



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

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IInd International Mini-Symposium

Heteroatom-Containing Reactive Intermediates

May 26th 2009

Program & Abstracts

Conference venue: University of Łódź, Faculty of Chemistry,
Str.-Tamka 12, Lecture room #016

Organizing committee:

Chairman:	Prof. dr. hab. Grzegorz Młostoń
Secretary:	dr. hab. Jarosław Romański
Member:	dr. Katarzyna Urbaniak

Program

- 1.55 pm *Invitation and opening*
- Session # 1: Chairman: Prof. Michał Pietrusiewicz**
- 2.00 – 2.30 pm SL-1 Peter Schreiner - *Hydroxycarbenes*
(Justus Liebig University in Giessen, Germany)
- 2.30 – 3.00 pm SL-2 Piotr Bałczewski - *Recent Progress in Phosphonate C-Radical Chemistry*
(Centre of Molecular and Macromolecular Studies,
Polish Academy of Sciences, Łódź, Poland)
- 3.00 – 3.30 pm SL-3 Anna Chrostowska - *Contribution of the UV-photoelectron Spectroscopy to the Electronic Structure Studies of the Heavier Group 14 Analogues of Carbenes and Radicals*
(University of Pau, France)
- 3.30 – 3.45 pm *Coffee break*
- Session # 2 Chairman: Prof. Bogdan Kryczka**
- 3.45 – 4.15 pm SL-4 Frank Jordan - *Defining States of Ionization and Tautomerization of the Thiamin Diphosphate Coenzyme on Enzymes*
(Rutgers, State University of New Jersey, United States)
- 4.15 – 4.45 pm SL-5 Bogdan Skalski - *Photochemistry of 5-Halogeno Derivatives of 4-Thiouridine*
(Adam Mickiewicz University in Poznań, Poland)
- 4.45 – 5.15 pm SL-6 Janusz Zakrzewski - *Novel Electrophilic C-C Bond-Forming Reactions of Ferrocene*
(University of Łódź, Poland)
- 5.15 – 5.30 pm *Coffee break*
- Session # 3 Chairman: Prof. Józef Drabowicz**
- 5.30 – 6.00 pm SL-7 Krzysztof Wojciechowski - *From Vicarious Nucleophilic Substitution to Aza-ortho-xylidenes*
(Institute of Organic Chemistry, Polish Academy of Sciences,
Warsaw, Poland)
- 6.00 – 6.30 pm SL-8 Heinz Heimgartner – *Honor Guest*
1,5-Dipolar Electrocyclizations – New Pericyclic Reactions of Thiocarbonyl Ylides
(University of Zurich, Switzerland)

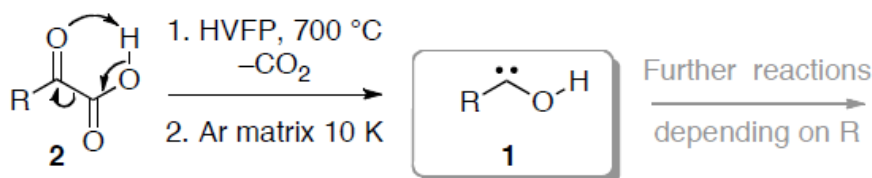
SL-1

Hydroxycarbenes

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Hydroxycarbenes (R–C–OH, **1**, Scheme 1) are prototypical donor-substituted carbenes that play a fundamental role in the class of synthetically valuable heterosubstituted carbenes as reagents and metal ligands. Paying tribute to the discoverer of such metallocarbene complexes, these types of structures (especially their higher analogues, the alkoxy-carbenes) are now referred to as Fischer carbenes.[1] Yet, attempts to prepare free alkoxy-carbenes through thermal decomposition of metal carbenes have failed.[2] The parent hydroxycarbene, **1a** (R=H) also plays an important role in deciphering the organic chemistry of small organic molecules in prebiotic earth and extraterrestrial environments because **1a** is implied in the thermal decomposition of glyoxylic acid (**2a**, R=H) that also gives rise to formic acid, CO, CO₂, H₂, and H₂O.[3] In the present talk we show that hydroxycarbenes **1** can be generated in a general fashion (R=OH, CH₃, OCH₃) thermally through high-vacuum flash pyrolysis (HVFP), subsequently be trapped in an argon matrix at 10 K, and be fully characterized spectroscopically.



The lecture will present firm experimental as well as high-level computational evidence for the first successful preparation of carbenes of type **1**, and will present their reactions that largely depend on the nature of the substituent R. For instance, while **1a** (R=H) disappears within only 2 h through H-tunneling under a very high barrier (ca. 30 kcal mol⁻¹), **1b** (R=OH) survives under matrix isolation conditions for at least several days.[4] Several new derivatives will be presented and discussed in detail.

References

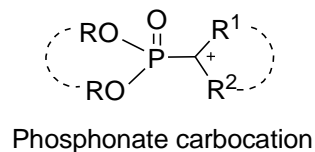
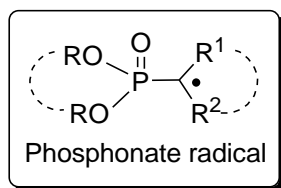
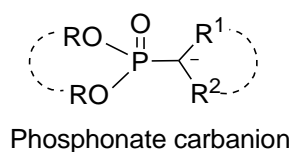
- 1 E. O. Fischer, A. Maasbol, *Angew. Chem. Int. Ed.* **1964**, *3*, 580.
- 2 M. A. Sierra, *Chem. Rev.* **2000**, *100*, 3591.
- 3 Schreiner, P. R., Reisenauer, H. P.; Pickard, F.; Simmonett, A. C., Matyus, E.; Allen, W. D.; Császár, A. G. *Nature* **2008**, *453*, 906. *Highlight*: G. Bucher, *Angew. Chem. Int. Ed.* **2008**, *47*, 6975.
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Recent Progress in Phosphonate C-Radical Chemistry

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In contrast to continuing development of α -carbanion chemistry of phosphonates as a method of functionalization of this class of synthetically, pharmacologically and agrochemically important compounds, chemistry of phosphonate C-centered radicals lagged behind for many years despite the potential capabilities of stabilization of both phosphonate carbanions, carbocations and radicals by the phosphoryl P(=O) group.



A recent progress in radical chemistry of C-C bond formation reactions as well as C-heteroatom (halogen, O, S, Se) and C-C bonds cleavage reactions, involving phosphonate C-centered radicals, will be presented with a special emphasis laid on achievements of recent years in the iodine atom transfer addition (I-ATRA) and cyclization (I-ATRC) reactions which were developed in our lab.

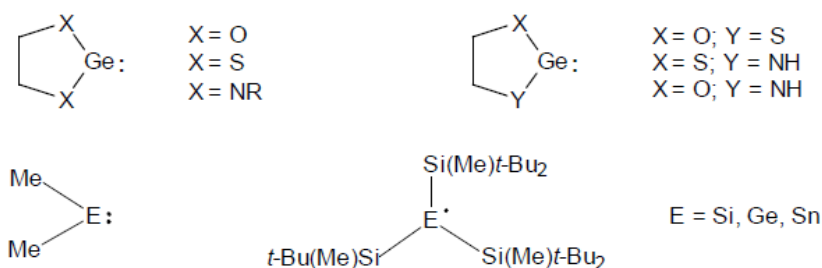
SL-3

Contribution of the UV-Photoelectron Spectroscopy to the Electronic Structure Studies of the Heavier Group 14 Analogues of Carbenes and Radicals

Anna Chrostowska

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In recent years, there have been a large number of experimental and theoretical studies devoted to understanding the trends in the electronic structures and reactivities of the silicon, germanium, and tin analogues of carbenes and radicals. Because the simplest congeners of these molecules are transient species, most studies of this type have been focused on derivatives bearing electronically and/or sterically stabilizing substituents. The study of simple derivatives is more challenging, requiring *in situ* generation of the species of interest from appropriate precursors and their direct spectroscopic detection. One particularly powerful tool for the characterization of the fundamental electronic properties of such molecules is UV photoelectron spectroscopy (UV-PES). Flash vacuum thermolysis (FVT) or vacuum gas solid reactions (VGSR) coupled with UV-PES proves to be especially suited to generate and analyze in real-time small amounts of short-lived species. In the present study such technique has been employed for the measurement of gas phase ionization energies of the series of the homo and heteroleptic O, N and S α,α' -disubstituted germanediyls $XYGe:$, the heavy carbene analogues $Me_2E:$ ($E = Si, Ge, Sn$) and radicals $(tBu_2MeSi)_3E\cdot$ ($E = Si, Ge, Sn$). The PE spectra have been analyzed with the aid of theoretical calculations [B3LYP/6-311G(d,p) for Si and Ge; B3LYP/SDD for Sn]. A general comparison of the electronic properties of the heavy carbene and radical species will be presented and discussed.



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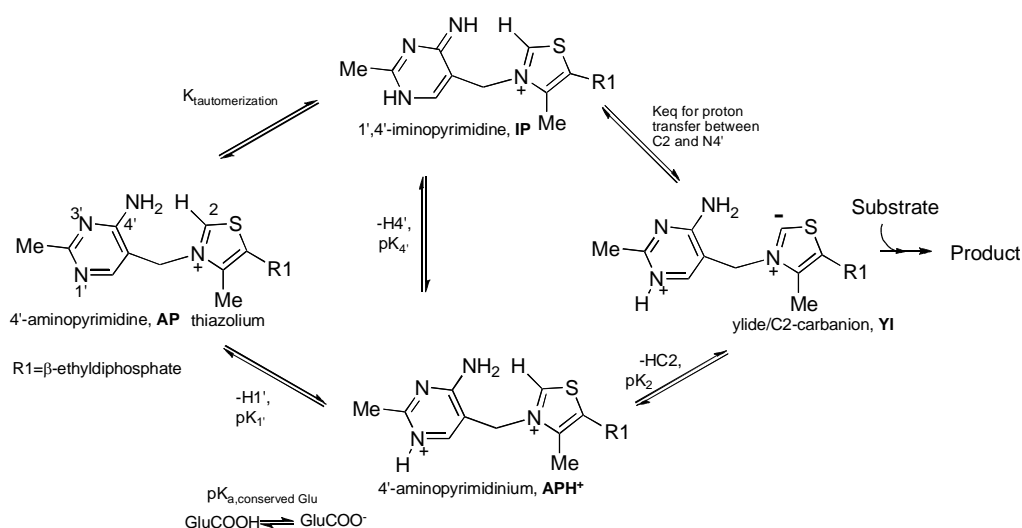
SL-4

Defining States of Ionization and Tautomerization of the Thiamin Diphosphate Coenzyme on Enzymes

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Thiamin diphosphate (ThDP) is the coenzyme derived from vitamin B1 and it comprises two aromatic rings, a thiazolium and a 4-aminopyrimidine ring. While the role of the thiazolium ring in catalysis has been known since the mid 1950's from the seminal work of R. Breslow at Columbia University, only more recently has a catalytic role been suggested and supported for the 4'-aminopyrimidine ring. The presentation will summarize currently available information regarding the state of ionization and tautomerization of the 4'-aminopyrimidine ring of ThDP on enzymes requiring this coenzyme. The thiazolium ring at its C2 atom forms a series of covalent intermediates with its substrates as an electrophilic catalyst (via the ylide in the Scheme), while the 4'-aminopyrimidine ring carries out intramolecular proton transfers, virtually unprecedented in coenzyme chemistry. Even more striking, the acid-base catalysis is assisted by the rare 1',4'-iminopyrimidine tautomer of the cofactor and there is evidence for the presence of all three forms of the 4'-aminopyrimidine from spectroscopic observations. An understanding of the state of ionization and tautomerization of the 4'-aminopyrimidine ring in each of the covalent and non-covalent intermediates provides important details about proton movements during catalysis. Circular dichroism spectroscopy, both steady state and time-resolved, has been crucial for obtaining this information since no other experimental method has provided such atomic detail so far.



Scheme 1. States of tautomerization and ionization of ThDP prior to substrate addition.

Recent review of the subject:

N. S. Nemeria, S. Chakraborty, A. Balakrishnan, F. Jordan (2009) FEBS Journal 276, 2432-2446.

SL-5

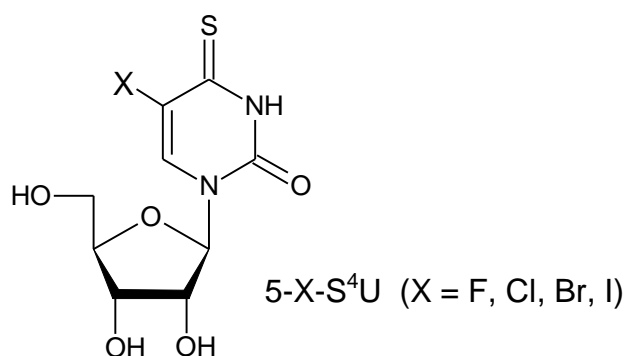
Photochemistry of 5-Halogeno Derivatives of 4-Thiouridine

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The 4-thiouracil as well as 5-halogenourracil (X = Br, I) chromophores have attracted considerable interest in recent years as efficient photocrosslinking agents in the studies of nucleic acids structure and their interactions with proteins.

In a search for new photolabels we turned our attention to 5-halogeno-4-thiouracil derivatives (5-X-S⁴U) bearing both of the above mentioned photochemically active functionalities.



As a part of our research goal to evaluate the potential of these compounds as photoprobes in nucleic acids we have undertaken systematic photophysical and photochemical studies of several 5-halogeno-4-thiouridines (X = F, Cl, Br, I). The results of these studies obtained in our lab over the last several years will be presented and discussed.

SL-6

Novel Electrophilic C-C Bond-Forming Reactions of Ferrocene

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Numerous applications of ferrocenyl compounds in various branches of science, ranging from homogenous catalysis and materials science to biochemistry and medicine, have stimulated the search of simple and efficient methods of functionalization of this metallocene.¹ In recent years, scientific interests of our group concentrated on the development of novel, electrophilic C-C bond-forming reactions of ferrocene aligned with modern requirements for synthetic methods such as atom-economy, step-economy and Green Chemistry. In the lecture our major achievements in this field will be presented:

- Friedel-Crafts acylation with acyl trifluoroacetates²
- acetoacetylation with diketene³
- alkenylation with β -ketoesters⁴, β - ketophosphonates⁵ and epoxides⁶
- carboxy- and carbothioamidation with KXCN (X = O, S)⁷
- Fujiwara-Moritani Pd(II)- catalyzed alkenylation with unsaturated esters.⁸

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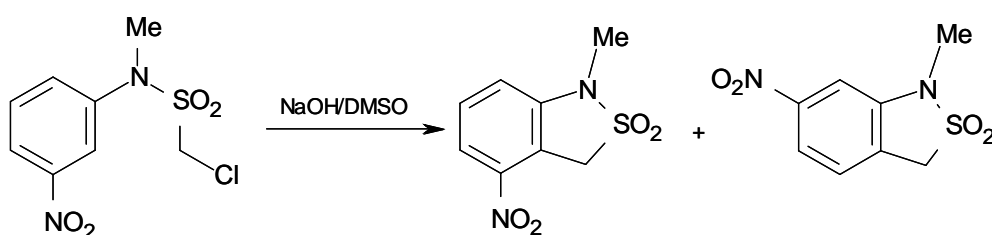
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- [2] D. Plažuk, J. Zakrzewski, *Synth. Comm.*, 34 (2004) 99.
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From Vicarious Nucleophilic Substitution to Aza-ortho-xylylenes

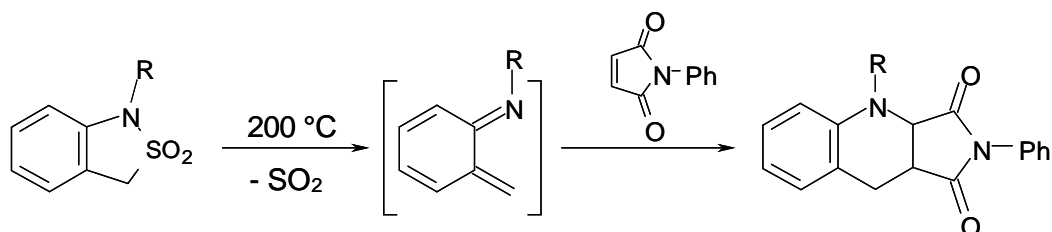
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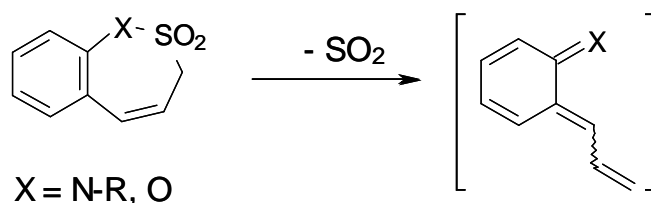
Intramolecular Vicarious Nucleophilic Substitution (VNS) in nitro derivatives of chloromethanesulfonanilides leads to 2,1-benzisothiazoline 2,2-dioxides (benzosultams).¹



Thermal extrusion of SO_2 from benzosultams leads to aza-ortho-xylylenes (quinonemethylene-imines).² These reactive 1-azadienes enter [4+2] cycloaddition reactions to form 1,2,3,4-tetrahydroquinoline derivatives³ or undergo a [1,5] sigmatropic hydrogen shift to form *ortho*-alkylaminostyrenes.⁴



The recent developments in this area, particularly reactions of azaxylylenes and their oxa analogues generated from seven-membered benzosultams and benzosultones will be presented.



1. Review on benzosultams: K. Wojciechowski, *Heterocycles* **2002**, 57, 1717-1740.
2. Review on aza-ortho-xylylenes: K. Wojciechowski *Eur. J. Org. Chem.* **2001**, 3587-3605.
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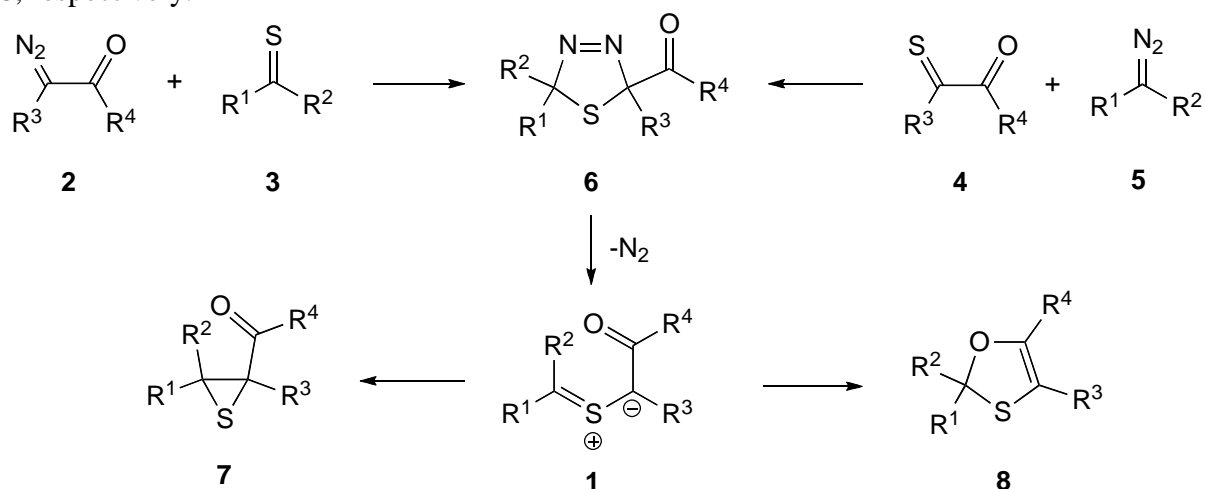
1,5-Dipolar Electrocyclizations – New Pericyclic Reactions of Thiocarbonyl Ylides

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Thiocarbonyl ylides proved to be useful building blocks for the synthesis of sulfur heterocycles [1,2]. Among other approaches, a convenient access to these reactive intermediates is the thermal decomposition of 2,5-dihydro-1,3,4-thiadiazoles, which are accessible by [2+3] cycloaddition of thiocarbonyl compounds with diazo compounds. In addition to *intermolecular* 1,3-dipolar cycloadditions and dimerizations, thiocarbonyl ylides undergo *intramolecular* stabilizations via 1,3-dipolar electrocyclization, 1,4-hydrogen shift, and *Wagner-Meerwein*-type reaction.

Acyl-substituted thiocarbonyl ylides **1** can be generated by the reaction of α -diazo ketones **2** with thiocarbonyl compounds **3** [3] or by treatment of α -thioxo ketones **4** with diazo compounds **5** [4] to give 1,5-dihydro-1,3,4-thiadiazoles **6** and subsequent N_2 -elimination. In the absence of external reagents, these reactive intermediates undergo competitive 1,3- and 1,5-dipolar electrocyclizations leading to thiiranes **7** and 1,3-oxathioles **8**, respectively.



In the presentation, relevant examples, scope and limitations of the reactions of **1** will be discussed. The focus will be on the extension to thiocarbonyl ylides of type **1**, which bear other π -systems as a substituent at C(α).

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