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# Oxidative Scission of Ethyl 2,2-Dimethoxycyclopropanecarboxylates with Lead Tetraacetate. Synthesis of the Unusual Anhydride Bis-Acetals

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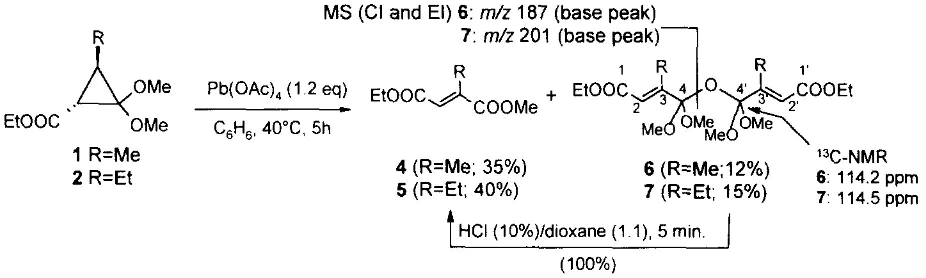
***Abstract.*** The reaction of ethyl 2,2-dimethoxycyclopropanecarboxylates **1-3** with lead tetraacetate ($Pb(OAc)_4$, LTA) in benzene leads to the oxidative scission of the $C_1$-$C_2$ bond. Monoalkylated fumaric acid diesters **4** and **5** are obtained from 3-alkylcyclopropanes **1** and **2**, respectively, along with dimeric species for which we propose the unusual anhydride bis-acetal structure **6** or **7**, respectively. Reaction of 3,3-dimethylcyclopropane **3** with LTA produces the 3-acetylsuccinate derivative **8** as the sole reaction product.

***Keywords***: Lead tetraacetate, vicinally substituted donor-acceptor cyclopropanes, fumarates, anhydride bis-acetals.

Vicinally substituted donor-acceptor cyclopropanes are versatile building blocks in organic synthesis and are used for the preparation of many types of compound.[1] The reactivity of these substances has been studied and, in particular, 2,2-dialkoxycyclopropanecarboxylic acid ethyl esters have been the subject of several investigations by our research group.[2] Nevertheless, little is known about their chemical behaviour in oxidising media. In a previous paper we reported that some of these compounds react with $RuO_4$ to give 2-alkyl-substituted methyl ethyl 3-oxobutanedioates by cleavage of the reactive $C_1$-$C_2$ $\sigma$ bond.[3]

We have now undertaken a study aimed at testing the reactivity of 2,2-dialkoxycyclopropanecarboxylic acid ethyl esters under a variety of oxidising conditions. In the present communication we report on the reaction of some of the above mentioned cyclopropanes, namely compounds **1-3** (Schemes 1 and 2) with $Pb(OAc)_4$ (LTA).[4] In particular, compounds **1** and **2** react with LTA in dry benzene at 40 °C to give 2-alkyl-substituted fumaric acid diesters **4** and **5**, respectively, by scission of the $C_1$-$C_2$ $\sigma$ bond (Scheme 1). Compound **4** is the known 1-methyl 4-ethyl mesaconate.[5] Unexpectedly, the reaction also produces in each case a dimeric compound for which we propose the anhydride bis-acetal structure **6** (from **1**) or **7** (from **2**) (Scheme 1) on the basis of NMR evidence, elemental analysis[6] carried out on compound **7**, MS data (Scheme 1), and the chemical behaviour exhibited by these substances under acidic conditions (**6** and **7** quantitatively converted into the corresponding fumarates **4** and **5**, respectively, in 10% aq. HCl/dioxane sol. (1:1), in 5 min.). Anhydride bis-acetals are very unusual compounds; only two examples of this type of substance can be found in the literature.[7]

**Scheme 1. Oxidative scission of cyclopropanes 1 and 2 with LTA.**



The reaction of the less reactive *gem*-dimethylcyclopropane **3** with LTA (Scheme 2) was accomplished in refluxing benzene and required seven days to go to completion. Monoacetate **8** was obtained as the sole reaction product in 62 % yield after HPLC purification. Spectral data exhibited by this compound well agree with structure **8**. Final proof for the structure shown came from reduction of the previously synthesised 2,2-dimethyl methyl ethyl 3-oxobutanedioate[3] with $NaBH_4$ in EtOH (r.t., 30 min.) followed by acetylation ($Ac_2O$/py, r.t., 16 h) that furnished a product identical to **8**.

From a mechanistic point of view, taking into account the push-pull nature of cyclopropanes **1-3**, it seems reasonable that $Pb(OAc)_4$ induces the scission of the $C_1$-$C_2$ bond in **1-3** by interacting with the $CO_2Et$ group as shown in Scheme 3. Attack of the released $AcO^-$ group at the cation portion $^+C(OMe)_2$ of this species would lead to intermediate **9**. The successive evolution of **9** can follow two paths. When $R^2$=H it could transform into fumarates **4** and **5** by loss of $Pb(OAc)_2$ and AcOH and collapse of the acetoxy ortho ester portion to a COOMe group (by loss of methyl acetate?), following path a. On the other hand,

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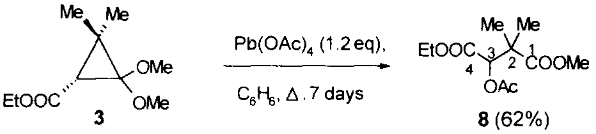
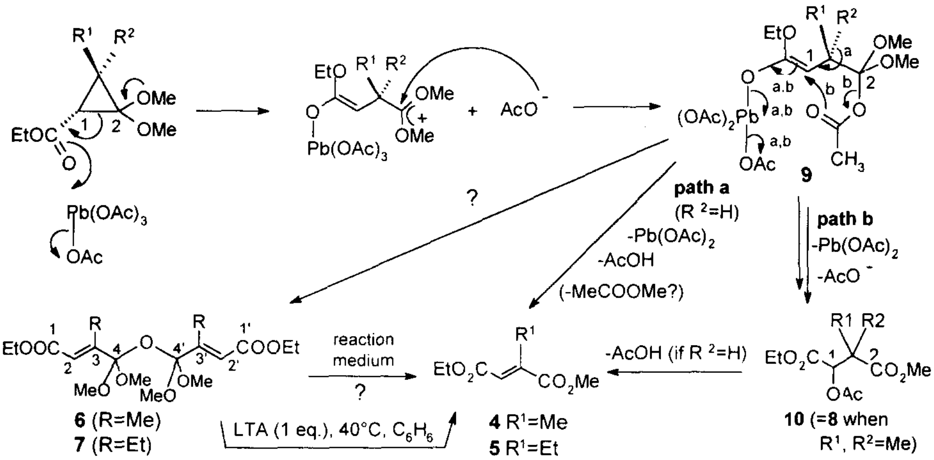
### Scheme 2. Oxidative scission of cyclopropane 3 with LTA



when $R^1=R^2=Me$ this path cannot be operative and **9** could give acetate **10** by migration of the AcO group from C-2 to C-1, assisted by loss of $Pb(OAc)_2$ and $AcO^-$, and concomitant formation of a COOMe group at C-2 (path b). It cannot be excluded that this path is always the most favourable and that fumarates **4** and **5** could be derived from intermediate **10** by loss of AcOH (if $R^2=H$). Indeed, reaction of **2** with LTA also produces 5% of the C-1 acetyl derivative (**10**: $R^1=Et$, $R^2=H$, Scheme 3) that has been isolated and characterised. However, this substance when dissolved in benzene in the presence of LTA (1 eq.) at 40°C has no tendency to convert to fumarate **5**. Analogous experiments conducted on fumarate **5** and on the dimeric species **7** showed that the former is recovered unmodified while the latter cleanly converts into **5** under the above conditions (60% conversion in 24 h, Scheme 3). It seems likely that this route could be in part operating in the reaction medium. What about the formation of dimers **6** and **7**? Do they originate in some way from the coupling of two molecules of intermediate **9** or of a species derived from it? At this stage any speculative reasoning seems hazardous. It cannot be excluded that the central oxygen in **6** and **7** derives from molecular oxygen since no care was taken to exclude it from the reaction medium during the reported experiments. Obviously, in this case a radical mechanism should be operative. Further experimental work is in progress to shed light on the nature of the process. As far as we know this is the first report on the LTA-induced scission of simple (not fused) cyclopropane compounds.

### Scheme 3. A mechanistic hypothesis explaining the reactivity of cyclopropanes 1-3 with LTA



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