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REACTIONS WITH LEAD TETRAACETATE. I.

OXIDATION OF SATURATED ALIPHATIC ALCOHOLS. PART 1

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IT was recently shown that various steroid alcohols could react with lead tetraacetate in non-polar solvents to give tetrahydrofuran (1,2) and tetrahydropyran derivatives (3), cyclization occurring when the position of and the distance between the reacting hydroxyl group and the δ - or ϵ -methyl, methylene or methine group were favourable to ring closure.

While in hydroxy steroids one or both of the reacting centers are geometrically fixed, this is not the case in acyclic alcohols. Because of free rotation, these alcohols can attain a large number of conformations, either favourable or unfavourable to the cyclization reaction. Moreover, some of the possible conformations could allow not only ring closure to five-membered heterocycles, but the formation of six-membered and higher cyclic ethers as well.

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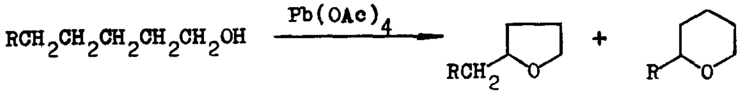
For that reason we have investigated the action of lead tetraacetate on saturated aliphatic alcohols with unbranched chains containing seven to nine carbon atoms. The reaction between primary alcohols, 1-heptanol (Ia) and 1-octanol (Ib), and the tetravalent lead compound (molar ratio 1:1), in boiling benzene, was completed after about one hour. The major products were pleasant smelling, volatile compounds, which did not contain carbonyl, hydroxyl or acetoxy groups. According to analytical data and I.R. spectra, these compounds were either tetrahydrofuran or tetrahydropyran derivatives.



I II III

a) $R = C_2H_5$; b) $R = \underline{n}\text{-}C_3H_7$

By comparison with authentic samples, synthesized by independent routes, it was proved that these ethers were 2-n-propyltetrahydrofuran (IIa) and 2-n-butyltetrahydrofuran (IIb), respectively. Their yields amounted to approximately 36-37%.[b] In addition, by careful gas-chromatographic separation of the oxide fractions, small amounts of the isomeric 2-alkyl tetrahydropyrans (III) were isolated, their yields not exceeding 3%. These compounds were identified by com-

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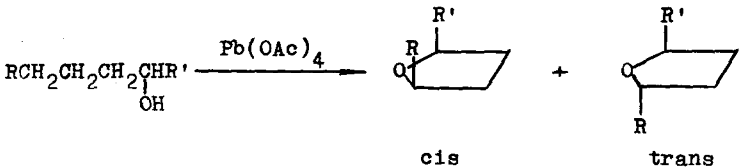
[b] By modification of the oxidation procedure and isolation technique, the yields of 2-alkyl tetrahydrofurans (II) were subsequently improved and amounted to about 50%.

parison of their retention times and I.R. spectra with those of authentic 2-ethyltetrahydropyran (IIIa) and 2-n-propyltetrahydropyran (IIIb).

Secondary alcohols, 2-octanol (IVa) and 5-nonanol (IVb), reacted more slowly than the primary alcohols, and about three hours in boiling benzene were needed for the complete consumption of lead tetraacetate (when the molar ratio used was 1:1). These alcohols furnished also oxide fractions which were separated by gas chromatography in two components.



IV V

a) $R = \underline{n}\text{-}C_3H_7$, $R' = CH_3$

b) $R = CH_3$, $R' = \underline{n}\text{-}C_4H_9$

It was shown that both these components were five-membered cyclic ethers, while the isomeric tetrahydropyrans were not found among the reaction products. In both cases (IVa and IVb) one of the oxido compounds proved to be identical with the 2,5-dialkyl tetrahydrofuran (V) prepared by Raney nickel hydrogenation of the corresponding furan derivative,[c] and

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[c] The Raney nickel hydrogenation of 2,5-dialkyl furans afforded only one isomeric form of the corresponding 2,5-dialkyl tetrahydrofurans.

the other oxide, on the basis of its I.R. spectrum, appeared to be the geometrical isomer. The fact that the cis and trans forms of V were obtained in nearly equal amounts (from IVa as well as from IVb), indicates that cyclization of aliphatic alcohols by means of lead tetraacetate is not a stereospecific reaction. The yields of 2-methyl-5-n-propyltetrahydrofuran (Va) and 2-methyl-5-n-butyltetrahydrofuran (Vb) were 30% and 20%, respectively.[d,e]

By increasing the amount of oxidizing agent to 1.5 and 2 moles (per mole of alcohol), the time required for complete consumption of lead tetraacetate was considerably increased, but the yields of cyclic ethers were not noticeably improved.

Other products of the oxidation of primary and secondary alcohols were the corresponding carbonyl derivatives, isolated in low yields (2-5%), the acetates of the starting alcohols and high-boiling, so far unidentified material. In addition, a certain amount of starting alcohol was always recovered unchanged, even when an excess of lead tetraacetate was used.

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[d] By improving experimental conditions, these yields were later increased to about 40% and 30%, respectively.

[e] After this work was completed, Eschenmoser et al. (4) reported the cyclization of an acyclic alcohol (in 15% yield) by means of lead tetraacetate.

Since cyclization of aliphatic alcohols by means of lead tetraacetate provides a direct and useful route to 2-alkyl tetrahydrofurans and 2,5-dialkyl tetrahydrofurans, the application of this reaction to other aliphatic alcohols is being the subject of further investigations.

A more detailed account of this work will appear elsewhere.

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