ICCST-XVI
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16th International Conference on the Chemistry of Selenium & Tellurium

August 26 – 29, 2025 in Halle (Saale)

Program & Abstracts

A Warm Welcome to the 16th International Conference on the Chemistry of Selenium and Tellurium!

On behalf of the international advisory board and the organizing team, it is my great pleasure to welcome all of you —familiar faces and new ones alike — to the 16th International Conference on the Chemistry of Selenium and Tellurium (ICCST) here in Halle an der Saale.

Since its inception with the first meeting in New York in 1971, the ICCST conference series has served as a unique meeting point for scientists from all over the world, with each conference being held at a different location every 3 years. It is known for its intimate atmosphere, which fosters open and productive discussions. This year, we are especially honored to hold our conference in the historic halls of the German National Academy of Sciences, the Leopoldina — a truly fitting venue for scientific exchange, where tradition and future-oriented research meet.

We would also like to take a moment to reflect on the legacy of the conference's founding spirit, Wolfgang H.H. Günther, who was instrumental in shaping this series until his passing in 2021. To honor his profound contributions to the field, we will be presenting the inaugural Wolfgang Günther Award for Lifetime Achievement and the Wolfgang Günther Award for Scientific Excellence in Selenium and Tellurium Chemistry.

This conference brings together approximately 70 participants from 17 countries and four continents. I am confident that this international mix of knowledge and experience will lead to inspiring conversations and fruitful new ideas. The wide range of presentations — from inorganic and organic chemistry to materials science, medicine, and biosciences — highlights the impressive diversity and relevance of selenium and tellurium chemistry.

I wish you a conference filled with new insights, opportunities to forge valuable scientific connections, and an enjoyable and rewarding time here in Halle.

Sincerely,

Ludger Wessjohann

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Program

Tuesday, August 26

9:30 Registration open (please bring your presentation stick!)

11:35 Light Lunch

Session 1 *Chair: Ludger Wessjohann*

12:15 Opening Ceremony

12:30 Plenary Lecture: **Robert J. Hondal** (*Univ. of Vermont, VT, USA*)
Oxidized ergothioneine as a substrate for thioredoxin reductase

13:15 Keynote Lecture: **Jacek Ścianowski** (*N. Copernicus Univ., Poland*)
Chiral selenides, diselenides and benzisoselenazolones - syntheses, transformations and bioactivity

13:45 Short Talk+: **Thomas Wirth** (*Cardiff Univ., United Kingdom*)
Control in Electroorganoselenium Chemistry

14:00 Short Talks: **Guilherme F. Botelho** (*U Federal do Rio de Janeiro, Brazil*)
Tribromoisocyanuric acid-mediated telescoped synthesis of 2-amino-4-arylselenazoles and its activity against *Meloidogyne incognita*
Erki Enkvist (*Univ. of Tartu, Estonia*)
Microsecond-Lifetime Photoluminescent Probes Based on Selenium Containing Protein Kinase Inhibitors
Javier Mateos (*Univ. of Vienna, Austria*)
Dicationic Diselenides – Bench-Stable Sources of Se(III) Radicals
Koh Sugamata (*Univ. of Tsukuba & Rikkyō Univ., Japan*)
Selenium- and tellurium-centered 2-Heteroallenes

14:45 Tea break

Session 2 *Chair: Sangit Kumar*

15:15 Invited Talk: **Victor Mamane** (*CNRS & Univ. of Strasbourg, France*)
Chalcogen Bonding Involving Tellurium: Study in Solution and Catalysis

15:45 Short Talks: **Laura Orian** (*Università degli Studi di Padova, Italy*)
Toward a rational design of ROS scavengers: does chalcogen matter?
Markus S. Seidl (*Univ. of Regensburg, Germany*)
Atypical S_N1 Reactions at Carbon Enabled by σ-Bond Quantum Poling
Magdalena Obieziurska-Fabisiak (*N. Copernicus Univ., Poland*)
Synthesis and bioactivity evaluation of *ortho*-substituted *β*-carbonyl phenyl selenides

16:30 Invited Talk: **Pavel Arsenyan** (*Latvian Inst. of Organic Synthesis, Latvia*)
Selenium in medicinal and material chemistry: a blessing and a curse

17:00 Invited Talk: **Vijay Pal Singh** (*Panjab University, India*)
Benzoselenazole Antioxidants with Potential Biological Applications against Oxidative Damage

17:30 Tea break

17:45 **Evening Lecture** (*"A Musical Surprise"*)

Program

Wednesday, August 27

Session 3 — *Chair: Thomas Wirth*

9:00 Plenary Lecture: **Anna Kipp** (*Friedrich-Schiller-Univ. Jena, Germany*)
Nutritional intake and homeostatic regulation of selenium

9:45 Keynote Lecture: **Barbara Nawrot** (*CBMM Łódź, Poland*)
2-Thio- and 2-Seleno-uridines – The Key Players of tRNA Transcriptomics

10:15 Short Talk+: **Vito Lippolis** (*Università degli Studi di Cagliari, Italy*)
Concurrent Intermolecular Halogen and Chalcogen Bonds in Bis(Pyridine)-Substituted Tellurophene-Dihalogen Adducts: Structural Insights and Reactivity Trends

10:30 Tea break

Session 4 — *Chair: Fabian Mohr*

11:00 Keynote Lecture: **Michio Iwaoka** (*Tokai Univ., Japan*)
Chemical and Biological Applications of Selenocysteine-Containing Peptides

11:30 Invited Lecture: **Christopher Williams** (*Vanderbilt Univ., TN, USA*)
Context-Dependent Roles of Selenoprotein P in Intestinal Inflammation and Tumorigenesis

12:00 Short Talks: **Avinash Chaurasia** (*Banaras Hindu Univ., India*)
Hg(II) and Pb(II) detoxification using *s*-triazine core-based N_3Se_3 type organoselenium moieties
Wei Cao (*Beijing Normal Univ., China*)
Selenium-Modified Melanins and their Radiation Protecting Properties *In Vivo*
Alessandro Rubbi (*Università degli Studi di Padova, Italy*)
Molecular Mechanisms of Poisoning: the Toxicity of Methyl Cadmium against (Seleno)Cysteine

12:30 Lunch

Session 5 — *Chair: Elżbieta Wojaczyńska*

13:45 Plenary Lecture: **Claus Jacob** (*Saarland Univ., Germany*)
From Organic Waste to Selenium Sulfide: A Bio-Based Synthetic Strategy

14:30 Keynote Lecture: **Huaping Xu** (*Tsinghua Univ., China*)
Non-Carbon Main Chain Polytelluoxane

15:00 Short Talks: **Laura G. Sarbu** (*"Alexandru Ioan Cuza" Univ., Romania*)
Selenium halide induced bridge formation in [2.2]paracyclophanes
Luca Sancineto (*Univ. of Perugia, Italy*)
Electrophilic selenylation of electron rich aromatics, a DoE guided approach
Shenghan Zhang (*Tsinghua University, China*)
Radiation Protection Polytelluroxane Material

15:30 Tea break

Session 6 *Chair: Vito Lippolis*

16:00 Short Talk+: **Hua Lu** (*Peking University, China*)
High-Throughput and Machine Learning-Assisted Synthesis of Selenopolypeptides for Biomedicine

16:15 Short Talks: **Graciela Mahler** (*Universidad de la República, Uruguay*)
Unveiling Selenosemicarbazones as Covalent Inhibitors of SARS-CoV-2 Main Proteases: Mechanistic Perspectives

Ryusei Hamano (*University of Tsukuba, Japan*)
Preparation of a Bulky Ferrocenyl Ligand Bearing a Selenium-coordinating Moiety and Its Application towards Isolable Oraganosilylenes

Chen-Wei Liu (*National Dong Hwa Univ., Taiwan*)
Atomically Precise Alloys Stabilized by Se-donor Ligands

17:00 Short Talks: **Lucian M. Birsa** (*"Alexandru Ioan Cuza" Univ., Romania*)
A New Bridge in [2.2]Cyclophanes: The Addition of Se_2Cl_2 to *Pseudo-Geminally* Substituted Bispropargylic Alcohols

Chaowei He (*Tsinghua University, China*)
Controlling Branching Morphology in Dynamic Selenium Crystal via Stress Engineering

Svastik Jaiswal (*IISER Bhopal, India*)
Directing Group Strategy for the Isolation of Organoselenium(VI) Benzoselenonates: Metal-Free Catalysts for Hydrogen Evolution Reaction

17:30 Keynote Lecture: **Vanessa do Nascimento** *(Univ. Federal Fluminense, Brazil*)
Chalcogeno-Functionalization as a Tool: From Supramolecular Catalysts to Bioactive Compounds

18:00 **Evening Special** (*"A Historical Surprise"*)

Program

Friday, August 29

Session 7 — *Chair: Antonio L. Braga*

9:00 Keynote Lecture: **Sangit Kumar** (*IISER Bhopal, India*)
Bidentate Ligand Derived Organochalcogens: Synthesis to Catalytic Applications

9:30 Keynote Lecture: **Francesca Marini** (*Univ. of Perugia, Italy*)
Electrophiles Containing Selenium at High Oxidation State: Insight into Reactivity and Biological Property

10:00 Invited Lecture: **Fabio De Moliner** (*The Univ. of Edinburgh, United Kingdom*)
Benzoselenadiazoles as tunable fluorophores and photosensitizers

10:30 Short Talk+: **Claudio Santi** (*Univ. of Perugia, Italy*)
Reimagining Selenium Role in Medicinal Chemistry: The Role of Se-S Bonds

10:45 Tea break

Session 8 — *Chair: Ludger Wessjohann*
Laudator: Ignacio Vargas-Baca

11:15 Keynote Lecture: **Ignacio Vargas-Baca** (*McMaster Univ., Canada*)
From Obscurity to Mainstream: The Rise of Chalcogen Bonding

11:45 Best Short Talks Prize & Laudatio Wolfgang HH Günther Award

12:15 Award Lecture: **Tristram Chivers** (*Univ. of Calgary, Canada*)

12:45 Award Lecture: **Jens Beckmann** (*Bremen Univ., Germany*)
Selenium and Tellurium Centered Radical Cations

13:15 Closing Ceremony with Preview 17th ICCST

13:30 Goodbye Coffee & Snacks

Abstracts Tuesday

Robert Hondal

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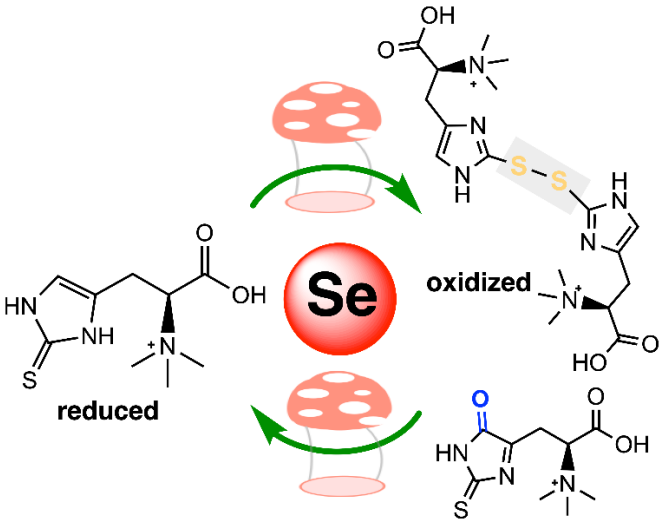
Oxidized ergothioneine as a substrate for thioredoxin reductase



(1.)**Hypothesis:** Oxidized forms of ascorbic acid are substrates for thioredoxin reductase. We wondered whether oxidized forms of ergothioneine, a vitamin-like molecule, could also be substrates for thioredoxin reductase. If so, then thioredoxin reductase could form a central axis for interacting with vitamin C, vitamin E, and ergothioneine.

(2.) **Methods:** We oxidized ergothioneine with either hydrogen peroxide or singlet oxygen. Oxidation of ergothioneine with hydrogen peroxide resulted in the disulfide form. We used light and the photosensitizer rose bengal to generate singlet oxygen, which oxidized ergothioneine to 5-oxo-ergothioneine (5-oxo-EGT). The oxidized products were verified by mass spectrometry and then these products were assayed for activity by thioredoxin reductase by monitoring the consumption of NADPH.

(3.) **Results:** The three oxidized forms of ergothioneine are ergothioneine disulfide (ESSE), 5-oxo-EGT, and ergothioneine radical (ES•). We were able to determine that both 5-oxo-EGT and ESSE were substrates for thioredoxin reductase in our activity assays. Using ESSE as a substrate, the values of k_{cat}

→ Program Tuesday

and K_M were determined to be 2900 ± 360 min^{-1} and 430 μM ± 105, respectively. For 5-oxo-EGT, the values of k_{cat} and K_M were determined to be 335 min^{-1} ± 50 and 91 μM ± 15, respectively. We were unable to measure the activity with ES• because unlike the ascorbyl radical, its lifetime is much shorter because it rapidly forms the disulfide, ESSE. Selenoneine, the selenium analogue of ergothioneine was also found to be a substrate when oxidized to the diselenide with hydrogen peroxide. The k_{cat} was much higher than ESSE, 6270 min^{-1} ± 790, but the K_M was significantly higher, 2335 μM ± 615. The activity of these substrates depended upon the presence of selenium in the enzyme as the truncated form of the enzyme lacked activity. We are currently exploring the role of ergothioneine as a superior scavenger of hypochlorous acid, which will also be discussed as these results are developing.

References:

Jenny KA, Mose G, Haupt DJ, Hondal RJ. Oxidized Forms of Ergothioneine Are Substrates for Mammalian Thioredoxin Reductase. Antioxidants (Basel). 2022 Jan 19;11(2):185. doi: 10.3390/antiox11020185. PMID: 35204068; PMCID: PMC8868364.

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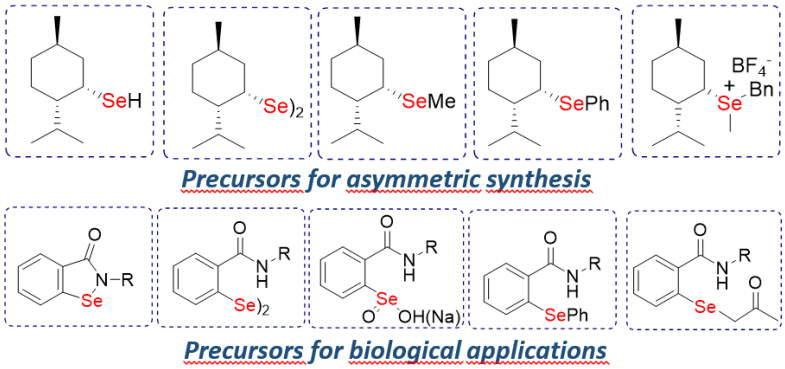
Chiral selenides, diselenides and benzisoselenazolones - syntheses, transformations and bioactivity

Magdalena Obieziurska-Fabisiak, Agata Paculа-Miszewska



Chiral organoselenium derivatives are an interesting alternative to classical reagents used in asymmetric synthesis. They have been used, for example, in methoxyselenenylation reactions, selenocyclization, addition of diethylzinc to aldehydes or synthesis of natural products [1]. On the other hand, due to the biological activity of organoselenium derivatives, searching for new reagents, including chiral ones, with antioxidant, antiviral, antibacterial or anticancer properties is an important research direction in modern organic synthesis [2]. During the lecture, the methods developed in our group for the synthesis of several groups of organoselenium derivatives, including selenides, diselenides, selenonium salts, phenylselenides, *β*-carbonylselenides, benzisoselenazolones, and selenenic acids and their salts, will be presented. The obtained derivatives were successfully used in asymmetric methoxyselenenylation, selenocyclization, synthesis of epoxides and cyclopropanes, and allylic alkylation reactions. They were also tested as antioxidants and anticancer, antibacterial, and antiviral agents.

References:

[1] Paculа-Miszewska A., Ścianowski J., at al. *Organoselenium reagents derived from natural compounds* ,in.: Chalcogen chemistry : fundamentals and applications / Lippolis Vito (R*ed.*), **2023**, London, RSC.
[2] Obieziurska-Fabisiak M., Pacula-Miszewska A., Ścianowski J., at al. *Organoselenium compounds as antioxidants*, Arkivoc **2023**, *5*, 212-235.

Control in Electroorganoselenium Chemistry

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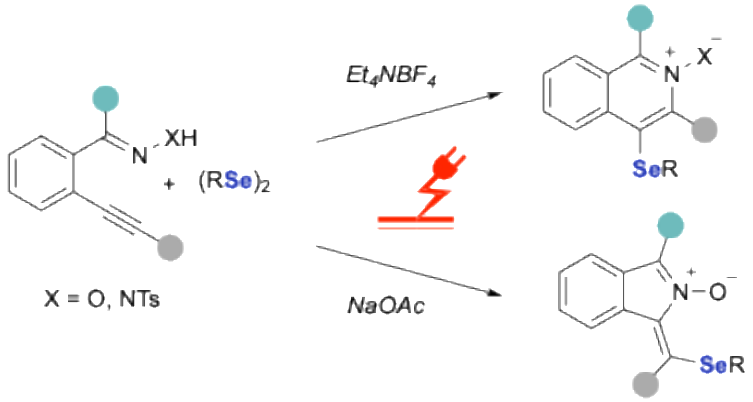

Can electrochemistry be used to control selenocyclizations?

We present a single-pass continuous flow electrolysis method enabling selective activation of diselenides and oximes to access seleno-substituted isoquinoline and isoindole derivatives. Mechanistic studies showed a radical pathway *via* iminoxyl radicals to isoindole *N*-oxides and an ionic mechanism leading to isoquinoline *N*-oxides. Our findings highlight the untapped potential of supporting electrolytes in regiodivergent electrochemical transformations and provide a sustainable and scalable platform for continuous flow approaches for synthesising selenium-containing heterocycles with biological relevance.

References:

[1] Automated Electrochemical Selenenylations: N. Amri, T. Wirth, *Synthesis* **2020**, *52*, 1751–1761.
[2] Continuous Flow Electroselenocyclization of Allylamides and Unsaturated Oximes to Selenofunctionalized Oxazolines and Isoxazolines. O. Alzaidi, T. Wirth, *ACS Org. Inorg. Au* **2024**, *4*, 350–355.
[3] Electrolyte-Controlled Regiodivergent Continuous Flow Electroselenocyclisations. S. Arepally, H. Gieman, T. Wirth, *submitted*.

→ Program Tuesday

Tribromoisocyanuric acid-mediated telescoped synthesis of 2-amino-4-arylselenazoles and its activity against *Meloidogyne incognita*

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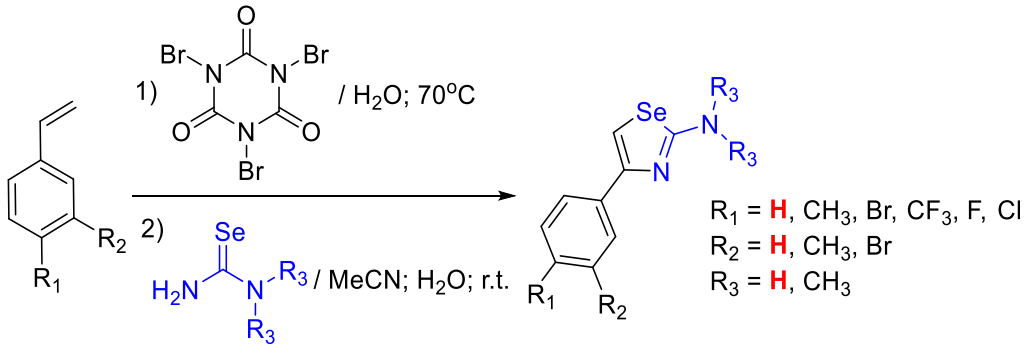

Selenazoles constitute a class of compounds of great medicinal and agriculture interest.[1] Although they are traditionally prepared via Hanztsch synthesis, this methodology has some disadvantages, such as the use of toxic and lacrimatory reagents. Therefore, we have studied the use of tribromoisocyanuric acid (TBCA) in telescopic preparation of heterocycles,[2] which present potential to be used in the control of plant-parasitic nematodes (PPNs) that pose a significant threat to global food production. Currently, PPNs account for over 30% of crop yield losses worldwide.[3] Therefore, the development of new products to control PPNs is of great interest and here we present a telescopic synthesis of 2-aminoselenazoles from substituted styrenes, mediated by TBCA. The protocol involves three reactions in one process: a tandem (co-bromination of styrene and oxidation of the formed bromohydrin by excess TBCA to give phenacyl bromides) followed by a telescoped condensation with selenoureas to give the corresponding 2-amino-4-arylselenazoles in 25–65% yield. When the selenazoles were tested against *Meloidogyne incognita*, which is a very destructive PPN,[3] 2-amino-4-phenylselenazole caused 100% nematode immobility (commercial nematicide: 100 %) and more than 60% nematode mortality (commercial nematicide: 56.7 %).

References:

[1] Koketsu, M.; Ishihara, H. *Curr. Org. Chem*. **2003**, *7*, 175.
[2] de Andrade, V. S. C.; de Mattos, M. C. S. *Synthesis* **2019**, *51*, 1841.
[3] Stucky, T. *et al*. *J. Appl. Microbiol*. **2024**, *35*, Ixae111.

Microsecond-Lifetime Photoluminescent Probes Based on Selenium Containing Protein Kinase Inhibitors

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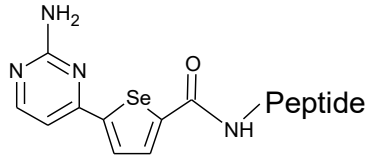
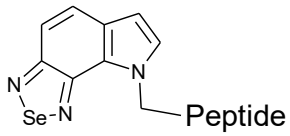
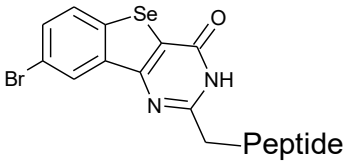


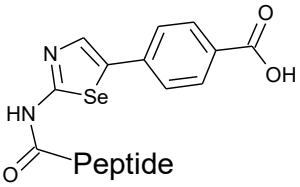
ACS Chem. Biol. 2011, **6**, 1052



Chem. Commun. 2014, **50**, 4096



RSC Adv. 2015, **5**, 96750



Bioorg. Med. Chem. 2018, **26**, 5062

We have discovered that binding of bicyclic and tricyclic sulfur- and selenium containing aromatic compounds to the active site of a protein kinase induced weak phosphorescence in water buffer solution at room temperature. Attachment of a fluorescent dye to these molecules lead to significant enhancement of the long-lifetime signals because of phosphor-sensitized delayed fluorescence through the Förster-type triplet-to-singlet energy transfer (TS-FRET). We have used these ARC-Lum probes for quantification of protein kinases in biological samples, screening of kinase inhibitors in displacement assays, and monitoring of activity of protein kinases in living cells through measurements of delayed luminescence.

Luminescence intensity of selenium containing ARC-Lum probes is 10-100 fold higher than that of their sulfur-containing counterparts, making these probes more valuable in practical applications. Higher signal intensity originates from the heavy atom effect of selenium that facilitates the inter-system crossing and emission from the excited triplet state of the donor phosphor (phosphorescence and TS-FRET).

Construction of selenium containing aromatic compounds is a challenging task, as the availability of the starting compounds is limited and synthetic procedures require optimization. Overall, we show that organic compounds possessing protein binding-induced long-lifetime photoluminescence have wide applicability for bio-medical research and encourage synthesis and testing of new selenium-containing aromatic compounds.

→ Program Tuesday

Dicationic Diselenides – Bench-Stable Sources of Se(III) Radicals

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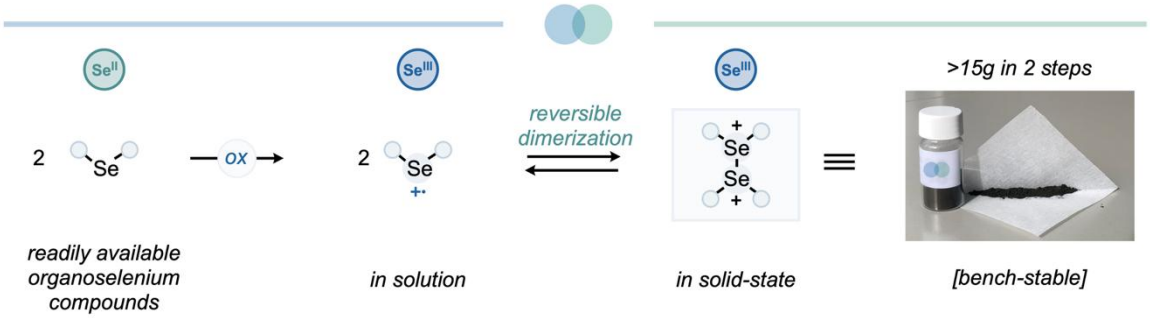

This talk presents the first contribution of our group to the field of organoselenium chemistry.[1]

Stable radicals that can be stored and handled under ambient conditions are valuable reagents in redox and radical-mediated processes due to their versatility and operational simplicity. We report the multigram-scale synthesis, isolation, and characterization of dicationic diselenides as bench-stable reservoirs of one-center/one-electron selenium radical cations – species that remain underexplored in organic synthesis.[2],[3] A key feature of these reagents is their selective, reversible head-to-head dimerization, which enables Se(III) radical formation in solution due to the low bond dissociation energy of the Se–Se σ-bond. The salts are stable under ambient conditions for over one month without requiring an inert atmosphere. Their reactivity includes oxidation and substitution reactions with hydrazines, alcohols, sulfinates, borates, silanes, and stannanes, including examples involving complex molecular architectures.

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Selenium- and tellurium-centered 2-Heteroallenes

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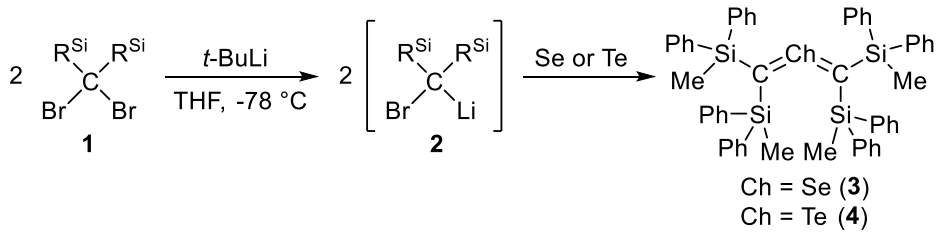
Allenes (>C=C=C<) contain a central carbon atom that shares two double bonds with two adjacent carbon atoms. The central carbon atom in such compounds is sp-hybridized, resulting in the formation of linear structures. Chalcogen-centered heteroallenes, formulated as E=Ch=E (E = R_2C and/or RN, Ch = S, Se), are considered as group 16 analogues of carbon-based allenes. These chalcogen-centered heteroallenes, however, exhbit different structures and properties compared to their carbon-based counterparts.[1] Recently, we reported the isolation and characterization of a stable sulfur-centered heteroallene, bis(methylene)-λ^4-sulfane $R^{Si}_2C=S=CR^{Si}_2$ (R^{Si} = $MePh_2Si$).[2] This compound exhibits extraordinary stability towards air, moisture, and heat, and its molecular structure shows the C_{2v} symmetry with a bent C=S=C moiety comprising a 3-center-4-electron π-bond. As a continuation of this work, we expected that the bis(methylene)-λ^4-selane and tellane provide more detailed structure in solution using ^{77}Se and ^{125}Te NMR spectroscopy. Additionally, the C=Se and C=Te moieties are expected to exhibit higher reactivity compared to the sulfur analogues.

In this presentation, we report the synthesis of the first stable bis(methylene)-λ^4-selane (**3**) and tellane (**4**). These compounds are synthesized via the reaction of elemental selenium and tellurium with the corresponding carbenoid (**2**), which is generated by the lithiation of bis(silyl)dibromomethane (**1**). The unique structures and reactivities of compounds **3** and **4** will be discussed.



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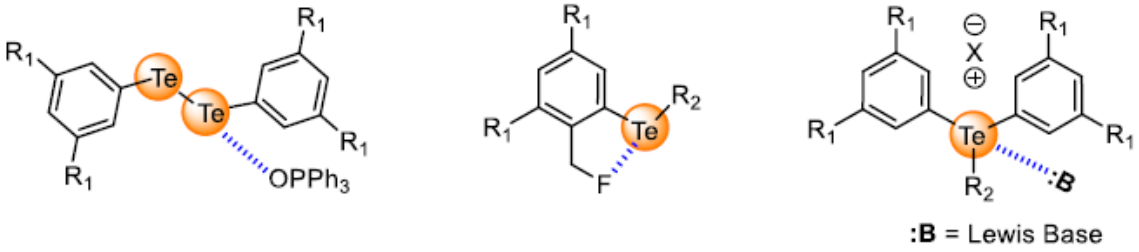
Chalcogen Bonding Involving Tellurium: Study in Solution and Catalysis



Chalcogen bond (ChB) is a non-covalent interaction, identified as such relatively recently, analogue to the now more common halogen bond (XB). Both are due to attraction between a nucleophilic entity (Lewis base) and an electrophilic region, called σ-hole, present on a halogen or a chalcogen atom. In contrast to monovalent halogens, chalcogen atoms exhibit two σ-holes due to their divalent character. Although comparable to hydrogen bond (HB) in term of strength, XB and ChB are highly directional in sharp contrast to HB. This interesting property has recently allowed the exploitation of ChB in many applications, including organocatalysis. As for XB, ChB strength depends on the polarizability of the chalcogen atom (S<Se<Te) and thus, chalcogen interactions involving tellurium are the strongest. Tellurium derivatives are thus becoming promising for applications based on σ-hole interactions. This presentation will focus on the latest results from our laboratory involving tellurium derivatives in solution [1] with a special focus on noncovalent catalysis [2].

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→ Program Tuesday

Toward a rational design of ROS scavengers: does chalcogen matter?

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ROS scavenging refers to the process by which biological or synthetic compounds neutralize reactive oxygen species (ROS), thereby preventing oxidative damage to cellular components. This mechanism is essential for maintaining redox homeostasis and is a central topic in redox biology, pharmacology, and aging research. The efficiency of ROS scavenging relies on several fundamental chemical reactions, whose thermodynamic and kinetic favorability is highly dependent on the molecular structure of the scavenger. For instance, the well-documented antioxidant activity of polyphenols underpins their recognized health benefits. However, a clear, systematic, and quantitative understanding of the structure–reactivity relationships governing ROS scavengers is still lacking. Developing such insight would enable the rational design of new compounds or the repurposing of existing ones. To address this gap, selected case studies will be presented, supported by accurate quantum mechanical analyses that reveal mechanistic and energetic details, shedding light on the influence of specific chemical motifs including the role of different chalcogens in ROS scavenging.

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→ Program Tuesday

Atypical S_N1 Reactions at Carbon Enabled by σ-Bond Quantum Poling

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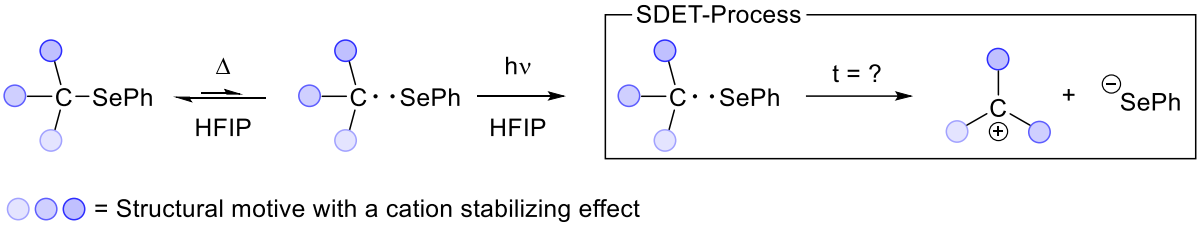

In classical S_N1 reactions, the heterolytic cleavage of polarized σ-bonds - typically between carbon and electronegative groups such as halides or sulfonates - leads to ion pair intermediates.[1] In contrast, homopolar bonds like C–Se (EN = 2.55 for both atoms) lack this intrinsic polarization and preferentially undergo homolysis under thermal or photochemical conditions, yielding radical pairs.[2] Conventional methods to induce heterolysis in such systems rely on stoichiometric activation of selenium, often at the expense of chemoselectivity.[3] We report a conceptually distinct approach in which C–Se bond cleavage is directed *via* sequential modulation of the substrate's electronic and vibrational states. Initial thermal homolysis generates a neutral radical pair, followed by selective photoexcitation of the selenium-centered radical. This triggers a stimulated doublet-doublet electron transfer (SDET) from the carbon-centered donor to the selenium acceptor, resulting in net heterolysis and formation of an ion pair from homopolar precursors.[4] The characteristic timescales of the SDET process have previously been determined by transient absorption spectroscopy using photothermally generated radicals. To provide synthetic validation, a series of radical clock substrates was employed. These radical clocks also offer insight into the relevant timescale of the SDET when initiated *via* thermophotonic activation. The obtained results support the proposed timing of the electron transfer and confirm the occurrence of SDET within distinct, experimentally resolvable temporal regimes. This method enables S_N1-type reactivity in substrates traditionally restricted to homolytic pathways, offering new avenues for selective bond activation via internal excitation control.

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→ Program Tuesday

Synthesis and bioactivity evaluation of *ortho*-substituted *β*-carbonyl phenyl selenides

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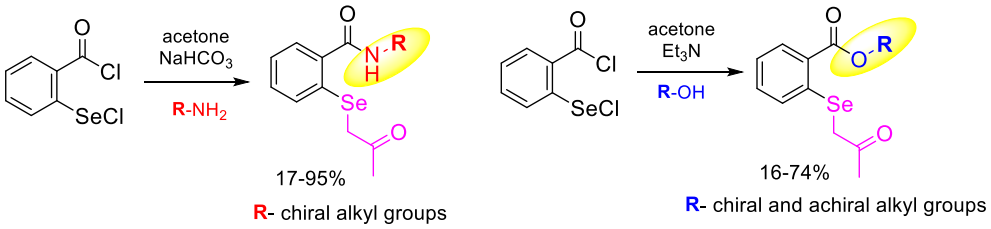

Organoselenium compounds are recognized for their significant antioxidant and anticancer properties, largely due to the reactivity of the selenium center and its ability to mimic selenoenzyme activity, such as that of glutathione peroxidase (GPx). This study explores a novel series of selenium-containing derivatives featuring a 2-(2-oxopropyl)selanyl moiety.[1,2] Two structural variants of *β*-carbonyl selenides were synthesized via efficient methodologies: those bearing *o*-amido groups substituted on nitrogen with chiral alkyl chains, and those incorporating *o*-ester groups substituted on oxygen with both chiral and achiral alkyl chains. For each pair of enantiomers and diastereomers, the influence of stereochemistry at individual carbon centers on antioxidant and antiproliferative activities was systematically evaluated. Ester substitution reduced H_2O_2-scavenging ability but improved free radical neutralization and enhanced antiproliferative activity compared to amide analogs.

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Selenium in medicinal and material chemistry: a blessing and a curse

Global refined selenium production is about 2,700 tons per year, with 17% used in nutrition and cosmetics and the rest in material production. Over the past two decades, research has confirmed selenium as an essential microelement for human health. It is a key component of GPx, an enzyme regulating cellular redox balance, and has antioxidant properties. Selenium supports immune function, slows HIV progression, reduces cardiovascular disease risk, and may help prevent certain cancers by influencing oxidative stress and cellular processes. Despite its essential role in health, selenium has a narrow therapeutic window, with toxic doses close to beneficial ones. Many industrial selenium compounds, such as sodium selenite, have high toxicity (LD_{50}: 8.1–12.1 mg/kg), comparable to potassium cyanide. In recent decades, researchers have explored selenium-containing molecules for their antioxidant, redox-modulating, antitumor, and antihypertensive properties. However, despite promising preclinical results, none of the thousands of synthesized selenium-based compounds have been approved as drugs.

This presentation will provide a critical analysis of our studies in anticancer research, beginning with ammonium selenites. While certain compounds, such as triethanolammonium and diisopropyl gamma-butyrobetaine, exhibited remarkable *in vivo* sarcoma suppression (up to 100%), their high toxicity posed a significant challenge, ultimately ruling out inorganic selenium as a viable option for anticancer drug development. To address these limitations, we investigated the incorporation of selenium into existing drugs by substituting sulfur, oxygen, or nitrogen atoms. This approach was applied to selective estrogen receptor modulators and degraders (SERM/SERD). Although the selenium-based analogue achieved a 30% reduction in breast cancer growth, its efficacy was deemed insufficient for further development. A more promising approach emerged from selenium-modified coumarins, inspired by Ayurveda and traditional medicine. In particular, a novel selenium-containing coumarin derivative, PA-27, was identified as an effective antimetastatic agent. PA-27 demonstrated outstanding suppression of tumor metastasis and formation in multiple *in vivo* models, with some mice showing complete tumor inhibition.

Targeting cancer metabolism offers a promising approach for selective tumor elimination. Pyruvate kinase M2 (PKM2), a key regulator of glucose metabolism in cancer cells, is an attractive therapeutic target. A novel class of selective PKM2 inhibitors was found, including a highly potent derivative (IC_{50} = 0.35 μM) that downregulates PKM2 mRNA, disrupts mitochondrial function, triggers oxidative stress, and exhibits broad cytotoxicity. Isoselenazolium chlorides inhibit PKM2 through an unusual mechanism, inducing a dysfunctional tetrameric assembly while acting as competitive inhibitors.

Despite the widespread use of selenium in the industrial production of various alloys, glass, quantum dots, LEDs, and solar cells, the application of organic selenium-containing compounds in OLED technology remains limited. However, in recent years, the incorporation of selenium, particularly in multiresonance thermally activated delayed fluorescence (MR-TADF) emitters, has emerged as a highly dynamic and rapidly growing research area. The role of selenium in the development of novel emissive materials for OLEDs will be explored including synthetic strategies for condensed selenophenes and polyaromatic hydrocarbons and nitrogen-containing hydrocarbons.

By highlighting key advancements, this presentation aims to outline promising directions for future research in drug discovery and smart material design.

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Benzoselenazole Antioxidants with Potential Biological Applications against Oxidative Damage

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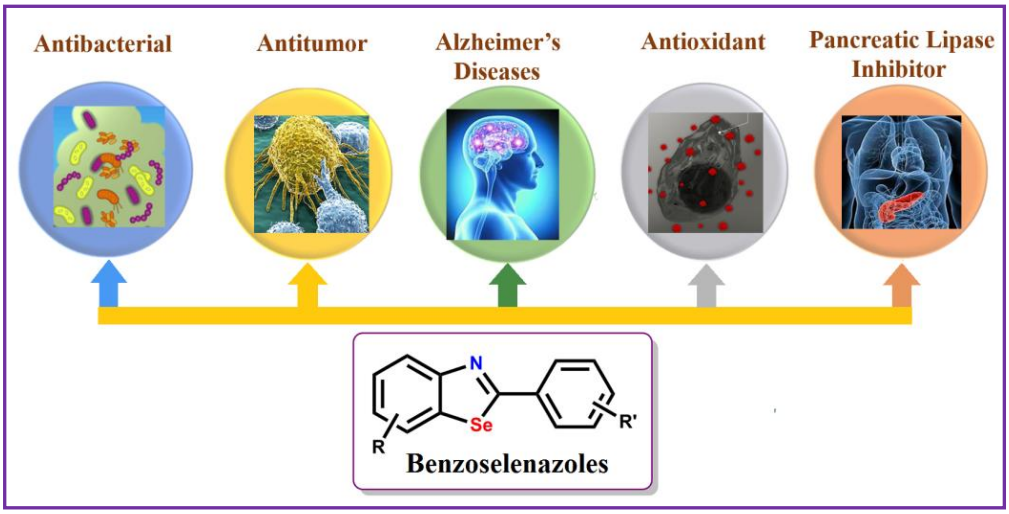

Benzoselenazoles have attracted a great attention of scientists due to their biological properties. One pot synthesis of benzoselenazoles was achieved from their corresponding diselenides and aryl aldehydes using acetic acid.[1-3] Benzoselenazoles carrying an anilide group in a very close proximity to the Se atom are found to be very good radical-trapping as well as hydroperoxide-decomposing antioxidants. They also exhibited the antimicrobial activity against *B. subtilis* and *P. aeruginosa* with minimum inhibitory concentration. The best compounds were found to inhibit the lipid peroxidation with a stoichiometric factor ≃ 2.2. Their *in vitro* antibacterial properties against the biofilm formation of *Bacillus subtilis* and *Pseudomonas aeruginosa* including molecular docking studies have been assessed. The potential applications including antioxidant, antitumor, antibacterial activities and inhibitors of pancreatic lipase have been identified.[4]

→ Program Tuesday

Molecular docking study of methyl substituted benzoselenazoles could also serve as effective inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2), with a response surface methodology (Box-Behnken Design) being used to evaluate the impact of different process variables on VEGFR-2 inhibition.[5] Overall, these results underscore the potential of 1,3-benzoselenazoles in medicinal chemistry, particularly as promising candidates for antioxidant activity and VEGFR-2 inhibition. Ferrostatin-based benzoselenazoles were also synthesized from *in situ* generated sodium selenolates and acid chlorides.[6] The ability of all benzoselenazoles as glutathione peroxidase and radical-trapping antioxidants has been investigated.

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6. R. Kadian and V. P. Singh, *unpublished results*.

Abstracts Wednesday

→ Program Wednesday

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Nutritional intake and homeostatic regulation of selenium

A balanced diet should ensure an adequate intake of essential nutrients. A vegetarian and vegan diet, in contrast to an omnivorous diet, is characterized by the avoidance of meat and fish or all foods of animal origin, respectively. In recent years, interest in these diets has increased significantly in Germany. However, this can result in an inadequate supply of essential trace elements such as selenium. Indeed, current study results demonstrate that the selenium status of vegans is reduced compared to omnivores resulting in lower levels of the circulating selenoproteins SELENOP and glutathione peroxidase (GPX) 3. Irrespective of the nutritional intake, serum levels of selenium also decrease with age and during inflammation. The combination of these aspects could significantly limit the cellular selenium supply resulting in lower selenoprotein expression and activity with functional consequences. The interplay of nutritional intake with physiological and pathophysiological characteristics is studied in mice of different sex and age as well as during inflammation feeding a selenium deficient mouse chow.

Regardless of the variations in the dietary selenium supply of mice, age-related changes were maintained indicating that these effects are driven by other mechanisms which could not be modulated by the dietary supply. Interestingly, aging and inflammation not only reduced circulating selenium concentrations but in parallel copper concentrations were upregulated and thus negatively correlated with serum selenium. The selenium homeostasis mainly depends on hepatic biosynthesis of SELENOP and SELENOP-mediated transport from the liver to e.g. the brain. Based on this, we hypothesized the direct effect of copper on SELENOP excretion resulting in the inverse regulation of the trace elements in hepatocytes and blood. Hepatic copper accumulation is a characteristic of Wilson's disease. Accordingly, SELENOP levels were low in the serum of Wilson's disease patients and Wilson's rats. Mechanistically, we proposed a disrupting effect of excessive copper on intracellular SELENOP transport resulting in its accumulation in the late Golgi. Our data indicates that besides the nutritional supply of selenium itself, additional factors such as copper status, age, and inflammation are important modulators of selenium homeostasis.

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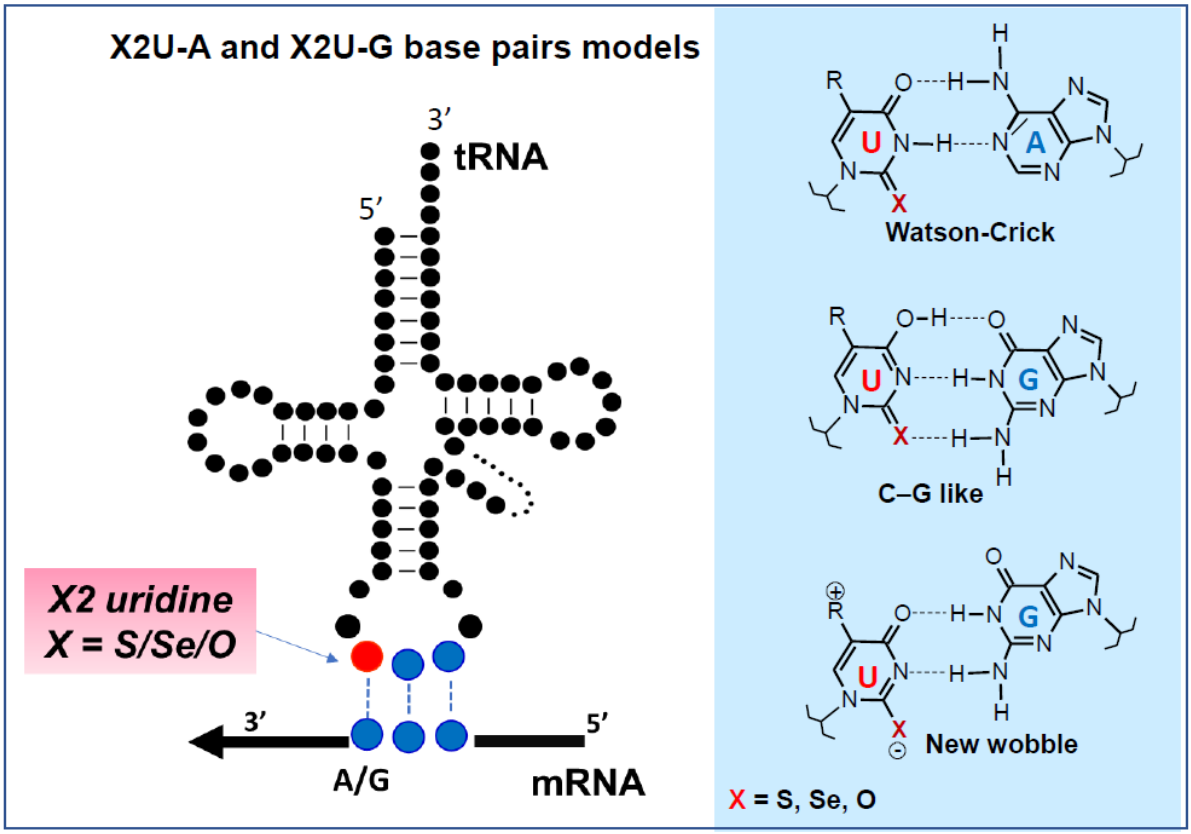
2-Thio- and 2-Seleno-uridines – The Key Players of tRNA Transcriptomics

Małgorzata Sierant, Katarzyna Kulik, Grażyna Leszczyńska,
Paulina Kuwerska, Patrycja Szczupak, Elżbieta Sochacka



tRNA molecules are among the most heavily and diversely modified RNA species. They undergo more than a hundred distinct chemical modifications that occur in different regions to stabilize the tRNA structure, ensure accurate codon-anticodon pairing, and fine-tune the overall efficiency and fidelity of protein synthesis. The most important tRNA modifications are found primarily in the wobble position of the anticodon loop (position 34, marked in red in the tRNA secondary structure, see Figure). These modifications are of central importance as they enable the tRNA to

pair with multiple codons, thereby expanding the decoding capacity and ensure that the genetic code is read accurately despite codon redundancy. **They include sulfur- and selenium-modified uridines with different substituents in position 5 of the uracil ring.** While 2-thiouridine modifications (R5S2U) occur in tRNA of all domains of life, the selenium-modified nucleosides (R5Se2U) are typically found in the tRNAs of certain bacteria. The modifications at the wobble position adjust the hydrogen-bonding potential of the uridine base and optimize it for precise recognition of the 5'-$N_1N_2A_3$ and 5'-$N_1N_2G_3$ (**A/G 3'-ending**) synonymous codons in mRNA.

In our studies, the function of R2S2U and R5Se2U in tRNA was elucidated. We proposed a two-step linear biosynthetic pathway of R5Se2U-tRNA from R5S2U-tRNA via its *S*-geranylated derivative catalyzed by tRNA 2-selenouridine synthase (SelU) [1,2]. The pH-dependent potentiometric titrations allowed to determine the p*K*a values of a series of modified R5S2Us and R5Se2Us and to confirm the hypothesis that 5-methylaminomethyl 2-thio- and 2-selenouridines (mnm55S2U and mnm5Se2U), due to the protonation of aminoalkyl group in cellular pH, can adopt a zwitterionic form to efficiently bind the G moiety following a "new wobble" base pair model [3-5] (see Figure). The other R substituted S2Us can form C-G-like base pairs with G [3]. The results of thermodynamic studies with R5S/Se2U-containing RNA duplexes suggest that the function of selenium in the wobble uridines of tRNA is to ensure the reading of the 3'-G-ending codons alongside the classical 3'-A-ending codons (bound in a Watson-Crick mode) [6]. In addition, the redox properties of selenium make Se2U particularly interesting [7], as it tends to be more reactive to oxidation than S2U [8], which could play an antioxidant role under cellular stress conditions while aiding accurate decoding. The conversion between sulfur and selenium modifications can be influenced by environmental or redox conditions, adapting the translational performance to cellular needs.

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Concurrent Intermolecular Halogen and Chalcogen Bonds in Bis(Pyridine)-Substituted Tellurophene-Dihalogen Adducts: Structural Insights and Reactivity Trends

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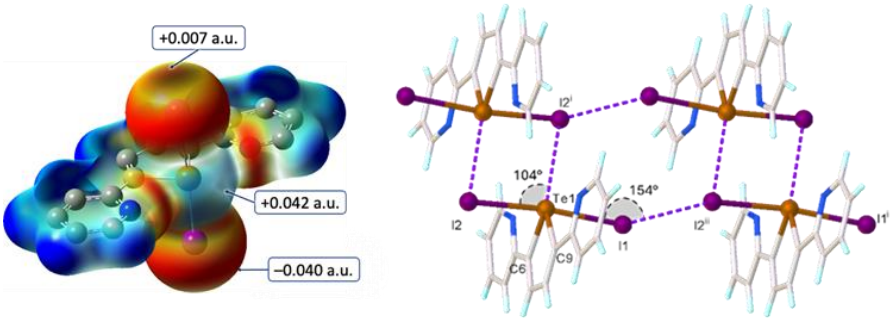

The reactivity of 2,5-bis(pyridine-2-yl)tellurophene[1] towards dihalogens XY (X = Y = I, Br, Cl; X = I, Y = Cl, Br) is explored, with a particular focus on the formation of oxidative addition adducts and the analysis of the non-covalent interactions (NCIs) governing the supramolecular architecture of the resulting compounds. Through a combination of structural characterization and theoretical calculations, the key factors influencing the formation of halogen bonds (XBs) and chalcogen bonds (ChBs) are identified, demonstrating how these interactions synergistically concur in determining the crystal packing in this class of compounds. The results provide new insights into the supramolecular chemistry of π-conjugated tellurophenes, a class of compounds of great interest for their optoelectronic properties.

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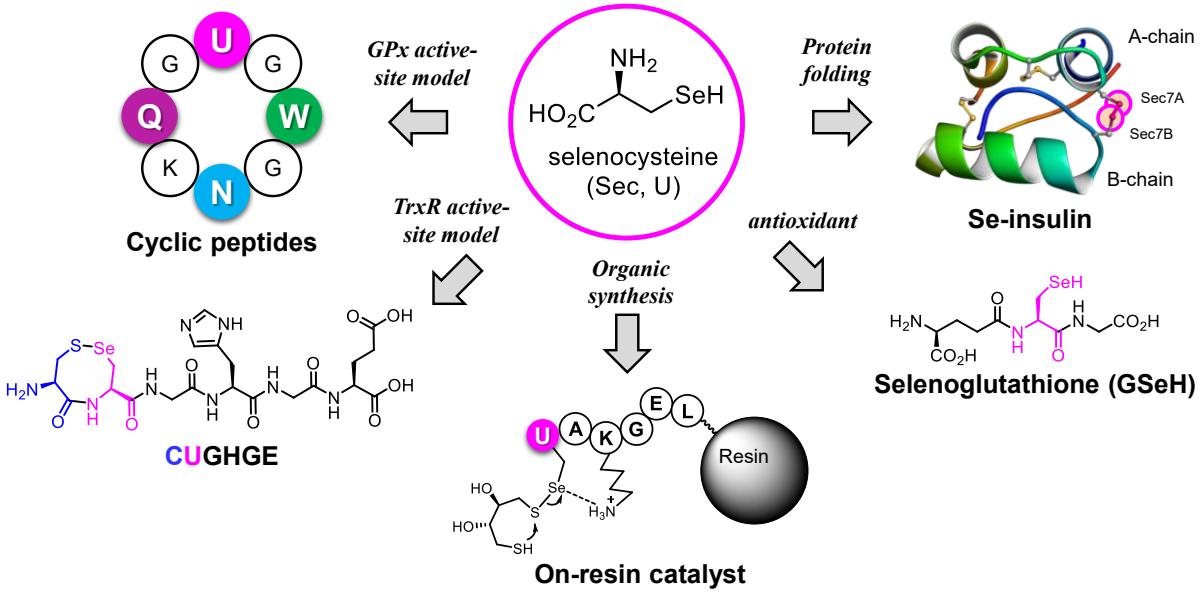
Chemical and Biological Applications of Selenocysteine-Containing Peptides



Introduction

Selenocysteine (Sec, U) is the 21st proteinogenic amino acid and is present in the active center of selenoenzymes. Our group is interested in the synthesis and applications of selenocysteine-containing peptides. Previously, we synthesized a cyclic selenopeptide that mimicked the structure of the catalytic tetrad in the active center of glutathione peroxidase (GPx) [1]. We also synthesized a linear selenopeptide modeling the active center of thioredoxin reductase (TrxR) and analyzed its TrxR-like catalytic activity, revealing that the NH···Se hydrogen bond formed between selenocysteine and histidine residues plays an important role in activating the thermodynamically stable Se-S bond [2]. In this study, we report (1) the development of on-resin selenopeptide catalysts, (2) the anti-stress functions of selenoglutathione (GSeH), and (3) the application of selenopetides to efficient folding of double-chain proteins.

→ Program Wednesday

Methods

The peptides containing selenocysteine (i.e., selenopeptides) were synthesized in liquid or solid phase using the Fmoc method. The resulting selenopeptides were purified by reversed-phase HPLC, and their structures were identified by mass spectrometry and amino acid analysis.

Results

(1) Development of on-resin selenopeptide catalysts [3]

Selenium is used as an efficient catalyst in organic synthesis, but it is toxic and post-reaction treatment is problematic. By supporting the selenium reagent on a resin, it is possible to recover selenium simply by filtering the solution after the reaction. Indeed, when the resin-supported selenopeptides were applied as catalysts to the oxidation reaction of thiols with hydrogen peroxide and the conversion reaction of unsaturated carboxylic acids to unsaturated lactones using ammonium sulfate as an oxidizing agent, the desired reactions proceeded as expected. It was also found that the catalysts can be reused for two or three times.

(2) Anti-stress functions of selenoglutathione (GSeH) [4]

GSeH, a selenium analog of GSH, is highly reactive and easily oxidized to the dimer GSeSeG [5]. We investigated the anti-stress functions of GSeSeG using HeLa cells. As a result, it was found that the cells pretreated with GSeSeG were less susceptible to oxidative stress caused by H_2O_2 as well as glycative stress caused by methylglyoxal (MG). It was proposed that the anti-stress effects were achieved by GSeSeG that penetrated into the cells, where GSeSeG was activated to GSeH enzymatically or non-enzymatically by glutathione reductase (GR) or high concentrations of GSH, respectively.

(3) Application to efficient folding of double-chain proteins [6]

The chemical synthesis of proteins consisting of two peptide chains, such as insulin, is considered difficult. We previously succeeded in efficiently synthesizing selenoinsulin, a selenium analog of insulin, by taking advantage of the fact that Se-Se bonds form preferentially over S-S bonds [7]. When the blood-glucose suppression effect of the obtained selenoinsulin was examined using diabetic model rats, it was found that in rats subcutaneously injected with selenoinsulin, the drop in postprandial blood glucose levels continued for more than 10 hours. Detailed analysis revealed that selenoinsulin is more likely to form oligomers at lower concentrations than wild-type insulin and also that the pharmacological action is sustained by forming oligomers. Recently, our group has also succeeded in synthesizing a selenium analog of relaxin, which has a similar structure to insulin, and has shown the possibility of applying the selenorelaxin to the treatment of endometriosis [8].

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Context-Dependent Roles of Selenoprotein P in Intestinal Inflammation and Tumorigenesis

Hypothesis / Scientific Question: We hypothesize that Selenoprotein P (SELENOP), a selenium-rich glycoprotein, plays context-specific roles in regulating intestinal inflammation and tumorigenesis. Specifically, SELENOP may either suppress or promote disease depending on the molecular environment, acting through redox regulation, selenium transport, and modulation of key immune and epithelial signaling pathways. This work seeks to define the conditions under which SELENOP functions protectively versus pathologically in colorectal cancer (CRC) and inflammatory bowel disease (IBD).

Methods: We used murine models of colitis and colitis-associated CRC to assess the impact of SELENOP deficiency or complete loss on disease severity and tumor formation. Transcriptomic profiling, including both bulk and single-cell RNA sequencing, was employed to examine SELENOP expression patterns in epithelial and immune compartments in both mice and humans. Bioinformatic analyses of publicly available single-cell RNA-seq datasets from human colon tissue were used to identify cell-type-specific expression patterns and associated signaling changes. Additionally, molecular and cellular assays were used to evaluate SELENOP's influence on oxidative stress responses, cytokine production, and signaling pathways such as WNT and NF-κB.

Results: Serum SELENOP levels inversely correlate with the risk of IBD and CRC in human studies. In experimental mouse models, partial SELENOP deficiency results in more severe colitis and increased tumor burden. Interestingly, complete genetic deletion of SELENOP confers protection against tumor development, suggesting a complex role for redox regulation in cancer progression. SELENOP appears to regulate both immune and epithelial cell functions, influencing redox balance and cytokine gene expression. Analysis of single-cell transcriptomic data reveals dynamic SELENOP expression across distinct epithelial subtypes and immune populations, with significant changes observed in the tumor microenvironment. Collectively, these findings support a model in which SELENOP has bimodal effects—serving protective roles in inflammation while potentially supporting tumorigenesis under certain conditions of chronic oxidative stress.

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Hg(II) and Pb(II) detoxification using *s*-triazine core-based N_3Se_3 type organoselenium moieties

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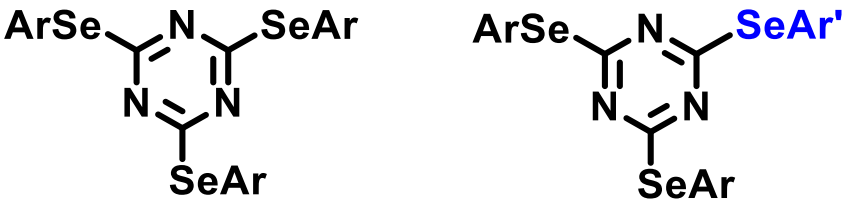

Figure: Chemical structure of *s*-triazine core-based N_3Se_3 type organoselenium moieties

Groundwater contamination of lead and mercury are significant environmental concerns due to their high toxicity to humans. It severely impacts human health, making effective removal from water sources crucial for safeguarding public health. There is an urgent need to develop effective and efficient systems to remove Hg^{2+} and Pb^{2+} from groundwater. As a means to achieve this, the successful and convenient synthesis of a few rigid tridentate organoselenium N_3Se_3 type species has been carried out. Our studies indicate that these rather simple **N_3Se_3** species show high uptake abilities for Hg^{2+} and Pb^{2+}. This novel approach may lead to the development of newer species for reducing mercury and lead contamination from aqueous medium.

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Selenium-Modified Melanins and their Radiation Protecting Properties *In Vivo*

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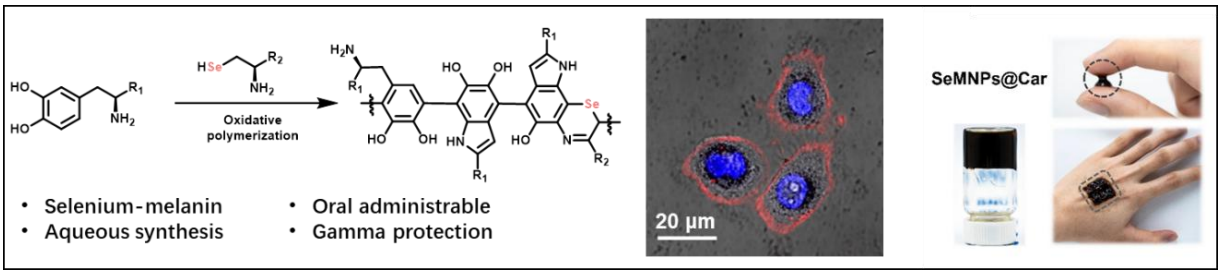

Melanin is a ubiquitous biomacromolecule in nature with a myriad of functions, including thermal regulation, radical scavenging, photoprotection, and radioprotection. Eumelanin and sulfur-containing pheomelanin are the most common subtype of melanin in human. Since selenium is a heavier chalcogen than sulfur, we hypothesize that if a selenium enriched melanin existed, it would be a better X-ray protector than pheomelanin because the X-ray absorption coefficient is proportional to the fourth power of the atomic number (Z). Compared with sulfur, selenium has lower electronegativity, higher nucleophilicity, and selenium compounds have unique bioactivities. We introduce this novel selenium analogue of pheomelanin through chemical and biosynthetic routes using selenocystine as a feedstock. We found selenomelanin effectively prevented neonatal human epidermal keratinocytes from G2/M phase arrest under high-dose X ray irradiation. The materials can be formulated into X-ray filtering hydrogel, and successfully protect mice skin in radiotherapy. Further, the selenomelanin increased mice survival to 100 % against 6 Gy total body γ-irradiation. This line of research showcases that bridging selenium chemistry with polymer synthesis creates new biomaterials for the urgent need of radiation protection.

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Molecular Mechanisms of Poisoning: the Toxicity of Methyl Cadmium against (Seleno)Cysteine

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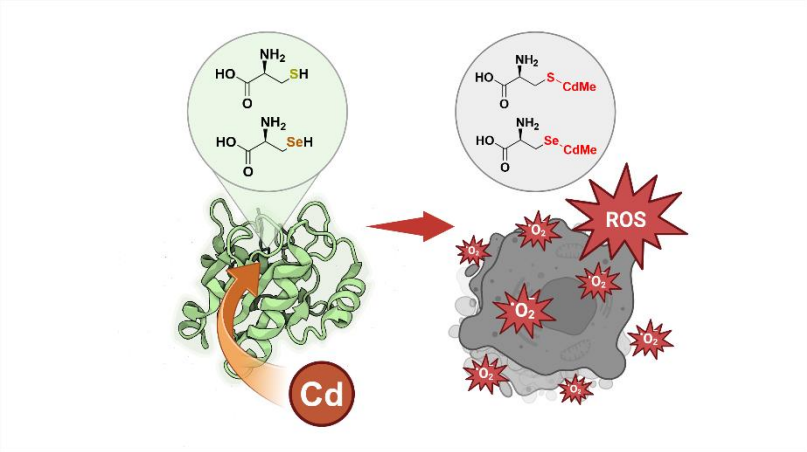

Cadmium has a high affinity for sulfur and selenium, a property strongly influencing its adverse biological effects. Thiol-based enzymes such as GPx and TRxR are primary targets of Cd-binding in organisms.[1] Although the symptoms of Cd toxicity are diverse, a rise in oxidative stress appears to be a unifying feature, due to the proliferation of reactive oxygen species and the disruption of redox balance in cells. Yet, intriguingly, the biochemistry of cadmium is not as well understood as that of other metals, prompting for deeper investigation.

Methylcadmium ($MeCd^+$) is a convenient model to study cadmium's pro-oxidant activity through computational approaches. We have therefore investigated *in silico* how $MeCd^+$ affects the peroxy-reducing potential of cysteine and selenocysteine (Cys/Sec), in comparison to previous findings on methylmercury toxicity (level of theory: BLYP-D3(BJ)/TZ2P).[2] Our results indicate that thiolate and selenolates groups within the catalytic sites of peroxidatic enzymes are significantly hampered by Cd-binding. Concomitantly, $MeCd^+$ binding facilitates the oxidation of protonated Cys and Sec residues by H_2O_2. Our results prompt for experimental investigation into these systems, which, besides broadening our limited understanding, will pave the route to the development of effective detoxification strategies.

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From Organic Waste to Selenium Sulfide: A Bio-Based Synthetic Strategy

Muhammad Jawad Nasim, Shahrzad Safinazlou, Eduard Tiganescu

Selenium sulfide, a key active ingredient in traditional anti-dandruff shampoos, is synthesized industrially from selenium dioxide (SeO_2) and hydrogen sulfide (H_2S) under acidic conditions. In a novel and environmentally conscious approach, we demonstrate that this reaction can also be performed using biogenic H_2S produced by sulfate-reducing bacteria (SRB). These robust microorganisms thrive not only on conventional growth media yet also digest nutrient-rich waste mixtures, such as cabbage juice combined with compost, or spoiled milk mixed with mineral water

Within these waste-based environments, SRBs metabolize naturally present D/L-lactate and sulfate to generate significant quantities of H_2S - up to 4.1 mM concentrations in the gas phase above standard cultures. This biogenic H_2S can be efficiently harvested from the fermentation headspace and directed into a separate reaction vessel containing SeO_2, leading to the formation of selenium sulfide without the need for complex purification steps

This method exemplifies a sustainable pathway for producing selenium compounds by valorizing organic waste and relying on the gas phase for purification. It highlights the potential of microbial biotransformation in selenium chemistry, with promising implications for both industrial and pharmaceutical applications

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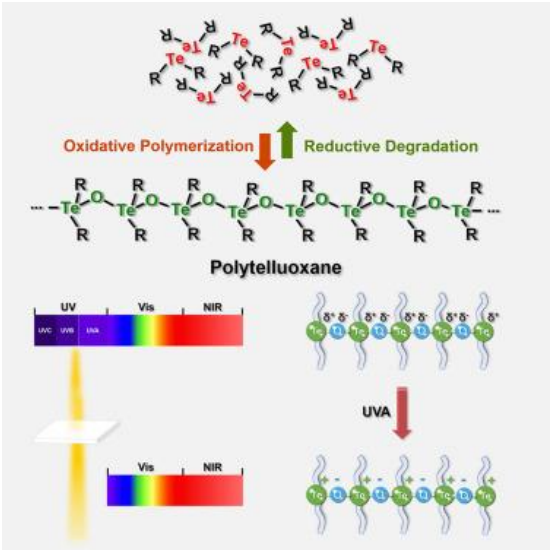
Non-Carbon Main Chain Polytelluoxane



In contrast to other main group elements, group VI elements are rarely observed to form long linear polymer main chains. We reported the synthesis and characterizations of polytelluoxane, a polymer with an inorganic main chain constituted of tellurium and oxygen, which may bridge the gap between inorganic oxides and macromolecules. Polytelluoxane has a flexible Te-O backbone and can be facilely synthesized and further processed into macroscopic materials. Because of its unique molecular structure, polytelluoxane is a transparent ultraviolet protection optical material and reveals a photocatalytic activity comparable with commercial catalysts. Moreover, polytelluoxane exhibited effective closed-loop recyclability with a recycle efficiency around 90% and a recycle number over 10. This work provided a prospective candidate for the development of flexible polymer devices and sustainable functional materials.

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Selenium halide induced bridge formation in [2.2]paracyclophanes

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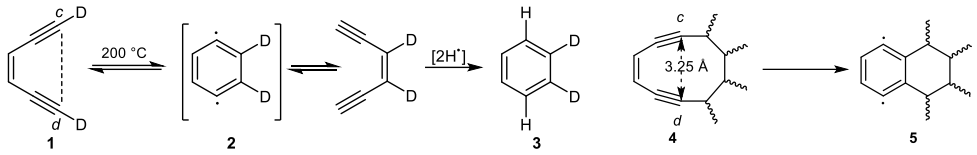
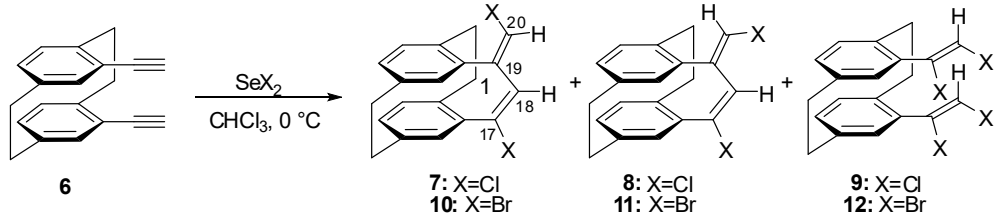
The thermal cyclization of (*Z*)-acyclic enediyne **1** to 1,4-dehydrobenzene **2** and via hydrogen abstraction to benzene **3** was studied in 1970s by Bergman.[1] A number of natural products, such as calicheamicin, esperamicin and dyneamicin, which contain the cyclic enediyne **4**, can generate a bicyclic 1,4-dehydrobenzene fragment **5**, which is capable of abstracting hydrogen atoms from DNA.[2] Studies on simple monocyclic enediynes revealed that the distance between the terminal carbon atoms of the triple bonds strongly affects the activation energy for ring closure. It was found that monocyclic enediynes in which the distance *cd* is less than 3.2 Å cyclize spontaneous at 25 °C (Scheme 1).[3]



Scheme 1. Cycloaromatization of enediynes

Functional groups in *pseudo-geminally* substituted [2.2]paracyclophanes often undergo highly specific reactions, due to the rigid framework and the short distance (3.09 Å) between the two aromatic rings within the [2.2]paracyclophane unit. Following the idea to use [2.2]paracyclophane as a spacer for model enediynes, we decided to investigate the synthesis of new enediynes analogs. Thus, an addition/elimination sequence of selenium halides to *pseudo-geminally* bisacetylene substituted [2.2]paracyclophanes leads to new bridges with an *endo-exo*-diene substructure. The reactions have been found to be sensitive to the substitution of the ethynyl group. The formation of dienes with a *zig-zag* configuration is related to that observed for nonconjugated cyclic diynes of medium ring size.[4]



Scheme 2. Reactions of selenium dichloride and selenium dibromide with *pseudo-geminal* bisacetylene **6**

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Electrophilic selenylation of electron rich aromatics, a DoE guided approach

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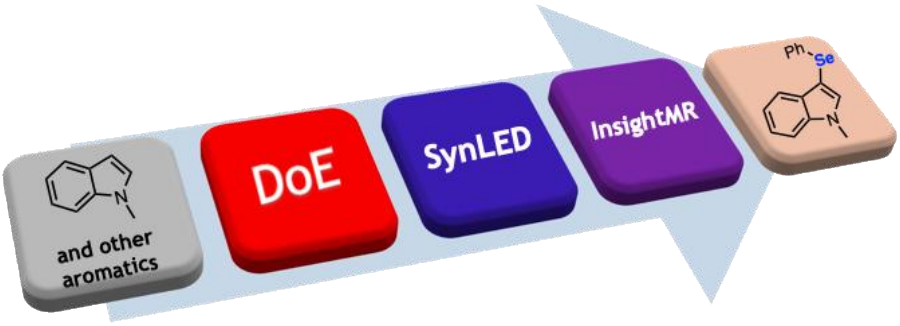
Optimizing reaction conditions is much like space exploration—except the terrain to be investigated is the so-called "experimental space." This space can, at times, be even more vast and complex than the cosmos itself. As such, a rational and efficient strategy to navigate this landscape is essential for maximizing the chances of identifying optimal conditions. Design of Experiments (DoE) paradigms provide a reliable roadmap to guide this exploration, enabling effective coverage of the experimental space with a manageable number of experiments.



This short lecture offers a concise overview of DoE paradigms, demonstrated using a free software tool [1], and their application in optimizing reaction conditions for the selenylation of electron-rich aromatics. In addition, On-line FlowNMR techniques were also implemented to study the reaction kinetic [2].

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Radiation Protection Polytelluroxane Material

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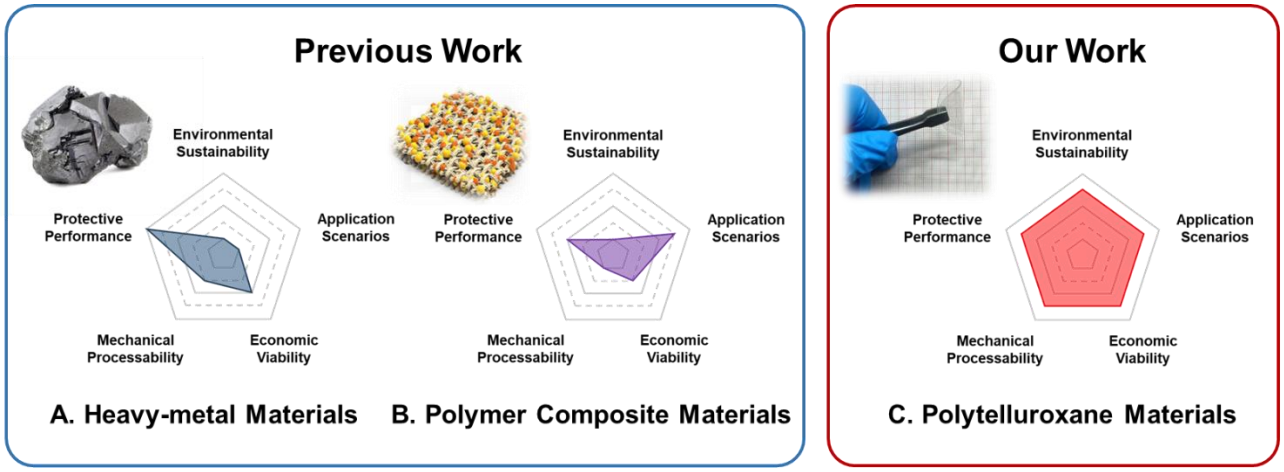

Traditional radiation protection materials predominantly depend on heavy-metal materials or corresponding polymer composite materials. While these systems have demonstrated utility across various applications, their intrinsic limitations pose significant challenges in scenarios requiring flexibility and lightweight. A notable example lies in interventional radiology, where clinicians must endure cumbersome lead aprons exceeding 10 kg to mitigate prolonged exposure to ionizing radiation. In our research, we successfully developed a tellurium-enriched polymer material for radiation protection through convenient oxidative polymerization of tellurium-containing compounds. The resultant material not only retains the advantages of fundamental polymers, such as adjustable mechanical modulus and recyclability, but also demonstrates outstanding performance in radiation protection that is comparable to or even surpasses commercial materials (Figure 1), revealing transformative potential for next-generation lightweight radiation protection solutions.

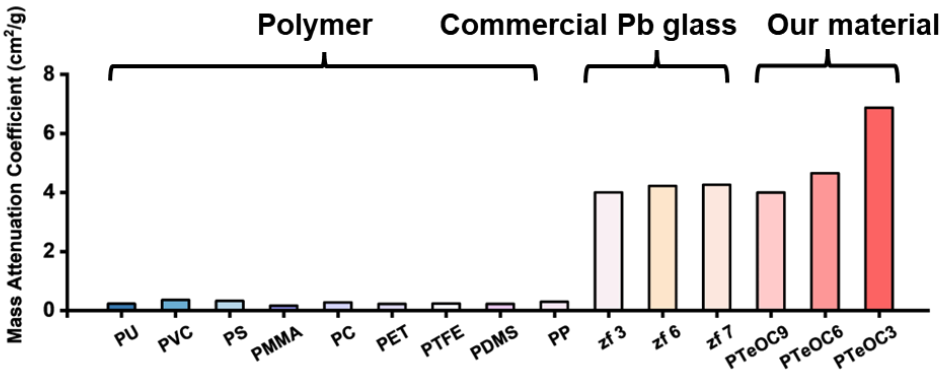

Figure 1. Comparison of Mass attenuation coefficient of different materials.

High-Throughput and Machine Learning-Assisted Synthesis of Selenopolypeptides for Biomedicine

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Selenoproteins, such as glutathione peroxidase and thioredoxin reductase, play crucial roles in biological redox processes. Dysfunction or misregulation of these proteins can disrupt the homeostasis of key redox species, leading to diseases such as inflammation and autoimmune disorders. Selenopolypeptides, as synthetic analogs of selenoproteins, hold great promise for advancing our understanding of selenium's biological functions and for developing novel therapeutic biomaterials. However, the design and synthesis of functional selenopolypeptides remain challenging and underexplored. In this talk, I will discuss our group's recent advances in the rational design and high-throughput synthesis of selenopolypeptides. By integrating automation and machine learning, we have established a build-synthesis-test-learn loop to efficiently discover functional selenopolypeptides with diverse applications, including artificial enzymes, anti-inflammatory agents, immunosuppressants, and synthetic antibodies.1-6

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Unveiling Selenosemicarbazones as Covalent Inhibitors of SARS-CoV-2 Main Proteases: Mechanistic Perspectives

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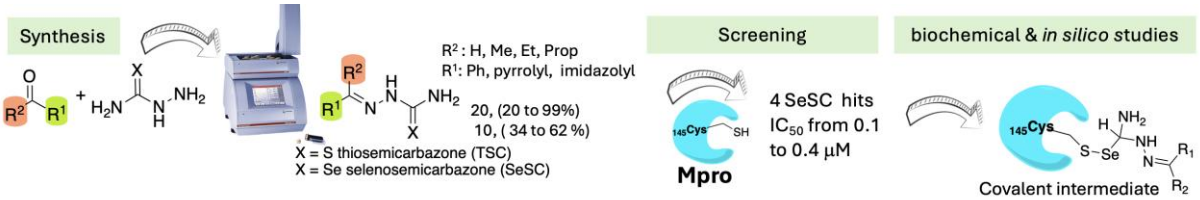

Coronaviruses (CoVs) are pathogenic single-stranded RNA viruses that cause severe respiratory illness in humans. Following entry into host cells, SARS-CoV-2 RNA is translated into polyproteins, which are processed by two essential viral proteases: the main protease (Mpro) and the papain-like protease (PLpro).[1] These enzymes are critical for viral replication and represent key targets for antiviral drug development. Since the 2019 outbreak, the highly conserved Mpro, responsible for cleaving viral polyproteins at eleven specific sites, has emerged as a particularly promising target. The structural and functional similarities between Mpro and other cysteine proteases prompted our interest, especially given our previous work identifying thiosemicarbazone (TSC) and selenosemicarbazone (SeSC) as potent inhibitors of cruzipain (Ki nM range), the cysteine protease from *Trypanosoma cruzi*.[2]

In this study, we synthesized a library of 30 compounds: 20 TSCs and 10 SeSCs, via condensation of the corresponding thio- or selenosemicarbazides with carbonyl com pounds using a monowave reactor in MeOH at 95ºC. These compounds were screened for their inhibitory activity against Mpro and PLpro. Four SeSCs and two TSCs exhibited IC_{50} values < 10 µM against Mpro, and four compounds showed similar potency against PLpro. The mechanism of inhibition of selected SeSC (CP224) was further examined by incubating Mpro and the inhibitor in the presence or absence of the reducing agent DTT. Results suggest that inhibition may involve covalent binding via a selenyl-sulfide bond between the selenium atom of CP224 and the catalytic Cys145 residue of Mpro. While CP224 showed strong inhibition under standard conditions, this effect was significantly reduced or abolished in the presence of 1 mM DTT, supporting a covalent mechanism of action. Notably, three SeSCs also demonstrated potent antiviral activity in cell-based assays, with IC_{50} values below 1 µM and high selectivity indices. These findings highlight SeSC as interesting candidates for further biochemical characterization and structure-guided optimization.

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Preparation of a Bulky Ferrocenyl Ligand Bearing a Selenium-coordinating Moiety and Its Application towards Isolable Oraganosilylenes

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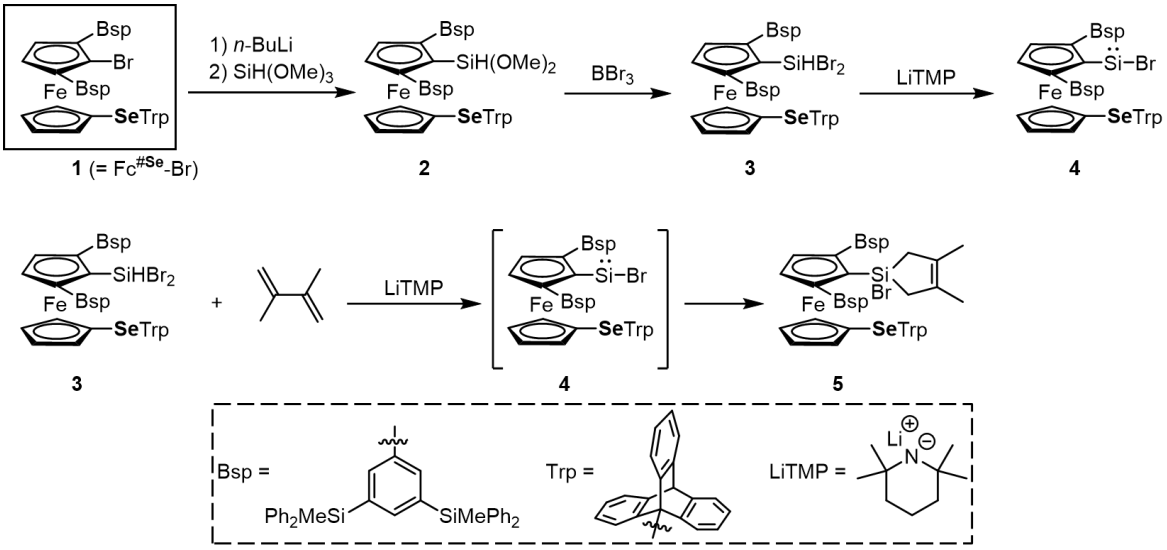

A selenide, a divalent selenium species, has the potential to act as an effective Lewis base due to its highly p-characterized lone pair. This study aims to investigate whether selenium can serve as an intramolecular donor site to a Lewis acidic center. From this perspective, we have successfully synthesized a sterically hindered ferrocenyl group ($Fc^{\#Se}$ –Br, **1**) featuring a selenium coordinating moiety, designed as a ligand to stabilize highly electrophilic species such as a silylene. A significant advantage of incorporating selenium lies in the existence of an NMR-active isotope, ^{77}Se. The spectroscopic handling allows us to observe the coordination behavior of the selenium atom to the central atom by 77Se NMR spectroscopy, providing valuable insights.

We have employed the selenium-substituted ferrocenyl ligand in the synthesis of a stable silylene, a highly electrophilic divalent silicon species whose isolation is notoriously challenging. This ligand provides both steric hindrance and electronic stabilization, which are crucial for stabilizing reactive species.

Here, we report the successful synthesis of the stable silylene bearing the bulky selenium-substituted ferrocenyl ligand, and its trapping reactions.

→ Program Wednesday

Atomically Precise Alloys Stabilized by Se-donor Ligands

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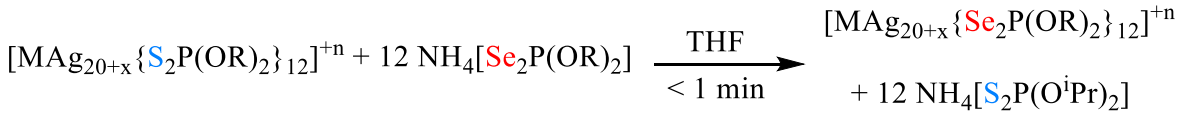
Unlike traditional nanoparticles with non-zero size distribution and non-defined structures, atomically precise nanoclusters (NCs) offer a far more controllable platform for exploring the relationships between structure, properties, and performances. In comparison with numerous examples of the NCs stabilized by S-donor ligands, structurally precise nanoclusters stabilized by Se-donor ligands are much rare. Synthetic challenge arising from the un-stability of selenolates in reducing condition required for alloy NCs formation discourages its product isolations. Very few examples of monometallic silver NC, stabilized by Se, have been reported to date, and bimetallic Ag-rich alloy clusters are absent. To overcome this challenge, ligand substitution offers an alternative post-synthetic modification protocol. Starting with a more facile synthesized S-protected NC, S-based ligands (dtp: $[S_2P(OR)_2]^-$) can be replaced with Se-based ligands (dsep: $[Se_2P(OR)_2]^-$) through a high-yield controlled process (Fig. 1). This approach allows for the successful isolation of rare and unique Se-protected NCs,[1] harnessing the benefits of selenium's strong interaction with coinage metals while circumventing the difficulties of direct synthesis.



M = Ag, Au, x = 0, n = 1; M = Ni, Pt, Pd, RhH, IrH, x = 0, n = 0; M = Rh, x = 1, n = 0; M = PtH, PdH, RhH_2, x = -1, n = 0

Figure 1: Synthesis of 8e Ag-rich alloys passivated by Se-donor ligands

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A New Bridge in [2.2]Cyclophanes: The Addition of Se_2Cl_2 to *Pseudo-Geminally* Substituted Bispropargylic Alcohols

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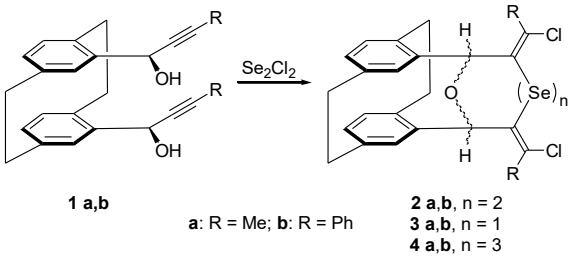
The regio- and stereospecific addition of monoselenium monochloride to *pseudo-geminally* substituted bispropargylic alcohols has been performed under high dilution conditions. The disproportionation reaction of selenium monochloride to selenium dichloride and triselenium dichloride leads to the corresponding divinylic mono- and triselenides. The treatment of bispropargylic alcohols **1** solution with 1 eq. of Se_2Cl_2 under high dilution conditions provided a mixture of three compounds which have been separated by PTLC. Besides the expected diselenide **2**, the isotopic pattern of molecular peaks unambiguously demonstrates the formation of a monoselenide **3** and a triselenide **4**. Moreover, the molecular mass of these selenides is in agreement with the above observation and corresponds to the structures described in Scheme 1.



1 a,b

a: R = Me; **b**: R = Ph

2 a,**b**, n = 2
3 a,**b**, n = 1
4 a,**b**, n = 3

Scheme 1

Vinylic selenides appear to have a promising future in organic synthesis, exploiting the combination of the unique reactivity of selenium with the reactivity of the carbon–carbon double bond. Oxidation of vinylic and divinylic selenides gives rise to the corresponding selenoxides, from which a number of acetylenic, allenic, or dienic products can be obtained by selenoxide *syn* elimination.

Controlling Branching Morphology in Dynamic Selenium Crystal via Stress Engineering

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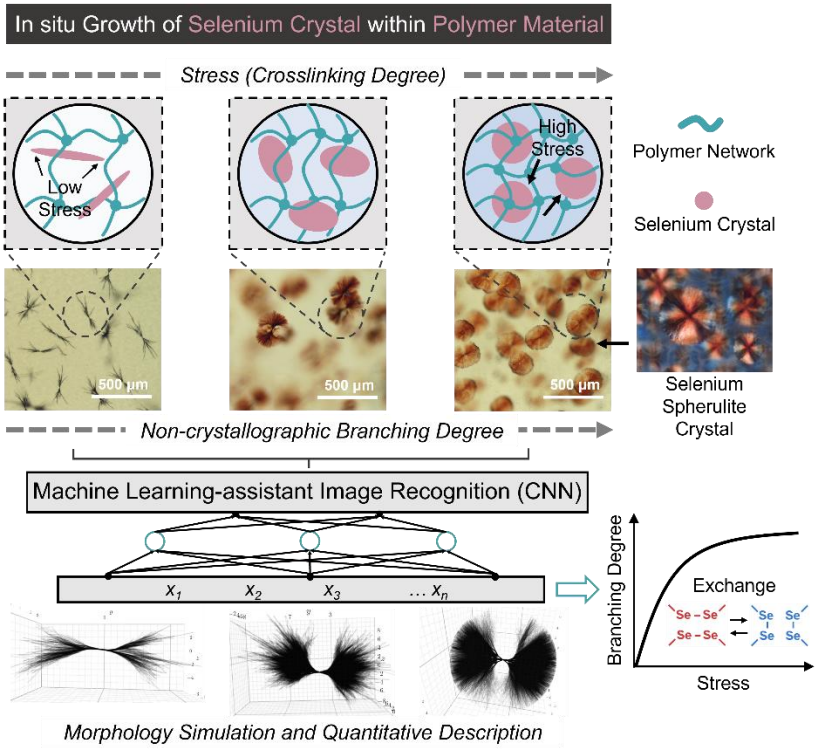

How stress influences the formation of non-crystallographic branching is an extremely challenging problem as it is nearly impossible to control the stress at the crystal growth front in conventional growth processes (melt quenching or solution precipitation).In this study, we constructed a sophisticated system that enables the in situ growth of selenium crystals within polymer materials, and for the first time, provided experimental evidence for relationship between stress and non-crystallographic branching. The stress can be precisely controlled by modulating the polymer crosslinking degree. We employed machine learning to quantitatively evaluate crystal morphology and found that the degree of branching increases with increasing stress, manifesting stress-responsive dynamic characteristics of selenium crystals, which arises from its polymer-like nature and the mechano-responsiveness of Se–Se bonds, which facilitate rapid lattice dislocation. This work offers a transformative paradigm for investigating the mechanisms by which stress governs non-crystallographic branching and for achieving controllable crystal morphologies. Insights obtained can also inspire other fields, such as the suppression of dendrites in lithium batteries.

→ Program Wednesday

Directing Group Strategy for the Isolation of Organoselenium(VI) Benzoselenonates: Metal-Free Catalysts for Hydrogen Evolution Reaction

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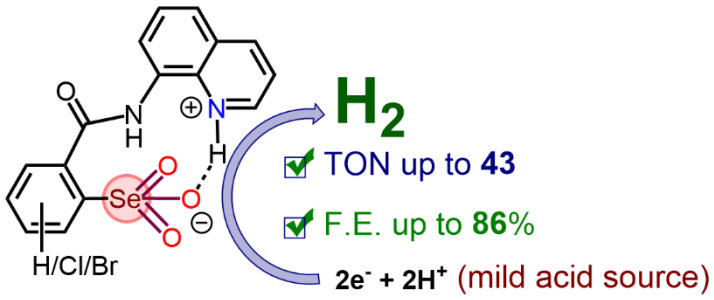
Abstract:

Currently, the very high demand for energy and the recent abrupt climate change enforce society to utilize a renewable and environment-friendly fuel H_2 gas. Recently, the demand for H_2 gas production has been immense as it could serve as an alternative, carbon-free green fuel (95 metric tons in 2022).[1] H_2 production is an intriguing approach to converting electrical energy to chemical energy (H_2). In this regard, scientists have developed a detailed mechanistic understanding to develop efficient electrocatalysts to produce hydrogen gas by reducing protons. However, non-innocent ligands or organic molecules have recently gained attention for hydrogen evolution reactions. These molecules could form a hydride intermediate (hydride with main group elements: N, P, S) and unlock the new catalytic possibilities by avoiding the M-H bond formation to follow the ligand-centered HER.[2] Very recently, we explored ligand-centered HER by metal-free hexavalent organoselenium Se(VI) electrocatalysts for hydrogen evolution reaction.[3] The unique ability of selenium to act as an electron reservoir and adjust its coordination site during the catalytic reaction could play a crucial role in the catalytic reaction.



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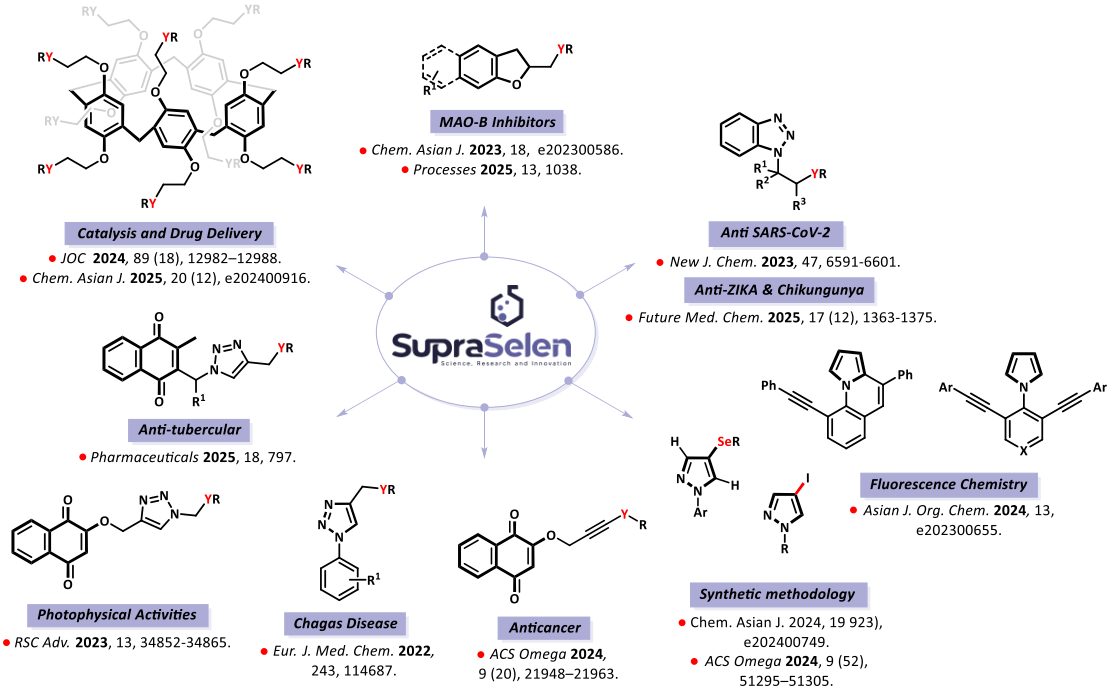
Chalcogeno-Functionalization as a Tool: From Supramolecular Catalysts to Bioactive Compounds



The development of methodologies to incorporate chalcogen to organic molecules is an important strategy in the obtention of promise compounds, since many of them have properties that can be applied in medicine and materials science. This talk will first discuss the development of selenium and tellurium-containing pillar[n]arenes as efficient catalysts in nucleophilic reactions under water. This class of macrocycles has a singular electron-rich cavity, easy functionalization and has been studied for several applications in the last years. The presentation will also provide a comprehensive overview of reported methods by our group, including green protocols, in discovery of new chalcogen biologically relevant molecules.

Abstracts Friday

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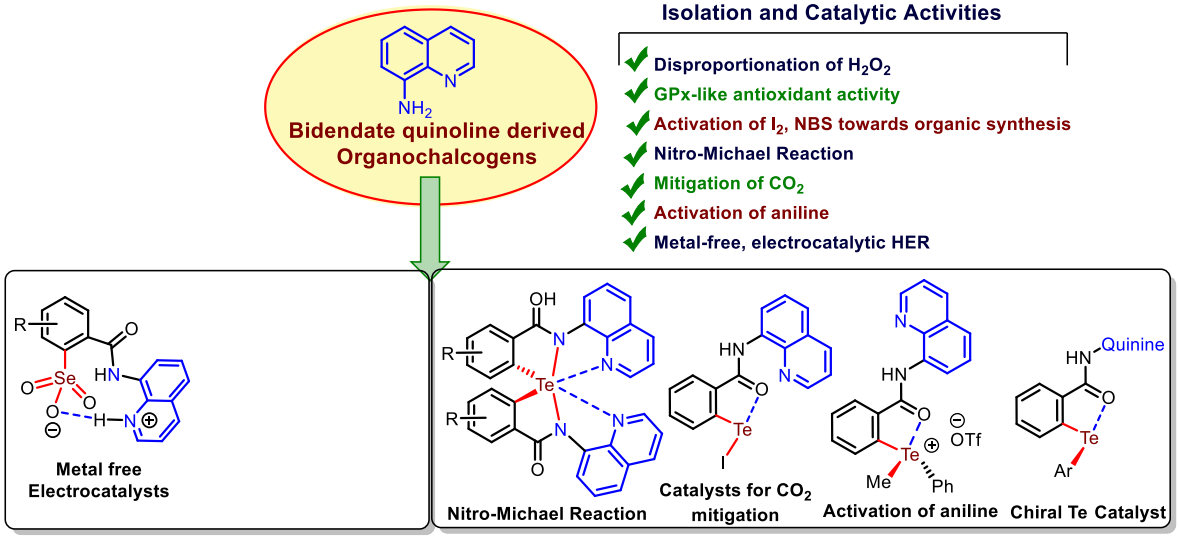
Bidentate Ligand Derived Organochalcogens: Synthesis to Catalytic Applications

Svastik Jaiswal, Deeksha Chaurasia, Sanhati Sharangi, Sumit Chandra Bhatt, Saket Jain, Monojit Batabyal



Scheme 1. Bidentate ligands derived organochalcogens and their catalytic activities

The bidentate quinoline ligand has widely been used exclusively as a directing group for TM-catalyzed C-H bond functionalization.[1] However, it has not been explored in organochalcogen (C-E, E = Se, Te). A quinoline-derived, intramolecular Se···N chalcogen bonded spiroselenuranes Se(IV) has been synthesized and explored for the disproportionation of H_2O_2 for the first time in organochalcogen chemistry, along with the catalytic organic transformation.[2] Synthesized and isolated new hexavalent selenium(VI) benzoselenonates using 8-amino quinolinyl directing ligand have also been made and further explored for metal-free, electrochemical hydrogen evolution reactions (HER).[3]

The maverick role of quinoline ligand in stabilizing synthetically challenging Te-N heterocycle, tellurenyl iodides, tellurenyl sulfides and tetravalent spirotelluranes have been studied in our group.[4-7] Synthesized organotellurides exhibited unique catalytic activities for nitro-Michael addition reaction, CO_2-mitiation and activation of the anilines towards urea formation.[4-7] Recently, we have synthesized chiral tellurides using

bidentate chiral ligand and studied their anantioselective catalytic reaction in arylseleno-Michael addition reaction.[8] In my talk at ICCST-16, I will discuss selenium(IV) molecules, their electrocatalytic activity to produce hydrogen gas[3] and chiral organotelluriums[8] and their enantioselective catalytic properties involving the concept of chalcogen bonding interactions will be discussed.[7]

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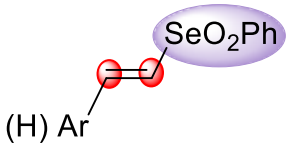
Electrophiles Containing Selenium at High Oxidation State: Insight into Reactivity and Biological Property

Coauthors: Damian Zarzecki, Maria Rachele Ceccarini, Tommaso Beccari, Luana Bagnoli, Claudio Santi



Michael acceptors

Dipolarophiles

- Domino reactions for the synthesis of carbo and heterocycles
- Asymmetric synthesis
- Thiol modifier activity
- Biological studies

Whereas the relevant role of sulfones in organic synthesis and bioorganic chemistry is well-established, the use of selenones has received considerably less attention. However, in the last years, our research group, alongside other groups, explored the reactivity of unsaturated selenones in challenging multicomponent cycloaddition/ elimination reactions, Michael-initiated domino processes, and organocatalyzed reactions for the asymmetric construction of carbon-carbon bonds also with applications in total synthesis of natural products [1]. These reactions take advantage of the electron-withdrawing nature, anion stabilizing effect, and good leaving group ability of the selenone moiety. Reactions are operationally simple and occur in mild reaction conditions, sometimes also in water. The reactivity of unsaturated selenones will be presented including our initial investigations on their thiol Michael reactivity. Thiol Michael reactions have emerged as an attractive strategy for protein chemical modification and bioconjugation with potential applications in medicinal chemistry [2,3]. For instance, α,β-unsaturated sulfonyl compounds have been studied as neuro-protective agents with potential application in neurodegenerative disorders [3]. They are believed able to covalently modify cysteine residues in the Keap1 protein, activating the Nrf2-pathway, which represents one of the most important cellular defense mechanisms against oxidative stress and xenobiotic damage. Inspired by the relevance of thiol modifier effects in the biological activity of organoselenium compounds [4], experiments in NMR tube with model thiols were performed to assess and monitor the thiol reactivity of unsaturated selenones and selenoxides, and collect

information on the reaction paths. Furthermore, some styryl selenones were synthesized and cell-based experiments were conducted to evaluate their neuroprotective activity, given the known effects of structurally related sulfones.

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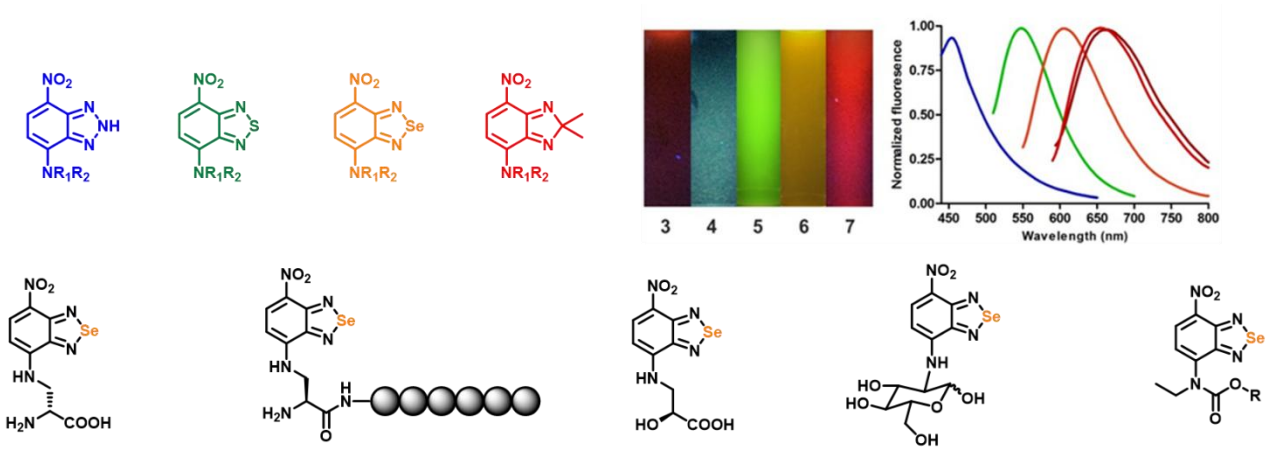
Benzoselenadiazoles as tunable fluorophores and photosensitizers

Eleni Nestoros, Ferran Nadal-Bufí, Deborah Seah, Zhi Ming Cheng, Maricarmen Ortega-Liebana, Sam Benson, Jun-Seok Lee, Asier Unciti-Broceta, Marc Vendrell



Recent advancements in optical bioimaging have driven the need for synthetic approaches that introduce minimal chemical reporters into biomolecules, while maintaining their biological activity and molecular recognition, and enhancing multiplexing potential. In particular, systematic replacement of heteroatoms within the scaffolds of known fluorophores has emerged as a powerful strategy to tune their optical properties and develop palette of probes where high optical diversity stems from minimal structural changes. Benzoselenadiazoles are Se-containing heterocycles with attractive fluorescent properties. They represent the heavier chalcogen analogues of the well known 7-nitro-2,1,3-benzoxadiazole (NBD) and display significant changes in photophysical behavior compared to their O- and S-containing counterparts due to heavy atom effect. This also results in more effective energy transfer to surrounding molecules, which enables the production of singlet oxygen species and makes them suitable for photodynamic therapy.

In this vein, we introduced SCOTfluors, a multicolor family of fluorescent benzodiazoles spanning from blue to NIR and containing bridging atoms as diverse as

N, O, S, Se and C, which have been successfully used to visualize the cellular transport of small molecules. The Se-containing analogues in this platform include a labelled glucose and a labelled lactate for the study of metabolism in cancer cells.[1] Furthermore, some of the smallest fluorescent amino acids were designed and we identified amine derivatized benzoselenadiazoles as scalable and photo stable amino acids for the straightforward solid-phase synthesis of fluorescent peptides. Benzodiazole amino acids retain the binding capabilities of bioactive peptides and display excellent signal-to-background ratios.[2]

Additionally, we showed that benzoselenadiazole-based metabolites can selectively eliminate pathogenic cells, such as bacteria and cancer cells, while sparing healthy ones, with high accuracy upon exposure to non-toxic visible light, thereby minimizing potential side effects in vivo.[3] We also demonstrated that the photocatalytic activity of benzoselenadiazole can be fully blocked by site-selective incorporation of small carbamate moieties and restored on demand upon uncaging with a wide range of molecular triggers, ranging from abiotic transition-metal catalysts to biocompatible stimuli.[4]

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Reimagining Selenium Role in Medicinal Chemistry: The Role of Se-S Bonds

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The chemistry of selenium–sulfur (Se–S) bonds is crucial for redox control and enzyme functionality, though their overall biological role remains insufficiently understood. Compounds containing selenium, especially those with Se–S linkages, show notable reactivity with thiols, affecting protein behavior and cellular responses to oxidative stress. This research utilizes such properties to examine the antiviral activity of selenium-based molecules against SARS-CoV-2. Due to the virus's ability to form immune-resistant variants, alternative treatments targeting conserved viral proteins like the main protease (Mpro) are urgently needed. A collection of benzisoselenazolones and diselenides was tested for Mpro inhibition, followed by in vitro assays to determine antiviral activity. Mechanistic understanding was achieved using density functional theory (DFT), molecular docking, and molecular dynamics simulations, identifying important interactions between proteins and ligands. Additionally, a bio-organic model was constructed to explore how these selenium compounds react with biologically relevant thiols, offering valuable data on their metabolic behavior. New findings from various biophysical techniques will be reported, providing enhanced understanding of the interaction between organoselenium molecules and Mpro, helping to elucidate their mode of action and antiviral promise.

Besides their immediate therapeutic value, the results also underscore the evolutionary significance of Se–S interactions in biology, emphasizing their role in maintaining redox balance and mediating host-pathogen dynamics. By linking basic chemical principles with applied virology, this work contributes to the informed development of innovative selenium-centered drugs.

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From Obscurity to Mainstream: The Rise of Chalcogen Bonding

Although it has long been recognized that molecules with heavy main-group atoms tend to form *secondary bonds*, i.e., short contacts with electron-rich centers, it was not until the turn of the century that this phenomenon began to be systematically investigated as a means to influence structure and properties. The term chalcogen bonding is now officially recommended by IUPAC.[1] While most experimental studies in this area focus on the solid state, some intermolecular interactions are strong enough to assemble well-defined discrete aggregates that remain stable in solution. Prominent examples of chalcogen bonding include derivatives of the 1,2-chalcogenazole ring, which spontaneously auto-associate. The tellurium *N*-oxides[2] form annular aggregates that persist in solution, host small molecules, serve as fullerene receptors, create macrocyclic transition-metal complexes, are resilient to tellurium halogenation, and are unreactive toward strong Lewis bases. However, mineral acids or boranes (BR_3, R = Ph, F) disrupt aggregation. Even larger rings are formed by the corresponding *N*-phenoxides. This presentation will provide an overview of the properties of these and closely related supramolecular systems.

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Selenium and Tellurium Centered Radical Cations

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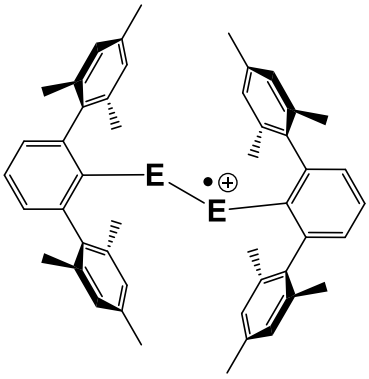
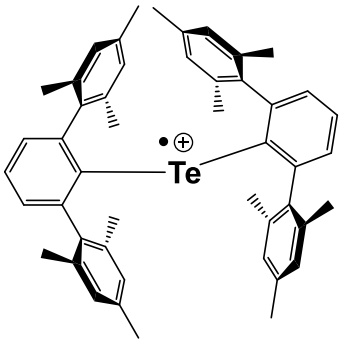
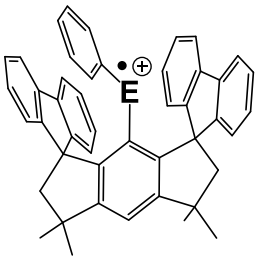
Ever since Gomberg's seminal discovery of the trityl radical in 1900, odd-electron species of the main group elements received considerable attention, which holds particularly true for sulfur centred radicals. Compared these, very few selenium and tellurium centered radicals are known. In this work, we report our effort to prepare kinetically stabilized radical cations, such as **I**, **II** and **II**, based upon selenium and tellurium.



I (E = Se, Te)



II



III (E = Se, Te)

The kinetic stabilization was achieved by the judicious choice of bulky and rigid *m*-terphenyl (**I**, **II**) and M^{S}Fluind substituents (**III**). The radical cations **I** – **III** were fully characterized by cyclovoltammetry (CV), electron paramagnetic resonance (EPR) spectroscopy and single crystal X-ray crystallography (scXRD). The experimental results are supported by DFT methods (e.g. of the spin density calculations).

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