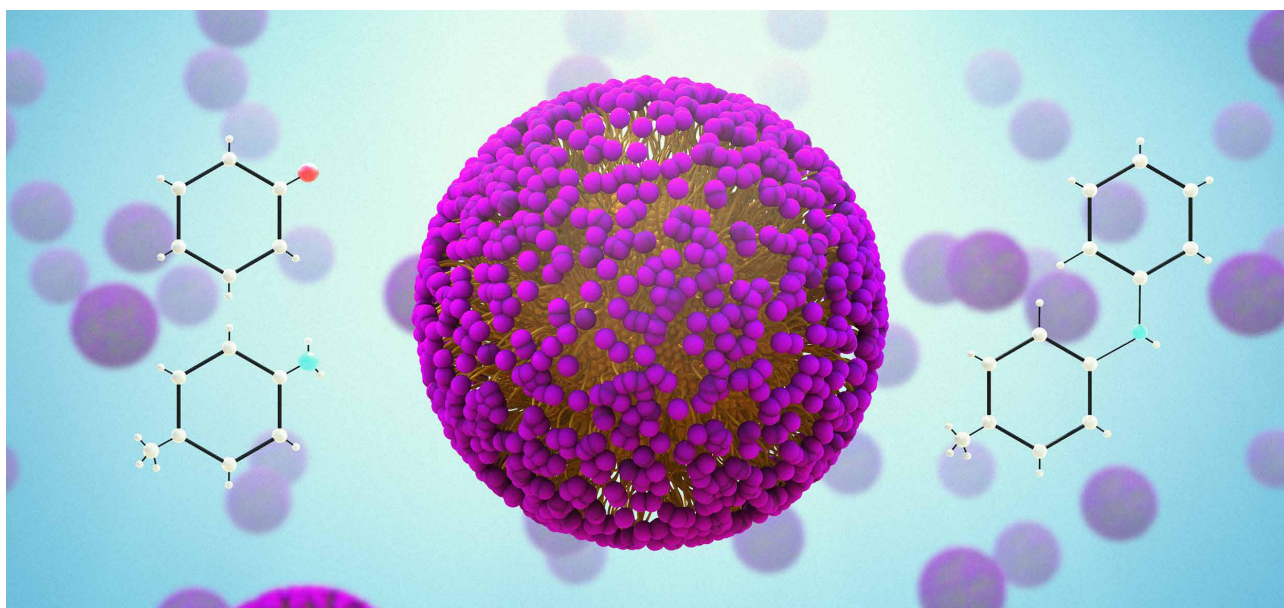


# Chemistry in Water

A revolutionary green technology to enable sustainable chemical syntheses



Chemistry in Water is a green 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.

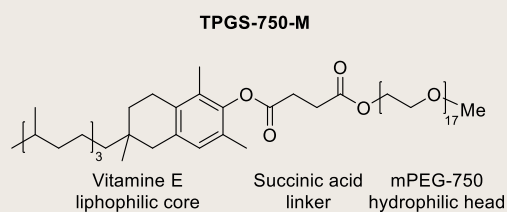
Reaction performance can be increased for improved yield and/or selectivity, while catalyst loading and energy consumption can be reduced.

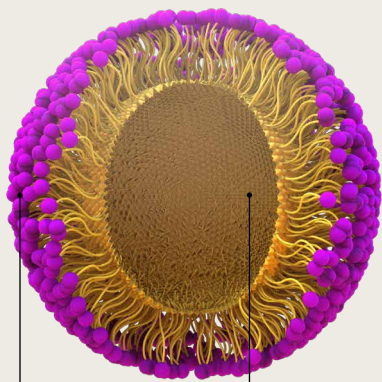
Thus, Chemistry in Water reduces the environmental impact and improves the sustainability of chemical syntheses.

## Surfactant

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

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





**Hydrophilic shell**  
Makes the micelle water soluble

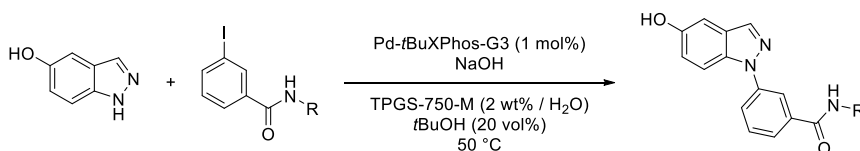
**Lipophilic core**  
Accommodates organic reactions

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

- Suzuki Miyaura couplings
- Stille couplings
- Heck couplings
- S<sub>N</sub>Ar reactions
- Aryl aminations
- Amide bond reactions
- C-H-activations
- Heterogeneous catalysis
- Peptide couplings
- Biocatalytic transformations

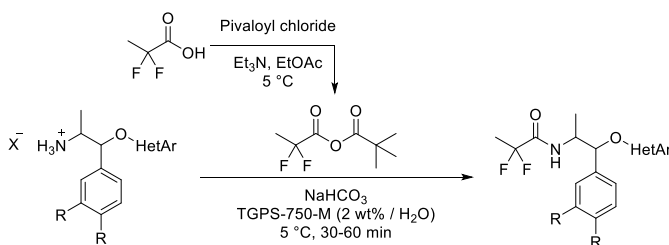
Evonik is working in collaboration with micellar technology pioneer, Professor Bruce Lipshutz of the University of California, Santa Barbara, to offer this highly sustainable technology for the industrial scale production of pharma intermediates and APIs.

### Example 1: Buchwald-Hartwig Coupling in water



- Dioxane replaced by water and *t*BuOH 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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