

## 94. A Note on Stereochemical Observations of the Deprotonation of Ethyl 2-Alkenoates

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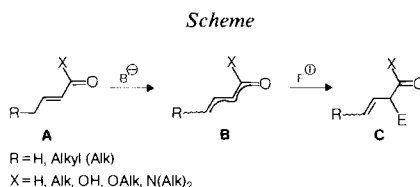
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### Summary

Deprotonation of ethyl (*E*)-2-alkenoates **1**, **3** and **4** yields after protonation the double bond migrated (3 *Z*)-isomers **5**, **7** and **9** as major products. In contrast, deprotonation and reprotonation of ethyl (*Z*)-2-pentenoate (**2**) gives the (3 *E*)-isomer **6** exclusively. These findings are explained by reaction paths starting from different ester conformations.

Dienolates of type **B** (*Scheme*) are usually derived from the corresponding  $\alpha,\beta$ -unsaturated species **A** (aldehydes, ketones, acids, esters, amides). It is well known that quenching of **B** with electrophiles gives rise to the nonconjugated,  $\alpha$ -substituted compounds **C** as major products [1-7]. If the electrophile is a proton, trapping most likely occurs at oxygen yielding the corresponding dienols which then tautomerize to **C**. In this case, the overall reaction sequence from **A** to **C** presents a double bond migration leading to the thermodynamically less favoured isomer [8].



The stereochemistry at the double bonds produced in these reactions has been recognized [6] but was studied only in the case of 2-hexenoic acid [3].

This paper gives an account of the configurational aspects of such double bond migrations starting from various ethyl 2-alkenoates such as ethyl (*E*)- and (*Z*)-pentenoates (**1**, resp. **2**), ethyl (*E*)-2-hexenoate (**3**) and ethyl (*E*)-5-methyl-2-hexenoate (**4**)<sup>1</sup>.

<sup>1</sup>) The synthesis of **1**, **3** and **4** was achieved by acid-catalyzed esterification of the corresponding acids [9], and of **2** from (*Z*)-2-pentenoic acid [10] by reaction with diazoethane. All compounds exhibited correct analytical data.

Under standard reaction conditions the esters were added dropwise to a slight excess (1.2 mol-equiv.) of a 0.5 M solution of LDA (lithiumdiisopropylamide) in THF/HMPT (hexamethylphosphoric triamide) (1.2 mol-equiv.) at  $-70^{\circ}$ . The enolates so formed were quenched after 15 min with saturated aqueous  $\text{NH}_4\text{Cl}$ -solution. After extraction and bulb-to-bulb distillation the products were compared with reference compounds<sup>2)</sup> on a GLC.-column.

The results are summarized in the *Table*. The (2*E*)-configured esters **1**, **3** and **4** give the (3*Z*)-alkenoates **5**, **7** and **9**, respectively, as the major products. The corresponding (3*E*)-isomers **6**, **8** and **10** were the minor products. In contrast, the ester with a (2*Z*)-configuration, **2**, gives the (3*E*)-isomer **6** exclusively.

The yields vary between 37 and 78%. The rest consists mostly of the 1,4-addition products of LDA to the starting esters, a reaction [12] known to occur when HMPT concentrations are low. Therefore, it is not surprising that the yields are dependent upon the amount of HMPT used. On the other hand, product distributions are practically independent of HMPT and base equivalents used as well as the concentration of the LDA solution.

When reexposed to the reaction conditions, products **5** and **6** were isolated unchanged in 75% yield. Hence the stereoselectivities observed for these double

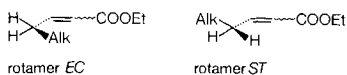
Table. Deprotonations of ethyl 2-alkenoates with LDA in THF/HMPT at  $-70^{\circ}$  followed by protonation with aq.  $\text{NH}_4\text{Cl}$  solution

Starting material <sup>a)</sup>	Products <sup>b)</sup> ethyl 3-alkenoates		Ratio	Overall (Σ) yield (%)
<b>1</b>	<b>5</b>	<b>6</b>	89:11	60 <sup>c)</sup>
" <b>1</b>	" <b>5</b>	" <b>6</b>	92:8	60 <sup>d)</sup>
" <b>1</b>	" <b>5</b>	" <b>6</b>	94:6	78 <sup>e)</sup>
" <b>1</b>	" <b>5</b>	" <b>6</b>	95:5	37 <sup>f)</sup>
<b>2</b>	" <b>5</b>	" <b>6</b>	0:100	56 <sup>c)</sup>
<b>3</b>	<b>7</b>	<b>8</b>	87:13	70 <sup>c)</sup>
<b>4</b>	<b>9</b>	<b>10</b>	56:44	64 <sup>g)</sup>

<sup>a)</sup> Purity > 97%. <sup>b)</sup> Products exhibiting GLC.-peaks greater than 0.5% (20 m GLC.-column packed with 20% SE-30 on Chromosorb W, 40-200°, 4°/min). Products exhibited correct MS.- and NMR.-data. <sup>c)</sup> 1.2 mol-equiv. of LDA and HMPT used. <sup>d)</sup> 2.4 mol-equiv. of LDA and HMPT used. <sup>e)</sup> 4.8 mol-equiv. of HMPT used, partly not dissolved. <sup>f)</sup> Molarity of LDA solution used was 0.05. 18% of **1** recovered. <sup>g)</sup> 2.4 mol-equiv. of HMPT used.

<sup>2)</sup> Syntheses of **6**, **8** and **10** were achieved from the corresponding acids by mild acid catalyzed esterification; the acids themselves were prepared according to the general procedure described in [11].

bond migrations must arise in the proton abstraction step and the (*E/Z*)-distributions could be explained by reaction paths starting from different conformations such as eclipsed (EC) and staggered (ST) rotamers.



It should be assumed that the eclipsed conformations lead to the (3*Z*)-configured products and the staggered conformations to the (3*E*)-configured ones. The product distributions, corrected with a statistical factor for different deprotonation possibilities would then express indirectly the conformation ratios of the corresponding starting esters. However, we do not know for certain, whether the product distributions are the result of thermodynamic or merely kinetic factors. For example, are the eclipsed rotamers of esters **1** and **3** really preferred<sup>3)</sup> or are these or closely related conformations simply more reactive? At least, it seems reasonable that the conformation ratios would depend upon the bulkiness of the alkyl (Alk) group.

The reaction sequence in which the (2*Z*)-configured ester **2** leads exclusively to **6** can easily be explained by steric reasons: conformation **2** (ST) prevails completely over the far more crowded rotamer **2** (EC).

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<sup>3)</sup> It is well-known that analogous eclipsed conformations are favored in case of saturated esters [13]. Therefore, it seems to be likely that this is also true for the vinylogous cases.