C. is open to objection for two reasons: first, the resins turn brown at this temperature and undoubtedly there is some change in composition; second, a constant weight cannot be obtained. When the resins are dried *in vacuo* there is no evidence of much change in composition and when completely dried there is practically no change in weight.

Great care should be taken in securing petroleic ether of suitable quality for the extraction of the soft resins. The practice in this laboratory is to make two distillations, starting with the commercial product sold by dealers (boiling point 40–60°) and each time taking the fraction distilling over under 45° C.

Acknowledgment is due Mr. B. Pilkington for valuable assistance given in making some of the analytical determinations given in this paper.

CONCLUSIONS.

1. A comparative study has been made of some of the present methods used for the determination of hard and soft resins in the hop and their defects pointed out.

2. A method has been proposed by the authors which they believe overcomes some of the objections to present methods.

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THE CHEMISTRY OF ANAESTHETICS, IV: CHLOROFORM.¹

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The career of chloroform has been chequered ever since its discovery, but especially since it has been used as an anaesthetic. The reasons for this are made apparent in this paper.

The report of this investigation has been subdivided as follows:

I. HISTORY.

II. USES.

III. MANUFACTURE: 1. *From Ethyl Alcohol.* 2. *From "Methylated Spirit."* 3. *From Acetone.* 4. *From Methane (Natural Gas).* 5. *From Carbon Tetrachloride.* 6. *Special Chloroforms of Foreign Manufacture.*

IV. PURIFICATION.

V. THE PHYSICAL CONSTANTS OF CHLOROFORM: 1. *Specific Gravity.* 2. *Boiling Point.*

VI. THE DECOMPOSITION OF CHLOROFORM: 1. *The Changes which Chloroform Undergoes upon Exposure to Air.* 2. *The Changes which Anaesthetic Chloroform Undergoes when a Current of Oxygen is Conducted through it.* 3. *The Decomposition of Chloroform Vapor upon Exposure to Gas Light, etc., during Administration.* 4. *The Effect of Agitation upon Anaesthetic Chloroform.* 5. *The Preservation of Chloroform.* 6. *The Storage of Anaesthetic Chloroform.*

VII. THE IMPURITIES OF ANAESTHETIC CHLOROFORM: 1. *Chemical Considerations.* 2. *Physiological Considerations.*

VIII. THE EXAMINATION OF ANAESTHETIC CHLOROFORM: 1. *The Tests for Odor.* 2. *Residue.* 3(a). *The Test with Sulphuric Acid.* 3(b). *The Test with Formalin—Sulphuric Acid.* 3(c). *Discussion of 3(a) and 3(b).* 4. *The Detection of Water in Chloroform.* 5. *The Detection and Estimation of Alcohol*

in Chloroform. 6. *The Detection of Acetone in Chloroform.* 7. *The Detection of Methyl Alcohol and other Methyl Compounds in Chloroform.* 8. *The Detection of Ethyl Ether in Chloroform.* 9. *The Detection of Acetaldehyde in Chloroform.* 10. *The Determination of the Acidity of Chloroform.* 11. *The Decomposition Products of Pure Chloroform.* 11(a). *The Detection of Carbonyl Chloride.* 11(b). *The Detection of Hydrochloric Acid.* 11(c). *The Detection of Chlorine.* 12. *The Detection of Chlorine Substitution Products.* 12(a). *"Chlorinated Decomposition Products."* 12(b). *The Occurrence of Ethyl Chloride in Chloroform.* 12(c). *The Occurrence of Ethylene Chloride in Chloroform.* 12(d). *The Detection of Carbon Tetrachloride.* 13. *Scheme for the Examination of Chloroform for Anaesthetic and Analytical Purposes, with Particular Reference to the Detection of Avoidable Impurities.* 14. *The Degrees of Purity of American Chloroforms.*

In this paper the grades of chloroform have been discriminated in accordance with the following classification, which the authors propose as a basis:

A. *Pure Chloroform.*—Absolute chloroform—chloroform free from alcohol and all impurities.

B. *Anaesthetic Chloroform.*—Chloroform complying with the pharmacopoeial requirements. Such chloroform contains ethyl alcohol (up to 1 per cent.) and small amounts of water.

C. *Commercial Chloroform.*—Chloroform which contains at least 99 per cent., by weight, of absolute CHCl_3 , but which may contain small amounts of "organic impurities."²

D. All other grades of chloroform should be classed as *impure commercial chloroform.*

E. The purity demanded of *laboratory chloroform*, or chloroform intended for analytical purposes, is entirely dependent upon the purpose for which it is intended. For ordinary reagent purposes, the grade specified under *anaesthetic chloroform* is suitable, and in general may be said to answer all such purposes; but in special cases *pure chloroform* may be required, and, when this is the case, it should always be prepared immediately before use, according to a method to be described in Section V, 1, A of this paper.

I. HISTORY.

Chloroform was discovered in 1831, yet it has been asserted that there are indications of an earlier acquaintance with the compound. For example, we are told by Hutman,² on the authority of Johannes Porta³ and Sir Walter Scott,⁴ that chloroform was known in former times and was then employed as a means of producing insensibility. Investigation shows that this statement is based upon misinterpretation.⁵

¹ See Section VII, 1, of this paper.

² *J. chim. med.*, [3] 4, 476.

³ "Magia Naturalis," 1619. It should be mentioned here that in 1589 Giambattista Porta used an essence made from hyoscyamus, solanum, poppy, and belladonna, enclosed in a lead vessel, for producing sleep by inhalation of the vapor.

⁴ "Letters on Demonology and Witchcraft," 1830.

⁵ Most ancient authors who pretend to treat of the wonders of "Natural Magic," give recipes for calling up phantoms by the inhalation of certain gases from burning medicated mixtures, generally of oils, and by the use of suffumigations of strong herbs (Hibbert's "Apparitions," p. 120). The ancient Egyptians, Assyrians, and Chinese were familiar with many vegetable substances (e. g., *cannabis indica*) capable of producing ecstatic, sedative and anodyne effects (Snow's "Chloroform and Other Anaesthetics," 1858; Bernard's "Leçons sur les Anesthésiques et sur l'Asphyxie," 1875;

¹ Read at the regular June meeting of the New York Section of the American Chemical Society, 1911.

Silliman¹ confused chloroform with ethylene dichloride, stating that it had been "long known to chemists under the name of 'oil of the Dutch chemists' and 'Dutch oil,' from its discovery in 1796 by an association of Dutch chemists."

In 1831, Liebig² obtained chloroform by the action of a water solution of potassium hydroxide on chloral and by treating acetone with bleaching-powder. Almost at the same time, however, Soubeiran³ obtained chloroform by the action of bleaching-powder on dilute alcohol, terming the product "ether bichlorique," and he was regarded as the discoverer of the compound until Liebig⁴ advanced his claim as having been the first to prepare it, although he originally believed the substance to be a new chloride of carbon. According to some authorities,⁵ Samuel Guthrie, an American, discovered chloroform simultaneously with Liebig and Soubeiran, and it has also been stated⁶ that his discovery antedates that of Liebig several months. Silliman⁷ stated in 1848 that "the production of 'chloric ether' so called, by the action of alcohol with bleaching-powders, was discovered almost simultaneously and without conference by our ingenious countryman, Samuel Guthrie, of Sackett's Harbor, New York, and by M. E. Soubeiran in France."

Liebig considered that he had prepared carbon trichloride whereas he actually obtained chloroform, and Guthrie confused his product with ethylene chloride; in both cases, the investigations were made in 1831 and published in the early part of 1832. Guthrie prepared chloroform without knowledge of the work of Liebig or Soubeiran, and is fully entitled to be credited with its independent discovery.⁸

Lyman's "Artificial Anaesthesia and Anaesthetics," 1883; and Dastre's "Les Anesthésiques," 1890). From the *Odyssey* (4, 220) we learn that Helen "cast a drug into the wine whereof they drank, a drug to lull all pain and anger and bring forgetfulness of every sorrow." Herodotus refers to the custom of the Scythians of inhaling the fumes of a kind of hemp; Dioscorides (*De Med. Mat.*, 4, 76) makes mention of the practice of boiling in wine the root of the "*Atropa Mandragora*" and of administering some of the decoction prior to surgical operations; and Pliny (35, 94) refers similarly to the powers of the mandrake. Mandragora appears to have been used to some considerable extent (*Galen, lib. 7*, 207; Lucian, "Demosthenes' Encomium," p. 36); it was employed in compounding the "spongia somnifera" of Theophrastus. The Bible and the Talmud also contain references to ancient practices of inducing sleep by artificial means. However, excepting the use of Memphis marble and vinegar as a local anaesthetic by the Romans, carotid compression and (later) mesmerism, vegetable narcotics only were used to assuage suffering and for the induction of unconsciousness until the foreshadowing of the modern system of anaesthesia by the discovery of nitrous oxide.

¹ *Am. J. Sci.*, [2] 5, 240.

² *Pogg. Ann.*, 23, 444; *Ann.*, 1, 31, 198.

³ *Ann. chim. phys.*, [2] 48, 131; *Ann.*, 1, 272; Soubeiran and Mailhe, *Ann.*, 71, 225.

⁴ *Ann.*, 162, 161.

⁵ E. G. Wurtz Flagg, "Ether and Chloroform," 1851, p. 18; and Turnbull, "Anaesthetic Manual," 1879, p. 87.

⁶ *Pop. Sci. Mon.*, 12, 738.

⁷ *Loc. cit.* See Silliman, *Am. Chemist*, 5, 86, for a full account of Guthrie's discovery.

⁸ The attention of Guthrie appears to have been directed to the preparation of "chloric ether" by reading a passage in a work by Silliman ("Elements of Chemistry," 2, 20), wherein it was stated that the alcoholic solution of "chloric ether" is of medicinal value. By the term "chloric ether" Silliman referred unmistakably to ethylene chloride, which Guthrie considered he had prepared in "spirituous solution," by the action of chloride of lime on alcohol of density 0.844, whereas he actually obtained an alcoholic solution of chloroform (*Am. J. Sci.*, [1] 21, 64). Silliman, commenting on Guthrie's original contribution (*Ibid.*, 408), stated that "we cannot say precisely what takes place during the distillation of alcohol

Dumas,¹ in 1834, showed that chloroform contains hydrogen, and later he determined its true formula.² Dumas obtained chloroform by boiling tri-chloroacetic acid with aqueous alkalis, and it was he who gave the compound its present name.³ Regnault⁴ proved that chloroform is the second substitution-product of methyl chloride; he termed it "ether hydrochlorique de méthylène bichlorure." Berzelius referred to chloroform as "formylsuperchlorid," and Mitscherlich as "chlorätherid."

II. USES.

Chloroform (methenyl trichloride; trichloro-methane; "formyl trichloride") is a colorless, limpid liquid possessing a sweet but somewhat burning taste and an agreeable characteristic odor. When pure, it is not combustible,⁵ but when mixed with alcohol it burns with a smoky flame edged with green. Chloroform is slightly soluble in water (0.822 gram in 100 grams at 20°) and it imparts to it a sweet taste. It is miscible in all proportions with absolute alcohol, ether, benzene, and petroleum spirit. It is soluble to a limited extent in aqueous alcohol. It may be made into an emulsion with water by means of saponin.⁶

Chloroform is used in medicine⁷ as an anaesthetic,⁸ stimulant,⁹ antispasmodic,¹⁰ antiseptic,¹¹ analgesic, from chloride of lime. It is, however, worthy of notice that, as alcohol is believed to be composed of olefiant gas and water... and as chloric ether has been heretofore produced by the combination of chlorine and olefiant gas, it seems hardly to admit of a doubt, that in distilling alcohol from chloride of lime, the latter gives its chlorine to the olefiant gas of a part of the former, and thus produces chloric ether, which passes over, in solution, in another portion of the alcohol, while the water of that portion of the alcohol which afforded the olefiant gas, or the water which may be supposed to be produced by a combination of the elements, is detained by the lime.¹² The question was raised, "Can any method be devised by which the alcohol can be detached from the chloric ether, and the latter obtained concentrated and in quantity?" Guthrie later (*Ibid.*, 22, 105, see also, Hayes, *Ibid.*, 163) found that this could be accomplished by distillation over sulphuric acid, and obtained an "ether" possessing a density of 1.486 and boiling at 166° F. In a communication to Silliman, he stated that "as chloric ether is said to have a specific gravity of only 1.22 at 45°, a boiling point at 152° F., and to be decomposed by sulphuric acid, evolving chlorine, you may have good reason to doubt the purity of my product or the accuracy of my estimate, but you can very readily verify the first, and I shall be found to be very near the truth with the latter."

¹ *Ann. chim. phys.*, [2] 56, 115; *Ann.*, 32, 113.

² *Ann. chim. phys.*, [2] 71, 353.

³ *Ibid.*, [2] 56, 120. To quote Dumas: "La formule.... correspond a un chlorure d'hydrogene carbone, qui est l'equivalent de l'acide formique anhydre.... C'est ce qui m'engage a la designer sous le nom de chloroforme."

⁴ *Ann. chim. phys.*, [2] 71, 377; *Ann.*, 33, 328; *J. prakt. Chem.*, 19, 210.

⁵ See Ommeganck, *Am. Chemist*, 5, 292.

⁶ *J. Soc. Chem. Ind.*, 1887, 382.

⁷ Seyffert (Z. f. Arbeiter-Wohlfahrtseinrichtungen, 10, 319; see also *Chem. Ind.*, 27, 379) has recommended the proposal of Weiskopf to use chloroform in cases of inhalation of nitrous fumes. Chloroform is used internally in colic, gastralgia, asthma, spasmodic coughing, atonic quinsy, hysteria, scarlet fever, neuralgia, cancer, hiccup, tic douloureux, etc.; and as an anaesthetic by inhalation in surgical operations. Externally, chloroform is used in a 20-50 per cent. liniment for rheumatism, neuralgia, colic, etc. It is used hypodermically in hydrocele. The maximum dose is 2 cc., and the usual dose is 0.6-1.3 cc. in solution.

⁸ Sir James Simpson, "New Anaesthetic," 1847, p. 7; *Illustrated London News*, December 4, 1847, 370/2. E. B. Simpson, *Century*, 25, 412; *Liv. Age*, 66, 720; *Mon. J. Med. Sci.*, September, 1847; *Ednb. Medico-Chir. Soc.*, November 11, 1848. J. Y. Simpson's "Anaesthesia," 1849, pp. 93, 145, 182, 193, 203. Chloroform of the density 1.48 was used by Simpson in 1847.

⁹ Formby (1845) mentioned this use of chloroform. See also, Simpson, *Mon. J. Med. Sci.*, December, 1847. Guthrie published an account of the therapeutic effects of chloroform as a diffusible stimulant in 1832.

¹⁰ Guillot proposed chloroform as an antispasmodic (*Ann. Therap.*, 1844, p. 35).

¹¹ As an antiseptic, chloroform prevents the growth of microorganisms,

counter-irritant, rubefacient, and as an antidote in cases of strychnine poisoning.

Anaesthetic chloroform, but more generally "technical" or "commercial" chloroform, is used technically (in electrotechnics, rubber industry, and photography) and in dentistry as a solvent. Chloroform is an important technical solvent; it dissolves fats, resins, one constituent part of caoutchouc, sulphur, phosphorus, iodine, many alkaloids and alkaloidal salts, as well as many other carbon compounds.¹

Reagent chloroform is generally of the density 1.48-1.489, and is employed as a solvent, for testing primary amines, for the detection of aniline, etc. Its most extensive use as a solvent in the laboratory is for dissolving alkaloids.

396,540 pounds of chloroform, valued at \$98,070, were produced in the United States in 1900; of this amount, 334,000 pounds were produced in New Jersey, and 62,540 pounds in New York. In 1905, 616,670 pounds, valued at \$165,604, were manufactured in this country.

III. MANUFACTURE.²

1. From Ethyl Alcohol.

A. Soubeiran³ showed that chloroform is formed by the action of bleaching-powder on dilute alcohol.⁴

When alcohol of various strengths is poured upon bleaching-powder, the distillate affords an oil which may be separated by fractionation. The amount of chloro-acetal (b. p., 150-160°) is therefore greatly diminished by diluting the alcohol.⁵

The theory of the process sometimes given is as follows: The bleaching-powder is supposed first to convert the alcohol into chloral, and then the lime which is present, or which is formed, splits this into calcium formate and chloroform.⁶

but it does not affect the action of soluble ferments (*J. Soc. Chem. Ind.*, 1886, 331). On the antiseptic applications of chloroform, see Robin, *Compt. rend.*, 30, 52; Augendre, *Ibid.*, 31, 679; Barnes, *Pharm. J.*, [3] 5, 441; Salkowski, *Chem. Repert.*, 1888, 166; and *Pharm. J.*, [3] 18, 315, 356, 855. Chloroform may be used as a preservative of mucilage and infusions. Munz (*Pharm. J.*, 1875, 967) proposed the use of chloroform as a test between chemical and living ferments.

¹ See, in this connection, Pettenkofer, *Jahresber.*, 1858, 363; Schlimpert, *Ibid.*, 1859, 405; Nowak, *Archiv. Pharm.*, [3] 3, 281; Hesse, *Pharm. J.*, [3] 4, 649. For a list of substances soluble, insoluble, and partly soluble in chloroform, see *Am. J. Pharm.*, 1852, 147.

² Only methods of commercial importance are considered.

³ *Loc. cit.*

⁴ See also, Bechamp, *Ann. chim. phys.*, [5] 22, 347. This process is usually conducted as follows: Bleaching-powder (40 parts), water (100-150 parts), alcohol (4-10 parts), and slaked lime (4-10 parts) are distilled together; the distillate separates in two layers, the lower one being chloroform, which is then purified. For papers on the manufacture of chloroform from alcohol and "chlorinated lime," see *Am. J. Pharm.*, 1862, 25, 42; 1868, 289. In *Chem. Ztg.*, 10, 338, is described the process used in Germany in 1886; in Gray's "Supplement to the Pharmacopoeia," 1846, p. 633, is described the process in general use in 1845; and in *Sci. Am.*, 95, 421, the French process is given by Boyer. On the manufacture of chloroform from bleaching-powder and ethyl alcohol, see especially Frerichs, *Am. Inst. of Chem. Eng.*, 1911.

⁵ Goldberg, *J. prakt. Chem.*, 132, 111. On the preparation of chloroform from alcohol, see, in addition, Soubeiran, *Compt. rend.*, 25, 799; Meurer, *Chem. Centr.*, 1848, 154; Carl, *Ibid.*, 1848, 236; Larocque and Hurault, *N. J. Pharm.*, 13, 97; Siemerling, *N. Br. Arch.*, 53, 23; Kessler, *N. J. Pharm.*, 13, 162; Ramdohr, *N. Br. Arch.*, 83, 280; Hirsch, *Ibid.*, 107, 137. The alcohol used should not contain fusel oil (Regnault and Hardy, *J. Pharm. Chim.*, [4] 30, 405) or higher alcohols.

⁶ Watts' "Dictionary of Chemistry," 2, 68 (1890).

Dott,¹ however, stated that the formation of chloroform from ethyl alcohol is best indicated by

Dott confirmed the observation of Finnemore² and Wade that a small proportion of ethyl chloride is formed in preparing chloroform from ethyl alcohol.³

B. According to the process of Schering,⁴ halogen salts of the alkalis or alkaline earths are electrolyzed in the presence of alcohol, acetone or aldehyde in a warm aqueous solution, carbon dioxide being passed continuously into the electrolyte during the process.

Kempf⁵ invented a process for the manufacture of chloroform by electrolyzing suitable halogen compounds of the alkalis and alkaline earths in alcoholic solution with constant heating; and Trechcinski⁶ prepared chloroform by the electrolysis of an aqueous-alcoholic solution of calcium chloride. The latter used platinum electrodes and the calcium chloride solution was contained in a glass vessel; the gases and chloroform vapor were conducted off through a tube to an absorption apparatus. The yield was found to be increased when alcohol was added to the spent electrolyte solution.

Although ethyl alcohol was formerly used for the production of chloroform, it is now largely, and almost entirely, replaced by acetone, and more recently carbon tetrachloride has become an important source.

2. From "Methylated Spirit."

Pure methyl alcohol does not yield chloroform when treated with bleaching-powder, although it is formed from commercial methyl alcohol.⁷ "Methylated chloroform," at one time extensively used in England, is chloroform prepared from wood spirit ("methylated spirit.")⁸ It is incorrect to suppose that "methylated chloroform" has received an actual addition of wood spirit, but such chloroform is liable to be much less pure than that obtained solely from ethyl alcohol. According to Allen,⁹ chloroform prepared from "methylated spirit" is more difficult to purify than that made from ethyl alcohol, but a product has been manufactured in England from the former source which appears to be equal in all respects to the more expensive article.¹⁰

¹ *J. Soc. Chem. Ind.*, 27, 6, 271.

² *J. Chem. Soc.*, 85, 938.

³ See ethyl chloride, Section VIII, 12(b).

⁴ German Patent 29,771, 1884; *Ber.*, 17, ref. 624. Also Dony-Henault, *Z. Elektrochem.*, 7, 57; Wäser, *Chem. Ztg.*, 34, 141.

⁵ English Patent 8,148, 1884; German Patent 29,771, 1884; French Patent 162,306, 1884; Belgian Patent 65,227, 1884.

⁶ *J. Russ. Phys.-Chem. Soc.*, 38, 734; *Pharm. Ztg.*, 51, 523.

⁷ Belohoubek, *Ann.*, 165, 349.

⁸ "Methylated spirit" is a mixture of rectified spirit with 10 per cent. of wood naphtha; it has been used in the manufacture of chloroform, owing to its being obtained duty-free (Thorpe).

⁹ "Commercial Organic Analysis," 1, 235 (1908). Although "methylated chloroform" is not on the American market, contamination with methyl alcohol is considered under that caption.

¹⁰ Allen is also authority for the statement that imperfectly purified "methylated chloroform" is specifically lighter than the pure substance, has an empyreumatic odor, and produces disagreeable sensations when inhaled. In some cases, we are told, such chloroform appears to be actually poisonous and produces general and rapid prostration. Such chloroform contains several units per cent. of a chlorinated oil, lighter than water and boiling at a much higher temperature than chloroform. A similar but different oil (heavier than water) has been detected in much smaller quantity

Gregory¹ found that the chloroform prepared from ethyl alcohol and wood spirit, when fully purified, is quite identical in all its properties, but that from the former is more easily purified. In fact, it may be asserted on the authority of Brown, Squibb, Schacht and Biltz² that properly purified chloroform is the same from whatever source it is obtained; however, Cross and also Spilsbury³ have expressed the opinion that chloroform made from ethyl alcohol is physiologically safer than that from methylated spirit and acetone. The latter opinion is a recent one (1909) and is substantiated, at least in part, by other evidence, but is totally incorrect when the chloroform is properly purified.⁴

3. From Acetone.

A. The preparation of chloroform from acetone was referred to by Liebig in 1832. Böttger, in 1848, showed how to prepare chloroform from acetates and from acetone, and stated that chloroform made from acetone directly was then to be had on the market, one ounce of acetone yielding 1 $\frac{1}{4}$ ounces of chloroform. The reason why this method of preparation was not generally followed up was doubtless attributable, as indicated by Squibb,⁵ to the erroneous statements of Siemerling (1848) and Wackenroder, adopted by such authorities as Gmelin and Watts, who for some reason failed to obtain anything like the proportion mentioned by Böttger. Thus, Watts⁶ stated, in 1874, that the manufacture of chloroform from acetone cannot be advantageously carried out, since the price of acetone is high and it yields only about one-third of its weight of chloroform when treated with chloride of lime. However, it may be shown that Siemerling used only about half of the theoretical proportion of chloride of lime, and that he apparently made no attempt to recover and treat again the acetone left unconverted.

Orndorff and Jessel⁷ found that the products formed by the action of bleaching-powder on acetone are chloroform, calcium hydroxide, calcium chloride, and calcium acetate. They considered it probable that the first action of the bleaching-powder is a substituting one, yielding trichloroacetone or methyl chloral, and that this is then acted on by calcium hydroxide formed at the same time, giving chloroform and calcium acetate:

Dott, however, states that the equation

in chloroform prepared from alcohol containing no methyl compounds; these oils may be totally eliminated by purification of the crude chloroform.

¹ *Mon. J. Med. Sci.*, May, 1850; *Pharm. J.*, **9**, 580.

² *Pharm. J.*, [3] **24**, 811.

³ *Ibid.*, [4] **29**, 660.

⁴ It has also been stated that headache frequently occurs among workmen while bottling chloroform made from methylated spirit, whereas the symptoms were not observed while manipulating chloroform derived from ethyl alcohol (*Ibid.*, [4] **18**, 515).

⁵ *J. Am. Chem. Soc.*, **1896**, 231.

⁶ "A Dictionary of Chemistry," **1**, 918. This statement was based on the results of Siemerling (*Arch. Pharm.*, [2] **53**, 23).

⁷ *Am. Chem. J.*, **10**, 366. Dott (*Pharm. J.*, **81**, 54) found that there are also considerable amounts of calcium carbonate and chlorate in the residual liquor obtained in preparing chloroform from acetone.

agrees well with his experimental results. This presentment of the reaction may be taken as representative.

B. Michaelis,¹ and Michaelis and Mayer² invented a process wherein rude acetates are subjected to dry distillation at high temperatures to remove the fluid products therefrom, which are then subjected to the action of a hypochlorite and the chloroform produced is condensed; the residual products of the dry distillation are converted into acetic acid or purified acetates. This process is used by an American firm.

C. Rumpf³ devised this process for the manufacture of chloroform from acetone:—acetone in a dilute state is periodically introduced into the bottom of a still containing chloride of lime solution, with agitation of the solution. The chloride of lime employed is more than five times the weight of the acetone, resulting in the chloroform produced equaling the acetone in volume. Rumpf based his patent upon the incorrect quotation from Watts. Squibb, to avoid litigation, and partly because he found that by taking an excess of acetone the hypochlorite is more economically and promptly utilized, and the resulting chloroform purer, while the unconverted acetone is easily recovered and again treated, proposed to use Siemerling's proportions, and to conduct the whole operation in an apparatus described by himself in 1857, and used for many years in the production of chloroform from alcohol.

In the process of Porsch,⁴ vapors from the dry distillation of an acetate, and chlorine gas, are continuously discharged, in opposite directions, under pressure, in an aqueous bath of an alkaline earth, as milk of lime, subjected to heat; the hydrochloric acid is separated from the resultant vapors and the chloroform vapors are condensed.

According to the patented process of Chute,⁵ wood spirit, containing ketonic impurities such as acetone, is treated with a hypochlorite, and the chloroform, which is thus produced, is isolated by diluting the reaction mixture with water, or with a saline solution, and then distilling off the chloroform.

D. Chloroform is now made from sodium chloride and acetone by electrolysis.⁶ However, there appears to be a strong prejudice in the pharmaceutical trade against chloroform from this

¹ U. S. Patent 322,194, 1885.

² English Patent 8,523, 1885; German Patent 36,514, 1886.

³ U. S. Patent 383,992, 1888. On the patents of Rumpf for the production of chloroform by the "acetone process," see Sadtler, *Pharm. Era*, **1889**, 376. Sadtler stated that the chloroform thus obtained is quite free from chlorinated side-products, but is nevertheless purified by treatment with sulphuric acid and careful washing, and then brought exactly to the pharmacopoeial standard.

⁴ U. S. Patent 573,483, 1896.

⁵ U. S. Patent 893,784, 1908.

⁶ In 1900, the following process was described (*Rev. Prod. Chim.*, **3**, 309): A 20 per cent. solution of sodium chloride is heated at 100° C. in a leaden still, and is kept agitated by means of carbon spatulas, which, at the same time, serve as anodes for the (5–6 ampere) current. Acetone is introduced into the bottom of the still and combines with the liberated chlorine to form acetone trichloride, which, in the presence of the sodium hydroxide, is decomposed with the formation of sodium acetate and chloroform. The latter is conveyed through a condenser and is collected in a suitable receiver. The yield was found to be 180 parts out of 210 theoretically possible. Klar (*Chem. Ind.*, **19**, 159) has also described the process for the preparation of chloroform in which acetone is chlorinated by chlorine evolved during the electrolysis of a 20 per cent. sodium chloride solution. Teeple (*J. Am. Chem. Soc.*, **26**, 536) has discussed very fully the electrolytic preparation of chloroform from acetone. He found that the conditions necessary for the successful preparation of chloroform by the electrolysis of a chloride in the presence of acetone are: A temperature below 25° C., absence of alkali, a high current density at the cathode and a low one at the anode. A good yield of chloroform may also be obtained by the action of chlorine upon calcium hydroxide solution containing acetone. This suggests that the electrolysis of a calcium chloride solution in the presence of acetone would be the best method of making chloroform, provided the high resistance of the deposits on the anode could be overcome. The process of Schering (1884), already referred to, specifically initiated the efforts which have been made to devise a satisfactory process for the production of chloroform from acetone electrolytically. See also, *Rev. Scienc.*, Feb., 1893.

source, which causes the manufacturers to be reluctant about divulging any information concerning the process.

When acetone is used for the preparation of chloroform, it should be previously purified¹ and this purification should be carefully conducted in order to prevent the formation of condensation compounds.²

It has been stated that chloroform made from acetone is not nearly so good an anaesthetic as chloroform made from ethyl alcohol;³ but this opinion is based upon the findings of Wade and Finnemore,⁴ that chloroform prepared from ethyl alcohol contains a very small proportion of ethyl chloride. When chloroform is properly made from purified acetone, careful purification will result in the production of pure chloroform.⁵

Chloroform is now being manufactured from acetone by at least three firms in this country,⁶ while anaesthetic chloroform prepared from crude chloroform from this source is being marketed with success by at least five manufacturing chemists.

4. From Methane (Natural Gas).

A. About 490,000,000,000 cubic feet of natural gas, valued at approximately \$71,000,000, are produced annually in the United States. In Pennsylvania, for example, many wells of 5,000,000 cubic feet daily capacity have been drilled. This gas contains 50-95 per cent. of methane,⁷ and, bearing in mind the demonstration of Regnault⁸ that chloroform is formed by the action of chlorine on methane in daylight and ultimately in sunlight, several investigators have sought to effect a chlorination in order to obtain substitution products. The ultimate object has been to produce a constant yield of an intermediate product.

B. In 1879, Mallet⁹ proposed passing chlorine and

¹ In *Am. J. Pharm.*, 1886, 321, is an account of a method for purifying acetone used in the preparation of chloroform.

² Dott, (*J. Soc. Chem. Ind.*, 27, 272) has called attention to the importance of the impurities which may be present in commercial acetone. He found that samples which indicated 99 per cent. by the iodoform and other methods gave about 7 per cent. distilling above 58°. This was first thought to be due to the presence of higher ketones or other bodies yielding iodoform, but Gibson suggested that it might possibly be caused by the presence of even 1 per cent. of a mixture of the condensation products of acetone (e. g., mesityl oxide, phorone, and mesitylene), which all have relatively high boiling points. It was found that on mixing pure acetone with 1 per cent. of the mixed condensation products it behaved on distillation and in its iodoform yield, and otherwise, like the samples referred to. When purifying acetone, therefore, manufacturers should avoid treatment with mineral acids or other method which is likely to cause formation of the condensation compounds. On the purity of acetone, see also Guttman, *Dingler's Polyt. J.*, 1894, 96; Klar, *J. Soc. Chem. Ind.*, 1897, 722.

³ Price, *Pharm. J.*, 23, 89.

⁴ *Loc. cit.*

⁵ J. F. MacFarlan & Co. (*The Lancet*, 1906, i, 747) have expressed the opinion that chloroform prepared from acetone is by no means generally accepted as inferior to chloroform prepared from alcohol, and consider that up to the present, insufficient evidence has been adduced to establish the view that it is actually inferior.

We may state here that, from our experience, anaesthetic chloroform manufactured from acetone has been found by American anaesthetizers to be fully as satisfactory as that from other sources.

⁶ The manufacture of chloroform from acetone has been carried on since 1885 in this country and since 1882 in Germany.

⁷ Pennsylvania natural gas contains from 50-99 per cent. total paraffins; Ohio gas, 90-93 per cent.; and West Virginia gas, 80-87 per cent.

⁸ *Ann. chim. phys.*, [2] 71, 380. See also, Dumas, *Ann.*, 33, 187; *Ann. chim. phys.*, [2] 73, 95.

⁹ U. S. Patent 220,397, October 7, 1879. Cf. U. S. Patents 880,900, March 3, 1908, and 1,009,428, November 21, 1911, of J. MacKaye.

methane through a body of porous material not acted upon by the chlorine, as prepared carbon, meanwhile maintaining the temperature between 30° and 90° C.

C. Later, Colin¹ made serious endeavors to manufacture and separate the chlorides of methane by the mutual combustion of chlorine and natural gas, mixed in suitable proportions within a retort. The gases were ignited and the reaction was maintained by an electric spark of proper tension, the chamber being kept at a proper temperature. After absorbing the hydrogen chloride from the product, the methyl chlorides were liquefied and attempts were made to thereby separate them. An experimental plant was installed for manufacturing chloroform from natural gas by this process at Allegheny, Penn.

Without discussing the suitability of the provisions made for the reactions in these two processes, it may be remarked that both were unsuccessful, mainly owing to the tendency of the methane, when chlorinated, to constantly produce either methyl chloride or carbon tetrachloride, as shown by Phillips.² The latter found that dichloromethane and chloroform are formed in relatively small quantities, and concluded that the manufacture of chloroform from natural gas, as indicated by his experiments, is likely to prove a difficult matter.³

D. The process of Elworthy for the manufacture of chloroform from methane is a decided improvement over the older ones, although future application only can decide its fate. In conjunction with Lance, Elworthy⁴ prepared methane by the synthetic method of Sabatier and Senderens,⁵ by passing a mixture of water-gas and hydrogen over heated nickel at 190-250° C.—one of the convenient methods of preparing methane, although any excess of carbon monoxide greatly retards the reaction. Elworthy and Lance passed methane properly mixed with chlorine through a series of thick-walled glass tubes exposed to direct or diffused sunlight, the light from an electric arc, etc., and their patent specifies dilution of the gases to avoid explosion.⁶

E. Pfeifer and Szaroasy⁷ have recently claimed a process for the production of halogen derivatives of hydrocarbons, consisting in treating methane with a halogen, or with a compound which liberates free halogen in the reaction chamber, under the action of the silent discharge.

We were informed that chloroform is now being made from natural gas by an American firm, and that such chloroform is known to the trade as "gas chloroform," but this appears to be incorrect, the source being carbon tetrachloride prepared from carbon disulphide and not methane.

¹ U. S. Patent 427,744, May 13, 1890.

² *Am. Phil. Soc.*, March 17, 1893.

³ *Am. Chem. J.*, 16, 362.

⁴ French Patent 353,291, May 15, 1905. See, in this connection, German Patent 222,919, November 5, 1909, of J. Walter; and *Allg. Osterr. Chem. Ztg.*, 29, 23.

⁵ *Compt. rend.*, 134, 9, 514.

⁶ Elworthy's death four years ago occurred before his process had been commercially demonstrated, and we have been informed that it is now very doubtful if the process can or will be carried out.

⁷ 12,058. D. Ann. P. 24,872, September 25, 1911.

5. From Carbon Tetrachloride.

Geuther found that chloroform results from the action of nascent hydrogen (from zinc and sulphuric acid) upon carbon tetrachloride;¹ and Damoiseau thought that chloroform might be profitably prepared by passing a mixture of methyl chloride and chlorine in the proper proportions through a long tube containing animal charcoal and heated between 250° and 350° C.² It was not until successful commercial processes for the production of carbon tetrachloride had been developed, however,³ that it was ascertained that chloroform may be advantageously prepared from carbon tetrachloride.⁴

The carbon tetrachloride used is prepared from carbon disulphide (the electric furnace product), and manufacturers in the United States state that it is so free from sulphur compounds that "no part of the distillate separated from a batch of 5000 pounds through a long fractionating column will show any

¹ *Ann.*, **107**, 212.

² *Compt. rend.*, **91**, 1071. See also, *Compt. rend.*, **92**, 42, 145; Vincent, *Jahresber. Chem. Technol.*, **1881**, 971.

³ As early as 1834 it was learned that carbon disulphide may be converted into carbon tetrachloride by chlorination (Kolbe, *Ann.*, **45**, 41; **54**, 146. See also, Hofmann, *Ibid.*, **115**, 264; Klasow, *Ber.*, **20**, 2376; Moneyrat, *Bull. soc. chim.*, [3] **19**, 262; Serra, *Gaz. chim. ital.*, **29**, 353). Müller and Dubois (Eng. Patent 19,628, 1893) devised a process for the production of carbon tetrachloride by the addition of finely divided iron to a mixture of carbon disulphide and sulphur chloride; cf. Eng. Patent 13,733 of 1901, of Urbain, wherein practically the same process is claimed, and U. S. Patent 753,325, dated March 1, 1904, of A. W. Smith. On the preparation of carbon tetrachloride, see Margosches, "Der Tetrachlorkohlenstoff," **1905**, pp. 4 and 15.

⁴ In 1896, the following method for the preparation of chloroform was described (*Chem. Rev.*, **1896**, 88): To 75 kg. of carbon tetrachloride are added, in the cold, 60 kg. of hydrochloric acid (22° B.) and 50 kg. of zinc, the whole being then heated in an autoclave. Hydrogen is liberated and reduces one atom of chlorine with the formation of hydrochloric acid which then attacks the zinc anew, and the cycle continues until the process is complete, a condition indicated by the formation of the hydrochloric acid. The upper layer of the substance is removed and the product refined. (See also, *Pharm. Centralh.*, **37**, 715; *Pharm. J.*, **57**, 377). "On the Preparation of Chloroform from Carbon Tetrachloride," see Gustavson, *Ber.*, **7**, 128; Eder and Valenta, *Chem. Ind.*, **20**, 249; *Pharm. Ztg.*, **41**, 22; Klar, *Chem. Ind.*, **19**, 159.

In 1902, A. W. Smith, of Cleveland, Ohio, devised a successful process of making chloroform from carbon tetrachloride. This process (*loc. cit.*) consists in the production of chloroform by the following steps: the action of heated sulphur upon heated carbon, so as to produce carbon disulphide; the action of chlorine upon sulphur, so as to produce sulphur chloride or dichloride; the action of sulphur chloride or dichloride upon carbon disulphide, so as to produce carbon tetrachloride; and, finally, the reduction of carbon tetrachloride, so as to produce chloroform. According to the specification of Smith, the reduction of the purified carbon tetrachloride to chloroform may be accomplished in a number of ways, "as by treating the tetrachloride with some substance or substances that will generate nascent hydrogen, such as an acid and a metal or an alkali and zinc or by electrolytic methods. This reaction may be much shortened in time by bringing the tetrachloride and acid used in the production of nascent hydrogen into more intimate contact with each other by the use of a mutual solvent for both tetrachloride and acid (ethyl or methyl alcohol)." Smith "found, however, that mechanical agitation of the tetrachloride with reducing substances answers the same purpose to a certain extent and is preferable".....and "that simple agitation of the tetrachloride with water and finely-divided iron without any acid or simply a trace of acid to start the reaction is one of the most efficient methods of reduction of the tetrachloride to chloroform," which "method is far cheaper than that involving the use of acids or most other reduction methods and possesses the added advantage that it can be readily controlled, so that little or no reduction to dichloromethane takes place." The process of Smith is in use by an American concern, and modifications have been put into effect and are now the subject of other patents under action. This company began the commercial manufacture of chloroform from carbon tetrachloride in 1902, and the present capacity is about 300,000 pounds per annum. At the present time, part of the product is being exported and is reported to be of satisfactory quality, complying with certain foreign pharmacopoeial requirements. ■

sulphur compounds by the most delicate tests known." The presence of carbon disulphide in the chloroform produced is guarded against by means of a process for removing carbon disulphide from the carbon tetrachloride used; when traces are present, the tetrachloride is fractionated in a high column still until the distillate will give no response with tests for the presence of carbon disulphide;¹ then the material remaining in the still is used for the manufacture of chloroform and the distillate is considered as commercial carbon tetrachloride, which is usually guaranteed to contain 99.7 per cent. of absolute CCl₄.

We have been informed that "technically pure" chloroform produced from disulphide tetrachloride may be recognized by its small content of carbon disulphide and carbon tetrachloride, and that such a grade also possesses a higher refractive index than other varieties. We have not examined any of this "technically pure" chloroform, but from our experience the anaesthetic grade conforms in full with the required pharmacopoeial standards.

6. Special Chloroforms of Foreign Manufacture.

Considerable quantities of chloroform are produced in Germany for domestic and foreign consumption.²

In addition to anaesthetic chloroform prepared by the action of bleaching-powder on alcohol and acetone (Chloroform Gehe, Riedel, Merck, Kahlbaum, de Haen, König, and Cotta), "Chloroform e Chloral," "Chloroform Pictet," and "Chloroform Anschütz" are found on the German market.

A. Chloral Chloroform.—Liebig found that chloroform might be prepared by distilling chloral with excess of aqueous potassium hydroxide, sodium hydroxide or baryta, or with milk of lime, repeatedly agitating the oily distillate with water, separating from the water as completely as possible by decantation, and then distilling with 6 or 8 times its volume of strong sulphuric acid in a perfectly dry apparatus. In 1870, chloral chloroform was sold under the name "English Chloroform" in Germany, and Hager, after an examination, expressed the opinion that chloroform from chloral was the purest then obtainable.³

The invention of Liebreich⁴ for preparations for the production of chloroform relates broadly to a product consisting of a dry mixture of chloral hydrate and alkali, which may be compressed into any convenient shape; on treatment with water, chloroform is pro-

¹ The detection and estimation of carbon disulphide in chloroform will be referred to later.

² In 1910, for example, 161,900 kg. of chloroform and chloral were exported, 19,000 kg. of which went to the United States: the average price is from 170–180 marks per 100 kg.

³ *Year-Book of Pharm.*, **1870**, 119. Hager found that "English chloroform" was really chloral chloroform containing 0.75–0.80 per cent. of alcohol. The addition of pure sulphuric acid to this chloral chloroform caused no coloration, while it was found to color slightly the ordinary grade of chloroform then in use. Evaporation of some of the substance on a watch-glass in the air was found to afford another means of testing the substance. When all but a few drops had disappeared, the ordinary chloroform residue was found to possess a disagreeable odor, while the other retained its pleasant odor. Versmann (*Pharm. J.*, [3] **2**, 63) also found that the residue of chloral chloroform possesses no foreign odor.

According to a later writer, however (Ahrends, *Pharm. Ztg.*, **1891**, 263), German chloroform is generally superior to that manufactured in England. This is as one would now suspect, since the British Pharmacopoeia is considerably less stringent than that of Germany.

⁴ Eng. Patent 15,930, 1904.

duced. The product of this process has been known as "Chloroform Liebreich," and "Chloroform-Scher-ing," now on the American market, is prepared from Liebreich's crystallized chloral hydrate.

Langgaard¹ examined the eight principal brands of chloroform obtainable in Germany, and found that chloral chloroform was the purest. As a general rule, however, all of the German chloroforms of anaesthetic grade are of good quality,² and the grade at present prescribed by the *Arzneibuch* is, at least in most cases, equal to chloroform prepared from chloral. It has been also claimed that chloral chloroform does not undergo decomposition, but this has been shown to be incorrect;³ in fact, like all the other pure preparations, "Chloroform e Chloral" decomposes if not preserved by the addition of, for example, a little alcohol.⁴

B. Chloroform Pictet.—This preparation is obtained by crystallization at -80° and then at -82° .⁵

Schacht⁶ has shown that although the Pictet chloroform is a good preparation, that obtained from the purest crystallized chloral hydrate is quite equal to it, and like the latter it requires the addition of a preservative.

C. Chloroform Anschütz.—More recently a special preparation under the name "Anschütz Salicylid Chloroform" or "Salicylchloroform" has been placed on the German market; it is obtained from a crystalline compound of salicylid, first prepared by Anschütz.⁷ According to the patented process of the latter, chemically pure chloroform is produced by decomposing by heat double compounds of chloroform and lactid-like condensation products derived from "ortho-phenol carbonic acids," as salicylid, and then condensing the pure chloroform; salicylid-chloroform is prepared by boiling salicylid in chloroform,⁸ and in this compound chloroform plays the same role as the water of crystallization in many crystalline salts, being obtained in a pure state by simple distillation therefrom.⁹ Salicylid-chloroform is said to be extensively used by anaesthetists in Russia, since it conforms to the pharmacopoeia of that country, and it is especially recommended by others for anaesthesia.

The comparative prices of anaesthetic chloroform prepared from acetone by means of bleaching-powder, chloroform from chloral by potassium hydroxide, "Chloroform Pictet," and "Chloroform Anschütz," are respectively, taking the first as a basis, 1, 3, 6, and 10.

¹ *Therap. Monatsh.*, May, 1902.

² The results obtained by the authors in the course of an examination of the principal German products will be given later.

³ See *Am. J. Pharm.*, **42**, 409.

⁴ See Schacht, *J. Soc. Chem. Ind.*, **1893**, 543; also *Preservation*. It is said that the vapor from chloral hydrate separates with difficulty from the vapor of chloroform, and that it is impossible to prevent contamination.

⁵ See *Purification*, where the process of Pictet is detailed.

⁶ *Loc. cit.*

⁷ *J. Soc. Chem. Ind.*, **1893**, 782. Cf. the analogous conduct of leprarin (Kassner, *Archiv. Pharm.*, **237**, 44). On $\text{CHCl}_3 \cdot 18\text{H}_2\text{O}$, see *Z. anal. Chem.*, **25**, 118.

⁸ U. S. Patent 535,270, 1895; German Patent 70,614, 1894.

⁹ Anschütz, *Ann.*, **273**, 94; Arends, *Chem. Ind.*, **16**, 78. The purity of this chloroform will be referred to in succeeding pages.

IV. PURIFICATION.

The crude chloroform prepared by the action of bleaching-powder on alcohol, by the action of bleaching-powder on acetone,¹ or by the electrolysis of solutions of chlorides of the alkalis or alkaline earths in alcohol or acetone² is not of so high a degree of purity as that obtained by the action of alkalis on previously purified chloral, and requires more careful purification before it is suitable for anaesthetic purposes. The extent of the purification necessary is, of course, dependent upon the purity of the materials used as well as upon the process employed, but especially upon the purpose for which the chloroform is intended.

A. The earliest methods for the purification of crude chloroform consisted in washing the distillate with water to remove alcohol,³ and then drying over calcium chloride, or sometimes rectifying without having previously dried the product. In 1848, the method was introduced whereby crude chloroform was purified by shaking with potassium hydroxide, drying over calcium chloride, and then rectifying; this method serves to remove chlorine⁴ and acids, but only partially eliminates alcohol and other probable contaminants.

Gregory⁵ purified chloroform by agitating it and leaving it in contact with sulphuric acid until the latter was no longer colored by it, then he removed the chloroform and placed it in contact with a small quantity of manganese dioxide to free it from "sulphurous acid." About 1860, the German custom was to rectify over concentrated sulphuric acid.⁶ At the present time treatment with sulphuric acid is generally resorted to and forms the most important stage of the purification of crude chloroform prepared from alcohol or acetone. Pure concentrated sulphuric acid has no action on chloroform itself unless

¹ See *Pharm. J.*, [3] **20**, 84.

² See *J. Soc. Chem. Ind.*, **1885**, 243.

³ When made from alcohol, crude chloroform contains considerable quantities of alcohol in solution, from which it may be separated by repeatedly washing with water. In order to wash a yield of 160-175 kg. of crude chloroform, about 800 liters of water are necessary to obtain anaesthetic chloroform, although this washing forms only one stage of the purifying process.

⁴ Kessler (*J. Pharm. Chim.*, [3] **13**, 162) found that chloroform may be freed from chlorine by agitation with potassium hydroxide, and suggested that it be further purified by drying over calcium chloride and then rectification. It has been stated by Pictet (U. S. Patent 489,592, 1893) that when chloroform containing hydrochloric acid and chlorine is neutralized with an alkali, there remains in the chloroform thus treated a series of heterogeneous bodies "consisting essentially of the series of the tetrachlorides of carbon which remain dissolved in the liquor" and no reagent known at present can serve for their detection or elimination.

⁵ *Proc. Roy. Soc. Ednb.*, **1850**, 391. According to Abraham (*Pharm. J.*, **10**, 24), chloroform, when thus purified, quickly decomposes, and is afterwards found to contain hydrochloric acid and free chlorine.

Guthrie, in 1832, found that "chloric ether may be entirely, or very nearly so, separated from alcohol by repeated rectification, from muriate of lime; it may thus be brought to the specific gravity of 1.44." However, "chloric ether, distilled off sulphuric acid, has a specific gravity of 1.486, or a little greater, and may be regarded as free from alcohol." He recommended that the "chloric ether" be finally washed with a concentrated solution of potassium carbonate.

⁶ The United States Pharmacopoeia of 1850 gave a process for preparing chloroform; this was transferred in 1860 to the *Materia Medica Catalogue*. "Chloroformum venale," or commercial chloroform, was introduced and also a formula for purifying chloroform; this was dropped in the Pharmacopoeia of 1890.

the operation is unduly prolonged,¹ but it decomposes some of the impurities which are commonly present and removes others. In the next place, the product is brought in contact with sodium carbonate,² or it is washed with lime water and then dried over calcium chloride.³ In any case, it should be finally distilled at a temperature not above 64°.⁴

One method of preparing anaesthetic chloroform from commercial chloroform manufactured from acetone, now in use by a prominent manufacturing chemist, consists in conducting the vapor of the commercial chloroform through concentrated sulphuric acid and then passing it through a tower containing crystallized sodium carbonate, after which treatment the purified chloroform is brought to pharmacopoeial strength. The commercial chloroform thus treated usually possesses a density of 1.485 at 25°/25°, and a sample examined by the authors conformed with all of the pharmacopoeial tests excepting the sulphuric acid test, thus indicating that it had been purified by washing with water alone.

B. Various other methods have been proposed for the purification of chloroform, especially when it has become contaminated with decomposition products. We have, for example, the method of Gibbs,

¹ Christison (*Pharm. J.*, **10**, 253) found that chloroform keeps well after being once treated with sulphuric acid, but that the continued action of that liquid, especially if it is contaminated with nitrous acid, exerts a decomposing action on it. Tilden (*Ibid.*, [3] **1**, 623) stated that the sulphuric acid used to purify chloroform must be free from all traces of nitrogen oxides, and it was his opinion that the decomposition of chloroform may be attributed to contamination of this kind. Redwood (*Ibid.*, [3] **12**, 734) was inclined to ascribe the improved quality of the British chloroform of 1882 to the care used in its manufacture, particularly to the attention paid to the purity of the sulphuric acid used in the purification. Clark, however, maintained that the presence of nitrous or nitric acids in the sulphuric acid was not the cause of the instability of chloroform. Both Clark and Dott considered "that the decomposition of chloroform is not probably due to the presence of nitric acid in the sulphuric acid" (*vide* Preston, *Ibid.*, **12**, 981). For a discussion of the action of sulphuric acid on chloroform, see *Decomposition*.

² Shuttleworth (*Am. Chemist*, **4**, 339) observed that in samples of chloroform imperfectly rectified, as that of the ordinary German manufacture of 1873, the impurities produced by the agencies of time, light, moisture, and atmospheric exposure are, after a lapse of some months, easily recognizable. Traces of sulphuric acid were found to quickly induce this change; and when that chemical has been employed as the purifying agent, and has not been completely removed by repeated washings and rectifications, the product will very soon give sharp indications of decomposition. The method of purification adopted by the British Pharmacopoeia of that time consisted in mixing the chloroform, after treatment with acid, with lime and calcium chloride, and then rectifying at once. Shuttleworth considered that the keeping qualities of the product would be much improved by agitating the chloroform, before rectification, with a solution of sodium carbonate, followed by water. Thorpe (*J. Chem. Soc.*, **37**, 196) purified chloroform by frequently agitating some purest commercial chloroform during several days with successive quantities of water, digesting the decanted liquid about a week with concentrated sulphuric acid, shaking the separated chloroform with recently heated potassium carbonate, and finally distilling. Chloroform thus purified possessed a density of 1.52637 at 0°/4° and a boiling point of 61.2°. Werner (*Arch. Pharm.*, [3] **25**, 1113) stated that his method of purification afforded a product found to be perfectly satisfactory for medicinal use during 10 years' experience. This method (*Ibid.*, [3] **12**, 481) consisted in shaking the chloroform up with one-fourth its volume of distilled water, removing the latter the next day, then agitating the chloroform with fused sodium carbonate and allowing the mixture to stand 24 hours. After removing the sodium carbonate, the residual product was distilled over a water-bath, the distillate coming over below 64° being used.

³ Thayer (*J. Phys. Chem.*, **3**, 36) found that traces of alcohol remained in chloroform even after the latter had been allowed to stand over calcium chloride for a long time. He purified chloroform by washing it repeatedly with water, then keeping it in contact with calcium chloride for two days, and finally decanting and distilling over fresh calcium chloride.

⁴ See Werner, *loc. cit.*; Thorpe, *loc. cit.*; Remys, *Archiv. Pharm.*, [3] **5**, 31; Michaelis and Mayer, *Polyt. J.*, **261**, 496.

wherein lead dioxide is employed;¹ that of Mentin, according to which the chloroform is distilled over 2 per cent. of paraffin at 61°;² and the recommendation of Shuttleworth³ that agitation with a dilute solution of sodium thiosulphate be employed.⁴

Yvon⁵ stated that he was enabled to obtain an absolutely pure chloroform by treatment with an alkaline potassium permanganate solution; this procedure is not a necessary one, however, and, as a result, has not come into use. Useless also, providing the chloroform has been brought to the proper state of purity prior to fractionation, is the French practice of distilling over poppy oil.⁶

C. Among the *special, technical methods of purification*, the process of Pictet, previously referred to in brief, depends upon cooling commercial chloroform to -80°; the solid bodies are removed by filtration. It is then cooled to below -80° and the non-crystallizable portions, which contain impurities, are removed; the chloroform is then distilled at a very low temperature and the middle 80 per cent. of the product is taken as "chemically pure" chloroform.⁷

¹ *Trans. N. Y. Acad. Med.*, **1**, 146. Gibbs suggested, in 1850, that chloroform possessing an acid reaction and probably containing chlorinated oils be treated with lead dioxide. Metcalfe (*Ibid.*) found that such treatment served to remove any disagreeable odor characteristic of such chloroform.

² *Ann. chim. farm.*, [4] **10**, 32.

³ *Am. Chemist*, **4**, 339. Shuttleworth recommended that chloroform which has been injured by time exposure be restored by agitating well with a dilute solution of sodium thiosulphate, separating from the supernatant liquid and washing with water, then separating and passing the chloroform through filter paper to free it from traces of moisture.

⁴ Although this method yielded an improved chloroform, Shuttleworth considered that when a "pure" preparation is desired, the impurities not removable by thiosulphate, those of a more stable character and possessing a higher boiling point than chloroform, be removed by distillation or by treatment with sulphuric acid.

⁵ *Mon. Sci.*, March, 1884, 262. Yvon found that chloroform prepared according to the French Pharmacopoeia of 1866, by agitation with water, leaving in contact with potassium carbonate, drying over calcium chloride, and finally rectifying, is sufficiently pure for anaesthetic purposes. He pointed out, however, that a still purer product could be obtained by modifications of this method.

⁶ The method official in the French Pharmacopoeia of 1899 for the purification of commercial chloroform was modified by Masson (*J. Pharm. Chim.*, **9**, 568), according to whose process crude commercial chloroform is first washed with water, the aqueous layer separated, and the chloroform shaken with 2.5 per cent. of its weight of sulphuric acid, and the operation being repeated with a fresh portion of acid, if necessary, the acid being left in contact with the chloroform for two or three days. The chloroform is then treated with 3 per cent. of its weight of sodium hydroxide solution (sp. gr. 1.33), which is left in contact also for two or three days. It is then washed with water, dried over calcium chloride, and 2.5 per cent. of poppy oil added. Distillation is then conducted into graduated receivers containing 0.2 per cent. by weight of alcohol for the amount of chloroform they are to contain. The important modifications in this process are the prolonged contact of the chloroform with the sodium hydroxide solution; the final distillation over poppy oil (it was then employed in the official process for a preliminary distillation); and the presence of a trace of alcohol in the receiver.

The "Chloroforme Officiel" of the present *Codex* (1908, p. 148) is prepared from rectified commercial chloroform by agitating with distilled water, decanting and filtering; shaking with sulphuric acid, then allowing to stand over sodium hydroxide; drying over calcium chloride, and finally distilling over poppy oil and adding alcohol (5/1000th part by weight of absolute ethyl alcohol).

See also, Maillard and Ranc, *Compt. rend. soc. biol.*, **61**, 483.

⁷ French Patent 215,911, 1891; U. S. Patent 489,592, 1893. See also, *J. Soc. Chem. Ind.*, **18**, 231. "On Some Peculiar Phenomena in the Solidification of Chloroform," see Pictet, *Compt. rend.*, **114**, 1245.

According to English Patent 15,514, 1891, the purification of chloroform is effected in a copper cylinder, surrounded by a jacket hermetically sealed at the top and bottom, and provided with an inlet and outlet pipe. A grating is fixed at the bottom of the cylinder on which any suitable filtering material can be placed, while a cock is attached below the grating for running off the contents of the cylinder. The object of the purification

On its introduction, it was announced that "Chloroform Pictet" had been experimentally proved to possess a capability of resisting the influence of sunlight for four days. Schacht and Biltz² therefore inferred that it contained alcohol, and their prediction that such was the case, without even having seen a sample, ultimately proved to be the case. Moreover, Schacht² found that "Chloroform Pictet" suffers the usual decomposition on washing to remove alcohol; and Biltz³ regarded the decomposition of chloroform under the influence of light and air as a natural characteristic of chloroform and not as a result of impurities.⁴ However, DuBois-Reymond⁵ stated that "Chloroform Pictet" is affected less by sunlight than any other chloroform with even the addition of alcohol.⁶

J. F. MacFarlane & Co.,⁷ separated the following relative quantities of "impurity" from "Chloroform Pictet" and a British product:

	Per cent.
From domestic product.....	0.0000512
From domestic product.....	0.0002050
From "Chloroform Pictet".....	0.0008200
From "Chloroform Pictet".....	0.0004100

Helbing and Passmore⁸ examined a large number of samples of chloroform which had been purified by Pictet's process, none of which, however, was anaesthetic chloroform—that is, all the samples were is to remove the various substances with which chloroform is invariably contaminated, from whatever source it is prepared, and is conducted in three stages: First, the chloroform in the cylinder is cooled down to -80° by allowing ethyl chloride, ethylene, "Pictet's liquid," etc., to evaporate in the jacketed space outside of the cylinder, and filtering the cold liquid mass; foreign bodies crystallizing above this temperature are thus removed, from which the liquid chloroform is filtered off through the above-mentioned grating. The second stage is to solidify the chloroform thus obtained by reducing the temperature of the cylinder to -82° , when about two-thirds of it freezes against the sides of the container; the remaining liquid is drained off and the solid chloroform is melted (according to Berthelot, chloroform melts at -70° ; Haase found the melting point to be -62° ; while Archibald and McIntosh reported -63.2°) and run out of the cylinder for the second time. The product thus obtained is finally subjected to distillation at a very low temperature under reduced pressure, the cylinder used in the previous stages of the purification now serving as the receiver; the first and last portions of the distillate are rejected, while the intermediate product, amounting to about 80 per cent. of the total, is obtained as "chemically pure chloroform."

¹ *J. Soc. Chem. Ind.*, **12**, 543. See also, *Western Drug.*, **1891**, 379.

² *Pharm. J.*, [3] **22**, 691.

³ *Ibid.*

⁴ See also, Biltz, *Ber. Pharm. Ges.*, **2**, 76, 247; Schacht, *Ibid.*, **2**, 69; Thilo, *Pharm. Ztg.*, **39**, 543.

⁵ *Pharm. Centralh.*, **32**, 658.

⁶ It will be shown under decomposition that the changes which occur in chloroform on exposure to air and light are accelerated by the presence of certain impurities. Had DuBois-Reymond made his comparisons of "Chloroform Pictet" with properly purified samples of anaesthetic chloroform, no such differences as he reported could have been observed.

⁷ *Brit. Med. J.*, **1892**, i, 525.

⁸ *Helbing's Pharm. Record*, March, 1892.

apparently alcohol-free. They found an average specific gravity of 1.5002 at $15^{\circ}/4^{\circ}$ in six specimens; a boiling point of $61.0-61.1^{\circ}$ at 756 mm.; and the usual tests with potassium dichromate and sulphuric acid, silver nitrate, and zinc iodide and starch gave negative results. The fractions obtained by distillation were examined and the specific gravity of each determined; in no case was any variation found beyond the limits of experimental error and the temperature rose in no case above 61.1° . In only one case did the residue amount to 0.00005 per cent., or 1 part in 2,000,000, and even then no bad odor was apparent.

The "Chloroform Pictet" examined by the authors possessed a density of 1.491 at $15^{\circ}/15^{\circ}$, and all the tests for the presence of allowable impurities and decomposition products gave negative results. Four other German products and one American anaesthetic chloroform, all of which were purified by chemical treatment, were found to be fully as pure, however, which supports the contention of the authors that purification by cryogenic means is not necessary to secure chloroform of anaesthetic grade.

DuBois-Reymond¹ has studied the physiological action of "Chloroform Pictet" and of the residue of foreign substances obtained in the process of Pictet. He found that the shape of the pulse waves and the frequency of respiration are about equally affected by both substances, the rate of respiration varying freely; that the pulse rate, compared in nineteen cases, is higher at the close of the experiments with the residue than with those with the purified chloroform; that the blood pressure in by far the greater number of experiments at the moment respiration ceases is higher after inhalation of the purified chloroform than after the inhalation of the impure residue; and, finally, that the residue causes stoppage of respiration much more quickly than does purified chloroform. DuBois-Reymond hardly conducted a sufficient number of physiological experiments to enable one to form a definite opinion of the physiological action of the commonly occurring impurities of commercial chloroform which are separated by means of the process of Pictet. In addition, the variable nature of these impurities, owing to the various processes of manufacture and the variability of the crude materials used therein, renders such an investigation of little value unless these facts were considered. This does not appear to have been the case.

(To be continued.)

¹ *Brit. Med. J.*, **1892**, i, 209.

LABORATORY AND PLANT

A MODIFIED WILEY EXTRACTION APPARATUS.

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Received November 13, 1911.

Of the making of extraction apparatus there is no end. In almost every laboratory special devices are in use, which have their advantages and dis-

advantages and their special applications, and each year witnesses the production of new forms or combinations. Of all forms of extraction apparatus, the Wiley apparatus¹ is probably the simplest and

¹ *J. Anal. Appl. Chem.*, **7**, 65; *J. Am. Chem. Soc.*, **1893**; Wiley, "Principles and Practice of Agricultural Analysis," Vol. III, pp. 48-52.