EXPERTISE AT UGENT

ORGANIC SYNTHESIS

FROM SMALL MOLECULES TO BIOCONJUGATES

UNIVERSITEIT GENT

OUR OFFER

STRATEGIC SYNTHESIS & DESIGN

THROUGH DEEP UNDERSTANDING OF (BIO) ORGANIC AND MEDICINAL CHEMISTRY

At UGent we focus on compounds, tools and synthetic methodology to support all aspects of life science research.
We have strong expertise in specific organic synthesis, chemical tool development and chemical technologies.

NOVEL CHEMICAL MATTER

- **Natural products and likes:** Natural product analogues are synthesized with less complicated or novel structures in order to produce biologically active compounds that exhibit activity profiles superior to that of the natural products they originate from. Through innovative synthetic methods and strategic target choice, we develop short synthetic schemes that allow a rapid assembly and straightforward analoging for such compounds, aiming for highly modular intermediates, with synthetic efficiencies approaching those that are typically achieved with 'flat' heterocyclic scaffolds. The development of new chemical synthesis methods allows access to targeted libraries of natural products and their analogues which can be used to gain more knowledge on the bioactive compounds present in extracts from various natural sources, their biological target and mechanism of action.
- **Heterocyclic scaffolds:** Chemical methodologies are being developed to synthesize new and innovative heterocyclic scaffolds for applications in the agrochemical and medicinal industry. Asymmetric syntheses of functionalized amino acid derivatives are developed, as new building blocks for heterocyclic and carbocyclic scaffolds, incorporating biologically interesting moieties. Focus goes to rational synthesis of various types of new heterocyclic compounds associated with specific biological activities to provide new SAR insights and to identify new leads for further development in medicinal chemistry.
- **Asymmetric (Bio)catalysis:** Exploration and application of enzyme-mediated functional group transformations.
- **Bioconjugated/modified Biomolecules:** We develop new and modular synthetic derivatisation strategies, based on caged reactive groups, which can be activated on demand for further reaction with moieties containing groups with complementary reactivity. Methods are being developed for the synthesis of labeled proteins and nucleic acids, chemically derivatised proteins, protein-drug conjugates and various bioconjugates.

NOVEL CHEMICAL TOOLS

Chemical tools, such as modified amino acid derivatives, peptides, fatty acids, carbohybrates (e.g. (amino)cyclitols and iminosugars) and other natural products, are developed via new synthetic strategies. These tools are applied in the study and management of biological processes with the general aim to collect more knowledge on biological processes on a molecular level which can be developed to applications in efficient sustainable agriculture, aquaculture and life sciences.

- **Crosslinking technologies:** The development of new methods for crosslinking of biomacromolecules such as peptides, proteins and oligonucleotides. Through the use of a furan moiety with inducible reactivity a method was developed for the site-selective introduction of covalent bonds between two binding partners.
- **Conjugate & linker technologies:** The preparation of various derivatives or analogues of biologically active and/or bio-derived molecules as a key step in biological research that uses small molecule tools. For this, direct derivatisation reactions are very useful to rapidly generate diverse chemical 'metabolites' for SAR-analysis and for preparing conjugates as chemical probes. We develop for e.g. versatile antifolate (methotrexate or trimethoprim) reagents that allow swift conjugation to small molecules. The resulting fusion compounds may be used for target identification/profiling via three hybrid methods or as protein dimerizers.
- **Labeling & probe technologies:** Design and use of novel labeling chemistries for site-specific labeling techniques. Design of new (non-bleaching) fluorescent or other molecular probes.
- **Flow & Microreactor chemistry:** Continuous flow methods in micro- and mesochannels is being developed for reactions that are difficult to scale up under batch conditions. The flow methodology is mostly preferable because of safety reasons, a good heat and mass transfer and constant product quality. A technology platform has been created with 7 different types of commercially available microreactors.

OUR OFFER

NATURAL PRODUCTS AND LIKES

HETEROCYCLIC SCAFFOLDS

NOVEL CHEMICAL MATTER

ASYMMETRIC (BIO)CATALYSIS

BIOCONJUGATED OR MODIFIED BIOMOLECULES

CROSSLINKING TECHNOLOGIES

CONJUGATE & LINKER TECHNOLOGIES

NOVEL CHEMICAL TOOLS

LABELLING & PROBE TECHNOLOGIES

FLOW & MICRO-REACTOR CHEMISTRY

OUR TOOLBOX

CHEMICAL TOOLBOX

Organic Synthesis Our teams have expertise in synthesizing novel monomers and initiators as well as in the chemical modification of available building blocks. We offer extensive organic synthesis and characterization facilities.

Methodology development in organic synthesis

- synthetic heterocyclic chemistry
- chemistry of small-ring azaheterocycles (aziridines, azetidines, bèta-lactams)
- carbohydrate and nucleoside chemistry
- (amino)phosphonate chemistry
- natural products chemistry
- development of novel synthetic methods allowing to obtain pure enantiomers (using a chiral catalyst)
- enzyme-catalyzed reactions for the synthesis of chiral building blocks.
- design and synthesis and screening of novel chiral ligands (as tools for application in asymmetric transition metal-catalyzed transformations with improved selectivity)
- click chemistry and (bio)orthogonal ligation methods
- strategies, methods and support for chemical genetics studies
- new modular organic building blocks for functional or sustainable materials

Flow chemistry

- microreactor technology
- homogeneous and heterogeneous catalysis in flow
- gas-liquid and multiphase reactions
- photochemical conversions in flow
- tube in tube set-ups

Solid phase synthesis of peptides and small heterocyclic peptidomimetics

- synthetic approaches via automated solid phase synthesis
- peptide synthesis, modification and conjugation
- methodologies for selective chemical modification of specific residues within peptides
- construction of conformationally restricted peptides

Solid phase synthesis of oligonucleotides and analogues

- oligonucleotide synthesis, modification and conjugation including DNA, RNA, 2'OMe RNA and PNA
- construction of reactive probes incorporating caged reactive functionalities for nucleic acid target identification
- antisense and antigene strategies

New labeling and conjugation methodologies

- synthesis of modified amino acids and nucleosides incorporating caged functionalities
- triggered activation by UV light, visible light or selective oxidation

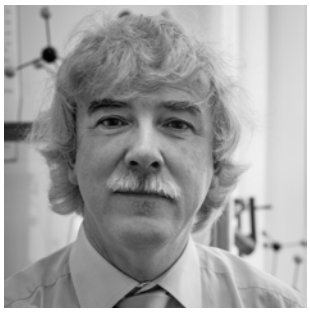
Characterisation and structure elucidation of unknown organic compounds

- expertise in interpretation of analytical data (NMR, MS) for complex molecules
- chemical analysis of unknown compounds or mixtures

in close collaboration with the ADVANCED CHEMICAL ANALYSIS CLUSTER

OUR EXPERT TEAM

PROF. CHRIS STEVENS
Synthesis, Bioresources and Bioorganic Chemistry (SynBioC)



PROF. JOHAN VAN DER EYCKEN
Laboratory for Organic and Bioorganic Synthesis

PROF. SERGE VAN CALENBERGH
Laboratory for Medicinal Chemistry

PROF. MATTHIAS D'HOOGHE
Synthesis, Bioresources and Bioorganic Chemistry (SynBioC)

PROF. SVEN MANGELINCKX
Synthesis, Bioresources and Bioorganic Chemistry (SynBioC)

PROF. JOHAN WINNE
Organic Synthesis Research Group

PROF. ANNEMIEKE MADDER
Organic and Biomimetic Research Chemistry

The **Laboratory for Medicinal Chemistry** belongs to the Faculty of Pharmaceutical Sciences. It mainly concentrates on the development of small molecule modulators of new (i.e., yet unexplored by approved drugs) targets. These modulators can be both enabling chemical tools to interrogate biology or therapeutically useful compounds. From a chemical point of view, much of our work is centered on the chemical synthesis of novel nucleoside and sphingolipid analogues. Our research interest also includes carbohydrate, phosphonate and bioconjugate chemistry. Several of the running projects deal with the design of new lead structures for the treatment of infectious diseases with unmet medical needs (malaria, TB, MRSA) and immune diseases.

The Laboratory for **Synthesis, Bioresources and Bioorganic Chemistry (SynBioC)** belongs to the Faculty of Bioscience Engineering. The SynBioC group focuses on diverse aspects of organic and bioorganic chemistry and has a broad range of collaborations with laboratories that are extensively testing the synthesized molecules. Innovative scaffolds and natural product analogues are screened in different activity domains (depending on the types of compounds). Compounds are being tested in oncology, analgesic, parasitic, fungicidal and bactericidal applications. In this research also SAR studies and SAR modelling is performed in order to increase the success in the development of biologically active structures.

The expertise of the Laboratory for **Organic and Bioorganic Synthesis** (Faculty of Science) is situated in the following fields:

- The total synthesis of complex natural products with biological activity. The research group is developing flexible synthetic routes allowing to obtain natural products as well as modified analogues such as other stereoisomers or analogues with a simplified structure.
- The design and synthesis of novel privileged scaffolds in solution and on solid phase, e.g. the development of small peptidomimetics composed of a central scaffold, which can be valorized against varying biological targets by decoration with customized side chains.
- The design and synthesis of novel chiral ligands for asymmetric transition metal catalysis.
- The development of non-bleaching fluorizers equipped with a linker for biological applications.
- The group has also expertise in the application of enzymes for asymmetric synthesis.

The main focus of the **Organic Synthesis Research Group** (Faculty of Science) is the chemical synthesis and derivatisation of target compounds with non-trivial carbon connectivities, such as those found in polycyclic Natural Products.

- The chemical synthesis part mainly involves the development of novel strategies and methods to assemble complex scaffolds, focusing on multiple bond forming steps such as cycloadditions and cascade reactions.
- For the chemical derivatisation part, the group focuses on the development of application-oriented versatile covalent ligation reactions to generate multiple derivatives from a single synthetic intermediate.
- As a major theme in the recent research, that encompasses both of the above general research topics, the group has started to design and target highly modular synthetic building blocks that allow a rapid exploration of Natural Product-like chemical space using simple and orthogonal functional group transformations.
- The concepts of versatile ligation reactions and modular building blocks in organic synthesis are also explored and applied in various collaborative research projects going from macromolecular and materials science to chemical biology.

The **Organic and Biomimetic Chemistry Research Group** is specialized in the design and synthesis of modified peptides and nucleic acids and methods for their conjugation and labeling.
More specifically, major research interests include:

- The construction of conformationally defined peptide architectures. Scaffold decoration, cyclisation and peptide stapling are used to impose a particular conformation and stability on the parent peptides. Method development for synthesis of dipodal and tripodal peptides on solid phase. The synthesized compounds can find applications as peptide vaccins, protein mimetics, DNA-binding ligands and artificial receptors or synthetic antibodies. More specifically, the use of cholic acid based steroid derivatives has been explored for the conformational restriction and metabolic stabilization of appended peptide chains.
- The development of new methods for crosslinking of biomacromolecules such as peptides, proteins and oligonucleotides. E.g. a very efficient furan-oxidation based crosslinking method has been developed for the site-selective labeling or introduction of covalent bonds between two binding partners.
- The design of novel reactive peptide and oligonucleotide based probes, including peptide nucleic acids, for applications in antisense and antigene strategies, protein and miRNA target identification and receptor pulldown.

Our UGent Organic Synthesis expert team is **member of the CBI cluster**. This initiative has been coined with the name of Chemistry to Foster Biology Innovation (CBI) and is a Flemish chemical biology cluster **linking the academic chemistry research with the biology community.**

www.CBIcluster.be

CONTACT INFORMATION

The Organic Synthesis cluster is supported by the business units **ChemTech** and **Discovere** and **GBEV**. They are the focal point for **industrial collaborations**.

ChemTech deals with chemistry and pharma and biotech companies that are looking for chemical expertise, chemical compounds and chemical tools. Discovere is active in biomedical and pharmaceutical research to promote early academic drug discovery. GBEV or Ghent Bio-Economy Valley deals with sustainable bioprocesses and green chemistry.

The business units facilitate and coordinate a set of **industrial projects** and manage a **strategic IP portfolio** and its licensing opportunities.

The business developers of ChemTech and Discovere and GBEV are at your disposal:

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