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1 The design of the EasyMax™ 102 makes it possible to manage two batches with completely different parameters.

Achieve usable results more quickly–that's the primary requirement in synthesis labs. A semiautomatic laboratory reactor system with integrated heating and cooling system helps to keep pace with the higher requirements.

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Faster and more reliable synthesis

Development work in an organic synthesis lab is characterized by a wealth of ideas, knowledge of materials, deep understanding of processes in chemistry – and the pace at which ideas need to be turned into reality. This makes it vital that laboratory apparatus functions reliably and is easy to operate.

The traditional round-bottomed flask, the oil and ice bath, heating mantles and cryostatic temperature regulators have all dominated the image of the chemical development lab for decades. They have the advantage of being relatively simple to handle and inexpensive to buy and operate. Yet they also have many disadvantages that make it harder or more time-consuming to implement new ideas.

Temperatures that are insufficiently known or not adequately kept, poor temperature consistency, the manual handling of highly toxic substances and limited reproducibility due to a lack of data records are problems that occur frequently in synthesis planning. This often means monotonous and cost-intensive repetitions of experiments. In addition, space in the fume cupboard is often limited, which can have a significant detrimental impact on the use of large heating baths or cryostatic temperature regulators and on the general possibilities of experiment setup.

Cooling without loud cryostatic temperature regulators, an easy control concept, high flexibility where space is tight, variable reactor volumes – these characteristics will depend on the needs of the modern organic synthesis laboratory.

Integrated heating and cooling system

To enable it to keep pace with the higher requirements in these laboratories, Mettler Toledo has collaborated with partners from the chemical and pharmaceutical industries to develop the EasyMax™ 102 (see Fig. 1).

This reactor system has been designed for preparative organic chemistry, and in particular for screening and optimization in chemical development processes. It comes with an integrated heating and cooling system that can be operated immediately without the expense of training. The system covers the whole temperature range from -25 to +180 °C, while the technology employed obviates the need to use a cryostatic temperature regulator even when working below room temperature.

Processing two batches at the same time

The design of the synthesis system allows two completely independent experiments with reactors of different volumes to be conducted at the same time. The chemical processes can be observed at all times and any necessary adjustments to

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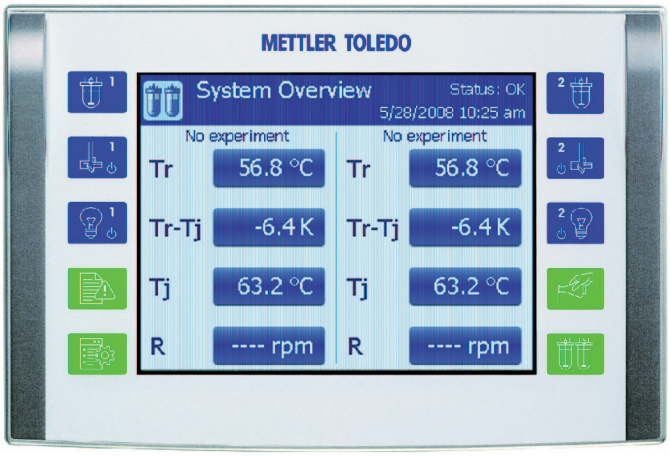
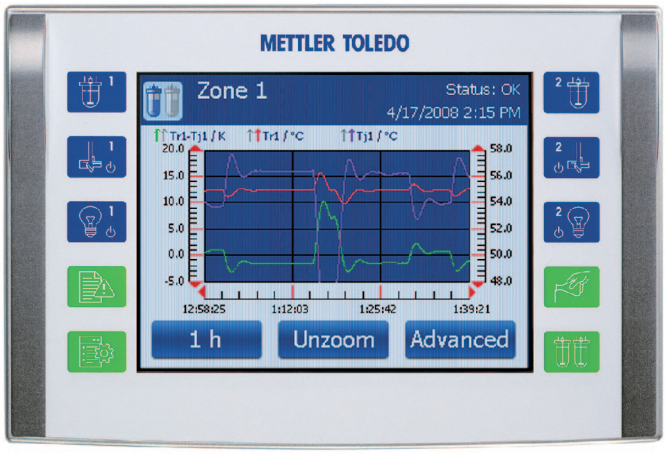


2 The test conditions are entered using a sensor screen.



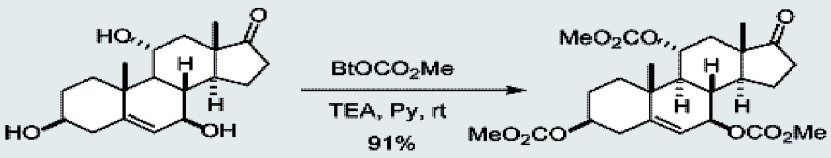
3 The screen also illustrates the course of the experiment in graph form.

the management of the reactions can be made at short notice.

The temperature ramp can be controlled fully automatically over a period of hours, opening up the possibility of unattended operation. All measuring data are recorded, delivering subsequent valuable information on the course of the reaction or the underlying kinetics. In many cases this information can be used to determine from a 100ml batch whether further development is sensible.

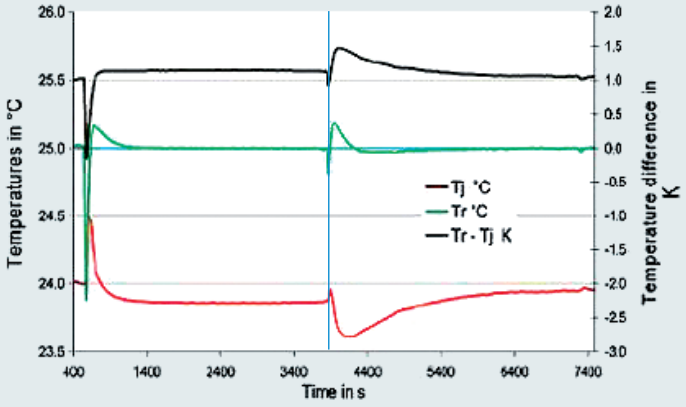
The EasyMax™ is operated entirely using a clear and well-designed sensor screen; no additional computer is required. All control elements are located on a small panel independent of the thermostat. Parameters such as temperature, agitator speed and dosage can be modified to the desired values in a matter of seconds (see Fig. 2).

The measured data are illustrated neatly as readings or graphs. The concept is rounded off with additional functionality such as zooming graphics, saving readings and actions, data transfer and analysis on a PC (see Fig. 5).



4 Simultaneous introduction of three protecting groups into a steroid hormone.
(Peter Wuts, Pharmacia, Kalamazoo/USA)

5 The influence of the catalyst dimethylaminopyridine (DMAP) on esterification.



Example: Introduction of protecting groups

The function is best illustrated by an example. Take, for instance, the simultaneous introduction of a protecting group for three hydroxyl groups.

Two questions arise:

- How can the progress of the reaction be monitored?
- How can the reaction end point be determined?

In this example, heatflow trending proved to be the best method for verifying the progress of the reaction. Heatflow trending is a qualitative method that observes the temperature difference (a measure of the flow of heat) between the reaction compound and the heating/cooling mantle outside the reactor. A glance at the temperature curves Tr, Tj and Tr-Tj reveals the start of the reaction (blue line), then an exponential decrease that allows certain conclusions to be drawn about the kinetics, and finally the reaction end point.

This method eliminates the need to take repeated samples over a longer period and then to analyze these samples. The procedure is particularly advantageous if unstable intermediate stages or highly toxic compounds are involved or if there is no suitable chromatographic or other analytical method available. At the same time, the corresponding information is available throughout the duration of the experiment and can be checked at any time.

Conclusion

EasyMax™ offers all the traits of a traditional round-bottomed flask – ease of use, mobility and a view of the chemical processes – alongside the advantages of automation. 24-hour operation with full logging and traceability of data is possible. LP

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