.5Hz), 7.57-7.55 (m, 2H), 7.36 (dd, 1H, J = 1.9, 2.0Hz), 7.24-7.23 (m, 3H), 7.17-7.12 (m, 3H), 6.57 (d, 1H, J = 8.4Hz), 4.96 (d, 1H, J = 15.8Hz), 4.86 (q, 2H, J = 4.6, 14.1Hz), 4.72 (d, 1H, J = 15.7Hz), 4.04 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)indolin-2-one [6f(iii)]

White solid; mp 206-208°C; Yield: 0.35g, 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 = 8.7Hz), 6.56 (d, 1H, J = 8.4Hz), 4.97 (d, 1H, J = 15.7Hz), 4.85 (q, 2H, J = 14.1, 15.6Hz), 4.74 (d, 1H, J = 15.7Hz), 3.87 (s, 3H); ^{13}C NMR (DMSO-d_6, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6g(i)]

Yellow solid; mp 198-200°C; Yield: 0.27g, 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 = 8.5Hz), 6.36 (d, 1H, J = 2.5Hz), 4.82(d, 1H, J = 14.2Hz), 4.73 (d, 1H, J = 14.2Hz), 3.97 (brs, 1H), 3.67 (s, 3H), 3.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxy-5-methoxy -1-methylindolin-2-one [6g(ii)]

White solid; mp 204-206°C; Yield: 0.31g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (s, 1H), 7.70 (d, 2H, J = 8.4Hz), 7.54 (d, 2H, J = 8.4Hz), 6.86 (dd, 1H, J = 2.4Hz), 6.74 (d, 1H, J = 8.5Hz), 6.39 (d, 1H, J = 2.4Hz), 4.78 (d, 1H, J = 14.2Hz), 4.73 (d, 1H, J = 14.2Hz), 4.33 (brs, 1H), 3.67 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-1-methylindolin-2-one [6g(iii)]

Yellow solid; mp 168-170°C; Yield: 0.28g, 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, 2.6Hz), 6.72 (d, 1H, J = 8.5Hz), 6.36 (d, 1H, J = 2.5Hz), 4.80 (d, 1H, J = 14.2Hz), 4.70 (d, 1H, J = 14.2Hz), 4.48 (brs, 1H), 3.86 (s, 3H), 3.68 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 175.2, 159.6, 156.6, 147.6, 136.1, 127.9, 127.1, 123.0, 120.8, 115.7, 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6h(i)]

Yellow solid; mp 196-198°C; Yield: 0.25g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, 1H, J = 3.1Hz), 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 = 8.0Hz), 6.66-6.64 (m, 1H), 4.79 (d, 1H, J = 2.8Hz), 4.74 (d, 1H, J = 13.0Hz), 3.17 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxy-1,5-dimethylindolin-2-one [6h(ii)]

Yellow solid; mp 208-210°C; Yield: 0.30g, 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 = 14.2Hz), 4.74 (d, 1H, J = 14.2Hz), 4.00 (brs, 1H), 3.17 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-1,5-dimethylindolin-2-one [6h(iii)]

Brownish solid; mp 204-206°C; Yield: 0.27g, 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 = 7.8Hz), 6.99-6.97 (m, 2H), 6.73 (d, 1H, J = 7.9Hz), 4.78-4.74 (m, 2H), 3.87 (s, 3H), 3.19 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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-1*H*-1,2,3-triazol-1-yl)methyl) indolin-2-one [6i(i)]

White solid; mp 148-151°C; Yield: 0.32g, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, 1H, J = 2.8Hz), 7.80 (d, 2H, J = 7.9Hz), 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 = 8.0Hz), 4.96-4.82 (m, 3H), 4.70 (d, 1H, J = 15.6Hz), 3.12 (brs, 1H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-3-hydroxy-5-methylindolin-2-one [6i(ii)]

White solid; mp 208-210°C; Yield: 0.36g, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.66 (d, 2H, J = 8.5Hz), 7.55-7.53 (m, 2H), 7.23-7.14 (m, 5H), 7.03 (d, 1H, J = 8.8Hz), 6.80 (s, 1H), 6.59 (d, 1H, J = 8.0Hz), 4.96 (d, 1H, J = 15.6Hz), 4.86-4.85 (m, 2H), 4.71 (d, 1H, J = 15.6Hz), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazol-1-yl)methyl)-5-methylindolin-2-one [6i(iii)]

Brown solid; mp 228-230°C; Yield: 0.33g, 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (s, 1H), 7.74 (d, 2H, J = 8.8Hz), 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 = 8.0Hz), 4.97 (d, 1H, J = 15.6Hz), 4.85 (q, 2H, J = 14.0Hz), 4.74 (d, 1H, J = 15.7Hz), 3.87 (s, 3H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7a)

Yellow solid; mp 200-202°C; Yield: 0.25g, 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 = 7.8Hz), 6.69 (d, 1H, J = 7.3Hz), 4.80 (d, 1H, *J* = 14.1Hz), 4.75 (d, 2H, *J* = 14.1Hz), 4.43 (q, 2H, *J* = 7.1Hz), 4.37 (brs, 1H), 3.20 (s, 3H), 1.42 (t, 3H, *J* = 7.2, 14.3Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7b)

Yellow solid; mp 138-140°C; Yield: 0.28g, 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* = 15.6Hz), 4.85-4.78 (m, 3H), 4.44 (q, 2H, *J* = 7.2Hz), 3.69 (brs, 1H), 1.43 (t, 3H, *J* = 7.1, 14.3Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7c)

White solid; mp 208-210°C; Yield: 0.27g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.34 (s, 1H), 7.36-7.33 (m, 1H), 6.88 (d, 1H, *J* = 2.1Hz), 6.79 (d, 1H, *J* = 8.4Hz), 4.79 (s, 2H), 4.43 (q, 2H, *J* = 7.1Hz), 3.19 (s, 3H), 1.43 (t, 3H, *J* = 7.2, 14.3Hz); ^{13}C NMR (DMSO-d_6, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7d)

Yellow solid; mp 120-122°C; Yield: 0.29g, 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* = 2.0Hz), 6.67-6.62 (m, 1H), 4.94 (d, 1H, *J* = 15.6Hz), 4.85-4.75 (m, 3H), 4.44 (q, 2H, *J* = 7.1, 14.2Hz), 4.06 (brs, 1H), 1.44 (t, 3H, *J* = 2.9, 7.1Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7e)

White solid; mp 196-198°C; Yield: 0.29g, 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* = 13.9Hz), 4.42 (q, 2H, *J* = 7.1, 14.2Hz), 4.23 (brs, 1H), 3.18 (s, 3H), 1.43 (t, 3H, *J* = 2.6, 7.1Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7f)

Yellow solid; mp 124-126°C; Yield: 0.31g, 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* = 1.9Hz), 6.60 (d, 1H, *J* = 8.4Hz), 4.92 (d, 1H, *J* = 15.7Hz), 4.85 (s, 2H), 4.75 (d, 1H, *J* = 15.7Hz), 4.42 (q, 2H, *J* = 7.1, 14.2Hz), 4.29 (brs, 1H), 1.42 (t, 3H, *J* = 7.2, 13.4Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7g)

Yellow solid; mp 176-178°C; Yield: 0.26g, 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.39 (s, 1H), 6.86 (dd, 1H, *J* = 2.5, 6.0Hz), 6.76 (d, 1H, *J* = 8.6Hz), 6.36 (d, 1H, *J* = 2.5Hz), 4.80 (d, 1H, *J* = 14.2Hz), 4.75 (d, 1H, *J* = 14.1Hz), 4.42 (q, 2H, *J* = 7.1, 14.2Hz), 4.36 (brs, 1H), 3.70 (s, 3H), 3.18 (s, 3H), 1.42 (t, 3H, *J* = 3.4, 7.1Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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)-1*H*-1,2,3-triazole-4-carboxylate (7h)

White solid; mp 168-170°C; Yield: 0.24g, 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (s, 1H), 7.16 (d, 1H, *J* = 7.9Hz), 6.75 (d, 1H, *J* = 8.0Hz), 6.63 (d, 1H, *J* = 10.8Hz), 4.77 (s, 2H), 4.45 (q, 2H, *J* = 7.2, 14.3Hz), 3.72 (brs, 1H), 3.20 (s, 3H), 2.28 (s, 3H), 1.44 (t, 3H, *J* = 4.6, 8.6Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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.

Ethyl 1-((1-benzyl-3-hydroxy-5-methyl-2-oxoindolin-3-yl)methyl)-1*H*-1,2,3-triazole-4-carboxylate (7i)

Brown solid; mp 96-98°C; Yield: 0.28g, 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* = 7.8Hz), 6.65-6.61 (m, 2H), 4.93 (d, 1H, *J* = 15.6Hz), 4.83 (s, 2H), 4.75 (d, 1H, *J* = 15.6Hz), 4.42 (q, 2H, *J* = 7.0, 14.1Hz), 4.19 (brs, 1H), 2.24 (s, 3H), 1.42 (t, 3H, *J* = 7.1, 13.2Hz); ^{13}C NMR ($CDCl_3$, 100MHz) 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.

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ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website. A copy of scanned spectra (^{1}H NMR, ^{13}C NMR and HRMS) can be found in the online version (file type, i.e., MS Word).

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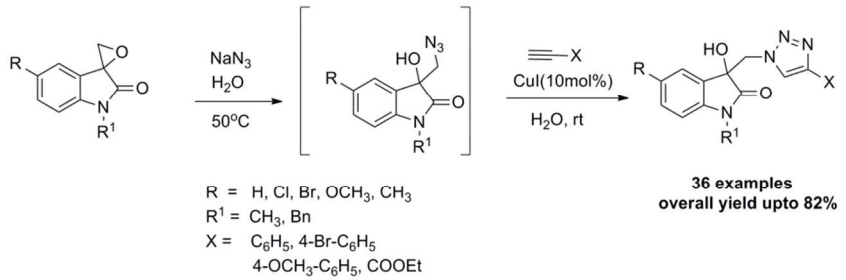
NaN3
H2O
50°C
CuI(10mol%)
H2O, rt
R = H, Cl, Br, OCH3, CH3
R1 = CH3, Bn
X = C6H5, 4-Br-C6H5
4-OCH3-C6H5, COOEt
36 examples
overall yield upto 82%