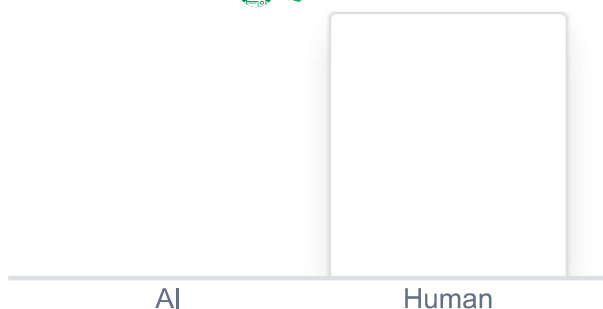




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1.4. Synthetic Organic Electrochemistry and Kolbe Electrolysis

Over the past decade, electrochemical synthesis has seen a renewal since organic chemists have sought to adopt green and effective ways of bond construction. Carbon-carbon bonds are produced by the Kolbe reaction, which uses electrochemical decarboxylative coupling. Even after over 100 years of research, the reaction has not been utilized extensively due to poor chemoselectivity and the requirement of precious metal electrodes.²⁷

Newer studies have shown additional, improved methods of non-Kolbe electrolysis of N-protected- α -amino acids using modern ElectraSyn 2.0 systems to enable electrochemical decarboxylative methoxylation under mild conditions.²⁸ This can be regarded as significant progress in the practical utilization of electrochemical procedures in amino acid chemistry.

In electrochemical synthesis of amino acids, special possibilities are given for simple access to complex structures that can hardly be prepared by classical methods. The capacity to form reactive radical intermediates under controlled conditions allows the production of quaternary carbon centers that are difficult to produce using other methods

The Kolbe electrolysis is a radical process, proceeding in two steps: electrochemical decarboxylation to give a radical intermediate, which then dimerizes during a radical reaction.³⁶

The equation below illustrates the general mechanism of Kolbe electrolysis. At the anode, the carboxylate ion undergoes oxidative decarboxylation, releasing carbon dioxide and generating an alkyl radical. These radical intermediates subsequently recombine to form a new carbon–carbon bond, typically yielding symmetrical hydrocarbons. This transformation is a classical example of electrochemical radical chemistry and demonstrates the ability of electrolysis to construct simple hydrocarbons directly from carboxylic acid salts.

Kolbe synthesis reaction can be generalized by the following equation:



In this reaction, R is a hydrocarbon functional group, e.g. an alkyl or aryl group, and CO_2 is carbon dioxide. In a carboxylate salt (either sodium acetate or potassium benzoate) aqueous solution containing a cathode and an anode, the reaction occurs in an electrolytic cell.

Water is reduced at the cathode to form hydrogen gas and hydroxide ions:



The carboxylate ions at the anode are oxidized to reactive radicals:



These radicals then react with water and the result is the hydrocarbons:



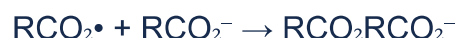
The Kolbe reaction normally forms hydrocarbons with relatively high molecular weight, which may not be easily isolated and purified. The reaction is also restricted to acids which are stable in the condition of the reaction used and mostly it demands high temperatures and large current densities.

Mechanistic Steps:

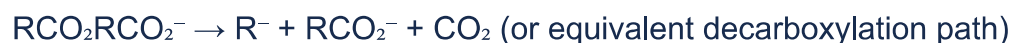
1. Radical Formation: The electron is removed by the carboxylate ion at the anode to produce a radical:



2. Dimerization: The radical dimerizes with another carboxylate ion to obtain a dimer:



3. Fragmentation: The dimer is fragmented into two carbanions:



4. Hydrocarbon Formation: The carbanions are reacted with water to produce hydrocarbons:



The resulting hydrocarbons may be further converted into other chemical products such as by oxidation or reduction.

This electro-oxidative decarboxylation of carboxylic acid salts results in radicals, which dimerize and is most effective in synthesis of symmetrical dimers, although in some cases can also be used with a mixture of two

carboxylic acids to produce unsymmetrical dimers.²¹ The trajectory to radical products (Kolbe electrolysis) and/or cationic intermediates (non-Kolbe electrolysis) is hampered primarily by the substituents in the α -position of the carboxylic acid as well as the experimental variables.³²

Interest in the Kolbe reaction has been renewed by recent progress in electrochemical apparatus and technique. Through controlled electrochemical systems, modern systems offer a precise nature of controlling current, potential, and reaction environment, which increases the yields and selectivity as compared to the traditional procedures. Addition of supporting electrolytes and properly selective bases have also been found as critical issues in determining the outcomes of the reaction.

1.4.1. The Benefits of Electrochemical Synthesis

Compared to the traditional synthetic methods, electrochemical methods are beneficial in the following aspects:

1. **Environmental Impact:** Electrochemical synthesis does not use stoichiometric oxidants and reducing agents hence has very little influence on the environment other than electricity. This complies with the concepts of green chemistry and reduces wastes.
2. **Mild Conditions:** When subjected to ambient conditions, electrochemical reactions can be performed without the need to use high-temperature or pressure that may destroy labile functional groups.
3. **Precise Control:** When using the modern electrochemical equipment, we can be able to measure the parameters of the reactions such as the current density, the potential and the time of reaction, and so on, with accuracy.
4. **Scalability:** Since the rate of electrochemical reactions can be varied with the current variations, then the reaction is scalable.
5. **Functional Group Tolerance:** Strong Electrochemical oxidation and reduction reactions tend to be mild and selective so that functional group tolerance is high.

1.4.2. Limitations and Challenges

Despite these advantages, the electrochemical synthesis suffers the following problems:

1. **Selectivity Problems:** There is a problem of chemoselectivity in most electrochemical reactions which results in the production of complex mixtures of products.
2. **Electrode Compatibility:** The type of electrode used could be a major determinant of the result of a given reaction and the best electrodes can be prohibitively expensive or hard to make.
3. **Restrictions on Substrates:** It is not possible to convert any type of substrate electrochemically, especially one that is insoluble in a suitable electrolyte solution.
4. **Scale-Up:** Electrochemical processes can be engineered to have mass transfer and heat dissipation engineering issues though are (in principle) scalable.

Special opportunities are provided in the electrochemical synthesis of amino acids to the easy access to

complex structures, which can barely be synthesized by classical methods. This ability to create reactive radical intermediates in controlled conditions makes it possible to prepare quaternary carbon centers that are hard to prepare by other techniques.

1.5. Project Aims and Objectives

This paper shall investigate the synthesis of alpha quaternary amino acid through Kolbe electrolysis reaction but of a particular interest in:

1. Conditions Optimization: careful investigation of base systems, electrolyte compositions, electrode material and the reaction conditions to get an optimum yield and selectivity performance.
2. Mechanistic Insight: Deliberation of the mechanistic facts of the reaction by characterizing the kinetics, spectroscopic characterisation and calculating a model.
3. Scalability Assessment: Reflection on the degrees to which scaling of the electrochemical reaction has been completed.
4. Substrate Scope: Investigations of the magnitude of scope of the amino acid substrates providing this synthesis.

The project will be grounded on the new achievements in the literature regarding the electrochemical organic synthesis and the special issue of the structure of quaternary centers construction in the amino acid systems. This will accomplish a sound and self doable procedure to the synthesis of α -quaternary amino acid via the combination of the current electrochemical apparatus along with the systemic maximization research. There can also be significant implications of the successful deployment of such a methodology in medicinal chemistry, which will provide access to new amino-acid units by which peptide-based therapies and materials are built. Environmental friendliness of electrochemical synthetic route also fits the contemporary requirement of green chemical-based process hence could have some advantages to the synthesis of pharmaceuticals where environmental consideration becomes important.