of these considerations seem then to emphasize the similarity pointed out before between the transformation of the acido (purpureo)-pentammine salts in aqueous solution into the aquo(roseo)-pentammine salts and the electrolytic dissociation of the strong electrolytes in water.

Summary.

1. A method of calorimetry has been developed in which only observations on a silver coulometer, and of time and electrical resistance are required.

2. It has been shown that the same sulfide of cobalt (Co_2S_3) is produced by the action of sodium sulfide on chloro- and aquo-pentammine cobalt chloride in aqueous solution.

3. The solubility of chloro-pentammine cobaltic chloride has been measured at several temperatures, and its heat of solution has been computed from these data, and found to be in fair agreement with the directly measured values.

4. The heats of solution in water of a number of acido- and aquo-pentammine cobaltic salts, and their heats of reaction with aqueous solutions of sodium sulfide have been measured. From these data the heats of transformation of the solid acido to the corresponding solid aquo ammines have been calculated.

5. The heats of transformation have been found to be antibat to the velocities of transformation, but probably symbat to the free energies of transformation, a reaction similar to that shown by the ionization of salts in water.

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NOTE.

An Interesting Colloid Gel.[1]—The structure of gels has been a question which has given rise to numerous investigations and we are still far from unanimity of opinion. Probably one of the factors which contributes to the difficulties of the problem is the complexity of the disperse material. Gelatin, for example, has been used in many investigations, but when we realize how inadequate our knowledge is regarding the chemical configuration of the gelatin molecule, and how easily proteins may be altered by physical or chemical factors, it is not surprising that the experimental results have been found to differ widely when different samples of gelatin are used. The same objections apply to agar-agar as apply to gelatin.

Aside from the complex organic substances, such as proteins, gums,

[1] Published with the approval of the Director as Paper No. 263, Journal Series, Minnesota Agricultural Experiment Station.

polysaccharides, etc., which show more or less true gel formation, we have silicic acid gels. Here again we have a material of more or less unknown composition. The method of preparing the sodium silicate sol and its past history as well as the concentration of acid by which it is converted into the silicic acid gel all play a part in the properties and behavior of the final gel.

There thus appears to be a need for some substance which can be prepared by anyone in pure form and which will easily set to a rigid gel. We believe that the dibenzoyl derivative of the amino acid *l*-cystine satisfactorily meets all of these requirements.

Preparation of dibenzoyl-*l*-cystine. — Two g. of cystine (prepared from human hair by hydrolysis with hydrochloric acid) was suspended in 100 cc. of water, and sufficient 10% sodium hydroxide solution was added to dissolve the amino acid. Ten g. of benzoyl chloride was then added and enough additional sodium hydroxide (in solution) to make a total of 6 g. The mixture was shaken vigorously until all odor of benzoyl chloride had disappeared. Upon acidification with hydrochloric acid the entire solution set to a stiff gel. This was broken up by agitation and thrown upon a Büchner funnel, and the liquid drained off by a strong suction. After filtering for several hours a felt of crystals of the benzoyl derivative remained upon the filter. This was washed with water and recrystallized from somewhat diluted alcohol, yielding long silky needles melting at 180–181° (uncorr.). Brenzinger[2] gives 180–181° (uncorr.) as the melting point of pure benzoyl cystine, whereas Goldmann and Baumann[3] give 156–158°. Undoubtedly 180–181° is the correct value.

Dibenzoyl cystine is insoluble in water, does not contain water of crystallization and in the crystalline state, at least, has no hydrophilic properties. It is readily soluble in most of the organic solvents and because of the presence of the benzoyl groups it is a relatively strong organic acid.

At the time we prepared our compound we had not consulted Brenzinger's paper but were relying on the data as given in various texts and handbooks. None of those consulted emphasized the gel-forming property. After we had prepared several samples of benzoyl cystine and had particularly investigated its gel-forming properties, we consulted Brenzinger's paper and found that he had recorded the gel formation. He states that if the alkaline solution of benzoyl cystine prepared from 2 g. of cystine as noted above is diluted to 3 liters before acidification with hydrochloric accid, the resulting mixture will be a rigid gel from which no water can be poured. Assuming a quantitative conversion of the cystine into the benzoyl derivative such a gel would have a concentration of 0.124% of benzoyl cystine.

Undoubtedly this observation of Brenzinger's would have attracted the attention of colloid chemists had it not been published at so early a date. The peculiar gel-forming properties of the substance led us to study it further. We found that we could readily prepare a rigid gel in

[2] Brenzinger, *Z. physiol. Chem.*, **16**, 537 (1892).

[3] Goldmann and Baumann, *ibid.*, **12**, 255 (1888).

which the concentration of the dibenzoyl derivative did not exceed 0.2% and that a gel of 0.1% concentration was rigid enough to hold its shape for a minute or more when the beaker containing the gel was inverted. We believe that these are the most dilute rigid gels that have ever been prepared artificially. Gelatin and silicic acid gels require considerably higher concentrations of the colloid material and even the natural gel in which frog eggs and salamander eggs are embedded and the natural gel of the jelly fish contain more solid material.

The Preparation of a 0.2% gel.—Two-tenths g. of pure benzoyl cystine was dissolved in a beaker in 5 cc. of 95% alcohol. While the contents were kept boiling hot, water was added until a volume of 100 cc. had been attained. At this point there was a slight opalescence but no evidence of precipitation or gel formation. The beaker was then covered and set aside to cool. In a short time, usually 2 to 3 hours but occasionally longer, the entire mass had set to a rigid gel comparable to a 5% gelatin gel. In no case was gel formation observed until a considerable period had elapsed after the contents of the beaker reached room temperature.

Properties of the Gel.—The gel was practically transparent, no change in opalescence being observed beyond that exhibited by the freshly prepared sol. The gel can be loosened from the walls of the beaker and will support its own weight for a long time. The beaker containing the gel may be left inverted for several hours without breaking the gel. However, in the course of several days some changes take place. The most noticeable one is the formation of opaque nuclei caused apparently by the aggregation of minute stellate groups of needles throughout the gel structure. This phenomenon is accompanied by syneresis or "bleeding" of the gel so that in the course of several weeks most of the benzoyl-cystine has separated in a definitely crystalline condition. When the freshly prepared gel is thrown upon a filter in a Büchner funnel and strong suction is applied, a limpid liquid filters slowly through and the benzoyl cystine remains practically quantitatively on the filter. Usually 8 to 10 hours are required to filter the liquid from 100 cc. of the gel. After filtration the thin "skin" of benzoyl cystine may easily be separated from the filter paper.

The Structure of the Gel.—The fact that the benzoyl-cystine may be filtered from the freshly prepared gel by the use of ordinary filter paper and suction argues for a relatively coarse degree of dispersion. Unfortunately we do not have access to a Zsigmondy ultramicroscope so that we are still somewhat in doubt as to the true gel structure. When a portion of the gel is viewed by dark-field illumination,[4] using a 4 mm. objective

[4] Using a Wenham-Sidentopf paraboloid and a special slide similar to that described by Lord (*J. Agr. Res.*, **17**, 170 (1919)) with the exception that the cavity in the slide was sufficiently large to allow the insertion of a portion of the gel approximating 5 × 5 mm. surface area and 1 mm. in thickness.

and 12.5 ocular, one observes a fibrillar structure as if the gel were composed of needle crystals of exceedingly small cross section. In fact, the cross section of the fiber is so small as to not be apparent when an oil immersion objective (1.9 mm. fluorite) was used. These fibrillar areas, however, could not be demonstrated to be continuous throughout the gel structure. In certain of our preparations they appeared to be discontinuous and surrounded by an area of approximately equal extent which was optically void. It is possible that the fibers were present in such an area, but we could not demonstrate them with our relatively crude ultramicroscope. Then again the areas in which the fibers could be demonstrated may possibly have been formed by crystal growth following the true gel formation, and may not be essential to the gel structure. Certain of the fibrillar areas apparently grow in opacity and size as the gel ages, serving as nuclei for the crystalline benzoyl-cystine noted earlier. This growth is however to be expected from the Noyes-Nernst rule governing the growth of crystals.

All of the available evidence, however, points to the benzoyl-cystine gel as having a fibrilar structure, the fibrils being exceedingly minute crystals of benzoyl-cystine. The evidence is incomplete, but if 0.2 g. of the non-hydrophilic benzoyl-cystine can form a crystal gel retaining 100 g. of water, such a phenomenon certainly has a profound bearing on the subject of gel formation and gel structure in other systems.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, HARVARD MEDICAL SCHOOL.]

THE RELATION BETWEEN THE MODE OF SYNTHESIS AND TOXICITY OF ARSPHENAMINE AND RELATED COMPOUNDS.[1]

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In the oldest and probably the most widely used method of preparing arsphenamine, 3-nitro-4-hydroxy-phenylarsonic acid is reduced by sodium hydrosulfite directly to arsphenamine base which is then converted into the dihydrochloride by solution in methyl-alcoholic hydrochloric acid and precipitated with ether. This procedure has led to wide variations in the toxicity of the product; some preparations kill at doses as low as 60 mg./kg., whereas others do not kill at 130 or 140 mg./kg. Believing that some

[1] This is the fourth of a series of studies on the properties contributing to the toxicity of arsphenamine being made under a grant from the United States Interdepartmental Social Hygiene Board to the Harvard Medical School; the work is under the general