Predicting Multicomponent Phase Equilibria and Free Energies of Transfer for Alkanes by Molecular Simulation

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Abstract: Configurational-bias Monte Carlo simulations in the Gibbs ensemble have been carried out to calculate (i) the boiling point diagram for the binary mixture of *n*-octane and *n*-dodecane at a pressure of 20 kPa, (ii) the 366 K isotherm for the binary mixture of supercritical ethane and *n*-heptane, and (iii) the free energies of transfer from a helium vapor phase at a pressure of 1 atm to an *n*-heptane liquid phase for the solutes n-pentane and *n*-hexane. Results are reported for three force fields (OPLS, SKS, and TraPPE) which all employ the united-atom description and Lennard–Jones nonbonded bead–bead interactions. The simulation methodology in conjunction with the TraPPE force field produces results in excellent agreement with experimental data. The simulated boiling points at 20 kPa are 342.7 ± 1.6 K (*n*-octane) and 423.8 ± 1.3 K (*n*-dodecane) compared to the experimental values of 349.1 and 431.3 K, respectively. For the ethane/*n*-heptane mixture the pressure dependence of the composition is very well reproduced. Free energies are calculated directly from the partitioning between the coexisting vapor and liquid phases without the need of multistep thermodynamic integration. The calculated free energies of transfer are −13.3 ± 0.3 kJ mol^{-1} (*n*-pentane) and −16.2 ± 0.5 kJ mol^{-1} (*n*-hexane), in good agreement with the experimental values of −13.7 ± 0.1 and −16.6 ± 0.1 kJ mol^{-1}. Our simulation methodology and the TraPPE force field have no pressure- or density-dependent parameters and can be utilized to perform calculations for a wide range of physical conditions which are outside the range of validity of most semiempirical solvation models and for which experiments are sometimes difficult to perform, such as phase equilibria at high temperatures and pressures.

Introduction

Knowledge of the phase behavior of hydrocarbons is of great importance in many technological applications, such as in oil refineries, for enhanced oil recovery, and for separation processes. Liquid alkanes can also serve as a zeroth-order model of the lipid bilayer,[1] and the alkane/air and water/air partition constants for a solute molecule can be combined to give information about the distribution of solutes in biological systems.[2] The position of chemical equilibria as well as the direction of all spontaneous chemical change is determined by free energies. The partition constant of solute *S* between phases α and β is directly related to the Gibbs free energy of transfer[3]

$$\Delta G_{S} = RT \, (\rho_{S}^{\alpha}/\rho_{S}^{\beta}) \tag{1}$$

where ρ_{S}^{α} and ρ_{S}^{β} are the number densities of S in the two phases at equilibrium. Whereas the determination of mechanical properties is now routine for computer simulation, the determination of free energies and other thermal properties, which depend on the volume of phase space, remains one of the most challenging problems.[4–6] Thermodynamic integration (TI) and

free energy perturbation (FEP) are the most widely used methods to calculate free energy differences and are available in many simulation packages.[5–8] These methods are based on reversibly mutating solute X into solute Y to calculate the free energy difference and require many successive simulations along the integration path. However, TI-FEP methods are not directly applicable to calculations of the free energy of transfer between two solvent phases.

The simulation technique used here is a combination of the Gibbs-ensemble Monte Carlo (GEMC) method[9] and the configurational-bias Monte Carlo (CBMC) algorithm.[10,11] GEMC utilizes two separate simulation boxes which are in thermodynamic contact, but do not have an explicit interface.[9] As a result, for a given state point the properties of the coexisting phases, such as the partitioning of solute molecules, can be determined directly from a single simulation. One of the GEMC steps involves the swapping of a molecule from one phase to the other, thereby equalizing the chemical potentials of each species in the two phases. Acceptance of these particle interchanges is often the rate limiting step in GEMC simulations, and to improve the sampling of insertions of flexible molecules, such as the alkanes, the CBMC technique is used. CBMC replaces the conventional random insertion of entire molecules with a scheme in which the chain molecule is inserted atom by atom such that conformations with favorable energies are preferentially found.[10]

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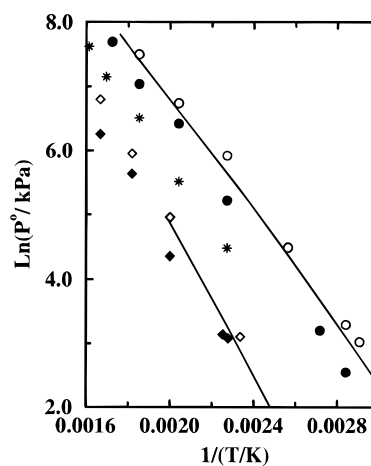(5) Kollman, P. A. *Chem. Rev.* **1993**, *93*, 2395–2417.
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The resulting bias in the CBMC swap step is then removed by using special acceptance rules.[12] A more detailed description of these simulation methods can be found in refs 13 and 14. GEMC-CBMC has been successfully applied to the calculations of single-component vapor-liquid phase equilibria of linear and branched alkanes,[15] alcohols,[16] and a fatty acid Langmuir monolayer.[17] The extension to multicomponent alkane mixtures described here introduces a case where the shorter alkane has a considerably higher acceptance rate in the swap move than the longer alkane. We take advantage of this by introducing the CBMC-switch move, which combines the GEMC identity switch[18] with CBMC chain interconversion,[19] such that molecule A is regrown as molecule B in one box, and B is regrown as A in the other box. This CBMC switch equalizes the difference of the chemical potentials of A and B in the two boxes. The conventional CBMC swap is used mainly to equalize the chemical potential of the shorter alkane in the two phases. In the case studied here, a mixture of *n*-octane and *n*-dodecane, the CBMC switch had an acceptance rate of at least two orders of magnitude higher than the *n*-dodecane swap. Thus the efficiency of the simulations was mainly limited by the acceptance rate for the *n*-octane swap. At an intermediate temperature of 390 K (using the TraPPE force field) the percentages of accepted octane-swaps, dodecane-swaps, and octane-dodecane switches were 0.083, 0.014, and 5.2, respectively.

Force Fields

Simulations were carried out for three different *n*-alkane force fields: OPLS (Optimized Potentials for Liquid Simulations),[20] SKS (Siepmann-Karaborni-Smit),[15a] and TraPPE (Transferable Potentials for Phase Equilibria).[21] These three force fields make use of the united-atom approach, *i.e.* methyl and methylene units are modeled as single pseudoatoms. Nonbonded pseudoatoms interact through Lennard-Jones 12−6 potentials with the following parameters: OPLS, $\epsilon_{CH_3}/k_B = 88.1$ K, $\epsilon_{CH_2}/k_B = 59.4$ K, $\sigma_{CH_3} = \sigma_{CH_2} = 3.905$ Å; SKS, $\epsilon_{CH_3}/k_B = 114.0$ K, $\epsilon_{CH_2}/k_B = 47.0$ K, $\sigma_{CH_3} = \sigma_{CH_2} = 3.93$ Å; TraPPE, $\epsilon_{CH_3}/k_B = 98.1$ K, $\epsilon_{CH_2}/k_B = 47.0$ K, $\sigma_{CH_3} = 3.77$ Å, $\sigma_{CH_2} = 3.93$ Å. The TraPPE force field differs from the other two in the respect that different sizes are used for the methyl and methylene beads (four-parameter model). The methylene parameters are identical in the SKS and TraPPE force fields. Thus both force fields yield very similar properties for high molecular weight *n*-alkanes, whereas the TraPPE force field is far superior for shorter alkanes.[21] The experimental critical constants of helium were used to obtain suitable Lennard-Jones parameters: $\epsilon_{He}/k_B = 3.95$ K, $\sigma_{He} = 3.065$ Å. Lorentz−Berthelot combining rules were used for the nonbonded interactions of unlike pseudoatoms, and no special

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Figure 1. Clausius−Clapeyron plot showing the logarithm of the vapor pressure versus the inverse temperature. The solid lines depict the experimental data (upper curve, *n*-octane[36]; lower curve, *n*-dodecane[24]). Open circles, filled circles, and stars show the simulation results of the TraPPE, SKS, and OPLS force fields for *n*-octane, respectively. Open and filled diamonds represent the TraPPE and SKS results for *n*-dodecane.

mixing rules were used to augment the interactions of unlike molecules. All Lennard-Jones potentials were truncated at 14.0 Å, and analytical tail corrections were applied.[22] For all force fields the pseudoatoms in a given alkane are connected by rigid bonds ($d_{CC}^{SKS,TraPPE} = 1.54$ Å, $d_{CC}^{OPLS} = 1.53$ Å); bond bending is governed by a harmonic potential[23] ($\theta^{SKS,TraPPE} = 114°$, $\theta^{OPLS} = 112°$, $k_\theta = 62500$ K rad^{-2}); and the dihedral motion is controlled by the OPLS potential.[20]

Results and Discussion

Boiling Points. The vapor pressures and vapor−liquid coexistence curves of pure *n*-octane and *n*-dodecane were determined from simulations by using the isometric (NVT) version of the Gibbs ensemble.[9a] The simulations were carried for 200 octane or dodecane molecules, and the production runs consisted of 5 000 to 25 000 MC cycles. A Clausius−Clapeyron plot of the vapor pressures can be used to calculate the boiling points of the pure substances (see Figure 1). It is clearly evident from Figure 1 that the vapor pressures obtained for the TraPPE force field are closest to the experimental data. The numerical values of the boiling points of octane at atmospheric pressure (values at a pressure of 20 kPa in brackets) are as follows: OPLS, 446.6 ± 1.8 K (387.4 ± 2.3 K); SKS, 416.3 ± 1.6 K (362.8 ± 1.8 K); and TraPPE, 393.8 ± 1.4 K (342.7 ± 1.6 K). The calculated boiling points for *n*-dodecane are as follows: SKS, 505.1 ± 2.8 K (438.1 ± 3.2 K); and TraPPE, 485.3 ± 1.0 K (423.8 ± 1.3 K). The statistical uncertainties in the calculated boiling points are remarkably small. The TraPPE boiling points agree very well with their experimental counterparts (398.9 and 489.5 K at atmospheric pressure and 349.1 and 431.3 K at 20 kPa).[24,25] In contrast, the SKS boiling points are shifted to slighly higher temperatures, and the OPLS boiling point for octane is close to the experimental value of decane (447.3 K at 1 atm).

Boiling Point Diagram. Simulations for the binary octane− dodecane mixture were performed in the NpT version of the

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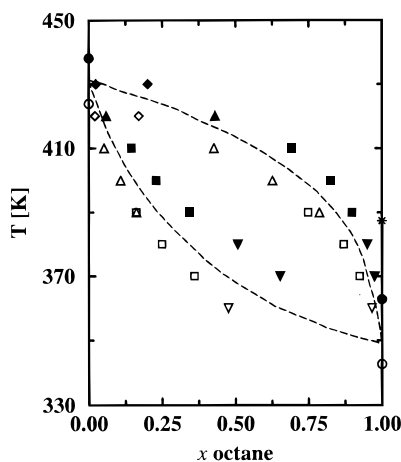
Figure 2. Boiling point diagram for the binary system *n*-octane and *n*-dodecane at $p = 20$ kPa. Open and filled symbols are used for the TraPPE and SKS force fields, respectively. The dashed line represents the experimental data.[24] The calculated boiling points for the pure substances are shown as circles (star for octane using the OPLS force field). Simulation results for binary mixtures are depicted as diamonds, upward-pointing triangles, squares, and downward-pointing triangles for simulations containing total mole fractions of *n*-octane of 0.1, 0.25, 0.5, and 0.75, respectively.

Table 1. Simulation Results for the Binary System Octane−Dodecane at 20 kPa Calculated for the TraPPE Force Field.

T [K]	x_t	x_{vap}	x_{liq}	ρ_{vap} [g cm^{-3}]	ρ_{liq} [g cm^{-3}]
360	0.75	0.965$_6$	0.476$_6$	0.00079$_1$	0.693$_3$
370	0.50	0.924$_{16}$	0.360$_{11}$	0.00077$_1$	0.690$_1$
380	0.50	0.869$_{21}$	0.249$_8$	0.00078$_1$	0.686$_1$
390	0.50	0.748$_7$	0.162$_{11}$	0.00081$_1$	0.682$_1$
390	0.25	0.787$_{24}$	0.163$_{16}$	0.00079$_1$	0.686$_1$
400	0.25	0.627$_{13}$	0.108$_{11}$	0.00082$_1$	0.677$_1$
410	0.25	0.427$_{14}$	0.052$_6$	0.00087$_1$	0.673$_2$
420	0.10	0.170$_4$	0.021$_1$	0.00094$_1$	0.667$_2$

^{a} x_t is the total octane molfraction for the GEMC simulation, e.g. a simulation with $x_t = 0.25$ is carried out using 50 octane and 150 dodecane molecules. x_{vap}, x_{liq}, ρ_{vap}, and ρ_{liq} are the mole fractions and specific densities for the vapor and liquid phases, respectively. The subscripts denote the standard deviations calculated from block averages of a length of 4000 MC cycles.

Gibbs ensemble.[9b] A total of 200 alkane molecules was used, and the relative amounts of each were varied to yield simulations with approximately equal numbers of molecules in the vapor and liquid phases. The production runs consisted of 20 000 and 5 000 MC cycles for the TraPPE and SKS force fields, respectively. For an equimolar mixture of octane and dodecane, 5 000 MC cycles take approximately 20 h of CPU time on an Intel PentiumPro (200 MHz) running under Linux. The calculated boiling point diagrams at $p = 20$ kPa are presented in Figure 2, and the numerical results for the compositions and densities are given in Table 1. The results obtained for both the TraPPE and the SKS force fields agree very well in both position and shape with the experimental phase diagram.[24] While the TraPPE force field yields results which are shifted slightly to lower temperatures (approximately 7 K over the entire range of compositions), the SKS boiling points are shifted upward by 8 to 12 K, and the OPLS results are shifted upward by more than 40 K.[26]

Supercritical Pressure Composition Diagram. The 366 K isotherm for the binary mixture of (supercritical) ethane and
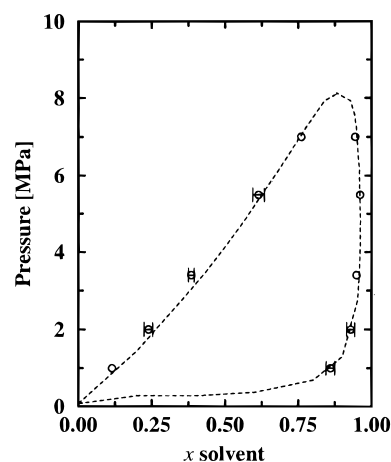
Figure 3. The 366 K isotherm for the binary system supercritical ethane and *n*-heptane. Open circles are used for the simulation data (obtained with the TraPPE force field). The dashed line represents the experimental data.[27] The statistical errors in the simulation data are only shown when larger in magnitude than the symbol size.

n-heptane is presented in Figure 3. The configurational-bias Monte Carlo simulations (20 000 MC cycles for the production runs) were carried out in the NpT Gibbs ensemble for a total of 400 molecules with use of the TraPPE force field. The experimental phase diagram[27] is very well reproduced, demonstrating that the TraPPE force field and the methodology also perform well at supercritical conditions and for alkanes with larger length ratios.

Free Energies of Transfer. Air/*n*-heptane partition constants for *n*-alkanes at $T = 298.15$ K and $p = 1$ atm have been measured by Eikens and Carr[28] using a modified head space chromatographic technique.[29] Due to the low vapor pressures of the *n*-alkanes studied, an inert gas has to be added to reach atmospheric pressure. We have used helium in our studies, whereas the experiments are carried out in air atmosphere.[30] The simulated systems contained 140 helium and 210 *n*-heptane molecules plus a small number of solute molecules. Production periods consisted of 60 000 to 80 000 MC cycles. Multiple partition constants can be measured in a single experiment by having sufficiently low concentrations of several solutes in the system. Inspired by this experimental technique, we have performed three simulations for the following combinations of solute molecules: (i) no solute (a binary mixture of helium and *n*-heptane), (ii) two *n*-pentane molecules (a ternary mixture), and (iii) two *n*-pentane plus two *n*-hexane molecules (a quaternary mixture). Figure 4 shows a comparison of the calculated Gibbs free energies of transfer obtained for the TraPPE force field with eq 1, the experimental results,[28] and the predictions from the semiempirical quantum mechanical solvation model AM1-SM4.[31] The agreement is very satisfactory, with our results falling in between the experimental and the AM1-SM4 results. For example, the calculated free energy of transfer for *n*-hexane is -16.2 ± 0.5 kJ mol^{-1}, and the

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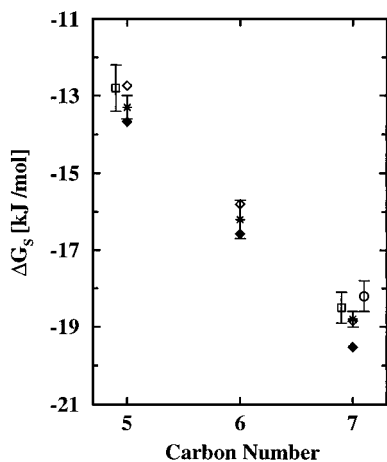
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Figure 4. Free energies of transfer from vapor phase to *n*-heptane liquid phase for *n*-pentane, *n*-hexane, and *n*-heptane. The experimental results[28] and the AM1-SM4 data[31] are depicted by the solid diamonds and open diamonds, respectively. The following symbols are used for the simulation results (see text): circles (no solute), squares (*n*-pentane solute), and stars (*n*-pentane and *n*-hexane solutes). For clarity, some of the simulation results have been shifted by ±0.1 on the *x*-axis.

corresponding experimental and AM1-SM4 results are −16.6 ± 0.1 and −15.8 kJ mol^{−1}, respectively. It is also evident that reliable free energies for multiple solutes can be obtained from one single simulation in the Gibbs ensemble. The statistical uncertainties (estimated from block averages) in the calculated free energies are smaller than 0.6 kJ mol^{−1} (or less than 5%), *i.e.* smaller than the statistical uncertainties typically associated with the creation/annihilation of a single methylene group in TI-FEP calculations.[32,33]

Conclusions

The combination of Gibbs-ensemble Monte Carlo and configurational-bias Monte Carlo methods allows the determination of free energies of transfer of multiple solutes in a single simulation and the calculation of multicomponent phase diagrams in a few simulations. In conjunction with the TraPPE alkane force field, results with a very high degree of accuracy and precision can be obtained. Since the GEMC-CBMC methodology allows for the direct determination of the partitioning of solute molecules, problems arising from the precise definition of the free energy of transfer[34] are circumvented. In this type of simulation molecules are always "complete" and ambiguities resulting from the coupling of a thermodynamic integration parameter to the individual parts of the force field are therefore avoided. The simulation methodology used in this report might offer significant advantages over more traditional free-energy methods. Our methodology and force field can be directly applied over a wide range of state points (*T*,*p*) which are outside the range of validity of semiempirical solvation models and where experiments are sometimes difficult to perform, such as high temperatures and pressures.[35]

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