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Degree of Rate Control: How Much the Energies of Intermediates and Transition States Control Rates

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Abstract: For many decades, the concept of a "rate-determining step" has been of central importance in understanding chemical kinetics in multistep reaction mechanisms and using that understanding to advantage. Yet a rigorous method for identifying the rate-determining step in a reaction mechanism was only recently introduced, via the "degree of rate control" of elementary steps. By extending that idea, we argue that even more useful than identifying the rate-determining step is identifying the rate-controlling transition states and the rate-controlling intermediates. These identify a few distinct chemical species whose relative energies we could adjust to achieve a faster or slower net reaction rate. Their relative energies could be adjusted by a variety of practical approaches, such as adding or modifying a catalyst, modifying the solvent, or simply modifying a reactant's molecular structure to affect electronic or steric control on the relative energies of the key species. Since these key species are the ones whose relative energies most strongly influence the net reaction rate, they also identify the species whose energetics must be most accurately measured or calculated to achieve an accurate kinetic model for any reaction mechanism. Thus, it is very important to identify these rate-controlling transition states and rate-controlling intermediates for both applied and basic research. Here, we present a method for doing that.

Introduction

In chemical kinetics involving any multistep reaction mechanism, the net reaction rate (i.e., the rate of formation of any chosen product or consumption of any chosen reactant) is generally a complex function of the rate constants for all of its elementary steps and the thermodynamics of all of its reaction intermediates.[1] However, under specific conditions, even the most complex mechanism can have a single rate-determining step (RDS), in which case the kinetic description can be greatly simplified. Whenever there is a single RDS, one is usually even able to derive a simple rate law for the net reaction rate involving only a few kinetic and thermodynamic parameters. Knowing the RDS has proven very powerful, since it provides not only kinetic rate laws but also great ideas about how to modify the reaction to achieve higher or lower rates as desired. For example, reaction rates have been modified to advantage by changing the conditions or the solvent, by adding a catalyst, or by modifying a reactant's molecular structure to control the relative energies or other properties of the transition state and reactant of that RDS. It is not obvious what one can do to improve the rates of a multistep reaction when there is not a single RDS, which is usually the case. We present here a method for identifying which transition states and intermediates really control the net rates of complex, multistep reaction mechanisms. Specifically, we define a "general degree of rate control" which quantifies the extent to which a differential change in the standard-state free energy of any given transition state or intermediate influences the net reaction rate. We argue that this degree of rate control is even more powerful than the rate-determining step concept, since one can more easily envision how to modify the energies of intermediates and transition states than to modify a step's rate constant. That is, it more directly connects the net rate with entities that one can hope to control to advantage. Also, since a single rate-determining step only exists under very limited conditions and it is much more likely that several steps control the net rate, this degree of rate control is much more widely applicable than is the RDS concept.

This new general degree of rate control to be presented here can only be calculated for reactions for which a microkinetic model has already been developed (i.e., for cases where estimates already exist for the forward and reverse rate constants for all the elementary steps in the mechanism); although as a concept that helps one to think about kinetics, it is much more broadly useful. Microkinetic models for complex reaction mechanisms have become common in the last few decades and are becoming more and more common all the time. The development of accurate and efficient computational codes for calculating the energies of intermediates and transition states have been particularly important in realizing this. Even in catalysis, it is now common to compute net reaction rates of complex mechanisms using microkinetic models where all or

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most of the rate constants have been calculated with density functional theory.[2−11] Equally important has been the development of more and more accurate and precise methods for measuring the energies of reaction intermediates and the rate constants for individual elementary steps. Importantly, the degree of rate control also should be a powerful aid to the development of more accurate microkinetic models, since it identifies which intermediates and transition states are most important to the net rate and thus which species' standard-state free energies or rate parameters must be measured or calculated most accurately. Since the net rate of even complex mechanisms typically depends on only a handful of such parameters,[1,12−14] its use to identify the critical parameters can greatly reduce the effort involved.

Degree of Rate Control for Elementary Step *i*, $X_{\mathrm{RC},i}$

In the past, much effort has been focused on identifying which elementary steps in complex mechanisms are important to the overall reaction rate, i.e., in identifying the rate-determining step or rate-limiting steps. To our knowledge, however, no method had been developed which unambiguously defines the rate-determining step until Campbell introduced the degree of rate control $X_{\mathrm{RC},i}$ for elementary step i,[15,16] which he defined as

$$X_{\mathrm{RC},i} = \frac{k_i}{r}\left(\frac{\partial r}{\partial k_i}\right)_{k_{j\neq i},K_i} = \left(\frac{\partial \ln r}{\partial \ln k_i}\right)_{k_{j\neq i},K_i} \tag{1}$$

where the partial derivative is taken holding constant the rate constants, k_j, for all other steps $j \neq i$ and the equilibrium constant, K_i, for step i (and all other steps too, since their forward and reverse rate constants are held fixed). Note that keeping K_i constant means that k_i and k_{-i} both must be varied by equal factors so that their ratio remains constant. (Within transition-state theory, this is accomplished by changing only the free energy for the transition state of step i but no other standard-state free energies of transition states, reactants, products, or intermediates, since the rate constant k_i equals $(k_BT/h)\exp(-\Delta G^{0,\mathrm{TS}}_i/RT)$, where $\Delta G^{0,\mathrm{TS}}_i$ is the difference in standard-state molar free energy between the transition state and the reactants, k_B is Boltzmann's constant, and h is Planck's constant. The equilibrium constant K_i equals $\exp(-\Delta G^{0,\mathrm{rxn}}_i/\mathrm{RT})$, where $\Delta G^{0,\mathrm{rxn}}_i$ is the difference in standard-state molar free energy between the products and the reactants. Since each of these free-energy changes breaks up into a sum of an enthalpy contribution (ΔH) and an entropy contribution ($-T\Delta S$) as $\Delta G = \Delta H - T\Delta S$, these rate constants and equilibrium constants break up into a product of terms that arises from enthalpy differences and entropy differences: $\exp(-\Delta \mathrm{G}/RT) = \exp(-\Delta H/RT)\exp(-\Delta S/R)$.

The larger the numeric value of $X_{\mathrm{RC},i}$ is for a given step, the bigger is the influence of its rate constant on the overall reaction rate r. A positive value indicates that increasing k_i will increase the net rate r, and such steps are termed rate-limiting steps (RLS). A negative value indicates the opposite, and such steps are termed inhibition steps. Campbell showed that for previously analyzed mechanisms at reaction conditions where it was widely recognized that there is a single rate-determining step (e.g., in numerous textbook examples) and the degree of rate control is equal to 1 for that step and 0 for all other steps. A value of $X_{\mathrm{RC},i}$ being unity can be taken as a strict definition of step i being the single rate-determining step.[15,16]

The degree of rate control seems to be conserved through the sum rule over all steps i in the mechanism[16]

$$\sum_i X_{\mathrm{RC},i} = 1 \tag{2}$$

Dumesic has proven this rule for any reaction scheme that leads to a single overall reaction.[17]

Campbell's degree of rate control $X_{\mathrm{RC},i}$ can only be quantitatively evaluated for microkinetic models (i.e., models with estimates of the rate constants for all the elementary steps). Indeed, it has found wide application in analyzing such models[4,5,9,10,18−37] and even in analyzing kinetic Monte Carlo models of catalytic mechanisms.[11]

Fundamentally, eq 1 implies changing the transition state of elementary step i while nothing else is changed in the reaction mechanism and determining how this influences the overall rate, r, of producing some specific product or consuming some specific reactant. More specifically, the standard state free energy of transition state i is changed while the energies and free

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energies of all other transition states, intermediates, and gas-phase species are kept constant. Hence, eq 1 probes the importance of one transition state's free energy in the full potential free-energy surface for the reaction.

Introducing the Degree of Thermodynamic Rate Control for an Intermediate *n*, $X_{\mathrm{TRC},n}$

By analogy, one would also like to know the importance of an intermediate's stability (thermodynamics) on the overall reaction rate of a complex mechanism. To do this, we would like to determine the relative change in the net rate r (to one product or from one reactant), when we stabilize that intermediate (decrease its standard-state molar free energy) by a tiny amount $\mathrm{d}G^0_{\mathrm{intermediate}}$ without changing anything else on the standard-state free-energy surface for the net reaction. We thus define the degree of thermodynamic rate control $X_{\mathrm{TRC},n}$ of intermediate n by

$$X_{\mathrm{TRC},n} = \frac{1}{r}\left(\frac{\partial r}{\partial\left(\dfrac{-G^0_n}{RT}\right)}\right)_{G^0_{m\neq n},G^{0,\mathrm{TS}}_i} = \left(\frac{\partial \ln r}{\partial\left(\dfrac{-G^0_n}{RT}\right)}\right)_{G^0_{m\neq n},G^{0,\mathrm{TS}}_i} \tag{3}$$

where the partial derivative is taken holding the standard-state Gibbs free-energy constant of all other intermediates $m \neq n$ ($G^0_{m\neq n}$) and Gibbs free energy of all transition states i constant ($G^{0,\mathrm{TS}}_i$). Here R is the universal gas constant and T is the absolute temperature. $X_{\mathrm{TRC},n}$ is dimensionless. Note that "standard state" here refers to the usual definition of standard state in thermodynamics, so that for each species, a specific reference condition must be defined, which includes in its choice a specific concentration value (or entropy). For example, for ideal gases in mixtures, that typically would be the pure gas at 1 bar pressure. A common choice for the standard state of a solute in a liquid solution is often unit mole fraction if the solution behaves close to an ideal solution, but for solutions that follow more closely the behavior of ideally dilute solutions, it may be a hypothetical state where the solute's concentration is either unit mole fraction or one molar concentration, but where its energy is the same as if it were ideally dilute (surrounded by solvent only). For adsorbates treated within a lattice gas model, common choices are 100% or 50% coverage of the lattice sites.

As shown in Figure 1, Campbell's degree of rate control answers the question: Suppose we could introduce a catalyst or catalyst modifier that incrementally lowered the free energy of the transition state for one elementary step, without changing anything else. By what fraction would this change the net rate, per unit change in that step's rate (where 1 unit = that steps's initial rate constant)? Similarly, this new degree of thermodynamic rate control answers the closely related question: Suppose we could introduce a catalyst or catalyst modifier that incrementally lowered the free energy of one intermediate, without changing anything else. By what fraction would this change the net rate, per unit change in free energy (in units of RT).

This is a very important question, since it gives direct information about which intermediate would be the most important to stabilize/destabilize. In all of the situations we will discuss below, the intermediates in question are adsorbed species on a catalyst's surface, in which case this might be accomplished by changing the catalyst material or by addition of surface modifiers. One can, however, imagine many other classes of reactions where this concept might be powerful. For example, the intermediate might be a solute in solution, in which case its stability might be controllable through changes in the solvent.

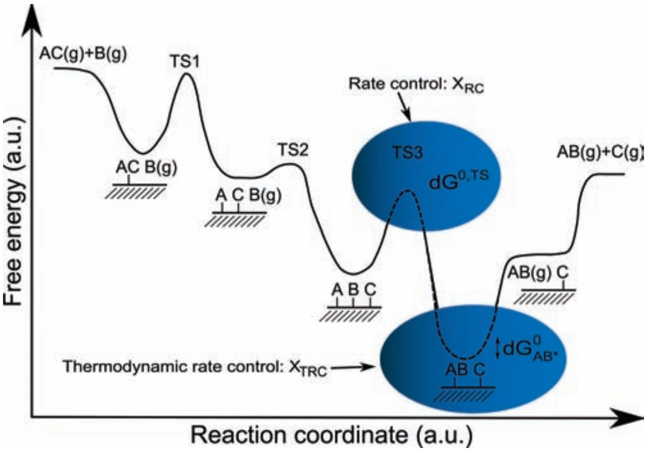

Figure 1. Schematic standard-state free-energy surface for the reaction AC(g) + B(g) → AB(g) + C(g), showing an incremental change in the standard-state free energy of one transition state TS3, as implied by the definition of Campbell's degree of rate control ($X_{\mathrm{RC},\mathrm{TS3}}$), and of one adsorbed intermediate AB*, as implied by the definition of the degree of thermodynamic rate control ($X_{\mathrm{TRC},\mathrm{AB}*}$).

Simple Example Calculation

To demonstrate the above concepts, we will analyze a simple Langmuir–Hinshelwood mechanism for solid-catalyzed reactions, with one RDS and all other steps quasi-equilibrated

$$(1)\ \ \mathrm{A} + * \rightleftharpoons \mathrm{A}* \qquad \text{(EQ)}$$

$$(2)\ \ \mathrm{B} + * \rightleftharpoons \mathrm{B}* \qquad \text{(EQ)}$$

$$(3)\ \ \mathrm{A}*+\mathrm{B}* \rightleftharpoons \mathrm{AB}*+* \qquad \text{(RDS)}$$

$$(4)\ \ \mathrm{AB}* \rightleftharpoons \mathrm{AB} + * \qquad \text{(EQ)}$$

where the asterisk (*) denotes a free site, X* a surface intermediate, X a gas-phase species, and $\rightleftharpoons$ forward and backward reaction arrows. The below rate law can be deduced from this mechanism by applying the quasi-equilibrium approximation

$$r = \frac{k_3\left(K_1K_2\dfrac{p_{\mathrm{A}}}{p^o}\dfrac{p_{\mathrm{B}}}{p^o} - \dfrac{1}{K_3K_4}\dfrac{p_{\mathrm{AB}}}{p^o}\right)}{\left(1 + K_1\dfrac{p_{\mathrm{A}}}{p^o} + K_2\dfrac{p_{\mathrm{B}}}{p^o} + \dfrac{1}{K_4}\dfrac{p_{\mathrm{AB}}}{p^o}\right)^2} \tag{4}$$

where k_3 is the rate constant of step 3, K_i is the equilibrium constant of step i, p_i is the partial pressure of species i, and p^o is the reference pressure. To simplify matters further, let us assume that step 3 is irreversible and the surface is almost saturated with A*, which means that the second term in the numerator is eliminated and all terms except the second term is eliminated in the denominator, resulting in the far simpler rate law

$$r = k_3\frac{K_2p_{\mathrm{B}}}{K_1p_{\mathrm{A}}} \tag{5}$$

Now the degree of thermodynamic rate control of each intermediate will be calculated by perturbing the Gibbs free energy of that intermediate. To further simplify, we do this here by perturbing the enthalpy part of the Gibbs free energy, while keeping all entropies constant. Thus, the enthalpy of A* is

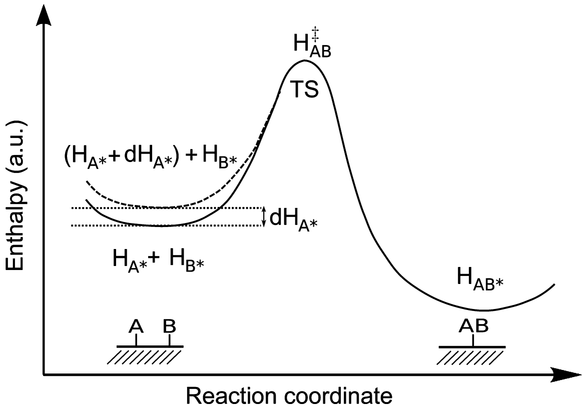

Figure 2. Schematic potential-energy surface, showing an incremental change in the standard-state free energy of one adsorbed intermediate (A*) via a simple change in its enthalpy; used to estimate the degree of thermodynamic rate control of A*.

perturbed by the amount dH while keeping all other enthalpies constant. Figure 2 illustrates this situation.

Before the enthalpy perturbation of A* we have the following enthalpies

$$H_{A*}, H_{B*}, H_{AB*}, H^{\ddagger}_{AB} \text{ and } E_A = H^{\ddagger}_{AB} - H_{A*} - H_{B*}$$

After the enthalpy perturbation of A* we have the following enthalpies

$$H_{A*} + dH, H_{B*}, H_{AB*}, H^{\ddagger}_{AB} \text{ and } E = H^{\ddagger}_{AB} - (H_{A*} + dH) - H_{B*}$$

This means that K_1 is perturbed to $K_1 \exp(-dH/(RT))$ and k_3 is perturbed to $k_3 \exp(dH/(RT))$ while K_2 remains constant. Applying eq 3 and substituting the Gibbs free energy with enthalpy (we perturb the Gibbs free energy by perturbing the enthalpy part only, just for simplicity of explanation), it is straightforward to show that $X_{TRC,A*} = -2$. This result shows that, if we stabilize A*, it decreases the rate strongly. This makes sense, since the surface is nearly saturated in A* already and it blocks free sites needed for B* and AB*. This negative value for the degree of thermodynamic rate control implies that this intermediate is a rate inhibitor under these conditions. Similarly, by changing the enthalpy of B* and AB*, it is easy to show that $X_{TRC,B*} = 0$ and $X_{TRC,AB*} = 0$. These results show that small changes in the stability of B* or AB* would not affect the net reaction rate under these conditions.

Relationship between the Degree of Rate Control of an Adsorbed Catalytic Intermediate and Its Surface Coverage for Surface-Catalyzed Reactions

By investigating many simple catalytic reaction mechanisms involving adsorbed reaction intermediates, we discovered that there is a simple link between the degree of thermodynamic rate control for any intermediate n and its coverage, θ_n

$$X_{TRC,n} = -\sigma \cdot \theta_n \tag{6}$$

where σ is the average number of sites required in the rate-limiting steps. Typically σ varies between 1 and 2 depending on the nature of the rate-limiting process, e.g., dissociative chemisorption requires two sites, bimolecular surface reaction requires two sites, molecular desorption requires one site, etc. Certainly noninteger values are possible if several elementary reactions are all rate limiting. Typically σ is more or less constant and $X_{TRC,n}$ becomes proportionate with the coverage of intermediate n.

A mathematical proof of eq 6 was not found. Nevertheless, in the simple example above, eq 6 holds. For example, the coverage of A* is ~1.0 and 2 sites are required in the RLS, so eq 6 gives $X_{TRC,A*} = -2$. Similarly, the coverages of B* and AB* are nearly 0, so $X_{TRC,B*} = 0$ and $X_{TRC,AB*} = 0$ according to eq 6, both consistent with the actual result above. Furthermore, by thorough analysis we also found that eq 6 also holds for several more complex examples involving both Langmuir–Hinshelwood as well as Michaelis–Menten enzyme kinetics. This work will be presented in detail elsewhere[38] and shows the utility of X_{TRC} in determining the key intermediates. Furthermore, the implications of eq 6 are consistent with the work of Dumesic, who concluded based on DeDonder analysis that the stability of intermediates is unimportant to kinetics, but only the stability of transition states is of importance, except if the intermediate has a nonzero coverage.[39,40]

The simple relationship in eq 6 between the kinetic importance of the thermodynamic stability of intermediates and their coverage may seem surprising, but it has some interesting and very important implications. First, the degree of thermodynamic rate control is always negative or zero, which means that the reaction rate will always decrease or remain unchanged if an intermediate is stabilized without also stabilizing associated transition states. On the other hand, destabilizing intermediates can increase the rate significantly, unless the key transition state(s) is (are) also destabilized. The trick in catalyst design/improvement is therefore to stabilize key transition states (those with positive X_{RC}) without stabilizing key intermediates too much, or to destabilize key intermediates (those with large negative X_{TRC}) without destabilizing related key transition states too much. (One could also destabilize the transition states of inhibition steps (those with negative X_{RC})).

General Degree of Rate Control That Applies to Both Transition States and Intermediates

The rate constant for step i is directly related to its standard-state molar free energy of activation ($\Delta G^{0\,TS}_i$) by

$$\ln(k_i/c) = -\Delta G^{0\,TS}_i/(RT) \tag{7}$$

where c is a constant (equal to $k_B T/h$ in simple transition-state theory for a first-order step, where k_B is Boltzmann's constant and h is Planck's constant). By taking the derivative of $\ln(k_i)$ in eq 7 and substituting the result into eq 1, Campbell's original $X_{RC,i}$ can be rewritten in terms of the standard-state free energy of the transition state for step i ($G^{0\,TS}_i$) as

$$X_{RC,i} = \frac{k_i}{r}\left(\frac{\partial r}{\partial k_i}\right)_{k_{j\neq i},K_i} = \left(\frac{\partial \ln r}{\partial \ln k_i}\right)_{k_{j\neq i},K_i} = \left(\frac{\partial \ln r}{\partial\left(\frac{-G^{0\,TS}_i}{RT}\right)}\right)_{G^{0\,TS}_{j\neq i},G^0_m} \tag{8}$$

The partial derivative here is taken holding the Gibbs free energy of all other transition states $j \neq i$ and all intermediates m constant, which is the same as holding the rate constants, k_j, of all other steps $j \neq i$ and the equilibrium constant, K_j, of all steps j constant. By comparing this to eq 3 above, we see that X_{RC} and X_{TRC} are really completely equivalent concepts, with X_{RC}

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varying just the standard-state free energy of one transition state i and X_{TRC} varying just the standard-state free energy of one intermediate n, with both energy changes in the same units (RT). Thus, one should think of both degrees of rate control as written in eq 3 or 8 as forms of the same general degree of rate control that applies to both transition states and intermediates, i.e., to all minima and saddle points in the multidimensional standard-state free-energy surface for the reaction. The value of $X_{\mathrm{RC},i}$ as defined by eq 1 or eq 8 reflects the relative effect of the standard-state free energy of any transition state i, and the value of X_{TRC} as defined by eq 3 reflects the effect of the standard-state free energy of any intermediate n. Therefore, their calculated values can be compared quantitatively to one another, to ascertain which transition state or intermediate is most critical and how critical it is compared to other critical transition states and intermediates. Computationally this is done by making a small decrease in one free energy (which for any transition state is equivalent to increasing one rate constant), holding all the other parameters in the microkinetic model constant as defined by eqs 1, 3, 6, and 8, and calculating the resulting fractional change in the net rate. These changes in standard-state free energies can result from changes in either the enthalpy or the entropy. An enthalpy change is associated with a change in the energy of a minimum and maximum in the potential-energy surface for the reaction, whereas an entropy change reflects only a change in the curvature of that potential-energy surface about a maximum or minimum (i.e., the freedom of motion of that species). Also, since the equilibrium constant, K_{M}, between the reactants of the net reaction and any transition state or intermediate, M, is related to their standard-state free energy difference by $K_{\mathrm{M}} = \exp[-(G^0_{\mathrm{M}} - G^0_{\mathrm{reactants}})/\mathrm{RT}]$, the derivatives with respect to $-G^0_{\mathrm{M}}/\mathrm{RT}$ in eqs 3 and 8, which define the degree of rate control, are equivalent to derivatives with respect to $\ln(K_{\mathrm{M}})$ instead.

Note that these degrees of rate control depend on reaction conditions (temperature, reactant concentrations, etc.), just as the rate-determining step may change with such conditions. They are strictly defined only for cases where every species is equilibrated to the same temperature T, although one might be able to gain insight into reaction models even where species are not thermally equilibrated, simply by choosing some reference temperature for the purpose of calculating the degrees of rate control.

How To Use the General Degree of Rate Control

The general degree of rate control is of great value since it identifies the kinetically critical transition states and intermediates (i.e., those with large magnitudes of their degree of rate control). This offers the potential to increase the net reaction rate by stabilizing one of these key transition states or destabilizing a key intermediate. In practice, it can be very difficult to accomplish these desired changes in relative stability, since intermediates and associated transition states may share structural similarities so that changing the free energy of one also changes the other in the same direction.[29,41] Nevertheless, it is certainly possible. Indeed, doing this underlies the very essence of the Sabatier principle for catalyst optimization and the common volcano plots of catalyst activity of metals versus their position in the Periodic Table: The best catalyst is the one that stabilizes the transition state the most without holding on to the reactants or products too tightly. This connection to the Sabatier principle has been shown beautifully by Dumesic[17] by combining the concept of X_{RC} with an analysis of the effects of intermediate stability on rates that is similar to, but quantitatively different than, the new X_{TRC} concept introduced here. These concepts go far beyond the single transition state usually imagined in the Sabatier principle, since in complex mechanisms there is not just one but many transition states and many intermediates and knowing which ones' free energies strongly influence the rate is critical.

One can easily see that X_{RC} and X_{TRC} are very important in catalyst design, since they clearly identify what one must do to improve the rates, at least in terms of changing the free energies of transition states and intermediates. Achieving these free-energy changes through specific structural changes in the catalyst material remains a big challenge, however. From the apparent validity of eq 6, it is realized that one can calculate X_{TRC} either by using the more complex eq 3 or by using the calculated coverage of intermediates in the simpler eq 6. As coverages are also accessible experimentally, this opens up a systematic route for catalyst improvement that may not require a full microkinetic model.

Using the general degrees of rate control to improve rates is not limited, however, to catalytic systems, since the relative stabilities of transition states and intermediates can also be modified without a catalyst by changing the solvent or by modifying a reactant's molecular structure to control the relative energies of key species in the mechanism (for example, by adding electron-donating or electron-withdrawing substituents or bulky groups that offer steric control).

The values of X_{RC} and X_{TRC} are also very important for improving microkinetic models for reactions, since they immediately identify which kinetic or energetic parameters need to be measured or computed with the highest accuracy (i.e., the ones upon which the rate depends most sensitively) to get the most accurate kinetic model. This is true of any multistep kinetic mechanism.

Thus, the general degree of rate control concept should have great applicability in a wide range of fields where kinetics of multistep mechanisms are important, such as catalysis, atmospheric modeling, and biological reaction systems, and even in the analysis of nonchemical systems such as competing rate processes to determine photovoltaic efficiency. Perhaps the most fundamental way to analyze any microkinetic model is to calculate the general degrees of rate control for all transition states and intermediates.

If one alters a reaction system in hopes of changing the stability of a transition state or intermediate to achieve a higher rate or selectivity based on this knowledge of their degrees of rate control, one must be aware that stabilizing a transition state (which can increase the net rate) will generally also stabilize the reactant and/or product of that elementary step (which could decrease the net rate) and vice versa. These energies (or free energies) are connected through the Brønsted relation (or the related linear free-energy relation), which states that the activation energy for an elementary step changes proportional to the change in its net reaction energy for a similar class of reactions, with a slope between zero and unity. Depending on the values of this slope and the values of X_{RC} and X_{TRC}, one can certainly find cases where real gains can be achieved in the

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(41) Nørskov, J. K.; Bligaard, T.; Logadottir, A.; Bahn, S.; Hansen, L. B.; Bollinger, M.; Bengaard, H.; Hammer, B.; Sljivancanin, Z.; Mavrikakis, M.; Xu, Y.; Dahl, S.; Jacobsen, C. J. H. *J. Catal.* **2002**, *209*, 275.

net reaction rate (see, for example, ref 42), and the values of X_{RC} and X_{TRC} will help one determine when it could be fruitful to try.

Dumesic introduced the concept of the "dimensionless sensitivity, s_i, of the overall rate with respect to the forward rate constant for one elementary step, k_i",[17] which is defined identically to Campbell's $X_{RC,i}$ in eq 1 above, except that the partial derivative is taken while holding all other rate constants fixed (including the reverse rate constant). This gives a very different value than X_{RC}, which varies the reverse rate constant for that step in proportion to its forward rate constant (thus holding the equilibrium constant for that step fixed) when taking the partial derivative. The new "degree of thermodynamic rate control" (X_{TRC}) which we introduce here is also similar to Dumesic's sensitivity (s_i). Dumesic's sensitivity (s_i) was independently applied by Meskine et al.,[11] whose verbal description of it makes it sound identical to our X_{TRC}. We emphasize, however, that it is distinctly different. Unlike in our definition of X_{TRC} in eq 3 above, in calculating s_i the free energy of the intermediate is not varied to see how it affects the net rate, but instead only the rate constant in *one* direction from that intermediate is changed, while holding its reverse rate constant unchanged. This is clearly different than our definition of X_{TRC}, which changes *all* the rate constant for *all* steps leading *from* that intermediate of interest (forward and backward), so as to be thermodynamically consistent with a simple standard-state free-energy change for that intermediate. This thermodynamically consistent change is the only type one could ever actually implement, so it is conceptually easier to envision. It more directly reflects the sensitivity of the net rate to changes in the energy of a given reaction intermediate and thus more directly reflects the errors in rate that result from errors in calculated energies or the improvements in rate that might be accomplished by chemical modifications. We offer the following points on how these related quantities (X_{TRC} versus s_i) are the same and how they differ. First, when the forward rate from an intermediate is huge compared to the reverse rate from that intermediate, s_i should scale with our X_{TRC}. However, when the intermediate has similar rates going in the forward and reverse directions, they will be quite different. Therefore, s_i will not scale with the coverage of the intermediate as does our X_{TRC} (eq 6), and so all of the discussion above that derives from eq 6 does not apply equally to s_i. Thus, all three concepts (s_i, X_{RC}, and X_{TRC}) are valuable and complimentary but very different. The physical significance of X_{TRC} and X_{RC} is more understandable than that of s_i, and they are thermodynamically consistent with simple changes in the reaction energy diagram, but s_i is not.

Meskine et al.[11] recently gave an elegant demonstration of the power of combining the analysis of both s_i and X_{RC} in analyzing complex kinetic processes where the rate constants are obtained from ab initio quantum computations. They showed that this is a very useful tool for understanding the propagation of errors from the electronic structure calculations to the statistical simulations in first-principles kinetic Monte Carlo simulations. The above discussion suggests that combining the analysis of X_{RC} and X_{TRC} would prove even more powerful, since the results should be easier to interpret physically. As a side note, their results also highlight the importance of properly considering adsorbate−adsorbate interactions in kinetic analyses of surface reactions. A single rate constant cannot apply to all adsobates of the same type, since their energy depends so strongly on the presence of nearest neighbors. Keeping track of the details of the neighbors can be complex but is essential and can be handled as they did. Alternatively, one might consider a more standard rate-equation approach, which would be simpler in principle. However, to get comparable accuracy one would need to define as separate "species" every possible set of nearest-neighbor configurations for a given adsorbate. To our knowledge, this has never been done with the rate-equation approach. As they showed, adsorbate islanding often occurs, which would make adsorbate kinetics even more complex to model within a rate-equation approach, if even possible.

Conclusions

The general degree of rate control is introduced here as a quantitative measure of the relative change in the net rate of a multistep reaction induced by a differential change in the standard-state free energy of any one of its transition states or intermediates, holding everything else constant. Its values can be calculated whenever a microkinetic model exists for the reaction mechanism. Large values of the degree of rate control identify the kinetically critical transition states and intermediates, which are few in number even for very complex mechanisms. This offers a very powerful approach to both applied and basic research, since it gives ideas for practical changes to improve net reaction rates (by modifying the reactants, solvent, or catalysts to control the relative energies of these key species) and to improve microkinetic models for complex mechanisms (by improving the accuracy of the kinetic parameters associated with these key species). It is similar to the concept of a rate-determining step but more direct to apply and much more widely applicable (since there is rarely a single rate-determining step).

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(42) Greeley, J.; Mavrikakis, M. *Nat. Mater.* **2004**, *3*, 810.