JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

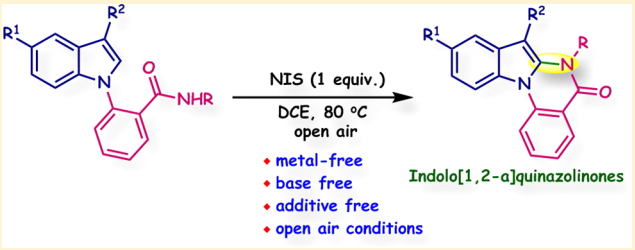
NIS Mediated Cross-Coupling of C(sp^2)−H and N−H Bonds: A Transition-Metal-Free Approach toward Indolo[1,2-*a*]quinazolinones

Sindhura Badigenchala and Govindasamy Sekar*

Department of Chemistry, Indian Institute of Technology Madras, Chennai, Tamil Nadu 600 036, India

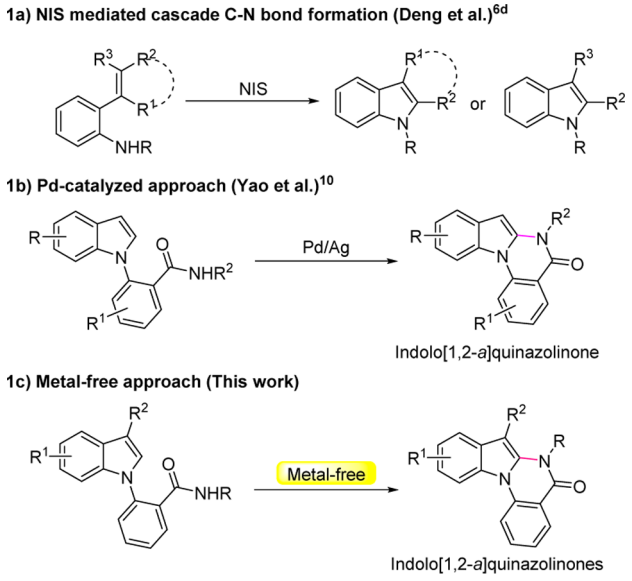
Supporting Information

ABSTRACT: A metal- and base-free protocol for intramolecular cross-coupling of C(sp^2)−H and N−H bonds using *N*-iodosuccinimide (NIS) has been demonstrated. This environmentally benign approach furnishes a series of substituted indolo[1,2-*a*]quinazolinones from the suitably fabricated indoles via C−N bond forming cyclization in 28−82% yield. A plausible mechanism is proposed for this cyclization based on the results of a control experiment. This methodology requires no additional metal catalyst, oxidant, or base. Furthermore, the synthetic utility of the protocol is demonstrated by performing a gram scale reaction.



C−N bond formation is considered as an important phenomenon in synthetic organic chemistry because of the ubiquitous nature of C−N bonds in various biologically active molecules.[1a] Apparently this field has gained immense interest from synthetic chemists, who are developing new strategies to transform a C−H/C−X bond into a C−N bond.[1] Apart from the classical C−H functionalizations, various transition metal catalyzed cross-coupling reactions have been extensively studied and efficiently applied for C−N bond formation/C−H amination reactions.[2] Although these methods are highly successful, they are associated with serious drawbacks such as use of expensive and toxic metal catalysts. In addition to this, most of the time these reactions require expensive ligands, additives, and cocatalysts. En route to overcome these complications, a wide variety of transition-metal-free methodologies have been developed.[3] Among these, iodine has attracted attention of chemists in recent years, as an alternative tool to metal catalysis. As a result, significant research has been done in this area and is still going on.[4] In particular, *N*-iodosuccinimide (NIS) has been proved highly efficient in various electrophilic cyclizations[5] and C−N bond forming reactions[6] to synthesize valuable nitrogen heterocycles. Deng et al. reported cascade C−N bond formation utilizing NIS to synthesize indoles (Scheme 1, **1a**).[6d] Recently NIS has been utilized for diastereoselective C−H amination for the synthesis of chiral ligands.[6f] Indole moiety is of particular importance among the heterocycles, because of its presence as a subunit in various bioactive compounds, and has been considered as a *privileged structure*.[7] Indolo[1,2-*a*]quinazolinones, comprising two important heterocyclic units, viz., indole and quinazolinone, have been known to have potent biological properties, and some of their derivatives have emerged as CK2 inhibitors.[8] Synthetic protocols for such promisingly bioactive indolo[1,2-*a*]quinazolinones are limited. Moreover the reported procedures involve multistep syntheses and use complex starting materials.[8,9] Recently, Yao et al. reported the synthesis of indolo[1,2-*a*]quinazolinones in which the key C−N bond formation has been attained by Pd-catalyzed intramolecular C−H amidation using a stoichiometric amount of silver salt as oxidant (Scheme 1b).[10]

Scheme 1. (a) NIS Mediated Cascade C−N Bond Formation. (b, c) Approaches for Indolo[1,2-*a*]quinazolinones



An alternative, simpler, inexpensive and metal-free protocol, which would be more general and environmentally friendly, is

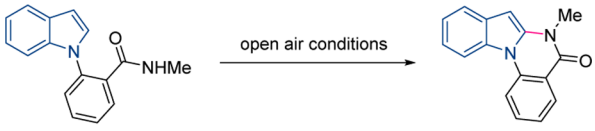
Received: May 4, 2017
Published: June 22, 2017

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

highly desirable and will have a significant impact in the field of transition-metal-free C−N bond formation (Scheme 1c). As part of our continuous efforts in developing metal-free methodologies for C−N bond formation,[11] we have recently reported iodine mediated intramolecular C2 amidation of indoles.[12] In continuation of our research in this field, herein we disclose a NIS mediated intramolecular cross-coupling of C(sp^2)−H and N−H bonds to construct indolo[1,2-*a*]-quinazolinones.

To initialize our study, compound **1a** was chosen as a model substrate. Initially, **1a** was subjected to our already-established intramolecular C2 sulfonamidation reaction conditions.[12] Unfortunately, this reaction was not fruitful and resulted in a complex reaction mixture, along with the unreacted **1a** (Table 1, entry 1). Later, based on the report of Deng et al., where NIS has been used for the cascade C−N bond formation reaction,[6d] the same reaction conditions were applied to the substrate **1a**. This reaction gave 20% yield of the **2a** (indolo[1,2-*a*]-quinazolinone) in 48 h (entry 3). Since the reaction was slow at room temperature, the same reaction was carried out at 60 °C in DCE solvent (entry 4). Convincingly, this reaction provided 54% of **2a** in 6 h (entry 4). Addition of base to this reaction disfavored the product formation (entry 5).

Table 1. Optimization of Reaction Conditions[a]



1a **2a**

Entry	Reagent (equiv.)	Solvent (2 mL)	Temp (°C)	Time (h)	Yield (%)
1.	I_2 (1.2)	CH_3CN	80	24	nd[b]
2.	I_2 (1.2)	CH_3CN	rt	24	nd[b]
3.	NIS (2)	DCM	rt	48	20
4.	NIS (2)	DCE	60	6	54
5.	NIS (2)	DCE	60	6	nd[b,c]
6.	NIS (2)	DCE	80	6	45
7.	NIS (1)	DCE	80	6	72
8.	NIS (1)	DCE	80	4	82
9.	NIS (1)	DCE	60	6	62
10.	NIS (1.2)	DCE	60	10	68
11.	NCS	DCE	80	12	nd[b]
12	NBS	DCE	80	8	54

[a]Reaction conditions: **1a** (0.5 mmol), NIS (0.5 mmol) in DCE (2 mL) at 80 °C under open air. [b]nd = not detected. [c]2 equiv of Cs_2CO_3 was added.

When the reaction was performed at 80 °C using NIS (2 equiv), 45% yield was isolated in 6 h (entry 6). It was suspected that the use of excess NIS (2 equiv) might be the cause of decomposition of the product (because other spots were seen in TLC), and a similar observation has been made in our previous methodology.[12] So, the amount of NIS was reduced to 1 equiv. To our delight, the yield of the product was increased to 72% (entry 7). However, the yield was slightly better (82%) when the same reaction was stopped at 5 h (entry 8). Further, changing reaction parameters and using other *N*-halosuccinimide reagents did not help in increasing the yield of **2a** (entries 9−12). After fixing the NIS equivalents and temperature, various solvents were screened to increase the yield of the product. Most of the solvents gave good yields of the products, however none of them were found to be superior to DCE.[13]

From the above series of screening reactions, the best optimized conditions were established as NIS (1 equiv) in DCE (2 mL) at 80 °C under open air (Table 1, entry 8). After establishing the optimized reaction conditions, the substrate scope of the methodology was surveyed. At first, the effect of substituents present on the indole ring system toward the C−N bond formation was studied, and results are depicted in Scheme 2.

Reaction proceeded very well with a broad spectrum of substrates and provided modest to good yields of the corresponding indolo[1,2-*a*]quinazolinones (Scheme 2). Substrates with substituents such as 5-methoxy (**1b**), 5-methyl (**1c**), and 3-methyl (**1d**) underwent reaction smoothly and gave corresponding cyclized products, **2b−2d**, in very good yields (70−76%). Substrates with mild electron withdrawing groups like 5-bromo (**1e**), 5-chloro (**1f**), and 6-chloro (**1g**) were well tolerated under the reaction conditions and afforded 60−72% yield of C−N bond formation products. But the presence of strong electron withdrawing 5-nitro substituent (**1h**) and 7-azaindole derived substrate (**1i**) completely suppressed the reaction. Substrate with 7-ethyl group (**1j**) on indole drastically reduced the yield of the product. This could be, probably, the steric effect of ethyl group at C7, disfavoring the orientation of amide group for cyclization. The structure of one of the products, viz., compound **2e**, was unambiguously established by single crystal XRD (see Supporting Information for details).

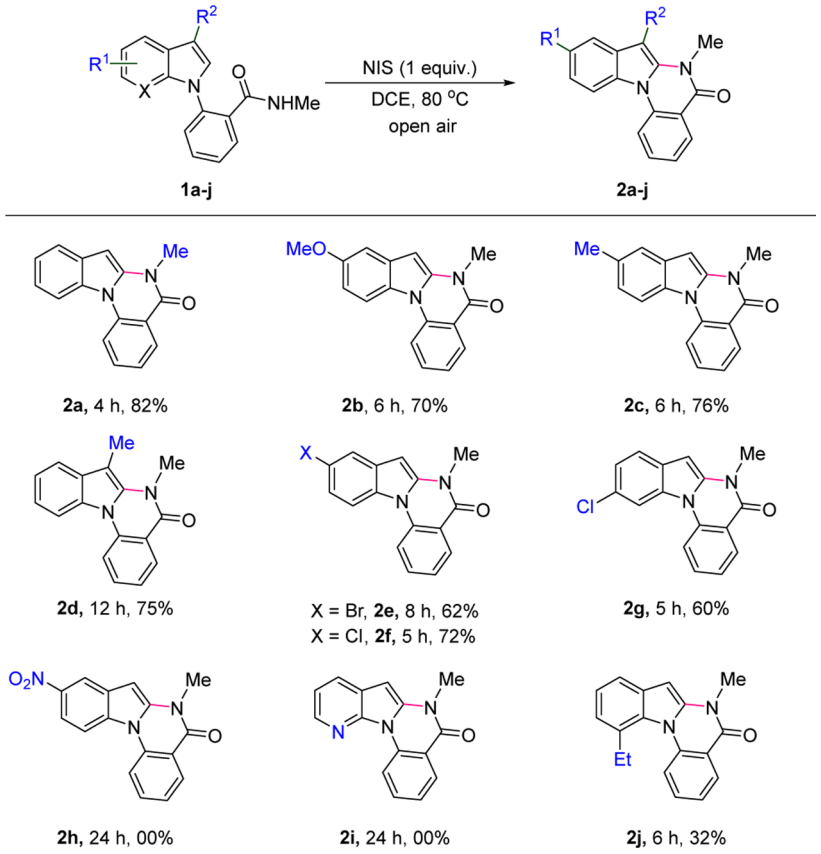
To further increase the scope of the methodology and to examine the effect of substituents on amide nitrogen, methyl substituent on the amide was replaced with aryl and benzyl groups (Scheme 3). Reaction was found to be sluggish in the case of *N*-phenyl substituted amides (**1k** and **1l**), and lesser yields of products were isolated (35% and 56%). In contrast, benzyl amide derived substrates underwent the transformation smoothly and the corresponding products were obtained in modest to good yields (53−77%). Unsubstituted benzyl amide (**1m**) gave 66% yield of the corresponding indolo[1,2-*a*]quinazolinone in 5 h. The established reaction conditions were found to be suitable for 5-methoxy, 5-bromo, and 6-chloro indole derivatives with benzyl substituted amide, delivering good yields of the desired products **2n**, **2o**, and **2p** respectively. When substrates with different substituents on benzyl group of amide (**1q** and **1r**) were subjected to cyclization conditions, they furnished the desired products **2q** and **2r** in 62% and 53% yield, respectively. In addition, *N*-furfuryl substituted amide **1s** also yielded 75% of **2s**. When substrates with unsubstituted amide (−$CONH_2$), **1t** and **1u**, were subjected to the reaction conditions, the corresponding products, **2t** and **2u**, were obtained in 34% and 28% yield, respectively.

After successfully exploring the substrate scope of the NIS mediated cyclization, the steric effect of substituents present on amide nitrogen toward the cyclization was studied by varying the alkyl groups on the amide (Table 2).

Furthermore, to prove the efficiency of the present methodology, a gram scale reaction was performed by scaling up the amount of **1a** to 1.5 g. Convincingly this reaction provided 78% of the **2a** under the optimized reaction conditions (Scheme 4).

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

Scheme 2. Substrate Scope with Substituted Indoles[a]



[a]Reaction conditions: Indole substrate (0.5 mmol), NIS (0.5 mmol) in DCE (2 mL) at 80 °C under open air.

We presume that the reaction might proceed via the initial C3 iodination of the substrate. To understand this and to gain insight into the reaction mechanism, a control experiment was carried out employing 2-methylindole-derived substrate **1y**. When **1y** was subjected to the standard reaction conditions, this exclusively gave C3 iodinated compound, **3**, in 75% yield (Scheme 5).

Based on the above control experiment and previous reports,[6d,14] we propose a plausible mechanism (Scheme 6), in which iodonium ion from *N*-iodo succinimide initially attacks C3 of indole and results in the unstable iminium ion, **4**. This is followed by the nucleophilic attack of amide nitrogen onto C2 of the indole. Since the reaction conditions are base free, succinimide ion might abstract proton from the amide nitrogen to give intermediate **5**. This intermediate **5** on elimination of HI gives the indolo[1,2-*a*]quinazolinone **2** as final product.

In summary, we have described an efficient methodology for C−N bond forming cyclization, employing NIS for cross-coupling of C−H and N−H bonds. This methodology is suitable for a wide range of substrates and provides a facile and convenient pathway to access a library of indolo[1,2-*a*]-quinazolinones. The steric bulkiness of substituents on amide nitrogen has been found to have a profound effect toward the cyclization. A control experiment has been carried out, and a plausible reaction mechanism is proposed based on the experimental result. In addition, gram scale synthesis has been performed to examine the synthetic utility of the protocol. This methodology is more advantageous owing to its operational simplicity. Furthermore, it offers an environmentally benign strategy which involves the use of NIS and avoids the use of complex starting materials, expensive metal catalysts, base, and extra additives.

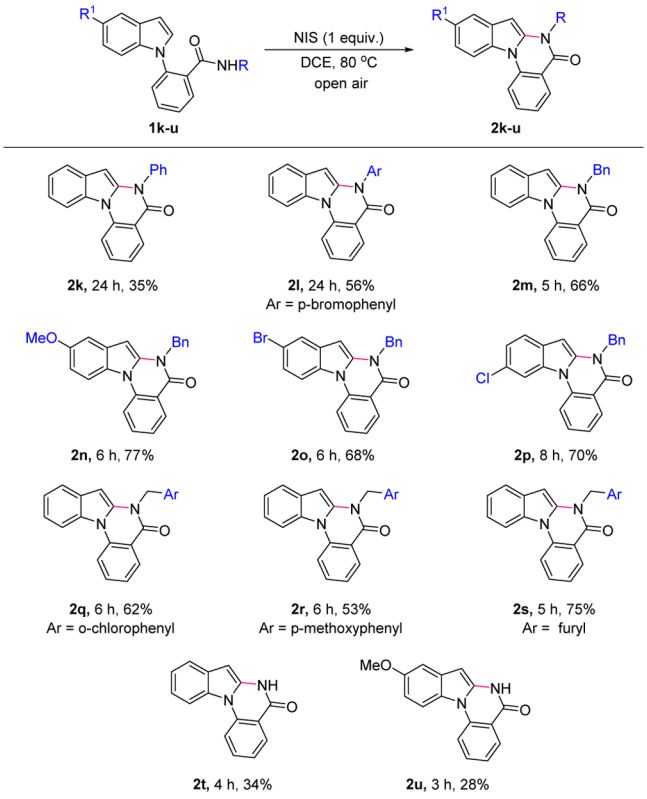
EXPERIMENTAL SECTION

General Considerations. All reactions were carried out under open atmosphere in reaction tubes using LR grade solvents without maintaining any inert conditions. All the solvents for the reactions were obtained from Fischer Scientific, India Pvt. Ltd., and were used directly without further distillation or drying. Reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F_{254} precoated plates (0.25 mm) and visualized by UV fluorescence quenching using appropriate mixture of ethyl acetate and hexanes. Silica gel (particle size: 100−200 mesh) was purchased from Avra synthesis Pvt. Ltd. India and used for column chromatography using hexanes and ethyl acetate mixture as eluent. Other reagents such as indole, NIS, 2-iodobenzoic acid, and methylamine were purchased from Spectrochem India Pvt. Ltd. Copper iodide was purchased from Alfa Aesar Company. Substituted indoles were obtained either from Spectrochem India Pvt. Ltd. or from Alfa Aesar Company. All the reactions were carried out in temperature controlled IKA magnetic stirrers. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 and 500 MHz instrument. ^{1}H NMR spectra are reported relative to Me_4Si (δ 0.0 ppm) or residual $CDCl_3$ (δ 7.26 ppm). $^{13}C\{^1H\}$ NMR are reported relative to $CDCl_3$ (δ 77.16 ppm). FTIR spectra were recorded on a Nicolet 6700 spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were recorded on a Q-Tof Micro mass spectrometer. Melting points were measured either on a Toshniwal melting point apparatus or on a Kofler-Heizitschmikroskop apparatus. The melting points were uncorrected.

All the indolylbenzamide substrates used in this methodology were prepared using the reported procedure.[10] All the substrates were prepared accordingly based on the amount required. 2-Iodobenzamide

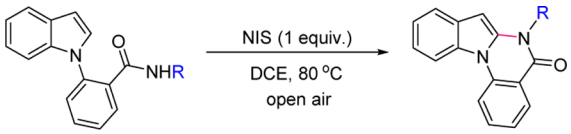
DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

Scheme 3. Substrate Scope with Substituted Amides and Indoles[a]



[a]Reaction conditions: Indole substrate (0.5 mmol), NIS (0.5 mmol) in DCE (2 mL) at 80 °C under open air.

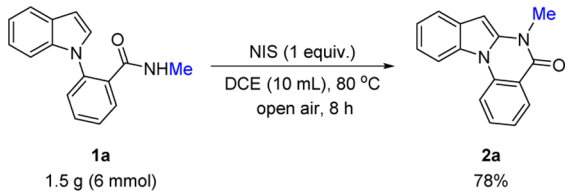
Table 2. Effect of Steric Bulkiness on Cyclization[a]



Entry	Substrate	Time (h)	Yield (%)
1	R = Me; **1a**	4	82
2	R = Et; **1v**	5	78
3	R = ^{i}Pr; **1w**	7	56
4	R = ^{t}Bu; **1x**	24	nd[b]

[a]Reaction conditions: Indole substrate (0.5 mmol), NIS (0.5 mmol) in DCE (2 mL) at 80 °C under open air. [b]nd = not detected.

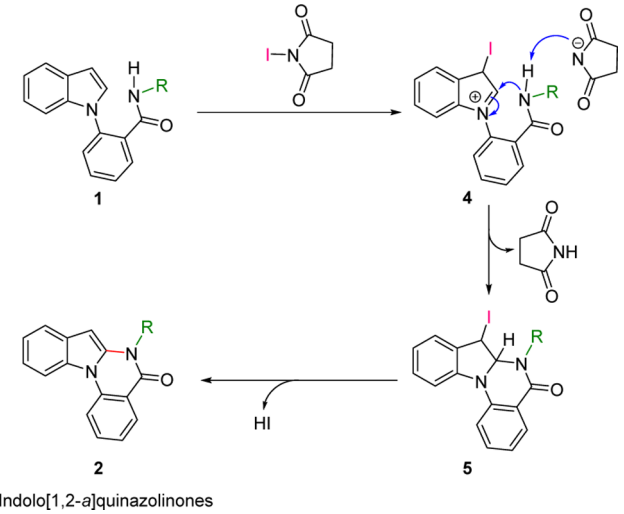
Scheme 4. Scalability of the NIS Mediated Indolo[1,2-*a*]quinazolinone Synthesis



was used in preparation of compounds **1t** and **1u** instead of *N*-substituted benzamide.

Scheme 5. Control Experiment

Scheme 6. Plausible Mechanism for NIS Mediated C−N Bond Formation



Typical Procedure for Preparation of Indolylbenzamides (1a−1y).[10] To a solution of 2-iodo-*N*-methylbenzamide (1.04 g, 4 mmol) and indole (562 mg, 4.8 mmol) in DMSO (1.5 mL/mmol) were added copper iodide (152.3 mg, 20 mol %) and potassium carbonate (1.1 g, 8 mmol). Then the reaction mixture was stirred at 80 °C until the complete conversion of 2-iodo-*N*-substituted benzamide as monitored by TLC. After the completion of reaction, the reaction mixture was filtered through Celite. The resulting filtrate was washed with brine solution and extracted with ethyl acetate. This organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to obtain crude product. The crude was then purified by column chromatography using hexane/ethyl acetate.

*2-(1H-Indol-1-yl)-N-methylbenzamide (**1a**):* white solid; yield 757 mg (63%); mp 152−154 °C [lit. 155−157 °C];[10] R_f 0.46 (30% ethyl acetate in hexanes); ^{1}H NMR (DMSO, 400 MHz, ppm) δ 2.42 (d, J = 4.4 Hz, 3H), 6.55 (dd, J = 1.6, 0.4 Hz, 1H), 7.0−7.07 (m, 2H), 7.16 (d, J = 8 Hz, 1H), 7.31 (d, J = 3.6 Hz, 1H), 7.39−7.46 (m, 2H), 7.49−7.56 (m, 3H), 8.12 (q, J = 4.4 Hz, 1H); ^{13}C{^{1}H} NMR (DMSO, 100 MHz) δ 25.9, 102.8, 110.3, 119.9, 120.6, 121.7, 127.3, 127.4, 128.4, 128.8, 129.4, 130.5, 134.9, 136.0, 138.3, 167.3; FTIR (KBr) 3437, 3103, 2923, 1644, 1601, 1544, 1512, 1492, 1459 cm^{-1}; GCMS (m/z) 250.10.

*2-(5-Methoxy-1H-indol-1-yl)-N-methylbenzamide (**1b**):* white solid; yield 264 mg (64%); mp 130−132 °C [lit. 128−130 °C];[10] R_f 0.43 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.52 (d, J = 4.8 Hz, 3H), 3.88 (s, 3H), 6.63 (d, J = 3.2 Hz, 1H), 6.86 (dd, J = 8.8, 2.4 Hz, 1H), 7.13 (d, J = 2.8 Hz, 1H), 7.19 (d, J = 3.2 Hz, 1H), 7.41 (dd, J = 7.8, 0.8 Hz, 1H), 7.49 (dt, J = 7.6, 1.6 Hz, 1H), 7.57 (dt, J = 7.6, 1.6 Hz, 1H), 7.93 (dd, J = 7.6, 2.4 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 26.8, 55.9, 102.9, 104.2, 111.1, 113.2, 127.8, 128.3, 129.3, 129.4, 131.0, 131.6, 132.2, 133.1, 136.4, 155.0, 167.2; FTIR (KBr) 3299, 3100, 3066, 2939, 2831, 1649, 1601, 1539, 1493, 1451 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{17}H_{16}N_2O_2Na$ 303.1109, found 303.1099.

*2-(5-Methyl-1H-indol-1-yl)-N-methylbenzamide (**1c**):* white solid; yield 228 mg (63%); mp 186−188 °C; R_f 0.43 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.51 (d, J = 5.2 Hz, 3H), 2.46 (s, 3H), 6.62 (d, J = 3.2, 0.8 Hz, 1H), 7.04 (dd, J = 8.4, 1.2

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 3.2 Hz, 1H), 7.42 (dd, J = 7.8, 0.8 Hz, 1H), 7.46−7.52 (m, 2H), 7.57 (dt, J = 7.6, 1.6 Hz, 1H), 7.94 (dd, J = 8.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 21.5, 26.8, 104.0, 110.0, 121.0, 124.7, 127.8, 128.2, 128.8, 129.2, 130.3, 131.0, 131.6, 133.1, 135.3, 136.5, 167.2; FTIR (KBr) 3326, 2919, 2856, 1624, 1486 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{17}H_{17}N_2O$ 265.1341, found 265.132.

*N-Methyl-2-(3-methyl-1H-indol-1-yl)benzamide (**1d**):* white solid; yield 220 mg (58%); mp 192−194 °C [lit. 195−197 °C];[10] R_f 0.43 (40% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.51 (d, J = 4.8 Hz, 3H), 2.38 (d, J = 0.8 Hz, 3H), 5.22 (bs, 1H), 7.01 (d, J = 0.8 Hz, 1H), 7.16−7.24 (m, 3H), 7.39 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 8 Hz, 1H), 7.56 (dt, J = 7.6, 1.6 Hz, 1H), 7.60−7.65 (m, 1H), 7.95 (dd, J = 8.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 9.7, 26.8, 110.3, 113.9, 119.4, 120.3, 123.1, 126.2, 127.8, 128.0, 129.5, 131.0, 131.6, 132.8, 136.6, 137.2; FTIR (KBr) 3316, 3055, 2918, 2859, 1644, 1600, 1545, 1492, 1459 cm^{-1}; GCMS (m/z) 264.00.

*2-(5-Bromo-1H-indol-1-yl)-N-methylbenzamide (**1e**):* white solid; yield 297 mg (66%); mp 185−186 °C [lit. 181−183 °C];[10] R_f 0.46 (50% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 4.14 (d, J = 5.2 Hz, 2H), 5.40 (s, 1H), 6.54 (d, J = 2.8 Hz, 1H), 6.67 (d, J = 7.2 Hz, 2H), 7.02 (d, J = 8.8 Hz, 1H), 7.10−7.16 (m, 2H), 7.16−7.24 (m, 3H), 7.37 (d, J = 7.6 Hz, 1H), 7.50−7.62 (m, 2H), 7.75 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 26.9, 103.8, 111.8, 114.2, 123.8, 125.9, 127.8, 128.7, 130.0, 130.5, 130.8, 131.7, 133.5, 135.6, 135.8; FTIR (KBr) 3331, 3105, 2921, 2852, 1626, 1547, 1513, 1488, 1454 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{13}N_2ONaBr$ 351.0109, found 351.0091.

*2-(5-Chloro-1H-indol-1-yl)-N-methylbenzamide (**1f**):* white solid; yield 210 mg (74%); mp 178−180 °C [lit. 182−184 °C];[10] R_f 0.45 (40% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.53 (d, J = 4.8 Hz, 3H), 6.65 (d, J = 3.2 Hz, 1H), 7.15 (d, J = 1.2 Hz, 2H), 7.24−7.27 (m, 1H), 7.41 (dd, J = 7.8, 1.2 Hz, 1H), 7.52 (dt, J = 3.6, 1.2 Hz, 1H), 7.59 (dt, J = 7.6, 1.6 Hz, 1H), 7.64 (t, J = 1.2 Hz, 1H), 7.90 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 26.9, 103.9, 111.4, 120.7, 123.3, 126.6, 127.8, 128.7, 129.9, 130.1, 130.8, 131.7, 133.5, 135.4, 135.9, 167.1; FTIR (KBr) 3316, 3108, 2924, 2854, 1621, 1515, 1486, 1450 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{13}N_2ONaCl$ 307.0614, found 307.0629.

*2-(6-Chloro-1H-indol-1-yl)-N-methylbenzamide (**1g**):* white solid; yield 225 mg (78%); mp 185−187 °C ; R_f 0.45 (40% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.57 (d, J = 4.8 Hz, 3H), 5.15 (s, 1H), 6.67 (d, J = 3.2 Hz, 1H), 7.15 (dd, J = 8.4, 1.6 Hz, 1H), 7.23 (s, 1H), 7.43 (dd, J = 7.8, 0.8 Hz, 1H), 7.52 (dt, J = 7.6, 1.2 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.84 (dd, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 26.9, 104.3, 110.3, 121.7, 122.2, 127.4, 127.8, 128.7, 129.0, 129.7, 130.8, 131.6, 133.6, 135.8, 137.3, 167.1; FTIR (KBr) 3285, 3101, 2935, 2871, 1628, 1560, 1490, 1458 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{16}H_{14}N_2OCl$ 285.0795, found 285.0804.

*2-(5-Nitro-1H-indol-1-yl)-N-methylbenzamide (**1h**):* yellow solid; yield 156 mg (38%); mp 186−188 °C; R_f 0.46 (70% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.51 (d, J = 4.8 Hz, 3H), 5.23 (bs, 1H), 6.80 (dd, J = 3.6, 0.8 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 7.35 (d, J = 3.2 Hz, 1H), 7.38 (dd, J = 7.8, 0.8 Hz, 1H), 7.50 (dt, J = 7.6, 1.6 Hz, 1H), 7.57 (dt, J = 7.6, 1.2 Hz, 1H), 7.76 (dd, J = 7.6, 1.6 Hz, 1H), 8.00 (dd, J = 9.0, 2.4 Hz, 1H), 8.56 (d, J = 2.4 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 26.9, 106.1, 110.4, 118.4, 118.5, 127.9, 128.1, 129.2, 130.3, 131.7, 132.2, 134.0, 135.3, 139.7, 142.6, 167.0; FTIR (KBr) 3315, 3102, 2925, 2853, 1647, 1512, 1461 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{13}N_3O_3Na$ 318.0855, found 318.0840.

*N-Methyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzamide (**1i**):* white solid; yield 163 mg (47%); mp 156−158 °C; R_f 0.46 (70% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.54 (d, J = 4.8 Hz, 3H), 6.08 (s, 1H), 6.62 (d, J = 3.6 Hz, 1H), 7.12 (1:1 q, J = 7.6 Hz, 1H), 7.4 (d, J = 3.6 Hz, 1H), 7.43 (dd, J = 7.6, 1.2 Hz, 1H), 7.48 (dt, J = 7.6, 1.6 Hz, 1H), 7.55 (dt, J = 7.6, 2.0 Hz, 1H) 7.73 (dd, J = 7.6, 1.6 Hz, 1H), 7.98 (dd, J = 7.6, 1.2 Hz, 1H), 8.26 (dd, J = 4.8, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 26.6, 101.9, 116.9, 121.1, 128.6, 128.6, 129.6, 130.0, 131.0, 134.9, 135.1, 143.8, 148.7, 168.1; FTIR (KBr) 3313, 3057, 2937, 2851, 1649, 1599, 1546, 1514, 1491 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{13}N_3ONa$ 274.0956, found 274.0985.

*2-(7-Ethyl-1H-indol-1-yl)-N-methylbenzamide (**1j**):* white solid; yield 143 mg (36%); mp 114−116 °C; R_f 0.47 (30% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 0.96 (t, J = 7.2 Hz, 3H), 2.31 (sep, J = 7.2 Hz, 2H), 2.45 (d, J = 4.8 Hz, 3H), 6.73 (d, J = 3.2 Hz, 1H), 7.05 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 3.2 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 7.35−7.40 (m, 1H), 7.51−7.59 (m, 3H), 8.06−8.12 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 14.6, 24.3, 26.9, 105.0, 119.3, 121.4, 123.5, 128.3, 129.1, 129.4, 129.8, 130.2, 131.0, 131.2, 133.5, 135.5, 138.9, 166.1; FTIR (KBr) 3308, 3058, 2930, 2874, 1650, 1602, 1531, 1489, 1450 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{18}H_{18}N_2ONa$ 301.1317, found 301.1328.

*2-(1H-Indol-1-yl)-N-phenylbenzamide (**1k**):* white solid; yield 324 mg (69%); mp 147−149 °C [lit. 151−153 °C];[10] R_f 0.56 (30% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 6.75 (d, J = 2.8 Hz, 1H), 6.84 (d, J = 7.6 Hz, 3H), 6.97 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 2H), 7.18−7.25 (m, 2H), 7.25−7.30 (m, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.59 (dt, J = 7.6, 1.2 Hz, 1H), 7.65 (dt, J = 7.6, 1.6 Hz, 1H), 7.70−7.75 (m, 1H), 8.12 (dd, J = 7.8, 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 105.0, 110.2, 120.3, 121.3, 121.5, 123.5, 124.6, 128.5, 128.7, 128.8, 128.9, 128.9, 131.7, 132.2, 133.3, 136.1, 137.0, 137.2, 164.0; FTIR (KBr) 3289, 3056, 2921, 2852, 1657, 1599, 1530, 1494, 1460 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{16}N_2ONa$ 335.1160, found 335.1156.

*N-(4-Bromophenyl)-2-(1H-indol-1-yl)benzamide (**1l**):* pale brown solid; yield 254 mg (54%); mp 110−112 °C; R_f 0.55 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 6.70 (d, J = 8.0 Hz, 2H), 6.74 (s, 1H), 6.82 (s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.62−7.75 (m, 2H), 8.08 (d, J = 7.2 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 105.1, 110.1, 117.2, 121.4, 121.5, 121.7, 123.6, 128.6, 128.7, 128.8, 129.0, 131.6, 131.7, 132.4, 133.0, 136.1, 136.3, 137.0, 164.0; FTIR (KBr) 3289, 3107, 3056, 2924, 2853, 1660, 1596, 1522, 1492, 1458 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{15}N_2ONaBr$ 413.0265, found 413.0251.

*N-Benzyl-2-(1H-indol-1-yl)benzamide (**1m**):* white solid; yield 336 mg (69%); mp 118−120 °C [lit. 113−115 °C;[10] R_f 0.45 (30% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 4.14 (d, J = 5.2 Hz, 2H), 5.44 (s, 1H), 6.61−6.68 (m, 3H), 7.07−7.16 (m, 3H), 7.17−7.23 (m, 4H), 7.41 (dd, J = 7.6, 1.2 Hz, 1H), 7.53 (dt, J = 7.6, 1.6 Hz, 1H), 7.59 (dt, J = 7.6, 1.6 Hz, 1H), 7.66−7.71 (m, 1H), 7.99 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 44.4, 104.4, 110.3, 121.0, 121.4, 123.2, 127.4, 127.7, 128.3, 128.6, 128.9, 131.0, 131.8, 133.4, 136.3, 137.0, 137.1, 166.4; FTIR (KBr) 3302, 3059, 3031, 2923, 2854, 1644, 1602, 1517, 1492, 1457 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{18}N_2ONa$ 349.1317, found 349.1338.

*N-Benzyl-2-(5-methoxy-1H-indol-1-yl)benzamide (**1n**):* pale brown semisolid; yield 277 mg (52%); R_f 0.45 (40% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.87 (s, 3H), 4.15 (d, J = 5.2 Hz, 2H), 5.62 (s, 1H), 6.47 (s, 1H), 6.55 (d, J = 3.2 Hz, 1H), 6.70 (d, J = 6.8 Hz, 1H), 6.82(dd, J = 8.8, 2.4 Hz, 1H), 7.08 (d, J = 9.2 Hz, 1H), 7.10−7.19 (m, 5H), 7.38 (dd, J = 7.8, 1.2 Hz, 1H), 7.49 (dt, J = 7.6, 0.8 Hz, 1H), 7.56 (dt, J = 7.6, 1.6 Hz, 1H), 7.94 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 44.4, 56.0, 103.0, 104.3, 111.1, 113.2, 127.4, 127.7, 128.2, 128.5, 128.5, 129.1, 129.4, 131.0, 131.8, 132.4, 133.3, 136.4, 137.1, 155.0, 166.3; FTIR (KBr) 3304, 3062, 3031, 2934, 2831, 1644, 1601, 1521, 1493, 1452 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{23}H_{20}N_2O_2Na$ 379.1422, found 379.1410.

*N-Benzyl-2-(5-bromo-1H-indol-1-yl)benzamide (**1o**):* white solid; yield 286 mg (47%); mp 104−106 °C; R_f 0.45 (40% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 4.14 (d, J = 5.2 Hz, 2H), 5.40 (s, 1H), 6.54 (d, J = 2.8 Hz, 1H), 6.67 (d, J = 7.2 Hz, 2H), 7.02 (d, J = 8.8 Hz, 1H), 7.10−7.16 (m, 2H), 7.16−7.24 (m, 3H), 7.37 (d, J = 7.6 Hz, 1H), 7.50−7.62 (m, 2H), 7.75 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 44.4, 103.9, 111.7, 114.2, 123.9, 125.9, 127.6, 127.7, 128.2, 128.6, 128.9, 129.8, 130.5, 130.9, 131.8, 133.7, 135.8, 136.9, 166.13; FTIR (KBr) 3286, 3063,

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

2924, 2855, 1644, 1601, 1515, 1493, 1456 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{22}H_{17}N_2ONaBr$ 427.0422, found 427.0446.

*N-Benzyl-2-(6-chloro-1H-indol-1-yl)benzamide (**1p**):* pale brown solid; yield 265 mg (46%); mp 186−188 °C; R_f 0.46 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.57 (d, J = 4.8 Hz, 3H), 5.15 (s, 1H), 6.67 (d, J = 3.2 Hz, 1H), 7.15 (dd, J = 8.4, 1.6 Hz, 1H), 7.23 (s, 1H), 7.43 (dd, J = 7.8, 0.8 Hz, 1H), 7.52 (dt, J = 7.6, 1.2 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.84 (dd, J = 7.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 26.9, 104.3, 110.3, 121.7, 122.2, 127.4, 127.8, 128.7, 129.0, 129.7, 130.8, 131.6, 133.6, 135.8, 137.3, 167.1; FTIR (KBr) 3288, 3062, 3033, 2924, 2855, 1646, 1604, 1514, 1458 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{22}H_{17}N_2ONaCl$ 383.0927, found 383.0952.

*2-(1H-Indol-1-yl)-N-(2-chlorobenzyl)benzamide (**1q**):* pale brown semisolid; yield 427 mg (69%); R_f 0.50 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 4.27 (d, J = 5.6 Hz, 2H), 5.64 (s, 1H), 6.56 (d, J = 3.2 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 7.00 (dt, J = 7.2, 1.2 Hz, 1H), 7.08−7.18 (m, 6H), 7.40 (dd, J = 7.6, 0.8 Hz, 1H), 7.52 (dt, J = 7.4, 1.2 Hz, 1H), 7.56−7.63 (m, 2H), 7.98 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 41.7, 104.4, 110.1, 120.8, 121.3, 122.9, 126.9, 128.2, 128.4, 128.7, 128.8, 129.2, 129.7, 130.8, 131.7, 133.3, 133.4, 134.7, 136.3, 136.9, 166.3; FTIR (KBr) 3288, 3060, 2925, 2856, 1650, 1603, 1518, 1491, 1464 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{22}H_{17}N_2ONaCl$ 383.0927, found 383.0912.

*2-(1H-Indol-1-yl)-N-(4-methoxybenzyl)benzamide (**1r**):* pale brown semisolid; yield 320 mg (70%); R_f 0.48 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.75 (s, 3H), 4.06 (d, J = 5.2 Hz, 2H), 5.34 (s, 1H), 6.53−6.58 (m, 2H), 6.60−6.64 (m, 3H), 7.19 (d, J = 2.8 Hz, 4H), 7.40 (dd, J = 7.6, 1.2 Hz, 1H), 7.52 (dt, J = 7.6, 1.2 Hz, 1H), 7.58 (dt, J = 7.6, 1.6 Hz, 1H), 7.66−7.70 (m, 1H), 7.97 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 43.8, 55.3, 104.5, 110.3, 113.9, 120.9, 121.3, 123.1, 128.3, 128.5, 128.6, 128.9, 129.0, 129.2, 130.9, 131.7, 133.5, 136.3, 137.1, 158.9, 166.2; FTIR (KBr) 3299, 3055, 3001, 2928, 2835, 1644, 1610, 1512, 1492, 1459 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{23}H_{20}N_2O_2Na$ 379.1422, found 379.1455.

*N-(Furan-2-ylmethyl)-2-(1H-indol-1-yl)benzamide (**1s**):* pale brown solid; yield 259 mg (57%); mp 82−84 °C; R_f 0.45 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 4.15 (d, J = 6.4 Hz, 2H), 5.48 (s, 1H), 5.75 (dd, J = 3.2, 0.8 Hz, 1H), 6.15 (dd, J = 3.2, 1.6 Hz, 1H), 6.63 (d, J = 3.2 Hz, 1H), 7.13 (dd, J = 2.0, 0.8 Hz, 1H), 7.16−7.22 (m, 4H), 7.42 (dd, J = 7.8, 1.2 Hz, 1H), 7.52 (dt, J = 7.6, 1.2 Hz, 1H), 7.59 (dt, J = 7.6, 2.0 Hz, 1H), 7.63−7.68 (m, 1H), 7.97 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 36.9, 104.5, 107.2, 110.2, 110.3, 120.8, 121.3, 123.0, 128.2, 128.4, 128.5, 128.8, 131.0, 131.8, 131.9, 136.4, 137.0, 142.0, 150.3, 166.1; FTIR (KBr) 3294, 3056, 2923, 2854, 1651, 1602, 1517, 1493, 1459 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{20}H_{16}N_2O_2Na$ 339.1109, found 339.1079.

*2-(1H-Indol-1-yl)benzamide (**1t**):* yellow solid; yield 260 mg (28%); mp 124−126 °C; R_f 0.50 (50% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 5.12 (s, 1H), 5.50 (s, 1H), 6.73 (d, J = 3.5 Hz, 1H), 7.17−7.22 (m, 3H), 7.23 (d, J = 3.5 Hz, 1H), 7.41 (dd, J = 7.7, 1.5 Hz, 1H), 7.54 (dt, J = 7.5, 1.5 Hz, 1H), 7.62 (dt, J = 7.5, 1.5 Hz, 1H), 7.67−7.70 (m, 1H), 8.04 (dd, J = 7.7, 1.5 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 104.7, 110.4, 121.0, 121.3, 123.2, 128.5, 128.6, 128.7, 128.9, 131.3, 132.2, 132.2, 136.6, 137.0, 168.0; FTIR (KBr) 3470, 3331, 3055, 1667, 1604, 1512, 1494 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{15}H_{12}N_2ONa$ 259.0847, found 259.0856.

*2-(5-Methoxy-1H-indol-1-yl)benzamide (**1u**):* yellow solid; yield 173 mg (36%); mp 118−120 °C; R_f 0.45 (50% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.86 (s, 3H), 5.14 (s, 1H), 5.40 (s, 1H), 6.65 (dd, J = 3.2, 0.8 Hz, 1H), 6.86 (dd, J = 9.2, 2.4 Hz, 1H), 7.10 (d, J = 8.8 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.20 (d, J = 3.2 H, 1H), 7.4 (dd, J = 7.6, 1.2 Hz, 1H), 7.53 (dt, J = 7.6, 1.6 Hz, 1H), 7.60 dt, J = 7.6, 1.6 Hz, 1H), 8.04 (dd, J = 7.8, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 55.9, 102.9, 104.4, 111.2, 113.3, 128.4, 128.5, 129.2, 129.4, 131.4, 132.1, 132.3, 132.3, 136.8, 155.1, 168.0; FTIR (KBr) 3444, 3334, 2991, 1662, 1605, 1493, 1476 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{15}N_2O_2$ 267.1134, found 267.1152.

*N-Ethyl-2-(1H-indol-1-yl)benzamide (**1v**):* brown solid; yield 196 mg (62%); mp 106−108 °C [lit. 106−108 °C];[10] R_f 0.48 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 0.49 (t, J = 7.2 Hz, 3H), 2.93−3.02 (m, 2H), 5.03 (s, 1H), 6.72 (d, J = 3.2 Hz, 1H), 7.14−7.25 (m, 4H), 7.43 (dd, J = 7.8, 1.2 Hz, 1H), 7.52 (dt, J = 7.6, 1.6 Hz, 1H), 7.59 (dt, J = 7.6, 1.6 Hz, 1H), 7.66−7.71 (m, 1H), 7.96 (dd, J = 8.0, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 34.7, 104.4, 110.3, 120.9, 121.3, 123.1, 128.1, 128.5, 128.5, 128.7, 131.0, 131.6, 133.7, 136.1, 137.1, 166.2; FTIR (KBr) 3297, 3059, 2929, 1645, 1520, 1491, 1458 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{17}H_{17}N_2O$ 265.1341, found 265.1371.

*N-Isopropyl-2-(1H-indol-1-yl)benzamide (**1w**):* white solid; yield 225 mg (39%); mp 98−100 °C; R_f 0.48 (30% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 0.55 (d, J = 4.8 Hz, 6H), 3.74−3.87 (m, 1H), 4.83 (d, J = 5.6 Hz, 1H), 6.73 (d, J = 3.2 Hz, 1H), 7.14−7.21 (m, 2H), 7.23 (d, J = 3.2 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.51−7.62 (m, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.98 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 21.9, 41.6, 104.4, 110.3, 120.9, 121.3, 123.2, 128.3, 128.7, 131.1, 131.6, 134.0, 136.1, 137.2, 165.2; FTIR (KBr) 3295, 3056, 2929, 2872, 1640, 1602, 1521, 1492, 1460 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{18}N_2ONa$ 301.1317, found 301.1335.

*N-(tert-Butyl)-2-(1H-indol-1-yl)benzamide (**1x**):* white solid; yield 273 mg (59%); mp 108−110 °C; R_f 0.50 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 0.83 (s, 9H), 4.89 (s, 1H), 6.74 (dd, J = 3.2, 0.4 Hz, 1H), 7.15−7.21 (m, 3H), 7.23 (d, J = 3.2 Hz, 1H), 7.40 (dd, J = 6.8, 1.6 Hz, 1H), 7.51−7.60 (m, 2H), 7.67−7.71 (m, 1H), 7.95 (dd, J = 7.4, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 28.0, 51.3, 104.3, 110.4, 120.9, 121.2, 123.2, 128.3, 128.4, 128.7, 128.8, 131.0, 131.4, 135.2, 135.9, 137.4, 165.2; FTIR (KBr) 3316, 3057, 2927, 1658, 1603, 1517, 1488, 1456 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{19}H_{20}N_2ONa$ 315.1473, found 315.1476.

*N-Methyl-2-(2-methyl-1H-indol-1-yl)benzamide (**1y**):* white solid; yield 190 mg (55%); mp 158−160 °C; R_f 0.45 (40% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.19 (s, 3H), 2.48 (d, J = 4.8 Hz, 3H), 5.06 (s, 1H), 6.45 (s, 1H), 6.95 (d, J = 7.6 Hz, 1H), 7.12 (q, J = 7.6 Hz, 2H), 7.31 (d, J = 7.2 Hz, 1H), 7.56−7.64 (m, 3H), 8.10 (d, J = 8.0 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 12.9, 26.3, 102.4, 109.8, 120.1, 120.8, 122.0, 128.6, 129.2, 129.9, 131.4, 131.9, 134.3, 134.7, 137.6, 138.0, 166.51; FTIR (KBr) 3303, 3056, 2927, 1652, 1604, 1549, 1490, 1457 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{17}H_{16}N_2ONa$ 287.1160, found 287.1141.

General Procedure for NIS Mediated Synthesis of Indolo-[1,2-*a*]quinazolinones (2a−w, 3). To a reaction tube containing a solution of 2-indolylbenzamide **1** (0.5 mmol) in DCE (2 mL) was added NIS (0.5 mmol, 113 mg), and the reaction mixture was stirred at 80 °C under the open air conditions, until the disappearance of starting material as monitored by TLC. After the completion of reaction, the obtained reaction mixture was then allowed to cool to room temperature and was washed with saturated $Na_2S_2O_3$ (to quench the I_2 formed by the oxidation of HI) and extracted with DCM. The combined organic layers were evaporated in a rotary evaporator to obtain crude product, which was then purified by column chromatography using hexane/ethyl acetate as eluent to obtain the product indolo[1,2-*a*]quinazolinones **2**.

*6-Methylindolo[1,2-a]quinazolin-5(6H)-one (**2a**):* greenish yellow solid; yield 102 mg (82%); mp 185−186 °C [lit. 181−183 °C];[10] R_f 0.48 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.49 (s, 3H), 5.91 (s, 1H), 7.16−7.20 (m, 2H), 7.20−7.26 (m, 1H), 7.50−7.54 (m, 1H), 7.60−7.66 (m, 1H), 7.92−7.97 (m, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.28 (dd, J = 8.0, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 30.5, 84.2, 113.1, 114.6, 116.5, 120.1, 121.4, 122.6, 123.5, 129.9, 131.4, 134.4, 138.2, 138.8, 158.8; FTIR (KBr) 2920, 1662, 1607, 1572, 1484 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{13}N_2O$ 249.1028, found 249.1005.

*9-Methoxy-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2b**):* greenish yellow solid; yield 97 mg (70%); mp 198−200 °C [lit. 198−200 °C];[10] R_f 0.50 (30% ethyl acetate in hexanes); ^{1}H NMR

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

($CDCl_3$, 400 MHz, ppm) δ 3.80 (s, 3H), 3.49 (s, 3H), 5.85 (s, 1H), 6.78 (d, J = 8.4 Hz, 2H), 6.98 (s, 1H), 7.16−7.27 (m, 1H), 7.63 (s, 1H), 7.82 (s, 1H), 8.03 (s, 1H), 8.28 (s, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 30.4, 55.8, 102.7, 110.0, 113.8, 114.2, 116.3, 123.2, 126.3, 129.9, 131.1, 134.4, 138.7, 155.8, 158.6; FTIR (KBr) 3103, 2925, 2828, 1661, 1500, 1489 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{14}N_2O_2Na$ 301.0944, found 301.0953.

9-Methyl-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2c**): greenish yellow solid; yield 99 mg (76%); mp 180−182 °C; R_f 0.55 (30% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 500 MHz, ppm) δ 2.46 (s, 2H), 3.54 (s, 3H), 5.88 (d, J = 0.5 Hz, 1H), 7.05 (dd, J = 8.5, 1.5 Hz, 1H), 7.28 (dt, J = 7.5, 1.0, 1H), 7.35 (s, 3H), 7.69 (dt, J = 7.8, 1.5 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 8.34 (dd, J = 7.8, 1.5 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 21.5, 30.4, 83.8, 112.7, 114.4, 114.4, 116.3, 120.0, 122.6, 123.2, 129.6, 129.8, 130.1, 132.0, 134.3, 138.1, 138.8, 158.8; FTIR (KBr) 2952, 1660, 1604, 1570, 1488, 1432 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{17}H_{15}N_2O$ 263.1184, found 263.1175.

6,7-Dimethylindolo[1,2-a]quinazolin-5(6H)-one (**2d**): yellow solid; yield 98 mg (75%); mp 208−210 °C; R_f 0.45 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.55 (s, 3H), 3.82 (s, 3H), 7.12−7.25 (m, 3H), 7.24−7.33 (m, 3H), 7.53−7.58 (m, 1H), 7.67 (dt, J = 7.6, 1.6 Hz, 1H), 7.97−8.02 (m, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.31 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 10.3, 32.3, 92.6, 112.8, 114.4, 116.3, 118.0, 121.7, 122.1, 123.1, 129.8, 130.2, 131.6, 133.5, 134.3, 139.0, 159.6; FTIR (KBr) 2918, 2855, 1651, 1568, 1480 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{17}H_{15}N_2O$ 263.1184, found 263.1159.

9-Bromo-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2e**): greenish yellow solid; yield 101 mg (62%); mp 230−232 °C [lit. 225−227 °C];[10] R_f 0.48 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.61 (s, 3H), 5.98 (d, J = 0.4 Hz, 1H), 7.32−7.40 (m, 2H), 7.73 (d, J = 2.0 Hz, 1H), 7.77 (dt, J = 8.0, 1.6 Hz, 1H), 7.92 (d, J = 9.2 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.40 (dd, J = 8.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 30.6, 114.3, 114.6, 115.9, 116.6, 122.6, 124.0, 124.0, 130.1, 130.2, 131.8, 134.6, 138.5, 139.2, 158.6; FTIR (KBr) 3038, 2935, 1656, 1437 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{11}N_2ONaBr$ 348.9952, found 348.9931.

9-Chloro-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2f**): greenish yellow solid; yield 101 mg (72%); mp 220−222 °C [lit. 216−218 °C];[10] R_f 0.48 (15% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.56 (s, 3H), 5.91 (s, 1H), 7.17 (dd, J = 9.0, 2.4 Hz, 1H), 7.33 (dt, J = 7.6, 0.4 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.42 (dt, J = 7.6, 1.6 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.36 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 30.5, 83.8, 113.9, 114.4, 116.6, 119.5, 121.3, 123.9, 128.2, 129.7, 130.1, 131.3, 134.5, 138.4, 139.3, 158.4; FTIR (KBr) 3033, 2919, 2848, 1671, 1618, 1597, 1489 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{11}N_2ONaCl$ 305.0458, found 305.0438.

10-Chloro-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2g**): greenish yellow solid; yield 84 mg (60%); mp 212−214 °C; R_f 0.48 (15% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 500 MHz, ppm) δ 3.54 (s, 3H), 5.92 (s, 1H), 7.21 (d, J = 7.5 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H) 7.46 (d, J = 8.5 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.93 (s, 1H), 8.05 (d, J = 8.5 Hz, 1H), 8.34 (d, J = 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 30.5, 84.0, 113.2, 114.4, 116.6, 120.6, 123.0, 124.0, 126.8, 128.4, 130.1, 131.4, 134.5, 138.3, 138.7, 158.3; FTIR (KBr) 3108, 2918, 2848, 1667, 1619, 1605, 1573, 1489 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{16}H_{11}N_2ONaCl$ 305.0458, found 305.0443.

11-Ethyl-6-methylindolo[1,2-a]quinazolin-5(6H)-one (**2j**): greenish yellow solid; yield 44 mg (32%); mp 100−102 °C; R_f 0.46 (15% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 1.21 (t, J = 7.2 Hz, 3H), 2.96 (q, J = 7.2 Hz, 2H), 3.60 (s, 3H), 6.01 (s, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.43 (t, J = 8 Hz, 2H), 7.63 (dt, J = 8.0, 1.6 Hz, 1H), 8.28 (dd, J = 8.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 15.0, 27.6, 30.6, 85.4, 117.4, 118.3, 122.7, 123.4, 123.9, 129.0, 130.1, 130.9, 131.6, 132.7, 138.8, 140.0, 159.6; FTIR (KBr) 3052, 2931, 2874, 2852, 1671, 1613, 1604, 1573, 1479 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{18}H_{17}N_2O$ 277.1341, found 277.1360.

6-Phenylindolo[1,2-a]quinazolin-5(6H)-one (**2k**): pale green solid; yield 54 mg (35%); mp 238−240 °C [lit. 226−228 °C];[10] R_f 0.56 (30% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.49 (s, 2H), 7.22−7.31 (m, 2H), 7.36 (t, J = 7.6 Hz, 1H), 7.47 (dd, J = 6.8, 1.6 Hz, 3H), 7.52−7.56 (m, 1H), 7.58−7.61 (m, 2H), 7.80 (dt, J = 8.0, 1.6 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.42 (dd, J = 7.6, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 86.3, 113.1, 114.8, 117.1, 120.1, 121.5, 122.7, 123.6, 128.5, 129.4, 129.7, 130.2, 130.3, 131.3, 134.9, 137.1, 139.3, 139.3, 158.6; FTIR (KBr) 3059, 1670, 1600, 1567, 1482, 1455 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{21}H_{15}N_2O$ 311.1184, found 311.1187.

6-(4-Bromophenyl)indolo[1,2-a]quinazolin-5(6H)-one (**2l**): pale green solid; yield 108 mg (56%); mp 290−292 °C; R_f 0.52 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.52 (s, 2H), 7.23−7.30 (m, 2H), 7.34−7.41 (m, 3H), 7.49 (d, J = 7.2 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.82 (t, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 8.0 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 86.3, 113.2, 114.9, 116.9, 120.2, 121.7, 122.8, 123.4, 123.8, 129.7, 130.4, 131.4, 133.5, 135.1, 136.1, 138.8, 139.4, 158.6; FTIR (KBr) 3087, 1666, 1597, 1565, 1482, 1459 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{13}N_2ONaBr$ 411.0109, found 411.0137.

6-Benzylindolo[1,2-a]quinazolin-5(6H)-one (**2m**): pale green solid; yield 107 mg (66%); mp 150−152 °C [lit. 157−159 °C],[10] R_f 0.58 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.33 (s, 2H), 5.98 (s, 1H), 7.20−7.28 (m, 3H), 7.28−7.37 (m, 3H), 7.39 (d, J = 7.2 Hz, 2H), 7.49−7.55 (m, 1H), 7.74 (t, J = 7.2 Hz, 1H), 8.00−8.07 (m, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.43 (d, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 47.6, 85.4, 113.1, 114.7, 116.4, 120.1, 121.4, 122.6, 123.6, 127.4, 127.8, 128.9, 129.9, 130.2, 131.2, 134.6, 135.7, 137.4, 139.1, 158.9; FTIR (KBr) 3052, 2925, 2851, 1666, 1618, 1601, 1571, 1484, 1457 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{22}H_{17}N_2O$ 325.1341, found 325.1367.

6-Benzyl-9-methoxyindolo[1,2-a]quinazolin-5(6H)-one (**2n**): greenish yellow solid; yield 136 mg (77%); mp 138−140 °C; R_f 0.43 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.75 (s, 3H), 5.24 (s, 2H), 5.83 (s, 1H), 6.75 (dd, J = 9.2, 2.4 Hz, 1H), 6.89 (d, J = 2.8 Hz, 1H), 7.16−7.19 (m, 1H), 7.20−7.26 (m, 3H), 7.31 (d, J = 7.2 Hz, 2H), 7.64 (dt, J = 8.0, 1.6 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.33 (dd, J = 8.0, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 47.6, 55.7, 85.4, 102.6, 110.1, 113.8, 114.2, 116.2, 123.2, 126.1, 127.4, 127.8, 128.9, 130.2, 131.0, 134.6, 135.8, 138.0, 139.0, 155.7, 158.9; FTIR (KBr) 3062, 2919, 2849, 1664, 1599, 1570, 1487, 1453 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{23}H_{18}N_2O_2Na$ 377.1266, found 377.1248.

6-Benzyl-9-bromoindolo[1,2-a]quinazolin-5(6H)-one (**2o**): greenish yellow solid; yield 137 mg (68%); mp 240−242 °C; R_f 0.48 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.36 (s, 2H), 5.96 (s, 1H), 7.28−7.36 (m, 4H), 7.39 (d, J = 7.6 Hz, 3H), 7.65 (d, J = 2.0 Hz, 1H), 7.80 (dt, J = 8.0, 1.6 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.46 (dd, J = 7.8, 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 47.7, 84.9, 114.3, 114.6, 115.8, 116.6, 122.7, 124.0, 127.1, 127.4, 127.9, 129.0, 130.0, 130.5, 131.7, 134.9, 135.5, 138.4, 138.7, 158.8; FTIR (KBr) 3061, 2921, 2851, 1664, 1605, 1570, 1484, 1460 cm^{-1}; HRMS (m/z) $[M + H]^+$ calcd for $C_{22}H_{16}N_2OBr$ 403.0446, found 403.0451.

6-Benzyl-10-chloroindolo[1,2-a]quinazolin-5(6H)-one (**2p**): greenish yellow solid; yield 125 mg (70%); mp 216−218 °C; R_f 0.55 (20% ethyl acetate in hexanes); ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.33 (s, 2H), 5.95 (s, 1H), 7.17−7.33 (m, 4H), 7.35−7.44 (m, 4H), 7.78 (t, J = 7.6 Hz, 1H), 8.02 (s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 47.7, 85.3, 113.2, 114.6, 116.6, 120.7, 123.0, 124.1, 126.9, 127.4, 127.9, 128.4, 128.9, 130.4, 131.4, 134.8, 135.6, 138.0, 138.6, 158.7; FTIR (KBr) 3030, 2921, 1669, 1599, 1566, 1481, 1458 cm^{-1}; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{15}N_2ONaCl$ 381.0771, found 381.0798.

6-(2-Chlorobenzyl)indolo[1,2-a]quinazolin-5(6H)-one (**2q**): greenish yellow solid; yield 111 mg (62%); mp 206−208 °C; R_f 0.52 (15%

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.47 (s, 2H), 5.89 (s, 1H), 7.05−7.13 (m, 2H), 7.18 (dt, J = 8.0, 2.4 Hz, 1H), 7.22−7.29 (m, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.50−7.54 (m, 1H), 7.80 (dt, J = 8.0, 1.6 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.45 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 45.1, 85.4, 113.1, 114.8, 116.4, 120.3, 121.6, 122.7, 123.7, 127.1, 127.3, 128.8, 129.8, 129.9, 130.4, 131.5, 132.8, 133.1, 134.9, 137.2, 139.2, 159.0; FTIR (KBr) 3044, 2923, 1658, 1613, 1597, 1567, 1478 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{22}H_{16}N_2OCl$ 359.0951, found 359.0981.

6-(4-Methoxybenzyl)indolo[1,2-a]quinazolin-5(6H)-one (**2r**): greenish yellow solid; yield 93 mg (53%); mp 182−184 °C; R_f 0.51 (15% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 3.74 (s, 3H), 5.27 (s, 2H), 6.03 (s, 1H), 6.83 (d, J = 8.4 Hz, 2H), 7.22−7.25 (m, 2H), 7.31−7.39 (m, 3H), 7.52−7.56 (m, 1H), 7.74 (dt, J = 7.8, 1.6 Hz, 1H), 8.01−8.07 (m, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.43 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 47.2, 55.4, 85.4, 113.1, 114.3, 114.7, 116.6, 120.1, 121.4, 122.6, 123.6, 127.9, 129.0, 130.0, 130.2, 131.3, 134.6, 137.5, 139.1, 158.8, 159.3; FTIR (KBr) 3051, 2932, 2837, 1667, 1617, 1606, 1571, 1512, 1485 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{23}H_{18}N_2O_2Na$ 377.1266, found 377.1295.

6-(Furan-2-ylmethyl)indolo[1,2-a]quinazolin-5(6H)-one (**2s**): pale green solid; yield 117 mg (75%); mp 224−226 °C; R_f 0.47 (15% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 5.32 (s, 2H), 6.26 (s, 1H), 6.30.6.34 (m, 1H), 6.46 (d, J = 3.2 Hz, 1H), 7.24−7.29 (m, 2H), 7.31−7.36 (m, 2H), 7.59−7.67 (m, 1H) 7.70−7.79 (m, 1H), 8.03−8.10 (m, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.41 (dd, J = 7.8, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 40.6, 85.1, 109.5, 110.7, 113.1, 114.7, 116.5, 120.3, 121.5, 122.6, 123.6, 130.0, 130.2, 131.4, 134.7, 137.3, 139.1, 142.5, 149.4, 158.5; FTIR (KBr) 3108, 2919, 2851, 1666, 1618, 1604, 1571, 1488, 1459 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{20}H_{14}N_2O_2Na$ 337.0953, found 337.0947.

Indolo[1,2-a]quinazolin-5(6H)-one (**2t**): pale yellow solid; yield 39 mg (34%); mp 256−258 °C; R_f 0.50 (35% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$:DMSO-d_6 (1:4), 400 MHz, ppm) δ 6.02 (s, 1H), 7.16−7.26 (m, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.51−7.62 (m, 1H), 8.20 (dd, J = 7.6, 1.2 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.44 (d, J = 8.4 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$:DMSO-d_6 (1:4), 100 MHz) δ 82.5, 113.0, 115.1, 116.6, 119.3, 120.4, 122.1, 123.4, 128.7, 129.8, 130.0, 134.9, 136.1, 138.8, 158.1; FTIR (KBr) 3427, 3084, 2954, 1683, 1601, 1476, 1460 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{10}N_2O$ 235.0871, found 235.0875.

9-Methoxyindolo[1,2-a]quinazolin-5(6H)-one (**2u**): pale yellow solid; yield 37 mg (28%); mp 272−274 °C; R_f 0.52 (40% ethyl acetate in hexanes); ^{1}H NMR (DMSO-d_6, 400 MHz, ppm) δ 3.78 (s, 3H), 5.96 (s, 1H), 6.79 (dd, J = 9.0, 2.4 Hz, 1H), 7.10 (d, J = 2.8 Hz, 1H), 7.38 (t, J = 3.6 Hz, 1H), 7.85 (dt, J = 1.6, 8.0 Hz, 1H), 8.12−8.20 (m, 2H), 8.36 (d, J = 8.4 Hz, 1H), 11.96 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz) δ 55.2, 82.7, 102.3, 108.8, 113.8, 114.7, 116.3, 123.3, 124.8, 128.7, 131.1, 135.1, 136.7, 138.6, 155.2, 158.1; FTIR (KBr) 3450, 3095, 2959, 1674, 1607, 1492, 1451 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{13}N_2O_2$ 265.0977, found 265.0961.

6-Ethylindolo[1,2-a]quinazolin-5(6H)-one (**2v**): pale green solid; yield 102 mg (78%); mp 105−107 °C [lit. 108−110 °C];[10] R_f 0.50 (15% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 1.33 (t, J = 7.2 Hz, 3H), 4.06 (q, J = 7.2 Hz, 2H), 7.12−7.25 (m, 3H), 5.94 (s, 1H), 7.13−7.23 (m, 3H), 7.48−7.52 (m, 1H), 7.61 (dt, J = 8.0, 1.6 Hz, 1H), 7.92−7.96 (m, 1H), 8.09 (d, J = 8.4 Hz, 1H), 8.27 9dd, J = 7.6, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 11.9, 39.4, 83.9, 113.1, 114.5, 116.7, 119.9, 121.2, 122.5, 123.4, 129.9, 130.3, 131.3, 134.3, 137.2, 138.9, 158.1; FTIR (KBr) 3051, 2934, 2852, 1667, 1616, 1598, 1571, 1484, 1460 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{17}H_{14}N_2ONa$ 285.1004, found 285.0998.

6-Isopropylindolo[1,2-a]quinazolin-5(6H)-one (**2w**): pale green solid; yield 77 mg (56%); mp 98−100 °C; R_f 0.50 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 1.69 (d, J = 7.2 Hz, 6H), 5.13 (s, 1H), 6.23 (s, 1H), 7.26−7.31 (m, 2H), 7.34 (dt, J = 7.6, 0.8 Hz, 1H), 7.61−7.64 (m, 1H), 7.75 (dt, J = 8.0, 1.6 Hz, 1H), 8.09−8.13 (m, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.38 (dd, J = 8.0, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 19.0, 49.2, 85.3, 113.1, 114.6, 117.6, 119.9, 121.3, 122.6, 123.5, 129.9, 131.0, 134.3, 136.7, 138.8, 158.9; FTIR (KBr) 2932, 1667, 1600, 1565, 1482, 1464 cm^{-1}; HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{17}N_2O$ 277.1342, found 277.1341.

2-(3-Iodo-2-methyl-1H-indol-1-yl)-N-methylbenzamide (**3**): brown solid; yield 146 mg (75%); mp 156−158 °C; R_f 0.46 (25% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 2.26 (s, 3H), 2.49 (d, J = 4.8 Hz, 3H), 5.03 (s, 1H), 6.92 (d, J = 8.0 Hz, 1H), 7.17 (dt, J = 7.0, 1.2 Hz, 1H), 7.23 (dt, J = 7.6, 0.8 Hz, 1H), 7.27−7.31 (m, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.57−7.65 (m, 2H), 8.02−8.07 (m. 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.7, 26.9, 61.3, 110.1, 121.0, 121.7, 123.4, 128.9, 129.6, 129.7, 130.6, 131.3, 131.9, 134.7, 138.0, 138.8, 166.4; FTIR (KBr) 3296, 3061, 2927, 2859, 1647, 1602, 1544, 1491, 1455 cm^{-1}; HRMS (m/z) [M + Na]$^+$ calcd for $C_{17}H_{15}N_2ONaI$ 413.0127, found 413.0146.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01080.

Solvent screening data, ^{1}H and ^{13}C NMR spectra for all compounds, and X-ray structure and brief crystal data of compound **2e** (PDF)

X-ray crystallographic file of compound **2e** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*Fax: (+91) 44-2257-4202. E-mail: gsekar@iitm.ac.in.

ORCID

Govindasamy Sekar: 0000-0003-2294-0485

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank DST (SB/S1/OC-72/2013) for funding. S.B. thanks UGC, New Delhi, for SRF. We thank IIT-Madras for infrastructure facilities.

■ REFERENCES

(1) (a) Hili, R.; Yudin, A. K. *Nat. Chem. Biol.* **2006**, *2*, 284. (b) Bariwal, J.; Van der Eycken, E. *Chem. Soc. Rev.* **2013**, *42*, 9283.

(2) (a) Louillat, M.-L.; Patureau, F. W. *Chem. Soc. Rev.* **2014**, *43*, 901. (b) Mailyan, A. K.; Eickhoff, J. A.; Minakova, A. S.; Gu, Z.; Lu, P.; Zakarian, A. *Chem. Rev.* **2016**, *116*, 4441. (c) Ruiz-Castillo, P.; Buchwald, S. L. *Chem. Rev.* **2016**, *116*, 12564. (d) Park, Y.; Kim, Y.; Chang, S. *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00644.

(3) (a) Aroncon, R. A. D.; Lin, C. S. K.; Vargas, C.; Luque, R. *Org. Biomol. Chem.* **2014**, *12*, 10. (b) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219.

(4) (a) Parvatkar, P. T.; Parameswaran, P. S.; Tilve, S. G. *Chem. - Eur. J.* **2012**, *18*, 5460 and references therein. (b) Xiang, L.; Yang, Y.; Zhou, X.; Liu, X.; Li, X.; Kang, X.; Yan, R.; Huang, G. *J. Org. Chem.* **2014**, *79*, 10641. (c) Mohammed, S.; Vishwakarma, R. A.; Bharate, S. B. *J. Org. Chem.* **2015**, *80*, 6915.

(5) (a) Kothandaraman, P.; Mothe, S. R.; Toh, S. S.-M.; Chan, P. W.-H. *J. Org. Chem.* **2011**, *76*, 7633. (b) Hu, Y.; Yi, R.; Wang, C.; Xin, X.; Wu, F.; Wan, B. *J. Org. Chem.* **2014**, *79*, 3052. (c) Grandclaudon, C.; Michelet, V.; Toullec, P. Y. *Org. Lett.* **2016**, *18*, 676. (d) Prabagar, B.; Nayak, S.; Prasad, R.; Sahoo, A. K. *Org. Lett.* **2016**, *18*, 3066.

(6) (a) Yan, Y.; Zhang, Y.; Zha, Z.; Wang, Z. *Org. Lett.* **2013**, *15*, 2274. (b) Zhang, J.; Zhang, G.; Wu, W.; Zhang, X.; Shi, M. *Chem. Commun.* **2014**, *50*, 15052. (c) Liu, T.; Mei, T.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2015**, *137*, 5871. (d) Li, Y.-L.; Li, J.; Ma, A.-L.; Huang, Y.-N.; Deng, J. *J. Org. Chem.* **2015**, *80*, 3841. (e) Santhi, J.; Baire, B. *Adv.*

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665

Synth. Catal. **2016**, *358*, 3817. (f) Ma, Y.-N.; Cheng, M.-X.; Yang, S.-D. *Org. Lett.* **2017**, *19*, 600.
(7) Schmidt, A. W.; Reddy, K. R.; Knoelker, H.-J. *Chem. Rev.* **2012**, *112*, 3193.
(8) Vangrevelinghe, E.; Zimmermann, K.; Schoepfer, J.; Portmann, R.; Fabbro, D.; Furet, P. *J. Med. Chem.* **2003**, *46*, 2656.
(9) Jiang, M.; Xiang, H.; Zhu, F.; Xu, X.; Deng, L.; Yang, C. *Org. Biomol. Chem.* **2015**, *13*, 10122.
(10) Kotipalli, T.; Kavala, V.; Janreddy, D.; Kuo, C.-W.; Kuo, T.-S.; Huang, H.-N.; He, C.-H.; Yao, C.-F. *RSC Adv.* **2014**, *4*, 2274.
(11) (a) Chandrasekar, S.; Sekar, G. *Org. Biomol. Chem.* **2016**, *14*, 3053. (b) Dutta, S.; Kotha, S. S.; Sekar, G. *RSC Adv.* **2015**, *5*, 47265. (c) Guha, S.; Rajeshkumar, V.; Kotha, S. S.; Sekar, G. *Org. Lett.* **2015**, *17*, 406. (d) Karthikeyan, I.; Arunprasath, D.; Sekar, G. *Chem. Commun.* **2015**, *51*, 1701. (e) Rajeshkumar, V.; Chandrasekar, S.; Sekar, G. *Org. Biomol. Chem.* **2014**, *12*, 8512.
(12) Badigenchala, S.; Rajeshkumar, V.; Sekar, G. *Org. Biomol. Chem.* **2016**, *14*, 2297.
(13) Refer to Table S1 for detailed solvent screening.
(14) Ghosh, S. K.; Nagarajan, R. *RSC Adv.* **2014**, *4*, 20136.

DOI: 10.1021/acs.joc.7b01080
J. Org. Chem. 2017, 82, 7657−7665