A synthesis of 3-substituted 3-hydroxyoxindoles via an indium-mediated Barbier-type allylation of isatins in PEG-400

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A simple procedure for the synthesis of 3-allyl-3-hydroxyoxindoles from isatins in PEG-400 using organoindium reagents generated *in situ* is described. A variety of isatins reactede with allyl bromides to give the target products with excellent yields in mild conditions.

Keywords: indium, allylation, PEG-400, 3-substituted 3-hydroxyoxindoles

The 3-substituted-3-hydroxy-2-oxindole scaffold has been shown to be at the core of several natural products with a wide spectrum of biological activities, such as convolutamydines,[1] donaxaridines[2] maremycins,[3] dioxibrassinines,[4] celogentin K,[5] 3′-hydroxy glucoisatisin,[6] and TMC-95A.[7] The development of practical methods for their preparation is of interest. 3-Substituted 3-hydroxyoxindoles are also encountered in a large variety of natural and artificial bioactive compounds and can be used for the total synthesis of natural products such as CPC-1[8,9] and flustraminol.[10,11] The formation of quaternary carbon centres by the addition of nucleophiles to ketone derivatives still constitutes a major challenge for synthetic chemistry.

Since 1988, when Araki *et al.* used indium for the first time as a mediating metal in Barbier-type additions of allyl bromide to carbonyl compounds,[12] indium attracted considerable attention from various groups working on the development of new synthetic methods. Because of its low toxicity, tolerance towards air and moisture and low ionisation potential,[13,14] indium metal-mediated carbon–carbon bond formation reactions, including the Barbier-type allylation of carbonyl compounds, have become a major topic in organic synthesis. Consequently, the synthesis of 3-substituted 3-hydroxyoxindoles by an indium-mediated Barbier-type allylation of isatins is a synthetically useful transformation. Nair *et al.* first reported the allylmetalation of isatins in anhydrous dimethylformamide,[15,16] while Gong *et al.* described the allylation of isatins in aqueous environment.[17] Recently, Alcaide *et al.* reported the preparation of 3-substituted 3-hydroxyoxindoles via the metal-mediated allylation, allenylation and propargylation reactions of isatins in aqueous media with full regioselectivity.[18] However, these reports of indium-mediated allylation reaction of isatins used dimethylformamide (DMF)[15,16] and an aqueous organic media (THF/H_2O)[17] which caused environmental contamination and health problems. Furthermore, the scope of the reaction was limited to isatin only and the reaction was carried in the presence of additives. Thus, there is a need to develop a generally applicable, mild and environmentally benign practical methodology. Recently, polyethylene glycol (PEG) has been found to be an interesting solvent system.[19] PEG is environmentally benign and hasapplications, in coupling,[20] substitution,[21] oxidation,[22] addition,[23] and reduction reactions.[24] To the best of our knowledge, the indium-mediated Barbier-type allylation of isatins in PEG-400 has not been reported. We now report a simple and convenient method for the preparation of 3-allyl-3-hydroxyoxindoles from isatins and allyl bromide by using PEG400 as green reaction medium and indium as the promoting metal reagent (Scheme 1).

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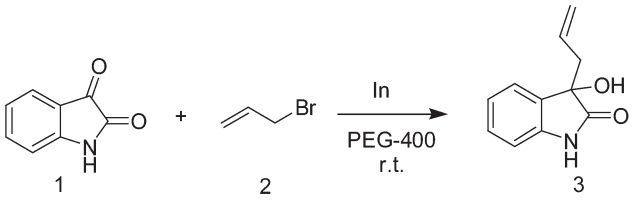


Scheme 1 Indium-mediated allylation of isatin in PEG-400.

Result and discussion

We initially selected isatin and allyl bromide as a model substrate for optimisation of the reaction conditions. Selected results from our screening experiments are summarised in Table 1. In our preliminary studies we found that, with pure water as the reaction media, the reaction proceeded at room temperature (r.t.) in 90 min and the corresponding product 3-allyl-3-hydroxyoxindole was obtained with excellent yield (Table 1, entry 1). The use of aqueous PEG-400 as a mixed solvent gave slow reaction (Table 1, entry 2). To our delight, PEG-400 as a reaction medium afforded a 99% yield of the desired product at r.t. for 5 min (Table 1, entry 3). Next, using a standard protocol we screened different metal mediators (zinc, tin). No products were observed (Table 1, entries 4, 5).

The scope of substrates was then investigated under the optimised reaction conditions. The results shown in Table 2 reveal that all the isatins were converted rapidly to give the corresponding 3-allyl-3-hydroxyoxindoles in excellent yields. We explored 2-methyl allyl bromide and 3-methyl allyl bromide as Barbier-type allylation reagents, affording the corresponding products with excellent yields of 97% and 98% respectively (Table 2, entries 2 and 3). Among the substituted isatins, both electron-donating groups and electron-withdrawing groups such as methyl, chloro, and bromo had no demonstrable effect on the yield of products (Table 2, entries 4–17). Those with *ortho* substituent such as 4-chloro and 4-bromo also gave excellent yields (Table 2, entries 7–9, 15 and 16). Note that for 4-substituted isatins as substrates and 3-methyl allyl bromide as Barbier-type allylation reagents, the reactions were reversible when the reaction time was extended

Table 1 Optimisation of allylation reaction conditions [a]

Entry	Reaction media (V/V)	Metal	Time/min	Yield /% [b]
1	H_2O	In	90min	97
2	$PEG\text{-}400/H_2O$=1:1	In	30min	98
3	PEG-400	In	5min	99
4	PEG-400	Zn	60min	NR C
5	PEG-400	Sn	60min	NR C

[a] Reaction conditions: isatin 1 mmol, indium powder 2 mol, allyl bromide 3 mmol in PEG-400 2 mL, r.t., TLC tracking.
[b] Isolated yield after flash column chromatography.
C NR, not reaction.

Table 2 Indium-mediated Barbier-type allylation of isatins

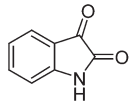
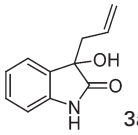
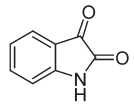
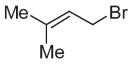
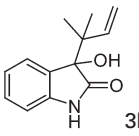
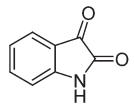
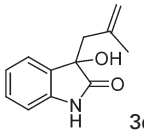
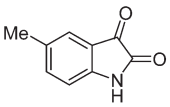
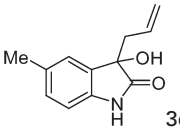
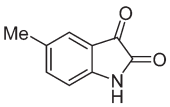
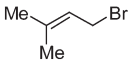
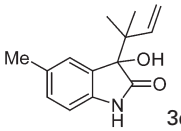
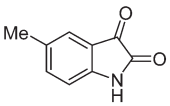
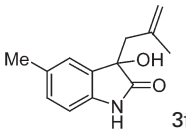
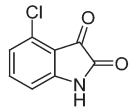
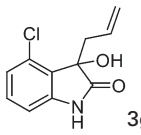
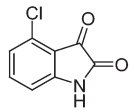
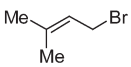
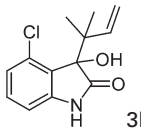
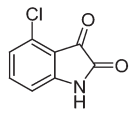
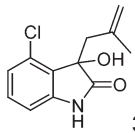
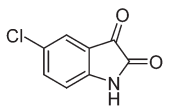
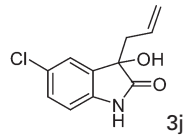
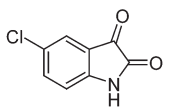
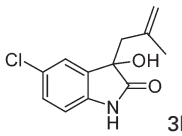
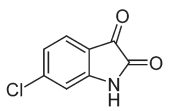
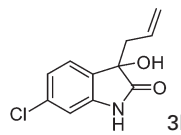
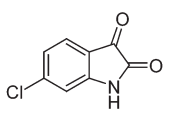
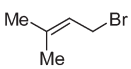
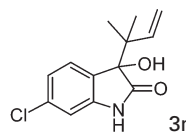
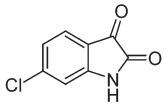
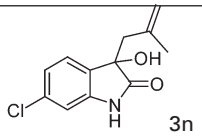
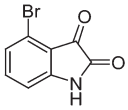
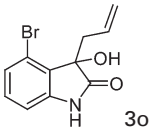
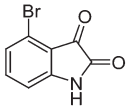
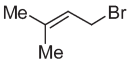
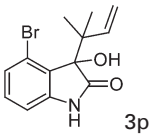
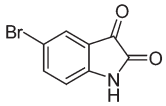
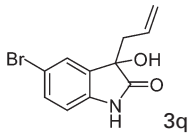
Entry[a]	Isatin	Allylbromides	Time /min	Product	Yield /%[b]
1			5	 3a	99
2			10	 3b	97
3			10	 3c	98
4			10	 3d	98
5			15	 3e	97
6			15	 3f	98
7			15	 3g	98
8			20	 3h	98
9			20	 3i	95
10			15	 3j	99
11			10	 3k	93
12			15	 3l	99
13			25	 3m	96

Table 2 *Continued*

Entry[a]	Isatin	Allylbromides	Time /min	Product	Yield /%[b]
14			25	 3n	97
15			25	 3o	96
16			30	 3p	93
17			20	 3q	96

[a] Reactions conditions: isatin 1 mmol, indium power 2 mmol, allyl bromide 3 mmol, PEG-400 2 mL, r.t., TLC tracking.
[b] Isolated yield after flash column chromatography.

(Table 2, entries 8 and 16). Interestingly, the reversible reactions were thoroughly expressed, when a drop of saturated NH_4Cl aqueous solution was added after the isatin has been consumed (confirmed by TLC). This may be attributable to the larger steric hindrance of the 4-substituent products. These indicate that indium-mediated allylation of isatins has a wide range of substrates, which can be used for large-scale synthesis of the corresponding 3-allyl-3-hydroxyoxindoles. These are important organic synthesis and medicinal intermediates.

Conclusion

In summary, we have devised a facile and simple procedure for the synthesis of 3-allyl-3-hydroxyoxindoles from isatins in PEG-400 using organoindium reagents generated *in situ*. A variety of isatins worked well with allyl bromides to give the target products with excellent yields under mild conditions. Future studies will focus on synthetic applications of the methods reported herein and the development of related C-C bond formation in PEG-400.

Experimental

All reagents were used as obtained from commercial sources except where mentioned. PEG-400 was AR grade and used directly. Indium with a purity of 99.9% were pressed into flakes and then cut into small pieces prior to use. Allyl bromide was redistilled for use. Melting points were determined on an XT-4 electrothermal Micro-melting-point apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-400 (400 MHz) spectrometer with TMS as an internal standard. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyser.

*Indium-mediated allylation of isatin (**1**); 3-allyl-3-hydroxy-1,3-dihydro-2H-indol-2-one (**3**); typical procedure*

A mixture of indium powder (2.0 mmol), allyl bromide (**2**; 3.0 mmol) and isatin (**1**; 1.0 mmol) was stirred in PEG-400 (2 mL) at r.t. until all the isatin has been consumed (confirmed by TLC). The mixture was extracted with Et_2O (3 × 2 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue eluting with hexane/ethyl acetate mixtures, gave analytically pure compound **3**. Spectroscopic and analytical data of **3** follow.

*3-Allyl-3-hydroxy-1,3-dihydro-2*H*-indol-2-one* (**3a**): Eluent: hexane–EtOAc (80:20); yield: 99%; colourless crystals; m.p. 151–152 °C (lit.[15] 150–152 °C). ^{1}H NMR ($CDCl_3$): δ 2.59–2.64 (m, 1H), 2.72–2.76 (m, 1 H), 2.80 (s, 1H), 5.12–5.17 (m, 2H), 5.67–5.71 (m, 1H), 6.58–7.49 (m, 3H), 7.49 (s, 1H). ^{13}C NMR ($CDCl_3$): 42.9, 75.9, 110.1, 120.7, 123.1, 124.6, 129.8, 130.0, 130.2, 140.1, 179.2. IR (film): ν (cm^{-1}) 3339, 2959, 1719, 1626, 1568, 1145, 923, 858, 546, 516. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.85; N, 7.40. Found: C, 70.15; H, 5.86; N, 7.78%.

*3-(1,1-Dimethylallyl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-one* (**3b**): Eluent: hexane–EtOAc (80:20); yield: 97%; colourless crystals; m.p. 181–182 °C (lit.[16] 182–183 °C). ^{1}H NMR ($CDCl_3$): δ 1.12 (s, 3H), 1.18 (s, 3H), 2.82 (s, 1H), 5.14 (d, J = 17.6 Hz, 1H), 5.23 (d, J = 10.8 Hz, 1H), 6.14–6.21 (m, 1H), 6.80–7.38 (m, 4H), 7.41 (s, 1H). ^{13}C NMR ($CDCl_3$): 19.9, 21.3, 42.6, 79.0, 108.9, 112.6, 120.5, 125.6, 128.6, 130.9, 142.0, 143.0, 178.7. IR (film): ν (cm^{-1}) 3431, 2927, 1567, 1145, 947, 858, 546, 517 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.89; H, 6.88; N, 6.42%.

*3-(2-Methylallyl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-one* (**3c**): Eluent: hexane–EtOAc (80:20); yield: 98%; colourless crystals; m.p. 187–188 °C. ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 3H), 2.54 (s, 2H), 2.76 (s, 1H), 4.54 (s, 1H), 4.78 (s, 1H), 6.74–7.10 (m, 3H), 7.19 (s, 1H). ^{13}C NMR ($CDCl_3$): 22.4, 45.7, 109.6, 115.7, 121.8, 124.0, 129.2, 129.8, 138.0, 139.2, 179.1. IR (film): ν (cm^{-1}) 3329, 2943, 1715, 1616, 1565, 1142, 912, 846, 541. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92, H, 6.45, N, 6.89. Found: C, 70.86; H, 6.42; N, 6.91%.

3-Allyl-3-hydroxy-5-methyl-1,3-dihydro-indol-2-one (**3d**): Eluent: hexane–EtOAc (80:20); yield: 98%; colourless crystals; m.p. 164–165 °C. ^{1}H NMR ($CDCl_3$): δ 2.54 (s, 3H), 2.65–2.70 (m, 2H), 2.75 (s, 1H), 5.10–5.14 (m, 2H), 5.64–5.70 (m, 1H), 6.54–7.45 (m, 3H), 7.47 (s, 1H). ^{13}C NMR ($CDCl_3$): 21.5, 42.8, 75.8, 110.0, 119.7, 122.8, 124.2, 129.4, 129.7, 128.9, 140.0, 179.1. IR (film): ν (cm^{-1}) 3338, 2946, 1627, 1564, 921, 853, 514. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92, H, 6.45, N, 6.89. Found: C, 71.14; H, 6.46; N, 6.90%.

3-(1,1-Dimethylallyl)-3-hydroxy-5-methyl-1,3-dihydro-2H-indol-2-one (**3e**): Eluent: hexane–EtOAc (80:20); yield: 97%; colourless crystals; m.p. 189–190 °C. ^{1}H NMR ($CDCl_3$): δ 1.10 (s, 3H), 1.12 (s, 3H), 2.57, (s, 3H), 2.92 (s, 1H), 5.10-5.11 (m, 2H), 5.63-5.67 (m, 1H), 6.64-7.37 (m, 3H), 7.35 (s, 1H). ^{13}C NMR ($CDCl_3$): 19.9, 21.3, 21.4, 42.7, 79.8, 108.9, 113.1, 120.1, 125.4, 128.0, 130.92, 141.7, 142.4, 178.2. IR (film): ν (cm^{-1}) 3435, 1569, 1148, 957, 864, 541. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70, H, 7.41, N, 6.06. Found: C, 72.97, H, 7.40; N, 6.08%.

*3-(2-Methylallyl)-3-hydroxy-5-methyl-1,3-dihydro-2*H*-indol-2-one* (**3f**): Eluent: hexane–EtOAc (80:20); yield: 98%; colourless crystals; m.p. 188–189 °C. ^{1}H NMR ($CDCl_3$): δ 1.40 (s, 3H), 2.51 (s, 3H), 2.63 (s, 2H), 2.68 (s, 1H), 4.52 (s, 1H), 4.78 (s, 1H), 6.70–7.17 (m, 3H), 7.13 (s, 1H). ^{13}C NMR ($CDCl_3$): 22.5, 22.2, 45.4, 109.1, 115.0, 121.1, 123.5, 129.1, 129.4, 137.5, 139.1, 179.0. IR (film): ν (cm^{-1}) 3359,

1712, 1568, 910, 854, 564 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 70.92, H, 6.45, N, 6.89. Found: C, 70.98; H, 6.49; N, 6.91%.

*3-Allyl-4-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3g**): Eluent: hexane–EtOAc (80:20); yield: 98%; colourless crystals; m.p. 209–211 °C. ^{1}H NMR ($CDCl_3$): δ 2.80 (s, 1H), 2.84-2.89 (m, 1H), 3.11–3.16 (m, 1H), 5.02 (d, *J* = 10.8 Hz, 1H), 5.45 (d, *J* = 17.2 Hz, 1H), 5.44–5.48 (m, 1H), 6.74–7.22 (m, 3H), 7.42 (s, 1H). ^{13}C NMR ($CDCl_3$): 75.3, 76.5, 108.4, 118.9, 122.3, 126.9, 128.6, 130.7, 130.9, 143.8, 177.6. IR (film): ν (cm^{-1}) 3431, 1721, 1567, 1144, 857, 546, 516. Anal. Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07, H, 4.51, N, 6.26. Found: C, 59.14; H, 4.50; N, 6.21%.

3-(1,1-Dimethylallyl)-4-chloro-3-hydroxy-1,3-dihydro-2H-indol-2-one (**3h**): Eluent: hexane–EtOAc (80:20); yield: 98%; colourless crystals; m.p. 193–194 °C. ^{1}H NMR ($CDCl_3$): δ 1.12 (s, 3H), 1.26 (s, 3H), 3.02 (s, 1H), 5.14–5.21 (m, 2H), 6.05–6.12 (m, 1H), 6.72–7.27 (m, 3H), 7.75 (s, 1H). ^{13}C NMR ($CDCl_3$): 21.0, 23.0, 82.1, 107.8, 112.1, 113.0, 127.4, 130.0, 143.5, 144.3, 178.5. IR (film): ν (cm^{-1}) 3444, 2952, 1640, 1415, 953, 514. Anal. Calcd for $C_{13}H_{14}ClNO_2$: C, 62.03, H, 5.61, N, 5.56. Found: C, 62.18; H, 5.58; N, 5.52%.

*3-(2-Methylallyl)-4-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3i**): Eluent: hexane–EtOAc (80:20); yield: 95%; colourless crystals; m.p. 232–233 °C. ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 3H), 2.58–2.61 (m, 2H), 2.96–3.00 (m, 1H), 4.20–4.24 (m, 1H), 4.52–4.60 (m, 1H), 6.72–7.20 (m, 3H), 10.46 (s, 1H). ^{13}C NMR ($CDCl_3$): 22.3, 45.4, 109.3, 114.5, 121.1, 123.0, 128.5, 128.5, 137.0, 138.4, 178.3. IR (film): ν (cm^{-1}) 3431, 2957, 1723, 1567, 1144, 857, 546 cm^{-1}. Anal. Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64, H, 5.09, N, 5.89. Found: C, 60.84; H, 5.05; N, 5.87%.

*3-Allyl-5-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3j**): Eluent: hexane–EtOAc (80:20); yield: 99%; colourless crystals; m.p. 177–178 °C. ^{1}H NMR ($CDCl_3$): δ 2.57–2.61 (m, 1H), 2.70–2.73 (m, 1H), 2.74 (s, 1H), 5.14–5.18 (m, 2H), 5.66–5.72 (m, 1H), 6.78–7.55 (m, 3H), 7.55 (s, 1H). ^{13}C NMR ($CDCl_3$): 64.9, 75.3, 110.8, 116.2, 121.8, 123.0, 125.0, 130.1, 139.0, 140.3, 179.4. IR (film): ν (cm^{-1}) 3414, 2959, 1717, 1568, 1142, 855, 546. Anal. Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07, H, 4.51, N, 6.26. Found: C, 59.14; H, 4.48; N, 6.24%.

*3-(1,1-Dimethylallyl)-5-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3k**): Eluent: hexane–EtOAc (80:20); yield: 93%; colourless crystals; m.p. 174–175 °C. ^{1}H NMR ($CDCl_3$): δ 1.11 (s, 3H), 1.16 (s, 3H), 2.84 (s, 1H), 5.12–5.26 (m, 2H), 6.14 (dd, J_1 = 10.8 Hz, J_2 = 17.6 Hz, 1H), 6.84–7.30 (m, 3H), 7.43 (s, 1H). ^{13}C NMR ($CDCl_3$): 19.9, 21.2, 42.7, 78.7, 108.9, 120.3, 127.0, 129.9, 132.9, 142.6, 143.7, 178.6. IR (film): ν (cm^{-1}) 3391, 1711, 1567, 1144, 858, 546. Anal. Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64, H, 5.09, N, 5.89. Found: C, 60.95; H, 5.12; N, 5.87%.

*3-Allyl-6-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3l**): Eluent: hexane–EtOAc (80:20); yield: 99%; colourless crystals; m.p. 202–203 °C. ^{1}H NMR ($CDCl_3$): δ 2.56–2.62 (m, 1H), 2.70–2.74 (m, 1H), 2.83 (s, 1H), 5.12–5.16 (m, 2H), 5.66–5.69 (m, 1H), 6.88–7.30 (m, 3H), 7.59 (s, 1H). ^{13}C NMR ($CDCl_3$): 43.5, 79.9, 110.2, 116.1, 122.3, 127.2, 127.3, 135.3, 141.3, 142.1, 179.2. IR (film): ν (cm^{-1}) 3351, 1722, 1147, 861, 546. Anal. Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07, H, 4.51, N, 6.26. Found: C, 59.57; H, 4.50; N, 6.27%.

*3-(1,1-Dimethylallyl)-6-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3m**): Eluent: hexane–EtOAc (80:20); yield: 96%; colourless crystals; m.p. 213–234 °C. ^{1}H NMR ($CDCl_3$): δ 1.11 (s, 3H), 1.16 (s, 3H), 2.84 (s, 1H), 5.12–5.26 (m, 2H), 6.14 (dd, J_1 = 10.8 Hz, J_2 = 17.6 Hz, 1H), 6.84–7.30 (m, 3H), 7.43 (s, 1H). ^{13}C NMR ($CDCl_3$): 19.9, 21.2, 42.7, 78.7, 108.9, 120.3, 127.0, 129.9, 132.9, 142.6, 143.7, 178.6. IR (film): ν (cm^{-1}) 3391, 1711, 1567, 1144, 858, 546 cm^{-1}. Anal. Calcd for $C_{13}H_{14}ClNO_2$: C, 62.03, H, 5.61, N, 5.56. Found: C, 62.15; H, 5.59; N, 5.54%.

*3-(2-Methylallyl)-6-chloro-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3n**): Eluent: hexane–EtOAc (80:20); yield: 97%; colourless crystals; m.p. 212–213 °C. ^{1}H NMR ($CDCl_3$): δ 1.57 (s, 3H), 2.67 (s, 2H), 2.80 (s, 1H), 4.67 (s, 1H), 4.84 (s, 1H), 6.87–7.29 (m, 3H), 7.31 (s, 1H). ^{13}C NMR ($CDCl_3$): 24.0, 46.1, 110.8, 116.6, 122.9, 126.0, 130.5, 130.8, 139.5.0, 139.9, 180.6. IR (film): ν (cm^{-1}) 3431, 1567 , 1144, 945, 857, 546 cm^{-1}. Anal. Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64, H, 5.09, N, 5.89. Found: C, 60.72; H, 5.05; N, 5.86%.

*3-Allyl-4-bromo-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3o**): Eluent: hexane–EtOAc (80:20); yield: 96%; colourless crystals; m.p. 232–233 °C. ^{1}H NMR ($CDCl_3$): δ 2.50–2.58 (m, 1H), 3.03–3.08 (m, 1H), 3.34 (s, 1H), 4.86 (d, *J* = 10.0 Hz, 1H), 4.96 (d, *J* = 16.8 Hz, 1H), 5.16–5.21 (m, 1H), 6.76–7.13 (m, 4H), ^{13}C NMR ($CDCl_3$): 77.1, 96.0, 108.9, 118.8, 119.0, 125.5, 128.6, 130.9, 144.1, 177.8. IR (film): ν (cm^{-1}) 3440, 3130, 1722, 1566, 1143, 95.2, 860, 546, 515 cm^{-1}. Anal. Calcd for $C_{11}H_{10}BrNO_2$: C, 49.28; H, 3.16; N, 5.22. Found: C, 49.85; H, 3.58; N, 5.17%.

*3-(1,1-Dimethylallyl)-4-bromo-3-hydroxy-1,3-dihydro-2*H-*indol-2-one* (**3p**): Eluent: hexane–EtOAc (80:20); yield: 93%; colourless crystals; m.p. 174–175 °C. ^{1}H NMR ($CDCl_3$): δ 1.09 (s, 3H), 1.12 (s, 3H), 2.50 (s, 1H), 5.76–5.91 (m, 2H), 5.99–6.01 (m, 1H), 6.71–7.07 (m, 3H), 10.24 (s, 1H). ^{13}C NMR ($CDCl_3$): 21.2, 23.3, 54.9, 82.4, 108.3, 112.2, 119.5, 126.3, 129.2, 130.2, 143.6, 144.6, 178.7. IR (film): ν (cm^{-1}) 3414, 1715, 1640, 1139, 1068,952, 863, 515 cm^{-1}. Anal. Calcd for $C_{13}H_{14}BrNO_2$: C, 52.72; H, 4.76; N, 4.73. Found: C, 52.87; H, 4.81; N, 4.81%.

3-allyl-5-bromo-3-hydroxy-1,3-dihydro-2H-indol-2-one **(3q):** Eluent: hexane–EtOAc (80:20); yield: 96%; colourless crystals; m.p. 217–218 °C (lit.[13] 215–217). ^{1}H NMR ($CDCl_3$): δ 2.41–2.62 (m, 3H), 4.93–4.97 (m, 2H), 5.40–5.44 (m, 1H), 6.93 (s, 2H), 7.14–7.22 (m, 2H), 10.39 (s, 1H). ^{13}C NMR ($CDCl_3$): 41.7, 74.9, 110.7, 113.2, 118.5, 126.5,130.7, 130.3,133.0,178.2, 140.0. IR (film): ν (cm^{-1}) 3428, 1721, 1568, 1144, 857, 546, 516 cm^{-1}. Anal. Calcd for $C_{11}H_{10}BrNO_2$: C, 49.28; H, 3.16; N, 5.22. Found: C, 49.24; H, 3.15; N, 5.28%.

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References

1 Y. Kamano, H.P. Zhang, Y. Ichihara, H. Kizu, K. Komiyama and G.R. Pettit, *Tetrahedron Lett*., 1995, **36**, 2783.
2 H.B. Rasmussen and J.K. MacLeod, *J. Nat. Prod*., 1997, **60**, 1152.
3 W. Balk-Bindseil, E. Helmke, H. Weyland and H. Laatsch, *Liebigs Ann*., 1995, 1291.
4 K. Monde, K. Sasaki, A. Shirata and M. Tagusuki, *Phytochemistry*, 1991, **30**, 2915.
5 H. Suzuki, H. Morita, M. Shiro and M. Kobayashi, *Tetrahedron*, 2004, **60**, 2489.
6 A. Frechard, N. Fabre, C. Pean, S. Montaut, M.T. Fauvel, P. Rollin and I. Fouraste, *Tetrahedron Lett.*, 2001, **42**, 9015.
7 J. Kohno, Y. Koguchi, M. Nishio, K. Nakao, M. Kuroda, R. Shimisu, T. Ohnuki and S. Komatsubara, *J. Org. Chem.*, 2000, **65**, 990.
8 C. Marti and E.M. Carreira, *Eur. J. Org. Chem.*, 2003, 2209.
9 H. Lin and S.J. Danishefsky, *Angew. Chem., Int. Ed.*, 2003, **42**, 36.
10 C.V. Galliford and K.A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748.
11 B.M. Trost and M.K. Brennan, *Synthesis*, 2009, 3003.
12 S. Araki, H. Ito and Y. Butsugan, *J. Org. Chem.*, 1988, **53**, 1831.
13 J. Podlech and T.C. Maier, *Synthesis*, 2003, 633.
14 Z. Du and Y. Li, *Prog. Chem*., 2010, **22**, 71.
15 V. Nair, S. Ros and C.N. Jayan, *Tetrahedron*, 2001, **57**, 9453.
16 V. Nair, S. Ros and C.N. Jayan, *J. Chem. Res., Synop.*, 2001, 551.
17 J.H. Gong, K.Y. Lee, J.S. Son and J.N. Kim, *Bull. Kor. Chem. Soc.*, 2003, **24**, 507.
18 B. Alcaide, P. Almendros and R. Rodrĺguez-Acebes, *J. Org. Chem.*, 2005, **70**, 3198.
19 J. Chen, S.K. Spear, J.G. Huddleston and R.D. Rogers, *Green Chem*., 2005, **7**, 64.
20 S. Chandrasekhar, C. Narsihmulu, S.S. Sultana and N.R. Reddy, *Org. Lett.*, 2002, **4**, 4399.
21 V.V. Namboodiri and R.S. Varma, *Green Chem.*, 2001, **3**, 146.
22 Z. Hou, N. Thetssen and W. Leitner, *Green Chem*., 2007, **9**, 127.
23 R. Kumar, P. Chaudhary, S. Nimesh and R. Chandra, *Green Chem.*, 2006, **8**, 356.
24 W. Wang, S. Lu, P. Yang, X. Han and Y. Zhou, *J. Am. Chem. Soc.*, 2003, **125**, 10536.