COSMO-RS Predictions of Aqueous Solubility: Application of Modified QSPR Equation to Estimate Gibbs Free Energy of Fusion

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Recently the COSMO-RS method originally developed for the prediction of liquid-liquid and liquid-vapor thermodynamical parameters based on application of conductor-like screening model (COSMO) and a statistical thermodynamics treatment of resulting polarization charge densities, has been modified to predict solubility of solids [1]. In this modification, the COSMO-RS equation that describes solubility of liquids:

$$\log(x_s) = (\mu_{self} - \mu_{solv})/RT\ln(10)$$

is replaced by more general one:

$$\log(x_s) = [\mu_{self} - \mu_{solv} - \max(0, \Delta G_{fus})]/RT\ln(10)$$

that could be applied for prediction of the solubility of both liquids and solids.

It was suggested that, due to computational difficulties for accurately predicting ΔG_{fus} **,** [1] to use a QSPR technique to generate the QSPR equation using an appropriate training set. Indeed, the equation obtained this way has been able to successfully predict solubility of many drugs and pesticides. However, more careful inspection of the results obtained in this manner revealed that the QSPR equation presented in [1] is not able to predict accurately the ΔG_{fus} values for nitro compounds of pesticides and drugs, in addition to representing military important classes of compounds as explosives and propellants. For example, the QSPR equation used in [1] predicts a negative ΔG_{fus}value (-7.08 kJ/mol) for trinitrotoluene(TNT).

Our current contribution presents another type of QSPR estimates for ΔG_{fus} which is based on an extended training set that includes most of the species presented in [1] and additionally several nitro compounds with known experimental water solubility. To develop new QSAR equations, we applied the Hierarchical Technology for Quantitative Structure - Activity Relationships (HiT QSAR) [2] based on the Simplex Representation of Molecular Structure (SiRMS) method [3]. This method has proved efficient in previous studies for solving different "structure-activity" problems.

As the result of HiT QSAR application, we obtained new QSPR equations which predict ΔG_{fus} much more accurately. For example we found that the error of solubility prediction for such explosives as TNT, CL-20, HMX and RDX is less then one log-unit.

References

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