The Polarisation and Charge-transfer (PCT) Theoretical Model for the Prediction and the Interpretation of the Relationship between Reactivity and Selectivity

By **Martin Godfrey**, Department of Chemistry, The University, Southampton SO9 5NH

A new theoretical model is presented for predicting when and how the selectivity of reagents with respect to substrates ought to vary with their reactivity. It incorporates a novel method of determining the effects of changing the nature of the reagent or the substrate on the nuclear structure of the reaction complex in its transition state. The model is shown to be capable of interpreting certain observed reactivity–selectivity behaviour which appears anomalous within the framework of orthodox theory. In particular departures from adherence to the Reactivity–Selectivity Principle and to Hammett-like correlation equations are interpreted.

THE relative abilities of two reagents to choose between a given pair of substrates in mechanistically similar reactions, are commonly assumed to follow the rule that the more reactive reagent is the less selective one.[1] This rule, which is known as the Reactivity–Selectivity Principle, may be rationalised with the aid of the Hammond Postulate, which effectively states that the transition state for the reaction of a given substrate occurs earlier along the reaction co-ordinate the more reactive the reagent.[1] Unfortunately, the Reactivity–Selectivity Principle has been shown to be by no means universally valid:[2-5] sometimes reagents of very different reactivity show similar selectivity, and sometimes the more reactive reagent of a pair is also the more selective one. The breakdown in the Reactivity–Selectivity Principle has been rationalised by Thornton[6] in terms of the transition state moving perpendicular to, as well as along, the reaction co-ordinate for the reference reaction. However, the problem of predicting the circumstances in which the various types of reactivity–selectivity behaviour ought to be expected, still remains unsolved.[3,4] In the present work we describe and discuss a novel approach to the solution of this problem which seems to us to have some merits. It builds on our previously reported[7,8] theoretical model for predicting (with apparent success) the circumstances in which different types of quantitative linear correlation between substituent effects on the same chemical or physical property of different compounds, or different chemical or physical properties of a particular compound, ought to be expected. Hence, a single theoretical model is obtained for both reactivity–selectivity relationships and linear free energy relationships. This feature is important since, as Johnson[2] has pointed out, the Hammond Postulate and Hammett's linear free energy relationship, both of which are widely used in analyses of reaction mechanisms, cannot hold simultaneously.

THEORY

The specific problem we have tackled here is that of designing a theoretical model for predicting qualitatively the variations in the nuclear (arrangement of atoms) and the electronic (arrangement of electrons) structures of a reactive molecular system in its transition state as the nature of the molecular system is varied. The basis of our model is the PCT (polarisation and charge-transfer) model for predicting the variations in the electronic structure of a molecular system in its ground state as the nature of the molecular system is varied. Popular models for predicting variations in electronic structure are unsuitable bases, because they suggest that single-variable quantitative linear correlations in organic chemistry ought not to occur in circumstances in which many statistically good correlations of this type have been found in practice.[7]

The PCT Theoretical Model for Electronic Effects.—It is assumed in this model that, except in the immediate vicinity of the source site, the changes in the electronic structure of a molecular system due to structural perturbations (such as substituent effects) are due primarily to PCT effects. In this section we briefly describe the origin and the transmission of PCT substituent effects on electron populations in any molecular system: more detailed accounts have been given elsewhere.[7,8] Each molecule, or molecular system, is divided into small sub-units each of which contains an orbital system that is topologically analogous to the π-system of ethylene.[8] The ethylene π-system, or its analogue, can self-polarise. Self-polarisation is due to the mixing of the orbitals with other orbital functions to give perturbed orbitals. Thus, for example, a vinylene sub-unit would polarise if the π-bonding orbital was mixed with a π-antibonding function. The self-polarisation of a sub-unit is a destabilising process but it will be allowed if it leads to an increase in the net stabilising effect of the interactions with other sub-units that is greater than the destabilising effect of the polarisation. These interactions between sub-units are of two kinds, coulombic and non-coulombic. Coulombic interactions are those which involve the net charges at the various atoms in the sub-units. Non-coulombic interactions are those which involve overlap between orbitals of one sub-unit and orbitals of a neighbouring sub-unit: they include charge-transfer interactions (HOMO–LUMO *etc.*) and overlap-repulsion interactions (HOMO–HOMO *etc.*). Self-polarisation which makes coulombic interactions more favourable is called coulombic polarisation, and self-polarisation which makes non-coulombic interactions more favourable is called non-coulombic polarisation. We shall see later that the non-coulombic polarisation phenomenon plays a key role in the PCT method for determining substituent effects on the nuclear structures of transition states.

Both coulombic and non-coulombic polarisation effects of substituents can be determined quantitatively from the results of MO calculations. We have previously obtained scales of such effects, the **F** and **S** scales respectively.[7]

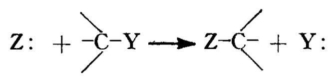
Substituents not only induce polarisation of adjacent sub-units, they also transfer charge to them. With most substituent groups, although not all, the amount of charge-transfer is proportional to the degree of non-coulombic polarisation. Hence, it can also be measured by the **S** scale. Thus, the effect of a substituent on the electron populations and their distributions in orbitals which are analogues of the ethylene π-orbitals, can usually be expressed in terms of its **F** and **S** values only. The electron populations and their distributions in the analogues of the vinylene σ-orbitals are assumed to be affected by substituents only through π–σ and analogous interactions. Hence the effect of a substituent on the total electron populations at any site within a sub-unit can also usually be expressed in terms of its **F** and **S** values only. A substituent has, by definition, no direct PCT effects on sub-units other than immediately adjacent ones. However it has indirect effects, since the changes in the sub-unit adjacent to the substituent will lead to changes in sub-units adjacent to that sub-unit, and so on through the whole molecular system. These indirect effects must, of course, also be expressible in terms of **F** and **S** values only. Hence we have the relationship (1), in which $\delta_X q$ represents the effect of a substituent X on the electron population, holding for all sites i in the molecular system. When $\delta_X \log k$ (where k is a reaction rate

$$\delta_X q_i = f_i(\mathbf{F} + g_i\mathbf{S}) \qquad (1)$$

constant) is directly proportional to some linear combination of the changes in electron population at the reaction site and at the sites immediately adjacent to it, then equation (2) must hold. [Equations (1) and (2) are examples of dual substituent parameter (DSP) correlation equations.]

$$\delta_X \log k_i = f_i'(\mathbf{F} + g_i'\mathbf{S}) \qquad (2)$$

The PCT Theoretical Analysis of the Classical S_N2 *Mechanism.*—The PCT model for reactivity–selectivity relationships will be described through the analysis of the alkyl-group migration reaction (3), which is assumed to follow the single-step S_N2 mechanism, and in which the nucleophile, Z, and the leaving group, Y, are variables. The model


$$\mathrm{Z{:}} + \mathrm{{>}C{-}Y} \longrightarrow \mathrm{Z{-}C{<}} + \mathrm{Y{:}} \qquad (3)$$

rests on the following assumption: The nuclear structure of the transition state is determined solely by non-coulombic interactions in the reacting molecular system, and in a series of similar reactions [*e.g.* reaction (3) with various Z and Y], the variation in the activation energy is determined principally by coulombic and steric interactions.

In reaction (3), the bond cleavage involves destabilising polarisation of the molecular sub-unit containing the bond to be broken, and the bond formation involves stabilising charge-transfer between the two sub-units containing the atoms to be joined. The polarisation and the charge-transfer processes are interdependent. The polarisation assists the charge-transfer, as with the non-coulombic polarisation effect of a substituent, and hence at least some of the energy loss due to the polarisation will be compensated for by an energy gain due to enhancement of the charge-transfer. Polarisation will occur spontaneously when all the energy loss is compensated for, but not otherwise. The amount of charge-transfer at a given nuclear structure of the reaction complex depends on the orientation and the separation of the sub-units containing the atoms to be joined (see below for a detailed analysis). At large distances of separation the polarisation could not occur spontaneously because the energy gain due to enhancement of the charge-transfer would not be sufficiently large to compensate fully for the energy loss due to the polarisation. However, this restraint on the polarisation should disappear when the distance of separation has decreased to a critical value. This critical nuclear structure for the reaction complex is assumed to determine the Z–C and the C–Y bond lengths in the transition state. The variation with the nature of Z and Y of the energy required to reach this critical nuclear structure is assumed to be the dominant factor in determining the corresponding variation in the activation energy for the reaction. The main contributions to the variation in the transition state energy come from the effects of coulombic PCT interactions between sub-units containing the atoms to be joined, and from the effects of non-PCT interactions. The non-PCT interactions are direct interactions involving sub-units of the reacting molecular systems other than those involved in the bond to be formed. The relevant sub-units involve, *inter alia*, those solvent molecules which are bound to the reactants. We shall use the term steric interactions to cover all non-PCT interactions.

For a given pair of reacting sub-units, the magnitudes of both coulombic and steric interactions must increase with decreasing separation of the reactants. Destabilising interactions will therefore make tighter (*i.e.* more product-like) transition state structures less stable than looser (*i.e.* more reactant-like) transition state structures. Steric interactions will usually be net destabilising. Coulombic interactions will be either destabilising or stabilising depending on the natures of the reacting sub-units.

The non-coulombic interactions which govern the nuclear structure of the transition state are now considered in detail for reaction (3). The orbitals directly involved in these interactions are, one occupied C–Y bonding orbital, one unoccupied C–Y anti-bonding orbital, and one non-bonding Z orbital. There will be a charge-transfer interaction involving the Z orbital as donor and the C–Y anti-bonding orbital as acceptor. The magnitude of this interaction is given by equation (4). It depends on: (i) the relative

$$E_{\mathrm{CT}} = (c_d c_a \beta_{da})^2/\Delta E \qquad (4)$$

energies (ΔE) of the donor and the acceptor orbitals; (ii) the amplitudes of the donor (c_d) and the acceptor (c_a) orbitals at the site of overlap; and (iii) the magnitude of the resonance integral, β_{da}, involving the overlapping atomic orbitals. The magnitude of the resonance integral should increase with decreasing separation of the sites of overlap, $r_{Z,C}$, along the line of maximum overlap.

The magnitude of the enhancement of the charge-transfer interaction energy resulting from the polarisation of the C–Y bond in the transition state structure, E_{CT}^*, is given by equation (5), in which δc_a is the change in amplitude of

$$E_{\mathrm{CT}}^* = (c_d \delta c_a \beta_{da})^2/\Delta E \qquad (5)$$

the acceptor orbital at the carbon atom due to the polarisation. The value of δc_a is assumed to be independent of the nature of Z. The energy loss resulting from the polarisation of the C–Y bond in the transition state will be given the symbol E_P^*. Hence, by the PCT model, equation (6) should hold.

$$E_{\mathrm{CT}}^* = E_P^* \qquad (6)$$

The predictions of the PCT model concerning the variations in the nuclear structure of the transition state and the activation energy with changes in the natures of Z and Y, will be considered in the next section. The main conclusions are summarised in the Scheme.

(a) Invariant transition state structure

(i) Coulombic control of differential reactivity

X_1Z_0 - - - - C —— Y

X_2Z_0 - - - - C —— Y

DSP for $\delta_X\log k$ when Y,Z_0 fixed

(ii) Coulombic control of selectivity

Z - - - C —— Y_0X_1

Z - - - C —— Y_0X_2

DSP for $\delta_X\log k$ when Z,Y_0 fixed

(iii) Steric control of differential reactivity

Z_0 - - - - C —— Y_1

Z_n - - - - C —— Y_1

Z_0 - - - - C —— Y_2

Z_n - - - - C —— Y_2

Parallel lines for $\delta_Y\log k_n$ *versus* $\delta_Y\log k_0$

(iv) Steric control of selectivity

Z_1 - - - - C —— Y_0

Z_1 - - - - C —— Y_n

Z_2 - - - - C —— Y_0

Z_2 - - - - C —— Y_n

Parallel lines for $\delta_Z\log k_n$ *versus* $\delta_Z\log k_0$

(b) Variable transition state structure

(i) Steric control of differential reactivity

Z_1 - - - - C —— Y

Z_2 - - - - - C —— Y

Hammond Postulate should hold

(ii) Steric control of differential reactivity coupled with coulombic control of selectivity

Z_1 - - - - C —— Y_0X_1

Z_1 - - - - C —— Y_0X_2

Z_2 - - - - - C —— Y_0X_1

Z_2 - - - - - C —— Y_0X_2

RSP for reactivity and selectivity of Z

DSP for $\delta_X\log k$ when Z,Y_0 fixed

(iii) Variable steric and coulombic involvement in both selectivity and differential reactivity

Z_1 - - - - C ——— Y_1

Z_2 - - - - - C —— Y_2

No RSP and no DSP

SCHEME

Predictions for S_N2 *Reactions.—Concerning when the nuclear structure of the transition state is invariant.* In terms of the previously reported PCT treatment of quantitative linear correlations, $\delta_Y\log k$ would have to be directly proportional to some linear combination of the changes in PCT electron population in the sub-unit containing the bond to be broken, for perfect DSP (dual substituent parameter) correlation to occur. This condition implies that the variation in the transition state energy with the nature of Y is due solely to variation in coulombic interaction energy and, hence, that the steric interaction energy at the transition state does not vary with the nature of Y. Since the steric interaction energy must vary markedly with the nuclear structure of the transition state, it follows that DSP correlations are permitted only when the nuclear structure of the transition state does not vary significantly with the nature of Y.

The constancy of the nuclear structure of the transition state implies invariance of the value of β_{da}, and hence, for a given ΔE, of E_{CT}^* and E_P^*. The value of E_P^* is unlikely to be even approximately independent of the nature of Y in the general case, but the variation ought to be relatively small among restricted sets of leaving groups which are linked to the central carbon atom by a common atom or by a common group of atoms (*e.g.* a set of $^-OSO_2X$ groups).

When the nuclear structure of the transition state is constant, the substrate selectivity of the nucleophile (*i.e.* the tendency of a nucleophile to choose between any pair of substrates) will be controlled by coulombic interactions unless, as discussed below, certain effects of differential solvation of the substrates are important. Coulombic control implies that the selectivity should depend only on the relative PCT electron populations and population distributions in the reactive sub-units of the substrates. Thus, if a common substituent was introduced into each of two substrates at corresponding sites, and this substituent had a purely additive effect on the PCT electron population and its distribution in each case, then there ought to be no change in the selectivity of the nucleophile. The introduction of the second substituent would, of course, affect the transition state energy, and hence the absolute rate of nucleophilic attack, in each case. Thus, the nucleophile would combine variable reactivity with constant selectivity. The cumulative effects of substituents on various measurable properties, including the logarithm of rate constant, are not strictly additive in practice. In PCT theory, the cumulative effects of substituents on electron population and its distribution, in a hydrocarbon, ought not to be additive, because the non-coulombic interactions involving one substituent must be affected by the polarisation of the hydrocarbon induced by the other substituents. Therefore there ought to be some variation of selectivity when a common second substituent is introduced into each of two substrates at corresponding sites, even if the nuclear structure of the transition state is not affected by the second substitution. The introduction of a substituent into a nucleophile should also affect the substrate selectivity of the nucleophile, through changing the coulombic interaction. Again this effect ought to be observable even if the nuclear structure of the transition state is not affected by the substitution.

Differential solute–solvent interactions in the pair of substrates or nucleophiles would lead to differential steric contributions to the activation energy. It is conceivable that these steric effects could compete with or even mask the coulombic effect, at least in certain cases.

When the effects of a set of nucleophiles with similar electronic characteristics but different steric characteristics (including different solvation energies) are compared, the nuclear structures of the transition states ought to be similar, but the energies of the transition states ought to be different. Thus, when the $\delta_Y\log k$ for reactions of various nucleophiles of this type with a set of substrates are plotted against $\delta_Y\log k$ for any one nucleophile, a set of parallel straight lines of unit slope ought to be obtained. Similarly, when the effects of a set of substrates with similar electronic characteristics but different steric characteristics are compared, a set of parallel straight lines again ought to be obtained when the $\delta_Z\log k$ for reactions of various substrates of this type with a set of nucleophiles, are plotted against $\delta_Z\log k$ for any one substrate.

Concerning when the nuclear structure of the transition state is not invariant. The constancy of the nuclear structure of the transition state ought to be lost when E_{CT}^* varies significantly with the nature of Y or Z. This will happen whenever ΔE or E_P^* varies significantly with the nature of

Y or Z. Let us now consider the implications of such variations, on nucleophilic reactivity, on substrate selectivity, and on DSP relationships.

When the nature of Z is changed so as to reduce ΔE significantly for any given Y, the value of $r_{Z.C}$ at the transition state ought to increase. Since the steric interactions will thereby become smaller, the new nucleophile ought to be more reactive than the original. Furthermore, since coulombic interactions fall off with increasing distance of separation, the constant of proportionality between $\delta_Y \log k$ and the change in PCT electron populations in the substrate should fall, and hence, the new nucleophile ought to be less selective than the original when the set of substrates is such that the nuclear structure of the transition state does not vary significantly with the nature of Y. This behaviour is in accord with the Reactivity–Selectivity Principle. In these circumstances DSP correlations are expected for $\delta_Y \log k$ with either nucleophile.

The nuclear structure of the transition state should vary with the nature of Y when E_{CT}^* varies significantly with the nature of Y. When Y is changed so as to reduce E_{CT}^* for any given Z, the value of $r_{Z.C}$ at the transition state ought to increase, with consequent reduction in steric interaction and hence increase in reaction rate. The way in which the substrate selectivity varies with the nature of the nucleophile in this case should be rather complicated since steric as well as coulombic factors are involved. The increment in $r_{Z.C}$ on changing the nature of Y should be very much greater the smaller the initial value of β_{da}^2, because of the great sensitivity of resonance integrals to the degree of separation of the overlapping orbitals. According to equation (5), for a given value of E_{CT}^*, β_{da}^2 should become smaller as ΔE becomes smaller, and hence the effect of changing Y on $r_{Z.C}$ should become greater as ΔE becomes smaller. Therefore, with nucleophiles which give rise to small values of ΔE, the effect of changing Y on $r_{Z.C}$ at the transition state, ought to be greater than with nucleophiles which give rise to larger values of ΔE. The smaller the value of ΔE, the faster the nucleophile will react. When the effects of steric interactions make the major contribution to the variation in transition state energy with the nature of Y, then, the greater the effect on $r_{Z,C}$ at the transition state of changing Y, the more selective the nucleophile might be in its choice of substrate. Thus, it is possible that the selectivity among a set of nucleophiles will increase with increasing reactivity. We argued above that when the major contribution to the variation in transition state energy with the nature of Y is made by the effects of coulombic interactions, the selectivity among a set of nucleophiles should decrease with increasing reactivity. Therefore, the relationship between reactivity and selectivity may depend qualitatively on the relative importance of the effects of steric interactions and the effects of coulombic interactions in contributing to the overall variation in transition state energy with the nature of Y.

DISCUSSION

We shall first analyse the results of some recent experimental studies on selectivity in S_N2 reactions in terms of the PCT model in order to illustrate the application of the model. We shall find that we sometimes reach different conclusions from other workers regarding the variation in the nuclear structure of the transition state in reaction series. It is important to realise that there are no experimental measures of transition state structure: experimental indicators (*e.g.* Hammett ρ values, and Grunwald–Winstein *m* values [1]) have significance only within the context of a particular theoretical model, and may give false information if the model is defective. On the other hand, selectivity and reactivity can be measured experimentally, and the ability of a theoretical model to predict these things can be tested.

Karton and Pross [4] have recently studied the effects of the nature of the leaving group on the selectivity of alkyl derivatives towards competing nucleophiles in S_N2 reactions. From the experimental data they drew up the following rules. (i) Where a set of leaving groups are joined to the substrate by a particular type of atom (*e.g.* oxygen) there is little variation in selectivity, but where a set of leaving groups are joined to the substrate by different types of atom there is usually considerable variation in selectivity. (ii) When the nature of the attacking atom is the same in a series of nucleophiles, the effect of the leaving group on selectivity is small, irrespective of the nature of the leaving group. (iii) There is no general simple correlation between the reactivity of the substrate and the selectivity; sometimes selectivity increases with increasing reactivity, sometimes it decreases, and sometimes it remains the same. These rules could just as easily have been formulated from the predictions of the PCT model detailed in the previous section.

Karton and Pross rationalised some of their findings using frontier molecular orbital theory. Their theoretical analysis took into account only the differential charge-transfer stabilisation of the reaction complexes that arise out of differences in ΔE. It is a very much simpler theoretical model than ours, but it is also much more limited in its ability to interpret observed behaviour, suggesting, for example, that selectivity should always vary directly with reactivity.

Harris *et al.*[3] have recently intepreted various experimental data for the effects of ring substituents on the rates of solvolysis in aqueous ethanol of benzyl chloride and benzyl tosylate, in terms of small substituent-induced variations in the nuclear structure of the transition state. Furthermore, they have used their results to infer the approximate absolute nuclear structure of the transition state. The experimental data indicate that as the electron-repelling power of the substituent increases, the differential reactivity for displacement by water as opposed to ethanol (k_W/k_E), the ratio of leaving group effects (k_{OTs}/k_{Cl}), and the value of the Grunwald–Winstein parameter *m* for the response to changes in solvent ionising power all increase. Using PCT theory, these experimental observations can be readily interpreted in terms of a transition state nuclear structure which does not vary with the nature of the substituent or with the nature of the nucleophile, and the absolute tightness of which is qualitatively unimportant. The variations in reactivity and selectivity may be taken to be controlled by the effects of coulombic interactions between the substituted benzyl group on the one hand, and the nucleophile and the leaving group on the other hand. The positive charge on the nucleophile is more dispersed in ethanol than in water, and consequently k_W should increase with increasing value of $\mathbf{F} + g'\mathbf{S}$ [the PCT indicator of electron-repelling power, see equation (2)] for the benzyl substituent, more rapidly than k_E does. The rate of increase of nucleophilic attack should be larger the more diffuse the negative charge on the leaving group. Since the negative charge is more dispersed in the tosylate ion than in the chloride ion, the ratio of leaving group effects (k_{OTs}/k_{Cl}) should increase with increasing value of $\mathbf{F} + g'\mathbf{S}$. Finally, as pointed out by Johnson *et al.*,[9] any variation in the value of the reaction constant in a Hammett-like equation with the polarity of the solvent, provides a sufficient condition for the value of m to vary with the nature of the substituent. In this paragraph we have demonstrated that the validity of the claim of Harris *et al.* to have measured transition state structure in the reactions studied, rests on the questionable validity of the assumptions on which their argument is based.

Young and Jencks [10] have argued that the observation of U-shaped Hammett plots in reactions of benzyl halides with nucleophiles does not necessarily mean either a change in mechanism or a change in the nuclear structure of the transition state, on going from electron-attracting to electron-repelling substituents in the benzene ring of the substrate. Their argument is based on the fact that the rate data fit a DSP quantitative linear correlation equation (in fact, a modified Yukawa–Tsuno equation). Using the PCT model we would reach the same conclusion. Furthermore, we would not dispute Young and Jencks' conclusion that the nuclear structure of the transition state does vary a little with the nature of the substituent in the benzene ring of the nucleophile, when the nucleophiles are a set of substituted anilines. It seems reasonable that the electronic character of the amino-group should be affected to a significant extent by changes in the electronic character of an attached substituted phenyl group.

The reactivities of substituted phenoxides [11] and thiophenoxides [12] also depend on the nature of the substituent in a way which is consistent with there being small variations in the nuclear structure of the transition state. However, sets of substrates with leaving groups having a common atom bonded to the central carbon atom show little variation in their selectivity for such nucleophiles, suggesting that there is no marked variation in leaving group effect on the nuclear structure of the transition state. Comparisons of iodide and sulphonate leaving group effects on reactivity and selectivity in reactions with phenoxides,[11] thiophenoxides,[12] and pyridines,[5] suggest similar leaving group effects on the nuclear structures of the transition states, and hence coincidently similar values of E_P*.

Having shown how the PCT model can successfully interpret experimental data in S_N2 reactions, we shall now consider briefly the extension of the model to some other reactions. In terms of the PCT approach, multi-step mechanisms for nucleophilic aliphatic substitution would occur if the polarisation energy for the C–Y bond were to be supplied by an electron-donating species other than the nucleophile, for example, from a solvent molecule (to give a loose ion-pair) or from a group attached to the central carbon atom (to give a tight ion-pair). Whether or not this should happen in a particular case ought to depend on the relative magnitudes of the effects of the factors (steric and cuolombic) which contribute to the transition state energy. Suppose in a particular example of a two-step reaction, the charge-transfer energy required to compensate for the polarisation energy for the C–Y bond could be most easily obtained when an α-phenyl group acted as the electron donor. Then the first step would be the formation of a benzyl-ion containing complex in which orbital overlap was optimised between the C–Y antibonding orbital and appropriate π-bonding orbitals of the α-phenyl group. In the second and product-forming step, orbital overlap would be optimised between the non-bonding orbital of the nucleophile and appropriate π-antibonding orbitals of the benzyl group belonging to the ion-pair, and the orbital overlap between the π-bonding orbitals of the α-phenyl group and the C–Y antibonding orbitals would be reduced from the level found in the isolated ion-pair. This latter step is analogous to the single step in the classical S_N2 mechanism. The difference is that the bond which is loosened is not the one which involves the leaving group for the reaction. Reactivity–selectivity behaviour in single-step reactions involving nucleophiles and ion-pairs or solvated ions ought, therefore, to be governed by the same factors that we described in our treatment of single-step S_N2 reactions.

The combination of constant selectivity and variable reactivity has been found in reactions between nucleophiles and cations. A striking example is provided by the protonation of α-substituted olefins in sulphuric acid studied by Tidwell and his co-workers.[13,14] Here log k gives a statistically good linear correlation with the substituent constant σ^+ even though the range of rate constants measured is over 10^{23}. In terms of PCT theory, this implies no significant variation in the nuclear structure of the transition state and coulombic control of the variations in transition state energy. If this interpretation was satisfactory, the precise value of the slope of the log k *versus* σ^+ plot for a set of ring substituents in styrene derivatives would be expected to vary somewhat with the nature of the other α-substituent, because the non-aryl substituent should influence the ease of polarisation of the olefin in the direction required to maximise orbital overlap with the aryl group, and hence influence the flow of electrons within the incipient carbonium ion. Electron-attracting groups ought to assist the process, and electron-repelling groups ought to hinder it. In accord with this prediction, the trifluoromethyl group has a larger negative ρ value than the hydrogen atom, whereas the methyl group and other electron-pushing groups have small negative ρ values.[14] Thus there is a small inverse reactivity–selectivity effect predicted without invoking variation in the olefin-to-proton separation in the transition state structure.

Having illustrated the application of the PCT model to the analysis of experimental studies on selectivity in S_N2 and other reactions, we now consider other theoretical approaches to variable reactivity–selectivity relationships in terms of the PCT model. The involvement of two independent factors for controlling variations in the energies of reacting species is found in other theories. For example, Salem[15] postulates charge control and overlap control. Since in PCT theory the magnitude of a steric interaction depends on the degree of orbital overlap, it is to be expected that the charge control *versus* overlap control analysis will be successful in problems in which any effects of variation in the nuclear structure of the transition state are not significant. However, this method of theoretical analysis does not yield information on the form of the relationship between reactivity and selectivity.

A theory which does permit interpretation of the Reactivity–Selectivity Principle and of departures from it, was proposed several years ago by Thornton.[6] In this theory the nuclear structure of the transition state is allowed to change perpendicular to as well as parallel to the reaction co-ordinate on the path of minimum energy, when the reactants change. Hence, in principle, the activation energy can change in a reaction series without there being any change in the structure of the transition state parallel to the original reaction co-ordinate. The problems of predicting how the transition state structure should vary and what effect the structural variation should have on the transition state energy cannot be tackled without additional theory. According to the PCT model, major changes in the electronic structure of the transition state can occur which are not accompanied by significant changes in the nuclear structure of the transition state parallel to the original reaction co-ordinate. The PCT model can be used to make predictions concerning the variations in the electronic and the nuclear structure of the transition state, and the effects of such structural variations on the energy of the transition state.

Conclusions.—The PCT model for reactivity–selectivity relationships is capable of providing self-consistent interpretations of observed departures from the Reactivity–Selectivity Principle in series of mechanistically similar reactions. In relating reactivity and reactivity–selectivity behaviour to variations in transition state structure (see Scheme), the following points emerge.

(i) Variations in the nuclear structure of the transition state due to changes in the nature of the reagent or the substrate in a reaction series, ought to result in variations in the energy of the transition state because of accompanying changes in steric interactions between the solvated reagent and the solvated substrate. (Metzger *et al.*[16,17] have assumed this result in their interpretation of certain reactivity–selectivity behaviour.)

(ii) The energy of the transition state also ought to be affected by changes in the electronic structure of either the reagent or the substrate because of accompanying changes in coulombic interactions between the reactants. Small changes in the electronic character of either the reagent or the substrate can produce significant changes in the coulombic interaction energy at the transition state, without producing changes in the nuclear structure of the transition state which are sufficiently large to result in significant changes in the steric interaction energy. These conditions are most likely to be approached when the reagents have a common atom at the site of attack and the leaving groups have a common atom at the site of attachment to the substrate. In these circumstances, the effects on the energy of the transition state of substituents in either the reagent or the substrate, ought to be accommodated quantitatively by DSP linear correlation equations.

(iii) In a concerted bond-breaking and bond-making process, the changes in the nuclear structure of the transition state that are parallel to the reaction co-ordinate are assumed to be governed by the requirement that the energy loss due to polarisation of the bond to be broken must be fully compensated by the accompanying energy gain in the charge-transfer interaction between the molecular sub-units involved in the bond to be made. (Before full compensation is possible the reaction complex must have reached a critical tightness, which corresponds to the nuclear structure of the transition state.)

(iv) Where variations in the nuclear structure of the transition state parallel to the reaction co-ordinate are insufficiently large to result in significant changes in the steric interaction energy, both the selectivities of the reagents with respect to the substrates and the differential reactivities of the reagents with respect to any one substrate, ought to be controlled by differences in the coulombic interactions between the reactants. Since invariant nuclear structure of the transition state implies only relatively small variations in electronic structure, the differential reactivities of the reagents are unlikely to be large enough to produce marked effects in what must be relatively small substrate selectivities.

(v) Where variations in the nuclear structure of the transition state parallel to the reaction co-ordinate are large enough to result in significant changes in the steric interaction energy, they ought to affect the selectivities of the reagents markedly. Where these structural variations are due to changes in the nature of the reagent only, that is, where changes in the nature of the substrate affect only the electronic structure, the selectivities of the reagents ought to be controlled by differences in the coulombic interactions between the reactants, but the differential reactivities of the reagents ought to be controlled by differences in steric interactions. In these circumstances the Reactivity–Selectivity Principle ought to be valid. Where changes in the nature of the substrate also affect the nuclear structure of the transition state, the selectivities of the reagents ought to be controlled by blends of (a) differences in the steric interactions between the reactants, and (b) differences in the coulombic interactions between the reactants. When the steric effects are greater than the coulombic effects, the reactivity–selectivity behaviour is not theoretically required to conform with the Reactivity–Selectivity Principle, and the more reactive of two reagents could be the more selective with respect to a pair of substrates in some cases.

[0/1217 *Received*, 1*st August*, 1980]

REFERENCES

[1] J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, p. 162.

[2] C. D. Johnson, *Chem. Rev.*, 1975, **75**, 755.

[3] J. M. Harris, S. G. Shafer, J. R. Moffatt, and A. R. Becker, *J. Am. Chem. Soc.*, 1979, **101**, 3295.

[4] Y. Karton and A. Pross, *J. Chem. Soc., Perkin Trans. 2*, 1979, 857.

[5] E. M. Arnett and R. Reich, *J. Am. Chem. Soc.*, 1978, **100**, 2930.

[6] E. R. Thornton, *J. Am. Chem. Soc.*, 1967, **89**, 2915.

[7] M. Godfrey, 'Correlation Analysis in Chemistry: Recent Advances,' eds. N. B. Chapman and J. Shorter, Plenum, New York, 1978, ch. 3.

[8] M. F. Duerden and M. Godfrey, *J. Chem. Soc., Perkin Trans. 2*, 1980, 330.

[9] I. Roberts, C. D. Johnson, and P. G. Taylor, *Tetrahedron*, 1977, **33**, 2123.

[10] P. R. Young and W. P. Jencks, *J. Am. Chem. Soc.*, 1979, **101**, 3288.

[11] E. S. Lewis and S. H. Vanderpool, *J. Am. Chem. Soc.*, 1977, **99**, 1946.

[12] E. S. Lewis and S. H. Vanderpool, *J. Am. Chem. Soc.*, 1978, **100**, 6421.

[13] V. M. Csizmadia, K. M. Koshy, K. C. M. Lau, R. A. McClelland, V. J. Nowlan, and T. T. Tidwell, *J. Am. Chem. Soc.*, 1979, **101**, 974.

[14] K. M. Koshy, D. Roy, and T. T. Tidwell, *J. Am. Chem. Soc.*, 1979, **101**, 357.

[15] L. Salem, *J. Am. Chem. Soc.*, 1968, **90**, 543.

[16] U. Berg, R. Gallo, and J. Metzger, *J. Org. Chem.*, 1976, **41**, 2621.

[17] U. Berg, R. Gallo, J. Metzger, and M. Chanon, *J. Am. Chem. Soc.*, 1976, **98**, 1260.