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## Diastereoselective addition of silvl metals to $\gamma$ -alkoxy substituted $\alpha$ , $\beta$ -unsaturated esters

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Dedicated to Professor Léon Ghosez on the occasion of his 70th birthday for his valuable contribution to organic chemistry

**Abstract**—Dimethylphenylsilyllithium adds to *Z*- $\gamma$ -alkoxy- $\alpha$ , $\beta$ -unsaturated esters to produce almost exclusively (i) the *anti*-adducts when the reaction is carried out in THF and (ii) the *anti*-adduct when carried out in the presence of HMPA. Poor stereocontrol is achieved with stereoisomeric *E*- $\gamma$ -alkoxy- $\alpha$ , $\beta$ -unsaturated esters. © 2004 Published by Elsevier Ltd.

As continuation of work aimed to produce methyl chrysanthemate by tandem addition of stannyl- and silylmetals **2** and acetone to  $\alpha,\beta$ -unsaturated esters,<sup>1</sup> we became interested in extending this reaction to related  $\gamma$ -alkoxy- $\alpha,\beta$ -unsaturated esters such as methyl 3-(2, 2-dimethyl-[1,3]dioxolan-4-yl)-acrylate **1** derived from D-glyceraldehyde acetonide<sup>2</sup> (Scheme 1). We expected to favour asymmetric induction leading to the enantioselective synthesis of the desired compound.<sup>3</sup>

We first reacted trimethylsilyllithium  $2a^{4a}$  with the enoate 1 and found that it adds quite selectively to the *Si*-face of the *Z*-stereoisomer *Z*-1 to produce the *anti*adduct  $3a_{Si}$  (7 equiv HMPA, THF, -78 °C, de 62%; Scheme 1, entry a) and with very poor stereocontrol from the *Re*-face of its *E*-diastereoisomer leading to the *syn*-adduct  $3a_{Re}$  (7 equiv HMPA, THF, -78 °C, de 12%; Scheme 1, entry e).

Although the carbon framework of the silyllithium is similar to that of its tin analogue (compare Scheme 1, entry a to Scheme 2, entry a), we felt that it was not secure to compare these results. In fact due to synthetic constraints, the presence of HMPA in the reaction involving the silyl derivative is required which is not the case with trimethylstannyllithium.



Scheme 1.

We have therefore prepared dimethylphenylsilyllithium **2b** which, unlike trimethylsilyllithium **2a**, can be generated in THF alone.<sup>4b</sup> We observed that, contrary to

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the previous case, it generates the *syn*-adduct  $3\mathbf{b}_{Re}$  in good yield from the Z-enoate 1, and with extremely high de (Scheme 1, entry c; compare to entry a).

We performed, in order to confirm the important role of HMPA in this facial stereocontrol, the reaction of **2b** with the Z-enoate Z-**1** in THF-HMPA (7 equiv., THF,  $-78 \degree$ C, 4 h). We found, as expected that it produces the *anti*-adduct **3b**<sub>Si</sub> resulting from the stereoselective attack on its *Si*-face (Scheme 1, entry b). The stereoselectivity proved to be much better than that observed from **2a** under the same experimental conditions (Scheme 1, compare entries a,b).

Diethylzincate<sup>4c</sup> **2c** behaves as its lithium analogue **2b** when the reactions are performed in THF. It reacts by the *Re*-face of the *Z*-enoate *Z*-**1** and offers the advantage of providing the *syn*-adduct **3b**<sub>*Re*</sub> with even higher stereocontrol (de 96 % instead of 90 %) and higher yield (Scheme 1, entry d, compare to entry c).

We were rather surprised to find that silyl metals react with very poor stereocontrol with the *E*-enoate *E*-1, whatever are the conditions used (de 8–28%; Scheme 1, entries e–h). This contrasts with the results reported above for the *Z*-diastereoisomer *Z*-1 (de 62–96%; Scheme 1, compare entries e–h to a–d).

This whole set of these results is quite exceptional, especially, the high control of the face of attack of silyllithium **2b** towards methyl Z-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate **1** in THF and the remarkably completely reversed facial stereocontrol found if the reaction is carried out in the presence of HMPA. We have ascertained, at least in the latter case that the reaction occurs under kinetic control. This has been achieved by determining the structures of the mixtures of products generated as described in Scheme 1, entry c ((i) THF, -78 °C, 4 h (ii) aq NH<sub>4</sub>Cl) or after addition of HMPA prior to the aqueous quench ((i) THF, -78 °C, 1 h (ii) HMPA, -78 °C, 3 h (iii) aq NH<sub>4</sub>Cl).

It is even more interesting to compare the behaviour of the trialkylsilyl metals to that of trialkylstannylmetals<sup>3</sup> which belong to the same family of compounds.

Both silyl-<sup>4a,b</sup> and stannyl-<sup>5a,b</sup> lithiums react in THF with extremely high stereocontrol on methyl Z-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate 1 but from different faces (*Re* and *Si*, respectively; Scheme 1, entry c and Scheme 2, entries a,b). The presence of HMPA in the reaction medium reverses the face of attack in the former case (Scheme 1, entries b,c) whereas as we have discovered in the present study it has no effect on the reaction involving tributylstannyllithium (Scheme 1, compare entries b,c).

Silyl-<sup>4c</sup> and stannyl-<sup>3</sup> zincates however both add to the same *Re*-face of methyl *Z*-3-(2,2-dimethyl-[1,3]dioxo-lan-4-yl)-acrylate **1** (Scheme 1, entry d; Scheme 2, entry d) and this trend is not reversed with its *E*-stereoisomer although the stereofacial differentiation is poorer (Scheme 1, entry h; Scheme 2, entry e).

The stereochemistry of each of the two diastereoisomers of **3**, has been ascertained by transforming them to the corresponding 4-(dimethylphenylsilanyl)-5-hydroxymethyldihydrofuran-2-ones  $\mathbf{6}_{anti}$  and  $\mathbf{6}_{syn}$  on tandem acid catalyzed dioxolane ring opening  $\gamma$ -hydroxyester ring closure (CF<sub>3</sub>CO<sub>2</sub>H, THF, 20 °C, 3 h, Scheme 3).<sup>6</sup>

The <sup>1</sup>H NMR spectra of  $\mathbf{6}_{anti}$  compares successfully with that already described in the literature for the same compound prepared from the silylcuprate and 5-hydroxy-methyl-5*H*-furan-2-one.<sup>6</sup> That of its stereoisomer  $\mathbf{6}_{syn}$  is as expected (Ha:  $\delta = 2.22$  ppm,  $J_{\text{HA}-\text{HB}} = 8.4$  Hz; Hb  $\delta = 4.674$  ppm,  $J_{\text{HA}-\text{HB}} = 8.4$  Hz).

Our results compare favourably with those already described by Smadja and co-workers, involving the tris(trimethylsilyl)silyl radical,<sup>7</sup> since they allow the stereo-selective synthesis of each of the two stereoisomers of **3**.

At present, we are unable to rationalize the whole set of results involving addition and cycloaddition reactions on  $\gamma$ -alkoxy- $\alpha$ , $\beta$ -unsaturated esters bearing a chiral  $\gamma$ -carbon on the basis of any known model (degenerated





non-chelated Felkin-Anh or chelated Cram model or another one).<sup>8</sup> We are working towards this end.

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