Large Scale Heterogeneous Continuous-Flow Microwave-Assisted Organic Synthesis

INNOVATION

The Cambrex Continuous-Flow Microwave-Assisted Organic Synthesis (CF-MAOS) heterogeneous technology is a breakthrough in the scale-up of microwave chemistry.

The technology is available for custom development and commercial manufacturing.

Operating conditions:

- Temperature: Room to 200°C
- Pressure: 1–20 bar
- Flow rate: 2–100 mL/min
- Dual feed vessels
- Dual receiver system
- Operation: 24 hour/7 days

For chemists who already use MAOS in the laboratory, the benefits of the technology are well known:

- Faster reaction rates
- Higher yields
- Improved purity

However, a lack of large-scale microwave reactors limits the use of microwave chemistry at commercial scale. Cambrex's solution is its CaMWave™ KiloLAB reactor, which scales up microwave heating as a continuous-flow reactor capable of handling solids, slurries and suspensions.

EXPERIENCE

The versatility of CaMWave™ technology allows laboratory MAOS protocols to be directly translated into the reactor leading to fast, efficient scale-up. The reactor has already processed more than 100 L in 24 hours to produce in excess of 20 kg of crystalline material.

Heterogeneous reactions carried out include:

- Pd-catalyzed Suzuki and cyanation reactions
- O-Alkylation reactions
- Hydrogenation reactions
- Nucleophilic substitution reactions

Larger CaMWave™ reactors are under development to manufacture more than 200 kg per day, along with cGMP versions. Their skid-mounted modular design utilizes current manufacturing plants to keep capital expenditure low while adding all the benefits of microwave heating and continuous-flow chemistry.

CAMBREX

Call Cambrex today

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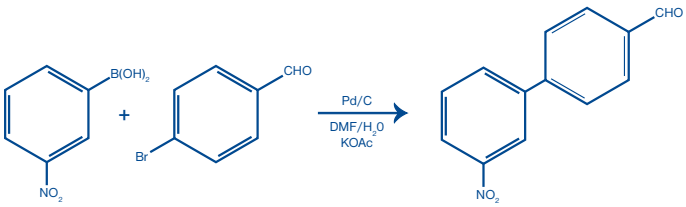
PERFORMANCE

Case Study 1

SCENARIO: A series of Suzuki reactions were studied under CF-MAOS using heterogeneous palladium catalysts.

Residence times were in minutes or seconds. Catalyst loadings were greatly reduced from the corresponding conventionally heated reaction. In one case, only 5 ppm catalyst was needed to give full conversion. No new impurities were observed and purity profiles were at least as good if not better than by conventional batch heating.

Example: Large volume manufacture



More than 140 L of the reaction mixture was processed continuously over 32 hours at 180°C to produce 22.3 kg product (88% yield) with 99.3% crude purity determined by HPLC.

OUTCOME: The Cambrex CF-MAOS methodology proved highly efficient and cost effective, resulting in:

- Shorter reaction time
- Less catalyst usage
- Decreased impurities
- Improved manufacturing cost
- Less waste produced
- Reduced scale-up time

Case Study 2

SCENARIO: Cambrex was presented with a difficult conventional reaction. Reaction parameters were quickly determined by microwave heating at laboratory scale. On the following day, 18 L of reaction mixture were processed by CF-MAOS yielding 2.6 kg of product, resulting in an estimated savings of four weeks in project time.

OUTCOME: The Cambrex CaMWave™ KiloLAB reactor significantly reduced production time. Other advantages over the conventional reaction included:

- Yield doubled over literature methods
- Off-the-shelf reagent used versus reagent preparation
- Substantial reduction of organic solvent used
- Simplified work-up
- Elimination of scale-up experiments

Production benefits

- Faster
- Cleaner reaction
- Scalable
- Cost-effective

Quality

- Higher product purity
- Lower impurity levels
- Reproducibility

Chemistry

- Broad range of reactions
- Slurry chemistry
- Solution chemistry
- Pressure reactions

Call us today to discuss the benefits and value we can bring to your program.

Winner of the 2009 CPhI Silver Innovation Award