(II) A sample of cymene oxidized at 80° for 14 days yielded formic acid, identified by the mercuric oxide test above.

Action of Water.—Fifty g. of *p*-cymene and 25 g. of water oxidized at the boiling point for 18 days gave 1.8 g. of *p*-tolylmethyl ketone, but no aldehyde and no acid.

tert.-Butylbenzene.—Twenty-five g. of *tert.*-butylbenzene treated with oxygen for 25 days at 102–104° gave only a trace of non-volatile residue.

Summary

1. The action of gaseous oxygen on aromatic hydrocarbons containing normal, secondary and tertiary alkyl groups has been studied and it has been found that oxidation takes place only at the carbon atom in the alpha position to the ring.

2. At least one hydrogen atom must be attached to the alpha carbon atom in order that oxidation may take place.

3. The presence of water inhibits the oxidation when at least two hydrogen atoms are attached to the alpha carbon atom, but favors it when only one hydrogen atom occupies that position. An explanation of this fact is suggested.

MINNEAPOLIS, MINNESOTA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

THE ALKYLATION OF HYDROXYNAPHTHOQUINONE
I. ORTHO-ETHERS

BY LOUIS F. FIESER

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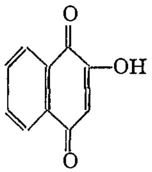
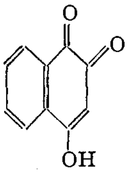
Although it has been known for some time that hydroxynaphthoquinone ("naphthalenic acid") may be prepared from derivatives of both α-naphthoquinone and of β-naphthoquinone, there is little evidence of a conclusive nature to indicate to which class of naphthoquinone derivatives the hydroxy compound belongs. In solution, the substance may consist of a tautomeric mixture of the two possible forms, and the possibility of the occurrence of a tautomeric change during the course of almost any reaction renders a solution of the problem by purely chemical means somewhat difficult.



p-Quinone form



o-Quinone form

O. Miller[1] sought to overcome this difficulty by preparing the silver

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[1] Miller, *J. Russ. Phys.-Chem. Soc.*, **43**, 440 (1911); **47**, 1536 (1915).

salt of the hydroxy compound and converting it, with ethyl iodide, into the ether. He supposed that the precipitation of the silver salt from the ammonium salt would not disturb a possible equilibrium between the tautomers, and further assumed that this silver salt, whether a single substance or a mixture of the salts derived from the two forms of the hydroxy compound, would react with an alkyl halide in such a manner that the silver atom would be replaced by the alkyl group. Carrying out this experiment, he obtained a mixture of ethers which he believed to be composed of eight parts of 4-ethoxy-1,2-naphthoquinone and one part of 2-ethoxy-1,4-naphthoquinone. He concluded that hydroxynaphthoquinone, in solution, consists of an equilibrium mixture in which the *p*- and *o*-quinone forms are present in the proportion of 1:8.

While one might object that both of the solid salts could not long exist in contact with a solution saturated with respect to both of them, because of the ease of interconversion by way of solution, dissociation and tautomeric change, this point need not be greatly stressed, for the second of Miller's assumptions can be tested in a simple manner. His assumption would require that portions of the same sample of the silver salt should always yield, with a variety of alkyl halides, the same proportion of the two isomeric ethers. If the proportion were not always the same, it is obvious that the yield of ethers cannot be regarded as an index of the composition of the silver salt or of the hydroxy compound. With a view to testing this point, and in order to obtain certain compounds required for a study of the structure of hydroxynaphthoquinone by an electrochemical method, the alkylation of this substance has been studied in some detail.

It is odd that at the time of Miller's publications a statement was to be found in the literature which apparently refutes his whole argument. Sachs, Berthold and Zaar[2] had already reported that the silver salt in question was converted, in 75% yield, into 2-methoxy-1,4-naphthoquinone by methyl iodide. However, it has now been found that the work of the German investigators as well as that of Miller was confused by the crystallization of eutectic mixtures containing about equal parts of the two isomeric ethers from solutions of the methylation or ethylation product. Separation of these mixtures by crystallization from alcohol, the solvent unfortunately employed in both Laboratories, is very difficult if not impossible. It has now been found that a rough separation may be effected by crystallization from benzene, which serves as a ready method of isolating the higher-melting, less soluble *o*-quinone ethers; and a more convenient method of separation is based on the fact that *o*-quinones generally form water-soluble bisulfite addition compounds, while substituted *p*-quinones usually do not react with sodium bisulfite. A third method, which is often of service in the isolation of the pure *p*-quinones, depends

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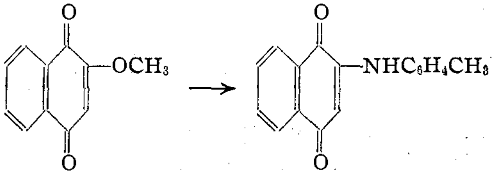
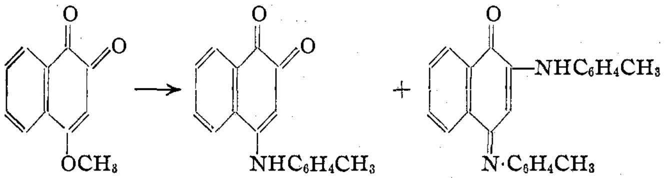
[2] Sachs, Berthold and Zaar, *Z. Farbenind.*, **6**, 81 (1907).

upon the very ready hydrolysis of the *o*-quinone ethers by dilute alcoholic hydrochloric acid, for under the same conditions, the isomers are not attacked.

Using these methods, the mixture described by Sachs and co-workers was separated into two unquestionably pure methoxynaphthoquinones, and these were characterized by conversion into the hydroquinones and hydroquinone diacetates, and by their reactions with amines. The ether readily soluble in bisulfite solution was shown to be an *o*-quinone by the formation of the known 6-methoxynaphthophenazine. Both methoxy compounds reacted readily with *p*-toluidine, giving the products indicated.





These reactions adequately establish the structures of the two methoxy compounds. Sachs and co-workers sought to prove the structure of the substance which is now known to be a mixture by comparing its oxime with the oxime obtained from the methyl ether of the condensation product of 1,2-naphthoquinone-4-sulfonate with methyl cyano-acetate. The two were considered to be identical. It is possible that only part of the mixture reacted, that a separation of the two oximes occurred on crystallization, or that the isomeric oximes cannot be distinguished by melting-point determinations. Beyond noting that the oximes do not melt but decompose on heating, I have made no attempt to settle the question.

The situation in the case of the ethyl ethers is somewhat similar. From the alkylation product, Miller[1] isolated two substances, one of which was pure 4-ethoxy-1,2-naphthoquinone while the other is now shown to be a mixture of the two isomers. Miller had shown that the *o*-quinone ether reacted with aniline to give anilino compounds similar to the toluidino compounds prepared, as indicated above, from the methyl ether, and a further proof of the structure is furnished by the conversion of the compound into 6-ethoxynaphthophenazine. The isomeric ether, 2-ethoxy-1,4-naphthoquinone, reacts with *p*-toluidine to give *p*-toluidino-α-naphthoquinone. That Miller obtained both anilino-α-naphthoquinone and anilino-naphthoquinone-anil from the low-melting substance which he regarded as the pure *p*-quinone ether is a further indication that he was dealing with a mixture of isomers. The anilino-naphthoquinone-anil must have come from the *o*-quinone ether present.

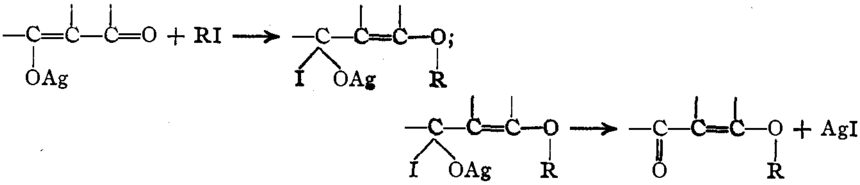
One diagnostic test available for distinguishing between other *o*- and *p*-quinonoid isomers is the solubility in bisulfite solution. Though all of the *o*-quinones studied dissolve readily in this reagent, the test should be applied with caution because most of the *p*-quinone ethers dissolve to a slight but perceptible extent. A second indication of structure is the color of the compounds: the *o*-quinone ethers are orange-yellow while the *p*-quinone ethers are pale yellow. The difference, though not great, is in conformity with the generalization of Hooker.[3] The surest distinction is found in the behavior of the ethers in the presence of acidic hydrolyzing agents. The *p*-quinone ethers may be crystallized from a dil. alcoholic hydrochloric acid solution without change, while the *o*-quinone ethers are completely hydrolyzed under these conditions.

Having thus found suitable methods of separating and identifying the isomeric ethers obtained from the silver salt, a series of alkylations with methyl, ethyl, *iso*propyl and *n*-butyl halides was carried out. The results of these experiments are tabulated in the experimental section. It was found that the proportion of *p*-quinone ether to *o*-quinone ether varies by as much as from 1:1.7 to 1:22, and that this proportion seems to depend upon the nature of the alkyl group, that of the halogen atom, and the experimental conditions. In general it may be said that the more reactive the alkyl halide used, the greater the relative amount of the *p*-quinone ether formed, and that this isomer is also somewhat favored by a high concentration of the alkyl halide. Hydroxynaphthoquinone was formed in some of the experiments and its production may possibly be due to hydrolysis of the *o*-quinone ether by the action of a trace of hydrogen halide, but even if this assumption is made it is found that the above conclusion is not materially altered. It seems clear, then, that the two isomeric ethers are not always formed in exactly the same proportions, and consequently Miller's assumption that the silver salt is a mixture of isomers, each of which can react with an alkyl halide in but one way, namely by replacement, is no longer tenable and another explanation of the production of isomeric ethers must be sought.

In view of the many cases in which alkylation apparently involves addition of the alkyl halide either to a double bond or to a 1,4-conjugated system[4] followed by elimination of the metal halide, it is reasonable to suppose that a similar reaction is responsible for the formation of one of the ethers, according to the following scheme

[3] Hooker, *J. Chem. Soc.*, **61**, 611 (1892). Hooker and Carnell, *ibid.*, **65**, 76 (1894).

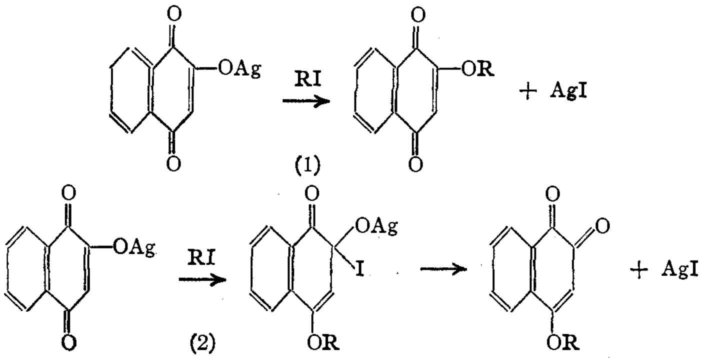
[4] For example, in the alkylation of anthranol, Meyer and Schlösser, *Ann.*, **420**, 126 (1920).



$$-\underset{\text{OAg}}{\underset{|}{C}}=\overset{|}{C}-\overset{|}{C}=O + RI \longrightarrow -\underset{\text{I}\ \ \text{OAg}}{\underset{\wedge}{C}}-\overset{|}{C}=\overset{|}{C}-\underset{\text{R}}{\underset{|}{O}};$$

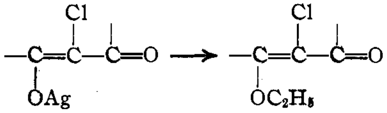
$$-\underset{\text{I}\ \ \text{OAg}}{\underset{\wedge}{C}}-\overset{|}{C}=\overset{|}{C}-\underset{\text{R}}{\underset{|}{O}} \longrightarrow -\underset{\text{O}}{\underset{\|}{C}}-\overset{|}{C}=\overset{|}{C}-\underset{\text{R}}{\underset{|}{O}} + AgI$$

while the other ether is formed by the normal replacement reaction. The alkylation products may thus be accounted for by assuming that two reactions take place concurrently and that the relative velocities of these reactions determine the relative amounts of isomers formed. The reactions may be written as follows.



But an equally consistent account of the course of the alkylation can be made on the assumption that the silver salt has the structure of a β-naphthoquinone derivative, rather than of a derivative of α-naphthoquinone as shown above. According to the latter view it is the *o*-quinone ether which is formed by the replacement reaction, while if the view outlined in the above equations is correct the *o*-quinone ether is formed by an addition reaction and it is the *p*-quinone ether which is produced by replacement. Now there are certain general characteristics of both replacement and addition reactions which should serve to distinguish between the two possibilities. A particularly noteworthy difference is that addition reactions are much more subject to the retarding influence exerted by suitably substituted groups than are replacement reactions. Thus, considering the esterification of acids by the Fischer method as involving an addition, the classical researches of Victor Meyer on steric hindrance make it clear that the silver salts of many *ortho*-disubstituted benzoic acids readily react, by replacement, with alkyl halides, while the corresponding acids can add alcohols only very slowly to give the same esters. If, then, the remaining hydrogen atom of the quinonoid nucleus of hydroxynaphthoquinone is replaced by a substituent atom or group, this substituent, being attached to the middle of the conjugated system regardless of which of the alternate formulas is considered, might be expected to decrease greatly the rate of the addition reaction without very materially affecting the rate at which replacement occurs. If one ether is formed exclusively, or in preponderant amount, this ether must owe its formation to a replacement reaction.

Miller[5] found that the silver salt of bromo-hydroxynaphthoquinone reacted with ethyl iodide to give none of the *o*-quinone ether but a mixture of the *p*-quinone ether and a considerable amount of the original hydroxy compound. Since the formation of much of the hydroxy compound renders this evidence somewhat uncertain, a similar experiment with chloro-hydroxynaphthoquinone was carried out to supplement Miller's result. On treating the silver salt of this compound with ethyl iodide without other solvent it was found that only 5% of the material was converted into the original hydroxy compound, while 89% of the remaining material was converted into the pure *p*-quinone ether. The *o*-quinone ether was entirely absent. The reaction may thus be formulated as involving only replacement, and this silver salt is thus shown to be an α-naphthoquinone derivative. New evidence that chloro-hydroxynaphthoquinone and hydroxynaphthoquinone are similarly constituted is furnished by reduction-potential data[6] and it is likely that the similarity extends to the silver salts, both of which are dark red in color. Consequently, it may be concluded that the alkylation of hydroxynaphthoquinone proceeds according to the formulation given above (Reactions 1 and 2), and that a consideration of the reaction furnishes some evidence that hydroxynaphthoquinone has the structure of a *p*-quinone.



$$-\underset{\text{OAg}}{\mathrm{C}}=\overset{\text{Cl}}{\mathrm{C}}-\overset{|}{\mathrm{C}}=\mathrm{O} \longrightarrow -\underset{\text{OC}_2\text{H}_5}{\mathrm{C}}=\overset{\text{Cl}}{\mathrm{C}}-\overset{|}{\mathrm{C}}=\mathrm{O}$$

The possibility of esterifying hydroxynaphthoquinone with an alcohol and a mineral acid was suggested by the pronounced ester-like properties of both types of ether. This esterification is readily accomplished, methyl alcohol reacting with particularly great rapidity. In every case the sole product was the *p*-quinone ether. The absence of any of the *o*-quinone ether is not significant of the structure of hydroxynaphthoquinone for it would be hydrolyzed under these conditions. Evidence of a sort, however, is furnished by the result of methylation with diazomethane. This reagent gives, with the greatest rapidity, nearly a 90% yield of the *p*-quinone ether. Of course, a tautomeric change may take place during the progress of this reaction but it seems unlikely, and the reaction may be regarded as supporting the *p*-quinonoid formula for hydroxynaphthoquinone. In accordance with this view, the esterification may be formulated as follows.

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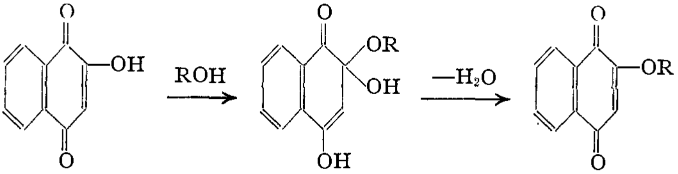
[5] Miller. *J. Russ. Phys.-Chem. Soc.*, **45**, 1467 (1913).

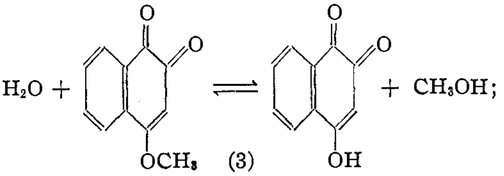
[6] Conant and Fieser, THIS JOURNAL, **46**, 1867 (1924).



The conjugated system of the quinone is thus regarded as equivalent to the carbonyl group of a carboxylic acid; it is involved in the esterification and it is responsible for the strongly acidic properties of the hydroxy compound and the ester-like properties of the ether.

This mechanism is supported by the fact that alcohols, in the presence of certain catalysts, readily add to quinone.[7] It furthermore brings into harmony the seemingly unrelated facts that the silver salts of chloro- and bromo-hydroxynaphthoquinone yield none of the *o*-quinone ether with alkyl halides, and that the corresponding hydroxy compounds cannot be esterified by the Fischer method.[8] Having formulated both reactions as involving 1,4 addition, it would be anticipated that a substituent attached to the conjugated system would retard or even prevent both reactions. It seems to be generally true that substituted hydroxyquinones cannot be esterified in the manner indicated, for several 2-alkyl-3-hydroxy-naphthoquinones conform to this rule. On the other hand, it is significant that 2,5-dihydroxybenzoquinone is readily converted into the dimethyl ether by methyl alcohol and hydrochloric acid.[9]

The ready hydrolysis of the *o*-quinone ethers, coupled with the ease of formation of the *p*-quinone ethers by esterification, permits a rather remarkable reaction: the *o*-quinone methyl ether is converted rapidly and completely into the *p*-quinone ether by warming with absolute methyl alcohol containing 3% of hydrogen chloride. Bearing in mind that esterification and hydrolysis are equilibrium reactions, this transformation can only be formulated in the following manner.



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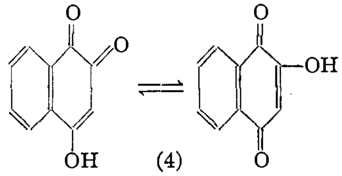
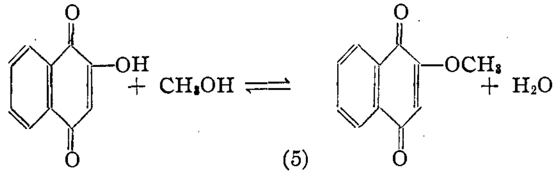


(4)



(5)

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[7] Knoevenagel and Bückel, *Ber.*, **34**, 3993 (1901).

[8] Zincke and Gerland, *Ber.*, **20**, 3221 (1887).

[9] Scholl and Dahll, *Ber.*, **57**, 81 (1925).

This reaction clearly indicates the necessity of regarding hydroxynaphthoquinone as a tautomeric substance, for the change must take place through the *o*-quinone form. Moreover, since there are no grounds for supposing that the equilibrium constants for Reactions 3 and 5 are vastly different, the obvious conclusion is that the point of equilibrium in Reaction 4 greatly favors the *p*-quinone form of hydroxynaphthoquinone. This conception is not in conflict with the results of the other alkylation experiments, and indeed all of the evidence taken together points to the conclusion that hydroxynaphthoquinone has the structure of a *p*-quinone, but that in solution a very small amount of the unknown tautomer, 4-hydroxy-1,2-naphthoquinone, is present in an equilibrium mixture.

Experimental Part

Preparation of Hydroxynaphthoquinone.—This compound was conveniently prepared by the action of sulfuric acid on ammonium 1,2-naphthoquinone-4-sulfonate. Owing to its greater solubility, this salt is more suitable than the sodium salt previously employed.[10] The product could be purified through the sodium salt (*a*) or better through the ether (*b*), 2-methoxy-1,4-naphthoquinone, which was obtained by the action of methyl alcohol and sulfuric acid on the quinone sulfonate. The reaction evidently involves replacement of the sulfonic acid group by hydroxyl, tautomeric change and esterification. By either method the yield was about 150 g. from 300 g. of β-naphthol.

Four hundred g. of 1-amino-2-naphthol-4-sulfonic acid was stirred into a paste with 800 cc. of water in a 2-liter beaker and the mixture cooled in an ice-bath. While the stirring was constantly maintained, 240 cc. of nitric acid (d., 1.41) was added in portions in the course of five to ten minutes. When the mixture began to froth, it was covered with a layer of ether which serves as an efficient subsident. Most of the material dissolved, gas was copiously evolved, and in about 15 minutes the quinone salt began to separate. In 15 minutes more the reaction was complete and 300 cc. of saturated ammonium chloride solution was added. After standing for one hour in the ice-bath, the orange-yellow crystals were collected, washed with 400 cc. of half-saturated ammonium chloride solution, air-dried at room temperature on a porous plate and finally dried to constant weight at 50-60°; yield, 363 to 375 g. (85-88%).[11]

(a) Three hundred and fifty g. of this crude ammonium salt was slowly stirred into 700 cc. of concd. sulfuric acid contained in a 3-liter beaker, the temperature being kept below 30° by occasional cooling in an ice-bath. After stirring had been continued for 15 minutes the yellow-brown solution was allowed to stand for one hour, poured into water and the dark precipitate of hydroxynaphthoquinone filtered off by suction and washed with water until the filtrate was light yellow. The crude product was dissolved in dil. sodium hydroxide solution, concd. alkali was then added and the sodium salt allowed to crystallize. When this salt was dissolved in water and the solution acidified, the hydroxyquinone was obtained as a light yellow precipitate and in almost pure condition; yield, 143 g. (60%).

(b) Three hundred g. of the ammonium salt was made into a paste with 400 cc. of

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[10] Ger. pat. 100,703.

[11] Compare Böniger, *Ber.*, **27**, **24** (1894).

absolute methyl alcohol in a 2-liter flask. The mixture was cooled in an ice-bath and constantly shaken while 75 cc. of concd. sulfuric acid was slowly added. The flask was warmed on the water-bath during continued shaking until the quinone sulfonate had all disappeared and a stiff paste of methoxynaphthoquinone was formed. Water was then added and the product was filtered off, washed with water, and with dil. ammonium hydroxide solution. The buff-colored product, while still moist, was heated with 1.5 liters of 2.5% sodium hydroxide solution until solution was complete (10 minutes), and the deep red solution was filtered and acidified. The hydroxynaphthoquinone which precipitated was pure yellow and compared favorably with samples purified by repeated crystallization of the sodium salt; yield, 106 to 116 g. (51–57%).

The loss of material occurs chiefly in the first step of the process, as the methoxy naphthoquinone, which melts within 3–4° of the correct temperature, is converted almost quantitatively into the hydroxy compound. For use in certain reactions, a sample of the hydroxyquinone was repeatedly crystallized from alcohol containing a trace of acetic acid. It consisted of glistening, pure yellow needles melting with decomposition at about 192°.

The SILVER SALT of hydroxynaphthoquinone was prepared in the following manner. One hundred g. of the quinone was covered with 1.5 liters of hot water and enough ammonium hydroxide added just to bring it into solution. In order to neutralize the slight excess of ammonia, dil. nitric acid was added until an appreciable precipitate persisted after prolonged stirring of the solution. The solution was then filtered and treated with the requisite quantity of silver nitrate solution; the dark red salt was washed thoroughly with water, alcohol and ether, and dried at 60°.

Methyl Ethers.—The substance described by Sachs, Berthold and Zaar[2] and regarded by them as pure 2-methoxy-1,4-naphthoquinone was prepared in the manner indicated by these authors. While the needles appeared to be homogeneous, they were not well formed. The melting point (146–147°) was not sharp and a minute crystal skeleton disappeared only 10–15° above this temperature. By fractional crystallization the material was found to be a mixture; a small amount of the *p*-quinone ether was isolated as the less soluble fraction after five crystallizations from alcohol, while on one crystallization of the mixture from ligroin-benzene the *o*-quinone ether separated in almost pure condition and the material from the mother liquor yielded the pure *o*-quinone ether on crystallization from alcohol. The separation was more easily accomplished by the use of bisulfite solution, which leaves the *p*-quinone ether almost completely undissolved. The isomer was recovered by the addition of sodium carbonate to the solution until no further separation took place. Thus, 2 g. of the crude alkylation product yielded 0.8 g. and 0.9 g., respectively, of the *para* and *ortho* isomers. An intimate mixture of equal parts of the two pure isomers (m. p. 183.5° and m. p. 190°) melted at 146–147° and possessed the characteristics of a eutectic mixture.

4-Methoxy-1,2-naphthoquinone.—This dissolves to a slight extent in boiling water, is sparingly soluble in ether or ligroin and moderately soluble in benzene or alcohol. It crystallizes from either of the latter two solvents, or from water, in beautiful, long, orange-yellow needles melting at 190°.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.2; H, 4.3; mol. wt., 188. Found: C, 70.5; H, 4.3; mol. wt. (Rast's method), 200.

The ether is hydrolyzed quantitatively by boiling for a few minutes with dilute alkali, and hydrolysis takes place rapidly in the cold when the material is in a finely divided condition. Thus alkali should not be used to decompose the bisulfite addition product, as much material is lost by hydrolysis; even sodium carbonate should not be used in too great excess. The ether is also hydrolyzed with great rapidity in the presence of mineral acids. Thus 1 g. of material was dissolved in 20 cc. of 85% alcohol containing 0.1 mole of hydrogen chloride per liter and the solution at once cooled. The material which was precipitated by the addition of water (0.8 g.) was completely soluble in dil. aqueous ammonia solution and proved to be hydroxynaphthoquinone. With methyl alcohol, in the absence of much water, hydrolysis is followed by esterification to give methoxy-α-naphthoquinone; on covering 2 g. of the *o*-quinone ether with 40 cc. of methyl alcohol containing 3% of hydrogen chloride and boiling, the orange-yellow crystals rapidly dissolved and the flask was soon filled with yellow needles of methoxy-α-naphthoquinone; yield, 1.8 g.; m. p., 183°.

Methoxy-β-naphthoquinone was reduced to *4-methoxy-1,2-naphthohydroquinone* by adding sodium hyposulfite to a suspension of 1 g. of material in 100 cc. of boiling water until a colorless solution resulted. The filtered solution deposited colorless needles on cooling, and these were collected in an atmosphere of nitrogen and crystallized from water containing a little hyposulfite and protected from the air. The material became slightly gray during drying and turned black in a few weeks. It decomposed at about 130°.

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.4; H, 5.3. Found: C, 69.1; H, 5.4.

The DIACETYL DERIVATIVE of the hydroquinone was obtained from the hydroquinone with acetic anhydride and sulfuric acid and also by the action of zinc dust, acetic anhydride and acetic acid on the quinone. Crystallized repeatedly from benzene-ligroin and from dil. alcohol, the substance formed colorless needles melting at 135°. It is very readily soluble in alcohol or benzene, sparingly soluble in ligroin or water.

Anal. Calcd. for $C_{15}H_{14}O_5$: C, 65.7; H, 5.1. Found: C, 65.4; H, 5.2.

An azine was prepared by boiling an alcoholic solution of equivalent weights of the quinone and *o*-phenylenediamine for ten minutes. The product which separated on cooling was nearly pure, and a further crystallization from methyl alcohol gave long, lemon-yellow needles of *6-methoxynaphthophenazine*, melting at 180°. It conformed to the description of Kehrmann and Messinger[12] who first obtained this substance, together with the N-methyl isomer, by alkylation of hydroxynaphthophenazine. They report a melting point of 176–177°.

The *semicarbazone* of methoxy-β-naphthoquinone was obtained as follows: 0.8 g. of the quinone was dissolved in an excess of boiling alcohol and a solution of 0.5 g. of semicarbazide hydrochloride and 0.7 g. of sodium acetate in a little water added. The solution was quickly filtered and then boiled under the reflux condenser for three hours when a copious crop of silken, yellow needles had formed. The substance, washed with water, alcohol and ether, melted at 246° with decomposition. It is very slightly soluble in the usual solvents and the nitrobenzene solution undergoes decomposition on boiling. Analysis of the crude material gave values agreeing approximately with the calculated values.

Anal. Calcd. for $C_{12}H_{11}O_3N_3$: C, 58.8; H, 4.5. Found: C, 58.3; H, 4.6.

It is possible that this is the substance obtained by Sachs and co-workers[2] from the mixture of isomers, for methoxy-α-naphthoquinone, under the conditions of the above experiment, gave no semicarbazone. These authors report a melting point of 237–238°.

Methoxy-β-naphthoquinone reacts readily with mono-amines. To a solution of 0.8 g. of the quinone in 500 cc. of boiling water 0.5 g. of *p*-toluidine was added and the solution warmed on the water-bath for one hour. The red precipitate was collected, digested with cold sodium bisulfite solution to remove a few crystals of unchanged quinone and extracted with hot methyl alcohol. The dissolved portion was recovered from solution by the addition of water. It was almost completely soluble in cold, dilute alkali and after precipitation from this solution and crystallization from alcohol, the substance

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[12] Kehrmann and Messinger, *Ber.*, **24**, 2174 (1891).

melted at 250° with decomposition. In crystalline form, solubility and point of decomposition, it corresponded exactly with a sample of 4(p-toluidino)-1,2-naphthoquinone[13] prepared from the corresponding sulfonate. The residue not dissolved by methyl alcohol constituted about half of the product and consisted of a dark red, crystalline powder melting at 175°. From benzene-ligroin it separated in large crystals with the characteristic metallic green luster of toluidino-naphthoquinone-toluide[14] and melted at 177°. It was identical with a sample (m. p., 177°) prepared by the action of p-toluidine on the methyl ether of p-toluidino-β-naphthoquinone in glacial acetic acid solution.

The methyl ether of toluidino-β-naphthoquinone, prepared by alkylation with dimethyl sulfate in alkaline solution, crystallized in beautiful, bright red crystals but melted at 147° and not at 150° as reported by Zincke and Brauns.[15]

Anal. Calcd. for $C_{18}H_{15}O_2N$: C, 78.0; H, 5.5. Found: C, 78.1; H, 5.9.

2-Methoxy-1,4-naphthoquinone dissolves in boiling water to about the same extent as the isomeric o-quinone ether, is slightly less soluble in alcohol and considerably more soluble in benzene. The crude material which is left as a residue after extracting the isomer from the alkylation product with bisulfite solution, as indicated above, is pinkish-brown in color. This color is not removed by repeated crystallization from organic solvents but disappears on a single crystallization from water. The pure substance forms yellow needles which are shorter and wider than those of the isomer. The difference in the color of the two isomers, though not great, is quite distinctive: the o-quinone is orange-yellow; the p-quinone is a somewhat pale, pure yellow. The melting point is 183.5°.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.2; H, 4.3; mol. wt., 188. Found: C, 70.0; H, 4.3; mol. wt. (Rast's method), 192.

This ether is hydrolyzed by dilute alkali about as readily as the isomer, but it is not easily hydrolyzed by mineral acids. A sample was crystallized from 85% alcohol 0.1 M in hydrogen chloride and not a trace of hydroxynaphthoquinone could be detected.

This ether, though a p-quinone, is appreciably soluble in bisulfite solution. After 1.00 g. of material had been stirred with 40 cc. of 10% bisulfite solution for 10 minutes in the cold, 0.90 g. remained undissolved, while 0.06 g. was recovered from the filtered solution by the addition of sodium carbonate solution. In another test extending for one and one-half hours, the amounts of dissolved and undissolved material collected were, respectively, 0.88 g. and 0.09 g. When the suspension was boiled, hydrolysis or some other reaction removed a part of the material.

Methoxy-α-naphthoquinone is prepared most readily by the Fischer esterification method. Thus 5 g. of pure hydroxynaphthoquinone was heated under a reflux condenser with 50 cc. of methyl alcohol containing 3% of hydrogen chloride. Before all of the material had dissolved, the methoxy derivative began to separate and soon gave a stiff paste. After 15 minutes the mixture was cooled and filtered; yield, 5.1 g.; m. p., 182.5–183.0°.

Diazomethane also converts hydroxynaphthoquinone exclusively into the α-naphthoquinone derivative. To an ethereal solution of diazomethane prepared from 2.7 cc. of nitrosomethyl-urethan was added 1 g. of the pure quinone. Although it is but sparingly soluble in ether, the quinone dissolved at once in this solution, and in about one minute the methoxy compound suddenly separated. The product (0.84 g.) melted at 181.5–182.0°; after one crystallization from alcohol the melting point was

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[13] Elsbach, *Ber.*, **15**, 686 (1882).

[14] Fuchs, *Ber.*, **8**, 1025 (1875).

[15] Zincke and Brauns, *Ber.*, **15**, 1970 (1882).

183.5°. Evaporation of the ethereal mother liquor left a slightly oily product which yielded 0.1 g. of the ether; m. p., 177°, on crystallization from water.

2-Methoxy-1,4-naphthohydroquinone was obtained in the manner indicated above for the isomer. The long, colorless needles which separated from water containing a little hyposulfite turned gray on drying. The point of decomposition was about 107°.

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.4; H, 5.3. Found: C, 69.3; H, 5.2.

The HYDROQUINONE DIACETATE crystallized from dil. methyl alcohol in the form of white needles melting at 129–130°. The substance is very readily soluble in alcohol, benzene or glacial acetic acid; it is less soluble in ligroin.

Anal. Calcd. for $C_{15}H_{14}O_5$: C, 65.7; H, 5.1. Found: C, 65.5; H, 5.3.

No reaction took place on boiling either an aqueous or an alcoholic solution of equivalent weights of methoxy-α-naphthoquinone and *p*-toluidine for one hour, but when glacial acetic acid was employed as the solvent the yellow solution rapidly became red and after it had boiled for ten minutes, dark red needles separated on cooling. The substance melted at 200°, the melting point of a sample of *p*-toluidino-α-naphthoquinone prepared from hydroxynaphthoquinone.[16] A mixed-melting-point determination established the identity of the two samples; yield from 0.8 g. of the quinone, 1 g.

Ethyl Ethers.—In an orienting experiment the silver salt of hydroxynaphthoquinone was allowed to react with ethyl iodide without other solvent, the excess of the halide was removed by evaporation, and the residue extracted with ether. The extraction was probably incomplete as the material obtained on evaporation of the ether represented only about half of the calculated amount. The experiment is mentioned only because the substance so obtained melted, after crystallization from dil. alcohol, at 96–7° and is thus to be regarded as the substance which Miller believed to be pure 2-ethoxy-1,4-naphthoquinone. Indeed, numerous crystallizations of the product from dil. alcohol failed to raise the melting point above 98°; but a single crystallization from benzene-ligroin was sufficient to show that the substance was a mixture, for long, orange-yellow needles separated from this solvent which melted sharply at 126°, the melting point of 4-ethoxy-1,2-naphthoquinone. That the initial material was a mixture of about equal parts of the two isomeric ethers was established by comparing its melting point with that of such a mixture of the pure compounds (m. p. 126° and m. p. 120°). The melting point was 97–98°, and a slight rise was produced by the addition of either component.

The ethylation of hydroxynaphthoquinone through the silver salt and the separation of the isomers by means of sodium bisulfite solution are described below. *4-Ethoxy-1,2-naphthoquinone,* first prepared by Baltzer,[17] was obtained in orange-yellow needles several centimeters in length by repeated crystallization from dil. alcohol; m. p., 126°. This is the only one of the quinones investigated that forms a bisulfite addition compound which is at all sparingly soluble in water. The compound separates from an aqueous solution containing an excess of sodium bisulfite in the form of large, colorless crystals which turn brown on keeping and which are very hygroscopic.

For the purpose of further identification, the quinone was converted into the hydroquinone diacetate, *1,2-diacetoxy-4-ethoxy-naphthalene,* by the action of zinc dust, acetic acid and acetic anhydride. Crystallized successively from alcohol, benzene-ligroin, and ligroin with the use of animal charcoal, the compound melted constantly at 108–109°, but a slight color persisted.

Anal. Calcd. for $C_{16}H_{16}O_5$: C, 66.6; H, 5.6. Found: C, 66.2; H, 5.7.

6-Ethoxynaphthophenazine was prepared by boiling an alcoholic solution of equivalent weights of the quinone and *o*-phenylenediamine for ten minutes. The product.

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[16] Elsbach, *Ber.*, **15**, 688 (1882).

[17] Baltzer, *Ber.*, **14**, 1900 (1881).

washed with methyl alcohol, melted at 158.5° and the melting point was not raised by further crystallization from benzene-ligroin. The compound forms fluffy, lemon-yellow needles. It is insoluble in cold alkali, dissolves in concd. sulfuric acid with development of the carmine-red color characteristic of azines, and is very readily soluble in benzene but much less soluble in alcohol or ligroin.

Anal. Calcd. for $C_{18}H_{14}ON_2$: C, 78.8; H, 5.1. Found: C, 78.6; H, 5.3.

2-Ethoxy-1,4-naphthoquinone is most conveniently prepared by the esterification method. After boiling a solution of 25 g. of hydroxynaphthoquinone in 300 cc. of absolute alcohol containing 3% of hydrogen chloride for eight hours, 25.2 g. of the ether and 2.4 g. of unchanged material were collected.

Crystallized from water, in which it is only sparingly soluble at the boiling point, the compound separates in the form of pale yellow needles, and one crystallization from this solvent serves completely to remove traces of oily or colored by-products often present in the crude material. Some brown material was repeatedly crystallized from dil. alcohol, dil. acetic acid and benzene-ligroin; the compound was obtained in the form of large, thick needles which, though animal charcoal had been freely used, were orange in color. Crystallization from water now gave a yellow product. The melting point is 120°.

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.3; H, 5.0. Found: C, 71.0; H, 5.0.

The solubility in most solvents is very nearly the same as that of the isomeric ether, but the *p*-quinone ether dissolves more readily in benzene. It is more soluble than the methyl ether in the usual solvents but dissolves to a slightly less extent in bisulfite solution. After 1.00 g. of material had been stirred with 10% bisulfite solution for ten minutes, 0.93 g. remained undissolved while 0.04 g. was recovered from the solution.

The hydroquinone diacetate, *1,4-diacetoxy-2-ethoxy-naphthalene*, is very readily soluble in ether, benzene, or alcohol; it is less soluble in ligroin or petroleum ether. Crystallized from suitable solvent pairs, it was obtained in the form of colorless crystals melting at 81.5°.

Anal. Calcd. for $C_{16}H_{16}O_5$: C, 66.6; H, 5.6. Found: C, 66.2; H, 5.6.

Ethoxy-α-naphthoquinone reacts with *p*-toluidine in the same manner as the methyl ether.

Alkylation Experiments.—In each of the following experiments 10 g. of the finely powdered silver salt was treated either with 1.1 molecular equivalents of an alkyl halide in 100 cc. of solvent, or with 35 cc. of the halide without other solvent. The dark red color of the silver salt enables the course of the reaction to be followed. Using methyl or ethyl iodide without a solvent the reaction went to completion in about five minutes with the development of considerable heat, while ethyl bromide reacted completely only in about three hours. When ether was employed as a diluent, the reaction was even slower; the mixture was boiled under the reflux condenser for about five hours, allowed to stand overnight, and boiled for two to three hours more after breaking up the solid matter with a stirring rod. Benzene is a much more suitable solvent both because the reaction proceeds more rapidly and because of its greater solvent power.

On completion of the reaction, the excess of halide or ether was distilled under diminished pressure and the residue extracted thoroughly with boiling benzene. The benzene solution was concentrated to a volume of about 50 cc. and cooled in ice. The mother liquor from this crystallization was evaporated to dryness in a vacuum. Both fractions were usually investigated as to melting point and solubility in ammonium hydroxide and sodium bisulfite solution, and it was often found that the first crystals consisted exclusively of the β-naphthoquinone ether and required no further attention. In general, however, it is sufficient to stir the combined product with successive portions of cold aqueous ammonia until the extract is no longer colored red by hydroxynaphthoquinone, and then with bisulfite solution until the extract gives no precipitate of the orange-yellow *o*-quinone ether on adding sodium carbonate solution.

The separation of the pairs of isomeric ethers by means of sodium bisulfite is not ideal because of the slight but definite solubility of the α-ethers, with the exception of the *n*-butyl ether, in solutions of this reagent.

Thus a mixture of 1.00 g. of each of the pure methyl ethers on treatment with 40 cc. of 10% bisulfite solution yielded 0.88 g. of the *p*-quinone ether and 1.06 g. of the *o*-quinone ether (m. p., 182–184°).

It is obvious that the separation is not quantitative and that the figures given in Table I indicate too high a yield of the *o*-quinone ethers at the expense of the *p*-quinone ethers. However, in view of other sources of error, such as the collection of most of the impurities along with the *p*-quinone ether, hydrolysis of some of the *o*-quinone ether by the carbonate solution, and the solubility of both ethers in water, I have made no attempt to correct for any of the errors in this first survey of the field.

TABLE I

YIELD OF ALKYLATION PRODUCTS FROM 10 G. OF THE SILVER SALT

Alkyl halide	Solvent	*p*-Quinone ether (insol. in $NaHSO_3$ soln.)		*o*-Quinone ether (sol. in $NaHSO_3$ soln.)		Hydroxy-naphthoquinone, g.
		G.	%[b]	G.	%[b]	
Methyl iodide	....	2.1	36	3.5	60	0.8
Methyl iodide	Ether	1.6	26	4.3	70	0.5
Ethyl iodide	....	1.6	22	5.4	75	...
Ethyl iodide	Ether	0.9	13	5.7	80	0.1
Ethyl bromide	....	0.3	4	6.3	88	...
*iso*Propyl bromide[a]	Benzene	?		3.9	70	1.7
n-Butyl iodide	Ether	1.5	18	5.6	68	...

[a] Considerable unidentified tar was formed.

[b] The amount of silver salt equivalent to the hydroxy compound produced has been deducted in calculating these percentage yields.

It should be noted that the residue insoluble in ammonium hydroxide or in bisulfite solution was almost pure in the case of the methyl derivative, that the ethyl and butyl derivatives were accompanied by small amounts of dark, oily products, while no pure substance could be isolated from the residue in the experiment with *iso*propyl bromide. In the former cases, the *p*-quinone ethers were purified by crystallization from water and compared with samples prepared by esterification.

4(n-Butoxy)-1,2-naphthoquinone separated from ligroin-benzene solution in the form of orange-yellow plates melting at 98°. It is more soluble than the ethoxy compound.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 72.7; H, 6.1.

2-(n-Butoxy)-1,4-naphthoquinone.—Five g. of hydroxynaphthoquinone was dissolved in 100 cc. of the alcohol, the solution was cooled rapidly to obtain a fine suspension of the material, and 20 cc. of concd. sulfuric acid was added. The mixture warmed considerably and most of the solid dissolved. After standing for ten hours considerable material had crystallized and the remainder was precipitated from the mother liquor with water. Dilute ammonia solution extracted 0.7 g. of unchanged material, leaving 4.5 g. of the ether; m. p., 104°. Crystallized from ligroin, the compound melted at 105.5° and formed brown-yellow needles. No perceptible quantity of the substance dissolved in cold bisulfite solution.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 72.9; H, 6.0.

4(isoPropoxy)-1,2-naphthoquinone crystallized from ligroin-benzene in the form of fine, orange-yellow needles melting at 126°.

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.2; H, 5.6. Found: C, 71.8; H, 5.6.

Ethylation of 2-Chloro-3-hydroxy-1,4-naphthoquinone.—A sample of this compound[8] melting at 213–214° was converted into the silver salt and 5.8 g. of the latter was covered with ethyl iodide. The reaction being slow in the cold, the mixture was heated to boiling for ten minutes. The excess of halide was then removed by evaporation in a vacuum and the residue extracted with benzene. This solution was shaken with ammonia solution, then with bisulfite solution dried and concentrated to a small volume. From the ammonium hydroxide solution there was recovered 0.2 g. of the chloro-hydroxy compound; no trace of material was found in the bisulfite extract; while the benzene solution yielded 3.7 g. of a yellow product melting at 96–97°. Crystallized repeatedly from ligroin, methyl alcohol, or benzene and petroleum ether, the compound melted constantly and sharply at 97–98°. It forms tufts of feathery needles which are of a deeper yellow color than the chlorine-free ether.

Anal. Calcd. for $C_{12}H_9O_3Cl$: Cl, 14.99. Found: 15.05.

The compound is very readily soluble in alcohol or benzene, and readily soluble in ligroin. When warmed with *p*-toluidine in glacial acetic acid solution it gave 2(*p*-toluidino)-3-chloro-1,4-naphthoquinone,[18] melting at 195°, while with aniline, the anilino compound,[19] melting at 202–203°, was formed. This shows that the compound is *2-ethoxy-3-chloro-1,4-naphthoquinone.* Zincke[20] states in a footnote that chloro-hydroxynaphthoquinone gives an ethyl ether which exists in two forms melting at 96–97° and 149–150°, both of which are different from 4-ethoxy-3-chloro-1,2-naphthoquinone (m. p., 148–149°) which he prepared in another manner, and both yielding the same chloro-anilino compound. No further details or analyses are given. It is evident that one of his compounds corresponds to the substance described above, but an explanation of his other reported form is still lacking.

Summary

1. Substances described in the literature as 2-methoxy- and 2-ethoxy-1,4-naphthoquinone are mixtures of these compounds with the isomeric 4-alkoxy-1,2-naphthoquinones.

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[18] Plagemann, *Ber.*, **15**, 487 (1882).

[19] Knapp and Schultz, *Ann.*, **210**, 189 (1881).

[20] Zincke, *Ber.*, **21**, 1043 (1883).

2. The silver salt of hydroxynaphthoquinone reacts with alkyl halides to give varying proportions of α-naphthoquinone-ether and β-naphthoquinone ether, the relative amount of the former increasing somewhat as the reactivity of the alkyl halide increases. The *p*-quinone ether is considered to be formed by normal replacement, while the formation of the *o*-quinone ether is regarded as involving 1,4 addition. The silver salt of chloro-hydroxynaphthoquinone reacts only in the first manner, giving the *p*-quinone ether.

3. Alkylation of hydroxynaphthoquinone with an alcohol and a mineral acid, or with diazomethane, yields exclusively the 2-alkoxy-1,4-naphthoquinone.

4. Consideration of these reactions, and of the behavior of the two types of ethers towards acid hydrolyzing agents, leads to the conclusion that in solution hydroxynaphthoquinone consists of a mixture of tautomers, with the orthoquinone form present in extremely small concentration.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE COUPLING ACTION OF THE GRIGNARD REAGENT
III. THE QUESTION OF THE FORMATION OF 1,2,3-TRIPHENYLPROPANE AND SIMILAR HYDROCARBONS IN THE COUPLING REACTIONS OF THE BENZYL HALIDES

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Introduction

In a study of the action of the Grignard reagent on alkyl halides, Späth[2] obtained products whose formation he attributed to a coupling reaction involving the combination of free alkyl and alkylene radicals assumed to exist as intermediates. By the action of various Grignard reagents on the benzyl halides he prepared a compound which he identified as 1,2,3-triphenylpropane (I). From ethylmagnesium bromide and benzyl chloride he obtained similarly a liquid which possessed the properties of α-ethyl-α,β-diphenylethane (II). Phenylmagnesium iodide with *p*-methoxybenzyl bromide gave a resinous solid to which Structure III was assigned.

Späth assumed that the first step in these reactions was the formation of free radicals and, further, that these free radicals were of two types—univalent and bivalent. The formation of compounds of the above-mentioned type is then explained by the coupling together of two of the alkyl radicals with one alkylene radical: $\mathrm{R}{-} + \mathrm{R}{-} + \mathrm{RCH}\!< \longrightarrow \mathrm{RCHRR}$.

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[1] National Research Fellow in Chemistry.

[2] Späth, *Monatsh.*, **34**, 1965 (1913).