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Baylis–Hillman carbonates in organic synthesis: a convenient one-pot strategy for nitrone–spiro-oxindole frameworks

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ABSTRACT

A facile one-pot protocol for synthesis of nitrone–spiro-oxindole frameworks via alkylation of nitromethane with carbonates of Baylis–Hillman alcohols, derived from isatins and cyclohex-2-enone derivatives, followed by reductive cyclization is described.

1. Introduction

In recent years there has been increasing interest in understanding the free radical mediated oxidative damage to cells because it is considered to be one of the major factors responsible for many diseases, such as neuro-degeneration, stroke, cancers etc.[1] After the initial studies on the applications of PBN (α-phenyl-*tert*-butylnitrone) and its derivatives for trapping free radicals in chemical systems, research work from various leading laboratories has been directed toward examining the utility of nitrones as spin traps in biological systems and many significant results were achieved in this direction.[1a–d,2] In fact the present day developments in synthetic and medicinal chemistry demand the design and synthesis of appropriate nitrone frameworks for addressing the problems of oxidative damage to tissues.[1d,3] Spirooxindole skeleton is another unique structural organization present in several natural products and biologically active molecules and therefore development of efficient and simple protocols for obtaining spirooxindole derivatives represents an attractive area of research in synthetic chemistry.[4] It occurred to us that molecules containing both nitrone skeleton and spirooxindole structural units might show interesting biological activities. In continuation of our interest on applications of the Baylis–Hillman (BH) adducts[5] in developing useful protocols for obtaining diverse classes of heterocyclic molecules of biological relevance we, herein, report a simple one-pot methodology for synthesis of interesting class of compounds (nitrone–spiro-oxindoles) containing both spirooxindole and nitrone skeletons using the Baylis–Hillman carbonates as starting materials.

The Baylis–Hillman (BH) reaction[6,7] occupies a special place in the list of carbon–carbon bond forming reactions because of its unique applications in producing highly useful densely functionalized molecules, which are commonly known as the Baylis–Hillman adducts. Due to the presence of proximal functional groups, BH-adducts have been extensively used in many synthetic transformations and also in the synthesis of several bioactive and natural products. There are some interesting reports on the applications of BH-adducts and their derivatives in the synthesis of various spirooxindoles[8] and also few reports are available for obtaining *N*-oxide derivatives.[3a,9] We have recently reported the Baylis–Hillman coupling between cyclohex-2-enone and isatin derivatives under the influence of titanium tetrachloride to produce the required BH-adducts (**1**).[10] Based on our experience in understanding the versatility of BH adducts we envisaged that the Baylis–Hillman carbonates (**2**) would serve as appropriate alkylators for obtaining the nitro-enone derivatives **3**, which in turn can be transformed into an interesting class of compounds (**4**) containing both the spirooxindole and nitrone frameworks as shown in the retro synthetic strategy (Scheme 1).

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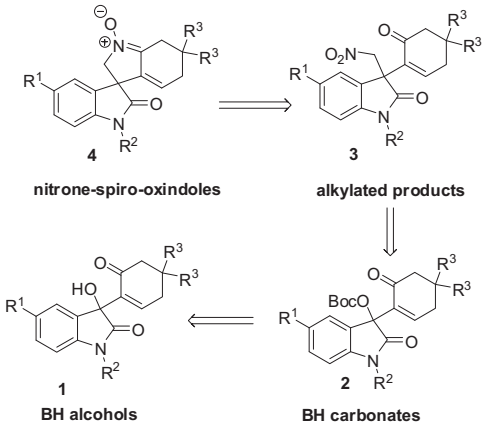
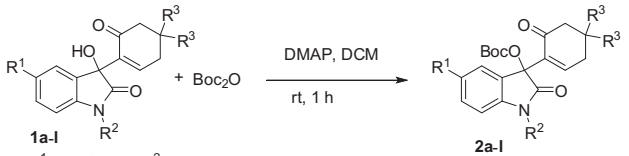


Scheme 1. Retro-synthetic strategy for synthesis of nitrone–spiro-oxindoles.

2. Results and discussion

Accordingly we have first prepared Baylis–Hillman adduct (**1a**) following the procedure developed in our laboratory[10] via the coupling of *N*-methylisatin and cyclohex-2-enone under the influence of $TiCl_4$. This allyl alcohol (**1a**) was converted into its carbonate derivative (**2a**) by treatment with Boc_2O (Table 1).[11]

Table 1
Synthesis of Boc-derivatives (**2a**–**l**) of BH-alcohols (**1a**–**l**)[a]



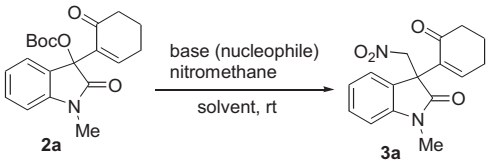
Entry	BH alcohol	R^1	R^2	R^3	Product[b]	Yield[c] (%)
1	**1a**	H	Me	H	**2a**	72
2	**1b**	H	Et	H	**2b**	74
3	**1c**	H	Bn	H	**2c**	83
4	**1d**	Cl	Me	H	**2d**	71
5	**1e**	Cl	Et	H	**2e**	78
6	**1f**	Cl	Bn	H	**2f**	80
7	**1g**	Br	Me	H	**2g**	79
8	**1h**	Br	Et	H	**2h**	74
9	**1i**	Br	Bn	H	**2i**	76
10	**1j**	Cl	Me	Me	**2j**	75
11	**1k**	Br	Me	Me	**2k**	86
12	**1l**	Cl	Et	Me	**2l**	79

[a] All reactions were carried out on a 20.0 mmol scale of Baylis–Hillman alcohols (**1**) with 22.0 mmol of Boc_2O in the presence of DMAP (1.0 mmol) in anhydrous DCM (see the procedure in Experimental section).
[b] All the compounds were obtained as solids and fully characterized.
[c] Isolated yields were based on the Baylis–Hillman alcohols.

We have performed alkylation of nitromethane with **2a** under various conditions (Table 2). Best results were obtained when **2a** (4 mmol) was treated with nitromethane (6 mmol) in the presence of DMAP (4 mmol) in dichloromethane (DCM) under nitrogen atmosphere at room temperature (25–30 °C) for 12 h thus providing the desired alkylated product, 3-nitromethyl-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**3a**),[12] in 82% isolated yield (Table 2, Entry 6).

We have next directed our efforts toward transformation of nitro-enone derivative (**3a**) into **4a** under different conditions. In this regard we obtained encouraging results when we have performed the reaction of **3a** (2 mmol) with Fe powder/HCl [Fe (12 mmol)/HCl (2N, 2 mL)] in EtOH[13] at room temperature

Table 2
Optimization: Alkylation of nitromethane with BH-carbonate (**2a**)[a]



Entry	Base/nucleophile	Solvent	Time (h)	Yield (%)
1	DABCO	DCM	48	N.R.
2	PPh_3	DCM	48	N.R.
3	Me_2S	DCM	48	N.R
4	DMAP	Toluene	48	53
5	DMAP	CH_3CN	48	50
6	**DMAP**	**DCM**	**12**	**82**[b]
7	DMAP	DCM	24	75[c]

[a] All reactions were carried out on a 2.0 mmol scale of Baylis–Hillman carbonates (**2a**) with 3.0 mmol of nitromethane in the presence of various nucleophiles (bases) (2.0 mmol) in different solvents at room temperature under N_2 atmosphere.
[b] Reaction was also carried out on a 4.0 mmol scale of Baylis-Hillman carbonates (**2a**) with 6.0 mmol of nitromethane in the presence of DMAP (4.0 mmol) in anhydrous DCM at room temperature under N_2 atmosphere.
[c] 1.0 mmol of DMAP was used.

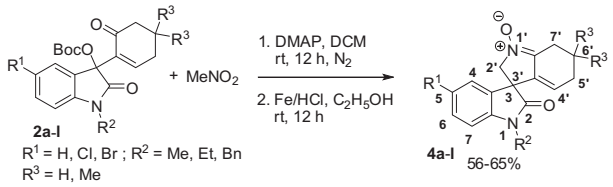
(25–30 °C) for 12h to provide [1-methylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4a**) in 69% yield (overall yield 57% starting from **2a**).

With a view to examining the possibility of performing both the steps in one-pot, we have treated the Baylis–Hillman carbonate **2a** (2 mmol) with nitromethane (3 mmol) in the presence of DMAP (2 mmol) in DCM at room temperature for 12 h and the resulting reaction mixture (after the solvent was removed under reduced pressure) was subsequently treated with Fe powder (12 mmol) and 2 N HCl (2 mL) in ethanol for 12 h at room temperature to provide the desired nitrone **4a** in 59% overall yield (after usual work-up followed by purification of the crude product, thus obtained, by silica gel column chromatography).

Structure of the molecule **4a** was established by spectral data analysis.[14] In the ^1H NMR spectrum of **4a**, C-6′ methylene protons appear as a multiplet at δ 1.71–1.92. The multiplets at δ 2.08–2.27 and δ 2.69–2.80 are attributed to methylene protons at C-5′ (or C-7′) and at C-7′ (or C-5′), respectively. Singlet at δ 3.26 arises due to N–*Me* Protons. Methylene protons at C-2′ appear as *ABq* at δ 4.21 & 4.47. Triplet at δ 5.39 is attributed to the olefinic proton at C-4′. Aromatic proton at C-7 appears as a doublet at δ 6.90. The remaining three aromatic protons appear as two multiplets one at δ 7.08–7.18 (2H) and the other one at δ 7.32–7.38 (1H). ^{13}C NMR spectrum of **4a** shows 16 signals corresponding to 16 carbons of the compound. Six aliphatic carbons show peaks at δ 20.02(C-4′), 21.28 (C-5'or C-6′), 24.59 (C-6′ or C-5′), 26.57 (N–*Me* carbon), 51.29 (C-3′), 68.66 (C-2′). Six aromatic, two olefinic and one iminium carbons appear at δ 108.48, 122.85, 123.48, 123.86, 129.06, 130.94, 137.42, 143.44, 143.91. Signal at δ 175.95 arises due to amide carbonyl carbon (N–**C**=O). HRMS (ESI) shows the exact mass of 269.1290 $(M+H)^+$ [exact mass calcd for (**4a**) $C_{16}H_{16}N_2O_2$+H $(M+H)^+$is 269.1290].

This is indeed a very encouraging result. We therefore have selected one-pot procedure to understand the generality of this methodology. We have prepared a representative class of the Baylis–Hillman adducts (**1a**–**l**) from selected isatins and cyclohexenone & 5,5-dimethylcyclohexenone and converted them into their carbonate derivatives **2a**–**l** (Table 1). We have then subjected these carbonates (**2a**–**l**) first to the reaction with nitromethane and then in situ produced alkylated products (**3a**–**l**) with Fe/HCl as in the case of **4a** to produce the resulting nitrone–spiro-oxindoles (**4a**–**l**) in 56–65% isolated yields (Table 3). Structures of the nitrone–spiro-oxindoles **4b** and **4j** were further confirmed by their

Table 3
Synthesis of nitrone–spiro-oxindole derivatives (**4a**–**l**)[a]



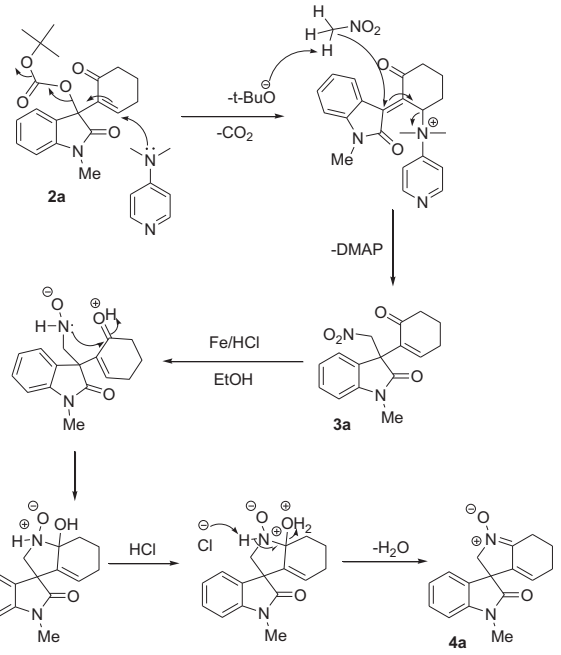
Entry	BH carbonate	R^1	R^2	R^3	Product[b]	Yield[c] (%)
1	**2a**	H	Me	H	**4a**	59
2	**2b**	H	Et	H	**4b**[d]	64
3	**2c**	H	Bn	H	**4c**	60
4	**2d**	Cl	Me	H	**4d**	61
5	**2e**	Cl	Et	H	**4e**	56
6	**2f**	Cl	Bn	H	**4f**	62
7	**2g**	Br	Me	H	**4g**	65
8	**2h**	Br	Et	H	**4h**	60
9	**2i**	Br	Bn	H	**4i**	64
10	**2j**	Cl	Me	Me	**4j**[d]	63
11	**2k**	Br	Me	Me	**4k**	58
12	**2l**	Cl	Et	Me	**4l**	61

[a] All reactions were carried out on a 2.0 mmol scale of Baylis-Hillman carbonates (**2**) with 3.0 mmol of nitromethane in the presence of DMAP (2.0 mmol) in anhydrous DCM, followed by reductive cyclization of the in situ generated nitro-enone derivatives using Fe powder (12.0 mmol) and HCl (2 N, 2.0 mL) in EtOH (10.0 mL) at room temperature.
[b] All the compounds were obtained as solids and fully characterized.
[c] Isolated yields were based on the Baylis–Hillman carbonates.
[d] Structures of these compounds were further confirmed by single crystal X-ray data analysis.[15]

single crystal X-ray data analysis (Fig. 1).[15] A plausible mechanism for obtaining nitrone–spiro-oxindoles (**4**) is presented in Scheme 2 taking **4a** as a model case.

3. Conclusions

In conclusion, we have developed an efficient one-pot methodology for the synthesis of nitrone–spiro-oxindoles (**4**) via alkylation of nitromethane with Baylis–Hillman carbonates (**2**) followed by reductive cyclization of the in situ generated nitro-enones **3** using Fe/HCl/EtOH in encouraging yields.



Scheme 2. Plausible mechanism for synthesis of nitrone–spiro-oxindoles **4**.

4. Experimental section

4.1. General remarks

Melting points were recorded on a Superfit (India) capillary melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO-FT-IR model 5300 spectrometer using solid samples as KBr plates and liquid sample as thin film between NaCl plates. For all the compounds ^{1}H NMR (400 or 500 MHz) and ^{13}C

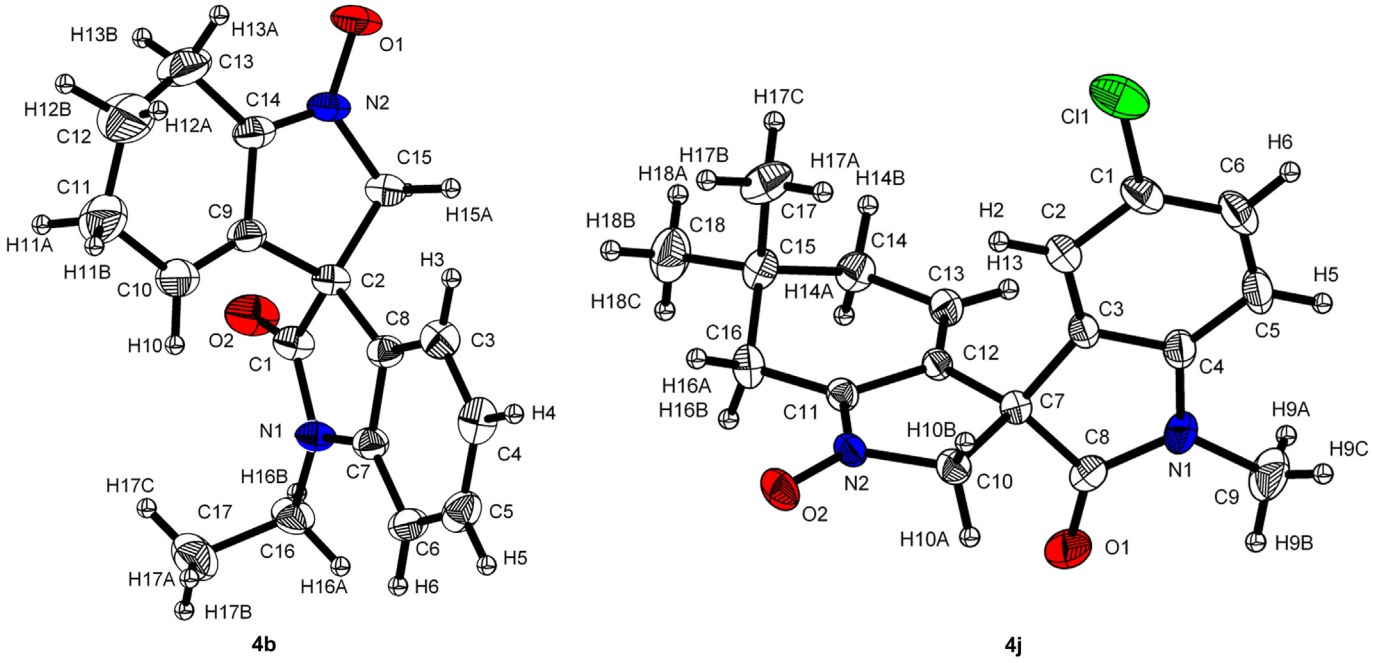


Fig. 1. ORTEP diagrams for compounds **4b** & **4j**.

NMR (100 MHz) spectra were recorded in deuterochloroform ($CDCl_3$) on a Bruker-AVANCE-400 and 500 spectrometers using tetramethylsilane (TMS, δ=0) as an internal standard at room temperature. HRMS spectra were recorded on Bruker maXis ESI-TOF spectrometer. The X-ray diffraction measurements were carried out at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ=0.71073 Å). The Baylis–Hillman alcohols **1a**–**l** were prepared via the reaction between cyclohex-2-enone (or 5,5-dimethylcyclohex-2-enone) with isatin derivatives under the influence of $TiCl_4$ following the known procedure.[10]

*4.1.1. Synthesis of 3-(tert-butoxycarbonyloxy)-3-(cyclohex-2en-on-2-yl)-1-methylindolin-2-one (**2a**). Representative procedure*: To a stirring solution of 3-hydroxy-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (20 mmol, 5.14 g) in anhydrous CH_2Cl_2 (40 mL) at 0 °C were added Boc_2O (22 mmol, 4.8 g, 5.0 mL) and DMAP (4-dimethylaminopyridine) (1.0 mmol, 0.122 g) in anhydrous CH_2Cl_2 (40 mL) drop-wise slowly (over half an hour) at the same temperature. After the addition, the stirring was continued at room temperature (25–30 °C) for 1 h. The reaction mixture was washed with aqueous hydrochloric acid (2 N, 2 mL) followed by saturated aqueous sodium bicarbonate solution (10 mL). Organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated. The crude product, thus obtained, was purified by column chromatography (40% ethyl acetate in hexanes) to provide the title compound as a brown solid in 72% (5.15 g) yield. R_f (50% EtOAc in hexanes) 0.32; mp:130–132 °C; IR (KBr): ν 1749, 1728, 1674, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.33 (s, 9H), 1.88–2.07 (m, 2H), 2.23–2.39 (m, 2H), 2.46–2.61 (m, 2H), 3.30 (s, 3H), 6.85 (d, 1H, J=8.0 Hz), 6.92–6.99 (m, 1H), 7.11 (dd, 1H, J=0.8 & 7.2 Hz)*, 7.29–7.35 (m, 1H), 7.64 (t, 1H, J=4.0 Hz), *not properly resolved; ^{13}C NMR (100 MHz): δ 22.09, 25.88, 26.61, 27.49, 38.52, 79.49, 83.13, 108.16, 122.14, 122.74, 126.97, 130.11, 136.02, 145.70, 148.25, 149.77, 173.16, 195.81; HRMS (ESI) exact mass calcd for $C_{20}H_{23}NO_5$+Na $(M+Na)^+$, 380.1474; Found, 380.1488.

*4.1.2. 3-(tert-Butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (**2b**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 74%; R_f (50% EtOAc in hexanes) 0.49; brown solid; mp 140–142 °C; IR (KBr): ν 1755, 1728, 1678, 1608 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.33 (s, 9H), 1.35 (t, 3H, J=7.2 Hz)*, 1.88–2.05 (m, 2H), 2.23–2.40 (m, 2H), 2.46–2.57 (m, 2H), 3.70–3.82 (m, 1H), 3.86–3.96 (m, 1H), 6.86 (d, 1H, J=7.6 Hz), 6.91–6.98 (m, 1H), 7.11 (dd, 1H, J=0.8 & 7.2 Hz), 7.27–7.33 (m, 1H), 7.62 (t, 1H, J=4.0 Hz), *one of the peak merged with singlet at δ 1.33; ^{13}C NMR (100 MHz): δ 11.59, 22.03, 25.80, 27.42, 34.86, 38.47, 79.49, 82.86, 108.13, 121.78, 122.90, 127.13, 129.92, 135.99, 144.78, 148.04, 149.67, 172.44, 195.57; HRMS (ESI) exact mass calcd for $C_{21}H_{25}NO_5$+Na $(M+Na)^+$, 394.1630; Found, 394.1634.

*4.1.3. 3-(tert-Butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (**2c**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 83%; R_f (50% EtOAc in hexanes) 0.60; white solid; mp: 124–126 °C; IR (KBr): ν 1758, 1735, 1683, 1612 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.40 (s, 9H), 1.86–2.10 (m, 2H), 2.25–2.46 (m, 2H), 2.49–2.62 (m, 2H), 5.05 (s, 2H), 6.63 (d, 1H, J=8.0 Hz), 6.89–6.98 (m, 1H), 7.11–7.20 (m, 2H), 7.25–7.32 (m, 1H), 7.33–7.41 (m, 2H), 7.57 (d, 2H, J=7.2 Hz), 7.69 (t, 1H, J=4.0 Hz); ^{13}C NMR (100 MHz): δ 22.14, 25.96, 27.61, 38.57, 44.79, 79.60, 83.11, 109.43, 122.19, 122.84, 127.05, 127.22, 127.36, 128.54, 129.98, 135.94, 136.14, 145.22, 148.34, 149.93, 173.40, 195.74; HRMS (ESI) exact mass calcd for $C_{26}H_{27}NO_5$+H $(M+H)^+$, 434.1967; Found, 434.1968.

*4.1.4. 5-Chloro-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2d**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 71%; R_f (50% EtOAc in hexanes) 0.40; brown solid; mp: 162–164 °C; IR (KBr): ν 1761, 1726, 1678, 1612 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.36 (s, 9H), 1.90–2.03 (m, 2H), 2.25–2.40 (m, 2H), 2.50–2.58 (m, 2H), 3.29 (s, 3H), 6.77 (d, 1H, J=8.0 Hz), 7.07 (d, 1H, J=2.0 Hz), 7.28 (dd, 1H, J=2.0 & 8.4 Hz)*, 7.65 (t, 1H, J=4.4 Hz), *one of the peak of dd merged with $CHCl_3$ peak; ^{13}C NMR (100 MHz): δ 22.06, 25.93, 26.75, 27.55, 38.48, 79.05, 83.51, 109.16, 123.26, 127.31, 128.69, 129.93, 135.68, 144.46, 148.81, 149.79, 172.76, 195.81; HRMS (ESI) exact mass calcd for $C_{20}H_{22}ClNO_5$+Na $(M+Na)^+$, 414.1084; Found, 414.1087.

*4.1.5. 5-Chloro-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (**2e**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 78%; R_f (50% EtOAc in hexanes) 0.50; brown solid; mp: 172–174 °C; IR (KBr): ν 1747, 1726, 1671, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.31 (t, 3H, J=7.2 Hz), 1.34 (s, 9H), 1.87–2.03 (m, 2H), 2.22–2.38 (m, 2H), 2.45–2.54 (m, 2H), 3.67–3.77 (m, 1H), 3.78–3.91 (m, 1H), 6.77 (d, 1H, J=8.0 Hz), 7.07 (d, 1H, J=2.0 Hz), 7.23 (dd, 1H, J=2.0 & 8.4 Hz), 7.60 (t, 1H, J=4.4 Hz); ^{13}C NMR (100 MHz): δ 11.52, 22.01, 25.87, 27.49, 35.08, 38.43, 79.05, 83.29, 109.15, 123.40, 126.97, 128.89, 129.78, 135.63, 143.54, 148.68, 149.71, 172.09, 195.65; HRMS (ESI) exact mass calcd for $C_{21}H_{24}ClNO_5$+H $(M+H)^+$, 406.1421; Found, 406.1418.

*4.1.6. 5-Chloro-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (**2f**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 80%; R_f (50% EtOAc in hexanes) 0.55; white solid; mp: 160–162 °C; IR (KBr): ν 1758, 1728, 1672, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 9H), 1.88–2.08 (m, 2H), 2.27–2.44 (m, 2H), 2.49–2.62 (m, 2H), 4.96 & 5.02 (ABq, 2H, J=16.0 Hz), 6.51 (d, 1H, J=8.0 Hz), 7.08–7.12 (m, 2H), 7.24–7.39 (m, 3H)*, 7.51 (d, 2H, J=7.2 Hz), 7.67 (t, 1H, J=4.0 Hz), *It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz): δ 22.16, 26.06, 27.70, 38.57, 44.96, 79.21, 83.63, 110.50, 123.36, 127.41, 127.48, 127.53, 128.71, 128.82, 129.91, 135.56, 135.83, 143.92, 149.04, 149.98, 173.08, 195.89; HRMS (ESI) exact mass calcd for $C_{26}H_{26}ClNO_5$+H $(M+H)^+$, 468.1578; Found, 468.1575.

*4.1.7. 5-Bromo-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2g**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 79%; R_f (50% EtOAc in hexanes) 0.47; brown solid; mp: 162–164 °C; IR (KBr): ν 1759, 1726, 1678, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.36 (s, 9H), 1.90–2.06 (m, 2H), 2.25–2.41 (m, 2H), 2.49–2.58 (m, 2H), 3.28 (s, 3H), 6.73 (d, 1H, J=8.0 Hz), 7.20 (d, 1H, J=2.0 Hz), 7.42 (dd, 1H, J=2.0 & 8.0 Hz), 7.64 (t, 1H, J=4.0 Hz); ^{13}C NMR (100 MHz): δ 22.07, 25.95, 26.76, 27.57, 38.48, 78.97, 83.60, 109.73, 114.57, 125.96, 129.01, 132.88, 135.67, 144.94, 148.94, 149.79, 172.71, 195.92; HRMS (ESI) exact mass calcd for $C_{20}H_{22}BrNO_5$+Na $(M+Na)^+$, 458.0579; Found, 458.0584.

*4.1.8. 5-Bromo-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (**2h**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 74%; R_f (50% EtOAc in hexanes) 0.53; brown solid; mp: 174–176 °C; IR (KBr): ν 1758, 1725, 1676, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, 3H, J=7.2 Hz), 1.36 (s, 9H), 1.89–2.06 (m, 2H), 2.25–2.41 (m, 2H), 2.49–2.56 (m, 2H), 3.69–3.80 (m, 1H), 3.81–3.94 (m, 1H), 6.75 (d, 1H, J=8.0 Hz), 7.21 (d, 1H, J=2.0 Hz), 7.41 (dd, 1H, J=2.0 & 8.4 Hz), 7.62 (t, 1H, J=4.0 Hz); ^{13}C NMR (100 MHz): δ 11.61, 22.11, 25.99, 27.60, 35.17, 38.53, 79.07, 83.47, 109.77, 114.31, 126.20, 129.33, 132.80, 135.74, 144.13, 148.83, 149.79, 172.11, 195.81; HRMS (ESI) exact mass calcd for $C_{21}H_{24}BrNO_5$+Na $(M+Na)^+$, 472.0736; Found, 472.0740.

*4.1.9. 5-Bromo-3-(tert-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (**2i**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 76%; R_f (50% EtOAc in hexanes) 0.61; yellow solid; mp:

170–172 °C; IR (KBr): ν 1753, 1730, 1672, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 9H), 1.91–2.08 (m, 2H), 2.28–2.44 (m, 2H), 2.49–2.62 (m, 2H), 4.96 & 5.02 (ABq, 2H, J=16.0 Hz), 6.47 (d, 1H, J=8.4 Hz), 7.21 (d, 1H, J=2.0 Hz), 7.23–7.30 (m, 2H)*, 7.31–7.36 (m, 2H), 7.51 (d, 2H, J=7.2 Hz), 7.67 (t, 1H, J=4.0 Hz), *It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz): δ 22.15, 26.06, 27.71, 38.56, 44.94, 79.12, 83.65, 111.03, 114.79, 126.05, 127.41, 127.48, 128.71, 129.17, 132.81, 135.52, 135.84, 144.42, 149.05, 149.98, 172.97, 195.89; HRMS (ESI) exact mass calcd for $C_{26}H_{26}BrNO_5$+H $(M+H)^+$, 512.1073; Found, 512.1069.

*4.1.10. 5-Chloro-3-(tert-butoxycarbonyloxy)-3-(5,5-dimethyl-cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2j**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 75%; R_f (50% EtOAc in hexanes) 0.58; yellow solid; mp: 158–160 °C; IR (KBr): ν 1752, 1736, 1676, 1615, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.99 (s, 3H), 1.02 (s, 3H), 1.36 (s, 9H), 2.15 & 2.18 (ABq, 2H, J=16.0 Hz), 2.42 (d, 2H, J=4.4 Hz), 3.28 (s, 3H), 6.77 (d, 1H, J=8.4 Hz), 7.07 (d, 1H, J=2.0 Hz), 7.27 (dd, 1H, J=2.0 & 8.4 Hz), 7.51 (t, 1H, J=4.4 Hz); ^{13}C NMR (100 MHz): δ 26.83, 27.61, 27.96, 28.17, 33.79, 39.96, 52.10, 79.07, 83.62, 109.24, 123.13, 127.40, 128.70, 130.03, 134.73, 144.56, 146.58, 149.82, 172.69, 196.15; HRMS (ESI) exact mass calcd for $C_{22}H_{26}ClNO_5$+Na $(M+Na)^+$, 442.1397; Found, 442.1397.

*4.1.11. 5-Bromo-3-(tert-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2k**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 86%; R_f (50% EtOAc in hexanes) 0.56; yellow solid; mp: 140–142 °C; IR (KBr): ν 1750, 1732, 1682, 1618, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.99 (s, 3H), 1.02 (s, 3H), 1.36 (s, 9H), 2.15 & 2.20 (ABq, 2H, J=16.0 Hz), 2.42 (d, 2H, J=4.4 Hz), 3.28 (s, 3H), 6.74 (d, 1H, J=8.4 Hz), 7.20 (d, 1H, J=2.0 Hz), 7.43 (dd, 1H, J=2.0 & 8.0 Hz), 7.51 (t, 1H, J=4.4 Hz); ^{13}C NMR (100 MHz): δ 26.80, 27.61, 27.92, 28.21, 33.79, 39.95, 52.09, 78.97, 83.63, 109.77, 114.58, 125.82, 129.03, 132.93, 134.73, 145.04, 146.58, 149.80, 172.57, 196.15; HRMS (ESI) exact mass calcd for $C_{22}H_{26}BrNO_5$+H $(M+H)^+$, 464.1073; Found, 464.1074.

*4.1.12. 5-Chloro-3-(tert-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-1-ethylindolin-2-one (**2l**).* Reaction time: 0.5 h (0 °C)+1 h (rt); yield: 79%; R_f (50% EtOAc in hexanes) 0.64; brown solid; mp: 168–170 °C; IR (KBr): ν 1750, 1676, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.99 (s, 3H), 1.02 (s, 3H), 1.33 (t, 3H, J=7.2 Hz), 1.36 (s, 9H), 2.16 & 2.20 (ABq, 2H, J=16.0 Hz), 2.39 & 2.45 (dABq, 2H, J=4.4 & 15.2 Hz), 3.68–3.80 (m, 1H), 3.81–3.94 (m, 1H), 6.79 (d, 1H, J=8.4 Hz), 7.06 (d, 1H, J=2.0 Hz), 7.22 (dd, 1H, J=8.4 & 2.4 Hz)*, 7.50 (t, 1H, J=4.4 Hz), *It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz): δ 11.63, 27.63, 28.09, 33.79, 35.21, 39.99, 52.13, 79.16, 83.48, 109.30, 123.35, 127.15, 129.01, 129.95, 134.81, 143.74, 146.47, 149.81, 172.10, 196.04; HRMS (ESI) exact mass calcd for $C_{23}H_{28}ClNO_5$+Na $(M+Na)^+$, 456.1554; Found, 456.1558.

*4.1.13. Synthesis of 3-nitromethyl-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**3a**).* To a stirring solution of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2a**) (4.0 mmol, 1.430 g) and nitromethane (6.0 mmol, 0.366 g, 0.33 mL) in anhydrous DCM (10 mL) was added DMAP (4.0 mmol, 0.488 g) at room temperature (25–30 °C). After stirring for 12 h at room temperature under N_2 atmosphere, solvent was removed and crude product thus obtained was purified by column chromatography (40% EtOAc in hexanes) to provide the desired product in 82% yield (0.985 g) as a white solid. R_f (50% EtOAc in hexanes) 0.29; mp: 140–142 °C; IR (KBr): ν 1709, 1676, 1630, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.84–2.06 (m, 2H), 2.30–2.55 (m, 4H), 3.31 (s, 3H), 5.03 & 5.60 (ABq, 2H, J=13.6 Hz), 6.88 (d, 1H, J=8.0 Hz), 6.94 (t, 1H, J=4.4 Hz), 7.00–7.09 (m, 1H), 7.28–7.36 (m, 1H), 7.50 (dd, 1H, J=0.8 & 7.6 Hz); ^{13}C NMR (100 MHz): δ 21.87, 26.39, 26.71, 39.22, 54.36, 76.54, 108.65, 122.90, 124.83, 127.70, 129.11, 134.70, 143.80, 149.38, 175.22, 197.69; HRMS (ESI) exact mass calcd for $C_{16}H_{16}N_2O_4$+H $(M+H)^+$, 301.1188; Found, 301.1191.

*4.1.14. Synthesis of [1-methylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4a**).* To a stirring solution of 3-nitromethyl-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one **3a** (2.0 mmol, 0.600 g) in ethanol (10 mL) at room temperature (25–30 °C) were added Fe powder (12.0 mmol, 0.672 g) and 2 N HCl (2.0 mL). After stirring at room temperature (25–30 °C) for 12 h the reaction mixture was diluted with ethyl acetate (20 mL) and stirred for a few minutes and filtered to remove iron impurities. The residue was washed with ethyl acetate (20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to column chromatography (silica gel, 2% EtOH in EtOAc) to provide **4a** in 69% (0.370 g) isolated yield as a brown solid. R_f (20% EtOH in ethyl acetate) 0.35; mp:180–182 °C; IR (KBr): ν 1718, 1610, 1587 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.71–1.92 (m, 2H)*, 2.08–2.27 (m, 2H), 2.69–2.80 (m, 2H), 3.26 (s, 3H), 4.21 & 4.47 (ABq, 2H, J=14.0 Hz), 5.39 (t, 1H, J=4.4 Hz), 6.90 (d, 1H, J=8.0 Hz), 7.08–7.18 (m, 2H), 7.32–7.38 (m, 1H), *It contains moisture peak; ^{13}C NMR (100 MHz): δ 20.02, 21.28, 24.59, 26.57, 51.29, 68.66, 108.48, 122.85, 123.48, 123.86, 129.06, 130.94, 137.42, 143.44, 143.91, 175.95; HRMS (ESI) exact mass calcd for $C_{16}H_{16}N_2O_2$+H $(M+H)^+$, 269.1290; Found, 269.1290.

*4.1.15. [1-Methylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4a**). Representative one-pot procedure*: To a stirring solution of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**2a**) (2.0 mmol, 0.715 g) and nitromethane (3.0 mmol, 0.183 g, 0.16 mL) in anhydrous CH_2Cl_2 (5 mL) at room temperature (25–30 °C) was added DMAP (2.0 mmol, 0.244 g). After stirring at the same temperature for 12 h under N_2 atmosphere, the solvent was removed under reduced pressure. The resulting residue was dissolved in ethanol (10 mL) and Fe powder (12.0 mmol, 0.672 g) and 2 N HCl (2.0 mL) were added. After stirring at room temperature (25–30 °C) for 12 h the reaction mixture was diluted with ethyl acetate (20 mL) and stirred for a few minutes and filtered to remove iron impurities. The residue was washed with ethyl acetate (20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to column chromatography (silica gel, 2% EtOH in EtOAc) to provide **4a** in 59% (0.319 g) isolated yield as brown solid.

Note: The spectral (IR, ^1H, & ^{13}C NMR, HRMS) data of this product (**4a**) was identical with that of the compound, obtained in a two-step protocol (Section 4.1.14).

*4.1.16. [1-Ethylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4b**).* Reaction time: 12 h+12 h; yield: 64%; R_f (20% EtOH in ethyl acetate) 0.45; brown solid; mp: 162–164 °C; IR (KBr): ν 1709, 1612, 1583 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.31 (t, 3H, J=7.2 Hz), 1.72–1.94 (m, 2H)#, 2.08–2.28 (m, 2H), 2.75 (t, 2H, J=6.8 Hz), 3.69–3.92 (m, 2H), 4.22 & 4.48 (ABq, 2H, J=14.0 Hz), 5.37 (t, 1H, J=4.4 Hz), 6.92 (d, 1H, J=8.0 Hz), 7.07–7.12 (m, 1H), 7.14–7.19 (m, 1H), 7.31–7.37 (m, 1H),* #It contains moisture peak. *Unresolved dd; ^{13}C NMR (100 MHz): δ 12.52, 20.00, 21.26, 24.59, 34.97, 51.22, 68.53, 108.60, 123.01, 123.25, 123.67, 128.97, 131.25, 137.58, 142.46, 143.95, 175.49; HRMS (ESI) exact mass calcd for $C_{17}H_{18}N_2O_2$+Na $(M+Na)^+$, 305.1266; Found, 305.1232.

Crystal data for **4b**: Empirical formula, $C_{17}H_{18}N_2O_2$; formula weight, 282.33; crystal color, habit: colorless, block; crystal dimensions, 0.36×0.28×0.25 mm^3; crystal system, triclinic; lattice type, primitive; lattice parameters, a=8.4050(6) Å, b=8.7609(6) Å, c=11.2366(8) Å; α=92.5970(10); β=109.0770(10); γ=108.3070(10);

V=732.23(9) Å^3; space group, P-1; Z=2; D_{cald}=1.281 g/cm^3; F_{000}=300; λ (Mo-K$_\alpha$)=0.71073 Å; R ($I\geq 2\sigma_1$)=0.0493, wR^2=0.1453. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **4b** CCDC # 923595).

*4.1.17. [1-Benzylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4c**).* Reaction time: 12 h+12 h; yield: 60%; R_f (20% EtOH in ethyl acetate) 0.48; white solid; mp: 162–164 °C; IR (KBr) : ν 1709, 1616, 1589 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.73–1.96 (m, 2H)$^{\#}$, 2.09–2.30 (m, 2H), 2.76 (t, 2H, J=6.8 Hz), 4.26 & 4.54 (ABq, 2H, J=14.0 Hz), 4.77 & 5.09 (ABq, 2H, J=15.6 Hz), 5.40 (t, 1H, J=4.4 Hz), 6.79 (d, 1H, J=8.0 Hz), 7.03–7.09 (m, 1H), 7.16 (dd, 1H, J=0.8 & 7.2 Hz)*, 7.18–7.23 (m, 1H), 7.26–7.38 (m, 5H), $^{\#}$It contains moisture peak. *unresolved dd; ^{13}C NMR (100 MHz): δ 20.02, 21.28, 24.67, 43.97, 51.29, 68.74, 109.46, 122.93, 123.48, 123.62, 127.11, 127.69, 128.70, 128.93, 130.98, 135.23, 137.68, 142.53, 143.75, 176.05; HRMS (ESI) exact mass calcd for $C_{22}H_{20}N_2O_2$+Na (M+Na)$^+$, 367.1422; Found, 367.1406.

*4.1.18. [1-Methyl-5-chlorolindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4d**).* Reaction time: 12 h+12 h; yield : 61%; R_f (20% EtOH in ethyl acetate) 0.43; brown solid; mp: 202–204 °C; IR (KBr): ν 1720, 1610, 1589 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.74–1.94 (m, 2H), 2.11–2.28 (m, 2H), 2.75 (t, 2H, J=6.8 Hz), 3.25 (s, 3H), 4.19 & 4.47 (ABq, 2H, J=14.0 Hz), 5.40 (t, 1H, J=4.4 Hz), 6.83 (d, 1H, J=8.0 Hz), 7.15 (d, 1H, J=2.0 Hz), 7.32 (dd, 1H, J=2.0 & 8.0 Hz); ^{13}C NMR (100 MHz): δ 20.12, 21.46, 24.81, 26.90, 51.52, 68.61, 109.61, 123.68, 124.53, 128.93, 129.19, 132.66, 137.04, 142.18, 144.13, 175.63; HRMS (ESI) exact mass calcd for $C_{16}H_{15}ClN_2O_2$+H (M+H)$^+$, 303.0900; Found, 303.0900.

*4.1.19. [1-Ethyl-5-chlorolindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4e**).* Reaction time: 12 h+12 h; yield: 56%; R_f (20% EtOH in ethyl acetate) 0.46; brown solid; mp 154–156 °C; IR (KBr): ν 1713, 1607, 1585 cm^{-1}; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 1.29 (t, 3H, J=7.0 Hz), 1.76–1.94 (m, 2H)$^{\#}$, 2.12–2.28 (m, 2H), 2.75 (t, 2H, J=7.0 Hz), 3.68–3.78 (m, 1H), 3.79–3.88 (m, 1H), 4.19 & 4.47 (ABq, 2H, J=14.0 Hz), 5.38 (t, 1H, J=4.5 Hz), 6.85 (d, 1H, J=8.0 Hz), 7.15 (d, 1H, J=2.0 Hz), 7.30 (dd, 1H, J=2.0 & 8.5 Hz), $^{\#}$It contains moisture peak; ^{13}C NMR (100 MHz): δ 12.68, 20.22, 21.53, 24.90, 35.42, 51.52, 68.64, 109.74, 123.87, 123.94, 128.79, 129.15, 133.17, 137.40, 141.31, 143.87, 175.26; HRMS (ESI) exact mass calcd for $C_{17}H_{17}ClN_2O_2$+H (M+H)$^+$, 317.1057; Found, 317.1056.

*4.1.20. [1-Benzyl-5-chlorolindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4f**).* Reaction time: 12 h+12 h; yield: 62%; R_f (20% EtOH in ethyl acetate) 0.56; white solid; mp: 100–102 °C; IR (KBr): ν 1715, 1610, 1583 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.68–1.88 (m, 2H)$^{\#}$, 2.06–2.24 (m, 2H), 2.69 (t, 2H, J=6.8 Hz), 4.15 & 4.45 (ABq, 2H, J=14.0 Hz), 4.68 & 4.99 (ABq, 2H, J=15.6 Hz), 5.34 (t, 1H, J=4.4 Hz), 6.63 (d, 1H, J=8.4 Hz), 7.07 (d, 1H, J=2.0 Hz), 7.11 (dd, 1H, J=2.0 & 8.4 Hz), 7.17–7.31 (m, 5H)*, $^{\#}$It contains moisture peak. *It contains CHCl$_3$ peak; ^{13}C NMR (100 MHz): δ 19.93, 21.28, 24.70, 44.10, 51.32, 68.44, 110.53, 123.52, 124.35, 127.07, 127.86, 128.72, 128.80, 128.91, 132.46, 134.79, 137.05, 141.08, 143.94, 175.56; HRMS (ESI) exact mass calcd for $C_{22}H_{19}ClN_2O_2$+H (M+H)$^+$, 379.1213; Found, 379.1210.

*4.1.21. [1-Methyl-5-bromoindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4g**).* Reaction time: 12 h+12 h; yield: 65%; R_f (20% EtOH in ethyl acetate) 0.44; brown solid; mp: 198–200 °C; IR (KBr): ν 1716, 1604, 1585 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.76–1.93 (m, 2H), 2.11–2.28 (m, 2H), 2.75 (t, 2H, J=6.0 Hz), 3.24 (s, 3H), 4.19 & 4.46 (ABq, 2H, J=14.0 Hz), 5.40 (t, 1H, J=4.4 Hz), 6.78 (d, 1H, J=8.4 Hz), 7.28 (d, 1H, J=2.0 Hz), 7.47 (dd, 1H, J=2.0 & 8.4 Hz); ^{13}C NMR (100 MHz): δ 20.13, 21.46, 24.82, 26.87, 51.44, 68.65, 110.08, 116.10, 124.37, 126.38, 132.08, 133.05, 137.05, 142.67, 143.96, 175.52; HRMS (ESI) exact mass calcd for $C_{16}H_{15}BrN_2O_2$+Na (M+Na)$^+$, 369.0215; Found, 369.0184.

*4.1.22. [1-Ethyl-5-bromoindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4h**).* Reaction time: 12 h+12 h; yield : 60%; R_f (20% EtOH in ethyl acetate) 0.49; brown solid; mp: 182–184 °C; IR (KBr): ν 1715, 1605, 1589 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.29 (t, 3H, J=7.2 Hz), 1.74–1.94 (m, 2H)$^{\#}$, 2.12–2.29 (m, 2H), 2.75 (t, 2H, J=6.8 Hz), 3.67–3.88 (m, 2H), 4.19 & 4.47 (ABq, 2H, J=14.4 Hz), 5.38 (t, 1H, J=4.8 Hz), 6.80 (d, 1H, J=8.4 Hz), 7.29 (d, 1H, J=2.0 Hz), 7.46 (dd, 1H, J=8.4 & 2.0 Hz), $^{\#}$It contains moisture peak; ^{13}C NMR (100 MHz): δ 12.69, 20.20, 21.53, 24.90, 35.41, 51.45, 68.63, 110.24, 115.96, 124.18, 126.63, 132.07, 133.51, 137.33, 141.79, 144.01, 175.17; HRMS (ESI) exact mass calcd for $C_{17}H_{17}BrN_2O_2$+Na (M+Na)$^+$, 383.0371; Found, 383.0364.

*4.1.23. [1-Benzyl-5-bromoindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4i**).* Reaction time: 12 h+12 h; yield: 64%; R_f (20% EtOH in ethyl acetate) 0.59; white solid; mp: 186–188 °C; IR (KBr): ν 1715, 1610, 1589 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.75–1.95 (m, 2H)$^{\#}$, 2.12–2.31 (m, 2H), 2.76 (t, 2H, J=6.8 Hz), 4.23 & 4.53 (ABq, 2H, J=14.0 Hz), 4.75 & 5.06 (ABq, 2H, J=15.6 Hz), 5.41 (t, 1H, J=4.4 Hz), 6.66 (d, 1H, J=8.4 Hz), 7.24–7.36 (m, 7H)*. $^{\#}$It contains moisture peak. *It contains CHCl$_3$ peak; ^{13}C NMR (100 MHz): δ 20.08, 21.40, 24.84, 44.23, 51.37, 68.66, 111.08, 116.10, 124.11, 126.36, 127.19, 128.01, 128.94, 131.91, 133.04, 134.86, 137.24, 141.68, 143.75, 175.56; HRMS (ESI) exact mass calcd for $C_{22}H_{19}BrN_2O_2$+H (M +H)$^+$, 423.0708; Found, 423.0704.

*4.1.24. [1-Methyl-5-chloroindolin-2-one]-3-spiro-3′-[6′,6′-dimethyl-2′,5′,6′,7′-tetrahyroindole 1′-oxide] (**4j**).* Reaction time: 12 h+12 h; yield: 63%; R_f (20% EtOH in ethyl acetate) 0.52; white solid; mp: 186–188 °C; IR (KBr): ν 1722, 1588 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.03 (s, 3H), 1.06 (s, 3H), 2.00 & 2.07 (dABq, 2H, J=4.8 & 18.0 Hz), 2.55 (s, 2H)*, 3.25 (s, 3H), 4.22 & 4.49 (ABq, 2H, J=14.0 Hz), 5.29 (t, 1H, J=4.8 Hz), 6.84 (d, 1H, J=8.4 Hz), 7.14 (d, 1H, J=2.0 Hz), 7.33 (dd, 1H, J=2.0 & 8.0 Hz), *It may be unresolved ABq; ^{13}C NMR (100 MHz): δ 26.97, 28.55, 28.64, 30.96, 34.91, 39.33, 51.33, 69.16, 109.66, 122.37, 123.58, 129.03, 129.26, 132.73, 136.47, 142.27, 144.35, 175.67; HRMS (ESI) exact mass calcd for $C_{18}H_{19}ClN_2O_2$+H (M+H)$^+$, 331.1213; Found, 331.1209.

Crystal data for **4j**: Empirical formula, $C_{18}H_{19}ClN_2O_2$; formula weight, 330.80; crystal color, habit: colorless, block; crystal dimensions, 0.32×0.24×0.12 mm^3; crystal system, monoclinic; lattice type, centrosymmetric; lattice parameters, a=15.6727(8) Å, b=10.8206(5) Å, c=19.7503(11) Å; α=90.00; β=103.779(5); γ=90.00; V=3253(3) Å^3; space group, C2/c; Z=8; D_{cald}=1.351 g/cm^3; F_{000}=1392; λ (Mo-K$_\alpha$)=0.71073 Å; R ($I\geq 2\sigma_1$)=0.0459, wR^2=0.1167. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **4j** CCDC # 923596).

*4.1.25. [1-Methyl-5-bromoindolin-2-one]-3-spiro-3′-[6′,6′-dimethyl-2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4k**).* Reaction time: 12 h+12 h; yield: 58%; R_f (20% EtOH in ethyl acetate) 0.55; white solid; mp:194–196 °C; IR (KBr): ν 1704, 1616, 1578 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.03 (s, 3H), 1.06 (s, 3H), 2.05 & 2.07 (dABq, 2H, J=4.8 & 18.0 Hz), 2.47–2.62 (m, 2H)*, 3.24 (s, 3H), 4.21 & 4.49 (ABq, 2H, J=14.0 Hz), 5.29 (t, 1H, J=4.8 Hz), 6.79 (d, 1H, J=8.0 Hz), 7.28 (d, 1H, J=2.0 Hz), 7.48 (dd, 1H, J=2.0 & 8.4 Hz), *Unresolved ABq; ^{13}C NMR (100 MHz) δ 26.97, 28.56, 28.71, 30.99, 34.96, 39.39, 51.30, 69.24, 110.15, 116.23, 122.30, 126.37, 132.19, 133.17, 136.52, 142.80, 144.30, 175.59; HRMS (ESI) exact mass calcd for $C_{18}H_{19}BrN_2O_2$+H (M+H)$^+$, 375.0708; Found, 375.0712.

*4.1.26. [1-Ethyl-5-chloroindolin-2-one]- 3-spiro-3′-[6′,6′-dimethyl-2′,5′,6′,7′-tetrahydroindole 1′-oxide] (**4l**).* Reaction time: 12 h+12 h; yield: 61%; R_f (20% EtOH in ethyl acetate) 0.59; white solid; mp: 184–186 °C; IR (KBr): ν 1704, 1605, 1582 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 1.02 (s, 3H), 1.07 (s, 3H), 1.29 (t, 3H, J=7.5 Hz), 2.00 & 2.07 (dABq, 2H, J=4.5 & 18.0 Hz), 2.54 (s, 2H)*, 3.68–3.88 (m, 2H), 4.22 & 4.50 (ABq, 2H, J=14.5 Hz), 5.26 (t, 1H, J=4.5 Hz), 6.84 (d, 1H, J=8.5 Hz), 7.14 (d, 1H, J=2.0 Hz), 7.31 (dd, 1H, J=2.0 & 8.0 Hz), *Unresolved ABq; ^{13}C NMR (100 MHz): δ 12.65, 28.53, 28.64, 30.94, 34.90, 35.38, 39.33, 51.25, 69.07, 109.76, 121.87, 123.67, 128.76, 129.15, 133.13, 136.70, 141.30, 144.14, 175.19; HRMS (ESI) exact mass calcd for $C_{19}H_{21}ClN_2O_2$+H $(M+H)^+$, 345.1370; Found, 345.1377.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.07.002.

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11. Preparation of carbonates of the BH adducts, derived from aldehydes and alkyl acrylate, is reported in the literature (see Ref: Feng, J.; Lu, X.; Kong, A.; Han, X. *Tetrahedron* **2007**, *63*, 6035–6041.) We have prepared the carbonates 2 following a similar procedure.
12. It is worth mentioning here that asymmetric alkylation of nitroalkanes with carbonates of BH alcohols, derived from isatin derivatives with methyl acrylate, was recently reoprted by Lu and co-workers (Ref. 8b).
13. For recent references on reduction of nitro group using Fe/HCl/EtOH see: Chen, B.-C.; Chao, S. T.; Sundeen, J. E.; Tellew, J.; Ahmad, S. *Tetrahedron Lett.* **2002**, *43*, 1595–1596.
14. One of the referees has suggested to present a brief discussion on characterization of structure of one of the nitrone–spiro-oxindole derivatives using spectral data. This is a very nice suggestion and we thank the referee for the same. Accordingly we present a brief discussion on the characterization of **4a** using spectral data.
15. Detailed X-ray crystallographic data is available from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK for compounds **4a** (CCDC # 923595) and **4j** (CCDC # 923596).