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Trityl Salt Catalyzed Aldol Reaction between α,β-Acetylenic Ketones and Silyl Enol Ethers

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In the presence of a catalytic amount of trityl salt, α,β-acetylenic ketones react with silyl enol ethers to afford the corresponding aldol adducts (1,2-addition products) stereoselectively in high yields. Naturally occurring monoterpenes, trans- and cis-tagetones, are synthesized by the use of this reaction.

α,β-Acetylenic ketones are readily available compounds and their conjugated systems are of great interest in connection with the competitive reactions of 1,2- vs. 1,4-addition. Concerning carbon-carbon bond forming reactions of these ketones, it was already reported that dialkylcopper lithiums react with α,β-acetylenic carbonyl compounds to produce the corresponding 1,4-addition products regioselectively.[1)] However, there have been few reports on the reaction of α,β-acetylenic ketones with other carbon nucleophiles, especially synthetically valuable enolate components.

In the previous papers, we have shown that, in the presence of a catalytic amount of trityl salts, α,β-unsaturated ketones (α,β-olefinic ketones) react with silyl enol ethers to afford the corresponding Michael adducts (1,4-addition products) stereoselectively in high yields.[2)] In the course of our investigations to develop new synthetic methodologies utilizing trityl salts as catalysts, we have focused on the reaction of α,β-acetylenic ketones and found that the treatment of α,β-acetylenic ketones with silyl enol ethers in the presence of a catalytic amount of trityl salt affords the corresponding aldol adducts (1,2-addition products) exclusively. In this communication, we would like to describe regio- and stereoselective aldol reaction (1,2-addition reaction) of α,β-acetylenic ketones with silyl enol ethers promoted by a catalytic amount of trityl salt and its application to the synthesis of naturally occurring monoterpenes, cis- and trans-tagetones.

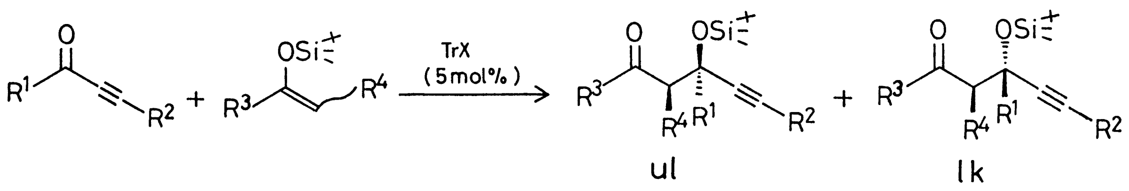
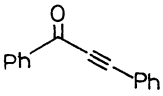
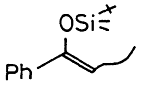
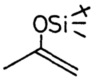
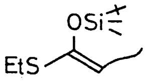
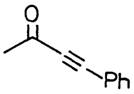
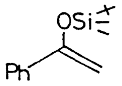
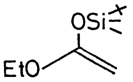
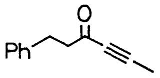
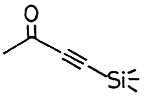


Table 1. The reaction of α,β-acetylenic ketones with silyl enol ethers[a)]

Entry	α,β-Acetylenic ketone	Silyl enol ether	TrX	Yield/%	ul/lk[b)]
1	 (1)	 (5)	$TrClO_4$	90	99/ 1
2	1	 (6)	$TrCl-SnCl_2$	71	——
3	1	 (7)	$TrClO_4$	85	87/13
4	 (2)	5	$TrClO_4$	69	95/ 5
5	2	 (8)	$TrClO_4$ $TrSbCl_6$ $TrCl-SnCl_2$	69 85 71	—— —— ——
6	2	6	$TrClO_4$	75	——
7	2	7	$TrClO_4$	97	83/17
8	2		$TrClO_4$	74	——
9	 (3)	5	$TrClO_4$	69	>99/ 1
10	3	6	$TrClO_4$	89	——
11	3	8	$TrClO_4$	quant.	——
12	 (4)	5	$TrClO_4$	85	>99/ 1
13	4	8	$TrClO_4$	97	——

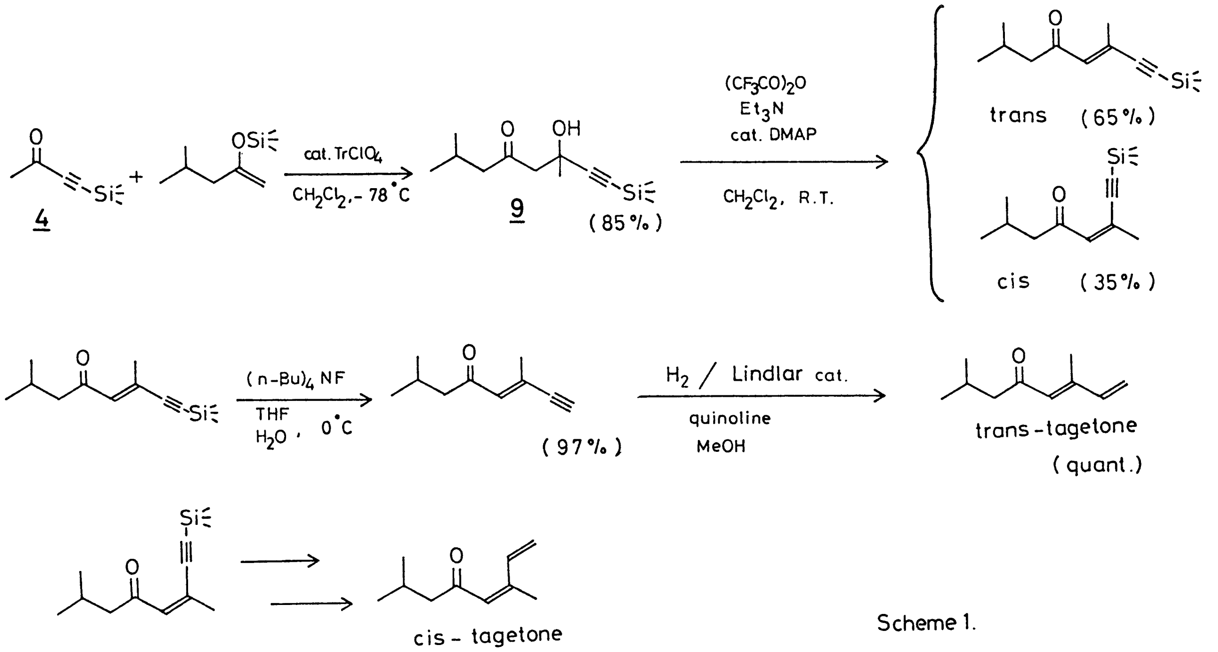
a) All the products gave satisfactory NMR and IR spectral data.

b) Diastereomer ratios were determined by HPLC and/or ^{13}C NMR.

In the first place, phenylpropargyl acetophenone(1) was chosen as a model, and the reaction of 1 with t-butyldimethylsilyl enol ether of propiophenone was tried in the presence of a catalytic amount of trityl perchlorate (5 mol%) in dichloromethane. The reaction smoothly proceeded at -78 °C and the corresponding aldol adduct (1,2-addition product) was obtained in 90% yield$^{3)}$ with excellent diastereoselectivity (ul/lk = 99/ 1).$^{4,5)}$ No Michael adduct (1,4-addition product) was observed in this reaction.

Next, to confirm the generality of this aldol reaction, several reactions of α,β-acetylenic ketones with silyl enol ethers were examined (Table 1). In every case, the reactions were completed at -78°C and only aldol adducts (1,2-addition products) were obtained in high yields with excellent diastereoselectivities. As the kinds of trityl salts (such as TrOTf, $TrSbCl_6$, $TrSnCl_5$, etc.$^{6)}$) had little effect on the yields and diastereoselectivities of the products, trityl perchlorate was employed as a representative. A new catalyst system, combined use of catalytic amounts of trityl chloride and tin(II) chloride,$^{7)}$ also effective in this reaction.

A typical procedure for the reaction of an α,β-acetylenic ketone with a silyl enol ether is as follows: A mixture of an α,β-acetylenic ketone (0.4 mmol), a silyl enol ether (0.44 mmol), and trityl perchlorate (5 mol%) in dichloromethane (3 ml) was stirred at -78 °C for an appropriate time (5-6 h). After the reaction was completed (checked by TLC), aqueous sodium hydrogen carbonate was added. The aqueous layer was extracted with dichloromethane, and the combined organic layers were dried. Then the solvent was removed under reduced pressure and the residue was chromatographed on silica gel.



Scheme 1.

The synthetic utility of this reaction is demonstrated in the facile synthesis of the naturally occurring monoterpenes, cis- and trans-tagetone[8)] as shown below (Scheme 1). In the presence of a catalytic amount of trityl perchlorate, 4-trimethylsilyl-3-butyn-2-one(4) reacted with silyl enol ether derived from isobutyl methyl ketone to afford the corresponding aldol adduct(9) in 80% yield (after hydrolysis). Dehydration of 9 was performed by the use of anhydrous trifluoroacetic acid and triethylamine in the presence of a catalytic amount of 4-(dimethylamino)pyridine,[9)] to produce cis- and trans-conjugated enynes (quant, cis/trans = 35/65). Desilylation (^{n}Bu$_4$NF/THF-H$_2$O) followed by hydrogenation (Lindlar catalyst) gave the corresponding naturally occurring cis- and trans-tagetones.

Thus, it was shown that the reaction of α,β-acetylenic ketones with silyl enol ethers, in the presence of a catalytic amount of trityl salt, proceeds regioselectively to afford the corresponding aldol adducts (1,2-addition products) in high yields with high stereoselectivities. It should be noted that this reaction is a useful tool for building a new carbon-carbon bond without losing synthetically versatile acetylene group.

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References

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5) The relative configuration of the major diastereomer was determined by X-ray crystallography.
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