Chapter 3

Applications of Carboxylic Acids in Organic Synthesis, Nanotechnology and Polymers

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Abstract

Carboxylic acids are versatile organic compounds. In this chapter is presented a current overview of the use of carboxylic acids in a different area as organic synthesis, nanotechnology, and polymers. The application carboxylic acids in these areas are: obtaining of small molecules, macromolecules, synthetic or natural polymers, modification surface of nanoparticles metallic, modification surface of nanostructure such as carbon nanotubes and graphene, nanomaterials, medical field, pharmacy, etc. Carboxylic acids can be natural and synthetic, can be extracted or synthesized, presented chemical structure highly polar, active in organic reactions, as substitution, elimination, oxidation, coupling, etc. In nanotechnology, the use of acid carboxylic as surface modifiers to promote the dispersion and incorporation of metallic nanoparticles or carbon nanostructure, in the area of polymer carboxylic acids present applications such monomers, additives, catalysts, etc. The purpose of this chapter is to emphasize the importance of carboxylic acids in different areas, highlighting the area of organic synthesis, nanotechnology and polymers and its applications.

Keywords: carboxylic acids, organic synthesis, nanotechnology, polymers, application

1. Introduction

Carboxylic acids are compounds with excellent chemical and physical properties, the most particular characteristics of this type of organic compounds, is their high solubility in polar solvents, as water, or alcohols, methanol, ethanol, etc. Chemical structure contains a carbonyl function (-C=O) and an hydroxyl group (OH), these groups interact easily with polar compounds, forming bridges of H, obtaining high boiling points. The carbonyl group (C=O) is considered a one of the most functional groups involved in many important reactions. The carboxylic acids are the most important functional group that present C=O.

This type of organic compounds can be obtained by different routes, some carboxylic acids, such as citric acid, lactic acid or fumaric acid are produced from by fermentation, most of these type of carboxylic acids are applied in the food industry. Historically, some carboxylic acids were produced by sugar fermentation. Synthetics route, there are different synthesis reactions such as reactions of oxidation from alcohols in the presence of strong oxidants such as $KMnO_4$, oxidation of aromatic compounds among other routes.

For example, citric acid is a carboxylic acid, can be obtained by different routes, synthetic, enzymatic and naturally occurring, is considered harmless and cheap, used in the food industry, because is non-toxic, has a thermal stability to the 175°C. Bian *et al.*, in 2017, reported the use of citric acid impregnated in porous material for the synthesis of Ni particles. They showed, that the presence of citric acid, is important in the dispersion of the Ni particles when are incorporate in porous materials, thus inhibiting the agglomeration [1].

Derivatives of carboxylic acid, as alkyl halides, esters, and amides, present different and important application in diverse areas. In the case of esters, these are obtained from the reaction between carboxylic acids and alcohols in presence of an acid catalyst usually H_2SO_4 with heat, this type of reaction is known as esterification. In the case of the amides, it is obtained in the presence of an amine, may be primary and secondary, with a carboxylic acid, in this reaction also can be used a catalyst and heat to accelerate the reaction.

Due to their chemical and physical characteristics, this type of organic compounds presents innumerable applications in the different areas, such as medicine, pharmacy, organometallic, polymer, nanotechnology, food, among others. Exist different reports, where study carboxylic acid, in the area organic synthesis, in 2008 Lazzarato *et al.*, reported the use of a carboxylic acid, salicylic acid type "aspirin-like", molecule obtained through a novel approach, where the phenol reaction to nitrooxy-acyl, this molecule present pharmaceutical properties [2].

In nanotechnology, the carboxyl acid, present in different applications, in 2016, Sáenz *et al.*, reported the use of organic carboxylic acids: tartaric acid, maleic acid, and malic acid, assisted the surface modification of multiple wall carbon nanotubes (MWCNTs) by ultrasonic radiation, with applications in the production of polymer nanomaterials. Finding that the modification with this type of carboxylic acids favors the dispersion of MWCNTs in the polymer matrix [3].

In the polymer area, also the carboxylic acids present important applications, in 2017 Oguz *et al.*, reported the obtain of "green composites" of Poli(lactic acid) and 10 wt % waste cellulose fibers, demonstrating that is easy, economical and sustainable its obtaining, this "green composites" presented improved tensile and impact properties [4]. Yasa *et al.*, reported the synthesis and characterization of polyol esters from iso-undecenoic and iso-undecanoic acids, using montmorillonite K10 clay as a catalyst, in presence of deionized water at a temperature of 250°C in an autoclave. This type of polymer presented applications like lubricant properties and good oxidation stability [5].

In general, the carboxylic acids presents applications in different areas, the propose of this chapter is to show a general panorama, about the applications of carboxylic in organic synthesis, nanotechnology, and polymer.

2. Use of carboxylic acids

2.1. Organic synthesis

The use of carboxylic acids in organic synthesis is a very wide area and the chemical transformations of this group to another have made it a very versatile functional group. These chemical transformations have seen improvement when they carry out through Green chemistry processes.

One of the methods to aim for energy efficiency (one of the principles of Green Chemistry) is to make reactions under microwave irradiation. The first report by this methodology was an esterification reaction with carboxylic acids and alcohols obtaining high yields in a short reaction time [6].

In addition to the esterification, the amidation reaction by a transformation of the carboxylic acids is also important because of the new covalent bond formed. This bond is of great importance because it can be found in a wide variety of molecules both in natural products and in small molecules with pharmacological activity [7–9]. Therefore, the development of new direct amidation reactions is important [10, 11]. One of those direct methodologies of amide formation is by reacting amines with carboxylic acids using toluene as a solvent [12] or using radiofrequency heating under neat conditions [13]. However this reagent-free pathway has limitations in the substrate scope.

On the other hand, Lanigan *et al.* reported a methodology in which they used simple borate esters that are efficient reagents for the direct synthesis of amides, using a variety of carboxylic acids and amines [14]. This reaction can be carried out openly to the air under acetonitrile reflux. The amidation product can be purified in a very simple way, in most cases, it only needs a simple filtration procedure using commercially available resins giving excellent yields (**Figure 1**). <http://pubs.acs.org/doi/abs/10.1021%2Fjo400509n>.

Another methodology in which microwave irradiation was used in the amidation reaction has proven to be an efficient synthesis of amides [15–18]. For example, Ojeda-Porras *et al.* [19] described a green methodology for the direct amidation (**3**) of carboxylic acids (**1**) and amines (**2**) using silica gel as a solid support (**Figure 2**).

In addition to the typical use of carboxylic acids in transformations other carbonyl groups, they can be used as a substrate in multicomponent reactions such as the well-known Ugi [20, 21]

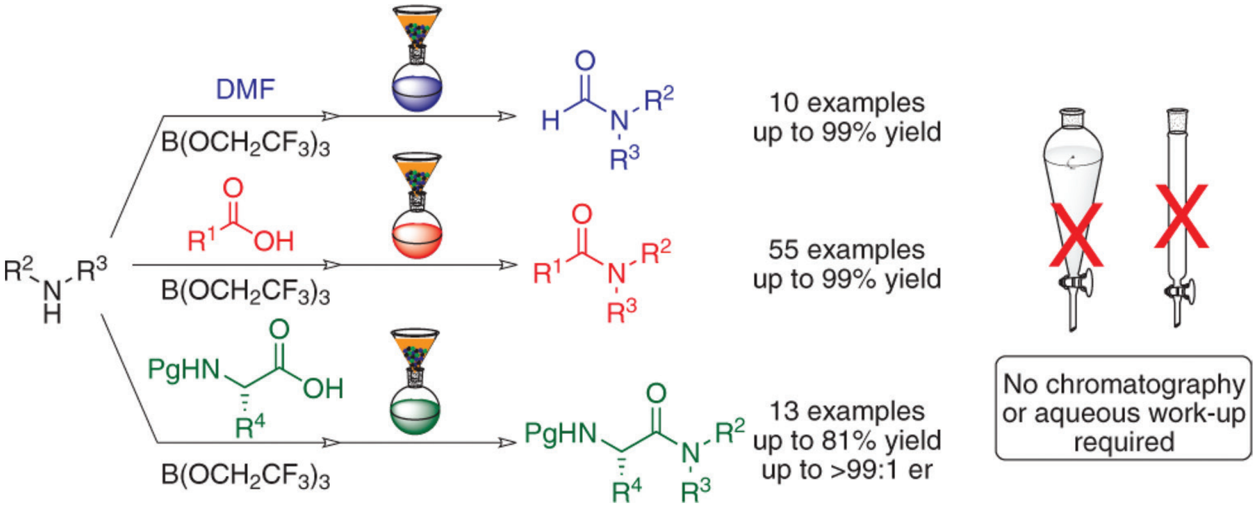

Figure 1. Carboxylic acids were used to obtain a variety of amides [12].

and Passerini [22, 23] reactions. An example is the reaction between an oxazolidine **4**, an isocyanide **5** and a carboxylic acid **6** to provides *N*-acyloxy ethylamino acid derivatives (**7**) (**Figure 3**) [24] so that it can be complemented with those structures that are produced by the well-established Ugi and Passerini reactions and they allow the generation of a chemical libraries.

As well, carboxylic acids can be used in organocatalytic reactions. As is in the case, carboxylic acid **11** can be used directly to obtain the *α*-hydroxy phosphonates **12**. The reaction was carried out in a simple way with a variety of aldehydes **8** and ketones **9** with trimethylphosphite **10** in the presence of catalytic amounts of pyridine 2,6-dicarboxylic acid **11** in water as a solvent. This generates a low cost and environmentally friendly methodology (**Figure 4**) [25].

Another example of using carboxylic acids as catalysts is by incorporating them into the structure of ionic liquids (IL). Jahani *et al.* described the condensation of 1,8-dioxo-octahydroxanthene **16** with 5,5-dimethyl-1,3-cyclohexanedione (**13**) and aldehyde derivatives **14** using carboxylic acid functionalized IL (**15**) under microwave irradiation (**Figure 5**) [25]. <https://creativecommons.org/licenses/by-nc-nd/4.0/> provides and offers the advantages of using IL and microwave irradiation are making the reaction an efficient and eco-friendly procedure.

Carboxylic acids present important applications in the pharmaceutical area, due to their chemical structure. Different methods have been developed for their detection, in medicines, in cosmetics, in food additives, etc. In 2015, Soham *et al.*, reported a selective chromogenic system, which not only can discriminate maleic acid vs. fumaric acid but can also differentiate

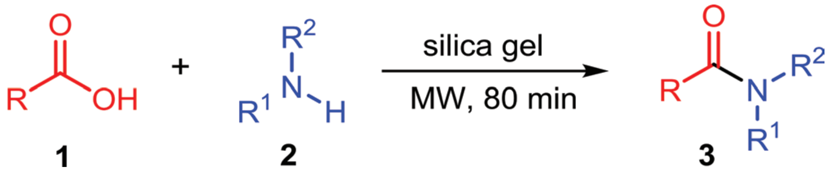

Figure 2. Amidation reaction via carboxylic acids and amines [17].

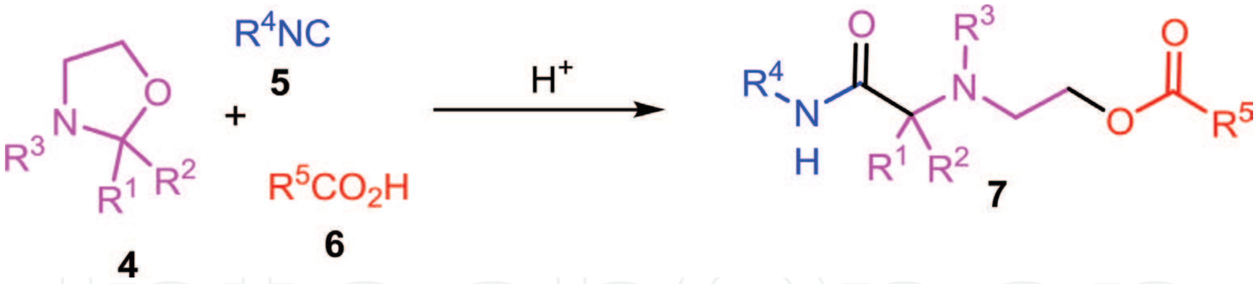

Figure 3. Use of carboxylic acid in a multicomponent reaction [24].

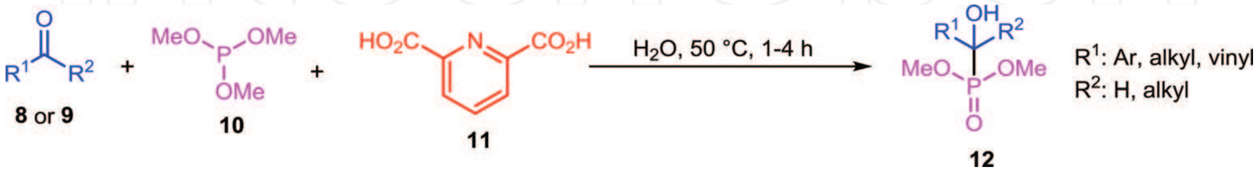

Figure 4. Carboxylic acid as a catalyst [25].

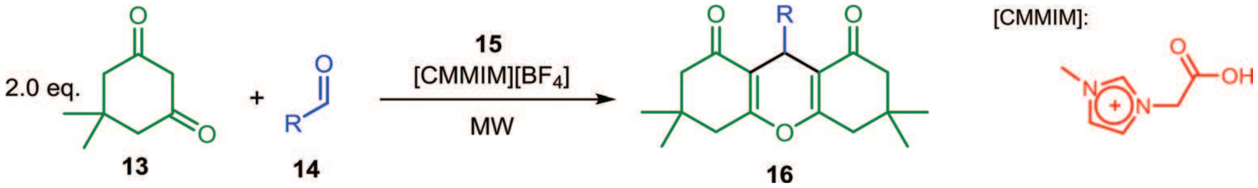

Figure 5. Carboxylic acid in ionic liquid in the multicomponent reaction [26].

maleic acid among diverse carboxylic acids. This method uses sharp colorimetric, as well as fluorogenic responses in both physiological conditions and food additives. The detection of this type of organic acids is very important. For example, maleic acid plays an important role in the organism because is a Krebs cycle inhibitor whereas, fumarate is produced in the Krebs cycle. Excessive consumption of maleic acid can cause different kidney diseases [27].

2.2. Nanotechnology

Recently carboxylic acids have been studied extensively, due to their important applications in the petrochemical, food industry, dyes, stabilizers and currently in nanotechnology [28]. This type of acid has become very important because it has been considered as a green solvent as part of the Eutectic Deep Solvents (DES), studied in 2003 by Abbott *et al.* [29] which are obtained by a mixture of hydrogen bond acceptor (such as a quaternary ammonium salt) and a hydrogen bond donor species (proton donating species). One of the most common acids is carboxylic acids, belonging to green solvents because they are not highly toxic and inexpensive [30].

One of the most important applications today of the carboxylic acids is the surface modification of the nanoparticles, this because during the synthesis of the nanoparticles by any methodology these tend to agglomerate due to the van der Waals forces and the absence of repulsive forces. In addition, oxidation at the surface of the nanoparticles causes instability which leads to aggregation [31]. One of the strategies to avoid this problem is to protect the colloidal particles with a passivating or stabilizing agent, which associates with the surface of the nanoparticles to keep them suspended, and therefore to prevent their aggregation [32]. In addition to acting as stabilizers, carboxylic acids also influence the solubility, reactivity, size and shape of nanoparticles [33]. Among other surface modifiers, the most used agents to stabilize the surface of the nanoparticles are polyvinylpyrrolidone (PVP), chitosan, starch, cellulose, and gelatin. Carboxylic acids serve as stabilizers for the preparation of nanoparticles, due to the carboxyl group provides coordination to the nanoparticles surface and therefore they stabilize. An example of this is oleic acid, which is widely used for the stabilization of nanoparticles, as well as for controlling the size and morphology of nanoparticles [34]. In this sense in 2008 Yang *et al*., obtained nanoparticles of Fe_3O_4 with sizes of 6–30 nm using oleic acid as surfactant or surfactant, this group of researchers functionalized the nanoparticles with carboxylic acids obtaining acid catalysts for the hydrolysis of carbohydrates, being able to observe that the acid functionalization can have large advantages in producing more active catalysts and thus an application in green processes [35]. On the other hand, Cabello *et al.* were able to surface functionalize multiwall carbon nanotubes using acetic acid and aniline, assisted by ultrasound, demonstrating the hydrophilic behavior of carbon nanotubes [36].

Hojjati *et al*., modified TiO_2 nanoparticles with carboxylic acid followed by polymerization with acrylic acid to obtain a well-dispersed nanoparticle in polyacrylic acid [37]. Armenalo used the carboxylic acid as a solvent to obtain CuS particles, finding several advantages with the use of this solvent because it favors the hydrolysis of the C-S bond thus producing a fast CuS supersaturation and a high speed of nucleation, favoring the growth of the particles and prevents agglomeration of the particles [38]. Qu *et al.* studied the chemical modification of nanoparticles of TiO_2 with carboxylic acids by the solvothermal method finding improvement in the photovoltaic performance of the TiO_2 nanoparticles despite being coated with carboxylic acid [39].

In other studies, it has been shown that the use of carboxylic acid as a surface modifier of nanoparticles can be easily redispersed in diverse matrix or solvents and improves properties as antibacterial activity [40]. In recent years, inorganic nanoparticles have been widely studied due to the excellent properties that they provide, due to their large surface area, emphasizing applications such as optical, catalytic, electrical, sensing, transport, magnetic, thermal conductivity, electromagnetic. These properties are the result of the large surface area that they possess. Metals such as gold, silver, palladium, and copper have been used to make inorganic nanoparticles of various shapes and sizes [41, 42]. The procedure and the conditions of synthesis of the nanoparticles directly influence its shape and size.

A wide variety of methods have been developed to synthesize metallic nanoparticles with different morphologies, as, nanotubes, nanodisks, nanofibers and others. In general, these procedures are classified into three groups: chemical methods, physical and biological methods.

Chemical methods are the most used, due to their ease of climbing [43]. The chemical reduction of metal salts in solution is the most commonly used method [44]. According to Slistan, the chemical reduction allows adequate control of the size, size distribution, and shape of nanoparticles [45].

In aqueous systems, the reducing agent is added or generated in situ, among the most commonly used reducing agents are sodium borohydride, hydrazine, and dimethylformamide, however in recent year's nontoxic and equally effective substances have been used, such as sodium citrate and glucose [46]. On the other hand, in non-aqueous systems, the solvent can also act as a reducing agent [47], such solvents can be alcohols such as polyethylene glycol, glycerol, and ethylene glycol, through which colloidal nanoparticles are obtained [48]. The advantage of these systems is that addition of reducing agents is not required, even synthesizing at room temperature [49]. Physical methods include electrochemical methods, laser ablation, thermolysis, microwave irradiation, and sonochemistry. For example, the thermolysis method involves the decomposition of solids at high temperature; through this process it is possible to obtain particles smaller than 5 nm [43].

Biologicals methods are developed using a metal salt and a reducing agent, which may be microorganisms, enzymes or plant extracts [49].

However, in general, the nanoparticles obtained by any methods tend to agglomerate due to the absence of repulsive forces and the forces of attraction of van der Waals [47]. Another common characteristic of metallic nanoparticles (Ag, Cu, etc.) is the oxidation of the surface causing instability of the nanoparticles and deriving in the aggregation of the same [31]. As a strategy to avoid these two major problems, the nanoparticles are modified superficially, to keep them stable in an aqueous solution and therefore to prevent their aggregation [50]. In addition to acting as stabilizers, surface modifiers also influence the solubility, reactivity, size, and shape of nanoparticles [33]. The surface modification of inorganic nanoparticles has today attracted attention, because they can be incorporated perfectly into some polymer, ceramic or metal matrix, improving the interaction between the two phases (the dispersed phase refers to the inorganic nanoparticles and the continuous phase is referred to the metallic, ceramic or polymer phase) formed nanocomposite or hybrid materials, combining the properties of the two phases [51, 52].

There are several types of surface modification such as chemical treatments, synthetic polymer grafts, the ligand exchange technique, among others; modification by chemical treatments may include reactions with metal alkoxides, carboxylic acid epoxides, silane coupling agents, among others; this being a convenient method to avoid the agglomeration of the nanoparticles and thus improve the dispersion [51], to achieve the surface modification of nanoparticles has been used ultrasonic irradiation as a technique that obeys the principles of green chemistry, because it reduces the use of solvents as well as energy. Another benefit of this technique is that the reaction mixture can be heated rapidly and uniformly, resulting in a shorter reaction time and a complete interaction avoiding the production of by-products [53].

Nanoparticles can be surface modified with adsorption of polymers on the surface, is one of the simplest methods to improve the dispersion of nanoparticles in aqueous systems. Nanoparticles with a hydrophilic behavior can be dispersed in polar solvents by modifying them with anionic or cationic polymeric dispersants. These dispersants generate repulsive forces between the particles and increase the dispersibility of the nanoparticles. In this case, the polycarboxylic acids, trioctylphosphine (TOPO), oleic acid and amines are examples of surfactants that modify nanoparticles of Al_2O_3, Fe_2O_3, TiO_2 and that can even be added during the synthesis of the nanoparticles [54].

The nanoparticles can also be functionalized with organic molecules with biological functions, e.g., lipids, vitamins, peptides, and sugars, in addition to other macromolecules such as proteins, enzymes, DNA and RNA. The combination of inorganic nanoparticles and biomolecules allows the use of these in biological systems because they combine unique properties for applications such as molecular recognition [55].

Another very important methodology found within the principles of green chemistry is the use of plasma to modify the surface of nanoparticles. Plasma surface modification is an effective and economical surface treatment technique for many nanoparticles.

This is a relatively simple, fast and dry method which has been used to modify the surface chemistry of different nanoparticles. It has also proved to be a versatile method since it allows the use of gases and/or organic molecules, whereby the surface modification can be adjusted to specific requirements, in other words, a particular functional group can be chosen.

This technique was originally implemented to modify the polymer surfaces, but in recent years has been used for the treatment of different nanoparticles [56]. The principle of the plasma polymerization technique is the creation of ionized and radical molecules by the bombardment of an electromagnetic field. These molecules and radicals can react with the surface of the substrate by erosion, removal, and deposition. As a result, the surface properties of the substrate will be modified.

Several organic molecules such as acrylic acid, pyrrole and styrene have been used in plasma to modify nanoparticles of zinc oxide, alumina and carbon nanofibers, respectively [57]. By this process it is possible to form a thin layer ranging from 1 to 3 nm in thickness.

The analytical methods used for characterizing the obtained nanoparticles are transmission electron microscopy (TEM) for size and shape determination, dynamic light scattering, fluorescence spectroscopy. Furthermore, binding of ligand molecules to metal nanoparticles can be probed by surface-enhanced Raman scattering.

Silver nanoparticles are recognized with antifungal and antibacterial properties and have applications in biosensing, antivirals against HIV-I, in water purification systems and paint products. In case of Au nanoparticles, these are used in cancer diagnosis and therapy, antiviral and antibacterial, MRI, biosensing applications. Magnetic nanoparticles have antimicrobial properties and are used in biomedicine such as drug delivery, magnetic resonance, and cancer treatment. The uses of TiO_2 nanoparticles that are also antimicrobial are in skin care products, nanomedicine, photocatalysis, gas sensor, wastewater to eliminate organic and inorganic pollutants. ZnO nanoparticles also have antimicrobial and anticancer properties, used in cosmetics, medical fillers, electronic and optoelectronic devices and gas sensors. The main applications of the nanoparticles of Al_2O_3 are in drug delivery, in membranes to eliminate pathogenic microorganisms, antimicrobial applications, removal of heavy metals from wastewater, in catalysis and in gas separation processes. On the other hand, the applications of SiO_2 nanoparticles are in biosensing, also serve as a carrier for antimicrobial applications, drug delivery, and tissue engineering [53].

Carboxylic acids are currently used as surface modifiers in carbon-based nanostructure: carbon nanotubes, single wall and multiple walls, graphene, nanofibers, etc., with the purpose of improving the dispersion in polar solvents such water, ethanol, methanol, ethyl acetate, etc. This type of superficial modifications can be carried out through different alternatives making use of green chemistry, which recommend the use of sustainable activation energies such as ultrasound, microwaves, plasma, that helps to reduce energy consumption and decrease the time of reaction in the surface modification.

2.3. Polymer

The carboxylic acids present applications in the obtaining of polymers, acting as monomers, additives, initiators, catalysts, dopants, etc. Currently, an area of great interest is the production of acidic polymers, with different applications, for example in electronic area required that present characteristics such as electron donors, high solubility in aqueous solvents, etc. [58].

As additive the carboxylic acids have been studied. In 2017, it was reported the study of a series of linear carboxylic acids whit different chain lengths of 6 trans-2-hexanoic acid carbon atoms (CA-6), trans-2-decanoic acid (CA-10), 9-tetradecanoic acid (CA-14), used as halogen-free additives-solvent, considered a sustainable and viable process useful for the production of polymeric films whit optical properties, whit potential application in solar cells. The conclusion of the study showed that increasing the length of the carboxylic acid chain changes the topology of the polymeric film [59].

Recent studies reported the use of acids polymers as dopants, to access and stabilize the electrically conducting states of conducting. The acids polymers are used for replace small-molecules acids as: poly(acrylic acid), poly(styrenesulfonate) (PSS), and poly(2-acrylamido-2-methyl-1-propanesulfonic acid), (2-acrylamido-2-methyl-1-propanesulfonic acid) (PAAMPSA), because its chemical nature, helps to stabilize the conduction of the polymers, in conclusion, the presence of an excess of carboxylic acid in the chemical structure promotes good dispersion, thus stabilizing the electric nature of the doped polymers [60].

In 2012 Shi *et al.*, reported the obtaining of two new blue transmissive donor-acceptor electrochromic polymers: a polymeric material synthesized by alternating copolymerization route and another random copolymerization, demonstrating that this type of polymeric materials having characteristic as higher water solubility. The results of this study, show that these polymeric acids, present electrochromic properties [61].

Recently Mohammadifar *et al.*, reported the reaction of cationic polymerization at room temperature and solvent free to obtain polyglycerol, the polymerization is classified as green polymerization, in this type of polymerization, citric acid participates as a donor of proton, promoting polymerization, it was reported that this type of polymerization does not require a purification process which indicates that the process is very sustainable, these types of polymers may be potential candidates for biomedical applications [62].

There are different types of polymer acids, natural or synthetic, for example, polylactic acid presents applications as polymeric acid antibacterial, due to its physical and chemical characteristics, the polylactic acid can be modified or incorporated whit other polymer matrices and form composites, it also presents high biodegradability and biocompatibility, which makes it a sustainable material [63–65].

Poly (methacrylic acid), is a peculiar material, its chemical structure consists of a polar backbone where the carboxylic acid is and rest of the structure is no polar. In 2017, Robin *et al.*, reported the study of behavior rheological of concentration of the poly (methacrylic acid) in aqueous solutions and influence in viscosity [66], the purpose of this study is know the physic-chemical of the polymeric material and to be able to formulate different composites, concluding that the poly (methacrylic acid) in aqueous solutions present a rheological behavior controlled by the balance between in the different interactions intramolecular as hydrogen-bonding [66]. Also the poly (methacrylic acid) is considered a biodegradable and sustainable polymeric material, used for the obtaining of biomaterials. Poly (methacrylic acid) brushes are highly susceptible to swelling in aqueous solution due to ionization of carboxylic groups presents in their chemical structure [67].

In general, the applications of carboxylic acid in the polymer are due to the presence of a polar group that helps solvate in aqueous systems, facilitating its processing.

3. Conclusion

In conclusion, the carboxylic acids have been widely applied in different areas, highlighting organic synthesis, nanotechnology and polymers, have been used in basic applications until relevant application. In organic synthesis, carboxylic acids can act as an organic substrate, reagents in reactions "*one step*" which are considered "green reactions" in some cases, also are used as catalysts, presents activity in substitution, addiction, condensation, polymerizations and copolymerization reactions. Actually, the research in organic synthesis is directed toward green reactions, easy, fast, economical, sustainable processes, the carboxylic acids are reagents that present a high reactivity, due to the chemical nature of the carbonyl group. In nanotechnology, the carboxylic acids are used as modifiers substrate in surface modifications of the nanostructure of carbon: CNT's or graphene, the proposal to obtain a polar surface thus improving the dispersion of the nanostructure of carbon in different polar matrices. The chemical nature of the carboxylic acids allows to carry out this type of application. Currently, in the area of polymeric materials, the carboxylic acids have been demonstrated that present important application as soluble polymer, degradation polymeric processes, obtain of composites and hybrid, a hydrophilic polymer, etc. It is considered that the application of the carboxylic acids is due to natural chemical, specifically by hydrophilic characteristic provided by the functional group. The research on the use of carboxylic acids, is very interesting, in this chapter were described some recent report. However, there are still vast challenges within this field that remain to explored.

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