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Gas phase reactions of dianions. 2. The effect of a second charge on S_N2 potential energy surfaces: an ab initio study

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Abstract

Ab initio calculations have been used to investigate the S_N2 reactions of model dianions with methyl bromide. Two dianion models were used. Model **A** consists of a series of ω-alkoxy carboxylates with charge separations of 5, 10, and 15 Å. Model **B** employs complexes of acetate and fluoride where the two anions are held at fixed separations of 5, 10, 15, 20, 25, and 30 Å. In each case, the carboxylate is used as the nucleophile in the S_N2 process. The results indicate that for initial charge separations of 15 Å or more, the second charge has only a modest effect on the barrier (<2.5 kcal/mol) and geometry (<0.04 Å) of the S_N2 transition state relative to a singly charged analog (acetate + methyl bromide). Consequently, dianions with moderately long initial charge separations provide S_N2 reactivity that is very similar to that of singly charged analogs. In contrast, large effects (barrier reductions >10 kcal/mol) are seen in the reactions of dianions with short charge separations (<10 Å). (Int J Mass Spectrom 192 (1999) 185–190) © 1999 Elsevier Science B.V.

Keywords: Dianion; S_N2; Electrostatic repulsion; Coulomb potential

1. Introduction

The development of electrospray ionization has allowed chemists access to multiply charged ions in the gas phase [1–4]. A characteristic feature of gas phase polyions is a substantial destabilization due to intramolecular electrostatic repulsion [5,6]. The destabilization can be modeled by a coulomb potential (E_{rep}), where r_i represents the distances between the charged groups and ϵ_i is the effective dielectric [7–10]

$$E_{\mathrm{rep}} = \sum_{i=1,n} q^2/\epsilon_i r_i \qquad (1)$$

Recent computational work on dianions and dications has shown that an effective dielectric constant near unity is appropriate for the region between like charges [11]. Experimental studies of proton transfer behavior [7,8] as well as photoelectron spectroscopy of dianions [12] have also suggested effective dielectrics near unity. For doubly charged ions with $\epsilon_i = 1$, Eq. (1) simplifies to

$$E_{\mathrm{rep}} = 333/r \text{ kcal/mol} \qquad (2)$$

where r is the distance between charge centers in angstroms as shown in Scheme 1.

From Eq. (2) it is clear that internal electrostatic repulsion can have a very significant effect on the stability of a doubly charged ion. For example, the

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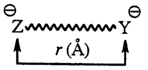
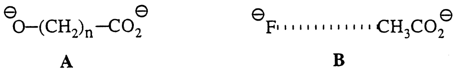


Scheme 1.



Scheme 2.

electrostatic repulsion in a dianion with $r = 10$ Å is approximately 33 kcal/mol. To put this in perspective, the electrostatic strain in this dianion is ~5 kcal/mol greater than the ring strain in cyclopropane! As a result, one might expect that coulomb repulsion would dominate the reactivity of doubly (multiply) charged ions. Obviously 20 kcal/mol or more of electrostatic repulsion will have a profound effect on the thermodynamics of the reactions of doubly charged ions, but the more important question is how does the electrostatic repulsion affect the kinetic reactivity of a doubly charged ion (relative to a singly charged analog). The importance of kinetic factors lies in the fact that doubly charged ions generally are studied under conditions where their reactions are irreversible so the rate constant is the only physically observable property. With the exception of hydration equilibria [13–15], experimental studies of gas phase dications and polycations have relied almost exclusively on kinetic factors for deducing thermodynamic properties such as ΔH_{acid} [7–10,16–22].

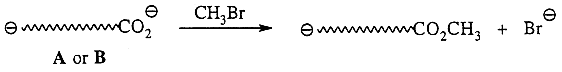
In a computational study of the proton transfer behavior of a dication, we have shown that the potential energy surface (E_{double}) can be modeled by superimposing a coulomb potential (E_{rep}) on the potential energy surface for the reaction of a singly charged analog (E_{single}) [23]

$$E_{\text{double}} = E_{\text{single}} + E_{\text{rep}} \tag{3}$$

In the present study, we have applied the same approach to a more complicated process, the S_N2 reaction of a dianion with methyl bromide. Two important questions need to be answered. (1) How does the second charge affect the S_N2 activation barrier and (2) does the presence of a second charge distort the S_N2 transition state. As noted previously, electrostatic repulsion in the dianion will make its reactions much more exothermic than those of singly charged analogs so “earlier” transition states are expected [24]. However, the coulomb repulsion is released over a very long reaction coordinate so the small increase in charge separation at the transition state will have only a modest energetic effect. As a result, the S_N2 transition state for the dianion may be very similar (geometrically and energetically) to that of a singly charged analog. If this is true, dianions could be used as surrogates to probe the inherent nucleophilic reactivity of gas phase anions (i.e. singly charged analogs). Of course this approximation can be valid only if the molecular forces associated with the S_N2 process are much larger than the electrostatic force from the dianion’s coulomb repulsion at the transition state. Because the electrostatic repulsion depends on the distance between the charges, this factor can be manipulated in the design of the dianion (i.e. the length of the spacer group between the two ionic sites).

To probe the effect of the initial coulomb repulsion on S_N2 potential energy surfaces, we have varied the charge separation in model dianions from 5 to 30 Å. Two types of dianion models have been used in this study (Scheme 2). Each employs a carboxylate as the nucleophile. (1) The dianion is modeled by an ω-alkoxy carboxylate (**A**) that has been locked into an extended conformation. In this case, the spacer group is an alkyl chain. The disadvantage of this approach is that very large systems are required to model long charge separations and the calculations become impractical. To alleviate this problem, a second approach was pursued. (2) The dianion is modeled by the combination of an acetate and a fluoride ion separated by a fixed distance (**B**). The spacer in this case is a vacuum, but as noted above, alkyl spacers provide an effective dielectric similar to a vacuum so this is not a severe approximation [11]. The validity of model **B** was tested by direct comparison to model **A** in three cases (charge separation = 5, 10, and 15 Å)

To investigate S_N2 processes, we have used the reactions of the dianions with methyl bromide to give esters (Scheme 3). This system was chosen because



Scheme 3.

we already have completed gas phase experiments on the reactions of carboxylate containing dianions with alkyl bromides [25]. The reaction was studied using model **A** with charge separations of approximately 5, 10, and 15 Å ($n = 3$, 7, and 11). With model **B**, charge separations of 5, 10, 15, 20, 25, and 30 Å were used.

2. Methods

Calculations were completed with the GAUSSIAN94 quantum mechanical package [26] on an SGI Octane, an IBM 39H, or an HP 735 computer. In model **A**, the system was locked into an extended conformation (all anti) and optimizations were completed at the Hartree-Fock (HF) and second order Møller-Plesset (MP2) levels. To reduce the size of the computational problem, nonstandard basis sets were employed in the optimizations. Specifically, a 6-31 + G(d) basis set was used for the oxygens, bromine, and two of the carbons (carboxylate and methyl bromide), whereas a 6-31G basis set was used for all other atoms. For the MP2 single point calculations on the MP2 geometries, a 6-31 + G(d, p) basis set was used on (C, H, O) and a 6-311 + G(d, p) basis set was used on Br.

In model **B**, the distance between the fluoride and acetate ions was fixed and all other parameters were optimized (in the ester product, an angle was fixed to prevent the ester from rotating and directing its OCH_3 group towards the F^-). Optimizations were completed at the HF and MP2 levels using a 6-31 + G(d) basis set on (C, H, O) and a 6-311 + G(d) basis set on Br. For the MP2 single point calculations on the MP2 geometries, a 6-31 + G(d, p) basis set was used on (C, H, O) and a 6-311 + G(d, p) basis set was used on Br.

Frequency calculations were completed in a few cases to ensure that the transition states had a single imaginary frequency. However, the energies listed in the tables do not include zero point vibrational energy corrections. These were not included because the goal of the work is to compare the potential energy surfaces of singly and doubly charged systems rather than to provide quantitatively accurate thermochemistry for the model systems.

Table 1
S_N2 transition state energies and reaction energies[a]

Charge separation (Å)[b]	Model **A**		Model **B**	
	E_{ts}	ΔE	E_{ts}	ΔE
5	−13.4	−106.4	−14.6	−106.1
10	−6.9	−79.0	−7.7	−75.6
15	−4.6	−65.7	−5.6	−65.3
20			−4.7	−60.0
25			−4.2	−56.9
30			−3.9	−54.7
Singly charged analog[c]			−3.2	−43.9

[a] Energies in kcal/mol relative to the separated reactants. Calculations at the MP2 level, see text for basis set.

[b] Nominal distances. In model **A**, the average O–O distance is ~0.9 Å longer than this value. In model **B**, the average F–O distance is ~0.6 Å longer than this value.

[c] Reaction of acetate with methyl bromide.

In the text, the nominal charge separations are listed. They correspond to the distance between the auxiliary charge (F^- or O^-) and the carboxylate carbon. More accurate measures of the charge separation are provided in Table 1.

3. Results and discussion

Table 1 contains data on the energetics of the S_N2 reactions of the dianions with methyl bromide. Comparing the results for dianions **A** and **B**, it can be that there is a satisfactory correspondence in the transition state energies (E_{ts}) with an average deviation of only about 1 kcal/mol. In each case, the transition state energy is somewhat higher in model **A**, but this is partly a result of the initial charge separations being slightly longer than in model **B**. The general accord between the models is not surprising because we have shown that alkyl spacer groups provide effective dielectrics similar to a vacuum [11]. Overall, the results indicate that model **B** provides S_N2 barriers

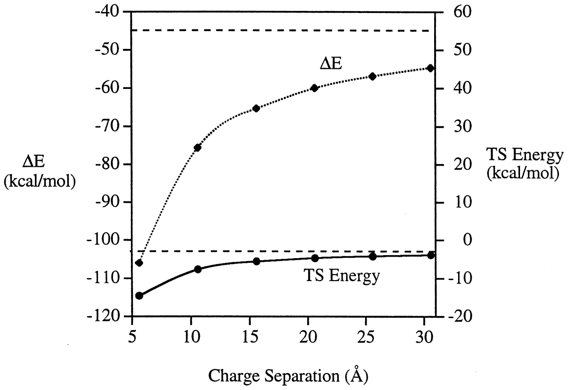


Fig. 1. Plot of reaction energy ΔE (dotted line) and transition state energy E_{ts} (solid line) as a function of the initial charge separation in the reactions of dianion model **B** with methyl bromide. Dashed lines represent the values for acetate + methyl bromide (singly charged analog).

that are essentially equivalent to those from the more computationally expensive model **A**. Good correspondence between models **A** and **B** is also seen in the reaction energies (ΔE).

In Fig. 1, the transition state energies and ΔE's of the S_N2 reactions of dianion **B** with methyl bromide are plotted against the initial charge separations in the dianion. In addition, values for the singly charged analog, acetate + methyl bromide, are indicated on the plot as dashed horizontal lines. In the plot, it is clear that the reaction energy (ΔE) varies dramatically as the initial charge separation is increased. For example, the reaction becomes 50 kcal/mol less exothermic in going from an initial charge separation of 5–30 Å. Even at 30 Å, the reaction is still 10 kcal/mol more exothermic than the singly charged analog. In contrast, the transition state energy varies much less with an increase in the initial charge separation. Going from 5 to 30 Å for the initial separation, the transition state energy changes by a little more than 10 kcal/mol. In fact, for initial charge separations of 15 Å or more, the transition state energy is very similar to that of the singly charged analog. Clearly only a small portion of the electrostatic repulsion is released at the transition state (about 10% for a 15 Å separation) and the second charge is having only a modest effect on the transition state energy in these cases. This is the expected result because in going to the transition state, the charge separation has increased by only a small amount. The increase in the charge separation at the transition state can be estimated in a straightforward way from the data. If we assume that the barrier is equal to the barrier of the singly charged analog minus the release of coulomb energy in reaching the transition state, the following equation can be generated:

$$E_{ts} = E_{ts}(\text{analog}) + q^2/\epsilon(r + x) - q^2/\epsilon r \qquad (4)$$

where r is the initial charge separation and x is the increase in charge separation at the transition state. Solving for x (assuming $\epsilon = 1$) gives a distance of roughly 2 Å, a very reasonable value for the increase in charge separation in an S_N2 process (2 Å puts the center of charge about midway between the nucleophile and leaving group). For dianions with initial charge separations of 15 Å or more, a 2 Å increase is relatively small and moderate energetic effects are seen, but this is not true for dianions with short initial charge separations. For example there is a 10 kcal/mol reduction in the S_N2 barrier for the dianion with an initial charge separation of 5 Å. Because coulomb effects play a large role in determining the activation barrier in dianions with initial charge separations of less than 10 Å, it is possible that these dianions would display reactivity that is markedly different than singly charged analogs.

The other important consideration is how the second charge affects the geometry of the S_N2 transition state. Because the reactions of the dianions are more exothermic, the Hammond postulate suggests that they should have earlier transition states than the singly charged analog [24]. In Fig. 2, two key distances from the transition state, C–Br (breaking) and C–O (forming), are plotted against the initial charge separations in the dianions. Again, values for the singly charged analog are indicated with dashed horizontal lines. In every case, the dianion has an earlier transition state (i.e. shorter C–Br distance and a longer C–O distance); however, the effect is very subtle for all the dianions with initial charge separations of 10 Å or more (deviations of less than 0.05 Å).

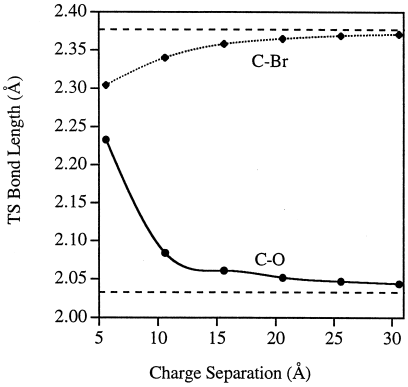


Fig. 2. Plot of breaking (C–Br) and forming (C–O) bond lengths in the transition states of the reactions of dianion model **B** with methyl bromide as a function of initial charge separation. C–Br is given with dotted line and C–O with a solid line. The corresponding bond lengths in the transition state of acetate + methyl bromide are shown with dashed lines.

With an initial separation of 5 Å, a much larger effect is seen in the C–O distance (~0.2 Å). Clearly when reasonably long initial charge separations are used (>15 Å), the second charge has almost no effect on the transition state geometry.

In Fig. 3, one-dimensional potential energy surfaces are given for model **B** ($r = 15$ Å) and the singly charged analog. For the reaction coordinate, the difference in the C–O (forming) and C–Br (breaking) distances is employed. It can be seen that the two potential energy surfaces have a very close fit in the region leading up to the transition state and only significantly diverge after the transition state where the majority of the coulomb repulsion is released. The close correspondence between the two curves offers a verification of the assumptions in Eq. (3).

Interesting insights can come from comparing the present results with those from our earlier study of the proton transfer reaction of a diammonium ion with ammonia [23]. In that work, we found that the actual barrier to proton transfer was negligible and that the rate determining process was the separation of the product complex (Fig. 4). This complex is characterized by a strong hydrogen bonding interaction and its breakdown leads to a significant rise in energy before the release of coulomb repulsion begins to dominate the potential energy surface. The net result is that the rate determining transition state occurs at a point much later on the reaction coordinate (the charge separation has increased by approximately 6 Å releasing ~15 kcal/mol in this example). Therefore, the

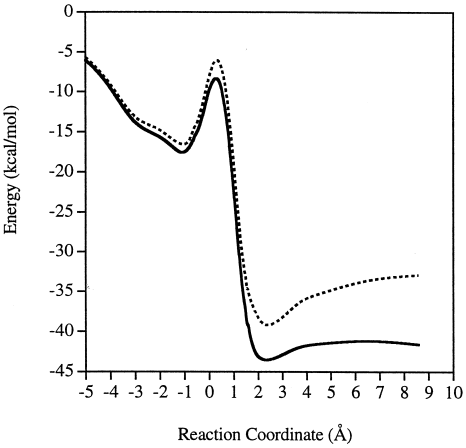


Fig. 3. One-dimensional potential energy surfaces for the reactions of methyl bromide with dianion model **B** (solid line) and acetate (dashed line). The initial charge separation in the dianion is 15 Å. Calculations at the HF/6-31 + G(d) level. The reaction coordinate corresponds to the difference between the breaking (C–Br) and forming (C–O) bond lengths (breaking − forming). Near the transition states, the points are determined with an intrinsic reaction coordinate calculation in GAUSSIAN94. Other points are determined by fixing one bond length and optimizing all other parameters.

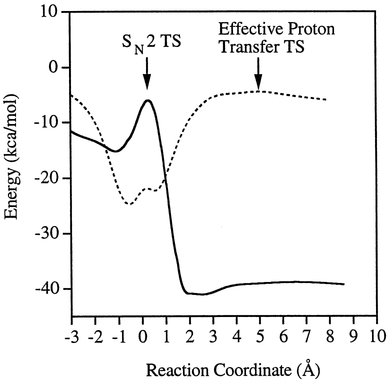


Fig. 4. One-dimensional potential energy surfaces for the S$_N$2 reaction of dianion model **B** (15 Å) with methyl bromide (solid line) and the proton transfer reaction of doubly-protonated 1,7-diaminoheptane with ammonia (dashed line). The reaction coordinate corresponds to the difference between the breaking and forming bond lengths (breaking − forming). Values for the proton transfer system are from a previous study [23].

release of coulomb energy at the transition state has a very significant effect on the kinetics even when the doubly charged ion has a fairly long initial charge separation. In contrast, S_N2 processes have sharp, well-defined barriers that occur early on the reaction coordinate. Moreover, S_N2 barriers are generally large and it is unlikely that separation of the product complex would be rate determining (see Fig. 3). The contrast in the results of these studies points to two distinct types of reactivity that can be expected with doubly charged ions (Fig. 4). In cases where the intrinsic barrier is large (e.g. S_N2 reactions), there will be a modest release of coulomb energy at the transition state and doubly charged systems with reasonable initial charge separations will model the reactivity of singly charged analogs. In reactions with little or no intrinsic barriers (e.g. proton transfers), very late transition states (i.e. product complex separation) lead to an extensive release of coulomb energy at the transition state and the reaction kinetics may differ significantly from singly charged analogs. In fact, this is the premise behind efforts to measure coulomb repulsion by the investigation of the acid/base behavior of doubly charged ions [7–10,16–22].

4. Conclusions

Ab initio calculations on the S_N2 reactions of model dianions with methyl bromide indicate that the second charge can have a relatively small effect on both the energy and geometry of the transition state. For example, with an initial charge separation of greater than 15 Å, the barrier is reduced by less than 2.5 kcal/mol and bond lengths in the transition state are altered by less than 0.04 Å. *As a result, dianions with initial charge separations of ~15 Å or more provide very good models for the* S_N2 *reactions of singly charged analogs*. Of course the modest barrier reductions will increase the rate constants of the dianion reactions, but general reactivity patterns such as substituent effects, regioselectivity, and competition with other mechanisms (i.e. $E2$ reactions) are likely to be very representative of those found in the reactions of singly charged analogs.

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