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Cobalt(II) Catalyzed Coupling Reaction of α,β-Unsaturated Compounds with Aldehydes by the Use of Phenylsilane.
New Method for Preparation of β-Hydroxy Nitriles, Amides, and Esters

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A new crossed coupling reaction of α,β-unsaturated nitriles with aldehydes was performed by using phenylsilane and a catalytic amount of bis(1,3-diketonato)cobalt(II) to give β-siloxy nitriles in good yields. Similarly, α,β-unsaturated amides and esters also reacted under the same conditions to afford β-siloxy amides or esters. The present reaction provides a new and facile method for preparation of β-hydroxy nitriles, amides, and esters.

The generation and reaction of organotransition-metal enolate$^{1)}$ is one of the current interests in organic synthesis and several C-C bond forming reactions were reported by using stoichiometric amount of enolates involving several transition metals (e.g., Ti, Zr, Mo, W, and Re).$^{2)}$ Recently, Rh catalyzed aldol-type reactions via oxygen-bound Rh enolates have been studied by using enol silyl ether or α,β-unsaturated esters as nucleophiles.$^{3)}$ However, little work is known$^{4)}$ on catalytic C-C bond forming reactions using other transition metal complexes as a catalyst. Now, we wish to report the first example of cobalt catalyzed coupling reaction of α,β-unsaturated compounds, especially unsaturated nitriles and amides, with aldehyde by using phenylsilane as hydrogen source.

Previously, we reported a series of bis(1,3-diketonato)cobalt(II) catalyzed oxygenations of olefinic compounds with O_2 and silane such as $Et_3SiH$$^{5)}$ or $PhSiH_3$$^{6)}$ as hydrogen source. Under these reaction conditions, it is assumed that formation and reaction of the key intermediate, alkyl-cobalt complex, was performed by the aid of silane. On the bases of this assumption, we attempt to realize a catalytic carbon-carbon bond forming reaction between an olefinic compound and an aldehyde by the combined use of hydrosilane and a catalytic amount of cobalt(II) complex.

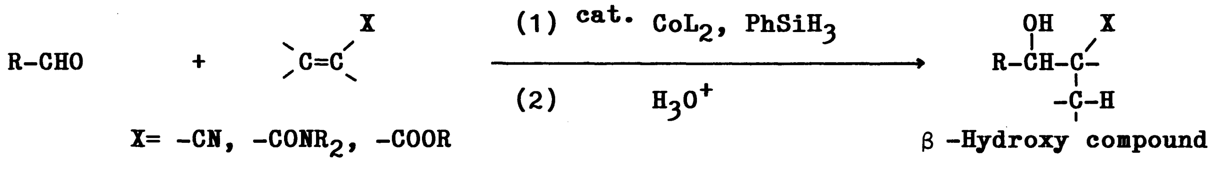

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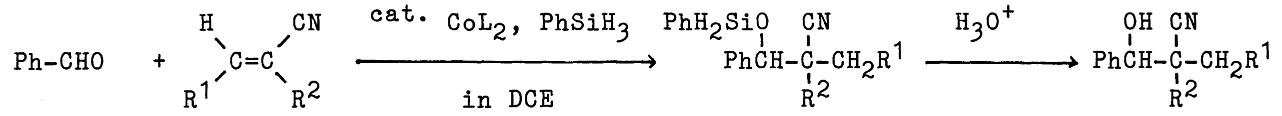
Table 1. Reaction of benzaldehyde and α ,β-unsaturated nitriles[a)]



$$\text{Ph-CHO} + \text{(R}^1\text{)(H)C=C(CN)(R}^2\text{)} \xrightarrow[\text{in DCE}]{\text{cat. CoL}_2\text{, PhSiH}_3} \text{PhCH(OSiH}_2\text{Ph)-C(CN)(R}^2\text{)-CH}_2\text{R}^1 \xrightarrow{H_3O^+} \text{PhCH(OH)-C(CN)(R}^2\text{)-CH}_2\text{R}^1$$

1 ; 2a R^1=H, R^2=H ; 2b R^1=Me, R^2=H ; 2C R^1=H, R^2=Me ; 3a-c ; 4a R^1=H, R^2=H ; 4b R^1=Me, R^2=H ; 4c R^1=H, R^2=Me

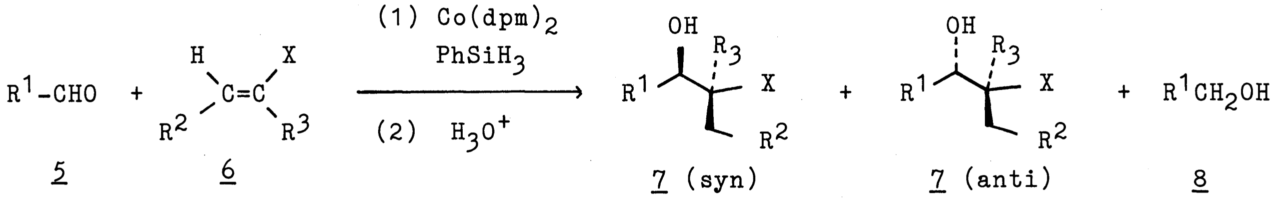
Entry	Nitriles 2	CoL_2[b)]	Temp /°C	Time /h	Yield of 4 /%[c)]	Yield of $PhCH_2OH$ /%[d)]
1	acrylonitrile	Co(acac)$_2$	70	3	70	5
2	acrylonitrile	Co(acac)$_2$	20	24	42	3
3	acrylonitrile	Co(dpm)$_2$	20	12	93	2
4	crotononitrile	Co(acac)$_2$	70	5	72	25
5	crotononitrile	Co(dpm)$_2$	20	12	92	5
6	methacylonitrile	Co(acac)$_2$	20	24	60[d)]	31

a) Under an argon atmosphere. Molar ratio of 1 : 2 : $PhSiH_3$: CoL_2 = 1 : 4 : 2 : 0.05. b) Co(acac)$_2$ was dried over 70 °C in vacuo. Co(dpm)$_2$ was purified by submilitaion. c) Isolated yield as a mixture of diastereomers (ratio = 50 : 50) d) Determined by GC.

Thus, to a 1,2-dichloroethane (DCE) solution of a catalytic amount of bis(acetylacetonato)cobalt(II) (Co(acac)2) (0.05 mmol) and phenylsilane (2 mmol) was added a DCE solution of acrylonitrile (2a) (4 mmol) and benzaldehyde (1) (1 mmol), and the reaction mixture was heated at 70 °C for 3 h. The coupling reaction proceeded smoothly to afford a β-siloxy nitrile 3a as the main product, and after quenching the reaction mixture with MeOH (20 ml) and 10% hydrochloric acid (2 ml), the desired β-hydroxy nitrile 4a was isolated by preparative TLC (silica gel) in good yield. At the same time, small amount of benzylalcohol was detected by GC analysis of the reaction mixture (Entry 1 in Table 1). Similarly, the respective coupling reactions of 1 with acrylonitrile (2a), crotononitrile (2b) and methacrylonitrile (2c) were examined by using several bis(1,3-diketonato)cobalt(II) complexes and it was found that bis(dipivaloylmethanato) cobalt(II) complex (Co(dpm)$_2$)[7)] showed excellent catalytic activities. For example, the reactions of 1 with 2a and 2b proceeded smoothly even at room temperature (20 °C) and the desired β-hydroxynitriles 4a and 4b were obtained in high yields (Entries 3 and 5). Although the simple reduction of 1 took place at the same time, methacrylonitrile also reacted with 1 to give β-hydroxy-

-dimethylnitrile 4c which is hardly prepared according to the conventional method. Thus the present reaction provided a novel and facile method for formation of new carbon-carbon bond between an α,β-unsaturated nitrile and an aldehyde.

Table 2. Reaction of aldehyde with α,β-unsaturated amide and ester[a)]



X = -NMe_2, -OMe

Entry	R^1	R^2	R^3	X	Temp /°C	Time /h	Yield of 7 /%[b)]	Syn:Anti[c)]	Yield of 8 /%[d)]
1	Ph	H	H	$CONMe_2$	20	2	95	80:20	3
2	PhCH=CH	H	H	$CONMe_2$	20	4	96	72:28	Trace
3	$PhCH_2CH_2$	H	H	$CONMe_2$	20	6	90	70:30	Trace
4	Ph	Me	H	$CONMe_2$	50	3	72	70:30	10
5	PhCH=CH	Me	H	$CONMe_2$	20	4	68	72:28	12
6	Ph	H	Me	$CONMe_2$	20	5	50	-	31
7	PhCH=CH	H	Me	$CONMe_2$	20	4	70	-	14
8	PhCH=CH	H	H	COOMe	20	20	80[e)]	50:50	10
9	$PhCH_2CH_2$	H	H	COOMe	20	20	62[e)]	50:50	14

a) Under an argon atmosphere. Molar ratio of Aldehyde : Amide : $PhSiH_3$: $Co(dpm)_2$ = 1 : 1.2 : 1.2 : 0.05. Molar ratio of Aldehyde : Ester : $PhSiH_3$: $Co(dpm)_2$ = 1 : 4 : 2 : 0.05. b) Isolated yield. c) All the diastereo isomers of amides were isolated by TLC (silica gel) and the stereochemistry were determined by comparing with the authentic samples (syn-isomers) prepared by reported method.[8)] d) Determined by GC. e) Isolated as mixtures.

Next, the coupling reaction of aldehyde with several α,β-unsaturated amides and esters were examined by using $Co(dpm)_2$ as a catalyst and the results are summarized in Table 2. All reactions were effectively catalyzed by Co(dpm)$_2$ to give the corresponding β-hydroxy amides and esters in good to high yields. It is noteworthy to refer that a certain extent of diastereoselectivity was observed in case of the reaction of the amides, for example, the ratio of syn and anti isomers was 80 : 20 in the reaction of 5a with 6a (Entry 1).

A typical procedure is described for the reaction of N,N-dimethylacrylamide with benzaldehyde; under an argon atmosphere, a solution of Co(dpm)$_2$ (21 mg, 0.05 mmol) and phenylsilane (130 mg, 1.2 mmol) in DCE (2 ml) was stirred for 5 min at room temperature (20 °C), to which were added slowly benzaldehyde (106 mg, 1 mmol) and N,N-dimethylacrylamide (119 mg, 1.2 mmol) in DCE (2 ml). After the solution was stirred for 2 h at room temperature, the volatile materials were evapolated under reduced pressure. To the residue, MeOH (2 ml), THF (2 ml) and 10% aqueous hydrochloric acid (1 ml) were added and stirred for 30 min and the organic materials were extracted with ethyl acetate and the combined organic extracts were washed with aqueous sodium bicarbonate, brine and dried over Na_2SO_4. After evapolation of the solvent, the residue was purified by preparative TLC (silica gel, hexane : AcOEt = 2:1) to give the two diastereoisomers of 3-hydroxy-2-methyl-3-phenyl-N,N-dimethylpropionamide respectively (syn-form, R_f= 0.4, 157 mg, 76% and anti-form, R_f= 0.3, 39 mg, 19%).

Although the detailed mechanism is not yet clear, it is assumed that a carbon-bound cobalt enolate could be generated by the addition of cobalt and hydrogen to unsaturated compounds, and successive coupling reaction of the cobalt enolates with aldehydes would occurred by the aid of phenylsilane to produce the β-siloxy nitriles, amides, and esters. Further studies directed to clarify the reaction intermediates of the present reaction are now under investigation.

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