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The Michael Reaction of O-Silylated Ketene Acetals with α,β-Unsaturated Esters Promoted by a Catalytic Amount of Aluminum Triflate

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The Michael reaction of O-silylated ketene acetals with α,β-unsaturated ester in the presence of a catalytic amount of aluminum triflate proceeds smoothly under mild conditions to afford the corresponding glutarates in good yields.

The Michael reaction of α,β-unsaturated esters is frequently employed as a useful method for carbon-carbon bond formation. Recently, a successful example of the Michael reaction of lithium enolates derived from carboxylic esters and amides to α,β-unsaturated esters has been reported by Yamaguchi et al.$^{1)}$ Contrary to these Michael reactions carried out under basic condition, the same reaction of α,β-unsaturated esters in the presence of a catalytic amount of Lewis acid remains unexplored.$^{2)}$

In the course of our investigation on new synthetic reactions using trityl cation, diphenylboryl triflate and hexachloroantimonate, various carbon-carbon bond forming reactions such as the aldol reaction,$^{3)}$ the Michael reaction to α,β-unsaturated ketones,$^{4)}$ the allylation reaction of acetals$^{5)}$ and the Friedel-Crafts acylation$^{6)}$ were developed.

These reactions are based on the characteristic ability of trityl cation and diphenylboryl reagents to activate the oxygen-containing functional groups such as acetals and carbonyl compounds by using only a catalytic amount of the promotor. In contrast to these results, neither trityl cation nor diphenylboryl reagents could effectively activate α,β-unsaturated esters in the reaction with silyl enol ether and so further investigation on a possible activation of these compounds was tried. In this communication, we wish to report the Michael reaction of O-silylated ketene acetals 2 to α,β-unsaturated ester 1 by use of a catalytic amount of aluminum triflate. It was found that, in the presence of a catalytic amount of aluminum triflate, α,β-unsaturated ester 1 smoothly reacts with 2 to afford the corresponding glutarate 3 in good yield.

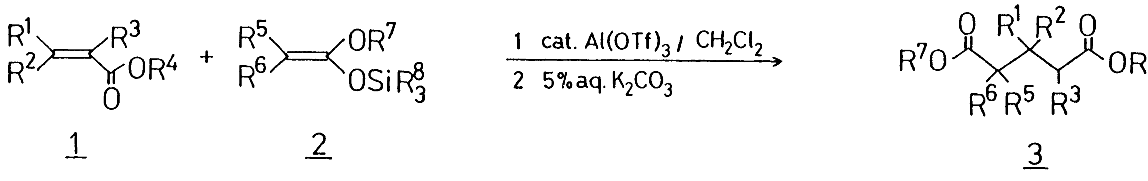
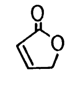


Table 1. The Michael reaction of 2 to 1 a)

Entry no.	α,β-Unsaturated ester b)	O-Silylated ketene acetal b)	Temperature/°C (Time/h)	Yield/% c)
1	(E)-MeCH=CHCO$_2$Me 1a	PhCH$_2$CH=C(OMe)OSiMe$_3$ 2a	r.t. (4)	85
2	1a	2a	-78 (14)	84
3	(E)-MeCH=CHCO$_2$Bn 1b	Me$_2$C=C(OMe)OSiMe$_3$ 2b	-23 (1)	84
4	(E)-PhCH=CHCO$_2$Me 1c	2a	r.t. (4)	89
5	1c	2a	-78 (14)	81
6	1c	2b	-23 (2)	89
7	1c	2b	-78 (14)	82
8	1c	H$_2$C=C(OEt)OSi^{t}BuMe$_2$ 2c	r.t. (4)	75
9	CH$_2$=C(Me)CO$_2$Et 1d	2a	0 (4)	62
10	1d	2a	-78 (14)	50
11	1d	2b	-23 (4)	61
12	(E)-MeO$_2$CCH=CHCO$_2$Me 1e	2b	r.t. (3)	66
13	CH$_2$=CHCO$_2$Me 1f	2a	r.t. (4)	27
14	1f	2a	-78 (5)	30
15	Me$_2$C=CHCO$_2$Me 1g	2a	r.t. (4)	9
16	Me$_2$C=C(CO$_2$Et)$_2$ 1h	2a	r.t. (6)	89
17	1h	2b	r.t. (6)	83
18	 1i	PhCH=C(OMe)OSiMe$_3$ 2d	-23 (2)	27

a) All reactions were carried out in the presence of aluminum triflate (0.10-0.17 equiv.). b) Molar ratio of 1 : 2 = 1.0 : 1.2 - 1.4 c) Isolated yield. Yields are based on α,β-unsaturated ester.

The results are summarized in Table 1. The features of the present reaction are as follows: (1) The reaction to β-monosubstituted acrylates proceeded smoothly under very mild conditions (-78 °C) or practical conditions (room temperature) to afford the corresponding glutarate in satisfactory yields. (2) In the case of the reaction using β,β-disubstituted acrylate, the product was obtained in low yield and the unsaturated ester was recovered. However, the addition to β,β-disubstituted methylenemalonate gave the desired product in high yield. (3) In the case of the addition to methyl acrylate, the desired product was obtained in low yield and polymeric substance resulted predominantly. (4) Conventionally employed organoaluminum reagents, such as $AlCl_3$ and Me_2AlOTf, are also effective for this type of reaction, however, yields are generally low.

Next, we examined the diastereoselectivity of the present reaction using diphenyl ketene methyl silyl acetal 2d and crotonate 4. The results are summarized in Table 2. From these results, it was shown that the substituents in the ester function of crotonate 4 remarkably influenced the diastereoselectivity of the reaction.

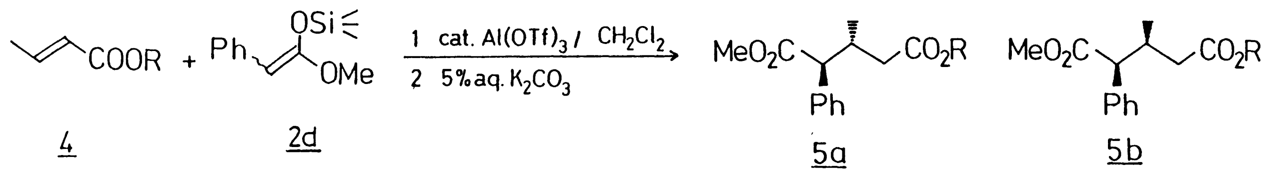


Table 2. The diastereoselectivity of the Michael reaction

R	Yield/% b)	5a : 5b c)
Me	84	1.5 : 1 d)
CH_2Ph	74	1 : 1 d)
^tBu	65	3.0 : 1 e)
Menthyl	82	4.0 : 1 e)

a) All reactions were carried out in the presence of aluminum triflate (0.20 equiv.) at -78 °C for 14 h.

b) Isolated yields. Yields are based on crotonate. 2d Z : E = 95 : 5.

c) See Ref. 7.

d) Diastereomeric ratio was determined by ^1H-NMR.

e) 5-Hydroxy-3-methyl-2-phenylpentanol was derived from the product by $LiAlH_4$-reduction. Diastereomeric ratio of this diol was determined by ^{13}C-NMR.

A typical reaction procedure is described for the synthesis of dimethyl 2-benzyl-3-methylglutarate (entry 2); under an argon atomosphere, to a CH_2Cl_2 solution (3 ml) of trifluoromethanesulfonic acid (33.8 mg, 0.23 mmol) was added 78 μl of Me_3Al (1 M in hexane, 0.078 mmol) at -78 °C. The mixture was stirred at -78 °C for 5 min and at room temperature for 30 min.[8] After cooling to -78 °C, solutions of methyl crotonate (43.9 mg, 0.44 mmol) in CH_2Cl_2 (2 ml) and benzylketene methyl trimethylsilyl acetal (149 mg, 0.63 mmol) in CH_2Cl_2 (2 ml) were successively added. The reaction mixture was stirred for 14 h at the same temperature, then quenched with 5% aq. K_2CO_3. The organic materials were extracted with CH_2Cl_2, and combined extracts were dried over Na_2SO_4. After the evaporation of the solvents, the residue was purified by preparative TLC (silica gel) to afford dimethyl 2-benzyl-3-methylglutarate (97.6 mg, 84%).

It is noted that the Michael reaction of O-silylated ketene acetals to α,β-unsaturated esters proceeds smoothly under mild condition in the presence of a catalytic amount of aluminum triflate, a promotor.

References

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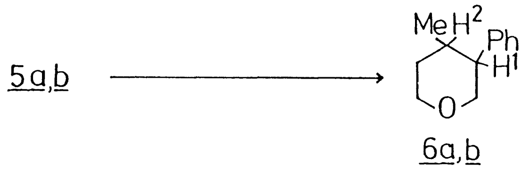
7) The configuration of 5a and 5b were determined by conversion to the tetrahydropyran 6a and 6b.[1] The coupling constant between proton H^1 and H^2 was J=4 Hz in 6a, J=11 Hz in 6b which indicates that the configuration of 6a is cis and that of 6b is trans.



8) Treatment of trifluoromethanesulfonic acid (3.0 mmol) with Me_3Al (1.0 mmol) in CH_2Cl_2 at room temperature gave aluminum triflate along with the evolution of CH_4 (3.0 mmol).

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