LACTONE STUDIES

(I) REACTION BETWEEN DIACETIN AND THIONYL CHLORIDE

(II) α-BENZYL-γ-BUTYROLACTONE AND RELATED COMPOUNDS

by

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To

My Parents

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The author wishes to express his appreciation and thanks to Dr. E. H. Charlesworth for his kind assistance and encouragement during the course of this work.

Thanks are due also to Mr. Barry Blackburn and Mr. Murray Morello for their help in obtaining the infrared spectra discussed herein.

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ABSTRACT

3-Chloro-1,2-propanediol diacetate is produced as a major product in the chlorination of diacetin. This is proved by the formation of 3-chloro-1,2-propanediol when the product of the reaction between diacetin and thionyl chloride is transesterified with ethyl alcohol. Di-(1,3-benzylideneglyceryl)sulfite is produced when 1,3-benzylideneglycerol is reacted with thionyl chloride in the presence of pyridine.

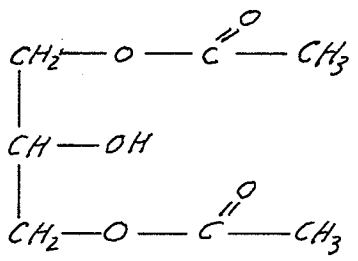
A monohydrazide is produced by reaction between α-carbethoxy-α-benzyl-γ-butyrolactone and hydrazine. Tars and oils are the main products when α-benzyl-γ-butyrolactone is oxidized.

TABLE OF CONTENTS

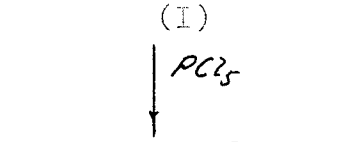
INTRODUCTION

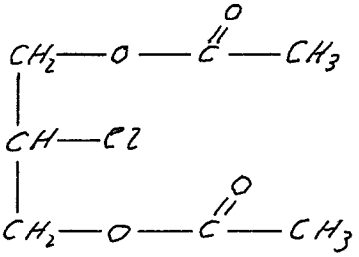
PART I..... (Reaction between diacetin and thionyl chloride.)

Results of the chlorination of the isomeric diacetins (glycerol diacetates) were reported by Wegscheider and Zmerzlikar (46) in 1913. Using phosphorus pentachloride they produced 2-chloro-1,3-propanediol diacetate (II) from 1,3-diacetin (I) and 1-chloro-2,3-propanediol diacetate (IV) from 1,2-diacetin (III). These reactions are shown below:



(I)





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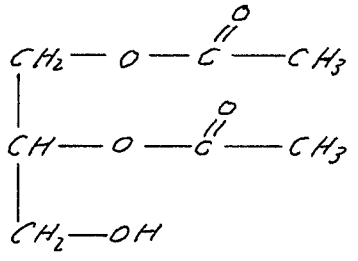

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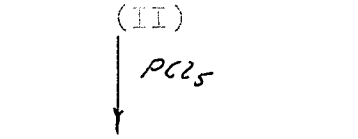
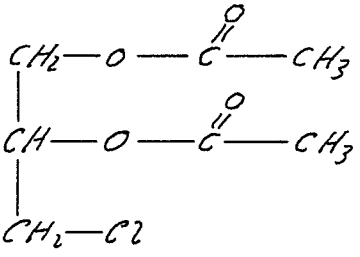
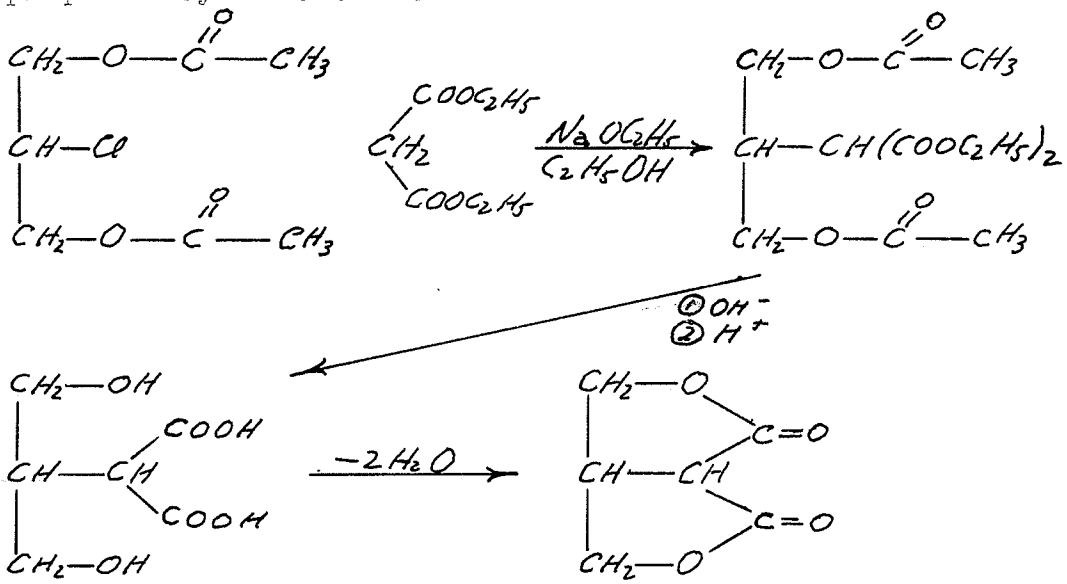




(IV)

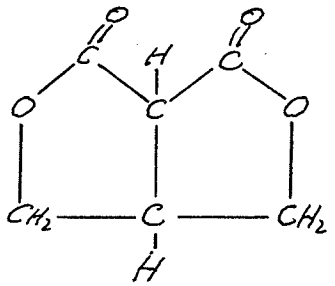
We became interested in compound III because it afforded the possibility of synthesizing the interesting

compound 2-carboxy-3,3'-dihydroxymethylacetic acid dilactone (V) via a malonic ester condensation. The proposed synthesis was:

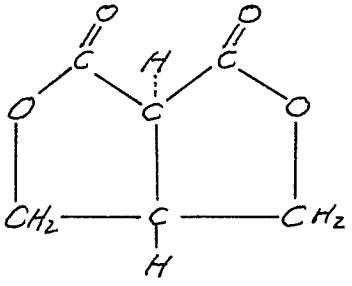


V

Studies with molecular models indicate that compound V can exist in two forms, one (Va) having the hydrogens on carbons 2 and 3 cis, the other (Vb) having these hydrogens trans.



Va

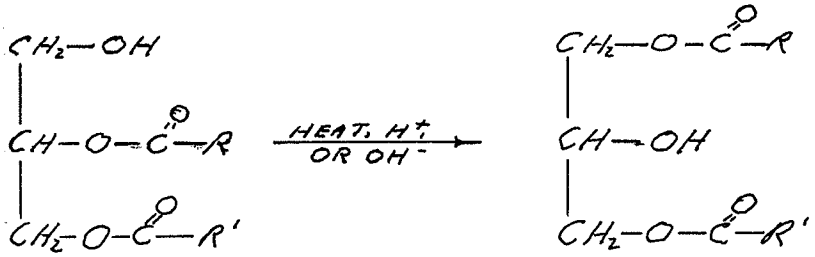


Vb

While this work was still in the early stages it became obvious that the preparation of compound III in

pure form from diacetin would be difficult because of the problem of acyl migration, which is discussed below. Hence this phase of the project is concerned solely with the reaction between thionyl chloride and diacetin and the characterization of the products therefrom.

In 1920, Fischer and coworkers (16) showed that migration of acyl groups in mono- and diglycerides (that is, glycerol esters with at least one free hydroxyl group present in the glycerol derived portion of the molecule) occurs readily on heating or in the presence of even small quantities of acid or base. Migration usually occurs from the 2-position to the 1-position. For example:



mixed 1,2-diglyceride mixed 1,3-diglyceride

For this reason, any synthesis which is designed to produce a glyceride (mono-, di-, or mixed tri-) of definite, known configuration is now accomplished by first putting protecting groups on glycerol hydroxyls which would otherwise be free to react and then removing the protecting groups under conditions which do

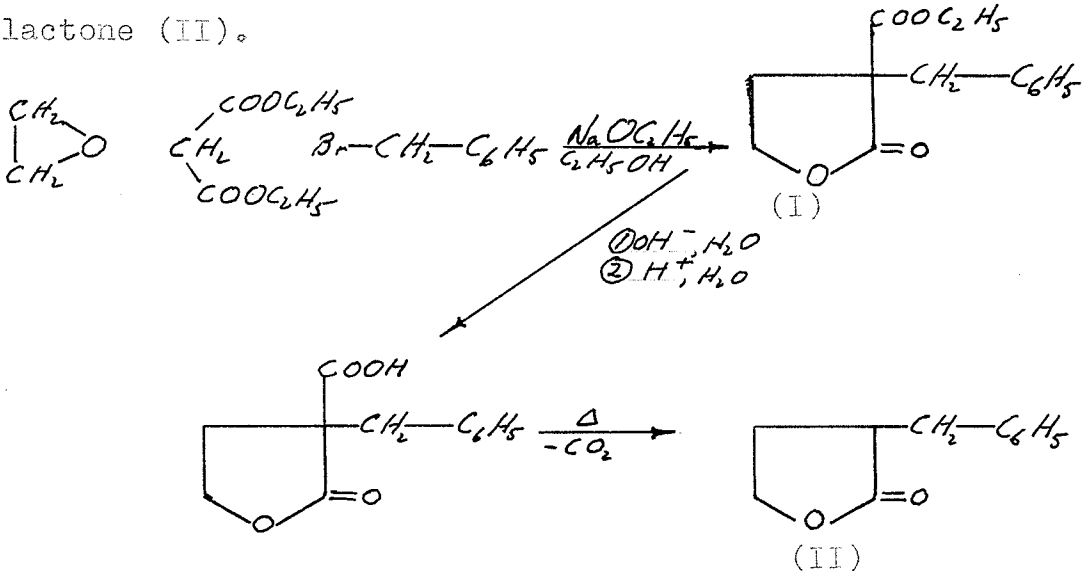
not promote migration of acyl groups. The use of protecting groups to minimize the effects of acyl migration in glyceride synthesis has become common only in the last forty years.

Wegscheider and Zmerzlikar (46) carried out their work before it was recognized that precautions should be taken to minimize the extent of acyl migrations in glyceride syntheses. Since one of the products of the reaction between phosphorus pentachloride and alcohols is hydrogen chloride, acyl (in this case, acetyl) migration would be expected to occur in the unreacted diacetin molecules during the course of the reaction. The isomerization would more probably affect the synthesis of 1-chloro-2,3-propanediol diacetate (IV), because of the noted tendency for migration to occur from the 2-position to the 1-position. A reexamination of the chlorination of the isomeric diacetins was therefore undertaken, using thionyl chloride as the chlorinating agent.

PART II..... (α-Benzyl-γ-butyrolactone and related compounds.)

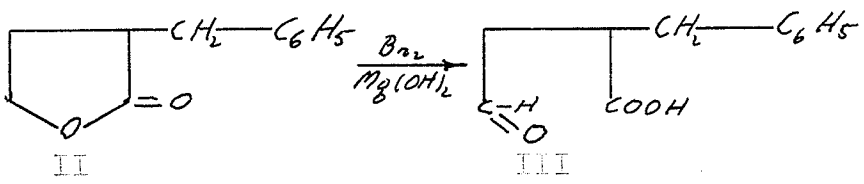
In 1960, Krushel (30), continuing the work of Charles-

worth et al (7, 8, 31, 32) on lactone structure and synthesis, prepared α-benzyl-γ-butyrolactone (II). He condensed equimolar quantities of ethylene oxide and benzyl bromide with diethyl malonate. α-Carbethoxy-α-benzyl-γ-butyrolactone (I) was formed spontaneously on reaction and after saponification followed by acidification and decarboxylation, this compound yielded α-benzyl-γ-butyrolactone (II).



Because compound I was rather poorly characterized by Krushel, a hydrazide derivative of it was prepared. A number of attempts were made to prepare 3-carboxy-4-phenyl-1-butanal (III) by mild oxidation of α-benzyl-γ-butyrolactone (II). In addition, Krushel's preparation

of α-benzylsuccinic acid (IV) by oxidation of α-benzyl-γ-butyrolactone was repeated. Confirmation of this synthesis was not realized and further work on this reaction will be necessary.



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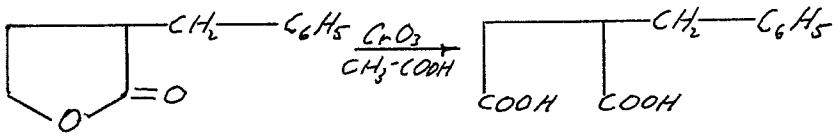


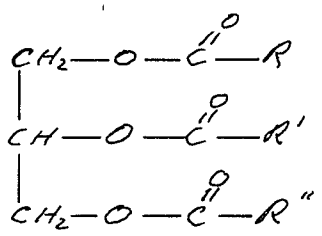
II IV

LITERATURE SURVEY

PART I..... (Reaction between diacetin and thionyl chloride.)

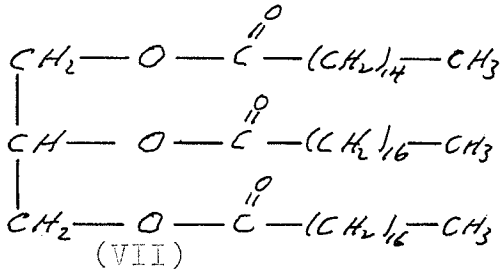
GLYCERIDE SYNTHESIS AND ACYL MIGRATION

The early studies of glycerides (fatty acid esters of glycerol) were prompted by Chevreul's discovery (9) in 1823 that most naturally occuring fats, plant and animal, belong to this class of compound. The general structure VI was proposed for fats:



(VI)

Usually, R, R', and R'' are not the same in naturally occuring glycerides. Without synthetic evidence, however, there is no way of determining the configuration of a given glyceride. Palmitodistearin, for instance, could be 1-palmito-2,3-distearin (VII) or 1,3-distearo-2-palmitin (VIII):



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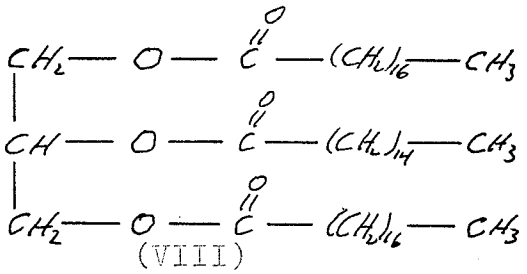
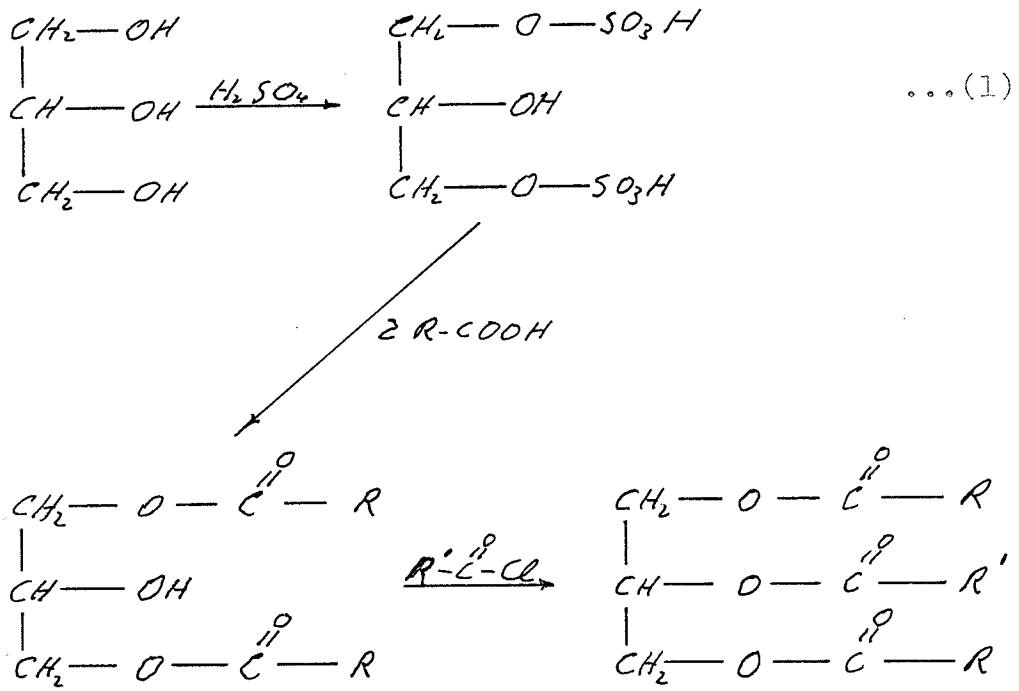
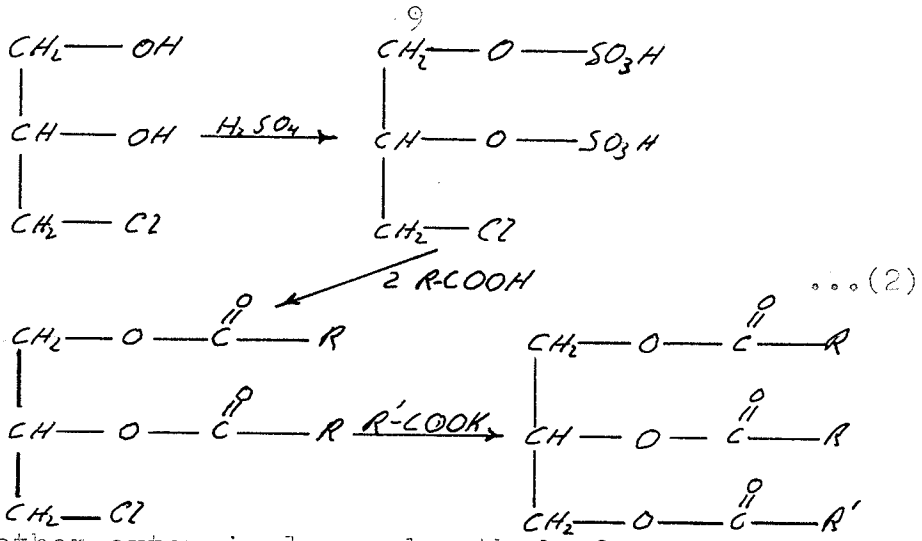


(VIII)

Simple triglycerides in which only one type of fatty acid residue is present were prepared by Garner (18), who heated a mixture of the fatty acid and glycerol under an atmosphere of carbon dioxide. This method is unsuitable for the preparation of pure mixed triglycerides in which more than one type of fatty acid is esterified; a mixture of all possible triglycerides is produced.

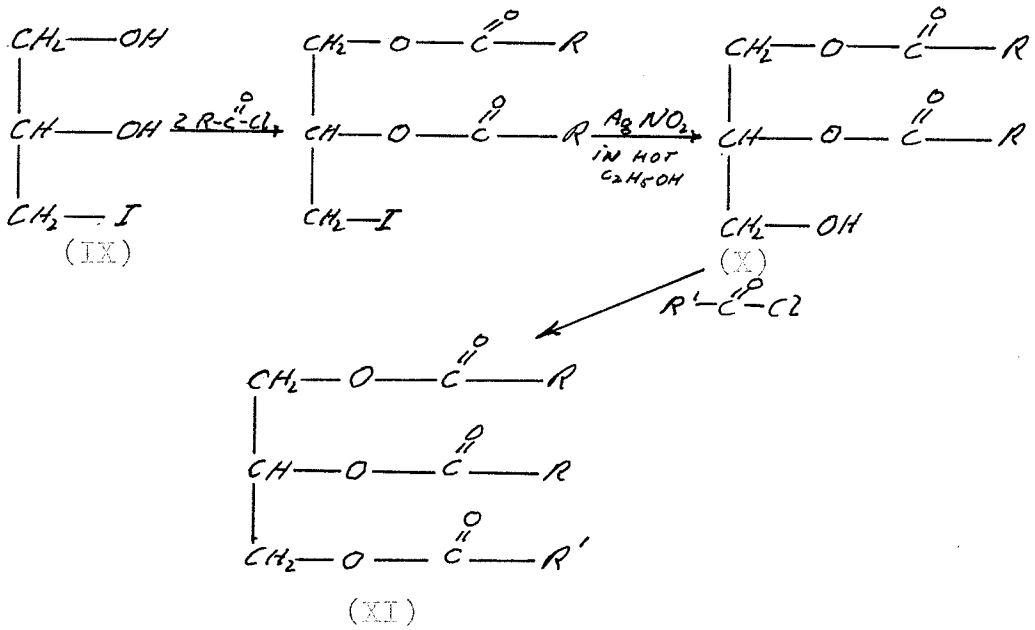
The first chemically versatile syntheses of pure mixed triglycerides were those of Grun et al (19, 21, 22). The preparation of a symmetrical (reaction 1) and an unsymmetrical (reaction 2) triglyceride containing two different fatty acid residues is shown:





...(2)

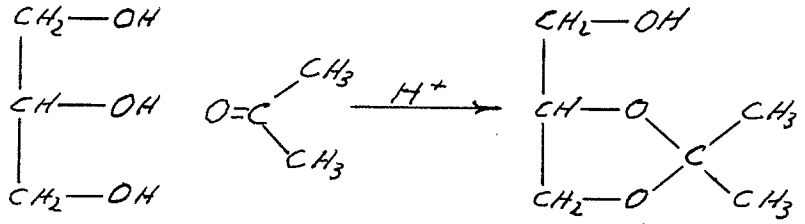
Another extensively used method of synthesis started with α-iodohydrin (IX), first producing an unsymmetrical diglyceride (X) and thence an unsymmetrical triglyceride (XI) according to the following scheme:



(IX) (X) (XI)

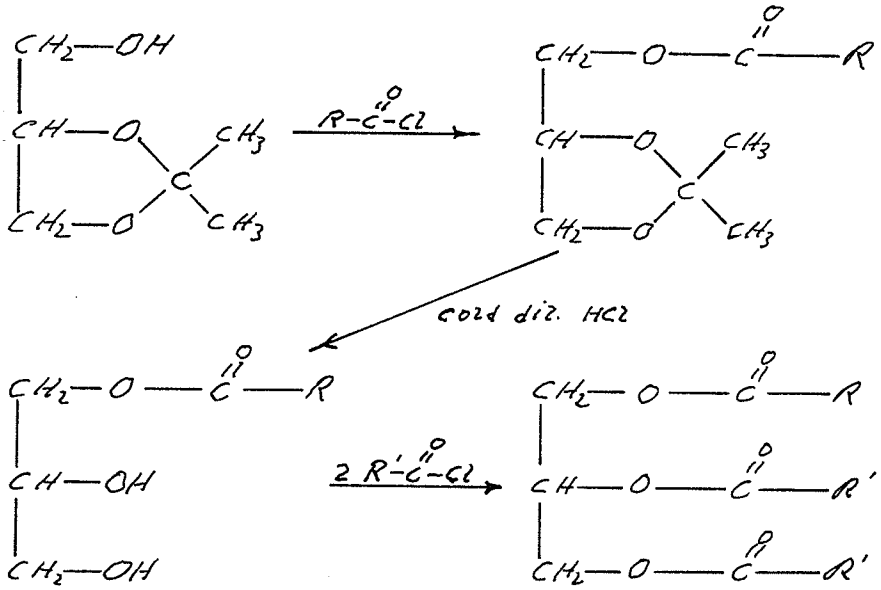
Fischer's demonstration (16) that shifting of acyl groups in mono- and diglycerides occurs at high temperatures and the later finding of Daubert and King (12) that small amounts of acid or base also catalyze this

shift, rendered suspect most early synthetic work. Fortunately this also served as a stimulus for the discovery of newer, more sophisticated techniques of glyceride synthesis. Fischer pioneered the use of 1,2-isopropylideneglycerol (XII) in the synthesis of unsymetrical triglycerides. The reagent is prepared by reaction of glycerol with acetone in the presence of a small amount of mineral acid.



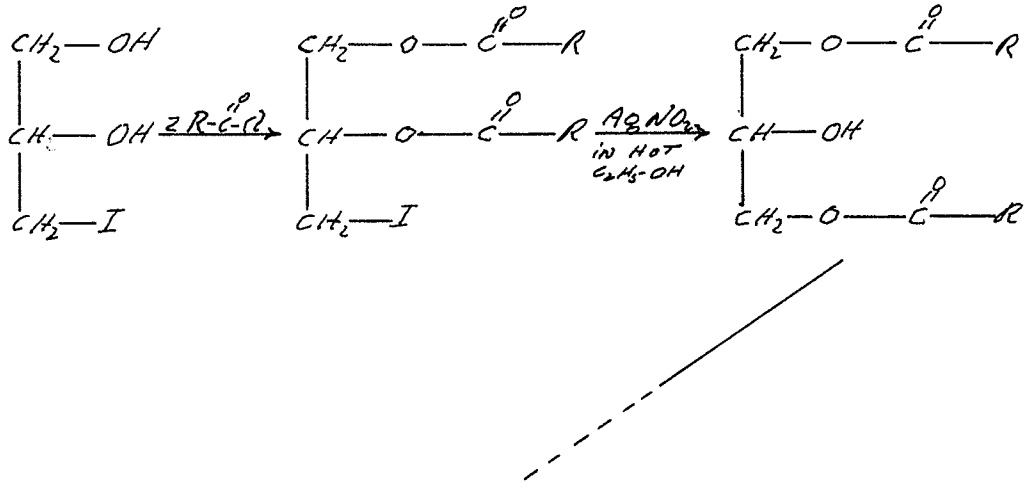
(XII)

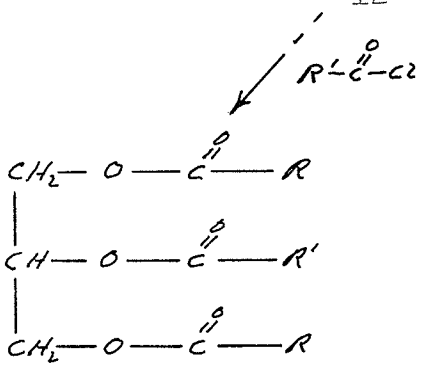
A typical unsymmetrical mixed triglyceride synthesis starting with 1,2-isopropylideneglycerol is shown below:



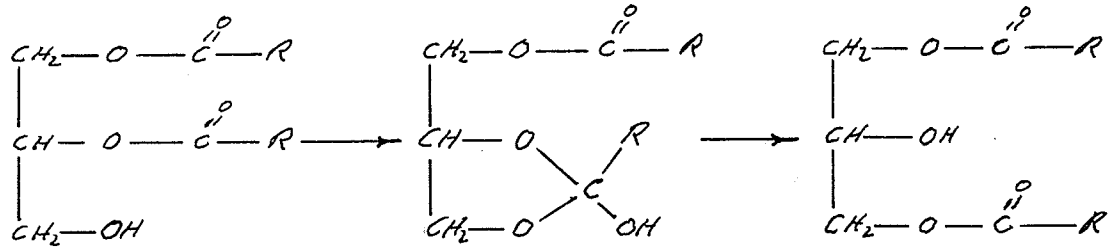
That cold dilute hydrochloric acid removes the acetone group without causing acyl migration was proved (20) by recondensation of the 1-monoglyceride with acetone. This reaction is succesful only for compounds with vicinal hydroxyl groups; thus, had the 2-monoglyceride been formed due to acyl migration during treatment of the isopropylideneglycerol ester with acid, the recondensation would have failed.

Fischer then compared the product obtained using this method of synthesis with that obtained using α-iodohydrin as the starting material. He found that the two were not the same. Since each had the same empirical formula and the product of the 1,2-isopropylideneglycerol method was definitely the unsymmetrical isomer, the product of the α-iodohydrin method must have been the symmetrical isomer. Therefore, the α-iodohydrin synthesis must proceed according to the following scheme, with acyl migration occuring on treatment with hot ethanolic silver nitrite, and not as previously given:





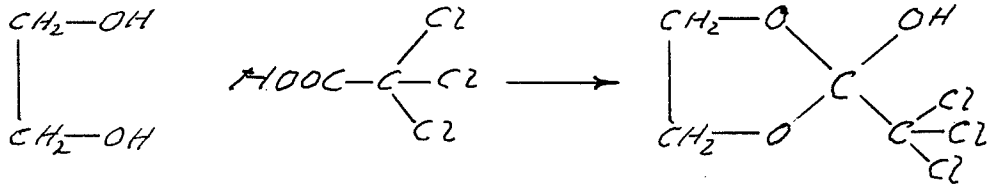
Fischer (16) proposed that the mechanism for the acyl shift in glycerides having free hydroxyls in the glycerol portion of the molecule proceeded through the formation of a 1,3-dioxolone intermediate (XIII) by migration of the hydroxyl hydrogen to the carbonyl oxygen on the adjacent acyl group:



(XIII)

Hibbert and Grieg (25) reasoned that an increase in the electronegativity of the -R group would favour the shift of hydrogen to the acyl oxygen and would therefore stabilize the dioxolone intermediate relative to the glyceride. They succeeded in preparing 2-hydroxy-2-trichloromethyl-1,3-dioxolone (XIV) by reacting ethylene glycol with trichloroacetic acid

and 2-hydroxy-2-trichloromethyl-4-chloromethyl-1,3-dioxolone (XV) by reacting epichlorohydrin with trichloroacetic acid.



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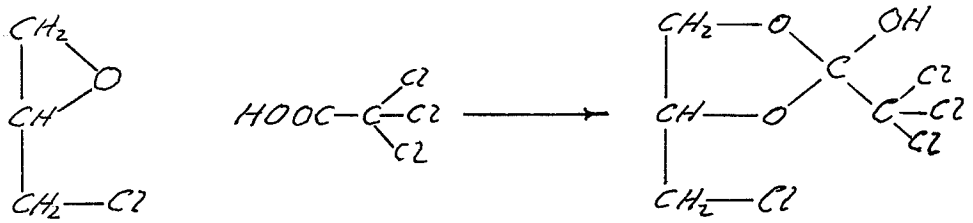
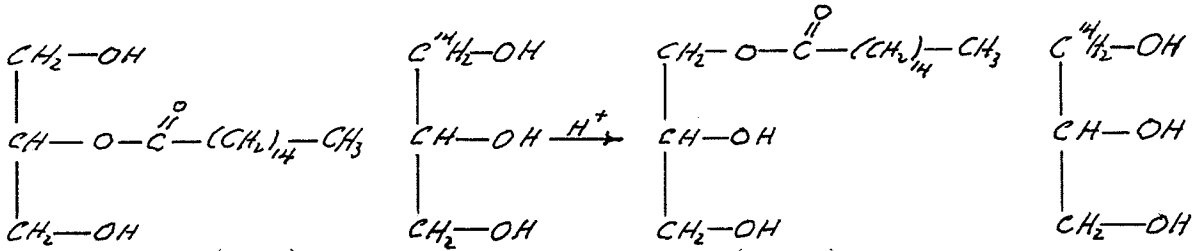


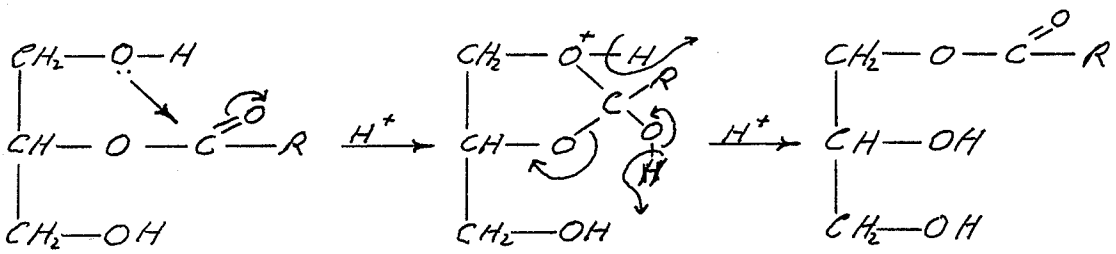
(XV)

Doerschuck (13) confirmed the intramolecular nature of the migration by carrying out the rearrangement of 2-monopalmitin (XVI) in the presence of glycerol-1-C^{14}. The 1-monopalmitin obtained (XVII) was C^{14} free.



(XVI) (XVII)

He proposed the general acid catalyzed mechanism:

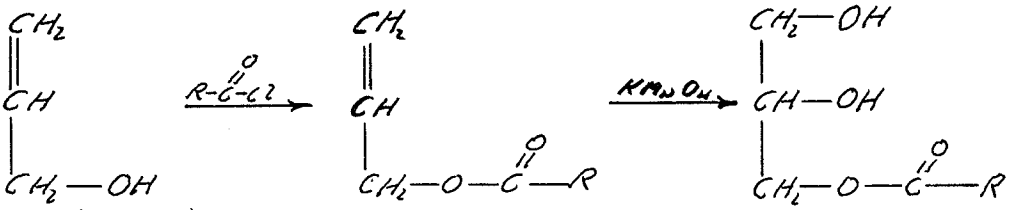


This is consistent with the facts that the benzoyl group does not migrate as readily as aliphatic acyl groups and that systems possesing -R's that are strongly electron-attracting exist as cyclic orthoesters (28).

Daubert and King (12) found that acyl migration occurs readily in the presence of acids or bases and moves the acyl group from the 2-position to the 1-position. Migration of both aromatic and aliphatic acyl groups occurs easily in the presence of 0.1N HCl or NH_4OH, and 0.0067N HCl or 0.013N NH_4OH causes migration of aliphatic acyl groups. These results, along with those of Fischer (16) illustrate the general unreliability of reports of mixed glyceride syntheses found in the literature prior to 1920.

With recognition of the phenomenon of acyl migration came a need for new techniques of glyceride synthesis, techniques designed to minimize migrations which would lead to impure products. The first rel-

iable method to satisfy this requirement was Fischer's 1,2-isopropylideneglycerol synthesis which, as was seen above, can be used to prepare both 1-monoglycerides and unsymmetrical mixed triglycerides. Fairbourne's 1-monoglyceride synthesis (14, 15) starts with the esterification of allyl alcohol (XVIII). The ester is then oxidized to a 1-monoglyceride with permanganate.



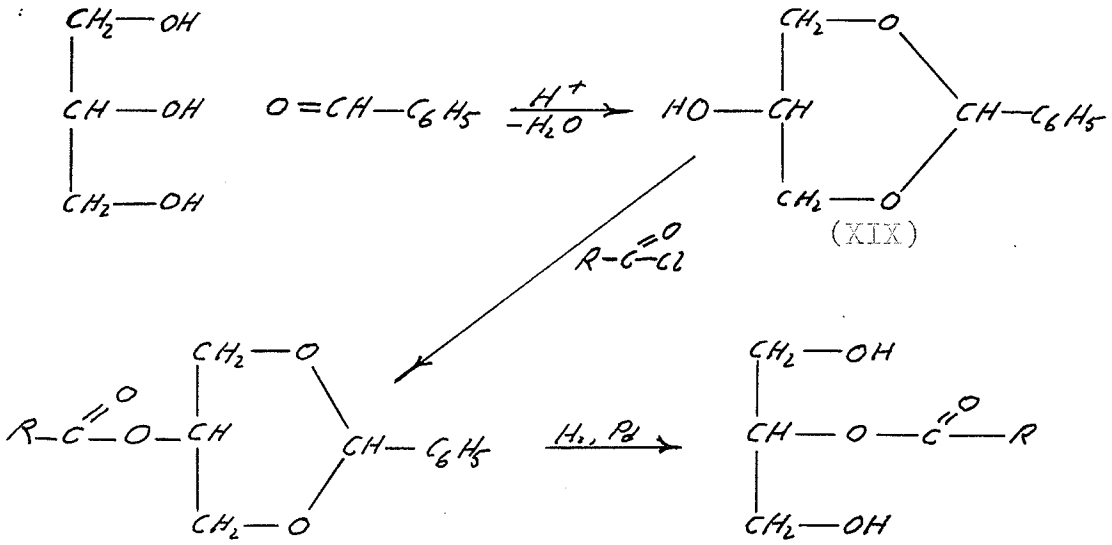
(XVIII)

More recent work (43) indicates that the purity of the final product of these reactions is only about ninety per cent, owing to side reactions. The 1,2-isopropylideneglycerol synthesis of 1-monoglycerides is the method commonly used today.

Because of the tendency for acyl migration to occur from the 2- to the 1-position, the synthesis of 2-glycerides must be accomplished in such a way that the final product is obtained under neutral conditions. The two common methods for preparing 2-glycerides, the 1,3-benzylideneglycerol (XIX) method (40, 45) and the glycerol-1,3-dityrityl ether (XX) method (11, 44), involve in-

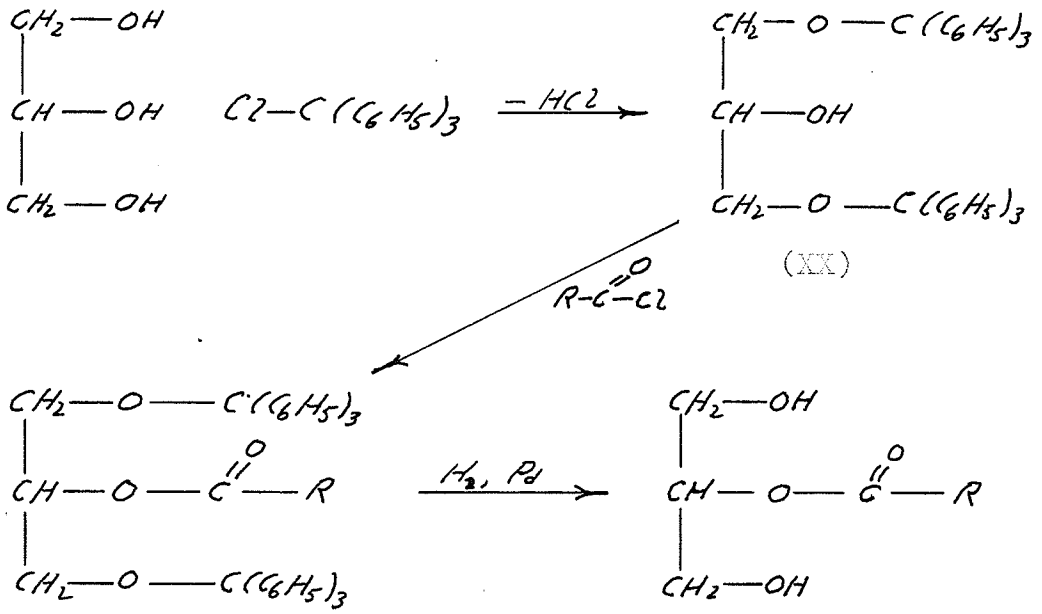
corporating the 1- and 3-hydroxyls of glycerol into an ether, reacting the 2-hydroxyl with an acid chloride, and then regenerating the 1- and 3-hydroxyls by hydrogenolysis.

I. 1,3-Benzylideneglycerol method.



(XIX)

II. Glycerol-1,3-dityrityl ether method.



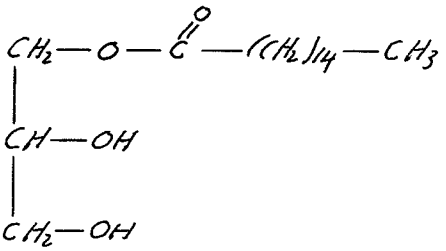
(XX)

GLYCERIDE INCLUSION COMPLEXES

The use of urea and thiourea inclusion complexes to separate straight-chain from branched-chain organic compounds is well documented (2, 3, 4, 23, 39). Urea and thiourea crystallize in such a way that long narrow channels are present in the crystal structure. When urea is allowed to crystallize in the presence of a straight-chain hydrocarbon (containing six or more carbons in the chain), alcohol (with six or more carbons in the chain), ketone (three or more carbons in the chain), or acid (four or more carbons in the chain), the latter tends to become fixed in the channels of the urea structure, forming an adduct (23). If a mixture of substrates is present, the straight-chain compounds will form adducts and the branched-chain compounds will not. This is widely used as a separation technique and is the basis for a patent on the commercial separation of hydrocarbons (27).

The use of this method for the separation of glycerol esters is discussed by Aylward and Wood (2, 3, 4) in a series of papers on glyceride separation. For example, they separated 2-monopalmitin (XVI) from 1-monopalmitin (XVII) by shaking a mixture of the two isomers in ether with a large excess of urea (4). 1-mono-

palmitin (XVII) formed a urea inclusion complex, 2-monopalmitin (XVI) did not.



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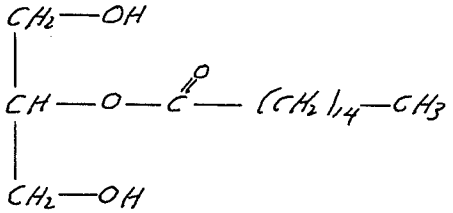
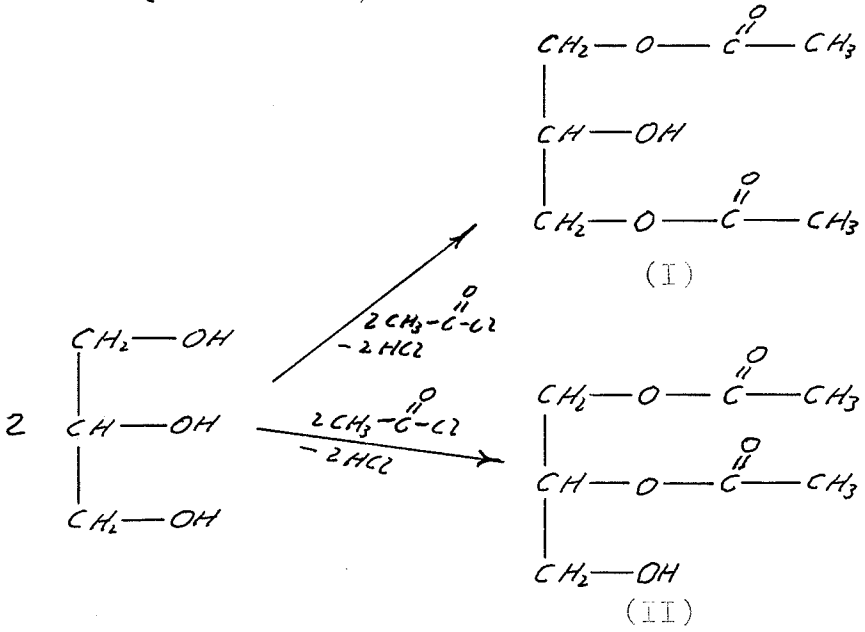


(XVI)

DIACETIN

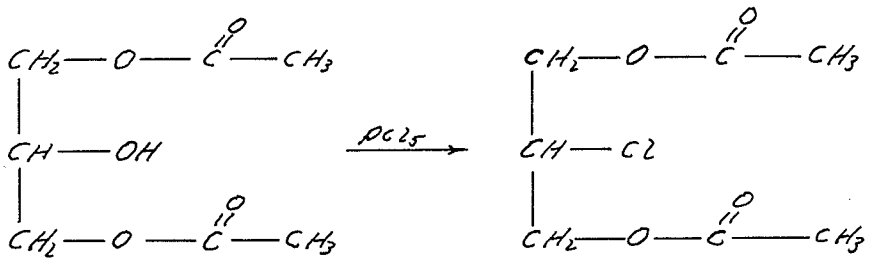
Industrially, diacetin is prepared by reaction between glycerol and acetyl chloride (26). A mixture of 1,2-diacetin (II) and 1,3-diacetin (I) results.



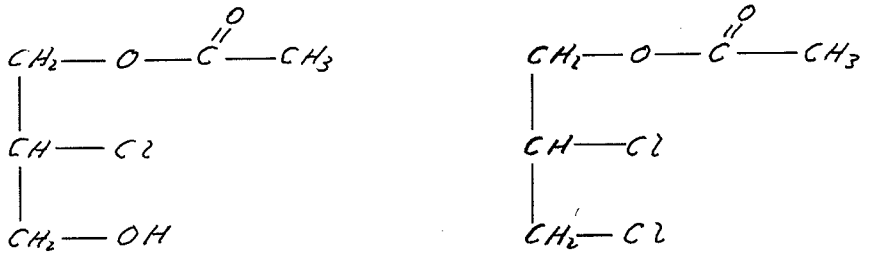
Nakamori (33, 34) discovered that the monoacetin

produced when acetic acid and glycerol react at 120 consists mainly of 1-monoacetin with a negligible amount of the 2-isomer. He concluded that the 1-hydroxyl has a much greater rate constant than the 2-hydroxyl and that diacetin consists mostly of the 1,3-isomer. Another explanation is that the difference in rate constant for esterification of the 1- and 2-hydroxyls is small but that the rate of acetyl migration is high for the 2-isomer and negligible for the 1-isomer.

Relatively little has appeared describing the chemical properties and reactions of diacetin. Wegscheider and Zmerzlikar's paper (46) on the chlorination of the isomeric diacetins is the only report on this topic in the literature. They prepared a mixture of 1,2- and 1,3-diacetin by reacting acetic acid with glycerol and separated the products by distilling under reduced pressure. They then chlorinated the two isomers separately and reported as products of the chlorination of 1,3-diacetin (I), 2-chloro-1,3-propanediol diacetate (II), 2-chloro-1,3-propanediol monoacetate (XXI), and 2,3-dichloro-1-propanol monoacetate (XXII).

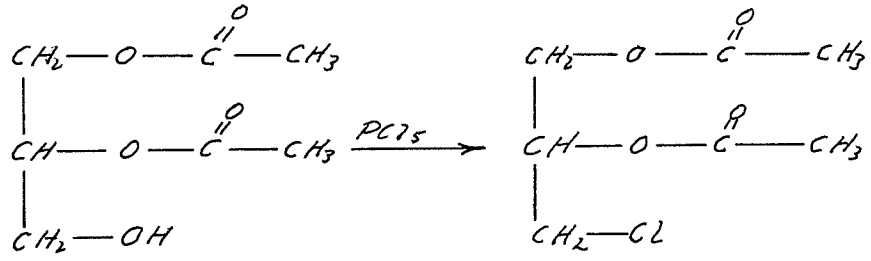


(II)



(XXI) (XXII)

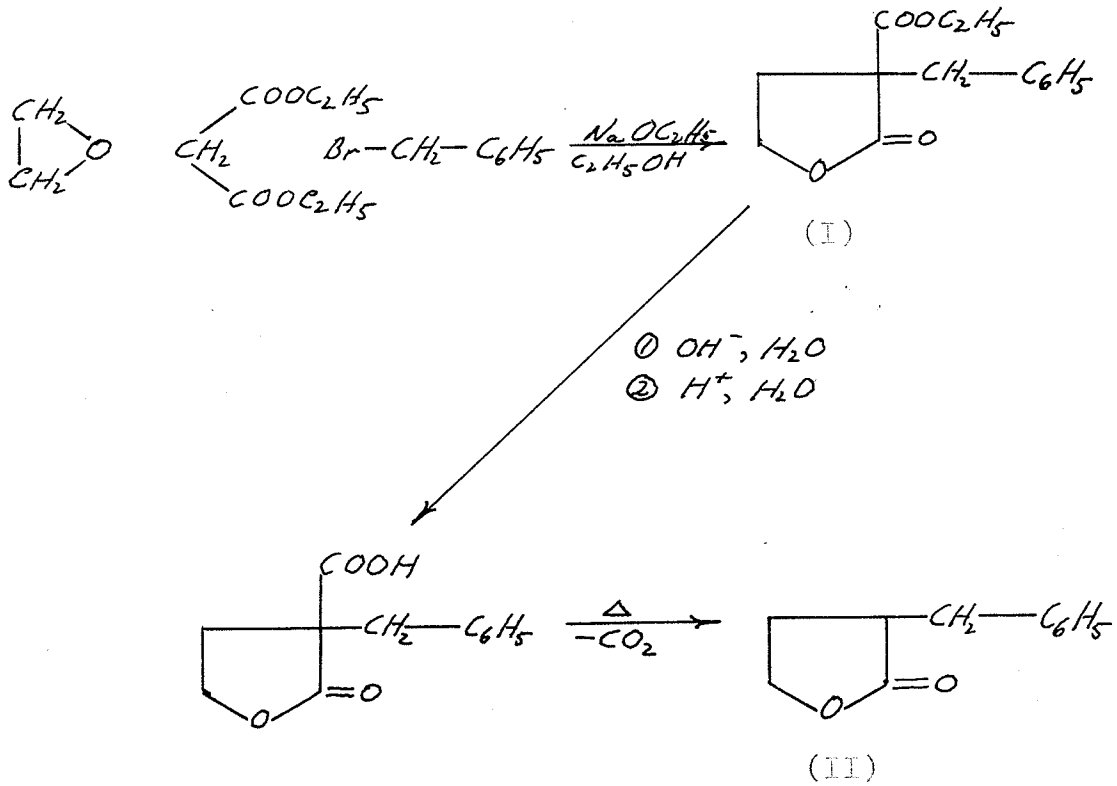
From the same reaction on 1,2-diacetin (II) they reported obtaining as products 1-chloro-2,3-propanediol diacetate (IV) and a chloropropanediol of undetermined structure.



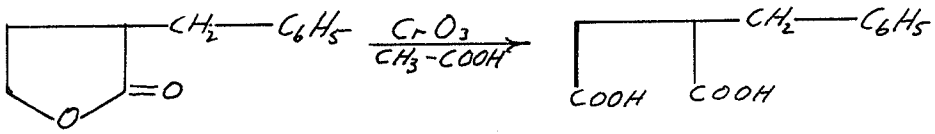
(IV)

PART II..... (α-Benzyl-γ-butyrolactone and related compounds.)

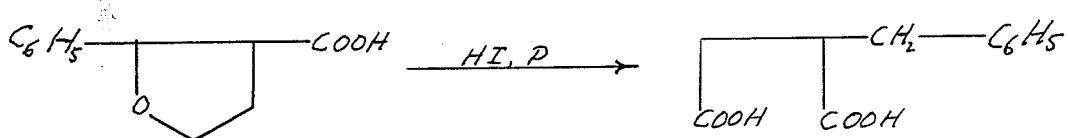
The studies of Charlesworth and coworkers on the synthesis and structure of various lactones have been surveyed in detail by Krushel (30). In extending this work, Krushel (30) prepared α-carbethoxy-α-benzyl-γ-butyrolactone (I) by condensation of equimolar quantities of ethylene oxide, diethyl malonate and benzyl bromide in the presence of sodium ethylate. On saponification, followed by acidification and decarboxylation, this compound yielded α-benzyl-γ-butyrolactone (II).



Chromic acid oxidation of α-benzyl-γ-butyrolactone (II) gave α-benzylsuccinic acid (IV), which melted at 159-160° as compared to a value of 160-161° given by Fittig and Shields (17). These authors had prepared this compound by refluxing α-phenylparaconic acid (V) in hydroiodic acid in the presence of red phosphorus.

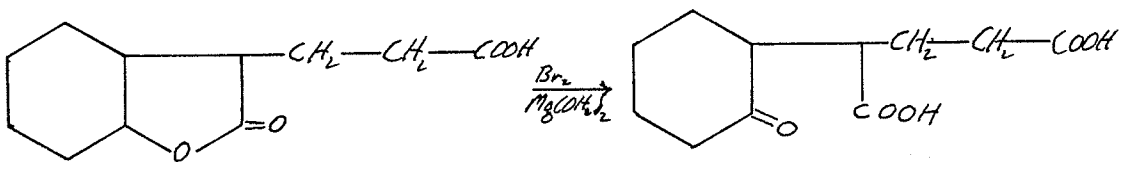


(II) (IV)



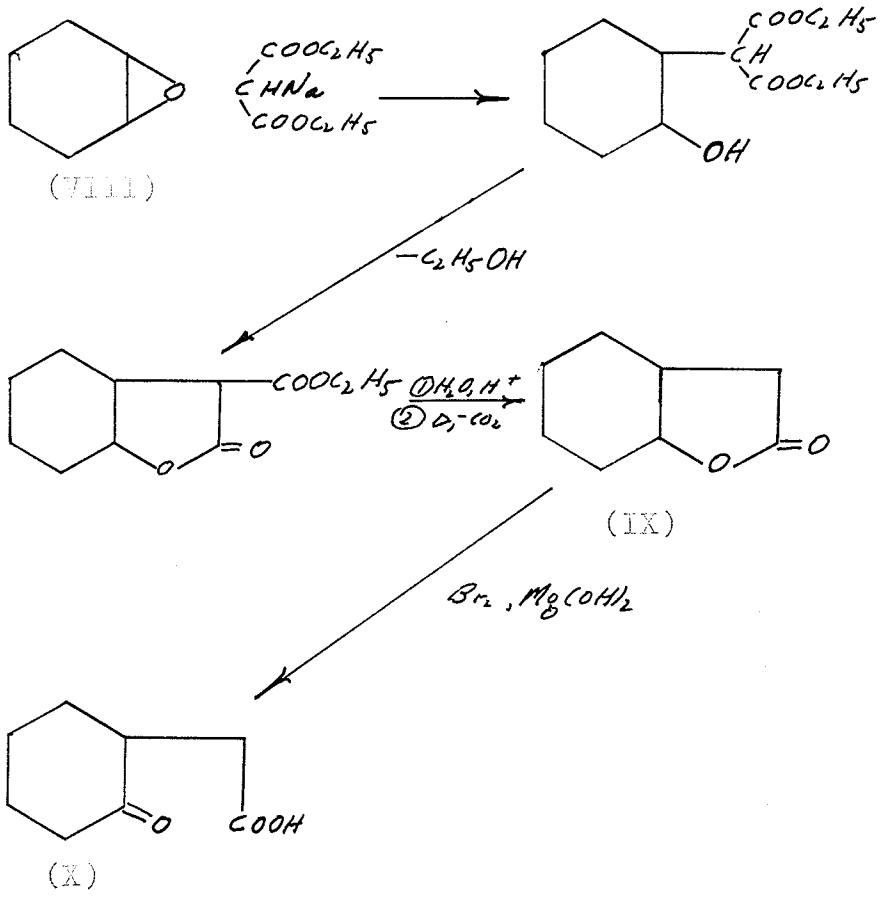
(V) (IV)

The first use of a mixture of bromine and magnesium hydroxide as a mild oxidizing agent for lactones was reported by Kendall, Osterberg, and Mackenzie (29) in 1926. They oxidized α-(2-hydroxycyclohexyl)glutaric acid lactone (VI) to α-(2-ketocyclohexyl)glutaric acid (VII) by using this reagent.

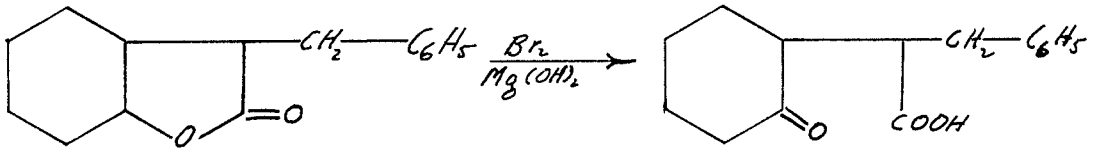


(VI) (VII)

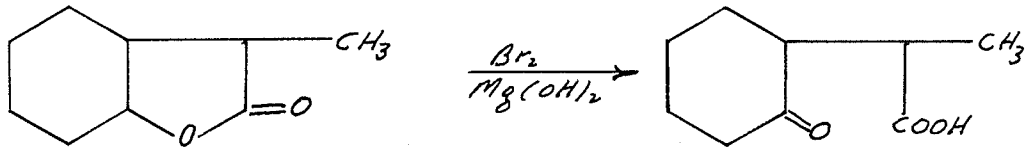
Subsequently, McRae, Charlesworth, and Alexander (31) oxidized cyclohexanolacetic acid lactone (IX), which had been prepared by Coffey (10) by condensation of cyclohexene oxide (VIII) with ethyl sodiomalonate. Using this procedure, they obtained 2-ketocyclohexyl-acetic acid (X).



Analagous oxidations on cyclohexanolbenzylacetic acid lactone (XI) and the γ-lactone of cyclohexanol-α-propionic acid (XIII) produced 2-ketocyclohexyl-benzylacetic acid (XII) and 2-ketocyclohexyl-α-propionic acid (XIV), respectively (31).



(XI) (XII)



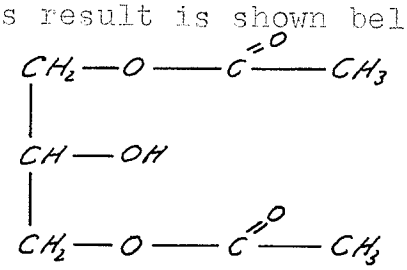
(XIII) (XIV)

DISCUSSION OF RESULTS

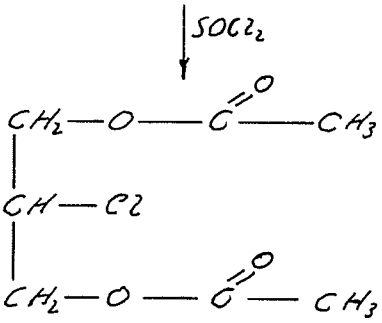
PART I..... (Reaction between diacetin and thionyl chloride.)

CHLORINATION OF DIACETIN

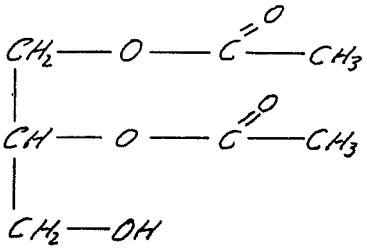
Analysis of the product of the reaction between diacetin and thionyl chloride gives a value for percentage of chlorine (37.40%) that is much too high if one assumes that the only reaction occuring is the chlorination of the isomeric diacetins. A chemically reasonable sequence of reactions which would explain this result is shown below:



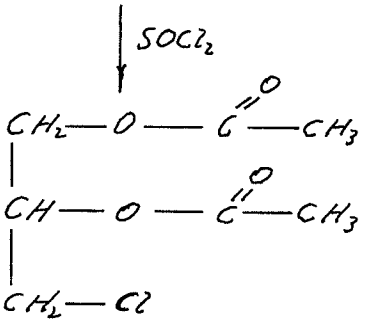
(I)



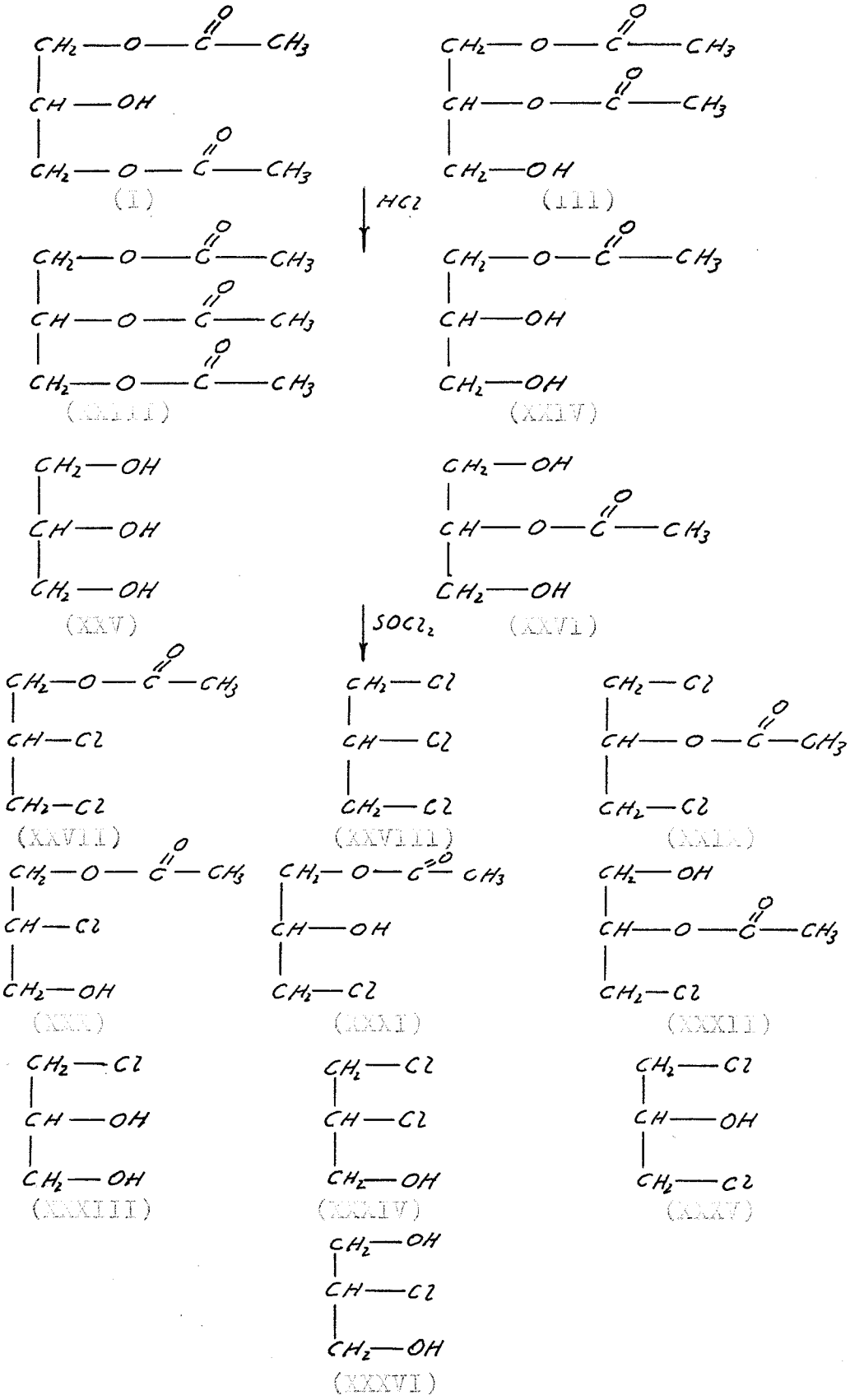
(II)



(III)



(IV)


HCl
SOCl2

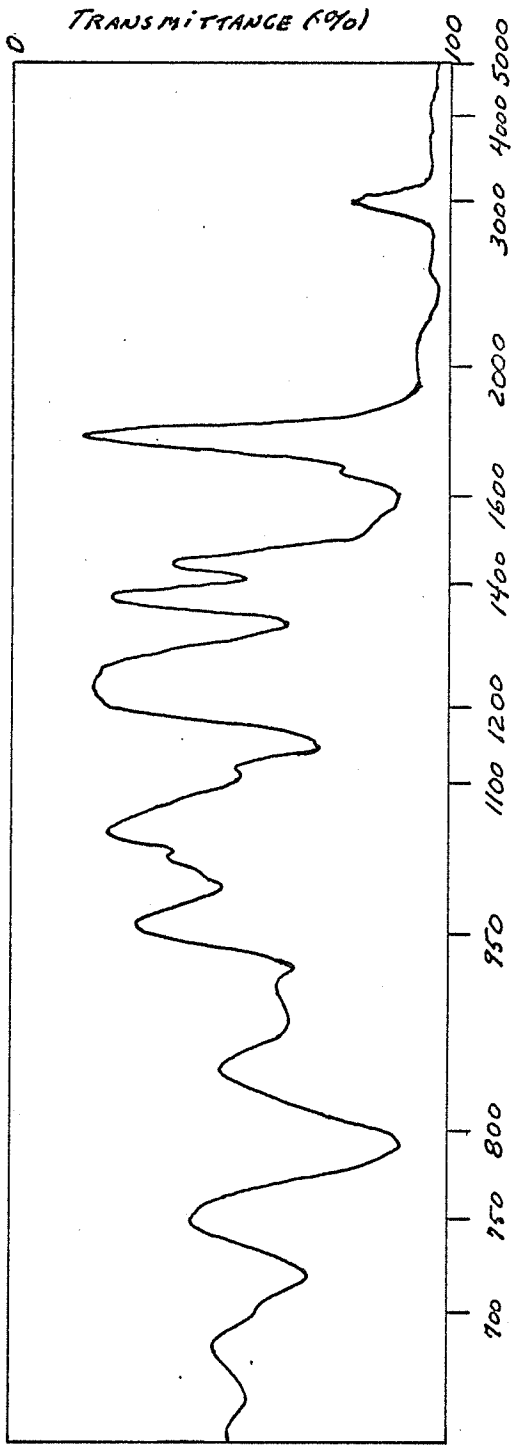
The first reaction, chlorination of the isomeric diacetins (I, III) to give 2-chloro-1,3-propanediol diacetate (II) and 1-chloro-2,3-propanediol diacetate (IV), produces hydrogen chloride. The hydrogen chloride then catalyses the transesterification reaction between 1,2- and 1,3-diacetin, yielding triacetin (XXIII), 1-monoacetin (XXIV), glycerol (XXV), and 2-monoacetin (XXVI). These last three compounds would in turn be chlorinated by thionyl chloride, giving a mixture of 2,3-dichloro-1-propanol acetate (XXVII), 1,2,3-trichloropropane (XXVIII), 1,3-dichloro-2-propanol acetate (XXIX), 2-chloro-1,3-propanediol-1- monoacetate (XXX), 3-chloro-1,2-propanediol-1-monoacetate (XXXI), 3-chloro-1,2-propanediol-2-monoacetate (XXXII), 3-chloro-1,2-propanediol (XXXIII), 2,3-dichloro-1-propanol (XXXIV), 1,3-dichloro-2-propanol (XXXV), and 2-chloro-1,3-propanediol (XXXVI). The reaction will be further complicated by acetyl migration, with 1,2-diacetin isomerizing to 1,3-diacetin, and by acid catalysed ester hydrolysis, producing alcohols from the various esters listed above.

One can therefore reasonably expect the reaction mixture to contain, in varying amounts, all of the compounds mentioned in the previous paragraph. The

solubilities of these compounds in water should be affected by substituents on the carbon chain as follows: the solubility should be increased by increasing substitution of hydroxyl groups and decreased by increasing substitution of chlorine atoms. As noted in the experimental section of this report, the reaction mixture is washed a total of six times; twice with water and four times with 5% sodium bicarbonate solution. Each time, the volume of washing solution is equal to the volume of the reaction mixture, about fifty milliliters. It is evident that under these conditions the mixture will become enriched in those molecules having a (relatively) high chlorine content. Triacetin (XXIII) is reasonably soluble in water and will be effectively removed from the mixture.

The infrared spectrum of the reaction product mixture (page 29) shows that the concentration of alcohols is negligible. Peaks at 1740-1760 $cm.^{-1}$ (sharp) and 1195-1260 $cm.^{-1}$ (broad) are attributed to acetate ester groups. A broad peak centered at 750 $cm.^{-1}$ indicates the aliphatic C-Cl bond. Peaks due to various aliphatic C-H bonds are found at 2950-3000 $cm.^{-1}$, 1430-1450 $cm.^{-1}$, and 1360-1380 $cm.^{-1}$. Any alcohols formed in the reaction must be either chlorinated by thionyl

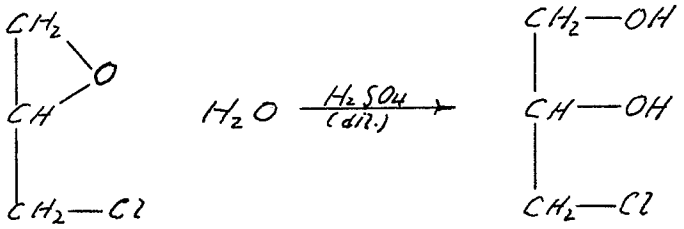
INFRARED SPECTRUM OF DIACETIN-THIONYL CHLORIDE PRODUCT MIXTURE



chloride or taken into the washing solution during purification of the crude product.

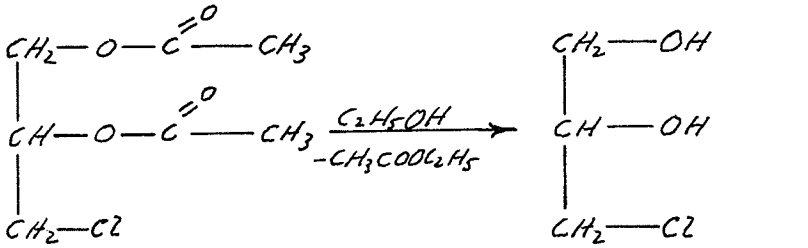
PRODUCTION OF 3-CHLORO-1,2-PROPANEDIOL BY TRANSESTERIFICATION OF THE DIACETIN-THIONYL CHLORIDE REACTION PRODUCT

The identification of the transesterification product as 3-chloro-1,2-propanediol (XXXIII) is based on the evidence of infrared spectroscopy. Synthetic 3-chloro-1,2-propanediol is prepared by hydrolysis of epichlorohydrin with dilute sulfuric acid:



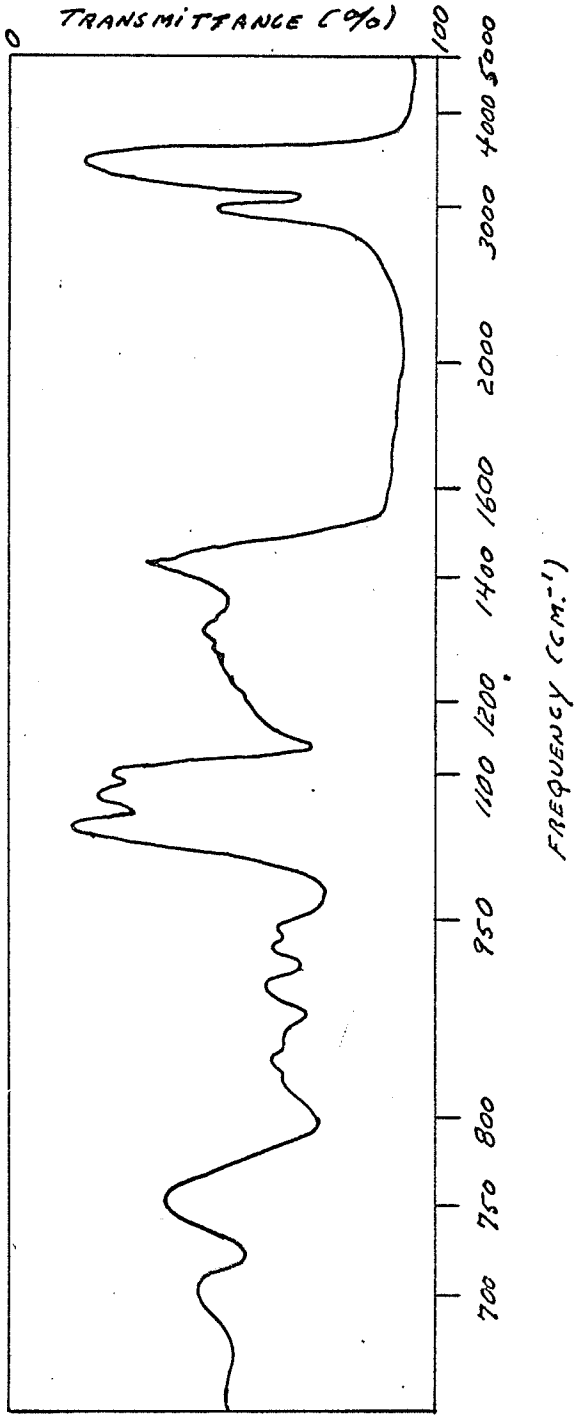
(XXXIII)

There is perfect correspondence, in both peak position and peak height, between the spectrum of the transesterification product (page 31) and that of synthetic 3-chloro-1,2-propanediol (page 32). The transesterification reaction, therefore, must be a reaction between ethanol and 3-chloro-1,2-propanediol diacetate (IV):

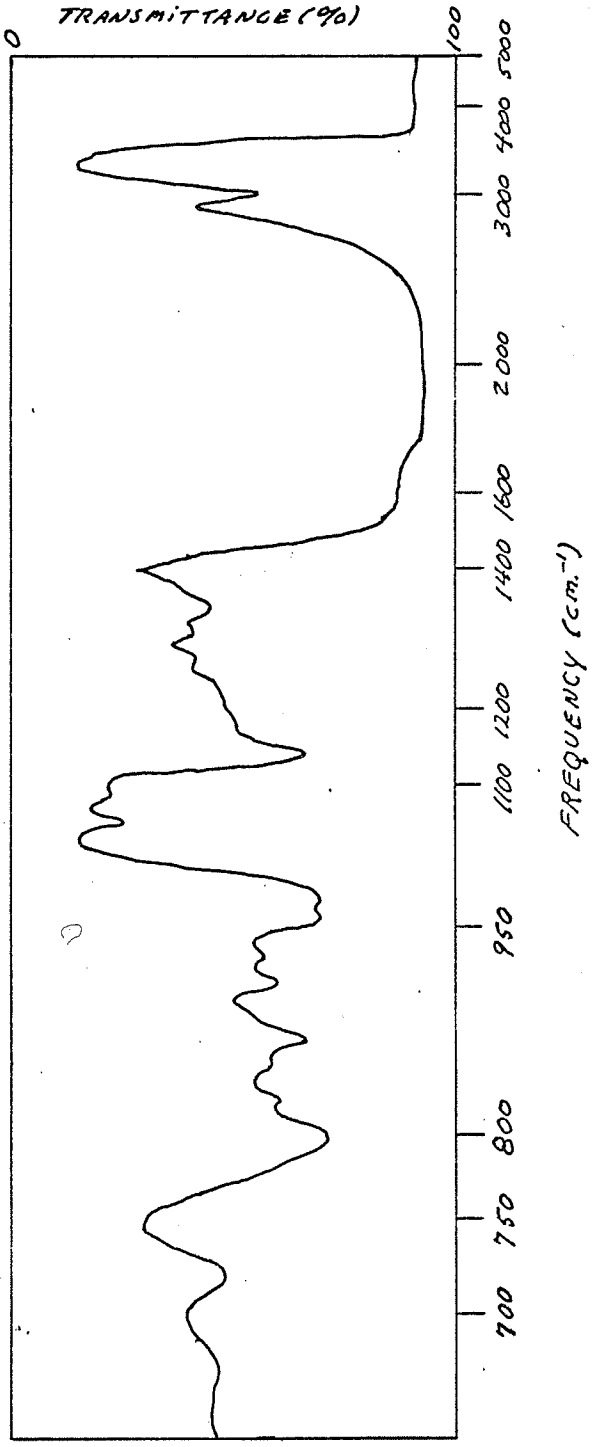


(IV) (XXXIII)

INFRARED SPECTRUM OF TRANSESTERIFICATION REACTION PRODUCT

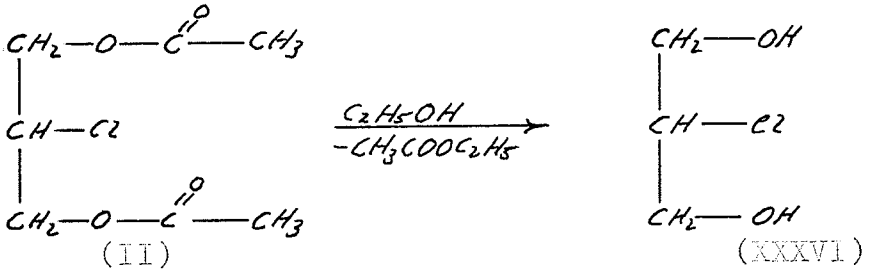


INFRARED SPECTRUM OF SYNTHETIC 3-CHLORO-1,2-PROPANEDIOL



The most prominent feature of the spectrum is a broad, strong alcoholic -OH absorption centered at 3300 cm.$^{-1}$. A broad peak centered at 750 cm.$^{-1}$ is again attributed to the C-Cl group. The peaks at 1740-1760 cm.$^{-1}$ and 1195-1260 cm.$^{-1}$, attributed to acetate ester groups in the spectrum of the diacetin-thionyl chloride reaction product, are absent in the spectrum of the transesterification product. The presence of aliphatic C-H linkages in the molecule is indicated by absorptions at 2900-2950 cm.$^{-1}$ and 1430-1440 cm.$^{-1}$.

One would expect that 2-chloro-1,3-propanediol (XXXVI), produced by reaction between 2-chloro-1,3-propanediol diacetate (II) and ethanol, should be found in the product of the transesterification reaction:



(II) (XXXVI)

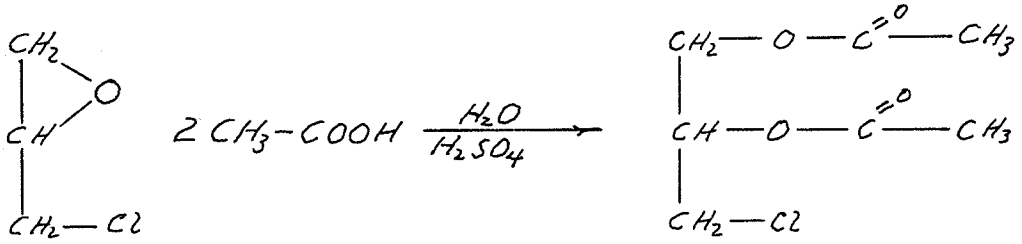
The fact that it is not found is difficult to explain. The possibility that the epichlorohydrin contains 2-chloro-1,3-propanediol as an impurity does not seem likely. If this were the case then the identity of the two spectra indicates that the relative concentration

The result of the transesterification experiment indicates that commercial diacetin consists mainly of the 1,2-isomer and that the reaction between diacetin and thionyl chloride gives 3-chloro-1,2-propanediol (IV) as a major product along with considerable amounts of di- and trichlorinated species derived from this substance and from 1,2-diacetin.

Hydrolysis of epichlorohydrin using dilute nitric acid solution as hydrolyzing agent obviously proceeds with the formation of nitrate esters of the alcoholic product. This is clearly shown by the presence of peaks at 1270-1280 $cm.^{-1}$ and 1640-1650 $cm.^{-1}$ in the infrared spectrum of the reaction product (page 36).

PREPARATION OF 3-CHLORO-1,2-PROPANEDIOL DIACETATE (IV)

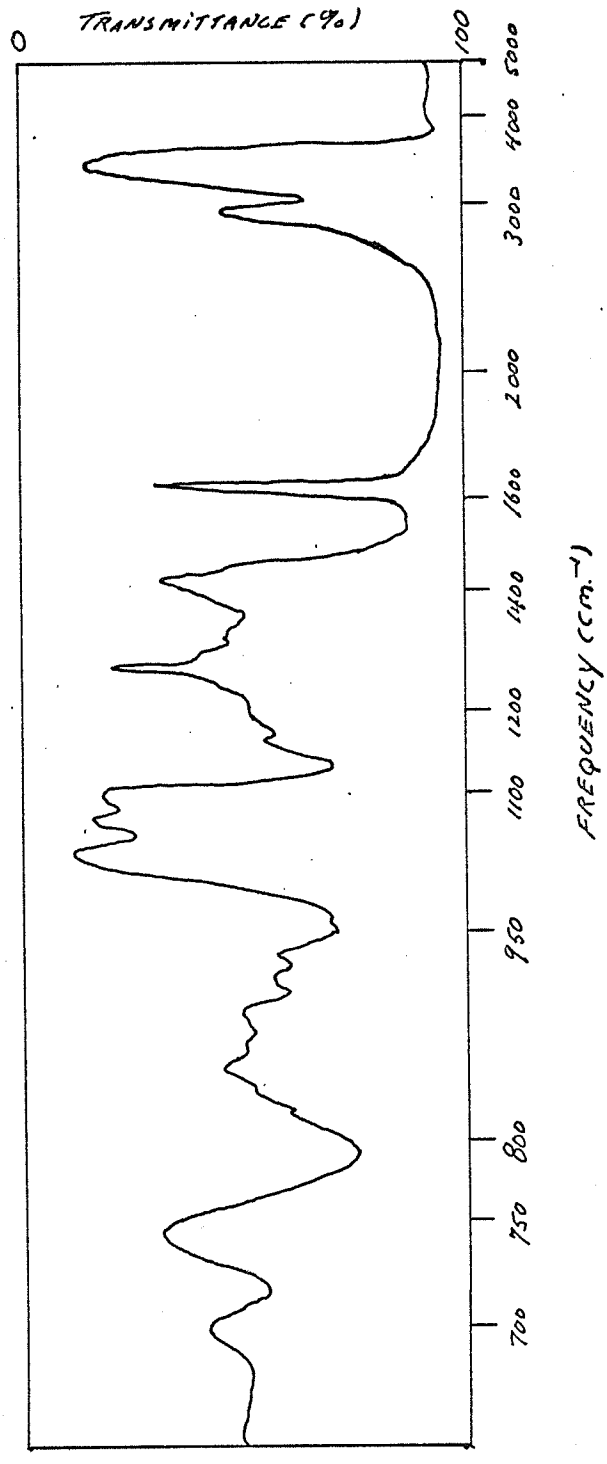
The production of 3-chloro-1,2-propanediol diacetate (IV) from epichlorohydrin and acetic acid is shown below:



(IV)

3-chloro-1,2-propanediol diacetate boils at sixty-four to sixty-seven degrees under a pressure of half a

INFRARED SPECTRUM OF PRODUCT FROM REACTION BETWEEN EPICHLOROHYDRIN AND DILUTE NITRIC ACID



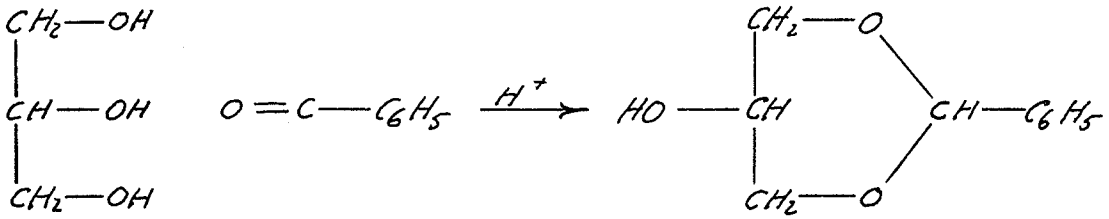
of 3-chloro-1,2-propanediol (XXXIII) and 2-chloro-1,3-propanediol (XXXVI) in the final product from both the hydrolysis and the transesterification reactions is the same. This is clearly asking too much of chance. Another possibility is that the two diols form an azeotropic mixture which distills at a constant temperature at a pressure of half a millimeter of mercury. No evidence for this was found in the literature. Furthermore, if commercial diacetin is postulated to consist of a mixture of the 1,2- and 1,3- isomers, then 2-chloro-1,3-propanediol would be expected to be a major product of the transesterification reaction, since 2-chloro-1,3-propanediol diacetate (II) is proposed to be a major product of the chlorination of such a mixture. The presence of 2-chloro-1,3-propanediol (XXXVI) in almost equal quantities as 3-chloro-1,2-propanediol (XXXIII) in the product of the hydrolysis of epichlorohydrin would mean that, far from being an impurity, 2-chloro-1,3-propanediol (or any precursor of this compound) is a major contaminant of epichlorohydrin.

It is seen that the supposition that commercial diacetin consists primarily of a mixture of the 1,2- and 1,3- isomers (33, 34) cannot be reconciled with the results of the transesterification experiment.

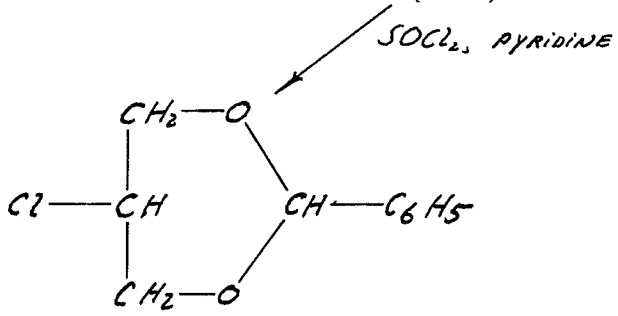
millimeter of mercury. Thus it is one of the low boiling components of the diacetin-thionyl chloride product mixture.

PREPARATION OF DI-(1,3-BENZYLIDENEGLYCERYL)-SULFITE (XXXVIII)

Having obtained 1,3-benzylideneglycerol (XIX) by condensation of benzaldehyde with glycerol according to the method of Hibbert and Carter (24), it was proposed to prepare 1,3-benzylidene-2-chloro-1,3-propanediol (XXXVII) from this by chlorination with thionyl chloride.



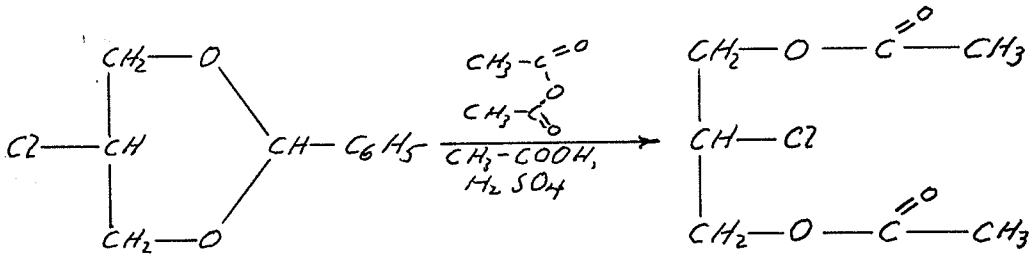
(XIX)



(XXXVII)

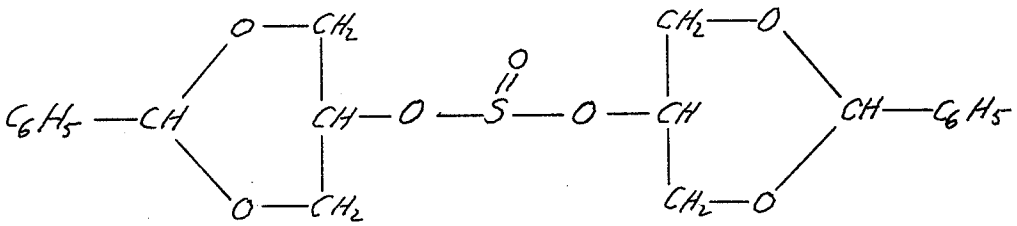
This last compound would then be reacted with an

acetylating mixture composed of acetic anhydride, acetic acid and sulfuric acid to produce 2-chloro-1,3-propanediol diacetate (II). This is the method of Senkus for preparing glycerol-1,3-diacetates (36).



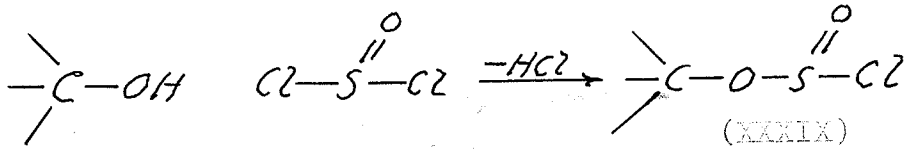
(II)

The chlorination step failed, producing instead of the expected product, di-(1,3-benzylideneglyceryl)-sulfite (XXXVIII).



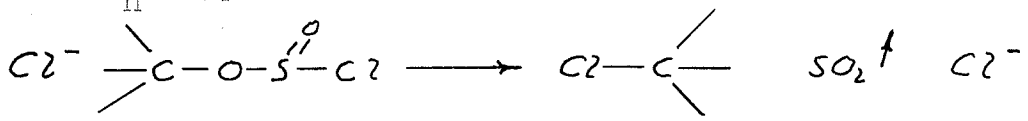
(XXXVIII)

The mechanism of chlorination of an alcohol by thionyl chloride in the presence of pyridine involves the initial formation of an alkyl chlorosulfite (XXXIX), with loss of hydrogen chloride.

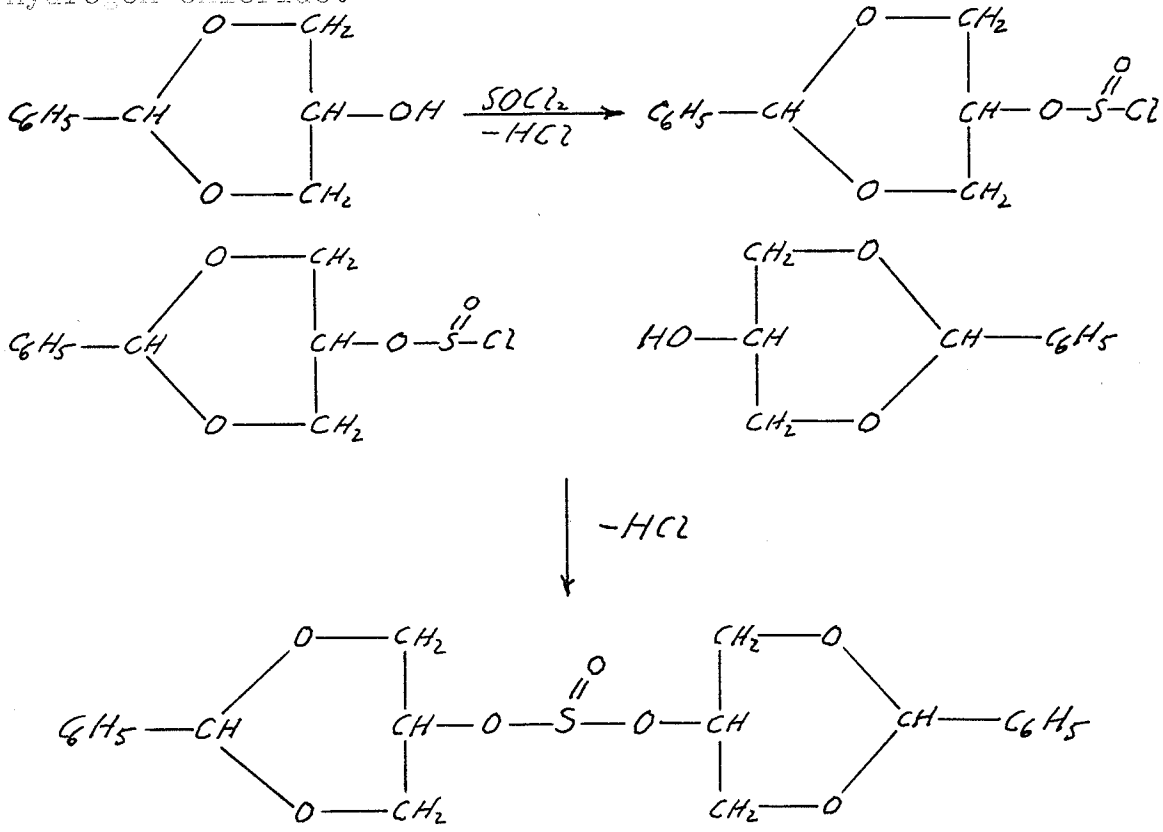


(XXXIX)

The pyridine reacts with the hydrogen chloride to give pyridinium chloride, the chloride ions of which attack the chlorosulfite-carrying carbon from the rear in an S_n2 type displacement.



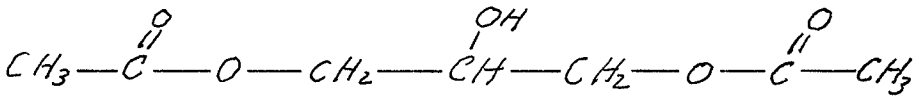
However, the alkyl chlorosulfite produced from 1,3-benzylidene glycerol presents obvious difficulties to this backside attack, approach to it being hindered because of its incorporation in a ring structure. Instead, the chlorosulfite reacts with a second alcohol molecule with the evolution of a second molecule of hydrogen chloride.



(XXXVIII)

UREA INCLUSION COMPLEXES

The separation of glycerol esters by formation of urea inclusion complexes has been applied mainly to glycerides of the higher fatty acids (2,3,4). Therefore, any conclusions drawn about the relative proportions of the isomeric diacetins in diacetin based on the failure of the compound to give such an inclusion complex cannot be expected to be as firm as those conclusions based on chemical evidence.



(I)

The diagram above emphasizes the straight chain structure of 1,3-diacetin (I). The chain length is nine atoms. On considering the chain length requirements for complex formation between urea and other organic molecules (23), one concludes that 1,3-diacetin is well suited to form such a complex. If a complex were formed on treatment of diacetin with urea it could be stated unequivocally that the included compound was 1,3-diacetin. The failure of the complex to form can be explained two ways: 1. Diacetin consists mainly of 1,2-diacetin, a compound whose non-linear structure prevents complex formation with urea.

2. Diacetin consists of a mixture of 1,2- and 1,3-diacetin. In this case the complex does not form because of an unanticipated structural or steric factor in the 1,3-diacetin molecule.

On the basis of previous work in the fields of urea inclusion complex formation in general (23) and glyceride-urea complexes in particular (2,3,4), hypothesis 1 seems the more reasonable of the two.

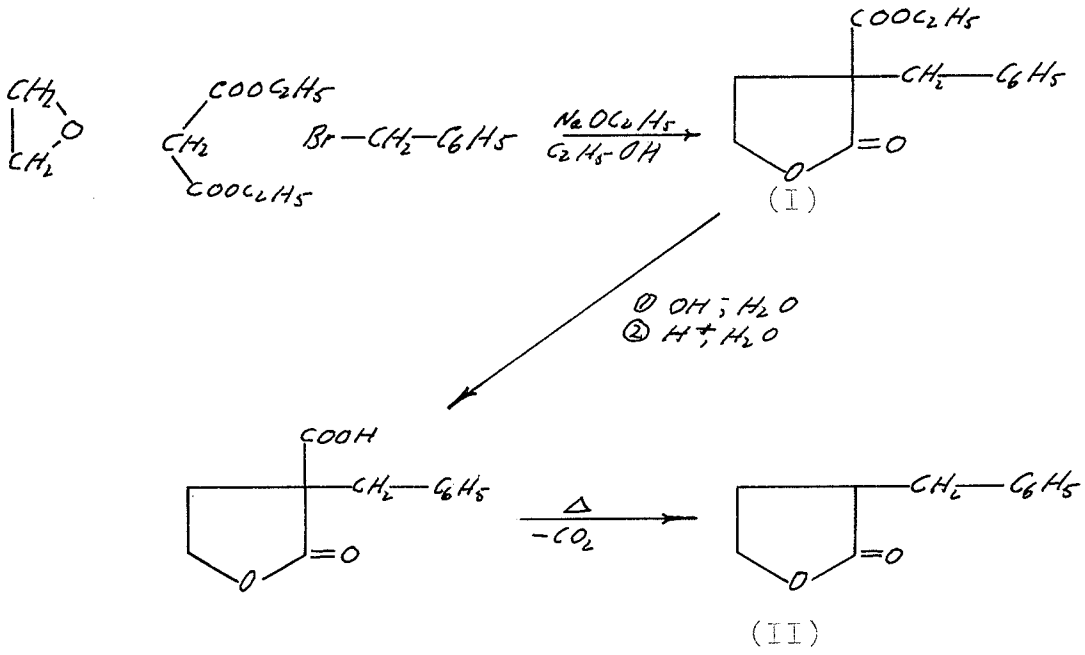
The failure of a complex to be formed on treatment of the diacetin-thionyl chloride product with urea cannot be taken as an assurance that 2-chloro-1,3-propanediol diacetate (II) is not present. In this molecule the presence of a chlorine atom may have an unforeseen effect on the ability of this molecule to form an adduct with urea.

PART II..... (α-Benzyl-γ-butyrolactone and related compounds.)

SYNTHESIS OF α-BENZYL-γ-BUTYROLACTONE (III)

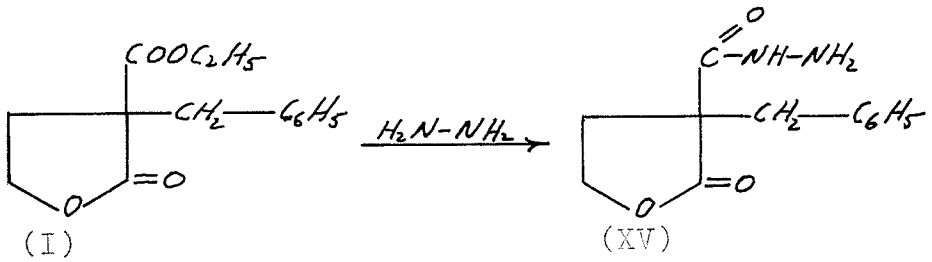
The method used to prepare α-benzyl-γ-butyrolactone (III) is originally due to Traube and Lehmann (41, 42), and the compound has also been similarly synthesized by McRae, Charlesworth, and Alexander (31) and by Krushel (30). The intermediate formed by condensation of diethyl malonate, benzyl bromide, and ethylene oxide loses ethyl alcohol

spontaneously to form α-carbethoxy-α-benzyl-γ-butyrolactone (I) which, on saponification followed by acidification and decarboxylation, is converted into α-benzyl-γ-butyrolactone (II).



PREPARATION OF HYDRAZINE DERIVATIVE OF α-CARBETHOXY-α-BENZYL-γ-BUTYROLACTONE (XV)

The formation of the monohydrazide derivative (XV) of α-carbethoxy-α-benzyl-γ-butyrolactone (IV) on treatment of this compound with hydrazine, rather than the



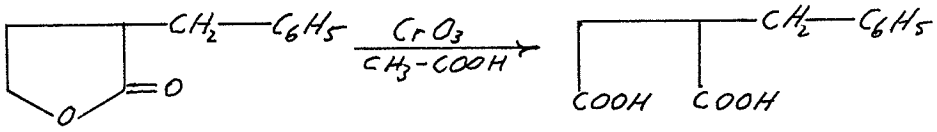
(I) (XV)

dihydrazide is not particularly surprising. It is known (38) that esters of alcohols of higher molecular weight than methyl or ethyl alcohol must be subjected to methanolysis before treatment with hydrazine or the hydrazide will fail to form. In this instance one therefore might expect only the acyclic ester group to react and this is what occurs.

OXIDATION OF α-BENZYL-γ-BUTYROLACTONE

Part of Krushel's proof of the structure of α-benzyl-γ-butyrolactone rests on his conversion of it, by chromium trioxide oxidation, to α-benzylsuccinic acid (IV) (30). After the lactone has been oxidized with chromium trioxide in acetic acid solution and the solution has been evaporated to a small volume, Krushel reports; "The remaining acetic acid was extracted with chloroform followed by a recrystallization from the same solvent. The chromium acetate was removed by extraction with ether, leaving white crystals on evapora-

tion." The white crystals prove to be α-benzylsuccinic acid (IV).

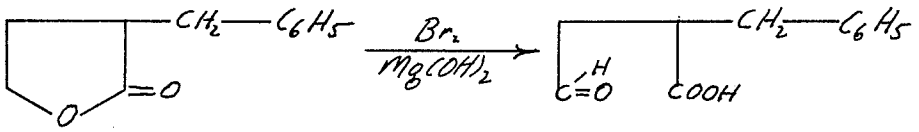


(II) (IV)

It is difficult to follow the logic of the above separation. Krushel did obtain the substituted succinic acid, but his method does not work. In fact, every attempt to obtain α-benzylsuccinic acid by oxidation of α-benzyl-γ-butyrolactone (chromium trioxide oxidation, potassium permanganate oxidation, and concentrated nitric acid oxidation) gave unresolvable oils as products. The oxidations were probably too drastic. The tendency for alkyl substituted benzenes to be converted to benzoic acid or a substituted benzoic acid on oxidation is well known. The oils obtained in these reactions may be assumed to be mixtures of the many possible compounds which could be formed in the stepwise oxidation of α-benzyl-γ-butyrolactone to benzoic acid. It is significant that the product of the concentrated nitric acid oxidation is yellow. This is an indication that under the conditions used, some nitration of the benzene ring has occurred.

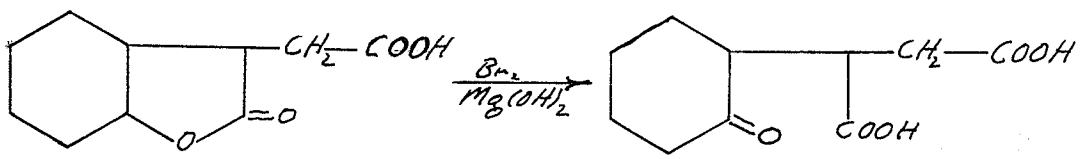
ATTEMPTED SYNTHESIS OF 3-CARBOXY-4-PHENYL-1-BUTANAL (III)

Investigation of the proposal that the use of a mild oxidizing agent (bromine and magnesium hydroxide in aqueous solution) to oxidize α-benzyl-γ-butyrolactone (II) would result in the formation of 3-carboxy-4-phenyl-1-butanal (III) shows that, as in the oxidation of the lactone to α-benzylsuccinic acid (IV), unresolvable oils are produced.



(II) (III)

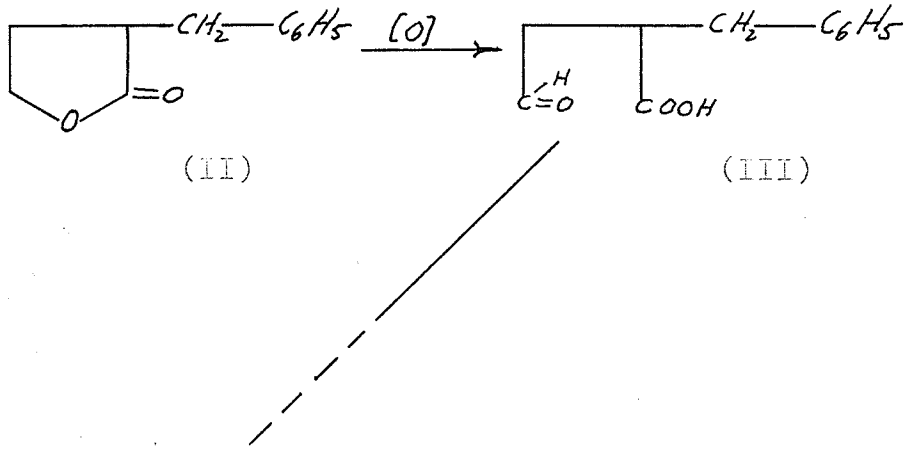
In this connection, it should be pointed out that previous applications of a mixture of bromine and magnesium hydroxide as an oxidizing agent for lactones have been in the field of cyclohexanol derived lactones. McRae, Charlesworth, and Alexander (31), for example, prepared 2-ketocyclohexylsuccinic acid (VII) by bromine and magnesium hydroxide oxidation of cyclohexanolsuccinic acid lactone (VI).



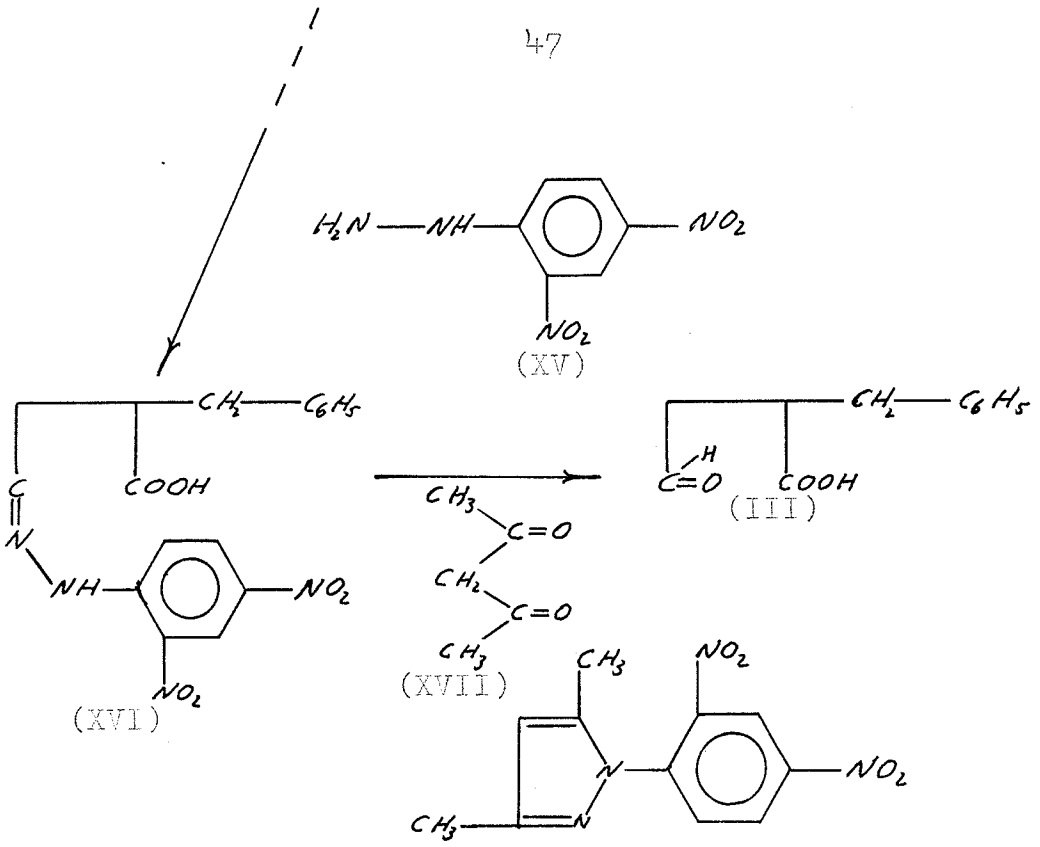
(VI) (VII)

As shown, oxidation occurs with the formation of a cyclohexanone which is substituted in the 2-position by a succinic acid residue. Further oxidation of a cyclohexanone, which would result in ring breakage, is difficult. The common laboratory preparation of cyclohexanone takes advantage of this fact (1). Thus, it does not follow that similar treatment of a butyrolactone would necessarily stop at the aldehyde stage.

A second approach to this synthesis was to oxidize α-benzyl-γ-butyrolactone (II) with potassium dichromate in the presence of 2,4-dinitrophenylhydrazine (XV). The 2,4-dinitrophenylhydrazine is present in order to react with the intermediate aldehyde (III), forming a 2,4-dinitrophenylhydrazone (XVI). This 2,4-dinitrophenylhydrazone, on reacting with acetylacetone (XVII), would regenerate the aldehyde (III) and form 1-(2,4-dinitrophenyl)-3,5-dimethylpyrazole (XVIII). This method is due to Reid and Muhe (35).



(II) (III)



(XV)

(XVI)

(XVII)

(III)

(XVIII)

The initial product does not appear to be the expected 2,4-dinitrophenylhydrazone (XVI). Its decomposition point is rather high (above 280) for this type of compound and its colour is yellow-green rather than red. The reaction is complicated by the fact that acids, as well as aldehydes and ketones, also react with 2,4-dinitrophenylhydrazine. The reaction of 2,4-dinitrophenylhydrazones with acetylacetone is a general one (35) and the failure of this compound to so react confirms the belief that it is not a true 2,4-dinitrophenylhydrazone.

EXPERIMENTAL

PART I..... (Reaction between diacetin and thionyl chloride.)

CHLORINATION OF DIACETIN

Commercial diacetin (70 g.) was placed in a two-necked round bottom flask (300 ml.) equipped with a magnetic stirrer, reflux condenser, and dropping funnel. Flask and contents were cooled in an ice bath and thionyl chloride (55 g.) was added dropwise over a space of ten to fifteen minutes. After the initial vigorous evolution of hydrogen chloride gas had subsided, the reactants were heated on a hot water bath to complete the reaction. When hydrogen chloride had ceased to be evolved the solution was cooled in an ice bath, then washed with an equal volume of water. The heavy non-aqueous layer from this washing was separated and then washed four times with an equal volume of dilute (5%) sodium bicarbonate solution. After one final washing with water, the liquid was dried overnight with magnesium sulfate. After drying, the liquid was separated from the salt by filtration and was distilled under reduced pressure. The liquid came over in the range 60-85° under a pressure of 0.5 mm. The total yield was 57.7 g.

The infrared spectrum of the product mixture (page 29) was taken on a Perkin-Elmer Model 21 infrared spectrophotometer with a thin layer of the liquid between sodium chloride plates as sample.

Analysis:

Found: C: 34.86% H: 4.93% Cl: 37.40%

Theoretical for (I) and (II), $C_7H_{11}ClO_4$:

C: 43.19% H: 5.66% Cl: 18.21%

TRANSESTERIFICATION OF PRODUCT FROM DIACETIN-THIONYL CHLORIDE REACTION

The product from the previous reaction (15 g.) was dissolved in 95% ethyl alcohol (35 ml.). This solution was refluxed on a steam bath for three hours. At the end of this time ethyl alcohol and ethyl acetate, formed by a transesterification reaction, were distilled off at atmospheric pressure and the liquid residue was redissolved in 95% ethyl alcohol (35 ml.). The reflux and distillation steps were then repeated (usually about four times) until the odour of ethyl acetate was not detectable in the distillate. The liquid residue was then dried overnight with magnesium sulfate. The dried liquid, after having been separated by filtration from the magnesium sulfate, was distilled under reduced pressure. The boiling point of the product was found

to be 72-73°/0.5 mm. The yield was 3.6 g.

The product gave a positive ceric nitrate test (37), indicating that it is a water soluble alcohol, and a positive test for halogen. The infrared spectrum of the compound (page 31) was obtained on a Perkin-Elmer Model 21 infrared spectrophotometer with a thin layer of the liquid between sodium chloride plates as sample.

HYDROLYSIS OF EPICHLOROHYDRIN

(a) With dilute sulfuric acid.

Epichlorohydrin (33 g.) was placed in a round bottom flask (200 ml.) equipped with a magnetic stirrer and flask and contents were cooled in an ice bath. Dilute (5%) sulfuric acid (85 ml.) was added to the this and the mixture was stirred and allowed to come to room temperature over a period of twelve hours. During this time the epichlorohydrin was completely hydrolyzed, as evidenced by the disappearance of the heavy organic layer from the mixture. The sulfuric acid solution was then distilled off under diminished pressure. The residual liquid was dried over magnesium sulfate and then distilled under reduced pressure. The boiling point of the product was 67-69°/0.5 mm. The yield was 16.9 g.

The infrared spectrum of the product (page 32)

was obtained on a Perkin-Elmer Model 21 infrared spectrophotometer with a thin layer of the liquid between sodium chloride plates as sample.

(b) With dilute nitric acid.

Epichlorohydrin (33 g.) was placed in a round bottom flask (200 ml.) equipped with a magnetic stirrer and flask and contents were cooled in an ice bath. Dilute (5%) nitric acid (85 ml.) was added to the cooled epichlorohydrin and the resulting mixture was stirred and allowed to come to room temperature over a period of twelve hours. During this time the epichlorohydrin was completely hydrolyzed, as evidenced by the disappearance of the heavy organic layer from the mixture. The nitric acid solution was distilled off under diminished pressure and the residual liquid was dried over magnesium sulfate. The dried liquid was distilled under reduced pressure and gave a product which boiled at 66-68°/0.5 mm. The yield was 18.1 g.

The infrared spectrum of the product (page 36) was obtained on a Perkin-Elmer Model 21 infrared spectrophotometer with a thin layer of the liquid between sodium chloride plates as sample.

PREPARATION OF 3-CHLORO-1,2-PROPANEDIOL DIACETATE (IV)

Glacial acetic acid (90 g.), concentrated sulfuric acid (15 ml.), and water (10 ml.) were mixed together in a two necked round bottom flask (300 ml.) equipped with a magnetic stirrer, reflux condenser, and dropping funnel. Flask and contents were cooled in an ice bath. Epichlorohydrin (46 g.) was added to this cold solution, dropwise and with stirring. A vigorous reaction ensued, accompanied by the evolution of a large quantity of heat. When this initial reaction had moderated, the solution was heated on a hot water bath for three hours. At the end of this time the reaction mixture was cooled in an ice bath and made basic with sodium hydroxide solution (6N). The liquid which separated was drawn off, dried with magnesium sulfate and distilled under reduced pressure. The product distilled over at 64-67°/0.5 mm.

Analysis:

Found: C: 42.03% H: 5.46% Cl: 18.81%

Theoretical for $C_7H_{11}ClO_4$: C: 43.22% H: 5.70% Cl: 18.24%

CONDENSATION OF BENZALDEHYDE WITH GLYCEROL

Method of Hibbert, H. and Carter, N. M. (24)

Benzaldehyde (100 g.) and glycerol (38.5 g.) were

placed in a Claisen distilling flask (300 ml.) and five drops of concentrated hydrochloric acid added. The mixture was then heated to 85-90° at 60-70mm., sufficiently high to allow the water produced in the condensation to distill off with a minimum loss of unchanged benzaldehyde. In three hours the reaction was complete, as evidenced by the non-separation of two layers when the flask was cooled in an ice bath. The condensation product was diluted with half its volume of ether and well shaken with a dilute (1%) solution of potassium carbonate (800 ml.) to remove the acid catalyst and any remaining glycerol. The ether solution was dried over magnesium sulfate and the ether removed on a steam bath, leaving a mixture of 1,2- and 1,3-benzylideneglycerol as a viscous, yellowish oil. A solution of this oil in a 4/3 mixture of ligroin and benzene deposited the 1,3- isomer as white, fine crystals on cooling. The 1,3-benzylideneglycerol, after recrystallization from ether, melted at 80-81°, as against the reported melting point of 83° (24).

PREPARATION OF DI-(1,3-BENZYLIDENEGLYCERYL)-SULFITE (XXXVIII)

Adaptation of original method of Hibbert, H. and Carter, N. M. (24) for preparing esters of 1,3-benzylideneglycerol.

1,3-benzylideneglycerol (2 g.) was dissolved in dry pyridine (5 g.) in a round bottom flask (50 ml.) equipped with a magnetic stirrer and a reflux condenser. Flask and contents were cooled in an ice bath and a solution of thionyl chloride (2 g.) in dry pyridine (10 g.) was added dropwise over a period of five minutes. The reaction mixture was heated on a hot water bath after the initial vigorous reaction had subsided. After heating, the mixture was poured into cold water (200 ml.). The product separated as a cream coloured precipitate. Recrystallization of this precipitate from 95% ethyl alcohol until a product of constant melting point was obtained yielded 0.7 grams of light, fluffy, white crystals whose melting point was 167-168°. The product gives a positive test for sulfur.

Analysis:

Found: C: 59.71% H: 5.73% S: 8.29%

Theoretical for $C_{20}H_{22}O_7S$: C: 59.12% H: 5.42% S: 7.90%.

A quantitative analysis for the sulfur content of this compound is being obtained.

ATTEMPTED SEPARATION OF DIACETIN-THIONYL CHLORIDE REACTION PRODUCT MIXTURE BY UREA ADDUCT FORMATION

Method of Aylward, F. and Wood, P. D. S. (4)

The reaction product (5 g.) was dissolved by heating in methanol (200 ml.). Urea (50 g.) was dissolved in this solution with stirring. After filtration, the solution was cooled to room temperature and the crystals formed were separated from the solution by filtration. These crystals were found to be pure urea, no adduct having formed.

ATTEMPTED SEPARATION OF DIACETIN BY UREA ADDUCT FORMATION

Method of Aylward, F. and Wood, P. D. S. (4)

Commercial diacetin (5 g.) was dissolved by heating in methanol (200 ml.). Urea (50 g.) was dissolved in this solution with stirring. The crystals which separated out of the solution after filtration followed by cooling to room temperature proved to be pure urea, no adduct having formed.

PART II..... (α-Benzyl-γ-butyrolactone and related compounds.)

PREPARATION OF α-BENZYL-γ-BUTYROLACTONE (II)

Method of Krushel (30) adapted from original method of Traube, W. and Lehmann, E. (41, 42)

Sodium (17 g.) was dissolved in absolute alcohol (300 ml.) in a flask (2 l.) equipped with stirrer. Diethyl malonate (120 g.) was added. The mixture was cooled in an ice bath and cold ethylene oxide (33 g.) in alcohol (80 ml.) was run in slowly. The mixture was cooled occasionally and on prolonged stirring went into solution. It was necessary to keep the mixture well cooled at this point for the reaction proceeded with the evolution of a great deal of heat. The condensate was allowed to sit overnight, and the next day ethyl alcohol (100 ml.) was added and the mixture stirred as benzyl bromide (130 g.) in alcohol (100 ml.) was added. After approximately ten minutes the mixture became very warm and more mobile as the sodium bromide separated. The mixture was allowed to react for two days at room temperature after which the ethyl alcohol was removed on a steam bath. The turbid and somewhat viscous matter remaining was treated twice with water to remove the sodium bromide. The oil which

separated was drawn off and the aqueous layer heated to drive off any alcohol. This was then treated with ether to remove any more oil and the ether extract then added to the oil. After treating the oil with magnesium sulfate it was distilled under reduced pressure, the following fractions being collected:

I	-100°/2 mm.	94.3 g.
II	100-140°/2 mm.	25.0 g.
III	140-146°/0.5-1 mm. ..	82.2 g.
IV	146-160°/0.5-1 mm. ..	38.7 g.
V	160-177°/0.5 mm.	13.3 g.

Fractions III, IV, and V were combined and redistilled under reduced pressure. They gave a fraction boiling at 150-158°/0.5 mm. which crystallized on standing in the refrigerator overnight. The melting point was 43-48°, and the total yield was 91 grams. This was α-carbethoxy-α-benzyl-γ-butyrolactone (1).

The lactone-ester prepared above (21 g.) was dissolved in alcohol (54 ml.) and sodium hydroxide solution (40 g. in 200 ml. water) added. The resulting clear solution was refluxed for twenty minutes and allowed to stand overnight. The next day the alcohol was removed by distillation until the temperature had reached 100°. The solution was then acidified with

concentrated hydrochloric acid and the oil which separated was extracted with ether and treated with magnesium sulfate. After evaporation of the ether the oil was decarboxylated in an oil bath at 160°. When the evolution of carbon dioxide had ceased, the oil was distilled. The fraction distilling over at 159-161°/8 mm. was collected and weighed (12.2 g.). This was α-benzyl-γ-butyrolactone.

PREPARATION OF HYDRAZINE DERIVATIVE OF α-CARBETHOXY-α-BENZYL-γ-BUTYROLACTONE (XV)

Method as described by Shriner, Fuson, and Curtin (38)

α-Carbethoxy-α-benzyl-γ-butyrolactone (4 g.) was added to 85% hydrazine hydrate (10 ml.) and the mixture was refluxed for fifteen minutes. Absolute ethyl alcohol was added until a clear solution was obtained. The mixture was then heated under reflux for two and a half hours. The alcohol was evaporated and the residue cooled in the refrigerator overnight. The white crystals so obtained were filtered under suction and on recrystallization from water melted at 177-179°.

Analysis:

Found: C: 63.25% H: 5.56% N: 11.37%

Theoretical for $C_{12}H_{14}N_2O_3$: C: 61.54% H: 5.98% N: 11.96%

ATTEMPTED PREPARATION OF α-BENZYLSUCCINIC ACID (IV)
(Method 1)

Method of Krushel (30)

α-Benzyl-γ-butyrolactone (3 g.) was added to glacial acetic acid (50 ml.) in a flask (250 ml.) equipped with a mechanical stirrer. The mixture was warmed to bring the liquids into solution and then allowed to cool to room temperature.

The oxidizing mixture was prepared by dissolving chromium trioxide (2.3 g.) in hot water (10 ml.). On cooling, glacial acetic acid (25 ml.) was added.

After this, the reaction flask and contents were cooled in an ice bath and kept cool while the addition of chromium trioxide solution took place over the course of half an hour.

After the addition, the solution was stirred for a few hours during which time it was allowed to come to room temperature and let stand for two days to complete the reaction. Isopropyl alcohol (20 ml.) was added to destroy the excess chromium trioxide and the whole evaporated under diminished pressure to a syrupy mass. The mass was extracted with chloroform, which removes some of the remaining acetic acid. The residue was then treated with ether to dissolve the succinic acid. On evaporation of the ether no product

was found. A repitition of the experiment, with ether extraction of the original syrupy mass obtained on evaporation of the reaction mixture yielded the same result.

ATTEMPTED PREPARATION OF α-BENZYLSUCCINIC ACID (IV)
(Method 2)

α-Benzyl-γ-butyrolactone (3 g.) was dissolved in 5N sodium hydroxide solution (25 ml.). To this solution was added dropwise a solution of potassium permanganate (2.8 g.) in water (40 ml.). The reaction mixture was allowed to remain at room temperature with stirring for twenty-four hours, after which time it was made acidic with sulfuric acid and extracted with ether. The oil obtained on evaporation of the ether was dissolved in 5N sodium hydroxide solution (15 ml.). On boiling this solution with Norite, filtering, and re-acidifying with sulfuric acid, the oil again separated. The oil solidified when immersed in liquid nitrogen, but became liquid again before it had reached room temperature. Prolonged cooling in the freezer compartment of the refrigerator did not cause the oil to solidify.

ATTEMPTED PREPARATION OF α-BENZYLSUCCINIC ACID (IV)
(Method 3)

α-benzyl-γ-butyrolactone (5 g.) was placed in a round bottom flask (100 ml.) equipped with a magnetic stirrer. Flask and contents were cooled in an ice bath and concentrated (70% min.) nitric acid (30 g.) was added, dropwise and with stirring. A few minutes after the addition of the acid was completed, reddish-brown nitrogen dioxide gas began to be given off. When the evolution of this gas had ceased, the solution was heated on a hot water bath for two hours. The nitric acid was then distilled off under reduced pressure and the small volume of yellow coloured liquid remaining in the flask was extracted with ether. The yellow coloured material was taken into the ether and on evaporation of the ether a yellow oil was obtained. Treatment of this oil with Norite as described under the preceeding heading was not effective as a purification technique. The oil was soluble in base and insoluble in acid.

ATTEMPTED SYNTHESIS OF 3-CARBOXY-4-PHENYL-1-BUTANAL (III)
(Method 1)

Method of McRae, J.A., Charlesworth, E.H., and Alexander, D.S. (31)

α-Benzyl-γ-butyrolactone (2.4 g.) was dissolved

in 5N sodium hydroxide solution (13 ml.) by heating to boiling; the solution was stirred mechanically while a hot solution of magnesium sulfate (6.9 g. of the heptahydrate in 5 ml. of water) was slowly added. The flask was cooled by immersion in an ice bath and the stirring continued while bromine (0.8 ml.) was added dropwise over the space of half an hour. The flask was surrounded by a fresh supply of ice and the reaction mixture was allowed to come to room temperature by standing overnight. Next morning the solution was acidified with concentrated (18N) sulfuric acid and a brown syrupy liquid separated. Attempts were made to purify this crude product by redissolving it in 5N sodium hydroxide solution and boiling it with Norite. After filtration and careful neutralization of the solution with sulfuric acid, it was evaporated to a small volume. The solution was extracted with ether and the ether distilled off, leaving behind a crude, oily substance. Further purifications with Norite effected no change in the state of this final product.

ATTEMPTED SYNTHESIS OF 3-CARBOXY-4-PHENYL-1-BUTANAL (III)
(Method 2)

α-Benzyl-γ-butyrolactone (9 g.) and 2,4-dinitro-

phenylhydrazine (2 g.) were dissolved in a solution of 18M sulfuric acid (10 ml.) in water (15 ml.). The mixture was heated to dissolve the lactone. To the resulting solution was added, over a space of thirty minutes, a solution of potassium dichromate (6 g.) in 18M sulfuric acid (4.5 ml.) and water (40 ml.). This mixture was then stirred under reflux for one hour, after which the organic layer was separated. The aqueous layer was extracted with ether and the ether extract, after evaporation of the ether, was added to the organic layer. The oily red liquid so obtained was placed in the refrigerator where it eventually solidified, forming a yellow-green solid. This solid, on recrystallization from ethyl alcohol, decomposed slowly above 280°.

This supposed 2,4-dinitrophenylhydrazone was then reacted with acetylacetone. The 2,4-dinitrophenylhydrazone (4.7 g.) was dissolved in ethyl alcohol (20 ml.) and to this was added a solution of acetylacetone (4 g.) in acetic acid (12 ml.). This solution was refluxed for thirty-six hours on a steam bath. At the end of this time the odour of acetylacetone was still easily detectable in the reaction mixture. The solution was extracted with sodium bisulfite solution

and made acidic with sulfuric acid. Even after this solution had stood for a week, no product separated.

SUMMARY

1. A study of the chlorination of commercial diacetin with thionyl chloride has shown that the reaction is not particularly clean, a variety of products being obtained. Possible reasons for this have been given.

2. The result of the transesterification of the diacetin-thionyl chloride product mixture with ethyl alcohol indicated that 1,2-diacetin is the major component of commercial diacetin and that 3-chloro-1,2-propanediol diacetate is a major product of the chlorination reaction. Attempts to prepare urea inclusion complexes from commercial diacetin and from the chlorination product were used to confirm the above finding. The results, while not as conclusive as the chemical evidence, were consistent with the above suggestion.

3. Di-(1,3-benzylideneglyceryl)sulfite has been prepared by reaction of 1,3-benzylideneglycerol with thionyl chloride.

4. The monohydrazide derivative of α-carbethoxy-α-

benzyl-γ-butyrolactone has been prepared.

5. A number of unsuccessful attempts have been made to oxidize α-benzyl-γ-butyrolactone to benzylsuccinic acid and to 3-carboxy-4-phenyl-1-butanal.

RECOMMENDATIONS FOR FURTHER WORK

1. The nuclear magnetic resonance spectrum of commercial diacetin could be obtained. If properly interpreted, this might give valuble information about the isomeric content of commercial diacetin.

2. The synthesis of a variety of compounds related to di-(1,3-benzylideneglyceryl)sulfite could be accomplished by starting with the condensation of glycerol with a substituted benzaldehyde.

3. 1,2-benzylideneglycerol could be obtained from the condensation of glycerol with benzaldehyde and the reaction of this compound with thionyl chloride could be studied.

4. Since Krushel's work on the oxidation of α-benzyl-γ-butyrolactone could not be reproduced, further work in this area will be necessary. In the preparation of 3-carboxy-4-phenyl-1-butanal by mild oxidation of α-benzyl-γ-butyrolactone, the use of milder oxidizing agents should be considered. Dilute nitrc acid might be used to advantage in this preparation.

BIBLIOGRAPHY

1. Anderson, L.C., Elderfield, R.S., Smith, P.A.S., and Bachmann, W.E. A Manual for the Organic Chemistry Laboratory. John Wiley and Sons, New York. 3rd Printing. 1964 p. 37

2. Aylward, F. and Wood, P.D.S. Chem. Ind. 1479 (1955)

3. Aylward, F. and Wood, P.D.S. Chem. Ind. 53-54 (1956)

4. Aylward, F. and Wood, P.D.S. Nature 177: 146 (1956)

5. Bergmann, M. and Carter, N.M. Z. Physiol. Chem. 191: 211-221. (1930)

6. Berthelot, M. Ann. Chim. Phys. 41: 216. (1854)

7. Charlesworth, E.H., McRae, J.A., and MacFarlane, H.M. Can. J. Research 21F: 55-64. (1943)

8. Charlesworth, E.H., Campbell, H.J. and Stachiw, D.L. Can. J. Chem. 37: 877-881. (1959)

9. Chevreul, M.E. Recherches sur les Corps Gras (1823)

10. Coffey, S. Rec. trav. chem. 42: 387-436. (1923)

11. Daubert, B.F. J. Am. Chem. Soc. 62: 1713-1714 (1940)

12. Daubert, B.F., and King, C.G. J. Am. Chem. Soc. 60: 3003-3005. (1938)

13. Doerschuk, A.P. J. Am. Chem. Soc. 74: 4202-4203 (1952)

14. Fairbourne, A. and Foster, G.E. J. Chem. Soc. 127: 2759-2764. (1925)

15. Fairbourne, A. and Toms, A. J. Chem. Soc. 1926: 3146-3148.

16. Fischer, E. Ber. 53B: 1621-1633. (1920)

17. Fittig, R. and Shields, J. Ann. 256: 91. (1890)

18. Garner, T.L. J. Soc. Chem. Ind. 47: 278-280 (1928)

19. Grun, A. Ber. 38: 2284-2287. (1905)

20. Grun, A. and Limpacher, R. Ber. 59b: 695-704. (1926)

21. Grun, A. and Schacht, P. Ber. 40: 1778-1791. (1907)

22. Grun, A. and Theimer, E. Ber. 40: 1792-1801. (1907)

23. Hagan, Sister Martinette Clathrate Inclusion Complexes. Reinhold Publishing Corp., New York. 1st Edition. 1962. p. 15

24. Hibbert, H. and Carter, N.M. J. Am. Chem. Soc. 51: 1601-1613. (1929)

25. Hibbert, H. and Grieg, M.E. Can. J. Research 4: 254-263. (1931)

26. I. G. Farbenindustrie, French Patent 664,770 Nov. 28, 1928.

27. I. G. Farbenindustrie, German Patent 869,070 Mar. 2, 1953.

28. Jackson, D.T. and King, C.G. J. Am. Chem. Soc. 55: 678-680. (1933)

29. Kendall, E.C., Osterberg, A.E., and MacKenzie, E.F. J. Am. Chem. Soc. 48: 1384-1401. (1956)

30. Krushel, K.E. M. Sc. Thesis, University of Manitoba (1960)

31. McRae, J.A., Charlesworth, E.H., and Alexander, D.S. Can. J. Research 21B: 1-12. (1943)

32. McRae, J.A., Charlesworth, E.H., Archibald, F. R., and Alexander, D.S. Can. J. Research 21B: 186-193. (1943)

33. Nakamori, I. J. Chem. Soc. Japan, Ind. Chem. Sect. 54: 456-458. (1951)

34. Nakamori, I. J. Chem. Soc. Japan, Ind. Chem. Sect. 55: 36-38. (1952)

35. Reid, W. and Muhe, G. Ann. 656: 119-126. (1962)

36. Senkus, M. J. Am. Chem. Soc. 68: 734-736. (1946)

37. Shriner, R.L., Fuson, R.C., and Curtin, D.Y. The Systematic Identification of Organic Compounds. John Wiley and Sons, New York. 4th. Edition. 1958. p. 110.

38. Shriner, R.L., Fuson, R.C., and Curtin, D.Y. The Systematic Identification of Organic Compounds. John Wiley and Sons, New York. 4th. Edition. 1958. p. 237.

39. Sixma, F. L.J. and Wynberg, H.A. A Manual of Physical Methods in Organic Chemistry. John Wiley and Sons, New York. 1st. Edition. pp. 147-149.

40. Stimmel, B.F. and King, C.G. J. Am. Chem. Soc. 56: 1724-1725. (1934)

41. Traube, W. and Lehmann, E. Ber. 32: 720-721. (1899)

42. Traube, W. and Lehmann, E. Ber. 34:1971-1983. (1901)

43. Vasquez Roncero, A., Fiestas, J., Mazuelos, F., and Martinez-Moreno, J.M. Fette u. Seifen 54: 550. (1952)

44. Verkade, P.E., van der Lee, J., De Quant, J.C., and van Buydewijr, E. de Roy Proc. Acad. Sci. Amsterdam 40: 580 (1937)

45. Verkade, P.E. and van Roon, J. D. Rec. trav. chim. 61: 831-834. (1942)

46. Wegscheider, R. and Zmerzlikar, F. Monatsh. 34: 1061-1087. (1913)