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SECTION A4

Propriétés chimiques et réactions nouvelles.

Chemical properties and new reactions.

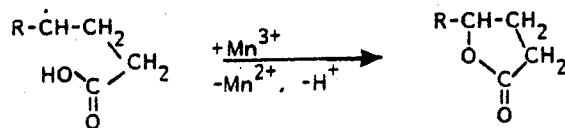
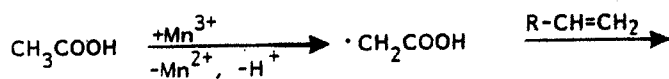
FREE RADICAL ADDITIONS TO METHYL OLEATE

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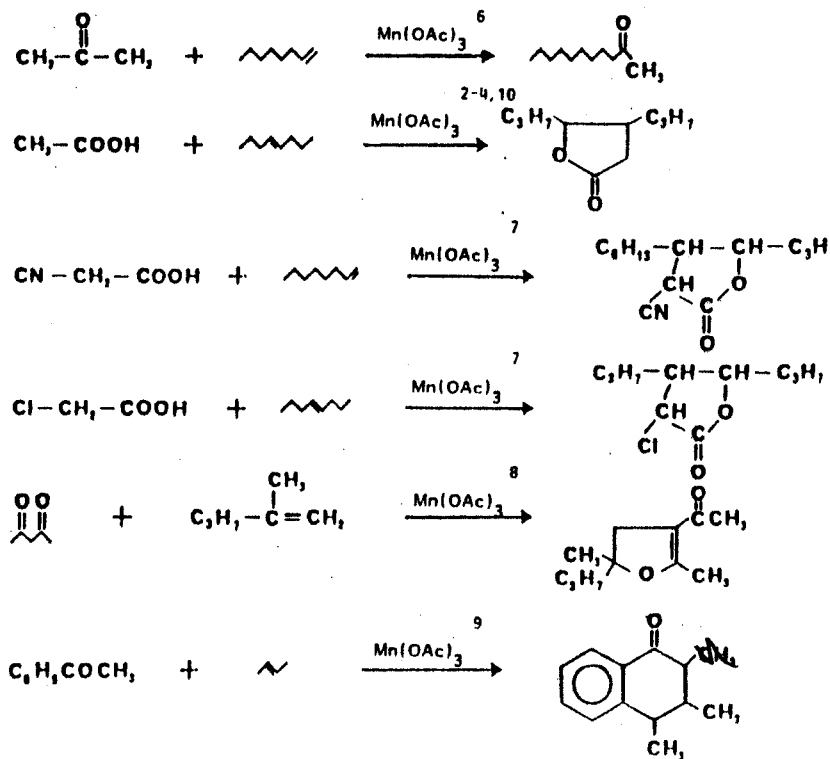
INTRODUCTION

Unsaturated fatty acids such as oleic acid are 1,2-dialkyl substituted alkenes, which can be functionalized by free radical addition to the C.C-double bond. Free radical addition especially of sulfur-, phosphorus- and carbon-centered radicals to methyl oleate and oleic acid have been described¹. We wanted to extend the spectrum of carbon-centered radical additions to methyl oleate. The double bond of methyl oleate is electron rich and therefore electrophilic carbon radicals are able to add to form functionalized and branched fatty acid compounds.

One method to generate electrophilic carbon-centered radicals is the oxidation of enolizable substrates with manganese(III)acetate. γ -lactones, are formed from olefines and acetic acid in one step in the presence of two equivalents of manganese(III) acetate²⁻⁴. The mechanism of lactone-annulation has been investigated in detail by Fristad et al.⁵.

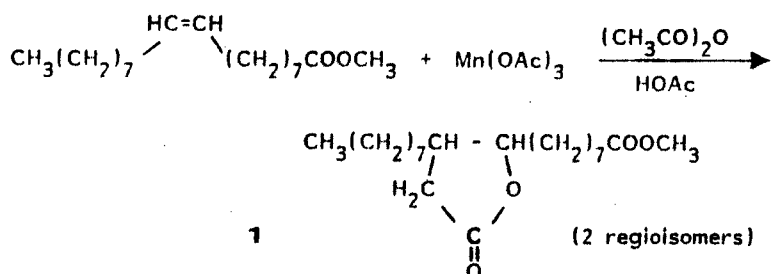


Some examples of the additions of enolizable substrates via electrophilic radicals to olefins (yields 30-100%) are given:



RESULTS AND DISCUSSION

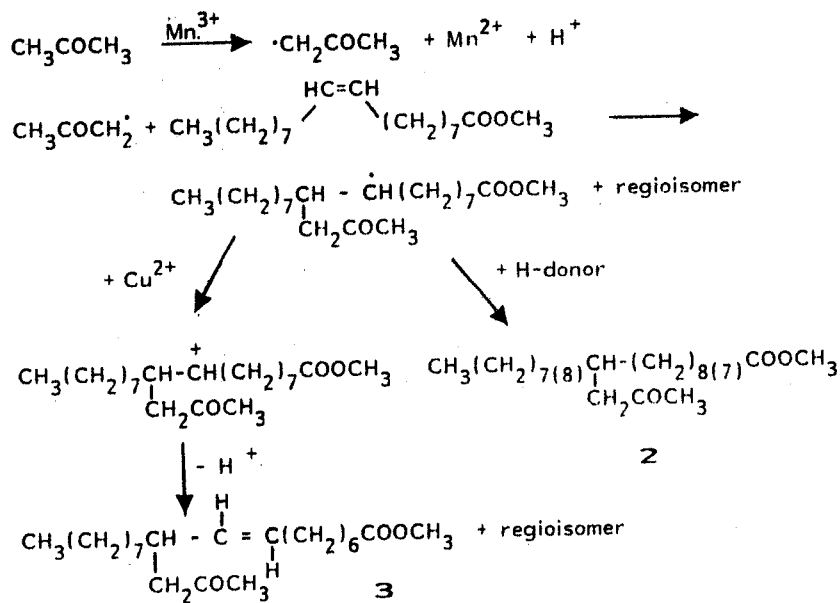
The reaction of methyl oleate with manganese(III)acetate in the presence of acetic acid and acetic anhydride gives 3,4-di-alkyl-substituted γ -lactones **1**. The degree of conversion of methyl oleate is 61% and the yield 54% (determined by GC).



Acetone as an enolizable compound is also a useful substrate for the reaction with manganese(III)acetate. Manganese(III)acetate oxidizes acetone to an acetylonyl radical which adds to the double bond of methyl oleate to form two regioisomeric adduct radicals. Now there are two possibilities for the radical to react:

1) with an H-donor (solvent or acetone) hydrogen transfer occurs and the regioisomeric methyl 9(10)-acetyonyl-stearates **2** are formed.

2) But addition of cupric acetate is an interesting method to form unsaturated branched fatty acid derivatives. Cupric acetate oxidizes the intermediate adduct radical to give a carbenium ion which forms a double bond by elimination of a β -proton¹¹ yielding E-methyl 9(10)-acetyonyl-10(8)-octadecenoate **3**. The stereospecific formation of the new double bond is remarkable.



The disadvantage of manganese(III)acetate as an oxidizing reagent is the use of an equimolar amount of manganese salt. We prepare manganese(III)acetate *in situ* by dropping a solution of potassium permanganate to a catalytic amount of manganese(II)acetate and apply only 20% of the manganese salt needed in the original procedure⁶. Another

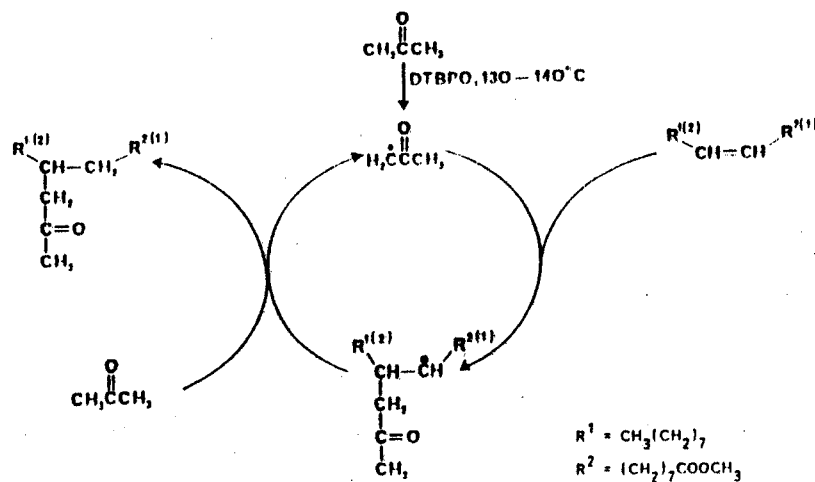
advantage of this method is an enhancement of the conversion of the oleate and of the yield of the addition product. Some results are listed in table 1.

Table 1: Manganese(III) Initiated Addition of Acetone to Methyl Oleate (100°C)

Ratio Mn(OAc) ₃ : methyl oleate	Conversion of methyl oleate [%]	Yield of addition product 2 [%] ^c
2.5 ^a	81	68
2.5 ^b	63	31
2.0 ^b	60	42
1.25 ^a	69	72
1.25 ^b	30	41
1.0 ^b	30	52

^a Manganese(III)acetate prepared *in situ*. ^b Manganese(III)acetate as salt. ^c GC; based on converted methyl oleate.

Addition of cupric acetate to the reaction mixture of methyl oleate, acetone, acetic acid and manganese(III)acetate generated *in situ* gives the regioisomeric addition-elimination products E-methyl 9(10)-acetyl-10(8)-octadecenoate **3** in 57% yield.



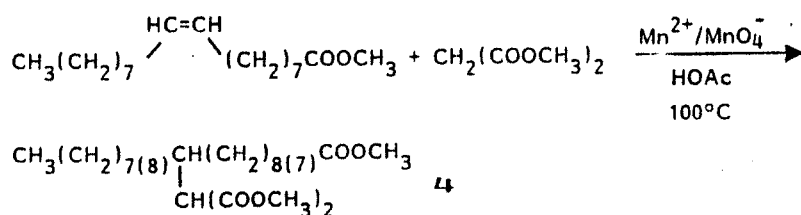
Acetone has been added to methyl oleate also in a free radical chain reaction initiated by di-tert.butylperoxide to yield the same addition product **2** as in the manganese(III) initiated addition. Some results are given in table 2.

Table 2: Di-tert.butylperoxide Initiated Addition of Acetone to Methyl Oleate (130 - 140°C).

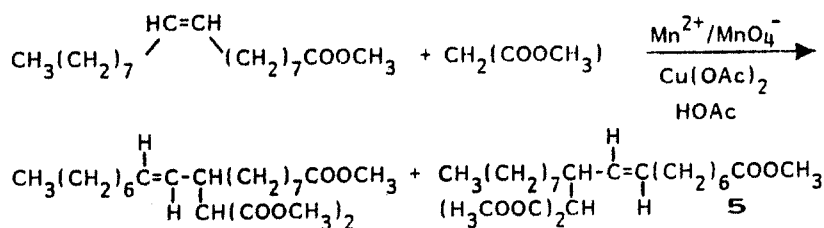
Ratio of educts ^a	Conversion of methyl oleate [%]	Yield of addition product 2 [%] ^b
10 : 1	53	86
4 : 1	82	76
2 : 1	84	55

^a Methyl oleate : di-tert.butylperoxide; solvens acetone. ^b 9(10)-Acetyl-stearate; based on converted methyl oleate.

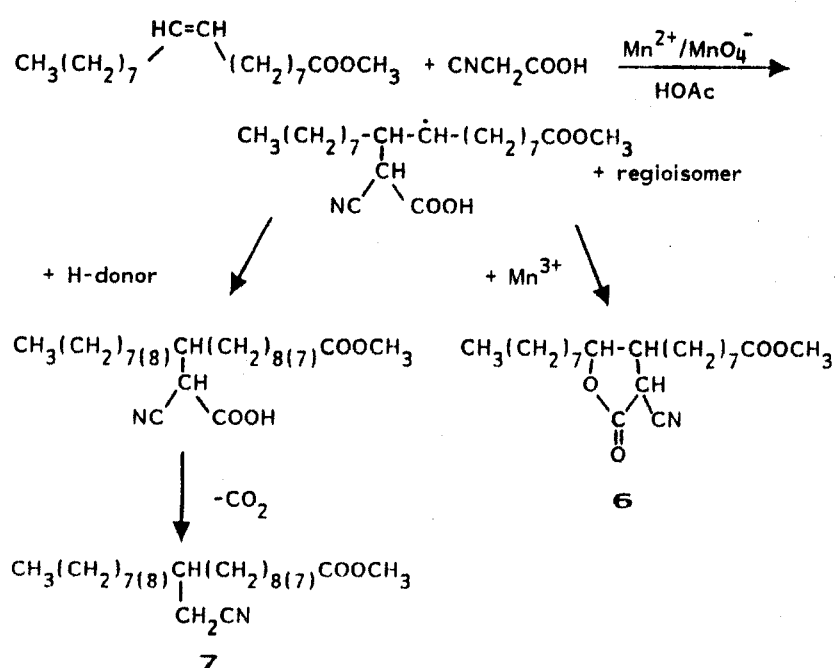
Di-alkyl malonates have been added to methyl oleate in the presence of manganese(III) acetate, prepared *in situ*, to form methyl 9(10)-(di-alkyl malonyl)-stearate **4**. With methyl or ethyl malonate the yields are 50 - 60% (GC).



Addition of cupric acetate forms analogously to the reaction with acetone the two regioisomeric E-methyl 9(10)-(dimethyl malonyl)-10(8)-octadecenoates **5** in 66% yield (conversion of methyl oleate : 65%).



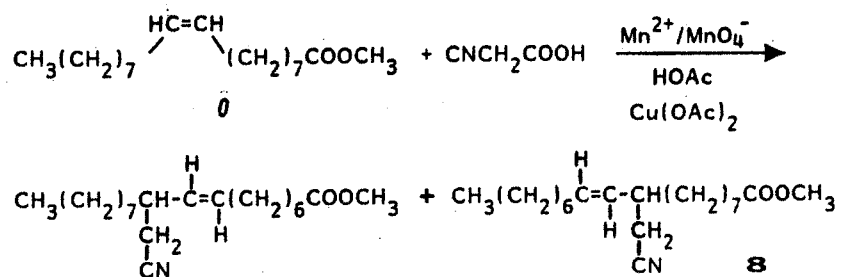
An interesting example is the reaction of cyano acetic acid and methyl oleate in the presence of manganese(III)acetate prepared *in situ*. In the first step manganese(III)acetate oxidizes the methylene group of cyano acetic acid to form a radical which adds to methyl oleate. Now there are two possibilities: 1) the intermediate adduct radical cyclizes to give the γ -lactone derivative **6** with simultaneous reduction of manganese(III). 2) The other variation is the transfer of a hydrogen atom from an H-donor to form the 9(10)-branched methyl stearate. Decarboxylation gives methyl 9(10)-(methylcyano)-stearate **7**.



The ratio of the products is variable. A large excess of cyano acetic acid (30 fold) as H-donor yields **7** as major product (30%) and the γ -lactone **6** as minor product. A smaller excess of cyano acetic acid (10 fold) leads to the γ -lactone **6** as major product (58%) and the nitrile is formed only in 6% yield. The degrees of conversion of methyl oleate are between 90% and 98%.

Addition of cupric acetate yields the unsaturated regioisomers E-methyl 9(10)-(cyanomethyl)-10(8)-octadecenoate **8** as major products (36%).

Cyclization to the lactone **6** occurs for 24%.



These examples show that radical additions to methyl oleate initiated with manganese(III)acetate, prepared *in situ*, is a useful method to form functionalized derivatives of fatty acids.

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