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双铑(II)/Xantphos 催化的 C—H 官能团化/烯丙基烷基化串联: 从 *N*-芳基-*α*-重氮-*β*-酮酯简便制备 3-酰基-3-烯丙基氧化吲哚衍生物

李芳洁[a,b] 卢 斌[b] 刘 阳*,[a] 王晓明*,[b,c]

([a] 肿瘤微环境响应药物研究湖南省重点实验室 湖南省分子靶标新药研究 南华大学 衡阳医学院药学院协同创新中心 湖南衡阳 421001)

([b] 中国科学院上海有机化学研究所 金属有机化学国家重点实验室 分子合成科学卓越创新中心 上海 200032)

([c] 中国科学院大学杭州高等研究院 化学与材料科学学院 杭州 310024)

摘要 从易于获得的 *N*-芳基-*α*-重氮-*β*-酮酰胺和烯丙基化合物出发, 利用新型的[Rh_2]/Xantphos 催化体系一锅法合成了各种 3-酰基-3-烯丙基的氧化吲哚衍生物. 这项工作的优点包括操作简便、反应条件温和、官能团兼容性良好和产物易于衍生化等. 初步的机理研究表明, 该反应可能经历卡宾诱导的 C—H 官能团化和 Rh(II)/Xantphos 催化的烯丙基烷基化串联过程. 此外, 选择 Xantphos 作为配体对于实现体系中的烯丙基烷基化过程至关重要.

关键词 双铑络合物; 重氮化合物; 氧化吲哚; 季碳中心; 接力催化

Dirhodium/Xantphos-Catalyzed Tandem C—H Functionalization/Allylic Alkylation: Direct Access to 3-Acyl-3-allyl Oxindole Derivatives from *N*-Aryl-*α*-diazo-*β*-keto Amides

Li, Fangjie[a,b] Lu, Bin[b] Liu, Yang*,[a] Wang, Xiaoming*,[b,c]

([a] *Hunan Provincial Key Laboratory of Tumor Microenvironment Responsive Drug Research, Hunan Province Cooperative Innovation Center for Molecular Target New Drug Study, School of Pharmacology, Hengyang Medical School, University of South China, Hengyang, Hunan 421001*)

([b] *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032*)

([c] *School of Chemistry and Materials Science, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, Hangzhou 310024*)

Abstract A novel [Rh_2]/Xantphos-catalyzed one-pot sequence for the synthesis of diverse 3-acyl-3-allyl oxindole derivatives from easily available *N*-aryl-*α*-diazo-*β*-keto amides and allylic compounds has been developed. The notable features of this work include ease of operation, mild reaction conditions, good functional group compatibility and facile diversification of the products. Preliminary mechanistic studies indicate a tandem carbene-induced C—H functionalization and Rh(II)/Xantphos catalyzed allylic alkylation process. Moreover, the choice of Xantphos as the ligand is critical to enable the allylic alkylation process in this catalysis.

Keywords dirhodium(II); diazo compounds; oxindoles; quaternary centers; relay catalysis

1 Introduction

Oxindole motif is a privileged heterocyclic skeleton pervasively encountered in the field of medicinal chemistry and is an important synthon in the total synthesis of natural products and pharmaceuticals (Figure 1).[1] Therefore, a variety of methods have been developed for the construction of these important scaffolds.[2] In addition, the functional groups on the fully substituted C(3)-site of the oxindoles often significantly affect their biological activity.

* Corresponding authors. E-mail: 2014001789@usc.edu.cn; xiaoming@sioc.ac.cn
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Notably, the synthesis of allylic derivatives from simple, readily available starting materials is an important research topic in synthetic organic chemistry, due to the high versatility of the allylic moiety for further functionalization.[3] Despite the great importance of allylic units in organic synthesis, the synthesis of oxindoles bearing allylic C(3)-all carbon quaternary centers is rare and remains a challenge, probably because of the increased steric hindrance encountered during the carbon-carbon bond formation. Thus, the development of new and efficient methods for the construction of this type of important structures is highly desirable to fully exploit biological potential of 3,3'-disubstituted oxindoles.

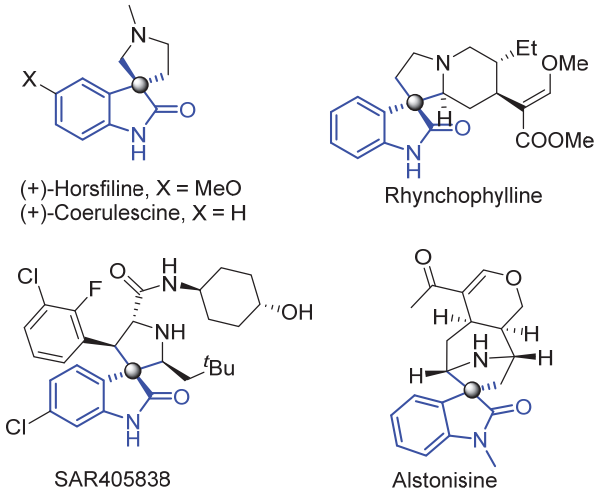
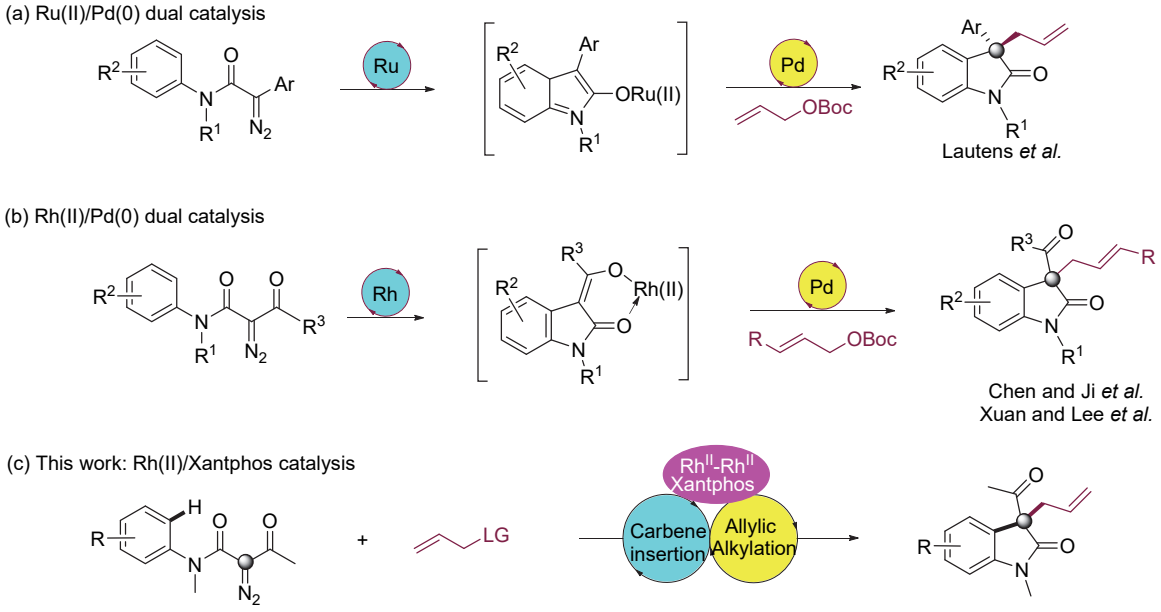


Figure 1 Selected examples of natural products and biologically active molecules

Transition metal-catalyzed intramolecular C—H insertion of diazo compounds has been emerged as a powerful tool for the synthesis of hetero- and carbocycles.[4-5] Especially, dual-catalysis has been emerged as an elegant strategy in the transformation of *N*-aryl *α*-diazo amides for the construction of 3,3'-disubstituted oxindoles frameworks.[6] Remarkably, Hu and coworkers developed a synergistic dual-catalysis strategy consisting of Rh(II)-carbene-induced C—H functionalization and subsequent electrophilic trapping by a chiral phosphoric acid-activated imine, whereby enantioselective synthesis of 3,3'-disubstituted oxindoles was achieved.[6a,b] Nevertheless, the construction of 3,3'-disubstituted oxindoles bearing an allylic C(3)-all carbon quaternary center through the reaction of diazo compounds remains elusive.[7-9] In 2016, Lautens and co-workers disclosed a cross-compatible Ru(II)/Pd(0) dual catalysis system to promote the divergent reaction of *N*-aryl *α*-diazoamides (Scheme 1a),[7a] wherein Ru(II)-associated oxindole enolate intermediate generated from Ru(II)-catalyzed intramolecular C-H insertion can undergo Pd(0)-catalyzed asymmetric allylic alkylation to selective construction of 3-allyl-3-aryl oxindoles. Later on, Ji and Chen *et al.*[7b] and Xuan and Lee *et al.*[7c] respectively reported a new Rh(II)/Pd(0) dual-catalysis system that enabled C—H functionalization and allylic alkylation cascades under mild conditions (Scheme 1b). In their work, allylic alkylation of Rh(II)-associated enolate intermediates (*in situ* formed from *N*-aryl-*α*-diazo-*β*-keto amides) with π-allyl Pd(II) intermediates proceeded in a chemo-selective manner to afford 3-allyl-3-acyl oxindoles. Despite these advancements through dual catalysis, it is still highly desirable to develop a new catalytic method for the synthesis of 3,3'-disubstituted oxindoles with allylic C(3)-all carbon quaternary centers.

As our continuous interest in MCRs under a novel dirhodium(II)/diphosphine catalytic system,[10-12] we herein report a $Rh_2(Oct)_4$/Xantphos-catalyzed selective C—H fun-



Scheme 1 Routes toward oxindoles bearing allylic C(3)-all carbon quaternary centers

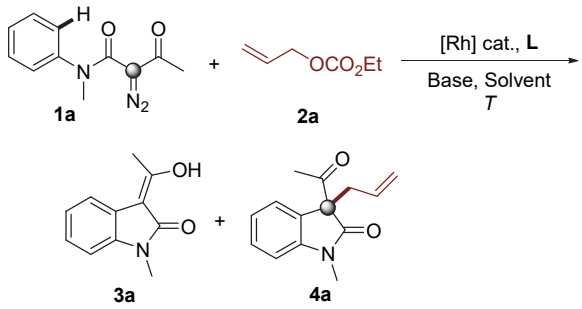
ctionalization of *N*-aryl-*α*-diazo-*β*-keto amides and subsequent allylic alkylation with allylic compounds under mild reaction conditions, affording various 3-allyl-3-acyl oxindole derivatives in good yields (Scheme 1c). Additionally, the salient features of this methodology include readily available starting materials, mild reaction conditions, ease of operation and potential opportunities for structural diversification. Furthermore, controlled experiments indicate that the Xantphos plays a vital role in enabling the allylic alkylation process in this novel catalysis.

2 Results and discussion

In our initial studies, the readily available *N*-aryl-*α*-diazo-*β*-keto amide (**1a**) and allyl ethyl carbonate (**2a**) were selected as the model substrates to survey practical reaction conditions. As shown in Table 1, the reaction of the two substrates in the presence of $Rh_2(Oct)_4$, Xantphos and Cs_2CO_3 in dichloroethane (DCE) at 50 ℃ for 6 h gave the target product **4a** in 51% yield. However, **4a** was not observed without using any base additives, instead **3a** was afforded in 83% yield (Entries 1, 2, Table 1). Following these results, various base additives were then tested and KOAc was identified as amongst the best additive by facilitating the formation of **4a** in 74% yield (Entry 3, Table 1). Additionally, solvents were also critical. The replacement of DCE with $PhCF_3$ further increased the yield to 88% (Entry 4, Table 1). Notably, other Rh(II) precursors such as $Rh_2(OAc)_4$ or $Rh_2(TFA)_4$, provided **4a** in much lower yields (0～7% yields, Entries 5, 6). When using $Rh(COD)_2(BF_4)$ as catalyst under otherwise identical conditions, the reaction cannot proceed (Entry 7). These results indicated that rhodium catalyst precursors play an important role in this reaction. Furthermore, brief ligand screening including BINAP, dppb, PPh_3, and ^{i}Pr-NHC [1,3-bis(2,6-diisopropylphenyl)imidazolium chloride] showed obvious ligand effects, and Xantphos was found to be optimal (Entry 4 vs. Entries 8～11). Next, the reaction temperature was also investigated, and raising or lowering temperature slightly decreased the yield of the product **4a** to 83% or 84%, respectively (Entries 12, 13). Remarkedly, the control experiments demonstrated the essential role of $Rh_2(Oct)_4$ and Xantphos in this catalytic system (Entries 14, 15).

With the optimal conditions in hands, the substrate scope of *N*-aryl-*α*-diazo-*β*-keto amide **1** was investigated. As depicted in Table 2, this catalytic system showed a good tolerance for diverse substituents with different steric hindrance and electronic properties on the aromatic ring. The reaction of *ortho*-methyl substituted substrate **1b** provided lower yield than that of **1a** (59% vs. 88% yield), probably due to the steric effect on the *ortho*-position of phenyl moiety. Additionally, substrates (**1c**～**1e**) with *para* electron-donating substitutes (including Me, ^{t}Bu, OMe) on the benzene ring were also competitive coupling partners in this reaction, giving the corresponding products in consistently good yields (74%～86% yields). Remarkably, the substrates with *para*-fluoro (**1f**), chloro (**1g**), and bromo

Table 1 Optimization of the reaction conditions[a]



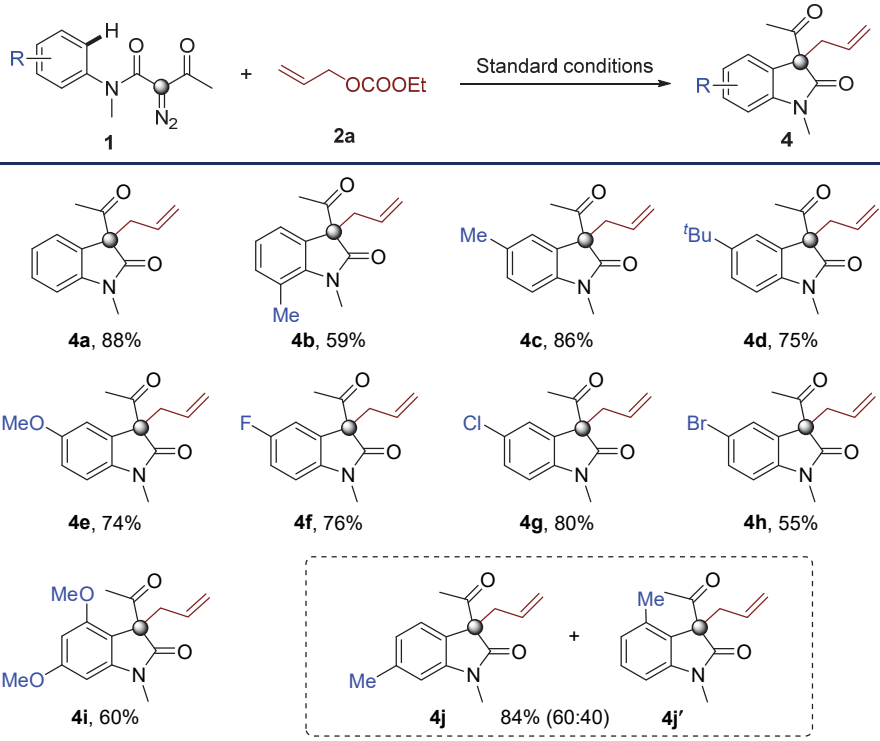
Entry	[Rh] cat.	Ligand	Base	Solvent	Yield[b]/%	
					3a	**4a**
1	$Rh_2(Oct)_4$	Xantphos	Cs_2CO_3	DCE	—	51
2	$Rh_2(Oct)_4$	Xantphos	—	DCE	83	0
3	$Rh_2(Oct)_4$	Xantphos	KOAc	DCE	—	74
4	**$Rh_2(Oct)_4$**	**Xantphos**	**KOAc**	**$PhCF_3$**	—	**88**
5	$Rh_2(OAc)_4$	Xantphos	KOAc	$PhCF_3$	—	＜1
6	$Rh_2(TFA)_4$	Xantphos	KOAc	$PhCF_3$	—	7
7	$Rh(COD)_2BF_4$	Xantphos	KOAc	$PhCF_3$	N.R.[c]	N.R.[c]
8	$Rh_2(Oct)_4$	BINAP	KOAc	$PhCF_3$	—	9
9	$Rh_2(Oct)_4$	dppb	KOAc	$PhCF_3$	—	7
10	$Rh_2(Oct)_4$	PPh_3	KOAc	$PhCF_3$	—	＜5
11	$Rh_2(Oct)_4$	^{i}Pr-NHC[d]	KOAc	$PhCF_3$	—	＜5
12[e]	$Rh_2(Oct)_4$	Xantphos	KOAc	$PhCF_3$	—	83
13[f]	$Rh_2(Oct)_4$	Xantphos	KOAc	$PhCF_3$	—	84
14	—	Xantphos	KOAc	$PhCF_3$	—	N.R.
15	$Rh_2(Oct)_4$	—	KOAc	$PhCF_3$	—	N.R.

[a] **1a** (0.2 mmol), **2a** (0.30 mmol), [Rh] catalyst (1.0 mol%), **L** (2.0 mol%), base (1.5 equiv.) in solvent (2.0 mL) at 50 ℃ under Ar for 6.0 h. [b] Yield was determined by ^{1}H NMR analysis of the crude mixture using nitromethane as an internal standard. [c] N.R.＝no reaction. [d] ^{i}Pr-NHC＝1,3-bis(2,6-diisopropylphenyl)imidazolium chloride. [e] At 30 ℃. [f] At 70 ℃.

(**1h**) on the phenyl moiety were also reactive in moderate to good yields (55%～80%), and the halogen substituents were well tolerated, thus offering their potential further transformation into more complex structures valuable in drug discovery. Furthermore, 3,5-dimethoxy substituted phenyl compound (**1i**) also worked well in this reaction under the standard conditions, delivering the corresponding multi-substituted product **4i** in 60% yield. Notably, the reaction of substrate **1j** bearing a *meta*-Me group on the phenyl ring led to a 60∶40 mixture of two regio-isomers (**4j** and **4j'**) in 84% total yield.

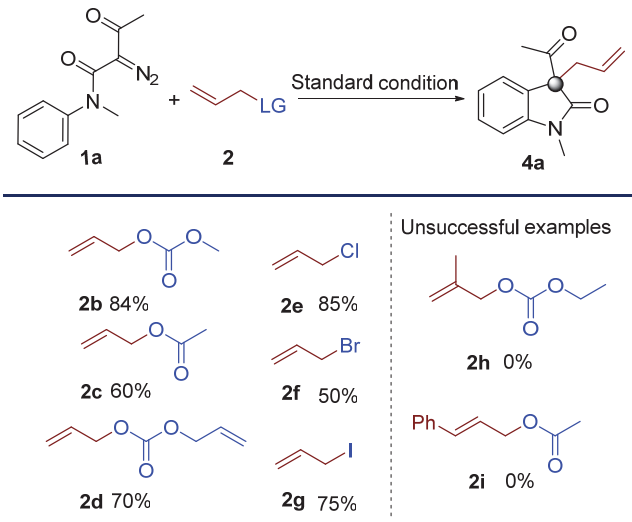
Subsequently, the substrate scope of allylic compounds **2** bearing different leaving groups was evaluated. As shown in Table 3, all the tested allylic alcohol esters **2b**～**2c** with different leaving groups transformed smoothly in this reaction under the standard conditions, furnishing the desired product **4a** in moderate to good yields (60%～84%). In addition, allylic halides (**2e**～**2g**) were also applicable to this reaction and delivered the target product **4a** in 50%～85% yields. Unfortunately, the reaction of 2-Me or 3-Ph substituted allylic compounds failed to give the corresponding products. Instead, compound **3a** was observed as the major product in these cases.

Table 2 Scope of *N*-aryl-*α*-diazo-*β*-keto amide **1**[a]



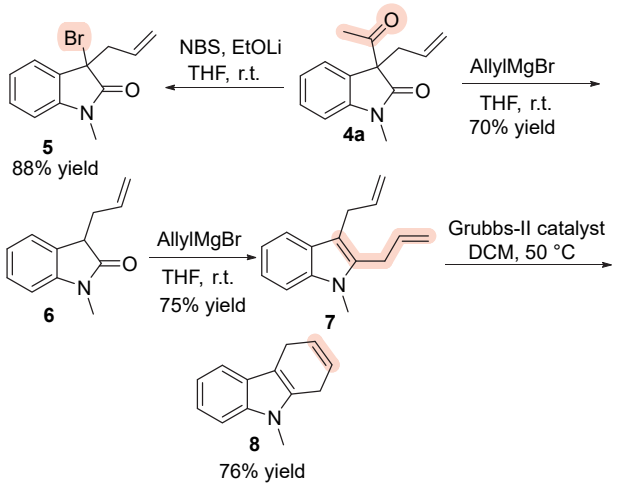
[a] Unless otherwise noted, all reactions were carried out using **1** (0.3 mmol), **2a** (0.45 mmol), $Rh_2(Oct)_4$ (1.0 mol%), Xantphos (2.0 mol%) and KOAc (1.5 equiv.) in $PhCF_3$ (2.5 mL) under Ar at 50 ℃ for 6.0 h. Isolated yields of the products are reported.

Table 3 Scope of allylic compounds **2**[a]



[a] Unless otherwise noted, all reactions were carried out using **1a** (0.3 mmol), **2** (0.45 mmol), $Rh_2(Oct)_4$ (1.0 mol%), Xantphos (2.0 mol%) and KOAc (1.5 equiv.) in $PhCF_3$ (2.5 mL) under Ar at 50 ℃ for 6.0 h. Isolated yields of the products are reported.

To demonstrate the synthetic utility of this protocol, further transformations of **4a** were carried out. As described in Scheme 2, a rapid deacylative bromination of **4a** was realized to afford the product **5** in 88% yield.[13] Furthermore, treatment of **4a** with allylmagnesium bromide which upon workup generated the deacylated oxindole **6** (70% yield), then allyl Grignard addition to the C(2) carbonyl group of **6** was achieved to provide the medicinally important 2,3-disubstituted indole **7** in 75% yield.[14] Finally, the ring-closing metathesis of **7** with Grubbs-II catalyst delivered the synthetically challenging dihydrocarbazole derivative **8** in 76% yield.

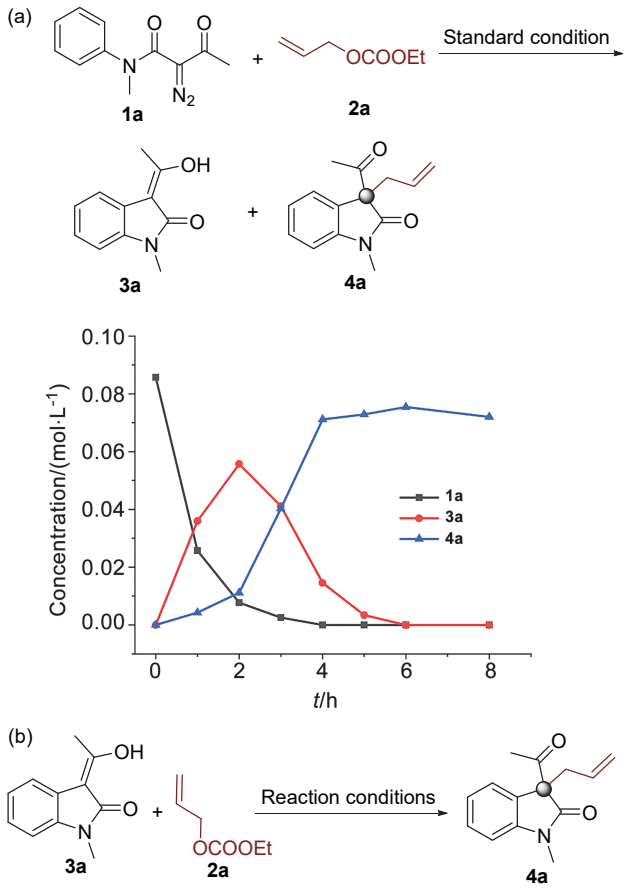


Scheme 2 Further transformations of **4a**

To investigate the possible pathway for this reaction, the reaction profile for the model reaction was monitored by ^1H NMR spectroscopy. As revealed in Scheme 3a, **1a** was completely consumed in 4.0 h period and the yield of C—H insertion product **3a** reached 66% in 2.0 h, accompanied by a steady increase in the amount of the final product **4a** until 6.0 h. Build-up and decay of **3a** during the course of the reaction suggested its intermediacy in the overall transfor-

mation. Furthermore, the reaction of isolated compound **3a** with allylic partner **2a** in the presence of $Rh_2(Oct)_4$, Xantphos, and KO^{t}Bu successfully gave the final product **4a** in 58% yield. In contrast, no **4a** was observed if lacking any component of $Rh_2(Oct)_4$, Xantphos, or KO^{t}Bu (58% vs 0%, Scheme 3b). These results suggest a stepwise pathway of this transformation, *i.e.*, the reaction most likely involves carbene-induced C—H functionalization followed by [Rh_2]/Xantphos-catalyzed allylic alkylation cascades, which is different from the well-known [Rh(II)$_2$] catalysis wherein a ylide/zwitterionic intermediate formed *in situ* was directly trapped by electrophiles.[15] The vital role of Xantphos ligand in this catalysis was probably due to the modification of the active center of the dirhodium complex through coordination, resulting in a novel catalytic activity in the allylic alkylation process.[10]

Based on the results herein and previous studies, a possible reaction pathway is proposed in Scheme 4. [Rh(II)$_2$] can first catalyze carbene insertion reaction, affording the Rh(II)-carbenoid intermediate **A**, which further undergoes [Rh(II)$_2$]-catalyzed C—H functionalization to afford the enolate intermediate **3a**. Additionally, complex **B** bearing a chelate-coordinated Xantphos can be afforded as an active species that can initiate the following allylic alkylation of intermediate **3a**.[10] The coordination of **2a** with dirhodium complex to form intermediate **C**. Then intermediate **C** undergoes oxidative addition with allylic substrate to form possible intermediate **D**. Subsequent nucleophilic attack by **3a** takes place with the assistance of a base to give the final product **4a** and regenerate the intermediate **B** (Scheme 4). However, the possibility of the formation of monorhodium species cannot be completely ruled out under the reaction conditions.



$Rh_2(Oct)_4$, Xantphos, KO^{t}Bu: 58% yield
Lacked any single component of $Rh_2(Oct)_4$, Xantphos, KO^{t}Bu: 0% yield

Scheme 3 Reaction profiles of the model reaction (a) and controlled experiments (b)

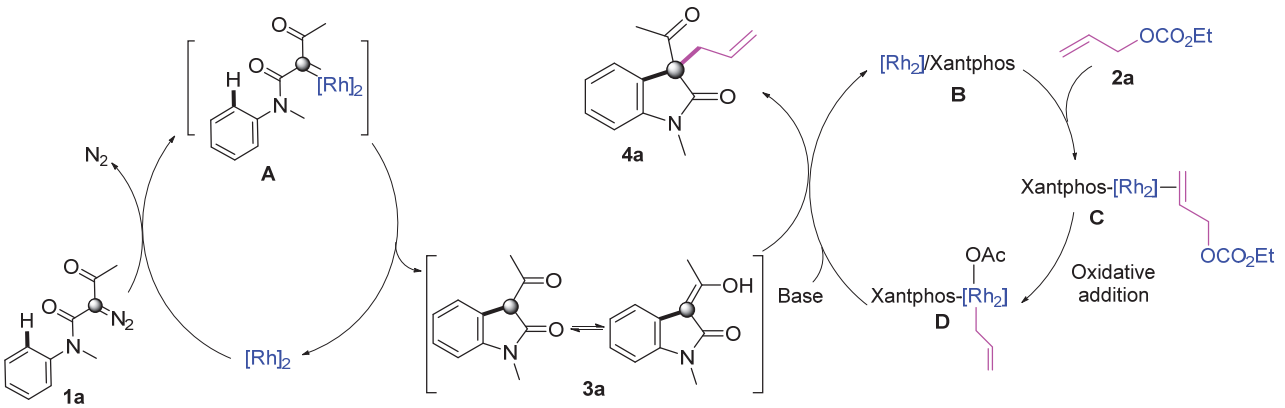
3 Conclusions

In summary, we have developed an efficient method toward the construction of diverse 3-acyl-3-allyl oxindole derivatives from *N*-aryl-*α*-diazo-*β*-keto amides and allylic compounds by employing a [Rh_2]/Xantphos catalysis. Moreover, ease of operation, mild reaction conditions, good functional group compatibility as well as facile transformations of the products constitute notable features of this work. Preliminary mechanistic experiments suggest that this transformation proceed through a relay carbene-induced C—H functionalization and Rh(II)/Xantphos-catalyzed allylic alkylation process.

4 Experimental section

4.1 General experimental information

Unless otherwise noted, all the reactions were carried



Scheme 4 Possible reaction pathway dirhodium/Xantphos-catalyzed tandem C—H functionalization/allylic alkylation

out an argon atmosphere condition and glassware were dried in an oven before use. Whole reagents were purchased from commercial sources and were used directly without further purification or prepared as described in the literature. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on Varian 400 MHz, Agilent 400 MHz or Bruker 400 MHz spectrometers. Chemical shifts (δ) were reported relative to internal TMS (^{1}H NMR: δ 0.000) or $CDCl_3$ (^{1}H NMR: δ 7.260; ^{13}C NMR: δ 77.16), respectively. Flash column chromatography was performed using 200～300 mesh silica gel. IR spectra were obtained on a Bruker Tensor 27 instruments with Bruker Platinum ATR accessory. HRMS (ESI) were determined on a Agilent 6224 TOF LC/MS. Shimadzu GC-2014 spectrometer using flame ionization detector and the heating procedure was established as follows: initial temperature 50 ℃, hold time 0.1 min, heating rate 15 ℃/min, reach temperature 150 ℃, hold time 3 min; heating rate 30 ℃/min, final temperature 280 ℃, hold time 7 min. NMR yield was determined by ^{1}H NMR using nitromethane as an internal standard before working up the reaction.

4.2 Typical experimental procedure for the two-component reaction

In an oven-dried 10 mL sealed tube equipped with a stir bar was added $Rh_2(Oct)_4$ (2.3 mg, 3.0×10^{-3} mmol, 1.0 mol%), Xantphos (3.5 mg, 6.0×10^{-3} mmol, 2.0 mol%), KOAc (42.4 mg, 4.5×10^{-3} mmol, 1.5 equiv.), under dry argon atmosphere, Then, anhydrous $PhCF_3$ (2.5 mL), allyl substrate **2** (0.45 mmol, 1.5 equiv.) and diazo compound **1** (0.30 mmol, 1.0 equiv.) was introduced, respectively. The resulting mixture was stirred at 50 ℃ for 6.0 h. After cooling to ambient temperature, the mixture was filtered and the clear filtrate was collected. After removing the solvents *in vacuo*, the crude product obtained was purified by flash column chromatography on silica gel to give the desired product.

3-Acetyl-3-allyl-1-methylindolin-2-one (**4a**):[7b] Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=15∶1). Yellow oil. 60.5 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38～7.34 (m, 1H), 7.18 (d, J=7.2 Hz 1H), 7.12～7.08 (m, 1H), 6.91～6.90 (m, 1H), 5.31～5.25 (m, 1H), 5.01 (d, J=16.8 Hz, 1H), 4.89 (d, J=10.4 Hz, 1H), 3.28 (s, 3H), 2.98～2.93 (m, 1H), 2.89～2.84 (m, 1H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.8, 174.5, 144.3, 131.5, 129.3, 127.0, 124.2, 123.2, 119.5, 108.6, 66.4, 37.5, 26.6 (one sp^3 C-atom missing due to overlap). HRMS-ESI calcd for $C_{14}H_{16}NO_2$ $[M+H]^+$ 230.1176, found 230.1176.

3-Acetyl-3-allyl-1,7-dimethylindolin-2-one (**4b**):[7b] Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate=10∶1, V∶V). White solid. 43.1 mg, 59% yield. m.p. 99～100 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.08～7.06 (m, 1H), 6.98～6.95 (m, 2H), 5.34～5.23 (m, 1H), 5.00 (d, J=16.8 Hz, 1H), 4.86 (d, J=10.0 Hz, 1H), 3.55 (s, 3H), 2.94～2.83 (m, 2H), 2.61 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.8, 175.3, 142.1, 133.1, 131.7, 127.5, 123.1, 122.0, 120.2, 119.4, 66.0, 37.7, 29.9, 26.5, 19.1. HRMS-ESI calcd for $C_{15}H_{18}O_2N$ $[M+H]^+$ 244.1332, found 244.1334.

3-Acetyl-3-allyl-1,5-dimethylindolin-2-one (**4c**):[7b] Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate=15∶1, V∶V). Yellow oil. 62.7 mg, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.16～7.14 (m, 1H), 6.99 (s, 1H), 6.80～6.78 (m, 1H), 5.35～5.24 (m, 1H), 5.01 (d, J=16.8 Hz, 1H), 5.01 (d, J=16.8 Hz, 1H), 4.89 (d, J=10.0 Hz, 1H), 3.26 (s, 3H), 2.96～2.83 (m, 2H), 2.34 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.0, 174.6, 141.9, 132.9, 131.6, 129.6, 127.0, 124.8, 119.4, 108.3, 66.5, 37.4, 26.6, 21.2 (one sp^3 C-atom missing due to overlap). HRMS-ESI calcd for $C_{15}H_{18}O_2N$ $[M+H]^+$ 244.1332, found 244.1334.

3-Acetyl-3-allyl-5-(*tert*-butyl)-1-methylindolin-2-one (**4d**): Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate=15∶1, V∶V). Yellow oil. 64.2 mg, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38～7.35 (m, 1H), 7.20 (d, J=2.0 Hz, 1H), 6.83 (d, J=8.4 Hz, 1H), 5.37～5.26 (m, 1H), 4.98 (d, J=16.8 Hz, 1H), 4.88 (d, J=10.0 Hz, 1H), 3.26 (s, 3H), 2.99～2.94 (m, 1H), 2.87～2.71 (m, 1H), 1.99 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.1, 174.7, 146.7, 141.9, 131.8, 126.7, 125.8, 121.4, 119.4, 107.9, 66.6, 37.6, 34.7, 31.6, 26.7, 26.6; IR (neat) ν: 2959, 1704, 1497, 1348, 1267, 1186, 1072, 919, 815, 560 cm^{-1}. HRMS-ESI calcd for $C_{18}H_{24}O_2N$ $[M+H]^+$ 286.1802, found 286.1802.

3-Acetyl-3-allyl-5-methoxy-1-methylindolin-2-one (**4e**):[7b] Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=10∶1). Yellow oil. 57.6 mg, 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.89～6.86 (m, 1H), 6.82～6.79 (m, 2H), 5.36～5.25 (m, 1H), 5.01 (d, J=16.8 Hz, 1H), 4.90 (d, J=10.0 Hz, 1H), 3.79 (s, 3H), 3.25 (s, 3H), 2.96～2.82 (m, 2H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.9, 174.2, 156.4, 137.8, 131.5, 128.2, 119.6, 113.8, 111.2, 109.0, 66.8, 55.9, 37.6, 26.7, 26.6. HRMS-ESI calcd for $C_{15}H_{18}O_3N$ $[M+H]^+$ 260.1281, found 260.1282.

3-Acetyl-3-allyl-5-fluoro-1-methylindolin-2-one (**4f**): Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=6∶1). Yellow oil. 56.4 mg, 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.08～7.03 (m, 1H), 6.97 (d, J=6.0 Hz, 1H), 6.84～6.81 (m, 1H), 5.36～5.26 (m, 1H), 5.02 (d, J=16.8 Hz, 1H), 4.91 (d, J=10.0 Hz, 1H), 3.26 (s, 3H), 2.95～2.83 (m, 2H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.3, 174.2, 159.5 (d, J=241.0 Hz), 140.2 (d, J=2.0 Hz), 131.0, 128.6 (d, J=8.0 Hz), 120.0, 115.6 (d, J=23.0 Hz), 112.6 (d, J=25.0 Hz), 109.0 (d, J=8.0 Hz), 66.7 (d, J=2.0 Hz), 38.0, 26.77, 26.73; ^{19}F NMR (376 MHz, $CDCl_3$) δ: −119.4 (m, 1F); IR (neat) ν: 3069, 1700, 1494, 1349, 1275, 1188, 925, 880, 824, 677, 560, 480 cm^{-1}. HRMS-ESI calcd for $C_{14}H_{15}O_2FN$ $[M+H]^+$ 248.1081, found 248.1081.

3-Acetyl-3-allyl-5-chloro-1-methylindolin-2-one (**4g**):[7b] Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=10∶1). Yellow oil. 63.1,

80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 (d, J=12.0 Hz, 1H), 7.19 (s, 1H), 6.81 (d, J=8.4 Hz, 1H), 5.36～5.24 (m, 1H), 5.03 (d, J=17.6 Hz, 1H), 4.93 (d, J=10.8 Hz, 1H), 3.25 (s, 3H), 2.97～2.81 (m, 2H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.1, 174.1, 142.8, 131.0, 129.3, 128.7, 128.6, 124.9, 120.1, 109.4, 66.5, 38.0, 26.8, 26.7. HRMS-ESI calcd for $C_{14}H_{15}O_2NCl$ $[M+H]^+$ 264.0786, found 264.0785.

3-Acetyl-3-allyl-5-bromo-1-methylindolin-2-one (**4h**): Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=5∶1). Yellow oil. 50.8 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49～7.47 (m, 1H), 7.33 (s, 1H), 6.78 (d, J=8.0 Hz, 1H), 5.34～5.25 (m, 1H), 5.03 (d, J=16.8 Hz, 1H), 4.93 (d, J=10.0 Hz, 1H), 3.25 (s, 3H), 2.95～2.82 (m, 2H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.1, 174.0, 143.3, 132.2, 131.0, 129.0, 127.6, 120.1, 115.9, 109.9, 66.4, 38.0, 26.8, 26.7; IR (neat) ν: 3069, 1705, 1605, 1486, 1418, 1338, 1182, 1085, 922, 809, 661, 539 cm^{-1}. HRMS-ESI calcd for $C_{14}H_{14}O_2NBrNa$ $[M+Na]^+$ 330.0100, found 330.0100.

3-Acetyl-3-allyl-4,6-dimethoxy-1-methylindolin-2-one (**4i**): Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=5∶1). Yellow oil. 52.1 mg, 60% yield. m.p. 72～73 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.17 (d, J=15.6 Hz, 2H), 5.28～5.17 (m, 1H), 4.97 (d, J=16.8 Hz, 1H), 4.81 (d, J=9.6 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.22 (s, 3H), 3.07～3.02 (m, 1H), 2.94～2.89 (m, 1H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.3, 174.3, 162.5, 156.7, 146.4, 132.5, 118.5, 105.7, 92.5, 88.7, 65.9, 55.7, 55.5, 34.8, 26.8, 26.1; IR (neat) ν: 2920, 1706, 1603, 1467, 1373, 1257, 1214, 1146, 1069, 822, 597 cm^{-1}. HRMS-ESI calcd for $C_{16}H_{20}O_4N$ $[M+H]^+$ 290.1387, found 290.1387.

3-Acetyl-3-allyl-1,6-dimethylindolin-2-one and 3-acetyl-3-allyl-1,4-dimethylindolin-2-one (**4j** and **4j'**): Purified by flash column chromatography (eluent: petroleum ether/ethyl acetate, V∶V=15∶1). Yellow oil. 61.2 mg, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28～7.26 (m, 0.75H), 7.06～7.04 (m, 0.40H), 6.92～6.87 (m, 1H), 6.76～6.72 (m, 1H), 5.36～5.25 (m, 0.40H), 5.21～5.10 (m, 0.64H), 3.27～3.26 (m, 2H), 3.17～2.81 (m, 2H), 2.41 (s, 1.15H), 2.19 (s, 1.83H), 1.97 (s, 1.12H), 1,78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.0, 200.1, 174.9, 174.1, 144.8, 144.4, 139.6, 135.3, 131.7, 131.7, 129.2, 125.6, 124.8, 124.1, 123.9, 123.8, 119.4, 118.8, 109.5, 106.3, 67.3, 66.3, 37.5, 34.8, 26.8, 26.6, 26.5, 26.1, 22.0, 17.9; IR (neat) ν: 2919, 1702, 1610, 1468, 1354, 1183, 1056, 918, 774, 739, 591 cm^{-1}. HRMS-ESI calcd for $C_{15}H_{18}O_2N$ $[M+H]^+$ 244.1332, found 244.1331.

Supporting Information Experimental procedures, the synthesis method of the starting materials, and compound characterization dat. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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