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The Reaction of Acetals with Silyl Enol Ethers Promoted by the Combination of Tin(II) Chloride and Organic Halide. Novel and Convenient Synthesis of α,β-Unsaturated Ketones

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Synopsis. Acetals react with silyl enol ethers to give condensation products in good yield by the action of a reactive halide such as acetyl chloride or methoxymethyl chloride along with a catalytic amount of $SnCl_2$. The procedure employing excessive amount of halide offers a novel and convenient method to synthesize conjugated enones.

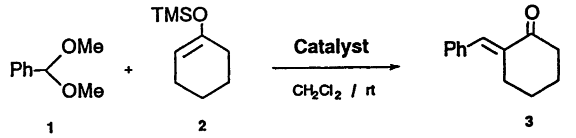
The carbon-carbon bond forming reaction between acetals and silyl enol ethers has received much interest in view of its usefulness as a mild and effective alternative to aldol condensation. Various catalysts such as $TiCl_4$,[1] $BF_3 \cdot OEt_2$,[2] trimethylsilyl trifluoromethanesulfonate (TMSOTf),[3] trityl perchlorate,[4] and phosphonium salts[5] have been reported to promote the reaction. Especially, in the last couple of years, considerable attention has been focused on the concept of a combined use of a weak Lewis acid and a neutral molecule that accelerate the carbon-carbon bond formation under essentially neutral conditions. Mukaiyama et al. reported that the combined use of $SnCl_2$ and trimethylsilyl chloride (TMSCl)[6] or trityl chloride,[7] both in catalytic amounts, can activate various carbonyl compounds and their derivatives to promote a wide variety of carbon-carbon bond formations.

In the course of our exploration on the usefulness of the reactions promoted by the combination of $SnCl_2$ and organic halide, we discovered that the reaction between acetals and silyl enol ethers can be directed either to β-alkoxy ketones, similar to the product of the Mukaiyama reaction, or further dealkoxylated α,β-unsaturated ketones depending on the molar ratio of the activator halide, RCl, such as acetyl chloride (AcCl) or methoxymethyl chloride (MOMCl).

Herein we wish to report this novel reaction which opens a mild and efficient route to α,β-unsaturated ketones under essentially neutral conditions.

In the first place, we undertook to examine the simple Mukaiyama-type reaction according to the following procedure. A mixture of benzaldehyde dimethyl acetal (**1**) and 0.05 molar amount of tin(II) chloride to the acetal was treated with trimethylsilyl enol ether of cyclohexanone (**2**) in dichloromethane, and then 0.05 molar amount of AcCl to the acetal was added at room temperature. After 1 h, the usual work-up of the reaction mixture afforded the aldol-type product, 2-(α-methoxybenzyl)cyclohexanone, quantitatively (*erythro*:*threo*=57:43). In contrast, when two molar amounts of AcCl to the acetal was employed, concomitant elimination has occurred to give (*E*)-2-benzylidenecyclohexanone (**3**) quantitatively without formation of acetylated products such as 2-acetylcyclohexanone (Eq. 1). To the best of our knowledge, this is the first example in which α,β-unsaturated ketone was obtained directly from acetal via carbon-carbon bond formation by simple one-step procedure. After the preliminary investigation in search of the optimum activator and its molar ratio with benzaldehyde dimethyl acetal (**1**) and 1-(trimethylsiloxy)cyclohexene (**2**) as standard substrates, we have tentatively chosen a combination of $SnCl_2$ and AcCl (or MOMCl) as the catalyst-activator system (molar ratio of acetal:$SnCl_2$:AcCl=1.0:0.05:2.0) (Table 1).

The reaction was carried out with substrates in various combinations from three types of silyl enol ether and three types of acetal along with AcCl or MOMCl as an activator (Eq. 2 and 3). As shown in



(1)

Table 1. The Effect of Catalyst-Activator System of the Reaction between Benzaldehyde Dimethyl Acetal and 1-(Trimethylsiloxy)cyclohexene[a]

Run	Catalyst (molar ratio to the acetal)	Time/h	Yield[b]/% of **3**
1	$SnCl_2$ (0.05)+AcCl (2)	2	100
2	$SnCl_2$ (0.05)+MOMCl (2)	1	95
3	$SnCl_2$ (0.05)+MOMCl (1)	1	79
4	$TiCl_4$ (0.1)+MOMCl (2)	1	trace
5	$ZnCl_2$ (0.1)+MOMCl (2)	1	74
6	$Sn(OTf)_2$ (0.05)+MOMCl (2)	1	69
7	$SnCl_2$ (0.05)+TMSCl (2)	2	58
8	$SnCl_2$ (0.005)+MOMCl (2)	1	91

a) Molar ratio of acetal: silyl enol ether=1:1.5. b) Isolated yield.

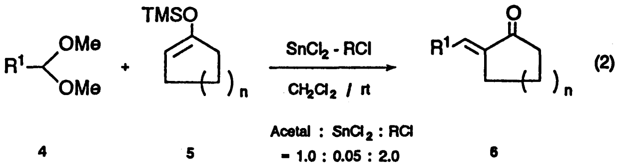


Table 2. Reaction between Acetals and 1-(Trimethylsiloxy)cycloalkenes[a]

Run	R^1	n[b]	RCl	Time/h	Yield/% of **6**
1	Ph	2	AcCl	2	100
2	Ph	2	MOMCl	1	95
3	Ph[c]	2	MOMCl	1	85
4	$PhCH_2CH_2$	2	MOMCl	3	92
5	$PhCH_2CH_2$	2	AcCl	3	78
6	$PhCH_2CH_2$	1	AcCl	6	71
7	(*E*)-CH_3CH=CH	2	AcCl	1	65
8	(*E*)-CH_3CH=CH	1	MOMCl	1	74

a) All samples gave satisfactory ^{1}H NMR and IR spectra. b) n+4=the number of ring size of cyclic silyl enol ether. c) Diethyl acetal was used in place of dimethyl acetal.

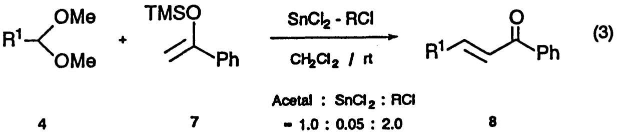


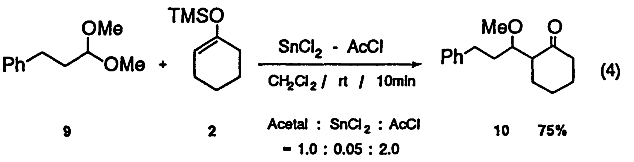
Table 3. Reaction between Acetals and α-(Trimethylsiloxy)styrene[a]

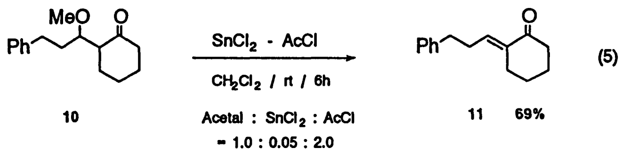
Run	R^1	RCl	Time/h	Yield/% of **8**
1	Ph	MOMCl	2	100
2	Ph	AcCl	1	100
3	$PhCH_2CH_2$	AcCl	12	73
4	$PhCH_2CH_2$[b]	AcCl	12	79

a) All samples gave satisfactory ^{1}H NMR and IR spectra. b) Reaction was carried out in the presence of molecular sieves 4A (Ref. 8).

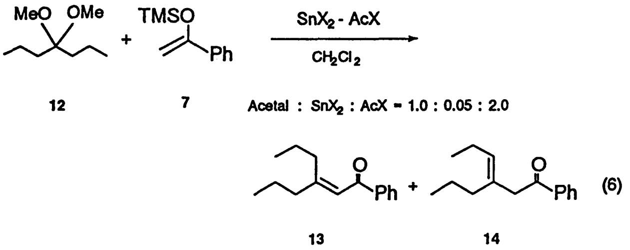
Tables 2 and 3, all combinations gave good to excellent yields of corresponding conjugated enones (dienones in the case of Runs 7 and 8 in Table 2) as a sole product without formation of acylated or alkylated products of silyl enol ethers.

A short time reaction (10 min) under the same conditions of Run 5 in Table 2 gave only β-methoxy ketone (**10**) in 75% yield (Eq. 4). Concerning the reaction mechanism, we have carried out a reaction in which an alleged primary condensation product, 2-(1-methoxy-3-phenylpropyl)cyclohexanone (**10**), was used as the starting material in place of combined acetal-silyl enol ether substrates. The result was completely identical with that of Run 5 in Table 2, thus confirming the intermediacy of the β-methoxy ketone.





Treatment of a mixture of 4-heptanone dimethyl acetal (**12**) and α-(trimethylsiloxy)styrene (**7**) in CH_2Cl_2 with $SnCl_2$–AcCl activator system at room temperature for 12 h gave α,β- and β,γ-unsaturated ketone in 88% combined yield (**13**:**14**=85:15) (Eq. 6). However, treatment with $SnBr_2$–AcBr activator system at room temperature for 1 h resulted in the reversal of selectivity (**13**:**14**=19:81).



In conclusion, the present one-step reaction of acetals and silyl enol ethers to form conjugated enones has an advantage that features experimental convenience and extremely mild reaction conditions.

Experimental

General Procedure. To a suspension of anhydrous tin(II) chloride (6.2 mg, 0.033 mmol) and benzaldehyde dimethyl acetal (105.6 mg, 0.70 mmol) in 2.5 ml of CH_2Cl_2 was added 1-(trimethylsiloxy)cyclohexene (176.6 mg, 1.04 mmol) in 1.5 ml of CH_2Cl_2 and AcCl (108.1 mg, 1.38 mmol) in 1 ml of CH_2Cl_2 successively at room temperature. The reaction mixture was stirred for 2 h at this temperature and was quenched with a phosphate buffer (pH 7). The organic materials were extracted with CH_2Cl_2 and dried over Na_2SO_4. (*E*)-2-Benzylidenecyclohexanone (129.3 mg, 100%) was isolated by thin layer chromatography on silica gel.

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References

1) T. Mukaiyama and M. Hayashi, *Chem. Lett.*, **1974**, 15; T. Mukaiyama, H. Ishihara, and K. Inomata, *ibid.*, **1975**, 527; H. Ishihara, K. Inomata, and T. Mukaiyama, *ibid.*, **1975**, 531.

2) T. Sato, M. Arai, and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 5827 (1977).

3) S. Murata, M. Suzuki, and R. Noyori, *J. Am. Chem. Soc.*, **102**, 3248 (1980).

4) T. Mukaiyama, S. Kobayashi, and M. Murakami, *Chem. Lett.*, **1984**, 1759.

5) T. Mukaiyama, S. Matsui, and K. Kashiwagi, *Chem. Lett.*, **1989**, 993.

6) N. Iwasawa and T. Mukaiyama, *Chem. Lett.*, **1987**, 463.

7) T. Mukaiyama, S. Kobayashi, M. Tamura, and Y. Sagawa, *Chem. Lett.*, **1987**, 491.

8) A. Ishida and T. Mukaiyama, *Chem. Lett.*, **1975**, 1167.