

## Energy Profile for a Nonconcerted S<sub>N</sub>2 Reaction in Solution

Jayaraman Chandrasekhar\* and William L. Jorgensen\*

Department of Chemistry, Purdue University  
West Lafayette, Indiana 47907

Received November 13, 1984

Gas-phase experiments have contributed significantly to the current revival of interest in solvent effects on bimolecular substitution reactions.<sup>1,2</sup> These investigations have provided striking evidence of the profound influence of solvation on rates and orders of nucleophilicity for S<sub>N</sub>2 reactions of anions with alkyl halides.<sup>1</sup> The kinetic data and quantum mechanical calculations<sup>2c,3</sup> have also revealed that the gas-phase reactions have double-well energy surfaces featuring ion-dipole complexes as minima. In contrast, the detailed shapes of the energy surfaces for these important reactions in solution are largely a matter of conjecture. Unimodal, concerted profiles without intermediates are widely assumed in the literature.<sup>1,2</sup>

Determination of reaction surfaces in solution is necessary for the refinement of mechanistic ideas on chemical reactivity. On the theoretical side, a significant advance was made in our recent report of the first a priori calculation of the free energy of activation profile for the S<sub>N</sub>2 reaction of Cl<sup>-</sup> + CH<sub>3</sub>Cl in water.<sup>4</sup> This example turned out to be closely consistent with the traditional unimodal picture, a finding subsequently supported by extended RISM calculations.<sup>5</sup> The loss of the ion-dipole complexes as minima follows from the relative strength of the water-chloride ion interactions. Switching to a solvent with diminished anion solvating ability should reduce the energy increase accompanying desolvation of the nucleophile. This could reintroduce the ion-dipole complexes as intermediates and, therefore, yield a nonconcerted reaction profile.<sup>4b</sup> Hydrocarbon solvents would be promising; however, they are experimentally unrealistic for solubility reasons. Consequently, we chose to determine the reaction profile in dimethylformamide (DMF). Such dipolar aprotic solvents are common media for anion-molecule S<sub>N</sub>2 reactions and typically provide rate increases of ca. 10<sup>5</sup> over aqueous conditions.<sup>1,2</sup> The expectations on the reaction profile were confirmed as presented here.

Intermolecular potential functions that provide excellent descriptions of the structures and properties of liquid amides in Monte Carlo (MC) statistical mechanics calculations have recently been reported.<sup>6</sup> For DMF at 25 and 100 °C, average errors of 1% for the heats of vaporization and densities were obtained.<sup>6</sup> The potential functions are in the usual Coulomb plus Lennard-Jones form that was also used for Cl<sup>-</sup> + CH<sub>3</sub>Cl in water.<sup>4</sup> In the latter case, the variations in charges and Lennard-Jones parameters for the substrate along the reaction path were determined from extensive quantum-mechanical studies of ClCH<sub>2</sub>Cl...H<sub>2</sub>O clusters.<sup>4</sup> For the simulation in DMF, the parameters reported previously for the substrate<sup>4</sup> and DMF<sup>6</sup> have been adopted. The transfer-

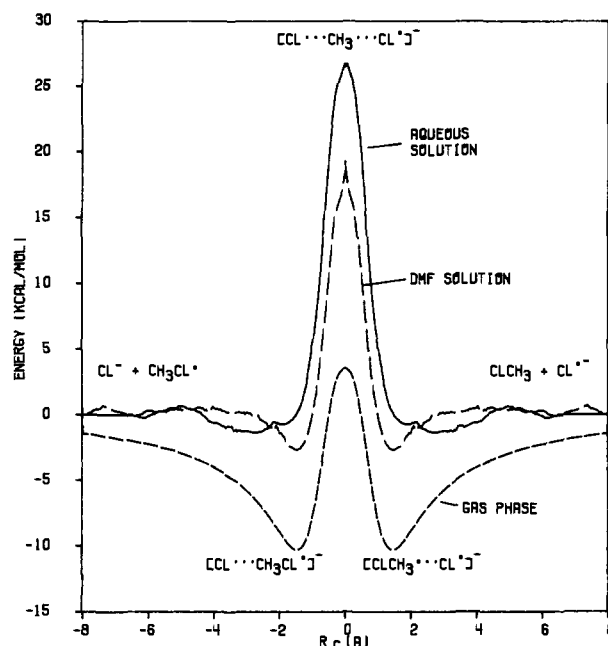


Figure 1. Calculated internal energies in the gas phase (short dashes) and the potential of mean force in DMF (long dashes) and in aqueous solution (solid curve) for the reaction of Cl<sup>-</sup> with CH<sub>3</sub>Cl as a function of the reaction coordinate,  $r_c$ , in angstroms.

ability was tested in part by performing an MC simulation for Cl<sup>-</sup> plus 128 DMF molecules using periodic boundary conditions and Metropolis and preferential sampling.<sup>7</sup> The computed enthalpy of solution for the chloride ion of  $-67 \pm 3$  kcal/mol at 25 °C and 1 atm compares favorably with the experimental estimate of  $-76$  kcal/mol, which has an uncertainty of ca.  $\pm 10$  kcal/mol.<sup>7,8</sup>

The procedure used for computing the free energy of activation profile for the reaction in DMF is analogous to the previous calculation in water.<sup>4</sup> The system consisted of the substrate plus 180 DMF molecules in a rectangular solid (ca.  $25 \times 25 \times 38$  Å) with periodic boundary conditions. Only the minimum-energy reaction path for the gas phase featuring collinear, backside displacement has been solvated. A series of seven MC simulations with importance<sup>9</sup> and preferential sampling were executed to span the reaction coordinate out to  $\pm 10$  Å. The reaction coordinate ( $r_c$ ) is defined as the difference between the two C-Cl distances; this enforces symmetry about the transition state. Both harmonic and exponential biasing functions were used for the importance sampling. The run for each of the seven "windows" consisted of an equilibration phase of at least  $10^6$  configurations followed by averaging over an additional  $2 \times 10^6$  configurations in the NPT ensemble at 25 °C and 1 atm. The relative probability of occurrence of values of  $r_c$ ,  $g(r_c)$ , was determined in each window. The results were spliced together at overlapping points to yield an overall  $g(r_c)$ . The "potential of mean force" is then given by  $w(r_c) = -kT \ln g(r_c)$ , and this provides an approximation to the transition state theory free energy of activation.

The free energy of activation profiles computed for the reaction in water and DMF are compared in the Figure 1. The gas-phase energy curve computed at the 6-31G\* level is also shown and is consistent with experimental data.<sup>4</sup> The free energy of activation minima would be less deep in the gas phase, ca.  $-5$  kcal/mol.<sup>4</sup> The ion-dipole minima are still clearly apparent in DMF, the well depth is  $-2.7$  kcal/mol with a barrier of 3.3 kcal/mol to dissociation. The computed maxima of the free energy of activation profiles,  $26.3 \pm 0.5$  kcal/mol in water and  $19.3 \pm 0.5$  kcal/mol

- (1) (a) Dougherty, R. C.; Roberts, J. D. *Org. Mass Spectrom.* **1974**, *8*, 77. (b) Dougherty, R. C. *Ibid.* **1974**, *8*, 85. (c) Bohme, D. K.; Mackay, G. I.; Payzant, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 4027. (d) Brauman, J. I.; Olmstead, W. N.; Lieder, C. A. *Ibid.* **1974**, *96*, 4030. (e) Olmstead, W. N.; Brauman, J. I. *Ibid.* **1977**, *99*, 4219. (f) Pellerite, M. J.; Brauman, J. I. *Ibid.* **1980**, *102*, 5993.
- (2) (a) Caldwell, G.; Magnera, T. F.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 959. (b) Magnera, T. F.; Caldwell, G.; Sunner, J.; Ikuta, S.; Kebarle, P. *Ibid.* **1984**, *106*, 6140. (c) Carrion, F.; Dewar, M. J. S. *Ibid.* **1984**, *106*, 3531. (d) Shaik, S. S. *Ibid.* **1984**, *106*, 1227. (e) Bohme, D. K.; Mackay, G. I. *Ibid.* **1981**, *103*, 978. (f) Bohme, D. K.; Raksit, A. B. *Ibid.* **1984**, *106*, 3447. (g) Henschman, M.; Paulson, J. F.; Hierl, P. M. *Ibid.* **1983**, *105*, 5509.
- (3) (a) Dedieu, A.; Veillard, A. In "Quantum Theory of Chemical Reactions"; Daudel, R.; Pullman, A.; Salem, L.; Veillard, A., Eds.; D. Reidel Publishers: New York, 1979; Vol. 1, p 69. (b) Wolfe, S.; Mitchell, D. J.; Schlegel, H. B. *J. Am. Chem. Soc.* **1981**, *103*, 7692, 7694. (c) Morokuma, K. *Ibid.* **1982**, *104*, 3732. (d) Urban, M.; Cernusak, I.; Kello, V. *Chem. Phys. Lett.* **1984**, *105*, 625.
- (4) (a) Chandrasekhar, J.; Smith, S. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1984**, *106*, 3049; (b) *Ibid.* **1985**, *107*, 154.
- (5) Chiles, R. A.; Rossky, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 6867.

- (6) Jorgensen, W. L.; Swenson, C. J. *J. Am. Chem. Soc.* **1985**, *107*, 569.  
(7) Chandrasekhar, J.; Spellmeyer, D. C.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1984**, *106*, 903.

- (8) (a) Bockris, J. O'M.; Reddy, A. K. N. In "Modern Electrochemistry"; Plenum Press: New York, 1970; Vol. 1, Chapter 2, p 106. (b) Cox, B. G.; Hedwig, G. R.; Parker, A. J.; Watts, D. W. *Aust. J. Chem.* **1974**, *27*, 477.  
(9) Patey, G. N.; Valleau, J. P. *J. Chem. Phys.* **1975**, *63*, 2334.

in DMF, may be compared with experimental values of 26.6 and 22.7, respectively.<sup>10,11</sup> However, the latter figure appears too high by 2-3 kcal/mol on the basis of correlations for a series of halide ion plus methyl halide reactions.<sup>11</sup> The simulation results show the correct trends in reactivity and that the rate retardation in solution is due to the expected preferential stabilization of the reactants over the more charge-delocalized transition state. Though the comparison with experiment is favorable, it should be emphasized that computational resources have not yet permitted us to include intramolecular vibrational effects or to explore the full multidimensional reaction surface in solution. However, the present results are consistent with the notion that the lowest energy reaction path in the gas phase may not be seriously perturbed in solution for the present case; certainly the stereochemistry is well-known to be the same.

The present results lead one to question the likelihood of concerted  $S_N2$  reactions in nonaqueous media, i.e., proceeding without the presence of intermediates.<sup>12</sup> Analyses of Brønsted plots for  $S_N2$  reactions in  $\text{Me}_2\text{SO}$  have also been recently interpreted in terms of a two-stage mechanism.<sup>13</sup> Obvious challenges are to define the optimal systems and conditions for occurrence of the ion-dipole complex and to directly detect the species in solution.<sup>14</sup>

(10) (a) Bathgate, R. H.; Moelwyn-Hughes, E. A. *J. Chem. Soc.* **1959**, 2642. (b) Alberty, W. J.; Kreevoy, M. M. *Adv. Phys. Org. Chem.* **1978**, *16*, 87.

(11) McLennan, D. J. *Aust. J. Chem.* **1978**, *31*, 1897.

(12) For discussion and definition of concertedness, see: Gilchrist, T. L.; Storr, R. D. In "Organic Reactions and Orbital Symmetry"; Cambridge University Press: Cambridge, 1972; p 5-9.

(13) Bordwell, F. G.; Cripe, T. A.; Hughes, D. L., unpublished results. See also: Hayami, J.; Tanaka, N.; Hihara, N.; Kaji, A. *Tetrahedron Lett.* **1973**, 385.

(14) Gratitude is expressed to the National Science Foundation and National Institutes of Health for support of this work. Computational assistance from J. D. Madura is also gratefully acknowledged.

## Dimer vs. Polymer Liquid Crystals: Alkyl Chain Flexibility via Deuterium NMR

Anselm C. Griffin

Department of Chemistry  
University of Southern Mississippi  
Hattiesburg, Mississippi 39406

Edward T. Samulski\*

Department of Chemistry and  
Institute of Materials Science U-136  
University of Connecticut  
Storrs, Connecticut 06208

Received February 11, 1985

Prolate, low molar mass mesogens—*monomeric liquid crystals* (MLCs)—can be readily functionalized and coupled to form oligomers of liquid crystals. In 1981 Griffin and Britt<sup>1</sup> showed that a flexible-center, "Siamese-twin" liquid crystal—a *dimer liquid crystal* (DLC) that is a precursor to *polymeric liquid crystals* (PLCs)—can be prepared by coupling two mesogenic cores with an aliphatic *spacer* chain. The textures and thermodynamic properties of several classes of DLCs have subsequently been reported.<sup>2</sup> Nematic melts of DLCs generally exhibit thermodynamic properties intermediate between those of MLCs and those of the corresponding PLCs. In particular, the oscillations in the nematic-isotropic transition temperature,  $T_{NI}$ , and the enthalpy and entropy of this transition with the number of me-

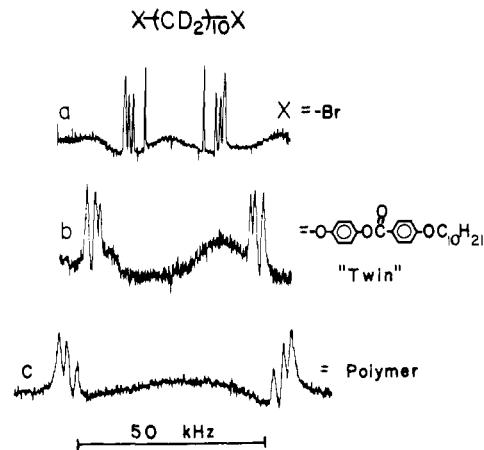
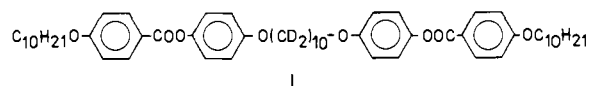


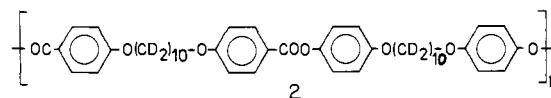
Figure 1.  $^2\text{H}$  NMR spectra of 1,10-disubstituted decane- $d_{20}$  chains; (a) and (b) are spectra of labeled solutes ( $\sim 2$  wt % in Merck Phase 5 at 300 K). Spectrum (c) is the polymer eutectic (see text) just below the  $T_{NI}$ .

thylenes in the spacer chain—the *even-odd* effect—are more exaggerated than that reported for corresponding MLCs approaching behavior characteristic of PLCs.<sup>1,2c,d</sup> In this paper we present a direct measurement of the spacer chain reorientation mobility in the nematic phases of a DLC and a PLC using deuterium NMR ( $^2\text{H}$  NMR). The temperature dependence of the quadrupolar splitting pattern of the labeled spacer chain in the DLC is similar to that reported for MLCs<sup>3</sup> while that exhibited by the PLC is fundamentally different. This observation implies that, despite the thermodynamic similarities of these two related classes of liquid crystals, in the DLC the conformational constraints on the spacer of the polymer precursor are considerably more relaxed than those operative in the polymer mesophase.

The DLC or "twin" mesogen **1** was prepared by reaction in



pyridine of 4-(*n*-decyloxy)benzoyl chloride with 4,4'-dihydroxy-1,10-diphenoxydecane- $d_{20}$  in a 2:1 molar ratio of acid chloride/bis(phenol). The deuterated bis(phenol) above was prepared from 1,10-dibromodecane- $d_{20}$ <sup>4</sup> by using a route previously described for the protonated analogue.<sup>5</sup> The corresponding PLC **2** was



prepared by the interfacial polycondensation reaction of 4,4'-dihydroxy-1,10-diphenoxydecane- $d_{20}$  and 4,4'-bis(chloroformyl)-1,10-diphenoxydecane- $d_{20}$  by a method described earlier.<sup>5</sup>

As the  $T_{NI} \approx 485$  K of the polymer is not accessible in the spectrometer, a eutectic mixture<sup>6</sup> of the related nematogen, *p*-phenylenebis(4-methoxybenzoate), and the labeled PLC (weight ratio 3:1 PLC/nematogen;  $T_{NI} \approx 455$  K) was studied. The  $^2\text{H}$  NMR spectra were recorded at 13.2 MHz after cooling the isotropic phases of the neat DLC **1** and the eutectic mixture containing the PLC **2** in the spectrometer. Macroscopically aligned uniaxial samples were rapidly produced ( $< 1$  minute) just below  $T_{NI}$  for both mesophases.

In nematic phases the DMR spectrum of a multiply labeled molecule is a superposition of quadrupolar splittings  $\Delta\nu_i$  the magnitudes of which reflect the efficacy of the molecular motion

(3) See, for example: Boden, N.; Clark, L. D.; Bushby, R. J.; Emsley, S. W.; Luckhurst, G. R.; Stockley, C. P. *Mol. Phys.* **1981**, *42*, 565.

(4) We thank Dr. D. Y. Yoon of the IBM Corporation, San Jose, CA, for a generous gift of this compound.

(5) Griffin, A. C.; Havens, S. J. *J. Polym. Sci., Polym. Phys. Ed.* **1981**, *19*, 969.

(6) Griffin, A. C.; Havens, S. J. *J. Polym. Sci., Polym. Lett. Ed.* **1980**, *18*, 259.

(1) Griffin, A. C.; Britt, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 4957.

(2) Blumstein, R. B.; Stickles, E. M.; Blumstein, A. *Mol. Cryst. Liq. Cryst.* **1982**, *82*, 205. (b) Blumstein, R. B.; Stickles, E. M. *Mol. Cryst. Liq. Cryst.* **1982**, *82*, 151. (c) Jin, J.-I.; Park, J.-H. *Mol. Cryst. Liq. Cryst.* **1983**, *92*, 149. (d) Emsley, J. W.; Luckhurst, G. R.; Shilstone, G. N.; Sage, I. *Mol. Cryst. Liq. Cryst.* **1984**, *102*, 223.