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An Efficient and Extremely Mild Catalyst System, Combined Use of Trityl Chloride and Tin(II) Chloride, in the Aldol and Michael Reactions

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The aldol reaction of silyl enol ethers with acetals or aldehydes, and the Michael reaction of silyl enol ethers with α,β-unsaturated ketones are efficiently catalyzed by the combined use of trityl chloride and tin(II) chloride under extremely mild conditions.

The reaction of rather stable carbon nucleophiles with activated carbonyl compounds is one of the most versatile synthetic tools for the carbon-carbon bond formation.1) Although Lewis acids such as $TiCl_4$, $SnCl_4$, $BF_3 \cdot OEt_2$, etc. are frequently employed in these reactions as useful promoters, it is still strongly desired to explore a new catalyst which accelerates the reactions under essentially neutral conditions.

Recently, we have reported that trityl salts are unique and excellent catalysts of several synthetic reactions.2) For examples, trityl salts effectively catalyze the aldol reaction of silyl enol ethers with acetals3) or aldehydes and syn(erythro) or anti(threo) aldol is obtained preferentially by the appropriate choice of trityl salts and silyl enol ethers.4) The Michael reaction of silyl enol ethers with α,β-unsaturated ketones is also catalyzed by trityl salts and 1,5-dicarbonyl compounds or intermediate silyl enol ether can be isolated under appropriate quenching conditions.5) One of the most characteristic features is that these reactions require only a catalytic amount of trityl salts, whereas the Lewis acid-promoted reactions6) generally require stoichiometric amounts of promoter. In the course of our investigations on the exploration of new possibility in the trityl salts-promoted reactions, we have found that the combined use of trityl chloride (Ph_3CCl=TrCl) and tin(II) chloride ($SnCl_2$) readily generates quite efficient active trityl species. In this communication, we wish to describe the aldol and Michael reactions of silyl enol ethers with aldehydes, acetals, and α,β-unsaturated ketones under essentially neutral conditions promoted by the above mentioned catalyst system.

Several examples of the aldol and Michael reactions are demonstrated in Table 1 and 2 respectively. In every case, the reactions smoothly proceeded at -78 °C and the adducts are obtained in high yields. Concerning the stereochemistry, syn(erythro) aldols were preferentially obtained by the reaction of acetals with trimethylsilyl enol ethers, whereas anti(threo) aldols were predominantly produced by the treatment of aldehydes with t-butyldimethylsilyl enol ethers. In the Michael reaction, the ul (anti) adducts[6] were obtained preferentially. These diastereoselectivities are almost consistent with those of the trityl salts-promoted aldol and Michael reactions.

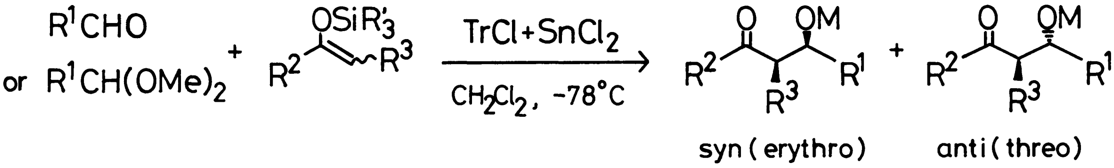
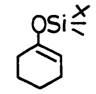
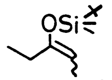
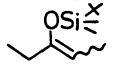
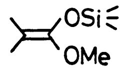
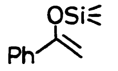
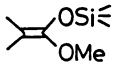
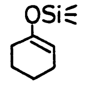
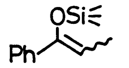
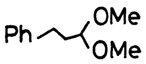
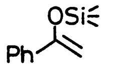
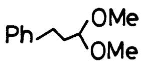
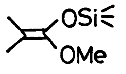


Table 1. The aldol reaction catalyzed by the combined use of trityl chloride and tin(II) chloride[a]

Entry	Aldehyde or Acetal	Silyl enol ether	Amounts of catalyst/mol%	Yield/%	syn:anti[b] (erythro:threo)
1	PhCHO		5	99	20 : 80
2	PhCHO		5	95	18 : 82
3	PhCHO		5	92	31 : 69
4	PhCHO		5	96	———
5			10	79	———
6			10	83	———
7	PhCH(OMe)$_2$		10	99	90 : 10
8	PhCH(OMe)$_2$		5	95	85 : 15
9			5	85	———
10			10	88	———

a) All products gave satisfactory NMR and IR spectra.
b) Determined by ^1H NMR.

A typical procedure is described for the reaction of t-butyldimethylsilyl enol ether of 3-pentanone with benzaldehyde; trityl chloride (0.05 mmol) and tin(II) chloride (0.05 mmol) was stirred in dichloromethane (1 cm^3) at room temperature for 30 min, and then the mixture was cooled to -78 °C. t-Butyl-

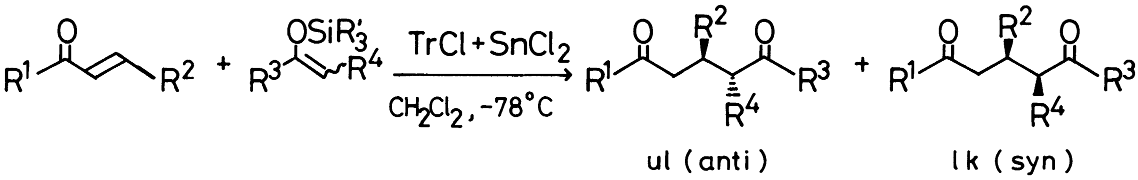
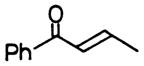
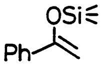
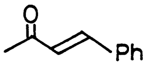
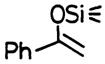
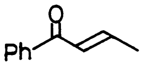
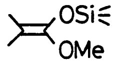
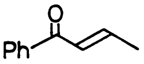
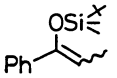
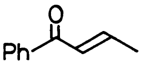
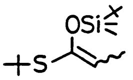
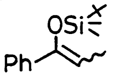
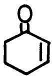
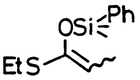
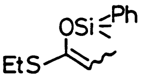


Table 2. The Michael reaction catalyzed by the combined use of trityl chloride and tin(II) chloride[a)]

Entry	α,β-Unsaturated ketone	Silyl enol ether	Amounts of catalyst/mol%	Yield/%	ul : lk (anti:syn)
1			5	82	———
2			5	88	———
3			5	81	———
4			5	84	> 95 : 5 [b)]
5			5	90	84 : 16 [c)]
6			10	79	83 : 17 [d)]
7			5	86	81 : 19 [d)]
8			5	88	85 : 15 [d)]

a) All products gave satisfactory NMR and IR spectra.

b) Determined by ^{13}C NMR.

c) Determined by ^{1}H NMR.

d) Determined by GC.

dimethylsilyl enol ether of 3-pentanone (1.1 mmol, E/Z=76/24) and benzaldehyde (1 mmol) in dichloromethane (4 cm^3) were added and the mixture was stirred for 100 min. Then aqueous sodium hydrogen carbonate was added and the aqueous layer was extracted with dichloromethane. The organic layer was dried and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel to yield 1-tert-butyldimethylsiloxy-1-phenyl-2-methyl-3-pentanone (94%, syn(erythro)/anti(threo) = 18/82).

Although the precise active species is not yet clear at this stage, we postulate the generation of a novel, active cationic species from trityl chloride and tin(II) chloride based on the results that neither trityl chloride nor tin(II) chloride promotes the above mentioned reactions. Actually, yellowish color appeared as soon as trityl chloride and tin(II) chloride are mixed in dichloromethane. After the mixture was stirred overnight at room temperature, solid tin(II) chloride still remained, and the aldol and Michael reactions proceed under this heterogeneous condition. The most characteristic and remarkable point is that this active promoter is prepared by just mixing *a neutral molecule and a weak Lewis acid*, and is enough to complete the reactions by using 5-10 mol% each of these reagents. These results show that fundamentally, synthetically valuable carbon-carbon bond forming reaction can be completed under essentially neutral conditions by simple procedures.

Quite recently, it was found in our laboratory that a similar active species is formed by the combined use of trimethylsilyl chloride and tin(II) chloride.8) This species is not yet made clear, however, the result is explained by assuming a possibility of making a covalently bonded interaction with electrophiles by taking account of the characteristic property of silicon atom.9) Different from this, the combination of trityl chloride and tin(II) chloride would generate a cationic species, which is easy to activate electrophiles. As demonstrated herein, the present cationic activators are novel and unique, enable the catalytic cycles, and have many synthetic and theoretical possibilities.

Further progress towards clarification of the active species as well as other synthetic reactions promoted by the combination of a neutral molecule and a weak Lewis acid is now in progress.

References

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4) S. Kobayashi, M. Murakami, and T. Mukaiyama, Chem. Lett., 1985, 1535.
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9) S. Murata, M. Suzuki, and R. Noyori, J. Am. Chem. Soc., 102, 3248 (1980); H. Sakurai, K. Sasaki, and A. Hosomi, Bull. Chem. Soc. Jpn., 56, 3195 (1983). See also Refs. 1 and 6.

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