University of Łódź
Faculty of Chemistry
Department of Organic & Applied Chemistry

Polish Chemical Society

III[rd] International Mini-Symposium

'Advances in Organocatalysis and Related Problems'

May 25[th] 2010

Program & Abstracts

Conference venue:

University of Łódź, Faculty of Chemistry, Tamka-Str. 12,

Lecture Room #016

Organizing committee:
Chairman: Prof. dr. hab. Grzegorz Mlostoń
Secretary: dr. hab. Jarosław Romański, Prof. UŁ

III[rd] International Mini-Symphosium

'Advances in Organocatalysis and Related Problems'

Program

13.55 *Invitation and opening*

Session #1: **Chairman: Prof. Janusz Zakrzewski**

14.00 – 14.30 **Filip Bures**
L-1 University of Pardubice, Czech Republic
α-Amino Acid- and Terpene-Derived Imidazole and Imidazoline Ligands in the Henry reaction

14.30 – 15.00 **Jacek Skarżewski**
L-2 Technical University of Wrocław, Poland
New Developments in Functionalization of Cinchona Alkaloids: Easy Access to Building Blocks for Modular Organocatalysts

15.00 – 15.30 **Dorota Gryko**
L-3 Institue of Organic Chemistry, Polish Academy of Sciences, Warszawa, Poland
L-Prolinethioamides – Efficient Organocatalysts for the Direct Asymmetric Aldol Reaction

15.30 – 15.45 *Coffee break*

Session #2 **Chairman: Prof. Józef Drabowicz**

15.45 – 16.15 **Zbigniew Kałuża**
L-4 Institue of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland
Synthesis of Alkaloid-like Ligands and their Application in Asymmetric Catalysis

16.15 – 16.45 **Piotr Kiełbasiński**
L-5 Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Łódź, Poland
Stereoselective biocatalytic transformations of heteroorganic compounds

16.45 – 17.15 **Michał Rachwalski**
L-6 University of Łódź, Poland
Chiral tridentate ligands as catalysts in asymmetric synthesis

17.15 – 17.45 **Korany A. Ali**
Guest Lecture National Research Centre, Cairo, Egypt
Convenient synthesis and reactions of some novel 2,6-bis(3-oxo-3-propanenitrile) pyridine derivatives

18.00 – 19.30 *Symphosium dinner*

α-Amino Acid- and Terpene-Derived Imidazole and Imidazoline Ligands in the Henry reaction.

Filip Bureš and Jiří Kulhánek

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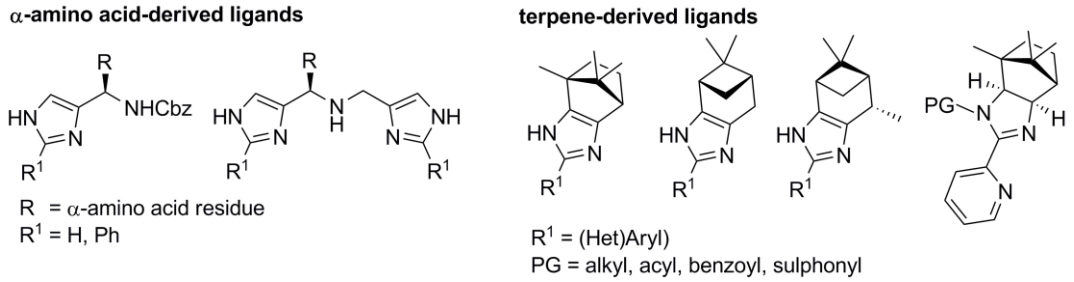
Chirial imidazole and imidazoline derivatives are remarkably interesting ligands and their (transition) metal coordinating properties enable preparation of various complexes with a wide application in asymmetric reactions such as the Henry reaction (nitroaldol condensation). Our synthetic approach to such molecules involves readily available and inexpensive chiral precursors such as α-amino acids or terpenes and subsequent building of the imidazole(ine) core. Recently, we have reported on several families of α-amino acid-derived[1] as well as terpene-annulated[2] imidazoles and imidazolines (Scheme 1).



Scheme 1. Nitrogen ligands featuring imidazole and imidazoline core.

The catalytic activities of the newly prepared ligands were tested in the asymmetric nitroaldol reaction achieving quantitative yields, quick reaction times, promising enantioselectivities as well as a good reaction control.

References:

1. (a) Bureš, F.; Kulhánek, J. *Tetrahedron:Asymmetry* **2005**, *16*, 1347; (b) Bureš, F.; Szotkowski, T.; Kulhánek, J.; Pytela, O.; Ludwig, M.; Holčapek, M. *Tetrahedron:Asymmetry* **2006**, *17*, 900; (c) Marek, A.; Kulhánek, J.; Ludwig, M.; Bureš, F. *Molecules* **2007**, *12*, 1183.
2. (a) Kulhánek, J.; Bureš, F.; Šimon, P.; Schweizer, W. B. *Tetrahedron:Asymmetry* **2008**, *19*, 2462; (b) Bureš, F.; Kulhánek, J.; Růžička, A. *Tetrahedron Lett.* **2009**, *50*, 3042.

New Developments in Functionalization of *Cinchona* Alkaloids: Easy Access to Building Blocks for Modular Organocatalysts

Jacek Skarżewski

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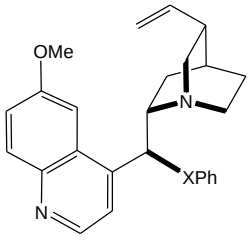
For many decades *Cinchona* alkaloids have been tried as chiral orgaonocatalysts and ligands. Their effectiveness in the reactions of different mechanism gained them recognition as *privileged catalysts*. However, the chemical transformations of their functionalities was rather limited and only recently the alkaloids have been shown to undergo useful transformations, thus broadening possibilities of their application.
In particular, an attempted substitution of the activated C9 hydroxyls often resulted in the unexpected outcomes, namely retention or inversion of configuration or even rearrangement of the quinoclidine skeleton.
Within our project on the preparation and use of chiral organochalcogen compounds in the asymmetric catalysis we have developed the successful synthesis of new C9 sulfur- and selenium-containing *Cinchona* derivatives **1**, chiral ligands suitable for the catalytic purpose. Thus, the respective chiral thioethers,[1a] selenoethers,[1b] and also epimeric sulfoxides[1c] (X-ray structure) were obtained and tested as N(sp^3), X-donating chiral ligands in the Pd-catalyzed allylic alkylation.
We have also succeeded in the introduction of a new carbon-carbon bond at the C9 center. The C9-halides reacted with various arylmagnesium bromides to afford the respective *epi*C9-arylated products **2** (X-ray structure).[2]
Yet another functionalization of the alkaloids has been achieved by their reaction with chloroacetic acid. The obtained products **3** were coupled with the C-protected amino acids and dipeptides.[3] The LAH reduction of **3** gave the corresponding primary alcohols, which were transformed into primary amines. Also the C9 primary amines were prepared directly by the same conversion of the native alkaloids. All these amino-derivatives were reacted with salicylic aldehydes and isothiocyanates to form the corresponding Schiff bases and thiourea-derivatives, different modular catalysts. Some of them have already been examined and the obtained results will be discussed.



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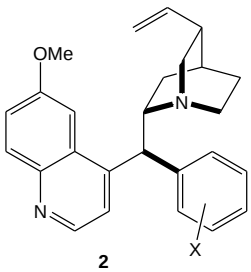

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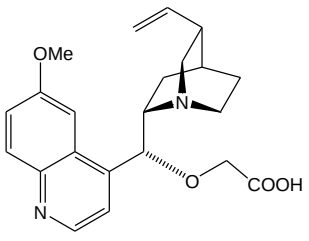

3

1. (a) Zielinska-Błajet, M.; Kucharska, M.; Skarżewski, J. *Synthesis* **2006**, 1176. (b) Zielinska-Błajet, M.; Siedlecka, R.; Skarżewski, J. *Tetrahedron: Asymmetry* **2007**, *18*, 131. (c) Wojaczyńska, E.; Zielińska-Błajet, M.; Turowska-Tyrk, I.; Skarżewski, J. *Tetrahedron: Asymmetry* **2010**, *21*, in press.
2. (a) P. J. Boratyński; Turowska-Tyrk, I.; Skarżewski, J. *Org. Lett*. **2008**, *10*, 385. (b) P. J. Boratyński; Skarzewski, J. *Synthesis* **2009**, 3113.
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L-Prolinethioamides – Efficient Organocatalysts for the Direct Asymmetric Aldol Reaction

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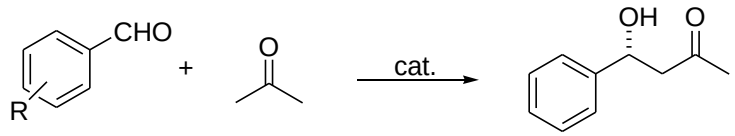
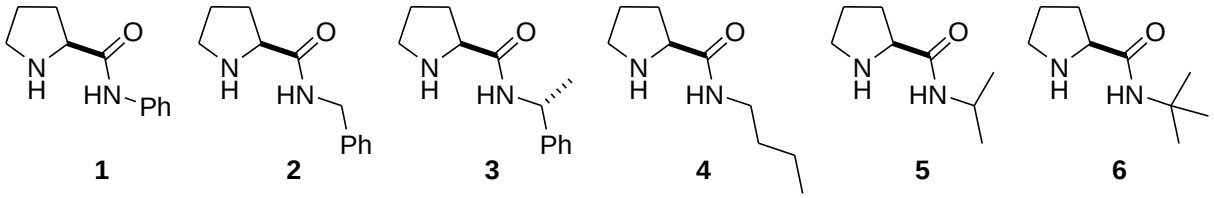
Since the discovery of L-proline catalysed asymmetric direct aldol reaction enormous efforts has been made to develop, improve and understand this powerful tool for the C-C bond formation. Elaboration of new organocatalysts has attracted great attention, since this metal-free process is environmentally friendly and can be easily carried out on a larger scale.

Our group has been interested in novel class of proline derivatives bearing thioamide moiety. A series of L- proline derived thioamides from various aliphatic and aromatic amines were synthesized and used as organocatalysts in the direct asymmetric aldol reaction. Compound **3** was found to be the most effective organocatalyst for the reaction of aromatic aldehydes with acetone giving 3-hydroxyketones with high yield and ee up to 99%. The addition of acid as an additive has a profound and appreciable effect on both the yield and stereoselectivity, at the same time the catalyst loading can be lowered to 2.5%. Furthermore, it was found that the reaction of cyclic ketones with various aldehydes could be run in the presence of water. The use of brine as the reaction medium further improved the yield and stereoselectivity of the discussed reaction.





1 **2** **3** **4** **5** **6**

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References

[1] Gryko D., Lipiński R. *Adv. Synth. Catal*.., **2005**, 347, 1984-1952
[2] Gryko D., Lipiński R*, Eur. J. Org. Chem*., **2006**, 3864-3876
[3] Gryko D., Zimnicka M., Lipiński R. *J. Org. Chem*., **2007**, 72, 964-970

L-4

Synthesis of Alkaloid-like Ligands and their Application in Asymmetric Catalysis

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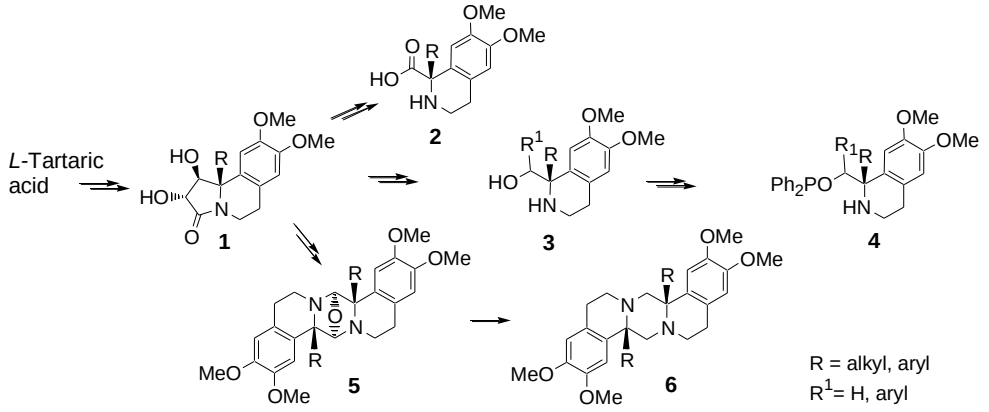
Enantiopure β-amino alcohols are among the most intensively utilized in asymmetric catalysis classes of compounds. They are employed as organocatalysts or ligands for metal based catalysis in a range of enantio-selective processes, *i.e.*: Baylis-Hillman reaction, Michael additions, reduction of ketones with $THF{\cdot}BH_3$ or hydride transfer reduction [1]. Furthermore, amino alcohols can be converted into variety of derivatives exploited in asymmetric synthesis, such as quaternary ammonium salts (PTC catalysts), diamines, amino phosphinites and phosphinites, (N,N- N,P- or P,P-ligands for transition metals based catalysis). The important sources of β-amino alcohols are alkaloids and amino acids. However, the limited number of cheap and easily available natural compounds, difficult modification of their complex structure and the occurrence predominantly in one enantiomerical form only, makes total synthesis of enantiopure β-amino alcohols an attractive alternative.



Scheme 1

Isoquinoline alkaloids due to their significant bioactivity [2] ***gather a lot of attention*** over recent years. In contrast to natural products containing quinoline skeleton *i.e. Cinchona* family, however, those compounds have never been applied in asymmetric catalysis. We have recently described a stereocontrolled synthesis of 10b-substituted hexahydropyrrolo-isoquinolines **1** from *L*-tartaric acid [3, 4]. Herein we report the synthesis of alkaloid-like ligands **2-6**, which structure was modelled on natural products, but lacking their complexity (Scheme 1). The application of obtained ligands in asymmetric processes such as hydride transfer reduction (comp. **2,3**), palladium catalysed allylic alkylation (comp. **4**) and desymmetrization of *meso*-diols (comp. **5, 6**) will be demonstrated.

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[1] Jacobsen, E.; Pfatz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*; Springer: New York,1999.
[2] Bentley, K. W. *The Isoquinoline Alkaloids*; Harwood Academic, Amsterdam, 1998.
[3] Mostowicz, D.; Wójcik, R.; Dołęga, G.; Kałuża, Z. *Tetrahedron Letters*, **45**, 6011-6015, 2004.
[4] Kałuża, Z.; Mostowicz, D.; Dołęga, G.; Mroczko, K.; Wójcik R. *Tetrahedron* **62**, 943-953, 2006.

Stereoselective Biocatalytic Transrormationa of Heteroorganic Compounds

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Enzymes, which are extremely efficient catalysts developed by nature to catalyze practically all the chemical reactions that take place in living organisms, have also been found capable of accepting and transforming unnatural, man-made substrates[1], also among them the heteroatom-containing ones[2]. The results of our recent investigations of enzyme-mediated stereoselective syntheses and transformations of chiral organosulfur and organophosphorus compounds, bearing stereogenic centres located either on a heteroatom or in a carbon side chain, will be reviewed. This will comprise: kinetic resolution of racemic hydroxymethylphosphinates and their P-borane analogues, dynamic kinetic resolution of β-hydroxyalkyl sulfones, and desymmetrization of bis-cyanomethyl sulfoxides[3] and phosphinoxides.[4] Mechanistic aspects of the reactions will be discussed. Finally, attempts at the application of enzyme catalytic promiscuity in lipase-promoted Michael addition of nucleophiles to to heteroorganic acceptors, will also be disclosed.

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Chiral Tridentate Ligands as Catalysts in Asymmetric Synthesis

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In the course of our studies we have become interested in developing a new strategy for the synthesis of chiral polydentate catalysts/ligands having a stereogenic sulfinyl group as one of the possible coordinating nucleophilic centres capable of binding organometallic reagents.[1] The synthetic pathway and attempts at the application of these ligands as catalysts in the asymmetric Henry reaction[2], enantioselective diethylzinc addition to aldehydes[3] and in a conjugate addition of diethylzinc to enones[4] will be presented.

1) M. Rachwalski, M. Kwiatkowska, J. Drabowicz, M. Kłos, W. M. Wieczorek, M. Szyrej, L. Sieroń, P. Kiełbasiński, *Tetrahedron: Asymmetry* **2008**, *19*, 2096.
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3) S. Leśniak, M. Rachwalski, E. Sznajder, P. Kiełbasiński, *Tetrahedron: Asymmetry* **2009**, *20*, 2311.
4) M. Rachwalski, S. Leśniak, P. Kiełbasiński, *Tetrahedron: Asymmetry* **2010**, submitted.

Guest Lecture

Convenient Synthesis and Reactions of Some Novel 2,6-Bis(3-oxo-3-propanenitrile) Pyridine Derivatives

Korany A. Ali

Organic Chemistry Department- National Research Centre- Egypt

Project 170(Science and Technology Development Fund)

Abstract

The versatile, hitherto unreported 2,6-bis(3-oxo-3-propanenitrile) pyridine (**2**) was prepared by the Claisen condensation reaction of pyridine 2,6-dicarboxylic acid ester **1** with acetonitrile in the presence of sodium hydride. Several new pyrazoles, isooxazoles, and pyrazolopyridazine derivatives have been synthesized by the reaction of 2,6-bis(3-oxo-3-propanenitrile) pyridine (**2**) with bidentate nucleophilic reagents and hydrazonyl chloride derivatives.