THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

For years we have had a fairly definite procedure for qualitative and quantitative analysis of inorganic compounds. Within the past decade attention has been given to the qualitative and quantitative analysis of organic compounds and steps are being made toward the development of procedures for similar analyses of organic compounds. The following paper by Dr. George D. Beal, of Mellon Institute of Industrial Research, is of special interest because the author is a leader in the field and he discusses the important subject of background necessary for the development of quantitative organic analysis.—C. B. JORDAN, *Editor.*

WHAT CONSTITUTES A PROPER FOUNDATION FOR THE STUDY OF QUANTITATIVE ORGANIC ANALYSIS.*

BY GEORGE D. BEAL.**, ***

When accepting the invitation to contribute this paper, it was the writer's intention to discuss, in a very general way, the prerequisites for the most effective teaching of organic analysis, or rather pharmaceutical assaying. The subject was therefore fixed as has been announced. Deeper reflection made evident the folly of attempting to review a curriculum in chemistry in a few pages. The paper will accordingly be limited to a discussion of one most essential prerequisite, a comprehensive course covering the fundamentals of quantitative analysis.

Thorough preparation in general chemistry and qualitative analysis is assumed, and also proper training in organic chemistry to accompany or follow the course that we are outlining here. To those who will object that what we are proposing herein is a part of the training of a chemist and not of a pharmacist, we make our reply at this point. Organic analysis, pharmaceutical assaying and clinical analysis are chemical subjects of an applied character. While the practice of these is becoming more empirical, and the list of arbitrary procedures to be followed by the laboratory technician is multiplying, the interpretation of data requires sound fundamental training, with a correct understanding of contributory factors.

Every teacher of analytical chemistry is disturbed, sooner or later, by the pleas of his students to be given practical work. The agricultural student wishes to plunge immediately into the analysis of soils and fertilizers, the budding chemist is anxious to get at coal or stainless steel and the pharmaceutical apprentice doubtless longs to begin upon the assay processes of the United States Pharmacopœia. Teachers generally agree that a proper training in the fundamental principles of quantitative analysis is essential for the student who proposes to master its technical applications and to interpret properly the data so obtained. What shall constitute this fundamental training?

Outline of the Laboratory Course.—The teaching of elementary quantitative analysis has two purposes. The first of these is to emphasize the quantitative character of chemical reactions. The second is to develop on the part of the student a technique that in addition to teaching specific procedures emphasizes exactness of operation. In the selection of laboratory experiments, the final application of these principles is made possible by adopting for teaching purposes those experiments that involve typical reactions and operations. Thus, tradition has it that in the list of gravimetric determinations shall be those of a halide ion, a sulphate ion, a trivalent metallic ion and one of the ions of the alkaline earth series.

The gravimetric determination of the halide is the basic method for the determination of chlorine, bromine, iodine and silver, the first three not only as halide ions but also after reduction from any other valency. The selection of the precipitating reagent illustrates the physico-chemical principles of ionization, solubility and solubility product. The preparation and handling of the solution involves the maintenance of acid reaction to prevent the precipitation of other ions. The colloidal character of the precipitate as first formed requires that it be coagulated by heat and electrolytes at the proper degree of acidity. Washing of the precipitate not only repeats the opportunity for the discussion of colloidal solutions and solubility product, but in the treatment of effective washing with a minimum of liquid suggests what will be taken up in the theory of extraction by immiscible solvents as the coefficient of distribution. Finally, if the precipitate is to be ignited, reduction by burning paper, reconversion by acids and volatility of salts must be discussed. In fact, if one were willing to spend the time upon it, and the temperament of the student would permit, the greater part of the theory of gravimetric analysis could be presented and demonstrated by means of a detailed study of this determination.

In the same way the analysis of a sulphate is not only a type determination but brings in as well the determination of all other forms of sulphur and suggests the determination of any acidic element in organic material. But since the points applicable to several specific determinations are the ones which warrant most emphasis in an elementary course, the determination of sulphate offers two of exceptional importance from the teaching standpoint. The first is the explanation of the contamination of precipitates by occlusion and double salt formation, while the second is the production of filterable precipitates of crystalline materials by crystal growth or digestion. Another reaction worthy of discussion at this time is the dissociation, by heat, of salts of relatively non-volatile bases with more volatile acids. Following this determination with that of iron or aluminum, the theories of hydrolysis and amphoteric reactions are introduced, with a reëmphasis, in certain cases, of the need for control of the state of oxidation. These, of course, represent only one series of determinations that may be used in the introduction to quantitative analysis.

Volumetric Analysis.—Opinions differ as to the proper place in the course for the introduction of volumetric analysis. The place assigned by tradition is following the gravimetric part. Some cases have come to our attention where it follows as a separate course. Some textbook authors treat it in a separate volume. On the other hand, some of our greatest teachers have used volumetric analysis as the introduction to the subject of analytical chemistry.

For my part, I have followed tradition, in devoting the second half of the semester to the subject, and have followed the new thought movement by placing it at the beginning. My real preference, followed for the last few years of my teaching experience, is for an introductory period for gravimetric analysis, then the treatment of volumetric analysis and last of all, combination analyses, involving both procedures, or more elaborate gravimetric analyses involving quantitative separations, double precipitations, etc. We really seem to have had the best results from this arrangement, and the reactions of the students have been exactly those that we looked for in outlining the program.

To begin with, all of quantitative analysis, aside from a very few empirical analyses such as the fire assay of ores, is based upon the theories of definite proportions and of combining weights. It requires less stretching of the students' imagination to calculate the percentage of chlorine in silver chloride, from that the weight in a precipitate of silver chloride and in turn the weight and percentage in an impure sodium chloride than it does to calculate the strength of an acetic acid solution from a volume of standard alkali; the normality factor of the same alkali and the weight of a hydrogen equivalent, or gram equivalent, of acetic acid. Precision in weighing is easier to develop than precision in measuring. Filtration is an operation which, while requiring great care to avoid loss, does not involve the regulation of volumes to a single drop. The student acquires a certain facility in the handling of laboratory apparatus before he begins titration and exact pipette measurements. Attention is also called to the progress of chemical reactions by rates of precipitation and coagulation and settling of precipitates.

Thoroughly understanding the law of definite proportions and the direct relations between samples and precipitates, the student is more ready to grasp the theory of normal solutions as based upon hydrogen equivalents, the gram equivalent system. From his gravimetric determination of chlorine he learns that since the weight of silver chloride is proportional to the sodium chloride in his sample in the ratio of their molecular weights, the silver nitrate required to form the precipitate must be likewise proportional. This suggests that if the concentration of the silver nitrate be known, and if the addition be stopped just at the end of precipitation, the volume of silver nitrate used will be a measure of the sodium chloride originally present. Having previously learned from the law of mass action that a very slight excess of precipitant is required for complete precipitation except when double salts are formed, and knowing that chromate ion will give a color with silver ion in solution, the thought of an end-point indicator as a convenience is suggested. And we now have the thought of volumetric analysis by standard solutions and colored indicators ready for elaboration into procedures based upon normal solutions, grams equivalent and indicators changing their color at certain hydrogen-ion concentrations.

Oxidation and reduction reactions naturally follow neutralization titrations, for the oxidizing power of solutions is measured by their ability to form water from hydrogen just as much as the power of bases to neutralize acids is measured by their ability to form water. Throughout volumetric analysis, the student should be required to determine the hydrogen equivalents of all solutions, and to standardize all solutions on a basis of normality. The policy of requiring the dilution of all solutions to exact decimals of normality is, in my opinion, a poor one.

The exercise is merely one in dilution, and the calculations thereafter become so mechanical that much of the educational value of volumetric calculations is lost.

It is unwise to attempt the teaching of analytical chemistry without explaining the reactions as far as possible, and yet simply, upon the basis of the modern theories of electrolytic dissociation. Aside from the practical applications now being made of these principles, qualitative and quantitative analysis offer the best means of demonstrating the phenomena due to ionization. Solubility of carbonates in acid with effervescence and the greater solubility of metallic sulphides in nitric than in hydrochloric acid demonstrate the removal of ionization repression. The chloride precipitation is illustrative of the common-ion effect in connection with the solubility product. Precipitation of aluminum by ammonia in the presence of ammonium chloride and the composition of magnesia mixture are other admirable demonstrations of common-ion effect. Again, the phenomenon of hydrolysis as regulated by the ionization of acids and bases in determining the stability of salts is well demonstrated by the hydrolysis of ferric sulphate and ferric acetate. While an elaborate presentation of hydrogen-ion control can be made only in a course in physical chemistry, the behavior of indicators in acidimetry and the buffer action of salts offer a very good demonstration in analytical chemistry.

The teacher has great latitude in the selection of special determinations, but they should always be selected with reference to their educational value, rather than as an instructor's hobby. There is one in particular which should never be omitted, the Kjeldahl method for organic nitrogen. This method with its modifications has many applications in organic analysis, both proximate and ultimate. The limitations of time, laboratory space and equipment and the preliminary preparation of the students impose certain limitations that must be observed in selecting additional experiments. Certainly however, in the field of volumetric analysis, acidimetry and alkalimetry, and oxidation and reduction including permanganate and iodine titrations should be included.

Analyzed Samples.—Proper teaching of quantitative analysis requires a careful preparation of samples. It is, in the writer's opinion, never justifiable to use pure salts as laboratory samples. In the first place, such samples invite dishonesty. Students have a pronounced tendency to compare samples and results, and careful inspection of notebooks is only one of the safeguards to be used. Samples should never be prepared with a view to misleading the students, but diluents, when used, should be those that necessitate certain obvious manipulations when preparing the sample for analysis. The complexity of the sample will also be governed by the amount of time available for each determination.

A suggested series of samples is as follows:

1. Mixtures of sodium or potassium chloride and sodium carbonate. These serve a manifold purpose. They may be used for the gravimetric and volumetric determination of chloride ion and for titration with standard acid and methyl orange as an experiment in alkalimetry. If potassium chloride is used, they are also available for separation of the alkali metals by chloroplatinic or perchloric acids. Such samples are non-hygroscopic under ordinary conditions. By substituting potassium sulphate for part of the sodium carbonate, they may be used for sulfate determinations.

2. Mixtures of ferric sulphate, sodium sulphate and sodium carbonate may be used for the determination of iron, gravimetrically by precipitation as the hydroxide with ignition to oxide, and volumetrically, after solution and reduction, by titration with permanganate and dichromate. They are ideal samples for the determination of the sulphate ion, as the filtrates resulting from a double precipitation of iron, when concentrated to an appropriate volume, are not only ready for sulphate precipitation, but give the student the experience of making a quantitative separation of two ions.

3. Limestone from Marblehead or Kelly's Island, Ohio, or Marblehead, Illinois, is easily soluble in hydrochloric acid, and is an excellent sample for the determination of insoluble matter, calculated as SiO_2, for the R_2O_3 group, and for calcium and magnesium. It is also easy to fortify this with respect to silica, R_2O_3 or magnesium by adding, respectively, silica flour, ferric oxide or magnesium carbonate.

4. For practice in the phosphate determination, Tennessee rock phosphate is an ideal material, and may be diluted with silica.

5. A solid acid is desirable for an experiment in acidimetry, rather than a standardized solution. Mixtures of potassium pyrosulphate and normal sulphate, tartaric acid and sodium tartrate or citric acid and sodium citrate are excellent for this purpose. The organic acids should be free from water of crystallization.

6. If it is desired to use an ore for the determination of iron by permanganate titration, hematite from the Lake Superior fields may be diluted with silica flour.

7. Some teachers like to use a water insoluble sample for practice in iodimetry. For this purpose there is nothing better than stibnite, or native antimony trisulphide, which may likewise be diluted with silica. The writer prefers stibnite to an arsenic compound, as it is necessary in the antimony analysis to add tartaric acid before dilution to prevent hydrolysis. An opportunity is also afforded to discuss the characteristics of metallic oxysalts.

8. As samples for the Kjeldahl determination, blood flour or blood meal is excellent. Wheat flour is a very good diluent for use here.

Preparation of Samples.—As fine grinding and thorough mixing of all samples is imperative, grinding the raw material with the diluent in a ball mill is the recommended procedure. Diluents should have a specific gravity approximating that of the original material in order to eliminate the danger of segregation.[1] Even with these precautions the entire bulk of each sample should be well mixed by rolling before parceling out the students' portions.

Volumetric Standards.—Every teacher is confronted with certain difficulties in the way of supplying appropriate reference materials for use in the evaluation of standard solutions. The standards should be as cheap as possible, must be permanent and require little preliminary preparation, and should not involve a lengthy series of reactions.

One of the most convenient standards for acidimetry is anhydrous sodium carbonate. Fortunately it is easy to obtain. Almost any so-called "C.P." grade will serve. As a matter of fact, one can go to a barrel of soda ash and, by scraping

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[1] G. F. Smith, L. V. and E. L. Gard, *Ind. Eng. Chem., Anal. Ed.,* 1 (1929), 228.

away any crust to remove surface contamination, scoop out reagent of a quality sufficient, with drying at 150° C., for the standardization of hydrochloric acid or a carbonate fusion for a silica determination.

Standardization of hydrochloric acid by precipitation of silver chloride is a good experiment to illustrate the use of a filtering crucible. Our experience is, however, that students obtain more reliable and useable values by titration of sodium carbonate.

The use of iron wire for standardization of permanganate and dichromate is well known. Pure iron is probably the best standard for dichromate. For permanganate we have, however, preferred to use sodium oxalate, which is both anhydrous and non-deliquescent.

Arsenous oxide is the logical standard for iodine, which in turn serves to standardize thiosulphate. Its use also affords an opportunity to discuss buffer action. While pure arsenous oxide is easily obtained, it must be carefully dried. It also has the disadvantage that the weight of the gram equivalent is low, so that very small samples must be weighed for the titration. Almost equally satisfactory results can be obtained by using standard permanganate or dichromate to liberate iodine from acidified potassium iodide,[1] titrating the iodine with thiosulphate and the thiosulphate in turn with the iodine solution to be standardized. The explanation of such an indirect method of standardization also has a considerable educational value.

Laboratory Teaching.—In this course the importance of laboratory teaching takes equal rank with class room presentations. Lectures to cover theoretical discussions are necessary. If, however, I had to choose between class room quizzes and laboratory quizzing, I would, except for the purpose of teaching stoichiometry, choose laboratory quizzing of individual students or small groups, at the laboratory desk. There, with everything before the student, incidental reactions may be discussed and demonstrated, errors in manipulation pointed out and various practical applications described. If time is available, and it should be made available, every student should be required to answer a questionnaire on each experiment before his sample or standard reagent is issued. A review of the questionnaire by the laboratory instructor may serve as the basis for the laboratory quiz. While chemical calculations may be reviewed at this time, at least one hour per week should be reserved for discussion, before the entire class, of stoichiometry. An abundance of problems should be ready, in order to have examples to illustrate any particular procedure. Patience in presentation, and insistence upon neatness and accuracy, will secure the maximum of success in teaching analytical chemistry.

The annual meeting of the Society of American Bacteriologists will be held December 29th to 31st at the Massachusetts Institute of Technology, under the presidency of Prof. S. Bayne-Jones; Dr. Barnett Cohen, of Johns Hopkins School of Medicine, is in charge of the program.

The Bouisson-Bertrand Institute, at Montpelier, France, has been authorized by the government to accept an annual subsidy of $10,000 from the Rockefeller Foundation. The money will be spent upon research into the cause and, if possible, promote the cure of Mediterranean fever, also known as Maltese fever.

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[1] Popoff and Chambers, *Jour. Amer. Chem. Soc.*, 45 (1923), 1358; Popoff and Whitman, *Ibid.*, 47 (1925), 2259.