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One-Pot Synthesis of γ,δ-Unsaturated Carbonyl Compounds from Allyl Alcohols and Vinyl or Isopropenyl Acetates Catalyzed by [IrCl(cod)]$_2$

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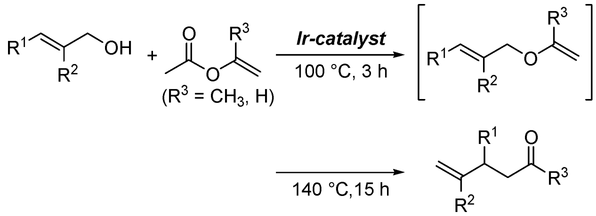


One-pot synthesis of γ,δ-unsaturated carbonyl compounds from allyl alcohols and vinyl or isopropenyl acetates was achieved through in situ generation of allyl vinyl ethers by the action of the [IrCl(cod)]$_2$ complex followed by Claisen rearrangement of the resulting ethers. For instance, the reaction of *trans*-2-methyl-3-phenyl-2-propen-1-ol with isopropenyl acetate in the presence of [IrCl(cod)]$_2$ (1 mol %) and Cs_2CO_3 (5 mol %) at 100 °C for 3 h followed by 140 °C for 15 h afforded 5-methyl-4-phenyl-5-hexen-2-one in 72% yield. When vinyl acetate was employed in place of isopropenyl acetate, 4-methyl-3-phenyl-4-pentenal was obtained in 83% yield.

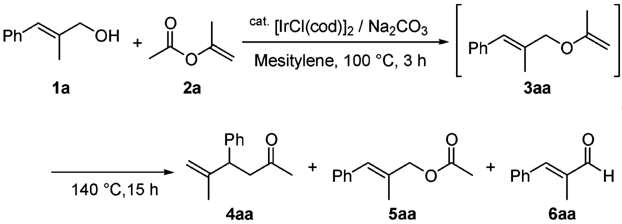
The Claisen rearrangement of allyl vinyl ethers is recognized as an attractive tool for the synthesis of olefins[1] in a stereoselective manner as well as for the creation of asymmetrical carbon centers.[2] Therefore, there have been several reports on the in situ generation of allyl vinyl ethers which are precursors for the Claisen rearrangement, e.g., acid-catalyzed decomposition of diallyl actates,[3] vinylation of haloethers,[4] Ru- and Ir-catalyzed rearrangement of diallyl ethers,[5] organoaluminum-promoted allyl vinyl ethers,[6] etc. The reaction of allyl alcohols with terminal alkynes catalyzed by Rh complexes is reported to lead to the Claisen rearrangement products.[7] Previously, we reported the rearrangement of allyl homoallyl ethers to γ,δ-unsaturated aldehydes induced by the [IrCl(cod)]$_2$ complex.[8] In this reaction, however, it is necessary to prepare independently allyl homoallyl ethers by etherification between allyl bromide and homoallyl alcohols derived from carbonyl compounds and allylmagnesium bromide. Therefore, if allyl vinyl ethers, which undergo the Claisen rearrangement, can be directly prepared by the vinylation of allyl alcohols with vinyl compounds such as vinyl acetate, this method would provide a very attractive route to γ,δ-unsaturated carbonyl compounds, since allyl alcohols are easily available from commercial sources. Fortunately, we have recently succeeded in performing the vinylation of alcohols with vinyl acetate using [IrCl(cod)]$_2$ complex, although the vinylation was very difficult to carry out by conventional methods.[9] Therefore, if the vinylation of allyl alcohols with vinyl acetate can be carried out by using [IrCl(cod)]$_2$, it may be possible to carry out a one-pot synthesis of γ,δ-unsaturated carbonyl compounds from allyl alcohols and vinyl or isopropenyl acetate through tandem reactions involving vinylation and Claisen rearrangement.

TABLE 1. Reaction of 1a with 2a under Various Conditions[a]

run	catalyst	base	yield[b] (%)			
			3aa	**4aa**	**5aa**	**6aa**
1	[IrCl(cod)]$_2$	Na_2CO_3	0	70	10	5
2	[IrCl(cod)]$_2$		0	0	49	11
3	$[\mathrm{Ir(cod)_2}]^+BF_4^-$	Na_2CO_3	0	58	10	9
4	[Cp*IrCl$_2$]$_2$	Na_2CO_3	0	2	1	84
5	[IrCl(cod)]$_2$	Cs_2CO_3	0	72	7	7
6	[IrCl(cod)]$_2$	NaOAc	0	68	10	6
7	[IrCl(cod)]$_2$	KOH	0	65	10	6
8[c]	[IrCl(cod)]$_2$	Na_2CO_3	30	30	13	8

[a] **1a** (0.5 mmol) was reacted with **2a** (6 mmol) in the presence of Ir complex (2 mol %) and base (5 mol %) in mesitylene (1.5 mL) at 100 °C for 3 h followed by 140 °C for 15 h. [b] Based on **1a**. [c] The second step was also carried out 100 °C for 15 h.

The reaction of *trans*-2-methyl-3-phenyl-2-propen-1-ol (**1a**) with isopropenyl acetate (**2a**) in the presence of [IrCl(cod)]$_2$ (2 mol %) was chosen as a model reaction and was carried out under various conditions (eq 1 and Table 1).



(1)

The reaction of **1a** with **2a** under the influence of [IrCl(cod)]$_2$ (2 mol %) and a base like Na_2CO_3 at 100 °C for 3 h followed by 140 °C for 15 h afforded the desired Claisen rearrangement

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TABLE 2. Reaction of Various Allyl Alcohols with 2a or 2b under the Influence of $[IrCl(cod)]_2$ [a]

run	allyl alcohol	acetate	product (yield/%)
1	**1a**	**2a**	**4aa** (72)
2	**1a**	**2b**	**4ab** (83)
3[b]	**1b**	**2a**	**4ba** (74)
4[b]	**1b**	**2b**	**4bb** (67)
5[b,c]	geraniol (**1c**)	**2a**	**4ca** (81)
6[b,c]	**1c**	**2b**	**4cb** (72)
7[b,c]	nerol (**1d**)	**2a**	**4da** (88)
8[b,c]	**1d**	**2b**	**4db** (69)

[a] The reaction was carried out using the same method as run 5 in Table 1. [b] $P(OPh_3)_3$ (0.04 mmol) was added in the second step. [c] The second step was carried out at 150 °C: **2a**, isopropenyl acetate; **2b**, vinyl acetate.

product, 5-methyl-4-phenyl-5-hexen-2-one (**4aa**), in 70% yield along with *trans*-2-methyl-3-phenyl-2-propenyl acetate (**5aa**) (10%) and *trans*-2-methyl-3-phenyl-2-propenal (**6aa**) (5%) (run 1). However, when the same reaction was carried out in the absence of Na_2CO_3 under these conditions, the normal ester exchange reaction between **1a** and **2a** took place as a major reaction to form **5aa**, but not the Claisen rearrangement product **4aa**, in 49% yield (run 2). In the present Ir-catalyzed reaction of **1a** with **2a**, isopropenylation of **1a** forming **3aa** competes with acetylation of **1a** forming **5aa**. It may be considered that the initial interaction of an Ir species with **2a** in preference to **1a** leads to the formation of **3aa**, while the Ir species first reacts with **1a** followed by **2a** to afford **5aa**. Therefore, it seems likely that an excess amount of **2a** with respect to **1a** is needed to obtain **3aa** as a major product.

A cationic complex, $[Ir(cod)_2]^+BF_4^-$, was less active than the $[IrCl(cod)]_2$ complex, and **4aa** was formed in a slightly lower yield (58%) (run 3). It is interesting that the $[Cp^*IrCl_2]_2$ complex produced dehydrogenation product **6aa** in high yield (84%) rather than the Claisen product **4aa** (run 4). In this reaction, **2a** was found to serve as a hydrogen acceptor of **1a**. This shows that the $[Cp^*IrCl_2]_2$ complex catalyzes the dehydrogenation of **1a** to **6aa** rather than the vinylation of **1a** with **2a** to **3aa**. Among the bases examined, Cs_2CO_3 was found to be the best additive and gave **4aa** in 72% yield (run 5). A strong base, KOH, was also used as a base for the present tandem Claisen rearrangement (run 7). When the reaction temperature was lowered to 100 °C, the rate of the Claisen rearrangement of **3aa** to **4aa** became very slow, and a considerable amount of **3aa** remained without rearrangement even after 18 h (run 8).

On the basis of these results, the reaction between allyl alcohols and vinyl or isopropenyl acetate was carried out, and the results are summarized in Table 2.

The reaction of **1a** with vinyl acetate (**2b**) under these conditions afforded the corresponding rearranged product, 4-methyl-3-phenyl-4-pentenal (**4ab**), in 83% yield (run 2). 3-Methyl-2-buten-1-ol (**1b**) reacted with **2a** to produce 4,4-dimethyl-5-hexen-2-one (**4ba**) in 74% yield (run 3). Similarly, the reaction of **1b** with **2b** afforded3,3-dimethyl-4-pentenal (**4bb**) in 67% yield (run 4). Geraniol (**1c**) underwent isopropenylation and vinylation with **2a** and **2b** followed by rearrangement to form the corresponding ketone **4ca** (81%) and aldehyde **4cb** (72%), respectively (runs 5 and 6). Nerol (**1d**) reacted with **2a** and **2b** to give the corresponding rearrangement products, **4da** and **4db**, in 88% and 69% yields, respectively (runs 7 and 8).

In conclusion, we have achieved a one-pot synthesis of γ,δ-unsaturated carbonyl compounds from allyl alcohols and vinyl or isopropenyl acetates by the use of Ir complexes.

Experimental Section

All starting materials were commercially available and used without any purification. GLC analysis was performed with a flame ionization detector using a 0.2 mm × 25 m capillary column (OV-1). ^1H and ^{13}C NMR were measured at 270 or 400 and 67.5 MHz, respectively, in $CDCl_3$ with Me_4Si as the internal standard.

A typical reaction procedure of the reaction of **1a** with **2a** is as follows: To a mixture of $[IrCl(cod)]_2$ (0.01 mmol) and Na_2CO_3 (0.025 mmol) in mesitylene (1.5 mL) were added **1a** (0.5 mmol) and **2a** (6 mmol) under Ar. The reaction mixture was stirred at 100 °C for 3 h followed by 140 °C for 15 h. The conversions and yields of products were estimated from the peak areas based on the internal standard technique using GC.

The products **4aa**,[10] **4ab**,[11] **4ba**,[12] **4bb**,[13] **4ca** and **4da**,[14] and **4cb** and **4db**[15] are known compounds and have been reported previously.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of **4aa**, **4ab**, **4ba**, **4ca**, and **4da**. This material is available free of charge via the Internet at http://pubs.acs.org.

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