Synthesis And Biotransformations Of Some Substituted Steroids by *Mucor plumbeus*

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Biotransformation

Biotransformation processes have been used by mankind for several thousand years. For example the biotransformation of ethanol to acetic acid (vinegar) by *Acetobacter* was most likely developed concomitantly with ethanol production from fermentable sugars by our ancestors in Babylon (Mesopotamia), Egypt, Mexico, and Sudan.

The biotransformation of ethanol to vinegar was probably the first true biotransformation process applied in an industrial manner. The glucose isomerase is an example of a biotransformation operated at scales typically seen in the petrochemical industry (∼5 million tones per year). This reaction converts glucose of starchy materials into high fructose syrups, which have enhanced sweetening properties but lower calorific values [6 OPRD].

The structures of drug molecules are becoming increasingly complex as scientists seek to improve potency, selectivity and safety. As a result many new drugs contain one or more chiral centers and are marketed as a single enantiomer pharmaceutical. Enzymatic reactions (Biotransformation) are often unique in their potential to produce fine chemicals in high optical purity. For example, cloned carbonyl reductases and alcohol dehydrogenases are used in a several instances to commercially produce fine chemicals in high optical purity.
Biotransformation is defined as the use of biological systems to perform chemical changes on compounds that are not their natural substrates. There are two major types of biotransformations. Xenobiotic (foreign to life) and biosynthetically directed biotransformations. In xenobiotic biotransformations, the substrate is foreign to the biological system. These biotransformations usually involve only one or two enzymatic steps and are catalysed by enzymes with wide substrate specificity. In the biosynthetically directed biotransformations, the substrate has a formal relationship to a natural biosynthetic intermediate (Fig. 1). These biotransformations exploit the flexibility of the biosynthetic pathways. Both types of biotransformations can be used for synthetic purposes. Biosynthetically directed biotransformations can be also used to reveal features of the biosynthesis.

Biotransformation offer many benefits when integrated with traditional synthetic chemistry, including more efficient, economical routes to target compounds; the ability to produce molecules that are difficult to
make using traditional organic synthesis; regio- and stereo-selective transformations; moderate reaction conditions; less side products and solvent waste, biotransformations are ‘environmentally friendly’ methodology.

1.1. Biotransformation advantages

- The ability of microorganisms, e.g., bacteria, to produce large amounts of biomass and a great variety of different enzymes in a short time.

- The chemo-, regio-, and enantioselectivity of enzymes, because of their small size bacteria have by far the largest surface-to-volume ratio in the living world, which allows them to maximize their metabolic rates because of a high exchange of molecules and metabolites through their surface.

- Microorganisms have great potential for inducing new or novel enzyme systems capable of converting foreign substrates.

- Microorganisms are capable of producing unique enzymes which are stable toward heat, alkali and acid.

- Umplung type reactions can be carried out.

- A combination of microbial transformation and chemical transformations (chemo-enzymatic synthesis) can be exploited for
المستخلص

تتضمن هذه الرسالة ثلاثة فصول: الفصل الأول يتحدث عن السمات المختارة للتحويل الحيوي، مميزاته، وعيوبه أيضا، شمل مسح للدوريات المرجعية عن الهيدروكسيلا الميكروبية باستخدام زراعة الفطر للمركبات الطبيعية.

الفصل الثاني: تم فيه مناقشة تحضير مواد مستبدلة من الاستيرويدات.- يمكن ان نقسم التحضيرات الى ثلاثة اقسام: (أ) تحضير هيدرازونات الاستيرويدات، (ب) تحضير هالوجينات الاستيرويدات، (ج) تحضير لاكتون الاستيرويدات. مع تناول الجزء العملي لهذا الفصل.

اما الفصل الثالث: يتناول التحول الحيوي للاستيرويدات المستبدلة مع الفطر موكور بلامبوس. تم التعرف على تركيب المركبات الناتجة باستخدام الطرق الطيفية. والملحق A يحتوي على طيف 13C NMR للمركبات التي حضرت خلال هذه الدراسة.
Abstract

This thesis includes three chapters: the first deals with selected aspects in biotransformation, advantages, disadvantages, which concerning the microbiological hydroxylation of natural products using fungi cultures.

The second chapter contains the work achieved. The synthesis of the substrates of substituted steroids.

The original of the work thesis divide into three parts: the first part a) synthesis of imino steroids, b) synthesis of halogenated steroids, c) synthesis of lactone steroids.

The second part report is the experimental part.

The third part deals with the biotransformation of the substituted steroids along by *Mucor plumbeus*, and the thesis was then ended with references.

The obtained compounds were identified deduced from spectroscopic methods.

Appendix A contains the carbon $^{13}$NMR table of the new compounds.
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1.4.2. β-Hydroxy-α-androstan-1V-phenyl hydrazone

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Chapter III: The Biotransformation of Imine Halogen and Lactone Steroids

Introduction

1.1. Results and Discussion

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1.1.2. Incubation of dehydroisoandrosterone (DHA)

1.1.3. The metabolism of different imino steroids by Mucor Plumbeus

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