Efficient Activation of Acetals, Aldehydes, and Imines toward Silylated Nucleophiles by the Combined Use of Catalytic Amounts of [Rh(COD)Cl]$_2$ and TMS-CN under Almost Neutral Conditions

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In the presence of a catalytic amount of a transition metal compound such as [Rh(COD)Cl]$_2$, Co(acac)$_2$, or NiCl$_2$, trimethylsilyl cyanide smoothly reacts with acetals to form α-methoxy carbonitriles in good yields. In the coexistence of catalytic amounts of [Rh(COD)Cl]$_2$ and TMS-CN, silyl enol ethers or ketene silyl acetals react with acetals, aldehyes, or imines to yield the corresponding coupling products in good yields under almost neutral conditions.

In recent years, various kinds of carbon–carbon bond forming reactions of carbonyl or related compounds with silylated nucleophiles have been developed.[1] Many reagents also have been employed for promotion of the above reactions and it becomes apparent that a stoichiometric amount of Lewis acid such as TiCl$_4$ or SnCl$_4$[2] is not necessarily required. For example, cyanation reactions of aldehydes, ketones, and epoxides with trimethylsilyl cyanide (TMS-CN)[3] are carried out by the use of a catalytic amount of Lewis acid such as ZnI$_2$, SnCl$_2$ or BF$_3$·Et$_2$O.[4] Another example shows that silyl enol ethers smoothly react with aldehydes, acetals or α,β-unsaturated ketones by the use of a catalytic amount of Lewis acid such as trimethylsilyl trifluoromethanesulfonate[5] or trityl perchlorate.[6] Most of these reactions, however, are carried out essentially under acidic conditions because of Lewis acid catalyst employed.

We initiated the present study in order to explore new types of catalysts which promote the reactions of carbonyl and related compounds with silylated nucleophiles under almost neutral conditions. First, based on the consideration that cyano group could coordinate to transition metal, cyanation of acetals with TMS-CN by using a catalytic amount of transition metal compound was tried. Then it was found that cyanation of acetals with TMS-CN proceeded under almost neutral conditions in the presence of a catalytic amount of transition metal compound such as di-μ-chloro-bis(1,5-cyclooctadiene)-dirhodium ([Rh(COD)Cl]$_2$), cobalt(II) acetylacetonate (Co(acac)$_2$), CoCl$_2$, or NiCl$_2$, as we have briefly reported in preliminary communications.[7] We have also briefly reported the efficient activation of acetals towards silyl enol ethers with a complex generated from [Rh(COD)Cl]$_2$ and TMS-CN.[7b] We now describe in full the results of our investigation on the above cyanation and aldol reactions promoted by using a catalytic amount of [Rh(COD)Cl]$_2$ under almost neutral conditions and further application to the possible use of the other silylated nucleophiles, and of electrophiles including aldehydes having basic substituents and imines.

Results and Discussion

Cyanation of Acetals. Concerning cyanation of acetals with TMS-CN under acidic conditions by the use of several Lewis acids, several examples are already known.[4] First, in order to carry out the cyanation of acetals with TMS-CN under very mild conditions without use of commonly employed Lewis acids, the reaction of (*E*)-cinnamaldehyde dimethyl acetal (**1**) with TMS-CN (1.5 equiv) in CH$_2$Cl$_2$ was tried in the presence of a catalytic amount of NiCl$_2$ (10 mol%) at room temperature and it was found that (*E*)-2-methoxy-4-phenyl-3-butenenitrile (**2**) was obtained in 96% yield. After screening other transition metal salts and detailed reaction conditions taking the above acetal **1** as a model substrate, it was found that **2** was obtained also in good yield when a catalytic amount of the other transition metal compound such as CoCl$_2$, Co(acac)$_2$, PdCl$_2$, or [Rh(COD)Cl]$_2$ was used. One of

Table 1. Cyanation of (*E*)-Cinnamaldehyde Dimethyl Acetal (**1**) with TMS-CN under Various Conditions[a]

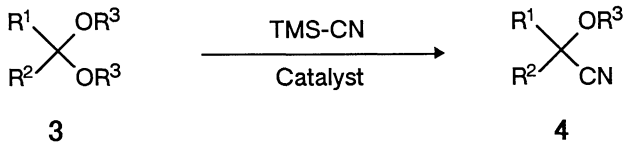
Entry	Catalyst	Solvent	Yield of **2**/%
1	NiCl$_2$	CH$_2$Cl$_2$	96
2	Ni(acac)$_2$	CH$_2$Cl$_2$	84
3	Ni(OAc)$_2$	CH$_2$Cl$_2$	87
4	CoCl$_2$	CH$_2$Cl$_2$	82
5	Co(acac)$_2$	CH$_2$Cl$_2$	82
6	PdCl$_2$	CH$_2$Cl$_2$	95
7	Pd(acac)$_2$	CH$_2$Cl$_2$	78
8[b]	[Rh(COD)Cl]$_2$	CH$_3$CN	88
9	Co(acac)$_2$	Toluene	81
10	Co(acac)$_2$	CH$_3$CN	92
11	Co(acac)$_2$	Et$_2$O	92
12	Co(acac)$_2$	Dioxane	90
13	Co(acac)$_2$	THF	89
14[c]	Co(acac)$_2$	DMF	79

a) Reactions were carried out by using 1.5 equiv of TMS-CN and 10 mol% of catalyst at room temperature for 3 h except for entries 8 and 14. b) 2 mol% of catalyst was used. c) Reaction time is 44 h.

the important notes of these reactions is that ether, dioxane, THF and DMF can be used as a reaction solvent different from the commonly known Lewis acids mediated reactions.

The mechanism of the reaction could be explained by considering that, in addition to the nucleophilic ability of TMS-CN, effective activation of acetal would be caused by TMS-CN; that is, positively charged trimethylsilyl group could be generated by coordination of cyano group of TMS-CN to transition metal,[8] and the acetal, activated by the interaction with the trimethylsilyl group, would readily be attacked by another TMS-CN to result in the formation of α-alkoxy carbonitrile and trimethylsilyl methoxide. To our knowledge, this is the first example to activate acetals by using this type of catalyst to effectively perform cyanation reaction.[9]

Next, various acetals[10] were treated with TMS-CN by the use of a catalytic amount of $NiCl_2$, $CoCl_2$, or [Rh(COD)Cl]$_2$ as a catalyst (see Scheme 1 and Table 2). The reactivity of the above mentioned cyanation of acetals was largely dependent on the sort of transition metals and solvents. For example *p*-methoxybenzaldehyde dimethyl acetal, relatively reactive acetal, react with TMS-CN by the use of $CoCl_2$ (Entry 5). On the other hand, 3-phenylpropanal dimethyl acetal, less reactive acetal, did not react with TMS-CN under the above conditions (Entry 17). The above reaction proceeded smoothly by the use of [Rh(COD)Cl]$_2$ in CH_3CN (Entry 18). It is noted that the strength of catalytic activity increases according to the following order; [Rh(COD)Cl]$_2$>$CoCl_2$>$NiCl_2$, and of solvents examined, CH_3CN was the most preferable.



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Scheme 1.

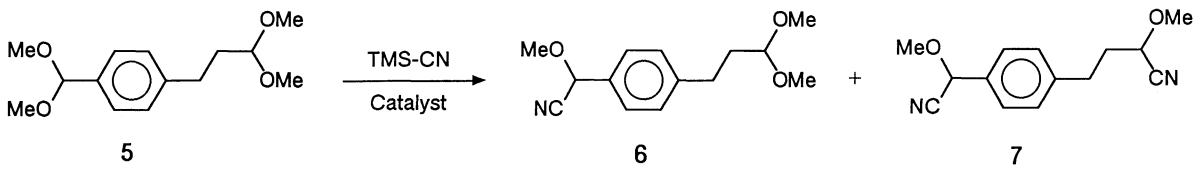
Based on the above results, it was suggested that selective cyanation would be realized between two acetal groups with different reactivities in one molecule by the choice of proper conditions. Reaction conditions of cyanation was screened taking bisacetal **5** as a model compound (Scheme 2) and it was shown that monocyano compound **6** was obtained without accompanying dicyano compound **7** by the use of 2.0 equiv of TMS-CN and 5 mol% of cobalt catalyst in CH_2Cl_2. On the other hand, **7** was obtained by the use of 3.0 equiv of TMS-CN and 2 mol% of [Rh(COD)Cl]$_2$ in CH_3CN as shown in Table 3.

Reaction of Acetals with Silylated Nucleophiles. The above results indicate that a complex formed from transition metal compounds such as [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 (**8**) of acetophenone in the coexistence of 2 mol% of [Rh(COD)Cl]$_2$ and 0.2 equiv of TMS-CN took place smoothly in CH_3CN at room temperature to give the desired 3-methoxy-1,5-diphenyl-4-penten-1-one (**9**) in 91% yield, as expected. While, in the absence of TMS-CN, the above reaction did not proceed at all. It is interesting to note that α-methoxy carbonitrile **2** was not isolated under the above conditions. After screening detailed reaction conditions (Table 4), it was

Table 2. Synthesis of α-Alkoxy Carbonitriles[a]

Entry	R^1	R^2	R^3	Catalyst	Solvent	Time/h	Yield/%
1	(*E*)-PhCH=CH	H	CH_3	$NiCl_2$	CH_2Cl_2	3	81
2	(*E*)-PhCH=CH	H	CH_3	$CoCl_2$	CH_2Cl_2	3	91
3	(*E*)-PhCH=CH	H	CH_3	[Rh(COD)Cl]$_2$	CH_3CN	3	88
4	*p*-MeO-C_6H_4	H	CH_3	$NiCl_2$	CH_2Cl_2	3	0
5	*p*-MeO-C_6H_4	H	CH_3	$CoCl_2$	CH_2Cl_2	1	90
6	*p*-MeO-C_6H_4	H	CH_3	Co(acac)$_2$	CH_2Cl_2	39	92
7	*p*-MeO-C_6H_4	H	CH_3	[Rh(COD)Cl]$_2$	CH_3CN	3	96
8	Ph	H	C_2H_5	$NiCl_2$	CH_2Cl_2	6	0
9	Ph	H	C_2H_5	$CoCl_2$	CH_2Cl_2	41	98
10	Ph	H	C_2H_5	Co(acac)$_2$	CH_2Cl_2	41	95
11	$CH_3(CH_2)_2CH$=CH	H	CH_3	$NiCl_2$	CH_2Cl_2	18	0
12	$CH_3(CH_2)_2CH$=CH	H	CH_3	$CoCl_2$	CH_2Cl_2	18	96
13	(*E*)-PhCH=CH	Ph	CH_3	$NiCl_2$	CH_2Cl_2	20	75
14	(*E*)-PhCH=CH	Ph	CH_3	$CoCl_2$	CH_2Cl_2	18	99
15	Ph	Ph	CH_3	$NiCl_2$	CH_2Cl_2	24	60
16	Ph	Ph	CH_3	$CoCl_2$	CH_2Cl_2	24	94
17	$PhCH_2CH_2$	H	CH_3	$CoCl_2$	CH_2Cl_2	18	0
18	$PhCH_2CH_2$	H	CH_3	[Rh(COD)Cl]$_2$	CH_3CN	3	93
19	$CH_3(CH_2)_8$	H	CH_3	$CoCl_2$	CH_2Cl_2	18	0
20	$CH_3(CH_2)_8$	H	CH_3	[Rh(COD)Cl]$_2$	CH_3CN	3	96

a) Reactions were carried out by using 1.5 equiv of TMS-CN and 2 mol% of catalyst at room temperature.



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Scheme 2.

Table 3. Selective Cyanation of 1-Dimethoxymethyl-4-(3,3-dimethoxypropyl)benzene (**5**)[a]

Entry	Catalyst	Equiv of TMS-CN	Solvent	Time/h	Yield/%	Ratio of **6**:**7**[b]
1	$Co(acac)_2$	2.0	CH_2Cl_2	18	83	100: 0
2	$CoCl_2$	2.0	CH_2Cl_2	15	87	100: 0
3	$Co(acac)_2$	2.0	CH_3CN	3	82	66: 34
4	$[Rh(COD)Cl]_2$	3.1	CH_2Cl_2	15	82	43: 57
5	$[Rh(COD)Cl]_2$	3.0	CH_3CN	3	88	0:100

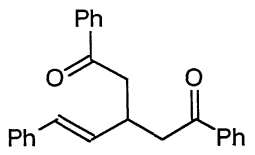
a) Reactions were carried out by using 5 mol% (Entries 1, 2, and 3) or 2 mol% (Entries 4 and 5) of catalyst at room temperature. b) Determined by ^1H NMR.

Table 4. Aldol Reaction between (*E*)-Cinnamaldehyde Dimethyl Acetal (**1**) and Trimethylsilyl Enol Ether (**8**) of Acetophenone under Various Conditions[a]

Entry	Solvent	Equiv of TMS-CN	Yield of **9**/%
1	CH_3CN	0	0
2	CH_3CN	0.05	21[b]
3	CH_3CN	0.2	91
4	CH_3CN	0.5	82
5	CH_3CN	1.0	56
6	CH_2Cl_2	0.2	79
7	THF	0.2	84
8	Toluene	0.2	78

a) Reactions were carried out by using 1.2 equiv of **8** and 2 mol% of $[Rh(COD)Cl]_2$ at room temperature for 3 h. b) Starting material **1** was recovered in 71% yield.

shown that the desired aldol adduct **9** 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 **9** decreased to 56% because of formation of by-product. This by-product was not α-methoxy carbonitrile **2** but identified as the mixture of **10** and **11** (37:63) by 500 MHz ^1H NMR measurement. The compounds **10** and **11** were formed by the addition of one more nucleophile **8** to initially formed aldol adduct **9** at C-3 or C-5 position. Similar to the cyanation of acetals, CH_3CN and THF can be used as a reaction solvent different from the commonly known Lewis acids mediated reactions.



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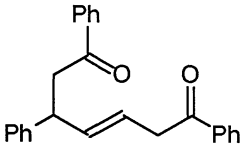

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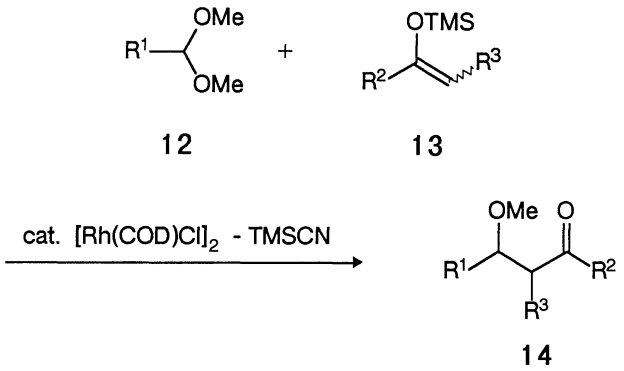


Scheme 3.

Several examples of the reactions of acetals with silyl enol ethers are demonstrated in Scheme 3 and the corresponding aldol adducts are obtained in good yields (see Table 5). In case of using less reactive acetals or silyl enol ethers than **1** or **8**, the yields of aldols increased by using more than 0.2 equiv of TMS-CN or more than 1.2 equiv of silyl enol ethers. Even under the above conditions, α-methoxy carbonitrile was not isolated. It suggests that silyl enol ether, more reactive nucleophile compared with TMS-CN, would preferentially attack the acetal activated by the interaction with positively charged trimethylsilyl group generated in situ by the coordination of cyano group of TMS-CN onto $[Rh(COD)Cl]_2$.

Concerning aldol reaction promoted by rhodium compounds, there are reported some reactions between aldehydes or acetal and silyl enol ethers promoted by cationic rhodium species such as $[Rh(COD)(DPPB)]ClO_4$ or $Rh_4(CO)_{12}$.[11] Recently, preparation of aldol type adducts from vinyl ketones, aldehydes, and hydrosilane by the aid of $Rh_4(CO)_{12}$ was also reported[12] and it was proposed there that rhodium enolate is generated initially as a key intermediate.

Table 5. Aldol Reaction of Acetals with Silyl Enol Ethers[a]

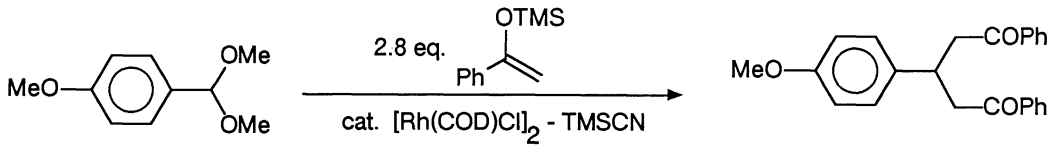
Entry	R^1	R^2	R^3	Equiv of **14**	Equiv of TMS-CN	Yield/%
1	Ph	Ph	H	0.2	1.5	97
2	*p*-MeO-C_6H_4	Ph	H	0.2	1.2	94
3	(*E*)-CH_3CH=CH	Ph	H	0.2	1.5	86
4	$PhCH_2CH_2$	Ph	H	0.2	1.5	98
5	$CH_3(CH_2)_8$	Ph	H	0.4	1.4	91
6[b]	*p*-MeO-C_6H_4	CH_3	H	0.2	1.4	87
7	*p*-MeO-C_6H_4	Ph	CH_3	0.4	1.4	89[c]
8	*p*-MeO-C_6H_4	$-(CH_2)_4-$		0.5	1.5	99[d]

a) Reactions were carried out by using 2 mol% of [Rh(COD)Cl_2] in CH_3CN at room temperature for 3 h except for Entry 6. b) 1 mol% of [Rh(COD)Cl]$_2$ was used. c) Syn : anti=71 : 29, determined by ^{1}H NMR. d) Syn : anti= 69 : 31, separated by preparative TLC (Silica gel).

Table 6. Reaction of Acetals with Ketene Silyl Acetals[a]

Entry	R^1	R^2	Equiv of **19**	Equiv of TMS-CN	Time/h	Yield/%
1	(*E*)-PhCH=CH	H	1.5	0.5	3	95[b]
2	(*E*)-PhCH=CH	CH_3	1.6	0.25	3	97
3	*p*-MeO-C_6H_4	H	1.4	0.5	3	89[b]
4	*p*-MeO-C_6H_4	CH_3	1.2	0.2	3	100
5	Ph	H	1.5	0.6	3	94[c]
6	Ph	CH_3	1.5	0.3	3	92
7	$PhCH_2CH_2$	H	1.5	0.5	13	73[d]
8	$PhCH_2CH_2$	CH_3	1.5	0.5	15	93

a) Reactions were carried out by using 2 mol% of [Rh(COD)Cl]$_2$ in CH_3CN at room temperature. b) Syn : anti= 50 : 50, determined by ^{1}H NMR. c) Syn : anti=48 : 52, separated by preparative TLC (Silica gel). d) Diastereomeric ratio was 52 : 48, determined by ^{1}N NMR. Relative configuration assignment was not made.



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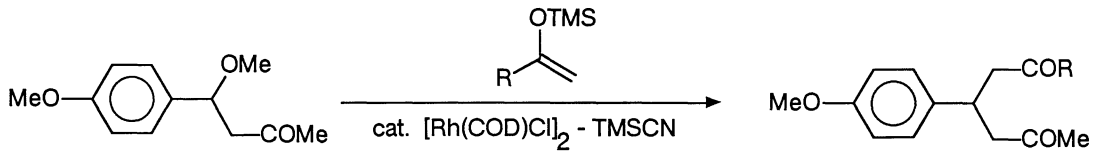
Scheme 4.



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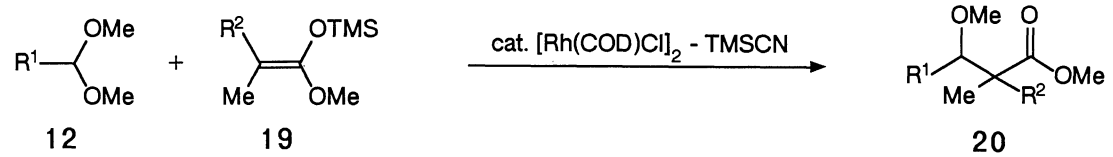
18a (R=Ph,79%)
18b (R=Me,75%)

Scheme 5.



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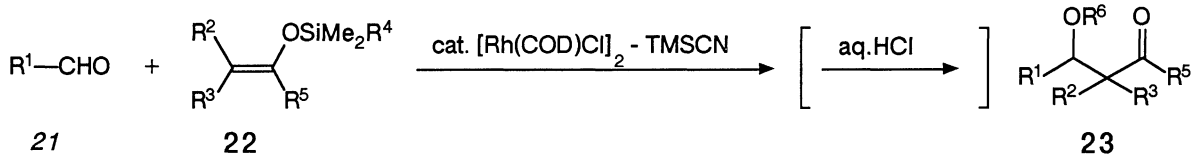
Scheme 6.

The formation of **10** indicates that acetals could react with 2 euqiv of silylated nucleophiles by increasing the amount of TMS-CN as a co-catalyst. The reaction of *p*-methoxybezaldehyde dimethyl acetal (**15**), relatively reactive acetal, with 2.8 equiv of **8** was tried by the use of 0.6 equiv of TMS-CN and 0.02 equiv of $[Rh(COD)Cl]_2$, and the desired product **16** was obtained in 79% yield (Scheme 4). In addition, it was also found that 2nd nucleophiles could react with aldol adducts prepared from acetals and 1st nucleophiles (for example, Scheme 5).

This new catalyst system of TMS-CN and $[Rh(COD)Cl]_2$ also smoothly promotes the reaction between acetals and ketene silyl acetals (Scheme 6) and some experimental results are shown in Table 6.

Reaction of Aldehydes and Silylated Nucleophiles. In order to extend the scope of effectiveness of the above mentioned new catalyst system, reactions between ketene silyl acetals and aldehydes were studied and it was found that corresponding β-hydroxy esters were obtained in good yields under almost neutral conditions. Several examples of the reactions are demonstrated in Table 7. It is interesting to note that aldehydes having basic substituents could also smooth-



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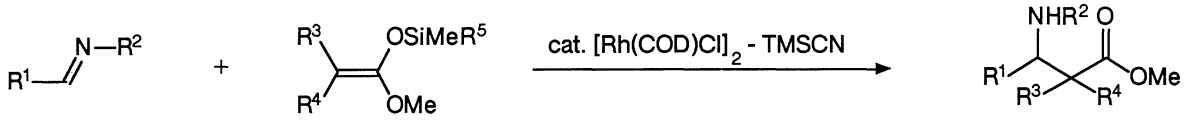
Scheme 7.

Table 7. Reaction of Aldehydes with Silylated Nucleophiles[a]

Entry	R^1	R^2	R^3	R^4	R^5	Time/h	R^6	Yield/%
1	*p*-MeO-C_6H_4	H	H	^{t}Bu	OMe	3	TBS	83
2	*p*-MeO-C_6H_4	H	Me	Me	OMe	3	H	96[b]
3	*p*-MeO-C_6H_4	Me	Me	Me	OMe	3	H	98
4	*p*-MeO-C_6H_4	H	H	Me	Ph	3	H	94
5	Ph	H	H	^{t}Bu	OMe	12	TBS	83
6	Ph	H	Me	Me	OMe	14	H	90[c]
7	Ph	Me	Me	Me	OMe	12	H	100
8	Ph	H	H	Me	Ph	3	H	70
9	$PhCH_2CH_2$	H	H	^{t}Bu	OMe	12	TBS	71
10[d]	*p*-Me_2N-C_6H_4	Me	Me	Me	OMe	15	TMS	89
11	2-Pyridyl	Me	Me	Me	OMe	16	H	73
12	2-Pyridyl	H	H	^{t}Bu	OMe	13	TBS	59

a) Reactions were carried out by using 1.4—1.7 equiv of **22**, 0.01—0.02 equiv of $[Rh(COD)Cl]_2$, and 0.4—0.6 equiv of TMS-CN in CH_3CN at room temperature except for Entry 10. b) Syn : anti=36 : 64, separated by preparative TLC (Silica gel). c) Syn : anti=44 : 56, separated by preparative TLC (Silica gel). d) Reaction was carried out in CH_2Cl_2.



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Scheme 8.

Table 8. Reaction of Imines with Ketene Silyl Acetals[a]

Entry	R^1	R^2	R^3	R^4	R^5	Solvent	Time/h	Yield/%
1	Ph	Ph	Me	Me	Me	CH_2Cl_2	14	96
2	Ph	Ph	H	Me	Me	CH_2Cl_2	15	75[b]
3	Ph	Ph	H	H	^{t}Bu	CH_2Cl_2	15	48
4	Ph	CH_2Ph	Me	Me	Me	CH_3CN	16	82
5	Ph	$CHPh_2$	Me	Me	Me	CH_3CN	3	82
6	2-Pyridyl	Ph	Me	Me	Me	CH_2Cl_2	14	97

a) Reactions were carried out by using 1.4—1.7 equiv of **25**, 0.01—0.02 equiv of $[Rh(COD)Cl]_2$, and 0.5—0.6 equiv of TMS-CN at room temperature. b) Syn : anti=67 : 33, determined by ^{1}H NMR.

ly react with ketene silyl acetals as shown in Entries 10, 11, and 12.

In these reactions, the yield of β-hydroxy esters is dependent on the molar ratio of TMS-CN to [Rh(COD)Cl]$_2$; that is, higher yields of β-hydroxy esters were achieved when 0.5 equiv of TMS-CN was used rather than when 0.2 equiv of TMS-CN was used.

Reaction of Imines and Ketene Silyl Acetals. The reaction of imines with ketene silyl acetals is one of the most fundamental methods for the preparation of β-amino esters. Most of these reactions generally require an equimolar amont of Lewis acid such as $TiCl_4$,[13] and there are reported a few examples on the above reaction carried out by using a catalytic amount of the promoter.[14]

The combined use of catalytic amounts of [Rh(COD)Cl]$_2$ and TMS-CN effectively activates aldehydes even those having basic substituents. It indicates that this catalyst system would be effective for the direct activation of imines under almost neutral conditions.

The reaction of *N*-benzylideneaniline with trimethylsilyl ketene acetal of methyl isobutyrate in the coexistence of 0.01 equiv of [Rh(COD)Cl]$_2$ and 0.5 equiv of TMS-CN in CH_2Cl_2 took place smoothly at room temperature to give the desired β-amino ester in 96% yield without accompanying the corresponding β-lactam. Several examples of the reactions of imines with ketene silyl acetals are demonstrated in Table 8 and the corresponding β-amino esters were obtained in good yields. On the other hand, when the reaction of imines derived from non-aromatic aldehydes such as pivaraldehyde or isobutyraldehyde with ketene silyl acetals were tried under the similar condition, no desired β-amino ester was isolated, instead β-amino carbonitrile, a simple adduct with TMS-CN, was detected in a small amount.

It is concluded that the use of a catalytic amount of transition metal compound such as [Rh(COD)Cl]$_2$ or $CoCl_2$, promotes the cyanation of acetals with TMS-CN and that the combined use of catalytic amounts of [Rh(COD)Cl]$_2$ and TMS-CN promotes the aldol type reactions between silylated nucleophiles and acetals, aldehydes including those having basic substituents or imines under almost neutral conditions.

This new catalyst system of combined use of [Rh(COD)Cl]$_2$ and TMS-CN will open further synthetic possibilities especially in carbon-carbon bond forming reactions under almost neutral conditions.

Experimental

All melting points were uncorrected. The IR spectra were determined on a Hitachi 270-30 or JASCO IRA-2 spectrometer. The ^{1}H NMR spectra were recorded with a Hitachi R-24B or a JEOL GSX-500 spectrometers with tetramethylsilane as an internal standard. The mass spectra were taken on a JEOL JMS-HX110 or a JEOL JMS-D300. Tetrahydrofuran and diethyl ether were freshly distilled from sodium benzophenone ketyl. Dichloromethane and acetonitrile were distilled from P_2O_5, successively distilled from CaH_2 and stored over Molecular Sieve. Purification of products were performed by column chromatography on silica gel (Merck, Art. 7734 Kieselgel 60) or preparative TLC on silica gel(Wakogel B-5F).

Dimethyl acetals were prepared by transacetalization of the corresponding aldehydes or ketones with trimethyl orthoformate in the presence of *p*-TsOH·H_2O, and purified by distillation. Trimethylsilyl cyanide was purified by distillation. Silyl enol ethers or ketene silyl acetals were prepared by silylation of the corresponding enolates of ketones or esters, and purified by distillation. Imines were prepared by dehydrate condensation of the corresponding aldehydes and amines in the presence of Molecular Sieve, and purified by distillation or recrystallization.

Preparation of α-Alkoxy Carbonitriles (4) (Table 2). A typical reaction procedure is described for (*E*)-cinnamaldehyde dimethyl acetal (**1**) with TMS-CN by the use of $NiCl_2$ as a catalyst (Entry 1): Under an argon atmosphere, a CH_2Cl_2 (3 ml) suspension of $NiCl_2$ (5.3 mg, 0.04 mmol) and trimethylsilyl cyanide (60.1 mg, 0.606 mmol) was stirred for 30 min at room temperature, to which was added (*E*)-cinnamaldehyde dimethyl acetal (73.6 mg, 0.413 mmol) in CH_2Cl_2 (1 ml). The reaction mixture was stirred for 3 h at room temperature and quenched with pH 7 phosphate buffer. The organic materials were extracted with CH_2Cl_2 and combined extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC (silica gel, hexane:AcOEt=5:1) to afford (*E*)-2-methoxy-4-phenyl-3-butenenitrile (**2**)[15] (68.6 mg, 0.396 mmol, 96%). IR(neat) 1675, 1655, 1495, 1450, 1190, 1120, 1095 cm^{-1}; ^{1}H NMR (CCl_4) δ=3.36 (3H, s), 4.62 (1H, d, *J*=5 Hz), 5.88 (1H, dd, *J*=16 Hz, 5 Hz), 6.64(1H, d, *J*=16 Hz), 7.10 (5H, s); MS, *m/z* 173 (M$^+$), 158, 142, 115.

Other analytical data are presented:

2-Methoxy-2-(4-methoxyphenyl)ethanenitrile (Entry 5). IR(neat) 1615, 1590, 1515, 1255, 1180, 1080, 1030 cm^{-1}; ^{1}H NMR (CCl_4) δ=3.34 (3H, s), 3.70 (3H, s), 4.95 (1H, s), 6.72 (2H, d, *J*=8 Hz), 7.21 (2H, d, *J*=8 Hz); MS, *m/z* 177 (M$^+$), 146. Found: *m/z* 177.0782. Calcd for $C_{10}H_{11}NO_2$: M, 177.0790.

2-Ethoxy-2-phenylethanenitrile[16] (Entry 9). IR(neat) 1495, 1455, 1090, 695 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.24 (3H, d, *J*=6.5 Hz), 3.3—3.8 (2H, m), 5.02 (1H, s), 7.18 (5H, s); MS *m/z* 161 (M$^+$), 149, 116.

(*E*)-2-Methoxy-3-heptenenitrile (Entry 12). IR(neat) 1675, 1495, 1195, 975 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.8—1.7 (5H, m), 1.9—2.3 (2H, m), 3.32 (3H, s), 4.43 (1H, d, *J*=5 Hz), 5.31 (1H, dd, *J*=15 Hz, 5 Hz), 5.90 (1H, dt, *J*=15 Hz, 7 Hz); MS, *m/z* 138 (M$^+$−1), 113, 71. Found: *m/z* 138.0928. Calcd for $C_{18}H_{12}NO$: M–H, 138.0919.

(*E*)-2,4-Diphenyl-2-methoxy-3-butenenitrile (Entry 14). IR(neat) 1495, 1455, 1070, 970, 750, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.36 (3H, s), 6.00 (1H, d, *J*=16 Hz), 6.87 (1H, d, *J*=16 Hz), 7.0—7.3 (10H, m); MS, *m/z* 249 (M$^+$), 218, 140. Found: *m/z* 249.1152. Calcd for $C_{17}H_{15}NO$: M, 249.1154.

2,2-Diphenyl-2-methoxyethanenitrile (Entry 16). Mp 53—54 °C; IR (KBr) 1490, 1450, 1200, 1175, 1095, 1075 cm^{-1}; ^{1}H NMR (CCl_4) δ=3.31 (3H, s), 7.2 (10H, m); MS, *m/z* 223 (M$^+$), 192. Found: C, 80.48; H, 5.83; N, 6.41%. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27%.

2-Methoxy-4-phenylbutanenitrile (Entry 18). IR (neat) 1600, 1495, 1450, 1110, 695 cm^{-1}; ^{1}H NMR (CCl_4) δ=2.1 (2H,

m), 2.7 (2H, m), 3.37 (3H, s), 3.76 (1H, t, J=6 Hz), 7.01 (5H, s); MS, m/z 175 (M^+), 160, 143, 105, 91. Found: m/z 175.0998. Calcd for $C_{11}H_{13}NO$: M, 175.0997.

2-Methoxyundecanenitrile (Entry 20). IR(neat) 1470, 1340, 1105 cm^{-1}; ^1H NMR (CCl_4) δ=0.8—1.7 (19H, m), 3.38 (3H, s), 3.83 (1H, t, J=6 Hz); MS, m/z 197 (M^+), 182, 171, 138, 71. Found: m/z 171.1749. Calcd for $C_{11}H_{23}O$: M–CN, 171.1749.

Preparation of Bisacetal 5. A solution of formylmethylenetriphenylphosphorane[17] (1.471 g, 4.83 mmol) and terephthalaldehyde (1.295 g, 9.66 mmol) in benzene (30 ml) was heated under reflux for 3 h. After evaporation of the solvent, the residue was purified by silica-gel column chromatography (hexane:AcOEt=4:1—2:1) to afford (*E*)-*p*-formylcinnamaldehyde[18] (0.578 g, 75%); mp 90—92 °C (decomp); IR (KBr) 1680, 1125, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.65 (1H, dd, J=16 Hz, 7 Hz), 7.43 (1H, d, J=16 Hz), 7.58 (2H, d, J=8 Hz), 7.83 (2H, d, J=8 Hz), 9.59 (1H, d, J=7 Hz), 9.88 (1H, s).

To a suspension of the above dialdehyde (1.58 g, 9.9 mmol) in methanol (30 ml) was added trimethyl orthoformate (2.55 g, 24 mmol) and $TsOH \cdot H_2O$ (10 mg). After the mixture was stirred for 3 h at room temperature, anhydrous K_2CO_3 was added and stirring was continued for an additional 0.5 h.

After evaporation of a filtrate of the reaction mixture, the residue was purified by distillation (bp 145—150 °C/3 mmHg, 1 mmHg≈133.322 Pa) to afford (*E*)-1-dimethoxymethyl-4-(3,3-dimethoxy-1-propenyl)benzene (1.77 g, 71%); ^1H NMR (CCl_4) δ=3.13 (6H, s), 3.18 (6H, s), 4.75 (1H, d, J=4 Hz), 5.18 (1H, dd, J=16 Hz, 4 Hz), 6.50 (1H, d, J=16 Hz), 7.13 (4H, s).

To a solution of the above bisacetal (1.75 g, 6.9 mmol) in THF (30 ml) was added 5% palladium–carbon (60 mg), and the mixture was stirred under hydrogen atmosphere for 15 h. After evaporation of a filtrate of the reaction mixture, the residue was purified by distillation (bp 141—142 °C/3.5 mmHg) to afford 1-dimethoxymethyl-4-(3,3-dimethoxypropyl)benzene (1.62 g, 92%); IR (neat) 1515, 1450, 1360, 1190, 1125, 1100, 1055 cm^{-1}; ^1H NMR (CCl_4) δ=1.6—1.9 (2H, m), 2.3—2.7 (2H, m), 3.15 (12H, s), 4.14 (1H, t, J=5.5 Hz), 5.17 (1H, s), 6.88 (2H, d, J=8 Hz), 7.10 (1H, d, J=8 Hz); MS, m/z 254 (M^+), 253, 223. Found: m/z 254.1506. Calcd for $C_{14}H_{22}O_4$: M, 254.1518.

Selective Cyanation of Bisacetal 5 (Table 3). **1-Cyanomethoxymethyl-4-(3,3-dimethoxypropyl)benzene(6)** (Entry 1). IR (neat) 1610, 1515, 1450, 1280, 1190, 1085 cm^{-1}; ^1H NMR (CCl_4) δ=1.6—2.0 (2H, m), 2.4—2.7 (2H, m), 3.17 (6H, s), 3.35 (3H, s), 4.15 (1H, t, J=5 Hz), 4.96 (1H, s), 7.00 (2H, d, J=8 Hz), 7.17 (2H, d, J=8 Hz); MS, m/z 249 (M^+), 217, 160, 75. Found: m/z 249.1363. Calcd for $C_{14}H_{19}NO_3$: M, 249.1365.

1-Cyanomethoxymethyl-4-(3-cyano-3-methoxypropyl)benzene (7) (Entry 5). IR (neat) 1610, 1515, 1460, 1185, 1115 cm^{-1}; ^1H NMR (CCl_4) δ=1.8—2.2 (2H, m), 2.6—2.8 (2H, m), 3.36 (6H, s), 3.79 (1H, t, J=6 Hz), 4.95 (1H, s), 6.97 (2H, d, J=8 Hz), 7.18 (2H, d, J=8 Hz); MS, m/z 244 (M^+), 217, 181, 159, 129. Found: m/z 244.1224. Calcd for $C_{14}H_{16}N_2O_2$: M, 244.1212.

Aldol Reaction of Acetals with Silyl Enol Ethers. A typical procedure is described for the reaction of trimethylsilyl enol ether (**8**) of acetophenone with (*E*)-cinnamaldehyde dimethyl acetal (**1**) (Table 4, Entry 3): Under an argon atmosphere, $[Rh(COD)Cl]_2$ (3.0 mg, 0.006 mmol) and TMS-CN (6.0 mg, 0.060 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 (70.1 mg, 0.365 mmol) and (*E*)-cinnamaldehyde dimethyl acetal (53.4 mg, 0.300 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 extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC (silica gel, hexane:AcOEt=5:1) to afford (*E*)-3-methoxy-1,5-diphenyl-4-penten-1-one (**9**)[19] (72.9 mg, 0.274 mmol, 91%); IR (neat) 1685, 1595, 1445, 1355, 1095, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.95 (1H, dd, J=16 Hz, 5 Hz), 3.26 (3H, s), 3.41 (1H, dd, J=16 Hz, 7 Hz), 4.35 (1H, m), 5.98(1H, dd, J=16 Hz, 7 Hz), 6.54 (1H, d, J=16 Hz), 7.1—7.9 (10H, m); MS, m/z 266 (M^+), 251, 234, 147, 105.

Other analytical data are presented (Table 5):

3-Methoxy-1,3-diphenyl-1-propanone[20] (Entry 1). IR (neat) 1685, 1600, 1580, 1450, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.96 (1H, dd, J=16 Hz, 5 Hz), 3.15 (3H, s), 3.52 (1H, dd, J=16 Hz, 8 Hz), 4.77 (1H, dd, J=8 Hz, 5 Hz), 7.2 (8H, m), 7.8 (2H, m).

3-Methoxy-3-(4-methoxyphenyl)-1-phenyl-1-propanone (Entry 2). IR (neat) 1685, 1610, 1515, 1245, 1095 cm^{-1}; ^1H NMR (CCl_4) δ=2.78 (1H, dd, J=16 Hz, 5 Hz), 3.05 (3H, s), 3.40 (1H, dd, J=16 Hz, 8 Hz), 3.65 (3H, s), 4.62 (1H, dd, J=8 Hz, 5 Hz), 6.63 (2H, d, J=9 Hz), 7.1 (5H, m), 7.7 (2H, m); MS, m/z 270 (M^+), 225, 238, 151. Found: m/z 270.1216. Calcd for $C_{17}H_{18}O_3$: M, 270.1256.

(*E*)-3-Methoxy-1-phenyl-4-hexen-1-one[21] (Entry 3). IR (neat) 1685, 1595, 1450, 1095 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.66 (3H, d, J=5 Hz), 2.83 (1H, dd, J=14 Hz, 5 Hz), 3.18 (3H, s), 3.22 (1H, dd, J=14 Hz, 7 Hz), 4.10 (1H, m), 5.0—6.0 (2H, m), 7.3 (3H, m), 7.7 (2H, m); MS, m/z 204 (M^+), 189, 157, 105.

3-Methoxy-1,5-diphenyl-1-pentanone[22] (Entry 4). IR (neat) 1685, 1595, 1450, 1260, 1095, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.9 (2H, m), 2.5—3.3 (4H, m), 3.25 (3H, s), 3.78 (1H, m), 7.0—7.3 (8H, m), 7.7 (2H, m); MS, m/z 268 (M^+), 236, 163, 105.

3-Methoxy-1-phenyl-1-dodecanone (Entry 5). IR (neat) 1690, 1600, 1450, 1360, 1265, 1100 cm^{-1}; ^1H NMR (CCl_4) δ=0.8—1.4 (19H, m), 2.5—3.3 (2H, m), 3.18 (3H, s), 3.7 (1H, m), 7.3 (3H, m), 7.7 (2H, m); MS, m/z 290 (M^+), 275, 258, 163, 105. Found: m/z 290.2236. Calcd for $C_{19}H_{30}O_2$: M, 290.2246.

4-Methoxy-4-(4-methoxyphenyl)-2-butanone (Entry 6). IR (neat) 1715, 1610, 1515, 1250, 1175, 1100, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.10 (3H, s), 2.50 (1H, dd, J=15 Hz, 5 Hz), 2.94 (1H, dd, J=15 Hz, 8 Hz), 3.10 (3H, s), 3.72 (3H, s), 4.48 (1H, dd, J=8 Hz, 5 Hz), 6.67 (2H, d, J=8.5 Hz), 7.02 (2H, d, J=8.5 Hz); MS, m/z 208 (M^+), 193, 161, 151. Found: m/z 208.1097. Calcd for $C_{12}H_{16}O_3$: M, 208.1099.

3-Methoxy-3-(4-methoxyphenyl)-2-methyl-1-phenyl-1-propanone (Syn:Anti=71:29, Mixture) (Entry 7). IR (neat) 1680, 1610, 1510, 1245, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.85 (0.29×3H, d, J=7.2 Hz), 1.35 (0.71×3H, d, J=6.4 Hz), 3.06 (0.29×3H, s), 3.18 (0.71×3H, s), 3.72 (0.71×3H, s), 3.8 (1H, m), 3.83 (0.29×3H, s), 4.40 (0.71×1H, d, J=7.9 Hz), 4.42 (0.29×1H, d, J=11.9 Hz), 6.76 (0.71×2H, d, J=7.9 Hz), 6.93 (0.29×2H, d, J=8.7 Hz), 7.2—7.6 (5H, m), 7.73 (0.71×2H, d, J=7.2 Hz), 8.03 (0.29×2H, d, J=8.7 Hz); MS, m/z 284 (M^+), 252, 237, 151. Found: m/z 284.1407. Calcd for $C_{18}H_{20}O_3$: M,

284.1412.

2-[Methoxy-(4-methoxyphenyl)methyl]cyclohexane (Entry 8). **Syn Isomer;** IR (neat) 1710, 1610, 1510, 1300, 1245, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.5—2.5 (9H, m), 3.14 (3H, s), 3.70 (3H, s), 4.57 (1H, d, J=4.5 Hz), 6.71 (2H, d, J=8.5 Hz), 7.05 (2H, d, J=8.5 Hz); MS, m/z 248 (M^+), 216, 151. Found: m/z 248.1416. Calcd for $C_{15}H_{20}O_3$: M, 248.1412.

Anti Isomer; IR (neat) 1705, 1610, 1510, 1300, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.5—2.5 (9H, m), 3.10 (3H, s), 3.73 (3H, s), 4.41 (1H, d, J=8 Hz), 6.74 (2H, d, J=8.5 Hz), 7.10 (2H, d, J=8.5 Hz); MS, m/z 248 (M^+), 216, 151. Found: m/z 248.1425. Calcd for $C_{15}H_{20}O_3$: M, 248.1412.

(*E*)-1,5-Diphenyl-3-styryl-1,5-pentanedione (10) and (*E*)-1,5,7-Triphenyl-3-heptene-1,7-dione (11). Under an argon atmosphere, [Rh(COD)Cl]$_2$ (5.7 mg, 0.011 mmol) and TMS-CN (36.5 mg, 0.368 mmol) were stirred in acetonitrile (3 ml) at room temperature for 30 min, to which was successively added trimethylsilyl enol ether of acetophenone (180.0 mg, 0.937 mmol) in acetonitrile (1.5 ml) and (*E*)-cinnamaldehyde dimethyl acetal (53.7 mg, 0.302 mmol) in acetonitrile (1.5 ml). The reaction mixture was stirred for 15 h at room temperature, then quenched with aqueous solution of $NaHCO_3$. The organic materials were extracted with ethyl acetate and combined extract was dried over Na_2SO_4. After evaporation of the solvent, the residure was purified by preparative TLC (silica gel, hexane:AcOEt=7:1) to afford the mixture of **10** and **11** (37:63) (47.5 mg, 44%); ^{1}H NMR ($CDCl_3$) δ=3.19 (0.63×1H, dd, J=17 Hz, 7 Hz, **11**), 3.36 (0.63×1H, dd, J=16 Hz, 6 Hz, **11**), 3.41 (0.37×4H, ABq d, J=16 Hz, 7 Hz, **10**), 3.62 (0.37×1H, m **10**), 3.69 (0.63×2H, d, J=7 Hz, **11**), 4.16 (0.63×1H, m, **11**), 5.74 (0.63×1H, dt, J=16 Hz, 6 Hz, **11**), 5.85 (0.63×1H, dd, J=16 Hz, 7 Hz, **11**), 6.29 (0.37×1H, dd, J=16 Hz, 8 Hz, **10**), 6.43 (0.37×1H, d, J=16 Hz, **10**), 7.15—7.6 (11H, m, **10** and **11**), 7.85—8.0 (4H, m, **10** and **11**); MS, m/z 354 (M^+), 336, 105. Found: m/z 354.1629. Calcd for $C_{25}H_{22}O_2$: M, 354.1620.

1,5-Diphenyl-3-(4-methoxyphenyl)-1,5-pentanedione (16). In the similar manner as described for **9**, *p*-methoxybenzaldehyde dimethyl acetal (44.7 mg, 0.245 mmol) was allowed to react with trimethylsilyl enol ether of acetophenone (131.3 mg, 0.683 mmol) by the use of [Rh(COD)Cl]$_2$ (2.1 mg, 0.004 mmol) and TMS-CN (13.8 mg, 0.139 mmol) to afford **16** (69.3 mg, 79%); mp 90—92 °C; IR (KBr) 1680, 1595, 1515, 1240, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.26 (4H, m), 3.62 (3H, s), 3.9 (1H, m), 6.58 (2H, d, J=8.5 Hz), 6.98 (2H, d, J=8.5 Hz), 7.2 (6H, m), 7.7 (4H, m); MS, m/z 358 (M^+), 239, 105. Found: C, 80.26; H, 6.26%. Calcd for $C_{24}H_{22}O_3$: C, 80.42; H, 6.19%.

3-(4-Methoxyphenyl)-1-phenyl-1,5-hexanedione (18a). In the similar manner as described for **9**, compound **17** (59.9 mg, 0.288 mmol) was allowed to react with trimethylsilyl enol ether of acetophenone (84.8 mg, 0.441 mmol) by the use of [Rh(COD)Cl]$_2$ (3.2 mg, 0.006 mmol) and TMS-CN (19.3 mg, 0.195 mmol) to afford **18a** (67.7 mg, 79%); mp 70—71 °C; IR (KBr) 1710, 1680, 1520, 1250, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.00 (3H, s), 2.75 (2H, d, J=7 Hz), 3.18 (2H, d, J=9 Hz), 3.65 (3H, s), 3.73 (1H, t, J=7 Hz), 6.63 (2H, d, J=9 Hz), 7.01 (2H, d, J=9 Hz), 7.3 (3H, m), 7.7 (2H, m); MS, m/z 296 (M^+), 239, 177, 105. Found: C, 76.96; H, 6.95%. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80%.

4-(4-Methoxyphenyl)-2,6-heptanedione (18b). Mp 73—74 °C; IR (KBr) 1710, 1520, 1370, 1245, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.99 (6H, s), 2.67 (4H, d, J=7 Hz), 3.60 (1H, t, J=7 Hz), 3.70 (3H, s), 6.67 (2H, d, J=9 Hz), 7.01 (2H, d, J=9 Hz); MS, m/z 234 (M^+), 177. Found: C, 71.65; H, 7.64%. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74%.

Reaction of Acetals with Ketene Silyl Acetals (Table 6). Reactions were carried out in the similar manner as described for **9**. Analytical data are presented:

Methyl (*E*)-3-Methoxy-2-methyl-5-phenyl-4-pentenoate[23] (Syn:Anti=50:50, Mixture) (Entry 1). IR(neat) 1740, 1455, 1195, 1170, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.11 (1.5H, d, J=7 Hz), 1.24 (1.5H, d, J=7 Hz), 2.7 (1H, m), 3.29 (1.5H, s), 3.32 (1.5H, s), 3.66 (1.5H, s), 3.73 (1.5H, s), 3.88 (0.5H, t, J=9 Hz), 3.94 (0.5H, t, J=7 Hz), 5.97 (0.5H, dd, J=16 Hz, 9 Hz), 6.12 (0.5H, dd, J=16 Hz, 7 Hz), 6.58 (0.5H, d, J=15 Hz), 6.61 (0.5H, d, J=16 Hz), 7.25—7.45 (5H, m); MS, m/z 234 (M^+).

Methyl (*E*)-3-Methoxy-2,2-dimethyl-5-phenyl-4-pentenate (Entry 2). IR (neat) 1730, 1465, 1270, 1130, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.13 (3H, s), 1.21 (3H, s), 3.22 (3H, s), 3.62 (3H, s), 3.84 (1H, d, J=8 Hz), 5.90 (1H, dd, J=16 Hz, 8 Hz), 6.46 (1H, d, J=16 Hz), 7.0—7.2 (5H, m); MS, m/z 248 (M^+), 217, 173, 147. Found: m/z 248.1429. Calcd for $C_{15}H_{20}O_3$: M, 248.1412.

Methyl 3-Methoxy-3-(4-methoxyphenyl)-2-methylpropanoate (Syn:Anti=50:50, Mixture) (Entry 3). IR(neat) 1735, 1610, 1510, 1245, 1165, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.86 (1.5H, d, J=7.1 Hz), 1.23 (1.5H, d, J=7.2 Hz), 2.74 (1H, m), 3.13 (1.5H, s), 3.20 (1.5H, s), 3.53 (1.5H, s), 3.75 (1.5H, s), 3.80 (1.5H, s), 3.82 (1.5H, s), 4.19 (0.5H, d, J=9.5 Hz), 4.34 (0.5H, d, J=7.1 Hz), 6.87 (1H, d, J=8.7 Hz), 6.90 (1H, d, J=8.7 Hz), 7.20 (1H, d, J=8.7 Hz), 7.21 (1H, d, J=8.7 Hz); MS, m/z 238 (M^+), 237, 207, 151. Found: m/z 238.1222. Calcd for $C_{13}H_{18}O_4$: M, 238.1205.

Methyl 3-Methoxy-3-(4-methoxyphenyl)-2,2-dimethylpropanoate (Entry 4). IR(neat) 1735, 1610, 1515, 1250, 1130, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.98 (3H, s), 1.10 (3H, s), 3.10 (3H, s), 3.62 (3H, s), 3.72 (3H, s), 6.71 (2H, d, J=9 Hz), 7.04 (2H, d, J=9 Hz); MS, m/z 252 (M^+), 221, 161, 151. Found: m/z 252.1339. Calcd for $C_{14}H_{20}O_4$: M, 252.1362.

Methyl 3-Methoxy-2-methyl-3-phenylpropanoate[24] (Syn:Anti=48:52) (Entry 5). **Syn isomer;** IR(neat) 1735, 1455, 1195, 1165, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.16 (3H, d, J=7 Hz), 2.64 (1H, qd, J=7 Hz, 7 Hz), 3.12 (3H, s), 3.42 (3H, s), 4.29 (1H, d, J=7 Hz), 7.09 (5H, s). **Anti isomer;** ^{1}H NMR ($CDCl_3$) δ=0.85 (3H, d, J=7 Hz), 2.73 (1H, dq, J=9 Hz, 7 Hz), 3.07 (3H, s), 4.14 (1H, d, J=9 Hz), 7.15 (5H, s); MS m/z 209 (M^++1), 193, 177.

Methyl 3-Methoxy-2,2-dimethyl-3-phenylpropanoate[19] (Entry 6). IR (neat) 1735, 1250, 1130, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.97 (3H, s), 1.08 (3H, s), 3.10 (3H, s), 3.60 (3H, s), 4.35 (1H, s,), 7.12 (5H, s); MS, m/z 223 (M^++1), 191, 121.

Methyl 3-Methoxy-2-methyl-5-phenylpentanoate[25] (Ratio of diastereoisomers was 52:48) (Entry 7). IR (neat) 1735, 1600, 1495, 1255, 1195, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.11 (0.52×3H, d, J=7.2 Hz), 1.18 (0.48×3H, d, J=7.2 Hz), 1.75—1.95 (2H, m), 2.55—2.85 (3H, m), 3.37 (0.52×3H, s), 3.38 (0.48×3H, s), 3.48 (1H, m), 3.67 (0.52×3H, s), 3.69 (0.48×3H, s), 7.15—7.3 (5H, m); MS, m/z 236 (M^+), 204, 146, 117, 91.

Methyl 3-Methoxy-2,2-dimethyl-5-phenylpentanoate[25] (Entry 8). IR (neat) 1735, 1455, 1275, 1130, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.10 (3H, s), 1.18 (3H, s), 1.5—1.9 (2H, m), 2.5—2.9 (2H, m), 3.3 (1H, m), 3.40 (3H, s), 3.58 (3H, s), 7.09 (5H, s); MS, m/z 250 (M^+), 218, 149, 117, 91.

Reaction of Aldehydes with Silylated Nucleophiles (Table 7).

(Procedure A) Reactions were carried out in the similar manner as described for **9**. Analytical data are presented:

Methyl 3-(*t*-Butyldimethylsilyloxy)-3-(4-methoxyphenyl)-propanoate (Entry 1). IR (neat) 1740, 1610, 1515, 1245, 1160, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ=−0.18 (3H, s), 0.00 (3H, s), 0.81 (9H, s), 2.42 (1H, dd, J=14 Hz, 5 Hz), 2.73 (1H, dd, J=14 Hz, 8 Hz), 3.56 (3H, s), 3.68 (3H, s), 5.00 (1H, dd, J=8 Hz, 5 Hz), 6.66 (2H, d, J=8.5 Hz), 7.08 (2H, d, J=8.5 Hz); MS, m/z 324 (M^+), 282, 278, 267. Found: m/z 267.1055. Calcd for $C_{13}H_{19}O_4Si$: M-^{t}Bu, 267.1053.

Methyl 3-(*t*-Butyldimethylsilyloxy)-3-phenylpropanoate (Entry 5). IR (neat) 1740, 1435, 1360, 1250, 1160, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ=−0.18 (3H, s), 0.00 (3H, s), 0.82 (9H, s), 2.6 (2H, m), 3.57 (3H, s), 5.01 (1H, dd, J=8 Hz, 5 Hz), 7.11 (5H, s); MS, m/z 295 (M^++1), 237, 185, 163. Found: m/z 237.0982. Calcd for $C_{12}H_{17}O_3Si$: M-^{t}Bu, 237.0947.

Methyl 3-(*t*-Butyldimethylsilyloxy)-5-phenylpentanoate (Entry 9). IR (neat) 1740, 1435, 1250, 1090, 835, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.03 (3H, s), 0.06 (3H, s), 0.88 (9H, s), 1.8 (2H, m), 2.4—2.8 (4H, m), 3.56 (3H, s), 4.10 (1H, m), 7.01 (5H, s); MS, m/z 323 (M^++1), 265. Found: m/z 265.1277. Calcd for $C_{14}H_{21}O_3Si$: M-^{t}Bu, 265.1260.

Methyl 3-(4-Dimethylaminophenyl)-2,2-dimethyl-3-trimethylsilyloxypropanoate (Entry 10). Mp 81—83 °C; IR (KBr) 3450, 1740, 1615, 1525, 1250, 1140, 1080, 880 cm^{-1}; ^1H NMR ($CDCl_3$) δ=−0.04 (9H, s), 0.95 (3H, s), 1.08 (3H, s), 2.86 (6H, s), 3.58 (3H, s), 4.81 (1H, s), 6.47 (2H, d, J=8.5 Hz), 6.94 (2H, d, J=8.5 Hz); MS, m/z 323 (M^+). Found: m/z 323.1896. Calcd for $C_{17}H_{29}NO_3Si$: M, 323.1917.

Methyl 3-(*t*-Butyldimethylsilyloxy)-3-(2-pyridyl)propanoate (Entry 12). IR (neat) 1745, 1590, 1470, 1435, 1255, 1165, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ=−0.05 (3H, s), 0.08 (3H, s), 0.88 (9H, s), 2.80 (2H, m), 3.58 (3H, s), 5.23 (1H, m), 6.9—7.6 (4H, m), 8.31 (1H, d, J=5 Hz); MS, m/z 296 (M^++1), 254, 238. Found: m/z 295.1633. Calcd for $C_{15}H_{25}NO_3Si$: M, 295.1604.

(Procedure B) A typical procedure is described for the reaction of *p*-methoxybenzaldehyde dimethyl acetal with trimethylsilyl ketene acetal of methyl propionate (Entry 2): Under an argon atmosphere, $[Rh(COD)Cl]_2$ (3.8 mg, 0.008 mmol) and TMS-CN (18.8 mg, 0.190 mmol) were stirred in CH_3CN (3 ml) at room temperature for 30 min, to which was successively added trimethysilyl ketene acetal of methyl propionate (E/Z>20) (106.1 mg, 0.663 mmol) in CH_3CN (1.5 ml) and *p*-methoxybenzaldehyde dimethyl acetal (60.3 mg, 0.443 mmol) in CH_3CN (1.5 ml). The reaction mixture was stirred for 3 h at room temperature, then to which was added 1 M HCl (1 M=1 mol dm^{-3}) solution (0.5 ml) and stirring was continued for an additional 20 min. After quenching with aqueous solution of $NaHCO_3$, the organic materials were extracted with ethyl acetate and combined extract was dreid over Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC (silica gel, hexane:AcOEt=3:1, twice) to afford methyl 3-hydroxy-3-(4-methoxyphenyl)-2-methylpropanoate[26] (Syn isomer 34.3 mg, anti isomer 61.5 mg, syn:anti=36:64, 96%).

Syn Isomer; IR (neat) 3450, 1735, 1610, 1515, 1250, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.10 (3H, d, J=7 Hz), 2.67 (D_2O exchange, 1H, qd, J=7 Hz, 5 Hz), 3.53 (3H, s), 3.67 (3H, s), 4.85 (D_2O exchange, 1H, d, J=5 Hz), 6.65 (2H, d, J=8 Hz), 7.03 (2H, d, J=8 Hz); MS, m/z 224 (M^+), 206, 137.

Anti Isomer; mp 55—56 °C; IR (KBr) 3450, 1720, 1515, 1250, 1170, 1040, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.93 (3H, d, J=7 Hz), 2.69 (1H, dq, J=8.5 Hz, 7 Hz), 2.90 (1H, d, J=4 Hz), 3.61 (3H, s), 3.67 (3H, s), 4.54 (1H, dd, J=8.5 Hz, 4 Hz), 6.63 (2H, d, J=9 Hz), 7.03 (2H, d, J=9 Hz); MS, m/z 224 (M^+), 208, 207, 151.

Other analytical data are presented:

Methyl 3-Hydroxy-3-(4-methoxyphenyl)-2,2-dimethylpropanoate (Entry 3). Mp 82—83 °C; IR (KBr) 3450, 1705, 1615, 1515, 1280, 1255, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.05 (3H, s), 1.10 (3H, s), 3.00 (1H, d, J=4 Hz), 3.60 (3H, s), 3.68 (3H, s), 4.70 (1H, d, J=4 Hz), 6.65 (2H, d, J=9 Hz), 7.03 (2H, d, J=9 Hz); MS, m/z 238 (M^+), 221, 205, 162, 137. Found: C, 65.72; H, 7.74%. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%,

3-Hydroxy-3-(4-methoxyphenyl)-1-phenyl-1-propanone (Entry 4). IR (neat) 3450, 1680, 1615, 1600, 1510, 1450, 1245 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.25 (2H, d, J=6 Hz), 3.49 (1H, d, J=2 Hz), 3.70 (3H, s), 5.07 (1H, m), 6.73 (2H, d, J=8.5 Hz), 7.1—7.4 (5H, m), 7.75 (2H, m); MS, m/z 256 (M^+), 239, 137, 105. Found: m/z 256.1111. Calcd for $C_{16}H_{16}O_3$: M, 256.1100.

Methyl 3-Hydroxy-2-methyl-3-phenylpropanoate[27] (Syn:Anti=44:56) (Entry 6). **Syn Isomer;** IR (neat) 3450, 1720, 1455, 1195, 1165, 765, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.10 (3H, d, J=7 Hz), 2.72 (D_2O exchange, 1H, qd, J=7 Hz, 4 Hz), 3.57 (3H, s), 4.96 (D_2O exchange, 1H, d, J=4 Hz), 7.14 (5H, s); MS, m/z 194 (M^+), 167, 149, 107.

Anti Isomer; mp 51—52 °C; IR (KBr) 3450, 1710, 1460, 1250, 1200, 1170, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.96 (3H, d, J=7 Hz), 2.73 (1H, dq, J=8 Hz, 7 Hz), 3.01 (1H, d, J=4 Hz), 3.61 (3H, s), 4.60 (1H, d, J=8 Hz, 4 Hz), 7.14 (5H, s); MS, m/z 194 (M^+), 177, 121, 107.

Methyl 3-Hydroxy-2,2-dimethyl-3-phenylpropanoate[27] (Entry 7). Mp 68—69 °C; IR (KBr) 3450, 1705, 1295, 1275, 1160, 1050, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.06 (3H, s), 1.11 (3H, s), 3.09 (1H, d, J=3.5 Hz), 3.58 (3H, s), 4.73 (1H, d, J=3.5 Hz), 7.08 (5H, s); MS, m/z 209 (M^++1), 191.

3-Hydroxy-1,3-diphenyl-1-propanone[28] (Entry 8). ^1H NMR ($CDCl_3$) δ=3.28 (2H, d, J=6 Hz), 5.24 (1H, t, J=6 Hz), 7.3 (8H, m), 7.8 (2H, m).

Methyl 3-Hydroxy-2,2-dimethyl-3-(2-pyridyl)propanoate (Entry 11). IR (neat) 3450, 1735, 1595, 1470, 1435, 1260, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.07 (3H, s), 1.16 (3H, s), 3.66 (3H, s), 4.85 (1H, br), 7.0—7.7 (3H, m), 8.40 (1H, m); MS, m/z 210 (M^++1), 185, 178. Found: m/z 178.0873. Calcd for $C_{10}H_{12}NO_2$: M-OCH_3, 178.0869.

Reaction of Imines with Ketene Silyl Acetals. (Table 8) A typical procedure is described for the reaction of *N*-benzylideneaniline with trimethylsilyl ketene acetal of methyl isobutyrate (Entry 1): Under an argon atmosphere, $[Rh(COD)Cl]_2$ (1.3 mg, 0.003 mmol) and TMS-CN (14.3 mg, 0.144 mmol) were stirred in CH_2Cl_2 (2 ml) at room temperature for 30 min. The reaction mixture was cooled to −78 °C, to which was successively added *N*-benzylideneaniline (53.7 mg, 0.297 mmol) in CH_2Cl_2 (1.5 ml) and trimethylsilyl ketene acetal of methyl isobutyrate (79.3 mg, 0.455 mmol) in CH_2Cl_2 (1.5 ml). The reaction mixture was warmed to room temperature and stirred for 14 h, then quenched with pH 7 phosphate buffer. The organic materials were extracted with CH_2Cl_2 and the combined extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC (silica gel, hexane:ether=9:1) to afford methyl 3-anilino-2,2-dimethyl-3-phenylpropanoate (80.4 mg, 0.284 mmol, 96%); mp 123—124 °C; IR (KBr) 3380, 1715, 1600, 1515, 1500, 1250, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.14 (3H, s), 1.25 (3H, s), 3.58

(3H, s), 4.4 (1H, br), 4.7 (1H, br), 6.3—7.0 (5H, m), 7.12 (5H, s); MS, *m/z* 284 (M^++1), 185, 182. Found: C, 76.19; H, 7.47; N, 4.85%. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94%.

Other analytical data are presented:

Methyl 3-Anilino-2-methyl-3-phenylpropanoate (Syn: Anti=67:33, Mixture) (Entry 2). Mp 85—86 °C; IR (KBr) 3450, 3350, 1745, 1720, 1605, 1510, 1285, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.16 (0.33×3H, d, J=7.1 Hz), 1.18 (0.67×3H, d, J=7.2 Hz), 3.0 (1H, m), 3.61 (0.67×3H, s), 3.63 (0.33×3H, s), 4.51 (0.33×1H, d, J=7.1 Hz), 4.71(0.67×1H, d, J=5.6 Hz), 6.5—6.9 (3H, m), 7.07 (2H, m), 7.2—7.3 (5H, m); MS, *m/z* 269 (M^+), 182. Found: C, 75.91; H, 7.31; N, 5.39%. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20%.

Methyl 3-Anilino-3-phenylpropanoate (Entry 3). Mp 107—108 °C; IR (KBr) 3400, 1725, 1605, 1515, 1440, 1295, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.71 (2H, d, J=6.5 Hz), 3.50 (3H, s), 4.35 (1H, br), 4.68 (1H, t, J=6.5 Hz), 6.2—7.2 (10H, m); MS, *m/z* 255 (M^+), 182. Found: C, 75.24; H, 6.83; N, 5.94%. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49%.

Methyl 3-Benzylamino-2,2-dimethyl-3-phenylpropanoate[29] (Entry 4). IR (neat) 3350, 1731, 1455, 1255, 1135 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.02 (3H, s), 1.11 (3H, s), 1.87 (1H, s), 3.45 (2H, ABq, J=13 Hz), 3.55 (3H, s), 3.81 (1H, s), 7.10 (5H, s), 7.15 (5H, s); MS, *m/z* 298 (M^++1), 196.

Methyl 3-Diphenylmethylamino-2,2-dimethyl-3-phenylpropanoate (Entry 5). Mp 90—91 °C; IR (KBr) 1725, 1460, 1250, 1135, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.03(3H, s), 1.12 (3H, s), 2.2 (1H, br), 3.56 (3H, s), 3.66 (1H, s), 4.36 (1H, s), 7.10 (15H, s); MS, *m/z* 374 (M^++1), 296, 272, 167. Found: C, 80.44; H, 7.10; N, 3.77%. Calcd for $C_{25}H_{27}NO_2$: C, 80.40; H, 7.29; N, 3.75%.

Methyl 3-Anilino-2,2-dimethyl-3-(2-pyridyl)propanoate (Entry 6). Mp 112—113 °C; IR (KBr) 3400, 1720, 1605, 1510, 1435, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.24 (6H, s), 3.60 (3H, s), 4.6 (1H, br), 6.4—7.1 (7H, m), 7.35 (1H, m), 8.37 (1H, m); MS, *m/z* 284 (M^+), 253, 183. Found: *m/z* 284.1520. Calcd for $C_{17}H_{20}N_2O_2$: M, 284.1525.

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