

## Reactivity and Selectivity, an Intersecting-state View †

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A recently developed intersecting-state model which estimates energy barriers of chemical reactions in terms of thermodynamic, geometric, and electronic factors is employed to discuss the validity of several reactivity relations, namely the postulates of Hammond and Leffler, various linear free energy relationships, and the reactivity-selectivity principle. It is shown that such rules and principles are obeyed when all the changes in reactivity are dominated by changes in the reaction energy. The breakdown of such rules can occur when other factors such as the transition-state bond order, bond lengths, and force constants of the reactive bonds play a dominating role in chemical reactivity. Examples are provided to illustrate the practical limitations of the current reactivity-selectivity relations.

The question of the relationship between reactivity and selectivity is of the utmost importance in organic chemistry, as demonstrated by the frequent review articles<sup>1-4</sup> and a special issue of *Isr. J. Chem.* dedicated to this problem (1985, vol. 26). This relation has been discussed in terms of the 'Reactivity Selectivity Principle' (RSP), which states that more reactive species tend to be less selective in their reactivity than less reactive ones. The principle has proved to be a useful mechanistic tool in organic chemistry, but the increasing number of exceptions raises the question of its value or limitation. One of the recent review articles<sup>1</sup> questions, 'The Reactivity-Selectivity Principle: Fact or Fiction?'

The relation between reactivity and selectivity is indeed complex, because many factors come into play and no simple general relationship between reactivity and selectivity exists. Very early in the development of chemical kinetics, relationships between rate and equilibrium constants were established by Brønsted and Pederson.<sup>5</sup> The quantitative understanding of these relations was greatly enhanced with the advent of the theory of Marcus,<sup>6</sup> which introduced the concept of kinetic [intrinsic energy barrier,  $\Delta G(0)^\ddagger$ ] and the thermodynamic (reaction energy,  $\Delta G^\circ$ ) control of chemical reactivity.

Chemical bond order has been shown to be an important factor in chemical reactivity in the BEBO theory<sup>7</sup> and in several reactivity indices of quantum chemistry.<sup>8</sup> Of particular relevance are the studies of Woodward and Hoffmann<sup>9</sup> and of Fukui<sup>10</sup> on the frontier orbitals which have revealed the existence of chemical processes where the bond order of the transition state is zero, the so-called 'forbidden reactions'.

As a result of the success of the theory of Marcus and similar approaches such as the BEBO and Agmon-Levine models,<sup>11</sup> it is understandable that efforts have recently been developed to locate the position of the energy barrier along the reaction co-ordinate,<sup>12,13</sup> and to derive a common formalism<sup>14</sup> for the different Marcus-type equations. This formalism, due to Murdoch,<sup>15</sup> has been shown to include the geometric distortion effects along and orthogonal to the reaction co-ordinate, employed by More O'Ferrall<sup>16</sup> and Thornton<sup>17</sup> among many others,<sup>4,18</sup> for the interpretation of substituent effects on the rates of several reactions and anti-RSP effects.

However other molecular factors, not explicit in the previous approaches, appear also to be important in controlling chemical reactivity. Koeppel and Kresge<sup>19</sup> have shown that the Brønsted coefficient is sensitive to vibrational force constants, and some

correlations between reaction rates and vibrational frequencies have been found.<sup>20</sup> Jones *et al.*<sup>21</sup> have also found correlations between reactivity and bond length.

The problem of reactivity and selectivity has been extensively discussed<sup>1-4,22,23</sup> in terms of several different models of chemical reactivity. These approaches represent, in most cases, mutually unrelated and single-cause models that cater specifically for certain types of problems. To deal with this problem one needs a model which embraces all the thermodynamic, electronic, and geometric factors which appear to control reaction rates. Such a model requires some degree of quantification, because without this it is difficult to assess the final outcome when some factors work in opposite directions. Recently we have developed a model (intersecting-state model, ISM)<sup>24</sup> along these lines, which appears to be adequate to deal with problems of reactivity and selectivity in the field of organic chemistry.

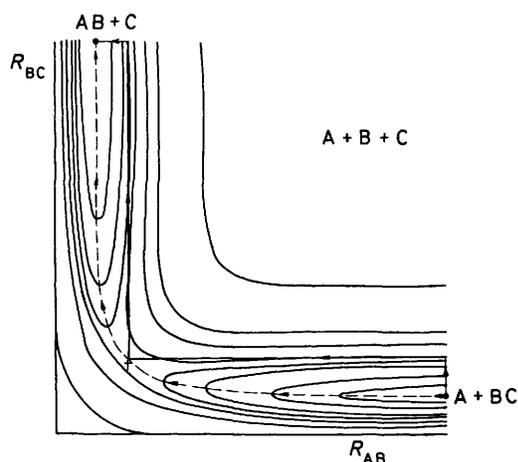
ISM encompasses the Marcus<sup>6</sup> and BEBO<sup>7</sup> theories as particular cases, includes rules such as the Brønsted relation,<sup>5</sup> the Evans-Polanyi<sup>25</sup> and Hammond postulates,<sup>26</sup> and quantifies the electronic allowedness of chemical reactions in terms of the 'transition state bond order'. Furthermore, the model appears to be general, and it has been applied with success to the study of a large variety of chemical reactions: atom transfer,<sup>24</sup> proton transfer,<sup>27</sup> methyl transfer,<sup>28</sup> sigmatropic shifts and cycloaddition reaction,<sup>29</sup> and nucleophilic substitutions.<sup>30,31</sup>

In the present paper we intend to employ ISM as a heuristic model for the study of the reactivity-selectivity principles and the analysis of their current limitations. Emphasis is given to the qualitative predictions which were gained through more detailed quantitative studies of prototype reactions.

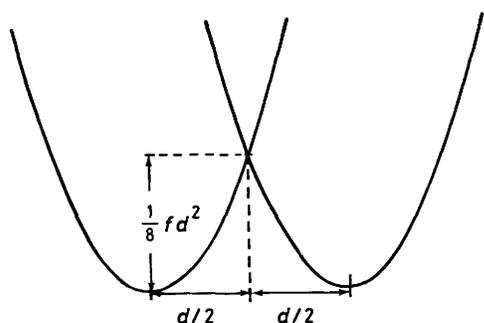
*The Intersecting-state Model.*—Figure 1 illustrates the potential energy surface for the reaction  $A + BC \longrightarrow AB + C$  in function of the bond distances  $R_{AB}$  and  $R_{BC}$ . The reaction is assumed to proceed without the bending of the linear  $ABC^\ddagger$  molecular species. The reaction path can be simulated by the following nonadiabatic path: (i) a BC stretch from the equilibrium bond length  $R_{BC}^e$  to  $R_{BC}^\ddagger$  at a constant  $R_{AB}$ ; (ii) a virtually isoenergetic path through the saddle point;  $R_{AB}$  decreases from a large distance to  $R_{AB}^\ddagger$  at a constant  $R_{BC}^\ddagger$ , etc.; (iii)  $R_{AB}^\ddagger$  decreases to the equilibrium value  $R_{AB}^e$  at a constant and large  $R_{BC}$ . This path justifies the estimation of the energy barrier through the intersection of the BC and AB potential energy curves, as shown in Figure 2 for a thermoneutral situation, and where  $d$  represents the sum of the bond extensions of BC and AB up to the transition state,  $d = (R_{AB}^\ddagger - R_{AB}^e) + (R_{BC}^\ddagger - R_{BC}^e)$ .

The height of the barrier depends not only on the shape of the potential energy curves (*i.e.* force constants,  $f$ , for harmonic

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**Figure 1.** Potential energy surface for the reaction  $A + BC \rightarrow AB + C$ ; (---) reaction path, (—) nonadiabatic path equivalent to an intersecting potential energy curve diagram



**Figure 2.** Intersection of the potential energy curves of BC and AB in the reaction  $A + BC \rightarrow AB + C$ , for oscillators of a common force constant  $f$  and with zero reaction energy;  $d$  represents the sum of the bond extensions of AB and BC up to the transition state, and the horizontal displacement of the potential energy curves

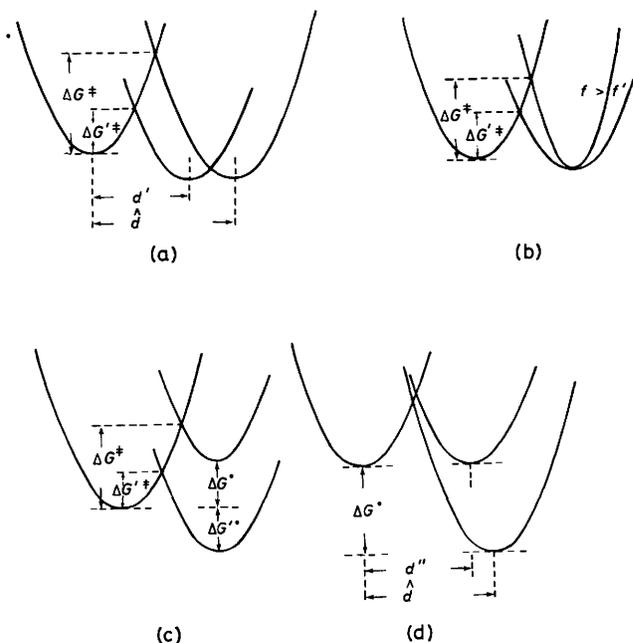
oscillators) and the reaction energy,  $\Delta G^\circ$ , but also on the parameter  $d$  (Figure 3). Since  $\Delta G^\circ$  and  $f$  can be obtained, in principle, from thermodynamic and spectroscopic data, the development of a general model for the calculation of  $\Delta G^\ddagger$  requires the establishment of a relationship between  $d$  and molecular structure. Such a relation was developed<sup>24</sup> from the Pauling relationship<sup>32</sup> between bond order,  $n$ , and bond length, and from the concept of 'mixing entropy' or 'configuration entropy' introduced by Agmon and Levine.<sup>11</sup> By minimizing the 'free energy' along the reaction co-ordinate equation (1) was

$$d = \left[ \frac{a' \ln 2}{n^\ddagger} + \frac{a'}{2} \left( \frac{\Delta G^\circ}{\lambda} \right)^2 \right] l \quad (1)$$

deduced, where  $l$  is the sum of the equilibrium bond lengths of reactant and product,  $n^\ddagger$  is the transition-state bond order which will be further explained below,  $\lambda$  is a measure of the capacity of the transition state to store the reaction energy, and  $a'$  is a constant ( $a' = 0.156$ ).

Such a model shows that the energy barrier,  $\Delta G^\ddagger$ , depends on:

\* The term bond order has normally a specific technical meaning. Here  $n$  is estimated by counting the number of bonding, nonbonding, and antibonding electrons.



**Figure 3.** Influence on the energy barrier,  $\Delta G^\ddagger$ , of the variation of: (a) the sum of the bond extensions,  $d$ ; (b) the force constants,  $f$ ; (c) the reaction energy,  $\Delta G^\circ$ , at a constant  $d$ ; (d) weak influence of  $\Delta G^\circ$  on the energy barrier when the entropy of the transition state is low and, consequently,  $d$  increases with an increase in  $|\Delta G^\circ|$

reactive bonds, normally in terms of the stretching force constants,  $f$ , of AB and BC ( $\Delta G^\ddagger$  decreases with a decrease in  $f$ ); (ii) the reaction energy  $\Delta G^\circ$ , in the normal region a decrease in  $\Delta G^\circ$  decreases  $\Delta G^\ddagger$ ; and (iii) the distance,  $d$ , between the minima of the two potential energy curves, *i.e.*, the energy barrier depends on the sum of the bond extensions in the transition state; a decrease in  $d$  decreases  $\Delta G^\ddagger$ . Whereas the factors considered in (i) and (ii) are present in any intersecting state model, the dependence of  $\Delta G^\ddagger$  on  $d$  is the novelty of ISM and requires further attention.

Three molecular factors affect the parameter  $d$ , namely the bond lengths ( $l$ ), the transition-state bond order ( $n^\ddagger$ ), and the energy parameter ( $\lambda$ ) associated with the 'configuration entropy' of Agmon and Levine.<sup>11</sup> The displacement of the potential energy curves is proportional to the equilibrium bond lengths of the reactive bonds. This has a simple physical meaning: when a bond length is small its bond extension is also small and when the equilibrium bond length is large its bond extension is also large.

At the transition state the reaction energy has to be accommodated by the activated complexes. If these species have few ways (low  $\Delta S^\ddagger$ ) and, consequently, a small capacity to store  $\Delta G^\circ$  ( $\lambda \ll |\Delta G^\circ|$ ) this energy can be viewed as stored in the reactive bonds, through further bond extensions; then  $d$  increases strongly with an increase in  $|\Delta G^\circ|$ . However if the activated complexes have many ways (high  $\Delta S^\ddagger$ ) and a large capacity to store energy ( $\lambda \gg |\Delta G^\circ|$ ), then virtually no reaction energy is stored in the reactive bonds and  $d$  is independent of  $\Delta G^\circ$ . Together with a common force constant for reactants and products, only the latter situation corresponds to the theory of Marcus.<sup>6</sup>

The sum of the bond extensions depends also on the electronic characteristics of the reactive chemical bonds in the transition state;  $d$  is higher when the transition-state bond order is smaller, *etc.* If one is dealing with single bonds ( $n = 1$ ), according to the BEBO model<sup>7</sup> the bond order is conserved

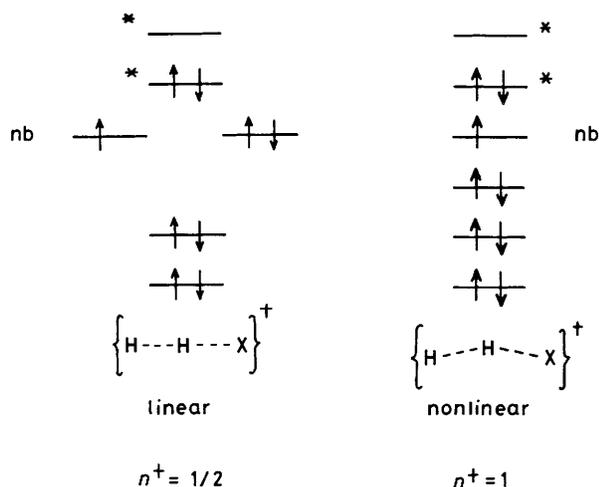


Figure 4. Molecular orbital energy diagram for  $\{\text{HHCl}\}^\ddagger$  activated complexes

along the reaction co-ordinate, *i.e.*,  $n_{\text{AB}} + n_{\text{BC}} = 1$ . At the transition state and for the thermoneutral situation then  $n^\ddagger = 1/2$ . However, we have shown<sup>24</sup> that when there are occupied non-bonding or antibonding low energy orbitals in reactants or products, such electrons can acquire a bonding character at the transition state. This electronic siphoning causes an increase in the transition-state bond order,  $n^\ddagger > 1/2$ , and a decrease in  $d$ . Generalized valence bond configuration interaction calculations for hydrogen abstraction  $\text{H} + \text{HX}$  support this view.<sup>33</sup> However, it is instructive to analyse the lack of conservation of chemical bond order in more detail.

To neglect the effect of  $\Delta G^\circ$  on  $d$  let us consider two reactions which are nearly thermoneutral:  $\text{H} + \text{HCl} \rightarrow \text{H}_2 + \text{Cl}$  ( $\Delta E^\circ = 9.2 \text{ kJ mol}^{-1}$ ) and the exchange reaction  $\text{H} + \text{ClH} \rightarrow \text{HCl} + \text{H}$  ( $\Delta E^\circ = 0$ ). In spite of involving the same molecular species, the first reaction has  $n^\ddagger = 1$  and the second  $n^\ddagger = 1/2$ .<sup>\*</sup> What is the cause of such a drastic difference?

Figure 4 illustrates the molecular orbital energy diagram for the linear  $\{\text{HHCl}\}^\ddagger$  activated complexes. The number of bonding and antibonding orbitals is the same and there are two non-bonding orbitals, essentially with an atomic  $p$  character. The electronic configuration  $\sigma_1^2 \sigma_2^2 p_x^2 p_y^1 \sigma_3^{*2}$  leads to the normal transition-state bond order  $n^\ddagger = 1/2$ . Such a transition state has features of an electronic excited state, because the electrons are not occupying all the lowest molecular orbitals. Nevertheless the occupancy of an antibonding orbital by a pair of electrons can be understood, because this is essential for the breaking of the HCl single bond in the reactants.

If the transition state is slightly non-linear, the chlorine  $p_x$  orbital in the plane of the  $\text{H}-\text{H}-\text{Cl}$  angle interacts with the  $1s$  hydrogen orbital and acquires a bonding character. As we have discussed elsewhere<sup>30</sup> and as shown in Figure 4, this leads to an increase in the transition-state bond order,  $n^\ddagger = 1$ . However for  $\{\text{HClH}\}^\ddagger$  the  $p_x$  chlorine atomic orbital appears to correlate with a molecular orbital with a non-bonding character,<sup>33</sup> *i.e.* the activated complex is linear. Consequently, the total bond order is conserved along the reaction co-ordinate and  $n^\ddagger = 1/2$ .

In principle the transition-state bond order  $n^\ddagger$  can be

considered as an empirical parameter of chemical reactivity, free from the effects of  $\Delta G^\circ$ ,  $f$ , and  $l$ . However, in general, it is possible to assign some physical meaning to it. In the vapour phase well defined  $n^\ddagger$  values ( $1/2; 1; 3/2$ ) have been found for hydrogen atom transfers between hydrides<sup>24</sup> and for methyl transfers,<sup>28</sup> but in solution this not the case. For example, vapour-phase reactions such as  $\text{X}^- + \text{CH}_3\text{Y} \rightarrow \text{XCH}_3 + \text{Y}^-$ , where X and Y are halogen atoms, have  $n^\ddagger \approx 1$  due to the siphoning of a pair of nonbonding electrons into the transition state.<sup>†</sup> In liquid solutions, owing to the interactions of these nonbonding pairs with solvent molecules  $n^\ddagger < 1$ . With hard nucleophiles and good accepting solvent molecules  $n^\ddagger \approx 0.5$ . Between these two extremes  $n^\ddagger$  varies with the nature of the solvent and of the nucleophiles, increasing with the increase of the softness of X and Y and with the decrease of the solvent acceptor number.<sup>28</sup> The transition-state bond order can vary also with the nature of the cations present in solution.

For reactions where charge is developed or cancelled, polar solvents can increase  $n^\ddagger$  at low  $\Delta G^\circ$  values. Such effects can lead to a decrease in  $d/l$  with a decrease in  $\Delta G^\circ$ , as found with some proton transfers.<sup>27</sup>

The transition-state bond order can also be increased through electronic siphoning of electron-rich substituents as revealed in sigmatropic shifts and cycloaddition reactions.<sup>29</sup> The loss of synchronicity of the reaction due to steric effects,<sup>34</sup> solvent viscosity, and lack of strong electronic-vibronic coupling<sup>29</sup> leads to a decrease in  $n^\ddagger$ . The participation in the reaction co-ordinate of bonds with  $n > 1$  leads also to an increase in  $n^\ddagger$ . For example, calculations for the isomerization of  $\text{CH}_3\text{NC}$  to  $\text{CH}_3\text{CN}$  lead to the stretching contribution for the barrier height  $\Delta G^\ddagger(\text{st}) = 117 \text{ kJ mol}^{-1}$  when only the C-N stretch is considered. However, when the reaction co-ordinate involves both a C-N and a C $\equiv$ N stretch, the barrier height is much smaller [ $\Delta G^\ddagger(\text{st}) 84 \text{ kJ mol}^{-1}$ ] and this fact is mainly due to an increase in  $n^\ddagger$ .

A similar kind of mechanism accounts for the normal acid behaviour of the carbon acid HCN.<sup>35</sup>

*The Hammond Postulate.*—A postulate which bears heavily on the reactivity-selectivity relations is that of Hammond.<sup>26</sup> It is usually interpreted as follows: transition states of highly exothermic reactions are similar in structure and energy to reactants, while the ones of highly endothermic reactions resemble products. Such a postulate is sometimes expressed in a quantitative relation, as proposed by Leffler:<sup>36</sup> the slope of a rate-equilibrium relationship,  $\partial \log k / \partial \log K = \gamma$ , measures the position of the transition state along the reaction co-ordinate. Those ideas were expressed earlier by Evans and Polanyi<sup>25</sup> and others, but lay dormant for two decades until revised and extended by Hammond.

According to ISM, the position of the transition state within the Hammond postulate can be measured by the ratio of the bond extension in reactant,  $x$ , with respect to the reactant bond extension of some reference reaction,  $x_{\text{R}}$ . As Figure 3 shows, the Hammond postulate is obeyed only if the reaction energy varies between the two reactions under comparison. However, if together with a decrease in  $\Delta G^\circ$  there is a strong decrease in the effective force constant,  $f$ , for the more endothermic reaction, or a strong increase in  $f$  of the more exothermic reaction, the Hammond postulate may not be valid. The same can be said for the extension parameter  $d$ . If  $d$  decreases for the more endothermic reaction or increases for the more exothermic process, the Hammond postulate may not be valid and even an 'anti-Hammond' effect can occur. The decrease in  $d$  can be due to an

\* Ref. 24 presents the study for the first reaction where the total bond order is not conserved. For the second reaction with a force constant  $f = 3.1 \times 10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ ,  $l = 1.275 \text{ \AA}$  the energy barrier is calculated to be  $\Delta E^\ddagger = 117 \text{ kJ mol}^{-1}$  with  $n^\ddagger = 1/2$  and  $\Delta E^\ddagger = 29 \text{ kJ mol}^{-1}$  with  $n^\ddagger = 1$ . Quantum mechanical calculations lead to barrier heights between 92 to 109  $\text{kJ mol}^{-1}$ .<sup>33</sup>

† Other reasons rather than the nonlinearity of the transition states can lead to the nonconservation of  $n$  such as the formation of weak charge-dipole complexes.

**Table 1.** ISM calculations for the Hammond and Leffler postulates<sup>a</sup>

Reaction Ref.	Pro-		$\Delta G^{\circ b}$	$\Delta G^{\ddagger c}$	$d/\text{\AA}$	$n^{\ddagger}$	$x/\text{\AA}$	$x/d$
	Reactant	duct						
1	2	2	-40	86	0.648	0.5	0.293	0.453
2	2	0.6	40	126	0.648	0.5	0.355	0.548
3	2	2	40	80	0.648	0.5	0.282	0.436
								0.590

<sup>a</sup>  $l_r + l_p = 3\text{\AA}$ ;  $d = (0.108/n^{\ddagger})(l_r + l_p)$ . <sup>b</sup> kJ mol<sup>-1</sup> Å<sup>-2</sup>. <sup>c</sup> kJ mol<sup>-1</sup>.

increase in  $n^{\ddagger}$ , a decrease in the reactive bond lengths, and/or a strong increase in  $\lambda$ .

If one considers the Hammond postulate in abstract terms, all the above mentioned factors can be important. However, for similar reactions the variations in  $f$  and  $l$  are usually not very significant. A longer chemical bond normally has a lower force constant and a shorter bond has a higher force constant.<sup>37</sup> This introduces a compensating effect for the barrier height and the position of the transition state. A practical example can illustrate this. For the H-atom exchange reactions  $\text{HX} + \text{H} \rightarrow$  the calculated barrier height varies only by 4 kJ mol<sup>-1</sup> for all the halogen atoms, within the harmonic approximation, in spite of the fact that  $f$  and  $l$  vary considerably between HF and HI [ $f(\text{HF})/f(\text{HI}) = 3$ ;  $l(\text{HI})/l(\text{HF}) = 1.8$ ]. Anharmonicities are negligible for the reaction with HF, but can be significant with HI. This leads to a greater effect on the barrier height  $\Delta E^{\ddagger}(\text{HF}) = 117$  and  $\Delta E^{\ddagger}(\text{HI}) = 69$  kJ mol<sup>-1</sup>, but the effect is negligible on the bond extensions.

Within the harmonic approximation, the barrier height for a chemical reaction with effective force constants  $f_r$  and  $f_p$  for reactants and products is given by equation (2) where  $x$  is estimated through equation (3) with  $d$  given by equation (1).

$$\Delta G^{\ddagger} = \frac{1}{2}f_r x^2 \quad (2)$$

$$\frac{1}{2}f_r x^2 = \frac{1}{2}f_p(d - x)^2 + \Delta G^{\circ} \quad (3)$$

Table 1 illustrates some calculations for typical values of  $f_r$ ,  $l_r + l_p$ , and  $\Delta G^{\circ}$ . Owing to the compensating effects of  $f$  and  $l$ , we will neglect, at present, the effect on  $x$ , as well as the effect of  $\lambda$  ( $\lambda \gg |\Delta G^{\circ}|$ ).<sup>\*</sup> We will concentrate therefore on the effect of  $n^{\ddagger}$ . Reaction (3) illustrates that, for example, an increase from  $n^{\ddagger} = 0.5$  to  $n^{\ddagger} > 0.635$  can invalidate the postulate of Hammond. Larger variations in  $n^{\ddagger}$  are found in several chemical reactions, as previously discussed. Variations of  $n^{\ddagger}$  can be attributed to changes in mechanism, e.g. from  $S_N1$  to  $S_N2$  as has been observed with water-exchange of hydrated metal ions.<sup>31</sup> However,  $n^{\ddagger}$  can vary also without a change in the reaction mechanism. Nucleophilic substitution reactions on methyl groups  $\text{X}^- + \text{CH}_3\text{Y} \rightarrow \text{XCH}_3 + \text{Y}^-$  are  $S_N2$  reactions, but  $n^{\ddagger}$  varies with the nature of the nucleophile and of the solvent. For example, for reactions in water  $n^{\ddagger}$  ranges between 0.54 (X and Y = F) to 0.70 (X and Y = I).<sup>28</sup> Methyl-transfer reactions are, therefore, good examples of anomalous selectivities<sup>38</sup> due to variations in the transition-state bond order, which, within

<sup>\*</sup> When  $f_r = f_p = f$ , equations (3) and (2) lead to  $\Delta G^{\ddagger} = [(fd^2/2) + \Delta G^{\circ}]^2/2fd^2$ . This equation is the familiar equation of Marcus with the intrinsic energy barrier  $\Delta G(0)^{\ddagger} = (1/8)fd^2$ . However, in the theory of Marcus  $d$  is independent of  $\Delta G^{\circ}$ , in contrast with ISM where  $d$  has a quadratic dependence on  $\Delta G^{\circ}$  scaled by the parameter  $\lambda$ . This parameter is a configuration entropy parameter, different from the repolarization parameter  $\lambda$  of the theory of Marcus.

**Table 2.** Calculations of the compensating effect of  $f$  and  $l$  at various reaction energies

Reaction	Pro-		$\Delta G^{\circ b}$	$\Delta G^{\ddagger b}$	$d/\text{\AA}$	$x/\text{\AA}$	$x/d$
	Reactant	duct					
1	2	2	0	105	0.648	0.324	0.5
2	2	1	0	105	0.782	0.324	0.41
3	2	2	40	126	0.648	0.355	0.548
4	2	1	40	129	0.782	0.360	0.460
5	2	2	-40	86	0.648	0.293	0.453
6	2	1	-40	82	0.782	0.287	0.367

<sup>a</sup> kJ mol<sup>-1</sup> Å<sup>-2</sup>. <sup>b</sup> kJ mol<sup>-1</sup>.

the present model, is the most important factor to invalidate the Hammond postulate. For example,  $x = 0.262$  for X = Cl and Y = F with  $\Delta G^{\circ} = -2$  kJ mol<sup>-1</sup> and  $n^{\ddagger} = 0.57$  and  $x = 0.294$  for X = OH and Y = Cl with  $\Delta G^{\circ} = -98$  kJ mol<sup>-1</sup> and  $n^{\ddagger} = 0.54$ ; the transition state of the more exothermic reaction is closer to the products.

The compensating effect of  $f$  and  $l$  depends on the reaction energy. Table 2 presents an illustrative calculation. Endothermicity enhances the effect of bond length and exothermicity enhances the force constant effect. Although for moderate changes in  $\Delta G^{\circ}$  such effects are not very significant, they can become dominant for very exo- or endo-thermic reactions. This can explain the increase in reactivity with an increase in bond length, observed for quite exothermic reactions,<sup>21</sup> because they are in fact dominated by the decrease in  $f$ . Furthermore, when the reaction co-ordinate involves more than one chemical bond in the reactants and in the products, the effective force constant for local mode oscillators can be estimated by  $f = (\sum f_i^2)^{1/2}$  where  $l = (1/m)\sum l_i^{2.9,30}$  and these effective  $f$  and  $l$  values have a weaker compensating effect, being dominated by the effect of  $f$ .

The Leffler postulate<sup>36</sup> is often associated with that of Hammond, but this is not always correct. The position of the transition state along the reaction co-ordinate should be measured by  $x/d$  and not strictly with respect to any reference reaction. Consequently, the Leffler coefficient is not necessarily identical to the Hammond postulate. As long as  $d$  is constant in a series of reactions, the Hammond and the Leffler postulates follow the same trend; compare, for example, reactions 1 and 3 or 1 and 5 in Table 2. However, when  $d$  varies owing to some variation of  $n^{\ddagger}$  and/or  $l$  the Hammond and the Leffler postulates can run in opposite directions; compare reaction 1/reference reaction and reaction 3/reference in Table 1 or reactions 1 and 4 in Table 2. In the latter example, an increase in endothermicity causes higher deformation in the reactants,  $x/x_R = 1.11$ , but places the transition state nearer the reactants.

As discussed later, the position of the transition state with respect to reactants and products is not necessarily given by  $\partial \log k / \partial \log K$ . Furthermore, any resemblance of the transition state to reactants or products can be misleading when the total bond order is not conserved. Under this situation the electronic structure of the transition state bears no resemblance to reactants and products, but has features of electronic excited states.<sup>30</sup>

**Linear Free Energy Relationships.**—Under this title we will consider the linear and the non-linear free energy relations such as the Brønsted and the Hammett-type relationships. The Brønsted relation has been discussed in detail for proton-

**Table 3.** Calculation of the position of the transition state ( $x/d$ ) and the Brönsted coefficient ( $\alpha$ ) for several ratios of the force constants of reactant and product<sup>a</sup>

$\Delta G^\circ/\text{kJ mol}^{-1}$	$f_r = 3$ $x/d$	$f_p = 2$ $\alpha$	$f_r = 3$ $x/d$	$f_p = 3$ $\alpha$	$f_r = 2$ $x/d$	$f_p = 3$ $\alpha$
-100	0.18	0.25	0.29	0.29	0.31	0.23
-50	0.32	0.41	0.40	0.40	0.43	0.33
0	0.45	0.55	0.50	0.50	0.55	0.45
50	0.57	0.67	0.60	0.60	0.68	0.59
100	0.69	0.77	0.71	0.71	0.82	0.75

<sup>a</sup>  $f/10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ .

transfer reactions.<sup>27</sup> In its usual expression the Brönsted coefficient,  $\alpha$ , is given by  $\log k = -\alpha pK + \text{const}$ . Within the harmonic approximation and for a common force constant of reactants and products, equation (4) applies on neglecting the

$$\alpha = \frac{1}{2} + \frac{\Delta G^\circ}{fd^2} \quad (4)$$

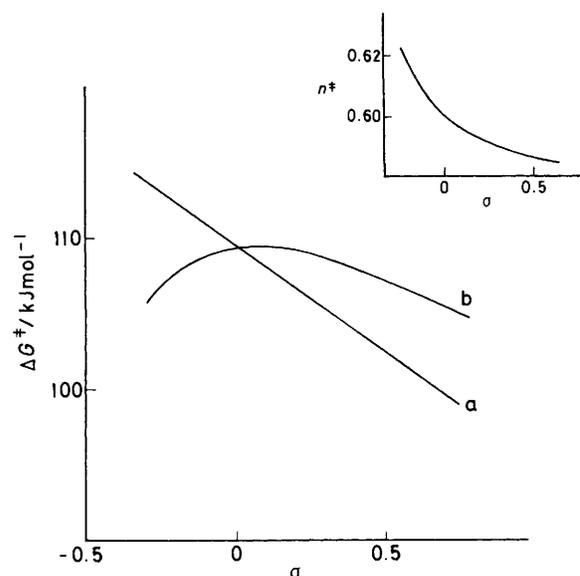
dependence of  $d$  on  $\Delta G^\circ$  ( $\lambda \gg |\Delta G^\circ|$ ). Under these conditions  $\alpha$  is a measure of the position of the transition state ( $x/d$ ). When  $f_r > f_p$  the Brönsted coefficient overestimates the progress of the reaction; the opposite effect occurs when  $f_r < f_p$  (Table 3).

Equation (4) shows that the Brönsted plots are curved and such a curvature depends on the intrinsic energy barrier  $\Delta G(0)^\ddagger = (1/8)fd^2$ . Therefore the curvature increases with a decrease in  $f$  and/or a decrease in  $l$  and/or an increase in  $n^\ddagger$ , and decreases with the opposite variation of these parameters. The latter effects can lead to virtually linear Brönsted plots.<sup>27</sup>

Variations in  $f$  and  $l$  can be found for different reaction types, but if one compares similar reactions, the main source of the non-validity of the Brönsted relation is the variation of  $n^\ddagger$ . For example, for proton-transfer reactions in water, the transition state bond order ranges from  $n^\ddagger = 0.55$  for a carbon acid such as  $\text{CH}_3\text{NO}_2$  to  $n^\ddagger = 0.95$  for HF, with the oxygen and nitrogen acids somewhere in the middle.<sup>27</sup> Sometimes  $n^\ddagger$  does not change drastically in a series of reactions to invalidate the Brönsted equation, but leads to anomalous coefficients,  $\alpha > 1$  or  $\alpha < 0$ , even far from the diffusion-controlled limit. Substituents can alter  $n^\ddagger$  and cause anomalous behaviour as, for example, with the reaction of 1-arylnitroalkanes with  $\text{OH}^-$  where a variation of  $n^\ddagger$  by  $\Delta n^\ddagger = 0.02$  for  $\Delta pK = 1.4$  accounts for an anomalous  $\alpha = 1.5$ .<sup>27</sup>

The Brönsted coefficient  $\alpha$  is occasionally associated with the extent of the chemical reaction, but this is only valid when  $f_r = f_p$ ,  $n^\ddagger$  does not vary, and  $\lambda \gg |\Delta G^\circ|$ . Otherwise,  $\alpha$  is not a measure of the extent of the reaction. Furthermore, for some reactions, such as proton transfer,<sup>27</sup>  $\lambda$  is not very high and all the reactivity relations can be further complicated by a significant increase of  $d$  with an increase in  $|\Delta G^\circ|$ . This effect tends to enhance the curvature of the Brönsted plots and can lead to values of  $\alpha > 1$  or  $\alpha < 0$ , even at constant  $n^\ddagger$ . The Brönsted coefficient depends on  $f$ ,  $n^\ddagger$ ,  $l$ , and  $\lambda$ . Consequently, the characterization of the changes in bond order and charge distribution of the transition-state structures in terms of  $\partial^2 \Delta G^\ddagger / \partial^2 \Delta G^\circ$  does not have universal applicability.

Pross<sup>2</sup> considers that there is a contradiction between the expected non-linear behaviour of the Brönsted relation and the overwhelming evidence for linear Hammett plots, to the extent that curvature, when found, is attributed to a change in the mechanism or in the identity of the rate-determining step. The question of the validity of linear free energy relations (l.f.e.r.) such as Hammett plots within the ISM formalism has been dis-

**Figure 5.** Calculated Hammett plots with  $f_r = f_p = 3 \times 10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ ,  $\Delta G^\circ = -28.5 \text{ kJ mol}^{-1}$  and (a)  $n^\ddagger = 0.6$ ; (b)  $n^\ddagger$  variable as shown in the insert

cussed in some detail elsewhere.<sup>39</sup> Linear kinetic Hammett plots are found when  $\lambda \gg |\Delta G^\circ|$  and  $n^\ddagger$  is constant within a reaction series. In general, Hammett plots are not very sensitive to variations in  $f$  and/or  $l$ . Their linearity results from the definition of the parameters involved. For a given kind of reaction we have shown that in a linear Hammett plot  $[\sigma_i = \log(K_i/K_R)]$  and  $\Delta G_i^\ddagger - \Delta G_R^\ddagger = -2.3RT \rho \sigma_i$   $\rho = [(2n^\ddagger + \epsilon)/8n^\ddagger \epsilon]^2$ . For bond-breaking–bond-forming processes it is reasonable to assume that changes in  $\Delta G^\circ$  are caused by changes in the potential energies of the reactive bonds and consequently one can consider that  $(\sigma \ln 2)^2 (f_r l_r^2 - f_p l_p^2) = \epsilon(\Delta G_i^\circ - \Delta G_R^\circ)$  along a reaction series.

There are situations where Hammett-type plots are not valid owing to a variation of  $n^\ddagger$ , but this does not imply a change in the reaction mechanism. For example, sigmatropic shift reactions of hexadienes do not obey Hammett l.f.e.r. because  $n^\ddagger$  varies due to electronic siphoning of substituents: hexa-1,5-diene,  $n^\ddagger = 0.5$ ; 2-phenylhexa-1,5-diene,  $n^\ddagger = 0.538$ ; and 2,5-diphenylhexa-1,5-diene,  $n^\ddagger = 0.575$ .<sup>29</sup>

Bordwell and Hughes<sup>40</sup> have reported an interesting case of curved Hammett plots. The substitution reactions of 9-substituted fluorenyl carbanions ( $9\text{-RF1}^-$ ) with  $\text{GC}_6\text{H}_4\text{CH}_2\text{-NMe}_2\text{C}_6\text{H}_4\text{Y}^+$  cations follow a l.f.e.r. with  $\sigma_Y$ . However, the reactions of  $9\text{-RF1}^-$  with  $\text{GC}_6\text{H}_4\text{CH}_2\text{Cl}^-$  have a curved Hammett plot with  $\sigma_G$ . When reaction energy dominates chemical reactivity good l.f.e.r. are normally observed. However, for some reactions substituents can alter both  $\Delta G^\circ$  and  $n^\ddagger$  in such a way that the two effects work in opposite directions on  $\Delta G^\ddagger$ . Under such circumstances non-l.f.e.r. can be observed, as it is illustrated in Figure 5. In reactions where there is a cancellation of charge,  $d/l$  is frequently independent of  $\Delta G^\circ$  within a significant  $\Delta G^\circ$  range. This corresponds effectively to an apparent constant  $n^\ddagger$  and  $\lambda \rightarrow \infty$ . Under such conditions good l.f.e.r. are observed with the Hammett  $\sigma$  coefficients (case a of Figure 5); when  $n^\ddagger$  varies with the nature of the substituents together with  $\Delta G^\circ$ , strongly curved Hammett plots can be observed (case b of Figure 5). Taking as the reference reaction  $\sigma = 0$ , the Hammond postulate is not obeyed.

*The Reactivity–Selectivity Principle.*—When two reagents  $X_i$  and  $X_j$ , with  $X_i$  more reactive than  $X_j$ , are allowed to react with

substrates  $Y_1$  and  $Y_2$  the Reactivity-Selectivity Principle (RSP) states that  $X_i$  not only will react faster with both substrates, but the ratio of the rate constants as  $(k_{i1}/k_{i2}) < (k_{j1}/k_{j2})$ , i.e.,  $X_i$  is less selective than  $X_j$ . If one defines selectivity as  $\ln(k_{i1}/k_{i2})$  then RSP describes a linear relationship between the decrease in selectivity and the increase in reactivity,  $\delta\Delta G^\ddagger = a \Delta G_R^\ddagger + \text{const.}$  with  $a > 0$ .

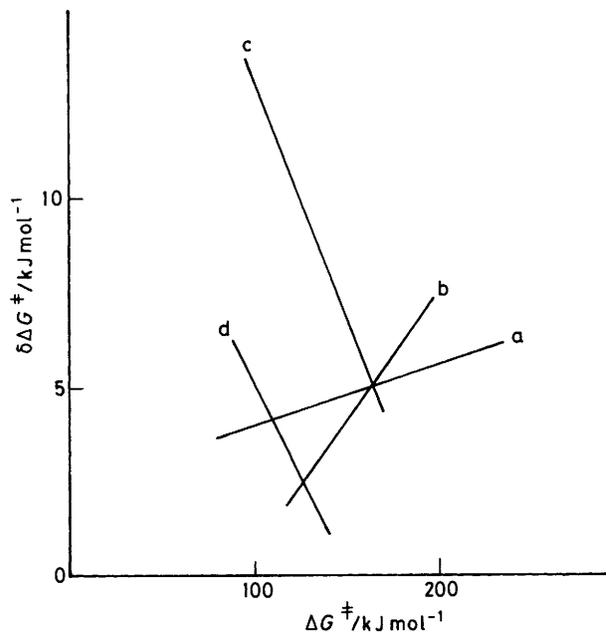
Figure 6 presents a calculation for several situations where the changes in reactivity are caused by changes in the reaction energy; in the normal region RSP is obeyed (case a). The selectivity can be increased by a decrease in  $\lambda$  (case b).

Molecular factors other than  $\Delta G^\circ$  can cause changes in reactivity.  $X_i$  can be more reactive than  $X_j$  owing to a smaller effective force constant or a lower  $d$  caused by an increase in  $n^\ddagger$  or a decrease in  $l$ . Under these conditions Table 4 shows ( $X_1$  versus  $X_2$ ) that when  $f$  decreases the more reactive species is also the more selective one and RSP is no longer obeyed. A good example of a breakdown of RSP is the nucleophilic aliphatic substitutions, e.g.  $\text{PhCOCH}_2\text{Br}$  is more reactive than  $\text{RBr}$  towards strong nucleophiles and is also more selective. This is a clear case where the higher reactivity of the  $\alpha$ -carbonyl derivative is due to an increase in  $n^\ddagger$ .<sup>28</sup> Anomalous selectivities have also been reported for methyl transfers to water.<sup>38</sup> Figure 6 illustrates how these anomalies can be interpreted in terms of the effects of  $n^\ddagger$  and  $\lambda$ . Such effects can also lead to Brønsted coefficients higher than 1. High  $\alpha$  values are expected when RSP fails, because they correspond to a large variation of  $\delta\Delta G^\ddagger$  ( $< 0$ ) due to a small decrease in  $\Delta G^\circ$ . Nevertheless the Hammond postulate is obeyed in agreement with the findings of Giese.<sup>3</sup>

It becomes an extremely difficult task to disentangle reactivity selectivity patterns when several factors work simultaneously, e.g., the reaction energy and the transition-state bond order. This is certainly the situation with the free radical reactions<sup>2,41</sup> and some examples can illustrate well the present discussion. When one compares the selectivity of  $\text{F}^\cdot$  and  $\text{Cl}^\cdot$  radicals to

abstractions at different hydrogens (Table 5) RSP is obeyed. However,  $\text{Br}^\cdot$  and  $\text{CH}_3^\cdot$  radicals are almost equally reactive, but  $\text{Br}^\cdot$  is ca. 10 times more selective, because for this radical  $n^\ddagger$  is much higher than for  $\text{CH}_3^\cdot$ . The radicals  $\text{Cl}^\cdot$  and  $\text{H}^\cdot$  have very different reactivities, but their selectivities towards secondary hydrogens are virtually identical; in this case the effect of  $n^\ddagger$  seems to compensate for the effect of  $\Delta E^\circ$ . Only for the tertiary hydrogens does the effect of  $\Delta E^\circ$  dominated and  $\text{H}^\cdot$  is ca. 6 times more selective than  $\text{Cl}^\cdot$ .

The reactions of  $\text{Br}^\cdot$  and  $\text{I}^\cdot$  provide another interesting



**Figure 6.** Calculated reactivity-selectivity relations: (a)  $f_r = f_p = 3 \times 10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ ,  $n^\ddagger = 0.5$ ,  $l = 3 \text{ \AA}$ ,  $\lambda \gg |\Delta G^\circ|$ ; the reactivity varies due to changes in  $\Delta G^\circ$ , variation in the reaction energy between  $Y_1$  and  $Y_2$   $\delta\Delta G^\circ = -10 \text{ kJ mol}^{-1}$ . (b) The same parameters as in (a) with  $\lambda = 280 \text{ kJ mol}^{-1}$ . (c)  $f$  and  $l$  as in (a),  $\lambda \gg |\Delta G^\circ|$ , and changes in reactivity due to the following parameters:

	$\Delta G^\circ/\text{kJ mol}^{-1}$	$n^\ddagger$	
$Y_1$	0	0.5	0.55
$Y_2$	-10	0.5	0.62

(d) The same parameters as in (c) except that  $\Delta G^\circ/\text{kJ mol}^{-1}$  is  $-50$  ( $Y_1$ ) and  $-60$  ( $Y_2$ ); associated with variations of  $n^\ddagger$  are variations in  $\lambda$ :

	$n^\ddagger$ ( $\lambda/\text{kJ mol}^{-1}$ )		
$Y_1$	0.5 (197)	0.55 (197)	0.6 (197)
$Y_2$	0.5 (197)	0.55 (228)	0.6 (283)

**Table 4.** Calculations for the Reactivity-Selectivity Principle

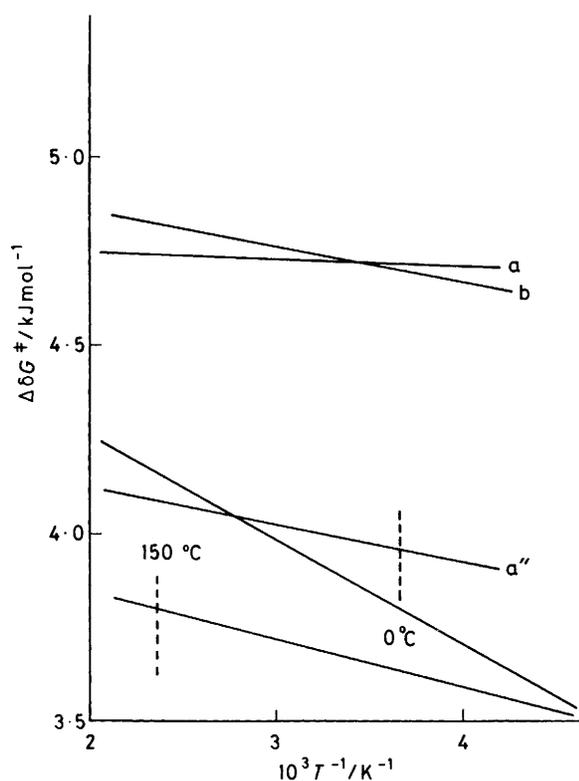
Reaction	$f_r^e$	$f_p^e$	$d/\text{\AA}$	$\Delta G^\circ^f$	$\Delta G^\ddagger^f$	$k_{X_1 Y_2} / k_{X_2 Y_1}^a$
$X_2 + Y_1$	2	2	0.648	0	105	53
$X_2 + Y_2$	2	2	0.648	-20	95.2	
$X_1 + Y_1^b$	2	2	0.648	-30	90.5	39
$X_1 + Y_2$	2	2	0.648	-50	81.5	
$X_1 + Y_1^c$	2	1	0.648	0	72	100
$X_1 + Y_2$	2	1	0.648	-20	60.7	
$X_1 + Y_1^d$	2	2	0.55	0	75.6	50
$X_1 + Y_2$	2	2	0.55	-20	66.0	

<sup>a</sup> Estimated at room temperature. <sup>b</sup> Effect of the reaction energy. <sup>c</sup> Effect of the force constant. <sup>d</sup> Effect of  $d$ , i.e. an increase in  $n^\ddagger$  or a decrease in  $l$ . <sup>e</sup>  $10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ . <sup>f</sup>  $\text{kJ mol}^{-1}$ .

**Table 5.** Selectivity of radicals towards C-H bonds<sup>a</sup>

Dominating effect	Radical	Primary	Secondary	Tertiary	$\Delta E^\circ(\text{CH}_4)$	$\Delta E^\ddagger(\text{CH}_4)$	$n^\ddagger^b$
$\Delta E^\circ$	$\text{F}^\cdot$	1	1.2	1.4	-134	5	1
	$\text{Cl}^\cdot$	1	4.3	7.0	0	16	1
$n^\ddagger$	$\text{Br}^\cdot$	1	80	1 700	67	75	1
	$\text{CH}_3^\cdot$	1	10	80	-4	73	1/2
$n^\ddagger$ (sec.)	$\text{Cl}^\cdot$	1	4.3	7.0	0	16	1
$\Delta E^\circ$ (tert.)	$\text{H}^\cdot$	1	4.8	40	0	50	1/2
$l$	$\text{Br}^\cdot$	1	80	1 700	67	75	1
	$\text{I}^\cdot$	1	18		138	142	1

<sup>a</sup> Data compiled in ref. 2, taken from J. A. Kerr in 'Free Radicals', ed. J. K. Kochi, Wiley, New York, 1973, vol. 1, ch. 1. <sup>b</sup> Ref. 24.



**Figure 7.** Effect of the temperature on the selectivity, with  $\Delta G^\circ(Y_2) - \Delta G^\circ(Y_1) = -10 \text{ kJ mol}^{-1}$ ,  $f_i = f_p = 3 \times 10^3 \text{ kJ mol}^{-1} \text{ \AA}^{-2}$ ,  $n^\ddagger = 0.5$ ,  $l = 3 \text{ \AA}$ : (a)  $\Delta G^\circ = -40 + 0.03T$ ; (b)  $\Delta G^\circ = -60 + 0.1T$ ; (a') and (b') as in (a) and (b) respectively but with  $\lambda = 279 \text{ kJ mol}^{-1}$ ; (a'') as in (a) with  $\lambda = 334 \text{ kJ mol}^{-1}$

example, because in spite of being more reactive, Br<sup>•</sup> is *ca.* 4.5 times more selective than I<sup>•</sup> towards secondary hydrogens. Since the reactions are very endothermic, as discussed previously, the effect of bond lengths dominates. This is a good example of the breakdown of RSP due to the effect of bond lengths, since there is not a compensating effect of  $l$  and  $f$ . In contrast I<sup>•</sup> is *ca.* 3 times more selective towards abstraction from CH<sub>3</sub><sup>•</sup> according to RSP.

The reaction energy and the transition-state bond order can vary with solvents and, consequently, these can have a great influence on the reactivity-selectivity relations as Giese has discussed in detail.<sup>3</sup> For example, the influence of solvents on the reaction of tetracyanoethylene (TCNE) with butyl vinyl ether and 2,3-dihydropropane obey RSP.<sup>3,42</sup> In this one-step cycloaddition zwitterionic species are formed and  $\Delta G^\circ$  decreases drastically with an increase in solvent polarity. Consequently,  $\Delta G^\circ$  dominates the effect of solvent on the reactivity-selectivity pattern. In contrast, the solvent influence on the reactivity-selectivity of the [2 + 2]-cycloadditions of diphenyl ketone with butyl vinyl ether and 2,3-dihydropyran does not verify RSP.<sup>3,43</sup> In this example the effect of solvent on  $n^\ddagger$  seems to dominate the overall process, because  $|\Delta G^\circ|$  is not very high. Another example is the reaction of arensulphonyl chlorides in the competition system aniline-3-chloroaniline.<sup>3,44</sup> RSP is verified with solvent variation ( $\Delta G^\circ$  effect dominates), but fails for substitution variation in the arensulphonyl chloride ( $n^\ddagger$  effect dominates).

Temperature influences the reaction energy of many reactions. An increase in  $|\Delta G^\circ|$  will favour RSP because  $\Delta G^\circ$  becomes the dominating reactivity factor, but a decrease in  $|\Delta G^\circ|$  contributes for the non-validity of RSP. For several chemical reactions isoselective temperatures can be found and

cases of a reversal in selectivity have been reported.<sup>3</sup> For example, at 0 °C CH<sub>3</sub><sup>•</sup> is more reactive and less selective than the t-undecyl radical in the competition system BrCCl<sub>3</sub>-CCl<sub>4</sub>, but at 130 °C CH<sub>3</sub><sup>•</sup> is more selective and more reactive than the t-undecyl radical;<sup>45</sup> the selectivity differences increase with increasing temperature above the isoselective temperature. These temperature effects can be attributed to the temperature dependence of  $\Delta G^\circ$  due to different  $\Delta H^\circ$  and  $\Delta S^\circ$  (Figure 7). These effects can be enhanced and changes on the isoselective temperature can occur when the square dependence of  $d/l$  on  $\Delta G^\circ$  is not negligible.

**Conclusions.**—In the literature there are several approaches to interpret the validity of the reactivity-selectivity relations. Possibly the most general, albeit qualitative, is the Configuration Mixing model (CM),<sup>23</sup> which considers that frequently the transition states need to be described in terms of the configuration of reactants and products and of another intermediate excited configuration, which can be dominant. This is equivalent to our concept of the non-conservation of the total bond order, because for these cases the transition states have features of electronically excited states. Nevertheless CM does not quantify  $n^\ddagger$  and does not take into account other molecular factors such as  $f$ ,  $l$ , and  $\lambda$ .

The same can be said for approaches which quantify structural effects perpendicular to the reaction co-ordinate, based essentially on Marcus-type equations.<sup>15,46,47</sup> Furthermore, these 'two-dimensional potential energy surfaces' have been criticized by Agmon,<sup>48</sup> because they bear no resemblance to potential energy surfaces familiar in molecular dynamics. Agmon has proposed an alternative model based on one-dimensional reaction energy curves, where effects of structures perpendicular to the reaction co-ordinate can be described by an upside-down free energy profile.<sup>48</sup> These procedures are essentially a way to circumvent the difficulties of the theory of Marcus in describing the progress of some reactions in terms of a single progress variable. Although keeping just 'one progress variable', as for any ordinary chemical reaction, ISM is more flexible than the theory of Marcus, and we have shown<sup>29</sup> that the present model includes models which consider structural effects perpendicular to the reaction co-ordinate.

Reactivity-selectivity relationships are a complex problem in chemical kinetics, because they depend on a great variety of electronic, thermodynamic, and geometric factors and not all of them work in the same direction. We have discussed in general terms the possible sources of the breakdown of such relationships, but it is obvious that more detailed mechanistic studies require the application of models, such as ISM, where the role of all the important factors is properly taken into consideration in a quantitative but extremely simple form.

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