interest to note the difference in behavior of the two aromatic aldehydes herein considered, and of methyl glyoxal (pyruvic aldehyde) towards silver and mercuric oxide in the presence of sodium hydroxide. Denis[1] found that with methyl glyoxal the benzilic acid rearrangement is practically not affected by the presence of the oxide of mercury or silver, while the two aromatic aldehydes give practically no other substance than the benzoic acid. In the case of benzoylformaldehyde with silver oxide and sodium hydroxide a trace of mandelic acid was obtained[2] but the main product was an almost quantitative yield of benzoic acid. In conclusion we wish to thank Mr. Evan Mahaffey, of this laboratory, for the carbon and hydrogen determinations of the osazone analysis given above.

COLUMBUS, OHIO.

[CONTRIBUTION FROM THE RESEARCH LABORATORY, ROOSEVELT HOSPITAL, NEW YORK.]

THE PREPARATION OF TRIBASIC PHENOLPHTHALATES.

BY P. A. KOBER AND J. THEODORE MARSHALL.

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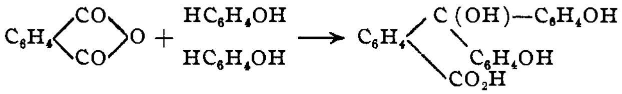
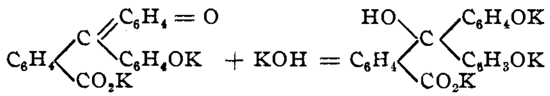
Introduction.

When Baeyer[3] heated phenol and phthalic anhydride in the presence of sulfuric acid, he did not obtain phenolphthalic acid as follows from the equation,



but obtained a substance having one molecule of water less; namely, a lactone or anhydride, which is called phenolphthalein.

Phenolphthalic acid has not yet been prepared, and according to Baeyer it does not exist. Recently the fading of the phenolphthalein color, due to excess of alkali, has been ascribed to the formation of salts of phenolphthalic acid.[4]



We determined from the study of the fading velocity, that the colorless substance was the product of one molecule of alkali and one molecule of dibasic alkali phenolphthalein.[5] On determining the concentration of the reacting substance at equilibrium, we found that the result agreed with the following equation:

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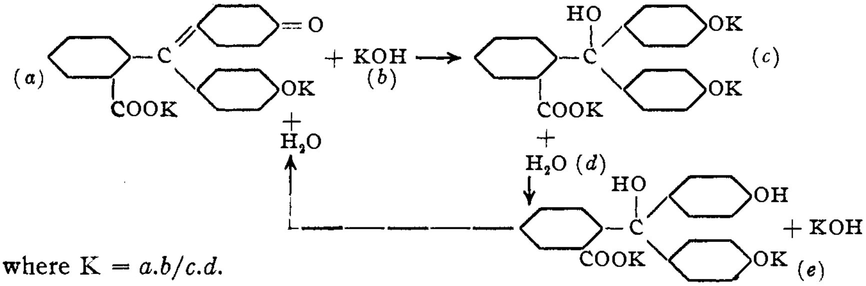
[1] *Am. Chem. J.*, 38, 585.

[2] *Ibid.*, 35, 131.

[3] Baeyer, *Ber.*, 4, 659 (1874).

[4] Green and Perkin, *J. Chem. Soc.*, 85, 389. Acree, *Am. Chem. J.*, 42, 122.

[5] Kober and Marshall, THIS JOURNAL, 33, 59 (1911).



where K = $a.b/c.d$.

These experiments support the hydration theory of the formation of alkaline phenolphthalates.

In a previous paper[1] we gave the description and analysis of tripotassium phenolphthalate in order to corroborate our theoretical deductions, but did not include the method of preparation. Therefore, it is the object of this paper to give the preparation and composition of these alkaline phenolphthalates.

Preparation of Phenolphthalates.

In the early part of the work we found that the colorless salt in solution was extremely unstable, returning in the absence of alkali to the colored form very quickly. This led to the belief that it existed only in the presence of free alkali. The finding of a few colorless crystals, which on being dissolved and heated yielded phenolphthalein, showed that the isolation of the salt was a possibility, and on applying deductions from the mass law the preparation of these salts offered no particular difficulty. Using the equilibrium formula $K = a.b/c.d.$ or $c = a.b/d.K.$, we found that a strong concentration of phenolphthalein (a) together with a strong concentration of alkali (b) on one hand, and a low concentration of water (d) on the other hand, gave us the most suitable concentrations for the production of alkali phenolphthalates (c). The low concentration of water was obtained by evaporating the reaction mixture in a vacuum.

Tripotassium Phenolphthalate.—To 100 grams of commercial phenolphthalein, mixed with sufficient hot water to form a thick paste, are added 200 to 300 grams of potassium hydroxide in the form of a hot saturated solution. The resulting solution is concentrated over a steam bath in a vacuum pan at a low pressure, until the liquid is filled with crystals. In this laboratory a good water pump gave us sufficient vacuum for this purpose. A capillary tube inserted as an inlet for air to the pan, which keeps the liquid in a state of agitation, was found advantageous. Rapid evaporation, which tends to cause the formation of crystals in too minute a form, is to be avoided. Usually the crystals can be filtered through a Buchner funnel, using filter paper

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[1] *Loc. cit.*

or asbestos, but if the crystals are too small or the mother liquid too viscous, a mat of rough asbestos fiber will serve satisfactorily. Suction is applied until most of the mother liquid has been removed and the crystals are nearly dry. The purification of the crystals is accomplished by removing the crystals from the filtering apparatus to a large dish or mortar and mixing them with cold benzene or petroleum ether containing 20–30 per cent. alcohol.

After thoroughly washing the crystals in this way five or six times, the crystals can be finally washed with a small quantity of 95 per cent. ethyl alcohol cooled to —10°, followed by one washing with absolute alcohol at a low temperature. The alcohol will dissolve all of the alkali and at the same time some tribasic salt. After filtering off all of the alcohol the crystals are washed with two portions of absolute ether, and immediately dried in a vacuum desiccator. To obtain perfectly colorless crystals, the washing and drying should be done quickly and under conditions of coolness and freedom from moisture. The yield varies from 60 to 80 per cent., depending on the number of washings. We give here the analysis of the salt as stated in our first paper:[1]

Calculated for $C_{20}H_{12}O_4K_3(OH).5H_2O$: C, 44.38; H, 4.27; K, 21.73
Found: C, 44.40; H, 4.37; K, 21.77

The crystals, upon microscopic examination, are revealed as colorless rhomboidal plates, which rapidly assume small, discrete, superficial areas of color, giving the mass when viewed microscopically, a pinkish tint. On careful heating they lose water and their crystallin form taking on an intense opaque purple color (the dibasic salt, see salt of Meyer and Spengler[2]) with a bronze iridescence, simulating in luster crystals of potassium permanganate. They retain their purple tint on cooling in the absence of moisture, but on exposure to air fade by passing through various tones of red to lighter colors, after which they deliquesce. Under ordinary conditions, the almost colorless salt is fairly stable, showing only a slight pink tint. The crystals are insoluble in ethyl ether, benzene and acetone, slightly soluble in amyl alcohol, but in water, and also in ethyl alcohol they dissolve rapidly with the production of very little color, especially if the temperature be kept at 0°. Upon long standing or boiling the aqueous solution intense color develops.

Trisoduim Phenolphthalate.—The isolation of the corresponding sodium salt involves considerable difficulties. As the sodium salt is more soluble and hydroscopic than that of potassium, it is necessary to evaporate to a greater concentration and in general to handle the product at a lower temperature. Large crystals are here very necessary for the successful isolation of the pure sodium salt.

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[1] *Loc. cit.*

[2] *Ber.*, **38**, 1318; **41**, 2446.

Although the general method of preparation of the sodium salt is the same as that of the potassium salt, yet the details of its preparation may be worth giving and are as follows:

One hundred and fifty grams of commercial phenolphthalein in an aqueous paste were treated with 200 grams of sodium hydroxide dissolved in the least quantity of hot water. After evaporating in a vacuum for an hour or more, large crystals filled the dish. The mother liquor was drawn off through a perforated plate with the aid of suction, and the crystals washed in turn with alcoholic benzene, alcohol and ethyl ether, at a temperature not above 0° as described under the preparation of the potassium salt. After drying, 170 grams of sodium phenolphthalate were obtained, making a yield of 63 per cent.

This process of purification of the sodium salt is not quite satisfactory; under the best of conditions the salt always contains from 0.6 to 0.7 per cent. excess of sodium, which is equivalent to 0.2 and 0.3 molecule above the required three molecules. Attempts to improve the purification by using acetone as a washing medium were unsuccessful, as a tendency of the acetone to react with the phthalates was observed similar to the action observed by Orndorff and Delbridge.[1]

On determining the amount of phenolphthalein and sodium, it was found that the results were fairly consistent with the formula

$$C_{20}H_{12}O_4Na_3(OH) + 6H_2O.$$

	Found.		Theor.
Phenolphthalein (less 2 atoms of hydrogen)....	60.0	60.7	61.9
Sodium....................................	14.2	14.1	13.5
$OH + 6H_2O$ (by difference)[2]................	25.8	25.2	24.5

Trisodium phenolphthalate crystallizes in simple rhombohedrons.[3] Its properties are similar to those of the potassium salt but it is more soluble and apparently less stable.

In general these alkaline phthalates are beautiful well defined, colorless crystals, and when kept in a cool and dry place are stable for months. Of the three molecules of alkali, two are easily neutralized, even by weak acids such as acetic, carbonic, etc. The third molecule of alkali, most probably joined to the carboxyl group, is fairly resistant, but is easily

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[1] Orndorff and Delbridge found that acetone readily formed a compound with tetrachlorogallein (*Am. Chem. J.*, **46**, 1 (1911)).

[2] In his article on the pharmacological action of the phthalates, Rowntree (*J. Pharmacol.*, May, 1911) gives, according to our investigation, two molecules of water of crystallization to the sodium salt. This datum, which was based on an alkalinity titration, is unfortunately incorrect as it was obtained under the wrong assumption that it was, like the potassium salt, free from excess of alkali.

[3] In our first paper we give in the addendum, the crystallization of the sodium salt as cubes. Although most of the crystals are cubical in appearance, they do not belong to that system.

displaced by mineral acids. The salts are insoluble in ethereal solvents and acetone, but are readily soluble in ethyl alcohol and water.

Summary.

(1) A description is given, for the first time, of a method for the isolation of tribasic phenolphthalates.

(2) Trisodium and tripotassium phenolphthalate are described.

We hope to apply this hydration method to other compounds, containing a phthalic acid group, such as the chloro and bromo derivatives of phenolphthalein, fluorescein, gallein, etc.

CONCERNING THE DECOMPOSITION OF URIC ACID BY MEANS OF DILUTE SODIUM HYDROXIDE SOLUTIONS.

By Clarence E. May.

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In recent years there have appeared in the literature three methods of biochemical importance, methods in which it seems to be the notion that by cutting down the dissociation of a given reagent, the activity of the reagent may be muzzled so that the desired action may be obtained without any side reactions taking place. The first of these methods to be proposed had to do with the determination of uric acid in urine, by the Folin-Shaffer method, wherein ammonium sulfate was added to prevent decomposition of the uric acid while precipitating the latter by means of ammonium hydroxide. In cutting down the dissociation of the ammonium hydroxide by having a large amount of ammonium sulfate present, the uric acid decomposition was diminished. The second method proposed was the Folin method for the determination of urea in urine. By having a large amount of magnesium chloride present along with the hydrochloric acid in the digestion mixture, it seemed that the dissociation of the acid was cut down and as a result the action of the acid on the non-urea constituents of urine was but slight.

Recently a modification of the Folin method for the ammonia estimation in urine was proposed by Steele[1] and in the modified method it was suggested that by the addition of a very large excess of sodium chloride it was possible to cut down the activity of the sodium hydroxide employed in the method to liberate the ammonia, since the dissociation of the caustic soda would be diminished by the presence of the sodium chloride. In other words, since the use of sodium hydroxide rather than sodium carbonate seemed necessary for the complete liberation of the ammonia in a mixture such as urine, the side action of the alkali on other urinary constituents would be prevented by the presence of an excess of sodium chloride.

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[1] *J. Biol. Chem.*, **8**, 365.