Silver or Copper Triflate-Catalyzed Amination of Silyl Enol Ethers

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Amination of silyl enol ethers with azo diester compounds proceeded smoothly in the presence of a catalytic amount of AgOTf or Cu(OTf)$_2$. Various types of silyl enol ethers reacted smoothly under these conditions and AgOTf gave better yields than Cu(OTf)$_2$ in most cases.

Amination at the α-positions of carbonyls provides one of the most efficient methods for synthesis of α-amino acids and their derivatives.[1] While several electrophilic aminations have been reported,[1] the reactions of silyl enol ethers with azo diesters are promising because the starting materials are stable and readily available and hydrazine groups produced are easily converted to amino groups by reductive N-N bond cleavage (Figure 1).[2,3] In previous reports, however, thermal conditions[4] or stoichiometric amounts of Lewis acids[2a,d-f] were required for the reactions of silyl enol ethers with azo diesters, and no general and catalytic protocols have been developed to the best of our knowledge. Here we report amination reactions of silyl enol ethers with azo diesters using silver or copper triflate (AgOTf, Cu(OTf)$_2$) as a catalyst.

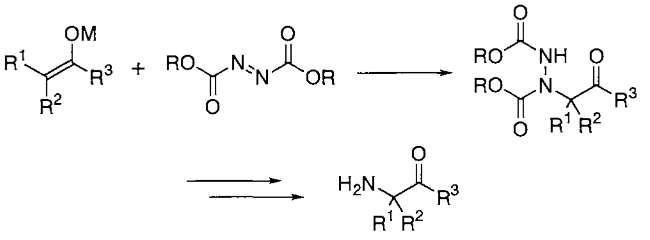


Figure 1. Amination of Enolates.

First, we examined the reaction of the silyl enol ether derived from *S*-ethyl propanethioate with dibenzyl azodicarboxylate (DBnAD) using a catalytic amount of a metal triflate (Table 1).[5] When Zn(OTf)$_2$, Fe(OTf)$_3$, Yb(OTf)$_3$, Zr(OTf)$_4$, or Hf(OTf)$_4$ was used, little rate enhancement was observed. On the other hand, while the reaction proceeded moderately in the presence of Sn(OTf)$_2$ or Sc(OTf)$_3$, the desired products were obtained in high yields when AgOTf or Cu(OTf)$_2$ was employed as the catalyst.

We then investigated the catalytic activities of AgOTf and Cu(OTf)$_2$ in the reactions of several silyl enol ethers with DBnAD (Table 2). When the amount of AgOTf or Cu(OTf)$_2$ was decreased in the reaction with the trimethylsilyl enol ether derived from *S*-ethyl propanethioate, the catalytic activity was maintained and the adduct was obtained in a high yield even when 1 mol% of AgOTf was used. In the reaction of the ketene silyl acetal derived from methyl isobutyrate, AgOTf gave a better yield of the desired adduct.[6] Moreover, the *tert*-butyldimethylsilyl group also worked well as a silyl moiety instead of the trimethylsilyl group. When more unreactive silyl enol ethers derived from ketones were examined, it was found that the reactions also proceeded smoothly in the presence of a catalytic amount of AgOTf or Cu(OTf)$_2$. Also in these cases, AgOTf showed higher activity than Cu(OTf)$_2$. For azo diester compounds, other azodicarboxylates reacted efficiently under these conditions; diethyl azodicarboxylate reacted with the silyl enol ether derived from propiophenone in the presence of 10 mol% AgOTf at 0 °C for 30 min to afford the desired amination adduct in 81% yield.

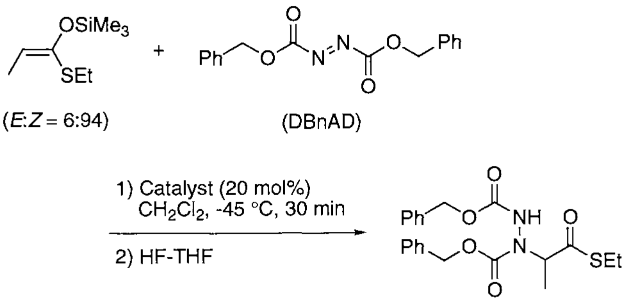


Table 1. Effect of Catalysts

Entry	Catalyst	Yield/%
1	—	12
2	Zn(OTf)$_2$	13
3	Zr(OTf)$_4$	16
4	Hf(OTf)$_4$	14
5	Yb(OTf)$_3$	14
6	Fe(OTf)$_3$	29
7	Sc(OTf)$_3$	40
8	Sn(OTf)$_2$	58
9	Cu(OTf)$_2$	89
10	AgOTf	92

A typical experimental procedure is as follows: To a stirred suspension of AgOTf (0.040 mmol) in CH$_2$Cl$_2$ (1.0 mL) was added DBnAD (0.44 mmol) in CH$_2$Cl$_2$ (0.5 mL) at the temperature shown in Table 2. After stirring for 10 min, a silyl enol ether (0.40 mmol) in CH$_2$Cl$_2$ (0.5 mL) was added dropwise, and the mixture was stirred at the same temperature. A 20% HFaq.-THF (1:1) solution was then added and the mixture was stirred for 1 h at room temperature. After being basicified with saturated aq. NaHCO$_3$, the aqueous layer was extracted with CH$_2$Cl$_2$. The organic layers were combined and dried over anhyd. Na$_2$SO$_4$. After filtration and concentration, the residue was purified by preparative thin layer chromatography on silica gel to afford the desired amination adduct.

In summary, amination reactions of silyl enol ethers with azo

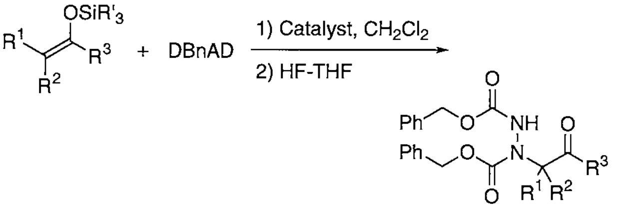
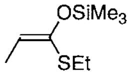
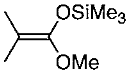
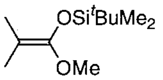
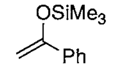
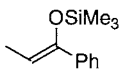
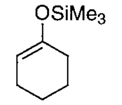


Table 2. Amination of Silyl Enol Ethers

Substrate	Catalyst/mol%	Conditions	Yield/%
 (*E*:*Z* = 6:94)	$Cu(OTf)_2$ (10)	-45 °C, 30 min	90
	$Cu(OTf)_2$ (5)	-45 °C, 30 min	86
	AgOTf (5)	-45 °C, 30 min	90
	AgOTf (1)	-45 °C, 30 min	91
	$Cu(OTf)_2$ (10)	-45 °C, 30 min	48
	AgOTf (10)	-45 °C, 30 min	97
	AgOTf (10)	0 °C, 30 min	95
	$Cu(OTf)_2$ (10)	0 °C, 2.5 h	70
	AgOTf (10)	0 °C, 30 min	91
	$Cu(OTf)_2$ (10)	0 °C, 2.5 h	39
	AgOTf (10)	0 °C, 30 min	84
	$Cu(OTf)_2$ (10)	0 °C, 2.5 h	39
	AgOTf (10)	0 °C, 30 min	91

diester compounds proceeded smoothly in the presence of a catalytic amount of AgOTf or $Cu(OTf)_2$. Various kinds of silyl enol ethers including those derived from esters, thioesters, and ketones worked well and AgOTf gave better results than $Cu(OTf)_2$. It is noted that all the examined reactions proceeded clearly using a small amount of the catalyst, and that the procedures are very simple. Further studies to develop asymmetric aminations with azo diester compounds using a chiral catalyst are in progress.

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References and Notes

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6 Side reactions predominated when the amination was performed without the catalyst.