

Innovation in Flow Chemistry for Accelerating the Critical Path to First-in-Human Trials



Arcinova flow technology ensures the delivery of

- **Velocity:** Compression of process steps and delivery time
- **Economy:** Driving down material, waste and reactor costs through process efficiency
- **Scalability/Safety:** Ease of Flow technology scaleup and elimination / control of hazards

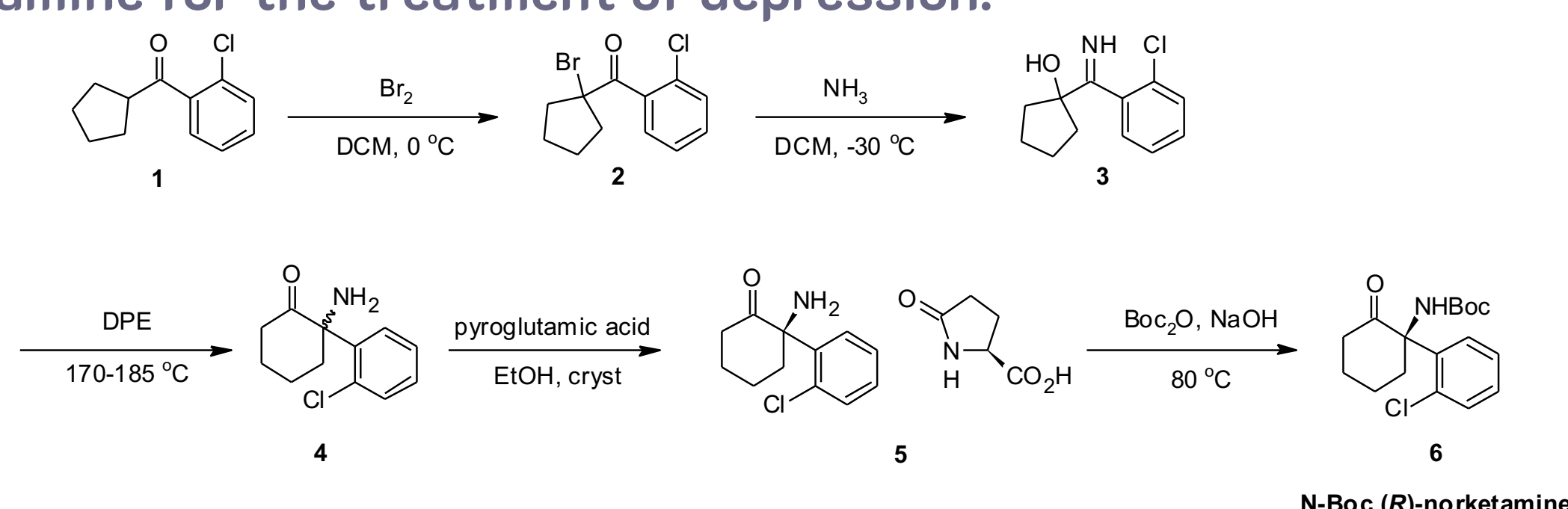
Advantages

- Improved product yield and purity
- Precise control of reaction parameters
- Safer processing of hazardous materials and reactions
- Simplified process scale-up
- Reduced equipment footprint and facility requirements
- On-line process monitoring and analysis
- Telescoping reactions and downstream processing



CASE STUDY: 2-Hydroxynorketamine

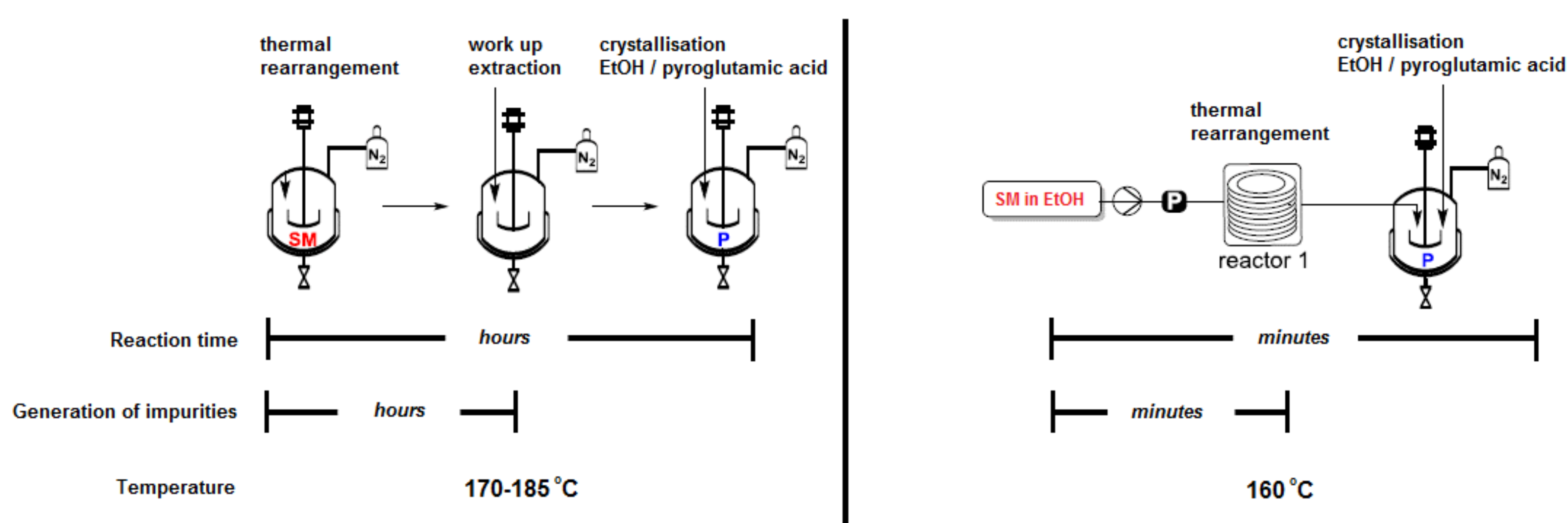
National Centre for Advancing Translational Sciences (NCATS) are in clinical trials with 2-hydroxynorketamine for the treatment of depression.



Straight forward and high yielding chemistry through to *N*-boc norketamine with the exception of the thermal rearrangement.

Thermal Rearrangement – Batch to Continuous Switch

Batch vs. Flow – Side-by-side comparison



- High boiling solvent required
- Long heating and cooling times
- Complex work up procedure
- Solvent switch before crystallisation
- Overall run time: 6-8 hours (inc. work up)
- Stages 1-4
- Yield: 60%
- Batch count: 24
- Weeks: 15
- Starting material: 18 kg

- Same solvent as crystallisation
- Decreased solvent usage
- No work up required
- Rapid heating and cooling
- Residence time: 20 minutes
- Stages 1-4
- Yield: 95%
- Batch count: 8
- Weeks: 4
- Starting material: 10 kg

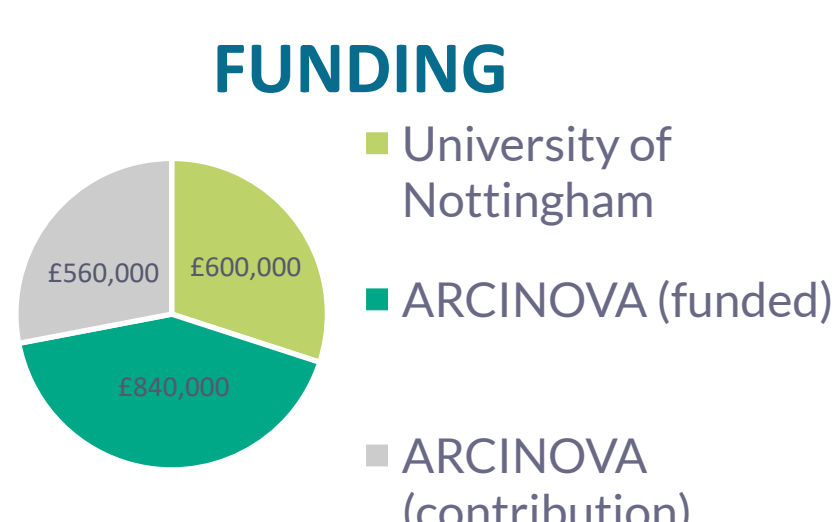
Key Points

- Yield was increased from 61% to 96% (over 2 steps) from batch to continuous
- Throughput was almost 4 kg/day
- Overall manufacturing time was decreased by 8 weeks
- Resource was made available for other projects

Flow Technology Development at ARCINOVA – FLOWINOVA

Project Aim: “Build a state of the art continuous manufacturing facility which will increase capacity and capability at ARCINOVA”

Project total: £2 million
Duration: 3 years



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