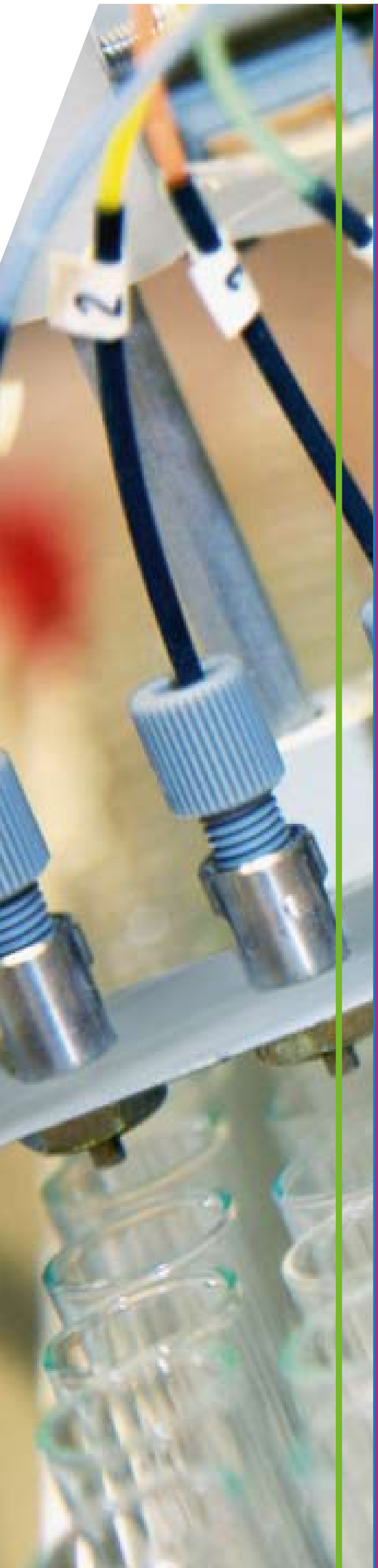
MERCACHEM

explores to lead

Library design and synthesis



Mercachem has an experienced group of skilled chemists that are involved in the design and synthesis of small focused libraries of tens to hundreds of compounds using parallel chemistry. An in-house developed work flow based on purpose designed 24-position aluminum blocks that hold glass vials maximize the efficiency of library synthesis balancing automation and throughput.

Parallel chemistry

Using this work flow Mercachem has shown that basically any chemistry can be made adaptable for parallelization and Mercachem has extensive experience with the following types of chemistry

- Amide formation
- Acylation
- Alkylation
- Palladium chemistry (Suzuki, Buchwald-Hartwig, Sonogashira)
- Reductions (using 48-position parallel autoclave)
- Grignard
- 1,3-dipolar cycloadditions
- 'Click' chemistry

In these library projects Mercachem combines its unprecedented knowledge of synthetic organic chemistry with pragmatic use of cheminformatics and computational chemistry. In general three distinct phases can be distinguished:

- Library design
- Feasibility study
- Library synthesis

Library design

When designing a library Mercachem attempts to create an information rich series of compounds that will enable further rapid development of a scaffold series by balancing the following factors:

- Robustness of the chemistry
- Availability of building blocks
- Number of synthetic steps
- Workup procedures
- Property profile (cLogP, polar surface area, pharmacophore features)
- Diversity oriented or focused design

Based on the design and selection of building blocks a virtual library will be enumerated (up to 50,000 structures) from which based on the desired properties a selection will be made of sufficient structures for the final library synthesis.

The design phase is followed by a feasibility study to explore the chemistry and to establish a robust synthetic protocol for the library synthesis.

Library synthesis

For the synthesis of the libraries Mercachem has a wide array of equipment available:

- 24-, 48- and 96-position reactor arrays
- Radley systems (-80°C to reflux)
- 48-position parallel autoclave
- Optix purification system
- CombiFlash system
- Preparative LC/MS systems (chiral and non-chiral)
- Microwave systems

All synthesized compounds are analyzed by LC/MS (purity depending on requirements 80 – 95%) and optionally by ^{1}H-NMR as well. On average these projects are completed in 2-4 months and require the use of 1-2 chemists.

Fragment library

Mercachem has developed a special fragment library (in collaboration with Pyxis Discovery) based on scaffolds occurring in drugs. In the design of the library special attention has been given to the fragment evolution of active fragments. Due to the fact that Mercachem understands the underlying chemistry small focused libraries can be designed and synthesized around the scaffolds of the original fragments.

In general due to the deep understanding of synthetic organic chemistry Mercachem is very well positioned to work on fragment evolution projects in which chemistry must be performed around specific exit vectors of the fragment.

Working with Mercachem ensures efficient execution of your library design and synthesis projects.

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