ACID-CATALYZED ADDITION OF ACID DERIVATIVES TO ETHYLENE OXIDE

By

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INTRODUCTION

Since its discovery by Wurtz (82) in 1859, ethylene oxide has been subjected to a great number of reactions with a wide variety of materials. One of the commercially important reactions of ethylene oxide is its telomerization with carboxylic acids, particularly long-chain ones, to form surface-active agents.

The purpose of the research covered by this thesis was to study new reactions of ethylene oxide with carboxylic acid precursors or derivatives. To that end, the acid-catalyzed addition of ketene, ethyl acetate, and acetonitrile to ethylene oxide was studied.

That further attention was in order was indicated by Kuhn (37) when he commented that "...research and development men must turn their studies to ethylene oxide, the precursor of ethylene glycol" as a solution to the present surplus production of ethylene glycol.

HISTORICAL

Preparation of Ethylene Oxide

The classical preparation of ethylene oxide, as described by Wurtz (82), is the dehydrohalogenation of ethylene chlorohydrin. This remains as the principal industrial process for the manufacture of ethylene oxide with some 390 million pounds produced in the United States in 1951 alone (6).

The second major process for producing ethylene oxide is the catalytic air oxidation of ethylene discovered by Lefort (42,69,70) in 1931. In 1951, 203 million pounds of ethylene oxide were produced by this process in the United States (6).

Both processes are extensively reviewed by Curme and Johnston (6) and by Goldstein (12).

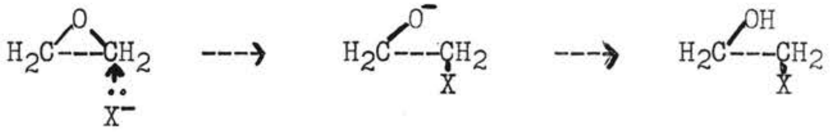
Physical properties

Ethylene oxide is a mobile liquid boiling at 10.7°C. As a liquid it is miscible in all proportions with water and forms azeotropic mixtures with hydrocarbons boiling in the range from -7 to +36° (22,23). Liquid ethylene oxide cannot be detonated, but the pure vapor is flammable and explosive as are air-ethylene oxide mixtures. A complete tabulation of the physical properties of ethylene oxide can be found in the American Chemical Society Monograph Number 114 (6).

Reactions with compounds containing active hydrogen

The principal reaction of ethylene oxide is the addition to it of compounds containing active hydrogen. In such a case the observed reaction is an opening of the ethylene oxide ring, the active hydrogen going to the oxygen and the remainder of the addend going to the carbon of the ethylene oxide.

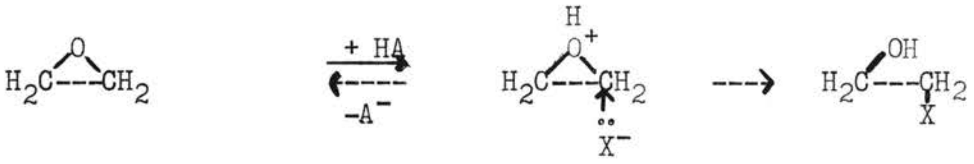
The mechanism by which this occurs is a nucleophilic displacement on carbon, with the ring oxygen atom as the displaced group (9). Such a displacement is illustrated below.



I II III

Displacement on the oxide itself gives II as an intermediate, which upon acquiring a proton gives III as a final product.

The displacement may also take place on the much more reactive conjugate acid of the oxide as illustrated by the following equation.



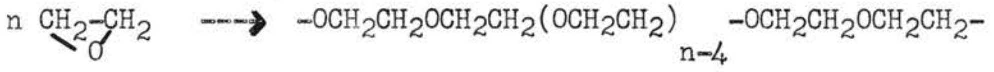
IV V

As a consequence of the ready attack on the conjugate acid of the oxide, acid catalysis of reactions of the oxide is very common.

The effective overall reaction observed in the addition of compounds containing active hydrogen to ethylene oxide is given by:

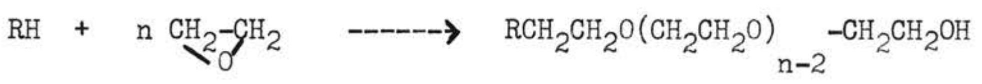
$$CH_2\text{-}CH_2 \; (\text{-O-}) + RH \longrightarrow R\text{-}CH_2CH_2\text{-}OH$$

A second major reaction undergone by ethylene oxide is its polymerization to form a polyethylene oxide chain as represented below.



$$n\ CH_2\text{-}CH_2 \; (\text{-O-}) \longrightarrow \text{-}OCH_2CH_2OCH_2CH_2(OCH_2CH_2)_{n-4}\text{-}OCH_2CH_2OCH_2CH_2\text{-}$$

Many of the commercially important materials (such as the surface-active agents) derived from ethylene oxide are a result of the combination of the two general reactions noted above. Thus an overall general reaction of ethylene oxide with active hydrogen compounds may be written as follows:



Since this study deals with the reaction of ethylene oxide with carboxylic acid precursors and derivatives a review of the known reactions of ethylene oxide with carboxylic acids and carboxylic acid derivatives is in order.

Ethylene oxide reacts readily with carboxylic acids to form mono- and diesters of the acids. The earliest example of such a reaction is the preparation of ethylene glycol monoacetate from ethylene oxide and glacial acetic acid by Wurtz (84).

The ethylene glycol esters so formed can react further to form the corresponding diesters. The general reaction can be represented by:

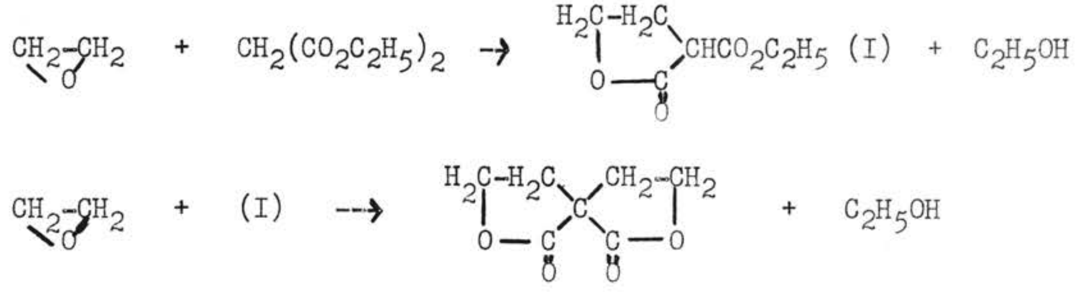
This reaction has been used for the preparation of surface-active agents by combining the hydrophobic hydrocarbon grouping present in a long-chain fatty acid with the hydrophilic grouping of a polyethylene glycol. Thus stearic acid has been condensed with six molecules of ethylene oxide to give a compound $CH_3(CH_2)_{16}COO(CH_2CH_2O)_5CH_2CH_2OH$ (12).

Dicarboxylic acids undergo similar reactions (76).

Reactions of this type are in general catalyzed by mineral acids such as sulfuric acid (20,21,26,28). Other catalysts which have been used are ferric chloride (36) and acidulated aluminum hydrosilicate (25).

Leland (43) condensed ethylene oxide with palmitic esters in the presence of metal halides to obtain materials which can be used as cutting oils. Ethylene oxide condensations with esters and ether-esters have also been promoted by zinc chloride, nickel chloride, or stannic chloride (30). However, the ethylene oxide condensations with these esters occur not at the ester linkage, but at some other active grouping such as a substituent hydroxyl group.

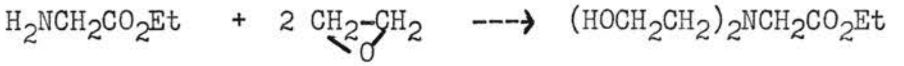
Pakendorf (53,54,55) condensed diethyl malonate with ethylene oxide in the presence of several catalysts such as piperidine, diethylamine and tris-2-hydroxyethylamine at room temperature to produce the lactone of 1,5-dihydroxypentane-3,3-dicarboxylic acid. The reaction can be represented by the following equations.



Using sodium ethoxide as a catalyst, Traube and Lehman (73) obtained ethyl 2-hydroxyethylmalonate and upon further heating obtained the monolactone.

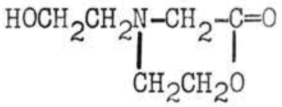
Pakendorf and Machus (56,57) obtained reactions between ethylene oxide and acetoacetic esters and cyclic <u>beta</u>-keto esters, similar to those obtained with malonic esters. A recent example is the preparation of acetylbutyrolactone, $CH_3C(O)\underline{CH-CH_2CH_2OC}=O$, by the action of ethylene oxide on acetoacetic esters in the presence of an aqueous solution of an alkali metal hydroxide (27).

The condensation of ethylene oxide with an ester of an amino acid in general gives reaction at the amino group. Thus, ethylene oxide and methyl anthranilate yield methyl N-2-hydroxyethylanthranilate (31), and ethylene oxide and the ethyl ester of glycine yield N,N-bis(2-hydroxyethyl)aminoacetic acid.



$$H_2NCH_2CO_2Et + 2\ CH_2\text{-}CH_2(O) \longrightarrow (HOCH_2CH_2)_2NCH_2CO_2Et$$ (32).

Upon heating, the latter compound loses alcohol to yield a lactone:



Other reactions similar to these have been reported (33,34,35).

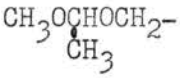
A comprehensive review of the reactions of ethylene oxide with active hydrogen compounds such as water, alcohols, phenols, ammonia, amines, mercaptans, hydrogen sulfide, hydrogen cyanide and hydrogen chloride can be found in books by Curme and Johnston (6) and Goldstein (12), and in a thesis by Durr (8).

Reactions with compounds not containing active hydrogen

Since the compounds chosen for the present study in condensations with ethylene oxide do not contain active hydrogen, it is now desirable to give a survey of known reactions of ethylene oxide with non-active hydrogen compounds.

The reaction involves the opening of the ethylene oxide ring, usually in the presence of an acid catalyst, the oxygen adding to the most positive part of the addend and the carbon to the most negative part. This is illustrated by the following general equation.

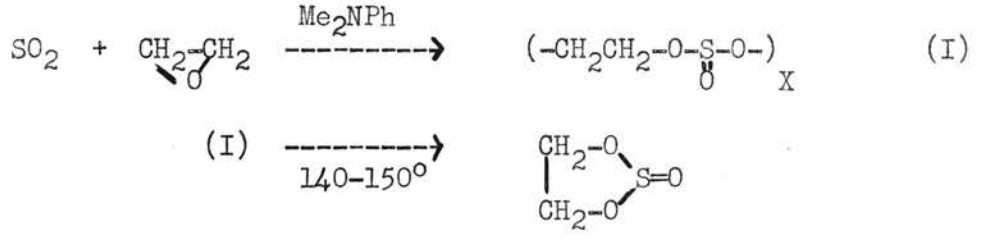
$$RX + CH_2\text{-}CH_2(O) \longrightarrow R\text{-}OCH_2CH_2\text{-}X$$

Durr (8) showed that acetals add to ethylene oxide or polyethylene oxide units in the presence of an acid catalyst such as boron trifluoride. Thus methylal and ethylene oxide yield $CH_3OCH_2CH_2OCH_2OCH_3$ and CH_3-$O(CH_2CH_2O)_2CH_2OCH_3$. Similarly the ethylal-ethylene oxide pair yields $C_2H_5OCH_2OCH_2CH_2OC_2H_5$ and dimethyl acetal-ethylene oxide yields  $CH_3O\underset{CH_3}{C}HOCH_2$-

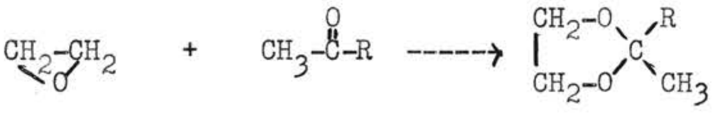
CH_2-OCH_3.

Upon heating ethylene oxide with acetic anhydride, Wurtz (83,84) obtained ethylene glycol diacetate. Other analogous reactions studied have been the condensation of phthalic anhydride with ethylene oxide (75), and succinic anhydride with ethylene oxide (74).

Sulfur dioxide (the anhydride of sulfurous acid) reacts with ethylene oxide in the presence of a tertiary amine to give a polymer. Heating the polymer at 140-150° gives the monomer, glycol sulfite (68).



Ethylene oxide and aldehydes react in the presence of a Lewis acid such as stannic chloride to form cyclic acetals (1,3-dioxolanes) (3). Cyclic ketals are formed in a similar manner but in poor yield from ethylene oxide and ketones by the use of either stannic chloride or boron trifluoride as a catalyst (3,61). Bersin and Willfang (2) found that conducting the ethylene oxide-aldehyde reaction in an inert solvent served to reduce the polymerization of ethylene oxide. A general equation for reactions of this type can be written:



In the case of aldehydes, R = H.

Maass and Boomer (45) have shown that at low temperatures (0°) ethylene oxide reacts with elementary bromine and chlorine to form the following oxonium compounds: $C_2H_4O{\cdot}Br$, $C_2H_4O{\cdot}2Br$, $C_2H_4O{\cdot}Cl$ and

$C_2H_4O\cdot 3Cl$. These formulas are not very intelligible but are quoted exactly. The composition of these compounds was determined from the eutectics of the freezing point curves of the halogen-ethylene oxide mixtures.

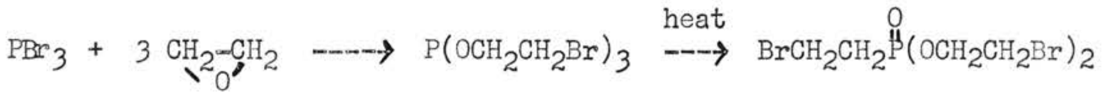
It was observed by Ribas and Tapia (62), that ethylene oxide in ether solution reacts with magnesium bromide to give $BrCH_2CH_2OMgBr\cdot(C_2H_5)_2O$. Upon hydrolysis this compound yielded ethylene bromohydrin, magnesium bromide and magnesium hydroxide.

In a similar fashion, $BeCl_2\cdot(C_2H_5)_2O$ reacts with ethylene oxide to yield $ClCH_2CH_2OBeCl\cdot(C_2H_5)_2O$ (51).

Ethylene oxide reacts with a variety of non-metallic halides to give the corresponding 2-haloethyl esters; these reactions are discussed in the following paragraphs.

Arsenious chloride reacts with ethylene oxide to give, after fifteen days, tris-2-chloroethyl arsenite (47). The reaction can also be applied to haloarsines.

Ethylene oxide reacts with phosphorus trichloride (29) and phosphorus tribromide (63) to yield the corresponding tris-2-haloethyl phosphite. Upon heating or distillation this rearranges to the corresponding phosphonic ester. This is illustrated for phosphous tribromide by the following equation:

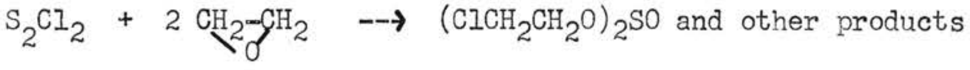


$$PBr_3 + 3\ \underset{\diagdown_{O}\diagup}{CH_2-CH_2} \longrightarrow P(OCH_2CH_2Br)_3 \xrightarrow{heat} BrCH_2CH_2\overset{O}{\overset{\|}{P}}(OCH_2CH_2Br)_2$$

Phosphorus oxychloride reacts with ethylene oxide in the presence of anhydrous hydrogen chloride (72), anhydrous aluminum chloride (7), or iron filings (44) as a catalyst to yield tris-2-chloroethyl phosphate.

Ethylene oxide and silicon tetrachloride (11,58,60) react to yield tetrakis-2-chloroethyl silicate. A number of alkyl and aryl halosilanes react with ethylene oxide in a similar fashion. Methyl, dimethyl, phenyl and diphenyl 2-chloroethylsiliconates have been prepared from ethylene oxide by this method (4,59,64).

Sulfur monochloride and ethylene oxide yield bis-2-chloroethyl sulfite (46) and side-reaction products while sulfuryl chloride yields 2-chloroethyl chlorosulfonate (48). These reactions are illustrated by the following equations:

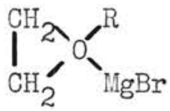


$$S_2Cl_2 + 2\ CH_2\text{-}CH_2(O) \longrightarrow (ClCH_2CH_2O)_2SO$$ and other products

$$SO_2Cl_2 + CH_2\text{-}CH_2(O) \longrightarrow ClCH_2CH_2OSO_2Cl$$

Reaction between ethylene oxide and acetyl iodide is extremely vigorous even at greatly reduced temperatures. However, a 74% yield of 2-iodoethyl acetate has been obtained from such a reaction carried out over a twenty-four-hour period (15). Similar reaction with acetyl chloride at 25° gives, after 44 days, a 95% yield of 2-chloroethyl acetate. Addition of a drop of concentrated hydrochloric acid to the acetyl chloride results in a completion of the reaction in two and one-half days with a 78% yield (15).

Ethylene oxide reacts with alkyl or aryl Grignard reagents to form primary alcohols containing two more carbon atoms than the reagents. Grignard (13,14) postulated the following intermediate in this reaction:



but such a structure is now unacceptable.

Huston and Agett (24) suggest the following series of reactions.

(1) $2\ RMgBr \rightleftharpoons MgBr_2 + R_2Mg$

(2) 

$$2\ CH_2{-}CH_2(O) + MgBr_2 \dashrightarrow Mg(OCH_2CH_2Br)_2$$

(3) $Mg(OCH_2CH_2Br)_2 + R_2Mg \dashrightarrow (RCH_2CH_2O)_2Mg + MgBr_2$

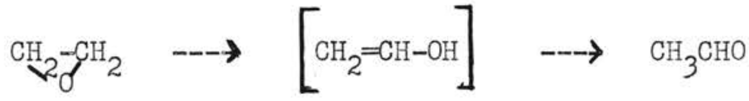
(4) $(RCH_2CH_2O)_2Mg + 2\ HOH \dashrightarrow 2\ RCH_2CH_2OH + Mg(OH)_2$

Ethylene oxide reacts with $MgBr_2$ as long as it is present. Huston and Agett (24) discuss the yields of alcohols prepared by means of the Grignard reagent from a number of alkyl and aryl halides.

Passage of ethylene oxide over an alkali bisulfate catalyst at 120° yields 1,4-dioxane (77). Similar treatment over an alkali hydroxide catalyst yields polyethylene glycols. Vapor-phase polymerization of ethylene oxide in the presence of acid catalysts such as sulfuric, phosphoric, or hydrochloric acid or boron trifluoride yields 1,4-dioxane and high-molecular-weight polyethylene glycols.

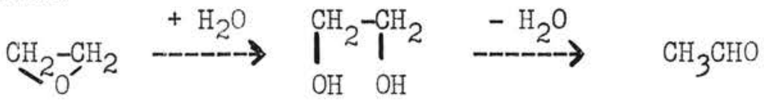
Ethylene oxide also undergoes thermal isomerization (at 300-400°) to acetaldehyde. Under the influence of dehydrating catalysts such as activated alumina, phosphoric acid or metallic phosphates (1) the isomerization takes place at 150-300°. In the latter case, ethylene glycol and other hydration products are obtained as by-products.

Two routes are postulated as possibilities for the isomerization. The first of these is a molecular rearrangement by way of the vinyl alcohol.



$$CH_2{-}CH_2(O) \dashrightarrow \left[CH_2{=}CH{-}OH\right] \dashrightarrow CH_3CHO$$

The other postulates a hydration to ethylene glycol followed by a dehydration.



$$CH_2{-}CH_2(O) \xrightarrow{+\ H_2O} \underset{OH\quad OH}{CH_2{-}CH_2} \xrightarrow{-\ H_2O} CH_3CHO$$

The reaction is highly exothermic ($\Delta H = -23.3$ Kcal.) and is essentially irreversible.

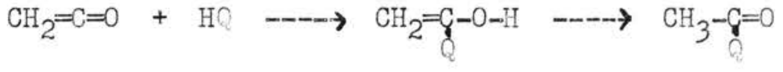
EXPERIMENTAL - PART A

ADDITION OF KETENE TO ETHYLENE OXIDE

Introduction

The best known reactions of ketene are those with compounds containing active hydrogen. Ketene behaves chemically as an anhydride of acetic acid (79). Thus with water it gives acetic acid, with alcohols it gives acetic acid esters, and with hydrogen chloride it gives acetyl chloride. An additional example of this behavior is the Friedel-Crafts reaction of ketene with benzene to form acetophenone (10).

The following equation illustrates the proposed mechanism for such reactions (79).

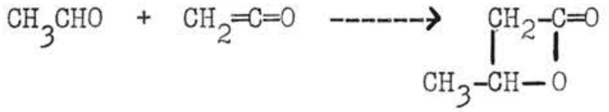


$$CH_2{=}C{=}O \; + \; HQ \; \dashrightarrow \; CH_2{=}\underset{Q}{C}{-}O{-}H \; \dashrightarrow \; CH_3{-}\underset{Q}{C}{=}O$$

In addition to its reaction with active hydrogen compounds, ketene also reacts with non-active hydrogen reagents. Noteworthy among the latter type are the dimerization of ketene to diketene, and the reactions of ketene with carbonyl compounds to form beta-lactones.

Examples of the latter type reactions are the condensations of ketene with formaldehyde, acetaldehyde and acetone to form, respectively, beta-propionolactone, beta-butyrolactone and beta-methyl-beta-butyrolactone (16).

An equation for the reaction with acetaldehyde is given below.



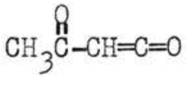
Such reactions have been catalyzed by Friedel-Crafts type catalysts or by non-Friedel-Crafts type catalysts such as boric acid or its esters (71).

All known ketenes dimerize when heated or when allowed to stand at room temperature or below for a sufficient length of time (17).

The dimers of ketoketenes are considered to be derivatives of cyclobutandione, as shown below for the dimer of dimethylketene.

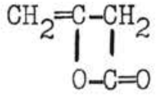
The dimers of aldoketenes are much more reactive than those of ketoketenes and as a result of their reactivity no universally accepted structure has been proposed.

Four different structures, which are shown below, have been proposed for diketene itself (17).

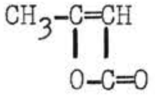


$CH_3\overset{O}{\overset{\|}{C}}{-}CH{=}C{=}O$

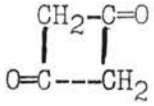
I



II



III



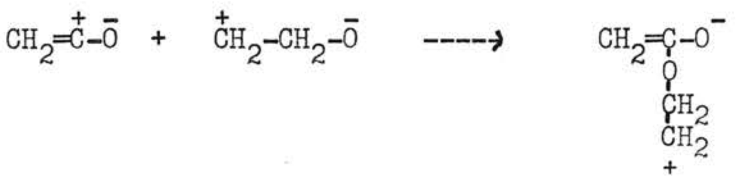
IV

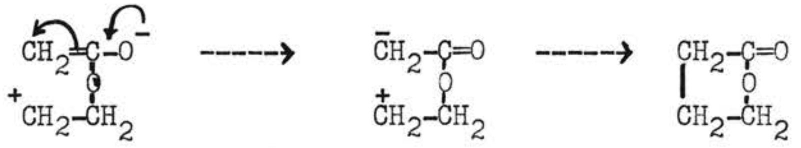
Arguments have been presented in the literature (84) for all four structures.

Since ethylene oxide can, under certain conditions, be considered as a precursor to acetaldehyde (which adds to ketene (16)), it was thought that the oxide itself might have a good chance for a similar reaction. The basis for this was the idea that, before reaction, the ethylene oxide ring opens to form a group which is electrophilic at one end and nucleophilic at the other. Such a group should react with ketene in the following manner:

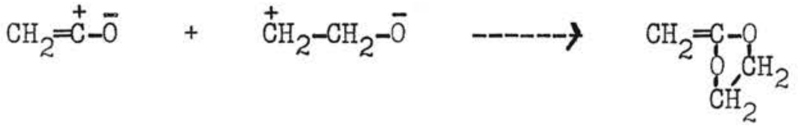
(1) 

(2) $CH_2{=}C{=}O \longrightarrow CH_2{=}\overset{+}{C}{-}\bar{O}$

(3)


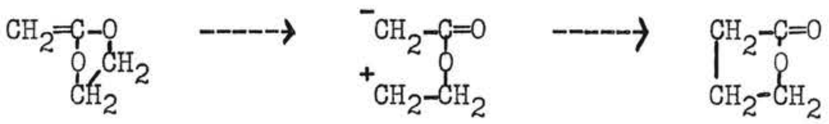
(4)


Another mechanism which suggests itself is shown by the following equations:



2-methylene-1,3-dioxolane

then rearrangement



The latter mechanism is however considered unlikely since the 2-methylene-1,3-dioxolane, a known compound, suggested as an intermediate is reported to undergo polymerization (50) rather than the rearrangement indicated above.

The expected gamma-butyrolactone has been prepared by other means (80).

In the present work it was hoped that acid catalysts could be used simultaneously to activate ketene and ethylene oxide which would then interact to form gamma-butyrolactone.

Procedures and Results

Preparation of ketene

The ketene for these studies was prepared by the pyrolysis of acetone, in a Vycor tube, over broken unglazed porcelain packing at 700° (52).

Liquid-phase reactions

The liquid-phase reactions were carried out with dioxane, ethyl ether and ethylene oxide itself serving as solvents. One uncatalyzed reaction was tried, but all other attempts utilized either phosphoric acid, sulfuric acid, or boron trifluoride as a catalyst.

Experiment 1. An attempt was made to cause a solution of ketene in dioxane to react with ethylene oxide in the absence of a catalyst. Ketene (200 ml. of a dioxane solution, equal to 0.16 mole ketene) was placed in a three-neck 500-ml. flask equipped with a power stirrer and placed in an ice bath. Liquid ethylene oxide (7 ml., 0.14 mole) was added dropwise with stirring over a period of about ten minutes. No evidence of reaction was noted. Stirring was continued and the mixture was allowed to warm up to room temperature. There was still no evidence of reaction at this point.

The reaction mixture was distilled and three fractions were collected: (a) 50-92° (22 ml.), (b) 92-115° (145 ml.), (c) residual liquid boiling above 115° (8 ml.). To see if any of the fractions might contain <u>gamma</u>-butyrolactone, each (a,b, and c) was tested with Tollens reagent. Properties listed for <u>gamma</u>-butyrolactone include reduction of ammoniacal silver nitrate and a boiling range of 203-204° (89° at 12 mm. Hg) (18). Reduction of silver ion was obtained with fraction (a). However, this was probably due to aldehydic impurities in the dioxane. Fractions (b) and (c) formed white precipitates, which may have been silver acetate and which became black after standing about an hour. Fraction (c) has a strong acetic smell which was probably due to hydrolysis of ketene to acetic acid by traces of moisture in the solvent. The white precipitate, assumed to be the slightly soluble silver acetate, was probably caused by the acidification of the Tollens reagent by fraction (b) and (c). A small amount of acetic acid in dioxane gave a white precipitate when added to Tollens reagent. One milliliter of fraction (c) required 27.41 ml. of 0.3400 N sodium hydroxide for neutralization to a phenolphthalein endpoint. After neutralization, fraction (c) gave a positive Tollens test.

The remainder of fraction (c) was neutralized with aqueous sodium hydroxide until a pH of 6 (as indicated by Hydrion paper) was reached. The neutralized solution was distilled and five fractions over the range 98-128° were collected in addition to a solid residue. Treatment of a portion of each fraction with Tollens reagent resulted in a negative test in each case. The solid residue gave a strongly positive Tollens test, possibly due to aldehydic materials held within the solid, which must have been essentially sodium acetate.

A 0.5-ml. portion of each fraction required 3 drops of saturated bromine water to impart a permanent coloration. Not enough bromine was required to suggest the presence of dioxane.

Treatment of 2-ml. portions of the distillate with 2,4-dinitrophenylhydrazine yielded a positive test in all cases. However, neither filtration nor centrifuge techniques yielded sufficient solid hydrazone for a capillary melting-point determination.

In light of these findings it was decided that none of the desired product was formed and that the positive Tollens test obtained in the initial phase of the experiment was indeed due to aldehydic impurities. Had any of the desired product been held in the acidic residue, it should have been released in the neutralization and distilled over with steam.

Experiment 2. This was an attempt to react a solution of ketene in dioxane with ethylene oxide using phosphoric acid as a catalyst.

Ketene (100 ml. of a dioxane solution, equal to 0.12 mole ketene) was placed in a three-neck 500-ml. reaction flask equipped with a power stirrer and placed in an ice bath. Four milliliters of 85% phosphoric acid were added as catalyst. Liquid ethylene oxide (5 ml., 0.1 mole) was added dropwise with stirring over a short time interval (about 7-10 minutes). No evidence of reaction was observed. Stirring was continued and the mixture allowed to warm up to room temperature. There was still no evidence of reaction.

An excess of anhydrous sodium carbonate (32 g.) was added to the mixture and shaken. A small amount of water was added to help form a slurry. After some gas evolution, the solids coagulated into a pasty mass and were separated from the liquid by filtration with suction. The filtrate was found to be neutral to litmus and was then distilled, six fractions being collected with boiling ranges and relative volumes as follows: (a) 50-80° (4.0 ml.), (b) 80-95° (8.9 ml.), (c) 95-100° (11.8 ml.), (d) 100-105° (42.2 ml.), (e) 105-110° (4.6 ml.), (f) residual liquid boiling above 110° (4.8 ml.).

The first fraction had a trace of acetone smell to it and the residual one a strong acetic smell. The acetone could be accounted for by the reasonable assumption that traces of it were carried over from the ketene generator into the solvent by the gas flow.

All six fractions were checked with Tollens reagent. Fraction (a) gave a strong positive test while (b) gave a weakly positive test. Both were assumed due to aldehydic impurities. The other fractions gave a fine white precipitate increasing in quantity from (c) to (f). The precipitate was again assumed to be silver acetate and to be caused by acidification of the Tollens reagent by acetic acid in the solution. One milliliter of fraction (f) required 29.04 ml. of 0.3400 N sodium hydroxide for titration to a phenolphthalein endpoint. After neutralization, (f) gave a positive Tollens test.

Since the acidic residue was so similar to the residue obtained from the uncatalyzed reaction, no further work was done with it.

The use of dioxane as a solvent was discontinued since the dioxane did not hold enough ketene to make it worth while.

Experiment 3. Ethylene oxide itself was used as a solvent for ketene, and sulfuric acid was used to catalyze the reaction.

A long test tube (25 x 200 mm.) equipped with a gas inlet tube reaching to the bottom, and an outlet tube at the top, was placed in an ice bath. A trap to remove uncondensed acetone was placed in an ice bath between the ketene generator and the gas inlet tube. The gas outlet tube was vented.

Liquid ethylene oxide (30 ml.) was placed in the tube and ketene (acetone-pyrolysis gas) was bubbled through it for three hours. Meanwhile, a 250-ml. three-neck flask was equipped with a power stirrer and immersed in an ice bath. Forty-nine grams (0.5 mole) of concentrated sulfuric acid were added to the flask. The solution of ketene in ethylene oxide was then added dropwise with stirring to the sulfuric acid over a period of about fifteen minutes. A very vigorous sputtering accompanied the addition. After all the solution had been added, stirring was continued at ice-bath temperatures for an additional thirty minutes and then the solution allowed to warm up to room temperature. The mixture became deep red during the addition of the solution but no further change was noted as the mixture warmed up to room temperature.

The acid solution was then slowly poured into 130 ml. of water containing 138 grams (1 mole) of potassium carbonate. This was a mistake in that only one-half mole of potassium carbonate was intended to be used. The resulting solution was brought to a pH of 6 to 7 (as indicated by Hydrion paper) with sulfuric acid.

Upon filtration the mixture yielded a solid white residue and a yellow filtrate.

Upon distillation of the yellow filtrate, no steam-volatile portion was obtained. Neither the distillate nor the residue gave a positive Tollens test.

Since the desired product is reported to be steam-volatile and to give a positive Tollens test, work on these reaction products was discontinued.

Experiment 4. A solution of ketene in ethylene oxide was prepared as described in Experiment 3. This solution was then added to 20 ml. (36.7 g., 0.37 mole) of concentrated sulfuric acid in a reaction apparatus as described above.

Again a vigorous reaction was noted and this time the reaction mixture stood at room temperature for four days before further processing was carried out. The acid mixture was poured into water and neutralized with sodium carbonate to a pH of 5 to 7 as indicated by Hydrion paper.

After neutralization, an orange oil was noted on a yellow aqueous layer. After separation of the layers, the aqueous layer was distilled between 95 and 104°. The distillation was stopped at 104° because of severe bumping. The distillate gave a negative Tollens test.

It was found that the distillate and residue contained faint traces of the smell of the orange oil. It was further noted that the orange oil was ether-soluble.

However, since it was unlikely to yield the desired product, and because the amounts of material were relatively small, work along this line was discontinued.

Experiment 5. The next objective was to pass a ketene-ethylene oxide solution mixture into a solution containing a catalyst.

Ketene from the pyrolysis of acetone was passed through a series of ice traps to remove acetone and then through a mineral oil bubbler (to give a rough measure of gas flow) into one arm of a glass "T" tube. Ethylene oxide from a cylinder was passed through a safety trap, then through another mineral oil bubbler into another arm of the "T" tube. The third arm of the "T" tube was connected to a two-way stopcock which would allow the gas mixture to be passed into the reaction apparatus, or to be vented.

The reaction apparatus consisted of a 500-ml. three-neck flask equipped with a power stirrer. One of the other necks was equipped with a glass inlet tube which extended almost to the bottom of the flask. The other end of the tube was connected to the ketene-ethylene oxide mixing "T" tube by a stopcock and a safety trap. The third neck of the flask was vented. The flask was placed in an ice bath.

Boron trifluoride was passed into 250 ml. of anhydrous ethyl ether in the reaction flask until the solution was pale yellow.

Then the mixture of ketene and ethylene oxide was run in at a rate of about 2 parts of acetone-pyrolysis gases to 1 part of ethylene oxide. Passage of the gas mixture into the boron trifluoride etherate was carried on for three hours. In this time the solution changed from pale yellow to a very dirty brown. The reaction mixture was poured into a three-liter round-bottom flask equipped with a long reflux condenser and the flask placed in an ice bath. Five hundred milliliters of distilled water were added slowly down the condenser. Then enough potassium carbonate solution was added to bring the mixture to a pH of 7 as indicated by Hydrion paper.

Upon standing, the solution formed two layers, a solid and a liquid layer. The aqueous liquid layer (containing some ether) was filtered and the red-orange filtrate set aside.

Distillation of a portion of the aqueous filtrate yielded no material giving a positive Tollens test.

The solid layer was extracted with ether and a deep red solution obtained. Upon removal of the ether, 6 ml. of a dark red viscous liquid remained. Part of this viscous dark red residue was thought to be due to dehydroacetic acid (6-methyl-3-aceto-2,4-pyrandione) which occurs as a residue in the distillation of impure diketene resulting from the dimerization of ketene (81). It seemed reasonable that dehydroacetic acid could be formed from ketene in the presence of boron trifluoride catalyst.

Distillation of the residue involved a maximum temperature of 245°. Since the boiling point of dehydroacetic acid is given as 270° (39)

it was concluded that if any of the acid was present, the amount was so small that it would not be worth further attempts at identification.

Experiment 6. The apparatus and the preparation of the boron trifluoride etherate were the same as in the previous experiment.

The gas ratio was changed to approximately equal parts of acetone-pyrolysis gases and ethylene oxide. This time the reaction was carried on for only an hour and forty-five minutes before the solution became extremely dark brown and viscous.

The reaction mixture was transferred to a 3-liter round-bottom flask as before and 400 ml. of ethyl ether added. Two layers were initially noted but they gradually became mixed. The mixture was neutralized with a thick potassium carbonate slush to a pH of 7 as indicated by Hydrion paper. The dark color of the solution disappeared to give a pale yellow-orange solution and a white solid.

Upon filtration to separate the white solid, two liquid layers were noted. The top (ether) layer was removed and treated with anhydrous sodium carbonate. The bottom layer was assumed to be aqueous.

Removal of the ether from the dried ethereal layer followed by a fractional distillation of the residue did not yield fractions with sharp temperature plateaus. A maximum temperature of 155° was obtained before signs of dryness and decomposition were noted in the stillpot. It was concluded that no gamma-butyrolactone was present since the boiling range of this material was not reached. No identification of the distillate was made.

The aqueous layer obtained above yielded a distillate boiling between 94 and 110°, the bulk (60%) of it between 98 and 101°. The possibility of gamma-butyrolactone being in the steam-volatile portion was ruled out when this portion gave a negative Tollens test. No identification of possible products obtained was made.

This concluded the ketene-ethylene oxide interaction attempts in the liquid phase. The remainder of such condensation attempts were made in the vapor phase as described below.

Vapor-phase reactions

Ketene was prepared as before. The pyrolysis gases were passed through two traps in series, immersed in ice, to remove unpyrolyzed acetone.

The acetone-pyrolysis gases were then mixed with ethylene oxide as described in experiment 5 above. After mixing, the gases were passed into the reaction apparatus.

The apparatus consisted of a 25 x 300 mm. tube open at both ends and bearing a side arm near each end. The tube was mounted vertically with the bottom fitted with a 24/40 joint which connected with a flask immersed in an ice bath. The flask was to collect any material which might condense in the tube and flow to the bottom. The top of the tube was fitted with a thermometer, the bulb extending down to the inlet tube mounted near the top of the 25 x 300 mm. tube. The large tube was filled with a Fiberglas plug up to the level of the lower inlet tube. The catalyst used was then poured in on top of the Fiberglas almost to the level of the upper inlet tube. Another plug of Fiberglas was put in on top of the catalyst. This gave about a 250 mm. column of catalyst.

The exterior of the 25 x 300 mm. tube was wrapped with nichrome resistance wire for heating purposes. The heat was controlled by means of a Powerstat.

The mixture of acetone-pyrolysis gases and ethylene oxide was passed into the catalyst chamber through the lower side arm. The reaction products and unchanged gases left the catalyst chamber through the upper tube and passed through two traps in series immersed in ice to condense the reaction products. The uncondensed gases were passed through a sodium hydroxide solution to remove excess ketene and then vented.

Experiment 1. Acidized alumina was used as a catalyst. The catlyst was prepared by mixing granular alumina with dilute sulfuric acid, draining off the acid, and drying the alumina with suction in the funnel. The air-dried alumina was then transferred to the catalyst chamber. The chamber was heated to between 150 and 200° and dry air pulled through it to finish drying the catalyst.

After the column had cooled to room temperature, a mixture of gases consisting approximately of two parts acetone-pyrolysis gases and one part of ethylene oxide was passed in. It was noted that the part of the catalyst struck by the gases became hot. This temperature was roughly estimated at 230-250° by holding a thermometer against the external wall of the catalyst chamber. It was further noted that the lower part of the catalyst gradually became black and also that the zone separating the clean from the blackened catalyst gradually moved up the tube. The temperature peak coincided (approximately) with the zone separating the clean from the blackened catalyst.

Running the reaction in this way for seventy minutes without external heat yielded 20 ml. of material, all boiling between 50 and 120°. This material was not identified.

Experiment 2. The catalyst was prepared as described above. The procedure used was the same as given above except that the catalyst chamber was heated to 210-230°. A temperature peak of about 240-250° was noted during the course of the reaction. This temperature peak coincided (approximately) with the gradual rise of the zone separating the blackened from the clean catalyst.

The passage of the gases through the catalyst was continued for 2.5 hours, at which time all the catalyst was black and no further evidence of reaction was noted. Fifty-five milliliters of a two-phase liquid product were obtained.

Physical separation of the two layers yielded 3.5 ml. of the upper layer, which was found to distill between 60 and 290°. No appreciable plateaus were observed, and no identification was attempted.

A rough fractional distillation of the lower layer yielded, besides single-phase distillates at low and high temperatures, a two-phase distillate between 91 and 102°. The single distillate and the upper portion of the two-phase one were combined (30 ml.) for precise fractional distillation. Further discussion of the aqueous lower phase (25 ml.) will be found under the discussion of the fractions from the precise distillation.

Fraction 1: A 1-ml. portion boiling at 21-30° was received. The boiling range and smell corresponded to that of acetaldehyde. The 2,4-dinitrophenylhydrazone of the distillate melted at 149-150° as compared to 147° for a literature value of the 2,4-dinitrophenylhydrazone of acetaldehyde (66).

Fraction 2: A 3-ml. portion boiling at 50-56° was received. No derivative was prepared since the fraction was thought to be a mixture of acetaldehyde and acetone.

Fraction 3: A 5-ml. portion boiling at 56-59° was received.

The boiling range and odor were that of acetone. The 2,4-dinitrophenylhydrazone melted at 125-126° as compared to a literature value of 126° (67).

Fraction 4: A 0.5-ml. portion boiling at 61-69° was received. The distillate gave a positive 2,4-dinitrophenylhydrazine test, but not a sharp-melting hydrazone. No further identification was attempted.

Fraction 5: A 0.5-ml. portion boiling at 69-75° was received. In general the distillate behaved in much the same way as fraction 4.

Fraction 6: A 2-ml., two-phase liquid portion boiling at 75-80° was received. Both layers absorbed bromine and yielded a positive 2,4-dinitrophenylhydrazine test.

Fraction 7: A 2-ml., two-phase liquid distillate boiling at 86-105° was received. Both layers absorbed bromine and yielded a positive 2,4-dinitrophenylhydrazine test.

Since fractions 6 and 7 seemed so similar, they were combined and a 2,4-dinitrophenylhydrazone of each layer was prepared. That from the lower layer melted at 178-82°, from the upper one at 183-4°. These values correspond most closely to the literature values for the 2,4-dinitrophenylhydrazone of crotonaldehyde, melting at 190° (66). The lowered melting points can be accounted for partially by the fact that the derivatives were not recrystallized, but merely washed with ethanol. The fact that the material was unsaturated increased the possibility of its being crotonaldehyde.

Fraction 8: A 0.4-ml. portion boiling from 105 to 118° was received. This fraction was not investigated.

Fraction 9: A 1-ml. portion boiling at 118-130° was received. The distillate smelled strongly of acetic acid but was not investigated further.

Fraction 10: A 1.5-ml. portion boiling at 162-180° was received. No further investigation was made.

Fraction 11: A 1-ml. portion boiling at 180-190° was received. No further investigation was made.

Fraction 12: A 4-ml. portion boiling at 190-194° was received. The stillpot went dry at this point. In addition to the fact that the boiling range was too low, there was little chance that the material contained any _gamma_-butyrolactone since the product gave a negative Tollens test and was water-insoluble. Its boiling range and mode of formation made it quite likely that the material was ethylene glycol diacetate. However, an attempt to form the N-benzylamide failed.

In general it can be seen that a number of rearrangements and condensations took place, but no detectable amount of _gamma_-butyrolactone was formed.

Experiment 3. Silica gel was used as a catalyst. Untreated granular silica gel was placed in the catalyst chamber and a mixture consisting of two volumes of acetone-pyrolysis gases to one volume of ethylene oxide was passed through the catalyst for a period of two hours. The reaction was not quite so exothermic as in the case of the acidized alumina. The exterior wall of the catalyst chamber was kept at 200-230°. The temperature of the exit gases gradually rose from 135 to 170°. The coincidence of the area dividing the clean from the blackened catalyst with the temperature peak in the catalyst chamber was again noted. When all the catalyst had blackened, the reaction stopped.

The reaction yielded 110-120 ml. of two liquid phases which readily formed a single phase upon mixing.

Fractional distillation gave the following fractions.

Fraction 1: A 7-ml. portion boiling at 20-30° was received. The boiling range and odor suggested acetaldehyde, which was identified by the melting point of the 2,4-dinitrophenylhydrazone.

Fraction 2: A 5-ml. portion boiling at 30-55° was received, but no further investigation was made.

Fraction 3: A 22-ml. portion boiling at 55-57° was received. The boiling range and odor suggested acetone, which was identified by the melting point of the 2,4-dinitrophenylhydrazone.

Fraction 4: A 1.5-ml. portion boiling at 63-84° was received. The two-phase distillate was not investigated.

Fraction 5: A 2-ml. portion boiling at 84-98° was received. A two-phase solution formed which readily absorbed bromine. On the basis of the behavior of fraction 7 from the acidized alumina, it is suggested that the solution contained crotonaldehyde. This could have been formed by an acid-catalyzed aldol condensation of the acetaldehyde formed by the rearrangement of ethylene oxide, followed by loss of water.

Fraction 6: A 35-ml. portion boiling at 98-110° was received. The same general ideas held here as in the case of fraction 5. The bulk of the fraction was probably water driven from the silica gel which was not dried beforehand owing to an oversight.

Fraction 7: A 2-ml. portion boiling at 113-119° was received. The distillate had a strong acetic odor. Preparation of an anilide via the acyl chloride yielded a product which melted at 112-113°. This compared favorably with the known melting point of 114° for acetanilide (65).

Fraction 8: A 2-ml. portion boiling at 119-134° was received which was probably a mixture of acetic acid and acetic anhydride. No attempt was made to prepare derivatives as proof.

Fraction 9: A 4-ml. portion boiling at 134-139° was received. The material was acetic anhydride (b.p. 138°), as proved by the conversion to the anilide, which melted at 114-115°.

Fraction 10: A 1-ml. portion boiling at 140-180° was received but not identified.

Fraction 11: A 2-ml. portion boiling at 182-184° was received but not identified.

Fraction 12: The stillpot went dry after a 1-ml. portion boiling at 184-185° was received. This fraction was not identified.

Both fractions 11 and 12 had an ester-like odor and probably contained some ethylene glycol diacetate. However, this was not proved in any way. The fractions were water-soluble but gave a negative Tollens test, which, combined with the low boiling range, ruled out the possibility that <u>gamma</u>-butyrolactone was present.

Experiment 4: Alumina was used as a catalyst. Granular (8-14 mesh) Harshaw activated alumina which had not been acidized was placed in the catalyst chamber and dried by heating the chamber to 120° and pulling dry air through it. A gas mixture consisting of two volumes acetone-pyrolysis gases to one volume ethylene oxide was passed through the catalyst for three hours, with the catalyst at about 200°.

As before, the area separating the clean from the blackened catalyst coincided with the peak of heat in the catalyst chamber. The surface separating the clean and blackened catalyst gradually moved up the column and, as before, reaction seemed to cease when the catalyst at the top of the column blackened. The exit gases were observed to have a temperature of 205° at this time.

Two immiscible layers were obtained. The layers were physically separated and separately distilled. No identification beyond separation of the fractions was made.

Distillation of the upper layer.

Fraction	Boiling Range	Yield of Distillate
1	64-67°	0.5 ml.
2	67-92°	less than 0.5 ml.
3	82-85°	1 ml.
4	95-140°	1 ml.
5	140-185°	1.5 ml.
6	185-200°	1 ml.
7	200-210°	1 ml.
8	210-215°	2 ml.
9	Pot Residue	5 ml.

Fractions 6 and 7 were water-insoluble and gave a negative Tollens test, ruling out any possibility of their containing gamma-butyrolactone.

Distillation of the lower layer.

Fraction 1: The boiling range was 20-30°; the yield, less than 0.5 ml. The material had a strong odor of acetaldehyde.

Fraction 2: The boiling range was 55-57°; the yield, about 3 ml. of material which had a strong odor of acetone.

Fraction 3: The boiling range was 60-90°; the yield, 2.5 ml. of liquid which was not identified.

Fraction 4: The boiling range was 90-110° with the stillpot going dry at 110°. The yield was 20 ml. of liquid with very little aldehydic smell. There is little chance that the liquid contained any gamma-butyrolactone, which would be steam-volatile, since the material gave a negative Tollens test.

Discussion

All attempts to prepare gamma-butyrolactone by uncatalyzed and acid-catalyzed liquid-phase and vapor-phase condensations of ketene with ethylene oxide were unsuccessful.

The only materials isolated and identified were products of rearrangement or side reactions of the reagents themselves.

The acetaldehyde obtained was presumed produced by thermal rearrangement of ethylene oxide. Some of the acetaldehyde evidently was converted to aldol, which then split out water and yielded crotonaldehyde, which was identified in the reaction products.

Traces of moisture in the apparatus and reagents reacted with ketene to form acetic acid which in turn with more ketene yielded acetic anhydride. Both acetic acid and acetic anhydride were identified in the reaction products.

Ethylene oxide then could react with the acetic anhydride to form ethylene glycol diacetate, the presence of which was suspected, but not positively proved.

It is possible that a specific set of conditions and a specific catalyst might be found for such a reaction but such a trial-and-error search was not undertaken at this time.

EXPERIMENTAL - PART B

ADDITION OF ESTERS TO ETHYLENE OXIDE

Introduction

Although no attempt to cause the reaction of ethylene oxide with an ester linkage has been reported in the literature, such a condensation did not seem unreasonable.

It was thought that the reactivity of the ester linkage might be somewhat similar to that of acid chlorides, acid anhydrides and acetals, all three of which are known to add to ethylene oxide.

The hoped-for reaction was the addition of carboxylic esters to ethylene oxide so as to form 2-alkoxyethyl carboxylic esters as illustrated by the following equation:

$$R-\overset{O}{\overset{\|}{C}}-OR' \quad + \quad n\ \underset{O}{CH_2-CH_2} \quad \text{--------}\!\!\rightarrow \quad R-\overset{O}{\overset{\|}{C}}-(OCH_2CH_2)_n OR'$$

Acid catalysis was chosen since it works well for acetals (8).

Since some esters of inorganic acids are readily hydrolyzed it was thought these might undergo a reaction with ethylene oxide similar to that of acetals. This is particularly true of the orthoesters, both of the inorganic acids and of the carboxylic acids.

Procedures and Results

Carboxylic Esters

The reaction chosen for study was the addition of ethyl acetate to ethylene oxide under a variety of conditions with the hope of obtaining 2-ethoxyethyl acetate. An excess of ethyl acetate over ethylene oxide was used to hold the reaction down to the introduction of only one ethylene oxide unit per ethyl acetate molecule.

Experiment 1: Ethyl acetate (88 grams, 1 mole) was placed in a three-neck 500-ml. flask equipped with a gas-dispersion tube and placed in an ice bath. Boron trifluoride was passed in until 29 grams (0.43 mole) had been added. Ethylene oxide (22 grams, 0.5 mole) was then added dropwise with shaking over a period of 30-40 minutes. Vigorous sputtering and gradual accumulation of dark, viscous material in the flask accompanied the addition of the ethylene oxide. After standing in an ice bath for two hours the reaction mixture was transferred to a 500-ml. round-bottom flask equipped with a long reflux condenser and placed in an ice bath. The reaction mixture was neutralized with sirupy potassium carbonate. About 20 ml. of water had to be added to effect the neutralization. The two-phase filtrate (clear dark red and colorless) was separated and each portion distilled through a three-bulb Snyder column.

Distillation of upper (organic) layer.

Fraction 1: A 40-ml. portion boiling at 71-73° was received. The water-white distillate had the boiling range of ethyl acetate-water azeotrope (22).

Fraction 2: A 15-ml. portion boiling at 73-90° was received. The fraction was mainly ethyl acetate.

Fraction 3: A 2-ml. portion boiling at 90-145° was received.

The fraction contained some 1,4-dioxane as evidenced by the formation of a bromine adduct melting between 65 and 66°. The literature melting point for the 1,4-dioxane-bromine adduct is 66° (19).

Fraction 4: A 2-ml. portion boiling at 155-185° was received.

Fraction 5: A 4-ml. portion boiling at 187-188° was received.

Fraction 6: A 4-ml. stillpot residue remained.

No identification was made of fractions four or six. Fraction 5 gave a positive ferric hydroxamate ester test and was considered to be ethylene glycol diacetate on the basis of the following physical property comparisons.

Property	Reaction Product	Ethylene Glycol Diacetate	Literature Reference
Boiling Range	187-188°/742 mm.	190.5°/760 mm.	(40)
Refractive Index	1.4165 to 1.4178 at 26°	1.4183 at 15°	(41)
Density, g./ml.	1.099 26°/26°	1.108 15°/15° 1.104 20°/20°	(41) (5)

Distillation of the lower (aqueous) layer.

Fraction 1: A 2-ml. portion boiling at 71-100° and containing some ethyl acetate was received.

Fraction 2: A 20-ml. portion boiling at 100-101° was received and presumed to be water since no dioxane odor was detected.

Fraction 3: Upon cooling, 5-10 ml. of a waxy material were obtained.

On the basis of the solubility data given below, it was decided that the waxy material was primarily a mixture of polyethylene glycols, commercially called Carbowax (49).

Water------------------Soluble

Methanol----------------Soluble

Ethanol-----------------Slightly soluble

Acetone----------------Very slightly soluble

Ethyl acetate----------Very slightly soluble

Toluene----------------Insoluble

Ethyl ether------------Insoluble

Experiment 2. Ethyl acetate (200 ml., 2 moles) was placed in a 500-ml. three-neck flask equipped with a power stirrer and placed in an ice bath. Boron trifluoride was added until the ethyl acetate had a pale yellow tinge. Ethylene oxide (88 grams, 2 moles) was added dropwise at 10-18° with stirring over a period of 1 1/2 hours. Vigorous sputtering and gradual accumulation of solid material again accompanied the ethylene oxide addition. Upon removal from the ice bath the reaction mixture slowly heated spontaneously to a maximum of 41° before cooling again to room temperature.

The solid was filtered off and saved. The filtrate was neutralized with potassium carbonate, the solids filtered off and discarded and the filtrate distilled.

Fraction 1: A 40-ml. portion of ethyl acetate-water azeotrope boiling at 71.5-74° was received.

Fraction 2: A 25-ml. portion boiling at 74-77° and consisting mainly of ethyl acetate was received.

Fraction 3: A 25-ml. portion boiling at 77-90° was received. The distillate consisted of ethyl acetate and some dioxane.

Fraction 4: A 15-ml. portion boiling at 90-110° was received. The distillate contained some 1,4-dioxane as evidenced by a melting range of 64-65° for the bromine adduct.

Fraction 5: A 5-ml. portion of water-white liquid boiling at 110-145° was received.

Fraction 6: A 1.5-ml. portion of water-white liquid boiling at 145-190° was received.

Fraction 7: A 3-ml. portion of water-white liquid boiling at 190-195° was received.

Fraction 8: A 0.5-ml. portion of water-white liquid boiling at 195-210° was received.

Fraction 9: A stillpot residue consisting of 5 ml. of deep brown liquid remained.

No product in the desired range was obtained. The hoped for 2-ethoxyethyl acetate boils at 156° (38). The high-boiling materials were considered to be ethylene glycol diacetate.

The solid residue from the reaction mixture which had been set aside was now treated with 150-200 ml. of water and neutralized with potassium carbonate. The mixture was filtered to remove solids and the filtrate distilled.

Fraction 1: A 175-ml. portion boiling at 99-102°, consisting mainly of water, was received.

Fraction 2: A 12-ml. portion of water-white liquid boiling at 180-184° was received.

Fraction 3: A 5-ml. yellow-brown distillate boiling at 191-198° was received.

The stillpot residue was a charred black solid.

Fraction 2 was redistilled through a precise column and a 10-ml. fraction boiling at 187-189° was received. This material was considered to be ethylene glycol diacetate.

Experiment 3: Ethyl acetate (100 ml., 1 mole) was placed in a 500-ml. three-neck flask equipped with a power stirrer and placed in an ice bath. Trichloroacetic acid (16.3 grams, 0.1 mole) was added as a catalyst. A solution of 22 grams (0.5 mole) ethylene oxide in 50 ml. (0.5 mole) ethyl acetate was added dropwise with stirring at such a rate as to maintain the temperature of the reaction between 2-3°.

Stirring at ice-bath temperatures was continued for 3.5 hours after which the mixture was allowed to come up to room temperature over a period of three hours and stirred for an additional hour. The mixture was then allowed to stand overnight before being neutralized with 6.9 grams (0.05 mole) anhydrous potassium carbonate. The solid was filtered off and the filtrate distilled through a 3-bulb Snyder column.

Fraction 1: A 0.5-ml. portion boiling at 45-58° was received.

Fraction 2: A 10-ml. portion boiling at 58-71° was received.

Fraction 3; A 10-ml. portion of ethyl acetate-water azeotrope boiling at 71-77° was received.

Fraction 4: A 104-ml. portion of ethyl acetate boiling at 77-79° was received.

Fraction 5: A 2-ml. portion boiling at 145-188° was received.

Fraction 6: A 2-ml. portion boiling at 188-210° was received.

Fraction 7: A 2-ml. portion of yellow liquid boiling above 210° was received. The stillpot went dry while this fraction was being received.

Fractions 1 to 3 were recombined for distillation through a precise column.

Fraction 1: The boiling range was 40-74°; the yield, 0.7 ml.

Fraction 2: The boiling range was 77-78°; the yield, 15-17 ml. of ethyl acetate.

No product boiling in the desired range was received. The other products were not identified.

Experiment 4. The apparatus and general procedure were the same as in the previous reaction, differing only in the catalyst used. Anhydrous stannic chloride (26 grams, 0.1 mole) was used as catalyst and the ethyl acetate-ethylene oxide solution was added at such a rate as to maintain the reaction temperature between 2 and 6°.

Small amounts of white solid were noted in the reaction mixture upon the addition of ethylene oxide. When about a quarter of the total ethylene oxide had been added the solids dissolved and were replaced by a clear solution. Toward the end of the ethylene oxide addition the solution again became somewhat cloudy.

The reaction mixture was allowed to warm up to room temperature and then to stand for 40 hours before being neutralized with 28 grams (0.2 moles) anhydrous potassium carbonate in 20 ml. of water. The neutralized mixture was filtered to remove the solids and the filtrate, which was yellow, distilled through an 8-bulb Snyder column.

Fraction 1: A 75-ml. yield of ethyl acetate-water azeotrope was obtained boiling between 71 and 77°.

Fraction 2: A 30-ml. yield of ethyl acetate was obtained, boiling between 77 and 78°.

Fraction 3: A 2-ml. yield of water-white liquid boiling at 80-125° was obtained. No dioxane was detected in the distillate.

Fraction 4: A 2-ml. yield of water-white liquid boiling at 125-130° was obtained.

Fraction 5: A 3-ml. yield of water-white liquid boiling at 130-150° was obtained.

Fraction 6: A 2-ml. yield of water-white liquid boiling from 150 to 165° was obtained.

Fraction 7: A 2-ml. yield of pale yellow liquid boiling at 165-175° was obtained.

Fraction 8: A 1.5-ml. yield boiling above 175° was obtained.

A black stillpot residue remained.

Fractions 3 to 8 were recombined for precise distillation.

Fraction 1: A 1-ml. yield of water-white liquid boiling up to 85° was obtained.

Fraction 2: The boiling range was 90-112°; the yield, 2-3 ml. The distillate had a very slight odor of 1,4-dioxane.

Fraction 3: A 5-ml. yield of water-white liquid boiling at 120-135° was obtained.

Fraction 4: A 4-ml. yield of water-white liquid boiling at 135-152° was obtained.

Fraction 5: A 1.5 ml. yield of water-white liquid boiling at 154-159° was obtained.

No material boiling in the desired range was received. The high-boiling material obtained was considered to be ethylene glycol diacetate.

Experiment 5: The apparatus and general procedure were the same as in the previous reaction, differing only in the catalyst used. Ten grams (0.1 mole) of concentrated sulfuric acid was used as a catalyst. The ethylene oxide was added at such a rate as to keep the temperature of the reaction mixture between 3 and 8°.

The reaction mixture was treated with 13.8 grams (0.1 mole) of anhydrous potassium carbonate to neutralize the catalyst. The solid was filtered off and the filtrate distilled.

Fraction 1: A 10-ml. portion of water-white liquid boiling between

61 and 70° was obtained.

Fraction 2: A 127-ml. portion of ethyl acetate-water azeotrope boiling between 70 and 76° was obtained.

Fraction 3: A 14-ml. portion of water-white liquid (with a strong pungent odor) boiling between 76 and 95° was obtained.

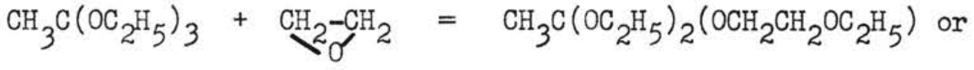
The stillpot went dry at 105°, accompanied by the formation of a black mass and smoke. This decomposition and the lack of higher-boiling materials was probably due to incomplete neutralization of the sulfuric acid.

No material boiling in the desired range was obtained.

<u>Other Esters</u>

A series of single experiments were conducted to study the reaction of ethylene oxide with ethyl orthoacetate, _n_-butyl nitrite, and _n_-butyl borate.

Experiment 1: The hoped for reaction between ethylene oxide and ethyl orthoacetate is expressed by the following equation:



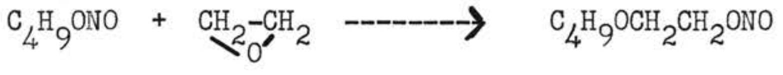
$$CH_3C(OC_2H_5)_3 + \underset{O}{CH_2-CH_2} = CH_3C(OC_2H_5)_2(OCH_2CH_2OC_2H_5)$$ or

similar products.

Boron trifluoride (4.5 g., 0.07 mole) was dissolved in 50 ml. of anhydrous ethyl ether in a 125-ml. erlenmeyer flask placed in an ice bath. To this was added dropwise with shaking a mixture of 5 ml. (0.1 mole) ethylene oxide and 5 ml. (0.03 mole) ethyl orthoacetate. Two layers were noted. The oily yellow bottom layer turned deep brown upon standing at room temperature for a half hour. The resulting mixture was neutralized by addition of sirupy potasssium carbonate with stirring until gas evolution ceased. The neutralized solution had a pH of about 8 as indicated by Hydrion paper. The mixture now consisted of a yellow solution and a white solid. The solid was filtered off and discarded while the liquid was dried over anhydrous sodium carbonate and then distilled. Primary products of distillation were ethyl ether and ethyl acetate. About 3.5 ml. of material boiling between 85-138° was received and about 1 ml. of unidentified amber liquid boiling above the boiling point of the orthoester remained.

In repetition of this work it would be desirable to maintain an excess of the ester over ethylene oxide and to insure the absence of any aqueous acid during the neutralization by addition of the reaction mixture to an excess of base.

Experiment 2: The hoped for reaction between n-butyl nitrite and ethylene oxide is expressed by the following equation:



$$C_4H_9ONO + \underset{O}{CH_2-CH_2} \dashrightarrow C_4H_9OCH_2CH_2ONO$$

Boron trifluoride (4.5 g., 0.07 mole) was dissolved in 50 ml. anhydrous ethyl ether in a 125-ml. erlenmeyer flask placed in an ice bath. To this was added dropwise with shaking a mixture of 5 ml. (0.1 mole) ethylene oxide and 6 ml. (0.05 mole) n-butyl nitrite. Vigorous sputtering accompanied the addition. A waxy film which turned brown upon warming to room temperature was formed on the bottom of the flask. Some nitrogen dioxide fumes were observed during the addition to the catalyst. After standing about 1 1/2 hours, the mixture was neutralized by the addition of sirupy potassium carbonate until gas evolution ceased, at which time the solution was neutral as indicated by Hydrion paper. The resulting white solid was filtered off and discarded and the orange filtrate distilled. The distillate consisted mainly of 1-butanol and about 1 ml. of a sweet-smelling material boiling between 135-145°. No identification of this material was made, but it might have been ethylene glycol monobutyl ether.

Experiment 3: The hoped for reaction between n-butyl borate and ethylene oxide is expressed by the following equation:

$$B(OC_4H_9)_3 + \underset{O}{CH_2\text{—}CH_2} \longrightarrow B(OC_4H_9)_2(OCH_2CH_2OC_4H_9)$$

and similar products.

Boron trifluoride (4.5 g., 0.07 mole) was dissolved in 50 ml. of anhydrous ethyl ether in a 125-ml. erlenmeyer flask placed in an ice bath. To this was added dropwise with shaking a mixture of 5 ml. (0.1 mole) ethylene oxide and 10 ml. (0.04 mole) of n-butyl borate. The addition proceeded smoothly though a white cloudy suspension was noted to form in the solution. Upon standing, the suspension formed a waxy film on the bottom of the flask. Upon warming to room temperature, this film became a deep brown. After standing at room temperature for 1.5 hours, the mixture was neutralized by the addition of sirupy potassium carbonate until gas evolution ceased. At this point the mixture was pale orange and contained a white solid. The solid was filtered off and discarded and the orange filtrate distilled. The distillation yielded primarily 1-butanol and 3 ml. of unidentified material boiling between 130 and 175°.

Discussion

Addition of ethyl acetate to ethylene oxide does not take place under the specified conditions of acid catalysis. Normal acid-catalyzed polymerization of ethylene oxide to p-dioxane and polyethylene oxides was observed. The observed formation of ethylene glycol diacetate is explained by assuming acid hydrolysis of the ethyl acetate in the presence of traces of moisture to form acetic acid which can react with ethylene oxide to yield ethylene glycol monoacetate. This latter material can then react with more acetic acid to form the ethylene glycol diacetate.

Vapor-phase trials over acidic and basic catalysts might give the desired results. Basic catalysts in solution might also be of value. However, neither of these general methods was studied in this work.

The results obtained from the single trials of other esters were inconclusive. Future work with the addition to orthoesters should include ethyl orthoformate which should have a better chance of succeeding than does ethyl orthoacetate. The ethyl orthoacetate was used in this work because it was at hand.

Future work on the addition of boric acid or nitrous acid esters to ethylene oxide should avoid the use of aqueous bases in working up the reaction mixture since both alkyl nitrites and alkyl borates are very readily hydrolyzed. A base such as ethanolamine should be satisfactory in deactivating the acid catalyst without the danger of hydrolysis of the products.

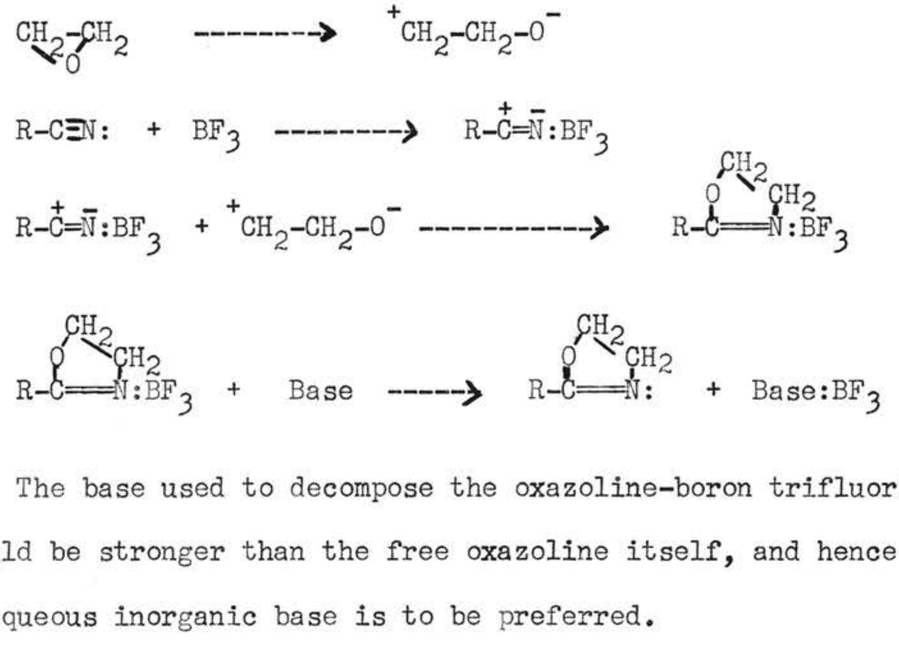
EXPERIMENTAL - PART C

ADDITION OF NITRILES TO ETHYLENE OXIDE

Introduction

Bogert and Roblin (3) showed that ethylene oxide would react with an aldehyde in the presence of a Lewis acid catalyst to yield a cyclic acetal (1,3-dioxolane).

It was thought that nitriles might undergo a similar reaction to yield 1,3-oxazolines. The sequence of reaction postulated for such a reaction using boron trifluoride as a catalyst is as follows:



The base used to decompose the oxazoline-boron trifluoride complex should be stronger than the free oxazoline itself, and hence the use of an aqueous inorganic base is to be preferred.

Procedure and Results

Acetonitrile was chosen for this study for a number of reasons. It is a typical nitrile and can be obtained at relatively low cost. Equally important is the fact that the hoped for product, 2-methyl-1,3-oxazoline, is a known material and therefore can be characterized with relative ease.

Preliminary Experiments

Experiment 1. Boron trifluoride (4.5 g., 0.07 mole) was dissolved in 50 ml. anhydrous ethyl ether in a 125-ml. erlenmeyer flask placed in an ice bath. To this was added dropwise and with shaking a mixture consisting of 5 ml. (0.1 mole) ethylene oxide and 5 ml. (0.1 mole) acetonitrile. Some sputtering occurred during the addition and a two-phase mixture resulted. Upon warming to and standing at room temperature for about thirty minutes the bottom layer assumed a pale yellow color and the consistency of mineral oil. After standing for two hours the mixture was neutralized by the addition of sirupy potassium carbonate until gas evolution ceased. The resulting white solid was filtered off, the filtrate dried over anhydrous sodium carbonate and distilled. In addition to recovery of some acetonitrile, some material boiling between 110-138° was obtained, and this gave a positive nitrogen test after sodium fusion. The material was thought to be 2-methyl-1,3-oxazoline but not enough was obtained for positive identification.

Experiment 2. Boron trifluoride (14 g., 0.2 mole) was dissolved in 100 grams (2.5 moles) of acetonitrile. This solution was placed in a 500-ml. three-neck flask equipped with a power stirrer and thermometer and placed in an ice bath.

Ethylene oxide (60.5 g., 1.38 moles) was dissolved in 64 grams (1.5 moles) acetonitrile. This mixture was added to the catalyst solution with stirring at such a rate as to maintain the temperature between 3-8°. Most of the time it was kept below 5°. A total of 6 1/2 hours was required for the addition. After the addition, stirring in the ice bath was continued as the ice was allowed to melt. Three and one-half hours were required to warm the bath up to 12°. At this time the solution was a cloudy white but no solid was noted. Stirring was continued overnight as the solution gradually warmed up to 18°.

The reaction mixture was then poured into 100 ml. of water containing 150-200 g. (large excess) of anhydrous potassium carbonate to neutralize the boron trifluoride. No violent reaction was noted although a small amount of heat was evolved. The solution was basic to Hydrion paper. The organic liquid was decanted off, dried over anhydrous sodium carbonate, and distilled.

In addition to acetonitrile azeotrope and acetonitrile itself, 2.5 ml. of material boiling from 109-112° at 745 mm. was obtained. The picrate of this material melted at 161-162°, which was in good agreement with the literature value of 163° for the picrate of 2-methyl-1,3-oxazoline (78). The free base itself is reported to boil at 109-111° (78). An unidentified high-boiling tarry residue was also obtained.

As the work progressed the chief difficulty encountered was the inability to consistently reproduce even the low yields occasionally obtained. It was uncertain whether the low yields were due to nonformation of product or to loss during isolation.

The work involved in adding acetonitrile to ethylene oxide in the presence of catalyst divided itself into three distinct sections.

A. To effect the addition itself in the presence of catalyst.

B. To neutralize or otherwise destroy the catalyst and liberate the basic product after the reaction.

C. To separate and purify the desired product.

A summary of the modifications of the above sections used for a number of reactions is given below.

A. The general procedure used was to dissolve the boron trifluoride in acetonitrile and then to this catalyst solution add a mixture of ethylene oxide and acetonitrile. In all cases the addition was made while the catalyst solution was being stirred by a mechanical stirrer. A vigorous reaction (sputtering) was noted when the ethylene oxide was added to the catalyst solution.

When the reaction flask was immersed in an ice bath during the addition, the yields of 2-methyl-1,3-oxazoline obtained were of the order of one to five percent based on ethylene oxide. When the reaction was carried out at 40-50° a yield of 10% was once obtained.

In all cases a large excess (4/1 and 5/1) of acetonitrile over ethylene oxide was maintained. The amount of catalyst was varied from 0.2 moles of boron trifluoride per mole of ethylene oxide to equimolar ratio. The higher catalyst concentrations proved to be most satisfactory.

Use of one mole of anhydrous hydrogen chloride as catalyst, four moles of acetonitrile and one mole of ethylene oxide with the reaction carried out at ice bath temperatures did not give any detectable amount of the desired oxazoline.

Refluxing equimolar portions of ethylene chlorohydrin and acetonitrile for 3 hours in the presence of a small amount of anhydrous hydrogen chloride followed by neutralization of the HCl did not yield any oxazoline.

B. The most satisfactory method of destroying the boron trifluoride after reaction seemed to be to stir the reaction mixture with an excess of sodium carbonate dissolved in a large volume of water. About 15-20 moles of water per mole of sodium carbonate was used. Use of such a large volume of water made it easier to stir the mixture which became quite thick after an hour or two of stirring. Neutralization seemed complete in 3 to 5 hours as evidenced by the fact that the mixture did not seem to become more viscous.

Other attempts to destroy the boron trifluoride after a low-temperature reaction consisted of treating the reaction mixture with either aqueous sodium hydroxide or distilling with a tertiary amine.

When the reaction mixture was treated with aqueous sodium hydroxide in slight theoretical excess none of the desired product was obtained. Instead a great deal of ammonia was evolved by the solution.

Separate portions of the mixture were distilled with tri-n-butylamine, triethanolamine, and 2,6-lutidine. After the excess acetonitrile had been distilled off it was hoped that the higher-boiling amine would complex with the boron trifluoride so as to liberate the desired product. No product was received when the reaction mixture from a low-temperature reaction was used.

C. An attempt to steam-distill the product from the neutralized reaction mixture and then break the resulting azeotrope with benzene did not prove satisfactory.

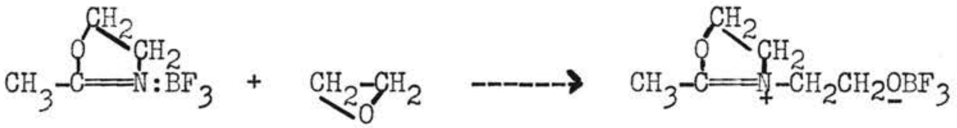
Since the above technique failed to give the desired 2-methyl-1,3-oxazoline in reproducible yields some attempts at extracting the neutralized reaction products were made in hope of obtaining the free base. A detailed description of such an experiment follows.

Acetonitrile (250 g., 6.1 moles) was placed in a one-liter three-neck flask equipped with a mechanical stirrer, a thermometer and an ice-water-cooled reflux condenser. Boron trifluoride was passed in until 148 g. (2.35 moles) had been absorbed. The flask was placed in a water bath at 40°. Ethylene oxide (114 g., 2.51 moles) was dissolved in 160 g. (4 moles) of acetonitrile and this mixture was added to the catalyst solution at such a rate as to keep the temperature between 45 and 70°. Most of the time it was kept at 48-52°. Vigorous sputtering accompanied the addition, which required four hours. The mixture was stirred at 40° for an additional 1.5 hours and then allowed to stay at room temperature overnight.

Three hundred grams of the reaction mixture were poured into one liter of water containing 320 grams of technical grade sodium carbonate. The mixture was stirred for five hours and then allowed to stand overnight. The clear sodium carbonate solution became filled with a gelatinous mass as the stirring proceeded.

The mixture was divided into two portions, and each portion extracted about ten times with 50-ml. portions of ethyl ether. The combined ether washings were dried over calcium chloride and the ether distilled off. None of the desired oxazoline was obtained.

It was thought that in addition to the formation of the 2-methyl-1,-3-oxazoline some other reaction was taking place which prevented the isolation of the free base. This belief was supported by the fact that in many instances all evidence of reaction ceased when two moles of ethylene oxide per mole of boron trifluoride had been added. It was thought that the following type of reaction might have occurred.



Such a process is known for pyridine-ethylene oxide reaction in the presence of boron trifluoride (51).

Condensation of ethylene oxide with acetonitrile followed by isolation or decomposition of the possible resulting quaternary salt was attempted.

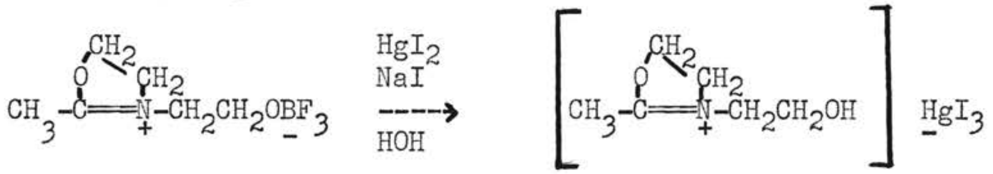
The condensation was carried out as described in the previous experiment except that only 4.5 moles of acetonitrile, 2 moles of ethylene oxide and 1 mole of boron trifluoride were used.

a. Sixty grams of the reaction mixture were distilled at room temperature and 30 mm. pressure to remove excess acetonitrile. Forty milliliters of tri-n-butylamine were added to the residue and arrangement for distillation made. The system, containing an air sweep, was maintained at 20-30 mm. pressure and the water bath temperature was varied from room temperature to 95°. No distillation was observed and hence it was concluded that the amine would not liberate any oxazoline present.

The amine was distilled off at 80-95° at 17-25 mm. pressure and heating of the residue was continued until a pot temperature of 245° was obtained at 20 mm. At this point a very small amount of yellow distillate with a pungent odor was received. The vapor temperature was 75°. During the heating the pot material changed from an amber-colored, moderately viscous mass to a deep brown waxy mass. Upon cooling the waxy residue was found to be water-soluble. No saltlike material was noted.

b. The acetonitrile was removed from another 60 grams of reaction mixture as in (a) and then the residue was gradually heated to a pot temperature of 260° at 20 mm. No distillation was observed even when the pot residue showed signs of decomposition. During the course of the heating the reaction mixture changed from an amber moderately viscous liquid to an extremely viscous red-brown liquid. Upon cooling, this residue was a muddy brown wax which was soluble in water. Apparently any existing complex cannot be broken thermally to give simpler products.

c. An attempt was made to form the mercuric iodide complex according to the following equation:



The acetonitrile was removed from another 60 grams of reaction mixture as in (a). The residue was then added to a suspension of 23 g. (0.05 mole) HgI_2 and 7.5 g. (0.05 mole) NaI in 100 ml. of water. The original suspension was red but after treatment with the reaction product, which was in theoretical excess, the red salt disappeared and was replaced by a viscous yellow oil.

Attempts to crystallize the oil by lowering the temperature to -12° failed.

Boiling a small amount of the oil resulted in its decomposition to a deep yellow-brown viscous mass.

Allowing the yellow oil to stand in a desiccator for several days resulted in the formation of some suspended crystals that could not be separated from the viscous oil.

At this point the prospects of clean nitrile-ethylene oxide reaction were so low that further study was abandoned.

Discussion

The above work indicated that the boron trifluoride-catalyzed addition of nitriles to ethylene oxide is not a satisfactory method for preparing the corresponding free oxazolines.

There are several lines of evidence that the oxazoline primarily formed adds another mole of ethylene oxide to give the quaternary ammonium compound even though excess nitrile is always present; evidently quaternization is faster than the primary addition. This reaction is not novel but not well known either; it has been reported only by Meerwein and coworkers (51), who found that pyridine-boron trifluoride, for instance, adds ethylene oxide to give $C_5H_5\overset{+}{N}CH_2CH_2O\overset{-}{B}F_3$, a betaine-type structure. It is also their work that suggested the attempts at precipitation with mercuric iodide. The evidence for quaternization in this case is (a) cessation of reaction with further ethylene oxide occurs after not <u>one</u> but <u>two</u> moles of ethylene oxide have been added per mole of boron trifluoride, (b) the boron trifluoride is so thoroughly complexed after reaction that addition of sodium carbonate produces little reaction. This surprising behavior is not that of amine-boron trifluoride complexes, which can be destroyed by stronger bases, but it <u>is</u> possible for the oxazoline betaine, in which the boron trifluoride is bonded through oxygen. $H(HOBF_3)$ and $H(ROBF_3)$ are strong acids, and do not have the boron-oxygen bond broken by neutralization. In other words, $C_5H_5\overset{+}{N}CH_2CH_2O\overset{-}{B}F_3$ and the corresponding oxazoline betaine are, like betaine itself, not convertible to the tertiary amine by treatment with inorganic alkali or an organic base. Betaine does under some circumstances decompose to give trimethylamine; similarly, as reported above, the betaine formed does occasionally give some free oxazoline, but not reproducibly and not in quantity.

The desired reaction might be achieved under the influence of acid catalysts other than boron trifluoride. The single trial of anhydrous hydrogen chloride as a catalyst at ice temperatures does not rule out the possibility of its use at a higher temperature.

Similarly there is a possibility of success in the vapor phase under the influence of a mildly acidic catalyst.

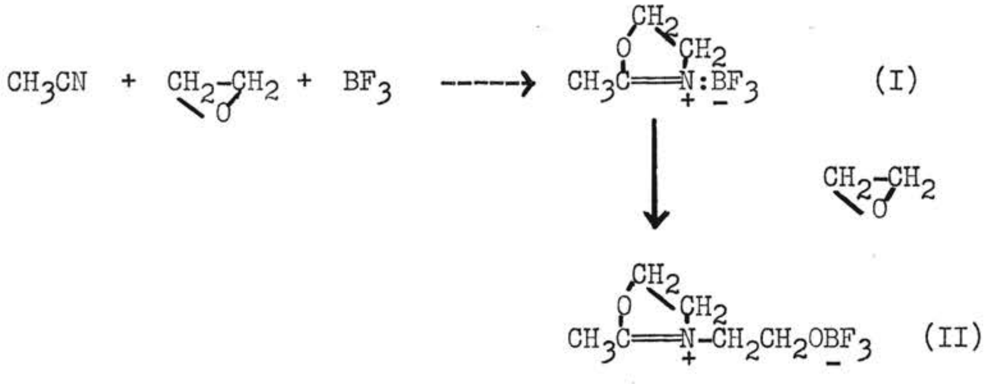
SUMMARY

No reaction could be produced between ketene and ethylene oxide under a variety of conditions. The reaction failed in dioxane with or without an acid catalyst, in ether with boron trifluoride catalyst, without solvent in liquid phase with sulphuric acid, and in vapor phase over silica gel or alumina, plain or acidized. Various products of polymerization or rearrangement of one or the other reagent were identified.

The acid-catalyzed reaction of ethyl acetate, tried as a typical ester, and ethylene oxide gave none of the desired adduct, 2-ethoxyethyl acetate. Only ethylene glycol diacetate and polymers of ethylene oxide were characterized as products.

Single experiments on adding n-butyl nitrite, n-butyl borate and ethyl orthoacetate to ethylene oxide were inconclusive.

The boron trifluoride-catalyzed addition of acetonitrile to ethylene oxide goes vigorously and apparently in high yield, but the quaternary betaine-type salt formed (II) will neither crystallize, yield crystalline derivatives, nor decompose readily and regularly to give the desired oxazoline.



Up to 10% of 2-methyl-1,3-oxazoline, the free base corresponding to (I), was obtained on occasion but not reproducibly. Evidence for the formation of (II) is entirely circumstantial but believed sound.

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