Transition-metal-catalyzed rearrangement of 5-alkynals to γ-alkynylketones and 1-cyclopentenylketones†

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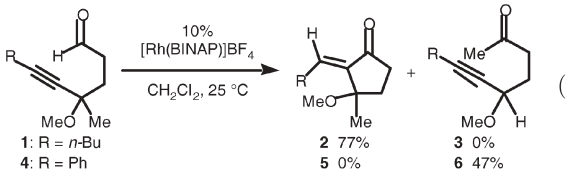
The transition-metal-catalyzed rearrangement of 5-alkynals to γ-alkynylketones and 1-cyclopentenylketones was developed using [Rh(P(OPh)$_3$)$_2$]BF$_4$ or Cu(OTf)$_2$ as a catalyst.

The transition-metal-catalyzed cyclo-isomerization of alkynyl carbonyl compounds leading to a variety of cyclic compounds has been developed though activation of alkynes by π-complexation to electrophilic transition metal complexes.[1–3] However, the reactions of γ-alkynyl carbonyl compounds including 5-alkynals in the presence of electrophilic transition metal complexes have been scarcely explored.[4] In this Communication, we describe the transition-metal-catalyzed rearrangement of 5-alkynals to γ-alkynylketones and 1-cyclopentenylketones. The substituents at the 4-position of 5-alkynals determine the selective formation of these two different products.

Recently, we reported the intramolecular hydroacylation of 5-alkynals leading to α-alkylidenecyclopentanones using [Rh(BINAP)]BF$_4$.[5,6] When 4-methoxy-4-methyl-5-decynal (**1**) was treated with 10% [Rh(BINAP)]BF$_4$ in CH$_2$Cl$_2$ at 25 °C, α-alkylidenecyclopentanone **2** was obtained in 77% yield. To our surprise, the reaction of 6-phenyl-5-hexynal **4** provided not the expected α-alkylidenecyclopentanone **5** but rather gave γ-alkynylketone **6** in 47% yield (eqn 1).

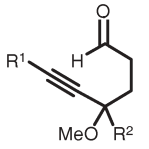
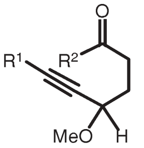
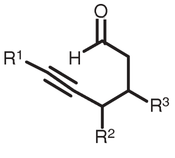
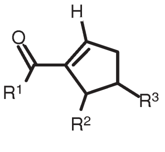


1: R = *n*-Bu
4: R = Ph
2 77%
5 0%
3 0%
6 47%

(1)

Various rhodium(I)/phosphine catalysts were examined to promote the rearrangement of **1** to γ-alkynylketone **3**. Among the catalysts examined, the use of cationic rhodium(I)/electron deficient monodentate phosphine complexes was effective for the rearrangement of **1** to **3**. Especially, the use of 10% [Rh(P(OPh)$_3$)$_2$]BF$_4$ gave **3** in 77% yield. Other electrophilic transition metal complexes, which are frequently used for activation of alkynes, were also examined. Although the use of PdCl$_2$[2c,3l–o] and PtCl$_2$[3c] led to unidentified mixtures, the use of 10% Cu(OTf)$_2$[3i,j] gave **3** in 69% yield. The reactions of a series of 4-methoxy-4-alkyl-5-alkynals were investigated in the presence of 10% [Rh(P(OPh)$_3$)$_2$]BF$_4$ or 10% Cu(OTf)$_2$ at 25 °C as shown in Table 1.[6] Both 6-phenyl- and 6-alkyl-5-alkynals cleanly afforded the corresponding γ-alkynylketones in good yield (entries 1–4). Although the yields of the ketone were decreased, 5% Rh or Cu catalyst can be used (entries 1 and 2). Although the reaction of 6-trimethylsilyl-5-alkynal using [Rh(P(OPh)$_3$)$_2$]BF$_4$ did not proceed even at elevated temperature (80 °C), the use of Cu(OTf)$_2$ at 80 °C gave the desired ketone in low yield (entry 5). The scope of 4-alkyl substituents was also investigated. Not only methyl, but also *n*-propyl and *i*-propyl substituted 5-alkynals can be used for this reaction (entries 6 and 7). Interestingly, in the absence of methoxy group, the intramolecular addition of aldehyde to alkyne proceeded at 50 °C to give 1-cyclopentenylketones (entries 8–11).[7,8]

Table 1 Catalytic rearrangement of 5-alkynals to γ-alkynylketones and 1-cyclopentenylketones[a]

Entry	Substrate		Product	Yield (%)[b]
				
1	R^1 = *n*-Bu	R^2 = Me		77 (64[d])
2[c]	R^1 = *n*-Bu	R^2 = Me		69 (66[d])
3	R^1 = Ph	R^2 = Me		71
4	R^1 = Cl(CH$_2$)$_3$	R^2 = Me		74
5[c]	R^1 = Me$_3$Si	R^2 = Me		24[d]
6	R^1 = *n*-Bu	R^2 = *n*-Pr		43
7	R^1 = *n*-Bu	R^2 = *i*-Pr		57
				
8	R^1 = *n*-Bu	R^2 = Me	R^3 = H	62
9	R^1 = *n*-C$_6$H$_{13}$	R^2 = *n*-Bu	R^3 = H	71
10	R^1 = *n*-C$_6$H$_{13}$	R^2 = H	R^3 = Me	47
11	R^1 = *n*-C$_{10}$H$_{21}$	R^2 = H	R^3 = H	43

[a] The reaction was conducted using [Rh(P(OPh)$_3$)$_2$]BF$_4$ (0.050 mmol), 5-alkynal (0.50 mmol), and solvent (2.0 mL) at 25 °C (CH$_2$Cl$_2$, entries 1–4, 6, and 7), 50 °C {(CH$_2$Cl)$_2$, entries 8–11}, or 80 °C {(CH$_2$Cl)$_2$, entry 5} for 15–110 h. [b] Isolated yield. [c] Cu(OTf)$_2$ was used as a catalyst in CH$_3$CN. [d] 5% Catalysts were used.

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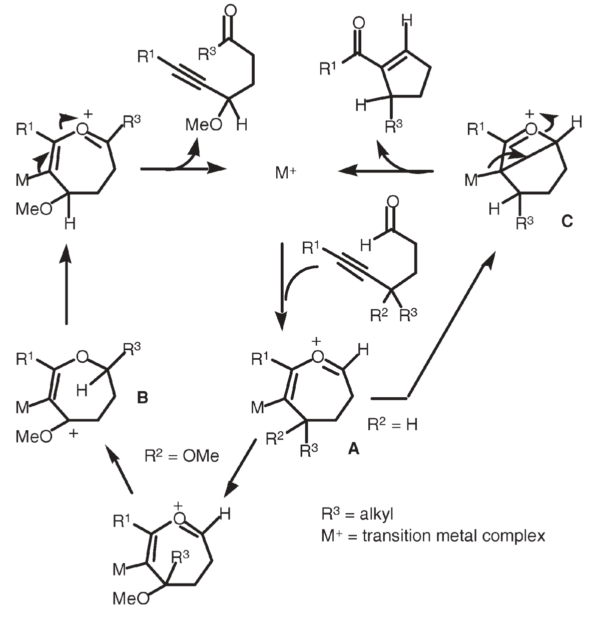
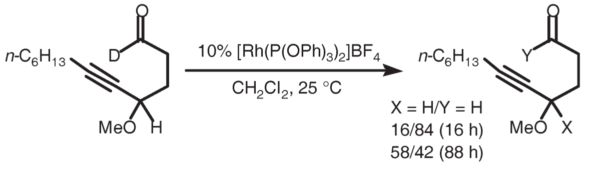
† Electronic supplementary information (ESI) available: experimental details. See http://dx.doi.org/10.1039/b508278a



Scheme 1

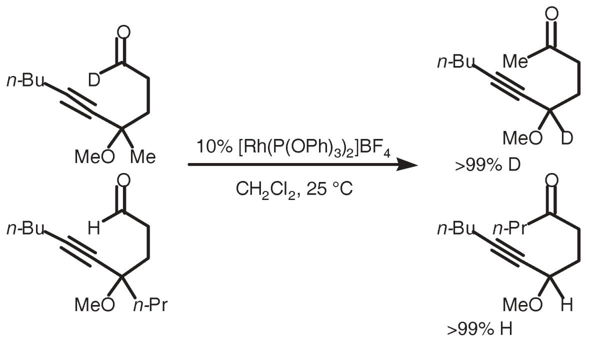
Although no reaction was observed when 4-methoxy-5-decynal was treated with 10% $[Rh(P(OPh)_3)_2]BF_4$ at 25 °C, we anticipated that exchange reaction between formyl hydrogen and propargylic hydrogen might occur instead of exchange reaction between formyl hydrogen and the propargylic alkyl group. Indeed, the exchange reaction between formyl deuterium and propargylic hydrogen proceeded slowly in the reaction of 1-deuterium-4-methoxy-5-decynal (eqn. 2).

Scheme 1 depicts a possible mechanism of these rearrangements. We believe that the coordination of an electrophilic transition metal complex would induce an attack of a carbonyl oxygen to an alkyne through an *endo* pathway leading to vinylmetal complex **A**.[9] In the case of 4-methoxy-5-alkynals (R^2 = OMe), exchange reaction between alkyl group (R^3) and formyl hydrogen proceeds *via* the oxygen-stabilized cationic intermediate **B** to form γ-alkynyl ketone and regenerates the transition metal complex. On the other hand, in the case of 5-alkynals (R^2 = H), a methathesis reaction proceeds *via* the cationic intermediate **C** to form 1-cyclopentenylketones.[7,8]

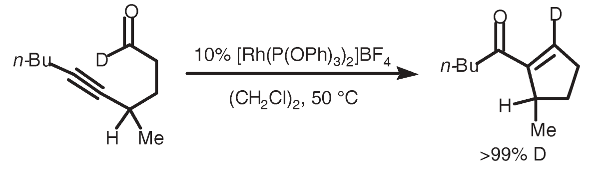


(2)

Consistent with these pathways, the reactions of 1-deuterium-5-alkynals led to stereospecific incorporation of deuterium in the propargylic position of γ-alkynyl ketone and the vinylic position of 1-cyclopentenyl ketone (eqn 3 and 4). Furthermore, through a crossover experiment, we have established that this transfer proceeds intramolecularly. Deuterium crossover was not observed in the reaction of a 1 : 1 mixture of a deuterated-5-alkynal and a nondeuterated-5-alkynal with $[Rh(P(OPh)_3)_2]BF_4$ (eqn 4).



(3)



(4)

In conclusion, we have developed the catalytic rearrangement of 5-alkynals to γ-alkynyl ketones and 1-cyclopentenyl ketones using $[Rh(P(OPh)_3)_2]BF_4$ or $Cu(OTf)_2$ as a catalyst. The substituents at the 4-position of 5-alkynals play an important role for the selection of two different rearrangement pathways.

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