PHENOL TESTS

I. A CLASSIFICATION OF THE TESTS AND A REVIEW OF THE LITERATURE

H. D. GIBBS

Senior Chemist, Division of Chemistry, Hygienic Laboratory, United States Public Health Service

INTRODUCTION

Chemists and biologists have found extensive use for tests of phenolic compounds. Compounds of this class are not only widely employed in industry but are distributed in liberal variety throughout the animal and vegetable kingdoms. Many are found by the biologists to occur naturally as products of metabolism; several are used as medicinals or antiseptics.

Their varied importance led to many methods of detection; and, since quantities available were often small, there has been continual effort to develop delicate color tests and wherever possible to make the tests specific. More than 40 of the tests vary in the character of the reagents, and these have been modified, improved and complicated in various ways so that now the tests described in the literature number more than 100.

It is of interest to note that while these tests are designed to detect phenols, very few of the reactions employed involve the hydroxyl group directly. They are brought about, mostly, through the influence of the phenolic group upon the remainder of the molecule, resulting, in a large number of instances, in ring substitution para to the hydroxyl group.

In some cases the hydroxyl group is modified in the course of the reaction, as in the case of oxidation to quinone, the nitroso reaction to oxime, the production of urethans, and in alkylization or acetylation. In practically all of the other tests the hydroxyl group remains intact in the final product of the reaction, subject, naturally in many cases, to the wandering of the labile hydrogen to produce tautomers. The oximes, produced by the nitroso reactions, are examples of the latter. (See second paper of this series.)

In cases where one or more of the hydroxyl groups remain in the final product, the acidic properties of this group determine the conditions under which color appears or changes of color take place.

It is to be noted that many of the tests enumerated for the phenolic group are produced with equal, or greater, facility by the amine group, in which case the reactions are usually much more complicated and quite apt to take place with the amine group directly.

The classification of many of the reactions involved in the phenol tests is simple; in some cases there is doubt regarding the exact character of the color formed, and in other cases no information is available upon which a logical classification can be based. I have endeavored to collect the important literature on the subject, and group the tests for purposes of simplicity and classification according to the chemistry of the reactions involved, wherever expedient.

A few of the tests have been satisfactorily applied on a quantitative basis for certain phenols; but the large majority is not susceptible of quantitative application, is not qualitatively specific for any phenol, and some of those that have been most employed by investigators are not specific for phenols as a class but are also given by many other substances not phenols. In employing such tests it is necessary that the investigator first be advised by some other means concerning the character of the material to be investigated. It is only then that many of the tests can be of any value and capable of intelligent application.

The very extensive literature treating of these tests is so widely scattered throughout chemical and other journals that much of it is not available to biologists. While the most of it is here presented no effort has been made to collect it all. However, it is believed that the references appended to this article together with those cited in the references will prove to comprise a fairly complete list. Since an article on the indophenols is in preparation, which will include extensive references to these compounds, only the necessary references to this very interesting class of substances are here included.

In addition to the literature compilation the chemistry of the first group, the nitroso colors, has been elucidated by the work described in the second paper of this series. This group includes the many and complicated color tests employing dilute nitric acid, nitrous acid, alkyl nitrites and the various reagents of this class containing mercury salts, Millon's, Hoffmann's, Plugge's, Lintner's reagents and others.

In a later paper a new application of the indophenol test will be elucidated. It has been studied quantitatively and has been found to be very delicate for some phenols. This review is presented with the hope that it will be of assistance to chemists and biologists and also for the purpose of giving perspective to the experimental work now in progress and which will be presented in subsequent articles.

CLASSIFICATION OF TESTS

A. Dye reactions

A considerable number of the color reactions employed for the detection of phenols can be classified as producing dyes of one of the following six groups.

1. Nitroso colors
2. Nitro colors
3. Azo colors
4. Di- or triphenylmethane colors
5. Xanthene colors
6. Indophenol colors

These will be considered in the order named.

1. Nitroso colors. Nitrous acid reacts with many phenols with the production of compounds giving colored solutions of nitroso derivatives. In the presence of a condensing agent, such as sulfuric acid, the nitroso compound is condensed with the phenol giving the well known Liebermann, indophenol test.

It has been very difficult to differentiate the various tests where nitrous acid is employed and to classify them definitely. In the case of some indophenol tests both classes of colors are undoubtedly present, and in other cases condensation of the nitroso derivatives may take place in other directions.

In the case of certain tests, Nickel (1890), without experimental evidence, expressed the opinion that red dyes were formed from the nitrosophenols produced in the test, and in the case of salicylic acid Lintner (1900) holds the same view.

Tests employing dilute nitric acid are also described. It seems improbable under the conditions, that the nitric acid is present in sufficient concentration to cause nitration and it appears most probable that the color is due to nitrous acid present in the nitric acid or formed by the reducing action of organic compounds present.

It is interesting in this connection to note the action of nitrogen tetroxide and nitrogen pentoxide. Houston and Johnson (1925) found that the former acts as nitrous acid (nitrosyl nitrate) while Haines and Adkins (1925) found the latter to be an excellent nitrating agent.

The use of nitric acid mixed with sulfuric acid or hydrochloric acid is also described. In the case of sulfuric acid there is produced a nitrating mixture and this test is described under the nitro colors. In the case of hydrochloric acid very active chlorine is liberated and while there may be the effect of nitrous acid on the phenol this test is more fully treated under the halogen tests.

All of these reactions except those definitely belonging to the indophenol or nitro class are described under this heading. This classification is justified as a result of some of the experimental work described in the second paper of this series.

a. Colors formed by dilute solutions of nitrous acid, nitrites (salts of nitrous acid, alkyl nitrites, ethyl nitrite, amylnitrite).

See previous discussion.

b. Colors formed by dilute solutions of nitric acid.

I have found that the use of the ordinary best reagent grade of nitric acid diluted, 3 drops in 10 cc. of water, will give a color with a phenol solution, 2 parts in 1000, when an equal volume of the dilute acid is added. The color which appears on standing 10 or 15 minutes appears the same as that produced by dilute solutions of nitrous acid. (See second paper of this series.)

c. Colors formed by dilute solutions of nitric acid in presence of various salts (mercuric sulphate, etc.).

This test is similar to the preceding except for the catalytic action of the mercury salts.

d. Colors formed by nitric acid and nitrous acid in presence of salts of mercury and some other metals.

In this group is classed the very important and much used Millon's reagent (a nitric acid solution of mercury) made in various slightly modified ways, Hoffmann's reagent (a solution of mercuric oxide in nitric acid with the addition of a trace of nitrous acid), Plugge's reagent (a solution of mercurous nitrate with the addition of some free nitrous acid) and Lintner's reagent (a solution of mercuric nitrate, sodium nitrite, acidified with sulfuric acid).

See second paper of this series.

References

Millon (1849)
Hoffmann (1853)
Meyer (1864)
Griessmayer (1871)
Plugge (1872)
Almén (1877)
Allen (1878)
Hirschsohn (1881)
Eykman (1882)
Fresenius (1883, 1889)
Nickel (1890)
Lintner (1900)
Perkin and Nierenstein (1905)
Bach (1911)
Elvove (1917)
Weiss (1920)
Chapin (1920)
Sen-Cupta (1921)
Salus (1922)
Huerre (1922)
Ware (1925)
Houston and Johnson (1925)
Haines and Adkins (1925)
Ekkert (1925)

2. Nitro colors. a. Nitration test. Many phenols can be nitrated to colored nitro derivatives. There is usually employed for this purpose a nitrating mixture of sulfuric and nitric acids. This reaction is one of the standard tests that has been used for a long time. In the case of phenol, picric acid results and by color comparisons of the acid or of its more highly colored salts with standards the test is made roughly quantitative.

References

Mulliken (1914, pg. 108)
Sen-Gupta (1921)
Huerre (1922)

3. Azo colors. The Peter Griess diazo reaction and the coupling of the diazo derivative with phenols to form dyes has been found to be susceptible to development for its great delicacy as tests for phenols and for that reason has been extensively employed.

a. Diazotized sulphanilic acid coupled with various phenols. Ehrlich made use of diazotized sulphanilic acid and other diazotized amines in testing biological material but Hanke and Koessler first attempted to develop the test on a quantitative basis.

b. Diazotized paranitraniline coupled with various phenols. This test, as applied in a qualitative way, has been very popular but it has remained for Palkin and Wales to add a very valuable contribution in recording the spectroscopic investigations of 45 phenols most encounteed in pharmaceutical preparations, which should render certain the identification of many of these compounds.

References

Ehrlich (1882, 1883, 1884)
Penzoldt and Fischer (1883)
Nickel (1890)
Limpricht (1891)
Amann (1896)
Riegler (1899)
Pauly (1904, 1905)
Formanek (1905, 1908, 1913)
Malacarne (1907)
United States Pharmacopoeia, 9 (1916)
Formanek and Knop (1917)
Chapin (1920)
Fox and Guage (1920, 1922)
Hanke and Koessler (1920, 1922)
Bell (1921)
Moir (1922)
Ellms, Marshall and Phillips (1922)
Theis and Benedict (1924)
Palkin and Wales (1924, 1925)
Wales and Palkin (1926)
Pyman (1926)

4. Di- or triphenylmethane colors. Various methods and reagents have been employed to perform this dye test. They produce brilliantly colored solutions of compounds which, in most cases, I believe should be classified in this group. The characteristics of the colors produced in many of the tests never have been sufficiently investigated, but from the mode of per-forming the tests, dyes analogous to the triphenylmethanes will be produced.

In general the test consists in the condensation of an aldehyde with a phenol. A large number of aldehydes has been employed, such as formaldehyde, acetaldehyde, other alkylaldehydes, methyl glyococoll, vanillin, furfural, benzaldehyde, p-hydroxybenzaldehyde and others.

Other compounds producing reactions comparable to the aldehydes, such as phosgene, iodoform, bromoform, chloroform, chloral, carbon tetrachloride, oxalic acid, dihydroxyacetone, etc., have been employed.

As condensing agents sulfuric acid, hydrochloric acid, alkalies and other substances have been used.

The most generally employed reagents are formaldehyde and sulfuric acid.

a. Marquis' reagent: Formaldehyde and sulfuric acid.

b. Ehrlich's reagent: Benzaldehyde and hydrochloric acid.

c. Guaraschi's test: Chloroform and alkali.

References

Kolbe (1861)
Baeyer (1872)
Guaraschi (1872)
Michler (1876)
Doebner (1878, 1879, 1880)
Nencki and Schmid (1881)
Sarauw (1882)
Nencki and Sieber (1882)
Lustgarten (1882)
Ihl (1885, 1889)
Udránszky (1888)
Schwarz (1888)
Crismer (1888)
Raupenstrauch (1888)
Geigy (1889)
Nickel (1890)
Desesquelle (1890)
Caro (1892)
Lambert (1892)
Marquis (1896)
Hehner (1896)
Barbet and Jandrier (1896)
Endemann (1897)
Melzer (1898)
Deniges (1898, 1909, 1911)
Hartwich and Winckel (1904)
Rhein (1907)
Silbermann and Ozorovitz (1908)
Pouget (1909)
Sanchez (1911)
United States Pharmacopoeia (1916, pg. 619)
Sieburg (1916)
Loele (1920)
Salus (1922)
Gomberg and Snow (1925)

5. Xanthene colors. a. Phthalic anhydride fusion. This test is essentially a fusion of phthalic anhydride with the phenol in presence of a condensing agent. The phenolphthaleins long have been known but the colors of various derivatives were not systematically investigated until the work of Gsell, and Formanek and Knop. The former measured the absorption spectra in the visible region of 20 phenolphthaleins and the latter investigators presented a critical review of the work and also prepared some phenol anthraquinone derivatives.

Many phenols can undoubtedly be thus identified but this means of investigation is limited to cases where a considerable quantity, (e.g., 0.1 g.) of the phenol is available to carry out the fusion.

References

Baeyer (1876)
Mulliken (1914, pg. 107)
Gsell (1916)
Formanek and Knop (1917)
Orndorff and Murray (1917)

6. Indophenol colors. The name "indophenols" was given by Köchlin and Witt to a class of dyes developed by them about 1880; but long before this, about 40 years, colors were produced in various ways which we now recognize as due to indophenols.

These colors can be produced by various reagents applied in a variety of ways and the tests can be made very delicate. The acid solutions of the free indophenols are red while the solutions of the alkali and ammonium salts are intense blue.

It is interesting to note that Parry (1924) ascribes the color produced by Mandelin's reagent (1884), a vanadate in sulfuric acid, to the formation of a vanadium type of indophenol colors $O{:}C_6H_4{:}VH\cdot C_6H_4\cdot OH$.

Previous to the work which will be described in a later paper of this series the tests have not been developed on anything but a qualitative basis. The new procedure depends upon indophenol formation which has been developed to a very delicate quantitative basis.

a. Liebermann test. Concentrated sulfuric acid containing nitrous acid. By this test the phenol is first partially converted to p-nitrosophenol which condenses through the agency of the sulfuric acid, with the phenol to form the indophenol.

Eijkman (1883) and Gutzkow (1889) employed amyl nitrite and sulfuric acid.

b. The simultaneous oxidation of an amine (p-aminophenol) and a phenol by a great variety of oxidizing agents will produce an indophenol. The oxidizing agent most commonly employed is hypochlorous acid.

c. Fluckiger test. This test depends upon the reaction of bromine upon the ammonium salt of a phenol. It produces an intense blue color and while it has not been investigated I believe it should be classed here and that the reaction is due to the bromine oxidation of the ammonium salt of the phenol rather than bromine substitution in the ring, although both may take place. It is well known that many oxidizing agents, including atmospheric air produce this reaction.

d. Quinonechloroimide tests. These tests employ various quinonechloroimides reacting with certain phenols to form indophenols and are fully treated in the experimental part of a later paper.

References

Berthelot (1859)
Lex (1870)
Neubauer (1872)
Salkowski (1872)
Jacquemin (1873)
Rice (1873)
Fluckiger (1873)
Liebermann (1874)
Cotton (1874)
Pollacci (1874)
Almen (1877)
Eijkman (1883)
Hager (1884, 1885)
Waller (1887)
Wurster (1887)
Gutzkow (1889)
Neubauer and Vogel (1890)
Manseau (1901)
Kühl (1905)
Raschig (1907)
Rodillon (1921)
Frieber (1921)
Parry (1921, 1924)

B. Halogen reactions

Halogenation tests have been applied extensively qualitatively and on a quantitative basis for detecting and estimating phenols. In many cases the methods are of considerable value in determining the identity of phenols, when sufficient quantities are available, since precipitates may be formed which can be purified and identified.

a. Iodination. Iodinated compounds of various phenols long have been known and the methods of preparation are numerous; among which may be mentioned the use of iodine dissolved in alkali, iodin in potassium iodide solutions, iodine and mercuric oxide, iodine in sodium phosphate, iodine monochloride, potassium iodide and hypochlorite solution, and arylsulphonhalogenamides.

Cofman (1919) has shown that the active substance in the iodination of phenols is hypoiodous acid, HOI, and that any method for the preparation of hypoiodous acid can be used for the preparation of iodophenols.

As a quantitative method it has proved in most cases unsatisfactory although for some phenols satisfactory methods have been worked out, Emery (1921). See also Volumetric Iodate Methods, Jamieson (1926).

b. Bromination. Brominated derivatives have been employed both for the quantitative estimation and qualitative detection of phenols. As reagents bromates, bromites and free bromine have been employed.

c. Chlorination. The contamination of city water supplies by phenols from by-product coke ovens, and chemical works of various kinds has been evident by the objectionable odor and taste resulting from the chlorination of these waters either by hydrochlorite or free-chlorine according to water works practices. Comparisons of some of the various tests for phenols by Ellms, et al., lead them to the conclusion that the odor and taste tests are the most delicate for the purposes of water investigation.

The so-called euchlorine test employs potassium chlorate and concentrated hydrochloric acid. A reaction produced by a mixture of nitric and hydrochloric acids is classified under this heading since the reagent will generate chlorine. However, the test may well be attributed to the action of nitrous acid. The compounds formed have not been investigated.

Arylsulfonhalogenamides,—chloramine T (p-toluenedisulfochloroamide), halazone (p-sulfodichloraminobenzoic acid), and compounds of the type $Ar \cdot SO_2NXM$ where X = halogen and M = sodium or potassium, have been employed in halogenation, giving colors with various phenols.

Vitali (1892) describes a test employing a reagent consisting of concentrated sulfuric acid into which are put a few crystals of potassium chlorate. On adding a few drops of the solution to be tested there is first developed a green color changing to blue, if phenol is present.

I have tried this test and find that it is given by two drops of an 0.008 M (1:1,300) phenol solution. The mechanism of the reaction has not been investigated but it is natural to attribute it to chlorine dioxide. It may not be correct to list this test under the head of chlorinations but it is placed here for want of a better classification. If the sulfuric acid is contaminated with small quantities of oxides of nitrogen the indophenol reaction must be considered as a possibility.

References

Landolt (1871)
Koppeschaar (1876)
Almén (1877)
Allen (1878)
Hirschsohn (1881)
Waller (1881)
Jacobson (1886)
Vitali (1892)
Kossler and Penny (1893)
Neuberg (1899)
Kahn (1907)
Dehn and Scott (1908)
Bougault (1908)
Skirrow (1908)
Mascarelli (1909)
Mooser (1909)
Neuberg and Hildescheimer (1910)
Liechti and Mooser (1911)
Seidell (1911)
Wilkie (1911)
Hensel (1912)
Schewket (1913)
Mulliken (1914, pg. 109)
Folin and Dennis (1915)
Guglialmelli (1917)
Cofman (1919)
Berthelot and Michel (1919)
Desvernes (1920)
Emery (1921)
MacLean and Thomas (1921)
Ellms and Lawrence (1922)
Heckner (1922)
Ellms, Marshall and Phillips (1922)
Roberts (1923)
Blaque (1923)
Vortmann (1923)
Jamieson (1926)

C. Salts of metals

Under this heading there are classified a large number of tests alphabetically arranged according to the metal employed in the reagent. Attempts to work out the chemistry of the reactions employed have been recorded in the literature in only a few cases.

A most natural arrangement of many of these reagents would place them definitely in the oxidizing class, the most obvious examples of which are, ferric chloride, dichromate, permanganate, etc. While such reagents undoubtedly act as oxidizing agents, the color formation is not to be explained so simply. Colored complexes may be formed with the metallic compounds, as has been definitely shown in the case of iron and titanium, and various condensations may take place with the oxidized phenols forming complex quinone derivatives. A number of the compounds of the metals entering into the reagents produce highly colored derivatives on reduction. In general it may be stated that in almost every case the color of the test is due to the reducing action of the phenol upon the salts of the metal or metals present and that the color of the oxidized phenol is not the predominating color of the reaction. It is therefore evident that in very few cases can these tests be made specific for any phenols and in fact the majority of them is undoubtedly not specific for phenols as a class, since any reducing substance will, in most cases, produce colors in the solutions of the reagents.

Antimony. A sulfuric acid solution of an oxide was employed by Levy (1886, 1887) to test a number of phenols and alkaloids. A number of other metals was also employed in the same way. See arsenic, bismuth, columbium, molybdenum, tantalum, tin, titanium and vanadium.

Arsenic. Angelo (1922) employed disodium arsenate (Na_2HAsO_4) and diammonium phosphate, $(NH_4)_2HPO_4$, either one producing a color when a small crystal is put into a 2 per cent phenol solution and then a small quantity of hydrogen peroxide added. The salts probably act as catalysts for the oxidation. See hydrogen peroxide test.

Guglialmelli (1916, 1917, 1918) devised tests employing arsenotungstic acid and arsenotungstomolybdic acid and compares the delicacy with 20 other of the known reagents. See also Lévy (1886, 1887).

Bismuth. See Levy (1886, 1887).

Cerium. Cerium sulphate gives a color with various phenols and it is stated that phenol can be made a very delicate test for cerium, 1 to 2000. Orlow (1907).

Chromium. Potassium dichromate has been employed as a reagent.

Cobalt. Bellucci and Chincini (1919) report that α-nitroso-β-naphthol gives a blood red color with cobalt compounds, is a very sensitive reagent and can be made the basis of a quantitative, colorimetric method for cobalt. Under certain conditions precipitates are obtained not only with cobalt but with other metals. Nickel (1888); Guglialmelli (1917).

Columbium. See Lévy (1886, 1887).

Gold. Auric chloride gives color reactions with phenols. Gugliamelli (1917); Fresenine (1883); Hirschsohn (1881).

The iron reagents. a. Ferric chloride. The blue color produced by ferric chloride reacting in solutions of many phenols has been a popular test for a long time. However, it is not very delicate. Sarauw (1882). Rashig (1907); Kahn (1907); Almén (1877).

Weinland and Binder (1912) describe certain phenol-iron complexes.

References

Waller (1902)
Sarauw (1882)
Hagar (1884)
Nickel (1890)
Bonanni (1900)
Desmouliére (1902)
Hantzsch and Desch (1902)
Rashig (1907)
Gibbs (1908)
United States Pharmacopoeia (1910)
Wienland and Binder (1912)
Mulliken (1914)

a. Ferric alum. A solution of ferric alum is often employed in place of ferric chloride. United States Department Agriculture Bureau of Chemistry Bulletin No. 107 (1907).

b. Ferricyanide and ferric chloride. Jendrassik's (1923) reagent, consisting of potassium ferricyanide and ferric chloride, was found by Bezssonoff (1924) to be sensitive reagent for o- and p-phenols due to the reducing action of the phenols forming Prussian blue.

c. Ferricyanide and ammonia. This reagent has been employed by Candussio (1900). Pummerer et al. (1922, 1925) isolated a colorless ketone by oxidizing o-cresol with potassium ferricyanide in sodium carbonate solution.

d. Ferrous sulfate in presence of tartrates has been employed by Mitchell (1923), Price (1924) in the quantitative estimation of certain phenols found in galls and tannins.

Manganese. Potassium permanganate in alkaline solution will oxidize many phenols. Mulliken (1914, pg. 79.)

Mercury. Denige's reagent (1898), an acid solution of mercuric sulfate, has been employed by Escaich (1920) to distinguish between α- and β-naphthol, since α-naphthol gives a brilliant color while β-naphthol forms a yellow precipitate.

Millon's reagent, mercury dissolved in nitric acid, and other reagents of the same type containing mercury, are treated under the heading of the nitroso dyes.

Molybdenum. Fröhde's reagent is a solution of molybdic acid in sulfuric acid. Davy (1878), Allen (1878), Guglialmelli (1917), Lévy (1886). For the tungsten-molybdenum phosphoric acid complexes see tungsten.

Nickel. Color compounds of the type $Ni(CN)_2 \cdot NH_3 \cdot C_6H_5 \cdot OH \cdot H_2O$ are described by Hofmann and Höchtlen (1903).

Phosphorous. Angelo (1922) employed diammonium phosphate and hydrogen peroxide in testing phenols. The former probably acts as a catalyst in the oxidation. See hydrogen peroxide test.

Platinum. Platinic chloride in some cases reacts somewhat similarly to gold. Fresenius (1883); Hirschsohn (1881).

Selenium. Levine (1920) states that selenious acid is a sensitive reagent for phenols and is of wide applicability.

Silver. Tollen's reagent, an ammoniacal solution of silver nitrate, is reduced by some phenols, especially many polyphenols. Mulliken (1914, fig. 22); Escaich (1920).

Sodium. Sodium peroxide has been employed as a test by Alvarez (1905).

Tantalum. See Lévy (1886, 1887).

Tin. See Lévy (1886, 1887).

Titanium. Hauser and Levite (1912, 1915) state that titanium salts form stable, colored complexes with phenols when two hydroxyl groups are present in the ortho position. An arseno-titanium reagent has been recommened by Guglialmelli (1917) who also employed a sulphotitanium test. Also see Lévy (1886, 1887); Déniges (1916).

Tungsten. Tungstic acid has been employed in tests for phenols; however, the test most employed has made use of a reagent composed of tungsten and molybdenum complexes with phosphoric acid.

Reagents of this character prepared in many ways and of varying compositions, have been proposed as qualitative and, by color comparison with standards of known composition, quantitative methods for detecting and estimating phenols and many other compounds. This type of test has been extensively used by biologists and others.

Wu (1920) made a study of these complexes and it has been shown that the color reactions are produced by reduction. The reagent prepared in various ways is very sensitive to mild reducing influences. The color reactions are not to be attributed, or at least only in small part to the colored oxidation products of the phenols. The reagent is therefore not specific for phenols or in fact for anything except a reducing influence. Ever since Folin and Denis (1912) proposed this reagent it has been widely employed.

Under the heading of the arsenic reagents there is described Guglialmelli's modification.

References

Folin and Macallum (1912)
Folin and Denis (1912, 1915, 1916)
Johns and Jones (1918)
Benedict and Theis (1918)
Folin and Wu (1919)
Gortner and Holm (1920)
Wu (1920)
Levine (1920)
Tisdall (1920)
Chapman (1921)
Donaldson (1921)
Scott (1921)
Bezssonoff (1921, 1922)
Levine and Burns (1922)
Ellms, Marshall and Phillips (1922)
Rakestraw (1923)
Henningsan (1923)
Goeffon and Nepveux (1923)
Cristol (1924)
Haas and Schlesinger (1924)
Vorce (1925)

Uranium. Uranium salts form colored complexes with phenols. Siemssen (1912); Aloy and Laprade (1905); Aloy and Rabaut (1914).

Vanadium. Mandelin's reagent is a solution of a vanadate in concentrated sulfuric acid.

References

Mandelin (1884)
Lévy (1886)
Bellier (1899)
Parry (1924)

Zinc. Zinc chloride is employed as a condensing agent in producing the phenol phthalein colors. Zinc chloride and zinc sulfate are used by Nickel (1890) in connection with nitrous acid reagents.

D. Tests not classified in the foregoing

a. Acetylation. Acetylation of phenols has been employed in some cases for quantitative measurements. Verley and Bölsing (1902); van Urk (1921).

b. Alkaloidal precipitation. Hesse (1876) found that certain alkaloids formed precipitates with phenol and indicated that these might be employed as tests.

c. Urethan test. Herzog (1907) employed diphenylcarbamylchloride to produce diphenylurethans from phenols and French and Wirtel (1926) made use of alpha-naphthylisocyanate in the formation of urethans. A number of urethans were analyzed and characterized by their melting points.

d. Electrometric titration. Various phenols have been estimated by this method. Kolthoff (1920); Bishop, Kittredge and Hildebrand (1922).

e. Enzyme test. Bourquelot (1906) showed that *Russula delica* contained an enzyme that gave colors with a large number of phenols. Schmalfuss (1924) employed an enzyme from the blood of larvae of *acta caja* to differentiate between many phenols by means of the color formation. Onslow and Robinson (1925) found an enzyme in potato tubers that acted on phenols.

Mamas (1923) found a peroxidase in melanotic tumors that acted on polyphenols when two hydroxyl groups are in the ortho position to each other.

f. Esterification. Various esterification tests can be employed to detect phenols. Hesse (1906) methylated isoborneol as a method of detection.

g. Hydrogen peroxide. Angelo (1922) obtained a fine rose or red color by oxidizing phenol with hydrogen peroxide in presence of diammonium phosphate or disodium arsenate. Without the addition of the salts the color development is much slower. For tests employing sodium peroxide see sodium. Wurster (1887); Kühl (1905).

h. Picrates. Goedike (1893) employed picric acid to precipitate various phenols; phenol, o-cresol, resorcinol, quinol, guaicol and other.

i. Wood test. Runge test. This test depends upon the formation of a blue color in a splinter of wood (usually pine) on treatment of the wood first with phenol and then with concentrated hydrochloric acid. With some phenols the color is red. This test is severely condemned by Khotinskii.

References

Runge (1834)
Dispensatory, U. S. (1870)
Waller (1881)
Tommasi and Tommasi (1881)
Udránszky (1888)
Khotinskii (1917)

DELICACY OF TESTS

Very few of the tests have any great degree of delicacy. The chlorine test as applied to potable waters, is claimed to be the most delicate and that even less than 1 part of phenol in 10,000,000 can be detected by the odor and taste.

Eykman claims 1:2,000,000 for the ethylnitrite test, and Wilkie 1:250,000 for the iodination test. The arsenotungstic, phosphotungstic-phosphomolybdic and the Millon reagents and the azo dye tests are stated to detect 1:1,000,000. The arylsulfonhalogenamides tests may be delicate in the case of β-naphthol, to 1:100,000 and the bromine test to 1:60,000. The ferric chloride test is not claimed to have a greater delicacy than 1:3,000 for phenol while for salicylic acid 1 part in 100,000 may be detected.

Various claims are made for some of the other tests, but it is evident that the delicacy depends not only upon the conditions of the reagent and the solutions of the phenols, but also upon the character of the phenol present. The delicacy of a test that is more or less general for a number of phenols may vary greatly with the different phenols.

BIBLIOGRAPHY

ABDERHALDEN, E. 1911 Biochemisches Handlexikon. 1 Band. Berlin, 533.

ALLEN, H. 1878 Note on molybdic acid as a test-agent. Pharm. J. & Trans. **9**, 74.

ALMÉN, A. 1876 Karbol-och salicylsyreaktioners olika känslighet. Upsala läk. Forhandlingar **11**, 393.

ALMÉN, A. 1877 Die relative Empfindlichkeit der Carbol- und Salicylsaure-reactionen. Arch. Pharm. [3] **10**, 44.

ALOY, J., ET LAPRADE, F. 1905 Sur und réactif des corps à fonction phénol. Bull. soc. chim. [3] **33**, 860.

ALOY, J., AND RABANT, C. 1914 Caractérisation de la morphine et des phenols a l'aide des sels d'uranium. Bull. soc. chim. [4] **15**, 680.

AMANN, J. 1896 Un nouveau procédé de dosage clinique des phenols de l'urine. Rev. medic. Suisse Romande **16**, 657.

ANGELO, B. 1922 Su di ima reazione chemica del fenolo. Arch. farm. sper. **33**, 190.

ARNOLD, C., UND WERNER, G. 1905 Unterscheidung von Phenolen und Kresolen Apoth.-Ztg. **20**, 925.

BACH, H. 1911 Kolorimetrische Bestimmung von Phenolen in Abwassern. Z. anal. Chem. **50**, 736.

BAEYER, A. 1872 Ueber die Verbindungen der Aldehyde mit den Phenolen. Ber. **5**, 25.

BAEYER, A. 1876 Ueber die Verbindungen der Phtalsäure mit den Phenolen. Ann. **183**, 1.

BARBET ET JANDRIER 1896 Différenciation des diverses aldéhydes an moyen des phénols et des divers phénols, an moyen des aldéhydes. Ann. chim. anal. **1**, 325.

BARBET ET JANDRIER 1896 Differentiation of aldehydes by means of phenols and vice versa. Analyst, **21**, 295.

BELL, W. H. 1921 A method for the detection of phenols produced by bacteria. J. Infect. Dis. **29**, 424.

BELLIER, J. 1899 Sur les réactions colorées de l'huile de sesame et sur trois reactions caractéristique nouvelles. Ann. chim. anal. **4**, 217.

BELLUCCI, J. E CHINCINI, A. 1919 I sali complessi interni in analitica quantitativa. Gazz. chim. ital. **49**, II, 187.

BENEDICT, S. R., AND THEIS, R. C. 1918 The colorimetric determination of phenols in the blood. J. Biol. Chem. **36**, 95.

BERTHELOT, 1859 Ueber das aus Anilin und Phensäure entstehende Violett. Repert. de Chim. 284. Through Chem. Zentr. 463.

Berthelot, A., and Michel, M. 1919 Sur l'emploi des sulfochloramides aromatiques comme réactifs. Bull. sci. pharmacol. **26**, 401.

Bezssonoff, N. 1922 Sur les reactions colorées des extraits antiscorbutiques et des polyphénols avec un acide phosphomolybdotungstique. Bull. soc. chim. biol. **4**, 83.

Bezssonoff, N. 1924 Sur la reaction proposee par Jendrassick (1923) pour caracteriser la vitamine B et our ses rapports avec la fonction phénol. Bull. soc. chim. biol. **6**, 35.

Bezssonoff, N. 1921 A simplified method of preparation of the Bezssonoff reagent for vitamin C and some polyphenols. Biochem. J. **17**, 420.

Bishop, E. R., Kittredge, E. B., and Hildebrand, J. H. 1922 Titrations in ethyl alcohol as solvent. J. Am. Chem. Soc. **44**, 135.

Blaque, G. 1923 Les plantes à thymol. Bull. sci. pharmacol. **30**, 201.

Bonanni, A. 1900 Die quantitative Bestimmung des Antipyrins, Tallins und Phenol auf optisohen Wege. Jahrsber. Fortschritte Tierchemie **30**, 122.

Bongault, J. 1908 Sur le procédé de Messinger et Vortmann pour le dosage de quelques phénols. Separation de l'acide salicylique. J. pharm. chim. [6] **28**, 145; Compt. rend. **146**, 1403.

Bourquelot, E. 1906 Sur l'emploi des enzyme comme réactifs dans recherches de laboratoire. I. Oxydases. J. pharm. chim. [6] **24**, 165.

Candussio, G. 1900 Ueber ein neues Reagens auf Phenolverbindungen. Chem. Ztg. **24**, 299.

Caro, N. 1892 Ueber Oxyaurine und Oxyaurincarbonsäuren. Ber. **25**, 939.

Caro, N. 1892 Ueber Oxyaurine und Oxyaurincarbonsäuren. II. Mittheilung. Ber. **25**, 2671.

Chapin, R. M. 1920 The diazometric determination. J. Ind. Eng. Chem. **12**, 568.

Chapin, R. M. 1920 A new method for the determination of phenol in the presence of certain other phenols. J. Ind. Eng. Chem. **12**, 771.

Chapin, R. M. 1921 The determination of cresol by the phenol reagent of Folin and Denis. J. Biol. Chem. **47**, 309.

Charabot, E. 1907 Revue des travaux récents sur les matières odorantes. Mon. sci. [4] **21**, 308.

Chattaway, F. D., and Hill, H. R. 1922 Interaction of diazonium salts and phenols. J. Chem. Soc. **121**, 2756.

Clark, W. M., Cohen, B., and Gibbs, H. D. 1925 Studies on oxidation-reduction. VIII. Methylene blue. Public Health Reports **40**, 1131. (Reprint No. 1017.)

Cofman, V. 1919 The active substance in the iodination of phenols. J. Chem. Soc. **115**, 1040.

Cohen, B., Gibbs, H. D., and Clark, W. M. 1924 Studies on oxidation-reduction. V. Electrode potentials of simple indophenols, each in equilibrium with its reduction product. Public Health Reports **39**, 381. (Reprint No. 904.)

Cotton, S. 1874 Nouvelles réactions colorées du phénate d'ammoniaque au sujet de l'acide érythrophenique. Bull. soc. chim. [2] **21**, 8.

Crismer, L. 1888 Das Resorcin als Reagens auf Chloral und Chloroform. Pharm. Ztg. **33**, 651.

Cristol, P. 1924 Quelques causes d'erreur dans les méthodes de dosage de l'acide urique et des phénol de l'urine par les methodes colorimetriques. Bull. soc. sci. méd. biol. Montpellier **5**, 456.

Davy, E. W. 1878 On a new chemical test for carbolic acid, and its useful applications. Chemical News **38**, 195.

Dehn, W. M., and Scott, S. F. 1908 Some characteristic color reactions produced by sodium hypobromite. J. Am. Chem. Soc. **30**, 1418.

Denigés, G. 1898 Sur les fonctions organiques pouvant se combiner au sulfate mercurique. Cas des acétones. Bull. soc. chim. [3] **19**, 754.

Denigés, G. 1909 Mecanisme des réactions colorées du type resorcinotartrique Bull. soc. chim. [4] **5**, 323.

Denigés, H. 1909 Sur la nature du groupement chromophore dans la réaction résorcinique de l'acide tartrique. Bull. soc. chim. [4] **5**, 19.

Denigés, G. 1909 Théorie des réactions colorées de la dioxyacétone eu milieu sulfurique. Sa généralisation. Compt. rend. **148**, 422.

Denigés, G. 1909 Réactions colorées de la dioxy-acétone. Compt. rend. **148**, 172.

Denigés, G. 1909 Le methylglyoxal reactif general de coloration en chimie analytique. Bull. soc. chim. [4] **5**, 649.

Denigés, G. 1911 Le methylglyoxal, réactif de l'acide salicylique et des es dérivés. Bull. soc. pharm. de Bordeaux. Through Ann. chim. anal. (1912) **17**, 19.

Denigés, G. 1916 Sur une réaction générale des alcaloïdes à fonction phenolique d'origine végétale on animale (morphine et dérivés, cupréin, adrénaline, etc.). Bull. soc. chim. [4] **19**, 308.

Desesquelle, E. 1890 Sur un mode recherche des phénols dans les urines. Compt. rend. soc. biol. [9] **2**, 101.

Desmouliere, A. 1902 Interpretation de l'action du perchlorure de fer sur l'acide salicylique, le salicylate de methyle, l'hydrure de salicyle et quelques autres composes phenolique. J. Pharm. chim. [6] **16**, 241.

Desvergnes, L. 1920 Method rapide d'analyse des acides phénolsulfoniques. Ann. chim. anal. [2] **2**, 211.

Dispensatory of United States 1870 13th ed., 342.

Dobiner, P. 1901 Bericht uber die Fortschritte der analytischen chemie. III. Chemischen Analyse organischer Körper. Ueber die Anwendung von Formaldehyde als Reagens auf Phenole berichtet Endemann. Z. anal. Chem. **40**, 667.

Doebner, O. 1878 Ueber die Bildung von Farbstoffen durch Einwirkung von Benzotrichlorid auf Phenole und tertiäre aromatische Basen. Ber. **11**, 1236.

Doebner, O. 1879 Über die Verbindungen des Benzotrichlorids mit Phenolen und tertiaren aromatischen Basen. II. Mittheilung. Ber. **12**, 1462.

Doebner, O. 1880 Ueber die Verbindungen des Benzotrichlorids mit Phenolen und tertiaren aromatischen Basen. III. Mittheilung. Ber. **13**, 610.

Donaldson, W. 1921 Detection of phenols in water. J. Ind. Eng. Chem. **13**, 848.

Ehrlich, P. 1882 Ueber eine neue Harnprobe. Z. klin. Med. **5**, 285.

Ehrlich, P. 1883 Einige Worte über die Diazoreaction. Deut. Med. Wochschr. **9**, 549.

Ehrlich, P. 1883 Ueber eine neue Harnprobe. Charite-Ann. **8**, 140.

Ehrlich, P. 1884 Ueber die Sulfodiazobenzol-Reaction. Deut. Med. Wochnschr. **10**, 419.

Ekkert, L. 1925 Noch eine Farbenreaktion der salpetrigen Saure und der Salpetersaure. Pharm. Zentralhalle **66**, 733.

Ellms, J. W., and Lawrence, W. C. 1922 The causes of obnoxious tastes and odors sometimes occurring in the Cleveland water supply. J. Am. Water Assoc. **9**, 463.

Ellms, J. W., Marshall, L. A., and Hillips, W. 1922 A discussion of the merits of recently developed tests for small amounts of phenolic compounds sometimes found in public drinking water supplies. Second Annual Report, Ohio Conference on Water Purification, 152.

Elvove, E. 1917 A colorimetric method for the estimation of the cresol or phenol preservative in serums. Hyg. Lab. Bull. **110**, 25.

Emery, W. O. 1921 Studies in synthetic drug analysis. VIII. Estimation of salicylates and phenol. J. Ind. Eng. Chem. **13**, 538.

Endemann, H. 1897 Formaldehyde as a reagent. Bull. Pharm. (Detroit) **11**, 365.

Escaich, A. 1920 3° Recherche du phenol ordinaire et de l'aniline. 4° Distinction entre le naphtol- et le naphtol-. J. pharm. chim. **22**, 140.

Eykman, J. F. 1882 Nitrous ether as a sensitive reagent for carbolic acid. New Remedies **11**, 340.

Fenton, H. J. H., and Barr, G. 1908 Some colour-reactions of organic acids with phenols. Proc. Camb. Phil. Soc. **14**, 386.

Fluckiger, F. A. 1873 Reactionen auf Kreosol und Phenol. Arch. der Pharm. cciii, 30.

Folin, O., and Denis, W. 1912 On phosphotungstic-phosphomolybdic compounds as color reagents. J. Biol. Chem. **12**, 239.

Folin, O., and Denis, W. 1915 A colorimetric method for the determination of phenols (and phenol derivatives) in urine. J. Biol. Chem. **22**, 305.

Folin, O., and Denis, W. 1916 The relative excretion of phenols by the kidneys and by the intestine. J. Biol. Chem., **26**, 507.

Folin, O., and Macallum, A. B. 1912 On the blue color reaction of phosphotungstic acid (?) with uric acid and other substances. J. Biol. Chem. **11**, 265.

Folin, O., and Wu, H. 1919 A revised colorimetric method for determination of uric acid in urine. J. Biol. Chem., **38**, 459.

Formánek, J. 1905 Die qualitative Spektraanalyse anorganische und organischer Körper. Berlin 2. Aufl.

Formánek, J. (unter Mitwirkung von E. Grandmougin) 1908–1913 Untersuchung und Nachweis organischer Farbstoffe auf spektroskopischem Wege. I. Teil. 2 Aufl. (1905) Berlin. II. Teil 1911 und (1913) Berlin.

Formánek, J., und Knop, J. 1917 Über den Nachweis der Phenole auf spektroskopischem Wege. Z. anal. Chem. **56**, 273.

Fox, J. J., and Guage, A. J. H. 1920 Note on the determination of tar acids in drainage from tarred roads. J. Soc. Chem. Ind. **39**, 260T.

Fox, J. J., and Guage, A. J. H. 1922 The determination of tar acids and tar bases in road drainage and mud. J. Soc. Chem. Ind. **41**, 173T.

French, H. E., and Wirtel, A. F. 1926 Alpha-naphthylisocyanate as a reagent for phenols and aliphatic amines. J. Am. Chem. Soc. **48**, 1736.

Fresenius, W. 1889 Chemische analyse organischer Körper. Z. anal. Chem. **28**, 244.

Frieber, W. 1921 Zum Nachweis von Phenol in Bakterienkulturen. Centr. Bakt. Parasitenk. I. Abt. Orig. **86**, 58. Abs. Bact. **5**, 383.

Geigy & Co., J. R. in Basel 1889 Verfähren zur Dorstellung beizenfärbender Triphenylmethanfarbstoffe. D.R.P. No. 49,970.

Gibbs, H. D. 1908 Methyl salicylate. I. The separation of salicylic acid from methyl salicylate and the hydrolysis of the ester. Philippine J. Sci. **3**, A, 101.

Gibbs, H. D., Cohen, B., and Cannan, R. K. 1925 Studies on oxidation-reduction. VII. A study of dichloro substitution products of phenol indophenol. Public Health Reports **40**, 649. (Reprint No. 1001.)

Goedike, R. 1893 Sur les combinations de l'acide picrique avec les phénols. Arch sciences biol. (St. Petersburg) **2**, 422.

Goiffon, R., et Nepveux, F. 1923 Appréciation colorimétrique des phenols urinaires. Compt. rend. soc. biol. **89**, 1213.

Gomberg, M., and Snow, H. R. 1925 The condensation of carbon-tetrachloride and phenol: aurin. J. Am. Chem. Soc. **47**, 198.

Gortner, R. A., and Holm, G. E. 1920 The colorimetric estimation of tyrosine by the method of Folin and Denis. J. Am. Chem. Soc. **42**, 1678.

Griessmayer, V. 1871 Ueber das Verhalten von Stärke und Dextrin gegen Jod und Gerbsaure. Ann. **160**, 40.

Gsell, H. 1916 Die Spektralanalytische Identifikation der Phenole. Z. anal. Chem. **55**, 417.

Guaraschi 1872 Correspondeuzen aus Florenz. Ber. **5**, 1055.

Guglialmelli, L. 1916 El acido arsenotungstico como reactivo de los phenoles. Anales soc. quim. Argentina **4**, 119.

Guglialmelli, L. 1916 El acido arsenotungsticomolibdico reactivo de los fenoles. Anales soc. quim. Argentina **4**, 183.

Guglialmelli, L. 1917 Un método general de dosimetria de los phenoles en los aceites esenciales. Anales soc. quim. Argentina **5**, 11.

Guglialmelli, L. 1917 Caracterization de los naftoles. Una nueva γ sensible reaccion del α-naftol. Anales. soc. quim. Argentina **5**, 97.

Guglialmelli, L. 1918 Los complejos arsenotungstico γ arsenotungstomolibdico como reactivos de las aminas fenolicas. Anales. soc. quim. Argentina **6**, 185.

Gutzkow, P. 1889 Farbenreactionen einiger Phenole und ihre Verwendung für die qualitative Analyse. Pharm. Ztg. **34**, 560.

Haas, G., and Schlesinger, E. F. 1924 Über den quantitativen Nachweis von freiem Phenol und Kresol in kleinen Blutmangen und seine prognostische Bedeutung bei Vergiftungsfällen. Arch. exp. Path. **104**, 56.

Hagar, H. 1884 Nachweis der Salpetersäure und Salpetrigsäure, der Nitrate und Nitrite, Neue Reactionsmethoden. (Mit theilweiser Rucksicht auf die Guttularmethode.) Pharm. Zentralhalle 25, N.F. 5, 289.

Hagar, H. 1885 Diphenylamin und krystall. Phenol als sehr scharfe Reagentien auf Nitrate, Nitrite, Salpetersäure und Salpeterigsaure. Pharm. Zentralhalle **26**, N.F. 6, 277.

Hagar, H. 1885 Napthol unter Beihülfe der Schwefelsaure ein scharfes Reagens auf Salpetersäure, Salpetrigsäure und freies Chlor. Pharm. Zentralhalle **26**, N.F. 6, 353.

Haines, L. B., and Adkins, H. 1925 The reaction of certain organic compounds with nitrogen pentoxide. J. Am. Chem. Soc. **47**, 1419.

Hanke, M. T., and Koessler, K. K. 1920 Quantitative colorimetric determination of tyrosine and tyramine (p-hydroxyphenylethylamine) and other phenols. J. Biol. Chem. **41** (Proc.) xlix.

Hanke, M. T., and Koessler, K. K. 1922 Studies on proteinogenous amines. XIV. A microchemical colorimetric method for estimating tyrosine, tyramine and other phenols. J. Biol. Chem. **50**, 235.

Hanke, M. T., and Koessler, K. K. 1922 Studies on proteinogenous amines. XV. A quantitative method for the separation and estimation of phenols including phenol, o-, m-, and p-cresol, p-oxyphenylacetic, p-oxyphenylpropionic and p-oxyphenylplactic acids, tyrosine, and tyramine. J. Biol. Chem. **50**, 271.

Hantzsch, A., und Desch, C. H. 1902 Ueber farbige organische Ferriverbindungen. Ann. **323**, 1.

Hartwich, C., und Winckel, M. 1904 Ueber das Vorkommen von Phloroglucin in Pflanzen. Arch. Pharm. **242**, 462.

Hauser, O., und Levite, A. 1912 Uber das Verhalten von Phenolen, Naphtholen und Phenol-carbonsäuren gegen vierwertiges Titan. Ber. **45**, 2480.

Hauser, O., und Levite, A. 1915 Uber das Verhalten von Phenolen, Naphtholen und deren Carbonsäuren gegen vierwertiges Titan. Ber. **48**, 213.

Hechmer, C. A. 1922 The probable formation of phenolic compounds by a chlorinated water in contact with a coal tar paint. J. Am. Water Works Assoc. **9**, 319.

Hehner, O. 1896 The detection of formalin. Analyst **21**, 94.

Hemmingsen, C. 1923 The determination of various monohydric phenols by the phenol reagent of Folin and Denis. Ind. Eng. Chem. **15**, 406.

Herzog, J. 1907 Diphenyl-harnstoffchloride als Reagens für Phenole. Ber. **40**, 1831.

Herzog, J. 1907 Diphenylharnstoffchlorid als Reagens für Phenole. Ber. pharm. Ges. **17**, 223.

Hesse, A. 1906 Ueber Pinen-chlorhydrat und Camphenchlorhydrat. Ber. **39**, 1127.

Hesse, O. 1876 Ueber einige Verbindungen von Schwefelcyanwasserstoff mit den wichtigeren Chinaalkaloïden. Ann. **181**, 48.

Hirsch, A. 1880 Ueber das Chinonchlorimide und änliche Substanzen. Ber. **13**, 1903.

Hirschsohn, E. 1881 Comparative experiments on the behavior of thymol and carbolic acid towards certain reagents. Pharm. J. and Trans. [3] **12**, 21.

Hoffmann, R. 1853 Reaction auf Leucin und Tyrosin. Ann. Chem. Pharm. **87**, 123.

Hofmann, K. A., und Höchtlen, F. 1903 Abnorme Verbindungen des Nickels. Ber. **36**, 1149.

Houston, B., and Johnson, T. B. 1925 Nitrogen tetroxide as a reagent for diazotization. J. Am. Chem. Soc. **47**, 3011.

Huerre, R. 1922 Quelques reactions de l'acide azotique sur les phenols et les diethers de la pyrocatechine et de l'homopyrocatechine. Bull. sci. pharmacol. **29**, 180.

Ihl, A. 1885 Phenole als reagentien für Kohlenhydrate. Chem. Ztg. **9**, 231.

Ihl, A. 1889 Farbenreactionen einiger ätherischer Oele. Empfindliche Reagentien für einige atherische Oele. Chem. Ztg. **13**, 264.

Jacobson, W. 1886 Ueber den Nachweis des Phenols im Thierkörper. Z. anal. Chem. **25**, 607.

Jacquemin, E. 1873 Acide érythrophenique, réaction monvelle du phénol et de l'aniline. Compt. rend. **76**, 1605.

Jamieson, G. S. 1926 Volumetric iodate methods. Chem. Catalogue Co. Inc.

Jendrassik, A. 1923 A color test for water soluble B. J. Biol. Chem. **57**, 129.

Johns, C. A., and Jones, D. B. 1918 The determination of tyrosine in proteins. J. Biol. Chem. **36**, 319.

Kahn, J. 1907 Bericht des Ansschusses betreffs Verfälschungen und Substitutionen. Deutsch-Amerik. Apoth. Ztg. **28**, 67.

Khotinskii, E. S. 1917 The so-called pyrrole reaction. J. Russ. Phys. Chem. Soc. **49**, 1, 149.

Kolbe, H. 1861 Vermischte Notigen. I. Rother Farbstoff aus Kreosot. Ann. **119**, 169.

Kolthoff, I. M. 1920 Die konduktometrische Titration von Phenolen. Z. anorg. allgem. Chem. **112**, 187.

Koppeschaar, W. F. 1876 Maas analytische Bestimmung des Phenols. Z. anal. Chem. **15**, 233.

Kossler, A., und Penny, E. 1893 Ueber die maass analytische Bestimmung der Phenole im Harn. Zeit. physiol. Chem. **17**, 117.

Kühl, H. 1905 Mitteiling über das Phenol. Pharm. Ztg. **50**, 1001.

Lambert, A. 1892 Sur une reaction des phenols. L'Union pharm. **33**, 17.

Landolt, H. 1871 Bromwasser als Reagens auf Phenol und verwandte Körper. Ber. **4**, 770.

Levine, V. E. 1920 A new color reaction for phenols based upon the use of selenious acid. Science **52**, 207.

Levine, V. E. 1920 The action of proteins on the phenol reagent of Folin and Denis. Science **52**, 612.

Levine, V. E., and Burns, B. C. 1922 The reaction of the molybdenum and tungstic reagents of Folin. J. Biol. Chem. **50**, (Proc.) liv.

Lévy, L. 1886 Sur quelques réactions colorées des acides titanique, niobique, tantalique, stannique. Compt. rend. **103**, 1074.

Lévy, L. 1886 Sur quelques réactions colorées des acides arsenique, vanadique, molybdique et arsenieux, ainsi que des oxydes d'antimoine et de bismuth. Compt. rend. **103**, 1195.

Lévy, L. 1887 Sur quelques réactions colorées des acides titanique, niobique, tantalique et stannique. J. pharm. chim. [5] **15**, 70.

Lex, R. 1870 Ueber einige neue Reactionen des Phenols. Ber. **3**, 457.

Liebermann, C. 1874 Ueber die Einwirkung der salpetrigen saure auf Phenole. Ber. **7**, 247.

Liebermann, C. 1874 Ueber die Einwirkung der salpetrigen Säure auf Phenole. Ber. **7**, 1098.

Liechti, P., und Mooser, W. 1911 Zur Bestimmung der Phenole in Rinderharn. Z. physiol. Chem. **73**, 365.

Limpricht, H. 1891 Über einige Azo verbindungen. Ann. **263**, 224.

Lintner, C. J. 1900 Ueber Mercurisalicylsaure und die Millon'sche Reaction. Z. angew. Chem. 707.

Loele, W. 1920 Die Phenolreaktion (Aldaminreaktion) und ihre Bedeutung für die Biologie. Wiener klin. Wochnschr. **33**, 1071.

Lührig, H., and Sartori, A. 1910 Jahrsbericht des chemischen Untersuchungsamtes der Stadt Breslau. April 1909 bis 31 März 1910. Through Chem. Ztg. **34**, 28 (1910).

Lustgarten, S. 1882 Über den Nachweis von Iodoform, Naphtol und Chloroform in thierischen Flüssigkeiten und Organen. Monatsh. **3**, 715.

MacLean, I. S., and Thomas, E. M. 1921 Observations on abnormal iodine values, with special reference to the sterols and resins. Biochem. J. **15**, 319.

Malacarne, M. 1907 Beitrag zum Nachweis der empyreumatischen Substauzen im Essig. Giorn. farm. chim. **56**, 49.

Mandelin, K. F. 1884 Pharm. Z. fur Russland. **22**, 345.

Manseau 1901 Neue Methoden zum qualitativen Nachweise und zur quantitativen Bestimmung der Carbolsäure. Bull. soc. pharm. **41**, 117.

Marquis, E. 1896 Ueber den Berbleib des Morphins im Organismus der Katse. Arb. d. Pharmakol. Inst. zu Dorpat herausgegeben von R. Kobert **14**, 117, Stuttgart.

Mascarelli, L. 1909 Sul dosamento del fenolo. Gazz. chim. ital. **39**, 180.

Mawas, J. 1923 Action des ferments oxydants des tumeurs mélaniques de la choroïde sur les phenols et leurs dérivés. Compt. rend. soc. biol. 88, 263.

Melzer, H. 1898 Beitrage zur forensichen Chemie. I. Nachweis von Phenol und Bittermandelöl (Benzaldehyd). Z. anal. Chem. **37**, 347.

Merk's Reagenzien-Nerzeichnis 1924 5th ed., Darmstadt.

Messinger, J., and Vortmann, G. 1890 Massanalytische Bestimmung der Phenole. Ber. **23**, 2753.

Meyer, L. 1864 Ueber die Hoffmann'sche Reaction auf Tyrosin. Ann. **132**, 156.

Michler, W. 1876 Synthese aromatischer Ketone mittelst Chlorkolenoxyd. Ber. **9**, 716.

Millon, E. 1849 Sur un réactif propre aux composes proteiques. Compt. rend. **28**, 40.

Mitchell, C. A. 1923 The colorimetric estimation of pyrogallol, gallotannin and gallic acid. Analyst **48**, 2.

Moir, J. 1922 A sensitive test for phenols. J. So. African Chem. Inst. **5**, 8.

Mulliken, S. P. 1914 A method for the identification of pure organic compounds. New York **1**, 87.

Neisser, M. 1921 Ueber Indol- und Phenolbildung durch Bakterien. Münch. Med. Wochschr. **68**, 1384.

Neubauer, C. 1872 Chemische Analyse organischer Körper. I. Qualitative Ermittelung organischer Körper. Ueber die Lex'sche Ammoniak-Chlorkalk-Reaction auf phenol. Z. anal. Chem. **11**, 316.

Neubauer, C., and Vogel, J. 1890 Analyse des Harnes 9 Auf. I. Abt. Weisbaden 78, 355.

Neuberg, C., and Hildescheimer, A. 1910 Die Bestimmung der Phenole im Rinderharn. Biochem. Z. **28**, 525.

Nencki, M., und Schmid, W. 1881 Ueber die Verbindungen der ein- und zweibasischen Fettsäuren mit Phenolen. J. prakt. Chem. [2] **23**, 549.

Nencki, M., and Sieber, N. 1882 Untersuchungen über die physiologische Oxydation. J. prakt. Chem. [2] **26**, 1.

Nickel, E. 1890 Die Farbenreactionen der Kohlenstoffverbindungen. 2nd Ed. Hermann Peters. Berlin.

Nölting, E., und Kohn, O. 1884 Ueber Azo- und Disazoverbindungen der Kresole. Ber. **17**, 358.

Official and Provisional Methods of Analysis. 1907 U. S. Dept. Agr. Bur. Chem. Bull. 107.

Onslow, M. W., and Robinson, M. E. 1925 VIII. The oxidation of certain parahydroxy compounds by plant enzymes and its connection with "tyrosinase." Biochem. J. **19**, 420.

Orlow, N. A. 1907 Ceroxyd als Reagens auf Phenole. Z. Oesterr. Apoth. Ver. **45**, 340.

Orndorff, W. R., and Murray, R. R. 1917 A new class of phthaleins—mixed phthaleins—formed by heating p-hydroxy benzoyl-6-benzoic acid with phenol. J. Am. Chem. Soc. **39**, 679.

Palkin, S., and Wales, H. 1924 Identification of phenols by means of the spectroscope. J. Am. Chem. Soc. **46**, 1488.

Palkin, S., and Wales, H. 1925 Azo dyes from alkaloids of ipecac root and their identification by means of the spectroscope. J. Am. Chem. Soc. **47**, 2005.

Palkins, S., and Wales, H. 1926 Dyes from the alkaloids of Ipecacuanha. A reply. J. Am. Chem. Soc. **48**, 836.

Parry, W. 1924 A color reaction for phenols. Giorn. farm. Chim. **72**, 245.

Pauly, H. 1904 Über die Konstitution des Histidins. Z. physiol. Chem. **42**, 508.

Pauly, H. 1905 Über die Einwirkung von Diazoniumverbindungen auf Imidazole. Z. physiol. Chem. **44**, 159.

Pelkan, K. F. 1922 The physiology of the phenols. I. A quantitative method for the determination of phenols in the blood. J. Biol. Chem. **50**, 491.

Penzoldt F., und Fischer, E. 1883 Neue Reaktion der Aldehyde. Ber. **16**, 657.

Perkin, A. G. 1905 Some oxidation products of the hydroxy benzoic acids and the constitution of ellagic acid. Part I. Trans. Chem. Soc. **87**, 1412.

Pharmacopoeia of the U. S. 1916 9th Revision. P. Blakiston Son & Co. Philadelphia.

Pinerua, E. y Alvarez 1905 A general colour reagent of the poly phenols, their isomers, and higher organic compounds. Chem. News **91**, 125.

Plugge, P. C. 1872 Eine neue Reaction auf Carbolsäure. Z. anal. Chem. **11**, 173.

Pollacci, E. 1874 Reattivi vecchi e reattivi nuovi del fenolo ordinario. Gazz. chim. ital. **4**, 8.

Pougnet, J. 1909 Un réactif général des phénols. Bull. sci. pharmacolog. **16**, 142.

Price, P. H. 1924 An attempt to extend Mitchell's colorimetric method to the estimation of catechol tannins. Analyst **49**, 361.

Pummerer, R., Melamed, D., und Puttfarckon, H. 1922 Die Dehydrierung von p-Kresol (VII. Mitteilung über die Oxydation der Phenole. Ber. **55**, 3116.

Pummerer, R., Puttfarcken, H., und Schopflacher, P. 1925 Die Dehydrierung von p-Kresol (VIII. Mitteilung über die Oxydation der Phenole.) Ber. **58**, 1808.

Pyman, F. L. 1926 Dyes from the alkaloids of Ipecacuanha. J. Am. Chem. Soc. **48**, 836.

Rakestraw, N. W. 1923 A quantitative method for the determination of phenols in blood. J. Biol. Chem. **56**, 109.

Raschig, F. 1907 Vorlesungsversuche aus der Chemie der anorganischen Sticksoffverbindungen. Ber. **40**, 4586.

Raschig, F. 1907 Die Eisenchlorid reaktion des Phenols und die chlorkalkreaction des Anilins. Z. angew. Chem. **20**, 2065.

Raupenstrauch, G. A. 1888 Ueber die Reaktionen einiger Phenole und analoger Körper mit Chloroform und Alkalien. Pharm. Ztg. **33**, 737.

Rettger, G. F. 1903 An experimental study of the chemical products of *Bacillus coli communis* and *Bacillus lactis aerogenes*. Am. J. Physiol. **8**, 284.

Rhein, M. 1917 Über die Bildung von Phenol im menschlichen Darm. Biochem. Z. **84**, 246.

Rice, C. 1873 New reaction for carbolic acid. Am. J. Pharm. **45**, 98.

Riegler 1899 Nouvelle méthode pour le dosage der phénol ordinaire et antres phénols. Bul. soc. Stiinte, Bucuresci, **8**, 51.

Roberts, E. 1923 Use of the salts of the arylsulphonhalogenoamides in the estimation and iodination of phenols. J. Chem. Soc. **123**, 2707.

Rodillon, G. 1921 Sur une reaction spécifique de l'acide phénolique. J. pharm. chim. [7] **23**, 136.

Rose, H. J., and Speer, F. W., Jr. 1920 Determination of phenols in ammonia still wastes. Am. Gas Assoc. Monthly **2**, 117.

Rowe, F. M. 1924 Colour Index, Society of Dyers and Colourists. Bradford, Yorkshire, 1.

Runge, F. F. 1834 Ueber einige Produkts der Steinkohlendestillation. Pogg. Ann. **31,** 65.

Salkowski, E. 1872 Ueber die Wirkung und das chemische Verhalten des Phenol (carbolsäure) im thierischen Organismus. Arch. Physiologie **5,** 335.

Salus, G. 1922 Zur Phenol- und Indolbildung durch Bakterien und zum Nachweis dieses Körper in Kulturen. Centr. Bakt. Parasitenk, Abt. I, **88,** 103.

Sanchez, J. A. 1911 Analyse systématique des composés à fonction phenoliques. Bull. soc. chim. [4] **9,** 1056.

Sarauw, A. 1882 Einwirkung von Phosgen auf Diazoamidokörper. Ber. **15,** 42.

Schewket, O. 1913 Über einige neue Farbenreaktionen von Di- und Triphenolen. Biochem. Z. **54,** 282.

Schamlfuss, H. 1924 Studien über die Bildung von Pigmenten. I. Abhandung. Sauerstoff, Chromogene und Ferment, I. Teil. Fermentforschung **8,** 1.

Schwarz, C. 1888 Üeber den direkten Nachweis von Chloral und Chloroform in Flussigkeiten. Pharm. Ztg. **33,** 419.

Scott, R. D. 1921 The detection of phenols in water. J. Ind. Eng. Chem. **13,** 422.

Seidell, A. 1911 New bromine method for the determination of aromatic phenols. Its special application to thymol. J. Wash. Acad. Sci. **1,** 196.

Sen-Gupta, N. N. 1921 Dephenolization in soil. J. Agr. Sci. **11,** 136.

Sieburg, E. 1916 Zur Kenntnis der Formaldehyd-Schwefelsäure-Reaktion. Biochem. Z. **74,** 371.

Siemmsen, J. A. 1912 Über die Einwirkung mehrwertiger Phenole auf Uransalze. Chem. Ztg. **36,** 353.

Silbermann, T., and Ozorovitz, N. 1908 Zur Erkennung und Identifizierung der zweiwertigen Phenole. Eine sehr empfindliche Resorcin-Reaktion. Bul. soc. Stiinte **17,** 41.

Skirrow, F. W. 1908 The determination of phenols in gas liquors. J. Soc. Chem. Ind. **27,** 58.

Theis, R. C., and Benedict, S. R. 1924 The determination of phenols in the blood. J. Biol. Chem. **61,** 67.

Tisdell, F. F. 1920 Estimation of phenolic substances in urine. J. Biol. Chem. **44,** 409.

Tommasi, T., und Tommasi, D. 1881 Ueber die Fichtenholz reaktion zur Entdeckung von Phenol im Urin. Ber. **14,** 1834.

Tsudji, M. 1919 Biological observations on the formation of phenol. J. Biol. Chem. **38,** 13.

Udránszky, L. v. 1888 Ueber Furfuralreactionen. Z. physiol. Chem. **12,** 355.

Urk, H. W. v. 1921 De Bepaling van Alkoholen en Phenolen in aetherische Olien door verestering mit Pyridine (Special Santalol, Menthol Eugenol). Pharm. Weekblad **58,** 1265.

Verley, A., und Bölsing, F. 1902 Ueber quantitative Esterbildung und Bestimmung von Alkoholen resp. Phenolen. Ber. **34,** 3354.

Vitali, D. 1892 Zum Nachweis von Saccharine. Z. anal. Chem. **31,** 89.

VORCE, L. R. 1925 Determination of minute amounts of phenols in polluted natural waters. Ind. Eng. Chem. **17**, 751.

VORTMANN, G. 1923 Ueber die Einwirkung von Jod auf alkalische Phenol-Lösung. Ber. **56B**, 234.

WALES, H., AND PALKIN, S. 1926 Identification of phenols by means of the spectroscope II. J. Am. Chem. Soc. **48**, 810.

WALLER, E. 1881 Phenol or carbolic acid: qualitative and quantitative tests. Chem. News **43**, 150.

WARE, A. H. 1925 The detection of plant phenols by the use of nitrites or nitric acid. Analyst **50**, 384.

WEINLAND, R. F., UND BINDER, K. 1912 Über die bei der Eisenchlorid-Reaktion des Breuzcatechins in alkalischer Lösung auftretende Rotfärbung I. Ber. **45**, 148.

WEINLAND, R. F., UND BINDER, K. 1912 Über die Eisanchlorid-Reaction des Breuzcatechins. II. Über violette Eisenbreuzcatechin-Verbindungen. Ber. **45**, 1113.

WEINLAND, R. F., UND BINDER, K. 1912 Über Eisenverbindungen der Phenole. III. Über Eisen Guajacol-Verbindungen. Ber. **45**, 2498.

WEISS, M. 1920 Colorimetrische Phenolbestimmung im Harn. Biochem. Z. **110**, 258.

WILKIE, J. M. 1911 A sensitive test for the detection of phenol and salicylic acid. J. Soc. Chem. Ind. **30**, 402.

WU, H. 1920 Contribution to the chemistry of phosphomolybdic acids, phosphotungstic acids and allied substances. J. Biol. Chem. **43**, 189.

WURSTER, C. 1887 Ueber Farbstoffbildung durch Wasserstoffsuperoxyd. Ber. **20**, 2934.