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Product Energy Deposition for CN + alkane H abstractions in Gas and Solution Phases

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Abstract

In this work, we report the first theoretical studies of post transition state dynamics for reaction of CN with polyatomic organic species. Using electronic structure theory, a newly developed analytic reactive PES, a recently implemented rare-event acceleration algorithm, and a normal mode projection scheme, we carried out and analyzed quasi-classical and classical non-equilibrium molecular dynamics simulations of the reactions CN + propane (R1) and CN + cyclohexane (R2). For (R2), we carried out simulations in both the gas phase and in a CH₂Cl₂ solvent. Analysis of the results suggests that the solvent perturbations to the (R2) reactive free energy surface are small, leading to product energy partitioning in the solvent that is similar to the gas phase. The distribution of molecular geometries at the respective gas and solution phase variational association transition states is very similar, leading to nascent HCN which is vibrationally excited in both its CH stretching and HCN bending coordinates. This study highlights the fact that *significant* non-equilibrium energy distributions may follow in the wake of solution phase bimolecular reactions, and may persist for hundreds of picoseconds despite frictional damping. Consideration of non-thermal distributions is often neglected in descriptions of condensed-phase reactivity; the extent to which the present intriguing observations are widespread remains an interesting question.

Introduction

Our fundamental understanding of chemical dynamics, kinetics, reactivity, and energy transfer in the gas phase has advanced considerably in the past few decades, and increasing efforts are underway to obtain similarly detailed insight into solution phase processes.¹⁻³ Solution phase chemical reactions are subject to a number of complications compared to their gas phase counterparts – including modifications of reactive potential energy surfaces by the solvent, solvent caging, and solvent friction,⁴ all of which combine to affect reaction rates,^{5,6} energy transfer,² and chemical dynamics.

The microscopic dynamics of a successful bimolecular reaction in solution may be heuristically broken into three consecutive stages. The first stage is generally diffusion limited and loosely analogous to a bimolecular gas phase collision probability, spanning the time during which the reactants navigate their individual solvent cages and approach the association transition state (TS). The second stage includes the time window during which the reaction may be defined as having occurred: following their encounter, there will be some ensemble averaged probability that the reactants' energy and orientation is favorable enough to undergo passage over the association TS. Averaged over a Boltzmann ensemble, the first two stages combine to yield the phenomenological kinetic rate coefficient for reaction. The third stage of reaction is the so-called post-transition state dynamics stage, during which the reactants relax to equilibrium following TS passage.

In the gas phase, a range of experimental and theoretical studies have demonstrated the prevalence of non-equilibrium (alternatively referred to as non-Markovian, or non-statistical) post-TS dynamics.^{7,8} While such post-TS dynamics are interesting *per se* in continued attempts to unravel the fundamental microscopic details of condensed phase chemical reactivity, it may be the case that their effects are even more far ranging than has generally been appreciated. For example, recent work suggests that non-equilibrium post-TS microphysics of solution phase bimolecular reactions may determine product ratios in reactions as ubiquitous as alkene hydroboration,^{7,9} which is a staple reaction in synthetic organic chemistry.

Numerous studies have been carried out to determine kinetic rate coefficients for bimolecular reactions in solution (i.e., stages 1 and 2 above). Also, several experimental and theoretical investigations have looked at the microscopic details of energy transfer and dynamics for unimolecular processes following photo-excitation.^{6,10-12} However, there have

been far fewer experimental and theoretical investigations of the post-transition state dynamics of thermal bimolecular reactions in solution, due to experimental and theoretical difficulties. On the experimental side, such investigations require very fast analytical methods that are capable of resolving solute features from solvent features. On the modeling side, computationally tractable yet accurate reactive potential energy surfaces (PESs) are required for the whole solute-solvent system, as well as methods for accurately addressing the rare event nature of bimolecular encounters in solution.

In this article, we present a molecular modelling study of the post transition state dynamics for CN + alkane H atom abstraction reactions in both the gas phase and a CH₂Cl₂ (dichloromethane) solvent, initiating our dynamics in the later phases of stage one (described above). The present study was carried out alongside recent time-resolved infrared (IR) post-TS measurements of nascent HCN for the reaction of CN + cyclohexane in solution, in which significant HCN vibrational excitation was observed.¹³ This finding differs somewhat from previous studies on the CN + CHCl₃ reaction by Hochstrasser and co-workers¹⁴ and by Crim and co-workers,¹⁵ who deduced that the nascent HCN is essentially thermal – leading to the conclusion that the solution phase reaction shows markedly different post-transition state dynamics than in the gas phase. Hochstrasser and Voth attributed this to solvent modifications of the PES, noting that the transition state region in the solution is shifted closer to the HCN product than in the gas phase.³

To the best of our knowledge, the work described in this article presents the first molecular dynamics study of abstraction mechanisms for reactions of CN + polyatomic organic molecules. In what follows, we investigated the following reactions



(R1) was investigated using gas phase *ab initio* quasiclassical direct dynamics. To investigate (R2), we used an analytic PES which we developed by fitting molecular mechanics force fields to coupled cluster (CCSD(T)) electronic structure theory energies. Subsequently, we carried out both gas and solution phase classical MD simulations using a recently developed MD rare-event acceleration algorithm.¹⁶ In all the simulations, we obtained normal mode energies from the (R1) and (R2) Cartesian dynamics by transforming to the normal mode frame. The MD simulations have afforded a level of detail which was inaccessible in the accompanying experiments, and show that: (1) that the degree of vibrational excitation at short time of both the C–H stretch and the bend in HCN is largely identical in the gas phase and in solution, (2) within the post TS region, the solution and gas phase reaction free energy

profiles are approximately identical, consistent with the fact that the observed post-TS dynamics at short times are very similar, and (3) in solution phase, the energy relaxation of the nascent excited HCN shows multiple timescales compared to the relaxation of HCN in pure solvent.

Methods

Ab Initio PES: Wave Function & DFT Approaches

In order to carry out *ab initio* direct dynamics to investigate energy disposal in HCN following CN hydrogen abstraction reactions, the first part of this study involved obtaining an accurate representation of an abstraction PES for reaction of CN with a small alkane. Given the computational expense of obtaining an accurate (R2) PES using high level electronic structure theory, we examined CN abstraction of a secondary H on propane (R1) as a reasonable proxy. An accurate representation of the (R1) potential energy surface (PES) is complicated because the CN radical is poorly described by typical spin-unrestricted methods, which produce significant spin contamination in this system, with consequently unreliable geometries and energies. Restricted open shell treatments produced more reliable energies and geometries, and we obtained an accurate representation of the energetics along the addition PES as follows: (1) Using unrestricted coupled cluster theory on a restricted open shell reference wave function (UCCSD-ROHF) in conjunction with the cc-pVDZ basis set, geometries along the reaction coordinate were obtained by performing relaxed scans along the secondary H—CN approach coordinate; and (2) single point energies along the reaction coordinate were obtained by carrying out further UCCSD(T)-ROHF calculations and extrapolating to the infinite basis set limit using the cc-pVDZ and cc-pVTZ basis sets. The extrapolation formula that we used to determine the infinite basis energy, E_∞ , is as follows:¹⁷

$$E_\infty = E_l - \frac{B}{(l+1)^4} \quad (1)$$

where E_l is the CCSD(T) energy obtained using a basis set with a maximum angular momentum basis function l .

Calculating the potential energy and gradient ‘on the fly’ during a classical trajectory study using the UCCSD(T) methods discussed above is computationally unaffordable. Our strategy was instead to use density functional theory (DFT), using a functional selected to reproduce fairly closely the more accurate CCSD(T) PES profile. In conjunction with the 6-

31G* basis set, we examined several different functionals including PBE, B1LYP, B3LYP, BB1K, and modified forms of BB1K. We also investigated the use of empirical dispersion corrections, but found that they had little effect. A restricted open shell treatment using the BB1K functional, modified to have 56% exact Hartree-Fock exchange, gave the best agreement with the CCSD(T) relative energies along the (R1) reaction path. All wavefunction based calculations in this work were carried out using the MOLPRO suite of programs, and all DFT calculations were carried out using the G03 suite of programs.¹⁸

Gas Phase Direct Dynamics

With the aforementioned modified BB1K functional and the 6-31G* basis set, we carried out quasiclassical direct dynamics calculations using a version of the VENUS dynamics package¹⁹ which we have locally modified to interface with arbitrary electronic structure theory packages. Initial selection of zero point energy corrected coordinates and momenta for CN and propane was performed using microcanonical normal mode sampling,²⁰ where the normal mode quantum numbers were selected from a 298 K vibrational Boltzmann distribution. Rotational and relative translational energies of each fragment were selected from 298 K Boltzmann distributions, with the orientation of each molecule randomly selected by rotation in the molecular center of mass (COM) Eckart frame. As there is no enthalpic barrier to reaction, there was no need to include additional kinetic energy along the association reaction coordinate in order to observe reactive events. Trajectories were initialized with a 4.5 Å center-of-mass separation between CN and propane fragments. In order to reduce the computational expense of these calculations, and given that our primary interest in this work is the post-transition state dynamics following H atom abstraction, we: (1) set the impact factor to zero, and (2) used importance sampling to increase the probability of selecting reactive trajectories – i.e., we only propagated those trajectories which had an initial H—CN separation of less than 4.0 Å. Trajectories which satisfied the importance sampling criteria were propagated 3000 steps using a velocity Verlet integrator and a timestep of 0.2 fs. We monitored total energy conservation for all reactive trajectories and discarded those which did not have an total energy conservation of better than 2.5% with respect to the difference between the initial total energy of CN + C₃H₈, and the final HCN + C₃H₇ potential energy.

CN + cyclohexane PES

Running a large number of solution phase trajectories using the direct dynamics techniques described above is computationally intractable. Consequently, we also used an analytical form of the PES which we fitted to the electronic theory data described above. The use of matrix representations to construct reactive PESs has been investigated by a number of previous workers, going back to Evans and Polyani,²¹ and our strategy is along those same lines. We constructed a reactive PES from a matrix representation of analytical molecular mechanics forcefields, $V(\mathbf{q})$, which are generally well-calibrated for simulations of non-reactive dynamics. The coordinate-dependent Hamiltonian, $\mathbf{H}(\mathbf{q})$, was represented using a symmetric $n \times n$ matrix, where the diagonal elements, $V_i(\mathbf{q})$, are the molecular mechanics energies for a particular connectivity arrangement, and ε_i are corresponding energy offsets associated with reaction endo- or exo-thermicity. The overall potential energy of the system for a given set of nuclear coordinates is then taken as the lowest eigenvalue, $\lambda_0(\mathbf{q})$, of $\mathbf{H}(\mathbf{q})$. In its simplest implementation, $n = 2$, and the system is described by a two-state Hamiltonian, in which state 1 corresponds to the reactant connectivity, while state 2 corresponds to the product connectivity. In this case, the Hamiltonian has the form:

$$H(\mathbf{q}) = \begin{bmatrix} V_1(\mathbf{q}) + \varepsilon_1 & H_{12}(\mathbf{q}) \\ H_{12}(\mathbf{q}) & V_2(\mathbf{q}) + \varepsilon_2 \end{bmatrix} \quad (2)$$

The values of ε_i are generally chosen so that the energies at the respective product and reactant geometries (P and R) give the correct energy of reaction, which is evaluated as $\lambda_0(\mathbf{q}=\text{P}) - \lambda_0(\mathbf{q}=\text{R})$. In the case that the respective coupling elements, $H_{12}(\mathbf{q}=\text{P})$ and $H_{12}(\mathbf{q}=\text{R})$, are close to zero near the product and reactant geometries, then the reaction energy is $(V_2(\mathbf{q}=\text{P}) + \varepsilon_2) - (V_1(\mathbf{q}=\text{R}) + \varepsilon_1)$.

In addition to the total system potential energy obtained via diagonalization of Eq (2), molecular dynamics approaches also require evaluation of energy gradients. While it is straightforward to write down an analytic expression for $d\lambda_0(\mathbf{q})/d\mathbf{q}$ for the case of a 2 dimensional Hamiltonian matrix, this approach is not feasible for the more general case of an n -dimensional Hamiltonian. The diagonal eigenvalue matrix, \mathbf{D} , may be written as

$$\mathbf{D} = \mathbf{U}^T \mathbf{H} \mathbf{U} \quad (3)$$

where \mathbf{U} is the eigenvector matrix, and the elements of \mathbf{D} , \mathbf{U} , and \mathbf{H} all implicitly depend on \mathbf{q} – i.e., they may be written as $\mathbf{D}(\mathbf{q})$, $\mathbf{U}(\mathbf{q})$, and $\mathbf{H}(\mathbf{q})$. The derivatives of the eigenvalues may then be calculated as

$$\frac{d\mathbf{D}}{d\mathbf{q}} = \mathbf{U}^T \frac{d\mathbf{H}}{d\mathbf{q}} \mathbf{U} \quad (4)$$

This is analagous to the Hellman-Feynmann approach, commonly written as

$$\frac{dE}{d\mathbf{q}} = \langle \psi(\mathbf{q}) | \frac{d\mathbf{H}}{d\mathbf{q}} | \psi(\mathbf{q}) \rangle \quad (5)$$

where E and ψ are the lowest eigenvalue and corresponding eigenfunction obtained from solution of the time independent Schrodinger equation. Eq (4) and (5) are accurate so long as the elements of $\mathbf{H}(\mathbf{q})$ are continuously differentiable in the neighborhood of \mathbf{q} .²²

One significant difficulty in a matrix representation of a reactive forcefield such as that in Eq (2) lies in representing the off-diagonal coupling elements, $H_{12}(\mathbf{q})$, and a number of different strategies for doing this have been proposed – e.g., the empirical valence bond (EVB) approach of Warshel and Weiss,²³ the approach of Chang and Miller,²⁴ and Truhlar’s multiconfigurational molecular mechanics (MCMM).²⁵ Because the system under investigation herein involves significant non-equilibrium dynamics, a reasonably accurate representation of the energetics along the reaction path is as important as the energies of the reactant and product states. The approach that we have taken in this work is similar in philosophy to the recently described distributed Gaussian approach,²⁶ wherein the off-diagonal coupling elements of $\mathbf{H}(\mathbf{q})$ are fit to gas-phase electronic structure theory results for some dynamically significant subset of \mathbf{q} . We represented the off diagonal coupling elements as a linear combination of Gaussian functions of the H–CN bond distance, r – i.e.,

$$H_{12}(r) = \sum_{i=1}^k A_i \exp\left(-\frac{1}{2}((r_{H-CN} - B_i)/C_i)^2\right) \quad (6)$$

where A_i , B_i , and C_i are the respective amplitude, center, and width parameters for a particular Gaussian function.

Increasingly accurate fits may be obtained with an increasing number of Gaussians, k ; however, in the interest of computational efficiency and to avoid over-fitting, it is also desirable to minimize k . In this work, we were able to accurately model the CCSD(T) reaction path between CN and a single cyclohexane hydrogen using two Gaussians (i.e., $k = 2$). This gives a total of six parameters which we fit to gas phase relaxed scans along the H–CN coordinate using a Levenberg-Marquardt non-linear least squares optimization algorithm with gradients which were calculated numerically. The goodness of fit was determined from a simple merit function

$$\chi^2(A_i, B_i, C_i; i \in k) = \sum_{r \in path} \left[\frac{\lambda_0(\mathbf{q} = r) - (\Delta E_{CCSD(T)/CBS}(r))}{\Delta E_{CCSD(T)/CBS}(r)} \right]^2 \quad (7)$$

where $\Delta E_{CCSD(T)/CBS}(r) = E_{CCSD(T)/CBS}(r) - E_{CCSD(T)/CBS}(\infty)$ - i.e., with respect to the reaction asymptote at ∞ . Eq (7) was found to satisfactorily weight both the low and high energies along the reaction path. For each trial set of parameters defining $H_{12}(\mathbf{q}=r)$, the set of values $\lambda_0(\mathbf{q}=r)$ was obtained through optimization of $\lambda_0(\mathbf{q}=r)$ with the H-CN coordinate, r , constrained to be identical to the corresponding value of r along the CCSD(T) reaction path. Hence the structures are not necessarily identical to those used in the CCSD(T) scans. However, inspection of both sets of structures along the reaction path shows that they are very similar, providing some support for the accuracy of the description of the potential energy surface away from the minimum energy path. Based on the good agreement that we obtain with the experiments (discussed below), our assumption that $H_{12}(\mathbf{q})$ does not change significantly in going from a gas phase reactive system to a solvated system appears reasonable. Additionally, we note that it would have been possible, albeit more computationally expensive, to make every hydrogen on the cyclohexane reactive by including additional terms in the matrix of equation (2); however, the quality of our results suggests that this additional computational expense is not necessary for the purposes of gaining insight into the solution phase post-TS dynamics.

CN + Cyclohexane Dynamics & Rare Event Acceleration

All of the CN + cyclohexane work described above was carried out using a locally modified version of the CHARMM software suite,²⁷ to which we have recently added code for carrying out reactive molecular dynamics with a generic n -state Hamiltonian matrix of the type shown in Eq (2). Fitting was carried out using a script to interface CHARMM with the Levenberg-Marquardt algorithm implementation available within the scientific python (SciPy) library. The diagonal elements of the Hamiltonian matrix were calculated using the unmodified Merck Molecular Mechanics force-field (MMFF) in CHARMM.²⁸ In its standard implementation, this force-field does not include any point charges on either the solvent or solute, which is reasonable given the fairly low polarity of all species involved here.

Both the gas phase and solution phase dynamics simulations used a leapfrog Verlet integration scheme, with NVT equilibration runs followed by subsequent NVE trajectories. In the gas phase, 250 stable equilibration temperature profiles were obtained with NVT runs lasting 100 ps (0.5 fs timestep) using Langevin integration with a friction coefficient of 50 ps^{-1} and a heat bath of 300K. The subsequent NVE trajectories had a duration of 100 ps and used a 0.1 fs timestep. The 250 solution phase NVT equilibration runs lasted 200 ps (0.5 fs timestep), with a Langevin friction coefficient of 10 ps^{-1} . The subsequent NVE trajectories

had a duration of 200 ps and used a 0.1 fs timestep. In the solution-phase NVT and NVE simulations, CN and C₆H₁₂ were solvated within a 23.7 Å³ periodic box filled with 125 molecules of CH₂Cl₂, corresponding to the experimental 298K CH₂Cl₂ density of 1.33 g/mL.²⁹ Finally, we also performed simulations of energy relaxation of HCN in a periodic box of neat CH₂Cl₂ solvent with $\nu \sim 1$ initial excitation placed in the CH stretch. This was done via 250 solution phase NVT equilibration runs, each of which lasted 200 ps (0.5 fs timestep), with a Langevin friction coefficient of 10 ps⁻¹, and constraining the C-H distance to have a value between 1.19 and 1.24 Å using the BXD algorithm (discussed below). In the subsequent NVE trajectories, which had a duration of 200 ps and used a 0.1 fs timestep, the BXD constraint was relaxed to allow the C-H stretch to relax to equilibrium.

On the timescale of the simulations, every single gas and solution phase CN + *c*-C₆H₁₂ trajectory was reactive – i.e., resulted in the HCN + *c*-C₆H₁₁ radical. The algorithm we used to accelerate the probability of obtaining reactive events is called AXD,¹⁶ which is a formally exact extension of TST, and which accelerates reactive events through implementing phase space constraints (via velocity inversion) in a fashion that conserves angular momentum, linear momentum, and energy.³⁰ As such, it works equally well for both NVT and NVE simulations, and we have recently shown that it conserves non-equilibrium behavior in the neighborhood of a TS so long as the distance between the phase space constraint and the TS is larger than the system's characteristic decorrelation length.³¹ In the NVT simulations reported above, we implemented a phase space constraint that maintained the H–CN distance to be between 2.5 and 4.0 Å. As discussed below, this constraint is well on the reactant side of the abstraction TS. In the NVE simulations, the 2.5 Å constraint was relaxed, allowing barrier crossing and subsequent abstraction to proceed with significant acceleration, essentially by preventing diffusion of the reactants away from one another.

To obtain the potential of mean force (PMF) along the C-H stretch in both the gas-phase and the solution-phase simulations, we used the recently developed BXD algorithm,¹⁶ in conjunction with the respective NVT simulation details described above. BXD is a multiple-constraint extension of AXD, which we have shown can be used to obtain accurate potentials of mean force. In the BXD simulations carried out as part of this work, we used 6 simulation boxes, with configuration space velocity inversion boundaries at 1.26, 1.36, 1.5, 1.7, 2.0, 4.0, and 6.0 Å. Convergence of the PMFs was monitored on each pass through the boxed configuration space. Both the AXD and BXD algorithms have recently been implemented in CHARMM.

HCN Normal Mode Analysis

For those reactive trajectories which yielded HCN using the methods described above, energy disposal in the nascent HCN was determined by projecting its space-fixed Cartesian velocities, $\dot{\mathbf{q}}(t)$, and coordinates, $\mathbf{q}(t)$, into the translational, rotational, and vibrational normal modes of HCN in its COM frame equilibrium geometry, \mathbf{q}_{eq} . In order to carry out this analysis, the nascent HCN was translated to its COM frame, and the least squares difference between the mass-weighted coordinates of the nascent HCN and those of the equilibrium HCN was minimized with respect to rigid-body rotations, using singular value decomposition – an operation which identical to placing the rovibrationally hot HCN into the Eckart frame of the equilibrium HCN, thereby minimizing rovibrational Coriolis coupling in the reference frame of the nascent HCN.³² Then, the projection of the Cartesian coordinates and velocities into the translational, rotational, and vibrational displacements of the equilibrium geometry was accomplished via the following relationships:³³

$$\begin{aligned}\Delta\mathbf{Q}(t) &= \mathbf{L}^{-1}\Delta\mathbf{q}(t) \\ \dot{\mathbf{Q}}(t) &= \mathbf{L}^{-1}\dot{\mathbf{q}}(t)\end{aligned}\tag{8}$$

where $\Delta\mathbf{q}(t) = \mathbf{q}(t) - \mathbf{q}_{eq}$ is the vector of Cartesian displacements from equilibrium of a particular HCN geometry. $\Delta\mathbf{Q}(t)$ and $\dot{\mathbf{Q}}(t)$ are the respective vectors of normal mode displacements and velocities. \mathbf{L} is a $3N \times 3N$ matrix obtained from diagonalization of the mass-weighted Hessian, whose column vectors are the Cartesian displacements of the 3 translations, 2 rotations, and $3N-5$ vibrations of HCN at equilibrium. The translational and rotational eigenvectors were obtained analytically in the usual way,³⁴ and the vibrational eigenvectors were obtained from diagonalization of the optimized HCN Hessian. To ensure orthogonality of these vibrational eigenvectors, we utilized a Gram-Schmidt algorithm. Owing to HCN's linear geometry, the total energy partitioned into the degenerate rotational degrees of freedom and bending vibrations is cylindrically symmetric about the molecular z -axis. Thus, we report rotational energies and bending energies as respective sums of the two degenerate rotations and vibrations.

Having determined $\Delta\mathbf{Q}(t)$ and $\dot{\mathbf{Q}}(t)$, the kinetic energy of the l th normal mode, $\mathbf{T}^l(t)$, was determined as

$$\mathbf{T}^l(t) = \sum_{i\alpha} \frac{m_i}{2} [\mathbf{L}_{i\alpha}^l \dot{\mathbf{Q}}^l(t)]^2\tag{9}$$

where m is the atomic mass, i runs over the atom indices, and α runs over the Cartesian x, y, z directions. It is important to point out that in our notation, the column vectors in \mathbf{L} are not the

raw vectors obtained from diagonalization of the mass-weighted Hessian; rather, they have been transformed from mass-weighted to Cartesian space, and subsequently normalized using the appropriate normalization constant, N_l . In the harmonic limit, the potential energy of the l th normal mode, $\mathbf{V}^l(t)$, may be determined as

$$\mathbf{V}^l(t) = \frac{1}{2} \mu_l \left[\omega_l \Delta \mathbf{Q}^l(t) \right]^2 \quad (10)$$

where ω_l is the frequency of the l th mode, and μ_l is the reduced mass of the mode, which is identical to N_l^2 .³⁵ The total energy in a particular mode, $\mathbf{E}^l(t)$, may then be calculated as

$$\mathbf{E}^l(t) = \mathbf{T}^l(t) + \mathbf{V}^l(t) \quad (11)$$

The method described above for determining total normal mode energies from the Cartesian positions and velocities is accurate in the limit of infinitesimally small displacements from the equilibrium geometry.^{33,35} In the limit of large non-equilibrium displacements such as considered in this work, the accuracy of Eq (11) falls off, primarily because Eq (10) ignores mode-mode couplings, treating the system potential energy as separable in the normal modes. The kinetic energy, on the other hand, *is* diagonal in the normal mode displacements. The virial theorem specifies that the total energy is equipartitioned between kinetic and potential contributions, so that the average total energy over a particular time window τ , may be calculated as:

$$\langle \mathbf{E}^l(t) \rangle_\tau \approx 2 \langle \mathbf{T}^l(t) \rangle_\tau \quad (12)$$

where the angled brackets indicate averages. This is the approach that we have adopted throughout this work, with all of the normal mode energies reported herein calculated using Eq (12). So long as τ spans several vibrational periods of the l th mode, then Eq (12) may be expected to give reasonably accurate results.³³ For the (R1) reactive trajectories, energy disposal in the nascent HCN was determined by averaging for the final 60 fs of each reactive trajectory. For the (R2) trajectories, where significantly more data points were available, the averaging was carried out with $\tau = 250$ fs.

Results and Discussion

Potential Energy Surfaces

Zero point energies for products and reactants of (R1), obtained using the UCCSD-ROHF/cc-pVDQ geometries and frequencies, as well as results from subsequent higher level single point energy calculations, are given in Table 1. The zero point corrected reaction

energy ($-28.4 \text{ kcal mol}^{-1}$) obtained using the infinite basis extrapolation described in Eq (1) is in good agreement with the experimental 298 K reaction enthalpy of $-29 \text{ kcal mol}^{-1}$,^{36,37} and the corresponding energy profiles, shown in Figure 1, are very similar to the analogous multireference results reported by Klippenstein and co-workers for CN + ethane.³⁸ The path shown in Figure 1 corresponds to a barrierless abstraction for the secondary hydrogen atoms on propane, with a linear approach of the CN to the hydrogen atom, both in terms of the C–H–C and the H–CN angles. Also shown in Figure 1 is the corresponding relaxed PES scan along the H–CN coordinate using the modified BB1K functional and the 6-31G* basis set. The BB1K/6-31G* reactant and product energies are given in Table 1.

Molecule		ZPE (UCCSD-ROHF/cc-pVDZ)	UCCSD(T)-ROHF/CBS	BB1K/6-31G*
reactants	CN	0.00482	-92.60272	-92.64883
	C ₃ H ₈	0.10407	-118.97403	-119.06339
products	HCN	0.01615	-93.31448	-93.36490
	C ₃ H ₇	0.08877	-118.30359	-118.39600
E(products-reactants)		-2.5	-25.9	-30.54

Table 1: Zero point energies (ZPE) and single point energies of the reactants and products obtained as described in the text. All energies are in Hartrees except for the final row, which gives the difference between the product and reactant energies, and is given in units of kcal mol^{-1} .

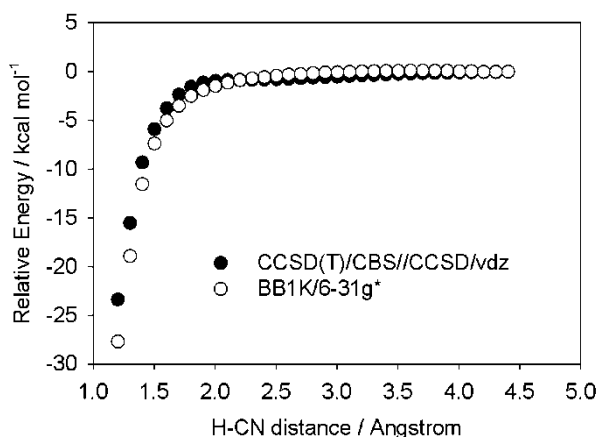


Figure 1: Relaxed (R1) scan energies along the H–CN distance using (i) the CCSD(T)/CBS//CCSD/vdz level of theory, and (ii) the reparameterized BB1K functional utilized in the direct dynamics simulations

For (R2), the off-diagonal coupling elements ($H_{12}(\mathbf{q})$ in Eq (2)) for the analytical EVB potential energy surface, were determined by minimizing Eq (7) using two Gaussian functions whose parameters (see Eq (5)) were determined by fitting to the CCSD(T) energy profile for (R1) shown in Figure 1. The energy difference between the offsets ($\epsilon_2 - \epsilon_1$ in Eq (2)) was fixed to $-20.7 \text{ kcal mol}^{-1}$ based on experimental data. According to the NIST

thermodynamics database, the 298K enthalpies of formation for CN and HCN are 104.00 and 31.05 kcal mol⁻¹, respectively. Combined with the experimental determination of D_{298K}^0 for C-H in cyclohexane (95.5 kcal mol⁻¹),³⁹ this gives $\Delta H_{298K}^{CN+C_6H_{12}} = -23.8$ kcal mol⁻¹. Based on cyclohexane frequency data taken from the NIST database as well as calculations by Klippenstein and coworkers carried out on the cyclohexyl radical,⁴⁰ the change in zero point energy for (R2) is ~ -3.1 kcal mol⁻¹, close to the value of -2.5 kcal mol⁻¹ for (R1) given in Table 1. Subtracting the change in zero point energy from the 298K experimental reaction enthalpy gives an approximate classical reaction energy of -20.7 kcal mol⁻¹.

Gaussian index	A (amplitude)	B (center)	C (width)
1	31.324	1.796	0.183
2	104.358	1.921	1.797

Table 2: Levenberg-Marquardt optimized parameters for the Gaussian functions making up H₁₂ in Eq (6)

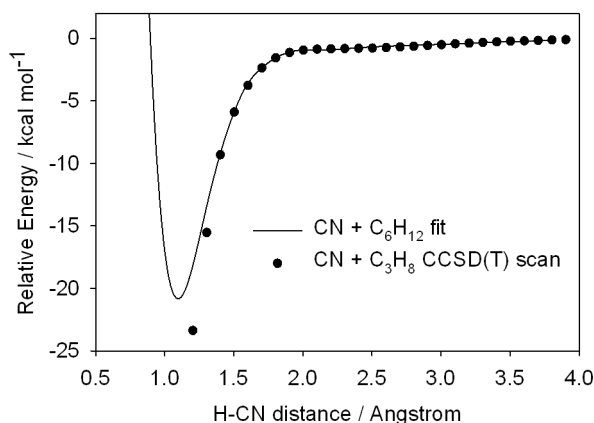


Figure 2: Relaxed scans along the H-CN distance coordinate using (i) CCSD(T)/CBS//CCSD/vdz electronic structure theory (•), and (ii) the (R2) analytical PES (—)

The parameters for the optimized Gaussians are given in Table 2. Figure 2 shows the comparison between relaxed potential energy scans along the H-CN coordinate using (i) the fitted Eq (2) analytical PES for (R2), and (ii) relaxed CCSD(T)/CBS//CCSD/vdz PES scans for (R1). As discussed above, the reaction energy less the zero point energy for (R2) was set to be slightly less exothermic than that for (R1) determined from the CCSD(T) calculations. This can be seen clearly in Figure 2. This does not however affect the quality of the fit in the early part of the reaction coordinate. Table 3 shows a comparison between the experimental HCN rotational constants and vibrational frequencies with those obtained at the modified BB1K/6-31G* level of theory, and using the MMFF.

	Moments of Inertia / amu Å ²	Frequencies / cm-1
Experiment	11.404	3312, 2097, 712 (× 2)
MMFF	11.516	3470, 2019, 777 (× 2)
BB1K/6-31G*	11.131	3612, 2349, 826 (× 2)

Table 3: Frequencies & Rotational Constants of HCN obtained from experiment (NIST database), the MMFF forcefield, and the modified BB1K/6-31G* model chemistry

Gas Phase Dynamics Results

CN + C₃H₈

A number of previous experimental and theoretical studies have examined reaction cross sections and product state distributions in the CN + H₂ → HCN + H reaction,⁴¹ those which examined nascent HCN product energy deposition reported excited HCN bending and CH stretching vibrations. To our knowledge, the results we report below represent the first theoretical study of product energy deposition for gas phase reactions of CN + *polyatomic* species, and represent a step toward addressing the extent to which qualitative Polanyi models are applicable to high dimensionality polyatomic systems.⁴²

Despite the fact that the (R1) quasi-classical direct dynamics we report below are too computationally intensive to provide quantitatively converged statistics, the results nevertheless yield significant qualitative insight. The point of these simulations was two-fold. First, the direct dynamics study of secondary H abstraction from propane by CN served as an additional reference to assess the quality of the results that we obtained using the analytical Hamiltonian for CN + cyclohexane. Second, we hoped to gain some qualitative insight into the experimental observations that the nascent HCN from various CN + RH reactions has hot C-H stretch and HCN bending modes, but thermal rotational and translational distributions.^{36,43}

A total of 56 reactive trajectories met the energy conservation criteria discussed above. The averaged results of the QCT calculations presented in Figures 2 - 5 show that the HCN product rotational and translational energies are very close to their thermal values at 298 K. Instead of the excess energy being deposited into HCN translational and rotational degrees of freedom, the dynamics results, shown in Figure 3 and Table 4, clearly show that the bulk of the excess energy goes into HCN vibrational excitation, with $\nu \sim 0.75$ in the H-C stretch, and significant excitation ($\nu \sim 3.95$) in the HCN bending mode, in qualitative agreement with the

experimental results. The bend excitation emerges as a particularly interesting dynamical result, especially given the fact that relaxed scans along the H—CN distance at both the CCSD-ROHF/cc-pVDZ and BBlK/6-31G* levels of theory show that the preferred HCN geometry is linear all along the reaction coordinate. As discussed in our recently published paper¹³ and further in what follows, the bend excitation derives from a very soft bending potential in the region of the association transition state, and from the greater statistical likelihood of CN approach vectors with an H—CN angle that deviates from 180°. In the region of the variational transition state (i.e., the free energy maximum, whose determination is discussed further below), the distribution of HCN bend angles is peaked from 140 – 160°.

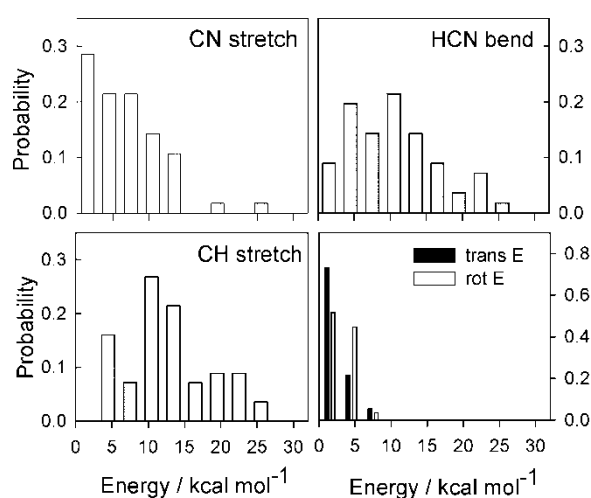


Figure 3: normalized distributions of energy deposited into each HCN degree of freedom for the (R1) BBlK gas phase quasiclassical direct dynamics carried out using VENUS. Results have been put in bins with a width of 3 kcal mol⁻¹.

<i>df</i> label (degeneracy)	Designation	CN + C ₃ H ₈ → HCN + C ₃ H ₇ (R1) using BBlK direct dynamics		CN + C ₆ H ₁₂ → HCN + C ₆ H ₁₁ (R2) using Eq 2 and MMFF	
		average energy / kcal mol ⁻¹	approximate ν	average energy / kcal mol ⁻¹	approximate ν
ν_1 (1)	C-N stretch	6.8	0.51	3.0	0.52
ν_2 (2)	bend	10.5	3.95	4.8	2.16
ν_3 (1)	C-H stretch	12.9	0.75	9.6	0.97
rotations (2)	N/A	3.2	—	0.6	—
translations (3)	N/A	2.6	—	0.9	—

Table 4: Average energy disposal in nascent HCN vibrational, rotational, and translational degrees of freedom (*df*). For the quasiclassical BBlK results, which included vibrational ZPE in the initial sampling, the approximate quantum numbers (ν) were obtained by subtracting the harmonic zero point energy from the average total energy, and then dividing by the energy of the appropriate BBlK harmonic vibrational frequency in Table 3. For the dynamics run using Eq 2 and the MMFF, which did not include initial vibrational ZPE, approximate quantum numbers were obtained simply through dividing by the energy of the appropriate MMFF harmonic frequency.

CN + *c*-C₆H₁₂

The gas phase $\text{CN} + c\text{-C}_6\text{H}_{12}$ results obtained using the Eq (2) analytic potential are in broad agreement with the gas phase results for (R1) discussed above. Figure 4 gives the normalized distributions of energy in each mode for the analytic MMFF classical dynamics results, and Figure 5 shows the time dependent energy in each of the HCN vibrational degrees of freedom upon passage over the variational TS for abstraction. Both figures show that the nascent HCN has excitation in both the CH stretch and the HCN bend beyond what would be expected for a 298K thermal distribution. According to the MMFF HCN frequencies in Table 3, the harmonic energy for one quantum of vibration in the CH stretch and HCN bend modes is $\sim 9.9 \text{ kcal mol}^{-1}$ and $\sim 2.2 \text{ kcal mol}^{-1}$ respectively. As shown in Figure 4 and Table 4, the CH stretching mode in the nascent HCN has an average energy of $\sim 9.6 \text{ kcal mol}^{-1}$, and the bending mode has an average energy of $\sim 4.8 \text{ kcal mol}^{-1}$, respectively corresponding to $\nu \sim 0.97$ and $\nu \sim 2.16$.

A direct quantitative comparison of the results in Figures 3 and 4 is complicated by the fact that: (1) the reactive systems are different; (2) the BB1K (R1) potential gave a reaction that was $\sim 10 \text{ kcal mol}^{-1}$ more exothermic than the MMFF analytic potential; and (3) the (R1) initial conditions included sampling of the normal mode vibrational energies, whereas the (R2) results did not. Nevertheless, both sets of dynamics results are in good qualitative agreement. They both reproduce the experimental observations of vibrational excitation in the nascent HCN bending and CH stretching modes, without accompanying translational and rotational excitation. Furthermore, alongside Figure 2, the results in Figure 4 and Table 4 suggest that the fitted analytic PES we developed using Eq (6) is sufficiently accurate to providing accurate modeling of the non-equilibrium solution phase dynamics which was a primary aim of this study.

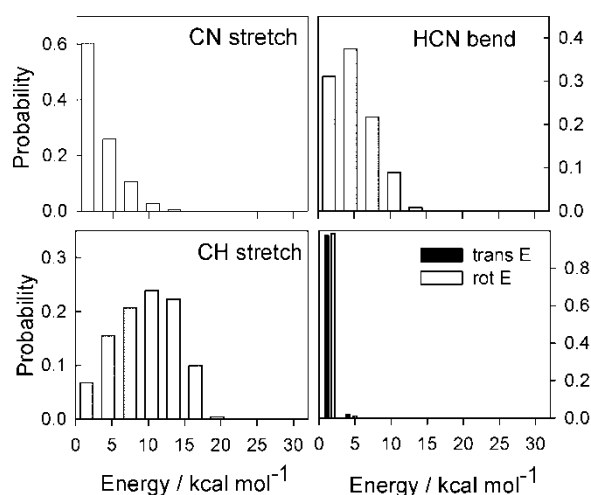


Figure 4: Normalized distributions of energy deposited into each HCN degree of freedom for the (R2) gas phase classical dynamics carried out using the Eq 2 analytical Hamiltonian in CHARMM. Results have been placed into bins with a width of 3 kcal mol⁻¹.

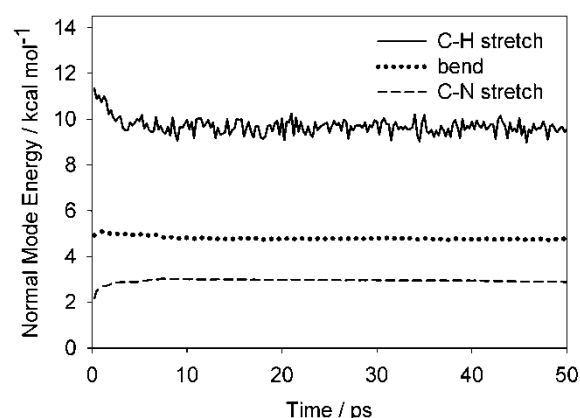


Figure 5: Time-dependent vibrational mode energies in the nascent HCN following (R2) gas phase simulations. Results shown are averaged over 250 reactive trajectories. After a few picoseconds, the results are essentially time independent.

Solution Phase Dynamics Results

Figure 6 shows the relative PMF for (R2) along the H–CN abstraction coordinate in both the gas-phase and solution-phase dynamics simulations, obtained using the BXD method. Despite the fact that the reaction is a barrierless process on the potential energy surface, both the gas-phase and solution-phase simulations show maxima in their respective PMFs. These maxima occur at very similar values of the reaction coordinate (~ 1.9 Å and 1.95 Å), and we have set the zero of both PMFs at this point. The origin of this maximum is primarily entropic,⁴⁴ corresponding to a reduction in relative fragment rotational and

translational degrees of freedom as CN approaches *c*-C₆H₁₂ to abstract a hydrogen atom. The potential of mean force in the reactant region is somewhat different in the gas phase and in solution, suggesting at first sight a significant difference in the rate constants for the two reactions. However, experiments show that the rate constants are in fact very similar. The solution phase data¹³ can be analyzed to provide a room temperature rate constant of $\sim 8.4 \times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ for the CN + *c*-C₆H₁₂ reaction. The rate constant at room temperature for the gas phase CN + *c*-C₆H₁₂ reaction has been measured as $\sim 2.7 \times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$,³⁹ very similar to the solution phase value. It is known⁴⁵ that relative free energies for bimolecular and association reactions cannot be obtained simply from inspection of numerically derived PMFs. In particular, the PMFs shown in Figure 6 are not fully converged with respect to sampling of all relative rotational orientations of the two reactants at large H–CN distances, and this may contribute to the apparent difference between the two curves in the reactant region. For the primary aim of this article, however, these differences are not significant, because the PMFs in the transition state and post-transition state regions are nearly identical, and it is these that determine the product energy partitioning.

Figure 7 depicts overlays taken from NVE simulations of the CN + *c*-C₆H₁₂ geometries at the moment of passage over the gas phase and solution phase free energy maxima, and shows that the range of geometries sampled in the gas and solution phases is largely similar. Taken together, Figures 6 and 7 suggest that the gross features of the dynamics en route to products following TS passage should be substantially similar in solution and in the gas phase.

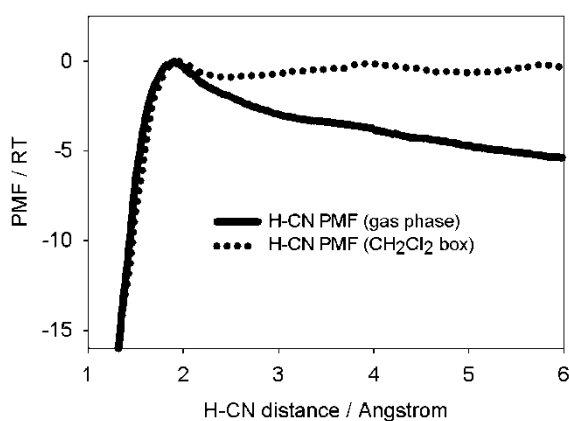


Figure 6: Plot of the PMF along the H-CN abstraction coordinate for (R2) in the gas phase, and solvated in a CH₂Cl₂ box

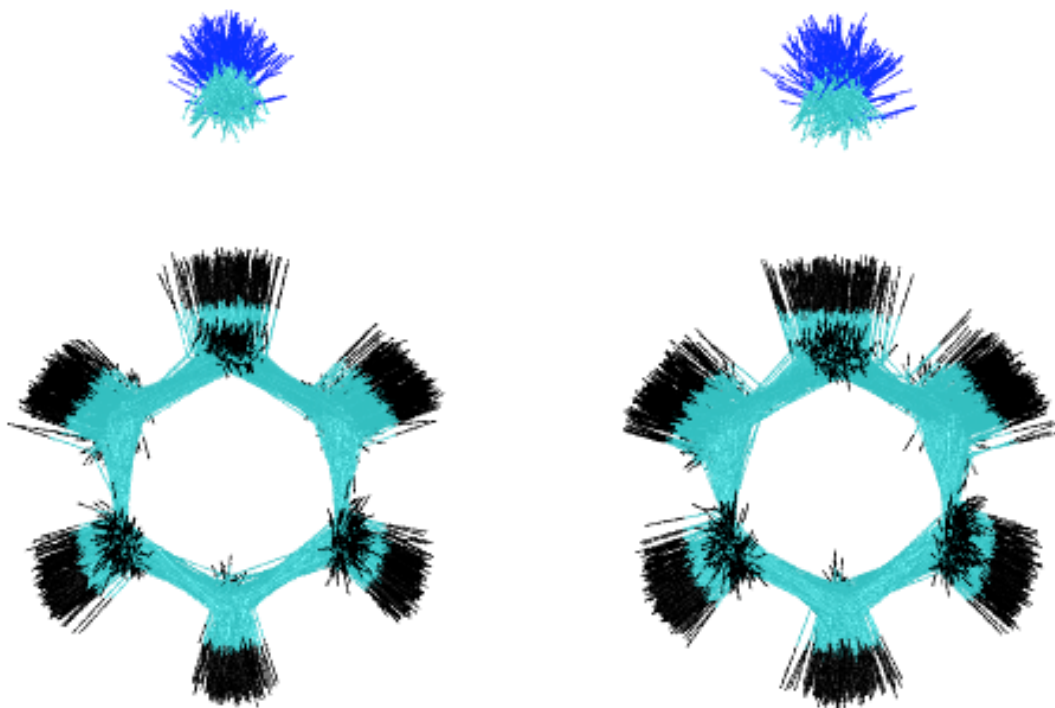


Figure 7: Superpositions of the ensemble of CN + *c*-C₆H₁₂ geometries at the point where they pass over their gas and solution phase free energy barriers. The left and right hand structures respectively correspond to the gas and solution phases. Their similarity explains in part why, at short times, the gas phase reaction specificity is similar to that in solution phase. The figures also shed light on the origin of the bend excitation, since the relative orientation of the CN with respect to *c*-C₆H₁₂ carves out a large range of H-CN angles.

Figure 8 shows normalized distributions of the energy deposition into the HCN degrees of freedom within the first picosecond following passage over the solution phase variational TS shown in Figure 6. The distributions are statistically identical to the corresponding CN + *c*-C₆H₁₂ gas phase distributions shown in Figure 4, consistent with the state specific vibrational excitation reported from our experimental studies,¹³ which show that HCN forms preferentially with $\nu = 1$ in the CH stretch and HCN bend excitation up to $\nu = 2$.

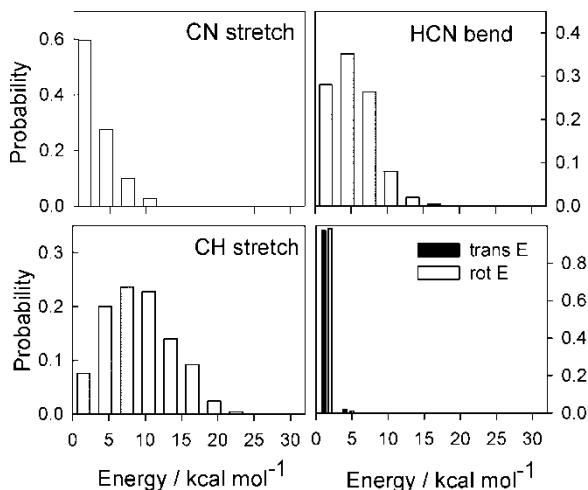


Figure 8: normalized distributions of energy deposited into each HCN degree of freedom for the (R2) solution phase classical dynamics carried out using the Eq 2 analytical Hamiltonian in CHARMM. Results have been placed into bins with a width of 3 kcal mol⁻¹

While the short-time vibrational energy deposition is essentially identical in both gas and solution phase owing to similarities in the post TS free energy profile in Figure 6, the same is not true for the time-dependent mode energies, which are shown in Figure 9 for the nascent HCN in the solution phase simulations (and Fig. 5 for the gas-phase calculations). Figure 9 clearly shows again that the average energy in each normal mode of the nascent HCN is similar to that in the corresponding gas phase reaction at very short times. At longer times, however, energy is dissipated to the solvent degrees of freedom. One of the most unexpected features of the data shown in Figure 9 is the fact that the energy decay profiles in each mode show distinct timescales – a fast decay at short times, and a slower decay at long times.

A comparison of the results obtained for HCN relaxation following on from $\nu \sim 1$ CH stretch excitation in neat solvent versus CH stretch relaxation in HCN following (R2) in the same solvent is shown in Figure 10. To a good approximation, the decay of CH excitation averaged over the ensemble of trajectories in the free CH₂Cl₂ solvent follows an exponential decay, which has been pointed out in other studies:¹²

$$\frac{\langle E_\nu(t) \rangle - \langle E_\nu(\infty) \rangle}{\langle E_\nu(0) \rangle - \langle E_\nu(\infty) \rangle} = \exp(-t/\tau) \quad (13)$$

where $\langle E_\nu(t) \rangle$ is the average energy at time t in mode ν (here the CH stretch), $\langle E_\infty(t) \rangle$ is the average equilibrium energy in mode ν (taken to be kT based on the equipartition principle), and $\langle E_\nu(0) \rangle$ is the average energy at $t = 0$. Using Eq 13, the decay of CH energy for HCN in a

periodic box of neat CH_2Cl_2 gives a value of $\tau \sim 736 \pm 531$ ps. The CH energy profile in Figures 9 and 10 was fit with a biexponential decay analogous to Eq 12 – i.e.:

$$\frac{\langle E_v(t) \rangle - \langle E_v(\infty) \rangle}{\langle E_v(0) \rangle - \langle E_v(\infty) \rangle} = A \exp(-t/\tau_1) + B \exp(-t/\tau_2) \quad (14)$$

where τ_1 and τ_2 are the respective time constants for decay at short times and long times, and A and B are constrained so that they sum to unity. Using Eq (14), the fitted value of the time constant for long-time decay for the CH stretch mode, τ_2 , has a value of $\sim 204 \pm 33$ ps, in close agreement with the experimental decay time constants of 144 ± 8 ps obtained from IR pump-probe experiments carried out on HCN in CH_2Cl_2 and ~ 1.0 M C_6H_{12} .¹³ The time constant for short-time decay, τ_1 , has a value of $\sim 7 \pm 0.2$ ps, more than an order of magnitude faster than τ_2 .

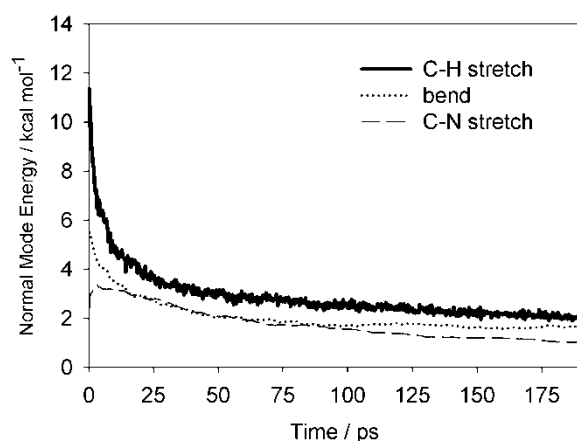


Figure 9: Time-dependent vibrational mode energies in the nascent HCN following abstraction of a hydrogen atom from $c\text{-C}_6\text{H}_{12}$ in the solution phase simulations. Results shown are averaged over 250 reactive trajectories.

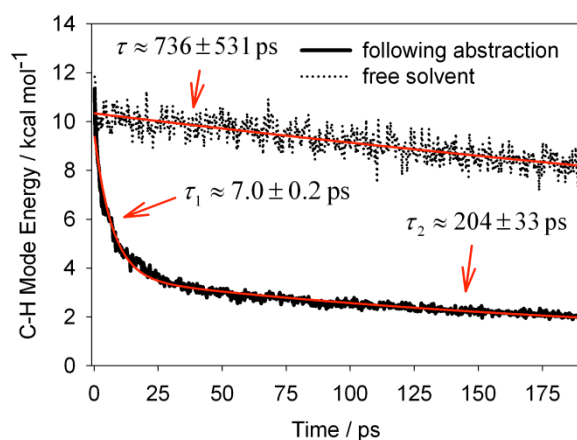


Figure 10: comparison of the relaxation of the CH stretch mode energy in HCN (1) following abstraction of a hydrogen atom from C_6H_{12} in CH_2Cl_2 solvent, and (2) following $\nu \sim 1$ excitation of the CH stretch mode in free CH_2Cl_2 solvent. For each curve, the results shown are averaged over 250 trajectories.

The observation of multiexponential vibrational energy decay in the product HCN after reaction in solution is intriguing. In the gas phase, intramolecular vibrational energy redistribution (IVR) can follow a complicated time course. In the present case, the gas phase and solution results suggest that the HCN product does not display significant IVR on the timescales considered here. The difference in the HCN energy relaxation profiles shown in Figure 10 arises because of time dependent energy relaxation efficiencies for HCN as it diffuses away from its *c*-C₆H₁₁ co-product into the bulk CH₂Cl₂ solvent. At short times, energy relaxation of the nascent HCN is extremely efficient given its proximity to *c*-C₆H₁₁, which serves as an efficient acceptor of the vibrational energy in the nascent HCN, and also facilitates fast energy transfer to the solvent. As the HCN and *c*-C₆H₁₁ diffuse away from one another through the CH₂Cl₂ solvent matrix, HCN energy relaxation to the solvent bath becomes less efficient, more closely resembling the relaxation decay profiles for isolated HCN in CH₂Cl₂. This explanation is qualitatively compatible with Fermi's Golden Rule – with the caveat that the density of accepting states for the HCN vibrational energy is effectively time dependent. A detailed analysis of these effects is beyond the scope of the present paper, but a combined theoretical and experimental analysis will be presented in a subsequent publication.⁴⁶

Conclusions

In this work, we report the first theoretical studies of post transition state dynamics for H atom abstractions of CN + polyatomic species. Using high-level electronic structure theory, a reparameterized density functional, a newly developed analytic reactive PES, and a recently implemented rare-event acceleration algorithm, we carried out both quasi-classical and classical non-equilibrium molecular dynamics simulations to investigate the reaction of CN with propane and cyclohexane in the gas phase and in a CH₂Cl₂ solvent. The results suggest that the solvent perturbations to the reactive free energy surface are small. This leads to very similar post-reaction product energy partitioning in both the gas and the solvent. In both sets of simulations, the nascent HCN is formed with vibrational excitation in both its CH stretching and HCN bending coordinates. The similarity in the energy deposition arises in part because of the similarity in the distributions of molecular geometries at the respective gas and solution phase variational association transition states, suggesting the utility of Polanyi type rules in qualitatively rationalizing the early time dynamical outcomes of solution phase

bimolecular reactions for polyatomic species. This study highlights the fact that non-equilibrium energy distributions following solution phase bimolecular reactions may persist for hundreds of picoseconds, despite frictional damping. In addition to the reactive solution phase dynamics, we also carried out non-equilibrium MD simulations for HCN in CH_2Cl_2 , and show that the HCN energy decay profile shows notable differences compared to HCN which is formed from a chemical reaction. We note that all the dynamics calculations performed in this work use either classical or quasi-classical trajectory propagation. This approach is not expected to yield quantitative agreement with experiment, even if an exact potential energy had been used. Nevertheless, the good agreement with experiment for the observed degree of vibrational excitation in the nascent products, and for the rate of decay by coupling to solvent, suggest that this classical approach captures the essential physics of vibrational energy transfer very well.^{11,12,47}

Within the molecular modeling community, the most widely used approaches for studying condensed phase chemical kinetics utilize thermostatted equilibrium MD, canonical rate theory, and Monte-Carlo Sampling. The implicit assumption with all of these approaches is that the timescales on which chemical reactions occur are much slower than (and consequently decoupled from) thermalization timescales. The present study shows that energy transfer in the post transition state region is in fact relatively slow, and, by microscopic reversibility, this must be true in the pre-transition state region for reactions similar to the reverse of that studied here. For the present system, none of the modeling suggests that the rate of the elementary chemical reaction being studied would deviate from that predicted by a statistical rate theory. However, non-thermal energy distributions as formed in the post transition state region might lead to breakdown of statistical theory for a hypothetical subsequent step. In this context, further theoretical and experimental studies will help unravel the extent to which such non-equilibrium dynamical effects are significant in other condensed phase chemical reactions of the sorts encountered in, e.g., biochemistry and synthetic chemistry.

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