JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

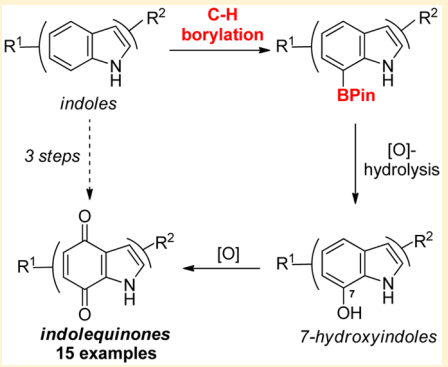
A Procedure for Transforming Indoles into Indolequinones

Andrew S. Eastabrook, Christy Wang, Emma K. Davison, and Jonathan Sperry*

School of Chemical Sciences, University of Auckland, 23 Symonds Street, Auckland, New Zealand

Supporting Information

ABSTRACT: A procedure that converts a series of structurally diverse, readily available indole derivatives to their corresponding indolequinones is described. The three-step route commences with an iridium catalyzed C−H borylation to give a 7-borylindole that upon oxidation−hydrolysis affords the 7-hydroxyindole. Subsequent oxidation provides the indolequinone.



INTRODUCTION

Compounds bearing the indolequinone pharmacophore have attracted widespread attention since the discovery of the natural product mitomycin C (MMC, **1**) and its subsequent clinical applications.[1] Unsurprisingly, the success of MMC has resulted in a plethora of synthetic indolequinones being developed,[2] including the MMC analogue apaziquone (E09, **2**), currently in advanced clinical trials as a treatment for bladder cancer.[3] Other biologically active natural indolequinones include the topoisomerase II inhibitor BE-10988 **3**,[4] the photoprotectant terreusinone **4**,[5] and exiguamine A **5**, a potent inhibitor of indoleamine-2,3-dioxygenase (IDO), an enzyme responsible for mobilizing the body's immune system against solid tumors[6] (Figure 1).

Due to their aforementioned biological properties, various methods have been developed for the preparation of indolequinones. Many existing methods involve the stepwise synthesis of an amino- or hydroxy/alkoxyindole **6** (from pyrroles[7] or arenes[8]) followed by oxidation to the desired indolequinone **7** (Scheme 1; A). An alternative method involves the annulation of a substituted quinone **8**, obviating the need for a final oxidation step (Scheme 1; B).[9,10]

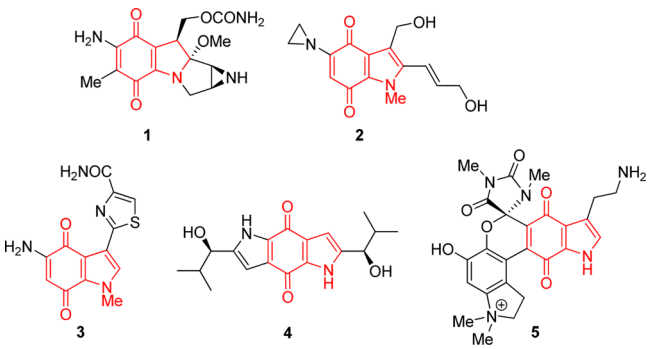
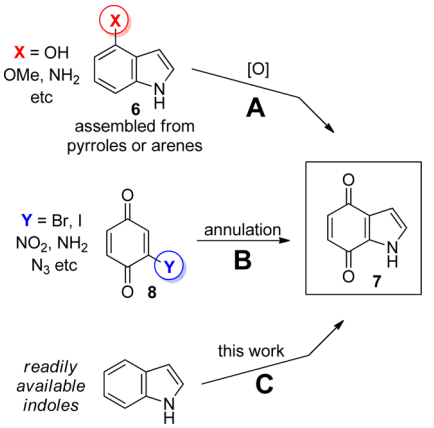


Figure 1. Biologically active indolequinones.

Scheme 1. Existing Approaches to Indolequinones (A and B) and Their Direct Assembly from Indoles (C)



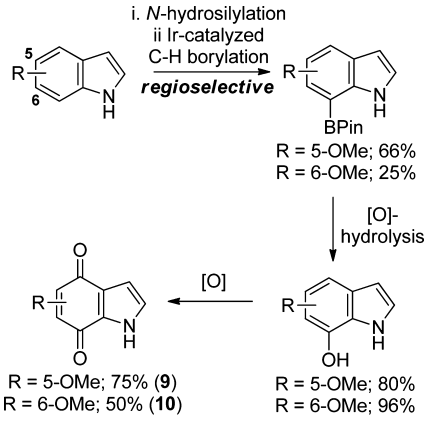
A versatile, topologically obvious synthesis of indolequinones from indoles would provide a valuable addition to the current synthetic repertoire (Scheme 1, C), an approach that requires selective functionalization of the benzo-fused ring in preference to the more reactive azole.[11] The vast majority of existing methods that convert indoles to indolequinones involve functionalizing the benzo-fused moiety of a 2,3-disubstituted indole, a substitution pattern that prevents reaction at the azole site.[12] Exceptions include the C4-oxidation of the indole ring in

Received: November 2, 2014

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

tryptamines and tryptophans using thallium salts[13] and the Dess–Martin periodinane-mediated oxidation of indoles to indolequinones, although this methodology is limited to substrates bearing a C5 benzylamide and a substituted indole nitrogen.[14] These limited methods prompted us to develop a synthetic route that would improve the scope of the direct indole → indolequinone transformation. Indeed, we recently demonstrated that subjecting 5- and 6-methoxyindole to a regioselective iridium-catalyzed C–H borylation[15] facilitated access to the indolequinones **9** and **10**, natural products isolated from the gastropod *Drupella fragum* (Scheme 2).[16] In

Scheme 2. C–H Borylation-Based Synthesis of Indolequinones 9 and 10[16]



these two examples, the excellent regiochemical outcome (i.e.: exclusive borylation at C7) can be attributed to the formation of a five-membered metallacycle upon C7–H bond cleavage, which is more favored than the four-membered metallacycle that would arise from C2–H bond cleavage.[15c] Using the results shown in Scheme 2 as a guide, a study to examine the range of indole substrates that are tolerated in this process was performed.

RESULTS AND DISCUSSION

Scheme 2 details the formation of 7-borylindoles from indoles that do not possess a substituent at C2 and hence the substrates had to be converted to the *N*-hydrosilylindole prior to the borylation. However, when using 2-substituted indoles in the borylation, the desired regiochemical outcome is governed by the indole N–H, which binds the active catalyst and directs borylation to the C7 site.[15b] Accordingly, a series of 2-substituted indoles were initially subjected to our synthetic methodology.[16a] 2-Methylindole, 2-phenylindole, and ethyl indole-2-carboxylate all proceeded through the synthetic process without incident, affording indolequinones **11**–**13**, respectively (Scheme 3). The 2,3- and 2,5-dimethylindolequinones **14** and **15** were also readily obtained from the corresponding dimethylindoles. Halogens are tolerated on both rings of the indole nucleus, illustrated by the synthesis of indolequinones **16**–**19**. An unprotected 5-aminoindole was converted to the indolequinone **20**, a useful example, as the biologically active indolequinones **1**–**3** (Figure 1) all possess a nitrogen substituent at this site. Indolequinone **21** was obtained without having to protect the tryptophol side chain. Tryptamine quinone **22** was also readily accessible, a notable result, as the existing method to convert tryptamines to tryptamine quinones employs highly toxic thallium salts.[13] This new approach[24] to tryptamine quinones described herein may find utility in the construction of pyrroloiminiquinones[17] and the synthesis of exiguamine analogues.[6,13b] Carbazole was readily converted to the carbazolequinone **23**,[18] a heterocyclic motif present in natural products including murrayaquinones A and B and koenigine-quinones A and B.[19] This methodology is compatible with the tetrahydrocarbazole and tetrahydro-*β*-carboline[20] ring systems, delivering indolequinones **24** and **25**, respectively. It is of note that the methodology described herein cannot be used if indolequinones bearing strong electron-withdrawing substituents on the quinone ring are required. Although electron-withdrawing groups on the indole carbocycle do not hinder the borylation and oxidation–hydrolysis steps, none of the resulting 7-hydroxyindoles **26**–**28** underwent oxidation to the corresponding indolequinones (Frémy's salt, CAN, salcomine/O_2). Nevertheless, this two-step route to 7-hydroxyindoles from indoles offers an efficient alternative to the existing synthetic methods used for assembling this heterocyclic motif.[21−23]

To conclude, a procedure that can be used to convert indoles to indolequinones has been developed. The three-step route commences with an iridium-catalyzed borylation to give a 7-borylindole that undergoes oxidation–hydrolysis to the 7-hydroxyindole and subsequent oxidation to the indolequinone. Although a range of indole derivatives work well in this process, it cannot be used to prepare indolequinones possessing strong electron-withdrawing substituents on the quinone ring, as they preclude the final oxidation step.

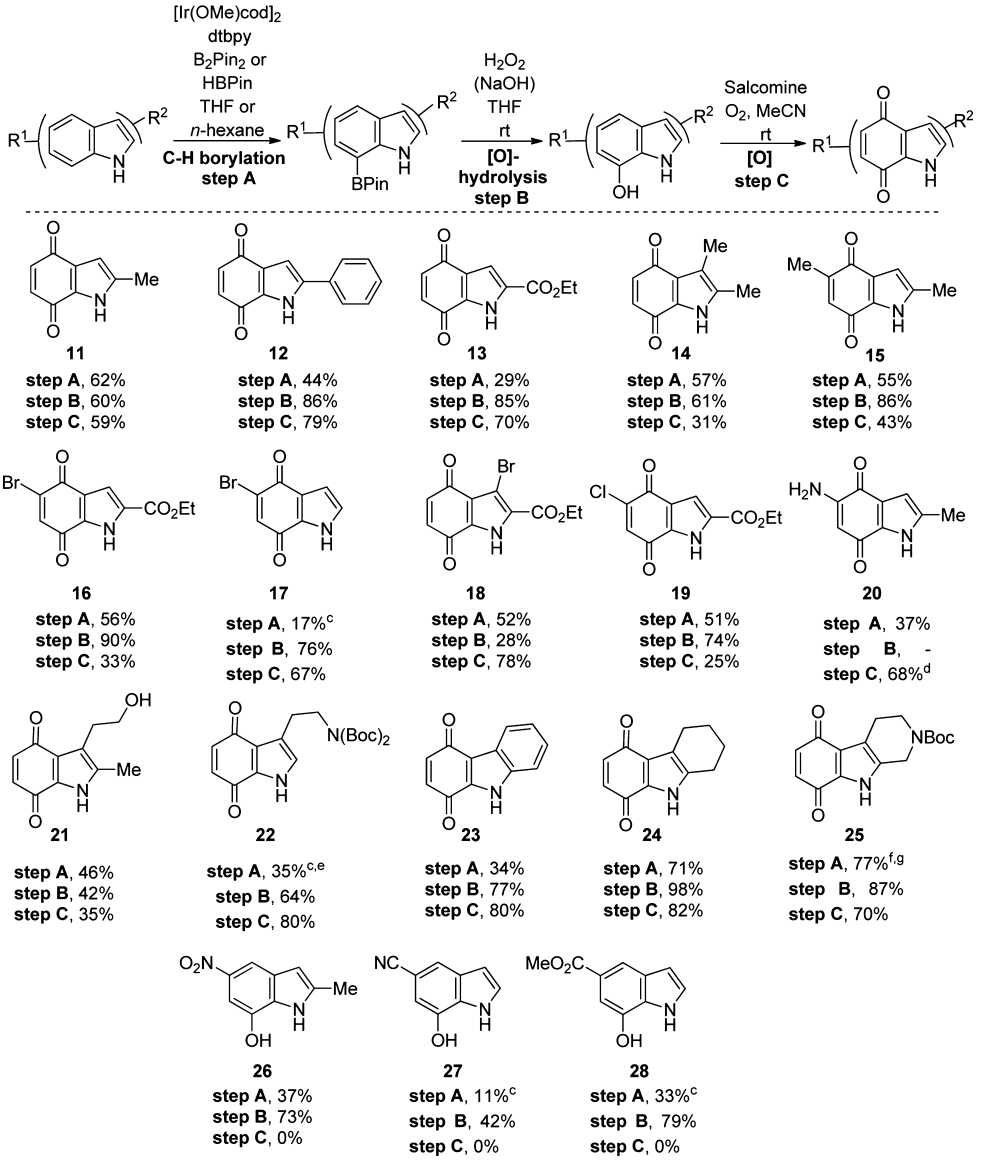
EXPERIMENTAL SECTION

All reactions were carried out in oven-dried glassware under a nitrogen atmosphere unless otherwise stated. Analytical thin layer chromatography was performed using 0.2 mm silica plates, and compounds were visualized under 365 nm ultraviolet irradiation followed by staining with either alkaline permanganate or ethanolic vanillin solution. Infrared spectra were obtained as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm^{-1}). Melting points were recorded on a melting point apparatus and are uncorrected. NMR spectra were recorded as indicated on an NMR spectrometer operating at 500, 400, and 300 MHz for ^1H nuclei and 125, 100, and 75 MHz for ^{13}C nuclei. Chemical shifts are reported in parts per million (ppm) relative to the tetramethylsilane peak recorded as δ 0.00 ppm in $CDCl_3$/TMS solvent, or the residual acetone (δ 2.05 ppm), chloroform (δ 7.24 ppm), DMSO (δ 2.50 ppm), or methanol (δ 3.31 ppm) peaks. The ^{13}C NMR values were referenced to the residual acetone (δ 29.9 ppm), chloroform (δ 77.1 ppm), DMSO (δ 39.5 ppm), or methanol (δ 49.0 ppm) peaks. ^{13}C NMR values are reported as chemical shift δ and assignment. ^1H NMR shift values are reported as chemical shift δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (J in hertz) and assignment. Assignments are made with the aid of DEPT 90, DEPT 135, COSY, NOESY, and HSQC experiments. High resolution mass spectra were obtained by electrospray ionization in positive ion mode at a nominal accelerating voltage of 70 eV on a microTOF mass spectrometer. Microwave-assisted reactions were performed in a CEM Discover Focused Microwave Synthesis System at 70 W.

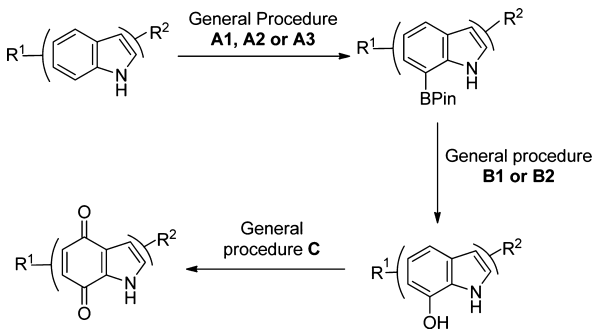
General Procedures. *General Procedure A1 (used with 2-substituted indoles).* A catalyst solution was prepared by adding pinacolborane (HBPin) or bis(pinacolato)diboron (B_2Pin_2) (1.0–1.5 equiv) to a solution of (1,5-cyclooctadiene)(methoxy)iridium(I) dimer {[Ir(OMe)cod]$_2$} (3–6 mol %) and 4,4′- di-*tert*-butyl-2,2′-dipyridyl (d^{t}bpy) (3–6 mol %) in THF or *n*-hexane (0.5 mL) with stirring until a deep red color appeared (1 min). The resulting solution was then transferred to a sealed tube containing the indole (0.2–1.0 mmol) in THF or *n*-hexane (0.5–5 mL), and the mixture was heated

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX–XXX

Scheme 3. Indolequinones from Indoles[a,b]



[a]Step A was generally performed using 1 mmol of indole, 1.5 equiv of the boron source, and 3−6 mol % catalyst and ligand. Oxidation−hydrolysis was performed on 0.1−0.8 mmol scale, with 1 mL of H_2O_2 and 1 mL of NaOH (1 M) per mmol of 7-borylindole. Oxidation was conducted on approximately 0.1 mmol scale. [b]All indolequinones were confirmed as para from the relevant NOE correlations. [c]The indole nitrogen was hydrosilylated prior to the C−H borylation to avoid C2 borylation. [d]The oxidation−hydrolysis (step B) gave a 1:1 mixture of 7-hydroxyindole and indolequinone which all converted to the indolequinone during workup and purification. [e]Conducting the borylation on Boc-tryptamine gave the C2-borylated product. Accordingly, the side chain has to be diBoc protected in order to obtain the desired 7-borylindole. [f]The borylation failed if the secondary amine was unprotected. [g]Borylation conducted under microwave irradiation.



at to 60 °C (unless specified otherwise) for 4 h (unless specified otherwise). The reaction mixture was cooled to room temperature and concentrated in vacuo and the crude residue purified by flash chromatography on silica gel eluting with *n*-hexane and ethyl acetate to give the 7-borylindole.

General Procedure A2 (N-diethylhydrosilylation−borylation; used on indoles with no substituent at C2). In a sealed tube equipped with a stirring bar and Teflon-lined screwcap was added $[Ru(p\text{-cymene})Cl_2]_2$ (3 mg, 0.005 mmol, 1 mol %), indole (0.5 mmol), diethylsilane (66 mg, 0.096 mL, 0.75 mmol), and toluene (0.5 mL). The mixture was heated at 90 °C for 15 h, and the volatile materials were removed under reduced pressure, affording the *N*-hydrosilylindole. In a separate vessel, a catalyst solution was prepared by adding B_2Pin_2 (190 mg, 0.75 mmol) to a solution of $[Ir(OMe)\text{-}cod]_2$ (10 mg, 0.015 mmol, 6 mol %) and d^{t}bpy (8 mg, 0.03 mmol, 12 mol %) in THF (0.5 mL) with stirring until a deep red color appeared (1−2 min). The resulting solution was then transferred to sealed tube

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

containing the freshly prepared *N*-hydrosilylindole in THF (1 mL), and the reaction mixture stirred at 90 °C in a sand bath for 15 h and then cooled to room temperature. Sodium acetate (3 M, 0.5 mL) was added, and the reaction mixture was stirred at room temperature for 6 h. Upon completion, the mixture was diluted with diethyl ether (20 mL) and water (20 mL). The aqueous layer was separated and extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel eluting with 4:1 *n*-hexane−ethyl acetate to give the 7-borylindole.

General Procedure A3 (N-dimethylhydrosilylation−borylation; used on indoles with no substituent at C2). During the preliminary stages of this study, we found general procedure A2 regularly gave unsatisfactory results, primarily due to the poor quality of diethylsilane we were supplied with. As a result, over time general procedure A3 became the *N*-hydrosilylation protocol of choice, which we found more reliable and logistically simpler than A2.

In a sealed tube equipped with a stirring bar and Teflon-lined screwcap was added indole (1 mmol) in THF (2 mL) followed by triethylamine (1.5 mmol) and dimethylchlorosilane (1.5 mmol). The reaction mixture was stirred at room temperature for 6−22 h and filtered through Celite, and the volatile materials were removed under reduced pressure, affording the *N*-hydrosilylindole. In a separate vessel, a catalyst solution was prepared by adding B_2Pin_2 (1.1−1.5 equiv) to a solution of $[Ir(OMe)cod]_2$ (0.5−6 mol %) and d^{t}bpy (0.5−3 mol %) in THF (1−2 mL) with stirring until a deep red color appeared (2 min). The resulting solution was then transferred to a sealed tube containing the freshly prepared *N*-hydrosilylindole in THF (2 mL), and the reaction mixture stirred at 80−85 °C in a sand bath for 16−19 h and then cooled to room temperature. Saturated sodium hydrogen carbonate (aq 1 mL) or sodium acetate (3 M aq, 0.5 mL) was added, and reaction mixture was stirred at room temperature for 1−2 h. Upon completion, the mixture was diluted with diethyl ether (20 mL) and water (20 mL). The aqueous layer was separated and extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel, eluting with the stated eluent to give the 7-borylindole.

General Procedure B1 (oxidation−hydrolysis). The following procedure was used if the 7-hydroxyindole products were sensitive to base:

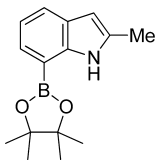
To a solution of 7-borylindole (0.03−0.8 mmol) in THF (2−5 mL) was added hydrogen peroxide (0.2−0.5 mL, 30% in water). The reaction mixture was stirred at room temperature for 1−4 h, diluted with ether (10 mL), washed with water (8 mL) and brine (8 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel eluting with *n*-hexane and ethyl acetate or diethyl ether to give the 7-hydroxyindole

General Procedure B2 (oxidation−hydrolysis; basic conditions). The following procedure was used if the 7-hydroxyindole products were stable to base:

To a solution of 7-borylindole (0.06−0.4 mmol) in THF (2.5−14 mL) at 0 °C was added equal volumes of hydrogen peroxide (0.03−0.4 mL, 30% in water) and sodium hydroxide (0.03−0.4 mL, 1 M solution). The reaction mixture was stirred at room temperature for 10 min, diluted with diethyl ether (10 mL), washed with water (8 mL) and brine (8 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel, eluting with *n*-hexane and ethyl acetate to give the 7-hydroxyindole.

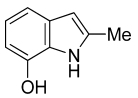
General Procedure C (oxidation). To a solution of 7-hydroxyindole (0.016−0.250 mmol) in acetonitrile (1−10 mL) was added salcomine (12−15 mol %), and the reaction mixture was stirred at room temperature under a balloon of oxygen for 4 h (unless stated otherwise). Silica gel (50 mg) was added, and the solvent concentrated in vacuo. The resulting residue was purified on a short pad of silica gel using the eluent stated, affording the desired indolequinone.

2-Methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole (11A). General procedure A1 was performed using 2-methylindole (131 mg, 1.00 mmol), $[Ir(OMe)cod]_2$ (1.5 mol %, 10



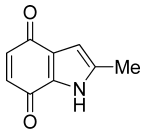
mg), d^{t}bpy (3 mol %, 8 mg), and B_2Pin_2 (1.5 equiv, 381 mg) in THF (1.5 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (159 mg, 0.62 mmol, 62%) as a pink solid, mp 64−70 °C (lit.[15b] oil); δ_H (300 MHz, $CDCl_3$) 8.85 (1 H, br s, NH), 7.62 (1 H, d, *J* 7.9, ArH), 7.55 (1 H, dd, *J* 7.1, 1.0, ArH), 7.06 (1 H, t, *J* 7.4, ArH), 6.20 (1 H, q, *J* 0.9, ArH), 2.49 (3 H, d, *J* 0.7, Me), 1.39 (12 H, s, 4 × Me); ^{1}H NMR spectrum was in agreement with the literature.[15b]

2-Methylindol-7-ol (11B). General procedure B2 was performed using **11A** (105 mg, 0.41 mmol), H_2O_2 (0.4 mL) and NaOH (1 M, 0.4



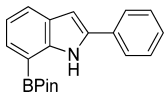
mL) in THF (12 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (36 mg, 0.24 mmol, 60%) as a yellow oil, ν_{max} (neat)/cm^{-1} 3390, 1582, 1451, 1306, 1258, 1030, 789, 728; δ_H (300 MHz, $CDCl_3$) 8.06 (1 H, br s, NH), 7.12 (1 H, d, *J* 7.9, ArH), 6.89 (1 H, t, *J* 7.8, ArH), 6.50 (1 H, dd, *J* 7.6, 0.7, ArH), 6.20 (1 H, m, ArH), 4.83 (1 H, br s, OH), 2.45 (3 H, d, *J* 0.8, Me); δ_C (100 MHz, $CDCl_3$) 140.9 (C), 135.2 (C), 131.4 (C), 125.7 (C), 120.0 (CH), 112.9 (CH), 105.9 (CH), 101.0 (CH), 13.8 (Me). HRMS [ESI, (M + H)$^+$] found 148.0764. $[C_9H_9NO + H]^+$ requires 148.0757.

2-Methylindole-4,7-dione (11C). General procedure C was performed using **11B** (34 mg, 0.23 mmol) and salcomine (12 mol



%, 9 mg) in acetonitrile (9 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (22 mg, 0.14 mmol, 59%) as a red solid, mp 168 °C (decomp); ν_{max} (neat)/cm^{-1} 3230, 3131, 3106, 2928, 1629, 1582, 1477, 1445, 1427, 1230, 1053, 1028, 828, 752, 732; δ_H (400 MHz, $CDCl_3$) 10.06 (1 H, br s, NH), 6.55 (2 H, s, 2 × CH), 6.37 (1 H, m, ArH), 2.40 (3 H, s, Me); δ_C (100 MHz, $CDCl_3$) 183.7 (C═O), 177.0 (C═O), 137.7 (CH), 137.4 (C), 136.4 (CH), 130.0 (C), 127.0 (C), 107.0 (CH), 13.3 (Me); HRMS [ESI, (M + Na)$^+$] found 184.0376. $[C_9H_7NO_2 + Na]^+$ requires 184.0369.

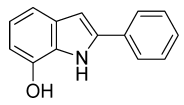
2-Phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole (12A). General procedure A1 was performed using 2-



phenylindole (193 mg, 1.0 mmol), $[Ir(OMe)cod]_2$ (1.5 mol %, 10 mg), d^{t}bpy (3 mol %, 8 mg), and HBPin (1.5 equiv, 0.22 mL) in *n*-hexane (2 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (140 mg, 0.44 mmol, 44%) as a colorless solid, δ_H (400 MHz, $CDCl_3$) 9.45 (1 H, br s, NH), 7.75 (1 H, d, *J* 7.6, ArH), 7.69 (2 H, d, *J* 8.4, 2 × ArH), 7.65 (1 H, d, *J* 6.8, ArH), 7.47 (2 H, dd, *J* 8.4, 7.6, 2 × ArH), 7.35 (1 H, t, *J* 7.6, ArH), 7.15 (1 H, t, *J* 7.6, ArH), 6.81 (1 H, d, *J* 2.4, ArH), 1.43 (12 H, br s, 4 × Me); The ^{1}H spectrum was in agreement with that reported in the literature.[15b]

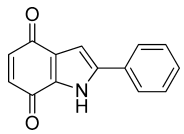
2-Phenyl-7-hydroxyindole (12B). General procedure B1 was performed using **12A** (255 mg, 0.8 mmol) and H_2O_2 (0.3 mL) in THF (10 mL). Purification using 7:3 *n*-hexane−ethyl acetate as eluent gave the title compound (144 mg, 0.69 mmol, 86%) as a pink solid, mp 146−148 °C; ν_{max} (neat)/cm^{-1} 3410, 3264, 3146, 1580, 1484, 1448, 1316, 1283, 1270, 1250, 1236, 1188, 1097, 966, 936, 799; δ_H (400

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX



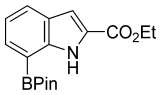
MHz, $CDCl_3$) 8.57 (1 H, br s, NH), 7.67 (2 H, dd, *J* 7.2, 1.2, ArH), 7.43 (2 H, t, *J* 7.6, ArH), 7.32 (1 H, d, *J* 7.6, ArH), 7.25 (1 H, d, *J* 7.2, ArH), 6.96 (1 H, t, *J* 7.6, ArH), 6.82 (1 H, d, *J* 1.2, ArH), 6.59 (1 H, d, *J* 7.2, ArH), 5.03 (1 H, br s, OH); δ_C (100 MHz, $CDCl_3$) 141.3 (C), 138.1 (C), 132.3 (C), 131.4 (C), 129.0 (2 × CH), 127.8 (CH), 126.6 (C), 125.2 (2 × CH), 120.5 (CH), 113.8 (CH), 106.9 (CH), 100.3 (CH); HRMS [ESI, $(M + Na)^+$] found 232.0734. $[C_{14}H_{11}NO + Na]^+$ requires 232.0733.

2-Phenylindole-4,7-dione (12C). General procedure C was performed using **12B** (50 mg, 0.24 mmol) and salcomine (15 mol



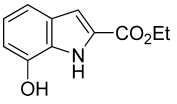
%, 12 mg) in acetonitrile (5 mL). Flash-column chromatography using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (42.1 mg, 0.19 mmol, 79%) as a red solid, mp 236 °C (decomp); ν_{max} (neat)/cm^{-1} 3259, 3124, 3103, 3059, 2923, 2163, 1975, 1729, 1634, 1585, 1512, 1488, 1467, 1426, 1352, 1291, 1268, 1211, 1200, 1060, 1029, 988, 971, 933, 917, 824, 794, 712, 686, 669; δ_H (400 MHz, DMSO-d_6) 13.04 (1 H, br s, NH), 7.94 (2 H, m, 2 × ArH), 7.44 (2 H, m, 2 × ArH), 7.37 (1 H, m, ArH), 7.06 (1 H, s, ArH), 6.71 (1 H, d, *J* 1.0, quinone CH), 6.66 (1 H, d, *J* 1.0, quinone CH); δ_C (100 MHz, DMSO-d_6) 183.2 (C═O), 176.6 (C═O), 139.3 (C), 137.1 (CH), 137.0 (CH), 131.3 (C), 130.2 (C), 128.9 (2 × CH), 128.4 (CH), 126.3 (C), 125.7 (2 × CH), 105.0 (CH); HRMS [ESI, $(M + Na)^+$] found 246.0529. $[C_{14}H_9NO_2 + Na]^+$ requires 246.0525.

Ethyl 7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)indole-2-carboxylate (13A). General procedure A1 was performed using

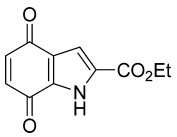


ethyl indole-2-carboxylate (189 mg, 1.0 mmol), $[Ir(OMe)cod]_2$ (1.5 mol %, 10 mg), d^{t}bpy (3 mol %, 8 mg), and HBPin (1.5 equiv, 0.22 mL) in *n*-hexane (2 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (90 mg, 0.29 mmol, 29%) as a colorless solid; δ_H (400 MHz, $CDCl_3$) 9.70 (1 H, br s, NH), 7.80 (1 H, d, *J* 8.0, ArH), 7.76 (1 H, dd, *J* 7.2, 2.0, ArH), 7.20 (1 H, d, *J* 2.0, ArH), 7.18−7.14 (1 H, dd, *J* 8.0, 6.8, ArH), 4.41 (2 H, q, *J* 7.2, CH_2), 1.41 (3 H, t, *J* 7.2, Me), 1.39 (12 H, s, 4 × Me). The ^1H spectrum was in agreement with that reported in the literature.[15b]

Ethyl 7-Hydroxyindole-2-carboxylate (13B). General procedure B1 was performed using **13A** (90 mg, 0.29 mmol) and H_2O_2

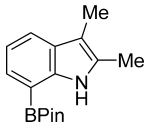


(0.35 mL) in THF (10 mL). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (50 mg, 0.24 mmol, 85%) as an orange solid, mp 196.6−200 °C; ν_{max} (neat)/cm^{-1} 3374, 3340, 2998, 2923, 2853, 2247, 1907, 1743, 1653, 1584, 1508, 1473, 1452, 1435, 1406, 1374, 1296, 1260, 1235, 1209, 1166, 1121, 1059, 1038, 1016, 978, 859, 823, 782, 754; δ_H (400 MHz, DMSO-d_6) 11.37 (1 H, br s, NH), 9.49 (1 H, br s, OH), 7.09 (2 H, m, 2 × ArH), 6.89 (1 H, t, *J* 7.6, ArH), 6.63 (1 H, d, *J* 7.2, ArH), 4.32 (2 H, q, *J* 7.2, CH_2), 1.34 (3 H, t, *J* 7.2, Me); δ_C (100 MHz, DMSO-d_6) 161.1 (C), 143.8 (C), 128.7 (C), 127.8 (C), 127.0 (C), 121.1 (CH), 112.7 (CH), 108.3 (CH), 108.2 (CH), 60.3 (CH_2), 14.2 (Me); HRMS [ESI, $(M + Na)^+$] found 228.0634. $[C_{11}H_{11}NO_3 + Na]^+$ requires 228.0631.



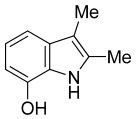
Ethyl 4,7-Dioxo-4,7-dihydroindole-2-carboxylate (13C). General procedure C was performed using **13B** (35 mg, 0.17 mmol) and salcomine (15 mol %, 8 mg) in acetonitrile (10 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (26 mg, 0.12 mmol, 70%) as a yellow solid, mp 169−172 °C; ν_{max} (neat)/cm^{-1} 3226, 2043, 2924, 1699, 1657, 1587, 1549, 1493, 1479, 1461, 1388, 1365, 1271, 1234, 1193, 1172, 1097, 1046, 1030, 1010, 846, 804, 781, 650, 633, 618; δ_H (400 MHz, DMSO-d_6) 13.68 (1 H, br s, NH), 7.07 (1 H, s, ArH), 6.76 (2 H, d, *J* 2.4, ArH), 4.30 (2 H, q, *J* 7.2, CH_2), 1.30 (3 H, t, *J* 7.2, Me); δ_C (100 MHz, DMSO-d_6) 182.5 (C═O), 177.6 (C═O), 159.6 (C═O), 138.0 (CH), 137.1 (CH), 133.9 (C), 133.0 (C), 128.7 (C), 111.6 (CH), 60.9 (CH_2), 14.0 (Me); HRMS [ESI, $(M + Na)^+$] found 242.0425. $[C_{11}H_9NO_4 + Na]^+$ requires 242.0424.

2,3-Dimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole (14A). General procedure A1 was performed using 2,3-



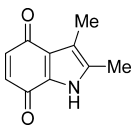
dimethylindole (100 mg, 0.69 mmol), $[Ir(OMe)cod]_2$ (3 mol %, 14 mg), d^{t}bpy (6 mol %, 11 mg), and B_2Pin_2 (1.1 equiv, 192 mg) in THF (1.5 mL total). Purification using 19:1 *n*-hexane−ethyl acetate as eluent gave the title compound (106 mg, 0.39 mmol, 57%) as a colorless solid, mp 89−93 °C; ν_{max} (neat)/cm^{-1} 3456, 2978, 1366, 1322, 1269, 1141, 1127, 851, 752, 681; δ_H (500 MHz, $CDCl_3$) 8.68 (1 H, br s, NH), 7.59 (1 H, d, *J* 7.9, ArH), 7.56 (1 H, dd, *J* 7.3, 1.0, ArH), 7.09 (1 H, t, *J* 7.4, ArH), 2.41 (3 H, s, Me), 2.24 (3 H, s, Me), 1.40 (12 H, s, 4 × BPin Me); δ_C (100 MHz, $CDCl_3$) 140.6 (C), 130.7 (C), 128.5 (C), 128.2 (CH), 121.5 (CH), 118.6 (CH), 106.6 (C), 83.8 (2 × C), 25.1 (4 × Me), 11.8 (Me), 8.5 (Me), 1 × C not observed; HRMS: [ESI, $(M + Na)^+$] found 294.1634. $[C_{16}H_{22}BNO_2 + Na]^+$ requires 294.1639.

2,3-Dimethylindol-7-ol (14B). General procedure B2 was performed using **14A** (75 mg, 0.28 mmol), H_2O_2 (0.28 mL), and



NaOH (1 M, 0.28 mL) in THF (10 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (28 mg, 0.17 mmol, 61%) as a colorless solid, mp >250 °C; ν_{max} (methanol)/cm^{-1}: 3387, 2919, 1577, 1496, 1463, 1314, 1223, 1100, 1051, 985, 777, 730; δ_H (500 MHz, $CDCl_3$) 7.89 (1 H, br s, NH), 7.10 (1 H, d, *J* 7.9, ArH), 6.92 (1 H, t, *J* 7.6, ArH), 6.50 (1 H, d, *J* 7.5, ArH), 4.88 (1 H, br s, OH), 2.36 (3 H, s, Me), 2.22 (3 H, s, Me); δ_C (125 MHz, $CDCl_3$) 140.7 (C), 131.9 (C), 131.0 (C), 124.7 (C), 119.5 (CH), 111.3 (CH), 107.8 (C), 106.0 (ArH), 11.7 (Me), 8.8 (Me); HRMS [ESI, $(M + H)^+$] found 162.0912. $[C_{10}H_{11}NO + H]^+$ requires 162.0913.

2,3-Dimethylindole-4,7-dione (14C). General procedure C was performed using **14B** (12 mg, 0.074 mmol) (12 mol %, 3 mg) in

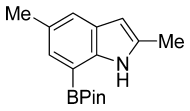


acetonitrile (2 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (4 mg, 0.023 mmol, 31%) as a red solid, mp 193 °C (decomp); ν_{max} (neat)/cm^{-1} 3202, 2923, 2853, 1630, 1581, 1568, 1489, 1439, 1391, 1376, 1350, 1250, 1086, 1037, 845, 762;

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

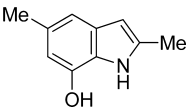
δ_H (500 MHz, $CDCl_3$) 9.14 (1 H, br s, NH), 6.51 (1 H, s, ArH), 6.50 (1 H, s, ArH), 2.27 (3 H, s, Me), 2.25 (3 H, s, Me); δ_C (125 MHz, DMSO-d_6) 184.5 (C), 175.6 (C), 137.1 (CH), 136.4 (CH), 134.7 (C), 124.1 (C), 123.0 (C), 117.2 (C), 10.2 (Me), 9.3 (Me); HRMS: [ESI, $(M + H)^+$] found 176.0711. $[C_{10}H_9NO_2 + H]^+$ requires 176.0706.

2,5-Dimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole (15A). General procedure A1 was performed using 2,5-



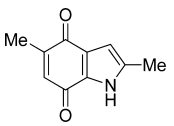
dimethylindole (100 mg, 0.689 mmol), $[Ir(OMe)cod]_2$ (3 mol %, 14 mg) d^{t}bpy (6 mol %, 11 mg), and B_2Pin_2 (1.1 equiv, 192 mg) in THF (1.5 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (103 mg, 0.380 mmol, 55%) as a pink solid, mp 85−89 °C; ν_{max} (neat)/cm^{-1} 3457, 2979, 2915, 1367, 1322, 1269, 1141, 1127, 851, 752, 681; δ_H (500 MHz, $CDCl_3$) 8.75 (1 H, br s, NH), 7.43 (1 H, s, ArH), 7.41 (1 H, d, *J* 1.1, ArH), 6.14 (1 H, q, *J* 1.1, ArH), 2.49 (3 H, s, Me), 2.44 (3 H, s, Me), 1.41 (12 H, s, 4 × BPin Me); δ_C (125 MHz, $CDCl_3$) 129.6 (C), 129.4 (CH), 128.6 (C), 128.2 (C), 125.4 (C), 123.3 (CH), 99.5 (CH), 83.8 (2 × C), 25.1 (4 × Me), 21.4 (Me), 14.1 (Me), 1 × C not observed; HRMS: [ESI, $(M + H)^+$] found 272.1827. $[C_{16}H_{22}BNO_2 + H]^+$ requires 272.1819.

2,5-Dimethylindol-7-ol (15B). General procedure B2 was performed using **15A** (100 mg, 0.37 mmol), H_2O_2 (0.37 mL), and



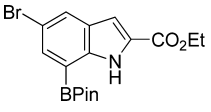
NaOH (1 M, 0.37 mL) in THF (14 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (51 mg, 0.32 mmol, 86%) as a pink solid, mp 138−139 °C; ν_{max} (methanol)/cm^{-1} 3348, 1631, 1588, 1524, 1491, 1455, 1411, 1351, 1319, 1244, 1133, 1062, 960, 813; δ_H (500 MHz, $CDCl_3$) 7.96 (1 H, br s, NH), 6.90 (1 H, s, ArH), 6.34 (1 H, s, ArH), 6.11 (1 H, t, *J* 1.2, ArH), 4.78 (1 H, s, OH), 2.43 (3 H, s, Me), 2.36 (3 H, s, Me); δ_C (126 MHz, $CDCl_3$) 140.5 (C), 135.3 (C), 131.6 (C), 129.7 (C), 124.7 (C), 112.5 (CH), 107.6 (CH), 100.5 (CH), 21.6 (Me), 13.8 (Me); HRMS: [ESI, $(M + H)^+$] found 162.0914. $[C_{10}H_{11}NO + H]^+$ requires 162.0913.

2,5-Dimethylindole-4,7-dione (15C). General procedure C was performed using **15B** (41 mg, 0.25 mmol) and salcomine (12 mol %,



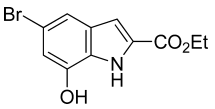
10 mg) in acetonitrile (6 mL). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (19 mg, 0.11 mmol, 43%) as an orange solid, mp 227−230 °C (decomp); ν_{max} (neat)/cm^{-1} 3212, 3137, 2924, 1667, 1638, 1603, 1428, 1190, 783, 746; δ_H (500 MHz, $CDCl_3$) 9.25 (1 H, br s, NH), 6.38 (1 H, q, *J* 1.6, ArH), 6.35 (1 H, d, *J* 2.4, ArH), 2.36 (3 H, s, Me), 2.07 (3 H, d, *J* 1.4, Me); δ_C (100 MHz, $CDCl_3$) 183.8 (C=O), 177.6 (C=O), 147.0 (C), 136.6 (C), 132.7 (CH), 130.5 (C), 127.0 (C), 107.1 (CH), 16.2 (Me), 13.2 (Me); HRMS: [ESI, $(M + H)^+$] found 176.0710. $[C_{10}H_9NO_2 + H]^+$ requires 176.0706.

Ethyl 5-Bromo-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole-2-carboxylate (16A). General procedure A1 was



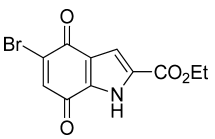
performed using ethyl 5-bromoindole-2-carboxylate (250 mg, 0.93 mmol), $[Ir(OMe)cod]_2$ (9 mg, 0.014 mmol, 1.5 mol %), d^{t}bpy (7.5 mg, 0.028 mmol, 3 mol %), and B_2Pin_2 (1.5 equiv, 355 mg) in THF (2 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (205 mg, 0.52 mmol 56%) as a colorless solid, mp 139−142 °C; ν_{max} (neat)/cm^{-1} 3452, 2983, 1710, 1537, 1360, 1292, 1229, 1177, 1139, 850, 743; δ_H (300 MHz, $CDCl_3$) 9.67 (1 H, br s, NH), 7.91 (1 H, d, *J* 1.8, ArH), 7.84 (1 H, d, *J* 1.8, ArH), 7.13 (1 H, d, *J* 2.2, ArH), 4.42 (2 H, q, *J* 7.1, CH_2), 1.45−1.40 (15 H, m, Me + 4 × BPin Me); δ_C (100 MHz, $CDCl_3$) 161.9 (C=O), 140.2 (C), 135.2 (CH), 128.7 (C), 128.4 (C), 128.2 (CH), 114.1 (C), 107.5 (CH), 84.6 (2 × C), 61.3 (CH_2), 25.1 (4 × Me), 14.5 (Me), 1 × C not observed; HRMS: [ESI, $(M + Na)^+$] found 416.0647. $[C_{17}H_{21}B^{79}BrNO_4 + Na]^+$ requires 416.0642.

Ethyl 5-Bromo-7-hydroxyindole-2-carboxylate (16B). General procedure B2 was performed using **16A** (150 mg, 0.38 mmol), H_2O_2



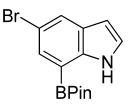
(0.4 mL), and NaOH (1 M, 0.4 mL) in THF (12 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (97 mg, 0.34 mmol, 90%) as a colorless solid, mp 205−207 °C; ν_{max} (neat)/cm^{-1} 3374, 3341, 2930, 1667, 1531, 1403, 1383, 1351, 1290, 1231, 1195, 1171, 1009, 885, 836, 766, 736; δ_H (400 MHz, acetone-d_6) 10.81 (1 H, br s, NH), 9.12 (1 H, br s, OH), 7.37 (1 H, d, *J* 1.7, ArH), 7.12 (1 H, s, ArH), 6.86 (1 H, d, *J* 1.7, ArH), 4.36 (2 H, q, *J* 7.1, CH_2), 1.37 (3 H, t, *J* 7.12, Me); δ_C (100 MHz, acetone-d_6) 161.8 (C=O), 145.6 (C), 131.1 (C), 129.7 (C), 116.6 (CH), 113.9 (C), 112.4 (CH), 108.5 (CH), 61.4 (CH_2), 14.6 (Me), 1 × C not observed; HRMS: [ESI, $(M + H)^+$] found 283.9920. $[C_{11}H_{10}{}^{79}BrNO_3 + H]^+$ requires 283.9917.

Ethyl 5-Bromoindole-4,7-dione-2-carboxylate (16C). General procedure C was performed using **16B** (60 mg, 0.21 mmol) and



salcomine (12 mol %, 8 mg) in acetonitrile (8 mL). Purification using 3:1 petroleum ether−ethyl acetate as eluent gave the title compound (20 mg 0.07 mmol, 33%) as a yellow solid, mp 155 °C (decomp); ν_{max}/cm^{-1} 3205, 3119, 2930, 1698, 1669, 1546, 1273, 1194, 1010, 876, 796, 783, 764; δ_H (300 MHz, $CDCl_3$) 10.37 (1 H, br s, NH), 7.30 (1 H, d, *J* 2.2, ArH), 7.24 (1 H, s, ArH), 4.43 (2 H, q, *J* 7.1, CH_2), 1.41 (3 H, t, *J* 7.1, Me); δ_C (75 MHz, $CDCl_3$) 175.2 (C=O), 174.3 (C=O), 160.2 (C=O), 141.1 (C), 137.8 (CH), 132.5 (C), 128.9 (C), 124.3 (C), 113.7 (CH), 62.3 (CH_2), 14.4 (Me); HRMS [ESI, $(M + Na)^+$] found 319.9531. $[C_{11}H_8{}^{79}BrNO_4 + Na]^+$ requires 319.9529.

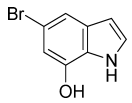
5-Bromo-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole (17A). General procedure A2 was performed using 5-



bromoindole (98 mg, 0.5 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (1 mol %, 3 mg), diethylsilane (1.5 equiv, 66 mg), $[Ir(OMe)cod]_2$ (10 mg, 0.015 mmol, 6 mol %), d^{t}bpy (8 mg, 0.03 mmol, 12 mol %), and B_2Pin_2 (1.5 equiv, 190 mg) to give the title compound (27 mg, 0.09 mmol, 17%) as a colorless oil; δ_H (400 MHz, $CDCl_3$) 9.23 (1 H, br s, NH), 7.87 (1 H, d, *J* 2.4, ArH), 7.73 (1 H, d, *J* 2.0, ArH), 7.27 (1 H, m, ArH, partially obscured by $CHCl_3$ peak), 6.49 (1 H, dd, *J* 2.4, 2.0, ArH), 1.39 (12 H, s, 4 × Me). ^{1}H spectrum was in agreement with that reported in the literature.[15c]

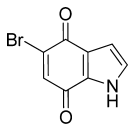
5-Bromo-7-hydroxyindole (17B). General procedure B1 was performed using **17A** (10 mg, 0.031 mmol) and H_2O_2 (0.2 mL) in THF (2 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (5 mg, 0.024 mmol, 76%) as a red oil, ν_{max}

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX



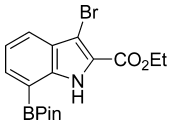
(neat)/cm^{-1} 3408, 2925, 1693, 1634, 1574, 1466, 1417, 1355, 1299, 1235, 1051, 868, 823, 764, 727; δ_H (400 MHz, acetone-d_6) 10.34 (1 H, br s, NH), 9.02 (1 H, br s, OH), 7.31 (1 H, t, J 2.8, ArH), 7.25 (1 H, d, J 1.6, ArH), 6.73 (1 H, d, J 1.6, ArH), 6.41 (1 H, dd, J 2.8, 1.6, ArH); δ_C (100 MHz, acetone-d_6) 145.1 (C), 132.1 (C), 126.5 (CH), 126.2 (C), 115.2 (CH), 112.5 (C), 109.5 (CH), 102.5 (CH); HRMS [ESI, (M − H)$^+$] found 209.9566. [C_8H_6BrNO − H]$^+$ requires 209.9560.

5-Bromoindole-4,7-dione (17C). General procedure C was performed using **17B** (5 mg, 0.024 mmol) and salcomine (12 mol



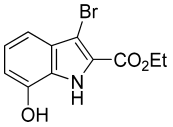
%, 0.9 mg) in acetonitrile (2 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (3.6 mg, 0.016 mmol, 67%) as an orange solid, mp 178 °C (decomp); ν_{max} (neat)/cm^{-1} 3238, 2923, 1645, 1570, 1489, 1380, 1248, 1194, 1105, 1017, 878, 806, 757, 664, 598; δ_H (400 MHz, DMSO-d_6) 12.92 (1 H, br s, NH), 7.30 (1 H, s, ArH), 7.28 (1 H, d, J 2.6, ArH), 6.65 (1 H, d, J 2.6, ArH); δ_C (100 MHz, DMSO-d_6) 174.9 (C═O), 174.5 (C═O), 138.2 (C), 137.6 (CH), 130.7 (C), 127.0 (CH), 123.7 (C), 108.9 (CH); HRMS [ESI, (M − H)$^+$] found 223.9358. [$C_8H_4{}^{79}BrNO_2$ − H]$^+$ requires 223.9353.

Ethyl 3-Bromo-7-(4,4,5,5−tetramethyl-1,3,2-dioxaborolan-2-yl)indole-2-carboxylate (18A). General procedure A1 was



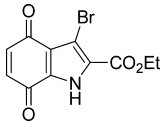
performed using ethyl 3-bromoindole-2-carboxylate (100 mg, 0.37 mmol), [Ir(OMe)cod]$_2$ (7.4 mg, 0.01 mmol, 3 mol %), d^{t}bpy (6.0 mg, 0.02 mmol, 6 mol %), and B_2Pin_2 (1.1 equiv, 104 mg) in THF (1.5 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (70 mg, 0.18 mmol, 52%) as a colorless solid, mp 142−146 °C; ν_{max} (neat)/cm^{-1} 3430, 2978, 2918, 2850, 2363, 1701, 1593, 1523, 1367, 1292, 1247, 1145, 1132, 858, 754, 677; δ_H (500 MHz, $CDCl_3$) 9.82 (1 H, br s, NH), 7.82 (1 H, d, J 7.2, ArH), 7.78 (1 H, d, J 7.5, ArH), 7.24 (1 H, dd, J 8.0, 6.9, ArH), 4.47 (2 H, q, J 7.1, CH_2), 1.47 (3 H, t, J 7.2, Me), 1.41 (12 H, s, 4 × BPin Me); δ_C (125 MHz, $CDCl_3$) 161.2 (C═O), 140.2 (C), 134.1 (CH), 127.1 (C), 124.8 (CH), 124.2 (C), 121.2 (CH), 97.8 (C), 84.3 (2 × C), 61.4 (CH_2), 25.1 (4 × Me), 14.4 (Me), 1 × C not observed; HRMS [ESI, (M + H)$^+$] found 394.0826. [$C_{17}H_{21}B^{79}BrNO_4$ + H]$^+$ requires 394.0823.

Ethyl 3-Bromo-7-hydroxyindole-2-carboxylate (18B). General procedure B2 was performed using **18A** (82 mg, 0.31 mmol), H_2O_2



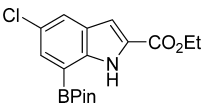
(0.3 mL), and NaOH (1 M, 0.3 mL) in THF (10 mL). Purification using 2:1 *n*-hexane−ethyl acetate gave the title compound (25 mg, 0.09 mmol, 28%) as a colorless solid, mp 187−192 °C; ν_{max} (neat)/cm^{-1} 3363, 3332, 2986, 2940, 1650, 1525, 1381, 1299, 1234, 1219, 1262, 1026, 782; δ_H (500 MHz, acetone-d_6) 10.84 (1 H, br s, NH), 8.91 (1 H, br s, OH), 7.11 (1 H, d, J 8.1, ArH), 7.05 (1 H, t, J 7.7, ArH), 6.81 (1 H, dd, J 7.2, 1.2, ArH), 4.40 (2 H, q, J 7.3, CH_2), 1.40 (3 H, t, J 7.2, Me); δ_C (125 MHz, acetone-d_6) 160.9 (C═O), 144.8 (C), 130.4 (C), 127.5 (C), 125.2 (C), 122.9 (CH), 112.4 (CH), 110.4 (CH), 97.9 (C), 61.6 (CH_2), 14.6 (Me); HRMS [ESI, (M + Na)$^+$] found 305.9726. [$C_{11}H_{10}{}^{79}BrNO_3$ + Na]$^+$ requires 305.9736.

Ethyl 3-Bromoindole-4,7-dione-2-carboxylate (18C). General procedure C was performed using **18B** (5.0 mg, 0.018 mmol) and



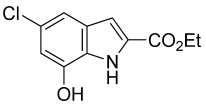
salcomine (12 mol %, 0.7 mg) in acetonitrile (1 mL). Purification using 3:2 *n*-hexane−ethyl acetate gave the title compound (4.1 mg, 0.014 mmol 78%), mp >300 °C; ν_{max} (neat)/cm^{-1} 3239, 2923, 2853, 1689, 1666, 1591, 1532, 1488, 1464, 1434, 1366, 1296, 1216, 1078, 1045, 1020, 1009, 847, 760, 671; δ_H (400 MHz, $CDCl_3$) 10.11 (1 H, br s, NH), 6.74 (2 H, q, J 10.2, ArH), 4.45 (2 H, q, J 7.2, CH_2), 1.44 (3 H, t, J 7.2, Me); δ_C (75 MHz, DMSO-d_6) 181.9 (C═O), 177.6 (C═O), 168.6 (C═O), 162.3 (C), 159.5 (C), 156.0 (C), 139.2 (CH), 136.9 (CH), 118.1 (C), 61.5 (CH_2), 14.5 (Me); HRMS [ESI, (M + Na)$^+$] found 319.9517. [$C_{11}H_8{}^{79}BrNO_4$ + Na]$^+$ requires 319.9529.

Ethyl 5-Chloro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole-2-carboxylate (19A). General procedure A1 was



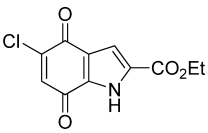
performed using ethyl 5-chloroindole-2-carboxylate (150 mg, 0.67 mmol), [Ir(OMe)cod]$_2$ (13 mg, 0.02 mmol, 3 mol %), d^{t}bpy (11 mg, 0.04 mmol, 6 mol %), and B_2Pin_2 (1.5 equiv, 256 mg) in THF (2 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (120 mg, 0.34 mmol, 51%) as a colorless solid, mp 91−95 °C; ν_{max} (neat)/cm^{-1} 3450, 2919, 2850, 1709, 1538, 1418, 1362, 1298, 1232, 1179, 1139, 864, 849, 745; δ_H (500 MHz, $CDCl_3$) 9.67 (1 H, br s, NH), 7.74 (1 H, d, J 2.0, ArH), 7.72 (1 H, d, J 2.0, ArH), 7.12 (1 H, d, J 2.1, ArH), 4.42 (2 H, q, J 7.1, CH_2), 1.42 (3 H, t, J 7.1, Me), 1.40 (12 H, s, 4 × Me); δ_C (125 MHz, $CDCl_3$) 161.8 (C═O), 139.9 (C), 132.7 (CH), 128.8 (C), 127.7 (C), 126.4 (C), 125.0 (CH), 107.5 (CH), 84.6 (2 × C), 61.2 (CH_2), 25.0 (4 × Me), 14.4 (Me), 1 × C not observed; HRMS [ESI, (M + H)$^+$] found 350.1341. [$C_{17}H_{21}B^{35}ClNO_4$ + H]$^+$ requires 350.1328.

Ethyl 5-Chloro-7-hydroxyindole-2-carboxylate (19B). General procedure B2 was performed using **19A** (120 mg, 0.34 mmol), H_2O_2



(0.3 mL), and NaOH (1 M, 0.3 mL) in THF (12 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (60 mg, 0.25 mmol, 74%) as a colorless solid, mp 202−204 °C; ν_{max} (neat)/cm^{-1} 3341, 2922, 1670, 1586, 1533, 1403, 1384, 1353, 1290, 1234, 1196, 901, 836, 767, 736; δ_H (400 MHz, acetone-d_6) 10.76 (1 H, s, NH or OH), 9.13 (1 H, s, NH or OH), 7.21 (1 H, d, J 1.6, ArH), 7.12 (1 H, s, ArH), 6.74 (1 H, d, J 1.9, ArH), 4.36 (2 H, q, J 7.1, CH_2), 1.36 (3 H, t, J 7.1, Me); δ_C (100 MHz, acetone-d_6) 161.8 (C═O), 145.4 (C), 130.4 (C), 129.8 (C), 127.5 (C), 126.6 (C), 113.4 (CH), 109.9 (CH), 108.7 (CH), 61.4 (CH_2), 14.6 (Me); HRMS [ESI, (M + H)$^+$] found 240.0419. [$C_{11}H_{10}{}^{35}ClNO_3$ + H]$^+$ requires 240.0422.

Ethyl 5-Chloroindole-4,7-dione-2-carboxylate (19C). General procedure C was performed using **19B** (50 mg, 0.20 mmol) and

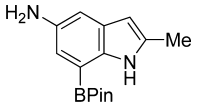


salcomine (12 mol %, 8 mg) in acetonitrile (8 mL) for 16 h. Purification was performed using 4:1 *n*-hexane−ethyl acetate to give

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

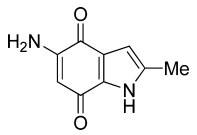
the title compound (13 mg, 0.05 mmol, 25%) as a yellow solid, mp 201−203 °C; ν_{max} (neat)/cm^{-1}: 3209, 3129, 2979, 2934, 1698, 1675, 1581, 1546, 1298, 1276, 1196, 1040, 1013, 876, 853, 795, 782, 763; δ_H (400 MHz, $CDCl_3$) 10.03 (1 H, br s, NH), 7.30 (1 H, s, ArH), 6.95 (1 H, s, ArH), 4.43 (2 H, q, *J* 7.1, CH_2), 1.41 (3 H, t, *J* 7.2, Me); δ_C (100 MHz, $CDCl_3$) 175.4 (C═O), 174.3 (C═O), 160.1 (C═O), 147.1 (C), 133.4 (CH), 132.5 (C), 129.0 (C), 124.7 (C), 113.4 (CH), 62.3 (CH_2), 14.4 (Me); HRMS: [ESI, (M + H)$^+$] found 254.0217. [$C_{11}H_8{}^{35}ClNO_4$ + H]$^+$ requires 254.0215

5-Amino-2-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole (20A). General procedure A1 was performed using 5-



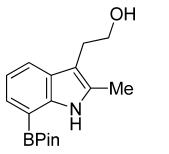
amino-2-methylindole[25] (100 mg, 0.68 mmol) [Ir(OMe)cod]$_2$ (14 mg, 0.02 mmol, 3 mol %), d^{t}bpy (11 mg, 0.04 mmol, 6 mol %), and B_2Pin_2 (1.1 equiv, 191 mg) in THF (1.5 mL total). Purification using 1:2 *n*-hexane−ethyl acetate as eluent gave the title compound (69 mg, 0.25 mmol, 37%) as a brown oil which was used immediately in the next step due to stability issues, δ_H (500 MHz, $CDCl_3$) 8.60 (1 H, br s, NH), 7.00 (1 H, d, *J* 2.3, ArH), 6.95 (1 H, d, *J* 2.2, ArH), 6.03 (1 H, q, *J* 1.1, ArH), 2.43 (3 H, d, *J* 0.7, Me), 1.37 (12 H, s, 4 × Me); δ_C (125 MHz, $CDCl_3$) 138.6 (C), 136.6 (C), 135.6 (C), 129.1 (C), 117.9 (CH), 109.3 (CH), 99.0 (CH), 83.8 (C), 25.0 (4 × Me), 14.0 (Me), 1 × C not observed.

5-Amino-2-methylindole-4,7-dione (20C). General procedure B2 was performed using **20A** (69 mg, 0.25 mmol), H_2O_2 (0.25 mL),



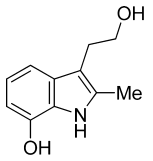
and NaOH (1 M, 0.25 mL) in THF (20 mL) gave a ∼1:1 mixture of 5-amino-7-hydroxyindole and the indolequinone which all oxidized to the latter during the purification process. Purification using 1:1 *n*-hexane−ethyl acetate gave the title compound (30 mg, 0.17 mmol, 68%) as a dark green solid, mp 198 °C (decomp); ν_{max} (neat)/cm^{-1}: 3271, 2921, 2852, 1666, 1625, 1589, 1568, 1498, 1446, 1388, 1248, 1223, 1174, 1103, 1070, 1039, 997, 973, 822, 781, 754, 712, 676; δ_H (500 MHz, DMSO-d_6) 12.08 (1 H, br s, NH), 6.91 (2 H, br s, NH_2), 6.13 (1 H, s, ArH), 5.22 (1 H, d, *J* 1.0, ArH), 2.18 (3 H, s, Me); δ_C (125 MHz, DMSO-d_6) 178.4 (C═O), 177.2 (C═O), 151.1 (C), 133.7 (C), 133.3 (C), 121.1 (C), 104.6 (CH), 96.8 (CH), 12.3 (Me); HRMS [ESI, (M + H)$^+$] found 177.0660. [$C_9H_8N_2O_2$ + H]$^+$ requires 177.0659.

2-Methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-tryptophol (21A). General procedure A1 was performed using 2-



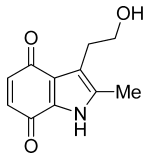
methyltryptophol[26] (179 mg, 1.02 mmol), [Ir(OMe)cod]$_2$ (20 mg, 0.03 mmol, 3 mol %), d^{t}bpy (16 mg, 0.06 mmol, 6 mol %), and B_2Pin_2 (1.5 equiv, 389 mg) in THF (2 mL total). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (141 mg, 0.47 mmol, 46%) as a colorless oil; ν_{max} (neat)/cm^{-1} 3450, 2977, 2930, 1370, 1327, 1271, 1140, 1124, 1044; δ_H (300 MHz, $CDCl_3$) 8.81 (1 H, br s, NH), 7.63 (1 H, d, *J* 7.8, ArH), 7.58 (1 H, dd, *J* 7.1, 0.8, ArH), 7.09 (1 H, t, *J* 7.5, ArH), 3.83 (2 H, q, *J* 6.3, CH_2), 2.99 (2 H, t, *J* 6.4, CH_2), 2.46 (3 H, s, Me), 1.40 (12 H, s, 4 × BPin Me), OH not observed; δ_C (75 MHz, $CDCl_3$) 140.8 (C), 132.6 (C), 128.6 (CH), 127.8 (C), 121.6 (CH), 119.0 (CH), 107.1 (C), 83.9 (2 × C), 63.1 (CH_2), 27.8 (CH_2), 25.1 (4 × Me), 12.0 (Me), 1 × C not observed; HRMS [ESI, (M + Na)$^+$] found 324.1745. [$C_{17}H_{24}BNO_3$ + Na]$^+$ requires 324.1744.

2-Methyl-7-hydroxytryptophol (21B). General procedure B2 was performed using **21A** (78 mg, 0.26 mmol), H_2O_2 (0.26 mL), and



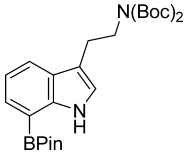
NaOH (1 M, 0.26 mL) in THF (5 mL). Product was filtered through a plug of silica using 1:1 *n*-hexane−ethyl acetate to give the title compound (21 mg, 0.11 mmol, 42%) as a brown oil which was used immediately in the next step due to stability issues.

3-(2-Hydroxyethyl)-2-methylindole-4,7-dione (21C). General procedure C was performed using **21B** (8 mg, 0.042 mmol) and



salcomine (12 mol %, 1.6 mg) in acetonitrile (1 mL). Purification using 1:1 *n*-hexane−ethyl acetate gave the title compound (3 mg, 0.015 mmol, 35%) as a red solid, mp 175 °C (decomp); ν_{max} (neat)/cm^{-1} 3445, 3196, 3126, 3035, 2923, 2853, 1630, 1580, 1491, 1452, 1379, 1261, 1047, 853, 763; δ_H (500 MHz, acetone-d_6) 11.21 (1 H, br s, NH), 6.48 (2 H, q, *J* 10.4, ArH), 3.66 (2 H, t, *J* 6.3, CH_2), 2.89 (2 H, t, *J* 6.8, CH_2), 2.33 (3 H, s, Me), OH not observed; δ_C (75 MHz, DMSO-d_6) 184.8 (C═O), 176.2 (C═O), 137.7 (CH), 136.8 (CH), 136.1 (C), 129.1 (C), 123.3 (C), 119.8 (C), 61.2 (CH_2), 28.4 (CH_2), 11.0 (Me); HRMS [ESI, (M + Na)$^+$] found 228.0623. [$C_{11}H_{11}NO_3$+Na]$^+$ requires 228.60631.

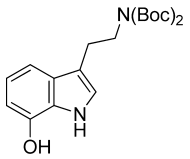
7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-*N*10-(di(*tert*-butoxycarbonyl))tryptamine (22A). General procedure A3 was



performed using *N*10-(di(*tert*-butoxycarbonyl))tryptamine[27] (360 mg, 1.0 mmol), triethylamine (152 mg, 1.5 mmol), and dimethylchlorosilane (142 mg, 1.5 mmol) in THF (3 mL) for 22 h followed by addition of [Ir(OMe)cod]$_2$ (20 mg, 0.03 mmol, 3 mol %), d^{t}bpy (16 mg, 0.06 mmol, 6 mol %) in THF (2 mL), and B_2Pin_2 (1.5 equiv, 380 mg) and the resulting mixture heated to 85 °C for 19 h. Desilylation was performed using sodium acetate for 2 h. Purification using 2:1 *n*-hexane−ethyl acetate as eluent gave the title compound (176.0 mg, 0.362 mmol, 35%) as a brown oil, ν_{max} (neat)/cm^{-1} 3460, 3360, 2981, 1735, 1692, 1345, 1328, 1129, 1110, 753, 684; δ_H (400 MHz, $CDCl_3$) 9.04 (1 H, br s, NH), 7.80 (1 H, d, *J* 7.7, ArH), 7.64 (1 H, d, *J* 7.0, ArH), 7.13 (1 H, t, *J* 7.5, ArH), 7.07 (1 H, d, *J* 2.2, ArH), 3.84 (2 H, m, CH_2), 3.05 (2 H, m, CH_2), 1.47 (18 H, s, 6 × Me), 1.38 (12 H, s, 4 × Me); δ_C (100 MHz, $CDCl_3$) 152.7 (2 × C), 141.6 (C), 129.4 (CH), 126.6 (C), 122.6 (CH), 122.1 (CH), 119.0 (CH), 112.7 (C), 83.9 (2 × C), 82.2 (2 × C), 47.5 (CH_2), 28.2 (6 × Me), 25.1 (4 × Me + CH_2), 1 × C not observed; HRMS [ESI, (M + Na)$^+$] found 509.2786. [$C_{26}H_{39}BN_2O_6$ + Na]$^+$ requires 509.2798.

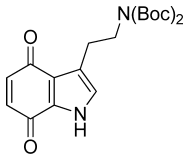
7-Hydroxy-*N*10-(di(*tert*-butoxycarbonyl))tryptamine (22B). General procedure B2 was performed using **22A** (55 mg, 0.11 mmol), H_2O_2 (0.03 mL), and NaOH (1 M, 0.03 mL) in THF (3 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (27 mg, 0.071 mmol, 64%) as a beige solid, mp 180−184 °C; ν_{max} (neat)/cm^{-1} 3379, 2976, 1764, 1586, 1367, 1133, 1092, 848, 731; δ_H (400 MHz, acetone-d_6) 9.84 (1 H, br s, NH), 8.36 (1 H, br s,

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX



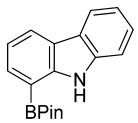
OH), 7.17 (1 H, d, *J* 7.9, ArH), 7.09 (1 H, s, ArH), 6.84 (1 H, t, *J* 7.7, ArH), 6.57 (1 H, dd, *J* 7.5, 0.8, ArH), 3.82 (2 H, m, CH_2), 2.98 (2 H, m, CH_2), 1.48 (18 H, s, 6 × Me); δ_C (100 MHz, $CDCl_3$/acetone-d_6) 152.4 (2 × C), 143.2 (C), 129.7 (C), 122.1 (CH), 119.4 (CH), 112.5 (C), 110.3 (CH), 106.0 (CH), 81.6 (2 × C), 47.1 (CH_2), 27.7 (6 × Me), 25.2 (CH_2); HRMS [ESI, (M + Na)$^+$] found 399.1875, [$C_{20}H_{28}N_2O_5$ + Na$^+$] requires 399.1890.

***N*10-(Di(*tert*-butoxycarbonyl))tryptamine-4,7-dione (22C).** General procedure C was performed using **22B** (6.0 mg, 0.016



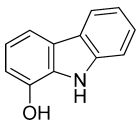
mmol) and salcomine (12 mol %, 0.6 mg) in acetonitrile (2 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (5.0 mg, 0.013 mmol, 80%) as a yellow solid, mp 129−132 °C; ν_{max} (neat)/cm^{-1} 3212, 2929, 1769, 1647, 1362, 1134, 1096, 1033, 850, 786; δ_H (400 MHz, $CDCl_3$) 9.13 (1 H, br s, NH), 6.86 (1 H, d, *J* 2.5, ArH), 6.58 (2 H, s, 2 × ArH), 3.88 (2 H, t, *J* 7.5, CH_2), 3.05 (2 H, t, *J* 7.5, CH_2), 1.46 (18 H, s, 6 × Me); δ_C (100 MHz, $CDCl_3$) 183.9 (2 × C═O), 177.3 (2 × C═O), 152.5 (C), 138.6 (CH), 135.7 (CH), 131.0 (C), 123.9 (CH), 123.5 (C), 123.1 (C), 82.2 (C), 45.9 (CH_2), 28.0 (6 × Me), 25.1 (CH_2); HRMS Found [M + Na]$^+$, 413.1678, [$C_{20}H_{26}N_2O_6$ + Na$^+$] requires 413.1683.

1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)carbazole (23A). General procedure A1 was performed using carbazole (84 mg,



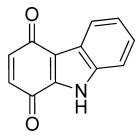
0.5 mmol), [Ir(OMe)cod]$_2$ (3 mol %, 10 mg), d^{t}bpy (6 mol %, 8 mg), and B_2Pin_2 (1.0 equiv, 130 mg) in THF (2.5 mL total) heating at 80 °C in a microwave[29] for 1 h. Purification using 2:1 *n*-hexane−ethyl acetate gave the title compound (50 mg, 0.17 mmol 34%), δ_H (400 MHz, $CDCl_3$) 9.20 (1 H, br s, NH), 8.23 (1 H, d, *J* 7.4, ArH), 8.12 (2 H, t, *J* 8.0, 2 × ArH), 7.91 (1 H, d, *J* 6.4, ArH), 7.55 (1 H, d, *J* 8.0, ArH), 7.47 (1 H, t, *J* 7.4, ArH), 7.28 (2 H, dd, *J* 13.6, 6.4, 2 × ArH), 1.47 (12 H, s, 4 × Me). The ^{1}H spectrum was in agreement with that reported in the literature.[15c]

Carbazol-1-ol (23B). General procedure B1 was performed using **23A** (25 mg, 0.085 mmol) and H_2O_2 (0.5 mL) in THF (5 mL).



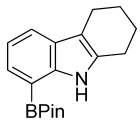
Purification using diethyl ether as eluent gave the title compound (12 mg, 0.065 mmol, 77%) as a colorless oil; δ_H (400 MHz, $CDCl_3$) 8.23 (1 H, br s, NH), 8.05 (1 H, d, *J* 7.8, ArH), 7.68 (1 H, d, *J* 7.8, ArH), 7.47−7.40 (2 H, m, 2 × ArH), 7.25−7.21 (1 H, m, ArH), 7.07 (1 H, t, *J* 7.8, ArH), 6.83 (1 H, d, *J* 7.8, ArH), 5.00 (1 H, br s, OH). The ^{1}H NMR spectrum was in agreement with that reported in the literature.[28]

Carbazole-1,4-dione (23C). General procedure C was performed using **24B** (14.2 mg, 0.071 mmol) and salcomine (12 mol %, 2.8 mg) in acetonitrile (5 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (11.2 mg, 0.057 mmol, 80%) as an orange solid, δ_H (400 MHz, acetone-d_6) 11.56 (1 H, br s, NH), 8.02 (1



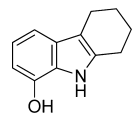
H, m, ArH), 7.53−7.51 (1 H, m, ArH), 7.33−7.21 (2 H, m, 2 × ArH), 6.60 (2 H, d, *J* 0.7, ArH). The ^{1}H NMR spectrum was in agreement with that reported in the literature.[28]

8-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3,4,9-tetrahydrocarbazole (24A). General procedure A1 was performed



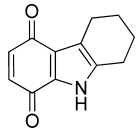
using 1,2,3,4-tetrahydrocarbazole (86 mg, 0.5 mmol), [Ir(OMe)cod]$_2$ (1.5 mol %, 5 mg), d^{t}bpy (3 mol %, 4 mg), and B_2Pin_2 (1.5 equiv, 190 mg) in THF (2.5 mL total) heating to 80 °C in a microwave[29] for 30 min. Purification using 4:1 *n*-hexane−ethyl acetate gave the title compound (105 mg, 0.35 mmol, 71%), δ_H (400 MHz, $CDCl_3$) 8.71 (1 H, br s, NH), 7.58 (2 H, t, *J* 6.3, ArH), 7.10 (1 H, t, *J* 7.6, ArH), 2.81 (2 H, t, *J* 5.6, CH_2), 2.73 (2 H, t, *J* 5.6, CH_2), 1.95−1.88 (4 H, m, 2 × CH_2), 1.41 (12 H, s, 4 × Me). The ^{1}H spectrum was in agreement with that reported in the literature.[29]

2,3,4,9-Tetrahydrocarbazol-8-ol (24B). General procedure B1 was performed using **24A** (50 mg, 0.168 mmol) and H_2O_2 (0.3 mL) in



THF (5 mL). Purification using diethyl ether as eluent gave the title compound (31 mg, 0.166 mmol, 98%) as a colorless oil, ν_{max} (neat)/cm^{-1} 3404, 2923, 2845, 1629, 1577, 1495, 1469, 1442, 1361, 1306, 1261, 1223, 1158, 1055, 939, 869, 821, 777, 732, 701; δ_H (400 MHz, DMSO-d_6) 10.32 (1 H, br s, NH), 9.21 (1 H, s, OH), 6.77 (1 H, d, *J* 7.6, ArH), 6.69 (1 H, t, *J* 7.6, ArH), 6.41 (1 H, dd, *J* 7.6, 0.8, ArH), 2.66 (2 H, t, *J* 5.2, CH_2), 2.56 (2 H, t, *J* 5.2, CH_2), 1.78 (4 H, m, 2 × CH_2); δ_C (100 MHz, DMSO-d_6) 142.8 (C), 133.7 (C), 129.2 (C), 125.1 (C), 118.6 (CH), 108.5 (CH), 108.3 (C), 105.0 (CH), 23.0 (CH_2), 22.9 (CH_2), 22.8 (CH_2), 20.9 (CH_2); HRMS [ESI, (M + H)$^+$] found 188.1068. [$C_{12}H_{13}NO$ + H]$^+$ requires 188.1070.

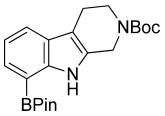
5,6,7,8-Tetrahydrocarbazole-1,4-dione (24C). General procedure C was performed using **24B** (26 mg, 0.086 mmol) and salcomine



(12 mol %, 3.4 mg) in acetonitrile (5 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (14.2 mg, 0.071 mmol, 82%) as an orange solid, mp 235 °C (decomp); ν_{max} (neat)/cm^{-1} 3200, 3105, 2927, 2854, 1740, 1641, 1579, 1558, 1516, 1479, 1459, 1428, 1373, 1271, 1242, 1186, 1150, 1136, 1071, 1055, 1029, 981, 958, 843, 788, 745; δ_H (400 MHz, DMSO-d_6) 12.35 (1 H, br s, NH), 6.56 (1 H, d, *J* 10.3, ArH), 6.48 (1 H, d, *J* 10.1, ArH), 2.63 (2 H, t, *J* 6.0, CH_2), 2.57 (2 H, t, *J* 5.6, CH_2), 1.76−1.67 (4 H, m, CH_2); δ_C (100 MHz, DMSO-d_6) 184.2 (C═O), 176.0 (C═O), 136.84 (CH), 136.82 (C), 136.6 (CH), 128.8 (C), 122.0 (C), 119.3 (C), 22.2 (CH_2), 22.1 (CH_2), 21.9 (2 × CH_2); HRMS [ESI, (M + H)$^+$] found 202.0867. [$C_{12}H_{11}NO_2$ + H]$^+$ requires 202.0863.

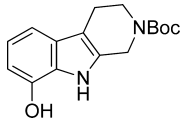
***tert*-Butyl 8-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydropyrido[3,4-*b*]indole-2-carboxylate (25A).** General procedure A1 was performed using *tert*-butyl 1,2,3,4-tetrahydropyrido-[3,4-*b*]indole-2-carboxylate (136 mg, 0.5 mmol), [Ir(OMe)cod]$_2$ (1.5 mol %, 5 mg), d^{t}bpy (3 mol %, 4 mg), and B_2Pin_2 (1.5 equiv, 190 mg)

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX



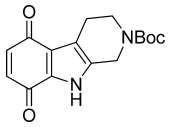
in THF (2.5 mL total) heating to 80 °C in a microwave[29] for 2 h. Purification using 4:1 *n*-hexane−ethyl acetate gave the title compound (153 mg, 0.385 mmol, 77%) as a colorless solid, mp 201−204 °C; ν_{max} (neat)/cm^{-1} 3446, 2978, 2930, 1735, 1688, 1615, 1594, 1492, 1466, 1379, 1347, 1323, 1304, 1259, 1237, 1212, 1144, 1127, 1099, 1045, 1020, 961, 916, 857, 753, 728; δ_H (400 MHz, $CDCl_3$) 8.80 (1 H, br s, NH), 7.61−7.58 (2 H, m, 2 × ArH), 7.10 (1 H, t, *J* 7.6, ArH), 4.68 (2 H, br s, CH_2), 3.77 (2 H, br s, CH_2), 2.80 (2 H, br s, CH_2), 1.50 (9 H, s, 3 × Me), 1.39 (12 H, s, 4 × Me); δ_C (100 MHz, $CDCl_3$) 155.2 (C═O), 141.4 (CH), 130.7 + 130.3 (C), 128.9 (C), 125.9 (C), 121.5 (CH), 119.0 (CH), 109.9 (C), 108.7 + 108.2 (C), 83.9 (2 × C), 79.9 (C), 42.7 + 42.4 (CH_2), 41.8 + 41.4 (CH_2), 28.5 (3 × Me), 25.0 (4 × Me), 21.2 + 21.0 (CH_2); HRMS [ESI, (M + Na)$^+$] found 421.2255. [$C_{22}H_{31}BN_2O_4$ + Na]$^+$ requires 421.2273.

***tert*-Butyl 8-Hydroxyl-3,4-dihydropyrido[3,4-*b*]indole-2-carboxylate (25B).** General procedure B1 was performed using **25A** (70



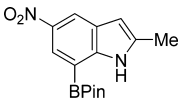
mg, 0.176 mmol) and H_2O_2 (0.3 mL) in THF (5 mL). Flash column chromatography using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (44 mg, 0.152 mmol, 87%) as a colorless oil; ν_{max} (neat)/cm^{-1} 3412, 3340, 2981, 2932, 2849, 1642, 1631, 1582, 1480, 1422, 1386, 1372, 1311, 1280, 1246, 1218, 1198, 1152, 1115, 1069, 1049, 981, 927, 875, 845, 813, 775, 682; δ_H (400 MHz, DMSO-d_6) 10.61 (1 H, br s, NH), 9.41 (1 H, s, OH), 6.84 (1 H, d, *J* 7.6, ArH), 6.75 (1 H, t, *J* 7.6, ArH), 6.48 (1 H, dd, *J* 7.6, 0.8, ArH), 4.53 (2 H, br s, CH_2), 3.66 (2 H, t, *J* 5.6, CH_2), 2.64 (2 H, t, *J* 5.6, CH_2), 1.44 (9 H, s, 3 × Me); δ_C (100 MHz, DMSO-d_6) 154.3 (C═O), 143.2 (C), 130.6 (C), 128.4 (C), 125.6 (C), 119.1 (CH), 108.7 (CH), 107.1 (C), 105.6 (CH), 79.0 (C), 42.3 + 42.1 (CH_2), 41.4 + 40.9 (CH_2), 28.1 (3 × Me), 21.2 (CH_2); HRMS [ESI, (M + Na)$^+$] found 311.1362. [$C_{16}H_{20}N_2O_3$ + Na]$^+$ requires 311.1366.

***tert*-Butyl 5,8-Dioxo-3,4,8,9-tetrahydropyrido[3,4-*b*]indole-2-carboxylate (25C).** General procedure C was performed using



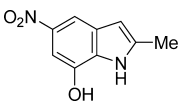
25B (22 mg, 0.076 mmol) and salcomine (12 mol %, 3 mg) in acetonitrile (5 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (16 mg, 0.053 mmol, 70%) as an orange solid, mp 247 °C (decomp); ν_{max} (neat)/cm^{-1} 3209, 2923, 1652, 1586, 1498, 1480, 1462, 1413, 1366, 1279, 1253, 1236, 1164, 1108, 1073, 1032, 976, 933, 874, 847, 785, 770; δ_H (400 MHz, DMSO-d_6) 12.53 (1 H, br s, NH), 6.60 (1 H, d, *J* 10.0, ArH), 6.54 (1 H, d, *J* 10.0, ArH), 4.45 (2 H, br s, CH_2), 3.57 (2 H, t, *J* 5.8, CH_2), 2.69 (2 H, t, *J* 5.8, CH_2), 1.43 (9 H, s, 3 × Me); δ_C (100 MHz, DMSO-d_6) 183.9 (C═O), 176.4 (C═O), 154.1 (C═O), 137.0 (CH), 136.5 (CH), 133.1 (C), 129.5 (C), 121.7 (C), 117.1 (C), 79.4 (C), 40.8 (CH_2), 29.0 (CH_2), 28.0 (3 × Me), 22.1 (CH_2); HRMS [ESI, (M + Na)$^+$] found 325.1155. [$C_{16}H_{18}N_2O_4$ + Na]$^+$ requires 325.1159.

2-Methyl-5-nitro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole (26A). General procedure A1 was performed using 2-



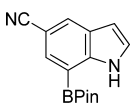
methyl-5-nitroindole (88 mg, 0.5 mmol), [Ir(OMe)cod]$_2$ (10 mg, 3 mol %), d^{t}bpy (8 mg, 6 mol %), and B_2Pin_2 (1.5 equiv, 190 mg) in THF (2.5 mL total) heating to 80 °C in a microwave[29] for 2 h. Purification using 3:2 *n*-hexane−ethyl acetate gave the title compound (55.9 mg, 0.185 mmol, 37%) as a crimson oil, ν_{max} (neat)/cm^{-1} 3438, 2981, 1592, 1561, 1520, 1468, 1373, 1312, 1268, 1204, 1185, 1138, 1072, 1009, 986, 963, 893, 851, 791, 752, 707, 691, 673; δ_H (400 MHz, $CDCl_3$) 9.15 (1 H, br s, NH), 8.48 (1 H, d, *J* 2.0, ArH), 8.45 (1 H, d, *J* 2.4, ArH), 6.34 (1 H, q, *J* 0.8, ArH), 2.51 (3 H, d, *J* 0.8, Me), 1.41 (12 H, s, 4 × Me); δ_C (100 MHz, $CDCl_3$) 144.3 (C), 141.5 (C), 138.8 (C), 127.8 (C), 123.7 (CH), 119.1 (CH), 102.1 (CH), 84.6 (2 × C), 82.9 (C), 25.0 (4 × Me), 14.0 (Me); HRMS [ESI, (M + Na)$^+$] found 325.1324, [$C_{15}H_{19}BN_2O_4$ + Na]$^+$ requires 325.1333.

2-Methyl-5-nitroindol-7-ol (26B). General procedure B1 was performed using **26A** (30 mg, 0.1 mmol) and H_2O_2 (0.3 mL) in THF



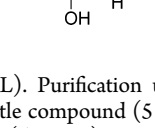
(5 mL). Purification using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (14 mg, 0.073 mmol, 73%) as an orange solid, mp 183−186 °C; ν_{max} (neat)/cm^{-1} 3377, 3307, 3088, 2922, 2852, 1708, 1639, 1573, 1520, 1471, 1386, 1315, 1271, 1244, 1232, 1146, 1102, 1078, 1067, 980, 950, 885, 868, 847, 817, 778, 737, 647; δ_H (400 MHz, DMSO-d_6) 11.62 (1 H, br s, NH), 10.49 (1 H, s, OH), 8.00 (1 H, d, *J* 2.0, ArH), 7.37 (1 H, d, *J* 2.0, ArH), 6.40 (1 H, m, ArH), 2.44 (3 H, s, Me); δ_C (100 MHz, DMSO-d_6) 142.6 (C), 140.8 (C), 138.8 (C), 129.6 (C), 128.6 (C), 108.1 (CH), 102.1 (CH), 99.2 (CH), 13.2 (Me); HRMS [ESI, (M + H)$^+$] found 193.0608. [$C_9H_8N_2O_3$ + H]$^+$ requires 193.0608.

5-Cyano-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole (27A). General procedure A3 was performed using 5-



cyanoindole (142 mg, 1.0 mmol), triethylamine (152 mg, 1.5 mmol), and dimethylchlorosilane (142 mg, 1.5 mmol) in THF (1 mL) for 6 h followed by addition of [Ir(OMe)cod]$_2$ (1.7 mg, 0.0025 mmol, 0.25 mol %), d^{t}bpy (1.4 mg, 0.005 mmol, 0.5 mol %), and B_2Pin_2 (1.05 equiv, 267 mg) in THF (1 mL) and the resulting mixture heated to 80 °C for 16 h. Desilylation was performed using sodium hydrogen carbonate for 1 h. Purification using 4:1 petroleum ether−ethyl acetate as eluent gave the title compound (29 mg, 0.11 mmol, 11%) as a colorless solid, mp 133−138 °C; ν_{max} (neat)/cm^{-1} 3348, 2982, 2223, 1372, 1301, 1207, 1137, 852, 739; δ_H (400 MHz, $CDCl_3$) 9.44 (1 H, br s, NH), 8.07 (1 H, dd, *J* 1.4, 0.5, ArH), 7.88 (1 H, d, *J* 1.6, ArH), 7.37 (1 H, dd, *J* 3.2, 2.4, ArH), 6.62 (1 H, dd, *J* 3.3, 2.1, ArH), 1.41 (12 H, s, 4 × BPin Me); δ_C (100 MHz, $CDCl_3$) 142.5 (C), 132.3 (CH), 129.0 (CH), 126.9 (C), 126.5 (CH), 120.8 (C), 103.1 (CH), 102.9 (C), 84.7 (2 × C), 25.1 (4 × Me), 1 × C not observed; HRMS [ESI, (M +Na)$^+$] found 291.1271. [$C_{15}H_{17}BN_2O_2$ + Na]$^+$ requires 291.1271.

5-Cyanoindol-7-ol (27B). General procedure B2 was performed using **27A** (20 mg, 0.075 mmol), H_2O_2 (0.08 mL), and NaOH (1 M,

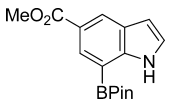


0.08 mL) in THF (2.5 mL). Purification using 4:1 *n*-hexane−ethyl acetate as eluent gave the title compound (5 mg, 0.032 mmol, 42%) as a brown solid, mp 173 °C (decomp); ν_{max} (neat)/cm^{-1} 3386, 3209, 2919, 2850, 2222, 1585, 1461, 1331, 1253, 1059, 824, 723; δ_H (400 MHz, acetone-d_6) 10.73 (1 H, br s, NH), 9.36 (1 H, br s, OH), 7.57 (1 H, d, *J* 0.8, ArH), 7.46 (1 H, d, *J* 3.2, ArH), 6.81 (1 H, d, *J* 0.9, ArH), 6.59 (1 H, d, *J* 3.1, ArH); δ_C (100 MHz, acetone-d_6) 144.8 (C), 130.7

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

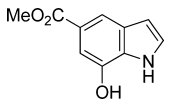
(C), 127.6 (CH), 121.2 (C), 119.1 (CH), 108.0 (CH), 103.9 (CH), 103.8 (C), 103.4 (C); HRMS [ESI, (M + H)$^+$] found 159.0551. [$C_9H_6N_2O$ + H]$^+$ requires 159.0553.

Methyl 7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-indole-5-carboxylate (28A). General procedure A2 was performed



using methyl indole-5-carboxylate (87 mg, 0.5 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (1 mol %, 3 mg), diethylsilane (1.5 equiv, 66 mg), [Ir(OMe)cod]$_2$ (10 mg, 0.015 mmol, 6 mol %), d^{t}bpy (8 mg, 0.03 mmol, 12 mol %), and B_2Pin_2 (1.5 equiv, 190 mg). Purification using 4:1 *n*-hexane−ethyl acetate as eluent to give the title compound (49.7 mg, 0.165 mmol, 33%) as a colorless solid, mp 140−144 °C; ν_{max} (neat)/cm^{-1} 3362, 2982, 1698, 1601, 1433, 1379, 1303, 1251, 1193, 1175, 1137, 1006, 974, 849, 774; δ_H (400 MHz, $CDCl_3$) 9.38 (1 H, br s, NH), 8.52 (1 H, d, *J* 1.4, ArH), 8.36 (1 H, d, *J* 1.4, ArH), 7.32 (1 H, t, *J* 2.8, ArH), 6.64 (1 H, dd, *J* 2.8, 2.0, ArH), 3.93 (3 H, s, OMe), 1.41 (12 H, s, 4 × Me); δ_C (100 MHz, $CDCl_3$) 167.2 (C), 142.4 (C), 131.3 (C), 129.7 (CH), 126.9 (C), 125.9 (CH), 124.5 (CH), 120.5 (C), 102.4 (CH), 83.1 (2 × C), 50.8 (Me), 24.0 (4 × Me); HRMS [ESI, (M + Na)$^+$] found 324.1376. [$C_{16}H_{20}BNO_4$ + Na]$^+$ requires 324.1380.

Methyl 7-Hydroxyindole-5-carboxylate (28B). General procedure B2 was performed using **28A** (20 mg, 0.066 mmol). Purification



using 1:1 *n*-hexane−ethyl acetate as eluent gave the title compound (10 mg, 0.052 mmol, 79%) as a colorless solid, mp 153.5−156.7 °C; ν_{max} (neat)/cm^{-1} 3402, 3376, 2951, 1690, 1634, 1589, 1460, 1437, 1368, 1335, 1292, 1241, 1224, 1201, 1093, 1051, 1002, 912, 877, 768, 718, 639; δ_H (400 MHz, acetone-d_6) 10.48 (1 H, br s, NH), 8.83 (1 H, br s, OH), 7.90 (1 H, d, *J* 1.2, ArH), 7.38 (1 H, t, *J* 2.4, ArH), 7.28 (1 H, d, *J* 1.6, ArH), 6.58 (1 H, dd, *J* 3.2, 2.0, ArH), 3.84 (3 H, s, Me); δ_C (100 MHz, acetone-d_6) δ 168.3 (C=O), 143.9 (C), 130.3 (C), 130.1 (C), 126.7 (CH), 123.1 (C), 116.3 (CH), 106.9 (CH), 104.2 (CH), 51.8 (Me); HRMS [ESI, (M + Na)$^+$] found 214.0476. [$C_{10}H_9NO_3$ + Na]$^+$ requires 214.0475.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all novel compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: j.sperry@auckland.ac.nz.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the Royal Society of New Zealand for support through the Marsden Fund (C.W. and J.S.) and the Rutherford Discovery Fellowship Scheme (A.S.E. and J.S.). The University of Auckland is thanked for the award of a Summer Research Scholarship (E.K.D.).

■ REFERENCES

(1) (a) Remers, W. A. *The Chemistry of Antitumour Antibiotics*; Wiley: New York, 1979. (b) Carter, S. K.; Crooke, S. T. *Mitomycin C: Current Status and New Developments*; Academic Press: New York, 1979. (c) Wolkenberg, S. E.; Boger, D. L. *Chem. Rev.* **2002**, *102*, 2477−2496. (d) Seow, H.; Penketh, P. G.; Baumann, R. P.; Sartorelli, A. C. *Methods Enzymol.* **2004**, *382*, 221−233. (e) Alcain, F. J.; Villalba, J. M. *Expert Opin. Ther. Pat.* **2007**, *17*, 649−665. (f) Andrez, J.-C. *Beil. J. Org. Chem.* **2009**, *5*, doi: 10.3762/bjoc.5.33. (g) Shelley, M. D.; Mason, M. D.; Kynaston, H. *Cancer Treat. Rev.* **2010**, *36*, 195−205.

(2) (a) Smitskamp-Wilms, E.; Hendriks, H. R.; Peters, G. J. *Gen. Pharm.* **1996**, *27*, 421−429. (b) Moody, C. J.; Swann, E. *Farmaco* **1997**, *52*, 271−279. (c) Jaffar, M.; Naylor, M. A.; Robertson, N.; Stratford, I. J. *Anti-Cancer Drug Des.* **1998**, *13*, 593−609. (d) Colucci, M. A.; Couch, G. D.; Moody, C. J. *Org. Biomol. Chem.* **2008**, *6*, 637−656.

(3) Phillips, R. M.; Hendriks, H. R.; Peters, G. J. *Br. J. Pharmacol.* **2013**, *168*, 11−18.

(4) Oka, H.; Yoshinari, T.; Murai, T.; Kuwamura, K.; Satoh, F.; Funaishi, K.; Okura, A.; Suda, H.; Okanishi, M.; Shizuri, Y. *J. Antibiot.* **1991**, *44*, 486−491.

(5) Li, X.; Lee, S. M.; Choi, H. D.; Kang, J. S.; Son, B. W. *Chem. Pharm. Bull.* **2003**, *51*, 1458−1459. (b) Wang, C.; Sperry, J. *Org. Lett.* **2011**, *13*, 6444−6447.

(6) Brastianos, H. C.; Vottero, E.; Patrick, B. O.; Van Soest, R.; Matainaho, T.; Mauk, A. G.; Andersen, R. J. *J. Am. Chem. Soc.* **2006**, *128*, 16046−16047.

(7) (a) Edsrtom, E. D. *Synlett* **1995**, 49−50. (b) Nobuhiro, J.; Hirayama, M.; Choshi, T.; Kamoshita, K.; Maruyama, S.; Sukenaga, Y.; Ishizu, T.; Fujioka, H.; Hibino, S. *Heterocycles* **2006**, *70*, 491−499. (c) Liebeskind, L. S.; Iyer, S.; Newell, C. F. *J. Org. Chem.* **1986**, *51*, 3065−3067. (d) Moore, H. W.; Perri, S. T. *J. Org. Chem.* **1988**, *53*, 996−1003.

(8) (a) Nakatsubo, F.; Cocuzza, A. J.; Keeley, D. E.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 4835−4836. (b) Cotterill, A. S.; Moody, C. J.; Roffey, J. R. A. *Tetrahedron* **1995**, *26*, 7223−7230. (c) Wang, Z.; Jimenez, L. S. *J. Org. Chem.* **1996**, *61*, 816−818. (d) Catrycke, M.-C.; Houssin, R.; Hénichart, J.-P.; Pfeiffer, B.; Renard, P.; Dassonneville, L.; Bailly, C. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2025−2030. (e) Colucci, M. A.; Reigan, P.; Siegel, D.; Chilloux, A.; Ross, D.; Moody, C. J. *J. Med. Chem.* **2007**, *50*, 5780−5789.

(9) (a) Acylaminoquinone tosylhydrazones: Akiba, M.; Kosugi, Y.; Takada, T. *J. Org. Chem.* **1978**, *43*, 4472−4475. (b) Nitroquinones: Parker, K. A.; Sworin, M. *Tetrahedron Lett.* **1978**, *26*, 2251−2254. (c) Azidoquinones: Kozuka, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2922−2927. (d) Aminoquinones: Tanaka, K.; Takanohashi, A.; Morikawa, O.; Konishi, H.; Kobayashi, K. *Heterocycles* **2001**, *55*, 1561−1568. (e) Weider, P. R.; Hegedus, L. S.; Asada, H.; D'Andreq, V. *J. Org. Chem.* **1985**, *50*, 4276−4281. (f) Wu, Y.-L.; Chuang, C.-P.; Lin, P.-Y. *Tetrahedron* **2001**, *57*, 5542−5549. (g) Chuang, C.-P.; Tsai, A.-I. *Tetrahedron* **2007**, *63*, 11911−11919. Bromoquinones: (h) Luly, J. R.; Rapoport, H. *J. Am. Chem. Soc.* **1983**, *105*, 2859−2866. (i) Hegedus, L. S.; Mulhern, T. A.; Mori, A. *J. Org. Chem.* **1985**, *50*, 4282−4288. (j) Comer, E.; Murphy, W. S. *ARKIVOC* **2003**, *vii*, 286−296. (k) Inman, M.; Moody, C. J. *Eur. J. Org. Chem.* **2013**, 2179−2187. (l) Iodoquinones: Chakraborty, M.; McConville, D. B.; Niu, Y.; Tessier, C. A.; Youngs, W. J. *J. Org. Chem.* **1998**, *63*, 7563−7567.

(10) For synthetic routes not covered by routes A and B in Scheme 1 (refs 8 and 9), see: (a) Saá, J. M.; Marti, C.; Raso-García, A. *J. Org. Chem.* **1992**, *57*, 589−594. (b) Vedejs, E.; Monahan, S. D. *J. Org. Chem.* **1997**, *62*, 4763−4769. (c) Parker, K. A.; Kang, S.-K. *J. Org. Chem.* **1979**, *44*, 1537−1540. Bauta, W. E.; Wulff, W. D.; Pavkovic, S. F.; Zuluzec, E. J. *J. Org. Chem.* **1989**, *54*, 3249−3252. (d) Visconti, A.; Moody, C. J. *Heterocycles* **2014**, *88*, 705−710.

(11) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608−9644.

(12) (a) Nitration−reduction: Natasuka, S.-I.; Ueda, K.; Asano, O.; Goto, T. *Heterocycles* **1987**, *26*, 65−68. (b) Hydroxyindole oxidation and then Thiele−Winter acetoxylation or reductive alkylation: Allen, G. R., Jr.; Poletto, J. F.; Weiss, M. J. *J. Am. Chem. Soc.* **1964**, *86*, 3877−3878. (c) Kametani, T.; Takahashi, K.; Ihara, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1976**, 389−393. Dakin oxidation: (d) Alamgir, M.; Mitchell, P. S. R.; Bowyer, P. K.; Kumar, N.; Black, D. S. *Tetrahedron* **2008**, *64*, 7136−7142.

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX

(13) (a) Tatsuta, K.; Imamura, K.; Itoh, S.; Kasai, S. *Tetrahedron Lett.* **2004**, *45*, 2847−2850. (b) Carr, G.; Chung, M. K. W.; Mauk, A. G.; Andersen, R. J. *J. Med. Chem.* **2008**, *51*, 2634−2637.
(14) Nicolaou, K. C.; Sugita, K.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2002**, *124*, 2221−2232.
(15) (a) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 3056−3058. (b) Sulanga, P.; Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E., Jr.; Smith, M. R., III. *J. Am. Chem. Soc.* **2006**, *128*, 15552−15553. (c) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 4068−4069. (d) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890−931. (e) Hartwig, J. F. *Chem. Soc. Rev.* **2011**, *40*, 1992−2002. (f) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864−873.
(16) (a) Wang, C.; Sperry, J. *J. Org. Chem.* **2012**, *77*, 2584−2587. (b) Fukuyama, Y.; Iwatsuki, C.; Kodama, M.; Ochi, M.; Kataoka, K.; Shibata, K. *Tetrahedron* **1998**, *54*, 10007−10016.
(17) (a) Antunes, E. M.; Copp, B. R.; Davies-Coleman, M. T.; Samaai, T. *Nat. Prod. Rep.* **2005**, *22*, 62−72. (b) Hu, J.-F.; Fan, H.; Wu, S.-B. *Chem. Rev.* **2011**, *111*, 5465−5491.
(18) Carbazole can be regioselectively oxygenated in the 1-position (40%) by lithiation of its 9-(1-pyrrolidinomethyl) derivative followed by quenching with bis(trimethylsilyl) peroxide: Katritzky, A. R.; Rewcastle, G. W.; de Miguel, L. M. V. *J. Org. Chem.* **1988**, *53*, 794−799.
(19) (a) Moody, C. J. *Synlett* **1994**, 681−688. (b) Knolker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303−4427. (c) Saha, C.; Chowdhury, B. K. *Phytochemistry* **1998**, *48*, 363.
(20) The iridium-catalyzed borylation of a similar tetrahydro-β-carboline has been reported: Meyer, F.-M.; Liras, S.; Guzman-Perez, A.; Perreault, C.; Bian, J.; James, K. *Org. Lett.* **2010**, *12*, 3870−3873.
(21) For discussions regarding the synthesis of 7-hydroxyindole, see: (a) Harada, H.; Fujii, A.; Kato, S. *Synth. Commun.* **2003**, *33*, 507−514. (b) Sugimori, D.; Sekiguchi, T.; Hasumi, F.; Kubo, M.; Shirasaka, N.; Ikunaka, M. *Biosci. Biotechnol. Biochem.* **2004**, *68*, 1167−1169. (c) Lerman, L.; Weinstock-Rosin, M.; Nudelman, A. *Synthesis* **2004**, *18*, 3043−3046. (d) Ishiyama, K.; Yamada, Y. *Tetrahedron Lett.* **2005**, *46*, 1021−1022 and references therein..
(22) For a variety of routes to more complex 7-hydroxyindoles: Bartoli: (a) Dobson, D.; Todd, A.; Gilmore, J. *Synth. Commun.* **1991**, *21*, 611−617. (b) Dalpozzo, R.; Bartoli, G. *Curr. Org. Chem.* **2005**, *9*, 163−178. Madelung: (c) Akao, A.; Sato, K.; Nonoyama, N.; Mase, T.; Yasuda, N. *Tetrahedron Lett.* **2006**, *47*, 969−972. Heck: (d) Charrier, N.; Demont, E.; Dunsdon, R.; Maile, G.; Naylor, A.; O'Brien, A.; Redshaw, S.; Theobald, P.; Vesey, D.; Walter, D. *Synlett* **2005**, 3071−3074. (e) Charrier, N.; Demont, E.; Dunsdon, R.; Maile, G.; Naylor, A.; O'Brien, A.; Redshaw, S.; Theobald, P.; Vesey, D.; Walter, D. *Synthesis* **2006**, 3467−3477. Reductive heteroannulation: (f) Cho, C. S.; Kim, T. K.; Yoon, S. W.; Kim, T.-J.; Shim, S. C. *Bull. Korean Chem. Soc.* **2001**, *22*, 545−546. Oxidative cleavage/cyclization of dihydronaphthalenes: (g) Ganton, M. D.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 574−582. (h) Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2008**, *10*, 997−1000.
(23) For the synthesis of a 7-hydroxyindole from the corresponding indole by directed metalation, see: Hartung, C. G.; Fecher, A.; Chapell, B.; Snieckus, V. *Org. Lett.* **2003**, *5*, 1899−1902.
(24) During the final stages of preparing this manuscript for submission, Movassaghi and co-workers reported a procedure for the C7-selective borylation of tryptophans, tryptamines, and 3-alkylindoles using a one-pot C2/C7-diboronation−C2-protodeboronation sequence; see: Loach, R. P.; Fenton, O. S.; Amaike, K.; Siegel, D. S.; Ozkal, E.; Movassaghi, M. *J. Org. Chem.* **2014**, *79*, 11254−11263.
(25) Robinson, M. W.; Overmeyer, J. H.; Young, A. M.; Erhardt, P. W.; Maltese, W. A. *J. Med. Chem.* **2012**, *55*, 1940−1956.
(26) Han, L.; Liu, C.; Zhang, W.; Shi, X.-X.; You, S.-L. *Chem. Commun.* **2014**, *50*, 1231−1233.
(27) Chakrabarty, M.; Kundu, T.; Harigaya, Y. *Synth. Commun.* **2006**, *36*, 2069−2077.
(28) Martin, T.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 235−240.
(29) Harrisson, P.; Morris, J.; Marder, T. B.; Steel, P. G. *Org. Lett.* **2009**, *11*, 3586−3589.

DOI: 10.1021/jo502509s
J. Org. Chem. XXXX, XXX, XXX−XXX