Synthesis of 2-phenylindoxyls

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Abstract
Described herein is a novel route to 2-phenylindoxyls. A previously undisclosed acid catalyzed reaction of *N*-hydroxyalkyl-3-acetoxy-2-phenylindoles gave the desired 2-phenylindoxyls, the identity of which was confirmed by 2D-NMR. The product structure represents a scaffold that could be exploited in a pharmaceutical or academic setting.

Keywords: 2-phenylindoxyl, 2D-NMR, 2-phenylindole

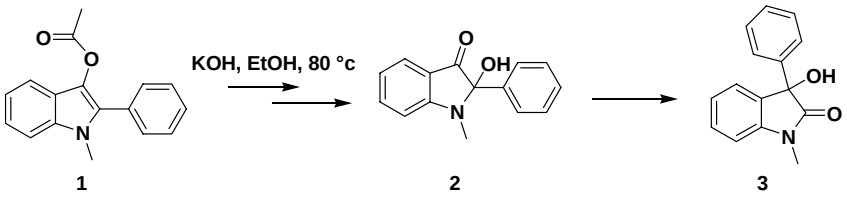
Introduction

Indoles are perhaps the most widely distributed heterocycles in nature, as the amino acid tryptophan is a constituent of almost every protein.[1] As such, the synthesis of indoles[2] and indole analogs, such as indoxyl[3] and oxindole,[4] have received considerable attention from synthetic organic chemists.

A number of different routes to 2-phenylindoxyls have been reported, including the addition of phenyl Grignard reagents to isatin[5] and alkyl grignard reagents to 2-phenyl-3*H*-indol-3-ones.[6] The 1,3-dipolar cycloaddition of 2-phenyl-3*H*-indol-3-one N-oxides to electron deficient alkenes also yields 2-phenylindoxyl skeletons, albeit containing a cyclic N-O bond.[7] Oxidative transformations yielding 2-phenylindoxyls include the reaction of 3-oxo-2,3-dihydroindoles with aryllead triacetate,[8] and the Baeyer-Villiger rearrangment of *N*-acetyl-2-phenyl-indole-3-carboxaldehyde.[9] *N*-acetyl-2-phenylindoxyl can also be formed from the selective hydrolysis of 1,3-diacetylindole.[10] The base-catalyzed rearrangement of 3*H*-Indol-3-ols have also been reported – one of many possibilities available for the synthesis of 2,2'-diphenyl indoxyls.[11]

A relatively straightforward route to 2-phenylindoxyls would be a valuable addition to the repertoire of reactions available to synthetic chemists. In this vein, hydrolysis of a 3-acetoxy-2-phenyl-indole precursor would seem to be a logical choice. It was previously reported by Sukari et al. that basic hydrolysis of 3-acetoxy-2-phenyl indoles **1** gave not the desired indoxyls, but rather dioxindoles **3** (Scheme 1).[12] Initial hydrolysis of the 3-acetoxy group was followed by

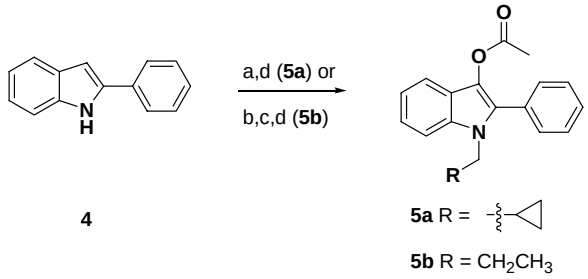
autooxidation and rearrangment. The autooxidation sequence (i.e. **1** → **2**) had ample precedent in the transformation of indoxyl to the dye indigo.[13]



Scheme 1. Basic hydrolysis of 3-acetoxy indoles.

Results and Discussion

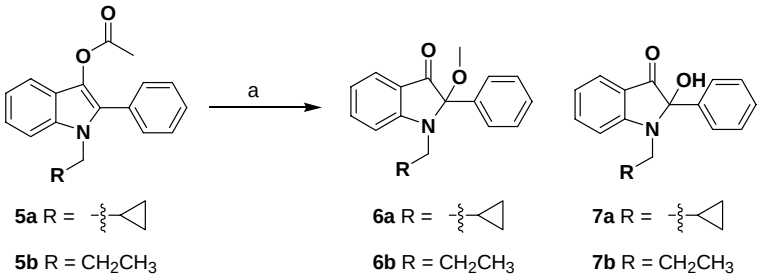
To the best of our knowledge the acidic hydrolysis of 3-acetyl-2-phenyl indoles had never been studied. Our investigation began with the synthesis of several *N*-alkyl-2-phenyl indole derivatives (Scheme 2). The hydrolysis precursors were prepared in 2-3 steps from commercially available indoles via sequential *N*-alkylation and oxidation with $Pb(OAc)_4$.[12] Alkylation of 2-phenyl indole **4** with cyclopropylmethyl bromide was followed by acetoxylation to give ester **5a**. Similarly, *N*-allylation, hydrogenation and acetoxylation provided ester **5b**.



Scheme 2. Synthesis of *N*-alkyl analogs. a) NaH, DMF, cyclopropylmethyl bromide. b) NaH, DMF, allyl bromide. c) H_2, Pd/C. d) CH_2Cl_2, $Pb(OAc)_4$.

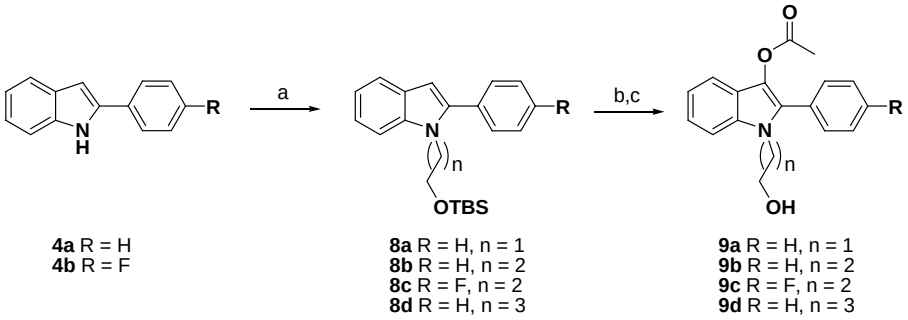
Basic hydrolysis (KOH, EtOH, 80 °C) of *N*-propyl indole **5a** gave a dioxindole,[14] in line with the findings of Sukari (*vida supra*). Acidic hydrolysis of *N*-alkyl-3-acetyl substrates **5** were carried out in methanol with a 2M solution of HCl and provided a mixture of 2-phenylindoxyls **6** and **7**. NMR (^1H, ^{13}C and DEPT) and GC-MS confirmed that the major product **6b** possessed a methoxy group at the 2-position and the minor product **7b** a hydroxyl group, respectively (Scheme 3). The structures of **6a** and **7a** were determined based on HPLC and GC-MS analysis and by analogy to the results seen for **6b** and **7b**. To account for the formation of structures **6** and **7**, we theorized that a radical or cation was forming at the benzylic position and was reacting

with solvent molecules. This prompted us to investigate whether the intermediate species could be trapped intramolecularly via attack by an alcohol tethered to the indole nitrogen.



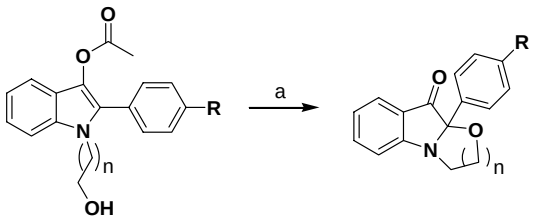
Scheme 3. Formation of 2-phenylindoxyls. a) 2M HCl, MeOH, RT.

Thus, we began the synthesis of *N*-hydroxyalkyl-3-acetoxy-2-phenyl indoles. *N*-Alkylation of 2-phenyl and 2-(*p*-fluoro)-phenyl indole **4** with TBS-protected bromo-alcohols proceeded in modest yield using NaH in DMF, followed by acetoxylation with LTA and removal of the TBS protecting group to give alcohols **9** (Scheme 4). The modest yield for the two steps was due to the low conversion of starting material in the acetoxylation reaction (see experimental).



Scheme 4. Synthesis of cyclization precursors. a) NaH, DMF, TBSO-$(CH_2)_n$-Br, n = 1,2,3. b) CH_2Cl_2, $Pb(OAc)_4$. c) THF, TBAF.

Acidic hydrolysis of *N*-hydroxyalkyl-3-acetoxy indole derivatives **9** provided cyclic 2-phenylindoxyl structures **10** and lent preliminary evidence to our hypothesis regarding the mechanism of the reaction (Scheme 5). All product structures were confirmed by a combination of 1D (DEPT, ^{13}C) and 2D-NMR experiments (gCOSY, gHMBC, gHMQC). The formation of indoxyls **10a** and **10d** was also accompanied by the formation of a side product[15] that accounted for the balance of the total yield in the reaction. The mechanism to account for the formation of the side product is currently under investigation and will be reported in due course.

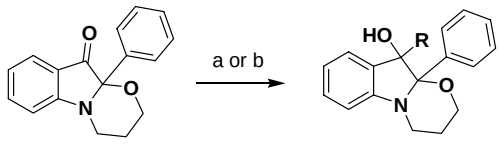


9 10

n	R	Starting material	Cyclized product	Yield
1	H	**9a**	**10a**	10%
2	H	**9b**	**10b**	76%
2	F	**9c**	**10c**	55%
3	H	**9d**	**10d**	16%

Scheme 5. Cyclization reaction. a) 2M HCl, MeOH, RT→70 °C

Indoxyl **10b** was also elaborated to show that it represented a potentially valuable scaffold for library synthesis. Reaction with MeLi and n-pentyl Grignard gave tertiary alcohols **11a** and **11b** by HPLC and GC-MS analysis (Scheme 6).



10b **11a** R = Me
11b R = Pent

Scheme 6. Reaction with nucleophiles. a) MeMgBr, THF. b) Pent-MgBr, THF

In summary, we have detailed a new synthesis of 2-phenylindoxyls. Our initial work showed that 2,2'-substitution was the only possibility due to the ease with which 2-phenylindoxyls were oxidized at the 2-position. *N*-hydroxyalkyl substitution provided novel cyclic 2-phenylindoxyl skeletons that could be elaborated with various nucleophiles. Work is underway to elucidate the mechanism under acidic conditions and will be reported in due course.

Experimental Section

General Procedures. All commercial reagents were used without further purification, unless otherwise noted. Anhydrous reactions were performed in flame-dried glassware under N_2. NMR spectra were recorded on a Varian 400 MHz spectrometer in deuterochloroform with

trimethylsilane (TMS) as an internal reference. Silica gel column chromatography was performed using an ISCO Combiflash system with detection at 254 nm on ISCO normal phase silica gel cartridges. HPLC was performed on a Hewlett Packard Series 1100 pump connected to an Agilent Zorbax RX-C18 5 μm, 4.6 X 250 mm column, with detection on a Hewlett Packard Series 1100 UV/Vis detector monitoring at 214 and 254 nm. The following linear gradient was used for all samples: Flow rate = 1 ml/min, Solvent A = H_20 w/0.05% TFA, Solvent B = MeCN w/0.05 % TFA. Time 0 min = 5 % Solvent B, time 4 min = 40 % Solvent B, time 8 min = 100 % Solvent B, 12 min = 5 % Solvent B, 20 min = 5 % Solvent B. GC-MS was performed on a Hewlett Packard 6890 Series GC System with an HP1 column (30 meters, 0.15 μ film thickness) coupled to a Hewlett Packard 5973 Series Mass Selective Detector. The following linear temperature gradient was used: 100°C for 5 minutes, then 20°C/min to 320°C. Hold @ 320°C for 10 minutes.

1-(Cyclopropylmethyl)-2-phenyl-1*H*-indol-3-yl acetate (5a). 2-Phenylindole (1.0 g, 5.17 mmol) was dissolved in anhydrous DMF (50 mL) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 248 mg, 6.21 mmol) was added and the resulting yellow solution was stirred at 0°C for 20 minutes. Cyclopropylmethyl bromide (600 μL, 6.21 mmol) was added and the yellow solution was allowed to warm to RT over 16 h. MeOH (5 mL) was added and the solution was poured into H_2O (100 mL) and washed with Et_2O (3 X 50 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→20 % EtOAc/hexanes yielded 1-(cyclopropylmethyl)-2-phenyl-1*H*-indole (292 mg, 23 %) as a clear oil. HPLC R_t = 11.44 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.82 (d, J = 7.70 Hz, 1H), 7.67-7.54 (m, 7H), 7.41 (at, 1H), 7.32 (at, 1H), 6.72 (s, 1H), 4.20 (d, J = 6.23 Hz, 1H), 1.23-1.19 (m, 1H), 0.54-0.49 (m, 2H), 0.20-0.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.4, 137.8, 133.6, 129.8, 129.6, 128.6, 128.5, 128.4, 128.1, 121.7, 120.7, 120.0, 110.4, 102.6, 48.2, 11.6, 4.2; GC-MS 13.38 min, M^+ 247. 1-(cyclopropylmethyl)-2-phenyl-1H-indole (273 mg, 1.11 mmol) was dissolved in anhydrous CH_2Cl_2 (11 mL) and Pb (IV) acetate (539 mg, 1.22 mmol) was added. The brown solution was stirred at RT for 16 h, then diluted with CH_2Cl_2 (30 mL), washed with brine (2 X 20 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→10 % EtOAc/hexanes yielded **5a** (100 mg, 29 %) as a white foam. HPLC R_t = 10.82 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.52-7.44 (m, 7H), 7.29-7.25 (m, 1H), 7.17 (at, 1H), 3.99 (d, J = 6.60 Hz, 2H), 2.25 (s, 3H), 1.07-1.03 (m, 1H), 0.42-0.37 (m, 2H), 0.04-0.012 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.1, 134.6, 130.5, 130.3, 130.2, 128.8, 128.7, 128.6, 122.6, 121.1, 120.2, 117.7, 110.7, 48.4, 20.8, 11.6, 4.4; GC-MS 14.3 min, M^+ 305.

2-Phenyl-1-propyl-1*H*-indol-3-yl acetate (5b). 2-Phenyl-1-propyl-1*H*-indole (1.4 g, 5.95 mmol) was dissolved in anhydrous CH_2Cl_2 (60 mL) and Pb (IV) acetate (2.9 g, 6.6 mmol) was added. The brown solution was stirred at RT for 16 h, then diluted with CH_2Cl_2 (100 mL), washed with brine (2 X 100 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→5 % EtOAc/hexanes yielded **5b** (400 mg, 34%) as a yellow solid. HPLC R_t = 10.9 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.54-7.41 (m, 7H), 7.28 (td, J = 6.97,

1.1 Hz, 1H), 7.21-7.17 (m, 1H), 4.08 (at, 2H), 2.27 (s, 3H), 1.76-1.70 (m, 2H), 0.80 (at, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.0, 134.3, 130.2, 130.0, 128.8, 128.5, 126.8, 122.4, 121.0, 120.1, 117.7, 110.4, 45.7, 23.5, 20.7, 11.4; GC-MS 13.7 min, M^+ 293.

2-Methoxy-2-phenyl-1-propylindolin-3-one (6b) and 2-hydroxy-2-phenyl-1-propylindolin-3-one (7b). 5b (155 mg, 0.53 mmol) was suspended in MeOH (10 mL) and 2.0 M HCl (530 µL, 1.06 mmol) was added. The solution was shaken at RT for 72 hours, then concentrated and purified by silica gel column chromatography with 0→20% EtOAc/hexanes to give **6b** (73 mg) as an orange oil and **7b** (21 mg) as an orange oil. **6b**: HPLC R_t = 10.82 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.56-7.30 (m, 7H), 6.82 (d, J = 8.43 Hz, 1H), 6.74 (t, J = 7.33 Hz, 1H), 3.31 (s, 3H), 3.25-3.17 (m, 1H), 3.09-3.03 (m, 1H), 1.65-1.59 (m, 2H), 0.89 (t, J = 7.33 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 199.0, 161.7, 138.8, 136.1, 128.8, 128.7, 126.4, 125.5, 118.5, 117.8, 107.9, 96.2, 51.7, 44.9, 22.2, 11.8; GC-MS 12.21 min, M^+ 281. **7b**: HPLC R_t = 9.86 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.53-7.49 (m, 2H), 7.41-7.32 (m, 4H), 6.77-6.71 (m, 2H), 3.32-3.25 (m, 1H), 3.10-3.02 (m, 1H), 1.63-1.57 (m, 2H), 0.86 (at, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 200.3, 160.9, 138.8, 136.5, 128.8, 128.7, 126.1, 126.1, 117.8, 117.0, 108.1, 91.3, 44.6, 22.3, 11.6; GC-MS 13.3 min, M^+ 267.

1-(Cyclopropylmethyl)-2-methoxy-2-phenylindolin-3-one (6a) and 1-(Cyclopropylmethyl)-2-hydroxy-2-phenylindolin-3-one (7a). 6a: HPLC R_t = 10.8 min, GC-MS 13.88 min, M^+ 293. **7a**: HPLC R_t = 9.91 min, GC-MS 13.93 min, M^+ 279.

Representative procedures for sequence of **4** → **8** (alkylation) and **8** → **9** (acetoxylation)

1-(2-*tert*-Butyldimethylsilyloxyethyl)-2-phenyl-1*H*-indole (8a). 2-Phenylindole (**4a**) (2.2 g, 11.7 mmol) was dissolved in anhydrous DMF (50 mL) and cooled to 0°C. NaH (60% dispersion in mineral oil, 702 mg, 17.5 mmol) was added and the resulting yellow solution was stirred at 0 °C for 20 minutes. 2-*tert*-butyldimethylsilyl-1-bromoethanol (2.72 g, 11.4 mmol) was dissolved in DMF (10 mL) and added dropwise to the indole solution. The yellow solution was allowed to warm to RT over 16 h. MeOH (5 mL) was added and the solution was poured into H_2O (100 mL) and washed with Et_2O (3 X 50 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→5 % EtOAc/hexanes yielded **8a** (1.69 g, 41%) as a clear oil. HPLC R_t = 13.3 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.65 (d, J = 7.70 Hz, 1H), 7.59-7.57 (m, 2H), 7.51-7.43 (m, 4H), 7.27-7.23 (m, 1H), 7.17 (at, 1H), 6.56 (d, J = 1.47 Hz, 1H), 4.31 (td, J = 1.83, 6.60 Hz, 2H), 3.86-3.82 (m, 2H), 0.80 (s, 9H), -0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.6, 138.0, 133.2, 129.9, 128.7, 128.3, 128.2, 121.8, 120.7, 120.1, 110.4, 102.6, 62.0, 46.1, 26.0, -5.5; GC-MS 14.1 min, M^+ 351.

1-(2-Hydroxyethyl)-2-phenyl-1*H*-indol-3-yl acetate (9a). 8a (1.69 g, 4.8 mmol) was dissolved in anhydrous CH_2Cl_2 (50 mL) and Pb (IV) acetate (2.35 g, 5.3 mmol) was added. The brown solution was stirred at RT for 16 h, then diluted with CH_2Cl_2 (100 mL), washed with brine (2 X 100 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→5 % EtOAc/hexanes yielded 1-(2-*tert*-butyldimethylsilyloxyethyl)-2-phenyl-1*H*-indol-3-yl acetate (560 mg, 28 %) as a yellow solid. HPLC R_t = 12.1 min, ^{1}H NMR

(400 MHz, $CDCl_3$) 7.57-7.47 (m, 7H), 7.30 (at, 1H), 7.20 (at, 1H), 4.27 (t, J = 6.60 Hz, 2H), 3.83 (at, 2H), 2.29 (s, 3H), 0.84 (s, 9H), -0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 169.9, 134.8, 130.3, 129.7, 128.8, 128.6, 127.1, 122.5, 121.0, 120.2, 117.6, 110.6, 62.0, 46.0, 25.9, 20.7, -5.54; GC-MS 14.75 min, M^+ 409. 1-(2-*tert*-butyldimethylsilyloxyethyl)-2-phenyl-1*H*-indol-3-yl acetate (558 mg, 1.36 mmol) was dissolved in anhydrous THF (14 mL) and 1.0 M TBAF in THF (2 mL, 2.0 mmol) was added. The clear orange solution was stirred for 40 min at RT, diluted with EtOAc and washed with H_2O (2 X 50 mL) and brine (50 mL). The organic extracts were dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→40% EtOAc/hexanes yielded **9a** (142 mg, 35%) as a yellow oil. HPLC R_t = 9.42 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.43-7.33 (m, 6H), 7.20 (at, 1H), 7.11 (at, 1H), 4.03 (t, J = 5.87 Hz, 2H), 3.53 (at, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.7, 134.5, 130.3, 130.3, 129.4, 128.8, 128.7, 126.8, 122.7, 120.9, 120.4, 117.5, 110.6, 61.2, 45.8, 20.7; GC-MS 13.9 min, M^+ 295.

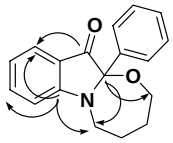
1-(3-*tert*-Butyldimethylsilyloxypropyl)-2-phenyl-1*H*-indole (8b). This compound was obtained as a clear oil in 53% yield using the general alkylation procedure outlined above. **8b**: HPLC R_t = 14.02 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.72 (d, J = 8.07 Hz, 1H), 7.59-7.46 (m, 5H), 7.30 (at, 1H), 7.21 (t, J = 7.70 Hz, 1H), 6.61 (s, 1H), 4.36 (t, J = 7.70 Hz, 2H), 3.60 (t, J = 5.87 Hz, 2H), 1.97-1.92 (m, 2H), 0.95 (s, 3H), 0.067 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.4, 137.7, 133.4, 129.5, 128.6, 128.3, 128.1, 121.7, 120.7, 120.0, 110.3, 102.4, 60.4, 41.3, 33.3, 26.1, -5.25; GC-MS 11.8 min, M^+ 365.

1-(3-Hydroxypropyl)-2-phenyl-1*H*-indol-3-yl acetate (9b). This compound was obtained as a colorless solid in 25% yield using the general acetoxylation procedure outlined above. **9b**: HPLC R_t = 9.46 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.51-7.42 (m, 7H), 7.26-7.13 (m, 3H), 4.28-4.25 (m, 2H), 3.42 (s, 3H), 2.24 (s, 3H), 1.86-1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.1, 134.4, 130.1, 129.9, 129.8, 128.9, 128.7, 127.0, 122.6, 121.0, 120.2, 117.7, 110.4, 59.6, 40.5, 32.7, 20.7; GC-MS 11.6 min, M^+ 309.

1-(3-*tert*-Butyldimethylsilyloxypropyl)-2-(4-fluorophenyl)-1*H*-indole (8c). This compound was obtained as a clear oil in 16% yield using the general alkylation procedure outlined above. **8c**: HPLC R_t = 13.68 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.64 (d, J = 7.70 Hz, 1H), 7.48-7.43 (m, 4H), 7.23 (at, 1H), 7.17-7.12 (m, 3H), 6.50 (s, 1H), 4.25 (t, J = 7.70 Hz, 2H), 3.53 (at, 2H), 1.90-1.84 (m, 2H), 0.87 (s, 10H), 0.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 164.0, 161.6, 140.3, 137.6, 131.3, 131.3, 129.5, 121.8, 120.7, 120.1, 115.8, 115.6, 110.3, 102.5, 60.3, 41.3, 33.3, 26.0, -5.3; GC-MS 11.8 min, M^+ 383.

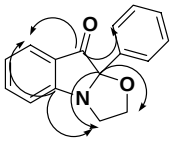
2-(4-Fluorophenyl)-1-(3-hydroxypropyl)-1*H*-indol-3-yl acetate (9c). This compound was obtained as a yellowish solid in 61% yield using the general acetoxylation procedure outlined above. HPLC R_t = 9.54 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.41-7.38 (m, 4H), 7.25-7.14 (m, 4H), 4.17 (t, J = 6.97 Hz, 1H), 3.38 (t, J = 5.87 Hz, 1H), 2.23 (s, 3H), 1.79-1.76 (m, 2H), 1.40 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.0, 164.2, 161.7, 134.3, 132.0, 131.9, 128.9, 125.8, 125.8, 122.8, 120.9, 120.3, 117.7, 116.2, 116.0, 110.4, 59.7, 40.6, 32.7, 20.7; GC-MS 14.7 min, M^+ 327.

1-(4-Hydroxybutyl)-2-phenyl-1*H*-indol-3-yl acetate (9d). This compound was obtained as a clear oil in 48% yield using the general acetoxylation procedure outlined above. **9d**: HPLC R_t = 9.55 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.51-7.38 (m, 7H), 7.25 (at, 1H), 7.16 (at, 1H), 4.12 (t, J = 7.33 Hz, 2H), 3.38 (t, J = 6.23 Hz, 2H), 2.25 (s, 3H), 1.73-1.66 (m, 2H), 1.34-1.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.1, 134.2, 130.1, 130.0, 129.9, 128.8, 128.6, 126.8, 122.5, 121.0, 120.1, 117.7, 62.1, 43.7, 29.7, 26.4, 20.7; GC-MS 12.4 min, M^+ 323.



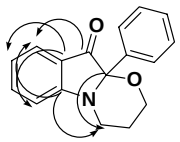
10d

Representative procedure ("cyclization") for synthesis of compounds **10a-d**: **9d** (74 mg, 0.23 mmol) was suspended in MeOH (2 mL) and 2.0 M HCl (230 µL, 0.46 mmol) was added. The solution was shaken at RT for 16 hours, then 6 M HCl (12 drops, ca. 60 µL) was added and the temperature was increased to 70°C. After 5.5 h the solution was cooled to RT and poured into sat'd aqueous $NaHCO_3$ (15 mL) and washed with Et_2O (3 X 30 mL). The combined organic washes were washed with brine (20 mL), dried (Na_2SO_4), filtered and concentrated. Purification by silica gel column chromatography with 0→25 % EtOAc/hexanes yielded **10d** (10 mg, 16%) as a fluorescent green oil. **10d**: HPLC R_t = 10.32 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.57-7.50 (m, 4H), 7.36-7.31 (m, 3H), 6.84 (d, *J* = 8.06 Hz, 1H), 6.74 (t, *J* = 7.33 Hz, 1H), 3.98-3.93 (m, 1H), 3.89-3.85 (m, 1H), 3.24-3.18 (m, 2H), 1.83-1.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) 200.9, 160.7, 138.5, 136.7, 129.0, 128.8, 126.5, 125.8, 119.2, 118.2, 108.9, 94.9, 66.3, 41.4, 30.5, 24.7; GC-MS 11.5 min, M^+ 279. Selected gHMBC couplings (see above): 200.9 → 7.5; 160.7 → 3.2, 7.4, 7.5; 94.9 → 3.2, 3.8, 3.9.



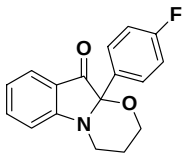
10a

This compound was obtained as a fluorescent green oil in 10% yield using the general cyclization procedure outlined above. **10a**: HPLC R_t = 9.87 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.66-7.60 (m, 4H), 7.41-7.37 (m, 3H), 7.11-7.05 (m, 2H), 4.10-4.04 (m, 2H), 3.69-3.63 (m, 1H), 3.58-3.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 197.2, 163.9, 137.8, 136.0, 128.9, 128.4, 126.5, 125.7, 122.8, 122.6, 114.8, 99.6, 67.9, 50.1; GC-MS 13.4 min, M^+ 251. Selected gHMBC couplings (see above): 200 → 7.62, 7.64; 164 → 3.65, 3.5, 7.64; 99 → 3.65, 4.05.



10b

This compound was obtained as a yellow solid in 76% yield using the general cyclization procedure outlined above. **10b**: HPLC R_t = 10.0 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.60-7.51 (m, 4H), 7.44-7.36 (m, 3H), 6.91 (d, J = 8.43 Hz, 1H), 6.80 (at, 1H), 3.96-3.81 (m, 3H), 3.46-3.39 (m, 1H), 2.05-1.97 (m, 1H), 1.40 (dd, J = 1.1, 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.4, 161.0, 138.0, 133.9, 129.2, 127.8, 126.6, 119.0, 118.9, 109.4, 90.6, 63.0, 40.0, 24.7; GC-MS 14.04 min, M^+ 265. Selected gHMBC couplings (see above): 197 → 7.6; 160 → 3.5, 7.6; 119 → 6.8, 6.98; 90 → 4.0.



10c

This compound was obtained as a fluorescent green oil in 55% yield using the general cyclization procedure outlined above. **10c**: HPLC R_t = 10.1 min; ^{1}H NMR (400 MHz, $CDCl_3$) 7.61-7.52 (m, 4H), 7.10 (at, 2H), 6.92 (d, J = 8.43, 1H), 6.83 (at, 1H), 3.97-3.90 (m, 2H), 3.85-3.78 (m, 1H), 3.45-3.37 (m, 1H), 2.05-1.95 (m, 1H), 1.60-1.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.2, 165.3, 162.0, 160.9, 138.0, 129.8, 129.7, 126.7, 119.3, 119.0, 116.3, 116.0, 109.6, 90.2, 62.9, 40.1, 24.6; GC-MS 12.35 min, M^+ 283.

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References and Notes

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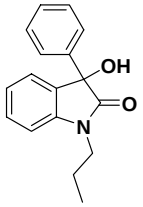
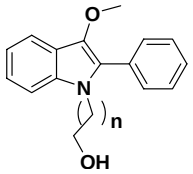
14. *N*-propyl dioxindole:



HPLC R_t = 9.31 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.39-7.26 (m, 6H), 7.06 (at, 1H), 6.91 (d, *J* = 7.70 Hz, 1H), 3.81-3.74 (m, 1H), 3.67-3.61 (m, 1H), 3.51 (s, 1H), 1.79-1.70 (m, 2H), 0.98 (t, *J* = 7.33 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 177.5, 143.0, 140.3, 131.8, 129.8, 128.6, 128.2, 125.2, 125.1, 123.3, 109.0, 77.9, 41.9, 20.7, 11.4; GC-MS 10.4 min, M^+ 267.

15. The structure of the side product has been tentatively identified:



Analytical data for n = 2: HPLC R_t = 9.67 min, ^{1}H NMR (400 MHz, $CDCl_3$) 7.69 (d, *J* = 7.83 Hz, 1H), 7.64-7.37 (m, 7H), 7.26-7.22 (m, 1H), 7.16-7.12 (at, 1H), 4.22 (at, 2H), 3.79 (s, 3H), 3.75 (at, 2H);^{13}C NMR (100 MHz, $CDCl_3$) 137.4, 134.6, 130.4, 128.6, 128.4, 128.1, 122.3, 121.1, 119.5, 118.1, 110.1, 62.0, 61.9, 45.8; GC-MS 14.1 min, M^+ 267.