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Palladium-Catalyzed Oxidation-Hydroxylation and Oxidation-Methoxylation of *N*-Boc Indoles for the Synthesis of 3-Oxoindolines

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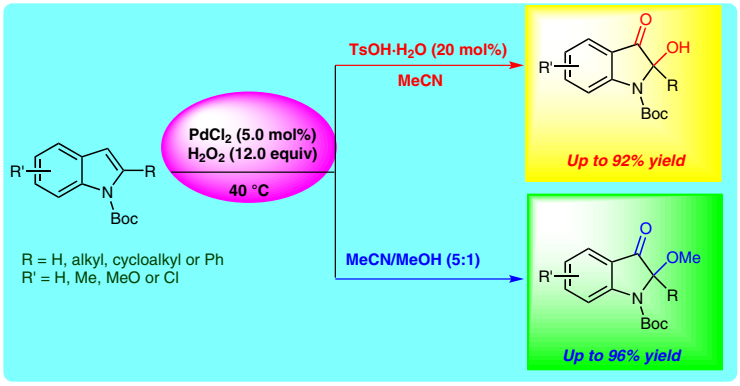

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Abstract The palladium-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles for the synthesis of *tert*-butyl 2-hydroxy(methoxy)-3-oxoindoline-1-carboxylates and their derivatives is developed. The process occurs readily using $PdCl_2$ as the catalyst and acetonitrile as the solvent to afford 3-oxoindolines in moderate to high yields. A mechanism for this Pd-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles is proposed.

Key words palladium, oxidation, hydroxylation, methoxylation, indole

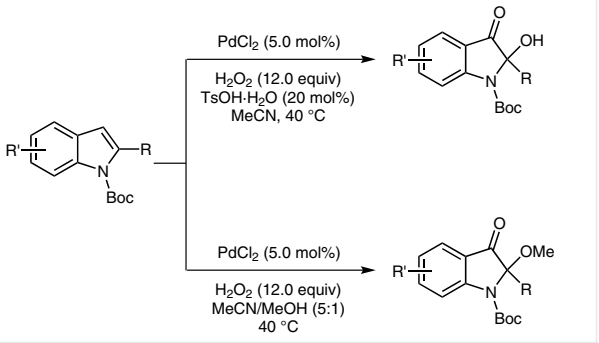
The oxidation process has been widely recognized as a powerful strategy for the synthesis of oxocyclic or oxo-heterocyclic compounds from the corresponding materials. However, only a small amount of effort has been devoted to the oxidation of aromatic and heteroaromatic compounds. In heteroaromatic compounds, indole and its derivatives are by far one of the most widely exploited.[1] The nucleophilic addition and Friedel–Crafts reactions of indoles have attracted significant attention for their extensive applications in the synthesis of natural products, pharmaceuticals and other fine chemicals.[2] As examples, 2-hydroxy-3-oxoindolines and 2-methoxy-3-oxoindolines are key building blocks in natural products and biologically active molecules.[3] The most effective method to obtain 2-hydroxy-3-oxoindolines and 2-methoxy-3-oxoindolines is via oxidation of their aromatic precursors due to the atom economy.

In recent decades, molybdenum pentoxide,[4] *meta*-chloroperoxybenzoic acid (*m*CPBA),[5] DDQ[6] and dimethyldioxirane[7] have been employed for the oxidation of indoles to construct oxoindolines, being the primary synthetic method to achieve this transformation. But there are many limitations to the process, such as toxic metal pollution, incompatibility with many functional groups, and low yields and selectivities. Fortunately, a few methods for the transition-metal-catalyzed oxidation of indoles have been reported. The Ru–porphyrin-catalyzed oxidation of *N*-Ts indoles to obtain 3-oxoindolines was achieved by Che and co-workers[8] using 2,6-Cl_2PyNO as the oxidant, which is efficient and highly selective. Recently, palladium-catalyzed oxidative dearomatization of indoles was reported by Guchhait's group[9] for the synthesis of C2-quaternary indolin-3-ones. Unfortunately, *tert*-butyl hydroperoxide (TBHP) (2.2 equiv) and MnO_2 (2.0 equiv) were employed in excess as oxidants. At the same time, palladium-catalyzed Wacker-type oxidation of *N*-Boc indoles for the preparation of 3-oxoindolines has been achieved in our group.[10] This result encouraged us to extend the application of the catalysis system to the oxidation of heteroaromatic precursors for the preparation of oxo-heterocyclic compounds.

In palladium-catalyzed oxidation reactions, the Wacker oxidation has played an extremely important role in industrial applications.[11] Pd-catalyzed Wacker-type oxidations of alkenes are typical for the synthesis of carbonyl compounds. Palladium-catalyzed oxidation of terminal olefins for the synthesis of methyl ketones with high conversion and selectivity has been reported by Mimoun's group[12] and the mechanism of the reaction was proposed. Subsequently, Sigman's[13] and Feringa's[14] groups reported the palladium-catalyzed Wacker-type oxidation of styrenes and ketones, respectively, with high selectivity. In addition, the copper-free Wacker-type oxidation of terminal olefins and internal olefins has been reported by Kaneda's group.[15]

However, palladium-catalyzed oxidation of indoles has rarely been reported recently. It is expected that palladium-catalyzed oxidations of indoles would provide an effective method for the synthesis of oxo-heterocyclic compounds. The Pd-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles using H_2O_2 as the oxidant is an interesting alternative. Herein, we report the Pd-cata-

lyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles (Scheme 1), which affords 2-hydroxy-3-oxoindolines in the presence of $TsOH·H_2O$ under mild reaction conditions, and 2-methoxy-3-oxoindolines in the presence of MeOH under the standard oxidation-hydroxylation conditions but without $TsOH·H_2O$.



Scheme 1 The oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles

Thus, in continuation of our research on the palladium-catalyzed oxidation of *N*-Boc indoles, 2-hydroxy-3-oxoindoline was found to be the main product. The initial experiment began with *tert*-butyl 2-methyl-1*H*-indole-1-carboxylate (**1a**) as the model starting material, H_2O_2 as the oxidant and $PdCl_2$ as the catalyst in ethyl acetate (EtOAc). The product, *tert*-butyl 2-hydroxy-2-methyl-3-oxoindoline-1-carboxylate (**2a**), was isolated in 18% yield (Table 1, entry 1). This product is different from that in our previous work in which $PdCl_2$ with stronger Lewis acidity was used as the catalyst.[10] This result encouraged us to adhere to our initial hypothesis that a Lewis acidic palladium catalyst can be applied for the catalyzed oxidation-hydroxylation of *N*-Boc indoles in the presence of an oxidant and water. Next, other solvents, catalysts and oxidants were evaluated to improve the yield of the product **2a**.

Firstly, MeOH (Table 1, entry 2), CH_2Cl_2 (entry 3), THF (entry 4), acetone (entry 5), DMF (entry 6), Et_2O (entry 7) and MeCN (entry 8) were tested as solvents to improve the yield of **2a** in the $PdCl_2$-catalyzed oxidation-hydroxylation. The results indicated that MeCN was the best solvent for the Pd-catalyzed oxidation-hydroxylation of *N*-Boc indoles affording an 81% yield. The reaction was inhibited completely when MeOH, CH_2Cl_2, DMF or Et_2O was used as the solvent in the presence of $PdCl_2$. The results indicated that the oxidant may lose its oxidative activity in MeOH and DMF and only trace amounts of the target product were detected (entries 2 and 6). Also, the water remains almost completely undissolved in CH_2Cl_2 and Et_2O, which results in only a trace amount of the target product being detected (entries 3 and 7). Due to the relatively good miscibility of water and THF, a 77% yield of the product was obtained (entry 4) when the reaction was carried out in THF. Next, other catalysts were evaluated to improve the yield of product **2a**. $Pd(OAc)_2$, $Pd(acac)_2$, $Pd(Quinox)Cl_2$, $CuCl_2$, and $FeCl_3$ were tested in the presence of H_2O_2 in MeCN, however, no improvements in the results were obtained (entries 9–13). In order to increase the activity of the oxidation-hydroxylation of *N*-Boc indoles, *tert*-butyl hydroperoxide (TBHP) was tested as the oxidant in the reaction, but only a trace amount of the desired product **2a** was detected (entry 14). This result indicated that H_2O_2 was the most effective oxidant in the $PdCl_2$-catalyzed oxidation-hydroxylation of *N*-Boc indoles for the preparation of product **2a**.

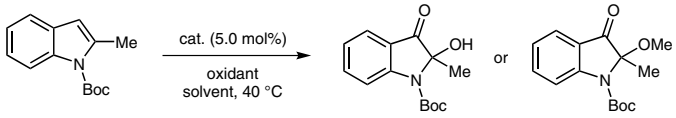
The above results were not satisfactory and a higher yield was desired. Based on the initial results, the Brønsted acid, *p*-toluenesulfonic acid ($TsOH·H_2O$) (10 mol%), was added in an attempt to improve the yield of product **2a**. This proved successful and an 87% yield of **2a** was obtained (Table 1, entry 15). Next, the effect of the amount of additive ($TsOH·H_2O$) on the reaction was investigated. A higher yield (92%) was observed when the amount of $TsOH·H_2O$ was increased to 20 mol% (entry 16), but the yield decreased significantly (to 61%) when 30 mol% of $TsOH·H_2O$ was added (entry 17).

Surprisingly, when MeOH was introduced into the reaction system (without $TsOH·H_2O$) to give the mixed solvent MeCN/MeOH (10:1) for the palladium-catalyzed oxidation-hydroxylation of *N*-Boc indole **1a**, *tert*-butyl 2-methoxy-2-methyl-3-oxoindoline-1-carboxylate (**3a**) was isolated as the product in 82% yield (Table 1, entry 18). Next, the ratio of the MeCN/MeOH mixed solvent (5:1, 2:1 and 1:1) was tested and yields of 90%, 76% and 69% (entries 19–21) were observed, respectively. The results indicated that the mixed solvent MeCN/MeOH (5:1) was the best choice for the palladium-catalyzed oxidation-methoxylation of *N*-Boc indole **1a**. It should be noted that no product was detected in the absence of a palladium catalyst or an oxidant (entries 22 and 23).

By optimization of the solvent, catalyst and oxidant, the best reaction conditions for the Pd-catalyzed oxidation-hydroxylation of an *N*-Boc indole were obtained: $PdCl_2$ (5.0 mol%) as catalyst, H_2O_2 (12.0 equiv) as oxidant with $TsOH·H_2O$ (20 mol%) in MeCN at 40 °C. The best reaction conditions for the Pd-catalyzed oxidation-methoxylation of an *N*-Boc indole were: $PdCl_2$ (5.0 mol%) as catalyst, H_2O_2 (12.0 equiv) as the oxidant in MeCN/MeOH (5:1) at 40 °C. Based on the optimized conditions, the substrate scope of the Pd-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles was examined and the results are shown in Table 2.

Under the optimized conditions, a range of *N*-Boc indoles **1a–l** was subjected to the palladium-catalyzed oxidation-hydroxylation and oxidation-methoxylation reaction (Table 2). For the indoles **1a–e** (entries 1–5) with different substituents at the 2- and/or 5-positions of indole, moderate to high isolated yields (66–96%) of **2** and **3** were

Table 1 Optimization of the Conditions for the Synthesis of **2a** and **3a**[a]



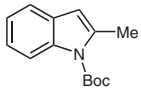
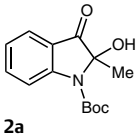
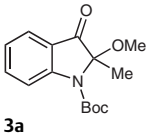
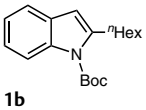
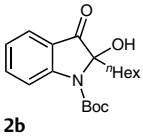
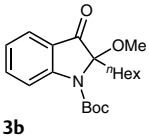
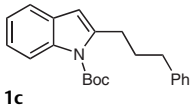
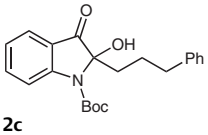
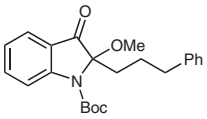
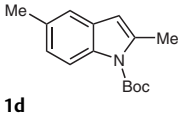
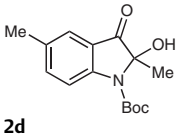
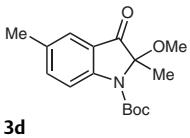
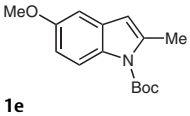
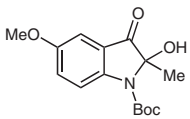
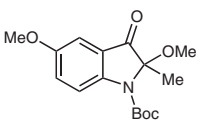
1a **2a** **3a**

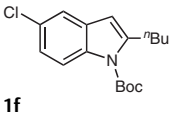
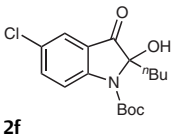
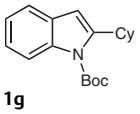
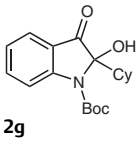
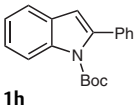
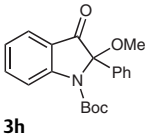
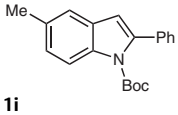
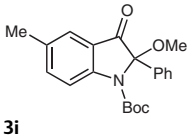
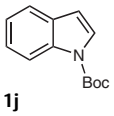
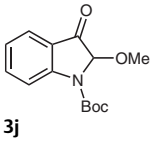
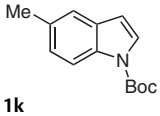
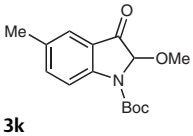
Entry	Cat.	Oxidant (wt%/equiv)	Solvent	Yield (%)[b]	
				2a	**3a**
1	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	EtOAc	18	N/A
2	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeOH	trace	N/A
3	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	CH_2Cl_2	trace	N/A
4	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	THF	77	N/A
5	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	acetone	41	N/A
6	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	DMF	trace	N/A
7	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	Et_2O	trace	N/A
8	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	81	N/A
9	$Pd(OAc)_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	78	N/A
10	$Pd(acac)_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	trace	N/A
11	Pd(Quinox)Cl_2	aq H_2O_2 (30 wt%/12.0)	MeCN	N/A	N/A
12	$CuCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	N/A	N/A
13	$FeCl_3$	aq H_2O_2 (30 wt%/12.0)	MeCN	N/A	N/A
14	$PdCl_2$	aq TBHP (70 wt%/3.0)	MeCN	trace	N/A
15[c]	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	87	N/A
16[d]	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	92	N/A
17[e]	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN	61	N/A
18	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN/MeOH (10:1)	N/A	82
19	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN/MeOH (5:1)	N/A	90
20	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN/MeOH (2:1)	N/A	76
21	$PdCl_2$	aq H_2O_2 (30 wt%/12.0)	MeCN/MeOH (1:1)	N/A	69
22	$PdCl_2$	–	MeCN	N/A	N/A
23	–	aq H_2O_2 (30 wt%/12.0)	MeCN	N/A	N/A

[a] Reaction conditions: **1a** (58 mg, 0.25 mmol), $PdCl_2$ (2.2 mg, 0.0125 mmol, 5.0 mol%), aq H_2O_2 (30 wt%, 3.0 mmol, 12.0 equiv) or aq TBHP (70 wt%, 0.75 mmol, 3.0 equiv), solvent (3.0 mL), 40 °C, 24 h.
[b] Yield of isolated product.
[c] TsOH·H_2O (4.8 mg, 0.025 mmol, 10 mol%) was added.
[d] TsOH·H_2O (9.5 mg, 0.05 mmol, 20 mol%) was added.
[e] TsOH·H_2O (14.3 mg, 0.075 mmol, 30 mol%) was added.

achieved under conditions A and B, respectively. However, for the 5-chloro-substituted indole **1f** (entry 6) and 2-cyclohexyl-indole (**1g**) (entry 7), only 47% and 63% isolated yields of **2f** and **2g** were obtained when the reactions were carried out under conditions A, and no target products were detected under conditions B. 2-Phenyl-substituted and 2-unsubstituted substrates **1h–k** (entries 8–11) underwent oxidation to afford the corresponding products in moderate yields (56–73%) under conditions B and unreacted starting materials were also recovered.

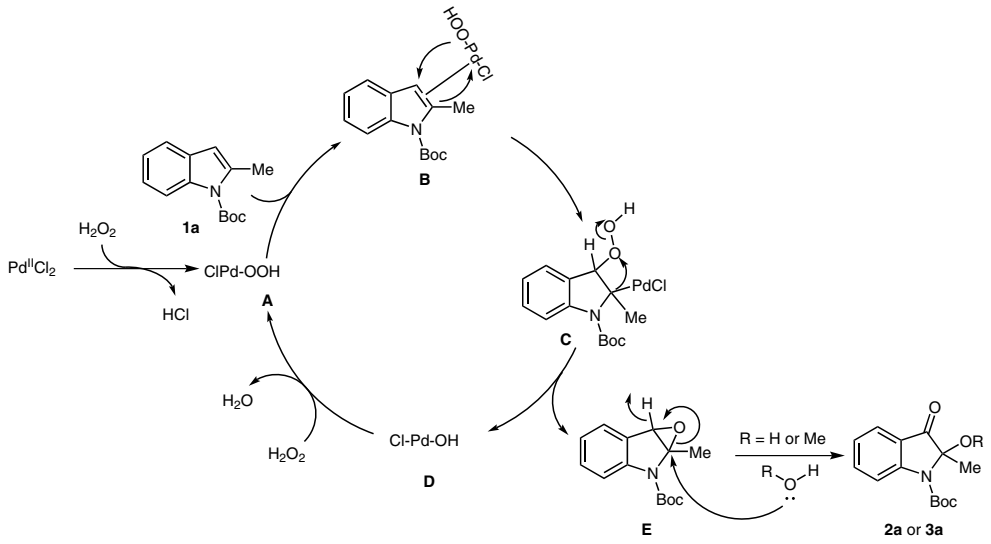
Table 2 Palladium-Catalyzed Wacker-Type Oxidation of *N*-Boc Indoles

Entry	Substrate	Product	Conditions[a]	Yield (%)[b]
1	 **1a**	 **2a**	A	92
		 **3a**	B	90
2	 **1b**	 **2b**	A	83
		 **3b**	B	88
3	 **1c**	 **2c**	A	83
		 **3c**	B	66
4	 **1d**	 **2d**	A	93
		 **3d**	B	96
5	 **1e**	 **2e**	A	74
		 **3e**	B	80

Entry	Substrate	Product	Conditions[a]	Yield (%)[b]
6	 **1f**	 **2f**	A	47
7	 **1g**	 **2g**	A	63
8	 **1h**	 **3h**	B	56
9	 **1i**	 **3i**	B	65
10	 **1j**	 **3j**	B	70
11	 **1k**	 **3k**	B	73

[a] Reaction conditions A: **1** (0.25 mmol), $PdCl_2$ (2.2 mg, 0.0125 mmol, 5.0 mol%), aq H_2O_2 (30 wt%, 3.0 mmol, 12.0 equiv), $TsOH{\cdot}H_2O$ (9.5 mg, 0.05 mmol, 20 mol%), MeCN (3.0 mL), 40 °C, 24 h. Reaction conditions B: **1** (0.25 mmol), $PdCl_2$ (2.2 mg, 0.0125 mmol, 5.0 mol%), aq H_2O_2 (30 wt%, 3.0 mmol, 12.0 equiv), MeCN/MeOH (5:1, 3.0 mL), 40 °C.
[b] Yield of isolated product.

The results indicated that the substrates with 2-phenyl-substituted and 2-unsubstituted groups (Table 2, entries 8–11) have no reactivity under conditions A, and no target products were detected when substrates containing large sterically hindered substituents such as *n*-butyl and cyclohexyl were reacted under conditions B (entries 6 and 7). Notably, the above optimum conditions are not appropriate for the oxidation of *N*-H, *N*-Me and *N*-Ac indoles owing to low selectivity. In addition, other alcohols, such as ethanol, isopropanol and benzyl alcohol, were tested in the palladium-catalyzed oxidation-alkoxylation of *N*-Boc indoles, however, almost all of the starting materials were recovered. We speculated that the oxidant may lose its oxidative activity in the presence of a relatively stronger reductive reagent (ethanol, isopropanol, benzyl alcohol).



Scheme 2 Proposed mechanism for the palladium-catalyzed oxidation-hydroxylation and -methoxylation of *N*-Boc indoles

Based on the reaction results and the known mechanism of the Pd-catalyzed Wacker oxidation of alkenes,[12] a possible mechanism for the Pd-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles is proposed in Scheme 2.

The activated palladium catalyst ClPd-OOH (**A**) may be produced from the palladium precursor $PdCl_2$ in the presence of hydrogen peroxide. The activated catalyst **A** could react with *N*-Boc indole **1a** to produce the palladium complex **B** and then further form the complex **C** under the standard reaction conditions. Next, a hydrogen-transfer process may occur to produce Cl-Pd-OH (**D**) and the epoxy intermediate **E**.[7b] The epoxy intermediate **E** is attacked by the nucleophilic reagent water promoted by TsOH to produce the target product **2a**. Compound **3a** was formed in the presence of the relatively stronger nucleophilic reagent MeOH without TsOH. The activated palladium catalyst **A** can be regenerated in the presence of H_2O_2.

We previously reported the synthesis of 3-oxoindoles under conditions employing the less Lewis acidic $Pd(acac)_2$ as the catalyst.[10] In contrast, $PdCl_2$ was used as a more Lewis acidic catalyst in this work. Besides, TsOH was used as the Brønsted acid for the synthesis of 2-hydroxy-3-oxoindoles **2** and MeOH was used as a more nucleophilic reagent for the synthesis of 2-methoxy-3-oxoindoles **3**. The main differences between both pieces of work are the catalyst and the additives employed.

In summary, using H_2O_2 as the oxidant, the palladium-catalyzed oxidation-hydroxylation and oxidation-methoxylation of *N*-Boc indoles has been successfully achieved with up to 93% and 96% yields, respectively. The reactions afforded 2-hydroxy-3-oxoindolines and 2-methoxy-3-oxoindolines with very high regioselectivity under similar conditions. The principle behind these reactions is expected to provide a new strategy to develop new types of catalytic oxidation of aromatic compounds.

All commercially available reagents were used without further purification. The starting materials **1a–k** were prepared according to reported methods.[10] Flash column chromatography was performed on Huanghai brand silica gel (200–300 mesh). TLC analysis was performed using Huanghai brand glass-backed plates coated with 0.2 mm silica gel. The chemical shifts for ^{1}H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of *d*-chloroform (77.23 ppm) as the internal standard. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplicities.

Oxidation-Hydroxylation of *N*-Boc Indoles; Typical Procedure

A mixture of *N*-Boc indole **1** (0.25 mmol) and $PdCl_2$ (2.2 mg, 0.0125 mmol, 5.0 mol%) in MeCN (3 mL) was added to a Schlenk flask (25 mL) and stirred at r.t. Following the addition of aq 30 wt% H_2O_2 (3.0 mmol, 12.0 equiv) and $TsOH{\cdot}H_2O$ (9.5 mg, 0.05 mmol, 20 mol%), the mixture was stirred at 40 °C until the reaction was finished. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (PE/EtOAc, 20:1 to 5:1).

tert-Butyl 2-Hydroxy-2-methyl-3-oxoindoline-1-carboxylate (2a)

Yield: 56.8 mg (88%); white solid; mp 95–97 °C.

IR (KBr): 3445, 2979, 2934, 1712, 1607, 1590, 1470, 1370, 1352, 1255, 1159, 1066, 989, 910, 840, 757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 9 H), 1.77 (s, 3 H), 7.13–7.17 (m, 1 H), 7.63–7.67 (m, 1 H), 7.77 (d, *J* = 7.6 Hz, 1 H), 7.92 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1, 28.4, 87.9, 116.4, 123.5, 125.0, 137.9, 150.9, 196.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_4Na$: 286.1055; found: 286.1056.

***tert*-Butyl 2-Hexyl-2-hydroxy-3-oxoindoline-1-carboxylate (2b)**

Yield: 62.6 mg (76%); colorless oil.

IR (neat): 3449, 2958, 2930, 1713, 1608, 1468, 1370, 1308, 1252, 1158, 1078, 756 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 6.8 Hz, 3 H), 1.18–1.23 (m, 8 H), 1.65 (s, 9 H), 2.20–2.24 (m, 2 H), 7.14 (dd, *J* = 7.6, 8.4 Hz, 1 H), 7.64–7.75 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 23.4, 28.6, 29.1, 29.9, 31.5, 37.2, 83.9, 90.4, 116.5, 122.0, 123.6, 124.8, 138.0, 196.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{27}NO_4Na$: 356.1838; found: 356.1835.

***tert*-Butyl 2-Hydroxy-3-oxo-2-(3-phenylpropyl)indoline-1-carboxylate (2c)**

Yield: 74.4 mg (80%); colorless oil.

IR (neat): 3444, 3062, 3026, 2977, 2931, 1712, 1607, 1467, 1369, 1317, 1253, 1162, 1114, 982, 942, 843, 755, 701 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.44 (m, 2 H), 1.55 (s, 9 H), 2.20–2.61 (m, 4 H), 7.05–7.25 (m, 6 H), 7.59–7.74 (m, 2 H), 7.93 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.3, 28.3, 35.5, 36.6, 83.7, 90.0, 116.4, 123.5, 124.6, 126.0, 128.39, 128.40, 137.9, 141.3, 196.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{25}NO_4Na$: 390.1681; found: 390.1696.

***tert*-Butyl 2-Hydroxy-2,5-dimethyl-3-oxoindoline-1-carboxylate (2d)**

Yield: 59.1 mg (86%); colorless oil.

IR (neat): 3449, 2979, 2933, 1712, 1622, 1586, 1492, 1371, 1354, 1255, 1159, 1068, 994, 973, 926, 827, 789, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 9 H), 1.75 (s, 3 H), 2.36 (s, 3 H), 7.45–7.48 (m, 1 H), 7.55 (s, 1 H), 7.87 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 28.4, 116.2, 124.6, 133.3, 139.0, 196.4.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_4$: 300.1212; found: 300.1215.

***tert*-Butyl 2-Hydroxy-5-methoxy-2-methyl-3-oxoindoline-1-carboxylate (2e)**

Yield: 52.4 mg (71%); white solid; mp 74–76 °C.

IR (KBr): 3443, 2978, 2934, 1709, 1492, 1370, 1330, 1273, 1158, 1112, 1067, 1031, 924, 836, 803, 786 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 9 H), 1.75 (s, 3 H), 3.82 (s, 3 H), 7.19–7.28 (m, 2 H), 7.84 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2, 28.6, 55.9, 83.7, 105.7, 117.8, 121.4, 127.1, 156.2, 196.5.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_5Na$: 316.1161; found: 316.1167.

***tert*-Butyl 2-Butyl-5-chloro-2-hydroxy-3-oxoindoline-1-carboxylate (2f)**

Yield: 36.0 mg (42%); colorless oil.

IR (neat): 3450, 2961, 2932, 1716, 1608, 1582, 1470, 1370, 1351, 1251, 1159, 1072, 993, 952, 832, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.80–1.28 (m, 7 H), 1.64 (s, 9 H), 2.14–2.32 (m, 2 H), 7.56–7.59 (m, 1 H), 7.69 (d, *J* = 2.4 Hz, 1 H), 7.92 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 22.4, 25.4, 28.4, 36.8, 90.7, 117.7, 124.0, 129.0, 137.5, 195.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{22}NO_4ClNa$: 362.1135; found: 362.1123.

***tert*-Butyl 2-Cyclohexyl-2-hydroxy-3-oxoindoline-1-carboxylate (2g)**

Yield: 50.8 mg (62%); colorless oil.

IR (neat): 3451, 2931, 2853, 1731, 1708, 1611, 1591, 1469, 1369, 1347, 1307, 1189, 1156, 1104, 1004, 935, 907, 876, 841, 756 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.14–2.04 (m, 19 H), 2.40–2.46 (m, 1 H), 7.13 (dd, *J* = 7.6, 8.4 Hz, 1 H), 7.59–7.63 (m, 1 H), 7.71 (d, *J* = 7.6 Hz, 1 H), 7.86 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9, 25.9, 26.1, 26.4, 27.6, 28.5, 45.1, 83.9, 92.6, 116.2, 122.7, 123.4, 124.2, 137.5, 151.2, 151.5, 196.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{25}NO_4Na$: 354.1681; found: 354.1677.

Oxidation-Methoxylation of *N*-Boc Indoles; Typical Procedure

A mixture of *N*-Boc indole **1** (0.25 mmol) and $PdCl_2$ (2.2 mg, 0.0125 mmol, 5.0 mol%) in MeCN/MeOH (5:1 v/v, 3 mL) was added to a Schlenk flask (25 mL) and stirred at r.t. Following the addition of aq 30 wt% H_2O_2 (3.0 mmol, 12.0 equiv), the mixture was stirred at 40 °C until the reaction was finished. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (PE/EtOAc, 50:1 to 20:1).

***tert*-Butyl 2-Methoxy-2-methyl-3-oxoindoline-1-carboxylate (3a)**

Yield: 59.6 mg (86%); white solid; mp 109–111 °C.

IR (KBr): 3124, 3048, 2980, 2932, 1708, 1604, 1586, 1466, 1307, 1258, 1170, 1054, 978, 967, 879, 841, 754, 706, 684 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 9 H), 1.69 (s, 3 H), 3.11 (s, 3 H), 7.14 (dd, *J* = 7.6, 8.4 Hz, 1 H), 7.65–7.69 (m, 1 H), 7.73 (d, *J* = 7.6 Hz, 1 H), 8.21 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 28.3, 51.7, 82.5, 92.7, 116.7, 121.3, 123.1, 124.0, 138.1, 150.8, 152.8, 198.7.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_4Na$: 300.1212; found: 300.1203.

***tert*-Butyl 2-Hexyl-2-methoxy-3-oxoindoline-1-carboxylate (3b)**

Yield: 68.2 mg (78%); colorless oil.

IR (neat): 2957, 2931, 2859, 1713, 1607, 1466, 1368, 1306, 1252, 1161, 1116, 1099, 1079, 927, 845, 758, 709 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.80–1.23 (m, 11 H), 1.61 (s, 9 H), 2.05–2.06 (m, 1 H), 2.41–2.42 (m, 1 H), 3.10 (s, 3 H), 7.13 (dd, *J* = 7.6, 8.4 Hz, 1 H), 7.64–7.71 (m, 2 H), 8.23 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 22.7, 28.5, 29.2, 31.5, 35.4, 51.6, 82.6, 95.5, 116.7, 122.5, 123.2, 123.7, 138.2, 151.1, 153.9, 199.4.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{29}NO_4Na$: 370.1994; found: 370.2003.

***tert*-Butyl 2-Methoxy-3-oxo-2-(3-phenylpropyl)indoline-1-carboxylate (3c)**

Yield: 58.7 mg (62%); colorless oil.

IR (neat): 3026, 2977, 2932, 1731, 1712, 1606, 1465, 1375, 1306, 1253, 1163, 1114, 1079, 927, 845, 756, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.85–1.37 (m, 3 H), 1.49 (s, 9 H), 2.10–2.59 (m, 3 H), 3.08 (s, 3 H), 7.05–7.24 (m, 6 H), 7.61–7.70 (m, 2 H), 8.21 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9, 28.3, 35.2, 35.9, 51.6, 82.6, 95.2, 116.8, 122.4, 123.3, 123.8, 126.1, 128.5, 128.7, 138.3, 141.6, 151.0, 153.9, 199.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{27}NO_4Na$: 404.1838; found: 404.1850.

***tert*-Butyl 2-Methoxy-2,5-dimethyl-3-oxoindoline-1-carboxylate (3d)**

Yield: 61.4 mg (84%); white solid; mp 139–141 °C.

IR (KBr): 2956, 2929, 1723, 1708, 1620, 1583, 1489, 1371, 1360, 1286, 1270, 1154, 1076, 1052, 839 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.56 (s, 9 H), 1.63 (s, 3 H), 2.32 (s, 3 H), 3.04 (s, 3 H), 7.43–7.46 (m, 2 H), 8.52 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7, 21.7, 28.5, 51.7, 82.5, 93.0, 116.7, 121.5, 123.7, 133.1, 139.3, 150.9, 151.0, 198.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{21}NO_4Na$: 314.1368; found: 314.1365.

***tert*-Butyl 2,5-Dimethoxy-2-methyl-3-oxoindoline-1-carboxylate (3e)**

Yield: 57.7 mg (75%); white solid; mp 118–120 °C.

IR (KBr): 2980, 2936, 1721, 1705, 1622, 1587, 1490, 1455, 1370, 1332, 1273, 1164, 1076, 1055, 846 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.57 (s, 9 H), 1.64 (s, 3 H), 3.06 (s, 3 H), 3.79 (s, 3 H), 7.10–7.25 (m, 2 H), 8.10 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 28.5, 51.8, 55.9, 62.3, 82.4, 93.2, 104.7, 118.2, 122.0, 126.5, 127.3, 147.8, 155.9, 198.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{21}NO_5Na$: 330.1317; found: 330.1324.

***tert*-Butyl 2-Methoxy-3-oxo-2-phenylindoline-1-carboxylate (3h)**

Yield: 44.5 mg (53%); colorless oil.

IR (neat): 2978, 2933, 1736, 1713, 1606, 1465, 1359, 1253, 1199, 1158, 1066, 1031, 993, 969, 901, 887, 843, 757, 743, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 9 H), 3.33 (s, 3 H), 7.16–7.39 (m, 6 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 8.36 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.0, 51.8, 82.4, 94.7, 116.5, 121.5, 123.6, 124.8, 125.1, 128.5, 137.1, 138.3, 151.0, 154.2, 196.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{21}NO_4Na$: 362.1368; found: 362.1364.

***tert*-Butyl 2-Methoxy-5-methyl-3-oxo-2-phenylindoline-1-carboxylate (3i)**

Yield: 52.3 mg (59%); white solid; mp 85–87 °C.

IR (KBr): 2978, 2932, 1732, 1713, 1620, 1586, 1491, 1358, 1254, 1155, 1119, 1069, 972, 914, 900, 829, 734, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (s, 9 H), 2.38 (s, 3 H), 3.32 (s, 3 H), 7.27–7.55 (m, 7 H), 8.24 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 28.0, 51.7, 82.2, 94.9, 116.3, 121.5, 124.4, 125.1, 128.5, 133.5, 137.2, 139.4, 151.1, 152.3, 196.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{23}NO_4Na$: 376.1525; found: 376.1533.

***tert*-Butyl 2-Methoxy-3-oxoindoline-1-carboxylate (3j)**

Yield: 42.5 mg (65%); colorless oil.

IR (neat): 2978, 2932, 1716, 1608, 1469, 1376, 1287, 1164, 1093, 1059, 758 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.61 (s, 9 H), 3.59 (s, 3 H), 4.21 (s, 1 H), 7.11–7.14 (m, 1 H), 7.60–7.72 (m, 2 H), 8.00 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5, 55.7, 56.5, 83.1, 87.1, 116.7, 122.3, 123.0, 123.5, 124.5, 137.2, 138.0, 151.3, 195.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_4Na$: 286.1055; found: 286.1056.

***tert*-Butyl 2-Methoxy-5-methyl-3-oxoindoline-1-carboxylate (3k)**

Yield: 46.9 mg (68%); colorless oil.

IR (neat): 3062, 3028, 2978, 2932, 1716, 1621, 1587, 1493, 1371, 1283, 1256, 1152, 1097, 1062, 826, 789, 763 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.60 (s, 9 H), 2.35–2.36 (m, 3 H), 3.58 (s, 3 H), 4.20 (s, 1 H), 7.43–7.49 (m, 2 H), 7.87 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 28.5, 55.9, 56.3, 82.9, 87.3, 116.5, 122.4, 124.2, 132.8, 133.3, 138.3, 139.0, 151.3, 196.0.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_4Na$: 300.1212; found: 300.1201.

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Supporting Information

Supporting information for this article is available online at https://doi.org /10.1055/s-0036-1589032.

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