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A Facile Access to Chiral Allenedicarboxylates by Deracemization Process[1]

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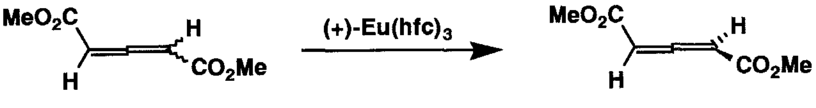
Abstract: Highly enantioselective deracemization route of chiral 2,3-pentadienedioates was achieved by complexation with the chiral organoeuropium reagent.

The deracemization process is known to be one of the most direct and efficient routes to prepare chiral molecules.[2] It has been investigated in several manners and its utility has been long recognized. However, high enantioselectivities were reported in few researches.[3] Here we describe the first successful approach to this methodology: preparation of chiral allenedicarboxylates using chiral organoeuropium complex.[4]

Our initial concern was to find an effective copper (II) reagent which posesses the chiral ligands with the appropriate structure.[5] However, observed asymmetric inductions were quite low regardless of the conditions. After a couple of attempts using other chiral organometallics, we noticed that the NMR shift reagent, Eu(hfc)3 is effective for this purpose.

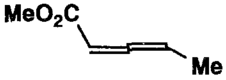
Racemic dimethyl 2,3-pentadienedioate[6] was resolved using 0.8 equiv. of (+)-Eu(hfc)3 in $CDCl_3$.[7] A pair of the diastereomeric peaks of the methoxyl group of the same intensities were observed at the chemical shift (δ) ca. 6.8 ppm with the difference (Δδ) of 0.06 ppm (270 MHz). But the peak at the higher field came to the major schielding from the light. After 9 days the ratio came to the maximum of 18:82 with only trace of decomposition. Addition of racemic dimethyl 2,3-pentadienedioate at this stage lowers the ratio again. This result showed that an enantiomeric drift should have occurred.

An excess amount of the europium catalyst (1.2 equiv.) improved the enantiomeric excess to 82%. These results were summarized in the Table 1.



(*S*) 82% e.e.

Table 1. Deracemization of Allenecarboxylates[a]

substrate	catalyst (equiv.)	solvent	e.e. (confg.)
	Cu(II) tartrate (2.0)	$CHCl_3$	7.4 (S)
		CH_2Cl_2	4.7 (S)
		$ClCH_2CH_2Cl$	4.2 (S)
	Cu(II) (Ts-Leu) (2.0)[b]	$CHCl_3$	9.6 (S)
		hexane [c]	0
	(+)-Eu(hfc)$_3$ (0.8)	$CHCl_3$ [d]	63.9 (S)
	(+)-Eu(hfc)$_3$ (1.2)	$CHCl_3$ [d]	82.0 (S)
	(+)-Eu(hfc)$_3$ (0.8)	$CHCl_3$ [d,e]	39.0 (S)
		$CHCl_3$ [d]	0
		$CHCl_3$ [d]	0

[a]All reaction were performed under argon atmosphere. The reaction time was 9 days. [b]Cu(II) (Ts-Leu): N-(4-methylphenylsulfonyl)-(L)-leucine, copper (II) salt. [c]The reaction time was 30 days. [d]The reaction was performed in a NMR tube. $CDCl_3$ was used as the solvent. The enantiomeric excess was measured directly by 270 MHz ^{1}H NMR (with a JEOL GMX-270 (PD = 100 sec.)). [e]The reaction mixture was irradiated by light.

The observed optical rotation ($[\alpha]_D^{20}$ = 29.4 (c, 0.408, methanol)) for the enantiomeric ratio of 40:60 with (+)-Eu(hfc)$_3$ showed that the absolute configuration of the major enantiomer is assigned as *S*, comparing with the calculated value (173 for (*S*)-isomer in methanol).[8]

Attempts using other 2,3-pentadienedioates, such as diethyl and diisopropyl esters, also led to enantiomeric drift. However, determination of the enantiomeric purity was failed due to the severe overlapping of the signals.[9] And the europium reagent was inert to 2,3-pentadienoates and 4-phenyl-2,3-butadienoates.[10]

Initially we assume the reaction mechanism as illustrated in Figure 1. Organoeuropium reagents are known to possess a strong Lewis acidity. First Eu(hfc)$_3$ preferably coordinates to the carbonyl oxygen of the alkoxycarbonyl group than to the double bond. The π-bond of the conjugated ester should be weakened by localization toward the Lewis acid. Racemization might take place thermally. The chiral environment of the ligands on the europium reagent enriches the favored isomeric complex. Irradiation by light caused the enaniomeric ratio to fall off. The photochemical path for racemization exsists independently. However, the plot of the enantiomeric excess does not follow the equation,[11] which was derived from the first-order approximation (Figure 2). The higher-order complexes and aggregates might participate to the deracemization process.[2,12]

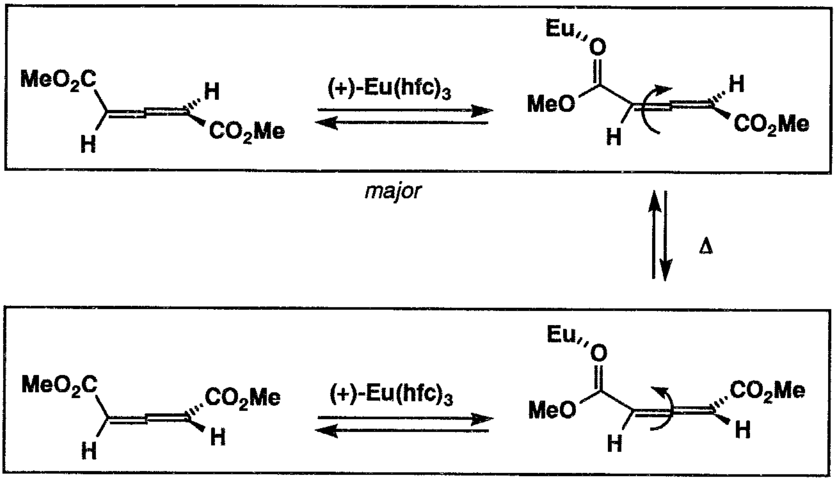


Figure 1. A possible mechanism for deracemization.

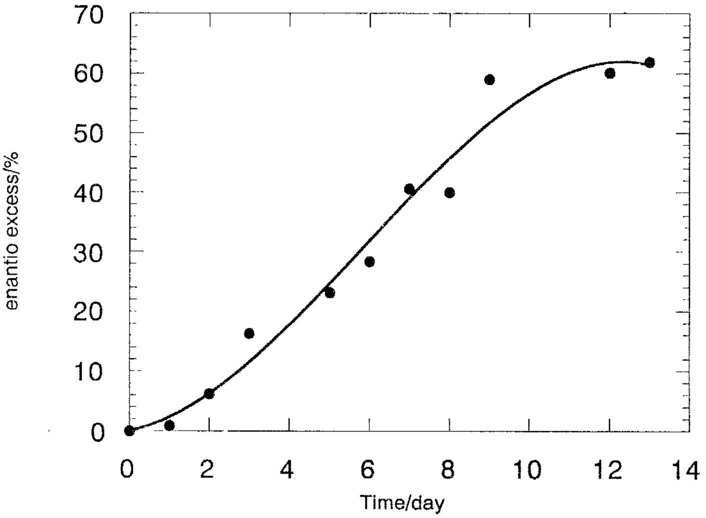


Figure 2. Plot of the time dependence of the enantiomeric excess (1.2 equiv. of (+)-Eu(hfc)$_3$ was used. The reaction conditions were not optimized.).

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9. Attempt in resolution of racemic allenecarboxylates by HPLC equipped with Daicel CHIRALCEL OD™ was failed.
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11. If we approximate the reaction rate as the first-order, the enantiomeric excess should change as described by the following equation:

$$\text{e.e.} = (\text{e.e.})_{\text{equilibrium}}(1-\exp(-kt))$$

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