

A Direct Approach to the Prediction of Substituent Effects on Transition State Structure

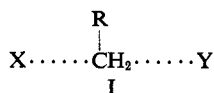
Judith Coburn Harris^{1a,b} and Joseph L. Kurz

Contribution from the Department of Chemistry, Washington University, Saint Louis, Missouri 63130. Received December 18, 1968

Abstract: An approach to the prediction of the effect of substituent changes on transition state structure which avoids the necessity for summing the independently estimated effects of the contributing normal modes is described. This approach leads to specific predictions of the directions of changes in lengths and orders of reacting bonds in SN2 transition states for those cases in which more than one possible response is permitted by Thornton's rules; these predictions are shown to be in better agreement with experimental evidence than those based on the reacting bond rule. Among the conclusions resulting from this analysis are three rules. (The first depends only on the form of the assumed potential function for the transition state; the other two depend also on an assumed model for predicting the relation between reacting bond length and the energy of interaction between the bond and the substituent.) (1) In any SN2 transition state, an electron-withdrawing substituent in the nucleophile or leaving group will increase the order of the reacting bond nearer to the substituent and decrease the order of the farther reacting bond. (2) If an SN2 transition state contains one negatively charged and one uncharged nucleophile, an electron-withdrawing substituent at the central atom will tend to decrease the order of the reacting bond to the negative nucleophile and increase the order of the reacting bond to the uncharged nucleophile. (3) If an SN2 transition state involves nucleophilic atoms from different rows of the periodic table, an electron-withdrawing substituent at the central atom will tend to increase the order of the reacting bond to the lighter atom, and decrease the order of the other reacting bond.

Any detailed interpretation of kinetic isotope and substituent effects in terms of the transition state theory of reaction rates requires a description of bond lengths and bond orders in the transition state and of the changes in these parameters which accompany changes in a substituent. Various approaches to the prediction of these quantities have been proposed, including the "Hammond postulate"² and the similar treatments of Wiberg,³ Streitwieser,⁴ and Leffler,⁵ the "reacting bond rule,"⁶ and, most recently, Thornton's rules.⁷ According to the Thornton model, the most general method of prediction yet presented, the introduction of a substituent into an activated complex, results in a perturbation, linear in the appropriate normal coordinate, of the vibrational potential for every normal mode of motion of the system. The effect of the substituent change on a given bond is obtained by summation of the separate effects on all normal modes which involve that bond.

Unfortunately, the prediction of substituent effects by this summation procedure is far from straightforward in a number of cases of interest. One such case is important in connection with current work in these laboratories which is directed toward the determination of X-C and C-Y bond orders in SN2 transition states of the form I. Thornton points out that when a substituent change is made in X or Y, the effects on the sym-



metric and antisymmetric normal stretching modes op-

pose one another in the reacting bond nearer to the substituent and reinforce in the more distant reacting bond. For such a substituent change, therefore, the Thornton model does not allow prediction of the direction of the change in length of the bond nearer to the site of substitution.

Another ambiguity arises if the structure of R in transition state I is modified. Increased electron supply at R should make extension of both the X-C and the C-Y bonds less difficult and, since motion perpendicular to the reaction coordinate involves extending both bonds, the Thornton rules predict that the substituent effect on this normal coordinate motion will be to lengthen both bonds. Motion parallel to the reaction coordinate, however, involves extending one bond and compressing the other; a given substituent change makes one of these individual bond length changes easier and the other more difficult. As a basis for predicting the substituent effect on the parallel mode, Thornton argues that, if two reacting bonds are equidistant from the substituent, the effect will be larger on whichever of the two bonds has the larger individual stretching force constant in the unperturbed activated complex. The net change in the parallel motion would then be determined by the effect on the stronger reacting bond. On the other hand, calculations based on simple models (*vide infra*) have led the present authors to the conclusion that the substituent effect on an individual reacting bond should be largely independent of its stretching force constant, but should correlate well, for instance, with the rows in the periodic table of the atoms bonded (which affects both bond lengths and force constants). Regardless of which of these sets of assumptions is made, there remains the question of whether the perpendicular or the parallel effect (which again oppose each other in one of the bonds) will be more important in determining the net change in transition state geometry. If X and Y are identical, the position of the transition state along the reaction coordinate is fixed by symmetry and any sub-

(1) (a) Née Judith I. Coburn; (b) National Science Foundation Graduate Fellow, 1968-1969.

(2) G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).

(3) K. B. Wiberg, *Chem. Rev.*, **55**, 732 (1955).

(4) A. Streitwieser, Jr., *ibid.*, **56**, 639 (1956).

(5) J. E. Leffler, *Science*, **117**, 340 (1953).

(6) C. G. Swain and E. R. Thornton, *J. Amer. Chem. Soc.*, **84**, 817 (1962).

(7) E. R. Thornton, *ibid.*, **89**, 2915 (1967).

stituent effect must be on the perpendicular motion. However, it seems probable that, as Thornton has suggested, the parallel effect might dominate the perpendicular if X and Y are of sufficiently different structure.

Much of this ambiguity arises from the fact that the substituent effect on each normal coordinate is estimated separately so that the contributions from all normal modes to changes in each bond length must be summed to obtain the predicted net change in bonding parameters. A more direct approach is to write the total potential function for the transition state in terms of individual bond force constants and then to apply a linear perturbation to that potential. The results of this procedure for a simple SN2 transition state model are given here.

Algebraic Criteria. If bending modes are excluded and X, Y, and CH₂R in I are approximated by point masses, the internal potential function for the transition state may be written in terms of two lengths, δ_{XC} and δ_{CY} , each of which is defined as the difference between the instantaneous value of the appropriate bond length in the system being considered and the equilibrium value of that bond length in the unperturbed transition state. Thus δ_{XC} for a perturbed system or a nonequilibrium configuration of the unperturbed system is given by eq 1.

$$\delta_{XC} = r_{XC} - (r_{XC}^{eq} \text{ for unperturbed system}) \quad (1)$$

The potential for the unsubstituted system is then given by eq 2, in which the k 's are individual bond force con-

$$V = \frac{1}{2}k_{XC}\delta_{XC}^2 + \frac{1}{2}k_{CY}\delta_{CY}^2 + \beta\delta_{XC}\delta_{CY} \quad (2)$$

stants, β is a coupling constant, and k_{XC} , k_{CY} , and β are positive. This form of the potential is identical with that⁸ which is known to give a satisfactory semiquantitative treatment of deuterium isotope effects in hydrogen transfer reactions. It is considered to be more realistic over a wide range of transition state symmetries than an alternative formulation in which $\beta = 0$ and the individual force constants are allowed to have opposite signs.

If the perturbation in transition state structure which is produced by introduction of a substituent is sufficiently small, then the corresponding perturbation in energy may be assumed to be linear in the individual bond lengths as in eq 3. (Exclusion of a term linear in $(\delta_{XC}\delta_{CY})^{1/2}$ is equivalent to the assumption that the

$$P = m_{XC}\delta_{XC} + m_{CY}\delta_{CY} + \text{constant} \quad (3)$$

change in direct interaction between X and Y produced by the substituent is small compared to the changes in interaction between X and C and/or C and Y.) The potential, V' , for the perturbed transition state is then given by eq 4. The values of δ_{XC} and δ_{CY} at which V'

$$V' = \frac{1}{2}k_{XC}\delta_{XC}^2 + \frac{1}{2}k_{CY}\delta_{CY}^2 + \beta\delta_{XC}\delta_{CY} + m_{XC}\delta_{XC} + m_{CY}\delta_{CY} + \text{constant} \quad (4)$$

has its stationary point are given by eq 5. Since the

$$\delta_{XC}' = \frac{m_{CY}\beta - m_{XC}k_{CY}}{k_{XC}k_{CY} - \beta^2}; \quad \delta_{CY}' = \frac{m_{XC}\beta - m_{CY}k_{XC}}{k_{XC}k_{CY} - \beta^2} \quad (5)$$

(8) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

unperturbed V has its stationary point at $\delta_{XC} = \delta_{CY} = 0$, δ_{XC}' and δ_{CY}' in eq 5 are equal to the increases in the two bond lengths which result from introduction of the substituent.

In considering the prediction of δ_{XC} and δ_{CY} values for various substituent changes, it should first be noted that if $\beta = 0$, the relations in eq 5 lead to Thornton's result, eq 6, for separate harmonic oscillators. That is,

$$\beta = 0; \quad \delta_{XC}' = \frac{-m_{XC}}{k_{XC}}; \quad \delta_{CY}' = \frac{-m_{CY}}{k_{CY}} \quad (6)$$

a substituent change which makes extension of a bond more difficult ($m > 0$) will cause a decrease in bond length ($\delta < 0$) for a vibration with a positive restoring force ($k > 0$), and will have a larger effect on the weaker of the two bonds. The cases of greatest interest, however, are those in which β^2 is greater than the product of the individual force constants, since it is only these systems which correspond to transition states, *i.e.*, systems for which the stationary point is a saddle point and the antisymmetric stretch has a negative restoring force. For such systems, although the expressions in eq 5 do not immediately reduce to a simple form, it is possible to predict relative values of δ_{XC} and δ_{CY} for a number of cases of interest.

Predictive Rules. Substitution in the Nucleophile.

The introduction of an electron-withdrawing substituent at X of I, for example, will cause a perturbation in which m_{XC} is negative and m_{CY} is positive. It follows from eq 5 that whenever $m_{XC}m_{CY}$ is negative, it is necessary that $\delta_{XC}\delta_{CY}$ be negative; the substituent in X must thus have opposite effects on the lengths of the two reacting bonds. Furthermore, if I is a transition state ($\beta^2 > k_{XC}k_{CY}$), it is necessarily δ_{XC} which is less than zero and δ_{CY} which is greater than zero. (If I were a stable species ($\beta^2 < k_{XC}k_{CY}$), the directions of these individual changes would be reversed.) The first rule, then, for the prediction of substituent effects on transition state structure may be stated as follows. *In any SN2 transition state, an electron-withdrawing substituent in the nucleophile or leaving group will shorten (increase the order of) the reacting bond nearer to the substituent and lengthen (decrease the order of) the farther reacting bond.* The validity of this rule is independent of any assumptions, other than those expressed in eq 2-4, about the nature of the bonding in the unperturbed transition state or about the mechanism of interaction between that species and the substituent. Furthermore, in applying the rule to the prediction of *directions* of changes in reacting bond lengths it is not necessary that the symmetry of the unperturbed system or the relative values of k_{XC} , k_{CY} , or β be specified (except, of course, that $\beta/(k_{XC}k_{CY})^{1/2}$ must be > 1).

In contrast to this facile prediction of the *directions* of changes in individual bond lengths, no general prediction of the relative *magnitudes* of those changes (*e.g.*, of $|\delta_{XC}/\delta_{CY}|$) can be made from eq 5. In order to predict relative magnitudes, values must be estimated for the ratios, $m_{XC}:m_{CY}$ and $\beta:(k_{XC}k_{CY})^{1/2}$. The m ratio may be estimated from the bond orders and lengths through the use of an electrostatic model for bonding in the transition state. The details of that model and the rationale for the assumed possible range of β are given in a later section of this paper; the results and implica-

Table I. Model Calculations of the Effect of an Electronegative Substituent in X on the Structure of an SN2 Transition State (I)

Transition State X-C-Y	n_{XC}	n_{CY}	$\frac{k_{XC}^a}{k_{CY}}$	$\left \frac{m_{XC}}{m_{CY}}\right ^b$	$\beta/(k_{XC}k_{CY})^{1/2} = 1.0^c$		$\beta/(k_{XC}k_{CY})^{1/2} = 1.2$	
					$\delta_{XC}/\delta_{CY}^e$	$\Delta n_{XC}^d/\Delta n_{CY}$	$\delta_{XC}^e/\delta_{CY}$	$\Delta n_{XC}^d/\Delta n_{CY}$
F-C-N	0.40	0.10	4.23	9.8	∓ 0.48	± 1.92	∓ 0.43	± 1.72
	0.25	0.25	1.06	3.0	∓ 0.97	± 0.97	∓ 0.88	± 0.88
	0.10	0.40	0.26	1.1	∓ 1.95	± 0.48	∓ 1.82	± 0.45
N-C-F	0.40	0.10	3.84	4.5	∓ 0.51	± 2.04	∓ 0.48	± 1.92
	0.25	0.25	0.94	1.8	∓ 1.03	± 1.03	∓ 0.98	± 0.98
	0.10	0.40	0.23	0.7	∓ 2.05	± 0.51	∓ 2.00	± 0.50
F-C-I	0.40	0.10	9.74	4.1	∓ 0.32	± 1.28	∓ 0.31	± 1.24
	0.25	0.25	2.41	1.6	∓ 0.64	± 0.64	∓ 0.63	± 0.63
	0.15	0.35	1.05	0.8	∓ 0.98	± 0.42	∓ 1.01	± 0.43
	0.10	0.40	0.61	0.5	∓ 1.29	± 0.32	∓ 1.34	± 0.33
I-C-F	0.40	0.10	1.64	6.3	∓ 0.78	± 3.12	∓ 0.69	± 2.76
	0.35	0.15	0.95	4.7	∓ 1.03	± 2.40	∓ 0.91	± 2.12
	0.25	0.25	0.41	2.6	∓ 1.58	± 1.89	∓ 1.68	± 1.68
	0.10	0.40	0.10	0.8	∓ 3.17	± 0.79	∓ 2.90	± 0.72

^a From eq 9, using single-bond force constants for C-F, C-N, and C-I of 5.6, 5.3, and 2.3 md/Å, respectively. ^b From eq 16, 17 (cf. Table IV), using $R = 3 \text{ \AA}$, $q_C = +0.5$. ^c From eq 5; the notation $(\delta_{XC}/\delta_{CY}) = \mp 0.48$ is to be interpreted as follows: δ_{XC} is negative (XC bond is shortened), δ_{CY} is positive (CY bond is lengthened), and $|\delta_{XC}| = 0.48|\delta_{CY}|$. ^d From eq 7; the \pm notation is to be interpreted as explained in footnote c. ^e As $\beta/(k_{XC}k_{CY})^{1/2}$ approaches unity, each individual δ value increases in magnitude without bound, but its sign depends on whether $\beta/(k_{XC}k_{CY})^{1/2}$ is greater or less than 1; the signs given are those for the limit approached from larger values of β (i.e., for the limiting case of a transition state rather than of a stable molecule).

tions of those calculations are discussed immediately below.

In any discussion of the magnitudes of the "effects" of a substituent on reacting bonds, it is important to distinguish between changes in bond lengths, δ_{XC} and δ_{CY} , and changes in bond orders, Δn_{XC} and Δn_{CY} . Such a distinction is necessary because it is not generally true that a larger value of $|\delta|$ implies a larger $|\Delta n|$; a given $|\delta|$ will correspond to a much larger $|\Delta n|$ for a strong bond than for a weak one. Furthermore, the most commonly used experimental probes for the strengths of reacting bonds, kinetic isotope, and substituent effects, are primarily probes for bond order (or for force constant and formal charge, which are proportional to bond order) rather than for bond length.

Table I summarizes the results of representative calculations of the effect of an electron-withdrawing⁹ substituent in X on the structure of the transition state, I. The hypothetical substituent change under consideration is the introduction of a unit positive charge 3 \AA from X and colinear with the X-C bond (II). The total bond order to carbon ($n_{XC} + n_{CY}$) was taken as 0.5 on the basis of unpublished interpretations of substituent effects in some similar substitution reactions; calculations based on total bond orders of 1.0 and 0.25 led to identical qualitative conclusions. Values of the $\delta_{XC}:\delta_{CY}$ ratio, rather than of the separate δ values (eq 5), are tabulated; this ratio is independent of the value of D_E (eq 16,17) and approaches a finite limit as $\beta:(k_{XC} \cdot k_{CY})^{1/2}$ approaches its lower bound of unity. The force constant for each bond was assumed to be proportional to the order of that bond (eq 9). The δ ratios were converted to ratios of Δn values according to eq 7,

$$\frac{\Delta n_{XC}}{\Delta n_{CY}} = \frac{n_{XC} \delta_{XC}}{n_{CY} \delta_{CY}} \quad (7)$$

which may be obtained by differentiation of eq 8.

The approximations inherent in the derivation of eq 5, in the model used for estimating the m ratio, and in the

(9) Although the model employed here is based on the field effect, the traditional terms ("electron donating" and "electron withdrawing") for classification of substituents, which would seem to imply an inductive model, have been retained.

assignment of values to k and β make the exact magnitudes of δ_{XC}/δ_{CY} and $\Delta n_{XC}/\Delta n_{CY}$ given in Table I of doubtful quantitative significance. However, their signs and their variations with changes in the parameters of the model should reveal the correct qualitative responses of the structure of a transition state to the perturbing substituent.

Inspection of Table I reveals that the relative magnitudes of Δn_{XC} and Δn_{CY} are strongly dependent upon both the nature of X and Y and the symmetry of the unperturbed transition state. Thus, no generally valid rule for predicting the effect of a substituent in X either on the symmetry of the transition state (as measured by $n_{CY} - n_{XC}$) or on the "tightness" of the transition state (as measured by $n_{XC} + n_{CY}$) can be stated. Predictions for individual special cases may be possible if independent evidence concerning the symmetry is available. Despite their low predictive value, however, the patterns of behavior revealed in Table I are of interest. First, the distinction between δ and Δn as measures of changes in transition state structure is dramatically demonstrated; in almost every instance, the bond which experiences the greater change in length is that which displays the smaller change in order. This reversal of relative magnitudes of δ and Δn reflects the fact that it is the bond with the smaller value of n (and/or the smaller k) which tends to exhibit the larger $|\delta|$. This is true even when the bond with the smaller value of n is the one which is farther from the substituent.

An interesting corollary of such behavior is that in a transition state in which $k_{XC} = k_{CY}$, the lengths of the two reacting bonds are affected equally, although in opposite directions, by the substituent change. Since $|m|$ is almost always larger for the nearer bond, other factors must exist which make the length of the farther bond inherently more sensitive to a substituent change. (This assertion is qualitatively the same as that deduced by Thornton:⁷ the separate effects of a substituent at X on the symmetric and antisymmetric normal stretching modes oppose one another in the nearer (X-C) bond but reinforce in the more distance (C-Y) bond.) If the SN2 transition state under consideration contains

Table II. Model Calculations of the Effect of an Electronegative Substituent at C on the Structure of an SN2 Transition State (I)

Transition State X-C-Y	n_{XC}	n_{CY}	$\frac{k_{XC}^a}{k_{CY}}$	$\frac{ m_{XC} ^b}{ m_{CY} }$	$-\beta/(k_{XC}k_{CY})^{1/2} = 1.0^a$		$-\beta/(k_{XC}k_{CY})^{1/2} = 1.2$	
					$\delta_{XC}^a/\delta_{CY}$	$\Delta n_{XC}^a/\Delta n_{CY}$	$\delta_{XC}^a/\delta_{CY}$	$\Delta n_{XC}^a/\Delta n_{CY}$
F-C-N	0.40	0.10	4.23	4.6	± 0.49	∓ 1.96	± 0.30	∓ 1.20
	0.30	0.20	1.58	2.5	± 0.78	∓ 1.17	± 0.44	∓ 0.66
	0.25	0.25	1.06	2.0	± 0.96	∓ 0.96	± 0.55	∓ 0.55
	0.20	0.30	0.70	1.7	± 1.17	∓ 0.78	± 0.67	∓ 0.44
	0.10	0.40	0.26	1.2	± 1.97	∓ 0.49	± 1.24	∓ 0.31
F-C-I	0.40	0.10	9.74	1.3	∓ 0.32	± 1.28	∓ 0.50	± 2.00
	0.30	0.20	3.65	0.9	∓ 0.56	± 0.84	∓ 0.88	± 1.32
	0.25	0.25	2.41	0.7	∓ 0.69	± 0.69	∓ 1.15	± 1.15
	0.20	0.30	1.62	0.6	∓ 0.79	± 0.52	∓ 1.41	± 0.94
	0.10	0.40	0.61	0.5	∓ 1.30	± 0.32	∓ 2.70	± 0.67

^a Refer to notes a, c, d, and e in Table I. ^b From eq 19 (cf. Table V), using $R = 3 \text{ \AA}$, $q_C = +0.5$.

two nucleophiles from the same row in the periodic table, the point at which $k_{XC} = k_{CY}$ will be that at which $n_{XC} = n_{CY}$. (This follows from eq 9 and the fact that the stretching force constant for an X-C bond is essentially independent of X across a row in the periodic table.) For such a transition state, then, n_{XC}/n_{CY} , $|\delta_{XC}/\delta_{CY}|$, and $|\Delta n_{XC}/\Delta n_{CY}|$ are all approximately unity; the net effect of electron withdrawal from X in a symmetric SN2 transition state is to shift the transition state along the reaction coordinate without changing its "tightness." If the two carbon-nucleophile reacting bonds in I have very different ground state single bond stretching frequencies, the point at which $k_{XC} = k_{CY}$, and hence $|\delta_{XC}| = |\delta_{CY}|$, will be one at which n_{XC} and n_{CY} will be unequal; it will then not be possible in general to predict the value of $|\Delta n_{XC}/\Delta n_{CY}|$. As this Δn ratio is the most accessible experimental measure of changes in transition state "tightness," the present model is not generally capable of unambiguous predictions of the results of such experiments. Nevertheless, the model does provide valuable insights into the interplay of the various factors which determine substituent effects on transition state structure.

Predictive Rules. Substitution at the Central Atom.

If an electron-withdrawing substituent is introduced at the central atom of an SN2 transition state, a model for estimation of m values must be invoked in order to predict even the directions of reacting bond length changes. (An exception is the case of a perfectly symmetrical transition state. As noted above, electron withdrawal from C in such a system must cause an equal shortening of both reacting bonds.) It is also necessary to assume values of $\beta/(k_{XC}k_{CY})^{1/2}$ in order to perform the model calculations. Application of the electrostatic model (described in a later section) for calculation of the m ratios leads to the results summarized in Table II for two representative transition states. The results of many similar calculations suggest two general rules for prediction of substituent effects. *If an SN2 transition state contains one negatively charged and one uncharged nucleophile, an electron-withdrawing substituent at the central atom will tend to decrease the order of the reacting bond to the negative nucleophile and increase the order of the reacting bond to the uncharged nucleophile. If an SN2 transition state involves nucleophilic atoms from different rows of the periodic table (i.e., atoms whose single bonds to carbon have significantly different force constants), an electron-withdrawing substituent at the central atom will tend to increase the order of whichever reacting bond has the larger single bond force constant (i.e., the reacting*

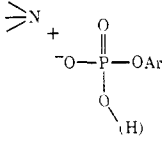
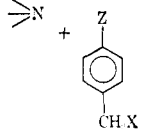
bond to the lighter atom) and decrease the order of the other reacting bond.

These two generalizations, hereafter referred to as the "q rule" and the "k rule," respectively, predict the directions of changes in transition state structure for a large number of experimentally accessible cases. For example, SN2 transition states containing any of the following pairs of nucleophiles are predicted by this model to respond to substituent changes according to the indicated rule: q rule, R_3N , F^- (or Cl^- , Br^- , I^-); H_2O , F^- (Cl^- , Br^- , I^-); k rule, F^- , Cl^- ; Cl^- , Br^- ; Br^- , I^- ; PhO^- , PhS^- ; OH^- , Cl^- (Br^- , I^-); R_3N , R_2S . It must also be admitted, however, that in some situations of interest these two rules are inadequate. If, for instance, the SN2 transition state contains F^- and R_2S as the nucleophiles, the k rule and q rule predict opposite effects of an electron-withdrawing substituent; in this particular case, the model calculations result in qualitatively different responses to the substituent change for different symmetries of the unperturbed transition state. Furthermore, if two nucleophiles are of the same charge type and from the same row in the periodic table (i.e., OH^- , F^-), neither the q rule nor the k rule is applicable; again the predicted response depends on the assumed symmetry. For those transition states to which they are applicable, utilization of the k rule and q rule requires a knowledge only of ground-state bonding parameters (nucleophile charge types and single bond force constants). As in the case of substitution at X, however, prediction of the magnitudes of these changes requires knowledge of the relative X-C and C-Y bond orders in the unperturbed transition state.

Experimental Evidence. The usefulness of any model for the prediction of substituent effects is severely limited by a lack of unambiguous empirical criteria for specific changes in transition state geometry. Such data as substituent effects on chlorine kinetic isotope effects in nucleophilic displacements on R-Cl, for example, though commonly treated as direct evidence for changes in the C-Cl bond length in the transition state, may reflect the effects of changes in the carbon-nucleophile bond length (and hence in the frequencies of the bending and symmetric stretching vibrations) as well. The interpretation of substituent effects on solvent sensitivity is also difficult since, as Parker and coworkers have recently shown,¹⁰ these may often be due primarily to ground-state effects and only secondarily to changes in the transition state itself. Furthermore, extreme care

(10) R. Alexander, E. C. F. Ko, A. J. Parker, and T. Broxton, *J. Amer. Chem. Soc.*, **90**, 5049 (1968).

Table III. Predicted and Observed Directions of Changes in Reacting Bond Order Caused by Electron Withdrawal from SN2 Transition States

Reactants	Site of electron withdrawal	Prediction	Observation	Conclusions
	Nucleophile	n_{PN} increases n_{PO} decreases	As pK_a ($\geq NH^+$) decreases, sensitivity to pK_a (ArOH) increases	n_{PO} decreases
	Phosphorus	n_{PN} increases	Change from $ArPO_3^{2-}$ to $ArHPO_3^-$ results in increased sensitivity to pK_a (ArOH) and pK_a ($\geq NH^+$)	n_{PN} increases
	Leaving group	n_{PO} decreases n_{PN} decreases n_{PO} increases		As pK_a (ArOH) decreases, sensitivity to pK_a ($\geq NH^+$) decreases
	Nucleophile	n_{CN} increases n_{CX} decreases	As pK_a ($\geq NH^+$) decreases, sensitivity to nature of leaving group increases	n_{CX} decreases
	Carbon	n_{CN} increases		As σ_z increases, sensitivity to nature of leaving group decreases, sensitivity to pK_a ($\geq NH^+$) increases
	Leaving group	n_{CX} decreases n_{CN} decreases	Change from $X = Cl$ to $X = Br$ leads to reduced sensitivity to pK_a ($\geq NH^+$)	n_{CX} increases n_{CN} decreases
		n_{CX} increases		

must be taken in analyzing any set of data in which the substitution involves changing one of the atoms involved in a reacting bond, since it is not at all obvious, for example, whether Br^- should be regarded as electron donating or electron withdrawing relative to Cl^- . In the small number of instances, however, in which multiple substituent effects have been examined in a single reaction, it appears that reliable conclusions can be drawn from the data and compared with predictions from theory. Two such cases are discussed below^{11,12} and the results summarized in Table III.

For electron withdrawal from one of the terminal groups of a three-center SN2 transition state, the present model predicts a shortening of the reacting bond nearer to the substituent and a lengthening of the more distant reacting bond. If it is assumed that any substituent change which decreases the proton basicity of the nucleophile may be regarded as increasing electron withdrawal from that nucleophile, and hence that Br^- may be described as "Cl⁻ plus an electron-withdrawing substituent," each conclusion in Table III concerning substitution at a terminal group is in agreement with the corresponding prediction.

That the apparent order of "increased electron withdrawal from the leaving group" for reactions in aprotic solvents should parallel the order of "decreased basicity of the leaving group toward a proton in water" is not surprising, since both of these are identical with the usual orders of carbon basicities and carbon nucleophilicities in aprotic solvents.^{13,14} For reactions in water or other protic solvents, it might have been expected that the order of increased electron withdrawal should follow that of decreased carbon nucleophilicities, which would require that Br^- be described as "Cl⁻ plus an electron-supplying substituent" since Br^- is a better nucleophile than Cl^- in water. In fact, analysis of the data of Swain and Thornton,¹⁵ who determined the

difference in the solvent deuterium isotope effect for hydrolysis of CH_3Cl and CH_3Br in water, indicates that even in aqueous solutions, where nucleophilicity and proton basicity orders differ, it is the decrease in proton basicity which parallels the increase in electron withdrawal from the leaving group. This result can be understood in terms of a model in which bonding in the transition state is primarily electrostatic; the central carbon then bears appreciable positive charge and is a relatively "hard" acid.¹⁶

For electron withdrawal from the central atom, the predictions of the present model for directions of changes in bond length are embodied in the q rule and the k rule. Each of the examples in Table III involves a neutral nucleophile, an amine, displacing a negative leaving group; one prediction, then, is that electron-withdrawing substituents on the central group should increase the order of the C-N bond. This prediction is in agreement with the conclusion from the data in each case. In the reaction of amines with benzyl halides, however, the second prediction, that the X-C bond order should be decreased, is not verified by observation. Although model calculations do indicate that *both* reacting bond orders are increased when $\beta/(k_{XC}k_{CY})^{1/2}$ is very large (greater than ca. 2 or 3, well outside the "reasonable range" estimated in a later section of this paper), there is no apparent reason to expect such behavior in this case.

In summary, of the eight predictions in Table III based on this model, which can be compared to experimental evidence, seven are in accord with that evidence. Although each of these eight predictions lies within the range of behavior permitted by Thornton's rules,⁷ those rules also permit the opposite predictions for the four cases involving substitution on the central atom. For comparison, application of the earlier reacting bond rule⁶ to these reactions leads to correct predictions for the four tested effects of substitution in a terminal group, but to incorrect predictions for three of the four effects of substitution at the central atom.

- (11) A. J. Kirby and A. G. Varvoglis, *J. Chem. Soc., B*, 135 (1968).
 (12) C. G. Swain and W. P. Langsdorf, Jr., *J. Amer. Chem. Soc.*, **73**, 2318 (1951).
 (13) E. R. Thornton, "Solvolysis Mechanisms," Ronald Press, New York, N. Y., 1964, p 162.
 (14) R. F. Rodewald, K. Mahendran, and R. Fuchs, *J. Amer. Chem. Soc.*, **90**, 6698 (1968).
 (15) C. G. Swain and E. R. Thornton, *ibid.*, **84**, 822 (1963).

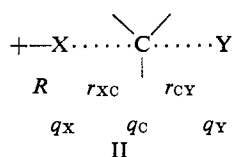
- (16) R. G. Pearson, *ibid.*, **85**, 3533 (1963); R. G. Pearson and J. Songstad, *ibid.*, **89**, 1827 (1967).

Table IV. Values of m_{XC} and m_{CY} for Substitution at X of I, Calculated from Eq 16 and 17^b

Transition state X-C-Y	n_{XC}	n_{CY}	q_X	q_Y	$\frac{k_{XC}^a}{k_{CY}}$	m_{CX} (units of e^2/D_E)	m_{CY} (units of e^2/D_E)
F-C-N	0.40	0.10	-0.60	+0.10	4.23	-0.205	+0.021
	0.25	0.25	-0.75	+0.25	1.06	-0.146	+0.049
	0.10	0.40	-0.90	+0.40	0.26	-0.078	+0.069
N-C-F	0.40	0.10	+0.40	-0.90	3.85	-0.184	+0.041
	0.25	0.25	+0.25	-0.75	0.94	-0.123	+0.070
	0.10	0.40	+0.10	-0.60	0.24	-0.058	+0.085
F-C-I	0.40	0.10	-0.60	-0.90	9.74	-0.187	+0.046
	0.25	0.25	-0.75	-0.75	2.41	-0.126	+0.079
	0.10	0.40	-0.90	-0.60	0.61	-0.058	+0.107
I-C-F	0.40	0.10	-0.60	-0.90	1.64	-0.220	+0.035
	0.25	0.25	-0.75	-0.75	0.41	-0.145	+0.056
	0.10	0.40	-0.90	-0.60	0.10	-0.061	+0.072

^a Refer to note *a* in Table I. ^b $R = 3 \text{ \AA}$, $q_C = +0.5$.

Electrostatic Estimation of m . The model system selected for calculation of the effects of substituents at a terminal position in an SN2 transition state is shown in II. The "substituent change" under consideration is



the introduction of a unit positive charge at a distance R , along the line of centers of X, C, and Y, from X in transition state I. The reacting bond orders, n_{ij} , distances, r_{ij} , force constants, k_{ij} , and the charges, q_i , are calculated from a point-charge electrostatic model for bonding and from the empirical relations between r , n , and k summarized by Johnston¹⁷ (eq 8-12). The values of m_{XC} and m_{CY} for the perturbation introduced by the

$$r_{ij} = r_{ij}(n_{ij} = 1) - 0.26 \ln n_{ij} \quad (8)$$

$$k_{ij} = n_{ij} k_{ij}(n_{ij} = 1) \quad (9)$$

$$q_X = q_X(n_{XC} = 1) - 1 + n_{XC} \quad (10)$$

$$q_Y = q_Y(n_{CY} = 1) - 1 + n_{CY} \quad (11)$$

$$q_C = 1 - n_{XC} - n_{CY} \quad (12)$$

positive charge are, from eq 3, given by eq 13 and 14. Since, for this model, P is given by eq 15 (where D_E is

$$m_{XC} = \left(\frac{\partial P}{\partial r_{XC}} \right)_{r_{CY}} \quad (13)$$

$$m_{CY} = \left(\frac{\partial P}{\partial r_{CY}} \right)_{r_{XC}} \quad (14)$$

$$P = \frac{e^2}{D_E} \left(\frac{q_X}{R} + \frac{q_C}{R + r_{XC}} + \frac{q_Y}{R + r_{XC} + r_{CY}} \right) \quad (15)$$

the effective dielectric constant, assumed to be the same for all three interactions), eq 13 and 14 for m_{XC} and m_{CY} become eq 16 and 17, respectively. It is interesting to

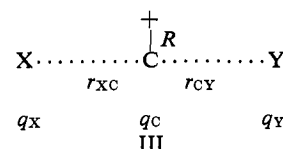
$$m_{XC} = -\frac{e^2}{D_E} \left\{ 3.85 n_{XC} \left[\frac{1}{R} - \frac{1}{(R + r_{XC})} \right] + \left[\frac{q_C}{(R + r_{XC})^2} + \frac{q_Y}{(R + r_{XC} + r_{CY})^2} \right] \right\} \quad (16)$$

(17) H. S. Johnston, "Gas Phase Reaction Rate Theory," Ronald Press, New York, N. Y., 1966, pp 72-83.

$$m_{CY} = -\frac{e^2}{D_E} \left\{ 3.85 n_{CY} \left[\frac{1}{(R + r_{XC} + r_{CY})} - \frac{1}{(R + r_{XC})} \right] + \left[\frac{q_Y}{(R + r_{XC} + r_{CY})^2} \right] \right\} \quad (17)$$

note that according to this model, the values of m_{XC} and m_{CY} are not mutually independent; the sensitivity of the X-C bond to substitution in X, m_{XC} , depends on q_Y and on r_{CY} . Some representative values of m_{XC} and m_{CY} for a number of assumed transition state structures are listed in Table IV.

The effect of a substituent at C in transition state I can be evaluated by a model completely analogous to that for substituents at X. In this case, the "substituent change" is the introduction of a unit positive charge at a distance, R , perpendicular to the line of centers of X, C, and Y, from C III. The interaction potential, P ,



caused by this substituent change is given by eq 18,

$$P = \frac{e^2}{D_E} \left\{ \frac{q_X}{(R^2 + r_{XC}^2)^{1/2}} + \frac{q_C}{R} + \frac{q_Y}{(R^2 + r_{CY}^2)^{1/2}} \right\} \quad (18)$$

which is symmetrical with respect to interchange of the "X" and "Y" labels. The expressions for m_{XC} and m_{CY} therefore have identical forms and are given by eq 19. Table V lists values of m for a number of X-C pairs.

$$m_{ij} = \frac{e^2}{D_E} \left\{ 3.85 n_{ij} \left[\frac{1}{R} - \frac{1}{(R^2 + r_{ij}^2)^{1/2}} \right] - \left[\frac{q_i r_{ij}}{(R^2 + r_{ij}^2)^{3/2}} \right] \right\} \quad (19)$$

Examination of eq 16, 17, and 19 reveals that the value of m for any given bond contains contributions from two terms. In eq 19, for example, the second term arises from a *direct electrostatic* interaction between the positively charged substituent and the terminal group; it will have opposite signs for uncharged ($q_X > 0$) and negatively charged ($q_X < 0$) nucleophiles. The first term in eq 19 is always positive and arises from the requirement that an increase in r_{XC} will make q_X

Table V. Values of m_{XC} for Substitution at C of I, Calculated from Eq 19^b

X-C	n_{XC}	q_X	k_{XC}^a (md/Å)	m_{XC} (units of e^2/D_E)
F-C	0.10	-0.90	0.56	0.060
	0.25	-0.75	1.40	0.075
	0.40	-0.60	2.24	0.088
N-C	0.10	+0.10	0.53	0.019
	0.25	+0.25	1.32	0.037
	0.40	+0.40	2.12	0.050
I-C	0.10	-0.90	0.23	0.069
	0.25	-0.75	0.57	0.103
	0.40	-0.60	0.92	0.131
S-C	0.10	+0.10	0.30	0.024
	0.25	+0.25	0.75	0.050
	0.40	+0.40	1.20	0.073

^a Refer to footnote a in Table I; the value of k_{CS} ($n = 1$) was taken as 3.0 md/Å. ^b $R = 3 \text{ \AA}$, $q_C = +0.5$.

more negative and q_C more positive, independently of the signs of q_X and q_C in the unperturbed transition state; this effect will always make an increase in r_{XC} more difficult. The behavior of this term thus correlates with the intuitive concept of an acid-base interaction between X and C; a positively charged substituent on C will make C a stronger acid and therefore always make it more difficult to increase r_{XC} .

For the case of electron withdrawal from X, the results of the model calculations indicate (Table IV) that m_{XC} is negative and m_{CY} is positive regardless of the signs of charges on X and Y. This is what is expected if the acid-base terms in eq 16 and 17 are always larger in magnitude than the direct electrostatic terms. For a substituent change at C, if X bears a negative charge in the unperturbed transition state, the acid-base and electrostatic terms are both positive. If, however, X bears a partial positive charge, the electrostatic term in eq 18 is negative and hence reduces the over-all value of m_{XC} . The tabulated m values show that, while m values are smaller for bonds involving neutral nucleophiles than for those involving negatively charged species, all m values are positive. In this case as well, therefore, the acid-base terms dominate the interaction.

The most dramatic conclusion to be deduced from Tables IV and V is that there is *no* correlation between the individual bond force constant and the value of m_{XC} for substitution either at X or at C. There is a significant increase in $|m_{XC}|$ as one proceeds down a column in the periodic table; this is a result of an increase in r_{XC} which leads to a relative increase in the magnitude of the acid-base contribution to m .

Estimation of Values of β . The lower limit to the value of β for any transition state I is inherent in the form of the potential (eq 2) which was originally chosen to describe the system. If there is to exist one normal mode of vibration, the antisymmetric stretch, with an imaginary frequency, the present model requires that $\beta/(k_{XC}k_{CY})^{1/2}$ be greater than one. This is a necessary and sufficient condition for the presence of downward curvature of the potential energy surface for passage along the reaction coordinate through the transition state.

The assignment of an upper limit to $\beta/(k_{XC}k_{CY})^{1/2}$ is more difficult. Bell¹⁸ has estimated that a value of $\beta = 2(k_{CX}k_{XY})^{1/2}$ gives a downward barrier curvature which is similar to the upward curvature of other parts of the potential energy surface. Since it seems likely that barriers are flatter, rather than steeper, than ordinary potential wells, $\beta/(k_{XC}k_{CY})^{1/2} = 2$ may be regarded as an upper limit for this ratio. There is reason to believe, however, that this is not a least upper bound.

A second criterion which might be applied in the attempt to assign an upper limit to β is that, as $\beta/(k_{XC} \cdot k_{CY})^{1/2}$ becomes very large, the probability of tunnelling through the potential energy barrier increases. In the case of hydrogen transfer reactions, such tunnelling may occur to an appreciable extent (*vide infra*) but in an SN2 reaction ("carbon transfer" between two nucleophiles) it is not believed that this phenomenon contributes significantly to the reaction rate. One possible approach to this problem is analogous to that applied by More O'Ferrall¹⁹ in his model calculation of isotope effects in hydrogen transfer reactions. Two possible forms of the dependence of $\beta/(k_{XC}k_{CY})^{1/2}$ on n_{XC} and n_{CY} were arbitrarily assumed; in the notation of the present authors these may be expressed as eq 20 and 21. For the reactions considered by More O'Ferrall,

$$\beta = [1 + (n_{XC}n_{CY})^2](k_{XC}k_{CY})^{1/2} \quad (20)$$

$$\beta = [1 + 2(n_{XC}n_{CY})^2](k_{XC}k_{CY})^{1/2} \quad (21)$$

in which "C" = H and $n_{XC} + n_{CY} = 1$, these equations gave maximum values of $\beta/(k_{XC}k_{CY})^{1/2}$ of 1.06 (eq 20) and 1.13 (eq 21). These maxima occur at $n_{XC} = n_{CY} = 0.5$ and correspond to tunnelling contributions to k_H/k_D of 20% and 50%, respectively. If $n_{XC} \neq n_{CY}$ (a less symmetric transition state) or if $n_{XC} + n_{CY} < 1$ (a "looser" transition state), the values of $\beta/(k_{XC}k_{CY})^{1/2}$ are even lower than those quoted above.

Since, to a first approximation, the magnitude of the tunnelling correction term is proportional to the reciprocal of the reduced mass for motion along the reaction coordinate, the same barrier curvature which results in a 30% tunnelling correction for hydrogen transfer should produce a 2-3% correction for a carbon transfer reaction. If the tunnelling correction for carbon transfer is assumed to be no larger than this, then $1.2(k_{XC}k_{CY})^{1/2}$ may be taken as an upper limit on β . This is probably a conservative estimate, since it is quite likely that, for SN2 reactions at carbon, $n_{XC} + n_{CY} < 1$. The allowed range of β values for an SN2 transition state, then, may be assumed to be $1.0 < \beta/(k_{XC}k_{CY})^{1/2} < 1.2$.

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(18) R. P. Bell, *Discussions Faraday Soc.*, **39**, 16 (1965).

(19) R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc., B*, 985 (1967).