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The Addition Reaction of Acetals to Activated Olefins under Extremely Mild Conditions

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In the presence of catalytic amounts of trimethylsilyl chloride and tin(II) chloride, or trityl chloride and tin(II) triflate, activated olefins smoothly react with acetals to afford the corresponding adducts in good yields.

The electrophilic additions to olefins are one of the most important reactions in organic synthesis and many electrophilic reagents have been developed.[1)] However, conventional addition reactions of acetals to even activated olefins require rather drastic reaction conditions[2)] and yields have not been improved in spite of the potential utility of this process leading to the widespread synthetic availability of acetals.[3)]

Recently, we have reported that combined use of trimethylsilyl chloride and tin(II) chloride[4)] or trityl chloride and tin(II) chloride[5)] generates an active species which effectively catalyzes the fundamental carbon-carbon bond forming reactions such as aldol reaction of acetals or aldehydes with silyl enol ethers and the Michael reaction of α,β-unsaturated ketones with silyl enol ethers. These reactions have advantage over the conventional methods in the mildness of the reaction conditions because these catalyst systems consist of a neutral molecule (TMSCl or TrCl) and a weak Lewis acid ($SnCl_2$). In the course of our investigations on new possibility in synthetic reactions promoted by the use of these new catalyst systems, we have focused to screen the capability of the catalysts for the activation of acetals toward weakly nucleophilic reagents. In the above mentioned reaction of acetals with silyl enol ethers, acetals are considered to be activated by the interaction of the catalyst to partly generate cationic species, which are attacked by silyl enol ethers to form new carbon-carbon bonds. Thus it is expected that these active species could also react with olefins to afford the intermediate cations by constructing new carbon-carbon bonds. These cations are trapped by alkoxide groups involved in the corresponding anion to give the adducts between acetals and olefins. In this communication, the addition reaction of acetals to activated olefins by the combined use of catalytic amounts of trimethylsilyl chloride and tin(II) chloride or trityl chloride and tin(II) chloride (tin(II) triflate) under extremely mild reaction conditions was studied.

At first, the reaction of 3-phenylpropionaldehyde dimethylacetal with 3,4-dihydro-2H-pyran was chosen as a model. It was carried out at 0 °C in dichloromethane in the presence of catalytic amounts of trimethylsilyl chloride and tin(II) chloride, and the desired corresponding adduct was obtained in 64% yield. Combined use of trityl chloride and tin(II) chloride also effectively catalyzed this reaction, however, neither tin(II) chloride, trimethylsilyl chloride, nor trityl chloride alone was effective (Table 1).

Next, the reaction of various activated olefins with acetals were examined (Table 2). Dihydropyran smoothly reacted with various acetals to afford the corresponding adducts in good yields. In the case of vinyl ethers, yields decreased slightly, however, this problem was overcome by the use of tin(II) triflate instead of tin(II) chloride. When styrene was employed as an olefin, the

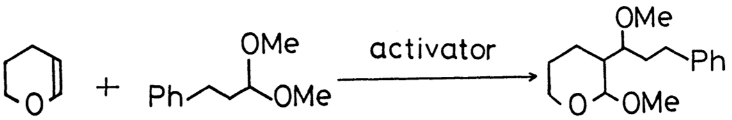
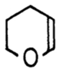
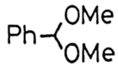
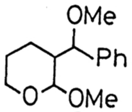
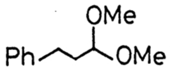
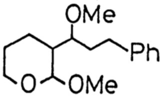
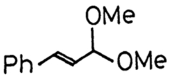
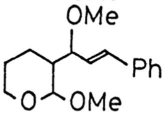
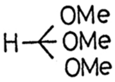
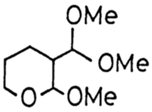
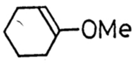
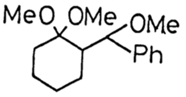
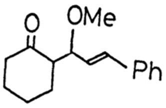
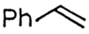
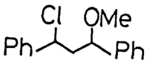
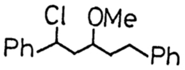


Table 1. The Effect of Catalyst

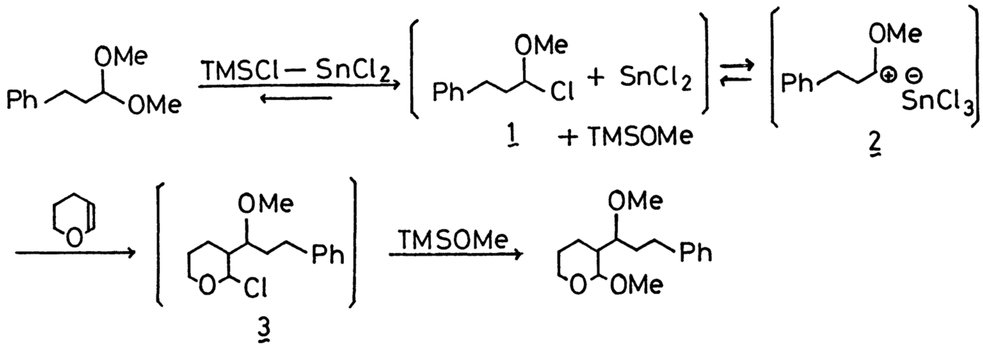
Activator	Yield/%
$SnCl_2$	7
$SnCl_2$ + MOMCl	58
$SnCl_2$ + TrCl	62
$SnCl_2$ + TMSCl	64
$SnCl_2$ + PhCOCl	39

Table 2. The Reaction of acetals with activated olefins[a)]

Olefin	Acetal	Catalyst	Product	Yield/%
	 (a)	$SnCl_2$+TMSCl		84 (70:14:13:3)[b),6)]
//	 (b)	$SnCl_2$+TMSCl		64[c)]
//	 (c)	$SnCl_2$+TMSCl		70[c)]
//		$SnCl_2$+TMSCl		55 (75:25)[b)]
	(a)	$Sn(OTf)_2$+TrCl		74[d)] (60:40)[b)]
//	(c)	$Sn(OTf)_2$+TrCl		77 (55:45)[b)]
	(a)	$SnCl_2$+1eq.TMSCl		80 (55:45)[b)]
//	(b)	$SnCl_2$+1eq.TMSCl		56 (55:45)[b)]

a) All the products gave satisfactory ^1H NMR and IR spectral data.
b) Diastereomer ratio determined by ^1H NMR. Relative configuration assignment was not made. c) A mixture of diastereomers. d) Quenched with NaOMe.

mixture of the desired adduct and the chloride was obtained in the presence of catalytic amounts of trimethylsilyl chloride and tin(II) chloride, while the chloride was exclusively produced in good yield when an equimolar amount of trimethylsilyl chloride and a catalytic amount of tin(II) chloride were employed. Based on these results, the mechanism of this reaction involving this chloride as the intermediate compound can be illustrated as follows; that is, the chloromethyl ether(1) seems to be initially produced by replacement of methoxy group of the acetal with chloride ion originated from trimethylsilyl chloride, followed by the addition of the second active species(2) generated from 1 and tin (II) chloride, to dihydropyran resulted in the formation of the intermediate chloride(3), which is in turn trapped by trimethylsilyl methoxide.



A typical procedure is described for the reaction of 3,4-dihydro-2H-pyran with benzaldehyde dimethylacetal; a mixture of trimethylsilyl chloride (0.06 mmol) and tin(II) chloride (0.06 mmol) in dichloromethane (2 cm^3) was stirred at 0 °C for 1 h. Dihydropyran (0.72 mmol) and benzaldehyde dimethylacetal (0.60 mmol) in dichloromethane (2 cm^3) were added to this mixture and stirring was continued for additional 1 h. Then aqueous sodium hydrogen carbonate was added and 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 the corresponding adduct (84%).

It is noted that, in the presence of catalytic amounts of trimethylsilyl chloride and tin(II) chloride (or trityl chloride and tin(II) chloride or tin(II) triflate), activated olefins such as 3,4-dihydro-2H-pyran, vinyl ethers, and styrene react with acetals to afford the corresponding adducts in good yields under extremely mild reaction conditions.

References

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2) O. C. Dermer and John J. Hawkins, J. Am. Chem. Soc., 74, 4595 (1952); O. N. Mikhant'eva et al., Deposited Doc. 1977, VINITI, 3061 - 77, 14pp; Chem. Abstr., 90, 167988y (1979); D. Elad and I. Rosenthal, J. Chem. Soc., Chem. Commun., 1966, 684.

3) T. Mukaiyama and M. Murakami, Synthesis, 1987, 1043.

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

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

6) Major diastereomer, ^{1}H NMR(CDCl$_3$) 7.36-7.23(m, 5H), 4.98(d, 1H, J=3.1 Hz), 3.98(d, 1H, J=10.2 Hz), 3.73-3.46(m, 2H), 3.45(s, 3H), 2.20-1.23(m, 4H), 1.03-0.80(m, 1H).

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