JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Homocoupling of 3-Halooxindole via Visible-Light Photocatalysis: A Mild Access to 3,3′-Bioxindoles

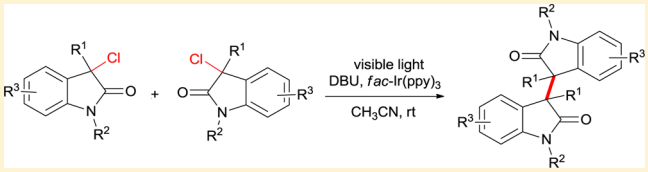
Wen-Liang Jia,[†] Jian He,[†] Jia-Jing Yang,[†] Xue-Wang Gao,[‡] Qiang Liu,*[,†] and Li-Zhu Wu*[,‡]

[†]State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, Gansu 730000, PR China

[‡]Key Laboratory of Photochemical Conversion and Optoelectronic Materials, Technical Institute of Physics and Chemistry, The Chinese Academy of Sciences, Beijing 100190, PR China

Supporting Information

ABSTRACT: This paper introduces a simple way to the homocoupling of tertiary halides induced by photocatalysis. This method features mild reaction conditions, excellent functional group tolerance, high yields, low photocatalyst loading and successful application to the highly sterically hindered systems. On the basis of the reaction results, a novel stable-radical-induced homocoupling reaction mechanism has been proposed.



INTRODUCTION

The coupling reactions of halogen compounds to form carbon−carbon bonds are among central methods of connecting two simpler molecules to generate a more complex one. The initial discovery by Wurtz et al. used alkali metal, such as sodium metal to reduce alkyl or benzyl halides, resulting in the homocoupling of two sp^3-carbon centers,[1] whereas the classic Ullmann reaction uses copper to induce homocoupling of aryl halides.[2] Because the synthetic applications of both the Wurtz coupling and classic Ullmann reaction are fairly limited, numerous reducing systems have thereafter been developed for the transformation, especially the transition metal-catalyzed coupling reactions of halides, which have advanced rapidly both in cross-electrophile coupling[3] and homocoupling. For example, Ni,[4] Ti[5] and Rh[6]-catalyzed reductive homocoupling of alkyl halides have been developed for the formation of $C(sp^3)-C(sp^3)$ bonds by using Zn, Et_2Zn or Mn as the reductant. More excitedly, this method has served as key steps for the total syntheses of many natural products. For example, the Movassaghi group has many excellent works on natural products syntheses by applying the Co-mediated homocoupling of C3-halogenated diketopiperazine as key step.[7] Overall, however, in most cases, metal-based reductants are essential for an efficient coupling of alkyl halides, and the reductive coupling of tertiary alkyl chlorides is still a challenge due to the associated difficulty in the formation of a C−C bond containing a vicinal all-carbon quaternary center.

The dimerization of indole and oxindole precursors, especially at C-3 position, has been always an attractive but challenging procedure.[8] Serving as key intermediates for the total syntheses of many natural products,[8,9] such as folicanthine, chimonanthine, calycanthine etc., the synthesis of 3,3′-bioxindoles rapidly caught organic chemists' attention. Maybe because of the highly steric hindrance, the initial attempts had low efficiency.[9a,10] Until 1994, the Rodrigo group obtained the dehydrogenative (±)dl-dimer (yield: 49−57%) and meso-dimer (yield: 8%) of ethyl 2-(1-methyl-2-oxoindolin-3-yl)-acetate at C-3 position and applied the former to achieve the total synthesis of (±) folicanthine successfully.[8] Even so, the harsh conditions, very long reaction time and many byproducts made it unfavorable. After that, several means to 3,3′-bioxindoles were reported, among which, either multiple procedures or excessive oxidants represented respective drawbacks.[9b−f]

Visible light photoredox chemistry is emerging as a powerful synthetic methodology owing to its attractive features such as mild and green conditions, excellent functional group tolerance, and high reactivity.[11] Recently, the group of Xiao described a visible-light-induced photocatalytic formyloxylation reaction of 3-alkyl-3-bromooxindole with water and DMF, in which the key intermediate 3-alkyl-2-oxoindolin-3-yl radical were generated by the electron transfer from the excited photocatalyst to 3-alkyl-3-bromooxindole.[12] In continuation of our interest in utilizing visible light to drive useful organic reactions,[13] we are intrigued by the structure of the 3-alkyl-2-oxoindolin-3-yl radical because this tertiary radical is stabilized by synergistic effect of electron-withdrawing carbonyl group and electron-donating aminophenyl group. The captodative stabilization and steric effect extend their lifetime and make homocoupling of 3-alkyl-2-oxoindolin-3-yl radical possible if other radical approaches are suppressed under proper photocatalytic conditions. Although several reports about dehalogenation-homocoupling induced by visible light were available,[14] the

Special Issue: Photocatalysis

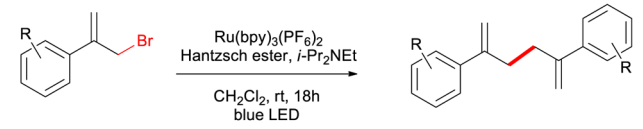
Received: May 4, 2016
Published: June 27, 2016

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

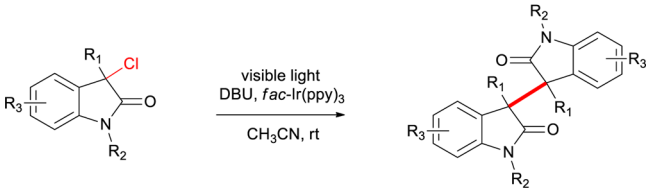
homocoupling of tertiary halides has not been researched before (Scheme 1). Herein, we report the first example of visible-light-driven construction of vicinal all-carbon quaternary center by homocoupling of 3-chloroxindole, which provide a mild and simple approach to 3,3′-substituted bioxindoles.

Scheme 1. Visible Light Induced Homocoupling of Halides[a]

a) Overman's work: primary halides, 2-arylallyl bromides are hard to access



b) Our strategy: direct construction of vicinal quaternary center

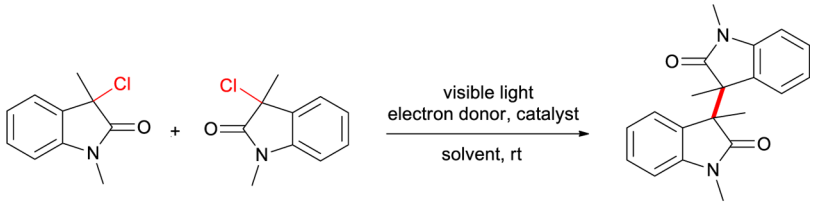


[a]Hantzsch ester = diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate, DBU = 1,8-diazabicyclo[5,4,0]undec-7-ene.

RESULTS AND DISSCUSSION

We initiated our investigations with **1a** (1.0 equiv) as the model substrate and DBU (1.0 equiv) as the electron donor. After 12 h of irradiation (blue LEDs, λ = 450 nm) in dry THF (0.06 M) with the loading of 0.5 mmol % *fac*-Ir(ppy)$_3$ as photocatalyst at room temperature, excitedly, **1b** was obtained in 57% isolated yield ((±) dl:meso = 1:2). After scrupulous evaluation of several solvents (Entries 2−5, Table 1), acetonitrile was found superior to others with **1b** yielding 82% (1.1:1). However, attention must be paid when DMF was used, we got the same product as the Xiao group's report without **1b** being obtained.[12] We then replaced DBU with other commonly used electron donors. DBN had a slightly lower efficiency than DBU, and we got **1b** in 76% (1.2:1) yield (Entry 6, Table 1). Other electron donors were not suitable for this transformation for lower yields (Entries 7−8, Table 1). The use of K_2CO_3 instead of DBU resulted in a trace amount of the desired product (Entry 9, Table 1), indicating that DBU merely act as an electron donor rather than a base. Next, enhancing the amount of DBU did not increase the yield of **1b** (Entries 10−11, Table 1), and 0.5 equiv of DBU reduced the yield nearly by half (Entry 12, Table 1). In addition, several typical photocatalysts were studied for their efficiency (Entries 13−16, Table 1). Ru(bpy)$_3$Cl$_2$ and Eosin B turned out to be useless to catalyze the reaction and Eosin Y and FIrPic were inferior to *fac*-Ir(ppy)$_3$, albeit obtaining **1b** in

Table 1. Optimization of Reaction Conditions



1a **1a** **1b**

entry[a]	solvent	electron donor	catalyst	yield (%)[b,c]
1	THF	DBU	*fac*-Ir(ppy)$_3$	57 (1:2)
2	DCM	DBU	*fac*-Ir(ppy)$_3$	76 (1:1)
3	**Acetonitrile**	**DBU**	***fac*-Ir(ppy)$_3$**	**82 (1.1:1)**
4	Acetone	DBU	*fac*-Ir(ppy)$_3$	34 (1:1)
5	DMF	DBU	*fac*-Ir(ppy)$_3$	No detect
6	Acetonitrile	DBN	*fac*-Ir(ppy)$_3$	76 (1.2:1)
7	Acetonitrile	DABCO	*fac*-Ir(ppy)$_3$	39 (1:2.5)
8	Acetonitrile	Et_3N	*fac*-Ir(ppy)$_3$	27 (1:1)
9[d]	Acetonitrile	–	*fac*-Ir(ppy)$_3$	Trace
10[e]	Acetonitrile	DBU	*fac*-Ir(ppy)$_3$	82 (1:1)
11[f]	Acetonitrile	DBU	*fac*-Ir(ppy)$_3$	80 (1:1)
12[g]	Acetonitrile	DBU	*fac*-Ir(ppy)$_3$	44 (1:1)
13	Acetonitrile	DBU	Ru(bpy)$_3$Cl$_2$	Trace
14	Acetonitrile	DBU	Eosin Y	51 (1:1.2)
15	Acetonitrile	DBU	Eosin B	Trace
16	Acetonitrile	DBU	FIrPic	75 (1.1:1)
17[h]	Acetonitrile	DBU	*fac*-Ir(ppy)$_3$	Trace
18	Acetonitrile	–	*fac*-Ir(ppy)$_3$	Trace
19	Acetonitrile	DBU	–	Trace

[a]Reaction conditions: **1a** (0.15 mmol, 1.0 equiv), electron donor (0.15 mmol, 1.0 equiv) and photocatalyst (0.00075 mmol, 0.5 mol %) in dry solvent (2.5 mL) was irradiated with two 3W blue LEDs lamp for 15 h. [b]Yield of the isolated product (averages of at least two separate runs). [c]The ratios in parentheses represent (±)dl: meso. [d]1.0 equiv of K_2CO_3 was used. [e]2.0 equiv of DBU was used. [f]3.0 equiv of DBU was used. [g]0.5 equiv of DBU was used. [h]No irradiation. DBN = 1,5-diazabicyclo[4.3.0]non-5-ene, DABCO = 1,4-diazabicyclo[2.2.2]octane, ppy = 2-phenylpyridine, Eosin Y = 2,4,5,7-tetrabromofluorescein sodium salt, Eosin B = 4,5-dibromo-2,7-dinitro fluorescein sodium salt, FIrPic = iridium(III)-bis[4,6-(difluorophenyl)-pyridinato-*N*,$C^{2'}$]picolinate.

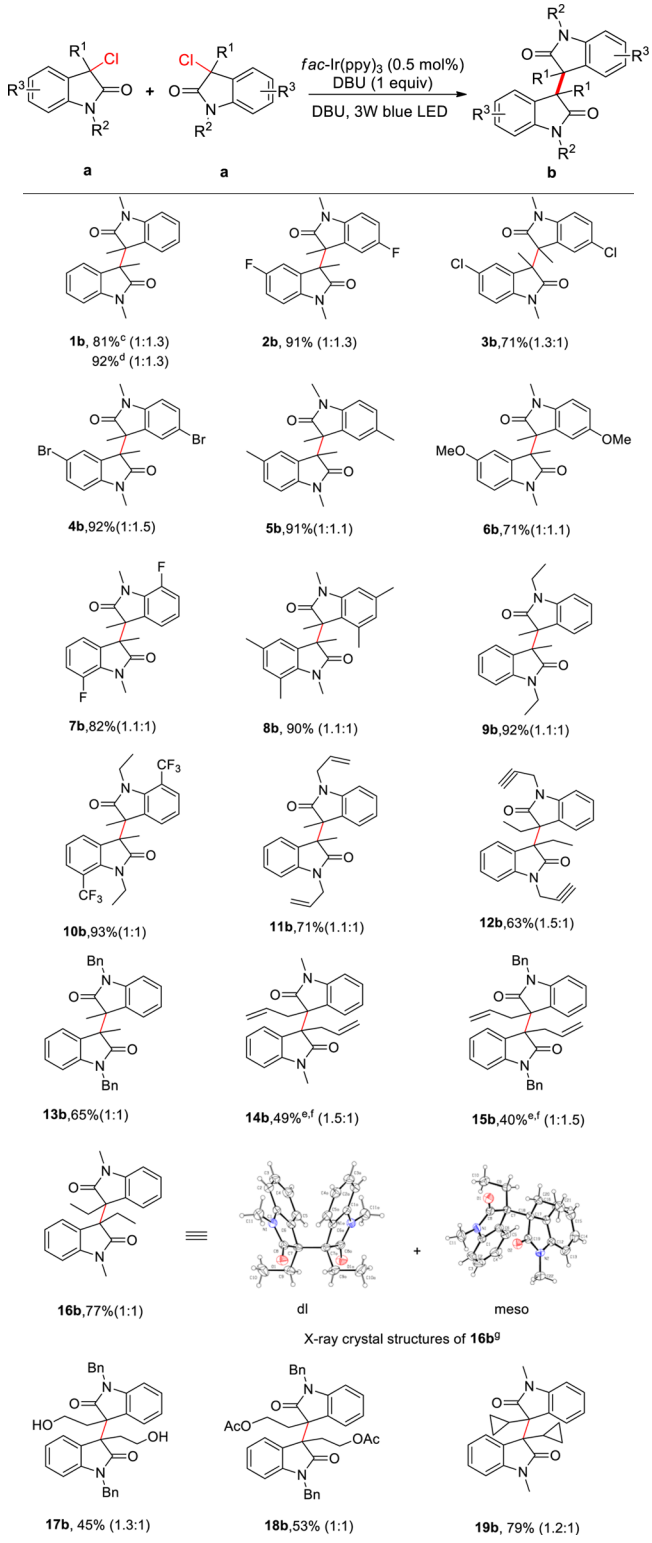
DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

51% and 75% yields, respectively. Moreover, control experiments established the importance of visible light, the electron donor and the photocatalyst, as no desired reaction was observed in the absence of light, DBU or *fac*-Ir(ppy)$_3$ (Entries 17−19, Table 1).

With the optimized conditions in hand, we next examined the generality of various substituted 3-halooxindoles in this visible-light-induced homocoupling protocol (Table 2). It was glad to see that the homocoupling of **1a** proceeded very well on a gram scale. The yield was similar to that obtained under standard reaction conditions, demonstrating the practicability of this visible-light driven photocatalytic process. When 3-bromoxindole **20a** was used instead of **1a**, the yield of **2b** was increased to 92%. Because alkyl chlorides are less reactive and more atom-efficient alternatives to alkyl bromides, 3-chloroxindoles were employed as the substrates for further studies. As shown in Table 2, 3-chloroxindoles with various substituents at C-5 and C-7 position of the benzene ring were found to undergo the desired homocoupling smoothly under the standard reaction conditions, affording the corresponding target products in 71−93% yields (Products **2b** to **8b**, **10b**, Table 2). In particular, halogen atoms in benzene ring are retained, thus providing an additional handle for further manipulation. Multisubstituted oxindole **8a** is also an excellent precursor, affording product **8b** in 90% yield. Next, various *N*-protected 3-chloroxindoles were tested, most of which can give satisfactory results (Products **9b** to **13b**, Table 2). The substrates protected by benzyl were also compatible with this new visible-light-driven homocoupling approach, although the reaction proceeded less efficiently. In contrast, unprotected and *t*-butyloxy carbonyl (Boc) protected 3-chloroxindoles failed to give the desired product. Finally, we examined 3-chloroxindoles with different substituents at C-3 position. In the case of 3-ethyl-3-chloroxindole, the two diastereoisomers of product **16b** were determined by X-ray crystallographic analysis. Notably, a number of key intermediates for the syntheses of natural products were obtained by altering substituents at C-3 position. For example, product **15b** has been employed to construct cyclotryptamine alkaloids[9e] by Trost et al. and product **17b** has been used to synthesize *meso*- and (−)-chimonanthine and (+)-calycanthine[9b] by Overman et al. In addition, the reaction of 3-cyclopropyl-3-chloroxindole produced **19b** without ring opening of the cyclopropane, which adds proof for our hypothesis that the 3-alkyl-2-oxoindolin-3-yl radical intermediate is stable.[15]

The photoluminescence of *fac*-Ir(ppy)$_3$ was quenched by 3-chloro-1,3-dimethylindolin-2-one **1a** with a rate constant of 87.7 L·mol^{-1}. In contrast, no significant quenching of *fac*-Ir(ppy)$_3$ took place in the presence of DBU (see Figure S2). This result indicated that the photoreaction is mainly initiated by the interaction between the excited *fac*-Ir(ppy)$_3$ and 3-chloro-1,3-dimethylindolin-2-one **1a**. On the basis of the results, a possible mechanism is proposed (Scheme 2). After absorbing a photon, [Ir^{III}] turns into excited [Ir^{III}]*. It is a strong reductant which can be oxidized to [Ir^{IV}] by 3-halooxindole via a single electron transfer (SET) process.[12] At the same time, 3-halooxindole was transferred to its radical anion, which can generate 3-alkyl-2-oxoindolin-3-yl radical after losing halide anion spontaneously. Successive SET between [Ir^{IV}] and DBU regenerates the photocatalyst and populates DBU radical cation. Further deprotonation of DBU radical cation can produce DBU radical, which should be oxidized to corresponding iminium ion.[16] Finally, the homocoupling of 3-

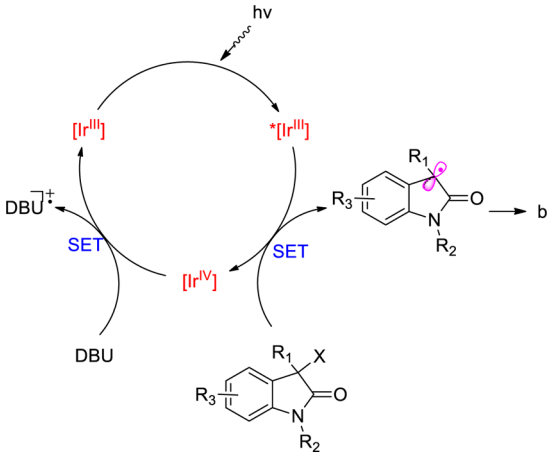
Table 2. Scope of Homocoupling of 3-Halooxindoles[a,b]



[a]Reaction conditions: **a** (0.15 mmol, 1.0 equiv), DBU (0.15 mmol, 1.0 equiv) and *fac*-Ir(ppy)$_3$ (0.00075 mmol, 0.5 mol %) in dry CH_3CN (2.5 mL) was irradiated with two 3W blue LED lamps for 15 h. [b]Yield of the isolated product (averages of at least two separate runs). The ratios in parentheses represent (±)dl: meso. [c]1.0 g of 3-chloro-1,3-dimethylindolin-2-one was used. [d]3-Bromo-1,3-dimethylindolin-2-one **20a** was used as the substrate. [e]Reactions were performed at −30 °C. [f]To achieve full conversion, the reaction time was prolonged to 24 h. [g]The ellipsoid contour percent probability level is 30%.

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

Scheme 2. Proposed Reaction Mechanism



alkyl-2-oxoindolin-3-yl radical affords the desired product **b**. Although Hashmi and co-workers have shown that the cross-coupling reaction can occur efficiently between α-aminoalkyl radical and alkynyl radical,[17] we only observed homocoupling reaction of 3-alkyl-2-oxoindolin-3-yl radical in the present case, and no cross-coupling reaction between DBU radical and 3-alkyl-2-oxoindolin-3-yl radical took place. The selectivity for the preferred homocoupling 3-alkyl-2-oxoindolin-3-yl radical may be attributed to the lower deprotonation rate of DBU radical cation, the higher steric hindrance of DBU radical and the less eletrophilicity of 3-alkyl-2-oxoindolin-3-yl radicals, which inhibit the cross-coupling process.[18]

CONCLUSIONS

In summary, we have developed a concise way to achieve homocoupling of tertiary halides in the presence of 0.5 mol % of the commercially available photocatalyst *fac*-Ir(ppy)$_3$, DBU, and visible light. With this method, a number of 3,3′-substituted bioxindoles including several key intermediates for the total syntheses of natural products were produced in good to excellent yields. The capacity to form vicinal all-carbon quaternary center readily demonstrates the inherent value of visible-light driven radical−radical couplings as a route to traditionally difficult bond constructions.[19]

EXPERIMENTAL SECTION

General Information. For product purification by flash column chromatography, silica gel (200−300 mesh) and light petroleum ether (PE) (bp. 60−90 °C) are used. All solvents were purified and dried by standard techniques, and distilled prior to use. Preparative TLC purification was performed on silica gel GF$_{254}$ TLC plates (20 cm × 20 cm, 0.5−1.0 mm). Experiments were conducted under an argon or nitrogen atmosphere, unless otherwise specified. NMR spectra were measured on 400 MHz instruments at room temperature. All new products were further characterized by HRMS (high-resolution mass spectrometry). HRMS spectra were obtained on a micrOTOF-Q instrument equipped with an ESI source or on a TOF instrument equipped with an EI source.

Preparation of 3-(2-Acetoxyethyl)indole.[20] Tryptophol (2.418 g, 15.0 mmol) was dissolved in 30 mL pyridine and 2.0 mL (21.00 mmol) acetic anhydride was added dropwise. After the mixture was allowed to stir for 15 h at room temperature, the solution was poured into 120 mL H_2O and stirred for another 20 min. The heterogeneous mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (30 mL × 4). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered through Celite and concentrated under reduced pressure. Purification by flash chromatography on silica gel using EtOAc-hexanes for elution provided the title compound as colorless oil.

Preparation of N-Benzyl-3-(2-((tert-butyldimethylsilyl)oxy)ethyl) indole.[21] Step 1: *tert*-Butyldimethylsilyl chloride (1.66 g, 11.0 mmol, 1.1 equiv) was added to a solution of tryptophol (1.61g, 10.0 mmol, 1.0 equiv) and imidazole (1.36 g, 20.0 mmol, 2.0 equiv) in DMF (50 mL) at 0 °C. The ice bath was then removed and the reaction mixture was stirred at room temperature for 3 h. The mixture was quenched with water (40 mL) and extracted with EtOAc (30 mL × 3), then the combined organic layers were washed with water (30 mL × 3), brine (30 mL), separated and dried over Na_2SO_4, then filtered and concentrated under reduced pressure. The residue was used directly for the next step without further purification.

Step 2: To a solution of the above TBS-tryptophol in DMF (50 mL) was added NaH (400.0 mg, 10.0 mmol, 1.0 equiv, 60% dispersion in mineral oil) at 0 °C. After stirring at 0 °C for 15 min and then at room temperature for 1 h, the reaction mixture was cooled to 0 °C, treated with BnBr (1.88 g, 11.0 mmol, 1.1 equiv) and then allowed to stir at room temperature for 12 h. After the reaction was complete (monitored by TLC), aqueous saturated $NaHCO_3$ (30 mL) was added slowly. The organic layer was separated and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with water (30 mL × 3), brine (30 mL), separated, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel using EtOAc-hexanes for elution provided the title compound as pale yellow oil.

Preparation of 3-Halooxindoles. *General Procedure A. Step 1: Preparation of N-Substituted Isatins.*[22] Substituted isatin (20.0 mmol) was dissolved in anhydrous DMF (80 mL), and the resultant solution was cooled to 0 °C, whereupon sodium hydride (0.95 g, 24.0 mmol, 60% dispersion in mineral oil,) was added in one portion and stirred for 10 min. Halide (30.0 mmol) was added slowly and the reaction mixture was stirred at 0 °C for 30 min before stirring overnight at room temperature. The reaction mixture was then poured into saturated aqueous NH_4Cl and extracted with EtOAc (30 mL × 4). The combined organic layers were washed with water (15 mL × 3) and brine (20 mL), then dried over Na_2SO_4, filtered, and concentrated to give the crude *N*-substituted isatin product. Careful purification by column chromatography on silica gel affords the pure product.

Step 2: Preparation of 3-Hydroxyoxindoles.[22d,23] The obove *N*-substituted isatin (34 mmol, 1.0 equiv) was dissolved in dry THF (200 mL) and the solution was cooled (−78 to 0 °C). Newly purchased Grignard reagent (51 mmol, 1.5 equiv) was added dropwise via a syringe to the solution. After that, the solution was warmed to room temperature slowly and continued to stir for another several hours. Saturated aqueous NH_4Cl (50 mL) was added and the mixture was extracted with CH_2Cl_2 (50 mL × 3). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4 and concentrated under reduced pressure to yield the crude product. Careful purification by column chromatography on silica gel offords 3-hydroxyoxindole.

Step 3: Preparation of 3-Chlorooxindole.[24] A solution of 3-hydroxyoxindole (28.1 mmol, 1.0 equiv) and pyridine (281.0 mmol, 10.0 equiv) in CH_2Cl_2 (200 mL) was stirred at 0 °C under Ar atmosphere for 15 min. Thionyl chloride (112.0 mmol, 4.0 equiv) was added dropwise and the solution was stirred at room temperature for several hours. Water (50 mL) was added and the mixture extracted with CH_2Cl_2 (50 mL × 3). The combined organic layers were washed with water (50 mL × 2), saturated aqueous $NaHCO_3$ (60 mL), brine (50 mL), dried with Na_2SO_4 and concentrated under reduced pressure to yield the crude product. The crude product was purified by column chromatography on silica gel.

General Procedure B. Step 1: General Synthesis of N-Methylindole.[25] To a stirred solution of indole (17.1 mmol) in dry DMF (25 mL), NaH (820 mg, 20.5 mmol 60% suspension in mineral oil) was added in portions under N_2 atmosphere at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 30 min. After cooling to 0 °C again, MeI (1.28 mL, 20.5 mmol) was added dropwise. The reaction mixture was warmed to room temperature again and stirred overnight. The mixture was quenched with water and the aqueous layer was extracted with ether (50 mL × 3). The

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

combined organic layer was washed with water (60 mL × 3), brine (50 mL), dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel.

Step 2: Preparation of 3-Chlorooxindole.[26] Substituted indole (15.25 mmol, 1.0 equiv) was dissolved in a mixture of THF (10 mL), *t*-BuOH (100 mL) and H_2O (1 mL). *N*-Bromosuccinimide (NBS) or *N*-chlorosuccinimide (NCS) (30.49 mmol, 2.0 equiv) dissolved in cooled THF (100 mL) was added dropwise to this vigorously stirred reaction system over a period of at least 1h. Then the mixture was leaved to warm to ambient temperature and stirred for another several hours. Evaporating the solvents under reduced pressure, the resulting residue was purified by column chromatography on silica gel.

*Preparation of **17a**. Step 1: Preparation of 1-Benzyl-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-3-chloroindolin-2-one.*[26] 1-Benzyl-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-1*H*-indole (15.25 mmol, 1.0 equiv) was dissolved in a mixture of THF (10 mL), *t*-BuOH (100 mL), Et_3N (31.5 mmol, 2.0 equiv) and H_2O (1 mL). *N*-Chlorosuccinimide (NCS) (30.49 mmol, 2.0 equiv) dissolved in cooled THF (100 mL) was added dropwise to this vigorously stirred reaction system over a period of at least 1h. Then the mixture was leaved to warm to ambient temperature and stirred for 5 h. Evaporating the solvents under reduced pressure, the resulting residue was purified by column chromatography on silica gel.

*Step 2: Preparation of **17a**.*[21] The above product (10.0 mmol, 1.0 equiv) was treated with treated with *tetra*-*N*-butylammonium fluoride (TBAF) (15.0 mmol, 1.5 equiv) in dry THF. After 24 h, the mixture was worked up and purified by column chromatography on silica gel to afford the desired product **17a**.

*3-Chloro-1,3-dimethylindolin-2-one (**1a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.2 Hz, 1H), 7.38−7.34 (m, 1H), 7.15−7.12 (m, 1H), 6.86 (d, J = 8.0 Hz, 1H), 3.25 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 142.1, 131.1, 130.1, 123.8, 123.4, 108.7, 61.8, 26.6, 25.9. MS (ESI) Calculated m/z for $[M + Na]^+$ = 218.1. Experimental m/z for $[M + Na]^+$ = 218.7. Characterization data obtained for **1a** matched those previously reported in the literature.[27]

*3-Chloro-5-fluoro-1,3-dimethylindolin-2-one (**2a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.16 (m, 1H), 7.08−7.03 (m, 1H), 6.79 (dd, J = 8.6, 4.0 Hz, 1H), 3.24, (s, 3H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 159.5 (d, J = 241 Hz), 138.0 (d, J = 2 Hz), 132.4 (d, J = 9 Hz), 116.5 (d, J = 24 Hz), 111.9 (d, J = 25 Hz), 109.4 (d, J = 8 Hz), 61.4, 26.7, 25.8. MS (ESI) Calculated m/z for $[M + Na]^+$ = 236.0. Experimental m/z for $[M + Na]^+$ = 235.9. HRMS (ESI, m/z) Calculated for $[C_{10}H_{10}ClFNO]$ $[M + H]^+$ 214.0435, found 214.0429.

*3,5-Dichloro-1,3-dimethylindolin-2-one (**3a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 2.0 Hz, 1H), 7.35−7.32 (m, 1H), 6.80 (d, J = 8.4 Hz, 1H), 3.24 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 140.6, 132.5, 130.1, 128.8, 124.4, 109.7, 61.2, 26.8, 25.8. MS (ESI) Calculated m/z for $[M + Na]^+$ = 252.0. Experimental m/z for $[M + Na]^+$ = 252.2. Characterization data obtained for **3a** matched those previously reported in the literature.[27]

*5-Bromo-3-chloro-1,3-dimethylindolin-2-one (**4a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 1.6 Hz, 1H), 7.47−7.44 (m, 1H), 6.74 (d, J = 8.4 Hz, 1H), 3.21 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 141.0, 132.9, 132.7, 127.0, 115.8, 110.2, 61.1, 26.7, 25.7. MS (ESI) Calculated m/z for $[M + NH_4]^+$ = 293.0. Experimental m/z for $[M + NH_4]^+$ = 293.4. HRMS (ESI, m/z) Calculated for $[C_{10}H_{10}BrClNO]$ $[M + H]^+$ 273.9634, found 273.9629.

*3-Chloro-1,3,5-trimethylindolin-2-one (**5a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 7.14 (d, J = 8.0 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 3.22 (s, 3H), 2.36 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 139. 6, 133.1, 130.9, 130.4, 124.5, 108.4, 62.0, 26.6, 25.9, 21.0. MS (ESI) Calculated m/z for $[M + H]^+$ = 210.1. Experimental m/z for $[M + H]^+$ = 210.3. Characterization data obtained for **5a** matched those previously reported in the literature.[27]

*3-Chloro-5-methoxy-1,3-dimethylindolin-2-one (**6a**).* The general method A was followed. After fast chromatography with EtOAc/PE (75%), further purification by chromatography (14.3% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 2.4 Hz, 1H), 6.89−6.86 (m, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.83 (s, 3H), 3.23 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 156.6, 135.4, 132.1, 114.7, 110.8, 109.2, 62.1, 55.9, 26.7, 26.0; MS (ESI) Calculated m/z for $[M + H]^+$ = 226.1. Experimental m/z for $[M + H]^+$ = 226.6. HRMS (ESI, m/z) Calculated for $[C_{11}H_{13}ClNO_2]$ $[M + H]^+$ 226.0635, found 226.0629.

*3-Chloro-7-fluoro-1,3-dimethylindolin-2-one (**7a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.21 (m, 1H), 7.11−7.03 (m, 2H), 3.47 (d, J = 2.8 Hz, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 147.7 (d, J = 243 Hz), 133.7, 124.0 (d, J = 6 Hz), 119.7 (d, J = 3 Hz), 118.1 (d, J = 19 Hz), 117.9, 61.4, 29.7 (d, J = 5 Hz), 26.1. MS (ESI) Calculated m/z for $[M + Na]^+$ = 236.0. Experimental m/z for $[M + Na]^+$ = 236.0. HRMS (EI, m/z) Calculated for $[C_{10}H_9FNOCl]$ $[M]^+$ 213.0357, found 213.0354.

*3-Chloro-1,3,5,7-tetramethylindolin-2-one (**8a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (s, 1H), 6.88 (s, 1H), 3.50 (s, 3H), 2.53 (s, 3H), 2.31 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 137.3, 134.3, 133.0, 131.7, 122.4, 120.1, 61.7, 30.0, 26.2, 20.7, 18.7. MS (ESI) Calculated m/z for $[M + H]^+$ = 224.1. Experimental m/z for $[M + H]^+$ = 224.5. HRMS (ESI, m/z) Calculated for $[C_{12}H_{15}ClNO]$ $[M + H]^+$ 224.0842, found 224.0837.

*3-Chloro-1-ethyl-3-methylindolin-2-one (**9a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.2 Hz, 1H), 7.36−7.32 (m, 1H), 7.13−7.09 (m, 1H), 6.88 (d, J = 8.0 Hz, 1H), 3.78 (q, J = 7.2 Hz, 2H), 1.89 (s, 3H), 1,29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 141.1, 131.1, 130.0, 123.9, 123.1, 108.8, 61.8, 35.1, 25.8, 12.4. MS (ESI) Calculated m/z for $[M + H]^+$ = 210.1. Experimental m/z for $[M + H]^+$ = 210.4. Characterization data obtained for **9a** matched those previously reported in the literature.[27]

*3-Chloro-3-ethyl-1-methyl-7-(trifluoromethyl)indolin-2-one (**10a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 1H), 7. 56 (d, J = 7.2 Hz, 1H), 7.23−7.18 (m, 1H), 3.44 (q, J = 2.4 Hz, 3H), 2.41−2.23 (m, 2H) 0.78 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 140.8, 131.7, 127.9 (q, J = 6 Hz), 127.7, 123.2 (q, J = 270 Hz), 122.7, 113.0 (q, J = 33 Hz), 63.3, 32.8, 29.2 (q, J = 7 Hz), 8.6. MS (ESI) Calculated m/z for $[M + NH_4]^+$ = 295.1. Experimental m/z for $[M + NH_4]^+$ = 259.4. HRMS (ESI, m/z) Calculated for $[C_{12}H_{12}ClF_3NO]$ $[M + H]^+$ 278.0559, found 278.0554.

*1-Allyl-3-chloro-3-methylindolin-2-one (**11a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.42 (m, 1H), 7.33−7.27 (m, 1H), 7.13−7.09 (m, 1H), 6.85 (d, J = 8.0 Hz, 1H), 5.89−5.79 (m, 1H), 5.25 (d, J = 1.2 Hz, 1H), 5.22−5.21 (m, 1H), 4.41−4.29 (m, 2H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$)

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

δ 174.0, 141.1, 130.8, 130.6, 130.0, 123.7, 123.3, 117.7, 109.5, 61.7, 42.4, 25.8. MS (ESI) Calculated m/z for $[M + H]^+$ = 222.1. Experimental m/z for $[M + H]^+$ = 222.3. HRMS (ESI, m/z) Calculated for $[C_{12}H_{13}ClNO]$ $[M + H]^+$ 222.0685, found 222.0680.

*3-Chloro-3-ethyl-1-(prop-2-yn-1-yl)indolin-2-one (**12a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (10% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.36 (m, 2H), 7.19−7.15 (m, 1H), 7.08 (d, J = 8.0 Hz), 4. 64 (dd, J = 17.6, 2. 4 Hz, 1H), 4.42 (dd, J = 17.6, 2.4 Hz, 1H), 2.39−2.25 (m, 3H), 0.81 (t, J = 7. 6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 140.8, 130.0, 129.0, 124.2, 123.7, 109.6, 76.2, 72.7, 65.4, 32.8, 29.6, 8.7. MS (ESI) Calculated m/z for $[M + Na]^+$ = 256.1. Experimental m/z for $[M + Na]^+$ = 256.0. HRMS (ESI, m/z) Calculated for $[C_{13}H_{13}ClNO]$ $[M + H]^+$ 234.0685, found 234.0680.

*1-Benzyl-3-chloro-3-methylindolin-2-one (**13a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (7.7% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.44 (m, 1H), 7.36−7.28 (m, 5H), 7.25−7.21 (m, 1H), 7.12−7.08 (m, 1H), 6.73 (d, J = 7.6 Hz, 1H), 4.99 (d, J = 16.0 Hz, 1H), 4.90 (d, J = 16.0 Hz, 1H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 141.2, 135.1, 131.0, 130.0, 128.9, 127.8, 127.1, 123.8, 123.4, 109.7, 61.8, 44.0, 25.9. MS (ESI) Calculated m/z for $[M + H]^+$ = 272.1. Experimental m/z for $[M + H]^+$ = 272.5. Characterization data obtained for **13a** matched those previously reported in the literature.[28]

*3-Allyl-3-chloro-1-methylindolin-2-one (**14a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (10% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.2 Hz, 1H), 7.38−7.33 (m, 1H), 7.14−7.10 (m, 1H), 6.85 (d, J = 8.0 Hz, 1H), 5.60−5.50 (m, 1H), 5.13−5.06 (m, 2H), 3.23 (s, 3H), 3.03 (m, 1H), 2.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 142.6, 130.1, 130.1, 129.0, 124.5, 123.2, 120.9, 108.6, 63.9, 43.1, 26.6. MS (ESI) Calculated m/z for $[M + Na]^+$ = 244.1. Experimental m/z for $[M + Na]^+$ = 244.3. HRMS (ESI, m/z) Calculated for $[C_{12}H_{13}ClNO]$ $[M + H]^+$ 222.0685, found 222.0680.

*3-Allyl-1-benzyl-3-chloroindolin-2-one (**15a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (7.7% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.42 (m, 1H), 7.35−7.26 (m, 5H), 7.25−7.20 (m, 1H), 7.11−7.07 (m, 1H), 6.71 (d, J = 8.0 Hz, 1H), 5.59−5.49 (m, 1H), 5.168 (dd, J = 17.2, 1.2 Hz, 1H), 5.10 (dd, J = 10.2, 0.7 Hz, 1H), 5.01 (d, J = 15.6 Hz), 4.85 (d, J = 16 Hz), 3.14−3.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 141.8, 135.1, 130.2, 130.1, 128.9, 127.8, 127.2, 124.5, 123.2, 121.2, 109.7, 63.9, 44.0, 43.2. MS (ESI) Calculated m/z for $[M + H]^+$ = 298.1. Experimental m/z for $[M + H]^+$ = 298.7. HRMS (EI, m/z) Calculated for $[C_{18}H_{16}ClNO]$ $[M]^+$ 297.0920, found 297.0928.

*3-Chloro-3-ethyl-1-methylindolin-2-one (**16a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.33 (m, 2H), 7.14−7.10 (m, 1H), 6.86 (d, J = 8.0 Hz, 1H), 3,23 (s, 3H), 2.29 (qd, J = 7.2, 2.4 Hz, 2H), 0.81 (t, J = 7. 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 142.8, 130.0, 129.2, 124.1, 123.3, 108.5, 65.6, 32.5, 26.5, 8.8. MS (ESI) Calculated m/z for $[M + Na]^+$ = 232.1. Experimental m/z for $[M + Na]^+$ = 232.4. HRMS (EI, m/z) Calculated for $[C_{11}H_{12}ClNO]$ $[M]^+$ 209.0607, found 209.0609.

*1-Benzyl-3-chloro-3-(2-hydroxyethyl)indolin-2-one (**17a**).* After fast chromatography with EtOAc, further purification by chromatography (20% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.6 Hz, 1H), 7.36−7.22 (m, 6H), 7.13−7.09 (m, 1H), 6.74 (d, 8.0 Hz, 1H), 4.94 (s, 2H), 4.06−3.99 (m, 1H), 3.70−3.62 (m, 1H), 2.70−2.63 (m, 1H), 2.50−2.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 141.6, 134.9, 130.3, 129.5, 128.9, 127.9, 127.2, 124.1, 123.6, 110.0, 64.4, 59.0, 44.2, 41.2. MS (ESI) Calculated m/z for $[M + H]^+$ = 302.1. Experimental m/z for $[M + H]^+$ = 302.9. HRMS (EI, m/z) Calculated for $[C_{17}H_{16}ClNO_2]$ $[M]^+$ 301.0870, found 301.0872.

*2-(1-Benzyl-3-chloro-2-oxoindolin-3-yl)ethyl acetate (**18a**).* The general method B was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.411 (d, J = 7.2 Hz, 1H), 7.36−7.28 (m, 5H), 7.26−7.22 (m, 1H), 7.12−7.08 (m, 1H), 6.73 (d, J = 8.0 Hz), 5.00 (d, J = 15.6 Hz, 1H), 4.90 (d, J = 15.6 Hz, 1H), 4.24−4.18 (m, 1H), 3.98−3.92 (m, 1H), 2.83−2.76 (m, 1H), 2.74−2.67 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 170.4, 141.9, 135.0, 130.4, 128.9, 128.7, 127.8, 127.1, 124.4, 123.4, 109.9, 63.0, 60.0, 44.1, 37.6, 20.4. MS (ESI) Calculated m/z for $[M + NH_4]^+$ = 361.1. Experimental m/z for $[M + NH_4]^+$ = 361.4. HRMS (EI, m/z) Calculated for $[C_{19}H_{18}ClNO_3]$ $[M]^+$ 343.0975, found 343.0987.

*3-Chloro-3-cyclopropyl-1-methylindolin-2-one (**19a**).* The general method A was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (11.1% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.47−7.45 (m, 1H), 7.43−7.39 (m, 1H), 7.14−7.08 (m, 1H), 3.17 (s, 3H), 1.72−1.65 (m, 1H), 0.73−0.64 (m, 2H), 0.62−0.55 (m, 1H), 0.38−0.32 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.0, 142.2, 130.4, 127.8, 124.2, 123.0, 109.4, 66.8, 26.4, 18.1, 3.0, 2.7. MS (ESI) Calculated m/z for $[M + H]^+$ = 222.1. Experimental m/z for $[M + H]^+$ = 222.8. HRMS (ESI, m/z) Calculated for $[C_{12}H_{12}NO]$ $[M\text{-}Cl]^+$ 186.0919, found 186.0913.

*3-Bromo-1,3-dimethylindolin-2-one (**20a**).* The general method B was followed. After fast chromatography with EtOAc/PE (50%), further purification by chromatography (7.7% EtOAc/PE) provided the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.2 Hz, 1H), 7.36−7.32 (m, 1H), 7.15−7.11 (m, 1H), 6.85 (d, J = 8.0 Hz, 1H), 3.25 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 141.8, 131.6, 130.1, 124.1, 123.4, 108.7, 52.4, 26.7, 26.4. MS (ESI) Calculated m/z for $[M + H]^+$ = 240.0. Experimental m/z for $[M + H]^+$ = 240.3. Characterization data obtained for **20a** matched those previously reported in the literature.[12]

General Procedure for the Visible Light Induced Homocoupling of 3-Halooxindole. In a 10 mL snap-cap vial equipped with a magnetic stirring bar and fitted with a septum, **a** (0.15 mmol, 1.0 equiv), DBU (0.15 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.00075 mmol, 0.5 mol %) were dissolved in CH_3CN (0.06 M). The mixture was bubbled with a stream of argon for 30 min through a syringe needle. The vial was then irradiated by using two 450 nm blue LED lamps for 15 h. Upon removal of solvent under vacuum, the residue was purified by flash chromatography on silica gel to afford pure **(±)dl b** and crude **meso b**. The **meso b** can be purified by preparative TLC.

*1,1′,3,3′-Tetramethyl-[3,3′-biindoline]-2,2′-dione (**1b**) (**(±)dl**).* In a 100 mL round-bottom flask equipped with a magnetic stirring bar and fitted with a septum, **a** (1.00 g, 3.12 mmol), DBU (475 mg, 3.12 mmol), *fac*-Ir(ppy)$_3$ (10.5 mg, 0.016 mmol) were dissolved in 50 mL CH_3CN. The mixture was bubbled with a stream of argon for 30 min through a syringe needle. The vial was then irradiated by using three 450 nm blue LED lamps for 15h. Upon removal of solvent under vacuum, the residue was purified by chromatography (14% EtOAc/PE) provided pure **(±)dl 1b** (375 mg, 45.8%) and crude **meso 1b**. The crude **meso 1b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (288 mg, 35.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 7.2 Hz, 2H), 7.05−7.00 (m, 2H), 6.85−6.81 (m, 2H), 6.45 (d, J = 7.6 Hz, 2H), 3.10 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 142.6, 131.1, 128.0, 122.8, 121.7, 107.3, 51.1, 25.7, 16.0. MS (ESI) Calculated m/z for $[M + H]^+$ = 321.2. Experimental m/z for $[M + H]^+$ = 321.3. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.23 (m, 2H), 6.89−6.85 (m, 2H), 6.72 (d, J = 8.0 Hz, 2H), 6.62 (m, J = 6.4 Hz, 2H), 2.98 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 143.7, 131.1, 128.5, 123.6, 121.6, 107.9, 51.6, 25.9, 17.3. MS (ESI) Calculated m/z for $[M + H]^+$ = 321.2. Experimental m/z for $[M + H]^+$ = 321.5. Characterization data obtained for **1b** matched those previously reported in the literature.[9f]

*5,5′-Difluoro-1,1′,3,3′-tetramethyl-[3,3′-biindoline]-2,2′-dione (**2b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 2b** (10.4 mg, 39.6%) and crude **meso 2b**. The crude **meso 2b** was further purified

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

by preparative TLC with EtOAc/PE (16.7%) as solvent (13.5 mg, 51.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86−6.83 (m, 2H), 6.79−6.74 (m, 2H), 6.45−6.42 (m, 2H), 3.13 (s, 6H), 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 158.9 (d, J = 239 Hz), 138.4, 132.5 (d, J = 9 Hz), 114.4 (d, J = 23 Hz), 111.2 (d, J = 25 Hz), 107.9 (d, J = 8 Hz), 51.3, 25.9, 16.1. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}F_2N_2O_2]$ $(M + H)^+$ 357.1414, found 357.1403. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02−6.97 (m, 2H), 6.69−6.66 (m, 2H), 6.41 (d, J = 7.2 Hz, 2H), 3.00 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 158.5 (d, J = 239 Hz), 139.7, 132.2 (d, J = 8 Hz), 114.9 (d, J = 23 Hz), 11.8 (d, J = 25 Hz), 108.4 (d, J = 8 Hz), 51.8, 26.1, 17.3. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}F_2N_2O_2]$ $(M + H)^+$ 357.1414, found 357.1404.

*5,5′-Dichloro-1,1′,3,3′-tetramethyl-[3,3′-biindoline]-2,2′-dione (**3b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 3b** (11.7 mg, 40.1%) and crude **meso 3b**. The crude **meso 3b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (9.0 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05−7.01 (m, 4H), 6.43 (d, J = 8.4 Hz, 2H), 3.12 (s, 6H), 1.73 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 141.1, 132.3, 128.1, 127.4, 123.5, 108.4, 51.3, 25.9, 15.6. MS (ESI) Calculated m/z for $[M + H]^+$ = 389.1. Experimental m/z for $[M + H]^+$ = 389.2. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.26 (m, 2H), 6.69 (d, J = 8.4 Hz, 2H), 6.61 (m, 2H), 2.98 (s, 6H), 1.66 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 142.3, 132.2, 128.6, 127.1, 124.1, 108.9, 51.8, 26.1, 17.1. MS (ESI) Calculated m/z for $[M + H]^+$ = 389.1. Experimental m/z for $[M + H]^+$ = 389.4. Characterization data obtained for **3b** matched those previously reported in the literature.[29]

*5,5′-Dibromo-1,1′,3,3′-tetramethyl-[3,3′-biindoline]-2,2′-dione (**4b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 4b** (13.2 mg, 36.8%) and crude **meso 4b**. The crude **meso 4b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (19.8 mg, 55.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.17 (m, 4H), 6.39−6.37 (m, 2H), 3.12 (s, 6H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 141.6, 132.5, 131.0, 126.2, 114.6, 109.0, 51.3, 25.8, 15.4. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}Br_2N_2O_2]$ $(M + H)^+$ 476.9808, found 476.9814. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 2H), 6.73 (m, 2H), 6.65 (d, J = 8.4 Hz, 2H), 2.97 (s, 6H), 1.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 142.8, 132.5, 131.6, 126.8, 114.3, 109.4, 51.8, 26.1, 17.0. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}Br_2N_2O_2]$ $(M + H)^+$ 476.9808, found 476.9802.

*1,1′,3,3′,5,5′-Hexamethyl-[3,3′-biindoline]-2,2′-dione (**5b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 5b** (11.2 mg, 42.9%) and crude **meso 5b**. The crude **meso 5b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (12.6 mg, 48.1%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 2H), 6.83 (dd, J = 7.9, 0.8 Hz, 2H), 6.34 (d, J = 8.0 Hz, 2H), 3.08 (s, 6H), 2.21 (s, 6H), 1.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 140.2, 131.2, 131.2, 128.1, 123.8, 106.9, 51.1, 25.7, 21.0, 16.0. HRMS (ESI, m/z) Calculated for $[C_{22}H_{25}N_2O_2]$ $(M + H)^+$ 349.1911, found 349.1915. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, J = 7.6 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 6.40 (m, 6H), 2.94 (s, 6H), 2.22 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 141.4, 131.1, 130.8, 128.5, 124.6, 107.3, 51.7, 25.9, 21.1, 17.2. HRMS (ESI, m/z) Calculated for $[C_{22}H_{25}N_2O_2]$ $(M + H)^+$ 349.1911, found 349.1904.

*5,5′-Dimethoxy-1,1′,3,3′-tetramethyl-[3,3′-biindoline]-2,2′-dione (**6b**) ((±)dl).* The general method was followed. Purification by chromatography (20% EtOAc/PE) provided pure **(±)dl 6b** (9.6 mg, 34%) and crude **meso 6b**. The crude **meso 6b** was further purified by preparative TLC with EtOAc/PE (25%) as solvent (10.6 mg, 37.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.742−6.736 (m, 2H), 6.60−6.58 (m, 2H), 6.41−6.39 (m, 2H), 3.70 (s, 6H), 3.11 (s, 6H), 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 155.6, 136.0, 132.4, 112.9, 110.0, 107.7, 55.8, 51.3, 25.9, 16.5. MS (ESI) Calculated m/z for $[M + H]^+$ = 381.2. Experimental m/z for $[M + H]^+$ = 381.3. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80−6.78 (m, 2H), 6.65−6.63 (m, 2H), 6.30 (m, 2H), 3.66 (s, 6H), 2.97 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 155.1, 137.4, 132.3, 113.0, 111.2, 108.1, 55.8, 51.9, 26.0, 17.4. MS (ESI) Calculated m/z for $[M + H]^+$ = 381.2. Experimental m/z for $[M + H]^+$ = 381.5. Characterization data obtained for **3b** matched those previously reported in the literature.[30]

*7,7′-Difluoro-1,1′,3,3′-tetramethyl-[3,3′-biindoline]-2,2′-dione (**7b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 7b** (11.5 mg, 43.0%) and crude **meso 7b**. The crude **meso 7b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (10.4 mg, 39.0%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89−6.84 (m, 2H), 6.82−6.77 (m, 4H), 3.32 (d, J = 2.8 Hz, 6H), 1.74 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 147.1 (d, J = 242 Hz), 133.8, 129.3 (d, J = 9 Hz), 122.5 (d, J = 7 Hz), 118.8 (d, J = 3 Hz), 116.2 (d, J = 19 Hz), 51.4, 28.2 (d, J = 6 Hz), 16.3. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}F_2N_2O_2]$ $(M + H)^+$ 357.1409, found 357.1405. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−6.97 (m, 2H), 6.86−6.81 (m, 2H), 6.44−6.42 (m, 2H), 3.21 (d, J = 2.8 Hz, 6H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 147.5 (d, J = 242 Hz), 133.6, 130.5, 122.1 (d, J = 7 Hz), 119.4 (d, J = 4 Hz), 116.6 (d, J = 19 Hz), 51.9, 28.4 (d, J = 6 Hz), 17.5. HRMS (ESI, m/z) Calculated for $[C_{20}H_{19}F_2N_2O_2]$ $(M + H)^+$ 357.1409, found 357.1414.

*1,1′,3,3′,5,5′,7,7′-Octamethyl-[3,3′-biindoline]-2,2′-dione (**8b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 8b** (13.3 mg, 47.1%) and crude **meso 8b**. The crude **meso 8b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (12.1 mg, 42.9%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (s, 2H), 6.57 (s, 2H), 3.36 (s, 6H), 2.27 (s, 6H), 2.18 (s, 6H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 137.9, 132.0, 131.9, 130.8, 121.5, 118.3, 50.7, 29.0, 20.6, 18.7, 16.2. HRMS (ESI, m/z) Calculated for $[C_{24}H_{29}N_2O_2]$ $(M + H)^+$ 377.2224, found 377.2216. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (s, 1H), 6.19 (s, 1H), 3.19 (m, 3H), 2.43 (s, 3H), 2.12 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 139.1, 132.3, 131.6, 130.4, 112.4, 118.7, 51.3, 29.2, 20.7, 18.8, 17.1. HRMS (ESI, m/z) Calculated for $[C_{24}H_{29}N_2O_2]$ $(M + H)^+$ 377.2224, found 377.2217.

*1,1′-Diethyl-3,3′-dimethyl-[3,3′-biindoline]-2,2′-dione (**9b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 9b** (12.6 mg, 48.2%) and crude **meso 9b**. The crude **meso 9b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (11.4 mg, 43.8%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 7.6 Hz, 2H), 7.05−7.01 (m, 2H), 6.82−6.79 (m, 2H), 6.52 (d, J = 7.6 Hz, 2H), 3.82−3.73 (m, 2H), 3.61 (m, 2H), 1.76 (s, 6H), 1.21 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 141.7, 131.4, 127.9, 123.7, 121.6, 107.5, 50.5, 30.5, 16.9, 12.5. MS (ESI) Calculated m/z for $[M + H]^+$ = 349.2. Experimental m/z for $[M + H]^+$ = 349.4. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.21 (m, 2H), 6.86−6.83 (m, 2H), 6.72 (d, J = 7.6 Hz, 2H), 6.61 (m, 2H), 3.73 (m, 2H), 3.40 (m, 2H), 1.67 (s, 6H), 0.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 142.9, 131.3, 128.3, 123.9, 121.4, 107.8, 51.3, 34.2, 17.3, 11.9. MS (ESI) Calculated m/z for $[M + H]^+$ = 349.2. Experimental m/z for $[M + H]^+$ = 349.4. Characterization data obtained for **9b** matched those previously reported in the literature.[31]

*3,3′-Diethyl-1,1′-dimethyl-7,7′-bis(trifluoromethyl)-[3,3′-biindoline]-2,2′-dione (**10b**) ((±)dl).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 10b** (17.0 mg, 46.8%) and crude **meso 10b**. The crude **meso 10b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (16.8 mg, 46.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.2 Hz, 2H), 6.95−6.91 (m, 2H), 3.28 (t, J = 2.4 Hz, 6H), 2.80−2.71 (m, 2H), 2.41−2.33 (m, 2H), 0.42 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 141.2, 130.6, 126.2 (q, J = 6.0 Hz), 126.1, 123.2 (q, J = 270.0 Hz), 121.0, 111.8 (q, J = 33.0 Hz), 56.3, 28.2 (q, J = 7.0 Hz), 21.2, 8.8. HRMS (ESI, m/z) Calculated for $[C_{24}H_{23}F_6N_2O_2]$ $(M + H)^+$ 485.1641, found 485.1649. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 2H), 6.98−6.95 (m, 2H), 6.68 (m, 2H), 3.13 (d, J = 2.0 Hz, 6H), 2.75 (m, 2H), 2.05 (m, 2H), 0.44 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 142.8, 130.7, 126.9, 126.7(q, J = 6.0 Hz), 123.4 (q, J = 294.7

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

Hz), 120.8, 112.2 (q, J = 33 Hz), 56.7, 28.5 (q, J = 6.0 Hz), 22.7, 8.6. HRMS (ESI, m/z) Calculated for $[C_{24}H_{23}F_6N_2O_2]$ $(M + H)^+$ 485.1641, found 485.1650.

*1,1′-Diallyl-3,3′-dimethyl-[3,3′-biindoline]-2,2′-dione (**11b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 11b** (10.4 mg, 37.2%) and crude **meso 11b**. The crude **meso 11b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (9.5 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 7.2 Hz, 2H), 7.03−7.00 (m, 2H), 6.84−6.80 (m,2H), 6.53 (d, J = 8.0 Hz, 2H), 5.79−5.69 (m, 2H), 5.20−5.13 (m, 2H), 4.37−4.32 (m, 4H), 4.26−4.20 (m, 2H), 1.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 141.9, 131.3, 131.2, 128.0, 123.7, 121.9, 118.0, 108.4, 50.6, 42.3, 17.2. HRMS (ESI, m/z) Calculated for $[C_{24}H_{25}N_2O_2]$ $(M + H)^+$ 373.1916, found 373.1902. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.20 (m, 2H), 6.88−6.85 (m, 2H), 6.72 (d, J = 7.6 Hz, 2H), 6.64 (m, 2H), 5.47−5.35 (m, 2H), 5.05−4.97 (m, 4H), 4.35−4.29 (m, 2H), 4.00 (dd, J = 16.3, 5.8 Hz, 2H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 143.0, 131.6, 131.2, 128.3, 123.8, 121.7, 117.2, 108.8, 51.4, 42.2, 17.7. HRMS (ESI, m/z) Calculated for $[C_{24}H_{25}N_2O_2]$ $(M + H)^+$ 373.1916, found 373.1905.

*3,3′-Diethyl-1,1′-di(prop-2-yn-1-yl)-[3,3′-biindoline]-2,2′-dione (**12b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 12b** (11.2 mg, 37.8%) and crude **meso 12b**. The crude **meso 12b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (7.4 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08−7.02 (m, 4H), 6.87−6.83 (m, 2H), 6.67 (d, J = 7.6 Hz, 2H), 4.51 (dd, J = 17.6, 2.4 Hz, 2H), 4.38 (dd, J = 17.6, 2.8 Hz, 2H), 2.82 (m, 2H), 2.37 (m, 2H), 2.18 (t, J = 2.4 Hz, 2H), 0.40 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 141.6, 128.4, 127.9, 123.5, 122.6, 108.0, 76.6, 72.1, 56.9, 28.8, 22.3, 8.6. HRMS (ESI, m/z) Calculated for $[C_{26}H_{25}N_2O_2]$ $(M + H)^+$ 397.1911, found 397.1904. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.24 (m, 2H), 6.92−6.89 (m, 4H), 6.59 (d, J = 5.6 Hz), 4.45 (dd, J = 17.6, 2.0 Hz, 2H), 4.12 (dd, J = 17.6, 2.4 Hz, 2H), 2.78 (m, 2H), 2.11 (m, 2H), 0.46 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 141.5, 128.4, 127.9, 123.5, 122.6, 108.0, 76.6, 72.1, 57.0, 28.8, 22.3, 8.6. HRMS (ESI, m/z) Calculated for $[C_{26}H_{25}N_2O_2]$ $(M + H)^+$ 397.1911, found 397.1903.

*1,1′-Dibenzyl-3,3′-dimethyl-[3,3′-biindoline]-2,2′-dione (**13b**) (**(±)dl**).* The general method was followed. Purification by chromatography (11.1% EtOAc/PE) provided pure **(±)dl 13b** (11.3 mg, 32%) and crude **meso 13b**. The crude **meso 13b** was further purified by preparative TLC with EtOAc/PE (12.5%) as solvent (11.7 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.14 (m, 10H), 7.09 (d, J = 8.0 Hz, 2H), 6.98−6.95 (m, 2H), 6.71−6.67 (m, 2H), 6.49 (d, J = 8.0 Hz, 2H), 5.04 (d, J = 16.0 Hz, 2H), 4.71 (d, J = 16.0 Hz, 2H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 141.8, 135.6, 131.3, 128.7, 128.4, 127.9, 127.6, 123.5, 122.1, 108.5, 50.7, 43.7, 17.7. HRMS (EI, m/z) Calculated for $[C_{32}H_{28}N_2O_2]$ $[M]^+$ 472.2151, found 472.2154. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.13 (m, 8H), 6.97 (m, 4H), 6.84−6.80 (m, 2H), 6.70 (m, 2H), 6.59 (d, J = 8.0 Hz, 2H), 4.94 (d, J = 15.6 Hz, 2H), 4.66 (d, J = 15.6 Hz, 2H), 1.81 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 142.9, 135.8, 131.4, 128.6, 128.4, 127.1(127.14), 127.1(127.05), 123.9, 122.0, 109.2, 51.3, 43.8, 18.6. HRMS (EI, m/z) Calculated for $[C_{32}H_{28}N_2O_2]$ $[M]^+$ 472.2151, found 472.2155.

*3,3′-Diallyl-1,1′-dimethyl-[3,3′-biindoline]-2,2′-dione (**14b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 14b** (8.1 mg, 29%) and crude **meso 14b**. The crude **meso 14b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (5.6 mg, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06−6.99 (m, 4H), 6.85−6.81 (m, 2H), 6.417 (d, J = 7.6 Hz, 2H), 5.10−4.97 (m, 4H), 4.77−4.74 (m, 2H), 3.67−3.62 (m, 2H), 3.07−3.01 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 143.3, 132.5, 128.2, 128.1, 123.4, 121.6, 118.8, 107.2, 55.9, 33.2, 25.6. MS (ESI) Calculated m/z for $[M + H]^+$= 373.3. Experimental m/z for $[M + H]^+$ = 373.5. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.22 (m, 2H), 6.89−6.85 (m, 2H), 6.69 (d, J = 8.0 Hz, 2H), 6.61 (d, J = 8.0 Hz, 2H), 5.15−5.05 (m, 2H), 4.97−4.93 (m, 2H), 4.77 (dd, J = 11.6, 1.6 Hz, 2H), 3.48 (dd, J = 12.0, 7.6 Hz, 2H), 2.94 (s, 6H), 2.89 (dd, J = 13.2, 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 144.6, 132.0, 128.5, 128.4, 124.1, 121.5, 119.2, 107.8, 56.5, 34.7, 25.8. MS (ESI) Calculated m/z for $[M + H]^+$ = 373.3. Experimental m/z for $[M + H]^+$ = 373.3. Characterization data obtained for **14b** matched those previously reported in the literature.[32]

*3,3′-Diallyl-1,1′-dibenzyl-[3,3′-biindoline]-2,2′-dione (**15b**) (**(±)dl**).* The general method was followed. Purification by chromatography (9.1% EtOAc/PE) provided pure **(±)dl 15b** (6.3 mg, 16%) and crude **meso 15b**. The crude **meso 15b** was further purified by preparative TLC with EtOAc/PE (11.1%) as solvent (9.4 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (m, 14H), 7.18 (d, J = 8.0 Hz, 2H), 6.94−6.91 (m, 2H), 6.73−6.70 (m, 2H), 6.36 (d, J = 7.6 Hz, 2H), 5.13 (d, J = 15.6 Hz, 2H), 5.09−5.05 (m, 4H), 4.82−4.79 (m, 2H), 4.48 (d, J = 15.6 Hz, 2H), 3.76 (dd, J = 14.6, 3.4 Hz, 2H), 3.12 (td, J = 8.0, 4.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 142.8, 135.5, 132.5, 128.6, 128.2, 128.0, 127.6, 127.5, 124.0, 121.9, 119.2, 108.4, 55.7, 43.7, 34.1. MS (ESI) Calculated m/z for $[M + Na]^+$ = 547.3. Experimental m/z for $[M + Na]^+$ = 547.7. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.12 (m, 4H), 6.98 (m, 2H), 6.86−6.82 (m, 1H), 6.69 (m, 1H), 6.54 (d, J = 7.8 Hz, 1H), 5.19−5.09 (m, 1H), 5.02 (dd, J = 17.0, 2.0 Hz, 1H), 4.83 (dd, J = 9.8, 2.2 Hz, 1H), 4.80−4.71 (m, 2H), 3.65−3.60 (dd, J = 12.4, 7.6 Hz, 1H), 3.01−2.96 (dd, J = 13.2, 10.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 143.9, 135.7, 131.8, 128.6, 128.5 (128.54), 128.5 (128.48), 127.1, 124.3, 121.8, 119.6, 109.1, 56.3, 43.8, 35.5, 29.7. MS (ESI) Calculated m/z for $[M + Na]^+$ = 547.3. Experimental m/z for $[M + Na]^+$ = 547.4. Characterization data obtained for **15b** matched those previously reported in the literature.[32]

*3,3′-Diethyl-1,1′-dimethyl-[3,3′-biindoline]-2,2′-dione (**16b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 16b** (10.2 mg, 39.0%) and crude **meso 16b**. The crude **meso 16b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (9.9 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−7.00 (m, 4H), 6.85−6.81 (m, 2H), 6.43−6.41 (m, 2H), 3.08 (s, 6H), 2.85−2.76 (m, 2H), 2.40−2.31 (m, 2H), 0.41 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 143.6, 128.7, 127.9, 123.1, 121.6, 107.1, 57.4, 25.5, 21.5, 8.9. HRMS (ESI, m/z) Calculated for $[C_{22}H_{25}N_2O_2]$ $(M + H)^+$ 349.1911, found 349.1914. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.22 (m, 2H), 6.88−6.84 (m, 2H), 6.70 (d, J = 8.0 Hz, 2H), 6.55 (m, 2H), 2.96 (s, 6H), 2.81−2.72 (m, 2H), 2.15−2.06 (m, 2H), 0.44 (t, J = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 144.8, 128.8, 128.3, 123.9, 121.4, 107.6, 57.9, 25.7, 23.0, 8.6. HRMS (ESI, m/z) Calculated for $[C_{22}H_{25}N_2O_2]$ $(M + H)^+$ 349.1911, found 349.1912.

*1,1′-Dibenzyl-3,3′-bis(2-hydroxyethyl)-[3,3′-biindoline]-2,2′-dione (**17b**) (**(±)dl**).* The general method was followed. Purification by chromatography (33% EtOAc/CH_2Cl_2) provided pure **(±)dl 17b** (10.0 mg, 25.0%) and crude **meso 17b**. The crude **meso 17b** was further purified by preparative TLC with EtOAc/CH_2Cl_2 (33%) as solvent (8.0 mg, 20%). ^{1}H NMR (400 MHz, d_6) δ 7.32−7.23 (m, 10H), 6.95−6.91 (m, 2H), 6.90−6.88 (m, 2H), 6.71−6.67 (m, 2H), 6.52 (d, J = 8.0 Hz, 2H), 5.15 (d, J = 16.0 Hz, 2H), 4.45−4.41 (m, 4H), 3.08−3.01 (m, 2H), 2.85−2.81 (m, 4H), 2.44−2.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 142.9, 135.6, 128.6, 128.3, 127.7, 127.6, 127.2, 124.1, 121.7, 108.7, 59.6, 54.2, 44.1, 32.0. MS (ESI) Calculated m/z for $[M + H]^+$ = 533.3. Experimental m/z for $[M + H]^+$ = 533.2. (meso): ^{1}H NMR (400 MHz, d_6) δ 7.22−7.17 (m, 8H), 7.00 (m, 4H), 6.84 (m, 2H), 6.67−6.45 (m, 4H), 4.70−4.63 (m, 4H), 4.48−4.45 (m, 2H), 3.00−2.92 (m, 4H), 2.73−2.68 (m, 2H), 2.40−2.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 143.9, 135.7, 128.9, 128.6, 128.1, 127.3, 127.1, 124.3, 122.0, 109.4, 59.3, 44.2, 34.0, 29.7. MS (ESI) Calculated m/z for $[M + H]^+$ = 533.3. Experimental m/z for $[M + H]^+$ = 533.4. Characterization data obtained for **17b** matched those previously reported in the literature.[9b,32]

*(1,1′-Dibenzyl-2,2′-dioxo-[3,3′-biindoline]-3,3′-diyl)bis(ethane-2,1-diyl) diacetate (**18b**) (**(±)dl**).* The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 18b** (12.5 mg, 27.0%) and crude **meso 18b**. The crude **meso 18b** was further purified by preparative TLC with EtOAc/PE (16.7%)

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

as solvent (12.1 mg, 26.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.26 (m, 10H), 7.01−6.94 (m, 4H), 6.68−6.64 (m, 2H), 6.43 (d, J = 8.0 Hz, 2H), 5.01 (d, J = 15.6 Hz, 2H), 4.61 (d, J = 15.6 Hz, 2H), 3.89 (d, J = 12.0, 6.0 Hz, 2H), 3.51 (td, J = 11.2, 6.0 Hz, 2H), 3.39−3.32 (m, 2H), 2.78−2.71 (m, 2H), 1.77 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 170.5, 142.8, 135.3, 128.7, 128.5, 127.72, 127.69, 126.9, 124.1, 122.1, 108.7, 6.9, 54.0, 44.1, 28.1, 20.1. HRMS (ESI, m/z) Calculated for $[C_{38}H_{37}N_2O_6]$ $(M + H)^+$ 617.2646, found 617.2636. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.13 (m, 4H), 6.99 (m, 2H), 6.83 (m, 1H), 6.66−6.56 (m, 2H), 4.86 (d, J = 15.7 Hz, 1H), 4.69 (m, 1H), 3.81−3.72 (m, 2H), 3.22 (m, 1H), 2.65−2.58 (m, 1H), 1.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 170.5, 143.8, 135.5, 128.9, 128.6, 127.9, 127.3, 127.0, 124.3, 122.1, 109.5, 60.7, 54.6, 44.1, 29.6, 20.4. HRMS (ESI, m/z) Calculated for $[C_{38}H_{37}N_2O_6]$ $(M + H)^+$ 617.2646, found 617.2632.

3,3′-Dicyclopropyl-1,1′-dimethyl-[3,3′-biindoline]-2,2′-dione (19b) ((±)dl). The general method was followed. Purification by chromatography (14% EtOAc/PE) provided pure **(±)dl 19b** (12.0 mg, 43.0%) and crude **meso 19b**. The crude **meso 19b** was further purified by preparative TLC with EtOAc/PE (16.7%) as solvent (10.0 mg, 35.8%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 7.2 Hz, 2H), 7.04−7.00 (m, 2H), 6.83−6.79 (m, 2H), 6.45 (d, J = 8.0 Hz, 2H), 3.07 (s, 6H), 2.34−2.27 (m, 2H), 0.810−0.746 (m, 2H), 0.66−0.59 (m, 2H), 0.53−0.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 142.9, 129.3, 127.9, 123.4, 121.6, 107.2, 55.8, 25.6, 11.5, 2.01, 2.05. HRMS (ESI, m/z) Calculated for $[C_{24}H_{25}N_2O_2]$ $(M + H)^+$ 373.1911, found 373.1904. (meso): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.22 (m, 1H), 6.81−6.78 (m, 1H), 6.70 (d, J = 7.6 Hz, 1H), 6.59 (m, 1H), 3.01 (s, 3H), 2.38−2.31 (m, 1H), 0.80−0.73 (m, 1H), 0.57−0.51 (m, 1H), 0.39−0.32 (m, 1H), (−0.42)−(−0.48) (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 145.2, 128.9, 125.9, 125.7, 121.1, 107.9, 56.4, 26.1, 11.3, 4.3, −0.5. HRMS (ESI, m/z) Calculated for $[C_{24}H_{25}N_2O_2]$ $(M + H)^+$ 373.1911, found 373.1904.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01045.

Characterization data, spectral data, and crystal data for **16b** (PDF)
Crystal data (CIF)
Crystal data (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: liuqiang@lzu.edu.cn.
*E-mail: lzwu@mail.ipc.ac.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the Ministry of Science and Technology of China (2013CB834804), NSFC (21572090 and 21172102), and the fundamental research funds for the central universities (lzujbky-2015-49).

■ REFERENCES

(1) Billington, D. C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 2.1.
(2) Fanta, P. E. *Chem. Rev.* **1964**, *64*, 613.
(3) (a) Durandetti, M.; Nédélec, J.-Y.; Périchon, J. *J. Org. Chem.* **1996**, *61*, 1748. (b) Everson, D. A.; Shrestha, R.; Weix, D. J. *J. Am. Chem. Soc.* **2010**, *132*, 920. (c) Everson, D. A.; Jones, B. A.; Weix, D. J. *J. Am. Chem. Soc.* **2012**, *134*, 6146.
(4) (a) Colon, I.; Kelsey, D. R. *J. Org. Chem.* **1986**, *51*, 2627. (b) Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203. (c) Peng, Y.; Luo, L.; Yan, C.-S.; Zhang, J.-J.; Wang, Y.-W. *J. Org. Chem.* **2013**, *78*, 10960.
(5) (a) Barrero, A. F.; Mar Herrador, M.; del Moral, J. F. Q.; Arteaga, P.; Arteaga, J. F.; Piedra, M.; Sánchez, E. M. *Org. Lett.* **2005**, *7*, 2301. (b) Barrero, A. F.; Mar Herrador, M.; del Moral, J. F. Q.; Arteaga, P.; Arteaga, J. F.; Diéguez, H. R.; Sánchez, E. M. *J. Org. Chem.* **2007**, *72*, 2988.
(6) Sato, K.; Inoue, Y.; Mori, T.; Sakaue, A.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *Org. Lett.* **2014**, *16*, 3756.
(7) (a) Movassaghi, M.; Schmidt, M. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3725. (b) Kim, J.; Ashenhurst, J. A.; Movassaghi, M. *Science* **2009**, *324*, 238. (c) Kim, J.; Movassaghi, M. *J. Am. Chem. Soc.* **2010**, *132*, 14376.
(8) Fang, C.-L.; Horne, S.; Taylor, N.; Rodrigo, R. *J. Am. Chem. Soc.* **1994**, *116*, 9480.
(9) (a) Hendrickson, J. B.; Goschke, R.; Rees, R. *Tetrahedron* **1964**, *20*, 565. (b) Overman, L. E.; Paone, D. V.; Stearns, B. A. *J. Am. Chem. Soc.* **1999**, *121*, 7702. (c) Guo, Ch.; Song, J.; Huang, J-Zh.; Chen, P.-H.; Luo, Sh-W.; Gong, L-Zh. *Angew. Chem., Int. Ed.* **2012**, *51*, 1046. (d) Liu, R.-R.; Zhang, J.-L. *Org. Lett.* **2013**, *15*, 2266. (e) Trost, B. M.; Osipov, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 9176. (f) Ghosh, S.; Chaudhuri, S.; Bisai, A. *Org. Lett.* **2015**, *17*, 1373.
(10) (a) Hall, E. S.; McCapra, F.; Scott, A. I. *Tetrahedron* **1967**, *23*, 4131. (b) Hino, T.; Kodato, S.; Takahashi, K.; Yamaguchi, H.; Nakagawa, M. *Tetrahedron Lett.* **1978**, *19*, 4913.
(11) For selective reviews, see: (a) Narayanam, J. M. R.; Stephenson, C. R. *Chem. Soc. Rev.* **2011**, *40*, 102. (b) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (c) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (d) Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176.
(12) Zou, Y.-Q.; Guo, W.; Liu, F.-L.; Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Green Chem.* **2014**, *16*, 3787.
(13) (a) Wei, X.-J.; Yang, D.-T.; Wang, L.; Song, T.; Wu, L.-Z.; Liu, Q. *Org. Lett.* **2013**, *15*, 6054. (b) Wang, L.; Ma, Z.-G.; Wei, X.-J.; Meng, Q.-Y.; Yang, D.-T.; Du, S.-F.; Chen, Z.-F.; Wu, L.-Z.; Liu, Q. *Green Chem.* **2014**, *16*, 3752. (c) Wang, L.; Wei, X.-J.; Jia, W.-L.; Zhong, J.-J.; Wu, L.-Z.; Liu, Q. *Org. Lett.* **2014**, *16*, 5842.
(14) (a) Hironaka, K.; Fukuzumi, S.; Tanaka, T. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1705. (b) Kern, J.-M.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1987**, 546. (c) Pratsch, G.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 11388.
(15) Beckwith, A. L. J.; Bowry, V. W. *J. Am. Chem. Soc.* **1994**, *116*, 2710.
(16) (a) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 539. (b) Pitre, S. P.; McTiernan, C. D.; Ismaili, H.; Scaiano, J. C. *ACS Catal.* **2014**, *4*, 2530.
(17) Xie, J.; Shi, S.; Zhang, T.; Mehrkens, N.; Rudolph, M.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2015**, *54*, 6046.
(18) (a) Fischer, H. *Chem. Rev.* **2001**, *101*, 3581. (b) Studer, A. *Chem. - Eur. J.* **2001**, *7*, 1159.
(19) Zuo, Z.-W.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2014**, *136*, 5257.
(20) Bajtos, B.; Pagenkopf, B. L. *Org. Lett.* **2009**, *11*, 2780.
(21) Han, L.; Liu, C.; Zhang, W.; Shi, X.-X.; You, S.-L. *Chem. Commun.* **2014**, *50*, 1231.
(22) (a) Trost, B. M.; Frederiksen, M. U. *Angew. Chem., Int. Ed.* **2005**, *44*, 308. (b) Shintani, R.; Inoue, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 3353. (c) Jiang, X.-X.; Cao, Y.-M.; Wang, Y.-Q.; Liu, L.-P.; Shen, F.-F.; Wang, R. *J. Am. Chem. Soc.* **2010**, *132*, 15328. (d) Trost, B. M.; Xie, J.; Sieber, J. D. *J. Am. Chem. Soc.* **2011**, *133*, 20611.
(23) Ma, S.; Han, X.-Q.; Krishnan, S.; Virgil, S. C.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 8037.
(24) Goldberg, F. W.; Magnus, P.; Turnbull, R. *Org. Lett.* **2005**, *7*, 4531.
(25) Su, Y.-M.; Hou, Y.; Yin, F.; Xu, Y.-M.; Li, Y.; Zheng, X.-Q.; Wang, X.-S. *Org. Lett.* **2014**, *16*, 2958.
(26) (a) Hinman, R. L.; Bauman, C. P. *J. Org. Chem.* **1964**, *29*, 1206. (b) Fuchs, J. R.; Funk, R. L. *J. Am. Chem. Soc.* **2004**, *126*, 5068.

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181

(27) Aoyama, H.; Omote, Y.; Hasegawa, T.; Shiraishi, H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1556.
(28) Thomson, J. E.; Kyle, A. F.; Gallagher, K. A.; Lenden, P.; Concellón, C.; Morrill, L. C.; Miller, A. J.; Joannesse, C.; Slawin, A. M. Z.; Smith, A. D. *Synthesis* **2008**, *2008*, 2805.
(29) Kato, T.; Inada, A.; Morita, Y.; Miyamae, H. *Chem. Pharm. Bull.* **1985**, *33*, 5270.
(30) Longmore, R. B.; Robinson, B. *Collect. Czech. Chem. Commun.* **1967**, *32*, 2184.
(31) Lee, H. J.; Lee, S.; Lim, J. W.; Kim, J. N. *Bull. Korean Chem. Soc.* **2013**, *34*, 2447.
(32) Ghosh, S.; Chaudhuri, S.; Bisai, A. *Chem. - Eur. J.* **2015**, *21*, 17479.

DOI: 10.1021/acs.joc.6b01045
J. Org. Chem. 2016, 81, 7172−7181