30th International Symposium on the Organic Chemistry of Sulfur

Abstracts

ISOCS-30

July 28 – August 02, 2024

Florence, Italy

HISTORY OF ISOCS

ISOCS meetings are well established international forums for the presentation and discussion of research results on the many aspects of sulfur chemistry. The importance of sulfur chemistry and responsiveness of the symposium to the needs of the participants has propelled this conference into a prestigious international meeting awaited by the scientific community. Sulfur meetings attract worldwide interest, bringing together chemists from all over the world, sharing their interest in the different areas of sulfur chemistry.

ISOCS 30 follows the long-dated tradition of these symposia, originating back from the first one held in a castle in Liblice, near Prague in 1964, exactly 60 years ago. The initial success of this conference led to its regular repetition every two years except 2020 due to covid-19 pandemic situation.

The conferences were convened in Europe until 1996, when the first conference in Asia was organized in Tsukuba, Japan. The conference then returned to Europe until 2002, when the first conference in the Western Hemisphere was held in Flagstaff, Arizona.

While the focus of these symposia has always been sulfur chemistry, areas of emphasis have changed. The areas originally emphasized were structure, mechanism and reactive intermediates. Then the emphasis shifted to stereochemistry, hypervalent sulfur and synthetic applications.

Currently the interest on synthetic chemistry, as well as on mechanisms and stereochemistry still continues, but there has also been expansion to biochemistry, medicinal chemistry, materials science and environmental issues. In all of these areas sulfur chemistry plays an important and key role.

ISOCS-30 in Florence has the aim to continue this prestigious series of events. Since ISOCS is being held in Italy for the fourth time, organizers have to opportunity to celebrate in 2024 the centenary of birth of Prof. Giorgio Modena, one of the fathers of Italian Organic Chemistry, and the centenary of the University of Florence.

The full listing of SOCS Symposia

1964 Liblice (Czech Republic)

1966 Groningen (The Netherlands)

1968 Caen (France)

1970 Venice (Italy)

1972 Lund (Sweden)

1974 Bangor (UK)

1976 Hamburg (Germany)

1978 Portoroz (Slovenia)

1980 Riga (Latvia)

1982 Bangor (UK)

1984 Lindau (Germany)

1986 Nijmegen (The Netherlands)

1988 Odense (Denmark)

1990 Lodz (Poland)

1992 Caen (France)

1994 Merseburg (Germany)

1996 Tsukuba (Japan)

1998 Florence (Italy)

2000 Sheffield (UK)

2002 Flagstaff (USA)

2004 Madrid (Spain)

2006 Saitama (Japan)

2008 Moscow (Russia)

2010 Florence (Italy)

2012 Czestochowa (Poland)

2014 Istanbul (Turkey)

2016 Jena (Germany)

2018 Tokyo (Japan)

2022 Guelph (Canada)

2024 Florence (Italy)

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GENERAL INFORMATION

The Symposium will start in the afternoon of ***Sunday July 28*** with the Registration (15:30-19:00) and the *Welcome mixer* (19:00-22:00) at the ***Natural History Museum, Botanical Garden***, Via Pier Antonio Micheli 3, Florence.

The Scientific sections will start on Monday July 29 (08:40) with the Opening Ceremony with the presence of the Rector of the University of Florence and the President of the Italian Chemical Society. The symposium venue is on the ***Campus Novoli*** of the University of Florence, Via delle Pandette, 9, 50127 Florence D6: Building ground floor ***conference location***.

The easiest way to reach the Symposium Venue from downtown (Alamanni-SMN Station) is ***T2- LINE - VESPUCCI*** ***and from Florence Airport is the*** ***T2 LINE – VESPUCCI*** tram line dropping off at "***SAN DONATO - Università***" station that is located 2-3 minutes walking distance from the D6 conference building (purchasing tickets).

Florence and its metro area are served by several bus lines. The bus company providing the service is called "*Autolinee Toscane*". Bus tickets can be bought from bars, tobacconists, newsagents, from automatic machines, and app. In the metropolitan area of Florence, all "urbano capoluogo" tickets and passes allow you to use urban trams and buses.

The price for a single ticket is € 1.70. Contactless payment is available on buses and tram for purchasing tickets on board using credit/debit cards, smartphones, and enabled wearables. Mastercard, Visa and American Express cards are accepted. Hold your card near the ticket validation machine. A green screen means you have successfully checked in. On urban lines, tap every time you board. If your journey involves changing buses or trams, you will not be charged additional tickets within the validity period (90 min) of the ticket purchased with the first tap. To purchase tickets for multiple people, download the app at bus.

Visit our website for additional information.

SOCIAL PROGRAM

➢ Sunday July 28, 2024

19:00-22:00 ***Welcome mixer***, Natural History Museum, Botanical Garden,
Via Pier Antonio Micheli 3, Firenze.

The Botanical Garden of Florence *Giardino dei Semplici,* founded on 1st December 1545 by Cosimo I de Medici, is the third most ancient botanical garden in the world after those of Pisa and Padua. Here, every day for almost 500 years, well-documented collections of living plants have been cared for, grown up and spread all around here for conservation, research and educational aims.

➢ Wednesday July 31, 2024

15:00-24:00 ***Social excursion to Siena with a Tuscany dinner***, Siena.

Siena, a city rich in history and culture and with a medieval charm that is still nearly intact today. The excursion, with a Tuscany dinner, will be at the “Contrada dell’Onda” garden.

➢ Thursday August 01, 2024

20:00-23:00 ***Banquet Panoramic B-Roof***, Grand Hotel Baglioni, Piazza dell’Unità Italiana 6, Firenze.

Partecipation requires the payment of the gold registration fee.

SCIENTIFIC PROGRAM

Plenary Lectures *(PL01 - PL06, 40 min. discussion included)*.

Invited Lectures *(IL01 - IL14, 30 min. discussion included)*.

Oral Communications *(OC01 - OC42, 20 min. discussion included)*.

Poster session *(P01 - P34).*

The poster session has been scheduled on Tuesday, July 30 in the same building, ground floor. Please refer to the Scientific Program to get the number assigned to the posters.

The area available for each poster is 70 cm (width) x 100 (height).

Material for mounting posters will be available at the Symposium desk.

Posters can be displayed from lunch time of Monday, July 29 till lunch time of Wednesday, July 31.

The WSeS-11 and the ISOCS-30 organizers have reached an agreement with Phosphorus, Sulfur, and Silicon and the Related Elements to jointly publish the proceedings of the two symposia.

PLANARY LECTURES

PL-01

A Sulfur-Handle for the Advanced Synthesis of Functionalized Chiral Amines

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Nitrogen-activated carbon-carbon double bonds present significant potential for constructing a diverse array of nitrogen-containing products. To broaden the utility of these substrates, our research focused on exploring the reactivity of promising enamide derivatives.

We developed innovative methods for the α,β-difunctionalization of enamides using a synergistic two-step strategy that combined asymmetric organocatalysis and photoredox catalysis. A pivotal aspect of our approach was employing thiol as a transient reaction partner which played a crucial in ensuring the success of these processes and enabling the synthesis of a diverse range of enantioenriched α,β-substituted amines.[1]

Additionally, we successfully implemented stereoselective enantioselective photocatalytic processes for synthesizing both α- and β-chiral amines. In these approaches, sulfoxide and sulfonyl groups proved to be ideal linchpins, facilitating selective transformations and ensuring high enantioselectivity.[2,3]

This lecture will present our contributions, emphasizing their application in synthesizing biologically active natural and synthetic compounds.

References

[1] D. Bouchet, T. Varlet, G. Masson, *Acc. Chem. Res*. **2022**, *55*, 3265.
[2] M. Leone, J. Milton, D. Gryko, L. Neuville, G. Masson, *Chem. Eur. J.* **2024**, *30*, e202400363.
[3] W.-Y. Ma, M. Leone, E. Derat, P. Retailleau, C. R. Reddy, L. Neuville, G. Masson, *Angew. Chem. Int. Ed.* **2024**, e202408154.

Recent Progress of Synthesis of Fluoro-sulfanyl Molecules

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The development of innovative synthetic methodologies for diversifying fluorinated structural motifs is crucial in medicinal chemistry as it expands the range of accessible molecules. In organic chemistry, pentafluoro-sulfanyl (-SF_5) groups and tetrafluoro-sulfanyl (-SF_4-) units have gained increasing attention as intriguing functional moieties. These groups consist of a sulfur(VI) atom bonded to five or four fluorine atoms, respectively. The presence of sulfur and multiple fluorine atoms endows these groups with exceptional electronegativity and lipophilicity, making them valuable and distinct modifying groups for modifying the chemical and physicochemical properties of the parent molecules. Furthermore, the SF_5 and SF_4 groups possess notable bulk and size, which influence molecular interactions and spatial arrangements. Although both groups share some similarities, the SF_5 moiety is typically employed as a terminal group, often regarded as a super trifluoromethyl (CF_3) group (Figure 1a), whereas the SF_4 unit functions as a connecting element. Notably, the trans-SF_4 unit linearly links two independent moieties, resembling an isosteric bridge akin to the alkyne, [1,1,1] bicyclopentane, cubane, or *p*-substituted phenyl connections (Figure 1b). These unique structural properties have garnered significant attention in pharmaceuticals, agrochemicals, and specialty materials, despite the limited availability of compounds featuring SF_5 and SF_4 groups. In this presentation, I will provide an overview of our advancements in the synthesis of SF_5 and SF_4 molecules.[1]

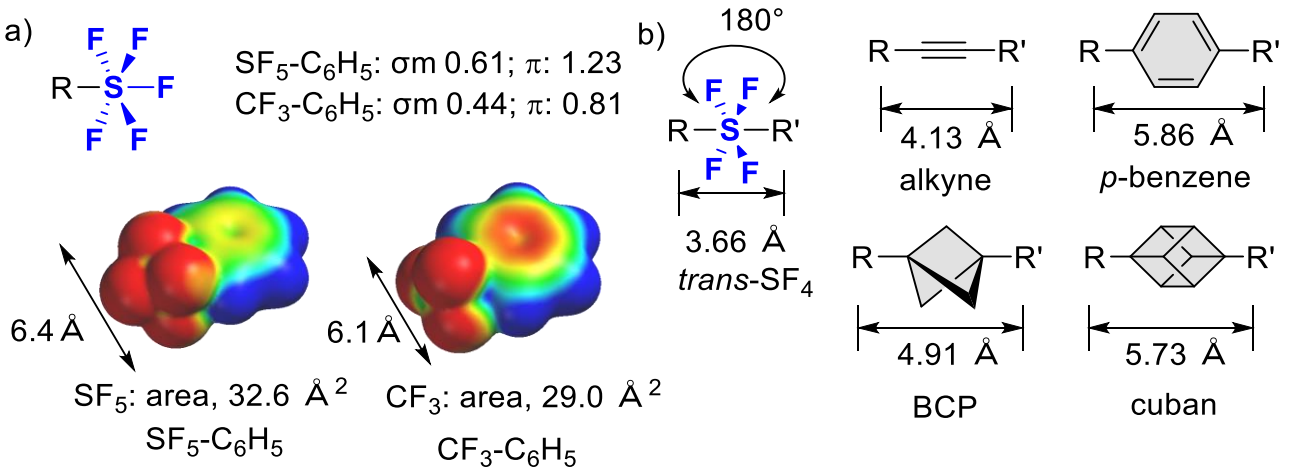

Figure 1. a) Comparison of selected factors of SF_5 and CF_3 groups of benzene derivatives.

b) Comparison of selected factors of SF_4-conenction and related units.

References

[1] S. Mori, K. Hada, N. Shibata, *J. Syn. Org. Chem. Japan,* **2023**, *81*, 428–438.

PL-03

New functional groups for synthetic and discovery chemistry

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Sulfonamides feature in >100 FDA approved drugs, and while the first examples date back to the 1930s they still appear in contemporary medicines. Defining new sulfonamide 'chemical space' can be challenging,[1] however, a simple O to N switch creates a new class of molecules; sulfonimidamides. A second O to N switch leads to a further functional group, this time known as sulfondiimidamides,[2] which are essentially unknown molecules. Although there are no commercial sulfonimidamide or sulfondiimidamide drugs, their presence in the medicinal chemistry patent literature is growing rapidly. Further atom-switching around a central S(VI)-core provides additional unexplored functional groups. In this lecture we will discuss new synthetic routes to these intriguing molecules,[3] and discuss their potential applications in medicinal and synthetic chemistry.

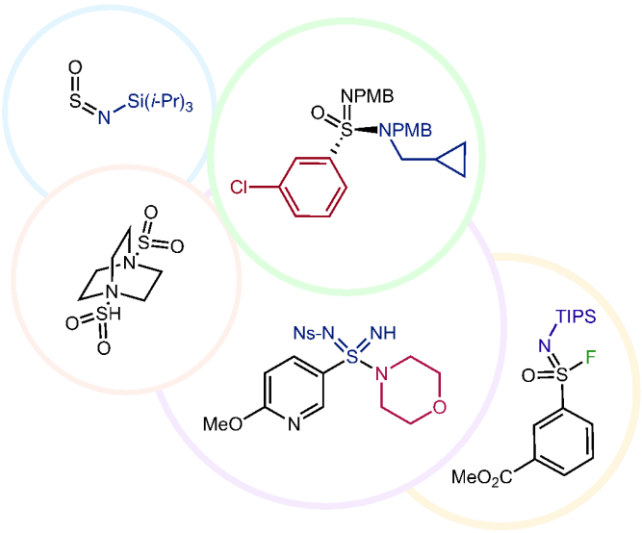

Figure 1.

References

[1] "Crafting chemical space with sulfur functional groups", Ze-Xin Zhang and Michael C. Willis, *Trends in Chemistry*, **2023**, *5*, 3–6.

[2] "Sulfondiimidamides as new functional groups for synthetic and medicinal chemistry", Ze-Xin Zhang and Michael C. Willis, *Chem* **2022**, *8*, 1137–1146.

[3] "Photocatalytic carboxylate to sulfinamide switching delivers a divergent synthesis of sulfonamides and sulfonimidamides", Jonathan A. Andrews, Jagadeesh Kalepu, Christopher F. Palmer, Darren L. Poole, Kirsten E. Christensen, Michael C. Willis, *J. Am. Chem. Soc.* **2023**, *145*, 21623–21629.

PL-04

Catalytic, Enantioselective *SYN*-Difunctionalization of Alkenes

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As some of the oldest organic chemical reactions known, the ionic additions of elemental halogens such as bromine and chlorine to alkenes are prototypical examples of stereospecific reactions, delivering vicinal dihalides resulting from *anti*-addition. Whilst the invention of enantioselective variants is an ongoing challenge, the ability to overturn the intrinsic *anti*-diastereospecificity of these transformations is also a largely unsolved problem. In this lecture, we describe the catalytic, *syn*-stereospecific dichlorination, diamination and oxyamination of alkenes, employing a group transfer catalyst based on a redox-active main group element (i.e., selenium). Thus, with a chiral diselenide (5 mol %) as the pre-catalyst, and an *N*-fluoropyridinium salt as the oxidant, a wide variety of functionalized cyclic and acyclic 1,2-disubstituted alkenes deliver *syn*-dichlorides, imidazolidinones, oxazolines, and oxazolidinones with exquisite stereocontrol and enantioselectivity. The latter two are readily converted to 1,2-diamines and 1,2-amino alcohols.

This lecture will describe the conceptual development, optimization, scope and limitations of the syn-functionalization and the ability to control the absolute configuration of the products as well. Finally, mechanistic investigations aided by computational analysis will be presented.

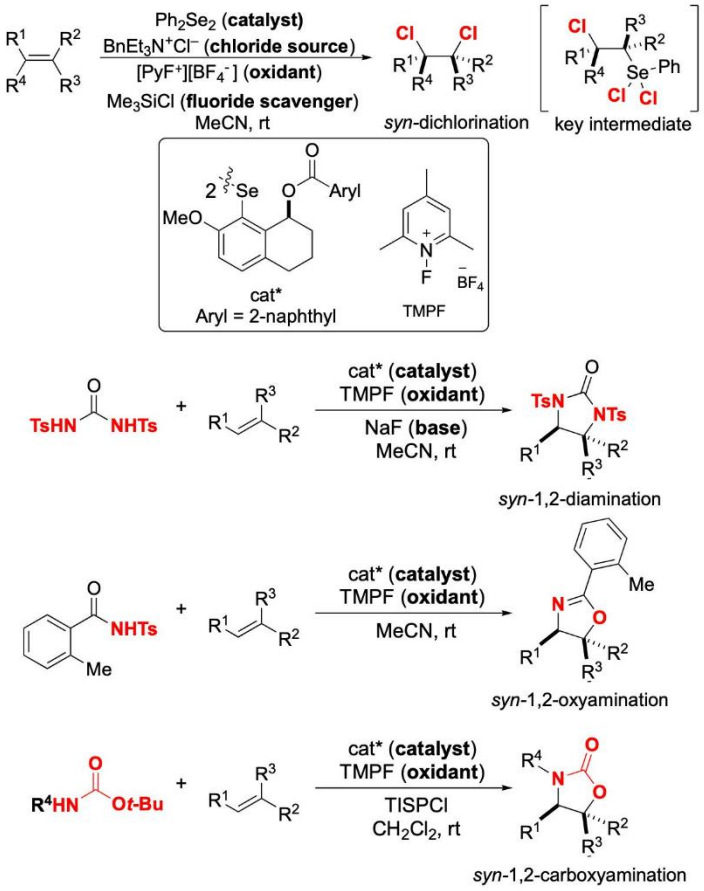

Figure 1.

PL-05

Sulfur compounds in the Bolm group: Syntheses and Applications

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Our recent approaches to sulfur compounds and applications of such molecules in organic synthesis will be presented. Some of the targeted products are shown in Figure 1.[1-9]

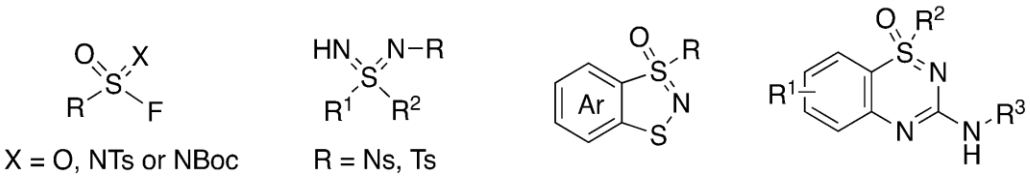

Figure 1. Sulfur compounds discussed here.

Besides solution-based processes, solvent-free transformations under mechanochemical conditions will be discussed.[10-12]

References

[1] Review: M. T. Passia, J.-H. Schöbel, C. Bolm, *Chem. Soc. Rev.* **2022**, *51*, 4890 – 4901.
[2] M. T. Passia, N. Bormann, J. S. Ward, K. Rissanen, C. Bolm, *Angew. Chem. Int. Ed.* **2023**, *62*, e202305703.
[3] R. Hommelsheim, S. Bausch, A. Selvakumar, M. M. Amer, K.N. Truong, K. Rissanen, C. Bolm, *Chem. Eur. J.* **2023**, *29*, e202203729.
[4] R. Hommelsheim. S. Bausch, R. van Nahl, J. S. Ward, K. Rissanen, C. Bolm, *Green Chem.* **2023**, *25*, 3021 – 3026.
[5] R. Hommelsheim, R. van Nahl, L. M. Hanek, J. Ward, K. Rissanen, C. Bolm, *Adv. Synth. Catal.*, **2024**, *366*, 717 – 724.
[6] P. Wu, J. S. Ward, K. Rissanen, C. Bolm, *Adv. Synth. Catal.* **2023**, *365*, 522 – 526.
[7] S. Pan, M. Passia, X. Wang, P. Wu, D. Ma, C. Bolm, *Adv. Synth. Catal.* **2023**, *365*, 31 – 36
[8] P. van Bonn, S. Soerensen, N. Schmitz, C. Bolm, *Adv. Synth. Catal.* **2024**, *366*, 725 – 732.
[9] P. Wu, J. Demerael, B. J. Statham, C. Bolm, *Chem. Sci.* **2024**, *15*, 5333 – 5339.
[10] M. M. Amer, R. Hommelsheim, C. Schumacher, D. Kong, C. Bolm, *Faraday Discuss.* **2023,** *241*, 79 – 90.
[11] M. Passia, M. M. Amer, J. Demaerel, C. Bolm, *ACS Sustainable Chem. Eng*. **2023**, *11*, 6838 – 6843
[12] S. Pan, F. Mulks, P. Wu, K. Rissanen, C. Bolm, *Angew. Chem. Int. Ed.* **2024**, *63*, e202316702.

PL-06

The Significance of Boron Interactions with Sulfoxides and Sulfenate Anions

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Sulfenate anions (RSO^-M^+)[1] are increasingly recognized as valuable sulfur nucleophiles. With the emergence of sulfenate anions comes an increase in the number of investigations probing their selective S-functionalization reactions. Many of these reactions call on interactions of the sulfenate oxygen and/or counterion with nearby functionality. The Schwan group[2-3] and others[4-6] have been probing these effects for stereoselective alkylation reactions. Our most recent work has explored the possibility of a boronate functionality interacting with the sulfenate oxygen and also with the oxygen of a proximal sulfoxide. This presentation will address some of our earlier work but will focus on recent practical and computational achievements assessing the capacity of boronates to direct selective sulfenate benzylation, via an S-O-B interaction. The talk will also address computational work probing the *syn*-elimination of b-boro sulfoxides, an alkene-forming reaction which also relies on a strong S-O-B interaction.

References

[1] A.B. Riddell, M.R.A. Smith, A.L. Schwan, *J. Sulfur Chem*., **2022**, *43*, 540–592.
[2] S.C. Söderman, A.L. Schwan, *J. Org. Chem.* **2013** *78*, 1638-1649.
[3] A.L. Schwan, *Eur. J. Org. Chem.* **2019**, 519-526.
[4] L. Zong, X. Ban, C.W. Kee, C.-H. Tan, *Angew Chem Int Ed*. **2014,** *53*, 11849–11853.
[5] J. Zhang, K. Suzuki, K. Ohmori *Org. Lett.* **2023**, *25*, 9036–9040.
[6] J. Zhang, V.V. Betkekar, K. Suzuki, K. Ohmori, *Synlett* **2023**, *34*, A–G.
[7] A.G. Durant, E.A. Nicol, B.M. McInnes, A.L. Schwan, *Org. Biomol. Chem*. **2022**, *20*, 649-657.

INVITED LECTURES

ISOCS-30

Radical-based Transformations through Reductive Activation of Alkylsulfones

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Organosulfones are versatile intermediates in organic synthesis because of the ease with which they permit facile structural modification through α-functionalization or conjugate addition.[1] Due to the inherent stability of sulfonyl groups, strong reducing agents are generally required for their removal. Recently, organosulfones have attracted considerable attention as a new class of electrophiles in cross-coupling reactions. Our group and others have developed several transition-metal catalyzed cross-coupling reactions of functionalized sulfones via carbon–sulfonyl (C–SO_2) bond activation.[2] Substituents on the sulfonyl group were found to provide a powerful new avenue for controlling reactivity. Building on these reports, next we envisioned that a controlled single electron reduction of sulfones would have the potential to establish a new method for the generation of carbon radicals under mild conditions. In this presentation, we will present radical-based transformations through C–SO_2 bond activation of alkylsulfones by use of reducing agents or visible-light photoredox catalysts.[3] This approach enables facile modifications of sp^3 carbon centers, highlighting the utility of organosulfones as redox-active substrates in organic synthesis.

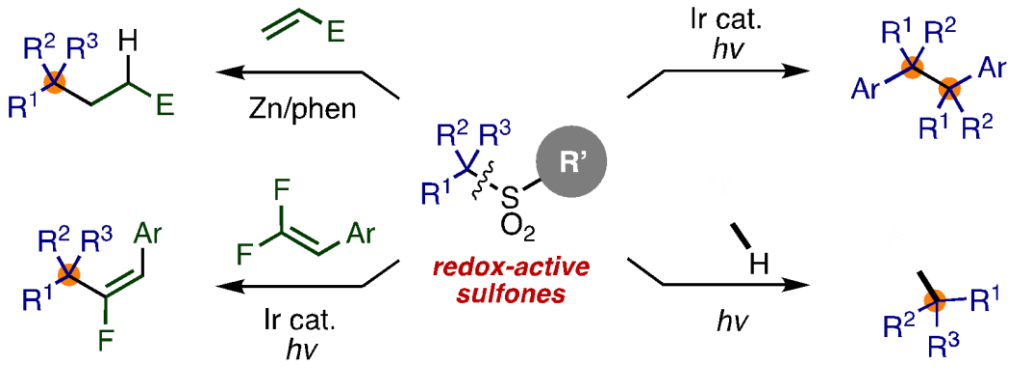

Figure 1. Radical-based transformations through C–SO_2 bond activation of alkylsulfones

References

[1] a) B. M. Trost, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107–124. b) B. M. Trost, C. A. Kalnmals, *Chem. Eur. J.* **2019**, *25*, 11193–11213.
[2] a) M. Nambo, Y. Maekawa, C. M. Crudden, *ACS Catal*. **2022**, *12*, 3013–3032. b) J. Corpas, S. H. Kim-Lee, P. Mauleon, R. G. Arrayas, J. C. Carretero, *Chem. Soc. Rev*. **2022**, *51*, 6774–6823. c) M. Nambo, C. M. Crudden, *Chem. Rec.* **2021**, *21*, 3978–3989.
[3] a) M. Nambo, Y. Tahara, J. C.-H. Yim, D. Yokogawa, C. M. Crudden, *Chem. Sci.* **2021**, *12*, 4866–4871. b) M. Nambo, K. Ghosh, J. C.-H. Yim, Y. Tahara, N. Inai, T. Yanai, C. M. Crudden, *ACS Catal.* **2022**, *12*, 9526–9532. c) Y. Tahara, K. Ghosh, M. Nambo, *Can. J. Chem.* **2023**, *101*, 491–496. d) R. Ohkura, M. Ohtsuka, J. C.-H. Yim, M. Nambo, C. M. Crudden, *Synlett* **2023**, *34*, 81–85.

Greening the Synthesis of Thiochromones and Benzothiazoles

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Thiocromones and benzothiazoles are valuable sulfur-containing heterocycles with important pharmacological activities.[1,2] The adoption of experimental procedures that embrace the principles of green chemistry has stood out as an alternative for the preparation of bioactive molecules.[3] In recent years, we have been dedicated to developing greener protocols for the synthesis of organochalcogen compounds (S, Se, and Te derivatives). In this lecture, we will present some recent examples of alternative approaches to prepare thiochromones and benzothiazoles. Atom-economic reactions, using environmentally benign reagents, and visible light are among the strategies that will be discussed (Figure 1).

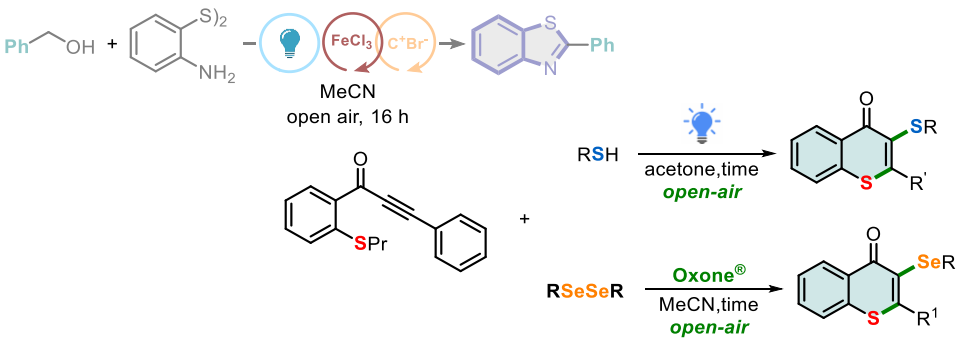

Figure 1. Syntheis of thiochromones and benzothiazoles.

References

[1] A. Rouf, C. Tanyeli, *Eur. J. Med. Chem.*, **2015**, *97*, 911−927.
[2] H.-K. Wang, K. F. Bastow, L. M. Cosentino, K.-H. Lee, *J. Med. Chem.*, **1996**, *39*, 1975−1980.
[3] S. Kar, H. Sanderson, K. Roy, E. Benfenati, J. Leszczynski, *Chem. Rev.*, **2022**, *122*, 3637−3710.
[4] L. H. Dapper, V. T. Mena, M. W. Rambo, F. B. Santos, N. R. Pineda, B. A. Iglesias, P. C. Piquini, M. S. Silva, E. J. Lenardão, F. Penteado, *ACS Sustain. Chem. Eng.*, **2024**, DOI: 10.1021/acssuschemeng.4c03149.
[5] R. H. Bartz, K. B. Silva, R. R. S. A. Santos, T. J. Peglow, E. J. Lenardão, B. A. Iglesias, F. Penteado, G. Perin, R. G. Jacob, ChemCatChem, **2023**, *15*, e202201557.
[6] R. H. Bartz, K. B. Silva, T. J. Peglow, A. M. Barcellos, R. G. Jacob, E. J. Lenardão, G. Perin, *Org. Biomol. Chem.*, **2022**, *20*, 8952−8961.

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The Contribution of Sulfenic Acid Intermediates in the Building-up of New Molecular Architectures

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During the last decades, the chemistry of the transient sulfenic acids has been exploited by our group in the efficient synthesis[1] of vinyl and alkyl sulfoxides *via* regio- and stereoselective additions to triple and double bonds, and of unsymmetrically substituted disulfides through the condensation of the transient species with thiols. Since the first works on the stereoselective Diels-Alder cycloaddition of enantiopure sulfinyldienes,[2] we have used these intermediates to synthesize a wide and varied library of a) sulfurated compounds bearing biologically relevant residues,[3] b) di- and tri-sulfoxides or disulfides useful in material chemistry[4] and in the biological field[5] and, lately, c) divinylsulfone reactive platforms, whose dual reactivity has been exploited in the construction of bolaamphiphilic species[5] and bolapolyphiles (Figure 1) precursors.

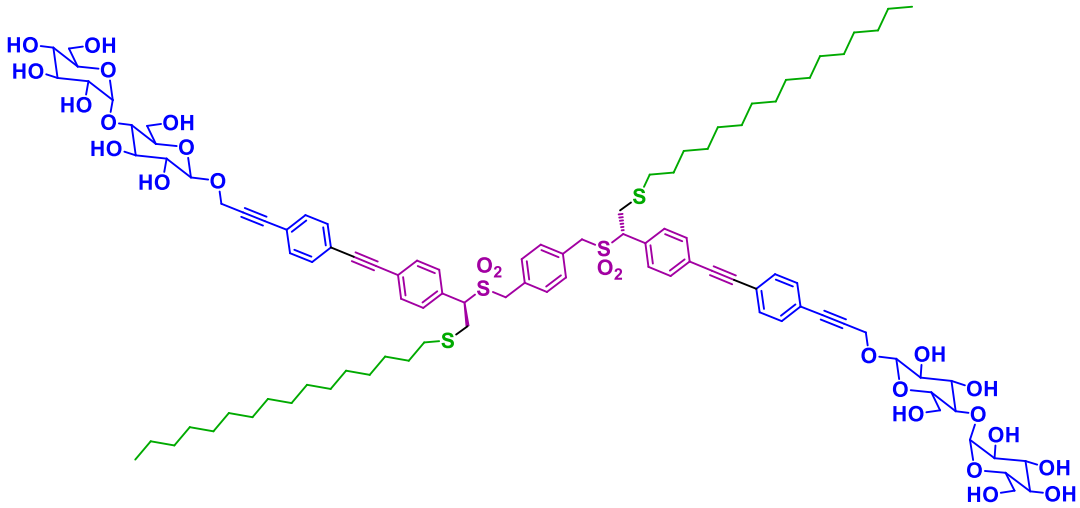

Figure 1. target bolapolyphile

This contribute will deal with the use of these versatile intermediates in our preparative chemistry, centring on the most recent results.

References

[1] A. Barattucci, M.C. Aversa, A. Mancuso, T. M. G. Salerno, P. Bonaccorsi, P., *Molecules*, **2018**, *23*, 1030-1033.
[2] M.C. Aversa, A. Barattucci, P. Bonaccorsi, P. Giannetto, D.N. Jones, *J. Org. Chem.*, **1997**, *62*, 4376–4384
[3] G. De Luca, P. Bonaccorsi, V. Trovato, A. Mancuso, T. Papalia, A. Pistone, M. P. Casaletto, A. Mezzi, B. Brunetti, L. Minuti, Andrea Temperini, A. Barattucci, M. R. Plutino, *New J. Chem.,* **2018**, *42*, 16436–16440.
[4] A. Barattucci, T. M. G. Salerno, F. H. Kohnke, T. Papalia, F. Puntoriero, P. Bonaccorsi, *New J. Chem.*, 2020, *44*, 19508–19514; P. Bonaccorsi, F. Marino-Merlo, A. Barattucci, G. Battaglia, E. Papaianni, T. Papalia, M. C. Aversa, A. Mastino *Bioorg. Med. Chem.*, **2012**, *20*, 3186–3195.
[5] P. Bonaccorsi, C. M. A. Gangemi, V. Greco, G. Gattuso, A. Barattucci *Org. Biomol. Chem.*, **2022**, *20*, 7448–7457.

IL-04

Synthesis and transformations of α,β-unsaturated sulfonyl fluorides and triflones

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Sulfonyl compounds are of great importance in organic synthesis and medicinal chemistry, and the interest deepened recently, when Sharpless introduced a new metal-free 'click'-type reaction, called SuFEx.[1] The process utilizes **sulfonyl fluorides** (SO_2F), which combine excellent stability and reactivity of the sulfonyl group, triggered with activators. However, in numerous cases the sulfonyl group remains intact, acting only as an electron-acceptor e.g. in conjugate addition to α,β-unsaturated systems. Recently, we described synthesis of β-arylethenesulfonyl fluorides via olefination of arylaldehydes,[2] and their organocatalytic enantioselective addition of malonates under high-pressure conditions (9 kbar).[3] Surprisingly, in similar transformations, a related class of sulfonyl derivatives – **triflones** (SO_2CF_3)[4] displayed a much higher reactivity, reacting under ambient pressure. The unexpected difference in electron-withdrawing properties of the fluorosulfonyl and trifluoromethylsulfonyl groups will be discussed in our lecture.[5]

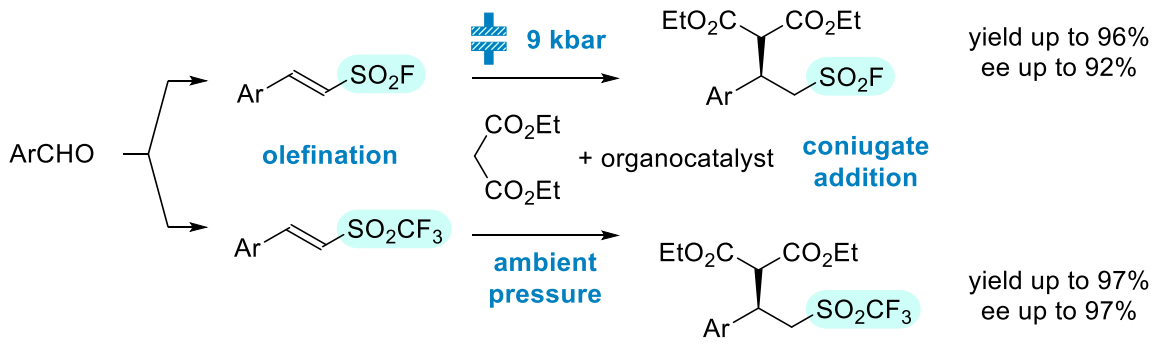

Figure 1. Synthesis and transformations of α,β-unsaturated sulfonyl fluorides and triflones.

References

[1] J. Dong, L. Krasnova, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2014**, *53*, 9430 – 9448.
[2] M. Tryniszewski, D. Basiak, M. Barbasiewicz, *Org. Lett.* **2022**, *24*, 4270 – 4274.
[3] M. Kopyt, M. Tryniszewski, M. Barbasiewicz, P. Kwiatkowski, *Org. Lett.* **2023**, *25*, 6818 – 6822.
[4] A. Budinská, H. Wennemers, *Angew. Chem. Int. Ed.* **2023**, *62*, e202300537.
[5] M. Kopyt, M. Tryniszewski, M. Barbasiewicz, P. Kwiatkowski, in preparation.

IL-05

Redneck chemistry: When sulfur meets selenium

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In order to be productive, chemistry is on the constant search for cheap and sustainable sources of raw materials which, ideally, should also have a low or no impact on the environment. In the fields of sulfur and selenium, hydrogen sulfide (H_2S)-rich spring and volcanic waters, often containing millimolar concentrations of (hydrogen)sulfide, represent such a widely distributed and readily available natural source[1–3]. In contrast to other forms of naturally occurring sulfur, such as sulfate or elemental sulfur, H_2S is chemically rather reactive under mild conditions and thus can be transformed easily to a range of valuable products, in water and occasionally even with the help of microorganisms[4].

Sulfur-rich water containing around 2.4 mM concentrations of sulfide has been collected at the spa town of Bad Nenndorf in Germany and converted in its native aqueous solvent to selenium disulfide ("SeS_2") by addition of SeO_2 and HCl. The product can be harvested and analyzed using CHN-S, EDX, ICP-OES in addition to FT-IR, powder diffraction and a Zetasizer. It is composed of nanoparticles with average diameters of around 400 nm, primarily consists of Se_2S_6 and Se_3S_5 rings, is vastly non-toxic and useful for medical, agricultural and cosmetic applications[5,6].

A similar redneck red selenium chemistry has been established with the kind assistance of microorganisms able to transform chemically simply sources of sulfur and selenium to valuable chalcogen nanomaterials. Thiophilic bacteria, such as *Thiobacilus thioparus*, for instance, feed on sodium sulfide as sulfur source and produce sulfur nanomaterials. Amazingly, even household yeast *Saccharomyces cerevisiae* can be employed to produce nanoparticles of red selenium and also of SeS_2[7,8]. Together, this redneck chemistry, despite looking somewhat trivial, requires considerable considerations, and eventually provides innovative solutions and materials, from natural sustainable (re-)sources and under mild conditions.

References

[1] L. Faulstich, S. Griffin,M.J. Nasim, M. I. Masood, W. Ali, S. Alhamound, Y. Omran, H. Kim, A. Kharma, K-H. Schäfer, R. Lilischkis, M. Montenarh, C. Keck, C. Jacob, *Int Biodeterior Biodegradation* **2017**, *119*, 678–686.

[2] A. Teleglów, J. Seremak, J. Golec, J. Marchewka, P. Golec, U. Marchewka, M. Maciejczyk, E. Golec, *Sci Rep* **2023**, *13*, 7960.

[3] J. Viegas, A.F. Esteves, E.M. Cardoso, F.A. Arosa, M. Vitale, L. Taborda-Barata, *Front Public Health* **2019**, *7*, 128.

[4] S. Giampaoli, F. Valeriani, G. Gianfranceschi, M. Vitali, M. Delfini, M.R. Festa, E. Bottari, V. Romano Spica, *Microchem. J.* **2013**, *108*, 210–214.

[5] G. Godse, K. Godse, *Cureus 16* (3), e57148.

[6] E. Tiganescu, A.Y. Abdin, A. Razouk, M.J. Nasim, C. Jacob, *Curr Opin Chem Biol* **2023**, *76*, 102365.

[7] F. Asghari-Paskiabi, M. Imani, H. Rafii-Tabar, M. Razzaghi-Abyaneh, *Biochem Biophys Res Commun* **2019**, *516* (4), 1078–1084.

[8] F.P. van den Ende, H. van Gemerden, Sulfide Oxidation under Oxygen Limitation by a Thiobacillus Thioparus Isolated from a Marine Microbial Mat. *FEMS Microbiol Ecol* **1993**, *13* (1), 69–77.

Design, Synthesis, and Biological Activity of Organosulfur/selenium Compounds for Environmental Stress Responses

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Animals and plants are exposed to many environmental stresses such as oxidative stress, dryness, heat, cold, and aging, and control of these stresses by chemicals is a critical subject to realize sustainable society. Pharmaceuticals are employed to treat brain diseases, allergies, and infections, and biostimulants to enhance plant resistivity. To control such complex stresses, small organic molecules are attractive because of availability of diverse approaches by fine-tuning their functions based on molecular structures, by administrating combinations of several compounds, and by time-dependently changing quantities. Among organic compounds, those containing heavy heteroatoms of the third & forth row of the periodic table, particularly sulfur and selenium, are attractive, because these heteroatoms are large, polarizable, oxidizable, and soft, and can well bind with biomacromolecules. Accordingly, suitable molecular design and efficient synthesis of heavy heteroatom compounds are needed to achieve biological activity for pharmaceuticals and biostimulants.[1] For molecular design, focused here are unsymmetric diheteroarylmethanes and related structures, which connect two multiple heteroatom groups by a single atom linker including sulfur and selenium.[2] These structures are characterized by involvement of multiple heteroatoms and by structural flexibility of the linkers, which facilitate binding with biomacromolecules and membrane permeation. In addition, many of these are new compounds which are patentable.[3] For the synthesis of organosulfur and selenium compounds, transition metal catalyzed methods are developed.

In order to broaden the scope of biological activities of heavy heteroatom compounds, cysteine disulfide derivatives are also developed, which are essential for the construction of protein three-dimensional structures and also for their biological functions. Their derivatives are designed, and synthetic methods are developed using transition metal catalysis, which directly reacts natural peptides in homogeneous water without using protecting groups (Figure 1).[4,5,6]

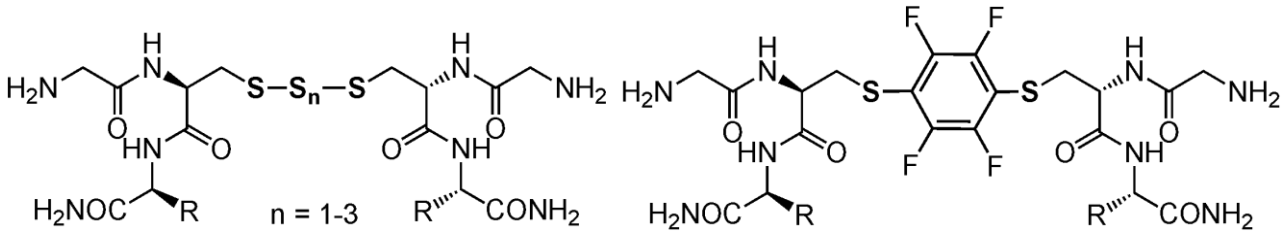

Figure 1. Functional organosulfur compounds synthesized by Rh-catalysis

References

[1] M. Arisawa, M. Yamaguchi, *Molecules*, **2020**, *25*, 3595 – 3630.
[2] M. Arisawa, *J of SJWS*, **2022**, *22*, 69 – 79.
[3] Patent: S. Moriguchi, M. Arisawa, K. Fukunaga, PCT/JP2020/38374, **2020**.
[4] M. Arisawa, K. Fukumoto, M. Yamaguchi, *ACS Catalysis*, **2020**, *10*, 15060 – 15064.
[5] K. Fukumoto, M. Yazaki, M. Arisawa, *Org. Lett.*, **2022**, *24*, 8176 – 8179.
[6] K. Fukumoto, M. Yazaki, M. Arisawa, *Asian J. Org. Chem.*, **2022**, *11*, e202200340.

Asymmetric Hydrothiolation, Hydroselenation and Hydrophosphination

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Asymmetric hydrofunctionalization of unsaturated bonds is an atom-economical and direct strategy for the synthesis of chiral molecules. Although high stereoselectivities and regioselectivities have been attained with electron-deficient C=C double bonds, achieving similar control with non-polar C=C bonds presents a significant challenge and is an area that has been infrequently addressed. Heterobicyclic alkenes, in particular, serve as versatile precursors for the generation of stereochemically complex structures. Their suitability stems from the inherent angle strain and the proximity of heteroatoms, which facilitate activation by transition metal complexes. Transition metal-catalyzed hydrofunctionalization for heterobicyclic alkenes using various heteroatom nucleophiles, including thiol,[1] selenium,[2] and phosphorus-based reagents,[3-5] have been successfully developed. These methodologies enable a concise, straightforward, and modular approach to access a range of previously unattainable chiral organosulfur, organoselenium, and organophosphorus compounds, which hold significant potential value.

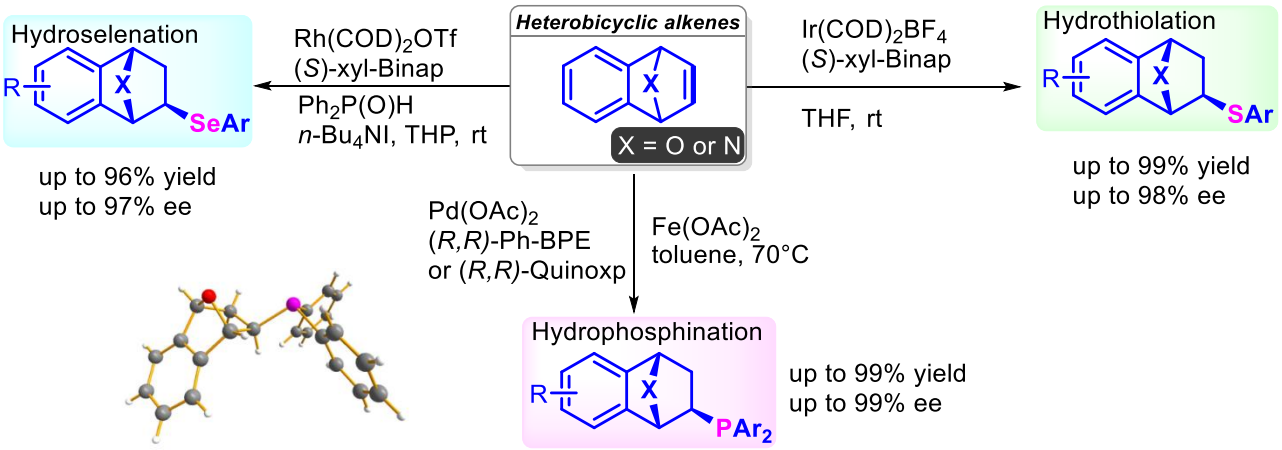

Figure 1

References

[1] Iridium-catalyzed asymmetric addition of thiophenols to oxabenzonorbornadienes. Li, S.-F.; Lu, Z.-W.; Meng, L.; Wang, J.* *Org. Lett.* **2016**, 18, 5276-5279.

[2] Rhodium-catalyzed enantioselective hydroselenation of heterobicyclic alkenes. Li, S.; Yang, Q.; Bian, Z.*; Wang, J.* *Org. Lett.* **2020**, *22*, 2781-2785.

[3] Asymmetric hydrophosphination of heterobicyclic alkenes: facile access to phosphine ligands for asymmetric catalysis. Lu, Z.; Zhang, H.; Yang, Z.; Ding, N.; Meng, L.; Wang, J.* *ACS Catal.* **2019**, *9*, 1457-1463.

[4] Enantioselective palladium-catalyzed hydrophosphinylation of allenes with phosphine oxides: facile access to chiral allylic phosphine oxides. Yang, Z.-P.; Wang, J.* *Angew. Chem. Int. Ed.* **2021**, *60*, 27288-27292.

[5] Palladium-catalyzed enantio- and regioselective ring-opening hydrophosphinylation of methylene cyclopropanes. Zhou, J.; Meng, L.; Lin, S.; Cai, B.; Wang, J.* *Angew. Chem. Int. Ed.* **2023**, *62*, e202303727.

IL-08

Contributing to the Renaissance of S(IV) and S(VI) Functional Groups

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Organosulfur compounds have historically played a pivotal role in organic chemistry, contributing significantly to the creation of innovative chemical structures and architectures.[1] Among these compounds, those containing a sulfur(VI) functional group have been extensively studied for over a century. However, there has been a renewed interest in sulfur(IV) and sulfur(VI) functional groups in recent years.[2]

Of particular interest are organosulfur compounds in which oxygen atoms are replaced by nitrogen atoms, resulting in unique compounds with significant relevance in drug discovery programs. This presentation will focus on our contribution in the development of synthetic methods for introducing nitrogen atoms onto sulfur atoms.[3-5]

Novel and efficient strategies for accessing uncommon sulfur(VI) functional groups, such as sulfoximines, sulfonimidates, and sulfonimidamides, as well as rather rare sulfur(IV) functional groups, including sulfinamidines and sulfinimidates, will be presented. Additionally, the integration of flow technology into these synthetic approaches to enhance their sustainability will be discussed.

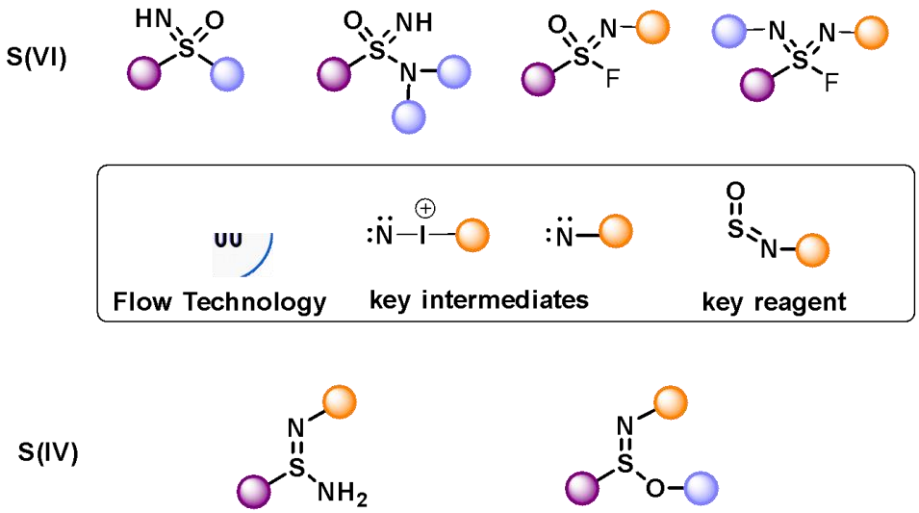

Figure 1. The chemical space of S(IV) and S(VI) functional groups.

References

[1] Feng, M.; Tang, B.; Liang, S. H.; Jiang, X. *Curr. Top. Med. Chem.* 2016, *16* (11), 1200−1216.
[2] M. Andresini, M. Colella, L. Degennaro, R. Luisi, *Org. Biomol. Chem.* **2023**, *21*, 7681.
[3] M. Andresini, A. Tota, L. Degennaro, J. A. Bull, R. Luisi, *Chem. Eur. J.* **2021**, *27*, 17293.
[4] M. J. Tilby, M. C. Willis, *Expert Opin. Drug Discov*. **2021**, *16*, 1227–1231.
[5] M. Frings, C. Bolm, A. Blum, C. Gnamm, *Eur. J. Med. Chem.* **2017**, *126*, 225.

IL-09

Expanding the molecular diversity of thiochromans using allenyl sulfones as substrates

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Thiochromans (X = S) are structural units found in an increasing number of molecules exhibiting biological activities.[1] Unlike the corresponding oxygen analogues (X = O), the development of synthetic methodologies to access these sulfur heterocycles has been scarcely investigated. The reported approaches are mainly based on annulation reactions, involving 2-sulfanylbenzaldehyde derivatives and electron-deficient alkenes as substrates.[2] Continuing with our interest towards allenyl sulfone chemistry,[3] we will present in this lecture an original route to highly functionalized thiochroman-4-ols using this family of allenes as electrophilic partners.[4] More precisely, the methodology we developed is based on the activation of the cumulene by unprecedented aromatic thiolates, prepared from the corresponding thioisatins. The optimization of the operating conditions, the study of the scope and limitations will be described. Furthermore, extension to the use of other structural types of electron-deficient allenes and last-stage derivatizations will be investigated.

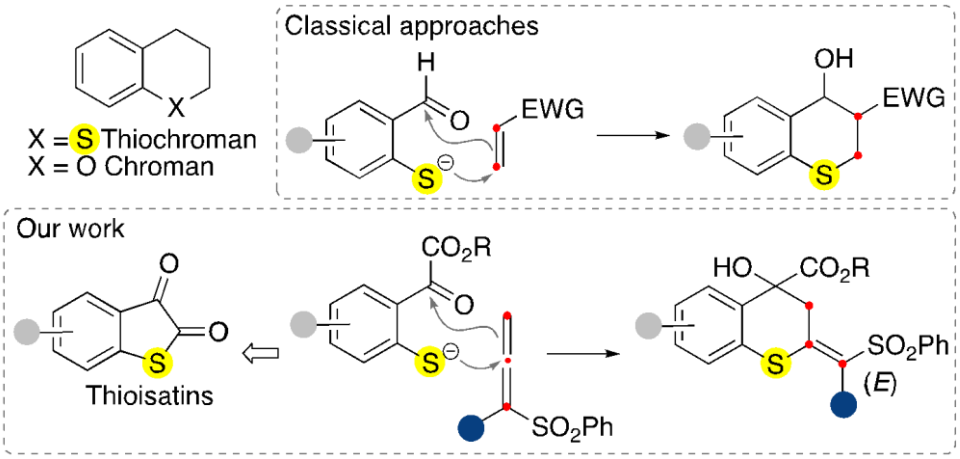

Figure 1

References

[1] (a) Q. Wu, S. Wu, J. Zou, Q. Wang, C. Mou, P. Zheng, Y. R. Chi, *Org. Lett.*, **2023**, 25, 3967–3971. (b) H. Mao, B.-W. You, L.-J. Zhou, T.-T. Xie, Y.-H. Wen, X. Lv, X.-X. Wang, *Org. Biomol. Chem.*, **2017**, *15*, 6157–6166.

[2] See for example: (a) Y. Mo, X. Zhang, Y. Yao, C. Duan, L. Ye, Z. Shi, Z. Zhao, X. Li, *J. Org. Chem.*, **2021**, *86*, 4448–4456. (b) Y.-P. Zhang, Y. You, J.-Q. Zhao, X.-M. Zhang, X.-Y. Xu, W.-C. Yuan, *J. Org. Chem.*, **2019**, *84*, 7984–7994. (c) H. Chen, C. Wang, D. Wen, Y. Deng, X. Liu, X. Liu, J. Zhang, W. Yan, *Synthesis*, **2019**, 51, 3327–3335.

[3] (a) T. Martzel, J.-F. Lohier, A.-C. Gaumont, J.-F. Brière, S. Perrio, *Eur. J. Org. Chem.*, **2018**, 5069–5073. (b) T. Martzel, J.-F. Lohier, A.-C. Gaumont, J.-F. Brière, S. Perrio, *Adv. Synth. Catal.*, **2018**, *360*, 2696–2706. (c) T. Martzel, J.-F. Lohier, A.-C. Gaumont, J.-F. Brière, S. Perrio, *Adv. Synth. Catal.*, **2017**, *359*, 96–106.

[4] To the best of our knowledge, there is a single precedent for the construction of thiochroman platforms from allenyl sulfones: M. P. Pavan, M. N. Reddy, N. N. B. Kumar, K. C. K. Swamy, *Org. Biomol. Chem.*, **2012**, *10*, 8113–8118.

IL-10

Chemical Tools and Models for Investigating Reactive Sulfur and Selenium Species

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Hydrogen sulfide (H_2S) is an important biological mediator involved in a wide array of physiological processes. Much of this activity is associated with often inseparable roles of reactive sulfur species, including persulfides (RSS^-), polysulfides (HS_n^-), and related molecules. In addition, emerging examples of reactive selenium species, including H_2Se, play complementary and often more potent roles in biological redox chemistry. A significant challenge in furthering our understanding of these highly reactive S and Se species has been the lack of chemical tools for delivery of these molecules in biological contexts and the lack of suitable model systems for investigating fundamental chemical reactivity. This presentation will focus on recent work from our group in two primary areas: (1) Developing responsive small molecule donors for H_2S and H_2Se,[1,2] and (2) Developing model systems to investigate the reactivity of dichalcogenide (RSS^-, $RSSe^-$, $RSeS^-$, and $RSeSe^-$).[2,3] Specifically, we will highlight approaches for H_2S delivery through intermediate release of COS, which is rapidly hydrolyzed to H_2S by carbonic anhydrase, as well as comparison to H_2Se-releasing analogues. In addition, we will describe the synthesis, characterization, and reactivity of synthetic dichalcogenides with other small biologically-relevant molecules, including transition metals.

References

[1] K.G. Fosnacht, J. Dorogin, P.M. Jefferis, M.H. Hettiaratchi, M.D. Pluth. *Angew. Chem. Int. Ed.*, **2024**, e202402353
[2] T.D. Newton, K. Li, J. Sharma, P.A. Champagne, M.D. Pluth. *Chem. Sci.* **2023**, 14, 7581-7588
[3] K. Li, L.N. Zakharov, M.D. Pluth. *J. Am. Chem. Soc.* **2023**, 14, 7581-7588

Chemical Tools for Regulating Reactive Sulfur Species

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Reactive sulfur species (RSS) such as hydrogen sulfide, hydrogen polysulfides, and persulfides play regulatory roles in many physiological and pathophysiological processes. The field of RSS physiology and pharmacology is rapidly growing in recent years, but a number of fundamental issues must be addressed to advance our understanding of their biology and clinical potential in the future. It is critical to investigate their chemistry and to develop useful tools/methods for regulating and tracking these species. The research in our laboratory focuses on the development of such methods and chemical tools. In this presentation, I will give an overview of our research in this field and discuss a few recent examples of specific RSS releasing agents, sensors, as well as scavengers (Figure 1).[1-4]

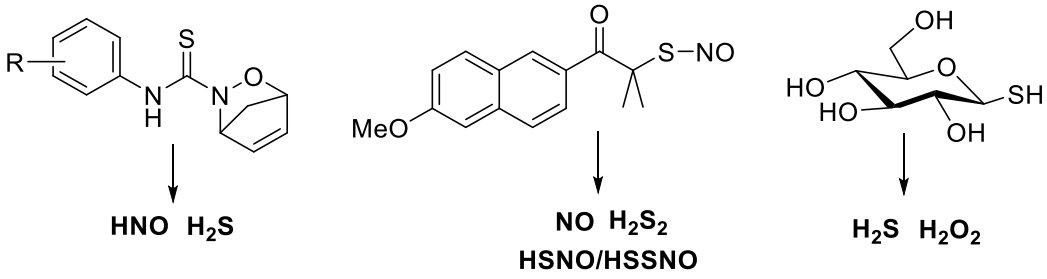

Figure 1. Examples of RSS releasing agents.

References

[1] X. Ni, X. Li, T. L. Shen, W. J. Qian, M. M. *J. Am. Chem. Soc*. **2021**, *143*, 13325-13332.
[2] S. S. Kelly, X. Ni, V. Yuen, M. N. Radford, M. Xian, *ChemBioChem* **2022**, *23*, e202200101.
[3] B. Roy, M. Shieh, S. Xu, X. Ni, M. Xian, *J. Am. Chem. Soc*., **2023**, *145*, 277-287.
[4] X. Ni, E. Marutani, M. Shieh, Y. Lam, F. Ichinose, M. Xian, M. *Angew. Chem. Int. Ed*. **2024**, *63*, e202317487.

IL-12

Up-cycling of waste Sulfur by inverse vulcanization: Novel macromolecular architectures for advanced photonics

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The recently arisen Inverse Vulcanization (IV) process represents an efficient and green method to up-cycle waste elemental Sulfur, which is an abundant by-product of oil and gas refining, and to achieve a new class of amorphous Sulfur-rich macromolecular materials christened inverse vulcanized polymers (IVPs).[1] Due to their peculiar nature consisting of polysulfide chains typically cross-linked by aromatic divinyl moieties, IVPs exhibit unique functional properties, such as dynamic covalent behaviour and self-healing capability. In particular, the high content of easily polarizable S-S bonds boasts very high refractive index and excellent transparency in the near infrared region (NIR), which makes IVPs appealing building blocks for photonic structures.[2] All-polymer photonic crystals are indeed technologically interesting for materials affordability, fabrication simplicity, versatility and scalability. However, their application in the field of light confinement is still limited by the low and similar refractive indices shown by most processable polymers in their transparency range.

In this research, IVPs with outstanding refractive index were synthetized using as cross-linking monomers purposely designed vinyl aromatic derivatives obtained by a single step Suzuky-Miyaura cross-coupling reaction.[3] Comonomer type and amount were varied to enhance both the optical behaviour and filmability, that is the properties technologically relevant for the application and industrial scale-up of the ensuing IVPs. These novel amorphous macromolecular architectures are indeed exploitable for a variety of applications for light emission control, spanning from free-standing dielectric mirrors (Distributed Bragg Reflectors) with very high reflectance and microcavities for NIR emitting lasers, to fabrication of metamaterials for advanced nanophotonics.

References

[1] W. J. Chung, J. J. Griebel, E. T. Kim *et al.*, *Nat. Chem.* **2013**, *5*, 518 – 524.
[2] C. Tavella, P. Lova, M. Marsotto, G. Luciano, M. Patrini, P. Stagnaro, D. Comoretto, *Crystals* **2020**, *10*, Art n. 154.
[3] C. Tavella, G. Luciano, P. Lova, M. Patrini, C. D'Arrigo, D. Comoretto, P. Stagnaro, *RSC Adv.* **2022**, *12*, 8924 – 8935.

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Project "PIVOT Sulfur-based Polymers from Inverse Vulcanization as high refractive index materials for planar photonic crystals: dielectric mirrors and microcavities" (IDROL 20583) funded by Compagnia di San Paolo (Italy).

Green Organosulfur Chemistry

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Element sulfur possesses its own circulation in the nature. However, fossil resources (coal, petroleum, sulfur-containing minerals, etc.) have been excessively consumed with increasing demands of human production and living[1]. The balance of sulfur circulation in nature has been partially disturbed. We implement our research via green chemistry strategies to assist the balance of sulfur circulation in the nature from two scientific models, which include high efficiency conversion of inorganic sulfur-containing salts. Based on the unique properties of electron and orbital arrangement of sulfur atom, our group has established a green sulfuration chemistry with "**3S**" (**S**melless, **S**table and **S**ustainable) concept, and developed a set of new sulfurating reagents[2] and corresponding methodologies. Through these strategies, the construction of sulfide[3], polysulfide, thiocarbonyl[4], sulfoxide, sulfone[5], and sulfoximide[6] in natural products, pharmaceuticals and organic materials were achieved comprehensively.

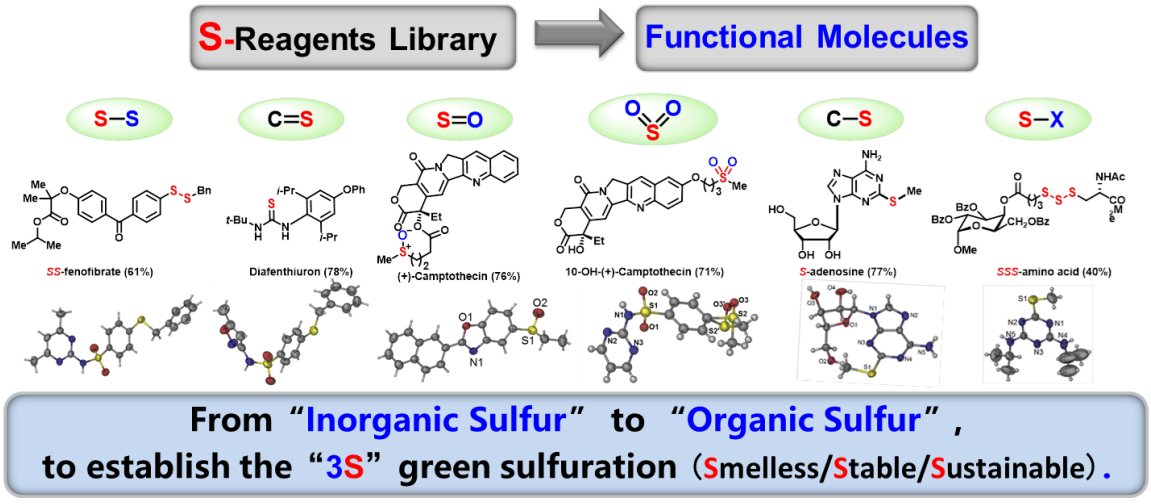

Figure 1. green organosulfur chemistry.

References:

[1] X. Jiang, *Sulfur Chemistry*, 376: 14 (Eds.: X. Jiang), Springer, Berlin, **2018**, pp. 285-324.
[2] S. Zhao, D. Zeng, M. Wang, X. Jiang, *Nat. Commun.*, **2024**, *15*, 727-735.
[3] Q. Yu, L. Bai, X. Jiang, *Angew. Chem. Int.* Ed., **2023**, *62*, e202314379.
[4] Y. Liao, S. Zhang, X. Jiang, *Angew. Chem. Int. Ed.*, **2023**, *62*, e202303625.
[5] Y. Meng, M. Wang, X. Jiang, *Angew. Chem. Int. Ed.*, **2020**, *59*, 1346-1353.
[6] D. Zeng, Y. Ma, W.-P. Deng, M. Wang, X. Jiang, *Nat. Synth*, **2022**, *1*, 455-463.

IL-14

Synthesis of *S*- and *N,S*-heterocycles by gold-catalyzed cyclizations

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Heterocycles containing sulfur or both nitrogen and sulfur atoms can be found in a broad range of drugs structures.[1,2] Recent research from our laboratory focused on the development of new synthetic strategies based on transition-metal catalysis (Pd,[3] Cu,[4] Rh,[5] Au[6,7]) to access original scaffolds belonging to this category. The presentation will cover our work dealing with the synthesis of benzothiophene and thiazepane derivatives (Figure 1) by gold-catalyzed domino reactions involving intramolecular carbone-sulfur bond formation.[6,7]

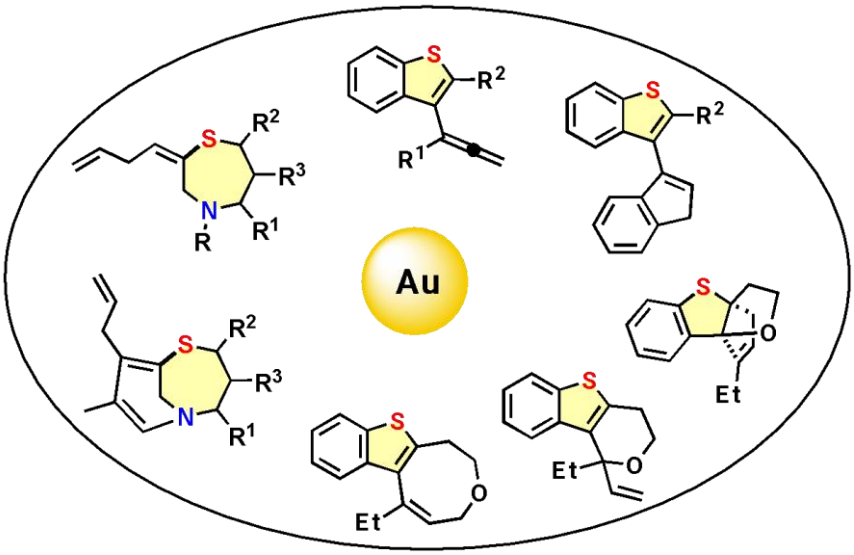

Figure 1.

References

[1] K. A. Scott, J. T. Njardarson, *Top. Curr. Chem.*, **2018**, 376: 5.
[2] A. Martinez, C. Gil, in *RSC Drug Discovery Series, Privileged Scaffolds in Medicinal Chemistry: Design, Synthesis, Evaluation*, Vol. (Ed.: S. Bräse N.), The Royal Society of Chemistry, **2015**, ch. 9, pp. 231 – 261.
[3] A. Basilio Lopes, P. Wagner, M. Gulea, *Eur. J. Org. Chem.*, **2019**, *2019*, 1361 – 1370.
[4] M. Choury, A. G. Blond, M. Gulea, *Eur. J. Org. Chem.*, **2021**, *2021*, 2203 – 2211.
[5] P. Wagner, M. Gulea, N. Girard, *Adv. Synth. Catal.*, **2024**, *366*, 2203 – 2211.
[6] M. Choury, P. Wagner, C. Rognan, G. Blond, M. Gulea, *Adv. Synth. Catal.*, **2022**, *364*, 3238 – 3244.
[7] C. Van Wesemael, N. Brach, M. Gulea, G. Blond, *Adv. Synth. Catal.*, **2022**, *364*, 4141 – 4145.

ORAL COMMUNICATIONS

ISOCS-30

OC-01

Designing Molecular Modifications for Sulfur-Centered Platforms with Nucleophilic C-1 Releasing Agents

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The direct transfer of a reactive nucleophilic CH_2X unit into an existing linkage enables the formal introduction of this moiety with the precisely defined degree of functionalization.[1] Upon the fine tuning of the reaction conditions governing the transformation, the initial homologation event can serve as the manifold for triggering unusual rearrangement sequences leading to complex architectures through a unique synthetic operation.[2] The direct – full chemoselective - conversion of a disulfide into the homologated dithioacetal (*via* a),[3] the telescoped homologation of a thiosulfonate to unsymmetrical oxothio-[4] and dithio-acetals[5] (*via* b) will illustrate these unprecedented concepts. Additionally, the homologation of a *N*-sulfinylimine will furnish the α-substituted methylsulfinamide core (*via* d).[6] The formal *ethylene* homologation through the consecutive installation of two methylene fragments onto isothiocyanates will be presented for assembling the unprecedented 4-membered imino-thietane ring.

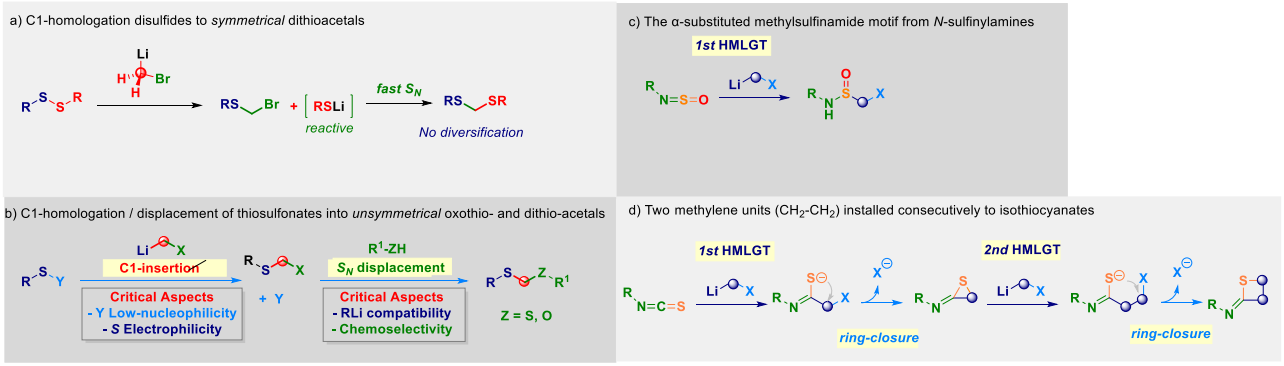

Figure 1. Nucleophilic homologations of *S*-electrophiles.

References

[1] a) L. Castoldi, S. Monticelli, R. Senatore, L. Ielo, V. Pace, *Chem. Commun.* **2018**, *54*, 6692-6704; b) R. Senatore, L. Castoldi, L. Ielo, W. Holzer, V. Pace, *Org. Lett.* **2018**, *20*, 2685-2688; c) M. Malik, R. Senatore, T. Langer, W. Holzer, V. Pace, *Chem. Sci.* **2023**, *14*, 10140-10146; d) *Homologation Reactions. Reagents, Applications and Mechanisms. Vol. 1 and 2,* V. Pace, Eds.,ISBN 978-3-527-34815-2; Wiley-VCH, Weinheim, 2023; e) V. Pace, L. Castoldi, E. Mazzeo, M. Rui, T. Langer, W. Holzer, *Angew. Chem. Int. Ed.* **2017**, *56*, 12677-12682; f) G. Parisi, M. Colella, S. Monticelli, G. Romanazzi, W. Holzer, T. Langer, L. Degennaro, V. Pace, R. Luisi, *J. Am. Chem. Soc.* **2017**, *139*, 13648-13651.
[2] a) L. Ielo, L. Castoldi, S. Touqeer, J. Lombino, A. Roller, C. Prandi, W. Holzer, V. Pace, *Angew. Chem. Int. Ed.* **2020**, *59*, 20852-20857; b) L. Ielo, S. Touqeer, A. Roller, T. Langer, W. Holzer, V. Pace, *Angew. Chem. Int. Ed.* **2019**, *58*, 2479-2484.
[3] V. Pace, A. Pelosi, D. Antermite, O. Rosati, M. Curini, W. Holzer, *Chem. Commun.* **2016**, *52*, 2639-2642.
[4] L. Ielo, V. Pillari, M. Miele, W. Holzer, V. Pace, *Adv. Synth. Catal.* **2020**, *362*, 5444-5449.
[5] L. Ielo, V. Pillari, N. Gajic, W. Holzer, V. Pace, *Chem. Commun.* **2020**, *56*, 12395-12398.
[6] M. Malik, R. Senatore, D. Castiglione, A. Roller-Prado, V. Pace, *Chem. Commun.* **2023**, *59*, 11065-11068.

Aromatic Metamorphosis of Thiophenes

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Aromatic skeletons are usually considered as being unbreakable due to their aromatic resonance energy. Compared with exocyclic decorations of aromatic compounds, little is known about endocyclic modifications such as substitutions of endocyclic atoms and atom insertions into the rings through partial disassembly of the cyclic skeletons and subsequent ring reconstruction. We are interested in developing a series of new synthetic methods to achieve endocyclic modifications of heteroarenes as a game-changing strategy in organic synthesis. Here I will present our endeavors to establish 'aromatic metamorphosis',[1] focusing on the transformations, or editing, of thiophenes and their benzo derivatives into other heteroles such as carbazoles,[2] dibenzophospholes,[3,4] and siloles.[4]

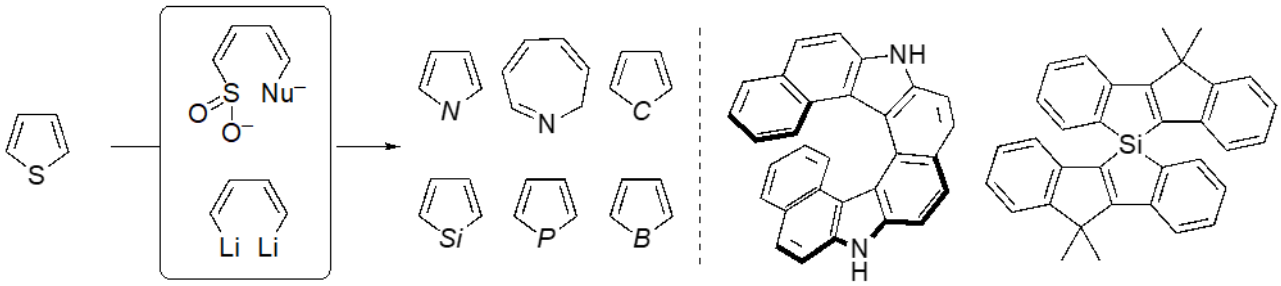

Figure 1. Transforming thiophenes into other heterocycles.

References

[1] (a) H. Yorimitsu, D. Vasu, M. Bhanuchandra, K. Murakami, A. Osuka, *Synlett* **2016**, *27*, 1765 – 1774. (b) K. Nogi, H. Yorimitsu, *Chem. Commun.* **2017**, *53*, 4055 – 4065. (c) H. Saito, H. Yorimitsu, *Chem. Lett.* **2019**, *48*, 1019 – 1028. (d) H. Yorimitsu, *J. Chin. Chem. Soc.* **2021**, *68*, 536 – 540.

[2] (a) M. Bhanuchandra, K. Murakami, D. Vasu, H. Yorimitsu, A. Osuka, *Angew. Chem. Int. Ed.* **2015**, *54*, 10234 – 10238. (b) A. Kaga, K. Nogi, H. Yorimitsu, *Chem. Eur. J.* **2019**, *25*, 14780 – 14784. (c) T. Yanagi, T. Tanaka, H. Yorimitsu, *Chem. Sci.* **2021**, *12*, 2784 – 2793.

[3] M. Onoda, Y. Koyanagi, H. Saito, M. Bhanuchandra, Y. Matano, H. Yorimitsu, *Asian J. Org. Chem.* **2017**, *6*, 257 – 261.

[4] A. Kaga, H. Iida, S. Tsuchiya, H. Saito, K. Nakano, H. Yorimitsu, *Chem. Eur. J.* **2021**, *27*, 4567 – 4572.

Cationic and Neutral Sulfur-Bridged [6]Helicenes

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Heterohelicenes are chiral *ortho*-condensed polyaromatics involving one or more heteroatoms in the helical backbone.[1] While neutral carbon analogues display absorption, fluorescence, electronic circular dichroism (ECD) and circularly polarized luminescence (CPL) in the blue range of the visible spectrum, cationic [*n*]heterohelicenes are welcome exceptions.[2] In fact, the extended delocalization provided by the triarylcarbenium framework allows longer visible wavelengths and even an access to NIR spectral region. The bridging heteroatoms are responsible for (i) stabilizing the carbenium species (pK_{R+}) and (ii) tuning the resulting (chir)optical properties. Herein, we present novel neutral and cationic [6]Helicenes containing sulfur as bridging atom, as well as oxidized analogues. Thanks to the lower donor ability of S compared to N and O atoms, the frontier molecular orbitals situation is strongly modified through a decrease in the energy of the LUMO orbitals in particular. Importantly, it results in a wide tuning of the optical properties. These compounds are configurationally stable benefitting, in addition, of the puckering of the S-ring induced by the longer C-S bonds (~1.755 Å).[3] Indeed, a very large increase of the helical curvature results and its impact on (chir)optical properties and chemical stability will be discussed during the presentation.

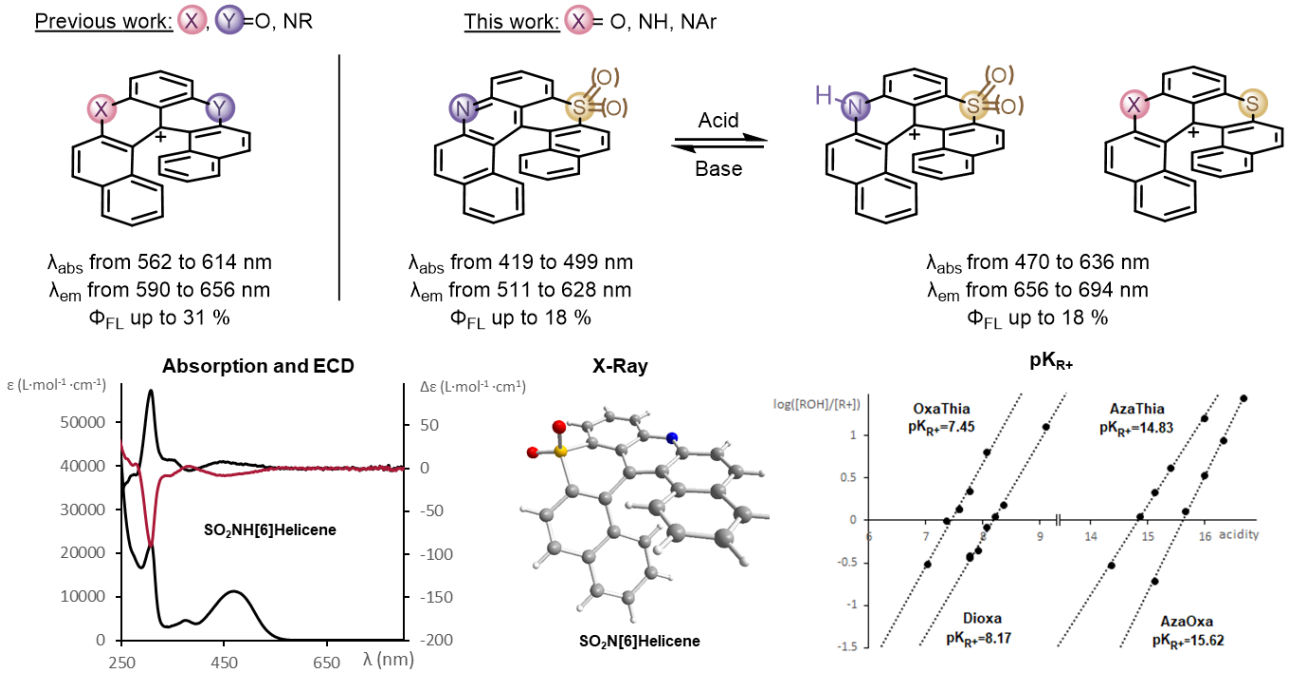

Figure 1

References

[1] K. Dhbaibi, L. Favereau, J. Crassous,*Chem. Rev.*, **2019**, *119*, 14, 8846-8953.
[2] J. Bosson; N. Bisballe, B. W. Laursen, J. Lacour, *Helicenes. Synthesis, Properties and Applications (Eds.: J. Crassous, I. G. Stara, I. Stary), Wiley-VCH*, **2022**, Chapter 4, 127-165.
[3] G. Lamanna, C. Faggi, F. Gasparrini, A. Ciogli, C. Villani, P. J. Stephens, F. J. Devlin, S. Menichetti, *Chem. Eur. J.*, **2008**, *14*, 5747-5750.

S-to-*Se* Substitution Strategy for Preparation of Insulin Superfamily Proteins

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Insulin, which has hypoglycemic activity, is a globular protein composed of two polypeptide chains (i.e., A- and B-chains), and its structure is stabilized by two interchain SS bridges ($C7^{A}$–$C7^{B}$ and $C20^{A}$–$C19^{B}$) and one intrachain SS linkage ($C6^{A}$–$C10^{A}$). Previously, our group reported that the [$C7U^{A}$,$C7U^{B}$] variant of bovine pancreatic insulin (SeIns), in which the solvent-exposed SS bond ($C7^{A}$–$C7^{B}$) is replaced by a diselenide (SeSe) bond, can be effectively synthesized via direct coupling of individual chains.[1] While SeIns has almost the same folded structure (**Fig. 1a**) as that of wild-type insulin (BPIns), it showed significantly higher resistance *in vitro* to insulin-degrading enzyme (IDE), which selectively recognize insulin monomer as a substrate. In this study, we aimed to further improve the efficiency of chemical synthesis of SeIns and to elucidate the relationship between the structure and biological functions of SeIns.

Optimizing the synthetic conditions for the oxidative chain assembly of the A- and B-chains, the target SeIns was generated in up to 72% yield that is comparable to the *in vitro* folding efficiency for single-chain proinsulin (**Fig. 1a**). When the resistance of BPIns to IDE was evaluated in the presence of SeIns, the degradation rate of BPIns became significantly slower than that of BPIns alone. Furthermore, the investigation on the intermolecular association properties of SeIns and BPIns using analytical ultracentrifugation suggested that SeIns readily forms oligomers not only with its own but also with BPIns. Moreover, the sustained hypoglycemic effect of SeIns on diabetic rats was observed (**Fig. 1b**). This presentation will describe the molecular mechanisms for the phenomena observed in the animal studies and the potential of SeIns as a long-acting formulation.

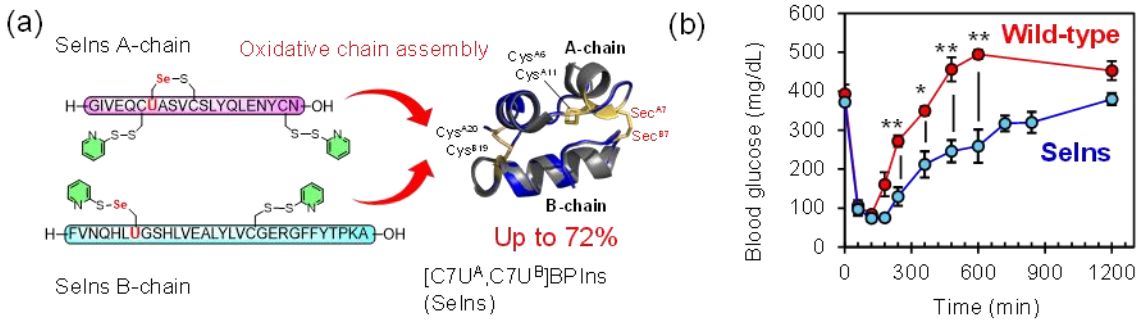

Figure 1. (**a**) One-step chain assembly of SeIns A- and B-chains to folded SeIns. Time course of blood glucose level in STZ-induced diabetic model rat following s.c. injection of insulin samples (100 units/mL of saline). The dosage of insulins was 150 μg/300 g rat. Data are shown as mean ± SEM. The symbols * and ** represent $p < 0.05$ and $p < 0.01$, respectively. The p-value was obtained from a t-test.

References

[1] K. Arai, *et al.*, *Angew. Chem. Int. Ed.*, **2017**, *56*, 5522–5526.
[2] K. Arai, *et al.*, *Commun. Chem.*, **2023**, *6*, 258.

Benzodithiophenes: key intermediates for the preparation of thiahelicenes

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Benzo[1,2-*b*:4,3-*b*']dithiophene derivatives (**BDT**) belong to an interesting class of thiophene-based aromatic π-conjugated compounds that are widely studied in the field of organic electronics and materials science.[1] Besides, **BDT** are key intermediates for the synthesis of inherently chiral helical systems such as tetrathia[7]helicenes (**7-TH**s).[2] In our ongoing studies on the synthesis and functionalization of **BDT**,[3] we have recently developed new methodologies for the preparation of [7]- and [5]-thiahelicenes, **7-TH**s and **5-2TH**s, respectively (Figure 1).

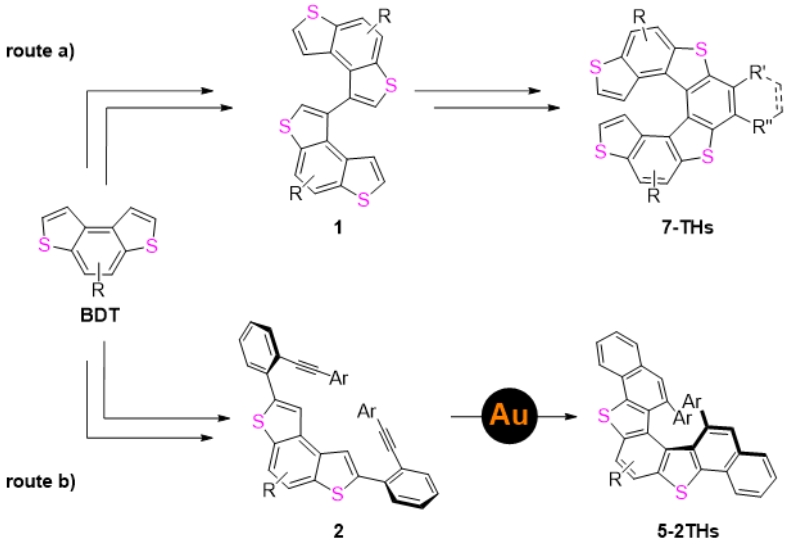

Figure 1. Synthesis of functionalized [5]- and [7]-thiahelicenes.

In this communication we present our results on the diversity-oriented synthesis of **7-TH**s exploiting transition metal-catalysed cross coupling reactions starting from bis(benzodithiophene) species **1** (Figure 1, route a),[4] along with the highly enantioselective synthesis of dithia[5]helicenes (**5-2TH**s) via double Au-catalysed hydroarylation of alkynes **2** (Figure 1, route b).[5]

References

[1] A. Bossi, S. Arnaboldi, C. Castellano, R. Martinazzo, S. Cauteruccio, *Adv. Optical Mater.*, **2020**, *8*, 2001018.

[2] E. Licandro, S. Cauteruccio, D. Dova, *Adv. Het. Chem.*, **2016**, *118*, 1 – 46.

[3] V. Pelliccioli, G. Dilauro, S. Grecchi, S. Arnaboldi, C. Graiff, F. M. Perna, P. Vitale, E. Licandro, A. Aliprandi, S. Cauteruccio, V. Capriati *Eur. J. Org. Chem.*, **2020**, 6981 – 6988.

[4] V. Pelliccioli, D. Dova, C. Baldoli, C. Graiff, E. Licandro, S. Cauteruccio, *Eur. J. Org. Chem.*, **2021**, 383 – 395.

[5] V. Pelliccioli, T. Hartung, M. Simon, C. Golz, E. Licandro, S. Cauteruccio, M. Alcarazo, *Angew. Chem. Int. Ed.*, **2022**, *61*, e2021145.

Amino-Acid Derived Dithiocarbamates – Building Blocks For Hard/Soft-Heterobimetallic Coordination Networks

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Dithiocarbamate-functionalized carboxylates (DTCCs) derived from amino acids can potentially coordinate to a hard (oxophilic) metal and to a soft (thiophilic) metal simultaneously (Figure 1, a). They are therefore attractive for the construction of heterobimetallic coordination polymers and networks, potentially able to form porous three-dimensional structures (metal-organic frameworks; MOFs). The CSS^- group is selectively complexed by late transition metals such as bivalent platinum[1,2] or copper,[3] affording DTCC metalloligands of different geometry. The free carboxylate groups are accessible to complex formation with various main-group and transition metals, e.g. zinc.[1] The resulting products contain polymeric chains, or two- or three-dimensional arrays of different porosity in the solid state (Figure 1, b).

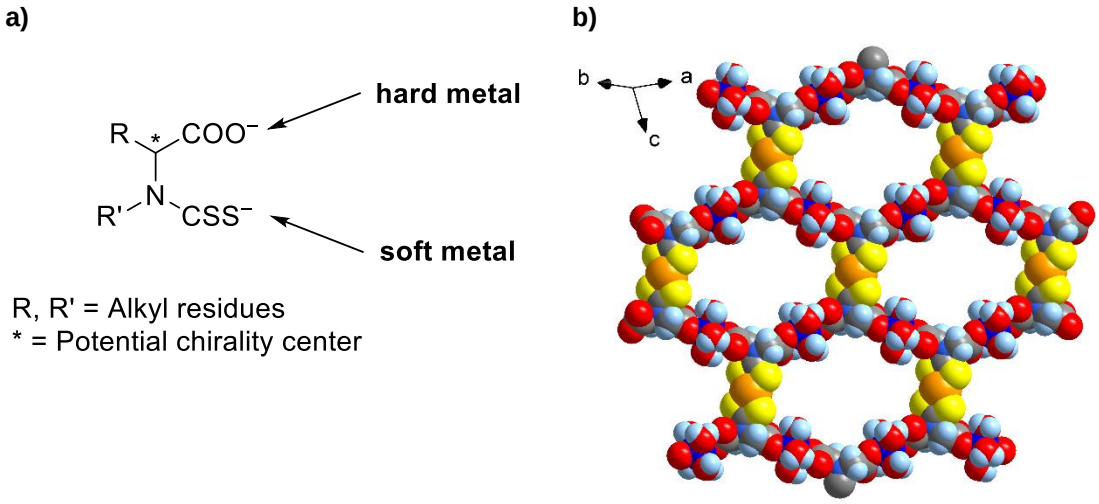

Figure 1. a) General structure of DTCC ligands and their potential ability to coordinate hard and soft metal centers selectively,[1] b) The porous layer structure of $Co_2[Pt\{SSC\text{-}N(CH_2COO)_2\}_2] \cdot n\ H_2O$, derived from iminodiacetic acid, in the crystal (non-coordinated crystal water omitted for clarity).[2]

References

[1] P. Liebing, J. Witzorke, F. Oehler, M. Schmeide, *Inorg. Chem.* **2020**, *59*, 2825–2832.
[2] P. Liebing, F. Oehler, J. Witzorke, M. Schmeide, *Cryst. Eng. Comm.* **2020**, *22*, 7838–7846.
[3] V. Behling, B. Kintzel, J. Heinrich, M. Hingel, J. Meyer, S. Greiner, P. Liebing, *Cryst. Growth Des.* **2023**, *23*, 7777–7788.

Poly(disulfide)s Toward Sustainability

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The overuse of nondegradable plastic has caused serious environmental pollution. The preparation of polymers with inherent recyclability through the design of new monomers is an effective way to solve environmental problems. To achieve the goal of a truly sustainable economy, thioctic acid was used as a monomer motif due to its intrinsic dynamic reversibility. By supplementing with various orthogonal supramolecular interactions, multifunctional poly(disulfide)s with controllable properties were developed, e.g., self-healing, adhesive, recyclable, and degradable. This report focuses on our developed poly(disulfide)s[1-4] toward sustainability.

References

[1] Y. Deng, Q. Zhang, C. Shi, R. Toyoda, D. H. Qu, H. Tian, B. L. Feringa, *Sci. Adv.* **2022**, *8*, eabk3286.
[2] Y. Deng, Q. Zhang, D.-H. Qu, H. Tian, B. L. Feringa, *Angew. Chem Int. Ed.* **2022**, *61*, e202209100.
[3] Y. Deng, Q. Zhang, B. L. Feringa, H. Tian, D. H. Qu, *Angew. Chem Int. Ed.* **2020**, *59*, 5278–5283.
[4] Y. Deng, Z. Huang, B. L. Feringa, H. Tian, Q. Zhang, D.-H. Qu, *ChemRxiv* **2023**, DOI:10.26434/chemrxiv-2023-gxm6p

OC-08

A novel bioresponsive self-immolative spacer based on aza-quinone methide reactivity for the controlled release of thiols

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Thiols are a special class of molecules that play an important role in biological systems.[1] As excellent electron donors, thiols readily bind metals in proteins and act as potent metalloenzyme inhibitors. In addition, due to their special redox potential, thiols play an important role in the control of redox homeostasis and in the scavenging of ROS and RNS (reactive oxygen and/or nitrogen species).[2] This wide range of activities makes thiols potentially useful compounds in therapy, although the diversity of targets often makes them non-selective. Stimulus-sensitive release of this moiety from conjugated prodrugs is limited to their conversion to disulfides, which have limited stability in various tissues and blood. Furthermore, the use of thiocarbonate or thiocarbamate as prodrugs is also limited by the instability of these groups in aqueous/organic media.[3]

We recently reported the first example of a molecular adaptor based on aza-quinone methide reactivity for the self-immolative release of directly linked thiols under biologically controllable conditions.[4]

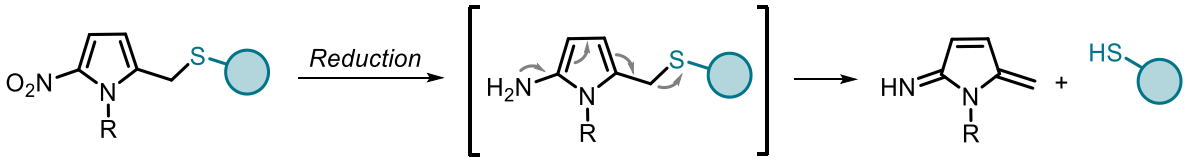

Figure 1. Release mechanism of NPYM.

5-Nitropyrrolylmethanol (NPYM), the designed self-immolative spacer, was tested for the release of thiols and other different functional groups, such as amines, phenols, sulfonamides and carboxyamides, under mild reduction conditions. its applicability in cells was also evaluated using ST7612AA1, a potent thiol-containing HDAC inhibitor with in vitro activity in the nanomolar range (IC50 = 50 nM on NCI-H460 cells) associated with a remarkable in vivo antitumour activity.[5]

References

[1] A.Y. Chen, R.N. Adamek, B.L. Dick, C. V. Credille, C.N. Morrison, S.M. Cohen, *Chem. Rev.,* **2019,** *119*, 1323–1455.
[2] S. Sun, B.L. Oliveira, G. Jiménez-Osés, G.J.L. Bernardes, *Angew. Chem. Int. Ed.*, **2018**, *57*, 15832–15835.
[3] A. Alouane, R. Labruère, T. Le Saux, F. Schmidt, L. Jullien, *Angew. Chem. Int. Ed.*, **2015**, *54*, 7492.
[4] E. Ermini, A. Brai, E. Cini, F. Finetti, G. Giannini, D. Padula, L. Paradisi, F. Poggialini, L. Trabalzini, P. Tolu, M. Taddei, *Chem. Sci*., **2024**, *15*, 6168-6177.
[5] F. M. Milazzo, L. Vesci, A. M. Anastasi, C. Chiapparino, A. Rosi, G. Giannini, M. Taddei, E. Cini, V. Faltoni, E. Petricci, *et al*., *Front. Oncol*. **2020**, *9*, 1534.

A Long-Lived Acyclic Triplet Aldimine Enables Modular Synthesis of Azetidines via An Intermolecular Aza-Paternò Büchi Reaction

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Saturated *N*-heterocycles are ubiquitous, abundant in nature in the form of alkaloid natural products[1] and a cornerstone of synthetic chemistry featuring in biologically active molecules in agrochemistry[2] and medicinal chemistry, where approximately 60% of all FDA approved drugs incorporate at least one *N*-heterocycle.[3] The result of incorporating azetidines imparts myriad desirable properties including improved stability to oxidative metabolism,[4] improved solubility[5] and structural rigidity.[6] In spite of their promise, azetidines are currently an underutilised scaffold in drug design accounting for only 6 approved drugs and this is as a direct consequence of the limitations in established methods for their synthesis.[7]

The ideal reaction to synthesize azetidines would be to take feedstock alkenes with modular, synthesisable imines and directly couple them together *via* an intermolecular [2+2] photocyclization, known as the aza Paternò-Buchi reaction, allowing for a direct and efficient method to synthesise azetidines via the use of 2 equally complex coupling partners.[8] The aza-Paternò-Büchi reaction remains under-developed due to the stringent structural and physical requirements for the imine substrate. Here we describe a more direct and challenging approach to this problem and design an acyclic aldimine that can be rapidly accessed from commercial starting materials, which upon excitation to the triplet state, undergoes the desired intermolecular addition into an unactivated alkene and subsequently forms a broad range useful azetidine products.

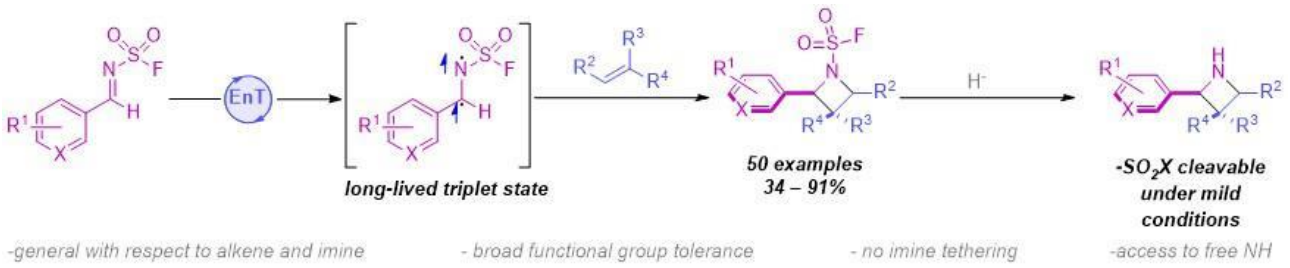

Figure 1.

References

[1] J. A. Joule, in *Adv. Heterocycl. Chem., Vol. 119* (Eds.: E. F. V. Scriven, C. A. Ramsden), Academic Press, 2016, 81-106.
[2] C. Lamberth, *Pest Manag. Sci.* **2013**, *69*, 1106-1114.
[3] E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257-10274.
[4] P. V. Fish, A. D. Brown, E. Evrard, L. R. Roberts, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1871-1875.
[5] A. Brown, T. B. Brown, A. Calabrese, D. Ellis, N. Puhalo, M. Ralph, L. Watson, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 516-520.
[6] M. R. Bauer, P. Di Fruscia, S. C. C. Lucas, I. N. Michaelides, J. E. Nelson, R. I. Storer, B. C. Whitehurst, *RSC Med. Chem.* **2021**, *12*, 448-471.
[7] D. R. Parmar, J. Y. Soni, R. Guduru, R. H. Rayani, R. V. Kusurkar, A. G. Vala, *Arch. Pharm.* **2021**, *354*, 2100062.
[8] A. D. Richardson, M. R. Becker, C. S. Schindler, *Chem. Sci.* **2020**, *11*, 7553-7561.

Mild redox reactions for switching functions of molecules

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Mild redox processes are frequently observed as a fundamental reaction in biological metabolism. The reactions between hydroquinone/quinone and disulfide/dithiol are known as representative ones among them. Recently we found a new fluorescence dye based on sulfur-substituted hydroquinone dimer, which showed nice blue fluorescence on irradiation by UV light.[1] We have developed a new bio-imaging material using this new dye.[2] The fluorescence of 2-sulfanylhydroquinone dimer **1** is sensitive to the substituents of the four phenolic hydroxyl groups. For example, the photoluminescence was active as long as less than two hydroxyl groups was acylated.[3] During the course of our investigation, we thought that it would be useful to detect chemical or physical events if the compound changed its properties responding to the mild redox conditions. In this presentation, we will show our recent examples of 2-sulfanylhydroquinone dimer derivatives that would be potential useful for sensing or responding to the redox conditions.

At first, we explored selective removal of the *O*-methyl groups in tetramethyl derivative of **1** in order to enhance the utility of the compound, and successfully developed selective preparation of mono-protected derivative **2**, which is photoluminescence active. Oxidative treatment of **2** quantitatively converted to the corresponding monoquinone **3**, which was fluorescence inert. Reductive treatment of **3** resulted in immediate formation of **2**, and we observed quick resuming of fluorescence. Thus, monoquinone **3** was potentially useful as a sensor of reductive atmosphere.[4]

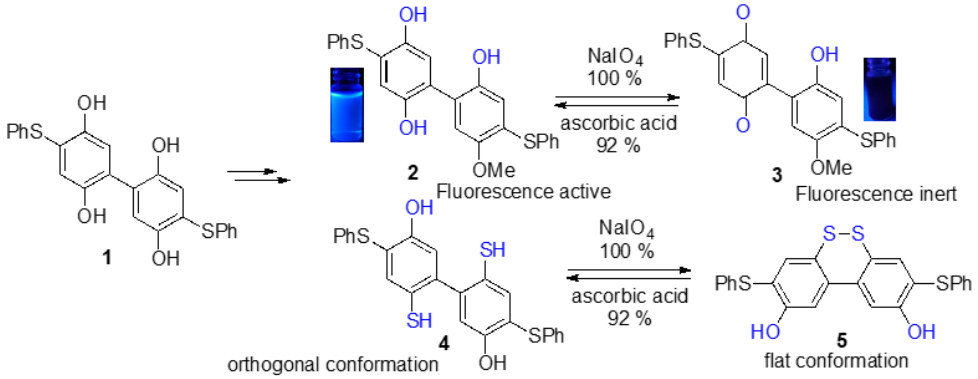

Figure 1. Modification of compound **1** to monoquinone **3** and dithiin **5**.

We next examined the conversion of the two phenolic hydroxyl groups to sulfur groups. Dithiol **4** and dithiin **5** were readily prepared using Newman-Kwart rearrangement and following oxidation. Interestingly the two aromatic units located almost flat conformation in dithiin **5**, while they twisted orthogonally in dithiol **4**. Thus, the dithiol/dithiin conversion is a promising new molecular switch based on conformational change, and we are currently examining to develop a functional molecule using this unit. We are investigating redox between quinone/hydroquinone that is also useful to change solubility of ionic liquids, which is going to be discussed in the presentation

References

[1] A. Kamimura, T. Nokubi, R. Watanabe, M. Ishikawa, K. Nasu, H. Uno, M. Sumimoto, *J. Org. Chem.* **2014***, 79,* 1068 - 1083.

[2] A. Kamimura, H. Umemoto, T. Kawamoto, T. Honda, *ACS Omega* **2021**, *6*, 9254-9262.

[3] A. Kamimura, S. Sakamoto, H. Umemoto, T. Kawamoto, M. Sumimoto, *Chem. Eur. J.* **2019**, *25*, 14081 – 14088.

[4] A. Kamimura, K. Abe, T. Kawamoto, *Arkivoc* **2024**, (2) 202312086.

Visible-Light-Induced Difunctionalisations of Alkynes with Arylsulfinates

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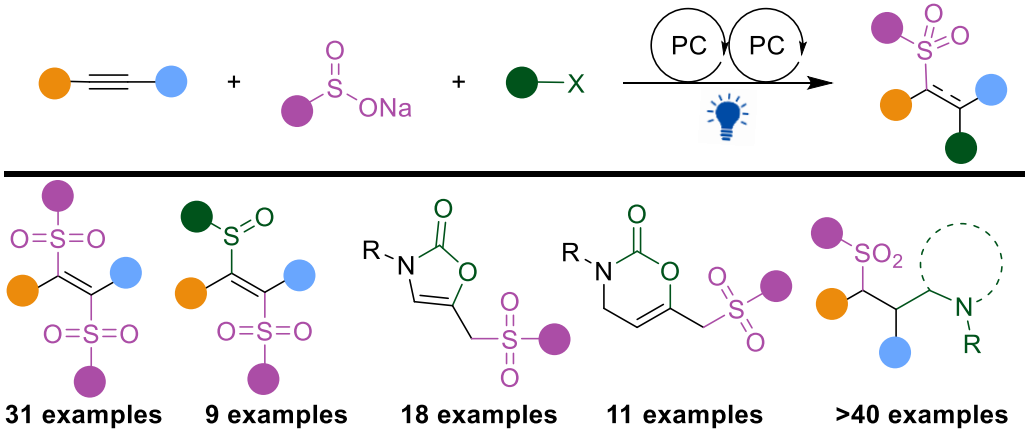
Organosulfones are an important class of organosulfur molecules and versatile synthons in organic chemistry.[1] Due to their importance in various fields, many synthetic strategies have been developed to synthesise sulfone-containing molecules.[2] Among them, radical sulfonylation is one of the most efficient approaches to access functionalized sulfones with high step- and atom-economy.[3] Recently, visible light-promoted reactions have played a promising role in organic synthesis because of demonstrated complex bond constructions under mild reaction conditions and visible light is environmentally benign.[4] In this context, we report on the radical difunctionalisation of alkynes under ambient conditions to access highly functionalised sulfones. We will present photochemical conditions and mechanistic investigations for (1) iodine-mediated tuneable disulfonylation of alkynes, (2) sustainable carboxylative sulfonylation of (homo)propargylic amines with CO_2, and (3) efficient metal-free three-component carbosulfonylation of alkynes with arylsulfinates.[5] We have also applied our carbosulfonylation method to the synthesis of sedum alkaloids.



Scheme 1. Difunctionalisation of alkynes with arylsulfinates.

References

[1] a) T. M. Monos, R. C. McAtee, C. R. J. Stephenson, *Science,* **2018**, *361*, 1369 – 1373; b) D. Kaiser, I. Klose, R. Oost, J. Neuhaus, N. Maulide, *Chem. Rev.,* **2019**, *119*, 8701 – 8780.
[2] S. P. Blum, K. Hofman, G. Manolikakes, S. R. Waldvogel, *Chem. Commun.,* **2021**, *57*, 8236 – 8249.
[3] a) P. J. Sarver, N. B. Bissonnette, D. W. C. MacMillan, *J. Am. Chem. Soc.,* **2021**, *143*, 9737 – 9743; b) K. Hofman, N.-W. Liu, G. Manolikakes, *Chem. – Eur. J.,* **2018**, *24*, 11852 – 11863.
[4] a) A. R. Nathan, D. A. Nicewicz, *Chem. Rev.,* **2016**, *116*, 10075 – 10166; b) G. E. M. Crisenza, P. Melchiorre, *Nat. Commun.,* **2020**, *11*, 803.
[5] a) M. Bhargava Reddy, E. M. McGarrigle, *Chem. Commun.,* **2023**, *59*, 7767 – 7770; b) M. Bhargava Reddy, E. M. McGarrigle, *Chem. Commun.,* **2023**, *59*, 13711 – 13714; c) M. Bhargava Reddy, V. E. Becker, E. M. McGarrigle, *submitted for publication*.

Diverse Courses of Oxidative Sulfonamidation of Unsaturated Compounds

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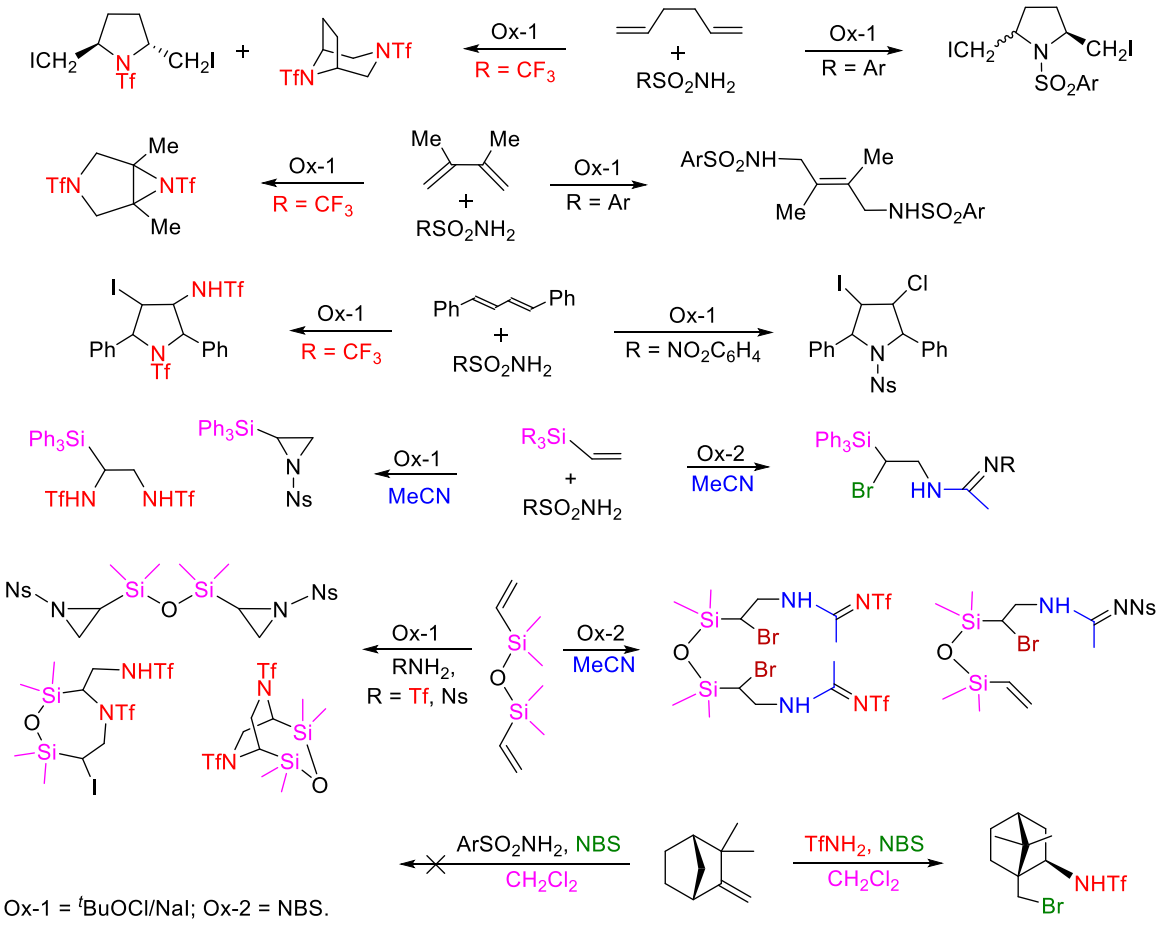
Oxidative sulfonamidation of alkenes is a convenient route to N-sulfonyl amidines and various heterocycles on their basis. Remarkably, the reaction is highly sensitive to many factors, such as the structure of the substrate, the solvent and the oxidant, and may follow different courses for fluorinated (triflamide) and non-fluorinated (arenesulfonamides) reagents. The substrates allowing to compare the reactivity of sulfonamides as the reagents are various dienes, vinylsilanes, and camphene. Most vivid examples showing the difference between the reactivity of triflamide and arenesulfonamides in the presence of different oxidants are given in Scheme 1.



Scheme 1. The diversity of reactivity of triflamide and arenesulfonamides in oxidative sulfonamidation.

References

[1] M. Yu. Moskalik, V. V. Astakhova, B. A. Shainyan, *Pure Appl. Chem.*, **2020**, *92*, 123–150.
[2] M. Yu. Moskalik, V. V. Astakhova, B. A. Shainyan, RSC Advances, **2020**, *10*, 40514–40528.
[3] V. V. Astakhova, M. Yu. Moskalik, B. A. Shainyan, *J. Organomet. Chem.*, **2021**, *951*, 122131.
[4] A. Ganin, M. Moskalik, I. Garagan, V. Astakhova, B. Shainyan, *Molecules*, **2022**, *213*, 6910.

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Photocatalytic Ring Expansion Of Alkenyl Sulfonium Salts In Flow

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Sulfonium salts, organic compounds with a positively charged sulfur atom which makes them prone to accept electrons, have been used vastly in organic synthesis to create a diversity of organic scaffolds.[1] These compounds have attracted the attention of chemist to use them in photocatalyzed reactions *via* single-electron transfer, where they can act as radical precursors of either stabilized or non-stabilized radicals.[2] Furthermore, the cationic nature of vinyl sulfoniums salts can also facilitate the reaction with radicals *via* Giese type additions, leading to interesting and recently new transformations.[3]

Considering this background, we combine the two reactivities explained above to obtain cyclic sulfides with different ring sizes. First, the reduction of the sulfonium salt with a suitable organophotocatalyst leads to the formation of a primary radical. This radical further reacts *via* Giese addition with the double bond, leading to the product in which the ring size was increased by two carbon atoms. This methodology has been successfully implemented into a flow system with a 10-minute residence time.

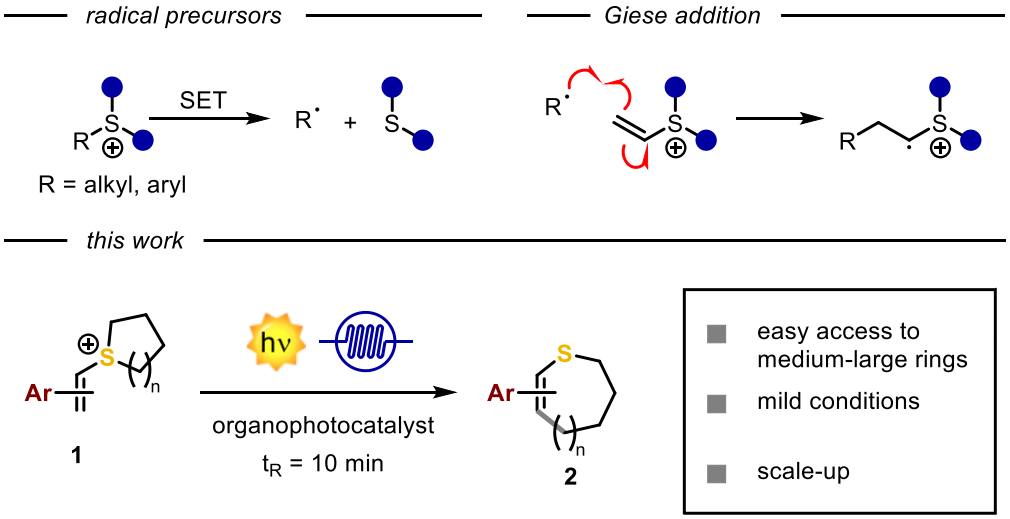

Figure 1. Sulfonium salts as radical precursors and Giese type acceptors (top) and photocatalytic ring expansion of sulfonium salts in flow (bottom).

References

[1] S. I. Kozhushkov , M. Alcarazo, *Eur. J. Inorg. Chem.* **2020**, 2486-2500.
[2] Á. Péter, G. J. P. Perry, D. J. Procter, *Adv. Synth. Catal.* **2020**, *362*, 2135–2142.
[3] S. Paul, D. Filippini, M. Silvi Silvi *J. Am. Chem. Soc.* **2023**, *145*, 2773−2778.
[5] A. Vega-Peñaloza, J. Mateos, X. Companyó, M. Escudero-Casao, L. Dell'Amico, *Angew. Chem. Int. Ed.* **2021**, *60*, 1082–1097.

Sulfur functionalization as a strategy to improve the bioactivity of natural phenolic compounds

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Nowadays, molecular scaffold manipulation of natural phenols is a currently pursued approach to boost or modulate their antioxidant properties and bioactivity.[1] In particular, conjugation of naturally occurring catechol compounds with biological thiols is a versatile and facile entry to a broad range of bioinspired multifunctional compounds for diverse applications in biomedicine and materials science. Noticeable examples of compounds with potentiated antioxidant activities are the human metabolite 5-*S*-cysteinyldopa, with high iron-induced lipid peroxidation inhibitory activity, 5-S-glutathionylpiceatannol a most effective inhibitor of nitrosation processes, and 5-*S*-lipoylhydroxytyrosol, and its polysulfides that, as will be presented, proved valuable oxidative-stress protective agents in various cellular models.[2] A distinguishing, yet puzzling, feature of the thiol-*o*-quinone reaction is the anomalous 1,6-type regiochemistry of the coupling reaction, leading mainly to C-5-linked adducts respect to the usual C-6 conjugates, an issue that has so far eluded intensive investigations. On this basis, to elucidate this regiochemistry, we report herein also a re-examination of the reaction of thiols with 4-methyl-*o*-benzoquinone (4-MBQ), modelling the natural DOPAquinone, by an integrated experimental and computational approach.[3] All the results have provided evidence that the addition of glutathione, cysteine, or benzenethiol to 4-MBQ, proceeds by a free radical chain mechanism triggered by the addition of thiyl radicals to the *o*-quinone that would thus open new vistas into a range of reactions and processes of biological relevance.[3]

Another strategy to manipulate phenolic compounds that is receiving considerable attention is sulfation. In this frame, herein we report the results of recent studies focused on the preparation and structural analysis (NMR, elemental analysis, MALDI-MS) of different sulfated oligomers of tyrosol obtained by the use of sulfur trioxide triethylamine complex and the evaluation of their antioxidant activity by chemical assays as well as of their anticoagulant activity both *in vitro* in human plasma by conventional clotting assays, and by the venous thrombosis model in mice.[4] In addition, the efficacy of the sulfated polymers as antifoulants with proven activity against anti-settlement of mussel (*Mytilus galloprovincialis*) plantigrade post-larvae as well as non-target marine organisms like Artemia Salina will be presented.[5]

References

[1] M.L. Alfieri, L. Panzella, R. Amorati, A. Cariola, L. Valgimigli, A. Napolitano, *Biomolecules,* **2022**, *1*, 1-24.
[2] A. Officioso, L. Panzella, F. Tortora, M.L. Alfieri, A. Napolitano, C. Manna, *Oxid. Med. Cell. Longev.*, **2018**, *2018*, 1-9.
[3] M.L. Alfieri, A. Cariola, L. Panzella, A. Napolitano, M. d'Ischia, L. Valgimigli, O. Crescenzi, *J. Org. Chem.,* **2022**, *87*, 4580-4589.
[4] M.L. Alfieri, L. Panzella, B. Duarte, S. Gonçalves-Monteiro, F. Marques, M. Morato, M. Correia-da-Silva, L. Verotta, A. Napolitano, *Biomacromolecules,* **2021**, *2*, 399-409.
[5] M.L. Alfieri, C. Gonçalves, J. Reis Almeida, M. Correia-da-Silva, L. Panzella, A. Napolitano, *Eur. Polym. J.,* **2024**, *208*, 112855.

Insights into the Cytotoxicity of Garlic-Related Trisulfides

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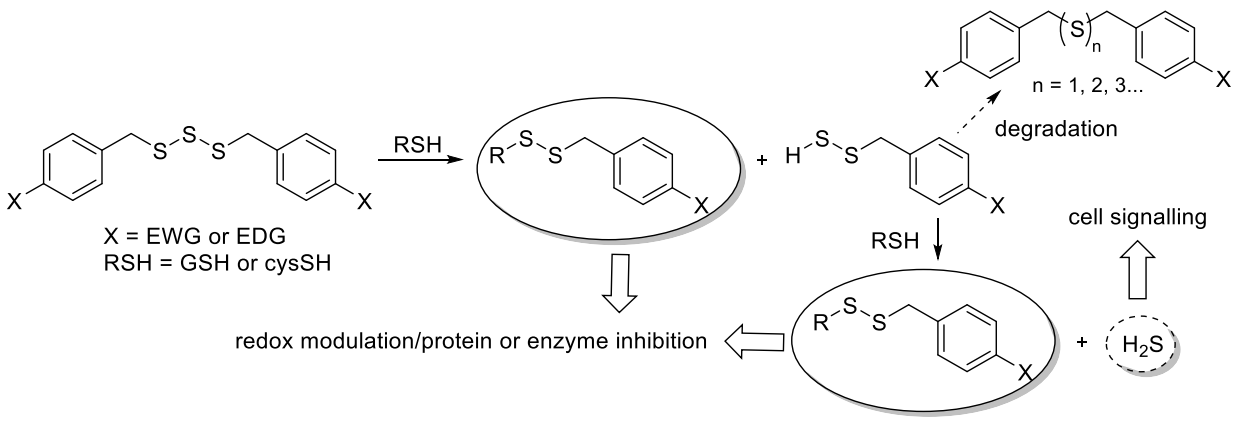
Garlic is a spice and medicinal plant that has been used since ancient times to promote health and fight disease. There are a number of small bioactive organosulfur compounds (OSC's) in garlic, with different sulfur-containing functional groups. These compounds are proposed to act on a molecular level by undergoing thiolysis exchange with a biological thiol, such as a cysteine residue on a protein. Many of the garlic OSCs, including the small thiophiles diallyl trisulfide (DATS) and ajoene, are natural anti-cancer agents. We have developed a synthetic route to access ajoene and unsymmetrical trisulfide derivatives,[1,2] which has enabled the synthesis of fluorescently tagged analogues as well libraries for studying structure-activity effects. Using tagged analogues, we have found that both ajoenes and trisulfides accumulate within the endoplasmic reticulum of cancer cells, where they interfere with protein folding and cause ER stress.[3] We have also found that a biotin-labelled ajoene causes widespread *S*-thiolation within the proteome of MDA-MB-231 breast cancer cells, where it targets functional and signalling pathways essential to the biology of cancer cells.[4] Synthesis and biological evaluation of trisulfide analogues, have revealed that they act on a number of pathways in cancer cells (Scheme 1). On a molecular level, it is proposed that the perthiol stability, which in turn is governed by its pK_a, determines the extent of cytotoxicity of the trisulfide.



Scheme 1. Cytotoxicity hypothesis of garlic-related trisulfides in cancer cells. Following *S*-thiolysis with a biological thiol within the cancer cell, a garlic-related trisulfide may produce a mixed disulfide leading to protein or enzyme inhibition. The byproduct perthiol appears to be key to the extent of cytotoxicity with EDG's enhancing perthiol stability which drives enhanced cancer cell cytotoxicity.

References

[1] Kaschula, C. H.; Hunter, R.; Stellenboom, N.; Caira, M. R.; Winks, S.; Ogunleye, T.; Richards, P.; Cotton, J.; Zilbeyaz, K.; Wang, Y.; Siyo, V.; Ngarande, E.; Parker, M. I. *Eur. J. Med. Chem.* **2012**, *50*, 236.
[2] Ali, D.; Hunter, R.; Kaschula, C. H.; De Doncker, S.; Rees-Jones, S. C. M. *J. Org. Chem.* **2019**, *84*, 2862.
[3] Kaschula, C. H.; Hunter, R.; Cotton, J.; Tuveri, R.; Ngarande, E.; Dzobo, K.; Schäfer, G.; Siyo, V.; Lang, D.; Kusza, D. A.; Davies, B.; Katz, A. A.; Parker, M. I. *Mol. Carcinog.* **2016**, *55*, 1213.
[4] Kusza, D. A.; Hunter, R.; Schäfer, G.; Smith, M.; Katz, A. A.; Kaschula, C. H. *J. Agric. Food Chem.* **2022**, *70*, 14679.

Vinyl sulfonimidamides as potential bioisosteres of acrylamides

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Covalent inhibitors have gained rising interest in medicinal and agricochemical industries, due to their high drug potency, long residence time and decrease drug resistance rate[1]. Acrylamides, being one of the most popularly used motifs, exhibits a wide range of biological activities[2-4] and has been used in over 10 approved drugs and 50 inhibitors[5].

Recently, Nomura etal. presented a cysteine active vinyl sulfonamide which enabled the degradation of the proteins BRD4, CDK4, BTK and more[6], which suggested vinyl sulfonamides as a potential bioisostere of acrylamides. On the other hand, sulfonimidamides, the aza-analogues of sulfonamides, possess several advantages over acrylamides and sulfonamides, including having a chiral center, an extra functional group for tuning reactivity and physiochemical properties. We postulated that vinyl sulfonimidamides could be potential bioisosteres of acrylamide, which could show a wide range of reactivities just by changing the functional group on its imidic nitrogen atom. Herein, we report the synthesis of various functionalized vinyl sulfonimidamides, and their reactivities with glutathione (GSH). Kinetic studies achieved using NMR spectroscopy showed that sulfonimidamies exhibit wide range of reactivities that are easily modified by small structural changes.

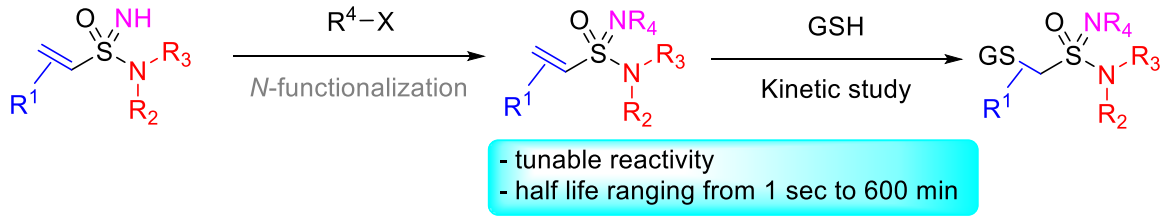

Figure 1. Synthesis and kinetic studies of vinyl sulfonimidamides with glutathione (GSH).

References

[1] J. Singh., R. C. Petter, T. A. Baillie, A. Whitty, *Nat. Rev. Drug Discov*, **2011**, *10*, 307 – 317.
[2] W. Zhou, H. Li, C. Xia, X. Zheng, W. Hu, *Bioorg. Med. Chem. Lett*. **2009**, *19*, 1861 – 1865.
[3] C. Nitsche, C. Steuer, C.D. Klein, *Bioorganic Med. Chem. J*, **2011**, *19*, 7318 – 7337.
[4] J. Fu, K. Cheng, Z. Zhang, R. Fang, H. Zhu, *Eur. J. Med. Chem*. **2010**, *45*, 2638 – 2643.
[5] H. Du, J. Gao, G. Weng, J. Ding, X. Chai, J. Pang, Y. Kang, D. Li, D. Cao, T. Hou, *Nucleic acids Res*, **2021**, *49*, 1122 – 1129.
[6] M. Lim, T. D. Cong, L. M. Orr, E. S. Toriki, A. C. Kile, J. W. Papatzimas, E. Lee, D. K. Nomura, *Acs Cent. Sci.* **2024**, ASAP. DOI: 10.1021/acscentsci.4c00286.
[7] P. Chinthakindi, T. Naicker, N. Thota, T. Govender, H. G. Kruger, P.I. Arvidsson, *Angew. Chem. Int. Ed*. **2017**, *56*, 4100 – 4109.

Metal-Free Thiolato Ligands for use as Photosensitizers: [FeFe]-Hydrogenase Mimic Complexes for Photocatalytic H_2 Production

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Photocatalytic H_2 production has attracted much attention due to its promise as a source of clean and green solar fuels. However, most artificial examples for H_2 production frequently involve rare transition metals either for the photosensitiser (**PS**), the catalytic active centre (**CAT**) or both. Conversely, [FeFe]-hydrogenases consisting of a thiolato coordinated cluster ([Fe_2S_2] cluster) as a **CAT** catalyses H_2 production very efficiently without noble metals[1]. Hence, applying [Fe_2S_2] complexes for photocatalytic H_2 production has seen a remarkable increase in interest[2]. In some examples, thiolato ligands have been modified as photosensitisers to build molecular dyads (**PS-CAT**) to overcome slow diffusion-controlled electron transfer processes between **PS** and **CAT**. Those reported **PS-CAT** molecules frequently consist of **PS** as a bidentate thiolato ligand (Figure 1, our previous example). Whereas, monodentate thiolato ligands can introduce two **PS**s in one molecule which potentially enhances the electron transfer (ET) from **PS** to **CAT**, however, to our knowledge, only one dyad working under UV irradiation has been reported[3].

Hence, we will report the new **PS-CAT** bearing two organic **PS**s designed as a donor-bridge-acceptor structure with the aim of efficient ET from **PS** to **CAT**. Using our facilitated synthetic method[4], **PS-CAT** was obtained in 69% yield by reaction of the corresponding thiol with $Fe_3(CO)_{12}$. The photocatalytic H_2 production activities of **PS-CAT** under 455 nm irradiations were tested and the turnover number reached 404 under optimised conditions. We are currently investigating the photophysical and photochemical properties of **PS-CAT** through (time-resolved) luminescence and ns-transient absorption spectroscopy and (scalar-relativistic) TD-DFT.

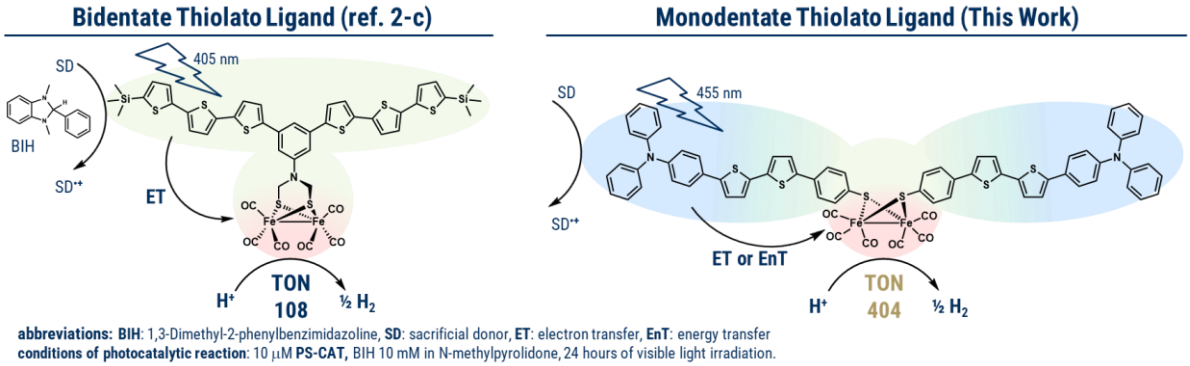

Figure 1. Molecular structures and photocatalytic activities (TON) of **PS-CAT**s.

References

[1] W. Lubitz, H. Ogata, O. Rudiger, E. Reijerse, *Chem. Rev*. **2014**, *114*, 4081 – 4148. [2] a) S. Ott, *et al*. *Coord. Chem. Rev*. **2021**, *448*, 214172 – 214206. b) W. Weigand, *et al*. *Angew. Chem. Int. Ed. Engl*. **2022**, *61*, e202202079; c) W. Weigand, *et al*. *ChemCatChem* **2024** DOI: 10.1002/cctc.202400247. [3] J.-H. Hou, *et al*. *Chem. Pap.* **2017**, *71*, 617 – 625. [4] W. Weigand, *et al*. *Dalton Trans.* **2023**, 52, 7421 – 7428.

OC-18

The role of selenium-sulfur bond in the biological activity of the selenorganic compounds: the case study of Ebselen®

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Sulfur and selenium are very representative as functional groups in different biomolecules which participates in the redox pattern of the cells.[1] The most representative examples are the cysteine residues involved in the thiol/disulfide-exchange reactions, essential in maintaining the cellular redox balance and keeping proteins in their active reduced state, and the selenocysteine residues of different selenoenzymes such as glutathione peroxidases (Gpx), iodothyronine deiodinases (DIO), thioredoxin reductases (TrxR), and methionine sulfoxide reductases (Msrs).[2] In a biological environment, organoselenium compounds can act as a redox modulator reacting as a nucleophile towards reactive oxygen species (ROS), or as an electrophile, towards reductive free thiols.[3] Both these pathways are strongly affected by the nature of the Se-S bond that can be formed between the selenium species and glutathione (GSH) or enzymatic free cysteines. As an example, there are several papers in which the antiviral activity against the SARS-CoV 2 virus is claimed as a direct interaction between the mild electrophilic selenium of Ebselen® with the cysteine 145 of the Main Protease (Mpro).[4] In a recently updated preprint, we demonstrated that in the presence of glutathione (GSH) Ebselen® cannot be the species that directly interact with the active cysteine because of a fast interaction of a glutathionated adduct.[5] To elucidate the mechanism biophysical and spectroscopic techniques, such as nanoDSF assay and waterLOGSY NMR, were applied.

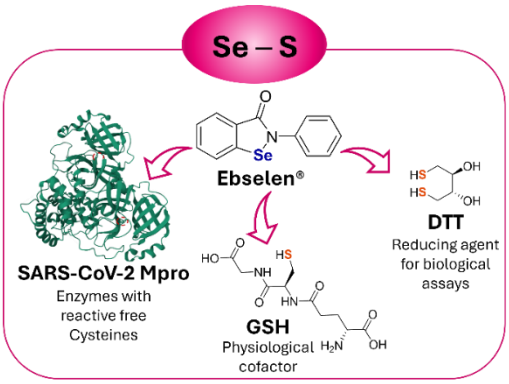

Figure 1. Study of the reactivity between Ebselen® and different thiols.

References

[1] C. Jacob et al., *Angew. Chem. Int. Ed.*, **2003**, 42, 4742-4758.
[2] H. J. Reich and R. J. Hondal, *ACS Chem. Biol.*, **2016**, 11, 4, 821–841
[3] C. Santi; F. Marini; E. J. Lenardão in Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments; (Eds.: V. K. Jain, K. I. Priyadarsini); The Royal Society of Chemistry, **2017** pp. 35 - 76.
[4] a) Z. Jin et al. *Nature,* **2020**, 582, 289–293. b) K. Amporndanai et al. *Nature Communications*, **2021**, 12, 3061.
[5] L. Sancineto et al. ChemRxiv. **2024**; doi:10.26434/chemrxiv-2024-0jxr0-v2

Cysteine Thioaldehydes: Photolytic Generation and Reactivity

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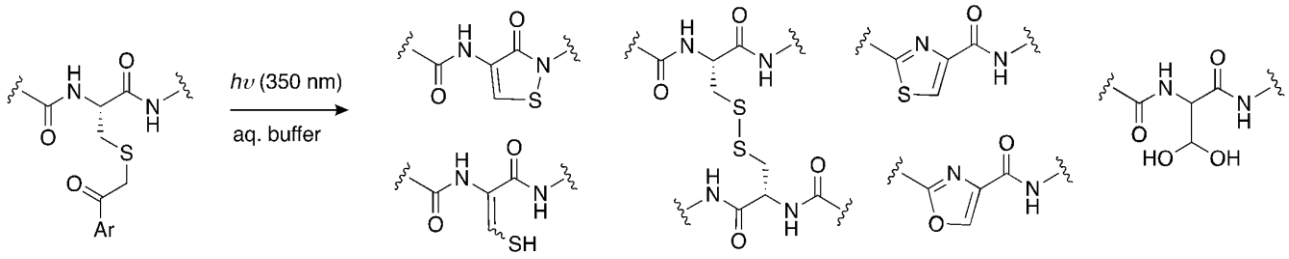
Cysteine thioaldehydes are reactive putative intermediates in penicillin and lanthipeptide biosynthesis, and in formylglycine generating enzyme (FGE) catalysed activation of sulfatases. In FGE catalysis, a superoxide-ligated Fe centre transforms a cysteine thiol into a thioaldehyde, which is proposed to undergo subsequent hydrolysis to the aldehyde.[1] Experimental study of thioaldehydes is challenging owing to their instability, but Norrish Type-II photolysis of phenacylsulfide derivatives is a convenient method for generating these species for further study and synthetic utility.[2] Inspired by the work of Lowe, who in the 1970s used this photolysis reaction to effect chemical cysteine-to-serine mutation within the active site of papain,[3] we explored the nature and reactivity of cysteine thioaldehydes by using NMR spectroscopy and mass spectrometry.

We found that phenacylsulfides bearing electron-withdrawing groups on the aromatic ring engender substrates with high propensity to photolyse through the desired Norrish Type II pathway while minimizing the ®-scission pathway, which leads to disulfides and oxidising enol radicals. For simple cysteine-containing peptides, S-alkylation with the requisite phenacylbromide (3,5-bis(trifluoromethyl) or 4-*N*,*N*,*N*-trimethylammonium) followed by photolysis in aqueous buffer leads to a mixture of cysteine enethiolate, isothiazolone and disulfide. The cysteine thioaldehyde intermediate undergoes rapid enolization to the enethiol (pK_a 4.3), which exists as the enethiolate at pH 7.4, where it is stable. Owing to the presence of enol radicals, which are generated through the competing ®-scission pathway, some of the enethiolate undergoes oxidation to the cysteine isothiazolone. At low pH values, the enethiol undergoes facile cyclocondensation into the cysteine thiazole derivative. Upon photolysis of cysteine-containing 15-mer peptides of the consensus sequence found in sulfatases, the formylglycine residue, existing as the gem-diol, was observed. The transformation was not observed for other shorter peptides. This result suggests that peptide secondary structure is important for favouring hydrolysis of the thioaldehyde over irreversible tautomerisation to the enethiol and amide backbone participation (Scheme 1).



Scheme 1. Product distribution of cysteine phenacylsulfide photolysis (*dependent on sequence*)

References

[1] M. J. Appel et al. *Proc. Nat. Acad. Sci.* **2019**, *116*, 5370 – 5375
[2] S. J. Collier, in *Science of Synthesis*, 27 (Eds: A. Padwa, D. Bellus), Thieme, Stuttgart, **2004**, pp. 177– 214
[3] P. I. Clark, G. Lowe, *Eur. J. Biochem*. **1978**, *84*, 293

OC-20

Uncatalyzed [3+2] annulation of 2-alkylenecyclobutanones with thiourea derivatives for the construction of cyclobuta-fused- imidazolidine-2-thiones and -thiazolidine-2-imines

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The development of novel methods for the selective preparation and functionalization of substituted cyclobutanes is of great utility and has received significant attention in organic synthesis.[1] In connection with our interest in strain-driven organic reactions for the synthesis of carbo- and heterocyclic skeletons,[2] we have successfully developed, a method for the synthesis of several cyclobuta-fused imidazolidine-2-thiones and -thiazolidin-2-imines in good to high yields under catalyst-free conditions. It involves an (3+2) annulation reaction starting from 2-alkylenecyclobutanones and thiourea derivatives (Figure 1).

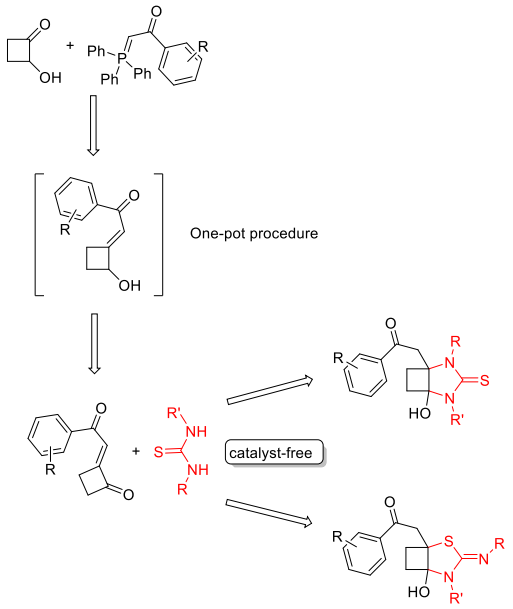

Figure 1. General scheme for the synthesis of cyclobuta-fused imidazolidine-2-thiones and -thiazolidin-2-imines.

References

[1] (a) J. C. Namsylo, D. E. Kaufmann, *Chem. Rev.,* **2003**, *103,* 1485-1538. (b) E. Lee-Ruff, G. Mladenova, *Chem. Rev.*, **2003**, *103,* 1449-1484. (c) N.-Y. Fu, S.-H. Chan, *in The Chemistry of Cyclobutanes*, eds. Z. Rappoport, J. F. Liebman, *Wiley, Chichester*, **2005**, 357–440. (d) Yang, Q. Jia, S. S. Song, X. Huang, *Nat. Prod. Rep.*, **2023,** *40,* 1094–1129. (e) M. R. van der Kolk, M. A. C. H. Janssen, F. P. J. T. Rutjes, D. Blanco-Ania, *ChemMedChem,* **2022,** *17* e202200020. (f) J. Li, K. Gao, M. Ming Bian, H. Ding, *Org. Chem. Front.*, **2020**, *7*, 136–154.
[2] (a) F. Cuccu, L. Serusi, A. Luridiana, F. Secci, P. Caboni, D. J. Aitken, A. Frongia, *Org. Lett.,* **2019**, *21*, 7755–7758; (b) L. Ghisu, N. Melis, L. Serusi, A. Luridiana, F. Soddu, F. Secci, P. Caboni, R. Guillot, D. J. Aitken, A. Frongia, *Org. Biomol. Chem*. **2019**, *17*, 6143-6147; (c) L. Serusi, F. Soddu, F. Cuccu, G. Peretti, A. Luridiana, F. Secci, P. Caboni, D. J. Aitken, A. Frongia, *Adv. Synth. Catal*. **2020**, *362*, 4159–4163; (d) V. Marras, P. Caboni, F. Secci, R. Guillot, D. J. Aitken, A. Frongia, *Org. Biomol. Chem.,* **2021**, *19*, 8912–8916. (e) S. Barranco, F. Cuccu, D. Liu, S. Robin, R. Guillot, F. Secci, V. Brenner, M. Mons, P. Caboni, D. J. Aitken, A. Frongia, *Eur. J. Org. Chem*. **2023**, e202300183.

In Vitro and *In Silico* Analysis of Neuroprotective Effects of Sulfur-Containing Dihydrobenzofurans

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Oxidative stress results from an imbalance between reactive species production and antioxidant defenses, increasing the brain's susceptibility to neurodegenerative and psychiatric diseases.[1] Changes in the expression or activity of neurotransmitter metabolism enzymes, such as monoamine oxidases (MAO), are also associated with mental disorders, including depression.[2] This study investigated the MAO-A inhibitory potential of five 2,3-sulfur-dihydrobenzofurans (2,3-SDHBF) and one 2,3-tellurium-dihydrobenzofurans (2,3-TeDHBF) through *in vitro* and *in silico* tests (Figure 1a). Screening of cerebral MAO-A activity in mouse brain showed inhibitory activity for compounds **2**, **4**, **5**, and **6**. Among sulfur compounds, compound **2** demonstrated superior scores in docking studies, yielding a value of -9.9 kcal/mol. In concentration-response curves, compound **2** (with S) inhibited MAO-A at concentration equal 25 µM. In summary, this study demonstrated the cerebral MAO-A inhibition properties of 2,3-DHBF, presenting potential as neuroprotective candidates.

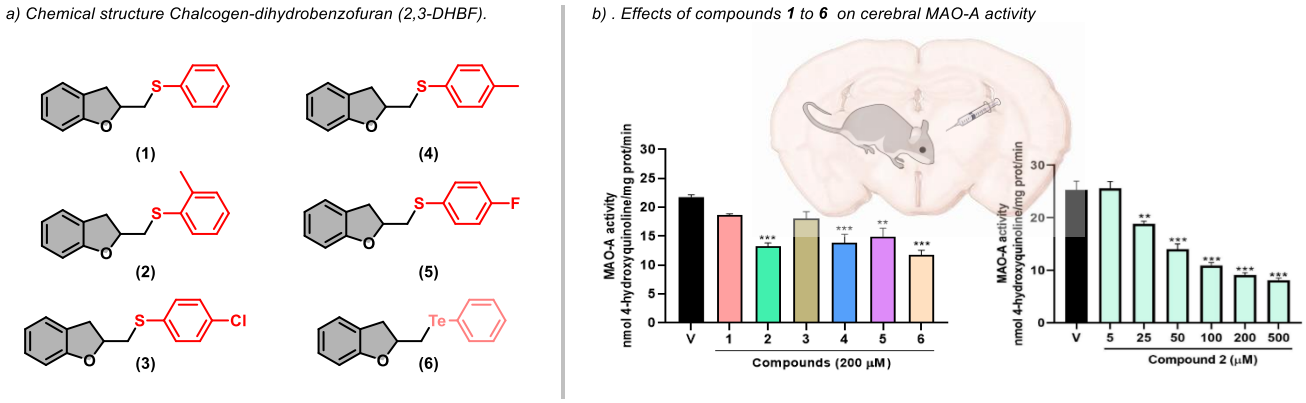

Figure 1. Sulfur and Telurium-Containing Dihydrobenzofurans and neuroprotective effects.

References

[1] V. Nascimento, *et al*., *Chem Asian J*, **2023**, *18*, e202300586.
[2] J. Grzelczyk, *et al. Food Chem,* **2021**, 348, 129108.

2-Azido Sulfoximines as Building Blocks for Benzothiadiazine Oxides in Metal-Catalysed Reactions

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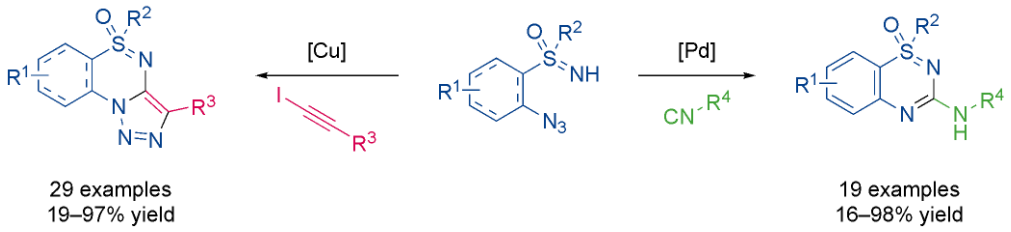
Sulfur- and nitrogen-containing heterocycles belong to privileged classes of compounds with numerous applications in medicinal chemistry and crop protection.[1] In recent years, sulfoximines (the mono-aza analogue of sulfones), have been of profound interest to medicinal chemists as bioisosteres for sulfones and sulfonamides.[2] In particular their corresponding heterocycles such as benzothiadiazine oxides have extensively been investigated for their biological activities.[3] Consequently, new synthetic methods towards sulfoximidoyl-containing heterocycles are of great interest.

Based on our work on sulfoximines and their corresponding heterocycles, we became interested in studying 2-azido sulfoximines as low-molecular building blocks for benzothiadiazine oxides. In this presentation, the synthesis of 2-azido sulfoximines and their application in metal-catalysed reactions with iodoalkynes[4] and isocyanides[5] (Scheme 1) will be discussed with special attention to mechanistic details.



Scheme 1. Copper- and palladium-catalysed cascade reactions of 2-azido sulfoximines.[4,5]

References

[1] a) J. Jampilek, *Molecules* **2019**, *24*, 3839; b) C. Lamberth, *Pest Manag. Sci.* **2013**, *69*, 1106 – 1114; c) S. Pathania, R. K. Narang, R. K. Rawal, *Eur. J. Med. Chem.* **2019**, *180*, 486 – 508; d) N. N. Makhova, L. I. Belen'kii, G. A. Gazieva, I. L. Dalinger, L. S. Konstantinova, V. V. Kuznetsov, A. N.Kravchenko, M. M. Krayushkin, O. A. Rakitin, A. M. Starosotnikov, L. L. Fershtat, S. A. Shevelev, V. Z. Shirinian, V. N. Yarovenko, *Russ. Chem. Rev.* **2020**, *89*, 55 – 124.
[2] a) U. Lücking, *Angew. Chem. Int. Ed.* **2013**, *52*, 9399 – 9408; b) P. Mäder, L. Kattner, *J. Med. Chem.* **2020**, *63*, 14243 – 14275; c) M. Frings, C. Bolm, A. Blum, C. Gnamm, *Eur. J. Med. Chem.* **2017**, *126*, 225 – 245.
[3] a) P. Stoss, G. Satzinger, *Chem. Ber.* **1976**, *109*, 2097 – 2106; b) Y. Zhou, T. Bertolini, L. Li, US20080292588, **2008**; c) Z. P. Shultz, J. M. Lopchuk, *Adv. Heterocycl. Chem.* **2022**, *138*, 61 – 158.
[4] R. Hommelsheim, S. Bausch, A. Selvakumar, M. M. Amer, K.-N. Truong, K. Rissanen, C. Bolm, *Chem. Eur. J.* **2023**, *29*, e202203729.
[5] R. Hommelsheim, S. Bausch, R. van Nahl, J. S. Ward, K. Rissanen, C. Bolm, *Green Chem.* **2023**, *25*, 3021 – 3026.

OC-23

Sulfur-Containing Organic Compounds for Solar Energy Conversion Technologies: from Molecular Properties to Device Performances

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Conjugated organic compounds with alternating donor-acceptor structures (D-π-A or D-A-D) find extensive application in various classes of devices for solar energy capture and conversion, where they can act as light harvesting materials, fluorescent emitters or charge transporting layers. Introduction of sulfur-containing fragments in the different sections of such compounds is a common strategy that allows to modulate their geometric, spectroscopic and electrochemical properties, or exploit specific interactions with the other device components (Figure 1).

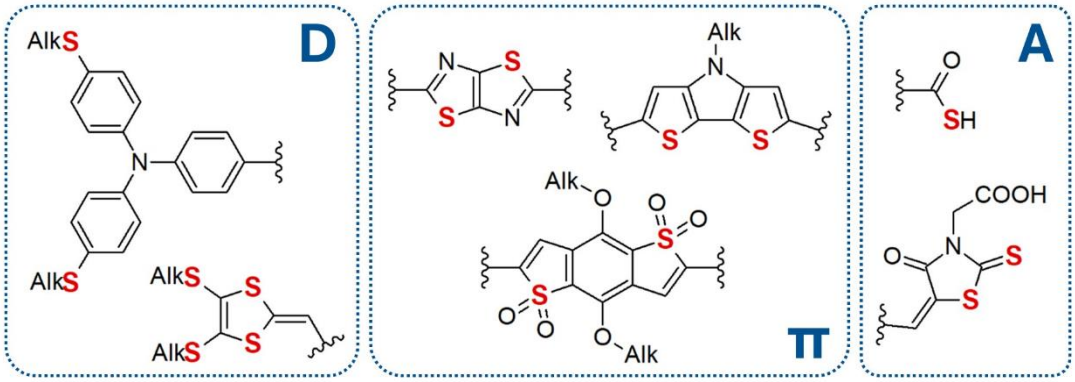

Figure 1. Examples of sulfur-containing fragments found in D-π-A compounds for solar energy conversion.

In this communication, we will present several examples showing the design, synthesis and application of sulfur-containing compounds in different solar conversion technologies, such as photovoltaic cells,[1-3] photo(electro)chemical systems for H_2 production[4] and luminescent solar concentrators,[5] highlighting the effect exerted by its incorporation on the individual properties of the molecules and the corresponding impact on the overall device performances.

References

[1] A. Dessì *et al.*, *Chem. Commun.* **2014**, *50*, 13952-13955.
[2] O. Bettucci *et al.*, *Eur. J. Org. Chem.* **2018**, 812-825.
[3] A. Dessì *et al.*, *Sust. Energy Fuels* **2021**, *5*, 1171-1183.
[4] O. Bettucci *et al.*, *ACS Appl. Energy Mater.* **2019**, *2*, 5600-5612.
[5] M. Bartolini *et al.*, *ACS Appl. Energy Mater*. **2023**, *6*, 4862-4880.

OC-24

Functionalization of CdSe Quantum Dot Films with [FeFe] Hydrogenase Mimics for Light-Driven Hydrogen Evolution

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CdSe quantum dots (QDs) have shown excellent light-harvesting properties, enabling them as well-established photo sensitizers (PS).[1] The functionalization with suitable co-catalysts, such as [FeFe] hydrogenase mimics (CAT) have demonstrated promising activity towards photocatalytic hydrogen generation. The direct bonding of the CAT to the QD surface by covalent linking via carboxylic groups was realized to keep the electron pathways as short as possible, supporting the transfer and accumulation of several needed electrons.[2] Our PS-CAT approach was further immobilized in a thin-film architecture on a glass substrate to overcome the limitations of colloidal stability and disadvantages of thiol ligands while performing hydrogen evolution reactions in aqueous solutions. Our proof-of-concept study achieved turnover numbers in the range of 360−580 (short linkers) and 130−160 (long linkers) and demonstrated the potential of the functionalized thin films.[3]

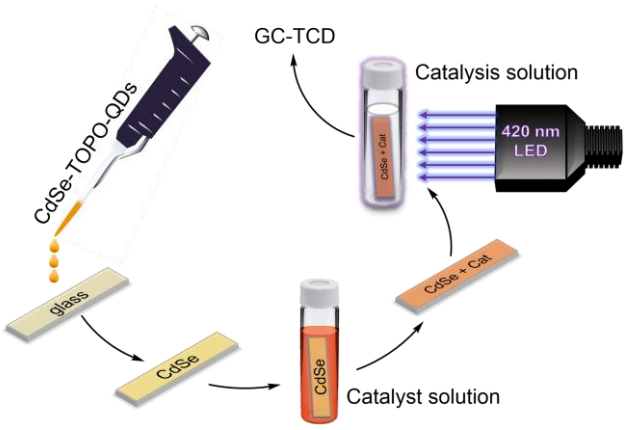

Figure 1. Schematic overview of the functionalization procedure of CdSe TOPO (trioctylphosphin oxide) QDs with [FeFe] hydrogenase mimics (Cat).[3]

References

[1] A. Schleusener, M. Micheel, S. Benndorf, M. Rettenmayr, W. Weigand, M. Wächtler, *J. Phys. Chem. Lett.* **2021**, *12*, 4385 - 4391.
[2] X.-B. Li, C.-H. Tung, L.-Z. Wu, *Nat. Rev. Chem*, **2018**, *2*, 160 - 173.
[3] S. Benndorf, A. Schleusener, R. Müller, M. Micheel, R. Baruah, J. Dellith, A. Undisz, C. Neumann, A. Turchanin, K. Leopold, W. Weigand, M. Wächtler, *ACS Appl. Mater. Interfaces*, **2023**, *15*, 18889 - 18897.

Conformationally-adaptive *thio*-hemicucurbiturils exhibit promiscuous anion binding by induced fit

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The conformational flexibility of single-stranded host molecules allows for more promiscuous host-guest complexation. Here, we show that a unique family of single-stranded anion receptors, *thio*-hemicucurbit[n]urils (*thio*-hCB[n], n = 6,8), which bind various anions *via* multiple hydrogen bonds and dispersion forces, exhibiting induced fit and conformational adaptation.[1] The *thio*-hCBs are readily accessible exclusively and quantitatively *via* template-driven mechanochemical synthesis from cyclic thiourea monomers. The solid-state structures of the various host-guest inclusion complexes reveal that these host molecules comprise a relatively rigid circular skeleton and eight or six rigid flaps that can easily change their tilt angle relative to the equatorial plane to maximize the guest binding interactions.

Competition and titration experiments monitored by ^{1}H and ^{19}F NMR provide additional information on the host-guest behavior and anion binding selectivity. The binding studies confirm that both *thio*-[cycH]-hCB[8] and *thio*-hCB[6] form a 1:1 complex with different anion guests through hydrogen bonding interactions. ITC titrations show that the *thio* analogs of hCB bind anions significantly more strongly than the *oxo* analog by two orders of magnitude, probably due to the higher polarizability of thiourea relative to urea. The anion binding selectivity follows the order of PF_6^- > BF_4^- ≈ ClO_4^- >> TfO^- for the octameric macrocycle. The hexameric macrocycle follows the order of I^- > Cl^- > Br^-.

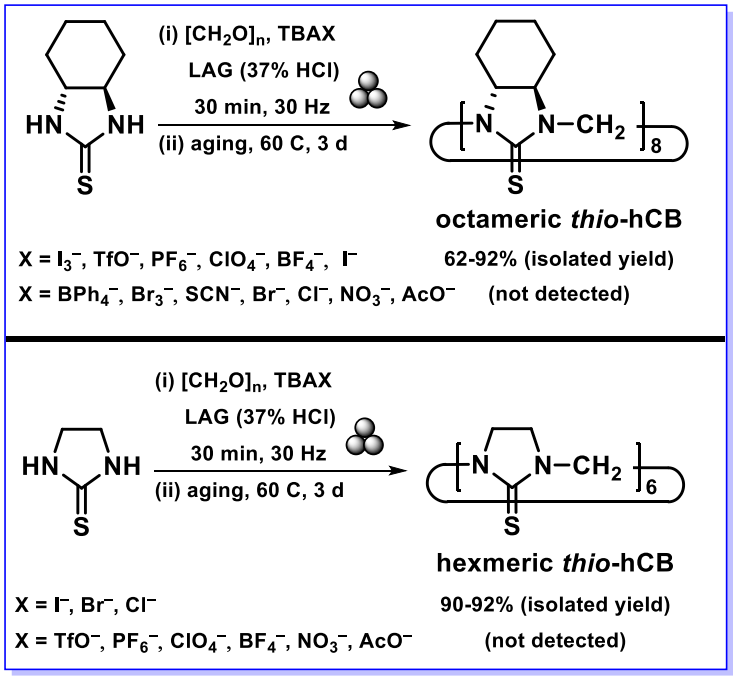

Figure 1. Mechanochemical synthesis of *thio*-hCB macrocycles.

References

[1] R. Gujjarappa, R. Khurana, N. Fridman, E. Keinan, O. Reany, *Cell Rep. Phys. Sci.*, **2024**, *submitted*.

Radical strain-release photocatalysis for the synthesis of azetidines

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The renascent interest on four-member rings has vastly widen the range of research and applications in medicinal chemistry discovery programs, guiding the scientific community to upgrade, rethink, and reinvent obsolete strategies for their crafting[1]. Such scenario has enlarged the tactical repertoire of drug hunters, particularly awakening the quasi-forgotten concept of strain-release[2]. However, in contrast to the tens of well-described strategies that access small carbocyclic derivatives, azetidines remain severely unexplored in both polar and radical realms[3,4]. Here is reported a general solution by introducing azabicyclo[1.1.0]butanes (ABBs) to the field of strain-release photocatalysis, showing that can be transformed directly to sulfonylazetidines through a one-step difunctionalization protocol[5]. Successful implementation requires the unprecedented addition of a transient sulfonyl radical to the nitrogen atom of ABB, followed by a carbon- and nitrogen-centred radical recombination. The chemistry is orchestrated by a novel organic photosensitiser (PS), which governs the key energy transfer process with various types of sulfonyl imine precursors. The radical intermediates are intercepted by the ABB *via* a radical strain-release process, providing access to azetidines in high chemical yields and in a single operation.

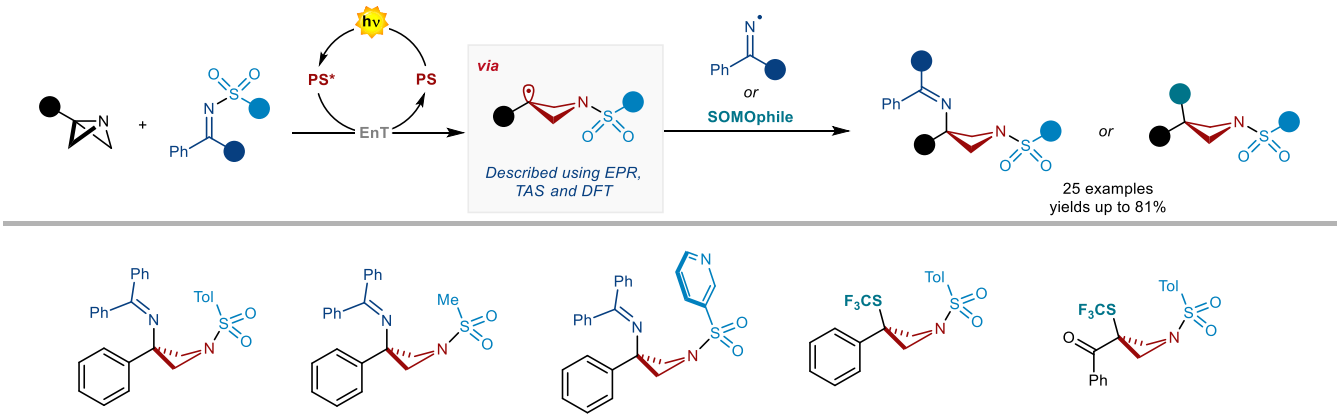

Figure 1. Difunctionalized azetidines

References

[1] M. R. Bauer, P. Di Fruscia, S. C. C. Lucas, I. N. Michaelides, J. E. Nelson, R. I. Storer, B. C. Whitehurst, *RSC Med. Chem.,* **2021**, *12*, 448-471.
[2] J. Turkowska, J. Durka, D. Gryko, *Chem. Commun*., **2020**, *56*, 5718-5734.
[3] M. Andresini, L. Degennaro, R. Luisi, *Org. Biomol. Chem*., **2020**, *18*, 5798-5810.
[4] P. Belloti, F. Glorius, *J. Am. Chem. Soc*., **2023**, *145*, 20716-20732.
[5] R. I. Rodríguez, V. Corti, L. Rizzo, S. Visentini, M. Bortolus , A. Amati, M. Natali, G. Pelosi, P. Costa, L. Dell' Amico, **2024**, ChemRxiv preprint DOI: 10.26434/chemrxiv-2024-f5g9p

Sustainable Poly(disulfide)s

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Understanding dynamic chemistry systems in Nature inspires chemists to design biomimetic synthetic materials. Disulfide bonds, the bonds that tie peptides, feature their dynamic covalent nature, that is reversible covalent bonds. Here we propose that making polymers with disulfide bonds can be a solution towards intrinsically dynamic materials. Unlike traditional plastics and noncovalent (supramolecular) polymers, poly(disulfides) can simultaneously exhibit chemical recycling ability and excellent mechanical performances. We will focus on the poly(disulfides) derived from thioctic acid, a natural small molecule, to show the promising applications of these intrinsically dynamic materials in self-healing elastomers, adhesives, and actuators. Then I will move to our recent discovery that hydrogen bonds are essential in the control of disulfide chirality and enable stereodivergent chirality transfer. We find that the formation of S−S---H−N hydrogen bonds in solution can drive conformational adaption to allow intramolecular chirality transfer, while the formation of C=O---H−N hydrogen bonds results in supramolecular chirality transfer to form antiparallel helically self-assembled solid-state architectures.

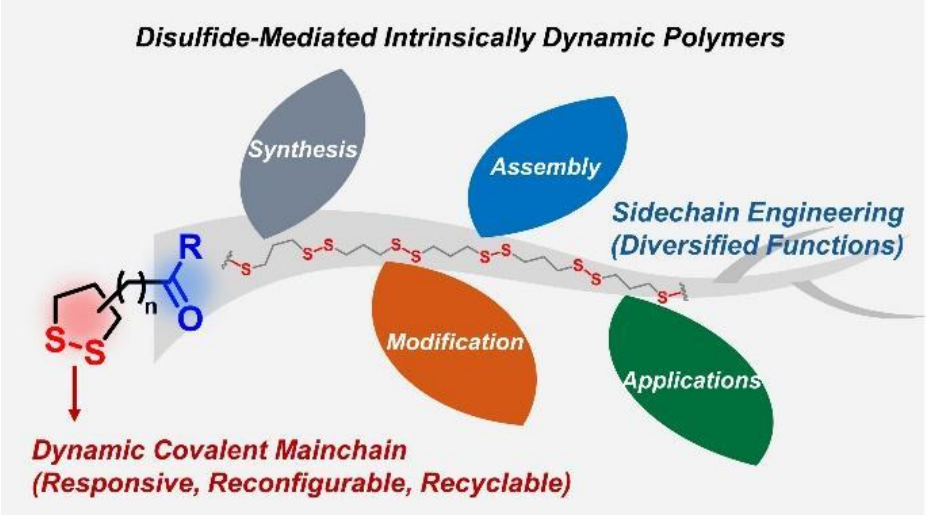

Figure 1. Conceptual illustration of poly(disulfide)s.

References

[1] **Q. Zhang**, C. Y. Shi, D. H. Qu, Y. T. Long, B. L. Feringa, H. Tian, *Sci. Adv.* **2018**, *4*, eaat8192.
[2] **Qi Zhang**, Y. Deng, H. Luo, C. Shi, G. M. Geise, B. L. Feringa, H. Tian, D. H. Qu, *J. Am. Chem. Soc.* **2019**, *141*, 12804-12814.
[3] **Qi Zhang**, Y. Deng, C. Shi, B. L. Feringa, H. Tian, D. H. Qu, *Matter*, **2021**, *4*, 1352-1364.
[4] **Q. Zhang**, D. H. Qu, B. L. Feringa, H. Tian, *J. Am. Chem. Soc.* **2022**, *144*, 2022–2033.
[5] **Q. Zhang**, S. Crespi, R. Toyoda, R. Costil, W. R. Browne, D. H. Qu, H. Tian, B. L. Feringa, *J. Am. Chem. Soc.* **2022**, *144*, 4376–4382.
[6] **Q. Zhang***, R. Toyoda, L. Pfeifer, B. L. Feringa*, *J. Am. Chem. Soc.* **2023**, *145*, 6976-6985.
[7] Y. Deng, Z. Huang, B. L. Feringa*, H. Tian, **Q. Zhang***, D. H. Qu*, *Nat. Comm.* **2024**, in press.

OC-28

Thiourea Oxidized Derivatives: The Unveiling Of Their Potentiality Through Solvent-less Techniques

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The synthesis of nitrogen heterocycles has always been a subject of interest in various fields of research. Among these, some of the most relevant are undoubtedly the pharmaceutical and biological fields due to the common occurrence of these derivatives in drugs and biomolecules.[1] Consequently, various procedures for their synthesis have been reported using several synthetic methodologies. Although they require a simple apparatus and perform well in terms of yield, they generally have different limitations due to the use of harsh reaction conditions along with the use of toxic solvents and reagents. With a view of improving the synthesis of these compounds and making such processes more sustainable, the use of oxidised thiourea derivatives has been considered. The sulphur present in thiourea can be converted to either a +2 or a +4 oxidation state, giving rise to thiourea dioxide (TDO) and thiourea trioxide (TTO), respectively. Both derivatives exhibit high electrophilicity on their carbon atom, implying the reversion of the nucleophilicity of thiourea to an electrophilic derivative. Furthermore, the oxidation state of sulphur itself can result in additional properties due to its reducing characteristics. By exploiting the advantages of their high reactivity, it was possible to use these oxidised derivatives in solvent-free techniques, namely Resonance Acoustic Mixing (RAM) and Ball-milling (BM), so that their yield can be maximised and their features can be studied more extensively.

Figure 1. Analysis of TDO and TTO potential through Resonance Acoustic Mixing (RAM) and Ball-milling (BM).

References

[1] S. M. Devine, M. P. Challis, J. K. Kigotho, G. Siddiqui, A. De Paoli, C. A. MacRaild, V. M. Avery, D. J. Creek., S. R. Norton, P. J. Scammells, *Eur. J. Med. Chem.*, **2021**, *221*, 113518.

Diverse Synthesis of Various Unsymmetrical Disulfides Facilitated by a Novel Disulfurating Reagent

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Disulfide bonds are prevalent in diverse fields, including medicinal chemistry, food chemistry, and materials science. Despite their wide applications, the synthesis of unsymmetrical disulfides is challenging[1-4] because conventional methods, such as the oxidation of thiols, tend to provide a mixture of symmetrical and unsymmetrical disulfides.

To address this issue, we designed and synthesized a new shelf-stable and easy-to-prepare bilateral disulfurating platform molecule, *N*-(morpholine-4-dithio)phthalimide (Figure 1A).[3] This reagent has amino and imide leaving groups that can be orthogonally transformed. Under acidic conditions, the amino leaving group undergoes selective protonation and thus can be displaced by various carbon nucleophiles, such as allyl trimethylsilanes, alkynyl silanes, and electron-rich arenes.[3] Meanwhile, the remaining phthalimide moiety is substituted by amines, thiols, and azlactones under basic or neutral conditions.[3-5] The combination of these transformations provides access to diverse unsymmetrical disulfides through two C−S bond-forming reactions in a time-efficient manner.

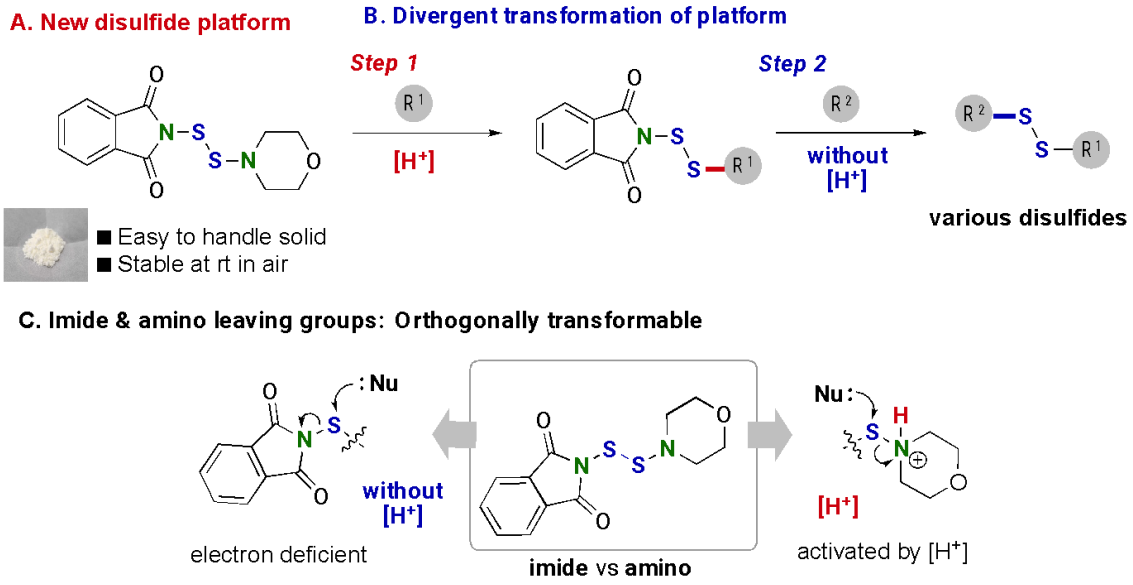

Figure 1. Modular synthesis of divergent unsymmetrical disulfides.

References

[1] J. Xue, X. Jiang, *Nat. Commun.* **2020**, *11*, 4170.
[2] K. Kanemoto, K. Furuhashi, Y. Morita, T. Komatsu, S.-i. Fukuzawa, *Org. Lett.* **2021**, *23*, 1582–1587.
[3] H. Asanuma, K. Kanemoto, T. Watanabe, S.-i. Fukuzawa, *Angew. Chem., Int. Ed.* **2023**, *62*, e202219156.
[4] H. Asanuma, K. Kanemoto, *Org. Lett.* **2024**, *26*, 438–443.
[5] H. Asanuma, K. Hosono, M. Iwata, Y. Takami, N. Yoshikai, K. Kanemoto, *ChemRxiv* **2024** (DOI: 10.26434/chemrxiv-2024-1vp1n).

Enantioselective Au-Catalyzed Synthesis of Thia[5]- and Thia[6]helicenes and Their Transformation into Bowl-shaped Pleiadenes

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Helicenes are an intriguing class of ortho-fused polyaromatic hydrocarbons that stand out by their distinct helical chirality. Especially heterohelicenes with their unique chemical and physical properties are predestined for technological applications in optoelectronics and others. Yet, the lack of enantioselective synthesis methods is the biggest limitation holding back further innovation.[1]

We have developed a novel and highly modular synthesis of new Thia[5(6)]helicenes *via* intramolecular alkyne hydroarylation using α-cationic chiral phosphonite Au(I)-catalysts achieving high enantioselectivities.[2] Furthermore, regioselective post-synthetic functionalization was explored to further increase the applicability of our method. The successful skeletal transformation of Thia[6]helicenes into either Aza[6]helicene or bowl-shaped pleiadenes, without loss of enantiopurity, was achieved. Comprehensive experimental and theoretical investigation of the racemization behavior as well as luminescence properties were carried out; absolute configuration for each compound was confirmed by X-Ray crystallography. In conclusion, we present a library of diverse Thiahelicenes synthesized in a highly enantioselective manner, allowing their comparison and the determination of relationships between their structure, conformational stability and chiroptical properties.

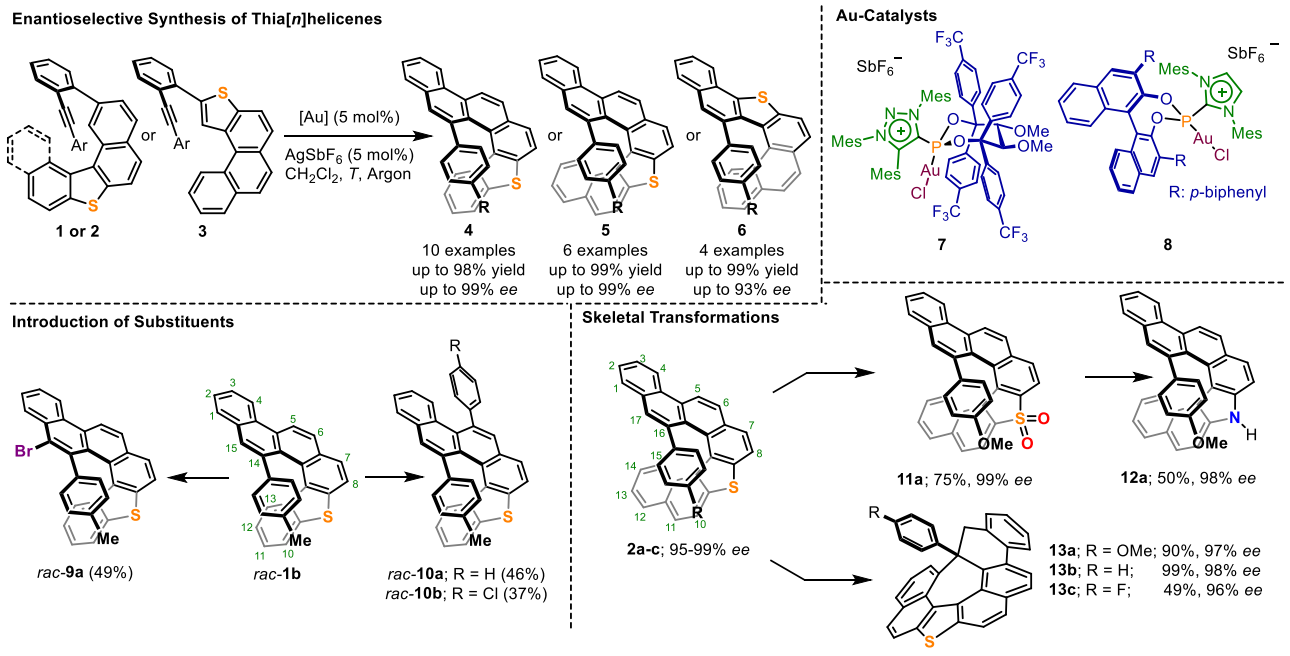

Figure 1: Enantioselective Synthesis of Thia[5]- and Thia[6]helicenes *via* intramolecular hydroarylation using α-cationic chiral phosphonite Au(I)-catalysts and their late-stage and skeletal transformation.[2]

References

[1] K. Dhbaibi, L. Favereau, J. Crassous, *Chemical Reviews*, **2019**, *119 (14)*, 8846 – 8953.

[2] W. Fu, V. Pelliccioli, M. von Geyso, P. Redero, C. Böhmer, M. Simon, C. Golz, M. Alcarazo, *Adv. Mater.,* **2023**, *35*, 2211279.

Modeling Reactive Persulfide Derivatives Utilizing Molecular Cavities

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Hydropersulfides (RSSH) and other polysulfur species are integral to a wide range of biological processes, including redox regulation, enzymatic activity, post-translational modifications, protective mechanisms against oxidative stress, metabolic pathways, signal transduction, and detoxification. Their dynamic and versatile nature allows them to contribute significantly to cellular homeostasis and overall organismal health. In the biological functions of hydropersulfides, reactive species generated by their oxidative modification, such as perthiosulfenic acids (RSSOH)[1] and *S*-nitrosopersulfides (RSSNO),[2] have been proposed to play crucial roles. However, chemical information on these species is very scarce because of their intrinsic instability; it was reported that RSSOH readily undergoes self-condensation[3] and that RSSNO is converted to the corresponding tetrasulfide with the release of nitric oxide.[2] Although their potential importance has been emphasized in the literature, no direct observation of RSSOH and RSSNO species has been reported. For the model studies of such biologically relevant reactive species, we have developed nano-sized molecular cavities and applied them to the stabilization of highly reactive intermediates.[4] Here, we report the first synthesis of RSSOH and RSSNO by utilizing cavity-shaped substituents (Figure 1). Their crystal structures and model studies on the biologically relevant reaction processes will also be delineated.

Figure 1. Perthiosulfenic acids and *S*-nitrosopersulfides stabilized by cavity-shaped substituents.

References

[1] D. E. Heppner, M. Hristova, T. Ida, A. Mijuskovic, C. M. Dustin, V. Bogdandi, J. M. Fukuto, T. P. Dick, P. Nagy, J. N. Li, T. Akaike, A. van der Vliet, *Redox Biol.*, **2018**, *14*, 379-385.

[2] J. Zarenkiewicz, C. Perez-Ternero, V. Kojasoy, C. McGinity, V. S. Khodade, J. S. Lin, D. J. Tantillo, J. P. Toscano, A. J. Hobbs, J. M. Fukuto, *Free Rad. Biol. Med.*, **2022**, 188, 459-467.

[3] E. Block, *J. Am. Chem. Soc.*, **1972**, *94*, 644-645.

[4] For recent examples, see: (a) T. Sano, R. Masuda, S. Sase, K. Goto, *Chem. Commun.*, **2021**, *57*, 2479-2482. (b) R. Masuda, R. Kimura, T. Karasaki, S. Sase, K. Goto, *J. Am. Chem. Soc.*, **2021**, *143*, 6345-6350. (c) R. Masuda, S. Kuwano, K. Goto, *J. Am. Chem. Soc.*, **2023**, *145*, 14184-14189.

OC-32

Organic electronic and optoelectronic materials based on thienothiophe and dithienothiophe

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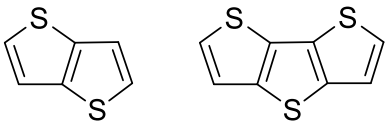
The heterocycles thienothiophenes (**1**, TT) and dithienothiophenes (**2**, DTT) possess two and three fused thiophenes, respectively, which are electron rich molecules [1-3]. As the orientations of the rings vary depending on the location of the sulfur atom, four and six isomers for TTs and DTTs can be depicted, respectively. They are particularly important as building blocks for numerous electronic and optical applications such as thin film transistors (OTFTs), light emitting diodes (OLED), photovoltatic cells, energy storage, electrochromic devices and sensors 1-5.



1 **2**

Figure 1.

References

[1] E. Cinar, T. Ozturk, *Chem. Rev.* "Thienothiophenes, Dithienothiophenes and Thienoacenes; Syntheses, Oligomers, Polymers and Properties, **2015**, 115, 3036 – 3140.

[2] Handbook of Thiophene-based Materials, I. F. Perepichka, D. F. Perepichka, Eds. John Wiley & Sons: Chichester, UK, 2009.

[3] "Dithienothiophenes" T. Ozturk, E. Ertas, O. Mert, *Tetrahedron*, **2005**, *61*, 11055.

[4] "Fused Thiophenes and Some Oligomers and Polymers Therefrom", Mehmet Emin Cinar and Turan Ozturk, Ed. John Joule, Thiophenes, Springer, "Top. Heterocycl. Chem." 2015, 39, 161-202.

[5] "Thiophene-Based Organic Semiconductors", Gulsen Turkoglu, M. Emin Cinar, Turan Ozturk, Topics in Current Chemistry, 2017, 375, 84 – 129.

New Reactions of Sulfur-Containing Aryl Benzyl Ethers

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We recently described the use of the *N*-butylamide group as an effective promoter of the [1,2]-Wittig rearrangement of aryl benzyl ethers and when it is in the *ortho*-position ring closure occurs to form 3-arylphthalides **1**.[1] In the case of the corresponding phosphonamidates, ring closure occurs without rearrangement to afford a new route to 2-aryl-2,3-dihydrobenzo[*d*][1,3-]oxaphospholes **2**.[2] We have now examined the corresponding sulfonamides **3** and find that Wittig rearrangement occurs readily followed by cyclisation to give benzo[*d*][1,2]thiazoline *S,S*-dioxides **4**. The method was applied to synthesis of compound **6** which has been reported to have anti-HIV activity[3], and structures of both it and its precursor **5** were confirmed by X-ray diffraction.

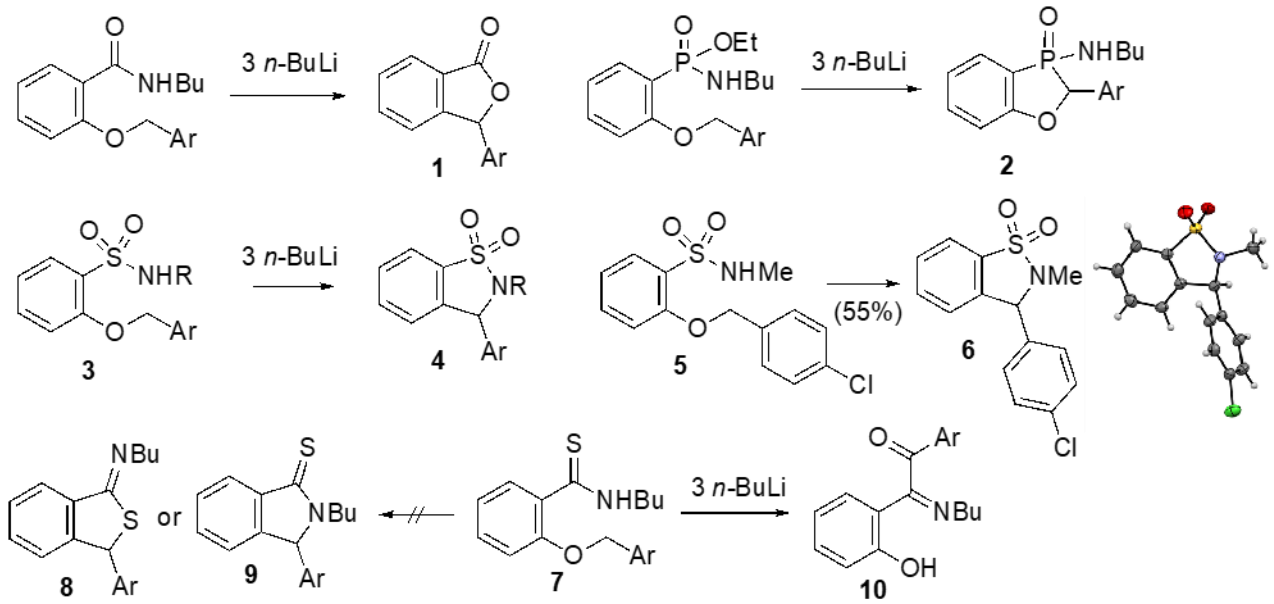

Figure1.

When we moved to the corresponding *N*-butylthioamides **7**, we expected Wittig rearrangement followed by cyclisation to give either benzo[*c*]thiophene-1-imines **8**[4] or 2,3-dihydroisoindole-1-thiones **9**[5] but in the event a completely different process is observed. Ring closure without rearrangement followed by loss of sulfur, hydrolysis and oxidation leads to the α-imino ketones **10**.

References

[1] R. A. Aitken, A. D. Harper, R. A. Inwood, A. M. Z. Slawin, *J. Org. Chem.*, **2022**, *87*, 4692–4701.
[2] R. A. Aitken, K. Ait Moulay, D. B. Cordes, R. A. Inwood, F. G. Jamieson, A. J. B. Nelson, A. P. McKay, *Organics*, **2024**, *5*, 12–31.
[3] D. Baker, B. Jiang, US Pat. 6353112 B1, **2002**.
[4] K. Kobayashi, Y. Shigemura, K. Ezaki, *Heterocycles*, **2015**, *91*, 526–536.
[5] K. Kobayashi, T. Nogi, *Heterocycles*, **2017**, *94*, 2262–2272.

"The Sulfur Dance" Around Arenes and Heteroarenes - the Reversible Nature of Nucleophilic Aromatic Substitutions

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Nucleophilic aromatic substitutions (NAS) are among the most frequently used reactions in organic chemistry.[1] Such exchanges of chemical components may occur by different mechanisms (S_NAr, $S_{RN}1$, cS_NAr, S_NArH). We will use the denomination S_NAr for representing these different mechanistic possibilities. Even if their reversibility was shown in rare cases,[2] it was overlooked in spite of a great number of S_NAr reactions reported since 1854.[3] We disclose here the features of a category of reversible NAS in view of their significance and generality in dynamic aromatic chemistry.[4] Exchange of sulfur components surrounding arenes and heteroarenes may occur at 25°C, in a process that one may call a "sulfur dance". These S_NAr systems present their own features and stimulate the implementation of reversible S_NAr in aromatic chemistry and in dynamic covalent chemistry (DCC). By varying conditions, covalent dynamics may operate to provide libraries of thiaarenes with some selectivity, or conversion of a hexa(thio)benzene asterisk into another one. The reversible nature of S_NAr is confirmed by three methods: a convergence of the products distribution in reversible S_NAr systems, a related product redistribution between two per(thio)benzenes by using a thiolate promoter, and from kinetic/thermodynamic data. A four-component dynamic covalent system further illustrates the thermodynamically-driven formation of a macrocycle (thiacalix[2]arene[2]pyrimidine).

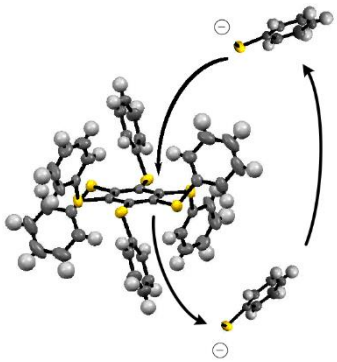
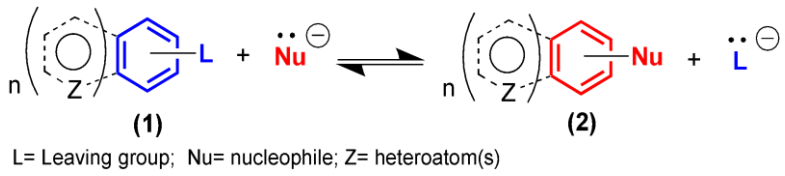


Figure 1. Exchange of sulfur components by dynamic S_NAr reactions



Scheme 1. Schematic representation of the reversibility of nucleophilic aromatic substitutions.

References

[1] D. G. Brown, J. Boström, *J. Med. Chem.* **2016**, *59*, 4443-4458.
[2] For an early discussion on reversible S_NAr : J. F. Bunnett, R. E. Zahler, *Chem. Rev.* **1951**, *49*, p. 301.
[3] a) Williamson and Scrugham, *Annalen* **1854**, *92*, 316-318; b) Pisani, *Compt. Rend.*, **1854**, *39*, 852-854.
[4] S. Gahlot, J.-L. Schmitt, A. Chevalier, M. Roy, M. Villa, P. Ceroni, J.-M. Lehn, M. Gingras, *Chem. Eur. J.* **2024**, e202400231 (https://doi.org/10.1039/D2CC05908H).

OC-35

t-Butylarylthio and selenophosphinic acids: Syntheses, structural studies and attempts to use them as chiral auxiliaries

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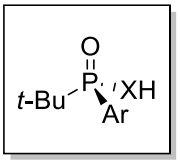
Chiral *t*-butylarylthio and selenophosphinic acids (**1** and **2**) may constitute an interesting group of chiral auxiliaries with a stereogenic phosphorus atom, relatively easily available as enantiomerically pure compounds. Research on this topic so far is basically limited to the synthesis and use as a chiral solvating agent (CSA) and a model compound in mechanistic studies of *t*-butylphenylthiophosphinic acid **1a**, which has been known in its enantiomerically pure form since the end of1970s[1,2]. This communication will present the selected results of research devoted to the synthesis (in racemic and enantiomerically pure form), determining the crystallographic structure and the use as chiral auxiliaries (including as precursors of chiral ionic liquids) of a broader group of *t*-butylarylthio and selenophosphinic acids **1** and **2**[3-5] (Figure 1).



1a-e, X= S
2a-e, X= Se

a, Ar = Ph
b, Ar = 1-Nph
c, Ar = 9-Antryl
d, Ar = *p*-MeO-C_6H_4
e, Ar = *p*-CF_3-C_6H_4

Figure 1 General structure of chiral *t*-butylarylthio and selenophosphinic acids **1** and **2**

References

[1] M. J. P. Harger, *Perkin Transaction II*, **1980**, 1505-1511.
[2] J. Drabowicz, P. Pokora-Sobczak, D. Krasowska, Z. Czarnocki, *Phosphorus, Sulfur and Silicon and the Related Elements*, **2014**,*189*, 977-991.
[3] J. Błaszczyk, B. Bujnicki, P. Pokora-Sobczak, G. Mielniczak, L. Sieroń, P. Kiełbasiński, J. Drabowicz, *Molecules* **2023,** *28,* 4298 DOI: org/10.3390/molecules28114298.
[4]. P. Pokora-Sobczak, PhD Thesis, Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Łódź, December **2023.**
[5] J. Drabowicz, P. Pokora-Sobczak, D. Krasowska, A. Zając, P Wach-Panfiłow, Polish Patent NR238674 .**2021.**

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The Potential Role of Iron Sulfide in the Prebiotic Chemistry

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The reaction of elemental iron and sulfur in water at room temperature is know since many years, although the characterization of the formed iron sulfide was still pending. We could show by use of diffraction methods that mackinawite (FeS) was formed under these exceptionally mild reaction conditions.[1] Iron sulfides also form the central components of the much-discussed theory of a chemoautotrophic origin of life in a primordial iron sulfur world.[2]

Mackinawite prepared after that protocol is highly reactive and it was found to reduce cyanide yielding a variety of organic sulfur compounds, alkyl thiols, alkyl di- and trisulfides, sulfur containing heterocycles like 1,2,4-trithiolane as well as carbon disulfide. The identification of the products was confirmed by GC-MS techniques and the carbon-carbon bond formations have been confirmed by use of ^{13}C isotope labelling experiments. Moreover, the constituents of the aqueous phase were characterized by using NMR spectroscopy.[3]

This reaction could be of primordial relevance because compounds are formed which are important for the origin of biologically relevant building blocks.[4]

References

[1] R. Bolney, M. Grosch,M. Winkler, J. van Slageren, W. Weigand, C. Robl, *RSC Adv.* **2021**, *11*, 32464.
[2] G. Wächtershäuser, *Prog. Biophys. Mol. Biol.* **1992**, *58,* 85-201.
[3] M. Grosch et al., *ChemSystemsChem* **2022**, e202200010.
[4] W. Martin, M. J. Russell, *Phil. Trans. R. Soc. B* **2007**, *362*, 1887-1925.

Making and Breaking of C–S Bonds Using Metal Catalysis

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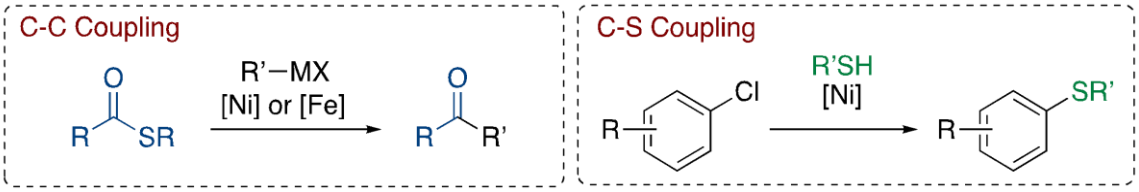
Our research interests focus on development of new methods for the synthesis and use of sulfur-containing compounds, such as thioesters and thioethers. They constitute valuable synthetic intermediates and target compounds for material chemistry and pharmaceutical applications.[1] Our aim is to develop efficient transformations employing non-precious metals as homogeneous catalysts.

We have demonstrated the usefulness of thioesters in cross coupling reactions with arylzinc reagents to generate ketones.[2] A defined nickel complex was employed as catalyst and a series of functionalized ketones was successfully obtained. The scope was later expanded to the coupling of thioesters with more reactive organomanganese reagents upon iron catalysis.[3]

Furthermore, we developed nickel-catalyzed coupling reactions of challenging aryl chlorides with thiols, whereby max. TOF of 800 h-1 was achieved.[4] A broad scope of substrates containing various functional groups and heterocyclic motifs was successfully converted. Further systematic studies of couplings of sterically hindered aliphatic thiols with a broad range of electrophiles, including ortho-substituted triflates, were conducted.



Scheme 1. Non-precious metal-catalyzed couplings of thioesters and thiols.

References

[1] a) K. A. Scott, J. T. Njardarson, *Top. Curr. Chem*. **2018**, *376*, 5; b) V. Hirschbeck, P. H. Gehrtz, I. Fleischer, *Chem. Eur. J.* **2018**, *24*, 7092 – 7107.

[2] P. H. Gehrtz, P. Kathe, I. Fleischer, *Chem. Eur. J.* **2018**, *24*, 8774 – 8778.

[3] V. J. Geiger, L. Lefèvre, I. Fleischer, *Chem. Eur. J.* **2022**, *28*, e202202212.

[4] a) P. H. Gehrtz, V. Geiger, T. Schmidt, L. Sršan, I. Fleischer, *Org. Lett.* **2019**, *21*, 50 – 55; b) R. M. Oechsner, J. P. Wagner, I. Fleischer, *ACS Catal.* **2022**, *12*, 2233 – 2243; c) R. M. Oechsner, I. H. Lindenmaier, I. Fleischer, *Org. Lett.* **2023**, *25*, 1655 – 1660; d) I. H. Lindenmaier, R. C. Richter, I. Fleischer, *Org. Chem. Front.* **2024**, DOI: 10.1039/d4qo00260a.

OC-38

Thiolated iminosugars as ligands for gold nanoparticles to address Gaucher disease

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Iminosugars are well known inhibitors of carbohydrate-processing enzymes and, in the last years, have shown attractive potential as therapeutics towards lysosomal storage disorders (LSDs), especially in the emerging pharmacological chaperone therapy (PCT)[1]. PCs are molecules able to bind and stabilize misfolded enzymes involved in these diseases, resulting in enzyme activity's enhancement. Recent studies showed that the multivalent presentation of a *N*-alkylated 3,4,5-trihydroxypiperidine iminosugar in dendrimeric scaffolds affords potent inhibitors and PCs of lysosomal enzyme GCase, the deficient enzyme involved in Gaucher LSD[2]. The efficacy of multivalency in modulating GCase activity, prompted us to multimerize the *N*-alkylated iminosugar with a 9-carbon chain (red moiety, Figure 1) using a thiol-ending linker (blue moiety, Figure 1) onto gold nanoparticles (AuNPs) as a scaffold. *In vitro* biological assays are ongoing to test the ability of these new nanosystems to act as PCs for GCase.

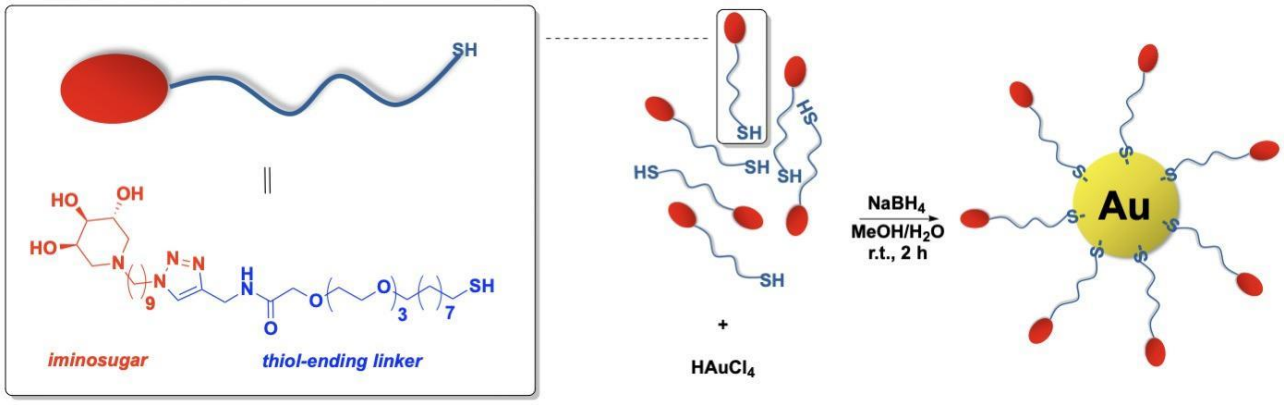

Figure 1. Multimerization of a thiol-ending *N*-alkylated iminosugar onto gold NPs by means of Au-S affinity.

References

[1] C. Matassini, F. Clemente, F. Cardona in *Carbohydrate-Based Therapeutics*, Eds.: R. Adamo, L. Lay, Wiley-VCH GmbH, Germany, **2023**, pp. 245 – 292.
[2] C. Vanni, F. Clemente, P. Paoli, A. Morrone, C. Matassini, A. Goti, F. Cardona *et al. ChemBioChem*, **2022**, *23*, e202200077.

Acknowledge

We acknowledge the support of the European Union by the Next Generation EU project ECS00000017 'Ecosistema dell'Innovazione' Tuscany Health Ecosystem (THE, PNRR, Spoke 4: Nanotechnologies for diagnosis and therapy).

Palladium-catalysed addition of aryl halides to *N*-sulfinylamines for the synthesis of sulfinamides

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Sulfinamides are versatile, synthetically useful intermediates and final motifs.[1-3] Traditional methods to synthesise sulfinamides generally require substrates with pre-installed sulfur centres. However, these precursors have limited commercial availability, and the associated synthetic routes often require harsh reaction conditions and highly reactive reagents, thus severely limiting their application. Herein, we report the synthesis of sulfinamides from aryl and alkenyl (pseudo) halides and *N*-sulfinylamines, enabled by palladium catalysis. The reactions use mild conditions and are achieved without the use of highly reactive pre-formed organometallic reagents, resulting in transformations of broad generality and high functional group tolerance. In particular, substrates featuring protic and electrophilic functional groups can be used successfully. Modification of complex aryl cores and natural product derivatives are used to demonstrate the utility of this method.

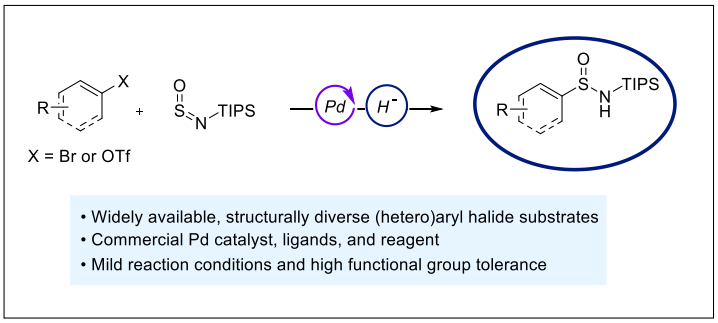

Figure 1. Palladium catalysed addition of aryl halides to N-sulfinylamines for the synthesis of sulfinamides

References

(1) Robak, M. T.; Herbage, M. A.; Ellman, J. A. Synthesis and Applications of tert-Butanesulfinamide. *Chem. Rev.* **2010**, *110* , 3600-3740.
(2) Lo, P. K. T.; Willis, M. C. Nickel(II)-Catalyzed Addition of Aryl and Heteroaryl Boroxines to the Sulfinylamine Reagent TrNSO: The Catalytic Synthesis of Sulfinamides, Sulfonimidamides, and Primary Sulfonamides. *J. Am. Chem. Soc.* **2021**, *143*, 15576-15581.
(3) Andrews, J. A.; Kalepu, J.; Palmer, C. F.; Poole, D. L.; Christensen, K. E.; Willis, M. C. Photocatalytic Carboxylate to Sulfinamide Switching Delivers a Divergent Synthesis of Sulfonamides and Sulfonimidamides. *J. Am. Chem. Soc.* **2023**, *145*, 21623-21629.

OC-40

Hydrogen Evolution through a photoactive Hydrogenase Mediator using Visible Light

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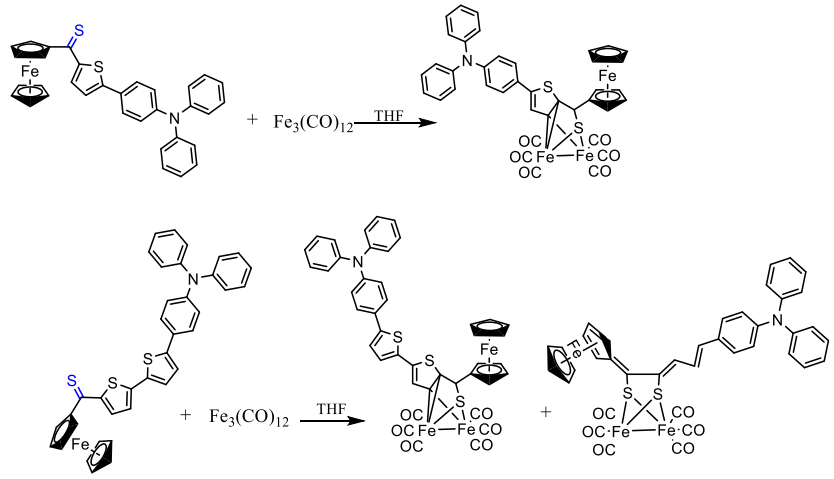
Nowadays the concerns about global warming and increasing demands of energy consumption has spurred much interest in developing eco-friendly and renewable energy technologies[3,4]. Molecular hydrogen (H_2) is considered as an energy carrier, and presently getting more popularity as an alternative fuel[3-5]. Natural [FeFe]- and [NiFe]-hydrogenases enzymes convert protons and electrons into H_2 with remarkably high rates at low overpotential. Photocatalytic H_2 generation through photoactive [FeFe]- hydrogenase mimic using visible light irradiation could make H_2 a real competitor to fossil fuels[1-5]. Thus, a series of novel photoactive hydrogenase mimics using triphenylamine (TPA) as electron donor, thiophene derivatives as π-conjugated molecules, and ferrocene moiety was designed for photocatalytic hydrogen evolution under visible light irradiation (Scheme 1).



Scheme 1. Synthetic pathways of the complexes.

References

[1] Alper, H., *et al*.; *J. Am. Chem. Soc*. **1973**, *95*, 4905–4913.
[2] Mlostoń, G. *et al*.; *Beilstein J. Org. Chem.* **2016**, *12*, 1421–1427.
[3] Basma, I., *et al*.; *J. Mol. Struct*. **2024**, *1295*, 136630.
[4] Daraosheh, A. *et al*.; *Eur. J. Inorg. Chem.* **2012**, 318–326.
[5] Buday, P. *et al*.; *Angew. Chem*. **2022**, *61*, 20.

Surface Chemical Functionalization of MoS_2 Derivatives with Strong Acids: Fostering Hydrogen Evolution Reaction under Alkaline Conditions

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Hydrogen is globally recognized as a key vector for driving the World towards a fossil fuel-free energy transition. Water electrolysis promoted by renewable sources represents the synthetic route of choice for producing hydrogen in a sustainable way. However, the exploitation of this technology is still limited by the lack of cheap, earth-abundant electrocatalysts able to promote Hydrogen Evolution Reaction (HER) in a wide pH range. In particular, HER conducted in alkaline conditions offers several technical and economic benefits but possesses intrinsically unfavorable kinetics with respect to the acidic medium. Therefore, the development of sustainable, non-critical electrocatalysts able to efficiently promote HER in alkaline media represents a challenging priority.[1-2]

On this ground, transition metal dichalcogenides (TMDs) and MoS_2 in particular have been extensively exploited in HER but their performance still appear unsatisfactory under alkaline conditions where kinetics are limited by slow water dissociation processes.[3] As an original approach to enhance TMDs HER performance in alkaline environment, we covalently decorated MoS_2 surface with Brønsted-acid end-capped aryl fragments featured by different acidic strength [*i.e*. carboxylic (Ar-COOH) and sulfonic (Ar-SO_3H)]. Chemical functionalization was found to stabilize the electrochemically active 1T phase and create an ideal surface microenvironment for running HER with kinetics virtually independent from the acidic/basic nature of the electrolyte. In particular, the ability of sulfone groups to establish strong H-bonds with water molecules is thought to vehicle their approach to the chalcogenide and facilitate the tunnelling of H-species to the MoS_2 surface (Figure 1). Materials synthesis, characterization and HER performance will be presented.[4]

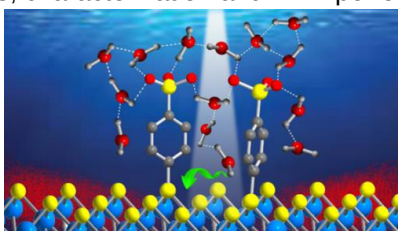

Figure 1. Representation of tunnelling of H-species at the MoS_2 surface.

References

[1] F. Qureshi, M. Yusuf, M. A. Khan, H. Ibrahim, B. C. Ekeoma, H. Kamyab, M. M. Rahman, A. K. Nadda, S. Chelliapan, *Fuel*, **2023**, *340*, 127574
[2] Y. Zheng, Y. Jiao, A. Vasileff, S. Z. Qiao, *Angew. Chem. Int. Ed*., **2018**, *57*, 7568-7579
[3] Y. Xu, R. Ge, J. Yang, J. Li, S. Li, Y. Li, J. Zhang, J. Feng, B. Liu, W. Li, *J. Energy Chem*., **2022**, *74*, 45-71
[4] *Manuscript in preparation*

Acknowledgments

The Italian MUR through the PRIN2022 project “MATISSE - A ‘Molecular Lift’ for the Control of the Metal Protrusion and Coordination Sphere in Single-Atom Catalysts for CO_2 Electroreduction” (2022K5SX27) and the European Union - NextGeneration EU through the Italian Ministry of Environment and Energy Security POR H2 AdP MMES/ENEA with involvement of CNR and RSE, PNRR - Mission 2, Component 2, Investment 3.5 “Ricerca e sviluppo sull’idrogeno”, CUP: B93C22000630006 are kindly acknowledged for financial support.

OC-42

Novel Heterocyclic And Condensed Compounds Based On Annulation And Cyclofunctionalization Reactions Of Electrophilic Chalcogen Reagents. Comparison Of The Reactivity of Sulfur, Selenium and Tellurium Halides

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New families of heterocyclic and condensed compounds have been developed based on annulation and cyclofunctionalization reactions of 2-quinolinesulfenyl, 8-quinolinesulfenyl, 2-pyridinechalcogenyl halides, chalcogen di- and tetrahalides with functional alkenes and natural compounds (eugenol, isoeugenol, anethole, thymol, and carvacrol derivatives). Some examples of the products are presented in the Scheme 1. 2-Quinolinesulfenyl chloride and bromide have been obtained for the first time. Comparison of the reactivity of sulfur, selenium and tellurium halides and the influence of the chalcogen nature on the reaction direction and product yields will be discussed.

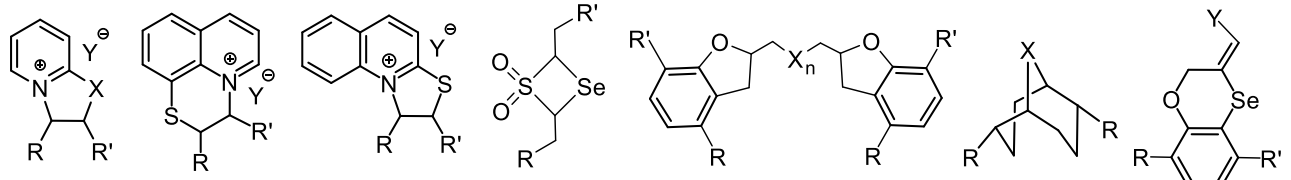

Figure 1. Examples of new families of heterocyclic and condensed organochalcogen compounds.

A novel methodology for the synthesis of condensed chalcogen heterocycles based on the one-pot annulation/functionalization reactions of chalcogen halides with unsaturated aromatic compounds combining electrophilic addition, aromatic substitution and nucleophilic substitution has been developed. Sulfur and selenium dihalides and tellurium tetrahalides were involved in a series of cyclofunctionalization reactions affording hitherto unknown heterocyclic and condensed organochalcogen compounds.

Previously, the possibility of using $SeCl_2$ and $SeBr_2$ in the synthesis of organoselenium compounds was shown for the first time in our laboratory.[1] The introduction of these reagents in organic synthesis has opened up opportunities for obtaining new classes of organoselenium compounds.

The regio- and stereoselective transannular addition/functionalization reactions of sulfur and selenium dihalides with 1,5-cyclooctadiene affording new 9-thia- and -selenabicyclo[3.3.1]nonane derivatives have been developed. New functionalized organochalcogen compounds with high glutathione peroxidase-like activity have been found. The developed reactions are based on atom-economic and environmentally safe synthetic approaches that allow obtaining products in high or quantitative yields. The antimicrobial activity of the obtained products has been evaluated and the compounds have been found that are superior in their activity to known antibiotics.

Financial support of Russian Science Foundation (Grant 22-13-00339) is gratefully acknowledged.

References

[1] V. A. Potapov, M. V. Musalov, M. V. Musalova, S. V. Amosova. *Curr. Org. Chem.* **2016**, *20*, 136-145.

POSTERS

ISOCS-30

P-01

Simultaneous Oxidative and Reductive C-S Bond Cleavage in *t*-Alkyl Aryl Sulfoxides Catalyzed by Tetrabutylammonium Decatungstate

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Tetrabutylammonium decatungstate, $(Bu_4N^+)_4W_{10}O_{32}^{4-}$, TBADT, is emerging as a powerful photocatalyst able to abstract hydrogen from several classes of organic compound including aliphatic hydrocarbons, aldehydes, amides and ethers. In the reaction of the excited state of decatungstate with thioethers, abstraction of the hydrogens α to the sulfur atoms of the substrates leading to dimers, $(R_2S[-H])_2$ is coupled with reduction of these substrates reduced form of the catalyst, $W_{10}O_{32}^{6-}$ generating the thioether anion radical. The latter than undergoes C-S bond cleavage to produce thiols, RSH and hydrocarbons, RH (Figure 1).[1]

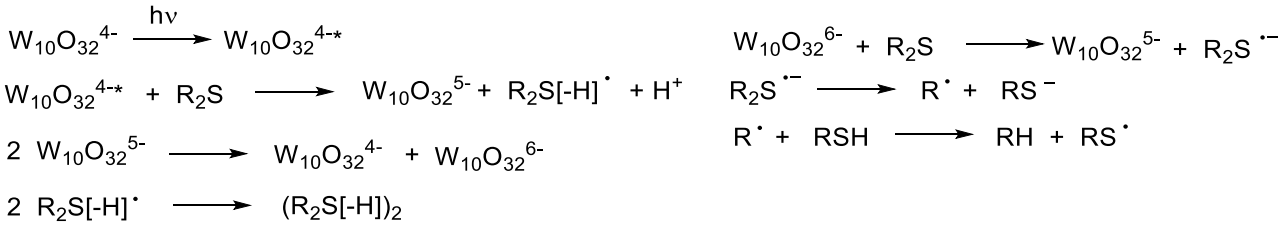

Figure 1. Oxidation of thioethers photocatalyzed by decatungstate.

Oxidation of sulfoxide by the decatungstate excited state has received almost no attention, thus. in this study, we have investigated the TBADT photocatalyzed oxidation of *t*-alkyl aryl sulfoxides. In the absence of α to sulfur C-H bonds the sulfoxide radical cations is formed which undergoes a very fast C-S fragmentation process leading to a *t*-alkyl cation and the phenyl sulfinyl radical.[2] This step is followed by another C-S fragmentation reactions in the reductive process leading to a *t*-alkyl radical and a phenylsulfenate anion (Figure 2). An unprecedented two-sequential oxidative/reductive C-S bond cleavage processes are observed by excitation of the TBADT photocatalyst.

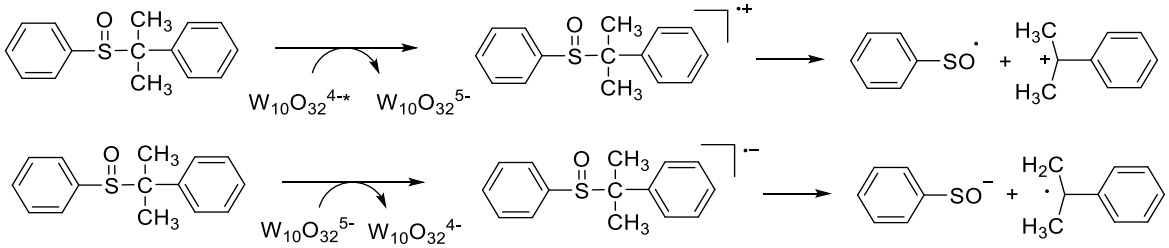

Figure 2. Oxidation of *t*-alkyl aryl sulfoxide photocatalyzed by decatungstate.

References

[1] R. C. Chambers, C. L. Hill, *J. Am. Chem. Soc.*, **1990**, *112,* 8427-8433.
[2] E. Baciocchi, T. Del Giacco, O. Lanzalunga, P. Mencarelli, B. Procacci, *J. Org. Chem.*, **2008**, *73*, 5675-5682.

P-02

Alkynyl Phenyl Selenides as Intermediates in the Metal-free Cyclization of *N*-Tosyl Homopropargyl Amides to γ-Lactams

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Organoselenium compounds have received considerable attention for their synthetic applications because they are useful reagents to introduce new functional groups into organic molecules under mild conditions. Specifically, functionalized alkynyl phenyl selenides have been employed in organic synthesis, as they are valuable intermediates for the selective preparation of substituted alkenes,[1] phenylseleno esters,[2] γ- and δ-lactones,[3] β[3]-amino acid derivatives,[4] (*Z*)-α-(phenylseleno)-sulfinyl and -sulfonyl alkenes.[5] Here, we present a new methodology to prepare γ-lactams using *N*-tosyl homopropargylic amides (Figure 1).

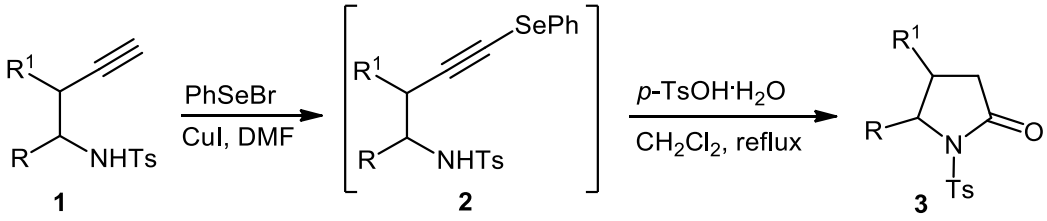

Figure 1. General scheme for the synthesis of γ-lactams

Thus, amides 1 reacted with PhSeBr in DMF and in the presence of CuI[6] to give the crude alkynyl selenide intermediates 2. The reaction of 2 with an excess of *p*-toluenesulfonic acid monohydrated in refluxing dichloromethane gave the corresponding *N*-tosyl γ-lactams 3 in good to excellent yields. Finally, DFT calculations were performed to shed light on the reaction mechanism of the conversion of alkynyl selenides **2** to γ-lactams **3**.

References

[1] M. Tingoli, M. Tiecco, L. Testaferri, A. Temperini, G. Pelizzi, A. Bacchi,*Tetrahedron*, **1995**, *51*, 4691-4695.
[2] M. Tiecco, L. Testaferri, A. Temperini, L. Bagnoli, F. Marini, C. Santi, F. Terlizzi, *Eur. J. Org. Chem*., **2004**, 3447-3451.
[3] M. Tiecco, L. Testaferri, A. Temperini, R. Terlizzi, L. Bagnoli, F. Marini, C. Santi, *Synlett,* **2006**, 587-590.
[4] A. Temperini, R. Terlizzi, L. Testaferri, M. Tiecco, *Chem. Eur. J*., **2009**, 15, 7883-7895.
[5] M. C. Aversa, A. Barattucci, P. Bonaccorsi, A. Temperini, *Eur. J. Org. Chem.,* **2011**, 5668-5673.
[6] A. L. Braga, C. C. Silveira, A. Reckziegel, P. H. Menezes, *Tetrahedron* Lett., **1993**, *34*, 8041-80444.

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Ca^{2+}-triggered allosteric disulfide/diselenide catalyst : potential regulator for cellular redox homeostasis

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Enzymes adroitly regulate their own enzymatic activities by altering peptidyl conformations around the active sites through association of a cofactor or partial chemical modification. Mimicking such the allosteric regulation mechanism of the actual enzymes would be useful in controlling the activity of artificial catalysts to accordingly exert the catalytic functions in cells[1]. Therefore, this study aims to develop biocompatible allosteric catalysts, which can modulate their catalytic activity in response to gap of Ca^{2+} concentration. First, diselenide (SeSe)- and SS-containing compounds were fused with a Ca^{2+}-ligand as an allosteric site. Coordination of Ca^{2+} into the molecules altered their own structures, decreasing the thermodynamic stability of the SeSe and SS bonds and hence readily converting into corresponding catalytically active selenol and thiol states (Figure 1). Herein, we applied these unique redox properties to kinetics control of three representative bio-related redox reactions, i.e., (A) oxidative folding, (B) reductive antioxidation, and (C) reductive degradation of proteins. The compounds effectively catalyzed oxidative folding and reduction of reactive oxygen species and protein SS bond in the presence of Ca^{2+}. In this presentation, we show the detailed molecular mechanisms and demonstrate that the synthetic compounds can be driven as an allosteric catalyst not only *in vitro*, but also in living cells.

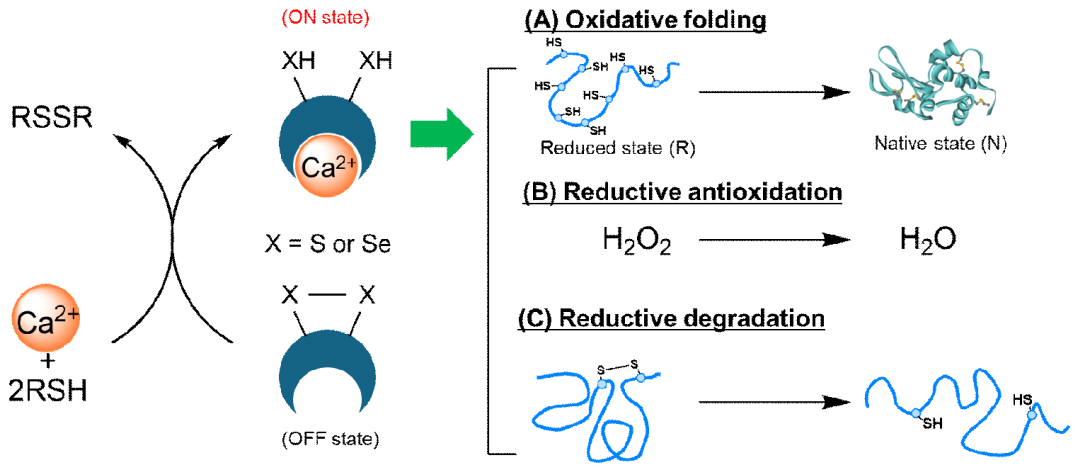

Figure 1. Diselenide and disulfide compounds activated by chelating Ca^{2+}.

References

[1] R. Mikami, *et al*., *ChemBioChem*, **2022**, *23*, e202100394.

P-04

Access to indole-fused sulfur-containing polycycles

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Polycyclic moieties are among a group of highly sought-after molecules, as they are often found to be a part of bioactive natural/synthetic compounds. Many polycyclic heterocycles possessing indolic core are among privileged structures because they display diverse range of biological activities. Particularly, indole derivatives functionalized at C-2 and C-3 positions are thought to be most promising to exhibit biological properties. Similarly, thiopyrans and fused-thiopyrans are of considerable interest due to their activities such as analgesic, anticancer, antihyperplasia, antiinflamatory, antibacterial, and antipsychotic. Despite many advances, a paucity of literature around sulfur-containing fused indoles still exists compared to indole-fused rings composed of C/N/O atom. Hence, in pursuit of novel bioactive chemical architectures the development of efficient and practical synthesis of indolyl moieties, fused with S-containing heterocycles is highly desirable in the current literature. Towards this endeavour our research efforts have led to the discovery of several elegant methods to access novel S-containing heterocycles in recent years. A summary of those findings along with some recent results will be presented.

P-05

Liquid Crystal-Based Inks via Michael Thiol-Acrylate Reaction for 3D printing

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Liquid Crystalline Elastomers (LCEs) stand out as among the materials studied for the development of artificial muscles, given their capability of responding to external stimuli such as light irradiation or temperature changes. However, their application in biological settings, particularly within the human body, presents challenges. Here, we employ 3D printing to create LCE structures serving as artificial muscles, responsive to thermal activation or visible light.The LC mixture is sinthetyze via Michael Thiol-Acrylate addition reaction. Additionally, we demonstrate their activation potential using LED arrays, enabling the possibility to develop of light-responsive biological interfaces for muscular support. Through precise control of alignment and geometries, diverse actuators are attainable, allowing tuneable complex deformations. Our study details the fabrication and characterization of LCE-based artificial muscles using cost-effective 3D printing, specifically employing Direct Ink Writing (DIW), a technique which can align the liquid crystals along the printing direction during the ink extrusion. LCEs show an elastomeric behavior with a Young Modulus in the range of MPa. The developed tension from photo and thermal-actuation test varies from 1 kPa to 400 kPa according to light intensity and irradiation time. Highly viscous oligomers based on diacrylate mesogens and dithiols, synthesized via a thiol-ene reaction, are used in DIW, with the inks containing an azobenzene dye for light actuation. Mechanical characterization and responsiveness to light and temperature are investigated post-printing, with structures adaptable for large-scale, custom-sized patches.

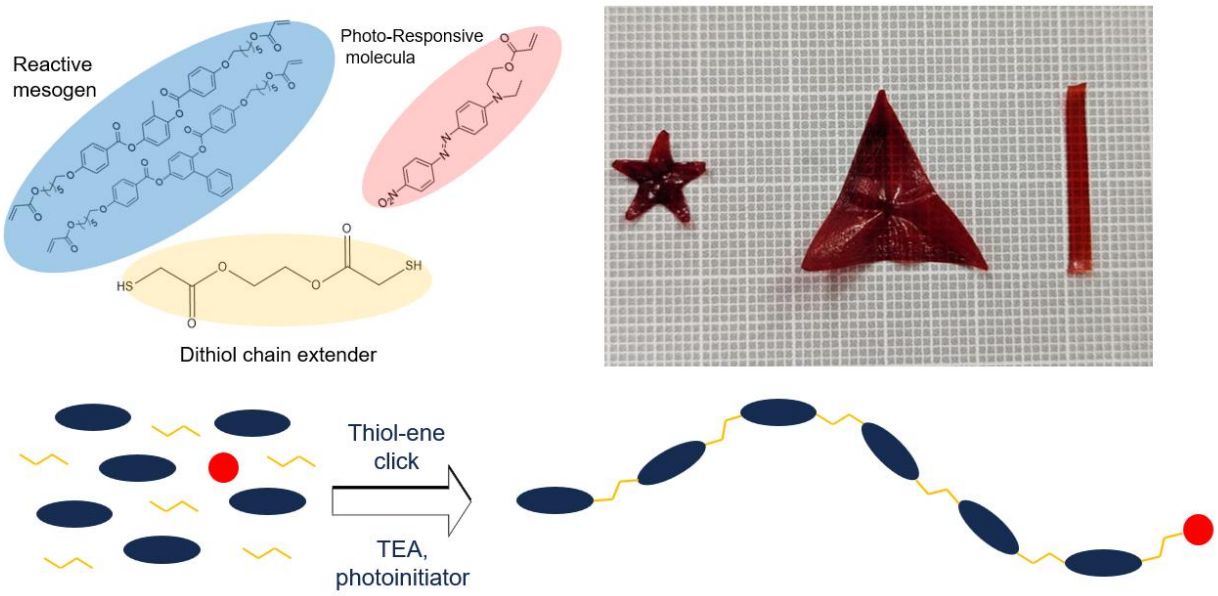

Figure 1. Synthesis of LC INK and 3D printed LCE.

References

[1] 1. S. Cai et al., Science Advances, 6, S29, **2020**.

Acknowledgment

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P-06

Synthesis of Triarylsulfonium Salts and their Applications in Organic Synthesis

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Sulfonium salts are a class of compound finding increased use in organic synthesis, notably in C-C bond formation.[1] Triarylsulfonium salts containing a pyridyl or polyfluorinated aryl ring represent underexplored examples of these salts. 2-Pyridyl and polyfluorinated arylboronic acids undergo rapid protodeboronation under aqueous conditions.[2] As a result these substrates give poor yields in certain C-C bond forming reactions, such as Suzuki-Miyaura cross-couplings. This suggests that alternative routes to incorporate these motifs would be highly valuable to organic chemists.

Presented here is a general strategy for the synthesis of triarylsulfonium salts containing a 2-pyridyl or polyfluorinated moiety.[3] An *S*-selective arylation procedure with iodonium salts has been developed. A range of sulfonium salts (>25 examples) showing good functional group and substitution pattern tolerance are shown. The resulting pyridylsulfonium salts were then applied in the transition metal-free synthesis of biaryls, the utility of which is highlighted by the synthesis of unsymmetrical bipyridine ligands.[4,5] Also presented here is work on the development of the applications of the polyfluorinated salts in organic synthesis, with a focus on ligand-coupling and photochemical reactions.[6]

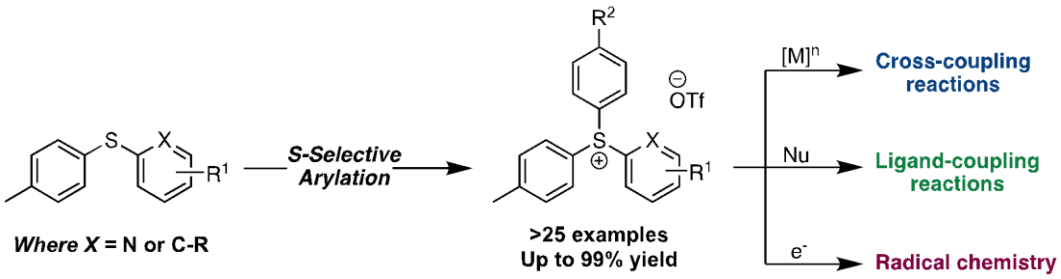

Figure 1. Synthesis and applications of pyridyl- and polyfluorinated sulfonium salts

References

[1] D. Kaiser, I. Klose, R. Oost, J. Neuhaus, N. Maulide, *Chem. Rev.* **2019**, *119*, 8701–8780.
[2] P. A. Cox, M. Reid, A. G. Leach, A. D. Campbell, E. J. King, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2017**, *139*, 13156–13165.
[3] V. K. Duong, A. M. Horan, E. M. McGarrigle, *Org. Lett*. **2020**, *22*, 8451–8457.
[4] A. M. Horan, V. K. Duong, E. M. McGarrigle, *Org. Lett*. **2021**, *23*, 9089–9093.
[5] L. Hallen, A. M. Horan, B. Twamley, E. M. McGarrigle, S. M. Draper, *Chem. Commun.* **2023**, *59*, 330-333.
[6] V. E. Becker, E. M. McGarrigle, *Manuscript in preparation.*

P-07

Sulfur- and Sulfone-Bridged *m*,*m*-Heteracalix[4]arenes

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Heteracalix[*n*]arenes[1] (*n* ≥ 4) are macrocyclic compounds, consisting of aromatic units bridged by oxygen, nitrogen, sulfur or other heteroatoms, capable of exhibiting molecular recognition properties.[2] These macrocycles may contain either carbocyclic or heterocyclic rings and their bridging atoms may be found in an *orto*, *meta* or *para* arrangement, or any combination thereof.

As part of our ongoing interest in calixarenes[3] and related aromatic macrocycles[4], we report here on a number of recently investigated sulfur-bridged calixarenes. In more detail, we describe the ionophoric properties of *m*,*m*-tetrathiacalix[2]arene[2]triazines **1a**,**b** towards halides,[5] along with the synthesis and structural features of the newly synthesised *m*,*m*-tetrathia[4]calixarene **2a** and *m*,*m*-tetrasulfone[4]calixarene **2b**.

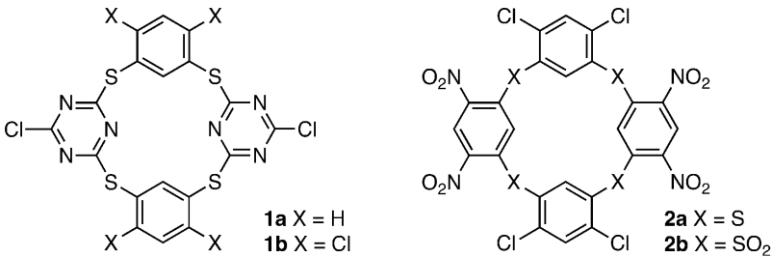

Figure 1. Tetrathiacalix[2]arene[2]triazines **1a**,**b**, tetrathia[4]calixarene **2a** and tetrasulfone[4]calixarene **2b**.

References

[1] M.-X. Wang, *Acc. Chem. Res.* **2012**, *45*, 182–195.
[2] D.-X. Wang, Q.-Y. Zheng, Q.-Q. Wang, M.-X. Wang, *Angew. Chem. Int. Ed.* **2008**, *47*, 7485–7488.
[3] M. F. Parisi, G. Gattuso, A. Notti, I. Pisagatti, S. Pappalardo. Calix[5]arene: from Capsules to Polymers. In *Calixarenes and Beyond*, Eds P. Neri, J. L. Sessler, M-X. Wang, Springer, **2016**, 95–111.
[4] a) C. Capici, D. Garozzo, G. Gattuso, A. Messina, A. Notti, M.F. Parisi, I. Pisagatti, S. Pappalardo, *Arkivoc* viii **2009**, *viii*, 199–211; b) N. Manganaro, G. Lando, C. Gargiulli, I. Pisagatti, A. Notti, S. Pappalardo, M. F. Parisi, G. Gattuso, *Chem. Commun.* **2015**, *51*, 12657–12660.
[5] I. Pisagatti, N. Manganaro, C. F. M. Mirabella, A. Pappalardo, G. Trusso Sfrazzetto, F. Nastasi, A. Notti, M. F. Parisi, G, Gattuso, *Tetrahedron Lett*, **2020**, *61*, 151911.

Sulfur-mediated Cycloaddition Reactions. A Potent Strategy Toward Glycosydic Antigens' Synthesis

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The hetero Diels-Alder reaction between glycans, as electron-rich dienophiles, and α,α'-dioxothiones, as electron-poor dienes, is an efficient strategy to prepare *O*-glycosides stereoselectively. A vast literature has been reported for the synthesis of α- or β-*O*-glycosides by using different glycans and dioxothiones.[1,2] Particularly interesting are derivatives **1**, **2** and **3** (Figure 1) obtained as single chemo-, regio- and stereoisomer.

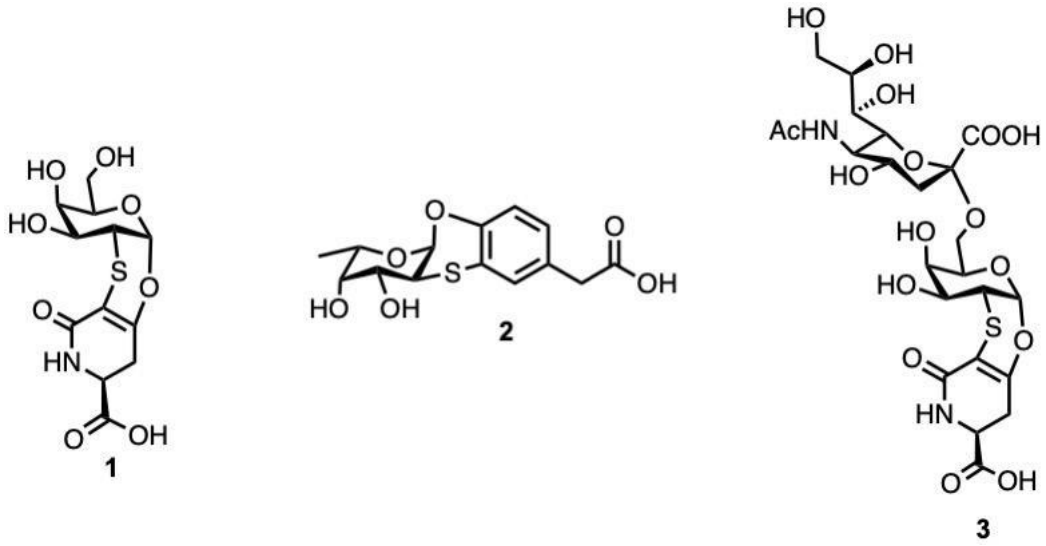

Figure 1. Structures of derivatives **1** - **3**.

Derivatives **1** and **3** are mimetics of MUC-1 Tn and STn antigens endowed with immunostimulant properties,[3,4] while **2** is a good ligand for bacterial lectins with affinity similar to the native ligand.[5]

References

[1] A. Bartolozzi, et al. *Org. Lett*. **2000**, *2*, 251-253.
[2] F. Venturi, et al. *Org. Chem.* **2004**, *69*, 6153–6155.
[3] A. Amedei, et al. *iScience 23*, **2020**, 101250.
[4] F. Papi, et al. *Org. Biomol. Chem*. **2020**, *18*, 7366-7372.
[5] S. Kuhaudomlarp, et al. *Chem. Sci.* **2020***, 47,* 12662–12670.

P-09

2-Azido Sulfoximines as Building Blocks for 3-Amino-Substituted Benzothiadiazine Oxides

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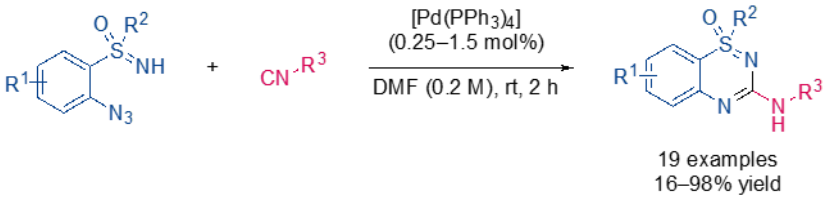
Initially discovered as a toxic side-product in the "agene process",[1] sulfoximines became omnipresent in drug discovery.[2] Based on their unique biophysical properties and high structural diversity they are often considered as bioisosteres of sulfones, sulfonamides and more recently alcohols.[1,2] In this context, academic and industrial research is also focusing on sulfoximidoyl-containing heterocycles such as benzothiadiazine oxides.[1-3]
Herein, we present our studies on the palladium-catalysed reaction of 2-azido sulfoximines with isonitriles for the synthesis of 3-amino-substituted benzothiadiazine oxides. Using [Pd(PPh$_3$)$_4$] as a commercially available and cheap pre-catalyst (0.25 – 1.5 mol%), the desired heterocycles are obtained under ambient reaction conditions in overall excellent yields within short reaction times. Furthermore, dealkylation of *N-tert*-butyl-substituted benzothiadiazine oxides gives access to the amine-free analogues, which could be used for further functionalisations.[4]



Scheme 1. Palladium-catalysed cascade reaction of 2-azido sulfoximines with isonitriles.[4]

Based on our experimental mechanistic studies and previously published experimental and *in silico* investigations,[5] a carbodiimide was proposed as a potential key intermediate.[4]

References

[1] U. Lücking, *Angew. Chem. Int. Ed.* **2013**, *52*, 9399 – 9408.
[2] a) P. Mäder, L. Kattner, *J. Med. Chem.* **2020**, *63*, 14243 – 14275; b) U. Lücking, *Chem. Eur. J.* **2022**, *28*, e202201993; c) M. J. Tilby, M. C. Willis, *Expert Opin. Drug Discovery* **2021**, *16*, 1227 – 1231; d) C. Gnamm, A. Jeanguenat, A. C. Dutton, C. Grimm, D. P. Kloer, A. J. Crossthwaite, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3800 – 3806.
[3] a) Z. P. Shultz, J. M. Lopchuk, *Adv. Heterocycl. Chem.* **2022**, *138*, 61 – 158; b) P. Stoss, G. Satzinger, *Chem. Ber.* **1976**, *109*, 2097 – 2106; c) R. D. Dillard, T. T. Yen, P. Stark, D. E. Pavey, *J. Med. Chem.* **1980**, *23*, 717 – 722; d) R. W. Buckheit Jr., V. Fliakas-Boltz, W. Don Decker, J. L. Roberson, C. A. Pyle, E. L. White, B. J. Bowdon, J. B. McMahon, M. R. Boyd, J. P. Bader, D. G. Nickell, H. Barth, T. K. Antonucci, *Antiviral Res.* **1994**, *25*, 43 – 56; e) G. D. Bartoszyk, D. J. Dooley, H. Barth, J. Hartenstein, G. Satzinger, *J. Pharm. Pharmacol.* **1987**, *39*, 407 – 408.
[4] R. Hommelsheim, S. Bausch, R. van Nahl, J. S. Ward, K. Rissanen, C. Bolm, *Green Chem.* **2023**, *25*, 3021 – 3026.
[5] A. J. Ansari, R. S. Pathare, A. K. Maurya, V. K. Agnihotri, S. Khan, T. K. Roy, D. M. Sawant, R. T. Pardasani, *Adv. Synth. Catal.* **2018**, *360*, 290 – 297.

Synthesis of Heterocyclic Tin Polysulfides Bearing Bulky Ferrocenyl Groups

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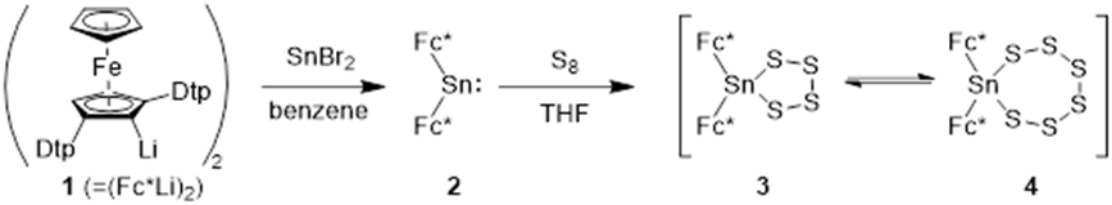
Although transition metal polysulfides are ubiquitous, chemistry of polysulfide compounds of heavier group 14 elements is less developed. It has been reported that the reaction of elemental sulfur with a stannylene, divalent organotin species, affords the corresponding heterocyclic tin polysulfides. Such a heterocyclic tin polysulfide is known as a precursor of stannanethione, tin-sulfur double-bond compounds.[1]
In this study, we have succeeded in the synthesis of heterocyclic tin polysulfide bearing bulky ferrocenyl groups by the sulfurization of bis(ferrocenyl)stannylene **2**. Stannylene **2** was synthesized by the reaction of monolithioferrocene **1**[2] with tin(II) bromide. The reaction of stannylene **2** with elemental sulfur afforded several heterocyclic tin polysulfides. The temperature variable NMR spectra indicated that they are in chemical equilibrium. Recrystallization of the reaction products from diethylether/methanol afforded single crystals suitable for an X-ray diffraction analysis. The results of X-ray diffraction analysis suggested the formation of tetrathiolane **3** and hexathiepane **4**. We will also discuss the desulfurization reaction of this cyclic tin polysulfides in the expectation of the generation of bis(ferrocenyl)stannanethione.



scheme 1. Synthesis of Tin Polysulfides Bearing Bulky Ferrocenyl Groups

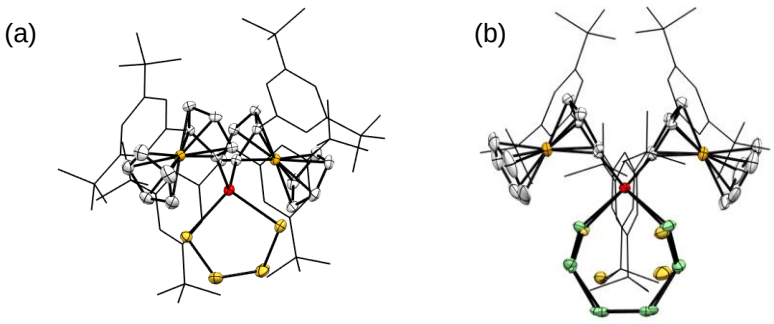


Figure 1. (a) ORTEP drawing (50% probability) of tetrathiolane **3**
(b) ORTEP drawing (50% probability) of disordered structures of **3** and **4**.

References

[1] M. Saito, N. Tokitoh, R. Okazaki, *J. Am. Chem. Soc.* **2004**, *126*, 15572-15582.
[2] T. Sasamori, Y. Suzuki, N. Tokitoh, *Organometallics* **2014**, *33*, 6696-6699.

Lipoic acid as a linker to Auranofin analogue on nanocellulose

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Cellulosic nanomaterials have stimulated interest in the scientific community due to their peculiar properties that make them particularly promising among nanostructured materials. Nanocellulose-based materials are naturally available, from waste materials, at low price and are, generally, characterized by a high biocompatibility.[1] Moreover, nanocellulose can be easily functionalized to produce materials with new properties and applications.

In this work we focused on the use of nanocellulose as a drug delivery support. Our aim is the functionalization of nanocellulose crystals with lipoic acid.

Lipoic acid will be used for the grafting of the pharmacophore of Auranofin, the gold complex Et_3PAuCl. As well, the presence of a glucose unit linked by a short PEG chain will enhance the selectivity of internalization in tumour cells.

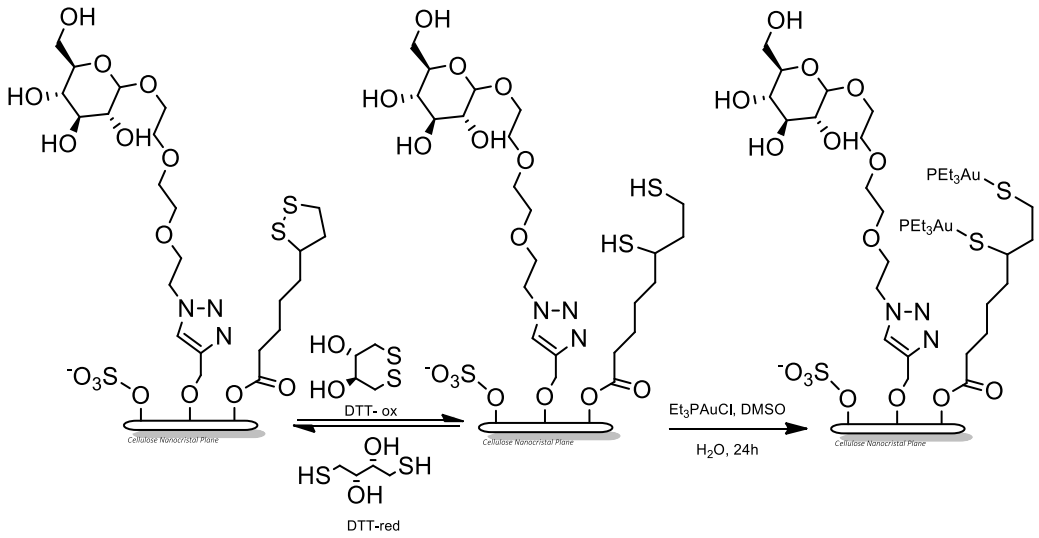

Figure 1. functionalization of the nanocellulose drug support.

References

[1] B. Thomas, M.C. Raj, J. Joy, A. Moores, G.L. Drisko, C. Sanchez, *Chem. Rev.*, **2018**, *118*, 11575-11625.

Acknowledge

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P-12

Chiroptical and Magneto-Optical Investigation of a Hetero[4]Helicene Radical Cation

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Dithiabridged triarylamine hetero[4]helicenes are an interesting class of chiral compounds characterized by a high racemization barrier, making them an attractive material for several applications.[1,2] Furthermore, they are characterized by rich redox chemistry, which allows for the reversible oxidation of the compounds. The obtained radical cations are stable at room temperature, allowing the isolation of the two configurationally stable enantiomers. In this contribution, we report on the use of chiroptical spectroscopies with the aim of investigating the effect of oxidation on the chiroptical responses considering ECD, VCD, NIR-CD, and MCD. In particular, while several vibrational circular dichroism (VCD) studies have been reported on radicals with transition metals,[3] the characterization of purely organic open-shell systems with VCD is still scarce. Oxidation of the molecular system shifts the first electronic transition towards the Near-IR (NIR) region at approximately 1250 nm and shows a variety of features in the visible range. The combination of these spectroscopic techniques and computational methodologies rooted in density functional theory allowed us a better comprehension of the spectroscopic properties of the systems and to shed some light on the chiroptical properties accessible via redox-switch (see Figure 1).

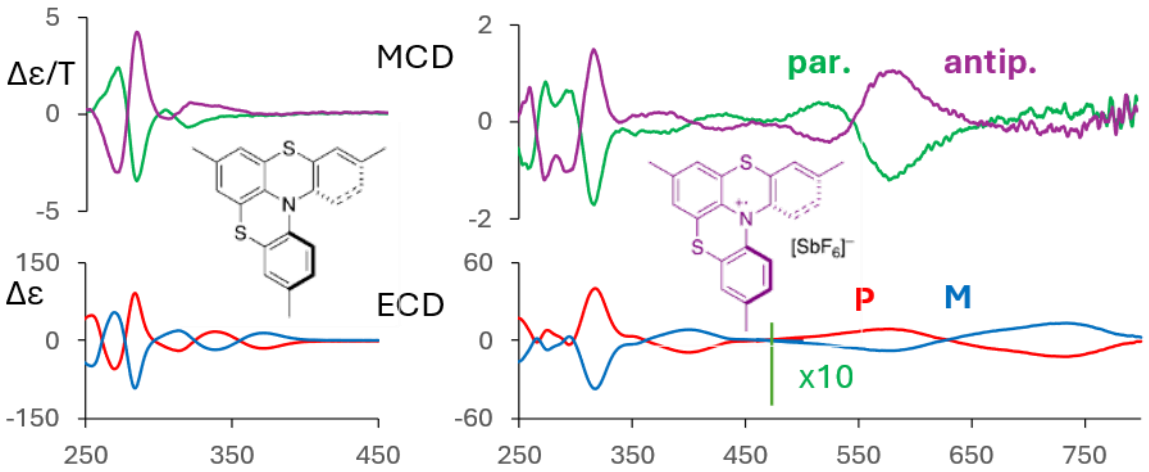

Figure 1. CD and MCD spectra of neutral (left) and cationic (right) [4]Helicene

References

[1] Menichetti, S. *et al. Chem. Commun.* **51**, 11452–11454 (2015).
[2] Longhi, G. *et al. J. Photochem. Photobiol. Chem.* **331**, 138–145 (2016).
[3] Nafie, L. A. *J. Phys. Chem. A* **108**, 7222–7231 (2004).

P-13

A library of sulfur-containing glycomimetics as next-generation of precision therapeutics in cancer treatment

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Since their discovery [4+2] inverse electron-demand hetero Diels-Alder (ihDA) reactions have prompted the interest of chemists worldwide.[1] Among them, ihDA reactions that include sulfur containing heterodienes have been widely employed to access to libraries of structurally different bioactive compounds that have found applications in biomedical field.[2] In this regard, glycomimetics, molecules that mimic the structural and functional features of natural carbohydrates, have been prepared by ihDA using glycals as electron-rich dienophiles.[2b-c] Today, these compounds are considered as valuable tools for advancing our understanding of the glyco-code and as therapeutics for a great variety of diseases.[3] Thus synthetic strategies that allow to easily access to such compounds with high degree of structural diversity are highly demanding.[2c, 3b]

In this context, owing to the support of a multidisciplinary and international network of collaborators,[4] we have recently provided a significant advancement in the field either in terms of the study of the reactivity of the glycals in the ihDA and in the implementation of the biological applications of the resulting sulfur-containing glycomimetics. In this communication, we describe our last contribution in the field in providing new insights on either the reactivity of glycals bearing 'unconventional' protective groups and on the identification of new sulfur-enriched heterodienes.[4] Our data foster the understanding of the mechanistic details and the reactivity of glycals/heterodienes in the ihDA and further widen the structural diversity of the glycomimetics that can be prepared. Unpublished data on the implications of our recent insights in the development of precision therapeutics in cancer settings will be also described.

References

[1] B. L. Oliveira, Z. Guo and G. J. L. Bernardes, *Chem. Soc. Rev.*, **2017**, 46, 4895–4950.

[2] a) C. Viglianisi, M. G. Bartolozzi, G. F. Pedulli, R. Amorati and S. Menichetti *Chem. Eur. J*, **2011**, 12396–12404. b) B. Richichi, A. Imberty, E. Gillon, R. Bosco, I. Sutkeviciute, F. Fieschi and C. Nativi, *Org. Biomol. Chem.*, **2013**, 11, 4086–4094. c) M. Cacciarini, S. Menichetti, C. Nativi and B. Richichi, *Curr. Org. Synth.*, **2007**, 4, 47–57.

[3] a) B. Ernst and J. L. Magnani, *Nat. Rev. Drug Discov.*, **2009**, 8, 661–677. b) A. Tamburrini, C. Colombo and A. Bernardi, *Med. Res. Rev.*, **2020**, 40, 495–531.

[4] a) K. C. Martin, J. Tricomi, F. Corzana, A. García-García, L. Ceballos-Laita, T. Hicks, S. Monaco, J. Angulo, R. Hurtado-Guerrero, B. Richichi and R. Sackstein, *Chem. Commun.*, **2021**, 57, 1145–1148. b) G. Biagiotti, L. Legnani, G. Aresta, M. A. Chiacchio and B. Richichi, *Eur. JOC*, **2022**, e202200769. c) R. Sackstein, B. Richichi and K. Martin, US20220211734A1, **2020**

Acknowledge

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When Curcumin lights up Sulfenic acid

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Sulfenic acids are useful intermediates for the formation of biologically important functional groups, such as sulfoxides, sulfones, disulfane moieties. Disulfides are regarded as dynamic-covalent bonds in biology.[1] In cells, they are stable in a redox environment of the extracellular area and are cleaved intracellularly. In continuing our research on the generation of sulfenic acids bearing natural residues, we have developed a procedure to obtain the sulfenyl moiety linked to the curcumin skeleton. Curcumin is the main yellow component of *Curcuma longa* L., of which is. It is a substance with numerous pharmacological properties and promising fields of applications. Despite its biomedical properties, our interest in curcumin was triggered by its fluorescent properties, that have been widely investigated.[2]

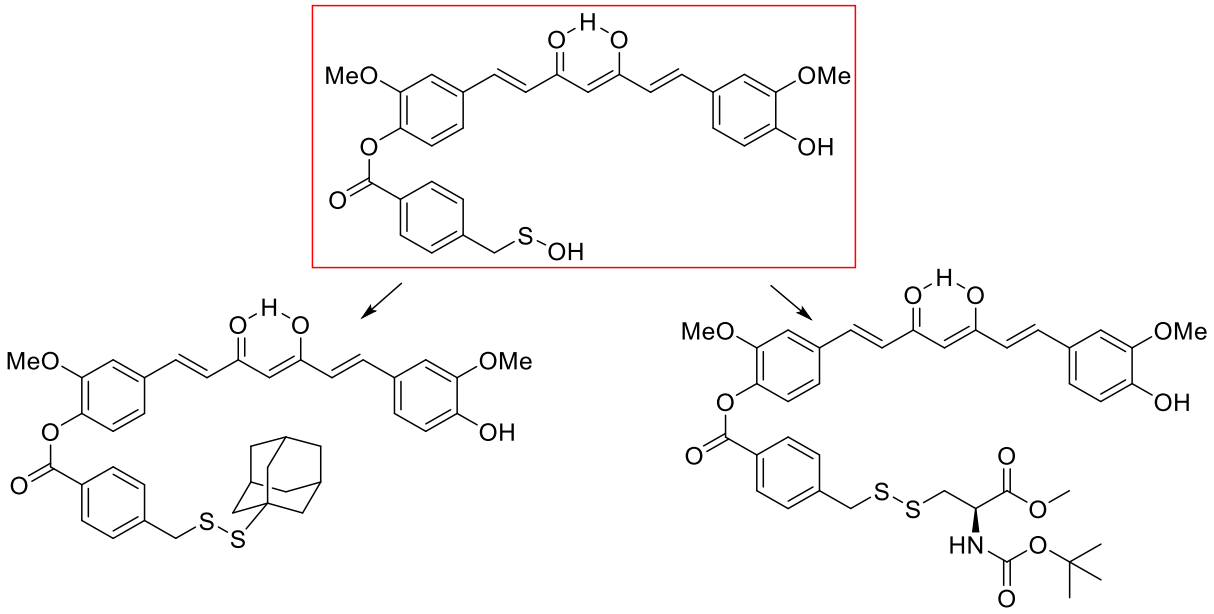

Figure 1. Curcumin-derived compounds.

In this poster communication we will describe how we achieved the generation of a curcumin-derived sulfenic acid and its involvement in: i) the formation of disulfide bonds with Cys-SH and GluSH, as biocompatible luminescent probe and potential sensor for the detection of biothiols,[3] ii) the linkage with adamantane (ADA)-SH and subsequent formation of the inclusion complex with a specific amphiphilic cyclodextrin for the synthesis of a curcumin drug delivery systems (Figure 1).

References

[1] C.M.A. Gangemi, E. D'Agostino, M. C. Aversa, A. Barattucci, P. M. Bonaccorsi,*Tetrahedron*, **2023**, *143*, 133550-133568.
[2] C.F. Chignell, P. Bilski, K.J. Reszka, A.G. Motten, R.H. Sik, T.A. Dahl, *Photochem. Photobiol*. **1994**, *59*, 295-302.
[3] A. Barattucci, T.M.G. Salerno, F.H. Kohnke, T. Papalia, F. Puntoriero, P. Bonaccorsi *New J. Chem*., **2020**,*44*, 19508-19514.

β-Lactams as inhibitors of SARS-CoV-2 M^{pro}

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The SARS-CoV-2 main protease (M^{pro}), which contains a cysteine-histidine catalytic dyad, plays a pivotal role in the viral replication process of SARS-CoV-2, thus making it an attractive therapeutic target[1]. Building on the proven efficacy of β-lactams as inhibitors of nucleophilic serine enzymes[2], our research has explored the potential of β-lactam derivatives, including penicillins, as potent inhibitors of viral cysteine proteases like M^{pro}. Specifically, we have developed low micromolar M^{pro} inhibitors (**Figure 1**) derived from clinically used antibacterial β-lactam drugs[3]. These compounds demonstrated that they can significantly inhibit the enzymatic activity of SARS-CoV-2 M^{pro} through the formation of a stable acyl-enzyme complex, as confirmed by mass spectrometric and crystallographic studies[3,4]. Our findings reveal the therapeutic potential of β-lactams as effective inhibitors of M^{pro}, offering a promising pathway for the development of novel antiviral treatments.

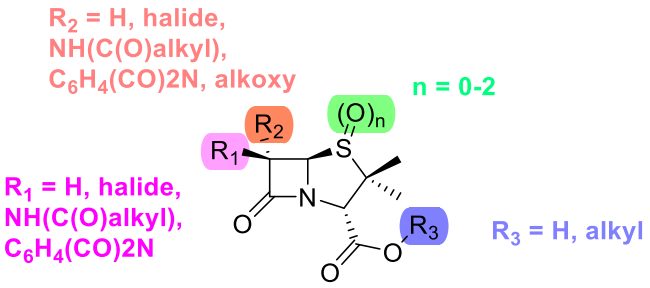

Figure 1. β-Lactam derivatives that can inhibit SARS-CoV-2 M^{pro}.

References

[1] Z. Jin *et al.*, *Nature,* **2020**, *582*, 289 – 293
[2] R.G. Finch, D. Greenwood, S.R. Norrby, R.J. Whitley, *Antibiotics and Chemotherapy*, W.B. Saunders, London, **2010**, pp. 170 – 225
[3] T.R. Malla *et al.*, *J. Med. Chem.*, **2022**, *65*, 7682 – 7696
[4] T.R. Malla *et al.*, *Chem. Commun.*, **2021**, 57, 1430 – 1433

P-16

Stereoselective Synthesis of Chloroalkene Dipeptide Isosteres with Sulfur-Centered Chirality via Remote Asymmetric Induction

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Alkene dipeptide isosteres[1], substituting the peptide bond with a structurally similar carbon-carbon double bond, confer hydrolysis resistance to peptides, making them valuable bioisosteres of peptide bonds. Chloroalkene Dipeptide Isosteres (CADIs) [2], which incorporate a chlorine atom as a carbonyl oxygen equivalent, allow for precise control over the dihedral angles of the peptide chain through a synergistic interplay of steric and stereoelectronic effects.[3] This property is beneficial for developing enzymatically stable and structurally defined peptidomimetics[4,5].

Herein, we present our investigation on the stereoselective synthesis of CADIs by diastereoselective allylic alkylation[5]. A key to our developed synthetic method is the 1,6-remote asymmetric induction based on the sulfur-centered chirality. DFT calculations highlight the critical role of hydrogen-bonding interactions between the α-hydrogen of electrophiles and the lone pair of the sulfur atom in the alkylation step, essential for achieving high stereoselectivity. This approach facilitates the rapid construction of Xaa-Asp-type CADIs in high yields, with excellent (*Z*)-selectivity and diastereoselectivity. The presentation will cover detailed reaction design, substrate scope, mechanistic insights including DFT calculations, and potential applications to biologically active peptides.

References

[1] A. Choudhary, R. T. Raines, *ChemBioChem*, **2011**, *12*, 1801-1807.
[2] H. Tamamura, T. Kobayakawa, *Meth. Enzymol.,* **2021**, *656*, 191-239.
[3] Y. Kodama, S. Takeo, J. Fujimoto, K. Sato, N. Mase, T. Narumi, *J. Org. Chem.*, **2022**, *87*, 2167-2177.
[4] H. Okita, Y. Kato, T. Masuzawa, K. Arai, S. Takeo, K. Sato, N. Mase, T. Oyoshi, T. Narumi, *RSC Adv*., **2020**, *10*, 29373-29377.
[5] T. Narumi, D. Toyama, J. Fujimoto, R. Kyan, K. Sato, K. Mori, J. T. Pearson, N. Mase, K. Takayama, *Chem Commun.*, **2024**, *60*, 3563-3566.

P-17

Synthesis of sulfur-containing *N*-heterocycles by mild reactions conditions: tetrazolo[1,5-*α*]quinolines and pyrazoles

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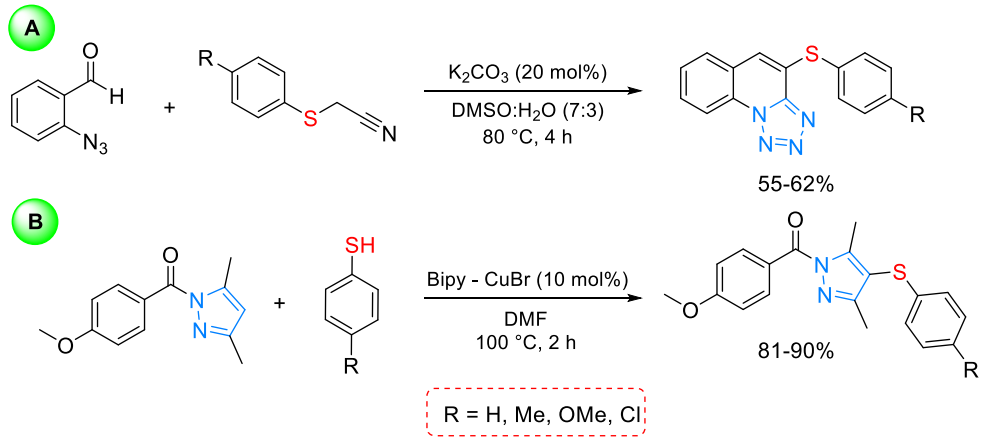
The development of new multifunctional molecules from the combination of two or more different pharmacophores in one molecule has been used as an effective strategy to design new drugs and promising results with different classes of compounds have been described.[1] Chalcogen-tetrazolo[1,5-*α*]quinolines and chalcogen-pyrazoles constitute interesting classes of molecules, which combine the importance of these nucleous[2,1] with an organochalcogen moiety.[3] Sulfur is an essential element, playing important roles in metabolic pathways, and the interest in its chemistry and pharmacology has increased in this century.[4] Based in our interest in developing new strategies to prepare potentially bioactive organochalcogen compounds, we propose a general methodology to access valuable 4-(phenylthio)tetrazolo[1,5-*α*]quinolines, through the intramolecular cyclocondensation between 2-azidobenzaldehyde and phenylthioacetonitriles using K_2CO_3 as base in a mixture of DMSO/H_2O as solvent (Scheme 1A). At the same time, the synthesis of thio-pyrazoles was also possible from the reaction between (3,5-dimethyl-1*H*-pyazole)(4-methoxyphenyl)methanone and substituted thiols mediated by Bipy-CuBr and using DMF as solvent in short reaction time (Scheme 1B). These methodologies are in accordance with some of the principles of Green Chemistry and presented a good functional group tolerance.



Scheme 1. Sulfur-containing *N*-heterocycles synthesized: (**A**) 4-(arylthio)tetrazolo[1,5-*α*]quinolines and (**B**) 4-(arylthio)-1*H*-pyrazoles.

References

[1] D.H. Oliveira, F.S. Sousa, P.T. Birmann, D. Alves, R.G. Jacob, L. Savegnago, *Pharmacol. Rep.* **2020**, *72*, 36–46.
[2] A.R.B. Tazeem, X. Han, F. Athar, *ChemistrySelect* **2016**, *1*, 5917–5922.
[3] A. Pinheiro, F. Busatto, B. Schaefer, P. Tomasini, I. Nunes, T. Machado, R. Cargnelutti, T. Aquino, K. Ferreira, A.M. Casaril, R.G. Jacob, L. Savegnago, D. Hartwig, J. Saffi, *J. Inorg. Biochem* **2022**, *237*, 112013.
[4] (a) T.A. Rouault, *Biometals* **2019**, *32*, 343–353. (b) D. Hartwig, J.E.R. Nascimento, L. Bettanin, T.B. Aquino, R.G. Jacob, E.J. Lenardão, *Curr. Green Chem.* **2020**, *7*, 179–200. (c) P.T. Birmann, A.M. Casaril, L. Abenante, F. Penteado, C.A. Brüning, L. Savegnago, E.J. Lenardão, *Curr. Med. Chem*. **2023**, *30*, 2357–2395.

Elucidation of Reactivity of a Cysteine Sulfenyl Iodide Utilizing a Molecular Cradle

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Cysteine sulfenyl iodides (Cys–SI) have attracted much interest in view of their important role as intermediates in various oxidative modification of cysteine thiol (Cys–SH) in proteins.[1] However, experimental elucidation of reactivity of Cys–SI remains challengeing because of their inherently instability due to disproportionation reaction to give disulfides and iodine. Recently, we have reported the isolation of cysteine sulfenic acid (Cys–SOH) through the use of a nano-sized molecular cardle as an *N*-terminal protecting group (denoted as a Bpsc group).[2] Moreover, we have also reported the synthesis of an isolable Cys–SI utilizing a Bpsc group.[3] Herein, we report the mechanistic study of reactions of the isolable Cys–SI with various nucleophiles. Nucleophilc reactions toward oxidatively modified sulfenyl compounds typically occur at their sulfur atom. The reactions of the isolable Cys–SI **1** with an oxygen nucleophile such as sodium hydroxide (**2a**), a nitrogen nucleophile such as lysine derivative **2b**, or a carbon nucleophile such as dimedone (**2c**), were found to produce the corresponding sulfenyl compounds **3** through the canonical pathway. However, the reaction of Cys–SI **1** with Cys–SH derivative **4** predominantly produced cysteine thiol **5**. When Cys–SH **4** was replaced by $BpqCH_2SH$ (**6**) having a bulky group,[4] the reaction of Cys–SI **1** with thiol **6** produced Cys–SH **5** and $BpqCH_2SI$ (**7**). These results indicate that the reaction of Cys–SI with hard nucleophiles such as oxygen, nitrogen, and carbon species proceeds on the sulfur atom of Cys–SI through the canonical pathway while the reaction of Cys–SI with soft nucleophiles such as sulfur species occur at the iodine atom of Cys–SI through the novel pathway, i.e., transiodination. Moreover, the reactions of sulfenyl chloride (Cys–SCl) **8**, sulfenyl bromide (Cys–SBr) **9**, or selenenyl iodide (Sec–SeI) **10** with Cys–SH **4** occured at their chalcogen atoms through canonical pathway. Such unique reactivity of Cys–SI is considered to be caused by the effect of σ-hole on the iodine atom.

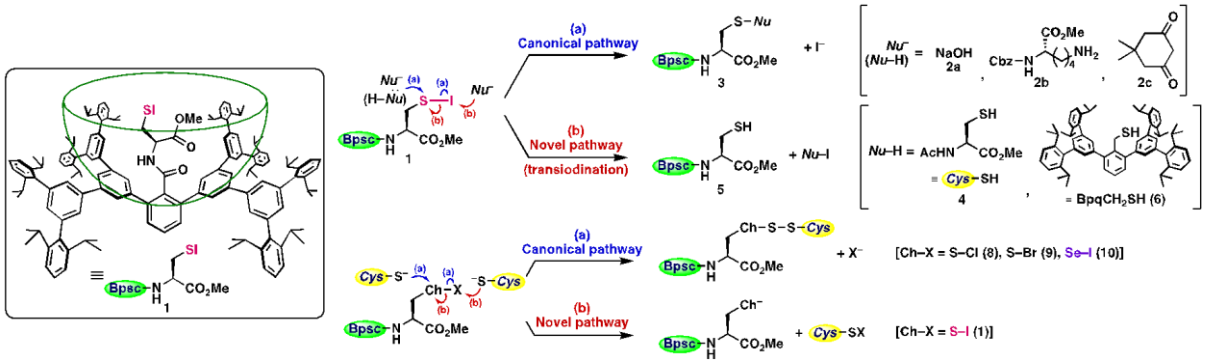

Figure 1.

References

[1] (a) H. Fraenkel-Conrat, *J. Biol. Chem.* **1955**, *217*, 373-381. (b) E. L. Thomas, T. M. Aune, *Biochemistry* **1977**, *16*, 3581-3586. (c) N. A. Kratochwil, A. I. Ivanov, M. Patriarca, J. A. Parkinson, A. M. Gouldworthy, P. d. S. Murdoch, P. J. Sadler, *J. Am. Chem. Soc.* **1999**, *121*, 8193-8203.

[2] T. Sano, R. Masuda, S. Sase, K. Goto, *Chem. Commun.* **2021**, *57*, 2479-2482.

[3] S. Otaka, T. Sano, S. Sase, S. Kuwano, K. Goto, *29th International Symposium on the Organic Chemistry of Sulfur*, PB10v, Gueiph, Canada (July 2022).

[4] S. Sase, Y. Aoki, N. Abe, K. Goto, *Chem. Lett.* **2009**, *38*, 1188-1189.

P-19

Intramolecular Cyclization of *N*-Cyano Sulfoximines for the Synthesis of Thiadiazine 1-Oxides and Thiadiazinone 1-Oxides

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Thiadiazine 1-oxide and thiadiazinone 1-oxide, a benzene-fused sulfoximine moiety, displayed interesting biological properties. Due to these properties, several synthetic strategies have been studied to further develop these derivatives. Although these approaches seem to be quite applicable, these procedures have several drawbacks such as noncommercial amination reagents and expensive transition-metal catalysts. Consequently, it is strongly required a practical method of synthesizing biologically active thiadiazine 1-oxide and thiadiazinone 1-oxide.

In this research, we have developed a new one-pot process for the synthesis of thiadiazine 1-oxides and thiadiazinone 1-oxides.[1,2]

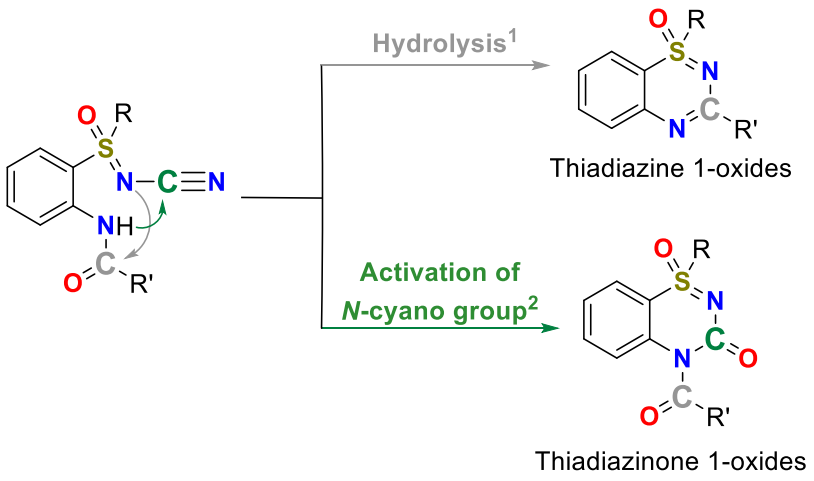

Figure 1. One-pot synthesis of thiadiazine 1-oxides and thiadiazinone 1-oxides.

References

[1] I. S. Oh, Y. J. Seo, J. Y. Hyun, H. J. Lim, D. -H. Lee, S. J. Park, *ACS Omega*, **2022**, *7*, 2160 – 2169.
[2] Y. J. Seo, E. Kim, I. S. Oh, J. Y. Hyun, J. H. Song, H. J. Lim, S. J. Park, *RSC Adv.*, **2023**, *13*, 24445 – 24449.

P-20

Synthesis and characterization of benzodithiophene-based atropisomers

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Heterobiaryl atropisomers are inherently chiral molecules that find numerous applications in manifold fields,[1] including asymmetric synthesis, drug discovery, material sciences and, more recently, in enantioselective electroanalysis. Our continuing interest in the study of intrinsically chiral thiophene-based systems,[2-3] let us to look for a versatile procedure to prepare a new class of benzo[1,2-*b*:4,3-*b*']dithiophene-based atropisomers, exploting the well-known palladium chemistry starting from the 1-bromo-benzodithiophene **1** as key intermediate (Figure 1).

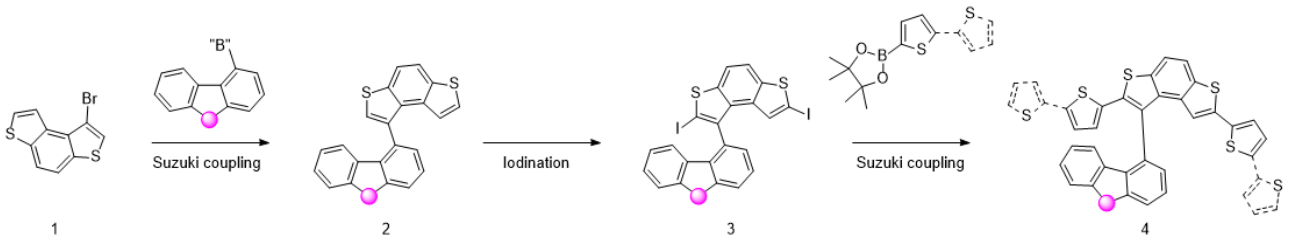

Figure 1. Synthesis of benzo[1,2-*b*:4,3-*b*']dithiophene-based atropisomers.

In this communication we present the synthesis of a library of benzo[1,2-*b*:4,3-*b*']dithiophene-based heterobiaryl atropisomers **2**-**4**, containing carbazole, dibenzofuran, dibenzothiophene, spirobifluorene units (Figure 1). The optical and structural properties of these molecules have been investigated by absorption/emission measurements and X-ray analyses. Moreover, a preliminary electrooligomerization study of functionalized atropisomers **4** has been performed, to evaluate their potential use as chiral sensors in enantioselective electrochemistry.

References

[1] J.K. Cheng, S.-H. Xiang, S. Li, L. Ye, B. Tan, *Chem. Rev*. **2021**, *121*, 4805 – 4902.
[2] V. Pelliccioli, D. Dova, C. Baldoli, C. Graiff, E. Licandro, S. Cauteruccio, *Eur. J. Org. Chem.*, **2021**, 383 – 395.
[3] V. Pelliccioli, F. Cardano G. Renno, F. Vasile, C. Graiff, G. Mazzeo, A. Fin, G. Longhi, S. Abbate, A. Rossetti, C. Villani, G. Viscardi, E. Licandro, S. Cauteruccio, *Catalysts*, **2022** ,*12*, 366.

P-21

Azasugar-based Sulfonamides as selective carbonic anhydrase inhibitors: probing the role of the triazole linker

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Carbonic Anhydrases (CAs; EC 4.2.1.1) are zinc metalloenzymes which play a crucial role both in physiological and pathological processes in humans. Therefore, the discovery of selective inhibitors towards one specific human isozyme (hCA) is an important target for drug development. By following the "sugar approach"[1] and considering our recent disclosure of two selective hCAs inhibitors based on glycomimetic-sulfonamide conjugates[2], new compounds **1** have been synthesized[3] by conjugating several benzenesulfonamides to a triazole-armed azasugar with different linkers (such as thioureido, ureido, amido and amine groups). These compounds were found to be potent selective inhibitors; some of them showed interesting data towards the therapeutically relevant hCAs II and VII isoforms involved in neuropathic pain. Based on the X-ray studies of the inhibitor-enzyme complexes, new analogues **2** lacking the triazole linker were synthesized in order to evaluate the influence of the heterocycle moiety on the enzymatic inhibition (Figure 1).

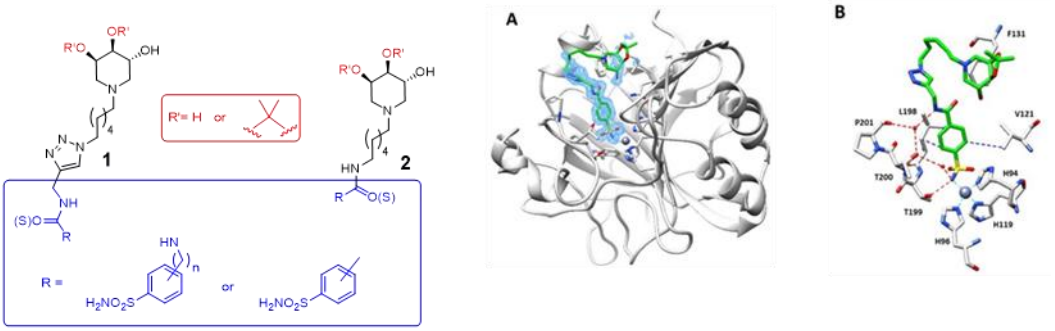

Figure 1. New azasugar-sulfonamide compounds **1**-**2** and X-ray studies (A and B).

Furthermore, the new compound series **1**-**2** were tested on different isoforms of bacterial carbonic anhydrase, with the aim of selectively inhibiting bacterial isoforms compared to human ones.

References

[1] J-Y. Winum, P. A. Colinas, C. T. Supuran, *Bioorg. Med. Chem. Lett.,* **2013**, *21*, 1419-1426.
[2] D. Pratesi, C. Matassini, A. Goti, A. Angeli, F. Carta, C. T. Supuran, R. Spanevello, F. Cardona, *ACS Med. Chem. Lett.,* **2020**, 727-731.
[3] D. Pratesi, A. Sodini, C. Matassini, F. Cardona, A. Angeli, F. Carta, M. Ferraroni, C.T. Supuran, A. Goti, *Eur. J. Org. Chem.,* **2021**, 2604-2614.

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The Nature and Chemical Utility of Proximal Boron Functionalities on the S-Alkylation of Sulfenic Acid Anions

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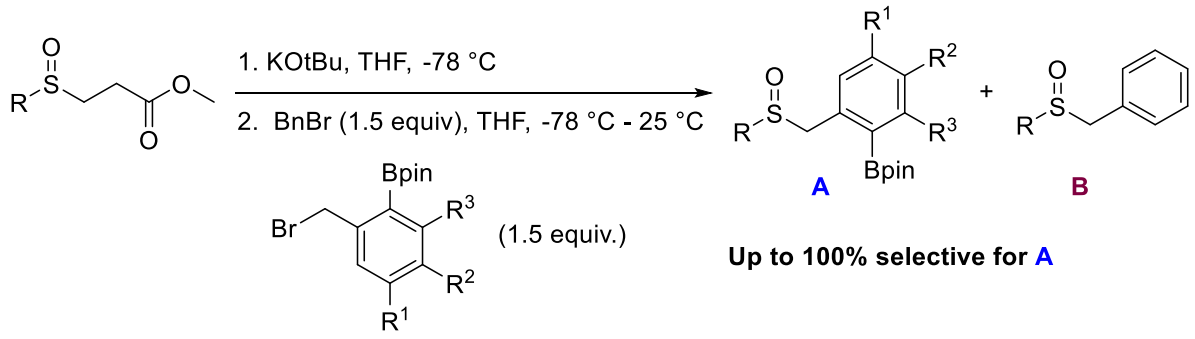
The S-functionalization chemistry of sulfenic acid anions, also known as sulfenate anions, represents an emerging method for the preparation of sulfoxides. Nearby functional groups can often influence the S-functionalization chemistry of sulfenate anions through non-bonding interactions.[1] Recently, several reports have illustrated the combination of the Lewis acidity of trivalent boron and Lewis basicity of sulfinyl groups to perform interesting chemistry.[2-4] Among these reports is a study by Benkovic and coworkers who investigated the reversible complexation of the oxygen of a sulfenate anion with the boron atom of boronic acids and a benzoxaborole.[2] This report illustrated that a reversible R-S-O-B bond forms between the sulfenate anion and the boron atom indicating that a proximal boron functional group could potentially influence the S-functionalization chemistry of sulfenate anions.[2] We decided to investigate this R-S-O-B interaction to probe if the initial complexation of a sulfenate oxygen to boron could direct and accelerate the S-alkylation chemistry of sulfenate anions. To date, 20 competition sulfenate alkylations have been performed between borylated and non-borylated electrophiles with the reactions being up to 100% selective for the boron containing electrophile. In the case of the aryl sulfenate anions, the selectivity of the reaction was directly dependent on the electronic effects on the sulfenate anion and thus Hammett analysis was performed to ascertain the origin of this selectivity. Two internal competition reactions have also been investigated and these reactions have been 100% selective for the more proximal electrophilic position with respect to the boron. The full details of our investigations are presented in the poster.



Scheme 1. General competition experiment investigating the effect of a proximal boron functionality on the S-alkylation chemistry of sulfenate anions.

References

[1] A. G. Durant, E. A. Nicol, B. M. McInnes, A. L. Schwan, Org. Biomol. Chem. **2022**, *20*, 649 – 657.
[2] C. T. Liu, S. J. Benkovic, *J. Am. Chem. Soc.* **2013**, *135,* 14544 – 14547.
[3] M. Čubiňák, V. Eigner, T. Tobrman, *Adv. Synth. Catal*. **2018**, *360*, 4604 – 4614.
[4] F. Takahashi, K. Nogi, H. Yorimitsu, *Eur. J. Org. Chem*., **2020**, 3009 – 3012.

P-23

Examining the Effect of Proximal Chiral Boronate Esters on the Stereoselective Alkylation of Sulfenate Anions

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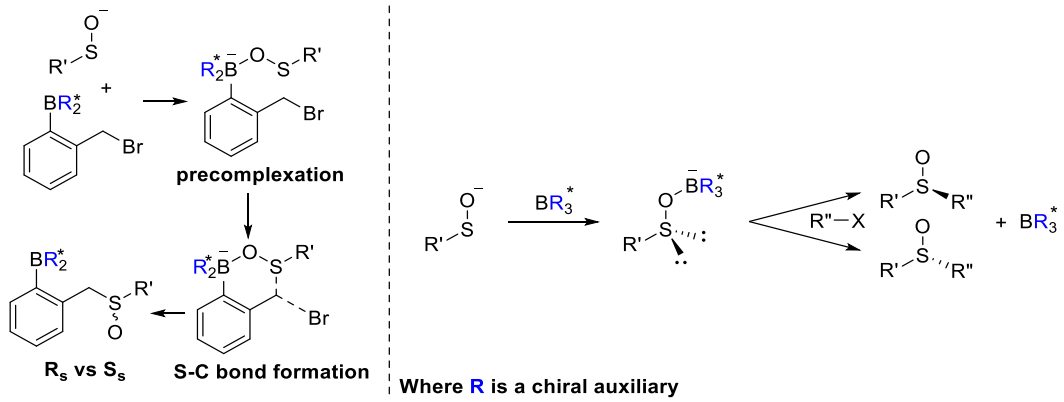
The stereoselective synthesis of sulfoxides has been at the forefront of organosulfur chemistry in recent years and a primary interest of those investigating the S-alkylation chemistry of prochiral sulfenate anions.[1] While the synthesis of enantiomerically and diastereomerically enriched sulfoxides has mostly centered around methods involving transition metal catalysis,[1] some recent reports have stereoselectively generated sulfoxides without expensive transition metals. The Perrio and Schwan groups were able to synthesize diastereomerically enriched sulfoxides via the S-alkylation of sulfenate anions generated with pendant chiral amine functionalities.[2,3] Additionally, the Perrio and Tan groups were able to stereoselectively synthesize sulfoxides from sulfenate anions using chiral phase transfer cinchonidinium and pentanidium salts.[4-5] With recent reports illustrating that reversible R-S-O-B bond formation can occur between a sulfenate anion and a trivalent boron species,[6] it was thought that a proximal chiral boron functionality could lead to the stereoselective S-alkylation of sulfenate anions. We decided to investigate this by performing S-alkylation reactions of sulfenate anions with chiral boronate containing electrophiles and by introducing chiral boron-based Lewis acids into a traditional sulfenate S-alkylation reaction to probe if the chiral boron will direct the stereochemical outcome of the reaction. To date, the S-alkylation of sulfenate anions with chiral boronate containing electrophiles has synthesized sulfoxides with diastereomeric ratios up to 84:16 and the presence of chiral boron containing Lewis acids in traditional sulfenate alkylation reactions have produced sulfoxides with moderate enantiomeric excesses.



Scheme 1. Effect of Chiral boron species on the S-alkylation of sulfenate anions.

References

[1] A. B. Riddell, M. R. A. Smith, A. L. Schwan, *J. Sulfur Chem.* **2022**, 1 – 53.
[2] F. Sandrinelli, S. Perrio, M-T. Averbuch-Pouchot, *Org. Lett*. **2002**, *4*, 3619 – 3622.
[3] S. C. Söderman, A. L. Schwan, *J. Org. Chem*. **2013**, *78*, 1638 – 1649.
[4] F. Gelat, A-C. Gaumont, S. Perrio, *J. Sulfur Chem*. **2013**, *34*, 596 – 605.
[5] L. Zong, X. Ban, C. W. Kee, C-H. Tan, *Angew. Chemie Int. Ed.* **2014**, *53*, 11849 – 11853.
[6] C. T. Liu, S. J. Benkovic, *J. Am. Chem. Soc.* **2013**, *135,* 14544 – 14547.

Expanding the toolbox of S(VI) electrophiles for covalent ligand discovery

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The large commercial success of cysteine-targeted covalent inhibitors has renewed interest in covalent drug discovery.[1] In order to expand the number of proteins that can be targeted with this covalent approach, we aim to explore the development of novel S(VI) electrophiles to target alternative nucleophilic amino acid residues. The aza analogues of sulfonamides, the sulfonimidamide and the sulfondiimidamide are emerging as viable functionalities and offer unique advantages over more developed motifs: unexplored chemical space, tunable basicity and solubility, and are stereogenic at sulfur.[2-4] A synthetic route to vinyl sulfondiimidamide derivatives has been developed utilising an amine elimination by *N*-oxide formation. Various protecting groups and conditions have been examined. A small library of S(VI) electrophiles has been synthesised utilising the developed method and reactivity trends within different S(VI) electrophile families with amino acid nucleophiles will be explored.

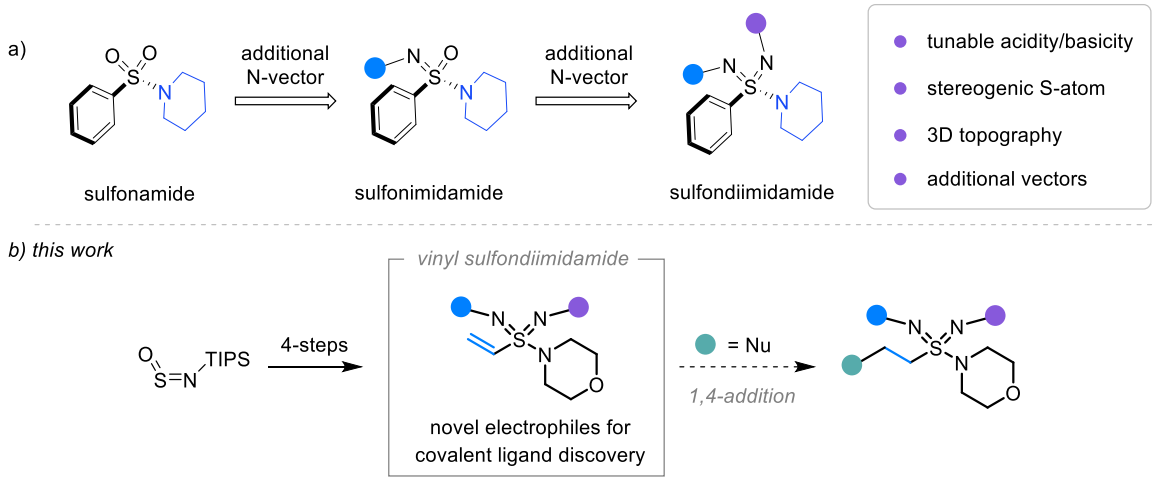

Figure 1. a) Benefits of sulfondiimidamides, b) Synthetic route towards vinyl sulfondiimidamides and their use as electrophilic warheads.

References

[1] S. E. Dalton, S. Campos, *ChemBioChem*, **2020**, *21*, 1080 – 1100.
[2] P. K. Chinthakindi, T. Naicker, N. Thota, T. Govender, H. G. Kruger and P. I. Arvidsson, *Angew. Chem. Int. Ed.*, **2017**, *56*, 4100 – 4109.
[3] Z.-X. Zhang, C. Bell, M. Ding and M. C. Willis, J. Am. Chem. Soc., **2022**, *144*, 11851 – 11858.
[4] Z.-X. Zhang and M. C. Willis, Chem, **2022**, *8*, 1137 – 1146.

Fast one-pot synthesis of aza-S(VI) fluorides from sulfinyl amines

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Hexavalent sulfur fluorides are strategic electrophilic reagents in organic synthesis enabling the linkage of S-O, S-N and S-C bonds[1]. While the preparation and use of sulfonyl fluorides have been widely explored, very little information about the synthesis and reactivity of sulfonyl fluoride aza-isosters, namely sulfonimidoyl fluorides and sulfondiimidoyl fluorides, is currently available[2,3]. Moreover, these compounds can be prepared through lengthy and time-consuming synthetic routes, that often require the generation of more reactive intermediates such as aza-S(VI) chlorides[4], or gaseous reagents[5]. Considering the great potential of such S(VI) derivatives in enabling the straightforward preparation of sulfur pharmacophores, here we present a fast one-pot synthesis of both sulfonimidoyl fluorides and sulfondiimidoyl fluorides starting from sulfinyl amines. The transformations proceed via nucleophilic addition of organometallic reagents to sulfinyl amines and sulfurdiimides[6,7], in turn prepared in situ from sulfinyl amines, followed by subsequent quenching with an electrophilic fluorine source. This process affords the products within a few minutes. Further reactions of such aza-S(VI) fluorides have also been investigated, disclosing their synthetic utility in the preparation of diverse S(VI) compounds.

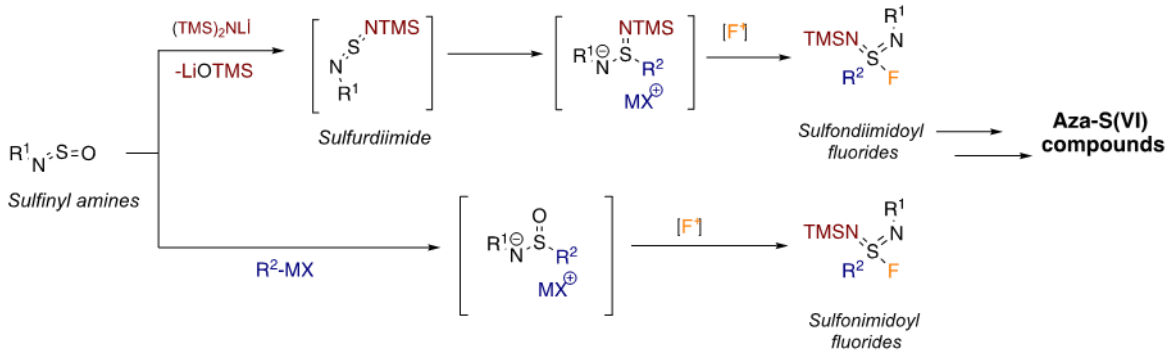

Figure 1. One-pot preparation of sulfonimidoyl fluorides and sulfondiimidoyl fluorides

References

[1] D. Zeng, Y. Ma, W. Deng, M. Wang, X. Jiang, *Angew. Chem. Int. Ed.* **2022**, *61*, DOI 10.1002/anie.202207100.
[2] S. Greed, E. L. Briggs, F. I. M. Idiris, A. J. P. White, U. Lücking, J. A. Bull, *Chem. Eur. J.* **2020**, *26*, 12533.
[3] Z.-X. Zhang, M. C. Willis, *Chem* **2022**, *8*, 1137.
[4] R. Kowalczyk, A. J. F. Edmunds, R. G. Hall, C. Bolm, *Org. Lett*. **2011**, *13*, 768.
[5] B. Gao, S. Li, P. Wu, J. E. Moses, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2018**, *57*, 1939.
[6] M. Andresini, S. Carret, L. Degennaro, F. Ciriaco, J. Poisson, R. Luisi, *Chem. Eur. J.* **2022**, *28*, DOI 10.1002/chem.202202066.
[7] M. Andresini, M. Colella, L. Degennaro, R. Luisi, *Org. Biomol. Chem.* **2023**, *21*, 7681.

Acknowledgement

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Approaches to the Parent 1,4- and 1,2-Thiazines

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Some years ago we described the generation and spectroscopic characterisation of the parent 4*H*-1,4-oxazine **1**.[1] So far this is the only parent fully unsaturated 6-membered heterocycle with one group 15 and one group 16 atom, although there is an isolated early report for formation of 1,4-thiazine as a stable liquid,[2] but this has not been subsequently reproduced. By examining a range of thermal precursors we believe we have generated the parent 1,4-thiazine **2** but find that it fragments under the conditions required for generation.

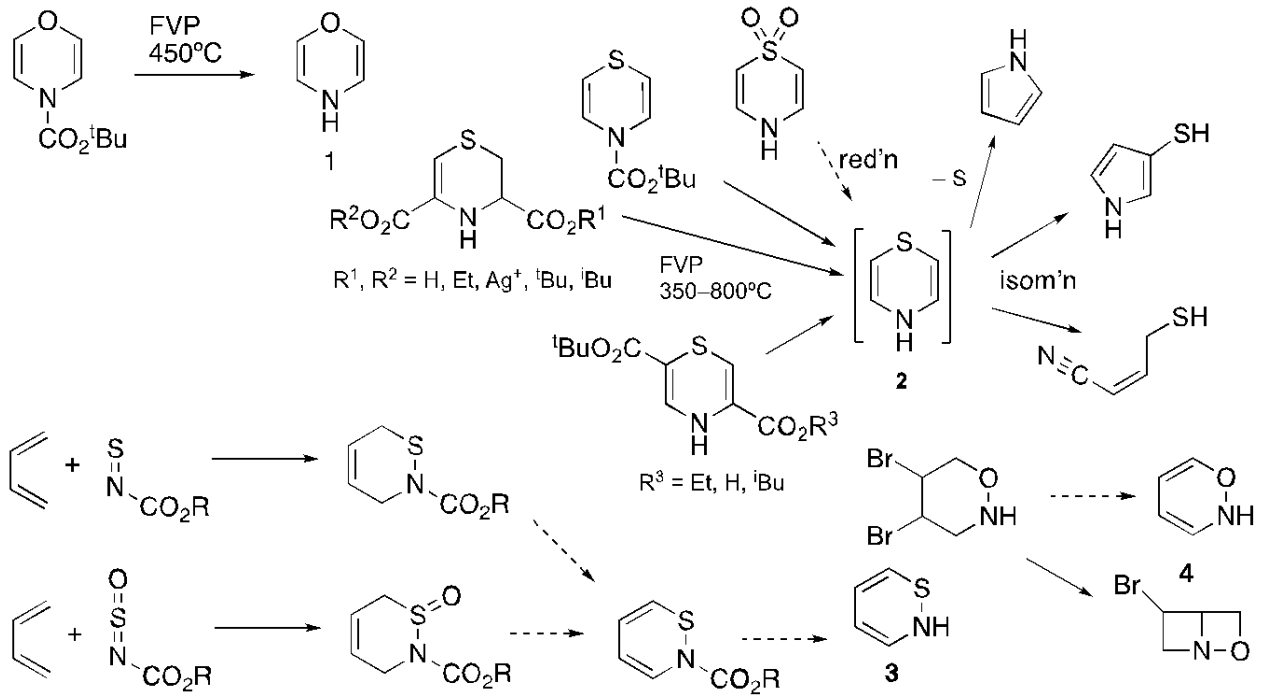

Figure 1

More recently, potential gas-phase pyrolysis precursors of the isomeric 1,2-thiazine **3** (as well as the analogous 1,2-oxazine **4**) have been prepared and the latest progress towards these fundamental but so far unknown heterocycles will be presented.

References

[1] R. A. Aitken, K. M. Aitken, P. G. Carruthers, M.-A. Jean, A. M. Z. Slawin, *Chem. Commun.*, **2013**, *49*, 11367–11369.
[2] C. Barkenbus, P. S. Landis, *J. Am. Chem. Soc.*, **1948**, *70*, 684–685.

P-27

Synthesis and applications of Liquid Crystal Elastomers prepared through thiol-acrylate polymerization

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Liquid crystalline elastomers (LCEs) are smart materials consisting of rubber-like polymers made by slightly crosslinked liquid crystalline networks. These materials have aroused great interest because they combine the entropic elasticity of classic elastomers with the orientational order at the molecular level and sensitivity to different external stimuli of Liquid Crystals. [1]

Thiol-ene polymerisation is a powerful and versatile tool to obtain main-chain LCEs starting from commercial diacrylate and dithiol terminated monomers. This reaction is extremely versatile and characterised by the absence of byproducts and side reactions. The polymerisation reaction can follow two different pathways. Michael's addition of the thiol moieties (nucleophilic) to the acrylate groups takes place when a base is added as a catalyst. On the other hand, in the presence of an opportune radical initiator, for example, a photoinitiator, different reactions of chain growth and radical transfer reactions contribute to the polymeric chain formation. Both mechanisms were used to develop materials opportunely optimised to find applications in different fields exploiting the peculiar behaviours of LCEs.

The radical photo polymerisation of a mesogenic diacrylate with 1,4-benzenedimethanethiol was conducted to obtain single-crystal liquid crystalline elastomeric (SC-LCE) films. SC-LCEs respond to an increase of the entropy in the system with a macroscopic and reversible contraction. This behaviour can be exploited to mimic the contraction of biological muscles. These materials were used in the REPAIR project to develop a bio-contractile unit to help the impaired mechanical cardiac function in heart failure affected patients.[2] The one-pot Michael's addition of a mesogenic diacrylate with dithiol and tetra thiol species was employed to obtain polydomain LCE films. Polydomain liquid crystalline elastomeric (PD-LCEs) films appear opaque due to the birefringence and the random orientation of each domain. PD-LCEs became transparent by applying an external mechanical force or heating the sample over a clearing point. These films were prepared and investigated as optical devices responsive to mechanical or thermic external stimuli able to switch reversibly from a brilliant white media able to scatter efficiently the light to a transparent media.[3]

References

[1] D. Martella, S. Nocentini et al., *Faraday Discuss.,* **2020**, *223*, 216–232.
[2] G.Vitale, B.Grandinetti, et al., *Macromol. Mater. Eng.,* **2022,** *307*, 2200187.
[3] Z.Wang, W.Fan, et al., *Extreme Mech. Letters,* **2017**, *11*, 42-48.

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P-28

Synthesis and Reactivity of Heavy Germanamides

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Kinetic stabilization afforded by bulky substituents has been successfully applied to the synthesis and isolation of highly reactive species containing heavier main group element.[1] Although keto-enol tautomerization reaction is one of the most important concepts in organic chemistry,[2] tautomerization has never been explored for the so-called heavy amides (double-bond compounds between heavier group 14 and 16 elements) because of difficulty in the synthesis and steric protection of the reactive heavy carbonyl bonds having an *alpha*-hydrogen.

In this study, we successfully synthesized and isolated heavy germaneamides having a hydrogen on the nitrogen atom by chalcogenation of the corresponding kinetically stabilized aminogermylene. In addition, we performed the proton abstraction reaction at the nitrogen atom of the heavy germaneamides thus obtained using potassium hexamethyldisilazide (KHMDS) as a base in the expectation of obatining the corresponding heavy iminols. As a result, the corresponding heavy imidates were obtained as a thermally stable colorless solid. The synthesis, structure, and reactivity of heavy germaneamides and imidates will be discussed.

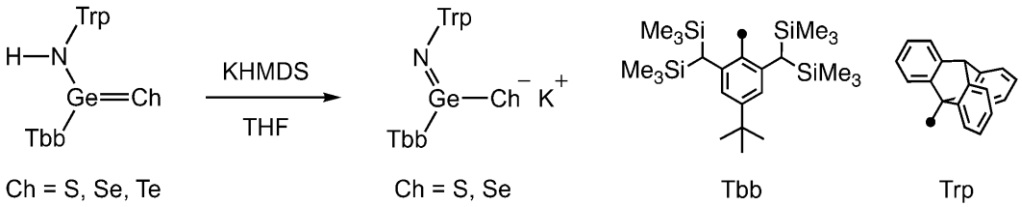

Figure 1

References

[1] Tokitoh, N., Okazaki, R. In *The Chemistry of Organic Silicon Compounds*, Vol. 2; Rappoport, Z., Apeloig, Y., Eds.; John Wiley & Sons: Chichester, 1998; pp 1063–1103; Weidenbruch, M. In *The Chemistry of Organic Silicon Compounds*, Vol. 3; Rappoport, Z., Apeloig, Y., Eds.; John Wiley & Sons: Chichester, 2001; pp 391–428.
[2] In *Tautomerism: Methods and Theories*; Antonov, L. Ed.; Wiley-VCH Verlag GmbH & Co.: Weinheim, 2014; pp 1–20.

P-29

Synthesis and study of the glutathione peroxidase-like properties of chalcogenolesters

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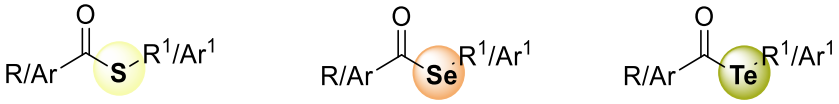
Chalcogenolesters (chalcogen = S, Se, Te; **Figure 1**) occupy a central position in chemical science and find broad application in organic synthesis, biology, medicinal chemistry, and material sciences.[1,2] In this contest, while the chemistry of thiolesters has been well established, selenolesters[3] and, especially, tellurolesters have been for less explored. The synthesis and the use of tellurolesters is significantly hampered by their limited stability.



Thiolester Selenolester Tellurolester

Figure 1. General structures of chalcogenolesters.

In this communication, the synthesis of selenolesters and tellurolesters will be reported. Selenols and tellurols (or tellurolates) smoothly react with acyl chlorides to afford the corresponding chalcogenolesters.[4]
The glutathione peroxidase-like properties of the synthesized compounds – which have been demonstrated to proceed through an oxidation-driven transesterification route – will also be discussed.[5]

References

[1] Y. Mutoh, in Chalcogen Chemistry, Fundamentals and Applications, (Eds: V. Lippolis, C. Santi, E. J. Lenardão, A. L. Braga), Royal Society of Chemistry, Croydon, UK, **2023**, pp. 27-52.
[2] T. Murai, in *Organoselenium Chemistry* (Ed: T. Wirth), Wiley-VCH, Weinheim, Germany, **2012**, pp. 257-281.
[3] L. L. Baldassari, D. S. Lüdtke, *Chem. Eur. J.* **2021**, *27*, 8656-8667.
[4] A. Angeli, F. Carta, S. Donnini, A. Capperucci, M. Ferraroni, D. Tanini, C. T. Supuran, *Chem. Commun.*, **2020**, *56*, 4444-4447.
[5] A. Capperucci, A. Petrucci, C. Faggi, D. Tanini, *Adv. Synth. Catal*., **2021**, *363*, 4256-4263.

Synthesis of 5'-Alkylseleno-substituted thymidine derivatives

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Selenium-containing organic compounds occupy a privileged position in organic synthesis and in biology. A growing number of organoselenium compounds have been demonstrated to possess antioxidant, enzyme modulator, anti-inflammatory activities.[1,2] On the other hand, nucleoside analogues represent a relevant class of bioactive compounds, with a variety of biological properties and applications in medicinal chemistry.[3] Nucleosides have been widely employed in cancer therapy and in antiviral chemo-therapy. For example, Zidovudine (or azidothymidine) is one of the FDA-approved drug for HIV treatment.[3,4]

In this context, the synthesis of selenium-containing nucleoside derivatives has emerged as a rewarding strategy to develop new drug candidates with antiproliferative properties. However, while arylseleno-substituted derivatives have been well studied,[5,6] alkyl-substituted analogues have not been explored yet. In this communication, our studies on the synthesis of 5'-alkylseleno-substituted thymidine derivatives with different molecular complexity through the functionalization of Zidovudine with alkyl selenols[7] will be discussed (**Figure 1**).

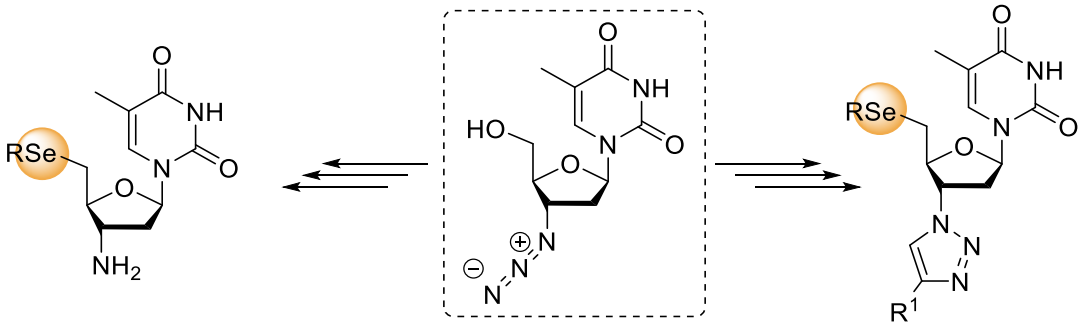

Figure 1. Structurally diverse 5'-seleno-substituted thymidine derivatives.

References

[1] E. J. Lenardão, C. Santi, L. Sancineto, *New Frontiers in Organoselenium Compounds*, Springer, Heidelberg, **2018**.

[2] G. Barchielli, A. Capperucci, D. Tanini, *Antioxidants*, **2022**, *11*, 251.

[3] S. Alaoui, M. Dufies, M. Driowya, L. Demange, K. Bougrin, G. Robert, P. Auberger, G. Pagès, R. Benhida, *Bioorg. Med. Chem. Lett*. **2017**, *27*, 1989–1992.

[4] E. Arts, D. Hazuda, *Cold Spring Harbor Perspect. Med*. **2012**, *2*, a007161.

[5] N. Quoos, L. Dornelles, J Buss, K. Rech Begnini, T. Collares, F. K. Seixas, F. Dutra Garcia, O. E. D. Rodrigues, *ChemistrySelect,* **2020**, *5*, 324-329.

[6] J. G. Leal, B. C. Piccoli, C. S. Oliveira, F. D'Avila da Silva, F. Bright Omage, J. B. T. da Rocha, M. S. Sonego, N. V. Segatto, F. Kommling Seixas, T. V. Collares, R. S. da Silva, J. M. Sarturi, L. Dornelles, Maria A. F. Faustino, O. E. D. Rodrigues, *New J. Chem*, **2022**, *46*, 22306-22313.

[7] D. Tanini, A. Capperucci, *Adv. Synth. Catal*. **2021**, *363*, 5360-5385

P-31

GPS-SH1: an innovative receptor for the determination of FKBP12

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The aim of the research activity is the design, assembly and the development of a device for rapid and efficient determination of the concentration of FKBP12 protein in biological fluids, i.e. CSF and blood. FKBP12 is a peptidyl-prolyl cis-trans isomerase with a well-established role in cancer, neurodegenerative processes and post-surgical anti-rejection response.[1] The proposed detection platform is constructed on a gold or silver coated support for Quartz-Crystal-Microbalance (QCM) measures. The QCM support is functionalized with a synthetic receptor, GPS-SH1, synthesized specifically to bind FKBP12[2], that allows to directly detect the untreated biological samples.
It has been demonstrated that the optimal binders for FKBPs expose the two contiguous carbonyl oxygens in the proline-mimetic chain and are characterized by a rigid quasi-cyclic structure mimicking the macrolide structure of the natural inhibitors FK506 and Rapamycin. Based on the above knowledge, we have designed and synthesized the GPS-SH1 receptor characterized by two different portions: a binding group for the unique recognition of FKBP12 and, on the other side, a linear chain ending with the thiol group so that it can be chemical adsorbed on the QCM sensor to form a Self-assembly-monolayer (SAM).

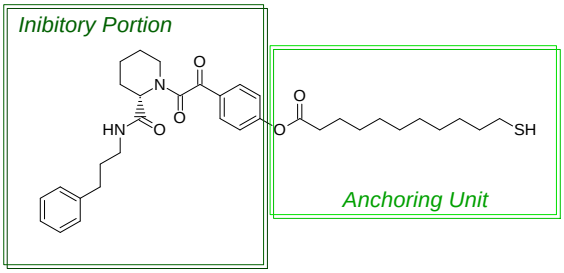

Figure 1. GPS-SH1 receptor

We investigated the adsorption of FKBP12 on QCM sensors with GPS-SH1 receptor SAMs and various spacers like 1-Dodecanethiol (C_{12}-SH) and Thiol-polyethylene glycol (PEG-SH), which can be anchored by their terminal thiol groups. Some interferents present in biological samples, such as BSA and IgG, were also tested on the proposed platform to demonstrate receptor selectivity for the protein of interest. After the addition of the proteins the sensors can be washed to be reconditioned and reused for different analyses.

References

[1] G. Caminati et al., International Publication Number WO2021/124269A1, **2021**.
[2] M. R. Martina et al., *J Med Chem.* **2013**, *56*, 1041-1051.

Acknowledgements

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P-32

Design, synthesis and resolution of chiral donor-acceptor dyads to study the CISS effect

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The focus of this research project is on the synthesis, resolution, and characterization of chiral donor-acceptor dyads, to explore the Chiral Induced Spin Selectivity (CISS) effect.[1] In our study, we used a thia-bridged[4]helicene as chiral donor[2], linked through bridges of various lengths, to a perylene diimide acceptor unit. Previous results demonstrated spin-filtering properties of thia-bridged[4]helicene anchored on gold surface.[3] Here, we studied the photoinduced electron transfer after photoexcitation of our dyads, through time-resolved optical and magnetic resonance spectroscopies.[4] The final aim is the direct spectroscopic detection of the CISS effect.

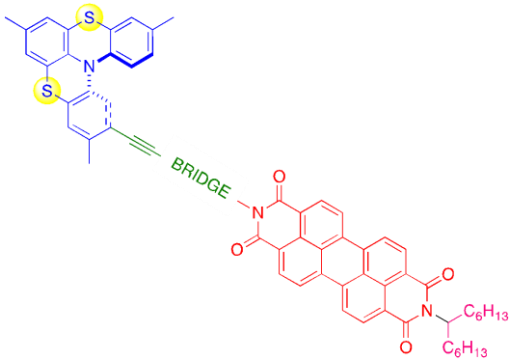

Figure 1. General Donor-Acceptor dyad.

In addition, we investigated the electronic properties of each donor-acceptor dyad, as well as the the interaction of the single enantiomers with circularly polarized light. Understanding the CISS effect at the molecular level will enable the design of new chiral organic devices with potential applications in the field of quantum information science.

References

[1] B. P. Bloom, Y. Paltiel, R. Naaman, D. H. Waldeck, *Chem. Rev.*, **2024**, *124*, 1950-1991.
[2] S. Menichetti, C. Faggi, M. Onori, S. Piantini, M. Ferreira, S. Rocchi, M. Lupi, I. Marin, M. Maggini, C. Viglianisi, *Eur. J. Org. Chem.*, **2019**, 168-175.
[3] N. Giaconi, L. Poggini, M. Lupi, M. Briganti, A. Kumar, T. K. Das, A. L. Sorrentino, C. Viglianisi, S. Menichetti, R. Naaman, R. Sessoli, M. Mannini, *ACS Nano*, **2023**, *17*, 15189–15198.
[4] A. Chiesa, A. Privitera, E. Macaluso, M. Mannini, R. Bittl, R. Naaman, M. R. Wasielewski, R. Sessoli, S. Carretta, *Adv. Mater.*, **2023**, *35*, 2300472.

Acknowledgements

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P-33

Dithia-aza[4]helicenes for Spintronics Devices

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The aim of the research project is the optimization of the synthesis of dithia-aza[4]helicenes (TA[4]HEL) with different types of functionalized-bridges for applications in molecular spintronics.
Dithia-aza[4]helicenes are a peculiar class of geometrically stable [4]helicenes, characterized by helical chirality because of the steric impediment between the terminal rings, that have found peculiar applications in material science.[1]
The conduction of a flowing current through a layer composed by chiral molecules, can be spin selective, promoting the transmission of electrons with a specific spin state. This effect, named Chirality-Induced Spin Selectivity (CISS) paved the way to new spintronic devices.[2]
The synthesis of TA[4]HEL was optimized since to introduce properly designed functionalized-bridges that allow their insertion on different two dimensional surfaces.
In particular we are studying, and we showed in this communication, the covalent functionalization of Highly Oriented Pyrolytic Graphite (HOPG) with these types of helicenes through the Tour reaction (*Figure 1*).

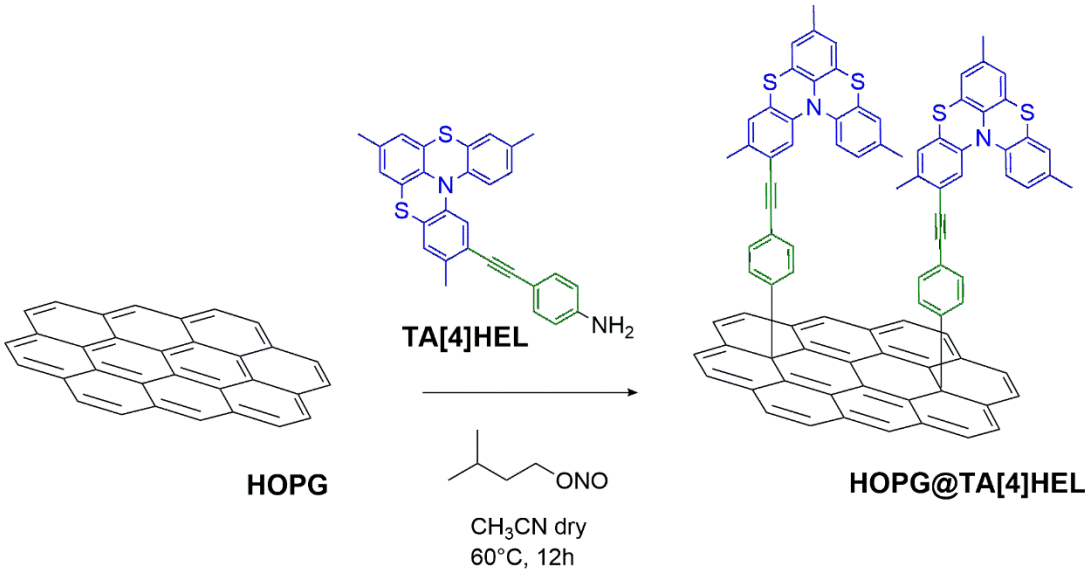

Figure 1.

The possibility of using these devices as spin filters, exploiting the CISS effect of chiral molecules, will be discussed as well.

References

[1] M. Lupi, O. Salmi, C. Viglianisi, S. Menichetti, *Adv. Synth. Catal.* **2023**, 365, 1705-1712
[2] N. Giaconi, L. Poggini, M. Lupi, M. Briganti, A. Kumar, T. K. Das, A. L. Sorrentino, C. Viglianisi, S. Menichetti, R. Naaman, R. Sessoli, M. Mannini, *ACS Nano 17* (15), 15189–15198.

P-34

Substrate- and Anion-Assisted Mechanochemical Synthesis of *thio*-Hemicucurbiturils

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The conformational flexibility of single-stranded host molecules allows for more promiscuous host-guest complexation. Here, we show that a unique family of single-stranded anion receptors, *thio*-hemicucurbit[n]urils (*thio*-hCB[n], n = 6,8), which bind various anions *via* multiple hydrogen bonds and dispersion forces, exhibiting induced fit and conformational adaptation.[1] The *thio*-hCBs are readily accessible exclusively and quantitatively *via* template-driven mechanochemical synthesis from cyclic thiourea monomers. Optimization reactions included the effect of the templating agent, the nature of the acid catalyst, and aging duration and temperature. Accordingly, we successfully prepared 6- and 8-membered *thio*-hemiCB[n]s in high selectivity. Ring-size selectivity was attributed to the nature of the building block. Acyclic oligomers vs. macrocycles were determined by choice of anion template.

The solid-state structures of the various host-guest inclusion complexes reveal that these host molecules comprise a relatively rigid circular skeleton and eight or six rigid flaps that can easily change their tilt angle relative to the equatorial plane to maximize the guest binding interactions. Competition and titration experiments monitored by various NMR techniques provide additional information on the host-guest behavior and anion binding selectivity. The binding studies confirm that both *thio*-[cycH]-hCB[8] and *thio*-hCB[6] form a 1:1 complex with different anion guests through hydrogen bonding interactions. ITC titrations show that the *thio* analogs of hCB bind anions significantly more strongly than the *oxo* analog by two orders of magnitude, probably due to the higher polarizability of thiourea relative to urea. The anion binding selectivity follows the order of PF_6^- > BF_4^- ≅ ClO_4^- >> TfO^- for the octameric macrocycle. The hexameric macrocycle follows the order of I^- > Cl^- > Br^-.

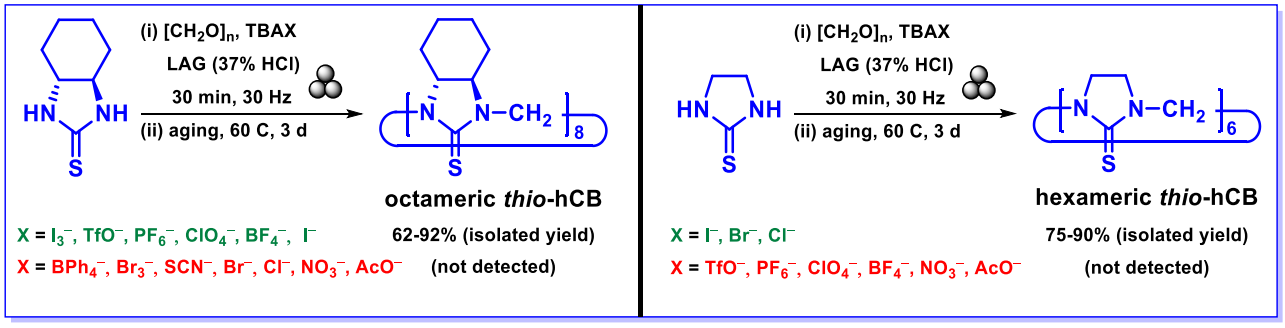

Figure 1. Mechanochemical synthesis of *thio*-hCB macrocycles.

References

[1] R. Gujjarappa, R. Khurana, N. Fridman, E. Keinan, O. Reany, *Cell Rep. Phys. Sci.* **2024**, *5,* 102011.

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