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LEAD (IV) ACETATE OXIDATION OF UNSATURATED CARBOXYLIC ACIDS, ESTERS AND AMIDES. THE MECHANISM OF THE REACTION

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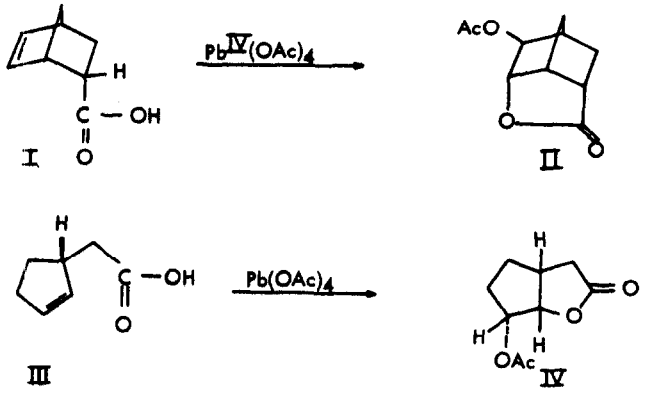
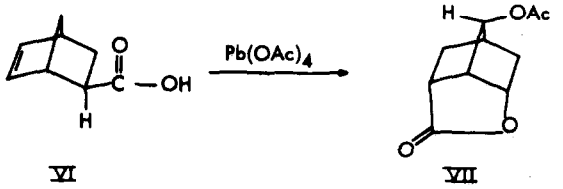
Lead tetraacetate oxidation of saturated carboxylic acids causes decarboxylation with formation of the corresponding lower acetate and alkene[1]. Kochi[2] has presented excellent evidence in support of a free radical chain mechanism for the oxidative decarboxylation.

In the case of certain unsaturated carboxylic acids the oxidation takes a markedly different course. Instead of oxidative decarboxylation, intramolecular acetoxy lactone formation occurs[3]. We wish to report on the synthetic utility of this reaction as well as the mechanistic pathway by which it proceeds. Typically endo-5-carboxy-bicyclo [2,2,1]hept-2-ene (I), upon lead tetraacetate oxidation in either benzene or pyridine, was found to yield acetoxy lactone II[4a] in 80% yield. Similar oxidation of Δ^2-cyclopentenyl acetic acid (III) yielded acetoxy lactone (IV)[5] in 70% yield. Only in the oxidation of endo-5-carboxybicyclo[2,2,2]oct-2-ene (V) was substantial decarboxylation observed, and about 15% of the known 5β-acetoxy-6α-hydroxybicyclo [2,2,2]octane 2α-carboxylic 6α-lactone (VI)[4b] was obtained[6].

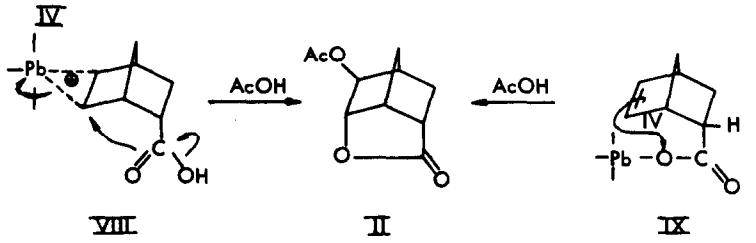


Lead tetraacetate oxidation of exo-5-carboxybicyclo[2,2,1]hept-2-ene (VI) yielded an acetoxy lactone isomeric with II in 70% yield. The isomer, m.p. 114-114.5°C $\nu c = 0$, 1725, 1775 cm^{-1} m/e 196, is assigned structure VII on the basis of its spin decoupled n.m.r. spectrum, fragmentation pattern in the high resolution mass spectrum and chemical degradation[7]. Saponification yielded the dihydroxy lactone, $\nu c = 0$, 1780 cm^{-1}, m.p. 203-204°. Oxidation with chromium trioxide-pyridine yielded the keto lactone, $\nu c = 0$, 1780 cm^{-1}; the derived 2,4-dinitrophenylhydrazone had m.p. 262-263°(d); $\nu c = 0$, 1780 cm^{-1}.



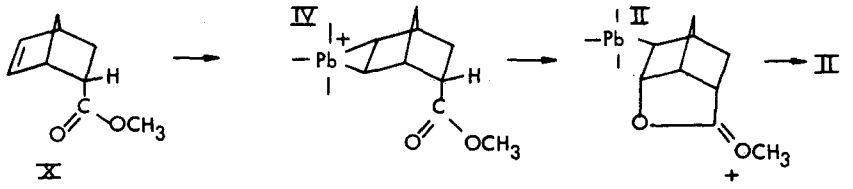
The mechanism(s) of the above cyclizations could involve either (a) initial electrophilic addition of lead tetraacetate to the double bond followed by intramolecular

nucleophilic opening by the carboxylate function (for I: VIII → II), or (b) initial lead carboxylate formation with cyclization proceeding via participation of the double bond (IX → II).

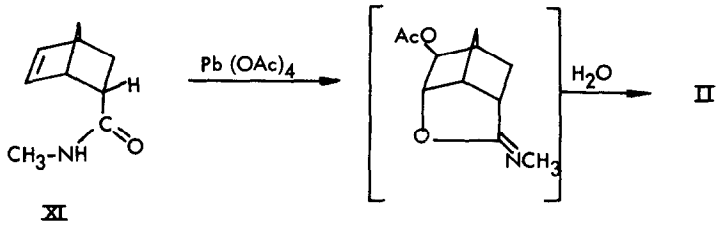


The first pathway is reasonable on the basis of the known reaction of norbornene with lead tetraacetate to yield 2,7-syn-diacetoxynorbornane[8]. On the other hand, the oxidative decarboxylation or endo-2-carboxynorbornane must certainly involve a lead carboxylate intermediate[9].

In order to decide between the two alternative sequences, the oxidation of methyl endo-5-carboxy bicyclo[2,2,1]hept-2-ene (X) was carried out. The same acetoxy lactone II was obtained as is formed in the oxidation of the free acid(I). Furthermore, the saturated analog, methyl endo-5-carboxybicyclo[2,2,1] heptane, is completely unreactive under the oxidation conditions. Thus, addition to the double bond followed by intramolecular opening by the carbomethoxy group is strongly indicated for the norbornene system.



In order to test the generality of such intramolecular participation in lead tetraacetate oxidations of olefins several other functional groups were examined[10]. Interestingly endo-N-methyl-5-carboxamidobicyclo [2,2,1] hept-2-ene (XI)[11] does not yield the corresponding acetoxy N-methyl lactam upon lead tetraacetate oxidation, but rather acetoxy lactone II[12].



XI

Lead tetraacetate oxidation of exo-N-methyl-5-carboxamido [2,2,1] hept-2-ene (XII)[11] yielded acetoxy lactone (VII). The saturated analogs, endo and exo-N-methyl carboxamido [2,2,1] heptane, do not react under the standard oxidation conditions.

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3. Intramolecular acetoxy lactone formation in the lead tetraacetate oxidation of unsaturated carboxylic acids has been reported by others, although for the most part the acetoxy lactone was only a minor product. For example, in the oxidation of methyl fumaropimarate, W. H. Ayer and C. E. McDonald, Canad. J. Chem., 43, 1429 (1965), and in the oxidation of norquassinic acid, Z. Valenta, A. H. Gray, S. Papadopoulos and C. Podesva, Tetrahedron Letters, 20, 25 (1960).

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5. R. K. Hill and A. G. Edwards, Tetrahedron, 21, 1501 (1965). The parent alcohol, 2,3-dihydroxy-1-cyclopentyl acetic acid α-lactone is reported. The acetate is new and has b.p. 118-120° (1.1mm), n_D^{22} 1.4778, ν_C = 0, 1782, 1725 cm^{-1}.

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7. Details of the structure proof of acetoxy lactone VII will be presented in the full paper. Correct analyses were obtained for all new compounds. Mass spectra were determined on an AEI MS-9 double focusing mass spectrometer.

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10. Intramolecular participation by the hydroxyl group in lead tetraacetate oxidation of unsaturated alcohols has already been observed in the norbornene series: R. M. Moriarty and K. Kapadia, Tetrahedron Letters, 1165 (1964).

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12. Lactone formation has been observed in the bromination of amides of 2,2-diphenyl-4-pentenoic acid, P. N. Craig, J. Am. Chem. Soc., 74, 129 (1952).