Catalyst-free aldol condensation of ketones and isatins under mild reaction conditions in DMF with molecular sieves 4 Å as additive†

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In the presence of molecular sieve (MS) 4 Å in DMF, a catalyst-free aldol condensation of a variety of aromatic and aliphatic ketones with isatins under mild reaction conditions has been developed. This approach may provide access to a wide range of 3-substituted-3-hydroxyindolin-2-ones in good to excellent yields.

Introduction

The indole nucleus, a common and important structural functionality of a variety of both natural and unnatural products, is probably the most well-known heterocycle.[1] In particular, the 3-substituted-3-hydroxyindolin-2-ones, one class of compounds bearing the indole skeletal structure, are found in several biologically active alkaloids and pharmacological agents[2] (Fig. 1). Owing to the significance of this structural motif, numerous elegant methodologies have been developed and continue to be explored for the construction of this structure.[3] Among them, the aldol addition of appropriate ketones to isatins should be one of the most concise and straightforward approaches to this kind of compounds.[4] Through careful examination of the existing literature procedures, we noted that nearly all existing methods for the aldol reaction of ketones with isatins inevitably required a base, a metal complex or an organic molecule serving as catalyst.[3d,3i,4,5] However, due to the fact that the highly reactive β-carbonyl group of isatin derivatives is susceptible to nucleophilic attack,[6] we envisioned that the aldol condensation between isatin derivatives and ketones might readily proceed catalyst-free under certain appropriate reaction conditions.

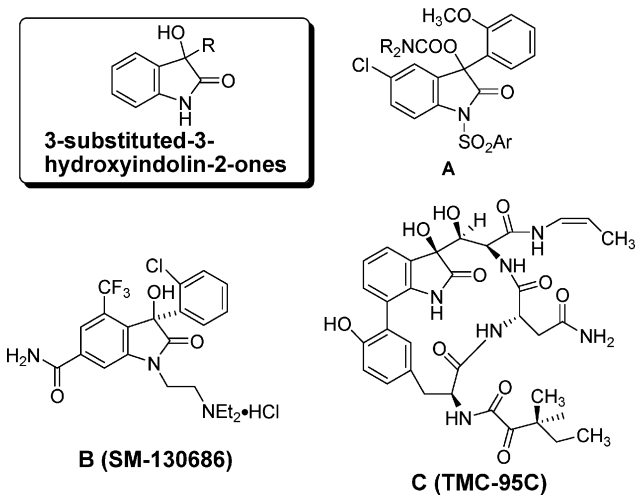

Fig. 1 Examples of biologically active 3-substituted-3-hydroxyindole-2-ones.

In view of the *12 Principles of Green Chemistry*,[7] catalyst-free reactions have been attracting more and more attention from organic synthesis chemists.[8] We recently have been trying to develop approaches to carry out reactions without any catalyst. Fortunately, we discovered that the aldol condensations of a variety of aromatic or aliphatic ketones with isatins proceeded smoothly at room temperature in DMF under catalyst-free conditions, and this approach may provide access to a wide range of 3-substituted-3-hydroxyindolin-2-ones derivatives in high yields. To the best of our knowledge, there are not any precedent protocols of this work for the preparation 3-substituted-3-hydroxyindolin-2-ones through the aldol condensation of isatins and ketones under catalyst free condition. Herein, we wish to describe our preliminary results about this work.

Results and discussion

To begin with, the addition of acetophenone **1a** to free isatin **2a** was examined to screen the optimal reaction conditions (Table 1). The desired adduct **3a** was obtained in very trace amount using THF as solvent at room temperature for 24 h (Table 1, entry 1). A variety of dry solvents, such as dioxane, CH_3CN, CH_2Cl_2, toluene, $CHCl_3$, DMSO and ethyl ether, were also tested respectively, but the results were disappointing (Table 1, entry 2). The desired product was not even obtained in the neat reaction using acetophenone **1a** as both solvent and substrate (Table 1, entry 3). Treatment of the model reaction in dry DMF at room temperature gave **3a** in 30% yield (Table 1, entry 4),[9] although the yield was low, we were encouraged to examine the reaction in detail to increase the yield. Fortunately, a noticeable increase in the reaction rate and the 88% yield of **3a** was obtained by adding 10 mg molecular sieves (MS) 4 Å to the reaction system as additive (Table 1, entry 4 *vs.* 5).[10] We supposed

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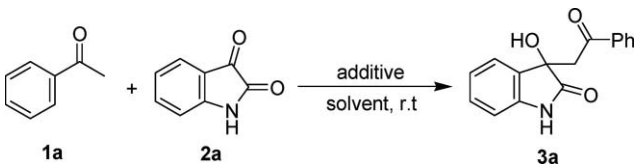
† Electronic supplementary information (ESI) available: ^{1}H NMR and ^{13}C NMR spectra. See DOI: 10.1039/b906684e

Table 1 Optimization of the reaction conditions[a]



1a **2a** **3a**

Entry	Solvent	Additive	Time/h	Yield (%)[b]
1	THF	—	24	trace
2	Dioxane (CH_3CN, CH_2Cl_2, toluene, $CHCl_3$, DMSO, ethyl ether)	—	24	—
3	neat	—	24	—
4	DMF	—	24	30
5	DMF	MS 4 Å	12	88
6	DMF	MS 3 Å	16	87
7	DMF	MS 5 Å	16	87
8	DMF	MS 4 Å	12	87[c]
9	NMP[d]	MS 4 Å	72	24

[a] All reactions were performed using isatin (1.0 mmol) and acetophenone (2.0 mmol) with 10 mg MS at room temperature. [b] Isolated yields of purified products. [c] Using 90 mg MS 4 Å as additive. [d] NMP is *N*-methyl-2-pyrrolidone.

that the molecular sieves might absorb the small amount of water present in the reaction system. Similar results were obtained at same reaction conditions when adding 10 mg MS 3 Å or MS 5 Å to the reaction system, respectively (Table 1, entries 6 and 7). We hoped to further increase the yield by adding 90 mg MS 4 Å, but found no significant improvement in the yield. Further examining NMP as solvent, the product **3a** was obtained only in 24% yield for 72 h (Table 1. entry 9). It is interesting that this reaction proceeded very well in DMF but worked poorly in other solvents. The exact reason for this is not clear, but we suppose that the DMF solvent acts like a poor base, which may have efficiently promoted this reaction with activated molecular sieves as additive under catalyst-free conditions. Accordingly, we chose dry DMF (solvent), 10 mg MS 4 Å (additive) and room temperature as the optimal reaction conditions.

With a set of optimized reaction conditions at hand, we firstly explored the scope of the reaction by using various aromatic ketones **1a–s** and isatin derivatives **2a–g**. The results are summarized in Table 2. It was found that all the reactions proceeded smoothly and afforded the desired adducts under the optimized reaction conditions. A wide range of acetophenone derivatives bearing electron-withdrawing (**1b–h**) and electron-donating (**1i–k**) groups on the phenyl ring could be employed in the aldol addition with free isatin (**2a**) and were nicely converted into corresponding products (**3b–k**) in moderate to good yields ranging from 66% to 94% (Table 2, entries 1–10). Strikingly, the reaction of **1h** addition to **2a** even completed in 3 h and provided the aldol adduct **3h** in as high as 95% isolated yield (Table 2, entry 7). The hetero-aromatic ketones, such as 2-thienyl (**1l**), 2-furanyl (**1m**) and 2-pyridyl ketones (**1n**) underwent the aldol reaction with free isatin (**2a**) to afford the products **3l**, **3m** and **3n** in 90%, 88% and 91% yield, respectively (Table 2, entries 11–13). Similar good results were observed in the cases of 1-acetonaphthone (**1o**) and 6-methoxy-1-acetonaphthone (**1p**) as substrates and the products were smoothly obtained in 80% and 90% yield, respectively, (Table 2, entries 14–15). Gratifying results were achieved in the examination of isatin derivatives bearing electron-withdrawing (**2b**, **2d** and **2e**) or electron-donating substituents (**2c**) at the phenyl ring (Table 2). It was found that all the isatin substrates worked well with aromatic ketones under the standard reaction conditions and afforded the desired aldol adducts in general over 70% yield (Table 2, entries 16–19).

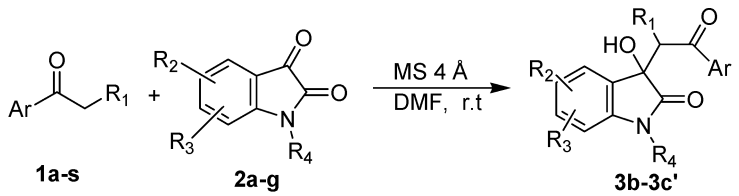
As a logical extension, we next studied the reactions of N-1 protected isatins **2f** and **2g** with ketones **1a**, **1k** and **1i**, respectively (Table 2, entries 20–25). It was found that in all cases the reactions proceeded smoothly and provided their corresponding products with good yields ranging from 80% to 95%. It was noteworthy that the *N*-benzyl adduct **3x** could be effectively achieved with 95% isolated yield in only 3 h at room temperature (Table 2, entry 23) and the *N*-methyl product **3w** could also be obtained with 89% isolated yield in 2.5 h (Table 2, entry 22). Further investigation on the scope of aromatic ketones was conducted by increasing the size of the alkyl substituent in acetophenone. As shown in Table 2, the substrates **1q**, **1r** and **1s** also worked well for the aldol condensation with free isatin **1a** (Table 2, entries 26–28). Generally, the aldol reaction tolerated a variety of different aromatic ketones and isatins and showed high reactivity in DMF with catalyst-free.

Encouraged by the above results, we hoped to further investigate the scope and limitations of this methodology, and so explored a series of aliphatic ketones as the aldol donors under the optimized reaction conditions. As shown in Table 3, the acyclic aliphatic ketones **1u**, **1v** and **1w** all reacted well with free isatin **2a** (Table 3, entries 1–3). However, in the case **1v** as substrate, the reaction only gave the adduct **3e′** with very high regioselectivity in 64% yield (Table 3, entries 2).[11] While using pentan-3-one **1w** as aldol donor, the product was obtained in 75% yield and 4.3 : 1 diasteroselectivity (Table 3, entries 2). On the other hand, the aldol reaction between cyclic aliphatic ketones **1x** and **1y** with free isatin **2a** also proceeded well under the optimized reaction conditions with as high as 87% yields, but the relatively poor diastereoselectivities of 2.6 : 1 and 1.1 : 1 were slightly imperfect (Table 3, entries 4–5). The success of the developed method prompted us to try conducting the reaction of acetone (**1u**) and 4,6-dibromoisatin (**2d**) under the optimal conditions to synthesise convolutamydine **A** (Table 3, entry 6), which was firstly isolated from the marine bryozoan species *Amathia convolute* by Kamano and co-workers in 1995, and its (*R*)-(+)-enantiomer was identified as an anti-leukemia agent (Table 3, entry 6).[12] The corresponding product **3i′** was smoothly obtained in 66% chemical yield under the optimized reaction conditions (Table 3, entry 6).

Conclusion

In conclusion, we have developed an efficient aldol reaction of a variety of aromatic and aliphatic ketones with isatins using DMF as solvent at room temperature under catalyst-free. Various desired products, 3-substituted-3-hydroxyindolin-2-ones, were smoothly obtained with good to excellent chemical yields. This approach has the following prominent advantages: (1) catalyst free, (2) very mild reaction condition, (3) high efficiency, (4) very wide-scope of substrate. Further investigation to develop

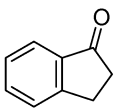
Table 2 Aldol condensation of aromatic acetones and isatins with catalyst-free[a]



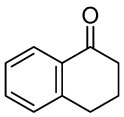
1a-s **2a-g** **3b-3c'**

Ar = C_6H_5, R_1= H **(1a)**
4-ClC_6H_4, R_1= H **(1b)**
3-ClC_6H_4, R_1= H **(1c)**
2-ClC_6H_4, R_1= H **(1d)**
4-$NO_2C_6H_4$, R_1= H **(1e)**
4-FC_6H_4, R_1= H **(1f)**
3-BrC_6H_4, R_1= H **(1g)**
4-BrC_6H_4, R_1= H **(1h)**
2-HOC_6H_4, R_1= H **(1i)**
4-MeC_6H_4, R_1 = H **(1j)**
4-$MeOC_6H_4$, R_1 = H **(1k)**

2-thienyl, R_1 = H **(1l)**
2-furanyl, R_1 = H **(1m)**
2-pyridinyl, R_1 = H **(1n)**
1-naphthyl, R_1 = H **(1o)**
6-MeO-1-naphthyl, R_1 = H **(1p)**
C_6H_5, R_1 = CH_3 **(1q)**



1r



1s

2a R_2 = H, R_3 = H, R_4 = H
2b R_2 = 5-Br, R_3 = H, R_4 = H
2c R_2 = 6-CH_3, R_3 = 7-CH_3, R_4 = H
2d R_2 = 4-Br, R_3 = 6-Br, R_4 = H
2e R_2 = 5-Br, R_3 = 7-Br, R_4 = H
2f R_2 = H, R_3 = H, R_4 = CH_3
2g R_2 = H, R_3 = H, R_4 = Bn

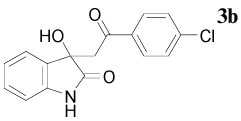
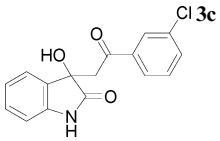
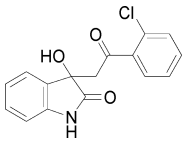
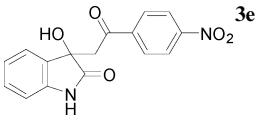
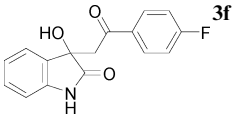
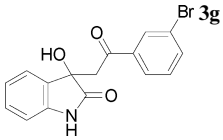
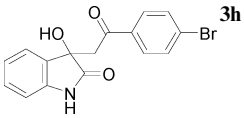
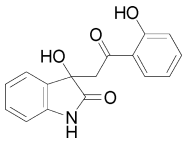
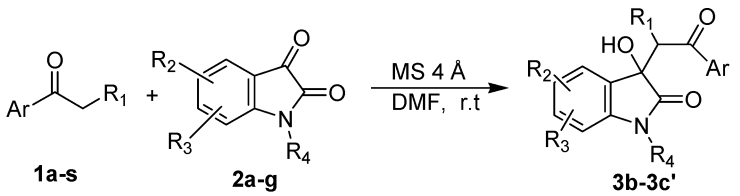
Entry	Ketones **1**	Isatins **2**	Products **3**	Time/h	Yield (%)[b]
1	**1b**	**2a**	 **3b**	48	88
2	**1c**	**2a**	 **3c**	48	80
3	**1d**	**2a**	 **3d**	9	87
4	**1e**	**2a**	 **3e**	48	80
5	**1f**	**2a**	 **3f**	16	80
6	**1g**	**2a**	 **3g**	10	87
7	**1h**	**2a**	 **3h**	3	94
8	**1i**	**2a**	 **3i**	16	66

Table 2 *(Contd.)*



1a-s **2a-g** **3b-3c'**

Ar = C_6H_5, R_1= H **(1a)**
4-ClC_6H_4, R_1= H **(1b)**
3-ClC_6H_4, R_1= H **(1c)**
2-ClC_6H_4, R_1= H **(1d)**
4-$NO_2C_6H_4$, R_1= H **(1e)**
4-FC_6H_4, R_1= H **(1f)**
3-BrC_6H_4, R_1= H **(1g)**
4-BrC_6H_4, R_1= H **(1h)**
2-HOC_6H_4, R_1= H **(1i)**
4-MeC_6H_4, R_1 = H **(1j)**
4-$MeOC_6H_4$, R_1 = H **(1k)**

2-thienyl, R_1 = H **(1l)**
2-furanyl, R_1 = H **(1m)**
2-pyridinyl, R_1 = H **(1n)**
1-naphthyl, R_1 = H **(1o)**
6-MeO-1-naphthyl, R_1 = H **(1p)**
C_6H_5, R_1 = CH_3 **(1q)**

1r **1s**

2a R_2 = H, R_3 = H, R_4 = H
2b R_2 = 5-Br, R_3 = H, R_4 = H
2c R_2 = 6-CH_3, R_3 = 7-CH_3, R_4 = H
2d R_2 = 4-Br, R_3 = 6-Br, R_4 = H
2e R_2 = 5-Br, R_3 = 7-Br, R_4 = H
2f R_2 = H, R_3 = H, R_4 = CH_3
2g R_2 = H, R_3 = H, R_4 = Bn

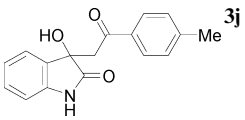
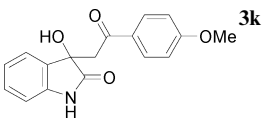
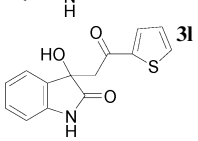
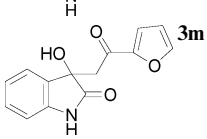
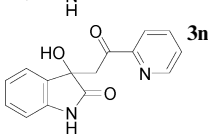
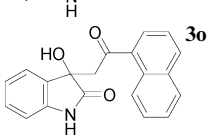
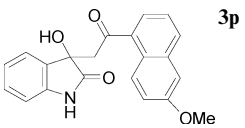
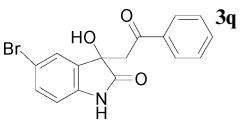
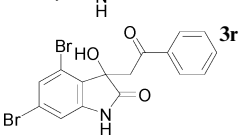
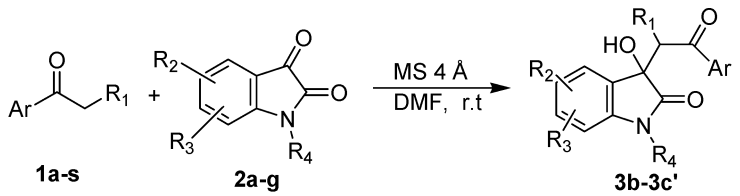
Entry	Ketones **1**	Isatins **2**	Products **3**	Time/h	Yield (%)[b]
9	**1j**	**2a**	 **3j**	18	87
10	**1k**	**2a**	 **3k**	48	89
11	**1l**	**2a**	 **3l**	24	90
12	**1m**	**2a**	 **3m**	20	88
13	**1n**	**2a**	 **3n**	12	91
14	**1o**	**2a**	 **3o**	42	80
15	**1p**	**2a**	 **3p**	24	90
16	**1a**	**2b**	 **3q**	20	80
17	**1a**	**2d**	 **3r**	24	82

Table 2 *(Contd.)*



1a-s **2a-g** **3b-3c'**

Ar = C_6H_5, R_1= H **(1a)**
4-ClC_6H_4, R_1= H **(1b)**
3-ClC_6H_4, R_1= H **(1c)**
2-ClC_6H_4, R_1= H **(1d)**
4-$NO_2C_6H_4$, R_1= H **(1e)**
4-FC_6H_4, R_1= H **(1f)**
3-BrC_6H_4, R_1= H **(1g)**
4-BrC_6H_4, R_1= H **(1h)**
2-HOC_6H_4, R_1= H **(1i)**
4-MeC_6H_4, R_1 = H **(1j)**
4-$MeOC_6H_4$, R_1 = H **(1k)**

2-thienyl, R_1 = H **(1l)**
2-furanyl, R_1 = H **(1m)**
2-pyridinyl, R_1 = H **(1n)**
1-naphthyl, R_1 = H **(1o)**
6-MeO-1-naphthyl, R_1 = H **(1p)**
C_6H_5, R_1 = CH_3 **(1q)**

1r **1s**

2a R_2 = H, R_3 = H, R_4 = H
2b R_2 = 5-Br, R_3 = H, R_4 = H
2c R_2 = 6-CH_3, R_3 = 7-CH_3, R_4 = H
2d R_2 = 4-Br, R_3 = 6-Br, R_4 = H
2e R_2 = 5-Br, R_3 = 7-Br, R_4 = H
2f R_2 = H, R_3 = H, R_4 = CH_3
2g R_2 = H, R_3 = H, R_4 = Bn

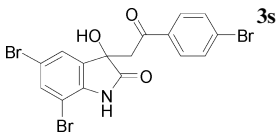
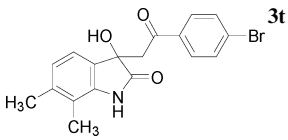
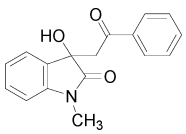
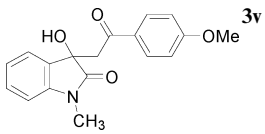
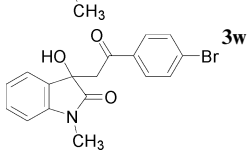
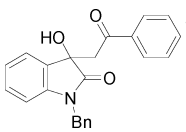
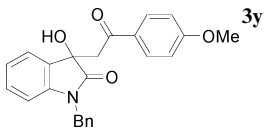
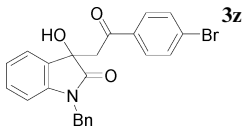
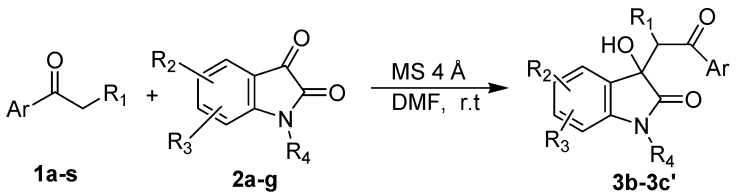
Entry	Ketones **1**	Isatins **2**	Products **3**	Time/h	Yield (%)[b]
18	**1i**	**2e**	**3s** 	36	70
19	**1i**	**2c**	**3t** 	16	84
20	**1a**	**2f**	**3u** 	12	90
21	**1k**	**2f**	**3v** 	24	87
22	**1i**	**2f**	**3w** 	2.5	89
23	**1a**	**2g**	**3x** 	3	95
24	**1k**	**2g**	**3y** 	24	80
25	**1i**	**2g**	**3z** 	5	90

Table 2 *(Contd.)*



1a-s **2a-g** **3b-3c'**

Ar = C_6H_5, R_1= H **(1a)**
4-ClC_6H_4, R_1= H **(1b)**
3-ClC_6H_4, R_1= H **(1c)**
2-ClC_6H_4, R_1= H **(1d)**
4-$NO_2C_6H_4$, R_1= H **(1e)**
4-FC_6H_4, R_1= H **(1f)**
3-BrC_6H_4, R_1= H **(1g)**
4-BrC_6H_4, R_1= H **(1h)**
2-HOC_6H_4, R_1= H **(1i)**
4-MeC_6H_4, R_1 = H **(1j)**
4-MeOC_6H_4, R_1 = H **(1k)**

2-thienyl, R_1 = H **(1l)**
2-furanyl, R_1 = H **(1m)**
2-pyridinyl, R_1 = H **(1n)**
1-naphthyl, R_1 = H **(1o)**
6-MeO-1-naphthyl, R_1 = H **(1p)**
C_6H_5, R_1 = CH_3 **(1q)**

1r **1s**

2a R_2 = H, R_3 = H, R_4 = H
2b R_2 = 5-Br, R_3 = H, R_4 = H
2c R_2 = 6-CH_3, R_3 = 7-CH_3, R_4 = H
2d R_2 = 4-Br, R_3 = 6-Br, R_4 = H
2e R_2 = 5-Br, R_3 = 7-Br, R_4 = H
2f R_2 = H, R_3 = H, R_4 = CH_3
2g R_2 = H, R_3 = H, R_4 = Bn

Entry	Ketones **1**	Isatins **2**	Products **3**	Time/h	Yield (%)[b]
26	**1q**	**2a**	**3a′**	24	91[c]
27	**1r**	**2a**	**3b′**	9	80[d]
28	**1s**	**2a**	**3c′**	36	63[e]

[a] All reactions were performed using isatins (1.0 mmol) and aromatic ketones (2.0 mmol) with 10 mg MS 4 Å in DMF at room temperature. [b] Isolated yields of purified products. [c] The diastereoselectivity was determined by ^{1}H NMR and erythro : threo = 3.4 : 1. [d] The diastereoselectivity was determined by ^{1}H NMR and erythro : threo = 3.4 : 1. [e] The diastereoselectivity was determined by ^{1}H NMR and erythro : threo = 8.1 : 1.

more efficient and convenient reactions from a green chemistry viewpoint is under way in our laboratory.

Experimental

General information

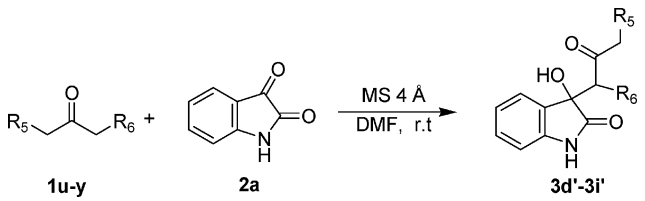
^{1}H NMR spectra were recorded on Bruker NMR spectrometers at 300 MHz. ^{13}C NMR spectra were recorded on Bruker NMR spectrometers at 75 MHz. IR spectra were recorded in KBr or neat on a Nicolet (MX-1E FT-IR) spectrometer. HRMS spectra were recorded on Bruker ESI-Q-TOF mass spectrometer, microTOF Q II. All melting points were uncorrected. All the reagents were purchased from commercial sources. Solvents used in this work are reagent grade and were purified by distillation prior to use. DMF solvent must be sufficiently refluxed in calcium hydride for 5 h and distilled from calcium hydride before use. MS 4 Å must be activated sufficiently before use.

General procedure for the aldol condensation reaction of ketones and isatins with catalyst-free

To a solution of isatins **2** (0.5 mmol) in freshly distilled DMF (1.5 mL) was added ketones **1** (1.0 mmol) in the presence of sufficiently activated MS 4Å (10 mg). The reaction mixture was stirred at room temperature for several hours and was monitored by TLC. When the isatins **2** fully disappeared, then the solvent was removed under reduced pressure to obtain the crude products. The crude products were purified by silica gel chromatography using ethyl acetate : petroleum ether = 1 : 3 to 1 : 1 as eluent to give the corresponding products **3**.

3-Hydroxy-3-(2-oxo-2-phenylethyl)indolin-2-one[13] **(3a).** White solid, mp 196.6–197.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.25 (brs, 1H), 7.88–7.86 (m, 2H), 7.60 (d, J = 7.2 Hz, 1H), 7.51–7.46 (m, 2H), 7.26 (d, J = 7.2 Hz, 1H), 7.18–7.12 (m, 1H), 6.87–6.79 (m, 2H), 6.05 (br s, 1H), 4.05 (d, J = 17.4 Hz, 1H), 3.56 (d, J = 17.4 Hz, 1H);^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.8,

Table 3 Aldol condensation of aliphatic acetones and isatins with catalyst-free[a]



Entry	Ketones **1**	Products **3**	Time/h	d.r. (erythro/threo)[b]	yield (%)[c]
1	**1u**	**3d′**	18	—	70
2	**1v**	**3e′**	14	—	64
3	**1w**	**3f′**	18	4.3 : 1	75
4	**1x**	**3g′**	14	2.6 : 1	87
5	**1y**	**3h′**	12	1.1 : 1	87
6	**1u**	**3i′**	20	—	66

[a] All reaction were performed using isatin (1.0 mmol) and ketones (2.0 mmol) with 10 mg MS 4 Å at room temperature. [b] The diastereoselectivity was determined with ^{1}H NMR. [c] Isolated yields of purified products.

73.0, 109.4, 121.1, 123.6, 127.9, 128.7, 128.9, 131.7, 133.4, 136.2, 142.9, 178.4, 196.5; IR (KBr) 3401.3, 3258.1, 3072.0, 2908.2, 1716.5, 1683.1, 1619.7, 1471.1, 1354.9, 753.7, 690.8 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{13}NNaO_3$ ([M + Na]$^+$): 290.0788, found: 290.0794.

3-Hydroxy-3-(2-oxo-2-(4-chlorophenyl)ethyl)indolin-2-one (3b). White solid, mp 196–197.4 °C;^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.28 (brs, 1H), 7.90 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 7.27 (d, J = 7.2 Hz, 1H), 7.16 (m, 1H), 6.88–6.80 (m, 2H), 6.09 (brs, 1H), 4.03 (d, J = 17.4 Hz, 1H), 3.57 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.8, 73.0, 109.4, 121.2, 123.7, 128.8, 129.2, 129.8, 131.6, 134.9, 138.4,. 142.9, 178.3, 195.6; IR (KBr) 3373.7, 3191.9, 3056.4, 3035.6, 2898.8, 1699.3, 1680.6, 1622.2, 1468.0, 1209.8, 747.7 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}ClNNaO_3$ ([M + Na]$^+$): 324.0398, found: 324.0393.

3-Hydroxy-3-(2-oxo-2-(3-chlorophenyl)ethyl)indolin-2-one (3c). White solid, mp 197.8–198.9 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.26 (brs, 1H), 7.88 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 6.87–6.78 (m, 2H), 6.07 (brs, 1H), 4.03 (d, J = 17.4 Hz, 1H), 3.55 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.8, 73.1, 109.5, 121.3, 123.7, 126.7, 127.6, 128.8, 129.9, 130.8, 131.6, 133.1, 138.0, 142.9, 178.3, 195.6; IR (KBr) 3372.4, 3193.5, 3057.0, 2899.5, 1695.5, 1681.1, 1584.3, 1486.2, 1210.1, 747.8 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}ClNNaO_3$ ([M + Na]$^+$): 324.0398, found: 324.0393.

3-Hydroxy-3-(2-oxo-2-(2-chlorophenyl)ethyl)indolin-2-one (3d). White solid, mp 189.5–190.5 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.31 (brs, 1H), 7.49–7.39 (m, 4H), 7.31 (d, J = 7.5 Hz, 1H), 7.21–7.16 (m, 1H), 6.91–6.83 (m, 1H), 6.82 (d, J = 7.5 Hz, 1H), 6.14 (brs, 1H), 3.89 (d, J = 16.8 Hz, 1H), 3.53 (d, J = 16.8 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 49.6, 73.1, 109.5, 121.3, 123.9, 127.3, 129.1, 129.3, 129.7, 130.4, 131.1, 132.5, 138.0, 142.8, 177.9, 198.7; IR (KBr) 3341.1, 3201.4, 3058.5, 2885.1, 1698.0, 1682.2, 1620.6, 1647.8, 753.5 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}ClNNaO_3$ ([M + Na]$^+$): 324.0398, found: 324.0393.

3-Hydroxy-3-(2-oxo-2-(4-nitrophenyl)ethyl)indolin-2-one (3e). White solid, mp 190.2–190.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.32 (brs, 1H), 8.28–8.12 (m, 4H), 7.29–6.84 (m,

4H), 6.15 (brs, 1H), 4.10 (d, $J = 15.3$, 1H), 3.64 (d, $J = 15.3$, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 46.3, 73.1, 109.5, 121.2, 123.8, 129.1, 129.4, 131.4, 140.7, 142.8, 149.9, 178.1, 195.9; IR (KBr) 3379.0, 3189.3, 3065.3, 2895.0, 1730.6, 1695.9, 1625.9, 1343.0, 1205.9, 746.4 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}N_2NaO_5$ ([M + Na]$^+$): 335.0638, found: 335.0639.

3-Hydroxy-3-(2-oxo-2-(4-fluorophenyl)ethyl)indolin-2-one (3f). White solid, mp 198.9–199.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.26 (brs, 1H), 7.97 (dd, J = 5.4, 8.7 Hz, 2H), 7.33–7.26 (m, 4H), 6.84 (dd, J = 7.8, 8.4 Hz, 2H), 6.06 (brs, 1H), 4.04 (d, J = 17.7 Hz, 1H), 3.56 (d, J = 17.7 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.7, 73.0, 109.4, 115.8, 121.1, 123.6, 128.9, 130.9, 133.0, 142.9, 163.4, 166.8, 178.3, 195.1; IR (KBr) 3379.3, 3196.1, 3059.6, 2898.5, 1699.9, 1679.1, 1619.1, 1468.6, 1229.5, 755.0 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}FNNaO_3$ ([M + Na]$^+$): 308.0693, found: 308.0701.

3-Hydroxy-3-(2-oxo-2-(3-bromorophenyl)ethyl)indolin-2-one (3g). White solid, mp 191.8–192.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.29 (brs, 1H), 7.99 (s, 1H), 7.89 (d, J = 5.7 Hz, 1H), 7.90 (d, J = 6.3 Hz, 1H), 7.45–7.44 (m, 1H), 7.28 (d, J = 5.4 Hz, 1H), 7.18–7.17 (m, 1H), 6.86–6.83 (m, 2H), 6.09 (brs, 1H), 4.08 (d, J = 17.2 Hz, 1H), 3.57 (d, J = 17.2 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.9, 73.0, 109.4, 121.2, 122.1, 123.8, 127.0, 129.0, 130.5, 130.9,131.5, 135.9, 138.2, 142.8, 178.2, 195.5; IR (KBr) 3395.6, 3342.3, 3281.5, 3061.2, 2901.1, 1726.0, 1680.0, 1620.7, 1471.5, 1206.9, 777.9 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}BrNNaO_3$ ([M + Na]$^+$): 367.9893, found: 367.9884.

3-Hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)indolin-2-one (3h). White solid, mp 194.1–194.7 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.28 (brs, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 6.9 Hz, 1H), 7.15 (d, J = 7.5, 1H), 6.88–6. 80 (m, 2H), 6.09 (brs, 1H), 4.05 (d, J = 17.4 Hz, 1H), 3.55 (d, J = 17.4, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.7, 73.0, 109.4, 121.2, 123.7, 127.6, 128.9, 129.9, 131.6, 131.8, 135.2, 142.9, 178.2, 195.8; IR (KBr) 3369.2, 3198.7, 3059.8, 2899.6, 1703.6, 1687.4, 1621.8, 1467.6, 1208.4, 987.8, 749.0 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{12}BrNNaO_3$ ([M + Na]$^+$): 367.9893, found: 367.9884.

3-Hydroxy-3-(2-oxo-2-(2-hydroxyphenyl)ethyl)indolin-2-one (3i). White solid, mp 197.2–197.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 11.34 (brs, 1H), 10.29 (brs, 1H), 7.81–7.79 (m, 1H), 7.47–7.45 (m, 1H), 7.27 (d, J = 7.2 Hz, 2H), 7.19–7.15 (m, 1H), 6.93–6.81 (m, 4H), 6.10 (brs, 1H), 4.10 (d, J = 17.7 Hz, 1H), 3.66 (d, J = 17.7 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 47.3, 72.9, 109.5, 117.6, 119.2, 120.8, 121.2, 123.6, 129.0, 130.7, 131.6, 136.0, 142.8, 160.1, 178.3, 201.4; IR (KBr) 3370.7, 3262.6, 3041.6, 2906.3, 1711.7, 1636.9, 1615.8, 1466.4, 1278.0, 1063.0, 751.2, 582.7 cm^1. HRMS (ESI): Calculated for $C_{16}H_{13}NNaO_4$ ([M + Na]$^+$): 306.0737, found: 306.0747.

3-Hydroxy-3-(2-oxo-2-*p*-tolylethyl)indolin-2-one (3j). White solid, mp 191.5–192.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.25 (brs, 1H), 7.78 (d, J = 8.1 Hz, 2H), 7.30–7.13 (m, 3H), 7.15 (m, 1H), 6.83 (dd, J = 7.2, 16.2 Hz, 2H), 6.04 (brs, 1H), 4.03 (d, J = 17.5 Hz, 1H), 3.54 (d, J = 17.5 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 21.1, 45.6, 73.0, 109.4, 121.1, 123.6, 128.0, 128.9, 129.2, 131.8, 133.8, 142.9, 143.8, 178.4, 195.9; IR (KBr) 3372.2, 3205.0, 3055.7, 2896.6, 1721.8, 1700.7, 1675.2, 1619.8, 1176.8, 754.9 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{15}NNaO_3$ ([M + Na]$^+$): 304.0944, found: 304.0951.

3-Hydroxy-3-(2-oxo-2-(4-methoxyphenyl)ethyl)indolin-2-one (3k). White solid, mp 181.2–183.7 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.25 (brs, 1H), 7.86 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 7.2 Hz, 1H), 7.18–7.12 (m, 1H), 7.00 (d, J = 8.7 Hz, 2H), 6.87–6.79 (m, 2H), 6.03 (brs, 1H), 4.01 (d, J = 17.4 Hz, 1H), 3.81 (s, 3H), 3.53 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.4, 55.5, 73.1, 109.4, 113.8, 121.1, 123.6, 128.9, 129.2, 130.3, 131.9, 142.9, 163.3, 178.4, 194.8; IR (KBr) 3381.4, 3194.4, 3053.9, 2901.4, 1722.1, 1697.4, 1668.4, 1600.5, 1468.9, 1256.6, 1166.8, 990.9, 579.9 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{15}NNaO_4$ ([M + Na]$^+$): 320.0893, found: 320.0897.

3-Hydroxy-3-(2-oxo-2-(thiophen-2-yl)ethyl)indolin-2-one (3l). White solid, mp 180.8–181.5 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.27 (brs, 1H), 7.97 (d, J = 12.0 Hz, 2H), 7.29–7.15 (m, 3H), 6.82 (dd, J = 7.2, 16.2 Hz, 2H), 6.12 (brs, 1H), 3.96 (d, J = 16.2 Hz, 1H), 3.48 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.9, 73.0, 109.5, 121.2, 123.8, 128.8, 129.0, 131.4, 133.9, 135.2, 142.8, 143.5, 178.2, 189.3, IR (KBr) 3374.5, 3302.2, 3055.7, 2900.5, 1701.5, 1653.8, 1617.0, 1413.0, 1225.9, 725.1 cm^{-1}. HRMS (ESI): Calculated for $C_{14}H_{11}NNaO_3S$ ([M + Na]$^+$): 296.0352, found: 296.0362.

3-(2-(Furan-2-yl)-2-oxoethyl)-3-hydroxyindolin-2-one (3m). White solid, mp 195.7–196.2 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.26 (brs, 1H), 7.92 (s, 1H), 7.46 (d, J = 3.6 Hz, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.13 (dd, J = 6.6, 7.5 Hz, 1H), 6.86–6.67 (m, 2H), 6.66 (d, J = 1.5 Hz, 1H), 6.11 (brs, 1H), 3.78 (d, J = 16.2 Hz, 1H), 3.30 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.2, 73.0, 109.4, 112.5, 119.1, 121.2, 123.9, 129.0, 131.1, 142.6, 147.9, 151.6, 178.0, 184.3; IR (KBr) 3342.7, 3297.2, 3096.2, 2917.8, 1723.4, 1657.1, 1617.8, 1461.9, 760.6 cm^{-1}. HRMS (ESI): Calculated for $C_{14}H_{11}NNaO_4$ ([M + Na]$^+$): 280.0580, found: 280.0579.

3-Hydroxy-3-(2-oxo-2-(pyridin-2-yl)ethyl)indolin-2-one (3n). White solid, mp 154.1–155.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.29 (brs, 1H), 8.74–7.92 (m, 1H), 7.94–7.91 (m, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 1.5 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.15–7.14 (m, 1H), 6.85–6.80 (m, 2H), 6.13 (brs, 1H), 4.28 (d, J = 17.7 Hz, 1H), 3.65 (d, J = 17.7 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 44.9, 73.0, 109.4, 121.1, 121.2, 123.6, 127.9, 128.9, 131.6, 137.6, 142.9, 149.2, 152.2, 178.3, 197.7; IR (KBr) 3441.3, 3303.8, 3263.6, 3083.9, 1715.9, 1697.1, 1618.0, 1470.3, 996.0, 768.8 cm^{-1}. HRMS (ESI): Calculated for $C_{15}H_{12}N_2NaO_3$ ([M + Na]$^+$): 291.0740, found: 291.0738.

3-Hydroxy-3-(2-(naphthalen-1-yl)-2-oxoethyl)indolin-2-one (3o). White solid, mp 170.5–172.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.32 (brs, 1H), 8.09 (d, J = 7.5 Hz, 2H), 8.02 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.52–7.46 (m, 2H), 7.34 (d, J = 7.2 Hz, 1H), 7.17 (d, J = 1.2 Hz, 1H), 6.86–6.80 (m, 2H), 6.14 (brs, 1H), 4.07 (d, J = 16.8 Hz, 1H), 3.73 (d, J = 16.8 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 49.1, 73.4, 109.5, 121.2, 123.8, 124.7, 124.9, 126.3,. 127.5, 128.1, 128.3, 128.9, 129.1, 131.5, 132.5, 133.3, 135.1,

142.8, 178.2, 200.7; IR (KBr) 3378.6, 3212.9, 3058.1, 2881.8, 1697.6, 1671.8, 1471.8, 777.2 cm^{-1}. HRMS (ESI): Calculated for $C_{20}H_{15}NNaO_3$ ([M + Na]$^+$): 340.0944, found: 340.0961.

3-Hydroxy-3-(2-(6-methoxynaphthalen-1-yl)-2-oxoethyl)indolin-2-one (3p). White solid, mp 205.6–207.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.27 (brs, 1H), 8.60 (s, 1H), 8.05 (d, J = 9.0 Hz, 1H), 8.02–7.79 (m, 2H), 7.37 (d, J = 2.4 Hz, 1H), 7.30–7.23 (m, 2H), 7.15 (d, J = 1.1 Hz, 1H), 6.86–6.80 (m, 2H), 6.09 (brs, 1H), 4.18 (d, J = 17.4 Hz, 1H), 3.90 (s, 3H), 3.66 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.5, 55.3, 73.1, 106.1, 109.3, 119.4, 120.9, 123.5, 123.8, 126.9, 127.3, 128.8, 131.0, 131.2, 131.5, 131.7, 136.9, 142.9, 159.4, 178.3, 195.9; IR (KBr) 3380.7, 3349.7, 3057.6, 2957.4, 2894.7, 1721.1, 1673.2, 1620.1, 1482.8, 1175.4, 748.8 cm^{-1}. HRMS (ESI): Calculated for $C_{21}H_{17}NNaO_4$ ([M + Na]$^+$): 370.1050, found: 370.1037.

5-Bromo-3-hydroxy-3-(2-oxo-2-phenylethyl)indolin-2-one (3q). White solid, mp 213.8–216.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.42 (brs, 1H), 7.89 (d, J = 7.2 Hz, 2H), 7.87–7.61 (m, 1H), 7.53–7.48 (m, 3H), 7.34 (dd, J = 6.3, 8.1 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.20 (brs, 1H), 4.16 (d, J = 17.8 Hz, 1H), 3.63 (d, J = 17.8 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.7, 73.0, 111.4, 112.9, 126.7, 127.9, 128.7, 131.5, 133.5, 134.4, 135.9, 142.3, 177.9, 196.6; IR (KBr) 3219.5, 2892.9, 1698.2, 1618.7, 1218.6, 827.0 cm^{-1}. HRMS (ESI): $C_{16}H_{12}BrNNaO_3$ ([M + Na]$^+$): 367.9893, found: 367.9889.

4,6-Dibromo-3-hydroxy-3-(2-oxo-2-phenylethyl)indolin-2-one (3r). White solid, mp 187.0–188.2 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.73 (brs, 1H), 7.91 (d, J = 7.5 Hz, 2H), 7.63–7.47 (m, 3H), 7.23 (s, 1H), 7.01 (s, 1H), 6.39 (brs, 1H), 4.46 (d, J = 18.3 Hz, 1H), 3.69 (d, J = 18.3 Hz, 1H);^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 44.2, 74.3, 111.9, 118.9, 122.4, 126.7, 127.8, 128.91, 128.97, 133.8, 135.5, 146.7, 177.4, 196.5; IR (KBr) 3369.1, 3305.2, 3083.0, 3033.5, 1712.1, 1686.7, 1676.7, 1611.0, 1349.3, 1218.2, 689.6 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{11}Br_2NNaO_3$ ([M + Na]$^+$): 445.9003, found: 445.9027.

5,7-Dibromo-3-hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)-indolin-2-one (3s). White solid, mp 142.7–145.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.81 (brs, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.72 (d, J = 8.1 Hz, 2H), 7.61 (s, 1H), 7.55 (s, 1H), 6.41 (brs, 1H), 4.20 (d, J = 18.3 Hz, 1H), 3.67 (d, J = 18.3 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 45.9, 73.8, 102.6, 113.5, 125.9, 127.9, 130.1, 131.8, 133.5, 134.7, 135.6, 142.0, 177.8, 196.0; IR (KBr) 3241.5, 2956.4, 2904.3, 1736.1, 1682.8, 1616.5, 1584.9, 1460.3, 1215.8, 1161.6, 1071.3, 567.6 cm^{-1}. HRMS (ESI): Calculated for $C_{16}H_{10}Br_3NNaO_3$ [M + Na]$^+$): 523.8103, found: 523.8084.

6,7-Dimethyl-3-hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)-indolin-2-one (3t). White solid, mp 179.8–181.2 °C ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.27 (brs, 1H), 7.82 (d, J = 7.8 Hz, 2H), 7.68 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 7.2 Hz, 1H), 6.67 (d, J = 7.2 Hz, 1H), 5.80 (brs, 1H), 3.99 (d, J = 17.4 Hz, 1H), 3.54 (d, J = 17.4 Hz, 1H), 2.16 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 13.1, 19.7, 45.8, 73.4, 117.4, 120.7, 122. 4, 127.6, 129.0, 130.0, 131.8, 135.3, 137.4, 141.5, 179.0, 195.8; IR (KBr) 3262.4, 2985.3, 2919.7, 1715.6, 1697.0, 1681.9, 1585.1, 1399.0, 1211.4 cm^{-1}. HRMS (ESI): Calculated for $C_{18}H_{16}BrNNaO_3$ ([M + Na]$^+$): 396.0206, found: 396.0226.

1-Methyl-3-hydroxy-3-(2-oxo-2-phenylethyl)indolin-2-one (3u). White solid, mp 176.5–178.0 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.88 (d, J = 7.2 Hz, 2H), 7.86–7.61 (m, 1H), 7.51–7.46 (m, 2H), 7.35–7.33 (m, 1H), 7.27–7.24 (m, 1H), 6.99–6.94 (m, 2H), 6.16 (brs, 1H), 4.15 (d, J = 17.7 Hz, 1H), 3.66 (d, J = 17.7 Hz, 1H), 3.15 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 25.9, 46.1, 72.7, 108.2, 121.8, 123.2, 127.9, 128.7, 129.1, 131.1, 133.5, 136.0, 144.4, 176.7, 196.5; IR (KBr) 338434, 3308.3, 3059.5, 2936.0, 1710, 1615.8, 1469.0, 1352.7, 767.4 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{15}NNaO_3$ ([M + Na]$^+$): 304.0944, found: 304.0949.

1-Methyl-3-hydroxy-3-(2-oxo-2-(4-methoxyphenyl)ethyl)-indolin-2-one (3v). White solid, mp 192.3–193.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.85 (d, J = 7.5 Hz, 2H), 7.33–7.26 (m, 2H), 7.00–6.98 (m, 4H), 6.11 (brs, 1H), 4.08 (d, J = 17.7 Hz, 1H), 3.81 (s, 3H), 3.57 (d, J = 17.7 Hz, 1H), 3.15 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 25.9, 45.7, 55.5, 72.7, 108.2, 113.8, 121.8, 123.1, 129.0, 130.3, 131.2, 144.4, 163.3, 176.8, 194.7; IR (KBr) 3362.3, 3089.5, 2952.5, 1689.8, 1672.0, 1599.4, 1265.2, 1169.2, 756.5 cm^{-1}. HRMS (ESI): Calculated for $C_{18}H_{17}NNaO_4$ ([M + Na]$^+$): 334.1050, found: 334.1060.

1-Methyl-3-hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)-indolin-2-one (3w). White solid, mp 165.0–166.2 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 1H), 7.29–7.27 (m, 1H), 6.99–6.93 (m, 2H), 6.20 (brs, 1H), 4.13 (d, J = 17.4 Hz, 1H), 3.65 (d, J = 17.4 Hz, 1H), 3.16 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 25.99, 46.0, 72.7, 108.3, 121.9, 123.3, 127.7, 129.2, 129.9, 130.9, 131.8, 135.0, 144.3, 176.6, 195.8; IR (KBr) 3340.8, 3060.7, 2930.5, 2902.4, 1687.5, 1617.6, 1588.8, 1470.9, 1071.0, 753.4 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{14}BrNNaO_3$ ([M + Na]$^+$): 382.0049, found: 382.0073.

1-Benzyl-3-hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)indolin-2-one (3x). White solid, mp 189.9–191.4 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.93 (d, J = 6.9 Hz, 2H), 7.61 (d, J = 6.6 Hz, 1H), 7.50–6.91 (m, 10H), 6.79 (d, J = 7.2 Hz, 1H), 6.37 (brs, 1H), 4.95 (s, 2H), 4.25 (d, J = 17.7 Hz, 1H), 3.78 (d, J = 17.7 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 42.8, 46.0, 72.9, 108.9, 122.0, 123.4, 127.3, 128.0, 128.5, 128.8, 129.0, 131.2, 133.6, 136.0, 136.5, 143.5, 176.9, 196.6; IR (KBr) 3401.0, 3321.2, 3261.2, 3074.3, 3031.6, 2908.2, 1715.0, 1696.9, 1681.5, 1349.8, 1215.8, 767.0 cm^{-1}. HRMS (ESI): Calculated for $C_{23}H_{19}NNaO_3$ ([M + Na]$^+$): 380.1257, found: 380.1249.

1-Benzyl-3-hydroxy-3-(2-oxo-2-(4-methoxyphenyl)ethyl)-indolin-2-one (3y). White solid, mp 161.0–162.9 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.91 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 7.5 Hz, 2H), 7.38–7.33 (m, 3H), 7.29 (d, J = 7.5 Hz, 1H), 7.18–7.13 (m, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.94–6.89 (m, 1H), 6.76 (d, J = 7.8 Hz, 1H), 6.31 (brs, 1H), 4.93 (s, 2H), 4.16 (d, J = 17.4 Hz, 1H), 3.81 (s, 3H), 3.70 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 42.8, 45.7, 55.6, 72.9, 108.9, 113.9, 121.9, 123.4, 127.3, 128.5, 128.9, 129.1, 130.4, 131.3, 136.5, 143.5, 163.4, 177.0, 194.8; IR (KBr) 3042.3, 3084.9, 3029.8, 2927.1, 1694.5, 1673.9, 1602.3, 1245.8, 1172.0, 772.5 cm^{-1}. HRMS (ESI): Calculated for $C_{24}H_{21}NNaO_4$ ([M + Na]$^+$): 410.1363, found: 410.1365.

1-Benzyl-3-hydroxy-3-(2-oxo-2-(4-bromophenyl)ethyl)indolin-2-one (3z). White solid, mp 184.5–184.9 °C; 1H NMR (300 MHz, $(CD_3)_2SO$) δ 7.84 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.35–7.25 (m, 4H), 7.19–7.13 (m, 1H), 6.95–6.90 (m, 1H), 6.77 (d, J = 7.5 Hz, 1H), 6.35 (brs, 1H), 4.92 (s, 2H), 4.19 (d, J = 17.4 Hz, 1H), 3.73 (d, J = 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 42.8, 45.9, 72.8, 109.0, 122.0, 123.5, 127.3, 127.8, 128.5,. 129.1, 130.1, 131.0, 131.8, 135.0, 136.4, 143.4, 176.8, 195.8; IR (KBr) 3326.7, 3085.4, 3060.4, 2924.8, 1704.3, 1686.9, 1614.6, 1467.6, 1654.5, 1347.3, 750.2 cm^{-1}. HRMS (ESI): Calculated for $C_{23}H_{18}BrNNaO_3$ ([M + Na]$^+$): 458.0362, found: 458.0374.

3-Hydroxy-3-(1-oxo-1-phenylpropan-2-yl)indolin-2-one (3a′). Major isomer: white solid, mp 140.4–142.7 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$,) δ 10.31 (brs, 1H), 7.99–6.10 (m, 9H), 6.10 (brs, 1H), 4.29 (q, J = 6.9 Hz, 1H), 1.04 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 12.09, 46.2, 47.7, 76.0, 109.4, 121.2, 125.1, 128.5, 128.72, 129.2, 130.4, 133.2, 137.4, 142.5, 178.1, 201.5; IR (KBr) 3315.5, 3215.3, 3061.2, 2990.4, 2936.4, 1700.8, 1678.0, 1624.5, 1475.2, 1185.5, 754.3 cm^1. HRMS (ESI): Calculated for $C_{17}H_{15}NNaO_3$ ([M + Na]$^+$): 304.0944, found: 304.0964.

Minor isomer: white solid, mp 140.4–142.7 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$,) δ 10.19 (brs, 1H), 7.99–6.10 (m, 9H), 6.09 (brs, 1H), 4.18 (q, J = 7.2 Hz, 1H), 1.40 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 12.5, 47.7, 75.8, 109.6, 121.2, 125.0, 128.3, 128.7, 129.2, 131.1, 136.3, 137.4, 142.6, 178.6, 200.8; IR (KBr) 3315.5, 3215.3, 3061.2, 2990.4, 2936.4, 1700.8, 1678.0, 1624.5, 1475.2, 1185.5, 754.3 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{15}NNaO_3$ ([M + Na]$^+$): 304.0944, found: 304.0964.

3-Hydroxy-3-(1-oxo-2,3-dihydro-1H-inden-2-yl)indolin-2-one (3b′). Major isomer: white solid, mp 183.1–185.2 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.38 (brs, 1H), 7.64–6.29 (m, 8H), 6.29 (brs, 1H), 3.63–3.09 (m, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 28.3, 53.1, 75.3, 109.5, 121.6, 122.9, 124.1, 126.6, 127.2, 129.2, 130.4, 134.8, 136.4, 142.5, 153.9, 177.9, 203.5; IR (KBr) 3272.7, 3058.6, 2910.1, 1734.9, 1699.9, 1621.8, 1472.8, 1287.5, 1204.7, 755.0 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{13}NNaO_3$ ([M + Na]$^+$): 302.0788, found: 302.0788.

Minor isomer: white solid, mp 183.1–185.2 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.31 (brs, 1H), 7.64–6.29 (m, 8H), 6.23 (brs, 1H), 3.63–3.09 (m, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 28.4, 52.4, 75.2, 109.6, 121.1, 122.8, 124.0, 126.7, 127.2, 129.1,130.4, 134.8, 136.8, 142.1, 153.3, 177.2, 203.7; IR (KBr) 3272.7, 3058.6, 2910.1, 1734.9, 1699.9, 1621.8, 1472.8, 1287.5, 1204.7, 755.0 cm^{-1}. HRMS (ESI): Calculated for $C_{17}H_{13}NNaO_3$ ([M + Na]$^+$): 302.0788, found: 302.0788.

3-Hydroxy-3-(1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)indolin-2-one (3c′). Major isomer: white solid, mp 213.8–214.6 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.29 (brs, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.54–6.78 (m, 7H), 6.08 (brs, 1H), 3.37–3.31 (m, 1H), 3.10–3.08 (m, 2H), 2.76–2.72 (m, 1H), 2.29–2.22 (m, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 23.4, 29.1, 54.9, 74.4, 109.5, 120.9, 124.5, 126.6, 128.6, 129.0, 130.3, 131.8, 132.2, 133.7, 143.7, 144.5, 178.8, 196.3; IR (KBr) 3276.4, 3060.3, 3022.0, 2927.5, 1727.0, 1674.4, 1473.4, 750.4 cm^{-1}. HRMS (ESI): Calculated for $C_{18}H_{15}NNaO_3$ ([M + Na]$^+$): 316.0944, found: 316.0955.

Minor isomer: white solid, mp 213.8–214.6 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.29 (brs, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.54–6.78 (m, 7H), 6.00 (brs, 1H), 3.37–3.31 (m, 1H), 3.10–3.08 (m, 2H), 2.76–2.72 (m, 1H), 2.29–2.22 (m, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 23.9, 28.8, 54.1, 74.4, 109.4, 121.2, 123.2, 126.3, 128.6, 128.9, 130.3, 131.8, 132.5, 133.6, 142.7, 144.4, 177.8, 197.6; IR (KBr) 3276.4, 3060.3, 3022.0, 2927.5, 1727.0, 1674.4, 1473.4, 750.4 cm^{-1}. HRMS (ESI): Calculated for $C_{18}H_{15}NNaO_3$ ([M + Na]$^+$): 316.0944, found: 316.0955.

3-Hydroxy-3-(2-oxopropyl)indolin-2-one (3d′). White solid, mp 171.9–172.8 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.23 (brs, 1H), 7.24 (d, J = 6.9 Hz, 1H), 7.20–7.15 (m, 1H), 6.93–6.77 (m, 2H), 6.00 (brs, 1H), 3.28 (d, J = 16.5 Hz, 1H), 3.03 (d, J = 16.5 Hz, 1H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 30.6, 50.3, 72.7, 109.5, 121.3, 123.8, 129.1, 131.6, 142.6, 178.3, 205.3; IR (KBr) 3365.8, 3316.8, 3064.4, 2896.6, 1720.5, 1621.8, 1470.8, 1182.4, 1088.9, 760.8 cm^{-1}. HRMS (ESI): Calculated for $C_{11}H_{11}NNaO_3$ ([M + Na]$^+$): 228.0631, found: 228.0639.

3-Hydroxy-3-(2-oxobutyl)indolin-2-one (3e′). White solid, mp 119.2–120.3 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.19 (brs, 1H), 7.24–7.14 (m, 2H), 6.90 (dd, J = 7.5, 0.6 Hz, 1H), 6.77 (d, J = 7.5 Hz, 1H), 5.95 (brs, 1H), 3.25 (d, J = 16.5 Hz, 1H), 2.97 (d, J = 16.5 Hz, 1H), 2.39–2.33 (m, 2H), 0.76 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 7.3, 35.7, 49.1, 72.7, 109.4, 121.2, 123.7, 128.9, 131.5, 142.5, 178.2, 207.4; IR (KBr) 3349.2, 2979.6, 2941.8, 1723.8, 1622.3, 1473.5, 1181.2, 776.5, 641.0 cm^{-1}. HRMS (ESI): Calculated for $C_{12}H_{12}NNaO_3$ ([M + Na]$^+$): 242.0788, found: 242.0798.

3-Hydroxy-3-(3-oxopentan-2-yl)indolin-2-one (3f′). Major isomer: white solid, mp 95.7–99.6 °C; 1H NMR (300 MHz, $(CD_3)_2SO$) δ 10.31 (brs, 1H), 7.26–7.10 (m, 2H), 6.95–6.90 (m, 1H), 6.77 (d, J = 7.5 Hz, 1H), 6.17 (brs, 1H), 3.22 (q, J = 7.2 Hz, 1H), 2.77–2.50 (m, 2H), 0.89 (d, J = 7.2 Hz, 3H), 0.90–0.71 (m, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 7.6, 10.9, 37.6, 50.0, 76.5, 109.5, 121.4, 125.3, 129.2, 129.4, 142.3, 177.9, 211.9; IR (KBr) 3291.1, 2978.1, 2938.5, 1978.1, 2938.5, 1713.3, 1621.6, 1472.0, 755.9 cm^{-1}. HRMS (ESI): Calculated for $C_{13}H_{15}NNaO_3$ ([M + Na]$^+$): 256.0944, found: 256.0949.

Minor isomer: white solid, mp 95.7–99.6 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.23 (brs, 1H), 7.26–7.10 (m, 2H), 6.95–6.90 (m, 1H), 6.77 (d, J = 7.5 Hz, 1H), 6.17 (brs, 1H), 3.21 (q, J = 7.2 Hz, 1H), 2.77–2.50 (m, 2H), 1.16 (d, J = 7.2 Hz, 3H), 0.90–0.71 (m, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 7.6, 10.7, 34.6, 52.4, 75.7, 109.6, 121.3, 124.6, 128.9, 130.9, 142.3, 178.4, 210.6; IR (KBr) 3291.1, 2978.1, 2938.5, 1978.1, 2938.5, 1713.3, 1621.6, 1472.0, 755.9 cm^{-1}. HRMS (ESI): Calculated for $C_{13}H_{15}NNaO_3$ ([M + Na]$^+$): 256.0944, found: 256.0949.

3-Hydroxy-3-(2-oxocyclopentyl)indolin-2-one (3g′). Major isomer: white solid, mp 138.2–140.0 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.28 (brs, 1H), 7.33 (d, J = 7.2 Hz, 2H), 7.17–6.84 (m, 1H), 6.77–6.72 (m, 1H), 5.97 (brs, 1H), 2.85 (t, J = 10.2 Hz, 1H), 2.22–1.74 (m, 6H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 20.2, 24.7, 40.3, 54.9, 75.1, 109.6, 121.3, 124.7, 129.3, 131.0, 142.9, 178.4, 216.5; IR (KBr) 3380.3, 2949.0, 2980.2, 2883.6, 1733.4,

1709.0, 1621.0, 1470.7, 770.2 cm^{-1}. HRMS (ESI): Calculated for $C_{13}H_{13}NNaO_3$ ([M + Na]$^+$): 254.0788, found: 254.0774.

Minor isomer: white solid, mp 138.2–140.0 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.28 (brs, 1H), 7.33 (d, J = 7.2 Hz, 2H), 7.17–6.84 (m, 1H), 6.77–6.72 (m, 1H), 5.92 (brs, 1H), 2.85 (t, J = 10.2 Hz, 1H), 2.22–1.74 (m, 6H); ^{13}C-NMR (75 MHz, $(CD_3)_2SO$) δ 19.7, 25.1, 40.3, 53.8, 75.1, 109.6, 121.8, 124.3, 129.2, 130.0, 142.4, 177.8, 216.8; IR (KBr) 3380.3, 2949.0, 2980.2, 2883.6, 1733.4, 1709.0, 1621.0, 1470.7, 770.2 cm^{-1}. HRMS (ESI): $C_{13}H_{13}NNaO_3$ ([M + Na]$^+$): 254.0788, found: 254.0774.

3-Hydroxy-3-(2-oxocyclohexyl)indolin-2-one (3h′). Major isomer: white solid, mp 175.0–177.0 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.18 (brs, 1H), 7.27 (d, J = 7.2 Hz, 1H), 7.17–7.11 (m, 1H), 6.87–6.76 (m, 1H), (d, J = 7.5 Hz, 1H), 5.80 (brs, 1H), 3.23 (dd, J = 5.1 Hz, 7.8 Hz, 1H), 2.56–2.48 (m, 1H), 2.32–2.30 (m, 1H), 2.08–1.48 (m, 6H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 24.5, 26.8, 27.8, 41.6, 57.5, 73.9, 109.5, 120.9, 124.9, 128.7, 130.9, 143.5, 178.8, 209.2, IR (KBr) 3334.7, 3235.6, 3059.6, 2937.7, 1718.3, 1702.6, 1618.2, 1470.3, 1175.4, 745.8 cm^{-1}. HRMS (ESI): Calculated for $C_{14}H_{15}NNaO_3$ ([M + Na]$^+$): 268.0944, found: 268.0951.

Minor isomer: white solid, mp 175.0–177.0 °C; 1H NMR (300 MHz, $(CD_3)_2SO$) δ 10.13 (brs, 1H), 7.22–7.14 (m, 2H), 6.88–6.77 (m, 2H), 5.72 (brs, 1H), 3.24 (dd, J = 5.1, 7.8 Hz, 1H), 2.37–2.26 (m, 2H), 2.08–2.01 (m, 2H), 1.83–1.47 (m, 4H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 24.7, 26.8, 27.8, 27.82, 42.3, 57.5, 73.7, 109.2, 121.1, 123.8, 128.7, 130.9, 143.5, 178.1, 209.9; IR (KBr) 3334.7, 3235.6, 3059.6, 2937.7, 1718.3, 1702.6, 1618.2, 1470.3, 1175.4, 745.8 cm^{-1}. HRMS (ESI): Calculated for $C_{14}H_{15}NNaO_3$ ([M + Na]$^+$): 268.0944, found: 268.0951.

4,6-Dibromo-3-hydroxy-3-(2-oxopropyl)indolin-2-one (3i′). White solid, mp 211.3–212.5 °C; ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 10.64 (brs, 1H), 7.28 (s, 1H), 6.94 (s, 1H), 6.24 (brs, 1H), 3.73 (d, J = 17.7 Hz, 1H), 3.15 (d, J = 17.7 Hz, 1H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 30.1, 48.4, 73.8, 111.9, 119.0, 122.5, 126.8, 128.8, 146.5, 177.4, 205.4; IR (KBr) 3392.6, 3169.2, 3032.0, 2903.3, 1716.4, 1609.7, 1434.9, 1362.0, 1327.2, 684.4 cm^{-1}. HRMS (ESI): Calculated for $C_{11}H_9Br_2NNaO_3$ ([M + Na]$^+$): 383.8841 found: 383.8847.

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11 In this case, the reaction took place preferentially at the C1 position of butan-2-one **1v** and gave **3e′** as the major regioisomer while the other regioisomeric product of C3 addition to isatin could hardly be determined by ^{1}H NMR.
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