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Formal Lossen Rearrangement/Alkenylation or Annulation Cascade of Heterole Carboxamides with Alkynes Catalyzed by CpRh^{III} Complexes with Pendant Amides

Takayuki Yamada,[a] Yu Shibata,[a] and Ken Tanaka*,[a]

Abstract: It has been established that a cyclopentadienyl (Cp) Rh^{III} complex with two aryl groups and a pendant amide moiety catalyzes the formal Lossen rearrangement/alkenylation cascade of *N*-pivaloyl heterole carboxamides with internal alkynes, leading to alkenylheteroles. Interestingly, the use of sterically demanding internal alkynes afforded not the alkenylation but the [3+2] annulation products ([5,5]-fused heteroles). In these reactions, the pendant amide moiety of the CpRh^{III} complex may accelerate the formal Lossen rearrangement. The use of five-membered heteroles may deter reductive elimination to form strained [5,5]-fused heteroles; instead, protonation proceeds to give the alkenylation products. Whereas, bulky alkyne substituents accelerate the reductive elimination to allow the formation of the [5,5]-fused heteroles.

Introduction

Transition-metal-catalyzed C-H bond functionalization has been actively studied because of its step and atom economical nature.[1] Especially, a commercially available pentamethylcyclopentadienyl rhodium(III) (Cp*Rh^{III}) complex is one of the most frequently used catalysts for the C-H bond functionalization, and numerous efficient transformations have been reported to date.[2] To improve catalytic activity and selectivity, several research groups have been developed rhodium(III) complexes with modified Cp ligands,[3] and many successful applications have been reported.[4–6] Interestingly, examples in which the reaction pathways are changed by modification of the Cp ligands have also been reported. For example, the Rovis group reported that the [2+1] annulation and carboamination of *N*-enoxyphthalimides with alkenes are catalyzed by isopropylcyclopentadienyl (Cp^{iPr}Cy) and tetramethyl(*tert*-butyl)cycopentadienyl (Cp^{*tBu}) ligands, respectively (Scheme 1a).[7a,b] The Chang group reported that the [4+2] and [4+1] annulations of *N*-acyloxybenzamides with enynones are catalyzed by rhodium(III) complexes with tetramethyl(cyclohexyl)cyclopentadienyl (Cp*Cy) and trimethyl(diethoxycarbonyl)cyclopentadienyl (Cp^{E}) ligands, respectively (Scheme 1b).[7c]

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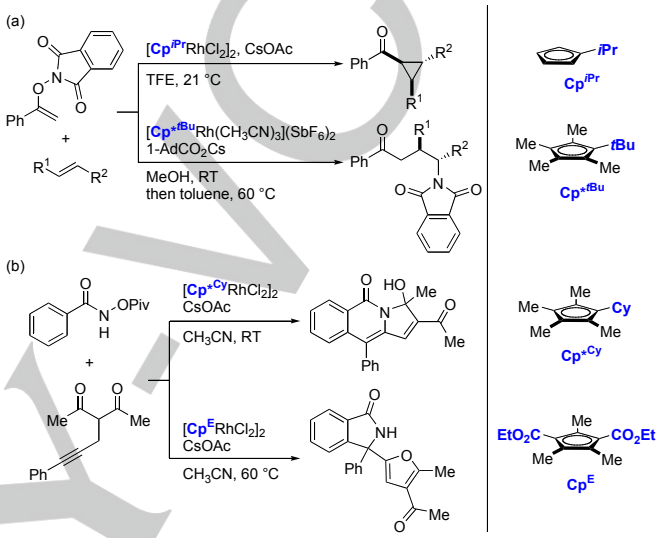
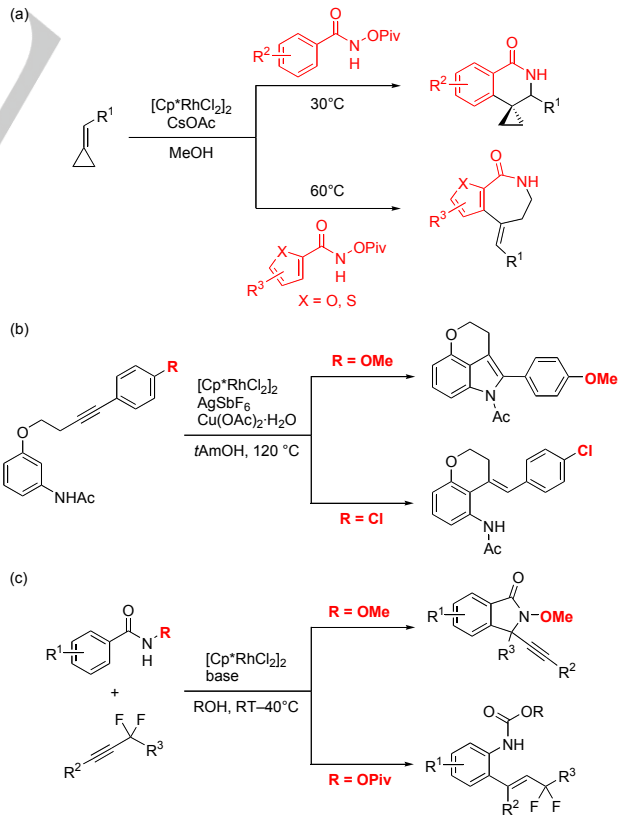


Scheme 1. Ligand-controlled changes of reaction pathways in rhodium(III)-catalyzed C-H bond functionalization. EWG = electron withdrawing group.



Scheme 2. Substrate-controlled changes of reaction pathways in rhodium(III)-catalyzed C-H bond functionalization.

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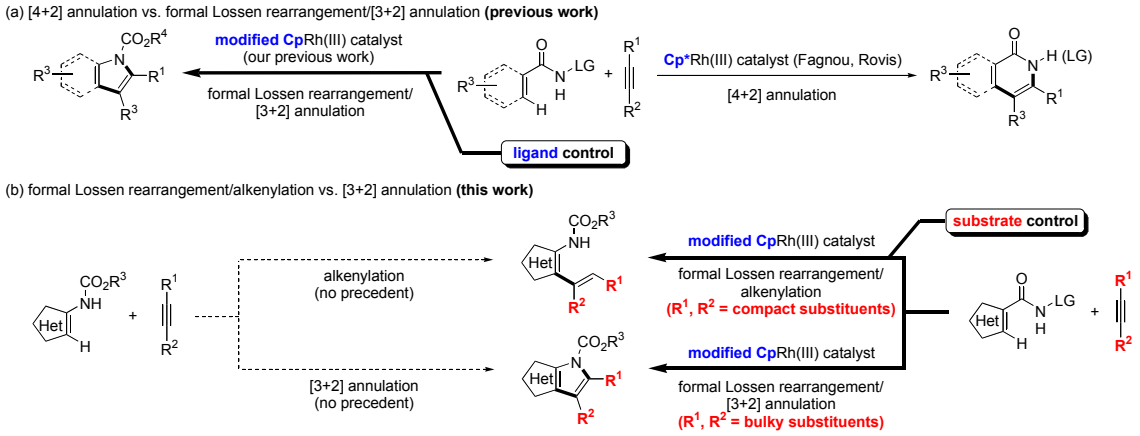

Scheme 3. Rhodium(III)-catalyzed annulation and alkenylation reactions. LG = leaving group.

Not only the ligand structure but also the substrate structure changes the reaction pathways.[8] For example, the Cui group reported that the reactions of methylenecyclopropanes with benzamides afford the [4+2] annulation products, but those with heterole carboxamides afford the [4+3] annulation products via β-carbon elimination followed by reductive elimination (Scheme 2a).[8a] The Xu and Liu groups reported that in the intramolecular reactions of anilides with alkynes, reductive elimination proceeds to give an annulation product when using an electron-rich alkyne, but protonation proceeds to give an alkenylation product when using an electron-deficient alkyne (Scheme 2b).[8b] The Loh and Feng groups reported that in the [4+2] annulation of *N*-acyloxybenzamides with internal alkynes, not reductive elimination but β-fluorine elimination or protonation proceeds to give [4+1] annulation[8c] or alkenylation[8d] products when using difluorinated internal alkynes (Scheme 2c). In these Cp^*Rh^{III}-catalyzed C-H bond functionalization reactions, substrate structures deter direct reductive elimination from rhodacycle intermediates.

In 2011, our research group reported the synthesis of an bis(ethoxycarbonyl)-substituted cyclopentadienyl rhodium(III) complex (Cp^ERh^{III}) via the rhodium(I)-catalyzed [2+2+1] cycloaddition of two ethyl 2-butynoates with triisopropylsilylacetylene, leading to a substituted silylfulvene, followed by its reductive complexation with $RhCl_3$ in ethanol.[9a] Pleasingly, this Cp^ERh^{III} complex showed significantly higher catalytic activity than the Cp^*Rh^{III} complex in the oxidative [3+2] annulation of anilides with internal alkynes.[9–11] Subsequently in 2017, we reported the synthesis of $CpRh^{III}$ complexes bearing a pendant amide moiety (Cp^ARh^{III}) via the rhodium(I)-catalyzed [2+2+1] cycloaddition of 1,6-diynes with cyclopropylideneacetamides, leading to substituted fulvenes, followed by their reductive complexation with $RhCl_3$ in ethanol.[12] Some of these Cp^ARh^{III} complexes also showed high catalytic activity in the oxidative [3+2] annulation of anilides with internal alkynes.[12–14] Interestingly, the use of the Cp^ARh^{III} complex in place of the Cp^*Rh^{III} complex changed the reaction pathways in the reactions of *N*-pivaloylbenzamides with internal alkynes. The Cp^ARh^{III} complex catalyzed not the previously reported [4+2] annulation, which is catalyzed by the Cp^*Rh^{III} complex (Scheme 3a, right),[15] but the formal Lossen rearrangement/oxidative [3+2] annulation cascade (Scheme 3a, left).[16,17]

In this paper, we have established that the substrate structure changes the reaction pathways in the Cp^ARh^{III} complex-catalyzed reactions. The use of *N*-pivaloyl heterole carboxamides in place of *N*-pivaloylbenzamides afforded not the formal Lossen rearrangement/oxidative [3+2] annulation products ([5,5]-fused heteroles) but the formal Lossen rearrangement/oxidative alkenylation products (alkenylated heteroles) (Scheme 3b, top right).[18] On the contrary, the use of bulky internal alkynes afforded not the alkenylated heteroles but [5,5]-fused heteroles (Scheme 3b, bottom right). Importantly, the above alkenylation and annulation products have not been prepared from the corresponding *N*-carbonyl aminoheteroles (Scheme 3b, left) due to their low stability and availability.[19]

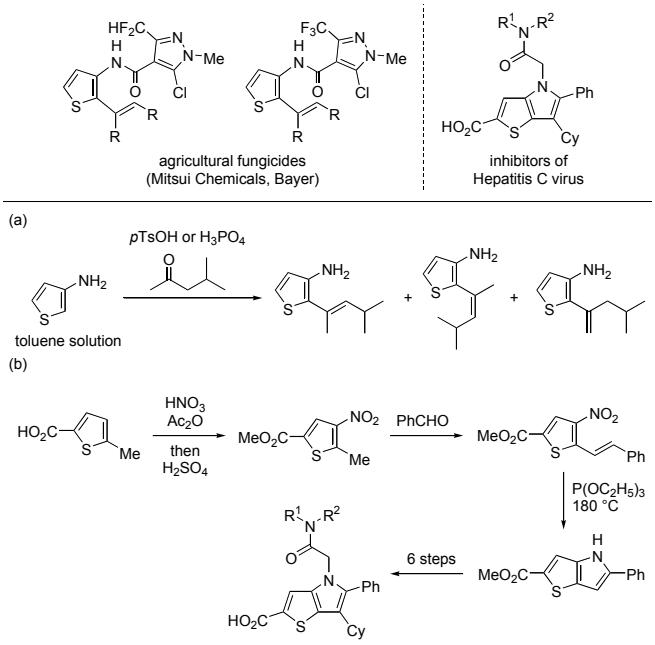

Figure 1. Structures and syntheses of biologically active alkenylated and [5,5]-fused thiophene derivatives.

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Furthermore, alkenylated and [5,5]-fused thiophene derivatives are found in biologically active compounds (e.g. agricultural fungicides[20] and inhibitors of the Hepatitis C virus[21], Figure 1, top), the syntheses of which are problematic. For example, the synthesis of the former compounds suffered from instability of the starting material (3-aminothiophene) and low regio- and stereoselectivities (Figure 1a),[20c] and the synthesis of the latter compounds suffered from the high-temperature reaction[21c] and long reaction steps[21c,d] (Figure 1b). Thus, the present cascade reactions involving the formal Lossen rearrangement of the stable *N*-pivaloyl heterole carboxamides might be synthetically useful.

Results and Discussion

As mentioned in the introduction, recent interests in the CpRh^{III} complex-catalyzed C-H functionalization are focused on modification of Cp ligands because this modification affects the catalytic activity and selectivity of their Rh^{III} complexes. The structures of the modified CpRh^{III} complexes, used in this research, are summarized in Figure 2. Newly developed Cp^{A}Rh^{III} complexes [Cp^{A4}RhCl$_2$]$_2$, [Cp^{A6}RhCl$_2$]$_2$, and [Cp^{A7}RhCl$_2$]$_2$ were prepared from the corresponding fulvenes **3aa**,[12] **3ba**,[12] and **3cb**, respectively, derived from 1,6-diynes **1a**–**c** and cyclopropylideneacetamides **2a**,**b**, by our previously reported protocol[12] in good yields.

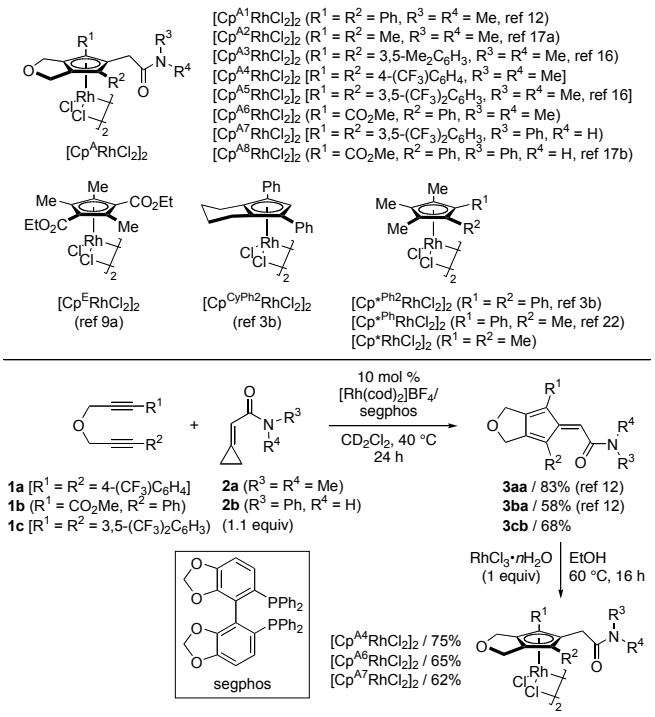
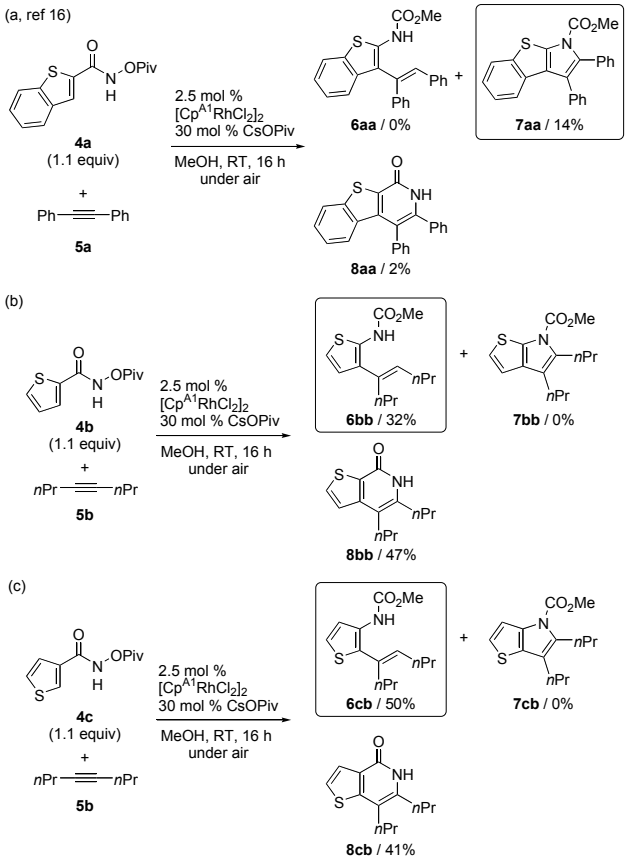


Figure 2. Structures and synthesis of modified CpRh^{III} complexes. cod = 1,5-cyclooctadiene.

In our previous report, the reaction of *N*-(pivaloyloxy)benzo[*b*]thiophene-2-carboxamide (**4a**) and diphenylacetylene (**5a**) using a Cp^{A1}Rh^{III} complex[12] as a catalyst afforded formal Lossen rearrangement/[3+2] annulation product **7aa** in low yield along with a trace amount of the non-rearranged [4+2] annulation product **8aa** (Scheme 4a).[16] Subsequently, we tested the reaction of *N*-(pivaloyloxy)thiophene-2-carboxamide (**4b**) and 4-octyne (**5b**) under the same reaction conditions. Unexpectedly, not [5,5]-fused heterole **7bb** but alkenylated thiophene **6bb** was generated in 32% yield along with non-rearranged [4+2] annulation product **8bb** in 47% yield (Scheme 4b). The use of *N*-(pivaloyloxy)thiophene-3-carboxamide (**4c**) instead of **4b** improved the yield of alkenylated thiophene **6cb** and decreased the yield of [4+2] annulation product **8cb** (Scheme 4c).



Scheme 4. Cp^{A1}Rh^{III} complex-catalyzed reactions of *N*-(pivaloyloxy)thiophene-carboxamides with internal alkynes.

Thus, the optimization of the reaction conditions to produce alkenylated thiophene **6cb** from **4c** and **5b** was studied systematically as shown in Table 1. With respect to the substituents on the Cp ring, the use of electron-rich Me (Cp^{A2})[17a] and 3,5-MeC$_6$H$_3$ (Cp^{A3})[16] derivatives decreased the yield of **6cb** and increased the yield of **8cb** (Table 1, entries 2 and 3), compared with the reaction using the Cp^{A1} ligand[12] (entry 1). On the contrary, the use of an electron-deficient 4-CF$_3$C$_6$H$_4$ (Cp^{A4}) derivatives increased the yield of **6cb** (entry 4). The use of more electron-deficient 3,5-(CF$_3$)C$_6$H$_3$ (Cp^{A5})[16] and CO$_2$Me/Ph (Cp^{A6}) derivatives dramatically increased the yield of **6cb** (entries 5 and 6). With respect to the amide substituents on the Cp ring, the use of Cp^{A7}, bearing the (*N*-

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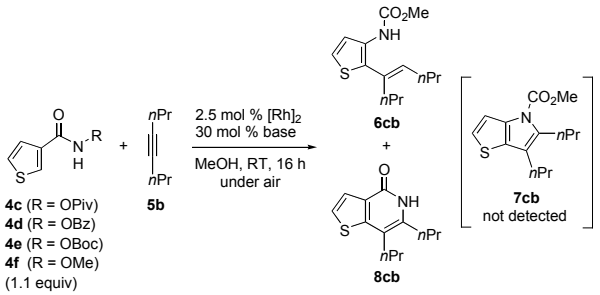
phenyl)carbamoylmethyl moiety, gave **6cb** in the highest yield (entry 7), although the use of the corresponding ester derivative (Cp^{A8})[17b] decreased the yield of **6cb** (entry 8). Screening of the leaving groups (**4d–f**, entries 9–11) and bases (entries 12–14) revealed that the use of OPiv and NaOAc further improves the yield of **6cb** (entry 14). The electron-deficient $Cp^{E}Rh^{III}$ complex was also effective for the formation of **6cb** (entry 15), but the yield did not exceed that using the $Cp^{A7}Rh^{III}$ complex (entry 14). Importantly, the use of a $Cp^{Cy\text{-}Ph2}Rh^{III}$ complex,[3b] the structure of which corresponds to the $Cp^{A1}Rh^{III}$ complex without the pendant amide moiety (entry 1), significantly lowered the yield of **6cb** (entry 16), Thus, not only the electron-deficient nature but also the presence of the pendant amide moiety may facilitate the formal Lossen rearrangement. The use of $Cp^{*Ph2}Rh^{III}$ and $Cp^{*Ph}Rh^{III}$ complexes[3b,22] further decreased the yields of **6cb** (entries 17 and 18), and the use of Cp* ligand afforded **8cb** exclusively (entry 19). It is worthy of noting that formal Lossen rearrangement/[3+2] annulation product **7cb** was not generated at all in all entries.

Table 1. Optimization of reaction conditions.[a]

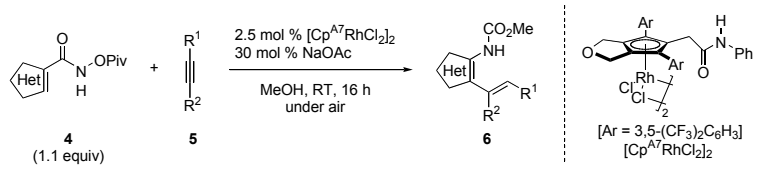


Entry	[Rh_2]	**4**	Base	Yield [%][b]	
				6cb	**8cb**
1	[$Cp^{A1}RhCl_2$]$_2$	**4c**	CsOPiv	50	41
2	[$Cp^{A2}RhCl_2$]$_2$	**4c**	CsOPiv	<2	84
3	[$Cp^{A3}RhCl_2$]$_2$	**4c**	CsOPiv	32	64
4	[$Cp^{A4}RhCl_2$]$_2$	**4c**	CsOPiv	63	26
5	[$Cp^{A5}RhCl_2$]$_2$	**4c**	CsOPiv	84	11
6	[$Cp^{A6}RhCl_2$]$_2$	**4c**	CsOPiv	84	11
7	[$Cp^{A7}RhCl_2$]$_2$	**4c**	CsOPiv	87	7
8	[$Cp^{A8}RhCl_2$]$_2$	**4c**	CsOPiv	81	14
9	[$Cp^{A7}RhCl_2$]$_2$	**4d**	CsOPiv	87	8
10	[$Cp^{A7}RhCl_2$]$_2$	**4e**	CsOPiv	82	9
11	[$Cp^{A7}RhCl_2$]$_2$	**4f**	CsOPiv	0	55
12	[$Cp^{A7}RhCl_2$]$_2$	**4c**	CsOAc	84	10
13	[$Cp^{A7}RhCl_2$]$_2$	**4c**	KOAc	87	9
14	**[$Cp^{A7}RhCl_2$]$_2$**	**4c**	**NaOAc**	**93**	**6**
15	[$Cp^{E}RhCl_2$]$_2$	**4c**	NaOAc	86	8
16	[$Cp^{Cy\text{-}Ph2}RhCl_2$]$_2$	**4c**	NaOAc	26	70
17	[$Cp^{*Ph2}RhCl_2$]$_2$	**4c**	NaOAc	18	71
18	[$Cp^{*Ph}RhCl_2$]$_2$	**4c**	NaOAc	4	88
19	[Cp*$RhCl_2$]$_2$	**4c**	NaOAc	0	98 (76[c])

[a] [Rh_2] (0.0025 mmol), base (0.030 mmol), **4** (0.11 mmol), **5b** (0.10 mmol), and solvent (0.5 mL) were used. [b] Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield.

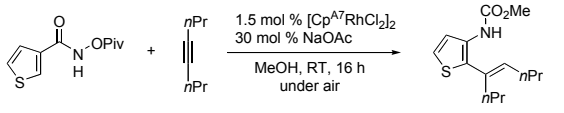
With the optimized reaction conditions in hand, we investigated the scope of the alkenylheterole synthesis, as shown in Scheme 5. With respect to the *N*-pivaloyl heterole carboxamides, the use of thiophene-3-carboxamide **4c** afforded the corresponding 2-alkenylthiophene **6cb** in high yield (entry 1). The reaction of furan-3-carboxamide **4g** afforded the desired 2-alkenylfuran **6gb** in moderate yield along with the non-rearranged [4+2] annulation product **8gb** (entry 2). Unfortunately, the reaction of 1*H*-pyrrole-3-carboxamide **4h** with **5b** was sluggish, and no coupling products were generated (entry 3). The bromo group on the thiophene ring (**4i**) was intact, and the desired product **6ib** was obtained in high yield (entry 4). The reaction of benzothiophene-3-carboxamide **4j** also afforded 2-alkenylbenzothiophen **6jb** in high yield along with formal Lossen rearrangement/[3+2] annulation product **7jb** in low yield (entry 5). Thiophene-2-carboxamide **4b** also reacted with **5b** to give the corresponding 3-alkenylthiophene **6bb** in moderate yield along with the non-rearranged [4+2] annulation product **8bb**, by using the $Cp^{A8}Rh^{III}$ complex (entry 6). Under the optimized conditions, the reaction of *N*-(pivaloyloxy)benzo[*b*]thiophene-2-carboxamide (**4a**) was reinvestigated, but the alkenylation reaction did not proceed, and the yields of annulation products decreased (entry 7). With respect of the internal alkynes, not only 4-octyne (**5b**) but also 6-dodecyne (**5c**) and diphenylacetylene (**5a**) could equally be employed (entries 8 and 9). Alkyl and phenyl-substituted unsymmetric internal alkynes **5d–f** were able to react with **4c** with good yields and regioselectivities (entries 10–12).

This cascade reaction could be carried out on a preparative scale, as shown in Scheme 6. The 1 mmol scale reaction with a low catalyst loading (1.5 mol % [Rh_2]) smoothly proceeded to give **6cb** in high yield of 93%.



Entry	4	5	Product / Yield	
1	**4c**	**5b**	**6cb** / 89%	
2	**4g**	**5b**	**6gb** / 47%	**8gb** / 9%
3	**4h**	**5b**	**6hb** / 0%	
4	**4i**	**5b**	**6ib** / 77%	
5	**4j**	**5b**	**6jb** / 76%	**7jb** / 10%
6[a]	**4b**	**5b**	**6bb** / 58%	**8bb** / 22%
7	**4a**	**5b**	**6ab** / 0%	**7ab** / 8%
			8ab / 6%	
8	**4c**	**5c**	**6cc** / 80%	
9	**4c**	**5a**	**6ca** / 88%	
10	**4c**	**5d**	**6cd** (**6cd'**) / 85% (**6cd**/**6cd'** = 89:11)	
11	**4c**	**5e**	**6ce** (**6ce'**) / 77% (**6ce**/**6ce'** = 89:11)	
12	**4c**	**5f**	**6cf** (**6cf'**) / 60% (**6cf**/**6cf'** = 87:13)	

Scheme 5. Scope of alkenylheterole synthesis. $[Cp^{A7}RhCl_2]_2$ (0.0050 mmol), **4** (0.22 mmol), **5** (0.20 mmol), NaOAc (0.060 mmol), and MeOH (1.0 mL) were used. Cited yields were of the isolated products. [a] $[Cp^{A8}RhCl_2]_2$ was used instead of $[Cp^{A7}RhCl_2]_2$.



Scheme 6 Preparative scale reaction.

Unexpectedly, the reaction of **4c** and bulky (cyclohexylethynyl)benzene (**5g**) gave strained [5,5]-fused heterole **7cg** as a major product along with alkenylated thiophene **6cg** and non-rearranged [4+2] annulation product **8cg** (entry 1, Table 2). Thus, we reinvestigated the catalysts for this formal Lossen rearrangement/oxidative [3+2] annulation of **4c** with **5g** (Table 2). The use of the $Cp^{A8}Rh^{III}$ complex that is more electron-deficient than the $Cp^{A7}Rh^{III}$ complex increased the yield of reductive elimination product **8cg**, and decreased the yield of formal Lossen rearrangement/protonation product **6cg**. However, the yield of formal Lossen rearrangement/reductive elimination product **7cg** was not changed (entry 2 vs entry 1). The more electron-deficient $Cp^{E}Rh^{III}$ complex was also tested, but the yields of **7cg** and **8cg** decreased simultaneously (entry 3). We anticipated that increasing the coordination ability of the pendant amide moiety would accelerate both the formal Lossen rearrangement and reductive elimination, which increase the yield of **7cg**. Pleasingly, the use of the $Cp^{A6}Rh^{III}$ complex

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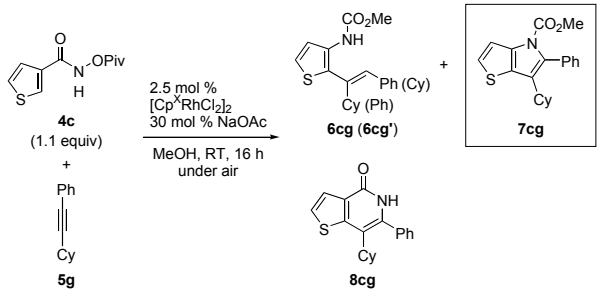
bearing the highly coordinative dimethylcarbamoyl group increased the yield of **7cg** to 55% (entry 4). As with the reaction of **4c** and **5b**, the use of the electron-rich $Cp^{A2}Rh^{III}$ complex predominantly afforded non-rearranged [4+2] annulation product **8cg** (entry 5).

Table 2. Screening of catalysts.[a]



Entry	$[Cp^XRhCl_2]_2$	Yield [%][b]		
		6cg+6cg' (6cg/6cg')[c]	**7cg**	**8cg**
1	$[Cp^{A7}RhCl_2]_2$	29 (71:29)	45	17
2	$[Cp^{A8}RhCl_2]_2$	9 (71:29)	45	29
3	$[Cp^{E}RhCl_2]_2$	9 (72:28)	35	20
4	**$[Cp^{A6}RhCl_2]_2$**	**11 (64:36)**	**55**	**22**
5	$[Cp^{A2}RhCl_2]_2$	0	2	72 (65[d])

[a] $[Cp^XRhCl_2]_2$ (0.0025 mmol), NaOAc (0.030 mmol), **4c** (0.11 mmol), **5g** (0.10 mmol), and MeOH (0.5 mL) were used. [b] Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [c] These compounds could not be isolated in pure forms. The yield and ratio were determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [d] Isolated yield. The product was isolated as a 94:6 mixture of regioisomers. See the Supporting Information.

The scope of the formal Lossen rearrangement/[3+2] annulation reaction is summarized in Scheme 7. Thiophene-3-carboxamide **4c** reacted **5g** to give 5-5 fused heterole **7cg** in moderate isolated yield (entry 1), but the reaction of furan-3-carboxamide **4g** and **5g** failed to afford the corresponding 5-5 fused heterole **7gg**, and non-rearranged [4+2] annulation product **8gg** was generated as a major product (entry 2). 2-Bromothiophene-4-carboxamide **4i** and benzothiophen-3-carboxamide **4j** reacted with **5g** to give the corresponding fused heteroles **7ig** and **7jg**, although the product yields were lower than that of **7cg** (entries 3 and 4). The reaction of thiophene-2-carboxamide **4b** and **5g** was also tested, while the yield of the corresponding [5,5]-fused heterole **7bg** was low and non-rearranged [4+2] annulation product **8bg** was generated as a major product (entry 5). With respect to the alkynes, not only cyclohexyl-substituted phenylacetylene **5g** but also sterically less demanding cyclopentyl- and isopropyl-substituted phenylacetylenes **5h** and **5i** could be employed to give the corresponding [5,5]-fused heteroles **7ch** and **7ci**, although their yields were lower than that of **7cg** (entries 6 and 7). Trimethylsilyl-substituted phenylacetylene **5j** could also react with **4c**, while the corresponding [5,5]-fused heterole **7cj** was obtained in low yield, and non-rearranged [4+2] annulation product **8cj** was generated as a major product (entry 8). Substituents on the phenyl group were also examined. When the $Cp^{A7}Rh^{III}$ complex was used instead of the $Cp^{A6}Rh^{III}$ complex, electron-rich methoxyphenyl-substituted alkynes **5k** and **5l** smoothly reacted with **4c** to give the corresponding [5,5]-fused heteroles **7ck** and **7cl** in good yields (entries 9 and 10). On the contrary, the reaction of **4c** and electron-deficient trifluoromethylphenyl-substituted alkyne **5m** afforded the corresponding [5,5]-fused heterole **7cm** in lower yield than that of **7ck** due to the formation of alkenylated product **6cm** (entry 11). These results indicate that not only steric but also electronic nature of substituents affects the selectivity between protonation and reductive elimination from rhodacycle intermediates. That is, the use of the electron-rich alkyne facilitates reductive elimination from the rhodacycle intermediate giving the [5,5]-fused heterole product, on the contrary, the use of the electron-deficient alkyne facilitates protonation giving the alkenylated product, as with the previously reported Cp^*Rh^{III} complex-catalyzed intramolecular reactions of anilides with alkynes.[8b]

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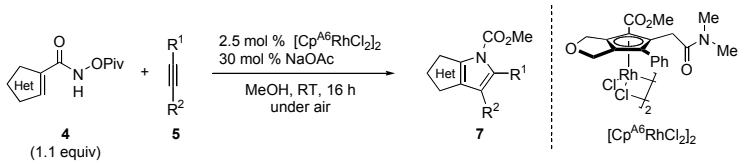
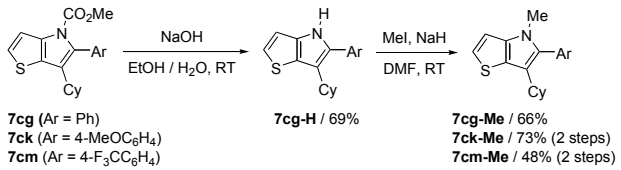


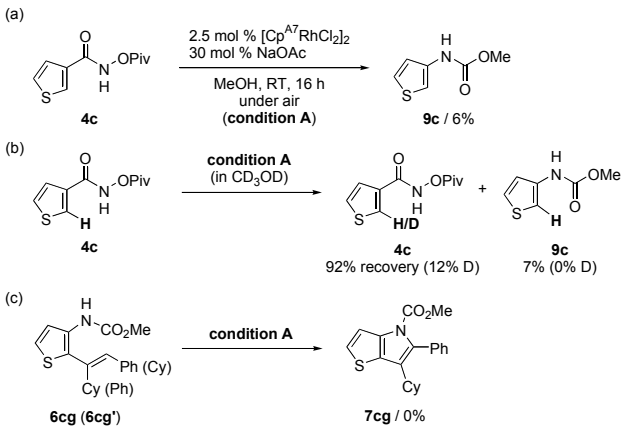
Entry	4	5	Product / Yield		Entry	4	5	Product / Yield	
1	**4c**	**5g**	**7cg** / 53%		7	**4c**	**5i**	**7ci** / 48%	
2	**4g**	**5g**	**7gg** / 0%	**8gg** (**8gg'**) / 47% (**8gg**/**8gg'** = 60:40)	8	**4c**	**5j**	**7cj** / 12%	**8cj** (**8cj'**) / 23% (**8cj**/**8cj'** = 67:33)
3	**4i**	**5g**	**7ig** / 26%		9[a]	**4c**	**5k**	**7ck** / 62%	
4	**4j**	**5g**	**7jg** / 37%		10[a]	**4c**	**5l**	**7cl** / 47%	
5	**4b**	**5g**	**7bg** / 6%	**8bg** / 21%	11	**4c**	**5m**	**7cm** / 34%	**6cm** (**6cm'**) / 29% (Ar = 4-$F_3CC_6H_4$) (**6cm**/**6cm'** = 90:10)
6	**4c**	**5h**	**7ch** / 33%						

Scheme 7. Scope of 5,5-fused heterole synthesis. $[Cp^{A6}RhCl_2]_2$ (0.0050 mmol), **4** (0.022 mmol), **5** (0.20 mmol), NaOAc (0.060 mmol), and MeOH (1.0 mL) were used. Cited yields were of the isolated products. [a] $[Cp^{A7}RhCl_2]_2$ was used instead of $[Cp^{A6}RhCl_2]_2$.

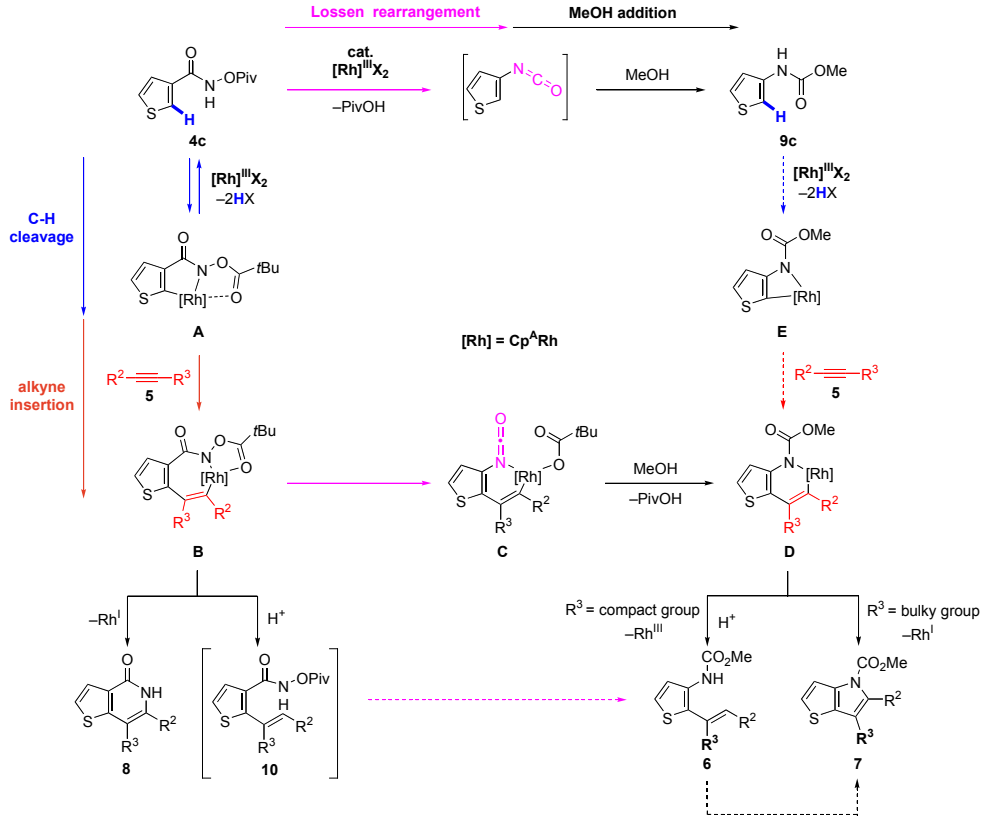
The synthetic transformation of the [5,5]-fused heterole products is shown in Scheme 8. Hydrolysis of **7cg** smoothly proceeded to give the corresponding N-H compound **7cg-H** in 69% yield. The subsequent methylation afforded the corresponding N-Me compound **7cg-Me** in 66% yield.[23] Similarly, **7ck** and **7cm** were transformed into the corresponding N-Me compounds **7ck-Me** and **7cm-Me** in 73% and 48% yields, respectively.[23]



Scheme 8. Transformations of [5,5]-fused heterole products.



Scheme 9. Mechanistic studies.



Scheme 10. Possible mechanisms for formation of **6**–**8** from **4c** and **5**.

To clarify the mechanism of this cascade process, the following experiments were conducted (Scheme 9). The reaction of **4c** with the $Cp^{A7}Rh^{III}$ complex under the present reaction conditions (condition A) gave the normal Lossen rearrangement product **9c** in low yield (Scheme 9a).[24] In the reaction of **4c** in CD_3OD under condition A, partial deuterium incorporation was observed only in the recovered substrate **4c** (Scheme 9b). These results indicate that **9c** may not be involved in the catalytic cycle. The reaction of **6cg** with the $Cp^{A7}Rh^{III}$ complex did not afford **7cg**, thus excluding the intermediacy of **6** for the formation of **7** (Scheme 9c).

Based on the above mechanistic studies, possible mechanisms for the formation of **6**–**8** are proposed, as shown in Scheme 10. First, cleavage of C–H bond of **4c** with $Cp^{A}Rh^{III}$ followed by insertion of **5** furnishes rhodacycle **B** via rhodacycle **A**. Direct reductive elimination from **B** affords non-rearranged [4+2] annulation product **8**. The formal Lossen rearrangement furnishes isocyanate **C**, and the addition of MeOH furnishes rhodacycle **D**.[16] When using a sterically less demanding internal alkyne, protonation of **D** proceeds to give alkenylheterole **6** and regenerates the $Cp^{A}Rh^{III}$ complex. On the contrary, the use of a sterically demanding internal alkyne facilitates reductive elimination from **D** to give [5,5]-fused heterole **7**. The thus liberated $Cp^{A}Rh^{I}$ complex is oxidized by air to regenerate the $Cp^{A}Rh^{III}$ complex. Although the formation of **D** via **9c** and **E** can be considered, this pathway may be excluded according to the experiments shown in Schemes 9a and 9b. Furthermore, sluggish progress of the normal Lossen rearrangement shown in Scheme 9a may exclude the formation of **6** from possible non-rearranged protonation product **10**.[25] The formation of **7** from **6** can also be considered, but the conversion of **6** to **7** did not proceed under the present reaction conditions, as shown in Scheme 9c.

Conclusions

In conclusion, we have established that the substrate structure changes the reaction pathways in the $Cp^{A}Rh^{III}$ complex-catalyzed reactions of heterole carboxamides with alkynes. A cyclopentadienyl (Cp) Rh^{III} complex, bearing two aryl groups and a pendant amide moiety, catalyzed the formal Lossen rearrangement/alkenylation cascade of *N*-pivaloyl heterole carboxamides with internal alkynes, leading to substituted alkenylheteroles. Interestingly, the use of sterically demanding internal alkynes afforded not the alkenylation but the [3+2] annulation products ([5,5]-fused heteroles). In these reactions, the pendant amide moiety of the $CpRh^{III}$ complex may accelerate the formal Lossen rearrangement. The use of five-membered heteroles may deter reductive elimination to form strained [5,5]-fused heteroles; instead, protonation proceeds to give the alkenylation products. Whereas, bulky alkyne substituents accelerate the reductive elimination to allow the formation of the [5,5]-fused heteroles. Mechanistic studies revealed that the present transformations involve the rhodium-

mediated formal Lossen rearrangement, not the base-mediated normal Lossen rearrangement.

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Keywords: Alkenylation • Cyclopentadienyl Complexes • C-H Bond Functionalization • Lossen Rearrangement • Rhodium

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[23] Regiochemistry of the products **7cg**, **7ck**, and **7cm** was determined by the NOESY spectra of **7cg-Me**, **7ck-Me**, and **7cm-Me**, respectively. See the Supporting Information.

[24] The use of $[Cp^*RhCl_2]_2$ or $RhCl_3{\bullet}nH_2O$ instead of $[Cp^{A7}RhCl_2]_2$, and the absence of the rhodium(III) complex did not afford **9c** at all.

[25] Non-rearranged protonation products **10** were not detected at all in any combination of substrates **4** and **5**.

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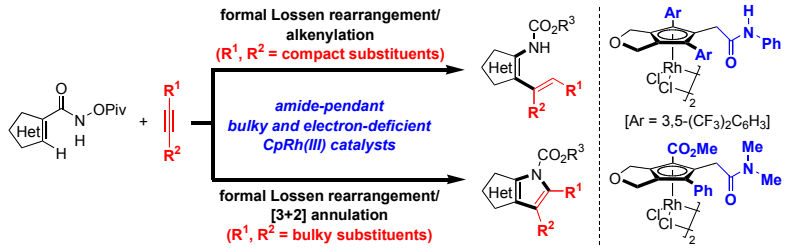

It has been established that a cyclopentadienyl (Cp) Rh^{III} complex with two aryl groups and a pendant amide moiety catalyzes the formal Lossen rearrangement/alkenylation cascade of *N*-pivaloyl heterole carboxamides with internal alkynes leading to substituted alkenylheteroarenes. Interestingly, the use of sterically demanding internal alkynes afforded not the alkenylation but the [3+2] annulation products ([5,5]-fused heteroles).

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