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Abstract of a thesis submitted to the Faculty of the Graduate School of the University of Maryland in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

THE ACTION OF
LEAD TETRAACETATE UPON
HYDROXYLATED FATTY ACIDS, ESTERS
AND RELATED COMPOUNDS

The oxidation of hydroxylated fatty acids, esters and related substances with lead tetraacetate (the Griegse reaction) has been studied. The oxidation of 9,10-dihydroxystearic acid yielded pelargonic aldehyde (n-nonanal) and azelaic half aldehyde (8-formyl-1-octanoic acid). Similarly, ethyl-9,10-dihydroxystearate yielded pelargonic aldehyde and the ethyl ester of azelaic half aldehyde; 9,10-dihydroxyoctadecanol yielded pelargonic aldehyde and 9-hydroxypelargonic aldehyde; 9,10,12-trihydroxystearic acid yielded α -nonenaldehyde and azelaic acid; hydroxylated castor oil yielded α -nonenaldehyde and azelaic acid.

The Griegse reaction has been modified and improved so that it is no longer necessary to isolate and purify either lead tetraacetate or the hydroxylated substances.

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By

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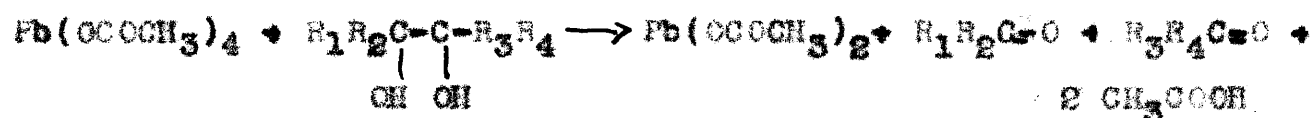
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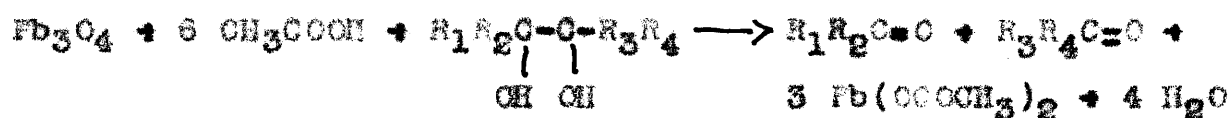
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I. INTRODUCTION

This investigation was undertaken for the purpose of studying the oxidizing action of lead tetraacetate on long chain hydroxylated fatty acids, esters, and related substances containing the α -glycol group ($-\overset{\text{OH}}{\underset{\text{OH}}{\text{C}}}-\text{C}-$) to produce aliphatic aldehydes. Since lead tetraacetate is prepared by the solution of red lead in glacial acetic acid, and since the oxidation of the hydroxy compounds is also carried out in acetic acid solution, it is merely necessary to dissolve the hydroxy compound in glacial acetic acid and to add the red lead in small portions. The lead tetraacetate which is formed reacts immediately with the hydroxy compounds in accordance with the following equations.



These equations may be combined.



This last reaction is the one upon which this investigation is based. The necessity of isolating and purifying lead tetraacetate is therefore obviated by utilizing the lead tetraacetate "in situ".

Since the hydroxylation of most of the unsaturated fatty materials is also carried out in acetic acid solution, in many cases it was found unnecessary to isolate and purify the hydroxylated derivative prior to treatment with red lead and acetic acid.

The aldehydes are one of the most reactive classes of organic compounds and a simple and economical method for preparing the higher aliphatic aldehydes would be very useful. The aldehydes may be used as intermediates in the preparation of fatty acids and alcohols, as starting materials in various types of condensations and syntheses, such as the aldol type condensation, acetal formation, the Knoevenagel synthesis, etc., and in the manufacture of plastics by combination with phenols, urea derivatives and amines. The aldehydes prepared in this investigation were pelargonic aldehyde (n-nonenal), azelaic half aldehyde (8-formyl-1-octanoic acid) and its ethyl ester, α -nonenal and 9-hydroxypelargonic aldehyde (8-formyl-1-octanol).

Pelargonic aldehyde has been isolated from rose oil (73), cinnamon oil (72), and lemon oil (69). It has been prepared synthetically by a variety of methods, most of which gave low yields of pelargonic aldehyde as well as undesirable by-products. It has been prepared by passing pelargonic acid over zinc dust at 300°C (46)(47), by vacuum distilling a mixture of the barium salts of formic and pelargonic acids (64), by the aqueous decomposition of the product formed from the reaction of octyl magnesium bromide with diethyl formamide (3), by distilling α -hydroxycapric acid at atmospheric pressure (1), and by passing a mixture of pelargonic and formic acids over titanium dioxide at 300°C (60), or over oxides of manganese (61). It has also been prepared by the exomolysis of oleic and elaidic acids (27)(28)(24)(44), oleyl alcohol (32), tetradecenoic

acid (71), and an aqueous solution of sodium oleate (27).

In a recent publication it was shown that pelargonic aldehyde could be prepared from 9,10-dihydroxystearic acid by oxidation with periodic acid (43).

Azelaic half aldehyde has been prepared by the ozonolysis of oleic, elaidic (24)(28)(29)(49) and ricinoleic acids (21). It has also been prepared by the oxidation of 9,10-dihydroxystearic acid with periodic acid (43). This aldehyde is very difficult to purify and keep for any length of time since it readily undergoes polymerization.

The ethyl ester of azelaic half aldehyde has been prepared by the ozonolysis of ethyl oleate (25).

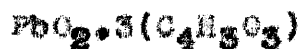
α -Nonenaldehyde has been prepared only with some difficulty. It has been prepared by treating heptaldehyde with malonic ester in a Knoevenagel synthesis (77), by the reduction of imide chlorides of the type $R-C(Cl)=NR'$ with chromous chloride (4), and from acrolein through a complex series of reactions (13).

α -Nonenaldehyde was also prepared by oxidizing 9,10,12-trihydroxystearic acid, prepared from ricinoleic acid, with lead tetracetate (78), but the investigators reported the aldehyde as 3-hydroxypelargonic aldehyde and not its dehydration product α -nonenaldehyde.

9-Hydroxypelargonic aldehyde was prepared in a pure state by the ozonolysis of oleyl alcohol (32). It was also prepared in an impure state by the oxidation of phloionolic acid, an acid present in cork, with lead tetracetate (78).

II. HISTORICAL

Since the time of Berzelius chemists have been aware that red lead (Pb_3O_4) is soluble in glacial acetic acid and a method for detecting and estimating certain impurities found in the commercial article has been based on this fact. The properties of this solution were little known until Jacquelin observed (39), as Dumas had before him, that a solution of red lead in aqueous acetic acid soon decomposed and deposited lead dioxide. He also found that the application of heat, as well as the addition of water, greatly accelerated the decomposition. He further observed that when he employed glacial acetic acid at $40^{\circ}C$ as the solvent, the solution deposited a crop of slender, colorless, oblique prisms on cooling. On filtering off these crystals of "acetate de bioxide de plomb", as he called them, and attempting to dry them between pieces of filter paper, Jacquelin found that they quickly turned brown decomposing into acetic acid and lead dioxide. On the addition of water this decomposition was complete and he was able to determine the percentage of acetic anhydride in the sample by titrating the aqueous solution with standard alkali. The lead was estimated as chloride in another sample. The results he obtained led him to adopt the following improbable formula for lead tetraacetate:



A few years later, Schönbein (65) made a similar observation on the solution of red lead in acetic acid. He

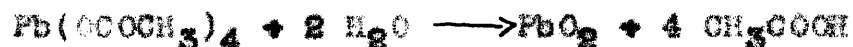
found that sulfuric acid precipitated only a part of the lead from this liquid leaving the "acetate of lead dioxide" in solution. Apparently Schönbein was not familiar with the work of Jacquelin nor did he appear to have obtained any crystals from his solution.

The first workers to recognize that lead tetraacetate was a definite chemical individual were probably Hutchinson and Pollard (36). They prepared lead tetraacetate by adding commercial red lead in small portions to hot glacial acetic acid until no more dissolved and lead dioxide commenced to precipitate out. The equation for this reaction is as follows:



The crystals which deposited on cooling were purified by recrystallization from hot glacial acetic acid. Several of the physical properties of lead tetraacetate are listed in Table I.

Hutchinson and Pollard found that lead tetraacetate was extremely sensitive to the presence of water and suggested that it might be used to detect moisture in gases. This property of lead tetraacetate may be used in its quantitative estimation as represented by the equation shown below.



* Lead Tetraacetate may also be prepared by the electrolysis of lead acetate in glacial acetic acid solution (53).

Table I. PHYSICAL PROPERTIES OF LEAD TETRAACETATE

M.P. 175°C (dec.)

$d_4^{16.9}$ 2.228

$d_4^{18.2}$ 2.218

Monoclinic, colorless, transparent prisms.

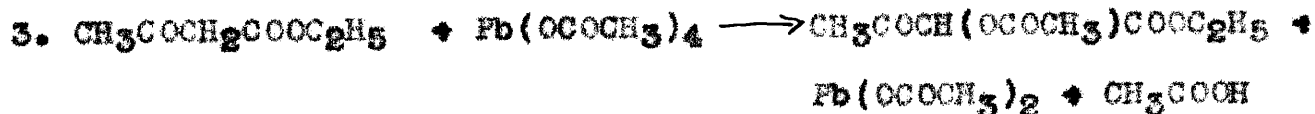
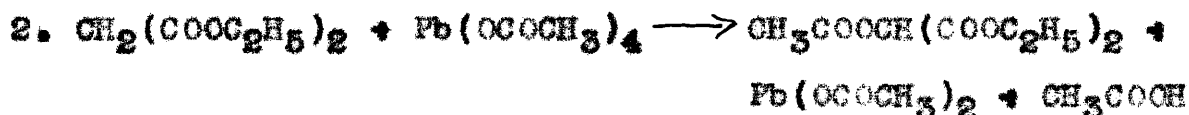
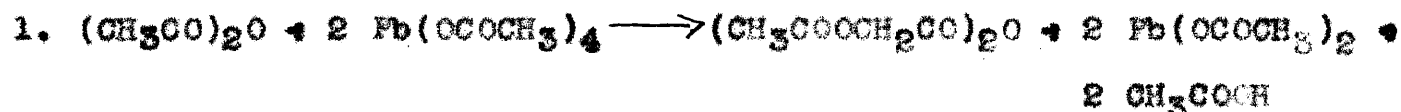
Soluble to the extent of 2.76 grams/100 grams of glacial acetic acid at 17°C.

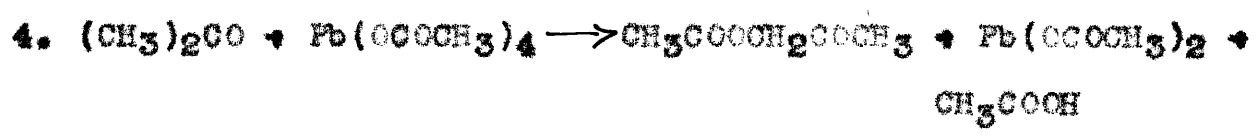
Easily soluble in cold chloroform, slightly soluble in ether and light petroleum and more so in benzene.

The acetic acid liberated may be titrated with standard alkali.

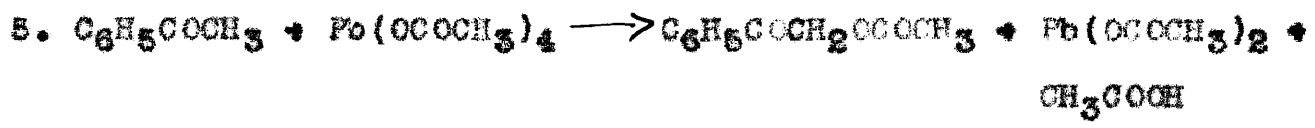
The work of Hutchinson and Pollard was devoted primarily to a study of the physical properties of lead tetraacetate. It was not until 1920 that Dimroth, Friedemann and Kämmerer (14) and Dimroth and Hilcker (15) found that lead tetraacetate could be used very effectively to oxidize certain hydroxyanthraquinone derivatives to anthraquinones. The attention in these last two pieces of research was not focussed on lead tetraacetate but on the diquinones obtained.

The first publication to devote itself to a study of the action of lead tetraacetate on various types of organic compounds was published by Dimroth and Schweizer in 1923 (16). They not only improved the method for preparing lead tetraacetate but showed that lead tetraacetate would react with certain compounds which contained hydrogen atoms alpha to a carbonyl or a carboxyl group. One or more alpha hydrogens are replaced by acetoxy groups (OCOCH_3). The following equations illustrate this mode of action of lead tetraacetate:

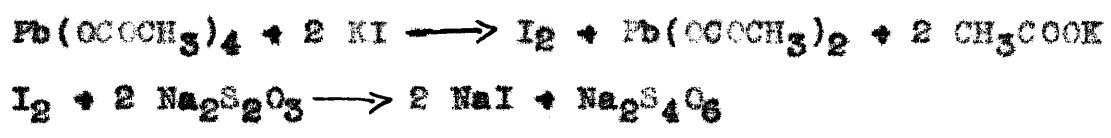




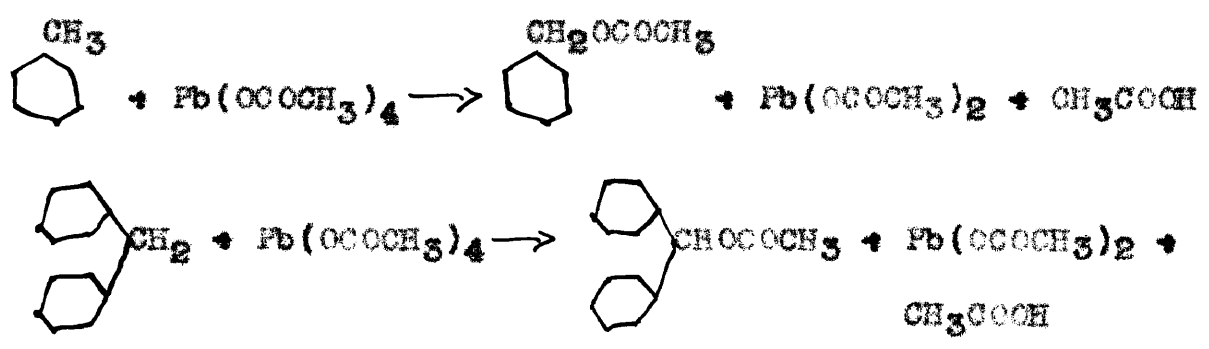
α,α-Diacetoxyacetone may be prepared by using a larger amount of lead tetraacetate and higher temperatures.

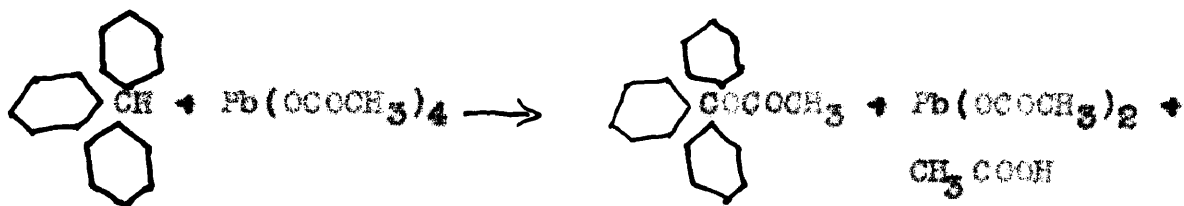


They found that lead tetraacetate may be employed to measure with a great deal of precision the lability of hydrogen atoms because the oxidation reaction may be followed by titrating the amount of unused lead tetraacetate according to the following equations:



In the case of homologues of benzene, they found that toluene, diphenylmethane and triphenylmethane were all oxidized to the acetates of the corresponding alcohols, the ease of oxidation increasing from toluene to triphenylmethane, benzene being unaffected.





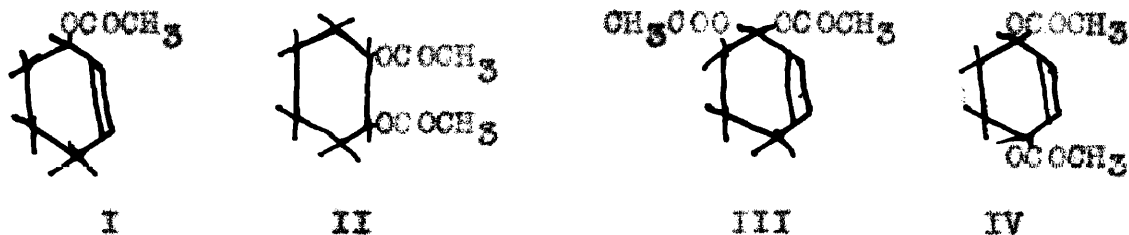
They also carried out a few experiments on the oxidation of unsaturated compounds. They found that anethole reacted smoothly with lead tetraacetate below 40°C to yield an acetylated derivative which was not definitely characterized. Hydrolysis of this product yielded 1-(p-methoxyphenyl)-1,2-propandiol in good yields. They merely mentioned the fact that stilbene reacted much more slowly than anethole to give a mixture of isomers, and safrole reacted very much more slowly than anethole. At the boiling point safrole reacted so violently that no products could be isolated.

In a very complete investigation, Griegee continued the work of Dimroth and Schweizer on the reaction of tetravalent lead salts with unsaturated hydrocarbons (7). He studied the preparation of lead tetraacetate, lead tetrapropionate, lead tetrabutyrate and lead tetrabenzoate and also their reactions with unsaturated hydrocarbons.

He found that lead tetraacetate reacted with unsaturated compounds primarily in two ways: (1) the simple addition of two acetoxy groups at the double bond, and (2) the replacement of hydrogen atoms by acetoxy groups, the double bond remaining unaffected. Usually both of the reactions took place concurrently.

Cyclohexene reacted with lead tetraacetate to yield mainly 2-cyclohexene-1-ol acetate (I) and cyclohexene-1,2-diol

diacetate (II). A small amount of a diacetate of cyclohexene-diol was also isolated. Its structure was believed to be either III or IV.



Indene reacted in essentially the same manner although the reaction was somewhat more complicated. Reaction took place in the five membered ring only.

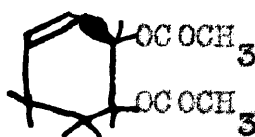
Cyclopentadiene reacted in the expected way to yield two main products, one of which was the result of a very interesting secondary reaction. The products were 3-cyclopentene-1,2-diol diacetate (V) and the monoacetate monoacetylglycolate of 3-cyclopentene-1,2-diol (VI), with the latter compound predominating.



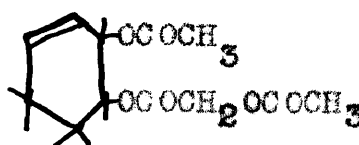
Compound VI resulted from the reaction of lead tetraacetate with V. This reaction is of the same type as that reported by Dimroth and Schweizer between acetone, acetic anhydride etc., and lead tetraacetate. The hydrogens in the acetoxy groups are alpha hydrogens and hence might be expected to react with lead tetraacetate.

Cyclohexadiene and lead tetraacetate yielded two products.

They were 3-cyclohexene-1,2-diol diacetate (VII) and the monoacetate monoacetylglycolate of 3-cyclohexene-1,2-diol (VIII).

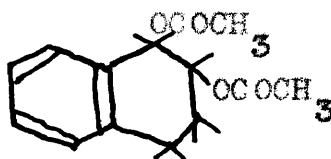


VII



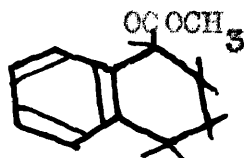
VIII

In addition to the above reactions, Criegee (7) found that a third type of reaction occurred to a lesser extent. This involved the dehydrogenation by lead tetraacetate of certain partially hydrogenated aromatic hydrocarbons. 9,10-Dihydroanthracene yielded a trace of anthracene when the reaction was carried out in acetic acid and a 30% yield of anthracene when the reaction was carried out in benzene. 1,4-Dihydronaphthalene gave a nearly quantitative yield of naphthalene. 1,2-Dihydronaphthalene gave a 20% yield of naphthalene, the remainder of the product being the diacetyl derivative of trans-1,2-dihydroxytetrahydronaphthalene (IX).



IX

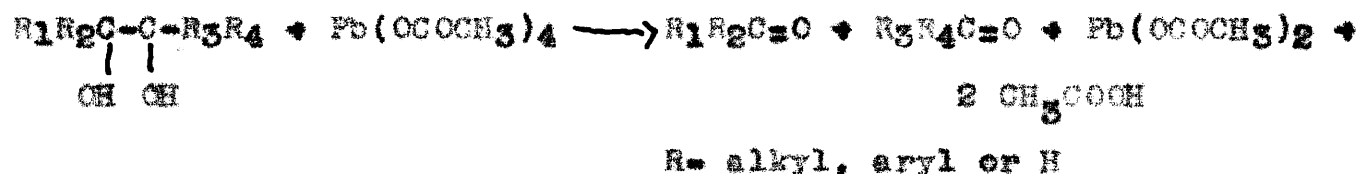
Tetrahydronaphthalene yielded 1-acetoxy-1,2,3,4-tetrahydronaphthalene (X).



X

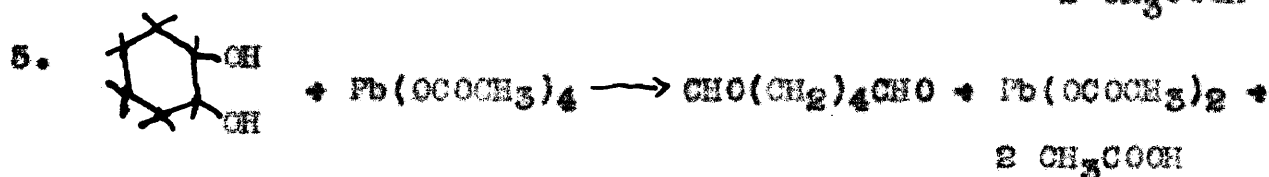
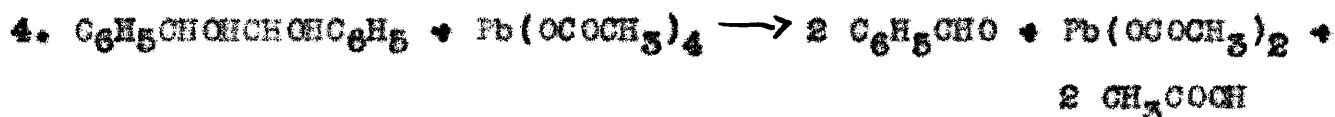
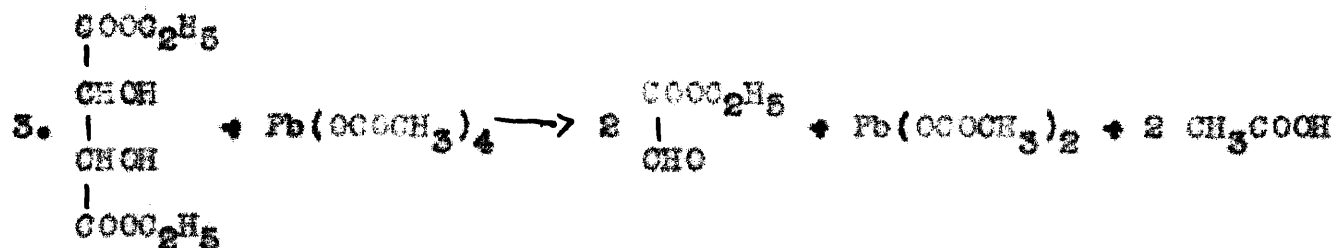
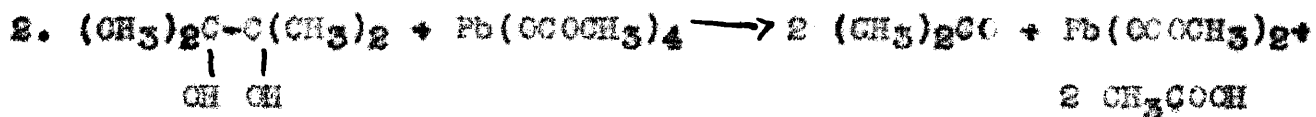
In a classic publication, Criegee (8) first demonstrated

that compounds which contained unsubstituted hydroxyl groups attached to two adjacent carbon atoms would react with lead tetraacetate. He showed that scission occurred between the carbon atoms holding the hydroxyl groups with the removal of two hydrogen atoms to yield aldehydes or ketones, depending on the nature of the other groups attached to the carbon atoms. The type equation for this reaction is as follows:

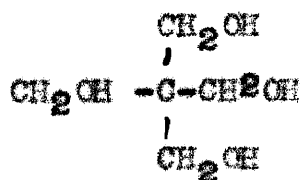


Although the mode of action of tetravalent lead salts on unsaturated compounds was complex and varied with the type of compound treated, the action of lead tetraacetate on 1,2-glycols was a smooth and usually almost quantitative reaction.

He found that the reaction was quite general, no exceptions being found in the large number of hydroxy compounds treated. He was able to prepare in very good yields two moles of formaldehyde from ethylene glycol, two moles of acetone from pinacol, two moles of ethyl glyoxylate from diethyl tartrate, two moles of benzaldehyde from hydrobenzoin, one mole of anisaldehyde from anetholeglycol, and from cis- and trans-cyclohexanediol-1,2 one mole of adipic dialdehyde. With polyhydroxy compounds such as the sugars, the reaction was naturally more complicated, although it worked satisfactorily to show the presence of adjacent hydroxyl groups in monosacetoneglucose.



The reaction leading to the production of aldehydes is extremely specific. The only compounds which will react with lead tetraacetate in this way are those which contain two free hydroxyl groups on adjacent carbon atoms. Monohydroxy compounds or those hydroxyl compounds which contain one or both of the hydroxyl groups substituted will not react. Particularly illuminating is the case of pentaerythritol (XI) which does not react in spite of its four hydroxyl groups because no two hydroxyl groups are attached to adjacent carbon atoms.



XI

The advantages of lead tetraacetate over other oxidizing agents are, (1) the oxidation may be carried out in a homogeneous medium, (2) the reaction is usually so rapid that low temperatures are required, (3) the oxidation stops at the aldehyde or ketone stage, and (4) the reaction gives comparatively high yields of aldehydes or ketones. This reaction may be used for the preparation of carbonyl compounds, for the qualitative detection of α -glycols and particularly as an aid in establishing the constitution of certain natural products.

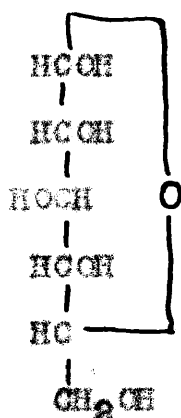
In a later paper, "glycol splitting", so called, was investigated more thoroughly by Criegee and his co-workers (12). They showed that lead tetraacetate would not only react with various types of compounds containing the α -glycol group ($\text{-}\overset{\text{OH}}{\text{C}}\text{-}\overset{\text{OH}}{\text{C}}\text{-}$), but would also react with α -hydroxy acids, α -amino acids and α -hydroxy amines. They studied the velocity of the reaction in various solvents and under varying conditions and advanced a mechanism for the oxidation of α -glycols with lead tetraacetate. Approximately 32 compounds were oxidized and the velocity of reaction in some cases was shown to be as much as 60,000,000 times as great as in others. Some of the compounds oxidized were cis- and trans-acenaphthenediol, cis- and trans-1,2-diphenylacenaphthenediol, cis- and trans-hydrindenediol, cis- and trans-cholestanetriol, meso-dimethyl tartrate, α -acetyl glycerol, etc. They found that cis-diol compounds reacted much faster than their trans-isomers, without exception. The greater part of this publication (12)

was devoted to a study of reaction mechanism and reaction rates, which will be discussed in the THEORETICAL section.

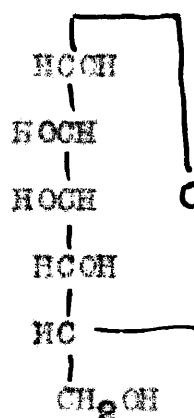
Since the prediction by Criegee (8) that lead tetraacetate could be used as an aid in establishing the constitution of both natural and synthetic products which contain the proper glycol structure, a great many papers have been published bearing out his prediction completely. The compounds studied have been of a great variety of types and no exceptions to the generality of this reaction have as yet been found.

Criegee, in a paper entitled "A New Method for the Determination of Ring Structure in Sugars and in Sugar Derivatives" (9), showed that lead tetraacetate could be used to determine the presence of at least two free adjacent hydroxyl groups in these types of compounds (cf. 48, 35). By measuring the amount of formaldehyde obtained and comparing it with the amount one would expect to get, it was possible to ascertain whether the end two carbon atoms in the sugar molecule were free or not. It was not sufficient merely to prove that formaldehyde was formed, but its quantitative estimation was essential since the presence of three or more free adjacent hydroxyl groups would give a mixture of formaldehyde and other aldehydes. Thus, d-glucose, if treated in this way should give no formaldehyde if it contains a pyranose ring (XII). This was borne out experimentally. d-Mannose (XIII) behaved in a similar manner. Since these reactions were carried out at comparatively low temperatures, no rearrangement would be expected. With but two exceptions out of the many

compounds studied, the structures as worked out by Irvine, Haworth, Freudenberg, etc., were corroborated.



XII



XIII

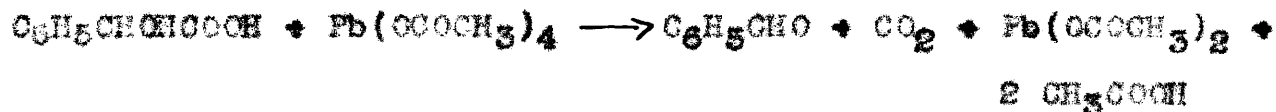
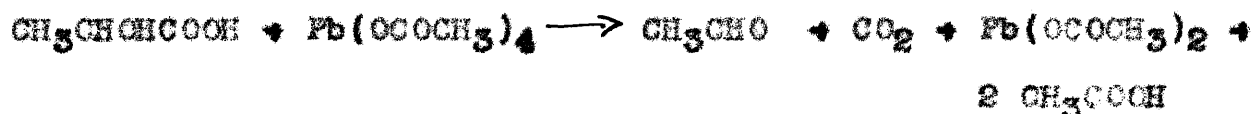
The position of the double bonds in certain plant pigments such as crocetin, bixin and others (41)(42) was determined by hydroxylation of the double bonds, scission of the resulting glycol with lead tetraacetate and identification of the resulting aldehydes and ketones.

That α -glyceromonephosphoric acid could be determined in the presence of the β -compound by utilizing lead tetraacetate was demonstrated by Carrarra (5) and Pyman and Stevenson (57). Since only the α -form reacted, by using an excess of lead tetraacetate and titrating the unused portion, the amount of α -compound was estimated.

Heilbron, Morrison and Simpson (31) showed that one of the double bonds in the ergosterol nucleus (either between C₅-C₆ or C₇-C₈) was particularly reactive. The addition of two hydroxyl groups took place only at this double bond as shown by the fact that a keto-aldehyde was obtained on treatment with lead tetraacetate. This type of compound would only occur if hydroxylation had occurred in one of the

rings. Similarly, hydrogenation took place at this same double bond. Ozonization of either the hydroxylated or hydrogenated product resulted in the formation of methyl isopropyl acetaldehyde, indicating that the side chain was unaffected by hydroxylation or hydrogenation.

It had been mentioned by Criegee that lead tetraacetate could be used to oxidize α -hydroxy acids. This was investigated in some detail by Ôeda (53). α -Hydroxy acids have analogous structures to 1,2-glycols and might be expected to react with lead tetraacetate in a similar manner. This was shown to be the case. Ôeda oxidized lactic, leucic, mandelic, β -phenyllactic and p-hydroxyphenyllactic acids. The reaction of this type may be illustrated by means of the lactic acid and mandelic acid oxidations.

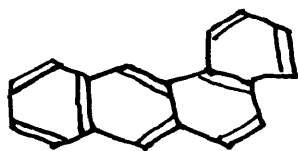


Oxidation of α -hydroxy acids may be carried out with other oxidizing agents but the reaction usually proceeds beyond the aldehyde stage and often does not give good yields of desired products. In the oxidation with lead tetraacetate, the reaction runs very smoothly at moderate temperatures and stops at the aldehyde stage.

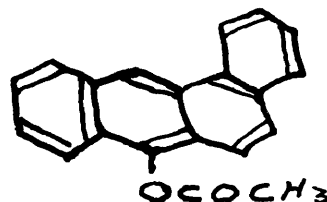
In a study of the esterification of higher fatty acids with glycerol, lead tetraacetate was used to good advantage

to distinguish between α - and β -glycerides (54). Lead tetraacetate has also been used to distinguish between mono- and di-triethylglycerol (70).

A very interesting reaction between lead tetraacetate and certain polynuclear aromatic compounds was reported recently by Mason and Herzberg (17). They found that 1,2-benzanthracene (XIV) reacted with lead tetraacetate to give the 10-acetoxy derivative (XV).

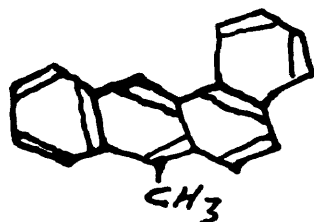


XIV

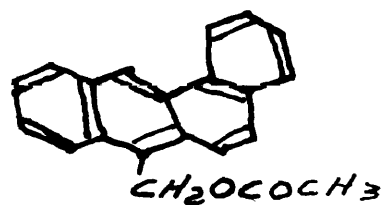


XV

Of the two none positions available, the less hindered none position at carbon 10 was the chief point of attack. That the none position at carbon 9 was hindered after reacting was shown by the fact that 10-methyl-1,2-benzanthracene (XVI) reacted with lead tetraacetate to give 10-acetoxymethyl-1,2-benzanthracene (XVII).



XVI

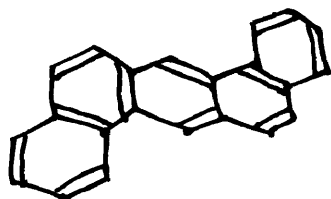


XVII

The oxidation of aliphatic side chains is not new (16)(17). That is obvious. It is that the methyl group is attached in preference to the none position 9. Mason and Herzberg (17)

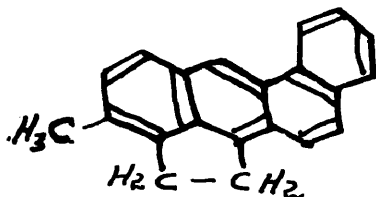
are inclined to attribute this effect to steric hindrance and it may be noted that the 9-position of 1,2-benzanthracene corresponds to position 4 in the phenanthrene system present in the molecule and that there are definite indications of hindrance at this position in phenanthrene.

As might be expected, 1,2,5,6-dibenzanthracene (XVIII) does not react with lead tetraacetate since both meso positions are subject to identical hindrance effects.

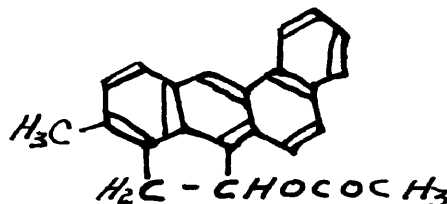


XVIII

In a continuation of this work (18), they found that methyleneanthrene (XIX) reacted with lead tetraacetate to give a new acetoxy derivative (XX) in 90% yield.



XIX



XX

3,4-Benzopyrene also yielded an acetoxy derivative in 90% yield, but the position of the acetoxy group was undetermined.

Up to the present time very little work has been done on the oxidation of hydroxylated fatty acids and related compounds with lead tetraacetate. In a study of the oxidation products of the unsaturated fatty acids of linseed oil (52), Nunn and Smedley-Maclean reported that the position of adjacent hydroxyl groups in dihydroxystearic acid and

sativic acid was determined by Criegee's method. It was the purpose of their investigation merely to show the presence and the position of the hydroxyl groups which they did by identifying certain of the aldehydic products.

Similarly, in an investigation of the constitution of two hydroxy acids isolated from cork (78), the position of adjacent hydroxyl groups was demonstrated by oxidation of the hydroxy acids with lead tetraacetate and identification of the aldehydic fragments. Thus, the constitution of phloionic acid (XXI) and phloionolic acid (XXII) was shown to be as follows:



XXI



XXII

The first publication to report the use of red lead and glacial acetic acid as the oxidizing agent instead of lead tetraacetate was that of Montignie (50). He warmed cholesterol with a mixture of red lead and acetic acid and hoped to obtain ketones. Although he isolated no ketones, he obtained a mixture of acetates.

Ward (74)(75) applied this modified procedure to the oxidation of certain terpenes. The terpene - - pinene, dipentene, terpinolene or α -terpinene - - was dissolved in glacial acetic acid and the red lead was slowly added. He found that the products obtained in this way were the same

as those obtained by using pure lead tetraacetate as the oxidizing agent. Ward, however, pointed out that

the ratio of low boiling to high boiling acetates is much higher when lead tetraacetate is used. Such differences are to be expected because a number of factors differ where red lead and acetic acid are used. Some of these factors include the acidity of the solution, the introduction of water from the reaction of red lead and acetic acid, and the presence of a solid phase with each addition of red lead.

These slight differences in action should not be observed in the oxidation of α -glycols by this modified method since only one mode of oxidation is possible, namely "glycol splitting". In the case of unsaturated compounds, it has already been pointed out that several types of reaction can and do take place. One reaction might be favored over the other under different conditions of acidity, percentage of water or the presence of a solid phase.

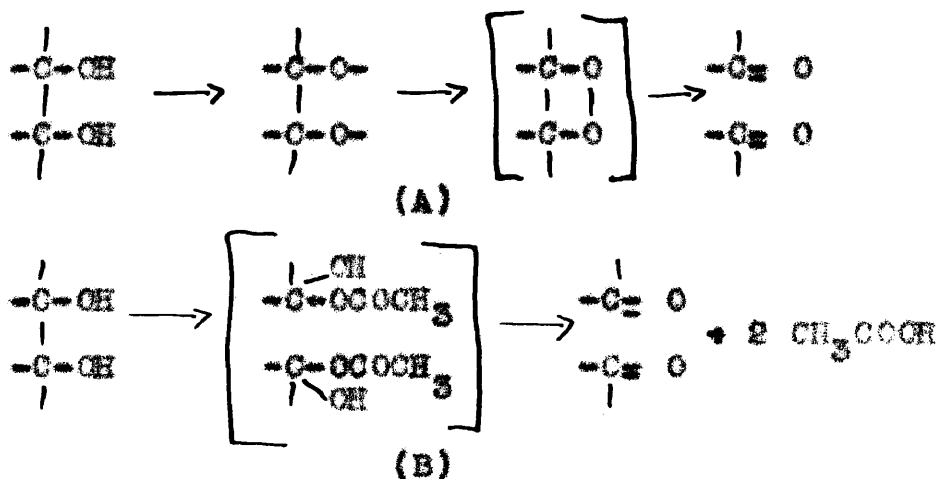
Although lead tetraacetate is not difficult to prepare, it can only be stored under strictly anhydrous conditions and the usual manipulations of the laboratory (weighing, transferring, etc.) cause decomposition of the substance to take place. Solution of the compound to be oxidized in glacial acetic acid and the addition of red lead in small portions eliminate the necessity of isolating lead tetraacetate, thereby saving a great deal of time and effort. As the lead tetraacetate is formed, it is used up in the oxidation. As far as can be ascertained, this method of oxidation has never been applied to compounds containing the α -glycol group prior to this investigation.

III. THEORETICAL

Mechanism

Almost all of the research attempting to elucidate the mechanism of the oxidation of α -glycols with lead tetraacetate has been carried out by Criegee and his co-workers.

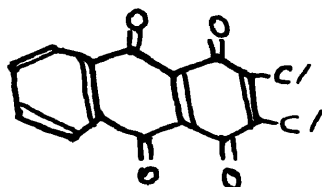
In 1931, Criegee stated (8) that only two possible reaction mechanisms for "glycol splitting" suggested themselves to him. Either the oxidizing agent removed two hydrogen atoms from the hydroxyl groups (A) or two acetoxy groups were added on to the molecule, analogous to the action of lead tetraacetate on unsaturated compounds (7)(8).



In the first case, a diradical was postulated as an intermediate product which could form a cyclic oxide, after a dehydrogenation had taken place. In the second case, mono-acetylated aldehydes or ketones were postulated as the primary reaction products. By splitting out acetic acid these yielded the corresponding carbonyl compounds.

The decision between the two possible mechanisms was arrived at by a process of elimination and not by the proof of the validity of one mechanism or the other. In unpub-

lished work of Dimroth and his co-workers, it had been shown that in those cases in which lead tetracetate undoubtedly acted as a dehydrogenating agent, such as in the oxidation of hydroxyanthraquinones to diquinones (14)(15), it may be substituted by a quinone of high oxidation potential such as dichloroquinizarinequinone (I).



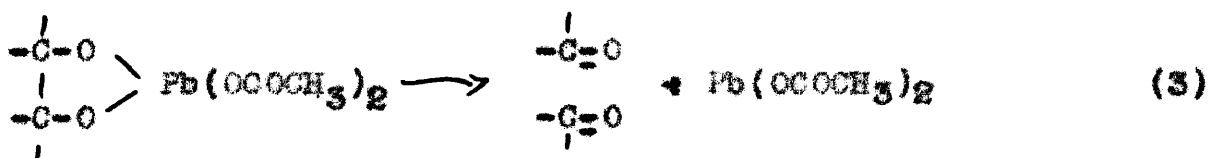
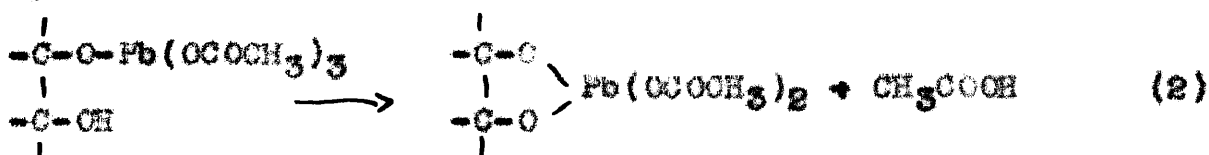
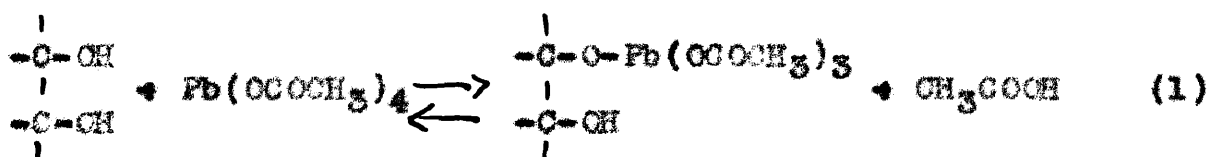
I

This quinone may be used not only to oxidize hydroquinone to quinone but also to oxidize 1,4-dihydronaphthalene to naphthalene. If "glycol splitting" were also a dehydrogenation, it should be possible to carry it out by means of this quinone. It turned out, however, that those glycols which reacted with lead tetracetate most rapidly were unaffected by this quinone under conditions analogous to those under which 1,4-dihydronaphthalene was smoothly dehydrogenated. Therefore, Griegee reasoned, since mechanism A was eliminated, the correct mechanism was B.

It is obvious that an attempt to prove which mechanism is correct by logic rather than by experimental evidence is exposing itself to the criticism that there are other possible mechanisms rather than just two. In fact, it was later shown by Griegee that an entirely different mechanism was the most plausible.

In a later publication (12), Criegee revised his ideas to a great extent concerning the reaction mechanism. This revision of the reaction mechanism was necessary for two reasons. First, the old mechanism did not explain why only free glycols reacted with lead tetraacetate. If either one of the hydroxyl groups was substituted no oxidation occurred. Second, if the basis of the reaction was, as Criegee expressed it, the addition of two pseudohalogen atoms "acetoxy" to the simple C-C bond in glycols analogous to the action of lead tetraacetate on the double bonds of olefines, it was difficult to understand why the reaction ran so much more slowly than the addition of true halogens to the double bond. He concluded that the initial point of attack in the molecule must be in the hydroxyl groups themselves.

After extensive experimental work, Criegee and his co-workers concluded that the following series of reactions represented "glycol splitting".



Reaction (1) was based on the analogous reaction between lead tetraacetate and monohydric alcohols. Reaction (2) was arrived at by a somewhat similar method of reasoning,

namely the ease of formation of five membered rings in the reactions between α -glycols and boric acid, acetone and arseno-acetic acid. As shown in Table II, cis-glycols react much more rapidly than corresponding trans-isomers. This should be the case if this mechanism is correct since ring closure can take place more readily when the hydroxyl groups are adjacent in space. Reaction (3) then followed from the first two and indicated how the carbonyl compounds were formed. It may be seen that by combining these three equations the general equation for "glycol splitting" may be arrived at. This reaction mechanism was corroborated by very extensive studies of reaction rates.

The speed of "glycol splitting" can be measured very easily by iodimetric titration. In acetic acid solution, the reaction follows the course of a bimolecular reaction. Table II shows the velocity constants in minutes at 20°C of the glycols studied. The table is arranged in order of decreasing speed. In all 32 compounds were examined.

The following conclusions may be drawn from this table:

- (1) The speed of oxidation of glycols varies considerably. In some cases the speed is as much as 60,000,000 times as fast as in others.
- (2) The speed of oxidation is usually extremely high. This may be made clearer by examining half life times instead of velocity constants. Half of the 32 compounds studied had half life times of one minute or less and twenty-six had half life values of one hour or less.
- (3) It can be seen from the table that the speed of oxidation is determined by steric influences. In all cases, in isomeric

TABLE II OXIDATION VELOCITY CONSTANTS

		Config. of OH Groups	Ring Size	k_{20°
1	Acenaphthenediol.....	cis	5	~120,000
2	Diphenylacenaphthendiol....	cis	5	33,100
3	Dimethylacenaphthenediol....	cis	5	28,600
4	Hydrindenediol.....	cis	5	27,800
5	α -Methyl mannofuranoside....	cis	5	>900
6	β -Anethole glycol.....	aliph.	...	330
7	β -Methyl isoeugenol glycol....	aliph.	...	>300
8	Diphenyldihydro- phenanthrenediol.....	cis	6	286
9	Diphenylacenaphthenediol....	trans	5	284
10	Cholestanetriol.....	cis	6	72.8
11	Tetrahydronaphthalenediol..	cis	6	40.2
12	Sannonic acid- γ -lactone....	cis	5	39
13	Diphenyldihydro- phenanthrenediol.....	trans	6	24.7
14	α -Anethole glycol.....	aliph.	...	19.7
15	Benzpinacol.....	aliph.	...	6.69
16	Cyclohexanediol.....	cis	6	5.04
17	d-Dimethyl tartrate.....	aliph.	...	2.17
18	Tetrahydronaphthalenediol..	trans	6	1.86
19	Gluconic acid- γ -lactone....	aliph.	...	1.2
20	meso-Dimethyl tartrate.....	aliph.	...	0.86
21	Monocetoneglucose.....	aliph.	...	0.63
22	Ethyl glucofuranoside.....	aliph.	...	0.55
23	Pinacol.....	aliph.	...	0.543
24	Hydrindenediol.....	trans	5	0.457
25	Cyclohexanediol.....	trans	6	0.224
26	α -Acetyl glycerol.....	aliph.	...	0.03
27	Dimethylacenaphthenediol....	trans	5	0.06
28	Ethylene glycol.....	aliph.	...	0.035
29	Acenaphthenediol.....	trans	5	0.03
30	Ethyl glucofuranoside- 5,6-carbonate.....	trans	5	<0.01
31	Arabonic acid- γ -lactone....	trans	5	<0.01
32	Cholestanetriol.....	trans	6	0.002

pairs of glycols, the cis-compound reacted much more rapidly than its trans-isomer. In fact, lead tetraacetate has been used to distinguish between cis- and trans- forms of glycols by measurement of reaction speed (2). It may also be seen on closer examination that the ratio of velocity constants for isomeric pairs of glycols (k_{cis}/k_{trans}) was very much greater in the case of five membered ring glycols than in the case of six membered ring glycols. This is shown in Table III for several pairs of cis-trans isomers. This property of lead tetraacetate may be used to determine ring size.

The role played by the acetic acid in "glycol splitting" is not merely that of a solvent. Acetic acid is represented on the right side of both equations (1) and (2). If the mechanism is correct, the concentration of acetic acid should play some part in the oxidation since the equilibrium point for these reactions would be displaced to the left by the presence of acetic acid. Displacing the equilibria in equations (1) and (2) to the left, would have as an over-all effect the slowing down of "glycol splitting". Whether this is actually so or not may be determined by carrying out the reaction in chemically indifferent solvents using the same concentrations of diol at the same temperature and measuring the half life times. Table IV shows the half life times using trans-cyclohexanediol at 20°C in various solvents.

TABLE III
RATIO OF OXIDATION
VELOCITY CONSTANTS AND RING SIZE

	Ring Size	Configuration of Hydroxyl Groups	k_{20°	$\frac{k_{cis}}{k_{trans}}$
Cyclohexanediol	6	cis	5.04	23
		trans	0.22	
Tetralin-1,2-diol	6	cis	40.2	21.6
		trans	1.88	
Hydrindenediol	5	cis	27800	59,000
		trans	0.47	
Acenaphthenediol	5	cis	120000	4,000,000
		trans	0.03	
Mannonic acid- γ - lactone	5	cis	39	3,900
Arabonic acid- γ - lactone	5	trans	0.01	
Diphenyldihydro- phenanthrenediol	6	cis	236	11.6
		trans	24.7	

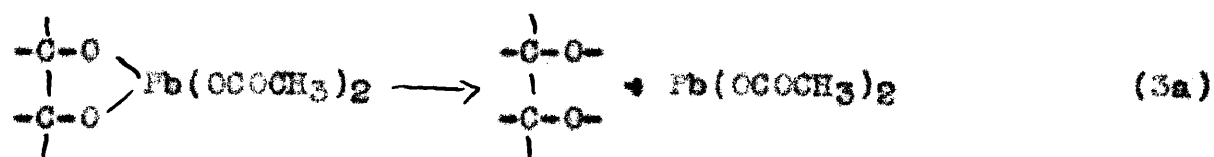
TABLE IV	Solvent	Half Life Time in Seconds
	Acetic Acid	4340
	Benzene	1.8
	Nitrobenzene	1.6
	Dichloroethane	1.1
	Tetrachloroethane	0.9

It can be seen that the rate of reaction in chemically indifferent solvents is many thousand times faster than in acetic acid. This fact has practical application in those cases where the desired oxidation goes so slowly in acetic acid at 20°C that side reactions are commencing to take place. Then an indifferent solvent may be substituted to good advantage so the reaction may go more rapidly even at room temperature.

This new mechanism for "glycol splitting", therefore, is consistent with all the experimental evidence and has a great deal of corroborative evidence in the field of kinetics studies to bear it out. It may be seen now why it is necessary to have unsubstituted hydroxyl groups. If merely one hydroxyl group were unsubstituted, only the reaction shown in equation (1) representing the first intermediate, could take place. It is difficult to see, however, how ring closure could take place as shown in equation (2). Experimental evidence bears out the fact that if either one of the hydroxyl groups is substituted, "glycol splitting" does not take place.

In later publications (10)(11), Grieges added one more intermediate equation to the mechanism of "glycol splitting". In the formation of the aldehydes or ketones

from the cyclic compound with the elimination of lead acetate, as shown in equation (3), no reason was given why there should be a rupture of the C-C bond. It was in this stage where the actual oxidation occurred, that is, the lead changed in valence from 4 to 2. An additional equation (3a) was therefore proposed which involved a free diradical. This equation took the place of equation (3) in the mechanism postulated previously.



The splitting out of lead acetate yielded, first, a 1,4-diradical with free valences on the oxygen. Criegee had previously shown (10) that in all cases in which a 1,4-diradical is formed or can be formed, splitting of the molecule occurs between atoms 2 and 3 (cf. 76). In a similar manner, it was reasonable to assume that the cyclic intermediate in "glycol splitting" yielded lead acetate and the carbonyl compounds through the formation of a 1,4-diradical.

Present Investigation

It was the purpose of the present investigation to study the action of red lead and acetic acid (lead tetraacetate) on long chain hydroxylated fatty acids, esters and alcohols containing the α -glycol group. Compounds suitable for the preparation of these hydroxylated compounds were the

relatively cheap and abundant fatty acids, esters and related compounds, which contained at least one ethylenic linkage. The starting materials in this investigation were oleic acid, ethyl oleate, oleyl alcohol, and castor oil. Various methods of hydroxylation were available but the method described by Hilditch (33) employing glacial acetic acid and 30% hydrogen peroxide was found to be most generally applicable and most desirable for several reasons. In the first place, most of the unsaturated compounds were soluble in the glacial acetic acid-hydrogen peroxide solution at the reaction temperatures. Furthermore, the same solvent, glacial acetic acid, was used in the preparation of lead tetraacetate from red lead and for its reaction with the hydroxylated compound. These circumstances made it unnecessary to isolate either the hydroxylated compound or the lead tetraacetate. It was merely necessary to add the red lead in small portions to the hydroxylation reaction mixture to which sufficient acetic acid had been added to take care of the red lead. The initial portions of red lead served to decompose excess hydrogen peroxide, while the remainder was utilized in the reaction with the hydroxylated compound. By isolating and purifying the hydroxylated compound, larger yields of the desired aldehydes were obtained, but it is doubtful whether the gain in yield of aldehydes compensated for the additional expenditure of time and materials.

It is reported, however, that this method of hydroxylation yields some of the hydroxy compound in the form of an acetylated derivative, the percentage of acetylated derivative increasing with the reaction temperature. These acety-

lated derivatives are not acted upon by lead tetracetate and the yield of aldehydes is therefore diminished. The percentage of acetylated derivatives may be held to a minimum by carrying out the hydroxylation at room temperature but more than a week is required for the completion of the reaction. The reaction may be speeded up by heating but its exothermic nature makes temperature control difficult, especially in large batches, and not only is the percentage of acetylated derivative increased but the total yield of products is decreased because of excessive decomposition of the hydrogen peroxide at the higher temperatures.

An improved method of hydroxylation, based on Hilditch's procedure, was developed whereby it was possible to carry out the reaction at relatively low temperatures in a few hours. At the same time the proportions of acetic acid and hydrogen peroxide to unsaturated compound were materially reduced and the recovery of the product was considerably simplified. The essential difference between Hilditch's method of hydroxylation and the improved method employed here, was that it was found to be a decided advantage to heat the solution of glacial acetic acid and hydrogen peroxide for one hour at 30°-35°C prior to adding it to the unsaturated compound. In the Hilditch procedure all three ingredients were mixed together and then heated. The temperature went out of control very easily when the reaction was carried out in this way.

There is little doubt that peracetic acid plays some part in the hydroxylation reaction. Its presence is indicated

by its peculiar odor. Evidence that peracetic acid plays some part in the hydroxylation is shown by the fact that acetylated derivatives are formed. If pure dihydroxystearic acid is boiled with a large excess of glacial acetic acid for some time, comparatively little acetylation takes place. If peracetic acid is postulated as playing some part in the hydroxylation, it can be readily seen that the addition of peracetic acid to the double bond would result in acetylated derivatives being formed. The addition of per-acids to double bonds is characteristic of that class of substances. The acetyl groups may be hydrolyzed to yield pure dihydroxy compounds. Additional evidence that peracetic acid plays some part in the reaction is shown by the fact that those substances which accelerate the decomposition of peracetic acid cause a diminution in yield of hydroxylated product (33).

In the second or oxidation stage, the hydroxylation reaction mixture was diluted with sufficient glacial acetic acid to make up the total quantity required or the purified hydroxy compound was dissolved in the required quantity of glacial acetic acid. Red lead was then added in small portions. The lead tetraacetate thus produced reacted with the long chain hydroxylated compound to split the carbon chain between the carbon atoms to which the hydroxyl groups were attached, yielding two aldehydes. The volatile aldehydes were usually recovered by steam distillation of the reaction mixture. From the residue the non-volatile aldehydes were usually separated by extraction with ether. These latter were difficult to purify in some cases and it was found more

feasible to oxidize them to the corresponding acid which could be readily purified.

When oleic acid was oxidized by means of dilute alkaline potassium permanganate solution or by means of hydrogen peroxide-glacial acetic acid, the high or low melting form of 9,10-dihydroxystearic acid was prepared. A word of explanation is necessary concerning the designations of "high" and "low" melting forms for 9,10-dihydroxystearic acid. When the double bond in oleic acid is saturated by the addition of two hydroxyl groups, two asymmetric carbon atoms are formed. These are indicated by asterisks in the formula for 9,10-dihydroxystearic acid shown below.



Since there are two asymmetric carbon atoms in this compound there should be four optically active forms or two racemic mixtures. As there is no reason for asymmetric synthesis taking place in the hydroxylation of the double bond, the product resulting should be optically inactive, and should be the racemic form. Such is the case. If the hydroxylation of oleic acid is carried out by means of alkaline potassium permanganate, the racemic mixture resulting has a higher melting point than the racemic mixture resulting from the hydroxylation of oleic acid by means of glacial acetic acid and hydrogen peroxide. Therefore, the racemic mixture with the higher melting point is called the high melting form and the racemic mixture with the lower melting point is called the low melting form of 9,10-dihydroxystearic acid. This

system is also employed in connection with other hydroxylated compounds of a similar type, e.g. those prepared from cleyl alcohol, ethyl oleate, etc. In the reaction with lead tetraacetate, both the high and low melting forms of 9,10-dihydroxystearic acid gave exactly the same products in the same yields, as might be expected. The ethyl esters of these substances also reacted in the same way.

Thus, when 9,10-dihydroxystearic acid was dissolved in glacial acetic acid and red lead added, the aldehydes were obtained in about 60-70% yields. Pelargonic aldehyde was obtained directly from the steam distillate in over 90% purity, and for further synthetic work could be used undistilled. Azelaic half aldehyde could only be purified by vacuum distillation which resulted in a diminution in yield since a rather large undistillable residue resulted on heating. It was found more feasible, usually, to oxidize it to azelaic acid which could be readily purified by recrystallization from water. The presence of the free carboxyl group in conjunction with carbonyl seemed to have the effect of causing the azelaic half aldehyde to undergo very rapid changes, particularly on steam distillation, which prevented satisfactory further treatment. This did not occur with the ethyl ester of azelaic half aldehyde.

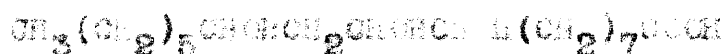
The ethyl esters of the high and low melting forms of 9,10-dihydroxystearic acid reacted with lead tetraacetate much more smoothly than the free acids giving pelargonic aldehyde and the ethyl ester of azelaic half aldehyde in about 90% yields and in a very high state of purity.

When oleic acid and ethyl oleate were hydroxylated with glacial acetic acid and hydrogen peroxide, and red lead added directly to the reaction mixture, pelargonic aldehyde was obtained in about 25-35% yields, based on the unsaturated compounds. These yields were almost as good as the yields obtained from the pure dihydroxy compounds, when the yields of aldehydes were calculated on the basis of the unsaturated compounds. No azelaic half aldehyde could be isolated from the oleic acid reaction mixture, although a small amount of azelaic acid could be obtained from it by oxidation. The ethyl ester of azelaic half aldehyde could be obtained in about a 12.5% yield and in a high state of purity by vacuum distillation of the reaction mixture obtained in the oxidation of ethyl oleate. The yield was quite small, however, and it was more feasible to prepare this ester from pure ethyl dihydroxystearate.

If one is interested solely in pelargonic aldehyde, it can be prepared most readily from the unsaturated compound as described above, without isolating the intermediate hydroxylated compound. The unrecrystallized 9,10-dihydroxystearic acid may be oxidized directly with lead tetraacetate. The yield of pelargonic aldehyde, based on oleic acid as the starting material, was somewhat higher than the yield in those experiments in which the hydroxy compound was not isolated, since here the acetyl groups were hydrolyzed prior to the lead tetraacetate oxidation. Azelaic acid was obtained in comparatively small yield.

Pure 9,10-dihydroxyoctadecanol-1 was dissolved in glacial acetic acid and oxidized by means of red lead. The aldehydes obtained were pelargonic aldehyde and 9-hydroxypelargonic aldehyde. These were separated by vacuum distillation and were obtained in about 70% and 30% yields respectively. Microcrystallized 9,10-dihydroxyoctadecanol-1 gave considerably smaller yields of aldehydes on being oxidized with lead tetracetate. No aldehydes could be obtained from cetyl alcohol when the hydroxylation reaction mixture was treated with red lead directly. The most satisfactory method of preparing 9-hydroxypelargonic aldehyde was from pure 9,10-dihydroxyoctadecanol-1.

9,10,12-Trihydroxystearic acid gave somewhat unexpected results in the oxidation with red lead and acetic acid. The volatile aldehyde obtained was α -nonenaldehyde instead of 3-hydroxypelargonic aldehyde, which would be expected from the structure of 9,10,12-trihydroxystearic acid.



In fact, for a time it was believed that the volatile aldehyde obtained was 3-hydroxypelargonic and not α -nonenaldehyde since the first derivative prepared from this aldehyde, the 3,4-diacetylacetonhydrazone, checked the melting point of the same derivative reported in the literature for 3-hydroxypelargonic aldehyde. The derivative reported in the literature (78), however, was also prepared from α -nonenaldehyde although the investigators were not aware of this. The first clue to the true identity of the aldehyde was given by mole-

cular refractivity data. Molecular refractivities were determined on the aldehyde and its corresponding acid and the values were found to check with the theoretical for the unsaturated compounds and not for the hydroxy compounds. The 2,4-dinitrophenylhydrazone and semicarbazone were prepared from the aldehyde, and the amide and p-bromophenacyl ester from the acid. The melting points of all solids were obtained and all the compounds were carefully analyzed. The melting points of the derivatives were found to check the melting points of the derivatives reported in the literature for α -nonenaldehyde and α -nonenoic acid prepared by totally different means. The analyses checked closely with the theoretical for the unsaturated aldehyde and acid. There was little doubt, therefore, that the volatile aldehyde prepared from trihydroxystearic acid was α -nonenaldehyde and not 3-hydroxypelargonic aldehyde. The yield of the aldehyde from trihydroxystearic acid was about 70%. Azelaic acid could be obtained from the residue in about 37% yield.

In connection with an investigation of the constitution of certain fatty acids present in cork, two investigators (78) had the occasion to prepare 9,10,12-trihydroxystearic acid from ricinoleic acid. They oxidized this hydroxy acid with lead tetraacetate and obtained an aldehyde which they merely stated was 3-hydroxypelargonic aldehyde and which would be expected since the structure of ricinoleic acid was known. No analytical data were given for this aldehyde or for its 2,4-dinitrophenylhydrazone whose melting point was reported. It seems almost certain that the aldehyde they obtained was

α -nonenaldehyde since they used the same starting material used in this investigation, and the melting point of their 2,4-dinitrophenylhydrazone checked the melting point of the 2,4-dinitrophenylhydrazone prepared in the present investigation. Fortunately, the conclusions they drew in their publication were unaffected by the actual structure of the aldehyde.

Caster oil also yielded α -nonenaldehyde in the oxidation with red lead and acetic acid. Approximately 16 grams of α -nonenaldehyde and 9 grams of azelaic acid were obtained from 100 grams of castor oil. In the case of castor oil it was more desirable to hydroxylate and then oxidize without isolating the intermediate hydroxylated material because all attempts to hydrolyze the acetyl groups added during the hydroxylation resulted in glyceride hydrolysis and because there was no method of purifying the hydroxylated material once it was isolated. Glyceride hydrolysis is undesirable because oxidation of the non-volatile residue seemed to proceed more satisfactorily when the carboxyl group was esterified. Castor oil was the best starting material for the preparation of α -nonenaldehyde because the best over-all yields were obtained from it and no intermediate hydroxylated compound had to be isolated.

The preparation of α -nonenaldehyde from 9,10,12-trihydroxystearic acid and from hydroxylated castor oil was somewhat unexpected since all the oxidations of hydroxylated compounds with lead tetracetate reported in the literature resulted only in glycol splitting without any side reactions.

Also, no unusual behavior had been observed in the oxidations of 9,10-dihydroxystearic acid and its ethyl ester, 9,10-dihydroxyoctadecanol-1 and in the other oxidations reported here. 9,10-Dihydroxyoctadecanol-1, which contains an hydroxyl group in addition to the α -glycol group, did not yield an unsaturated aldehyde upon oxidation. It seems reasonable to assume, therefore, that a normal type of scission occurred in the oxidations of 9,10,12-trihydroxystearic acid and hydroxylated castor oil. The hydroxyaldehyde thus prepared contained an hydroxyl group in the β -position and because the α -hydrogen atoms in aldehydes are particularly reactive, dehydration to yield the α, β -unsaturated aldehyde could reasonably have occurred. In the light of this theory concerning the formation of α -nonenaldehyde, it may be safely stated that lead tetraacetate (prepared and utilized "in situ") reacts with hydroxylated fatty acids, esters and related compounds in a manner analogous to that previously reported for the action of lead tetraacetate on hydroxylated compounds, and the mechanism proposed by Criegee and his co-workers (10) (11)(12) may be applied without alteration.

IV. EXPERIMENTAL

In this investigation, the oleic acid used was of U.S.P. grade and was marketed as olive elaine. The oleyl alcohol was also of good quality and was a pale yellow liquid having a pleasant fatty odor. The ethyl oleate employed was the Eastman Kodak Practical grade. The castor oil was a colorless oil of U.S.P. grade. Some of the chemical properties of these substances are tabulated in Table V.

TABLE V PROPERTIES OF MATERIALS USED

	: Neut. Equiv. :		: Iodine No. :		: Saponification :	
	: Found :	: Calc. :	: Found :	: Calc. :	: Found :	: Calc. :
Oleic Acid	: 290 :	: 282 :	: 91.9 :	: 89.9 :	: ... :	: ... :
Oleyl Alcohol	: ... :	: ... :	: 97.8 :	: 94.6 :	: ... :	: ... :
Ethyl Oleate	: ... :	: ... :	: 79.0 :	: 81.8 :	: 305 :	: 310 :
Castor Oil	: ... :	: ... :	: 84.0 :	: 82-90 :	: 179.9* :	: 177-187* :

*Saponification Number

The red lead used was a fine powdered commercial product which contained not less than 95% Pb_3O_4 . All the other chemicals used were of C.P. or analytical reagent quality.

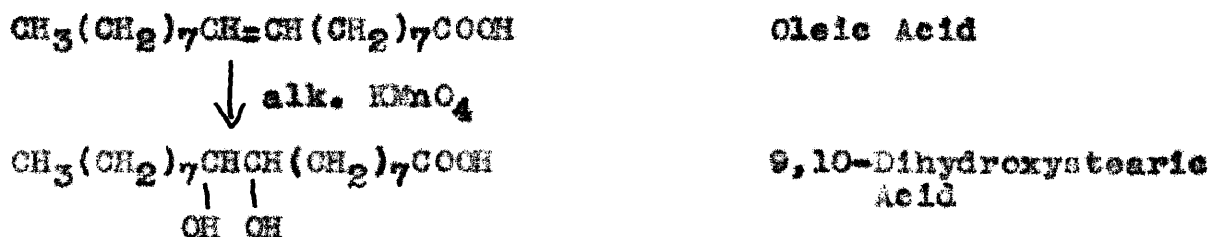
All melting points reported are corrected values.

Combustions were run using the apparatus described by Phillips and Hellbach (55).

For convenience, the discussion relating to the oxidations of hydroxy compounds with lead tetraacetate may be divided into three parts, (1) oxidations in which pure hydroxy compounds were used, (2) oxidations in which the hydroxy compounds were isolated but not purified, and (3) oxidations in which the hydroxy compounds were oxidized without being isolated from the hydroxylation mixture.

Oxidations in which pure hydroxy compounds were used.

Preparation of 9,10-Dihydroxystearic Acid (High Melting):



This substance was prepared essentially according to the methods of Le Sueur (45) and Saytzeff (62).

126 grams of oleic acid (.45 mole) was dissolved in 1100 cc. of water containing 38 grams of potassium hydroxide (.68 mole). The solution was well stirred and cooled to 0°C, becoming quite viscous at this stage. By means of a dropping funnel, a solution containing 126 grams of potassium permanganate (.80 mole) in 1900 cc. of water was added slowly. At no time was the temperature allowed to rise above 10°C and the stirring was kept very rapid throughout. After all the permanganate had been added the stirring was continued until the reaction had reached room temperature. The reaction mixture was then allowed to stand overnight to permit the coagulation of the manganese dioxide. The precipitate of man-

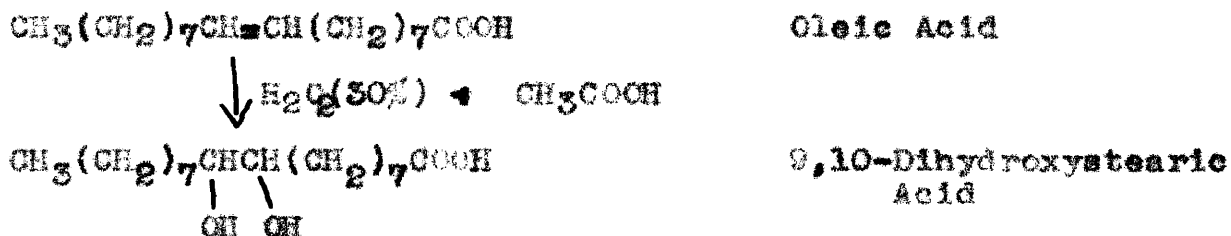
ganese dioxide was filtered and washed several times with boiling water. In order to remove all the soap from the manganese dioxide, it was necessary to transfer the precipitate to a large beaker, add boiling water and stir the mixture well. This was filtered and the aqueous solution was combined with the main filtrate. The combined filtrates were cooled to about 10°C and acidified with dilute sulfuric acid. The curdy, white precipitate of 9,10-dihydroxystearic acid was filtered by suction, washed with cold water several times to remove excess sulfuric acid and sucked as dry as possible. It was recrystallized from 95% ethyl alcohol or ethyl acetate.

Yield: 57 grams or 40%

Neutralization Equivalent: Found 315-320
Calc. (C₁₈H₃₆O₄) 316

Melting point: 129-130°C Literature 130.5-131°C (62)

Preparation of 9,10-Dihydroxystearic Acid (Low Melting):



This substance was prepared by a modification of the method described by Hilditch (55).

567 grams of 30% hydrogen peroxide (5.0 moles) was dissolved in 1800 cc. of glacial acetic acid at room temperature and heated on the steam bath for one hour at 80-85°C. This solution was cooled under the tap to about 25°C and 708 grams of oleic acid (2.5 moles) was added. The solution was stirred occasionally by hand. The reaction was exothermic and the

temperature rose rapidly to about 65°C, the solution becoming homogeneous about that time. The temperature continued to rise slowly to a maximum of about 72°C. The solution was then allowed to cool to room temperature. The exothermic reaction continued for some time after the maximum temperature was reached as evidenced by the fact that the temperature fell very slowly. The reaction mixture was allowed to stand overnight. It was filtered free of a waxy solid prior to its being poured into hot water, although this was not found to be essential. The mixture was then poured into 6000 cc. of hot water and the whole well shaken. After a clean separation into two layers had been obtained, the aqueous layer was siphoned off. The residual oil was dissolved in 4000 cc. of water containing 750 cc. of 6 N sodium hydroxide and heated for about two hours on the steam bath to hydrolyze the acetyl groups added during the course of the reaction. For convenience in handling, the solution was divided into two parts and the dihydroxystearic acid precipitated by means of 6 N hydrochloric acid while the solutions were still hot. The mixtures were cooled until the dihydroxystearic acid floating on the surface had solidified. The lower aqueous layers were rejected. The solid cakes were combined and remelted in 3000 cc. of hot water containing a small amount of hydrochloric acid and the mixture was then thoroughly stirred. This washing with water was found to be essential for the preparation of a pure product because it removed inorganic salts and soap which were mechanically included in the dihydroxystearic acid and which could not be

removed by subsequent recrystallizations. Omission of this step yielded a product with a neutralization equivalent from forty to sixty units too high. The oil was again allowed to separate and solidify. The dihydroxystearic acid was separated from the aqueous layer and recrystallized from 95% ethyl alcohol.

Yield: 353 grams or 45%

Neutralization Equivalent:	Found	314-320
	Calc. (C ₁₈ H ₃₆ O ₄)	316

Melting point:	89-91°C	Literature 95°C (33)
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Preparation of Ethyl 9,10-Dihydroxystearate (High Melting):

This compound was prepared from the dried, unrecrystallized high melting 9,10-dihydroxystearic acid whose synthesis was described previously.

The crude dihydroxystearic acid prepared from 189 grams of oleic acid (.67 mole) was dissolved in 500 cc. of hot 95% ethyl alcohol, and 500 cc. of carbon tetrachloride and 5 grams of concentrated sulfuric acid were added. The solution was slowly distilled through a long Vigreux column into a 500 cc. separatory funnel until about 250 cc. of distillate had been collected. The distillate came over at 62°C and was a ternary mixture of ethyl alcohol, carbon tetrachloride and water (54). The distillate separated into two layers in the separatory funnel. The upper layer consisted of 65% ethyl alcohol, 25% water and 10% carbon tetrachloride. The lower layer consisted of carbon tetrachloride, ethyl alcohol and small amounts of water. The lower layer was drawn off and dried for a few minutes over anhydrous potassium carbonate and returned to the

system. The relatively small upper layer was discarded. This process was continued until two layers no longer formed. The single layer was then dried and returned in the same way. The process was continued until no more turbid drops came over. This was considered the end of the reaction. The total time for the reaction varied with the amount of water in the dihydroxystearic acid and the size of the batch. When the reaction was complete about 500 cc. of distillate was collected. The residue in the distillation flask was filtered hot and the filtrate was chilled in the refrigerator. A white, apparently amorphous solid separated on cooling. It was recrystallized from 95% ethyl alcohol.

Yield: 90 grams or 39% (Based on oleic acid)

Saponification Equivalent:	Found	349
	Calc. ($C_{20}H_{40}O_4$)	344

Melting point:	95-96°C	Literature 99°C (68)
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Preparation of Ethyl 9,10-Dihydroxystearate (Low Melting):

This ester was prepared from the crude, unrecrystallized low melting dihydroxystearic acid, the preparation of which has already been described. It was prepared in almost the same way as the high melting ester. The only variation in the procedure was necessitated by the fact that this ester is more soluble in alcohol than the high melting compound. The residue in the distillation flask was filtered hot at the end of the reaction after 500 cc. of distillate had been collected, but on being cooled a very poor yield of ester was obtained because of its high solubility in ethyl alcohol. It was necessary to reheat the solution to boiling and add hot

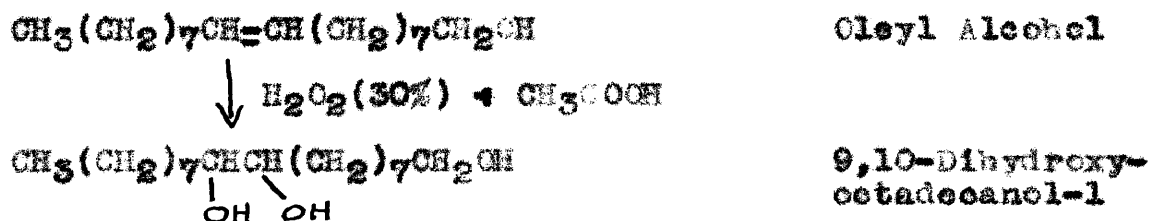
water until the solution was slightly turbid. Alcohol was then added until the solution was clear and sufficient alcohol was added in excess so that the ester came out of solution in the crystalline state instead of an oil on being chilled. The ester was recrystallized in the same fashion using a small quantity of Darco. It formed small white crystals.

Yield: 49 grams or 29% (Based on 141 grams of oleic acid)

Saponification Equivalent: Found 347
Calc. (C₂₀H₄₀O₄) 344

Melting point: 56.5-58.5°C Literature 59-60°C (66)

Preparation of 9,10-Dihydroxyoctadecanol-1 (Low Melting):



This trihydric alcohol was prepared by the method of Collin and Hilditch (6) employing the improvements described under the preparation of the low melting 9,10-dihydroxystearic acid.

225 grams of 30% hydrogen peroxide (2.0 moles) was dissolved in 720 cc. of glacial acetic acid at room temperature and heated on the steam bath for one hour at 80-85°C. The solution was then cooled under the tap to about 25°C and 268.5 grams of oleyl alcohol (1.0 mole) was added. The solution was stirred occasionally by hand. The reaction was extremely exothermic, the temperature rising very rapidly to 68°C, at which time the solution became homogeneous. The

temperature continued to rise to about 72°C where it remained for some time and then fell very slowly. After standing overnight, the solution was poured into 2400 cc. of hot water and stirred well. The lower aqueous layer was siphoned off after a clean cut separation into two layers had been obtained. The residual oil was neutralized with 1 N alcoholic potassium hydroxide and a one liter excess was added. This alkaline solution was refluxed for two hours. The alcohol was evaporated and the product was thrown out as an oil by the addition of 2000 cc. of hot water. In one experiment the use of cold water to precipitate the alcohol resulted in the formation of a thick emulsion which could not be filtered and could be handled only with great difficulty. The mixture was well stirred to remove as much alkali as possible from the oil and then allowed to cool until the oil had solidified. The lower aqueous layer was poured off and the solid cake was remelted and stirred with hot water. This was allowed to cool and the oil to solidify. The solidified product, which was yellow-brown in color, was broken into small pieces, transferred to a large dish, and allowed to dry in the air. It was then recrystallized once from ethyl acetate using Darco. A white crystalline product was thus obtained. A purer product may be obtained by an additional recrystallization. For the purposes of this investigation this was unnecessary.

Yield: 138 grams or 46%

Melting point: 73-75°C Literature 82-82.5°C (6)

Preparation of 9,10,12-Trihydroxystearic Acid (Low Melting):

Since the samples of ricinoleic acid at our disposal had undergone so many internal changes, castor oil was used as the starting material. This was an advantage since it would have been necessary to hydrolyze the castor oil to obtain a good sample of ricinoleic acid, and then, after the hydroxylation, to hydrolyze the acetylated hydroxy compound in order to obtain the free trihydroxy compound. Using castor oil as the starting material, one hydrolysis served to hydrolyze the acetyl groups and saponify the glyceride.

225 grams of 30% hydrogen peroxide (2.0 moles) and 820 cc. of glacial acetic acid were mixed and heated together for one hour at 80-85°C. The solution was cooled under the tap to 25°C and 311 grams of castor oil (approximately .33 mole of triricinolein) was added. The mixture was stirred occasionally by hand. The temperature rose rapidly to about 70°C at which point the solution became homogeneous. The temperature of the reaction mixture fell slowly and the solution was allowed to stand overnight. The acetic acid was removed by steam distillation and the residual white, viscous oil was refluxed for two hours with 1000 cc. of 10% sodium hydroxide solution. The solution was then acidified while hot with dilute sulfuric acid. The 9,10,12-trihydroxystearic acid separated out as an oil and solidified as a light brown solid on cooling. The lower aqueous layer was poured away, the solid remelted with boiling water and the whole stirred. Enough sulfuric acid was added so that the

oil floated on the surface of the solution. The mixture was again allowed to cool and the lower aqueous layer was discarded. The solid cake was dissolved in hot 95% ethyl alcohol, Darco added and the mixture filtered hot. The alcoholic solution was allowed to cool slowly and the small white crystals of 9,10,12-trihydroxystearic acid were filtered off and dried. It is important to avoid using too much ethyl alcohol in the recrystallization since the acid is fairly soluble in this solvent.

Yield: 92 grams or approximately 28%

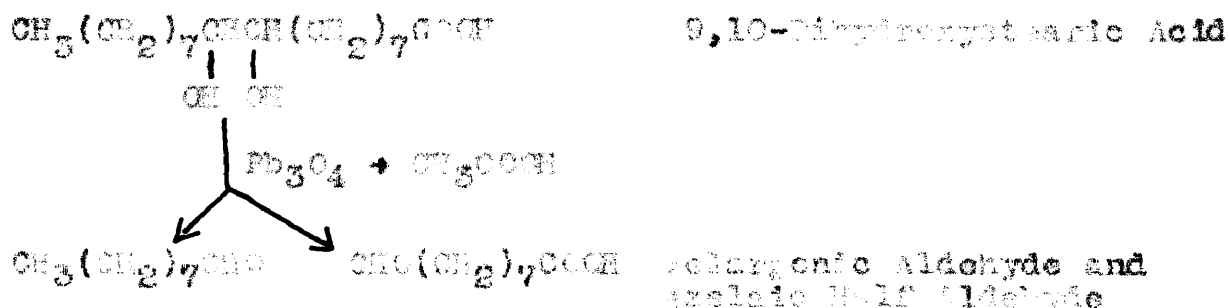
Neutralization Equivalent: Found 337
Calc. ($C_{18}H_{36}O_8$) 332

Melting Point: 108-109°C Literature 110-111°C (30)

Iodine Number: 0.8

The question arose later on in this investigation whether the above mentioned method of hydroxylation of castor oil caused a dehydration to take place splitting out water between carbons twelve and thirteen, because in the subsequent lead tetraacetate oxidation of this hydroxy compound α -nonenaldehyde was obtained instead of the expected 3-hydroxypelargonic aldehyde. It seems evident from the iodine number of the above product that it is completely saturated. The neutralization equivalent and melting point bear out the fact that the compound is 9,10,12-trihydroxystearic acid. The dehydration, therefore, must occur at some later stage and not during the hydroxylation.

Oxidation of 9,10-Dihydroxystearic Acid with Red Lead and
Glacial Acetic Acid:



No difference was observed between the low and high melting forms of 9,10-dihydroxystearic acid in their reaction with red lead and acetic acid. The low melting form was more soluble in glacial acetic acid at the reaction temperatures (55-65°C) and because it could be prepared more easily in large batches than the high melting form, it was used in most of the experiments.

63.2 grams of 9,10-dihydroxystearic acid (.2 mole) was dissolved in 500 cc. of glacial acetic acid at 55-65°C in a 1-liter 3-necked flask fitted with a very efficient stirrer and a thermometer. 151 grams of red lead (.22 mole) was added in small portions (5-10 grams) through a 40 mesh sieve, with rapid stirring, at all times. Each successive portion of red lead was added only after the previous portion had been completely decolorized. The reaction was only slightly exothermic and there was no difficulty in maintaining the temperature between 55-65°C throughout the addition of red lead. After the last portion of red lead had been added, the reaction was considered complete when a drop of the reaction solution placed on a few crystals of leuco-malachite green gave no green coloration. This indicated the absence of all

oxidizing agent from the solution and the stirring was then stopped. The reaction mixture was worked up in either of the following two ways: (1) The reaction mixture was diluted with 500 cc. of water and steam distilled until no more oily drops came over. The distillate was extracted with ether, the ether solution washed twice with water, then with a solution of sodium bicarbonate (9 grams/100 cc. of water) until the lower aqueous layer was alkaline, and then with water until the washings were neutral. The ether solution was dried over anhydrous calcium sulfate and filtered. The ether was evaporated under reduced pressure. The residue consisted of a colorless oil with a sharp, although not unpleasant, odor. This oil proved to be pelargonic aldehyde. The steam distillation residue was cooled down to room temperature and extracted with ether. The ether solution was washed with water until free of lead and acetic acid and dried over anhydrous calcium sulfate. The ether solution was filtered and the ether evaporated under reduced pressure. The residue was a pale yellow viscous oil which solidified on cooling. This proved to be mainly azelaic half aldehyde (8-formyl-1-octanoic acid).

(2) The alternate method of working up the reaction solution was to dilute it with 500 cc. of water and extract it twice with 500 cc. portions of ether. The combined ether solutions were washed with water until free of lead and acetic acid and dried over anhydrous calcium sulfate. The solution was filtered and the ether evaporated under reduced pressure. The residue was a pale yellow limpid oil. This oil was chilled in the refrigerator to about -10°C to throw out the azelaic

acid formed by the auto-oxidation of the azelaic half aldehyde. This precipitate was filtered off and washed with a small amount of petroleum ether, which dissolved small amounts of adhering aldehydes without dissolving any azelaic acid. The azelaic acid was further purified by recrystallization from hot water. The residual oil from the azelaic acid separation was then vacuum distilled giving a clean cut separation of the two aldehydes. If very pure products were desired a vacuum distillation of the aldehydes was essential. However, for most purposes, the aldehydes as prepared by method (1) were pure enough and could be isolated in a shorter time.

The following examples serve to show the yields of products obtained by the two methods of isolating the aldehydes. Employing the first method described, 20 grams of pelargonic aldehyde (71% yield) and 22 grams of azelaic half aldehyde (64% yield) were obtained from 63.2 grams of 9,10-dihydroxystearic acid. Employing the second method described, 63.2 grams of 9,10-dihydroxystearic acid yielded 4 grams of azelaic acid and 56 grams of oil to be vacuum distilled. The fractions obtained and their boiling ranges are shown below.

Fraction	Boiling Range	Wt. in Grams	Identity
1	55-90°C/15 mm	4	Unidentified
2	90-100°C/15mm	16	Pelargonic Aldehyde (57% yield)

At this point the temperature began to fall and then shot up rapidly.

3	145-155°C/15 mm	8	Pelargonic Acid
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The temperature fell again at this point and then rose again very rapidly.

Fraction	Boiling Range	Wt. in Grams	Identity
4	195-197°C/15mm	14	Azelaic Half Aldehyde (41% yield)
Residue		8	
Condensate in dry ice trap		5	

The identity of the various products obtained was determined in the following ways:

Pelargonic Aldehyde. As isolated by steam distillation, it was found to contain approximately 94% pelargonic aldehyde determined by the hydroxylamine hydrochloride method (58). When this material was purified by vacuum distillation or isolated by vacuum distillation according to method (2), it was found to contain approximately 99-100% pelargonic aldehyde.

The oxime was prepared according to the method of Bagard (1), and was recrystallized twice from petroleum ether. It formed long, flat, colorless needles. Melting point 62-63°C. Literature 64°C (1).

The 2,4-dinitrophenylhydrazone was prepared in the manner described by Shriner and Fuson (67). It was recrystallized twice from 95% ethyl alcohol and was obtained in almost quantitative yield as long, golden yellow needles. Melting point 106-106.5°C. Literature 106-106.4°C (52). Because of some ambiguity in the literature concerning the melting point of this derivative, carbon and hydrogen analyses

were run.

Found:	Carbon	55.6%	Hydrogen	6.95%
		55.8		6.90
Calc.: (C ₁₅ H ₂₂ O ₄ N ₄)		55.9		6.88

50 grams of pelargonic aldehyde, on being aerated for four hours in the aerator described by Sensenbrenner and Stubbs (66), was converted to pelargonic acid in 94% yield. The reaction was quite exothermic, the temperature rising from 22°C to 45°C in a short time. The aeration mixture was vacuum distilled yielding pure pelargonic acid. Boiling point 142-150°C/13 mm (40). Melting point 11-12°C (59). The *p*-bromophenacyl ester of this acid was prepared according to the method of Hann, Reid and Jamieson (22) and formed pearly flakes which melted at 64-65°C (56) after two recrystallizations from 95% ethyl alcohol. Literature 63.5°C (56).

The aeration mixture need not be vacuum distilled to purify the pelargonic acid in order to prepare ethyl pelargonate from it. The reaction mixture was dissolved in a large excess of 95% ethyl alcohol which contained 1% concentrated sulfuric acid and was refluxed for three hours. The solution was washed with water until free of sulfuric acid, washed with sodium bicarbonate solution until free of pelargonic acid and with water until neutral. The oil was dried over anhydrous calcium sulfate, filtered and vacuum distilled. Ethyl pelargonate was isolated in a 60% yield. It was a colorless limpid oil with a pleasant fruity odor similar to apple cider.

Saponification Equivalent:	Found	185;186
	Calc. (C ₁₁ H ₂₂ O ₂)	186.3

Pelargonic Acid. This substance was not a primary product of the oxidation reaction but was obtained because of the ease of auto-oxidation of pelargonic aldehyde. This acid was identified as described under pelargonic aldehyde by means of its melting point, boiling range, the melting point of its p-bromophenacyl ester and the boiling range and saponification equivalent of its ethyl ester.

Azelaic Half Aldehyde. This substance was very prone to undergo spontaneous polymerization (43). Previous investigations have indicated the difficulty in working with this compound because of its extreme instability (21)(27)(28). This same difficulty was met here and it was impossible to keep this aldehyde for any length of time before it became worthless for any further use. It was best purified by vacuum distillation. Boiling point 195-197°C/15 mm. (21). Vacuum distillation resulted in a decrease in yield of this aldehyde since heating accelerated its polymerization and decomposition. On cooling, it formed a white amorphous mass. Melting point 40-42°C. Literature 38°C (43).

Neutralization Equivalent:	Found	177
	Calc. (C ₉ H ₁₆ O ₃)	172

The semicarbazone of this aldehyde was prepared (67) and was obtained as a white powder on recrystallization from ethyl alcohol. Melting point 161-162°C. Literature 162°, 163°C (21)(27).

From one mole of dihydroxystearic acid, 130 grams of azelaic half aldehyde was isolated by the steam distillation method described above. This material was dissolved in a

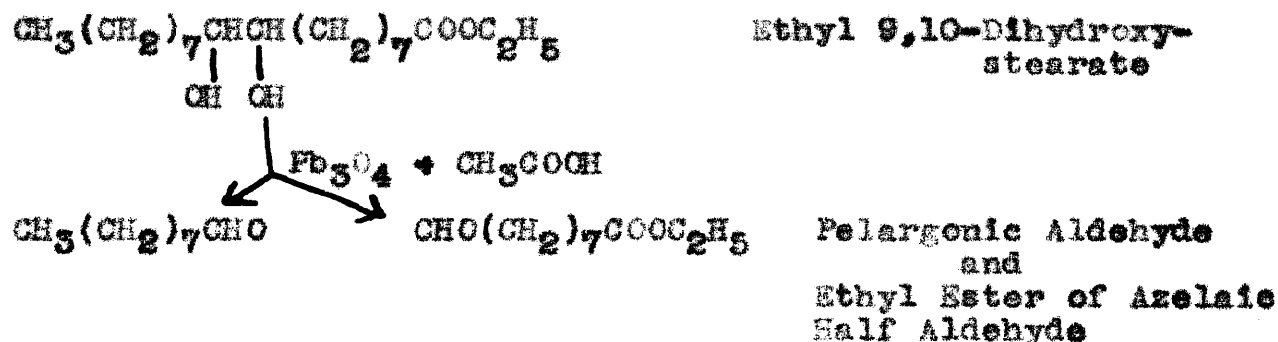
slight excess of 5% sodium hydroxide solution so that the pH was 8-9. With very rapid stirring, a solution of 237 grams (1.5 moles) of potassium permanganate in 2640 cc. of water was added all at once. The solution tended to foam over in some experiments and a small amount of benzene was used to break the foam, if necessary. The temperature rose quite rapidly to 75°C. The stirring was continued for 15 minutes after the permanganate color had disappeared. The oxidation mixture was allowed to stand overnight to permit the settling and coagulation of the manganese dioxide to take place. The manganese dioxide was filtered off and washed several times with small portions of boiling water. The precipitate was transferred to a large beaker and stirred up with about one liter of boiling water. This was filtered off and the filtrate combined with the main filtrate. The solution was evaporated to about three liters and acidified while hot with dilute sulfuric acid. A pale yellow oil was thrown out, and the mixture was filtered. Most of the oil was retained by the filter paper. The small quantity of oil which passed through the filter was removed by boiling the filtrate with a small quantity of Darco. The solution was refiltered and allowed to cool in the refrigerator. The crystals of azelaic acid were filtered off, washed with cold water until free of sulfuric acid and recrystallized from hot water. The azelaic acid weighed 47 grams (25% yield based on dihydroxystearic acid), and melted at 104-106°C. A mixed melting point with an authentic specimen of azelaic acid was unchanged.

All attempts to oxidize the half aldehyde with hydrogen

peroxide were unsuccessful with the aldehyde dissolved in either sodium hydroxide, sodium carbonate, sodium bicarbonate or acetic acid solution. Only extremely small amounts of azelaic acid could be obtained.

Azelaic Acid. This substance was also a secondary product of the reaction and was isolated as indicated under method (2). Purification was effected by dissolving the azelaic acid in hot water containing a small quantity of Darco, filtering and allowing the azelaic acid to crystallize slowly. It formed large, flat, pearly flakes. Melting point 104-106°C. A mixed melting point with an authentic sample gave no depression.

Oxidation of Ethyl 9,10-Dihydroxystearate with Red Lead and Acetic Acid:



Again no difference in behavior was observed between the high and the low melting forms.

69 grams of ethyl 9,10-dihydroxystearate (.2 mole) was dissolved in 500 cc. of glacial acetic acid at 55-65°C. 151 grams of red lead was added exactly as described under the oxidation of 9,10-dihydroxystearic acid. At the completion of the reaction as determined by the leuco-malachite green test, the solution was diluted with 500 cc. of water and steam distilled until no more pelargonic aldehyde came

over. The steam distillate was worked up in the same way as that from 9,10-dihydroxysebacic acid. The residue, however, was extracted with ether, washed with water until free of lead, and then with sodium bicarbonate solution until free of acidic impurities. The ether solution was washed with water until neutral and dried over anhydrous calcium sulfate. The solution was filtered and the ether evaporated under reduced pressure. The residue was a pale yellow, slightly viscous oil and proved to be the ethyl ester of azelaic half aldehyde.

25 grams of pelargonic aldehyde were obtained (88% yield) and 36 grams of the ethyl ester of azelaic half aldehyde (90% yield).

Pelargonic Aldehyde. The method of identification of this compound has already been described.

Ethyl Ester of Azelaic Half Aldehyde. This ester was very susceptible to auto-oxidation but did not polymerize to any appreciable extent on standing, as far as could be ascertained. On standing exposed to the air it gained in weight and its percentage of free acid increased very rapidly. Very little has been reported in the literature concerning this ester. As initially isolated from the steam distillation residue, it had a saponification equivalent of 192.0 (Calc. $(C_{11}H_{20}O_2)$ 200.1). It may be vacuum distilled more satisfactorily than the free acid, although again a somewhat large, dark colored residue was obtained. The pure ester was a colorless oil with a pleasant odor and boiled at 153-160°C/14 mm. (26) and at 100-102°C/1 mm. The pure product had a

saponification equivalent of 198.5-201.5.

Found:	Carbon	65.9%	Hydrogen	10.2%
		65.8		10.1
Calc.:(C ₁₁ H ₂₀ O ₃)		66.0		10.1

All attempts to prepare the semicarbazone yielded oils which could not be made to crystallize.

This ester formed a 2,4-dinitrophenylhydrazone in quantitative yields, which crystallized as glistening yellow needles from 95% ethyl alcohol. The melting point was constant after three recrystallizations. Melting point 63-64°C.

Found:	Carbon	53.6%	Hydrogen	6.35%
		53.5		6.34
Calc.:(C ₁₇ H ₂₄ O ₆ N ₄)		53.7		6.36

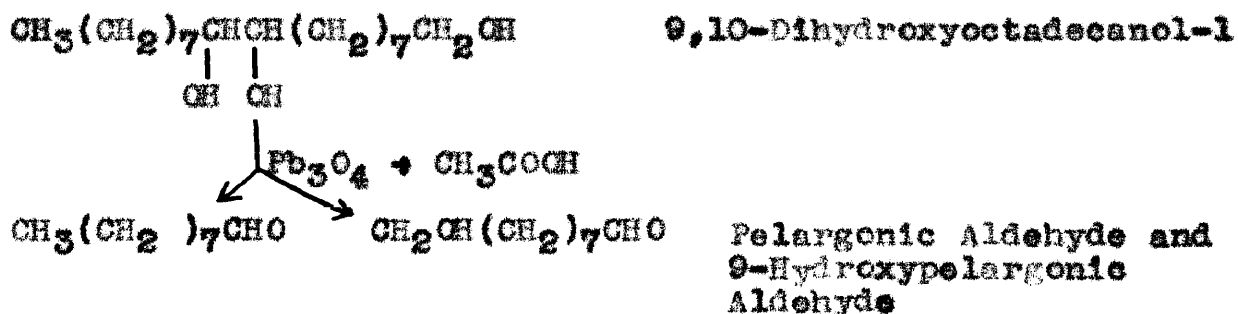
The refractive index and density of this aldehyde were determined at 25°C.

$$n_{\text{Abbe}}^{25^\circ} \quad 1.4348 \qquad d_4^{25^\circ} \quad 0.9380$$

From these values the molecular refractivity was calculated.

Found:	55.7
Calc.:(C ₁₁ H ₂₀ O ₃)	54.5 (20)

Oxidation of 9,10-Dihydroxyoctadecanol-1 (Low Melting) with Red Lead and Glacial Acetic Acid:



151 grams of 9,10-dihydroxyoctadecanol-1 (.5 mole) was dissolved in 1230 cc. of glacial acetic acid and oxidized

by means of 377 grams of red lead (.55 mole) as described previously. After the reaction was complete, the reaction mixture was diluted with about 2500 cc. of water and well shaken. The mixture was then extracted with two 1000 cc. portions of ether. The combined ether extracts were washed with water until free of lead, with sodium bicarbonate solution until free of acidic substances and then with water until neutral. The ether solution was dried over anhydrous calcium sulfate and filtered. The ether was removed under reduced pressure and the residual pale yellow, pleasant smelling oil was vacuum distilled. In this way 50 grams of pelargonic aldehyde (70% yield) boiling from 80-90°C/14 mm. and 40 grams of 9-hydroxypelargonic aldehyde (51% yield) boiling from 153-175°C/14 mm. were obtained.

Pelargonic Aldehyde. This fraction contained over 98% free pelargonic aldehyde (58). The boiling point of pelargonic aldehyde was also determined at two other pressures. The boiling points were 49-52°C/1 mm. and 35-37°C/.1 mm.

9-Hydroxypelargonic Aldehyde. This aldehyde was a white waxy solid and tended to clog up the condenser if precautions were not taken. It melted from 41-44°C unrecrystallized and from 55-56°C after two recrystallizations from xylene. Literature melting point 58°C and boiling point 155-157°C/14 mm. (32). The pure aldehyde was a snow white solid with a very pleasant odor.

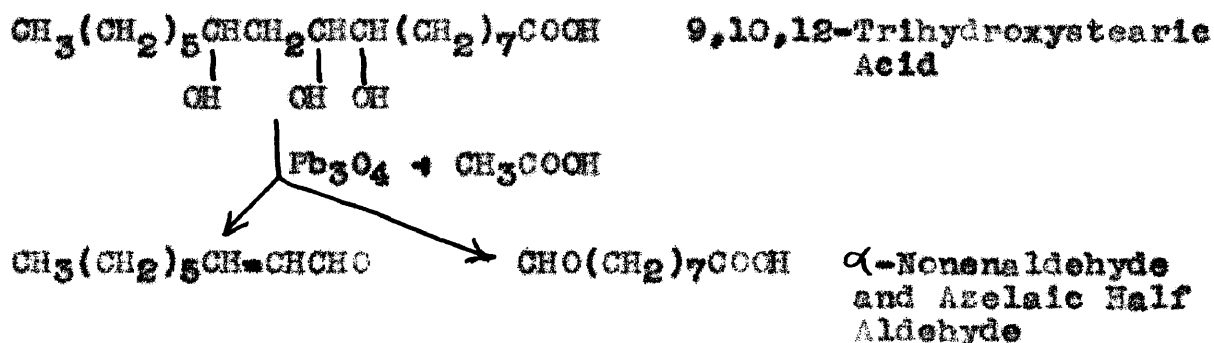
Found:	Carbon	68.2%	Hydrogen	11.6%
		68.2		11.5
Calc.:(C ₉ H ₁₈ O ₂)		68.3		11.5

All attempts to prepare the benzoate and 3,5-dinitrobenzoate yielded uncrystallizable oils.

The percentage of aldehyde was found to be 98.5% by the method employed by Iddles and his co-workers (37)(38).

The boiling ranges of this aldehyde at other pressures were found to be 119-125°C/1 mm. and 106-120°C/.1 mm.

Oxidation of 9,10,12-Trihydroxystearic Acid (Low Melting)
with Red Lead and Glacial Acetic Acid:



The oxidation was carried out in the manner already described using 66.4 grams of 9,10,12-trihydroxystearic acid (.2 mole), 151 grams of red lead (.22 mole) and 500 cc. of glacial acetic acid. The reaction mixture was worked up according to the first method described under dihydroxystearic acid.

The aldehyde which was isolated from the steam distillate was a pale yellowish-green oil with a sweet but slightly rancid odor. This aldehyde was believed to be 3-hydroxypelargonic aldehyde at first, but subsequent investigation proved it to be α -nonenaldehyde. From the above-mentioned amount of trihydroxystearic acid, 20 grams of α -nonenaldehyde of 94% purity (58) was obtained. This was a 67% yield.

No attempt was made to purify the azelaic half aldehyde. It was oxidized directly to azelaic acid. As isolated from the steam distillation residue, the azelaic half aldehyde was a light brown viscous oil. It was dissolved in enough 5% sodium hydroxide solution so that the pH was about 8-9. To this well stirred solution at room temperature a solution of 44 grams of potassium permanganate (.28 moles) in 500 cc. of water was added all at once with very efficient stirring. The temperature rose rapidly to about 68°C. The solution was stirred for fifteen minutes after the permanganate color had disappeared. After the manganese dioxide had settled, the mixture was filtered and the residue of manganese dioxide washed with boiling water several times. The precipitate was transferred to a beaker and washed thoroughly with about 250 cc. of boiling water. This was filtered and the filtrates were combined and evaporated to about one liter. The hot solution was acidified with dilute sulfuric acid. The solution became milky and a small quantity of oil floated to the surface. The solution was heated to boiling with a small quantity of Darco and filtered. The filtrate was allowed to cool and the azelaic acid which crystallized out was filtered off, washed free of sulfuric acid and dried. It formed small white crystals. The yield of azelaic acid was 14 grams or 37% based on the trihydroxystearic acid.

α -Nonenaldehyde. The aldehyde was purified by vacuum distillation under reduced pressure and boiled from 56-58°C/.1 mm. It is hard to conceive of any dehydration taking place at this temperature and it should be noted that the

chemical properties of the pure vacuum distilled aldehyde and the aldehyde as obtained from the steam distillate were practically identical.

This aldehyde, dissolved in carbon tetrachloride, absorbed bromine very rapidly (5% bromine in carbon tetrachloride). Pelargonic aldehyde also took up bromine in a parallel experiment, but much more slowly and with the evolution of fumes of hydrobromic acid. This test indicated that the compound was unsaturated. The steam distillate aldehyde, which had not been vacuum distilled, reacted similarly.

The density and refractive index of the purified compound were determined and the molecular refractivity calculated from these values.

	$n_{\text{Abbe}}^{25^\circ}$	1.4502	$d_{40}^{25^\circ}$	0.8418
Found:		44.7		
Calc.:($\text{C}_9\text{H}_{16}\text{O}$)		43.3 (20)		

It will be observed that the experimental value for the molecular refractivity is slightly higher than the calculated one and is to be expected in a compound with a conjugated system of double bonds.

Carbon and hydrogen values were obtained on the pure, freshly distilled aldehyde.

Found:	Carbon	77.0%	Hydrogen	11.4%
		76.8		11.8
Calc.:($\text{C}_9\text{H}_{16}\text{O}$)		77.1		11.8

The aldehyde, either the highly purified samples or the steam distillation product, formed a semicarbazone (67)

in 70% yield which crystallized as small white needles from 95% ethyl alcohol. The melting point was constant after two recrystallizations from 95% ethyl alcohol using Darcos. This derivative melted at 165-165.5°C. Literature 163°C (4).

Found:	Carbon	60.8%	Hydrogen	9.85%
		60.7		9.76
Calc.:(C ₁₀ H ₁₉ ON ₃)		60.8		9.71

All attempts to prepare the oxime of this aldehyde yielded uncrystallizable oils.

The 2,4-dinitrophenylhydrazones formed small orange-red needles from 95% ethyl alcohol in 90% yield. It melted sharply at 126°C after two recrystallizations.

Found:	Carbon	56.3%	Hydrogen	6.23%
		56.3		6.26
Calc.:(C ₁₅ H ₂₀ O ₄ N ₄)		56.2		6.29

By passing air through samples of the aldehyde for 27 hours at room temperature, the corresponding acid, α -nonenoic acid, was prepared in 97% yield. The apparatus used was the aerator containing the sintered glass disk, as described by Senseman and Stubbs (56). The air oxidation was only slightly exothermic and was very easily managed. This acid was readily purified by vacuum distillation but for the purposes of derivatives the aeration reaction mixture served just as well.

The pure acid boiled from 135-138°C/5 mm. and was an almost colorless oil with a somewhat sharp, rancid odor. It had a neutralization equivalent of 156.5 Calc.(C₉H₁₆O₂) 156.2 and a melting point of 0-1°C. Literature +3°C (51).

Found:	Carbon	69.2%	Hydrogen	10.3%
		69.1		10.4

Calc.: (C₉H₁₆O₂) Carbon 69.2% Hydrogen 10.3%

This acid took up bromine dissolved in carbon tetrachloride very rapidly with no evolution of hydrobromic acid. Its density and refractive index were also determined from which the molecular refractivity was readily calculated.

$n_{\text{Abbe}}^{25^\circ}$	1.4561	$d_{40}^{25^\circ}$	0.9286
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Found: 45.7

Calc.: (C₉H₁₆O₂) 44.8 (20)

Again the experimental value was slightly high as might be expected in a compound with a conjugated system of double bonds.

The p-bromophenacyl derivative of this acid was prepared (22) and was recrystallized to constant melting point from 95% ethyl alcohol. It formed glistening, pearly flakes which melted sharply at 77.5-78°C.

Found:	Carbon 57.8%	Hydrogen 5.85%	Bromine 22.6%
	57.7	5.92	

Calc.: (C ₁₇ H ₂₁ O ₃ Br)	57.8	5.99	22.6
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The amide of the acid was prepared according to the method described by Shriner and Fuson (67). It was recrystallized from aqueous methanol (Darco) to constant melting point. After three recrystallizations it melted at 130-130.5°C, and formed glistening plates. Literature 126-127°C (23).

It will be seen that the properties of the unsaturated aldehyde and its corresponding acid, as well as those derivatives of these substances which have been reported previ-

ously in the literature, check fairly well with the literature for α,β -unsaturated compounds prepared by totally different means. Likewise, the other properties of these compounds which have been determined check very well with the values calculated for the unsaturated compounds and not with those calculated on the basis of hydroxy compounds.

Oxidations in which the hydroxy compounds were isolated but not purified.

Oxidation of Unrecrystallized 9,10-Dihydroxystearic Acid
(Low Melting) with Red Lead and Glacial Acetic Acid:

The dihydroxystearic acid used in this experiment was the unrecrystallized solid cake prepared by the oxidation of oleic acid with hydrogen peroxide and acetic acid, as described previously. The solid cake was broken into small pieces and allowed to dry before being used in the lead tetraacetate oxidation. From 282 grams of oleic acid (1.0 mole), 288 grams of crude dihydroxystearic acid was obtained. This material was dissolved in 2200 cc. of glacial acetic acid at 55-65°C and 754 grams of red lead (1.1 moles) was added in the usual way. At the completion of the reaction, the reaction solution was diluted with 1500 cc. of water and steam distilled until no more oily drops came over. The steam distillate was worked up as described previously and 51 grams of pelargonic aldehyde of 95% purity was obtained. This was a 36% yield based on the oleic acid used. Starting with pure dihydroxystearic acid, the yield of pelargonic aldehyde based on oleic acid was 32%. It is quite obvious that it is un-

necessary to purify the dihydroxystearic acid if only palar-
gonic aldehyde is desired. However, the impurities which
remain in the dihydroxystearic acid are retained in the
residue after distillation with steam and interfere with the
subsequent operations. The steam distillation residue con-
sisted of a brown oil floating on the surface of the water.
This was extracted with ether and the ether was washed with
water until free of lead and acetic acid. The ether was
evaporated and the residual oil was dissolved in a slight
excess of 5% sodium hydroxide solution so that the pH was 8-9.
To this solution at room temperature was added as rapidly as
possible a solution of 92 grams of potassium permanganate
(.58 mole) in 1100 cc. of water with very efficient stirring.
The temperature rose rapidly from 30°C to 65°C and to prevent
frothing over, a small amount of benzene had to be added. The
permanganate color disappeared almost immediately but stirring
was continued for an additional 15 minutes. The reaction
mixture was allowed to stand over night and then filtered.
The precipitate of manganese dioxide was washed twice with
boiling water and then transferred to a large beaker where
it was stirred well with about 1000 cc. of boiling water.
The manganese dioxide was filtered off and the filtrates were
combined. The combined filtrates may be evaporated down to
about two liters at this point or later as described. The
solution was cooled, acidified with 20% sulfuric acid and
chilled in the refrigerator. The small amount of oil which
had separated on acidification, solidified on cooling, and
was removed mechanically by means of a spatula, the azelaic

acid being left behind. The solution was evaporated down to about two liters, and filtered hot after the addition of a small amount of Darco. The azelaic acid which precipitated on cooling was filtered off and recrystallized again from hot water. It formed small white crystals.

Yield: 11 grams or 6% based on oleic acid. Melting point and mixed melting point 104-106°C.

Oxidation of 9,10-Dihydroxyoctadecanol-1 (Low Melting) with Red Lead and Glacial Acetic Acid:

The dry, unrecrystallized 9,10-dihydroxyoctadecanol-1 (about 278 grams) which was prepared from 268.5 grams of oleyl alcohol (1.0 mole) was dissolved in 2200 cc. of glacial acetic acid at 55-65°C. To this solution was added in the usual way 754 grams of red lead with very efficient stirring. After the reaction was complete, the solution was poured into 2200 cc. of water and well shaken. The mixture was extracted twice with 1000 cc. portions of ether, the ether solution washed with water until free of lead, with sodium bicarbonate solution until free of acidic products and then with water until neutral. The ether solution was dried over anhydrous calcium sulfate, filtered and the ether was evaporated under reduced pressure. The residual light brown oil was vacuum distilled. In this way, 38 grams of pelargonic aldehyde (27% yield based on oleyl alcohol) of 99% purity was obtained having a boiling range from 40-42°C/.1 mm. Similarly, 36 grams of 9-hydroxypelargonic aldehyde (23% yield based on oleyl alcohol) was obtained having a boiling range from 99-120°C/.1 mm. and melting from 42-45°C. It was recrystallized twice from xylene

and then melted at 52-54°C. A mixed melting point with an authentic specimen of 9-hydroxypelargonic aldehyde melting at 53-56°C, melted at 53-55°C.

Oxidation of the Crude Hydroxylation Product of Castor Oil
with Red Lead and Glacial Acetic Acid:

As will be described later, castor oil may be hydroxylated and then oxidized without the isolation of the hydroxy derivative--the so-called continuous method. It was thought that the presence of hydrogen peroxide in the reaction mixture in the continuous process interfered with the subsequent red lead oxidation. It was considered a good plan to isolate the hydroxylated derivative of castor oil and then dissolve it in glacial acetic acid to which red lead could then be added. In this way, there would be no hydrogen peroxide to contend with and the percentage of water would be less than in the continuous method. It was also believed that after the hydroxylated product was isolated, some procedure could be devised for hydrolyzing the acetyl groups without affecting the glyceride, thereby giving an increased yield of aldehydes. The advantage in keeping the carboxyl groups blocked is that the dangers of polymerization of the azelaic half aldehyde fraction is lessened and a more effective oxidation of the aldehyde to the acid is possible. It was found, however, that isolating the hydroxylated product was of no advantage, and no procedure could be devised for preferential acetyl group hydrolysis. The yields of α -nonenaldehyde and azelaic acid were the same as in the continuous process. Since the continuous method effects such large savings of time and

materials, it is superior to the above method.

The method which was employed in an attempt to remove acetyl groups without altering the glyceride part of the molecule was to suspend the hydroxylated product in a solution of sodium tetraborate, sodium bicarbonate or sodium carbonate and then pass steam through the mixture. The first two solutions used caused no appreciable hydrolysis of any sort to take place. The last solution caused the hydrolysis to go too far and was therefore undesirable.

Oxidations in which the hydroxy compounds were oxidized without their isolation from the reaction mixture

Hydroxylation and Oxidation of Castor Oil:

For the sake of simplicity of calculation, castor oil was considered to be 100% triricinolein. Although this is not strictly correct, the residual material does not affect the results appreciably. 225 grams of 30% hydrogen peroxide (2.0 moles) was dissolved in 820 cc. of glacial acetic acid and the solution heated from 80-85°C for one hour. This solution was cooled under the tap to 25°C and mixed with 311 grams of castor oil (approximately .33 mole). The mixture was stirred occasionally and the temperature rose to about 70°C in about thirty minutes at which point the solution became homogeneous. The temperature remained at its maximum point for some time and then commenced to fall very slowly, which indicated that the reaction was continuing. The solution was allowed to stand overnight and then diluted with 1380 cc. of glacial acetic acid. To this well stirred so-

lution at 55-65°C, 754 grams of finely powdered red lead (1.1 moles) was added. The first additions of red lead served to decompose excess hydrogen peroxide as evidenced by the very rapid decolorization of the solution and the evolution of large amounts of gas. When the hydrogen peroxide was completely decomposed, the red color disappeared less rapidly and the red lead had to be added at a slower rate. The reaction was allowed to run to completion, the reaction mixture diluted with one liter of water and then steam distilled until no more oil came over. The steam distillate was extracted with ether, the ether solution washed twice with water, with sodium bicarbonate solution until free of all acidic impurities, and again with water until neutral. The ether solution was dried over anhydrous calcium sulfate, filtered, and the ether evaporated under reduced pressure. The residue was a greenish yellow liquid with a sweet, somewhat rancid odor. This liquid was α -nonenaldehyde and from 311 grams of castor oil about 50 grams were obtained. The freshly prepared material contained approximately 94% α -nonenaldehyde (58).

The residue which consisted of a brown oil floating on top of an aqueous layer, was cooled and extracted with ether. The ether solution was washed free of lead and the ether evaporated. The brown viscous oil which remained probably consisted of mixed glycerides of azelaic half aldehyde, saturated fatty acids and acetyl derivatives of hydroxy fatty acids. This residue was dissolved in 1000 cc. of glacial acetic acid to which 225 grams of 30% hydrogen

peroxide was added. The solution was allowed to stand at room temperature for approximately 24 hours and then heated on the steam bath until the maximum temperature was reached and then removed. The solution was allowed to cool down to room temperature and then was steam distilled free of acetic acid. The supernatant liquid was poured off and the residual pale yellow oil was refluxed with 1000 cc. of 10% sodium hydroxide solution for about three hours. The alkaline solution was acidified with sulfuric acid while hot and filtered as free of the oil floating on the surface as was possible. To remove the small amount of oil which came through, the filtrate was boiled with a small amount of Darco and filtered. The filtrate was allowed to cool slowly. The azelaic acid which precipitated out, was filtered, washed free of sulfuric acid and dried. 27 grams of azelaic acid were thus obtained. Melting point 104-106°C.

The oil which was filtered off solidified to a dark brown waxy solid. It weighed about 220 grams. No definite products could be identified from it. Glycerol is recoverable from the aqueous solution.

Hydroxylation and Oxidation of Ethyl Oleate:

310 grams of ethyl oleate (1.0 mole) was hydroxylated in the manner previously described using 225 grams of 30% hydrogen peroxide and 1120 cc. of glacial acetic acid. The additional acetic acid was necessary in order to keep the ethyl oleate in solution. The maximum temperature of the exothermic reaction was 61°C. After standing overnight,

1080 cc. of glacial acetic acid was added and the solution was warmed to 55-65°C. 754 grams of red lead (1.1 moles) was added as previously described. After the reaction was complete, the solution was diluted with one liter of water and steam distilled until no more oil came over. The steam distillate was extracted with ether and the ether solution washed twice with water, with sodium bicarbonate solution until free of acidic impurities, and again with water until neutral. The ether solution was dried over anhydrous calcium sulfate, filtered, and the ether evaporated under reduced pressure. The residue was a practically colorless, pleasant smelling oil which proved to be pelargonic aldehyde. This material contained 93% pelargonic aldehyde (58) and weighed 47 grams. This was a 33% yield based on the ethyl oleate.

The steam distillation residue was extracted with ether, the ether solution washed with water until free of lead, and with sodium bicarbonate solution until free of acidic impurities. The ether solution was dried over anhydrous calcium sulfate, filtered, and the ether evaporated. The residue weighed 263 grams and was a dark brown oil. It was vacuum distilled. The fraction boiling from 95-115°C/1 mm. proved to be the ethyl ester of azelaic half aldehyde. It had a saponification equivalent of 201.5 (Theory 200.3) and contained 96.8% aldehyde (58). The yield based on ethyl oleate was 12.5%. It formed a 2,4-dinitrophenylhydrazone in quantitative yield which melted at 63-64°C. A mixed melting point with an authentic sample remained unchanged.

Hydroxylation and Oxidation of Oleic Acid:

This substance did not react satisfactorily when oxidized by the continuous method.

282 grams of oleic acid (1.0 mole) was hydroxylated in the usual manner by means of 225 grams of 30% hydrogen peroxide (2.0 moles) and 720 cc. of acetic acid. At the conclusion of the reaction 1480 cc. of glacial acetic acid was added, the solution warmed to 55-65°C and 754 grams of red lead (1.1 moles) was added. When the reaction was complete, the solution was steam distilled and the steam distillate was worked up as described under the oxidation of 9,10-dihydroxystearic acid.

33 grams of pelargonic aldehyde was thus obtained of 94% purity (58). This was a 23% yield based on oleic acid.

It was not possible to isolate any azelaic half aldehyde from the steam distillation residue by vacuum distillation. By potassium permanganate oxidation only 4 grams of azelaic acid could be obtained.

It appears, then, as if the continuous hydroxylation and oxidation of oleic acid is not as satisfactory a method for preparing aldehydes as the oxidation of 9,10-dihydroxystearic acid, either pure or crude.

Oleyl alcohol also gave poor results when treated by the continuous method. The vacuum distillation of the reaction product bumped very badly and did not give a clean cut fractionation. Here again it was more desirable to start with a pure dihydroxy compound in the oxidation with lead tetraacetate.

It is most probable that the substances interfering with the continuous process are acetylated derivatives, since the hydrolysis of the reaction products gave hydroxy compounds in fairly good yields which reacted satisfactorily in the oxidation stage.

Other oils, namely peanut and olive, were treated by means of the continuous method, and pelargonic aldehyde and azelaic acid were obtained in much smaller yields than the products obtained from castor oil. The experiments were run in the same way as the castor oil experiments except that more acetic acid had to be used in the hydroxylation step because of the lower solubility of these oils in the hydroxylation mixture. A correspondingly smaller additional quantity of acetic acid was added for the oxidation stage in order to make the total amount of acetic acid used 2200 cc.

V. SUMMARY

The oxidation of hydroxylated fatty acids, esters and related substances with lead tetraacetate (the Criegee reaction) has been studied. The oxidation of 9,10-dihydroxystearic acid yielded pelargonic aldehyde (n-nonanal) and azelaic half aldehyde (8-formyl-1-octanoic acid). Similarly, ethyl-9,10-dihydroxystearate yielded pelargonic aldehyde and the ethyl ester of azelaic half aldehyde; 9,10-dihydroxyoctadecanone yielded pelargonic aldehyde and 9-hydroxypelargonic aldehyde; 9,10,12-trihydroxystearic acid yielded α -nonenaldehyde and azelaic acid; hydroxylated castor oil yielded α -nonenaldehyde and azelaic acid.

The Criegee reaction has been modified and improved so that it is no longer necessary to isolate and purify either lead tetraacetate or the hydroxylated substances.

VI. LITERATURE CITED

- (1) Bagard, P.
--Bull. soc. chim. [4], 1, 308, 319, 352 (1907)
- (2) Bartlett, P. D. and Hawley, A.
--J. Am. Chem. Soc. 60, 2416 (1938)
- (3) Bouveault, M. L.
--Bull. soc. chim. [3], 31, 1322 (1904)
- (4) v. Braun, J., Rudolph, W., Kröper, H. and Finkernelle, W.
--Ber. 67, 269 (1934)
- (5) Carrarra, G.
--Giorn. chim. ind. applicata 14, 236 (1932)
- (6) Collin, G. and Milditch, T. P.
--J. Chem. Soc. 1933, 246
- (7) Criegee, R.
--Ann. 481, 263 (1930)
- (8) Criegee, R.
--Ber. 64, 260 (1931)
- (9) Criegee, R.
--Ann. 495, 211 (1932)
- (10) Criegee, R.
--Ber. 68, 658 (1935)

- (11) Criegee, R.
--Angew. Chem. 50, 153 (1937)
- (12) Criegee, R., Kraft, L., and Rank, B.
--Ann. 507, 159 (1933)
- (13) Delaby, R. and Guillot-Allegre, S.
--Bull. sec. chim. 53, 301 (1933)
- (14) Dimroth, O., Friedemann, O., and Kämmerer, H.
--Ber. 53, 481 (1920)
- (15) Dimroth, O. and Hilcker, V.
--Ber. 54, 3050 (1921)
- (16) Dimroth, O. and Schweizer, R.
--Ber. 56, 1375 (1923)
- (17) Fieser, L. F. and Hershberg, E. B.
--J. Am. Chem. Soc. 60, 1895 (1938)
- (18) Fieser, L. F. and Hershberg, E. B.
--J. Am. Chem. Soc. 60, 2542 (1938)
- (19) Fieser, L. F. "The Chemistry of Natural Products
Related to Phenanthrene", 2nd ed., pp. 13-14, New
York, Reinhold Publishing Corp. (1937)
- (20) Gilman, H. "Organic Chemistry--An Advanced Treatise",
1st ed., Vol. II p. 1712, New York, John Wiley and
Sons, Inc. (1938)

- (21) Haller, A. and Brochet, A.
--Compt. rend. 150, 496 (1910)
- (22) Hann, R., Reid, E. K., and Jamieson, G.
--J. Am. Chem. Soc. 52, 818 (1930)
- (23) Harding, V. J. and Weizmann, C.
--J. Chem. Soc. 97, 299 (1910)
- (24) Harries, C.
--Ber. 42, 446 (1909)
- (25) Harries, C.
--Ann. 374, 288 (1910)
- (26) Harries, C.
--Ann. 374, 366 (1910)
- (27) Harries, C. and Thieme, G.
--Ann. 343, 357 (1905)
- (28) Harries, C. and Türk, H. O.
--Ber. 39, 3753 (1906)
- (29) Harries, C. and Türk, H. O.
--Ann. 343, 354 (1905)
- (30) Hazura, K.
--Monats. 9, 469 (1888)
- (31) Heilbron, I. M., Morrison, A. L. and Simpson, J. C. F.
--J. Chem. Soc. 1933, 302

- (43) King, G.
--J. Chem. Soc. 1938, 1826
- (44) Kobata, Y.
--J. Agr. Chem. Soc. Japan 11, 709 (1935)
- (45) Le Sueur, H. R.
--J. Chem. Soc. 79, 1313 (1901)
- (46) Mailhe, A.
--Bull. soc. chim. [4], 5, 619 (1909)
- (47) Mailhe, A.
--Chem.-Zeit. 35, 242 (1909)
- (48) McClenahan, W. S. and Hockett, R. C.
--J. Am. Chem. Soc. 60, 2061 (1938)
- (49) Molinari, E. and Barosi, C.
--Ber. 41, 2794 (1908)
- (50) Montignie, E.
--Bull. soc. chim. [5], 1, 1280 (1934)
- (51) Noorduyn, A. C.
Rec. trav. chim. 38, 331 (1919)
- (52) Nunn, L. C. A. and Smedley-Maclean, I.
--Biochem. J. 29, 2742 (1935)
- (53) Ôeda, H.
--Bull. Chem. Soc. Japan 9, 8 (1934)

- (54) Organic Syntheses, Collective Vol. I p.258 (1932)
- (55) Phillips, M. and Hellbach, R.
--J. Assoc. Official Agr. Chem. 11, 393 (1928)
- (56) Powell, S. G.
--J. Am. Chem. Soc. 53, 1171 (1931)
- (57) Pyman, F.L. and Stevenson, H.A.
--J. Chem. Soc. 1934, 448
- (58) Reclaire, A. and Frank, R.
--Perfumery Essent. Oil Record 29, 212 (1938)
- (59) Reid, E. E. and Ruhoff, J. R.
--Organic Syntheses 16, 60 (1936)
- (60) Sabatier, P. and Mailhe, A.
--Compt. rend. 154, 561 (1912)
- (61) Sabatier, P. and Mailhe, A.
--Compt. rend. 158, 916 (1914)
- (62) Saytzeff, A.
--J. prakt. Chem. [2], 35, 300 (1886)
- (63) Schall, H. C. and Melzer, W.
--Z. Electrochem. 26, 474 (1922)
- (64) Schimmel and Co.
--German patent 126,736 (1901)
- (65) Schönbein, C. F.
--J. prakt. Chem. 74, 315 (1858)

- (66) **Sensman, C. E. and Stubbs, J. J.**
 --Ind. Eng. Chem. 24, 1184 (1932)
- (67) **Shriner, R. L. and Fuson, R. C.** "The Systematic Identification of Organic Compounds", pp. 138-149, New York, **John Wiley and Sons, Inc.** (1936)
- (68) **Smil, K. C.**
 --Rec. trav. chim. 49, 675 (1930)
- (69) **v. Soden, H. and Rojahn, W.**
 --Ber. 34, 2810 (1901)
- (70) **Verkade, P. K.**
 --Rec. trav. chim. 67, 824 (1938)
- (71) **Wagner, A.**
 --Allgem. Ol-Fett. Ztg. 24, 340 (1927)
- (72) **Wahlbaum, H. and Nüchig, O.**
 --J. prakt. Chem. [2], 66, 47 (1902)
- (73) **Wahlbaum, H. and Stephan, K.**
 --Ber. 33, 2308 (1900)
- (74) **Ward, K.**
 --J. Am. Chem. Soc. 60, 326 (1938)
- (75) **Ward, K.**
 --U.S. Patent 2, 080,752 (1937)
- (76) **Wittig, G. and v. Lupin, P.**
 --Ber. 61, 1627 (1928)
- (77) **Zaer, S.**
 --Ber. Schimmel and Co., Akt. Ges. 1929, 299
- (78) **Zetsche, F. and Weber, T.**
 --J. prakt. Chem. 150, 140 (1938)