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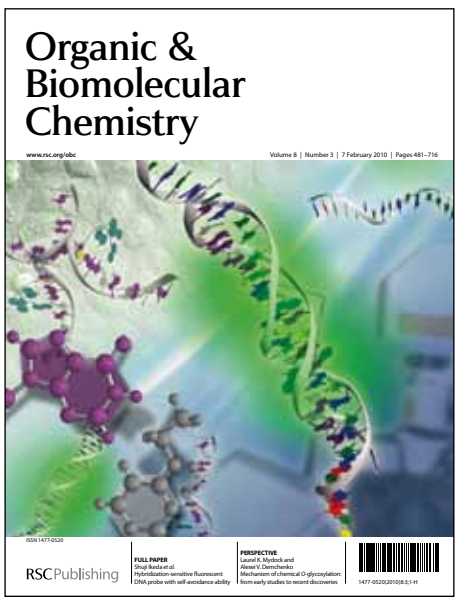

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ARTICLE TYPE

Rhodium-Catalyzed Three-Component Reaction of 3-Diazooxindoles with Indoles and Isatin-Derived Ketimines: A Facile and Versatile Approach to Functionalized 3,3',3''-Trisindoles

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A simple, facile and efficient $Rh_2(OAc)_4$-catalyzed three-component reaction of 3-diazooxindoles with indoles and isatin-derived N-Boc ketimines towards a variety of functionalized 3,3',3''-trisindoles in high yields with moderate to excellent diastereoselectivities has been developed. This methodology provides an ideal approach for the direct introduction of indole and oxindole onto an isatin moiety at the 3-position.

Introduction

Indole and oxindole derivatives are very useful building blocks for the construction of biologically valuable indole-containing alkaloids.[1] Among them, the bisindoles and 3,3',3''-trisindoles are particularly intriguing for their widespread existence and exhibition of a wide range of biological activities such as antibacterial, antiprotozoal and anti-inflammatory behavior (Figure 1).[2] Therefore, developing efficient methodologies for the synthesis of such compounds is highly desirable. To this aspect, a variety of elegant synthetic protocols have been developed for the synthesis of bisindoles,[2f,3] as well as for the construction of functionalized 3,3',3''-trisindoles involving metal-catalyzed reactions,[4] Brønsted acid mediated processes,[5] and other methods.[6] Very recently, we reported a gold-catalyzed intramolecular cycloisomerization of 1,1-bis(indolyl)-5-alkynes, affording a convenient method for the synthesis of bis(indloe) derivatives with good regio- and enantioselectivity.[7]

The reaction of α-diazo carbonyl compounds with transition metals is a well studied method for generation of transient electrophilic carbenoids, which can undergo an array of attractive transformations such as cyclopropanations, C-H or heteroatom-H insertions, cycloaddition reactions and ylide formations.[8] Recently, Hu[9] reported that the carbenoids could react with a nucleophilic indole substrate and then generate a suspected zwitterionic intermediate.[10] This intermediate could undergo either rapid proton transfer to afford C-H insertion products;[3a-3d] or subsequently be trapped by electrophiles such as activated imines[9] or ethyl glyoxylate.[3e] As part of our ongoing interest in exploring novel routes for synthesis of bis- or trisindole derivatives, we considered to trap the zwitterionic intermediate by using isatin as the electrophile. However, due to the rapid 1,2-proton shift process,[3a-3d] C-H functionalized byproduct **5** was obtained as the sole product (Scheme 1). Therefore, finding a suitable electrophile is vital for the three-component reaction. In this paper, we selected isatin-derived N-Boc ketimines as the electrophiles to react with 3-diazooxindoles and indoles as substrates, in expectation to afford the desired functionalized 3,3',3''-trisindoles (Scheme 1).

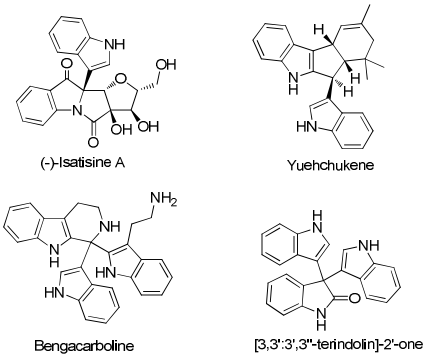

Figure 1. Bioactive compounds containing bisindoles and 3,3',3''-trisindoles.

Results and Discussion

Initial examinations using 1-benzyl-3-diazoindolin-2-one **1a**, 1-methyl-1*H*-indole **2a** and tert-butyl (1-benzyl-2-oxoindolin-3-ylidene)carbamate **3a** as the model substrates in the presence of $Rh_2(OAc)_4$ were aimed at screening the optimal conditions and the results are summarized in Table 1. Upon adding the solution of **1a** via a syringe over 1 h into the mixtures of **2a** and **3a** in the presence of 10 mol% $Rh_2(OAc)_4$, tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4a** was obtained in 96% yield with >20/1 dr in toluene at room temperature (Table 1, entry 1). While, if **1a** was added in one portion, the yield of **4a** decreased remarkably, though no significant change of diastereoselectivity (Table 1, entry 2). To our delight, by reducing the catalyst

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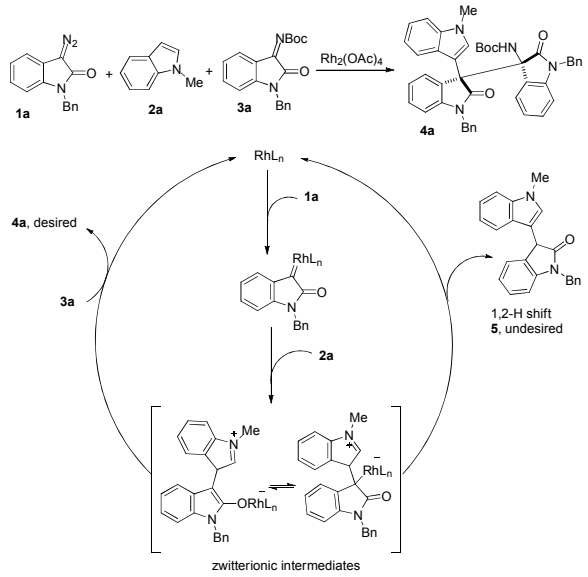
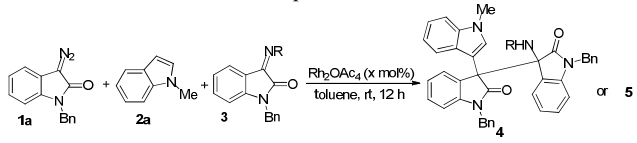
loading of $Rh_2(OAc)_4$ to 5 mol%, the corresponding product **4a** was still furnished in 94% yield with > 20/1 dr, which are chosen as the optimized conditions for this reaction (Table 1, entry 3). Moreover, when other isatin-derived ketimines such as N-PMP **3b**, N-Ts **3c** or N-NHTs **3d** were employed as substrates, only the corresponding byproducts **5** were obtained, indicating that using tert-butyl (1-benzyl-2-oxoindolin-3-ylidene)carbamate **3a** as the electrophile was crucial for this three-component reaction (Table 1, entries 4-6).



Scheme 1. Proposed mechanism for the three-component reaction of **1a**, **2a**, and **3a**.

Table 1. Optimization of Conditions for $Rh_2(OAc)_4$-Catalyzed Three-Component Reaction



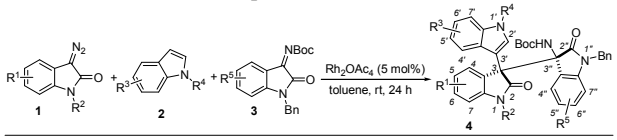
entry[a]	R	x	yield [%][b]	dr[c]
1	Boc, **3a**	10	**4a**, 96	>20:1
2[d]	Boc, **3a**	10	**4a**, 61	>20:1
3	Boc, **3a**	5	**4a**, 94	>20:1
4	PMP, **3b**	5	**5**, 83	-
5	Ts, **3c**	5	**5**, 74	-
6	NHTs, **3d**	5	**5**, 77	-

[a] To the mixture of **2a** (0.1 mmol), **3** (0.12 mmol) and $Rh_2(OAc)_4$ (x mol%) in toluene (0.5 mL) was added a solution of **1a** (0.12 mmol) in toluene (1.0 mL) via a syringe pump over 1 h. [b] Isolated yield. [c] The diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [d] To the mixture of **2a** (0.1 mmol), **3** (0.12 mmol) and $Rh_2(OAc)_4$ (x mol%) in toluene (0.5 mL) was added a solution of **1a** (0.12 mmol) in toluene (1.0 mL) in one portion.

With the optimized reaction conditions in hand, the substrate scope was next explored and the results are shown in Table 2. At first, using 1-methyl-1*H*-indole **2a** and tert-butyl (1-benzyl-2-oxoindolin-3-ylidene)carbamate **3a** as the model substrates, we investigated different 3-diazooxindoles **1** bearing different *N*-substituted groups (Table 2, entries 1-2). Both *N*-protecting methyl and methoxymethyl (MOM) groups were tolerable in this reaction, as for substrates **1b** and **1c**, giving desired adducts **4b** and **4c** in high yields with excellent diastereoselectivities (Table 2, entries 1-2). Next, various indoles **2** possessing different substituents on the aromatic ring and *N*-protecting groups were tested (Table 2, entries 3-9). A wide range of substituents R^3 having different electronic properties at the C4', C5', or C6' position of indoles did not have significant electronic impact on this reaction, smoothly affording the corresponding 3,3',3''-trisindoles **4d-4h** in 70-97% yields with 5/1->20/1 diastereoselectivities (Table 2, entries 3-7). It is noteworthy that several functional groups including nitrile (**2c**) or ester group (**2e**) on the aryl residue are well tolerated (Table 2, entries 4 and 6). In addition, using 1*H*-indole **2g** without any protecting group and 1-benzyl-1*H*-indole **2h** as the substrates, the reactions also proceeded successfully to give the corresponding adducts **4i** and **4j** in high yields along with excellent diastereoselectivities under the standard conditions (Table 2, entries 8-9). Several halide or dihalide substituted 3-diazooxindoles **1d-1f** were also employed as substrates, and the expected functionalized 3,3',3''-trisindoles **4k-4m** were aquired in satisfactory yields of 90-94% and good dr values (Table 2, entries 10-12). Finally, an array of isatin-derived N-Boc ketimines that exhibit diverse electronic and steric effects were studied using 1-benzyl-3-diazoindolin-2-one **1a** and 1-methyl-1*H*-indole **2a** as the model substrates (Table 2, entries 13-18). Different ketimines **3e-3j** with single or multiple diverse substituents R^5 at the C5', C6', or C7' position of isatins could readily participate in this reaction, providing the desired products **4o-4s** in 91-94% yields with 5/1->20/1 diastereoselectivities and, no significant electronic effect was observed (Table 2, entries 14-18). When a methyl group (R^5) was introduced at the C4' position of isatin, the by-product **5** derived from the two-component reaction of **1a** and **2a** was formed in 86% yield rather then the desired product **4n**, presumably because the electrophile trapping reaction was prohibited due to the steric hindrance of methyl group (Table 2, entry 13). Moreover, the relative configuration of **4a** has been confirmed by its X-ray diffraction. The ORTEP drawing of **4a** is shown in Figure 2 and its CIF data are summarized in Supporting Information.

Based on our experimental results and previously reported studies,[8s] we tentatively proposed transition states **I** and **II** to explain the observed stereochemical outcome of the reaction (Scheme 2). In **TS-II**, the large steric repulsions between the sterically bulky rhodium species and the aromatic ring of isatin as well as the large N-Boc group and aromatic ring of indole disfavoured the formation of **4**. But, in **TS-I**, the possible π-π stacking interaction between two aromatic rings of isatins and the less steric repulsions facilitated the production of **4**.

Table 2. Substrate Scope for $Rh_2(OAc)_4$-Catalyzed Three-Component Reaction



entry[a]	R^1/R^2	R^3/R^4	R^5	yield [%][b]	dr[c]
1	H/Me, **1b**	H/Me, **2a**	H, **3a**	**4b**, 90	10:1
2	H/MOM, **1c**	H/Me, **2a**	H, **3a**	**4c**, 87	>20:1
3	H/Bn, **1a**	5'-Me/Me, **2b**	H, **3a**	**4d**, 97	5:1
4	H/Bn, **1a**	5'-CN/Me, **2c**	H, **3a**	**4e**, 96	>20:1
5	H/Bn, **1a**	6'-Br/Me, **2d**	H, **3a**	**4f**, 95	9:1
6	H/Bn, **1a**	6'-COOMe/Me, **2e**	H, **3a**	**4g**, 92	5:1
7	H/Me, **1b**	4'-Cl/Me, **2f**	H, **3a**	**4h**, 70	10:1
8	H/Me, **1b**	H/H, **2g**	H, **3a**	**4i**, 93	11:1
9	H/Me, **1b**	H/Bn, **2h**	H, **3a**	**4j**, 94	>20:1
10	5-F/Me, **1d**	H/Bn, **2h**	H, **3a**	**4k**, 90	12:1
11	6-Br/Me, **1e**	H/Bn, **2h**	H, **3a**	**4l**, 94	5:1
12	5, 7-Cl_2/Me, **1f**	H/Bn, **2h**	H, **3a**	**4m**, 93	5:1
13	H/Bn, **1a**	H/Me, **2a**	4''-Me, **3e**	**4n**, n. d.[d]	n. d.[d]
14	H/Bn, **1a**	H/Me, **2a**	5''-F, **3f**	**4o**, 93	11:1
15	H/Bn, **1a**	H/Me, **2a**	6''-Me, **3g**	**4p**, 94	7:1
16	H/Bn, **1a**	H/Me, **2a**	6''-Br, **3h**	**4q**, 91	8:1
17	H/Bn, **1a**	H/Me, **2a**	7''-CF_3, **3i**	**4r**, 94	>20:1
18	H/Bn, **1a**	H/Me, **2a**	5''-Cl, 7''-Me, **3j**	**4s**, 92	5:1

[a] To the mixture of **2** (0.1 mmol), **3** (0.12 mmol) and $Rh_2(OAc)_4$ (5 mol%) in toluene (0.5 mL) was added a solution of **1** (0.12 mmol) in toluene (1.0 mL) via a syringe pump over 1 h. [b] Isolated yield. [c] The diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [d] Not detected; 86% byproduct **5** was obtained.

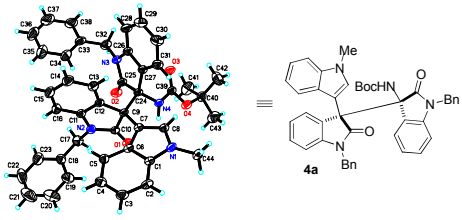
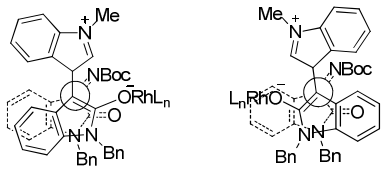


Figure 2. X-ray Crystal Structure of Product **4a**.



Scheme 2. Proposed transition states.

In conclusion, a facile and versatile $Rh_2(OAc)_4$-catalyzed three-component reaction of 3-diazooxindoles with indoles and isatin-derived N-Boc ketimines has been developed. On the basis of *in situ* generation of an active zwitterionic intermediate through 3-diazooxindole and indole in the presence of $Rh_2(OAc)_4$, and subsequent trapping by isatin-derived N-Boc ketimines, the reaction proceeded efficiently furnishing a spectrum of 3,3',3''-trisindoles from readily available starting materials in high yields with moderate to excellent diastereoselectivities. Further investigations expanding the substrate scope of this reaction as well as the applications of this protocol to natural product synthesis are in progress.

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Experimental Section

General Remarks. MP was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Infra-red spectra were measured on a spectrometer. ^{1}H NMR spectra were recorded for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; ^{19}F NMR spectra were recorded for a solution in $CDCl_3$ with $CFCl_3$ as the external reference. *J*-values are in Hz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure. All reactions were performed under argon using standard Schlenk techniques.

3-Diazooxindoles **1a**, **1b**, **1d** were prepared according to the previously reported procedures.[11] Indoles **2** were prepared according to the previously reported procedures.[12] Isatin-derived N-Boc ketimines **3** were prepared according to the previously reported procedures.[13]

General procedure for Rhodium-Catalyzed Coupling Reaction of 3-Diazooxindoles with Indoles and Isatin-Derived Ketimines

To the mixture of indoles **2** (0.1 mmol), isatin-derived N-Boc ketimines **3** (0.12 mmol) and $Rh_2(OAc)_4$ (2.2 mg, 5 mol%) in toluene (0.5 mL) was added a solution of 3-diazooxindoles **1** (0.12 mmol) in toluene (1.0 mL) *via* a syringe pump over 1 h. When the addition was completed, the reaction mixture was further stirred for 12 hours and then directly subjected to flash column chromatography (petroleum ether/EtOAc, 8:1 to 2:1) to afford the corresponding pure products **4.**

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4a** (major isomer): a colorless solid, 94% yield (65 mg), >20:1 dr. M.p.: 127-130 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.23-1.39 (m, 9H, CH_3), 3.86 (s, 3H, CH_3), 4.39 (d, *J* = 15.2 Hz, 1H, CH_2), 4.70 (d, *J* = 16.0 Hz, 1H, CH_2), 4.86 (d, *J* = 16.0 Hz, 1H, CH_2), 5.17 (d, *J* = 15.2 Hz, 1H, CH_2), 5.74 (s, 1H, ArH), 6.18 (d, *J* = 8.0 Hz, 1H, ArH), 6.54-6.57 (m, 2H, ArH), 6.67-6.73 (m, 2H, ArH), 6.79-6.87 (m, 3H, ArH), 7.08-7.19 (m, 9H, ArH), 7.23-7.29 (m, 4H, ArH), 7.96 (s, 1H, ArH), 8.22 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.2, 33.3, 44.2, 44.5, 54.5, 67.1, 80.2, 107.6, 109.0, 109.4, 109.9, 119.3, 120.9, 121.7, 122.1, 122.2, 125.9, 126.2, 126.8, 127.1, 127.17, 127.2, 127.4, 128.5, 128.6, 129.39, 129.4, 131.2, 135.4, 135.5, 137.0, 143.8, 144.6, 154.8, 174.8, 176.5. IR (CH_2Cl_2) ν 3319, 3059, 2978, 2926, 1717, 1697, 1609, 1486, 1465, 1365, 1276, 1158, 1104, 1075, 1018, 956, 898, 877, 734, 697, 661 cm^{-1}. MS (ESI) *m/z* (%): 689.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{41}N_4O_4^+$ (M^++H) requires 689.3128, found: 689.3139.

tert-butyl-1-benzyl-3-(1-methyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4b** (major isomer): a colorless solid, 90% yield (55 mg), 10:1 dr. M.p.: 130-133 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.23-1.38 (m, 9H, CH_3), 3.27 (s, 3H, CH_3), 3.84 (s, 3H, CH_3), 4.40 (d, *J* = 16.0 Hz, 1H, CH_2), 4.58 (d, *J* = 16.0 Hz, 1H, CH_2), 5.81 (d, *J* = 6.0 Hz, 1H, ArH), 6.41 (d, *J* = 8.4 Hz, 1H, ArH), 6.52 (d, *J* = 7.6 Hz, 1H, ArH), 6.65 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.76-6.85 (m, 4H, ArH), 6.93 (d, *J* = 8.0 Hz, 1H, ArH), 7.09-7.17 (m, 6H, ArH), 7.27 (d, *J* = 8.4 Hz, 1H, ArH), 7.36 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H, ArH), 7.84 (s, 1H, ArH), 8.22 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 33.1, 33.2, 44.1, 54.3, 67.1, 80.1, 107.3, 108.6, 108.9, 109.3, 118.1, 119.1, 119.4, 121.0, 121.6, 122.0, 122.1, 122.6, 125.8, 126.2, 126.8, 127.1, 127.3, 127.8, 128.5, 129.1, 129.3, 129.5, 131.2, 135.5, 137.0, 144.6, 154.8, 174.8, 176.1. IR (CH_2Cl_2) ν 3311, 3055, 2977, 2923, 1717, 1698, 1610, 1489, 1467, 1368, 1276, 1161, 1131, 1067, 1028, 911, 882, 750, 697 cm^{-1}. MS (ESI) *m/z* (%): 613.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{38}H_{37}N_4O_4^+$ (M^++H) requires 613.2815, found: 613.2809.

tert-butyl-1-benzyl-3-(1-(methoxymethyl)-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4c** (major isomer): a colorless solid, 87% yield (56 mg), >20:1 dr. M.p.: 128-131 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.23-1.39 (m, 9H, CH_3), 3.28 (s, 3H, CH_3), 3.86 (s, 3H, CH_3), 4.40 (d, *J* = 16.0 Hz, 1H, CH_2), 4.64 (d, *J* = 16.0 Hz, 1H, CH_2), 5.16 (d, *J* = 11.2 Hz, 1H, CH_2), 5.23 (d, *J* = 11.2 Hz, 1H, CH_2), 5.77 (d, *J* = 4.4 Hz, 1H, ArH), 6.36 (d, *J* = 8.4 Hz, 1H, ArH), 6.54 (d, *J* = 8.0 Hz, 1H, ArH), 6.65 (dd, *J* = 6.8 Hz, 6.8 Hz, 1H, ArH), 6.76-6.87 (m, 4H, ArH), 7.09-7.20 (m, 7H, ArH), 7.25 (d, *J* = 6.8 Hz, 1H, ArH), 7.35 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H, ArH), 7.86 (s, 1H, ArH), 8.09

(s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 33.1, 33.2, 44.2, 56.5, 67.1, 72.1, 80.2, 107.4, 108.9, 109.4, 110.1, 118.3, 119.1, 119.5, 120.7, 121.1, 121.7, 122.0, 122.6, 123.0, 125.8, 126.2, 126.7, 127.1, 128.5, 129.4, 129.7, 131.2, 133.2, 135.4, 137.0, 143.0, 144.6, 154.7, 174.6, 176.9. IR (CH_2Cl_2) ν 3325, 3055, 2978, 2931, 1717, 1610, 1485, 1466, 1366, 1275, 1159, 1123, 1093, 1028, 1008, 910, 881, 736, 700, 664 cm^{-1}. MS (ESI) *m/z* (%): 643.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{39}H_{39}N_4O_5^+$(M^++H) requires 643.2920, found: 643.2908.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1,5-dimethyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4d** (major isomer): a colorless solid, 97% yield (68 mg), 5:1 dr. M.p.: 133-136 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.40 (m, 9H, CH_3), 2.09 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 4.40 (d, *J* = 15.2 Hz, 1H, CH_2), 4.71 (d, *J* = 15.2 Hz, 1H, CH_2), 4.84 (d, *J* = 16.0 Hz, 1H, CH_2), 5.19 (d, *J* = 16.0 Hz, 1H, CH_2), 5.73 (d, *J* = 5.6 Hz, 1H, ArH), 6.11 (s, 1H, ArH), 6.53-6.56 (m, 2H, ArH), 6.67 (d, *J* = 8.0 Hz, 1H, ArH), 6.78-6.86 (m, 3H, ArH), 6.95 (d, *J* = 8.0 Hz, 1H, ArH), 7.10-7.20 (m, 9H, ArH), 7.26-7.39 (m, 3H, ArH), 7.77 (s, 1H, ArH), 8.26 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.5, 28.2, 33.2, 44.2, 44.3, 54.4, 66.9, 80.0, 107.1, 108.8, 108.9, 109.8, 121.0, 121.9, 122.1, 123.2, 125.8, 126.2, 126.9, 127.0, 127.07, 127.1, 127.3, 127.35, 127.8, 127.9, 128.2, 128.3, 128.46, 128.5, 128.8, 129.0, 129.1, 129.3, 131.2, 135.3, 135.47, 135.5, 143.8, 144.5, 154.7, 174.7, 176.5. IR (CH_2Cl_2) ν 3312, 3051, 2971, 2925, 1716, 1608, 1491, 1468, 1367, 1276, 1159, 1090, 1027, 972, 909, 870, 734, 698 cm^{-1}. MS (ESI) *m/z* (%): 703.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{45}H_{43}N_4O_4^+$ (M^++H) requires 703.3284, Found: 703.3275.

tert-butyl-1-benzyl-3-(1-benzyl-3-(5-cyano-1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4e** (major isomer): a colorless solid, 96% yield (68 mg), >20:1 dr. M.p.: 144-147 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.40 (m, 9H, CH_3), 3.91 (s, 3H, CH_3), 4.41 (d, *J* = 15.6 Hz, 1H, CH_2), 4.70 (d, *J* = 15.6 Hz, 1H, CH_2), 4.88 (d, *J* = 16.0 Hz, 1H, CH_2), 5.14 (d, *J* = 16.0 Hz, 1H, CH_2), 5.69 (s, 1H, ArH), 6.48 (s, 1H, ArH), 6.58-6.60 (m, 2H, ArH), 6.73-6.88 (m, 4H, ArH), 7.09-7.19 (m, 4H, ArH), 7.20-7.27 (m, 6H, ArH), 7.33-7.41 (m, 3H, ArH), 8.08 (s, 1H, ArH), 8.16 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.2, 33.5, 44.3, 44.6, 54.2, 66.8, 80.6, 102.7, 109.2, 109.5, 110.3, 110.5, 120.4, 122.1, 122.6, 124.6, 125.5, 126.0, 126.4, 126.5, 126.7, 127.0, 127.1, 127.2, 127.5, 127.7, 127.9, 128.6, 128.8, 129.7, 130.1, 133.4, 135.0, 135.3, 138.5, 143.6, 144.6, 154.7, 174.5, 176.1. IR (CH_2Cl_2) ν 3323, 3053, 2978, 2923, 2221, 1720, 1698, 1610, 1487, 1467, 1456, 1367, 1276, 1163, 1079, 1017, 899, 803, 733, 698 cm^{-1}. MS (ESI) *m/z* (%): 731.3 (100) [M^++NH_4]; HRMS (ESI) Calcd. for $C_{45}H_{43}N_6O_4^+$ (M^++NH_4) requires 731.3346, found: 731.3340.

tert-butyl-1-benzyl-3-(1-benzyl-3-(6-bromo-1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4f** (major isomer): a colorless solid, 95% yield (73 mg), 9:1 dr. M.p.: 137-140 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.39 (m, 9H, CH_3), 3.83 (s, 3H, CH_3), 4.40 (d, *J* = 16.0 Hz, 1H, CH_2), 4.68 (d, *J* = 16.0 Hz, 1H, CH_2), 4.85 (d, *J* = 15.2 Hz, 1H, CH_2), 5.16 (d, *J* = 15.2 Hz, 1H, CH_2), 5.71 (s, 1H, ArH), 6.12 (d, *J* = 8.8 Hz, 1H, ArH), 6.55-6.58 (m, 2H, ArH), 6.69 (d, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.75-6.87 (m, 4H, ArH), 7.08-7.21 (m, 9H, ArH), 7.28-7.44 (m, 3H, ArH), 7.87 (s, 1H, ArH), 8.18 (s, 1H, NH).^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 33.3, 44.2, 44.5, 54.3, 66.9, 80.2, 108.2, 108.5, 109.0, 109.9, 112.4, 114.8, 115.5, 120.0, 121.7, 122.0, 122.2, 122.3, 122.6, 125.6, 126.0, 127.2, 127.4, 128.1, 128.5, 128.6, 129.1, 129.4, 129.5, 131.8, 133.9, 134.9, 135.2, 135.4, 137.4, 137.9, 143.7, 144.6, 154.7, 174.6, 176.2. IR (CH_2Cl_2) ν 3319, 3059, 2978, 2927, 1716, 1696, 1609, 1486, 1466, 1365, 1275, 1160, 1103, 1075, 1017, 955, 898, 879, 733, 697 cm^{-1}. MS (ESI) *m/z* (%): 767.2 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{40}BrN_4O_4^+$ (M^++H) requires 767.2233, found: 767.2227.

methyl 3-(1-benzyl-3-(1-benzyl-3-(tert-butoxycarbonyl)-2-oxoindolin-3-yl)-2-oxoindolin-3-yl)-1-methyl-1H-indole-6-carboxylate **4g** (major isomer): a colorless solid, 92% yield (68 mg), 5:1 dr (two isolated isomers). M.p.: 99-102 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25-1.39 (m, 9H, CH_3), 3.89 (s, 3H, CH_3), 3.94 (s, 3H, CH_3), 4.41 (d, *J* = 15.9 Hz, 1H, CH_2), 4.68 (d, *J* = 16.2 Hz, 1H, CH_2), 4.86 (d, *J* = 16.2 Hz, 1H, CH_2), 5.16 (d, *J* = 15.9 Hz, 1H, CH_2), 5.73 (s, 1H, ArH), 6.23 (d, *J* = 8.7 Hz, 1H, ArH), 6.55-6.59 (m, 2H, ArH), 6.70 (d, *J* = 8.1 Hz, 1H, ArH), 6.82-6.88 (m, 3H, ArH), 7.08-7.32 (m, 11H, ArH), 7.40 (d, *J* = 8.7 Hz, 1H, ArH), 8.05 (s, 1H, ArH), 8.12 (s, 1H, ArH), 8.20 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 33.5, 44.2, 44.5, 51.9, 54.3, 66.9, 80.3, 108.4, 109.0, 110.0, 111.7, 120.0, 120.2, 120.4, 122.1, 122.3, 122.7, 123.2, 125.6, 126.1, 127.1, 127.4, 128.4, 128.5, 128.6, 128.8, 129.5, 129.6, 130.2, 134.3, 135.2, 135.4, 136.4, 143.7, 144.6, 154.8, 167.8, 174.6, 176.3. IR (CH_2Cl_2) ν 3366, 3051, 2982, 2928, 2088, 1709, 1610, 1533, 1484, 1465, 1434, 1363, 1312, 1265, 1227, 1162, 1096, 1078, 1030, 902, 832, 751, 734, 698, 670 cm^{-1}. MS (ESI) *m/z* (%): 747.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{46}H_{43}N_4O_6^+$ (M^++H) requires 747.3177, found: 747.3179.

methyl 3-(1-benzyl-3-(1-benzyl-3-(tert-butoxycarbonyl)-2-oxoindolin-3-yl)-2-oxoindolin-3-yl)-1-methyl-1H-indole-6-carboxylate **4g'** (minor isomer): a colorless solid. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.40 (m, 9H, CH_3), 3.86 (s, 3H, CH_3), 3.95 (s, 3H, CH_3), 4.36 (d, *J* = 15.2 Hz, 1H, CH_2), 4.53 (d, *J* = 16.0 Hz, 1H, CH_2), 5.10 (d, *J* = 16.0 Hz, 1H, CH_2), 5.37 (d, *J* = 15.2 Hz, 1H, CH_2), 5.97 (d, *J* = 8.4 Hz, 1H, ArH), 6.31 (d, *J* = 7.6 Hz, 1H, ArH), 6.55-6.58 (m, 2H, ArH), 6.74-6.78 (m, 2H, ArH), 6.95-6.98 (m, 2H, ArH), 7.12-7.19 (m, 3H, ArH), 7.21-7.41 (m, 10H, ArH), 7.99 (s, 1H, ArH), 8.72 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.4, 33.4, 44.3, 44.5, 51.9, 55.9, 65.1, 80.3, 105.4, 108.3, 108.7, 111.7, 111.8, 118.3, 120.1, 121.7, 122.3, 122.7, 122.73, 125.2, 126.8, 127.2, 127.4, 127.5, 127.8, 128.0, 128.2, 128.4, 128.6, 128.9, 129.0, 129.3, 129.5, 130.1, 134.9, 135.4, 135.9, 136.6, 142.5, 143.1, 154.0, 168.0, 173.8, 177.0.

tert-butyl-1-benzyl-3-(3-(4-chloro-1-methyl-1H-indol-3-yl)-1-methyl-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4h** (major isomer): a colorless solid, 70% yield (45 mg), 10:1 dr. M.p.: 142-145 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25-1.37 (m, 9H, CH_3), 3.05 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 4.33 (d, *J* = 16.2 Hz, 1H, CH_2), 5.06 (d, *J* = 16.2 Hz, 1H, CH_2), 6.14 (d, *J* = 7.5 Hz, 1H, ArH), 6.29 (d, *J* = 7.8 Hz, 1H, ArH), 6.65 (dd, *J* = 7.5 Hz, 7.5 Hz, 1H, ArH), 6.81-6.86 (m, 2H, ArH), 6.88-7.02 (m, 4H, ArH), 7.13-7.35 (m, 8H, ArH), 9.04 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.0, 28.3, 33.6, 44.0, 57.2, 66.7, 80.2, 103.0, 107.3, 107.8, 108.1, 121.0, 121.4, 121.5, 121.9, 122.9, 124.1, 124.6, 127.2, 127.4, 127.5, 127.8, 128.5, 128.8, 129.1, 129.4, 129.8, 135.4, 137.6, 138.6, 142.7, 144.4, 153.6, 174.4, 177.9. IR (CH_2Cl_2) ν 3321, 3044, 2979, 2920, 1717, 1611, 1479, 1465, 1393, 1368, 1340, 1303, 1286, 1248, 1147, 1099, 1019, 1003, 925, 887, 838, 735, 698 cm^{-1}. MS (ESI) *m/z* (%): 647.2 (100)

[(M^++H]; HRMS (ESI) Calcd. for $C_{38}H_{36}ClN_4O_4^+$ (M^++H) requires 647.2420, found: 647.2422.

tert-butyl-3-(3-(1H-indol-3-yl)-1-methyl-2-oxoindolin-3-yl)-1-benzyl-2-oxoindolin-3-ylcarbamate **4i** (major isomer): a colorless solid, 93% yield (56 mg), 11:1 dr. M.p.: 153-156 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.37 (m, 9H, CH_3), 3.28 (s, 3H, CH_3), 4.38 (d, *J* = 16.0 Hz, 1H, CH_2), 4.58 (d, *J* = 16.0 Hz, 1H, CH_2), 5.80 (d, *J* = 6.4 Hz, 1H, ArH), 6.43 (d, *J* = 8.0 Hz, 1H, ArH), 6.52 (d, *J* = 7.6 Hz, 1H, ArH), 6.66 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.76-6.83 (m, 4H, ArH), 6.94 (d, *J* = 8.0 Hz, 1H, ArH), 7.07 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H, ArH), 7.12-7.17 (m, 4H, ArH), 7.26 (s, 1H, ArH), 7.32-7.39 (m, 2H, ArH), 7.98 (s, 1H, ArH), 8.24 (s, 1H, NH), 8.52 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 29.6, 44.1, 54.3, 67.1, 80.1, 108.6, 108.9, 111.3, 118.0, 119.7, 120.8, 121.4, 121.5, 122.0, 122.1, 122.6, 125.8, 126.2, 126.8, 127.1, 127.2, 127.8, 128.45, 128.5, 129.1, 129.3, 129.5, 135.4, 136.3, 144.5, 144.6, 154.7, 174.7, 176.0. IR (CH_2Cl_2) ν 3329, 3053, 2977, 2925, 1705, 1611, 1490, 1467, 1369, 1276, 1162, 1067, 906, 750, 697 cm^{-1}. MS (ESI) *m/z* (%): 599.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{37}H_{35}N_4O_4^+$ (M^++H) requires 599.2658, Found: 599.2647.

tert-butyl-1-benzyl-3-(3-(1-benzyl-1H-indol-3-yl)-1-methyl-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4j** (major isomer): a colorless solid, 94% yield (65 mg), >20:1 dr. M.p.: 134-138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.28 (m, 9H, CH_3), 3.30 (s, 3H, CH_3), 4.39 (d, *J* = 15.6 Hz, 1H, CH_2), 4.55 (d, *J* = 15.6 Hz, 1H, CH_2), 5.37 (s, 2H, CH_2), 5.80 (d, *J* = 7.6 Hz, 1H, ArH), 6.51 (d, *J* = 7.6 Hz, 1H, ArH), 6.59-6.67 (m, 2H, ArH), 6.73 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.80-6.85 (m, 3H, ArH), 6.94 (d, *J* = 8.0 Hz, 2H, ArH), 7.07 (dd, *J* = 8.4 Hz, 8.4 Hz, 1H, ArH), 7.12-7.19 (m, 6H, ArH), 7.23 (d, *J* = 8.4 Hz, 1H, ArH), 7.28-7.38 (m, 4H, ArH), 7.81 (s, 1H, ArH), 8.24 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 27.8, 29.3, 43.7, 49.7, 53.9, 66.8, 79.7, 107.8, 108.3, 108.5, 109.5, 119.3, 121.0, 121.4, 121.5, 121.7, 125.4, 125.6, 125.8, 126.0, 126.3, 126.6, 126.7, 127.4, 128.1, 128.3, 128.5, 128.7, 128.9, 129.2, 130.5, 135.1, 136.2, 136.9, 144.2, 154.3, 174.4, 175.6. IR (CH_2Cl_2) ν 3313, 3051, 2977, 2926, 1719, 1692, 1610, 1490, 1466, 1367, 1276, 1161, 1131, 1077, 1028, 906, 882, 750, 697 cm^{-1}. MS (ESI) *m/z* (%): 689.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{41}N_4O_4^+$ (M^++H) requires 689.3128, found: 689.3114.

tert-butyl-1-benzyl-3-(3-(1-benzyl-1H-indol-3-yl)-5-fluoro-1-methyl-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4k** (major isomer): a colorless solid, 90% yield (64 mg), 12:1 dr. M.p.: 125-128 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.23-1.28 (m, 9H, CH_3), 3.27 (s, 3H, CH_3), 4.42 (d, *J* = 15.6 Hz, 1H, CH_2), 4.60 (d, *J* = 15.6 Hz, 1H, CH_2), 5.36 (s, 2H, CH_2), 5.50 (dd, *J* = 1.8 Hz, 8.4 Hz, 1H, ArH), 6.60 (d, *J* = 7.8 Hz, 1H, ArH), 6.65 (d, *J* = 7.8 Hz, 1H, ArH), 6.74 (dd, *J* = 7.5 Hz, 7.5 Hz, 1H, ArH), 6.79-6.86 (m, 2H, ArH), 6.89-6.94 (m, 3H, ArH), 6.97-7.05 (m, 1H, ArH), 7.09 (dd, *J* = 7.5 Hz, 7.5 Hz, 1H, ArH), 7.15-7.20 (m, 6H, ArH), 7.23-7.27 (m, 2H, ArH), 7.29-7.39 (m, 2H, ArH), 7.78 (s, 1H, ArH), 8.18 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 26.8, 28.1, 44.2, 50.1, 54.6, 67.0, 80.2, 107.5, 108.9 (d, *J* = 8.3 Hz), 109.0, 110.0, 114.1 (d, *J* = 25.1 Hz), 116.0 (d, *J* = 23.5 Hz), 119.9, 121.2, 122.0 (d, *J* = 5.0 Hz), 125.8, 126.6, 126.7, 126.8, 127.2, 127.3, 127.8, 128.5, 128.7, 128.8, 128.9, 129.6, 130.8, 135.4, 136.6, 137.1, 140.6, 144.4, 155.9 (d, *J* = 247.5 Hz), 159.5, 174.5, 175.7. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$) δ -120.4. IR (CH_2Cl_2) ν 3311, 3051, 2976, 2925, 1717, 1699, 1604, 1485, 1470, 1368, 1351, 1276, 1252, 1159, 1110, 1064, 1028, 911, 879, 843, 735, 701 cm^{-1}. ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$) δ -120.4. MS (ESI) *m/z* (%): 707.3 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{40}FN_4O_4^+$ (M^++H) requires 707.3034, Found: 707.3029.

tert-butyl-1-benzyl-3-(3-(1-benzyl-1H-indol-3-yl)-6-bromo-1-methyl-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4l** (major isomer): a colorless solid, 94% yield (72 mg), 5:1 dr. M.p.: 127-130 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.33 (m, 9H, CH_3), 3.27 (s, 3H, CH_3), 4.37 (d, *J* = 15.6 Hz, 1H, CH_2), 4.71 (d, *J* = 15.6 Hz, 1H, CH_2), 5.35 (s, 2H, CH_2), 6.62 (d, *J* = 8.0 Hz, 1H, ArH), 6.56 (d, *J* = 8.0 Hz, 1H, ArH), 6.70-6.77 (m, 3H, ArH), 6.83-6.91 (m, 3H, ArH), 7.07-7.13 (m, 2H, ArH), 7.15-7.17 (m, 3H, ArH), 7.22-7.38 (m, 8H, ArH), 7.72 (s, 1H, ArH), 8.12 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 28.1, 31.9, 44.3, 50.1, 54.0, 66.9, 80.1, 107.5, 109.0, 110.0, 112.1, 120.0, 121.3, 121.4, 121.9, 122.0, 123.4, 124.9, 125.5, 125.8, 126.1, 126.7, 126.8, 127.2, 127.26, 127.3, 127.5, 127.8, 128.5, 128.7, 128.8, 129.4, 130.8, 135.3, 136.6, 137.1, 144.5, 145.8, 154.5, 174.6, 175.8. IR (CH_2Cl_2) ν 3323, 3051, 2974, 2922, 1716, 1600, 1489, 1465, 1455, 1364, 1275, 1258, 1159, 1099, 1075, 1028, 965, 912, 883, 843, 809, 732, 697 cm^{-1}. MS (ESI) *m/z* (%): 767.2 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{40}BrN_4O_4^+$ (M^++H) requires 767.2233, Found: 767.2226.

tert-butyl-1-benzyl-3-(3-(1-benzyl-1H-indol-3-yl)-5,7-dichloro-1-methyl-2-oxoindolin-3-yl)-2-oxoindolin-3-ylcarbamate **4m** (major isomer): a colorless solid, 93% yield (70 mg), 5:1 dr. M.p.: 124-127 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25-1.33 (m, 9H, CH_3), 3.63 (s, 3H, CH_3), 4.39 (d, *J* = 15.6 Hz, 1H, CH_2), 4.68 (d, *J* = 15.6 Hz, 1H, CH_2), 5.38 (s, 2H, CH_2), 5.44 (s, 1H, ArH), 6.53 (d, *J* = 7.8 Hz, 1H, ArH), 6.72 (d, *J* = 7.5 Hz, 1H, ArH), 6.77 (dd, *J* = 7.5 Hz, 7.5 Hz, 1H, ArH), 6.87 (dd, *J* = 7.8 Hz, 7.8 Hz, 1H, ArH), 6.96-7.03 (m, 3H, ArH), 7.05-7.12 (m, 2H, ArH), 7.15-7.21 (m, 2H, ArH), 7.24-7.40 (m, 8H, ArH), 7.82 (s, 1H, ArH), 8.00 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.1, 30.2, 44.3, 50.2, 54.3, 67.1, 80.4, 106.9, 108.8, 110.1, 115.8, 117.9, 120.1, 120.7, 122.1, 124.9, 125.9, 126.4, 126.6, 126.8, 127.1, 127.3, 127.5, 127.6, 127.9, 128.6, 128.7, 128.8, 128.9, 129.7, 130.55, 130.6, 131.4, 135.3, 136.6, 137.0, 139.2, 144.4, 154.6, 174.2, 176.0. IR (CH_2Cl_2) ν 3325, 3062, 2978, 2924, 1716, 1611, 1577, 1487, 1464, 1366, 1275, 1253, 1160, 1118, 1075, 1028, 918, 861, 738, 697 cm^{-1}. MS (ESI) *m/z* (%): 757.2 (100) [M^++H]; HRMS (ESI) Calcd. for $C_{44}H_{39}Cl_2N_4O_4^+$ (M^++H) requires 757.2349, found: 757.2346.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-5-fluoro-2-oxoindolin-3-ylcarbamate **4o** (major isomer): a colorless solid, 93% yield (66 mg), 11:1 dr. M.p.: 115-118 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.26-1.41 (m, 9H, CH_3), 3.86 (s, 3H, CH_3), 4.40 (d, *J* = 15.6 Hz, 1H, CH_2), 4.65 (d, *J* = 16.0 Hz, 1H, CH_2), 4.85 (d, *J* = 16.0 Hz, 1H, CH_2), 5.16 (d, *J* = 15.6 Hz, 1H, CH_2), 5.82 (s, 1H, ArH), 6.22 (d, *J* = 7.6 Hz, 1H, ArH), 6.46 (dd, *J* = 4.0 Hz, 8.0 Hz, 1H, ArH), 6.58 (dd, *J* = 6.8 Hz, 6.8 Hz, 1H, ArH), 6.69-6.90 (m, 5H, ArH), 6.95-7.01 (m, 1H, ArH), 7.09-7.37 (m, 11H, ArH), 7.90 (s, 1H, ArH), 8.25 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.2, 33.3, 44.4, 44.5, 53.4, 67.3, 80.5, 109.3 (d, *J* = 8.1 Hz), 109.5, 110.0, 114.2 (d, *J* = 25.3 Hz), 115.7 (d, *J* = 22.9 Hz), 119.5, 120.8, 121.9, 122.2, 122.7 (d, *J* = 5.4 Hz), 126.7, 127.1, 127.2, 127.4, 127.6, 128.1, 128.4, 128.6, 128.65, 129.6, 131.0, 135.2, 135.3, 137.1, 140.7, 143.8, 154.8, 158.5 (d, *J* = 238.6 Hz), 174.6, 176.2. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ -120.1. IR (CH_2Cl_2) ν 3385, 3062, 2978, 2924, 1714, 1702, 1610, 1507, 1469, 1424, 1368, 1348,

1249, 1160, 1130, 1067, 1020, 912, 878, 845, 810, 736, 699, 669 cm^{-1}. MS (ESI) *m/z* (%): 707.3 (100) $[M^+H]$; HRMS (ESI) Calcd. for $C_{44}H_{40}FN_4O_4^+$ (M^++H) requires 707.3034, found: 707.3028.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-6-methyl-2-oxoindolin-3-ylcarbamate **4p** (major isomer): a colorless solid, 94% yield (66 mg), 7:1 dr. M.p.: 122-125 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.47 (m, 9H, CH_3), 2.23 (s, 3H, CH_3), 3.86 (s, 3H, CH_3), 4.39 (d, *J* = 15.6 Hz, 1H, CH_2), 4.66 (d, *J* = 16.0 Hz, 1H, CH_2), 4.85 (d, *J* = 16.0 Hz, 1H, CH_2), 5.16 (d, *J* = 15.6 Hz, 1H, CH_2), 5.82 (d, *J* = 2.8 Hz, 1H, ArH), 6.23 (d, *J* = 8.4 Hz, 1H, ArH), 6.37 (s, 1H, ArH), 6.53-6.57 (m, 1H, ArH), 6.63-6.74 (m, 3H, ArH), 6.80-6.85 (m, 2H, ArH), 7.08-7.19 (m, 8H, ArH), 7.26-7.39 (m, 4H, ArH), 7.92 (s, 1H, ArH), 8.22 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 21.9, 28.2, 33.2, 44.1, 44.4, 54.5, 66.9, 80.0, 109.3, 109.7, 109.8, 118.9, 119.3, 120.9, 121.0, 121.6, 122.1, 122.3, 122.5, 122.7, 124.3, 125.7, 126.3, 126.8, 127.0, 127.2, 127.3, 127.9, 128.5, 128.6, 128.7, 129.3, 131.2, 133.3, 135.4, 135.7, 137.0, 139.4, 143.8, 144.6, 154.8, 175.1, 176.6. IR (CH_2Cl_2) ν 3324, 3055, 2977, 2926, 1719, 1618, 1610, 1487, 1466, 1366, 1276, 1162, 1115, 1077, 1016, 899, 848, 749, 698 cm^{-1}. MS (ESI) *m/z* (%): 703.3 (100) $[M^+H]$; HRMS (ESI) Calcd. for $C_{45}H_{43}N_4O_4^+$ (M^++H) requires 703.3284, found: 703.3280.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-6-bromo-2-oxoindolin-3-ylcarbamate **4q** (major isomer): a colorless solid, 91% yield (70 mg), 8:1 dr. M.p.: 135-138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.43 (m, 9H, CH_3), 3.85 (s, 3H, CH_3), 4.38 (d, *J* = 16.0 Hz, 1H, CH_2), 4.63 (d, *J* = 15.2 Hz, 1H, CH_2), 4.88 (d, *J* = 16.0 Hz, 1H, CH_2), 5.13 (d, *J* = 15.2 Hz, 1H, CH_2), 5.89 (d, *J* = 4.4 Hz, 1H, ArH), 6.38 (d, *J* = 8.0 Hz, 1H, ArH), 6.62-6.71 (m, 3H, ArH), 6.74-6.84 (m, 3H, ArH), 6.96-7.04 (m, 2H, ArH), 7.11-7.39 (m, 11H, ArH), 7.80 (s, 1H, ArH), 8.29 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 28.2, 33.3, 44.3, 44.5, 54.2, 66.7, 80.5, 109.3, 109.4, 110.1, 112.2, 118.7, 119.1, 119.5, 121.1, 121.2, 121.8, 122.4, 123.1, 124.5, 125.0, 126.0, 126.3, 126.6, 127.1, 127.2, 127.3, 127.4, 127.8, 128.1, 128.7, 129.6, 131.2, 133.1, 134.9, 135.2, 137.1, 143.7, 145.9, 154.8, 174.8, 176.2. IR (CH_2Cl_2) ν 3318, 3059, 2978, 2923, 1718, 1695, 1603, 1485, 1466, 1367, 1276, 1159, 1110, 1064, 1018, 898, 878, 843, 735, 697, 670 cm^{-1}. MS (ESI) *m/z* (%): 767.2 (100) $[M^+H]$; HRMS (ESI) Calcd. for $C_{44}H_{40}BrN_4O_4^+$ (M^++H) requires 767.2233, found: 767.2231.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-2-oxo-7-(trifluoromethyl)indolin-3-ylcarbamate **4r** (major isomer): a colorless solid, 94% yield (71 mg), >20:1 dr. M.p.: 133-136 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25-1.41 (m, 9H, CH_3), 3.83 (s, 3H, CH_3), 4.64 (d, *J* = 17.2 Hz, 1H, CH_2), 4.76 (d, *J* = 17.2 Hz, 1H, CH_2), 4.88 (d, *J* = 16.0 Hz, 1H, CH_2), 5.01 (d, *J* = 16.0 Hz, 1H, CH_2), 5.86 (d, *J* = 3.6 Hz, 1H, ArH), 6.69-6.78 (m, 5H, ArH), 6.86 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.94 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 7.04-7.19 (m, 8H, ArH), 7.23-7.32 (m, 4H, ArH), 7.57 (d, *J* = 7.6 Hz, 1H, ArH), 7.66 (s, 1H, ArH), 8.33 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) 28.2, 33.1, 33.2, 44.4, 47.0, 65.5, 80.6, 106.9, 108.6, 109.4, 110.3, 119.6, 120.7, 121.4, 121.7, 122.1, 122.8, 125.1, 125.4, 125.8, 126.0 (q, *J* = 268.5 Hz), 126.1, 126.5, 126.7, 127.0, 127.7, 127.9, 128.1, 128.60 (q, *J* = 33.1 Hz), 128.62, 129.0, 129.2, 129.8, 130.4, 131.5, 134.9, 136.1, 137.2, 143.0, 143.7, 154.9, 175.8, 176.9. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ -54.8. IR (CH_2Cl_2) ν 3310, 3040, 2978, 2928, 1716, 1699, 1609, 1596, 1491, 1470, 1452, 1438, 1368, 1332, 1282, 1252, 1160, 1122, 1097, 1020,967, 904, 888, 834, 790, 735, 697 cm^{-1}. MS (ESI) *m/z* (%): 774.3 (100) $[(M^++NH_4]$; HRMS (ESI) Calcd. for $C_{45}H_{43}F_3N_5O_4^+$ (M^++NH_4) requires 774.3262, found: 774.3254.

tert-butyl-1-benzyl-3-(1-benzyl-3-(1-methyl-1H-indol-3-yl)-2-oxoindolin-3-yl)-5-chloro-7-methyl-2-oxoindolin-3-ylcarbamate **4s** (major isomer): a colorless solid, 92% yield (68 mg), 5:1 dr. M.p.: 130-133 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.24-1.44 (m, 9H, CH_3), 2.06 (s, 3H, CH_3), 3.84 (s, 3H, CH_3), 4.70 (br, 2H, CH_2), 4.83 (d, *J* = 16.0 Hz, 1H, CH_2), 5.11 (d, *J* = 16.0 Hz, 1H, CH_2), 5.94 (s, 1H, ArH), 6.59 (d, *J* = 7.6 Hz, 1H, ArH), 6.69-6.74 (m, 3H, ArH), 6.82 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H, ArH), 6.88-7.05 (m, 2H, ArH), 7.12-7.42 (m, 12H, ArH), 7.75 (s, 1H, ArH), 8.21 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 18.7, 28.3, 33.2, 44.5, 45.9, 56.6, 65.1, 80.5, 109.0, 109.3, 109.5, 110.2, 119.0, 119.6, 120.5, 120.9, 121.3, 121.9, 122.0, 124.0, 125.7, 126.2, 126.7, 127.1, 127.4, 128.0, 128.4, 128.6, 128.8, 129.2, 129.6, 131.5, 132.5, 132.8, 133.2, 135.2, 136.5, 137.3, 141.5, 143.9, 153.9, 176.0, 176.8. IR (CH_2Cl_2) ν 3325, 3062, 2977, 2928, 1716, 1608, 1486, 1466, 1366, 1276, 1160, 1077, 1029, 913, 870, 839, 738, 697 cm^{-1}. MS (ESI) *m/z* (%): 737.3 (100) $[M^+H]$; HRMS (ESI) Calcd. for $C_{45}H_{42}ClN_4O_4^+$ (M^++H) requires 737.2895, found: 737.2892.

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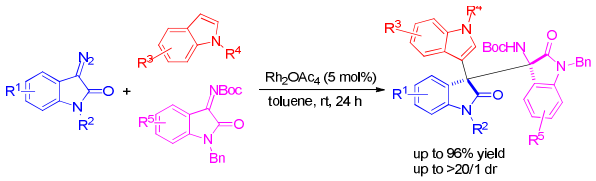
Rhodium-Catalyzed Three-Component Reaction of 3-Diazooxindoles with Indoles and Isatin-Derived Ketimines: A Facile and Versatile Approach to Functionalized 3,3',3''-Trisindoles



A variety of functionalized 3,3',3''-trisindoles could be produced in high yields with moderate to excellent diastereoselectivities via $Rh_2(OAc)_4$-catalyzed three-component reaction of 3-diazooxindoles with indoles and isatin-derived N-Boc ketimines

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