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ACTIVATION OF KETENE SILYL ACETALS BY 10-METHYLACRIDINIUM PERCHLORATE: A NOVEL CATALYSIS IN MUKAIYAMA REACTION

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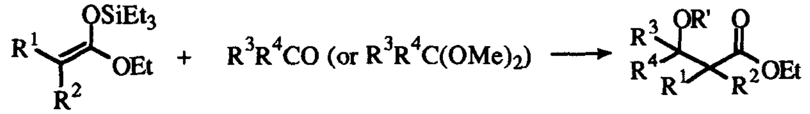
Abstract: 10-Methylacridinium perchlorate (**1**) effectively promotes various reactions of ketene silyl acetals: aldol and Michael addition products are obtained with aldehydes, ketones, acetals, and α-enones. *The reactions exhibit unusual dependency upon* **1***, namely the yields are* excellent when a catalytic amount of **1** is employed whereas no desired products are accessible by the use of **1** in a stoichiometric quantity. A novel catalytic cycle is proposed.

Increasing attention has been paid to reaction of ketene silyl acetals with carbonyls, acetals, or α-enones (Mukaiyama reaction).[1] Since Lewis acids play a key role in promotion of the reaction, a number of efforts have been devoted to search for more effective promotors. As part of our studies in this field,[2] we have found that 10-methylacridinium perchlorate (**1**)[3] serves well to this end, in particular, for activation of β,β-disubstituted ketene silyl acetals. Of great interest with this system *is that the reactions are dramatically dependent upon the dosage of* **1**. The use of a catalytic amount of **1** is crucial for the efficient aldol and Michael addition reactions whereas the yields of the desired products sharply decrease with increasing quantity of **1**. Elucidation of this anomaly is the subject of this letter, too.

To a dichloromethane solution of **1** (5 mol%) were added the β,β-dimethyl-substituted ketene silyl acetal **2a** (1.3 equiv) and a carbonyl or acetal compound (1 equiv) (eq. 1). After the solution had been stirred for 1-6 h, the aldol products were obtained in good yields (Table 1). On the other hand, yields were somewhat diminished with monomethyl-substituted and unsubstituted derivatives, **2b** and **2c**. The Michael reaction with α-enones (eq. 2) gave the similar results (Table 2). Note that quaternary carbon centers are readily connected.

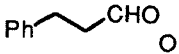
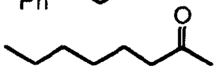
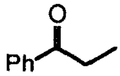
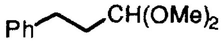
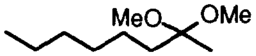
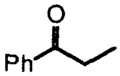
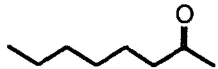


(1)

2

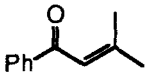
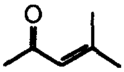
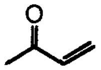
(2)

Table 1. Aldol Reaction[a]

2	R^1	R^2	carbonyl or acetal	reaction time, h	yield, %
2a	Me	Me	PhCHO	6	88
				4	98
				4^b	94
				4^b	79
			$PhCH(OMe)_2$	1	98
				4	91
				4	89
2b	Me	H	PhCHO	4^b	90
			$PhCH(OMe)_2$	4^b	55
				4^b	60
2c	H	H	PhCHO	4^b	67
			$PhCH(OMe)_2$	4^b	59
				4^b	81

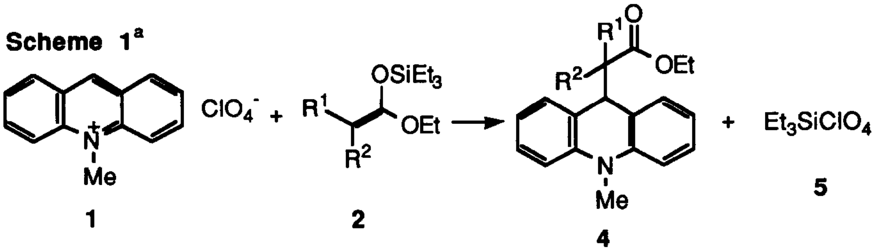
[a] Reaction conditions: **2**/carbonyl (or acetal)/**1** = 1.2: 1: 0.05, CH_2Cl_2, rt.
[b] At -78 °C.

Table 2. Michael Addition[a]

2	α-enone	yield, %
2a	 (**3**)	98
		99
		93
2b	**3**	53
2c	**3**	53

[a] Reaction conditions: **2**/α-enone/**1** = 1.2: 1: 0.05, CH_2Cl_2, -78 °C, 4 h.

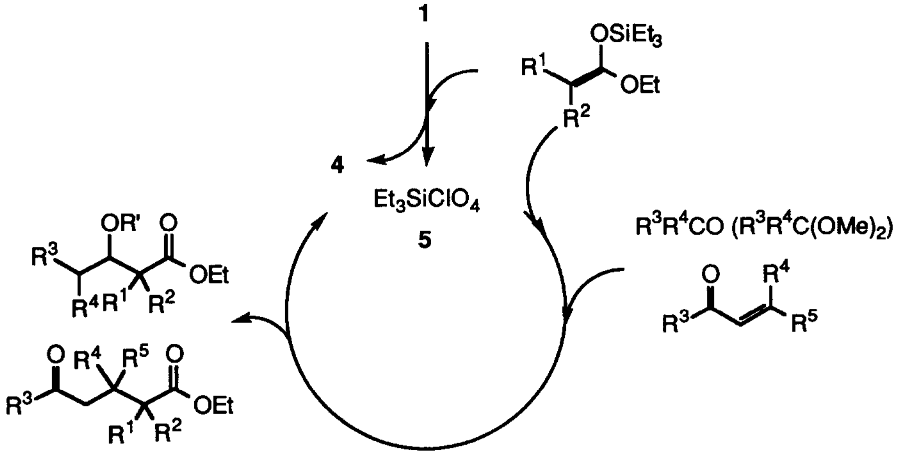
Scheme 1[a]



2	**4**, yield (%)
2a	80
2b	50
2c	31

[a] Reaction conditions: CH_2Cl_2, -78 °C, 4 h.

Scheme 2



Next, we found that employment of a stoichiometric amount of **1** drastically reduced the yields in the above reactions. For example, a dichloromethane solution of **1** (1 equiv) and **2a** (1 equiv) was stirred for 15 min at -78 °C and then the α-enone **3** (1 equiv) was added to the solution. After the solution was stirred for 4 h at this temperature, the Michael adduct was obtained only in 28% yield. When **1** and **2a** were stirred for 1 h before the addition of **3**, no adduct was formed. These results led us to suppose that **1** was not a real catalyst. In fact, alkylation products **4** was produced upon treatment of **1** with ketene silyl acetals (1 equiv) at -78 °C (Scheme 1).4) It then turned out that **4** did not work as a promotor of the Mukaiyama reactions at all. We therefore deduce the genuine active species to be triethylsilyl perchlorate (**5**) which has been formed simultaneously although this compound has not been isolated. The reactions employing separately prepared **5**5) in place of **1** afforded quite analogous results to support the effectiveness of **5**.6) The above outcome leads us to delineate the present reactions as given in Scheme 2. The initial step is the generation of **5**, which triggers the reaction of the electron-deficient centers with the unchanged ketene silyl acetal. In other words, one of the reactants serves as a precursor of the catalyst. Since the alkylation of **1** precedes the aldol or Michael rèaction, the use of an equivalent amount of this compounds completely consumes the ketene silyl acetal which otherwise should be supplied to the reaction with an electrophile. The remarkable effect of the dosage of **1** is apparent on this basis.

The reasons for lower yields with **2b** and **2c** are two-fold. First, the rate of alkylation of **1** is slower than that of **2a** as is seen from the results in Scheme 1. Secondly, **2b** and **2c** themselves are less reactive than **2a** in the Mukaiyama reactions.7)

In summary, **1** has proved to work as an efficient activator of ketene silyl acetals. Due to the neutral and air-stable properties, **1** would find versatile synthetic applications, especially for aldol and Michael products bearing quaternary carbons. In a strict sense, "catalyst" is regarded as a substance which reduces the activation energy but hardly affects equilibrium of the reaction. Consequently, the catalyst is not involved in the stoichiometry of the reactants and products. However, this sense is violated frequently and the extreme case is "auto-catalysis" where one of the reaction products catalyzes the reaction through which the catalyst itself has been produced. The novel catalysis presented in this paper constitutes the opposite extreme where one of the reactants is forced to react by the self-created catalyst.

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References

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(3) S. Fukuzumi, S. Kuroda, and T. Tanaka, *J. Chem. Soc., Chem. Commun.*, **1986**, 1553. S. Fukuzumi and T. Kitano, *J. Am. Chem. Soc.*, **112**, 3246 (1990).

(4) The alkylation will be discussed in more detail elsewhere.

(5) The compound was prepared from Et_3SiH and Ph_3CClO_4 according to the Lambert's method: J. B. Lambert, J. A. McConnell, W. Shilf, and W. J. Schultz, Jr., *J. Chem. Soc., Chem. Commun.*, **1988**, 455.

(6) To the best of our knowledge, this is the first examples which show that organosilyl perchlorates catalyze the Mukaiyama reactions. Formation of Me_3SiClO_4 was suggested in electrochemical reactions of silyl nucleophiles in the presence of perchlorate salts. It was concluded however that the actual promotor was not the silyl perchlorate but an electrogenerated acid: S. Torii, T. Inokuchi, S. Takagishi, H. Hiroke, H. Kuroda, and K. Uneyama, *Bull. Chem. Soc. Jpn.*, **60**, 2173 (1987).

(7) The unusual reactivity of the more hindered ketene silyl acetals will be reported shortly.

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