

522e A Computer-Aided Methodology for Solvent Selection for Reactions: Robust Design Formulation

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Given the important role played by solvents in chemical processing, significant research effort has been devoted to the development of systematic methods for solvent selection. However, much of this effort has been focused on separations, and there has been little work on the design of solvents that can enhance reaction rates, in spite of the significant gains that can be achieved by optimizing the choice of reaction medium (Cox).

To address this issue, we propose an iterative approach that combines experimental work with computations for the design of solvent for a reaction. A key issue is to identify a relationship that links certain specific solvent properties to the reaction rate in a way that can quantify solvent effects on a particular reaction. We propose the use of the multi-parameter solvatochromic equation (Abraham et al., 1987), simple and easily applicable, which correlates solvent properties (empirical solvatochromic parameters and cohesive energy density parameter) with the logarithm of the reaction rate constant. We obtain the values of the solvent parameters used in this equation by group-contribution prediction techniques we have recently developed. These prediction techniques use UNIFAC first-order groups to make further integration with previous solvent design approaches easier. We aim to develop a tool that can be adapted to plant-wide process integration and allows balancing reaction rate against other processing requirements.

The proposed methodology consists of three steps. The first step is concerned with the development of a model of solvent effects on the reaction. It involves gathering reaction rate data for eight predetermined solvents and generating the solvatochromic equation by fitting the coefficients by linear regression. The solvents should be chosen in such a manner as to cover a wide range of polarity and classes of chemicals. The second step is an optimization step in which the design problem is formulated as an MINLP and solved using standard techniques. The first objective we consider is to identify a solvent in which the reaction rate constant under given conditions is maximized. Implementation of integer cuts allows the generation of successive candidate molecules. However, since we build our model based on kinetic data in a few solvents only, and then use it for further extrapolation, there is significant uncertainty associated with the model coefficients. We use global sensitivity analysis to evaluate this effect on the model. We then evaluate the impact of uncertainty on the solvents designed. We first formulate the design problem for a large number of different combinations of the values of the coefficients and find the optimal design for each problem. Next, we use the results obtained over the whole uncertainty space to generate a number of coefficient clusters from which a few uncertain scenarios are generated. These are then used to formulate and solve a robust design problem formulation.

The methodology is tested through application to classes of reactions where solvent effects are known to be significant such as solvolysis of alkyl halides and Menschutkin reaction. The uncertainty analysis reveals the solution of the deterministic design problem is quite robust. Relatively few optimal solvents are generated from a large design space.

References:

1. Abraham, M.H., Doherty, R.M., Kamlet, M. J., Harris, J.M. and Taft, R.W. (1987). Linear Solvation Energy Relationships. Part 37. An Analysis of Contributions of Dipolarity-Polarisability, Nucleophilic Assistance, Electrophilic Assistance, and Cavity Terms to Solvent Effects on t-Butyl Halide Solvolysis

Rates. *Journal of the Chemical Society – Perkin Transactions 2*, 913-920. 2. Cox, B.G. (1994). *Modern Liquid Phase Kinetics*. Oxford University Press.