3′-Arsonic Acid.—The alkali solution of the crude product was yellow with red fluorescence, which fluorescence was not observed in the case of the purified arsonic acid.

4′-Arsonic Acid.—Addition of the diazo mixture to the alkaline arsenite solution immediately caused the latter to turn almost black, and the precipitate which separated when this mixture was heated was dark red.

2′-Arsonic Acid.—Attempts to prepare this acid by the method used for the 3′- and 4′-isomers proved futile. The yield of alkali-soluble material averaged only about 7%, and no arsonic acid could be isolated from it.

Summary

1. By condensing the monothiosulfuric acid of *p*-amino-dimethylaniline with nitrobenzaldehydes, 2-nitrophenylbenzothiazoles have been obtained, reduction of which gave the corresponding amino derivatives, from which in turn arsonic acids were prepared. In one of these initial aldehyde condensations, the intermediate benzal derivative was isolated and identified.
2. By similar reactions, using hydroxybenzaldehydes, the corresponding 2-*o*- and -*p*-hydroxyphenyl-benzothiazoles have been secured, and the *meta* isomer from the *m*-amino derivative.
3. The new compounds described are the following: the 2-phenyl, 2-(*o*-, *m*- and *p*-nitrophenyl), 2-(*o*-, *m*- and *p*-aminophenyl) and 2-(*o*-, *m*- and *p*-hydroxyphenyl) derivatives of 6-dimethylamino-benzothiazole; 2-phenyl-6-dimethylamino-benzothiazole-3′- and -4′-arsonic acids; 2-(*p*-dimethylaminophenyl)-6-dimethylamino-benzothiazole and the intermediate anil.

New York, N. Y.

[Contribution from the Cleveland Clinic]

THE PREPARATION OF A STABLE COLLOIDAL SOLUTION OF LEAD

By M. Telkes

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When Sir William Blair Bell[1] announced the results of his treatment of cancer by colloidal lead, the need at once became apparent of finding a method of preparing colloidal solutions of lead which would be stable and which could be used for intravenous injection. It was to find such a method that the studies were undertaken which are reported here. Our problem was to prepare a solution which could be boiled and could be kept for a long time without precipitation, and at the same time would have a rather high concentration and could be prepared without the aid of protective colloids.

A search of the literature has supplied abundant data concerning methods for preparing colloidal lead and lead compounds. Bredig ob-

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[1] Bell and others, *Lancet*, 1, 537 (1926).

tained colloidal lead by a method originally used by him in the preparation of metal hydrosols, the essential feature of which is an electric spark maintained between two lead electrodes submerged in water, 30–110 v. and 5–10 amp. being used. This method was slightly modified by Billiter, who substituted iron or zinc electrodes covered with a thin coating of lead for the lead electrodes used by Bredig.

By means of alternating and oscillating currents, Svedberg[2] obtained colloidal metal solutions in organic solvents. As a further improvement he enclosed the arc to protect it from the cooling action of the liquid, and as a result was able to obtain a purer and more concentrated colloidal solution of much higher degree of dispersity. The colloid thus obtained, however, always contains particles of different sizes. A certain percentage of the metal forms coarse particles, whereas the finely grained metal remains in solution. The coarse particles are probably formed by the action of the liquid on the molten metal, while the fine particles which form the real colloid are doubtless produced by the condensation of the metal vapor in the liquid. When a metal solution is prepared, the coarse particles are soon precipitated, the amount of this precipitate being very considerable, especially for metals with a low melting point like lead. According to Svedberg's results, this sediment includes about 50–60% of the total amount of lead dispersed between the electrodes. Naturally, the coarse particles cannot be used for intravenous injection, as they would cause thrombosis. The colloidal lead solutions thus prepared are grayish-black, and all those which are dispersed in water are stable only for a few days. Svedberg obtained stable solutions of lead in methyl alcohol and *iso*butyl alcohol, but these cannot be used for intravenous injection.

The low stability of the lead hydrosols is due to the chemical reaction of water and air on the finely divided lead. The colloidal solution is brown in high dilution and turns black as the concentration is increased. If a freshly prepared solution is allowed to stand, in a few hours it turns gray, and in two or three days a grayish-white powder is precipitated, the precipitation taking place more quickly when air is passed through the solution.

Protective colloids do not prevent precipitation of the colloidal lead; moreover, it has been shown that the use of protective colloids is not desirable because of their possible secondary effects such as, for instance, the effects of colloidal silver solutions. However, gelatin (0.4%), as used by Bell, appears to have no secondary effects; or instead of gelatin a solution of gum acacia might be used, as Bayliss found that intravenous injections of a 6% solution of gum acacia have no secondary effects, but even with this solution no permanent stabilization can be effected.

The grayish-white precipitate described above was collected and analyzed

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[2] Börjeson, *Dissertation*, Upsala, **1921**.

for lead, and we found that the lead content varied slightly in relation to the rate of precipitation. On an average the lead content of the precipitate amounted to 78%. The lead content of lead carbonate is 77.6%, while that of lead hydroxide is 85.9%. The above figures indicate, therefore, that lead carbonate is the principal constituent of the precipitate and that the cause of precipitation is most probably the carbon dioxide of the air which is dissolved in the water. This was further proved by the finding that in a colloid, formed in water, which had been boiled to expel the carbon dioxide and kept in air protected from carbon dioxide, the precipitation was retarded.

The question which we had to answer was whether the precipitation is due to the water or to the air dissolved in the water. To decide this, the water was boiled and cooled in a hydrogen atmosphere, and was then saturated with hydrogen, by passing the gas through it for one-half to one hour. The colloidal solution was then prepared in this water saturated with hydrogen, the passage of hydrogen being continued throughout the preparation. When the current was turned on, the colloidal lead streamed from the spark in brown clouds and the whole solution turned black. When the black solution was kept in a sealed glass container without having come into contact with air, and in a hydrogen atmosphere, it remained black. The particles of larger diameter settled quickly and no more particles were precipitated afterwards. The sediment adhered to the glass wall and was black in color. When the sealed glass bulb was opened and the solution of colloidal lead was exposed to the air, it turned gray in a few hours and in two or three days the lead was precipitated as a grayish-white powder. When 1 or 2 cc. of air was passed into 100 cc. of colloidal solution in a hydrogen atmosphere, only a small part of the lead solution was precipitated as a grayish-white powder, while the remainder of the solution invariably remained black. This experiment proved that the air is the cause of the precipitation, and if the colloid is kept in a hydrogen (or nitrogen) atmosphere it can be kept stable for months.

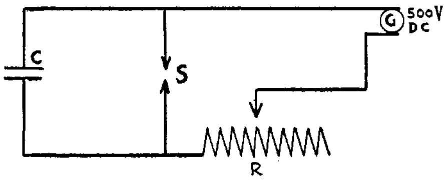

Fig. 1.

Apparatus

The apparatus used for the preparation of colloidal lead is constructed by using the enclosed arc and the method of undamped oscillations.

A generator producing 500 v. direct current is used. The capacity (*C*) of 0.034 microfarad is connected parallel to the spark micrometer (*S*),[3] and the current intensity can be regulated by the resistance *R* (see Fig. 1).

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[3] The spark micrometer was made by Mr. V. Seitz of the Electro-Mechanical Engineering Department of the Cleveland Clinic.

The lead electrodes can be replaced and the connecting wires are mounted in the isolating glass tube. The lead electrodes are measured before and after each experiment, the difference in their values giving the total amount of dispersed lead. A silica tube is fastened to the lower lead electrode, and is fitted closely to it. The upper electrode is made somewhat smaller in diameter, so that it can be moved up and down by the micrometer screw. The silica tube is provided with a hole 3 mm. in diameter and is adjusted so as to bring this hole directly in front of the spark.

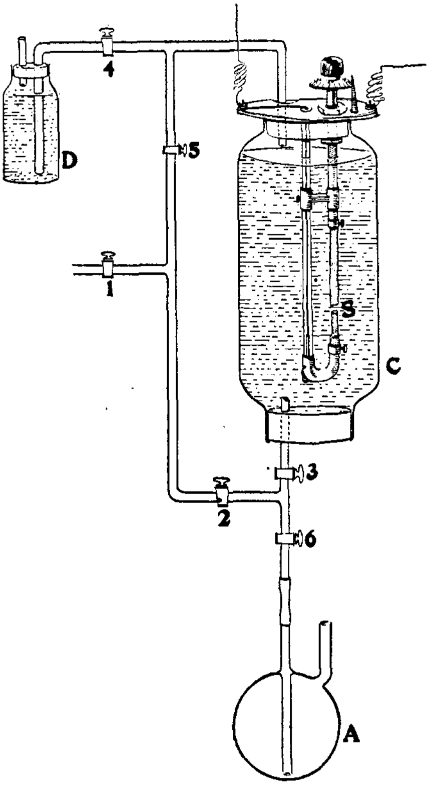

Fig. 2.

When the spark micrometer is in use it is placed in a glass vessel *C* (Fig. 2) with a capacity of about 600 cc., which is filled with conductivity water. This vessel is provided with the necessary tubes for conducting hydrogen gas, which is conducted from a Kipp generator through washing bottles and Stopcocks 1 and 2; it passes through the water and leaves the vessel through Stopcock 4 and then passes through the bottle *D*, which is filled with water to make the system air-tight. The hydrogen gas is passed through *C* for a preliminary period of half an hour, and during the period of sparking.

When the current is sent through the electrodes the spark is blown out into the liquid and the colloid rises in black clouds. When the colloid has reached a sufficient concentration, Stopcock 3 is closed, Stopcock 6 is opened, and the glass container *A*, in which the colloid is preserved, is filled with hydrogen in the following manner.

It is first completely filled with distilled water. Then some of the colloidal solution is allowed to run down to fill the tubing closed by Stopcock 6. Stopcocks 2 and 6 are then opened and hydrogen is allowed to stream through for a few minutes to expel the air. Then the container is connected to the glass tube by means of rubber tubing, which is attached to the longer glass tube reaching into the container. The other glass tube is connected with a bottle by means of rubber tubing. The hydrogen forces out the water and fills the container, and when it is filled with the gas, Stopcocks 2 and 4 are closed and 3, 5 and 6 are opened. The hydrogen is now going through Stopcock 5 and forcing the colloidal solution through 3 and 6 into the container. When this is almost filled, Stopcocks 3 and 5 are closed, 2 is opened, and hydrogen is passed through for about ten minutes. After this, the two tubes of the container are sealed by fusion.

A part of the colloidal solution is analyzed for lead by the chromate titration method of Diehl.[4] The colloid is dissolved in acetic acid, and a measured amount of 0.1 *N* potassium dichromate solution is added. The lead chromate precipitate is filtered and the excess of potassium dichromate is measured with sodium thiosulfate.

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[4] Diehl, *Z. anal. Chem.*, **19**, 306 (1880).

The total amount of lead dispersed per minute by 500 v., using a capacity of 0.034 microfarad and a current of 1 amp., is 0.012 g.

Summary

1. It is shown that the precipitation of lead hydrosols is due to the oxygen and carbon dioxide of the air.
2. An apparatus is described by means of which the colloidal solution can be prepared under an indifferent atmosphere and can be rendered more stable.
3. Thus far we have not been able to maintain a stable solution of a higher concentration than 0.2%.

CLEVELAND, OHIO

NOTE

Aluminum Amalgam as an Agent for the Reduction of Phenylsulfone Chlorides to Thiophenols.—Aluminum amalgam in alcohol-ether solution has long been known to be a neutral and, therefore, desirable reducing agent in many cases.[1] Nevertheless, it has not been used in general for the reduction of aromatic sulfone chlorides to thiophenols, as it has been found that the amalgams sometimes split off the sulfonic group, replacing it with hydrogen. Thus, sulfocinnamic acid is reduced upon treatment with aluminum amalgam to cinnamic acid or even further.[2]

α-Naphthol-2,4-disulfonic acid is known to be reduced with sodium amalgam to α-naphthol-2-sulfonic acid. However, in the tested cases where an aromatic sulfone chloride was reduced in alcohol-ether solution, this tendency to split off the sulfonic group was not found to be great, especially when the reaction was not allowed to become too violent.

With reactions which are, at least to a certain extent, analogous to that with aluminum amalgam reported here, metallic calcium only has been used previously for the reduction of aromatic sulfone chlorides to the corresponding thiophenols in acid-ether-alcohol solution.[3]

The advantages of the reduction with aluminum amalgam apply particularly well to the intended reactions; thus, it is possible to regulate the intensity of the hydrogen evolution by the gradual addition of water, and the separation of the formed mercaptans, especially in the case of amphoteric substances, is facilitated. In addition, by this method, the careful control of the temperature[4] which is sometimes necessary is not essential, as the intensity of the reduction can be regulated, as already mentioned.

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[1] (a) Wislicenus, *J. prakt. Chem.*, **54**, 18 (1896). (b) Cohen and Ormandy, *J. Chem. Soc.*, **57**, 811 (1890).

[2] Moore, *Ber.*, **33**, 2014 (1900).

[3] Beckmann, *Ber.*, **38**, 904 (1905).

[4] Zincke, *Ber.*, **51**, 755 (1918).