

Extractum Cubebæ, By-Product:—In the manufacture of Extract of Cubebs the Oil of Cubebs can be obtained as a by-product by simply re-distilling the exhausted drug.

Three hundred pounds of drug will yield, from fifty to sixty pounds of extract. The exhausted drug, in turn, will yield ten to twelve pints of Oil of Cubebs which complies with all U. S. P. requirements.

Fluid Orange Soluble, By-Product:—Oil of Orange may be obtained in the manufacture of Fluid Orange Soluble by distilling the separated oil.

Eight hundred pounds of drug, yielding sixteen hundred pints of Fluid Orange Soluble, will give a corresponding yield of ten to fourteen pints of oil of orange.

In the production of pharmaceutical products, the manufacturer has called to his aid every mechanical device whereby he may keep pace with pharmaceutical progress.

Vacuum-stills and dryers, mixers, granulators, mills, etc., enable the manufacturer to produce, within two or three days, the same amount of finished product that would ordinarily require one or two weeks to manufacture.

Thus the human factor has largely been eliminated and manual labor superseded by mechanical aids which enable the producer to manufacture with greater accuracy and to market preparations of a better quality.

MANUFACTURING LABORATORIES, BRISTOL-MYERS COMPANY, August 7th, 1914.

AMYL NITRITE; ITS PREPARATION, PURITY AND TESTS.

FRANK O. TAYLOR, PH. C.

From time to time during the past thirty-five years there have appeared articles on amyl nitrite dealing with the manufacture, impurities, assay and therapeutic effects. A number of these record investigations of the quality of commercial grades of amyl nitrite, chiefly by some method of assay and in a less number of cases by fractional distillation, together with some qualitative tests for aldehyde, nitropentane, etc. The collective evidence of these shows that the quality of much of the amyl nitrite on the market has always been inferior and, further, that the improvement following the publication of these investigations and criticisms has been by no means marked.

At the risk of re-treading ground already well explored the writer desires to record here results obtained in both experimental and practical work during some years past, to call attention to a number of facts of which he has seen no published mention and suggest higher standards and better tests than are now universally included in the various pharmacopœias. The pharmacopœial requirements are in some things too rigid and in others not sufficiently severe. The following brief *resume* of the requirements of a number of pharmacopœias is given so that proper comparison may easily be made, reserving comment on these statements until later:

Definition and Description.—Of the nine pharmacopœias examined only two, the U. S. and British, include a definition as distinguished from the description.

*Read at the Rochester Meeting of the A. C. S.

U. S. P.—"A liquid containing about 80 percent. of amyl (chiefly iso-amyl) nitrite ($C_5H_{11}NO_2$), together with variable quantities of undetermined compounds."

B. P.—"A liquid produced by the interaction of amylic alcohol which has been distilled between 262° and 270° F. (127.7° to 132.2° C.) and nitrous acid. It consists chiefly of iso-amyl nitrite, $C_5H_{11}NO_2$, but contains also the nitrites of the homologous series."

The description of amyl nitrite as regards color, odor, volatility and general physical characteristics is practically the same in all the pharmacopœias examined.

Specific Gravity.—The *U. S. P.* gives 0.865-0.875 at 25 C. which agrees with 0.870-0.880 at 15° C. as stated by the British, German, Austrian and Japanese pharmacopœias; the Italian gives 0.870-0.890; the Swiss and Belgian give 0.870-0.900, and the French gives about 0.88.

Boiling Point.—The *U. S.* and French pharmacopœias indicate 96° - 99° but the French gives among other tests a qualifying statement to the effect that amyl nitrite should completely distill below 110° . The German, Swiss Austrian, Italian and Japanese pharmacopœias state the boiling point as 97° - 99° , the Belgian gives about 99° while the British more properly makes the following statement:

"Submitted to distillation, about 70 percent. passes over between 194° and 212° F. (90° and 100° C.), the bulb of the thermometer not dipping below the surface of the residual liquid."

Acidity.—All except the Swiss pharmacopœia give some test for acidity, for typical examples of which the *U. S. P.* and *Ph. G.* tests are given here:

U. S. P.—"If 1 cc. normal potassium hydrate *V. S.* and 10 cc. of water be mixed with a drop of phenolphthalein *T. S.*, then 5 cc. of amyl nitrite added, and the tubes inverted a few times, the red tint of the aqueous layer should still be perceptible (limit of free acid)."

Ph. G.—"5 c. c. of amyl nitrite shall not neutralize the alkaline reaction of a mixture of 0.1 c. c. ammonia and 1 c. c. of water."

Aldehyde.—All nine of the above-mentioned pharmacopœias give a test for aldehydes of which that of the *U. S. P.* is typical.

"A mixture of 1.5 cc. of silver nitrite *T. S.* and 1.5 cc. of alcohol with a few drops of ammonia water should not become brown or black if 1 cc. of amyl nitrite be added and the mixture gently heated."

Water.—All except the Italian and Swiss pharmacopœias direct that amyl nitrite when cooled to 0° C. should not become turbid, showing absence of water.

Assay.—Only the *U. S. P.* and *B. P.* include a process for assay which in each case is an adaptation of the well-known gasometric estimation of nitric oxide produced by the reaction of the nitrite with potassium iodide and sulphuric acid.

As will be shown, much of the amyl nitrite on the market does not come up to the standard of strength which can be profitably attained on a commercial scale and certain impurities not detectable by any of the above tests may be present. It has been the intention therefore to collect published data, add to it results of a number of experiments and fix upon a standard severe enough to exclude therapeutically undesirable products and lenient enough to admit a grade commer-

cially obtainable and as definite as the complex nature of an acceptable amyl nitrite will permit.

AMYL ALCOHOL USED.

Commercial amyl alcohol is well known to be far from a pure substance and even the grades below that of highest purity contain notable quantities of impurities. Besides the active and inactive or iso-amyl alcohols which are always present together, there may be found iso-butyl, normal propyl and ethyl alcohols and often other of the various amyl, butyl and propyl alcohols. The action of nitrous acid on such mixtures would give very varied results, hence it is essential that an alcohol be used which is as pure as can be made without unduly increasing its cost.

The boiling point of amyl alcohol is variously stated and it would seem that some of the earlier investigators of amyl nitrite failed to distinguish between the active amyl and iso-amyl alcohols, or as they are sometimes known, the α - and β -iso-amyl alcohols.

Umney in 1870 (Pharm. Jour. (3) 1, 422) in an article on amyl nitrite states that amyl alcohol boils at 132°.

Tanner in 1872 (Pharm. Jour. (3) 2, 421) states that it boils when pure at 132° and for making amyl nitrite should distill "near 132°."

Dott in 1878 (Pharm. Jour. (3) 9, 172) says: "There is an amylic alcohol or mixture of alcohols boiling at 128°-129°."

The following year Greene (Am. Jour. Pharm., 1879, 65) in criticizing this paper of Dott's says that iso-amyl alcohol, "when carefully separated from fusel oil by fractional distillation, boils constantly at 132°. Portions may be obtained which when fractionated in an imperfect apparatus may pass entirely at 128° to 129°, but, if these be subjected to several careful rectifications in a suitable fractionating apparatus, they may be entirely resolved into the alcohol, boiling at 132° and iso-butylic alcohol boiling at 109°." He considers an alcohol distilling between 128° and 132° as pure enough for making amyl nitrite.

Dott (Pharm. Jour. (3) 10, 231) replies to Greene and reiterates his statement of the boiling point of amyl alcohol, bringing experimental proof of the same.

Squibb (Ephemeris II, 701) gives "about 132°" as the proper boiling point for alcohol to be used in amyl nitrite manufacture.

Dunstan & Williams in 1888 (Pharm. Jour. (3) 19, 487) gives 127° to 132° as the boiling point of the amyl alcohol of commerce and says, "in the portions of fusel oil which has been repeatedly fractionated between 127°-132° there is said to be usually about 13 percent. of the active alcohol. These alcohols cannot be separated by fractional distillation, since the α -amyl alcohol boils at 128° and the β -amyl alcohol at 131°." (This last statement is evidently a misprint as the boiling points of these alcohols should be reversed.)

Curtman before the A. Ph. A. in 1892 (Proc. A. Ph. A., 1892, 159) states that what is usually sold as "purified amyl alcohol" is the fraction of fusel oil between 125° and 140°.

Researches in pure chemistry, carried on at different times, have shown the boiling point of the active alcohol to be 128° and that of the iso-amyl to be

131.5°. A boiling point of 128°-132° will include both but exclude the chief portion of impurities, while a range of 130°-132° admits an alcohol consisting chiefly of iso-amyl alcohol.

METHODS OF PREPARATION.

Having obtained a properly purified alcohol, four general methods present themselves as suitable for producing amyl nitrite. *First*, direct heating with nitric acid; *second*, heating with nitric acid, sulphuric acid, and copper; *third*, by reaction between alkali-nitrite, sulphuric acid and amyl alcohol; and, *fourth*, by producing nitrous gas with nitric acid and arsenous acid or starch, and passing this through the alcohol. Other methods of less importance have been advocated but they have not received application except in a small way.

The first method is that originally proposed by Balard the discoverer of amyl nitrite, and has had numerous advocates, notable among them being John M. Maisch, (*Am. Jour. Phar.*, 1871, 146) and E. R. Squibb (*Ephemeris* 11, 701). Maisch states that the yield of nitrite distilling between 95° and 100° is small and mentions the fact that amyl nitrite, aldehyde, ethyl-amyl ether and hydrocyanic acid are also formed. The nitric acid and amyl alcohol are heated together carefully and all that product of the reaction collected which distills below 100° C. This is purified by washing with a solution of potash or potassium carbonate to remove acids and then distilled; all that comes over below 96° and above 100° being rejected. This will lead to the rejection of much amyl nitrite if the nitrite is not dried before distillation, for, as will be seen later, amyl nitrite and water distill together as a binary mixture at about 80°. Squibb distilled off all below 100° and purified by agitation with a solution of sodium carbonate, then rectified, rejecting only the portion above 100°, removing water subsequently by freezing. This obviates the difficulty connected with the purification of Maisch, but is liable to introduce another, tho in much less degree, for a binary mixture of iso-amyl alcohol and water distills at 95°. It is therefore always preferable to both wash with the alkaline solution and dry thoroughly before rectification.

A. B. Tanner (*Pharm. Jour.* (3) 2, 421) advocates the second method, the product of the reaction being distilled as made, below 98°. This is washed with solution sodium hydroxide and rectified over fused potassium carbonate, the portion distilling between 95° and 100° being collected for medicinal use. This method is liable to produce still more impurities than the first and however well they may be separated by fractionation the amyl nitrite so produced can by no means be considered a pure product and the yield will also be low.

The third method will undoubtedly produce the purest product, giving at the same time, if carefully carried out, a good yield. This process however is not suited to manufacture on a large scale tho excellently adapted for purely scientific work. A very pure alcohol is necessary and the increased expense of production is not justified by the greater purity of the product as the difference is not sufficient to cause any marked difference in therapeutic action. Greene (*Am. Jour. Pharm.*, 1879, 65) says that "a fair yield may be obtained" in this manner. He heats potassium nitrite with the amyl alcohol on a water bath and gradually adds sulphuric acid diluted with an equal volume of water. The amyl nitrite distills

over and has to be purified by washing with potassium carbonate solution, drying with the fused salt and distilling; all that passes over below 100° being retained. This process is objectionable because of the heat being applied during the reaction. Dunstan and Wooley (Pharm. Jour. (3) 19, 487) give a process for the manufacture of iso-butyl nitrite which is exactly the same as that which they use for amyl nitrite. The quantities were calculated according to the equation:—

$2C_5H_{11}OH + H_2SO_4 + 2NaNO_2 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O$ and a slight excess of sodium nitrite used. The acid was gradually mixed with the alcohol, the mixture cooled and poured very slowly to the bottom of a solution of the sodium nitrite in three parts of water, keeping the whole cooled to 10° or 12°. The amyl nitrite formed floats on the aqueous layer and is washed with alkaline carbonate solution and dried over fused potassium carbonate. If absolutely pure reagents are used, the amyl nitrite so formed requires no distillation and is almost perfectly pure. With less pure grades of alcohol, distillation must be resorted to.

The fourth process is more frequently recommended than any other. Umney (Pharm. Jour. (3) 1, 422) says that "true amyl nitrite should be made by passing nitrous acid into amyl alcohol" and proceeds to define the nature of the alcohol.

Hilger (Archiv. d. Pharm., 1874, 485) recommends the production of nitrous acid from arsenous and nitric acids and passing this gas into amyl alcohol until no odor of the alcohol remains. This method of determining the end of the process is both crude and unpleasant, as an attempt to detect amyl alcohol in the nitrite by odor will demonstrate. D. B. Dott (Pharm. Jour. (3) 9, 172) also considers this process much better than that using nitric acid, but does not compare it to third process given here.

The investigations of Williams and Smith (Pharm. Jour. (3) 16, 499) have shown the variation in yield of amyl nitrite due to the use of nitric acid of different strengths for generating the nitrous acid. Herein lies one of the chief objections to the process, that the nature of the gas given off when nitric acid reacts with arsenous acid is complex, and variable according to temperature and strength of acid.

Stenhouse and Groves in 1877 (Jour. Chem. Soc., 1877, i, 545) call attention to the variable composition of the gases so formed and recommended nitric acid of specific gravity 1.30-1.31 and a temperature of 70° as giving the most N_2O_3 . Lunge (Berichte 17, 1641) says that acid of 1.35 specific gravity produces large quantities of N_2O_3 along with N_2O_4 and that acid of specific gravity 1.5 produces chiefly N_2O_4 with some N_2O_3 . Ramsey and Cundall in a research on the oxides of nitrogen (Jour. Chem. Soc., 1885, 197), in which they employed arsenious acid, and nitric acid of specific gravity 1.5, state that "arsenious oxide when heated with nitric acid gives a liquid containing N_2O_3 according to the equation $2HNO_3 + AS_2O_3 + nH_2O = N_2O_3 + AS_2O_3 + (n + 1) H_2O$. In the gaseous state, however, they claim that N_2O_3 does not exist but dissociates into NO and a mixture of NO_2 and N_2O_4 , the N_2O_4 , they assume, reacting with water as follows: $2N_2O_4 + H_2O = 2HNO_3 + N_2O_3$. Williams and Smith (vide supra)

say that "it is stated in chemical works that this gas (N_2O_4) acting upon amyl alcohol is broken up into nitrous acid (N_2O_3) and nitric acid." They made a practical test of conditions governing the production of a gas best adapted to making amyl nitrite and found their results agreed with this statement and with those of Ramsey and Cundall; giving also evidence confirmatory of Lunge's assertions. An acid of specific gravity 1.5 gave a low yield of amyl nitrite as would be expected if N_2O_4 were chiefly produced and decomposed into N_2O_3 and nitric acid. Their best results were obtained with acid of 1.35-1.36 specific gravity and this they recommended as best, as would be anticipated from the researches cited above.

E. Rennard (Pharm. Centr., 1874, 236) in a review of methods for making amyl nitrite also considers this method best, but uses starch or sugar for producing the nitrous gas.

CHEMICAL AND PHYSICAL CHARACTERISTICS.

The descriptions of Amyl Nitrite in the various pharmacopœias differ somewhat in details but in most cases do not indicate as great a variation from an absolutely pure product as is actually the case. In view of this it will be of interest here to consider at some length the characteristics of amyl nitrite, its allied nitrites and other possible impurities.

Of the definitions quoted, that of the U. S. P. is probably best as it merely states the percentage strength of the amyl nitrite and does not remark concerning the nature of the impurities.

The B. P. is contradictory as it states that "other nitrites of the homologous series" are present but specifies that amyl nitrite shall be made from amyl alcohol distilling between 127.7° and 132.2° , which excludes homologous alcohols. If this requirement on the alcohol is not observed the other statement will then be true.

Other pharmacopœias give no definition, which tends to give the idea that medicinal amyl nitrite should be a pure substance, especially in view of the boiling-point requirement.

As previously noted the different pharmacopœias give a range of specific gravity from 0.870 to 0.900. D. B. Dott (Pharm. Jour. (3) 9, 172) gives .877 as the exact specific gravity, while Dunstan and Williams (Pharm. Jour. (3) 19, 487) give .874 ($15^\circ/15^\circ$) as the correct figures for pure amyl nitrite. In view of the fact that secondary propyl nitrite has a specific gravity of 0.871; secondary butyl nitrite, 0.874; tertiary butyl nitrite, 0.8715; and iso-butyl nitrite, 0.876, all according to Cash and Dunstan (Proc. Roy. Soc., 49, 314), and there may be present impurities of both higher and lower specific gravity than amyl nitrite, the specific gravity alone is of but little importance and not at all indicative of purity.

The qualitative tests for aldehyde and free acid are of value, especially the latter. Free acid is not liable to be present in well made amyl nitrite immediately after manufacture, but may be generated through decomposition on standing when improperly protected.

As regards the boiling point much variation of statement exists. For example the U. S. P. says: "At about 96° - 99° it boils yielding an orange-colored vapor."

It is uncertain whether this means that a good amyl nitrite begins to boil at about this temperature, or, what seems more obvious, that it distils wholly between these degrees. Furthermore, the vapor of amyl nitrite is colorless when seen in shallow layers, such as the thickness of a distilling flask of half a liter capacity. The orange colored vapors first given off on boiling amyl nitrite are in reality strongly reddish tinted and are simply mixtures of N_2O_3 and N_2O_4 , which are very soluble in amyl nitrite. In distilling amyl nitrite, after these first colored vapors have been driven off, there is no further evolution of a similar character. It is difficult to obtain any amyl nitrite by the nitrous-acid method which will not show a trace of this orange vapor, but it is obtainable with much less difficulty by the sodium nitrite-sulphuric acid method.

Now, as will be seen later, if the amyl nitrite is supposed to distil wholly or in great part between 96° and 99° , we have a demand for an impossible range of temperature for a commercial article. Several pharmacopœias demand the still smaller range of 97° - 99° . On the other hand the B. P. requires that on distillation about 70 percent. pass over between 90° and 100° . This is a rational and wholly attainable standard.

Coming now to statements of various experimenters, we find marked difference in the temperatures given as the exact boiling point of pure amyl nitrite. Balard, the discoverer of amyl nitrite (Ann. Chim. et Phys. (3) 12, 318) gives 96° as its boiling point. Umney (Pharm. Jour. (3) 1, 422) gives 98° - 99° . Guthrie (Jour. Chem. Soc., 1859, 245) in an article on "Nitrite of Amyl and Its Derivatives" says: "Nitrite of Amyl, when perfectly dry, boils at 99° C. in a glass vessel in contact with platinum wire, under a pressure of 756 mm. A small quantity of moisture depresses the boiling point two or three degrees, apparently by diminishing the cohesion of the liquid." Tanner (Am. Jour. Pharm., 1872, 21) says that, "The portion which distills between 95° and 100° C. is collected as amyl nitrite sufficiently pure for medicinal use." Hilger (Archiv. d. Pharm., 1874, 485) states that it has a boiling point of 94° - 95° . This, and the high specific gravity he assigns (.902), agrees much better with these characteristics of tertiary amyl nitrite as given by Bertoni (Gazz. Chim. Ital., 16,515) (specific gravity .903 and boiling point 92° - 93°) than they do with the statements of other observers on α - and β -amyl nitrites. It appears probable that he may have had a more or less pure tertiary amyl nitrite. For preparing amyl nitrite he recommends the nitrous acid process and collects the distillate from 90° to 95° for use. Greene (Am. Jour. Pharm., 1879, 65) confirms Balard's statement, saying, "It boils constantly at 96° ." Williams and Smith (Pharm. Jour. (3) 16, 499), after remarking on the difference in recorded boiling points, say, "Probably 95° or 96° may be the correct point; our experiments rather tend to confirm that temperature as the correct one." Cash and Dunstan (Proc. Roy. Soc., 49,314) give the boiling point of α -amyl nitrite as 97° and β -amyl nitrite at 95° - 96° , the mixture boiling at 96° - 97° , the one being derived from α -amyl alcohol (B. P. 131.5 $^\circ$) and the other from the β - or active amyl alcohol (B. P. 128 $^\circ$). The researches of Dunstan and his associates on amyl nitrite and homologous nitrites are the most complete published and are undoubtedly the most authoritative.

From the above variety of boiling points it is evident that some observers did not have pure material and that the kind of alcohol used, whether active or inactive, even tho well purified, makes a difference in the boiling temperature. Experimental results to be given later tend to confirm the statements of Dunstan.

PHYSIOLOGICAL ACTION.

Any extended discussion of the physiological action of amyl nitrite is out of place here but before entering into the merits of methods of standardizing amyl nitrite as given in the pharmacopœias and elsewhere it will be of interest to consider the physiological effects of amyl nitrite and allied compounds so that we can better judge of the worth of assay methods as indicating medicinal value. In doing this we will quote briefly from the very thorough and painstaking research of Cash and Dunstan on "The Physiological Action of the Nitrites of the Paraffine Series, Considered in Connection with Their Chemical Constitution." (Philosophical Transactions 1893 B, 505-640.) The only account the writer has seen of it in any other place likely to be seen by pharmaceutical chemists is a brief and wholly inadequate abstract in the *Pharmaceutical Journal* (3) 25, 313).

After the discovery of amyl nitrite it was more fully investigated by Guthrie (*Jour. Chem. Soc.*, 1859, 245) who called attention to its power of causing flushing of the face and acceleration of the heart's action. It was considered as little more than a chemical curiosity until Dr. W. B. Richardson brought it to the attention of the British Association for the Advancement of Science in 1863 by a report on the "Physiological Properties of the Nitrite of Amyl" and showed it to be the most powerful known drug for increasing the action of the heart, and in 1864 he extended his investigations. Dr. Lauder Brunton by publication of results of his work in 1867 and 1870 did much toward increasing its use as a medicine. Valuable primarily in diseases of the circulatory system it has been advocated for numerous other affections in which a vascular excitant is desired. In 1888 Brunton and Bokenham (*Pharm. Jour.* (3) 19, 491) while investigating the effect of amyl nitrite on blood pressure found that the B. P. substance was more powerful than an absolutely pure amyl nitrite. This anomalous and unexpected result was explained by the work of Cash and Dunstan as due to the presence of iso-butyl nitrite which they found to be more powerful than the iso-amyl compound.

Their work dealt with ten related nitrites and their comparative action on the pulse and blood pressure is indicated in the following table, the numerals showing the order of activity.

	Sp. Gr.	Boiling Point.	Acceleration of Pulse.	Reduction of Blood Pressure.	Duration of Subnormal Pressure.
Methyl Nitrite.....		12°	1	4	10
Ethyl Nitrite.....		17°	2	2	9
Primary Propyl Nitrite...	0.895	48°	3	1	1
Secondary " " ...	0.871	39.5°	4	10	2
Primary Butyl " " ...	0.911	76°	5	3	5
Secondary " " ...	0.874	68.5°	6	8	6
Tertiary " " ...	0.8715	63°	8	9	7
Iso-Primary " " ...	0.876	67°	7	7	3
α-Iso-Amyl " " ...	0.874	97°	9	5	4
β- " " " ...	0.874	95-96°			
Tertiary Amyl " " ...	0.890	92°	10	6	8

Having demonstrated the action of these nitrites they say: "In conclusion, the following are the principal facts which have been established with reference to the connection between the various phases of the physiological action of these nitrites and their chemical constitution.

In respect of all phases of the physiological action, the secondary and tertiary nitrites are more active than the corresponding primary compounds. This is to be chiefly attributed, not to the direct physiological effect of the secondary and tertiary groups, but to the great facility with which these compounds suffer decomposition.

In respect of the acceleration of the pulse, the power of the nitrites varies directly as their molecular weights, and they therefore fall into an order identical with that of the homologous series. This same relationship, increase of activity corresponding with rise in molecular weight, may also be traced, though less uniformly, in their power of reducing blood pressure and of inducing muscular contraction.

This order appears to be the result, not so much of the direct influence of the substituted methyl groups, as of the increased chemical instability which their substitution confers on the higher members of the series.

In respect of the duration of subnormal pressure, as well as of the rapidity with which muscular contraction ensues, the activity of the nitrites is expressed by an order which is for the most part the reverse of that presenting their power in accelerating the pulse, reducing blood-pressure, and contracting muscular fibre, this order being in general contrary to that of the homologous series. In these respects the more volatile nitrites of low molecular weight, and containing, therefore, relatively more nitroxyl, are the most active. It is probable that these simple nitrites more readily attach themselves to constituents of blood and muscle, and thus act more quickly than the higher compounds in inducing muscular contraction, whilst their greater stability causes their effect, i. e., reduction of blood-pressure, to endure for a greater length of time than that of the higher and more easily decomposed bodies."

Besides the effect of these homologous nitrites, which is quite similar to that of amyl nitrite, we have that of numerous oxidation products. Thus we may find valerianic aldehyde, valerianic acid, amyl valerianate, nitropentane and unknown products which have the power even in minute quantity of producing violent and lasting headache. We shall also show later that pyridine nitrate is produced by the nitrous acid process and its presence may be expected. This makes it probable that the unknown bodies mentioned above may be pyridine derivatives. Hydrocyanic acid is mentioned by some, while others report that they are unable to find it. While we have made no extended examination for HCN, we have found no reason for concluding it was present in amyl nitrite of the nitrous acid process. Considering the poisonous properties of the pyridine compounds however, it is obvious that crudely prepared amyl nitrite may be extremely deleterious.

METHODS OF VALUATION.

Several methods of assay have been proposed but the most practical for pharmaceutical use is the nitrometer method first proposed by Allen for spirit of nitrous ether and subsequently applied by him to amyl nitrite. This is adopted in both the U. S. P. and B. P. (To be continued.)

OUR NEW OFFICERS.

CASWELL ARMSTRONG MAYO, PH. G.,
SIXTY-SECOND PRESIDENT, AMERICAN PHARMA-
CEUTICAL ASSOCIATION.

Caswell Armstrong Mayo, who was installed as the sixty-second President of the American Pharmaceutical Association on Saturday, August 29, 1914, at the conclusion of the Detroit meeting, was born in Columbus, Miss., July 5, 1862. He received his early education and his preliminary training in pharmacy in his native town. He was graduated from the Philadelphia College of Pharmacy in 1887, while employed in the pharmacy of William Procter, Jr., Company. He was assistant editor of the *Druggists' Circular* for a little over five years, editor of the Drug Department of the *Oil, Paint and Drug Reporter* for about a year, editor of *Merck's Market Report* for three months, in 1892, and succeeded Dr. Frederick A. Castle and Dr. Charles Rice as editor of the *American Druggist*, with which the *Pharmaceutical Record* was consolidated on the death of its editor, Prof. P. W. Bedford. Mr. Mayo has attended every meeting of the Association since 1888, with two exceptions, and has taken an active part in its affairs. He served for seventeen years as Chairman of the Committee on Transportation and on numerous other committees, and has been Historian, Chairman of the Section on: Historical Pharmacy, Secretary of that Section, Member of the Council, and a Vice-President of the Association. He is a widower, and resides with his four children in Brooklyn, N. Y.

<>

WILLIAM BAKER DAY, PH.G.,
THE NEWLY-ELECTED SECRETARY OF THE
ASSOCIATION.

In the selection of Professor W. B. Day as its General Secretary the Association has made a wise and an admirable choice. Becoming a member of the Association in 1895 he has done yeoman work in its behalf. In every position to which he has been appointed by the Association he has shown eminent ability and capacity, and he may be depended upon to give to the organization the same loyal service in the high and responsible position to which he has been chosen.

As past President of the Association he brings to the position a full knowledge of its duties, and is a most worthy and fitting suc-

cessor of Procter, Parrish, Maisch, Remington, Caspari and Beal. In his hands every member may be assured that the traditions of



the office will be fully maintained and that the affairs of the Association will be carried on with dignity, zeal and faithfulness.

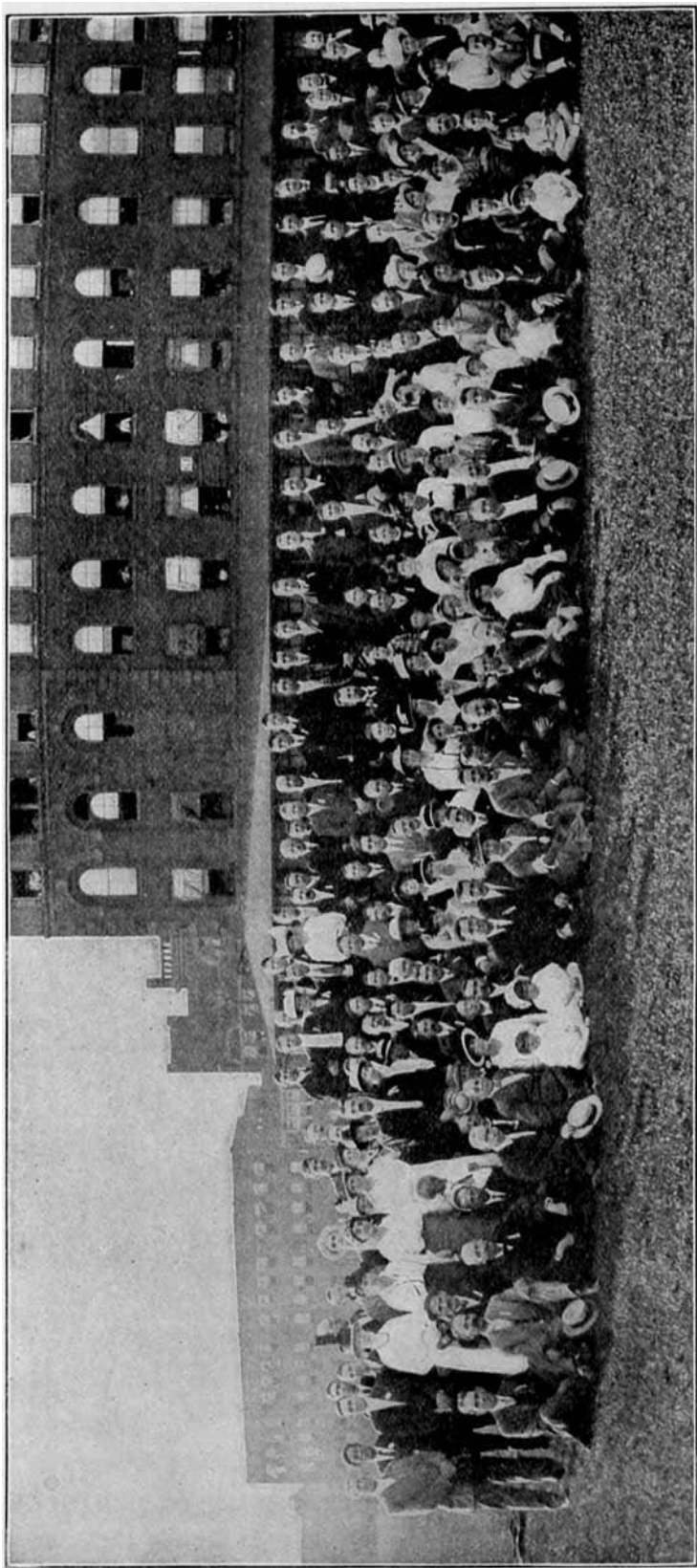
<>

CONVENTION ENTERTAINMENTS.

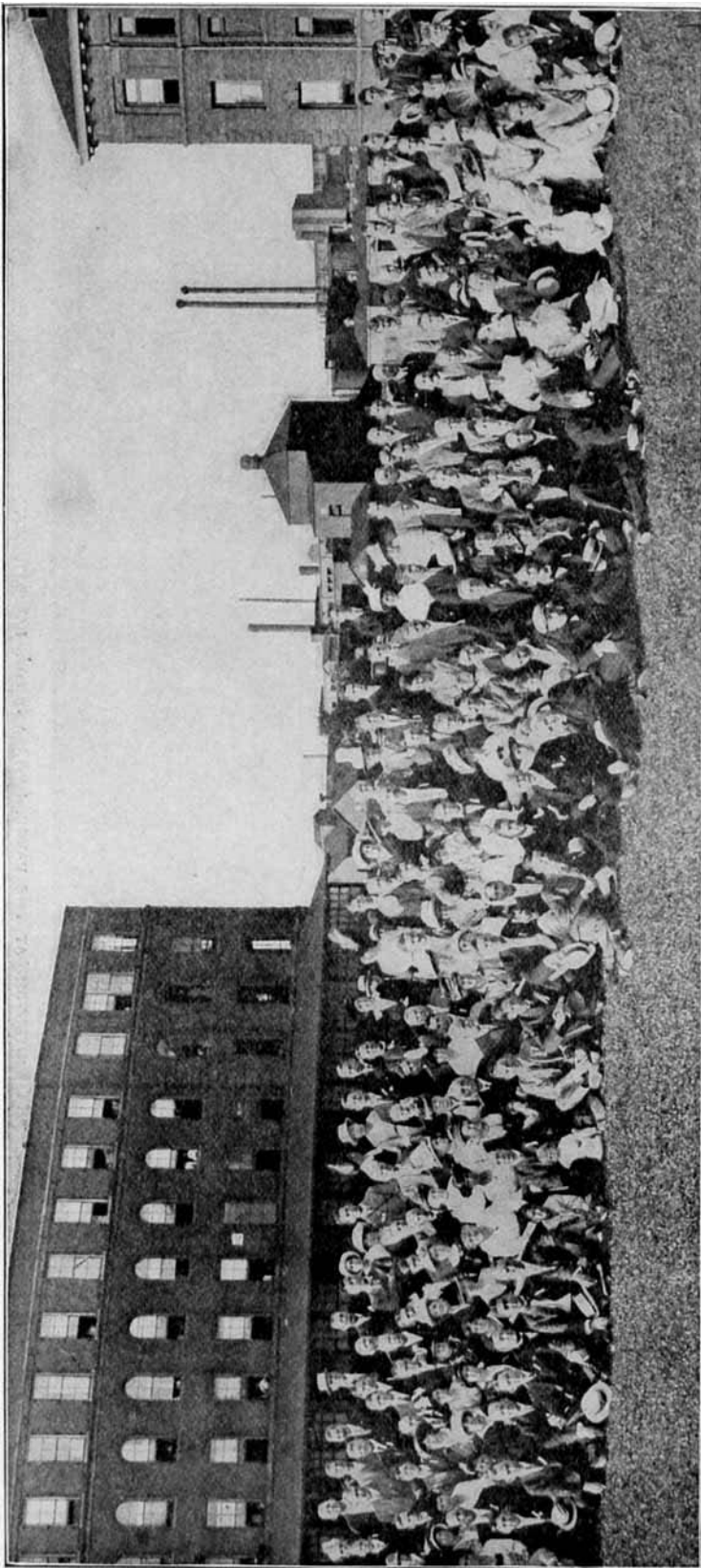
The Entertainment Committee, under the Chairmanship of Mr. O. W. Gorenflo, assisted by a Ladies' Committee, consisting of Mesdames Webster, Rennie, Mann, Mason, Scoville, Hall, Weaver, Francis and Stevens, were indefatigable in their efforts to make the meeting most pleasurable to every person in attendance.

On Monday evening the magnificent ballroom and the adjacent rooms was the scene of a most enjoyable occasion, that of the Presidents' reception and ball. In the receiving-line were President and Mrs. Beringer and the past Presidents of the Association with their ladies, and also the President of the Michigan State Pharmaceutical Association, Mr. D. G. Look. The rooms were thronged with a large and fashionable gathering until a late hour.

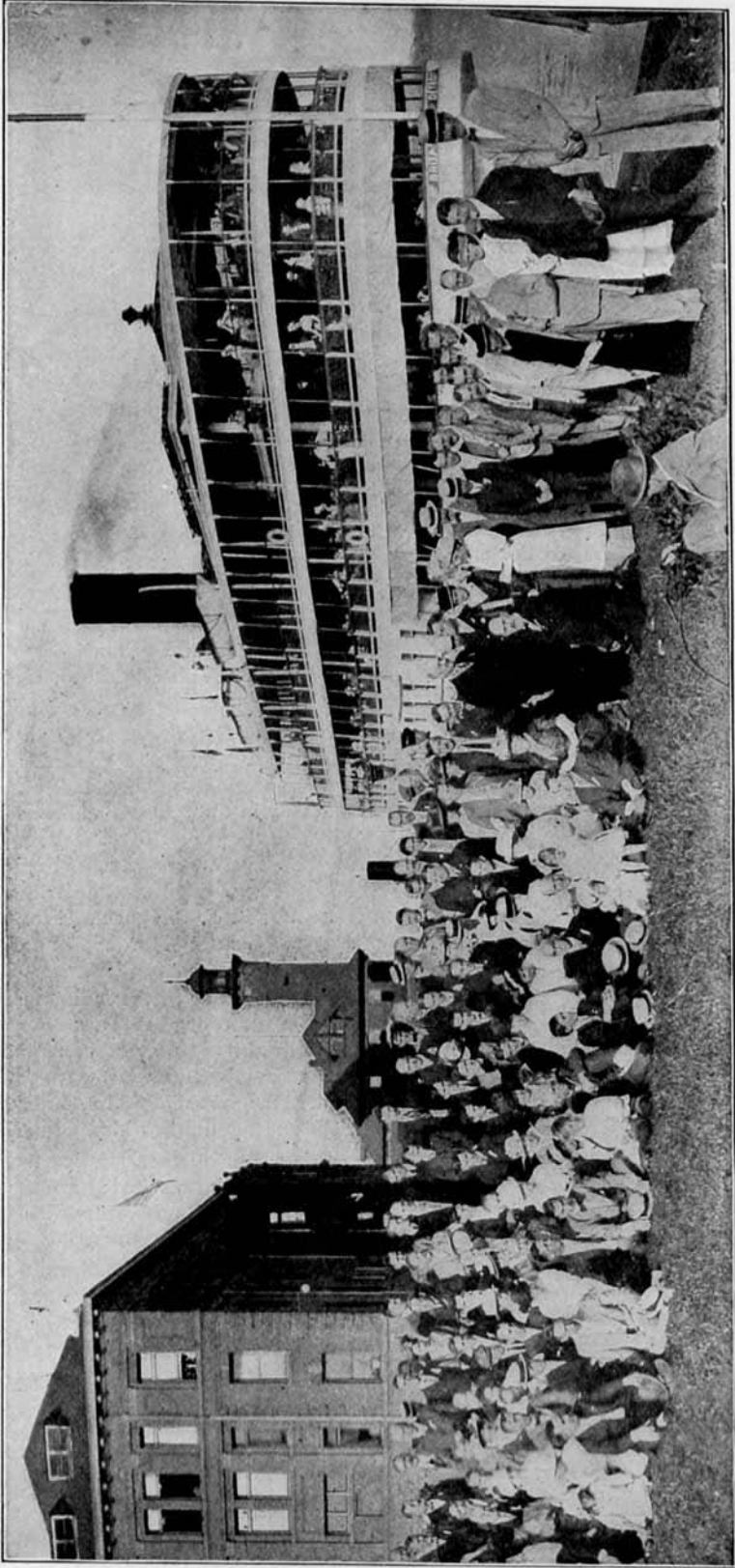
The ladies' excursion, given by the firm of Nelson, Baker & Co. was a most delightful function. The ladies were taken to Bois Blanc Island (Bob-Lo) where they were en-



THE CONVENTION AT THE PARKE, DAVIS AND CO.'S LABORATORIES.



THE CONVENTION AT THE FARKE, DAVIS AND CO.'S LABORATORIES. (2)



THE CONVENTION AT THE PARKE, DAVIS AND CO.'S LABORATORIES. (3)

tertained until a late hour, and where a fine dinner was served in unexceptionable style.

On Wednesday the alumni of the different colleges represented at the Convention met at luncheon together, the most elaborate of the functions being that of the Philadelphia College of Pharmacy at the Hotel Pontchartrain, at which Mr. Frank G. Ryan, the President of the Parke, Davis Co., acted as host. The Massachusetts College of Pharmacy Alumni held their lunch at the Hotel Ste. Claire, under the presidency of Mr. F. W. Archer.

Wednesday afternoon a card-party for the ladies was held in the parlors of the Hotel Pontchartrain, at which Mrs. H. M. Whelpley and Mrs. George M. Andrews were the prize-winners.

Wednesday evening the ladies were the guests of F. F. Ingram & Co. and F. A. Thompson & Co. at the Temple Theatre, while the gentlemen were being entertained most royally at the Wayne Gardens by Frederick Stearns & Co.

On Thursday afternoon, Parke, Davis & Co. entertained the entire Convention with a steamer-excursion to St. Clair Flats, which trip also included an inspection of the magnificently equipped laboratories of the firm. Supper was served on the boat and the party did not return until a late hour in the evening. The excursion through the Flats was one long to be remembered by those who participated in the trip.

Friday afternoon a general auto-ride was enjoyed by all those who desired, and the party was taken through the residential section of Detroit, along its beautiful boulevard, and to beautiful Belle Isle, probably one of the most magnificent public parks in America. Its Zoological Gardens and Aquarium were most enjoyable points of interest for all who participated in this excursion. It is but fair to say that the completeness with which every detail of these various functions was carried out, deserved and received the warmest encomiums of every person who participated in them.

*In Detroit Life Was Worth
Living Every Day.*

Proceedings of the Local Branches

"All papers presented to the Association and its branches shall become the property of the Association, with the understanding that they are not to be published in any other publication than those of the Association, except by consent of the Committee on Publication."—By-Laws, Chapter X, Art. III.

Reports of the meetings of the Local Branches should be mailed to the Acting Editor on the day following the meeting, if possible. Minutes should be *plainly* written, or typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly, and manuscript should be signed by the reporter.

<>

CINCINNATI.

The Outing Committee of the Cincinnati Branch, A. Ph. A., planned for a delightful day at White Villa, Ky., about eighteen miles from Cincinnati.

Nearly every member with their families attended and enjoyed a good chicken dinner, games, boating, bathing and a good time generally in the coolness and shade of White Villa, as the guests of mine host, Mr. J. M. Myers. There were speeches by President E. H. Thiesing, Frank H. Freericks, National Delegate; C. T. P. Fennel, Theo. D. Wetterstroem, Charles Harding, Fred Ott and others.

The first prize in the ladies' guessing contest, for guessing the nearest number of Jequirity beans, prayer beans and jumble beads, contained in a jar, went to Miss Lula Faller, the second to Mrs. Frank H. Freericks and the third to Mrs. Otto Kistner.

Prizes also offered, guessing the weight of entire package, resulted: First prize, Mrs. Scallan; second prize, Mrs. Jackson; third prize, Miss Helen Heister.

The lady guessing the nearest number of polka dots in a polka-dot bow was Mrs. Freericks for first prize; Mrs. Kotte, second prize, and Mrs. Vocke, for third prize.

Sugar-coated pellets, contained in a jar, were nearest estimated in number by Mrs. Kistner, for first prize; Mrs. Weissmann, for second prize, and Miss Heister, for third prize.

The geography game resulted in the first