investigated. There are two serious objections to such a mechanism for the entire reaction, but it is possible for chain reactions to contribute a few per cent. to the total.

4. Our own experiments, and recalculation of Pease and Durgan's data in the light of our work on methane production, suggest a lower value for the equilibrium constant of the dehydrogenation reaction than has been obtained in previous experimental work. This new value is in far better agreement with statistical mechanical calculations than were the earlier values.

PHYSICAL CHEMISTRY SECTION
U. S. BUREAU OF MINES
PITTSBURGH, PENNA.

RECEIVED FEBRUARY 8, 1937

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

Two-Step Oxidation of Benzoin to Benzil

BY L. MICHAELIS AND E. S. FETCHER, JR.

The purple color which arises during the oxidation of benzoin to benzil has been known for many years, and the various conditions under which it can be produced have been studied by a number of authors.[1-4] It may be best observed on addition of sodium hydroxide to an alcoholic solution of a mixture of benzil and benzoin. The colored substance arising under this condition has been fully shown to be on an oxidation level between benzil and benzoin.[1,2,5,6] As far as an attempt to interpret its structure has been made, it usually has been considered as a bimolecular compound[4,7] supposedly comparable to the quinhydrones, which also had been considered to be bimolecular. Another interpretation adopted, but without reliable proof, by some authors[3-5] is that of a unimolecular radical. Since many quinhydrones have now been proved to be semiquinone radicals[8] it was suggestive to investigate the nature of the purple substance with those methods developed for the study of the quinhydrones.

$$\underset{\text{I}}{C_6H_5COCOC_6H_5} \quad \underset{\text{II}}{C_6H_5COCOHC_6H_5} \quad \underset{\text{III}}{C_6H_5COCHOHC_6H_5}$$

If this purple substance be a radical such as II, it would have the same molecular size as benzoin (III) or benzil (I). If it be a molecular compound of benzil and benzoin the molecular size would be a multiple. The customary procedures for the determination of molecular weights are of no avail in this case. But there are at least two methods that might be used. One is the potentiometric method which has been applied successfully to the solution of the problem for many organic dyestuffs.[8] A number of unfavorable circumstances obviate its use in the present case. Another method, referred to in a previous paper[9] as the dilution test, is readily applicable under the requisite experimental conditions, and is just as reliable.

To carry out this test, equivalent weights of the oxidized and the reduced forms of the system, *i. e.*, benzil and benzoin, are dissolved in a solvent in which the intermediate purple compound is formed spontaneously. Two experiments are carried out in which nothing but the volume of the solvent is varied. A color comparison of the two solutions is made in tubes of the same diameter by examination through the whole length of the tubes, thus comparing the total amounts of the colored substance. If the substance be a radical this amount will be independent of the volume; if it be a bimolecular compound the color intensity will be inversely proportional to the volume.

This statement, however, is true[9] only if the amount of the colored substance, in equilibrium with the two parent substances, is but a small fraction of that which can arise *in maximo*. This amount is dependent on the concentration of alkali, increasing with it. This influence of the alkalinity can be accounted for by the same argument that has been presented for anionic semiquinones.[9] The alkali concentration should be

---

[1] More recent papers are: A. Weissberger, H. Mainz, and E. Strasser, *Ber.*, **62B**, 1942 (1929).

[2] A. Weissberger, E. Strasser and H. Mainz, *Ann.*, **478**, 112 (1930).

[3] Ben B. Corson and R. W. McAllister, THIS JOURNAL, **51**, 2822 (1929).

[4] A. Weissberger, *Ber.*, **65B**, 1815 (1932).

[5] W. E. Bachmann, THIS JOURNAL, **53**, 2758 (1931).

[6] A. Weissberger, W. Schwarze and H. Mainz, *Ann.*, **481**, 68 (1930).

[7] E. Beckmann and T. Paul, *ibid.*, **266**, 6 (1891).

[8] L. Michaelis, *Chem. Reviews*, **16**, 243 (1935).

[9] L. Michaelis, THIS JOURNAL, **58**, 873 (1936).

chosen so that the minimum conveniently measurable intensity of color is produced. For this case the ratio of color formed with a given concentration of parent substances, compared with that formed in very strong alkali, will be extremely small, and thus suitable for the experiment.

It will be shown that the color, even under the above strict condition, is practically independent of the volume. The very slight deviations are not in such a direction as to be expected if the purple substance were a bimolecular compound, but in the opposite direction. The deviations are so slight as to be almost within the limits of error. They will be properly discussed. At any rate the experiment furnishes a definite proof that the purple substance has the same molecular size as benzil and benzoin. This fact fully establishes the identity of this compound as being a radical and not a bi- or polymeric compound. This, then, is the first case where all the features of the semiquinone theory, which deals with substances of the quinoid type, may be transferred to a compound, the characteristic groups of which are aliphatic.

Experimental

The apparatus shown in Fig. 1 was constructed to allow of the preparation of the colored intermediate in the absence of oxygen, to which it is sensitive, in two solutions of different concentrations under otherwise exactly comparable conditions. It consists essentially of a buret connected, through a mixing chamber, to a ground joint to which can be attached either of two cylindrical cells (A) and (B) with plane glass ends. (These are shown enlarged in the figure.) These cells have the same over-all length, but one (A) contains a glass partition in such a position that one chamber of the cell is about one-seventh the total length of the other cell (B). The other chamber of A contains the same alcoholic sodium hydroxide in which the benzoin and benzil are dissolved, so that when the cells have been filled with the benzoin–benzil solution, the comparison of color intensity is made through equal lengths of solution. The internal length of the small chamber of A is 19.3 mm., that of B is 138.7 mm.; the ratio is 7.19. The buret is fed by an all-glass siphon from a flask containing alcoholic sodium hydroxide. Before a series of experiments the entire system (including the alcoholic sodium hydroxide) is freed of oxygen by evacuating with an oil pump and flushing with nitrogen. The traps shown contain alcohol, in order that the concentration of the solutions will not be changed by evaporation.

The procedure adopted was as follows: one of the cells was attached to the mixing chamber which previously had been flushed with nitrogen; the gas was then passed through the cell for ten minutes, and both outlets closed. The mixing chamber and cell were detached from the buret and equivalent weights of benzil and benzoin were introduced into the mixing chamber which, with the cell, was replaced and rinsed thoroughly with nitrogen. The requisite amount—depending on which cell was being used—of alcoholic sodium hydroxide was measured into the mixing chamber from the buret, and stirred by the gas stream until the solid had dissolved completely. This solution was run into the cell which was stored in the dark until the same operations had been repeated with the other cell, and the two could be compared. About an hour elapsed between the times of filling the two cells.

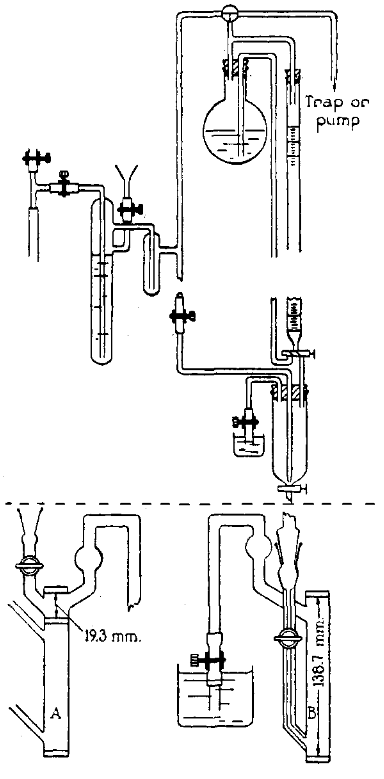

Fig. 1.

The benzil and benzoin were commercial products of high purity; 12.5 mg. of the former and 12.6 mg. of the latter were used. The alcohol—95% ethyl alcohol—was boiled just before dissolving the roughly weighed pellets of sodium hydroxide. The light precipitate of sodium carbonate which formed settled to the bottom of the flask in the course of several hours, and the solution was perfectly clear, except for a barely perceptible yellow tinge. The concentration of the sodium hydroxide was about 0.19% as calculated from the weight of the sodium hydroxide and the volume of alcohol; the solution was not titrated, since an accurate knowledge of the concentration is of no significance to this work. This concentration had been chosen from preliminary tests as that which gives about the right (low) intensity of color with the amounts of benzoin and benzil used.

The color intensity of two cells was compared visually. In every case (the experiment was repeated nine times) the intensities were nearly the same; in fact, the more dilute solution—which, if the color were due to a dimer, would have about one-seventh the color of the concentrated solution—actually was always a little darker by 15 or 20%.

This was estimated simply by pouring out solution from the long tube into the side-arm until the intensities matched, then measuring the column of liquids. The order in which the cells were prepared made no difference in this ratio. That the compound is stable, certainly within the time of the experiment—and actually much longer—is proved by the fact that if one cell were prepared and left overnight, and the next day a fresh solution were prepared in the other cell, a change in the ratio could barely be observed. The observed deviation from a 1:1 ratio seems to be just outside the limits of error even by this rough method of estimation.

Although for the problem in question this deviation is insignificant, an attempt at its explanation is worth while. There are at least two circumstances both of which could cause a slight deviation in the observed direction. First, benzoin is an acid, very weak indeed, but able to neutralize a small fraction of the sodium hydroxide used. The amount neutralized in per cent. of the total sodium hydroxide is greater in the experiment with the smaller volume, so that the concentration of sodium hydroxide is a little greater in the longer tube and hence its color is deeper. On reducing the total concentration of benzil and benzoin (2.50 and 2.55 mg., respectively, instead of 12.5 and 12.6 mg.) and using the same concentration of alkali, the ratio remained the same (1:0.85) whereas if the above explanation were correct, it would approach 1:1. As the variation of the concentration must be kept within rather narrow limits for technical and optical reasons, and because the accuracy of the color comparison is low, this experiment is not conclusive. Still it is unlikely that this explanation is sufficient.

Second, it is possible that a dimerization of the purple radical to a bimolecular species having a less intense or no color, takes place to a noticeable extent. As this dimerization would involve a bimolecular reaction it would proceed to a smaller extent in the experiment with larger volume. In any event, if there be a dimeric compound formed at all, it must be in equilibrium with the radical. Obviously even if some bimeric compound be formed it is not the purple compound.

An explanation for the fact that this radical is a surprisingly stable compound may be found in the perfect symmetry of its structure. Its formula written in the ionized form as it will exist in sufficiently alkaline solution shows the odd electron on one of the two oxygen atoms: $C_6H_5CO^-COC_6H_5$. The probability that it may belong to the other O atom is the same. So, there is a resonance, enhanced by the proximity of the two O atoms sharing the electron. This resonance contributes to the stability of the radical and shifts the equilibrium in its favor. It is the same principle which has been applied previously to the explanation of the stability of the semiquinone radicals.[8]

The knowledge acquired hereby may be used for a discussion of the process of oxidation of benzoin to benzil. When a solution of benzoin in alcoholic sodium hydroxide is exposed to an oxidant such as oxygen or iodine, it is easy to observe that the oxidation proceeds in two steps, the intermediate being the radical. Unless the conditions of alkalinity are such as to make possible the formation of the radical, no oxidation occurs. There are two reasons why the observation of the two successive steps is easy in this case. One is the high concentration of the radical obtainable due to its stability, the other is the fact that the disappearance of the radical by oxidation with oxygen or iodine is instantaneous, but its reëstablishment after the consumption of the oxidizing agent is slow. This slowness is due to the fact that that form of benzoin best accessible to oxidation is its enolic form. This form has been shown by Weissberger[2,10–12] to arise rather slowly from the ketonic form. This author showed that the enolization is so slow that its rate is the limiting factor for the rate of autoxidation of benzil.

So it can be seen that the oxidation, which as a whole is bivalent, will proceed only if the conditions are such as to allow it to proceed in two successive univalent steps. It may be that in many other cases less accessible to experimentation the mechanism of bivalent oxidation is quite similar. It will be the task of further research to investigate to what extent this example can serve as a model for the oxidation of organic compounds in general.

The theory of Franck and Haber, and Haber and Willstätter,[13–15] seems to be related to the one presented here. There is, however, a fundamental difference. The radicals suggested by these authors are supposed to start a chain re-

---

(10) A. Weissberger, A. Dörker and W. Schwarze, *Ber.*, **64B**, 1200 (1931).

(11) A. Weissberger, *J. Chem. Soc.*, 223 (1935).

(12) A. Weissberger and W. Bach, *ibid.*, 226 (1935).

(13) J. Franck and F. Haber, *Sitzber. preuss. Akad. Wiss.*, 250 (1931).

(14) F. Haber, *Naturwissenschaften*, **19**, 450 (1931).

(15) F. Haber and R. Willstätter, *Ber.*, **64**, 2844 (1931).

action which according to conditions may break sooner or later. The final state of the system depends on kinetic factors. The process of oxidation in our example is a reversible process. Provided benzoin is fed with the oxidizing agent continuously at a sufficiently slow rate, the gradual oxidation of benzoin to benzil is a continuous shift of thermodynamical equilibria.

Summary

The purple substance on an oxidation level between benzil and benzoin is a radical of the same molecular size as benzil and benzoin. Its stability is due to resonance. The oxidation of benzoin to benzil on adding an oxidizing agent such as oxygen or iodine proceeds in two successive univalent steps. Oxidation does not proceed at all unless the conditions, especially those of alkalinity, are such as to allow the existence of the radical in equilibrium with benzoin and benzil.

NEW YORK, N. Y. RECEIVED MARCH 31, 1937

[CONTRIBUTION FROM THE BURROUGHS WELLCOME AND CO., U. S. A., EXPERIMENTAL RESEARCH LABORATORIES]

Some N-Aryl Barbituric Acids. III

BY JOHANNES S. BUCK

There has recently appeared in this Journal[1] a description of some colored barbituric acids, the object of the work being to obtain a hypnotic which would preferentially stain certain tissues. In the paper mentioned it is the 5-carbon atom which carries the chromophore. The author has been working recently with N-aryl barbituric acids[2] and it seemed that these offered greater possibilities in the way of colored hypnotics, as there would be less chance of destroying the pharmacological properties if substitution were carried out on the N-aryl group.

1-Phenyl-5,5-diethylbarbituric acid[2,3] was nitrated, and gave approximately equal amounts of the meta- and para-nitro derivatives. These were readily reducible to the corresponding amino compounds. These latter behave as typical aromatic amines, the amino group being acylated and diazotized readily. The diazonium group is replaceable by hydroxyl, chlorine, etc., and may also be coupled with a variety of amines and phenolic compounds to give typical azo dyes. 1-*p*-(Phenylazo)-phenyl-5,5-diethylbarbituric acid (prepared by condensation) is included for check in the pharmacological work, which will be reported elsewhere.

Dox[4] has described an ethylene-N,N′-bis-(5,5-diethylbarbituric acid), prepared from ethylene diurea and ethyl diethylmalonate. The analogous *m*-phenylene- and the *p*-phenylene-N,N′-bis-(5,5-diethylbarbituric acid) have been made by condensing 1-*m*- and 1-*p*-ureidophenyl-5,5-diethylbarbituric acids with the same ester, and these are described in the present work.

Experimental

1-Nitrophenyl-5,5-diethylbarbituric Acids.—Twenty-six grams of 1-phenyl-5,5-diethylbarbituric acid was ground up and dissolved in 100 cc. of concd. sulfuric acid at −5°. During one hour a solution of 4.30 cc. of fuming nitric acid (sp. gr. 1.50) in 25 cc. of concd. sulfuric acid was dropped in. After a further hour the solution was poured onto crushed ice and, after standing, the solid was filtered off and washed with water. The reaction mixture was stirred mechanically throughout, and the temperature held at −3 to −5°, by means of ice–salt cooling. The conditions given are critical.[5]

Prolonged fractional crystallization from alcohol gave small amounts of the meta and paranitro compounds, the major portion being inseparable by any reasonable amount of effort. The nitro compounds were orientated by reduction to the corresponding amino compounds, whose structure was known. For practical purposes the mixed nitro compounds, after one recrystallization from alcohol, were reduced directly and the amino compounds then separated by fractional crystallization.

1-Aminophenyl-5,5-diethylbarbituric Acids.—Eighteen and three-tenths grams of the mixed nitro compounds, ground up and suspended in 150 cc. of 95% alcohol, was reduced catalytically (platinum oxide at room temperature). A considerable proportion of the crude para compound separates toward the end of the reduction and is filtered off. This product and the material obtained from the filtrate are then crystallized fractionally until pure, a laborious operation in view of the close similarity between the meta and para compounds. There is so obtained approximately equal amounts of two compounds melting at 226 and 234° when pure. No third isomer was found.

The compound of m. p. 234° was identified as the para compound by direct comparison (mixed m. p., etc.) with

---

[1] Pierce and Rising, THIS JOURNAL, **58**, 1361 (1936).

[2] Buck, *ibid.*, **58**, 1284, 2059 (1936).

[3] Hjort and Dox, *J. Pharmacol.*, **35**, 155 (1929).

[4] Dox, THIS JOURNAL, **55**, 1230 (1933).

[5] *Cf.* Bousquet and Adams, *ibid.*, **52**, 224 (1930).