JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Synthesis of 2-Amino-3-hydroxy-3*H*-indoles via Palladium-Catalyzed One-Pot Reaction of Isonitriles, Oxygen, and *N*-Tosylhydrazones Derived from 2-Acylanilines

Haoke Chu, Qiang Dai, Yan Jiang, and Jiang Cheng*

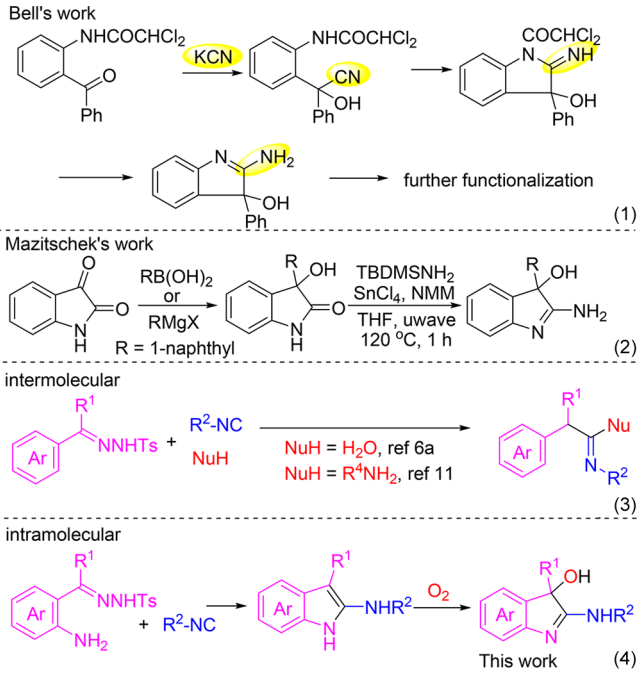
School of Petrochemical Engineering, Jiangsu Key Laboratory of Advanced Catalytic Materials & Technology, Jiangsu Province Key Laboratory of Fine Petrochemical Engineering, Changzhou University, Changzhou 213164, P. R. China

Supporting Information

ABSTRACT: A cyanide-free one-pot procedure was developed to access 2-amino-3-hydroxy-3*H*-indoles, which involved: (1) *in situ* formation of ketenimines by the reaction of *N*′-(1-(2-aminophenyl)ethylidene)-*p*-tosylhydrazones with isonitriles; (2) the intramolecular nucleophilic attack of ketenimines by the amino in phenyl furnishing the ring closure leading to 2-aminoindoles; (3) the oxidation of 2-aminoindoles by O_2 leading to 2-amino-3-hydroxy-3*H*-indoles. This strategy represents not only a key compliment to the sporadic synthetic methods toward 2-amino-3-hydroxy-3*H*-indoles but also progress in *N*-tosylhydrazone, isonitrile, and ketenimine chemistry.

2-Amino-3-hydroxy-3*H*-indoles possess activity against *Plasmodium falciparum*, serving as antimalarials with potent in vivo activity.[1] However, its biological activity is virtually unexplored, which is at least partly due to sporadic synthetic methodologies.[2] To date, only two practical methods were reported. One is the annulation of 2′-aroylacylanilides with cyanide developed by Bell (Scheme 1, eq 1).[3] Mazitschek demonstrated the other procedure involving the addition of aryl boronic acids to isatins followed by treatment with *tert*-butyldimethylsilyl amine (Scheme 1, eq 2).[4] Therefore, further development of practical methods involving either new reaction partners or pathways toward such frameworks remains a highly desired goal for organic chemists.

Scheme 1. Nucleophilic Attack on *in Situ* Formed Ketenimine via Reaction of *N*-Tosylhydrazone and Isonitrile



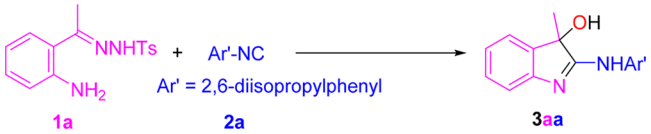
Meanwhile, ketenimines are versatile intermediates in organic synthesis.[5] Cai pioneered the study on *in situ* formation of ketenimines[6] whereby direct reaction between isonitriles[7−9] and *N*-tosylhydrazones[10−12] as the carbene precursors. Afterward, intermolecular nucleophilic attack of the *in situ* formed ketenimines by H_2O produced amides (Scheme 1, eq 1).[6a] This strategy was further developed by us in palladium-catalyzed MCRs to access amidines, where amines served as nucleophiles (Scheme 1, eq 3).[13] We expect the intramolecular nucleophilic attack on the *in situ* formed ketenimines, albeit without preceding reports, could furnish ring closure toward 2-aminoindoles, which, subsequently, is oxidized by O_2 allowing access to 2-amino-3-hydroxy-3*H*-indoles quickly (Scheme 1, eq 4).[14] Herein, we wish to report such a synthetic pathway, which represents not only a key compliment to the sporadic synthetic methods toward 2-amino-3-hydroxy-3*H*-indoles but also progress in *N*-tosylhydrazone, isonitrile, and ketenimine chemistry.

Initially, we tested the reaction of *N*′-(1-(2-aminophenyl)-ethylidene)-*p*-tosylhydrazone (**1a**, 1.0 equiv), 2,6-diisopropylphenyl isonitrile (**2a**, 1.2 equiv) in the presence of $Pd(OAc)_2$ (5 mol %), PPh_3 (10 mol %), and LiOH (3.0 equiv) in dioxane under N_2 at 120 °C for 5 h (Table 1, entry 1). To our delight, 2-((2,6-diisopropylphenyl)amino)-3-methyl-3-hydroxy-3*H*-indole **3aa** was isolated in 44% yield after further heating the reaction mixture under O_2 at 60 °C for 1 h (Table 1, entry 1). $Pd(acac)_2$ provided a comparable yield (50%, Table 1, entry 2).

Received: May 16, 2017
Published: July 13, 2017

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267−8272

Table 1. Selected Results for Screening the Optimized Reaction Conditions[a]



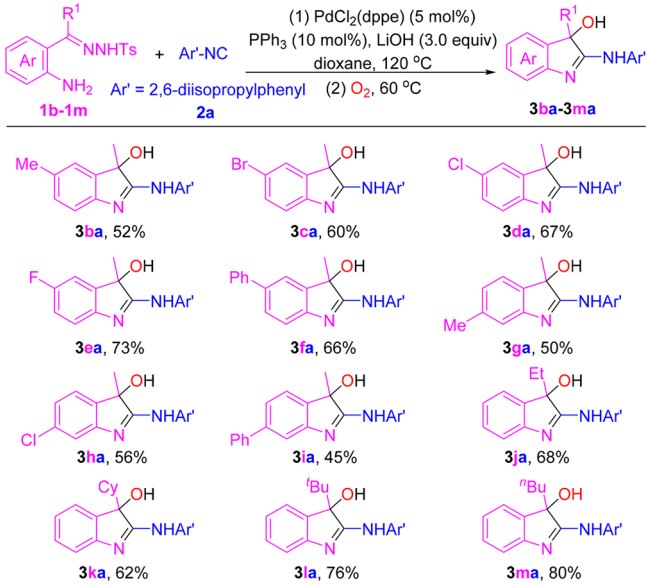
entry	catalyst	ligand	solvent	yield (%)[b]
1	$Pd(OAc)_2$	PPh_3	dioxane	44
2	$Pd(acac)_2$	PPh_3	dioxane	50
3	$Pd(MeCN)_2Cl_2$	PPh_3	dioxane	70
4	$PdCl_2$(dppe)	PPh_3	dioxane	73
5	$PdCl_2$(dppf)·CH_2Cl_2	PPh_3	dioxane	62
6	$Pd(cod)Cl_2$	PPh_3	dioxane	58
7	$PdCl_2$(dppe)	P(*p*-tolyl)$_3$	dioxane	36
8	$PdCl_2$(dppe)	P(2-furyl)$_3$	dioxane	68
9	$PdCl_2$(dppe)	PCy_3	dioxane	45
10	$PdCl_2$(dppe)	–	dioxane	33
11	–	–	dioxane	NR
12	$PdCl_2$(dppe)	PPh_3	THF	65
13	$PdCl_2$(dppe)	PPh_3	DMF	<5
14	$PdCl_2$(dppe)	PPh_3	toluene	<5
15[c]	$PdCl_2$(dppe)	PPh_3	dioxane	27
16[d]	$PdCl_2$(dppe)	PPh_3	dioxane	<5

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), Pd catalyst (0.01 mmol, 5 mol %), ligand (0.02 mmol, 10 mol %), and LiOH (0.6 mmol, 3.0 equiv) in solvent (2 mL) under N_2, 120 °C for 5 h in a sealed tube, then under O_2, 60 °C for 1 h Cs_2CO_3. [b]Isolated yield. [c]Cs_2CO_3 instead of LiOH. [d]LiO^{t}Bu instead of LiOH.

Pleasingly, $Pd(MeCN)_2Cl_2$ increased the yield to 70% (Table 1, entry 3), while $PdCl_2$(dppe) gave the best yield (73%, Table 1, entry 4). $PdCl_2$(dppf)·CH_2Cl_2 and $Pd(cod)Cl_2$ slightly decreased the reaction efficiency to 62% and 58%, respectively (Table 1, entries 5 and 6). The ligands, such as tri(4-methylphenyl)phosphine (36%, Table 1, entry 7), tri(2-furyl)phosphine (68%, Table 1, entry 8), and tricyclohexylphosphine (45%, Table 1, entry 9) were inferior to PPh_3. In the absence of PPh_3, the yield dramatically decreased to 33% (Table 1, entry 10), while no reaction took place in the absence of both palladium and PPh_3 (Table 1, entry 11). Replacing dioxane with THF slightly decreased the reaction efficiency (65%, Table 1, entry 12), while DMF and toluene resulted in no reaction (Table 1, entries 13 and 14). The reaction was inhibited when LiOH was replaced with Cs_2CO_3 or LiO^{t}Bu (Table 1, entries 15 and 16).

Once the optimized conditions were established, the scope and limitation of substituted *N*′-(1-(2-aminophenyl)-ethylidene)-*p*-tosylhydrazones were studied (Scheme 2). As expected, the procedure ran smoothly to access 2-amino-3-methyl-3-hydroxy-3*H*-indole derivatives with various substituents at the 5- and 6-position in moderate to good yields (**3ba**–**3ia**). A series of functional groups, such as methyl, bromo, chloro, and fluoro, were compatible with the reaction conditions, which provided handles for potentially further functionalization. Notably, the diversity was further increased as the 3-alkyl in 2-amino-3-hydroxy-3*H*-indoles was not limited to methyl. The 3-ethyl (**3ja**, 68%), cyclohexyl (**3ka**, 62%), *tert*-butyl (**3la**, 76%), and *n*-butyl (**3ma**, 80%) analogues were all isolated in good yields, while disappointingly 3-aryl products were isolated in trace amounts. The structure of **3aa** was established by X-ray crystallographic analysis (see Supporting Information).[15]

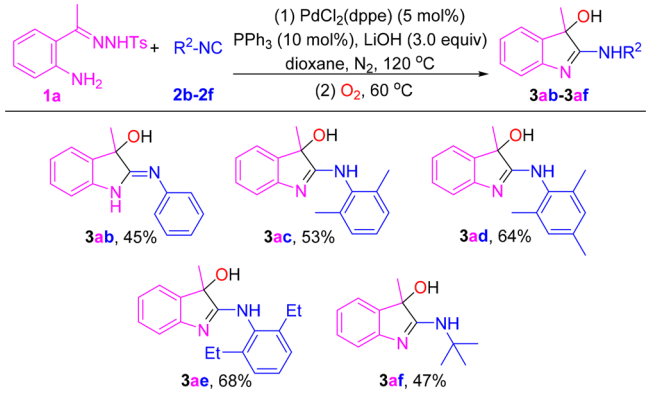
Scheme 2. Substrate Scope of Substituted *N*-Tosylhydrazones[a]



[a]Reaction conditions: **1b**–**1m** (0.2 mmol), **2a** (0.24 mmol), $PdCl_2$(dppe) (0.01 mmol, 5 mol %), PPh_3 (0.02 mmol, 10 mol %), and LiOH (0.6 mmol, 3.0 equiv) in dioxane (2 mL) under N_2, 120 °C for 5 h in a sealed tube, then under O_2, 60 °C for 1 h.

Afterward, the scope of isonitriles was studied (Scheme 3). The hindrance on the phenyl of isonitrile was beneficial for this transformation. For example, phenyl isonitrile provided **3ab** in 45% yield, while the 2,6-dimethyl, 2,4,6-trimethyl, and 2,6-diethyl analogues produced the corresponding 2-amino-3-hydroxy-3*H*-indoles in 53% (**3ac**), 64% (**3ad**), and 68% (**3ae**) yields, respectively. Notably, *tert*-butyl isonitrile took part in this transformation, and 2-*tert*-butylamino-3-methyl-3-hydroxy-3*H*-indole **3af** was isolated in 47% yield. *n*-Hexylisonitrile did not work utilizing the procedure. The structure of **3ab** was established by X-ray crystallographic analysis (see Supporting Information).[16] Notably, in this case, the C=N bond in the N–C=N linkage located outside of the ring.

Scheme 3. Substrate Scope of Isonitriles[a]

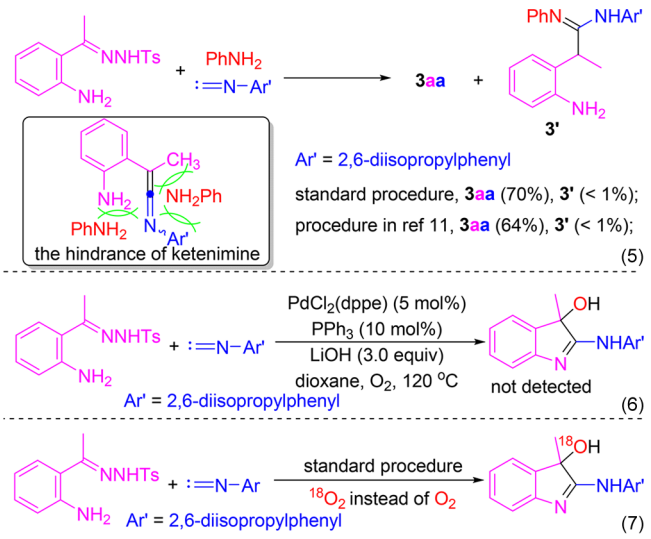


[a]Reaction conditions: **1a** (0.2 mmol), **2b**–**2f** (0.24 mmol), $PdCl_2$(dppe) (0.01 mmol, 5 mol %), PPh_3 (0.02 mmol, 10 mol %), and LiOH (0.6 mmol, 3.0 equiv) in dioxane (2 mL) under N_2, 120 °C for 5 h in a sealed tube, then under O_2, 60 °C for 1 h.

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267–8272

Some experiments were conducted to gain some insight into this procedure. In the competitive experiments, under either the standard procedure or the procedure in ref 11, 2-((2,6-diisopropylphenyl)amino)-3-methyl-3-hydroxy-3*H*-indole **3aa** was isolated as the sole product and no product whereby the intermolecular nucleophilic attack was detected at all (Scheme 4, eq 5). This may be ascribed to the hindrance of the

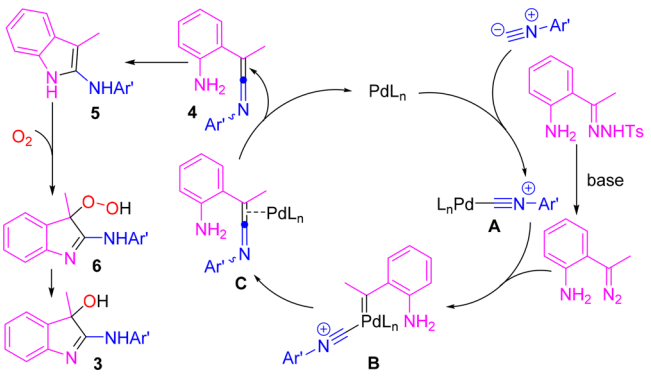
Scheme 4. Preliminary Mechanism Study



presumed ketenimine intermediate (Scheme 4, eq 5). During the transformation, 2-aminoindoles were occasionally detected, which were not stable enough to be isolated. The product **3aa** could not be detected when the reaction was conducted in one pot under an oxygen atmosphere (Scheme 4, eq 6). Moreover, no ^{18}O was detected in the final product by adding $H_2{}^{18}O$ to the standard procedure. However, ^{18}O was totally incorporated in the hydroxy group of the product when the reaction was conducted under $^{18}O_2$ atmosphere (Scheme 4, eq 7).

Based on the experimental results, a proposed mechanism was outlined in Scheme 5. First, the coordination of palladium

Scheme 5. A Tentative Mechanism



with isonitrile formed complex **A**. Then, under basic conditions, sequential deprotonation and detosylation of *N*′-(1-(2-aminophenyl)ethylidene)-*p*-tosylhydrazone took place to produce a diazo compound, which reacted with palladium complex **A** toward a palladium carbene **B**, along with the extrusion of N_2. Second, **B** converted to the palladium complex **C** via migratory insertion. After the dissociation of palladium to enter the catalytic cycle, the intramolecular attack of ketenimine **4** by the amino in the phenyl ring furnished the ring closure leading to 2-aminoindole **5**. Finally, the oxidation of **5** by O_2 produced the final product 2-amino-3-hydroxy-3*H*-indole via the formation of 2-amino-3-peroxy-3*H*-indole.[14]

In conclusion, we have developed a palladium-catalyzed cascade one-pot reaction of *N*′-(1-(2-aminophenyl)ethylidene)-*p*-tosylhydrazones, isonitriles, and O_2 toward 2-amino-3-hydroxy-3*H*-indoles. This procedure involved the following: the sequential *in situ* formation of ketenimines; intramolecular nucleophilic attack of ketenimines by amino; and oxidation by O_2. It represents a practical synthetic method toward 2-amino-3-hydroxy-3*H*-indoles, rendering progress in *N*-tosylhydrazone, isonitrile, and ketenimine chemistry.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. ^1H and ^{13}C NMR spectra were recorded at ambient temperature on a 300 or 400 MHz (75 or 100 MHz for ^{13}C) NMR spectrometer. NMR experiments are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (δ 7.26 or 77.0 ppm), acetone-d^6 (δ 7.26 or 77.0 ppm), or DMSO-d^6 (δ 2.50 or 39.50 ppm) as the internal standard. The coupling constants J are given in Hz. Column chromatography was performed using EM Silica gel 60 (300–400 mesh). High-resolution mass spectra (HRMS) were obtained using a micro TOF II focus spectrometer (ESI).

Experimental Procedure. *General Procedure for 2-Amino-3-hydroxy-3H-indoles.* A 20 mL Schlenk tube equipped with a stir bar was charged with **1** (0.2 mmol), **2** (0.24 mmol, 1.2 equiv), $PdCl_2$(dppe) (5.8 mg, 5 mol %), PPh_3 (5.2 mg, 10 mol %), LiOH (48.0 mg, 0.6 mmol), and dioxane (2 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred under N_2 at 100 °C in an oil bath. After 5 h, the tube was cooled to room temperature and poured with O_2. The mixture was stirred at 60 °C for another 1 h. After completion, 5 mL of brine were added, and the mixture was extracted with EtOAc (3 × 2 mL). The organic layer was collected and concentrated in vacuum. The residue was purified by flash column chromatography on silica gel with petroleum ether–EtOAc as the eluent to give the desired product.

*2-((2,6-Diisopropylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3aa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3aa** (47.0 mg, 73% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.2 Hz, 1H), 7.22–7.15 (m, 4H), 6.99 (t, J = 7.4 Hz, 1H) 6.62 (d, J = 7.7 Hz, 1H), 6.52 (s, 1H), 4.09 (s, 1H), 3.12–3.02 (m, 2H), 1.83 (s, 3H), 1.25–1.16 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 143.0, 141.3, 139.6, 139.1, 132.2, 129.4, 124.1, 123.8, 123.6, 123.3, 121.8, 109.0, 75.4, 28.2, 27.7, 27.3, 23.8, 23.8, 23.6, 23.2; GCMS (EI) calcd for $C_{21}H_{26}N_2O$ 322, found 322; HRMS (ESI) m/z calcd for $C_{21}H_{27}N_2O$ $(M + H)^+$ 323.2118, found 323.2119; IR (KBr) 3414, 3060, 2962, 2926, 2867, 1687, 1620, 1588, 1484, 1471, 1384, 1362, 1325 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-3,5-dimethyl-3-hydroxy-3H-indole (**3ba**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ba** (35.1 mg, 52% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.22–7.16 (m, 3H), 7.00 (d, J = 7.8 Hz, 1H), 6.55 (d, J = 7.7 Hz, 1H), 6.40 (s, 1H), 3.76 (s, 1H), 3.11–3.02 (m, 2H), 2.34 (s, 3H), 1.84 (s, 3H), 1.25–1.15 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 143.2, 139.5, 139.0, 139.0, 132.1, 131.4, 129.7, 124.5, 124.0, 123.5, 123.3, 108.7, 75.4, 28.2, 27.7, 27.3, 23.7, 23.7, 23.6, 23.2, 20.9; GCMS (EI) calcd for $C_{22}H_{29}N_2O$ 336, found 336; HRMS (ESI) m/z calcd for $C_{22}H_{29}N_2O$ $(M + H)^+$ 337.2274, found 337.2274; IR (KBr) 3474, 3415, 2961, 1637, 1617, 1458, 1384, 1339 cm^{-1}.

*5-Bromo-2-((2,6-diisopropylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3ca**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ca** (48.2 mg, 60% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.20–7.13

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267–8272

(m, 4H), 6.56 (d, J = 8.1 Hz, 1H), 6.47 (s, 1H), 3.94 (s, 1H), 3.05−2.95 (m, 2H), 1.80 (s, 3H), 1.22−1.12 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 142.7, 139.8, 139.4, 138.9, 133.8, 129.3, 127.1, 124.4, 124.3, 123.6, 123.4, 110.0, 75.4, 29.7, 28.2, 27.8, 27.3, 23.7, 23.6, 23.2; GCMS (EI) calcd for $C_{21}H_{25}BrN_2O$ 400, found 400; HRMS (ESI) m/z calcd for $C_{21}H_{26}BrN_2O$ $(M + H)^+$ 401.1223, found 401.1212; IR (KBr) 3416, 2962, 2926, 2868, 1685, 1638, 1618, 1560, 1459, 1384, 1326 cm^{-1}.

*5-Chloro-2-((2,6-diisopropylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3da**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3da** (47.7 mg, 67% yield) as a yellow solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.12 (s, 1H), 7.45 (s, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.12−7.04 (m, 3H), 6.72 (d, J = 7.2 Hz, 1H), 6.09 (s, 1H), 3.11−2.97 (m, 1H), 2.96−2.76 (m, 1H), 1.61 (s, 3H), 1.12−1.08 (m, 12H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 131.4, 123.1, 122.7, 74.8, 27.8, 27.0, 23.9, 23.6, 23.3, 23.0; GCMS (EI) calcd for $C_{21}H_{25}ClN_2O$ 356, found 356; HRMS (ESI) m/z calcd for $C_{21}H_{26}ClN_2O$ $(M + H)^+$ 357.1728, found 357.1730; IR (KBr) 3547, 3474, 3414, 3235, 2958, 2866, 1668, 1638, 1616, 1478, 1457, 1436, 1384, 1322 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-5-fluoro-3-methyl-3-hydroxy-3H-indole (**3ea**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ea** (49.6 mg, 73% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.12 (m, 4H), 6.86 (t, J = 8.7 Hz, 1H), 6.56−6.53 (m, 1H), 6.48 (s, 1H), 3.09−2.98 (m, 2H), 2.03 (s, 1H), 1.81 (s, 3H), 1.23−1.13 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 158.7 (d, J_{C-F} = 239.0 Hz), 142.8, 139.3 (d, J_{C-F} = 53.0 Hz), 137.2, 133.6, 124.3, 123.6, 123.4, 115.8, 115.6, 111.8, 111.6, 109.5 (d, J_{C-F} = 7.0 Hz), 75.6, 28.2, 27.7, 27.3, 23.7, 23.6, 23.2, 21.0; GCMS (EI) calcd for $C_{21}H_{25}FN_2O$ 340, found 340; HRMS (ESI) m/z calcd for $C_{21}H_{26}FN_2O$ $(M + H)^+$ 341.2024, found 341.2022; IR (KBr) 3436, 2963, 2928, 2868, 1691, 1629, 1488, 1438, 1384, 1362, 1327 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-3-methyl-5-phenyl-3-hydroxy-3H-indole (**3fa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3fa** (52.6 mg, 66% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.56−7.54 (m, 2H), 7.44−7.41 (m, 3H), 7.32 (t, J = 7.3 Hz, 1H), 7.22−7.16 (m, 3H), 6.72 (d, J = 7.8 Hz, 1H), 6.56 (s, 1H), 3.08−3.02 (m, 2H), 2.04 (s, 1H), 1.87 (s, 3H), 1.24−1.17 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 143.0, 140.9, 140.7, 139.5, 139.0, 135.5, 132.6, 128.8, 128.4, 126.8, 126.8, 124.2, 123.6, 123.4, 122.8, 109.3, 75.4, 28.2, 27.8, 27.3, 23.7, 23.6, 23.6, 23.2; GCMS (EI) calcd for $C_{21}H_{30}N_2O$ 398, found 398; HRMS (ESI) m/z calcd for $C_{27}H_{31}N_2O$ $(M + H)^+$ 399.2431, found 399.2437; IR (KBr) 3435, 3060, 2962, 2926, 2867, 1691, 1623, 1600, 1508, 1479, 1464, 1438, 1384, 1362, 1326 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-3,6-dimethyl-3-hydroxy-3H-indole (**3ga**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ga** (33.8 mg, 50% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.5 Hz, 1H), 7.20−7.11 (m, 3H), 6.81 (d, J = 7.5 Hz, 1H), 6.46 (s, 1H), 6.43 (s, 1H), 3.39 (s, 1H), 3.04−2.98 (m, 2H), 2.29 (s, 3H), 1.80 (s, 3H), 1.21−1.14 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 143.2, 141.6, 139.8, 139.4, 139.0, 129.1, 124.0, 123.6, 123.5, 123.3, 122.4, 109.8, 75.2, 29.7, 28.2, 27.8, 27.2, 23.6, 23.6, 23.2, 21.7; GCMS (EI) calcd for $C_{22}H_{28}N_2O$ 336, found 336; HRMS (ESI) m/z calcd for $C_{22}H_{29}N_2O$ $(M + H)^+$ 337.2274, found 337.2276; IR (KBr) 3463, 2961, 2926, 2867, 1686, 1654, 1630, 1559, 1507, 1458, 1384, 1326 cm^{-1}.

*6-Chloro-2-((2,6-Diisopropylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3ha**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ha** (40.1 mg, 56% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 7.8 Hz, 1H), 7.18−7.12 (m, 3H), 6.96 (d, J = 7.9 Hz, 1H), 6.64 (s, 1H), 6.51 (s, 1H), 3.56 (s, 1H), 3.02−2.94 (m, 2H), 1.79 (s, 3H), 1.21−1.14 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 142.7, 142.5, 139.3, 138.9, 135.1, 130.4, 124.8, 124.4, 123.6, 123.4, 121.9, 109.7, 74.9, 29.7, 28.2, 27.8, 27.2, 23.6, 23.5, 23.2; GCMS (EI) calcd for $C_{21}H_{25}ClN_2O$ 356, found 356; HRMS (ESI) m/z calcd for $C_{21}H_{26}ClN_2O$ $(M + H)^+$ 357.1728, found 357.1727; IR (KBr) 3438, 2962, 2926, 2968, 1693, 1617, 1560, 1485, 1458, 1325 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-3-methyl-6-phenyl-3-hydroxy-3H-indole (**3ia**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ia** (36.0 mg, 45% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.51 (m, 3H), 7.44−7.40 (m, 2H), 7.37−7.33 (m, 1H), 7.28−7.21 (m, 4H), 6.91 (s, 1H), 3.10−3.00 (m, 2H), 2.08 (s, 1H), 2.07 (s, 1H), 1.90 (s, 3H), 1.24−1.19 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 140.8, 131.3, 128.8, 127.6, 127.1, 125.0, 124.1, 123.8, 123.5, 121.4, 75.6, 29.7, 28.3, 27.8, 27.0, 23.8, 23.5, 23.4; GCMS (EI) calcd for $C_{27}H_{30}N_2O$ 398, found 398; HRMS (ESI) m/z calcd for $C_{27}H_{31}N_2O$ $(M + H)^+$ 399.2431, found 399.2427; IR (KBr) 3463, 2961, 2927, 1685, 1626, 1560, 1507, 1458, 1437, 1384, 1339 cm^{-1}.

*2-((2,6-Diisopropylphenyl)amino)-3-ethyl-3-hydroxy-3H-indole (**3ja**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ja** (45.9 mg, 68% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.2 Hz, 1H), 7.20−7.12 (m, 4H), 6.99 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.5 Hz, 1H), 6.48 (s, 1H), 3.37 (s, 1H), 3.10−3.01 (m, 2H), 2.23−2.18 (m, 2H), 1.23−1.12 (m, 12H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 142.9, 141.8, 139.1, 138.6, 129.9, 129.1, 124.1, 123.8, 123.2, 123.0, 121.4, 108.6, 76.4, 33.2, 27.7, 27.4, 23.6, 23.3, 23.2, 23.0, 7.5; GCMS (EI) calcd for $C_{22}H_{28}N_2O$ 336, found 336; HRMS (ESI) m/z calcd for $C_{22}H_{29}N_2O$ $(M + H)^+$ 337.2274, found 337.2274; IR (KBr) 3456, 2962, 2918, 2849, 1685, 1637, 1622, 1470, 1384, 1325 cm^{-1}.

*3-Cyclohexyl-2-((2,6-diisopropylphenyl)amino)-3-hydroxy-3H-indole (**3ka**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ka** (48.4 mg, 62% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.3 Hz, 1H), 7.20−7.10 (m, 4H), 6.98 (t, J = 7.4 Hz, 1H), 6.62 (d, J = 7.7 Hz, 1H), 6.44 (s, 1H), 3.11 (hept, J = 6.7 Hz, 1H), 2.95 (hept, J = 6.7 Hz, 1H), 2.87 (s, 1H), 2.17−2.09 (m, 2H), 1.86−1.68 (m, 4H), 1.34−1.10 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 143.2, 142.4, 139.4, 138.8, 129.8, 129.3, 124.9, 124.0, 123.5, 123.3, 121.5, 108.8, 80.5, 48.3, 28.1, 27.8, 26.9, 26.5, 26.3, 26.1, 26.0, 23.9, 23.6, 23.5, 23.3; GCMS (EI) calcd for $C_{26}H_{34}N_2O$ 390, found 390; HRMS (ESI) m/z calcd for $C_{26}H_{35}N_2O$ $(M + H)^+$ 391.2744, found 391.2744; IR (KBr) 3466, 3059, 2960, 2929, 2854, 1725, 1686, 1619, 1470, 1384, 1325 cm^{-1}.

*3-(tert-Butyl)-2-((2,6-diisopropylphenyl)amino)-3-hydroxy-3H-indole (**3la**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3la** (55.5 mg, 76% yield) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.5 Hz, 1H), 7.21−7.10 (m, 4H), 6.95 (t, J = 7.5 Hz, 1H), 6.59 (d, J = 7.8 Hz, 1H), 6.31 (s, 1H), 3.12 (hept, J = 6.8 Hz, 1H), 3.06 (s, 1H), 2.88 (hept, J = 6.7 Hz, 1H), 1.26−1.12 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 143.3, 142.7, 139.3, 138.6, 130.4, 129.2, 126.1, 124.0, 123.6, 123.3, 121.0, 108.6, 82.5, 38.8, 28.3, 27.7, 24.1, 23.8, 23.7, 23.4, 23.3; GCMS (EI) calcd for $C_{24}H_{32}N_2O$ 364, found 364; HRMS (ESI) m/z calcd for $C_{24}H_{33}N_2O$ $(M + H)^+$ 365.2587, found 365.2591; IR (KBr) 3474, 2961, 2929, 2869, 1683, 1638, 1618, 1469, 1384, 1362, 1325 cm^{-1}.

*3-(n-Butyl)-2-((2,6-diisopropylphenyl)amino)-3-hydroxy-3H-indole (**3ma**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ma** (58.3 mg, 80% yield) as a yellow solid: ^{1}H NMR (100 MHz, $CDCl_3$) δ 7.41 (d, J = 7.4 Hz, 1H), 7.20−7.11 (m, 4H), 6.99 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 6.49 (s, 1H), 3.09 (s, 1H), 3.07−2.97 (m, 2H), 2.20−2.16 (m, 2H), 1.27−1.12 (m, 16H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 143.2, 142.1, 139.3, 138.9, 130.4, 129.4, 124.3, 124.0, 123.5, 123.3, 121.7, 109.0, 78.3, 40.4, 28.0, 27.8, 25.7, 23.9, 23.5, 23.5, 23.3, 22.9, 13.9; GCMS (EI) calcd for $C_{24}H_{32}N_2O$ 364, found 364; HRMS (ESI) m/z calcd for $C_{24}H_{33}N_2O$ $(M + H)^+$ 365.2587, found 365.2589; IR (KBr) 3416, 2959, 2931, 2868, 1685, 1638, 1619, 1470, 1384, 1325 cm^{-1}.

*3-Methyl-2-(phenylamino)-3-hydroxy-3H-indole (**3ab**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ab** (21.3 mg, 45% yield) as a yellow solid: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.93 (s, 1H), 7.36−7.28 (m, 3H), 7.22−7.16 (m, 1H), 7.10 (d, J = Hz, 1H), 7.04−6.99 (m, 1H), 6.97−6.92 (m, 1H), 5.10 (s, 1H), 1.58 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 129.9,

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267−8272

129.6, 123.2, 122.8, 122.6, 120.2, 25.9; GCMS (EI) calcd for $C_{15}H_{14}N_2O$ 238, found 238; HRMS (ESI) m/z calcd for $C_{15}H_{15}N_2O$ $(M + H)^+$ 239.1179, found 239.1181; IR (KBr) 3450, 3418, 2935, 1642, 1617, 1450, 1380, 1333 cm^{-1}.

*2-((2,6-Dimethylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3ac**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ac** (28.1 mg, 53% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.1 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.09−7.07 (m, 2H), 6.99−6.95 (m, 2H), 6.64 (s, 1H), 6.51 (s, 1H), 4.43 (s, 1H), 2.15 (s, 6H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.55, 129.4, 128.3, 123.7, 121.8, 109.0, 75.4, 27.3, 17.7; GCMS (EI) calcd for $C_{17}H_{18}N_2O$ 266, found 266; HRMS (ESI) m/z calcd for $C_{17}H_{19}N_2O$ $(M + H)^+$ 267.1492, found 267.1500; IR (KBr) 3457, 2926, 1685, 1621, 1560, 1469, 1384, 1326 cm^{-1}.

*2-((2,4,6-Trimethylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3ad**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ad** (35.8 mg, 64% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.0 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.90 (s, 2H), 6.62 (s, 1H), 6.49 (s, 1H), 4.35 (s, 1H), 2.29 (s, 3H), 2.12 (s, 6H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 129.3, 128.9, 123.7, 121.8, 60.4, 21.0, 20.7, 17.6, 14.1; GCMS (EI) calcd for $C_{18}H_{20}N_2O$ 280, found 280; HRMS (ESI) m/z calcd for $C_{18}H_{21}N_2O$ $(M + H)^+$ 281.1648, found 281.1652; IR (KBr) 3415, 2966, 2924, 2855, 1684, 1637, 1620, 1570, 1470, 1384, 1325 cm^{-1}.

*2-((2,6-Diethylphenyl)amino)-3-methyl-3-hydroxy-3H-indole (**3ae**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3ae** (40.0 mg, 68% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.1 Hz, 1H), 7.19−7.05 (m, 4H), 6.98 (t, J = 7.4 Hz, 1H), 6.61 (d, J = 7.2 Hz, 1H), 6.50 (s, 1H), 3.92 (s, 1H), 2.58−2.49 (m, 4H), 1.81 (s, 3H), 1.17 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 144.5, 141.3, 134.9, 134.4, 132.1, 129.4, 126.5, 126.3, 123.8, 121.8, 109.0, 75.3, 27.2, 24.6, 24.0, 14.4, 14.2; GCMS (EI) calcd for $C_{19}H_{22}N_2O$ 294, found 294; HRMS (ESI) m/z calcd for $C_{19}H_{23}N_2O$ $(M + H)^+$ 295.1805, found 295.1806; IR (KBr) 3439, 3061, 2966, 2930, 2873, 1686, 1620, 1589, 1471, 1452, 1384, 1326 cm^{-1}.

*2-(tert-Butylamino)-3-methyl-3-hydroxy-3H-indole (**3af**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gives **3af** (20.5 mg, 47% yield) as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.20−7.13 (m, 3H), 6.86 (t, J = 7.2 Hz, 1H), 4.93 (s, 1H), 2.90 (s, 1H), 1.44 (s, 9H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 155.3, 136.8, 129.8, 121.4, 121.2, 117.0, 80.6, 52.0, 28.7, 25.7; GCMS (EI) calcd for $C_{13}H_{18}N_2O$ 218, found 218; HRMS (ESI) m/z calcd for $C_{13}H_{19}N_2O$ $(M + H)^+$ 219.1492, found 219.1497; IR (KBr) 3408, 2970, 2928, 1623, 1599, 1574, 1532, 1458, 1384, 1366, 1339 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01195.

X-ray crystallographic data for **3aa** (CIF)

X-ray crystallographic data for **3ab** (CIF)

^1H and ^{13}C NMR spectra for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*jiangcheng@cczu.edu.cn

ORCID

Jiang Cheng: 0000-0003-2580-1616

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Nos. 21272028 and 21572025), "Innovation & Entrepreneurship Talents" Introduction Plan of Jiangsu Province, the Key University Science Research Project of Jiangsu Province (15KJA150001), Qing Lan Project of Jiangsu Province, Jiangsu Key Laboratory of Advanced Catalytic Materials &Technology (BM2012110), and Advanced Catalysis and Green Manufacturing Collaborative Innovation Center for financial supports. H.C. thanks the Research Innovation Program for College Graduates of Jiangsu Province (Grant No. KYZZ15-0304) for financial support.

■ REFERENCES

(1) (a) Barker, R. H., Jr.; Urgaonkar, S.; Mazitschek, R.; Celatka, C.; Skerlj, R.; Cortese, J. F.; Tyndall, E.; Liu, H.; Cromwell, M.; Sidhu, A. B.; et al. *Antimicrob. Agents Chemother.* **2011**, *55*, 2612. (b) Mazitschek, R.; Clardy, J. C.; Wirth, D.; Wiegand, R.; Urgaonkar, S.; Baniecki, S. M. L.; Cortese, J.; Celatka, C.; Xiang, Y.; Skerlj, R. et al. PCT Int. 2011, WO 201105369.

(2) (a) Wittig, G.; Kleiner, H.; Conrad, J. *Liebigs Ann. Chem.* **1929**, *469*, 1. (b) Ishizumi, K.; Inaba, S.; Yamamoto, H. *J. Org. Chem.* **1974**, *39*, 2581.

(3) (a) Bell, S. C.; Wei, P. H. L. *J. Heterocycl. Chem.* **1969**, *6*, 599. (b) Sakiyama, F.; Nakazawa, T. *Chem. Lett.* **1979**, *8*, 587.

(4) Urgaonkar, S.; Cortese, J. F.; Barker, R. H.; Cromwell, M.; Serrano, A. E.; Wirth, D. F.; Clardy, J.; Mazitschek, R. *Org. Lett.* **2010**, *12*, 3998.

(5) For reviews of ketenimine, please see: (a) Lu, P.; Wang, Y. *Chem. Soc. Rev.* **2012**, *41*, 5687. (b) Zhang, W.; Xu, W.; Kuang, C. *Youji Huaxue* **2015**, *35*, 2059. (c) Allen, A. D.; Tidwell, T. T. *Chem. Rev.* **2013**, *113*, 7287. (d) Alajarin, M.; Marin-Luna, M.; Vidal, A. *Eur. J. Org. Chem.* **2012**, *2012*, 5637. (e) Kim, S. H.; Park, S. H.; Choi, J. H.; Chang, S. *Chem. - Asian J.* **2011**, *6*, 2618. (f) Wentrup, C.; Finnerty, J. J.; Koch, R. *Curr. Org. Chem.* **2010**, *14*, 1586. (g) Lu, P.; Wang, Y. *Synlett* **2010**, *2010*, 165.

(6) (a) Zhou, F.; Ding, K.; Cai, Q. *Chem. - Eur. J.* **2011**, *17*, 12268. (b) Yan, X.; Liao, J.; Lu, Y.; Liu, J.; Zeng, Y.; Cai, Q. *Org. Lett.* **2013**, *15*, 2478.

(7) For reviews on isonitriles, please see: (a) Zhang, B.; Studer, A. *Chem. Soc. Rev.* **2015**, *44*, 3505. (b) Wilson, R. M.; Stockdill, J. L.; Wu, X.; Li, X.; Vadola, P. A.; Park, P. K.; Wang, P.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 2834. (c) Zhu, J. *Eur. J. Org. Chem.* **2003**, *2003*, 1133. (d) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177. (e) Spagnolo, P.; Nanni, D. In *Encyclopedia of Radicals in Chemistry, Biology and Materials*; Chatgilialoglu, C., Studer, A., Eds.; Wiley: 2012; Vol. 2, pp 1019−1057.

(8) (a) Vlaar, T.; Maes, B. U. W.; Ruijter, E.; Orru, R. V. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7084. (b) Lang, S. *Chem. Soc. Rev.* **2013**, *42*, 4867. (c) Qiu, G.; Ding, Q.; Wu, J. *Chem. Soc. Rev.* **2013**, *42*, 5257. (d) Song, B.; Xu, B. *Chem. Soc. Rev.* **2017**, *46*, 1103. (e) Giustiniano, M.; Basso, A.; Mercalli, V.; Massarotti, A.; Novellino, E.; Tron, G. C.; Zhu, J. *Chem. Soc. Rev.* **2017**, *46*, 1295.

(9) For selected recent examples, see: (a) Leifert, D.; Artiukhin, D. G.; Neugebauer, J.; Galstyan, A.; Strassert, C. A.; Studer, A. *Chem. Commun.* **2016**, *52*, 5997. (b) Zhang, Y.; Ao, Y.-F.; Huang, Z.-T.; Wang, D.-X.; Wang, M.-X.; Zhu, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 5282. (c) Zhang, Z.; Xiao, F.; Huang, B.; Hu, J.; Fu, B.; Zhang, Z. *Org. Lett.* **2016**, *18*, 908. (d) Buyck, T.; Pasche, D.; Wang, Q.; Zhu, J. *Chem. - Eur. J.* **2016**, *22*, 2278. (e) Li, S.; Lowell, A. N.; Yu, F.; Raveh, A.; Newmister, S. A.; Bair, N.; Schaub, J. M.; Williams, R. M.; Sherman, D. H. *J. Am. Chem. Soc.* **2015**, *137*, 15366. (f) Zhang, J.; Lin, S.-X.; Cheng, D.-J.; Liu, X.-Y.; Tan, B. *J. Am. Chem. Soc.* **2015**, *137*, 14039. (g) Wang, Y.; Wang, H.; Peng, J.; Zhu, Q. *Org. Lett.* **2011**, *13*, 4604.

(10) For reviews on *N*-tosylhydrazones, please see: (a) Zhang, Y.; Wang, J. *Top. Curr. Chem.* **2012**, *327*, 239. (b) Jadhav, A. P.; Ray, D.; Rao, V. U. B.; Singh, R. P. *Eur. J. Org. Chem.* **2016**, *2016*, 2369. (c) Liu,

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267−8272

Z.; Wang, J. *J. Org. Chem.* **2013**, *78*, 10024. (d) Liu, Z.; Zhang, Y.; Wang, J. *Youji Huaxue* **2013**, *33*, 687. (e) Xiao, Q.; Zhang, Y.; Wang, J. *Acc. Chem. Res.* **2013**, *46*, 236. (f) Shao, Z.; Zhang, H. *Chem. Soc. Rev.* **2012**, *41*, 560.

(11) For selected recent examples, please see: (a) Zhang, Z.; Liu, Y.; Ling, L.; Li, Y.; Dong, Y.; Gong, M.; Zhao, X.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 4330. (b) Zhou, L.; Ye, F.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2010**, *132*, 13590. (c) Zhang, Z.; Liu, Y.; Gong, M.; Zhao, X.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1139. (d) Zhou, P.-X.; Ye, Y.-Y.; Liang, Y.-M. *Org. Lett.* **2013**, *15*, 5080. (e) Liu, X.; Ma, X.; Huang, Y.; Gu, Z. *Org. Lett.* **2013**, *15*, 4814. (f) Khanna, A.; Maung, C.; Johnson, K. R.; Luong, T. T.; Van Vranken, D. L V. *Org. Lett.* **2012**, *14*, 3233.

(12) (a) Tsai, A. S.; Curto, J. M.; Rocke, B. N.; Dechert-Schmitt, A.-M. R.; Ingle, G. K.; Mascitti, V. *Org. Lett.* **2016**, *18*, 508. (b) Zhou, P.-X.; Ye, Y.-Y.; Ma, J.-W.; Zheng, L.; Tang, Q.; Qiu, Y.-F.; Song, B.; Qiu, Z.-H.; Xu, P.-F.; Liang, Y.-M. *J. Org. Chem.* **2014**, *79*, 6627. (c) Wu, X.-X.; Zhou, P.-X.; Wang, L.-J.; Xu, P.-F.; Liang, Y.-M. *Chem. Commun.* **2014**, *50*, 3882. (d) Chen, Z.; Yan, Q.; Liu, Z.; Xu, Y.; Zhang, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 13324.

(13) Dai, Q.; Jiang, Y.; Yu, J.-T.; Cheng, J. *Chem. Commun.* **2015**, *51*, 16645.

(14) For the oxidation of 2-aminoindoles by O_2, please see: (a) Benincori, T.; Sannicolò, F. *J. Org. Chem.* **1988**, *53*, 1309 and references therein. (b) Golubeva, G. A.; Portnov, Y. N.; Kost, A. N. *Chem. Heterocycl. Compd.* **1973**, *9*, 471. (c) Kost, A. N.; Portnov, Y. N.; Golubeva, G. A.; Popova, A. G.; Mushket, B. *Chem. Heterocycl. Compd.* **1980**, *16*, 917.

(15) The molecular structure of **3aa** was determined by X-ray crystallographic analysis. CCDC 1497965 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(16) The molecular structure of **3ab** was determined by X-ray crystallographic analysis. CCDC 1497966 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

DOI: 10.1021/acs.joc.7b01195
J. Org. Chem. 2017, 82, 8267−8272