

# Heidolph Instruments GmbH & Co.KG - Synthesis 1 Product Profile

## Newly Developed Parallel Synthesiser with High Efficiency and Variability

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### Parallel synthesis; liquid phase; solid phase; combinatorial chemistry

In the sector of modern drug and materials research, the method of parallel synthesis is gaining more and more importance. In addition to liquid phase synthesis, solid-phase-supported substance preparation can be used efficiently. With the help of the recently developed instrument design *Synthesis 1*, both variants can be implemented under either classical reaction conditions as well as highly demanding reaction conditions.

### Parallel synthesis: Concept & advantages

Parallel synthesis makes it possible to prepare and examine a variety of chemical compounds that are prepared by the same procedure, but that differ in the type or arrangement of the underlying synthetic building blocks. The goal here is fast and effective discovery of novel drugs, materials, or catalysts, and optimisation of chemical reactions. Such substance libraries are necessary in the modern pharma research sector, since new drug targets are constantly being identified by genomics and proteomics, that can also be examined very quickly for their biological activity with the help of automated high-throughput screening procedures.

Parallel synthesis differs from classical combinatorial procedures in that substance libraries are not produced in a mixture, but definite reaction products are formed in spatially separated reaction vessels. Besides the classical reaction in solution or by mixing educts and reagents with no solvents, parallel synthesis can also be used in the area of solid-phase-supported synthesis. This had its origin in peptide synthesis (solid phase peptide synthesis, SPPS) and has very recently been extended to non-peptide organic reactions (solid phase organic synthesis, SPOS). In both cases, the support is by means of a suitable resin on which synthetic building blocks or reagents are immobilised through chemical anchor groups (linkers).

### *Synthesis 1*: Areas of use & special features

Heidolph Instruments, with *Synthesis 1*, with our collaboration, has developed a design that as a model meets the multiple and individual requirements of parallel liquid and solid phase synthesis on a laboratory scale. Added to this is the capability of time-saving and gentle workup. Because of its high variability, the design of *Synthesis 1* permits a multitude of applications in the areas of pharma research, development of new molecular materials and in the search for and optimisation of chemical reactions and novel catalysts. Depending on the configuration of the instrument module, *Synthesis 1* can be used for parallel liquid and solid phase synthesis or for simultaneous evaporation. Because of a full complement of technical details, even demanding reaction conditions, for example exclusion of moisture or oxygen or precisely controlled low temperature, can be realised with *Synthesis 1*.

*Synthesis 1* offers optimal visual reaction control for both liquid phase and solid phase synthesis, by a circular arrangement of reaction vessels, which consist of glass or PTFE and PFA. Furthermore, there is the best accessibility of all samples because of rotatable reaction platforms. Individual seals on the reaction vessels



*Synthesis 1* product range

have precluded the risk of contamination. Separate heating zones make it possible to set four different reaction zones. In this way, both elevated temperatures and low temperatures can be set precisely, with the assistance of a cryostat. Condensation zones permit the recondensation of solvents without making it necessary to use reflux condensers.

The reaction vessels for solid phase synthesis are distinguished by the fact that the resin does not stick to the inside of the vessel due to the nature of the material. The ground joint, a valve and the tubing connector to the suction drain are accommodated in the bottom section of the vessel; they are provided to collect rinse solvents in a beaker or to isolate the products in test tubes after completion of the synthesis. This suction device can be controlled visually. The glass vessels for liquid phase synthesis have standardised screw threads. A septum, valve and vacuum or inert gas connector are integrated into both vessel platforms. *Synthesis 1* can be optionally equipped with a multi-vapouriser that makes simultaneous concentration possible in all of the connected reaction vessels.

Mixing in the reaction vessels is done with the help of especially rugged and low vibration shaking technology. The frequency of the shaking apparatus can be adjusted continuously, up to a maximum of 1000 rpm.

The design of *Synthesis 1* provides for a modular principle. Thus the base station can be optionally equipped with a platform for 16, 20 or 24 reaction vessels, each containing 42, 25 or 8 ml, for solid phase synthesis. The liquid phase platform can be delivered for twelve 50 ml reaction vessels, sixteen 25 ml vessels, or a maximum of twenty-four 10 ml reaction vessels. The instrument technology permits it to be equipped not only with the maximum possible number of reaction vessels, but also with any smaller number of vessels.

### Working with *Synthesis 1* in the laboratory

In recent months we have used *Synthesis 1* intensively for our research activities in the field of liquid and solid-phase-supported drug synthesis. My co-workers are enthused by the multiple capabilities of the instrument, but also by the stable operation and precision of control.

Prof. Peter Gmeiner  
Dr. Stefan Löber

### Brief resumé of Dr. Peter Gmeiner

Born in 1959. Pharmaceutical State Exam, Munich University (1983). Doctorate with F. Eiden, Munich

(1983–1987). Post-doctorate, University of California, Berkeley, with H. Rapoport (1987–1988). Graduate in Pharmaceutical Chemistry (1992). Professor of Pharmaceutical Chemistry (C3), Bonn University (1994–1996). Professor of Pharmaceutical Chemistry (C4), Erlangen-Nuremberg University (since 1996). Recipient of the Johann-Wolfgang-Döbereiner Prize of the German Pharmaceutical Association. Member of the Board of Directors of the Medicinal Chemistry Professional Group of the GDCh. The research interests of Professor Gmeiner are directed towards the design of solid-phase-supported and stereoselective drug synthesis and the in-vitro testing of CNS-active receptor agonists and antagonists. In the teaching sector, Professor Gmeiner co-ordinates the new Master Study programme in Molecular Life Science in Erlangen, as well as the revised Pharmacy programme.

### Brief resumé of Dr. Stefan Löber

Born in 1971. Food chemistry course, Erlangen-Nuremberg University (1991–1996). Research with G. Eisenbrand, at Kaiserlautern University (1996–1997). Doctorate with P. Gmeiner, Erlangen (1997–2000). Scientific Assistant in Pharmaceutical Chemistry, Erlangen-Nuremberg University (2000–2003). Since May, 2003, Academic Council z.A. The research interests of Dr. Löber are directed towards the solid and liquid phase synthesis of potential CNS-receptor ligands and the development of new polymer-bound linkers.

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