CHEMISTRY LETTERS, pp. 1875-1878, 1985.

A FACILE COUPLING REACTION OF VINYL KETONES WITH ALDEHYDES CATALYZED BY RHODIUM(I) HYDRIDE COMPLEX

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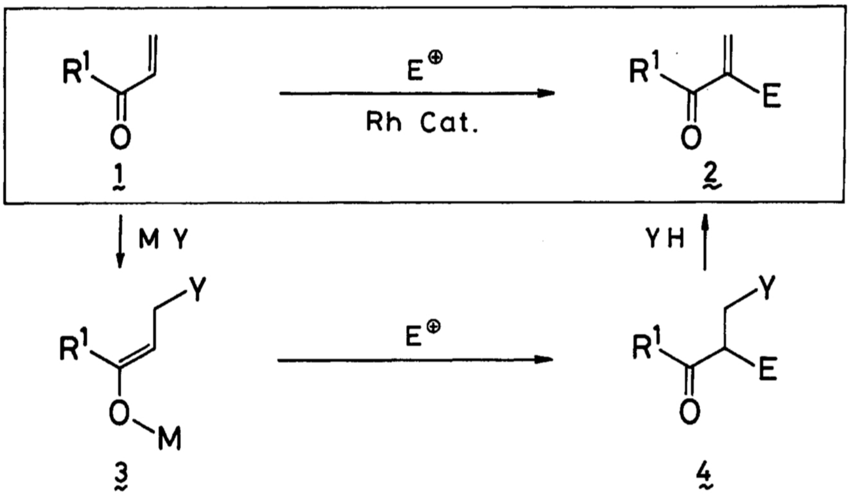
A convenient α-hydroxyalkylation of vinyl ketones is accomplished by the coupling reaction of vinyl ketone and aldehyde, where rhodium(I) enolate derived from $HRh(PPh_3)_4$ plays an important role in the carbon-carbon bond forming step.

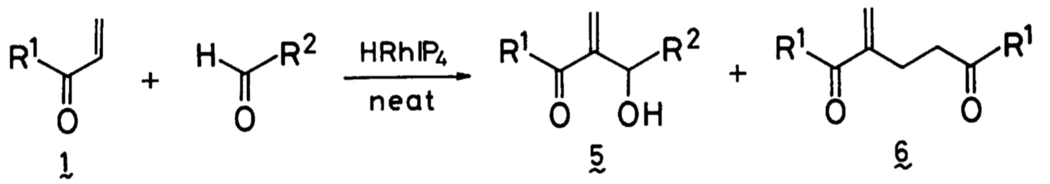
Since introduction of an electrophile to the sp^2-hybridized α position of α, β-unsaturated ketones is an important operation, some attractive approaches have been proposed from the various points of view.[1, 2] Central to their approaches was the three steps procedure [2] composed of Michael type addition of M-Y to **1**, attack of electrophile to **3**, and elimination of H-Y from **4** as shown in Scheme 1. Such a strategy, however, requires inevitable use of an equimolar amount of M-Y which is relatively expensive or troublesome to use. A more convenient and possibly more direct approach for the conversion of **1** to **2** could be realized by exploiting a new catalytic cycle including transition metal complexes. We describe herein an important role of $HRh(PPh_3)_4$ for the coupling reaction of **1** with aldehydes.



MY = $LiSiMe_2Ph$ [2a)]
$IMgSPh$ [2b)]
Bu_2BSPh [2c)]
R_2BSePh [2d)]
Me_2AlSPh [2e)]
$Me_3SiSePh$ [2f)]

Scheme 1.

Previously, we pointed out the putative intervention of rhodium enolate complex **7** formed by Michael type addition of $HRh(PPh_3)_4$ to α,β-enone in the synthesis of α-trimethylsilyl ketones.[3] If intermediate **7** has enough nucleophilicity to aldehyde, aldol type carbon-carbon bond formation could be attained under the almost neutral conditions. In fact, two types of coupling product **5** and **6** (ratio **5**/**6** = 85/15)[4] were obtained in the preliminary reaction of 3-buten-2-one with an equivalent of propanal by the assist of 1 mol% of HRh(PPh$_3$)$_4$ at 105 °C. While it is critical to use no solvent for the acceptable yield of products in the present reaction, the predominant formation of **5** stimulates us to delve further because of the formal accomplishment of the process **1** ⟶ **2**. The formation of **6** can be decreased by the use of two moles of aldehyde and the addition of small amount of alcohol. The results are summarized in Tables 1 and 2 where the extension of an analogous coupling is shown for some types of aldehyde and vinyl ketone.



(1)

Table 1. Coupling reaction of 3-buten-2-one with propanal[a]

Entry	Catalyst[b] (mol%)	Alcohol[c]	Conditions Temp/°C	Time/h	Product[d] **5**:**6**	Yield of **5**[e] %	Turnover of Rh
1	HRh(PPh$_3$)$_4$ (1.0)	none	105	2	93:7	47	48
2	HRh(PPh$_3$)$_4$ (0.6)	none	40	40	96:4	17	28
3	HRh(PPh$_3$)$_4$ (0.9)	EtOH	105	2	90:10	57	62
4	HRh(PPh$_3$)$_4$ (0.8)	^{i}PrOH	105	2	93:7	62	74
5	HRh(PPh$_3$)$_4$ (0.8)	^{i}PrOH	40	40	97:3	78	92
6	HRh(PPh$_3$)$_4$ (0.8)	C	105	2	92:8	61	73
7	HRh(PPh$_3$)$_4$ (0.9)	C	40	20	98:2	83	92
8	HRh(PPh$_3$)$_4$ (0.9)	D	105	2	93:7	76	86
9	HRh(PPh$_3$)$_4$ (0.4)	^{i}PrOH	40	43	97:3	57	157
10	HRh(PPh$_3$)$_4$ (0.1)	^{i}PrOH	40	160	97:3	58	457
11	A (1.0)	none	105	2	100:0	63[f]	--
12	B (1.0)	none	110	2	84:16	43	41
13	PPh$_3$ (4.2)	none	40	20	77:23	40[f]	--

a) Reactions were conducted on a 5 mmol scale without solvent in a sealed tube using a mixture of 3-buten-2-one/propanal = 1/2.

b) A;[(COD)Rh(DIPHOS)]$^+$PF$_6^-$/H$_2$, B;HRh(PPh$_3$)$_4$/4PBu$_3$.

c) Ca. 20 mol% of alcohol was added. C;2-Methyldiphenylsilylheptan-1-ol, D;2-Trimethylsilylheptan-1-ol.

d) The ratio was determined by capillary GLC analyses (PEG-HT Bonded, 25 m column).

e) Isolated yield.

f) Contaminated by unidentified product.

Table 2. Coupling reaction of 1 with aldehydes[a)]

Entry	1 R^1	Aldehyde R^2	Conditions Temp/°C	 Time/h	Yield of 5 [b)] %	Turnover of Rh
1	Me	Et	40	40	78	92
2	Me	Propyl	40	40	61	45
3	Me	1-Methylethyl	43	42	70	74
4	Me	2-Methylpropyl	43	41	76	82
5	Me	Ph	40	20	18	26
6	Et	Et	105	2 [c)]	45	52
7	Pentyl	Et	41	30	63	36
8	Octyl	Et	43	30	70	97
9	Cyclohexyl	Et	45	40	79	65
10	1-Ethylpentyl	Et	43	30	58	46
11	Ph	Et	43	38	37	37

a) Reactions were conducted on a 5 mmol scale without solvent in a sealed tube using a mixture of 1/aldehyde/^{i}PrOH/HRh$(PPh_3)_4$ = 1/2/0.2/0.01.

b) Isolated yield.

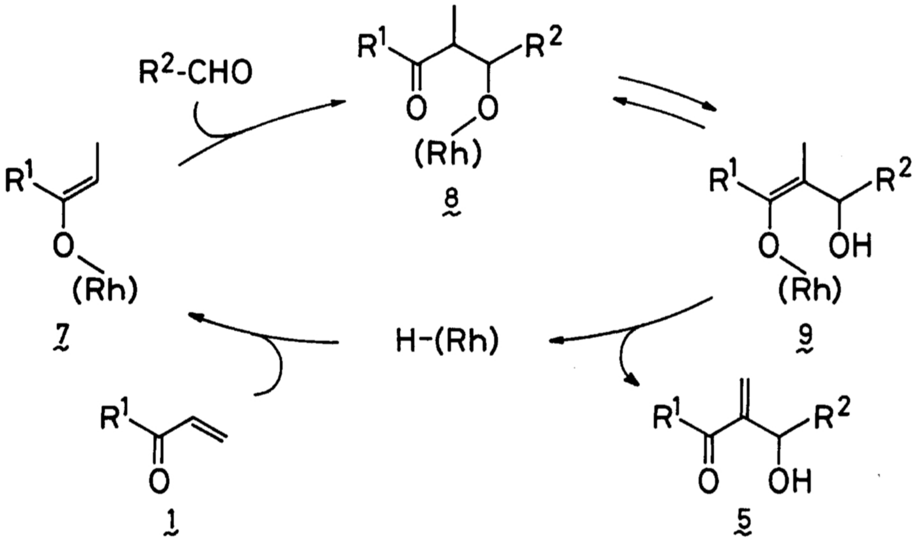
c) 2-Methyldiphenylsilylheptan-1-ol was added instead of 2-propanol.

Triphenylphosphine itself can catalyze the similar process via phosphonium betaine intermediate,[5)] however, the participation of another catalytic species can be suggested in Eq. 1 on the basis of the following observations; (1) the solvent interferes the coupling reaction,[6)] (2) addition of 10–20 mol% of alcohol enhances turnover number of catalyst (compare entries 2 and 5 in Table 1), and (3) addition of PBu_3 into catalyst does not change the reaction course[7)] (entry 12 in Table 1).

While it is premature to rationalize the mechanistic details in the present coupling reaction, it is noteworthy that rhodium enolate complex like 7 has been proposed in the interaction of 4-phenyl-3-buten-2-one with HRh$(PPh_3)_4$.[8)] Nucleophilic attack of 7 to aldehyde resulting 8, and the concomitant equilibration to 9 may be linked to the formation of 5 as shown in Scheme 2.

Anyway the present method is the first example catalyzed by rhodium(I) complex and promises a new route to stereoselective synthesis of aldol derivatives by the subsequent selective hydrogenation of the methylene group in 5.

The author (I. M.) thanks to The Kurata Foundation for the Kurata Research Grant.



Scheme 2.

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4) These two compounds were isolated by column chromatography on silica gel and characterized by the IR, NMR, and MS spectra. The ratio was determined by capillary GLC analyses (PEG-HT Bonded, 25 m column).

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6) When benzene was used as a solvent, the yield of 5 dropped sharply to 2% even in the presence of 3 mol% of $HRh(PPh_3)_4$.

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(Received September 19, 1985)