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THE FIRST EXAMPLE OF ALDOL REACTIONS BETWEEN TRIMETHYLSILYL ENOL ETHERS AND ALDEHYDES BY THE AID OF RHODIUM COMPLEX

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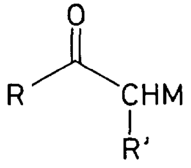
Summary: Crossed aldol reaction of trimethylsilyl enol ether with aldehyde is successfully performed with the aid of catalytic amount of rhodium complex, [(COD)Rh(DPPB)]$^+$X$^-$ (X = PF_6 and ClO_4) or $Rh_4(CO)_{12}$, under neutral conditions.

The generation and reactions of organotransition-metal enolates have witnessed the burgeoning interest in organic synthesis. Several carbon-bound transition-metal enolates (type **1**) have been generated and isolated.[1 - 5] These are relatively stable and insufficient to the subsequent carbon-carbon bond formation unless the conversion to η^3-enolates (type **2**) is possible.[4, 6]

On the other hand, enolates of type **3** have been generated *in situ* by reactions involving complexes of early transition-metals (Ti and Zr) and shown stereoselectivity in their aldol reactions with aldehydes.[7 - 9] It has been reported that the intermediacy of rhodium enolates (type **2** or **3**) is quite important in the rhodium catalyzed coupling reaction of vinyl ketone and aldehyde which resembles an aldol type carbon-carbon bond formation.[10]



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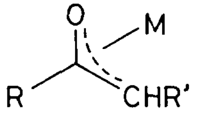

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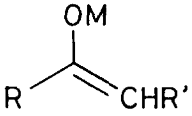

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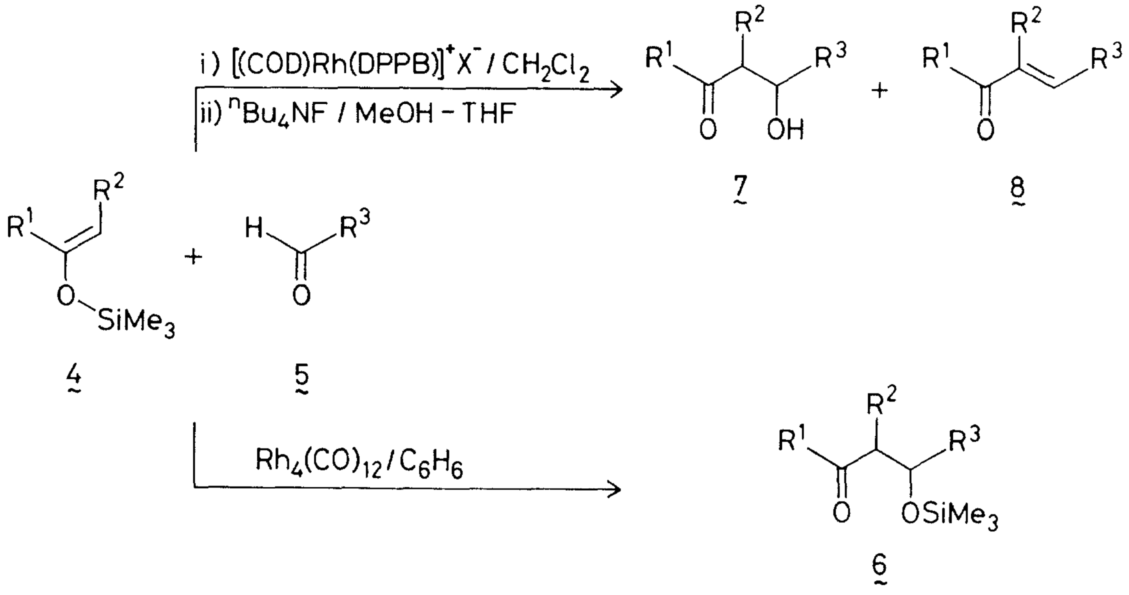
The feasibility of the presence of rhodium enolate stimulates us to utilize trimethylsilyl enol ethers as a facile and general enolate source. In line with the motive we report here the first rhodium catalyzed aldol reaction between trimethylsilyl enol ethers and aldehydes under almost neutral conditions.

Thus, a dichloromethane solution of trimethylsilyl enol ether **4a** (R^1 = Me, R^2 = H) (2 mmol) and hexanal (2.2 mmol) was heated at 100 °C for 15 h in a sealed tube contained 2 mol% of [(COD)Rh(DPPB)]$^+PF_6^-$ [COD = 1,5-cyclooctadiene, DPPB = bis(1,4-diphenylphosphino)-butane]. The reaction mixture diluted with hexane was filtered and concentrated. Since the resulting oily liquid was composed of two aldol type products, β-siloxy ketone **6a**, and the subsequently protodesilylated β-hydroxy ketone **7a**, the residue was protodesilylated in a mixed solution of MeOH-THF including catalytic amount of $^{n}Bu_4N^+F^-$, to give pure **7a** in 66 % yield following a column chromatography on silica gel.

The formation of the protodesilylated product **7a** was not suppressed even under milder conditions in the presence of $[(COD)Rh(DPPB)]^+PF_6^-$. An analogous cationic complex $[(COD)Rh(DPPB)]^+ClO_4^-$ catalyzed aldol reactions more effectively (Entry 2 and 3 in Table 1), however, the content of **6a** decreased. The subsequently dehydrated product α,β-unsuturated ketone **8a** was the sole product under forcing conditions (Entry 1 in Table 1). The results are summarized in Table 1.

The anionic part of the complex also affects the aldol type reaction significanty. When $[(COD)Rh(DPPB)]^+BF_4^-$ was used as catalyst, only 9% of **6a** was obtained after heating for 15 h at 100 °C. Several other neutral complexes, $HRh(PPh_3)_4$, $HRh(PPh_3)_3$, $HClRu(PPh_3)_3$, $H_4Ru(PPh_3)_3$, and $Cl_2Pd(CH_3CN)_2$, had no catalytic activity in the reaction of **4a** and hexanal. These observations make us hesitate to conclude the crucial intervention of rhodium metal in the reaction, because the extremely high catalytic activity of $Ph_3C^+ClO_4^-$ for aldol reaction has been reported previously.[11] However, the effective activity of $Rh_4(CO)_{12}$ as a catalyst suggests strongly the important role of rhodium metal in the analogous aldol reaction. Although it has been reported that the reaction of silyl enol ethers with aldehydes



Scheme 1.

Table 1. Aldol reactions with the aid of $[(COD)Rh(DPPB)]^+X^-$.

					Yield % a)			
Entry	Silyl enol ether		Aldehyde	Conditions	X = PF_6		X = ClO_4	
	R^1	R^2	R^3	°C/h	**7**	**8**	**7**	**8**
1	Me	H	$^nC_5H_{11}$	100/15	66	0	0	77
2	Me	H	$^nC_5H_{11}$	100/0.25	12	0	74	0
3	Me	H	$^nC_5H_{11}$	40/20	7	0	70	0
4	Me	H	Cyclohexyl	100/18	20	0	25	0
5	Ph	H	$^nC_5H_{11}$	100/15	53	0	0	26b)
6	Ph	H	$^nC_5H_{11}$	100/0.25			5	25b)
7	$-(CH_2)_4-$		$^nC_5H_{11}$	100/15	19	0	0	0
8	Et	Me	Et	100/15			0	22
9	Et	Me	Ph	100/25			20	10

a) Isolated yield after protodesilylation.

b) Silyl enol ether was consumed, but acetophenone was recovered.

Table 2. Aldol reactions with the aid of $Rh_4(CO)_{12}$.

Entry	Silyl enol ether		Aldehyde	Conditions	Yield of **6** a)	Syn:Anti
	R^1	R^2	R^3	°C/h	%	
1	Me	H	$^nC_5H_{11}$	100/21	71	
2	Me	H	$^nC_5H_{11}$	40/23	0	
3	Me	H	$^nC_5H_{11}$	100/2	57	
4	Me	H	Cyclohexyl	100/20	35	
5	Me	H	Ph	100/16	61	
6	$-(CH_2)_4-$		$^nC_5H_{11}$	100/21	71	56:44
7	$-(CH_2)_4-$		Cyclohexyl	100/18	52	56:44
8	$-(CH_2)_4-$		Ph	100/17	83	56:44
9	Et	Me	$^nC_5H_{11}$	100/20	0	
10	Et	Me	Ph	100/19	54	50:50

a) Isolated yield.

proceeded under neutral conditions by using a high-pressure technique (10 kbar),[12] no coupling product **6a** was observed in the reaction of **4a** with hexanal (100 °C, 25 h) in the absence of any rhodium complexes.

A reaction of **4a** (2 mmol) and hexanal (1.5 mmol) was catalyzed by 2 mol% (on Rh atom) of $Rh_4(CO)_{12}$ in benzene to give **6a** as the sole product in 71 % yield after bulb to bulb distillation. Neither protodesilylation nor dehydration of **6a** was observed in all cases. The results are summarized in Table 2.

In contrast to the successful intermolecular carbon-carbon bond formation, the stereoselectivity is not satisfied in the rhodium catalyzed aldol reaction (Entry 6, 7, 8, and 10 in Table 2). However, it should be stressed that crossed aldol reactions between trimethylsilyl enol ethers and aldehydes could be performed with the aid of rhodium complexes under the neutral conditions. Although the mechanistic aspect of the reaction is not clear in the present time, the intermediacy of rhodium enolate in the catalytic cycle is a plausible elucidation like as the examples reported previously.[10, 13, 14] Further studies are now in progress.

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References and Notes

1. R. B. Silverman, and D. Dolphin, J. Am. Chem. Soc., 98, 4633 (1976).
2. D. Milstein, and J. C. Calabrese, J. Am. Chem. Soc., 104, 3773 (1982).
3. D. Milstein, J. Am. Chem. Soc., 104, 5227 (1982).
4. J. J. Doney, R. G. Bergman, and C. H. Heathcock, J. Am. Chem. Soc., 107, 3724 (1985).
5. Y. Aoyama, T. Yoshida, and H. Ogoshi, Tetrahedron Lett., 26, 6107 (1985).
6. Y. Ito, H. Aoyama, T.Hirao, A. Mochizuki, and T. Saegusa, J. Am. Chem. Soc., 101, 494 (1979).
7. D. A. Evans, and L. A. McGee, Tetrahedron Lett., 21, 3975 (1980).
8. Y. Yamamoto, and K. Maruyama, Tetrahedron Lett., 21, 4607 (1980).
9. J. R. Stille, and R. H. Grubbs, J. Am. Chem. Soc., 105, 1664 (1983).
10. S. Sato, I. Matsuda, and Y. Izumi, Chem. Lett., 1875 (1985).
11. T. Mukaiyama, S. Kobayashi, and M. Murakami, Chem. Lett., 447 (1985).
12. Y. Yamamoto, K. Maruyama, and K. Matsumoto, J. Am. Chem. Soc., 105, 6963 (1983).
13. I. Matsuda, S. Sato, and Y. Izumi, Tetrahedron Lett., 24, 2787 (1983).
14. S. Sato, I. Matsuda, and Y. Izumi, Tetrahedron Lett., 24, 3855 (1983).

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