

Recent Designer Surfactants in Micellar Catalysis

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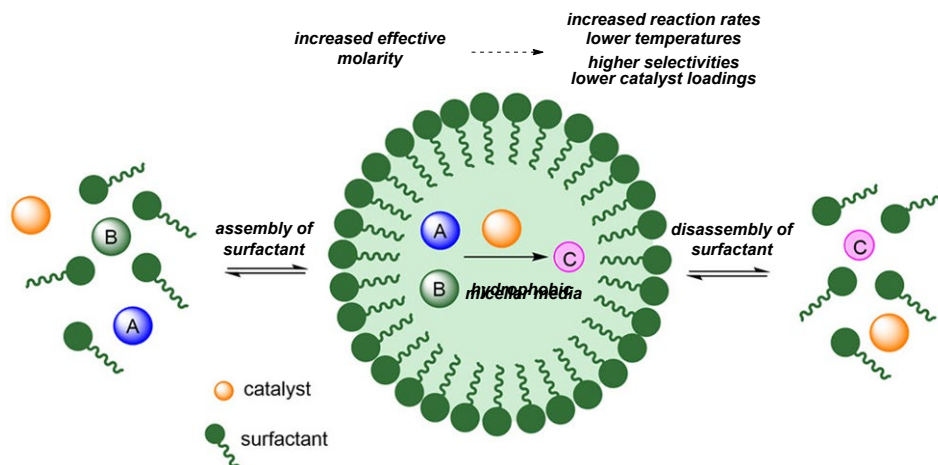
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INTRODUCTION

Micellar catalysis allows for myriad organic transformations to be performed in aqueous mediums with the added benefits of lower temperatures and catalyst loadings. It is proposed that the origins of this rate acceleration, relative to

performing the same reactions “on water,” stems from an increased effective molarity of water-insoluble reactants and catalysts within the surfactant’s hydrophobic micellar cores. Consequently, many reactions, traditionally performed in the absence of water, can minimize their use of organic solvent and allow for more environmentally sustainable processes with lower E-factors. This route towards greener chemistries has been motivation for a series next generation surfactants, allowing the synthetic chemist to harness reactivity in conditions traditionally thought unlikely.¹ This literature seminar will focus on recent designer surfactants reported by Lipshutz and Handa and their applications in modern day organic synthesis.²⁻⁵

Scheme 1. Overview of Micellar Catalysis



NOK: A PHYTOSTEROL-BASED SURFACTANT

Scheme 2. TPGS-750-M and SPGS-550-M (“Nok”)



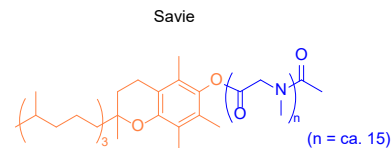
Lipshutz’s third generation surfactant, SPGS-550-M or otherwise known as Nok, differs from its second generation predecessor, TPGS-750-M, via substitution of the α -tocopherol lipophilic motif with the more economically sustainable plant steroid, β -sitosterol. The simple, two-step synthesis of Nok entails the subsequent installations of the succinic acid linker and poly(ethylene glycol) methyl ether onto the lipophilic moiety. Similar to previous generations, Nok is able to facilitate a variety of

reactions, including named cross couplings and cross olefin metatheses, using in many cases water as the sole solvent.²

SAVIE: A BIODEGRADABLE SURFATANT

Lipshutz's newest designer surfactant, Savie, is a biodegradable alternative to previous generations and demonstrates enhanced emulsification capabilities. Although the lipophilic α -tocopherol motif is retained from the second generation surfactant, the hydrophilic portion consists of a DMF-like polysarcosine chain. This surfactant has been shown to broaden the scope of chemistries harnessable by previously reported surfactants, especially in the context of difficult to solubilize substrates that often require the addition of organic co-solvents to the aqueous medium. Moreover, the polysarcosine functionality is thought to adopt random coil conformations in water, unlike homopolypeptide chains which favor ordered secondary structures which could inhibit micellar catalysis.

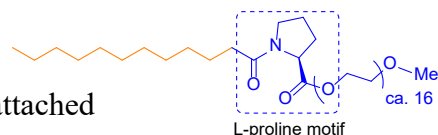
Scheme 3. Savie



PS-750-M: AN ENHANCED POLARITY SURFACTANT

PS-750-M, designed by the Handa group, differs from the aforementioned surfactants via its structurally simpler, lipophilic *n*-undecyl functionality and hydrophilic L-proline motif covalently attached to a poly(ethylene glycol) methyl ether terminus. The L-proline linker was strategically chosen to enhance polarity near the micellar core to imitate polar, aprotic solvents as envisioned by the Handa group. Such enhanced polarity is thought to allow this surfactant to facilitate the C(sp³) – C(sp²) cross coupling of polar nitroalkanes and aryl bromides using *t*-BuXPhosPd(allyl)OTf as the precatalyst.⁴ Moreover, this same surfactant has been shown to accommodate Ni(0)Pd(0) nanoparticles within its micellar interior. These unique nanocatalysts have been shown to facilitate the selective deprotection of Cbz protected anilines via hydrogenolysis. Notable examples contain functionalities prone to cleavage in traditional hydrogenolysis conditions, including aryl ethers.

Scheme 4. PS-750-M



REFERENCES

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