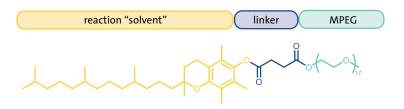
Quick Start Guide to Micellar Catalysis

GENERAL OVERVIEW



- Amphiphiles aggregate into micelles in water
- Mild reaction conditions
- ✓ Reduced organic solvent use
- ✓ Single reaction medium for different types of chemistry
- Potential for reduced catalyst loading (both metal and enzyme)

RECENT INDUSTRY APPLICATIONS

LSZ102 (Novartis)
Kilogram scale Suzuki Miyaura Cross Coupling
Org. Process Res. Dev. 2020, 24, 1536.

TAK -954 (Takeda)

Manufacturing process developed in water *Green Chem.*, 2021, 23, 788.

GETTING STARTED

Commercially Available Surfactants

Where do I begin?

- Many surfactants commercially available (Sigma -Aldrich)
- Can be purchased neat or in solution
- Start with 2 wt% in water (1 -5 wt% optimal)
- 0.1M to 0.5M reaction concentration is the most ideal
- For air -sensitive reactions, use degassed water (sparge with N₂)
- Store in inert atmosphere (up to 6 months)

REACTION SCREEN

| Recommended | Inital 12 Exp. | Screen | Screen

Gauge reaction amenability with initial screen

Things to Consider

Before Reaction

- ✓ Choice of Surfactant
- ✓ Amount of co -solvent (5 -20%)
- Dosing rate of reagents
- Temperature (above 60°C may degrade surfactant)
- pH (extreme pH may degrade surfactant)
- ✓ Lipophilicity of reagents

Work-up

- ✓ Direct drop crystallization
- ✓ Product precipitation *via*
 - H₂O addition
 - Co-solvent evaporation
- ✓ Extractive work -up
- Traditional crystallization

Insider Knowledge

- √ Vigorous stirring is key! (barring biocatalysis)
- Avoid splashing above solvent level
- For most cases, surfactant solution should be added last
- For reaction monitoring, remove aliquot while reaction is stirring

Disadvantages

- Insufficient solubility of substrate
- Hydrolysis of highly reactive intermediates
- Challenges with some heterogeneous reaction mixtures
- Large quantities of solvent use during extraction may negate environmental benefits

REACTION TYPES =

olefin metathesis peptide couplings biocatalysis Heck coupling Stille coupling

Suzuki - Miyaura S NAr C - H activation tandem reactions reductive amination

Sonogashira Nitro reductions Buchwald - Hartwig Amination