A molecular dynamics and Monte Carlo study of solvent effects on the conformational equilibrium of *n*-butane in CCl_4[a),b)]

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We report on a computer simulation study of the gauche–trans conformational equilibrium of *n*-butane in liquid carbon tetrachloride solvent. The study is made possible by implementing an exact statistical mechanical theorem which relates the full intramolecular distribution function for a butane molecule to that of a hypothetical species which does not possess a large potential barrier separating the trans and gauche states. In addition to determining the trans–gauche equilibrium constant, the potential of mean torsion, that is, the reversible work required to alter the conformation is determined as a function of the dihedral angle. Recent theoretical work is compared with these computer experiments, and while qualitative agreement is found, the approximate theory overestimates the solvent effect. Finally, the change in solvent structure in response to a conformational change in the solute is determined.

I. INTRODUCTION

When a polyatomic molecule is dissolved in a liquid, both the static and dynamic properties associated with its internal degrees of freedom may be altered from the gas phase values. A rigorous statistical mechanical theory describing conformational structures of nonrigid molecules dissolved in liquid solvents has been provided by Pratt and Chandler[1,2] and some of the computationally tractable approximations that can be made have been explored for model systems of *n*-butane dissolved in liquid carbon tetrachloride, *n*-butane, and *n*-hexane.[3,4] The dynamics of isomerization of small nonrigid molecules in liquid solvents have also been explored using time correlation function methods.[5]

The *n*-butane molecule is perhaps the simplest nonpolar molecule with only one appreciable conformational degree of freedom. In this and subsequent articles we will employ computer simulation techniques to examine the effects of nonassociated solvent (carbon tetrachloride) on the statics and dynamics of the isomerization of *n*-butane.

Recent advances in technique have greatly enhanced the practicality of simulating nonrigid polyatomic molecules via the molecular dynamics (MD) method. The classical way of treating such systems involved construction of the equations of motion in generalized coordinates employing the formalisms of Hamilton or Lagrange. While unconstrained dynamical models for flexible molecules have been investigated,[6,7] the SHAKE method of constraint dynamics has been employed in the MD simulation of *n*-butane and higher order alkanes[8] and a macromolecule, bovine protein trypsin inhibitor.[9] SHAKE avoids the difficulties of explicitly determining a set of equations in generalized coordinates. The method allows the use of equations of motion in Cartesian form, the most natural form for the evaluatuion of interparticle forces for most model potentials. A further very important advantage of the method is that it allows the elimination of irrelevant internal degrees of freedom through the introduction of additional holonomic constraints.

In this article, we discuss the method and results of an MD computer simulation and two Monte Carlo (MC) simulations of a simple classical isomerization of a nonrigid polyatomic molecule (*n*-butane) in a nonassociated liquid solvent (carbon tetrachloride). We focus attention on the static properties of the isomerization; the equilibrium ratio of *trans* and *gauche* conformation, x_g/x_t; the distribution function $s(\phi)$ of the dihedral angle ϕ of the butane molecule; the reversible work, $W(\phi)$, which gives the Helmholtz free energy change in the solvent when the butane molecule is rotated from a dihedral angle of zero to ϕ; and the radial distribution of solvent particles around a solute molecule.

Our study confirms the qualitative conclusions arrived at by Pratt *et al.*[3] concerning the solvent effects on the conformational structure of *n*-butane in simple liquid solvents. However, we do find significant quantitative differences between the results of the approximate calculations for $W(\phi)$ and the "exact" simulation results reported here.

II. METHODOLOGY AND BACKGROUND

In the MD simulation carried out in this study, the system contains 122 CCl_4 molecules, each represented by a single Lennard-Jones sphere interacting with its neighbors via a truncated and shifted pair potential

$$u(r) = \begin{cases} u_{LJ}(r) - u_{LJ}(r_c), & 0 \le r \le r_c \\ 0, & r > r_c, \end{cases} \tag{1}$$

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[b)]This research was carried out when one of the authors (DC) was on leave from the University of Illinois at Columbia University during the 1977-1978 academic year.

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where r is the interparticle distance, r_c is the cutoff distance, and

$$u_{LJ}(r) = 4\epsilon_1\left[\left(\frac{\sigma_1}{r}\right)^{12} - \left(\frac{\sigma_1}{r}\right)^{6}\right]. \tag{2}$$

For CCl_4 the cutoff distance is taken as $r_c = 2.50\sigma_1$, the "diameter" is $\sigma_1 = 5.27$ Å, and the well depth is $\epsilon_1 = 373\,^\circ\mathrm{K}\,k_B$. The mass of a CCl_4 particle was taken to be $m = 2.55\times10^{-22}$ g.

The system also contains one butane molecule represented by a chain of four interconnected Lennard-Jones spheres (representing methyl groups). The three C–C bond lengths were fixed at 1.53 Å and the two angles between adjacent C–C bonds were fixed at the tetrahedral angle, 109° 28'. The mass of each methyl particle was taken to be one fourth the mass of a butane molecule, i.e., 2.41×10^{-23} g. The well depth $\epsilon_2 = 84\,^\circ\mathrm{K}\,k_B$ and diameter $\sigma_2 = 3.92$ Å have been used previously by Ryckaert and Bellemans[10,11] in MD simulations of neat liquid n-butane. These parameters would characterize the Lennard-Jones potential between two methyl particles on different n-butane molecules. We assume that the methyl particles interact with the solvent molecules via the truncated and shifted pair potential

$$v(r) = \begin{cases} v_{LJ}(r) - v_{LJ}(r_c), & 0 \le r \le r_c \\ 0, & r > r_c, \end{cases} \tag{3}$$

where r is the solvent–methyl interparticle distance,

$$v_{LJ}(r) = 4\epsilon_{12}\left[\left(\frac{\sigma_{12}}{r}\right)^{12} - \left(\frac{\sigma_{12}}{r}\right)^{6}\right], \tag{4}$$

where $\epsilon_{12} = (\epsilon_1\epsilon_2)^{1/2}$, and $\sigma_{12} = \frac{1}{2}(\sigma_1 + \sigma_2)$. The cutoff r_c is the same for solvent–solvent and solvent–methyl interactions in our simulation.

The truncation of Lennard-Jones potentials is widely used in computer simulations[12,13] and significantly reduces the number of pairs contributing to the total potential and hence the computer time. The shifts[14] $u_{LJ}(r_c)$ and $v_{LJ}(r_c)$ ensure the continuity of u and v, respectively. If the unshifted, truncated potentials were used, conservation of energy would require that a particle crossing into or out of a sphere of radius r_c drawn about any other particle in the system would experience an impulse (instantaneous change in momentum). In molecular dynamics the forces are truncated at r_c. The potentials corresponding to these truncated forces are the truncated and shifted potentials, u and v.

Ryckaert and Bellemans[10,11] have reported a semi-empirical intramolecular potential, $V_b(\phi)$, which is a slight revision of an earlier one proposed by Scott and Scherage,[15]

$$\begin{aligned} V_b(\phi) = [&2.216 + 2.904\cos\phi - 3.134\cos^2\phi \\ &- 0.731\cos^3\phi + 6.268\cos^4\phi \\ &- 7.523\cos^5\phi]\ \text{kcal/mole}, \end{aligned} \tag{5}$$

which has minima $V_b(0) = 0$ (*trans* conformer) and $V_b(\pm 2\pi/3) = 0.70$ kcal/mole (*gauche* conformer) and maxima $V_b(\pm\pi/3) = 2.95$ kcal/mole and $V_b(\pm\pi) = 10.7$ kcal/mole (*cis* conformer). A plot of $V_b(\phi)$ is shown in Fig. 1.

The normalized configurational distribution corresponding to this potential is

$$s^{(0)}(\phi) = \exp[-\beta V_b(\phi)] \Big/ \int_{-\pi}^{\pi} d\phi' \exp[-\beta V_b(\phi')], \tag{6}$$

where β^{-1} is Boltzmann's constant times the tempera-

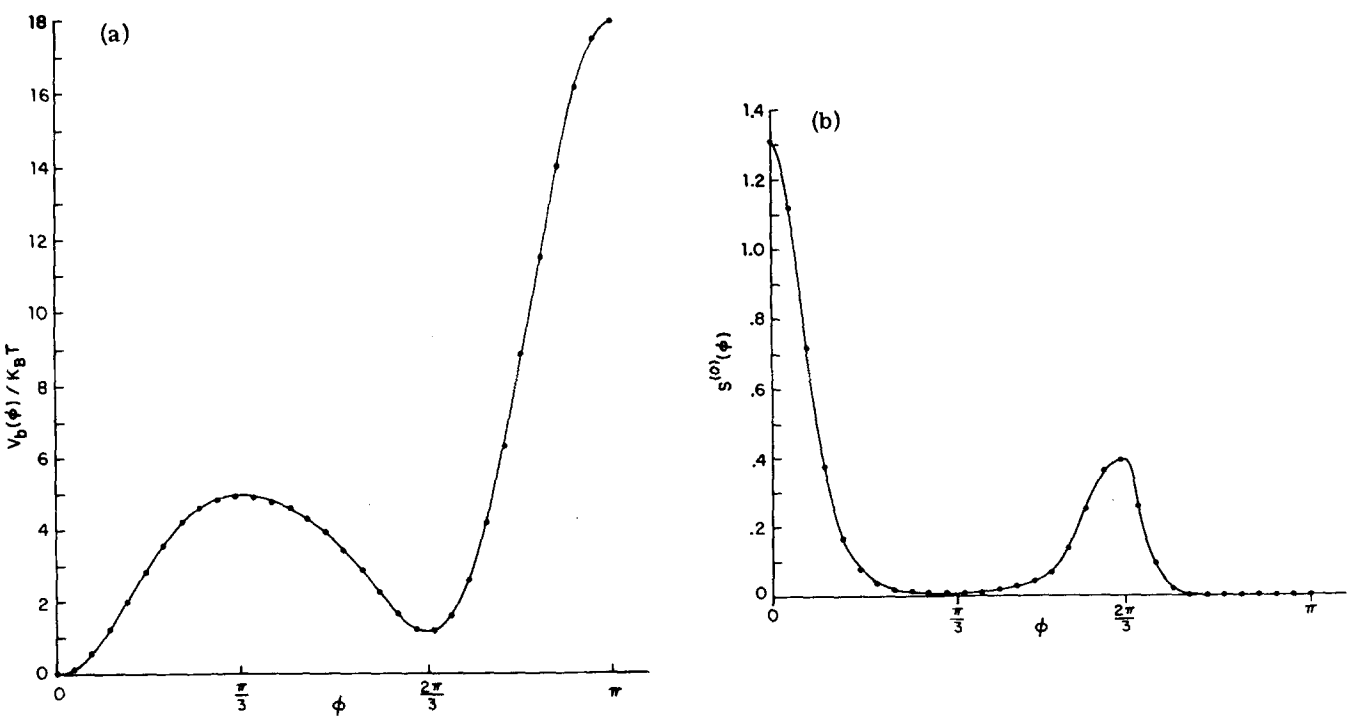

FIG. 1. (a) Intramolecular potential $V_b(\phi)/k_BT$ for n-butane at 300 °K and (b) the corresponding distribution function $s^{(0)}(\phi)$ of for the dihedral angle ϕ. Only nonnegative ϕ are shown since $V_b(\phi)$ and $s^{(0)}(\phi)$ are symmetric about $\phi = 0$.

ture, k_BT. This distribution is correct for an ideal gas of *n*-butane molecules. It is plotted in Fig. 1. The fractions of molecules in the *trans* and *gauche* states are defined, respectively, by

$$x_t^{(0)} \equiv \int_{-\pi/3}^{\pi/3} d\phi s^{(0)}(\phi); \quad x_g^{(0)} = 1 - x_t^{(0)}. \tag{7}$$

The equilibrium constant $K = x_g/x_t$ for the *trans–gauche* isomerization reaction in an ideal gas at $T = 300\,^\circ\mathrm{K}$ is

$$K^{(0)} = (x_g^{(0)}/x_t^{(0)}) = 0.54. \tag{8}$$

In solution, the solvent–solute forces can alter the distribution $s(\phi)$ from its gas phase value. Indeed, Pratt *et al.*[3] have predicted that the liquid environment will increase the percentage of *gauche* species from that found in the gas. To study the solvent induced shifts in $s(\phi)$ one may consider performing an MD simulation in which the total potential is

$$V = \sum_{i>j=5}^{126} u(r_{ij}) + \sum_{i=5}^{126} \sum_{j=1}^{4} v(r_{ij}) + V_b(\phi), \tag{9}$$

where the first sum represents the solvent–solvent interactions, the second sum represents the solvent–solute interactions, and $V_b(\phi)$ is the intramolecular potential.

A computer simulation based on the potential given in Eq. (9) does not seem practical. The problem is associated with the intramolecular barriers which separate the *gauche* states from the *trans* state. The barriers are sufficiently high compared to k_BT that relatively few *trans–gauche* transitions would occur during the length of time of a standard computer simulation run. Hence, insufficient time would have elapsed to establish *trans–gauche* equilibrium. Due to the difficulties described above, previous computer simulations[6,10,11] have not led to informative statements concerning the solvent effects on the *trans–gauche* equilibrium in *n*-butane.

Fortunately, a rigorous statistical mechanical result suggests a method be which the problem can be avoided. In particular, note that

$$s(\phi) = \langle \delta(\phi_1 - \phi) \rangle, \tag{10}$$

where ϕ_1 denotes the dihedral angle for a tagged *n*-butane molecule, and the pointed brackets indicate the equilibrium ensemble average. If this average is performed in the canonical ensemble, it is easy to see that

$$s(\phi) = cy(\phi) \exp[-\beta V_b(\phi)], \tag{11}$$

where c is a normalization constant, and

$$y(\phi) = \langle \delta(\phi_1 - \phi) \rangle'. \tag{12}$$

Here, the primed average is over an ensemble in which the single tagged *n*-butane molecule has been switched to a hypothetical species for which $V_b(\phi) = 0$.

In our simulation, the intramolecular potential, $V_b(\phi)$, for the single *n*-butane molecule was omitted. As a result, averages evaluated with the simulation correspond to those of the primed ensemble. The problem of poor statistics due to infrequent *trans–gauche* transition is alleviated to a large extent since the intramolecular potential barrier has been removed. The distribution function of dihedral angles obtained from the simulation is, according to Eq. (12), the function $y(\phi)$. The full distribution function, $s(\phi)$, is determined from $y(\phi)$ by applying Eq. (11). Along with providing a means of obtaining good statistics for the *trans–gauche* equilibrium, our simulation procedure also provides enough sampling of intermediate states that it is possible to determine the solvent effects on the barrier to internal rotations. This additional information is useful when considering the solvent shifts on rates of isomerization (which is the subject of a future paper).

The initial conditions for the MD simulation were chosen in the following manner. The solvent particles were placed in a $5\times5\times5$ simple cubic lattice in a cubic box with periodic boundaries. Three solvent particles near the center of the box were removed and the four methyl particles of the butane molecule were placed in the vacated space. The volume of the box was chosen so that the dimensionless solvent density has the value $\rho\sigma_1^3 = 0.9375$. With this choice, the total number of molecules in our system (123) per unit volume is identical to that in liquid CCl_4 at atmospheric pressure and room temperature, namely 6.303×10^{-3} Å^{-3}. Solvent molecular velocities were sampled from a Maxwell–Boltzmann distribution corresponding to 300 °K. The butane molecule was initially assigned no kinetic energy.

The equations of motion of the solvent particles were integrated using the Verlet algorithm[13] and those of the methyl particles were integrated by a combination of the Verlet algorithm and the SHAKE method[8] of constraint dynamics. A time step of 0.005τ, where $\tau = (m\sigma_1^2/48\epsilon_1)^{1/2}$ was used in the integration. The velocities of all particles in the system were rescaled at 2000 time step intervals until a stable temperature near 300 °K was reached. The system was allowed to relax for an additional 4000 time steps to ensure equilibrium was reached. The trajectory of the equilibrated system was followed for 90 000 time steps (450τ); energy conservation was better than 0.05%. At each time step the value of the dihedral angle of the butane molecule was computed and a histogram over 128 equal subintervals of the full range $-\pi$ to π was accumulated. To improve the statistics of the histogram for $y(\phi)$, the calculation was extended to 2050τ using a step size of 0.01τ; energy conservation was still better than 0.1%. The equilibrium portion of the trajectory required roughly 8.5 h of CPU time on an IBM 360/91 computer.

In addition to the MD experiment described above, two Monte Carlo (MC) experiments on the model system were performed for the purposes of determining the solvent structure near the solute. In one, the butane molecule was held fixed in the *trans* configuration while the solvent configurations were sampled via a force-bias scheme.[16,17] The system was allowed to equilibrate for 4000 passes then equilibrium sampling was continued for 24 000 passes. A similar MC experiment was performed with the butane molecule held fixed in the *gauche* configuration. The equilibrium portion of the sampling in the two MC experiments required roughly 5.5 h of CPU time.

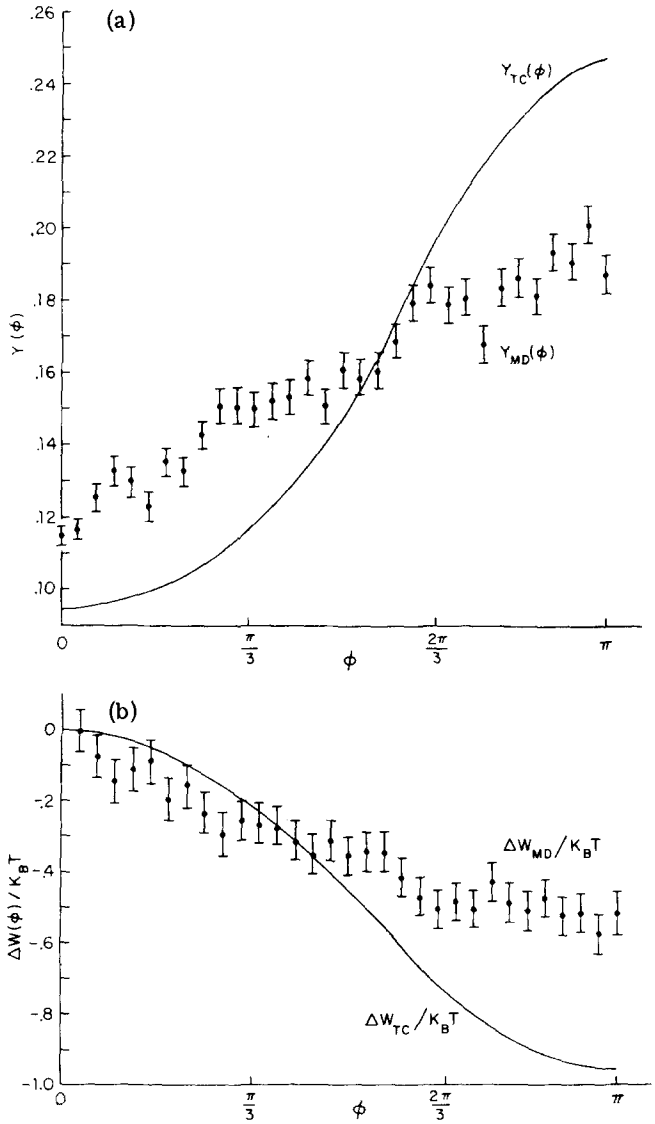

FIG. 2. (a) Cavity distribution function $y(\phi)$ and (b) potential of mean torsion, $\Delta W(\phi)/k_BT$ from the molecular dynamics simulation (data points) and the two-cavity approximation (solid curves). The error bars are ± one standard deviation.

III. RESULTS

In Fig. 2 the distribution function $y(\phi)$ (which is an even function) is plotted for $0 \leq \phi \leq \pi$. The 128 bin histogram accumulated in our MD simulation was condensed to 64 bins by doubling the bin width, then further condensed to 32 bins using the symmetry of $y(\phi)$. The result is shown in Fig. 2 with the statistical (± one standard deviation) error bars shown for each point. The solid curve, $y_{TC}(\phi)$ is calculated from the two-cavity approximation for $y(\phi)$ proposed by Pratt *et al.*[3] Both distributions shown in Fig. 2 have been normalized so that

$$2\int_0^\pi y(\phi)d\phi = 1. \tag{13}$$

The approximate two-cavity prediction is in qualitative agreement with the computer simulation result. However, the comparison shown in Fig. 2 indicates that the two-cavity approximation overestimates the solvent effect on $s(\phi)$.

The potential of mean torsion, defined by

$$W(\phi) = V_b(\phi) + \Delta W(\phi), \tag{14}$$

where

$$\Delta W(\phi) = -k_BT \ln[y(\phi)/y(0)] \tag{15}$$

is the Helmholtz free energy change of the solvent (or equivalently, the reversible work performed) when the butane molecule is rotated from a dihedral angle of 0 to ϕ. Our MD simulation is therefore an example of computer calorimetry.[18] The absence of an internal potential for butane in our model system and the relatively slow variation of $\Delta W(\phi)$ (see Fig. 2) with respect to ϕ assures that the butane molecule would not become locked in some preferred conformer and that all dihedral angles would be efficiently sampled.

The MD result for $\Delta W(\phi)$ graphed in Fig. 2 shows that the solvent effect on the conformational free energy lowers the *gauche* state energy relative to the *trans* by roughly $\frac{1}{2}k_BT$. The approximate two-cavity model[3] predicts a somewhat larger shift of about $\frac{3}{4}k_BT$. The solvent effect on the conformational statistics is assessed by computing equilibrium constants. By combining the MD result for $y(\phi)$ with Eq. (10) and integrating the resulting $s(\phi)$ to obtain populations we find $K = 0.80$. The two-cavity model gives $K_{TC} = 1.0$ which is in qualitative agreement with the MD result in the sense that both predict a solvent shift in the same direction from the ideal gas result which is $K^{(0)} = 0.54$. However, as with the other properties described above, it is seen that the two-cavity theory overestimates the size of the solvent shift.

It is of considerable interest to determine how the structure of the solvent changes in response to the change in the conformation of the molecule. Two Monte Carlo experiments were carried out. In one simulation, the n-butane molecule was held fixed in the *trans* configuration while the solvent configurations were sampled via a force-bias scheme. In the other simulation, the n-butane molecule was held fixed in a *gauche* configuration. The pair correlation function $g^{(E)}(r|\phi)$ and $g^{(I)}(r|\phi)$ were determined for $\phi = 0$ (*trans*) and $\phi = 2\pi/3$ (*gauche*). Here E and I refer, respectively, to end and interior methyl groups; and $g^{(E)}(r|\phi)$ and $g^{(I)}(r|\phi)$ are the pair correlation functions describing the distribution of solvent particles around the end and interior methyl particles, respectively, for a butane molecule with a fixed dihedral angle ϕ. These functions are plotted in Fig. 3.

It should be noted that the first peak of $g^{(E)}(r|trans)$ is smaller than that of $g^{(E)}(r|gauche)$ indicating that in the *gauche* configuration, the end methyl groups are less shielded from solvent particles than in the *trans* configuration. It should also be noted that the first peak in $g^{(I)}(r|gauche)$ is higher than that in $g^{(I)}(r|trans)$ indicating that the interior sites are more exposed to the solvent in the *gauche* configuration than in the *trans* configuration.

IV. CONCLUSIONS

The MD simulation described in this article demonstrates the feasibility of studying conformational equi-

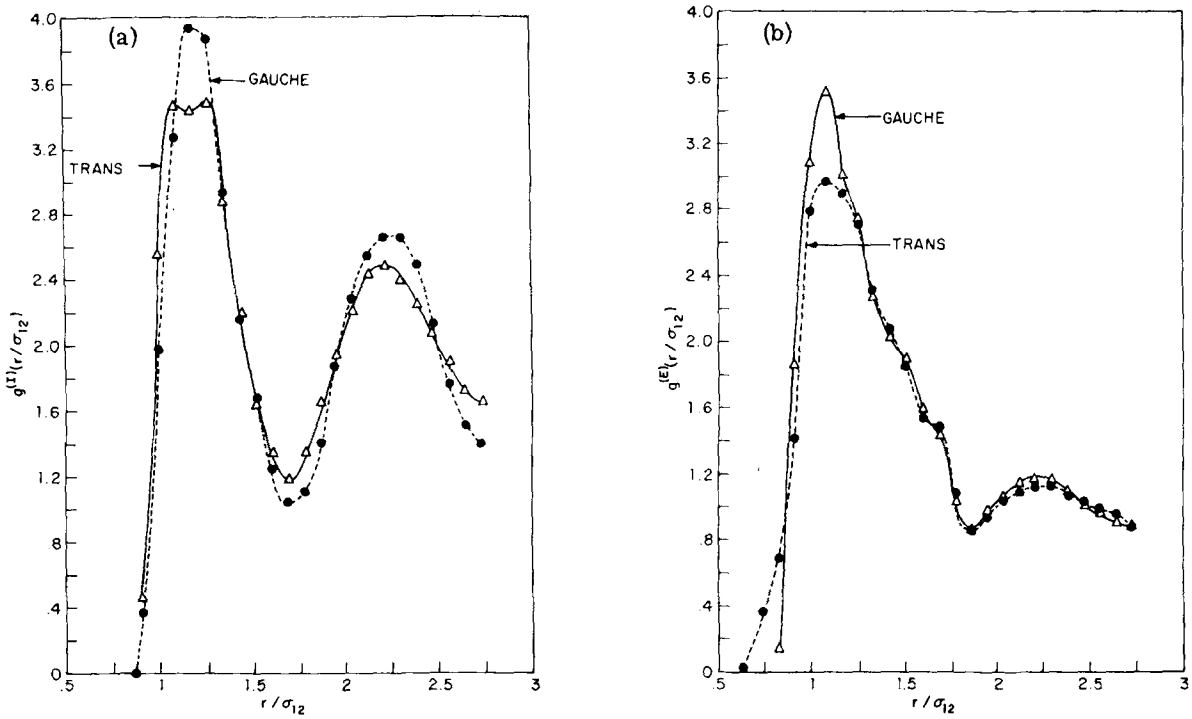

FIG. 3. (a) Pair correlation function $g^{(I)}(r|trans)$ (shown by solid line and triangles) which gives the radial distribution of solvent particles about interior methyl particles when the butane molecule is held fixed in the *trans* configuration. The other curve (dashed line and circles) is the corresponding distribution $g^{(I)}(r|gauche)$ for a butane molecule in the *gauche* configuragion. (b) Radial distribution function $g^{(E)}(r|trans)$ (shown by solid line and triangles) of solvent particles about end methyl particles of *trans* n-butane and the corresponding function $g^{(E)}(r|gauche)$ (dashed line and circles) for *gauche* n-butane.

libria of small chain molecules in liquids. Our results show that the conformational structure of the nonpolar n-butane molecule is significantly affected by the simplest of solvents: the Lennard-Jones fluid. This finding is in qualitative accord with the predictions of Pratt and Chandler.[1,3] It is in marked disagreement with more common ideas concerning chain molecules dissolved in liquids. Indeed, Flory[19] expresses the view that because "disorder prevails" in the liquid state "The *average* potential (describing the free energetics for changing the dihedral angle of an n-butane molecule in a liquid) should therefore correspond closely to its unperturbed form, and the system of molecules may be pictured as populating the configuration space, i.e., the space$\cdots$of the molecule, according to a Boltzmann distribution over the intramolecular energy, intermolecular effects being ignored." The computer simulation results reported here show that this picture is wrong. The reason is that neighboring molecules in a liquid are strongly correlated to one another. The local structure, i.e., correlations, of a liquid can often accommodate one solute species more easily than another. In the present case, the spherical Lennard-Jones solvent particles used to mimic CCl_4 molecules seem to be able to build a liquid structure more easily when they are near a *gauche* n-butane molecule than when they are near a *trans* molecule. Undoubtedly, this is due in part to the fact that the *gauche* conformer is closer to being spherical than the *trans* conformer.

It is probably not correct to explain the solvent shift we have found by a simple free volume argument which says that the species excluding the smallest volume from the solvent is the species favored by the solvent. Indeed, our results indicate that there seems to be no appreciable difference between excluded volumes of the *trans* and *gauche* conformers of n-butane. We draw this conclusion from our calculations of $g^{(E)}(r|\phi)$ and $g^{(I)}(r|\phi)$. Notice that the changes in $g^{(E)}(r|\phi)$ in going from *trans* to *gauche* are nearly identical in size but opposite in sign to those in $g^{(I)}(r|\phi)$. This behavior implies that the total number of solvent particles in the first coordination shell surrounding the n-butane molecule does not change when the molecule changes conformational state. Thus, while the shape of the n-butane solute changes when passing from *trans* to *gauche*, the excluded volume it produces does not.

The traditional ideas[20] on solvent shifts of conformational equilibria in nonassociated solvents have focussed attention on the free energetics of altering charge distributions in a dielectric media. Of course, n-butane has no significantly polar groups. Further, our model for it contains no charge distribution, and our solvent (nonpolarizable Lennard-Jones particles) has the vacuum dielectric constant, $\epsilon = 1$. Thus, the point of view which attributes solvent shifts to dielectric effects can say nothing about the phenomena we have investigated in this article. But, as the entries in Table I suggest, our calculations do have direct bearing on the traditional approach. Consider the first two rows. The molecules considered have similar shapes. Thus, packing effects should be nearly the same. But 1,2-dibromoethane goes from a nonpolar to a polar species as the molecule changes from *trans* to *gauche* states. If electrostatics were important, $K/K^{(0)}$ should be larger for 1,2-dibro-

TABLE I. The *trans–gauche* equilibrium constant, $K = x_g/x_t$, for disubstituted ethanes in solution relative to the gas phase value, $K^{(0)}$. All values are for room temperature and 1 atm pressure.

Molecule	Solvent	Solvent ϵ	$K/K^{(0)}$
$CH_3–CH_2CH_2–CH_3$	Simulated CCl_4	1[a]	1.5[a]
$Br–CH_2CH_2–Br$	CCl_4	2.2	1.6[b]
$Br–CH_2CH_2–Br$	C_6H_6	2.3	4.9[b]

[a]From computer simulation reported herein. CCl_4 solvent is modeled as a nonpolarizable Lennard-Jones fluid. Hence, in the simulation $\epsilon = 1$.
[b]From data compiled by Abraham and Bretschneider (Ref. 21).

moethane in CCl_4 than for our simulation of *n*-butane in CCl_4 since a dielectric solvent is supposed to stabilize the polar species relative to the gas phase. But in fact $K/K^{(0)}$ is the same for both systems. The third row is presented to show that large solvent shifts can be found even when the dielectric constant is not large. Presumably that large shift must have something to do with specific interactions between the bromine groups and benzene. However, independent of what precisely is happening in that system, it is clear that the effects cannot be correctly attributed to dielectric phenomena. Indeed, the entries of the first two rows in Table I imply that electrostatics has noting to do with the solvent shift for 1,2-dibromoethane in CCl_4.

While the earlier approximate predictions of Pratt *et al.*[3] agree in a qualitative sense with the simulation results, it is clear that the two-cavity model for $y(\phi)$ is not accurate enough to be quantitatively reliable. A more accurate theory will undoubtedly have to grapple with the fact that $y(\phi)$ is actually a four-point cavity distribution function.[1,3] The two-cavity model tries to avoid the difficulties associated with multipoint correlation functions by approximating the four-cavity *n*-butane molecule by two cavities. This approximation reduces $y(\phi)$ to a two-point correlation function. Unfortunately, the approximation incurs noticeable errors such as overestimating the *trans-gauche* equilibrium constant by 20%. We believe that one incidental benefit of this article is that the results reported provide a benchmark with which theories for multipoint correlation functions can be tested.

Pratt *et al.*[3] make an additional approximation that is worth checking. They assume that the solvent contribution to the conformational structure of *n*-butane is primarily an entropic effect due to the packing of neighboring solvent molecules, represented by hard spheres, around the *n*-butane solute. As a result, attractive solute–solvent interactions are ignored. This idea could be tested by performing a simulation like the one described herein but with the attractive branches of the Lennard-Jones potentials removed.[21] We have not done this. But our results for $g^{(I)}(r|\phi)$ and $g^{(E)}(r|\phi)$ suggest that the approach taken by Pratt *et al.* may be correct. Recall that when changing ϕ, an increase in $g^{(E)}(r|\phi)$ is accompanied by a decrease of the same size in $g^{(I)}(r|\phi)$, and vice versa. This behavior implies that while the number of solvent molecules at a certain distance from a particular CH_n group does depend on the conformational structure, the total number does not. As a result, the average solvent–solute potential energy will be insensitive to the conformational structure of the *n*-butane solute. Presumably, the same insensitivity also holds for the solvent–solvent potential energy. Unfortunately, it is difficult to acquire the statistics needed for a quantitative verification of these ideas. One would need information about the potential energy change produced by altering only one of the 123 molecules.

Obviously, there are many directions in which this research can be extended. Our most important finding is that by focusing attention on $y(\phi)$, simulation studies of conformational equilibria in liquids are practical even though conformational transitions in a real system are infrequent.

[1]D. Chandler and L. R. Pratt, J. Chem. Phys. **65**, 2925 (1976).
[2]L. R. Pratt and D. Chandler, J. Chem. Phys. **66**, 147 (1977).
[3]L. R. Pratt, C. S. Hsu, and D. Chandler, J. Chem. Phys. **68**, 4202 (1978).
[4]C. S. Hsu, L. R. Pratt, and D. Chandler, J. Chem. Phys. **68**, 4213 (1978).
[5]D. Chandler, J. Chem. Phys. **68**, 2959 (1978).
[6]T. A. Weber, J. Chem. Phys. **69**, 2347 (1978).
[7]P. T. Rossky and M. Karplus, Solvation: A Molecular Dynamics Study of a Dipeptide in Water, preprint (1978).
[8]J. Ryckaert, G. Ciccoti, and H. J. C. Berendsen, J. Comput. Phys. **23**, 327 (1977).
[9]W. F. van Gunsteren and H. J. C. Berendsen, Mol. Phys. **34**, 1311 (1977).
[10]J. P. Ryckaert and A. Bellemans, Chem. Phys. Lett. **30**, 23 (1975).
[11]J. P. Ryckaert and A. Bellemans, Faraday Discuss. Chem. Soc. (to be published).
[12]A. Rahman, Phys. Rev. A **136**, 405 (1964).
[13]L. Verlet, Phys. Rev. A **159**, 98 (1967).
[14]M. Rao and D. Levesque, J. Chem. Phys. **65**, 3233 (1976).
[15]R. A. Scott and H. A. Scheraga, J. Chem. Phys. **44**, 3054 (1966).
[16]C. Pangali, M. Rao, and B. J. Berne, Chem. Phys. Lett. **55**, 413 (1978).
[17]M. Rao, C. Pangali, and B. J. Berne, preprint (1978).
[18]C. H. Bennett, J. Comput. Phys. **22**, 245 (1976).
[19]P. J. Flory, *Statistical Mechanics of Chain Molecules* (Wiley, New York, 1969).
[20]R. J. Abraham and E. Bretschneider, in *Internal Rotation in Molecules*, edited by W. J. Orville–Thomas (Wiley, New York, 1974).
[21]J. D. Weeks, D. Chandler, and H. C. Andersen, J. Chem. Phys. **54**, 5237 (1971).