



Invited Speaker  
**Dr. Hervé Raps**



# THE SECOND YEAR

*Doctoral Students' Day*

Villa Arson, 06100 Nice

**JULY** | **19<sup>th</sup>** | **2024**



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# Schedule

8:45

*Welcome of the participants*

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9:05

Opening of the Day - Welcome Speech

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9:15

Keyu MAO

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9:30

Alex WASCHTSCH

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9:45

Alice RAVEZ

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10:00

Fakhri-Eddin LAHFAIDH

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10:15

Anastasiia PIDVOROTNIA

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10:30

*Coffee Break*

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11:00

Invited Speaker - Dr. Hervé RAPS

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11:30

Matthieu JORANDON

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11:45

Sandra LITWIN

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12:00

Jean-Baptiste COFFIN

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12:15

Awards - Closing Ceremony

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12:25

*Lunch Buffet*

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13:30

*End*

## Silver and ruthenium complexes in molecular chemistry: towards green chemistry and sustainable development

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In the context of the key principles of “Green chemistry”,<sup>1</sup> the development of efficient, clean and mild strategies to access cyclized and functionalized molecules is highly important in the field of organic chemistry. We got interested in the reactivity of enynes in the presence of silver and ruthenium complexes. The enantioselective cyclization of functionalized 1,6-enynes was tackled. We showed that silver hexafluoroantimonate<sup>2</sup> catalyzed intramolecular [4+2] cycloaddition reaction of amide-1,6-enynes, providing tricyclic and tetracyclic compounds. Asymmetric unprecedented reaction conditions in the presence of Ag salts and chiral phosphine ligands were also investigated and afforded the enantioenriched cyclic amides in good yields. In parallel, the preparation of functionalized polycyclic azaborine skeletons via a ruthenium-mediated ring-closing enyne metathesis transformation<sup>3</sup> of alkynyl B-anthranilamide (aam) has been developed. B(aam) tethered enynes were engaged with Grubbs catalyst affording the corresponding exo-cyclic compounds in good yields (25 examples, yields up to 89%).<sup>4</sup> This methodology was efficiently optimized and was performed in dimethyl carbonate<sup>5</sup> as green solvent which overall provided a direct access to functionalized azaborine scaffolds.

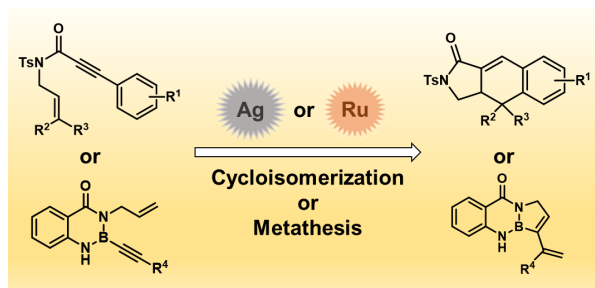


Figure 1: Silver and ruthenium complexes in enyne cycloisomerization reactions

### References

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- [5] (a) Miao, X.; Fischmeister, C.; Bruneau, C.; Dixneuf, Pierre H. *ChemSusChem: Chemistry & Sustainability Energy & Materials*, 2008, 1, 813-816. (b) Fiorani, G.; Perosa, A.; Selva, M. *Green Chem.*, 2018, 20, 288-322.

# WASCHTSCH

Alex

## Development of nonlinear optical polymers using modified natural flavonols from renewable sources

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One of the key elements of the optoelectronic communication systems is the optical signal modulator, generally made from inorganic electrooptic (EO) materials. Despite huge advantage in chemical and thermal stability over organic EO materials, they are worse in performance [1]. In turn, the main problems of organic EO materials remain their low thermal stability and vanishing EO-properties over time due to relaxation processes. Thus, here we are concentrating on enhancing of sustainable organic EO materials based on flavonols.

Flavonols are plant-based compounds, mainly used in pharmacy. Their  $\pi$ -conjugated core with separated donor and acceptor groups, make them promising candidates for NLO materials [2]. Additionally, their rigid aromatic structure with several hydroxyl groups, which already used in thermostable plastics [3], should also improve thermal stability of EO properties for materials base thereon[2]. However, significantly lower first hyperpolarizability  $B$  values of natural flavonols, compared with that in typically used NLO materials [4], prompt us for further chemical modifications of their donor and/or acceptor units. Here we considered two general ways (see Fig.1): introduction of cyano-containing groups instead of carbonyl group, and introduction of amino- or dialkylaminogroups instead of hydroxyl groups.

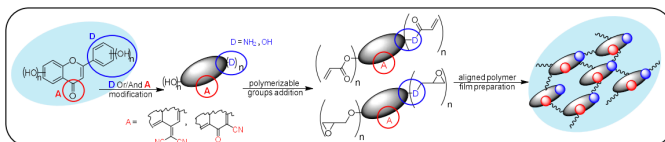


Figure 1: General strategy for EO polymers based on modified flavonols

We selected the most potent flavone-based candidates(Fig.2) by comparison of the values of their first hyperpolarizability  $B_{tot}$ , obtained through quantum-chemical simulation with DFT method, using B3LYP hybrid potential with 6-311++ G(d,p) basis. Thus, we concluded that while donor modification can lead utmost to ~30% improvement of  $B_{tot}$  value, whereas the acceptor improvement can increase it up to 2-4 times.

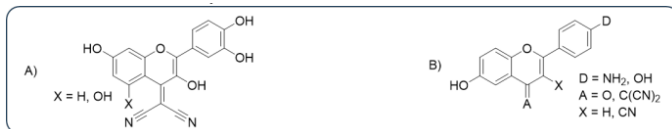


Figure 2: Selected NLO chromophores based on A) natural flavonols B) synthetic flavone structures

### References

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## Synthesis of 7-chloro-6-methoxy-mellein and analogs

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Marine-based metabolites are recognized as source of molecular and structural diversity. Despite this unending source of inspiration, the supply of those metabolites remains limited and represents a major challenge for next years. Present in several species of fungi and microorganisms, halogenated melleins display promising and intriguing biological properties, such as antibacterial and antifungal activities [1]. The study of the biosynthetic pathway of these compounds suggests that melleins are precursors of other metabolites. Our next objective will be to gain access to these complex metabolites [2].

Synthesis of 7-chloro-6-methoxy-mellein, as a racemic mixture, firstly described by Henderson *et al.* in 1982, was performed in 5 steps with an overall yield of 9.5% [3]. Due to the interesting biological activities of chlorinated melleins, we conceived a new synthetic route for the enantioselective preparation of 7-chloro-6-methoxy-mellein (**7b**) and its analogs. Our synthetic plan will provide 7-chloro-6-hydroxy-mellein (**7a**), as a model molecule, in 6 steps (Figure 1). The four first steps, were reached without trouble, in moderate to good yields for methoxy- and hydroxy- derivatives, respectively 26% (**5b**) and 69% (**5a**) overall yields. We are now focusing on the direct-*ortho*-metalation and enantioselective cyclisation steps by introduction of (*S*)- or (*R*)-Propylene oxide, and later the chlorination step. This synthetic route (Figure 1) would provide a convenient access to various halogenated analogs, starting from cheap and commercially available starting materials.

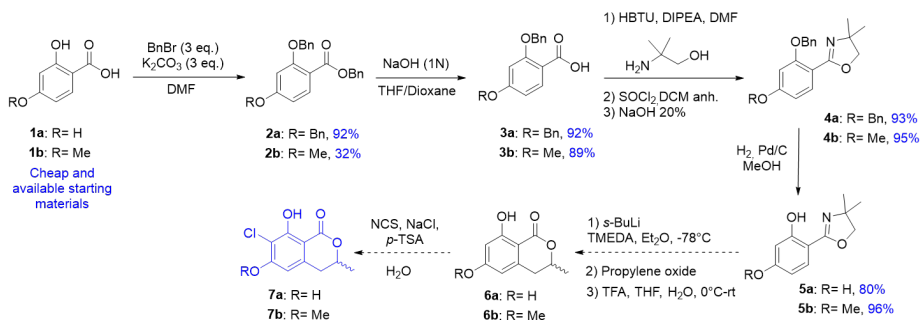


Figure 1: Planned synthesis of 7-chloro-6-methoxy-mellein

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# LAHFAIDH

*Fakhri-Eddin*

## Exploring and understanding the recycling of a biobased epoxy thermoset via saponification

*Fakhri-Eddin Nadir LAHFAIDH, Nathanaël Guigo, Luc Vincent, Nicolas Sbirrazzuoli*

Our world is facing unprecedented environmental challenges, with plastic waste being one of its major contributors. As traditional recycling methods such as mechanical recycling are displaying limits, chemical recycling and its recent development emerges as an interesting option to address the plastic waste issue while advancing towards a more sustainable future. In parallel, thermosetting resins account for 10 % of the global plastic production. However, this class of material is not prone to mechanical recycling and their chemical recycling or reprocessing can be foreseen.

This presentation will focus on a solvolysis-based recycling method of a flexible biobased thermoset. An in-depth methodology for in-situ monitoring and quantifying the solvolysis over time will be presented. Various techniques were employed to achieve this. The temperature dependence was investigated, providing a comprehensive kinetic analysis of the solvolysis process. The kinetic data allowed the development of a simulation tool, effective for extrapolation at different temperatures. In addition, the valorisation of the recycled product will be highlighted, showcasing the potential to reprocess biobased thermosets into fresh materials. The properties of these recycled samples were studied with a focus on their thermal and mechanical properties. This systematic approach not only enhances the understanding of the chemical processes during solvolysis but also paves the way for precise control and optimization.

This work aims to increase the sustainability of biobased thermoset resins by considering the recycling approach.

Better known as  
*Nadir*



# PIDVOROTNIA

Anastasia

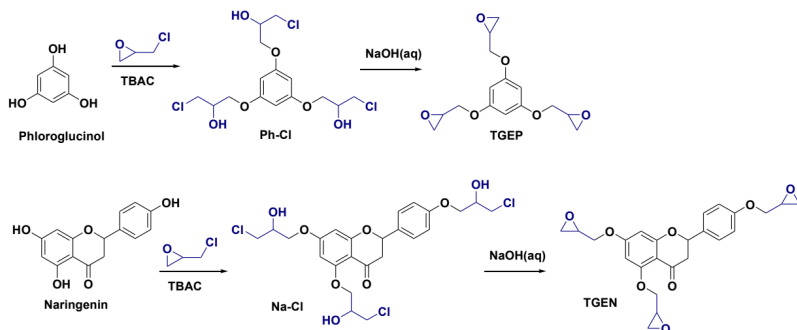
## High performance, recyclable and sustainable by design natural polyphenol-based epoxy polyester thermosets

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Possessing high thermo-mechanical properties and chemical resistance, epoxy resins are widely used in industry. However, along with the demand for epoxy resins, there is the problem of toxicity and non-environmental friendliness of the starting materials in their production [1]. To replace the known endocrine disruptor Bisphenol-A in the synthesis of epoxy monomers, we used the triglycidyl esters of phloroglucinol and naringenin. Their mixture with anhydrides in the presence of an amine initiator gave thermosetting resins with good performance characteristics.

The resulting thermosets exhibited impressive properties, including elevated glass transition temperatures (ranging from 134 to 199 °C), high cross-link density, gel content exceeding 99%, and exceptional resistance to high temperatures (ultimate oxygen index of approximately 28 to 33%). Also, polyaromatic thermosets exhibited remarkable mechanical properties, with Young's modulus of approximately 1.26 to 1.68 GPa and elastic modulus at 25 °C (ranging from 2.7 to 3.5 GPa)[2].



### References

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## Ocean pollution and human health

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Ocean pollution is a growing threat to human health, both directly and through its impact on the ecosystem services provided by the oceans, and climate change acts as a threat multiplier.

The sources of ocean pollution are multiple: chemical pollutants (heavy metals, hydrocarbons), organic pollutants (phosphorus, nitrogen) and, of course, plastics, but their origin is easier to determine: 80% of marine pollution is land-based and comes from human activities. Widespread, this pollution has increasingly negative effects on human health and well-being, both directly and through the degradation of ecosystem services provided by the ocean (food, economic). Like other forms of pollution, ocean pollution disproportionately affects the most vulnerable populations and communities.

Climate change acts as a multiplying threat: directly, with, for example, an increase in the intensity, frequency and geographical distribution of toxic algae proliferation, or the development of bacteria favored by rising seawater temperatures and changing salinity, but climate change can also act indirectly: an increase in extreme weather events in coastal and river areas (storms, floods, submersions) leads to an influx of pollution into the ocean.

The fight against climate change, through the reduction of greenhouse gas emissions and the transition to renewable energies, must also be accompanied by specific measures to reduce and control ocean pollution, which have already proven their effectiveness: the development of marine protected areas, efficient wastewater and effluent treatment systems, protection against extreme events of waste treatment infrastructures in coastal and river areas, and above all the reduction of waste at source: agricultural discharges, industrial discharges and pollution by plastics. The support and application of international regulations, such as the future binding international treaty on plastics, is a guarantee of the success of these measures.

# JORANDON

Matthieu

## Development of a catalytic methodology for oxepane synthesis to target HIF-1

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Cancer stands as the second leading cause of death worldwide and remains a significant challenge for the medicinal chemistry.<sup>1</sup> Hypoxic cancers are widely associated to a poor prognosis due to a strong therapy resistance. Tumor cells rely on the hypoxia-inducible transcription factor 1 (HIF-1) to cope with low oxygen levels. Composed of two subunits  $\alpha$  and  $\beta$ , HIF-1 is responsible for the transcriptional induction of series of genes involved in the cell proliferation.<sup>2</sup> In this context, the HIF-1 $\alpha$  subunit, overexpressed during a hypoxic stress, emerged as a important target for anticancer drug discovery. Although few inhibitors had been identified, none of them had been clinically approved as they suffer from a lack of selectivity.<sup>3</sup> A promising solution might be provided by the sea. Sodwanones, a class of triterpenoids isolated from the marine sponge *Axinella weltoni*, demonstrated a great cytotoxicity through the inhibition of HIF-1 activation in breast and prostate tumor cells.<sup>4</sup> Their very interesting oxepane scaffold, present in various natural products with significant biological activities (i.e. anti-inflammatory, antitumoral, antibacterial, antifungal), highlights their potential in the research for novel anticancer drugs.<sup>5</sup>

This work is focused on the development of a novel catalytic and biomimetic approach to access a series of sodwanone western fragments, as they feature an interesting cyclohexane-oxepane subunit (Figure 1). Methods to access to seven membered-ring cyclic ethers have been widely explored. Oxepane motif is usually obtained via a cyclization step through the addition of alcohols on an electrophilic site (epoxides, allenenes, activated olefins, ...), mediated by an excess of Lewis acids such as boron trifluoride etherate.<sup>6</sup> Our methodology is based on the use of a catalytic amount of Lewis superacids, (i.e. bismuth (III) triflates) to trigger an epoxide-opening cascade reaction. Among the various cyclic ethers obtained, we formed several oxepane derivatives, corresponding to smaller fragments of the sodwanones. The ongoing biological studies of those scaffolds should provide essential information about the involvement of the oxepane motif in the overall sodwanones activity against HIF-1. Applied to more complex sesquiterpenes, this methodology would provide new avenues for hypoxic cancer therapy via HIF-1 targeting.

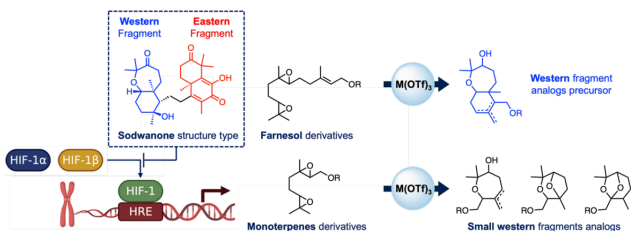


Figure 1: General overview of the project

### References

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## **Understanding the solvent dissolution of styrene-acrylonitrile (SAN) employing calorimetry and FTIR for envisioning the physical recycling of acrylonitrile-butadiene-styrene**

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The recycling of plastics has been a major issue to tackle for the past 50 years. Indeed, the pollution of the environment has been reinforced by plastic landfilling. Acrylonitrile-butadiene-styrene (ABS) is a commonly used plastic in the automotive and electronic industries that is formulated with different additives such as pigments, flame retardants, and fillers. Hence, finding a recycling strategy leading to a recycled ABS material with virgin-like mechanical and thermal properties is of great interest. According to the complexity of and the variety in ABS compositions, physical recycling is a promising solution. Indeed, it would enable the removal of polybutadiene rubber (PBR) particles and additives from the styrene-acrylonitrile (SAN) matrix via dissolution/precipitation. Thus, the dissolution of the SAN was performed in various solvents selected from their Hansen solubility parameters. In situ monitoring of the polymer dissolution by calorimetry, Fourier Transform Infrared Spectroscopy (FTIR), and dynamical mechanical analysis (DMA) allowed the investigation of thermodynamic and kinetic aspects of the dissolution process. The main steps in the dissolution process of SAN were identified and quantified, and the results will be used to aid the ongoing investigations of physical solvent-based dissolution for plastic recycling.



## Opportunities and Challenges of Artificial Intelligence and Big Data in the Fragrance Industry

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The advent of Artificial Intelligence (AI) and Big Data has initiated a significant transformation in scientific research. AI has the capability to process vast amounts of data and discern meaningful patterns within them. This presentation aims to explore the potential research opportunities and inherent limitations of AI and Big Data within the context of the perfumery industry.

Despite the existence of databases such as The Good Scent Company, ScenTree, and FF Willey, their scale and structure do not align with the criteria typically associated with big data. A major challenge for AI in the fragrance domain is the scarcity of accessible data.

Unlike sectors such as finance or healthcare, where extensive datasets are readily available to researchers, the perfume industry faces a deficit in comprehensive and diverse data necessary for AI to yield substantial results. The available information often restricts AI's capacity to generate accurate and generalizable insights due to its limited, proprietary, and fragmented nature.

To address these challenges, enhanced cooperation and collaboration among stakeholders in the fragrance industry are crucial. Perfumers, fragrance houses, ingredient manufacturers, and researchers must collaborate to share knowledge and data, thereby creating larger and more representative datasets. This collaborative effort would facilitate the development of more precise and pertinent AI models, capable of capturing the intricate nuances of olfactory preferences, consumer behavior, and the emotional impact of fragrance ingredients.

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**THANK YOU**  
*For your participation*