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What is a Good Approximation for the Transition State of an S_N2 Reaction?*

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It has been previously proposed, based on a qualitative application of the Curve Crossing model, that the transition state for a reaction is found in the *vicinity* of the crossing point of reactant and product electronic configurations. Computational data on S_N2 reactions are found to support this contention and the application of this result for the Leffler-Hammond postulate are discussed.

INTRODUCTION

Some years ago, based on a qualitative application of the Curve Crossing model, we suggested that the transition state for a chemical reaction is in the vicinity of the crossing point of reactant and product electronic configurations.[1a] This suggestion is very useful because it can be used to characterise the transition state by providing information regarding both its charge distribution and its structure. Indeed, for the S_N2 reaction of an anionic nucleophile, N^-, with a neutral substrate R-X, the electronic distribution in the transition state is likely to be approximated by equal negative charges on the nucleophile and the leaving group, and this is true *regardless of the position of the TS along the reaction coordinate.*[1] Thus our conclusion questioned the validity of the Leffler-Hammond postulate,[2] which implies that geometric progression and charge development along the reaction coordinate are controlled by the exothermicity of the reaction, and related to one another in a simple linear fashion.

Recently Shi and Boys[3] computed charge distribution for S_N2 transition states, $(N{---}CH_3{---}X)^-$ (N, X = H, OH, F, Cl) at relatively high levels of theory (up to MP2/6-31++G**). The data obtained by these workers enables the qualitative conclusions an-

* Dedicated to Professor Dionis E. Sunko on the occasion of his seventieth birthday.

ticipated from the Curve Crossing model to be critically assessed within a large enough data set. In this paper we wish to show that these calculations: (a) support our prediction regarding the location of the TS at the crossing point of the reactant and product configurations, and (b) confirm the lack of a general relationship between the position of the TS along the reaction coordinate and its degree of charge development.

DISCUSSION

In the past we have concluded, in conflict with the Leffler-Hammond postulate,[2] that »charge development in the TS is in general unrelated to the position of the TS along the reaction coordinate.«[1a] Our conclusion derives from an analysis of the S_N2 reaction using the Curve Crossing model.[1,4] According to the model, the S_N2 reaction profile is most simply generated from the intersection of two energy curves. These are obtained from plots of energy against reaction coordinate for the two Heitler-London valence bond structures, **1** and **2**, as illustrated in Figure 1. Since the crossing point

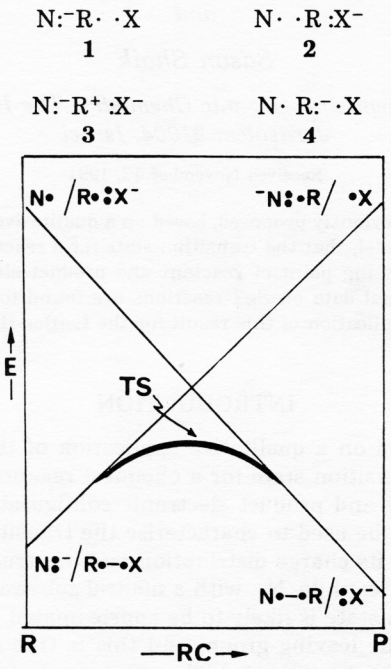

Figure 1. Energy diagram showing the crossing of two Heitler-London valence bond forms for $N:^- + RX \rightarrow NR + :X^-$ as a function of the reaction coordinate. The bold line indicates the ground state reaction profile as a result of the avoided crossing. Spin pairing is indicated by the two electrons (symbolized by dots) connected by a line.

is the point of highest energy, it was reasonably assumed that the TS will correspond closely to the geometry of the crossing point. Given that at the crossing point the description of the reaction surface is expressed by the mixture of **1** and **2** in equal proportions Eq. (1), it follows that the charges on N and X, q_N and q_X are expected

$$TS \sim 1/\sqrt{2}\{(N{:}^{-}R\cdot\ \cdot X) + (N\cdot\ \cdot R{:}X^{-})\} \quad (1)$$

to be the same. The important point is that the charge equality, $q_N = q_X$, that derives from Eq. (1), holds true *regardless of the position of the TS along the reaction coordinate.*[1a]

Two qualifications need to be made to the above statements.[1a]

(a) A two-configuration description of the reaction profile is clearly a simplified one. In practice other configurations will mix into the wave function that describes the reaction surface. Mixing in of carbocation, **3**, and carbanion, **4**, configurations will modify the TS charge on N and X from the value of 0.5 expected from the TS description of Eq. (1). However, if we assume that the mixing in of **3** and **4** occurs at the crossing point of **1** and **2** and does not shift the position of the TS away from this crossing point, then the charge on N and X will remain the same, though clearly it will no longer equal 0.5, as implied in Eq. (1). In fact, since **3** is lower in energy than **4**, the charges of N and X will exceed 0.5 as expressed in Eq. (2a) and (2b).

$$TS \sim 1/\sqrt{2}\{(N{:}^{-}R\cdot\ \cdot X) + (N\cdot\ \cdot R{:}X^{-})\} + \lambda(N{:}^{-}R^{+}\ {:}X^{-}); \quad (2a)$$

$$|q_N| \sim |q_X| > 0.5 \quad (2b)$$

Mixing in of *very* high energy asymmetric configurations, $N^{+}\ R^{-}{:}\ {:}X^{-}$ and $N^{-}{:}\ {:}R^{-}\ X^{+}$, *will* modify the charge equality, but not to any significant extent, due to the slight mixing of these high energy forms.[5] Thus Eq. (2b) should provide a good approximation for the TS charge distribution.

(b) The effect of curve skewing may also lead to a breakdown of the charge equality assumption.[6] Thus for example, for very exothermic (or endothermic) reactions, the position of the TS may not coincide with the position of the crossing point. This is illustrated in Figure 2. In the particular case illustrated, the TS *does* exhibit reactant-like charge distribution (*i.e.*, $|q_N| > |q_X|$). The curve skewing effect is however not

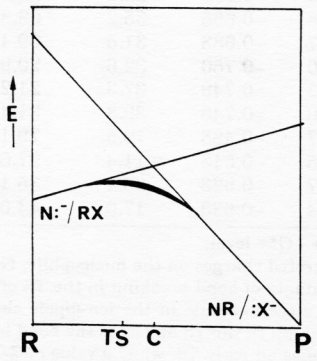

Figure 2. A schematic representation of the curve skewing effect, where the transition state (TS) position after the avoided crossing does not correspond with the position of the crossing point, (**C**). **R** and **P** are reactants and products (or their gas phase clusters in a gas phase reaction), respectively.

a hard rule in exothermic and endothermic reactions, as evidenced by existing quantitative studies of curve crossing.[7,8]

Analysis of Computational Results

Shi and Boyd conducted integrated charge analysis with the 6-31++G** basis set at three levels.[3] The lowest level was RHF where the charge analysis was performed on the RHF optimized TS, and the highest level was MP2/ 6-31++G** where both the charge analysis and geometry optimization were performed at the MP2 level.

Table I presents the MP2 charges and reaction ergonicity, ΔE, for both first row (H, NH_2, OH, F, CN, NC, and CCH, entries 1–9) and second row (SH, Cl, entries 10–13) groups.[3b] From Table I it can be seen that essentially all of the transition states with first row groups (entries 1–9) have symmetric or almost symmetric charge distribution, in accord with our prediction that $q_N \sim q_X$ Eq. (2). It is particularly noteworthy that this equality exists *despite* the extreme range of endo-exothermicity of the reactions (+46.2 to –86.4 kcal/mol), and the fact that in geometric terms the TS's are highly asymmetric. For example, the charges on H (–0.70) and NC (–0.71) in H--R--NC are essentially identical despite it being the system of highest exothermicity (–86.4 kcal/mol) within the Table I. So certainly for the family of transition states composed from first row groups, we see that the assumption of $q_N \sim q_X$ holds remarkably well.

Turning to the family of transition states with second row groups (entries 10–13, Table I), we see that, here, the assumption of charge equality does *not* hold. However

TABLE I

Integrated TS Charges in [N--R--X]⁻ from Ref. 3b[a]

Entry	[N--R--X]⁻	q_N[b]	q_X[b]	%CX‡[c]	%CN‡[c]	%CX‡–%CN‡[d]	ΔE[e]	
1	H--R--NH_2	–0.597	–0.603	31.4	56.8	–25.4	–21.9	(–20.9)
2	H--R--OH	–0.643	–0.635	25.4	71.1	–45.7	–44.6	(–41.8)
3	H--R--F	–0.700	–0.679	17.7	83.7	–66.0	–68.1	(–60.9)
4	H--R--NC	–0.698	–0.705	22.9	80.3	–57.4	–86.4	(–73.7)
5	H--R--CCH	–0.598	–0.655	35.2	63.3	–28.1	–34.9	(–30.0)
6	H--R--CN	–0.617	–0.683	31.5	69.4	–37.9	–60.1	(–48.6)
7	F--R--NH_2	–0.700	–0.750	32.6	20.9	+11.7	+46.2	
8	F--R--OH	–0.723	–0.749	37.3	21.2	+16.1	+23.5	(+17.6)
9	F--R--CN	–0.746	–0.746	39.8	31.4	+8.4	+ 8.0	
10	H--R--SH	–0.637	–0.488	19.5	79.1	–59.6	–70.8	(–57.1)
11	H--R--Cl	–0.725	–0.513	11.4	97.6	–86.2	–95.4	(–86.9)
12	F--R--SH	–0.757	–0.628	26.4	35.1	+8.7	– 2.7	
13	F--R--Cl	–0.814	–0.623	17.0	44.0	–27.0	–27.3	(–22.8)

[a] Data obtained at the MP2/6-31++G** level.

[b] q_N and q_X are Bader type[10] integrated charges on the nucleophile, N, and leaving group, X, respectively.

[c] %CX‡(%CN‡) refers to the percentages of bond breaking in the TS of C–X (C–N) with respect to the C–X (C–N) bond length in the ground state molecule in the ion-dipole clusters.[11]; Thus: $\%CX^{\ddagger} = 100(d^{a}CX - d^{o}CX)/d^{o}CX$. Here d^{a} is the bond length in the TS and d^{o} is the bond length in the molecule in the cluster.

[d] A value of %CX‡–%CN‡ < 0 signifies an early TS, while a value of %CX‡–%CN‡ > 0 signifies an late TS.

[e] Energy change for the reaction: $N^- + CH_3–X \rightarrow N–CH_3 + X^-$. Values out of parentheses refer to energy differences from free reactants to free products, while the values in parentheses refer to the energy difference between the ion-dipole clusters of reactants and products, *i.e.*, to the central process $N^-/CH_3–X \rightarrow N–CH_3/X^-$.

it is hard to attribute the charge asymmetry in these cases to the high exothermicity or the earliness of the transition state. For example, the reaction in Table I, entry 12 is almost thermoneutral yet it possesses a reactant-like charge distribution. We cannot provide an unequivocal explanation for the failure of the charge equality to hold in the second row systems, though it may well be linked to a recent observation by Perrin,[9] who demonstrated that Bader electronic charge distribution[10] tends to deplete the charge of large atoms in favor of the smaller atoms, irrespective of their relative electronegativities. In fact, for all the systems containing second row elements (Table I, entries 10–13) the second row atom bears a smaller charge than the first row atom. A further possibility is that the curve skewing effect is, for some reason, more pronounced for second row atoms.

Whatever the reason for the inequality in the charges in the second row examples, the entire data set certainly does not support the Leffler-Hammond idea suggesting a relationship between charge distribution and reaction exothermicity – there is no global correlation between charge distribution and ΔE. A plot of the charge asymmetry ($q_N - q_X$) against ΔE is one of total scatter, with a correlation coefficient of just 0.085. In contrast with this lack of correlation, there is a very good global correlation between ΔE and the *geometric* asymmetry of the TS, as measured by the difference in percentages of bond cleavage $\%CX^{\ddagger}$–$\%CN^{\ddagger}$.[11] A plot of $\%CX^{\ddagger}$–$\%CN^{\ddagger}$ against ΔE (from cluster to cluster), for the systems of Table I, is illustrated in Figure 3, and shows a good linear correlation between the two quantities (correlation coefficient 0.97) in agreement with earlier conclusions by Shaik *et al.*[11a] using data based on the 4-31G basis set. In other words, the Leffler-Hammond idea, that more exothermic reaction will be earlier in geometric terms, *is* supported by the data. It is only for the TS charges and their assumed synchronous change with geometry that the Leffler-Hammond postulate breaks down.

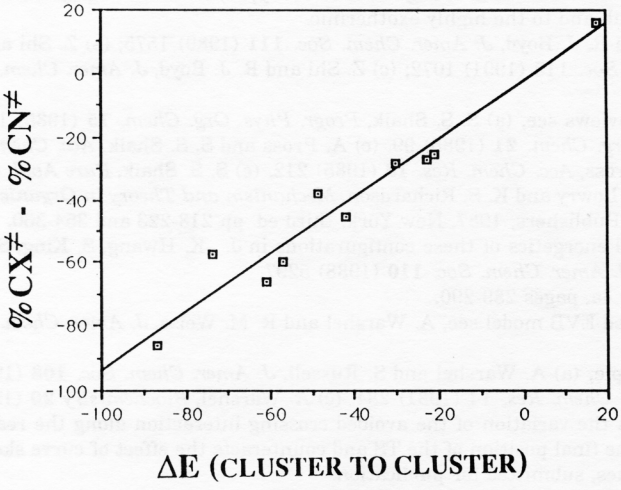

Figure 3. Plot of the degree of geometric progression along the reaction coordinate, as measured by $\%CX^{\ddagger}$–$\%CN^{\ddagger}$ against the reaction exothermicity (kcal/mol) from reactants' ion-dipole cluster to products' ion-dipole cluster.[11a] Data from Ref. 3b and 3c.

CONCLUSION

An analysis of the computational data of Shi and Boyd[3] for the S_N2 reaction lends support to our conclusions derived from the Curve Crossing model.[4] Thus a good approximation for the TS of an organic reaction is expected to be at the crossing point of the two Heitler-London configurations that describe reactants and products. The charge distribution in the TS can then be estimated from the average charges of the Heitler-London configurations by adding the contributions of the main secondary structures (*e.g.*, **3**, for S_N2). The analysis suggests that the relationship between TS charge distribution and TS geometry, derived from the Leffler-Hammond postulate, must be of limited validity. The computational results of Shi and Boyd[3] indeed show that reaction exothermicity and charge distribution are not related in the simple manner which is often assumed,[13] though reaction exothermicity and geometric progression along the reaction coordinate do correlate in the expected fashion.

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REFERENCES

1. (a) A. Pross and S. S. Shaik, *Tetrahedron Lett.* **22** (1982) 5467. (b) S. S. Shaik, *J. Amer. Chem. Soc.* **103** (1981) 3692. (c) A. Pross and S. S. Shaik, *J. Amer. Chem. Soc.* **103** (1981) 3702. (d) A. Pross and S. S. Shaik, *J. Amer. Chem. Soc.* **104** (1982) 187. (d) S. S. Shaik and A. Pross, *J. Amer. Chem. Soc.* **104** (1982) 2708.
2. (a) J. E. Leffler, *Science* **117** (1953) 340. (b) G. S. Hammond, *J. Amer. Chem. Soc.* **77** (1955) 334. Actually, the original Hammond postulate (Ref. 2b) refers to the similarity between transition states and high energy intermediates. However, the conventional wisdom extends the exothermicity over the entire range of reaction types, from the highly endothermic, through thermoneutral, and to the highly exothermic.
3. (a) Z. Shi and R. J. Boyd, *J. Amer. Chem. Soc.* **111** (1989) 1575; (b) Z. Shi and R. J. Boyd, *J. Amer. Chem. Soc.* **113** (1991) 1072; (c) Z. Shi and R. J. Boyd, *J. Amer. Chem. Soc.* **112** (1990) 6789.
4. For recent reviews see, (a) S. S. Shaik, *Progr. Phys. Org. Chem.* **15** (1985) 197. (b) A. Pross, *Adv. Phys. Org. Chem.* **21** (1985) 99. (c) A. Pross and S. S. Shaik, *Acc. Chem. Res.* **16** (1983) 363. (d) A. Pross, *Acc. Chem. Res.* **18** (1985) 212. (e) S. S. Shaik, *Pure Appl. Chem.* **63** (1991) 195. (f) T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, Harper and Row Publishers, 1987, New York, third ed. pp 218-223 and 354-360.
5. See computed energetics of these configurations in J. –K. Hwang, S. King, S. Creighton, and A. Warshel, *J. Amer. Chem. Soc.* **110** (1988) 5297.
6. See reference 4a, pages 289-290.
7. For the related EVB model see, A. Warshel and R. M. Weiss, *J. Amer. Chem. Soc.* **102** (1980) 6218.
8. See for example, (a) A. Warshel and S. Russell, *J. Amer. Chem. Soc.* **108** (1986) 6569. (b) A. Warshel, *Acc. Chem. Res.* **14** (1981) 284. (c) A. Warshel, *Biochemistry* **20** (1981) 3167. (d) In S_N1 reactions the variation of the avoided crossing interaction along the reaction coordinate determines the final position of the TS and counteracts the effect of curve skewing. H. J. Kim and J. T. Hynes, submitted for publication.
9. C. L. Perrin, *J. Amer. Chem. Soc.* **113** (1991) 2865.
10. (a) R. F. W. Bader, *Acc. Chem. Res.* **8** (1975) 34. (b) R. F. W. Bader, *Acc. Chem. Res.* **18** (1985) 9.
11. (a) S. S. Shaik, H. B. Schlegel, and S. Wolfe, *J. Chem. Soc., Chem. Commun.* (1988) 1322. (b) S. S. Shaik, *Acta Chem. Scand.* **44** (1990) 202. (c) S. S. Shaik, H. B. Schlegel, and S. Wolfe, *Theoretical Aspects of Physical Organic Chemistry. The S_N2 Transition State*, Wiley, New York, 1992.

12. As explained in reference 11a, the plot should strictly refer to the ΔE from cluster to cluster. With some assumptions the correlation may be used with ΔE values from reactants to products (correlation coefficient of 0.95). For a recent related paper see: S. Wolfe and C. –K. Kim, *J. Amer. Chem. Soc.* **113** (1991) 8056.
13. For a recent analysis see: S. Hoz, *Acta Chem. Scand.*, in press.

SAŽETAK

Što je dobra aproksimacija za prijelazno stanje S_N2 reakcije?

Addy Pross i Sason Shaik

Primjena modela »presijecanja krivulja« pokazuje da se prijelazno stanje za S_N2 reakciju nalazi u blizini točke presijecanja energija elektronskih konfiguracija reaktanta i produkta. Računski podaci podupiru ovaj zaključak.