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A Short Review on Artificial Enzymes

Naga Jyothi. B, G. Sravani and Sruthi. K*

Department of Pharmaceutical Chemistry, RBVRR Women's College of Pharmacy, Osmania University, Hyderabad, India.

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***Corresponding Author Email:** sruthik.207@gmail.com

Abstract

Enzymes are outstanding biological catalysts which accelerate rate of reaction even upto 10,0000times more and are essential for all life sustaining reactions. like digestion, metabolism, growth healing etc. Recent utilization of enzymes includes the development of biosensors, food industry, technological applications and agricultural applications has prompted a drastic progress in the recent era. Their high degree of usage and lack of handiness stepped in developing them unnaturally.

Artificial enzymes can be defined as synthetic organic molecules that are not generally proteinaceous but contain an active site with functional group and are able to replicate the role of an enzyme. As they are prepared from chemical moieties they are also called as "chemzymes". The present review is focused on the development of artificial enzymes, their mechanisms and their wide applications together with long run prospects where research is often needed to be taken up to supply varied artificial enzymes with increasing wants.

Keywords

Chemzymes, Artificial hydrolytic enzymes, Self replicating molecules.

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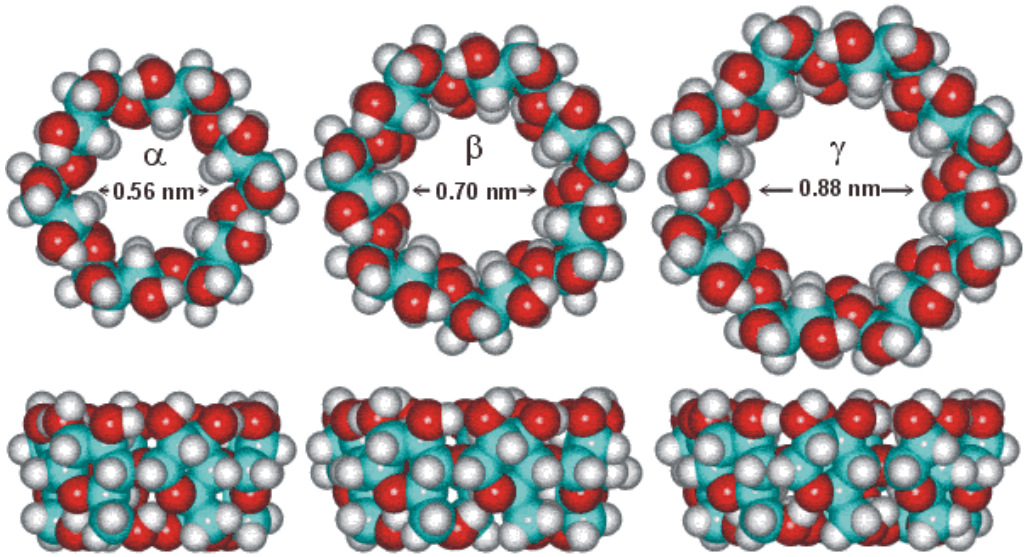
INTRODUCTION

Chemzymes are the synthetic molecules with replicating roles of natural enzymes. Inspite of having catalytic activity they have advantage of tunable structures and excellent tolerance to experimental conditions, low cost and purely synthetic routes of preparation.Also, various forms of mimics like polymeric, dendrimeric, supramolecular, nanoparticulateetc are available. They are extremely robust and are not recognized by body natural degrading enzymes. Characteristic property of these artificial enzymes is that their binding site is offered by structures like crown ethers, cyclodextrin, cryptands etc most oftenly cyclodextins offers a best fit model. Thus, researchers have developed most of enzymes concerning cyclodextrins as binding site [1].

Various forms of cyclodextrins are:

They are obtained by degradation of starch which are water-soluble ring-shaped oligomers composed of 4-C1 chair conformation α-(1,4-D) glucopyranoside units. They are available in three different forms varying with number of glucose units present in them.[1]



Some important classes of artificial enzymes[1,2] are:

1) Mimics of enzymes that use thiamine pyrophosphate as coenzyme.

2) Artificial hydrolytic enzymes include:

- Chymotrypsin mimics
- Metalloenzyme mimics
- Artificial ribonucleases
- Artificial enolases, esterases and aldolases.

3) Cytochrome p450 mimics

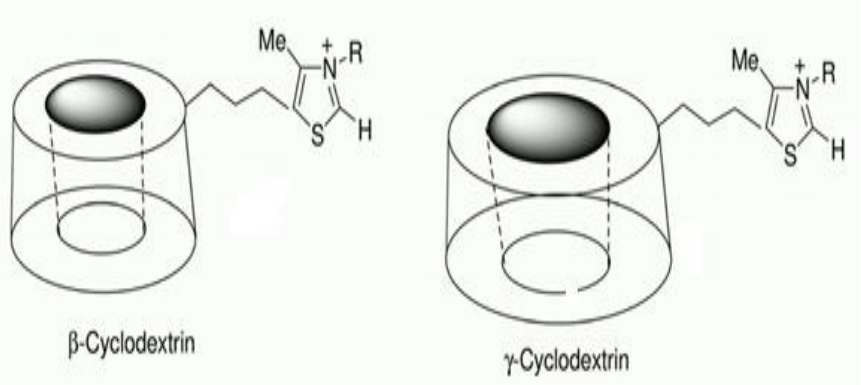
4) Conjugate addition

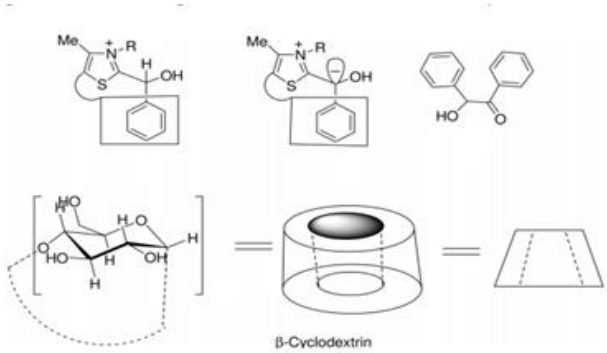
5) Cycloaddition.

6) Self replicating molecules.

1)Mimics of enzymes using Thiamine pyrophosphate (TPP) as coenzyme: Examples of such enzymes are pyruvate decarboxylase, transketolase etc which are involved in citric acid cycle.

Mechanism: Thiazolium ring of thiamine pyrophosphate forms a stable anion which is responsible for enzymatic activity. Thus, Artificial enzymes with thiazolium ring of TPP into Cyclodextrin units are prepared with both β&γcyclodextrins and benzoin condensation reaction can be observed in them which is a similar analogous function of TPP in carboxylase. In this benzaldehyde binds to cyclodextrin and are converted into thiazolium adducts which form benzylic anion that react with other benzaldehyde forming benzoin with150 folds higher rates. γ - cyclodextrin with 8 glucose units offered best binding site for two benzaldehydes .[2]



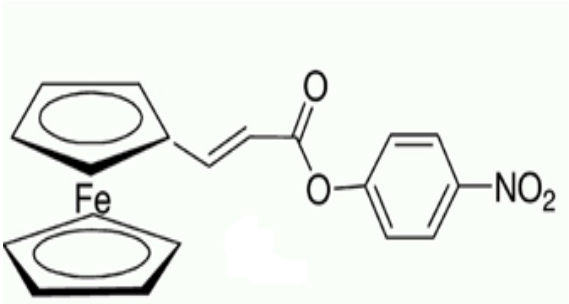


2)Artificial hydrolytic enzymes:

Chymotrypsin mimics: This enzyme is involved in cleavage of peptide bond by hydrolysis whose active site consist of histidine, serine, aspargine groups.

Mechanism: Imidazole of histidine plays a bifunctional catalytic role where first acts as an acid then as general base and serine –OH group as nucleophile.

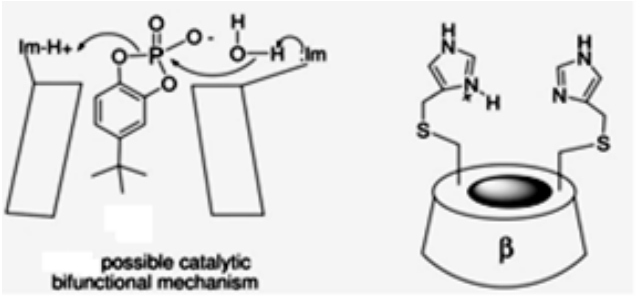
Cyclodextrin based artificial enzymes were prepared which react with substrate by acylating -OH group of cyclodextrins. Best combination gave fitting of substrate Para nitrophenyl ester of ferroceneacrylic acid and Acceleration relative to hydrolysis increased to 1 M folds than with normal chymotrypsin .[2]



Artificial Ribonucleases: Ribonucleases are the enzymes which cleave RNA by acid base catalysis without metal ions.

Mechanism: Catalysis is performed by two imidazoles of histidine units one as free base and other protonated as acid.Basic imidazole delivers water molecule to phosphate group of bound substrate while imidazolium ion of other protonated as the leaving group .

To mimic such activity β-cyclodextrins with bisimidazoles were prepared and hydrolysis of cyclic phosphate of 4- t- butyl catechol was studied which have shown similar effects as with of ribonucleases.[2]

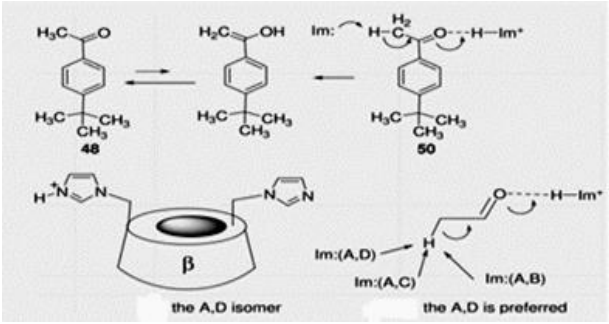


Artificial enolases and aldolases: These are the other examples for bifunctiona lCatalytsts, enolases are involved in penultimate step of glycolysis whereas aldolases in reversible conversion of fructose-1,6bisphosphate to glyceraldehyde-3-phosphate and dihydroxy acetone phosphate.

Mechanism: Acidic imidazole binds to –CO and basic imidazole removes neighboring methyl proton.

Bis imidazole cyclodextrin of three isomeric forms were prepared which have bifunctional activity and promote enolization.Three isomers can achieve

geometries but, A,D isomer is more preferred for this reaction, as they remove proton in non linear attack.[2]

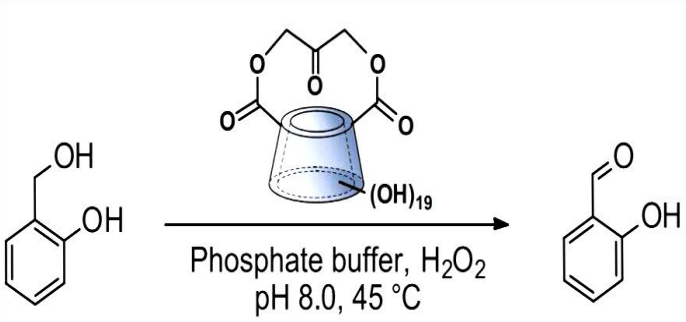


Oxidation: It is a corner stone reaction involved in both organic and biological processes. oxidase enzyme of cytp450 are involved in conversion of more polar components enabling in easy elimination and responsible for metabolizing wide variety of compounds.

List of few important Cyclodextrin derivatives for oxidation mimics are:

- Ketodiester bridged cyclodextrins
- Ditrifluoromethyl ketones (amines and alcohols oxidation)
- β6 Amino/β3 Amino Cyclodextrin with EDTA and cerium (involved in luminal catalysis)
- 2-Deoxy-2- Telluroβ-Cyclodextrin
- 1,2 benzisoselenazol-3(2H) one moiety

Oxidation of benzyl alcohol is the most prominent example with a catalysis rate of 60,000.

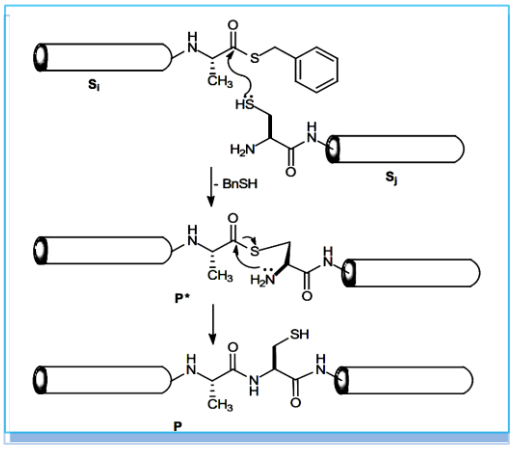


Enzymes like superoxide dismutases and glutathione peroxidase are mainly involved in antioxidant effect which prevents free radical reaction that cause aging, cardiovasculardiseases,endemic diseases etc.

Mimics of such valuable enzymes are

- 1,2 benzisoselenazol-3(2H)-one moiety.
- 2-deoxy,2-telluro β-cyclodextrin.

Self-replicating Molecules: These are interesting subgroup in which molecules have ability in replicating their own synthesis. It was reported by Ghadiri and his collaborators in which a peptide act as template for its own synthesis.



1.Transthiol esterification.

2.Intermediate P* intramolecular rearrangement.

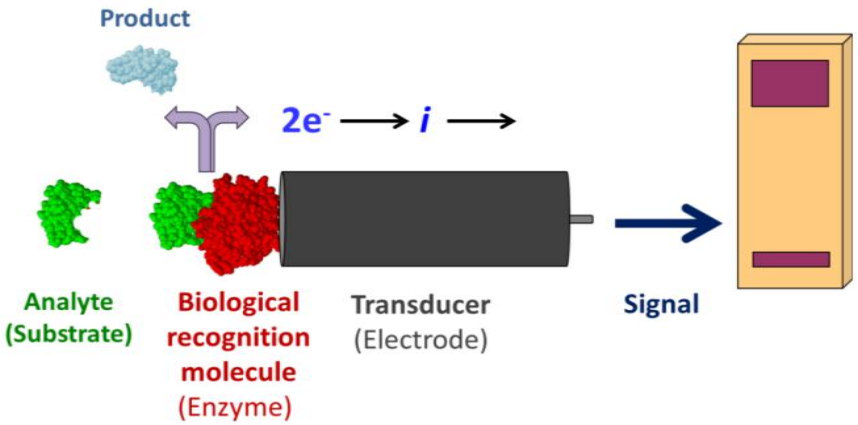
3.Fragments are bounded on α helical template forming complex

Two peptides are joined by ligase type reaction and such template enhanced the reaction rate over 4,000 times. In the first step there is nucleophilic attack of the N-terminal cysteine sulfhydryl group from Sj to the C-terminal thiolester of electrophile Si. Followed by intramolecular S-N acyl transfer to produce amide bond. Then these fragments are bound to helical template to form complex that facilitates their ligation.

More recently a diels alder reaction is catalyzed by its own product, latter acting as template for cycloaddition.[1]

APPLICATIONS:

- They are used in the selective synthesis of amino acids, steroids etc.[3]
- Ribonuclease enzymes are synthesized which mimics the hydrolysis of RNA.[3]
- Development of anti- cocaine catalytic antibodies which are programmable class of artificial enzymes. These incorporated antigenic cocaine analogues which when injected into mice by hybridoma technology successfully identified several families of anti-cocaine antibodies. Among them more efficient is MAB15A10 which is sufficient to block cocaine induced reinforcement.[4]
- They also find their application as environmental biosensors, pharmaceuticals etc[5,6].



- Used in the treatment of cancer and abola virus infections[7].
- Helpful in understanding the mechanism of natural enzyme catalysis.
- Chemzymes which are stripped down version of natural enzymes are also used to breakdown toxins inside fruits and vegetables[8].
- A Danish scientist successfully neutralised glycoside **esculin** a toxin that causes muscle twitching lack of co-ordination, paralysis etc, which is found in horse chest nuts[9].

- Artificial enzymes are also used to reduce carbondioxide emission by converting them into carbonates. [10] Natural enzymes are incapable of coping with extreme conditions of industrial plants. They developed enzyme which mimic carbonic anhydrase that accelerate the conversion of carbon dioxide to carbonates. These carbonates can be used in baking soda, lime manufacturing etc., thus a solution for global warming.
- Immobilized artificial carbonic anhydrase model are used for CO_2 sequestration.[11]
- Chemzymes can be mass produced using chemical process when large amount of product is required.
- Artificial enzymes make fuel from water and may decrease dependence on coal and soil.[12,13]

- Synthetic enzymes in the form of artificial genetic material known as XNA are even attainable to cleave the oncogene and as they don't exist in nature it will be worked for longer time than DNA or RNA.

FUTURE PERSPECTIVES:

- A remarkable progress in field of artificial enzymes has been made and still it is an area of active research, few areas of developments are:
- With the exciting advancements in sphere of chemistry in bio catalysis form an easy use of enzymes in a very little flask of laboratory to fully dilated their applications to use as highly added valuable molecules like natural products that are terribly tough to access and are doubtless quite valuable candidates are to be more focused .
- Highly useful enzymes are still to be unlocked with their synthetic modes of mimicking them and thus,artificial enzymes are going to be the future of synthetic chemistry.
- Enzymatic remedies for acute poisoning, metabolic diseases, genetic disorders etc are to be developed.
- Enzymes that are capable of performing pericyclic transformations with high efficiency and selectivity are still to be optimized.
- Efforts are to be more concerned in further developing defined geometrically directed functionalization, good binding properties, more environment friendly features.

CONCLUSION:

Like natural enzymes these synthetic molecules are capable of powering simple biochemical reactions effectively and they kick start process enabling reaction to happen at necessary rates .This introduction of enzyme mimics and their comprehensive summary of advances and current standing of their applications seeks to inspire researchers to perfect design & synthesize more effective mimics and tailor their functionality to better wide range of applications. The sector of synthetic chemistry struggles to reinvite and shift their focus on to emulating and engineering enzymes. Further, researches promise to offer new insights into the origins of life, as well as providing a potential starting point for an entirely new generation of drugs and diagnostics

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