

## Synthetic and Mechanistic Study of Organic Reactions in the Aqueous Media

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Considering that between one half to three quarters of the annual resource inputs to industrial economies are returned to the environment as wastes within a year,<sup>1</sup> it is imperative that the chemical community implements all necessary steps to cut down the amount of waste generated in synthetic processes. It is a well-known fact that organic solvents represent the major contributor to chemical waste. For example, in multistep synthetic processes, such as pharmaceutical manufacture, amounting to ca. 85% of the total mass of chemicals involved in the process.<sup>2</sup>

Water is the most abundant and environmentally friendly solvent in nature. Yet, its application in organic synthesis is currently very limited.<sup>3,4</sup> Since most organic compounds have a low water solubility, much emphasis has been placed on the development of organic microenvironment in the aqueous phase by adding small-molecule surfactants, e.g. micellar catalysis.<sup>5</sup> The necessity to use such additives or co-solvents significantly reduces the attractiveness of water as a reaction medium. It is also worth remembering that unless the aqueous phase is efficiently recycled or easily decontaminated, mere performance of an organic reaction in water does not necessarily result in an environmentally clean process.<sup>6</sup>

We have demonstrated that simple sodium salts can completely reverse the selectivity of organic transformations in aqueous media by moving the reactants between the two phases. In the case of the Passerini reaction, when the reaction was performed in water it resulted with a mixture of two products. While using the salting-out sodium sulfate led to the Passerini product, the salting-in tosylate lead to the complete reversal of the reactivity providing the hydrolysis product exclusively.

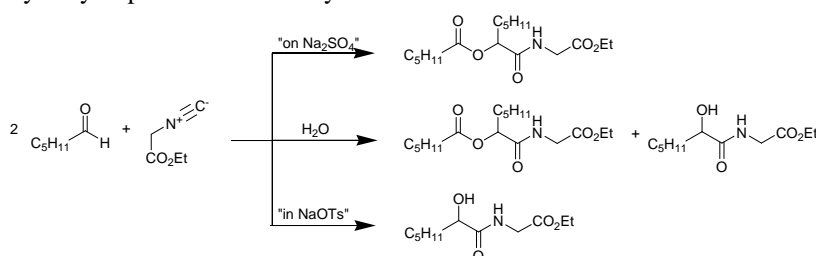


Fig. 1 – Competitive formation of "on Water" and "in Water" Passerini reaction products in the presence of sodium salts.

Furthermore, the use of the "salting-in" salt and a small excess of the nucleophile gives significantly higher yields than the use of the saturated solution of the nucleophile alone.

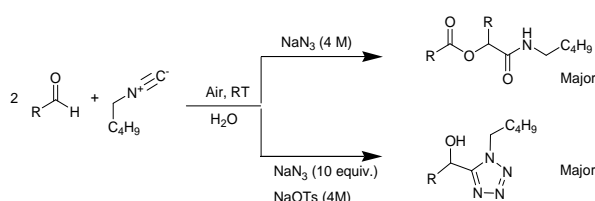


Fig. 2 – Reactive intermediate trapping under the "in Water" or "in NaOTs" conditions

The aqueous phases could be recycled several times without influence the reaction selectivity and reactivity making a good case for a truly sustainable organic synthesis, novel and "green" at the same time.

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