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Review of the PhD thesis titled "Biomimetic carbon-carbon bond formation: synthesis of ulosonic acids" by Osama El-Sepelgy

The title 3-deoxy-2-ulosonic acids are a family of widely distributed natural seven carbon carbohydrates, of which 3-deoxy-α-arabino-hept-2-ulosonic acid (DAH), 3-deoxy-α-manno-oct-2-ulosonic acid (KDO) and 3-deoxy-glycero-D-galacto-non-2-ulosonic acid (KDN) are the most common members. These sugars have been demonstrated to play a crucial role in a variety of biochemical and biological processes. The family of ulosonic acids has provided potential therapeutic leads for the development of inhibitors of corresponding enzymes. Discovery of these properties has propelled, during the last twenty years, a growing interest of academic and industrial laboratories in the synthesis of known and new high-carbon carbohydrates with improved activities and specificities. The group of Prof. Jacek Młynarski from Jagiellonian University has successfully entered the competition. Mr. Osama El-Sepelgy from this group has recently written a PhD thesis which is now the subject of the present review.

The thesis concerns three synthetic aspects: direct aldol reaction of pyruvic acid derivatives, synthesis of ulosonic acids and Bronsted acid catalyzed enantioselective synthesis of chromones. It should be said that the dissertation is built in a non-classical way. Presented thesis is a collection of publications, which the candidate is a co-author of. Each chapter consists of a brief introduction and copies of publications/supporting information.

Original results are preceded by basic information on the synthesis and properties of ulosonic acids. This part of the thesis corresponds well with the presentation of the experiments performed by the candidate. The Author reports a catalytic asymmetric aldol reaction of pyruvic aldehydes with sugar derived aldehydes catalyzed by transition metal-based chiral Trost or Shibasaki catalysts. This methodology allowed the first catalytic synthesis of 3-deoxy-2-ketoacid precursors through direct aldol reaction of sugar aldehydes with pyruvic acid

derivatives. A variety of pyruvate derivatives were efficiently activated under the developed protocol, including 2-acetylthiazole, which is a fundamental achievement when compared to previously published methodologies for the synthesis of ulosonic acids. The second publication focuses on biomimetic direct aldol reaction of pyruvate esters with chiral aldehydes. The candidate shows that direct aldol reactions of hindered pyruvate esters with sugar aldehydes is efficiently promoted by dinuclear metal complexes or chiral Cinchona alkaloid organocatalysts. The described methodology enables a flexible entry to both syn- and anti-configured aldols - key intermediates in the biomimetic approach to ulosonic acids.

The third section was based on experiments performed in the laboratory of Prof. Christophe Schneider in Leipzig. This section contains its own introduction and experimental part. It describes a highly enantioselective synthesis of chromones. The key step is a chiral phosphoric acid-catalyzed asymmetric benzylation of 1,3-dicarbonyl compounds. The presented methodology has a broad scope, resulting in construction of the corresponding 4*H*-chromones in excellent yields and enantioselectivities. I am sure that these results will be published in the near future as well.

I've found a few typographical errors in the submitted copy. This is a common problem, bearing no great importance and cannot influence my excellent opinion on the reviewed thesis.

I would like to stress that the thesis provides very interesting material. The described transformations are simple and effective, asserting the candidate's knowledge, creativity and understanding of the chemistry of natural products and their mimics. All reported reactions were carefully performed, products were obtained in good or even excellent yields and they were well characterized by NMR spectroscopy and MS. These facts affirm the candidate's excellent acquaintance with modern organic chemistry.

I am strongly convinced that the thesis of Mr. Osama El-Sepelgy perfectly fulfills all international standards of the PhD degree in organic chemistry. Therefore I recommend to the Jagiellonian University, Department of Organic Chemistry the granting of the PhD degree to Mr. Osama El-Sepelgy. In addition, I submit a request to award a (*cum laude)* distinction to Mr. Osama El-Sepelgy's dissertation.

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