Synthetic Methods

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Transition-Metal-Catalyzed Rearrangement of Allenyl Sulfides: A Route to Furan Derivatives**

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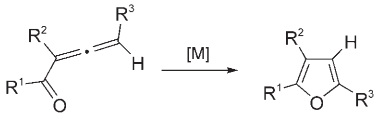
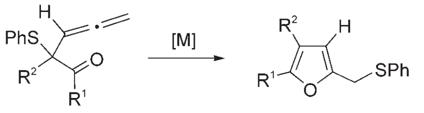
Allene chemistry has attracted considerable attention in recent years. In particular, the transition-metal-catalyzed reaction of allene derivatives bearing an α substituent, such as hydroxy, carbonyl, carboxy, thio (sulfanyl), and amino groups, has led to many synthetically useful transformations.[1,2] One important reaction among them is the transition-metal-catalyzed cyclization of allenyl ketones to afford furans in a straightforward manner [Eq. (1)].[3] Furans are important heterocycles and are present as key structural units in many biologically important natural products and pharmaceutical substances.[4] Furans are also widely used as building blocks in organic synthesis.[5] The development of novel and efficient approaches to furan derivatives has been an active research area over the past decade.[6]



(1)

[M]: Rh^I, Ag^I, Pd^{II}, Pd^0, Au^{III}

In relation to our investigation on [2,3]-sigmatropic rearrangements of sulfide ylides generated from metal carbenes and propargylic sulfides,[7] we have studied the transition-metal-catalyzed reaction of allenyl sulfides. The reaction proceeds through 1,4 migration of the sulfanyl group to afford furan derivatives [Eq. (2)].[8] The reaction presumably involves a metal carbene intermediate, which is trapped intramolecularly by a carbonyl group. Based on this transformation, we have developed a one-pot sequential catalytic process that gives furan products directly from diazocarbonyl compounds and propargyl sulfide. We report herein the preliminary results of this study.

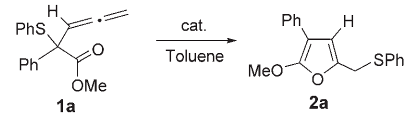


(2)

[M]: Ru^{II}, Pt^{II}, Rh^{II}

The allenyl sulfide **1a**, which can be easily obtained by a Cu^I- or Rh^{II}-catalyzed reaction of methyl phenyldiazoacetate and phenyl propargyl sulfide,[7,9] was treated with various transition-metal catalysts (Table 1). AuCl or $[Au(PPh_3)Cl]$, which are efficient catalysts for the cycloisomerization of α-thioallenes,[2a] were not effective with **1a** (Table 1, entries 1, 2); Rh^{II} carboxylates were next examined: $Rh_2(O_2CCF_3)_4$ was found to effectively catalyze the reaction of **1a** in toluene at 80 °C to afford furan **2a** in 67% yield (Table 1, entry 4). $Rh_2(OAc)_4$ gave only trace amount of **2a** (Table 1, entry 5) and treatment of **1a** with 5 mol% of $PtCl_2$ gave **2a** in a slightly higher yield compared to $Rh_2(O_2CCF_3)_4$ (Table 1, entry 6). Ru^{II} complexes were also tested (Table 1, entries 7–9). To our delight, $[\{RuCl_2(p\text{-cymene})\}_2]$ was highly efficient and afforded **2a** with an excellent yield in 1 h at 80 °C in toluene (Table 1, entry 8). The reaction also occurred at room temperature, but it took much longer (Table 1, entry 9).

Table 1: Reaction of **1a** with various transition-metal complexes.



Entry	Catalyst[a]	*T* [°C]	*t* [h]	Yield [%][b]
1	AuCl	80	17	trace[c]
2	$[Au(PPh_3)Cl]$	80	12	n.r.[c]
3	AuCl + AgOTf	80	17	n.r.
4	$Rh_2(O_2CCF_3)_4$	80	4.5	67
5	$Rh_2(OAc)_4$	80	12	trace
6	$PtCl_2$	80	4.5	73
7	$[Ru(PPh_3)_3Cl_2]$	80	4.5	50
8	**$[\{RuCl_2(p\text{-cymene})\}_2]$**	**80**	**1**	**93**
9	$[\{RuCl_2(p\text{-cymene})\}_2]$	25	23	88

[a] Reactions were carried out with 5 mol% catalyst except for Rh^{II} catalysts, of which 1 mol% was used. [b] Yield of isolated product after column chromatography. [c] Most of the starting material was recovered. n.r. = no reaction. The best result is highlighted in bold.

A reaction mechanism is proposed in Scheme 1: the phenylsulfanyl group attacks the terminal carbon atom of the metal-activated allene moiety to give a five-membered

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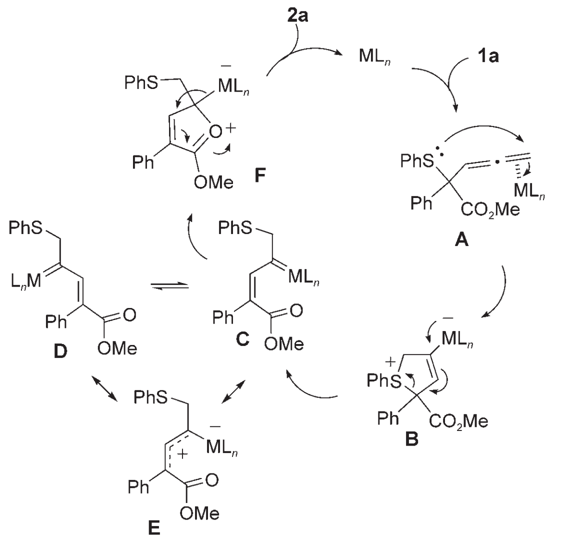


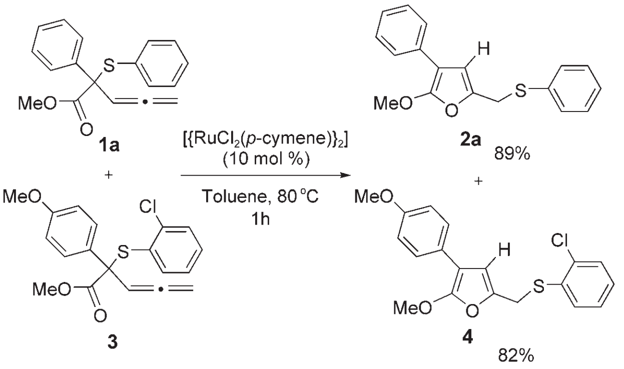
Scheme 1. Mechanistic hypothesis for the formation of furans according to Equation (2).

thiolanium ion species, **B**. Metal carbenes, **C** and **D**, are then generated from **B** through 1,4 migration of the phenylsulfanyl group. These metal carbenes can be viewed as metal-stabilized allylic cations with resonance structure **E**. Therefore, *trans/cis* isomerization occurs readily, and **C** and **D** are in rapid equilibrium. From **C**, the carbonyl oxygen atom interacts with the electron-deficient carbene carbon atom, which leads to the formation of **2a**. This step, to afford a carbonyl ylide, is a well-known process in transition-metal-catalyzed reactions of diazo compounds.[9b,c,10] Moreover, Hashmi and co-workers recently reported that the reaction of gold carbene species with a carbonyl oxygen atom is the key step in the synthesis of arene oxides and arenes by gold-catalyzed reaction of furans.[11]

The selective attack of the terminal position of the allene moiety by the phenylsulfanyl group may be attributed to the favorable formation of a five-membered ring. However, the possibility cannot be ruled out that this attack may arise from efficient generation of a metal carbene and its subsequent reactions. Attack of the internal double bond will not generate a metal carbene species. Besides, from **D** (Scheme 1) formal insertion into an aromatic C–H bond by metal carbenes should give indene derivatives.[12] No indene products are observed in this process as the reaction of an electron-deficient metal carbene with a carbonyl oxygen atom is more favorable than formal insertion into an aromatic C–H bond.[9b,c,10]

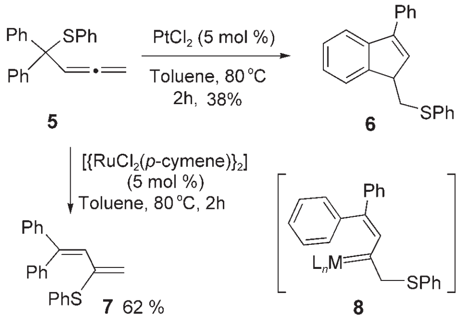
The key point of this mechanism is the formation of metal carbene intermediates. Although there are rare precedents, metal carbenes have been supposed to be intermediates in transition-metal-catalyzed reactions of allenes.[2h,3c,d] Hashmi and co-workers have suggested a palladium carbene intermediate in a palladium(II)-catalyzed reaction of allenyl ketones.[3c,d] In a similar transition-metal-catalyzed reaction of propargyl acetate, metal carbenes have been suggested as intermediates.[13]

To substantiate the above-hypothesized reaction mechanism, several experiments have been carried out. First, the crossover experiment with a mixture of **1a** and **3** as the substrates resulted in the isolation of furan derivatives, **2a** and **4** (Scheme 2). No crossover products were detected, which suggests that migration of the sulfanyl group is intramolecular in accordance with the mechanism proposed in Scheme 1.



Scheme 2. Crossover experiment with two different allenyl sulfides.

Second, the allenyl sulfide **5**, in which the methoxycarbonyl group of **1a** is replaced with a phenyl group, was investigated (Scheme 3). The $PtCl_2$-catalyzed reaction gave

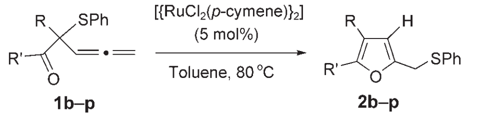


Scheme 3. Catalytic reaction with allenyl sulfide, **5**.

indene derivative **6**, presumably formed through formal C–H insertion of the metal carbene intermediate **8**.[12] When **5** was subjected to [{$RuCl_2$(*p*-cymene)}$_2$], 1,3-butadiene derivative **7** was identified as the major product. The formation of **7** can be rationalized by 1,2-sulfur migration from the metal carbene intermediate.[14] Although extensive investigation is still required to firmly establish the reaction mechanism, these experiments provide evidence to support the hypothesis shown in Scheme 1.

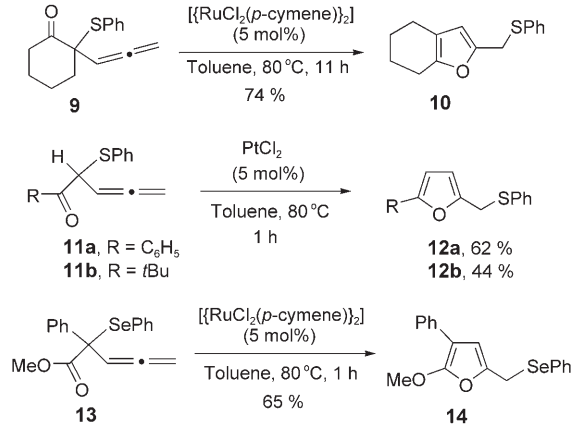
The scope of this catalytic reaction is demonstrated by a series of allenyl sulfides, **1b–p**, **9**, **11a,b**, and allenyl selenide **13**, which are summarized in Table 2 and Scheme 4. The tertiary allenyl sulfides **1b–p** (Table 2), which bear various substituents, all gave good to excellent yields of the corresponding furan products under the optimized reaction conditions with [{$RuCl_2$(*p*-cymene)}$_2$] as catalyst. Cyclic tertiary allenyl sulfide **9** also worked well under the same conditions. However, for secondary allenyl sulfides **11a** and **11b** the Ru^{II} catalyst gave a complex mixture, while catalysis with

Table 2: [{RuCl$_2$(*p*-cymene)}$_2$]-catalyzed reaction of **2b–p**.



Entry	Allene **1**, R, R′	*t*	Yield [%][a]
1	**1b**, 4-ClC$_6$H$_4$, OMe	1 h	95
2	**1c**, 2,4-Cl$_2$C$_6$H$_3$, OMe	1.5 h	74
3	**1d**, 4-MeOC$_6$H$_4$, OMe	10 min	91
4	**1e**, 3-MeC$_6$H$_4$, OMe	30 min	81
5	**1f**, 1-naphthyl, OMe	3 h	70
6	**1g**, 3-ClC$_6$H$_4$, Me	2 h	80
7	**1h**, 2-ClC$_6$H$_4$, Me	2 h	78
8	**1i**, 2-thienyl, OEt	1 h	93
9	**1j**, Ph, H	1 h	99
10	**1k**, 4-BrC$_6$H$_4$, H	1 h	98
11	**1l**, 4-MeOC$_6$H$_4$, H	1 h	98
12	**1m**, *trans*-CH$_3$CH=CH–, OEt	1 h	83
13	**1n**, CH$_3$C(O), CH$_3$	48 h	60
14	**1o**, EtOC(O), OEt	23 h	60
15	**1p**, Me, H	12 h	74

[a] Yields of isolated products after column chromatography.

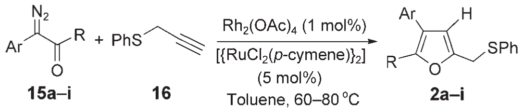


Scheme 4. Catalytic reaction with allenyl sulfides, **9**, **11a,b**, and allenyl selenide **13**.

5 mol% of PtCl$_2$ afforded the furan products **12a** and **12b** in moderate yields, together with a complex mixture as by-products (Scheme 4). No products as a result of direct furan formation without migration of the sulfanyl group could be identified.[15] It is noteworthy that the catalytic reaction with allenyl selenide **13** also proceeded with the Ru^{II} catalyst.

As the allenyl sulfides are obtained from the Cu^{I}- or Rh^{II}-catalyzed reactions of α-diazocarbonyl compounds and propargyl sulfide, it is conceivable that a one-pot reaction may be possible by carrying out the two catalytic reactions without separation of the allenyl sulfides (Table 3). Thus, the reaction of diazo compounds **15a–i** with propargyl sulfide **16** was first catalyzed with 1 mol% Rh$_2$(OAc)$_4$ in toluene at 60 °C. After the [2,3]-sigmatropic rearrangement was completed, 5 mol% of [{RuCl$_2$(*p*-cymene)}$_2$] was added and the reaction mixture was heated to 80 °C. As shown in Table 3, the one-pot reaction worked well with various diazo substrates and gave the furan products in high yields.

Table 3: One-pot sequential catalytic reactions with two catalysts.

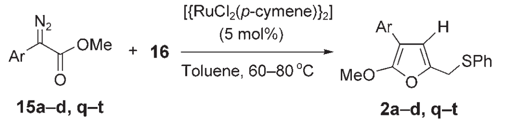


Entry	Diazo substrate **15**, Ar, R	*t*[a]	Yield [%][b]
1	**15a**, C$_6$H$_5$, OMe	1 h	81
2	**15b**, 4-ClC$_6$H$_4$, OMe	1 h	90
3	**15c**, 2,4-Cl$_2$C$_6$H$_3$, OMe	1.5 h	72
4	**15d**, 4-MeOC$_6$H$_4$, OMe	10 min	83
5	**15e**, 3-MeC$_6$H$_4$, OMe	30 min	84
6	**15f**, 1-naphthyl, OMe	3 h	50
7	**15g**, 3-ClC$_6$H$_4$, Me	2 h	73
8	**15h**, 2-ClC$_6$H$_4$, Me	2 h	62
9	**15i**, 2-thienyl, OEt	1 h	82

[a] Reaction time for second step. [b] Yields of isolated products after column chromatography.

Recently, the use of a single transition-metal catalyst to mediate two or more transformations in a single synthetic operation has emerged as a new research area.[16] We have observed that [{RuCl$_2$(*p*-cymene)}$_2$] can also catalyze the reaction of α-diazocarbonyl compounds with propargyl sulfide to afford allenyl sulfides. Naturally, [{RuCl$_2$(*p*-cymene)$_2$}] was then tested as a single catalyst in this one-pot sequential catalytic reaction. As shown in Table 4, with the exception of two substrates (Table 4, entries 3, 4), the Ru^{II} complex catalyzed the two reactions sequentially and gave the corresponding furan products in moderate yields. The two exceptions arose because of inefficiency and low selectivity of the first catalytic reaction, that is, the generation of the allenyl sulfide. Finally, as Rh$_2$(O$_2$CCF$_3$)$_4$ can also catalyze the allenyl sulfide rearrangement (Table 1, entry 4), we attempted its use as the only catalyst in the one-pot reaction. The corresponding furan product was obtained, however, the yield was low with isolation of a considerable amount of allenyl sulfide.

Table 4: One-pot sequential catalytic reactions with one catalyst.



Entry	Diazo substrate **15**, Ar	*t*	Yield [%][a]
1	**15a**, C$_6$H$_5$	1 h	52
2	**15b**, 4-ClC$_6$H$_4$	1 h	67
3	**15c**, 2,4-Cl$_2$C$_6$H$_3$	18 h	–[b]
4	**15d**, 4-MeOC$_6$H$_4$	30 min	–[b]
8	**15q**, 3-MeOC$_6$H$_4$	1 h	68
6	**15r**, 4-MeC$_6$H$_4$	1 h	45
7	**15s**, 3-ClC$_6$H$_4$	1 h	61
5	**15t**, 4-BrC$_6$H$_4$	1 h	54

[a] Yields of isolated products after silica-gel column chromatography. [b] Diazo compound decomposed, but no furan product was identified.

In summary, we have reported an unprecedented 1,4 migration of the sulfanyl group in a transition-metal-catalyzed reaction of allenyl sulfides. The reaction gives multisubstituted furan products in good to excellent yields. Furthermore, in combination with a metal-catalyzed [2,3]-sigmatropic rearrangement, a one-pot sequential catalytic transformation of α-diazocarbonyl compounds to furan derivatives has been developed.[17] This one-pot catalytic process is highly atom-economic and involves remarkable bond reorganizations.

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