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

Polish Chemical Society

# IV$^{th}$ International Mini-Symposium

# *'Metal containing substrates and metal catalyzed reactions'*

## May 24$^{th}$ 2011

Acknowledgement

The City of Łódź Office for financial support

# *Program & Abstracts*

*Conference venue*:

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

Lecture Room #1-022

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

# IV$^{th}$ International Mini-Symposium
## *'Metal containing substrates and metal catalyzed reactions'*

## Program

*13.55* *Invitation and opening*

### *Session #1:* *Chairman: Prof. Piotr Kiełbasiński*

**14.00 – 14.30** **Wolfgang Weigand**
***L-1*** Friedrich Schiller University, Jena, Germany
*From Iron-sulfide to Membrane-bound [FeFe] Hydrogenase Models*

**14.30 – 15.00** **Antoni Pietrzykowski**
***L-2*** Warsaw University of Technology, Warszawa, Poland
*Progress in Synthesis of Cyclopentadienylnickel Compounds and Their Application as Initiators in Polymerization of Vinyl Monomers*

**15.00 – 15.30** **Bogna Rudolf**
***L-3*** University of Lodz, Łódź, Poland
*Metallocarbonyl Complexes of Iron, Molybdenum and Tungsten as Irreversible and Reversible Inhibitors of Papain*

*15.30 – 15.45* *Coffee break*

### *Session #2* *Chairman: Prof. Piotr Kaszyński*

**15.45 – 16.15** **Daniel Gryko**
***L-4*** Institue of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland
*The Synthesis of Pyrrole Derivatives via Direct Arylation*

**16.15 – 16.45** **Arkadiusz Chworoś**
***L-5*** Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Łódź, Poland
*Oxidative Damage of Nucleic Acids Using Metalloporphyrin*

**16.45 – 17.15** **Oleg Demchuk**
***L-6*** Maria Curie-Skłodowska University, Lublin, Poland
*Novel Ligands for a"Greener" and Asymmetric Cross Coupling Reactions*

**17.15 – 17.45** **Ahmed Ali**
***Guest Lecture*** National Research Centre, Cairo, Egypt
*The Utility of Carbon Disulphide and Lawesson's Reagent for Synthesis of Different Bioactive Sulfur Fused Heterocycles*

## *L-1*

# From Iron-sulfide to Membrane-bound [FeFe] Hydrogenase Models

T. Alpermann[a], U.-P. Apfel[a], K. Rüdel[b], A. Fahr[b], G. Mloston[c], W. Weigand[a]

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[c]*University of Lodz, Faculty of ChemistryDepartment of Organic & Applied Chemistry Tamka 12, 91-403 Lodz, Poland*

In 1845, Berzelius [1] has reported the geochemically and primordially important reaction (1) of iron sulfide with hydrogensulfide to form pyrite, which was forgotten for many decades.

$$FeS + H_2S \rightarrow FeS_2 + H_2S;\ \Delta G°_r = -26.9\ kJ\ mol^{-1},\ 25\ °C,\ 1\ bar \quad (1)$$

The Berzelius can be seen as a primordial model for the hydrogenase enzyme. In other words, the structure of catalytically active Fe,S centres of Fe,S proteins are not inventions of the biological world, rather they are mimicking these iron sulfur minerals that are older and which themselves have catalytic activity in the absence of protein.
In that presentation, first we will report on the compartmentation of $Fe^{2+}$ in vesicles [2]. Through addition of $H_2S$ releasing agents (e.g. $(NH_4)_2S$ or $Na_2S$) iron sulphide could be precipitated inside these vesicles, which can seen as a very simple and primitive cell system containing a primordial hydrogenase model. On the other hand we will present results on the synthesis of novel molecular [FeFe] hydrogenase models.

### References

[1] J. J. Berzelius, *Traite´ de Chimie. 2; Didot: Paris,* **1845**
[2] T. Alpermann K. Rüdel, R. Rüger, F. Steiniger, S. Nietzsche, S. Förster, A. Fahr, W. Weigand, *Orig. Life Evol. Biosph.* **2011**, *41*, 103–119

## *L-2*

# Progress in Synthesis of Cyclopentadienylnickel Compounds and Their Application as Initiators in Polymerization of Vinyl Monomers

**Włodzimierz Buchowicz, Andrzej Kozioł, Antoni Pietrzykowski**

*Warsaw University of Technology, Faculty of Chemistry, Noakowskiego 3, 00-664 Warszawa, Poland*

Synthesis of substituted nickelocenes, especially with substituents bearing polar functional groups, is a difficult task. Formation of a very limited number of such compounds has been reported so far[1]. Since olefin metathesis has been recently established as a valuable tool in the synthesis of inorganic and organometallic compounds[2], we have successfully applied alkene metathesis in nickel coordination spheres to synthesize several novel nickelocene derivatives, including *ansa*-nickelocenes[3] and carbonyl-substituted nickelocenes (Figure 1)[4].

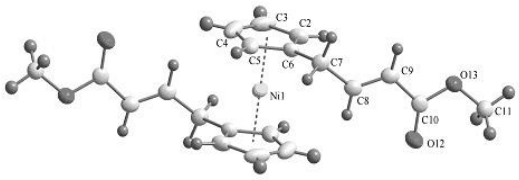
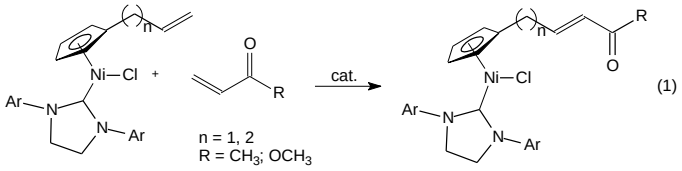



Figure 1. The molecular structure of 1,1′-bis(4-methoxy-4-oxo-2-butenyl)nickelocene

We have also found that cyclopentadienylnickel(II) compounds of the formula [NiCp(X)(L)] (X = Cl, Br or $CH_3$; L = NHC, $PR_3$), activated by methylalumoxane (MAO) could be applied as intiators in polymerization of vinyl monomers[5,6]. Selectivecross metathesis of [NiCl($C_5H_4R$)($H_2$IMes)] with α,β-unsaturated carbonyl compounds (Eq. 1) led to the formation of novel Ni(II) compounds with functionalized cyclopentadienyl ligands[6].




Syntheses, structures and properties of these compounds will be discussed and their catalytic activity will be compared with unsubstituted cyclopentadienylnickel(II) compounds of the formula [NiCp(X)(L)].

**References:**

[1] Hart, W.P. *et al. J. Am. Chem. Soc.* **1980**, *102*, 1196; Conway, B.G. *et al. Organometallics,* **1985**, *4*, 688.

[2] Bauer, E. B.; Gladysz, J. A., in *Handbook of Metathesis*, Grubbs, R. H., Ed.; Wiley-VCH, Weinheim, Germany, **2003**, Vol 2, pp 403-431 and references cited therein.

[3] Buchowicz, W.; Jerzykiewicz, L. B.; Krasińska, A.; Losi, S.; Pietrzykowski, A.; Zanello, P. *Organometallics* **2006**, *25*, 5076.

[4] Buchowicz, W.; Szmajda, M. *Organometallics* **2009**, *28*, 6838.

[5] Buchowicz, W.; Kozioł, A.; Jerzykiewicz, L.B.; Lis, T.; Pasynkiewicz, S.; Pęcherzewska, A.; Pietrzykowski, A. *J. Mol. Catal. A-Chem.* **2006**, *257*, 118.

[6] Buchowicz, W.; Wojtczak, W.; Pietrzykowski, A.; Lupa, A.; Jerzykiewicz, L. B.; Makal, A.; Woźniak, K. *Eur. J. Inorg. Chem.* **2010**, 648.

## *L-3*

# Metallocarbonyl Complexes of Iron, Molybdenum and Tungsten as Irreversible and Reversible Inhibitors of Papain

**Bogna Rudolf**

*Department of Organic Chemistry, Faculty of Chemistry,*
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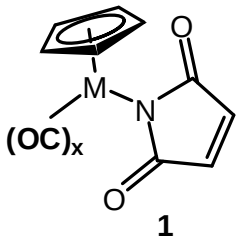
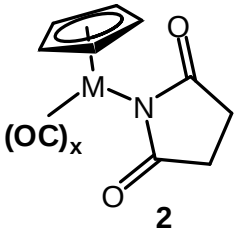
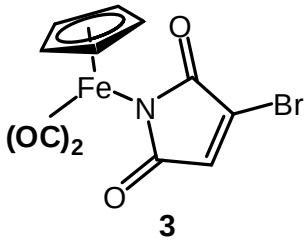
Cysteine proteases could be responsible for several serious diseases related to tissue degeneration due to abnormalities in the functioning of the catalytic site cysteine. Papain is a sulfhydryl protease from the fruit of the tropical papaya tree and it is homologous to mammalian cathepsin B. The catalytic activity of this enzyme is easily inhibited by chemical compounds reacting with sulfhydryl groups e.g. by maleimide derivatives. We have found that the metallocarbonyl complexes **1** bearing a maleimide function were irreversible inhibitors of the enzyme papain [1]. To get further insight into the binding mechanism of these compounds we synthesized analogous complexes **2** that lacked the ethylenic bond responsible for alkylation of the cysteine 25 thiol group in the papain's catalytic pocket. We performed kinetic studies of the interaction of the synthesized complexes **1**, **2** with papain [1,2].




**1**




**2**




**3**

M=Fe; x=2
M=W; Mo; x=3

It has been reported recently that the bromomaleimides react rapidly and selectively with cysteine residues to form thiomaleimides which can be cleaved with a TCEP (tris(2-carboxyethyl)phosphine) to regenerate the cysteine derivative [3]. We synthesized the metallocarbonyl complex **3** bearing a bromomaleimide moiety and studied its behavior towards papain.

[1] P. Haquette, M. Salmain, K. Svedlung, A. Martel, B. Rudolf, J. Zakrzewski, S. Cordier, T. Roisnel, C. Fosse, G. Jaouen, *ChemBioChem*, **2007**, *8*, 224-231.
[2] B. Rudolf, M. Salmain, A. Martel, M. Palusiak, J. Zakrzewski, *J. Inorg. Biochem.,* **2009**, *103*, 1162-1168.
[3] M. E. B. Smith, F. F. Schumacher, C. P. Ryan, L. M. Tedaldi, D. Papaioannou, G. Waksman, S. Caddick, J. R. Baker, *J. Am. Chem. Soc.* **2010**, *132*, 1960-1965.

## L-4
# The Synthesis of Pyrrole Derivatives via Direct Arylation

**Daniel T. Gryko**

[a] *Institute of Organic Chemistry Polish Academy of Sciences, Warsaw, Poland*

[b] *Faculty of Chemistry, Warsaw University of Technology, Warsaw, Poland*

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Among various heterocyclic rings, pyrrole, due to its unprecedented reactivity and broad utilization, is one of the most fascinating ones. Pyrroles are abundant in natural products, medicinal agents, and serve as a number of intermediates in multistep syntheses. Thus, many synthetic methods are known for the construction and derivatization of pyrrole ring and this field of research is as vigorous now as it was one hundred years ago. Aryl-substituted pyrrole derivatives can be prepared *via* Suzuki coupling of *N*-substituted-2-bromopyrroles with boronic acids or from *N*-protected pyrrole boronic acids esters and aryl bromides. These strategies however cannot be applied to *N*-alkylpyrroles since bromo-derivatives of these compounds lack *N*-electron-withdrawing protecting group and hence are not stable. Additionally, the overall process, including the prefunctionalization of the substrates with boronic acids and halides, is neither atom economic nor green.

Among the new concepts for linking two different aryl units together direct arylation were significantly explored within the last 15 years. We initially developed an efficient protocol for regioselective *C2*-arylation of pyrrole core in the presence of palladium complex with KF/AgOAc activator system. This methodology can be characterised by relatively mild conditions and short reaction times that are especially noteworthy compared to other related procedures for direct arylation of pyrrole core. Under these conditions variety of *N*-substituted pyrrole derivatives can be arylated with the range of aryl iodides, bearing both electron-donating and electron-withdrawing substituents, giving 2-arylpyrroles in 30-80% yield.

Subsequently, we managed to develop three efficient metal-free protocols for direct arylation of pyrrole derivatives. We proved that transformation of *N*-alkyl- and *N*-arylpyrroles into 2-arylated products can be mediated by KOAc in ionic liquids possessing basic anion. 2-Arylated products were obtained in good yields (up to 72%) and with high regioselectivity.

We proved that *t*-BuOLi alone can transform pyrrole derivatives into their 2-arylated derivatives. Reaction proceeds smoothly between pyrroles, bearing *N*-alkyl, *N*-aryl groups, and variety of aryl iodides and bromides, bearing both electron-donating and electron-withdrawing groups. High yields of products (up to 92 %) were reached, however 15-times excess of pyrrolic substrate is needed. During attempts to expand the scope of that catalytic system to other electron rich aromatic heterocycles, I discovered unprecedented regioselectivity in arylation of indolizine.

## *L-5*

# Oxidative Damage of Nucleic Acids using Metalloporphyrin

**Arkadiusz Chworoś**

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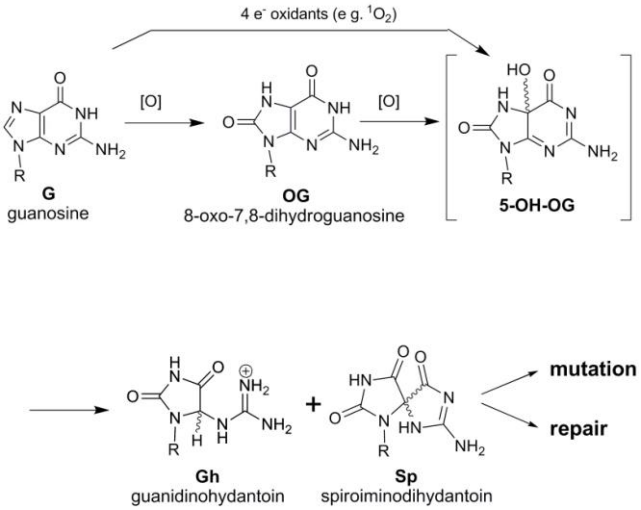
Oxidative damage of cellular DNA and RNA is one of the most important issues concerning proper cell function and its life. Many internal processes and external factors can lead to the radical oxidation, and if not repaired to DNA mutation. It is believed that reactive oxygen species (ROS) are directly responsible for oxidative stress; however they can be formed under several conditions (metal oxidation, enzyme triggered radical anion formation). Ultraviolet (UV) radiation itself can cause several types of DNA and RNA damage (photochemical modification, crosslinking and oxidative damage). Carcinogenic toxins (for instance those present in tobacco smoke), alkylating agents are also known to be responsible for the formation of damaged DNA and RNA. The 8-oxoguanosine is often identified and major product of DNA oxidation; however the mechanism of its formation was until recently not fully understood. It is even less know about the oxidative damage of RNA.

In our study we use the cationic metalloporphyrin with manganese(III) coordinated as a central ion inside the porphyrin ring (Mn-TMPyP). This chemical nuclease was activated by $KHSO_5$ into a high-valent metal-oxo species and able to oxidize guanine in a controlled manner. Under these conditions we were able to characterize previously unknown dehydro-guanidinohydantoin residue. Actually such a functionalized tetrakis-methylpyridiniumyl porphyrin can triggered two types of DNA oxidation, one of which is specifically DNA sequence dependant.




Acknowledgements: this research was supported by Ministry of Science and Higher Education in Poland under joined LCC (Toulouse, France) and the CMMS PAS (Lodz, Poland) program.

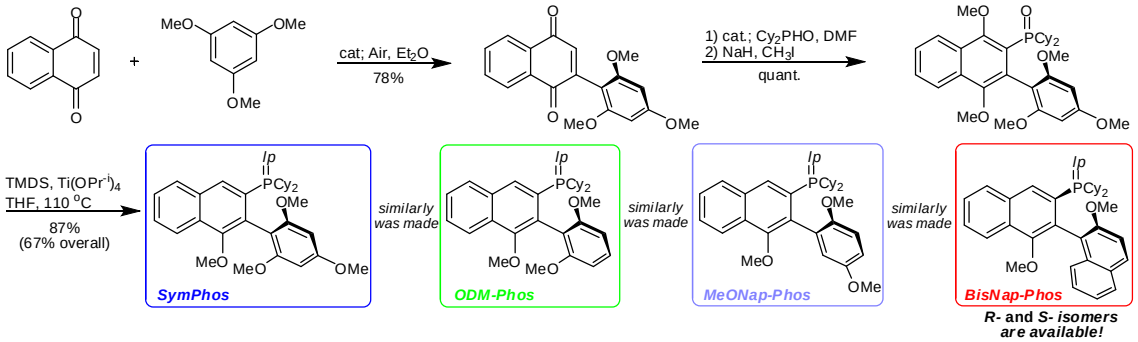
## L-6

# Novel Ligands for a "Greener" and Asymmetric Cross Coupling Reactions

**Oleg M. Demchuk**

*Department of Organic Chemistry, Maria Curie-Skłodowska University, 20-614, Lublin, Gliniana 33, Poland, Oleh.Demchuk@UMCS.Lublin.pl*

Successful realisation of the difficult cases of Suzuki, Negishi, Heck etc. coupling reactions is only possible when well tuned catalysts, usually based on the phosphine palladium complexes, are utilised. The particular place in the range of efficient ligands for cross coupling reactions occupy electronically reach and bulky biaryl core based ligands of C,P- type of complexation due to their extremely high activity and potential ability to posses an chiral axis as well as additional chirality at phosphorus atom. Herein we are intended to demonstrate that new catalysts based on transition metal complexes of novel easily available in large scale and prepared by straightforward modular approach phosphines, could be efficient enough to promote difficult cross coupling reactions run in "greener" conditions (water, open flask, low temperature, no toxic waste). An inexpensive 3-step synthetic pathway starting from naphthoquinone and leading to highly active scalemic ligands has been therefore developed. The sequence of high yielding, catalysed by bismuth or rhodium complexes, oxidative arylation of naphthoquinone gave the key 2-arylnaphthoquinone intermediates used next for facile, as well as catalysed by bismuth, Michael addition of secondary phosphine oxides. Subsequent O-methylation and reductions of the resulting products gave access to the target air-stable phosphine ligands in excellent overall yields. Also we decided to use properly substituted biaryls to introduce an atropoisomeric chirality into the phosphine structure. Thus the same approach was applied in the synthesis of nonracemic atropoisometric ligands.




Several transition metal complexes of the obtained ligands were utilised in the model cross coupling, CH activation and asymmetric hydrogenation reactions giving the corresponding products in good to excellent yield and good ee. The details of these studies and some other issues will be discussed.

## *Guest Lecture*

# The Utility of Carbon Disulphide and Lawesson's Reagent for Synthesis of different Bioactive Sulfur Fused Heterocycles

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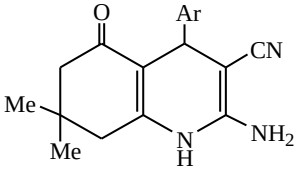
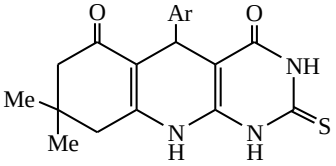
[b]*Chemistry Department, El-Aflaj Girls College, El-Kharj University Kingdom of Saudi Arabia.*

[c]*Chemistry Department Faculty of Science, Ain Shams University, Cairo, Egypt.*

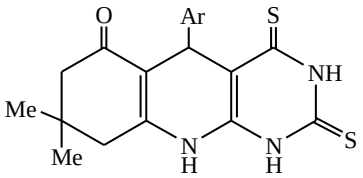
Hexahydroquinoline derivatives **1a,b** reacted with $CS_2$ in different concentrations to yield the corresponding adducts **2a,b** and **3a,b** respectively. Carrying out the same reactions in acetone as solvent produced the modified new products **4a,b**. The interaction of pyrazolopyridine derivatives **5a-b** with $CS_2$ under the same previous conditions furnished the isolated products **6a-d** & **8a-d**, respectively. Studying the behaviour of **1a,b** towards Lawesson's reagent (LR) in different concentrations, formed the final adducts **9a,b** and **10a,b**. On the other hand, the reaction of **5a,b** with LR formed the corresponding sulfur heterocycles **11a-d** and **12a-d**. The structure of the all newly synthesized compounds was confirmed with the spectroscopic and micro analytical data. The antimicrobial activity of the synthesized compounds was examined.



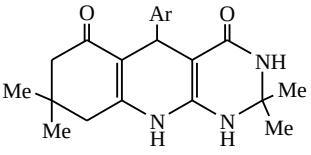
**1a,b**



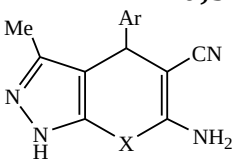
**2a,b**



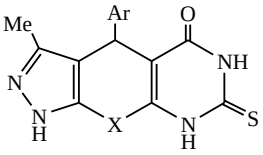
**3a,b**



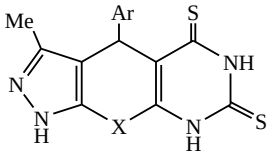
**4a,b**



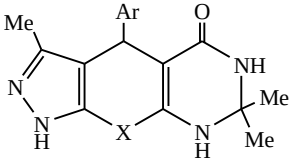
**5a-d**



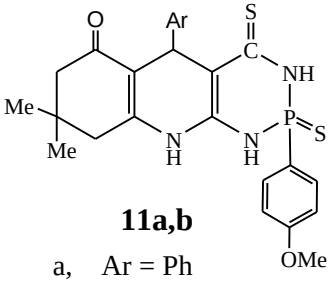
**6a-d**



**7a-d**



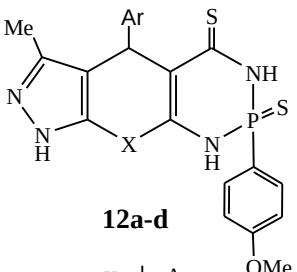
**8a-d**



**11a,b**

a, Ar = Ph

b, Ar = Cl-$C_6H_4$



**12a-d**

| | X | Ar |
|---|---|---|
| a, | O | $NMe_2$-$C_6H_4$ |
| b, | O | $NO_2$-$C_6H_4$ |
| c, | NH | Ph |
| d, | NH | Cl-$C_6H_4$ |