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An Essentially Mild and Efficient Catalyst System for the Activation of Carbonyl Compounds and Their Derivatives. The Combined Use of Trimethylsilyl Chloride and Tin(II) Chloride

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An essentially mild and efficient catalyst system, the combined use of trimethylsilyl chloride and tin(II) chloride, is effectively employed for the activation of acetals, aldehydes, orthoesters, and α,β-unsaturated ketones to accomplish the reaction with silyl enol ethers to give the corresponding addition products in good yields.

New catalyst systems for fundamental carbon-carbon bond forming reactions are highly desirable and one of the most frequently employed promoters is Lewis acid, which generates electron deficient carbon centers to accelerate the reaction with various nucleophiles. Conventionally, various Lewis acids such as $TiCl_4$, $SnCl_4$, or $BF_3 \cdot Et_2O$ have been employed for this purpose, however, stoichiometric amounts of the reagents are usually required.1) Recently, several new catalysts such as trimethylsilyl triflate2) and trityl perchlorate3) have been introduced as effective catalytic promoters. However, most of these reagents are composed of superacids, and it is still desirable to explore a more effective and mild catalyst system, which would be useful in synthetic procedures involving acid or base sensitive compounds.

In this communication, we would like to report our new and unique finding that an essentially mild and efficient catalyst system, the combined use of trimethylsilyl chloride(TMSCl) and tin(II) chloride, can activate various carbonyl compounds and their derivatives and promote a wide variety of carbon-carbon bond forming reactions.

First, we examined various catalyst systems taking the Michael reaction of trimethylsilyl enol ether of cyclohexanone and phenylpropenylketone as a model, and the results are summarized in Table 1.

As shown in Table 1, when $ZnCl_2$ or $SnCl_2$, a weak Lewis acid, was employed alone, no reaction took place. Also, TMSCl did not promote the reaction at all. On the contrary, when a mixture of TMSCl and $SnCl_2$ or $ZnCl_2$ was employed, the reaction was dramatically accelerated and the Michael adduct was obtained in good yield. The most noteworthy point was that a combined employment of a catalytic amount of these two reagents (TMSCl and $SnCl_2$) promoted the Michael reaction efficiently, and the product was obtained in 90% yield.

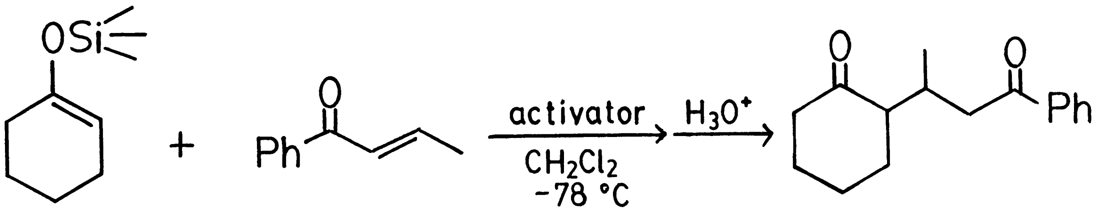


Table 1. Examination of the Catalyst System$^{a)}$

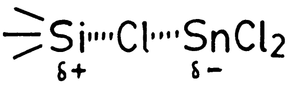
Activator	Reaction time/h	Yield/%
3.4 equiv. TMSCl	2.5	0
1.3 equiv. $MgCl_2$	2.5	0
1.3 equiv. $MgCl_2$ + 1.7 equiv. TMSCl	2.5	0
1.3 equiv. $ZnCl_2$	2.5	0
1.2 equiv. $ZnCl_2$ + 2.6 equiv. TMSCl	2.5	53
0.14 equiv. $ZnCl_2$ + 0.23 equiv. TMSCl	19	33
1.3 equiv. $SnCl_2$	2.5	0
1.3 equiv. $SnCl_2$ + 2.4 equiv. TMSCl	2.5	86
0.10 equiv. $SnCl_2$ + 0.18 equiv. TMSCl	15	90

a) Molar ratio of silyl enol ether : unsaturated ketone = 1.0 : 0.8.

Next, we examined several kinds of reactions employing a catalytic amount of TMSCl and $SnCl_2$.

As shown in Table 2, this catalyst system was also effective for the activation of aldehydes, acetals, (aldol-type reaction), α,β-unsaturated ketones (the Michael-type reaction), and orthoester, and in most cases, the reaction proceeds smoothly at -78 °C to give the corresponding adducts in good yield. It should be noted that this new catalyst system was active enough to generate cationic species comparable to trimethylsilyl triflate or trityl perchlorate without using such superacids.

At present, we assume that the active point of this catalyst system is silicon, which is able to attack preferentially on the oxygen atoms of the carbonyl compounds, and the following two active intermediates could be postulated.$^{4)}$



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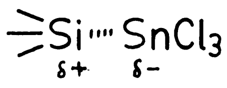


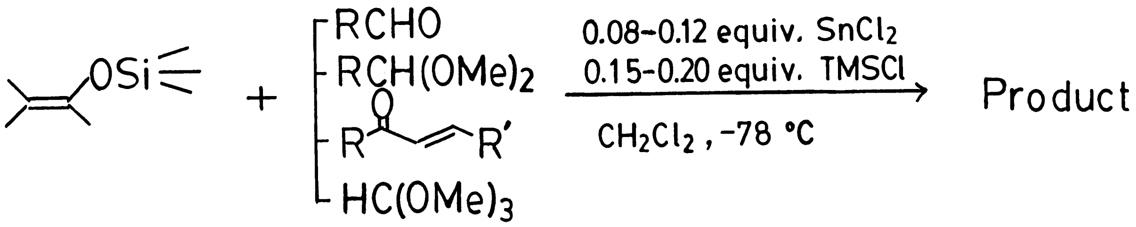
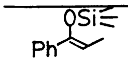
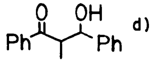
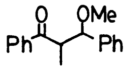
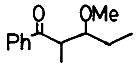
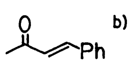
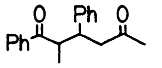
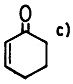
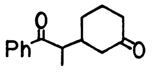
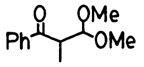
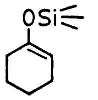
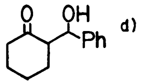
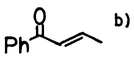
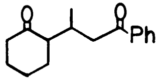
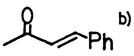
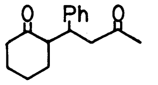
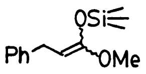
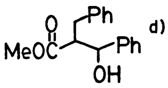
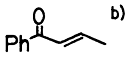
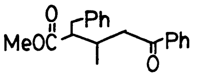


Table 2. Reaction of Various Silyl Nucleophiles and Electrophiles.

Nucleophile	Electrophile	Product	Reaction time/h	Yield/%	Diastereomer f) ratio
	PhCHO a)	 d)	1.5	88	65 : 35
	$PhCH(OMe)_2$ a)		1.5	90	85 : 15
	$C_2H_5CH(OMe)_2$ a)e)		2	69	85 : 15
	 b)		23	97	90 : 10
	 c)		23	89	70 : 30
	$HC(OMe)_3$ a)		15	85	—
	PhCHO a)	 d)	3	82	70 : 30
	 b)		15	90	65 : 35
	 b)		13	93	55 : 45
	PhCHO a)	 d)	3	85	60 : 40
	 b)		15	84	50 : 50

a) Molar ratio of silyl enol ether : electrophile = 1.0 : 1.2
b) Molar ratio of silyl enol ether : electrophile = 1.0 : 0.8
c) Molar ratio of silyl enol ether : electrophile = 1.0 : 0.5
d) Partially obtained as its trimethylsilyl ether.
e) This reaction was carried out at -40 °C.
f) Determined by ^1H or ^{13}C NMR spectra. Relative stereochemistry was not rigorously assigned.

Representative procedure is described for the reaction of silyl enol ether of propiophenone and benzaldehyde; To a CH_2Cl_2 suspension (1 ml) of $SnCl_2$(10 mg, 0.05 mmol)) was added a CH_2Cl_2 solution (1.5 ml) of enol silyl ether of propiophenone (131 mg, 0.64 mmol) and benzaldehyde (74 mg, 0.70 mmol) and a CH_2Cl_2 solution (0.5 ml) of TMSCl (11 mg, 0.10 mmol) successively at -78 °C. The reaction mixture was further stirred for 1.5 h at this temperature, and the reaction was quenched with 10% citric acid solution. The organic materials were extracted with ethyl acetate twice, and the combined extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by silica gel thin layer chromatography to give the product in 88% yield.

Thus, we have succeeded in devising a new catalyst system just by combining neutral molecule (TMSCl) and very mild Lewis acid ($SnCl_2$) to generate active cationic species, which effectively activates carbonyl compounds and their derivatives. We are currently continuing studies to clarify the reactive species of this unique activation and to examine the further applicability of this system.

References

1) For example, see; W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, Berlin (1983), pp. 206-227.
2) R. Noyori, S. Murata, and M. Suzuki, Tetrahedron, 37, 3899 (1981); See also; H. Sakurai, K. Sasaki, and A. Hosomi, Tetrahedron Lett., 22, 745 (1981).
3) T. Mukaiyama, S. Kobayashi, and M. Murakami, Chem. Lett., 1984, 1759; S. Kobayashi, M. Murakami, and T. Mukaiyama, ibid., 1985, 953; 1985, 1535.
4) For some related systems which might have the same active species; S. Danishefsky and T. Kitahara, J. Am. Chem. Soc., 96, 7807 (1974); H. Oshino, E. Nakamura, and I. Kuwajima, J. Org. Chem., 50, 2802 (1985).

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