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KO^{t}Bu-Mediated Synthesis of Dimethylisoindolin-1-ones and Dimethyl-5-phenylisoindolin-1-ones: Selective C−C Coupling of an Unreactive Tertiary sp^3 C−H Bond

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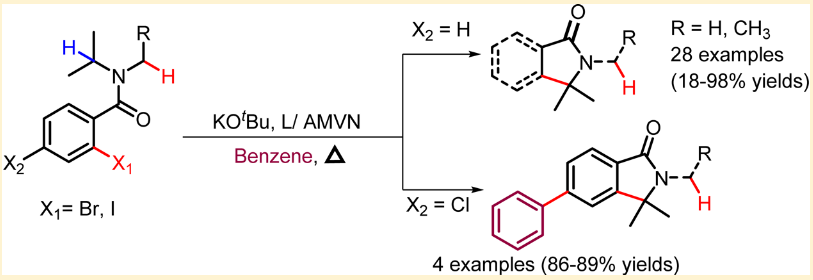
Supporting Information



ABSTRACT: A new reaction for the synthesis of dimethylisoindolinones has been presented from 2-halo-*N*-isopropyl-*N*-alkylbenzamide substrates and KO^{t}Bu by the selective C−C coupling of an unreactive tertiary sp^3 C−H bond. The reaction manifested an excellent selectivity toward a tertiary sp^3 C−H bond over primary or *sec* C−H bond. Moreover, biaryl C−C coupling along with alkyl−aryl C−C coupling can be achieved in one pot using dihalobenzamides for the synthesis of biaryl 5-phenylisoindolin-1-ones. It seems that the reaction proceeds via a radical pathway in which the aryl radical translocates via 1,5-hydrogen atom transfer (HAT), forming a tertiary alkyl carbon-centered radical. The generated tertiary alkyl radical could attack the benzamide ring in a 5-*exo*/*endo*-trig manner followed by the release of an electron and a proton, leading to a five-membered isoindolinone ring. HAT seems to be responsible for the selective functionalization of the tertiary alkyl group over primary and secondary C−H bonds.

■ INTRODUCTION

Selective functionalization of unreactive tertiary alkyl C−H bonds for carbon−carbon coupling reactions is highly desirable for the synthesis of organic molecules bearing a quaternary carbon center. For the functionalization of a C−H bond, a transition-metal catalyst, particularly palladium, is often employed for carbon−carbon coupling reactions. Transition-metal-free approaches are also being studied for the construction of carbon−carbon bonds as an alternative. Recently, the use of potassium *tert*-butoxide reagent for the promotion of carbon−carbon bond formation has aroused interest in synthetic chemistry due to its ready availability and nontoxicity. KO^{t}Bu-mediated inter- and intramolecular sp^2−sp^2 and activated sp^3−sp^2 carbon−carbon coupling reactions have been reported in recent times.[1−4] Herein, we present the KO^{t}Bu-mediated synthesis of isoindolin-1-ones from 2-halo-*N*-isopropyl-*N*-alkylbenzamide substrates by the selective C−C coupling of an unreactive tertiary sp^3 C−H bond, which has not been reported by any method (Scheme 1). The only recent report is on Ni-catalyzed synthesis of isoindolinones.[5] Nonetheless, the reaction was noted to be unselective toward secondary and tertiary alkyl C−H bonds.

The isoindolin-1-one core is present in a broad range of biologically relevant molecules having a wide range of medicinal properties such as anti-inflammatory, antihypertensive, anti-ulcer, and antileukemic.[6] As a result, several synthetic routes have been developed for the preparation of isoindolinones such as Grignard or lithiation procedures, reduction of phthalaldehyde, and transition-metal-catalyzed constructions.[7,8] Nonetheless, there is only one report on the synthesis of dimethylisoindolin-1-one **1** bearing a quaternary carbon center in the ring in which 2-isoindoline-1,3-dione is converted into indolinone by the reaction of zinc, followed by the addition of potassium amide base and methyl iodide.[9] On the other hand, several methods on the coupling of activated alkyl C−H bonds with aniline rings have been studied for the synthesis of oxindole, a moiety closely related to isoindolin-1-one.[10] A method which is transition metal free and requires readily accessible substrates and reagents would be highly desirable for the synthesis of isoindolinones. *N*,*N*-Diisopropylamide is used as an ortho directing and protecting group for acids for ortho-

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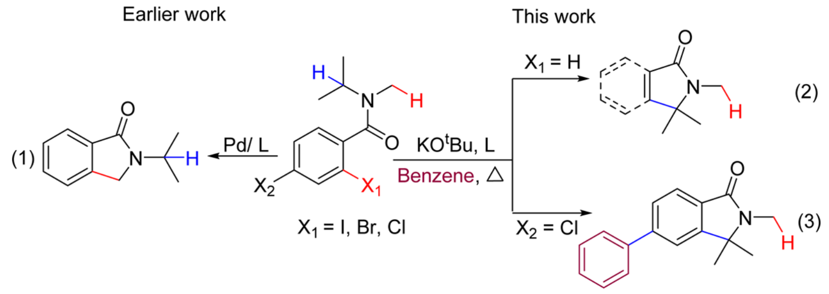
Scheme 1. C−C Coupling in 2-Halo-*N*,*N*-dialkylbenzamide

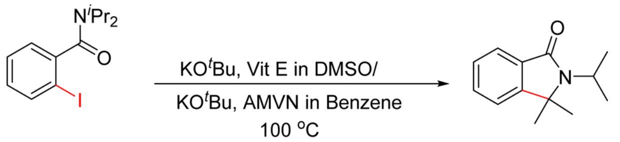


metalation reactions and is noted to be unreactive even in the presence of a strong base such as *t*-BuLi.[11] Palladium-catalyzed C−H functionalization in carboxamide has been reported; however, Pd shows selectivity toward the methyl group over a tertiary C−H bond (Scheme 1, eq 1).[12] Here, selective formation of a tertiary alkyl−aryl carbon−carbon bond is realized while studying intermolecular biaryl coupling in 2-iodo-*N*,*N*-diisopropylbenzamide (Scheme 2).[13] The presented reaction shows excellent selectivity toward a tertiary C−H bond over primary methyl and secondary ethyl C−H bonds (Scheme 1, eq 2). Moreover, arylation of the benzamide ring could be achieved along with alkylation in one pot from 4-chloro-2-iodobenzamides (Scheme 1, eq 3).

■ RESULTS AND DISCUSSION

We started optimizing the reaction conditions using 2-iodo-*N*,*N*-diisopropylbenzamide in various solvents using KO^{t}Bu (Scheme 2). Optimization of the reaction conditions is presented in the Supporting Information (Table S1, page S2; for the crystal structure of isoindolinone **1**, see Figure S126, page S131). Potassium *tert*-butoxide alone was noted to be ineffective in benzene; however, it yielded 86% of isoindolinone **1** in DMSO and 10% substrate was recovered. Addition of a catalytic amount (5 mol %) of vitamin E, a phenolic natural product, to the reaction mixture not only led to the complete conversion of the substrate into isoindolinone **1** but also reduced the reaction time from 12 to 3 h. 2-Bromo- and 2-chloro-*N*,*N*-diisopropylbenzamide substrates were found to be less reactive in DMSO; however, they gave a good yield of **1** in benzene in the presence of the radical initiator azomethylvaleronitrile (AMVN).

Scheme 2. Optimization of Reaction Conditions

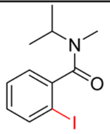
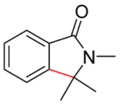
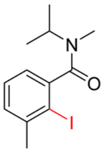
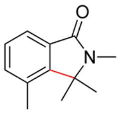
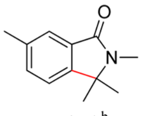
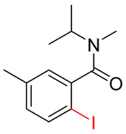
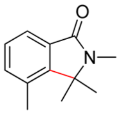
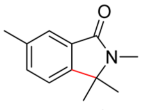
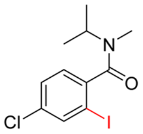
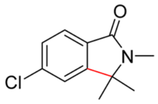
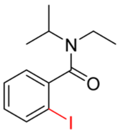
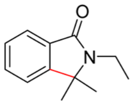
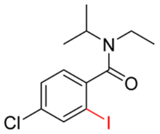
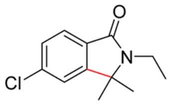
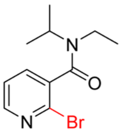
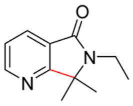
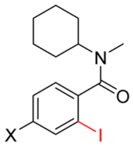
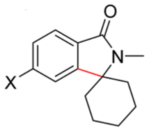
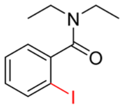
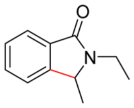
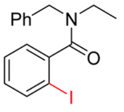
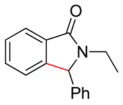
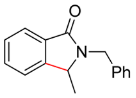
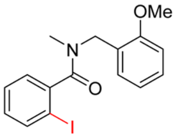
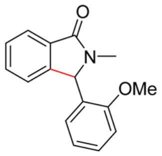
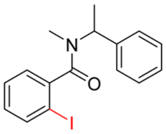
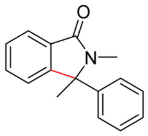
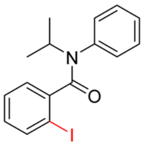
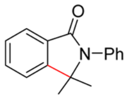
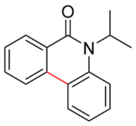


1 (98%)

After screening for various reaction conditions, we decided to use vitamin E as an additive in DMSO for iodo substrates and AMVN as a radical initiator in benzene for bromo- and chlorobenzamides. Various *N*-alkyl-substituted 2-halobenzamides were explored to study the selectivity in the KO^{t}Bu-mediated alkyl−aryl coupling reactions (Table 1). We began with *N*-methyl-*N*-isopropyl substrates (entries 1−4, Table 1) and noticed that the reaction showed excellent selectivity toward a tertiary isopropyl C−H bond over a methyl C−H bond, as **1−4** were obtained exclusively under the optimized reaction conditions. We have also studied the memory of positions in the reaction by using 2-iodo-*N*-isopropyl-*N*,3-dimethylbenzamide and 2-iodo-*N*-isopropyl-*N*,5-dimethylbenzamide substrates (entries 2 and 3, Table 1). Both substrates gave nearly the same ratio (64:36 vs 70:30) of isomers **3a** and **3b**, which suggests that the memory of the positions is not the determining factor for the selective formation of regioisomers in this study. Next, selectivity toward an ethyl vs an isopropyl group was studied (entries 5−7, Table 1). To our delight, the tertiary isopropyl C−H bond showed reactivity over the ethyl C−H bond in the C−C coupling reaction and dimethylisoindolinones **5−7** were obtained in good yields. Interestingly, benzamides having a cyclohexyl substitutent (entries 8 and 9, Table 1) also underwent C−C coupling reactions and 2′-methylspiro[cyclohexane-1,1′-isoindolin]-3′-ones **9** and **10** were obtained selectively in 94 and 93% yields, respectively. After this, *N*,*N*-dialkylbenzamides having only primary or secondary C−H bonds were studied in the reaction (entry 10, Table 1). *N*,*N*-Diethyl-2-iodobenzamide gave a 26% yield of C−C coupled product **10** and the reaction was observed to be sluggish. *N*,*N*-Dimethyl-2-iodobenzamide substrate did not produce even traces of C−C coupled product, which demonstrated the selectivity of this reaction toward a tertiary C−H bond. Next, *N*-methyl-*N*-benzylic-2-iodobenzamide substrates were used in KO^{t}Bu-mediated alkyl−aryl C−C coupling (entries 11−13, Table 1). The reaction showed selectivity toward the benzylic C−H bond and benzylic isoindolinones **11−13** were obtained as major products. In the end, selectivity toward aromatic versus isopropyl C−H bonds was evaluated by using *N*-isopropyl-*N*-phenyl-2-iodobenzamide substrate. Unfortunately, the reaction was selective toward sp^2 C−H bonds and yielded a 70:30 ratio of phenanthridinone **14b**, an sp^2−sp^2 C−C coupled product, and indolinone **14a**, an sp^3−sp^2 C−C coupled product, respectively.

Next, benzamide ring substituted substrates were investigated in the KO^{t}Bu-mediated reaction (entries 2−4 and 6−9, Table 1, and Table 2). Various functional groups such as nitro, chloro, methyl, methoxy, and dimethoxy have shown compatibility with the reaction conditions. A substrate with the chloro substituent para to the amide functionality gave the single regioisomers **4**, **6**, **9**, and **15** (entries 4, 6, 9, Table 1, and entry 1, Table 2). A 3-nitrobenzamide substrate also gave one regioisomer, **16**, as the major product (entry 2, Table 2). 2-Chloro-*N*,*N*-diisopropyl-5-nitrobenzamide failed to provide a C−C coupled product and yielded a hydroxylated product, 2-hydroxy-*N*,*N*-diisopropyl-5-nitrobenzamide (see the Experimental Section). Next, dimethoxybenzamide substrate also afforded the single regioisomer **17** (entry 3, Table 2). On the other hand, methyl-substituted benzamides (entries 2 and 3, Table 1, and entry 4, Table 2) gave the two regioisomers **3a**,**b**

Table 1. Coupling of *N*-Alkyl-Substituted Arylbenzamides

Entry	Substrate	Isoindolinone (Yield)[a]
1		 **2** (90)
2[b]		 **3a** (70)  **3b** (20)[b]
3[b]		 **3a** (68)  **3b** (18)[b]
4		 **4** (92)
5		 **5** (89)
6		 **6** (92)
7[c]		 **7** (75)
8 9		 **8** X, H (94) **9** X, Cl (93)
10		 **10** (26)
11[b]		 **11a** (68)  **11b**(10)[b]
12		 **12** (60)
13		 **13** (70)
14[b]		 **14a** (27)  **14b** (64)[b]

[a] Isolated yields. Isoindolinones were obtained from iodo substrates by using KO^{t}Bu (3 equiv) and vitamin E (5 mol %) in DMSO (procedure A). [b] Two regioisomers were obtained, and both were isolated. [c] Isoindolinone **7** was obtained from the bromo substrate using KO^{t}Bu (3 equiv) and AMVN (10 mol %) in benzene (procedure B).

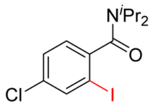
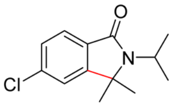
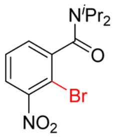
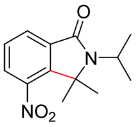
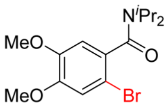
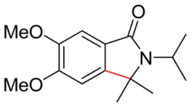
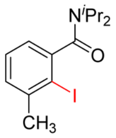
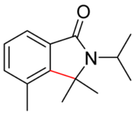
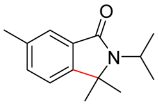
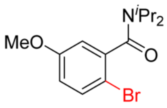
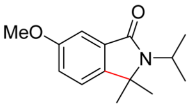
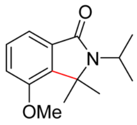
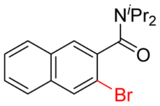
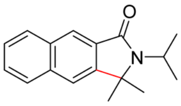
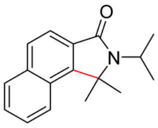
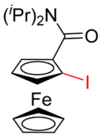
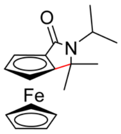
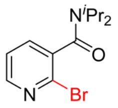
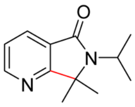
and **18a**,**b**, respectively. Similarly, 5-methoxy-substituted benzamide reacted to give the two regioisomers **19a**,**b** (entry 5, Table 2). After exploring benzene-based substrates, we tested different aryl *N*,*N*-diisopropylcarboxamides under the reaction conditions (entry 7, Table 1, and entries 6−8, Table 2). To our delight, not only naphthyl and pyridyl amides but also ferrocenylamide showed amenability to the reaction conditions and produced the respective novel ferrocenylisoindolinone **21** quantitatively. The structure of ferrocenylisoindolinone **21** has also been established by an X-ray single-crystal structure study (see the Supporting Information, Figure S127, page S132).[14]

After exploring the tertiary sp^3 C−H bond coupling reaction, we envisioned synthesizing isoindolinones containing a biaryl core in a single pot (Scheme 3). Biaryl cores are privileged structures having numerous applications in pharmaceuticals, agrochemicals, and materials.[15]

For this purpose, readily accessible 4-chloro-2-iodo-*N*,*N*-dialkylbenzamides were exploited in the KO^{t}Bu-mediated reaction. In the presence of excess KO^{t}Bu, the reaction yielded the desired biaryls, 5-phenylisoindolin-1-ones **23**−**26**, in 86−89% yields in one pot on heating for a longer period of time. The coupling of 4-chloro-2-iodo-*N*,*N*-diisopropylbenzamide with benzene only occurred in the presence of AMVN initiator under the harsh reaction conditions. The formation of 5-phenylisoindolinone **23** was not observed under the vitamin E catalyzed reaction conditions. 5-Phenylisoindolinone **23** has also been characterized by an X-ray single-crystal structure study (see the Supporting Information, Figure S128, page S133). It is worth noting that the reaction proceeds in a sequential manner: first the intramolecular alkyl−aryl C−C coupled product isoindolinone **1** was formed, followed by sp^2−sp^2 biaryl coupling of **1** with benzene leading to biaryl **23**.[16]

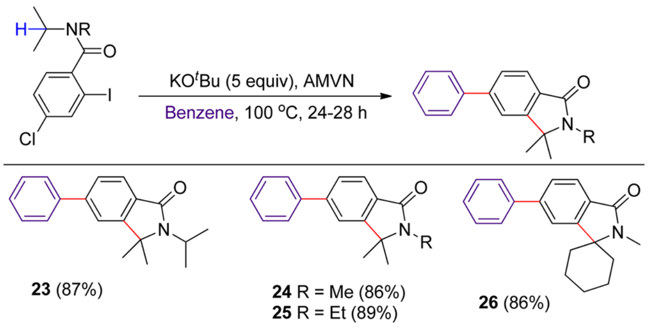
A plausible mechanism is depicted in Scheme 4, and detailed vitamin E catalyzed and AMVN-mediated mechanisms are presented in the Supporting Information (pages S2−S3). On the basis of the regioselective tertiary sp^3 C−H bond functionalization over methyl or ethyl substituents in this study and KO^{t}Bu-mediated biaryl coupling reactions,[1−3] it is reasonable to assume that the reaction proceeds via a radical pathway. It seems that the electron transfer from KO^{t}Bu to 2-iodobenzamamide leads to the radical anion **I**, as in the presence of vitamin E the rate of reaction increases considerably, which is a good one-electron donor in the radical chain reactions.[17] Radical anion **I** may produce phenyl radical **II**

Table 2. Coupling of 2-Iodo-*N*,*N*-diisopropylarylamides[a]

Entry	Substrate	Product	Yield (%)
1			**15** (96)
2[b]			**16** (44)
3[b]			**17** (67)
4[c]		 **18a**  **18b**	**18a** (80) **18b** (18)
5[d]		 **19a**  **19b**	**19a/19b** (68)
6[c]		 **20a**  **20b**	**20a** (60) **20b** (34)
7			**21** (96)
8[b]			**22** (79)

[a] The reaction was carried out on a 1 mmol scale using 2-halobenzamide substrates. Procedure A was applied for iodo substrates and procedure B was applied for bromo susbstrates. [b] The formation of a single isomer was noted and established by GC-MS analysis of the crude reaction mixture. [c] Two regioisomers were obtained, and both were isolated. [d] The combined yield for both isomers is presented, and the isomers were not separated.

Scheme 3. Synthesis of 5-Phenylisoindolinones

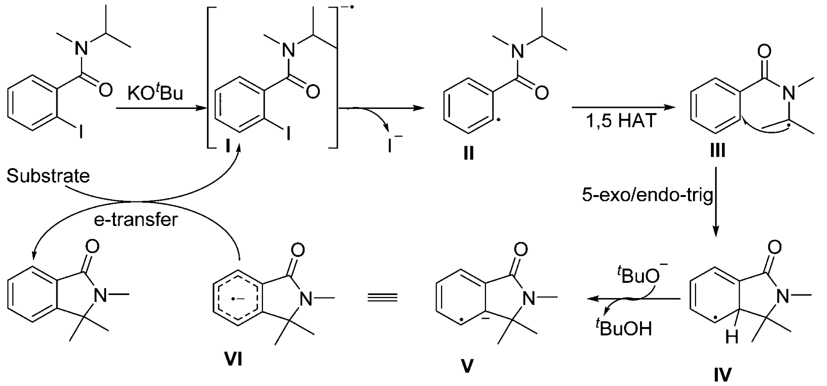


upon the release of iodide. 1,5-Hydrogen atom transfer reaction led to the tertiary alkyl radical **III**. This seems to be the key step in this transformation and could be the reason for the excellent selectivity toward a tertiary C−H bond. The alkyl radical **III** would attack the benzamide ring in a 5-*exo*/*endo*-trig manner, leading to the cyclohexadienyl radical **IV**. Abstraction of a proton from radical **IV** would give radical anion **V**. Finally radical anion **V** donates an electron to the 2-iodobenzamide substrate, leading to the radical anion **I** and thus completing the radical chain reaction with the concomitant release of isoindolinone **1**. Biaryl isoindolinone **23** could be realized by the coupling of 5-chloro-2-isopropyl-3,3-dimethylisoindolin-1-one **15** with benzene (see the proposed mechanism in the Supporting Information, page S4).[1,2c]

■ SUMMARY

In conclusion, a transition-metal-free selective carbon−carbon coupling of an unreactive tertiary alkyl C−H bond has been achieved, which has not been reported earlier by any method.

Scheme 4. Proposed Mechanism for sp^3-C−H Coupling



Potassium *tert*-butoxide mediated coupling of a tertiary sp^3 C−H bond was successfully employed with a series of 2-halobenzamides such as ferrocene-, pyridine-, and naphthalene-derived substrates to furnish diversified isoindolinones. The presented methodology enables the construction of biologically relevant isoindolinone and biarylisoindolinone organic molecules from monohalo- and dihalobenzamides, respectively, in a single pot. Further application and understanding of the reaction, particularly the enantioselective version, are currently in progress in our laboratory.

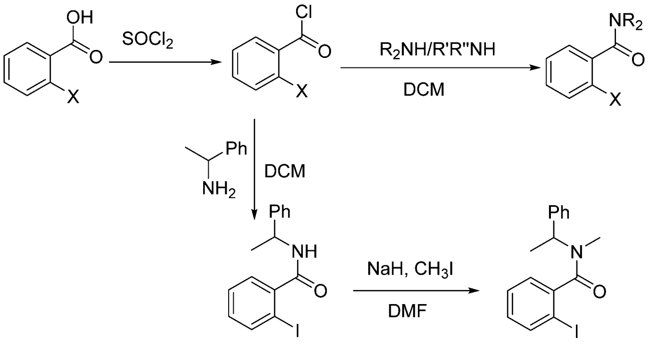
EXPERIMENTAL SECTION

General Experimental Details. All NMR experiments were carried out on a 400 MHz spectrometer. $CDCl_3$ and NMR chemical shifts are reported in ppm referenced to the solvent peaks of $CDCl_3$ (7.26 ppm for ^1H and 77.16 (±0.06) ppm for ^{13}C, respectively). High-resolution mass analysis was performed on a quadrupole time of flight (Q-TOF) mass spectrometer equipped with an ESI source (positive). DMF and DMSO with seal septa and 1,10-phenanthroline were used as received. Benzene and mesitylene were dried over calcium hydride and freshly distilled before use. Potassium *tert*-butoxide (98% purity) was used as purchased and stored in a desiccator. Silica gel (100−200 mesh size) was used for column chromatography. TLC analysis of reaction mixtures was performed using silica gel plates. Isoindolinones **1**,[9] **5**,[18] **8**,[19] **10**,[5] **11a**,[20] **11b**,[21] **13**,[22] **14a**,[23] and **14b**[10i] are known, and the rest of the isoindolinones are unknown. Substituted benzoyl chlorides were prepared from the respective benzoic acids by refluxing with excess thionyl chloride and otherwise prepared according to the reported procedure. Excess thionyl chloride was removed under vacuum, and the resulting residue was used for amide preparation without further purification. Substrates: 2-iodo-*N*,*N*-diisopropylbenzamide (substrate for **1**),[24] 2-iodo-*N*-phenylethylbenzamide[13a] (precursor for 2-iodo-*N*-methyl-*N*-phenylethylbenzamide), *N*,*N*-diethyl-2-iodobenzamide[25] (substrate for **10**), 4-chloro-2-iodo-*N*,*N*-diisopropylbenzamide[26] (substrate for **15**), 2-bromo-*N*,*N*-diisopropyl-4,5-dimethoxybenzamide[7] (substrate for **17**), 2-iodo-*N*,*N*-diisopropyl-3-methylbenzamide[27] (substrate for **18a**,**b**), 2-bromo-*N*,*N*-diisopropyl-5-methoxybenzamide[28] (substrate for **19**), 2-iodo-*N*,*N*-diisopropylferrocenecarboxamide[11b] (substrate for **21**), and 2-hydroxy-*N*,*N*-diisopropyl-5-nitrobenzamide[29] are also known, and analytical data correlate well with the reported values.

General Procedures for the Synthesis of 2-Halo Tertiary Benzamides. Substrates for isoindolinones **1**−**22** (except **13**) were prepared by following Scheme 5. The substrate for **13** was prepared by using NaH and methyl iodide. The 2-halo tertiary benzamides substrates show *E*/*Z* rotational isomerism, as observed in ^1H and ^{13}C NMR spectra.

General Procedures for Amide Synthesis: Synthesis of 2-Iodo-*N*,*N*-diisopropylbenzamide Substrate for 1). To a stirred solution of 2-iodobenzoyl chloride (266 mg, 1.0 mmol) in DCM (10 mL) were added dropwise diisopropylamine (152 mg, 1.5 mmol) and triethylamine (203 mg, 2.0 mmol) in DCM (10 mL) using a dropping funnel at 0 °C. After complete addition, the reaction mixture was stirred for 5 h. After this 10% HCl aqueous solution (40 mL) was added to the reaction mixture. The resulting solution was extracted with DCM (20 mL × 3), and the DCM layer was washed with water (30 mL) and dried over Na_2SO_4. The organic layer was concentrated on a rotary evaporator under vacuum. A white solid was obtained. Yield: 298 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.53 Hz, 1H), 7.13 (dd, J = 7.54 Hz, J = 1.54 Hz, 1H), 7.01 (dt, J = 7.74 Hz, J = 1.54 Hz, 1H), 3.61−3.45 (m, 2H), 1.58 (d, J = 6.87 Hz, 3H), 1.55 (d, J = 6.87 Hz, 3H), 1.25 (d, J = 6.70 Hz, 3H), 1.05 (d, J = 6.70 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 144.1, 139.3, 129.5, 128.2, 125.9, 92.3, 51.3, 46.1, 20.8, 20.7, 20.1. LRMS: m/z 332.0, calculated for $C_{13}H_{18}INO + H^+$ 332.1.

Scheme 5. Synthesis of 2-Halo Tertiary Benzamides



General Procedures for the Synthesis of Isoindolinones. Isoindolinones were synthesized from 2-iodobenzamides by following procedure A. 2-Bromo and 2-chloro substrates were converted into products by following procedure B.

Procedure A for the Synthesis of 2-Isopropyl-3,3-dimethylisoindolin-1-one (1). A sealed tube (25 mL) containing 2 mL of dry DMSO was charged with 2-iodo-*N*,*N*-diisopropylbenzamide (464 mg, 1.4 mmol), vitamin E (30 mg, 0.07 mmol), and KO^{t}Bu (474 mg, 4.2 mmol) under N_2. The resulting reaction mixture was refluxed for 3 h at 100 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, water (110 mL) was added. The resulting brownish white solution was stirred for 30 min and extracted with ethyl acetate (20 mL × 3), dried over Na_2SO_4, and concentrated under vacuum. The resulting white crystalline solid was purified by flash column chromatography. Yield: 278 mg, 98%.

Procedure B. In a 15 mL capacity sealed tube containing 5 mL of benzene, the substrate (304 mg, 1 mmol), AMVN (25 mg, 0.1 mmol, 10 mol %), and potassium *tert*-butoxide (358 mg, 3.1 mmol, 3 equiv) were heated to 100 °C. The progress of the reaction was monitored by TLC. The reaction mixture was refluxed for 3 h at 100 °C. After completion of the reaction, water (100 mL) was added to the resulting brownish white solid and the mixture was stirred for 30 min. The resulting solution was extracted with ethyl acetate (20 mL × 3) and dried over Na_2SO_4. The organic layer was concentrated on a rotary evaporator under vacuum. The resulting crude reaction mixture was purified by column chromatography using hexane/ethyl acetate (8/2) on silica to give the desired isoindolinone **1**. Yield: 176 mg, 87%.

*2-Isopropyl-3,3-dimethylisoindolin-1-one (**1**) from 2-Iodo-N,N-diisopropylbenzamide.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 3.59−3.55 (m, 1H), 1.48 (d, *J* = 8.0 Hz, 6H), 1.39 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 151.3, 132.0, 131.2, 127.8, 123.1, 120.6, 63.3, 44.5, 25.4, 20.5. LRMS: *m/z* 204.1, calculated for $C_{13}H_{17}O$ N + H^+ 204.1.

*2-Iodo-N-isopropyl-N-methylbenzamide (Substrate for **2**).* 2-Iodo-*N*-isopropyl-*N*-methylbenzamide was prepared using 2-iodobenzoyl chloride and *N*-methyl-*N*-isopropylamine, which gave a white semisolid. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.78 (m, 2H), 7.38−7.34 (m, 2H), 7.19−7.14 (m, 2H), 7.07−7.01 (m, 2H), 5.02 (m, 1H), 3.64 (m, 1H), 2.97 (s, 3H), 2.64 (s, 3H), 1.26−1.05(s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.3, 143.3, 141.7, 139.4, 139.1, 129.9, 128.5, 128.2, 126.8, 126.4, 92.5, 92.3, 50.0, 44.1, 29.6, 25.7, 20.6, 20.2. HRMS: *m/z* 303.0094, calculated for $C_{11}H_{14}INO$ 303.0120.

*2,3,3-Trimethylisoindolin-1-one (**2**).* Compound **2** was prepared by following procedure A, which gave a white solid. Yield: 156 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.24 Hz, 1H) 7.51 (t, *J* = 7.24 Hz, 1H) 7.43−7.38 (m, 2H) 3.01 (s, 3H) 1.43 (s, 6H). ^{13} C NMR (400 MHz, $CDCl_3$) δ167.2, 151.5, 131.4, 130.91, 128.0, 123.6, 120.6, 62.1, 24.9, 23.9. HRMS: *m/z* 175.0968, calculated for $C_{11}H_{13}NO$ 175.0997.

*2-Iodo-N-isopropyl-N,3-dimethylbenzamide (Substrate for **3**).* 2-Iodo-*N*-isopropyl-*N*,3-dimethylbenzamide was prepared using 2-iodo-3-methylbenzoyl chloride and *N*-methyl-*N*-isopropylamine. A white solid was obtained. Yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (t, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 8.0 Hz, 2H) 6.93(d, *J* = 8.0 Hz, 2H), 5.06−5.00 (m, 1H), 3.69−3.63 (m, 1H), 2.96 (s, 3H), 2.62 (s, 3H), 2.45 (d, *J* = 4.0 Hz, 6H), 1.24 (d, *J* = 4.0 Hz, 6H), 1.20 (d, *J* = 4.0 Hz, 3H), 1.05 (d, *J* = 4.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.9, 144.4, 142.9, 142.6, 129.3, 128.6, 128.3, 129.2, 123.9, 123.6, 99.4, 99.1, 49.9, 44.0, 25.6, 20.6, 20.2, 19.5, 18.7. HRMS: *m/z* 317.0274, calculated for $C_{12}H_{16}INO$ 317.0277.

*2,3,3,4-Tetramethylisoindolin-1-one (**3a**) from 2-Iodo-N-isopropyl-N,3-dimethylbenzamide.* Following general procedure A, a white solid was obtained, which was purified by column chromatography hexane/EtOAc (8/2) on silica gel. This gave two fractions: first fraction, white solid **3a**; second fraction, white solid **3b**. Yield for **3a**: 0.132 g (70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 3.0 (s, 3H), 2.50 (s, 3H), 1.50 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 148.4, 133.9, 131.7, 131.6, 128.0, 121.3, 62.8, 23.5, 22.5, 18.7. HRMS: *m/z* 189.1134, calculated for $C_{12}H_{15}NO$ 189.1154.

*2,3,3,6-Tetramethylisoindolin-1-one (**3b**) from 2-Iodo-N-isopropyl-N,3-dimethylbenzamide.* Second fraction. Yield: 0.038 g (20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 3.00 (s, 3H), 2.41 (s, 3H), 1.41 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 148.9, 137.9, 132.4, 131.0, 123.8, 120.4, 61.9, 25.0, 23.9, 21.3. HRMS: *m/z* 189.1147, calculated for $C_{12}H_{15}NO$ 189.1154.

*2-Iodo-N-isopropyl-N,5-dimethylbenzamide (Substrate for **3a**,**b**).* This substrate was prepared from 2-iodo-4-methylbenzoyl chloride and *N*-methyl-*N*-isopropylamine. Yield: 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (t, *J* = 8.0 Hz, 2H), 6.94 (t, *J* = 4.0 Hz, 2H), 4.96 (m, 1H), 3.62 (m, 1H), 2.91 (m, 1H), 2.60 (m, 1H), 2.24 (s, 6H), 1.21 (d, *J* = 4.0 Hz, 6H), 1.16 (d, *J* = 4.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.3, 143.2, 143.1, 139.0, 138.8, 138.7, 138.5, 130.92, 130.90, 127.6, 127.1, 88.4, 88.1, 49.9, 44.0, 29.6, 25.6, 21.0, 20.9, 20.6, 20.3. HRMS: *m/z*: 317.0251, calculated for $C_{12}H_{16}INO$ 317.0276.

*2,3,3,4-Tetramethylisoindolin-1-one (**3a**) and 2,3,3,6-Tetramethylisoindolin-1-one (**3b**).* The ratio of **3a** and **3b** is 64:36, obtained from 2-iodo-*N*-isopropyl-*N*,5-dimethylbenzamide substrate. This is similar to the ratio obtained from 2-iodo-*N*-isopropyl-*N*,3-dimethylbenzamide substrate. ^{1}H NMR of **3a**,**b** (400 MHz, $CDCl_3$): ratio 64:36, δ 7.67 (d), 7.61 (t), 7.32 (d), 7.27 (t), 3.01 (s), 3.00 (s), 2.49 (s), 2.40 (s), 1.50 (s), 1.41 (s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 167.2, 148.9, 148.4, 137.93, 137.92, 132.4, 131.7, 131.5, 131.0, 128.0, 123.8, 121.3, 120.4, 62.9, 61.9, 25.0, 23.9, 23.5. 22.5, 21.3, 18.7.

*4-Chloro-2-iodo-N-isopropyl-N-methylbenzamide (Substrate for **4** and **24**).* 4-Chloro-2-iodo-*N*-isopropyl-*N*-methylbenzamide was prepared using 4-chloro-2-iodobenzoyl chloride and *N*-methyl-*N*-isopropylamine. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.07 (q, *J* = 4.0 Hz, 2H), 4.99−4.92 (m, 1H), 3.62−3.55 (m, 1H), 2.93 (s, 3H), 2.60 (s, 3H), 1.23−1.18 (m, 9H), 1.04 (d, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 169.5, 141.72, 141.70, 138.8, 138.5, 134.8, 134.7, 128.8, 128.6, 127.6, 127.1, 92.7, 92.5, 50.1, 44.4, 25.8, 20.6, 20.2. HRMS: *m/z* 336.9739, calculated for $C_{11}H_{13}NOICl$ 336.9730.

*5-Chloro-2,3,3-trimethylisoindolin-1-one (**4**) from 4-Chloro-N-methyl-2-iodo-N-isopropylbenzamide.* Compound **4** was prepared by following procedure A. White solid. Yield: 0.192 g (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 3.0 (s, 3H), 1.44 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9, 153.1, 137.8, 129.4, 128.6, 124.9, 121.3, 61.9, 24.8, 24.0. HRMS: *m/z* 209.0592, calculated for $C_{11}H_{12}NOCl$ 209.0607.

*N-Ethyl-2-iodo-N-isopropylbenzamide (Substrate for **5**).* *N*-Ethyl-2-iodo-*N*-isopropylbenzamide was prepared using 2-iodobenzoyl chloride and *N*-ethyl-*N*-isopropylamine. Yield: 70%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (t, *J* = 7.81 Hz, 2H), 7.37−7.33 (m, 2H), 7.22−7.14 (m, 2H), 7.05−7.01 (m, 2H), 3.64−3.53 (m, 3H), 3.32−3.02 (m, 3H), 1.34−1.23 (m, 12H), 1.06−0.98 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.0, 143.4, 139.3, 139.1, 129.8, 129.7, 128.2, 128.1, 127.2, 126.3, 92.9, 92.5, 50.5, 46.2, 39.3, 35.4, 21.24, 21.19, 16.3, 14.4. HRMS: *m/z* 317.0255, calculated for $C_{12}H_{16}INO$ 317.0277.

*2-Ethyl-3,3-dimethylisoindolin-1-one (**5**) from N-Ethyl-2-iodo-N-isopropylbenzamide.* Compound **5** was prepared by following procedure C. White semisolid. Yield: 0.168 g (89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 6.0 Hz, 1H), 7.41 (m, 1H), 7.34 (m, 1H), 3.49 (q, *J* = 4.0 Hz, 2H), 1.46 (s, 6H), 1.28 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 151.6, 131.4, 128.5, 127.9, 123.4, 120.6, 62.8, 33.4, 26.0, 14.7. HRMS: *m/z* 190.1249, calculated for $C_{12}H_{15}NO$ + H^+ 190.1232.

*4-Chloro-N-ethyl-2-iodo-N-isopropylbenzamide (Substrate for **6** and **25**).* 4-Chloro-*N*-ethyl-2-iodo-*N*-isopropylbenzamide was prepared using 4-chloro-2-iodobenzoyl chloride and *N*-ethyl-*N*-isopropylamine. Yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 7.11 Hz, *J* = 1.85 Hz, 2H), 7.38−7.34 (d, *J* = 7.31 Hz, 2H), 7.16−7.08 (m, 2H), 3.63−3.53 (m, 3H), 3.33−3.02 (m, 3H), 1.35−1.27 (m, 12H), 1.07−1.00 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 169.1, 141.9, 141.8, 138.8, 138.5, 134.6, 134.5, 128.6, 128.5, 127.9, 127.0, 93.1, 92.7, 50.5, 46.4, 39.4, 35.5, 21.23, 21.20, 16.3, 14.3. HRMS: *m/z* 350.9876, calculated for $C_{12}H_{15}ClINO$ 350.9887.

*5-Chloro-2-ethyl-3,3-dimethylisoindolin-1-one (**6**) from 4-Chloro-N-ethyl-2-iodo-N-isopropylbenzamide.* Compound **6** was prepared by following procedure A. White solid. Yield: 0.205 g (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.37 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 3.48 (q, *J* = 4.0 Hz, 2H), 1.46 (m, 6H), 1.28 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 153.2, 137.7, 129.6, 128.5, 124.8, 121.3, 62.6, 34.1, 25.9, 14.7. HRMS: *m/z* 224.0833, calculated for $C_{12}H_{14}ClNO$ + H^+ 224.0842.

*2-Bromo-N-ethyl-N-isopropylnicotinamide (Substrate for compound **7**).* White semisolid. Yield: 85%. ^{1} H NMR (400 MHz, $CDCl_3$): δ 8.38−8.37 (m, 2H), 7.62−7.54 (m, 2H), 7.28−7.25 (m, 2H), 4.72−3.02 (m, 6H), 1.30−1.22 (m, 12H), 1.05−0.96 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 165.7, 149.64, 1.64.0, 147.2, 147.0, 136.5, 136.0, 133.6, 133.4, 122.6, 122.4, 50.6, 46.4, 39.1, 35.5, 21.3, 20.9, 20.4, 20.0, 16.3, 14.3. HRMS: *m/z* 270.0361, calculated for $C_{11}H_{15}BrN_2O$ 270.0368.

*6-Ethyl-7,7-dimethyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-5-one (**7**).* Compound **7** was prepared by following procedure B. White semisolid. Yield: 0.143 g (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (dd, *J* = 4.8, 1.35 Hz, 1H), 8.02 (dd, *J* = 7.6, 1.35 Hz, 1H), 7.30−7.26 (m, 1H), 3.49 (q, *J* = 7.0 Hz, 2H), 1.48 (s, 6H), 1.27 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 165.6, 152.1, 131.7, 124.5, 123.1, 63.9, 34.1, 24.3, 14.6. HRMS: m/z 191.1208, calculated for $C_{11}H_{14}N_2O + H^+$ 191.1184.

*N-Cyclohexyl-2-iodo-N-methylbenzamide (Substrate for **8**).* N-Cyclohexyl-2-iodo-*N*-methylbenzamide was prepared using 2-iodobenzoyl chloride and *N*-cyclohexyl-*N*-methylamine. Yellowish solid. Yield: 98%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78−7.73 (m, 2H), 7.33−7.28 (m, 2H), 7.13−7.08 (m, 2H), 7.02−6.96 (m, 2H), 4.58−4.50 (m, 1H), 3.11−3.03 (m, 1H), 2.94 (s, 3H), 2.61 (s, 3H), 1.92−1.39 (m, 20H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.3, 143.5, 143.4, 139.3, 139.1, 129.84, 129.82, 128.5 128.2, 126.8, 126.3, 92.5, 92.4, 58.5, 52.4, 31.0, 30.9, 30.7, 27.1, 25.7, 25.6, 25.4, 25.1. HRMS: m/z 343.0420, calculated for $C_{14}H_{18}INO$ 343.0433.

*2′-Methylspiro[cyclohexane-1,1′-isoindolin]-3′-one (**8**).* Compound **8** was prepared by following procedure A. White semisolid. Yield: 202 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 3.69, 1H), 7.72 (d, *J* = 3.69, 1H), 7.45−7.37 (m, 2H), 2.96 (s, 3H), 1.94−1.82 (m, 8H), 1.38−1.36 (m, 2H). ^{13} C NMR (400 MHz, $CDCl_3$): δ 167.5, 150.6, 130.6, 127.8, 123.8, 123.4, 114.1, 64.4, 32.9, 24.7, 24.3, 22.4. LRMS: m/z 216.2, calculated for $C_{14}H_{17}ON + H^+$ 216.1.

*4-Chloro-N-cyclohexyl-2-iodo-N-methylbenzamide (Substrate for **9** and **26**).* 4-Chloro-*N*-cyclohexyl-2-iodo-*N*-methylbenzamide was prepared using 4-chloro-2-iodobenzoyl chloride and *N*-cyclohexyl-*N*-methylamine. Yield: 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (dd, *J* = 12, 2 Hz, 2H), 7.33 (dt, *J* = 8, 2 Hz, 2H), 7.07 (q, *J* = 8 Hz, 2H), 2.96 (s, 3H), 2.64 (s, 3H), 1.96−0.99 (m, 22H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 169.5, 142.0, 138.8, 138.5, 134.7, 128.8, 128.6, 127.6, 127.0, 92.7, 92.5, 58.6, 52.6, 31.0, 30.9, 30.7, 29.7, 29.2, 27.2, 25.6, 25.5, 25.4, 25.1. HRMS: m/z 378.0131, calculated for $C_{14}H_{17}ClINO + H^+$ 378.0122.

*6′-Chloro-2′-methylspiro[cyclohexane-1,1′-isoindolin]-3′-one (**9**) from 4-Chloro-N-cyclohexyl-2-iodo-N-methylbenzamide.* Compound **9** was prepared by following procedure A. White solid. Yield: 232 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 12.0 Hz, 1H), 7.75 (t, *J* = 2.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.01 (s, 3H), 1.96−1.84 (m, 8H), 1.46−1.41 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 152.0, 136.8, 128.4, 124.9, 123.9, 111.8, 64.3, 32.7, 24.6, 24.3, 22.4. HRMS: m/z 250.1006, calculated for $C_{14}H_{16}ClON + H^+$ 250.0999.

*N,N-Diethyl-2-iodobenzamide (Substrate for **10**).* *N,N*-Diethyl-2-iodobenzamide was prepared using 2-iodobenzoyl chloride and diethylamine. Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.06 Hz, 1H), 7.35 (t, *J* = 7.63 Hz, 1H), 7.18 (dd, *J* = 7.63 Hz, *J* = 1.64 Hz, 1H), 7.03 (dt, *J* = 7.73 Hz, *J* = 1.64 Hz, 1H), 3.91−3.75 (m, 1H), 3.35−3.21 (m, 1H), 3.13−3.09 (m, 2H), 1.27 (t, *J* = 7.14 Hz, 3H), 1.04 (t, *J* = 7.14 Hz, 3H). ^{13} C NMR (100 MHz, $CDCl_3$): δ 170.1, 142.9, 139.2, 129.9, 128.2 126.9, 92.8, 42.8, 38.9, 13.9, 12.5. LRMS: m/z 304.0, calculated for $C_{11}H_{14}INO + H^+$ 304.0.

*2-Ethyl-3-methylisoindolin-1-one (**10**) from N,N-Diethyl-2-iodobenzamide.* Compound **10** was prepared by following procedure A. White solid. Yield: 45 mg (26%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 6.0 Hz, 1H), 7.44 (d, *J* = 4.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 4.56 (q, *J* = 6.0 Hz, 1H), 3.98−3.94 (m, 1H), 3.32−3.28 (m, 1H), 1.46 (d, *J* = 8.0 Hz, 3H), 1.25 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 146.9, 131.3, 128.1, 126.8, 123.5, 121.8, 55.2, 34.6, 18.2, 13.8. LRMS: m/z 176.1, calculated for $C_{11}H_{13}NO + H^+$ 176.1.

*N-Benzyl-N-ethyl-2-iodobenzamide (Substrate for **11a,b**).* N-Benzyl-*N*-ethyl-2-iodobenzamide was prepared using 2-iodobenzoyl chloride and *N*-benzyl-*N*-ethylamine. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (t, *J* = 7.19 Hz, 2H), 7.46 (d, *J* = 7.31 Hz, 2H), 7.39−7.22 (m, 10H), 7.14 (d, *J* = 7.15 Hz, 2H), 7.09−6.99 (m, 2H), 5.07 (d, *J* = 14.64 Hz, 1H), 4.51 (d, *J* = 14.64 Hz, 1H), 4.38−4.28 (m, 2H), 4.01−3.97 (m, 1H), 3.08−3.03 (m, 3H), 1.24 (t, *J* = 7.16 Hz, 3H), 1.01 (t, *J* = 7.11 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.6, 142.6, 142.3, 139.4, 139.2, 136.9, 136.3, 130.1, 130.0, 128.8, 128.7, 128.5, 128.4, 128.2, 127.7, 127.5, 127.3, 127.2, 127.1, 92.9, 92.6, 51.5, 46.7, 42.2, 39.2, 13.3, 11.8. HRMS: m/z 365.0261, calculated for $C_{16}H_{16}INO$ 365.0277.

*2-Ethyl-3-phenylisoindolin-1-one (**11a**) from N-Benzyl-N-ethyl-2-iodobenzamide.* Procedure A was followed for the synthesis of **11a**,**b**. A white solid was obtained, which was purified by column chromatography with hexane/EtOAc (8/2) on silica gel. This gave two fractions; first fraction, white solid **11a**; second fraction, white solid **11b**. Yield of **11a**: 161 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 4.0 Hz, 1H), 7.47−7.41 (m, 2H), 7.38 (dd, *J* = 8.0, 3.0 Hz, 2H), 7.34−7.29 (m, 3H), 7.26−7.24 (m, 2H), 3.54−3.45 (m, 1H), 3.13−3.05 (m, 1H), 1.03 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 148.9, 138.6, 132.6, 130.7, 129.5, 128.50, 128.47, 126.2, 123.2, 122.6, 91.4, 34.3, 14.3. HRMS: m/z 238.1233 calculated for $C_{16}H_{15}NO + H^+$ 238.1232.

*2-Benzyl-3-methylisoindolin-1-one (**11b**).* Second fraction. Yield: 24 mg (10%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 4.0 Hz, 1H), 7.45 (t, *J* = 6.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 4H), 5.32 (d, *J* = 12.0 Hz, 1H), 4.37 (q, *J* = 4.0 Hz, 1H), 4.24, (d, *J* = 12.0 Hz, 1H), 1.41 (d, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 147.0, 137.3, 131.7, 131.5, 128.7, 128.1, 128.0, 127.6, 123.9, 121.9, 55.0, 43.7, 18.0. HRMS: m/z 236.1073, calculated for $C_{16}H_{15}NO - H^+$ 236.1075.

*2-Iodo-N-(2-methoxybenzyl)-N-methylbenzamide (Substrate for **12**).* 2-Iodo-*N*-(2-methoxybenzyl)-*N*-methylbenzamide was prepared using 2-iodobenzoyl chloride and 1-(2-methoxyphenyl)-*N*-methylmethanamine. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.97 Hz, 2H), 7.47−7.45 (m, 1H), 7.39−7.35 (m, 1H), 7.32−7.26 (m, 2H), 7.23−7.21 (m, 3H), 7.11 (d, *J* = 7.20 Hz 1H), 7.06−7.00 (m, 2H), 6.97−6.90 (m, 2H), 6.88 (d, *J* = 8.20 Hz, 1H), 6.81 (d, *J* = 8.20 Hz, 1H), 4.85−4.77 (m, 2H), 4.34 (s, 2H), 3.84 (s, 3H), 3.74 (s, 3H), 3.03 (s, 3H), 2.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 170.8, 157.7, 157.3, 142.9, 142.6, 139.2, 139.1, 130.1, 130.03, 129.99, 128.9, 128.7, 128.5, 128.4, 128.1, 127.5, 127.2, 124.6, 124.0, 120.7, 120.5, 110.35, 110.31, 93.0, 92.3, 55.4, 55.1, 49.6, 44.7, 36.1, 32.6. HRMS: m/z 381.0210, calculated for $C_{16}H_{16}INO_2$ 381.0226.

*3-(2-Methoxyphenyl)-2-methylisoindolin-1-one (**12**) from 2-Iodo-N-(2-methoxybenzyl)-N-methylbenzamide.* Compound **12** was prepared by following procedure A. White solid. Yield: 0.152 g (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.0 Hz, 3H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 8.0 Hz, 3H), 3.95 (s, 1H), 3.02 (s, 3H), 3.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 171.0, 155.3, 151.7, 148.9, 143.3, 138.9, 133.8, 131.4, 126.8, 123.1, 119.0, 118.9, 112.4, 65.8, 39.8, 13.7. HRMS (APCI): m/z 254.1170, calculated for $C_{16}H_{15}NO_2$ + H 253.1181.

*2-Iodo-N-methyl-N-(1-phenylethyl)benzamide (Substrate for **13**).* 2-Iodo-*N*-methyl-*N*-(1-phenylethyl)benzamide was prepared by using NaH and CH_3I. 2-Iodo-*N*-phenylethylbenzamide (598 mg, 1.7 mmol) was dissolved in dry DMF, to this was added NaH (280 mg, 7.0 mmol) portionwise at 0 °C, and the mixture was stirred for 30 min at this temperature under N_2. Methyl iodide (0.65 mL, 10 mmol) was added dropwise at 0 °C under N_2. After this, the reaction mixture was stirred at room temperature for 4 h. The resulting reaction mixture was slowly poured over ice and extracted with ethyl acetate (20 mL × 3), and the extract was dried over Na_2SO_4 and concentrated under vacuum. The resulting yellowish oil was purified by column chromatography using hexane/ethyl acetate (8/2) on silica gel. The resulted product was obtained as a thick liquid which solidified on standing. Yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.79 (m, 1H), 7.51−7.25 (m, 6H), 7.22−7.02 (m, 2H), 6.24−4.73 (m, 1H), 2.94−2.45 (m 3H), 1.70−1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 170.6, 143.0, 142.9, 140.2, 140.1, 139.5, 139.2, 130.1, 130.01, 128.7, 128.5, 128.2, 127.94, 127.87, 127.7, 127.5, 126.9, 126.7, 126.2, 93.3, 92.7, 56.72, 56.67, 50.42, 29.4, 27.7, 18.4. HRMS: m/z 365.0267, calculated for $C_{16}H_{16}INO$ 365.0277.

*2,3-Dimethyl-3-phenylisoindolin-1-one (**13**).* Compound **13** was prepared by following procedure A. White semisolid. Yield: 166 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 6.51, 1H), 7.41 (t, *J* = 6.72, 2H), 7.32−7.27 (m, 3H), 7.17−7.13 (m, 3H), 2.87 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 168.2, 151.9, 139.9, 131.9, 130.6, 128.9, 128.1, 127.9, 126.1, 123.7, 121.8, 67.2, 24.7, 22.5. HRMS: m/z 238.1248, calculated for $C_{16}H_{15}ON + H^+$ 238.1232.

*2-Iodo-N-isopropyl-N-phenylbenzamide (Substrate for **14**).* 2-Iodo-*N*-isopropyl-*N*-phenylbenzamide was prepared using 2-iodobenzoyl chloride and *N*-benzyl-*N*-isopropylamine. Yield: 90%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.57 (d, J = 7.9 Hz, 1H), 7.23–7.21 (m, 5H), 7.04 (t, J = 7.4 Hz, 1H), 6.97 (dd, J = 7.4 Hz, J = 1.5 Hz, 1H), 6.74 (dt, J = 7.9 Hz, J = 1.5 Hz, 1H), 5.21–5.12 (m, 1H), 1.20 (d, J = 6.7 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 169.8, 142.9, 138.9, 137.9, 130.4, 129.3, 128.5, 128.2, 128.0, 127.1, 93.6, 46.9, 20.9. HRMS: m/z 366.0365, calculated for $C_{16}H_{16}INO + H^+$ 366.0355.

*3,3-Dimethyl-2-phenylisoindolin-1-one (**14a**).* Following procedure A, a white solid was obtained, which was purified by column chromatography hexane/EtOAc (8/2) on silica gel. This gave two fractions: first fraction, white solid **14a**; second fraction, white solid **14b**. Yield for **14a**: 63 mg (27%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.49 (m, 5H), 7.26 (d, J = 7.4 Hz, 2H), 1.50 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.7, 151.7, 135.8, 132.0, 130.5, 129.7, 129.4, 128.2, 128.1, 124.3, 120.9, 64.5, 26.8. LRMS: m/z 238.2, calculated for $C_{16}H_{15}NO + H^+$ 238.1.

*5-Isopropylphenanthridin-6(5H)-one (**14b**).* Second fraction. White solid. Yield for **14b**: 152 mg (64%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.50 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.79 (t, J = 7.8 Hz, 1H), 7.60 (d, J = 8.6 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.27 (t, J = 7.4 Hz, 1H), 5.62–5.31 (m, 1H), 1.69 (d, J = 7.0 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 162.0, 137.3, 133.5, 132.3, 128.9, 128.6, 127.8, 126.4, 123.6, 122.1, 121.4, 120.1, 115.9, 47.4, 19.9. LRMS: m/z 238.2, calculated for $C_{16}H_{15}NO + H^+$ 238.1.

*4-Chloro-2-iodo-N,N-diisopropylbenzamide (Substrate for **15**).* 4-Chloro-2-iodo-*N*,*N*-diisopropylbenzamide was prepared using 4-chloro-2-iodobenzoyl chloride and diisopropylamine. Yield: 90%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.80 (d, J = 4.0 Hz, 1H), 7.32 (dd, J = 8.0, 2.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 3.45–3.56 (m, 2H), 1.56 (d, J = 8.0 Hz, 3H), 1.53 (d, J = 8.0 Hz, 3H), 1.24 (d, J = 4.0 Hz, 3H), 1.04 (d, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 169.0, 142.7, 138.7, 134.2, 128.6, 126.5, 92.4, 51.3, 46.1, 20.8, 20.0. HRMS: m/z 366.0146, calculated for $C_{13}H_{17}INOCl + H^+$ 366.0122.

*5-Chloro-2-isopropyl-3,3-dimethylisoindolin-1-one (**15**).* Compound **15** was prepared by following procedure A. White semisolid. Yield: 228 mg (96%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.67 (d, J = 8.0 Hz, 1H), 7.35 (dd, J = 2.0, 8.0 Hz, 1H), 7.30 (d, J = 3.0 Hz, 1H), 3.63–3.56 (m, 1H) 1.52 (d, J = 8.0 Hz, 6H), 1.44 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.2, 152.8, 137.5, 130.5, 128.5, 124.6, 121.2, 63.1, 44.7, 25.3, 20.4. HRMS: m/z 238.1017, calculated for $C_{13}H_{16}NOCl + H^+$ 238.0999.

*2-Bromo-N,N-diisopropyl-3-nitrobenzamide (Substrate for **16**).* 2-Bromo-*N*,*N*-diisopropyl-3-nitrobenzamide was prepared using 2-bromo-3-nitrobenzoyl chloride and diisopropylamine. Yellowish solid. Yield: 98%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.71 (d, J = 8.45 Hz, 1H), 7.47 (t, J = 7.76 Hz, 1H), 7.34 (d, J = 7.07 Hz, 1H), 3.57–3.47 (m, 2H), 1.55 (t, J = 6.33, 6H), 1.24 (d, J = 6.69 Hz, 3H), 1.07 (d, J = 6.69 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.2, 150.8, 143.1, 129.5, 128.7, 124.6, 111.2, 51.4, 46.4, 20.8, 20.7, 20.5, 19.9. HRMS: m/z 328.0406, calculated for $C_{13}H_{17}BrN_2O_3$ 328.0423.

*2-Isopropyl-3,3-dimethyl-4-nitroisoindolin-1-one (**16**) from 2-Bromo-N,N-diisopropyl-3-nitrobenzamide.* Compound **16** was prepared by following procedure B. Yellowish semisolid. Yield: 109 mg (44%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.25 (d, J = 8.0, 1H), 8.12 (d, J = 7.40, 1H), 7.61 (t, J = 8.0, 1H), 3.72–3.66 (m, 1H), 1.68 (s, 6H), 1.57 (d, J = 3.42, 6H). ^{13}C NMR (400 MHz, CDCl$_3$): δ 182.1, 143.6, 140.4, 140.3, 129.5, 127.8, 123.5, 66.2, 45.0, 22.5, 20.3. HRMS: m/z 248.1161, calculated for $C_{13}H_{16}N_2O_3$ 248.1161.

*2-Bromo-N,N-diisopropyl-4,5-dimethoxybenzamide (Substrate for **17**).* 2-Bromo-*N*,*N*-diisopropyl-4,5-dimethoxybenzamide was prepared from 2-bromo-4,5-dimethoxybenzoyl chloride and diisopropylamine. Yield: 89%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.94 (s, 1H), 6.61 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.62–3.56 (m, 1H), 3.49–3.42 (m, 1H), 1.51 (d, J = 6.8 Hz, 6H), 1.18 (d, J = 6.8 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 168.1, 149.3, 148.6, 132.2, 115.4, 109.3, 109.0, 56.19, 56.17, 51.2, 45.9, 21.0, 20.7, 20.5, 20.0. LRMS: m/z 344.0, calculated for $C_{15}H_{22}BrNO_3 + H^+$ 344.0.

*2-Isopropyl-5,6-dimethoxy-3,3-dimethylisoindolin-1-one (**17**).* Compound **17** was prepared by following procedure B; the reaction mixture was heated for 12 h. White semisolid. Yield: 177 mg (67%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.23 (s, 1H), 6.75 (s, 1H), 3.93 (t, 3H), 3.90 (t, 3H), 3.64–3.57 (m, 1H), 1.52 (d, J = 8.0 Hz, 6H), 1.43 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.4, 152.4, 149.5, 144.8, 124.2, 105.0, 102.9, 62.9, 56.23, 56.20, 44.6, 25.6, 20.58. HRMS: m/z 263.1493, calculated for $C_{15}H_{21}NO_3$ 263.1521.

*2-Iodo-N,N-diisopropyl-3-methylbenzamide (Substrate for **18a,b**).* 2-Iodo-*N*,*N*-diisopropyl-3-methylbenzamide was prepared using 2-iodo-3-methylbenzoyl chloride and diisopropylamine. White solid. Yield: 90%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.21 (t, J = 7.4 Hz, 1H), 7.14(d, J = 6.7 Hz, 1H), 6.89 (d, J = 6.9 Hz, 1H), 3.61–3.55 (m, 1H), 3.53–3.46 (m, 1H), 2.5 (s, 3H), 1.59 (d, J = 6.8 Hz, 3H), 1.55 (d, J = 6.8 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H), 1.04 (d, J = 6.7 Hz, 3H), ^{13}C NMR (100 MHz, CDCl$_3$): δ 170.4, 145.3, 142.6, 128.9, 128.2, 123.0, 99.1, 51.1, 45.9, 28.8, 20.74, 20.70, 20.68, 19.9. GCMS: m/z 345.0, calculated for $C_{14}H_{20}INO$ 345.1.

*2-Isopropyl-3,3,4-trimethylisoindolin-1-one (**18a**).* Following procedure A, a white solid was obtained which was purified by column chromatography with hexane/EtOAc (8/2) on silica gel. This gave two fractions: first fraction, white solid **18a**; second fraction, white solid **18b**. Yield: 174 mg (80%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.62 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 3.66–3.59 (m, 1H), 2.47 (s, 3H), 1.55 (d, J = 8.0 Hz, 6H), 1.53 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.2, 148.1, 133.7, 132.6, 131.5, 127.9, 120.9, 64.2, 44.3, 22.9, 20.5, 18.7. HRMS: m/z 218.1544, calculated for $C_{14}H_{19}ON + H^+$ 218.1545.

*2-Isopropyl-3,3,6-trimethylisoindolin-1-one (**18b**).* Second fraction. White solid **18b**. Yield: 39 mg (18%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.56 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 3.65–3.58 (m, 1H), 2.40 (s, 3H), 1.53 (d, J = 8.0 Hz, 6H), 1.44 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.4, 137.8, 132.2, 131.4, 123.4, 120.3, 115.6, 55.6, 44.6, 25.5, 21.3, 20.5. HRMS: m/z 218.1526, calculated for $C_{14}H_{19}ON+ H^+$ 218.1545.

*2-Bromo-N,N-diisopropyl-5-methoxybenzamide (Substrate for **19**).* 2-Bromo-*N*,*N*-diisopropyl-5-methoxybenzamide was prepared using 2-bromo-5-methoxybenzoyl chloride and diisopropylamine. White solid. Yield: 85%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.39 (d, J = 8.7 Hz, 1H), 6.72 (dd, J = 8.8, 2.9 Hz, 1H), 6.68 (d, J = 2.9 Hz, 1H), 3.75 (s, 3H), 3.64–3.54 (m, 1H), 3.52–3.43 (m, 1H), 1.55–1.52 (m, 6H), 1.21 (d, J = 6.6 Hz, 3H), 1.04 (d, J = 6.67 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.9, 159.0, 140.8, 133.6, 115.6, 111.9, 109.2, 55.6, 51.15, 45.97, 20.9, 20.7, 20.5, 20.0. LRMS: m/z: 314.2, calculated for $C_{14}H_{20}BrNO_2 + H^+$ 314.1.

*2-Isopropyl-6-methoxy-3,3-dimethylisoindolin-1-one (**19a**) and 2-Isopropyl-4-methoxy-3,3-dimethylisoindolin-1-one (**19b**) from 2-Bromo-N,N-diisopropyl-5-methoxybenzamide.* Procedure B was followed. A white solid was obtained, which was purified by column chromatography with hexane/EtOAc (8/2) on silica gel. This gave a mixture of **19a** and **19b**. White solid. Yield: 158 mg (68%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.38–7.32 (m, 2H), 7.20 (d, J = 12.0 Hz, 2H), 7.04 (dd, J = 4.0, 8.0 Hz, 1H), 6.95 (dd, J = 4.0, 8.0 Hz, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.65–3.58 (m, 2H), 1.54 (m, 6H), 1.52 (d, J = 4.0 Hz, 12H), 1.43 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ.157.2, 154.2, 135.0, 134.1, 134.0, 133.8, 129.3, 121.5, 119.5, 115.3, 112.9, 105.92, 105.9, 63.4, 63.0, 55.7, 55.4, 44.6, 44.2, 25.5, 22.8, 20.5. HRMS: m/z 233.1398, calculated for $C_{14}H_{19}O_2N$ 233.1416.

*1-Bromo-N,N-diisopropyl-2-naphthamide (Substrate for **20**).* This substrate was prepared by using 2-bromonaphthoyl chloride and diisopropylamine. White solid. Yield: 89%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.29 (d, J = 8.4 Hz, 1H), 7.82 (dd, J = 8.4 Hz, J = 2.2 Hz, 2H), 7.61 (td, J = 7.1 Hz, J = 1.2 Hz, 1H), 7.55–7.51 (m, 1H), 7.26 (d, J = 8.4 Hz, 1H), 3.68–3.60 (m, 1H), 3.58–3.49 (m, 1H), 1.64 (d, J = 6.8 Hz, 3H), 1.61 (d, J = 6.8 Hz, 3H), 1.21 (d, J = 6.6 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 168.6, 138.0, 133.7, 132.1, 128.5, 128.2, 127.9, 127.3, 127.0, 123.5, 118.9, 51.2, 46.0, 20.8, 20.72, 20.70, 20.2. HRMS: m/z 334.0781, calculated for $C_{17}H_{20}BrNO + H^+$ 334.0807.

*2-Isopropyl-3,3-dimethyl-2,3-dihydro-1H-benzo[f]isoindol-1-one (**20a**) from 3-Bromo-N,N-diisopropyl-2-naphthamide.* Following procedure B, a white solid was obtained, which was purified by column chromatography with hexane/EtOAc (8/2) on silica gel. This gave two fractions: first fraction, white solid **20a**; second fraction, white solid **20b**. Yield obtained for **20a**: 152 mg (60%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.28 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.74 (s, 1H), 7.56−7.48 (m, 2H), 3.71−3.64 (m, 1H), 1.59 (d, J = 8.0 Hz, 6H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.0, 146.9, 135.1, 133.1, 130.3, 129.5, 128.0, 127.3, 126.1, 123.3, 119.4, 63.4, 44.8, 26.2, 20.6. HRMS: m/z 253.1459, calculated for $\mathrm{C_{17}H_{19}ON}$ 253.1467.

*2-Isopropyl-1,1-dimethyl-1H-benzo[e]isoindol-3(2H)-one (**20b**).* Yield: 86 mg (34%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.04 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.87 (q, J = 8.0 Hz, 2H), 7.63−7.56 (m, 2H), 3.80−3.72 (m, 1H), 1.72 (s, 6H), 1.61 (d, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.4, 147.7, 135.8, 130.1, 130.0, 129.3, 126.9, 126.7, 126.69, 123.7, 119.8, 64.4, 44.5, 24.8, 20.7. HRMS: m/z 253.1446, calculated for $\mathrm{C_{17}H_{19}ON}$ 253.1467.

*N,N-Diisopropyl-2-iodoferrocenecarboxamide (Substrate for **21**).* This compound was prepared by following a literature procedure.[12] Yield: 95%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 4.42 (s, 1H), 4.34 (s, 5H), 4.27 (s, 1H), 4.16 (s, 1H), 3.61 (s, 1H), 3.40 (s, 1H), 1.49 (s, 6H), 1.09 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.3, 73.6. 72.8, 67.6, 66.8, 50.8, 45.9, 40.5, 20.8. LRMS: m/z 440.0, calculated for $\mathrm{C_{17}H_{22}ONIFe + H^+}$ 440.0.

*Ferrocenylisoindolinone (**21**).* Compound **21** was prepared by following procedure A. Orange solid. Yield: 300 mg (96%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 4.59 (s, 1H), 4.25−4.20 (m, 7H), 3.48 (s, 1H), 1.72 (s, 3H), 1.51 (d, J = 4.0 Hz, 3H), 1.47 (d, J = 4.0 Hz, 3H), 1.29 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 170.5, 104.3, 70.7, 69.6, 60.7, 60.1, 45.0, 28.7, 27.2, 20.7, 20.6. HRMS: m/z 311.0963, calculated for $\mathrm{C_{17}H_{21}ONFe}$ 311.0973.

*2-Bromo-N,N-diisopropylnicotinamide (Substrate for **22**).* 2-Bromo-*N,N*-diisopropylnicotinamide was prepared using 2-bromonicotinoyl chloride and diisopropylamine. White solid. Yield: 95%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.37 (s, 1H), 7.53 (dd, J = 7.52 Hz, J = 1.71 Hz, 1H), 7.27−7.24 (m, 1H), 3.58−3.47 (m, 2H), 1.54 (t, J = 6.5 Hz, 6H), 1.23 (d, J = 6.57 Hz, 3H), 1.05 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 165.5, 149.3, 147.0, 135.5, 134.2, 122.6, 51.3, 46.2, 20.9, 20.6, 20.5, 19.9. HRMS: m/z 284.0507, calculated for $\mathrm{C_{12}H_{17}BrN_2O}$ 284.0524.

*6-Isopropyl-7,7-dimethyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-5-one (**22**).* Compound **22** was prepared by following procedure B. Yellowish semisolid. Yield: 162 mg (79%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.66 (dd, J = 5.0, 1.4 Hz, 1H), 8.03 (dd, J = 7.6, 1.4 Hz, 1H), 7.34−7.31 (m, 1H), 3.75−3.64 (m, 1H), 1.55 (d, J = 6.8 Hz, 6H), 1.52 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 169.4, 165.4, 151.9, 131.5, 125.5, 123.1, 64.5, 44.9, 23.8, 20.5. HRMS: m/z 205.1357, calculated for $\mathrm{C_{12}H_{16}N_2O + H^+}$ 205.1341.

Typical Procedure for the Synthesis of 5-Phenylisoindolin-1-ones. 2-Isopropyl-3,3-dimethyl-5-phenylisoindolin-1-one (23) from 4-Chloro-2-iodo-*N,N*-diisopropylbenzamide (Procedure C). In a 15 mL capacity sealed tube containing 5 mL of benzene, 4-chloro-2-iodo-*N,N*-diisopropylbenzamide (511 mg, 1.4 mmol), AMVN (35 mg, 0.14 mmol, 10 mol %), and potassium *tert*-butoxide (818 mg, 7.3 mmol) were heated to 100 °C. The progress of the reaction was monitored by TLC. The reaction mixture was refluxed for 28 h at 100 °C. After completion of the reaction, water (100 mL) was added to the resulting brownish white solid and the mixture was stirred for 30 min. The resulting solution was extracted with ethyl acetate (20 mL × 3), and the extract was dried over Na$_2$SO$_4$. The organic layer was concentrated on a rotary evaporator under vacuum. The resulting crude reaction mixture was purified by column chromatography using hexane/ethyl acetate (8/2) on silica to give the desired 2-isopropyl-3,3-dimethyl-5-phenylisoindolin-1-one (**23**). White solid. Yield: 340 mg (87%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.83 (d, J = 8.0 Hz, 1H), 7.62−7.58 (m, 3H), 7.50 (s, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.37 (t, J = 8.0 Hz, 1H), 3.69−3.62 (m, 1H), 1.56 (d, J = 8.0 Hz, 6H), 1.51 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.1, 152.0, 144.7, 140.8, 130.9, 128.9, 127.9, 127.5, 127.2, 123.6, 119.4, 63.3, 44.7, 25.6, 20.5. HRMS: m/z 280.1715, calculated for $\mathrm{C_{19}H_{21}ON + H^+}$ 280.1701.

*2-Methyl-3,3-dimethyl-5-phenylisoindolin-1-one (**24**) from 4-Chloro-N-methyl-2-iodo-N-isopropylbenzamide.* Compound **24** was prepared by following procedure C. White solid. Yield: 216 mg (86%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.87 (d, J = 8.0 Hz, 1H), 7.64−7.57 (s, 4H), 7.46 (t, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 3.04 (s, 3H), 1.49 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 178.4, 152.2, 147.9, 128.9, 128.0, 127.5, 127.3, 123.9, 119.5, 100.0, 99.1, 62.2, 25.0, 24.0. HRMS: m/z 251.1295, calculated for $\mathrm{C_{17}H_{17}NO}$ 251.1310.

*2-Ethyl-3,3-dimethyl-5-phenylisoindolin-1-one (**25**) from 4-Chloro-N-ethyl-2-iodo-N-isopropylbenzamide.* Compound **25** was prepared by following procedure C. White solid. Yield: 236 mg, 89%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.86 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 8.0 Hz, 3H), 7.54 (s, 1H), 7.45 (t, J = 6.0 Hz, 2H), 7.38 (t, J = 6.0 Hz, 1H), 3.53 (t, J = 6.0 Hz, 2H), 1.52 (s, 6H), 1.32 (t, J = 6.0 Hz, 3H) . ^{13}C NMR (100 MHz, CDCl$_3$): δ 167.2, 152.3, 144.8, 140.7, 130.0, 128.9, 128.0, 127.5, 127.3, 123.8, 119.4, 62.9, 34.1, 26.1, 14.8. HRMS: m/z 266.1553, calculated for $\mathrm{C_{18}H_{19}NO + H^+}$ 266.1545.

*2′-Methyl-6′-phenylspiro[cyclohexane-1,1′-isoindolin]-3′-one (**26**) from 4-Chloro-N-cyclohexyl-2-iodo-N-methylbenzamide.* Compound **26** was prepared by following procedure C. White solid. Yield: 215 mg (86%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.92 (d, J = 8.0 Hz, 2H), 7.65 (dd, J = 8.0, 2.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 7.39 (t, J = 8.0 Hz, 1H), 3.05 (s, 3H), 2.01−1.88 (s, 8H), 1.52−1.47 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 175.5, 151.3, 144.0, 130.6, 129.0, 127.9, 127.6, 127.3, 124.0, 122.4, 100.0, 64.4, 32.9, 24.8, 24.3, 22.6. HRMS: m/z 291.1611, calculated for $\mathrm{C_{20}H_{21}NO}$ 291.1623.

2-Chloro-N,N-diisopropyl-5-nitrobenzamide. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.13 (dd, J = 8.0, 2.0 Hz, 1H), 8.06 (d, J = 2.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 3.59−3.48 (m, 2H), 1.55 (dd, J = 8.0, 2.0 Hz, 6H), 1.22 (d, J = 8.0 Hz, 1H), 1.10 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 164.9, 146.7, 139.2, 137.2, 130.9, 124.2, 121.9, 51.5, 46.4, 20.5, 20.1. HRMS: 284.0904, calculated for $\mathrm{C_{13}H_{17}ClN_2O_3}$ 284.0928.

2-Hydroxy-N,N-diisopropyl-5-nitrobenzamide. This compound was prepared by following procedure B; a white solid was obtained. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.15 (dd, J = 8.0, 2.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 3.88 (s, 2H), 1.40 (d, J = 8.0 Hz, 12H). HRMS: m/z 267.1323, calculated for $\mathrm{C_{13}H_{18}N_2O_4 + H^+}$ 267.1345.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Tables, figures, and CIF files giving details for the optimization of reaction conditions, mechanistic details, NMR spectra, HRMS spectra of unknown compounds, and crystallographic data (CCDC file 968215 for **21**, 968216 for **23**, 968217 for **1**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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