Chapter - II
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INTRODUCTION

A number of organic compounds have been synthesized through conventional chemical methods at different conditions. Various research efforts have been and continue to be directed towards the development of processes to synthesize many organic compounds. Electroorganic chemistry is a new sub-field of chemistry, which permits to produce a very large number of chemical compounds.

Drug synthesis is a fast growing field and the number of compounds generated daily by the pharmaceutical industry is continuously increasing. The nature of the pharmaceutical business is changing rapidly. Time line and quality of results are becoming more important to improve the research and development for pharmaceutical companies. The necessity of developing new experimental strategies and analytical methods for the synthesis of these compounds become a real challenge.

Electrochemistry is the name given to the study of electrode reactions not only in batteries but also in the synthetic processes and general redox reactions of molecules [1].
Electrochemistry is expected to be used in many industrial processes in the future science and it generally leads to lower emissions of pollutants.

2.1 Electroorganic synthesis

Electroorganic synthesis can provide an exciting alternative to traditional organic synthesis. Oxidation or reduction reaction steps which are difficult to be operated in traditional routes, may proceed more easily and efficiently with electroorganic synthesis. Greatly simplified product separations, selective transformations and reduced waste can also be achieved with electroorganic synthesis [2].

Every electroorganic synthesis should be preceded by a measurement of the dependence of the electrolytic current on the potential of the working electrode for the given substrate and for a given composition of the solution to be electrolyzed. The application of electric current for preparing organic substrates had already begun 150 years ago [3]. At that time, Faraday attempted to oxidize electrolytically, the salts of aliphatic acids for the formation of corresponding alkanes. The actual beginning, however, is considered to be the year 1849, when Kolbe interpreted the above reaction and used it purposefully in the synthesis of alkanes. In 1898, Haber prepared phenyl hydroxylamine and aniline selectively by electrolytic reduction of nitrobenzene, he found that phenyl hydroxylamine results at less negative potentials and four electrons per molecule of nitrobenzene are consumed in its formation. When the reduction of nitrobenzene was performed at more negative potentials, aniline was prepared with the consumption of six electrons. In this way, a discovery was made which had a decisive importance for the further development of electroorganic synthesis [4].
The practical performance of electroorganic reactions was made easier by the potentialstat, constructed by Hickling in 1942. This device, when working with a three-electrode system, automatically keeps the potential of the working electrode at the required constant value with a reference electrode. In consequence of this technical innovation, a relatively rapid development of organic electrosynthesis was initiated in the mid 1950s and has lasted until now with the development of spectral and electroanalytical procedures as well as that of more advanced separation and isolation methods.

The importance of electrosynthesis of this "old - new" discipline for the present industrial society may be confirmed by the engineering solution of the consumption of highly efficient working cells. However, the developments in the 1980s proved that the most suitable field of application is the preparation of relatively small quantities of valuable fine chemicals. The famous method used in the nylon synthesis is more or less an exception. The discipline resulting in this way and the electrosynthesis makes use of the electrolysis in liquid media for preparing organic compounds or preparing reagents for further application in organic synthesis.

In its simplest form, an organic preparative reaction can be compared with a chemical reaction, which is followed by the isolation of the required product. In practical performance of both a laboratory preparation and an industrial process, the chemical reaction is often not completely satisfactory and convenient. The reaction need not necessarily follow the required path and may lead to side reactions and to the formation of side products, isomers and polymers. The literature concerning preparative procedures of organic chemistry published as early as in the first decades of this century,
point to the fact that, in oxidations and reductions, electrosynthesis could be more convenient than classical organic synthesis [5,6]

Electrons are the purest and cleanest reagents in the world. Direct transfer of electrons to or from a target molecule can perform reduction or oxidations respectively, without spent reagents complicating isolation or producing a waste stream. In addition, the electrosynthesis provides unique mechanistic pathways and thus different selectivities from traditional organic synthesis. In some cases, oxidizing or reducing power can be controlled by the electrode potential as well as the functional group differentiation.

Using electrochemical techniques, an initial screening can show whether or not a compound is electronegative and at what voltage. We can also estimate how many electrons are involved in the process and assess the relative stability of the intermediate formed by electron transfer. This analysis suggests the likely success of an electrochemical approach.

Electroorganic approach has currently fascinated academicians and industrial researchers, because of its high potential prospects for industrial venture [7].

Electroorganic chemistry is a multidisciplinary science overlapping the vast field of organic chemistry, physical chemistry, biochemistry, chemical engineering and material science. As a branch of organic chemistry, its principal aim is to enhance synthetic possibilities for academic and industrial ventures. In the present context, organic electrochemistry is of relevance to the synthesis of organic compounds, nature of electron transfer process and investigation into the electron generation and study of transient intermediates [8]. Many electrochemical methods, e.g., polarography and cyclic
voltammetry can be used to elucidate the mechanism of the electrochemical reactions and to select the reaction parameters, on rational grounds [9-12].

Over the past 25-30 years, the use of electrochemistry as a synthetic tool in organic chemistry has increased remarkably [13-15]. According to Pletcher and Walsh [16] more than 100 electroorganic synthetic processes have been piloted at levels ranging from a few tons up to more than 100 tons. A broad spectrum of applications of electrochemical methods in organic synthesis is increasing their use in the pharmaceutical industry [17,18].

In recent years, the number of investigations of organic electrochemistry has been increasing. The electrochemistry affords a facile and precise way to generate highly energetic intermediates via control of the electrode potential. It is important to note that, one electron exchanged over a potential difference of 1 volt amounts to injecting 1 eV in a molecule, i.e., approximately 23 kcal/mole. Owing to the possibility of performing electrochemistry over a potential difference of several volts, it is easily perceptible that the method may involve energies comparable to those of most chemical bonds and most activation energies. Thus highly energetic intermediates may be generated under mild and precisely controlled conditions. Another useful aspect of electrochemical generation of intermediates is related to the current flow through the cell.

Indeed, the current is a direct measure of production rate and also an important parameter in product selectivity. The cost of electricity is foreseen to increase less rapidly than that of traditional chemicals. For an organic chemist, the study of electrochemistry also gives the spin-off benefit that many of the electroanalytical results
may be useful for investigations of ordinary chemical reactions. Chief advantage of electrochemical reactions compared to chemical one is the effective contribution to pollution control [19-22], because the electron is a non-polluting reagent and electrochemical reactions are easy to control automatically.

2.2 Electrocatalytic hydrogenation

Electrochemical technology comes a long way in its applications to synthesis of chemicals. The benefits afforded by the electrochemical route include precise and easier control of reactions, low operating temperatures, minimum waste by-products and reduced running cost. Fast developing electrochemical engineering and electrolytic hydrogenation help in developing catalytic specific electrodes with better selectivity enhancing their utility in electrosynthesis.

Successful electrosynthetic process depends on finding electrode materials, reaction selectivity and current efficiency for the intended chemical change. For large scale industrial processes, the overpotentials may also need to be low, while certainly the electrode materials must be resistant to corrosion and must maintain their performance throughout the service life of the cell.

It has long been known that trace metal ions in the catholyte can lead to detrimental changes in the cathode surface. For example, low levels of Ni\(^{2+}\) or Fe\(^{2+}\) in solution can lead to deposition of the metals and hence an increase in hydrogen evolution [23]. Recently, it has been recognized that the addition of low metal ion concentration to the catholyte in some systems, forms continuously renewed reproducible surfaces [24, 25].
In organic synthesis, catalytic hydrogenation is an important procedure because it commonly permits selective reduction under very mild conditions, than compared to those used for electron transfer initiated reduction using redox reagents. In comparison, electrocatalytic reductions are seldom attempted although they offer the possibility of very selective reduction at much less negative potentials than when the initial step is electron transfer. The literature does have some potentially useful examples of electrocatalytic hydrogenation such as phenol to cyclohexanol on rhodium [26], acetophenone to ethyl benzene on platinum [27] and estratetraene to 8-α-estradiol methyl ether on nickel or palladium [28]. The electrocatalytic hydrogenation is having more selectivity to obtain unusual products than to reduce energy consumption.

Electrocatalytic hydrogenations have been carried out since the beginning of the century [29-32]. It has been suggested that electrochemical reductions in aqueous media on cathode of spongy transition metals, might involve reaction of unsaturated substance with adsorbed hydrogen [33]. This has been confirmed in a number of mechanistic studies of electrocatalytic hydrogenation on Raney nickel [34-36], nickel black [37,38] and Raney ruthenium - iridium surfaces [39].

The electrocatalytic hydrogenation of an unsaturated organic molecule in aqueous or mixed aqueous organic media involves the formation of chemisorbed hydrogen at a cathode with a low hydrogen overvoltage (transition metal) by reduction of water or hydronium ion. Hydrogenation reaction between the adsorbed substrate [(Y = Z) M] and the chemisorbed hydrogen can be represented through the following equation:
Electrochemically generated hydrogen is an attractive process, which avoids the necessity for a supply of hydrogen gas. A number of catalytic cathode surfaces have been examined including Pb, Ni, Pt, Pd, and Rh for the reduction of acetophenone [40], phenol [41], alkenes [42], glucose [43,44], diamines and ammonitriles [45,46], benzene, aniline and nitrobenzene [47-49], aldehydes [50] and enones [51,52]. The electrocatalytic hydrogenations of soyabean oil and edible oils have also been carried out in recent years [53-55]. Nickel surfaces have been most frequently used because of the relatively low cost and the possibility of preparing a high surface area coated by Raney-nickel process. Raney nickel particles can be attached to the cathode [56] then activated by alkali treatment [57]. This type of surfaces has been employed for the electrochemical hydrogenation of polycyclic hydrocarbons, nitrobenzene, glucose and enones. It has been made of teflon coating for attaching nickel particles more firmly to the cathode for the reduction of enones [58]. However, the most practical finely divided nickel surface is one prepared by electrochemical deposition from a nickel salt solution. Such a nickel black deposited on copper was used by Ischiwata [59] for the electrochemical hydrogenation of benzalacetones. Lam and Pletcher [60] have introduced the concept of a continuously renewed nickel surface on carbon, where a nickel salt in the electrolyte is reduced with the organic substrate.
The study of electrocatalytic hydrogenation on surfaces that are reproducible may be fully characterized. We also wished to prepare the catalytic surface \textit{in situ} in the electrolysis cell by using a catholyte, which contains a low concentration of the appropriate metal ions. It was hoped that, such procedures lead to reproducible surfaces in their equilibrium state for the electrolysis conditions to surfaces and perhaps the more active catalysts. This catalyst would be prepared and used in an oxygen free medium at potential, where the deposit is cathodically protected and the surface would be continuously renewed by low rate deposition of further catalyst. Nickel surfaces are cheap, widely used in heterogeneous catalysis and have been used with some success in organic electrosynthesis. Further more, the new generation of hydrogen evolution cathodes is based on nickel electrodes and they operate at very low overpotentials [61-63].

It may be noted that, nickel has been in use for the electrocatalytic hydrogenation of several functional groups. De Hempitme and Coworkers [64,65] have reported that the synthetically most useful procedures are used on Raney nickel [66-71]. Filardo \textit{et al.} [72] have also described an electrochemical procedure using DMF for the preparation of nickel catalyst for high pressure hydrogenation.

Electrocatalytic hydrogenation modifies the overall rates of an electrochemical rather than a chemical reaction. Thus interested in dealing with electrochemical reaction is selectivity, yield and efficiency which are maximized in the electron transport that will take place at the electrode/ electrolyte interface. Electrode potential may be used as the driving force for reaction rather than temperature and pressure.
Modern organic electrochemist intends to combine the search for new reactions with the aim of optimizing the efficiency and useful synthetic procedures. Economical as well as environmental pressures has led chemists to attempt to increase the selectivity of the reactions, while avoiding the formation of polluting by-products and using the more simple reaction conditions.

In this context, the importance of electrocatalytic hydrogenation has been increasing for the valuable advantages, notably in terms of selectivity and efficiency. Indeed, low valent metal electrodes like nickel, lead and palladium can react with many functional groups, thus allowing numerous C-C bond forming reactions.

Electrocatalytic hydrogenation has the following advantages over conventional catalytic hydrogenations. Firstly, the kinetic barrier due to splitting of hydrogen molecule is completely bypassed, as is the transport of the poorly soluble hydrogen molecule. Thus the hydrogen gas, elevated temperature and pressure can be avoided. Secondly, the fact that a cathodic potential is applied, the catalyst in electrocatalytic hydrogenation can in some cases diminish the adsorption of positions [73-75].

The advantage of electrocatalytic hydrogenation over catalytic hydrogenation and direct electrochemical reduction make it a method of general interest for the hydrogenation of functional groups in organic molecules. Electrohydrogenations in synthesis have been reported at various high area catalytic electrodes such as nickel [76-96], platinum [97-100], palladium and rhodium [101-110]. The electrohydrogenated functional groups include triple bonds, double bonds, aromatic rings, heterocycles, nitro groups and hydrazines.
The efficiency of electrocatalytic hydrogenation is determined by the competition between hydrogenation and hydrogen evolution. The active rates of these two processes are affected by the strength of bond to be hydrogenated and by a number of factors, which enhance the adsorption of organic substrate. Hydrogenation is dependent on electrode surface, substrate concentration, current density, nature of solvent, reaction temperature and supporting electrolyte.

This should convince all that electrochemistry provides the real synthetic method. It is commonly said that, the electrochemical method requires complex and expensive devices. However, important progress has also been making it simpler and not too expensive. Large number of electrochemical reactions is now run at constant current, thus requiring very simple electric power supplies compared to those used for controlled potential reaction [111]. In addition, undivided cells are increasingly employed, thus avoiding the use of separators, which are not efficient when used with polar aprotic solvent and require the use of large amounts of supporting electrolyte. The metallic ions derived from the anode increase the conductivity and can also influence the reactivity of the chemical intermediates. It has allowed the use of quite simple electrolytic devices, which can be more easily scaled up than divided cells. This device can be used for direct as well as catalytical reactions [112].

2.3 Electrochemical carboxylation

Many studies have been devoted to the electrochemical reduction of organic halides in aprotic solvents in the presence of electrophiles with the aim of forming carbon - carbon or carbon - heteroatom bonds [113, 114].
In many cases, the organic halide is less easily reduced electrochemically than its coreagent, or the derived intermediate (radical or anion) reacts faster with a proton (or hydrogen) donating molecule (residual water, solvent, organic supporting electrolyte) than with the electrophile.

Some authors have attempted to overcome these drawbacks by using low valent metal electrodes [112, 115, 116]. Electrochemical approaches have greatly increased the selectivity of many reactions. However, even these improved methods suffer constraints imposed by the electrochemistry itself: (1) most frequently reductive electrolysis is carried out in an undivided cell at cathode surface. (2) Electrolytes are frequently performed at controlled potential and constant current density.

Most of these restrictions, notably the anolyte - catholyte separation, can be suppressed by the use of consumable anode made of a readily oxidized metal. Anodic oxidation of metals has been used in many electrochemical methods leading to organo metallic compounds from their carbanions [117].

Silvestri [118, 119] and Perchon [112, 120] reported that electrochemical carboxylation of organic halides for carbonyl compounds readily takes place under an atmospheric pressure of carbon dioxide to give the carboxylic acids in high yields when a sacrificial anode, such as magnesium or aluminum metal is used in the electrosynthesis. Tokuda et al. [121-127] already reported efficient electrochemical carboxylation of various organic substrates using a magnesium anode.

Electrochemical carboxylation is one of the most useful methods for the fixation of carbondioxide into organic substrates. Even in the atmospheric pressure of
carbondioxide, electrochemical carboxylation took place efficiently by the use of a reactive metal anode such as magnesium, aluminum and zinc [112, 119]

An important development in electroorganic synthesis has been achieved with the electrocarboxylation of organic halides and the electroreductive coupling of organic halides with a variety of electrophiles [119, 120]

\[
\text{E.g.} \quad \text{RX} + 2e^- + \text{CO}_2 \rightarrow \text{Acids}
\]

The following reaction is closely related to organometallic synthesis, where the reduction takes place by metal instead of electricity. The electrosynthetic utility has the valuable advantages over the conventional synthetic routes and it can be easily performed on a preparative scale.

The mechanism can be schematically given as follows, for a divalent anode derived ion:

At anode: \( M \rightarrow M^{2+} + 2e^- \)

At cathode: \( \text{RX} + 2e^- \rightarrow \text{R}^- + \text{X}^- \)

In solution: \( \text{R}^- + \text{E}^+ \rightarrow \text{RE}^+ \)

Overall reaction: \( \text{RX} + \text{M} + \text{E}^+ \rightarrow \text{RE} + \text{MX}^+ \)

This transformation is electron assisted organometallic reaction and has performed in usual solvent and involving massive metal. Actually, it has been clearly demonstrated that the reaction does not proceed in the absence of electricity. In most cases at least 2F/mole current is required, i.e., stoichiometric amount of electricity.
For the above reaction, the relative production potentials of all components should be in the proper order: (1) the metallic ion generated by the oxidation of the anode has to be reduced at more negative potential than the halide (2) when the halide is reduced more easily than the electrophile \( E^+ \), electroorganic synthesis by low valent metal electrode can be used associated with consumable anode.

Thus the process is mainly characterized by its simplicity. At the laboratory scale, a very simple electrical power source is used, making the method accessible at moderate cost.

This method has several advantages over the normal carboxylation process, as (1) it is one-step reaction (2) the experimental conditions are mild as a result of using massive metals and non-flammable solvents and operating out or near room temperature (3) the selectivity of some reactions can be increased.

In the carboxylation of benzylhalide, the use of magnesium ions avoids the formation of the ester by trapping the carboxylate.

For a given reaction, the nature of the anodic metal plays a decisive role. The ions formed in the anodic oxidation should not be reduced more readily than the organic halide. Thus in the electrocarboxylation reaction, magnesium or aluminum can be used for benzyl halides, whereas magnesium is performed with the less readily reduced organic halides.

For three decades, much work has been devoted to the electrochemical carboxylation of organic substrates. Generally halogen compounds are unsaturated and good leaving groups. Most of the organic halide reactions are give the successful results from easily reducible compounds. Electrochemical synthesis involving \( \text{CO}_2 \) by the use
of sacrificial anodes without diaphragm cells are widely applied on a laboratory scale and in some cases have been scaled up to the pilot plant stage or industrial production. In several cases, noteworthy improvements have been observed in yield and selectivity of the products with conventional diaphragm electrolytic systems.

A broad definition of sacrificial anodic process considered, extends to all those metal electrodes for the anodic polarisation, the oxidation of the metal is favoured for thermodynamic and kinetic reactions, with respect to all the other reactions involving the species present in the neighbourhood of the electrode.

Sacrificial anodes have been proposed essentially on a laboratory scale, for the performance of quite a large number of electrochemical synthetic reactions in non-aqueous media. In this case, re-deposition of the metal at the cathode is generally undesired, the cathodic reaction being useful to the synthetic process. In this connection, it should be considered that the redox potential of reaction is generally shifted towards more negative values by the formation of complex compounds between metal ions and the electrolyte medium:

\[ M \rightarrow M^{n+} + n\text{e}^- \]

With a proper choice of the metal as anode, it is possible to undivided cells for the performance of cathode processes leading to easily oxidable products, instead of using diaphragm or membranes. This methodology has resulted, particularly with advantage in the arrangement of high pressure small scale electrochemical reaction [128]. Interesting results have also been obtained in the synthesis of various important compounds [129-136] via combined anodic and cathodic reactions.
2.4 Non-steroidal anti-inflammatory drugs

Health is of prime importance to a man and he wants to get cured in the least possible time whenever he falls ill. This desire has resulted in the use of a large number of synthetic organic compounds as medicines. In recent years, the practice of giving a number of drugs together has very much increased.

Most of the world's scientific literature deals with the topic of non-steroidal anti-inflammatory drugs (NSAID). An attempt has been made to be as complete as possible, however the several hundred of compounds have been reported to exhibit anti-inflammatory activity in animal models.

Fewer than 200 anti-inflammatory compounds are assigned generic names. Of these, only a portion has been used in clinical trials for which some data have been reported. A smaller portion of these compounds successfully completed clinical trials are approved and marked for use in the treatment of inflammatory diseases like arthritis. Thus by focusing NSAIDs with generic names that are either marked somewhere in the world or have some published clinical data. In addition, use of these criteria provides some assurance that the more interesting NSAIDs, those that have actually achieved therapeutic utility in patients with inflammatory diseases [137-140].

Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of medications that possess analgesic and anti-pyretic activities. They are used for reducing pain and inflammation in a large variety of musculoskeletal disorders, menstrual cramps, fever etc. Non-steroidal anti-inflammatory drugs are perhaps the most popular new group of medication on the market today [141]. They are used on a frequent basis both in the home and health care facilities for a diverse number of medical disorders. These drugs
are available in both prescription and non-prescription forms. This new group of medications is highly effective and welcome new comers to the world of Pharmacology [142-144]. Generally drugs in these groups are used to treat all kinds of pain, including rheumatoid arthritis, osteoarthritis, pain caused by autoimmune disease and physical trauma. The successful progress of pharmacology in the treatment of several diseases has led to the development of a powerful pharmaceutical industry.

NSAIDs can be categorized into three classes (1) benzoic derivatives with salicylic group, anthranilic compounds with mafenamic acid and niflumic acid (2) aryl acetic acid compound and (3) α-arylpropionic acids. Benoxaprofen, Carprofen, Pranoprofen, Proizunic acid, Flurbiprofen, Isoprofen, Flunoxaprofen and Pirprofen are being prepared independently in several laboratories, Boots, Distal Products (Lilly) and Cilage (Janssen) of Great Britain, Theraplix, Specia, Roussel and Bouchara of France, Syntex of USA, Mochida, Yoshimotl, and Sankyo of Japan, Hoffmann La Roche and Geigy of China and Carlo Erba of Italy since 45 years [145]. This class of drugs is widely used to control the symptoms of arthritis and related connective tissue diseases [146].

2.5 Significance and scope of the work

In 1942 Hunsdiecker [147] reported that carboxylic acids could be prepared by electrochemical hydrogenation in presence of sulphuric acid with lead cathode and was later developed by Birch [148] making use of two phase system. Electrochemical approach is very convenient for the hydrogenation of unsaturated hydrocarbons, benzaldehydes, acetophenones and unsaturated fatty acids [87,149].

$$R-\text{CH}=\text{CH-R}^1 + 2\text{H}^+ \rightarrow R-\text{CH}_2\text{CH}_2\text{-R}^1$$
In 1964 Wawzonek [150] reported that carboxylic acids could be prepared by electrochemical reduction performed in presence of carbon dioxide of the corresponding benzyl halides with a mercury cathode in a two compartment cell and was later improved by Barzer [151] making use of conventional diaphragm systems Alky, benzyl and allyl halides are quite easily electrocarboxylated [152,153]. Even aryl bromides or chlorides can be carboxylated in the presence of catalysts [154,155].

\[ R-X + CO_2 + 2e^- \rightarrow R-COO^- + X^- \]

These reactions appear to the particularly undesirable in case of the synthesis of carboxylic acids from valuable precursors. A considerable improvement of the synthesis came from the use of low valent metal electrodes. The electrochemical reduction of \( \alpha \)-aryl acrylic acids and benzyl halides is an interesting method and is a convenient way to obtain carboxylic acids [156-171].

Electrochemically generated hydrogen is an attractive process that avoids the necessity for the supply of hydrogen gas. This hydrogen can be used for the reduction of olefinic bond [172]. Similarly, fixation of carbon dioxide by using it as a C1-building block in chemical synthesis has gained considerable interest, stimulated by environmental considerations and by its abundant availability. Carbon dioxide can be employed as a single carbon source through the formation of low carbon number organic compounds [173,174]. In the presence of other functionalised organic compounds, such as alkyl halides, unsaturated hydrocarbons and carbonyl compounds possess one or two additional carbon atoms in the backbone [175-178].
Electrolysis of $\alpha$-aryl acrylic acids and organic halides generally gives low yields of the corresponding products. Earlier studies in this area have supported much progress in electrocatalytic reactions. Some catalysts can improve the yield and current efficiencies of electrosynthetic reactions [154,179].

A new and interesting anodic dissolution of various metals to cathodic reactions involving $\alpha$-aryl acrylic acids and organic halides catalysed by metal electrodes and it has been proposed recently for the performance of numerous electroorganic synthesis by using an undivided cell. This electrocatalytic system is used in order to improve the yield and selectivity of electrode reactions. Several transition metal electrodes have shown good catalytic properties in the synthesis of non-steroidal anti-inflammatory drugs (NSAIDs) by electrochemical hydrogenation and electrocarboxylation.

In this case, it has been recognized that, with a few exceptions, direct reactions are difficult, owing to the numerous concurrent pathways existing for the electrogenerated intermediates. However, the use of transition metal catalysts may improve the effectiveness of synthetic reactions considerably, affording generally high yields of carboxylic acids.

Synthesis of the non-steroidal anti-inflammatory category of drugs start from aryl carbonyl compounds, which can be prepared by selective electrophilic acylation and converted by many different routes to the final drug. Initially, the Willgerold-Kindler reaction [180] was the method of choice to achieve this conversion, its synthetic utility is, however, limited by (1) the reaction conditions, which involve high temperature and high pressures (2) the tedious and rather complicated isolation technique and (3) the yield of the products, which in many cases is modest and variable.
Though there are so many conventional chemical methods used for the preparation of drugs and pharmaceuticals, the yields are poor, process are cumbersome, most hazardous chemicals like cyanides are to be handled [145,181-188] and a series of multistep chemical reactions are to be used [189,190]. To avoid this difficulty and introducing the electrochemical process, which has clear advantage by using plentiful electrodes that should serve for the purpose and environment friendly.

Electrochemical synthesis is one of the most important technologies of synthetic field and the many people are unaware of its wide-ranging significance. It plays a crucial role in various aspects of human progress in the efficient manufacture of many kinds of drugs and pharmaceuticals and protecting the environment. This is an extremely active research area, new catalysts are being designed and new processes being devised that aim to produce cleaner electrochemical processes. This laboratory level micro scale process is more efficient and less polluting by using suitable electrode materials and the key aim is to find a way of producing valuable drugs and pharmaceuticals more cheaply. Most of the times, the surface of electrode acts as a catalyst and the mechanism of the electrode processes involves specific interactions between the surface and solution phase.

Electroorganic synthetic procedures have been proposed in order to improve the yield and selectivity of electrochemical hydrogenation and carboxylation. Several transition metal electrodes have shown good catalytic properties for the synthesis of NSAIDs. The electrocatalytic hydrogenation of α-aryl acrylic acids is a new and convenient method for the synthesis of non-steroidal anti-inflammatory drugs (NSAIDs).
Electrochemically generated hydrogen is an attractive process, which avoids the necessity for the supply of hydrogen gas.

Electrochemical conversion of ketones to alcohols, olefins to alkanes and nitro compounds to amino compounds by electrocatalytical hydrogenation at nickel surface has been achieved. The formation of the product was favoured at low concentration of substrate and high current density. Nickel surfaces have been most frequently used, because of the relatively low cost and possibility of preparing a high surface area. Most of the electrochemical reductions occur via amon radical, carbanion and other intermediates in solution. There is another type of reduction that occurs at a cathode whose surfaces are able to stabilise hydrogen atoms by adsorption and is closely related to catalytic hydrogenation. The electron transfer reaction means the reduction form of proton, to give adsorbed hydrogen atoms.

The electrochemical carboxylation of organic halides is a promising procedure for the synthesis of carboxylic acids. In the field of carbon-carbon bond formation involving carbon dioxide, we have been interested in the reactivity of organic halides with carbon dioxide using low valent metal electrodes for the synthesis of NSAIDs.
This presents an obvious advantage over the direct reduction, since the above process allows the reductive activation of an organic substrate at a potential generally less negative than that of its direct reduction. Low-valent transition metals are versatile reagents prone to activate carbon-carbon double bonds and carbon-halogen bonds in the electroreduction reactions [191,192].

Due to continuous increase in growth and demand for the prevention and treatment of disease, drugs and pharmaceuticals play an important role in our daily life. It is needed to prepare the drugs and pharmaceuticals as much as possible to meet the tremendous demand. The present investigation is mainly associated with the development of novel electroorganic synthetic procedures for the synthesis of Benoxaprofen, Carprofen, Pranoprofen, Protazinic acid, Flurbiprofen, Isoprofen, Flunoxaprofen, Pirprofen and 6-Aminonicotinic acid from their respective precursors by electrochemical hydrogenation and carboxylation. The electroorganic synthesis is performed with various combinations of solvents and supporting electrolytes at the different electrode materials.
The following Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are chosen for study:

- Benoxaprofen
- Protizinic acid
- Carprofen
- Pranoprofen
- Isoprofen
- Flurbiprofen
- Flunoxaprofen
- Piprofen
- 6-Aminonicotinic acid