



Figure 6. Schematic representation of the triplet cyclopropylidene (**3**) → allene (**6**) interconversion and the isomerization of **6** by in-plane (**6** → [**12**] → **6**) and by rotation (**6** → [**13**] → **6**). Best estimated relative energies (kJ mol⁻¹): stable structures (●); transition structures (+).

6), it cannot lie on the lowest energy path from **14** to **6**. Rather, at some point between **14** and **6** before **12** is reached, torsion at one or both methylene groups must set in. It is of interest to note that if only one of the methylene groups rotates through 90° then **14** would convert to **13**. As **13** itself is a transition structure for geometric isomerization of **6**, it also cannot lie on the reaction coordinate **3** → [**14**] → **6**. As a consequence, each of the methylene groups must ultimately rotate through an angle of 90° but in an unsymmetrical fashion. By allowing the geometry to relax without symmetry constraints from **14** to **6**, it is apparent that the single most important factor is the relaxation of the C₁C₂C₃ angle. As a consequence, the C₁C₂C₃ bond system becomes almost linear (close to structure **12**) before rotation and rebending allow the equilibrium geometry **6** to be attained.

The preceding description of the conversion **3** → **6** is substantially different from that found by Pasto and co-workers,¹¹ who may have restricted their investigation to structures with C_s symmetry. Although they guessed that the C₁C₂C₃ angle of their transition structure was close to 88°, the value found for **14**, they found a rapid disrotatory motion around the transition structure to give a nonplanar structure followed by gradual flattening of the methylene group while ring opening continued to **6**. Their estimated barrier at the 4-31G level, 80 kJ mol⁻¹, is somewhat higher than that found in this investigation at the 3-21G level, 64 kJ mol⁻¹, or at the 6-31G level, 69 kJ mol⁻¹. Our best estimate for the barrier after inclusion of polarization functions and correction for changes in correlation energies and zero-point vibrational energies is 99 kJ mol⁻¹. Thus the conversion of cyclopropylidene to allene on the triplet potential energy surface is substantially more hindered than that on the singlet surface, the latter barrier being 48 kJ mol⁻¹.

Concluding Remarks

Ab initio calculations with gradient techniques and inclusion of correlation have revealed the detailed mechanisms of the cyclopropylidene → allene conversion on both the singlet and triplet potential energy surfaces. The singlet reaction has an activation energy of 48 kJ mol⁻¹. The reaction coordinate branches prior to passage over chiral and enantiotopic transition structures. Elucidation of the transition structures (**10** and **10'**) has enabled a rationale to be presented for the high degree of stereoselectivity on the basis of steric factors observed for the conversion of anti-substituted cyclopropylidenes to allenes, and for the very low degree of stereoselectivity observed in the case of syn substitution. The analogous reaction of triplet cyclopropylidene is hindered by a higher barrier, 99 kJ mol⁻¹. Here the transition structure (**14**) is reached by means of a nonrotatory but unsymmetrical rupture of the bond opposite to the carbene site.

Registry No. Cyclopropylidene, 2143-70-6; allene, 463-49-0.

Generalization of the Born Equation to Nonspherical Solvent Cavities

Joel I. Gersten[†] and Anne Marie Sapse*

Contribution from the Department of Physics, City College of the City University of New York, New York, New York 10031, and the Science Department, John Jay College of the City University of New York, New York, New York 10031. Received August 30, 1984

Abstract: Solvent effects on the methylamine-acetic acid complex are studied by embedding the molecule in a spheroidally shaped cavity and employing the generalized Born equation. The solvent effect is found to stabilize the zwitterion but not enough to make it more stable than the neutral complex.

I. Introduction

Lack of agreement between gas-phase calculations and experimental solution data is probably due to the solute-solvent interaction. For a charged solute in a polar solvent the Born equation¹ approximates this interaction by placing the solute molecule in a spherical solvent cavity. The ion is idealized as a point particle at the center of a sphere. The solvent is treated as a continuum whose electrical properties are embodied in its dielectric constant, ϵ . The electrostatic hydration energy is then given by

$$U = -\frac{Q^2}{2a} \left[1 - \frac{1}{\epsilon} \right] \quad (1)$$

where Q is the solute's net charge and a is the radius of the spherical cavity. This formula has been applied to numerous problems of practical interest in the literature.² Two sources of error in this expression are first that the solute molecule, in reality, consists of a distribution of charge corresponding to the distorted atomic charge clouds positioned around the atomic locations in

(1) Born, M. *Phys. Z.* **1920**, *1*, 45.

(2) See, for example: Aue, B. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 318.

[†] City College of the City University of New York.

* John Jay College of the City University of New York.

space and second that many molecules or molecular complexes are not spherical and as such should not be necessarily put in a spherical solvent cavity.

The first of these difficulties has been addressed by numerous authors³ over the years. In our previous work⁴ we approximated the molecular charge distribution by calculating the Mulliken charge population on atoms in the framework of the Hartree-Fock approximation using Gaussian basis sets. The resulting set of discrete charges was then put inside a spherical cavity. Then, following a simple procedure,⁴ we expanded the interaction energy in an infinite series of Legendre polynomials which describe the monopole, dipole, quadrupole, octupole, and higher poles effects and used

$$U = \frac{1}{2} \sum_{n=0}^{\infty} \frac{(n+1)(1-\epsilon)}{n+(n+1)\epsilon} \sum_{j=1}^N \sum_{k=1}^N Q_j Q_k \frac{(r_j r_k)^n}{a^{2n+1}} P_n(\bar{r}_j \bar{r}_k) \quad (2)$$

where Q_j denotes the net charge on the j th atom, N is the total number of atoms, and \bar{r}_j locates the j th atom in space. This method, applied to the determination of the basicity of a series of amines⁴ as well as to other systems such as the OH^- solvation in water and the Lithium affinities of some bases,⁵ leads to an improved agreement with experiment as well as to a better understanding of the phenomena involved.

In this work, we address ourselves to the second aforementioned approximation. Indeed, many systems are far from spherical: some are planar, in many cases fitting better inside an oblate spheroidal cavity; some are quasilinear, fitting better inside a prolate spheroidal cavity. The problem of solvation energy of a distribution of charge in spheroidal and ellipsoidal cavities has been studied by several research groups.⁶ The example treated in this work is the methylamine-acetic acid complex. In a previous work one of the authors and co-worker⁷ studied, using quantum mechanical Hartree-Fock calculation, some amino acid-amino acid interactions, modeled by guanidium (for arginine) and methylamine (for lysine) hydrogen bonded to a formate ion or an acetate ion as a model for the carboxyl groups on amino acid residues. The questions answered for gas-phase calculations in that work were primarily if the zwitterion complex is more stable than the neutral-neutral species complex or vice versa and secondly if there is a barrier to the proton transfer from one species to the other. Such data are relevant for a series of biochemical problems, some at the molecular level of vision and some for enzymatic reactions. It was found that while the guanidium formate ion complex is a zwitterion, the methylamine-acetic acid complex is neutral. These results are significant for hydrophobic pockets in enzymes. However, in aqueous media the water-complex interaction could reverse the conclusion arrived at in the gas phase. Consequently, the water interaction is described by placing the methylamine-acetic acid as zwitterion and as neutral-neutral species in a nonspherical cavity and the energy is calculated. Note that if the simple Born equation given by eq 1 were to be applied, the interaction would vanish since there is no net charge in either complex. Our calculation takes into account all higher-order pole effects as well as the physical shape of the molecule.

II. Theory

In order to describe precisely how the calculation is performed, let us briefly review the theory.⁶ Let the molecule be composed of N point charges Q_j located at the positions \bar{r}_j inside a spheroidal cavity in the solvent. Let the semimajor and semiminor axes of the

cavity will be denoted by a and b , respectively, and let $f = (a^2 - b^2)^{1/2}$ and $\xi_0 = a/f$. One wishes to calculate the strength of the electrostatic interaction between the molecule and the solvent. The solvent is characterized as a dielectric liquid with static dielectric constant ϵ .

The interaction energy is obtained from the expression

$$U = (1/2) \sum_{j=0}^N Q_j \Phi_j \quad (3)$$

where Φ_j is the potential at the position of the j th ion due to the other ions and the induced charge on the surface of the cavity. Φ_j may be determined by solving the Poisson equation and matching boundary conditions on the surface. The result is⁶

$$U = \frac{1}{2} \left[\frac{1}{\epsilon} - 1 \right] \sum_{n=0}^{\infty} \sum_{m=0}^n \frac{F_n^m}{\Delta_n^m} [(\gamma_n^m)^2 + (\sigma_n^m)^2] \quad (4)$$

Here γ_n^m and σ_n^m are generalized multipole moments defined by

$$\gamma_n^m = \sum_{j=1}^N Q_j P_n^m(\xi_j) P_n^m(\eta_j) \cos m\phi_j \quad (5a)$$

$$\sigma_n^m = \sum_{j=1}^N Q_j P_n^m(\xi_j) P_n^m(\eta_j) \sin m\phi_j \quad (5b)$$

where ξ_j , η_j , ϕ_j are the prolate spheroidal coordinates of the j th ion, and

$$F_n^m = \frac{1}{f} [2 - \delta_{m,0}] (-)^m (2n+1) \left[\frac{(n-m)!}{(n+m)!} \right]^2 \quad (6)$$

and

$$\Delta_n^m = \frac{P_n^m(\xi_0)}{Q_n^m(\xi_0)} - \frac{1}{\epsilon} \frac{[P_n^m(\xi_0)]'}{[Q_n^m(\xi_0)]'} \quad (7)$$

Here $P_n^m(\xi_0)$ and $Q_n^m(\xi_0)$ are associated Legendre functions of the first and second kind, respectively.

In evaluating the electrostatic energy some care must go into selecting the cavity dimensions into which the molecule will fit. Our procedure was as follows. We randomly selected values for the semimajor and semiminor axes a and b as well as the Euler angles defining the orientation of the cavity relative to the molecule and the position coordinates of the center of the cavity. If the molecule fit inside the cavity, the cavity was deemed an acceptable candidate for consideration. A search was made for the cavity with minimum surface area which would enclose the molecule. The reason for wanting minimum area is that this would minimize the surface energy associated with the cavity formation. The walls of the cavity were kept a van der Waals radius away from the ions of the molecule in order to account for the steric repulsion of the atoms. Comparing eq 4 and 2 we see that the result for the spheroidal cavity is complicated by the fact that a summation over contributions from the individual azimuthal indices " m " is required. This is as expected, since the rotational symmetry of the spherical cavity has now been degraded to an axial symmetry of the spheroidal cavity. Another way of stating this is that now the energy of interaction depends sensitively on the orientation of the molecule relative to the axis of the cavity.

In this paper we will focus our attention primarily on a prolate spheroidal cavity. The case of an oblate spheroidal cavity may be obtained from this case by noting that the parameters ξ_0 and f become imaginary numbers if $b > a$. The same formulas that were derived are applicable, one need only continue them into the complex plane.

The charges on the atoms were obtained from Mulliken population calculations with the 6-31G* basis set,⁸ as implemented by the GAUSSIAN 80 program.⁹

(3) Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351, 713. Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486. Dogonadze, R. R.; Kornyshev, A. A. *Phys. Status Solidi B* **1972**, *53*, 439; **1973**, *55*, 843. Dogonadze, R. R.; Kornyshev, A. A. *J. Chem. Soc., Faraday Trans. 2* **1974**, *70*, 1121. Friedman, H. L. *Mol. Phys.* **1975**, *29*, 1533. Schmidt, P. P. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 703. For a recent review see: Tapia, O. In "Molecular Interactions"; Rajtajczak, H., Orville-Thomas, W. J., Eds.; Wiley: New York, 1982; p 47.

(4) Gersten, J. I.; Sapse, A. M. *J. Phys. Chem.* **1981**, *85*, 3407.

(5) Gersten, J. I.; Sapse, A. M. *J. Comput. Chem.*, in press.

(6) Harrison, S. W.; Nolte, H. J.; Beveridge, D. L. *J. Phys. Chem.* **1976**, *80*, 2580. Felder, C. E. *J. Chem. Phys.* **1981**, *75*, 4679. Rinaldi, D.; Ruiz-Lopez, M. F.; Rivail, J. L. *J. Chem. Phys.* **1983**, *78*, 834.

(7) Sapse, A. M.; Russell, C. S., to be published.

(8) Hariharm, B. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(9) Brinkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; DeFrees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. GAUSSIAN 80, Department of Chemistry, Carnegie-Mellon University, Pittsburgh, PA 15213.

Table I. Electrostatic Energies for Methylamine–Acetic Acid Zwitterion (A) and Neutral–Neutral Species (B), for a Cavity with $a = 5.43 \text{ \AA}$ and $b = 4.22 \text{ \AA}$

N	$U(A)$ (kcal/mol)	$U(B)$ (kcal/mol)
2	-5.67	-0.76
3	-7.47	-2.07
4	-9.04	-2.21
5	-9.27	-2.31
6	-9.29	-2.33
7	-9.31	-2.37
8	-9.33	-2.40
9	-9.36	-2.42
10	-9.36	-2.44
11	-9.36	-2.44
12	-9.36	-2.44

Table II. Electron Populations and Coordinates for the Two Molecules

j	Q_j	X_j (Å)	Y_j (Å)	Z_j (Å)
Zwitterion (A)				
1	7.85	0	0	0
2	0.52	0	0	1.01
3	0.52	0.97	0	-0.30
4	6.37	-0.66	1.22	-0.49
5	0.75	-0.13	2.10	-0.13
6	0.79	-0.67	1.23	-1.57
7	0.79	-1.69	1.26	-0.13
8	0.58	-0.40	-0.87	-0.30
9	5.26	2.50	0	1.45
10	8.75	1.53	0	2.19
11	8.74	2.67	0	0.24
12	6.54	3.89	0	2.10
13	0.84	4.43	0.89	1.79
14	0.86	3.78	0	3.18
15	0.84	4.43	-0.89	1.79
Neutral–Neutral Species (B)				
1	7.94	0	0	0
2	0.59	0	0	1.00
3	6.28	-0.97	0.95	-0.56
4	0.82	-0.73	1.96	-0.23
5	0.83	-0.93	0.92	-1.64
6	0.85	-1.97	0.70	-0.23
7	0.66	-0.33	-0.93	-0.19
8	5.25	2.41	0	2.04
9	8.58	1.34	0	2.54
10	8.75	2.70	0	0.73
11	6.56	3.65	0	2.93
12	0.81	4.25	88	2.73
13	0.80	3.35	0	3.97
14	0.81	4.25	-0.88	2.73
15	0.47	1.85	0	0.27

III. Results

In Table I we compare the electrostatic energy of the methylamine–acetic acid zwitterion (A) and neutral–neutral complex (B) for a cavity with $a = 5.43 \text{ \AA}$ and $b = 4.22 \text{ \AA}$. Values of U are given for various values of N , the largest value of N appearing in a truncated version of eq 4, in order to show the convergence. We note that significant contributions come from the first four multipoles. A table of ionic charges and coordinates for these

Table III. Electrostatic Energies for Zwitterion (A) and Neutral–Neutral Species (B), for a Cavity with $a = 4.43 \text{ \AA}$ and $b = 3.21 \text{ \AA}$

N	$U(A)$ (kcal/mol)	$U(B)$ (kcal/mol)
2	-11.57	-1.64
3	-17.77	-6.04
4	-24.57	-6.75
5	-26.25	-7.19
6	-26.83	-7.61
7	-27.22	-8.44
8	-27.87	-9.54
9	-28.14	-10.40
10	-28.37	-11.64
11	-28.49	-12.17
12	-28.54	-12.95

molecules is given in Table II. Note that the zwitterion, which has more charge separation than the neutral–neutral complex, also has the stronger electrostatic interaction with the cavity.

This conclusion remains unchanged if the dimensions of the cavity are changed. In Table III we repeat the results of Table I but for $a = 4.43 \text{ \AA}$ and $b = 3.21 \text{ \AA}$. Two facts are to be noted for this smaller cavity. The first is that the size of the electrostatic interaction is larger than it was in Table I. The other is that the contributions from the higher order multipoles are more significant and hence the convergence of the summation is slower. The result that the molecule with the greater charge separation has the greater interaction, however, remains the same.

In this paper we have considered two molecules, the zwitterion and the neutral–neutral complex associated with the methylamine–acetic acid complex. This case was somewhat special in that the size and shape of the cavity was identical for both molecules. In a more general situation we might be comparing molecular conformations for which the sizes and shapes were different. As long as both molecules could be encapsulated in a spheroidal cavity the present theory would be applicable. However, in discussing the energetics of the problem one must then take into account the surface energy of the cavity, which is the energy per unit area, σ_s , multiplied by the surface area. Thus the surface energy is

$$R_s = 2\pi\sigma_s(\xi_0^2 - 1)^{1/2}[\sin^{-1}(1/\xi_0) + \xi_0^{-1}(1 - \xi_0^{-2})^{1/2}] \quad (8)$$

For a sphere whose radius is 4 \AA in water at $20 \text{ }^\circ\text{C}$, this energy is roughly 21 kcal/mol . The difference in U_s for two configurations can help stabilize one or another of the configurations, just as the Coulomb contribution to the solvation energy can.

Examining the tables one notices that the zwitterion acquires in solution an extra Coulombic stability between 7 and 15 kcal/mol. When these values are compared to the extra stability of the neutral–neutral complex in the gas phase, found to be 18.39 kcal/mol at the 6-31G* level of calculations, it is to be presumed that in solution the neutral–neutral complex will be as stable as the zwitterion.

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Registry No. Methylamine, 74-89-5; acetic acid, 64-19-7.