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THE STEREOSELECTIVE MICHAEL REACTION BETWEEN SILYL ENOL ETHERS AND α,β-UNSATURATED KETONES BY THE USE OF TRITYL PERCHLORATE AS A CATALYST

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The Michael adducts are obtained with good to excellent ul selectivity by treating silyl enol ethers with α,β-unsaturated ketones in the presence of a catalytic amount of trityl perchlorate.

The Michael reaction is one of the most important methods for carbon-carbon bond formation.[1] However, in the conventional Michael reactions carried out under basic conditions, side reactions such as undesired condensations, self-condensation of substrates, and enolization or cyclization of products often occurred.[1a,b] These disadvantages can be overcome by the $TiCl_4$-promoted Michael reaction of silyl enol ethers with α,β-unsaturated ketones,[2] and this reaction has been used for the preparation of the key intermediates in the syntheses of natural products.[3]

Concerning the stereochemistry of the carbon-carbon bond-forming process of this reaction, few investigations have been made.[4] Recently, Heathcock et al.[5] examined the stereochemistry of the Lewis acid ($TiCl_4$, $SnCl_4$ etc.) promoted Michael reaction, and Yamaguchi et al.[6] reported that Li enolates of simple esters stereoselectively added to α,β-unsaturated esters.

In the previous paper,[7] we have shown that trityl perchlorate is an efficient catalyst in the Michael reaction between silyl enol ethers and α,β-unsaturated ketones. This reaction has the advantages that the reaction proceeds smoothly by the catalytic use of trityl perchlorate as an activator and that the reaction products, both 1,5-dicarbonyl compounds and the intermediate adducts, the synthetically valuable silyl enol ethers, are easily isolated. In the course of our investigations to find further potential utility of this reaction, we have examined the stereochemistry in detail and found that it proceeds stereo-selectively under proper reaction conditions. In this communication, we wish to describe the trityl perchlorate catalyzed ul selective[8] Michael reaction.

In the first place, 2-cyclohexen-1-one was chosen as a model of a cyclic α,β-unsaturated ketone, and was treated with silyl enol ether of propiophenone. The reaction conditions such as the kind and the amount of trityl salts, solvents, reaction temperature, and reaction time were screened, and it was found that there was no effect of the kind of trityl salts on the stereochemistry though it is known that the counter anions of trityl salts greatly influence the stereo-

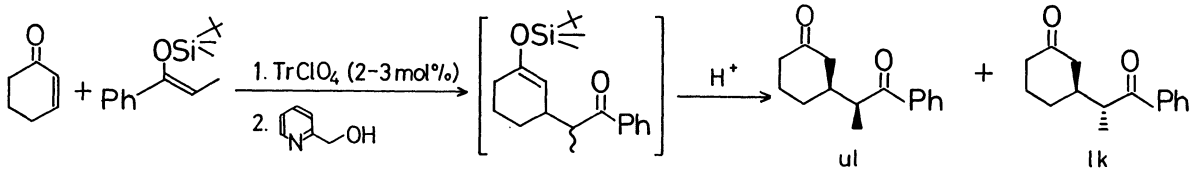


Table 1. The reaction of 2-cyclohexen-1-one with silyl enol ether of propiophenone

Entry	TrX	Solv.	Temp/°C	Time	yield/%	ul / lk[a)]
1	$TrClO_4$	CH_2Cl_2	-45	1 h	63	77 : 23
2	$TrPF_6$	CH_2Cl_2	-45	1 h	66	78 : 22
3	$TrSnCl_5$	CH_2Cl_2	-45	1 h	62	79 : 71
4	$TrClO_4$	CH_2Cl_2	-78	1 h	71	80 : 20
5	$TrClO_4$	CH_3CN	-45	3 h	61	84 : 16
6	$TrClO_4$	$CH_3CN:CH_2Cl_2$ (1.7:1)	-78	3 h	69	83 : 17
7	$TrClO_4$	CH_2Cl_2	-45	12 s	10	77 : 23
8	$TrClO_4$	CH_2Cl_2	-45	1 d	70	78 : 22

a) Determined by GC.

chemistry of the aldol reaction.[9)] The best result was obtained when the reaction was carried out at -78 °C in a mixture of acetonitrile and dichloromethane (1.7 : 1.0) in the presence of a catalytic amount of trityl perchlorate (Table 1).[10)] As the diastereomer ratio of the product is independent of the reaction time, the reaction proceeds probably under kinetic control.

Next, the reaction of 1-phenyl-2-buten-1-one, a model of an acyclic α,β-unsaturated ketone,with (E)-trimethylsilyl enol ether derived from 3-pentanone was investigated. It was carried out at -45 °C in dichloromethane to produce the corresponding Michael adduct in 51% yield and a ratio of ul(anti)/lk(syn) = 59:41.

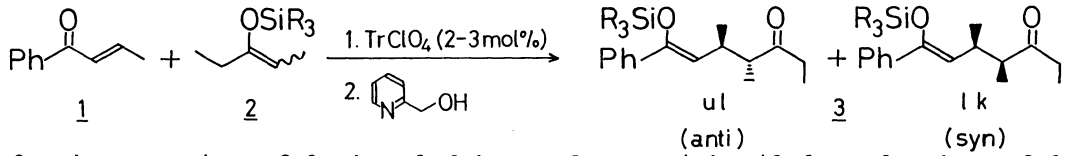


Table 2. The reaction of 1-phenyl-2-buten-1-one with silyl enol ether of 3-pentanone

Entry	R_3		Solv.	Temp/°C	Yield/%	ul(anti)/lk(syn)[a)]
1	Me_3	E	CH_2Cl_2	-45	51	59 : 41
2	$PhMe_2$	E	CH_2Cl_2	-45	44	70 : 30
3	Et_3	E	CH_2Cl_2	-45	70	71 : 29
4	$^tBuMe_2$	E	CH_2Cl_2	-45	81	77 : 23
5	$^tBuMe_2$	Z	CH_2Cl_2	-45	75	83 : 17
6	$^tBuMe_2$	Z	CH_2Cl_2	-78	84	85 : 15
7	$^tBuMe_2$	Z	$CH_3CN:CH_2Cl_2$ (1.7:1)	-78	47	84 : 16

a) Determined by ^1H NMR.

In order to improve the diastereomer ratio, several reaction parameters were further examined and found that the effect of the substituents on silicon of enolates plays a significant role on the diastereoselectivity (Table 2). The ul(anti) Michael adduct was preferentially obtained when (Z)-t-butyldimethylsilyl enol ether was employed (84%, ul(anti)/lk(syn) = 85:15).

Several examples of the reaction between α,β-unsaturated ketones and silyl enol ethers in Table 3 show that the ul Michael adducts are produced predominantly. Particularly in the case of using silyl enol ethers derived from aromatic ketones, ul adducts are obtained almost exclusively.

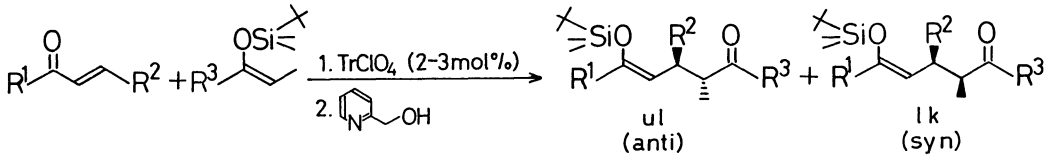
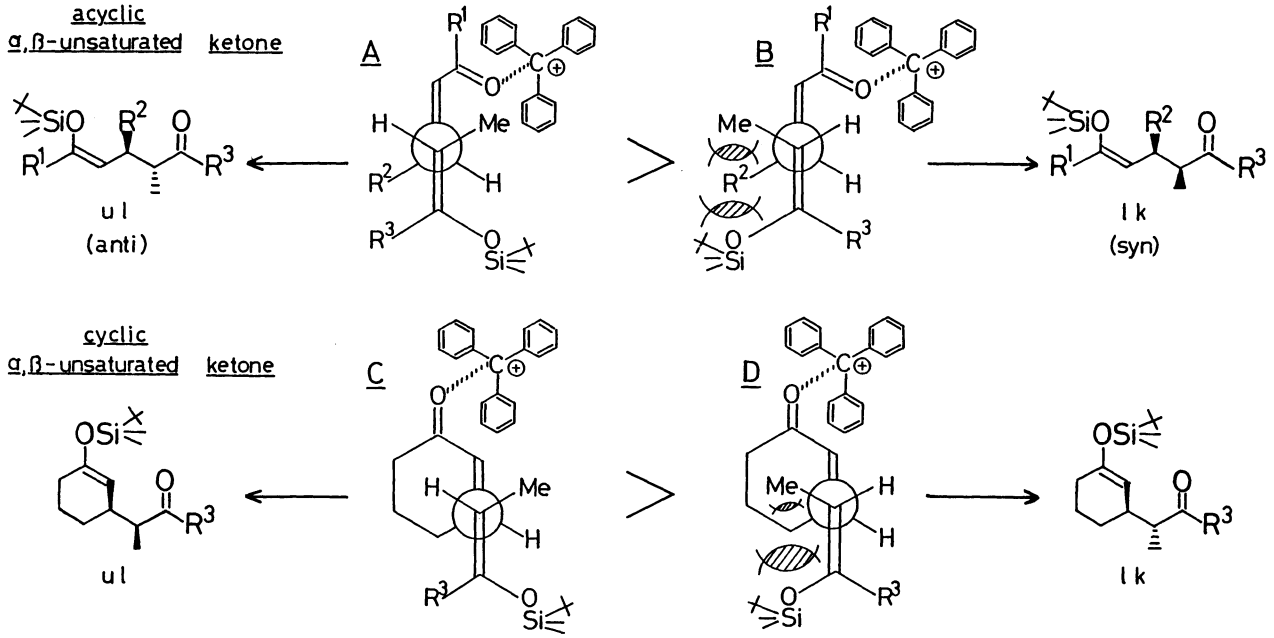


Table 3. The reaction of silyl enol ethers with α,β-unsaturated ketones

Entry	R_1	R_2	R_3	Solv.	Temp/°C	Yield/%	ul(anti)/lk(syn)
1	Me	Me	Et	$CH_3CN:CH_2Cl_2$ (1.7:1)	-78	54	84 : 16
2	Me	Me	Ph	CH_2Cl_2	-78	64	>95 : 5
3	Ph	Me	Et	CH_2Cl_2	-78	84	85 : 15
4	Ph	Me	Ph	CH_2Cl_2	-78	81	>95 : 5
5	Ph	Ph	Et	CH_2Cl_2	-78	81	74 : 26
6	Ph	Ph	Ph	CH_2Cl_2	-45	75	>95 : 5
7	Me	Ph	Et	CH_2Cl_2	-78	75	73 : 27
8	Me	Ph	Ph	CH_2Cl_2	-78	81	>95 : 5
9	$-(CH_2)_3-$		Et	CH_2Cl_2	-78	68	54 : 46
10	$-(Ch_2)_3-$		Ph	$CH_3CN:CH_2Cl_2$ (1.7:1)	-78	69	83 : 17

This ul selectivity is explained by assuming the open transition state as shown below (Fig. 1). Namely, sterically large trityl cation initially interacts with the α,β-unsaturated ketone, and the activated α,β-unsaturated ketones are attacked by the silyl enol ether with bulky siloxy group in such a way that the steric hindrance between trityl cation and t-butyldimethylsiloxy group can be minimized. Transition state A is favoured over transition state B in an acyclic α,β-unsaturated ketone, and transition state C is preferred to transition state D in a cyclic α,β-unsatureted ketone because of both the gauche interaction between R^2 and Me and the steric hindrance between R^2 and t-butyldimethylsiloxy group.

A typical reaction procedure is described for the reaction of (E)-1-phenyl-2-buten-1-one (1) with (Z)-t-butyldimethylsilyl enol ether of 3-pentanone (2, Z/E = 92/8); the mixture of 1 (0.5 mmol), 2 (0.55 mmol), and trityl perchlorate (2—3 mol%) in dichloromethane (3 ml) was stirred at -78 °C for 1 h. Pyridinemethanol[11] was added and the reaciton mixture was diluted with dry low to medium boiling petroleum ether. After filtlation, the solvent was removed under reduced pressure and the residue was separated by deactivated silica gel[12] column chromatography



to afford 7-t-butyldimethylsiloxy-4,5-dimethyl-7-phenyl-6-hepten-3-one (3) (84%, ul(anti)/lk(syn) = 85/15).

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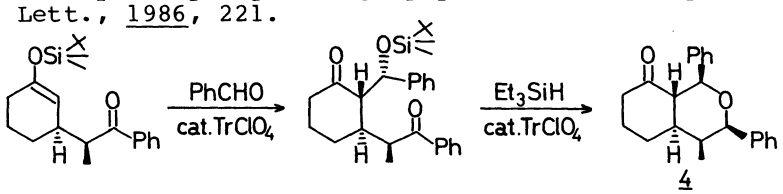
10) The configuration of the major diastereomer was assigned by transformation into the tetrahydropyrane derivative (4). The stereostructure of 4 was confirmed by X-ray crystallography. See, S. Kobayashi and T. Mukaiyama, Chem. Lett., 1986, 221.



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11) The intermediate silyl enol ethers are isolated more effectively by the use of pyridinemethanol than that of pyridine.
12) A mixture of silica gel (WAKO GEL C-200) and water (6:1).

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