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General synthesis of mono-, di-, and tri-acetylated indoles from indolin-2-ones

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ABSTRACT

Having developed the one-pot triacetylation of indolin-3-ones, we have now devised a simple two-step reaction sequences to produce di- and mono-acetylated indoles from indolin-2-ones. The indolin-2-ones were first subjected to acetylation in the presence of acetic anhydride and a catalytic amount of *N*,*N*-dimethylaminopyridine to give 2-acetoxy-1,3-diacetylindoles. Subsequently, an enzyme-assisted deacetylation resulted in the chemoselective deprotection of the acetoxy group to produce 1,3-diacetyl-2-hydroxyindoles. However, a chemical deacetylation of 2-acetoxy-1,3-diacetylinoles under mild basic or acidic conditions resulted in the formation of 3-acetyl-2-hydroxyindoles.

1. Introduction

The indole nucleus is a basic skeletal framework for a large number of biologically and industrially relevant molecules.[1] The importance of indole and its myriad derivatives is evident from the growing volume of chemical literature found on them in the field of pharmaceutical/medicinal chemistry,[2] natural products,[3] agro-chemicals,[4] and synthetic chemistry.[5] Given the high significance of indole-based molecules, there is a rising need for the development of efficient and practical synthesis of substituted indoles. Our research group is actively involved in exploring the chemistry of substituted indoles to develop the synthesis of newer indole-based heterocycles.[6,7]

Protection and deprotection steps are an integral part of organic synthesis and are routinely applied in multistep synthetic transformations.[8] Some of the desirable criteria for designing synthetic procedures for the introduction and removal of protecting groups are selectivity, higher yields of the reaction, clean conversion, and their easy manipulation.[9] Among various protections, the acetyl group is heavily used for the protection of heteroatoms (N, O, and S).[8]

In addition to chemical deprotection procedures, which may[10] or may not be selective, enzyme-assisted chemo- and regio-selective deprotection of multiply acylated compounds can be employed. Enzyme-catalyzed reactions have become very popular in organic synthesis[11] and are often employed as a green and sometimes an only alternative to achieve selectivity in the reaction outcomes. Besides being highly selective in nature, the enzyme-catalyzed reactions are generally high yielding, clean, and use very mild reaction conditions (room temperature). *Candida antarctica* lipase B (CALB), commercially available in immobilized form (Novozyme® 435), is a hydrolase enzyme known for its promiscuity and efficient catalysis of transesterification reactions in organic solvents.[12–15]

The indolin-2-one moiety is a useful precursor for the synthesis of indole derivatives.[16] In our preliminary study,[6] while pursuing the acetyl protection of the N-1 position of indolin-2-one (**1**), we disclosed an unprecedented multiple acetylation on the indolin-2-one (**1**) framework in the presence of a catalytic amount of *N*,*N*-dimethylaminopyridine (DMAP) in acetic anhydride. This resulted in the synthesis of 2-acetoxy-1,3-diacetylindole (**2**) in excellent yields where three nucleophilic sites, namely N-1, O at C-2 and C-3, were acetylated in just one step.[6] Earlier Beccalli et al. had reported a triacylation of 3-(2-aryl-1-hydroxyethylidene)indol-2(3*H*)-one moieties using ethyl formate.[17] However, in their reaction multiple acylation occurred only at the heteroatoms. Furthermore, the acetylation of 1-alkylated indolin-2-ones in the presence of DMAP resulted in the chemoselective synthesis of 3-acetyl-1-alkyl-2-hydroxyindoles in one step.[6] To make the easily obtainable per-acetylated indole products synthetically more attractive, we

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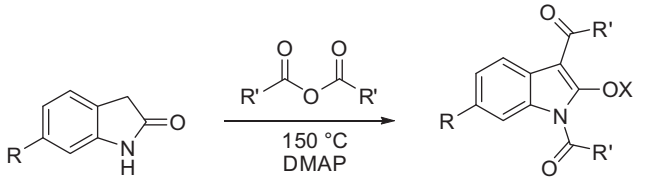
envisioned selective as well as complete deprotection of relatively labile acetyl groups on heteroatoms. Altogether, the strategy of triacetylation of indolin-2-ones followed by selective as well as complete deacetylation could give us an easy access to mono- and di-acetyl substituted 2-hydroxyindoles.

To systematically conclude our preliminary study[6] on the acetylation of indolin-2-ones, we have examined the chemoselective acetylation and deacetylation of variously substituted indolinones in this report. The multi-acetyled products were subjected to deacetylation under enzyme-catalyzed transesterification and chemical hydrolysis conditions to produce *O*-deacetylated and *N*,*O*-dideacetylated products, respectively. Herein, we wish to report a general syntheses of 3-acetyl-2-hydroxyindoles, 1,3-diacetyl-2-hydroxyindoles, and 2-acetoxy-1,3-diacetylindoles from indolin-2-ones in excellent yields.

2. Results and discussions

Acetylation of indolin-2-one (**1**) at N-1 using acetic anhydride is well documented in the literature,[18] however, a one-pot multiple acetylation on this framework was unprecedented until our preliminary report was published recently.[6] DMAP is a general catalyst well-known to catalyze acylation, alkylation, carbonylation, dehydration, esterification, nucleophilic substitution, etc. reactions involving a variety of functional groups.[19] The results of our preliminary investigation are summarized here. A systematic investigation of this unique reaction revealed the triacetylated indole derivative being the exclusive product in the case of acetic anhydride (Table 1, entries 1 and 2). However, when higher anhydrides namely propanoic and butyric anhydrides were used as acyl group donors,

Table 1
Multiple acylation on indolin-2-ones **1** and **2**

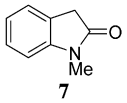
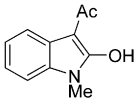
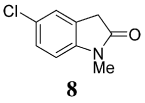
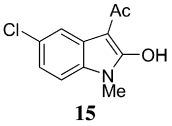
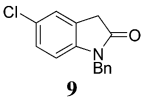
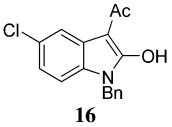
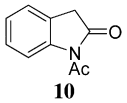
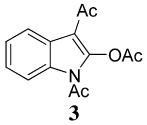
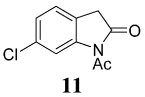
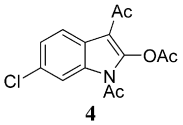
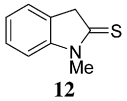
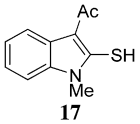
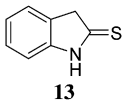
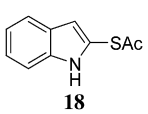
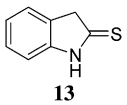
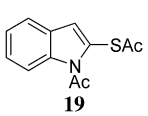


Entry	Substrate	Anhydride (R′)	Reaction time (h)	Product (% yield)
1	**1**	Me	4	**3** (95)
2	**2**	Me	1	**4** (93)
3	**1**	Et	4	**5** (76)
4	**1**	Pr	4	**6** (82)

the acylation occurred at only two positions, N and 3-C, in the major product (Table 1, entries 3 and 4). A trace amount of (>5%) of triacylated product was also isolated from the reaction mixture in these cases. It is likely that the steric bulk imparted by longer chain acyl groups might be slowing the formation of the triacylated products.

To exhibit the substrate variability, 1-alkylindolin-2-ones, indoline-2-thione, and 1-alkylindolin-2-thione, obtained using literature procedures,[20,21] were included in the preliminary study. Rather interesting results were obtained with these substrates when subjected to the acetic anhydride/DMAP reaction condition. 1-Alkylindolin-2-one (**7**–**9**) and 1-methylindoline-2-thione (**12**) were chemoselectively monoacetylated to 3-acetyl-1-alkyl-2-hydroxyindoles **14**–**16** and 3-acetyl-1-alkyl-2-mercaptoindole (**17**), respectively (Table 2). Whereas, in the case of indoline-2-thione (**13**) the acetylation first occurred at S (Table 2, entry 7), while a prolonged heating

Table 2
Acetylation on 1-substituted indolin-2-ones (**7**–**11**) and indoline-2-thiones (**12**, **13**)

Entry	Substrate	Product	Reaction time (h)	Product (% yield)
1	 **7**	 **14**	4	81
2	 **8**	 **15**	4	78
3	 **9**	 **16**	4	80
4	 **10**	 **3**	4	94
5	 **11**	 **4**	4	90
6	 **12**	 **17**	2	71
7	 **13**	 **18**	1	94
8	 **13**	 **19**	4	78

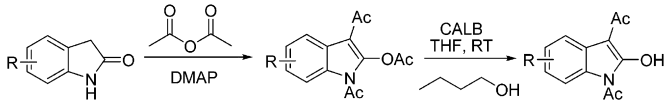
of the reaction mixture led to the diacetylation at N and S producing 1-acetyl-1*H*-indol-2-yl ethanethioate (**19**, Table 2, entry 8). On the contrary, the presence of an electron withdrawing acetyl group in **10** and **11** was detrimental to the chemoselectivity. In these cases the triacetylated indole was isolated as a major product of the reaction (Table 2, entries 4 and 5).

Previously, the syntheses of 3-acetyl-1-alkyl-2-hydroxyindoles have been reported in three steps starting from substituted anilines.[22,23] Our one-step facile formation of 3-acetyl-1-alkyl-2-hydroxyindoles (**14**–**16**) in good yields from easily available starting materials represents a very simple and inexpensive alternative procedure to access this framework.

To further widen the substrate scope of the triacetylation reaction, we selected a range of variously substituted indolin-2-ones (**20**–**26**) with variations in functional groups and the position of their substitution on the indole ring. The indolin-2-ones **21**, **22**, **25**, and **26** were obtained from commercial sources, whereas **20**, **23**, and **24** were synthesized from corresponding isatins using literature

procedure. The indolin-2-ones were then subjected to acetic anhydride and 1 mol % DMAP at 150 °C to obtain the 2-acetoxy-1,3-diacetylindoles. As shown in Table 3, the reaction time for the acetylation reaction of substituted indolin-2-one was generally shorter than that for the unsubstituted analog **1**. In most cases the reaction was completed within 2 h, whereas indolin-2-one (**1**) required 4 h to undergo completion. The isolation of the desired multi-acetylated products was straight forward. The reaction

Table 3
Multiple acylation on indolin-2-ones and indoline-2-thiones followed by CALB-catalyzed chemoselective O-deacetylation



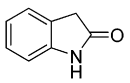
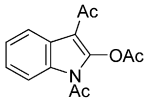
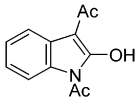
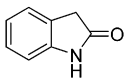
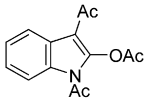
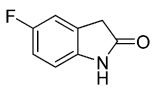
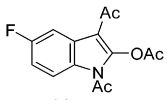
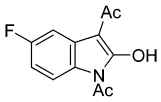
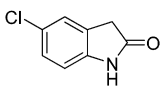
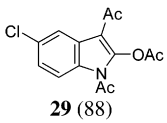
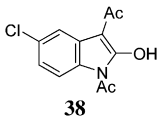
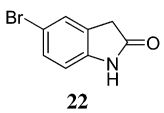
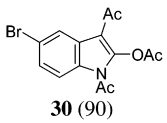
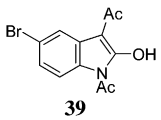
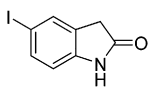
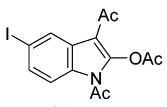
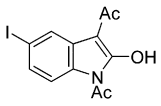
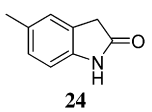
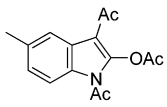
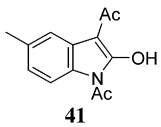
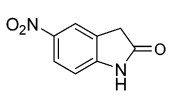
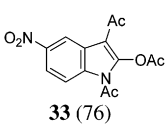
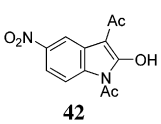
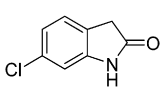
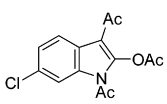
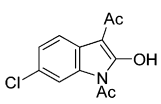
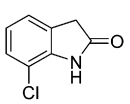
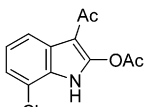
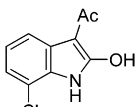
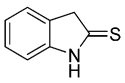
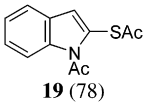
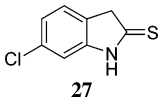
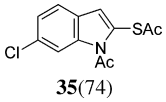
Entry	Indolin-2-one	Product (% yield)	Reaction time (h)	Product[a]	Reaction time (h)
1	 **1**	 **3** (93)	4	 **36**	1
2	 **1**	 **3** (93)	4	No reaction	1 Control (no enzyme)
3	 **20**	 **28** (91)	2	 **37**	1
4	 **21**	 **29** (88)	2	 **38**	1
5	 **22**	 **30** (90)	2	 **39**	1
6	 **23**	 **31** (81)	2	 **40**	1
7	 **24**	 **32** (95)	2	 **41**	1
8	 **25**	 **33** (76)	4	 **42**	4
9	 **2**	 **4**	1	 **43**	1
10	 **26**	 **34** (95)	2	 **44**	3

Table 3 (*continued*)

Entry	Indolin-2-one	Product (% yield)	Reaction time (h)	Product[a]	Reaction time (h)
11	 **13**	 **19** (78)	1	No reaction	72
12	 **27**	 **35**(74)	4	No reaction	72

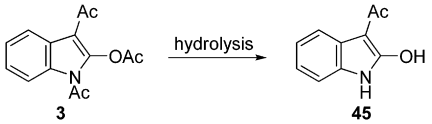
[a] The products were obtained in quantitative yields in all the cases.

mixture was stripped off of the excess acetic anhydride under high vacuum. The resulting residue was suspended in cold methanol and the precipitate obtained was vacuum filtered followed by a wash with hexanes. The triacetylation proceeded efficiently in almost all cases (Table 3), except for 5-nitro indolin-2-one (**25**) where the product yield was slightly lower (entry 8). The result obtained for the acetylation of 7-chloroindolin-2-one (**26**) was anomalous with respect to other indolinones. A diacetylated product **34** was obtained in which the 3-C and the O at C-2 of **26** were acetylated but the N-1 remained free from acetyl substitution (Table 3, entry 10). This anomaly in the reactivity of **26** might be caused by the steric hindrance imparted by the chloro group being present in close proximity to the N-1. The thione analog **27** underwent diacetylation analogous to indoline-2-thione (Table 3, entries 11 and 12). To obtain an additional example of a multi-acetylated indole, acetylation of compound **6** was attempted in the presence of acetic anhydride and DMAP. Interestingly, the butanoyl group on N of **6** was substituted with the acetyl group **6a** under this reaction condition.

After having synthesized a number of 2-acetoxy-1,3-diacetylindoles, we set out to study selective deacetylations to produce indole derivatives amenable to further chemical manipulations. The acetyl group at heteroatoms (N, O, and S) are chemically labile under hydrolytic conditions and can be deprotected simultaneously. To achieve selective deacetylation, we chose to employ the commercially available immobilized enzyme CALB (Novozyme® 435) to carry out the desired transformations. The motivation of using enzyme-assisted reactions in lieu of chemical conditions also stems from their 'green' properties, such as clean and quantitative conversion, mild conditions, catalyst recycling, and low waste production. In a test reaction, a solution of 1,3-diacetyl-2-hydroxyindole (**3**) in THF was mixed with the enzyme CALB and 1-butanol as acetyl acceptor. The enzyme was not introduced in the control reaction mixture and only consisted of a solution of compound **3** and 1-butanol in THF. The reaction mixtures were shaken vigorously at room temperature and the progress was monitored by thin layer chromatography (TLC). After the reaction was completed (1 h) the enzyme was filtered off, the solvent was evaporated under vacuum and the product was analyzed by NMR. We were quite pleased to observe that a chemoselective O-deacetylation took place in quantitative yield to produce the desired product **36** (Table 3, entry 1). Under the control reaction conditions, the compound **3** did not undergo any transformation in 1 h and only the starting material was isolated from the reaction mixture. After validating the enzyme-assisted chemoselective O-deacetylation reaction, eight 2-acetoxy-1,3-diacetylindoles and two thioesters were subjected to the deacetylation reaction. As shown in Table 3, the enzymatic deacetylation proceeded in quantitative yields in all the cases. There was a marked difference in the reactivity of 2-acetoxy-1,3-diacetyl-5-nitroindole (**33**) and 2-acetoxy-1-acetyl-7-chloroindole (**34**) where the reaction rate was found to be somewhat slower toward the deacetylation reaction. The relatively high polarity of these compounds might be causing the slowdown in the enzymatic transformation reaction. Furthermore, the thioesters **19** and **35** were not found to be the substrates for the enzyme studied. No transformation was observed for **19** and **35** even after 72 h of stirring (Table 3, entries 11 and 12).

Chemically, 2-acetoxy-1,3-diacetylindole (**3**) contains an ester and an amide group. Owing to extra stability of the amide functionality, it is possible to selectively perform chemical hydrolysis of the ester group in the presence of an amide group.[10] Thus, we attempted to effect selective ester hydrolysis of 2-acetoxy-1,3-diacetylindole (**3**) to ascertain if there is any merit in the use of the enzyme-assisted deacetylation process described in this report. As shown in Table 4, four hydrolytic conditions were chosen to carry out the desired transformation. The reaction conditions were selected so as to represent mild and relatively harsh acidic and basic conditions for the desired hydrolysis. The hydrolysis was found to be significantly slower under acidic conditions relative to the basic conditions. However, the reactions resulted in indiscriminate deacetylation leading to 3-acetyl-2-hydroxyindole in all cases (Table 4). The best result was obtained in 5% NaOH/THF (1:1) at room temperature followed by acidification with dil HCl (Table 4, entry 3). Although the chemical deacetylation did not afford the desired selective O-deacetylation, the double deacetylation of 2-acetoxy-1,3-diacetylindole (**3**) represents a novel and mild method for the synthesis of 3-acetyl-2-hydroxyindole (**45**) from indolin-2-one. The synthesis of **45** has been reported previously starting from *o*-acetoacetochloroanilide in the presence of potassium amide/ammonia in 67% yield.[24] Another group reported the synthesis of related 3-acetyl-6-bromooxindole from 6-bromooxindole in three steps.[25] In this synthesis the acetyl group was indirectly installed at the 3 position by first acetylating 6-bromooxindole and treating 1-acetyl-6-bromooxindole with triethyl orthoacetate followed by a basic cleavage of the resulting enol ether. Also, it was interesting to note that the product of chemical deacetylation **45**, despite being a 1,3-diketone, is stable under harsh basic conditions unlike normal 1,3-diketones.[26] This stabilization is presumably due to the aromatic effect of the indole nucleus.

Table 4
Chemical deacetylation of 2-acetoxy-1,3-diacetylindole **3**



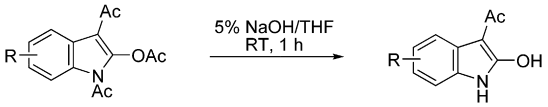
3 **45**

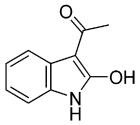
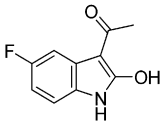
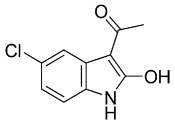
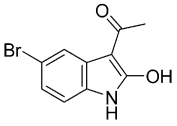
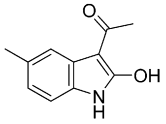
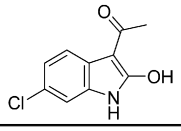
Entry	Reaction conditions	Reaction time (h)	% Yield
1	5% HCl/THF (1:1), rt	24	97
2	5% HCl/THF (1:1), 80 °C	12	94
3	5% NaOH/THF (1:1), rt	1	95
4	5% NaOH/THF (1:1), 80 °C	1	95

To further investigate and consolidate the results of double deacetylation, under chemical conditions several 2-acetoxy-1,3-diacetylindoles **4**, **28**–**30**, and **32** were subjected to the base-

promoted hydrolysis. The results shown in Table 5 indicate that the chemical hydrolysis went smoothly in all the cases in excellent yields. No significant substitution effect was observed in the reaction and the hydrolysis was complete within 1 h.

Table 5
Chemical deacetylation of 2-acetoxy-1,3-diacetylindoles **3**, **4**, **28**–**30**, and **32**



Entry	Triacetylated indole	Product	Product (% isolated yield)
1	**3**		**45** (91)
2	**28**		**46** (88)
3	**29**		**47** (89)
4	**30**		**48** (83)
5	**32**		**49** (85)
6	**4**		**50** (88)

3. Conclusions

The development of efficient and practical strategies to further expand the diversity of indole-based heterocycles is highly desirable in organic synthesis. We have developed a simple synthesis of *N*-substituted 3-acetyl-2-hyroxyindoles starting from indolin-2-ones, which can be used as building blocks to access newer indole heterocycles. *N*-Alkylated 3-acetyl-2-hydroxyindoles can be directly obtained upon treating *N*-alkylated indolin-2-one with acetic anhydride in the presence of a catalytic amount of DMAP. The strategy for the synthesis of *N*-acetylated 3-acetyl-2-hyroxyindoles involves two steps starting from indolin-2-ones. First, the indolin-2-one moieties are peracetylated in the presence of acetic anhydride and DMAP leading to 2-acetoxy-1,3-diacetylindoles in excellent yields. Subsequently, CALB enzyme-catalyzed chemoselective deacetylation gave rise to 1,3-diacetyl-2-hydroxyindoles in overall excellent yields. The use of an enzyme-catalyzed transformation makes this step environmentally friendly. On the contrary, the deacetylation under mild chemical conditions led to a non-selective removal of the acetyl groups from N and O of 2-acetoxy-1,3-diacetylindoles to give 3-acetyl-2-hydroxyindoles in excellent yields. The multiple acetylation followed by a chemical double deacetylation reaction sequence represents a new, efficient and general procedure for the synthesis 3-acetyl-2-hydroxyindoles.

4. Experimental

4.1. General

All reagents and solvents were used as supplied by commercial sources without further purification. Melting points were measured using a MEL-TEMP II apparatus and are uncorrected. Precoated fluorescent silica gel TLC plates were used to monitor the progress of the reactions. IR spectra were recorded on a Nicolet MAGNA-IR 560 Spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained by a Bruker AV300 spectrometer. Chemical shifts of the ^{1}H NMR spectra are reported in parts per million (ppm) downfield from tetramethylsilane. The GC–EIMS mass spectra were recorded using Varian-450 GC instrument equipped with Varian 240-MS IT mass spectrometer. HR-ESIMS spectra were obtained at the Department of Chemistry, Dalhousie University, by Mr. Xiao Feng.

4.2. General procedure for the synthesis of indolin-2-ones from isatins

A mixture of substituted isatin (12.3 mmol), hydrazine hydrate (368 mmol), potassium hydroxide (245 mmol), and ethylene glycol (242 mmol) were heated at 100 °C for 1 h. The reaction mixture was cooled on ice bath and acidified using concd HCl (drop wise addition) along with vigorous stirring. The precipitated product was vacuum filtered and washed with hexanes to give substituted indolin-2-ones in 90–95% yield.

4.3. General procedure for DMAP-catalyzed acetylation of indolin-2-ones and indoline-2-thiones

Appropriate indolin-2-one or indoline-2-thione (0.3 g) was mixed with acetic anhydride (3 mL) and 4-dimethylaminopyridine (DMAP, 1 mol %). The mixture was heated at 150 °C in a round-bottomed flask equipped with an air condenser and $CaCl_2$ guard tube. The reaction time for each reactant is provided in Tables 2 and 3. After the completion of the reaction excess acetic anhydride was evaporated under reduced pressure. The solid residue obtained in the case of the triacetylated products was suspended in cold methanol and vacuum filtered. The product collected was thoroughly washed with hexane and dried. In the case of mono and diacetylated products the solid residue was purified using flash column chromatography (FCC) (silica gel, hexanes/ethyl acetate).

*4.3.1. 1,3-Diacetyl-1H-indol-2-yl acetate (**3**).* Yield 95%. Mp: 137–139 °C (methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (d, J=8 Hz, 1H), 7.61 (d, J=7.5, 1H), 7.34 (dd, J=8, 8 Hz, 1H), 7.21 (dd, J=8, 8 Hz, 1H), 2.74 (s, 3H), 2.72 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.9, 167.8, 167.0, 161.8, 137.8, 129.1, 124.9, 122.9, 121.6, 116.3, 115.5, 27.0, 21.3, 19.0. FT-IR ν_{max} (KBr): 3471, 1757, 1742, 1698, 1460, 748 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 259 (M^+, 5), 217 (40), 175(100), 150 (35), 129 (10). ESI-HRMS (amu): calcd $C_{14}H_{13}NNaO_4$ $[M+Na]^+$: 282.0742; found $[M+Na]^+$: 282.0745.

*4.3.2. 3-Diacetyl-6-chloro-1H-indol-2-yl acetate (**4**).* Yield 93%. Mp: 166–168 °C (methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.53 (d, J=8 Hz, 1H), 7.19 (d, J=8 Hz, 1H), 2.74 (s, 3H), 2.71 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 167.5, 166.8, 162.4, 138.4, 134.7, 125.0, 123.6, 120.1, 116.9, 114.7, 26.9, 21.3, 19.1. FT-IR ν_{max} (KBr): 3128, 1747, 1710, 1655, 1466, 742 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 293 (M^+, 3), 253 (13) 251 (38), 211 (34), 209

(100), 162 (35), 129 (7). ESI-HRMS (amu): calcd $C_{14}H_{12}ClNNaO_4$ $[M+Na]^+$: 316.0353; found $[M+Na]^+$: 316.0353.

*4.3.3. 1,1′-(2-Hydroxy-1H-indole-1,3-diyl)dipropan-1-one (**5**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 76% yield. Mp: 73–74 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.69 (s, 1H), 8.36 (d, J=7.5 Hz, 1H), 7.35 (m, 2H), 7.24 (m, 2H), 3.18 (q, 2H), 2.82 (q, 2H), 1.34 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.2, 174.7, 172.3, 135.4, 125.6, 124.7, 122.6, 119.2, 116.5, 100.6, 32.2, 27.6, 9.6, 8.4. FT-IR ν_{max} (KBr): 2934, 1717, 1661, 1475, 738 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 245 (M^+, 28), 289 (100), 150 (75), 133 (15). ESI-HRMS (amu): calcd $C_{14}H_{15}NNaO_3$ $[M+Na]^+$: 268.0950; found $[M+Na]^+$: 268.0937.

*4.3.4. 1,1′-(2-Hydroxy-1H-indole-1,3-diyl)dibutan-1-one (**6**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 82% yield. Mp: 52–54 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.70 (s, 1H), 8.35 (d, J=8.5 Hz, 1H), 7.36 (s, 1H), 7.24 (m, 2H), 3.16 (t, J=7.5 Hz, 2H), 2.78 (t, J=7.5 Hz, 2H), 1.85 (m, 4H) 1.12(m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.5, 173.9, 172.3, 135.5, 125.9, 124.7, 122.6, 119.2, 116.6, 101.1, 40.5, 36.0, 19.2, 17.8, 14.0, 13.8. FT-IR ν_{max} (KBr): 2952, 1713, 1670, 1457, 743 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 273 (M^+, 15), 203 (100), 160 (48), 133 (22). ESI-HRMS (amu): calcd $C_{16}H_{19}NNaO_3$ $[M+Na]^+$: 296.1263; found $[M+Na]^+$: 296.1261.

*4.3.5. 1-(2-Hydroxy-1-methyl-1H-indol-3-yl)ethanone (**14**)*[22a]. The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 81% yield. Mp: 110–111 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.67 (br s, 1H), 7.37 (d, J=7.5 Hz, 1H), 7.23 (d, J=7.5 Hz, 1H), 7.12 (dd, J=8 Hz, 1H), 6.95 (d, J=8 Hz, 1H), 3.35 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.9, 171.0, 138.9, 125.2, 122.2, 122.1, 119.7, 108.4, 101.7, 25.6, 20.3. FT-IR ν_{max} (KBr): 3058, 2932, 1655, 1466, 748 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 189 (M^+, 100), 174 (80), 147 (17), 91 (24). ESI-HRMS (amu): calcd $C_{11}H_{11}NNaO_2$ $[M+Na]^+$: 212.0687; found $[M+Na]^+$: 212.0683.

*4.3.6. 1-(5-Chloro-2-hydroxy-1-methyl-1H-indol-3-yl)ethanone (**15**)*[22b]. The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 78% yield. Mp: 126–128 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 13.56 (br s, 1H), 7.34 (s, 1H), 7.21 (d, J=8.5 Hz, 1H), 6.88 (d, J=8.5 Hz, 1H), 3.36 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.3, 170.9, 137.3, 127.6, 124.9, 123.7, 119.8, 109.1, 101.2, 25.8, 20.4. FT-IR ν_{max} (KBr): 3441, 1653, 1486, 708 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 225 (33), 223 (M^+, 100), 210 (30), 208 (85), 117 (33). ESI-HRMS (amu): calcd $C_{11}H_{10}ClNNaO_2$ $[M+Na]^+$: 246.0298; found $[M+Na]^+$: 246.0294.

*4.3.7. 1-(1-Benzyl-5-chloro-2-hydroxy-1H-indol-3-yl)ethanone (**16**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 80% yield. Mp: 127–128 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 13.52 (br s, 1H), 7.32 (m, 6H), 7.09 (d, J=8.5 Hz, 1H), 6.77 (d, J=8.5 Hz, 1H), 5.04 (s, 2H), 2.48 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.7, 170.9, 136.3, 135.7, 128.9, 127.8, 127.7, 127.2, 124.9, 123.8, 119.8, 110.1, 101.1, 43.4, 20.5. FT-IR ν_{max} (KBr): 3031, 1660, 1434, 750 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 301 (17), 299 (M^+, 54), 179 (7), 91 (100). ESI-HRMS (amu): calcd $C_{17}H_{15}ClNO_2$ $[M+H]^+$: 300.0791; found $[M+H]^+$: 300.0777.

*4.3.8. 1-(2-Mercapto-1-methyl-1H-indol-3-yl)ethanone (**17**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 71% yield. Mp: 164–166 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 15.66 (br s, 1H, D_2O exchangeable), 7.52 (d, J=7.5 Hz, 1H), 7.30 (m, 2H), 7.18 (d, J=7.5, 1H), 3.73 (s, 3H), 2.66 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.3, 177.6, 141.2, 125.6, 125.1, 123.2, 120.3, 112.1, 109.3, 29.3, 22.7. FT-IR ν_{max} (KBr): 2935, 1595, 1443, 747 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 205 (M^+, 100), 190 (100), 117 (14). ESI-HRMS (amu): calcd $C_{11}H_{12}NOS$ $[M+H]^+$: 206.0640; found $[M+H]^+$: 206.0629.

*4.3.9. S-1H-Indol-2-yl ethanethioate (**18**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 94% yield. Mp: 101–103 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.66 (br s, 1H, D_2O exchangeable), 7.64 (d, J=8 Hz, 1H), 7.39 (d, J=8 Hz, 1H), 7.26 (dd, J=8 Hz, 1H), 7.16 (dd, J=7.5 Hz, 1H), 6.73 (s, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.9, 137.8, 127.9, 123.4, 121.3, 120.8, 120.4, 111.1, 109.9, 30.1. FT-IR ν_{max} (KBr): 3343, 1685, 1438, 1110, 743 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 191 (M^+, 100), 149 (37), 121 (10). ESI-HRMS (amu): calcd $C_{10}H_9NNaOS$ $[M+Na]^+$: 214.0303; found $[M+Na]^+$: 214.0290.

*4.3.10. S-1-Acetyl-1H-indol-2-yl ethanethioate (**19**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 78% yield. Mp: 52–54 °C (hexanes/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (d, J=8.5 Hz, 1H), 7.60 (d, J=7.5 Hz, 1H), 7.41 (dd, J=7.5 Hz, 1H), 7.30 (dd, J=7.5 Hz, 1H), 7.03 (s, 1H), 2.79 (s, 3H), 2.47 (s, 3H). D_2O exchange experiment did not result any change in ^{1}H NMR spectrum. ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.3, 170.0, 138.3, 128.6, 126.2, 123.6, 122.4, 122.1, 121.0, 116.0, 29.8, 27.1. FT-IR ν_{max} (KBr): 3347, 3011, 1690, 1440, 749 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 234 (M^+, 100), 191 (20), 149 (47). ESI-HRMS (amu): calcd $C_{12}H_{11}NNaO_2S$ $[M+Na]^+$: 256.0408; found $[M+Na]^+$: 256.0410.

*4.3.11. 1,3-Diacetyl-5-fluoro-1H-indol-2-yl acetate (**28**).* Melting point: 133–135 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (dd, J=9.0, 5.0 Hz, 1H), 7.30 (dd, J=8.7, 2.7 Hz, 1H), 7.04 (ddd, J=9.0, 9.0, 2.7 Hz, 1H), 2.73 (s, 6H), 2.45 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.1, 168.9, 168.2, 164.5, 161.2 (d, $^1J_{C-F}$=242 Hz), 135.0, 124.1 (d, $^3J_{C-F}$=9 Hz), 118.7 (d, $^3J_{C-F}$=9 Hz), 116.6 (d, $^2J_{C-F}$=24 Hz), 116.0, 111.2 (d, $^2J_{C-F}$=26 Hz), 27.4, 21.8, 19.6. FT-IR ν_{max} (KBr): 3452, 3122, 1738, 1700, 1650, 1474, 1194, 815 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{12}FNNaO_4$ $[M+Na]^+$: 300.0643; found $[M+Na]^+$: 300.0644.

*4.3.12. 1,3-Diacetyl-5-chloro-1H-indol-2-yl acetate (**29**).* Melting point: 127–128 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25 (d, J=8.9 Hz, 1H), 7.57 (s, 1H), 7.30 (d, J=8.5 Hz, 1H), 2.73 (s, 6H), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.1, 167.6, 167.2, 163.7, 136.4, 130.5, 129.2, 123.4, 117.8, 114.9, 27.3, 21.7, 19.5. FT-IR ν_{max} (KBr): 3436, 1701, 1163, 1014, 882 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{12}ClNNaO_4$ $[M+Na]^+$: 316.0347; found $[M+Na]^+$: 316.0345.

*4.3.13. 1,3-Diacetyl-5-bromo-1H-indol-2-yl acetate (**30**).* Melting point: 121–123 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.20 (d, J=8.4 Hz, 1H), 7.73 (s, 1H), 7.45 (d, J=8.1 Hz, 1H), 2.73 (s, 6H), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.2, 171.0, 167.1, 163.7, 136.8, 132.0, 129.0, 126.2, 123.8, 118.2, 115, 27.3, 21.7, 19.5. FT-IR ν_{max} (KBr): 3442, 1699, 1670, 1618, 1456, 1370, 1164 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{12}BrNNaO_4$ $[M+Na]^+$: 359.9842; found $[M+Na]^+$: 359.9846.

*4.3.14. 1,3-Diacetyl-5-iodo-1H-indol-2-yl acetate (**31**).* Melting point: 93–95 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): 8.09 (d, J=8.7, 1H), 7.94 (s, 1H), 7.63 (d, J=8.5, 1H), 2.72 (s, 6H), 2.45 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.0, 171.1, 167.2, 163.4, 138.0, 135.1, 132.2, 128.2, 124.1, 118.5, 88.9, 27.3, 21.6, 19.5. FT-IR ν_{max} (KBr): 3444, 1736, 1645, 1457, 1368, 1162 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{12}INNaO_4$ $[M+Na]^+$: 407.9703; found $[M+Na]^+$: 407.9683.

*4.3.15. 1,3-Diacetyl-5-methyl-1H-indol-2-yl acetate (**32**).* Melting point: 120–123 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15 (d, J=8.1 Hz, 1H), 7.37 (s, 1H), 7.12 (d, J=8.2 Hz, 1H), 2.70 (s, 3H), 2.68 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.1, 168.4, 167.4, 161.7, 136.0, 134.6, 130.3, 123.8, 121.9, 116.4, 116.0, 27.3, 21.8, 21.7, 19.4. FT-IR ν_{max} (KBr): 3452, 2913, 1750, 1742, 1654, 1479,

1174, 818. ESI-HRMS (amu): calcd $C_{15}H_{15}NNaO_4$ $[M+Na]^+$: 296.0893; found $[M+Na]^+$: 296.0889.

*4.3.16. 1,3-Diacetyl-5-nitro-1H-indol-2-yl acetate (**33**).* Melting point: 132–134 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.52 (s, 1H), 8.47 (d, J=9.0 Hz, 1H), 8.26 (d, J=7.8 Hz, 1H), 2.79 (s, 3H), 7.78 (s, 3H), 2.53 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.2, 167.3, 167.0, 165.8, 145.0, 142.3, 125.1, 122.7, 118.6, 116.7, 114.0, 27.3, 21.7, 19.7. FT-IR ν_{max} (KBr): 3432, 1773, 1700, 1653, 1559, 1347, 1159 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{12}N_2NaO_6$ $[M+Na]^+$: 327.0588; found $[M+Na]^+$: 327.0568.

*4.3.17. 3-Acetyl-7-chloro-1H-indol-2-yl acetate (**34**).* Melting point: 179–180 °C (methanol). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.09 (br s, 1H, D_2O exchangeable), 7.39 (d, J=7.7 Hz, 1H), 7.21 (d, J=8.1 Hz, 1H), 6.27 (dd, J=8.0, 7.9 Hz, 1H), 2.72 (s, 3H), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.6, 167.4, 162.4, 136.8, 128.7, 123.3, 123.2, 122.2, 116.8, 115.3, 21.7, 18.7. FT-IR ν_{max} (KBr): 3440, 2995, 1759, 1716, 1653, 1178, 794 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_{10}ClNNaO_3$ $[M+Na]^+$: 274.0241; found $[M+Na]^+$: 274.0023.

*4.3.18. 1-Acetyl-6-chloro-1H-indol-2-yl ethanethioate (**35**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 74% yield. Melting point: 70–72 °C (hexanes/ethyl acetate). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 (s, 1H), 7.47 (d, J=8.3 Hz, 1H), 7.25 (d, J=8.4 Hz, 1H), 6.94 (s, 1H), 2.75 (s, 3H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 193.3, 170.3, 139.0, 132.8, 127.3, 124.7, 123.4, 122.2, 121.9, 117.0, 30.2, 27.4. FT-IR ν_{max} (KBr): 1705, 1412, 1310, 1210, 833, 601 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_{10}ClNNaO_2S$ $[M+Na]^+$: 290.0013; found $[M+Na]^+$: 290.0003.

*4.3.19. 1-(1-Acetyl-2-hydroxy-1H-indol-3-yl)butan-1-one (**6a**).* The product was isolated using FCC (silica gel, hexanes/ethyl acetate) in 81% yield (methanol). Melting point: 95–97.5 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.52 (br s, 1H, D_2O exchangeable), 8.35 (d, J=7.0 Hz, 1H), 7.40 (d, J=7.0 Hz, 1H), 7.28–7.26 (m, 2H), 3.17 (t, J=7.3 Hz, 2H), 2.53 (s, 3H), 1.83 (m, 2H), 1.09 (t, J=7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.7, 174.1, 172.2, 135.8, 126.3, 125.0, 123.1, 119.5, 116.9, 101.9, 40.9, 21.3, 18.1, 14.1. FT-IR ν_{max} (KBr): 3441, 2962, 1629, 1459, 1192, 718 cm^{-1}. ESI-HRMS (amu): calcd $C_{14}H_{14}NO_3$ $[M-H]^-$: 244.0979; found $[M-H]^-$: 244.0972.

4.4. General procedure for CALB-catalyzed O-deacetylation of 2-acetoxy-1,3-diacetylindoles

Appropriate 2-acetoxy-1,3-diacetylindole (0.2 g) was mixed with CALB enzyme (0.2 g) and 1-butanol (1 equiv) in THF (6 mL). The mixture was shaken vigorously (180 rpm) at ambient temperature. The reaction time for each reactant is provided in Table 3. After the completion of reaction the enzyme was filtered off and the filtrate was rotary evaporated to obtain 1,3-diacetyl-2-hydroxyindoles in quantitative yields.

*4.4.1. 1,3-Diacetyl-2-hydroxyindole (**36**).* Melting point: 98–99 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.45 (s, 1H, D_2O exchangeable), 8.33 (d, J=8.0 Hz, 1H), 7.38 (d, J=6.7 Hz, 1H,), 7.28–7.25 (m, 2H), 2.78 (s, 3H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.9, 172.4, 171.0, 135.7, 126.4, 125.1, 123.1, 119.6, 116.9, 102.0, 27.3, 21.3. FT-IR ν_{max} (KBr): 3452, 3125, 1718, 1670, 1375, 1175, 780 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_{11}NNaO_3$ $[M+Na]^+$: 240.0631; found $[M+Na]^+$: 240.0626.

*4.4.2. 1,3-Diacetyl-5-fluoro-2-hydroxyindole (**37**).* Melting point: 140–142 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.63 (br s, 1H, D_2O exchangeable), 8.31 (dd, J=9.0, 5.0 Hz, 1H), 7.08 (dd, J=8.9, 2.6 Hz, 1H), 6.96 (ddd, J=9.0, 9.0, 2.6 Hz, 1H), 2.77 (s, 3H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.9, 172.3, 170.8, 160.4 (d, $^1J_{C-F}$=242 Hz), 131.6, 124.7 (d, $^3J_{C-F}$=9.5 Hz), 118.1 (d, $^3J_{C-F}$=9 Hz), 112.7 (d, $^2J_{C-F}$=24 Hz), 106.9 (d, $^2J_{C-F}$=26 Hz), 101.7, 27.2, 21.3. FT-IR ν_{max} (KBr): 3456, 3011, 1762, 1700, 1474, 1195, 815 cm^{-1} ESI-HRMS (amu): calcd $C_{12}H_{10}FNNaO_3$ $[M+Na]^+$: 258.0537; found $[M+Na]^+$: 258.0531.

*4.4.3. 1,3-Diacetyl-5-chloro-2-hydroxyindole (**38**).* Melting point: 145–147 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.41 (br s, 1H, D_2O exchangeable), 8.18 (s, 1H), 7.25–7.16 (m, 2H), 2.72 (s, 3H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.1, 171.9, 170.8, 133.8, 130.6, 126.0, 124.6, 119.5, 117.9, 101.2, 27.1, 21.4. FT-IR ν_{max} (KBr): 3444, 1712, 1635, 1368, 1169, 810 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_9ClNO_3$ $[M-H]^-$: 250.0276; found $[M-H]^-$: 250.0275.

*4.4.4. 1,3-Diacetyl-5-bromo-2-hydroxyindole (**39**).* Melting point: 140–144 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.49 (s, 1H, D_2O exchangeable), 8.20 (d, J=8.4 Hz, 1H), 7.46 (s, 1H), 7.36 (d, J=8.4 Hz, 1H,), 2.75 (s, 3H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.2, 171.9, 170.8, 134.4, 129.0, 125.1, 122.4, 118.4, 118.3, 101.2, 27.2, 21.5. FT-IR ν_{max} (KBr): 3425, 3068, 1699, 1624, 1457, 1373, 1289, 830 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_9BrNO_3$ $[M-H]^-$: 293.9771; found $[M-H]^-$: 293.9773.

*4.4.5. 1,3-Diacetyl-5-iodo-2-hydroxyindole (**40**).* Melting point: 129–131 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.42 (br s, 1H, D_2O exchangeable), 8.02 (d, J=8.4, 1H), 7.58 (s, 1H), 7.54 (d, J=8.4 Hz, 1H), 2.72 (s, 3H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.1, 171.3, 170.9, 135.1, 128.2, 125.4, 118.7, 100.9, 89.2, 27.3, 21.6. FT-IR ν_{max} (KBr): 3445, 3125, 1750 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_9INO_3$ $[M-H]^-$: 341.9633; found $[M-H]^-$: 341.9644.

*4.4.6. 1,3-Diacetyl-5-methyl-2-hydroxyindole (**41**).* Melting point: 109–112 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.40 (br s, 1H, D_2O exchangeable), 8.16 (d, J=7.6 Hz, 1H), 7.13 (s, 1H), 7.04 (d, J=8.0 Hz, 1H), 2.73 (s, 3H), 2.47 (s, 3H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.5, 172.5, 170.9, 134.7, 133.5, 127.0, 123.1, 120.2, 116.1, 102.0, 27.2, 21.8, 21.3. FT-IR ν_{max} (KBr): 3444, 1700, 1653, 1559, 1177, 810 cm^{-1}. ESI-HRMS (amu): calcd $C_{13}H_{13}NNaO_3$ $[M+Na]^+$: 254.0771; found $[M+Na]^+$: 254.0771.

*4.4.7. 1,3-Diacetyl-5-nitro-2-hydroxyindole (**42**).* Melting point: 149–150 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.43 (br s, 1H, D_2O exchangeable), 8.45 (d, 1H, J=8.8 Hz), 8.21–8.15 (m, 2H), 2.80 (s, 3H), 2.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.8, 172.0, 171.0, 145.2, 139.6, 124.1, 122.2, 116.8, 114.5, 100.8, 27.2, 21.7. FT-IR ν_{max} (KBr): 3440, 1717, 1653, 1558, 1506, 1170 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_9N_2O_5$ $[M-H]^-$: 261.0517; found $[M-H]^-$: 261.0503.

*4.4.8. 1,3-Diacetyl-6-chloro-2-hydroxyindole (**43**).* Melting point: 134–136 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.37 (s, 1H, D_2O exchangeable), 8.39 (s, 1H), 7.30–7.21(m, 2H), 2.77 (s, 3H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.2, 172.1, 170.8, 137.6, 136.1, 132.0, 125.2, 120.1, 117.5, 101.4, 27.2, 21.5. FT-IR ν_{max} (KBr): 3444, 3125, 1706, 1310, 817, 620 cm^{-1}. ESI-HRMS (amu): calcd $C_{12}H_9ClNO_3$ $[M-H]^-$: 250.0276; found $[M-H]^-$: 250.0265.

*4.4.9. 3-Acetyl-7-chloro-2-hydroxyindole (**44**).* Melting point: 117 °C (THF). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.46 (br s, 1H, D_2O exchangeable) 7.35–7.05 (m, 3H), 2.5 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): 175.9, 172.2, 133.7, 125.3, 124.7, 123.4, 118.6, 116.5, 102.6, 20.9. FT-IR ν_{max} (KBr): 3444, 2962, 1744, 1559, 1540,772 cm^{-1}. ESI-HRMS (amu): calcd $C_{10}H_9ClNO_2$ $[M+H]^+$: 210.0316; found $[M+H]^+$: 210.0321.

4.5. General procedure for chemical deacetylation of 2-acetoxy-1,3-diacetylindoles

Appropriate 2-acetoxy-1,3-diacetylindoles (0.2 g) was mixed with 5% NaOH and THF (1:1 v/v, 4 mL). The mixture was stirred at room temperature for 1 h. The THF was evaporated under reduced pressure

and the residue was acidified using 1 M HCl to pH 2. The precipitated product was filtered off and washed with hexanes (Table 5).

*4.5.1. 3-Acetyl-2-hydroxyindole (**45**).* Melting point: 195–197 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.47 (br s, 1H, D_2O exchangeable), 8.81 (br s, 1H, D_2O exchangeable), 7.38 (s, 1H), 7.18–7.04 (m, 3H), 2.50 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.3, 173.0, 136.5, 125.7, 123.1, 122.5, 120.3, 110.7, 102.5, 20.8. FT-IR ν_{max} (KBr): 3448, 3166, 3027, 1675, 1464, 1290, 744 cm^{-1}. ESI-HRMS (amu): calcd $C_{10}H_8NO_2$ $[M-H]^-$: 174.0561; found $[M-H]^-$: 174.0549.

*4.5.2. 3-Acetyl-5-fluoro-2-hydroxyindole (**46**).* Melting point: 218–222 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.09 (br s, 1H, D_2O exchangeable), 8.31 (dd, J=8.9, 2 Hz, 1H), 6.92–6.89 (m, 2H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.6, 172.9, 159.10 (d, $^1J_{C-F}$=238 Hz), 132.1, 124.3 (d, $^3J_{C-F}$=9 Hz), 112.1 (d, $^2J_{C-F}$=24 Hz), 110.9 (d, $^3J_{C-F}$=9 Hz), 107.8 (d, $^2J_{C-F}$=26 Hz), 101.6, 20.8. FT-IR ν_{max} (KBr): 3423, 3161, 1666, 1473, 1285, 899 cm^{-1}. ESI-HRMS (amu): calcd $C_{10}H_9FNO_2$ $[M+H]^+$: 194.0612; found $[M+H]^+$: 194.0613.

*4.5.3. 3-Acetyl-5-chloro-2-hydroxyindole (**47**).* Melting point: 239–240 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.37 (s, 1H), 7.32 (s, 1H), 7.15 (d, J=6.5 Hz, 1H), 6.93 (d, J=8.4 Hz, 1H), 2.48 (s, H), 2.20 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.6, 172.4, 134.4, 127.8, 125.3, 124.5, 120.2, 111.2, 101.7, 20.8. FT-IR ν_{max} (KBr): 3445, 3169, 1667, 1445, 1292, 814 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 209 (M^+, 100), 191 (50), 163(27), 138 (22). ESI-HRMS (amu): calcd $C_{10}H_9ClNO_2$ $[M+H]^+$: 210.0322; found $[M+H]^+$: 210.0308.

*4.5.4. 3-Acetyl-5-bromo-2-hydroxyindole (**48**).* Melting point: 201–202 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 13.50 (s, 1H), 8.20 (d, 1H, J=8.7 Hz), 7.47 (s, 1H), 7.36 (d, 1H, J=8.7 Hz), 2.75 (s, 3H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.9, 172.5, 135.1, 128.3, 125.2, 123.3, 115.5, 111.9, 101.2, 21.1. FT-IR ν_{max} (KBr): 3419, 1704, 1622, 1288 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 253 (M^+, 70), 209 (75), 191 (72), 97 (75). ESI-HRMS (amu): calcd $C_{10}H_7BrNO_2$ $[M-H]^-$: 251.9660; found $[M-H]^-$: 251.9670.

*4.5.5. 3-Acetyl-5-methyl-2-hydroxyindole (**49**).* Melting point: 214–215 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.50 (s, 1H), 7.18 (s, 1H), 6.99 (d, 1H, J=8.0 Hz), 6.90 (d, 1H, J=8.0 Hz), 2.48 (s, 3H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.0, 173.0, 134.2, 131.9, 126.3, 123.2, 121.0, 110.3, 101.8, 21.8, 20.8. FT-IR ν_{max} (KBr): 3455, 3172, 1669, 1614, 1287, 860 cm^{-1}. GC–MS (EI): m/z (% relative abundance) 189 (M^+, 100), 143 (10). ESI-HRMS (amu): calcd $C_{11}H_{11}NNaO_2$ $[M+Na]^+$: 212.0687; found $[M+Na]^+$: 212.0685.

*4.5.6. 3-Acetyl-6-chloro-2-hydroxyindole (**50**).* Melting point: 228–230 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.90 (br s, 1H, D_2O exchangeable), 7.26 (s, 1H), 7.08 (dd, J=8.2, 2 Hz, 1H), 7.01 (s, 1H), 2.47 (s, 3H). FT-IR ν_{max} (KBr): 3452, 3219, 1682, 1247 cm^{-1}. ESI-HRMS (amu): calcd $C_{10}H_7ClN_2$ $[M-H]^-$: 208.0171; found $[M-H]^-$: 208.0167.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.11.105.

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