

Optical Properties of the Crystals.—The optical properties of the crystals were determined by the immersion method⁷ which has been used successfully by one of the authors in the identification of several types of organic compounds.⁸ The 3,5-dinitrobenzoyl derivatives of the phenols were most satisfactorily studied in solutions of potassium mercuric iodide in glycerol and water, although for rapid determinative work, oily liquids consisting of mixtures of mineral oils, monochloronaphthalene and methylene iodide can be used.

The results obtained are given in Table II. Because of the peculiar cleavage properties of the 3,5-dinitrobenzoyl derivatives of eugenol and isoeugenol the optical properties of the crystals could not be determined with any degree of accuracy and therefore are not included in the table.

Summary

1. A method for the preparation of the 3,5-dinitrobenzoyl derivatives of phenols is described. This method can be conveniently used for the identification of phenols.
2. The melting points and the optical properties of the crystals of the 3,5-dinitrobenzoyl derivatives of several phenols were determined.
3. Methods for the preparation of creosol and of 1-*n*-propyl-3-methoxy-4-hydroxybenzene are given.

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THE REARRANGEMENT OF SATURATED ALKYL PHENYL ETHERS. SYNTHESIS OF ISOPROPYL PHENOL AND CRESOLS¹

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Theoretical Part

In an earlier publication² a report was given on the condensation of olefins with phenols under the influence of concentrated sulfuric acid in the cold. The results obtained differed from those already reported in the literature, ethers being obtained and not the corresponding substituted phenols. It was suggested that the condensation process used by the other authors brought about rearrangement of the ethers first formed.

⁷ Wilson and Keenan, *J. Assoc. Official Agr. Chem.*, **13**, 389 (1930).

⁸ Keenan, *J. Biol. Chem.*, **62**, 163 (1924); *J. Wash. Acad. Sci.*, **16**, 433 (1926); Keenan and Weisberg, *J. Phys. Chem.*, **33**, 791 (1929).

¹ Constructed from the second half of the thesis presented by Samuel Natelson to the Faculty of the Graduate School of New York University in candidacy for the degree of Doctor of Philosophy, 1931. Presented at the Indianapolis meeting of the American Chemical Society, April 3, 1931.

² Niederl and Natelson, *THIS JOURNAL*, **53**, 272 (1931).

Koenigs,³ and Schrauth and Quasebarth⁴ used a mixture of sulfuric and acetic acids as condensing agents and obtained the corresponding substituted phenols on warming. This condensation process is close to the one employed by the authors, concentrated sulfuric acid in the cold, yet the results were different.

For the conclusive proof of the reaction mechanism offered in such condensations, it was necessary that it be shown that saturated alkyl phenyl ethers would rearrange under the conditions used by Koenig. In all the ethers obtained (*sec*.-amyl phenyl and cresyl ethers; di-isobutyl phenyl and cresyl ethers) the oxygen is at a secondary or tertiary carbon atom. Since no data on the rearrangement of such types of compounds could be found in the literature, the simplest case, the various isopropyl phenyl and cresyl ethers, was then chosen for study.

There have been numerous cases of rearrangement already reported.⁵

Where the alkyl group is a negative one, mere heat is necessary.⁶ As the alkyl group becomes less and less negative, various reagents, such as zinc chloride and hydrogen chloride, have to be used to effect rearrangement.^{5b,e}

A mixture of concentrated sulfuric and glacial acetic acid should then be an excellent means for rearranging alkyl phenyl ethers. This reagent has the advantage of bringing the whole reaction mixture into homogeneous solution, while at the same time the concentration of the active rearranging agent, sulfuric acid can be reduced to any desired quantity. The ease with which the resultant product may be isolated is apparent, it only being necessary to add water to separate the rearranged product.

From the reactions studied there appears to be very little side reaction, the only product obtained other than the rearranged ether being the original ether itself, which can be again subjected to rearrangement.

The mechanism for this type of rearrangement as offered by Van Alphen involves oxonium formation. Kursanov suggests hydrolysis of the ether to the phenol and the alkyl halide and then recombination with the formation of a substituted phenol. Neither of these authors explains the rearrangement of alkyl ethers in the absence of a rearranging agent. Claisen's mechanism is a special one and requires the presence of the unsaturation in the alkyl residue. From Latimer's considerations,⁷ the

³ Koenigs and Carl, *Ber.*, **24**, 3889 (1891).

⁴ Schrauth and Quasebarth, *ibid.*, **57**, 856 (1924).

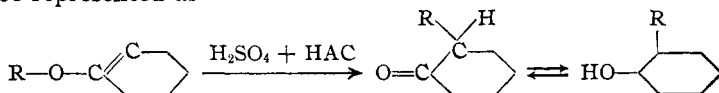
⁵ (a) Claisen, *Ann.*, **237**, 261 (1887); **401**, 21-119 (1914); *Z. angew. Chem.*, **36**, 478-9 (1923); *Ber.*, **58b**, 275-81 (1925); **45**, 3157-66 (1912); (b) Van Alphen, *Rec. trav. chim.*, **46**, 799 (1927); (c) Heller, *Ber.*, **45**, 418 (1912); (d) Bucherer and Grolee, *ibid.*, **39**, 986 (1906); (e) Kursanov, *J. Russ. Phys.-Chem. Soc.*, **48**, 1172-4 (1914); (f) Eijkman, *Chem. Centr.*, **I**, 1597 (1904); **I**, 814 (1905); (g) Smith and Niederl, *THIS JOURNAL*, **53**, 806 (1931).

⁶ Claisen and Godesberg, *Ann.*, **418**, 69-120 (1919).

⁷ Latimer, *THIS JOURNAL*, **51**, 3185 (1929).

substituted phenol structure is a more stable configuration than that of the ether and therefore when placed in a suitable medium or under suitable conditions, readjustment to the more stable configuration should be expected.

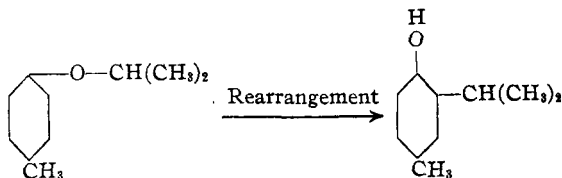
Drawing an analogy from keto-enol tautomerism and rearrangement of vinyl alkyl ethers to the corresponding aldehydes, the series of reactions may be represented as



As mentioned before, the ethers chosen for study were the isopropyl phenyl and cresyl ethers. Some of these ethers and the corresponding phenols obtained after rearrangement had not been previously prepared and had to be characterized.

The complete identification of the substituted phenols formed would involve determination of the position of the alkyl groups introduced. This would permit us to draw conclusions and generalizations which would be of great value in the identification and structure proof of a number of new longer chain phenols obtained by a similar process and to be described later.

The rearrangement of isopropyl *p*-cresyl ether was first studied. The reaction went smoothly and the rearranged phenol was isolated.

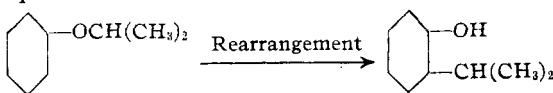


The isopropyl group could migrate to the ortho position only, the para position being occupied and meta rearrangement being rare.

The rearrangement of isopropyl phenyl ether gave rise to a product the main portion of which distilled in the neighborhood of the boiling point of *o*-isopropyl phenol as reported in the literature.⁸

The product obtained on treating this product with bromoacetic acid was identical with that reported in the literature for *o*-isopropylphenoxyacetic acid.⁹

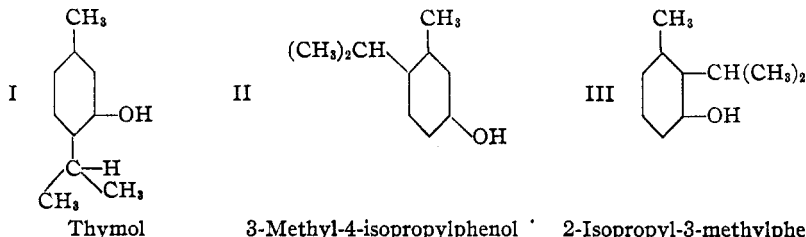
The product therefore appears to be identical with *o*-isopropylphenol and the alkyl group in the ether has apparently migrated ortho to the hydroxyl group



⁸ Spica, *Gazz. chim. ital.*, 9, 442 (1879); *Jahresb.*, 663 (1880).

⁹ Fileti, *Gazz. chim. ital.*, 16, 129 (1886).

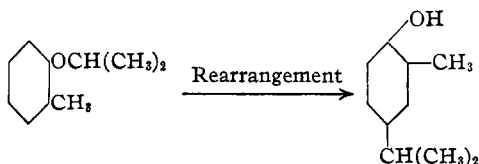
It was expected that by the rearrangement of the isopropyl *m*-cresyl ether, thymol would be obtained. Actually a strong odor of thymol was observed, the total product boiling between 230–240°. From the fraction boiling between 231–235° a derivative with bromoacetic acid was made which melted 4° lower than that of thymol. According to Crum-Brown's rule there are three isomeric products possible upon the introduction of an isopropyl group into *m*-cresol.



Of these only I (thymol) has been identified conclusively. A condensation product furnished by Read¹⁰ was studied and was found to be different from thymol and the rearranged isopropyl *m*-cresyl ether.

Usually upon treatment of an alcohol with phenol in the presence of a condensing agent the alkyl radical enters in a position para to the hydroxyl group.¹¹ Structural Formula II may then be assigned to these types of products. The only possible structure for the substituted phenol obtained from isopropyl *m*-cresyl ether by the rearrangement process mentioned before, would then be Formula I or III, which would be in harmony with the fact observed that whenever the ortho positions are free migration to this place is preferred. Formula III would involve readjustment to a position which should be particularly non-reactive due to such phenomena as steric hindrance. A definite stand as to the position occupied is not being taken until the behavior of this compound is studied further.

The rearrangement of the *o*-cresyl isopropyl ether gave rise to a product which was identified by its physical and chemical properties and by its bromine derivative as *p*-isopropyl-*o*-methylphenol. The compound appears to be identical with that obtained by Kelbe and Spica,¹² the structure of which is given as



¹⁰ (a) Read, Sharp and Dohme, private communication; (b) Mazzara, *Gazz. chim. ital.*, **12**, 505 (1882).

¹¹ Senkowski, *Ber.*, **24**, 2974 (1891); Anschütz and Beckerhoff, *ibid.*, **28**, 407 (1895).

¹² Kelbe, *Ann.*, **210**, 40 (1881); Spica, *Gazz. chim. ital.*, **12**, 552 (1882).

With a methyl group occupying an ortho position, migration para to the hydroxyl group appears to be favored.

Experimental Part

Preparation of Isopropylphenyl and Cresyl Ethers.—One molecular weight of the phenol or cresol was placed in a three-necked flask fitted with a reflux condenser. Fifty-eight grams (excess) of finely powdered potassium hydroxide was added and the whole heated with a low flame, when a homogeneous viscous mass is formed; 125 g. (excess) of isopropyl bromide was then slowly added through a dropping funnel extending below the level of the liquid. Constant warming was necessary to keep the whole mass from solidifying. After all the halide had been added refluxing was continued for two hours more. The mass was allowed to cool and then 500 cc. of water was added to dissolve the separated sodium bromide. A light oil appeared at the top of the liquid. This was removed in a separatory funnel and washed successively with 10% alkali and then twice with water. The separated light yellow oil was dried over calcium chloride and then distilled. One fractionation was sufficient to give a colorless constant boiling oil.

Rearrangement of Isopropylphenyl and Cresyl Ethers.—The rearrangement mixture consists of a solution of 150 cc. of concentrated sulfuric acid in sufficient glacial acetic acid to make up to a liter; 80 cc. of the ether prepared as above was placed in a flask fitted with a reflux condenser and a calcium chloride addition tube; 200 cc. of the rearrangement mixture was added and the whole shaken. Two layers are formed at first, but the mixture becomes homogeneous on warming. The solution was then refluxed gently for five hours. The temperature of the solution on refluxing is constant between 125–130°. The reaction mixture was then allowed to stand overnight. It assumed a deep red color. The whole was transferred to a 500-cc. separatory funnel and 200 cc. of water added. Sufficient solid hydrated sodium carbonate was added to neutralize the sulfuric acid (180 g.). The separatory funnel was then filled with a saturated salt solution. On standing, a heavy viscous oil separated to form the upper layer. The lower layer was allowed to drain off and discarded and the upper layer extracted with 10% potassium hydroxide solution. The alkali-insoluble portion was redistilled to reclaim unchanged ether. The alkali extract was neutralized with cold concentrated hydrochloric acid, ice being thrown in to keep the reaction mixture cool, when a deeply colored oil separated. The mixture was extracted with ether, the ether distilled off and the residue fractionated.

From 72 g. of ether, 39 g. of rearranged alkali-soluble product was obtained, and 16 g. of unchanged ether in the case of *m*-cresyl isopropyl ether. This corresponds to a 54% yield on the basis of the total ether at the outset, or a 70% yield taking into consideration the ether recovered.

Preparation of Isopropylphenoxy- and Cresoxyacetic Acids.—About one gram of the substituted phenol was weighed out carefully on an analytical balance. The exact quantity of 1 *N* potassium hydroxide was added and the whole gently warmed. A slight excess of bromoacetic acid was weighed into a separate flask and carefully neutralized with 1 *N* potassium hydroxide. The two solutions were mixed and then gently boiled for five minutes. Decolorizing charcoal was added and the whole filtered while hot. While still warm the calculated quantity of concentrated hydrochloric acid was added and the mixture allowed to stand. The separated crystalline product was filtered off and recrystallized from hot water.

Isopropylphenyl Ether.¹³—A colorless oil with an odor resembling anise; b. p. 178°, sp. gr. 0.975 (20°), n_D^{20} 1.4992.

¹³ Perkin, *J. Chem. Soc.*, 69, 1187, 1250 (1896).

***o*-Isopropylphenol (2-Oxy-1-isopropylbenzene).**⁸—Colorless oil with phenolic odor, soluble in alkali. Its alcoholic solution gave a deep violet color with ferric chloride solution; b. p. 213–214°, sp. gr. 1.012 (20°), n_D^{20} 1.5315.

***o*-Isopropylphenoxyacetic Acid.**⁹—White needle-like crystals; soluble in hot water; m. p. 130° (uncorr.).

Anal. Calcd. for $C_9H_{12}O$: C, 68.04; H, 7.27; neut. equiv., 194. Found: C, 68.21; H, 7.62; neut. equiv., 200.

Isopropyl *o*-Cresyl Ether.—Light oil with a characteristic aromatic odor; b. p. 192° (uncorr.), sp. gr., 0.953 (20°), n_D^{20} 1.5040.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 80.15; H, 9.39.

6-Oxy-1-methyl-3-isopropylbenzene (2-Methyl-4-isopropylphenol).¹²—Colorless liquid with phenolic odor; b. p. 232–234° (uncorr.), sp. gr. 0.989 (20°), n_D^{20} 1.5178.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 80.29; H, 9.38.

(2-Methyl-4-isopropylphenoxy)-acetic Acid.—Prepared from the above compound by treating it with bromoacetic acid as described above; m. p. 87–88° (uncorr.).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69; neut. equiv., 208. Found: C, 68.97; H, 7.46; neut. equiv., 203.

2,4,5-Tribromo-6-oxy-1-methyl-3-isopropylbenzene.¹⁴—Prepared by treating the 2-methyl-4-isopropylphenol in water with an excess of bromine. Upon recrystallization from alcohol lustrous, golden-yellow plates were obtained; m. p. 223° (uncorr.).

Isopropyl *m*-Cresyl Ether.—Faint pleasant aromatic odor; b. p. 195°, sp. gr. 0.931 (20°), n_D^{20} 1.4959.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 80.32; H, 8.95.

(3 - Oxy - 1 - methyl - *x* - isopropylbenzene), 3 - Methyl - *x* - isopropylphenol.—Odor strongly resembles that of thymol, alkali soluble. Its alcoholic solution was colored a deep lavender by ferric chloride solution; b. p. 230–235°, sp. gr. 0.994 (20°), n_D^{20} 1.5280.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 79.84; H, 9.39.

***x*-Isopropyl-*m*-cresoxyacetic Acid.**—Prepared from the above compound; small white crystals soluble in hot water; m. p. 141° (uncorr.).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69; neut. equiv., 208. Found: C, 69.43; H, 7.85; neut. equiv., 213.

***y*-Isopropyl-*m*-cresoxyacetic Acid (3-Methyl-*y*-isopropylphenoxyacetic Acid).**—This compound was prepared from a condensation product (b. p. 95–110° (4 mm.)),^{10a} m. p. 125–126° (uncorr.).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69; neut. equiv., 208. Found: C, 69.75; H, 7.36; neut. equiv., 209.

Isopropyl *p*-Cresyl Ether.—Strong disagreeable odor with a trace of anise; b. p. 195° (84°, 12 mm.), sp. gr. 0.927 (20°), n_D^{20} 1.4952.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 80.10; H, 9.39.

4-Oxy-1-methyl-3-isopropylbenzene (4-Methyl-2-isopropylphenol).—Characteristic odor, rather disagreeable; alkali soluble. Gives rise to a purple color with ferric chloride in alcohol solution. In aqueous solution, a greenish turbidity is obtained with ferric chloride; b. p. 234–237° (uncorr.), sp. gr. 0.989 (20°), n_D^{20} 1.5277.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 79.80; H, 9.36.

(4-Methyl-2-isopropylphenoxy)-acetic Acid.—Long silky needles; soluble in hot water, difficultly soluble in the cold; m. p. 126° (uncorr.).

¹⁴ Jesurun, *Ber.*, 19, 1414 (1886).

Anal. Calcd. for $C_{12}H_{18}O_8$: C, 69.23; H, 7.69; neut. equiv., 208. Found: C, 69.43; H, 7.53; neut. equiv., 212.

The quantitative determinations were performed microanalytically according to Pregl.¹⁵

Acknowledgment is made here to Mr. Franz K. Silbert of this Laboratory for performing the analyses, and to Mr. Louis Krautmann for his assistance in preparing some of the above mentioned compounds.

Summary

Saturated alkyl phenyl ethers (isopropylphenyl and cresyl ethers) were rearranged to the corresponding substituted phenols by means of a mixture of concentrated sulfuric and glacial acetic acid. Proofs for the probable structure of the products obtained were advanced and a general rule as to the way of migration of the alkyl groups was given.

As the possibility of rearranging even short chain, saturated phenyl ethers has now been demonstrated, a series of related problems such as the rearrangement of some of the more important phenyl ethers of mono and poly functional alkanes are now being investigated.

The physiological properties of the substituted phenols mentioned before are being studied.

NEW YORK, N. Y.

[COMMUNICATION NO. 460 FROM THE KODAK RESEARCH LABORATORIES]

EFFECT OF NEUTRAL SALTS ON THE RATE OF HYDROLYSIS OF CELLULOSE ACETATE IN ACETIC ACID SOLUTIONS¹

BY J. T. FUESS AND C. J. STAUD

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Introduction

The effect of the presence of neutral salts of the alkali metals on the rate of chemical reactions has been the subject of the investigation of several workers in recent years. The published results appear to have been concerned mostly with crystalloids. L. E. Bowe² has investigated the effect of sodium chloride and sodium bromide on the rate of saponification of ethyl acetate by hydrochloric acid. Grube and Schmid³ studied the hydrolysis of cyanamide to urea by nitric acid in the presence of nitrates, and the saponification of ethyl acetate by hydrochloric acid in the presence of alkali and alkaline earth chlorides. Hawkins⁴ worked on the

¹⁵ Pregl, "Quantitative Organic Micro Analysis," Blakiston's Sons, Philadelphia, 1930.

¹ Study carried out under the direction of H. LeB. Gray, Superintendent of the Organic Research Laboratory.

² Bowe, *J. Phys. Chem.*, **31**, 298 (1927).

³ H. Grube and G. Schmid, *Z. physik. Chem.*, **119**, 19 (1926).

⁴ J. E. Hawkins, University of Pennsylvania, "Thesis," 1927.