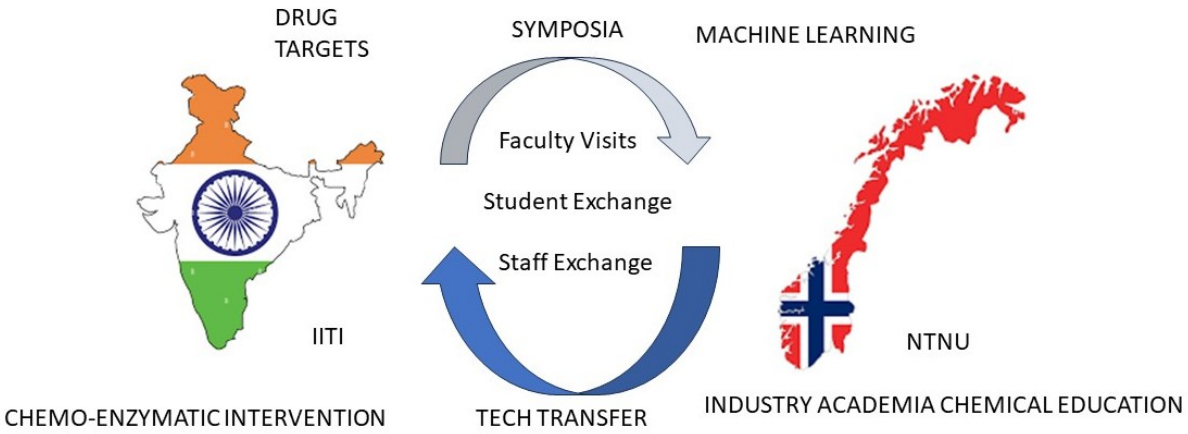
NTNU
Faculty of Natural Sciences
Department of Chemistry
and Biomedical Science

Sustainable Drug Synthesis, State of the Art 2026

NTNU, Trondheim, Norway, June 25th-27th, 2026



SPECIAL HONORARY LECTURERS

Professor Sergio Riva. ITALY Professor Jennifer Littlechild, UK,

https://www.ntnu.edu/ikb/india-collaboration

Distinguished guest

It gives me great pleasure to welcome you all to the conference **Sustainable Drug synthesis- State of the Art 2026**. The conference is organised at Department of Chemistry and Biomedical Sciences, Norwegian University of Science and Technology in Trondheim 25th to 27th of June 2026 under the INDO-NORWEGIAN project "Sustainable Synthesis of Drug Targets, Machine Learning, Chemoenzymatic Resolution and Advancing Tech-transfer Chemical Education in India and Norway" funded by Norwegian Directorate for Higher Education and Skills (HK-dir and University Grants Commision (USG, India). The project INCP2 funded by the two directorates are supporting 12 Indo-Norwegian projects. The collaboration are supported by both Embassies and several Innovation bodies.

The conference gathers 30 delegates from both academia and industry from seven countries presenting and discussing research progress on the topics of sustainable drug synthesis.

A little background of the project: Professor Debayan Sarkar approached the undersigned in august 2024 and suggested to write a joint application to the INCP2 project. The main focus should be green synthesis of enantiopure drugs, with focus on biocatalysis from the Norwegian side and photocatalysis on the Indian side. A future goal should be photobiocatalysis!

We are honoured to welcome Professor Dr. Jennifer Littlechild as the honorary opening lecturer: Professor Littlechild is the Vice President of European Society of Applied Biocatalysis (ESAB) and Professor at University of Exeter, United Kingdom. Professor Sergio Riva is Professor and Research Executive at Instituto de Scienze e Technologie Chimiche Giulio Natta, Milano in Italy and will give the honorable closing lecture.

We are grateful for the support from SyncoZymes Co., Ltd, (Shanghai, China) during the last 10 years. The enzyme gifts have given both successful and not so successful results, but all results are valuable, even though it is not easy to report low enantiomeric excess of products.

We are very happy that CEO Dr. Wei Zhu and assistant manager Ms Yiye Zhu from SyncoZymes have accepted our invitation to the conference. We are looking forward to fruitful discussions about the many enzyme preparations we have received in the past years. And as a delegate at the conference, you might even be able to secure a special deal on enzymes and equipment for your research!

ESAB is thanked for giving free registration to ESAB 4th Digital congress November 23.-25.- 2026 for the best student presentation.

I hereby also express my thanks to the Scientific Committee of the conference and to the Organizing Committee, in special Truls, Mathilde, Ivar, Chistina and Alexandre.

With that, I wish you all an inspiring conference with fruitful discussions here in (rainy) Trondheim!

On behalf of the Scientific Committe

Elisabeth E. Jacobsen
Conference chair and Treasurer of ESAB

Programme

Thursday June 25, 2026

09:30-10:00	**Registration**	R5 area
Session Chair: Elisabeth Jacobsen		
10:00-10:30	**Opening of the Conference** Words of welcome: Chair of Conference, Prof. Dr. **Elisabeth Jacobsen** *Chiral Drugs for Cardiovascular Diseases 2020-2026*	R5
10:30-11:15	**Honorary Opening Lecture** Prof. Dr. **Jennifer Littlechild**, University of Exeter, UK *Thermophilic Genomes and Metagenomes as a Source of Novel Enzymes for Industrial Biocatalysis*	R5
11:15-11:45	Prof. Dr. **Eirik Sundby**, NTNU, Trondheim, Norway *Pyrrolopyrimidines and Purines As Csf1r Inhibitors*	R5
11:45-12:15	Coffee break	R5 area
12:15-12:45	Prof. Dr. **Armanda Cordova**, Mid Sweden University, Sundsvall, Sweden *Heterogeneous catalysis and selective Programming of Polysaccharides*	R5
12:45-13:15	Senior Director R&D Dr. **Huiling Liu,** Chiron AS, Trondheim, Norway *New Psychoactive Substances: Chemistry, Synthesis and Societal Impact*	R5
13:15-14:15	**Lunch break**	Element Cantina
Session chair: Ivar Skogvik		
14:15-14:45	CSO Dr. **Susanta Samajdar** Aurigene Oncology Limited, Indore, India *Discovery and Development of Proximity Inducing Agents: Aurigene Oncology´s Contribution to Neo-PPI Driven Pharmacology*	R5
14:45-15:15	Prof. Dr. **Marcelo Cristianini,** State University of Campinas, Sao Paulo, Brazil *High-Pressure Processing: A Gentle Strategy for Tailoring Polymer Functionality and Extracting Sensitive Bioactives*	R5
15:15-15:45	Prof. Dr. **Sulalit Bandyopadyhay,** NTNU, Trondheim, Norway *Scalable Synthesis Method for Drug Encapsulation in Polymer Nanoparticles*	R5
16:00	**Dinner**	D3-114

Bringing enzymes to chemistry

Immobilized CALB

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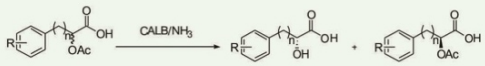
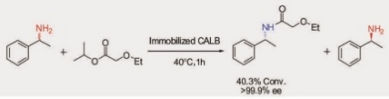
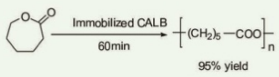
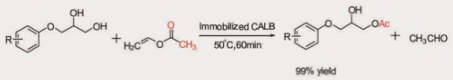
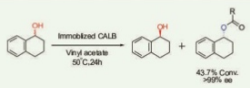
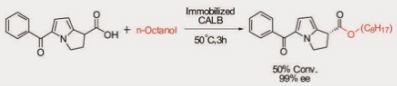
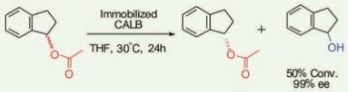
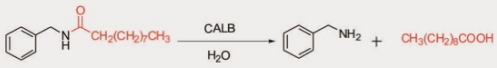
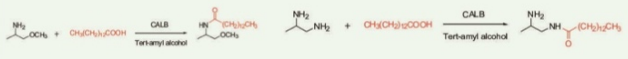
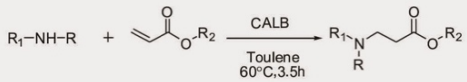
Application Examples

Example 1(Aminolysis)(1) :	
Example 2(Aminolysis) (2) :	
Example 3(Ring opening polyester synthesis) (3) :	
Example 4(Transesterification, regioselective of hydroxyl group) (4):	
Example 5(Transesterification, kinetic resolution of racemic alcohols)(5):	
Example 6(Esterification, kinetic resolution of carboxylic acid) (6) :	
Example 7(Esterolysis, kinetic resolution) (7) :	
Example 8(Hydrolysis of amides) (8) :	
Example 9(Acylation of amines) (9) :	
Example 10(Aza-Michael addition reaction) (10) :	

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Friday June 26, 2026

Session chair: Mathilde Aanerud		
09:00-09:45	Prof. Dr. **Debayan Sarkar,** IIT, Indore, India *Precision Dearomatisation with Arene – π- Tribromide Complex and Visible Light Catalysis*	R5
09:45-10:15	Prof. Dr. **Roland Wohlgemuth**, Lodz University of Technology, Lodz, Poland *Sustainable Drug Synthesis – an overview.*	R5
10:15-10:45	CEO Dr. **Wei Zhu,** Syncozymes, Co. LTD, Shanghai, China	
10:45-11:15	**Coffee break**	R5 area
11:15-11:45	Dr. **Joachim Mossige,** University of Oslo, Oslo, Norway *From OpenSPIM to FlowSPIM: Enhancing The Versatility of a Light Sheet Microscope Through an Iterative Design Process*	R5
11:45-12:15	Dr. **Niladri Sekhar Roy**, IIT, Indore, India *Flavin-Based Photodynamic Inactivation as a Sustainable Approach for Extending the Post-Harvest Shelf Life of Fresh Produce in India*	R5
12:15-12:45	Prof. Dr. **Astrid Silva De Wijn**, NTNU, Trondheim, Norway *A Computational Dynamic Model For Drug Resistance and Treatmend Selection in Enzyme Inhibition Treatment*	
12.45:13.45	**Lunch break**	Element Cantina
Session chair: Christina Pettersen		
13:45-14:05	**Truls Rossbach Hammer**, NTNU, Trondheim, Norway *Chemoenzymatic Synthesis for Chiral Pharmaceutical Intermediates and Biologically Active Lipid Derivatives*	R5
14:05-14:35	Dr. **Subarna Roy**, IIT, Indore, India *Visible Light-induced Crossed [2+2] Cycloaddition of Aryl Terminal Olefins via Energy Transfer Catalysis*	R5
14:35-14:55	MSc. **Morten André Gundersen**, NTNU, Trondheim, Norway *Lipase Catalyzed Synthesis Of Enantiopure Precursors And Derivatives For β-Blockers Practolol, Pindolol And Carteolol*	R5
14:55-15.15	MSc. **Ivar Skogvik**, NTNU, Trondheim, Norway *Chemo-Enzymatic Synthesis of Building Block for Tramadol And Enzymatic Reversibility Analysis*	R5
15:30-	**Dinner**	D3-114

Saturday June 27, 2026

Session chair: Jennifer Littlechild		
09:30-10:00	Dr. **Majid Ahmad Ganie,** IIT, Indore, India *Flavin-Photocatalyzed Benzylic Functionalization, Spirocyclization, and Spiroepoxidation of Phenols*	
10:00-10:20	MSc. **Fredrik Bjørnes,** NTNU, Trondheim, Norway *Chemo-Enzymatic Synthesis of Enantiopure Beta-blocker (+)-Nebivolol*	R5
10.20-11:00	Prof. Dr. **Rafi Ahmad**, University of Inland Norway, Hamar, Norway *Superbugs vs. Super Tech*: *How AI and Genomics Are Reshaping the Battle Against Infection and Antimicrobial Resistance*	
11:00-11:20	MSc. **Christina Glenna Pettersen**, NTNU, Trondheim, Norway *Chemo-Enzymatic Synthesis of Enantiopure Building Blocks for (S)-Verapamil and Derivatives*	R5
11:20-12:05	**Special Honorary Concluding Lecture** Prof. Dr. **Sergio Riva,** Scitec-CNR, Milano, Italy *Chemo-Enzymatic Synthesis of Pharmaceuticals: Examples from a Forty Years Research Activity*	R5

Scientific Committee

Elisabeth Jacobsen, NTNU, Trondheim, Norway Treasurer of European Society of Applied Biocatalysis (ESAB)
Debayan Sarkar Department of Chemistry, IIT, Indore, India
Roland Wohlgemuth, Lodz University of Technology, Lodz, Poland President of ESAB
Jennifer Littlechild University of Exeter, Exeter, UK Vice President of ESAB

Local Organising Committee

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Morten Andre Gundersen Dept. of Chemical engineering, NTNU (IKP), Trondheim, Norway
Mathilde Herring Aanerud, IKB, NTNU, Trondheim, Norway
Christina Glenna Pettersen, IKB, NTNU, Trondheim, Norway
Ivar Skogvik, IKB, NTNU, Trondheim, Norway
Truls Rossbach Hammer, IKB, NTNU, Trondheim, Norway
Alexandre Murat, IKB, NTNU, Trondheim, Norway
Kristofer Gunnar Paso, IKP, NTNU, Trondheim, Norway

LECTURE ABSTRACTS

L1. Thermophilic Genomes and Metagenomes as a source of Novel Enzymes for Industrial Biocatalysis

Jennifer A. Littlechild

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Enzymes identified in thermophilic genomes and metagenomes are providing new novel biocatalysts for Industrial Biocatalysis. These enzymes have evolved under different evolutionary pressures and often have new catalytic properties and stereoselectivity when compared to previously identified proteins. They are finding new applications industrially and are important to enhance the enzyme 'tool box' that is available for new sustainable processes to produce important new pharmaceuticals and healthcare products. These enzymes are not only naturally evolved for stability to temperature but are also stable to solvents and the addition of other formulation additives. They can also have novel protein folds which have not been identified in other know protein structures.

This lecture will illustrate a selection of important enzyme examples including aminoacylase, carbonic anhydrase, carboxyl esterase, epoxide hydrolase, transketolase, transaminases, sugar isomerase and cyclic di-phosphoglycerate synthetase. These enzymes can be further optimised for specific processes by both rational and directed evolution using 'state of the art' microfluidics.

1. Biocatalysis as Key to Sustainable Industrial Chemistry
   Alcántara A, Domínguez de María P, Littlechild J, Schürmann M, Sheldon R and Wohlgemuth, R (2022) ChemSusChem, e202102709, 1-11
2. The structure of a novel thermophilic esterase from the Planctomycetes species, *Thermogutta terrifontis* reveals an open active site due to a minimal cap domain. Sayer C, Szabo Z, Isupov MN, Ingham C, Littlechild J.A. (2015). Front. Microbiol. 11, 1294
3. A 'Split-Gene' Transketolase from the Hyper-thermophilic bacterium *Carboxydothermus hydrogenoformans*: Structure and Biochemical Characterization James P, Isupov M, De Rose S A, Sayer C, Cole I S and Littlechild J A (2020) Front. Microbiol. 11:592353.
4. New thermophilic α/β class epoxide hydrolases found in metagenomes from hot environments Ferrandi E, Sayer C, De Rose S, Guazzelli E, Marchesi C, Saneei V. Isupov M, Littlechild, J and Monti D (2018) Front. Bioeng. and Biotechnol, 6, 144
5. Discovery and characterization of thermophilic limonene-1,2-epoxide hydrolases from hot spring metagenomics libraries Ferrandi, C, Sayer C, Isupov, M, Annovazzi C, Marchesi C, Lacobone G, Peng X, Bonch-Osmolovskaya, E, Wohlgemuth R, Littlechild J. and Monti D. FEBS J (2015) 282, 2879-2894
6. Biochemical and Structural Characterisation of a Novel D-Lyxose Isomerase from the Hyperthermophilic Archaeon *Thermofilum* sp. De Rose SA, Kuprat T, Isupov MN, Reinhardt A, Schönheit P and Littlechild JA (2021) Front. Bioeng. Biotechnol. 9:711487
7. Functional and structural insights into a thermostable (S)-selective amine transaminase and its improved substrate scope by protein engineering Patti S, De Rose, S, Isupov, M, Alunno M. Riva. S, Ferrandi E, Littlechild J, Monti D, (2025) Applied Microbiology and Biotechnology 109:180
8. Discovery and Characterization of Novel 2-Phosphoglycerate Kinase and Cyclic 2,3-DiphosphoglyceratSynthase from Thermophilic (Meta) Genomes (2026) Patti, S, De Rose, S Isupov M , Kublanov ,I Alunno, I, Riva,S Bassanini I, Dore E, Stracke, C, Siebers, B, Ferrandi, Littlechild, J and Monti, D (2026) Catalysts, 16, 305

L2. Pyrrolopyrimidines and Purines as Csf1r Inhibitors

(or How to eradicate microglia)

Eirik Sundby and Bård Helge Hoff

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The colony-stimulating factor 1 receptor (CSF1R) is a tyrosine kinase expressed among others in monocytes, macrophages, microglial cells, and bone-resorbing osteoclasts. Activation of CSF1R and downstream signalling pathways is necessary for normal function of these cell types. However, in some diseases, overexpression of CSF-1 and/or elevated activity of CSF1R cause a misbalance of the immune cell phenotypes. Thus, CSF1R inhibitors might have therapeutic relevance in cancers, CNS disorders, and bone diseases. We have investigated pyrrolopyrimidines and purines as CSF1R inhibitors [1-4]. An X-ray co-crystal structure of one of the frontrunner inhibitors allowed for rational design and indentification of numerous compounds with higher activity than the reference drug PLX3397 in enzymatic studies. Hurdles for progressing these inhibitors into lead compounds will be discussed, along with their kinase activation state preferences. Finally, *in vivo* studies will be presented demonstrating efficient blood–brain barrier penetration, effective microglial depletion, and therapeutic efficacy in murine models of multiple sclerosis and ALS.

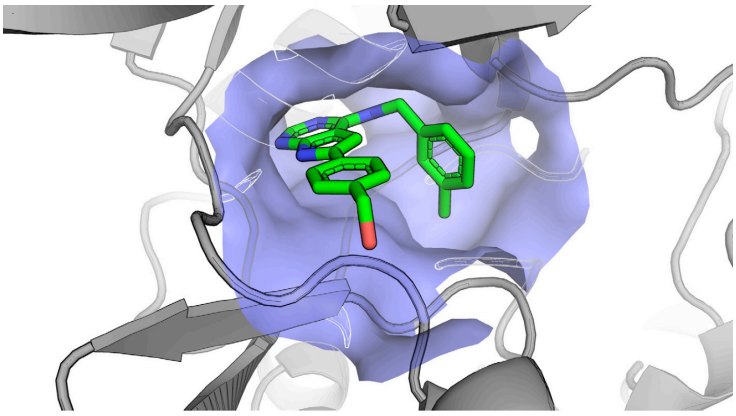

Figure 1: Front view of CSF1R inhibitor co-crystallesed with the CSF1R kinase domain.

[1] Bjørnstad, F.; Havik, S.; Aarhus, T. I.; Mahdi, I.; Unger, A.; Habenberger, P.; Degenhart, C.; Eickhoff, J.; Klebl, B. M.; Sundby, E.; Hoff, B. H., Pyrrolopyrimidine based CSF1R inhibitors: attempted departure from fatland. *European Journal of Medicinal Chemistry* **2024**, 265, 116053.
[2] Aarhus, T. I.; Teksum, V.; Unger, A.; Habenberger, P.; Wolf, A.; Eickhoff, J.; Klebl, B.; Wolowczyk, C.; Bjørkøy, G.; Sundby, E.; Hoff, B. H., Negishi Cross-Coupling in the preparation of benzyl substituted pyrrolo[2,3-d]pyrimidine based CSF1R inhibitors. *European Journal of Organic Chemistry*. **2023** *26*, e202300052,
[3] Aarhus, T. I.; Eickhoff, J.; Klebl, B.; Unger, A.; Boros, J.; Choidas, A.; Zischinsky, M.-L.; Wolowczyk, C.; Bjørkøy, G.; Sundby, E.; Hoff, B. H., A highly selective purine-based inhibitor of CSF1R potently inhibits osteoclast differentiation. *European Journal of Medicinal Chemistry* **2023**, *255*, 115344.
[4] Aarhus, T. I.; Bjørnstad, F.; Wolowczyk, C.; Larsen, K. U.; Rognstad, L.; Leithaug, T.; Unger, A.; Habenberger, P.; Wolf, A.; Bjørkøy, G.; Pridans, C.; Eickhoff, J.; Klebl, B.; Hoff, B. H.; Sundby, E., Synthesis and development of highly selective pyrrolo[2,3-d]pyrimidine CSF1R inhibitors targeting the autoinhibited form. *Journal of medicinal Chemistry* **2023**, *66*, 6959–6980.

L3. Heterogenous Catalysis and Selective Programming of Polysaccharides

Armando Cordova

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Renewable polysaccharides are emerging not only as sustainable feedstocks but also as programmable materials for catalyst design and selective synthesis. This lecture will highlight how heterogeneous catalysis and molecular-level control of polysaccharide structure can be combined to create recyclable catalytic systems and sustainable routes to pharmaceutically relevant molecules. Examples ranging from cellulose-supported asymmetric catalysts and metal nanocatalysts to the valorization of lignocellulosic biomass into aromatic building blocks and bioactive compounds will be presented. Together, these studies demonstrate how catalysis and renewable materials can contribute to the next generation of green and efficient drug synthesis.

L4. New Psychoactive Substances: Chemistry, Synthesis and Societal Impact

Huiling Liu

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7041Trondheim, Norway

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New Psychoactive Substances (NPS) represent a rapidly evolving class of compounds designed to mimic the effects of controlled drugs while evading legal restrictions. Over the past two decades, their proliferation has posed significant challenges to public health, regulatory agencies, and the scientific community. This presentation provides an overview of the chemistry and societal impact of NPS, highlighting their structural diversity and the strategies used to generate novel analogues.

From a chemical perspective, NPS arise from modifications of known psychoactive scaffolds, including phenethylamines, synthetic cannabinoids, cathinones, and opioids. Even minor structural changes - such as functional group substitutions or alterations to molecular frameworks - can lead to substantial differences in potency, receptor selectivity, and toxicity. The rapid pace of these modifications complicates analytical detection and pharmacological characterization.

Driven by market demand and regulatory pressures, new variants are continually introduced, often outpacing existing analytical and legal frameworks. This dynamic landscape presents ongoing challenges for forensic identification and monitoring.

Beyond chemistry, NPS are associated with unpredictable effects, increased toxicity, and limited clinical understanding. Their widespread availability through global and digital markets further amplifies their societal impact.

Addressing the NPS challenge requires coordinated efforts across chemistry, toxicology, public health, and policy, supported by improved analytical capabilities, monitoring systems, and adaptive regulatory strategies.

L5. Discovery and Development of Proximity Inducing Agents: Aurigene Oncology's Contribution to Neo-PPI Driven Pharmacology

Susanta Samajdar

Aurigene Oncology Limited
Indore, India

e-mail: susanta_s@aurigene.com

The past decade has witnessed a paradigm shift in drug discovery, moving beyond classical occupancy-driven inhibition toward event-driven pharmacology that exploits chemically induced protein proximity. Proximity inducing agents (PIAs) — encompassing heterobifunctional degraders (PROTACs), molecular glue degraders, and non-degradative proximity inducers — operate by engineering neo-protein–protein interactions (neo-PPIs) that are absent in normal biology, thereby redirecting the cell's own enzymatic machinery to modulate target protein fate. This mechanistic framework dramatically expands the druggable proteome, enabling therapeutic intervention against transcription factors, scaffolding proteins, and other targets historically considered intractable to small molecule approaches.

Aurigene Oncology has built a fully integrated proximity inducer discovery engine — the A-PROX platform — that combines solid phase library screening, direct-to-biology chemistries, proprietary ternary complex assays, structure-based design, and computational modelling to systematically prosecute neo-PPI space across oncology targets. This talk will describe our journey from platform conception to clinical-stage assets, highlighting the scientific principles, key learnings, and translational strategies that have shaped our portfolio.

We will present case studies spanning multiple target classes. First, the discovery of potent, paralogue-selective SMARCA2 degraders that achieve deep and durable target knockdown while sparing SMARCA4, culminating in an IND-approved clinical candidate — the first SMARCA2 degrader to enter clinical development. Second, the rational design of SMARCA4-selective degraders that exploit the synthetic lethality between SMARCA4 loss and residual SWI/SNF complex activity in SMARCA4-driven cancers. Third, the development of paralogue-selective p300 degraders with exceptional selectivity over CBP, designed to exploit synthetic lethality in CBP-mutant hematologic and solid malignancies, and to address p300-dependent oncogenic transcription in prostate and other cancers. Fourth, progress on a pan-KRAS degrader program targeting one of oncology's most recalcitrant drivers.

Collectively, these programs illustrate how a systematic, platform-driven approach to neo-PPI pharmacology can convert proximity biology into differentiated, clinically actionable therapeutics. We will discuss emerging opportunities in non-degradative proximity induction, the expanding E3 ligase landscape, and the next frontier of induced proximity beyond the ubiquitin–proteasome system.

Biography: Dr. Samajdar serves as the Chief Scientific Officer at Aurigene Oncology Limited, bringing over 25 years of experience in synthetic and medicinal chemistry research within diverse sectors of Indian industries and academia. He earned his Ph.D. in Synthetic Organic Chemistry from the **Indian Association for the Cultivation of Science (IACS) in Kolkata**. Subsequently, he pursued Post-Doctoral training in anti-cancer drug discovery at MD Anderson Cancer Centre in Houston, TX.
Dr. Samajdar has spearheaded multi-disciplinary drug discovery teams, resulting in the successful delivery of more than 20 preclinical development candidates spanning the Oncology and Inflammation

therapeutic domains. Several of these molecules are in the different phases of clinical development. His proficiency extends across various therapeutic modalities, encompassing small molecules, antibodies, antibody drug conjugates (ADCs), Targeted Protein degradation (TPD), and Natural Products.

He has tackled a range of target classes such as Transcription factors, GPCRs, Ion channels, Proteases, Kinases, NHRs, Epigenetic effector proteins etc. With a prolific track record, Dr. Samajdar has amassed over 100 patents and publications. He has been affiliated with Aurigene since March 2012, contributing his expertise in anti-cancer drug discovery and exploring newer avenues in Oncology research.

L6. High-Pressure Processing: A Gentle Strategy for Tailoring Polymer Functionality and Extracting Sensitive Bioactives

Marcelo Cristianini

State University of Campinas, Sao Paulo, Brazil
e-mail: mcristianini@unicamp.br

L7. Scalable Synthesis Method for Drug Encapsulation in Polymer Nanoparticles

Sulalit Bandyopadyhay

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Polymeric nanoparticles are attractive carriers for hydrophobic and sensitive therapeutics, but many established preparation routes suffer from multistep processing, poor reproducibility, and limited scalability. Flash nanoprecipitation (FNP) — the rapid, turbulent micro mixing of a polymer- and cargo-bearing organic stream against an aqueous antisolvent stream in a multi-inlet vortex mixer - offers a continuous, robust, and inherently scalable alternative, governed by a well-defined interplay of mixing, supersaturation, nucleation, and growth time scales [1]. This talk presents our work using FNP to encapsulate both organic and inorganic payloads within poly(lactic-co-glycolic acid) (PLGA), a biodegradable and biocompatible matrix.

We first show how the operating and system variables of the FNP process (polymer concentration, flow-rate ratio, solvent, surfactant) govern the size, size distribution, and colloidal stability of bare PLGA nanoparticles [2], and how these conditions translate into efficient loading of the anticancer drug paclitaxel, with loading efficiencies reaching around 90% depending on the process conditions. Building on this baseline, we demonstrate co-encapsulation of superparamagnetic iron oxide nanoparticles (IONPs) to impart magnetic functionality. Hydrophobic IONPs, prepared by either thermal decomposition or co-precipitation followed by oleic acid coating, were phase-transferred and encapsulated in PLGA, with loading efficiencies tunable through the size and hydrophobicity of the starting IONPs, reaching up to ~43% [2]. Finally, co-encapsulation of paclitaxel with IONPs yielded magnetically responsive carriers in which an alternating magnetic field triggered roughly a fourfold increase in drug release relative to the field-free case [3]. All formulations showed good biocompatibility across the cell lines tested. Together, these results position FNP as a versatile and scalable route to functional, stimuli-responsive drug-delivery nanoparticles.

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L8. Precision Dearomatisation With Arene – π- Tribromide Complex and Visible Light Catalysis

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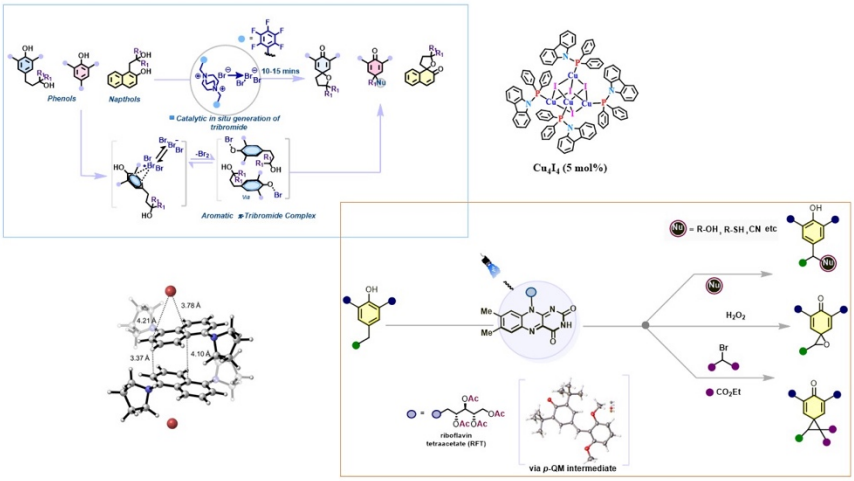
Dearomatization reactions have always attracted enough attention as they cater interesting chemical transformations in organic synthesis that facilitate the generation of three-dimensional structures from two-dimensional precursors and thus put forward the best access towards achieving Molecular Complexity. Aromaticity imparts extraordinary stability to the structures due to delocalization of pi electrons. In this regard many synthetic protocols of dearomatization are available. However,a general platform for the oxidative aromatization of common feedstocks is few. Our group has reported the first recognition Tribromide complexes in a number of Dearomative Transformations. The objective has been to understand an unknown Arene π- Tribromide complex Intermediate which would be a major breakthrough towards this direction.

Concurrently, we aim to develop a catalytic, visible-light-driven strategy for transforming abundant and inexpensive planar Arenols and other aromatic core into valuable, complex three-dimensional chiral scaffolds via dearomatization. Its significance lies in overcoming the inherent stability of aromatic rings using a novel *in situ* generated electrophilic tribromide catalyst (Br_3^-), formed synergistically via photo redox processes. The tribromide is sufficiently electrophilic to break inherent aromatic stabilization of 2D cores to provide access to 3D core skeletons in one pot transformation. para-Quinone methides (p-QMs) are versatile, transient electrophilic dearomatized intermediates in organic synthesis, enabling a range of transformations such as cycloadditions, nucleophilic additions, and cascade reactions. The photogenerated *p*-QMs undergo efficient transformations, including benzylic functionalization, spirocyclization, and spiroepoxidation, delivering rapid access to benzylic scaffolds and structurally complex sp^3-rich spirocyclic frameworks



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L9. Sustainable Drug Synthesis

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Over the last eight decades the development and manufacturing of diagnostics and therapeutics have enabled tremendous progress of human health on our planet by saving and improving the lives of a large number of humans suffering from inherited and acquired diseases. When human health gets out of balance and is affected negatively by diseases, biological resources in the biosphere of our planet are key for the synthesis of drugs. [1] Around half of the new drugs approved between 1981 and 2019 are related to biological resources, either directly as biological macromolecules, unaltered natural products, botanical drugs, or indirectly as natural product derivatives, vaccines, or mimics of a natural product[2] Complex interactions of drugs with humans and their activities with the natural environment go beyond the individual level and link planetary health also to planetary boundaries.[3,4] The interfaces between sustainability and drugs, their interactions with humans and their way of synthesis, are important at various scales, and the evolving nature of sustainable drugs for precision medicine requires also a concomittant adaptation of sustainable manufacturing processes, as illustrated by the paths to sustainable statin drugs.[5] The molecular economy from starting materials via the intermediates to the active pharmaceutical ingredients provides a frame work for biocatalytic syntheses of numerous drug precursors. Biocatalytic reaction steps for the most challenging reactions which can only be done via chemical protection-deprotection schemes or not at all, or for transitioning from fossil-based to biobased raw materials, are best taken into consideration early on in the retrosynthetic analysis and route design for sustainable synthesis.[6,7] The rapidly growing biocatalytic reaction platforms support the sustainable synthesis of more complex pharmaceuticals from simple building blocks.[8-10]
The identification and overcoming of bottlenecks to complete conversion and product recovery[11] will further contribute towards the increasing use of biocatalysis, from one-step and multi-step reactions to biocatalytic total synthesis, in the sustainable drug synthesis.[12]

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L10. SyncoZymes' Story with Enzymes Development and Their Application in Pharmaceutical Industry

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The lecture will focus on syncosymes´s history from the foundation in 2007 up util now, showing the factory for enzymes, food ingredient, intermediates, APIs and formulations. With the 80 series of enzymes, Syncozymes can supply enzymes for a broad range of enzyme catalysed reactions. The factory has an annual capacity to produce over 100 tons of coenzyme NAD-family products and custom batches of enzyme preparations reaching tonnage levels.

L11. From Openspim to Flowspim: Enhancing The Versatility of a Light Sheet Microscope Through an Iterative Design Process

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Light sheet microscopy is ideal for the 3D imaging of large biological specimens, yet systematic documentation on adapting microscope designs to diverse experimental requirements remains limited. We present the iterative process used to design and build a modular light-sheet microscope and adapt it to different sample types and experimental conditions. Starting from a stripped-down OpenSPIM platform, we gradually make our microscope more versatile by implementing new hardware, such as additional laser channels and optical filters, and new protocols for sample handling. In its final iteration, FlowSPIM is a new flow-based incubation technique for 3D tissue culture.

Bio Joachim is a mechanical engineer from NTNU, with a Ph.D. in microfluidics from the University of Oslo. He was a postdoc at Stanford University and at UCSB to learn about interfacial dynamics, polymer systems and protein diffusion, with human health applications. He then worked as a teacher of fluid mechanics at the Norwegian University of Life Sciences, and developed "kitchen flows" as an affordable and accessible learning strategy. Back at the University of Oslo, he developed a 3D imaging platform to unravel how cells work in concert to form organs. Applications of his research span from water treatment to contact lens development and drug testing.

L12. Flavin-Based Photodynamic Inactivation as a Sustainable Approach for Extending the Post-Harvest Shelf Life of Fresh Produce in India

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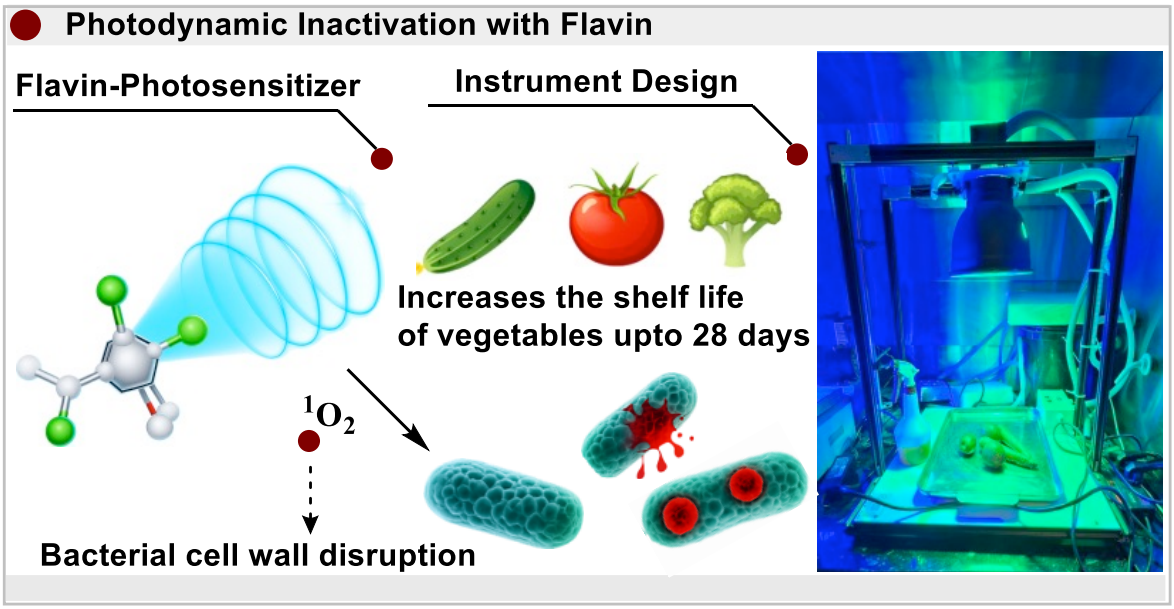
The integration of riboflavin derivatives as biocompatible photosensitizers into an IoT-enabled portable device addresses longstanding challenges in perishable goods storage, high energy burdens, and microbial spoilage for small and marginal farmers in India. A safe and biocompatible photosensitizer, in combination with blue LED, steps up to generate reactive oxygen species (ROS) that rapidly and irreversibly disrupt microbial cell envelopes, proteins, and nucleic acids. The protocol achieves selective pathogen inactivation while overcoming critical limitations of conventional preservation techniques, such as limited penetration depth, oxidative damage to food quality associated with ultraviolet irradiation, radical-induced off-flavors and structural degradation from ultrasonication. Shotgun metagenomic analysis further demonstrated that treatment with cationic salt and Boc-Lysine-protected riboflavin derivatives markedly reduced microbial diversity, underscoring the microbial efficacy of the platform. By substantially extending post-harvest shelf life and enhancing food safety, this technology offers a mass-saleable, environmentally sustainable alternative to energy-intensive cold storage.



L13. A Computational Dynamic Model For Drug Resistance and Treatmend Selection in Enzyme Inhibition Treatment

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Resistance to therapy is a major clinical obstacle to treatment of cancer and communicable diseases. Inhibitory drug selection in treatment of patients where the disease is showing resistance to therapy is often guided by IC_{50} or fold-IC_{50} values. We construct a model for the treatment of chronic myeloid leukaemia (CML), a blood cancer that has been extensively studied and is used as a model for targeted therapy and use this model to contest the use of fold-IC50 values as a guide for treatment selection. If time allows, I will also show some results on combination treatments.

L14. Chemo-enzymatic Synthesis of Pregabalin (Lyrica)

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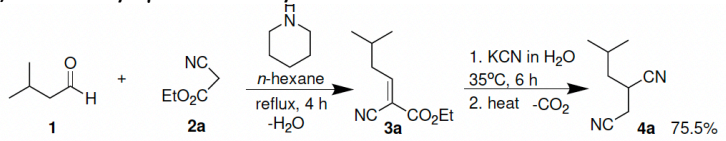
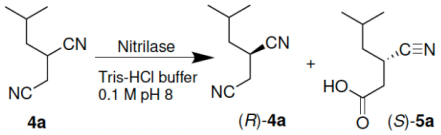
A chemoenzymatic approach for synthesis of enantiopure pregabalin has been investigated with nitrilases and nitrile reductases from Syncozymes Co., LTD, Shanghai, China (Scheme 1 and 2). The drug is used in the treatment of epilepsy, neuropathic pain, fibromyalgia, restless legs syndrome, opioid withdrawal, generalized anxiety disorder (GAD) and postherpetic neuralgia (a type of nerve damage that can result from shingles). The drug is manufactured by several pharmaceutical companies, where the most known trade names are Axalid and Lyrica. The IUPAC name of the Active Pharmaceutical Ingredient (API) is (*S*)-3-isobutyl-γ-aminobutyric acid.

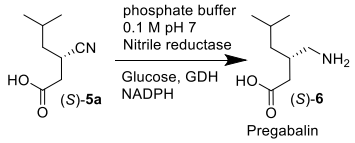


Scheme 1. Synthesis of racemic building block **4a** for nitrilase catalysed kinetic resolution.



Scheme 2. Nitrilase catalysed kinetic resolution of **4a** yielding (*S*)-**5a** (low yield)

Racemic 2-isobutylsuccinonitrile (**4a**) was synthesized in high yield and high purity by a Knoevenagel condensation of 3-methylbutanal (**1**) and ethyl 2-cyanoacetate (**2a**) followed by a conjugate addition of cyanide and decarboxylation. **4a** was then subjected to kinetic resolution using 21 nitrilase variants provided by Syncozymes. The isolated yield of (*S*)-**5a** was low, which will be optimised. Several of the nitrilases exhibited little or no measurable conversion in the kinetic resolution of **4a**, which require further testing. Significant differences in activity and stereoselectivity were also observed in the different reactions.



Scheme 3. Attempted nitrile reductase-catalysed nitrile reduction of (*S*)-**5a** to give (*S*)-**6** (pregabalin)

The subsequent reduction of (*S*)-**5a** to pregabalin ((*S*)-**6**) by nitrile reductase ES-NRED-102 did not result in detectable product formation.

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L15. Visible light-induced Crossed [2+2] Cycloaddition of Aryl Terminal Olefins via Energy Transfer Catalysis

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Cyclobutanes are high-value synthetic targets in medicinal chemistry, yet their assembly is often hindered by significant ring strain (roughly 26–27 kcal.mol^{-1})[1] and the limitations of classical photochemical [2+2] cycloadditions.[2] While recent advances in visible-light energy transfer[3,4] and photoredox[5] catalysis have improved functional group tolerance, many methods remain restricted to homodimerization or the use of specific internal and electron-biased olefins.[2] Crossed [2+2] cycloadditions involving simple aryl terminal styrenes remain significantly underexplored.

This work describes a visible-light-mediated methodology for the crossed [2+2] cycloaddition of aryl terminal styrenes utilizing an iridium-based photocatalyst. By overcoming the thermodynamic and kinetic barriers that typically favour homodimerization, this approach enables the efficient synthesis of diverse, multi-substituted cyclobutanes from readily available terminal alkene precursors.

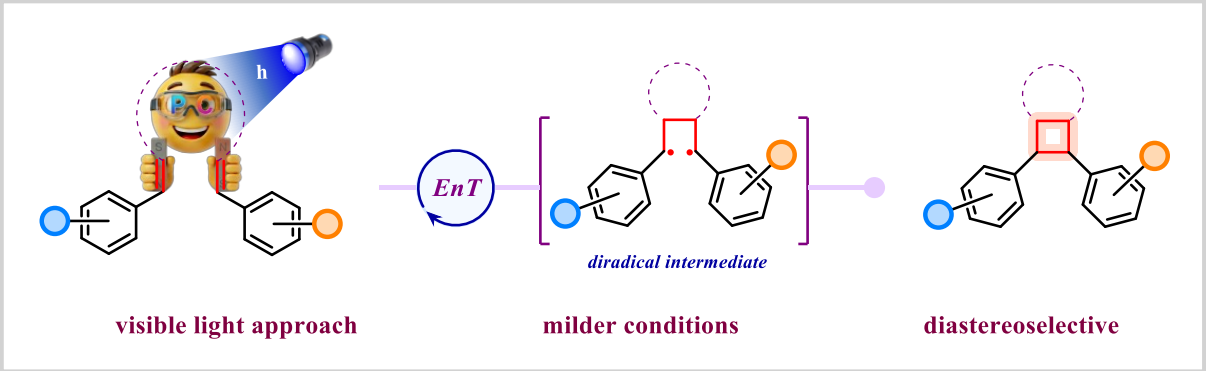

Figure 1. Visible light-induced crossed [2+2] cycloaddition of aryl terminal olefins.

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L16. Lipase Catalyzed Synthesis of Enantiopure Precursors and Derivatives for β-Blockers Practolol, Pindolol and Carteolol

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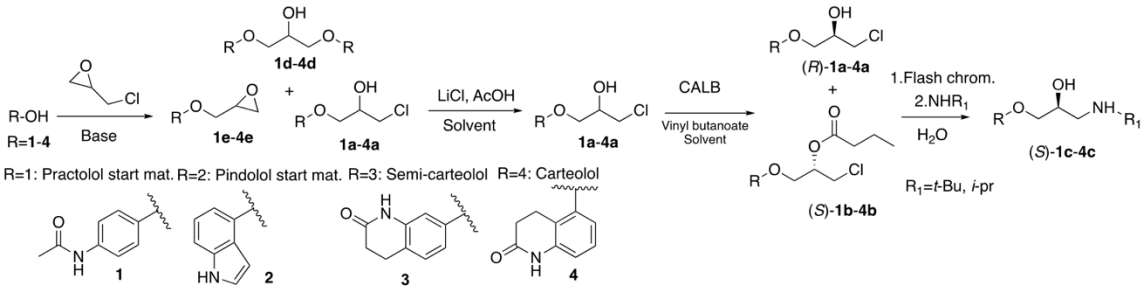
High blood pressure (hypertension) and heart failure are severe global health problems. In Norway, approximately 30% of all deaths are caused by cardiovascular diseases [1]. Approximately 26 million people worldwide live with heart failure, and approximately seven million deaths are caused by hypertension annually [2]. Heart failure cannot be cured, but may be treated by medications in order to increase quality of life for the patients. Both heritage (genetic) and lifestyle may lead to increased risk of cardiovascular diseases. Risk factors for cardiovascular diseases, such as reduced activity, eating more sugar and salt, increased stress, obesity and overweight, may be reasons for the increasing health problems worldwide [3].

Chlorohydrins as building blocks for several β-blockers have been synthesized in high enantiomeric purity by chemo-enzymatic methods. The yield of the chlorohydrins increased by the use of catalytic amount of base. The reason for this was found to be the reduced formation of the dimeric by-products compared to the use of higher concentration of the base. An overall reduction of reagents and reaction time was also obtained compared to our previously reported data of similar compounds.



Scheme 1. Building blocks (*R*)-**1a**-**4a** synthesized in 92–97% *ee* for use in synthesis of the *S*-enantiomers of the β-blockers practolol, pindolol and derivatives of carteolol ((*S*)-**1c**-**4c**).

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L17. Chemo-Enzymatic Synthesis of Building Block for Tramadol and Enzymatic Reversibility Analysis

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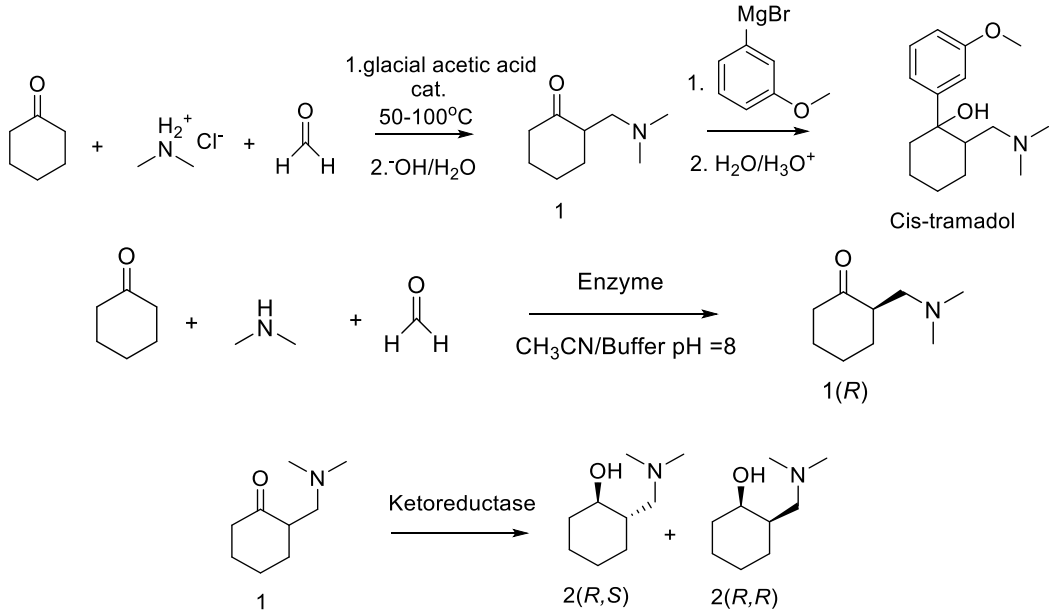
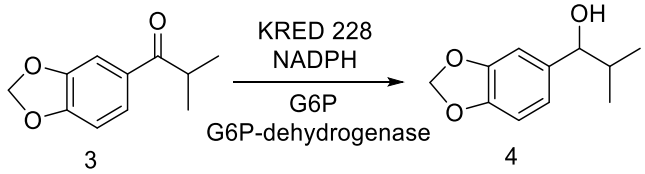
Tramadol is a commonly used painkiller used in hospitals for moderate to intense pains. It has been shown that the (*R,R*)-enatiomer has a 20 times higher affinity to the μ-opioid receptor. [1] In the industrial synthesis of tramadol only cis-tramadol is generated[2] without any assistance in determining. This means that the second chiral center is determined by the first one. By doing an asymmetric synthesis of the building block (1) or a kinetic resolution one can generate pure (*R,R*)-tramadol. Enzymatic synthesis showed selectivity and byproduct problems. The different ketoreductases tested for kinetic resolution showed no activity on 1.



Previous results from doing an asymmetric synthesis of 1-(benzo[d][1,3]dioxol-5-yl)-2-methylpropan-1-ol (3) from 1-(benzo[d][1,3]dioxol-5-yl)-2-methylpropan-1-one showed that the enatiomeric excess decreased (ee) from 67% to 49% when the reaction was run for a longer time. The enzyme used was shown to deracemize racemic 4. Suggesting that the regenation of glucose-6-phosphate was the cause of lowering ee.



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L 18. Flavin-Photocatalyzed Benzylic Functionalization, Spirocyclization, and Spiroepoxidation of Phenols

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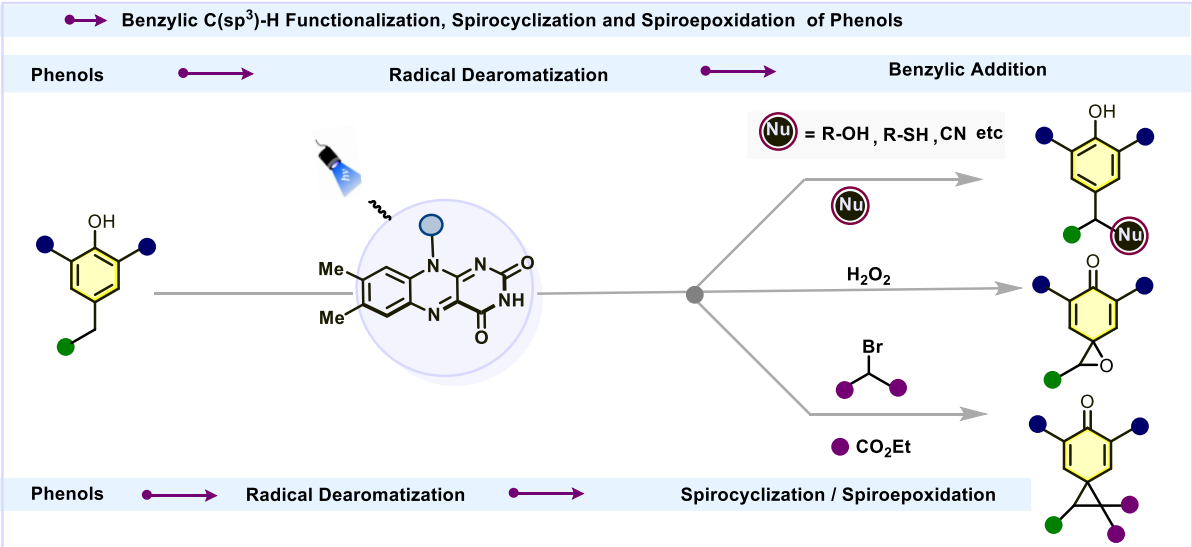
para-Quinone methides (*p*-QMs) represent a class of highly versatile, transient electrophilic synthetic intermediates in organic synthesis, enabling a diverse range of transformations such as cycloadditions, nucleophilic additions, and cascade reactions. (Scheme 1). Conventionally, these ephemeral species are generated *in situ* via acid- or base-mediated activation of phenols prefunctionalized with a leaving group (e.g., hydroxyl, halide, or sulfonate) at the benzylic position or through oxidation of phenols employing toxic heavy metals (e.g., lead, silver, or bismuth).

We report a novel photocatalytic approach for *in situ* generation of *p*-QMs directly from simple phenolic precursors, thereby circumventing the need for benzylic prefunctionalization or transition-metal reagents. The photogenerated *p*-QMs undergo efficient downstream transformations, including benzylic functionalization, spirocyclization, and spiroepoxidation, thereby enabling rapid access to benzylic scaffolds and structurally complex sp^3-rich spirocyclic frameworks.



Scheme 1.

L19. Chemo-Enzymatic Synthesis of Enantiopure Nebivolol enantiomers

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The American Heart Association reported in March 2019 their update on heart diseases and stroke statistics. The report states that the prevalence of high blood pressure in the United States between 2013-2016 was 46% of the total population at ages 20 years and older. It was the cause of death for 82,735 Americans in 2016 and costed the American society approximately $ 55.9 billion in the period 2014-2015 [1]. A class of drugs that have been used both in cardiovascular and non-cardiovascular treatment are the β-adrenergic blocking agents (betablockers). This class of drugs were introduced into clinical medicine in the early 1960's, and since then, the findings of these drugs have led to a discovery of the importance of the sympathetic nervous system in the pathophysiology of a wide variety of cardiovascular and non-cardiovascular disorders [2]. However, most betablockers are marketed with the racemic API, with the S-enantiomer as the most active, leaving the R-enantiomer as a non-active compound, or as a compound causing several unwanted side effects. FDA considers the wrong enantiomer as an impurity and demands for pure enantiomers as marketed drugs, not racemates [3].

Synthesis protocols for enantiopure building blocks and *S*-enantiomers of both (+)- and (-)-enantiomers of nebivolol (Fig. 1) will be presented [4].

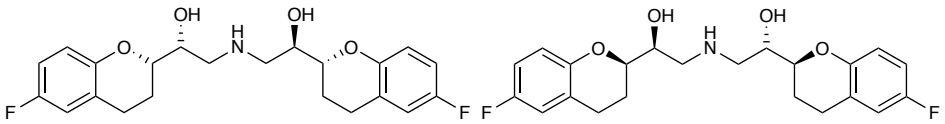

Figure 1. (*S,R,R,R*)-2,2'-Azanediylbis(1-(6-fluorochroman-2-yl)ethanol ((+)-nebivolol), left, and (*R,S,S,S*)-2,2'-azanediylbis(1-(6-fluorochroman-2-yl)ethanol ((−)-nebivolol) right.

[1]. E. J. Benjamin *et al. Circulation* **2019**, *139* (10), e526-e528.
[2]. J. W. Black and B. N. C. Prichard. *Br. Med. Bull.* **1973**, *29*, (2), 163.
[3]. FDA, *Chirality* **1992**, *4*, (5), 338.
[4]. F. Bjørnes *et al*. *Topics in Catalysis,* **2025,** *68* (11-12) 1058.
[4]. E. F. Hoem *et al. Catalysts,* **2026**, *16*, 256-273

L20. *Superbugs vs. Super Tech:* How AI and Genomics Are Reshaping the Battle Against Infection and Antimicrobial Resistance

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Antimicrobial resistance (AMR) represents one of the most urgent global health threats of the 21st century, undermining the effectiveness of life-saving treatments and jeopardizing modern medicine. Misuse and overuse of antibiotics are estimated to contribute to nearly 5 million deaths annually worldwide, accelerating the spread of resistant pathogens. Without effective intervention, AMR could claim up to 10 million lives per year by 2050 and impose a cumulative economic burden exceeding $1 trillion.

A major challenge in combating AMR lies in the time required for accurate diagnosis. Conventional bacterial culture methods typically require 2-4 days to identify pathogens and determine appropriate antibiotic treatment. In critical conditions such as sepsis, this delay necessitates immediate empirical treatment, often involving broad-spectrum or inappropriate antibiotics, further driving resistance.

This project addresses two major clinical burdens, including sepsis and urinary tract infections, by advancing strategies to better understand, clinically manage, and prevent AMR. We aim to develop rapid, point-of-care diagnostic tools that significantly reduce time-to-result while improving diagnostic accuracy. By integrating genomics and artificial intelligence, we propose a novel diagnostic prototype that delivers results within 4-5 hours.

This approach represents a transformative step toward precision antimicrobial therapy, enabling timely and targeted treatment decisions, reducing unnecessary antibiotic use, and strengthening antimicrobial stewardship. Ultimately, this work has the potential to mitigate the global impact of AMR, preserve the efficacy of existing antibiotics, and save millions of lives.

L 21. Chemo-Enzymatic Synthesis of Enantiopure Building Blocks for (S)-Verapamil and Derivatives

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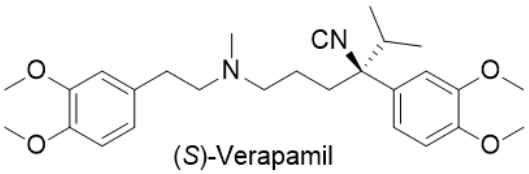
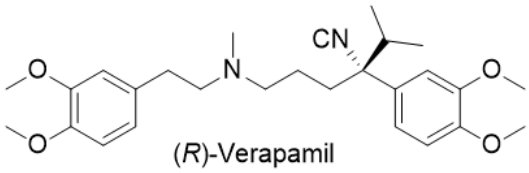
Verapamil is a calcium channel blocker (CCB) used in the treatment of cardiovascular diseases. Verapamil is available as a racemate containing both the *S*- and *R*-enantiomer[1]. The enantiomers have similar pharmacological effects, but (*S*)-verapamil is more pharmacologically potent than the *R*-isomer and has a larger volume of distribution[2]. The objective of this thesis was to synthesise (*S*)-verapamil through a more sustainable synthesis pathway than previously reported, using enzymes. The first attempted synthesis route was discontinued due to racemisation in the final synthetic step, an issue that was attempted to be mitigated in the second synthesis pathway.



(*S*)-Verapamil



(*R*)-Verapamil

In the current pathway, 4-bromo-1-(3,4-dimethoxyphenyl)butan-1-one (**3a**) was successfully synthesised in 73% yield and >99% purity through a Friedel–Crafts acylation. Subsequently, 6-bromo-3-(3,4-dimethoxyphenyl)-2-methylhexan-3-ol (**4b**) was synthesised in 22.7% yield and >99% purity (NMR) via a Grignard reaction. The kinetic resolution of compound 4b was unsuccessful with both Candida antarctica lipase A (CALA) and Candida antarctica lipase B (CALB).

The first pathway was initiated from 3,4-dimethoxybenzaldehyde (**1b**), where a Grignard reaction yielded 1-(3,4-dimethoxyphenyl)-2-methylpropan-1-ol (**2b**) in 32.7% yield and 94% purity (NMR). Compound **2b** underwent a promising kinetic resolution with CALA, giving a 23% yield, 77% enantiomeric excess (*ee*) and 60% conversion. This optimisation was achieved through a Design of Experiments (DOE) approach.

[1]. Petersen, A. S.; Barloese, M. C. J.; Snoer, A.; Soerensen, A. M. S.; Jensen, R. H. Verapamil and Cluster Headache: Still a Mystery. A Narrative Review of Efficacy, Mechanisms and Perspectives. *Headache* **2019**, *59*, 1198–1211, DOI: 10.1111/head.13603

[2]. Busse, D.; Templin, S.; Mikus, G.; Schwab, M.; Hofmann, U.; Eichelbaum, M.; Kivist¨o, K. T. Cardiovascular effects of (R)- and (S)-verapamil and racemic verapamil in humans: a placebo-controlled study. *Eur. J. Clin. Pharmacol*. **2006**, *62*, 613–619, DOI: 10.1007/s00228-006-0154-7

L22. Chemo-Enzymatic Synthesis of Pharmaceuticals: Examples From a Forty Years Research Activity

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The synthesis of active pharmaceutical ingredients (APIs) typically requires the installation and manipulation of functional groups and stereogenic centers following complex synthetic schemes, usually relying on protecting and deprotecting steps, generating high amounts of waste.

During the years, biocatalysis has established itself as a valuable tool for API synthesis thanks to its numerous advantages, such as superior regio-, stereo-, and enantioselectivity of the (optimized) enzymes, shorter multi-step synthetic routes, mild reaction conditions, reduced amounts of waste and fewer side products.

In this presentation the discussion of some relevant examples from the recent literature will be combined with the presentation of the results collected in forty years of research activity in our CNR Institute.

Examples will be related to the exploitation of hydrolases, oxidoreductases and, more recently, transferases, in water or in organic solvents.

1. Our reviews on this topic:

a) G. Carrea, S. Riva, "Properties and synthetic applications of enzymes in organic solvents", *Angew. Chem. Int. Ed.* **39**, 2226 (2000).
b) D. Monti, G. Ottolina, G. Carrea, S. Riva, "Redox reactions catalyzed by isolated enzymes", *Chem. Rev*. **111**, 4111-4140 (2011),
c) E.E. Ferrandi, S. Bertuletti, D. Monti, S. Riva, "Hydroxysteroid Dehydrogenases: An Ongoing Story", *Eur. J. Org. Chem..,* **issue 29**, 4463 (2020).

Biography

Dr Sergio Riva is Emeritus Research Director at the Institute of Chemical Sciences and Technologies (SCITEC) of the Italian National Research Council (CNR), where he has been working from 1984 to 2025. He was an adjunct professor at the University of Modena and Reggio Emilia from 2000 to 2022. He obtained his Laurea in Chemistry from Milano University in 1983 and his "Diploma di Specialità" in Organic Synthesis from the Milano Politecnico in 1989. He spent a year (1987) at MIT (Cambridge, USA) working with Professor A. Klibanov on the research area of biocatalysis in organic solvents. In 1993, he was awarded the *Ciamician Medal*, and in 2023, he received the *Quilico* Medal from the Organic Chemistry Division of the Italian Chemical Society both motivated by his research in biocatalysis. His scientific contributions are documented in more than 240 publications and patents, focusing on the isolation and characterisation of various enzyme groups and the synthetic applications of these biocatalysts.

POSTER ABSTRACTS

P1. Towards Inversion of the Absolute Configuration of Methyl (*R*)-3-(benzoylthio)-2-methylpropanoate

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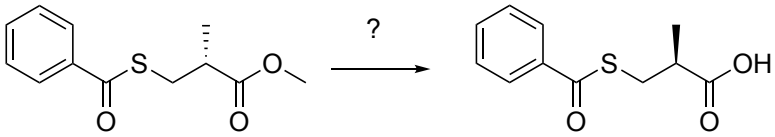
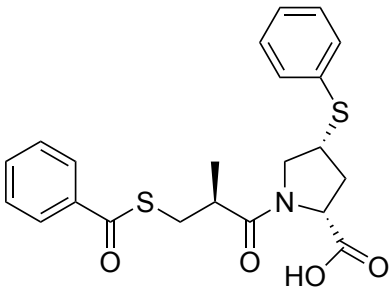
Methyl (*S*)-3-(benzoylthio)-2-methylpropanoate is a chiral building block for Zofenopril, an angiotensin Converting Enzyme (ACE) inhibitor used to treat hypertension. The drug is proven more efficient than other similar drugs. Synmax co. LTD in Taipei, Taiwan, produces methyl (*S*)-3-(benzoylthio)-2-methylpropanoate from a racemic mixture, where the *R*-enantiomer is difficult to convert to the right enantiomer and thus gives a high economic loss due to the low atomic efficiency.

Several attempts in order to inverting the methyl group on methyl (*R*)-3-(benzoylthio)-2-methylpropanoate to obtain methyl (*S*)-3-(benzoylthio)-2-methylpropanoate have been performed: Racemisation *via* enolates and hydroxylation with different Cytochrome P450 (CYP450) with subsequent elimination and methylation with a proS-enzyme.



Chilral builiding block of Zofenopril



Zofenopril

If one of these protocols are successful, it represents a promising step toward sa more efficient and sustainable synthesis of Zofenopril.

1. Ambrosioni, E. *Am. J. Cardiovasc. Drugs*. **2007**, *7* (1) 17

P2. Chemo-Enzymatic Synthesis of Enantiopure Building Block for Verapamil and Derivatives

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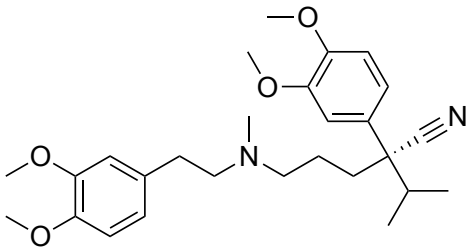
A chemo-enzymatic protocol for synthesis of the chiral side chain of the calcium-channel blocking drug (*S*)-Verapamil ((*S*)-5-((3,4-dimethoxyphenethyl)(methyl)amino)-2-(3,4-dimethoxyphenyl)-2-isopropylpentanenitrile) will be presented, Fig. 1.

Verapamil is the trivial name of the racemic active pharmaceutical ingredient (API) of multiple pharmaceuticals, such as Isoptin® and Calaptin®. The drugs are used for treatment of high blood pressure, control of ventricular rate and prevention of migraine headaches[1].



(*S*)-Verapamil

Fig. 1.

The main action of the drug is the calcium channel blocking activity of the *S*-enantiomer (shown). (*R)*-Verapamil, however, exhibits low calcium channel selectivity and inhibits mostly sodium channels. It has also been demonstrated that (*S*)-Verapamil is four times more potent than (*R*)-Verapamil in effect on heart rate and blood pressure. Due to this, (*S*)-Verapamil should be administered as single enantiomer API, as it would allow the treatment to be more efficient with potential reduction of undesirable effects.

A protocol for synthesis of the racemic piperonal derivative will also be described.

1. Curtis, M. J.; Walker, M. J. A. *Br. J. Pharmacol*. **1986**, *89* (1), 137.

P3. Chemo-Enzymatic Synthesis of Enantiopure Building Block for Tramadol

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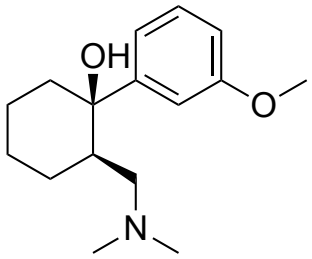
Tramadol ((1*R*,2*R*)-2-((dimethylamino)methyl)-1-(3-methoxyphenyl)cyclohexan-1-ol) as shown in Fig. 1 is sold under the brand names Ultram, Cozip and Ultracet among others. The drug is an opioid pain-relief medication and a serotonin - norepinephrine reuptake inhibitor (SNRI) used to treat moderately to severe pain, f. inst in cancer patients[2-4]. The *R,R*-enantiomer is 10 times more potent than the *S,S*-enantiomer, however, the drug is still marketed with racemic API.

We aim to obtain the chiral building block for the *R,R*-enantiomer with an asymmetric Mannich Reaction catalysed by *Aspergillus melleus* acylase.



(1*R*,2*R*)-Tramadol

1. Leppert, W. *Pharmacological Reports*, **2009**, *61* (6), 978
2. Grond, S and Sablotzki, A. *Clinical Pharmacokinetics*, **2004**, *43* (13), 879
3. Lee, C. R, McTavish, D., Sorkin, E. M. *Drugs*, **1993**, 46 (2), 313

P4. Synthesis of amphiphilic tartaric acid derivatives for antibiotic testing

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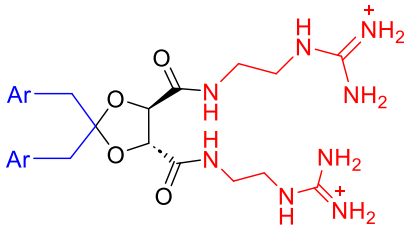
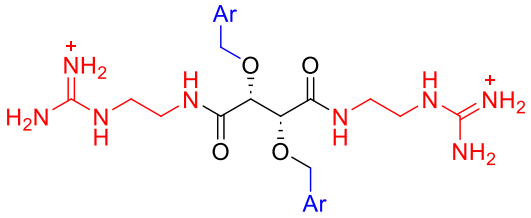
A continued increase in the consumption of antibiotics is accelerating the rate of development for antibiotic resistance.[1,2] The synthesis of novel antibiotic compounds is an important avenue to combat this growing threat.[3]

Taking inspiration from antimicrobial peptides isolated from marine life,[4] as well as other synthetic classes of amphiphilic compounds,[5] has given the background to design a series of tartaric acid derived target compounds.

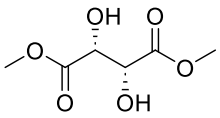
This poster will show our latest synthetic work towards both **T1** and **T2** from dimethyl-tartrate, Ar = Aryl.



T1



T2



(+)-Dimethyl-*L*-tartrate

1. Zalewska, M.; Błażejewska, A.; Czapko, A.; Popowska, M. *Front. Microbiol*. **2021**, 12.
2. Blair, J.; Webber, M.; Baylay, A.; Ogbolu, D.; Piddock, L. *Nat. Rev. Microbiol*. **2015**, 13, 42.
3. Tacconelli, E.; Carrara, E.; Savoldi, A.; Harbarth, S.; Mendelson, M.; Monnet, D. L.; et al *Lancet Infect Dis*, **2018**, 18, 318.
4. Hanssen, K. Ø.; Cervin, G.; Trepos, R.; Petitbois, J.; Haug, T.; Hansen, E.; Amdersen, J. H.; Pavia, H.; Hellio, C.; Svenson, J. *Mar. Biotechnol*, **2014**, 16, 684.
5. Paulsen, M. H.; Engqvist, M.; Ausbacher, D.; Anderssen, T.; Langer, M. K.; Haug, T.; Morello, G. R.; Liikanen, L. E.; Blencke, H.-M.; Isaksson, J.; Juskewitz, E.; Bayer, A.; Strøm, M. B.; *J. Med. Chem*. **2021**, 64, 11395.

P5. Chemo-Enzymatic Synthesis Of Enantiopure Vasodilator (–)-Nebivolol

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The American Heart Association reported in March 2019 their update on heart diseases and stroke statistics. The report states that the prevalence of high blood pressure in the United States between 2013-2016 was 46% of the total population at ages 20 years and older. It was the cause of death for 82,735 Americans in 2016 and costed the American society approximately $ 55.9 billion in the period 2014-2015 [1].

A class of drugs that have been used both in cardiovascular and non-cardiovascular treatment are the β-adrenergic blocking agents (betablockers). This class of drugs were introduced into clinical medicine in the early 1960's, and since then, the findings of these drugs have led to a discovery of the importance of the sympathetic nervous system in the pathophysiology of a wide variety of cardiovascular and non-cardiovascular disorders [2]. We have for some time developed efficient chemo-enzymatic protocols for synthesis of several betablockers [3a-e]. Here, we present our protocol for the enantiopure vasodilator (–)-Nebivolol, fig. 1. Due to the four stereogenic centra in the molecule there are 16 possible isomers when no catalysts is used in the synthesis. However, due to symmetry, there are 10 possible isomers. We have achieved to produce the (*R,S,S,S*)-nebivolol or (–)-nebivolol.

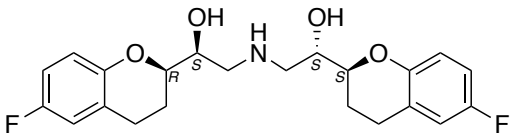

Figure 1. (–)-Nebivolol, (*R,S,S,S*)-nebivolol.

[1]. E. J. Benjamin, *et al. Circulation* **2019**, *139* (10), e56-e528.
[2]. J. W. Black and B. N. C. Prichard. *Br. Med. Bull.* **1973**, *29*, (2), 163
[3]. a) M. A. Gundersen *et al., Catalysts,* **2021,** *11,* 503**.** b) S. H. Troøyen, *et al. Catalysts* **2022**, *12*, 980. c) S. H. Troøyen and E. E. Jacobsen. *Catalysts,* **2022**, *12*, 1645. d) L. H. Y. Bocquin and E. E. Jacobsen. *Catalysts* 2023, *13*, 54. e) P. L. Bøckmann and E. E. Jacobsen. *Topics in Catalysis*, **2024**, 1-9.

P6. Towards A Green Synthesis of Precursors to Ormeloxifene: A Selective Estrogen Receptor Modulator

Marcin Makosa-Szczygiel, Petter Daleng, Marius Chareun, Sunniva Sørlien Bjerkeengen, Erling Løklingholm Leivestad and Elisabeth Egholm Jacobsen

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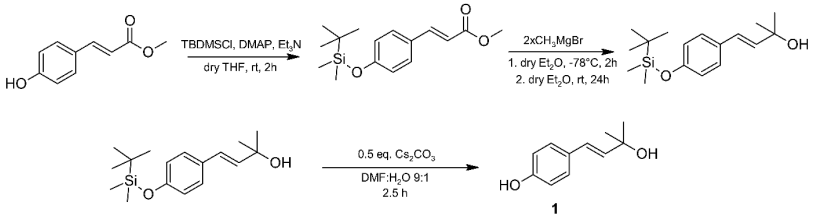
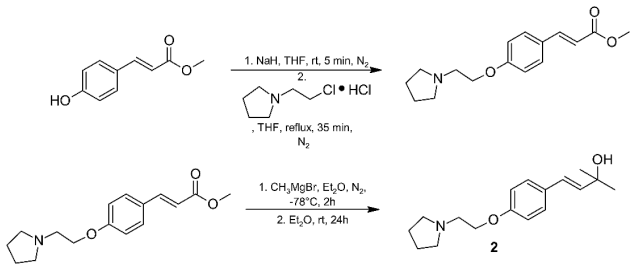
Ormeloxifene is the only female birth control pill that is non-hormonal, which means it exhibits almost none of the side effects commonly associated with other contraceptives [1][2]. As part of a novel pathway to ormeloxifene, two precursors thereof have been synthesized: 4-[(*1E*)-3-hydroxy-3-methylbut-1-en-1-yl]phenol (**1**) (Scheme 1), and (*E*)-2-methyl-4-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)but-3-en-2-ol (**2**) (Scheme 2).



Scheme 1: Synthesis of 4-[(*1E*)-3-hydroxy-3-methylbut-1-en-1-yl]phenol (**1**).



Scheme 2: Synthesis of (*E*)-2-methyl-4-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)but-3-en-2-ol (**2**).

Enzymatic epoxidation of **2** has been attempted using two genetically engineered peroxidases: Eucodis 012 and Eucodis 013. Compound **1** is an aryl allylic alcohol, meaning it has great potential as a future precursor to pharmaceutical compounds. (*E*)-2-Methyl-4-(4-(2-(pyrrolidin-1-yl)ethoxy)phenyl)but-3-en-2-ol (**2**) is also an aryl allyl alcohol and thereby shares the same potential as compound **1** in addition to being presented as a novel compound.

[1]. Kumar, S.; Rai, R.; Agarwal, G. G.; Dwivedi, V.; Kumar, S.; Das, V. A Randomized, Double-Blind, Placebo-Controlled Trial of Ormeloxifene in Breast Pain and Nodularity. *Natl Med J India* **2013**, *26* (2), 69–74.
[2]. Brahmachari, S.; Bhagat, V.; Patil, P.; Vasuniya, V. Evaluating the Effect of Ormeloxifene on Multiple Fibroadenomas and Mastalgia. *J. Pharm. Bioallied Sci.* **2021**, *13* (Suppl 2), S1386.

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