# Chemo- and Regioselective Synthesis of Functionalized 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones via a Redox-Neutral Rhodium(III)-Catalyzed [4+1] Annulation between Indoles and Alkynes

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**Abstract.** Alkynes generally serve as $C_2$ synthons in transition-metal-catalyzed C−H annulations, herein, exploiting electron-deficient alkynes as unconventional $C_1$ synthons, the chemo- and regiospecific synthesis of functionalized 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones via a redox-neutral rhodium(III)-catalyzed [4+1] annulation of *N*-carbamoyl indoles has been achieved. This process is characterized by high chemo- and regioselectivity, broad substrate scope, good tolerance of functional groups, moderate to high yields and mild redox-neutral conditions, thus affording a robust approach to access valuable 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones.

**Keywords:** Rhodium; Indole; Alkyne; C−H activation; [4+1] annulation; $C_1$ synthon

## Introduction

Indole-fused heterocycles are regarded as privileged structures as they are widely found in natural products[1] and active pharmaceutical ingredients.[2] Therefore, the construction of indole-fused heterocycles has captured wide attention of the synthetic community,[3] who are invariably pursuing to develop efficient and straightforward methods to access these scaffolds. With the significant progress made in transition-metal (TM)-catalyzed C−H activations assisted by directing groups in recent decades,[4] the strategy of C−H annulations between various coupling partners and indole substrates has emerged as the prior strategy to assemble indole-fused heterocycles because of its high efficiency, convenience, and step/atom-economy.[5,6] Within this field, alkynes are frequently used coupling partners, which normally serve as $C_2$ synthons to fulfil [n+2] cycloaddition in C−H annulations of indoles.[6a, c-e, g, h, j, l-q, u-w] Although TM-catalyzed C−H annulations of

other aromatic substrates using alkynes as $C_1$ synthons have made some breakthrough in recent years,[7] to the best of our knowledge, examples of exploiting alkynes as $C_1$ synthons to fulfil [n+1] cycloaddition in C−H annulations of indoles are still rare.[8] In addition, among the indole substrates employed, *N*-carbamoyl indoles are hot substrates, not only because the carbamoyl directing group[9] is simple to install onto a large number of readily available indole materials, but also because different annulation modes could be provided by *N*-carbamoyl indoles. The reported C−H annulations between *N*-carbamoyl indoles and alkynes could be classified into two categories. (i) [3+2] annulation for the synthesis of 3*H*-pyrrolo[1,2-*a*]indol-3-ones via Co,[10a] Ru,[10b] Re,[10c] Rh[10d, e] catalysis (Scheme 1a); (ii) [4+2] annulation for the synthesis of pyrimido[1,6-*a*]indol-1(2*H*)-ones via Rh[11] catalysis (Scheme 1b). Of note, alkynes display as normal $C_2$ synthons in the abovementioned two types of annulations. Despite the remarkable achievements made, however, the [4+1] annulation of *N*-carbamoyl
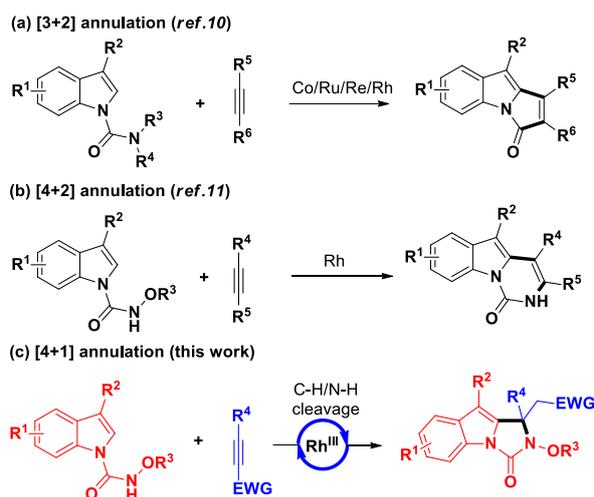
**Scheme 1**. C−H annulations between *N*-carbamoyl indoles and alkynes.

indoles with alkynes as $C_1$ synthons for the synthesis of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones has not been reported yet to date. This reflects the challenge in realizing such a transformation and prompts us to explore this new type of connection. Specifically, the first challenge is to identify suitable alkyne partners as $C_1$ synthons as they generally act as $C_2$ synthons in TM-catalyzed C−H annulations.[12] The control of chemoselectivity by developing a proper catalytic system to achieve [4+1] annulation from strong competitive background reactions including [3+2] annulation[10], [4+2] annulation[11] as well as C−H alkenylation[13] is the second foreseeable challenge. The third challenge is the control of regioselectivity between indole C2 and C7 positions, and two alkyne carbons when unsymmetrical alkynes are employed. With our interests in indole compound synthesis[14] and Rh(III)-catalyzed C−H functionalization,[10d, 11d, 13g, 15] herein we report the Rh(III)-catalyzed chemo- and regioselective [4+1] annulation between *N*-carbamoyl indoles and electron-deficient alkynes for the assembly of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones (Scheme 1c). Notably, this reaction is characterized by the following valuable features. (i) Alkynes are used as unconventional $C_1$ synthons to fulfil an unusual [4+1] annulation, which is rare as alkynes normally act as $C_2$ synthons to undergo [n+2] cycloaddition in C−H annulations of indoles; (ii) a highly chemoselective [4+1] annulation, in which the competitive background reactions such as [3+2], [4+2] annulation and C−H alkenylation are inhibited; (iii) a highly regiospecific [4+1] annulation with the C−H activation occurred at C2 over C7 position of the indole and C−C/C−N bonds both formed at the distal sp hybridized carbon of the alkyne moiety; (iii) a mild redox-neutral transformation without the addition of any external oxidants, which results in good compatibility of various functional groups. Despite the elegant synthesis of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones from indoles with hazardous diazo compounds,[11a, 16] 4-hydroxyphenylboronic

acid under silver oxidants[17] or isocyanides under air oxidation[18], our method stands as the first example of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one synthesis via a redox-neutral Rh(III)-catalyzed [4+1] annulation of *N*-carbamoyl indoles exploiting alkynes as $C_1$ synthons. Regarding the large occurrence of the 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one motif in pharmaceutical agents (Figure 1),[19] our approach is quite attractive as it offers a facile and rapid access to highly functionalized 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones from readily available materials through Rh(III)-catalyzed chemo- and regioselective [4+1] annulation.
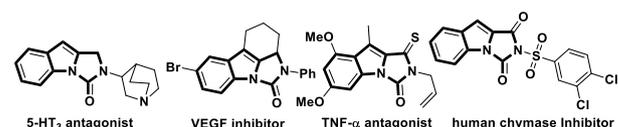


**Figure 1**. Representative bioactive molecules containing the 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one motif.

## Results and Discussion

Initial screening experiments were performed with indole **1aa** and ethyl propiolate **2aa** as the model substrates, and the informative results were shown in Table 1. At first, substrates **1aa** and **2aa** were treated with various metal catalysts in DCE at 60 °C for 24 h using NaOAc as the additive. Only a slight amount of *aza*-Michael addition products **3aa'** or **3aa''** were observed with CoCp$_2$*PF$_6$, [RuCl$_2$(*p*-cym)]$_2$, Pd(OAc)$_2$ and [Cp*IrCl$_2$]$_2$ (entries 1-4). Pleasingly, the desired [4+1] annulation product **3aa** was afforded chemoselectively in 44% yield when [Cp*RhCl$_2$]$_2$ was employed as the catalyst (entry 5). Then, with [Cp*RhCl$_2$]$_2$ as the catalyst and NaOAc as the additive, a screening of diverse solvents revealed that increasing the polarity of the solvent seemed unbeneficial, and DCE was still the best choice (entries 6-13). Next, a series of additives were investigated in DCE. Additives such as KOAc, CsOAc and Na$_2$CO$_3$, which show stronger basicity than NaOAc, only promoted the formation of the *aza*-Michael addition products **3aa'** or **3aa''** (entries 14-16). To our delight, NaOPiv·H$_2$O turned out to be a better additive, with which product **3aa** was obtained in 56% yield without the formation of the byproducts **3aa'** and **3aa''** (entries 17). Subsequently, in order to further improve the reaction yield, an extra acid additive was added into the reaction (entries 18-20) regarding acid additives could promote Rh(III)-catalyzed C–H activations in some cases.[20] As a result, benzoic acid, pivalic acid and HOAc all could improve the yield of **3aa** significantly, and HOAc was proved to be the best acid additive, with which substrate **1aa** was fully consumed and the desired product **3aa** was obtained with a high yield (83%). Moreover, decreasing the reaction temperature to 50 °C led to a lower yield (72%) of **3aa** because of the incomplete consumption of materials (entry 21), while increasing the temperature to 70 °C was

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**Table 1.** Optimization of the reaction conditions.[a]
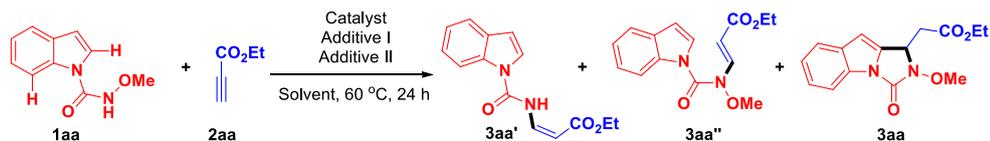


| Entry | Catalyst | Additive I | Additive II | Solvent | Yield (%)[b] | | |
|---|---|---|---|---|---|---|---|
| | | | | | 3aa' | 3aa'' | 3aa |
| 1 | CoCp$_2$*PF$_6$ | NaOAc | - | DCE | <5 | 11 | 0 |
| 2 | [RuCl$_2$(p-cym)]$_2$ | NaOAc | - | DCE | 0 | <5 | 0 |
| 3 | Pd(OAc)$_2$ | NaOAc | - | DCE | trace | trace | 0 |
| 4 | [Cp*IrCl$_2$]$_2$ | NaOAc | - | DCE | <5 | <5 | 0 |
| 5 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | DCE | trace | 0 | 44 |
| 6 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | Toluene | trace | 0 | 41 |
| 7 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | DCM | trace | 0 | 43 |
| 8 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | THF | <5 | <5 | trace |
| 9 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | Acetone | 12 | 15 | <5 |
| 10 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | CH$_3$CN | 0 | 0 | 21 |
| 11 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | 1,4-dioxane | <5 | <5 | 0 |
| 12 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | EtOH | <5 | 0 | <5 |
| 13 | [Cp*RhCl$_2$]$_2$ | NaOAc | - | DMF | 0 | 0 | 0 |
| 14 | [Cp*RhCl$_2$]$_2$ | KOAc | - | DCE | 18 | 21 | 10 |
| 15 | [Cp*RhCl$_2$]$_2$ | CsOAc | - | DCE | 26 | 29 | <5 |
| 16 | [Cp*RhCl$_2$]$_2$ | Na$_2$CO$_3$ | - | DCE | 23 | 24 | 0 |
| 17 | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | - | DCE | 0 | 0 | 56 |
| 18 | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | C$_6$H$_5$CO$_2$H | DCE | 0 | 0 | 65 |
| 19 | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | Pivalic acid | DCE | 0 | 0 | 82 |
| **20** | **[Cp*RhCl$_2$]$_2$** | **NaOPiv·H$_2$O** | **HOAc** | **DCE** | **0** | **0** | **83** |
| 21[c] | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | HOAc | DCE | 0 | 0 | 72 |
| 22[d] | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | HOAc | DCE | <5 | 9 | 70 |
| 23[e] | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | HOAc | DCE | 0 | 0 | 82 |
| 24[f] | [Cp*RhCl$_2$]$_2$ | NaOPiv·H$_2$O | HOAc | DCE | 0 | 0 | 76 |
| 25 | [Cp*RhCl$_2$]$_2$ | - | HOAc | DCE | 0 | 0 | 0 |
| 26 | - | NaOPiv·H$_2$O | HOAc | DCE | 0 | 0 | 0 |

[a] Reaction conditions: **1aa** (0.25 mmol), **2aa** (0.3 mmol), catalyst (5 mol%), additive I (0.5 mmol), additive II (0.5 mmol), solvent (4.0 mL), 60 °C, 24 h. [b] Isolated yields. [c] The reaction was performed at 50 °C. [d] The reaction was performed at 70 °C. [e] **2aa** (0.375 mmol) was used. [f] [Cp*RhCl$_2$]$_2$ (2.5 mol%) was used.

beneficial for the generation of the byproducts **3aa'** and **3aa''**, and thus also resulted in a lower yield (70%) of **3aa** (entry 22). Attempts to further improve the yield of **3aa** by increasing the amount of alkyne **2aa** to 1.5 equivalents turned out to be unsuccessful, and a comparable yield (82%) of **3aa** was observed in this case (entry 23). This result makes sense as 1.2 equivalents of alkyne **2aa** was enough to have indole **1aa** fully consumed. In addition, reducing the amount of the catalyst [Cp*RhCl$_2$]$_2$ from 5 mol% to 2.5 mol% caused a lower yield (76%) of **3aa** as well owing to the incomplete conversion of indole **1aa** (entry 24). At last, control experiments showed that the catalyst [Cp*RhCl$_2$]$_2$ and the additive NaOPiv·H$_2$O were both essential for the title [4+1] annulation (entries 25 and 26). In this way, the catalytic system consisting of [Cp*RhCl$_2$]$_2$/NaOPiv·H$_2$O/HOAc was identified for the title [4+1] annulation. Of note, the products of background [3+2]/[4+2] annulation were not detected during optimization of the reaction conditions,

indicating the excellent chemoselectivity of this process.

With the optimal reaction conditions identified, we checked the substrate scope of indoles at first with **2aa** as the reaction component (Table 2). In general, the reactions of a broad range of indoles **1** substituted at R$^1$-R$^3$ with **2aa** occurred smoothly, providing the chemo- and regioselective [4+1] annulation products **3** in good to excellent yields. For instance, indoles bearing halogens (F, Cl, Br, I) at C4-C7 positions underwent this transformation successfully to give products **3ab-3al** in 74-98% yields. The reactions of indoles having electron-donating groups (Me, MeO) at C4-C7 positions worked well to provide products **3am-3as** in 59-91% yields. Likewise, the reactions of indoles with electron-withdrawing substituents (CO$_2$Me, CN, NO$_2$, CF$_3$) at C5 position took place uneventfully to deliver products **3at-3aw** in 12-92% yields. Impressively, indoles bearing C3 substituents (Me, Bn, CH$_2$CN, CH$_2$CO$_2$Et), which cause an obvious steric hindrance near the reaction site, could

**Table 2**. Scope of the indoles.[a,b]
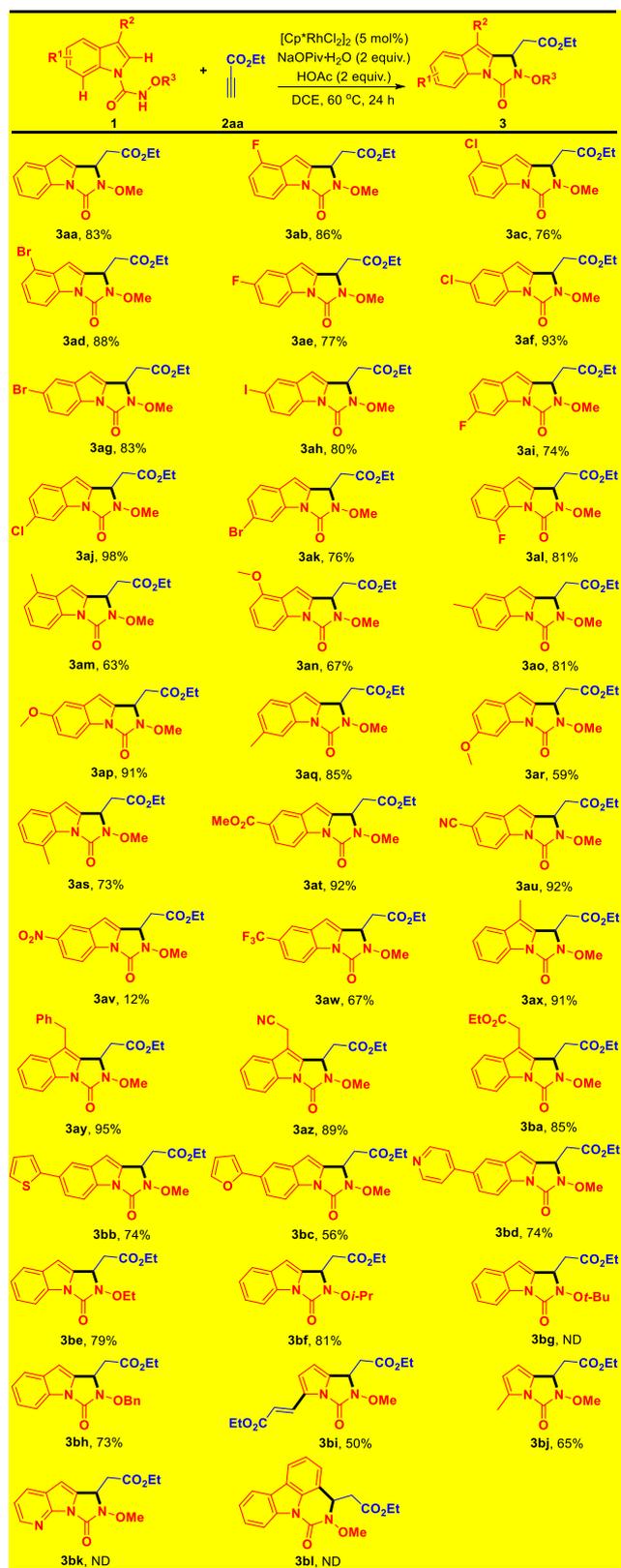


[a] Reaction conditions: **1** (0.25 mmol), **2aa** (0.3 mmol), [Cp*RhCl₂]₂ (5 mol%), NaOPiv·H₂O (0.5 mmol), HOAc (0.5 mmol), DCE (4.0 mL), 60 °C, 24 h. [b] Isolated yields. ND = not detected.
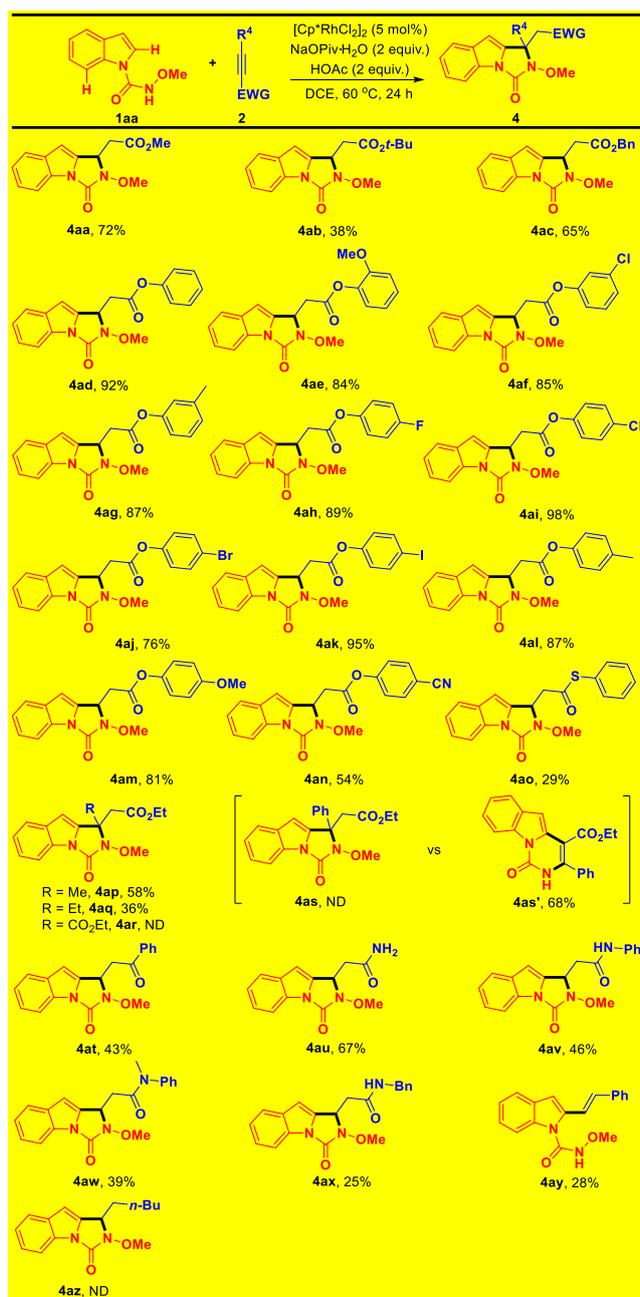
undergo the reaction to provide products **3ax-3ba** in 85-95% yields. Gratifyingly, indoles carrying heterocycles such as thiophene, furan and pyridine at C5 position were well tolerated, affording products **3bb-3bd** in 56-74% yields. In addition, this process could also be applicable to indoles bearing diverse alkyl groups (Et, *i*-Pr, Bn) at R³, which underwent this [4+1] annulation smoothly to assemble products **3be**, **3bf** and **3bh** in 73-81% yields. By contrast, the reaction of indole substrate possessing a bulky *t*-Bu group at R³ failed to react to produce the corresponding product **3bg** but with the recovery of the materials, maybe because of the steric hindrance caused by the huge *t*-Bu group. Pleasingly, the transformation was also compatible with *N*-carbamoyl pyrroles. Interestingly, the reaction of C2 and C5 both unsubstituted pyrrole gave [4+1] annulation/C−H alkenylation product **3bi** in 50% yield, while the reaction of pyrrole bearing a Me group at C2 provided the [4+1] annulation product **3bj** in 65% yield. By comparison, *N*-carbamoyl 7-azaindole and *N*-carbamoyl carbazole could not be converted into the corresponding products **3bk** and **3bl**, respectively, but with the recovery of the materials.

We next examined the substrate scope of alkynes with **1aa** as the reaction partner (Table 3). Alkyl propiolates such as methyl/*tert*-butyl/benzyl propiolates reacted smoothly to give products **4aa**-**4ac** in 38-72% yields. Similarly, a variety of phenyl propiolates having halogens, electron-donating or electron-withdrawing groups (EWG) on the benzene ring could also participate in this reaction to provide products **4ad-4an** in 54-98% yields. *S*-phenyl prop-2-ynethioate could also be converted into the corresponding product **4ao**, albeit with a lower yield. Pleasingly, internal alkynes like ethyl but-2-ynoate and ethyl pent-2-ynoate were also tolerated, and the desired products **4ap** and **4aq** were obtained with moderate yields. By contrast, diethyl acetylenedicarboxylate failed to react to provide the corresponding [4+1] annulation product **4ar**. The reaction of ethyl phenylpropiolate gave the [4+2] annulation product **4as'** in 68% yield rather than the [4+1] annulation product **4as**. Besides, the reaction of 1-phenylprop-2-yn-1-one could take place to afford the desired product **4at** with 43% yield. Moreover, a series of propiolamides were also proved to be suitable substrates, and the desired products **4au-4ax** were obtained with moderate to good yields (25-67%). Phenylacetylene could interact with **1aa** under optimal conditions, but providing the C−H alkenylation product **4ay** rather than the desired [4+1] annulation product. The reaction of 1-hexyne with **1aa** gave a complex mixture, in which the desired product **4az** was not detected.

To further demonstrate the efficiency of this methodology, the gram-scale reaction between **1aa** and **2aa** was performed under standard conditions (Scheme 2a). Impressively, the desired product **3aa** was obtained in a comparable yield (81%) as the small-scale reaction, indicating the Rh(III)-catalyzed [4+1] annulation could be easily scaled up. Additionally, this protocol could also find its

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**Table 3**. Scope of the alkynes.[a,b]



Conditions shown: 1aa + 2 → [Cp*RhCl₂]₂ (5 mol%), NaOPiv·H₂O (2 equiv.), HOAc (2 equiv.), DCE, 60 °C, 24 h → 4

**4aa**, 72%  |  **4ab**, 38%  |  **4ac**, 65%
**4ad**, 92%  |  **4ae**, 84%  |  **4af**, 85%
**4ag**, 87%  |  **4ah**, 89%  |  **4ai**, 98%
**4aj**, 76%  |  **4ak**, 95%  |  **4al**, 87%
**4am**, 81%  |  **4an**, 54%  |  **4ao**, 29%
R = Me, **4ap**, 58%; R = Et, **4aq**, 36%; R = CO₂Et, **4ar**, ND  |  **4as**, ND  vs  **4as'**, 68%
**4at**, 43%  |  **4au**, 67%  |  **4av**, 46%
**4aw**, 39%  |  **4ax**, 25%  |  **4ay**, 28%
**4az**, ND

[a] Reaction conditions: **1aa** (0.25 mmol), **2** (0.3 mmol), [Cp*RhCl₂]₂ (5 mol%), NaOPiv·H₂O (0.5 mmol), HOAc (0.5 mmol), DCE (4.0 mL), 60 °C, 24 h. [b] Isolated yields. ND = not detected.

application in the modification of natural products. Taking melatonin[21] (an animal hormone) as an example, it could undergo the sequential carbamoylation/[4+1] annulation to produce the melatonin derivative **5aa** containing the imidazo[1,5-a]indole motif in a high yield (Scheme 2b).

An investigation of the directing groups disclosed that 1H-indole-1-carboxamide **1aa-1** or N-methyl-1H-indole-1-carboxamide **1aa-2** could not undergo the [4+1] annulation under standard conditions but with the recovery of the starting materials (Scheme 3), suggesting the alkoxy group like MeO linked to the amide N is essential for this reaction. This result is in
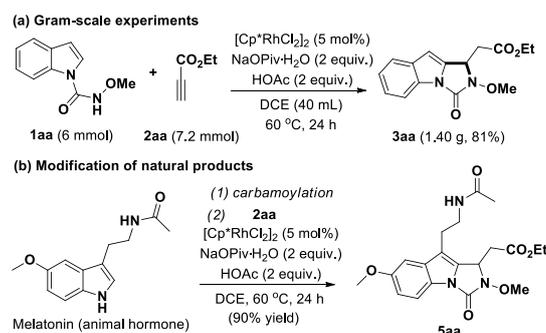


**Scheme 2**. Gram-scale experiments and modification of natural products.

accordance with the recent reports employing the carbamoyl as the directing group,[9e,13f] and we speculated that the alkoxy group like MeO may assure the amide N to have an appropriate electronic property which could enable its coordination to the rhodium catalyst to start the catalytic cycle.
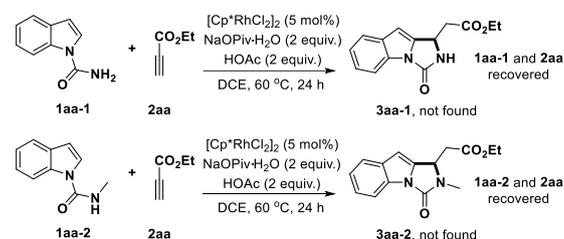


**Scheme 3**. Investigation of the directing groups.

Isotope labeling experiments were carried out to probe the reaction mechanism. When indole **1aa** was subjected to CD₃OD under standard conditions, 82%, 92% and 91% deuteration at C2, C3 and C7 positions of **1aa** was observed respectively (Scheme 4a). This indicates the step of C−H bond cleavage is reversible. The reaction between **1aa-D** and **2aa** under standard conditions gave undeuterated product **3aa** (Scheme 4b). Kinetic isotope effect (KIE) study through intermolecular competition experiment resulted in a low KIE value of 0.82 (Scheme 4c), suggesting the C−H bond cleavage step was unlikely to be rate-determining. Moreover, when the model reaction between **1aa** and **2aa** was performed in a shorter time (1 h), the C−H alkenylation species **3aa-I** was isolated along with the desired [4+1] annulation product **3aa** (Scheme 4d). This suggests the C−H alkenylation species may act as the reaction intermediate. At last, a rhodacycle complex A was detected by HRMS when indole **1aa** was treated with a stoichiometric amount of [Cp*RhCl₂]₂ (Scheme 4e), indicating the coordination of **1aa** to the catalyst and the following twofold deprotonation maybe involved.

To better understand how the C−H alkenylation intermediate **3aa-I** was converted into the [4+1] annulation product **3aa**, a set of control experiments were performed with isolated **3aa-I** (Table 4). Heating cannot promote the conversion (entry 1),
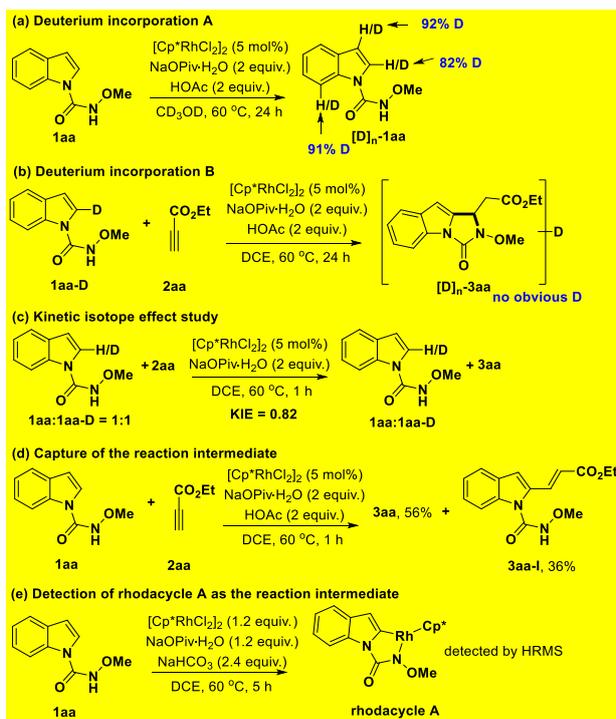
**Scheme 4**. Preliminary mechanism studies.

**Table 4.** Study on the conversion of **3aa-I** to **3aa**.[a]



| Entry | Catalyst | Additive I | Additive II | Yield of 3aa (%)[b] |
|-------|----------|-----------|------------|---------------------|
| 1 | - | - | - | 0 |
| 2 | [Cp*RhCl₂]₂ | - | - | 0 |
| 3 | - | NaOPiv·H₂O | - | 96 |
| 4 | - | - | HOAc | <5 |
| 5 | [Cp*RhCl₂]₂ | NaOPiv·H₂O | - | 94 |
| 6 | [Cp*RhCl₂]₂ | - | HOAc | 0 |
| 7 | - | NaOPiv·H₂O | HOAc | 95 |
| 8 | [Cp*RhCl₂]₂ | NaOPiv·H₂O | HOAc | 93 |
| 9[c] | - | NaOPiv·H₂O | - | 95 |

[a] Reaction conditions: **3aa-I** (0.125 mmol), catalyst (5 mol%), additive I (0.25 mmol), additive II (0.25 mmol), DCE (2.0 mL), 60 °C, 24 h. [b] Isolated yields. [c] NaOPiv·H₂O (20 mol%) was used.

neither do [Cp*RhCl₂]₂ and/nor HOAc (entries 2, 4 and 6). However, NaOPiv·H₂O was found to be able to promote the conversion efficiently, affording the product **3aa** in 96% yield (entry 3). Moreover, the combination use of [Cp*RhCl₂]₂ and/or HOAc with NaOPiv·H₂O did not affect the function of NaOPiv·H₂O (entries 5, 7 and 8). At last, 20 mol% NaOPiv·H₂O was proved to be enough to complete the conversion, indicating this conversion was catalyzed by NaOPiv·H₂O. By contrast, compounds **3aa'** and **3aa''** were both excluded as the reaction intermediates for the generation of product **3aa** as both of them could not be converted into the desired product **3aa** under standard conditions but with the recovery of the starting materials (Supporting Information).

Based on the literature reports[12a, e, 13d, 22] and the results of our mechanistic studies, a plausible reaction mechanism was proposed in Scheme 5. Initially, an active catalyst Cp*Rh(OPiv)₂ may be produced by ligand exchange of [Cp*RhCl₂]₂ with NaOPiv, then the Rh(III)-catalyzed site-selective C–H activation at indole C2 position takes place to yield rhodacycle **A**. The following regioselective insertion of the alkyne into the Rh–C bond of **A** gives intermediate **B**. The polarization of the C≡C bond by the EWG is believed to guarantee the regioselectivity as well as reactivity. Then, intermediate **B** undergoes intramolecular *aza*-Michael addition to afford intermediate **C** (path a). The subsequent protonation of intermediate **C** provides products **4** with the regeneration of the catalyst. Alternatively, intermediate **B** may undergo reductive elimination to produce intermediate **D** (path b), which is converted into the desired products **4** through a NaOPiv-catalyzed intramolecular *aza*-Michael addition. The additive HOAc may protonate the oxygen atom of the carbonyl in EWG to accelerate the *aza*-Michael addition step to promote the whole transformation.
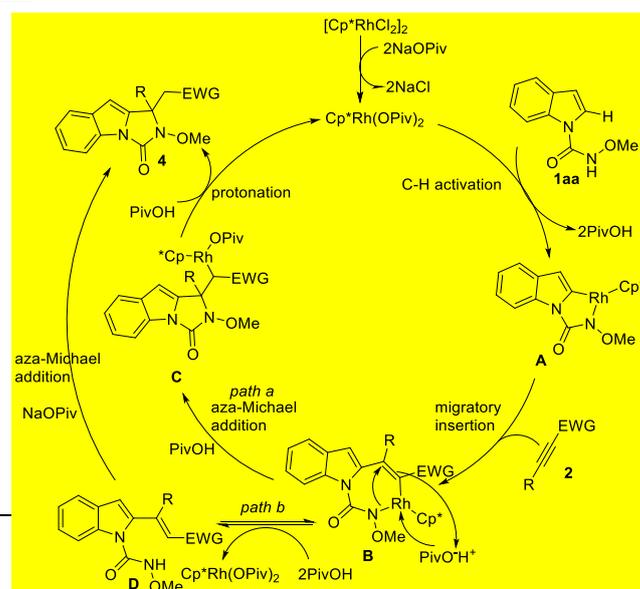


**Scheme 5.** A plausible reaction mechanism.

# Conclusion

In conclusion, exploiting electron-deficient alkynes such as propiolates, propiolamides and ynones as unconventional $C_1$ synthons, we have achieved the chemo- and regioselective synthesis of functionalized 1$H$-imidazo[1,5-$a$]indol-3(2$H$)-ones via a redox-neutral rhodium(III)-catalyzed [4+1] annulation of $N$-carbamoyl indoles. This method features high chemo- and regioselectivity, broad substrate scope, good compatibility of functional groups, moderate to high yields and mild redox-neutral conditions. Further applications of the $C_1$ synthons identified here in fulfilling [n+1] annulations with other aromatic substrates and pharmacological studies of the functionalized 1$H$-imidazo[1,5-$a$]indol-3(2$H$)-ones are in progress in our laboratory.

## Experimental Section

**General Procedure for the Rhodium-Catalyzed Chemo- and Regioselective [4+1] Annulation between Indoles and Alkynes**

To a mixture of indoles **1** (0.25 mmol), [Cp*RhCl$_2$]$_2$ (5 mol%), NaOPiv·H$_2$O (0.5 mmol) in a 25 mL Schlenk tube was added a solution of HOAc (0.5 mmol) in DCE (2.0 mL) and a solution of alkynes **2** (0.3 mmol) in DCE (2.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 60 °C in an oil bath for 24 h. After removal of the solvent, the residue was purified by flash chromatography on silica gel to give the desired products.

## Acknowledgements

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Chemo- and Regioselective Synthesis of Functionalized 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones via a Redox-Neutral Rhodium(III)-Catalyzed [4+1] Annulation between Indoles and Alkynes

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