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Efficient Activation of Acetals toward Nucleophiles with $[Rh(COD)Cl]_2$ Catalyst. New Method for the Preparation of Aldols from Acetals and Silyl Enol Ethers by the Combined Use of Catalytic Amounts of $[Rh(COD)Cl]_2$ and Trimethylsilyl Cyanide

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In the presence of a catalytic amount of $[Rh(COD)Cl]_2$, di-μ-chloro-bis(1,5-cyclooctadiene)dirhodium, trimethylsilyl cyanide smoothly reacts with acetals derived from aliphatic, unsaturated and aromatic aldehydes to form the corresponding α-cyano derivatives in high yields. In the coexistence of catalytic amounts of $[Rh(COD)Cl]_2$ and trimethylsilyl cyanide, silyl enol ethers also react with acetals to yield the corresponding aldol adducts under almost neutral conditions.

Reactions between acetal and silyl nucleophiles are important tools for carbon-carbon bond formation.$^{1)}$ Most of these reactions are carried out under acidic conditions by the promotion of Lewis acids such as $TiCl_4$, $SnCl_4$ or by the use of salts with anions of very strong acids such as trimethylsilyl trifluoromethanesulfonate or trityl perchlorate, etc. In the previous paper$^{2)}$, we reported that in the presence of a catalytic amount of transition metal salts such as $NiCl_2$ or $CoCl_2$, trimethylsilyl cyanide (TMS-CN) smoothly reacts with acetals derived from aromatic and α,β-unsaturated carbonyl compounds to form the corresponding α-cyano derivatives under almost neutral conditions. Under the above conditions, however, acetals of saturated aldehydes hardly react with TMS-CN. Then, in order to perform the cyanation of acetals of saturated aldehydes, the reaction of 3-phenylpropanal dimethyl acetal (3) with TMS-CN (1.5 equiv.) in CH_3CN was tried in the presence of 2 mol% of $[Rh(COD)Cl]_2$, di-μ-chloro-bis(1,5-cyclooctadiene)dirhodium, at room temperature and it was found that 1-methoxy-3-phenylpropionitrile was obtained in 93% yield within 3 h. Similarly, the reaction of the other acetals with TMS-CN gave the corresponding α-cyano derivatives in high yields (Table 1).

Based on the above results, it was suggested that a complex formed from $[Rh(COD)Cl]_2$ and TMS-CN would be effective for the activation of acetals. The possible activation of acetals, protected carbonyl compounds, under almost neutral conditions led us to study on aldol reaction between silyl enol ethers and acetals in the presence of the above complex. The reaction of acetal 1 with trimethylsilyl enol ether of acetophenone(5) in the coexistence of 2 mol% of

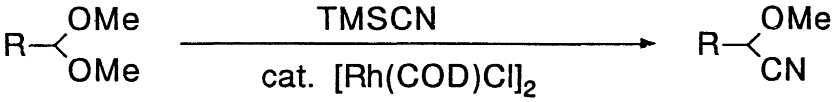
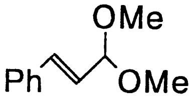
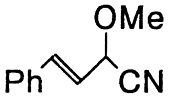
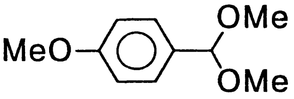
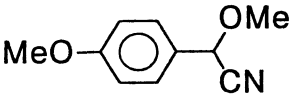
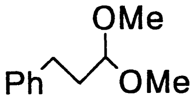
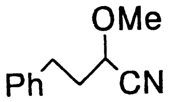
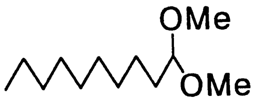
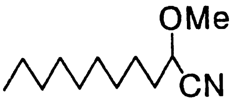
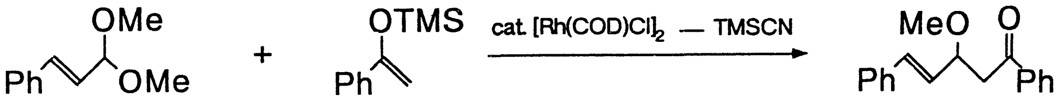


Table 1. Cyanation of acetals$^{a)}$

Entry	Substrate	Product	Yield/%
1	 1	 7	88
2	 2		96
3	 3		93
4	 4		96

a) Reactions were carried out by using 1.5 equiv. of TMS-CN and 2 mol% of $[Rh(COD)Cl]_2$ in CH_3CN at room temperature for 3 h.



1 5 6

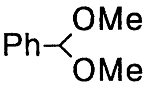
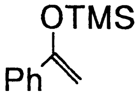
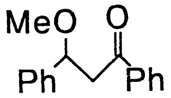
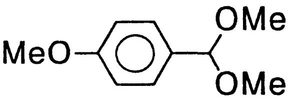
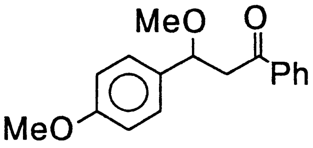
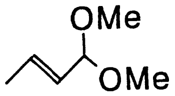
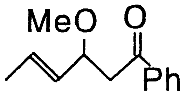
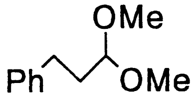
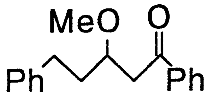
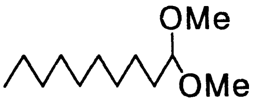
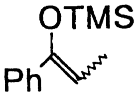
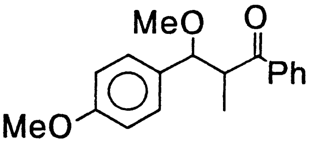
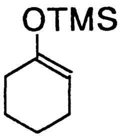
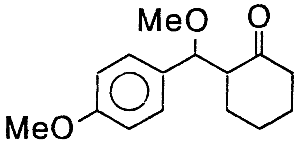
Table 2. Examination of reaction conditions$^{a)}$

Entry	Solvent	Mol% of TMS-CN	Yield of 6/%
1	CH_3CN	0	0
2	CH_3CN	5	21$^{b)}$
3	CH_3CN	20	91
4	CH_3CN	50	82
5	CH_3CN	100	56
6	CH_2Cl_2	20	79
7	THF	20	84
8	Toluene	20	78

a) Reactions were carried out by using 1.2 equiv. of 5 and 2 mol% of $[Rh(COD)Cl]_2$ at room temperature for 3 h.
b) Starting material 1 was recovered in 71% yield.

$[Rh(COD)Cl]_2$ and 20 mol% of TMS-CN took place smoothly in CH_3CN at room temperature to give the desired product 6 in 91% yield, as expected. It is

Table 3. Reactions of acetals with silyl enol ethers[a)]

Entry	Acetal		Silyl enol ether		Product	Yield/%
1		8		5		97
2[b)]		2		5		94
3		9		5		86
4		3		5		98
5[c)]		4		5		80
6	2			10		87[d)]
7	2			11		92[e)]

a) Reactions were carried out by using 1.5 equiv. of silyl enol ethers, 2 mol% of $[Rh(COD)Cl]_2$ and 20 mol% of TMS-CN in CH_3CN at room temperature for 3 h except for entries 2 and 5.

b) 1.2 equiv. of 5 was used.

c) 50 mol% of TMS-CN was used.

d) syn:anti=7:3, determined by ^1H NMR measurement.

e) syn:anti=7:3, separated by preparative TLC (silica gel).

interesting to note that α-cyano derivative 7 was not isolated under the above conditions. While, in the absence of TMS-CN, the above reaction did not proceed at all. After screening detailed reaction conditions (Table 2), it was shown that the desired aldol adduct 6 was obtained in high yield when the reaction was carried out with 20 mol% of TMS-CN as a co-catalyst. On the other hand, when 1 equiv. of TMS-CN was used, the yield of 6 decreased to 56% because of formation of unidentified by-product.3) One of the important notes of the present reactions is that CH_3CN and THF can be used as a reaction solvent different from the commonly known Lewis acids mediated reactions.

Several examples of the reactions of acetals with silyl enol ethers are demonstrated in Table 3 and the corresponding aldol adducts are obtained in good yields.

Concerning aldol reactions promoted by rhodium compounds, there reported some reactions between aldehydes or acetals and silyl enol ethers promoted by cationic rhodium species such as $[Rh(COD)(DPPB)]ClO_4$ or $Rh_4(CO)_{12}$.4) Recently, preparation of aldol type adducts from vinylketones, aldehydes and hydrosilane by the aid of $Rh_4(CO)_{12}$ was also reported5) and it was proposed there that rhodium enolate is generated initially as a key intermediate.

Typical procedure is described for the reaction of trimethylsilyl enol ether of acetophenone with benzaldehyde dimethyl acetal (Table 3, entry 1): Under an argon atmosphere, $[Rh(COD)Cl]_2$ (0.004 mmol) and TMS-CN (0.04 mmol) were stirred in acetonitrile (3 ml) at room temperature for 30 min, to which was added a mixture of trimethylsilyl enol ether of acetophenone (0.2 mmol) and benzaldehyde dimethyl acetal (0.3 mmol) in acetonitrile (2 ml). The reaction mixture was stirred for 3 h at the same temperature, then quenched with aqueous solution of $NaHCO_3$. The organic materials were extracted with ethyl acetate and combined extracts were dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC (silica gel, n-hexane:AcOEt=5:1) to afford 1,3-diphenyl-3-methoxy-1-propanone (0.193 mmol, 97%).

Although the detailed mechanism is not yet made clear, it is assumed that acetal would be activated by the interaction with positively charged trimethylsilyl group generated by the coordination of cyano group of TMS-CN onto $[Rh(COD)Cl]_2$. Then, silyl enol ethers, more reactive nucleophile compared with TMS-CN, would preferentially attack the activated acetal to result in the formation of aldol adducts.

It is noted that the use of a catalytic amount of $[Rh(COD)Cl]_2$ promotes the cyanation of acetals including acetals of saturated aldehydes with TMS-CN and that, in addition, the combined use of catalytic amounts of $[Rh(COD)Cl]_2$ and TMS-CN promotes the aldol reaction between acetals and silyl enol ethers under almost neutral conditions. Further studies directed to the possible use of the other nucleophiles and electrophiles are currently in progress.

References

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2) T. Mukaiyama, T. Soga, and H. Takenoshita, Chem. Lett., 1989, 997.

3) An unidentified by-product is not α-cyano derivative 7, (E)-1-methoxy-4-phenyl-3-butenonitrile.

4) S. Sato, I. Matsuda, and Y. Izumi, Tetrahedron Lett., 27, 5517 (1986); S. Sato, I. Matsuda, and Y. Izumi, ibid., 28, 6657 (1987); M. T. Reetz and A. E. Vougioukas, ibid., 28, 793 (1987).

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