

REACTIVITY AND SELECTIVITY CONTROL BY REACTANTS AND PRODUCTS.

A GENERAL RELATIONSHIP BETWEEN THE SELECTIVITY AND THE POSITION OF THE TRANSITION STATE.

Alain ARGILE and Marie-Françoise RUASSE

Institut de Topologie et de Dynamique des Systèmes, Université Paris VII,  
associé au C.N.R.S., 1, rue Guy de la Brosse, 75005 PARIS.

*Abstract - Although the reactivity-selectivity principle and the frontier molecular orbital theory lead to opposed reactivity-selectivity relationships, they lead to an identical transition state position-selectivity relationship. The transition state position is generally reactant- and product-dependent. The RSP which neglects reactant effects and the FMO which neglects product effects can be considered as the two limits of the general rule.*

The reactivity-selectivity principle, RSP, which implies a linear relationship between the decrease in selectivity and the increase in reactivity, has been a useful empirical tool for the prediction and interpretation of reactivity for many years.<sup>1</sup> Initially based on the chemist's intuition, the RSP has since received fundamental backing from the Hammond-Leffler postulate.<sup>2</sup> However, over the last few years, it has been widely criticized because many exceptions have been reported.<sup>3</sup> Recently, several authors sought to define its limitations and range of applicability by reexamining the basic assumptions involved.<sup>4</sup> There are two types of explanation for the failure of the principle; incorrect applications (such as unwarranted comparisons between reactions involving quite different effects, complex mechanisms involving a compensation of effects acting in opposite directions,...) and fundamental contradictions (as in the case of the orbital-controlled reactions where the RSP is inapplicable). This note is an attempt to determine the nature of and the reasons for the contradiction between the two most currently used approaches to reactivity, the RSP and the frontier molecular orbital, FMO, theory,<sup>5</sup> since this very contradiction directly questions the reality of the RSP itself. Such an analysis makes it possible to define the limits of each approach and the pitfalls to be avoided in any interpretation of reactivity.

Leffler's explanation of the RSP is based on the rate-equilibrium relationship (1) which assumes a continuous variation of the reactivity with the free energy variations  $\delta\Delta G_0$  of the reaction.<sup>2</sup>

$$\delta\Delta G^\ddagger = \alpha\delta\Delta G_0 \quad (1)$$

From expression (1), three relationships can be deduced. Firstly, as can be seen<sup>6</sup> in Fig. 1a, the stabler the products, the higher the reactivities. Therefore, the selectivity  $\delta\Delta G^\ddagger$  is inversely proportional to the reactivity. Secondly, since  $\alpha$  reflects the position of the

transition state, the greater the reactivity, the earlier the transition state, as stated in the Hammond postulate.<sup>2,7</sup> Finally, it follows that the later the transition state, the higher the selectivity.

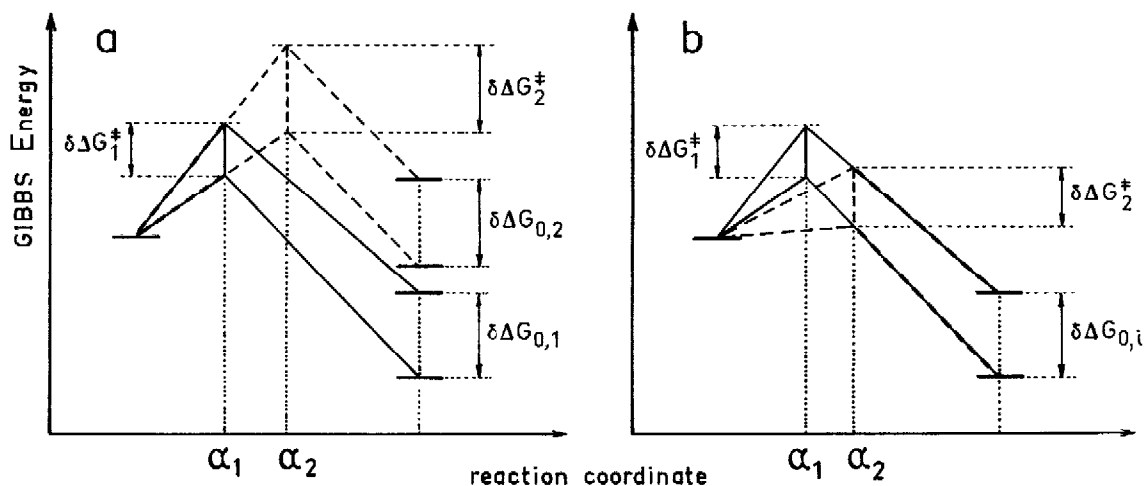


Fig. 1 : THE EFFECT OF A CHANGE IN REACTIVITY ON SELECTIVITY. a) Change in the products: The HAMMOND-LEFFLER approach. The selectivity  $\delta\Delta G^\ddagger$  increases as  $\Delta G^\ddagger$  increases; b) Change in the reactants: the FMO approach. The selectivity  $\delta\Delta G^\ddagger$  increases as  $\Delta G^\ddagger$  decreases.

In contrast to the RSP which has an empirical basis,<sup>8</sup> the FMO theory approach to reactivity is based on the physical nature of the chemical bond. In this theory, a reaction is described in terms of the interactions between the frontier orbitals of the reactants.<sup>5</sup> The reactivity is then inversely proportional to the energy difference between the orbitals involved in the reaction.<sup>5,9</sup>

$$\log k = \frac{A}{\Delta E_{\text{FMO}}} + B \quad (2)$$

In this approach, the three relationships between the reactivity, the selectivity and the transition state position are the following. Firstly, the selectivity increases with increasing reactivity: as seen from eq. (2), the smaller the energy difference between two reactants, the greater the influence of a perturbation in one of them.<sup>10</sup> This relationship is represented in Fig. 1b where the energy curves of the reactants are assumed to be straight lines, the slopes of which correspond to the stabilization energies  $\Delta E_{\text{FMO}}$ .<sup>5</sup> Secondly, the transition state occurs later as reactivity increases: this is demonstrated by the fact that the amount of charge transfer between the combining orbitals is inversely related to the difference between them.<sup>10,11</sup> Finally, the relationship between the selectivity and the transition state position ensues from the association of the first two: the later the transition state, the higher the selectivity.

Thus, although neither the RSP nor the Hammond-Leffler postulate are verified by the FMO theory, either one leads to the same relationship between the selectivity and the transition state. Since this relationship emerges from two quite different approaches, it appears that

any more general approach should take into account the transition state position. Therefore, the factors on which this position is dependent must be determined.

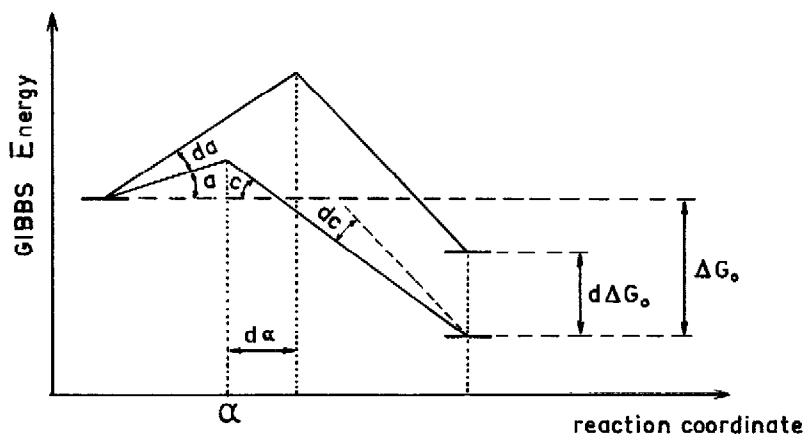


Fig. 2 :  $\alpha$ , the transition state position as a function of the reagents defined by  $a$ , the slope of the reaction pathway starting from reactants, and of the products defined by  $\Delta G_0$  and  $c$  the slope of the pathway leading to products.

The geometrical analysis of a simplified energy profile diagram<sup>12,13</sup> (Fig. 2) gives the value of the transition state position as a function of the reactants and the products.

$$\alpha = \frac{\Delta G_0 + c}{a + c} \quad (3)$$

Differentiation of eq. (3) as a function of each variable leads to eq. 4

$$d\alpha = \frac{1}{a + c} \left| \underset{A}{d\Delta G_0} + (1 - \alpha)\underset{B}{dc} - \alpha da \right| \quad (4)$$

in which A reflects the influence of the products and B that of the reactants on the transition state. The sign of the variation thus depends on the relative magnitude of A and B. Taking eq. (4) and setting  $da = dc = 0$  gives the Hammond-Leffler approach where  $d\alpha$  depends only on  $d\Delta G_0$ , whereas setting  $dc = d\Delta G_0 = 0$  gives the FMO approach. When both A and B contribute, they can cancel each other, in which case the transition state position varies only slightly although reactant and product energies vary widely; they can also oppose each other, in which case the transition state can move towards either the reactants or the products.

Our inspection of the FMO theory and of the RSP shows the existence of a generally valid relationship between selectivity and the transition state position. However, it is useful to know how the transition state position varies with reactivity which, experimentally, is the most available value. Mok and Nye<sup>13</sup> have obtained such a relationship by using an energy diagram

analogous to that of Fig. 2 :

$$\Delta G^\ddagger = \phi \Delta E_{\text{FMO}} + (1 - \phi) \Delta G_o \quad (5)$$

in which  $\phi = c/(a + c)$ .

As shown by eq. (5), it is possible to obtain a simple relationship as a function of either energy variation when one of the terms is negligible. Therefore, the classical RSP or FMO relationships can be considered as the two limits of the general rule. The FMO theory applies to reactant-dependent reactions with an early transition state, whereas the RSP applies to product stability-dependent reactions with a late transition state. When the transition state is about halfway along the reaction pathway, eqs. (4) and (5) must be integrally considered; in this case it is difficult to predict how the reactivity varies with the reactants or products.<sup>14</sup> Thus, in order to avoid misleading conclusions, it appears essential that any interpretation of the reactivity in terms of either theory must be based at least on an estimation of the transition state position.<sup>15,16</sup>

#### NOTES AND REFERENCES

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