

Streamlined Workflow: Modern Microwave and Flash Techniques

Martin Keil, Frederic Meistermann

Talk Overview

Streamlining the workflow

- **Biotage, the leading provider of tools for rapid synthesis and purification**
- **Microwave Assisted Synthesis**
 - Initiator as an highly reliable and safe mw system
- **ISOLERA flash purification instrument**
 - Intelligent software features
 - Highest purity of compound fractions

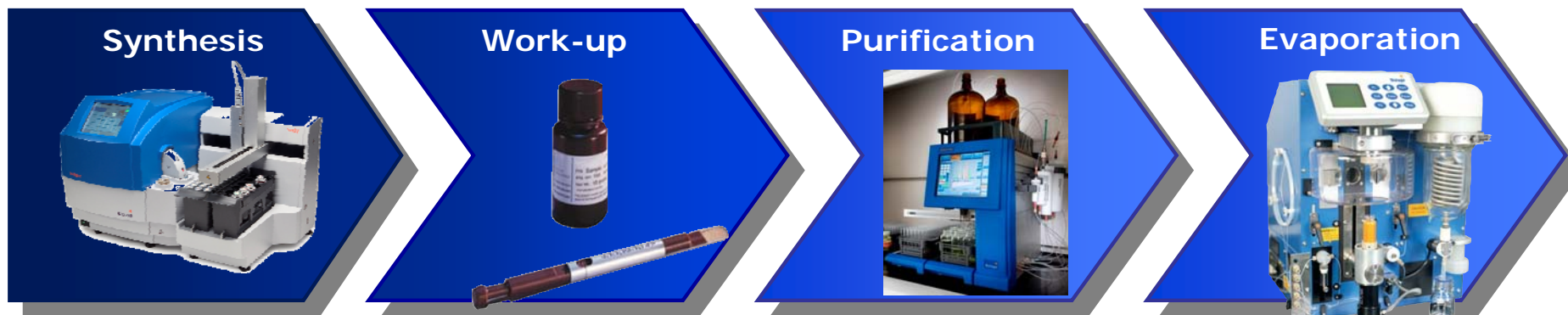
Biotage offers a whole concept for the discovery chemistry area

Biotage Discovery Chemistry

- Largest range of innovative and integrated discovery chemistry tools for synthesis, work-up, purification, evaporation and sample preparation.
- Solutions for research and development through clinical trials and manufacturing
- Product synergies work together to improve drug discovery and remove process bottlenecks. *Accelerate Synthesis, Accelerate Purification (ASAP)*



Discovery Chemistry Tools



Microwave Synthesis

- Extremely fast reactions
- High yield and purity
- Enables “impossible” reactions
- Reproducible

Solid-bound Reagent and Scavenger and SPE

- Simplifies purification
- Facilitates reaction chemistry

Automated flash purification

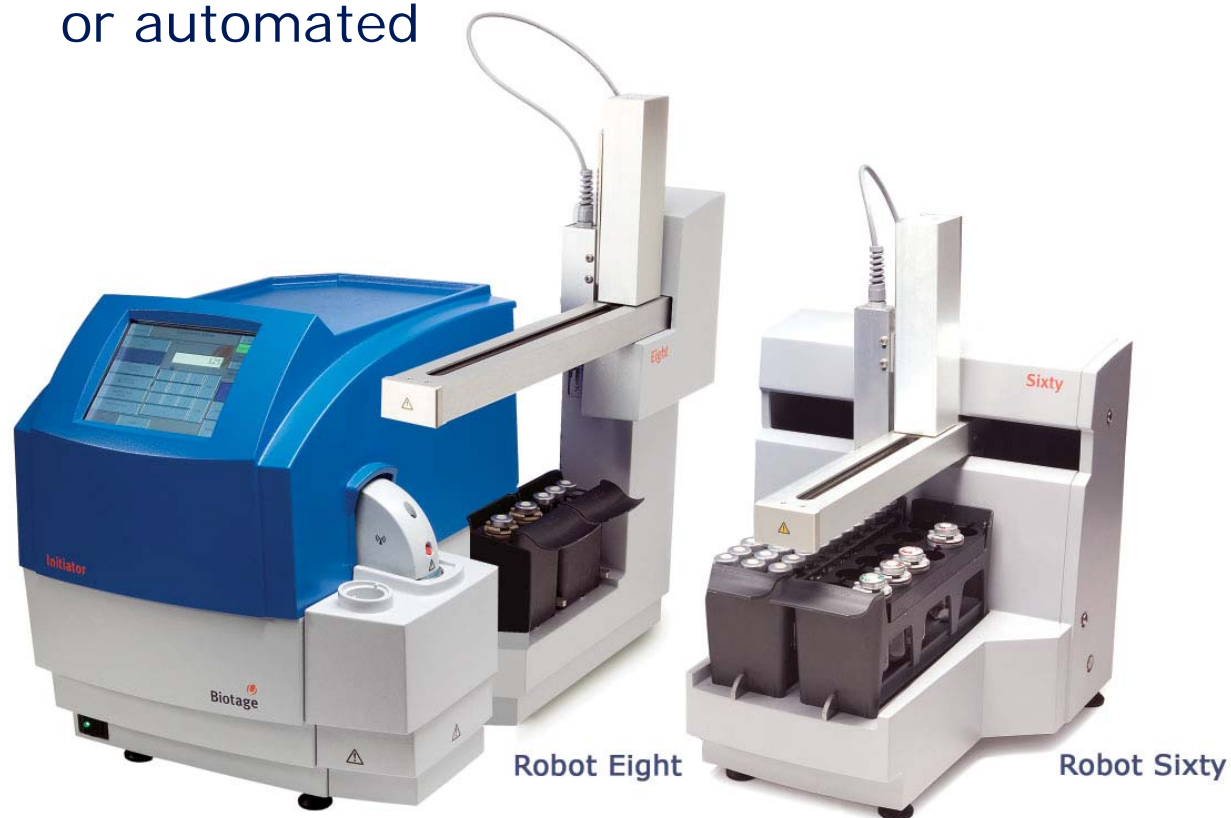
- multi cartridges in unattended operation
- TLC to gradient method development

Rapid solvent evaporation

- Organic solvents & water
- Flexible formats
- Flow or batch mode
- Effective re-dissolution

Modular Initiator™ Product Line

- A small and upgradeable microwave synthesis platform
- The system is controlled *via* a touch screen
- Can run rxn volumes of 0.2-20 mL (EXP) either manually or automated



Initiator's improved heating performance

Initiator 2.0 introduces *Amplified Microwave Power (AMP)* for increased heating performance

- Biotage offers the only single mode system to use **400W** power to heat the sample, with **minimal overshoot** and **accurate temperature** control
- In general, 30-50% improvements can be expected
- Plus new enhanced performance specifically for non- polar solvent

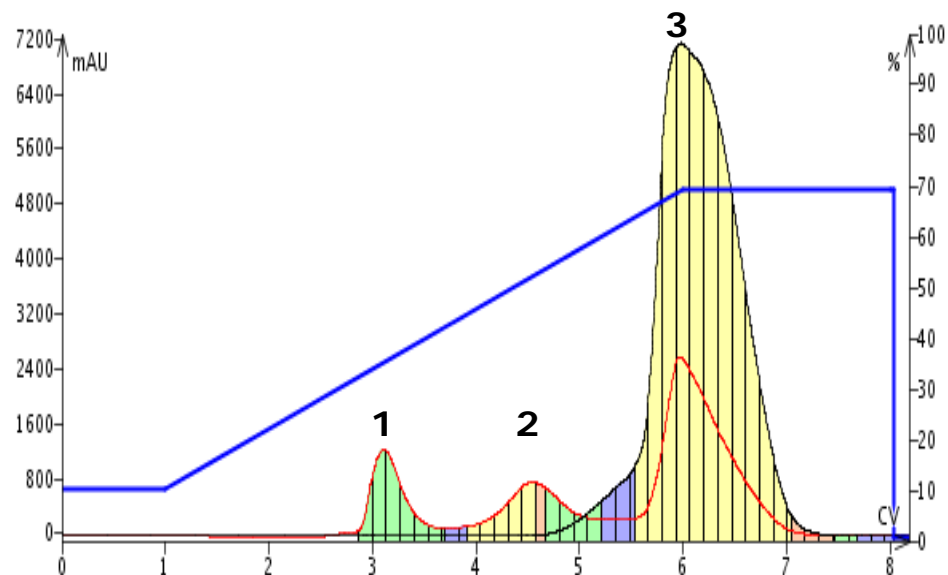
ISOLERA Flash Purification System

- State-of-the-art automated open access and multi user flash purification system
- Touchscreen graphic user interface with new, intuitive software
- Calculates gradient and suggests column and loading capacities, just from Rf data of one TLC run
- Unsurpassed purification capability: fractionation at two wavelengths simultaneously for highest purity of compound fractions
- Large fraction collection volume
 - Up to 9.60 liters or even unlimited volume when operated in cycles
- New leak detector: sensitive detection of all types of solvents



Two wavelengths fractionation

- Collect compounds otherwise missed using a single wavelength
- Increase compound recovery
 - Compound 1
 - At 254 nm 100%
 - At 330 nm 0%
 - Compound 2
 - At 254 nm 100%
 - At 330 nm 0%
 - Compound 3
 - At 254 nm 93.8%
 - At 330 nm 94.3%
- Mixed fractions separately collected



Conditions

System: Isolera One
Cartridge: SNAP 50g KP-SIL
Solvent A: Heptane
Solvent B: Ethyl Acetate
Gradient: 10% B for 1 CV
10%-70% B in 5 CV
70% B for 2 CV
Flow rate: 40 mL/min
Load: 1.5g via Samplet
 λ 1 (red): 254 nm
 λ 2 (black): 330 nm
Fractionation: Low slope

ISOLERA feature: TLC to Gradient

- **TLC-to-gradient: state of the art calculation of gradient from TLC conditions**
- **Calculated from Rf data of one TLC run: just type in solvent composition in the TLC chamber and Rf values of TLC spots**
- **Calculation of loading capacities and proposals for cartridge / column selection**

Conclusion

New Strategies:

- *Microwave Synthesis* and *Automated Flash Chromatography* are powerful tools in the synthetic labs
- Initiator mw system offers most accurate control of rxns and best in class safety
- ISOLERA flash system's intelligent software calculates gradient and suggests cartridge and loading capacities, just from Rf data of one TLC run
- Highest purity of compound fractions by automated fractionation at two wavelengths simultaneously
- Combining the two modern techniques speeds up the process of rapid compound production
- Beyond the above: Biotage is the leading provider for synthesis resins and scavengers for easier workup, or for new evaporation techniques for fast solvent removal of even high boiling solvents