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LANTHANOID TRIFLATES CATALYZED REACTION OF A SILYL YNOLATE WITH ALDIMINES[†]

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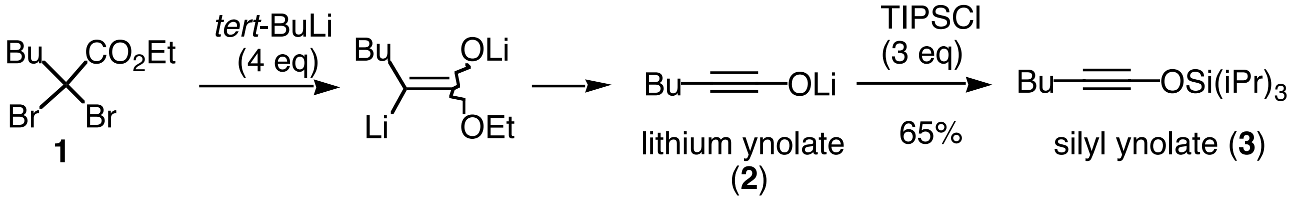
Abstract – A silyl ynolate, prepared from α,α-dibromo ester in one-pot, reacts with *N*-(*p*-methoxyphenyl)aldimines in the presence of a catalytic amount of lanthanoid triflates to provide α,β-unsaturated amides with high *E* selectivity.

Recently, we have developed a new and convenient method for the generation of lithium ynolates *via* the cleavage of ester dianions prepared from readily available α-bromo[1] or α,α-dibromo esters (Scheme 1).[2] The unique characteristics of ynolates[3] have been demonstrated in our reports on the reactions with carbonyl compounds.[4] Previously, we also reported that lithium ynolates react with *N*-sulfonyl aldimines to afford β-lactams.[5] However, *N*-benzyl- or *N*-(*p*-methoxyphenyl)aldimines (*N*-PMP aldimines) were not effective even in the presence of strong Lewis acids. These non-activated imines would be more advantageous than *N*-sulfonylimines, because of the facile preparation and removal of *N*-substituents. Compared to lithium ynolates, silyl ynolates (silyl ynol ether) are thought to be effective for the reaction of imines activated by Lewis acids. Kowalski reported the reaction of silyl ynolates with aldehydes in the presence of a stoichiometric amount of $TiCl_4$;[6] however, there have been no reports on this type of reaction with imines.[7] Herein, we describe the first example of the reaction of a silyl ynolate with *N*-PMP aldimines in the presence of a catalytic amount of lanthanoid triflates.



Scheme 1

A triisopropylsilyl ynolate (silyl ynol ether, **3**) was easily synthesized by the reaction of triisopropylsilyl chloride[8] with lithium ynolate (**2**) generated from a dibromo ester in one-pot (Scheme 1). At first, we attempted the reaction of aldimine (**4**, R: Ph) in the presence of $TiCl_4$ (0.2 eq), but the reaction did not proceed. In recent years, lanthanoid trifluoromethansulfonates (triflates) have been found to be effective for the activation of imines without decomposition of silyl enolates and imines.[9] Thus, we tried the reactions using these catalysts. A typical experimental procedure is exemplified by the following: to a slight suspension of the imine (**4**, 0.5 mmol) and a Lewis acid (0.19 mmol) in acetonitrile was added a solution of TIPS ynolate (**3**, 0.75 mmol) in acetonitrile at 0 ℃. After being stirred for 3 h, the reaction mixture was allowed to warm to room temperature for 18 h. After quenching with saturated aqueous $NaHCO_3$ solution, the usual workup gave a crude mixture, which was purified by column chromatography on SiO_2.

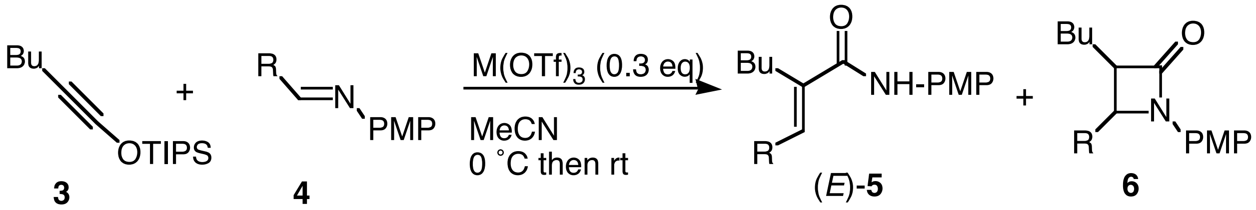


Table. The $M(OTf)_3$ catalyzed reactions of silyl ynolates with *N*-PMPimines

Entry	R	$M(OTf)_3$	Amide (**5**)(%)	*E*/*Z*[a)]	β-Lactam (**6**)(%)[b]
1	Ph	Sc	35	100/0	4
2	Ph	Y[c]	52	100/0	0
3	Ph	La	22	100/0	9
4	Ph	Pr	43	100/0	22
5	Ph	Nd	38	100/0	13
6	Ph	Sm	32	100/0	0
7	Ph	Eu	45	100/0	0
8	Ph	Gd	62	100/0	7
9	Ph	Gd[c]	57	100/0	7
10	Ph	Tb	46	100/0	15
11	Ph	Dy	61	100/0	4
12	Ph	Ho	56	100/0	6
13	Ph	Er	54	100/0	7
14	Ph	Tm	36	100/0	16
15[d]	Ph	Yb	38	100/0	0
16	Ph	Lu	56	100/0	0
17	(E)-PhCH=CH-	Gd	56	86/14	0
18	α-naphthyl	Gd	62	75/25	0
19	β-naphthyl	Gd	58	75/25	0

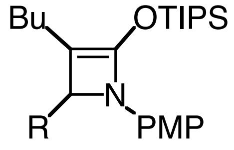
a) The E/Z ratios of **5** were determined by ^{1}H-NMR. The stereochemistry was determined by NOE experiments. b) Only a *cis*-isomer was isolated. c) In the presence of H_2O (3 eq for $M(OTf)_3$). d) In EtCN.

As shown in the Table, using various metal triflate catalysts we obtained α,β-unsaturated amide (**5**) as a major product with excellent (*E*)-selectivity in good to moderate yields along with a small amount of β-lactam (**6**). To our knowledge, this is the first example of the reaction of a non-activated aldimine[10] with an ynolate. The best yield of **5** was obtained when $Gd(OTf)_3$ was used. As Kobayashi[11] proposed that in the presence of water, lanthanoid triflates are transformed into a more active metal cation species, $Ln(H_2O)_n^{3+}$, water (3 eq for the catalyst) was added to the reaction mixture with $Gd(OTf)_3$. The rate of the reaction seemed to be faster, although the yield of **5** was somewhat lower (Table, Entry 9).

Using three kinds of *N*-PMP aldimines, the $Gd(OTf)_3$-catalyzed reactions were examined (Table, Entries17~19). The α,β-unsaturated amides were obtained as a mixture of *E* and *Z* isomers with preferential formation of *E*. Interestingly, β-lactams were not observed at all.

The mechanism of the reactions would be concerted or stepwise [2+2] cycloaddition followed by electrocyclic thermal ring-opening of the azetine intermediates (**7**).[4,6,7] The generation of β-lactams (**6**) as side products indicates the intervention of **7**.[12] Additional investigation is required to clarify the mechanism, including the stereochemical outcome.

In conclusion, we have succeeded in the lanthanoid triflates catalyzed reaction of *N*-PMP imines with a silyl ynolate for the first time. The results described herein also demonstrate the synthetic utility of ynolates.



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REFERENCES AND NOTES

†Dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

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