solid potassium hydroxide (50 g.) added over a 30-min. period so that the temperature did not rise above 70°. Formaldehyde (15 ml. of 40% solution) was added and the temperature maintained between 75° and 85° for 3.5 hr., an additional 10 ml. of formaldehyde being added at the end of the first hour. The reaction mixture was acidified, and the white solid which formed was collected on a filter and washed with sodium bicarbonate solution, yielding 9.4 g. (77.6% yield) of crude 1,8-naphthalide melting at 129–148°. Recrystallization (charcoal treatment) from an ethyl acetate–petroleum ether (b.p. 60–71°) mixture yielded 5.7 g. (47% yield) melting at 155–157°. This is the same melting point reported by Fuson and Munn.[9]

The infrared spectrum showed a lactone carbonyl band at 5.8 μ and a C—O—C band at 9.2 μ.

1,8-Naphthalenedialdehyde (VIII). A slurry of III (5.0 g.) with 50 ml. of methanol was treated with 10 g. of potassium iodide and 10 ml. of glacial acetic acid. An exothermic reaction liberating iodine occurred. After 1 hr., the iodine was reduced with 10% sodium thiosulfate solution and the solvent evaporated in an air blast. An oil (4.1 g.) separated, which did not crystallize on standing overnight. The oil gave a positive test with 2,4-dinitrophenylhydrazine, and its infrared spectrum showed the presence of OH and carbonyl groups. Criegee[11] reports that the dialdehyde exists as a monohydrate, which would explain the presence of the OH band. One gram of the oil was allowed to react with 2.6 g. of *p*-nitrophenylhydrazine in ethanol containing a few drops of glacial acetic acid. Filtration yielded 0.9 g. (39% yield) of the bis(*p*-nitrophenylhydrazone) as red needles which melted at 227° dec. Criegee reports a melting point of 229° for this derivative.[11]

Anal. Calcd. for $C_{24}H_{18}N_6O_4$: C, 63.40; H, 3.97; N, 18.53. Found: C, 62.90; H, 4.15; N, 18.40.

Ozonolysis in t-butyl alcohol. Ten grams of acenaphthylene dissolved in 100 ml. of *t*-butyl alcohol was treated with 3.6 g. of ozone as described previously. After flushing with dry oxygen, a portion of the solution was frozen in a Dry Ice–acetone bath and the *t*-butyl alcohol removed by lyophilization for 5 hr. at 0.1 mm. while maintaining the sample at −30°. A sample of the white sticky solid was analyzed immediately for *t*-butoxy content.

Anal. Calcd. for $C_{16}H_{18}O_4$: *t*-butoxy, 26.0. Found: 13.6.

The infrared spectrum of the unstable solid showed a broad OH band at 2.8–3.0 μ and a carbonyl band at 5.8 μ.

Titration of an aliquot of the *t*-butyl alcohol solution showed 60 mmoles of active oxygen, which is 92% of the theoretical value of 66. The solution gave a positive carbonyl test with 2,4-dinitrophenylhydrazine reagent, a positive hydroperoxide test with lead tetraacetate, and a negative test for hydrogen peroxide with titanium^{III} chloride.

The remainder of the *t*-butyl alcohol solution was steam-distilled to remove the alcohol, yielding 11.3 g. of a yellow oil which solidified. By extraction with benzene, 6.4 g. of 1,8-naphthaldehydic acid IV melting at 161–165° was obtained.

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PITTSBURGH 13, PA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WYOMING]

Formation of Phenols in the Reductive Ozonolysis of Aryl Allyl Ethers. Product Analysis with Gas-Liquid Chromatography[1]

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The reductive ozonolysis of a series of *para*-substituted aryl allyl ethers has been found to proceed essentially normally to give more than 75% yield of the corresponding 2-phenoxyethanol. The small amount of phenolic product, estimated from gas chromatograms, is largely due to alkaline cleavage of the ether bond during the reduction procedure. Similar experiments with crotyl phenyl ether have resulted in no significant quantity of phenolic product. These results stand in contrast with some abnormal ozonolyses of allylic compounds in the literature.

Abnormal or unexpected products from the ozonolysis of allylic compounds in nonhydroxylic solvents have been noted by a number of investigators.[3] In the studies with a variety of allylic structures Young[4] and his collaborators reported, in addition to the expected acetic acid, 15% of formic acid obtained in the ozonization and subsequent oxidation of crotyl phenyl ether. A similar treatment of crotyl *p*-nitrophenyl ether yielded 8% of formic acid. The formation of this product, found in the analysis for volatile acids, has been explained in terms of the hydrolytic cleavage of an abnormal or rearranged ozonide resulting from the influence of unshared electron pairs on an electro-negative atom joined to the allylic system. Comparable results[5] were obtained in our laboratories in experiments with oxidative ozonolysis of other aryl allyl ethers which yielded an unexpected phenolic substance. The products isolated from the ozonization-oxidation treatment of allyl (I) and γ-ethylallyl (II) ethers of methyl *o*-cresotinate were *o*-cresotinic acid (IV) as well as the expected 2-carboxy-6-methylphenoxyacetic acid (III). Since a test of the effect of the acidic and alkaline conditions accompanying the oxidation and hydrolysis steps showed that they were responsible for no

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(1) Much of the work reported here was presented at the Ozone Symposium, Division of Organic Chemistry, American Chemical Society, September 1959, Atlantic City, N. J.

(2) Research Corporation Fellow, 1957–58.

(3) P. S. Bailey, *Chem. Revs.*, **58**, 925 (1958).

(4) W. G. Young, A. C. McKinnis, I. D. Webb, and J. D. Roberts, *J. Am. Chem. Soc.*, **68**, 293 (1946).

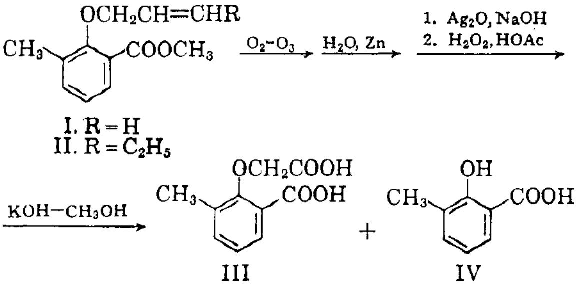
(5) S. J. Rhoads, R. Raulins, and R. D. Reynolds, *J. Am. Chem. Soc.*, **76**, 3456 (1954).

TABLE I

RESULTS OF REDUCTIVE OZONOLYSIS EXPERIMENTS

Ether	Yield[a] from Ozonolysis, %	Composition of Product Mixture[b]		Phenol[d] due to $LiAlH_4$, %
		2-Phenoxyethanol,[c] %	Phenol,[c] %	
$C_6H_5OCH_2CH{=}CH_2$	88	93.9	4.4	2.3
p-$CH_3C_6H_4OCH_2CH{=}CH_2$	77	95.1	4.1	1.5
p-$CH_3OC_6H_4OCH_2CH{=}CH_2$	89	97.2	2.2	1.5
p-$ClC_6H_4OCH_2CH{=}CH_2$	76	94.1	3.6	1.6
$C_6H_5OCH_2CH{=}CHCH_3$	80	91.9	6.6	2.3

[a] % theory, based on the normal product, 2-phenoxyethanol. [b] This is the crude product mixture from O_2—O_3 treatment, followed by lithium aluminum hydride. [c] Weight per cents were calculated from peak areas in chromatograms. They are average values for duplicate runs. [d] Due to treatment of pure 2-phenoxyethanol samples with lithium aluminum hydride under simulated reaction conditions.



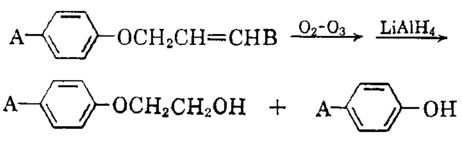
I. R = H
II. R = C_2H_5

III

IV

more than 5% of the o-cresotinic acid formed, 8–30% of phenolic product was attributed to some abnormality in the ozonizations. This may be explained in terms of either the abnormal ozonide of Young[4] or a rearrangement of the now widely accepted zwitterion intermediate of Criegee.[6] The reaction which frees a methylene carbon atom as formic acid will also produce a phenolic product. These studies have been directed to the phenolic product as an index to abnormality in ozonization.

This investigation was initiated for the purpose of determining the effect of a selected series of substituents on the course of the ozonization of aryl allyl ethers in nonhydroxylic solvents. The results from the analysis of the nonvolatile products of the reductive cleavage of the ozonization intermediates were used as a measure of the abnormal ozone attack.



A = H, CH_3, OCH_3, Cl when B = H
A = H when B = CH_3

The sensitivity of the ether bond to both the acidic and alkaline conditions required in the oxidative workup procedures dictated the choice of a reductive procedure for these studies. It was hoped that an adaptation of the Greenwood[7] method of cleavage of the peroxidic intermediates with lithium aluminum hydride would prove sufficiently mild, though alkaline, that the ether bonds would be left intact. The product analysis then consisted of the determination of a mixture of a phenol and a 2-phenoxyethanol.

Gas chromatographic analysis[8] was applied to the crude product mixtures. Plots of sample weight vs. peak area (in mm.^{2}) made from chromatograms for a series of weighed mixtures of authentic samples of each phenol-alcohol pair showed a linear relationship which permitted the use of peak areas as a direct measure of weight composition of the ozonolysis product mixtures. The accuracy of the method within the weight ranges concerned was ±1 weight per cent.

Ozonization reactions were carried out on five-mmole samples of allylic ethers whose chromatograms indicated that they were completely phenol-free. The hexane solutions of peroxidic materials were reduced immediately by the addition of twenty mmoles of lithium aluminum hydride in ether. Following the hydrolysis of the lithium aluminum salts the organic products were extracted into an ether-hexane layer and dried. Removal of solvents with a rotary evaporator left a crude product ready for GLC analysis. Samples of this mixture, dissolved in benzene, were injected into the Vapor Fractometer.[9]

Mild reduction conditions and inverse addition of reducing agent were used to minimize any possible alkaline cleavage of the ether bonds of the peroxidic intermediates. However, a 300% excess of lithium aluminum hydride was required to complete the reduction of all of the ozonization products present as shown by extra peaks in the

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(6) R. Criegee, *Record Chem. Progr.* (*Kresge-Hooker Sci. Lib.*), **18**, 111 (1957).

(7) F. L. Greenwood, *J. Org. Chem.*, **20**, 803 (1955).

(8) Preliminary investigations with allyl phenyl ether led to the estimation that an abnormal attack of ozone might lead to the formation of as little as 5% by weight of phenol in the product mixture. This necessitated the development of a quantitative method for estimating phenolic material in this concentration in the presence of large amounts of the corresponding 2-phenoxyethanol. Analyses of infrared and ultraviolet spectra of these mixtures were found to be unsatisfactory for such quantitative estimates. However, the method of gas-liquid chromatography was applicable.

(9) Perkin-Elmer Model 154C. See Experimental for details.

chromatograms and positive sodium iodide tests obtained with samples in which a smaller amount of the reducing agent was employed. To test the stability of the ether bond to this excess of lithium aluminum hydride, phenol-free samples of the 2-phenoxyethanols were dissolved in ether and hexane and subjected to the same excess lithium aluminum hydride treatment as the ozonization products received.

Table I shows the results of the experiments with five allylic ethers. The percentages of phenolic product are all small and of the same order of magnitude. In the last column are results from the treatment of the 2-phenoxyethanols with lithium aluminum hydride. Recoveries of the alcohols were practically quantitative. However, in all cases, although the chromatograms of the starting materials had shown only a single peak for the alcohol, the product chromatograms included, in addition, a small peak for the phenol due to the lithium aluminum hydride action on the ether bond. Since prolonged treatment of 2-phenoxyethanol with 2*N* sulfuric acid yielded no phenol due to acid cleavage of the ether bond, the phenol percentages in this last column are a measure of the amounts which can be attributed to the reduction conditions following the ozonizations.

A completely rigorous treatment necessitated establishing that the ether bond of the first formed ozonization intermediate was not cleaved by lithium aluminum hydride. In the light of the Criegee[6] mechanism for ozonization, phenoxyacetaldehyde seemed a likely intermediate. A pure sample of this compound was prepared and subjected to lithium aluminum hydride reduction. Table II compares the percentages of phenolic product obtained in the procedures studied. Phenol was obtained in an amount equal to that observed in lithium aluminum hydride cleavage of 2-phenoxyethanol. This fact suggests strongly that the ether bond of this first aldehydic ozonization product is not rapidly cleaved under these reduction conditions but rather that the phenoxyacetaldehyde undergoes the expected immediate reduction to 2-phenoxyethanol which then suffers the same ether bond cleavage as was observed when it was treated directly with lithium aluminum hydride.

TABLE II

PHENOL AS A PRODUCT FROM OZONIZATION AND REDUCTION REACTIONS

Compound	Treatment	Phenol Obtained, %
$C_6H_5OCH_2CH{=}CH_2$	O_2—O_3, $LiAlH_4$	4.4
$C_6H_5OCH_2CH_2OH$	$LiAlH_4$	2.3
$C_6H_5OCH_2CHO$	$LiAlH_4$	2.4

From the results of these reductive ozonolysis experiments two conclusions may be reached. First, little phenol is formed by an abnormal attack of ozone on the aryl allyl ether molecules studied. The differences between total phenol and that formed by alkaline attack on the ether bond are close to the accuracy of the analytical method, ±1 weight per cent. Even in an inert, nonhydroxylic solvent, then, the ozonization of these allyl aryl ethers is essentially normal.[10] Second, within the series of *para* substituted ethers studied, no effect of the nature of the *para* substituent on the composition of the products formed has been observed.

These results, contrasting with those obtained from the oxidative ozonolysis of similar allylic systems, raise a question concerning the origin of abnormal products (*vide supra*). We feel that the reaction conditions subsequent to the action of ozone may be responsible in some cases for the so-called abnormal products. The very small amount of phenolic material obtained in the product mixtures of this study suggests that sufficiently mild conditions for working up the peroxidic intermediates from ozonization may largely eliminate the substances which have been attributed to abnormal attack.

Comparison of the oxidative ozonolysis results[4,5] with those reported in this study points to the need for a systematic examination of the effects of substituents, both in allylic side chains[11] and in ring positions, on the course of ozonization under a variety of conditions. The investigation is continuing.

EXPERIMENTAL[12]

Preparation and purification of materials. Phenols. Commercially available samples were purified by distillation, carefully protected from moisture. Properties of the fractions used for quantitative studies were as follows: phenol, b.p. 172–173° (592 mm.), m.p. 40.2–40.6°; *p*-cresol, b.p. 192–193° (584 mm.), m.p. 33.9–35.0°; *p*-methoxyphenol, b.p. 232–234° (587 mm.), m.p. 56.2–57.4°; *p*-chlorophenol, b.p. 209–211° (589 mm.), m.p. 42.6–43.7°.

Ethers. The ethers were prepared by the method of Claisen and Eisleb.[13] Their properties were: allyl phenyl ether, b.p. 70–71° (7 mm.), n_D^{20} 1.5217 (lit.[14] b.p. 80–84° at 13 mm., n_D^{20} 1.5218); *p*-cresyl allyl ether, b.p. 80–81° (7 mm.) (lit.[13] b.p. 91° at 12 mm.); *p*-methoxyphenyl allyl ether, b.p. 74–75° (0.2 mm.) (lit.[15] b.p. 70.0–70.5° at 0.1 mm.); *p*-chlorophenyl allyl ether, b.p. 78–79° (2 mm.) (lit.[13] b.p. 106–107° at 12 mm.); crotyl phenyl ether, b.p.

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(10) The absence of abnormal products from ozonizations carried out in methanol has previously been discussed by N. A. Milas and J. T. Nolan, Jr., *Adv. in Chemistry Series*, 21, 136 (1959).

(11) There was a small increase in per cent of phenol in the crotyl phenyl ether result as compared with that of allyl phenyl ether (Table I). Possibly the γ-methyl exerts an influence on the initial ozone attack which is at least as important as that of the ether oxygen.

(12) All melting points are corrected. Ozonizations were carried out using a Welsbach Model T-19 Ozonator.

(13) L. Claisen and O. Eisleb, *Ann.*, 401, 21 (1913).

(14) E. M. Filachione, J. H. Lengel, and W. P. Ratchford, *J. Am. Chem. Soc.*, 72, 840 (1950).

(15) H. L. Goering and R. R. Jacobson, *J. Am. Chem. Soc.*, 80, 3277 (1958).

89–90° (10 mm.) (lit.[4] b.p. 89° at 10 mm.). Each sample was checked by gas chromatography for homogeneity and absence of phenol just prior to ozonization.

Alcohols. 2-Phenoxyethanol, Eastman yellow label, was distilled, b.p. 86–87° at 0.8 mm., n_D^{20} 1.5386. 2-*p*-Cresoxyethanol and 2-(*p*-chlorophenoxy)ethanol were prepared by the method of Powell[16] utilizing sodium salts of the phenols and ethylene chlorohydrin in aqueous solution. Observed properties for these alcohols were: 2-*p*-cresoxyethanol, white crystalline solid, m.p. 45.5–46.2° (lit.[17] m.p. 44–45°); 2-(*p*-chlorophenoxy)ethanol, colorless liquid, b.p. 122–123° at 1.3 mm., *p*-nitrobenzoate, m.p. 89.4–90.6° (lit.[17] m.p. 90–91°). 2-(*p*-Methoxyphenoxy)ethanol was prepared by the method of Bentley, Haworth, and Perkin as described by Dunstan[18] from the sodium salt of *p*-methoxyphenol and ethylene chlorohydrin in absolute ethanol. The shiny, white needles, recrystallized from hexane, melted at 72.1–73.1°, *p*-nitrobenzoate,[19] m.p. 97–98° (lit.[18] m.p. of alcohol, 70°, of *p*-nitrobenzoate, 96°). These alcohols were shown to be free of phenol contaminants by GLC analysis.

Lithium aluminum hydride solutions used in reductive procedures were prepared by refluxing 0.5 g. of lumps (Metal Hydrides, Inc.) with 100 ml. of specially dried reagent grade ether for 10 hr. An assay of this saturated solution showed that it contained 1.26×10^{-1} mmoles/ml. Such solutions were used for all reductions.

Reductive ozonolysis of p-cresyl allyl ether. All ozonolyses were carried out in the following manner. In a gas washing bottle with fritted cylinder was placed a 0.7436-g. (5.02 mmoles) sample of *p*-cresyl allyl ether dissolved in 150 ml. of specially purified hexane (washed with permanganate, sulfuric acid, sodium hydroxide, water, than dried over sodium wire and distilled, b.p. 60–61°/588 mm.). The solution was cooled in an ice-salt bath to −6° and ozonized with an ozone stream which furnished ozone at a concentration of 0.4 mmole/l. of gas. After the addition of 17.7 l.[20] of gas, a stream of nitrogen was bubbled through to remove dissolved oxygen and ozone. The cloudy hexane solution was then transferred quantitatively with dry ether to a three-necked flask fitted with a spiral condenser protected from moisture, a dropping funnel, and a "Vibro-Mixer." To the stirring, cold (0–3°) solution was added, dropwise, 165 ml. of an ether solution containing 20 mmoles of lithium aluminum hydride. After a 45-min. reflux period the mixture was cooled again to 3° and hydrolyzed with ice and 60 ml. of 2*N* sulfuric acid. The organic products were extracted into an ether-hexane layer, filtered through anhydrous sodium sulfate and dried over magnesium sulfate. Removal of solvents with a rotary evaporator left a crude yellow oily product, 77% yield, calculated as 2-*p*-cresoxyethanol. A duplicate run on 1.05 mmoles in a Mini-lab batch reactor assembly[21] gave checking results.

Gas chromatography. A Perkin-Elmer, Model 154C Vapor Fractometer was used. A two meter "C" column packed with a dimethylsiloxane polymer adsorbed on Celite afforded practical separations of components into symmetrical, cleanly resolved peaks for the ethers, phenols, and alcohols studied. Preliminary investigations with pure authentic samples of the phenols and alcohols and mixtures thereof resulted in the selection of optimum cabinet temperatures, 171–206°, and helium flowrates, 69–72 ml./min. for the analyses.

Carefully weighed authentic mixtures of phenols and alcohols were dissolved in benzene in small volumetric flasks. Hamilton microliter syringes were used to measure the volumes (3–30 µl.) injected into the vapor fractometer. The ratios of paper areas (mm.^{2}) for phenolic to alcoholic product were found to check closely with the ratios of sample weights in the solutions chromatographed. Plots of sample weights *versus* paper areas (in mm.^{2}) gave straight lines, indicating that the paper areas could be used as a direct measure of the weight composition of a mixture. Repetition of procedures showed that the accuracy of the method was within ± one weight per cent.

The crude ozonolysis product mixtures were dissolved in benzene. Samples of sizes 3 µl. to 20 µl. were used, depending upon the solubility and concentration of components and the need for maximum response to the small amounts of phenols present. The chromatograms showed peaks for solvent benzene, phenol, phenoxyethanol, and less than 2% of unidentified impurity.

Stability of ether bond to reduction and hydrolysis conditions. One mmole of 2-(*p*-methoxyphenoxy)ethanol (phenol-free) was dissolved in 100 ml. of hexane and 30 ml. of ether in a three-necked flask fitted with a dropping funnel, spiral condenser protected from moisture and a "Vibro-Mixer." To the stirring, cold (−5°) solution 12 ml. of lithium aluminum hydride solution was added dropwise. After some additional stirring the solution was allowed to warm to room temperature and then refluxed for 15 min. The cloudy mixture was again cooled and treated cautiously with bits of ice until hydrogen evolution was essentially complete. Then 10 ml. of 2*N* sulfuric acid was added and the usual separation, extraction, and drying procedures followed. Removal of solvent by means of a rotary evaporator left 0.160 g. of white solid, 95% recovery. The chromatogram of a 20 µl. sample of this solid in benzene solution showed two peaks whose retention times and areas indicated 98.5% of 2-(*p*-methoxyphenoxy)ethanol and 1.5% of *p*-methoxyphenol.

Similar treatments of the other phenoxyethanols with lithium aluminum hydride resulted in better than 92% recovery of starting material which included the small percentage of phenolic cleavage product reported in the last column of Table I.

One mmole of 2-(*p*-methoxyphenoxy)ethanol dissolved in ether, was allowed to stand in the cold with 13 ml. of 2*N* sulfuric acid for an hour with intermittent shaking. Following the standard separation, extraction, drying, and solvent removal procedure, the solid which remained showed a chromatogram with a single peak for the alcohol. No *p*-methoxyphenol was detected in this tracing.

Phenoxyacetaldehyde was prepared by the lead tetraacetate oxidation[22] of α-glyceryl phenyl ether (3-phenoxy-1,2-propanediol).[23] Every precaution was taken to remove moisture from all reagents and to exclude it during the course of the reaction. To a 500-ml. three-necked flask fitted with a stirrer, dropping funnel protected from moisture, and a thermometer was added 8.86 g. (0.02 m.) of recrystallized lead tetraacetate (Arapahoe Chemicals, Inc.) and 150 ml. of dried benzene. Temperature inside the flask was maintained below 15° with an ice-water–salt bath during the dropwise addition of a benzene solution of 3.36 g. (0.02 mole) of dried α-glyceryl phenyl ether. The mixture was stirred for 2 hr. while the temperature was maintained at

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(16) S. J. Powell, *J. Am. Chem. Soc.*, **45**, 2708 (1923).

(17) D. R. Boyd and E. R. Marle, *J. Chem. Soc.*, **105**, 2117 (1914).

(18) W. J. Dunstan, *J. Chem. Soc.*, 755 (1946).

(19) Prepared by the method described in R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, 1956, p. 212.

(20) The quantity of ozone was calculated to include that required to saturate the solvent plus 10% over the theoretical amount for one double bond. Preliminary studies had shown that less than this amount resulted in the presence of unchanged ether in the product mixture.

(21) Ace Glass Incorporated, Vineland, N. J.

(22) L. F. Hatch and S. S. Nesbitt, *J. Am. Chem. Soc.*, **67**, 39 (1945).

(23) The method of *Organic Syntheses* was used for preparing the ether from glycerol α-chlorohydrin and sodium phenoxide in absolute ethanol. Use of excess chlorohydrin ensured a product uncontaminated with unchanged phenol as indicated by the gas chromatogram and a negative phosphomolybdic acid test.

15–26°. Lead acetate was removed by filtration and the filtrate was washed thoroughly with water and sodium bicarbonate. After the removal of benzene on the rotary evaporator the remaining liquid was vacuum distilled. A fraction of b.p. 60–63° (1 mm.) was found by gas chromatographic analysis to be phenol-free.

A 0.162-g. sample of this phenoxyacetaldehyde was dissolved in 35 ml. of specially dried ether and reduced with a fourfold excess of lithium aluminum hydride in the Minilab reactor. The chromatogram of the benzene solution of the crude product showed 96.8% of 2-phenoxyethanol and 2.4% of phenol and less than 1% of unchanged aldehyde.

Reductive ozonolysis of crotyl phenyl ether. Crotyl phenyl ether was checked for homogeneity by gas chromatography using a two meter Perkin-Elmer "K" column. A single symmetrical peak indicated the absence of phenol or other impurities. A 1.1-mmole sample was dissolved in 25 ml. of dried hexane, cooled to −6°, and ozonized in the Minilab reactor assembly with a 10% excess of ozone. The peroxidic products in hexane were reduced with 400% of the required lithium aluminum hydride solution. Following hydrolysis, extraction, drying, and solvent removal, 0.134 g. (80%) of a pale yellow oil was obtained. Vapor fractometry of this material in benzene solution at a cabinet temperature of 216° on a Perkin-Elmer "K" column gave a fractogram from which weight per cents were determined. The results are recorded in Table I.

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LARAMIE, WYO.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF KANSAS]

Oxidation of 1-(3,4-Dimethoxyphenethyl)-3-ethyl-4-(carboxaldehyde diethylacetal)pyridinium Bromide by Potassium Ferricyanide

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3-Ethylpyridine-4-carboxaldehyde diethylacetal was converted to a quaternary ammonium salt by treatment with 3,4-dimethoxyphenethyl bromide. Oxidation of the salt by potassium ferricyanide in alkaline solution gave approximately equal amounts of 1-(3,4-dimethoxyphenethyl)-4-(carboxaldehyde diethylacetal)-5-ethyl-2-pyridone and 1-(3,4-dimethoxyphenethyl)-3-ethyl-4-(carboxaldehyde diethylacetal)-2-pyridone. The former pyridone was also prepared in an unequivocal manner by oxidation of 1-(3,4-dimethoxyphenethyl)-2-methyl-4-(carboxaldehyde diethylacetal)-5-ethylpyridinium bromide with iodine in pyridine solution and treatment of the resultant product with sodium hydroxide solution.

The subject of the preparation of pyridones by the oxidation of *N*-alkylpyridinium salts with potassium ferricyanide in alkaline solution has been reviewed recently.[1] With respect to the problem of orientation in the oxidation of 1-alkyl-3-substituted pyridinium salts, it has been reported that when the 3-substituent is alkoxycarbonyl,[2] 3-pyridyl,[3,4] *N*-methyl-3-pyrrolidyl,[3,4] 6,7-methylenedioxy-2-quinolyl,[5] 2-methyl-4-thiazolyl,[6] cyano,[7] carboxyl,[7] or phenyl,[8,9] pyridone formation takes place at the 6-position in the major if not the sole reaction path. However, when the 3-substituent is methyl, ethyl, or bromo, pyridone formation occurs at the 2-position exclusively.[7,10,11]

There has been a controversy as to which pyridone is formed on oxidation of nicotinamide methiodide. Some workers have reported that pyridone formation takes place at the 2-position,[7,12] while another has claimed that oxidation occurs at the 6-position.[13] The point has been clarified by Pullman and Colowick, who have shown that nearly equal amounts of the two isomeric pyridones are formed.[14] The claim of predominance of one pyridone over the other in earlier reports was attributed to the previous workers having effected preferential extraction of one or the other of the two possible isomers in the course of the isolation procedure.

Various suggestions have been advanced in an attempt to explain for the whole series of known reactions the preferential formation of one or the

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