ISOMERIZATION DYNAMICS IN LIQUIDS BY MOLECULAR DYNAMICS*

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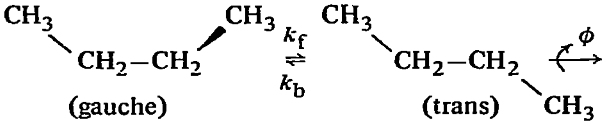
Two molecular dynamics studies are made of isomerization dynamics of *n*-butane dissolved in liquid CCl_4 and in a rigid matrix Rate constants for the gauche ⇌ trans isomerization, determined from the long-time behavior of reactive flux, differ considerably from transition state theory Reactive fluxes (and rates) for the liquid and rigid matrix agree, eliminating viscous continuum models

1. Introduction

Reaction dynamics in liquids involve fundamentally different processes than in gases. Because molecules undergoing a chemical transformation are in continuous interaction with neighboring solvent molecules, the motions of the reactant, product and solvent molecules are highly correlated, and "cage" or "packing effects" may be very important. Although much talked about, these cage effects are not understood at the microscopic level.

To better understand reaction dynamics in liquids we have chosen to study, by computer experiment, the simple isomerization reaction



in which *n*-butane undergoes a gauche–trans isomerization. The stage for this work is set by our previous molecular dynamics and Monte Carlo studies of *n*-butane in liquid CCl_4 [1]. The basic thrust of that study was to show how solvent packing shifts the position of equilibrium towards the gauche state. An important aspect of that work was the determination of the reversible work required to change the molecular conformation from the trans state ($\phi = 0$) to a conformation with a given dihedral angle ϕ This work, $W(\phi)$, is the free energy change for the process, and is called the "potential of mean torsion" It contains the energy and entropy changes that accompany the conformation change – changes that come in part from the reorganization of the solvent around the molecule. Having a quantitative determination of $W(\phi)$ enables us to determine the transition state theory rate constant for the reaction and to compare this with the exact result coming from the full molecular dynamics simulation described here.

Liquid state reactions are often treated by stochastic theories In isomerization reactions the problem is to describe how a reaction coordinate moves over energy barriers separating the stable conformational states of the molecule. In a liquid it is usually assumed that interactions with the solvent molecules are so frequent and so strong that the reaction coordinate executes a small step random walk (diffusion process) over the barrier. The resulting rate constants depend on the barrier heights as well as on the curvature of

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the intramolecular potential, and hydrodynamic parameters such as the viscosity. One of the simplifying features of this approach is that *inertial effects* (i.e., effects associated with the free intramolecular motion between strong solvent interactions) are ignored. This approach is in marked contrast to transition state theory according to which the rate constants are proportional to the equilibrium population of the molecules at the barrier heights and are independent of dynamical parameters such as the viscosity.

The molecular dynamics study represented here allows us to test these ideas. We compare the reaction dynamics of *n*-butane dissolved in a simple liquid chosen to model carbon tetrachloride, and in a rigid but random environment. The difference between the two simulations is that in the fluid the solvent molecules are free to move whereas in the rigid environment they are "frozen". The particles and the initial configurations for the liquid and rigid are identical. We find that the reactive fluxes for these two systems are very similar and in fact cannot be distinguished from each other to within the error bars. Thus the rate constants cannot depend on the "solvent viscosity", because in the fluid, η is finite, whereas in the rigid environment it is indeterminate. Had we not performed the comparitive simulation with the rigid environment, and had we only made comparisons on the basis of rate constants, we could have convinced ourselves that the Kramer's small step diffusion model with the viscosity of simulated CCl_4 was valid.

2. Molecular modeling and methodology

In this study, the system contains 122 CCl_4 molecules – each represented by a single Lennard-Jones sphere and contains one butane molecule represented by a chain of four interconnected Lennard-Jones spheres (representing methyl groups). The potential model is given schematically in fig. 1. The masses adopted and the parameterization of the intermolecular potentials are described in ref. [1].

The *n*-butane molecule is perhaps the simplest nonpolar molecule which undergoes a trans–gauche isomerization. If we label the *n*-butane molecule sequentially, the reaction coordinate for this transformation is the dihedral angle, ϕ, between the plane containing carbons 1, 2, 3 and the plane containing carbons 2, 3, 4.

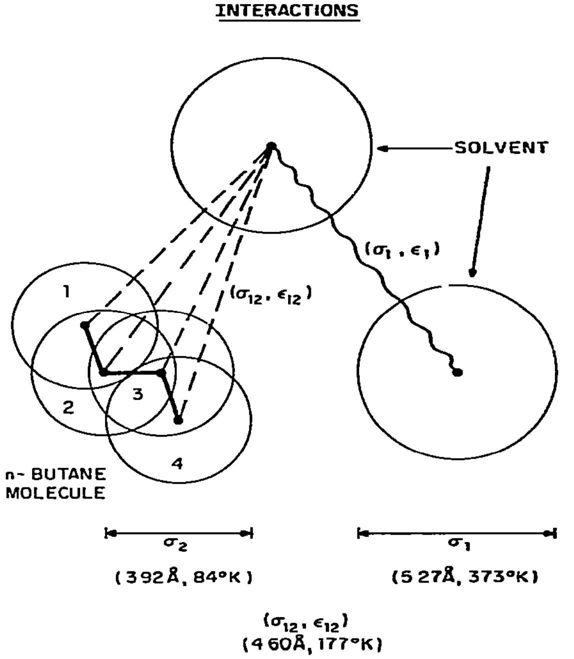

Fig. 1. Potential model for *n*-butane in CCl_4. The Lennard-Jones spheres are drawn to scale. The interaction between the (CH_n) sites on the butane and the CCl_4 spheres are given by a L.J. 12–6 potential with $\sigma_{12} = 4.60$ Å and $\epsilon_{12} = 177$ K.

The potential energy for the isolated molecule is taken to be

$$V = V_b(\phi) + \tfrac{1}{2} K_b \sum_{i=1}^{3} (b_{i+1,i} - b_0)^2 + \tfrac{1}{2} K_\theta \sum_{i=1}^{3} (\cos\theta_{i+1,i} - \cos\theta_0)^2 \qquad (1)$$

The first term, $V_b(\phi)$, corresponds to the potential of the reactive degree of freedom. This is taken to be the potential fitted to experiments by Scott and Scheraga [2] and, more recently, by Ryckaert and Bellemans [3], and given by eq. (5) in ref. [1]. For our purpose a plot of $V_b(\phi)$ is shown in fig. 2. The second and third terms in eq. (1) specify a harmonic model for the stretching of the C–C bonds and the bending of the C–C–C bond angles. The harmonic force constants are taken to be $K_b = 3.5 \times 10^7$ J/nm^{2}mole, $K_\theta = 1.8 \times 10^5$ J/mole and the equilibrium bond lengths and bond angles are $b_0 = 1.53$ Å and $\theta_0 = 109°28'$ respectively. These are the values used by Helfand and

Weber in their stochastic molecular dynamics studies of n-alkanes [4,5].

Molecular dynamics simulations involve the brute force solution of the classical equations of motion of solute plus solvent subject to the whole system being in some initial microscopic state. Were we to start with n-butane in either the gauche or trans state, it would librate in these states before gaining enough energy from the solvent to surmount the energy barrier that separates the gauche and trans states (cf. fig. 2). Thus much time would be wasted on non-reactive dynamics. The strategy adopted here is to start with a set of "transition state configurations" of molecule plus solvent and to follow the trajectories for each of these starting points. We then calculate the reactive flux.

$$k(t) = 2\langle\dot{\phi}(0)\delta(\phi(0) + \tfrac{1}{3}\pi)H_T(\phi(t))\rangle\,. \tag{2}$$

Here $\phi(0)$, $\phi(t)$ and $\dot{\phi}(0)$ respectively denote the dihedral angle at the initial time 0 and at a time t later and $\dot{\phi}(0)$ is the initial dihedral velocity. $H_T(\phi(t))$ is so defined that

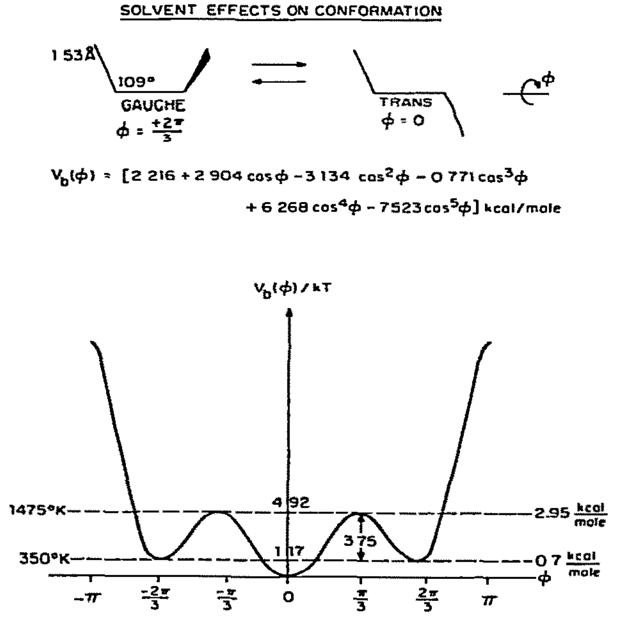

Fig 2. The intramolecular potential of n-butane is given by the Scott–Scherega potential pictured above in units of kT at room temperature The reactive degree of freedom is the dihedral angle ϕ.

$$H_T(t) = 1, \quad -\tfrac{1}{3}\pi \leqslant \phi(t) \leqslant \tfrac{1}{3}\pi\,;$$
$$= 0, \quad \text{otherwise}. \tag{3}$$

Only those trajectories contribute to eq. (2) for which the butane is initially at the transition state $\phi_T = -\frac{1}{3}\pi$ (because of the delta function) and which at time t are to be found in the trans well. This reactive flux has several interesting properties [6,7].

$$\lim_{t\to 0+} k(t) = k_{TST}\,, \tag{4}$$

where k_{TST} is the reactive flux in the transition state theory approximation and the forward (gauche to trans) rate constant in that approximation is $x_g^{-1} k_{TST}$, where x_g is the mole fraction of the gauche conformer.

The plateau value of $k(t)$, should it exist, gives the forward rate constant,

$$k_f = x_g^{-1} k_{plat}\,. \tag{5}$$

Thus $k(t)/k_{TST}$ measures the fractional error in transition state theory. Its plateau value is the transmission coefficient. From (2) and (4) the transition state rate constant is found to be

$$k_{TST} = \langle|\dot{\phi}|\rangle' S(-\tfrac{1}{3}\pi)\,, \tag{6}$$

where $S(\phi)$ is the probability distribution of finding the conformation ϕ (in this case $\phi = -\frac{1}{3}\pi$), and the primed brackets, $\langle\ \rangle'$, indicate the equilibrium average with ϕ constrained to the transition state. As mentioned earlier we have already determined $S(\phi)$ in a previous paper [1], and can thus determine k_{TST}.

The initial conditions for the MD simulation were chosen in the following manner. The solvent particles were placed on a 5 × 5 × 5 simple cubic lattice in a cubic box with periodic boundaries. The volume of the box was chosen so that the dimensionless solvent density is $\rho\sigma_1^3 = 0.9375$, which is appropriate for the liquid at 1 atm pressure and room temperature. 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 in such a way that the dihedral angle of n-butane is $\phi_T = -\frac{1}{3}\pi$, and the bond lengths and bond angles were given their equilibrium values. A force-bias Monte Carlo simulation was then carried out on the system with the constraint that the dihedral angle remained fixed at its transition state value $\phi_T = -\frac{1}{3}\pi$. All other degrees of freedom are allowed to change.

Starting with the lattice configuration with the butane at the center, the system was equilibrated for 1000 passes at a temperature of $T = 300$ K. The Monte Carlo run was then continued for 3200 passes. The configuration after every 100 passes was saved. Since the mean squared displacements rapidly became linear, the run was continued for 680 more passes and every tenth configuration was saved. Thus in all, 100 "independent" *transition state configurations* were generated

The solvent particle momenta were sampled from the Maxwell distribution function with $T = 300$ K. The momenta of the methyl groups on n-butane were importance sampled as follows. Because the dihedral velocity, $\dot{\phi}(0)$ can be expressed in terms of the cartesian velocities $\{\dot{X}_n(0)\}$ of the four methyl groups as $\dot{\phi}(0) = \Sigma_{i=1}^{12} a_i(\{\dot{X}_n(0)\})X_i(0)$, the reactive flux can be expressed as

$$k(t) = [S(\phi_T)/(2\pi\beta M)^{1/2}]$$
$$\times \sum_{i=1}^{12} \int \mathrm{d}\mathbf{\Gamma}[(P_i^{(+)}(\mathbf{\Gamma}) - P_i^{(-)}(\mathbf{\Gamma})] a_i(\{X_n\}) H_T(\phi) ,$$

where

$$P_i^{(\pm)}(\mathbf{\Gamma}) = \frac{\dot{X}_i \theta(\pm \dot{X}_i) \delta(\phi - \phi_T) \exp(-\beta H)}{\int \mathrm{d}\mathbf{\Gamma} \dot{X}_i \theta(\pm \dot{X}_i) \delta(\phi - \phi_T) \exp(-\beta H)} .$$

Here $\theta(X)$ is the unit step function and $\mathbf{\Gamma}$ denotes a point in phase space. The $k(t)$ involves 24 integrals. For each integral one must sample the phase points from a given $P_i^{(\pm)}(\mathbf{\Gamma})$. From the definition of $P_i^{(\pm)}(\mathbf{\Gamma})$, it is clear that the configurations should be sampled from $\delta(\phi - \phi_T)\exp(-\beta V)$. This is done by the force-bias Monte Carlo scheme. It is also clear that the cartesian velocities are to be sampled from $\dot{X}_i \theta(\pm \dot{X}_i) \times \exp(-\beta T)$. Each of the 24 integrals are evaluated by sampling (100 independent configurations) × (3 velocity samplings per configuration) for a total of $3 \times 100 \times 24 = 7200$ trajectories.

Each "transition state configuration" and each sampling of the momenta defines an initial microscopic state. The equations of motion of the total system (n-butane molecule plus 122 CCl_4 molecules) were integrated using the Verlet algorithm. The time step of the integration is 0.007 τ, where $\tau = (m_1 \sigma_1^2/\epsilon_1)^{1/2}$. Here, m_1, σ_1, and ϵ_1 are the mass, diameter and well depth of the solvent molecules. Thus for each transition configuration, many trajectories of length $t = 0.7\tau$ were generated, each corresponding to a different momentum sampling. A total of 7200 trajectories were used to evaluate $k(t)$.

Having chosen the 100 initial configurations and the initial momentum, two sets of trajectories were generated, one for the full system in which solvent plus solute is allowed to move, and one in which the solvent is frozen in each initial configuration. Thus, two systems are simulated. a *fluid system*, and a *random rigid environment*.

3. Results and discussion

The ratio of $k(t)/k_{TST}$ is plotted in fig. 3. This quantity clearly decays on two time scales. There is a rapid initial decay followed by a long time decay, or plateau region. The existence of this region implies [6,7] that the linear rate law of chemical kinetic phenomenology describes the system at times long compared to the initial decay time; that is

$$\mathrm{d}\bar{N}_G(t)/\mathrm{d}t = k_f \bar{N}_g(t) - k_b \bar{N}_t(t) , \tag{7}$$

where $\bar{N}_g(t)$ and $\bar{N}_t(t)$ are the average numbers of gauche and trans molecules at time t and k_f and k_b are the rate constants. It is a simple matter to show that if unimolecular phenomenology is correct, then after a short time the normalized reactive flux $k(t)/k(0+)$ should behave as $\lambda e^{-t}/\tau_{rxn}$ where $\tau_{rxn}^{-1} = k_f + k_b$ is the kinetic relaxation time and $\lambda \equiv \tau_{rxn}^{-1}/(\tau_{rxn}^{TST})^{-1}$ where TST designates the transition state value of τ_{rxn}^{-1}. τ_{rxn}^{TST} can be computed using $(\tau_{rxn}^{TST})^{-1} = (x_g x_t)^{-1} k(0+)$ and evaluating $k(0+)$ from eq. (6).

The simulation results for $k(t)/k(0+)$ are fitted by the function

$$k(t)/k(0+) = (1 - \lambda)e^{-k_1 t} + \lambda e^{-k_2 t} , \tag{8}$$

where $\lambda \equiv k_2 \tau_{rxn}^{TST}$. Best fits were obtained by varying k_1 and k_2 while fixing τ_{rxn}^{TST} at a value that was calculated independent of any dynamics. This value of τ_{rxn}^{TST} requires the knowledge of the dihedral distribution function, $S(\phi)$, for flexible butane in our CCl_4-like solvent (cf. eq. (2)). $S(\phi)$, for rigid butane in the same solvent was calculated in ref. [1]. From this value of $S(\phi)$ one obtains the distribution for flexible butane using Fixman's theorem as discussed in ref. [8]. Values for $1/\tau_{rxn}^{TST}$ and best fit values for k_1 and $k_2 = 1/\tau_{rxn}$ are listed in table 1.

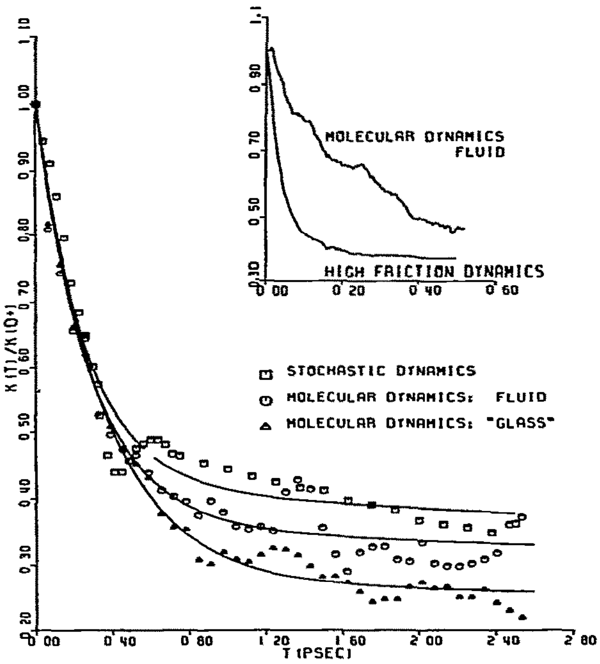

Fig. 3. The reactive flux divided by its initial value (the TST value) as a function of time. The data for the stochastic dynamics ($\alpha = 0.2 \times 10^{13}$ s^{-1}), the fluid and rigid matrix ("glass") systems are plotted along with their best fit of these curves to a sum of two exponentials (see text). The discontinuity in the graph for the fluid system at 1.3 ps is due to the difference in statistics, i.e., the first half is averaged over 7200 trajectories yielding error bars of ±0.04 (unitless), while the second half contains the extension of only the first 480 trajectories with error bars of ±0.1. For the "glass" plot, error bars are about ±0.04 for all points. The stochastic dynamic result is also discontinuous in its statistics, before 0.6 ps, 10000 trajectories are used, while after 0.6 ps only 2200 trajectories are used, yielding error bars of ±0.01 and ±0.025 respectively. In the inset the fluid graph is again shown but this time compared with the high friction dynamic results ($\zeta = 0.96 \times 10^{-9}$ g/s which was averaged over 10000 trajectories with error bars of ±0.01.

Table 1

	Rigid environment	Fluid
$1/\tau_{rxn}^{TST}$	2.0×10^{11} s^{-1}	2.0×10^{11} s^{-1}
$1/\tau_{rxn}$	0.54×10^{11} s^{-1}	0.70×10^{11} s^{-1}
k_1	5.8×10^{12} s^{-1}	7.1×10^{12} s^{-1}
$\lambda = \tau_{rxn}/(\tau_{rxn}^{TST})^{-1}$	0.276	0.361

The deviation of $\lambda \equiv \tau_{rxn}^{-1}/(\tau_{rxn}^{TST})^{-1}$ from unity shows that there are considerable deviations from transition state theory. This is entirely expected. More than 50% of the trajectories rapidly recross the transition state due to interactions with the solvent. In fact λ could be regarded as a "transmission coefficient" over the barrier.

It is of interest to compare molecular dynamics in the fluid to predictions of the high viscosity (small step diffusion) Kramers theory. To do this we assume that each of the four spheres (representing the CH_3 and CH_2 groups) experience a hydrodynamic drag specified by the same friction constant and we further assume that there is no hydrodynamic interaction between the spheres. This friction constant is related to the translational self-diffusion constant of the *n*-butane molecule by $\zeta = kT/4D$ (a result found from the free draining limit). A brownian dynamics simulation was carried out for *n*-butane in which the four spheres experience a fluctuating force which is consistent (through the second fluctuation dissipation theorem) with the friction constant used. The plateau value of the reactive flux, λ, was thus computed as a function of ζ and it was found that [9] for $\zeta > 3.5 \times 10^{-9}$ g/s,

$$\lambda = [(0.65 \pm 0.03) \times 10^{-9}\ \mathrm{g/s}]\,\zeta^{-1}\,. \tag{9}$$

This is the high friction non-inertial regime of the Fokker–Planck theory; that is, it is the Kramers small step diffusion theory of the reaction rate.

To estimate ζ we apply Stokes law with slip boundary conditions‡

$$\zeta = 2\pi\eta\sigma\,. \tag{10}$$

Here σ is the diameter of the spheres representing the CH_3 groups (3.92 Å for our model of *n*-butane) and η is the shear viscosity of the solvent. For the Lennard-Jones fluid at the temperature and density of our simulation [11], $\eta \approx 0.5$ cP. It should be noted that real liquid CCl_4 has a viscosity close to 1 cP. This higher value is due to the translation rotation coupling present in the molecular fluid but absent in the simple Lennard-Jones model of our simulation [12]. The Lennard-Jones value of η yields $\zeta = 1.2 \times 10^{-9}$ g/s, a value outside the asymptotic high friction limit

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‡ Recent work on molecular hydrodynamics shows that slip rather than stick boundary conditions apply to small molecules. See ref. [10].

given by eq. (9). If we use this estimate of ζ in eq (9) we find

$$(k_{\mathrm{plat}}/k_{\mathrm{TST}})_{\mathrm{Kramers}} \approx 0.5\,. \tag{11}$$

This result is close enough to the simulation result of 0.36 to suggest that the Kramers theory might be an adequate representation of the dynamics. In fact, if ζ is set equal to

$$\zeta = 0.96 \times 10^{-9}\ \mathrm{g/s}\,, \tag{12}$$

the Kramers small step diffusion model gives the reactive flux shown in the inset of fig. 3 (labelled high friction dynamics). For this value of ζ, it can be seen from this figure that the plateau values and thereby the rate constants are in agreement. Unfortunately it can also be seen that the reactive fluxes themselves are in complete disagreement We are thus forced to conclude that the small step diffusion model does not represent the observed isomerization dynamics. Further, it should noted from fig 3 that the reactive flux for the reaction in the rigid environment is the same as that for the fluid (to within experimental error). Here there is no solvent viscosity. The solvent is frozen and has no momentum transport. The similarity of the relaxation in fluid and the glass-like system shows that viscous continuum model for isomerization in our system is not valid.

In the rigid environment, the collisions of the methyl particles with the rigidly fixed solvent molecules enables momentum and energy to be transferred between various intramolecular modes and particularly from and to the reactive mode. No energy is transferred to or from the solvent. The solvent merely provides a crystal field coupling of the internal degrees of freedom The molecular motion in the short-ranged forces of the solvent cage gives rise to collisional pulses of couplings between the different internal degrees of freedom. In a one-dimensional model, the "reaction coordinate collision rate" will be an effective rate, that is, it will be dependent on the efficiency of the collision to cause energy transfer between the reactive modes and the other modes. It is of interest to see whether a simple collisional model can describe the dynamics in the fluid and in the rigid matrix. Recently, the effective dynamics model used by Montgomery et al. [6] has been extended to n-butane [9]. Each site on the n-butane molecule undergoes thermalizing collisions with a collision rate α. Fig. 3 shows that the reactive flux of this model can be fit to the molecular dynamics results if the collision rate is taken to be

$$\alpha = 0.2 \times 10^{13}\,\mathrm{s}^{-1}\,. \tag{13}$$

This collision rate is in accord with estimates of the gas kinetic rate, indicating the collisions with the individual sites are effective with respect to momentum and energy transfer to the reaction coordinate. Of course this collision model is overly simplified. It ignores correlation, in collisional events, the structure of the fluid, etc. Nevertheless, we regard this result as being of some interest.

It is important to note that our simulations involve a solvent with large mass and a solute of small mass $m_{\mathrm{CH_4}}/m_{\mathrm{CCl_4}} = 0.11$. Thus the solvent molecules move slowly compared to the solute. It is for this reason that rigid matrix simulation might be expected to be in rough agreement with the fluid simulation. In the case of less massive solvent molecules, the agreement might not be observed. Nevertheless, our simulation serves to point to the weakness of viscous continuum models or molecular hydrodynamic models for the reactive and energy transfer processes. It also hints at a possible theoretical approach to the computation of rate constants.

A word of caution is necessary at this juncture. In the random rigid environment, it is expected that in each solvent configuration there will be a well-defined reactive flux. At long times this flux will decay as $k_2(\{X\})\cdot e^{-k_2(\{X\})t}$, where $k_2(\{X\})$ is the kinetic rate constant $(1/\tau_{\mathrm{rxn}})$ for that particular configuration of solvent molecules. Thus the long time flux for the whole set of configurations should behave like $\langle k_2(\{X\})\, e^{-k_2(\{X\})t}\rangle$, where the average is taken over the configurational distribution function $p(\{X\})$ of the rigid environment. This can be developed in a cumulant expansion giving

$$k(t) \to \langle k_2\rangle \exp(-\Gamma t - \Lambda^2 t^2/2! + ..)\,, \tag{14}$$

where

$$\Gamma = \langle k_2^2\rangle/\langle k_2\rangle, \quad \Lambda^2 = \langle k_2^3\rangle/\langle k_2\rangle - (\langle k_2^2\rangle/\langle k_2\rangle)^2\,. \tag{15}$$

Clearly for the glass-like system, the reactive flux will be exponential at long times only if the distribution of relaxation rates is very narrow (sharp). In general, the flux will be non-exponential and the usual linear phenomenology should not be valid; that is, the usual rate constants cannot be defined. In the limit where the distribution is uniform, the reactive flux will decay as powers t^{-1}.

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