Hybridization as a Metric for the Reaction Coordinate of Chemical Reactions

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Abstract: The reaction coordinate is usually chosen to be a simple function of the bonds that are broken or formed in a chemical reaction. Although such an approach is adequate for the analysis of isolated reaction processes, it does not provide a general metric that allows ready comparison between different chemical reactions. In this paper, we introduce hybridization as a unifying metric for the degree of structural progress in organic reaction processes and illustrate the usefulness of such an analysis by reference to the Hammond postulate and electrocyclic reactions.

Chemical reactions are normally considered to be processes that form and break bonds, and it is traditional to measure the progress of a reaction by reference to some function of the interatomic distances that undergoes a significant change during the chemical transformation.[1,2] While this approach is convenient, it does not provide a general metric of reaction progress. This is because such a scheme introduces one arbitrary and one ill-defined boundary condition.

Consider a dissociation process in which a bond is broken during a reaction (Figure 1a). The initial coordinate for the representation of the reaction progress will usually be chosen as some function of the equilibrium length of the bond to be broken (R_R). In general, the bonds in molecules are of variable length, and this bond length will not be transferable to other reactions. At the final point in the process, the products will be at infinity with respect to one another (R_P), and such a boundary condition cannot provide a scale of measure.
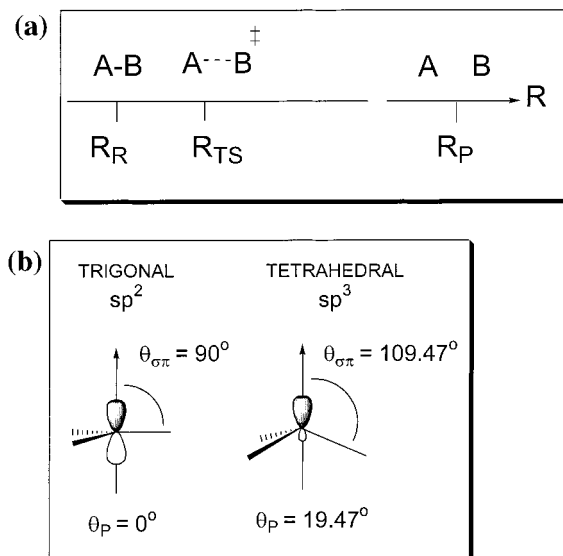
Although it might be thought that this is of little consequence, we shall argue that there is a great deal of value in adopting a unified and general metric for the reaction coordinate of chemical processes because this allows comparisons between a variety of disparate reactions and has important ramifications for the Hammond postulate.[3] We adopt a modern statement[4] of the Hammond postulate: "The structure of a transition state resembles the structure of the nearest stable species. Transition states for endothermic steps structurally resemble products, and transition states for exothermic steps structurally resemble reactants." Although the Hammond postulate depends on the structural evolution of reactants to products along a reaction coordinate, the nature of the essential structural characteristic-(s) has remained undefined. The Hammond postulate is central to the practice of organic chemistry because it provides a connection between the kinetics and thermodynamics of reaction processes. The success of a given reaction usually depends on kinetics, but most of the reasoning in organic chemistry is based
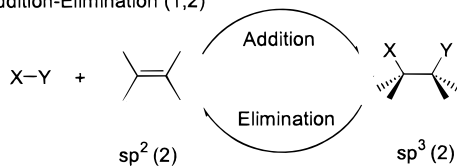

Figure 1. (a) Conventional reaction coordinate for a dissociation reaction, where R is a function of the bond(s) broken in the reaction. R_R is the function value for the reactant A−B. R_P is the function value for the products (A and B at infinity). R_{TS} is the function value for the transition state (A···B). Such a reaction coordinate system cannot provide a general and unified metric of reaction progress (see text). (b) Proposed reaction coordinate boundary conditions for reactions involving conversions between sp^2 and sp^3 hybridization.

on thermodynamics; it is therefore of the utmost importance to broadly and precisely define the underlying structural basis of the postulate.

Most textbooks[4] conclude that there are six classes of chemical reactions in organic chemistry: (1) additions, (2) eliminations, (3) substitutions, (4) rearrangements, (5) reduction−oxidations, and (6) combinations of classes 1−5. Of the five distinct classes of reaction, only class 5 does not necessarily involve a change in hybridization. Not all of these hybridization changes are of the same type, but we have found that a surprisingly small number of distinct rehybridizations are involved in all of organic chemistry (at least within the simple theoretical treatment introduced below). In fact, most organic reactions (classes 1−4) simply involve a transition between sp^2

(1) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; VCH: Weinheim, 1970; Chapter 3.

(2) Salem, L. *Electrons in Chemical Reactions*; Wiley: New York, 1982; Chapter 2.

(3) Hammond, G. S. *J. Am. Chem. Soc.* **1955,** *77,* 334−338.

(4) McMurry, J. *Organic Chemistry*; Brooks Cole: Pacific Grove, CA, 1996; Chapter 6.

and sp^3 hybridizations in the reacting atoms of some combination of the reactants, products, reaction intermediates, and transition states of the reaction (the extension to other cases, such as the transition between sp and sp^2 hybrids, is straightforward). This is exemplified in the reaction types illustrated below.
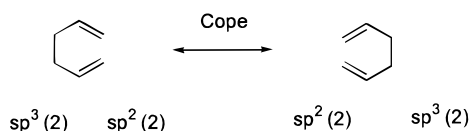
Addition-Elimination (1,2)

sp^2 (2)   sp^3 (2)

Substitution (3)

sp^3 sp^2 sp^3

Rearrangement (4)

Cope
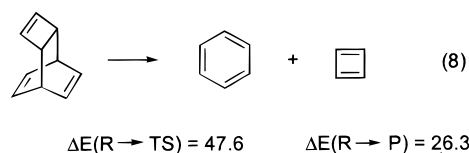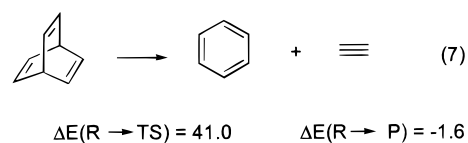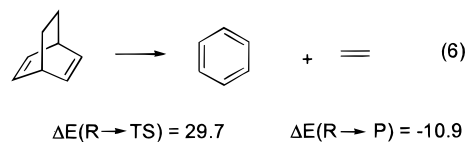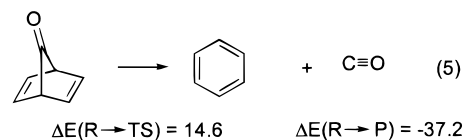
sp^3 (2)   sp^2 (2)   sp^2 (2)   sp^3 (2)
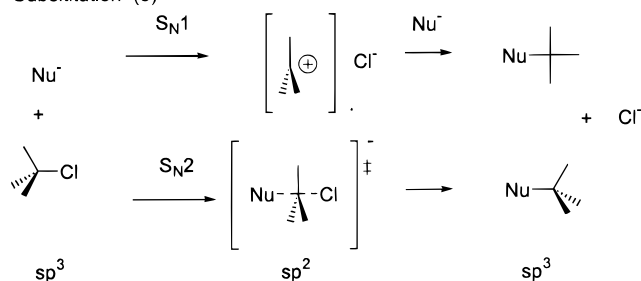
We therefore suggest hybridization as the unifying reaction coordinate metric (Figure 1b). In most cases, it is possible to associate an *ideal* initial and final hybridization with the atoms that are involved in the bond forming and breaking in chemical reaction processes, and together these provide well-defined boundary conditions for the reaction metric. The most common reaction processes involve conversions among sp^2 and sp^3 hybrids in the reacting atoms (vide infra). The use of the π-orbital axis vector (POAV) analysis makes it possible to solve analytically for the intermediate hybridizations,[5,6] and thus, a general metric may be obtained for almost any organic reaction process. The hybridization metric that is introduced here is structurally based and is valid for the reactants, products, transition states, and intermediates of many organic reaction processes. The adoption of this reaction metric makes possible for the first time the application of the Hammond postulate in a quantitative manner across a variety of reactions.

We illustrate the method with a series of simple reverse Diels−Alder cycloaddition reactions of varying exothermicity. We calculated the structures and energies of (5)−(8) along the dissociation pathways using the B3LYP/6-31G* method; see Table 1.[7−10] This level of theory has been shown to provide

(5) Haddon, R. C.; Scott, L. T. *Pure Appl. Chem.* **1986**, *58*, 137−142.

(6) Haddon, R. C. *J. Am. Chem. Soc.* **1986**, *108*, 2837−2842.

(7) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Peterson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, L. A.; Zakrezewski, V. G.; Orvitz, J. V.; Foresman, J. B.; Cioslowsi, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian-94*, Revision D.1; Gaussian, Inc.: Pittsburgh, PA, 1995.

(8) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(9) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.

(10) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372−1377.

Table 1. Pyramidalization Angles (θ_P, deg) and Hybridizations of the Stationary Points

reaction	reactant	transition state	product
(5)	$\theta_P = 13.23$, sp$^{2.373}$	$\theta_P = 9.71$, sp$^{2.187}$	$\theta_P = 0$, sp^2
(6)	$\theta_P = 17.30$, sp$^{2.722}$	$\theta_P = 9.38$, sp$^{2.173}$	$\theta_P = 0$, sp^2
(7)	$\theta_P = 18.31$, sp$^{2.841}$	$\theta_P = 9.16$, sp$^{2.165}$	$\theta_P = 0$, sp^2
(8)	$\theta_P = 17.50$, sp$^{2.745}$	$\theta_P = 6.90$, sp$^{2.091}$	$\theta_P = 0$, sp^2

$\Delta E(R \rightarrow TS) = 14.6$ $\Delta E(R \rightarrow P) = -37.2$ (5)

$\Delta E(R \rightarrow TS) = 29.7$ $\Delta E(R \rightarrow P) = -10.9$ (6)

$\Delta E(R \rightarrow TS) = 41.0$ $\Delta E(R \rightarrow P) = -1.6$ (7)

$\Delta E(R \rightarrow TS) = 47.6$ $\Delta E(R \rightarrow P) = 26.3$ (8)

fairly satisfactory descriptions of organic structures and reactions.[11,12] The transition states were located in all cases, and the force constant matrix was shown to possess a single negative eigenvalue. The energies of the products and transition states (kcal/mol) relative to the reactants are given in the equations (the results are in good agreement with prior high level calculations).[13−15]

In Figure 2, we show the reaction profiles of these reactions as a function of the pyramidalization angle (θ_P) (bottom axis) and POAV1 hybridization (top axis).[5,6] In POAV1 theory, the π-orbital axis vector is defined as that vector which makes equal angles ($\theta_{\sigma\pi}$) to the three σ-bonds at a conjugated carbon atom, and the pyramidalization angle is obtained as $\theta_P = (\theta_{\sigma\pi} - 90)°$ (Figure 1b). The σ-bond hybridization (sp^n) is given by $n = 2/(1 - 3\sin^2\theta_P)$. Although we originally intended to plot these curves as a direct function of hybridization, the results dissuaded us from this mode of analysis. As may be seen from Table 1 and Figure 2, the transition states of most of the reactions occur in the vicinity of sp$^{2.2}$ hybridization. Thus, a linear plot of hybridization is quite asymmetric for these reactions. Reaction 7 is almost thermoneutral [$\Delta E(R \rightarrow P) = -1.6$ kcal/mol], and based on the current understanding of the Hammond postulate, it would be expected to have a transition state midway between reactants and products. We found that the transition state for this reaction was characterized by a pyramidalization angle of $\theta_P = 9.16°$. As shown in Figures 1 and 2, the ideal pyrami-

(11) Johnson, B. G.; Gill, P. M. W.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 5612−5626.

(12) Wiest, O.; Black, K. A.; Houk, K. N. *J. Am. Chem. Soc.* **1994**, *116*, 10336−10337.

(13) Clifford, S.; Bearpack, M. J.; Bernardi, F.; Olivucci, M.; Robb, M. A.; Smith, B. R. *J. Am. Chem. Soc.* **1996**, *118*, 7353−7360.

(14) Bachrach, S. M.; Magdalinos, P. *THEOCHEM* **1996**, *368*, 1−6.

(15) Birney, D. M.; Ham, S.; Unruh, G. R. *J. Am. Chem. Soc.* **1997**, *119*, 4509−4517.
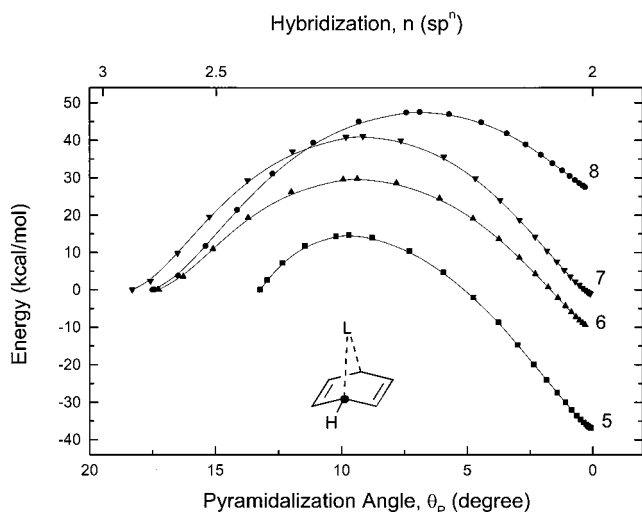
Figure 2. Energy of reaction as a function of pyramidalization angle and hybridization (defined by the C−H and two C−C bonds shown in the structure, where L is the leaving group), of the bridgehead carbon atoms (denoted by •). The numbers on the curves refer to the processes shown in the reaction scheme.
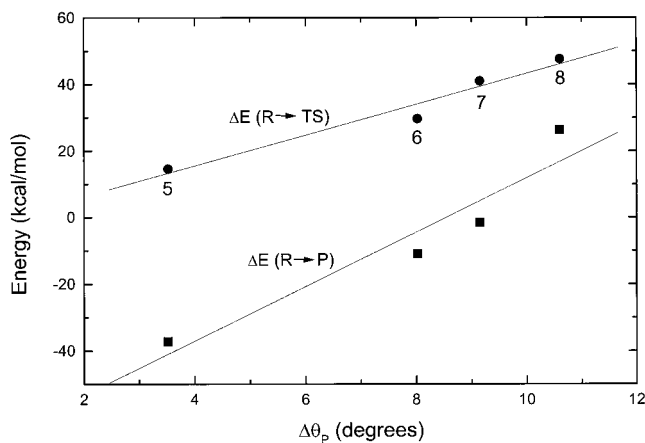

Figure 3. Reaction (■) and activation energies (●) as a function of change in pyramidalizaton angle.

dalizations are sp^2, $\theta_P = 0°$, and sp^3, $\theta_P = 19.47°$, with a midpoint value of $sp^{2.19}$, $\theta_P = 9.74°$. Thus, the pyramidalization angle conforms rather well to the conventional notion of the Hammond postulate, and we chose this parameter to provide the scale between sp^2 and sp^3 hybridization. It is important to note that although the scale is not linear in hybridization, the boundary conditions for the metric remain intact, and the interpretation of the reaction process is now reduced to a single geometric variable.

Figure 2 reproduces the central tenets of the Hammond postulate with regard to structure along the reaction pathway. Endothermic reactions have transition-state structures that are more productlike, whereas exothermic reactions have transition-state structures that are more reactantlike.

Although our analysis supports the basic features of the Hammond postulate, there are some caveats. The POAV analysis provides an absolute scale of reaction structures, and Figure 2 shows that for the exothermic reactions (5)−(7) the transition states occur at much the same value of the reaction coordinate [θ_P (TS) = 9.71° (5), 9.38° (6), 9.16° (7), 6.9° (8)]. Thus in terms of the hybridization approach to the Hammond postulate, it is not that the structure of the transition state resembles the reactants but that the structure of the reactant resembles the structure of the transition state in the case of exothermic reactions. Thus in the case of (5), in which the bond angles of the reactant are not ideal (angle strain), it is appropriate to view the reaction as being more advanced at the reactant stage rather than the conventional view of an early transition state. The endothermic process (8) is in full accord with the conventional picture of the Hammond postulate, with a late transition state.

Figure 3 reproduces the central tenets of the Hammond postulate with regard to the relationship between the kinetics and thermodynamics of reactions. In this plot, we show the enthalpies and activation energies for the reactions as a function of the separation of reactant structure from transition-state structure, based on the hybridization metric. Both the thermodynamics (enthalpy of reaction) and kinetics (activation energy) of the reactions correlate quite well with the reaction metric.

We believe that the current study provides the first general, quantitative application and verification of the Hammond

postulate.[16] The POAV hybridization analysis will provide a widely applicable and unified view of organic reactions and will expand the usefulness of the concepts of hybridization and the Hammond postulate. We have recently shown that the hybridization metric can provide information on bond making and breaking and the degree of concertedness in chemical reactions.[17]

Finally we consider the relationship of the hybridization metric of chemical reactions to the traditional approaches that rely on some function of the bonds that are broken or formed during the reaction. The most general approaches to this problem are the minimum energy path (MEP) and its companion, the intrinsic reaction coordinate (IRC) method.[18−21] In both of these approaches, all of the molecular degrees of freedom are treated along the minimum energy reaction pathway between reactant and product. The MEP was used to obtain the data in the present paper.[7]

As noted earlier, the usual procedure for following a chemical reaction is to identify a bond that is broken or formed in the reaction and to use some function of this bond to force changes in the location of the structure on the potential surface. In this way, a particular variable is used to *control* the reaction progress. The present approach is complementary to this part of the procedure and should be considered as an *indicator* of the progress of a chemical reaction. An indicator is useful if it is transferable and provides a general measure of a property. Such an indicator can then be used to compare this property in different systems. In this study, the hybridization metric or indicator provides a comparison of reaction progress in related chemical systems, and this allows a quantitative test of the Hammond postulate.

(16) For other approaches to quantifying the Hammond postulate, see: Cioslowski, J. *J. Am. Chem. Soc.* **1991**, *113*, 6756−6760. Maity, D. K.; Majumdar, D. K.; Bhattachryya, S. P. *THEOCHEM* **1995**, *332*, 1−20.
(17) Haddon, R. C.; Chow, S.-Y. *Pure Appl. Chem.*, in press.
(18) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363−368.
(19) Truhlar, D. G.; Garrett, B. C. *Acc. Chem. Res.* **1980**, *13*, 440−448.
(20) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154−2161.
(21) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523−5530.