

A new reaction: lead(IV) acetate-mediated oxidative fragmentation of homoallylic alcohols

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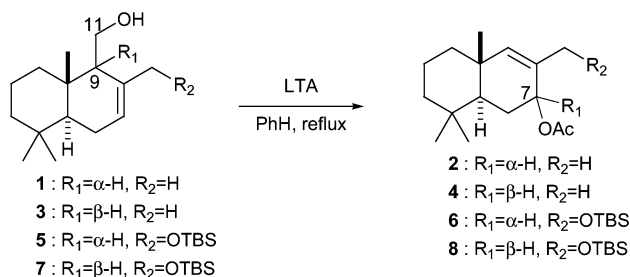
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Treatment of a homoallylic alcohol with lead(IV) acetate in refluxing benzene for 2 hours results in an oxidative cleavage to give a carbonyl compound and an allylic acetate with high yield.

Lead(IV) acetate (a.k.a. LTA, *lead tetraacetate*) has since long ago been recognized as one of the most highly versatile and useful oxidants available to the organic chemist, despite its relatively high toxicity.¹ To highlight just a few important classical applications, LTA finds use in the oxidative cleavage of vicinal diols,² the decarboxylation of acids,³ and the remote functionalization of alcohols.⁴ Recently, some new applications were found, as in the preparation of aryl lead triacetates, that find use in the direct arylation of nucleophiles,⁵ and a very interesting multistage hetero-domino transformation,⁶ both examples allowing access to unique carbon substitution patterns.

During the course of research intended to synthesize new bioactive compounds from locally abundant and easily available drimanic terpene alcohols,⁷ we found that when a boiling solution of drimenol (**1**)⁸ in benzene was treated with one equivalent of LTA, a smooth reaction occurred, to give a single product, identified as 11-nordrimanic acetate **2** (Scheme 1).⁹ Acetate **2** resulted from a broken C-9/C-11 β -bond of **1**, with concomitant loss of carbon atom C-11, together with the appearing of a new acetate group at carbon C-7. Interestingly, the C-9 α -H in **1** prevailed also as an α -H in **2**, but now in carbon C-7, so we reasoned that there was a chance that our new reaction could show some stereoselectivity as an added value. This fact was confirmed on a series of related drimanic alcohols (Table 1, entries 1–4).[†] In all cases analogous results, with the stereochemistry of C-7 on the product reflecting that of C-9 in the starting material, was observed.



Scheme 1 First example of the LTA oxidative fragmentation.

Table 1 Results of the oxidative fragmentation of several homoallylic alcohols. For their structures, see Scheme 1 and Fig. 1[†]

Entry	Substrate	Product	Yield (%)
1	1	2	87
2	3	4	85
3	5	6	80
4	7	8	81
5 ^a	9	—	—
6	12	13	85
7 ^a	14	—	—

^a See main text for a full explanation.

In order to evaluate the applicability of this reaction, and to learn more on its behavior, we decided to run our reaction with a set of different homoallylic alcohols (Table 1). When cholesterol (**9**, entry 5) was submitted to reaction, the starting material was consumed only after 20 days of continuous reflux and in the presence of a 20-fold excess of LTA, giving a very complex mixture of compounds containing no ketone or aldehyde, that after a very tedious chromatographic separation, produced two diastereomeric epoxide-acetate products: **10** (3% yield) and **11** (2.5% yield).¹¹ This result showed clearly that for our reaction to take place, both the unsaturation and the OH group had to be accessible by the Pb active species from the same side of the molecule. This feature limits the reaction scope but, at the same time, makes it more interesting and intriguing. A confirmation of the reaction behavior came from the next two experiments. When *endo*-5-norbornen-2-ol (**12**, entry 6) was submitted to reaction with LTA, it smoothly produced aldehyde-acetate **13** in good yield. In contrast, when epimeric *exo*-alcohol **14** (entry 7) was submitted to identical conditions, no product was observed even after a 24 h reflux. Again, *exo*-alcohol **14** did not allow complexation of the OH and C=C double bond to take place by an intermediate metal species.

A mechanistic rationalization for this reaction, which is in agreement with our observations is shown in Scheme 2. The first step should be a ligand exchange of one of the acetate groups on LTA by the unsaturated alcohol **15**, with concurrent expulsion of one molecule of AcOH, to produce complex **16**.¹⁰ Next step might be the release of the carbonyl compound product **17**, by a

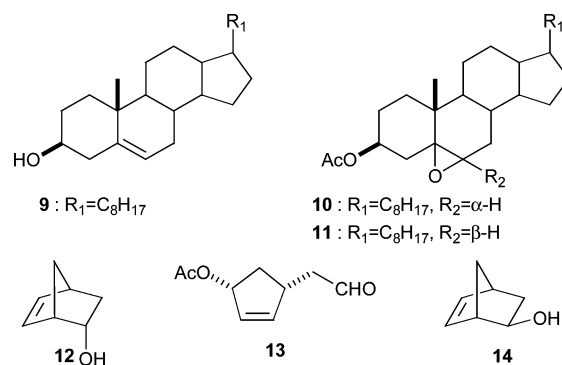
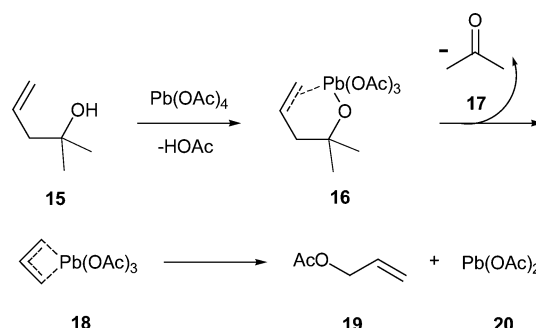


Fig. 1 Starting materials used, and products obtained.



Scheme 2 Mechanistic rationale for the LTA-mediated oxidative fragmentation of homoallylic alcohols.

fragmentation of complex **16** β -bond, presumably to produce a π -allyl complex of type **18**,^{12,13} that finally would transform into an allyl acetate of type **19**, by a ligand coupling reaction between the complexed allyl group and one acetate group bonded to Pb,¹⁴ and simultaneous release of lead(II) acetate (**20**).¹⁵ At this point, we can not rule out the intermediacy of radical or cationic species.¹⁶

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Notes and references

† General procedure for the LTA oxidative fragmentation of homoallylic alcohols: Fragmentation of **1** to **2**: to a solution of **1** (36 g, 0.162 mol) in benzene (500 mL), LTA (71.8 g, 0.162 mol) was added. The resulting colorless to slightly yellow solution was heated to reflux for 2 h, or until TLC analysis showed the total consumption of the starting material. A white to grayish precipitate of lead(II) acetate appeared, that had to be filtered off, and the filtrate was diluted with EtOAc, washed several times with water, dried, and evaporated. If the aqueous phase became dark brown (a sign that too high an excess of LTA was being used, that turned into PbO₂ by reaction with water), a dilute hydrochloric acid wash, followed by a NaHCO₃ wash helped in handling the organic phase. Compound **2** (35.3 g, 87% yield) was obtained as a colorless oil after column chromatography.

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- Lead(II) acetate precipitated during the reaction due to its very low solubility in non-polar solvents, and was fully characterized.⁹ No other Pb species were observed.
- There are previously reported examples of reactions of Pb(IV) with both radical¹⁰ and cationic⁵ intermediates.