Asymmetric Michael reaction in/on water catalyzed by chiral amines

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Asymmetric conjugated addition is a useful method for carbon-carbon bond formation. Both inter- and intramolecular Michael reactions are often a key step in synthesis of biologically active compounds. For this reason, constant search for new, effective catalysts of this process is an always present concern for scientists. In last few years there was observed dynamic growth of organocatalysis, which uses small organic molecules as catalysts. Special interest gathers reactions carried out in aqueous media due to its ecological benefits, safety and total cost of the process.

Herein, I presented possibility of conducting Michael reaction of aldehydes and nitroolefines in aqueous media catalysed by primary amines and secondary aminoalcoholes. I showed that addition of water to organic solvent improves yield and selectivity of the reaction. This methodology I used in synthesis of Michael adducts of β-nitrostyrene to a number of aldehydes. Chiral, commercially available (1*S*,2*S*)-1,2-diphenylethylenediamine effectively promoted reaction of more demanding α,α-disubstituted aldehydes, leading to products with high enantioselectivity (up to 98% *ee*). I proposed also transition state model for the reaction of β-nitrostyrene and isobutyric aldehyde, catalysed by diamine, explaining stereochemistry of the product.

Finally, I accomplished synthesis of biologically active compound. My attention was drown by warfarin – anticoagulating drug used in *thrombosis* therapy. Reaction was conducted in water. I used ultrasound bath to enable emulsification of reaction components. I proposed crystallisation, as an alternative method for purifying the product of the reaction of 4-hydroxycumarine and benzylideneacetone. The main advantage of this method was that it excluded use of expensive silica gel chromatography from the procedure and led to optically pure (*S*)-warfarin. I used this methodology in synthesis of warfarin derivatives to show universality of proposed approach.