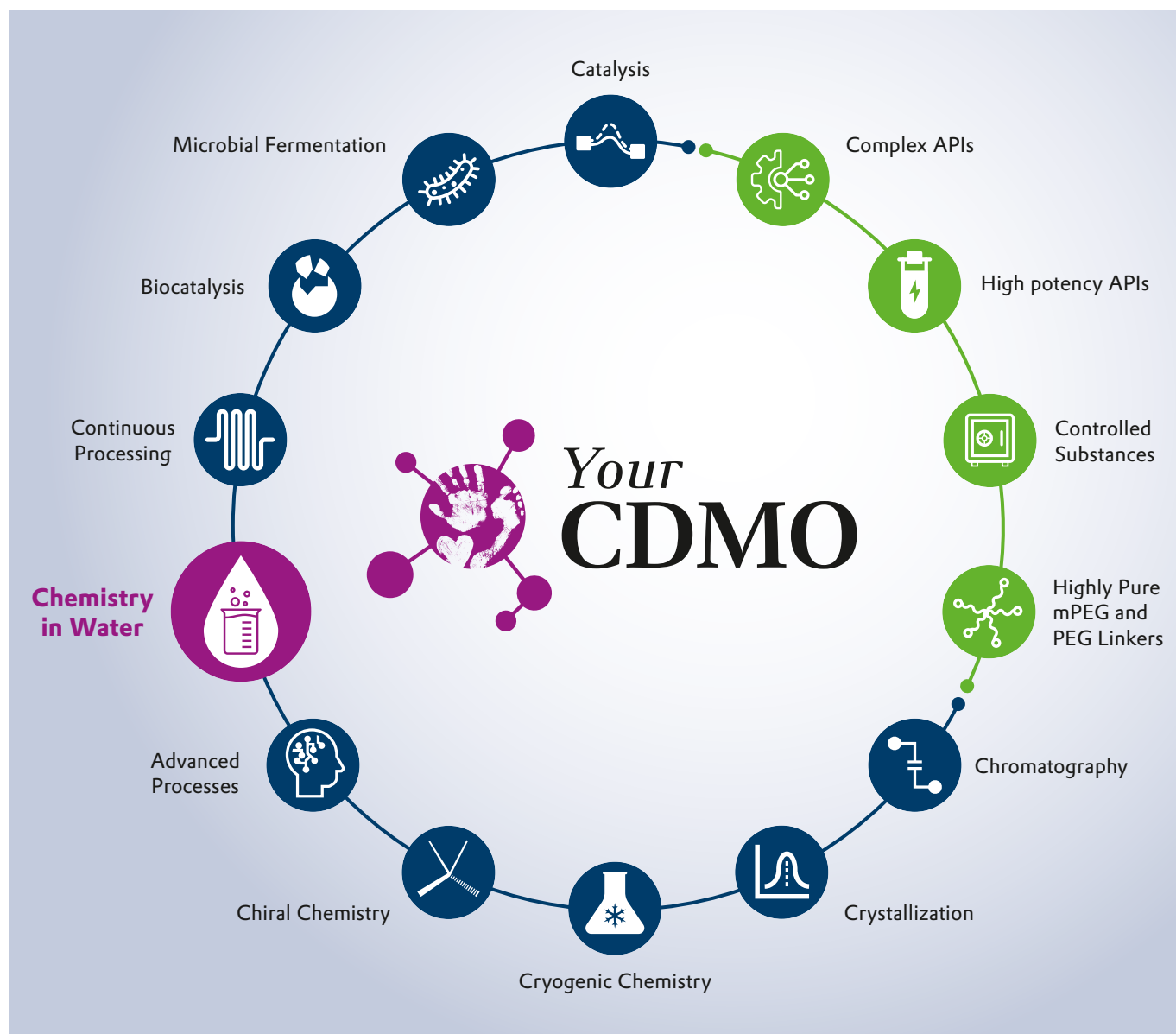


Chemistry in Water

Micellar catalysis for API synthesis with less organic solvent



- 1 Significant reduction of organic solvent use
- 2 Enhanced reaction rates and selectivity through micellar catalysis
- 3 Ready to use for a broad type of reactions

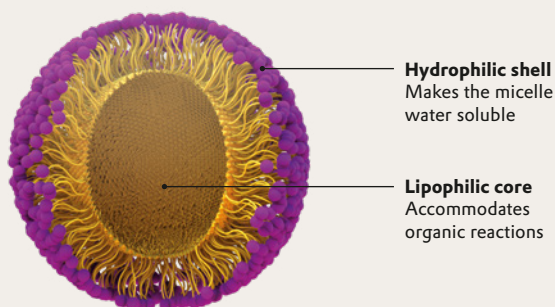
Chemistry in Water is a technology that allows classical organic reactions and the synthesis of active pharmaceutical ingredients and intermediates to be carried out in water.

Benefits

The technology significantly reduces the use of organic solvents and therefore the waste created during chemical production.

Reaction performance can be increased for improved yield and/or selectivity, while catalyst loading and energy consumption can be reduced.

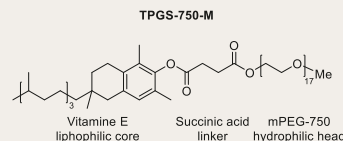
As a result, Chemistry in Water can help reduce solvent waste, catalyst use and energy demand in chemical synthesis.



Surfactant

The technology is based on Vitamin-E derived designer surfactants such as TPGS-750-M, that self-assemble into micelle-shaped nano-reactors. These micelles enable organic reactions, which are generally run in organic solvents, to be performed in water.

TPGS-750-M is fully removable below the Limit of Quantification (LOQ).



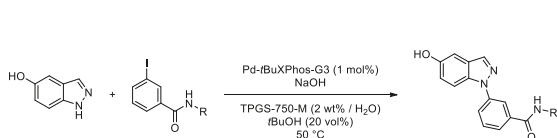
Chemistry in Water can be applied in a broad range of reaction types, including:

- Suzuki-Miyaura couplings
- Stille couplings
- Heck couplings
- S_NAr reactions
- Aryl aminations
- Amide bond reactions
- C-H-activations
- Heterogeneous catalysis
- Peptide couplings
- Biocatalytic transformations

Evonik is working in collaboration with micellar technology pioneer, Professor Bruce Lipshutz of the University of California, Santa Barbara, to offer this technology for the industrial scale production of pharma intermediates and APIs.

Example 1

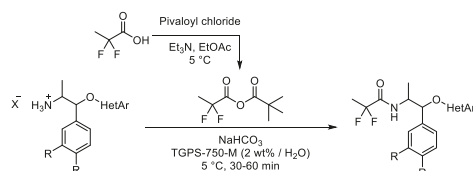
BUCHWALD-HARTWIG COUPLING IN WATER



- Dioxane replaced by water and tBuOH as co-solvent
- Reduced catalyst loading from 5 mol% to 1 mol%
- Reduced reaction temperature from 100 °C to 50 °C

Example 2

AMIDE COUPLING WITH IN SITU FORMED MIXED ANHYDRIDE IN WATER



- MeTHF substituted by water
- Improved regioselectivity, no formation of pivaloated byproduct
- Short reaction sequence without need for freebasing

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