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Synthesis of 1*H*-Indole-2,3-dicarboxylates via Rhodium-catalyzed C−H Annulation of Arylhydrazines with Maleates

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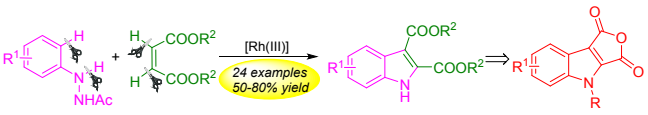


ABSTRACT: This work describes the one-step synthesis of 1*H*-indole-2,3-dicarboxylates through C−H activation. The rhodium-catalyzed tandem C−H activation and annulation of 2-acetyl-1-phenylhydrazines with maleates proceeded smoothly in the presence of additive NaOAc and oxidant Ag_2CO_3 and produced the corresponding indole derivatives, 1*H*-indole-2,3-dicarboxylates, in satisfactory to good

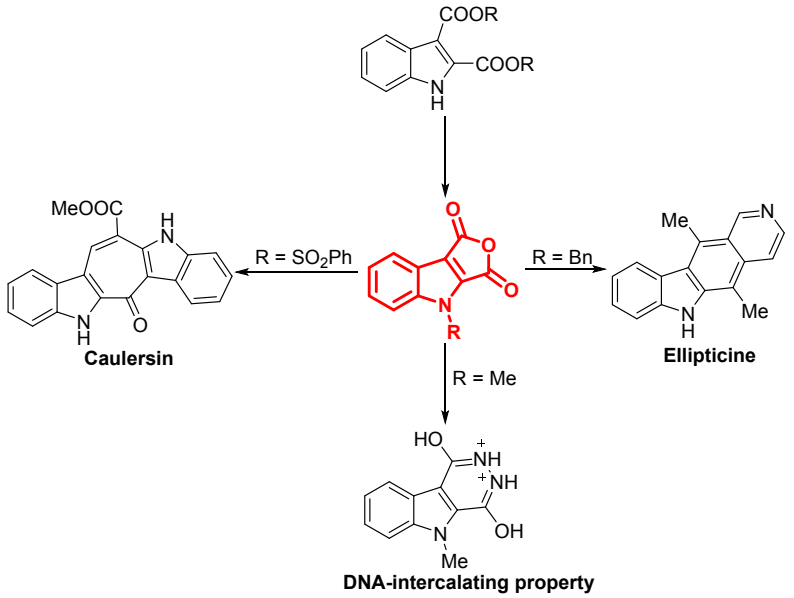
yields. A variety of useful functional groups are tolerated on benzene ring including halogen atoms (F, Cl, Br, and I) and methoxycarbonyl groups.

INTRODUCTION

Furo[3,4-*b*]indole-1,3(4*H*)-dione units are important synthons for the synthesis of numerous commercial drugs and natural bioactive products[1] and are generally synthesized from 1*H*-indole-2,3-dicarboxylates (Scheme 1).[2] Intermediate 1*H*-indole-2,3-dicarboxylates can be obtain from the palladium-catalyzed annulation of aniline derivatives with esters of acetylenedicarboxylic acids via multiple-step procedure (Scheme 2a).[3] The transition metal-catalyzed direct functionalization of C−H bond is more economical and effective than traditional molecule transformation. Therefore, it is highly desirable to develop a method involving the direct C−H bond activation for the synthesis of 1*H*-indole-2,3-dicarboxylates with wide substrate scope, mild reaction conditions, and high atomic economy.[4] The cleavage strategy of transition metal-catalyzed aromatic C−H bonds usually requires a suitable directing group linked on the aromatic substrate,[5] such as the hydrazine group for indole synthesis.[6-9] Maleimides,[6] diaryl acetylenes,[7,8] and diazoketoesters[9] were successfully used as partners in the rhodium (Rh)-catalyzed annulation of arylhydrazines[10]. The Rh-catalyzed intramolecular annulation of hydrazine-tethered alkynes was also reported for indole synthesis.[11] To our knowledge, a few of precedents of the direct annulation of arylhydrazines with olefin partners for synthesis of indoles has been reported. Herein, Rh-catalyzed C−H activation

and annulation of arylhydrazines with maleates were conducted to obtain 1*H*-indole-2,3-dicarboxylates that can be easily transformed into furo[3,4-*b*]indole-1,3(4*H*)-diones (Scheme 2b).[12]

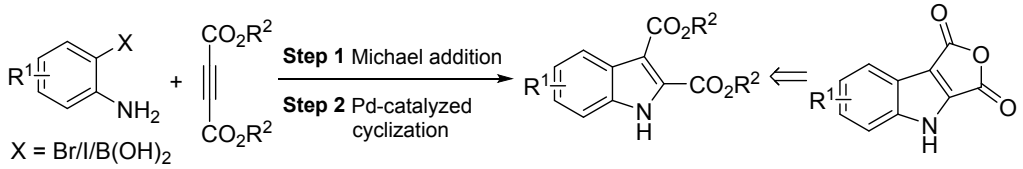
Scheme 1. Representative Synthetic Applications of Furo[3,4-*b*]indole-1,3(4*H*)-diones.



Scheme 2. Synthetic Strategies to Access 1*H*-Indole-2,3-dicarboxylates.

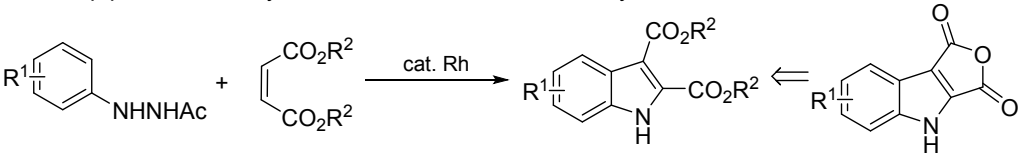
Previous work:

a) Multiple-step procedure for synthesis of 1*H*-indole-2,3-dicarboxylates



This work:

b) One-step procedure for synthesis of 1*H*-indole-2,3-dicarboxylates via C-H bond activation

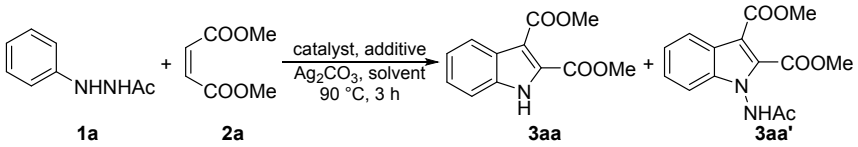


RESULTS AND DISCUSSION

Encouraged by our success on indole synthesis using arylhydrazines and maleimides as substrates,[6] we initially examined the annulation reaction using 2-acetyl-1-phenylhydrazine (**1a**) and maleic anhydride as starting materials in the presence of a Rh catalyst. However, no product was obtained, and the starting materials were recovered. **1a** was then reacted with dimethyl maleate (**2a**) in the presence of a Rh catalyst and generated the desired product, dimethyl 1*H*-indole-2,3-dicarboxylate (**3aa**). Therefore, the reaction of **1a** and **2a** was chosen as a model to optimize the reaction conditions, and the results are summarized in Table 1. The catalysts were first checked using Ag_2CO_3 as oxidant in 1,2-dichloroethane (DCE) at 90 °C under nitrogen atmosphere (entries 1−5). A cationic Rh catalyst favors the C−H activation of arylhydrazines.[6] Combination of $[Cp^*RhCl_2]_2$ and $AgSbF_6$, $[Cp^*Co(CO)I_2]$ and $AgSbF_6$ or $[RuCl_2(p\text{-cymene})]_2$ and $AgSbF_6$ was employed. The desired **3aa** was obtained in 59% yield when $[Cp^*Rh(MeCN)_3](SbF_6)_2$ was used as the catalyst (entry 2). Other different solvents, namely, toluene, methanol (MeOH), acetonitrile (MeCN), and 1,4-dioxane were subsequently screened using $[Cp^*Rh(MeCN)_3](SbF_6)_2$ as the catalyst. DCE was found to be the best solvent (entry 2 vs. entries 1 and 6–9). The reason may be that the starting materials have better solubility in DCE. And **3aa** yield was finally increased to 78% by introducing a base, namely, sodium acetate (NaOAc) (entry 10). Product **3aa** was not formed in the absence of $[Cp^*Rh(MeCN)_3](SbF_6)_2$, although substrate **1a** completely

disappeared (entry 11). Therefore, the subsequent annulations of various 2-acetyl-1-arylhydrazines with maleates were carried out using $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (5 mol%), NaOAc (25 mol%), and Ag_2CO_3 (2.0 eq.) in DCE at 90 °C under nitrogen atmosphere for 3 h.

Table 1. Reaction Condition Screening[a]



1a **2a** **3aa** **3aa'**

entry	catalyst	additive	solvent	yield (%) **3aa**/**3aa′**
1	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	44/23
2	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	DCE	59/15
3	$[Cp^*Co(CO)I_2]$	$AgSbF_6$	DCE	NR[b]
4	$[Cp^*Co(MeCN)_3](SbF_6)_2$	None	DCE	NR[b]
5	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	DCE	NR[b]
6	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	Toluene	NR[b]
7	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	MeOH	NR[b]
8	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	CH_3CN	NR[b]
9	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	Dioxane	NR[b]
10[c]	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	None	DCE	78/trace
11[c]	none	None	DCE	NR[b,d]

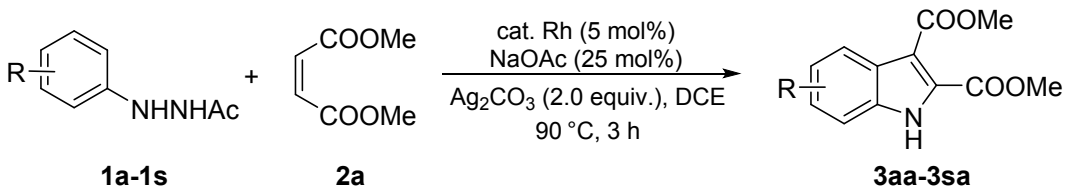
[a]Reaction conditions: *N*-phenylacetohydrazide (**1a**, 0.2 mmol, 30.0 mg), dimethyl maleate (**2a**, 0.4 mmol, 57.7 mg), catalyst (5 mol%), $AgSbF_6$ (10 mol%), and Ag_2CO_3 (2 equiv.) in solvent (1.0 mL) at 90 °C under a nitrogen atmosphere for 3 h. [b]No reaction was observed; the starting material **2a** was recovered. [c]25 mol% of NaOAc was used. [d]The substrate **1a** was decomposed.

The Rh-catalyzed annulation reactions of 2-acetyl-1-arylhydrazines **1a**–**1s** with dimethyl maleate (**2a**) were conducted under optimized conditions. The results are summarized in Scheme 3. When 2-acetyl-1-arylhydrazines **1b**–**1d** bearing a methyl (Me) group on the *para*-, *meta*-, or *ortho*-position were tested in the reaction of **2a**, 80%, 72%,

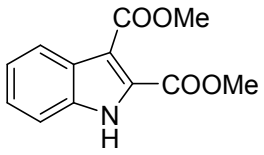
and 66% yields of dimethyl 1*H*-indole-2,3-dicarboxylate products **3ba**–**3da** were obtained, respectively. The structure of **3da** was confirmed by X-ray crystallography. The result from two Me groups substituted substrate **1e** was similar with mono-substituted one, product **3ea** was obtained in 71% yield. Other electron-donating groups were also investigated under optimized reaction conditions. The reactions of 2-acetyl-1-arylhydrazine substrates **1f**–**1i** with methoxy (MeO), *normal*-butyl (^{n}Bu), *tert*-butyl (^{t}Bu), and phenyl (Ph) group on the *para*-positions of benzene rings proceeded smoothly to produce the desired products **3fa**–**3ia** in good yields (71%–80%). Similar to that of **1d,** this transformation was affected by steric hindrance, substrate **1i** bearing a Ph group on the *ortho*-position gave the product **3ja** in only 54% yield. Halogen-substituted 2-acetyl-1-arylhydrazine **1k**–**1p** were demonstrated to be suitable substrates in this reaction, no matter which kind of halogen atom (F, Cl, Br, or I) linked to the benzene ring, the reactions proceeded smoothly to furnish halogenated products **3ka**−**3pa** in satisfactory yields (69%−76%). We believed further manipulation based on the C−X bond may produce useful compounds. The desired products **3qa** and **3ra** were also obtained in relatively low yields (53 and 50%, respectively) when substrates **1q** and **1r** bearing a strong electron-withdrawing group (methoxycarbonyl (COOMe) or trifluoromethyl (CF_3)) on the *para*-positions of benzene rings. These results are consistent with literature,[13] which suggested that the benzene ring with lower electron density is not conducive to C−H activation. The substrate *N*'-(naphthalen-1-yl)acetohydrazide (**1s**) was finally examined, and the expected product

3sa was obtained in 67% yield.

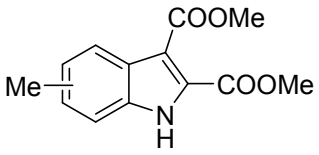
Scheme 3. Rh-Catalyzed Annulation of Various 2-Acetyl-1-arylhydrazines with Dimethyl Maleate[a,b]



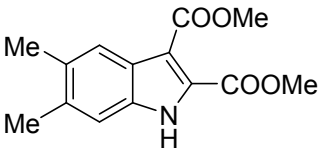
1a-1s **2a** **3aa-3sa**



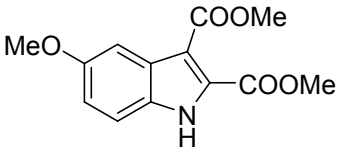
3aa, 78%



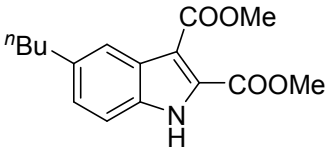
3ba, *o*-Me, 80%
3ca, *m*-Me, 72%
3da, *p*-Me, 66%



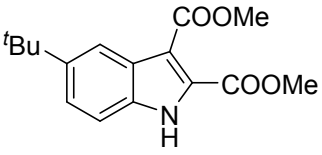
3ea, 71%



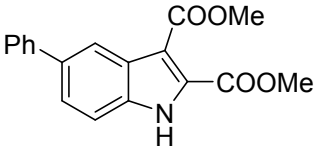
3fa, 80%



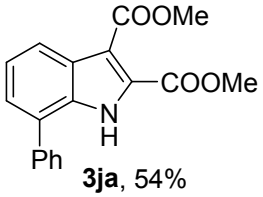
3ga, 75%



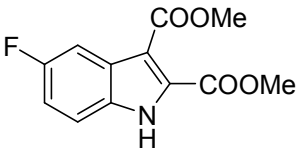
3ha, 76%



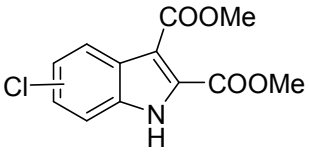
3ia, 71%



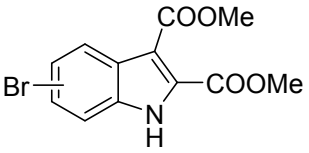
3ja, 54%



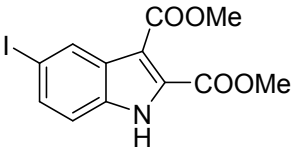
3ka, 76%



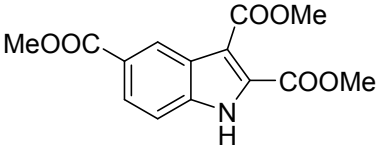
3la, *p*-Cl, 73%
3ma, *m*-Cl, 69%



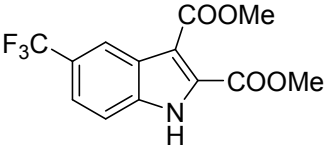
3na, *p*-Br, 75%
3oa, *m*-Br, 69%



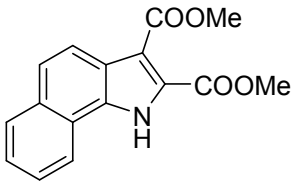
3pa, 73%



3qa, 53%



3ra, 50%



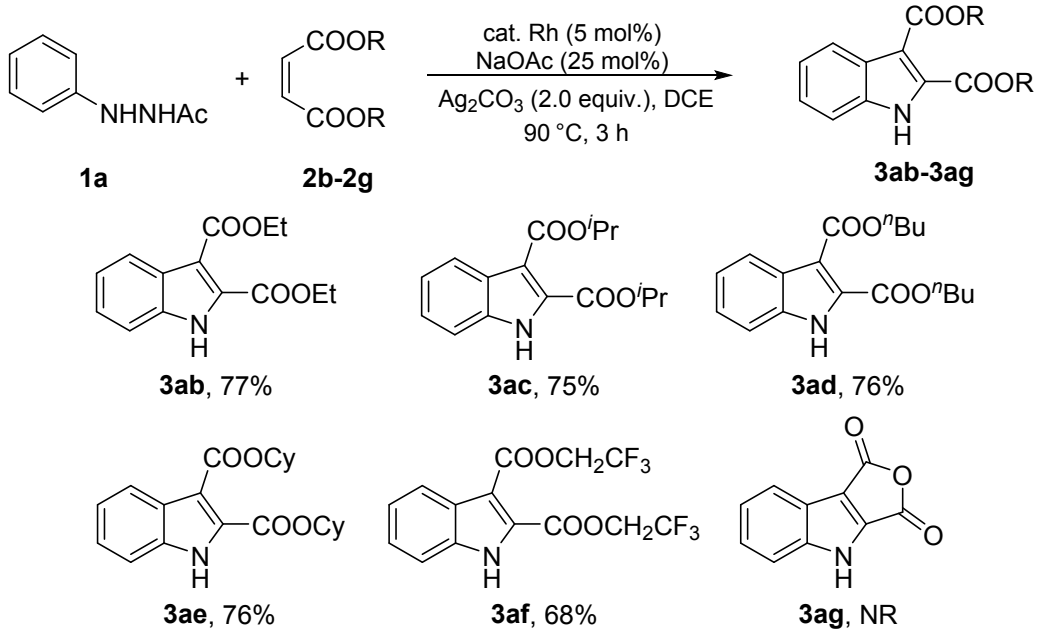
3sa, 67%

[a]Reaction conditions: arylhydrazines (**1a-1s**, 0.2 mmol), dimethyl maleate (**2a**, 0.4 mmol, 57.7 mg), $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (5 mol%, 8.3 mg), Ag_2CO_3 (0.4 mmol, 110.2 mg), NaOAc (25 mol%, 4.1 mg) in DCE (1.0 mL) at 90 °C under a nitrogen atmosphere for 3 h.

Scheme 4 shows the results obtained from the reactions of **1a** with various maleates. The maleates **2b**–**2f** coupled with **1a** generated the corresponding indoles **3ab**–**3af** in

satisfactory yields (68%–77%). Unfortunately, no reaction was observed when the mixture of **1a** and **2g** was treated under the established reaction conditions.

Scheme 4. Rh-Catalyzed Annulation of 2-Acetyl-1-phenylhydrazine with Various Maleates[a,b]

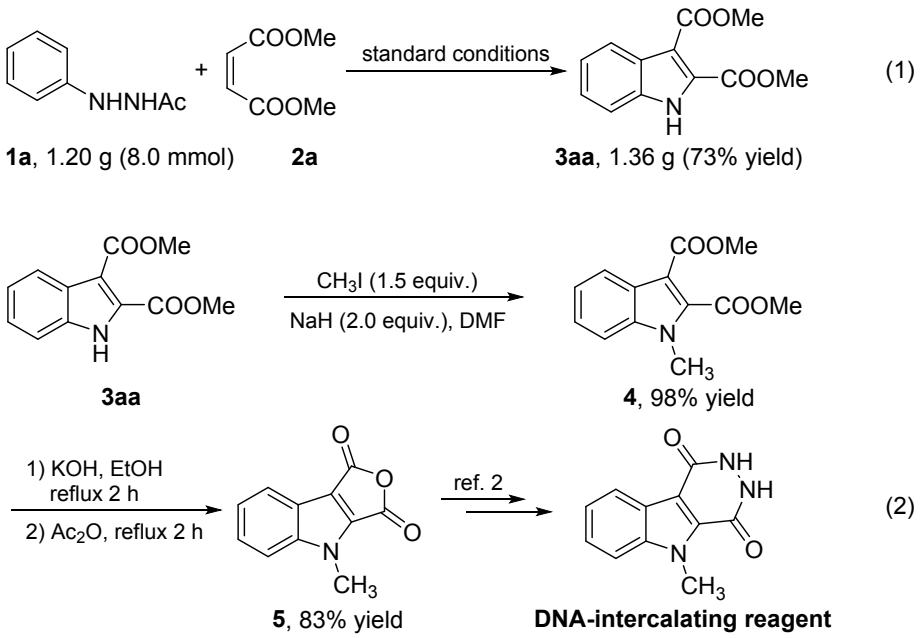


[a]Reaction conditions: 2-acetyl-1-phenylhydrazine (**1a**, 0.2 mmol, 30 mmg), maleate (**2b-2g**, 0.4 mmol), $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (5 mol%, 8.3 mg), Ag_2CO_3 (0.4 mmol, 110.2 mg), NaOAc (25 mol%, 4.1 mg) in DCE (1.0 mL) at 90 °C under a nitrogen atmosphere for 3 h.

To demonstrate the practicality of this new methodology, gram-scale synthesis of **3aa** was carried out under the standard conditions (Scheme 5, Eq. 1). Approximately 1.36 g of **3aa** was obtained with 73% yield when the reaction was performed on an 8.0 mmol scale. This result indicated that the scale-up reactions also proceeded smoothly without loss of efficiency. The product **3aa** was easily converted into product **5**[12] through *N*-methylation,

ester hydrolysis, and acid dehydration. The product **5** has been utilized as a key intermediate for the construction of DNA-intercalating reagents (Scheme 5, Eq. 2).[2]

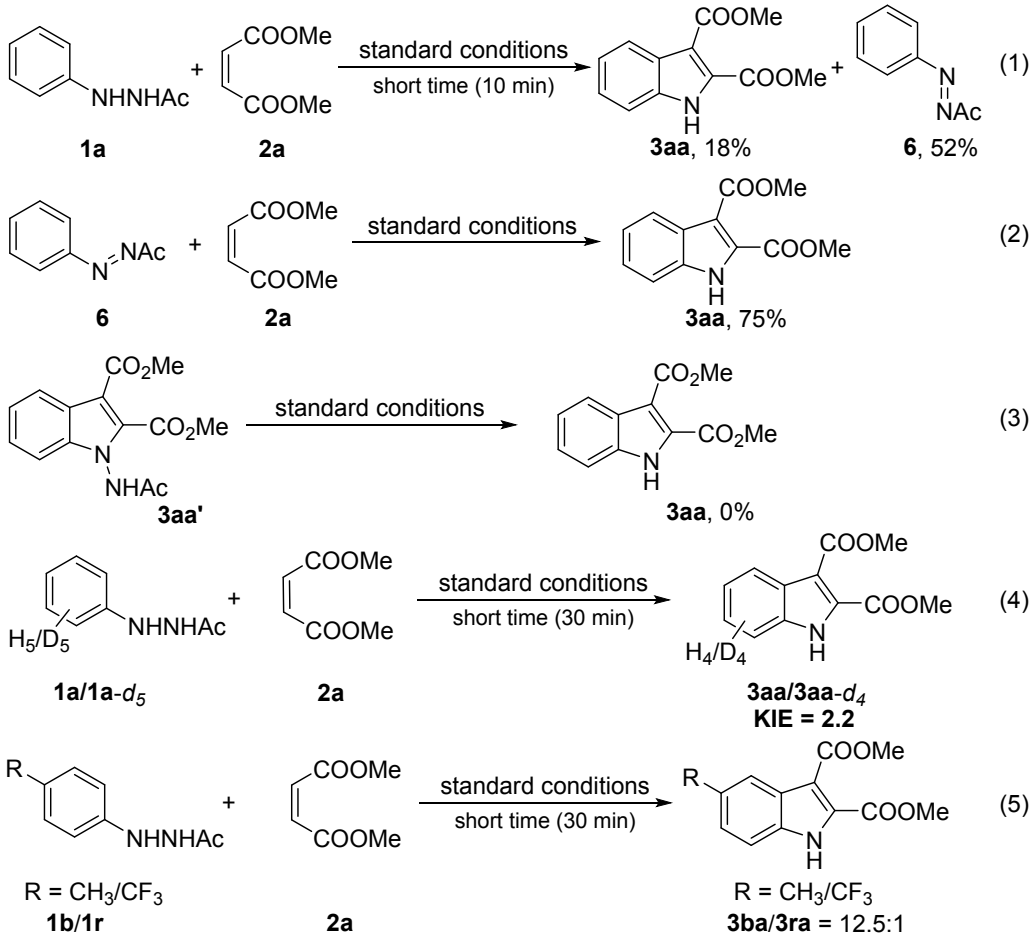
Scheme 5. Gram-scale Synthesis and Derivatization of **3aa**



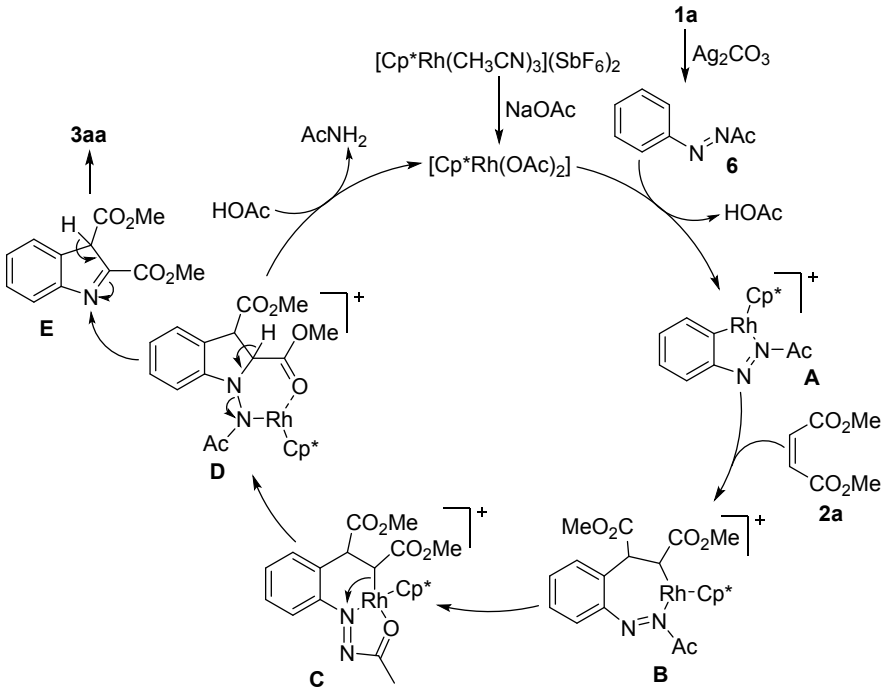
A series of experiments were conducted to probe the reaction mechanism (Scheme 6). The major product 2-phenyl-1-acetyldiazene (**6**) was formed under the standard conditions in a short time. This indicates that 2-acetyl-1-phenylhydrazine can easily be transformed into intermediate **6** in situ in the presence of an oxidant (Eq. 1). The product **3aa** was obtained in 75% yield when **6** reacted with **2a** under standard conditions (Eq. 2). By-product **3aa′** could not be converted to **3aa** under the standard conditions and therefore is not the intermediate for **3aa** generation (Eq. 3). The kinetic isotope effect

determined from an intermolecular competition by reacting 1:1 mixture of **1a** and **1a-**d_5 (KIE value of approximately 2.2) suggested that the cleavage of the aromatic C−H bond was the rate-determining step (Eq. 4). A 12.5:1 ratio of **3ba** to **3ra** was observed in the intermolecular competition between **1b** and **1r** (Eq. 5), indicating that the reaction proceeds through electrophilic C−H bond activation.

Scheme 6. Control Experiments.



Scheme 7. Proposed Mechanism



Scheme 7 shows a plausible mechanism for this indole synthesis on the basis of previous reports[8] and current experimental outcomes. First, the cationic Rh catalyst species $[Cp^*Rh(OAc)_2]$ is formed through the reaction of the precatalyst $[Cp^*Rh(MeCN)_3](SbF_6)_2$ with the base NaOAc. **1a** is oxidized by Ag_2CO_3 to give 2-phenyl-1-acetyldiazene (**6**) in situ. Cationic five-membered rhodacyclic intermediate **A** is formed through the coordination of **6** to rhodium and the subsequent *ortho* C−H bond activation processes. The insertion of the olefin moiety in **2a** to C−Rh bond then produces intermediate **B**, followed by rearrangement to generate more stable six-membered coordinately saturated Rh species **C**, thereby *β*–hydride elimination reaction does not take place. Instead, intramolecular nucleophilic addition occurs to produce intermediate **D**, which undergoes N−N bond cleavage to generate intermediate **E** and regenerate catalytic species $[Cp^*Rh(OAc)_2]$. Finally, **E** transpires aromatization to give *N*-free indole **3aa**.[14]

In summary, a convenient and efficient method for synthesis of 1*H*-indole-2,3-dicarboxylates has been developed. As far as we know, the first successful example of rhodium-catalyzed C−H annulation of arylhydrazines with maleates to obtain 1*H*-indole-2,3-dicarboxylates is reported in this paper. In addition, this method can tolerate diverse functional groups and can be applied to obtain a rather wide range of indole.

EXPERIMENTAL SECTION

General Information.

Solvents were purified by standard techniques without special instructions. ^{1}H and ^{13}C NMR spectra were recorded on a 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C); DMSO-d_6 was used as a solvent. The chemical shifts are reported in ppm (δ), and the coupling constants J are given in Hz. The peak patterns are indicated as follows: s, singlet; d, doublet; m, multiplet. IR spectra were recorded on a FT-IR spectrometer. High resolution mass spectra were recorded on a GC-TOF mass spectrometer. TLC was carried out on SiO_2, and the spots were located with UV light.

The starting materials **1a**–**1q**, **2b**, **2c**, **2e**, and **2f** were synthesized according the literatures.[7,15]

General Procedure for the Rh-Catalyzed Annulation Reaction

A reaction flask was charged with a mixture of *N*-arylacetohydrazide (**1**, 0.2 mmol),

maleate (0.4 mmol, 2.0 equiv.), $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (8.3 mg, 0.01 mmol, 5 mol%), NaOAc (4.1 mg, 0.05 mmol, 25 mol%), Ag_2CO_3 (110.2 mg, 0.4 mmol, 2.0 equiv.), and DCE (1.0 mL). The reaction mixture was stirred at 90 °C by IKA plate for 3 h under N_2 atmosphere, and then was cooled to room temperature. The solvent was removed under reduced pressure, and the residue obtained was purified via silica gel chromatography (eluent: petroleum ether/ethyl acetate = 4:1) to give product **3**.

Dimethyl 1*H*-indole-2,3-dicarboxylate (**3aa**): White solid (36.4 mg, 78% yield), mp 122−124 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.52 (s, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.38−7.35 (m, 1H), 7.28−7.25 (m, 1H), 3.99 (s, 3H), 3.97 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.7, 161.5, 134.9, 128.1, 126.8, 125.9, 122.8, 122.6, 112.0, 111.9, 52.7, 51.9; IR (KBr): 3311, 2951, 2919, 1704, 1537, 1442, 1332, 1252, 1221, 1072, 770, 750 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{11}NO_4$: 233.0688 $[M]^+$; found: 233.0695.

Dimethyl 5-methyl-1*H*-indole-2,3-dicarboxylate (**3ba**): White solid (39.6 mg, 80% yield), mp 136−138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.47 (s, 1H), 7.83 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 3.99 (s, 3H), 3.96 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.8, 161.5, 133.3, 132.2, 128.0, 127.9, 127.1, 121.9, 111.6, 111.3, 52.6, 51.8, 21.6; IR (KBr): 3298, 2948, 2920, 1691, 1532, 1439, 1343, 1254, 1152, 1065, 801, 776 (cm^{-1}); HRMS (EI) calcd for $C_{13}H_{13}NO_4$: 247.0845 $[M]^+$; found: 247.0850.

Dimethyl 6-methyl-1*H*-indole-2,3-dicarboxylate (**3ca**): White solid (35.6 mg, 72% yield), mp 129−131 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.35 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.20 (s, 1H), 7.10 (s, 1H), 3.98 (s, 3H), 3.96 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR

($CDCl_3$, 100 MHz) δ 164.7, 161.5, 136.3, 135.3, 127.4, 124.8, 124.7, 122.4, 111.9, 111.5, 52.6, 51.8, 21.9; IR (KBr): 3304, 2947, 2919, 1730, 1682, 1532, 1447, 1327, 1257, 1072, 810, 784 (cm^{-1}); HRMS (EI) calcd for $C_{13}H_{13}NO_4$: 247.0845 $[M]^+$; found: 247.0851.

Dimethyl 7-methyl-1*H*-indole-2,3-dicarboxylate (**3da**): White solid (32.6 mg, 66% yield), mp 132−134 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.54 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.19−7.14 (m, 2H), 3.98 (s, 3H), 3.95 (s, 3H), 2.52 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.8, 161.8, 134.7, 127.9, 126.5, 126.1, 122.8, 121.4, 120.2, 112.3, 52.7, 51.9, 16.6; IR (KBr): 3261, 2953, 1744, 1699, 1545, 1446, 1374, 1260, 1162, 1099, 964, 752 (cm^{-1}); HRMS (EI) calcd for $C_{13}H_{13}NO_4$: 247.0845 $[M]^+$; found: 247.0854.

Dimethyl 5,6-dimethyl-1*H*-indole-2,3-dicarboxylate (**3ea**): White solid (36.8 mg, 71% yield), mp 153−155 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.26 (s, 1H), 7.79 (s, 1H), 7.18 (s, 1H), 3.98 (s, 3H), 3.96 (s, 3H), 2.36 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.9, 161.5, 135.9, 133.9, 132.0, 127.1, 125.4, 122.2, 111.9, 111.4, 52.6, 51.8, 20.7, 20.3; IR (KBr): 3310, 2917, 2849, 1726, 1686, 1528, 1445, 1276, 1198, 1064, 782, 767 (cm^{-1}); HRMS (EI) calcd for $C_{14}H_{15}NO_4$: 261.1001 $[M]^+$; found: 261.1011.

Dimethyl 5-methoxy-1*H*-indole-2,3-dicarboxylate (**3fa**): White solid (42.1 mg, 80% yield), mp 176−178 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.54 (s, 1H), 7.47 (s, 1H), 7.33 (d, J = 12.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 3.98 (s, 3H), 3.95 (s, 3H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.9, 161.4, 156.1, 130.1, 128.2, 127.7, 117.8, 113.0, 111.1, 102.5, 55.7, 52., 51.8; IR (KBr): 3287, 2943, 2922, 1721, 1688, 1525, 1463, 1260, 1162, 972, 841, 819 (cm^{-1}); HRMS (EI) calcd for $C_{13}H_{13}NO_5$: 263.0794 $[M]^+$; found: 263.0803.

Dimethyl 5-butyl-1*H*-indole-2,3-dicarboxylate (**3ga**): White solid (43.4 mg, 75% yield), mp 84−85 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.53 (s, 1H), 7.83 (s, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.72 (t, J = 8.0 Hz, 2H), 1.68−1.60 (m, 2H), 1.40−1.35 (m, 2H), 0.93 (t, J = 8.0 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.9, 161.6, 137.4, 133.5, 128.0, 127.3, 127.1, 121.3, 111.7, 111.4, 52.7, 51.8, 35.9, 34.2, 22.4, 14.0; IR (KBr): 3315, 2954, 2859, 1708, 1357, 1459, 1343, 1249, 1099, 1063, 811, 774 (cm^{-1}); HRMS (EI) calcd for $C_{16}H_{19}NO_4$: 289.1314 [M]$^+$; found: 289.1325.

Dimethyl 5-(*tert*-butyl)-1H-indole-2,3-dicarboxylate (**3ha**): White solid (44.0 mg, 76% yield), mp 145−146 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.47 (s, 1H), 8.02 (s, 1H), 7.47 (d, J = 10.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 4.00 (s, 3H), 3.96 (s, 3H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 165.0, 161.5, 145.7, 133.2, 127.9, 126.8, 124.8, 117.9, 111.9, 111.5, 52.6, 51.8, 34.9, 31.6; IR (KBr): 3318, 2954, 2928, 1707, 1536, 1440, 1343, 1249, 1154, 1065, 810, 774 (cm^{-1}); HRMS (EI) calcd for $C_{16}H_{19}NO_4$: 289.1314 [M]$^+$; found: 289.1320.

Dimethyl 5-phenyl-1*H*-indole-2,3-dicarboxylate (**3ia**): Yellow solid (43.9 mg, 71% yield), mp 118−120 °C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.70 (s, 1H), 8.13 (s, 1H), 7.68−7.59 (m, 4H), 7.49−7.47 (m, 2H), 7.37−7.33 (m, 1H), 3.93 (s, 3H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 164.5, 161.8, 141.4, 135.3, 135.2, 130.9, 129.4, 127.4, 126.7, 125.0, 119.6, 113.9, 109.9, 53.1, 52.0; IR (KBr): 3312, 2951, 2924, 1706, 1537, 1459, 1375, 1345, 1251, 1165, 1072, 761 (cm^{-1}); HRMS (EI) calcd for $C_{18}H_{15}NO_4$: 309.1001 [M]$^+$; found: 309.1012.

Dimethyl 7-phenyl-1*H*-indole-2,3-dicarboxylate (**3ja**): Yellow solid (33.4 mg, 54% yield), mp 111−113 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.31 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.60−7.58 (m, 2H), 7.56−7.52 (m, 2H), 7.47−7.43 (m, 1H), 7.37−7.33 (m, 2H), 4.01 (s, 3H), 3.97 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.5, 161.3, 137.7, 132.9, 129.5, 128.3, 128.2, 128.1, 127.3, 126.6, 125.6, 123.1, 121.9, 112.4, 52.8, 51.9; IR (KBr): 3296, 2952, 2923, 1705, 1452, 1448, 1241, 1120, 1068, 809, 759, 702 (cm^{-1}); HRMS (EI) calcd for $C_{18}H_{15}NO_4$: 309.1001 $[M]^+$; found: 309.1006.

Dimethyl 5-fluoro-1*H*-indole-2,3-dicarboxylate (**3ka**): Yellow solid (38.2 mg, 76% yield), mp 156−158 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.56 (s, 1H), 7.73 (dd, J = 4.0, 8.0 Hz, 1H), 7.37 (dd, J = 4.0, 8.0 Hz, 1H), 7.15−7.10 (m, 1H), 3.98 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.2, 161.2, 159.3 (d, J = 238.0 Hz), 131.3, 129.8, 127.4 (d, J = 11.0 Hz), 115.4, 115.1, 113.1 (d, J = 10.0 Hz), 111.7 (d, J = 5.0 Hz), 107.7, 107.5, 52.9, 51.9; IR (KBr): 3279, 2923, 1772, 1719, 1487, 1399, 1196, 1134, 1076, 1046, 743, 621 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}FNO_4$: 251.0594 $[M]^+$; found: 251.0603.

Dimethyl 5-chloro-1*H*-indole-2,3-dicarboxylate (**3la**): Yellow solid (39.1 mg, 73% yield), mp 187−189 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.54 (s, 1H), 8.05 (d, J = 4.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.31 (dd, J = 4.0, 8.0 Hz, 1H), 3.99 (s, 3H), 3.98 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 164.0, 161.1, 133.1, 129.4, 128.6, 127.7, 126.6, 122.2, 113.1, 111.3, 52.9, 52.0; IR (KBr): 3330, 2951, 2922, 1683, 1530, 1449, 1348, 1219, 1086, 946, 869, 767 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}ClNO_4$: 267.0298 $[M]^+$; found: 267.0308.

Dimethyl 6-chloro-1*H*-indole-2,3-dicarboxylate (**3ma**): Yellow solid (36.9 mg, 69% yield), mp 228−230 °C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.75 (s, 1H), 7.91 (s, 1H),

7.54 (d, J = 2.0 Hz, 1H), 7.25 (dd, J = 4.0, 8.0 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 164.1, 161.5, 136.0, 131.2, 130.0, 124.9, 123.5, 123.2, 112.8, 109.7, 53.2, 52.1; IR (KBr): 3308, 2952, 2917, 1735, 1681, 1530, 1448, 1250, 1133, 1058, 811, 785 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}ClNO_4$: 267.0298 $[M]^+$; found: 267.0309.

Dimethyl 5-bromo-1*H*-indole-2,3-dicarboxylate (**3na**): Yellow solid (46.8 mg, 75% yield), mp 202−204 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.40 (s, 1H), 8.22 (d, J = 4.0 Hz, 1H), 7.46 (dd, J = 4.0, 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 3.99 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.0, 161.0, 133.3, 129.1, 128.3, 125.4, 116.2, 113.4, 111.2, 52.9, 52.0; IR (KBr): 3300, 2952, 2922, 1705, 1537, 1445, 1338, 1215, 1167, 10786, 803, 768 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}BrNO_4$: 310.9793 and 312.9773 $[M]^+$; found: 310.9790 and 312.9778.

Dimethyl 6-bromo-1*H*-indole-2,3-dicarboxylate (**3oa**): Yellow solid (43.1 mg, 69% yield), mp 232−234 °C. ^1H NMR (DMSO-d_6, 400 MHz) δ 12.75 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.69 (s, 1H), 7.37 (d, J = 12.0 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 164.1, 161.5, 136.4, 131.0, 125.7, 125.1, 123.8, 118.1, 115.8, 109.8, 53.2, 52.1; IR (KBr): 3311, 2953, 2917, 1736, 1681, 1567, 1445, 1334, 1251, 1076, 926, 787 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}BrNO_4$: 310.9793 and 312.9773 $[M]^+$; found: 310.9791 and 312.9776.

Dimethyl 5-iodo-1*H*-indole-2,3-dicarboxylate (**3pa**): Yellow solid (52.4 mg, 73% yield), mp 202−203 °C. ^1H NMR (DMSO-d_6, 400 MHz) δ 12.81 (s, 1H), 8.26 (d, J = 2.0 Hz, 1H), 7.61−7.58 (m, 1H), 7.37 (d, J = 12.0 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 164.0, 161.5, 134.7, 133.4, 131.2, 130.2, 128.4,

115.8, 108.4, 87.1, 53.2, 52.1; IR (KBr): 3300, 2949, 2920, 1702, 1533, 1443, 1338, 1294, 1218, 1133, 1076, 768 (cm^{-1}); HRMS (EI) calcd for $C_{12}H_{10}INO_4$: 358.9655 $[M]^+$; found: 358.9650.

Trimethyl 1*H*-indole-2,3,5-tricarboxylate (**3qa**): White solid (30.9 mg, 53% yield), mp 172−174 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.90 (s, 1H), 8.76 (s, 1H), 8.03 (dd, J = 4.0, 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.5, 164.1, 161.1, 137.2, 129.6, 126.8, 126.2, 125.8, 124.6, 113.0, 112.0, 52.9, 52.2, 52.1; IR (KBr): 3303, 2953, 2925, 1716, 1620, 1542, 1437, 1286, 1245, 1167, 1062, 762 (cm^{-1}); HRMS (EI) calcd for $C_{14}H_{13}NO_6$: 291.0743 $[M]^+$; found: 291.0749.

Dimethyl 5-(trifluoromethyl)-1*H*-indole-2,3-dicarboxylate (**3ra**): White solid (30.1 mg, 50% yield), mp 162−164 °C. ^1H NMR (DMSO-d_6, 400 MHz) δ 13.07 (s, 1H), 8.25 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 163.9, 161.5, 137.1, 132.7, 129.4, 126.7, 125.3, 124.0, 123.4 (q, J = 56.0 Hz), 121.5, 119.5 (q, J = 9.0 Hz), 114.6, 110.0, 53.3, 52.2; IR (KBr): 3312, 2954, 1745, 1713, 1543, 1444, 1342, 1204 1112, 822, 761, 677 (cm^{-1}); HRMS (EI) calcd for $C_{13}H_{10}F_3NO_4$: 301.0562 $[M]^+$; found: 301.0567.

Dimethyl 1*H*-benzo[*g*]indole-2,3-dicarboxylate (**3sa**): Yellow solid (38.0 mg, 67% yield), mp 205−207 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 10.57 (s, 1H), 8.25 (d, J = 4.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.60−7.50 (m, 3H), 4.03 (s, 3H), 3.99 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.9, 161.8, 132.0, 131.1, 128.9, 126.3, 126.1, 125.9, 123.8, 123.7, 121.3, 120.7, 120.6, 113.7, 52.8, 52.0; IR (KBr): 3316,

2953, 2918, 1727, 1692, 1526, 1446, 1263, 1103, 818, 775, 749 (cm^{-1}); HRMS (EI) calcd for $C_{16}H_{13}NO_4$: 283.0845 $[M]^+$; found: 283.0850.

Diethyl 1*H*-indole-2,3-dicarboxylate (**3ab**): Colorless oil (40.2 mg, 77% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ 9.42 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.29−7.25 (m, 1H), 7.20−7.16 (m, 1H), 4.41−4.34 (m, 4H), 1.39−1.32 (m, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.3, 161.1, 134.9, 128.2, 126.9, 125.8, 122.6, 122.4, 112.2, 111.9, 61.9, 60.8, 14.4, 14.2; IR (neat): 3310, 2980, 2924, 1701, 1536, 1438, 1375, 1330, 1218, 1068, 1023, 750 (cm^{-1}); HRMS (EI) calcd for $C_{14}H_{15}NO_4$: 261.1001 $[M]^+$; found: 261.1008.

Diisopropyl 1*H*-indole-2,3-dicarboxylate (**3ac**): White solid (43.4 mg, 75% yield), mp 66−68 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.40 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.39−7.35 (m, 1H), 7.29−7.27 (m, 1H), 5.41−5.31 (m, 2H), 1.48 (s, 3H), 1.46 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.3, 161.1, 134.9, 128.2, 126.9, 125.8, 122.6, 122.4, 112.2, 111.9, 61.9, 60.8, 14.4, 14.2; IR (KBr): 3319, 2981, 2933, 1731, 1541, 1452, 1375, 1253, 1182, 1107, 1064, 750 (cm^{-1}); HRMS (EI) calcd for $C_{16}H_{19}NO_4$: 289.1314 $[M]^+$; found: 289.1322.

Dibuty 1*H*-indole-2,3-dicarboxylate (**3ad**): White solid (48.2 mg, 76% yield), mp 62−64 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.47 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.29−7.25 (m, 1H), 7.20−7.16 (m, 1H), 4.34−4.29 (m, 4H), 1.74−1.66 (m, 4H), 1.43−1.37 (m, 4H), 0.93−0.86 (m, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.4, 161.3, 134.9, 128.2, 126.8, 125.8, 122.6, 122.4, 112.3, 112.0, 65.8, 64.8, 30.9, 30.6, 19.4, 19.1, 13.8, 13.7; IR (KBr): 3313, 2960, 2933, 1702, 1541, 1434, 1331, 1217, 1182, 1121, 1070, 750 (cm^{-1}); HRMS (EI) calcd for $C_{18}H_{23}NO_4$: 317.1627 $[M]^+$; found: 317.1633.

Dicyclohexyl 1*H*-indole-2,3-dicarboxylate (**3ae**): White solid (56.2 mg, 76% yield), mp 173−175 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.31 (s, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.36−7.33 (m, 1H), 7.26−7.23 (m, 1H), 5.13−5.05 (m, 2H), 2.11−2.07 (m, 2H), 2.02−1.98 (m, 2H), 1.84−1.81 (m, 4H), 1.69−1.57 (m, 6H), 1.51−1.41 (m, 4H), 1.36−1.30 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 163.6, 160.3, 134.7, 128.5, 126.8, 125.6, 122.5, 122.2, 112.9, 111.8, 74.6, 73.4, 31.9, 31.6, 25.5, 25.4, 24.0, 23.7; IR (KBr): 3290, 2923, 2855, 1702, 1540, 1454, 1334, 1259, 1181, 946, 768, 742 (cm^{-1}); HRMS (EI) calcd for $C_{22}H_{27}NO_4$: 369.1940 $[M]^+$; found: 369.1931.

Bis(2,2,2-trifluoroethyl) 1*H*-indole-2,3-dicarboxylate (**3af**): White solid (50.2 mg, 68% yield), mp 147−149 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.43 (s, 1H), 8.09 (d, J = 12.0 Hz, 1H), 7.50−7.42 (m, 2H), 7.36−7.32 (m, 1H), 4.81−4.74 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 161.8, 158.6, 135.1, 126.9, 126.8 (d, J = 6.0 Hz), 124.1, 123.2 (q, J = 182.0 Hz), 121.4, 112.2, 111.3, 60.9 (q, J = 56.0 Hz), 60.8 (q, J = 74.0 Hz); IR (KBr): 33324, 2972, 2915, 1743, 1693, 1525, 1454, 1285, 1166, 961, 767, 746 (cm^{-1}); HRMS (EI) calcd for $C_{14}H_9F_6NO_4$: 369.0436 $[M]^+$; found: 369.0428.

Dimethyl 1-methyl-1*H*-indole-2,3-dicarboxylate (4):[2] Ice-colded solution of **3aa** (233.2 mg, 1.0 mmol) in DMF (10 mL) was treated with NaH (80.0 mg, 2.0 equiv.) and methyl iodide (212.9 mg, 1.5 equiv.), and then the mixture was stirred at 75 °C by oil bath for 8 h. The reaction was quenched with saturated aqueous solution of NH_4Cl, and the product was extract with EtOAc. The combined organic layers were washed with water and brine, and then the organic layers were dried with Na_2SO_4. The residue obtained through filtration and concentration was purified via silica gel chromatography (eluent: petroleum ether/ethyl acetate = 8:1) to give 242.3 mg (98%) of **4** as a yellow oil

(242.3 mg, 98% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (d, J = 8.0 Hz, 1H), 7.34 (s, 2H), 7.30−7.25 (m, 1H), 4.01 (s, 3H), 3.91 (s, 3H), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 164.6, 163.3, 136.9, 134.8, 125.3, 124.5, 123.0, 122.4, 110.2, 108.1, 53.1, 51.5, 31.5.

4-Methyl-1*H*-furo[3,4-b]indole-1,3(4*H*)-dione (5):[12] A mixture of dimethyl 1-methylindole-2,3-dicarboxylate (**4**, 123.6 mg. 0.5 mmol) and KOH (112.2 mg, 4.0 equiv.) in ethanol was treated under reflux for 2h. The mixture was cooled to 0 °C and the precipitated potassium salt was collected and redissolved in water (5 mL). The solution was acidified to pH 2.0 with hydrochloric acid (5 M) to give brown solid dicarboxylic acid, which was used directly in the following synthesis step. Dicarboxylic acid in acetic anhydride (15 mL) was treated under reflux by oil bath for 2 h. The solvent was removed under reduced pressure, and the residue obtained was purified via silica gel chromatography (eluent: petroleum ether/ethyl acetate = 10:1) to give product **5** (83.5 mg, 83%). mp 209−211 °C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.10 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.38−7.34 (m, 1H), 7.29−7.25 (m, 1H), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 166.7, 163.6, 136.9, 136.8, 125.6, 124.5, 122.8, 122.3, 111.6, 107.0, 32.2.

1-(phenyldiazenyl)ethan-1-one (6):[16] A reaction flask was charged with a mixture of substituted 2-acetyl-1-phenylhydrazine (**1a**, 0.2 mmol, 30 mmg), dimethyl maleate (**2a**, 0.4 mmol, 57.7 mg), $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (8.3 mg, 5 mol%), NaOAc (4.1 mg, 25 mol%), Ag_2CO_3 (110.2 mg, 0.4 mmol, 2.0 equiv.) and DCE (1.0 mL). The reaction mixture was stirred at 90 °C by IKA plate for 10 min under N_2 condition, and then was rapidly cooled to room temperature. The solvent was removed under reduced pressure,

and the residue obtained was purified via silica gel chromatography (eluent: petroleum ether/ethyl acetate = 8:1 to 4:1) to give **6** (15.3 mg, 52%). Red oil (13.6 mg, 46% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, J = 8.0 Hz, 2H), 7.57−7.51 (m, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 188.6, 151.5, 133.6, 129.4, 123.7, 21.3.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.xxxxxxx.

Copies of ^{1}H and ^{13}C NMR spectra for all compounds (PDF)

Crystallographic information for **3da** (CIF)

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Notes

The authors declare no competing financial interest.

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