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Thesis

Retrosynthesis analysis; a way to design a retrosynthesis map for Pyridine and pyrimidine ring

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Abstract

Pyridine and pyrimidines are amongst the most important, well known heteroaromatic rings, owning to their bioactive importance. Herein, an idea about how to design the synthetic pathway for these rings using retrosynthesis analysis techniques.

Introduction

Chemical synthesis is exceptionally located at the heart of organic chemistry, or now a day used to call by medicinal chemistry; due to its influence on our lives and health [1]. For illustration, many of today's medicines are synthetic, in predominantly are heterocyclic related compounds [2]. According to Corey 1989" To the field of synthetic chemistry belongs an array of responsibilities which are crucial for the future of mankind, not only with regard to the health, material and economic needs of our society, but also for the attainment of an understanding of matter, chemical change and life at the highest level of which the human mind is capable". The field of total (ideal) synthesis has a noticeable history and an inspiring future [3,4]. This report aimed to clarify the issue of how to design an ideal synthesis [5], for heterocyclic bioactive rings (namely; Pyrazole, Isoxazoles and imidazoles, as an example for 5-membered rings; Pyridine and Pyimidine, as an example for 6-membered). Compering between Retrosynthesis tree and ideal synthetic schemes.

Discussion

To prepare an organic compound (target, TGT), we need a readily obtainable starting materials and reagents. This process usually begins with the design of a synthetic plan (Strategy). Retrosynthetic analysis is a problem solving procedure for transforming the (TGT) gradually to more simpler structures (Synthon), through a pathway known as retrosynthesis tree, which finally leads to commercially available starting materials for a chemical synthesis [3], as revealed in figure 1. How to design a retrosynthesis tree First, Idea deal with where the disconnect occur [6-8], as revealed in figure 2. Second; for heterocyclic aromatic ring, we have to deal with saturated system, all unsaturated bonds must resolve. Third; synthetically equivalents synthons are to be given in its simplest way, synthetic equivalent in case of heteroaromatc ring mainly consist of active methylene and dicarbonyl compounds [9].

Pyridine as 6-membered heteroaromatic ring is one of most important bioactive compounds, naturally and synthetically occurred [10-12]. For Pyridine synthesis; main pathway is Hantzsch pyridine synthesis, where (α, β-unsaturated compound is added to active methylene as ethtyl acetoacetate (EAA) [13-17], also Knorr synthesis

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is available , by adding 1,5-dicarbonyl to heteroatom to give pyridine [18-20]. Micheal addition is also one of possible pathway [12,21]. Retrosynthesis tree of pyridine are discussed aside with its synthetically available pathways, is revealed in figure 3. Pyrimidine, is considered as most important ring as main components of DNA and privilege structure for dozen of bioactive drugs [22,23]. Using same steps as pyridine synthesis, as revealed in figure 4, retrosynthesis pathways for design pyrimidine synthesis. One of most applicable pathway is reaction between urea derivatives as (thiourea, guanidines) with 1,3-ducarbonyl compounds [24-28].

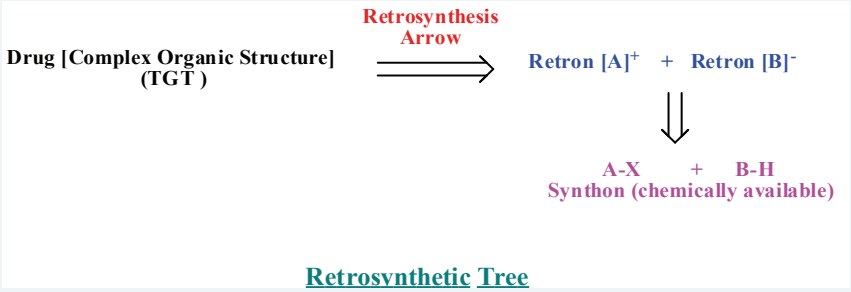

Figure 1: Target Molecules retrosynthesis tree.

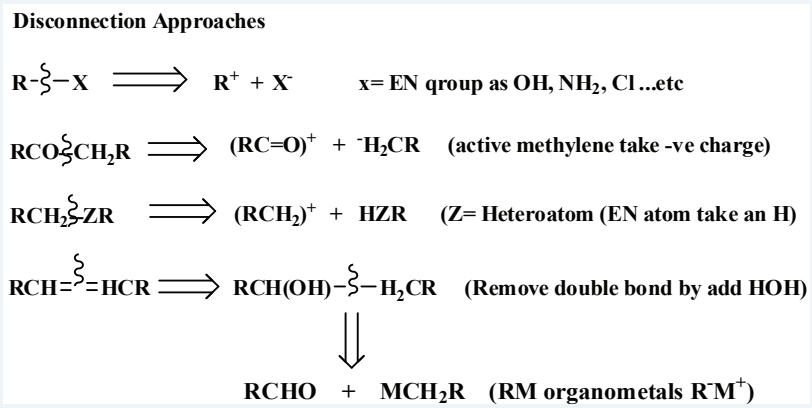

Figure 2: Main Disconnecting approaches in retrosynthesis.

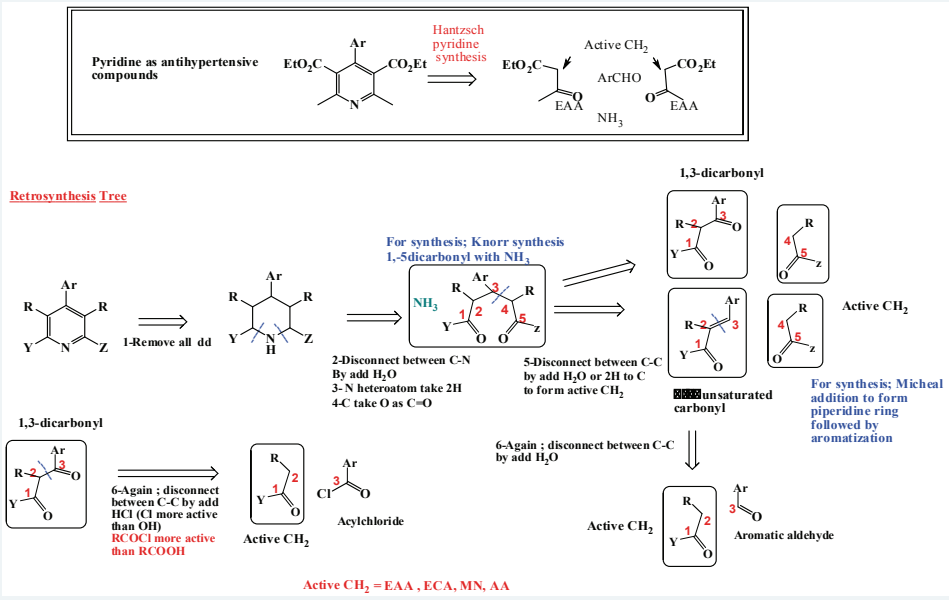

Figure 3: Retrosynthesis Tree for Pyridine.

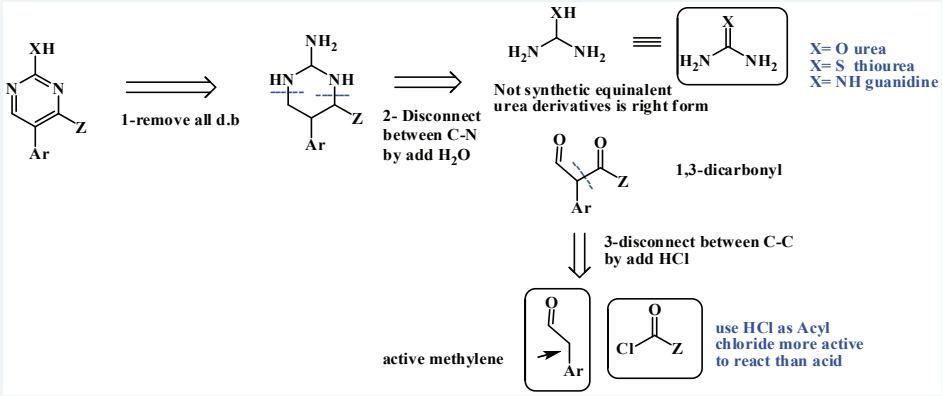

Figure 4: Retrosynthesis analysis for pyrimidine.

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