5.2×10^{-5} M^{-1} at 24 °C and 2.3×10^{-5} M^{-1} at 0 °C. These values are obviously only approximate.

References and Notes

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(2) Some of the results and interpretations reported here have appeared earlier in communications: (a) J. M. Timko and D. J. Cram, *J. Am. Chem. Soc.*, **96**, 7159 (1974); (b) J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel, and D. J. Cram, *ibid.*, **96**, 7097 (1974).

(3) (a) D. W. Griffiths and M. L. Bender, *Adv. Catal. Relat. Subj.*, **23**, 209 (1973); (b) J. H. Fendler and E. J. Fendler, "Catalysis in Micellar and Macromolecular Systems", Academic Press, New York, N.Y., 1974, Chapter 11.

(4) (a) E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, and D. J. Cram, *J. Am. Chem. Soc.*, **99** 2564 (1977); (b) S. S. Moore, T. L. Tarnowski, M. Newcomb, and D. J. Cram, *ibid.*, submitted for publication.

(5) C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 2495, 7017 (1967).

(6) We warmly thank the following people: (a) Dr. G. W. Gokel, who prepared this compound; (b) Dr. K. Koga, who first prepared this compound which was reported in ref 2b.; (c) Dr. M. Newcomb, who first prepared this compound.

(7) W. N. Haworth and W. G. M. Jones, *J. Chem. Soc.*, 667 (1944).

(8) P. A. Finan, *J. Chem. Soc.*, 3917 (1963).

(9) (a) British Patent 911 221; *Chem. Abstr.*, **58**, 9027f (1963); (b) A. K. Bose and B. Lal, *Tetrahedron Lett.*, 3937 (1973).

(10) R. I. Abraham and H. J. Bernstein, *Can. J. Chem.*, **37**, 1056 (1959).

(11) (a) F. H. Newh, *Adv. Carbohyd. Chem.*, **6**, 83 (1951); (b) British Patent 887 360; *Chem. Abstr.*, **57**, 2193 (1962).

(12) After our preliminary report of this compound (ref 2a), D. N. Reinhoudt and R. T. Gray, *Tetrahedron Lett.*, 2105 (1975) also described it in a preliminary report.

(13) (a) H. E. Winberg, F. S. Fawcett, W. E. Mochel, and C. W. Theobald, *J. Am. Chem. Soc.*, **82**, 1428 (1960); (b) D. J. Cram, C. S. Montgomery, and G. R. Knox, *ibid.*, **88**, 515 (1966); (c) F. Vogtle and P. Neumann, *Synthesis*, 85 (1973).

(14) (a) I. Gault, B. J. Price, and I. O. Sutherland, *Chem. Commun.*, 540 (1967); (b) S. M. Rosenfeld and P. M. Keehn, *ibid.*, 120 (1974).

(15) I. Goldberg, *Acta Crystallogr., Sect. B*, **31**, 754 (1975).

(16) (a) J. Dale and K. Daasvtn, *J. Chem. Soc., Chem. Commun.*, 295 (1976); (b) G. W. Gokel, D. J. Cram, C. L. Liotta, H. P. Harris, and F. L. Cook, *J. Org. Chem.*, **39**, 2445 (1974).

(17) (a) J. W. Ensley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy' Vol. 1, Pergamon, Oxford, 1965, p 481; (b) R. Helder and H. Wynberg, *Tetrahedron Lett.*, 4321 (1973).

(18) (a) D. Gagnaire and P. Monzeglio, *Bull Soc. Chim. Fr.*, 474 (1965); (b) M. L. Mihailovic, R. I. Mamuzic, L. Zigic-Mamuzic, J. Bosnjak, and Z. Cekovic, *Tetrahedron*, **23**, 215 (1967).

(19) R. E. Sievers, Ed., "Nuclear Magnetic Resonance Shift Reagents", Academic Press, New York, N.Y., 1973.

(20) F. de Jong, D. N. Reinhoudt, and C. J. Smit [*Tetrahedron Lett.*, **17**, 1371 (1976)] observed that in extractions of t-BuNH$_3^+$PF$_6^-$ from water into CDCl$_3$ containing host **4**, that nonhydrated 1:1 complexes of host–guest were formed in the CDCl$_3$ layer. With hosts *whose rings were larger than 18-membered*, hydrated 2:2 complexes were formed at high host concentrations. The only host of our study whose ring is larger than 18-membered is **17**, and its complex might possibly be dimeric and hydrated. The 1:2 host-to-guest complex of F. de Jong, D. N. Reinhoudt, C. J. Smit, and R. Huis [*Tetrahedron Lett.*, **51**, 4783 (1976)] is a postulated *reaction intermediate* that explains the mechanism for the exchange of free t-BuNH$_3^+$PF$_6^-$ with a 1:1 complex between t-BuNH$_3^+$PF$_6^-$ and 18-crown-6.

(21) D. Live and S. I. Chan, *J. Am. Chem. Soc.*, **98**, 3769 (1976).

(22) (a) The GAUSSIAN 70 series of programs (W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, QCPE No. 236, Indiana University, Bloomington, Ind.) with STO-3G basis set were used (W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, **51**, 2657 (1970).

(23) S. Z. Perry and H. Hibbert, *Can. J. Res., Sect. B*, **14**, 77 (1936).

(24) M. L. Mednick, *J. Org. Chem.*, **27**, 398 (1962).

(25) R. A. Hales, J. W. LeMaistre, and G. O. Orth, Jr., U.S. Patent 3 071 599; *Chem. Abstr.*, **59**, 576a (1964).

(26) M. Kulku, *Can. J. Res., Sect. B*, **23**, 106 (1945).

(27) S. De Bernardo, M. Weigele, V. Toome, K. Manhart, W. Leimgruber, P. Böhler, S. Stein, and S. Undenfriend, *Arch. Biochem. Biophys.*, **163**, 390 (1974).

(28) W. M. Clark and H. A. Lubs, *J. Biol. Chem.*, **25**, 479 (1916).

Gas-Phase Nucleophilic Displacement Reactions

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Abstract: Displacement reactions of each of a variety of anionic nucleophiles reacting with each of a variety of neutrals have been studied by pulsed ion cyclotron resonance (ICR) spectroscopy. Rate constants for these reactions are interpreted in terms of a three-step reaction sequence. RRKM calculations are used to obtain information about the energy of transition states. The origin of the barrier to reaction in solution is discussed.

Bimolecular nucleophilic substitution (S_N2) reactions have been one of the most widely studied families of reactions in chemistry. For many years they were the favorites of physical organic chemists. The history of their study closely parallels and is sometimes responsible for the development of ideas such as structure-reactivity relationships, linear free energy relationships, steric inhibition, kinetics as a probe of mechanism, stereochemistry as a probe of mechanism, and solvent effects. Since the basic properties of the mechanism have been well-known for a long time; they are discussed in detail in most physical organic chemistry texts and other books as well.[1-5]

$$X^- + RY \rightarrow Y^- + RX$$

The reaction was first recognized to be first order in both nucleophile (X^-) and substrate (RY) by Hughes, Ingold, and co-workers.[6] It is thus distinct from the first-order S_N1 process, which involves dissociation of the substrate into a carbonium ion (R^+) and anion (Y^-) in the rate-determining first step. The S_N2 reaction was envisioned as proceeding in one step, with formation of the new bond occurring synchronously with cleavage of the old bond. The reaction has been shown to give inversion of configuration at the site of attack, implying backside attack at carbon. As a result, the rate of the reaction is very sensitive to steric hindrance to backside attack. Alkyl groups attached to the carbon under attack greatly inhibit the reaction.

In addition to the structure of the substrate, the nature of the nucleophile and leaving group affect the overall reaction rate. Many attempts have been made to correlate nucleophilicity, which is a kinetic property of a nucleophile measured by its rate constant for an S_N2 reaction, with thermodynamic properties such as basicity, polarizability, and redox potential. These attempts have generally failed except for nucleophiles of related structure, such as substituted phenoxide ions. The overall rates of S_N2 reactions have been found to be strongly solvent dependent. Often the rate of a reaction will increase by orders of magnitude on switching from a protic solvent such as methanol to a dipolar aprotic one such as DMSO. Winstein even found that the nucleophilic order of the halides in protic solvents ($I^- > Br^- > Cl^- > F^-$) was reversed in acetone solvent.[7]

Parker has used the dependence of reaction rates on the solvent, coupled with the relative solvation energies of the reactants in various solvents, to deduce the relative solvation energies of the transition states for the reactions.[8] He has shown much about transition state structures in this manner.

Although the effects of the solvent can be used in this way to deduce properties of the reaction, these effects often interfere with the study of the intrinsic (solvent free) properties. For instance the greater reactivity of iodide ion relative to the other halides and of thiophenoxide relative to phenoxide has often been ascribed to their greater polarizability. In this view the more polarizable anions can respond to a greater need for electron density near the substrate and thus react more quickly. From studies in aprotic solvents and now in the gas phase this view is known to be wrong. The order is simply a reflection of the lesser solvation energy of the more polarizable anions, which enhances their reactivity in protic solvents.

Recently there have been two approaches to deduction of the inherent gas-phase properties of S_N2 reactions. Theoretical studies of the potential energy surfaces for several reactions have resulted from improvements in calculational techniques.[9] Except possibly for the simplest of these systems ($H^- + CH_4 \rightarrow H^- + CH_4$) the calculations are probably quantitatively inaccurate due to the large number of electrons involved and the problems associated with calculating energies of negatively charged species. The other approach, made possible by advances in experimental techniques, has been to study the ion-molecule reactions in the gas phase. Results of Bohme and co-workers[10-13] and from our laboratory[14] have shown that there is a wide variation of rates for S_N2 reactions in the gas phase. Dougherty and co-workers have observed stable adducts between anions and alkyl halides in a high-pressure mass spectrometer.[15] These adducts, which can correspond to intermediates in the S_N2 reactions, vary in stability from 8.6 to 14.4 kcal/mol. In our laboratory the neutral products of several reactions have been identified.[16] The reactions were shown to proceed with inversion of configuration at the carbon atom in the gas phase, just as in solution.

In this paper we report the results of a number of new rate measurements on S_N2 reactions in the gas phase. Variations in the nucleophile (X^-), leaving group (Y^-), and alkyl substrate (R) lead to a wide range of rate constants. We also report experiments which show that there is a barrier to halide exchange in the adduct between chloride ion and methyl bromide. Variations in this barrier height for different combinations of reactants are responsible for the variations in rates for the overall S_N2 reactions. These rates are discussed in terms of nucleophilicity, leaving group ability, and steric hindrance. Comparisons are made with rates in solution, which are many orders of magnitude slower. Finally, we report the results of RRKM calculations on several reactions, showing the dependence of the overall rate on the height of the intermediate potential barrier. From these calculations and the experimental rates, the heights of the intermediate barriers can be estimated.

Experimental Section

For all of the nonkinetic experiments in this work a Varian V-5900 ion cyclotron resonance spectrometer was used.[17] Either pulsed double resonance or ion ejection were used to confirm each reaction.[17] Marginal oscillator frequencies of 112, 153, and 307 kHz were used. Rate constants were measured on a pulsed ion cyclotron resonance spectrometer.[18] The marginal oscillator frequency was varied between 153 and 612 kHz. Pressure measurements were made with a Varian Model 971-0014 ionization gauge which was calibrated for each neutral gas in the pressure range 10^{-5} to 10^{-4} Torr against an MKS Baratron capacitance manometer. The operating pressures for the experiments were between 1×10^{-6} and 5×10^{-5} Torr. This method gave a rate constant of 1.12×10^{-9} cm^3 molecule^{-1} s^{-1} for the reaction $CH_4^+ + CH_4 \rightarrow CH_5^+ + CH_3$, which has an average literature rate constant of 1.11×10^{-9} cm^3 molecule^{-1} s^{-1} from many different techniques.[19]

For slow reactions ($k < \sim 1 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1}), where nonreactive ion loss was competitive with reactive loss, the rate of disappearance of the reactant ion was corrected in the following way. The rate of nonreactive ion loss of the product was measured after the reaction was over. From that and the empirical expression[20]

$$k_{11} \propto m^{1/2}/H^2\mu^{1/2} \qquad (1)$$

where m is the mass of the ion, H is the magnetic field strength, and μ is the reduced mass of the ion-neutral molecule collision pair, the rate constant for nonreactive ion loss of the reactant ion could be found. Then the rate constant for the reaction was calculated from this and the observed rate of disappearance of the reactant ion. Independently, eq 1 was checked and found to be fairly accurate for a number of different ions and magnetic field strengths under conditions where there was only nonreactive ion loss. This method of correcting for ion loss gave reproducible results. Our previously reported[14] rate constant for the reaction $Cl^- + CH_3Br \rightarrow Br^- + CH_3Cl$ is in error because no correction was made for nonreactive ion loss.

A frequent criticism of rate constants measured by ICR is that the ions may not be thermalized before they react. This possibility was checked by several methods. First, if nonexponential decays were observed for the reactant ion concentration, the data were not used. This would indicate that the rate constant was changing with time due to relaxation of excited ions by nonreactive collisions. Second, in some cases a nonreactive neutral gas was entered. If the reactant ions were excited and were reacting at a different rate than thermal ions, then collisional deactivation by the added neutral gas would be expected to change the observed rate constant. If this was found to be the case, the data were not used. Third, the kinetic energy dependence of S_N2 reactions was independently measured and found to be very weak up to a few electron volts.[21]

The following sources were used for generation of the negative ions by electron impact. The approximate electron energy (absolute value of filament voltage minus trapping voltage) is indicated in electron volts for each compound: F^- from NF_3 (0.5–1.5), Cl^- from CCl_4 or $CHCl_3$ (0.0–1.0), Br^- from $CH_2{=\!=}CHCH_2Br$ (1.0–2.0), CH_3O^- from CH_3OOCH_3 (1.0–2.5), OH^- from H_2O (6.1), CN^- from HCN (2.0–3.5), CH_3S^- from CH_3SSCH_3 (1.5), Cl_2^- and $COCl^-$ from $COCl_2$ (20), CF_3Cl^- and $COCl^-$ from CF_3COCl (30), and Br_2^- from Br_2 (1–10). All of these were obtained from commercial sources except NF_3, which was obtained from Dr. S. K. Brauman at SRI, CH_3OOCH_3, which was synthesized by a literature method,[22] and HCN, which was generated from KCN and H_2SO_4 at room temperature on a vacuum line.

Methyl chloride and methyl bromide (Matheson, >99.5%) were used without further purification. Methyl trifluoroacetate (Pierce), anisole (Aldrich), and 1-chloro-2,2-dimethylpropane (MCB) were distilled at atmospheric pressure and checked for purity by gas chromatography (Hewlett-Packard F and M Model 700 gas chromatograph equipped with a dual flame ionization detector; 15% β,β-oxydipropionitrile on Chromosorb P, 60/80 mesh column).

Results

Several experiments were performed on the adduct of chloride ion with methyl bromide to determine its chemical behavior. Although this adduct has been observed by third-body stabilization in a high-pressure mass spectrometer,[15a] at the low pressure ($<10^{-4}$ Torr) in an ICR, this is not possible. Therefore, the adduct was formed by transfer of a chloride ion from three species to methyl bromide:

$$CF_3Cl^- + CH_3Br \rightarrow ClCH_3Br^- + CF_3$$

$$Cl_2^- + CH_3Br \rightarrow ClCH_3Br^- + Cl$$

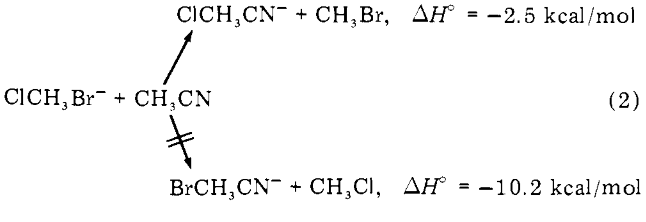
$$COCl^- + CH_3Br \rightarrow ClCH_3Br^- + CO$$

Ions of the correct masses and isotope ratios were observed (129:131:133 = 3:4:1). The reactions were confirmed by double resonance irradiation of the reactant ions. The adducts formed in this manner could transfer a chloride ion, but not a bromide ion, to acetonitrile and 1,1-difluoroethane:[23]

Table I. Rate Constants, Reaction Efficiencies, and Heats of Reaction for S_N2 and Related Reactions

Reaction	Rate constant, 10^{-9} cm^3 molecule^{-1} s^{-1}	Reaction efficiency[a]	$\Delta H°$, kcal mol^{-1} [b]
(1) $OH^- + CH_3Cl \rightarrow Cl^- + CH_3OH$	1.6	0.68	−47.5
(2) $F^- + CH_3Cl \rightarrow Cl^- + CH_3F$	0.80	0.35	−28.5
(3) $CH_3O^- + CH_3Cl \rightarrow Cl^- + CH_3OCH_3$	0.49	0.25	−39.3
(4) $CH_3S^- + CH_3Cl \rightarrow Cl^- + CH_3SCH_3$	0.078	0.045	−31.0
(5) $^{37}Cl^- + CH_3{}^{35}Cl \rightarrow {}^{35}Cl^- + CH_3{}^{37}Cl$	~0.006	~0.003	0.0
(6) $CN^- + CH_3Cl \rightarrow Cl^- + CH_3CN$	<0.001	<0.0005	−27.2
or CH_3NC			−12.3
(7) $OH^- + CH_3Br \rightarrow Br^- + CH_3OH$	1.9	0.84	−55.7
(8) $F^- + CH_3Br \rightarrow Br^- + CH_3F$	0.60	0.28	−36.7
(9) $CH_3O^- + CH_3Br \rightarrow Br^- + CH_3OCH_3$	0.72	0.40	−47.5
(10) $CH_3S^- + CH_3Br \rightarrow Br^- + CH_3SCH_3$	0.14	0.091	−39.2
(11) $Cl^- + CH_3Br \rightarrow Br^- + CH_3Cl$	0.012	0.0070	−8.2
(12) $CN^- + CH_3Br \rightarrow Br^- + CH_3CN$	0.02	0.01	−35.4
or CH_3NC			−20.5
(13) $^{81}Br^- + CH_3{}^{79}Br \rightarrow {}^{79}Br^- + CH_3{}^{81}Br$	<0.01	<0.008	0.0
(14) $OH^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3OH$	1.4	0.47	−68.2
(15) $F^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3F$	1.1	0.39	−49.2
(16) $CH_3O^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3OCH_3$	1.0	0.43	−60.0
(17) $CH_3S^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3SCH_3$	0.50	0.25	−51.7
(18) $Cl^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3Cl$	0.045	0.021	−20.7
(19) $CN^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3CN$	0.03	0.01	−47.9
or CH_3NC			−33.0
(20) $Br^- + CF_3CO_2CH_3 \rightarrow CF_3CO_2^- + CH_3Br$	~0.005	~0.003	−12.5
(21) $OH^- + PhOCH_3 \rightarrow PhO^- + CH_3OH$	0.08	0.03	−38.3
(22) $F^- + PhOCH_3 \rightarrow PhO^- + CH_3F$	0.08	0.03	−19.3
(23) $CH_3O^- + PhOCH_3 \rightarrow PhO^- + CH_3OCH_3$	0.024	0.012	−30.1
(24) $CH_3S^- + PhOCH_3 \rightarrow PhO^- + CH_3SCH_3$	<0.005	<0.003	−21.8
(25) $CN^- + PhOCH_3 \rightarrow PhO^- + CH_3CN$	~0.007	~0.003	−18.0
or CH_3NC			−3.1
(26) $CD_3O^- + CH_3OCH_3 \rightarrow CH_3O^- + CH_3OCD_3$	<0.001	<0.0005	0.0
(27) $F^- + (CH_3)_3CCH_2Cl \rightarrow Cl^- + (CH_3)_3CCH_2F$	0.49		−29.1
(28) $CH_3S^- + (CH_3)_3CCH_2Cl \rightarrow Cl^- + (CH_3)_3CCH_2SCH_3$	<0.01		−31.2
(29) $(CH_3)_3CO^- + (CH_3)_3CCH_2Cl \rightarrow Cl^- + (CH_3)_3CCH_2OC(CH_3)_3$	<0.01		−38.5
(30) $CH_3O^- + (CH_3)_3CCO_2CH_2CH_3 \rightarrow (CH_3)_3CO_2^- + CH_3CH_2OCH_3$	0.2		
(31) $CH_3O^- + (CH_3)_3CCO_2CH_2CH_3 \rightarrow CH_3CH_2O^- + (CH_3)_3CCO_2CH_3$	0.5		
(32) $CH_3S^- + CH_3SH \rightarrow SH^- + CH_3SCH_3$	0.8	0.5	−12.3
(33) $CN^- + CH_3CO_2H \rightarrow CH_3CO_2^- + HCN$	0.37	0.19	−2.9

[a] The reaction efficiency is the fraction of collisions which result in reaction. The collision rate constants were calculated by the average dipole orientation (ADO) method.[51] [b] Enthalpies of reaction were calculated from thermochemical data from the following sources. Heats of formation of CH_3F, CH_3Cl, CH_3Br, CH_3OH, CH_3OCH_3, CH_3SCH_3, CH_3CN, CH_3NC, CH_3CO_2H, and CH_3SH are from ref 24b, and $PhOCH_3$ from J. D. Cox and G. Pilcher, "Thermochemistry of Organic and Organometallic Compounds", Academic Press, London, 1970. Heats of formation of neopentyl fluoride, chloride, and bromide were calculated by group additivity (S. W. Benson, "Thermochemical Kinetics", Wiley, New York, N.Y., 1968). Heats of formation of OH^-, F^-, and CN^- are from JANAF Thermochemical Tables, 1974 Supplement, *J. Phys. Chem. Ref. Data*, **3,** 311 (1974); Cl^-, Br^-, and HS^- from ref 24a; CH_3O^- from R. T. McIver, Jr., and J. S. Miller, *J. Am. Chem. Soc.*, **96,** 4323 (1974). $\Delta H_{f,298}°(CH_3S^-) = -11.7$ kcal mol^{-1} from $D°(CH_3S\text{-}H) = 88$ kcal mol^{-1} (J. A. Kerr, *Chem. Rev.*, **66,** 465 (1966)) and $EA(CH_3S) = 42.1$ kcal mol^{-1} (K. J. Reed, Ph.D. Thesis, Stanford University, 1975). $\Delta H_f°(PhO^-) = -41.8$ kcal mol^{-1} from DH-EA(PhOH) = 33.3 kcal mol^{-1} (T. B. McMahon and P. Kebarle, *J. Am. Chem. Soc.*, **98,** 3399 (1976)) and $D°(H_2) = 104.2$ kcal mol^{-1}. $\Delta H_f°(CF_3CO_2H) - \Delta H_f°(CF_3CO_2CH_3) = 8.9$ kcal mol^{-1} (K. Hiraoka, R. Yamdagni, and P. Kebarle, *J. Am. Chem. Soc.*, **95,** 6833 (1973)).



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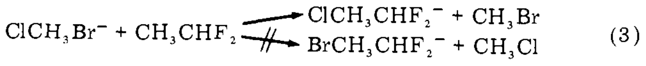

(3)

Careful searches for the bromide-acetonitrile adduct and bromide-1,1-difluoroethane adduct were made under conditions where the signals for the corresponding chloride adducts were strong and the double resonance signals for the reactions leading to the formation of these adducts were also strong.

Several unsuccessful attempts were made to form the bromide-methyl chloride adduct. Br_2^- formed from bromine would not transfer a bromide ion to methyl chloride and no CF_3Br^- or $COBr^-$ could be found from electron impact on trifluoroacetyl bromide.

The results of the kinetic studies of S_N2 reactions are summarized in Table I. The estimated accuracy of the rate constants is ±20% for those reactions faster than 1×10^{-10} cm^3 molecule^{-1} s^{-1} and ±30% for the slower reactions. However, the relative rates should be more dependable than that. Also in Table I are the efficiencies and exothermicities for each reaction.

Discussion

Mechanism. The wide variation in rates for the reactants in Table I is extremely unusual. Often in the field of ion-molecule reactions, generalizations can be made about various families of reactions: proton transfers involving localized charged

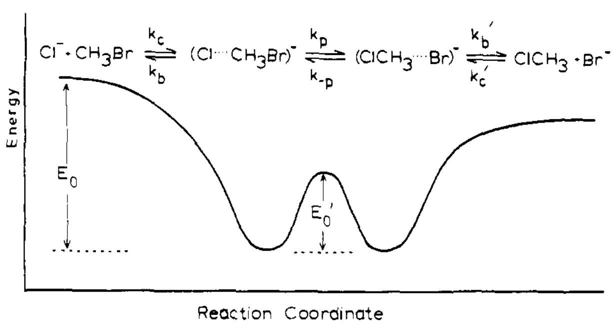

Figure 1. Mechanism and potential energy surface for a representative nucleophilic displacement reaction.

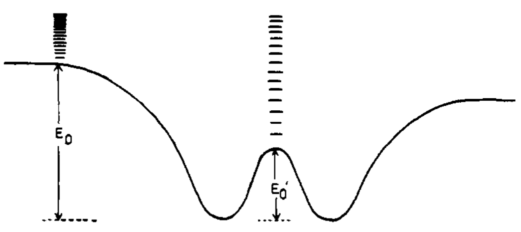

Figure 2. Pictorial representation of internal energy level spacings for an S_N2 reaction in the gas phase.

species are fast,[25] proton transfers involving delocalized charged species are slow,[26] hydride transfers are slow,[27] etc. However, the reactions in Table I span the range from almost collision controlled to too slow to be observed. This variation is best explained by a "double-well" potential with a secondary barrier, as shown in Figure 1. How this view of the reaction can explain the smooth variations in rate will be explained later. First some alternative explanations will be considered.

Many ion-molecule reactions are undoubtedly slow because they have some dynamic, entropic, or steric constraints which are difficult to overcome. Not enough is known about many slow reactions to pinpoint the origin of their problems. The S_N2 reactions are all structurally similar, so there is no reason for some of them to have problems of this nature while others do not.

It is not possible to explain the observed rates on the basis of a single-well potential. Because of the symmetric nature of reaction 4 the complex with equal chlorine bond lengths must

$$Cl^- + CH_3Cl \underset{k_b}{\overset{k_c}{\rightleftharpoons}} Cl \cdots CH_3 \cdots Cl^- \underset{k_{-p}}{\overset{k_p}{\rightleftharpoons}} CH_3Cl + Cl^- \quad (4)$$

be either an intermediate at the bottom of a potential well or a transition state at the top of a potential barrier. If it is a stable intermediate and there are no other intermediates then $k_p = k_b$ and the overall rate will be $k_c/2$. If there is no barrier to formation of the complex, then k_c is the collision rate constant. Experimentally, the overall rate is about 0.3% of the collision rate, so there cannot be a single intermediate without any barriers to its formation.

Is a single symmetrical intermediate with a barrier to its formation possible? This would entail a rise in potential energy as the ion and molecule approach, followed by a drop to the intermediate. However, the simple electrostatic attractive force between the two particles becomes substantial at greater distances than chemical forces which are due to overlapping molecular orbitals. Therefore there must first be a drop in potential energy before any chemical barrier. If this were the case, symmetry requires a similar barrier on the other side of the intermediate. The overall surface would then have three wells. All of the experimental data (thus far) can be explained by a double-well surface, so we will use this simpler model.

Referring to Figure 1, if $k_b > k_p$ then the overall rate of the reaction will be less than half of k_c, the collision rate. The relative values of k_b and k_p will determine the overall rate of the reaction. Making the assumption that k_{-p} is negligible, the overall bimolecular rate is given by (5).

$$k_{bi} = \frac{k_c k_p}{k_b + k_p} \quad (5)$$

This assumption is valid for the reactions in this study for the following reasons. For the exothermic reactions $k_b' > k_b$ because it is energetically favored and the two reactions are similar entropically. Thus once a complex passes over the central barrier it will mostly go on to products. For the thermoneutral reactions we know from the experimental rate that $k_b' = k_b \gg k_p$, so once the central barrier is overcome the complex will preferentially decompose to the products.

Given that the double-well potential in Figure 1 is qualitatively accurate, how can a central barrier lower than the barrier to give the reactants slow down the overall reaction? As shown below, the answer is that the back reaction (k_b) is greatly favored by entropy. Physically this means that the internal energy levels for the back reaction are much more closely spaced than those for the forward reaction at equal internal energies. This is shown diagrammatically in Figure 2. The partitioning of the intermediate in the two directions is determined by the ratio of the number of microscopic pathways in each direction (within the constraints of conservation of angular momentum). Therefore even though the forward direction may be energetically favored, it can be substantially slower than the reverse reaction. Just how much slower depends on the relative energy level spacing, which depends in turn on the energy difference between the two barriers as well as the oscillator frequencies for the two transition states. Assuming that the internal energy of the intermediate is randomized, nothing need be known about its structure, stability, or energy levels in order to calculate the partitioning in the two pathways. This principle will be utilized in the quantitative estimates of the central barrier heights which will come later.

The variation in rates for the S_N2 reactions is the result of variations in the size of the secondary barriers. A barrier which is at the same potential energy as the separated reactants will slow the reaction considerably. All other factors being equal (which is certainly not true) every rate can be accommodated by a single barrier height, or more exactly a difference in barrier heights for the forward (k_p) and back (k_b) reactions.

A qualitative prediction of this model and the Bell-Evans-Polanyi principle[28] is that the more exothermic reactions should be faster. Since the transition state involves partial formation of the new bond and breaking of the old bond, the overall energy of the reaction should be partially reflected in the energy of the transition state. As can be seen by examining Table I there is very rough correlation between rate and exothermicity. However there must be other factors which also influence the rates, since the correlation is only a rough one. These will be discussed later.

This double-well potential is supported by other experiments. The ones described above (reactions 2 and 3) indicate that there is a barrier to exchange of the two halide ions in the adduct. Formed in the manner described it is most likely a loose ion-molecule complex held together by ion-dipole and ion-induced dipole forces. Dougherty et al.[15a] have measured its stability as 10.9 kcal/mol relative to chloride ion and methyl bromide. This is in the correct range for complexes bound by simple electrostatic forces. Riveros et al.[29] have reported a similar experiment on the adduct between chloride and methyl chloride:

$$CO^{35}Cl^- + CH_3{}^{37}Cl \longrightarrow {}^{35}Cl\cdots CH_3{}^{37}Cl^-$$

$${}^{35}Cl\cdots CH_3{}^{37}Cl^- + CH_3CF_3 \longrightarrow {}^{35}ClCH_3CF_3{}^- + CH_3{}^{37}Cl$$

$${}^{35}Cl\cdots CH_3{}^{37}Cl^- + CH_3CF_3 \nrightarrow {}^{37}ClCH_3CF_3{}^- + CH_3{}^{35}Cl$$

Here also the adduct is unsymmetrical, with only the chloride isotope which was added able to transfer to another neutral molecule. There is no proof from these experiments that these adducts are "backside" attachments of the halide ions to the carbon atoms, even though this would be the most stable configuration resulting from the ion-dipole force due to the direction of the dipole moment in methyl halides. Another possibility would be a structure such as **1.**

$$[CH_3\text{-}Cl\text{-}Cl]^-$$

1

That this is not the case is supported by the inability of Dougherty et al.[15] to observe adducts between halide ions and bridgehead halides.

The double-well potential has also been calculated by a variety of theoretical methods.[9] In these calculations the height of the barrier separating the two wells varies widely from reaction to reaction using the same computational techniques. Unfortunately they also vary widely for the same reactions using different techniques. The calculations are probably quantitatively inaccurate, but the qualitative picture of a double-well potential should be correct.

Nucleophilicity and Leaving Group Ability. The reaction efficiencies in Table I represent intrinsic reactivities in the absence of the complicating effects of a solvent. Most of the methyl compound efficiencies are reorganized in Table II along with some of the efficiencies reported by Bohme et al.[13] Almost all of our presently reported values are somewhat smaller than the previously reported ones,[13] which were measured in a flowing afterglow apparatus. The origin of these discrepancies is not known, but the exact absolute values are not important for the following discussion and conclusions. Comparisons of these efficiencies provide some useful insights into the intrinsic nature of nucleophilicity, leaving group ability (LGA), and steric hindrance. Since the definitions of these three properties are purely kinetic ones, the model for the reactions described above is not necessary. However it is reassuring that the basis of the kinetic differences is indeed energetic, just as in solution.

The concept of nucleophilicity has been around a long time, and no discussion of S_N2 reactions would be complete without mention of the factors which influence it. The order of the anionic nucleophilicity which is found in this study is:

$$OH^- > F^- \sim CH_3O^- > CH_3S^- \gg Cl^- > CN^- > Br^-$$

The first three of these are very potent nucleophiles (eff > 0.25). Reversals (not very substantial ones) can be seen as the leaving group is varied, especially in Bohme's data (H^- and NH_2^- are also very good nucleophiles). Methylthiolate is somewhat less nucleophilic, and then there is greater than an order of magnitude drop in efficiency to the three poor nucleophiles. Although the number of nucleophiles is limited, some of the factors influencing their reactivity are clear.

(1) Methyl Cation Affinity. In solution, nucleophilicity is often correlated with basicity. Often these linear free energy relationships are quite good within one family of nucleophiles but fail for comparisons of nucleophiles with different charged atoms. The comparison of thermodynamic basicity with kinetic nucleophilicity reflects the Bell-Evans-Polanyi principle mentioned above. Another difference besides the static-dynamic one is that the former involves proton affinity while the latter involves methyl cation affinity. In the gas phase the thermodynamic methyl cation affinities (defined as the heat of reaction of $X^- + CH_3^+ \rightarrow CH_3X$) are known, so the comparison of these with kinetic carbon affinities can be made. The exothermicities of the reactions of nucleophiles with a single substrate reflect the thermodynamic affinities. With methyl chloride these follow the order:

nucleophile:	$H^- >$	$NH_2^- >$	$OH^- >$	$CH_3O^- >$	$CH_3S^- \sim$	$F^- \sim$	$CN^- >$	Cl^-
$\Delta H°$, kcal/mol:	86.3	69.2	47.5	39.3	31.0	28.5	27.2	0

The relative efficiencies, on the other hand, follow the order:

nucleophile:	$OH^- \sim$	$NH_2^- >$	$F^- \sim$	$H^- \sim$	$CH_3O^- >$	$CH_3S^- >$	$Cl^- >$	CN^-
rel eff:	210	210	120	120	83	15	1	<0.07

This order is followed roughly for the other leaving groups in Table II but some reversals occur. For instance fluoride is a better nucleophile than methoxide toward methyl chloride but the order is reversed with methyl bromide. This and the other reversals are very modest, however, and they are all for the very good nucleophiles. The thermodynamic order above is different from the kinetic order. Hydride, methylthiolate, and cyanide are anomalously slow. This can be accounted for on the basis of the next factor.

Table II. S_N2 Reaction Efficiencies[a]

	CH_3F	CH_3OPh	CH_3Cl	CH_3Br	CH_3O-$COCF_3$
NH_2^-	(0.0076)		(0.63)	(0.48)	
OH^-	(0.011)	0.03	0.68	0.84	0.47
			(0.62)	(0.43)	
F^-		0.03	0.35	0.28	0.39
			(0.83)	(0.59)	
H^-	(0.002)		(0.35)	(0.43)	
CH_3O^-	(0.0074)	0.012	0.25	0.40	0.43
			(0.68)	(0.61)	
CH_3S^-	(≤0.0006)		0.045	0.091	0.25
			(0.065)	(0.35)	
Cl^-	*b*	*b*	0.003	0.0070	0.021
				(0.012)	
CN^-	(≤0.003	~0.003	<0.0005	0.01	0.01
			(<0.0002)	(0.016)	
Br^-	*b*	*b*	*b*	<0.008	

[a] Values in parentheses are from ref 13. [b] Endothermic reactions.

(2) Charge Concentration. The fact that anions with a localized charge are better gas phase nucleophiles than those with a delocalized charge was first recognized by Bohme and Young.[10] They found that benzyl anions were very poor nucleophiles despite the fact that they have very large methyl cation affinities. The delocalization of the charge on the cyanide anion could account for its lack of reactivity. Although hydride and methylthiolate anions have their charge localized on one atom, both of them are very diffuse. It is often pointed out from solution studies that polarizable nucleophiles are better than nonpolarizable ones because they can respond better to demand for charge reorganization (e.g., $CH_3S^- > CH_3O^-$ and $I^- > Br^- > Cl^- > F^-$). From the present results it can be seen that just the opposite is the case and that the higher nucleophilicity of polarizable anions in solution is purely an artifact of solvation effects. The intrinsic nucleophilicities follow the reverse order of the polarizabilities (e.g., $CH_3O^- > CH_3S^-$ and $F^- > Cl^- > Br^-$). This could be due to a stronger interaction between the more concentrated molecular

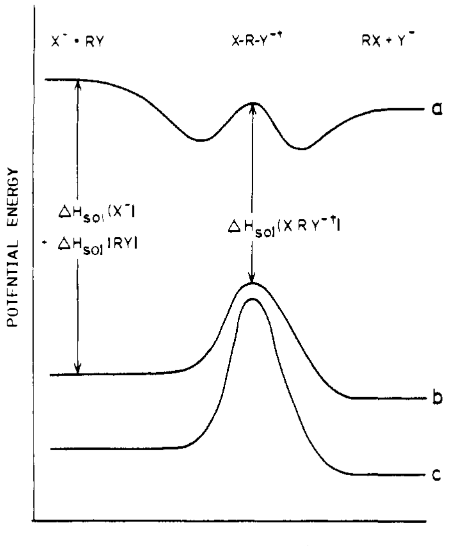

Figure 3. Representative reaction coordinate diagrams for a nucleophilic displacement reaction in the gas phase (a) and in dipolar aprotic (b) and protic (c) solvents.

orbitals of the anion with the carbon center. It could also be simply a reflection of the greater thermodynamic methyl cation affinities of the smaller anions.

Cyanide ion is a much poorer nucleophile than would be expected from its thermodynamic carbon affinity. One possible explanation for this is that the nitrogen end of the nucleophile has the greater charge concentration and is the end which attacks the carbon. This would lead to the less stable neutral product, methyl isocyanide. The proton transfer reaction 33 in Table I, on the other hand, is not anomalously slow despite the fact that formation of HNC would be endothermic. Apparently the low nucleophilicity of cyanide ion is not reflected in its proton abstraction ability.

Reaction efficiencies for five leaving groups are presented in Table II (six including reaction 26 from Table I). The relative order of exothermicities for these groups and any nucleophile (numbers are for methoxide) are:

substrate:	$CH_3O\overset{O}{\overset{\parallel}{C}}CF_3$ >	CH_3Br >	CH_3Cl >	CH_3OPh >	CH_3F >	CH_3OCH_3
$\Delta H'$, kcal/mol:	60.0	47.5	39.3	29.4	10.8	0

The relative rate order with methoxide as the nucleophile is exactly the same:

substrate:	$CH_3O\overset{O}{\overset{\parallel}{C}}CF_3$ >	CH_3Br >	CH_3Cl >	CH_3OPh >	CH_3F >	CH_3OCH_3
rel rate:	58	54	34	12	1	<0.07

The order of the first three leaving groups does not hold for all of the other nucleophiles, however. For instance, with hydroxide it is

$$CH_3Br > CH_3Cl > CH_3O_2CCF_3$$

and with fluoride it is

$$CH_3O_2CCF_3 > CH_3Cl > CH_3Br$$

The order does stay constant besides the reversals within these three very fast leaving groups. Apparently the ease of breaking the CH_3-LG bond plays a dominant part in the rate of the reaction until the exothermicity becomes large, and then secondary factors take over.

The fact that there is not an absolute scale of LGA's proves that there is some kind of communication, or coupling, between the nucleophile and leaving group during the reaction. This is best accommodated as an effect on the energy of the transition state. If there is a stabilizing influence on the transition state because of a favorable interaction between the nucleophile and leaving group, then the reaction will be faster than in the absence of the interaction. This phenomenon has also been observed in solution for S_N2 reactions and discussed by Bunnett[30] and Pearson and Songstad.[31] The latter authors have explained the behavior in terms of the principle of hard and soft acids and bases (HSAB).[32] When the nucleophile and leaving group have similar properties (hardness or softness) the reaction rates are relatively fast. Hard bases are defined as having a donor atom of low polarizability and high electronegativity (F^-, OH^-, NH_2^-, CH_3O^-, PhO^-, $CF_3CO_2^-$). Soft bases, on the other hand, have a donor atom of high polarizability and low electronegativity (CH_3S^-, CN^-, Br^-). Chloride ion is a borderline case in this classification.

The accelerating effect of having a hard nucleophile and leaving group or a soft nucleophile and leaving group is secondary to the other factors discussed above, such as exothermicity. It becomes most evident when the behavior of F^-, CH_3S^-, and CN^-, which have very similar thermodynamic methyl cation affinities (and therefore exothermicities) are compared. The nucleophilic order of these three is $F^- > CH_3S^- > CN^-$ for the leaving groups in Table IV, probably due to the effect of charge concentration. However, when their efficiencies with CH_3Cl and CH_3Br are compared, the secondary "symbiotic" effect takes over. Thus hard fluoride ion displaces chloride faster than bromide while soft methylthiolate and cyanide displace bromide much faster than chloride. Due to effects like this it is impossible to establish an absolute scale of either nucleophilicity or leaving group ability.

Solvent Effects. Another factor which greatly affects the reactivity of S_N2 reactions is the medium in which they are carried out. Parker has extensively studied the solvent effects on these reactions by comparing rates and reactant solvent activity coefficients in a variety of polar protic and polar aprotic solvents.[8] By doing this he has identified the effects of solvation of the reactants and transition states and discussed them in some detail. By comparing the rates in solution with those in the gas phase we can learn much about the absolute effect of the solvent rather than the relative effects of different solvents.

A comparison of the rates of some selected reactions in three solvents and in the gas phase is given in Table III. The most striking difference in the rates is their absolute magnitude. There is a rate acceleration of several orders of magnitude on switching from the protic solvents water and methanol to the polar aprotic dimethylformamide. The comparison between DMF and the gas phase is even more dramatic. The primary influence on the rate differences in the solvation energy of the reactant anion relative to the transition state. This is demonstrated pictorially in Figure 3. It has been discussed for protic vs. aprotic solvents by Parker[8] and for solution vs. gas phase by Dewar and Dougherty.[34]

Figure 3 provides a good background for a qualitative discussion of the solvent effects on these reactions. It is well-known that charge localized ions are better solvated than charge delocalized ions.[8,35] Since the charge is more localized on the reactant anion than the transition state for S_N2 reactions, the former will be better solvated than the transition state. This results in a greater drop in potential energy of the reactants compared to the transition state. For many reactions the energy barrier in the gas phase is lower than the energy of the reactants, as shown in Figure 3. The differential solvation of the reactants and transition state is solely responsible for the increase in this energy barrier to a value greater than the reactants. Because of the specific interaction of hydrogen bonding, protic solvents are more sensitive to charge localization than aprotic solvents. Therefore the differential solvation of reactants and transition state is greater for protic

Table III. Absolute Rates in Various Media of S_N2 Reactions at 25 °C (log k in $M^{-1}\,s^{-1}$)

Reactants	H_2O	CH_3OH	DMF	Gas phase
$OH^- + CH_3F$	−6.2[a]			10.2[b]
$OH^- + CH_3Cl$	−5.2[a]			12.0
$OH^- + CH_3Br$	−3/9[A]			12.0
$F^- + CH_3Cl$	−7.8[a]			11.7
$F^- + CH_3Br$	−6.5[a]			11.6
$F^- + CH_3I$	−7.2[a]	∼−7.3[d]		
$CH_3O^- + CH_3Br$				11.6
$CH_3O^- + CH_3I$		−3.6[c]		
$Cl^- + CH_3Cl$				9.6
$Cl^- + CH_3Br$	−5.3[a]	−5.2[c]	−0.4[c]	9.9
$Cl^- + CH_3I$	−5.5[a]	−5.5[c]	0.5[c]	
$CN^- + CH_3Br$				10.3[b]
$CN^- + CH_3I$	−3.2[c]	−3.2[c]	2.5[c]	
$Br^- + CH_3Br$				<9.8
$Br^- + CH_3I$	−4.4[c]	−4.1[c]	0.1[c]	

[a] Reference 33. [b] Reference 13. [c] Reference 8. [d] R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90,** 319 (1968).

solvents. This is the origin of the great rate enhancement in polar aprotic solvents.[36]

In addition to the striking difference in absolute rates in different media, there are differences and reversals in relative rates. For instance, the halogen nucleophilic order $I^- > Br^- > Cl^- > F^-$ had long been ingrained in the hearts of chemists from the results of innumerable rate studies with a variety of leaving groups. However these studies were carried out in the traditional protic solvents such as water, methanol, or mixed aqueous solvents. Winstein and his co-workers discovered that in acetone, when care was exercised to avoid ion pairing, this order was reversed.[37] In other polar aprotic solvents and in the gas phase the order is $F^- > Cl^- > Br^- > I^-$.

These reversals can also be understood in terms of differential solvation of reactants and transition state. Through a series of gas phase and solution acidity measurements and the enthalpies of solution of the parent acids, Arnett et al. have arrived at the enthalpy of solution of three halide ions in DMSO. They are, in kcal/mol, Cl^- (−76.7), Br^- (−66.5), and I^- (−62.0).[35] Even though the smaller halides are solvated more strongly, the differential solvation of reactants and transition state does not change enough to reverse the reactivity of the halide ions. On switching to a protic solvent, however, the differences in the halide solvation energies become even greater. The enthalpies of transfer from DMSO to methanol are: in kcal/mol at 298 K, Cl^- (−2.5), Br^- (+0.1), and I^- (+2.7).[38] This further increase in relative solvation of the smaller halides in methanol is enough to reverse their order of reactivity, since the solvation of the transition states is not as sensitive to solvent changes as the solvation of the reactant anions.

The LGA of the halide ions in solution ($I^- > Br^- > Cl^- > F^-$) is similar to that in the gas phase ($Br^- > Cl^- > F^-$). This is not surprising since it is the solvation of the free anion which seems to be of most importance, and solvation of the product has no influence on the forward rate of the reaction.

Steric Hindrance. The concept of steric hindrance to reaction is an old one for S_N2 reactions. Indeed, perhaps the first recognition of this concept was by Hofmann in his study of the reactions of ortho substituted anilines with methyl iodide.[39] Most studies since then have involved structural changes in the substrate rather than the nucleophile. They have been described and summarized well by Ingold.[1] The reactions are impeded both by substitution at the α carbon (e.g., methyl, ethyl, isopropyl, and *tert*-butyl) and the β carbon (e.g., ethyl, *n*-propyl, isobutyl, and neopentyl).

Table IV. Steric Effects on S_N2 Reaction Rates in the Gas Phase

Nucleophile	$k_{(CH_3)_3CCH_2Cl}/k_{CH_3Cl}$
F^-	0.61
CH_3S^-	<0.10
$(CH_3)_3CO^-$	<0.01[a]

[a] $k_{CH_3Cl} = 0.8 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1} from ref 10.

In order to study the effect of steric hindrance on gas phase S_N2 reactions, three reaction rates were measured with neopentyl chloride as the substrate. They are listed in Table I and are reproduced in Table IV as fractions of the corresponding rate with methyl chloride. The magnitude of the rate depression for F^- might at first seem very small. In solution, rate depressions are normally several orders of magnitude on switching from a methyl to a neopentyl substrate.[1] However, this can be easily explained by the mechanism in Figure 1. For $F^- + CH_3Cl$ the central barrier is rather small, as reflected in the high efficiency (0.35) of reaction. The steric effect of the *tert*-butyl group in neopentyl chloride increases the central barrier but still does not depress the rate by much since the barrier is still well below the potential energy of the reactants. On the other hand, for CH_3S^- the central barrier is high enough with methyl chloride to cause a low efficiency (0.045). Therefore the raising of the barrier by the steric effect greatly depresses the rate of the reaction. For $(CH_3)_3CO^-$ the reaction with methyl chloride is very efficient (0.5), indicating that there is a small central barrier. However, when $(CH_3)_3CO^-$ reacts with neopentyl chloride, there is sufficient steric interaction to depress the rate substantially. This effect is not seen with the smaller nucleophile F^-.

The trends in steric effects presented here support the proposed mechanism and origin of the rate variations for gas phase S_N2 reactions. They provide a convenient method of modifying the height of the central barrier and observing the resulting effect on the rate of reaction.

Quantitative Model

It is possible to calculate overall rate constants (or relative efficiencies) from the model presented above (Figure 1 and eq 5). In this section RRKM calculations are presented for several systems at various values of the unknown parameter $E_0' - E_0$. The reaction efficiencies are critically dependent on this parameter, so it can be inferred from the experimental efficiency.

In applying RRKM theory we are making the statistical assumption that the energy is randomized among all the internal modes of the intermediate complex and that all the microscopic pathways to products are equally probable. By application of suitable counting methods for the number of internal energy states of the two transition states, the partitioning of the intermediate complex in the two paths (k_b and k_p in Figure 1) can be calculated. RRKM theory is one way of doing this. It is well established in the field of unimolecular reactions and has been described in detail.[40,41]

In order for the statistical assumption to hold, the reactions must proceed via a long-lived intermediate complex rather than by a direct mechanism. Although there is no proof that this is true, past experiments suggest that reactions of this complexity at thermal energies should involve the formation of a long-lived complex.[42] There are several other pieces of evidence which support the applicability of a statistical theory to these reactions:

(1) The adducts have been directly observed in a high-pressure mass spectrometer for a number of reactant pairs.[15] This proves that at least some of the collisions result in long-

Table V. Parameters Used in the Calculation of Reaction Efficiencies for $Cl^- + CH_3Br \rightarrow Br^- + CH_3Cl$[a]

	Transition state A $[Cl^- \cdots CH_3Br]^\dagger$	Transition state B $[Cl \cdots CH_3 \cdots Br]^{-\dagger}$
ν_i[b]	3057 (2)	3057 (2)
	2935 (1)	2972 (1)
	1443 (2)	1448 (2)
	1305 (1)	1284 (1)
	954 (2)	1133 (2)
	611 (1)	200 (3) or 300 (3)
I_i, σ_i[b]	37.0, 3 (2)	
I^+/I	3.0	

[a] Degeneracies are in parentheses. Frequencies (ν_i) are in cm^{-1}, moment of inertia (I_i) is in amu $Å^2$, and σ_i is the symmetry number for the internal rotor. [b] CH_3Br frequencies and moments of inertia were taken from G. Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules", Van Nostrand-Reinhold, New York, N.Y., 1945.

lived complexes that can be stabilized by collision with a third body.

(2) Trajectory calculations on ion-polar molecule collisions indicate that multiple collisions (up to 2000) occur during any one encounter between an ion and molecule.[43] This behavior greatly enhances the T → V energy transfer and the chances for randomization of the internal energy.

(3) There have been several successful applications of statistical theories to other ion-molecule reactions which do not involve an adjustable parameter (e.g., barrier height).[44]

There is a good precedent in the literature for finding barrier heights by the general method presented here. Trotman-Dickenson and co-workers[45] have varied the barrier height for HF elimination from a number of alkyl fluorides in order to fit the observed rate constant for this reaction from chemically activated molecules, e.g.,

$$CH_2F + CH_2CH_3 \rightarrow CH_3CH_2CH_2F^* \rightarrow CH_3CH{=}CH_2 + HF$$

The barrier height for the second reaction derived by this method (E_0 = 56.9 kcal mol^{-1}) is the same as that derived from thermal decomposition of *n*-propyl fluoride. Agreement is very good for the many other systems studied also. In the present systems,

$$X^- + RY \rightleftarrows XRY^{-*} \rightarrow Y^- + RX$$

there is no method for studying the thermal decomposition of the intermediate ion, so the barrier height must be derived from the behavior of the chemically activated species.

Method. The basic RRKM equation is

$$k(E) = G(E - E_0)/hN(E) \tag{6}$$

where $G(E - E_0)$ is the sum of vibrational and internal rotation quantum states for the transition state up to energy $E - E_0$ and $N(E)$ is the density of states for the intermediate complex. The ratio of the two rate constants for a complex which can decompose by two pathways is

$$\frac{k'(E)}{k(E)} = \frac{G'(E - E_0' - \Delta E_{rot})}{G(E - E_0)} \tag{7}$$

Here $k'(E) = k_p$ and $k(E) = k_b$ (see Figure 1) at a specific energy E. ΔE_{rot} is a correction to the internal energy of the transition state for k_p which accounts for the fact that some energy must be constrained to be in the external rotations (and is therefore not available for the vibrational and internal rotational quantum states) in order to conserve angular momentum.[46] It can be calculated by

$$\Delta E_{rot} = (1 - I'/I)kT \tag{8}$$

where I' and I are the moments of inertia for the two transition states. In order to get the overall ratio of rate constants (7) must be integrated over the energy distribution function. When $k_b(E) > k_p(E)$, this ratio is approximately:

$$\frac{k_p}{k_b} = \int_{E_0}^{\infty} \frac{G'(E - E_0' - \Delta E_{rot})}{G(E - E_0)} F(E)\,dE \tag{9}$$

For this type of chemical activation the distribution function is given by:[47]

$$F(E) = \frac{G(E - E_0)e^{-E/kT}}{\int_0^{\infty} G(E - E_0)e^{-E/kT}\,dE} \tag{10}$$

Combining (9) and (10) gives

$$\frac{k_p}{k_b} = \frac{\int_{E_0}^{\infty} G'(E - E_0' - \Delta E_{rot})e^{-E/kT}\,dE}{\int_{E_0}^{\infty} G(E - E_0)e^{-E/kT}\,dE} \tag{11}$$

This ratio can be manipulated to give the overall reaction efficiency ($k_p/(k_b + k_p)$) and therefore the overall bimolecular rate constant by eq 5.

The sums of states in eq 11 were evaluated by a direct counting of vibrational states using seven frequency groups and a classical counting of internal rotational states.[48] The integrals were evaluated numerically.

(1) $Cl^- + CH_3Br$. In order to calculate the sums of states in (11) it is necessary to know or estimate the vibrational frequencies and the moments of inertia for the internal rotors. The transition state for k_b is easily chosen. Because of the long-range attraction between the ion and molecule, the transition state, which is taken to be where the sum of the inherent potential energy and the centrifugal energy reach a maximum,[46] is at a large separation of the two species (> ca. 7 Å, and it depends on the impact parameter). At this distance the oscillator frequencies are those of free CH_3Br, and the remaining internal degrees of freedom are the reaction coordinate and a two-dimensional free rotor corresponding to a tumbling of the CH_3Br (the third dimension of this tumbling is one of the external rotations). The parameters for the calculation are reproduced in Table V.

The frequencies for the second transition state are not so easily chosen. In a recent study on isotope effects on S_N2 reactions, the frequencies of the transition state for the reaction

$$PhS^- + n\text{-}BuCl \rightarrow Cl^- + n\text{-}BuSPh$$

were determined based on a number of assumptions.[49] Most of the frequencies for the transition state in the present study were changed proportionately from CH_3Br in the same way as those in the isotope effect study were changed from *n*-BuCl. The remaining oscillators are the symmetric Cl-C-Br stretch and two degenerate Cl-C-Br bends. In the very crudely analogous compound PCl_5 these oscillator frequencies are 394 and 335 cm^{-1}. They should be lower in $ClCH_3Br^-$ because of the reduced bound orders and heavier Br. Calculations were performed with both 200- and 300-cm^{-1} frequencies for these three oscillators. The frequencies are summarized in Table V.

(2) $CH_3O^- + CH_3Br$. The parameters for the two transition states in this system were chosen in the same way as those for the previous one. The frequencies and moments of inertia for CH_3O^- were taken to be the same as those of CH_3F except for the C-O stretch, which was taken from CH_3OH. The parameters are reproduced in Table VI. The frequencies have been grouped for the direct counting procedure by taking the

Table VI. Parameters Used in the Calculation of Reaction Efficiencies for $Cl^- + n\text{-}BuBr \rightarrow Br^- + n\text{-}BuCl$[a]

	Transition state A $[Cl^-\cdots n\text{-}BuBr]^\dagger$	Transition state B $[Cl\cdots n\text{-}Bu\cdots Br]^{-\dagger}$
ν_i	2924 (9)	2924 (9)
	1429 (7)	1434 (8)
	1193 (8)	1182 (7)
	709 (7)	753 (6)
	280 (2)	280 (2)
	197 (2)	199 (5)
	100 (1)	100 (1)
I_i, σ_i	220.0, 1 (2)	
I^+/I	3.0	

[a] See Table V for explanation and units.

Table VII. Parameters Used in the Calculation of Reaction Efficiencies for $CH_3O^- + CH_3Br \rightarrow Br^- + CH_3OCH_3$[a]

	Transition state A $[CH_3O^-\cdots CH_3Br]^\dagger$	Transition state B $[CH_3O\cdots CH_3\cdots Br]^{-\dagger}$
ν_i	3004 (6)	3004 (6)
	1466 (3)	1548 (2)
	1445 (2)	1466 (3)
	1222 (3)	1284 (1)
	1033 (1)	1182 (2)
	952 (2)	1099 (3)
	611 (1)	200 (5)
I_i, σ_i	8.4, 1 (1)	1.65, 3 (1)
	37.0, 3 (2)	
	10.9, 3 (2)	
I^+/I	3.0	

[a] See Table V for explanation and units.

geometric mean of the individual frequencies for each group.[48]

(3) $Cl^- + n$-BuBr. The two transition state models are chosen as before. The frequencies for n-BuBr were estimated from those of n-BuH and EtBr.[50] The frequencies have been grouped as above. The parameters are reproduced in Table VII.

Results and Discussion

The results of the RRKM calculations for the four systems are shown in Figure 4. There are several observations which can be made about these results:

(1) Even though the barriers may be substantially below the potential energy of the reactants, they can lead to significantly reduced reaction efficiencies.

(2) The relative barrier heights ($\Delta E_0^\dagger = E_0' - E_0$) required to reproduce the experimental efficiency for the $Cl^- + CH_3Br$ reaction are −0.3 and −0.7 kcal mol^{-1} for the two transition state models. Considering the uncertainty in transition state frequencies this should only be taken as an approximate range of barrier heights. Nevertheless, it is reassuring that the two values are close despite the very different frequencies. The exact values of these frequencies are not nearly as critical as the difference in barrier heights.

(3) The relative barrier height which corresponds to the experimental efficiency for the $CH_3O^- + CH_3Br$ reaction is 8.8 kcal mol^{-1}.

(4) The reason for the large discrepancy in the curves for Cl^- and CH_3O^- is the fact that the latter is polyatomic. As a result of the three extra degrees of freedom due to its rotations, the channel to reactants (where these degrees of freedom are internal rotations in the transition state) is favored over the channel to products (where they are vibrations).

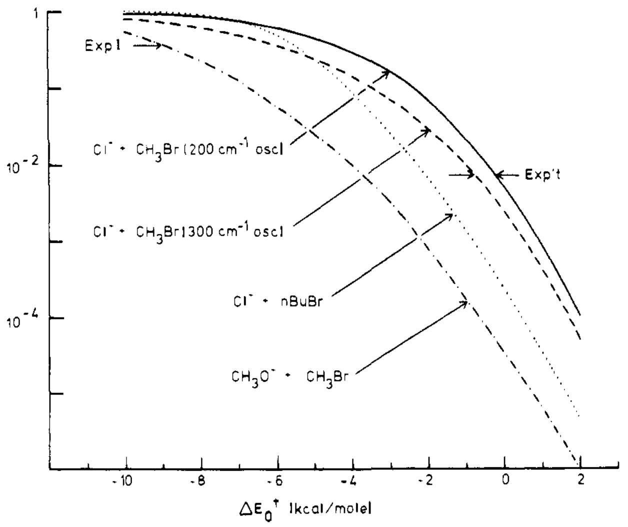

Figure 4. Calculated reaction efficiencies for nucleophilic displacement reactions as a function of the difference in barrier heights ($E_0' - E_0$ in Figure 1). The arrows indicate the experimental efficiencies for two of the reactions. The RRKM calculations were done using the input parameters in Tables V, VI, and VII.

(5) For $Cl^- + n$-BuBr, the effect of the extra vibrational degrees of freedom is to slow down the reaction at large barrier heights and speed it up at low barrier heights. The reason for this is that the sum of states for the purely vibrational transition state (the one leading to products) grows much faster relative to the vibrational-rotational transition state due to the extra degrees of freedom.

(6) Minor changes in structure (e.g., substituting F^- for Cl^- or CH_3Cl for CH_3Br or CH_3S^- for CH_3O^-) give curves very close to those for the analogous reactions in Figure 4.

From the above treatment and various literature values, the enthalpies of solution of the transition state ($\Delta H°_{sol}(X\text{-}R\text{-}Y^{-\dagger})$ in Figure 3) can be found for X = Cl and RY = CH_3Br from the approximate[52] eq 12.

$$\Delta H°_{sol}(X\text{-}R\text{-}Y^{-\dagger}) = \Delta H°_{sol}(X^-) + \Delta H°_{sol}(RY) + E_a\ (\text{in } H_2O) - \Delta E_0^\dagger\ (\text{gas phase}) - 2RT \quad (12)$$

$$\Delta H°_{sol}(Cl^-) = -76.3\ \text{kcal/mol} \quad (\text{ref 35 and 38})$$

$$\Delta H°_{sol}(CH_3Br) = -6.8\ \text{kcal/mol} \quad (\text{ref 52})$$

$$E_a(\text{in } H_2O) = 24.7\ \text{kcal/mol} \quad (\text{ref 33})$$

$$\Delta E_0^\dagger(\text{gas phase}) = -0.3\ \text{kcal/mol} \quad (\text{this work; 200 cm}^{-1}\text{ oscillators})$$

$$\Delta H°_{sol}(Cl\text{-}CH_3\text{-}Br^{-\dagger}) = -58.7\ \text{kcal/mol in } H_2O\ \text{AT } 25\ °C$$

Thus the solvation enthalpy of the transition state is about 24.4 kcal/mol less than the solvation enthalpy of the reactants. This is the primary origin of the 15 orders of magnitude rate acceleration in the gas phase over aqueous solution.

The barrier heights of the models presented here are not meant to be absolute quantitative predictions. The model is one which has been proposed to explain the experimental results but it has not been proven to be correct. Qualitatively, the trends should be correct, but it is only an approximation quantitatively.

Conclusion

The mechanism in Figure 1 can account for all of the available experimental and theoretical evidence on S_N2 gas phase reactions. The ion and molecule collide at a rate determined by the long-range attractive force between them. The competition between decomposition of the resulting collision complex to reactants and passage over the central barrier to the second ion–molecule complex determines the overall efficiency of the reaction. The most important factor which affects this efficiency is the height of the central barrier. Variation in this height leads to a wide range of reaction rates. These rates, which are intrinsic rates in the absence of the complicating effects of solvent, are dependent on the nature of the nucleophile, substrate, and leaving group. The intrinsic nucleophilicities and leaving group abilities have been determined. In addition, there is a secondary effect on the rates due to a coupling between the nucleophile and leaving group. Steric inhibition due to alkyl groups on the substrate can be substantial.

S_N2 reactions are the first ionic reactions to be extensively studied both in solution and in the gas phase. They are orders of magnitude slower in solution due to a preferential solvation of the reactants (principally the ion) over the transition state. The relative order of nucleophilicity is similar in the gas phase and dipolar aprotic solvents and is very different from the one found in protic solvents. Leaving group abilities are very similar for all three.

There have been many comparisons between solution and gas phase thermodynamic quantities, but there have not been many comparisons of kinetic processes in the two phases. One reason for this is that the details of the gas phase mechanisms are often difficult to determine. Hopefully the approach in this paper can be applied to other ion–molecule reactions not only in order to understand the gas phase reactions but also so that comparison with reactions in solution can be made.

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References and Notes

(1) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969.
(2) S. R. Hartshorn, "Aliphatic Nucleophilic Substitution", Cambridge University Press, London, 1973.
(3) R. W. Alder, R. Baker, and J. M. Brown, "Mechanism in Organic Chemistry", Wiley-Interscience, London, 1971.
(4) A. Streitwieser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York, N.Y., 1963.
(5) E. S. Amis and J. F. Hinton, "Solvent Effects on Chemical Phenomena", Academic Press, New York, N.Y., 1973.
(6) J. L. Gleave, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 236 (1935).
(7) S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Lett.*, 9, 24 (1960).
(8) A. J. Parker, *Chem. Rev.*, **69**, 1 (1969).
(9) (a) A. Dedieu and A. Veillard, *J. Am. Chem. Soc.*, **94**, 6730 (1972); (b) W. Th. A. M. van der Lugt and P. Ros, *Chem. Phys. Lett.*, **4**, 389 (1969); (c) J. J. C. Mulder and J. S. Wright, *ibid.*, **5**, 445 (1970); (d) C. D. Ritchie and G. A. Chappell, *J. Am. Chem. Soc.*, **92**, 1819 (1970); (e) V. Dyczmons and W. Kutzelnigg, *Theor. Chim. Acta*, **33**, 239 (1974); (f) P. Baybutt, *Mol. Phys.*, **29**, 389 (1975); (g) F. Keil and R. Alrichs, *J. Am. Chem. Soc.*, **98**, 4787 (1976); (h) R. F. W. Bader, A. J. Duke, and R. R. Messer, *ibid.*, **95**, 7715 (1973); (i) H. B. Schlegel, K. Mislow, F. Bernardi, and A. Bottoni, in press.
(10) D. K. Bohme and L. B. Young, *J. Am. Chem. Soc.*, **92**, 7354 (1970).
(11) L. B. Young, E. Lee-Ruff, and D. K. Bohme, *Chem. Commun.*, 35 (1973).
(12) D. K. Bohme, G. I. Mackay, and J. D. Payzant, *J. Am. Chem. Soc.*, **96**, 4027 (1974).
(13) K. Tanaka, G. I. Mackay, J. D. Payzant, and D. K. Bohme, *Can. J. Chem.*, **54**, 1643 (1976).
(14) J. I. Brauman, W. N. Olmstead, and C. A. Lieder, *J. Am. Chem. Soc.*, **96**, 4030 (1974).
(15) (a) R. C. Dougherty, J. Dalton, and J. D. Roberts, *Org. Mass Spectrom.*, **8**, 77 (1974); (b) R. C. Dougherty and J. D. Roberts, *ibid.*, **8**, 81 (1974); (c) R. C. Dougherty, *ibid.*, **8**, 85 (1974).
(16) (a) C. A. Lieder and J. I. Brauman, *J. Am. Chem. Soc.*, **96**, 4028 (1974); (b) C. A. Lieder and J. I. Brauman, *Int. J. Mass Spectrom. Ion Phys.*, **16**, 307 (1975).
(17) J. L. Beauchamp, *Ann. Rev. Phys. Chem.*, **22**, 527 (1971).
(18) (a) R. T. McIver, Jr., *Rev. Sci. Instrum.*, **41**, 555 (1970); (b) R. C. Dunbar and R. T. McIver, Jr., *Int. J. Mass Spectrom. Ion Phys.*, 7, 741 (1971).
(19) W. T. Huntress, J. B. Laudenslager, and R. F. Pinizzotto, *Int. J. Mass Spectrom. Ion Phys.*, **13**, 331 (1974).
(20) T. E. Sharp, J. R. Eyler, and E. Li, *Int. J. Mass Spectrom. Ion Phys.*, **9**, 421 (1972).
(21) C. A. Lieder, Ph.D. Thesis, Stanford University, 1974.
(22) P. L. Hanst and J. G. Calvert, *J. Phys. Chem.*, **63**, 104 (1959).
(23) Thermochemistry calculated from $D(Cl^- - CH_3Br) = 10.9$ kcal/mol (ref 15a); $D(Cl^- - CH_3CN) = 13.4$ and $D(Br^- - CH_3CN) = 12.9$ (R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, **94**, 2940 (1972); $\Delta H_f°(Cl^-) = -54.3$ and $\Delta H_f°(Br^-) = -50.9$ (ref 24a); $\Delta H_f°(CH_3Cl) = -20.6$ and $\Delta H_f°(CH_3Br) = -9.0$ (ref 24b).
(24) (a) K. W. Egger and A. T. Cocks, *Helv. Chim. Acta*, **56**, 1516 (1973); (b) D. R. Stull, E. F. Westrum, Jr., and G. C. Sinke, "The Chemical Thermodynamics of Organic Compounds", Wiley, New York, N.Y., 1969.
(25) D. K. Bohme, "Interactions Between Ions and Molecules", P. Ausloos, Ed., Plenum Press, New York, N.Y., 1975, p 489.
(26) W. E. Farneth and J. I. Brauman, *J. Am. Chem. Soc.*, **98**, 7891 (1976).
(27) M. Meot-Ner and F. H. Field, *J. Am. Chem. Soc.*, **97**, 2014 (1975).
(28) M. J. S. Dewar and R. C. Dougherty, "The PMO Theory of Organic Chemistry", Plenum Press, New York, N.Y., 1975, pp 212–220.
(29) J. M. Riveros, A. C. Breda, and L. K. Blair, *J. Am. Chem. Soc.*, **96**, 4030 (1974).
(30) (a) J. F. Bunnett, *J. Am. Chem. Soc.*, **79**, 5969 (1957); (b) J. F. Bunnett and J. D. Reinheimer, *ibid.*, **84**, 3284 (1962).
(31) (a) R. G. Pearson and J. Songstad, *J. Org. Chem.*, **32**, 2899 (1967); (b) R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967).
(32) R. G. Pearson, Ed., "Hard and Soft Acids and Bases", Dowden, Hutchinson, and Ross, Inc., Stroudsburg, Pa., 1973.
(33) R. H. Bathgate and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 2642 (1959).
(34) Reference 28, p 234.
(35) E. M. Arnett, D. E. Johnston, and L. E. Small, *J. Am. Chem. Soc.*, **97**, 5598 (1975).
(36) One factor which has not been considered here but which should not be forgotten is ion pairing or ion aggregation. Clearly these effects will slow down the overall rate by stabilizing the reactant anion relative to the transition state. It is assumed in this and the following discussion that the anions are free from interactions with counterions. For an example of the complications which ion aggregation can cause, see the following reference.
(37) S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Lett.*, 24 (1960).
(38) B. G. Cox, *Annu. Rep. Prog. Chem.*, **70** (Section A) (1973).
(39) (a) A. W. Hofmann, *Ber.*, **5**, 704 (1872); (b) *ibid.*, **8**, 61 (1875).
(40) P. J. Robinson and K. A. Holbrook, "Unimolecular Reactions", Wiley-Interscience, New York, N.Y., 1972.
(41) W. Forst, "Theory of Unimolecular Reactions", Academic Press, New York, N.Y., 1973.
(42) For an excellent general discussion of intermediate complex and direct mechanisms, see R. Wolfgang, *Acc. Chem. Res.*, **3**, 48 (1970).
(43) J. V. Dugan, Jr., J. H. Rice, and J. L. Magee, *Chem. Phys. Lett.*, **3**, 323 (1969).
(44) (a) S. E. Buttrill, Jr., *J. Chem. Phys.*, **52**, 6174 (1970); (b) C. E. Klots, *ibid.*, **64**, 4269 (1976); (c) W. N. Olmstead, M. Lev-On, D. M. Golden, and J. I. Brauman, *J. Am. Chem. Soc.*, **99**, 992 (1977).
(45) P. Cadman, A. W. Kirk, and A. F. Trotman-Dickenson, *J. Chem. Soc., Faraday Trans. 1*, 72, 996 (1976).
(46) E. V. Waage and B. S. Rabinovitch, *Chem. Rev.*, 70, 377 (1970).
(47) Reference 41, p 208 ff.
(48) W. L. Hase and D. L. Bunker, Quantum Chemistry Program Exchange No. 234, Indiana University. The subroutine in this RRKM program was used intact except for the addition of the capability to handle two-dimensional rotors.
(49) R. L. Julian and J. W. Taylor, *J. Am. Chem. Soc.*, **98**, 5238 (1976).
(50) T. Shimanouchi, *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.*, "Tables of Molecular Vibrational Frequencies, Part 1" (1967).
(51) (a) T. Su and M. T. Bowers, *J. Chem. Phys.*, **58**, 3027 (1973); (b) T. Su and M. T. Bowers, *Int. J. Mass Spectrom. Ion Phys.*, **12**, 347 (1973).
(52) This equation is inexact because the measured Arrhenius activation energy is the difference between the average energy of the reacting molecules and the average energy of the nonreacting molecules, which is not always equal to the ground state potential energy difference between the reactants and the transition state. The $2RT$ is a standard state correction to E_a (D. M. Golden, *J. Chem. Educ.*, **48**, 235 (1971)) and part of the difference between E_0 and E_a (ref 41, p 170).