Angelic acid and a crystalline substance, which is probably an unstable sesquiterpene alcohol, were recovered from the saponification products of the balsam. Both are minor constituents.

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Organic Reactions with Boron Fluoride. V. The Rearrangement of Isopropylphenol, *o*-, *m*- and *p*-Cresyl Ethers

BY F. J. SOWA,[1] H. D. HINTON AND J. A. NIEUWLAND

In a previous publication[2] it was shown that the rearrangement of alkyl phenyl ethers could be accomplished by the use of boron fluoride as the rearranging agent and that the position occupied by the migrating group was similar to that of an earlier report.[3]

Later,[4] a procedure was outlined by which propylene could be condensed with phenol, using boron fluoride as a catalyst. It was noted, during the rearrangement of alkyl phenyl ethers, that if the reaction were allowed to take place spontaneously or if the temperature were raised considerably during the reflux process, in the presence of boron fluoride, several higher boiling fractions other than the first rearranged products were isolated. This investigation has been a study of the rearrangement of isopropyl phenyl and cresyl ethers under the conditions just mentioned. The experimental work gives some information that deals directly with the course of condensation and rearrangement of alkyl aryl ethers using boron fluoride as the agent.

Huston and his collaborators[5] investigated the action of benzyl alcohol on *o*-, *m*- and *p*-cresol in the presence of aluminum chloride. They obtained monobenzyl and dibenzyl cresols. Niederl and Natelson[3,6] studied the rearrangement of saturated alkyl phenyl and cresyl ethers but they did not report the isolation of any phenols other than the mono-substituted isopropylphenol or cresols.

If boron fluoride is passed into isopropyl phenyl ether without cooling, the mixture becomes quite warm and then a violent reaction takes place. Among the products of the reaction from 250 g. of the ether are: the phenols, phenol (90 g.), 2-isopropylphenol (34 g.), 2,4-diisopropylphenol

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[1] From the third part of the Dissertation presented by Frank J. Sowa to the Committee on Graduate Study of the University of Notre Dame in partial fulfilment of the requirements for the Degree of Doctor of Philosophy, June, 1933.

[2] Sowa, Hinton and Nieuwland, THIS JOURNAL, **54**, 2019 (1932).

[3] Niederl and Natelson, *ibid.*, **53**, 1928 (1931).

[4] Sowa, Hinton and Nieuwland, *ibid.*, **54**, 3694 (1932).

[5] Huston, *ibid.*, **52**, 4484 (1930); *ibid.*, **53**, 2379 (1931); *ibid.*, **54**, 1506 (1932).

[6] Niederl and Natelson, *ibid.*, **54**, 1063 (1932).

(44 g.) and 2,4,6-triisopropylphenol (28 g.); the ethers, phenyl isopropyl (trace), 2-isopropylphenyl isopropyl (trace), 2,4-diisopropylphenyl isopropyl (32 g.) and 2,4,6-triisopropylphenyl isopropyl ether (12 g.).

When isopropyl *p*-cresyl ether was treated in a manner similar to that of isopropyl phenyl ether, several higher boiling fractions were likewise separated. They are: the phenols, 4-methylphenol, 4-methyl-2-isopropylphenol, 4-methyl-2,6-diisopropylphenol; the ethers, 4-methyl-2-isopropylphenyl isopropyl and 4-methyl-2,6-diisopropylphenyl isopropyl ether.

The following compounds were separated after isopropyl *o*-cresyl ether was rearranged: the phenols, 2-methylphenol, 2-methyl-4-isopropylphenol and 2-methyl-4,6-diisopropylphenol; the ethers, 2-methyl-4-isopropylphenyl and 2-methyl-4,6-diisopropylphenyl isopropyl ether.

By treating isopropyl *m*-cresyl ether under a little milder condition than for the foregoing ethers, the following fractions were obtained:

Fraction	I	II	III	IV	V	VI
B. p., °C.	190–197	198–203	229–235	235–237	237–244	252–262

Fraction (I) was identified as isopropyl *m*-cresyl ether. Fraction (II) was shown to be *m*-cresol. Fractions (III, IV and V) were examined by Niederl and Natelson.[6] They were successful in proving that fraction (III) in their experiment was thymol; that fraction (V) was 3-methyl-4-isopropylphenol and that fraction (IV) was a mixture of fractions (III) and (V). In this investigation the phenoxyacetic acid derivatives of fractions (III) and (V) were identical with thymoxyacetic acid and 3-methyl-4-isopropylphenoxyacetic acid, respectively. After many fractionations, (IV) passed into fractions (III) and (V). It was necessary to prove the structure of fraction (VI). Thymyl isopropyl ether was rearranged by means of boron fluoride. Complete rearrangement took place and only one product was isolated. The latter product was identical with the product in fraction (VI). The isopropyl ether of fraction (V) was rearranged with boron fluoride and again a compound having the same physical properties as the compound in fraction (VI) was obtained. This evidence seems to support fraction (VI) as being 3-methyl-4,6-diisopropylphenol.

By refluxing the rearrangement mixture of *m*-cresyl isopropyl ether for just a little longer time than in the above experiment, one additional compound is formed; namely, 3-methyl-4,6-diisopropylphenyl isopropyl ether and none of the original ether was reclaimed. When 3-methyl-4,6-diisopropylphenol was treated by the reaction of Williamson,[7] an ether was obtained which was identical with the above mentioned compound. Meyer and Bernhauer[8] treated *m*-cresol with isopropyl alcohol in the presence of sulfuric acid and reported that the products obtained boiled between 210–260°. They reported only one compound, 3-methyl-4-

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(7) Williamson, *J. Chem. Soc.*, **4**, 106 (1851).

(8) Meyer and Bernhauer, *Monatsh.*, **53** and **54**, 737 (1929).

isopropylphenol. It is believed that the higher boiling fractions likely contained some of the products isolated in this investigation.

The rearrangement of isopropyl phenyl ether may be visualized as taking place through a series of migration reactions. For example, in the formation of 2,4,6-triisopropylphenyl isopropyl ether by the rearrangement of isopropyl phenyl ether, the process may consist of a series of inter- and intra-molecular reactions in which the isopropyl group is transferred from oxygen to oxygen or from oxygen to carbon. Since all of the compounds that would appear in such a series of reactions have been isolated in a greater or smaller quantity, this series is undoubtedly almost a true representation of one course that this rearrangement may take. The 2,4-diisopropylphenyl isopropyl ether may donate its isopropyl group to 2,4,6-triisopropylphenol to form an ether of the latter and then the 2,4-diisopropylphenol formed may receive another isopropyl group from phenyl isopropyl ether.

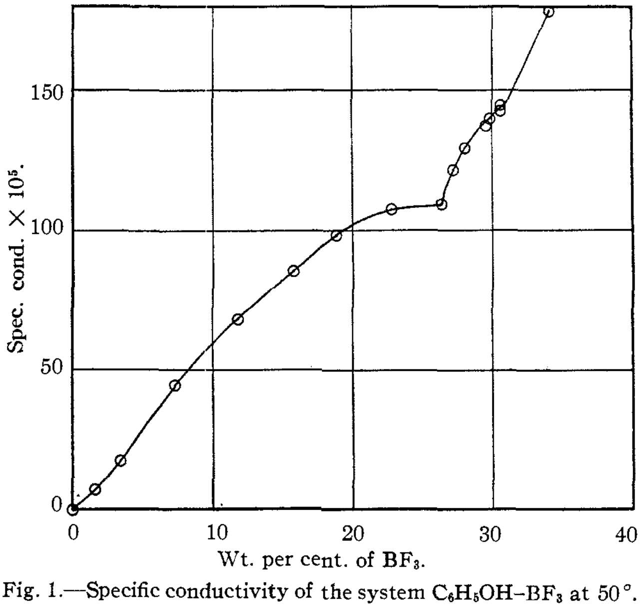

Fig. 1.—Specific conductivity of the system C_6H_5OH–BF_3 at 50°.

The conductivities of the system phenol–boron fluoride were determined. Figure 1 is the curve representing these conductivities. An examination of this curve makes it obvious that by the addition of boron fluoride to phenol the specific conductivity of phenol rapidly increases. At 26.5% boron fluoride, the specific conductivity increases at even a greater rate than at first. This increase is indicative of compound formation. Twenty-six and one-half per cent. by weight of boron fluoride corresponds exactly to one mole of boron fluoride and to two moles of phenol. Gasselin[9]

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(9) Gasselin, *Ann. chim. phys.*, [7] **3**, 67 (1894).

observed that one mole of boron fluoride was absorbed by two moles of phenol.

Various acids absorb unsaturated hydrocarbons to form addition compounds. Likewise, the acid formed by the addition of boron fluoride to phenol adds propylene[4] to form isopropyl phenyl ethers. This represents one course of the condensation with subsequent rearrangement. For these reactions the reader is referred to an earlier[4] article. This does not, however, eliminate one other possibility, namely, the direct nuclear condensation of the olefin hydrocarbon with the alkyl phenyl ether.

Anisole could not be rearranged under the conditions ordinarily employed in these reactions. It was thought that if propylene could be condensed with anisole in the presence of boron fluoride, then in the formation of substituted phenyl ethers the rearrangement of the ether would not necessarily be an intermediate step. Since propylene could be condensed readily with anisole in the presence of boron fluoride with the isolation of 2-isopropylphenyl methyl ether and higher condensation products, it was concluded that direct nuclear condensation is very likely. The 2,4,6-triisopropylphenyl isopropyl ether, like anisole, under similar conditions, was unaffected by boron fluoride. However, in the presence of phenol and boron fluoride, it readily releases its isopropyl group, attached to the oxygen, to the phenol present. A small amount of phenol with some of the original ether and all of the possible phenols and ethers up to and including 2,4,6-triisopropylphenol, were isolated.

The next question to arise was the transfer of an alkyl group from one benzene nucleus to a second benzene molecule. A mixture of 2,4,6-triisopropylphenol, boron fluoride and phenol was heated for a short time. About one-half of the phenol and substituted phenol originally used was recovered. The 2-isopropylphenol and the 2,4-diisopropylphenol were isolated but no ethers were detected. Landolph[10] treated anethole with boron fluoride and removed the propenyl group. He identified anisole as one product and isolated two other compounds each having a higher percentage of carbon than anethole.

One mole of boron fluoride is absorbed by one mole of an alkyl phenyl ether to form a definite compound.[11] It is this compound that rearranges to form a substituted phenol.

Niederl and Natelson[12] isolated phenyl ethers as intermediates in the preparation of substituted phenols and proposed that the ether formation was a necessary step in the addition of unsaturated hydrocarbons to phenols. Some of the results in this article seem to indicate that this may be true in a number of cases but is not necessarily always the case. However, our work is not conclusive on this point.

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(10) Landolph, *Compt. rend.*, **86**, 602 (1878).

(11) Meerwein and Maier-Hüser, *J. prakt. Chem.*, **134**, 51–81 (1932).

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

The ethers 2-isopropylphenyl, 2,4-diisopropylphenyl and 2,4,6-triisopropylphenyl isopropyl ethers may be prepared by direct nuclear condensation with propylene from rearrangements previously[4] outlined. Again, the lower phenols may be built up by the rearrangement of any alkyl phenyl ether.

An inspection of the different lines of approach will make it obvious that there are several methods by which nearly every compound reported here may be synthesized. Nearly every compound reported in this investigation was also prepared by the condensation method with propylene.

Experimental

Preparation of Alkyl Phenyl and Cresyl Ethers.—The preparation of these compounds was accomplished by two different methods, namely, the modified Williamson[7] method and the condensation[4] method with propylene. Only a few minor changes were made in the methods referred to above.

Rearrangement of Alkyl Phenyl and Cresyl Ethers.—The procedure for rearrangements was outlined in a previous article.[2] As followed in this paper, the procedure must be slightly modified. In the modified method, the temperature is allowed to rise

TABLE I

PHYSICAL CONSTANTS OF COMPOUNDS PREPARED

	B. p. °C. 745 mm. (uncorr.)	Sp. gr., 25°	n^{25}_{D}
Isopropyl phenyl ether	178	0.9351	1.4944
2-Isopropylphenol	212–214	.9929	1.5263
2-Isopropylphenyl isopropyl ether	225–227	.9192	1.4948
2,4-Diisopropylphenol	228–230	.9825	1.5224
2,4-Diisopropylphenyl isopropyl ether	248	.9432	1.5095
2,4,6-Triisopropylphenol	249	.9497	1.5118
2,4,6-Triisopropylphenyl isopropyl ether	263	.9132	1.4982
2-Methylphenyl isopropyl ether	191	.9266	1.4943
2-Methyl-4-isopropylphenol	231–235	.9736	1.5204
2-Methyl-4-isopropylphenyl isopropyl ether	241–242	.9233	1.4997
2-Methyl-4,6-diisopropylphenol	253–256	.9477	1.5123
2-Methyl-4,6-diisopropylphenyl isopropyl ether	257–259	.9313	1.5058
4-Methylphenyl isopropyl ether	197	.9228	1.4933
4-Methyl-2-isopropylphenol	233–236	.9741	1.5224
4-Methyl-2-isopropylphenyl isopropyl ether	241–243	.9228	1.5002
4-Methyl-2,6-diisopropylphenol	249–250	.9661	1.5193
4-Methyl-2,6-diisopropylphenyl isopropyl ether	257–259	.9461	1.5137
3-Methylphenyl isopropyl ether	197	.9232	1.4940
3-Methyl-6-isopropylphenyl isopropyl ether	233	.9056	1.4913
3-Methyl-4,6-isopropylphenol	261	.9445	1.5135
3-Methyl-4,6-diisopropylphenyl isopropyl ether	262	.9460	1.5127
Methyl phenyl ether (anisole)	154	.9884	1.5150
2-Isopropylphenyl methyl ether	200	.9475	1.5047
	M. p. uncorr., °C.		
3-Methyl-6-isopropylphenoxyacetic acid	145		
3-Methyl-4-isopropylphenoxyacetic acid	126		
m-Cresyl benzoate	55		

with the addition of boron fluoride and in nearly every case a spontaneous reaction took place which marked the end of the rearrangement. If the rearrangement was incomplete after the addition of boron fluoride, the mixture was refluxed from one-half to three-quarters of an hour. The purification was the same except that 15% potassium hydroxide was used.

Preparation of Phenoxyacetic Acid Derivative.—This preparation was described by Koelsch.[13] He used an alkaline solution and chloroacetic acid, then extracted the phenoxyacetic acid derivative with ether. During this work the ether extraction was eliminated, since it seemed to be unnecessary for the compounds prepared.

Conductivity Measurements.—The usual Kohlrausch assembly was used for conductivity measurements. The phenol had a specific conductivity of 72.30×10^{-8}.

Summary

The synthesis of the possible substituted phenols and phenyl alkyl ethers up to and including the trialkylphenyl isopropyl ethers has been accomplished by the rearrangement of the isopropyl phenyl or cresyl ether and by the condensation of propylene with phenol or cresol.

Intra- and inter-molecular rearrangements have been shown to take place in the same reaction.

The direct nuclear condensation of propylene with alkyl phenyl ethers has been shown experimentally to be a probable step in condensation reactions.

The conductivities for the system phenol–boron fluoride have been determined.

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[13] Koelsch, THIS JOURNAL, **53**, 304 (1931).

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The *p*-Xylylmethylpyrazolones and Some Derivatives

BY RALPH C. HUSTON, HAROLD M. SELL AND HARLOW R. BRIGHAM

In a study of the *p*-xylylpyrazolones, the compounds listed in the table have been prepared from *p*-xylylhydrazine and its acetyl derivative.

The hydrazine was prepared in 68% yield by the method of Demonbreun and Kremer,[1] so modified that exact molecular quantities of reagents were used and the temperature was not allowed to rise above −5° during either the diazotization or the reduction. It boiled at 120° (4 mm.) and melted[2] at 76–77°.

Acylation of the hydrazine was accomplished by refluxing with glacial acetic acid. When recrystallized from water, N′-acetyl-N-(2,5-dimethylphenyl)-hydrazine melted[3] at 104–106°.

Condensation of *p*-xylylhydrazine with ethyl acetoacetate gave 1-*p*-

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[1] Demonbreun and Kremer, *J. Am. Pharm. Assn.*, **12**, 589 (1923).

[2] Willgerodt and Lindenberg, *J. prakt. Chem.*, [2] **71**, 389 (1905).

[3] Willgerodt and Lindenberg, *ibid.*, [2] **71**, 408 (1905), give 196° as the melting point.