Book Reviews

COSMO-RS from Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design. By A. Klamt. Elsevier: Amsterdam, The Netherlands, 2005. 246 pp. $US 165. ISBN 0-444-51994-7.

The acronym COSMO stands for Conductor Like Screening Model, and COSMO-RS refers to the COSMO model with Realistic Solvation and its application to the prediction of the thermodynamic properties of fluid mixtures. This book is in part a very personal account of the history of the development of COSMO and COSMO-RS and its application initially to partition coefficients, then to the thermodynamic properties of liquid mixtures related to the chemical potential and its temperature derivate, and then extension of the method to be a tool for drug design. The goal of most researchers who study thermophysical properties of fluids is to be able to explain their results in terms of molecular interactions. It was anticipated that this goal would be achieved through theories firmly grounded in statistical mechanics or massive calculation based on Monte Carlo or molecular dynamics simulation using realistic intermolecular potentials. While we have mastered both theory and simulation, a realistic intermolecular potential that will describe complex polar multi-atom molecules remains elusive with no solution presently in sight.

COSMO-RS is a serious attempt to provide a molecular interpretation of properties of fluid mixtures derived from the chemical potential of the components and their variation with temperature (LLE, VLE, partition coefficients, Henry's constant, excess enthalpy, and infinite dilution activity coefficients). COSMO-RS makes no claim to predict properties related to the pressure derivative of the chemical potentials (*PVT* properties including excess volumes). Prior to the advent of COSMO-RS, we have tried to explain mixture properties based on speculative hand-waving arguments or on group contribution schemes, which require a massive database of measured properties to derive the group contributions to the residual portion of the excess Gibbs function.

The book is eminently readable. In the introduction the limitations of various quantum mechanical approaches to describe chemical thermodynamics are discussed. These methods provide a detailed description of the electron density and thus are primarily applicable to non-interacting molecules in a vacuum. The discussion also includes the limitations of molecular dynamics or Monte Carlo methods for complex systems that require a plethora of parameters, including bond lengths, bond angles, and electrostatic and dispersive force descriptions, many having to be adjusted too reproduce experimental data for either the pure fluid or the mixture. The role and limitations of group contribution schemes are also outlined.

Chapter two introduces the concept of placement of molecules in a dielectric continuum with a resultant reaction field due to polarization, leading to solvation models. It was in 1991 that Klamt, then a metal physicist, was asked to look at the implementation of the self-consistent reaction field approach into a semi-empirical quantum code to account for solvation effects during the calculation of quantative structure−activity relationships (QSAR). This work lead to a very efficient conductor-like variant (COSMO). Chapter 3 discusses the limitation of this model while Chapter 4 offers a way out by introducing an energy of misfit approach. Chapter 5 deals primarily with entropy and concludes with an expression similar to the UNIFAC combinatorial term. The preeminent chapter is 6, the basis COSMO-RS. A COSMO calculation determines the polarization charge density on the COSMO surface. The average charge density σ over a surface area of radius 0.5 nm is then used to calculated the σ profile, which is the histogram of the amount of surface that has a charge density between ($\sigma - d\sigma/2$) and ($\sigma + d\sigma/2$). A qualitative picture of the interactions between molecules can be inferred by comparison of their σ profiles. An integration over the surface involving the σ profiles of both components leads to an expression for the residual of the chemical potential, from which other thermodynamic properties may be estimated. Chapter 7 includes refinements to the model, and Chapter 8 discusses applications to chemical engineering thermodynamics, while Chapters 9 and 10 discuss further applications of COSMO-RS in the physical sciences. Chapter 11 introduces some fascinating applications to life sciences with particular emphasis on drug design. Chapter 12 is a summary of the advantages and limitations of the COSMO-RS approach. Here Klampt honestly admits: "The COSMO-RS method is a fruitful compromise between empirical and oversimplifying group contribution methods used for a long time in chemical engineering and the basically more rigorous molecular dynamics or Monte Carlo approaches, ..." Other limitations include the inability to derive quantities related to the pressure dependence of the chemical potential and transport properties.

The book is easy to read as well as enlightening. It should be compulsory reading for those researchers attempting to explain their measured thermodynamic properties of mixing by invoking hand waving molecular interaction arguments.

The book includes a demonstration disk of the COSMOtherm program, a limited number of COSMO files, the manual, and tutorial. I still do not find the program intuitive, but those more savvy with computer programs might fare better.

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