Pergamon

Tetrahedron Letters, Vol. 37, No. 17, pp. 3005-3008, 1996

0040-4039/96 $15.00 + 0.00

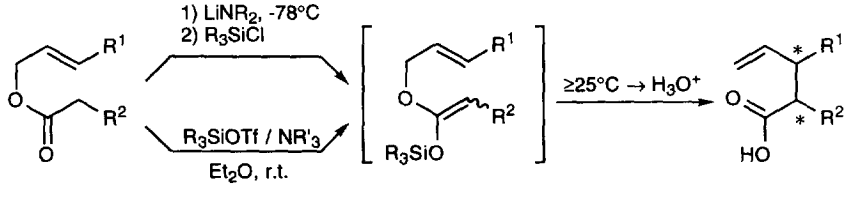
S0040-4039(96)00485-6

Stereochemical Control in the Silyl Triflate-Mediated Claisen Rearrangement of Allylic Esters

Masatada Kobayashi, Katsuhisa Masumoto,[1] Ei-ichi Nakai, and Takeshi Nakai*
Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan

Abstract: *The titled Claisen modification is shown to proceed with a remarkably high level of diastereoselection and asymmetric transmission by virtue of the proper choice of the combination of the silyl triflate and the tertiary amine used.*

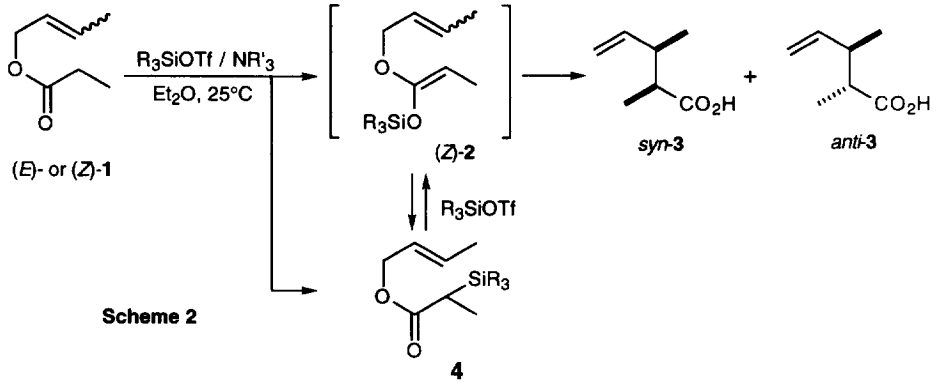
The ester enolate Claisen rearrangement, *i.e.*, the Ireland-Claisen rearrangement, enjoys widespread application in organic synthesis.[2,3] The key feature of the Claisen variant is its ability to control the relative stereochemistry of the two newly created chiral centers through the highly (*E*)- or (*Z*)-selective formation of the enolate by the choice of the solvent (Scheme 1). In practice, however, the Ireland procedure requires the use of a strong base such as lithium amides, the rather tedious low temperature technique (-78 °C), and severely anhydrous conditions. Thus, a more convenient alternative variant had been highly desired which is applicable to *base-sensitive* substrates and can be conducted around ambient temperature with an equally high level of stereocontrol. Recently our group[4] and others[5] have reported that the Claisen rearrangement of some allylic esters can be effected by trimethylsilyl triflate in the presence of triethylamine at room temperature, while the inherent complexity arises in terms of the *O- vs. C*-silylation of esters[6] (Scheme 1). Despite its great potential, however, no systematic study has been made on the stereochemical aspect of the new Claisen variant. We now wish to report that the silyl triflate-mediated Claisen rearrangement, *when conducted by the proper combination of the silyl triflate and the tertiary amine used*, provides a remarkably high degree of diastereoselection and asymmetric transmission.



Scheme 1

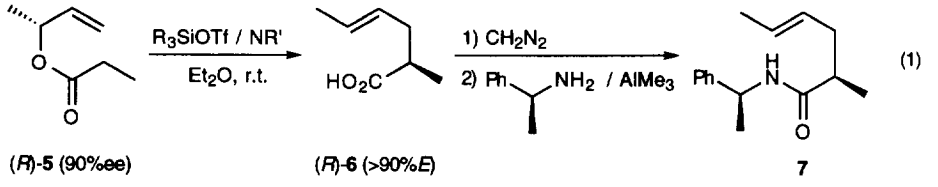
At the outset, we examined the distereoseletivity of the Claisen rearrangement of (*E*)- and (*Z*)-crotyl propanoate (**1**) using various combinations of silyl triflates and tertiary amines (Scheme 2). The results given in Table 1 reveal that the present Claisen variant exhibits the *E*-to-*syn* and *Z*-to-*anti* diastereoselection, the degree depending markedly upon the natures of the silyl triflate and the amine used. Significant enough, the use of the combination of a bulky silyl triflate and a bulky amine provides the highest degrees of diastereoselection which are significantly higher than those reported for the Ireland variant[2] (entries 5 and 7). The observed sense of diastereoselection indicates that the enolsilylation leads selectively to the (*Z*)-ketene

silyl acetal **2**[7] which then rearranges via the usual chair-like transition state. Interestingly, monitoring of the reaction by NMR showed that at an early stage the *C*-silylated ester **4** was predominantly formed as expeted,[6] and then **4** gradually decreased, while the Claisen product **3** was built up, suggesting that the reaction involves as a bypath the (*Z*)-selective conversion[7] of **4** into **2** promoted by the silyl triflate. In fact, similar treatment of (*E*)-**4** once isolated with *10 mol% of TMSOTf in the absence of any amine* afforded the Claisen product **3** in comparable yield and essentially the same diastereomeric ratio.[8]



Scheme 2

Moreover, the present Claisen variants of (α-alkyl)allyl esters such as 1-buten-3-yl and 1-octen-3-yl propanoates, even when the combination of Me_3SiOTf and NEt_3 was used, exhibited an extremely high (*E*)-selectivity (>99%) over the newly formed olefinic bond. Most significantly, we also found that the *asymmetric* version of the enantio-enriched substrate (*R*)-**5**, when conducted by using the combination of the bulky silyl triflate and the bulky amine, proceeded with a remarkably high degree of asymmetric transmission to give (*E*, *R*)-**6** (eq 1).[9] The highest %transmission thus observed is significantly higher than that (90%) reported for the Ireland variant.[10]



R_3SiOTf / NR_3	% Yield	Opt. purity of (*R*)-**6***	1.4-transfer of chirality
Me_3SiOTf / NEt_3	74	44%ee	49%
t-$BuMe_2SiOTf$ / NEt_3	72	66%ee	73%
t-$BuMe_2SiOTf$ / $(c\text{-Hex})_2NMe$	66	86%ee	96%

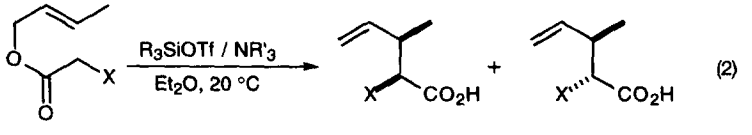
*Determined by HPLC analysis of the *N*-(*S*)-α-phenethyl amide **7** which was prepared by applying the Weinreb procedure (ref 11).

Table 1. The silyl triflate-mediated Claisen rearrangement of (*E*)- and (*Z*)-**1**

Entry	Substrate	R_3SiOTf	NR'_3	%Yield	*syn* : *anti*[a]
1	(*E*)-**1**	Me_3SiOTf	NEt_3	89	76 : 24
2			$(c\text{-Hex})_2NMe$	92	80 : 20
3		$t\text{-BuMe}_2SiOTf$	NEt_3	70	86 : 14
4			*N*-ethylpiperadine	79	89 : 11
5			$(c\text{-Hex})_2NMe$	69	92 : 8
Cf[b]		[LDA, $t\text{-BuMe}_2SiCl$, THF, -78 °C]			13 : 87
		[LDA, $t\text{-BuMe}_2SiCl$, THF-HMPA, -78 °C]			86 : 14
6	(*Z*)-**1**	$t\text{-BuMe}_2SiOTf$	NEt_3	89	7 : 93
7		$t\text{-BuMe}_2SiOTf$	$(c\text{-Hex})_2NMe$	62	4 : 96
Cf[b]		[$t\text{-BuMe}_2SiCl$, LDA, THF-HMPA -78 °C]			14 : 86

[a] Determined by GLC analysis of the corresponding methy ester. [b] Cited from ref 2c.

Next, the range of the applicable substrates was investigated. Unfortunately, applications of the present procedure to (α,γ–dialkyl)allyl esters were failed, instead yielding the acids arising from the ester cleavage, presumably because of the substantial stabilization of the forming allylic carbocations by the two alkyl groups. This is a serious drawback of the present Claisen variant, compared to the Ireland variant. However, the (α-*n*-pentyl–γ-trifluoromethyl)allyl acetate, where the CF_3 group could *de*stalize the carbocation concerned, did undergo the Claisen rearrangement without a detectable extent of the ester cleavage, albeit very sluggish.[12] On the other hand, a key merit of the present Claisen variant is its applicability to base-sensitive halogenated substrates. As shown in eq 2, the rearrangements of (*E*)-crotyl chloro- and bromoacetate (**8**) were found to proceed smoothly to give the Claisen products (**9**) in good yields and high diastereoselectivities.[13] Once again, use of the combination of the bulky silyl triflate and the bulky amine attains the highest diastereoselectivity.



(*E*)-**8** *syn*-**9** *anti*-**9**

X in **8**	R_3SiOTf	NR'_3	% Yield	*syn* : *anti*[a]
Cl	Me_3SiOTf	NEt_3	90	70 : 30
	$t\text{-BuMe}_2SiOTf$	NEt_3	86	84 : 16
		$(c\text{-Hex})_2NMe$	60	92 : 8
Br	Me_3SiOTf	NEt_3	58	75 : 25
	$t\text{-BuMe}_2SiOTf$[b]	$(c\text{-Hex})_2NMe$	82	90 : 10

[a] Determined by GLC analysis of the corresponding methyl ester. [b] Five equivalents of the triflate were used to accelerate the reaction.

In summary, we have convincingly demonstrated that the silyl triflate-mediated Calisen variant, when the combination of the silyl triflate and the tertiary amine is properly chosen, provides high levels of (*E*)-selection, diastereoselection, and 1,4-asymmetric transmission, which are comparable to or slightly higher than those of the Ireland variant. Thus, the present Claisen variant offers a convenient alternative to or compliments the widely-utilized Ireland-Claisen rearragement. Further application of the presnt Claisen variant is in progress in our laboratories.

Acknowledgment: This research was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan.

References and Notes

1. A visiting research fellow from Sumitomo Chemical Co., Ltd., Osaka.
2. (a) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 5897. (b) Ireland, R. E.; Willard, A. K. *Tetrahedron Lett.* **1975**, 3975. (c) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, 98, 2868. (d) Ireland, R. E.; Wilcox, C. S. *Tetrahedron Lett.* **1977**, 2839.
3. Reviews: (a) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423. (b) Wipf, P. *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: New York, **1991**; Vol. 5, p 827.
4. Yokozawa, T.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1984**, *25*, 3991. Also see: Yokozawa, T.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1984**, *25*, 3987.
5. (a) Funk, R. L.; Olmstead, T. A.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298, and references cited therein. (b) Schreiber, S. L.; Smith, D. B. *J. Org. Chem.* **1989**, *54*, 9. (c) Angle, S. R.; Amaiz, D. O. *Tetrahedron Lett.* **1989**, *30*, 515.
6. Review on *C- vs. O*-silylation of esters with silyl triflates: Emde, H. *Synthesis* **1982**, 1.
7. The (*Z*)-selection observed here is explicable in terms of essentially the same *noncyclic* mechanism advanced for explaining the (*Z*)-selection in the metal ester enolate formations: Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099.
8. For the *thermal* Claisen rearrangement of allylic (α-trimethylsilyl)esters: Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735.
9. The absolute configuration was assigned by the sign of the optical rotation (*cf.* ref 10): (*E, R*)-**6**, $[\alpha]_D^{20}$ -10.6°(*c* 1.00, Et_2O); its methyl ester, $[\alpha]_D^{20}$ -17.6°(*c* 1.12, Et_2O). The stereospecificity of (*R*)-**5** to (*R*)-**6** is understood as a result of the (*Z*)-selective formation of the ketene silyl acetal followed by the Claisen shift via the usual chair-like transition state.
10. Nagatsuma, M.; Shirai, F.; Sayo, N.; Nakai, T. *Chem. Lett.* **1984**, 1393.
11. Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, 4171.
12. In this reaction a considerable amount of the *C*-silylated ester was also formed (*ca.* 40% yield).
13. The *syn* configuration of the major Claisen product was assigned by the conversion of its methyl ester into the *anti*-α-amino ester via the S_N2 reaction with NaN_3 and then hydrogeneation (H_2, Pd/C) followed by its GLC comparison with an authentic *L*-isoleucine methyl ester (*anti* configuration).

(*Received in Japan* 14 *February* 1996; *revised* 6 *March* 1996; *accepted* 7 *March* 1996)