Reflexiones

Luigi chiozza. The chemistry of organic acids

Luigi Chiozza. La química de los ácidos orgánicos.

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Resumen

Luigi Chiozza (1828-1889) fue un químico italiano que llevó a cabo un estudio detallado de la preparación, propiedades y reacciones de los ácidos orgánicos. Durante el estudio de la reacción del sulfuro de ammonio y el ácido cinámico, descubrió el compuesto nuevo carbostyril (2-hydroxiquinoline). También sintetizó el ácido monoclorobenzoico (ácido *o*-clorobenzoico), preparado tratando con agua el producto de la cloración del ácido salicílico por el pentacloruro de fósforo. Solo, o con Gerhardt, desarrolló procesos eficientes para la síntesis de anhídridos simples of mixtos, de ácidos, así como numerosas amidas primarias, secundarias y ternarias. Su trabajo más importante fue síntesis de la vainilla (aldehído cinámico).

Palabras clave

Amidas; anhídridos; canela; vainilla

Abstract

Luigi Chiozza (1828-1889) was an Italian chemist who made a detailed study of the preparation, properties, and reactions of organic acids. While studying the reaction of ammonium sulfide with nitrocinnamic acid, he discovered the new compound, carbostyril (2-hydroxyquinoline). He also synthesized monochlorobenzoic acid (*o*-chlorobenzoic acid) by treating the chlorination product of salicylic acid with phosphorus pentachloride with water. Alone, or with Gerhardt, he developed efficient processes for the preparation of simple and mixed acid anhydrides, as well as numerous new primaries, secondary, and ternary amides. His most important work was the artificial production of the essence of cinnamon (i.e., cinnamic aldehyde).

Keywords

Amides, anhydrides cinnamon; vanilla

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Life and career (Guareschi, 1908; Morpurgo, 1929; Gaudiano, 1981)

Luigi Chiozza (Figure 1) was born in Trieste on December 20, 1828, the son of Teresa Kircher Valloghino (1798-1859) and Giuseppe Chiozza (1789-1833), who managed a soap factory founded by his father Carlo Luigi (1754-1831) in Trieste. Luigi took his basic education at the Instituto Mathés in Geneva, where he was charmed by his chemistry teacher Jean-Charles Galissard de Marignac (1817-1894), a professor at the Geneva University and famous for his determination of the atomic mass of many elements and the discovery of gadolinium and ytterbium. In 1845, after his graduation, he enrolled in the school of practical-industrial chemistry of the Società d'Incoraggiamento d'Arti e Mestieri in Milan, then directed by Antonio Giovanni Kramer (1806-1853), a former student of August Laurent (1807-1853). After a couple of years, he moved to Paris to continue his study of chemistry at the Collège de France, under the guidance of Charles Frédéric Gerhardt (1816-1856), until 1849 when he returned to the Milan school. The following year, his uncle Giorgio Antonio Chiozza left him heir to his factory Ditta L. Chiozza & Figlio on condition that he abandon his studies and take over the direction of the factory. Chiozza gave up this substantial inheritance and after a study trip to Austria, Germany, and England, returned to Gerhardt, to participate actively in his research on organic synthesis, for almost three years. He then returned to Milan as assistant to Kramer, to whom he succeeded (1854) in the direction of the school and in the chair of chemistry.

In 1857 Chiozza married Pisana di Pomperò, who died a year later, after giving birth to their daughter Teresa. This painful event led Chiozza to leave his position at the school, which was then led by Agostino Frapolli, and retire to Scodovacca, Friuli. In 1862 he married Teresa de Stabile; three children were born of his union, Giuseppe, Angela, and Antonio. There, after a few years, he mounted his own private laboratory and reinitiated his research activities directed towards improving the agricultural production and natural resources of the region. His most important achievement was the establishment in Cervignano of a wheat starch factory obtained with a particular processing method, which was then enlarged and transformed into a rice starch factory. In 1876 he was granted a patent for a process the separation of maize sprouts for the manufacture of white flours and other derivatives (Chiozza, 1881). This work earned him an award at the Philadelphia exhibition of 1876. In 1880, Chiozza presented a project (*Progetto per la Creazione di una Febbrica di Soda all'Ammoniaca*) to the presidency of the Pazin Salt Pans Consortium to exploit the marine salt industrially in a soda factory using the ammonia method. Chiozza also played an important role in the establishment of the Pontebbana railway.

Luigi Chiozza passed away died in Scodovacca (Udine) on May 21, 1889, after suffering from cardiac and renal disease; he was buried in the local cemetery (Guareschi, 1908; Morpurgo, 1929; Gaudiano, 1981).

Scientific activities

Most of the scientific work of Chiozza, alone or with Charles Gerhardt, his mentor, was about the preparation, properties, and reactions of organic acids. Here we present the main features of this activity.

Cinnamic acid

In 1847, Émile Kopp (1817-1875) reported the composition of the balsam of Tolu and that it contained a free acid and a resin little soluble in alcohol. Further analysis indicated that the free acid was cinnamic acid (Kopp, 1847). This fact was demonstrated by the conversion of the acid to nitrocinnamic acid, which was sparingly soluble in alcohol, while benzoic acid and nitrobenzoic acid were very soluble. In addition, distillation of the resins transformed them mostly into benzoic acid. Treatment of cinnamic acid with concentrated nitric acid transformed it first into nitrocinnamic acid, then into benzoic acid, and finally, into nitrobenzoic acid. Dissolution of nitrobenzoic acid in an alcoholic solution of ammonium sulfide, followed by mild heating, resulted in the formation of two substances, one a true yellow resin, the other, an alkaloid. The latter was solid, colorless, crystallizable in mamelons, insoluble in water, soluble in alcohol and ether, and forming salts that hardly crystallized (Kopp, 1847).

In 1849, Gustave Chancel (1822-1890) reported the results of his study of the products of the dry distillation of calcium benzoate and the separation of a crystalline substance that he named benzophenone (Chancel, 1849). Benzophenone was insoluble in water and very soluble in alcohol and ether; it melted at 46 °C and boiled at 315 °C. Treated with hot fuming nitric acid it converted into dinitrobenzophenone. According to Chancel, dinitrobenzophenone was the origin of the oxygenated alkaloid, flavine, that Laurent and him and had separated during the dry dissolution of calcium benzoate by nitric acid, followed by treatment with ammonium sulfide (Chancel, 1849; Laurent & Chancel, 1848).
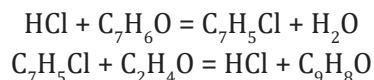
All these results led Chiozza to study in detail the action of ammonium sulfide on nitrocinnamic acid (Chiozza, 1852a). His results were substantially different from those of Kopp. He justified the difference stating that Kopp had conducted his experiments using an alcoholic solution of nitrocinnamic acid when it was known that the action of hydrogen sulfide and ammonium sulfide on alcoholic solutions of nitro derivatives was quite different from that when in aqueous solutions. Boiling a solution of nitrocinnamic acid in ammonium sulfide resulted in the precipitation a large amount of sulfur. Saturating the liquid residue with HCl produced a liquor strongly colored by a resin. Concentration by evaporation resulted in the precipitation of small brown crystals soiled with the resin. The crystals were separated and purified by repeated solution in boiling water. Elemental analysis indicated that they contained, by weight, 74.6% carbon, 5.0% hydrogen, 10.0% nitrogen, and 10.4% oxygen, corresponding to the formula C_9H_7NO. Chiozza named this new substance *carbostyril* (today, 2-quinolone).

The formula of nitrocinnamic acid is $C_9H_7NO_4$, hence carbostyril may be formed by a simple deoxidation of the nitro acid. Carbostyril was found not to be acid or basic, to be very soluble in boiling water, alcohol, and ether, and insoluble in ammonia. According to Chiozza, carbostyril seemed to be a volatile alkaloid like aniline, or the nitrile of an acid like carbanilic acid, in which the aniline had been replaced by styryl (a hypothetical radical

found in certain derivatives of styrene and cinnamic acid; called also *cinnyl*, or *cinnamyl*) (Chiozza, 1852a).

Angelic and cinnamic acids

According to Chiozza, the reaction of essence of Roman chamomile with KOH went through three very distinct stages; the first one was a simple combination between the reagents, yielding a gelatinous, reddish mass from which the water again separated the unaltered chamomile oil. The second one occurred after further moderate heating; an exothermic reaction took place accompanied by the release of a mixture of hydrogen and the vapors of the hydrocarbon of the essence. The result was an almost dry saline mass composed of potassium angelate mixed with the excess of KOH employed. Treatment of the potassium salt with a dilute acid released the angelic acid, which floated as a slightly colored oil. Upon cooling, this layer solidified as a mass of beautiful crystals (Chiozza, 1853b). These first two phases of the reaction had already been observed by Charles Gerhardt in his work about the preparation of angelic acid from the essence of Roman chamomile (Gerhardt, 1848).

Chiozza repeated the experiments of Gerhardt and noticed that the acid often remained liquid, and, in this case, it possessed a penetrating odor of glacial acetic acid. This last effect called Chiozza's attention because angelic acid was homologous to acrylic and oleic acid (monounsaturated fatty acids), known to give acetic acid under the influence of oxidizing agents. This assumption was confirmed by heating a mixture of KOH and potassium angelate and noticing the abundant release of hydrogen. According to Chiozza, this additional reaction should be considered the third stage of the reaction between KOH and chamomile essence. After it, treatment of the liquid with sulfuric acid yielded a mixture of acetic and propionic acids, and no angelic acid (Chiozza, 1853b).

Chiozza remarked that this procedure allowed the easy preparation of substantial quantities of propionic acid in a high state of purity. In addition, he mentioned that when angelic acid was partially decomposed, it remained in solution in acetic and propionic acids, forming on the surface of the liquor an oleaginous and in crystallizable layer, which presented a penetrating odor, offering some analogy to that valerianic acid. The presence of the latter was confirmed with silver and barium salts. The action of KOH on these three acids could be expressed by the following equations:

$$C_3H_4O_2 \ + 2KOH = C_2H_3OOK + CHOOK + H_2$$
Acrylic acid   K formiate

$$C_5H_8O_2 \ + \ 2KOH = C_2H_3OOK + C_3H_5OOK + H_2$$
Angelic acid   K propionate

$$C_{18}H_{34}O_2 + 2KOH = C_2H_3OOK + C_{16}H_{31}OOK + H_2$$
Oleic acid   K palmitate

The next step was examination of cinnamic acid, which exhibited with benzoic acid the same relations as angelic acid with propionic acid. It was known that cinnamic acid gave benzoic acid under the influence of oxidizing agents, but acetic acid was not mentioned among the products of this reaction. The results were as expected, heating potassium cinnamate with an excess of KOH, resulted in an abundant liberation of hydrogen and the complete transformation of cinnamic acid into benzoic and acetic acids, accompanied by
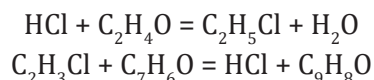
the formation a little amount of salicylic acid as the result from the secondary action of KOH on benzoic acid. Chiozza tried the same reaction with coumaric acid but failed in collecting enough acetic acid among the products of KOH on this body to be able to ascertain its presence by analysis (Chiozza, 1853b).

Aldehydes from the acids

Chiozza wrote that his results about the splitting experimented by certain organic acids under the influence of molten KOH, led him to study the possibility of obtaining the aldehydes corresponding to these acids (Chiozza, 1856). The first step was performing the reverse reaction, that is, the synthesis of cinnamic acid or cinnamaldehyde, using benzoic and acetic elements. He found that under slight heating, a mixture of acetaldehyde and benzaldehyde saturated with HCl, turned dark brown while releasing a lot of the HCl and a large fraction of the aldehyde, which escaped the reaction and decreased the yield. After a few minutes, the mixture became cloudy with the separation of water droplets. Upon distillation, the first fraction consisted of non-reacted benzaldehyde; this was followed by a small quantity of a liquid, which, purified by several rectifications and washings with alkaline solutions, proved to be cinnamaldehyde. It smelled as natural cinnamon oil, especially very strongly when the substance began to resinify itself. In the fresh state, it was neutral to reagent papers and perfectly clear and almost colorless. On exposure to air, it quickly became acid and then colored. Prolonged exposure completely resinified it. This highly inefficient method was modified replacing by sulfuric acid the HCl and operating in closed vessels. Chiozza believed that the reaction between the two aldehydes was an esterification like the one between an organic acid in the presence of alcohol and HCl. It was also possible that HCl reacted with one or the other of the two aldehydes, forming the chlorides C_2H_3Cl (vinyl chloride) or C_7H_5Cl (chloromethylbenzene) which, by reacting in turn with the aldehydes, regenerated HCl and produced cinnamon, $\dot{C}_9H_8O$, according to the following equations:

$$HCl + C_7H_6O = C_7H_5Cl + H_2O$$
$$C_7H_5Cl + C_2H_4O = HCl + C_9H_8O$$

or

$$HCl + C_2H_4O = C_2H_5Cl + H_2O$$
$$C_2H_3Cl + C_7H_6O = HCl + C_9H_8O$$

Chiozza believed that the inefficiency of his method could be easily overcome by using sulfuric acid instead of HCl and conducting the process in a closed vessel (Chiozza, 1856).

Salicylic acid

In 1846 August Cahours reported that the reaction of phosphorus pentachloride with certain volatile organic acids having 2 or 3 equivalents of oxygen yielded phosphoryl chloride, HCl, and the corresponding acyl chloride. For example, with benzoic it was (Cahours, 1846):

$$C_7H_6O_2 + PCl_5 = C_7H_5OCl + HCl + POCl_3$$
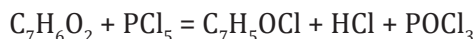
According to Chiozza, it could be assumed that the first product of the reaction was a compound of formula $C_7H_6ClO_2$, which afterwards decomposed into benzoyl chloride and

HCl (Chiozza, 1852b). In this case, the reaction consisted simply in the replacement of one equivalent of oxygen by one equivalent of chlorine. This assumption was proven correct by the results of the reaction of salicylic acid, except that in this case, the product did not decompose immediately into salicyloyl chloride ($C_7H_5ClO_2$) and HCl, but into its isomer, monochlorobenzoic acid and HCl.

Rectification of the product of the reaction and collection of the fraction passing between 200° and 250 °C, yielded a liquid with a suffocating odor, which decomposed slowly in contact with cold water and immediately with boiling water into monochlorobenzoic acid hydrochloride, $C_7H_5ClO_2$,HCl, and HCl. The purified acid appears as shiny needles, vey soluble in boiling water, melting a few degrees higher than that of benzoic acid, and sublimating without decomposition. (Chiozza, 1852b). Chiozza added that John Stenhouse (1809-1880) had already synthesized this acid in a very impure form, during the chlorination of benzoic acid (Stenhouse, 1845).

Mixed acid anhydrides

According to Gerhardt, the best procedure for preparing a mixed anhydride was based on the double decomposition of the chlorides of different monobasic acids, or their potassium or sodium salts, in the same manner that double ethers were produced by treating the potassium salt of an alcohol with the chloride of a different alcohol (Gerhardt, 1853). He added that Cahours was the author of an excellent procedure for preparing the chlorides of many organic acids. It consisted in treating the acid with phosphorus pentachloride and separating by distillation the acid chloride from the phosphorus oxychloride chloride produced simultaneously (see above). Nevertheless, the Cahours method was appropriate only when the resulting chloride had a higher boiling point than that of the phosphorus oxychloride (105.8 °C). More volatile chlorides could not be separated completely by distillation from the accompanying phosphorus oxychloride (Gerhardt, 1853).

Moreover, the action of phosphorus pentachloride upon organic acids was not a simple double decomposition. Actually, in consisted of several successive stages, as shown by the release of HCl; the first stage was the formation of a hydrochloride of the chloride, followed by its split into chloride and HCl. Gerhardt believed that phosphorus oxychloride, and not phosphorus pentachloride, was to phosphoric acid what benzoyl chloride was to benzoic acid. Consequently, phosphoryl chloride was the one that gave the corresponding chloride. This assumption was easily tested: phosphoryl chloride acted energetically of many salts; at room temperature it produced a phosphate and a volatile chloride; thus, with sodium benzoate it produced benzoyl chloride, with sodium cumate, cumyl chloride, etc. Phosphoryl chloride was extremely advantageous for preparing the chlorides as well as the anhydrides of monobasic acids, according to the way it was employed. Used in slight excess (no more than 3 molecules of salt per molecule of oxychloride) it produced the chloride; used in less than one molecule per six of the salt, it generated the corresponding anhydride. Gerhard mentioned that it was possible to prepare large amounts of phosphorus oxychloride by distilling a mixture of one part of phosphorus pentachloride with one-half part of oxalic acid, perfectly dry (Gerhardt. 1853).

Gerhardt went on to describe the preparation and properties of several simple and double anhydrides, among them, formic, acetic, butyric, valeric, cinnamic and benzoic anhydrides, cuminic-benzoic, cinnamic-benzoic, etc. (Gerhardt, 1853).

Chiozza used the procedure described by Gerhardt to of several new simple and mixed anhydrides, among them, valeric (pentanoic), valeric-benzoic, caprylic (octanoic), caproic (hexanoic), pelargonic (nonanoic), pelargonic-benzoic, angelic, benzoic-angelic, nitrocinnamic, and cumyl anhydrides (Chiozza. 1853ac).

Potassium valerate was the salt most appropriate to perform the experiments. The reaction of 6 equivalents of the salt with one of phosphorus oxychloride was highly exothermic and resulted in the immediate disappearance of the intolerable smell of the oxychloride and transformation of the mixture into a saline mass, impregnated with a slightly smelling thick oil, composed of valeric anhydride. This compound was purified by treatment with a dilute solution of potassium carbonate, followed by extraction with ether, evaporation of the ether, and agitation with calcium chloride. Elemental analysis of the purified anhydride indicated that it contained, by weight, 64.5% carbon, 9.4% hydrogen, and 26.1% oxygen, corresponding to the formula $C_{12}H_{18}O_3 = (C_6H_9O)-O-(C_6H_9O)$. It was a limpid oil, having density 0.934 at 15 °C, boiling at 215 °C and irritating the eyes. In contact with humid air, it transformed slowly into hydrated valeric acid (Chiozza, 1852d, 1853ac).

The valeric-benzoic mixed anhydride was prepared by reacting benzoyl chloride with potassium valerate. The reaction was exothermic, and the pertinent anhydride as purified in the same manner as valeric anhydride. It appeared as a limpid oil, heavier than water, and inert to reactive papers. Treated with alkalis it split into potassium and benzoic valerate; treated with aniline it yielded valeranilide, a crystalline substance, little soluble in boiling water, soluble in alcohol and ether, and boiling at 115 °C, without decomposition. The mixed anhydride of pelargonic and benzoic acid, $(C_7H_8)-O-(C_9H_{17}O)$, was prepared in the same manner (Chiozza, 1853ac).

Gerhard wrote that chemists had been unable to isolate acid anhydrides, in spite that the dualistic theory admitted they were present in monobasic acids such as benzoates, acetates, cinnamates, butyrates, etc. (Gerhard, 1852). It was not understood why it was impossible to withdraw a water molecule from the hydrated monobasic acids to convert them to acid anhydride, as was easily done with dibasic acids. According to Gerhardt, this occurred because the dualistic theory was wrong, on the one hand, monobasic acids did not contain a water molecule, on the other hand, dibasic acids contained the basic hydrogen necessary for the elimination of a water molecule. The dualistic theory did not negate the existence of substances containing *twice* all the elements of a monobasic acid less a water molecule. Gerhardt went on to demonstrate how this fact could be brought into being (Gerhard, 1852).

Thus, Gerhardt prepared benzoic anhydride by the double decomposition of two benzoic compounds, an alkaline derivative and benzoyl chloride. A mixture of one molecule of sodium benzoate and one molecule of benzoyl chloride, heated in a sand bath at 130 °C, turned into a limpid liquid. Heated a few degrees higher resulted in the precipitation of sodium chloride. The residue, washed with water and sodium carbonate, solidified as oblique prisms, melting at 33 °C, volatile without decomposition, and having an elemental composition equivalent to $C_{14}H_{10}O_3$. This substance was transformed immediately to benzoic acid hydrate by water or alkaline hydroxides. Acetic anhydride was prepared by a similar procedure. Treatment of both acid anhydrides with aniline transformed them into benzanilide and acetanilide, respectively. Gerhardt added that he had discovered that phosphorus oxychloride could be used advantageously to prepare the organic chlorides necessary for the preparation of acid anhydrides (Gerhardt, 1852).

Gerhardt wrote that the composition of these acid anhydrides contained twice the acid radical and negated the existence of water in the monobasic acid, in addition, the ratio of the two radicals contained in their constitution was the same as that into an alcohol and its ether. To reinforce this assumption, Gerhardt also prepared the anhydride of mixtures of two acids, i.e., cinnamic and benzoic, cumic (*p*-isopropylbenzoic acid), and acetic, and cumic and benzoic (Gerhardt, 1852).

Chiozza wrote that Gerhardt results allowed assuming that the anhydride contained twice the oxygenated group present in the ordinary acid (Chiozza, 1852c). In addition, they allowed assuming that the radicals themselves could be obtained by reacting the chlorides of the oxygenated groups with metallic combinations of the aldehydes. Of the latter, potassium cuminol (cumaldehyde), $C_{10}H_{11}KO$, was the most accessible one; it could be easily prepared by heating cuminol with potassium in a covered platinum crucible. Reaction with cumyl chloride resulted in liquefaction of the mixture; slight heating converted it into a pasty state and the separation of potassium chloride (Chiozza, 1852c), according to

$$C_{10}H_{11}KO + C_{10}H_{11}OCl = (C_{10}H_{11}O)(C_{10}H_{11}O) + KCl$$
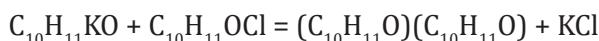
Cumyle appeared as a pasty oil, heavier than water, very little odorous. Slight heated, it released an agreeable odor like geranium. It was slightly soluble in cold alcohol and very soluble in boiling alcohol. It boiled above 300 °C while decomposing into cuminic acid and other less oxygenated products. Elemental analysis indicated that its composition was $C_{20}H_{22}O_2$ (Chiozza, 1852c).

Gerhardt and Chiozza added more information to the preparation of acid anhydrides (Gerhardt & Chiozza, 1853a). The usual procedure for preparing a mixed anhydride consisted in reacting the chloride of a monobasic acid with the alkaline salt of another monobasic acid (i.e., acetyl chloride and potassium benzoate). This was not the result when reacting the chloride of a monobasic acid with the alkaline salt of a *dibasic* acid. Instead of a mixed anhydride, the product consisted in a mixture of *two simple anhydrides*. For example, treating sodium succinate with benzoyl chloride yielded a mixture of succinic anhydride and benzoyl anhydride, instead of succinic-benzoyl anhydride. The same results were obtained with other dibasic acids such as oxalic, carbonates, suberates, sebacates, etc. The salts of dibasic acids contained all the elements of the corresponding acid anhydride but *also* the element of a oxide. Hence, two successive reactions took place: (1) the split of the salt into an acid anhydride and oxide, and (2) the reaction between this oxide and the chloride. The manner that hydrated acids reacted with phosphorus pentachloride allowed identifying if they were monobasic or dibasic. With dibasic acids the reaction took place in two stages; with monobasic acids it required only one stage (Gerhardt & Chiozza, 1853a).

Gerhardt and Chiozza published two additional memoirs about the nature of amides, which completed their view about the constitution and classification of organic compounds (Gerhardt & Chiozza, 1853b, 1856). They believed that most organic compounds could be derived from a very small number of types belonging to mineral chemistry, such as water, HCl, ammonia, etc. The terms derived from each type had no identical properties, but their properties were in progression. In this order of ideas, the same type contained simultaneously the acids, the bases, and neutral compounds. Acids were located at one end of the series, bases at the opposite end, and neutral substances in between. Calling the two extremes as positive and negative, then organic radicals such as methyl, ethyl, and phenyl, which originated from the substitution of the hydrogen of the preceding types, produced

derivatives more or less like bases, while other groups or radicals, such as acetyl, benzoyl, cumyl, gave rise, by a similar substitution, to negative derivatives, that is to say. bodies more or less like acids.

Gerhardt and Chiozza discussed in particular, the compounds belonging to the ammonia types, and went on to describe the preparation and properties of a large number of new chemical species (e.g., dibenzanilide, benzoyl salicylamide, cumyl salicylamide, etc.). One of the conclusions of this work was the attachment of amides to the ammonia type, like the amines prepared by Charles-Adolph Würtz (1817-1884) (Würtz, 1849) and August Wilhelm Hofmann (1818-1892) (Hofmann, 1849), with the difference that now the hydrogen had been replaced by acid groups instead of hydrocarbon groups. From this research, also came the concept that amides were to acids what compound ammonia was to alcohols; in their own words: "if we call monobasic acid a water molecule in which the hydrogen atom has been replaced by a negative radical, we shall say that the amide corresponds to the neutral salt of such an acid represented by an ammonia molecule in which the hydrogen atom has been replaced by the same negative radical, acetyl, benzoyl, sulfophenyl, etc. Amides of this sort (primary amides) have been produced thus far by the action of heat on the neutral salt, by the reaction between ammonia and the neutral ether, or by the reaction of ammonia and the corresponding acid chloride. Our experiences show that monobasic acids are also capable of yielding the amides corresponding to acid salts; in fact, our secondary amides correspond to bi-salts and our ternary amides to tri-salts. In these two classes of amides two or three hydrogen atoms of the ammonia molecules are replaced by the same negative radical or by different negative radicals". They named these compounds primary amides, secondary amides, and tertiary amides (Gerhardt & Chiozza, 1853b, 1856).

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