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OXIDATION OF PHENOLS
BY TETRAVALENT CERIUM

by

Walter Rogers Spencer

A Dissertation Submitted to the
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Major Subject: Analytical Chemistry

Approved:

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In Charge of Major Work

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Head of Major Department

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Dean of Graduate College

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TABLE OF CONTENTS

Page

INTRODUCTION

History

All compounds in which there is direct bonding of hydroxyl to aromatic nucleus, are grouped in a chemical class and known as phenols. Discovery of phenolic individuals, however, preceded by many years any understanding of their structural relationship.

Pyrogallol, obtained by Scheele in 1786, was the first phenol to be described, and owes its surprisingly early recording to the fact that it arises from the heating of gallic acid, a natural plant substance. Since the observations of Scheele, every one of the twelve hydroxybenzenes, except the pentahydroxy compound, has been satisfactorily described, together with a multitude of phenols containing non-hydroxy substituents.

It was not until 1834 that Runge (1) encountered the prototype of the class. Investigating the more volatile fractions of coal tar, he discovered phenol itself and the three nitrogenous bases, pyrrole, analine and quinoline besides. The name, carbolic acid, which he proposed for the phenol, is still used in pharmacy. Runge also recorded the important observations that phenol has denaturing effect on proteins and the power to prevent or check decay, but he was mistaken in believing that his carbolic acid was pure.

Seven years later, Laurent (2) succeeded in preparing crystalline phenol from coal gas oil. He analyzed the substance, and, believing it to contain water, assigned the formula, $C_{12}H_{10}O \cdot H_2O$, and a name, phenyl hydrate. Also published was his opinion that Runge's carbolic acid might be impure phenyl hydrate.

The structural nature of phenols became quickly deduced following the general acceptance of Kekule's formula for benzene, and the fact demonstrated by Hunt in 1849 that phenol arises from that parent compound.

Preparation

Phenol was not an article of commerce until after 1867, when Wurtz (3) discovered that aromatic sulfonates, however resistant they might be to aqueous alkali, could still be converted to phenolates by fusion with potassium hydroxide. Thanks to improved methods, a vast amount of phenol is now recovered directly from coal tar, but the demand for phenol has increased so greatly that chemical production of it from benzene is also employed on a large scale.

Besides the important sulphonic acid process, there are newer methods in which aryl halide intermediates are hydrolyzed by aqueous alkali (4). With most halides, and particularly chlorobenzene, elevated temperatures and pressures are necessary. A batch process used in Europe employs autoclaving with a copper salt catalyst. In America, the Dow Chemical Company has developed a continuous method in which the reaction mixture slowly passes through a long pipe. The German Raschig process features both catalytic air-oxidation of a hot hydrochloric-benzene mixture to give the chlorobenzene, and almost quantitative recovery of the acid following hydrolysis. The overall effect is therefore a simple air-oxidation of benzene to phenol.

In the laboratory, it is possible within certain limits to replace hydrogen with hydroxyl by means of successive nitration, reduction, diazotization and hydrolytic reactions; likewise the nitro and amino groups, which are simply steps in the foregoing total operation. Some individual amines do not require the diazotization step, but may be hydrolyzed directly to phenols. A degradative process, decarboxylation of hydroxy-aromatic acids, is occasionally useful, and was used by Scheele for producing pyrogallol. Many other, less general methods for arriving at individual phenols have been invented, an interesting example being the dehydrobromination of 2,4-dibromomenthone to thymol. Benzene itself can be oxidized in considerable yields, to phenol-dihydroxybenzene mixtures by the action of hydrogen peroxide in the presence of ferrous sulfate (5).

Occurrence

It may not be correct to state that phenol as such is found in coal and related natural substances. There is indeed a likelihood that the phenol arises from chemical reactions accompanying the distilling operation. But coal distillation, nevertheless, produces phenol from a naturally occurring material.

Because of their general reactivity, and especially the ease with which they are oxidized, phenols do not occur in large quantities even in the biologic world. Their existence there in small amounts, nevertheless, is widespread and of extreme significance.

Phenols and phenol ethers are found in such agreeable substances as thyme, clove, nutmeg and wintergreen. Less fortunate is the presence of the irritant, urushiol, in poison ivy (6). There are free phenols in wood resins, in plant leaves and in fruits. Combined with saccharides as tannin-like compounds or in simple glycosidic fashion, phenols are again broadly distributed.

Animal organisms excrete a part of aromatic protein residues as free phenol at high dilution, but do not generally seem to harbor as wide a variety of simple phenolic materials as do plants. Among the more complicated phenols which play a vital part in animal existence are adrenaline, thyroxine, vitamins E and K, and some sterols.

Importance

The ease with which phenols themselves suffer oxidation has led to their application in the protection of a number of commodities that are seriously susceptible to oxidative deterioration. To accomplish this, a relatively small amount of compound, perhaps an aminophenol, is mixed with the material to be stabilized. Since many so-called auto-oxidation reactions are of the chain type and depend upon the building up of minute concentrations of initiating substances, small quantities of inhibitor, exerting a strategic reducing influence, may prevent the accumulation of critical amounts of reaction initiators, and thus prevent the larger consequences. Successful applications of this principle have been made in the fields of food, chemicals, petroleum products, paint and rubber. The controlling or extinguishing of polymerizations has been accomplished through the use of phenols (7) acting in a somewhat similar fashion.

A further utilization of phenolic reducing power is encountered in the field of photography, where hydroquinone, catechol, pyrogallol and p-aminophenol have long been used as developers. Superior results from the developing process have been obtained by adding a soluble sulfite to the reaction, and it has been shown that the sulfite participates actively (8).

While the importance of phenols as antiseptics in general therapy is not increasing at present, they have been of paramount significance here, first by enabling Lister to accomplish aseptic surgery, and in succeeding years making possible its universal application. Today, phenols still find extensive use in the related field of decontamination.

From the standpoint of consumption, the synthetic resin industry is the most important peacetime user of phenols. Since the commercialization of phenol-formaldehyde reactions by Baekeland, there has been ever-increasing demand for the resulting plastics. Modification of plastic properties as a function of preparative method and/or admixture of new ingredients, has proved both a stimulus and a response to widening use.

Phenols are also employed as starting materials and intermediates in the synthesis of many substances, nylon being an outstanding example.

Both hexamethylenediamine and adipic acid, the materials of nylon production, are obtained by means of reactions starting with phenol. During World War I, the manufacture of picrate explosives consumed as much phenol as did the entire economy in the following decade. Dye synthesis, relatively less important from a volume standpoint, remains as a conspicuous use.

Of passing interest, is the utilization of alkaline pyrogallol solutions as oxygen absorbers, a practice formerly universal, but now destined to decline in the face of competition from newly-available inorganic reducing agents.

Recently it has been observed that the heavier noble gases enter into combination with certain solid phenols (9,10). The substances arising in this way may properly be spoken of as compounds if one accepts a definition which emphasizes stability and stoichiometric constancy. It appears, however, that shape and size of crystal interstices is the critical factor in their formation, and not the usual bonding between atoms. There is not sufficient reason as yet for assuming that this behavior is peculiar to phenols.

Statement of the Problem

The aims of this thesis are to describe the reaction of sulfatocerate on phenols; to show how it may be used in analytical operations; to explain the nature of the reaction and the constitution of the product; and to set these observations in perspective by an examination of existing knowledge on the general subjects of phenol analysis and oxidation.

REVIEW OF THE LITERATURE

Detection

The development of single, specific tests, reliable in mixtures, and covering both classes and individual compounds, is the final goal of research in qualitative analysis. Unattained though this may be, there has been encouraging progress, even in the difficult problem with phenols.

Although numerous instances of interference by other classes exist, the main confusion in detecting and estimating phenols is caused by amines, whose oxidation and substitution reactions are similar. Sometimes, the mere demonstration of elementary nitrogen will eliminate a question, but not, for instance, in the case of 8-hydroxyquinoline. Likewise, it may prove simple to test with the classifying solvents in which the ordinary mono-functional amines and phenols distinguish themselves. This is not practicable, however, if specimens are dilute solutions, nor when a presence of other functional groups changes the solubility pattern.

In the following section will be given a number of procedures for detecting phenols. Some of these methods yield extremely precise and specific information.

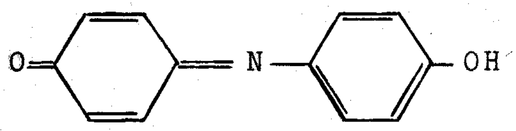
Pure substances in solution

As one knows, solid phenol, or its water solutions may be sensed by odor. For solutions, the threshold of human perception lies in the vicinity of one part phenol per three thousand parts water. Fish, however, seem able to detect it in lower orders of magnitude, and have been used for this purpose (12).

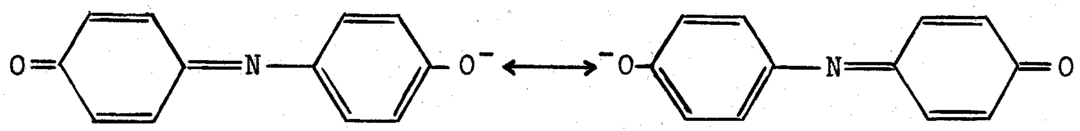
Ferric chloride, a qualitative phenol reagent of long standing, forms intensely colored complexes of various hue with most members of the class, and may be used in alcoholic solutions with substances that are insufficiently soluble in water. Amines do not interfere, but enols, if not too dilute, give a positive test.

The Lieberman reaction is another standard test for phenols, and consists of the forming of an intense red coloration on addition of nitrous acid to a phenol solution. Indophenols are considered to be the products, since they may form by action of phenols on nitrosophenols. A color change caused by liberation of the indophenol anion is observed upon neutralization of the excess acid. This anion, formulating as a symmetrical mesomer, is very stable. Nitrous acid is supplied to the reaction by adding nitrite salt to the acid solution.

Indophenol formation by a different route is the basis of the most sensitive chemical test on record for phenols, and has been popularized by Gibbs (13). It consists in treating a very dilute aqueous solution, buffered near pH-9.4, with 2,6-dibromoquinonechloroimide. Concentrations of phenol as low as 1:20,000,000 give a sensible color within an hour; higher concentrations, within shorter time intervals.



An indophenol



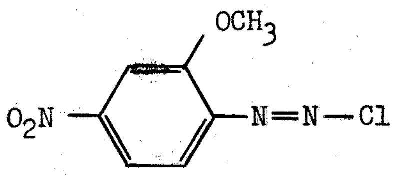
The indophenol anion

The particular brom-substituted reagent was selected by Gibbs as the best of all substances tested (13) and appears still to be regarded as such (14). The method has been checked (15) and modified (15,16), using techniques of concentration which permit the reliable estimation of phenol and cresol in water in parts per billion. The Gibbs method, as it is known, is both sensitive to amines, and insensitive to para-substituted phenols; the latter characteristic, however, can be used for demonstrating the condition of para-substitution.

Color reaction of many phenols with metavanadic acid has been described (17), and may involve indophenol formation analogous to the Lieberman phenomenon. Here, the rôle of nitrogen is filled by its chemical relative, vanadium.

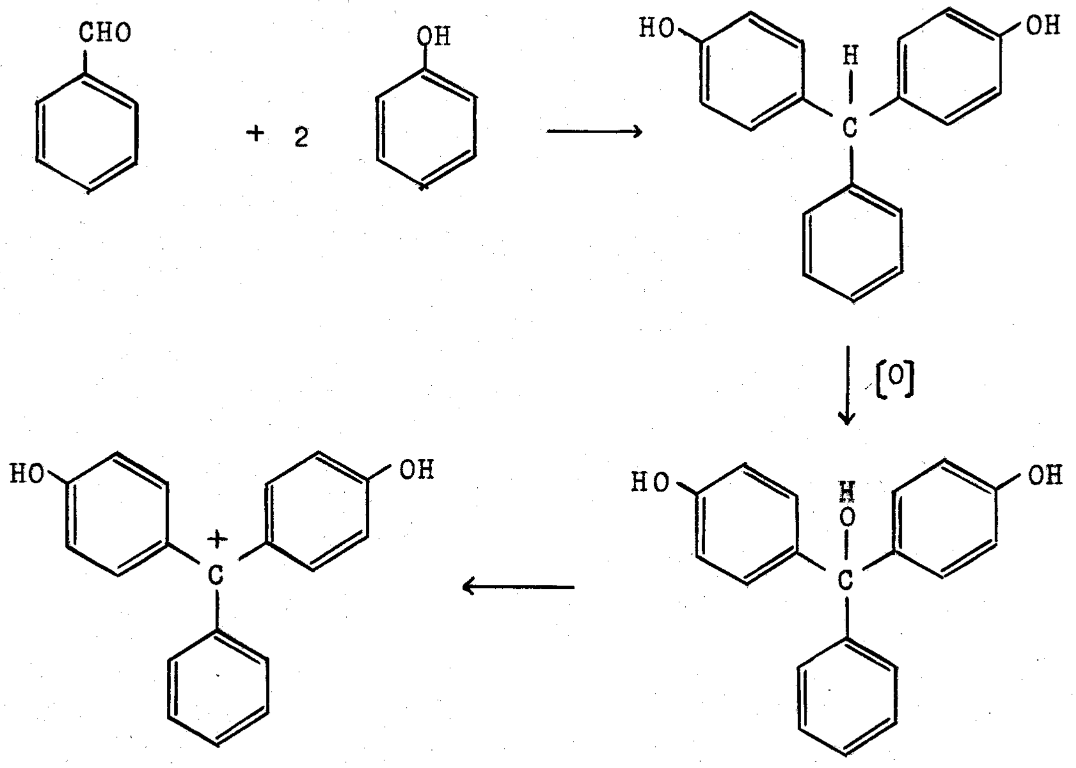
Although not entirely specific, the Millon-type tests can still be used advantageously in phenol detection. The procedure appears to have originated as a qualitative reaction for proteins, but owes its effectiveness in this to the fortuitous occurrence of the phenolic tyrosine units in most proteins. The reagent, a nitric acid solution of mercury, is frequently modified under the same name. It is clear from the action of tyrosine, that para-substitution constitutes no such restriction on the Millon test as it does in some other circumstances. Like tyrosine, p-cresol gives a positive response. The Millon reactions have been surveyed by Gibbs (18).

In the treatment of small samples, there is a method, published by Kondo (19), which utilizes the microscope for examining precipitates. It employs the so-called *echtrotsalz B*, a substituted benzenediazonium compound, as the precipitant. Samples need be no larger than a drop on a slide, nor more concentrated than 1:100,000. Spot plate technique may be substituted for the microscopic, but does not give the better result.



Echtrotsalz B

Phenols undergo the Komarowsky reaction, in which a sulfuric acid solution of an aromatic aldehyde serves as reagent. Salicylaldehyde is commonly used. It has been thought that carbonyl oxygen, together with the parahydrogen atoms of two phenol molecules becomes eliminated as water. One of the attached phenol residues is also oxidized to the quinoid state, which gives the coloration. At present it is felt, however, that quinoid structure is not involved, and that the Komarowsky phenol reaction may instead be pictured:



As previously mentioned, para-hydrogen atoms are required in the phenols. In addition, the phenol group itself must be free; phenolic ethers do not react. It may be mentioned that while the Komarowsky procedure, as applied to alcohols and olefinic substances, gives rise to colors through quite different chemical reactions, the classes indicated constitute a practical source of confusion that is just as serious as though they reacted in exactly the same way.

A simple test suggested by Escaich (20) is said to give preliminary quantitative information in addition to the qualitative. The method consists of treating the phenol solution with successive small amounts of the following dissolved reagents: ammonia, sodium peroxydisulfate and silver nitrate. Phenol, if present at less than 1:20000, causes the appearance of a yellow coloration. At higher concentrations, the color is blue. Amines also react.

There is a review covering some of these and many other color reactions of phenols, authored by Gibbs (21). The various tests are presented in organized form. Their scope and limitations are discussed.

Mixtures

Due to such factors as indistinguishable behavior by two or more substances, interactions between components, or discharge of the reagent by other than the intended processes, the detection of individual compounds in mixtures by chemical means is fraught with difficulty. Furthermore, even when a measure of success is achieved, the results are usually of poorer quality than those obtained from pure unknowns.

Among the chemical tests, the ferric chloride is sufficiently reliable for general use. Enols give the test, but may usually be distinguished by their sensitivity to carbonyl reagents.[1] Certain other substances, of which mercaptoacetic acid is an organic example,

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[1] The latter property is shared, however, by certain phenols, notably the meta-oriented polyhydroxybenzenes.

and thiocyanate ion an inorganic, give intense colorations with iron (III).

Recently, a new qualitative reagent for phenols has been introduced, nitrato-cerate (22,23), which is a ceric oxide solution in nitric acid. Such a test solution gives colors with alcohols, but precipitates with phenols. Other common organic substances containing only carbon, hydrogen and oxygen, do not usually interfere, but amines and heterocyclic nitrogen compounds also yield precipitates. The test begins to fail on both phenols and alcohols at a carbon atom content near ten, but it would seem that the method offers much promise.

Ware (24) has stated that phenol or ortho-cresol may be detected in most mixtures by a short sequence of operations using Millon-type reagents.

The best general procedure in the chemical analysis of mixtures, however, is the carrying out of preliminary separations. Thus, in the case of the nitrato-cerate test, extraction of an organic sample with aqueous acid, or the acidification of its water solution prior to its extraction with an immiscible solvent, will accomplish a separation of nitrogenous base from weakly acidic phenol. Phenolic mixtures may be obtained from general mixtures by alkali-extraction of the latter, and precipitation of the extracted phenols by carbon dioxide. They are, of course, less difficult to analyze than the general mixture.

It seems likely at present, that purely chemical methods, particularly in mixture analysis, will suffer continued displacement by instrumental techniques, wherein advantage is taken of subtler dissimilarities in compounds. Infra-red absorption spectra of pure substances, for instance, are so characteristic that analogy with the fingerprint suggests itself. Simple qualitative analysis by such a method is becoming only a matter of correlation with catalogued patterns. For reasons similar to those already mentioned, the problem of mixtures is again more difficult, but it has been solved in numerous cases by locating wave lengths at which single components absorb more strongly than the rest. By extension of the same idea, presence of functional groups themselves may be determined. The phenolic function can be shown in this way, relatively independently of other factors, and becomes our closest approach to a universal test. The large importance here ascribed to instrumental methods is based not only on present levels of attainment, but also the rapidity with which they have been gained. Detection of substances at very low concentrations in either pure solution or in mixtures, however, can still be best accomplished by chemical testing.

Identification

Color and precipitation reactions

Classification tests. In studying particular compounds, it is usually necessary and always desirable to organize them into classes, in which individuals or sub-classes share some identifying quality. Pyrimidal repetition of this principle is the pattern of systematic qualitative analysis.

This pattern for phenols is quite incomplete. But there do exist, methods for establishing phenolic nature, i.e. detection, and also a few reactions by which the number and/or orientation of hydroxyl groups may be learned.

Medley (25) has observed a reaction in which monohydroxy and polyhydroxybenzenes differentiate themselves. Basic lead acetate gives a precipitate, usually in the cold, with the common phenols. Precipitates of monovalent phenols can be dissolved in chloroform, while others are not soluble. This short cut could, on occasion, eliminate a necessity for an absolute procedure involving molecular weight determinations, elementary analyses and acylation.

If a phenol is known to be monovalent, the question of para-substitution may be resolved either by its behavior in the Gibbs reaction (15) or in the Komarowsky (26). But this is often unnecessary, since common individual compounds are generally distinguishable. In more unusual cases, infra-red spectra have also been used. This line of investigation is bound to continue. Friedel (27) by means of infra-red absorption data, has arranged twenty-two simple phenols into four classes as a function of their different states of ortho-substitution.

Some peculiarities of polyhydric phenols have been recorded by several investigators. Thomas (28), using a solution of ethanolamine molybdate in alcohol, has obtained intense red colorations from catechol, gallic acid and pyrogallol. A similar color arising from benzoquinone differs in being stable towards acid. Over fifty common phenols which lack the vicinal polyhydroxy characteristic, tested negatively. Precipitation of the same compounds by excess trivalent rare earth ion has been reported by Fernandes (29). He does not mention gallic acid. Trivalent cerium is said to cause a violet precipitate, whereas precipitates of other rare earths are white. Medley (25) has observed pyrogallol and catechol to precipitate in the water solution of normal lead acetate, while the basic acetate is required to precipitate others.

An additional method for distinguishing this configuration is that of Brauer (30), using a molybdiphosphate reagent. The first reaction is noted, and also any change brought about on addition of ammonia. The color sequence given by catechol and pyrogallol is green to blue; by hydroquinone and hydroxyhydroquinone, blue without change; and by resorcinol and phloroglucinol, no color to blue. The test is said to indicate these configurations as they occur in larger molecules, as well as to differentiate the di- and trihydroxybenzene isomers.

Precipitation of two meta-dihydroxy compounds, resorcinol and orcinol, by the basic nitrate of mercury, has been reported by Cremer (31), and may be specific in wider applications. The occurrence is noted even in dilute solutions. Hydroquinone, phenol and ortho-cresol give no response. Catechol gives a black precipitate.

Ranedo (32) has used the reagent, 1-diazo-2-napthol-4-sulfonic acid, followed by ammonia, in a color reaction that appears to be selective for the meta-dihydroxy configuration. Resorcinol, orcinol and phloroglucinol solutions all become intensely red, while the response of pyrogallol is weak. Other phenols either react differently or not at all.

Para-dihydroxy orientation in the simpler molecules gives the unique property of quinhydrone formation on partial oxidation. Substitution does not generally obviate the effect, unless it be extreme. In this connection, it has been shown by Michaelis and Schubert (33) that duro-quinone, the tetramethyl derivative of para-benzoquinone, does not form a quinhydrone.

One reaction, discovered by Feigl and Feigl (34), appears to be characteristic of vicinal trihydroxy phenols. A positive test is the formation of a flocculent violet precipitate when an ammoniacal solution of the unknown is warmed with orthophenanthroline. Natural tannins, gallic acid and pyrogallol show positive reaction even in minute concentrations, while catechol, phloroglucinol and resorcinol give no response. Hydroquinone reacts weakly.

By the judicious use of classifying reactions, one may frequently resolve a confusion between specific individual substances when their individual tests are non-distinctive. Finally, classification reactions in general, may always be thought of as analytical tools in the study of mixtures.

Tests for individual phenols. A very large number of such tests, differing in their scope of applicability, have been reported.

Certain procedures, for instance, may distinguish only between two or three possibilities. Such a test is that of Castiglioni (35) in differentiating the napthols. Both of these isomers are precipitated from acid solutions by formalin, but the precipitate from alpha-napthol gives a blue coloration in alkali. The method of Afanas'ev (36) in treating the same problem, consists in reacting the phenol with N-chloro-p-toluene-sulfonamide in aqueous solution. Alpha napthol causes a violet coloration; beta napthol, a yellow. The three dihydroxybenzenes show conspicuously different behavior towards basic mercuric nitrate, as stated by Cremer (31).

Jackson and Dehn (37) have used Manseau's reagent, hexamethylenetetramine in sulfuric acid, as a color-testing reagent for diverse compounds, including a number of phenols. The greatest advantage of the Manseau test lies in distinguishing position isomers from one another, and certain other closely related compounds. For this reason, either some foreknowledge or additional testing is usually required. Their reaction with the Manseau reagent clearly differentiates the hydroxybenzoic acids, thymol from carvacrol, and gallic acid from pyrogallol.

Gibbs (18) and Ware (24) have pointed out specific differences in the action of Millon-type reagents on various phenols, allowing their identification. Often, the procedure takes the form of two or more separate tests, wherein the reagent, or some other factor may be modified. By noting spontaneous color changes and the effects of heating, Ekkert (38) has succeeded in differentiating a number of phenols with a sulfuric solution of sodium arsenate. All cresols give similar colors, however, and consequently are not suited to this test. The acid metavanadate reactions of Parry (17) are interesting, as are the colors reported by Giral (39), which phenols give on their treatment with selenium dioxide in sulfuric acid.

In what is probably the first report on the reaction of phenols with cerium, Orlow (40) has proposed it as a qualitative test for both the organic substances and for cerium. Although he mentions the quadrivalent state of cerium specifically, and also the supposed oxidation of tannin by the reagent, there is uncertainty as to whether or not Orlow understood the oxidative nature of the phenol precipitation. Cerium(III) salts, and those of neodymium, have been reported as having no effect on tannins. It is somewhat surprising in this connection that the rare earth ions studied by Fernandes (29) should precipitate pyrogallol, a tannin constituent.

A miscellaneous, but possibly useful observation by Krauskopf and Ritter (41), is that resorcinol produces an intense violet coloration in ammoniacal cobalt solutions. Zinc, nickel and cadmium are similarly active, but their colors are bluish and less intense. Slotta and Neisser (42) have demonstrated that catechol and hydroquinone precipitate iodoform slowly, while resorcinol acquires but a pink hue in hypoidite solution.

Tests for individual phenols in mixtures. Less effort is expended now than formerly in perfecting tests of purely qualitative nature, since the need for quantitative information is also of the greatest importance. Consequently, many of the distinguishing phenomena which might be entered at this point, will instead appear under the heading of quantitative procedures. Few, if any, of the older schemes for detection and identification could not be utilized in one degree or another for quantitative information as well, and many have indeed been so modified. This chronological drift, of course, is the pattern of advancement in analytical operations.

In the search for improved methods, or in the investigation of new substances, the first exploration should be towards applying a known reaction of classification. For example, the fact that the Gibbs reagent[1] fails to react with para-substituted phenols, suggests its use on such compounds as p-cresol and thymol in testing their purity.

An interesting study of one complex mixture has been made by Sanchez (43), whose system consists of the nine phenols, catechol, resorcinol, hydroquinone, pyrogallol, pholoroglucinol, vanillin, and the acids, salicylic, gallic and tannic. By his scheme of systematic qualitative analysis, this investigator has resolved both the entire mixture, and its lesser combinations.

Qualitative demonstration of cresol in phenol can be achieved with a vanillin reagent, by the method of Ware (44); of resorcinol in phenol, by the method of Kuznetzov (45), in which the reagent, 4-diazo-3,5-benzenedisulfonic acid, colors with resorcinol only.

The discovery of chromatographic techniques and their extension to diverse applications, has opened up a new field in qualitative analysis. There will no doubt be steady advancement towards the quantitative basis, for the self-evident advantages to be gained through a relatively easy separation of mixture components are attractive. Chromatography has already been applied in the analysis

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[1] This thesis, p. 10

of phenol mixtures by Bielenberg and Fischer (46), whose method involves coupling the phenols with diazonium salts. These workers have been able to identify the individual phenols in an eight-component mixture. Hossfeld (47) has subsequently claimed that his sulfonic diazo reagent and use of paper chromatography give improved results.

Characteristic derivatives

In addition to the commoner phenol derivatives, for which melting points are listed in standard laboratory texts (48), the literature contains valuable information.

Examples of the less common substances, for which data are given, are the para-nitrophenyl acetates of Ward and Jenkins (49); phenoxyacetic amids of Nametkin, Mel'nikov, Baskakov and Bokarev (50); allophanates of Sah, Gih, Kang and Shou-cheng (51); and the 3,5-dinitrobenzazides of Sah and Tsu-sheng (52).

Occasionally, the appearance of a precipitated derivative is used as the identifying characteristic. Rosenthaler (53) has obtained the azo-derivatives of a number of phenols. Microscopic examination of these precipitates identifies them, and consequently the phenol out of which they arise. In a similar operation reported by Kondo (19), the 2-methoxy homologue of the Rosenthaler reagent is utilized.

Study of the absorption spectra of their pthalein derivatives has enabled Formanek and Knop (54) to identify twenty-four phenols.

Both acid and alkaline solutions are used. Wales and Palkin (55) have employed the absorption spectra of para-nitro-diazo derivatives to characterize an additional number. Absorption spectra in three different solvents are required for the positive identification of certain individuals.

Methods for Quantitative Analysis

Pure substances in solution

The oldest method. The fact that phenols are soluble in aqueous alkali was first observed by Runge (1), who isolated the phenolic fraction of coal tar by extraction of the latter with limewater and subsequent acidification of this phase. It was natural, therefore, that the first general method for quantitative phenol estimation was shaking a known volume of organic mixture with a strongly alkaline water solution, and observing the volume change suffered by the oil. The transparent inaccuracies and limitations of this crude method were the driving force toward improved techniques.

Halogenation. Koppeschaar (56) appears to have introduced the first superior analytic method for phenols. The procedure bears the name of its inventor, and has survived throughout seven decades. Its principle is the determination of bromine required for halogenating a phenol, and the procedure consists in adding to the phenol solution, a known amount of bromine that is more than sufficient to react, conversion of the excess bromine to iodine with potassium iodide, and titration of this iodine with standard thiosulfate. Since in the overall process one molecule of phenol consumes six atoms of bromine,[1] the data obtained can be used to show the amount of phenol originally present. In order to prevent the escape of volatile materials, this procedure is carried out in iodine flasks.

Reagent bromine may be added in two ways: simply as bromine water, or as bromate, followed by excess bromide and acid. In the latter case, the limiting factor is bromate, which becomes quantitatively reduced. A known charge of bromine is thus set free in the solution. There is the advantage with this variation that all the bromine gets into the flask in the first place, and that very little can escape during the time for adding acid and stoppering.

If sufficient care be exercised, phenol and meta-cresol may be determined with errors of only tenths of a per cent by the Koppeschaar method.

Danckwortt (57) has studied the problem of the cresols, and his results indicate that only meta-cresol is satisfactorily brominated within the customary fifteen-minute waiting period. Ortho- and para-cresol require up to seventy-two hours. Pieters (58) has checked the Koppeschaar method along with an iodometric procedure, and found satisfactory agreement. Bielenberg and Goldhahn (59), however, in

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[1] In the initial bromination of phenol, bromine substitution occurs at three nuclear positions and also at the oxygen atom, where Br remains reactive towards iodide and its valence corresponds to the hypobromous state. Reduction of this bromine atom to bromide therefore liberates two atoms of iodine, and the gross effect is as though no hydroxyl reaction were involved.

extending the method to resorcinol, hydroquinone and phloroglucinol, state that erroneously low results are suffered in the analysis of these compounds, and similarly in the instances of ortho-and para-cresol. Accordingly, they have modified the Koppeschaar procedure by eliminating the iodine steps and back-titrating the excess bromine directly with standard arsenite or thiosulfate. Results using this procedure are higher, excepting the cases of phenol and meta-cresol, than those obtained by the regular method, but it is not stated that these higher results are in agreement with theory.

A shortage of iodide salts in Germany following World War II has resulted in two Koppeschaar modifications. The one of Riemschneider (60) substitutes sodium sulfite for potassium iodide. Bromide ion produced from excess bromine by the sulfite reagent, together with the bromide previously released by the substitution reaction, is determined, its difference from the total bromine calculated, and the phenol estimated by the quantity of bromine it has withdrawn. Poethke, (61) in a subsequent publication, criticizes the Riemschneider method on grounds that it requires too many standard solutions. Poethke's suggestion is that standard arsenite be used in place of the iodide, and the excess arsenite titrated. Precision of less than five tenths per cent is claimed.

A discussion of direct bromometric procedures has been given by Kolthoff (62). Three general methods exist: First, the precipitate, 2,4,6-tribromophenol bromide, may be recovered, washed, dried and weighed; second, the liberated hydrogen bromide titrated with alkali after destruction of the excess bromine by mercurous chloride; and third, by iodometric determination of the fourth bromine atom.[1] Methods one and three give results about two per cent low, while method two is usually high in similar degree. The iodination of phenol in cold, weakly alkaline solutions by free iodine, gives the product 2,4,6-tri-iodophenol exclusively, and consumes six iodine atoms per mole of phenol. Three iodide ions appear in the solution. The quantitative adaptation of this reaction has been proposed by Hamann (63). Also reporting an iodination method are Slotta and Neisser (42), in whose hands, the alkaline iodine solution, that is, hypoidite, has appeared to give good results in a number of cases. The procedure is to treat neutral phenol solutions with a known quantity of iodine, add alkali, and after a time interval followed by acidification, to titrate the excess reagent with thiosulfate. Catechol and hydroquinone suffer ring-cleavage, but their reactions still conform to simple stoichiometry, the former compound consuming ten iodine atoms, and the latter, twelve.

Iodination may also be accomplished through the use of iodine chloride. Gengrinovitch (64) has reported a satisfactory analysis of phenol, resorcinol, beta-napthol and oxine. The phenol is titrated directly with the reagent, starch-iodide indicator being used. It is emphasized that the iodine chloride reagent possesses the following

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[1] This thesis, footnote 1, p. 24.

advantages: non-volatility, high sensitivity towards phenols, convenience, freedom from absorption by the precipitates, and low cost.

Colorimetry. The ferric chloride coloration with phenols appears to be one example of a general qualitative test which is not easily adaptable to quantitative use. Babkin (65) has attempted the application, but without any encouraging success, and has admitted that his method may produce results deviating by as much as twenty per cent.

Bach (66) has studied the Millon-type color phenomena, as has Gibbs (18). The former reports that his procedure, which includes boiling, furnishes stable colorations that are reproducible for phenol. Concentrations of this substance, however, must be above five p.p.m. Gibbs outlines his own efforts and reviews the work of others.

Colorations obtained through the use of the Gibbs reagent[1] have been found serviceable in quantitative analysis of phenols at extreme dilutions, and undoubtedly constitutes one of the very finest procedures wherever it is applicable. Papers by Gibbs (13), Basavilbaso (16), and by Ettinger and Ruchhoft (15), have explained the procedures and limitations, and suggested modifications for specific purposes.

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[1] This thesis, p. 9.

Some miscellaneous color reactions employed in quantitative analysis are titanium salts with phenol in chloroform (67), diazonium coupling (55) and ethanolamine-molybdate complexation.(28) The titanium colors suffer interferences from such hard-to-avoid substances as water, ethanol and ether, but the exceptionally sharp specificity of ethanolamine-molybdate reagent[1] for the catechol and gallic acid classes, would seem to indicate promise in the field of mixtures.

Gravimetric measurement. Halogenated phenols obtained in the iodine and bromine reactions, are generally sufficiently stable and insoluble to be used for quantitative measurements. They are not easy to wash and dry, however, as Koppeschaar (56) has mentioned. Individual reactions must usually be studied to determine exact composition and the conditions assuring reproducibility. Kolthoff (62) has discussed the use of halogenated phenols in gravimetric determination.

Another reagent giving insoluble reaction products with phenols is formaldehyde, which has been applied by Castiglioni (35) for the determination of the napthols, and by Sage and Fleck (68) for the determination of ortho and meta-cresol. Aldehyde precipitates may be dried at 100°, which is not the usual case with those of the halogens.

Riegler (69) has obtained an insoluble azo dye from phenol and a nitro-diazonium reagent. This precipitate, also stable at 100°,

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[1] This thesis, p. 16.

gives the investigator a 98-99 per cent accounting for the phenol in a 100 mg. sample.

Oxidimetric titration. The application of this type of measurement to the determination of phenols in general has suffered the disadvantage that simple stoichiometry is the exception, and that the extent of reaction with most reagents is too sensitive a function of conditions to be consistently reproduced. It is one purpose of this thesis to show how a relatively new reagent, sulfato-cerate, may be used to advantage in empirical determinations.

Sulfato-cerate has already been used by Furman and Wallace (70) in the oxidimetric analysis of that atypical phenol, hydroquinone. The reaction is a rigidly precise, bivalent oxidation, whose quinone product is not affected by the reagent under the experimental circumstances. Kolthoff and Lee (71), in checking the sulfato-cerate method, have shown it to be capable of 0.02% precision and accuracy. Ferrous-orthophenanthroline is the prescribed internal indicator.

Petsov (72) and Kolthoff (73) have both accomplished the same oxidation of hydroquinone by means of acid dichromate reagent. According to Petsov, it is best to titrate the oxidant with a hydroquinone solution, adding diphenylamine indicator after the color of the dichromate has begun to fade. There is only remote possibility that a dichromate method will ever be employed in preference to the sulfato-cerate method for hydroquinone.

Oxidimetric determination of phenol has been reported by Rassow and Schultsky (74), who employ the sulfuric acid-dichromate reagent.

Potentiometric titration. The course of analytical oxidations is frequently followed through use of instrumental indication. Sven (75), in such titrimetric determinations of phenol and thymol, has used a sodium nitrite-hydrochloric acid reagent. Kolthoff (73) has studied the oxidation of hydroquinone both by iodine and by dichromate. Iodimetric oxidation is satisfactorily quantitative when the solution is buffered with carbonic acid and bicarbonate. Quinone is said to poison the platinum electrode rapidly, necessitating strong heating to revive its activity.

Acidimetric titration. The titration of phenol as a weak acid in aqueous solution has been achieved by Kolthoff (76). Presumably, the process might apply to a number of phenols, but it is stated that polyhydroxybenzenes become air-oxidized during their attempted analysis. A dilute, carbonate-free sodium hydroxide reagent is used, and the indicator, resorcin yellow, is an azo dye sulfonate. Accuracy in the neighborhood of one per cent may be expected.

Conductimetric titration. The method has been used by Kolthoff (77) in the reaction of phenol with sodium hydroxide. More precise analyses are to be expected with moderately concentrated reagents than with highly diluted ones. A twenty-five milliliter sample of tenth-normal phenol, treated with normal sodium hydroxide, gives a result only one tenth per cent away from theoretical. Duyckaerts (78) has tested the technique for the oxidation of oxine with bromate at 50°. In this titration, current is a function of bromide concentration, which increases until the equivalence point, and then decreases as excess bromate oxidizes it to bromine. Inaccuracy in this operation was around a half per cent.

Polarography. Oxidation of pyrogallol in solutions about .0001 molar at the dropping mercury electrode has been studied by Vlček and Špalek (79). It is reported that the anodic half-wave potential is a negative linear function of pH, and that diffusion current is proportional to the pyrogallol concentration. The procedure is therefore suitable for quantitative use. Although phloroglucinol takes up atmospheric oxygen, its solutions show no polarographic activity.

Laitinen and Kolthoff (80) have used the stationary micro-electrode in the anodic oxidation of hydroquinone. A diffusion current proportional to reactant concentration within one per cent is reported. At least a two-minute interval is required for the diffusion current to become constant. The solid anode oxidation of hydroquinone, catechol and resorcinol has been described by Skobets and Atamanenko (81), who obtain sharply defined polarographic waves except in the case of resorcinol. In the latter there is destructive oxidation, i.e. irreversibility. The wave form first rises to a sharp maximum, falls, then ascends continuously.

Miscellaneous. The titration of the lower monohydric phenols by standard para-nitrobenzenediazonium solution has been suggested by Chapin (82). Reagent is mixed as needed, from separate solutions of para-nitroaniline in nitric acid, and sodium nitrite. Basic lead acetate buffers the reaction satisfactorily. The end-point, determined externally, is presumably the formation of a contrasting dye on the spot plate caused by free reagent in the main solution.

Barac (83), in the analysis of blood for phenol, has turned to ultra-violet absorption spectra. He has found for the phenolic absorption band at 2807 Å ., an extinction coefficient of 2400. The case is Beer's-Law-dependent.

Interaction of beta-napthol and malic acid, promoted by strong acid and heating, has been observed by Leininger and Katz (84). The strong fluorescing ability brought on by the change can be used to determine either compound. To estimate beta-napthol, its evaporated solution is treated with a small amount of malic acid in sulfuric acid, heated at about 90° C. for one-half hour, and after cooling, made up to standard volume. This solution is read by means of an electrofluorimeter.

Mixtures

Instrumentation. The infra-red absorption technique has already been mentioned as a powerful and fast-developing tool in qualitative analysis.[1] Its direct application to quantitative studies is also well under way (85). Details for the rapid analysis of cresylic acid-phenol mixtures have been given by Whiffen and Thompson (86), who use a carbon disulfide solvent. Absolute errors in their results amount to about two per cent. The same authors have also made a preliminary study of xylenol spectra, explaining how their findings may be adapted to the quantitative determination of these substances. Friedel, Pierce and McGovern (87), employing the same solvent, have

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[1] This thesis, p. 15.

studied solutions of similar mixtures and reported satisfactory analytical results. Correlation of structure with absorption spectra has been worked out on a more-or-less individual band basis (27)(86), and also by characteristic band patterns found between 5 to 6 microns. Such knowledge lays the necessary foundations for analytic application.

Light absorption spectrophotometry has been employed by Willard and Wooten (89) to estimate a single poly-hydroxy phenol of the catechol or resorcinol type. The buffered, aqueous sample is reacted with iodine, excess of this being carefully destroyed after a period, and a quantity of acetone added. Transmittancy at 725 millimicrons is finally read and interpreted empirically. If a meta-dihydroxy phenol be iodinated in the presence of catechol, a dark-colored addition compound is formed, the amount of which is limited by the substance not in excess, and whose acetone solution may be determined colorimetrically. Phenols and cresols do not interfere.

Robertson, Ginsberg and Matsen (90) have studied cresylic acid-phenol mixtures by means of the ultraviolet absorption of their vapors. Two to three per cent accuracy has been obtained, and the presence of phenol demonstrated at concentrations as low as three tenths per cent.

Specific reactions. From the standpoint of the present investigation, the most interesting example encountered is that reported by Rao, Rao and Sastri (91), namely that hydroquinone may be quantitatively oxidized in the presence of phenol and cresols by a vanadic acid reagent without interference from these substances. The reaction is carried out at 50° C. with sulfuric solutions of sodium vanadate, an oxalic acid catalyst, and diphenylbenzidine indicator. The authors state that results are comparable to those obtained by sulfato-cerate oxidimetry, and point out that the latter cannot be used in the presence of the other phenols because of reaction of these to form colored precipitates.

Under certain conditions which involve reagent concentration, heating, and time intervals, Chapin (92) has observed sufficiently selective action by phenol with Millon's reagent to permit its analysis in cresylic acid mixture. Miklashevskaya (93) has determined the ratio of phenol to cresol in mixtures by utilizing the fact that a hot acid permanganate solution oxidizes phenol to water and carbon dioxide only, whereas cresol oxidation gives acetic acid in addition.

The very low solubility of the lead-catechol precipitate has been noted by Jones, Prahl and Taylor (94) and also by Böck and Lock (95). Quantitative analysis of catechol by this reaction has been proposed by both groups of authors, the former with regard to commercial preparations of resorcinol, and the latter, to the mixture of three dihydroxybenzenes. In such a mixture, catechol is precipitated by lead acetate from a neutral solution, and hydroquinone oxidized by sufficient ferric chloride. The resulting quinone can be extracted with chloroform and reduced with hydriodic acid, free iodine then being titrated. Phenol does not interfere, nor does the resorcinol. Other meta-hydroxyphenols are equally passive. This procedure is said to become a sensitive qualitative test for hydroquinone when starch indicator is used to show trace quantities of iodine.

Miscellaneous. A large difference in the time required for bromination makes possible the determination of meta-cresol in the presence of the cresol isomers.[1] Ortho-meta-cresol mixtures have been analyzed by Sage and Fleck (68) using formaldehyde precipitation. In the absence of cineole, both cresols are thrown down together, but only ortho-cresol reacts with formaldehyde in its presence.

Certain binary mixtures, when dissolved in a standard weight-ratio of hot water, show clouding temperatures that are characteristic of composition. Paris and Vail (96) have determined some of these data for phenol, cresol and xylenol binaries, while Stevens and Nickels (97) have applied the technique to butylated cresols as well. The latter workers include some data on the freezing temperatures of these mixtures.[2] The meta-para-cresol mixture has been investigated by Savitt, Goldberg and Othmer (98), who use colorimetry on a nitrosated sample. This method, while accurate to about one percent, is empirical, and the preparation of standard curves for

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[1] This thesis, p. 24.

[2] Freezing points are of necessarily limited usefulness, since the data taken do not identify the component freezing out of the liquid. It is required that this be known in order to distinguish compositions lying on opposite sides of a eutectic. Moreover, in some systems, there may be more than one eutectic, enlarging the problem.

different total concentrations is required. The same authors have submitted a review of existing analytical methods for cresols in addition to their experimental contribution.

Zahner and Swann (99) have achieved a separation of phenol from cresylic acid mixture by chromatography, this being followed by separate analysis of the single component. Ninety-eight per cent of the phenol present in the sample can be accounted for.

Oxidation

There is the dilemma, in attempting to define oxidation, that the familiar statements having to do with electron loss do not include a multitude of cases, also though of as oxidative, where the electron pair of a covalent bond shifts only a little with respect to a given atom. On the other hand, a broadening of the limits to include all such modifications in polarity brings every chemical change into consideration. Oxidation, therefore, is to be thought of as an arbitrary concept, covering a number of common phenomena and involving relatively large changes in atomic polarities but not set apart from chemical reaction in general by any natural discontinuity (100).

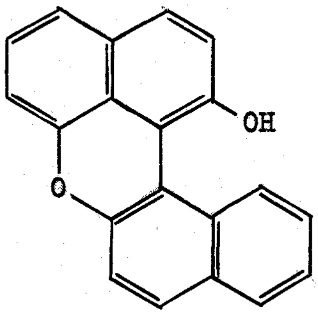
Few, if any substances ordinarily regarded as oxidants, are without effect on phenols, but their actions are diverse, not thoroughly understood, and frequently appear to generate more than one type of product. Behavior of individual phenols towards a given oxidant is scarcely less varied, one rough generality being, however, that susceptibility towards oxidation increases with pH and the number of hydroxyl groups.

Fieser (101) has attempted to indicate the relative susceptibilities towards oxidation precisely by the so-called critical oxidation potential, and his results are in agreement with the rule set forth above. The author defines critical oxidation potential as that of an oxidizing solution which causes a barely sensible reaction in five minutes. Several redox couples have been used, the experimenter not fully realizing at the time that idiosyncrasies in the action of different oxidants prevent their simple electrode potentials from being a reliable common denominator. Pennington and Ritter (102), in a more recent investigation, have emphasized this.

Alkaline conditions

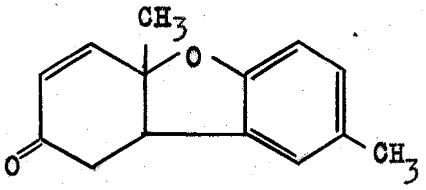
The reason why phenols become more sensitive to oxidation under alkaline conditions is that there the phenoxyl proton becomes acquired by the more strongly basic hydroxyl ion, forming water, and leaves the phenolic residue charged with an extra electron. This negative charge, by mesomerization, increases electron density throughout the entire ion.

Ferricyanide. This oxidant has been used by Pummerer (103) throughout most of his extensive labors in phenol oxidation, and on beta-napthol in particular. The beta-napthol product is said to be hydroxybinapthaleneoxide. Loss of hydrogen by hydroxybinapthaleneoxide, i.e., oxidation, results in colored solutions whose behavior is of great interest (104).



Hydroxybinapthaleneoxide

Phenol and the cresols react with the reagent to form a variety of products, conspicuous among these being hydroxybiphenyls and amorphous resins. The oxidation of para-cresol results in forming considerable quantities of a ketone, $C_{14}H_{14}O_2$, whose structure has been elucidated by the discoverer. (105)



Pummerer's ketone

<u>Peroxydisulfate</u>. The oxidation of phenols to hydroquinones by this reagent under alkaline conditions, is known as the Elbs persulfate oxidation, and results in hydroxylation. A noticeable tendency towards para-orientation exists in the presence of this

alternative, but ortho-compounds may form if the para configuration is blocked. Baker and Brown (106) have studied this reaction, and give their data on a number of phenols, as well as an extensive bibliography. Sulfate ion-radical is visualized as the acting species.

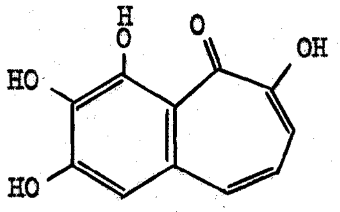
Eller (107), using similar reagents, has allowed more extensive reaction to occur so that the major product consists of so-called humic acid. This amorphous, insoluble and dark-colored substance arises from any of the common phenols, intermediate stages supposedly involving hydroquinones, catechols and hydroxyhydroquinones. The reaction, carried out on hydroxyhydroquinone itself, gives a product containing 58.16 per cent carbon and 3.16 per cent hydrogen. Except for the instances of salicylic and pyrogallic acids, carbon dioxide does not evolve, and ring structures therefore are thought to survive intact. They are considered to be oxidized to quinoid structure. The use of air or hydrogen peroxide in alkaline solutions gives the investigator similar materials.

Silver ion in the presence of sulfite. The common reaction in photographic development does not result in quinone formation, but in a symmetrically disulfonated hydroquinone that shows no further reducing action on silver (8). The speed of hydroquinone or sulfite acting alone on silver halide, is less than that of their combination. Quinhydrone clearly cannot form in these developers.

Air. Dihydroxybenzenes are observed by Triebs (108) to air-oxidize in alkaline solution, through their quinones in the cases of catechol and hydroquinone, to insoluble resins. Resorcinol, incapable of passing through a similar condition, still gives rise to a comparable product. One such resin, obtained directly from parabenzoquinone, consists of alkali-soluble and alkali-insoluble fractions, each of which gives the same elementary analysis.

Air-oxidized vicinal and meta-polyhydroxybenzenes have been studied polarographically by Vlček, Špalek, Krátký and Havlíček (109), apparently with the purpose of determining whether the reactions were reversible. Only the pyrogallol sample gave a cathodic wave, indicating that this substance first oxidizes to its hydroxyquinone; a second cathodic wave is thought to correspond with reduction of purpurogallin, which is also formed in pyrogallol oxidation. It is therefore apparent that the other compounds investigated suffer destructive oxidation immediately. The experiments have been conducted in the pH range 4.0-10.4.

An oxidation of purpurogallin itself has also been noted under these conditions by Haworth and Moore (110), who have shown that the benzenoid ring is destroyed leaving a substituted tropolone.



Purpurogallin

Neutral conditions

Peroxymonosulfate. Phenol oxidation by this reagent, according to the procedure of Bamberger and Czerkis (111), forms catechol and quinhydrone as main products, the former predominating.[1] The same products are also obtained in acid solution. Bamberger (112) has reacted para-cresol with this oxidant and warmed the mixture, whereas the first-mentioned experiment on phenol has been carried out at room temperature. Paratoluquinol, 1-methyl-cyclohexadiene-2,5-ol-1-one-4, is the product, but the yield is not good. Also obtained are several amorphous fractions.

Benzoyl peroxide. The findings of Cosgrove and Waters (113) show that monohydric phenols react in boiling chloroform with this radical-producing reagent, to give monobenzoates of corresponding catechols. The processes are of considerable interest because certain of them include an apparent displacement of substituents by the attacking radical. The phenomenon may also be explained as an acyl and hydrogen atomic exchange, involving no rupture of phenoxide bonds. Reaction of ortho-cresol, for instance, gives 2-hydroxy-6-methylphenyl benzoate in detectable yield, while the para-cresol product is 2-hydroxy-4-methylphenyl benzoate in larger quantity. It appears that where it is possible for the attacking group to enter a position

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[1] Compare the Elbs oxidation, this thesis, p. 38.

lying ortho-para to hydroxyl and methyl groups already present, it happens so. Where this geometry does not exist, transpositions establishing such configurations occur. Rather unexpectedly smoother reaction and higher yield are associated with the latter situation.

Methylene blue. Reaction of phenols with methylene blue does not occur spontaneously, but requires activation. Carter (114) has demonstrated the sustaining effect of ultra-violet radiation, while Wieland (115) has promoted the reaction with palladium black. Methylene blue acts merely as a hydrogen acceptor. Oxygen, if used instead of the dye, is consumed under the same circumstances.

Gold chloride. Chloride solutions of this noble metal are reduced at a neutral solution reaction by hydroxybenzenes, effectiveness of these increasing with the number of hydroxyls. Gold metal appears in the form of colored sols. Blue, green and red are noted, depending on the identity of the phenol and its concentration (116).

Air. Oxidation of pure phenol and cresol samples takes place in the presence of light and/or moisture, causing the materials to become colored. The nature of the change was once a subject of controversy, it being maintained by some that only impurities could be responsible. Gibbs (117), however, showed by isolating the colored substances, that they are the quinoid and hydroxylated derivatives of the phenols themselves.

Acid conditions

Quinone. Pummerer, Dally and Reissinger (118) have observed a reaction, catalyzed by aluminum chloride, in which phenol and cresols combine with this substance to form 2,5-di-[4-hydroxyphenyl]-benzoquinone. There must be concurrent dehydrogenation of the two intermediate mono- and di-substituted hydroquinones, but atmospheric oxygen seems to be sufficient for accomplishing this. The reaction has also been referred to by Meyer (119), who employs the same solvent, carbon bisulfide, but no catalyst. A darkening in color appears to accompany both the first and second substitutions.

Formal similarities appear between this phenomenon, the alkaline sulfite,[1] and the analido-quinone reactions (120).

Ferric ion. It would seem that dihydroxy-biaryls are preferentially generated by this oxidant, at least with regard to napthol oxidation. Formation of 1,1'-bi-napthol-2,2' by the treatment of beta napthol in boiling water with ferric chloride solution has been recorded by Pummerer, Prell and Rieche (121). The product precipitates from the reaction mixture in yields of around ninety per cent.

Ioffe and Krichevtsov (122), utilizing similar conditions and alpha-napthol, have achieved a ninety-six per cent yield of isomeric products. Only two substances are stated to be produced, 4,4'-binapthol and 2,2'-binapthol. Separation of these is based on their

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[1] This thesis, p. 39.

different solubilities in hot benzene.

Lead dioxide. Ortho-cresol, dissolved in an ether-acetic acid mixture, has been treated with the lead reagent by Goldschmidt, Schulz and Bernard (123). The presence of 2,2'-dihydroxy-3,3'-dimethylbiphenyl can be demonstrated in the product, but the bulk of the material is resinous. This latter substance, of average molecular weight around 315, is alkali-soluble and shows hydroxyl reactivity towards dimethyl sulfate. It is also soluble in the common organic solvents, gives some cresol on pyrolysis, and has the carbon-hydrogen analysis, 78.8%-6.44%.

Peracetic acid. Henderson and Boyd (124) have reacted hydrogen peroxide-acetic acid mixture with several common phenols including the cresols and phenol itself. Hydroxylation, preferentially para-oriented, is the mode of action observed. Limited quinone formation from hydroquinones so produced also takes place. Oxidation of para-cresol, however, gives 4-methylcatechol as the sole product. Thymol and carvacrol are repeatedly hydroxylated, the same compound, tetrahydroxycymene and some corresponding quinone appearing in both cases. Para-t-butylphenol becomes triply hydroxylated under the conditions imposed.

According to Boesekin (125,126,127), concentrated peracetic acid reacts with phenol to give cis-cis-muconic acid and quinone in approximately equal amounts. It thus appears that ortho or para hydroxylation first occurs, followed by quinoidization and cleavage of the ortho-quinone to the aliphatic acid. This muconic acid product is not encountered in the oxidation of phenol by other reagents.

Para-benzoquinone, diphenoquinone, 2,4,6-trisubstituted phenols, muconic acid and benzene are all stable to excess of this reagent, but napthalene is oxidized to 2,3-benzomuconic acid. Para-substituted phenols, which cannot give rise to para-quinones, react entirely in the alternate fashion and become beta-substituted muconic acids.

Halate. There is a strong tendency for these oxidants to cause ring substitution by halogen.[1] Hofmann (128) has reacted phenol with potassium chlorate in hydrochloric acid solution, and obtained tetrachlerobenzoquinone, also known as chloranil. A number of organic substances, including analine and salicylic acid, give the same product.

Cook and Louden (129) have noted that pyrogallol is smoothly oxidized to purpurogallin in cold aqueous solution by sodium iodate.

Electrochemical. Anoidic oxidation of phenol and catechol has been carried out by Fichter and Ackermann (130), together with the identification of a number of reaction products. The reactants are electrolyzed in one normal sulfuric acid solution under conditions of low current density. In the oxidation of phenol itself, there are obtained o,o'- and p,p'-diphenols, 2-hydroxydiphenylether, hydroquinone and catechol. The opinion is ventured that the diphenols may be intermediates in catechol and hydroquinone formation.

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[1] This behavior is understandable in view of the usual reaction of halate and halogenide to produce the free element.

If catechol is used as a starting material, high molecular weight substances are formed, together with certain amounts of volatile fatty acids, the latter probably being products of cathodic reduction of maleic acid and other ring fragments. Hydroquinone is not as extensively oxidized as catechol under the conditions of experiment.

Ortho- and para-cresols become oxidized to the biphenyl derivatives, 3,3'-dimethyl-4,4'-diphenyl and 5,5'-dimethyl-2,2'-diphenol respectively. Presence of the corresponding hydroquinones is demonstrated, and also methyl-p-benzo-quinone in the ortho-cresol sequence. It is stated that para cresol also gives the compound, 3,3'-dimethyl-2,2'-dihydroxydiphenylether.

A larger amount of resinous material is obtained from phenol in the presence of alkali.

Consideration of the anodic process has led Klemenic (131) to conclude that the primary reaction at this electrode is the oxidation of hydroxyl ion to hydroxyl radical. Diffusion of the latter agent into the solution and its attack on the dissolved reactant occur in sequence.

Hydrogen peroxide. Considerable interest in this reagent has been shown by a number of experimenters, most of whom have used it in conjunction with a ferrous salt. It is now believed (132,133) that a reaction between these substances occurs, which might be formulated:

$$H_2O_2 + Fe^{++} \longrightarrow Fe(OH)^{++} + {}^{\cdot}OH$$

Thus, the active species in this reagent mixture, as in electrolytic oxidation, is apparently the hydroxyl radical.

The effects on phenol produced by the hydrogen peroxide-ferrous salt reagents has been observed by Magidson and Preobrashenski (134), Goldhammer (135) and Chwala and Pailer (136). All have used dilute solutions, little or no heating, and reaction times of the order of twenty-four hours. The iron salt is usually dissolved with the phenol prior to addition of peroxide. Catechol and hydroquinone as main products are reported by each group, catechol appearing to predominate somewhat. Magidson mentions the precipitation of a resin in the phenol oxidation, and also a separate experiment in which small yields of guiacol arise from the oxidation of anisole. Pyrogallol occurs in the experiments of both Goldhammer and Chwala, purpurogallin being mentioned, in addition, by the former.

Ortho-cresol oxidation, studied by Ono and Oyamada (137), shows a resinous product and para-toluhydroquinone. The resin has been shown to consist at least partly of polyhydroxyphenyl derivatives, some of which appear to be coupled with iron.

Cross, Bevan and Heiberg (5), using benzene as the reactant, have obtained a conversion of three-quarters of the starting material. Phenol, and its oxidation products, catechol and hydroquinone, together with resin, are reported.

Para-cresol, two meta-xylenenol isomers and mesitol have been oxidized by Cosgrove and Waters (133). Products obtained from para-cresol are stated to be identical with those of alkaline ferricyanide oxidations conducted by Pummerer (105). This formation of biphenyl derivatives appears to be common, except in the case of mesitol. One product identified in the latter reaction is di-[3,5-dimethyl-4-hydroxyphenyl]- methane.

An experiment in hydrogen peroxide oxidation has been reported by Bader (138), in which a molybdate salt is substituted for the usual ferrous compound. This method, used on beta-napthol, produces a more complex product than that of the ferric chloride procedure,[1] namely 4-[2-hydroxynapthyl]-napthoquinone-1,2. It is illustrative of specificity in the actions of different reagents.

Sulfato-cerate. The general use of this oxidant has been described at length (139,140). Further understanding of its action with regard to phenolic compounds, is the topic of this thesis.

Useful application of sulfato-cerate in the quantitative analysis of hydroquinone has been mentioned.[2] Smith, Ruaoff and Wawzonek (14) have discovered that para-hydroxychromans and coumarans behave in similar fashion, yielding substituted para-benzoquinones. Their reaction, carried out in 50 per cent ethanol, can be used for quantitative analysis as well as for preparative purposes.

Mention of phenol sensitivity towards tetravalent cerium in general, has been made by Orlow (40), and by Rao, Rao and Sastri (91).

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[1] This thesis, p. 43.

[2] This thesis, p. 29.

Nitrato-cerate. Solutions of ceric oxide in nitric acid possess a higher oxidation potential than do corresponding sulfuric reagents, and their action on phenol solutions, is noticeably more extensive. Few, if any qualitative differences exist, however (142).

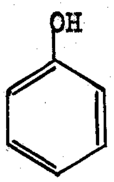
Ceric perchlorate. At present it is believed that cerium forms no complex anion with perchlorate (143) and consequently that this acid solution may be a reagent of somewhat different nature. Its effect on ortho-cresol has been observed by Duke (142). Immediate precipitation of a curdy product occurs, as it does with both sulfate- and nitrato-cerates, but the continuous further attack on this material, also characteristic of the other reagents, proceeds in the perchloric acid at a very much faster rate.

General. Under the the heading of quinone synthesis, Cason (144) has collected a large amount of thoroughly documented information in the oxidation of individual phenols.

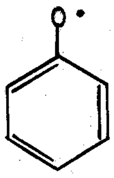
Mechanistic considerations

From the foregoing evidence, it appears that two general types of change may occur in the oxidation of phenols: hydroxylation; and the dehydrogenative coupling of aromatic neuclei. The former may comprise the entire reaction, precede ring cleavage or quinone formation, or take place simultaneously with other processes. Coupling, often involving two molecules only, may be more extensive, and while carbon-carbon linkage between rings is the commoner, aromatic ethers are occasionally met. It seems evident that the resinous materials frequently appearing in phenol oxidations are manifestations of the latter reaction type and that in peroxide reactions substituted phenols show predisposition towards resin formation, in contrast with phenol itself. Sulfato-cerate, on the other hand, acts to produce resins in nearly quantitative yield from monohydric phenols generally, and hydroxylation by this reagent, if it occurs, is not important by comparison.

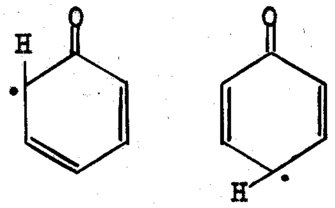
The most far-reaching investigation into the nature of phenolic oxidation has been conducted by Pummerer (103), whose findings conclusively indicate that a dehydrogenation is involved initially. Abstraction of the hydroxyl H-atom is visualized, the phenolic residue retaining an odd electron. Pummerer calls this fragement by the name, aroxyl. Such a molecule might be expected to form a symmetrical dimeric peroxide, but experimental evidence indicates that only insignificant ~~amounts~~ of such compounds arise. The explanation, given by Pummerer, is that the aroxyl radical may become modified spontaneously through simple electronic rearrangement to the so-called keto-methyl structures, the odd electron then appearing at an ortho or para position.



Phenol



Aroxyl
radical

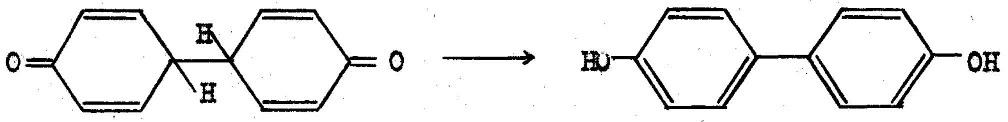


Keto-methyl radicals

Dimerization of these radicals would give rise to carbon-carbon bonding that is observed in biphenyls, while the combination of aroxyl with keto-methyl results in an ether linkage.[1]

The views of Pummerer have been specifically reiterated by Goldschmidt, Schulz, Bernard (123), and by Cosgrove and Waters (133).

In the formation of diphenols, it is of course necessary that a tautomeric shift take place, effecting transfer of the non-aromatic hydrogen atoms to oxygen:



Although keto-methyl dimers have not been isolated in the oxidation of phenol itself, a corresponding substance is actually obtained in the oxidation of anthrol by alkaline ferricyanide (145). That the H-atom shift may occur freely in less ponderous molecules, is evidenced by those reactions in which a phenol arises from the dehydrogenation of hydroaromatic ketones (146).

The question of which hydrogen is actually removed first is not absolutely determined. Ionization of phenol, followed by loss of an electron, is clearly equivalent to the abstraction of hydrogen, and would appear reasonable. Such consideration, especially in terms of alkaline conditions, no doubt influenced Pummerer towards this preference. Cosgrove and Waters (133), however, are rather of the opinion

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[1] Such ideas have explained a number of phenomena, including the inertness of phenolic meta-positions toward electron-seeking reactants. Extending this line of thought has led to the important concepts of the homogeneous mesomer, and resonance stabilization.

that ortho-hydrogen is directly abstracted, and that aroxyl appears as a secondary product after tautomeric shift by the hydroxyl H-atom. Their feeling is based largely on the observed substitution by benzoate radical in the benzoyl peroxide reaction with phenols.[1] It seems more likely, however, that neither mode of dehydrogenation covers all cases of phenol oxidation.

The conjectured involvement of hydroxyl radical in certain oxidizing processes[2], makes clear how one type of phenol oxidation can come about. Hydrogen atom seizure from the nucleus, leaves a trivalent carbon atom, which is subsequently attacked by a second hydroxyl. It is not as easy to understand how the dimerization phenomenon, almost quantitative in ceric oxidations, can proceed to such an extent using the same initial step. Substantial attack by mobile oxidizing fragments as in the first instance, should certainly be noticable. These consequences, of course, do appear to fit many cases, but they indicate for the case of cerium, a different path of reaction.

A formal similarity between hydroxyl radical and fluorine atom has been pointed out by Klemenc (126) who reinforces his idea with theoretical considerations. If this concept be granted, hydrogen peroxide may be thought of as a pseudo-halogen, and its reaction with phenol as analogous to ordinary substitution. Conceivably, the case may extend to the benzoyl peroxide reagent.

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[1] This thesis, p. 41.

[2] This thesis, p. 46.

Interesting new approaches to the problem of substitution are now being made in the study of deuterium exchange reactions with phenols (147). It is probable that out of these may come, in one way or another, further insight into the chemical nature of aromatic compounds and their reactions.

Dehydrogenation of phenols by palladium black, thought by Wieland (115) to proceed in wide applications, has been seriously questioned by Gillespie and Liu (148). The contradictory evidence is strong in theory, but does not satisfactorily explain why a recovery of hydrogen from spent palladium was achieved by Wieland.

The unique phenomenon of pyrogallol oxidation by a variety of reagents may be of small significance to the general problem. But the nature of the purpurogallin product has mystified chemists since its discovery by Girard (149) in 1869. Solution of this riddle is now thought to be accomplished, and the initial stages of the oxidation, as conceived by Critchlow, Haworth and Pauson (150), may be closely compared with those of the beta napthol reaction with hydrogen peroxide and molybdate.[1]

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[1] This thesis, p. 48.

EXPERIMENTAL WORK

Materials and Equipment

The experiments to be described were carried out almost entirely with simple apparatus. A Christian Becker Chainomatic analytical balance was utilized in all weighing operations except those of carbon and hydrogen determination. Such measurements in the latter operation were taken on the Ainsworth microchemical balance. A set of N. B. S. standard weights was used to calibrate effects of the laboratory analytical weights when they rest on the left-hand pan.

Volumetric apparatus, burettes and pipettes, was of the Kimbal Exax brand. Two burettes and a 50 ml. pipette used for dispensing quantitative reagents were calibrated at temperatures near 27° C. by weight of solution delivered. Correction factors so determined, like those previously established for the analytical weights, have been applied to every subsequent measurement.

Colorimetric internal indicators being unsatisfactory in the phenol-cerium oxidations, it proved convenient to employ the bimetallic electrode. Two different electronic instruments were used alternately from time to time, the G. Frederick Smith Electron Beam Sectrometer, and the Fisher Titrimeter. No difference in the behavior of these instruments is possible under the conditions of application, however, since they serve only to amplify potential difference between the electrodes. Their indicating electron ray tubes are of the same type.

The Electron Beam Sectrometer is equipped with an electrode consisting of two straight wires, mounted in a plastic head, and which may be immersed two to three inches in the solutions to be studied. The Fisher Titrimeter, contrarily, incorporates the electrodes with a rotating glass stirrer. This electrode, when used in stationary manner, is entirely too sluggish to be of value, and when rotated by the Fisher motor, does not give sufficient stirring action. An inference drawn from the former circumstances has been that larger electrode area is associated with faster indicating action. With regard to this assumption, a home-made electrode assembly was devised from large elements, eighth-inch wolfram rodding and sixteen gauge platinum wire, the two parts being mounted in a cork. This arrangement gave more satisfactory results with the electron Beam Sectrometer than did its regular electrode, and was equally well suited to the Fisher Titrimeter. Both these instruments were carefully checked against orthophenanthroline indicator, and found to agree within 0.01 ml. of tenth-normal reagent.

Precipitated solids were separated from liquids either by filtration through Pyrex sintered glass of medium aperture, or by centrifugation in an International Clinical Centrifuge. A conventional carbon and hydrogen train on the semi-micro scale was used in the elementary analysis of materials so examined. Melting temperatures employed in the cryoscopic determination of average molecular weights, were obtained by use of the precision melting point apparatus described by Merriam (151), coupled with a Sargent M0450 thermometer, which is graduated in tenths of degrees.

The organic substances investigated in the following experiments are not of reagent grade, but were drawn from various stocks on hand. A number of the latter were from the stores of the organic chemistry division of Iowa State College. Phenol itself, however, came from a fresh source.[1] The cresols, of quality comparable to the Eastman practical, have been redistilled before use. All are liquids, indicating in the cases of the ortho and para compounds, the presence of soluble impurities, probably water in large part. These cresols become tinged with color over a period of time, even when stored in the dark, as has been reported by Gibbs (117). Cresols were stored in, and dispensed from 30 ml. glass-stoppered dropping bottles.

Reagent grade inorganic chemicals and visual indicator have been used throughout: ferric sulfate and potassium thiocyanate of Baker and Adamson; Mohr's salt of Merck; ceric acid sulfate and ortho-phenanthroline monohydrate of the G. Frederick Smith Chemical Co.

Observations

Description of the reaction

Sulfato-ceric acid solutions react instantly, irreversibly and completely with phenol in dilute acid solution and at room temperature, producing flocculent, colored precipitates whose spongy appearance recalls hydrous ferric oxide to mind. Similar reaction has been noted

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[1] Merck and Co., Inc., Rahway, N. J. Merck Silver Label. 98 - 100% phenol.

for other monohydric phenols oxidised and for the dihydric resorcinol.

The procedure, fixed unless otherwise explained, as to add, with brisk mechanical stirring and without delay, a known amount of standard sulfato-cerate to the phenol sample previously dissolved in about 50 ml. of dilute acid; to allow a definite time interval; and finally to back-titrate the excess cerate. Dilute acid used to dissolve the phenol and likewise for making up the redox standards, was prepared throughout the entire series of experiments, as 100 ml. of concentrated sulfuric acid diluted with distilled water to a volume of 1 gallon. The pH of this, and reagent solutions prepared from it, is close to 1.0. Normalities of the cerate oxidant and the ferrous reductant standards are about one tenth.

The addition of 50 ml. of cerate solution to a 0.1 g. carbolic sample according to the method given, causes an immediate blackening, which appears solution-like for a few seconds, but changes shortly to a visibly non-homogeneous condition. The precipitate, a spongy, reticulate solid, settles gradually to the bottom of the vessel after stirring has ceased, and leaves a clear, pale-yellow supernatant liquid. This liquid, when filtered free of the precipitate, was observed to yield a very small additional quantity of precipitated matter after a few days, but whether slow chemical reaction of active materials in residual concentration is represented, or simply the re-agglutination of solids passed by the filter, has not been determined.

Reactions on larger phenol samples, in which all the cerate is consumed at once, show the same initial darkening effect, but a precipitate which becomes progressively lighter in color, approaching a rusty-brown-violet hue, in contrast to the deep brown-black obtained in the conventional procedure. Solid precipitate is formed, even by a few drops of cerate reagent on excess phenol.

Oxidant uptake and precipitate weight as time functions

Data were obtained by the standard method[1] described above, using 50 ml. as the fixed volume of sulfato-cerate, and specified time intervals in the separate runs. Oxidation reactions were carried out in 150 ml. tall-form beakers, and the decantation washing of precipitates in 500 ml. beakers, also of the tall-form variety. Figures 1 and 2 show the general disposition of apparatus employed in the described operations. By using suitable numbers of operations and decanting ratios, dilution effects of about one thousand were secured. It may be stated, however, that the process is tedious, and that as the inorganic matter is leached away, there is increasing tendency for the precipitates to disperse as sols. Particularly is this true of the ortho-cresol precipitates. Recovery of the solids subsequent to their washing, was done by suction filtration. Wads of glass wool placed over the sintered glass filtering surfaces may have facilitated matters. There was some small loss during these manipulations, arising in the passage of peptized solids through the filters and/or dispersion into the decanted liquids.

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[1] This thesis, p. 57.

Figure 1

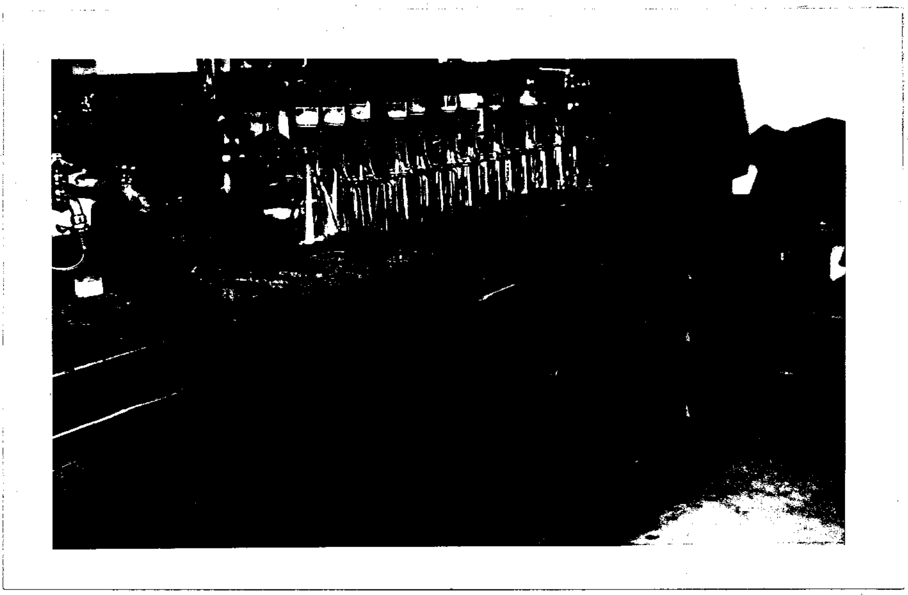

Figure 2

Drying to constant weight required two to four days, and was done in the vacuum desiccator over magnesium perchlorate. It is believed that the product may actually be stable to oven temperatures of 105° C., and that the slight charring observed when oven-drying was tried, might have been brought about by traces of sulfuric acid.

In parallel operations using centrifugation, the data gathered agree substantially with those of filtration. But they are not more consistent, and their tendency to be higher may be partially discounted by consideration of their higher ash content. Colloidal sol formation, moreover, is as serious to one type of operation as it is to the other.

Phenol. Data with regard to this substance are presented in Table 1, page 61.

Ortho-cresol. Data with regard to this substance are presented in Table 2, page 62.

Meta-cresol. Data with regard to this substance are presented in Table 3, page 63.

Para-cresol. Data with regard to this substance are presented in Table 4, page 64.

Generalizations. There appears to be a tendency in these reactions, for the weight of the precipitate to increase for a time, reach a maximum within an hour or less, and then fall continuously. It is possible that destructive oxidation may proceed eventually to the complete conversion of resinous to soluble products with this

Table 1

Phenol: Oxidant Consumption and Precipitate Weight As a Function of Reacting Time

Part a: Filtrative Precipitate Separation

Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Apparent eq. wt.	Ppt. grams	Ppt. wt. ÷ samp. wt.
.1219	1	3.54	29.1	34.4	.1138	.93
.1210	3	3.80	31.4	31.8	.1158	.96
.1260	7	4.10	32.5	30.8	.1220	.97
.1181	15	4.06	34.4	29.1	.1158	.98
.1149	45	4.17	36.3	27.6	.1130	.98
.1008	204	4.28	42.5	23.5	.0994	.98
.0515	912	3.60	70.0	14.3	.0463	.90
Part b: Centrifugative Precipitate Separation						
.1009	1	3.03	30.0	33.3	.0950	.94
.1021	3	3.24	31.7	31.6	.0980	.96
.1000	3	3.16	31.6	31.6	.0976	.98
.0999	30	3.61	36.1	27.7	.1005	1.01

Table 2

Ortho-cresol: Oxidant Consumption and PrecipitateWeight as a Function of Reacting Time

Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Apparant eq. wt.	Ppt. grams	Ppt. wt. ÷ samp. wt.
Part a: Filtrative Precipitate Separation						
.1214	1	2.34	19.3	51.8	.0959	.79
.1198	3	2.38	19.8	50.5	----	----
.1232	7	2.52	20.4	49.0	.1003	.82
.1206	15	2.55	21.2	47.2	.0935	.78
.1249	45	2.83	22.6	44.2	.0911	.73
.1221	180	3.19	26.1	38.3	.0700	.57
.0567	1216	2.16	38.1	26.3	.0082	.15
Part b: Centrifugative Precipitate Separation						
.1003	1	1.92	19.1	52.3	.0830	.83
.0998	1	1.96	19.7	50.7	.0866	.87
.1004	3	1.97	19.6	51.0	.0870	.87
.0997	30	2.14	21.5	46.5	.0819	.82

Table 3

Meta-cresol: Oxidant Consumption and Precipitate Weight as a Function of Reacting Time

Part a: Filtrative Precipitate Separation

Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Apparent eq. wt.	Ppt. grams	Ppt. wt. ÷ samp. wt.
.1212	1	3.26	26.9	37.2	.1180	.97
.1223	3	3.39	27.7	36.1	.1194	.98
.1257	7	3.73	29.7	33.7	.1246	.99
.1265	15	3.92	31.0	32.3	.1271	1.00
.1208	45	4.04	33.4	29.9	.1229	1.02
.1157	180	4.33	37.4	26.7	.1161	1.00
.0532	1003	3.37	63.4	15.8	.0174	.33
Part b: Centrifugative Precipitate Separation						
.0999	1	2.66	26.6	37.6	.1000	1.00
.1004	3	2.89	28.8	34.7	.1033	1.03
.1001	30	3.29	32.9	30.4	.1001	1.00

Table 4

Para-cresol: Oxidant Consumption and Precipitate Weight as a Function of Reacting Time

Part a: Filtrative Precipitate Separation

Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Apparent eq. wt.	Ppt. grams	Ppt. wt. ÷ samp. wt.
.1217	1	1.90	15.6	64.1	.1040	.86
.1259	3	1.97	15.7	63.7	.1072	.85
.1241	7	2.05	16.5	60.6	.1052	.85
.1232	15	2.15	17.4	57.5	.1044	.85
.1219	45	2.35	19.3	51.8	.0979	.80
.1255	180	2.93	23.4	42.7	.0908	.72
.1244	1302	4.71	37.8	26.4	.0689	.55

Part b: Centrifugative Precipitate Separation

Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Apparent eq. wt.	Ppt. grams	Ppt. wt. ÷ samp. wt.
.0997	1	1.58	15.8	63.3	.0867	.87
.0999	3	1.62	16.2	61.7	.0860	.86
.1000	30	1.88	18.8	53.2	.0858	.86

reagent, as it does with ceric perchlorate within short periods. Meta-cresol precipitate, after about 100 hours in excess sulfato-cerate, showed dissolution effects extending far beyond those observed in the shorter experiments. Data on para-cresol, although they show no maximum, do not obviate the probability that such a peak value occurs within the first minute. The ortho-cresol peak is reached shortly after this, and significantly earlier than are the maxima for phenol and meta-cresol precipitates. Dissimilarities of reaction setting these two pairs of substances apart, certainly must be related to the degree of ortho-para substitution existing in the parent phenols.

Gross appearance of the precipitates is changed by prolonged oxidation. Dark-colored materials appear to grow lighter, while the pure-white character of freshly precipitated para-cresol is replaced by light yellow. In addition, the spongy, flocculent, state is changed to a non-reticulate, somewhat muddy one. Destruction of the former appears also to come about by drying, since the powdered resin, re-suspended in water, does not take on its previous character, at least not within a short period. Conversion can be achieved with the alkali-soluble substances, by dissolving them so, and reprecipitating with acid. The resulting matter is indistinguishable from the original.

Behavior of other phenols

Monohydric phenols in the benzene and napthalene series react towards sulfato-cerate in the same way as do phenol and the cresols, so that it seems permissible to describe this oxidative precipitation as a class reaction. An exception in the series mentioned has been observed in the behavior of di-iodotyrosine, which forms a precipitate only under modified conditions. The example of para-hydroxy chromans and coumarans (141) appears also as a variation.[1]

Except for resorcinol, the polyhydric phenols investigated do not show precipitation behavior. Hydroquinone reacts with sulfato-cerate, becoming oxidized to para-benzo-quinone, which is practically stable towards cerate excesses, but which even in the absence of the latter, slowly decomposes to insoluble materials over a period of days. The orange-red color assumed by freshly oxidized catechol solutions is almost certainly due to ortho-benzoquinone formation. Spontaneous changes occurring subsequently are similar to those with the para isomer, but very much faster. It was possible in the catechol experiment, to recover the solid product in usable amounts within one day.

Pyrogallol gives dark coloration, but no precipitate, and little, if any, gas evolution. Salicylic acid and thymol yield typical precipitates of brown and white colors respectively, but these phenols were not further investigated because of their limited solubility. Methyl salicylate as a saturated solution, gives no precipitate in the regular procedure, but in the presence of large quantities of acetic acid, enough material dissolves to give a copious dark brown product.

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[1] It is not unlikely, however, that in sulfuric acid solutions, these compounds may exist in equilibrium with their hydrolysis products. A free hydroquinone would consequently be submitted to the action of the oxidant.

Rather slow dissolution of solid napthol particles was overcome in the following way: A sample, sufficiently small to be dissolved, was treated with a minimum quantity of 5 per cent sodium hydroxide, and the regular acid medium subsequently added with stirring.

Table 5, page 68, contains oxidation and precipitate weight data wherever taken, on these additional phenols, together with a partial repetition on phenol and cresols for the sake of comparison. The repeated data have been taken from the b-sections of Tables 1, 2, 3 and 4, since catechol and resorcinol precipitate weights were obtained in the centrifuging procedure.

Nature of the precipitates

Molecular weight. Since the oxidized phenols are thought not to be homogeneous substances, but mixtures, average molecular weight values must result from the following determinations. Little more than a general order of magnitude is therefore considered as established; not precise information on which to base formulas. In view of the foregoing and also the point of practical convenience, the cryoscopic method was selected.

Apparatus used in making these observations has been referred to.[1] The solvent chosen was benzophenone whose solutions show a molar freezing point depression of 9.8 centigrade degrees (152). Preparation of the mixtures was carried out in midget test tubes 11 x 45 mm., which

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[1] This thesis, p. 55.

Table 5

Oxidation and Precipitate Formation of Various Phenols

Substance	Sample grams	Minutes of time	Mileq. of ox.	Mileq. of ox. per g.	Eq. ox. per mole	Ppt. wt. ÷ samp. wt.	Color of ppt.
Catechol	.0999	1	2.13	21.3	2.34	.51	muddy black*
	.0998	3	2.64	26.4	2.90	.51	
Resorcinol	.1003	1	4.26	42.5	4.68	1.07	dark red
	.1007	3	4.55	45.1	4.97	1.07	
Hydroquinone	.1002	1	1.84	18.4	2.02		no ppt.
	.1008	3	1.85	18.4	2.02		
Pyrogallol	.0997	5	3.06	30.7	3.87		no ppt.
Alpha-napthol	.0304	1	.31	10.1	1.46	---	blue-violet
	.0316	15	.40	12.6	1.81	---	
Beta-napthol	.0312	1	.43	13.7	1.97	---	tan
	.0314	15	.57	18.3	2.63	---	
Para-hydroxy-acetophenone	.1187	1	1.98	16.7	2.27	---	olive-gray
	.1204	15	2.27	18.9	2.56	---	
Di-iodotyrosine	.0747	15	.71	9.5	4.09		no ppt.
Phenol**	.1009	1	3.03	30.0	2.82	.94	dark brown
	.1021	3	3.24	31.8	2.99	.96	
Ortho-cresol	.1003	1	1.92	19.1	2.06	.83	dark brown
	.1004	3	1.97	19.6	2.12	.87	
Meta-cresol	.0999	1	2.66	26.6	2.88	1.00	red
	.1004	3	2.89	28.8	3.11	1.03	
Para-cresol	.0997	1	1.58	15.8	1.71	.87	white
	.0999	3	1.62	16.2	1.75	.86	

*The catechol precipitate appears only after long standing.

**Phenol and cresol data re-submitted from Tables 1,2,3 and 4.

permit easy and effective stirring of the melts. These latter were poured onto watch glasses to crystallize. Two melting-point samples were run simultaneously on each substance tested, one sample coming from the watch glass, and the other from the residue adhering to the inside of the mixing tube. Neither the phenol nor the meta-cresol precipitates could be entirely dissolved in benzophenone, and meta-cresol was considered no further. But an acetone extract of phenol precipitate was tested.

Molecular weight values obtained in the manner described, are presented in Table 6, page 70.

Elementary analysis. There were no deviations from customary procedure in obtaining carbon and hydrogen data. A rapid weighing of the samples was required, however, since they are appreciably hygroscopic. This was accomplished by first determining as closely as possible on the analytical balance, a pre-setting for the micro-chemical instrument which would eliminate the need for changing weights while the sample was on the pan. Materials were protected both before and after weighing in a micro-desiccator containing magnesium perchlorate. Before connection of absorption tubes to the train, the samples were dried in the combustion tube for a few minutes by a current of warm oxygen.

Table 7, page 71, shows the elementary analyses obtained for a number of substances. Some interesting calculations may be based on these data. For instance, it can be shown in terms of a material

Table 6

Apparent Molecular Weights of Oxidized Phenols

Substance	Minutes of time ox.	Sample grams	Benzophenone grams	Melting temp.	ΔT	Molecular weight
Benzophenone				48.4		
Oxidized ortho-cresol	1	.0374	.2019	45.4	3.0	580
				45.6	2.8	620
	3	.0334	.4816	47.2	1.2	540
				47.2	1.2	540
	3	.0467	.2014	44.3	4.1	530
				44.2	4.2	520
Oxidized para-cresol	3	.0403	.2077	44.8	3.6	510
				45.0	3.4	540
	1000	.0274	.1976	45.9	2.5	520
				46.0	2.4	540
Oxidized phenol*	1	.0277	.2200	46.7	1.7	700
				46.8	1.6	740

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* Acetone-soluble fraction of phenol precipitate did not quite dissolve in benzophenone. Molecular weight values shown are therefore known to be high.

Table 7

Elementary Analysis of Oxidized Phenols

Substance	Minutes of time ox.	Per cent carbon on ashless basis	Per cent hydrogen on ashless basis	Per cent oxygen by difference	Per cent ash
Phenol		76.61	6.43	16.96	
Oxydized phenol	1	75.68	4.11	20.21	0.13
Sol. fraction	1	75.58	4.12	20.30	0.39
Oxidized phenol	1000	74.60	3.88	21.52	0.06
Cresols		77.73	7.46	14.80	
Oxidized o-cres.	1	76.47	5.52	18.01	0.28
	3	76.49	5.59	17.92	0.25
Oxidized m-cres.	1	75.01	5.28	19.71	0.22
Oxidized p-cres.	3	77.33	5.94	16.73	0.48
	1000	74.66	5.56	19.78	0.29
	1000	74.61	5.18	20.21	0.29
	5	77.43	6.02	16.55	0.18
Zn-dust dist.	5	80.66	6.44	12.90	0.00
Dihydroxybenzenes		65.47	5.50	29.06	
Oxidized resorcinol	1	52.70	3.51	43.79	1.00
Oxidized catechol	1	56.33	3.43	40.24	4.75

balance on carbon, how large a fraction of the phenol reactants have been involved in precipitate formation; and the figures arrived at for phenol, ortho-cresol, meta-cresol and para-cresol are 95, 86, 96 and 99 per cent respectively. Since the recovery of the solid precipitate is not absolute, the values given should be regarded as minimum fractions.

By calculating the moles of oxygen gained per mole of carbon, there being no gain or loss in the latter, and knowing the number of carbon atoms per unit residue, it becomes possible to show a gain of 0.124 moles of oxygen per reacting molecule in the case of para cresol after 5 minutes of oxidizing time. The three-minute figure for ortho-cresol is 0.231. If the oxygen increase is the result of hydroxylation, it may be seen that one hydroxyl group for each eight residues would be added in para-cresol, and one for four in ortho-cresol. Oxygen per cent, assumed to be a difference between larger figures, should not be considered as a quantity sufficiently exact to establish such a ratio. But rather, it is simply demonstrated that oxygen addition is not the more important of the two types of phenol oxidation so far as the sulfato-cerate reagent is concerned. Evidence is to be presented which indicates that the hydroxyl group is indeed present in the oxidized phenols, though only in small degree.

In the example of the zinc-dust reduction product of para-cresol,[1]

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[1] This thesis, p. 71.

similar arithmetic operations show oxygen loss of 0.284 atom per ring residue. As a rule, the zinc reaction affects the phenolic oxygen preferentially, and it is therefore inferred that the ratio of ring residues to reduced hydroxyl groups may be three or four to one. The significance in this is thought to lie in a reasonable correspondence between para-cresol uptake in oxygen and the phenolic content of its oxidation product. Although quinoid oxygen is known to react with zinc dust in special instances (153), the situation at hand is believed to be the more ordinary case. It is reasonably certain, moreover, that the oxygen remaining in the product is of quinoid character.

Infra-red absorption spectra. Six samples altogether were submitted for observation: one each of oxidized phenol, ortho-cresol, meta-cresol and para-cresol, which had reacted for less than five minutes; and two others of phenol and meta-cresol, which had reacted for about 1000 minutes.

Infra-red spectroscopy on Nujol mulls of these substances, shows that they are very similar in constitution. All the resins tested showed an absorption band at 3.0 microns, the region usually associated with hydroxyl responses. Absence of any absorption at 7.0 microns is taken to indicate that aromatic ring units are not present in numbers. There is absorption by all the samples at 6.1 to 6.3 microns, which probably denotes the quinoid structure. Little contrast was noted between spectra of heavily oxidized specimens and the others.

Characteristic absorption bands of the cresols in the region of 750 - 800 reciprocal centimeters have been observed by Whiffen and Thompson (86) and have been used by these investigators in cresol analysis. With the exception of the para-cresol resin, which absorbs somewhat at 815 reciprocal centimeters, no such absorption was found with the oxidized substances.

Infra-red absorption data were taken by means of a Baird Associates Infra-red Recording Spectrophotometer, Model B.

Solubility in various media. None of the resins is water-soluble or acid-soluble in any sensible degree. Some, however, are dissolved completely by 5 per cent sodium hydroxide, and all are visibly affected in the reagent.[1] Acetic acid and acetone are both good solvents for these substances.

Acidification of their alkaline solutions reprecipitates most of the resins, exceptions being those of resorcinol and catechol. The acetone-soluble component of the phenol resin, dissolved in alkali and titrated with dilute sulfuric, begins to precipitate at pH 7.5. At this stage, it does not appear to flocculate, but shows only as a haziness in the liquid. The haziness increases with lowering of the pH, and agglutination takes place around pH 4.0.

Table 8 indicates results obtained with 5 ml. volumes of various solvents about 10 mg. of solid. The tendency for the resins to become

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[1] Such effects as particle swelling and color change were observed.

Table 8

Solubility in Different Solvents of Oxidized Phenols

Substance oxidized	Minutes in reaction	Ether	Acetone	Benzene	5% NaOH	5% $NaHCO_3$	Conc. H_2SO_4
Phenol	1	partial	partial	no	partial	no	no
	1000	no	partial	no	partial	no	no
Ortho-cresol	1	complete	complete	partial	complete	no	complete (brown)
Meta-cresol	1	partial	partial	no	partial	no	no
Para-cresol	1	large	complete	large	partial	no	complete (brown)
	1000	slight	complete	partial	complete	slight	complete (red)
Para-hydroxy-acetonphenone	1	slight	large	slight	complete	no	complete (brown)
Alpha-napthol	1	slight	large	slight	large	no	partial (brown)
Beta-napthol	1	partial	large	partial	large	no	complete (purple)
Resorcinol	1	slight	slight	slight	partial	slight	no
Catechol	1	slight	partial	slight	partial	slight	complete (brown)

more insoluble with increasing degree of oxidation has been observed in the meta-cresol product as well as in those of phenol and para-cresol. No evidence has appeared which indicates that this phenomenon is not general. Acetone-soluble resins and the evaporated acetone extracts of other resins are also alkali-soluble. Conversely, the resins reprecipitated by acid from sodium hydroxide solutions, are acetone-soluble. Alkali-insoluble materials appear to take up inorganic substances from caustic solutions, as their acquired ash content indicates. No significant amount of ash remains after ignition of the corresponding acetone and ether-insoluble residues.

Other qualities. With the para and ortho-cresol substances as exceptions, the phenolic resins produced by cerium oxidation are nearly infusible, decomposing as they soften. Meta-cresol and phenol resins usually decrepitate under strong heating. In the oxygen atmosphere of the combustion tube, small, incandescent particles may be emitted. Glowing-cinder type of burning is also possible but the correlation of these behaviors with sample history has not been accomplished.

Para-cresol precipitate not only melts, but may actually be distilled at atmospheric pressure. Its liquid is pale yellow. There is some possibility, therefore, that in the zinc-dust distillation of this substance,[1] part of the charge may have distilled through the hot metal without reacting. Precaution against this consisted in overlaying the reaction with a layer of pure zinc dust, and heating

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[1] This thesis, p. 73.

this layer strongly before the reaction mixture itself.

Para-cresol precipitate will also coalesce under boiling water to form a massive biscuit of glassy character.[1] Ortho-cresol resins behave similarly in hot solutions.

A number of the precipitates were tested for peroxide character with iodide and starch. Oxidation of the iodide to iodine, indicated by the intense color of the latter with the starch, constitutes the positive reaction. Since iodide may become oxidized under other influences also, the reaction is not at all specific for peroxides. Quinoid character, plausibly resulting from phenol oxidation, may bring about the same effect, but other structures, conceivably resulting, i.e. hydroxyl, ether and biaryl, would show no oxidizing action in iodide.

Table 9

Reaction of the Oxidized Phenols with Iodide

Material	Reaction
Blank	negative
Tertiary butylperoxide	strongly positive
Ortho-cresol resin	positive
Meta-cresol resin	positive
Para-cresol resin	weakly positive
Para-hydroxyacetophenone	positive
Alpha-napthol	positive

Table 9 contains the results obtained in the so-called peroxide test on several oxidized phenols. Each resin was dissolved in acetic

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[1] Changes leading to the biscuit stage are, in order, shrinking, fissioning and softening. This sequence, except for the softening, is strikingly similar to that occurring as the same substance becomes dry on filters.

acid, containing a little sulfuric, heated, and a dry-ice pellet added. This was followed by a milliliter of saturated potassium iodide and the solution allowed to cool. Continuous exclusion of air from the reaction is accomplished by the evolving carbon dioxide. Dilute, boiled starch was finally mixed in.

Identification of an intermediate

A saturated water solution of phenol at room temperature, 500 ml., was mixed quickly with 300 ml. of tenth-normal sulfato-cerate. The solids produced were recovered by filtration, and extracted with hot water. From the cooled extract, a crystalline substance eventually separated. This material proved by its melting behavior, to be 2,2'-dihydroxybiphenyl, a compound studied at length by Diels and Bibergeil (154). These investigators found that when the substance is crystallized from aqueous solution, it forms as a hydrate with a melting point of 71 - 3°; that further heating drives off the water, after which a re-solidification occurs; and that the dehydrated substance melts at about 109°. The compound obtained by sulfato-cerate oxidation of phenol was observed to melt at 70°, subsequently solidify, and become completely re-liquified at 115°. When treated in acid solution with sulfato-cerate reagent, it gave a precipitate closely resembling that of phenol, but of somewhat lighter color.

Quantitative analysis of phenols

If reaction conditions are maintained sufficiently constant, the sulfato-cerate oxidation of phenols may be employed as a method for their quantitative analysis. It is much more rapid than the Koppeschaar procedure,[1] both as to time consumed per sample, and also the period required before any result can be obtained. Since the cerium reagent is not high in cost, and may actually be regenerated by a simple process (155), cerate oxidimetry is quite inexpensive. Finally, the cerate method is applicable without procedural modification, to any of the simpler phenols mentioned. Whole-number stoichiometry is not observed, however, save in the oxidation of hydroquinone.

In order to reproduce results, it is necessary to follow a selected procedure explicitly, particularly with respect to the time interval in which cerate acts on the organic material. Concentration of excess oxidant is also a sensitive variable, obviating the purely linear relationship between oxidant consumed and weight of substance. There is the temperature factor, of course, and though it is not spectacular, it may, for instance, affect ortho-cresol results to the extent of 1 per cent per degree.

The routine used was as follows: Samples of from .025 to .200 g. were oxidized to obtain the empirical relationship of sample weight against oxidant consumed. Weighing was done by subtracting the weight of a tared 150 ml. tall-form beaker from the combined weight

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[1] This thesis, p. 23.

of beaker and sample. To reduce the effects of moisture absorption and evaporation, sample dispensation and measurement were done without delay. About 50 ml. of dilute sulfuric acid, pH 1.0, were placed in the beaker, and the mechanical stirrer used to hasten the dissolution of the phenol. The stirrer, a glass rod flattened in the last half-inch and running at the full speed of a small motor, was operated continuously throughout the remainder of the experiment. While the dissolution operation progressed, 50 ml. of tenth-normal oxidizing standard were drawn from the calibrated burette into a clean, 125 ml. Erlenmeyer flask. The oxidant was quickly added to the phenol solution from this vessel, residual quantities of reagent being either rinsed into the reaction, or titrated separately. After an exact time interval, 3 minutes in these trials, the tenth-normal reducing solution was run in from a full burette at its maximum flow rate, and sharply arrested as the signal tube shadow reached its widest position. Very close attention is required in the latter manipulation. Data were taken and calculations made in the usual manner, and from the function thus established, it became possible to determine unknown quantities of the given phenol. Tables 10 and 11 show data obtained in the foregoing manner for two common phenols, ortho-cresol and para-cresol.

Because of a tendency for the precipitate to accumulate in thin films on the electrodes, it is necessary between analyses to rinse them with sodium hydroxide solution and to wipe away any insoluble

Table 10

Ortho-cresol: Empirical Relationship of Sample Weight to Oxidant Consumed

Sample grams	Mileq. cerate reduced	Mileq. per gram sample	Temperature
.0238	.523	21.97	27.0
.0460	.984	21.40	27.5
.0645	1.351	20.95	28.0
.0863	1.778	20.60	28.5
.1118	2.278	20.38	28.0
.1499	2.994	19.97	28.5
.1700	3.326	19.57	28.5

Table 11

Para-cresol: Empirical Relationship of Sample Weight to Oxidant Consumed

Sample grams	Mileq. cerate reduced	Mileq. per gram sample	Temperature
.0234	.396	16.93	28.0
.0489	.830	16.97	28.0
.0677	1.143	16.87	28.0
.1071	1.734	16.19	28.0
.1261	2.013	15.97	28.0
.1347	2.166	16.08	28.0

residue. The effect of coatings on the electrode is to seriously delay its response. This electrode problem, not immediately appreciated by the writer, a continuously changing normality of the reducing solution, and temperature changes in the room, prevented the demonstration of any reproducibility better than plus-or-minus 2 per cent.

Duke (156) has reported a method for the stabilization of ferrous sulfate solutions by the use of lead amalgam. The complication of temperature changes should not be as important henceforth as it has been in the past, due to the widening use of air-conditioning. An ultimate precision may therefore be expected which far exceeds the one reported, perhaps on the order of two to three parts per thousand.

An attempt was made to analyze a binary mixture by assuming that two phenols, ortho-cresol and phenol itself, for example, behave in solution together exactly as they would in separate solutions. Knowing the oxidant required per gram of each substance, and also the ratios of precipitate weight to reactant weight, it becomes possible to deduce the composition of the mixture as a function of its total oxidant uptake and precipitate yield. Data and calculated results of this experiment are presented in Table 12.

A fairly constant total weight was used deliberately in order that variations in excess oxidant concentration be minimized. These results, although of poor precision, illustrate the method and show that considerable success might yet be achieved through improvement of the technique.

Table 12

Analysis of a Binary Mixture by a Simultaneous Equation Method

Phenol grams	Ortho-cresol grams	Mileq. ox. consumed	Mileq. ox. calc. by add.	Precipitate grams	Apparent g. phenol	Apparent g. ortho-cresol
---	.1201	2.42	---	.1026	---	---
.0274	.0895	2.53	2.66	.1005	.018	.097
.0291	.0943	2.71	2.81	.1063	.024	.097
.0580	.0607	2.94	3.01	.1035	.060	.054
.0593	.0609	2.95	3.07	.1008	.069	.041
.0896	.0300	3.35	3.40	.1093	.092	.024
.0896	.0318	3.37	3.43	.1114	.090	.030
.1241	---	3.86	---	.1198	---	---

Attempted Oxidation of Di-iodotyrosine to Thyroxine with Sulfato-cerate

The propensity of di-iodotyrosine for slowly becoming air-oxidized to thyroxine, was first observed by von Mutzenbecher (157). Johnson and Tewkesbury (158) have also reported on the phenomenon, confirming it and interpreting the reaction in terms of Pummerer's radical intermediates.[1]

Although the ether linkage appears to be somewhat uncommon in phenol oxidation products, it seems to occur in certain instances (130, 133). There appeared a possibility in view of these considerations that the action of sulfato-cerate on di-iodotyrosine might bring about faster reaction and higher yield.

The first experiment was carried out by the usual procedure. A very rapid darkening occurred, and no precipitation. After the titration of excess oxidant, the solution was extracted with chloroform, and the aqueous color observed to pass into the organic layer. In this solvent, the coloration was violet, indicating that the substance involved is iodine. In about 2 minutes of oxidizing time, the di-iodotyrosine reduced 2.2 equivalents of cerate on a molar basis, and in 15 minutes, 4.1 equivalents.

In a second type of procedure, an amount of tenth-normal oxidant equal to one equivalent per mole of substrate, was added slowly to the di-iodotyrosine solution. There was no precipitate, but a light

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[1] This thesis, p. 50.

brown color appeared. By diluting the cerate reagent about twenty-five times, forming the di-iodotyrosine solution with as dilute acid as possible, and using an oxidant equivalent per mole of di-iodotyrosine of 0.95, a flocculent white precipitate was obtained. It was of apparently similar character to the precipitates of other phenols. Some ether-soluble material remained in solution. This seemed to be of acidic nature, since it dissolved in 5 per cent alkali, but not in bicarbonate. Thyroxine itself is not soluble in ether.

The precipitate became dark colored on standing, and dried to a light brown. It contained a substantial amount of ash. The extract of the fresh precipitate with alcoholic alkali, when acidified with acetic acid, did not yield any thyroxine on standing.

Electron-exchanging Capability of the Meta-cresol Precipitate

The experiments of Cassidy (159,160) on polymerized vinylhydroquinone show that electron-exchanging resins can be made. They are thought to function as semi-quinones whose dismutation is hindered by the chain structure. Since quinoid structure and chains of rings are probably present in the cerate-oxidized phenols, an experiment was devised for determining whether these resins might show electron exchange properties also.

A 10 ml. burette, mounted over a suction flask, was used as a column. It was packed with a glass-wool plug overlaid with a centimeter of pure sand, and finally a mixture of sand and meta-cresol resin. About 3.0 grams of resin were taken, and an equal volume of sand, so that the burette became about two-thirds filled. It was assumed that the sand would allow a freer liquid flow through the column.

Purification of the sand was done by boiling it at length both in nitric acid and in hydrochloric acid. The resin was prepared from 5.41 grams of meta-cresol and an amount of oxidant slightly in excess of the previously-observed three-minute uptake. Concentrations were used which corresponded with those of previous oxidations. Excess oxidant was destroyed after 3 minutes, and the precipitate washed exhaustively. The dried product weighed 5.29 grams.

The column was filled with a 0.12 normal solution of titanous sulfate, allowed to stand overnight, and flushed with dilute sulfuric acid. By the hydrogen peroxide test, titanium showed in the column effluent until about 75 ml. of wash liquid had passed through.

Ten ml. of saturated ferric sulfate in dilute acid were introduced into the column and drawn through, followed by 50 ml. of dilute acid. Thiocyanate gave only a trace of color with the last portion of the liquid. The 60 ml. of iron solution were titrated with standard cerate, and required 0.74 ml. of the tenth-normal reagent. Sixty ml. of dilute acid, also drawn through the column, required less than 0.25 ml. In a repetition of this, corresponding values of 0.66 and 0.26 ml. were obtained. Sixty ml. of ordinary dilute acid were over-titrated by one drop of the cerate, as was also a solution of

10 ml. ferric sulfate diluted with 50 ml. of dilute acid.

It seems apparent from these observations that electron-exchanging capability exists in this resin. Experiments involving the exclusion of air and/or use of a different oxidant might demonstrate the effect more strikingly.

DISCUSSION AND CONCLUSIONS

Value of Sulfato-cerate as an Analytical Reagent for Phenols

It has been shown that the oxidative precipitation of monohydric phenols is a class reaction. By its use, such phenols may generally be distinguished from other organic substances, excepting only the aromatic amines and heterocyclic nitrogen compounds.

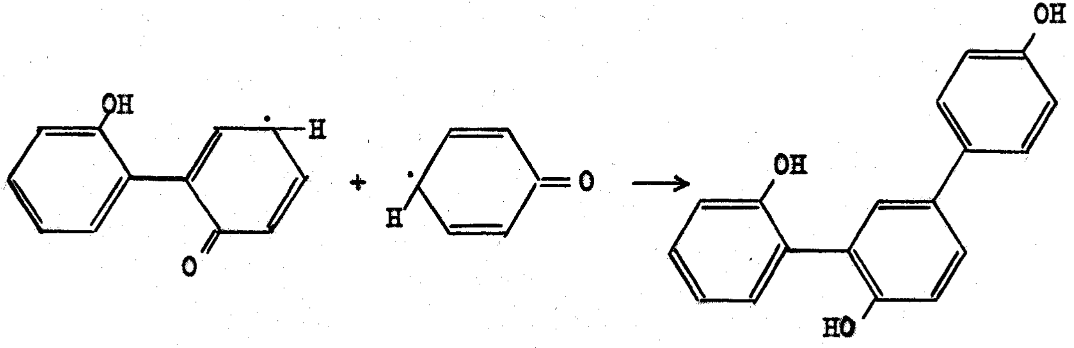
Since few, if any pairs of the precipitated resins are entirely similar with respect to color, mechanical appearance and solubility behavior, the sulfato-cerate reagent allows the easy identification of individual phenols. In addition, some of the polyhydric phenols which did not form precipitates with sulfato-cerate, showed characteristic color changes in solution. There is finally a peculiar reducing capacity in the sulfato-cerate reaction associated with each phenol, provided that experimental conditions are maintained constant. The practicability of quantitative procedures based empirically on sulfato-cerate reduction has been demonstrated, and a possibility of determining binary mixtures suggested.

Unique breadth of application, plus the low cost, stability and handling ease of sulfato-cerate reagents, make probable their ever-widening use in the chemical study of phenols.

Nature of the Reaction

The characteristics which differentiate the sulfato-cerate-phenol reactions most noticeably from other oxidations, are high velocity at room temperature, large yield of one type of product, specificity for phenols, and stability of quinone products towards the reagent. It appears evident, in view of the latter fact, that resin formation resulting from the polymerization of quinones (107) does not explain the cerate phenomena.

Most understandable would be a stepwise buildup of polyphenyl structure by the addition of Pummerer keto-methyls to singly dehydrogenated polynuclear radicals.[1]



Repetition of the process must take place as long as the concentration of keto-methyl radicals is sufficiently high, or until some factor related to molecular size, prevents the cerate from dehydrogenating the polyphenol.

Oxidation of phenols and polyphenols to radical fragments by

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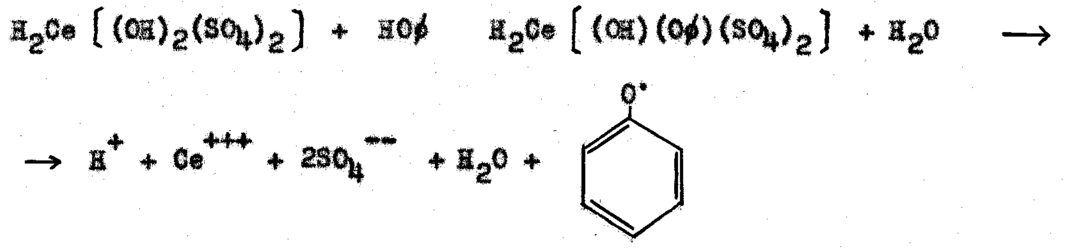
[1] Details in the formation of a diphenol are thought to be represented in this thesis, pages 50, 51.

the cerium reagent is probably accomplished through the momentary combination of phenoxide ion in the cerate complex. In this condition, the phenol becomes oxidized and the cerium reduced by single electron transfer:



$$H_2Ce\left[(OH)_2(SO_4)_2\right] + HO\phi \quad H_2Ce\left[(OH)(O\phi)(SO_4)_2\right] + H_2O \longrightarrow$$

$$\longrightarrow H^+ + Ce^{+++} + 2SO_4^{--} + H_2O +$$

Arguing for such a process is the demonstrated ability of nitratocerate complexes to react with ethanol (161).

If the hydroxyl radical were present during the reaction in considerable concentrations, the building up of chains of rings would be continually terminated by hydroxylation, but in view of the high molecular weights observed, this does not take place extensively. However, since zinc-dust distillation removes oxygen from the one resin so treated,[1] and the infra-red spectra of several resins indicate the presence of hydroxyl groups, it is not unlikely that hydroxylation does occur in some degree.

Quinoid structure, clearly evident in the precipitates by their oxygen content, color, unbroken ring structure and lack of aromatic character, might reasonably arise whenever a pair of hydroxyl groups in the required orientation are attacked simultaneously. This is clearly bound to occur more completely as the supply of keto-methyl

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[1] This thesis, p. 71.

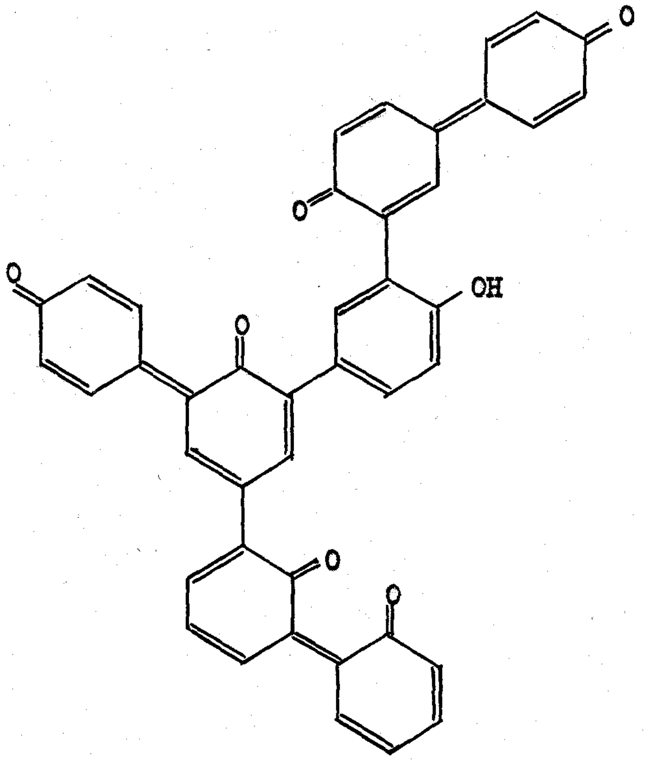
radicals diminishes. If hydroxylation precedes quinone formation, those hydroxyls oriented outside the pattern for quinone formation, will remain intact. It is also conceivable, however, that hydroxyl groups may arise after the quinone configuration has been established (162)(163).

Because ortho and para compounds are so nearly identical in their reactions, it is possible for a variety of branched and unbranched patterns to emerge. One type of product which probably results from the sulfato-cerate oxidation of phenol is illustrated on page 91b.

Suggestions for Further Study

It is believed that the sulfato-cerate reagent shows large promise in the field of phenol analysis, and consequently deserves further investigation. Among the broad regions which the writer feels might profitably be explored are the following:

1. Correlation of precipitate volume after standardized centrifuging, and the amount of phenol. If this measurement could be substituted for the weighing of resins, it would render the determination of binary mixtures by the cerate method more attractive.
2. Investigation of the reaction as carried out in the presence of foreign substances. There are a number of organic classes, stable towards sulfato-cerate, and which probably would not interfere.



Conceivable molecule of oxidized phenol

3. The use of reaction solvents other than dilute sulfuric acid. A number of phenols whose solubility in aqueous media is excessively low, might be identified and analyzed in such solvents as acetic acid.
4. Experimentation with different analytical procedures. It is not impossible that the direct titration of the phenol with cerate might be developed.
5. Further observations on effects of various reaction conditions on molecular weights and elementary analyses of the precipitates. Time, substrate concentration, oxidant concentration and temperature are possible variables.
6. Use of the cerate oxidation to manufacture resins containing a desired functional group.

SUMMARY

A brief account of the discovery and early investigations on phenol itself has been given, and the subsequent rise in commercial importance of this compound traced. Some useful applications of phenols as a class have been enumerated.

Literature bearing on the detection, identification and quantitative analysis of phenols, and on their reactions with various oxidizing agents has been surveyed. Interpretations of phenol oxidation reactions by a number of investigators have been reviewed and generalization attempted.

Observations by the writer on the sulfato-cerate oxidation of phenols have been described. The typical reaction is an almost instantaneous oxidative precipitation whereby the phenol in its near entirety becomes changed to a resinous mass. Only aromatic amines and some heterocyclic nitrogen compounds may be confused with phenols in this phenomenon. Differing colors and solubility behavior of the individual resins may be used to identify them and consequently the phenol out of which they arise.

If temperature, time and concentrations are reproduced, the amount of sulfato-cerate reduced by a given quantity of a phenol, is constant and it is characteristic of the individual substance. By oxidizing known amounts of phenols in a standard procedure and charting the data, unknown quantities of the corresponding substances

may be estimated. Weights of the pure resins may also be used for quantitative analysis. In view of its wide applicability, economy and convenience, the sulfato-cerate reagent is expected to assume increasing importance in phenol chemistry.

The precipitates have been investigated as to average molecular weight, elementary analysis, infra-red absorption spectra and solubility behavior. It has been concluded that the precipitates are essentially polynuclear quinones containing four to seven six-membered rings, and that they arise from the repeated combination of aroxyl radicals. Cerium reagents are unique in the extent to which they force this type of reaction.

Application of the sulfato-cerate reagent to the oxidation of di-iodotyrosine has been tested with the possibility of forming thyroxine as the question. Thyroxine was not observed to be formed under the conditions imposed, however. The resin obtained from the sulfato-cerate oxidation of meta-cresol has been observed to possess a small amount of electron-exchanging capability.

It is suggested that the phenol-sulfato-cerate phenomena may be made increasingly useful through further investigation.

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