

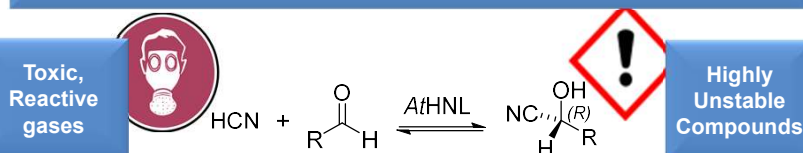
A multi-step biocatalytic approach for the continuous generation and use of HCN towards chiral O-acetylcyanohydrins

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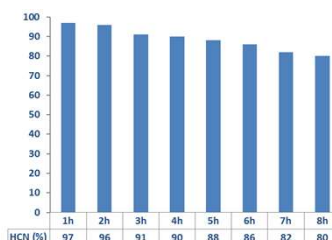
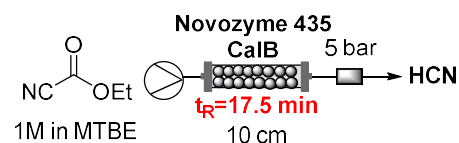


Preparation of chiral cyanohydrins catalysed by (*R*)-selective Hydroxynitrile Lyase from *Arabidopsis thaliana* (AtHNL): batch vs flow



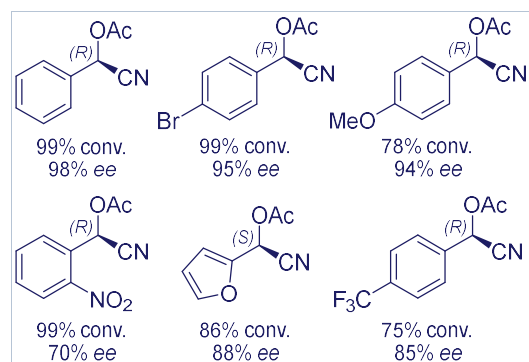
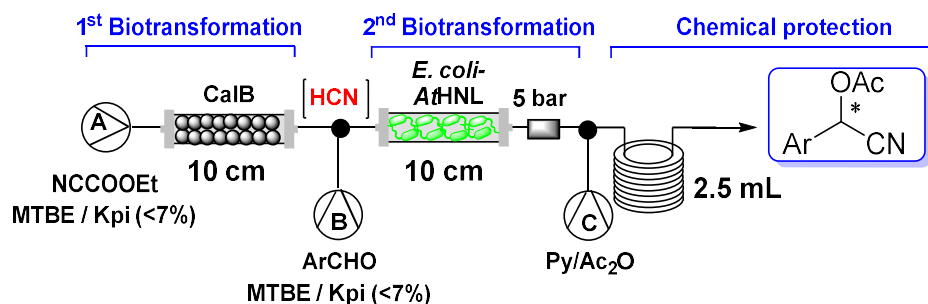
Batch	Reversible reaction	Enzymatic reaction vs chemical reaction	Handling of HCN	Unstable compounds
	Residence time and reactor design	Solvent system	Cascade process	In-line protection
Flow				

Generation of HCN in flow from alternative cyanide source



- ✓ Handling of toxic dissolved gas as reagent
- ✓ Safety and environmental profile
- ✓ Scale-up
- ✓ Streamline multi-step synthesis

Three-step chemo-biocatalytic cascade towards *O*-protected chiral cyanohydrins in micro-aqueous solvent system



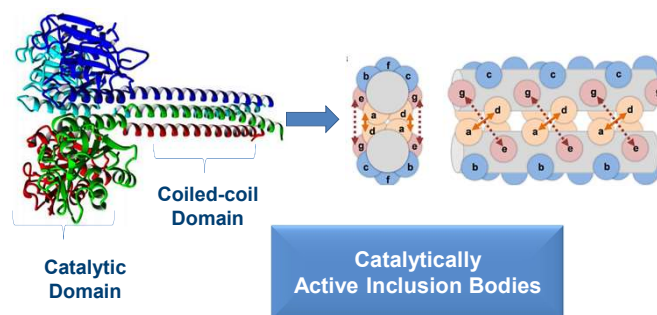
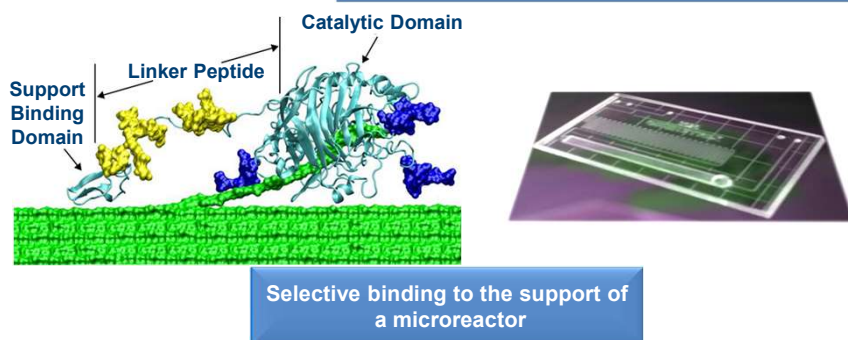
CalB and AtHNL were employed in a robust continuous telescoped process, involving the *in situ* HCN generation followed by addition to aldehydes. High stereocontrol was observed in the subsequent hydrocyanation reaction. An in-line chemical acetylation enabled stabilisation of the newly formed cyanohydrins, giving access to a class of *O*-acetylcyanohydrins with good to excellent conversions and ee values over three steps (75 – 99% conversion; 40 – 98% ee).

Batch:
 1st Step: 2 h
 2nd Step: 1 h
 HCN: 3 eq

Flow Plug Reactor:
 1st Step: 17.5 min
 2nd Step: 4.38 min
 HCN: 2 eq

Synlett 2015, 262–266

Work in progress: use of cell crude extract containing "Naturally immobilised" Enzyme



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