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A Significant Substituent Effect on the Stereochemistry of the Trityl Salt-Catalyzed Michael Reaction†

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In the presence of a catalytic amount of trityl salts, silyl enol ethers of thioesters react with α-substituted α,β-unsaturated cyclic ketones to afford the corresponding Michael adducts in good yields with excellent 1k diastereoselectivities.

In the previous paper,[1] we have shown that, in the presence of a catalytic amount of trityl salts, silyl enol ethers of thioesters react with α,β-unsaturated ketones to produce the corresponding Michael adducts in high yields with excellent ul stereoselectivities. Herein we wish to describe a significant substituent effect on the stereochemistry of the Michael reaction between silyl enol ethers of thioesters and α-substituted α,β-unsaturated cyclic ketones promoted by a catalytic amount of trityl salts.

There are various kinds of fused ring systems containing an angular methyl group in sesquiterpenes, diterpenes, triterpenes, or steroids etc. Considering the effective synthesis of these compounds, the stereoselective Michael reaction of α-methyl α,β-unsaturated cyclic ketones with carbon nucleophiles is one of the most convenient synthetic methods for the construction of the necessary carbon skeleton. From this point of view, we studied on the stereoselective Michael reaction of 2-methyl-2-cyclopentenone with silyl enol ethers.

In the first place, the reaction of 2-methyl-2-cyclopentenone (1) with (Z)-1-dimethylphenylsiloxy-1-ethylthiopropene (2Z)[2] was carried out in the presence of a catalytic amount of trityl hexachloroantimonate.[3] The corresponding Michael adduct was obtained in 71% yield with disappointing low selectivity (ul/lk= 67/33).[4] However, 1k adduct was obtained with high diastereoselectivity (ul/lk=12/88) when (E)-1-dimethylphenylsiloxy-1-ethylthiopropene (2E), the geometrical isomer, was employed as an enolate component. This result encouraged us towards the stereoselective synthesis of 1k adducts. The several reaction parameters such as the effect of substituents of thioester and silicon, the geometry of enolates, and the kind of trityl salts were examined to improve the diastereoselectivity, and it was found that 1k adduct was exclusively obtained by the use of the silyl enol ether of t-butyl thioester. In this reaction, the t-butyl

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†This paper is dedicated to the late Professor Ryozo Goto, Kyoto University.

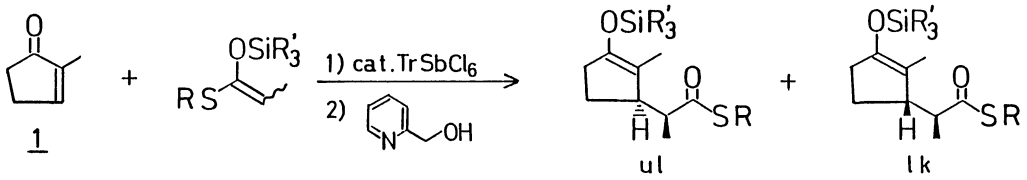
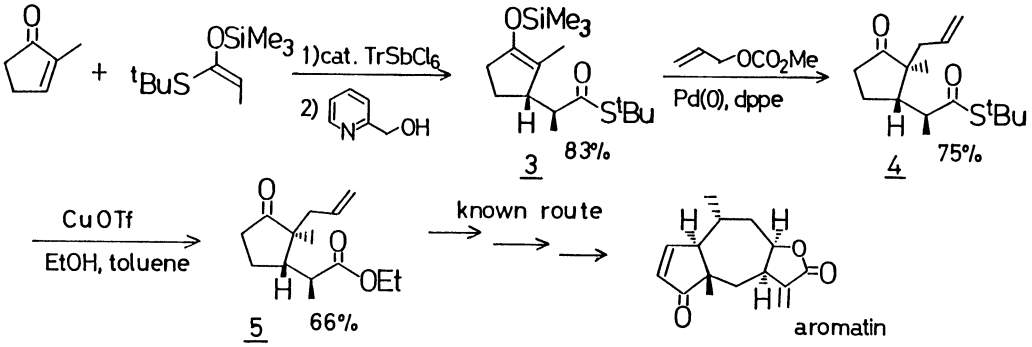


Table 1. The Michael reaction of 2-methyl-2-cyclopentenone with silyl enol ethers of thioesters

Entry	R	R'_3	Yield/%	ul:lk
1	Et	$PhMe_2$ (Z)	71	67:33
2	Et	$PhMe_2$ (E)	80	12:88
3	Et	$^tBuMe_2$ (E)	77	17:83
4	Ph	$^tBuMe_2$ (Z)	83	16:84
5	^{t}Bu	$PhMe_2$ (E)	58	<5:>95
6	^{t}Bu	$^tBuMe_2$ (E)	73	<5:>95
7	^{t}Bu	Me_3 (E)	83	<5:>95
8	^{t}Bu	$^tBuMe_2$ (Z)	57	5:95

thioester group is essential and both the substituent on silicon and the geometry of enolates have little effect on the diastereoselectivity (Table 1).

The stereochemistry of the major diastereomer was determined by the derivation to the aromatin intermediate. Treatment of the Michael adduct (3) with allyl methyl carbonate in the presence of a catalytic amount of Pd(dppe)(bis(diphenylphosphino)ethane)[5] afforded the allylated ketone (4) in 75% yield. Transesterification of 4 was carried out by the use of a large excess of copper(I) trifluoromethanesulfonate (benzene complex) and ethanol in refluxing toluene[6] to give the corresponding ethyl ester (5) in 66% yield. The 270 MHz ^{1}H NMR spectral data of 5 were in complete agreement with those of the literature.[7]



This excellent lk selection exemplified by the present trial prompted us to confirm the generality of this reaction to provide a versatile synthetic tool for constructing desired fundamental carbon skeletons as well as the clarification of the transition state.

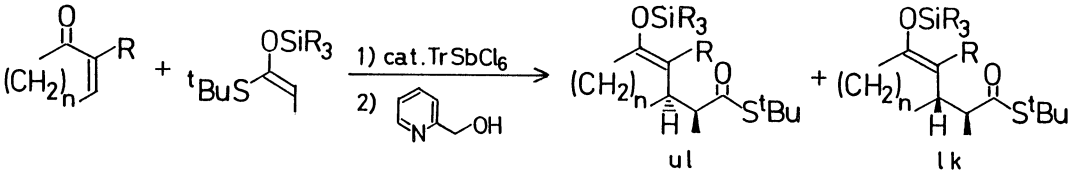
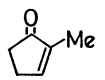
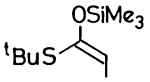
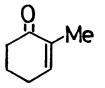
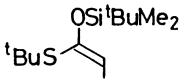
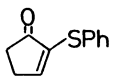
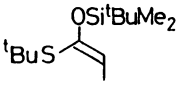
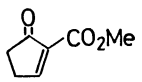
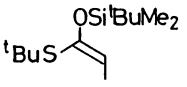


Table 2. The reaction of α-substituted α,β-unsaturated cyclic ketones with silyl enol ethers of thioesters

Entry	α,β-Unsaturated ketone	Silyl enol ether	Yield/%	ul/lk
1			83	< 5:>95 a)
2			78	< 5:>95 a)
3			85	< 5:>95 a)
4			73	10:90 b)

a) Determined by GC and ^{13}C NMR.

b) Separated by TLC.

Several α-substituted α,β-unsaturated cyclic ketones were examined as shown in Table 2. In every case, the lk Michael adducts are obtained in good yields with excellent diastereoselectivities.

It was assumed that this high lk selectivity was mainly ascribed to the α-substituents of α,β-unsaturated ketones involved in the open chain transition state as shown in Fig. 1. Transition state A would be favorable over B because of the gauche interaction between R and the methyl group.

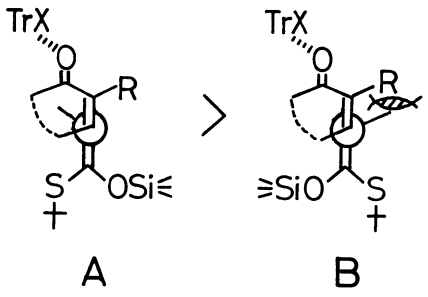
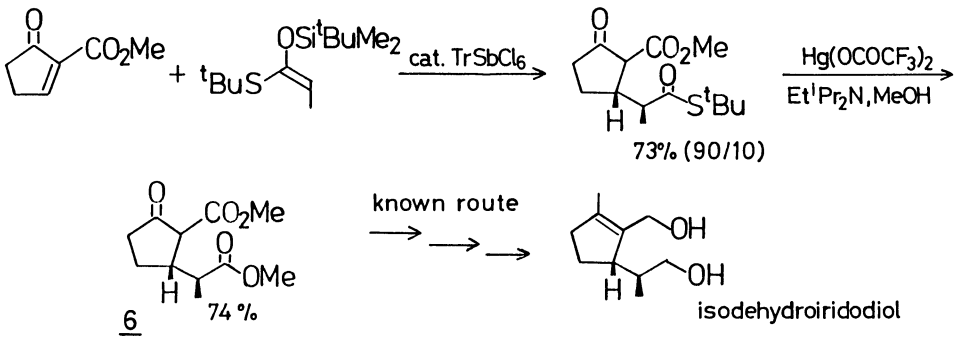
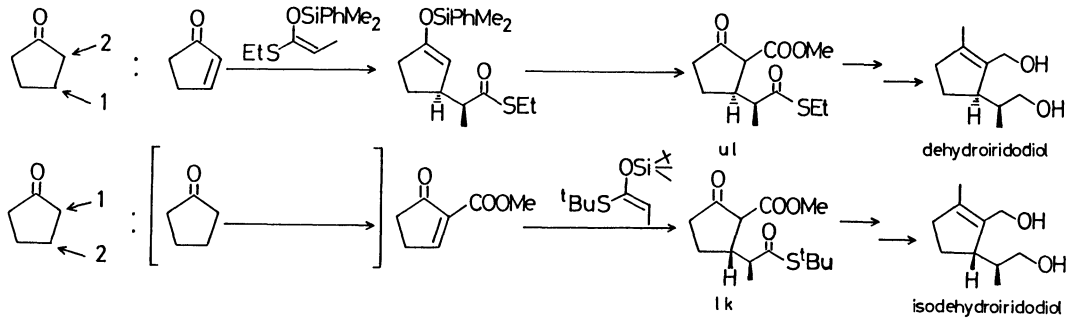


Fig. 1.

The synthetic utility of the present reaction is obvious from the stereoselective formal synthesis of isodehydroiridodiol intermediate[8] according to the following equation, i.e. the synthetic intermediate 6 was prepared by the two-step procedure starting from methyl 5-oxo-1-cyclopentenecarboxylate.[10]



We have already shown the stereoselective synthesis of dehydroiridodiol, the stereoisomer of isodehydroiridodiol, by the use of the trityl salt-catalyzed Michael reaction of 2-cyclopentenone with (Z)-1-dimethylphenylsiloxy-1-ethylthiopropene as a key step.[1] Of these two approaches, the first example for the synthesis of dehydroiridodiol is performed by the ul-selective Michael reaction followed by introducing α-side chain, while the second isodehydroiridodiol synthesis is achieved by the opposite lk-selective Michael reaction caused by the pre-introduced α-side chain of the α,β-unsaturated ketone. Namely, in these syntheses of two isomeric natural products, the stereochemistry is controlled by changing the order of introducing the side chains. This new possibility of stereocontrolled syntheses is now under investigation to apply to the syntheses of other natural products.



References

1) T. Mukaiyama, M. Tamura, and S. Kobayashi, Chem. Lett., 1986, 1817.
2) In this paper, the stereochemical descriptors E and Z of silyl enol ethers of thioesters are employed as they correspond to ketene silyl acetals.
3) Commercially available from Aldrich Chemical Company.
4) For definition of the ul/lk convention, see D. Seebach and V. Prelog, Angew. Chem., Int. Ed. Engl., 21, 654 (1982).
5) J. Tsuji, I. Minami, and I. Shimizu, Chem. Lett., 1983, 1325.
6) S. Masamune, Y. Hayase, W. Schilling, W. K. Chan, and G. S. Bates, J. Am. Chem. Soc., 99, 6756 (1977).
7) J-M. Fang, J. Org. Chem., 47, 3464 (1982).
8) M. Yamaguchi, K. Hasebe, S. Tanaka, and T. Minami, Tetrahedron Lett., 27, 959 (1986).
9) S. Masamune, S. Kamata, and W. Schilling, J. Am. Chem. Soc., 97, 3515 (1975).
10) J. N. Marx and G. Minaskanian, Tetrahedron Lett., 1979, 4175.

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