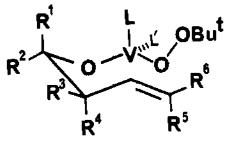
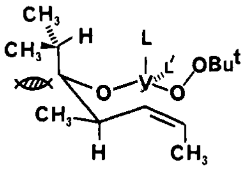
conformation which is quite useful for discussion purposes. We



A

have investigated six different substitution types and our results are summarized in Table I. In all cases, the observed selectivity is in accord with that form of A which minimizes steric interactions among the various substituents according to commonly accepted principles of conformational analysis. We believe the very high asymmetric inductions that we have obtained for a number of these substrates are entirely predictable on the same grounds.

Entries 1, 9, and 10 show selectivities of $>$100:1 since the favored transition state in these cases has R^1 = R^4 = H and R^3 = R^5 = alkyl. Formation of the minor isomer requires a severe 1,3-interaction (R^4 = R^5 = alkyl) and is, therefore, highly disfavored. The same is true for entries 11–15 even though R^1 is now constrained to be alkyl in order to avoid a severe R^4–R^5 interaction. For R^1 = Me, this appears to be well tolerated although the reaction rate slows considerably. However, with R^1 = *i*-Pr (entry 13) no chair conformation is free of a severe 1,3-interaction (see B) and competition with boat conformations leads



B

to a much poorer asymmetric induction. Removal of the indicated Me–Me interaction by changing R^1 from iso-propyl to *n*-pentyl (entry 14) again allowed highly selective epoxide formation (94:6 product ratio).

The above cases fit the category of 1,2-relative asymmetric induction in Bartlett's terminology.[2a] Entries 2 and 4 indicate that high 1,3-induction is also possible in the V^{5+}/TBHP system. This selectivity is lost in the case of the corresponding (*E*)-olefin (entry 3) since energetically competitive boat forms are possible.[9]

Finally, we were especially interested in the structure type characterized by entries 5–8. The possibility exists that vanadium could be trigonal bipyramidal in these reactions, and a preliminary predictive model has been formulated on this basis.[10] Such a model fails when applied to this substrate class. The tetrahedral vanadate ester formulation, on the other hand, nicely accounts for the $\sim$5:1 selectivity observed on the basis of preferred chain form A (R^2 = R^3 = alkyl).[11]

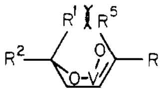
We have found the principles outlined here to be consistent not only with our own experimental results but also with those previously reported in the literature.[10,12] In particular, the bishomoallylic alcohol cases studied by Kishi[12a] are easily rationalized in terms of a similar 7.5-membered-ring[7c] transition state.[13]

Our results now open the door to rational synthetic planning based on this efficient epoxidation methodology. The facility with which four contiguous chiral centers have been assembled in a predictable manner with virtually complete stereocontrol (entries 9–12 and 15) testifies to the power of this synthetic approach. Numerous applications in complex acyclic synthesis will undoubtedly follow.

Acknowledgment. We thank Professor D. A. Evans for introducing us to the exceptional utility of fused silica capillary gas chromatography columns for determining isomer distributions.

---

[9] In boat conformation i, a severe R^1–R^5 interaction occurs (R^5 = alkyl) as long as a lone pair of the coordinated peroxide oxygen is aligned in the plane of the olefin π cloud as has been suggested by Sharpless[10] for peracid epoxidations.



i

Without this requirement, it is difficult to account for the substantial selectivities observed for entries 2 and 4. Consequently, we employ this constraint when evaluating the transition-state models for every substrate.

[10] Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63–73.

[11] At this point in time, we can only view the tetrahedral vanadate ester formulation as a very highly successful predictive model. However, we do feel our results lend support to the proposed mechanism for this reaction (Scheme III in ref 10) with the added refinement of an early (reactant-like) transition state.

[12] (a) Fukuyama, T.; Vranesic, B.; Negri, D. P.; Kishi, Y. *Tetrahedron Lett.* **1978**, 2741–2744. (b) Johnson, M. R.; Nakata, T.; Kishi, Y. *Ibid.* **1979**, 4343–4346. (c) Johnson, M. R.; Kishi, Y. *Ibid.* **1979**, 4347–4350. (d) Kozikowski, A. P.; Schmiesing, R. J.; Sorgi, K. L. *Ibid.* **1981**, 2059–2062. (e) Hiyama, T.; Kimura, K.; Nozaki, H. *Ibid.* **1981**, 1037–1040.

[13] Analysis of this considerably more flexible system is simplified by minimizing steric interactions between the *tert*-butyl of the hydroperoxide and the alkyl groups on the more substituted side of the double bond. This again emphasizes the importance of considering all ligand–substrate interactions in these reactions.[6]

Theoretical Studies of S$_N$2 Transition States. 1. Geometries

Saul Wolfe* and David John Mitchell

Department of Chemistry, Queen's University
Kingston, Ontario, Canada K7L 3N6

H. Bernhard Schlegel[†]

Department of Chemistry, Wayne State University
Detroit, Michigan 48202

Received June 17, 1981

The establishment of rate–equilibrium[1] or structure–reactivity[2] relationships is a common feature of experimental investigations of reaction mechanisms. Extensive experience has led to the view that such phenomenological effects provide information concerning the structures and properties of transition states if it is valid to postulate that these properties are related in some well-defined manner to properties of the reactants and the products. In this and the following communication we present relationships between the calculated geometries and energies of S$_N$2 transition states and calculated properties of the reactions. There is remarkable agreement between these theoretical results and the postulates of physical organic chemistry.

Our work was inspired by the outstanding series of experimental contributions by Brauman and his co-workers[3] concerning the

---

[†] Fellow of the Alfred P. Sloan Foundation, 1981–1983.

[1] Brönsted, J. N. *Chem. Rev.* **1928**, *5*, 231–338. (b) Hammett, L. P. *Ibid.* **1935**, *17*, 125–136. (c) Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963.

[2] (a) Olson, A. R. *J. Chem. Phys.* **1933**, *1*, 418–423. (b) Ogg, R. A.; Polanyi, M. *Trans. Faraday Soc.* **1935**, *31*, 604–620. (c) Evans, M. G.; Polanyi, M. *Ibid.* **1935**, *31*, 875–894. (d) Bell, R. P. *Proc. R. Soc., Ser. A.* **1936**, *154*, 414–429. (e) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* **1936**, *32*, 1333–1360. (f) Evans, M. G.; Polanyi, M. *Ibid.* **1938**, *34*, 11–29. (g) Wigner, E. *Ibid.* **1938**, *34*, 29–41. (h) Evans, M. G. *Ibid.* **1938**, *34*, 49–57. (i) Hughes, E. D. *Ibid.* **1938**, *34*, 185–202. (j) Leffler, J. E. *Science (Washington, D.C)* **1953**, *117*, 340–341. (k) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338. (l) Burgi, H.-B. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 460–473. (m) Chapman, N. B.; Shorter, J., Eds. "Correlation Analysis in Chemistry. Recent Advances"; Plenum Press: New York, 1978.

[3] (a) Brauman, J. I.; Olmstead, W. N.; Lieder, C. A. *J. Am. Chem. Soc.* **1974**, *96*, 4030–4031. (b) Farneth, W. E.; Brauman, J. I. *Ibid.* **1976**, *98*, 7891–7898. (c) Olmstead, W. N.; Brauman, J. I. *Ibid.* **1977**, *99*, 4219–4228. Inversion of configuration in gas-phase S$_N$2 reactions has been observed by: Wolf, A. P.; Schueler, P.; Pettijohn, R. R.; To, K.-C.; Rack, E. P. *J. Phys. Chem.* **1979**, *83*, 1237–1241. To, K.-C.; Rack, E. P.; Wolf, A. P. *J. Chem. Phys.* **1981**, *74*, 1499–1500.

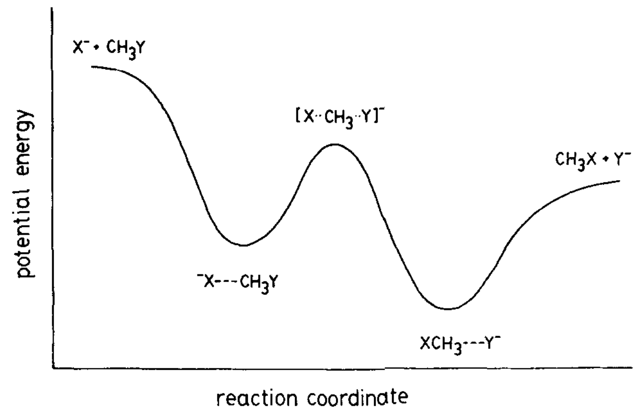


Figure 1. Reaction coordinate proposed by Brauman[3] for the gas-phase displacement reaction $X^- + CH_3Y \rightarrow XCH_3 + Y^-$.

observation, analysis, and interpretation of gas-phase S_N2 reactions. These studies suggest that, in the absence of solvent,[4] the reaction coordinate will have the form shown in Figure 1; the minima in this reaction coordinate are ion–molecule complexes or clusters, and the central barrier is the highest energy point on the minimum energy reaction path from cluster to cluster and can be identified with the classical concept of an S_N2 transition state. A particularly important experimental finding is that, with some reasonable assumptions,[5] the central barrier heights can be interpreted in terms of Marcus theory, a rate–equilibrium relationship[6] that has also been applied successfully to proton-transfer[7] and alkyl-transfer[8] reactions in solution.

A number of ab-initio molecular orbital calculations of S_N2 transition states have already appeared in the literature[9] and are consistent with the reaction coordinate depicted in Figure 1. However, no systematic investigation of the geometries of the transition states and the energetics of the reactions has been performed, probably because of the difficulties associated with the complete geometry optimization of ion–molecule complexes and transition structures.[10] Such problems have been overcome by the development of efficient techniques for the calculation of forces or gradients[11] and by a modification of the conjugate gradient method to search for transition structures.[12] These methods have been incorporated into the GAUSSIAN 80 program system[13] and are particularly well suited to the treatment of systems containing strongly coupled variables or weak intermolecular forces. The latter problem exists in the ion–molecule complexes. The former problem is present in the computation of S_N2 transition structures, because the bond-making and bond-breaking coordinates are strongly coupled to each other and to the umbrella motion of the substituents on the central carbon.

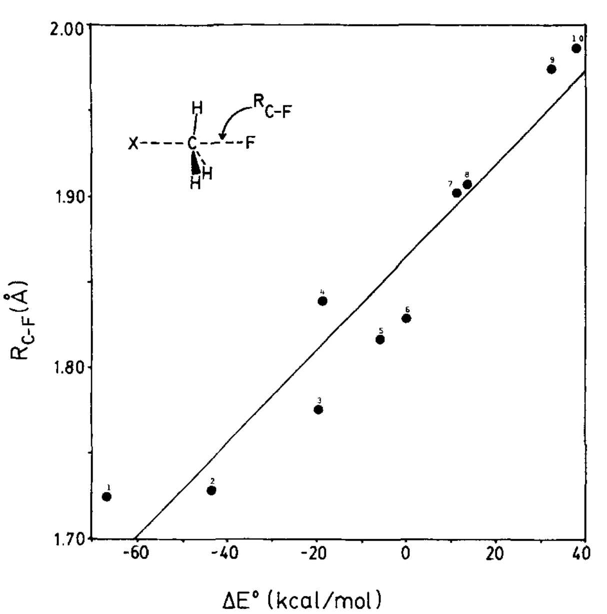


Figure 2. Plot of the C–F bond lengths in $[X–CH_3–F]^-$ transition structures vs. the calculated energies of reaction in the direction $X^- + CH_3F \rightarrow XCH_3 + F^-$. Data points 1–10 refer to X = H, H_2N, HO, HCC, CH_3O, F, NC, HOO, C*N*, FO.

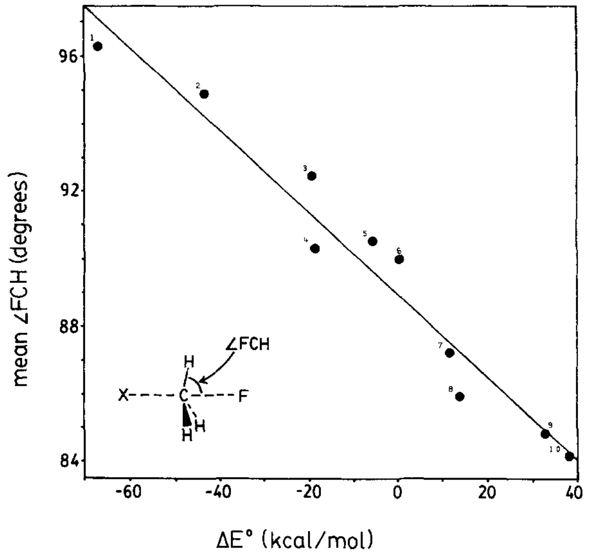


Figure 3. Plot of the FCH bond angles in $[X–CH_3–F]^-$ transition structures vs. the calculated energies of reaction in the direction $X^- + CH_3F \rightarrow XCH_3 + F^-$. Data points 1–10 are the same as for Figure 2.

Extensive test calculations by the present authors and by others[14] reveal that the 4-31G basis set reproduces the form of the S_N2 reaction coordinate and is reliable for the geometries of interest. Although energies calculated at this level are less reliable, experimental trends in heats of reaction are reproduced.[15]

Figure 2 shows the relationship between calculated C–F bond lengths and calculated heats of reaction in the direction $X^- + CH_3F \rightarrow CH_3X + F^-$ for ten transition states $[X–CH_3–F]^-$. Figure 3 is the complementary relationship associated with the mean FCH bond angles of these transition states. As the reaction becomes progressively less exothermic, the C–F bond lengths increase from 1.725 to 1.986 Å, and the FCH angles decrease from

---

(4) For recent work on the role of solvation in S_N2 reactions and the manner in which hydration of the entering and leaving groups alters the gas-phase reaction coordinate, see: Bohme, D. K.; Mackay, G. I. *J. Am. Chem. Soc.* **1981**, *103*, 978–979 and references to earlier publications by the same group cited therein. See also: Benson, S. W.; Nangia, P. S. *Ibid.* **1980**, *102*, 2843–2844.

(5) Pellerite, M. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1980**, *102*, 5993–5999.

(6) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155–196 and references cited therein. See also: Murdoch, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 4410–4418. Miller, A. R. *Ibid.* **1978**, *100*, 1984–1992.

(7) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354–360. Albery, W. J. *Annu. Rev. Phys. Chem.* **1980**, *31*, 227–263.

(8) Albery, W. J.; Kreevoy, M. M. *Adv. Phys. Org. Chem.* **1978**, *16*, 87–157.

(9) See, e.g.: Dedieu, A.; Veillard, A. *J. Am. Chem. Soc.* **1972**, *94*, 6730–6738. Bader, R. F. W.; Duke, A. J.; Messer, R. R. *Ibid.* **1973**, *95*, 7715–7721. Keil, F.; Ahlrichs, R. *Ibid.* **1976**, *98*, 4787–4793. Schlegel, H. B.; Mislow, K.; Bernardi, F.; Bottoni, A. *Theor. Chim. Acta* **1977**, *44*, 245–256. Ishida, K.; Morokuma, K.; Komornicki, A. *J. Chem. Phys.* **1977**, *66*, 2153–2156. Fujimoto, H.; Kosugi, N. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2209–2214. Talaty, E. R.; Woods, J. J.; Simons, G. *Aust. J. Chem.* **1979**, *32*, 2289–2291.

(10) Müller, K. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1–13.

(11) See: Pople, J. A.; Krishnan, R.; Schlegel, H. B.; Binkley, J. S. *Int. J. Quantum Chem.: Quantum Chem. Symp.* **1979**, *13*, 225–241 and references cited therein.

(12) Schlegel, H. B., submitted for publication.

(13) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; Defrees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. *QCPE* **1980**, *13*, 406.

(14) Frisch, M.; Pople, J. A., unpublished results.

(15) For the series of reactions $X^- + CH_3F \rightarrow XCH_3 + F^-$, calculated exothermicities follow the trend $H^- > H_2N^- > HO^- > HCC^- > CH_3O^- > F^- > NC^- > HOO^- > CN^- > FO^-$. The experimental trend is $H^- > H_2N^- > HCC^- > HO^- > CH_3O^- > F^- > NC^- > HOO^- > CN^-$.

Table I. Application of Equation 2 to S_N2 Transition Structures[a]

X	Y	n_X	n_Y	total bond order[b]
F	H	0.593	0.406	0.999
F	OH	0.546	0.455	1.001
F	CCH	0.491	0.510	1.001
F	NH_2	0.591	0.421	1.012
F	CN	0.442	0.558	1.000
F	OOH	0.438	0.566	1.004
F	OCH_3	0.509	0.492	1.001
H	NH_2	0.482	0.513	0.995
H	OH	0.445	0.549	0.994
H	CCH	0.423	0.570	0.993
H	CN	0.389	0.610	0.999
HO	CN	0.426	0.583	1.009

[a] Calculated a_X values (Å) from eq 1 are as follows: H, 0.936; CCH, 0.959; CN, 0.948; NH_2, 0.795; OH, 0.691; OCH_3, 0.687; OOH, 0.703; F, 0.600. [b] Average value 1.001, $\sigma_n = 0.004$.

96.3 to 84.2°. This is the Bell–Evans–Polanyi–Leffler–Hammond effect:[2,16] *the more exothermic the reaction, the more closely the transition structure resembles the higher energy reactants.*

Linear fits to these data give, for Figure 2, $r = 0.952$ and, for Figure 3, $r = 0.976$. Linear correlations have also been found for $[X-CH_3-OH]^-$ transition states (R_{CO}, $r = 0.967$; $\angle HCO$, $r = 0.994$) and $[X-CH_3-H]^-$ transition states (R_{CH}, $r = 0.977$; $\angle HCH$, $r = 0.996$). Such correlations suggest that these geometrical parameters of the transition structure are influenced more by the thermochemistry of the reaction than by electronic interactions between the entering and leaving groups.[17] It is particularly noteworthy that Figures 2 and 3 include cyanide/isocyanide, an "ambident nucleophile", and the "alpha-nucleophiles" hypofluorite and hydroperoxide. No unusual geometrical effects are observed with these nucleophiles.[18]

Our calculated geometries can also be employed to test the postulate of conservation of bond order along the reaction coordinate.[19] For an S_N2 reaction, this corresponds to $n_X + n_Y = 1$, where n_X and n_Y are the bond orders of C–X and C–Y, respectively, and can be obtained from bond lengths using the Pauling relationship[20] (eq 1). The proportionality constants a_X

$$R - R_e = a_X \ln (n_X) \tag{1}$$

were calculated from the transition structures for the degenerate reactions $X^- + CH_3X \rightarrow CH_3X + X^-$, in which $n_X = 0.5$ and R_e is the C–X bond length in CH_3X (see footnote to Table I). In the cross-reactions $X^- + CH_3Y \rightarrow CH_3X + Y^-$, conservation of bond order requires that

$$n_X + n_Y = \exp[(R_{e_X} - R_X)/a_X] + \exp[(R_{e_Y} - R_Y)/a_Y] = 1 \tag{2}$$

As can be seen in Table I, this behavior is observed uniformly in the transition structures.

The conservation of bond order in the transition state, coupled with the relations between reaction energy and bond length or bond angle, allows accurate estimation of transition-state geometries from properties of the reactants and products alone. These findings are being used successfully to extend the study of S_N2 transition structures reported here.

Acknowledgment. This research has been supported by grants from the Natural Sciences and Engineering Research Council of Canada and the Petroleum Research Fund, administered by the American Chemical Society. We gratefully thank the Advisory Research Committee of Queen's University and Wayne State University for generous allocation of computing funds.

Supplementary Material Available: Geometries and energies of all transition structures and ion–molecule complexes discussed in this and the following communication (6 pages). Ordering information is given on any current masthead page.

---

(16) Dewar, M. J. S. "The Molecular Orbital Theory of Organic Chemistry"; McGraw-Hill: Toronto, 1969; pp 284–288.

(17) Preliminary results indicate that correlations analogous to those reported here also exist with higher quality basis sets.

(18) Liebman, J. F.; Pollack, R. M. *J. Org. Chem.* **1973**, *38*, 3444–3445.

(19) Johnston, H. S. "Gas Phase Reaction Rate Theory"; Ronald Press: New York, 1966. Dunitz, J. D. *Philos. Trans. R. Soc. London, Ser. B* **1975**, *272*, 99–108. Agmon, N. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 388–404. *Int. J. Chem. Kinet.* **1981**, *13*, 333–365.

(20) Pauling, L. *J. Am. Chem. Soc.* **1947**, *69*, 542–553.

Theoretical Studies of S_N2 Transition States. 2. Intrinsic Barriers, Rate–Equilibrium Relationships, and the Marcus Equation

Saul Wolfe* and David John Mitchell

Department of Chemistry, Queen's University
Kingston, Ontario, Canada K7L 3N6

H. Bernhard Schlegel†

Department of Chemistry, Wayne State University
Detroit, Michigan 48202

Received June 17, 1981

The reaction coordinate shown in Figure 1 for the gas-phase displacement $X^- + CH_3Y \rightarrow XCH_3 + Y^-$ is characterized by two energy minima, corresponding to reactant (**1**) and product (**3**) ion–molecule clusters, separated by a central barrier (**2**), corresponding to the S_N2 transition state. As discussed by Brauman and his co-workers,[1] such a reaction coordinate is consistent with the observation that the process proceeds at less than the collision rate, even when **2** has lower potential energy than the reactants, because partitioning of **1** in the direction of the reactants is favored entropically. With this interpretation, and model RRKM calculations, it has been found[2] that the energy difference between the reactants and the central barrier **2** (here termed $\Delta E^b{}_{X,Y}$) can be correlated with the efficiency of the reaction.

Figure 2 shows a plot, based on 4-31G level calculations with full geometry optimization of all structures, of $\Delta E^b{}_{X,Y}$ vs $\Delta E°$, the calculated energy of reaction. No simple correlation between these quantities is apparent. That this is not an artifact of the computations may be seen from the experimental data of Bohme[3] and Brauman,[2] wherein reactions having similar $\Delta H°$ may proceed with very different efficiencies. Thus, although the *geometries* of S_N2 transition states correlate well with the heats of reaction (the Bell–Evans–Polanyi–Leffler–Hammond effect[4]), their energies do not, and it must be concluded that the *efficiency* of a gas-phase S_N2 reaction is not controlled solely by the enthalpy change.

The origin of such behavior has been treated in a number of rate–equilibrium relationships developed for elementary reactions,[5,6] which relate the reaction rate not only to $\Delta E°$ ($\Delta G°$) but also to certain intrinsic properties of the system. For an S_N2 reaction these properties are associated with the nature of X and Y. The Marcus equation (eq 1) has already been applied suc-

$$\Delta E^{\ddagger}{}_{X,Y} = \tfrac{1}{2}[\Delta E^{\ddagger}{}_{X,X} + \Delta E^{\ddagger}{}_{Y,Y}] + \tfrac{1}{2}\Delta E + \{(\Delta E)^2/8[\Delta E^{\ddagger}{}_{X,X} + \Delta E^{\ddagger}{}_{Y,Y}]\} \tag{1}$$

---

† Fellow of the Alfred P. Sloan Foundation, 1981–1983.

(1) Farneth, W. E.; Brauman, J. I. *J. Am. Chem. Soc.* **1976** *98*, 7891–7898.

(2) Olmstead, W. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219–4228.

(3) Tanaka, K.; Mackay, G. I.; Payzant, J. D.; Bohme, D. K. *Can. J. Chem.* **1976**, *54*, 1643–1659.

(4) Wolfe, S.; Mitchell, D. J.; Schlegel, H. B. *J. Am. Chem. Soc*, preceding paper in this issue.

(5) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155–196 and references cited therein. *J. Phys. Chem.* **1968**, *72*, 891–899. Cohen, A. O.; Marcus, R. A. *Ibid.* **1968**, *72*, 4249–4256. Murdoch, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 4410–4418.

(6) (a) Agmon, N.; Levine, R. D. *Chem. Phys. Lett.* **1977**, *52*, 197–201. (b) Agmon, N. *J. Chem. Soc., Faraday Trans. 2*, **1978**, *74*, 388–404. (c) Miller, A. R. *J. Am. Chem. Soc.* **1978**, *100*, 1984–1992. (d) Levine, R. D. *J. Phys. Chem.* **1979**, *83*, 159–170. (e) Agmon, N.; Levine, R. D. *J. Chem. Phys.* **1979**, *71*, 3034–3041. (f) Agmon, N. *Int. J. Chem. Kinet.* **1981**, *13*, 333–365.