

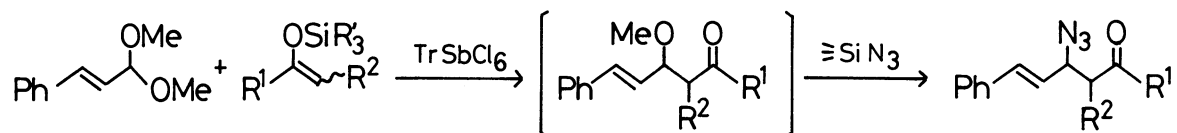
Facile Synthesis of γ,δ -Unsaturated β -Azido Carbonyl Compounds
via Successive Nucleophilic Additions on Cinnamaldehyde Dimethyl Acetal
Catalyzed by Trityl Hexachloroantimonate

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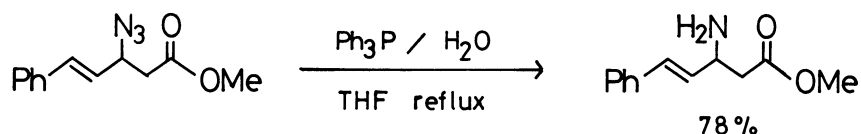
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In the presence of a catalytic amount of trityl hexachloroantimonate, cinnamaldehyde dimethyl acetal successively reacts with silyl enol ethers or ketene silyl acetals and azido-trimethylsilane, to afford the corresponding γ,δ -unsaturated β -azido carbonyl compounds in good yields.

In the previous papers, we have demonstrated that trityl salts such as TrClO_4 , TrOTf , TrSbCl_6 , etc., are quite efficient catalysts for the reaction of acetals with silyl enol ethers¹⁾ and for the reaction of secondary and tertiary allyl methyl ethers with various silyl nucleophiles.²⁾ As silyl enol ethers or ketene silyl acetals regioselectively react with α,β -unsaturated dimethyl acetals in the presence of a trityl salt to give functionalized allyl methyl ethers,³⁾ we could take an advantage of these intermediate methyl ethers to substitute the methoxy group with second silyl nucleophiles. In this communication, we wish to describe the formation of γ,δ -unsaturated β -azido carbonyl compounds by one-pot reaction of cinnamaldehyde dimethyl acetal (as a model of aromatic α,β -unsaturated acetals) with two different silyl nucleophiles successively, at first a silyl enol ether or a ketene silyl acetal and then azidotrimethylsilane as shown below.



In each case, the intermediate allyl methyl ethers react with azido-trimethylsilane in a clean α -regioselective manner leading to γ,δ -unsaturated β -azido carbonyl compounds in good yields (Table 1). Furthermore the azido function is selectively reduced to the corresponding amine according to the Staudinger reaction.⁴⁾



A typical procedure is the following: after stirring a solution of trityl hexachloroantimonate⁵⁾ (0.02 mmol), cinnamaldehyde dimethyl acetal (0.5 mmol) and

Table 1. Synthesis of γ,δ -unsaturated β -azido carbonyl compounds

Entry	R ¹	R ²	R' ₃	Yield/%	(diastereomer ratio)
1	Ph	H	Me ₃	85	——
2	OMe	H	^t BuMe ₂	67	——
3	OSiMe ₃	Me	Me ₃	70 a)	(1 : 1) ^{b)}
4	OSiMe ₃	Me	^t BuMe ₂	76 a)	(1 : 1) ^{b)}
5	S ^t Bu	H	Me ₃	81	——
6	SEt	Me	^t BuMe ₂	73	(60:40) ^{c)}
7	S ^t Bu	Me	Me ₃	78	(64:36) ^{c)}
8	S ^t Bu	Me	^t BuMe ₂	72	(61:39) ^{c)}

a) The product is a carboxylic acid. Some impurities still remained after purification. b) Determined by ¹H NMR. c) Determined by HPLC.

a silyl nucleophile (0,5 mmol) in dichloromethane (3.5 ml) for 1 h at -78 °C, azidotrimethylsilane (1.25 mmol) in dichloromethane (1 ml) was added and the mixture was warmed up to -23 °C. Then, a solution of trityl hexachloroantimonate (0.02 mmol) in dichloromethane (0.5 ml) was added dropwise. After 2 h at -23 °C, aqueous sodium hydrogen carbonate was added and the aqueous layer was extracted with dichloromethane. The organic layer was dried and the solvent was removed in vacuo. The residue was chromatographed on silica gel to yield the desired compounds.

Although the present method is limited to aromatic α,β -unsaturated acetals (aliphatic ones give different results concerning regioselectivity), the resulting compounds may be valuable intermediates in the synthesis of β -lactams in the carbapenem series⁶⁾ based on the known method of facile cyclization of β -amino esters in the presence of bases.⁷⁾ Further studies with such respect are now in progress.

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