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Article

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Rhodium(III)-Catalyzed Oxidative Coupling of *N*-Phenylindole-3-carboxylic Acids with Alkenes and Alkynes via C4–H and C2–H/C2'–H Bond Cleavage

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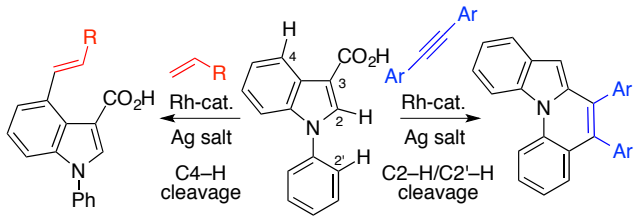
KEYWORDS: rhodium catalyst; oxidative coupling; C–H bond cleavage; indole; carboxylic acid.



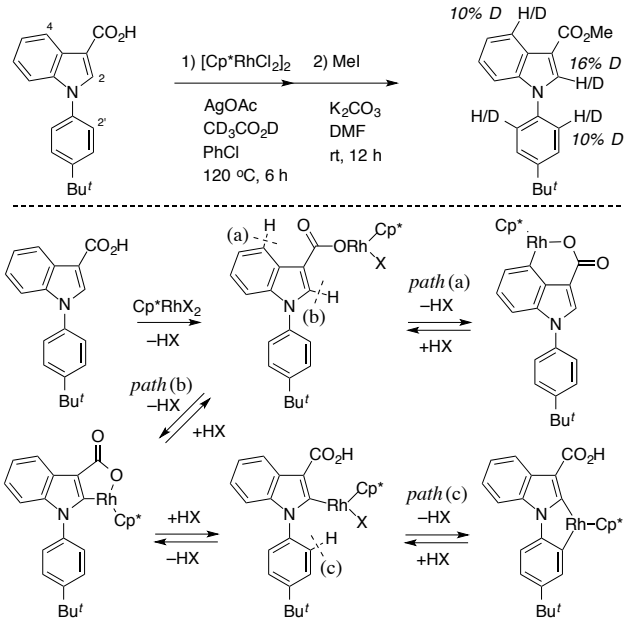
ABSTRACT: The rhodium(III)-catalyzed direct alkenylation of *N*-phenylindole-3-carboxylic acids with alkenes including acrylate ester, acrylamide, and acrylonitrile proceeds smoothly at the C4-position through regioselective C–H bond cleavage directed by the carboxyl group. In marked contrast, the indole substrates react with diarylacetylenes accompanied by cleavage of the C2–H and C2'–H bonds and decarboxylation to produce 5,6-diarylindolo[1,2-*a*]quinolone derivatives. DFT calculations have suggested that the smooth insertion of an alkene to a C4-rhodated six-membered metallacycle intermediate leads to the C4 alkenylated products, while the latter annulation at the C2 and C2' positions is attributable to facile reductive elimination in the corresponding seven-membered metallacycles formed by the double C-H bond cleavage and alkyne insertion.

INTRODUCTION

Since variously substituted indoles can be seen in a broad range of biologically active natural and unnatural compounds, the development of regioselective substitution methods on indole skeletons has been of substantial importance in organic synthesis field. As one of the most powerful, straightforward tools for the regioselective substitution on aromatic compounds, the transition-metal-catalyzed C–H bond functionalization utilizing directing groups[1] has been extensively studied, and the direct methods have been employed for derivatizing indoles. Most of such reactions on indoles with use of C-3 directing groups take place on the more electron-rich pyrrole ring (C-2), although those at the phenyl ring (C-4) are observed in some cases.[2] For the former examples, we reported the palladium-, rhodium-, and ruthenium-catalyzed oxidative coupling reactions of indole-3-carboxylic acids as well as those of indole-2-carboxylic acids with

alkenes and alkynes through cleavage of the C2–H bond (or C3-H bond in the case of the 2-carboxylic acids).[3] The carboxylic function is especially useful as it can be used in further derivatization reactions and also removable after the coupling event. To obtain mechanistic information about the rhodium-catalyzed reaction, we examined the H/D exchange reaction of *N*-(4-Bu^{t}C$_6$H$_4$)phenylindole-3-carboxylic acid as a representative substrate, which allows the assignment of each of the protons in its ^{1}H NMR analysis, by using CD_3CO_2D as a D-source (Scheme 1). Interestingly, we observed the deuterium incorporation at the C4- and C2'-positions in addition to the expected C2-position. Thus, the C–H bond cleavage steps, i.e. paths (a), (b), and (c) appear to be reversible. This observation encouraged us to develop new site-selective functionalization methods for indole-3-carboxylic acid derivatives under rhodium catalysis.

Scheme 1. H/D Exchange of *N*-(4-Bu^{t}C$_6$H$_4$)phenylindole-3-carboxylic acid



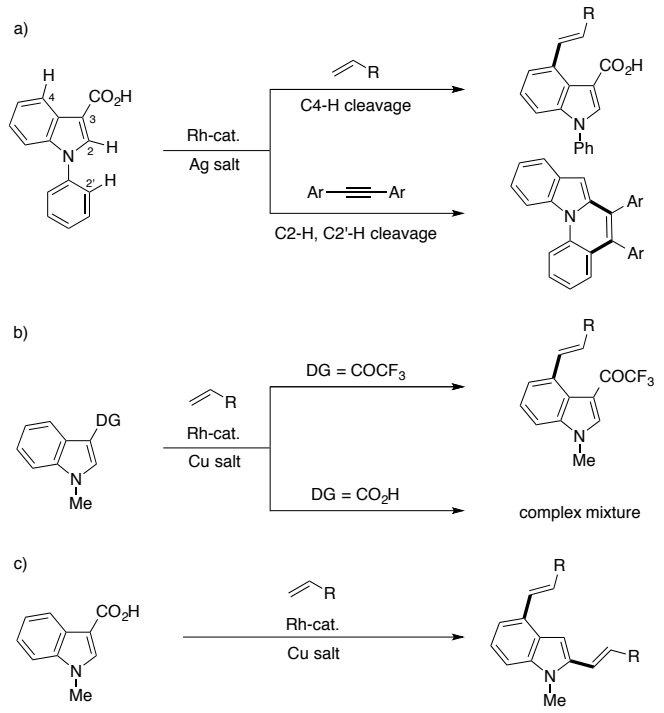
In the above context of our studies, we have found that *N*-phenylindole-3-carboxylic acids undergo oxidative alkenylation at the C4-position upon treatment with alkenes such as acrylates in the presence of a Cp*Rh(III) catalyst and a silver salt oxidant (Scheme 2a). In marked contrast, it has been observed that *N*-phenylindole-3-carboxylic acids couple with diarylacetylenes under similar conditions through cleavage of the C2-H and C2'-H bonds accompanied by decarboxylation to produce 5,6-diarylindolo[1,2-*a*]quinolone derivatives.[4] Although similar tetracyclic compounds, which are fluorescent in the solid state, could also be obtained under palladium catalysis,[3c] the product yields were moderate to low and the substrate scope was rather limited.

Recently, the ruthenium- and palladium-catalyzed C4-alkenylation of indole nuclei utilizing formyl-[5] and sulfonylamino-directing groups,[6] respectively, were reported. Afterward, Prabhu and co-workers demonstrated that the C4-alkenylation of 3-(trifluoroacetyl)indoles can be achieved under rhodium catalysis (Scheme 2b).[7] However, under their conditions, the reaction utilizing a carboxyl directing group gave a complex mixture.[7a] After the initiation of this work, Zhang and co-workers disclosed that treatment of indole-3-carboxylic acids with alkenes by using a rhodium catalyst and a copper oxidant leads to dialkenylation at the C2- and C4-positions and spontaneous decarboxylation to produce 2,4-dialkenylated indole derivatives (Scheme 2c).[8] In the present case, only the C-4 mono-alkenylation occurs and the carboxyl group remains in the alkenylated products. As a preliminary attempt, we have combined the C4-alkenylion with the subsequent coupling with an alkyne in a one-pot manner.

Furthermore, we have performed DFT calculations to provide rational insight into the different site-selectivity in the reactions with alkenes and alkynes: The dominant origins of such C2/C4

selectivity have been little known. These results for the experimental and theoretical studies are described herein.

Scheme 2. Regioselective C–H Bond Functionalization of Indoles



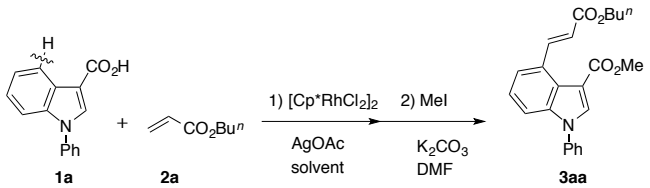
RESULTS AND DISCUSSION

Coupling with Alkenes

In an initial attempt, *N*-phenylindole-3-carboxylic acid (**1a**) (0.2 mmol) was treated with butyl acrylate (**2a**) (0.4 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.005 mmol, 2.5 mol %) and AgOAc (0.4 mmol) in PhCl under N_2 at 120 °C for 12 h. As a result, the desired C4-alkenylated product was selectively formed, and it was successively methyl-esterified for its quantification to afford methyl (*E*)-4-(3-butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3aa**) in 57% GC yield (Table 1, entry 1). The use of other solvents such as *o*-xylene, *tert*-amyl alcohol,

dioxane, and DMF diminished the yield of **3aa** (entries 2-5). In PhCl, Ag_2CO_3 was found to be as effective as AgOAc (entry 6). Interestingly, decreasing the reaction temperature to 80 °C enhanced the yield to 77% (entry 8). However, a further decrease to 60 °C reduced it to 61% (entry 9).

Table 1. Reaction of *N*-Phenylindole-3-carboxylic Acid (**1a**) with Butyl Acrylate (**2a**)[a]



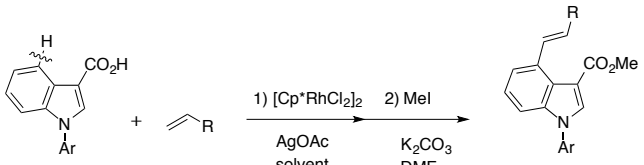
entry	solvent	temp (°C)	yield (%)[b]
1	PhCl	120	57
2	*o*-xylene	120	41
3	Am^{t}OH	120	41
4	dioxane	120	23
5	DMF	120	11
6[c]	PhCl	120	57
7	PhCl	100	72
8	PhCl	80	77 (75)
9	PhCl	60	61

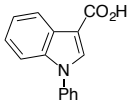
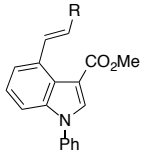
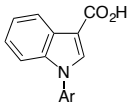
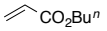
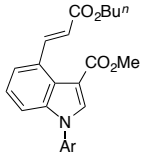
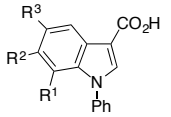
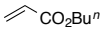
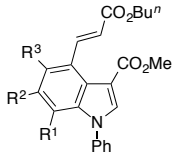
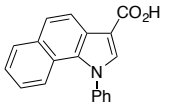
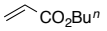
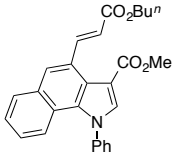
[a] Reaction conditions: 1) **1a** (0.2 mmol), **2a** (0.4 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), AgOAc (0.4 mmol) in solvent (2 mL) under N_2 for 12 h, unless otherwise noted: 2) With the addition of MeI (1.2 mmol), K_2CO_3 (0.6 mmol), and DMF (2 mL) at rt for 12 h. [b] GC yield based on the amount of **1a** used. Value in parentheses indicates yield after purification. [c] Ag_2CO_3 (0.2 mmol) was employed in place of AgOAc.

Under the conditions in entry 8 of Table 1, the reactions of **1a** with various alkenes **2b**-**h** were next examined (Table 2). A series of acrylate esters **2b**-**f** reacted with **1a** regioselectively to produce the corresponding C4-alkenylindole derivatives **3ab**-**af**, as in the coupling of **1a** and **2a** (entries 1-5). Besides the esters, *N*,*N*-dimethylacrylamide (**2g**) and acrylonitrile (**2h**) could also be employed for the present coupling to give the C4-alkenylated products **3ag** and **3ah**, respectively (entries 6 and 7). In contrast to these electron-deficient alkenes, styrene was less reactive to give only a trace amount of an alkenylated product. Under similar conditions, *p*-

methyl-, *tert*-butyl-, and chloro-substituted phenylindole-3-carboxylic acids **1b**-**d** reacted with **2a** to afford **3ba**-**da** (entries 8-10). 7-Methyl, 6-chloro, and 5-methoxy indole substrates **1e**-**g** also underwent the coupling with **2a** to form **3ea**-**ga** (entries 11-13). A benzo-fused indole substrate, 1-phenyl-1*H*-benzo[*g*]indole-3-carboxylic acid (**1h**) was also alkenylated at the C4 position under standard conditions to produce **3ha** in 73% yield (entry 14).

Table 2. Reaction of *N*-Arylindole-3-carboxylic Acids **1** with Alkenes **2**[a]



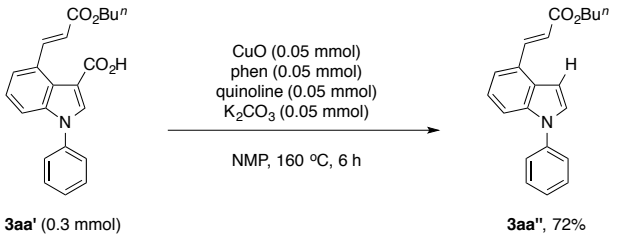
entry	1	2	product	yield (%)[b]
				
1	**1a**	**2b**: R = CO_2Bu^i	**3ab**: R = CO_2Bu^i	64
2		**2c**: R = CO_2Bu^t	**3ac**: R = CO_2Bu^t	68
3		**2d**: R = CO_2Cy	**3ad**: R = CO_2Cy	65
4		**2e**: R = CO_2Et	**3ae**: R = CO_2Et	66
5		**2f**: R = CO_2Me	**3af**: R = CO_2Me	68
6		**2g**: R = $CONMe_2$	**3ag**: R = $CONMe_2$	71
7		**2h**: R = CN	**3ah**: R = CN	54
				
8	**1b**: Ar = 4-MeC_6H_4	**2a**	**3ba**: Ar = 4-MeC_6H_4	77
9	**1c**: Ar = 4-$Bu^tC_6H_4$		**3ca**: Ar = 4-$Bu^tC_6H_4$	77
10	**1d**: Ar = 4-ClC_6H_4		**3da**: Ar = 4-ClC_6H_4	50
				
11	**1e**: R^1 = Me, R^2 = R^3 = H	**2a**	**3ea**: R^1 = Me, R^2 = R^3 = H	74
12	**1f**: R^2 = Cl, R^1 = R^3 = H		**3fa**: R^2 = Cl, R^1 = R^3 = H	67
13	**1g**: R^3 = OMe, R^1 = R^2 = H		**3ga**: R^3 = OMe, R^1 = R^2 = H	56
				
14	**1h**	**2a**	**3ha**	73

[a] Reaction conditions: 1) **1** (0.2 mmol), **2** (0.4 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), AgOAc (0.4 mmol) in PhCl (2 mL) at 80 °C under N_2 for 12 h, unless otherwise noted: 2) With the addition of MeI (1.2 mmol), K_2CO_3 (0.6 mmol), and DMF (2 mL) at rt for 12 h. [b] Isolated yield.

In addition, the decarboxylation[9] of a 4-alkenylated indole-3-carboxylic acid was examined. As expected, treatment of (*E*)-4-(3-butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylic

acid (**3aa'**) under Goossen's conditions[9a] gave (*E*)-4-(3-butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole (**3aa''**) in 72% yield (Scheme 3).

Scheme 3. Decarboxylation of **3aa'**

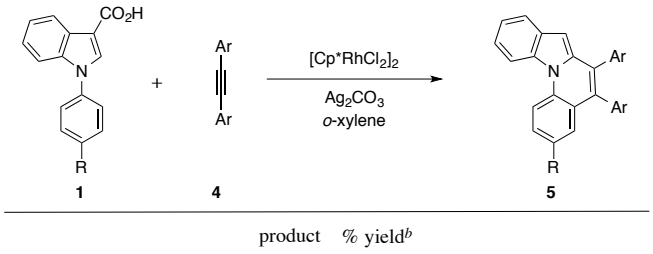


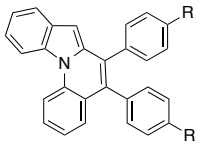
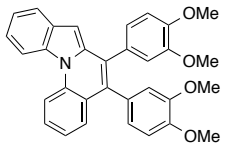
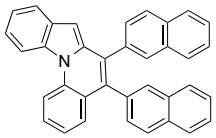
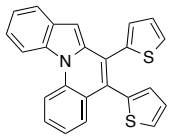
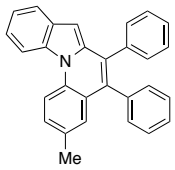
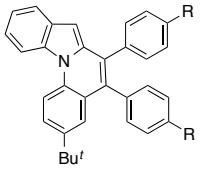
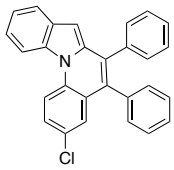
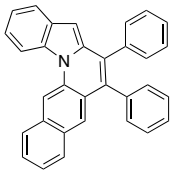
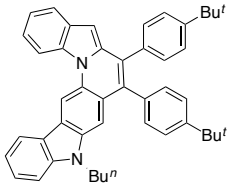
Coupling with Alkynes

As described above, the reaction of **1a** with diphenylacetylene (**4a**) proceeded through cleavage of the C2–H and C2'–H bonds and decarboxylation to give rise to an indolo[1,2-*a*]quinolone framework.[10] Thus, treatment of **1a** (0.3 mmol) with **4a** (0.2 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.005 mmol, 2.5 mol %) and Ag_2CO_3 (0.2 mmol) in *o*-xylene under N_2 at 120 °C for 24 h afforded 5,6-diphenylindolo[1,2-*a*]quinolone (**5aa**) in 78% yield (Table 3). Variously substituted diphenylacetylenes **4b**-**h** also coupled with **1a** to produce **5ab**-**ah** in fair to good yields. The reactions of di(2-naphthyl)- (**4i**) and di(2-thienyl)- (**4j**) acetylenes with **1a** could be conducted in similar manners to give **5ai** and **5aj**. The reaction of 4-octyne was sluggish to give the corresponding annulated product in a poor yield (> 20%). In addition to **1a**, *N*-(*p*-substituted phenyl)-, *N*-(2-naphthyl)-, and *N*-(9-Bu^{t}carbazol-3-yl)indole-3-carboxylic acids **1b**-**d**,**i**,**j** reacted

with **4a** or **4d** to give the corresponding tetra-, penta-, and hexacyclic products **5ba**-**da**, **5cd**, **5ia**, and **5jd**.

Table 3. Reaction of *N*-Arylindole-3-carboxylic Acids **1** with Alkynes **4**[a]

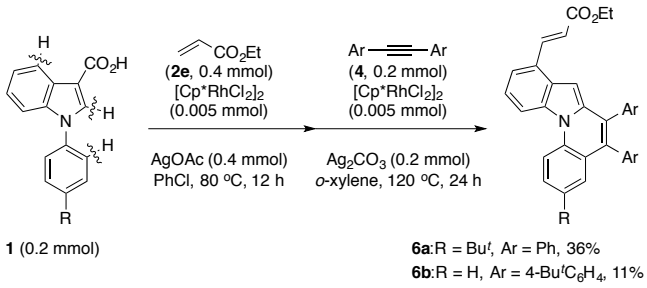


product	% yield[b]
 **5aa**: R = H	78
5ab: R = Me	86
5ac: R = OMe	70
5ad: R = Bu^t	70
5ae: R = Cl	75
5af: R = Br	73
5ag: R = CF_3	56
 **5ah**	84
 **5ai**	70
 **5aj**	32
 **5ba**	79
 **5ca**: R = H	84
5cd: R = Bu^t	87
 **5da**	89
 **5ia**	70
 **5jd**	32

[a] Reaction conditions: **1** (0.3 mmol), **4** (0.2 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), Ag_2CO_3 (0.2 mmol) in *o*-xylene (2 mL) at 120 °C under N_2 for 24 h, unless otherwise noted. [b] Isolated yield based on the amount of **4** used.

We next examined the one-pot three-component coupling[11] of **1c**, **2e**, and **4a** through the C4-alkenylation and successive alkyne annulation at the C2- and C2'-positions. Thus, **1c** (0.2 mmol) was treated with **2e** (0.4 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.005 mmol) and AgOAc (0.4 mmol) in PhCl under N_2 at 80 °C for 12 h. After evaporation of the solvent under vacuum, **4a** (0.2 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), Ag_2CO_3 (0.2 mmol), and *o*-xylene were added and heated at 120 °C under N_2 for 24 h. From the resulting reaction mixture, the corresponding three-component coupling product **6a** was isolated in 36% yield (Scheme 4). Similarly, the three-component coupling of **1a**, **2e**, and **4d** furnished **6b**, albeit with a low yield.

Scheme 4. Three-Component Coupling



DFT Calculation for Acrylonitrile Insertion

In order to clarify the cause of the different site-selectivity in the reactions with alkenes and with alkynes on *N*-arylindole-3-carboxylic acids **1**, DFT calculations were performed for the insertion reaction of acrylonitrile (**2h**) as well as that of diphenylacetylene (**4a**) into three rhodacycles **A**, **B**, and **C** (Figure 1). The rhodacycles **A**, **B**, and **C** are likely involved as the intermediates in the present coupling reactions as implied by Scheme 1. Six possible insertion positions are indicated by **I** - **VI** in Figure 1. In the acrylonitrile insertion reaction, there are four

transition states (TS) per an insertion position due to the orientation of the cyano group. Therefore, 24 insertion TSs and intermediates were calculated for the acrylonitrile insertion reactions.

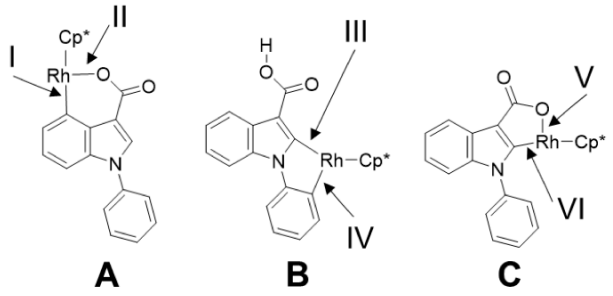


Figure 1. Six possible alkene and alkyne insertion positions (**I** - **VI**) in rhodacycle intermediates **A**, **B**, and **C**.

The 24 intermediates of the acrylonitrile insertion with the activation free energy ($\Delta G^{\ddagger}$) and the reaction free energy (ΔG) are shown in Figure S1 (see Supporting Information). The insertion reaction, in which the acrylonitrile is inserted into **Position I** with the cyano group orienting to the Rh side as shown in Figure 2, has the lowest activation free energy among the 24 insertion reactions. The result shows that the acrylonitrile kinetically advantageously inserts into **Position I**, which is consistent with the experimental observation that the alkenes are coupled at the C4-position of the indole substrate.

Figure 2 shows the Gibbs free energy diagram for the entire reaction from the insertion reaction to the β-hydrogen elimination. The Gibbs free energy is a relative value based on the energy of the rhodacycle intermediate **A** and acrylonitrile. Acrylonitrile coordinates to Rh of **A** to form π-complex intermediate **D**. Then, acrylonitrile inserts into the Rh-C bond of **D** leading to

intermediate **D-IM1** via transition state **D-TS1**. The activation free energy and reaction free energy of the insertion reaction are 9.0 and –16.0 kcal mol^{-1}, respectively, indicating that this reaction proceeds rapidly.

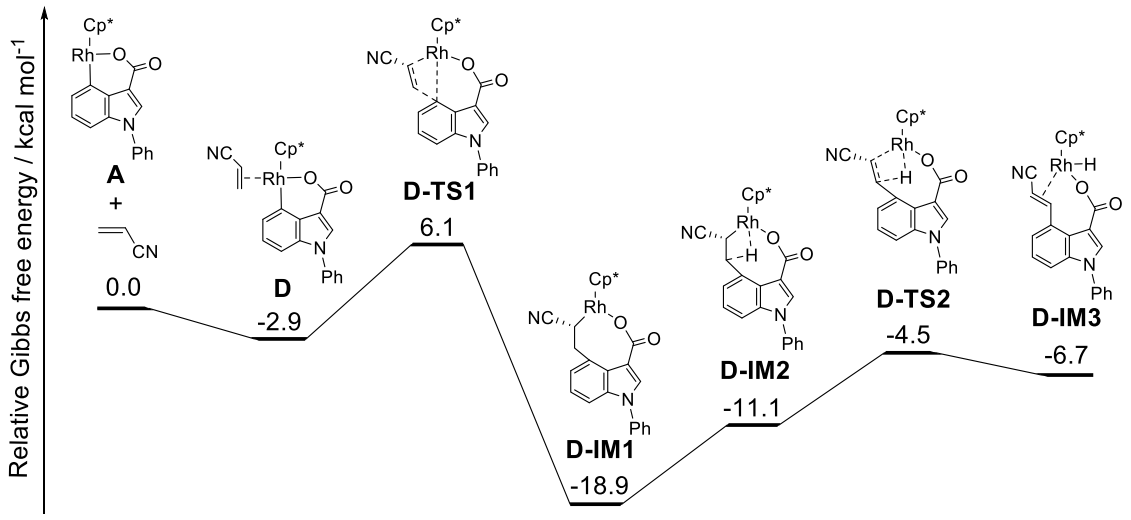


Figure 2. Gibbs free energy diagram in the insertion reaction of acrylonitrile to rhodacycle intermediate **A**. The relative Gibbs free energy are given in kcal mol^{-1}.

A β-hydrogen approaching to Rh is necessary to undergo β-hydrogen elimination in the intermediate **D-IM1**. However, as shown in Figure 3(a), Rh and β-hydrogen are spatially separated (3.278 Å) in **D-IM1**. Therefore, we searched for another conformer in which the β-hydrogen is placed proximally to Rh. As a result, a metastable conformer **D-IM2** with the Rh and β-hydrogen distance of 1.872 Å was found, as shown in Figure 3(b). **D-IM2** was 7.8 kcal mol^{-1} less stable than **D-IM1**. This indicates that the β-hydrogen transfer proceeds after changing the conformation from **D-IM1** to **D-IM2**.

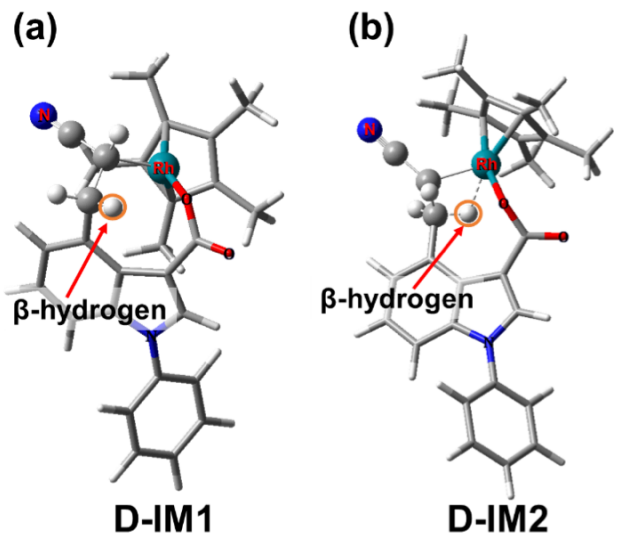


Figure 3. Structures of (a) conformer **D-IM1** and (b) meta-stable conformer **D-IM2**.

The length of β C-H bond proximal to Rh of **D-IM2** is extended to 1.166 Å, while that of **D-IM1** is 1.088 Å. This bond extension indicates the presence of an agostic interaction. The activation free energy of the β-hydrogen transfer from **D-IM2** through **D-TS2** to **D-IM3** was 6.5 kcal mol^{-1}. The low activation free energy may be due to the agostic interaction. This indicates that the conformational change to **D-IM2** induces the β-hydrogen transfer promptly.

In summary, the activation free energy of the acrylonitrile insertion into **Position I** leading to **D-IM1** was the lowest activation free energy among the possible 24 insertion reactions. After changing the conformation from **D-IM1** to **D-IM2**, a β-hydrogen elimination easily proceeds to form C4-coupled precursor **D-IM3**. Therefore, the regioselectivity of the coupling with alkenes is ascribed to the activation free energy of the insertion reaction (**D-TS1**).

DFT Calculation for Diphenylacetylene Insertion

In the diphenylacetylene insertion reaction, there is one transition state (TS) per an insertion position shown in Figure 1. Thus, DFT calculations were performed for the six types of insertion reactions. The Gibbs free energy diagram is shown in Figure 4. The Gibbs free energy is a relative value based on the energy of the rhodacycle intermediates **A**, **B**, or **C** and diphenylacetylene. Coordination of a diphenylacetylene to Rh in **A**, **B**, and **C**, leads to π-complex intermediates **E**, **F**, and **G**, respectively. The diphenylacetylene inserts into the Rh-C or Rh-O bond of **E**, **F**, and **G** via the six types of TSs (**E-TS1**, **E-TS2**, **F-TS1**, **F-TS2**, **G-TS1**, and **G-TS2**) forming the intermediates **E-IM1**, **E-IM2**, **F-IM1**, **F-IM2**, **G-IM1**, and **G-IM2**. The reaction from **G** to **G-IM2** has the lowest activation free energy of 11.3 kcal mol^{-1} with a negative value of the reaction free energy in the six insertion reactions. However, the anticipated product **G-P** by reductive elimination in **G-IM2** was not detected at all in our experiments. Therefore, the activation free energy of the insertion reaction does not simply determine the regioselectivity of the coupling with alkynes.

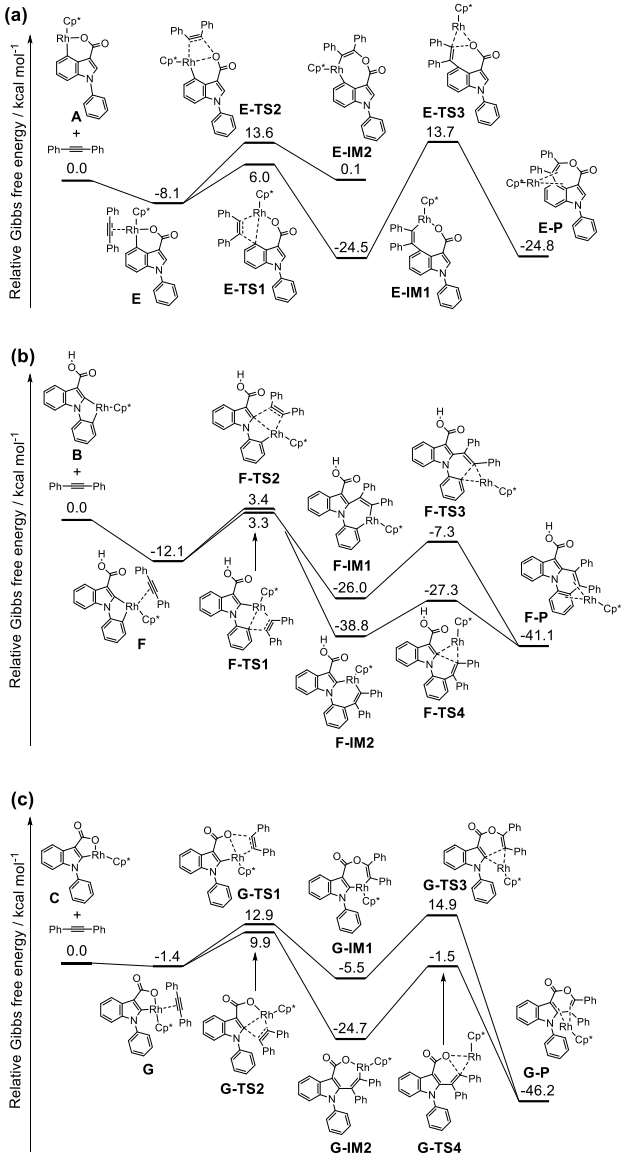


Figure 4. Gibbs free energy diagram in the 4 types of insertion reactions of diphenylacetylene to the rhodacycle intermediates (a) **A**, (b) **B**, and (c) **C**. The relative Gibbs free energies are given in kcal mol^{-1}.

The insertion intermediates lead to the coupling products **E-P**, **F-P**, and **G-P** by the reductive elimination of Rh. Although we carefully explored TS of the reductive elimination of **E-IM2**, it

was not found. The reductive elimination of **E-IM1** has an activation free energy of 38.2 kcal mol^{-1}, which is higher than that of the reverse reaction of the diphenylacetylene insertion (30.5 kcal mol^{-1}), indicating that the reductive elimination of **E-IM1** is slower than the diphenylacetylene desorption. This is consistent with the experimental observation that the alkyne did not couple at the C4-position at all.

The activation free energies of the reductive elimination of **F-IM1** and **F-IM2** are 18.7 and 11.4 kcal mol^{-1}, respectively, which are significantly lower than that of the reductive elimination of **E-IM1** (38.2 kcal mol^{-1}) and the diphenylacetylene desorption of **F-IM1** and **F-IM2** (29.3 and 42.2 kcal mol^{-1}). This result shows that the reductive eliminations of **F-IM1** and **F-IM2** proceed to form the coupling product **F-P**, which corresponds to the C2/C2'-coupled product observed in our experiments. Therefore, the experimental observation that diphenylacetylene reacted at the C2- and C2'-positions can be explained by the low activation free energy of reductive eliminations in **F-IM1** and **F-IM2**.

The activation free energy of the reductive elimination of **G-IM1** and **G-IM2** (20.4 and 23.2 kcal mol^{-1}) are higher than that of the reductive eliminations of **F-IM1** and **F-IM2** (18.7 and 11.4 kcal mol^{-1}), indicating that the reductive elimination of **G-IM1** and **G-IM2** is slower than that of **F-IM1** and **F-IM2**. This is consistent with the fact that the coupling reaction of the *N*-phenylindole with alkynes predominantly gave the products coupled at the C2- and C2'-positions.

CONCLUSIONS

We have demonstrated that *N*-phenylindole-3-carboxylic acids undergo alkenylation at the C-4 position on treatment with alkenes such as acrylate ester, acrylamide, and acrylonitrile in the

presence of a rhodium(III) catalyst and a silver salt oxidant via regioselective C–H bond cleavage. On the other hand, we have observed that the indoles react with diarylacetylenes through cleavage of the C2–H and C2'–H bonds and decarboxylation to selectively furnish the corresponding annulated products in good yields even under similar conditions. A one-pot three-component coupling of the mother substrate *N*-phenylindole-3-carboxylic acid with an alkene and an alkyne has also been shown.

Since the site-selective introduction of functional substituents onto arenes and heteroarenes involving indoles[2] is currently of substantial importance, we have also performed DFT calculations to provide rational insight into the observed different site-selectivity with alkenes and alkynes in the present catalytic system. As a result, it has been suggested that the smooth insertion of an alkene to a C4-rhodated metallacycle intermediate is the key for the selective alkenylation. As for the annulation with alkynes at the C2 and C2' positions, the facile reductive elimination in the corresponding alkyne-inserted seven-membered metallacycles seems to be the key factor. The information obtained in this work would be helpful in designing new catalytic substitution reactions on benzo-fused heteroarenes of importance medicinal and materials chemistry.

EXPERIMENTAL SECTION

General. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz for $CDCl_3$ solutions. HRMS data were obtained by APCI using a TOF mass spectrometer. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm x 25 m). The structures of all products listed below

were unambiguously determined by ^{1}H and ^{13}C NMR with the aid of NOE, COSY, HMQC, and HMBC experiments.

N-Arylindole-3-carboxylic acid **1a-j**[8,12] and alkynes **4b-h,j**[13] and **4i**[14] were prepared according to published procedures.

The following experimental procedures may be regarded as typical in methodology and scale.

Rh-Catalyzed Reaction of *N*-Arylindole-3-carboxylic acids 1 with Alkenes 2. To a 20 mL two-necked flask with a reflux condenser, a balloon, and a rubber cup were added *N*-arylindole-3-carboxylic acid **1** (0.2 mmol), alkene **2** (0.4 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol, 3 mg), AgOAc (0.4 mmol, 67 mg), dibenzyl (ca. 30 mg) as internal standard, and chlorobenzene (2 mL). Then the resulting mixture was stirred under nitrogen at 80 °C (bath temperature). After cooling, CH_3I (1.2 mmol), K_2CO_3 (0.6 mmol, 83 mg), and DMF (2 mL) were added and the resulting mixture was stirred under air at room temperature for 12 h. Then the reaction mixture was diluted by ethyl acetate (100 mL). The organic layer was washed by water (100 mL, three times) and dried over Na_2SO_4. After evaporation of the solvents under vacuum, product **3** was isolated by column chromatography on silica gel using hexane–ethyl acetate as eluent. Further purification by GPC (gel permeation chromatography) was performed, if needed.

Calculation Method

The DFT calculations were employed by the long-range and dispersion corrected ωB97X-D functional.[15] The 6-311G(d,p) basis set was used for H, C, N, and O atoms.[16] The Stuttgart-Dresden SDD effective core potential basis set[17] was used for Rh atom with an additional f polarization function ($\zeta_{f(Rh)}$=1.350).[18] The solvent effect of *o*-xylene was taken account by the Polarizable Continuum Model using the integral equation formalism (IEFPCM)[19] for DFT calculations. Acrylonitrile and diphenylacetylene were selected as the alkene and alkyne

molecules, respectively. The optimized molecular structures were verified by vibrational analysis; equilibrium structures did not have imaginary frequencies and transition state structures had only one imaginary frequency corresponding to the reaction coordinate. Additionally, the intrinsic reaction coordinate (IRC) calculations[20] were carried out to check whether the transition state leading to the reactant and the product. Gibbs free energies were calculated by using the unscaled vibrational frequencies. All calculations were carried out using the Gaussian 16 program.[21]

Characterization Data of Products

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3aa**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange oil; 57 mg (75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3H), 1.50 (sext, J = 7.4 Hz, 2H), 1.74 (quint, J = 6.9 Hz, 2H), 3.93 (s, 3H), 4.26 (t, J = 6.6 Hz, 2H), 6.42 (d, J = 15.8 Hz, 1H), 7.29 (d, J = 7.9 Hz, 1H), 7.46-7.49 (m, 4H), 7.55-7.59 (m, 3H), 8.12 (s, 1H), 9.30 (d, J = 16.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.4, 31.0, 51.7, 64.4, 110.0, 112.7, 118.5, 121.5, 123.7, 125.1, 125.5, 128.4, 129.6, 130.0, 137.0, 138.1, 138.2, 146.0, 165.0, 167.6; HRMS m/z calcd for $C_{23}H_{24}NO_4$ ($[M+H]^+$) 378.1700, found 378.1699.

Methyl (*E*)-4-(3-Isobutoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3ab**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange oil; 48 mg (64%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (d, J = 6.7 Hz, 6H). 2.08 (sep, J = 6.7 Hz, 1H), 3.92 (s, 3H), 4.04 (d, J = 6.6 Hz, 2H), 6.43 (d, J = 15.3 Hz, 1H), 7.24-7.35 (m, 1H), 7.46-7.50 (m, 4H), 7.54-7.60 (m, 3H), 8.12 (s, 1H), 9.32 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 28.1, 51.7, 70.7, 110.0, 112.7, 118.5, 121.5, 123.7, 125.2, 125.5, 128.4, 129.58, 130.0, 136.9,

138.1, 138.2, 145.9, 165.0, 167.6; HRMS *m/z* calcd for $C_{23}H_{24}NO_4$ ([M+H]$^+$) 378.1700, found 378.1698.

Methyl (*E*)-4-(3-(*tert*-Butoxy)-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3ac**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange oil; 51 mg (68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58 (s, 9H), 3.92 (s, 3H), 6.37 (d, *J* = 15.8 Hz, 1H), 7.23-7.36 (m, 1H), 7.45-7.49 (m, 4H), 7.55-7.59 (m, 3H), 8.12 (s, 1H), 9.23 (d, *J* = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 51.7, 80.2, 110.0, 112.5, 120.4, 121.4, 123.6, 125.1, 125.5, 128.4, 129.7, 130.0, 136.9, 138.1, 138.2, 144.8, 165.0, 166.9; HRMS *m/z* calcd for $C_{23}H_{24}NO_4$ ([M+H]$^+$) 378.1700, found 378.1680.

Methyl (*E*)-4-(3-(Cyclohexyloxy)-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3ad**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange solid; 49 mg (65%); mp 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29-1.61 (m, 7H), 1.81-1.97 (m, 4H), 3.93 (s, 3H), 6.42 (d, *J* = 15.8 Hz, 1H), 7.25-7.30 (m, 1H), 7.45-7.49 (m, 4H), 7.54-7.59 (m, 3H), 8.12 (s, 1H), 9.27 (d, *J* = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.9, 25.7, 31.9, 51.7, 72.5, 110.0, 112.6, 119.1, 121.5, 123.6, 125.1, 125.4, 128.4, 129.6, 130.0, 136.9, 138.1, 138.2, 145.6, 165.0, 166.9; HRMS *m/z* calcd for $C_{25}H_{26}NO_4$ ([M+H]$^+$) 404.1856, found 404.1865.

Methyl (*E*)-4-(3-Ethoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (**3ae**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange oil; 46 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, *J* = 7.1 Hz, 3H), 3.94 (s, 3H), 4.32 (q, J = 7.1 Hz, 2H), 6.42 (d, *J* = 15.8 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.45-7.49 (m, 4H), 7.55-7.59 (m, 3H), 8.13 (s, 1H), 9.29 (d, *J* = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 51.7, 60.5, 110.0, 112.8, 118.5, 121.6, 123.7, 125.1, 125.5, 128.4, 129.6, 130.0, 137.0, 138.1, 138.2, 146.0, 165.0, 167.5; HRMS *m/z* calcd for $C_{21}H_{20}NO_4$ ([M+H]$^+$) 350.1387, found 350.1372.

Methyl (*E*)-4-(3-Methoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (3af): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange solid; 46 mg (68%); mp 107-110 °C; ^{1}H NMR (400 MHz, CDCl3) δ 3.86 (s, 3H), 3.94 (s, 3H), 6.42 (d, J = 15.8 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.46-7.50 (m, 4H), 7.55-7.59 (m, 3H), 8.13 (s, 1H), 9.31 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 51.76, 51.83, 109.9, 112.8, 118.1, 121.6, 123.7, 125.1, 125.5, 128.5, 129.5, 130.1, 137.1, 138.1, 138.2, 146.3, 165.0, 167.9; HRMS *m/z* calcd for $C_{20}H_{18}NO_4$ ([M+H]$^+$) 336.1230, found 336.1221.

Methyl (*E*)-4-(3-(Dimethylamino)-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole-3-carboxylate (3ag): purified by column chromatography on silica gel (hexane/EtOAc = 3:1); orange solid; 49 mg (71%); mp 153-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (s, 3H), 3.22 (s, 3H), 3.94 (s, 3H), 6.82 (d, J = 15.3 Hz, 1H), 7.26 (t, J = 7.9 Hz, 1H), 7.44-7.50 (m, 4H), 7.52-7.59 (m, 3H), 8.10 (s, 1H), 9.05 (d, J = 15.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.0, 37.7, 51.8, 110.2, 112.0, 118.3, 121.3, 123.6, 124.9, 125.5, 128.3, 130.0, 130.8, 136.6, 138.0, 138.3, 143.4, 165.0, 167.3; HRMS *m/z* calcd for $C_{21}H_{21}N_2O_3$ ([M+H]$^+$) 349.1547, found 349.1546.

Methyl (*E*)-4-(2-Cyanovinyl)-1-phenyl-1*H*-indole-3-carboxylate (3ah): purified by column chromatography on silica gel (hexane/EtOAc = 3:1); orange solid; 33 mg (54%); mp 128-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 5.85 (d, J = 16.5 Hz, 1H), 7.29 (t, J = 7.9 Hz, 1H), 7.46-7.53 (m, 5H), 7.55-7.60 (m, 2H), 8.14 (s, 1H), 9.21 (d, J = 16.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.8, 96.1, 109.6, 113.7, 119.0, 120.9, 123.7, 124.8, 125.5, 128.6 (overlapped), 130.1, 137.3, 137.9, 138.2, 152.0, 164.8; HRMS *m/z* calcd for $C_{19}H_{15}N_2O_2$ ([M+H]$^+$) 303.1128, found 303.1114.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-(*p*-tolyl)-1*H*-indole-3-carboxylate (3ba): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange solid; 60 mg

(77%); mp 99-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3H), 1.50 (sext, J = 7.4 Hz, 2H), 1.74 (quint, J = 6.9 Hz, 2H), 2.46 (s, 3H), 3.92 (s, 3H), 4.26 (t, J = 6.6 Hz, 2H), 6.42 (d, J = 15.8 Hz, 1H), 7.26 (t, J = 7.8 Hz, 1H), 7.32-7.41 (m, 4H), 7.44 (d, J = 8.2 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 8.09 (s, 1H), 9.31 (d, J = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.4, 21.3, 31.0, 51.7, 64.4, 109.6, 112.8, 118.4, 121.4, 123.5, 125.1, 125.3, 129.5, 130.6, 135.6, 137.1, 138.3, 138.5, 146.0, 165.0, 167.6; HRMS *m/z* calcd for $C_{24}H_{26}NO_4$ ($[M+H]^+$) 392.1856, found 392.1866.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-(4-*(tert*-butyl)phenyl)-1*H*-indole-3-carboxylate (**3ca**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange solid; 67 mg (77%); mp 105-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3H), 1.40 (s, 9H), 1.51 (quint, J = 7.5 Hz, 2H), 1.93 (sext, J = 6.9 Hz, 2H), 3.92 (s, 3H), 4.26 (t, J = 6.6 Hz, 2H), 6.42 (d, J = 15.8 Hz, 1H), 7.26 (t, J = 7.9 Hz, 1H), 7.38-7.41 (m, 2H), 7.49 (dd, J = 0.72, 8.2 Hz, 1H), 7.55-7.58 (m, 3H), 8.11 (s, 1H), 9.31 (d, J = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.4, 31.0, 31.5, 34.9, 51.7, 64.4, 109.6, 112.9, 118.4, 121.4, 123.5, 125.0, 125.1, 126.9, 129.5, 135.5, 137.1, 138.2, 146.0, 151.6, 165.0, 167.6; HRMS *m/z* calcd for $C_{27}H_{32}NO_4$ ($[M+H]^+$) 434.2326, found 434.2338.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-(4-chlorophenyl)-1*H*-indole-3-carboxylate (**3da**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); orange solid; 41 mg (50%); mp 134-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3H), 1.50 (sext, J = 7.5 Hz, 2H), 1.74 (quint, J = 6.8 Hz, 2H), 3.93 (s, 3H), 4.26 (t, J = 6.6 Hz, 2H), 6.42 (d, J = 15.8 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 7.40-7.50 (m, 3H), 7.53-7.59 (m, 3H), 8.08 (s, 1H), 9.27 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.4, 31.0, 51.8, 64.5,

110.4, 112.4, 118.7, 121.7, 123.9, 125.1, 126.7, 129.7, 130.3, 134.3, 136.6, 136.7, 138.0, 145.7, 164.8, 167.6; HRMS *m/z* calcd for $C_{23}H_{23}ClNO_4$ ([M+H]$^+$) 412.1310, found 412.1326.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-7-methyl-1-phenyl-1*H*-indole-3-carboxylate (**3ea**): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); white solid; 59 mg (74%); mp 244.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.4 Hz, 3H), 1.45-1.54 (m, 2H), 1.69-1.76 (m, 2H), 1.95 (s, 3H), 3.89 (s, 3H), 4.25 (t, *J* = 6.6 Hz, 2H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 7.37-7.39 (m, 2H), 7.46-7.51 (m, 4H), 7.93 (s, 1H), 9.26 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 19.2, 19.6, 30.8, 51.5, 64.1, 108.9, 117.2, 121.2, 124.2, 125.3, 126.4, 127.2, 127.8, 128.9, 129.0, 137.0, 139.0, 140.1, 145.9, 164.9, 167.6; HRMS *m/z* calcd for $C_{24}H_{26}NO_4$ ([M+H]$^+$) 392.1856, found 392.1831.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-6-chloro-1-phenyl-1*H*-indole-3-carboxylate (**3fa**): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); white solid; 55 mg (67%); mp 198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.4 Hz, 3H), 1.45-1.54 (m, 2H), 1.69-1.76 (m, 2H), 3.91 (s, 3H), 4.25 (t, *J* = 6.6 Hz, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 7.42-7.48 (m, 3H), 7.49-7.52 (m, 2H), 7.55-7.60 (m, 2H), 8.09 (s, 1H), 9.22 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 19.2, 30.8, 51.6, 64.4, 109.9, 112.2, 119.6, 121.5, 123.5, 125.3, 128.6, 129.6, 130.0, 130.5, 137.3, 137.5, 138.4, 144.4, 164.4, 167.1; HRMS *m/z* calcd for $C_{23}H_{23}ClNO_4$ ([M+H]$^+$) 412.1310, found 412.1343.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-5-methoxy-1-phenyl-1*H*-indole-3-carboxylate (**3ga**): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); colorless gum; 47 mg (56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.44-1.54 (m, 2H), 1.69-1.77 (m, 2H), 3.90 (s, 3H), 3.93 (s, 3H), 4.25 (t, *J* = 6.7 Hz, 2H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.98 (d, *J* = 9.1 Hz, 1H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.45-7.47 (m, 3H), 7.53-7.57 (m, 2H),

8.07 (s, 1H), 9.04 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 19.2, 30.9, 51.6, 56.6, 64.1, 109.4, 109.9, 112.7, 116.3, 121.3, 125.1, 127.0, 128.1, 129.9, 132.8, 137.3, 138.1, 141.0, 155.9, 165.1, 168.7; HRMS *m/z* calcd for $C_{24}H_{26}NO_5$ ($[M+H]^+$) 408.1805, found 408.1820.

Methyl (*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-benzo[*g*]indole-3-carboxylate (**3ha**): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); white solid; 65 mg (73%); mp 228.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.0 (t, *J* = 7.4 Hz, 3H), 1.47-1.56 (m, 2H), 1.72-1.79 (m, 2H), 3.93 (s, 3H), 4.28 (t, *J* = 6.6 Hz, 2H), 6.53 (d, *J* = 15.7 Hz, 1H), 7.16-7.22 (m, 2H), 7.37-7.40 (1m, 1H), 7.47-7.51 (m, 2H), 7.57-7.63 (m, 3H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.95 (s, 1H), 9.17 (dd, *J* = 0.6, 15.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 19.2, 30.9, 51.6, 64.3, 110.2, 118.5, 120.8, 121.8, 122.5, 123.0, 124.8, 126.2, 127.3, 128.5, 129.4, 129.4, 129.9, 131.2, 132.0, 136.7, 140.7, 146.3, 165.1, 167.4; HRMS *m/z* calcd for $C_{27}H_{26}NO_4$ ($[M+H]^+$) 428.1856, found 428.1864.

(*E*)-4-(3-Butoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-indole (3aa''): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); yellow solid; 69 mg (72%); mp 65-67 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.2 Hz, 3H), 1.47 (sext, *J* = 7.2Hz, 2H), 1.72 (quin, *J* = 6.6 Hz, 2H), 4.25 (t, *J* = 15.9 Hz, 2H), 6.65 (d, *J* = 15.9Hz, 1H), 6.97 (dd, *J* = 0.6, 3.3 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.39-7.58 (m, 8H), 8.13 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 19.0, 30.9, 64.4, 102.0, 112.6, 118.5, 120.6, 122.4, 124.7, 126.98, 127.01, 128.4, 129.3, 129.7, 136.5, 139.4, 143.1, 167.6; HRMS m/z calcd for $C_{21}H_{22}NO_2$ $[M+H]^+$ 320.16505, found 320.16447.

5,6-Diphenylindolo[1,2-*a*]quinoline (**5aa**):[3e] purified by column chromatography on silica gel (hexane/EtOAc = 20:1); yellow solid; 58 mg (78%); mp 196-199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (s, 1H), 7.10-7.28 (m, 10H), 7.35 (t, J = 8.2 Hz, 2H), 7.40-7.44 (m, 2H), 7.61 (t, J

= 7.2 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 8.52 (d, J = 8.5 Hz, 1H), 8.67 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.8, 114.5, 115.4, 121.4, 122.0, 122.1, 122.7, 125.5, 127.1, 127.3, 128.01, 128.04, 128.46, 128.47, 130.35, 130.39, 131.2, 131.3, 132.9, 133.4, 136.4, 137.5, 137.6, 137.7; HRMS *m/z* calcd for $C_{28}H_{20}N$ ($[M+H]^+$) 370.1590, found 370.1599.

5,6-Di(*p*-tolyl)indolo[1,2-*a*]quinoline (**5ab**):[3c] purified by column chromatography on silica gel (hexane/EtOAc = 20:1); green solid; 68 mg (86%); mp 219-220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.34 (s, 3H), 6.45 (s, 1H), 7.06-7.11 (m, 6H), 7.12-7.17 (m, 2H), 7.20 (ddd, *J* = 0.8, 7.2, 7.2 Hz, 1H), 7.35 (ddd, *J* = 0.8, 8.4, 8.4 Hz, 1H), 7.40-7.44 (m, 2H), 7.60 (ddd, *J* = 1.6, 7.2, 7.2 Hz, 1H), 7.75 (dd, *J* = 0.8, 8.0 Hz, 1H), 8.52 (dd, *J* = 0.8, 8.4 Hz, 1H), 8.66 (dd, *J* = 0.8, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 21.5, 98.7, 114.5, 115.4, 121.3, 121.9, 122.0, 122.6, 125.8, 125.9, 128.3, 128.5, 128.8, 130.2, 130.4, 131.0, 131.2, 132.8, 133.4, 134.5, 134.8, 136.4, 136.6, 136.8, 138.0; HRMS *m/z* calcd for $C_{30}H_{24}N$ ($[M+H]^+$) 398.1903, found 398.1904.

5,6-Bis(4-methoxyphenyl)indolo[1,2-*a*]quinoline (**5ac**):[3c] purified by column chromatography on silica gel (hexane/EtOAc = 20:1); green solid; 60 mg (70%); mp 264-267 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.809 (s, 3H), 3.811 (s, 3H), 6.47 (s, 1H), 6.80-6.84 (m, 4H), 7.10 (d, *J* = 6.8 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.35 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.42 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.46 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.61 (dd, *J* = 1.6, 7.6, 7.5 Hz, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.66 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.30, 55.31, 98.6, 113.5 (overlapped), 114.5, 115.4, 121.3, 121.9, 122.0, 122.7, 125.9, 128.3, 128.4, 129.8, 130.4, 131.0, 131.5, 132.3, 132.7, 133.4, 136.3, 138.1, 158.5, 158.6; HRMS *m/z* calcd for $C_{30}H_{24}NO_2$ ($[M+H]^+$) 430.1802, found 430.1801.

5,6-Bis(4-*tert*-butylphenyl)indolo[1,2-*a*]quinoline (**5ad**):[3e] purified by column chromatography on silica gel (hexane/EtOAc = 20:1); green solid; 67 mg (70%); mp 278-280 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 18H), 6.55 (s, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.22-7.25 (m, 5H), 7.35 (ddd, *J* = 0.8, 7.2, 7.2 Hz, 1H), 7.42 (ddd, *J* = 1.6, 7.2, 7.2 Hz, 1H), 7.53 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.61 (ddd, *J* = 1.6, 7.2, 7.2 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.67 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4 (overlapped), 34.6 (overlapped), 98.6, 114.5, 115.4, 121.3, 121.8, 121.9, 122.6, 124.6 (overlapped), 125.6, 128.2, 128.5, 130.0, 130.5, 130.9, 131.4, 133.1, 133.4, 134.5, 134.7, 136.4, 137.9, 149.8, 149.9; HRMS *m/z* calcd for $C_{36}H_{36}N$ ($[M+H]^+$) 482.2842, found 482.2847.

5,6-Bis(4-chlorophenyl)indolo[1,2-*a*]quinoline (**5ae**):[3e] purified by column chromatography on silica gel (hexane/EtOAc = 10:1); yellow solid; 66 mg (75%); mp 253-256 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 1H), 7.12 (ddd, *J* = 2.0, 2.0, 8.5 Hz, 2H), 7.17-7.25 (m, 3H), 7.27-7.31 (m, 4H), 7.34-7.40 (m, 2H), 7.45 (ddd, *J* = 1.4, 8.4, 8..4 Hz, 1H), 7.64 (ddd, *J* = 1.6, 8.6, 8.6 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.0, 114.5, 115.6, 121.5, 122.3, 122.4, 122.9, 124.9, 128.2, 128.58 (overlapped), 128.63, 128.9, 130.3, 130.4, 131.67, 131.70, 132.4, 133.4, 133.5, 135.7, 135.8, 136.4, 137.1; HRMS *m/z* calcd for $C_{28}H_{18}Cl_2N$ ($[M+H]^+$) 438.0811, found 438.0811.

5,6-Bis(4-bromophenyl)indolo[1,2-*a*]quinoline (**5af**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); yellow solid; 77 mg (73%); mp 242-344 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 1H), 7.05 (dd, *J* = 1.2, 8.4 Hz, 2H), 7.13 (dd, *J* = 1.2, 8.4 Hz, 2H), 7.23 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.42-7.47 (m, 5H), 7.64 (ddd, *J* = 1.6, 8.4 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 8.52 (d, *J* = 8.8 Hz, 1H), 8.67 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.1, 114.5, 115.6, 121.5, 121.6, 121.7, 122.2, 122.4,

122.9, 124.9, 128.2, 128.9, 130.3 (overlapped), 131.5, 131.6, 131.8, 132.0, 132.8, 133.5, 136.2, 136.3, 136.4, 137.0; HRMS *m/z* calcd for $C_{28}H_{18}Br_2N$ ($[M+H]^+$) 527.9787, found 527.9782.

5,6-Bis(4-(trifluoromethyl)phenyl)indolo[1,2-*a*]quinoline (**5ag**):[3c] purified by column chromatography on silica gel (hexane/EtOAc = 10:1); yellow solid; 57 mg (56%); mp 240-243 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (s, 1H), 7.25-7.33 (m, 4H), 7.38-7.41 (m, 3H), 7.48 (ddd, *J* = 2.0, 7.2, 7.2 Hz, 1H), 7.55-7.58 (m, 4H), 7.65-7.70 (m, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 8.54 (d, *J* = 8.4 Hz, 1H), 8.70 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.3, 114.5, 115.7, 121.6, 122.4, 122.7, 122.8, 124.1 (q, *J* = 272.0 Hz, overlapped), 124.6, 125.3 (q, *J* = 3.8 Hz), 125.4 (q, *J* = 3.8 Hz), 128.1, 129.2, 129.5 (q, *J* = 32.5 Hz), 129.7 (q, *J* = 32.5 Hz) 130.1, 130.2, 130.3, 130.4, 130.7, 131.5, 131.8, 133.5, 136.5, 136.6; HRMS *m/z* calcd for $C_{30}H_{18}F_6N$ ($[M+H]^+$) 506.1338, found 506.1337.

5,6-Bis(3,4-dimethoxyphenyl)indolo[1,2-*a*]quinoline (**5ah**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); green solid; 82 mg (84%); mp 204-207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 6H), 3.89 (s, 6H), 6.57 (s, 1H), 6.66-6.92 (m, 5H), 7.24 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.37 (ddd, *J* = 0.8, 8.0, 8.0 Hz, 1H), 7.43 (ddd, *J* = 1.2, 8.4, 8.4 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.62 (ddd, *J* = 1.6, 7.2 7.2 Hz, 1H), 7.78 (dd, *J* = 0.8, 8.0 Hz, 1H), 8.53 (dd, *J* = 0.8, 8.8 Hz, 1H), 8.67 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.89 (overlapped), 55.91 (overlapped), 98.7, 110.58, 100.64, 110.7, 114.5, 115.4, 121.3, 122.0, 122.1, 122.8, 123.5, 125.6, 125.9, 128.39, 128.42, 129.7, 130.1, 130.3, 130.4, 131.0, 132.6, 133.4, 136.3, 137.8, 148.0, 148.1, 148.5, 148.6; HRMS *m/z* calcd for $C_{32}H_{28}NO_4$ ($[M+H]^+$) 490.2013, found 490.2014.

5,6-Di(naphthalen-2-yl)indolo[1,2-*a*]quinolone (**5ai**): purified by column chromatography on silica gel (hexane/EtOAc = 20:1); yellow solid; 66 mg (70%); mp 205-208 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 6.47 (s, 1H), 7.18 (ddd, J = 0.8, 8.0, 8.0 Hz, 1H), 7.34-7.48 (m, 9H), 7.63-7.75 (m, 9H), 7.87 (s, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.72 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.0, 99.1, 114.5, 115.5, 121.4, 122.1 (overlapped), 122.8, 125.7, 126.0, 126.09, 126.11 (overlapped), 126.2, 127.73, 127.77 (overlapped), 127.81, 128.2, 128.6 (overlapped), 129.1, 130.4, 131.4, 132.4, 132.6, 133.0, 133.11, 133.13, 133.2, 132.49, 133.5, 135.0, 135.1, 136.5, 137.9; HRMS *m/z* calcd for $C_{36}H_{24}N$ ($[M+H]^+$) 470.1903, found 470.1903.

5,6-Di(thiophen-2-yl)indolo[1,2-*a*]quinoline (**5aj**): purified by column chromatography on silica gel (hexane/EtOAc = 20:1); yellow solid; 24 mg (32%); mp 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 7.01-7.05 (m, 2H), 7.06 (dd, J = 3.2, 4.8 Hz, 1H), 7.15 (dd, J = 1.2, 3.6 Hz, 1H), 7.25-7.29 (m, 1H), 7.34 (dd, J = 1.2, 5.2 Hz, 1H), 7.37-7.40 (m, 2H), 7.46 (ddd, J = 1.2, 8.4, 8.4 Hz, 1H), 7.62-7.66 (m, 2H), 7.82 (d, J = 7.2 Hz, 1H), 8.51 (d, J = 8.4 Hz, 1H), 8.65 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.9, 114.5, 115.4, 121.7, 122.2, 122.5, 123.0, 125.3, 125.9, 126.5, 126.6, 126.8, 126.9, 127.2, 128.6, 128.9, 129.1, 129.7, 129.96, 129.97, 130.3, 136.3, 137.85, 137.92; HRMS *m/z* calcd for $C_{24}H_{16}NS_2$ ($[M+H]^+$) 382.0719, found 382.0718.

3-Methyl-5,6-diphenylindolo[1,2-*a*]quinoline (**5ba**):[10] purified by column chromatography on silica gel (hexane/EtOAc = 40:1); green solid; 61 mg (79%); mp 194-196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 6.43 (s, 1H), 7.16-7.33 (m, 11H), 7.34 (ddd, J = 0.8, 7.2, 7.2 Hz, 1H), 7.40-7.44 (m, 2H), 7.76 (d, J = 8.0 Hz, 1H), 8.51 (d, J = 8.8 Hz, 1H), 8.57 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 98.5, 114.4, 115.3, 121.3, 121.8, 121.9, 125.4, 127.1, 127.2, 128.00, 128.02, 128.5, 129.4, 130.3, 130.4, 131.2, 131.3, 132.2, 132.9, 133.3, 134.4, 137.61, 137.63, 137.8; HRMS *m/z* calcd for $C_{29}H_{22}N$ ($[M+H]^+$) 384.1747, found 384.1748.

3-*tert*-Butyl-5,6-diphenylindolo[1,2-*a*]quinoline (**5ca**): purified by column chromatography on silica gel (hexane/EtOAc = 20:1); green solid; 71 mg (84%); mp 210-211 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 1.26 (s, 9H), 6.44 (s, 1H), 7.18-7.30 (m, 10H), 7.35 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.40-7.44 (m, 2H), 7.66 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.61 (*J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.6, 34.8, 98.6, 114.6, 115.3, 121.5, 122.0, 122.1, 125.2, 125.3, 126.0, 127.2, 127.4, 128.1, 128.2, 130.5, 130.6, 131.3, 131.4, 133.46, 133.51, 134.4, 137.7, 137.9, 138.0, 145.6; HRMS *m/z* calcd for $C_{32}H_{28}N$ ($[M+H]^+$) 426.2216, found 426.2214.

3-*tert*-Butyl-5,6-bis(4-*tert*-butylpheny)lindolo[1,2-*a*]quinolone (**5cd**): purified by column chromatography on silica gel (hexane/EtOAc = 20:1); green solid; 111 mg (87%); mp 248-249 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.275 (s, 9H), 1.282 (s, 9H), 1.291 (s, 9H), 6.52 (s, 1H), 7.07-7.15 (m, 5H), 7.22-7.34 (m, 3H), 7.34 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.41 (ddd, *J* = 1.2, 6.8, 6.8 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.65 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.60 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 31.4, 34.6, 98.2, 114.4, 115.0, 121.2, 121.5, 121.7, 124.5, 124.6, 125.0, 125.2, 125.6, 125.9, 129.7 130.0, 130.4, 130.9, 131.2, 133.3, 133.4, 134.2, 134.5, 134.9, 136.7, 137.9, 145.3, 149.7, 149.8; HRMS *m/z* calcd for $C_{40}H_{44}N$ ($[M+H]^+$) 538.3468, found 538.3474.

3-Chloro-5,6-diphenylindolo[1,2-*a*]quinoline (**5da**):[10] purified by column chromatography on silica gel (hexane/EtOAc = 40:1); green solid; 72 mg (89%); mp 279-280 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 1H), 7.15-7.18 (m, 2H), 7.21-7.31 (m, 8H), 7.35-7.39 (m 2H), 7.45 (ddd, *J* = 1.2, 8.4 8.4 Hz, 1H), 7.55 (dd, *J* = 2.8, 8.4 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 8.45 (d, *J* = 8.8 Hz, 1H), 8.59 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.5, 114.3, 116.6, 121.6, 122.3, 122.4, 127.2, 127.47, 127.50, 127.7, 128.07, 128.11, 128.2, 128.3, 130.2, 130.4, 131.1, 132.0, 132.5, 133.4, 134.9, 136.7, 137.3, 137.4; HRMS *m/z* calcd for $C_{28}H_{19}ClN$ ($[M+H]^+$) 404.1201, found 404.1201.

6,7-Diphenylbenzo[*g*]indolo[1,2-*a*]quinoline (**5ia**): purified by column chromatography on silica gel (hexane/EtOAc = 20:1); yellow solid; 59 mg (70%); mp 276-278 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 1H), 7.21-7.35 (m, 10H), 7.38 (d, J = 7.6 Hz, 1H), 7.42 (dd, J = 0.8, 8.0 Hz, 1H), 7.4-7.58 (m, 2H), 7.75 (t, J = 8.4 Hz, 2H), 7.81 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 8.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.1, 111.8, 114.3, 121.6, 122.1, 122.8, 125.1, 126.3, 127.1, 127.2, 127.3, 127.4, 127.8, 128.1, 128.2, 128.3, 129.4, 130.37, 130.38, 131.3, 131.6, 133.1, 133.2, 134.59, 134.62, 137.5, 137.56, 137.60; HRMS m/z calcd for $C_{32}H_{22}N$ ($[M+H]^+$) 420.1747, found 420.1745.

9-Butyl-6,7-bis(4-(*tert*-butyl)phenyl)-9*H*-benzo[2,3]indolizino[6,5-*b*]carbazole (**5jd**): purified by column chromatography on silica gel (hexane/EtOAc = 10:1); yellow solid; 40 mg (32%); mp 341-343 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, J = 7.3 Hz, 3H), 1.25-1.28 (m, 2H), 1.30 (s, 9H), 1.32 (s, 9H) 1.75 (quint. J = 6.9 Hz, 2H), 4.10-4.18 (m, 2H), 6.57 (s, 1H), 7.09-7.25 (m, 6H), 7.29-7.36 (m, 3H), 7.37-7.42 (m, 3H), 7.52 (m, 2H), 7.80 (d, J = 7.4 Hz, 1H), 8.34 (d, J= 7.7 Hz, 1H), 8.76 (d, J = 8.1 Hz, 1H), 9.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 20.4, 30.9, 31.5 (overlapped), 34.62, 34.65, 42.6, 98.5, 106.3, 107.6, 108.9, 114.2, 118.9, 120.9, 121.3, 121.5, 121.7, 122.7, 123.0, 124.65, 124.68, 125.3, 126.5, 130.1, 130.2, 130.4, 130.7, 131.0, 133.7, 133.8, 135.1, 135.2, 136.9, 137.8, 142.1, 149.79, 149.81; HRMS m/z calcd for $C_{46}H_{47}N_2$ ($[M+H]^+$) 627.3734, found 627.3742.

Ethyl (*E*)-3-(3-(*tert*-Butyl)-5,6-diphenylindolo[1,2-*a*]quinolin-8-yl)acrylate (**6a**): purified by GPC; yellow solid; 40 mg (36%); mp 153-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 9H), 1.33 (t, J = 7.1 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 6.58 (d, J = 16.0, 1H), 6.75 (s, 1H), 7.17-7.20 (m, 2H), 7.22-7.25 (m, 2H), 7.26-7.32 (m, 6H), 7.42 (dd, J = 8.1, 8.1 Hz, 1H), 7.45 (d, J = 2.3 Hz, 1H), 7.66-7.70 (m, 2H), 8.15 (d, J = 16.0 Hz, 1H), 8.56 (d, J = 8.6 Hz, 1H), 8.59 (d, J = 8.8 Hz,

1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 31.4 (overlapped), 34.6, 60.6, 96.5, 115.2, 116.0, 118.2, 120.5, 121.6, 125.2, 126.1, 126.6, 127.2, 127.5, 128.0 (overlapped), 128.3, 130.1, 130.3 (overlapped), 131.0, 131.1, 134.0, 134.4, 137.3, 137.4, 142.6, 145.9, 167.6; HRMS *m/z* calcd for $C_{37}H_{34}NO_2$ ([M+H]$^+$) 524.2584, found 524.2603.

Ethyl (*E*)-5,6-bis(4-(*tert*-butyl)phenyl)indolo[1,2-*a*]quinolin-8-yl)acrylate (**6b**): purified by column chromatography on silica gel (hexane/EtOAc = 19:1); yellow solid; 13 mg (11%); mp 268-270 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 9H), 1.23 (s, 9H), 1.26 (t, *J* = 7.2 Hz, 3H), 4.19 (q, *J* = 7.2 Hz, 2H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.54 (s, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 7.16-7.19 (m, 5H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.47-7.61 (m, 3H), 8.11 (d, *J* = 16.0 Hz, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 8.56 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 31.3 (overlapped), 34.5 (overlapped), 60.4, 96.5, 115.4, 116.0, 118.0, 120.3, 121.5, 123.0, 124.5, 124.8, 125.6, 126.5, 128.4, 128.6, 129.8, 130.2, 130.7, 131.2, 134.0, 134.1 (overlapped), 134.2, 135.9, 138.8, 142.5, 149.8, 150.0, 167.5; HRMS *m/z* calcd for $C_{41}H_{42}NO_2$ [M+H]$^+$ 580.32155, found 580.32183.

ASSOCIATED CONTENT

Supporting Information. Results for additional experiments, ^{1}H and ^{13}C NMR spectra of products, 24 intermediates of the acrylonitrile insertion with the activation free energy and the reaction free energy in the DFT calculations (Figure S1), and atomic coordinates of all calculated molecules (XYZ file). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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