Educación Química

Refexión

Charles-Joseph Tanret: natural principles

Charles-Joseph Tanret: principios naturales

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Resumen

Charles Tanret (1847-1917) fue un químico y farmacéutico francés que dedicó la mayor parte de su vida al aislamiento de nuevos alcaloides y la química de los azúcares. A su mérito le debemos la preparación de digital cristalina, el aislamiento de ergotinina, cornutina y ergosterol del cornezuelo de centeno, vincetoxina de la raíz de ***Asclepias***, isohesperidina, hesperidina, etc. de la cáscara de naranja amarga, quebrachitol de la corteza de quebracho blanco, levosina de centeno maduro, trigo y cebada, el glucósido piceína de las hojas de abeto y su derivado piceol, la síntesis de levoglucosano a partir de piceol, y la síntesis de alcaloides artificiales por la reacción entre el amoniaco y la glucosa.

Palabras clave: cornutina; ergosterol; ergotinina; isohesperidina; levoglucosano; levosina; piceína; quebrachitol.

Abstract

Charles Tanret (1847-1917) was a French chemist and pharmacist who devoted most of his life to the isolation of new alkaloids and the chemistry of sugars. To his credit we owe the preparation of crystalline digitalis, the isolation of ergotinin, cornutin, and ergosterol from rye ergot, vincetoxin from the root of ***Asclepias***, isohesperidin, hesperidin, etc. from the peel of bitter orange, quebrachitol from the bark of white quebracho, levosine from ripe rye, wheat, and barley, the glucoside picein from the leaves of spruce fir, and its derivative piceol, the synthesis of levoglucosan from piceol, and the synthesis of artificial alkaloids by the reaction between ammonia and glucose.

Keywords: cornutin; ergosterol; ergotinin; isohesperidin; levoglucosan; levosine; picein; quebrachitol.

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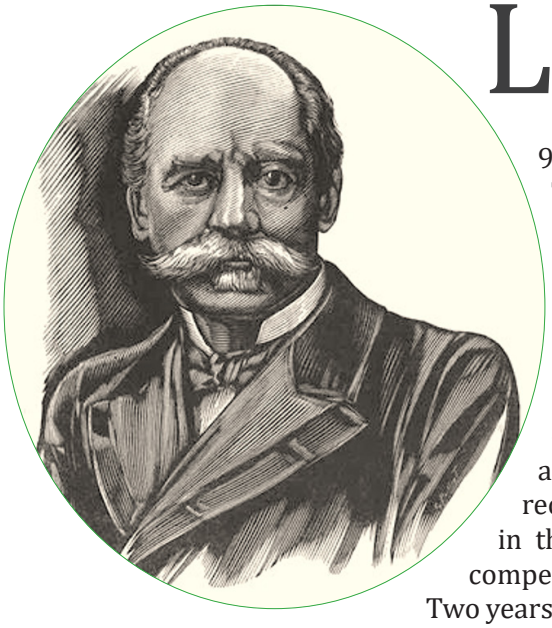

FIGURE 1: Charles Tanret (1847-1917).

Life and career (Anonymous, 2022; Lestel, 2021; Delvincourt, 1968, 1980; Kraemer, 1919; André, 1918; Delépine, 1918).

Charles Joseph Tanret (Figure 1) was born on August 9, 1847, in Joinville (Haute-Marne, France) the son of Thomas Charles Tanret, a modest hosier and winemaker, and Françoise Armance Larché. He took his basic education at the Petit Séminaire of Langres and after graduation and receiving his diploma of baccalaureate ès-lettres, he returned to Joinville and began a three-year apprenticeship in a local pharmacy. This was a program of practical studies leading to the degree of pharmacist of second class, the lowest level in the profession, and a prerequisite to start formal academic studies. After receiving his internship validation certificate, he enrolled in the École Supérieure de Pharmacy and in 1868 won by competition a position of intern in the public hospitals of Paris. Two years later, he resigned this position to enroll in the army during the Franco-Prussian war. In 1871, after the end of the war, he won again an intern competition and restarted his academic studies. During this period, he attended the chemistry courses given by Antoine-Jerôme Balard (1802-1876) and Marcellin Berthelot (1827-1907) at the College de France. In 1872, he received his degree of Pharmacien de 1er classe, after successfully defending a thesis devoted to the study of albumen (Tanret, 1872). Afterward, he returned to work with Berthelot, for two years. He then opened his own business in Troyes, where he also began to research alkaloids. Seven years later, he returned to Paris and opened a laboratory to produce alkaloids. In 1880, he stopped all commercial activities to devote himself fulltime to research. During the First World War, he devoted much of his efforts to develop an anti-chlorine mask to protect the French soldiers menaced by poisonous gases.

In 1874, Tanret married Marie Decluy; two children (Lucie and Georges Charlemagne) were born of this union.

Tanret passed away in Paris, on July 27, 1917, victim of an acute pulmonary edema.

Tanret participated actively in professional and public activities and was rewarded accordingly. He was a member of the Société de Pharmacie, of the Société de Thérapeutique, of the Société de Chimique de Paris and its President in 1897, and an honorary member of the Philadelphia College of Pharmacy. In 1889, he was appointed Chevalier of the Légion d'Honneur. The Académie des sciences awarded him the 1879 Barbier Prize for his discovery of ergotinin and pelletierin (Tanret, 1875b, 1878, 1880), and the 1895 Jecker prize for his work about the isolation and characterization of several new alkaloids. He received the first prize of the section Chemical and Pharmacy Arts of the 1889 Universal Exposition.

Scientific contribution

Tanret wrote about 100 papers and books (i.e., Tanret, 1880) about his research activities in organic, inorganic, and analytical chemistry, plant principles, sugars, alkaloids, etc. As customary for candidates to a scientific academy, he prepared a booklet describing his

research activities and achievements (Tanret, 1895-1899). In addition to the few subjects presented below, Tanret studied the poisonous effects of little hemlock (Æthusia cynapium) (Tanret, 1882); determined the composition of terpinol (Tanret, 1885e), studied the chemistry of the nitrogen derivatives of turpentine (Tanret, 1887ab, 1888) and the salts of caffeine (Tanret, 1891a); isolated the alkaloid pelletierin from the bark of pomegranate (Tanret, 1878); determined the composition and properties of the inulin of *Atractylis* (Tanret, 1893a); compared the composition and the analytical capability of the different reagents known under the names potassium iodomercurate and iodized potassium iodide (Tanret, 1893b); made a detailed study of the different inulins, their preparation and properties (Tanret, 1893cd); separated the carbohydrates present in the Jerusalem artichoke (Tanret, 1893e); studied the molecular modifications of glucose and other sugars, (Tanret, 1895a, 1896a), filtrates, stirred with chloroform studied the composition and properties of different fungi (Tanret, 1896b, 1897ab); etc.

Crystalline digitalis

Tanret wrote that the information available about digitalis, a drug obtained from the dry leaves of common foxglove (*Digitalis purpurea*), was incomplete and contradictory (Tanret, 1875a). No clear information was available of the chemical state of the drug in the plant, although it was generally believed that it was present in the form of a tannate. This had led to an extraction process based on exhaustion of the powdered leaves with water or alcohol, followed by treatment of the filtered extract with lead acetate to separate the digitalis from the tannin. This supposition did not seem logical because the active compound could be removed directly by alcohol and chloroform and then become precipitable by tannin. In fact, the above information suggested that digitalis was present in foxglove in a state of freedom, or combined with a body different from tannin, acting like an acid, and yielding a compound soluble in alcohol and chloroform (Tanret, 1875a).

Based on these assumptions, Tanret developed an alternative extraction technique process based on the solubility of digitalis tannate in alcohol, its insolubility in chloroform, and its easy decomposition in alcoholic solution by zinc oxide or yellow mercuric (II) oxide. In this method, the foxglove leaves, coarsely pulverized, were leached repeatedly with alcohol of 25% by volume, and the collected alcoholic filtrates stirred with chloroform and left to stand. The separated chloroform phase was colored deep brownish green and contained digitalis, digitaline (digitoxin), chlorophyl, and plant fats. It was washed with water to eliminate the residual alcohol and then mixed with a concentrated solution of tannin. The precipitated digitalis tannate was separated and purified by extraction with alcohol, mercury (II), yellow oxide (or zinc oxide), and animal carbon. The pure material was separated by evaporation. A microscopic examination showed that the crystalline material was composed of needles radiating from the center. According to Tanret, his procedure was very fast and gave a high yield (Tanret, 1881a).

Ergotinin

In 1875, Tanret reported to the Académie des sciences that he had isolated from rye ergot a new, solid, and non-volatile alkaloid, which he proposed naming *ergotinin*, to avoid confusion with several ill-defined substances that carried the name *ergotin*. Ergotinin was present in rye ergot in very small quantities and was very labile in air, making its extraction difficult and delicate. (Tanret, 1875b).

To separate the alkaloid, Tanret ground the rye ergot to a coarse powder and extracted it twice with boiling alcohol of 86°, until he obtained two parts of filtrate per part of the rye ergot. The filtrate was concentrated by boiling and then left to cool. This resulted in the separation of a solid resin, an extraction liquid, and a floating layer of fatty liquor. The pertinent phases were washed with ether exempt from alcohol. The fatty matter was dissolved in ether and the filtrate treated several times with sulfuric acid of 20% wt. to retain the ergotin as sulfate. The filtered aqueous solution of the alkaloid sulfate was washed with ether to remove the remaining fat, the sulfate split with concentrated KOH, the ergotinin recovered with ether, and the ethereal solution left to evaporate in the absence of air. The extraction liquid was distilled in a stream of air and the passing aqueous stream found to contain methylamine and a very odorous substance. Most to the ergotinin remained in the final syrupy residue of the distillation process. As before, this residue wastreated with sulfuric acid, neutralized with KOH, and the ergotinin recovered with ether. Tanret remarked that distillation of the extractive liquor with concentrated NaOH or KOH produced almost no ergotinin but a very large amount of ethylamine (Tanret, 1875b).

Tanret described ergotinin as a solid having a strong alkaline reaction, capable of neutralizing acids and precipitating the double iodide of mercury and of potassium, potassium iodide, phosphomolybdic acid, tannin, gold chloride, platinum chloride, and brominated water. It was soluble in alcohol, chloroform, and ether, and extremely labile in contact with air. Treated with sulfuric acid of medium concentration, it produced a yellow-colored solution, which then turned intense blue violet (Tanret, 1875b).

In 1884, the toxicologist Rudolph Kobert (1854-1918) reported that he had extracted from rye ergot three new principles, which he called ergotinic acid, sphacelinic acid and cornutin. He made no claim regarding the chemical purity of his new materials, indicating that he was only interested in their physiological properties (Kobert, 1884). This publication brought a strong reply from Tanret, regarding the results reported for the compounds cornutin and ergotinin (Tanret, 1885a).

According to Tanret, Kobert claimed that cornutin was different from ergotinin and that its separation was based upon of its easy solubility in alcohol and the property that it had of being removed from its alkaline solutions by stirring with ethyl acetate. The very low yield in cornutin did not allow determining its chemical composition. Kobert's process delivered very similar amounts of ergotinin and cornutin, sometimes more cornutin, sometimes. More ergotinin. The only noticeable differences were that cornutin was more soluble than ergotinin, and that it was extremely toxic while ergotinin was not. According to Kobert, cornutin was not the principle on which the ergot acted on the uterus. "If in some animals it produced clonic and toxic convulsions as well as movements of the viscera and uterus, these movements were different from the tetanic contractions (tetanus uteri) caused by ergot and unable to help. To the expulsion of the fetus" (Kobert, 1844). Tanret added that Kobert believed that ergotinin had no effect on the uterus, although some physicians had reported a positive effect. This was probably due to the possible presence of small impurities of cornutin (Tanret, 1885a).

Tanret had the following objections to Kobert's conclusions; (1) The preparation of cornutin required exposing an acid solution of ergotinin to air, for a long or short time. It was a known fact that ergotinin was labile to the action of air; it became colored and eventually showed little of the reactions that Kolbert attributed to cornutin. To Tanret, this meant was

simply more or less profoundly altered ergotinin; (2) cornutin had only been tested on animals, while ergotinin had been in medical practice for several years. The medical results indicated that ergotinin lowered the body temperature, it decreased its pulse rate and caused the vessels to contract by acting on the muscle fiber. Some possible side effects were, nausea, colic, and vomiting, particularly at the beginning of its use. In parturient women it induced, sometimes, vomiting, and toxic accidents at a dose of one milligram. Tanret's own experience indicated that 0.25 mg of ergotinin, corresponding to 0.25 g of ergot, were sufficient to control port-partum hemorrhages. In other words, medical evident proved that ergotinin was not an inert physiological principle (Tanret, 1885a).

The above information was repeated in another publication, which included details of the ergotinic acid (ergotinsaüre), sphacelinic acid (sphacelinsaüre), and cornutin, prepared by Kobert, as well as more physiological evidence about the effects of ergotinin (Tanret, 1885b).

Ergosterol

In 1899 Tanret reported that he had discovered in the rye ergot a crystalline substance, having properties very similar to animal cholesterol or its plants isomers, but very different composition. He suggested naming his new compound *ergosterin* (today: *ergosterol*) to recall this relationship (Tanret, 1889a).

The separation process of ergosterin consisted in extracting rye ergot repeatedly with alcohol, followed by distillation of most of the alcohol, extraction of the residue with ether, and distillation of the ethereal extract to eliminate the solvent. The residual oily mass was filled with crystals, which were filtered off with a pump and fog paper and purified by several crystallizations, first in alkaline alcohol to saponify the accompanying oil, and then in pure alcohol. The yield was about 0.2 per 1000 (Tanret, 1889a).

Ergosterin crystallized from alcohol in pearly flakes and from ether in fine needles. It melted at 154 °C and boiled at 185 °C/20 mmHg. Its relative density was 1.040 and was levorotarory with rotatory power $[\alpha]_D = -114^0$ (1 g in 30 cm^3 of 5% solution chloroform). It was completely insoluble in water, little soluble in cold or hot chloroform, and partially soluble in cold alcohol and ether, and much more in the boiling solvents. Elemental analysis indicated that it contained, by weight, 84.85% carbon, 11.15% hydrogen, and 4.00% oxygen, corresponding to the formula $C_{52}H_{40}O_2$,H_2O_2. The water of hydration was eliminated by drying at 110 °C, or (preferable) under vacuum (Tanret, 1889a).

According to Tanret, ergosterin oxidized slowly in air, turning colored and odorous. Around 100 °C, this alteration was very rapid. Tanret described the composition, formula, and properties (relative density, rotatory power, etc.) of the formic, acetic, and butyric esters. All three were crystallizable. The chemical analysis indicated that like cholesterol, ergosterin was a monoatomic alcohol. Ergosterin was not attacked by a concentrated and boiling alkaline solution. With nitric acid, HCl, and ferric chloride it gave the color reactions of cholesterol, but with sulfuric and chloroform the result was totally different: the ergosterin dissolved completely and the chloroform became slightly colored violet. With cholesterol, the chloroform was initially orange-yellow, and then red and violet. This reaction served to differentiate between ergosterin and cholesterin (Tanret, 1889a).

Vincetoxin

The aqueous solution of the hydro-alcoholic extract of the root of *Asclepias* (vincetoxicum, white swallowwort) had the curious property of turning cloudy by heat, and clear again on cooling. In 1885 Tanret discovered that this property was due to the presence of a new glucoside that he proposed naming *vincetoxin*. Vincetoxin existed in two varieties, one insoluble in water, the other soluble (Tanret, 1885c).

Tanret separated the glucoside by mixing a coarse powder of Asclepias with limewater and leaching the mixture with water. The filtrate was treated with sodium chloride and the precipitate separated, washed with salt water, and then extracted with chloroform. The extract was mixed with animal black, distilled to eliminate the solvent, and the residue treated successively with alcohol, ether, and water. Evaporation of the lower aqueous phase yielded the water-soluble vincetoxin. The upper ethereal layer was treated with alkaline water to remove an acid resin, and then with diluted sulfuric acid. The liquor was then neutralized and distilled to dryness. This constituted the vincetoxin insoluble in water. Tanret believed that both varieties had the same composition, and rotary power, $[\alpha]_D$ = - 50°, and main chemical reactions, but different molecular structure. His results showed that vincetoxin did not contain nitrogen; elemental analysis indicated that the soluble and insoluble varieties contained, by weight, 61.04% carbon and 7.79% hydrogen, and 61.61% carbon and 8.50% hydrogen, respectively, corresponding to the formula $C_{16}H_{12}O$, and showing it was a glucoside (Tanret, 1885c).

Soluble vincetoxin appeared as a slightly yellowish non-crystallizable powder, slightly sweet and bitter, and very soluble in water, alcohol, and chloroform, but insoluble in ether. Its aqueous solutions become cloudy with heat and turned clear again on cooling. Insoluble vincetoxin was non-crystallizable, insoluble in water, and very soluble in alcohol, ether, and chloroform. The pertinent solution became milky at a temperature lower than that of soluble vincetoxin alone. Vincetoxin was precipitated by many salts, especially sodium chloride. Although it was not an alkaloid, it precipitated in the presence of iodated potassium iodide and a mineral acid (Tanret, 1885c).

Bitter orange peel immediate principles

In 1886 Tanret reported that he had separated five immediate principles from the peel of bitter orange (Tanret, 1886). For this purpose, he macerated the peel with alcohol of 60° and distilled the extract to eliminate the solvent. Treatment of the residue with chloroform produced two liquid phases. The chloroform phase was distilled to dryness and the residue extracted with cold alcohol, leaving a crystalline powder (a). The alcoholic extract was evaporated with tannin and the tannate formed, separated, decomposed with limewater, and distilled in the presence of animal carbon, leaving a resinous product (b). The chloroform phase, left alone, resulted in the precipitation of a yellowish crystalline mass, (c), which was separated. The remaining liquor was treated with lead acetate, followed by sulfuric acid, and sodium sulfate. The resulting floating sticky layer was dried and separated with absolute alcohol into an extract (d) and a residue (e) (Tanret, 1886).

Tanret analyzed these five substances, with the following results: (a) was a weak, white, and tasteless acid, non-volatile, insoluble in water and ether, sparingly soluble in cold alcohol, and more in boiling alcohol and chloroform. This acid reacted with alkalis forming

soluble non-crystallizable salts decomposable by CO_2. Elemental analysis indicated that it contained, by weight, 64.84% carbon, 7.51% hydrogen, and 27.65% oxygen, corresponding to the formula $C_{44}H_{28}O_{14}$. The overall yield, per weight, was about 0.50 per 1000. Substance (b) was non-crystallizable, extremely bitter, softening about 12 °C, and rotatory power $[\alpha]_D$ = -28°. It was sparingly soluble in water, very soluble in boiling water, and soluble in ether, alcohol, and chloroform. Heated with acids, it did not give glucose. Elemental analysis indicated that it contained, by weight, 61.14% carbon, 6.57% hydrogen, and 32.29 oxygen. Tanret believed that this component was related to hesperic acid, $C_{22}H_{28}O_7$, having 61.85% carbon and 6.57% hydrogen. The over yield was, by weight, about 1 in 1000 (Tanret, 1886).

Component (c) was a glucoside having the same elemental composition as hesperidin, $C_{44}H_{26}O_{24}$ (today: $C_{28}H_{34}O_{15}$), which Tanret named *isohespiridin*. Isohespiridin appeared as microscopic needles, bitter, rotatory power $[\alpha]_D$ = -89°, and soluble in boiling water, alcohol, and ethyl acetate. The overall yield, by weight, was from 4 to 30 per 1000. Component (d) was identified as aurantiamarina, the glucoside which gave all its bitterness to bitter orange peel. It was very soluble in water and alcohol and insoluble in ether and chloroform, and had rotatory power $[\alpha]_D$ = -60°. Elemental analysis indicated that it contained, by weight, 53.04 - 53.48% carbon and 6.36 - 6.16% hydrogen. The overall yield was, by weight, 15 to 95 per 1000. The insoluble white powder (e), crystallizing as white silky needles, was identified has hesperidin. The overall yield was, by weight, from 0 to 6 per 1000 (Tanret, 1886).

Sugars from quebracho (*Aspidosperma quebracho*)

In 1889 Tanret reported the isolation of two new sugars from the bark of white quebracho (Tanret, 1889b). This result was achieved by extracting with alcohol of 50° a mixture of pulverized quebracho bark and limewater. The filtrate was concentrated, neutralized with acetic acid, followed by treatment with lead subacetate and precipitation of the sugar with ammoniacal lead acetate. The lead precipitate was washed, decomposed with diluted sulfuric acid, and concentrated to a syrupy material. The sugar solute was separated, redissolved in water, decolorized with charcoal, and then evaporated to dryness. The overall yield was about 1 g per kg of bark. Tanret named his new sugar *quebrachite* (today*: quebrachitol*) to indicate its origin. Elemental analysis indicated that the composition of quebrachite corresponded to the formula $C_{14}H_{14}O_{12}$. This assumption was confirmed by the products of its decomposition with hot hydriodic acid:

$$C_{14}H_{14}O_{12} + HI = C_{12}H_{12}O_{12} + C_2H_3I$$

(Tanret is using the old value of the atomic mass of carbon), which indicated that quebrachite was the monomethyl ether of a particular inosite. (Tanret, 1889b).

Tanret reported that quebrachite was a crystalline solid, appearing as anhydrous rhomboidal prisms with a very sweet flavor, having relative density 1.54/0 °C, rotatory power at $[\alpha]_D$ = -80°, melting at 186°-187 °C, and boiling around 210 °C while sublimating into needles. It fermented only with brewer's yeast, did not react with Fehling's liquor and basic lead acetate, and was not attacked by alkaline solutions and diluted boiling acids. It reacted with sulfuric acid at 100 °C, forming; quebrachisulfuric acid, a levorotatory compound.

The inosite produced by hydrogen iodide appeared as very shiny prismatic needles, with rotatory power $[\alpha]_D$ = -55°, melting point 238 °C, boiling in vacuum around 250 °C and sublimating. It effloresced in air and was soluble in water, partially soluble in cold and boiling alcohol, and insoluble in ether (Tanret, 1889b).

Levosine

Tanret wrote that during experiments carried out with the purpose of understanding the ripening of barley, wheat, and rye, he had succeeded in isolating a well-defined carbohydrate, which the chemical analysis usually included under the generic name of dextrins. This new substance was levorotary and for this reason he proposed naming it *levosine* (Tanret, 1891b).

Levosine was separated be exhausting ground rye with alcohol of 50º and treating the filtrate with alcohol of 94º, which deposited a large quantity of gum. After decantation, the mixture was distilled, and the residue precipitated with barite and limewater. The solid was separated by filtration and decomposed with CO_2. Evaporation of the filtrate left levosin contaminated with 0.50 to 1% of calcium. To purify it, it was redissolved in alcohol of 60°, mixed with diluted sulfuric acid, and reprecipitated again with alcohol of 95°. Elemental analysis of levosine dried at 110 ºC, showed that his global formula was $C_{48}H_{40}O_{40}$ or $(C_{12}H_{10}O_{10})_4$, that is, the same as starch and dextrin, Raoult's method, showed that the molecular mass was 652 for the first formula, and 648 for the second. Exposure of the anhydrous material to the atmospheric air formed the monohydrate $(C_{12}H_{10}O_{10},H_2O_2)_4$ (Tanret, 1891b).

Tanret described levosin as a white, amorphous, and almost tasteless body, of relative density 1.62, melting point 160 °C, and rotatory power $[\alpha]_D$ = -36°. It was very soluble in water and very diluted alcohol, and almost insoluble in alcohol of 95%. It did not reduce Fehling's liquor, did not ferment with brewer's yeast or diastase, and was not attacked by alkaline solutions. Tanret described the synthesis and properties of the barium, and calcium salts, and the product of the reaction with ammoniacal lead acetate. Levosine was a polyatomic alcohol, forming triacetic and tetraacetic esters and di and trinitrates. It did not stain with iodine and was oxidized by nitric acid into oxalic acid (Tanret, 1891b).

Alkaloids from ammonia and glucose

Tanret remarked that his long experience with the action of ammonia on essential oils had indicated the clear formation of alkaloids (Tanret, 1885d). He thought of interest to investigate whether other bodies with alcoholic functions would also produce the same reaction. The fact that glucose gave remarkable results, led him to study the action of ammonia on sugar and to find if not only ammonia but also other of its compounds, such as ethylamine, methylamine, etc., also produced alkaloids. He speculated that this way of producing artificial alkaloids would someday throw light on the synthesis of these compounds in plants, as well as in putrefaction. In his first publication, he restricted himself to describe the synthesis of two of the alkaloids obtained by the action of ammonia on glucose (Tanret, 1885d).

Basically, the experimental procedure consisted in heating a mixture of 60 parts of glucose and 100 parts of pure ammonia in a sealed tube, for thirty to forty hours at 100 °C. The resulting blackish syrup was found to contain, among others, free ammonia, ammonium carbonate, formic acid, and alkaloids. The latter were extracted with enough chloroform, acidified with 1/10 sulfuric acid to obtain an acid aqueous liquid. This resulted in a mixture of sulfates, ammonia, and very basic alkaloids, which could be freed with sodium carbonate and purified by additional extraction with chloroform or ether and distillation of the solvent.

In this manner, Tanret was able to separate two new alkaloids, which he named *glucosines,* one boiling at 136 °C (α-glucosine) the other, at 160 °C (β-glucosine) (Tanret, 1885d).

Glucosines were described as very volatile liquids, colorless, very refractive, with a sharp odor, and without optical activity. α-Glucosine had relative density 1.038 at 0 °C. Elemental analysis indicated that it contained, by weight, 66.60% carbon, 7,40% hydrogen, and 26% nitrogen, corresponding to the formula $C_{12}H_8N_2$. β-glucosine had relative density 1.012 at 0 °C, and contained, by weight, 69.27% carbon, 7.39% hydrogen, and 22.70 nitrogen (total: 99.36%), corresponding to the formula $C_{14}H_{10}N_{2.}$ (Tanret, 1885d).

Tanret found that both glucosines had the same chemical properties. As typical alkaloids, their acid solutions precipitated the double iodide of mercury and potassium, tannin, brominated water, etc. They were slightly alkaline and were removed by chloroform from their acidic solutions. He studied the action of various chemicals on the glucosines, among them, metal salts such as cupric and iron sulfates, and ferric chloride, mercury (II) chloride, potassium ferricyanide, gold chloride, platinum chloride, HCl, hydrogen iodide, nitrous and nitric acids, etc. For example, glucosines turned blue a solution of cupric sulfate, yellow one of ferric sulfate, and brown one of ferric chloride, and reduced potassium ferricyanide. They produced a yellow precipitate with gold chloride and a mixture of colored salts with platinum chloride acidulated with HCl. With dry gaseous HCl they gave the crystallized hydrochlorides $C_{12}H_8N_2$,HCl and $C_{14}H_{10}N_2$,HCl. Glucosines were not attacked by nitrous acid, chromic acid, and mercuric oxide. They were attacked vigorously by nitric acid, with release of nitrous vapors, CO_2, and hydrocyanic acid, leaving a residue of oxalic acid. Additional testing indicated that they were not amides (Tanret, 1885d).

Picein

In 1894, Tanret announced the discovery of a new glucoside, *picein*, in the leaves of the spruce fir *Pinus picea* (Tanret, 1894a). This substance was obtained by macerating finely chopped fir twigs with a boiling dilute solution sodium bicarbonate The filtrate was precipitated successively by basic lead acetate and ammoniacal lead acetate, followed by decomposition by acid sulfuric, filtration and neutralization with magnesium oxide, and filtration and evaporation to a clear syrup. This syrup was mixed with magnesium sulfate and then exhausted with ethyl acetate. The filtrate was mixed with sodium bicarbonate, distilled, and the residue extracted with boiling alcohol. On cooling, the solution precipitated crystalline picein monohydrate at the rate of 0.50 to 3 g per kg of twigs, depending on the season the twigs were collected. Elemental analysis of picein dried at 100 °C indicated that it contained, by weight, 56.32 to 56.38% carbon and 6.20 to 6.20% hydrogen, corresponding to the formula $C_{14}H_{18}O_7$,H_2O. Picein was anhydrous when it settled from its solution in absolute alcohol (Tanret, 1894a).

According to Tanret, picein crystallized in silky prismatic needles, bitter, and sparingly soluble in cold water and much more in boiling water. It was very soluble in cold alcohol and ethyl acetate, and insoluble in ether and chloroform. It was levorotatory with $[\alpha]_D$ = -84° and $[\alpha]_D$ = -78^0 dissolved in 70° alcohol The anhydrous picein melted at 194 °C and was hydrolyzed by emulsin into glucose and piceol (70.80% carbon and 6.15% hydrogen) according to the equation (Tanret, 1894a):

$$\underset{\text{Picein}}{C_{14}H_{18}O_7} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Piceol}}{C_8H_8O_2}$$

Picein was not precipitated by tannin or by lead sub-acetate. Heated with acetic anhydride in the presence of solid zinc chloride, it gave the tetraacetic ether $(C_{14}H_{10}O_3)(C_2H_4O_2)_4$, which crystallized and melted at 170 °C. This result indicated that picein was simultaneously ether and alcohol (Tanret, 1894a).

Tanret reported that piceol melted at 109 °C, and that it was soluble in cold water and much more in boiling water, and in solutions of alkaline carbonates, without displacing CO_2. It combined with alkalis forming crystalline salts, and with acetic and benzoic acids. These results indicated that piceol behaved like a phenol (Tanret, 1894a).

Levoglucosan

As shown above, acids and emulsin, split picein into piceol and water. Tanret found that the effect of baryta water at 100 °C was completely different: it transformed picein into a glucose anhydride or glucosan. This result also took place with other glucosides like salicin and coniferin. The new glucosan differed in its physical properties, in particular the sense of its rotatory power, from the dextrorotatory glucosan, which was formed when the glucose was kept for some time at 170 °C. For this reason, Tanret decided to name it *levoglucosan* (Tanret, 1894b).

Basically, levoglucosan was prepared by heating the glucoside mixed with twenty times its weight of barite water, in a sealed flask for four hours at 100 °C. The barite was then precipitated with CO_2 and the filtrate extracted with ether to eliminate the residual piceol. The aqueous filtrate was concentrated by evaporation and then extracted with boiling acetic acetate. The solvent was eliminated by distillation, leaving as residue impure crystalline levoglucosan, which was purified by recrystallizing from water. The yield of the process was close to the theoretical one. Elemental analysis indicated that levoglucosan contained, by weight, 44.63% carbon and 6.35% hydrogen, corresponding to the formula $C_6H_{10}05$. Raoult's method indicated the molecular mass was Determination of the molecular mass 166.8, These values were approximately those of a glucose anhydride. (Tanret, 1894b).

According to Tanret, levoglucosan was a crystalline sweet substance, melting at 178 °C and sublimating without decomposition, specific gravity 1.59; levorotatory with rotary power $[\alpha]_D$ = -66.5° in aqueous solution at 10% and below, $[\alpha]_D$ = -81.5 ° in solution at 50%, $[\alpha]_D$ = -70.5° with absolute alcohol, and $[\alpha]_D$ = -77.5°, with acetic acetate. These values changed little with temperature. It was very soluble in water, alcohol, and ethyl acetate, and slightly soluble in ether. Heated with acids it formed ordinary, dextrorotatory, fermentable, and reducing glucose. However, levoglucosan itself, was not fermentable with brewer's yeast or emulsin and did not reduce Fehling's liquor (Tanret, 1894b).

Tanret prepared the benzoic and acetic esters of levoglucosan. Levoglucosan benzoate, $C_6(H_2O)_2(C_7H_6O_2)_3$ was a white powder, little soluble in water, alcohol, and ether. Levoglucosan acetate, $C_6(H_2O)_2(C_2H_4O_2)_{3,}$ crystallized in fusible needles melting at 107°-108 °C; and rotatory power $[\alpha]_D$ = -45.5° in alcoholic solution (Tanret, 1894b).

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