Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
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Cite this: *Org. Biomol. Chem.*, 2021, **19**, 3173

# Sulfur-controlled and rhodium-catalyzed formal (3 + 3) transannulation of thioacyl carbenes with alk-2-enals and mechanistic insights†

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Received 22nd January 2021,
Accepted 15th March 2021

DOI: 10.1039/d1ob00116g

rsc.li/obc

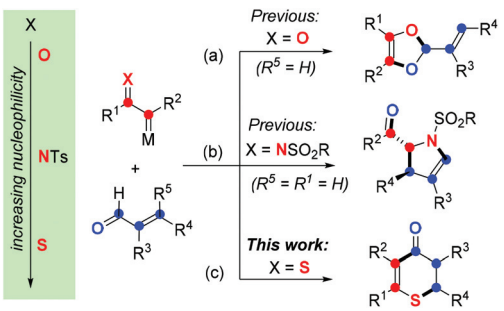
A rhodium-catalyzed denitrogenative formal (3 + 3) transannulation of 1,2,3-thiadiazoles with alk-2-enals is achieved, producing 2,3-dihydrothiopyran-4-ones in moderate to excellent yields. An inverse KIE of 0.49 is obtained, suggesting the reversibility of the oxidative addition of thioacyl Rh(I) carbenes to alk-2-enals. The late-stage structural modifications of steroid compounds are realized. Moreover, our studies show that thioacyl carbenes have different reactivities to those of α-oxo and α-imino carbenes, and highlight the importance of heteroatoms in deciding the reactivities of heterovinyl carbenes.

## Introduction

The transannulations of heterovinyl transition-metal-carbenes with unsaturated compounds represent some of the most important approaches to heterocycles. Transition metal catalyzed transannulations of α-oxo and α-imino carbenes have provided various elegant constructions of structurally diverse oxa- and azacycles, respectively.[1,2] Since 2016, Gevorgyan's,[3] Lee's,[4] and Nakajima and Nishibayashi's[5] groups demonstrated that thioacyl carbenes (also referred to as thiavinyl carbenes) were able to transannulate with alkynes, alkenes, nitriles, and phosphaalkynes to give five-membered thiacycles in the presence of a rhodium catalyst. It must be mentioned that it is Gevorgyan's group that made seminal breakthroughs in generating α-imino and thioacyl carbenes and disclosing their reactivities.[3a,6] Nowadays, one of the central and important research areas in the thioacyl carbene field is to exploit new transannulative partners and explore new and unique reactivities of thioacyl carbenes.

Alk-2-enals are versatile building blocks in the synthesis of heterocycles and natural products.[7] Initially we envisioned that they might be potential transannulative partners of thioacyl carbenes. A literature survey revealed that the transition metal-catalyzed transannulations of alk-2-enals with α-oxo and α-imino carbenes had been exploited. As reported by Alonso and coworkers in 1985,[8] with a Cu(II) catalyst, the α-oxo carbenes generated from α-diazoketones underwent (3 + 2) transannulation with the C=O bonds of alk-2-enals to produce 1,3-dioxoles (Scheme 1a). In 2013, a novel reaction of alk-2-enals and α-imino carbenes derived from *N*-sulfonyl-1,2,3-triazoles was developed by Miura and Murakami's group to stereoselectively synthesize *trans*-2,3-disubstituted 2,3-dihydropyrroles (Scheme 1b).[9] Mechanistically, the (3 + 2) transannulation of α-imino carbenes with the formyl group of alk-2-enals and a subsequent ionic rearrangement of the resultant 4-oxazoline intermediates were involved. In these two cases, these two types of products were virtually decided by the electrophilic nature of acyl carbenes and α-imino carbenes. In other words, the different electronegativity and nucleophilicity of heteroatoms in the heterovinyl metal–carbenes led to different reactivities.

On the basis of the reports mentioned above and from our background of sulfur chemistry[10] and carbene chemistry,[11] we envisioned that replacement of the respective oxygen atom or




**Scheme 1** Reactions of α-oxo, α-imino, and α-thioxo metal carbenes with alk-2-enals.

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†Electronic supplementary information (ESI) available: Detailed experimental procedures, analytical data and copies of NMR ($^{1}$H, $^{19}$F, and $^{13}$C) spectra of products **1–6**, **12** and **13**; copies of $^{1}$H NMR spectra of crude reaction mixtures. CCDC 1919688. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ob00116g

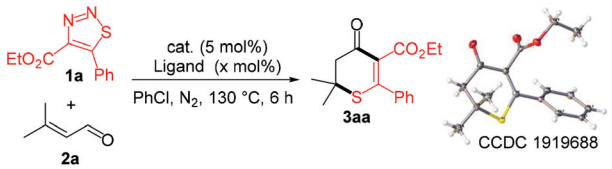
$NSO_2R$ group of the aforementioned two classes of carbenes with the sulfur atom might enable a new transannulation mode in the reaction of alk-2-enals. By harnessing the stronger nucleophilicity of the sulfur atom in the thioacyl group, we, herein, realize a formal (3 + 3) transannulation of thioacyl Rh–carbenes with alk-2-enals, giving 2,3-dihydrothiopyran-4-ones as products (Scheme 1c). Our studies highlight the importance of heteroatoms in heterovinyl carbenes in deciding their reactivity, and provide a novel method to construct 2,3-dihydrothiopyran-4-ones,[12] which are important intermediates in organic synthesis and the preparation of high electrical conductivity materials, and also show some biological activities.[13]

## Results and discussion

### Optimization of conditions

The optimization of reaction conditions was performed by using 1,2,3-thiadiazole **1a** as the α-thioxo carbene precursor and 3-methylcrotonaldehyde (**2a**) as a transannulation partner (Table 1, for more details see Table S1 in the ESI†). Under standard conditions, the desired (3 + 3) product **3aa** was isolated in 72% yield (entry 1). No reaction occurred without the ligand DPPF (entry 2). The use of $[RhCp^*Cl_2]_2$ led to a slightly lower 63% yield (entry 3). Changing the selected diphosphine ligands did not afford as good results as using DPPF (entries 4–8). Monodentate ligands, whether electron-deficient triarylphosphines (entries 9–11) or electron-rich phosphinates (entries 12 and 13), only gave a trace amount of product **3aa**. Using toluene as a solvent gave a moderate 54% yield (entry 14). Reactions at lower temperature gave poor results (entries 15 and 16). Even under the optimal conditions (entry 1), **1a** was not completely consumed, and some unidentified mixtures, as shown by $^1$H NMR, were also isolated.

Table 1 Optimization of reaction conditions[a]



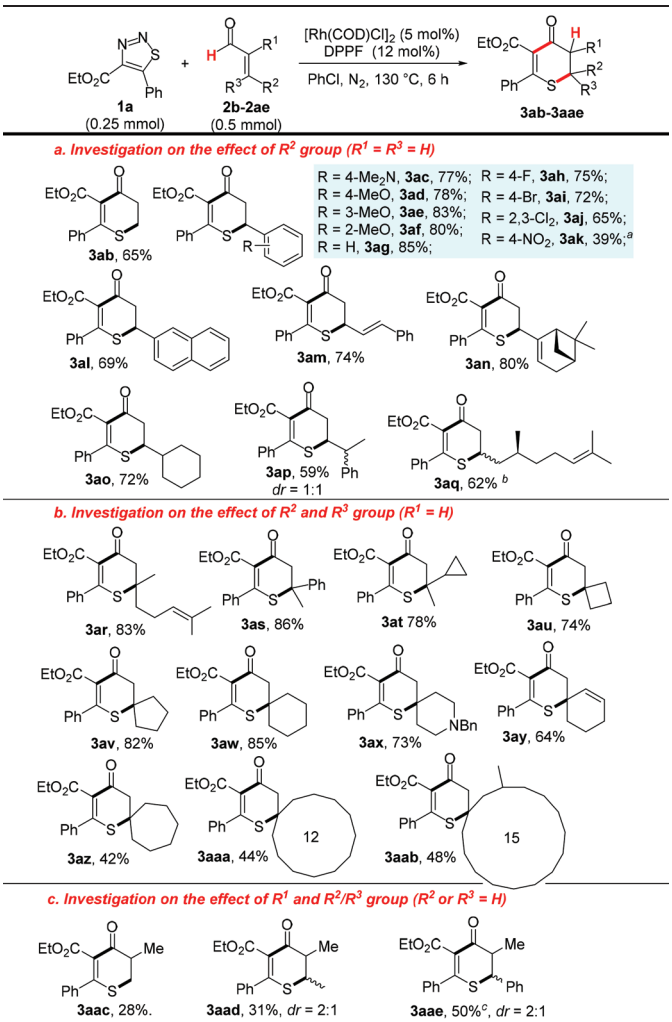

| Entry | Cat. | Ligand (mol%) | Yield[b] (%) |
|---|---|---|---|
| 1 | $[Rh(COD)Cl]_2$ | DPPF (12) | 72 |
| 2 | $[Rh(COD)Cl]_2$ | — | Trace |
| 3 | $[RhCp^*Cl_2]_2$ | DPPF (12) | 63 |
| 4 | $[Rh(COD)Cl]_2$ | DPPM (12) | Trace |
| 5 | $[Rh(COD)Cl]_2$ | DPPE (12) | 6 |
| 6 | $[Rh(COD)Cl]_2$ | DPPP (12) | 8 |
| 7 | $[Rh(COD)Cl]_2$ | DPPB (12) | 15 |
| 8 | $[Rh(COD)Cl]_2$ | DPPPenta (12) | 3 |
| 9 | $[Rh(COD)Cl]_2$ | $PPh_3$ (24) | Trace |
| 10 | $[Rh(COD)Cl]_2$ | $P(4\text{-}CF_3C_6H_4)_3$ (24) | Trace |
| 11 | $[Rh(COD)Cl]_2$ | $P(C_6F_5)_3$ (24) | Trace |
| 12 | $[Rh(COD)Cl]_2$ | $P(OEt)_3$ (24) | Trace |
| 13 | $[Rh(COD)Cl]_2$ | $P(OPh)_3$ (24) | Trace |
| 14[c] | $[Rh(COD)Cl]_2$ | DPPF (12) | 54 |
| 15[d] | $[Rh(COD)Cl]_2$ | DPPF (12) | 3 |
| 16[e] | $[Rh(COD)Cl]_2$ | DPPF (12) | Trace |

[a] Reactions were performed using **1a** (0.25 mmol) and **2a** (0.50 mmol) under the indicated conditions. [b] Yield obtained by column chromatography. [c] Toluene as the solvent. [d] Reaction temperature 100 °C. [e] Reaction temperature 60 °C.

### Substrate scope and substituent effect

In our previous work on the (3 + 3) transannulation of thioacyl carbenes with alk-2-ynals,[14] some examples of the (3 + 3) transannulation of thioacyl carbenes with alk-2-enals were divulged. However, alk-2-enals **2** possess more substituents ($R^1$, $R^2$, $R^3$ in Table 2) at the α- and β-positions. Thus, it is necessary to further disclose the details of the transannulations of alken-2-als with thioacyl carbenes. The substrate scope and substituent effect of alk-2-enals on the (3 + 3) transannulation have been studied and the results are presented in Table 2.

Table 2 Scope of alk-2-enals




[a] Together with 21% yield of 4-nitrostyrene and 24% recovery of 4-nitrocinnamaldehyde (**2k**). [b] The dr could not be determined by $^1$H NMR. [c] 10 mol% $[Rh(COD)Cl]_2$, 24 mol% DPPF, 12 h.

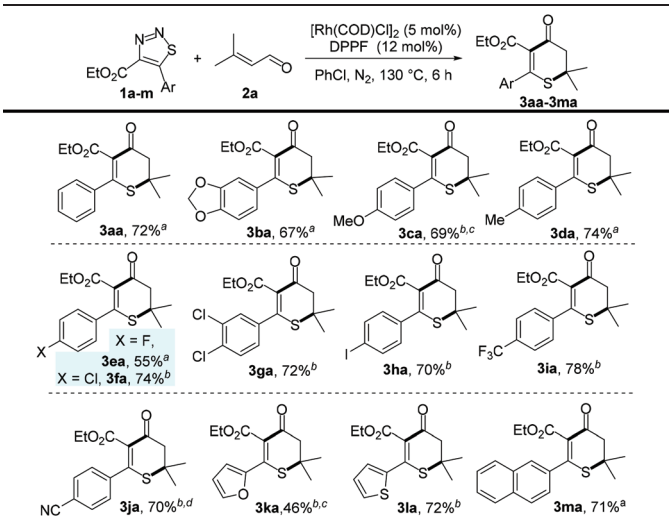
We first investigated the β-substituent effect of (*E*)-alk-2-enals **2c–2q** by reacting them with thiadiazole **1a** under the optimal conditions (Table 2a). Compared with the reaction of acrylaldehyde ($R^1$ = $R^2$ = $R^3$ = H, **2b**), the presence of a β-substituent ($R^2$) greatly facilitated the transannulations, and the product yields were improved to 39–80% (**3ac–3ap**). The electronic properties of β-aryls were relevant to the yields. Strong electron acceptors such as the nitro group on the aryl group gave **3ak** in a lower yield of 39%. The reaction of 3-(naphthalen-2-yl)acrylaldehyde (**2l**) and thiadiazole **1a** furnished **3al** in 69% yield, showing their excellent reactivity toward (3 + 3) transannulation. The (3 + 3) transannulation was promoted by the β-alk-1-enyl groups of alk-2-enals **2m** and **2n**, regardless of their steric hindrance, and the desired products **3am** and **3an** were isolated in 74% and 80% yields, respectively. Also investigated was the β-alkyl effect of alk-2-enals **2o** and **2p**. The branched secondary alkyls (**2o** and **2p**) and long-chain branched primary alkyl (**2q**) did not suppress the transannulations, with the desired products obtained in 59–72% yields. Notably, when a steric center was present in alk-2-enals **2**, two diastereomers were generated (**3ap** and **3aq**) because a new stereocenter (C6 position) was forged in 2,3-dihydrothiopyran-4-ones when the transannulation occurred.

Alk-2-enals **2r–2ab** with two β-substituents ($R^2$ and $R^3$) were also tested (Table 2b). The reactions of β,β-dimethyl (**2a**, Table 1), β-methyl-β-(4-methyl)pent-3-enyl (**2r**), β-methyl-β-phenyl (**2s**), and β-cyclopropyl-β-methyl enals (**2t**) with **1a** took place readily, and the desired products **3aa**, **3ar**, **3as**, and **3at** were isolated in 70–86% yields. In Lee's report, alkenes readily reacted with 1,2,3-thiadiazole **1a** under similar conditions. However, in our work, the trisubstituted (**2q** and **2r**) and disubstituted alkene (**2m** and **2y**) moieties remained intact. In addition, the ring-opening of cyclopropane moieties was frequently involved in Rh(I)-catalyzed carbocycle syntheses.[15] However, they were well tolerated under our conditions. These cases indicated the priority of alk-2-enals over alkenes and cyclopropanes when they reacted with thioacyl Rh–carbenes. The reactions of β,β-(1,*n*-alkylidene)enals or their analogues **2u–2ab**, namely, $R^2$ and $R^3$ were connected together, gave spiro products **3au–3aab** in moderate to good yields. The ring size of these cycloalkylideneacetaldehydes and their analogues, together with other factors, if any, largely affected the transannulations. The four-, five-, and six-membered enals **2u–2y** transannulated well to give the desired spiro products **3au–3ay** in 64–85% yields, while those with seven-, twelve-, and fifteen-membered rings only gave the corresponding spiro products **3az–3aab** in moderate 42–48% yields.

The α-monosubstituted and α,β-disubstituted alkenals **2ac–2ae** showed low activity toward the (3 + 3) transannulation with thioacyl Rh–carbenes, and the desired products **3aac–3aae** were isolated in only 28–50% yields (Table 2c). These examples demonstrated that the presence of an α-substituent of alkenals **2** disfavored the desired (3 + 3) transannulation.

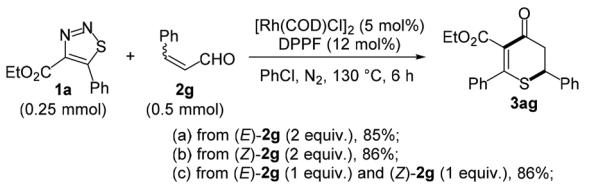
On the other hand, the scope of 1,2,3-thiadiazoles **1** was also screened by reacting with 3-methylbut-2-enal (**2a**) under the optimal conditions (Table 3). A variety of ethyl 5-aryl-1,2,3-thiadiazole-4-carboxylates **1** were able to undergo the transannulation to give the desired 2,3-dihydrothiopyran-4-ones **3** in 46–78% yields of the isolated products. The well-tolerated functional groups include but are not limited to methyl-enedioxy, halogen atoms, cyano, fur-2-yl, and thiophen-2-yl. However, the reaction of 5-(fur-2-yl) thiadiazole (**1k**) gave a relatively low yield of 46%. Lee and coworkers have demonstrated that aryl nitriles were viable substrates to undergo (3 + 2) transannulation with thioacyl Rh(I)–carbenes derived from 1,2,3-thiadiazoles. However, in the case of **1j**, the cyano group survived.

Table 3 Scope of 1,2,3-thiadiazoles




[a] 0.25 mmol of **1**, 0.5 mmol of **2a**, and 1 mL PhCl were used. [b] 0.1 mmol of **1**, 0.3 mmol of **2a**, 10 mol% $[Rh(COD)Cl]_2$, 24 mol% DPPF, 20 mol% $AgBF_4$, and 0.5 mL PhCl were used. [c] Reaction for 12 h. [d] Reaction for 10 h.

In the above reports, most of the β-monosubstituted alkenals **2b–2p** possessed the *E*-configuration. We studied the configuration effect of the alkenyl moiety on the (3 + 3) transannulation. With 2 equivalents of (*E*)-**2g** or (*Z*)-**2g**, the same product **3ag** was obtained in 85% or 86% yield, respectively (Scheme 2a and b). With 1 equivalent of (*E*)-**2g** and 1 equivalent of (*Z*)-**2g**, **3ag** was also obtained in 86% yield (Scheme 2c). These results show that the (*Z*)- or (*E*)-configurations of alken-2-als do not affect their reactivity toward the formal (3 + 3) transannulations.




Scheme 2 Effect of the configuration of alkenals **2g**.

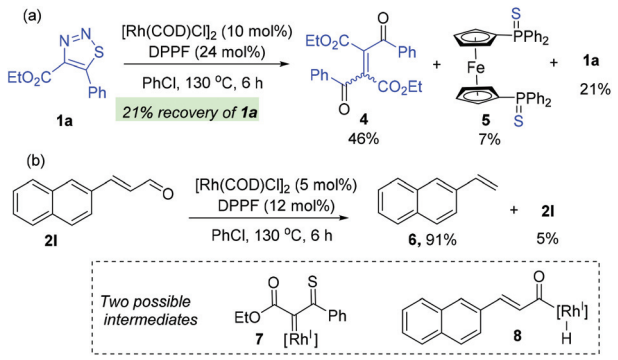
### Mechanistic studies and proposal

We sought to probe the key intermediates in the present formal (3 + 3) transannulation of alk-2-enals **2**. Although thioacyl Rh–carbenes were proposed as intermediates in Gevorgyan's, Lee's, and Nakajima and Nishibayashi's work to react with alkynes, alkenes, nitriles, and phosphaalkynes,[3–5] they were never probed, isolated or characterized. Initially, we attempted to isolate the thioacyl Rh–carbenes by directly mixing thiadiazole **1a** with $[Rh(COD)Cl]_2$ and different bidentate phosphine ligands. However, none of the trials prevailed. For example, heating **1a**, $[Rh(COD)Cl]_2$, and DPPF at 130 °C for 6 h caused the decomposition of thiadiazole **1a**, and the carbene dimer **4** and bisphosphine sulfide **5** were isolated in 46% and 7% yields, respectively, together with the recovery of **1a** in 21% yield (Scheme 3a). Apparently, compound **4** was generated from dimerization of the thioacyl Rh–carbene, with the desulfurization occurring before or after the dimerization. The lost sulfur was partially accepted by the phosphine ligand. In other words, the presence of the carbene dimer **4** was indirect evidence for the existence of thioacyl carbenes. Recently, Bao and coworkers proposed that the denitrogenation of 1,2,3-thiadiazoles promoted by the Rh(I) catalyst might not afford the commonly proposed α-thiavinyl Rh-carbenoid intermediates, based on their DFT calculation results on the Rh(I)-catalyzed transannulation of 1,2,3-thiadiazoles with alkenes, alkynes, and nitriles.[16] However, our experimental result (Scheme 3a) suggested the carbene intermediates. Additionally, alk-2-enal **2l** was also subjected to the optimal conditions, and decarbonylation product **6** was isolated in 91% yield, together with 5% recovery of **2l** (Scheme 3b). It was evidenced that the acyl rhodium hydride was involved as the key intermediate in the decarbonylation of alkenals.[17] The above two intermediate probing experiments suggested that thioacyl Rh–carbenes or acyl rhodium hydrides were probably involved in the dehydrogenative transannulation of alk-2-enals **2** and thiadiazoles **1**.

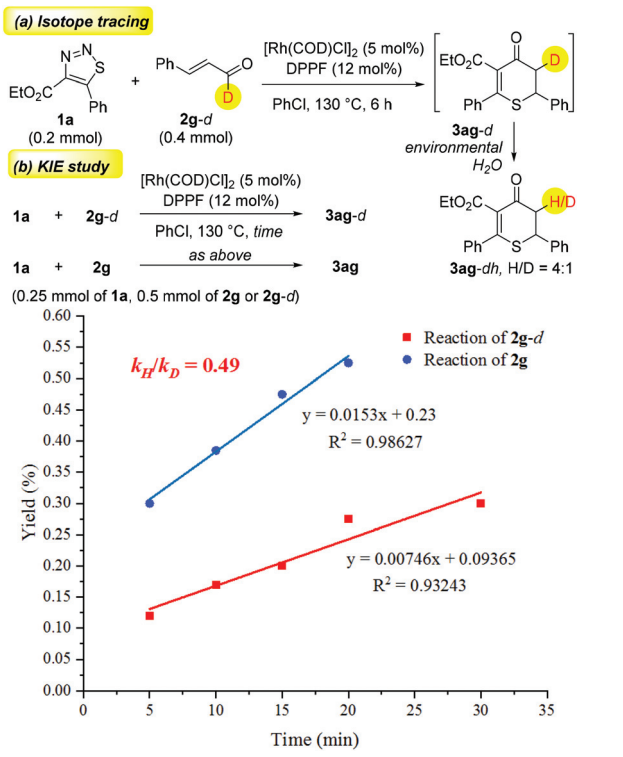
In our previous work on the Rh-catalyzed transannulation between alk-2-ynals and 1,2,3-thiadiazoles **1**,[14] we proposed a 1,1-hydroacylation and subsequent 6-*endo*-*dig* cyclization mechanism involving the Rh-catalyzed 1,1-hydroacylation of thioacyl carbenes with the formation of the acyl rhodium hydride as the turnover-limiting step. In the mechanism, a primary kinetic isotope effect (KIE) with $k_H/k_D$ = 3.07 was observed. Since alk-2-enals **2** are structurally different from alk-2-ynals, does the present transannulation of alk-2-enals follow the same mechanism as that of alk-2-ynals?

To answer this question, we first performed an isotope tracing experiment by reacting thiadiazole **1a** with cinnamaldehyde-*d* (**2g**-*d*) (Scheme 4a). The desired product **3ag**-*dh* was isolated in 55% yield, and the deuterium atom of **2g**-*d* was partially transferred to the 5-position of **3ag**-*dh*, and a 4 : 1 H/D ratio was determined by the $^1$H NMR analysis of **3ag**-*dh*. The low deuterium incorporation was attributed to the highly acidic C–D bonds of intermediate **3ag**-*d*, and probably resulted from D–H exchange of **3ag**-*d* with environmental water during purification or the NMR test. This result also implied that it was inappropriate to use the intermolecular competition experiment with equimolar **2g**-*d* and **2g** in one pot to determine the KIE of the transannulation. Thus, we performed the KIE studies using the initial rate method with two parallel experiments of **2g**-*d* and **2g** (Scheme 4b). To our surprise, an inverse primary KIE of $k_H/k_D$ = 0.49 was obtained, in sharp contrast with our previous KIE studies ($k_H/k_D$ = 3.07) on the transannulation of alk-2-ynals and 1,2,3-thiadiazoles **1**. Therefore, the current transannulation mechanism appeared to be different from that for the alk-2-ynal transannulation.

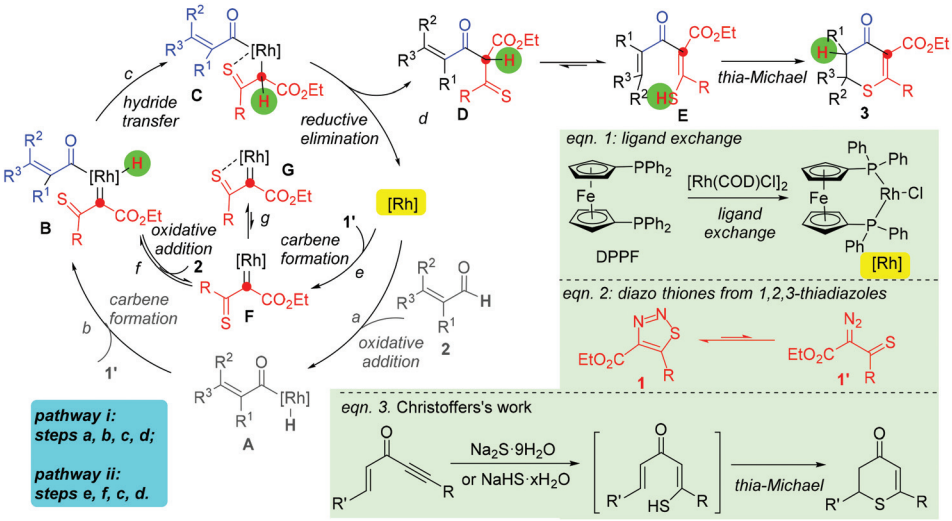
Based on the intermediate probing experiments, two plausible mechanistic pathways are proposed (Scheme 5). The ligand exchange between DPPF and $[Rh(COD)Cl]_2$ affords an




Scheme 3 Key intermediate probing experiments.




Scheme 4 (a) Isotope tracing experiment; (b) KIE studies using the initial rate method.




**Scheme 5** Proposed mechanism involving thioacyl Rh–carbenes.

active catalyst [Rh] (eqn (1)). In pathway i, the catalyst [Rh] undergoes an oxidative addition to form acyl rhodium hydrides **A** (step a). Subsequently, denitrogenative carbene formation between thiadiazoles **1** (possibly *via* their diazo form **1′**) and **A** occurs to give carbene intermediates **B** (step b). Alternatively, in pathway ii, the first decomposition of thiadiazoles **1** gives thioacyl carbenes **F** (step e). Because of the relatively high nucleophilicity of the sulfur atom of the thioacyl group, we suggest that the sulfur coordinates with the center Rh(I) metal to render stabilized carbenes **G** (step g). Oxidative addition of **F** to alk-2-enals **2** also furnishes **B** (step f). The formation of oxonium ylides from **F** and aldehydes is not considered, as these intermediates probably lead to direct (3 + 2) or (3 + 4) transannulations, not in accordance with our (3 + 3) transannulations.[18] Intramolecular 1,2-hydride transfer of **B** delivers intermediates **C** (step c), whose reductive elimination regenerates the catalyst and produces β-thioacyl enones **D** (step d). Tautomerization of **D** to **E** followed by intramolecular thia-Michael addition delivers the desired products **3**, which is in high accordance with Christoffers's synthesis of 2,3-dihydrothiopyran-4-ones from pent-1-en-4-yn-3-ones and sodium sulfide or sodium hydrosulfide in the presence of water (eqn (3)).[19]

We believe that the KIE ($k_H/k_D$) may play an important role in distinguishing the two mechanistic pathways. The key differences between the two mechanistic pathways (i and ii) rely on how intermediates **B** are formed (steps a and b, or steps e and f). Pathway i features acyl rhodium hydrides **A**, and is quite similar to that of the alk-2-ynal transannulation proposed in our previous work.[14] Pathway ii is characteristic of thioacyl carbenes **F**, and is consistent with various transannulations reported by Gevorgyan's,[3] Lee's,[4] and Nakajima and Nishibayashi's[5] groups. In the case of Rh(I)-catalyzed reactions involving acyl hyrides **A**, for example, hydroacylations of ketones and alkenes with aldehydes[20] as well as decarbonylation of aldehydes,[21] primary KIEs varying from 2.4 to 2.9 were observed by numerous groups. In our previous work associated with hydroacylation of carbenes with aldehydes,[14] a primary KIE of 3.07 was observed. In these reports, the irreversible oxidative addition of Rh(I) to the formyl C–H bond (step a), which leads to the formation of acyl rhodium hydrides **A**, is proposed as the rate-determining step. In addition, KIEs of 1.4–1.7 were also reported for other hydroacylation reactions, indicating that migratory insertion (similar to step c) or reductive elimination (similar to step d) might act as the rate-determining step.[22] In light of the above reports, if the denitrogenative transannulation of 1,2,3-thiodiazoles **1** and alk-2-enals **2** follows pathway i, a KIE of around 2.4–3.07 or 1.4–1.7 might be obtained, depending on which step is the rate-determining step. However, in fact, we measured a KIE of 0.49, and this could not be explained by the mechanism of pathway i.

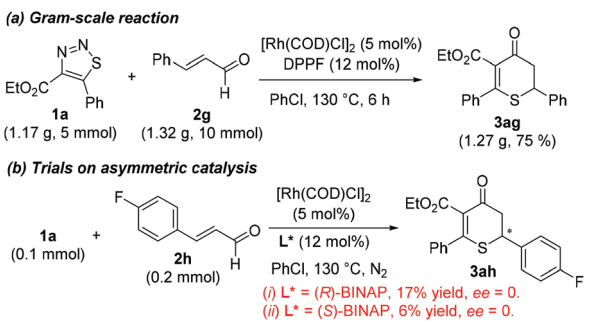
Faced with the contradiction, we turned to the mechanism of pathway ii, and now the key problem is how to explain the inverse KIE of 0.49. Within this pathway, the first step involves the irreversible denitrogenative carbene formation, and has no relation to the KIE. The hydride transfer (step c) or reductive elimination (step d), according to the aforementioned previous work,[18–20] occurring either irreversibly fast,[20,21] or relatively slow to contribute to a KIE of 1.4–1.7,[22] cannot account for a KIE of 0.49. Recent advances on the equilibrium isotope effect (EIE) have revealed that a low inverse KIE value (for example, less than 0.6) in the C–H activation process may arise from the equilibrium between oxidative addition and reductive elimination.[23] Inspired by this, we suggest the oxidative addition of carbene-ligated Rh(I) (**F**) to alk-2-enals **2** (step f) to form carbene-ligated acyl rhodium hydrides **B** reversibly. The EIE value is theoretically the ratio of the forward and reverse KIEs. In step f, intermediates **F** are the reactants and **B** are the products. Thus, oxidative addition from **F** to **B** is the forward reaction, and reductive elimination from **B** to **F** is the reverse reaction. Obviously, the thioacyl carbene ligand is important to render step f reversible. From a simple electronic perspective,

the coordination of thioacyl carbenes with the catalyst [Rh] makes the metal center more electron-rich (16e configuration of **F**, and 18e configuration of **G**), and lowers their ability to undergo oxidative addition. On the other hand, the electronic richness of the metal center (18e configuration) of **B** grants them a high tendency to undergo reductive elimination. As a result, a reversibility between **F** and **B** emerges and leads to an EIE of 0.49. Thus, the mechanism containing thioacyl carbenes **F** (pathway ii) is plausibly favored.

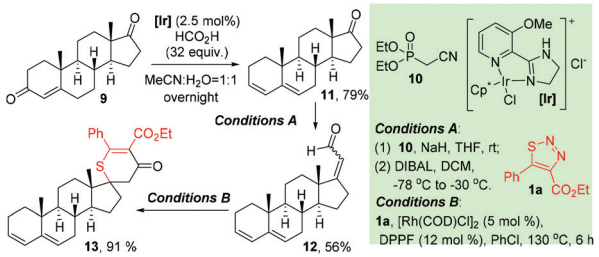
Returning to Scheme 1, the transannuloselectivity can be well explained. Both the α-oxo and α-imino carbenes are electrophilic, and the carbenic centers directly react with the nucleophilic oxygen atom of the alk-2-enals to form ylide intermediates; subsequent cyclization (for Scheme 1a)[8] or rearrangement–cyclization (for Scheme 1b)[9] gave the desired five-membered cycles. It is the electrophilic nature of the two kinds of carbenes that governs the transannuloselectivity toward five-membered products. However, in the case of thioacyl carbenes, it is the reversible oxidative addition between the carbene-ligated metal and alk-2-enals that decides the transannuloselectivity toward six-membered cycles; the carbene center does not directly participate in the formation of the C(carbene)–C(formyl) bond. In other words, the α-oxo and α-imino carbenes act as actor ligands, while the thioacyl carbenes act as spectator ligands. Such a reactivity difference is attributed to the heteroatoms of the α-heterovinyl groups of the three types of carbenes.

### Gram-scale synthesis and trials on asymmetric catalysis

The transannulation was scaled up to a gram-scale synthesis. For example, the reaction of 1.17 g of thiodiazole **1a** with 1.32 g of cinnamaldehyde (**2g**) gave 1.27 g of the desired product **3ag** in 75% yield (Scheme 6a). The possibility of realizing an asymmetric catalytic reaction by changing the bidentate DPPF ligand to other chiral bisphosphine ligands was also exploited. However, the use of the (*R*)- or (*S*)-BINAP ligand did not render any optically active product (Scheme 6b). The results are in high accordance with the proposed mechanism in which the chiral center in the final product is formed by an intramolecular thia-Michael addition of nonchiral intermediate **E**, having no concern with the bisphosphine ligand.




Scheme 6 Gram-scale synthesis and trials on asymmetric catalysis.




Scheme 7 Modification of androst-4-en-3,17-dione.

### Synthetic applications

Our current rhodium-catalyzed formal (3 + 3) transannulation can be used in the late-stage structural modification of naturally occurring products. As exemplified in Scheme 7, by using our previously developed iridium-catalyzed reduction–elimination process, androst-4-en-3,17-dione (**9**) was readily converted to steroidal 3,5-dien-17-one **11**;[24] transformation of ketone **11** to enal **12** and subsequent transannulation with thioacyl Rh–carbene derived from thiadiazole **1a** gave pentacyclic product **13** in 91% yield, with the diene moiety excellently tolerated.

## Conclusions

We have realized a sulfur-controlled and rhodium-catalyzed formal denitrogenative (3 + 3) transannulation of 1,2,3-thiadiazoles with alk-2-enals, affording structurally diverse 2,3-dihydrothiopyran-4-ones in moderate to excellent yields, with good substrate scope and functional group tolerance. The substituent effects of alk-2-enals are investigated. The presence of an α-substituent suppresses the transannulation, while the other substituents promote the transannulation. Detailed mechanistic studies, especially the inverse KIE of $k_H/k_D$ = 0.49, suggest an equilibrium of oxidative addition and reductive addition between thioacyl rhodium carbenes and thioacyl carbene-ligated acyl rhodium hydrides. The present formal (3 + 3) transannulation has been demonstrated to be applicable in the late-stage structural modification of naturally occurring products. Moreover, the importance of the heteroatoms of heterovinyl carbenes in deciding their reactivities toward transannulations is demonstrated.

## Conflicts of interest

There are no conflicts of interest to declare.

## Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (No. 21602010 to Z. Y.) and the

Fundamental Research Funds for the Central Universities (XK1802-6 to Z. Y. and J. X.; No. 12060093063 to Z. Y.).

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