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Ester Enolate Claisen Rearrangement via Boat-Like Transition State

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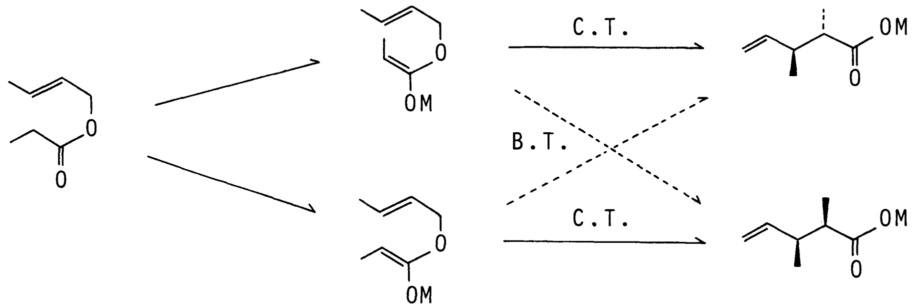
The Claisen rearrangement of ester enolates with appropriate metal ions bearing bulky cyclopentadienyl ligands was found to proceed through a boat-like transition state leading to the products with the different configuration from that expected from a chair-like transition state.

The ester enolate Claisen rearrangement reaction is a very useful tool for acyclic stereocontrol and has been widely used in natural product syntheses.[1) One of the valuable features of this reaction is that either syn- or anti-2,3-dialkyl carboxylic acid can be derived selectively from a common starting material through the selective formation of each geometrically isomeric enolate (Scheme 1).[2)



Scheme 1.

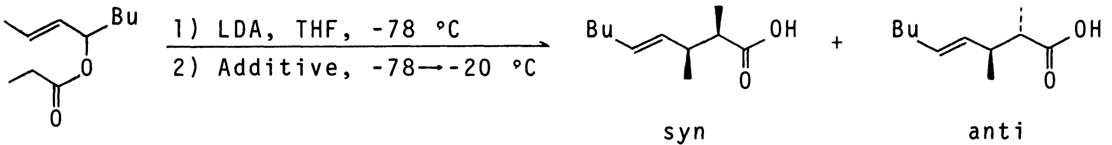
It is well known that the enolate Claisen rearrangement usually proceeds through a chair-like transition state (C.T.).[2) Therefore, if the reaction is constrained to proceed through a boat-like transition state (B.T.) by some means, the reversed diastereoselection of the product can be expected from an enolate of the same geometry, as indicated by dotted lines in Scheme 1 .

The modification in the transition state along this line is considered to be realized by the introduction of a bulky[3) ligand of concave type onto the counter ion metal, causing a steric repulsion between the ligand and the allyl double bond to destabilize the C.T., as depicted in Fig. 1. As one of such systems, we examined the cyclopentadienyl ligands system[4) in combination with several metal ions and could thereby obtain the products which could be interpreted to be formed through the B.T.

Fig. 1.

All the enolates examined here were derived from the kinetically formed lithium enolates (LDA in THF)$^{2)}$ by adding the appropriate additives. The geometry of the lithium enolate is considered to be retained during the exchange of its counter cation under the conditions.

The results of the rearrangement of (E)-2-octen-4-yl propionate (1) are shown in Table 1.



1

syn

anti

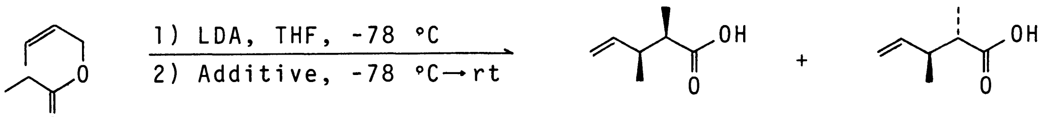
Table 1. Enolate Claisen rearrangement of (E)-2-octen-4-yl propionate

Entry	Additive	Yield/%	syn	:	anti$^{a,b)}$
1	Me_3SiCl	80	7	:	93
2	Et_2AlCl	33	18	:	82
3	$Cl_2Zr(OiPr)_2$	30	35	:	65
4	Cp_2TiCl_2	86	57	:	43
5	Cp_2ZrCl_2	78	67	:	33
6	Cp_2HfCl_2	90	70	:	30
7	$(Me_5Cp)_2ZrCl_2$	-			

a) The ratio of diastreomers was determined by ^{1}H NMR (400 MHz). b) The geometry of the newly formed double bond in both the syn- and anti-products was exclusively E (>20 : 1).

Rearrangement of 1 via the silylketene acetal showed high anti-selectivity reflecting the (E)-geometry$^{5)}$ of the enolate and the C.T.$^{2)}$ (entry 1). However, with other counter ions examined, though the diastereoselectivity was dependent on the nature of metals and ligands, syn-selectivity was obviously enhanced by the use of cyclopentadienyl ligands, suggesting the increased participation of the B.T. (entries 4-6). The highest syn-selectivity was observed with the Cp_2ClHf-enolate. However, the reaction of much bulky $(Me_5Cp)_2ClZr$-enolate did not give any rearrangement products.

The rearrangements of (Z)-2-butenyl propionate (2) were next examined. The results are shown in Table 2. The reversal in diastereoselectivity from the silylketene acetals (syn) to Zr- or Hf-enolate (anti) was also observed here reflecting the (Z)-geometry of the allyl moiety.



2

syn

anti

Table 2. Enolate Claisen rearrangement of (Z)-2-butenyl propionate

Entry	Additive	Yield/%	syn[a]	:	anti
1	Me_3SiCl[b]	24	83	:	17
2	t-$BuMe_2SiCl$[b]	57	83	:	17 (89 : 11)[c]
3	Cp_2ZrCl_2	18	15	:	85
4	Cp_2HfCl_2	16	13	:	87

a) The ratio of diastereomers was determined by ^{1}H NMR (400 MHz). b) The reaction mixture was refluxed for 3 h. c) The number in the parentheses was taken from reference 2.

The rearrangement of (E)-2-octen-4-yl α-benzyloxyacetate which has been known to give (Z)-enolate on treatment with LDA,[6] was then examined. In this case, however, both the silylketene acetals and the Cp_2ClM-enolates gave a high syn-selectivity as shown in Table 3. It has already been established that the enolate Claisen rearrangement of the silylketene acetals derived from glycolate esters proceeds through C.T.[6] The reason why Cp_2ClM-(Z)-enolate also proceeds through C.T. is unclear at present.[7]

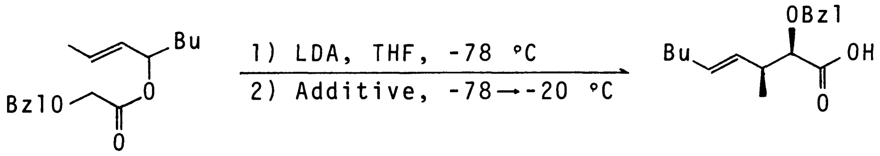


Table 3. Enolate Claisen rearrangement of (E)-2-octen-4-yl α-benzyloxyacetate

Entry	Additive	Yield/%	syn[a]	:	anti
1	Me_3SiCl	81	95[b]	:	5
2	Cp_2ZrCl_2	66	92[b]	:	8
3	Cp_2HfCl_2	74	93[b]	:	7

a) The ratio of diastereomers was determined by ^{1}H NMR (400 MHz). b) The geometry of the newly formed double bond was exclusively E.

Finally, the rearrangement of (R)-1-hepten-3-yl propionate was examined and, as expected, the enolate with Cp_2ClZr ion showed the sense of chirality transfer opposite to that observed with the silylketene acetal (Table 4).

In a typical experiment, (E)-2-octen-4-yl propionate (100 mg) was added to a solution of LDA (0.68 mmol, 1.2 equiv.) in THF (5 ml) at -78 °C. After stirring for 30 min, a solution of Cp_2HfCl_2 (292 mg, 1.2 equiv.) in THF (3 ml) was added to the solution. The mixture was, then, allowed to warm to -20 °C and kept for 48 h. The mixture was quenched with 1 mol dm^{-3} HCl and extracted with ether. The ethereal so-

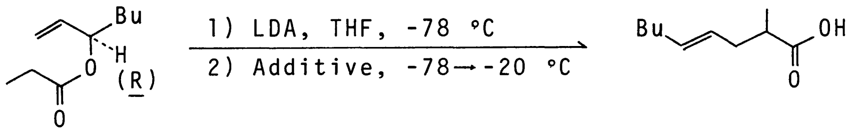


Table 4. The Claisen rearrangement of (R)-1-hepten-3-yl propionate

Entry	Additive	Yield/%	Config. at C2[a,b)]	Chirality transfer/%
1	Me_3SiCl	72	S	79
2	Cp_2ZrCl_2	72	R	55

a) The absolute configuration was determined by chemical correlation to methyl (S)-2-methylnoanoate through the sequence, i) treatment with diazomethane and ii) hydrogenation (H_2/Pd-C). b) The geometry of newly formed double bond was exclusively E.

lution was dried over Na_2SO_4, filtered through a celite column, and treated with CH_2N_2. After the concentration, the residue was passed through a short silica gel column. The filtrate was concentrated and the isomeric ratio was determined by ^1H NMR.

References

1) For a recent review, see; R. K. Hill, "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, Orland (1984), Vol. 3, pp. 503-572.
2) R. E. Ireland, R. H. Mueller, and A. K. Willard, J. Am. Chem. Soc., 98, 2868 (1976).
3) A mere increase of the bulkiness of the ligand in this type of reaction has been mentioned to rather result in the destabilization of the B.T.: M. Nagatsuma, F. Shirai, N. Sayo, and T. Nakai, Chem. Lett., 1984, 1393.
4) D. A. Evans and L. R. McGee, J. Am. Chem. Soc., 103, 2876 (1981). The steric effect of the cyclopentadienyl group in the aldol condensation reaction between Cp_2ClZr-enolates and aldehydes was discussed.
5) The nomenclature of the enolate geometry follows the proposal of Evans: Priority is given to the alkoxide oxygen bearing the metal ion in sequence rule assignment of ester enolates. D. A. Evans, "Asymmetric Synthesis" ed by J. D. Morrison,Academic Press, Orland (1984), vol. 3, pp. 1-110.
6) T. Sato, K. Tajima, and T. Fujisawa, Tetrahedron Lett., 24, 729 (1983); J. Kallmerten and T. J. Gould, ibid., 24, 5177 (1983); S. D. Burke, W. F. Fobare, and G. J. Pacofsky, J. Org. Chem., 48, 5221 (1983) and reference 3.
7) As for the transition state of zirconium mediated aldol reaction, Evans et al. proposed that the (E)-enolate reacts through B.T., while (Z)-enolate through C.T (references 8). The same argument may be extended to explain the result of the present enolate Claisen rearrangement.
8) D. A. Evans and L. R. McGee, Tetrahedron Lett., 21, 3975 (1980); D. A. Evans, J. V. Nelson, and T. R. Taber, "Topics in Stereochemistry," ed by N. L. Allinger, E. L. Eliel, and S. H. Silen, John Wiley & Sons, New York, 1982, Vol. 13, pp. 1-115; Y. Yamamoto and K. Maruyama, Tetrahedron Lett., 21, 4607 (1980). However, Yamamoto and Maruyama has proposed an acyclic transition state for the aldol reaction of zirconium enolates.

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