Rev. CENIC Cienc. Quím.; Vol. 52. (2): 265-282. Año. 2021. e-ISSN: 2221-2450.

REVISION BIBLIOGRAFICA

LOUIS BOUVEAULT

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Recibido: 2 de noviembre de 2021; **Aceptado:** 11 de noviembre de 2021;

ABSTRACT

Louis Bouveault (1864-1909), a French chemist and physician who found that the action of sodium upon nitriles resulted in the formation of monosodium derivatives where the sodium atom was attached to the carbon atom closest to the group -CN. He studied in detail the synthesis of many new compounds, among them, *β*-ketone nitriles, primary alcohols, fatty acids, etc. His most important contribution is the Bouveault synthesis of aldehydes, a one-pot substitution reaction that replaces an alkyl or aryl group with a formyl using a disubstituted formamide. He illustrated his reaction by preparing valeraldehyde, benzaldehyde, decyl aldehyde, etc. He studied in detail the separation and properties of numerous plant extracts, among them, rhodinol, rhodinal, lemon grass, lemonals, citronellol, etc. The oxime of citronellal, a stable aldehyde, acted by acetic anhydride, yielded the corresponding nitrile. Bouveault and Gourmand carried the total synthesis of rhodinol.

Keywords: aldehydes, Bouveault aldehyde synthesis, ethyl cyanide, *β*-ketone nitriles, nitrile saponification, plant extracts, primary alcohols.

RESUMEN

Louis Bouveault (1864-1909), un químico y médico francés que descubrió, que la acción del sodio sobre los nitrilos resultaba en la formación de derivados mono sódicos en los cuales el átomo de sodio estaba unido al átomo de carbono más cercano al grupo -CN. Estudió en detalle la síntesis de una gran variedad de nuevos compuestos, entre ellos *β*-cetonitrilos, alcoholes primarios, ácidos grasos, etc. Su contribución más importante es la síntesis Bouveault de aldehidos, una reacción de substitución de un paso para reemplazar el grupo alquilo o arilo por el grupo formilo usando una formamida di substituida. El ilustró su reacción preparando valeraldehido, benzaldehído, aldehído decílico, etc. Bouveault estudió en detalle la separación y propiedades de un gran número de extractos de plantas, entre ellos, rodinol, rodinal, hierba de limón, lemonals, citronelol, etc. La oxima de citronelal, un aldehído estable, reaccionaba con el aldehído acético para producir el nitrilo correspondiente. Bouveault y Gourmand realizaron la síntesis total del rodinol.

Palabras claves: alcoholes primarios, aldehídos, Bouveault síntesis de aldehídos, *β*-cetonitrilos, cianuro de etilo, extractos de plantas, saponificación de nitrilos, separación de ácidos grasos.

Este articulo no presenta conflicto de intereses.

INTRODUCTION

Life and career (Béhal, 1913; Anonymous, 2020)

Louis Bouveault was born on 11 February 11, 1864, in Nevers, France, the son of Marie Pauline Arbelot and Théophile François Adolphe Bouveault, an architect. He took his basic education in his hometown and then at the Lyçée Saint Louis in Paris, a public institution dedicated to preparing the students to enter the Grand Écoles. In 1880 he received his diploma Bachelier ès Lettres diploma and in 1881 his Bachelier és Sciences diploma. In 1883 he was admitted to the École Polytechnique and left in 1885 because he did not feel that the military discipline was appropriate to his spirit. He then joined the laboratory of Adrien Armand Maurice Hanriot (1854-1933) at the Faculty of Medicine of Paris, as préparateur of practical works. In 1886 he received his degree of Licencié ès Science Physiques and in 1890 his doctorate in physical sciences, after successfully defending a thesis about ketone nitriles and their derivatives (Bouveault, 1890a). He was then appointed, by competition, as class's inspector of schools of the Department of the Seine. Simultaneously with this position he continued his studies at the Faculty of Medicine and in 1892 he received the degree of Docteur ès Médicine, after defending a thesis about the chemistry of avian tuberculosis (Bouveault, 1891-1892). He then begun a successful academic career: In 1892 he was appointed adjunct professor at the Faculty of Medicine in Lyon, in 1894 lecturer of general chemistry at the Faculty of Sciences of Lyon, and in 1898 lecturer of general chemistry at the Faculty of Sciences of Lille. In Lyon he worked on the chemistry of camphor and terpenes and with Philippe Barbier (1842-1922) on plant essences. In 1899 he transferred to the University of Nancy to take charge of the course of organic chemistry and 1900 he was promoted to adjunct professor. In 1901 he moved to Paris to replace Auguste Béhal (1859-1941) as lecturer of organic chemistry at the Faculty of Sciences. The high quality of his academic work earned him nominations of Officier d'Académie (1895) and Officier de l'Instruction Publique (1900) (two appointments awarded to distinguished academics). In his last years he worked as entrance examiner of the École Polytechnique.

The high value of his research earned him one-third of the 1896 Jecker Prize and the 1903 (full) Jecker Prize (and the Berthelot Medal) of the Académie des Science of France. Bouveault occupied several important positions in the Société de Chimie de France: Vice secretary (1889-1892), member of the Council (1902), Vice President (1905), and President (1907). In 1907 he was appointed Chevalier de la Légion d'Honneur. He was also secretary of the International Commission of Chemical Nomenclature (1889-1892), secretary of the International Congress of Chemical Nomenclature (Geneva, 1892) President of the Chemical Section of the French Society for the Advancement of Chemistry, etc. (Béhal, 1913; Anonymous, 2020)

In 1895 Bouveault married Marguerite Joséphine Nivault; one son (Marie Louis René) was born of this union.

Bouveault passed away in Paris on September 5, 1909. He was buried at the Cimetière du Sud (Montparnasse).

Scientific contribution

Bouveault was a very prolific writer; despite his short life (45 years) he published about 200 papers mainly on new synthesis processes of organic compounds, on natural principles, and the structure of camphor and the preparation and properties of many of its derivatives. As customary for candidates to the Académie, he published a booklet describing the results of his scientific research (Bouveault, 1908a). In 1907 he

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failed twice in this attempt, first to Henry Le Chatêlier (1850-1930) during the election to replace Henri Moissan (1852-1907, 1906 Nobel Prize for Chemistry) and then to Emil Jungfleish (1839-1916), during the election to replace Marcelin Berthelot (1827-1907).

In addition to the subjects described below, he studied compounds with cyclic formula having several nitrogen atoms (Bouveault, 1889); the phenomenon of optical isomerism in compounds having a closed ring formula (Bouveault, 1894); the synthesis of aldehydes and aromatic acids by means of aluminum chloride (Bouveault, 1896a); he developed a method for preparing aromatic aldehydes (Bouveault, 1896b); he studied α-acetylfuran and its presence in wood tar (Bouveault, 1897a); several derivatives of guaiacol (Bouveault, 1897b); the application of Friedel-Craft's method to the preparation of aromatic ketones and aldehydes (Bouveault, 1897c); the electrolysis of sodium ethyl succinate (Bouveault, 1899d); the direct nitration in the fatty series (Bouveault & Wahl, 1900); he synthesized rhodinamine (Bouveault, 1903b);[15] etc. Here we describe a few of his results. The work with François Antoine Philippe Barbier (1842-1922) on natural products has been discussed in another publication (Wisniak, 2020).

Ethyl cyanide

In 1887 Louis Henry reported that sodium replaced easily one of the hydrogen atoms of the group -CH_2 of malononitrile CN-CH_2-CN because of its vicinity to two electronegative groups -CN (Henry, 1887). This finding led Adrien Armand Maurice Hanriot (1854-1933) and Bouveault to investigate if cyanoacetic acid (malonic acid mononitrile) reacted in the same manner (Hanriot & Bouveault, 1889a). Their results indicated that the action of sodium on nitriles resulted in the formation of mono sodium derivatives in which the sodium was attached to the carbon atom closest to the group -CN. Addition of the sodium in small pieces to a solution cyanoacetic acid in dry ether resulted in the release of ethane and the formation of the highly unstable derivative CH_3-CHNa-CN, as a white powder (Hanriot & Bouveault, 1889a).

The instability of the sodium derivative led Hanriot and Bouveault to transform it into alkyl derivatives by means of alkyl iodides, to elucidate its constitution: the white precipitate, washed with absolute ether and then treated with ethyl iodide, transformed the sodium into sodium iodide, accompanied by the formation of valeronitrile, boiling at 125 ^{0}C, according to

CH_3-CHNa-CN + C_2H_5I = NaI + CH_3-CH(C_2H_5)-CN

This result was substantiated by the fact that the reaction of CH_2Na-CH_2-CN with ethyl iodide resulted in the formation of normal valeronitrile, CH_3-(CH_2)$_2$-CN, boiling at 140 ^{0}C (Hanriot & Bouveault, 1889a).

The basic reaction was carried at room temperature by adding the sodium to a solution of propionitrile in ether. The process was exothermal, and the mixture entered promptly into ebullition. A large amount of ethane was released accompanied by a small amount of hydrogen and deposition of a white powder. The purified powder reacted lively with ethyl iodide yielding sodium iodide that was eliminated by water washes. The remaining liquid was purified and found to be a mixture of two liquids, one boiling at 125^0 and the other at 195 ^{0}C. Rectification of the mother ethereal solution yielded propionitrile and a crystalline body melting at 48 ^{0}C. (Hanriot & Bouveault, 1889a).

Hanriot and Bouveault described valeronitrile as a liquid boiling at 125 ^{0}C and containing, by weight, 72.01% carbon, 10.91% hydrogen, and 17.81% nitrogen (not

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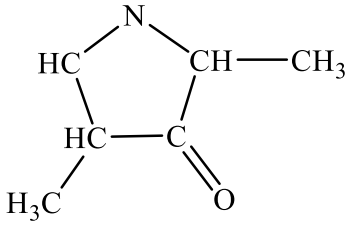
100%). The liquid boiling at 195 ^{0}C was found to contain, by weight, 67.97% carbon, 9.45% hydrogen, 10.05% nitrogen, and 12.53%, corresponding to the formula $C_8H_{13}NO$. The presence of oxygen was unexpected and for this reason the reaction was repeated with methyl iodide. Now the reaction was more violent and for this reason the reagent was added slowly to the sodium derivative. The product consisted exclusively of a substance containing, by weight, 67.3% carbon, 9.3% hydrogen and 11.43% nitrogen, corresponding more or less to the formula C_7H_4NO, boiling at 175 ^{0}C, having relative density 0.9451 (0 ^{0}C) and molecular weight 121. To find if the oxygen came from the ether, Hanriot and Bouveault repeated the reaction using benzene instead. The reaction was now lively and faster. The sodium iodide was separated by filtration and the filtrate distilled. The only fraction passed at a temperature higher than 175 ^{0}C and was decomposed by HCl into ammonium chloride and an oily liquid identical with the one boiling a 175 ^{0}C. Hanriot and Bouveault interpreted this result by assuming that the high boiling compound contained an -NH group that the HCl replaced by an oxygen atom, with separation of ammonium chloride. In other words, it had to have the formula $C_7H_{12}N_2$ (the original oxygen eliminated as water) and the pertinent chemical equations were as follows (Hanriot & Bouveault, 1889a):

$Na + 2C_3H_5N + CH_3I = NaI + C_7H_{12}N_2 + H$

$C_7H_{12}N_2 + H_2O + HCl = NH_4Cl + C_7H_{11}NO$

The next step was to determine the functionality of oxygen within the molecule and the constitution of the molecule. Treatment with phenylhydrazine hydrochloride yielded a well-defined hydrazone, melting at 80 ^{0}C, indicating the presence of a carbonyl group. In addition, three methyl groups were present, two belonging to the two molecules of ethyl cyanide participating in the reaction, and the third originating from methyl iodide. Furthermore, the compound could not be a nitrile because boiling KOH did not attack it. In addition, the compound was neutral, indicating that it was not an amine or an imide. Hence the nitrogen had to be part of the nucleus of the molecule. All these facts led Hanriot and Bouveault to suggest that the new substance had the structure



Hanriot and Bouveault proposed naming the five-member ring of $C_7H_{11}NO$ *β-pyrolone* and the full compound, *trimethylpyrolone* (Hanriot & Bouveault, 1889a).

Hanriot and Bouveault also described the preparation and properties of dimethylethylpyrolone, dimethylpyrolonimide, and dimethylpyrolone (Hanriot & Bouveault, 1889a).

Hanriot and Bouveault heated a mixture of the compound $C_7H_{11}NO$ with concentrated HCl, in a closed tube to 140^0-150 ^{0}C and on opening noted a strong pressure of CO_2. It contained an abundant deposit of ammonium chloride and an oil lighter that HCl and boiling at 113^0 to 114 ^{0}C, which was identified as ethyl isopropyl carbonyl, C_2H_5-CO-$CH(CH_3)_2$. The same experiment with the compound $C_8H_{13}NO$ yielded ethyl α-butyl carbonyl, C_2H_5-CO-$CH(CH_3)(C_2H_5)$, boiling between 134^0 and

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135 ^{0}C. The formation of ammonium chloride indicated that both primitive molecules had to contain a -CN group that HCl transformed into a carbonyl group, -CO-. In both cases, the reaction with HCl could be represented by the equation (Hanriot & Bouveault, 1889b):

$C_6H_8RNO + 2H_2O + HCl = NH_4Cl + CO_2 + C_5H_9RO$

This equation led Hanriot and Bouveault to reject the formula they had proposed previously where the sodium was attached to the nitrogen. The new evidence indicated that the sodium had be connected to a carbon atom, which in the case of the ketone was attached to the new alkyl group introduced into the molecule, as follows (Hanriot & Bouveault, 1889b):

C_2H_5-CN + CH_3-CHNa-CN = C_2H_5-C(NH)-C(CH_3)Na-CN. The action of methyl iodide on this product would yield

$$C_2H_5\text{-}C(NH)\text{-}\underset{\displaystyle CH_3}{\underset{|}{C}}\text{-}CN \quad \text{which HCl would transform into the body} \quad C_2H_5\text{-}CO\text{-}\underset{\displaystyle CH_3}{\underset{|}{C}}\text{-}CN$$

(Hanriot & Bouveault, 1889b).

β-Ketone nitriles

As mentioned before, these substances were the subjects of Bouveault's doctoral (and of many publications before and after) (Bouveault, 1890abcde, 1892; Bouveault & Wahl, 1905ab).

Bouveault wrote that Jean-Baptiste André Dumas (1800-1884) had made known that the cyano esters of alcohols (alkyl cyanides) and acid nitriles constituted one chemical function. Hence nitriles, like alcohols, could also be divided into primary, secondary, and tertiary nitriles (Bouveault, 1890ae, 1892). Since all primary alcohols could be represented by the general formula R-CH_2-OH it followed that all primary nitriles would be represented by R-CH_2-CN. It was also known that the vicinity of strong electronegative group communicated to hydrogen atom the faculty of being replaced by metals. In this way nitromethane CH_3-NO_2, having the strongly electronegative group -NO_2, would have one of the hydrogen atoms of its -CH_3 group replaced by a sodium atom and become sodate nitromethane, a true salt. Since the group -CN was also strongly electronegative the question could be asked if primary nitriles R-CH_2-CN did not have the same property of having one of hydrogen atoms being replaced by metals, making viable the combinations R-CHNa-CN. As shown previously, (Hanriot & Bouveault, 1889a) had found that a solution of ethyl cyanide in absolute ether reacted vividly with sodium giving place to a white precipitate, highly deliquescent, which turned liquid in contact with humid air. This compound had been treated with an iodide dissolved in alcohol to replace the sodium by an alkyl radical. This allowed the separation of a new nitrile having the constitution CH_3-CH(C_2H_5)-CN, a result of the reaction

CH_3-CHNa-CN + C_2H_5I = CH_3-CH(C_2H_5)-CN + NaI

This finding had led Bouveault to the synthesis of many secondary nitriles, having the general formula CH_3-CH(R)-CN, by reacting the corresponding sodate with the alkyl iodide RI. This nitrile was not the only product of the reaction; it was always

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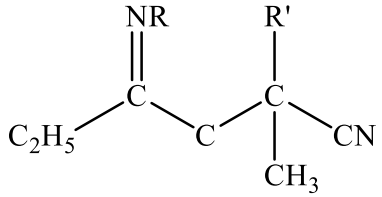
accompanied by an oily liquid that was split by ammonia into ammonium chloride and a compound of formula $C_8N_{12}NO$.

Bouveault was able to prove that the reaction between sodium and propionitrile produced not only the sodate derivative but also sodium cyanide derived from the total decomposition of the nitrile into a sodate polymer of constitution C_2H_5-C(NH)-C(CH_3)Na-CN, by the reaction C_2H_5-CN + CH_3-CHNa-CN = C_2H_5-C(NH)-C(CH_3)Na-CN. The reaction of the latter with C_2H_5I yielded NaI and the compound C_2H_5-C(NH)-C(C_2H_5)(CH_3)CN, the oily liquid mentioned above. HCl transformed this substance into ammonium chloride and a liquid of formula C_2H_5-CO-C(C_2H_5)(CH_3)(CN), boiling at 195 ^{0}C. This new compound constituted a sample of a new series of substances that were simultaneously ketone and nitrile. The first terms of the series could be obtained by replacing the ethyl iodide by methyl iodide:
C_2H_5-CO-C(CH_3)(CH_3)CN and C_2H_5-CO-CH(CH_3)-CN, both being *β-ketone nitriles* (Bouveault, 1890abe, 1892).

Bouveault studied in detail the properties of these three new nitriles. He found that they could be transformed into the corresponding esters by treating their alcoholic solution with dry HCl. This property allowed the synthesis of new numerous *β*-ketone esters. He also found that heating these nitriles with concentrated HCl in a sealed tube at 120 ^{0}C, transformed them into the corresponding acid, which was not stable at 120 ^{0}C, decomposing into a ketone, CO_2 and ammonium chloride, according to the equation:
C_2H_5-CO-CH(CH_3)-CN + HCl + $2H_2O$ = C_2H_5-CO-CH(CH_3)(CH_3) + CO_2 + NH_4Cl

The *β*-ketone nitriles combined with aromatic amines, such as aniline yielding water and imide derivatives of general formula



Where R represented an aromatic monoatomic radical, and R' an alkyl group. Bouveault described the preparation and properties of the compounds corresponding to aniline, *o*-toluidine, *p*-toluidine, mesidine, and *α*- and *β*-naphthylamine (Bouveault, 1890ac).

Consideration of the three homologue nitriles showed that the simplest one, of formula
C_2H_5-CO-CH(CH_3)-CN was simultaneously a ketone and a secondary nitrile, while the other two were ketones and tertiary nitrile. This difference was brought to light by their reaction with phenylhydrazine. The tertiary *β*-ketone nitriles reacted as common ketones yielding the corresponding hydrazone; the secondary nitrile (methylpropionylnitrile) yielded a basic product having a closed ring, pertaining to the pyrazole series, *phenylethylmethylamidopyrazole* (Bouveault, 1890ad):

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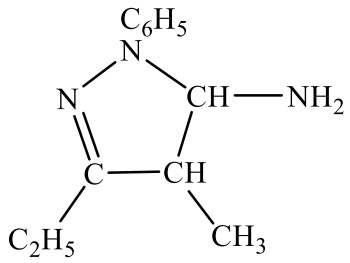

Separation of fatty acids

According to Bouveault, aromatic acids were generally crystallizable and yielded solid derivatives, and thus could be separated and characterized when in a mixture. This was not the case with fatty acids, they were normally liquid and their crystallized derivatives were few and hard to obtain. For these reasons they were usually characterized by their physical properties or the physical properties of their esters. In order to overcome this problem Bouveault went on to find a reagent that would yield a stable derivative, easy to purify and to regenerate the acid, once purified (Bouveault, 1899c). For this purpose he tried a large number of amides, anilides, and *p*-toluides, capable of forming crystalline derivatives. The amides seemed advantageous; they could be prepared easily and with reasonable yields. Unfortunately, they were very soluble in the different solvents and generated supersaturated solutions, making their separation very laborious. They also failed when dealing with mixtures of two or more isomers. The anilides and toluides exhibited the same shortcomings; in addition, they regenerate the acid with difficulty. The phenylhydrazides crystallized quite well but when the molecular weight became higher the fusion point decreased and the solubility increased. In addition, it was very difficult to regenerate the acid (Bouveault, 1899c).

Eventually Bouveault found that tetrachlorhydroquinone satisfied the requirements. Heated with an acid chloride under reflux, it combined giving place to a mono and a diacid derivative according to the equations

$C_6Cl_4(OH)_2 + 2R\text{-}CO\text{-}Cl = 2HCl + C_6H_4(OCO\text{-}R)(OCO\text{-}R')$

$C_6Cl_4(OH)_2 + R\text{-}CO\text{-}Cl = 2HCl + C_6H_4(OCO\text{-}R)(OH)$

Bouveault reported that the diacid derivatives were always crystallized, very soluble in ether, benzene, chloroform, less soluble in petroleum ether, sparingly soluble in cold methanol and cold ethanol, very soluble in hot methanol and ethanol, and insoluble in water. They were easily purified and appeared as white compounds, well crystallized, very stable, unaffected by air, and not attacked by diluted acids and alkalis. They were rapidly split by alcoholic KOH, with easy regeneration of the acid. These properties characterized all saturated or unsaturated fatty acids capable of forming chlorides (Bouveault, 1899c).

According to Bouveault, the diacid derivatives of tetrachlorhydroquinone could be used not only to characterize the acid but also to separate their mixtures. For this purpose it was enough to transform the mixture into the corresponding methyl or ethyl esters, which could then be separated easily by distillation (Bouveault, 1899c).

The monoacid derivatives were separated easily from the diacid esters by their solubility in diluted alkali; they were also crystallizable and could be used as the control in the case where the melting points were identical or very similar. They were more soluble in the alcohols than the diacid derivatives and less soluble in petroleum ether. Bouveault gave a detailed description of the preparation method of tetrachlorhydroquinone and its fatty acid derivatives (Bouveault, 1899c).

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Bouveault aldehyde synthesis

Bouveault wrote that the extreme plasticity of aldehydes of the fatty series made them an interesting material for the synthesis of other organic substances (Bouveault, 1904a). Unfortunately, the known methods for these syntheses were complicated and somehow expensive. For this reason, he decided to search for a new procedure that would overcome these limitations. In his first paper on the subject, he reported an exhaustive description of the most important methods for preparing aldehydes, including their disadvantages. For this purpose, he classified these methods in seven groups. The first six groups started from a substance having a carbon chain of the same length as the desired product: (1) hydrolysis, (2) hydration, (3) isomerization, (4) dehydration, (5) oxidation, and (6) hydrogenation. The seventh method started from a material having a different number of carbon atoms than the desired aldehyde; if the number was larger, the procedure employed was a degradation, if the number was smaller, the procedure was a synthetic one (Bouveault, 1904a). For example, hydrolysis methods started from derivatives of aldehydes, such as acetals, imines, oximes, hydrazones, phenylhydrazones, and semicarbazones. Hydration procedures involved the monosubstituted acetylenic hydrocarbons of formula R-C≡CH. Substances that could be isomerized to aldehydes were the homologues of *β*-substituted vinyl alcohol, R-CH=CH(OH), and the homologues of ethylene oxide. Acid dehydration materials such as solid zinc chloride and diluted sulfuric acid transformed the primary and secondary glycols into a mixture of aldehydes and ketones and the primary and tertiary glycols, into aldehydes. Primary alcohols could be dehydrogenated by means of platinum black, manganese dioxide and sulfuric acid, and the chromic mixture. Aldehydes could be obtained by hydrogenation of unsaturated αβ aldehydes, saturated acids, and their anhydrides and chlorides. Aldehydes could also be prepared by the decomposition of secondary acids or alcohols, etc. (Bouveault, 1904a).

Within the synthetic procedures, Bouveault mentioned that he and Wahl had developed a process for the gradual synthesis of saturated fatty aldehydes that permitted passing from the species R-CHO to the following homologue, R-CH_2-CHO (Bouveault & Wahl, 1903c). This method consisted in dehydrating by means of a solution of zinc chloride in acetic acid the products of the condensation of aldehydes and nitromethane, R-CH(OH)-CH_2-NO_2 = H_2O + R-CH=CH-NO_2. These unsaturated nitro compounds were then hydrogenated by means of the aluminum amalgam yielding neatly the oxime of the next homologue aldehyde [R-CH=CH-NO_2 +2 H_2 = R-CH_2-CH=NOH + H_2O], from which the aldehyde could be easily separated. This procedure had the inconvenience of requiring an aldehyde as starting material. Clearly, it would be more advantageous to start from an acid or an alcohol. Bouveault and Gustave Louis Blanc (1872-1927) had solved this problem by showing that the primary alcohols were more appropriate than the acids (the Bouveault-Blanc method in which an ester is reduced to primary alcohols using absolute alcohol and metallic sodium) (Bouveault & Blanc, 1903a). The question then reduced to how to transform RX into R-CHO, which perhaps could be solved using Edmond Blaise's (1872-1939) finding that nitriles could be transformed into ketones by means of Grignard's reagent (Blaise, 1901). Unfortunately, the HCN and the formamide (and all its derivatives containing a hydrogen atom connected to an oxygen or nitrogen atom) to be used were decomposed by HCl. These restrictions led to use a formic acid

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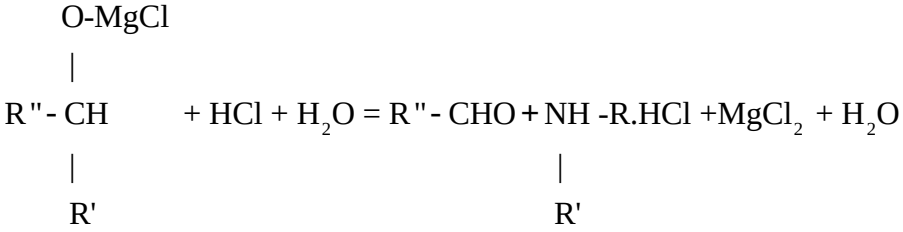
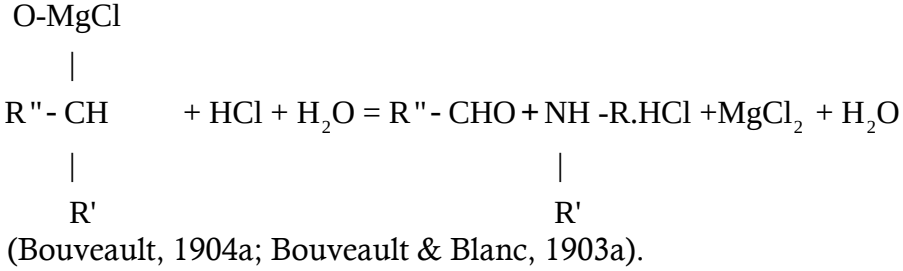
or carbonyl derivative completely blocked. Bouveault found that the most appropriate were the disubstituted formamides, which reacted according to



Treatment with a diluted mineral acid transformed the organometallic compound into the desired aldehyde:



(Bouveault, 1904a; Bouveault & Blanc, 1903a).

The next publication described in detail the Bouveault procedure for the synthesis of aldehydes (Bouveault & Blanc, 1904b). It was divided into four parts: (1) preparation of the raw materials, (2) operation procedure, (3) secondary reactions, and (4) aldehydes prepared by means of disubstituted formamides. Bouveault used as raw materials dimethyl, diethyl and piperidinyl formamide, and methyl and ethyl formanilide. The first three were prepared very easily and in large yield by heating an equimolar mixture of the base and the acid. Distillation provided formyl piperidine immediately; the lower homologues required a more complex process. Bouveault described formyldiethylamide as a colorless liquid, boiling at 68 ^{0}C (15 mmHg), miscible in water, and coloring litmus paper strong red. Methyl and ethyl formanilide were prepared by an alcoholic solution of formanilide with one molecule of the pertinent iodide, in a closed vase at 100 ^{0}C and treating the product with water and distillation. They boiled at 133-134 ^{0}C and 140 ^{0}C (20 mmHg), respectively (Bouveault and Blanc, 1904b).

The pertinent aldehydes could be prepared with any of these derivatives; the best yields were obtained with the aromatic formamides. The organomagnesium compounds used were based on isobutyl chloride, isoamyl chloride, chlorocyclohexane, bromobenzene, benzyl chloride, octyl chloride, nonyl chloride and *β*-phenylethyl chloride, C_6H_5-CH_2-CH_2Cl. The product of the reaction was treated with water acidulated with sulfuric acid; the aldehyde was present in the ethereal phase. Fractional distillation of the latter provided the aldehyde R-CHO, mixed with the alkyl chloride. The reaction produced several byproducts, for example, the hydrocarbon R-R and a small amount of a complex alkaline molecule (Bouveault & Blanc, 1904b).

Bouveault and Blanc described some of the aldehydes prepared from disubstituted formamides: valeraldehyde from the reaction of formopiperidide with isobutyl chloride-magnesium; isobutyl (boiling at 122 ^{0}C) from amyl chloride and dimethylformamide; benzaldehyde from bromophenyl magnesium and methylformanilide, etc. Decyl aldehyde, prepared from nonyl chloride, was a liquid boiling at 91 ^{0}C (11 mmHg); its semicarbazone melted at 102 ^{0}C (Bouveault & Blanc, 1904b).

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Plant extracts

Between 1895-1896 François Antoine Philippe Barbier (1842-1922) and Bouveault reported that the reaction between semicarbazide and the essence of lemon grass (*Andropagon citratus*) produced three semicarbazones melting at 135^0, 160 ^{0}C, and 171 ^{0}C. A more detailed study of the ones melting at 135^0 and 171 ^{0}C had led them to conclude that the essence contained at least two aldehydes differing between them on the location of the double bond and having an ethylenic stereoisomerism (Barbier & Bouveault, 1895, 1896c). Bouveault washed, dried, and pulverized the raw product of the reaction with semicarbazide, and then extracted the powder repeatedly with boiling ether (Bouveault, 1899a). The hot filtrate, upon cooling, deposited a mass of crystals melting a 135 ^{0}C. The new filtrate left on the filter a semicarbazone, which was washed with ether and then dissolved with alcohol. Upon cooling, the alcoholic extract deposited flaky crystals, melting at 171 ^{0}C, insoluble in cold alcohol and in ether. Bouveault found that the same products were obtained from the extracts of citral and of the aldehydes originating from the oxidation of licareol or geraniol, although in different proportions (Bouveault, 1899a).

Bouveault prepared the semicarbazone by three different procedures: (1) Reacting an alcoholic solution of the aldehyde with an equimolar mixture of semicarbazide hydrochloride and sodium acetate; (2) mixing an aqueous solution of semicarbazide hydrochloride and a solution of aldehyde in glacial acetic acid; and (3) using a neutral alcoholic solution of semicarbazide. The resulting semicarbazone was purified as indicated before and then reacted with citral (lemonal). The results indicated that the product was a mixture of two isomers melting at 164^0 and 171 ^{0}C, and crystallizing as needles and flakes, respectively. After a few additional tests, Bouveault concluded that the essence of lemon grass contained two isomers of lemonal, one stable, corresponding to the semicarbazone melting at 164^0, and another, unstable and corresponding to the semicarbazone melting at 171 ^{0}C; the first one transformed onto the second in an alkaline medium, and the opposite, in an acid medium. Bouveault added that although at present there were no procedures that allowed differentiating between stereoisomers and positional isomers; both lemonals could be represented by the formula $C(CH_3)_2$=CH-CH_2-CH_2-$C(CH_3)$=CH-CHO, 2,6-dimethyl-2,6-ol-8, and present ethylene stereo isomerization due to the group -$C(CH_3)$=CH(CHO) or $C(CH_3)_2$=CH-CH_2-CH_2-CH=$C(CH_3)$-CH_2-CHO, 2,5-dimethyl-2,6-ol-8. He believed there were serious reasons to accept the second configuration: (1) no aldehyde was known to have ethylene stereo isomerization, and (2) both lemonals were present in the essence of lemon grass, hence the corresponding oxime should also be a mixture of two isomers, as well as the resulting nitriles, a fact not confirmed by experience. In other words, the observed isomerism was due only to a displacement of the double bond (Bouveault, 1899ab).

Another work compared the alcohols rhodinol and citronellol (Bouveault, 1900a). Bouveault wrote that citronellol, $C_{10}H_{10}O$, was a primary alcohol corresponding to the unsaturated aldehyde citronellal discovered by Frank Despard Dodge in the essence of citronelle (Andropogon nardus) (Dodge, 1889). Dodge described it as a liquid boiling between 117^0-118 ^{0}C (17 mmHg), having relative density 0.8565 at 17.5 ^{0}C, rotatory power $[\alpha]_D = 4^020'$, and yielding citronellol by hydrogenation. Barbier and Bouveault discovered rhodinol in the essences of pelargonium and roses, mixed with geraniol (lemonol) $C_{10}H_{18}O$. Rhodinol was a colorless liquid boiling at 110 ^{0}C (10

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mmHg), relative density 0.874, and $[\alpha]_D$ varying between -2^0 and -4^0, depending on the sample. Strong oxidation of rhodinol yielded dimethyl acetone and *β*-methyladipic acid. Rhodinal was a very unstable aldehyde that transformed spontaneously into menthone, $C_{10}H_{18}O$ (Barbier & Bouveault, 1896b). Citronellal was a very stable aldehyde; its oxime was transformed by acetic anhydride into the corresponding nitrile. A solution of sodium acetate in acetic acid transformed it into *isopulegol*, an unsaturated cyclic alcohol. The chromic mixture oxidized this alcohol into *isopulegone*, $C_{10}H_{16}O$ (Bouveault, 1900ab).

Barbier and Bouveault also found that the chromic mixture oxidized rhodinol to rhodinal, an aldehyde that isomerized spontaneously and partially (Barbier & Bouveault, 1896c). Rhodinal yielded two isomeric semicarbazones, one melting at 115^0-116 ^{0}C and the other at 186 ^{0}C. The first one was very soluble in neutral solvents and was not decomposed by diluted acids; the second one was little soluble in alcohol and almost insoluble on ether, allowing its easy separation. Barbier and Bouveault identified the first as the semicarbazone of rhodinal and the second as the semicarbazone of menthone, the isomer of rhodinal. Diluted acids split it into menthone. Bouveault reported that the semicarbazone melting at 186 ^{0}C contained 62.07% carbon, 10.21% hydrogen, and 27.72% oxygen. A solution of this semicarbazone in alcohol of 93^0 had rotatory power $[\alpha]_D$ = 20' (tube of 2 dm) (Barbier & Bouveault, 1896c).

In his last publication Bouveault and Gourmand described the total synthesis of rhodinol as a proof of its constitution (Bouveault & Gourmand, 1904). They mentioned that Barbier and Bouveault had shown that a mixture of the two alcohols geraniol and rhodinol formed the largest portion of the essences of roses and of *Pelargonium odoratissimum*. The first one had a very pleasant smell and had been found in numerous essences; the second had been found only in the two essences mentioned above and for this reason had been given a the particular name of rhodinol (Barbier & Bouveault, 1896a). In this work they applied the method developed by Bouveault and Blanc to convert esters into the corresponding primary alcohols. This procedure had the advantage that in the case of the esters of acids αβ unsaturated it also led to the hydrogenation of the double bond (Bouveault & Blanc, 1903ab). Application of this procedure to ethyl geraniate CH_3-C(CH_3)=CH-($CH2)_2$-C(CH_3)=CH-$COOC_2H_5$ generated ethyl rhodinate. Bouveault and Gourmand described this ester as a colorless liquid, smelling like fruit and boiling at 115 ^{0}C (10 mmHg). Treated with sodium and absolute alcohol it released racemic rhodinol, $C_{10}H_{20}O$, boiling at 110 ^{0}C (10 mmHg) and having relative density 0.877. This alcohol smelled strongly like roses, it did not have rotatory power, and had the same properties of the rhodinol extracted from the essence of roses or the essence of pelargonium. Its identity and composition was further confirmed by preparing its pyruvate and semicarbazone, and comparing them with the same derivatives obtained from natural rhodinol (Bouveault & Gourmand, 1904).

Synthesis of primary alcohols

Bouveault wrote that methanol, ethanol, propanol, isobutanol, and amyl alcohols were easily prepared by distillation of wood or by the fermentation of glucose. All the remaining alcohols of the fatty series were hard to obtain. Four methods were available for preparing these alcohols; two of them, due to Charles-Adolph Würtz (1817-1884) (Würtz, 1862) and Charles Friedel (1832-1899) (Friedel, 1862), employed

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the corresponding acid as starting material, and the other two, the corresponding lower alcohol. In the first method the aldehyde R-CHO was reduced by means of the sodium amalgam or zinc and acetic acid; the aldehyde was first prepared by the Pyria method (calcination of a mixture of the calcium salt of the acid R-COOH with calcium formate). In the second method a chloride or anhydride of the acid was reduced with the sodium amalgam or the couple zinc-copper. This method was inefficient because in addition to the alcohol R-CH_2OH it produced the aldehyde R-CHO, and an ester of the acid R-CH_2-O-CO-R as byproducts. Both methods were hard to execute and had a relatively low yield (Bouveault, 1903a, 1904a).

The third method, proposed in 1899 by Marcel Guerbet (1861-1938), consisted in condensing an equimolar mixture of an alcohol with its alkoxide or with a different alcohol at high temperature in a closed tube (Guerbet, 1899). The fourth method was based on the reaction of 1,3,5-trioxane with organomagnesium derivatives (Grignard & Tissier, 1902):

R-Mg-Cl + CH_2O = R-CH_2-O-Mg-Cl

R-CH_2-O-Mg-Cl + H_2O = Mg(OH)Cl + R-CH_2OH

This procedure required the alkyl halide to be able to combine with magnesium and form an organomagnesium derivative, a condition not satisfied by the halide of ternary alcohols. Bouveault and Blanc selected the first two procedures because acids were the most available reagents (Bouveault & Blanc, 1903a, 1904a).

It was known that acids and salts could not be reduced to alcohols, hence it was indispensable to avoid that the reduction process be accompanied by saponification. For this reason, Bouveault and Blanc started their work using the reduction of fatty esters by means of sodium, under diverse conditions (Bouveault & Blanc, 1903a, 1904a). The methyl or ethyl ester was dissolved in ether exempt of alcohol and the solution put on top of a layer of water. Addition of the sodium in small pieces resulted in a lively reaction, the rate of addition was controlled to maintain the mixture in a boiling state and until all the sodium had dissolved. The NaOH formed dissolved promptly in the water layer thus avoiding saponification. The nascent hydrogen reduced the ester according

R-$COOC_2H_5$ + $2H_2$ = R-CH_2OH + C_2H_6O

R-$COOC_2H_5$ + 4Na + $3C_2H_6O$ = R-CH_2OH + $4C_2H_5ONa$

The mixture was then steam distilled; the first fraction was composed of ethanol (or methanol), followed by the new alcohol. The new alcohol was separated from the water by means of ether. The resulting mixture was redistilled to eliminate the residual water. The experiments with methyl caprylate (octanoate) indicated that more than 50% of caprylic acid had been converted to 1-octanol; the rest was sodium caprylate mixed with a small amount of the glycol C_7H_{15}-$(CHOH)_2$-C_7H_{15}, which distilled at about 200 ^{0}C (10 mmHg) and crystallized upon cooling. According to Bouveault and Blanc, this was a general process that could be applied to all the saturated fatty acids, except formic acid, that is, only to R-CH_2-COOH, R(R')CH-COOH, and (R)(R')(R)C-COOH. It was only necessary to modify the extraction process of the new alcohol, when its molecular mass became too high (Bouveault & Blanc, 1903a, 1904ab).

Since the amides held a close relation to the esters Bouveault and Blanc speculated that the above reaction could also be used to convert them into primary alcohols according to the equation (Bouveault & Blanc, 1904ab):

R-$CO-NH_2$ + 4Na + $3C_2H_6O$ = R-CH_2ONa + $3C_2H_5ONa$ + NH_3

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The experimental results justified this assumption: the reaction proceeded under the same conditions as with the esters, although with a much lower yield, especially due to the formation of the amide R-CH_2-NH_2. The preparation of amides was more difficult than that of esters and for this reason this potential procedure would be advantageous in very few cases. Bouveault and Blanc mentioned that the transformation of amides in alcohols was not a new process, in 1874 Icilio Guareschi (1847-1918) had reported the reduction of benzamide to benzyl alcohol and benzaldehyde using an HCl solution of the sodium amalgam (Guareschi, 1874). Afterwards, others had reported the reduction of acetamide to ethanol, of fencholenamide to the corresponding alcohol, the hydrogenation of amides to alcohols, of sebacic amide into 1,10-decanediol, etc. For their part, Bouveault and Blanc reported the transformation of the amides of caproic, pelargonic, and phenylacetic acids into their corresponding alcohol. They dissolved the amide in absolute alcohol and poured the solution over sodium located inside a flask provided with a refrigerated condenser. A lively reaction took place with release of ammonia. Once the sodium had disappeared, water was added, and the alcohol produced separated by steam distillation. The alcohol was detached from the accompanying water by agitating the solution with diluted HCl. Bouveault and Blanc used this procedure to prepare *n*-hexanol, *n*-nonanol, and 1-phenylethanol (Bouveault & Blanc, 1904ab).

Bouveault and Blanc reported that they had applied the above method to a series of aliphatic acids to verify if it applied to all of them. The results indicated that formic acid was the only exception (Bouveault & Blanc, 1904c). This experiment was carried on treating amyl formiate with sodium and amyl alcohol, to avoid the difficult separation of methanol and ethanol. The course of the experiment was the same as described above. No methanol was found in the aqueous and in the amyl alcohol layer; in addition, all the formic acid was found to be present as sodium formate in the alkaline layer. Application of the method to amyl acetate with amyl alcohol and sodium produced ethanol, but in very low yields. The reduction of 100 g of methyl butyrate with sodium and ethanol yielded 30 g of butanol, boiling at 116 ^{0}C. Reaction of this butanol with carbanile (phenyl isocyanate) yielded the phenylurethane as colorless needles, melting at 57 ^{0}C, and being very soluble in organic solvents, except petroleum ether. Methyl caprylate yielded 1-octanol, boiling at 96 ^{0}C (17 mmHg). Its acetate was a colorless liquid, smelling like fruits, and boiling at 98 ^{0}C (15 mmHg). Bouveault and Blanc reported the preparation and properties of several additional aliphatic alcohols, among them, 1-nonanol and 1-decanol (Bouveault & Blanc, 1904c).

Bouveault and Blanc also applied the method to the preparation of a variety of acids derived from the di- and triderivatives of acetic acid, (R)(R')CH-COOH and ((R)(R')(R")C-COOH (Bouveault & Blanc, 1904d). For example, to methylhexylacetic acid prepared from the caprylate of castor oil. This acid was a colorless liquid, boiling at 136 ^{0}C (17 mmHg) and relative density 0.9098 at 4 ^{0}C. The corresponding alcohol, methylhexylethanol (2-methyl-octanol-1) was prepared by reduction of ethyl methylhexylacetate. This alcohol was a sweet smelling liquid, boiling at 89^0-99 ^{0}C (16 mmHg) and relative density 0.8418 at 4 ^{0}C. Bouveault and Blanc also reported the successful reduction of hexahydrobenzoic acetate to hexahydrobenzyl alcohol (cyclohexylmethanol). This alcohol boiled at 82 ^{0}C (11 mmHg) and had a relative density of 0.946 at 4 ^{0}C (Bouveault & Blanc, 1904d).

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Application of the method to ethyldimethyl acetate yielded 2,2-dimethylbutane-ol-1, a colorless liquid, smelling like camphor, boiling at 135 ^{0}C, having relative density 0.844 at 4 ^{0}C, which could be cooled down to -15 ^{0}C, without crystallization (Bouveault & Blanc, 1904d).

Further publications detailed the application of the method to dibasic acids (Bouveault & Blanc, 1904e), unsaturated esters (Bouveault & Blanc, 1904f), esters containing the oxy function (Bouveault & Blanc, 1904g), acid alcohols and ketonic acids (Bouveault & Blanc, 1904h), etc.

This process was the subject of several patents, for example, US Patent 868252 (Bouveault & Blanc, 1907).

Saponification of nitriles

The need to saponify dimethylbenzonitrile led Bouveault to look into this reaction in detail (Bouveault, 1893). Various procedures were available for saponifying nitriles. The most general consisted in heating in a water bath a mixture of the nitrile with an alcoholic solution of KOH. Unfortunately, the process was very slow, had a poor yield, and produced the desired acid mixed with brown resinous substances hard to eliminate. In other procedures, the nitrile was heated with concentrated HCl in a closed tube. This method provided good yields and products relatively pure. Regrettably it was frequently necessary to heat the contents to temperatures higher than 200 ^{0}C, with the resulting decomposition of the nitrile. In addition, the tubes sometimes exploded at these high temperatures. Diluted sulfuric acid easily saponified the nitriles of the fatty series, but not so the aromatic ones (Bouveault, 1893).

None of these methods was appropriate for saponifying dimethylbenzonitrile. After trying different approaches Bouveault found an alternative handy procedure based on the transformation of the nitrile into the amide. For this purpose he dissolved the nitrile in sulfuric acid of 85%, left the mixture under heating for several hours in a water bath, and then poured it into cold water. The resulting amide precipitated practically pure and in almost theoretical yield. Bouveault found that with nitriles that did not dissolve in sulfuric acid of 85% it was necessary to repeat the process with acid of 90%. The process was inappropriate if this second stage also failed. The benzamide was then decomposed by addition of cold HCl, followed by a drop-wise addition of a concentrated solution of sodium nitrite (Bouveault suggested several alternatives for this process). The resulting benzoic acid was perfectly pure and the yield almost 100%. Bouveault believed that a very small amount of a nitroso derivative of benzamide, C_6H_5-CO-NH-NO, was also formed that eventually decomposed into benzoic acid and nitrogen; he failed in all his attempts to verify this phenomenon (Bouveault, 1893).

Bouveault used his method successfully with benzonitrile, α-naphthonitrile, and β-naphthonitrile (Bouveault, 1893).

Synthesis of aldehydes from alcohols

In 1903 Paul Sabatier (1854-1941 and Jean-Baptiste Senderens (1856-1937) published three papers reporting the catalytic action exerted by copper on primary alcohols (Sabatier & Senderens, 1903). They found that between 200^0 and 350 ^{0}C the alcohols were decomposed into the corresponding aldehyde with release of hydrogen, according to R-CH_2OH = R-CHO + H_2. At higher temperatures part of the aldehyde decomposed into the alkane and carbon monoxide, R-CHO = RH + CO. The same results were produced by nickel, but in a more reduced range of temperatures.

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Unfortunately, the operating procedure allowed preparing only small amounts of the aldehydes. In both cases, the reactor was a horizontal tube full with copper particles and heated to the desired temperature. The pertinent aldehyde was fed as a gas and the ensuing product collected in a condenser cooled by a mixture of ice and salt (Sabatier & Senderens, 1903).

Bouveault went on to investigate the possibility of conducting the reaction in an apparatus easier to control and allowing the conversion of any volatile primary alcohol into the pertinent aldehyde (Bouveault, 1908b). He found that these conditions were easily satisfied by a *vertical* reactor, made of a glass or copper tube of 25 to 30 mm diameter, heated electrically, and controlled by a rheostat. One end of the tube, reduced to 10 mm diameter, served to introduce the alcohol as a vapor. The copper was introduced as cupric oxide that was then reduced at 300 ^{0}C in the apparatus by means of hydrogen. The reduction process took about 8 hours in a tube 80 cm long. A rubber tube provided with a clamp controlled the flow of the aldehyde vapor. The exiting vapor, containing a substantial proportion of aldehyde, was directed to a distillation column. The aldehyde residue was recycled to the vapor generator. A reactor containing one meter of catalyst was able to produce about 500 g of aldehyde per 8 hours of work (Bouveault, 1908).

Bouveault found that the apparatus was not very efficient for aldehydes boiling above 200 ^{0}C because of their inherent thermal instability. Reducing the temperature of the catalyst column to 200^0 to 250 ^{0}C generally solved the problem. The catalysis was not so strong but the process was helped by the vacuum action produced by removal of the hydrogen produced.

In general, the distilled product contained between 50 to 80% of the pure aldehyde, depending on the rate of distillation. Bouveault was able to produce easily the saturated ten-carbon aldehyde (C_{10}), as well as phenylethyl aldehyde (Bouveault, 1908).

Secondary alcohols were found to easily yield the corresponding ketones. Alcohols containing a complex function, such as acyloins (α-hydroxyketones), were converted into diacetones without difficulty. *β*-Hydroxy esters were converted into *β*-ketone esters and hydrogen. Unsaturated alcohols were converted into the corresponding aldehyde and then hydrogenated into the saturated aldehyde (Bouveault, 1908).

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Este articulo no presenta conflicto de intereses.