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$Eu(fod)_3$-catalyzed tandem regiospecific rearrangement of divinyl alkoxyacetates and Diels–Alder reaction

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Abstract

Unsymmetrical divinyl alkoxyacetates (such as **7a**) undergo a $Eu(fod)_3$-catalyzed regiospecific allylic rearrangement to form C_5-substituted (*E*)-2-ethoxy-1,3-dienes at room temperature. When the rearrangement of **7a** was carried out in the presence of maleic anhydride, a tandem allylic rearrangement and Diels–Alder reaction occurred to give the adduct **11**. Reactions of other dienophiles in this tandem procedure were examined. © 2000 Elsevier Science Ltd. All rights reserved.

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The lanthanide complexes $Ln(fod)_3$ and related analogs modified by chiral ligands have been used as Lewis acid catalysts in organic synthesis.[1] The $Ln(fod)_3$ catalysts are efficient for promoting the cycloaddition of electron-rich dienes with aldehydes.[2] Other reactions catalyzed by $Ln(fod)_3$ include 1,3-dipolar cycloadditions,[3a] ene reactions,[3b] radical-mediated allylation,[3c] and the ring closure of vinylic epoxy alcohols.[3d] Recently, Koreeda's group reported that $Eu(fod)_3$ promoted a stereospecific rearrangement of allylic methoxyacetates.[3e] In contrast to Pd(II) catalysts, $Eu(fod)_3$ is compatible with alkynyl group(s).[3e] We have successfully applied this rearrangement to the synthesis of *cis*-enediynes.[4] We report now on a regiospecific rearrangement of unsymmetrical divinyl esters and a tandem allylic rearrangement and Diels–Alder reaction under $Ln(fod)_3$ catalysis.

We first examined $Ln(fod)_3$ catalysts for the rearrangement of the symmetrical divinyl ester **3** (Scheme 1).[5] The (*E*,*E*)-divinylcarbinol **2** was prepared according to the literature procedure.[6] Addition of $BnOCH_2C{\equiv}CLi$ to methyl formate gave the alcohol **1** which was reduced to **2** by using excess Red-Al[7] (0°C, 12 h, 46%). The methoxyacetate **3** was prepared from **2** in 87% yield under the DCC–DMAP conditions. We used four $Ln(fod)_3$ catalysts (Ln = Pr, Eu, Er, Yb) for promoting the rearrangement of **3**. With 10 mol% of the catalyst, the reaction was completed

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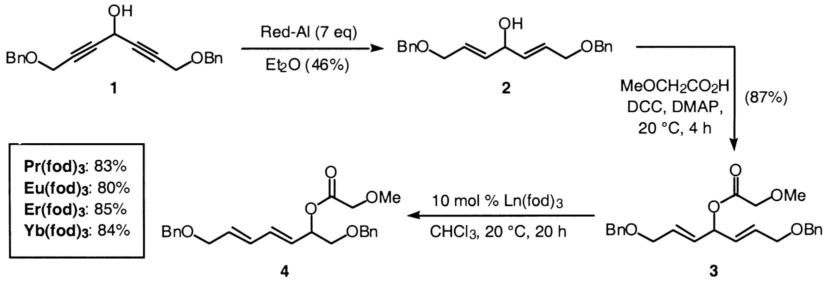
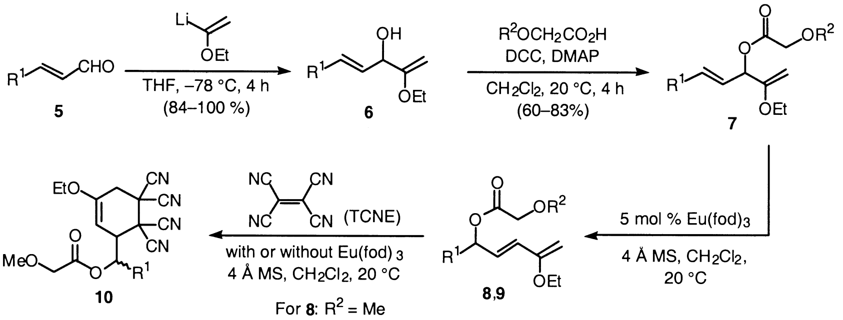


Scheme 1.

within 20 h in $CHCl_3$ at room temperature and the diene **4** was isolated in 80–85% yield. Because the product **4** cannot be separated from **3** on a silica gel TLC plate, the reaction mixture was checked by ^1H NMR spectroscopy and the characteristic signals of **3** were not detected.

We envisaged the unsymmetrical divinyl substrates **7** as the precursors of electron-rich 1,3-dienes based on the assumption that a regiospecific allylic rearrangement is possible. To test this idea, we synthesized two series of esters **7** (R^2 = Me and PMB) from α,β-unsaturated aldehydes **5** (Scheme 2). Addition of α-ethoxyvinyllithium prepared from ethyl vinyl ether and *t*-BuLi[8] to **5** at –78°C gave the alcohols **6**. Condensation of **6** with methoxyacetic acid or *p*-methoxybenzyloxyacetic acid under the DCC–DMAP conditions afforded **7**. The PMB ether is cleaved by DDQ under mild conditions.[9] It provides an opportunity to manipulate the PMB-containing ester group after the rearrangement.



Scheme 2.

Rearrangement of **7** was carried out in CH_2Cl_2 at room temperature by using 5 mol% $Eu(fod)_3$. The results are summarized in Table 1. We found that it is necessary to use molecular sieves to prevent the dienes from hydrolysis by moisture. We isolated the α,β-unsaturated methyl ketones from the reactions where the molecular sieves were not added. Rearrangement of **7** is regiospecific as only the C_5-substituted (*E*)-1,3-dienes **8** and **9** were formed. The methoxyacetates are slightly more reactive compared to the *p*-methoxybenzyloxyacetates. Increase of the catalyst loading from 5 to 10 mol% reduced the reaction time accordingly (for **8c** in Table 1, entry 3). Overall, the $Eu(fod)_3$-catalyzed rearrangement is general and the 1,3-dienes are formed in good to excellent yields.

Table 1
Eu(fod)$_3$-Catalyzed regiospecific rearrangement of **7**[a]

Entry	R^1	**8** (R^2 = Me) t (h), yield (%)	**9** (R^2 = PMB) t (h), yield (%)
1	**7a**: Me	**8a**: 60, 85	**9a**: 70, 61
2	**7b**: Et	**8b**: 60, 90	**9b**: 70, 71
3	**7c**: *n*-Pr	**8c**: 16, 81[b]	**9c**: 70, 80

[a] All reactions were carried out at 0.1 M of **7**. [b] 10 mol % of Eu(fod)$_3$ was used. PMB = *p*-MeOC$_6$H$_4$CH$_2$.

The dienes **8a–c** were reacted with tetracyanoethylene (TCNE) (Table 2). In the absence of Eu(fod)$_3$, **10b** was formed from **8b** and TCNE at room temperature for 8 h (51%) as an inseparable mixture. After a prolonged reaction (24 h), the yield of **10b** slightly increased to 55% (entries 2 and 3). In a similar manner, reaction of **8a** and **8c** with TCNE furnished **10a** (50%) and **10c** (60%) as an inseparable mixture, respectively (entries 1 and 5). We found that in the presence of 5 mol% Eu(fod)$_3$, cycloaddition of the diene **8b** with TCNE furnished **10b** in 58% yield (entry 4). This result showed that Eu(fod)$_3$ catalyzes the Diels–Alder reaction of **8b** with TCNE (entry 4 versus entry 3).[10]

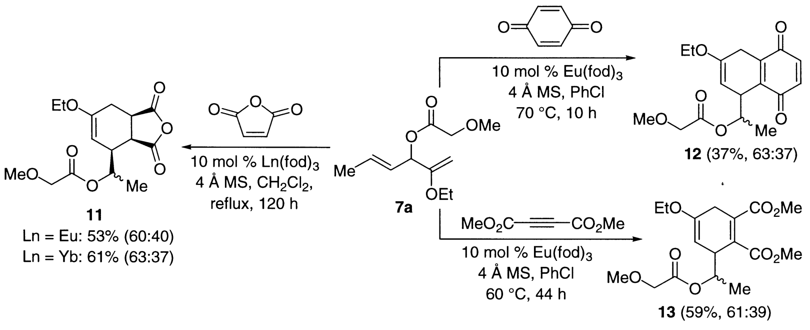
Table 2
Stepwise versus tandem Diels–Alder reaction[a]

Entry	R^1	Stepwise (from **8**) t (h), yield (%), dr[b]	Tandem (from **7**) t (h), yield (%), dr[b]
1	**a**: Me	**10a**: 24, 50, 55:45[c]	**10a**: 10, 65, 59:41[d]
2	**b**: Et	**10b**: 8, 51, 56:44[c]	
3	**b**: Et	**10b**: 24, 55, 56:44[c]	
4	**b**: Et	**10b**: 10, 58, 56:44[d]	**10b**: 10.5, 56, 61:39[d]
5	**c**: *n*-Pr	**10c**: 24, 60, 50:50[c]	**10c**: 18.5, 64, 57:43[e]

[a] Reactions were carried out at 0.1 M of **7** or **8**. [b] Diastereomeric ratio of the adduct was determined by ^{1}H NMR. [c] No Eu(fod)$_3$ was used. [d] 5 mol % of Eu(fod)$_3$ was used. [e] 10 mol % of Eu(fod)$_3$ was used.

Next, we used **7a–c** in a tandem allylic rearrangement and Diels–Alder reaction (Table 2).[11] For example, a mixture of **7a**, TCNE, and 5 mol% Eu(fod)$_3$ in CH$_2$Cl$_2$ was stirred for 10 h to give **10a** in 65% yield (entry 1). The reaction time of the tandem procedure is significantly shorter than the rearrangement of **7a** into **8a** (Table 1, entry 1) because of the equilibrium between **7a** and **8a**. In the tandem reaction, the diene **8a** formed reacted with the dienophile to give the adduct **10a**. Thus, the return path from **8a** to **7a** was suppressed. Similarly, the cycloadducts **10b** and **10c** were formed directly from **7b** and **7c** with TCNE, respectively. With a large alkyl group in **7c**, steric effects came into play to slow down the Diels–Alder reaction. It is evident that the tandem procedure is better than the stepwise reaction. The overall chemical yield is higher for the tandem reaction with a slight enhancement in the diastereoselectivity.

We investigated the tandem allylic rearrangement and Diels–Alder reaction of **7a** with other dienophiles (Scheme 3). Treatment of **7a** and maleic anhydride with 10 mol% Eu(fod)$_3$ in refluxing CH_2Cl_2 for 120 h afforded **11** in 53% yield as a 60:40 inseparable mixture. The cycloaddition should follow the *endo* selectivity.[10] Yb(fod)$_3$ catalyzed the same tandem reaction with a similar efficiency. The bicyclic compound **12** was obtained from **7a** and 1,4-benzoquinone through the tandem reaction sequence followed by air oxidation (Scheme 3). We found that **12** gradually decomposed at higher temperatures. By limiting the reaction in chlorobenzene at 75°C for 10 h, **12** was isolated in 37% yield as a 63:37 inseparable mixture. The tandem reaction of **7a** with dimethyl acetylenedicarboxylate also occurred at 60°C in chlorobenzene and **13** was obtained in 59% yield as a 61:39 inseparable mixture.



Scheme 3.

In summary, we have established the Eu(fod)$_3$-catalyzed regiospecific rearrangement of the unsymmetrical divinyl esters **7** to form the C_5-substituted (*E*)-1,3-dienes **8** and **9** under mild conditions. This provides an efficient alternative method for the preparation of 2-alkoxy-1,3-dienes.[12] We also developed a tandem allylic rearrangement of the alkoxyacetates **7** and Diels–Alder reaction of the resultant 1,3-dienes using a single Lewis acid catalyst, Eu(fod)$_3$. Application of the Ln(fod)$_3$-catalyzed rearrangement of allylic esters in organic synthesis is under way in our laboratory.

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