

Diffusion and Disequilibrium for Rapid Bimolecular Reactions in Solution: Influence of the Back-Reaction

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Abstract: The influence of reversibility and diffusion on the rate constant of rapid bimolecular reactions in solution is explored with statistical nonequilibrium thermodynamics. For reactions with stoichiometry $A + B \rightleftharpoons C$, we find that in dilute solution the Smoluchowski–Collins–Kimball steady-state expression for the rate constant is valid only when the steady state is sufficiently far from equilibrium (as determined by the criterion $\Delta G \ll -RT \ln [k^0/4\pi D'R]$). Comparable results hold for bimolecular reactions with other stoichiometries. On the basis of these considerations, we put forward two caveats in the interpretation of experimental data: (1) for measurements in an equilibrium ensemble (e.g., equilibrium perturbation techniques), the bimolecular rate constant equals the intrinsic rate constant and is *not* diffusion dependent; (2) while the Smoluchowski–Collins–Kimball expression is valid at steady states sufficiently far from equilibrium, the ratio of the forward to the reverse rate constants does *not* equal the equilibrium constant. The implications of these caveats for the interpretation of experimental data, including acid–base neutralization reactions, are discussed.

I. Introduction

The theory of rapid bimolecular chemical reactions in solution has a rich history beginning with Smoluchowski's original work in 1917.¹ Smoluchowski's idea of describing the rate constant for rapid reactions using the diffusion equation was later improved in a number of ways by Debye,² Collins and Kimball,³ and others.⁴ The predictions of time-dependent and steady-state relaxation rates based on this work have been verified repeatedly in a number of simple systems in dilute solution.⁵ While the extension of the Smoluchowski theory to more concentrated solutions and to reactants involved in competing reactions (e.g., fluorescence) is difficult, we have recently shown how to deal with these and other transport effects on rapid bimolecular reactions using statistical nonequilibrium thermodynamics.^{6–8} In this paper, we deal with reversible reactions and the influence of diffusion and disequilibrium on the steady-state bimolecular rate constant.

Disequilibrium in a chemical reaction can have a number of effects on the reaction rate. For example, in the gas phase, chemical disequilibrium can modify translational energy distributions^{9,10} as well as the distribution of internal states.¹¹ These modifications can be significant for flash photolysis induced⁹ or hot-atom reactions¹⁰ but seem to be small for thermal bimolecular reactions except under special conditions.¹¹ Translational and internal-state effects caused by disequilibrium are generally much smaller in solution because of the shorter collisional relaxation time scale. This can be circumvented by selectively populating internal electronic states, as one does to measure excited-state acid association rate constants.¹² Here, however, we are interested in another effect, namely, the change in the average configurational arrangement of one type of reactant around another. This phenomenon is important for so-called "diffusion-controlled" reactions⁴ in solution, i.e., rapid bimolecular reactions that have small or negligible activation energies. For diffusion-controlled reactions,

the spatial distribution of reactants determines the bimolecular encounter frequency and, thereby, the reaction rate constant, which can be several orders of magnitude smaller than its gas-phase value. For some reactions of this sort, e.g., the recombination of iodine atoms, excited vibrational states seem to play a role.¹³ Thus, we also explore how disequilibrium with respect to an intervening excited state perturbs the spatial distribution of reactants.

There are many types of rapid bimolecular reactions in solution for which the back-reaction is sufficiently slow that it causes a negligible effect on the spatial distribution of reactants, e.g., fluorescence quenching and radical–radical recombination. Acid–base neutralization¹⁴ reactions, on the other hand, can have dissociation rate constants as large as 10^{10} s^{-1} . For these reactions, the influence of the reverse reaction may have a significant effect on the spatial distribution of reactants since it provides a "source" to replenish the reactant pairs that are depleted by the bimolecular "sink". In fact, in a previous investigation of the reinjection of receptors in biological membranes after capture by coated pits,¹⁵ we found that the back-reaction can eliminate completely the effect of diffusion on the rate of capture of receptors. Here we explore this phenomenon further by examining bimolecular reactions in solution. A number of mechanisms and stoichiometries are investigated, including $A + A \rightleftharpoons A_2$, $A + B \rightleftharpoons C$, and $A + B \rightleftharpoons A-B \rightleftharpoons C$. In the latter reaction, the species $A-B$ might correspond to an excited internal state of the product, C , or an "encounter" complex. We obtain explicit results for the radial distribution function for reactants in dilute solutions for these reactions, while for the first reaction we examine for completeness both concentration effects and two methods of driving the reaction away from equilibrium.

Using the radial distribution function, we calculate the observed bimolecular rate constants, k^{obs} , for these reactions. In dilute solution for the reaction $A + B \rightleftharpoons C$, our result takes the particularly simple form

$$k^{\text{obs}} = k_{\text{SCK}}[1 + \exp(\Delta G/RT)k^0/4\pi D'R] \quad (1)$$

where

$$k_{\text{SCK}} = k^0/(1 + k^0/4\pi D'R) \quad (2)$$

is the usual Smoluchowski–Collins–Kimball (SCK) expression for the bimolecular rate constant and ΔG is the Gibbs free energy for the reaction. Three cases of this expression are notable: (1) If the ensemble is at equilibrium, $\Delta G = 0$ and the observed rate

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constant is the intrinsic rate constant *no matter how fast* the intrinsic rate constant, k^0 . (2) When the steady state is sufficiently far from equilibrium to the left, i.e., $\Delta G \ll -RT \ln(k^0/4\pi D'R)$, one recovers the SCK expression. (3) When the steady state is sufficiently far to the right, i.e., $\Delta G \gg -RT \ln(k^0/4\pi D'R)$, there are large deviations from the SCK expression. The implication of this result is discussed for experimental measurements of bimolecular reaction rate constants, especially for acid-base neutralization reactions.

II. Dimerization

The simplest example of a reversible bimolecular chemical reaction is the dimerization reaction⁶



Here the bimolecular rate constant is k^{obs} , and the unimolecular decomposition rate constant for the reverse reaction is k . In solution, the rate constant for the reverse reaction may be dependent on viscosity due to internal motions that have nothing to do with translational diffusion.¹⁶ Although we will be interested exclusively in the effect of translational diffusion on the bimolecular reaction rate, we return to a discussion of the viscosity dependence of the reverse rate constant in section IV. Except as indicated in section III, we ignore the possibility of excited internal states and assume, therefore, that the value of k is a constant.

To calculate the steady-state bimolecular rate constant for this reaction, we use the formula⁶⁻⁸

$$k^{\text{obs}} = k^0 g_{AA}(R) \quad (4)$$

where k^0 is the collisional or "intrinsic" rate constant and $g_{AA}(R)$ is the A-A radial distribution function evaluated at the reaction radius, R . Equation 4 is a special case of the general expression connecting the rate constant and the radial distribution function. We use it simply because it involves the same level of approximation employed in the usual Smoluchowski theory. We also restrict our attention to the value of the observed rate constant in a uniform steady state. In this case, $g_{AA}(r)$ is the steady-state radial distribution function.

It is possible to maintain a uniform steady state for the dimerization reaction in several ways. We consider first the use of a steady, uniform source (or sink) of monomer and dimer. Thus, on the average, one has

$$d\bar{\rho}_A/dt = -2k^{\text{obs}}\bar{\rho}_A^2 + 2k\bar{\rho}_{A_2} + 2K \quad (5)$$

$$d\bar{\rho}_{A_2}/dt = k^{\text{obs}}\bar{\rho}_A^2 - k\bar{\rho}_{A_2} - K$$

where the overbars represent average number concentrations and K is a constant. At steady state one finds that

$$K = k^{\text{obs}}\rho_A^{\text{ss}2} - k\rho_{A_2}^{\text{ss}} \quad (6)$$

According to statistical nonequilibrium thermodynamics,¹⁷ fluctuations around the steady-state values ρ_A^{ss} and $\rho_{A_2}^{\text{ss}}$ satisfy stochastic differential equations. These equations can be used, as is outlined in the Appendix and elsewhere,⁶⁻⁸ to obtain the density-density correlation function and, then, the radial distribution at steady state. Carrying out the details one finds that

$$g_{AA}(r) = 1 - (K/\rho_A^{\text{ss}2}) \left[\frac{\exp(-\xi_1 r)}{2\pi D_A r} + \frac{k[\exp(-\xi_1 r) - \exp(-\xi_2 r)]}{2\pi D_A D_{A_2} r (\xi_2^2 - \xi_1^2)} \right] \quad (7)$$

where

$$\xi_1^2 = \frac{4k^{\text{obs}}\rho_A^{\text{ss}}}{D_A} + \frac{k}{D_{A_2}} \quad \xi_2^2 = \frac{4k^{\text{obs}}\rho_A^{\text{ss}} + k}{D_A + D_{A_2}} \quad (8)$$

Three things are notable in eq 7. First, $g_{AA}(r) = 1$ when K

vanishes, i.e., at equilibrium. Thus, the radial distribution function agrees with the correct equilibrium formula, as it is guaranteed to in general by the thermodynamic structure of the theory.¹⁸ Second, in the limit that k is small, the second term in brackets in eq 7 is negligible and $K/\rho_A^{\text{ss}2} \approx k^{\text{obs}}$ so that the radial distribution function reduces to the usual Smoluchowski form in the absence of the reverse reaction. Third, when k is not negligible, the input term K can be positive or negative. In the latter case the radial distribution function can exceed unity at $r = R$. We discuss this point in detail below.

The inverses of the terms ξ_1 and ξ_2 in eqs 7 and 8 are correlation lengths whose values determine the influence of the bimolecular ($1/k^{\text{obs}}\rho_A^{\text{ss}}$) and unimolecular ($1/k$) lifetimes on this reaction, as described previously.^{5-8,17} The bimolecular lifetime effect is generally significant only at concentrations above 10^{-3} M. The effect of the unimolecular lifetime, however, can persist even in dilute solution. In fact, noting that in dilute solution $\xi_2^2 - \xi_1^2 = -kD_A/D_{A_2}(D_A + D_{A_2})$, it is easily shown that eq 7 reduces to

$$g_{AA}(r) = 1 - \frac{k^{\text{obs}} - k\rho_{A_2}^{\text{ss}}/\rho_A^{\text{ss}2}}{2\pi D_A r} \left\{ \frac{D_{A_2} + D_A}{D_A} \exp(-r[k/D_A + D_{A_2}]^{1/2}) - \frac{D_{A_2}}{D_A} \exp(-r[k/D_{A_2}]^{1/2}) \right\} \quad (9)$$

Although the term in braces is always positive, its size depends on the reverse rate constants and the diffusion constants. For $k \leq 10^8$ s⁻¹, however, its value will be close to unity for small molecules ($D \sim 10^{-5}$ cm² s⁻¹). Indeed, k must be of order 10^{11} s⁻¹ for this term to differ appreciably from unity even for r near the reaction radius, R .

To calculate the bimolecular rate constant, eq 9 is used in conjunction with eq 4.⁵⁻⁸ After rearrangement, one easily finds that

$$k^{\text{obs}} = k^0 [1 + (k\rho_{A_2}^{\text{ss}}/\rho_A^{\text{ss}2})B/2\pi D_A R] / [1 + k^0 B/2\pi D_A R] \quad (10)$$

where B is the expression in braces in eq 9. As we have already noted, the value of k^{obs} at equilibrium is k^0 . Thus, with the principle of detailed balance, which applies at equilibrium, eq 10 can be rewritten with $k^0/k = K^e$, the equilibrium constant for this reaction. Recalling further the thermodynamic identity for the Gibbs free energy for the reaction in dilute solution

$$\Delta G = -RT \ln K^e + RT \ln (\rho_{A_2}^{\text{ss}}/\rho_A^{\text{ss}2}) \quad (11)$$

eq 10 becomes

$$k^{\text{obs}} = \left(\frac{k^0}{1 + k^0/2\pi D_A \bar{R}} \right) [1 + \exp(\Delta G/RT)k^0/2\pi D_A \bar{R}] \quad (12)$$

with $\bar{R} = R/B$, the apparent reaction radius as modified by the influence of the unimolecular lifetime.

The first term in eq 12 is recognized as the usual SCK result, corrected for the identity of reactants and the bimolecular lifetime.^{5,6,8} Because B will be close to unity unless k is quite large, this term is essentially unchanged by the back-reaction. In the second term, the quantity $\exp(\Delta G/RT)$ is a measure of the distance that the reaction is from equilibrium, which can be very significant. Thus, at equilibrium when $\Delta G = 0$, it cancels the denominator in the first term, yielding $k^{\text{obs}} = k^0$, as expected, while when $k \rightarrow 0$, $\Delta G \rightarrow -\infty$ and one recovers the usual SCK result, also as expected. Intermediate situations are possible, as illustrated in Figure 1 in which k^{obs}/k^0 is plotted as a function of $\ln(k^0/2\pi D_A \bar{R})$ for various values of $\Delta G/RT$. In panel A of that figure, one finds results for $\Delta G/RT \leq 0$, which correspond to a net input of A at the steady state (i.e., $K > 0$). For $\Delta G/RT \ll 0$, these curves converge to the usual limiting far-from-equilibrium results of Smoluchowski, Collins, and Kimball. In panel B, the results

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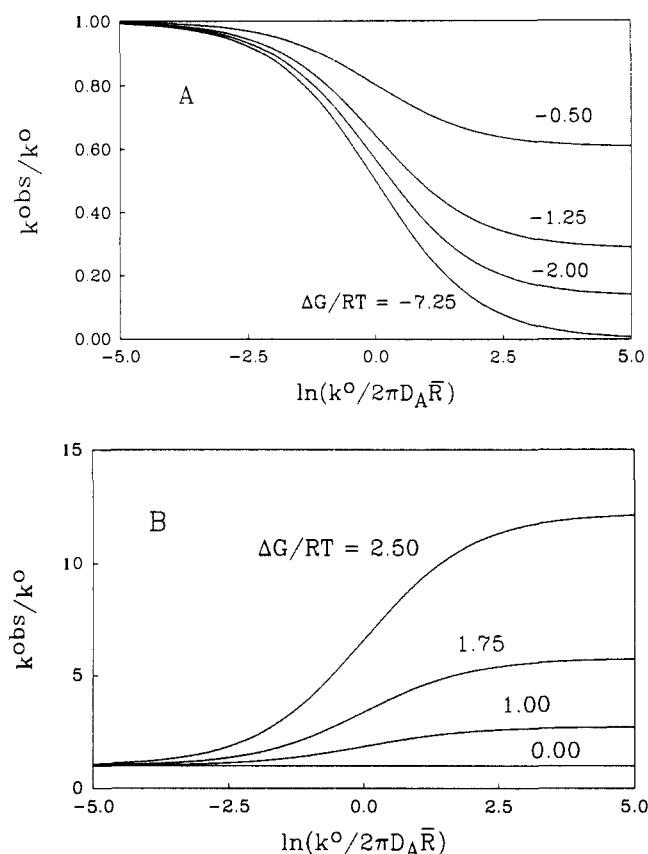
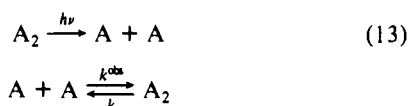


Figure 1. Panel A: effect of different negative values of $\Delta G/RT$ on the observed bimolecular rate constant as a function of $k^0/2\pi D_A \bar{R}$ (cf. eq 12). Panel B: similar results for $\Delta G/RT > 0$. Note that as $\Delta G/RT \rightarrow -\infty$, the curve converges on the usual Smoluchowski–Collins–Kimball result.

for $\Delta G/RT \geq 0$ (an input of product A_2 into the system) are shown. Notice that under these conditions the observed rate constant can greatly exceed the collisional rate constant, k^0 , even if the ratio $k^0/2\pi D_A \bar{R}$ is rather small.

The origin of the effect of disequilibrium on the observed reactant rate is easily understood. Imagine sitting on an “average” A molecule. According to eq 4, the average density of A at a distance R away determines the reaction rate. In the usual Smoluchowski theory, this density is determined by two kinetic processes, diffusion and the intrinsic (collisional) reaction rate—diffusion being important only when it is slow enough that it cannot replenish reactants removed at R by reactive collisions. When back-reaction is possible, the local concentration of A at R is further replenished by the process $A_2 \rightarrow A + A$. In fact, when the forward and reverse processes balance, as they do at equilibrium, the net result of reaction is to leave the average density unchanged and, thus, diffusion has no effect on the reaction. On the other hand, if the back-reaction is sufficiently slow—as is usually assumed—the formation of geminate pairs has little impact and, thus, only diffusion and the bimolecular collision rate have an effect. The extent of disequilibrium and its sign are clearly important since they determine whether removal of A–A pairs by the forward reaction or their reinjection by the reverse reaction will have the greater influence on the density at the reaction radius. In fact, if disequilibrium at the steady state favors the product A_2 (i.e., $\Delta G > 0$), then the density at the reaction radius will be increased above its equilibrium value. It is this latter effect that is described quantitatively in Figure 1B.

Similar conclusions are reached if we use the following photochemical mechanism to drive the dimerization reaction to steady state:



From previous work,⁶ we find that in dilute solution

$$g_{AA}(r) = 1 - \frac{k^{obs}k^*}{2\pi D_A r(k+k^*)} \left\{ \frac{D_A - D_{A_2}}{D_A} \exp(-r[k/D_A + D_{A_2}]^{1/2}) + \frac{D_{A_2}}{D_A} \exp(-r[k/D_{A_2}]^{1/2}) \right\} \quad (14)$$

It is easy to see for small molecules that the term in braces is near unity unless k is greater than 10^8 s^{-1} . Using eq 4 and a notation to that in eq 10, we find that

$$k^{obs} = k^0 / (1 + f k^0 / 2\pi D_A \bar{R}) \quad (15)$$

where \bar{B} is now defined by the braces in eq 14 and $f \equiv k^*/k + k^*$. Using eq 15 along with a little algebra involving the steady-state condition for this mechanism, i.e.

$$k^{obs} \rho_A^{ss2} = (k + k^*) \rho_{A_2}^{ss} \quad (16)$$

it is not difficult to show that

$$f = \frac{1 - \exp(\Delta G/RT)}{1 + (k^0/2\pi D_A \bar{R}) \exp(\Delta G/RT)} \quad (17)$$

from which it follows that

$$k^{obs} = \left[\frac{k^0}{1 + k^0/2\pi D_A \bar{R}} \right] [1 + \exp(\Delta G/RT) k^0/2\pi D_A \bar{R}] \quad (18)$$

in dilute solution. Equation 18 has precisely the same dependence on the deviation from equilibrium as found for the uniform driving mechanism in eq 12. Note, however, that the photochemical mechanisms can only increase the density of A molecules in the system, thus leading only to negative values of ΔG .

While the two methods of driving the steady state (uniformly or photochemically) produce the same dependence of the bimolecular rate constant on Gibbs free energy difference, their dependence on other parameters is different. For example, for a sufficiently large reverse rate constant, k , the term in braces in eq 14 can become negative. This increases the radial distribution function at R beyond its equilibrium value, producing a value of k^{obs} in eq 18 that is greater than k^0 . Something comparable is seen when one retains the density-dependent terms in the correlation lengths for photochemical driving. If one calculates k^{obs} as a function of k^* with the total number of A molecules fixed, one finds that $k^{obs} = k^0$ at $k^* = 0$ (equilibrium) and that k^{obs} decreases to a minimum and then increases again at values of k^* that depend on k . These differences with the uniform driving mechanism are due to the fact that the photochemical production of A from A_2 produces local geminate pairs, while the uniform mechanism injects A molecules randomly into solution. In this way, the photochemical mechanism augments the local-pair production due to the back-reaction, ultimately swamping the loss of pairs due to the bimolecular step.

III. Other Stoichiometries

The conclusions regarding the dependence of the bimolecular rate constant on the back-reaction rate for the dimerization reaction can be extended to reactions with other stoichiometries. The steady-state radial distribution function, $g_{AB}(r)$, is easily obtained in dilute solution for the reaction

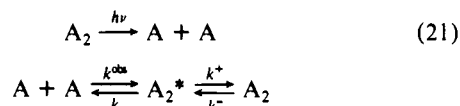


with use of computer-assisted algebra.¹⁹ For uniform inputs, this leads to an expression for the bimolecular rate constant analogous to that for the dimerization reaction, namely

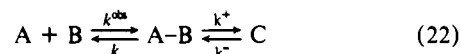
$$k^{obs} = [k^0 / (1 + k^0/4\pi D' \bar{R})] [1 + \exp(\Delta G/RT) k^0/4\pi D' \bar{R}] \quad (20)$$

where $D' = D_A + D_B$. Again one finds that the apparent reaction radius, \bar{R} , is modified by the back-reaction when k is on the order of 10^8 s^{-1} or larger. As before, eq 20 reduces to the familiar SCK expression when $\Delta G/RT \ll 0$ and gives $k^{\text{obs}} = k^0$ when the ensemble is at equilibrium.

For completeness, we consider the following two reaction schemes



and



in which an intermediate species, A_2^* or $A-B$, precedes the stable molecule, A_2 or C . Indeed, Eigen and co-workers¹⁵ have introduced ion pairs (analogous to the intermediate $A-B$) in their analysis of experimental rates of acid-base neutralization reactions, while recent experiments on iodine recombination²¹ have uncovered excited vibrational and electronic states analogous to A_2^* . Thus, it seems important to assess the effect of such intermediates on the bimolecular rate constant. For these reactions, we find the same formal expressions for the observed rate constants as given in eqs 18 and 20, *except* that the free energy difference ΔG is now for the steps $A + A \rightleftharpoons A_2^*$ and $A + B \rightleftharpoons A-B$, respectively. Since additional unimolecular rate constants (i.e., k^+ and k^-) are involved in these schemes, the effective reaction radius, \bar{R} , will depend on several additional characteristic lengths. As before, this effect remains negligible as long as all the unimolecular rate constants are not too large.

IV. Relationship to Other Theories

There are several existing theories of diffusion effects on reversible reactions,²² the most widely used being that of Eigen.²³ Eigen's ideas were developed in order to analyze kinetic data on acid-base neutralization reactions,^{15,20} which are invariably reversible and for which equilibrium constants are usually well-known. In Eigen's theory, a contact ion pair $A-B$ is identified as an intermediate in the neutralization reaction, as in eq 22. Regarding eq 22 as a mass action law scheme and eliminating transient intermediate $A-B$ give the rate law

$$d\bar{\rho}_A/dt = -k_R\bar{\rho}_A\bar{\rho}_B + k_D\bar{\rho}_C \quad (23)$$

where the overbars represent bulk concentrations and the apparent recombination and dissociation rate constants are

$$k_R = \frac{k^{\text{obs}}k^+}{k + k^+} \quad k_D = \frac{kk^-}{k + k^+} \quad (24)$$

Equation 23 gives rise to a single relaxation time

$$\tau = \frac{1}{k_R(\bar{\rho}_A + \bar{\rho}_B) + k_D} \quad (25)$$

as found experimentally for "normal" protolytic reactions.¹⁵

According to Eigen,^{20,23} the value of k^{obs} in these equations should be taken from the steady-state Smoluchowski theory as modified by Debye to correct for ionic forces. The value of k is assumed to be given by microscopic reversibility as

$$k = k^{\text{obs}}/K^e_1 \quad (26)$$

where K^e_1 is the equilibrium constant for ion-pair formation, e.g., the first step in eq 22. Several attempts^{22,23} have been made to justify eq 26 by applying a Smoluchowski-type theory to the back-reaction. By appropriate modification of boundary con-

ditions, one can, in fact, obtain eq 26. This boundary condition treats the $A-B$ pair as a source of B molecules, with a sink at infinity. If the reaction is far from equilibrium, this approach leads to the correct low-density radial distribution function of B molecules around a central $A-B$ pair, e.g., in the absence of interactions $g_{B,A-B}(r) = R/r$. To calculate the rate constant, k , however, Eigen uses the flux from the source, which implies that translational diffusion of the $A-B$ pair alone determines the reverse rate constant. A simple consequence of Eigen's theory is that

$$k_R/k_D = K^e_1K^e_2 = K^e \quad (27)$$

where from microscopic reversibility $K^e_2 = k^+/k^-$ is the equilibrium constant for the second step in eq 22 and K^e is the overall equilibrium constant. Under conditions of diffusion control, one has further that $k \ll k^+$ so that eq 24 implies

$$k_R = k^{\text{obs}} \quad k_D = k/K^e_2 \quad (28)$$

These are the equations used by Eigen and others to analyze acid-base neutralization reactions.^{15,20} Equation 26 and the assumption that k^{obs} is given by the Smoluchowski-Debye expression are the key ingredients of this analysis.

To examine the validity of these assumptions, we look separately at equilibrium states and nonequilibrium steady states. In equilibrium ensembles, it is well-known that eq 26 is valid. Indeed, as we discussed in the previous sections, it is a rather general consequence of statistical nonequilibrium thermodynamics. On the other hand, it is not true at equilibrium that k^{obs} depends on the diffusion constant. At equilibrium, the bimolecular rate constant is determined by an average over the canonical distribution function,^{17,24} and, as shown explicitly in sections II and III, the rate constant has the value $k^{\text{obs}} = k^0$. Related results have been obtained recently for reversible reactions by Szabo and Agmon²⁵ using a time-dependent version of the Smoluchowski theory. Thus, while one of the basic tenants of Eigen's theory is valid at equilibrium, namely that the ratio of the forward and reverse rate constants can be obtained from the equilibrium constant, it is not true that k^{obs} depends on the diffusion constant. This has important implications for the analysis of data obtained by perturbation methods around equilibrium.

For steady states that are maintained sufficiently close to equilibrium, we saw in section III that the effect of diffusion on k^{obs} depends on the distance away from equilibrium as measured by ΔG_1 , the Gibbs free energy of reaction for the first step in eq 22. Explicitly

$$k^{\text{obs}} = [k^0/(1 + k^0/4\pi D'\bar{R})][1 + \exp(\Delta G_1/RT)k^0/4\pi D'\bar{R}] \quad (29)$$

Thus, even in a steady-state ensemble—unless conditions are such that $\Delta G_1/RT \ll -\ln(k^0/4\pi D'\bar{R})$ —the bimolecular rate constant is not equal to the usual Smoluchowski expression.

It seems unlikely that eq 26 ever will be valid in steady ensembles far from equilibrium unless $k^0/4\pi D'\bar{R} \ll 1$. Our view on this is motivated by two considerations. First, forget about the idea of an ion-pair intermediate, so that the reaction mechanism is simply given by $A + B \rightleftharpoons C$. Thus, the reverse reaction rate constant is determined by the lifetime of the bound state, C . This lifetime is a function of the molecular interaction potential, the distribution of thermal energies, and solvent effects, including viscosity. For a bound species, viscous effects are determined by frictional damping on crossing the barrier to the unbound state. The effect is described reasonably well by the Kramers theory,^{16,21} which does not require a knowledge of the distribution of the unbound reactant pairs that is important for calculating the bimolecular rate constant. Thus, if an ion pair can be distinguished from an unbound $A-B$ pair only by their close proximity, then it is not necessary to include it explicitly in the calculation. This implies that our results for the reversible reaction $A + B \rightleftharpoons C$ are valid. On the other hand, if an ion pair is a species distinct

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from a "free" A-B pair, it must involve some sort of bound state between A and B. In this case, however, the preceding argument implies that the Kramers theory, not the Smoluchowski theory, must be used to calculate the reverse rate constant and that eq 26 is not valid. In either case, eq 26 would not be valid for steady states sufficiently far from equilibrium unless $k^0/4\pi D'R \ll 1$.

V. Implications for Analysis of Experimental Data

There are many important diffusion-controlled reactions for which the back-reaction has a negligible effect. Rates of fluorescence-quenching reactions,²⁶ for example, are measured by populating an excited state by radiation. Since the rate of repopulation of this excited state by the reverse of the quenching process is negligible, the quenching reaction is always far from equilibrium under normal experimental conditions.⁷ Thus, the back-reaction will have a negligible effect on the quenching rate constants, as is well-supported by experimental evidence.^{7,27}

Other types of rapid reactions, including acid-base neutralization reactions, are often studied close to or under equilibrium conditions. For example, much of the work of Eigen and collaborators²⁰ on proteolytic reactions utilized small perturbations around equilibrium²⁷ to measure recombination rates. The time or frequency response in these experiments is determined by linearizing kinetic equations around the equilibrium state. As a consequence, the values of rate constants are determined by an *equilibrium ensemble*. As we have seen, this implies that the bimolecular rate constant, k^{obs} , has its intrinsic value, k^0 , dictated by thermal equilibrium. This value is independent of diffusional effects since the distribution of reaction pairs at equilibrium is determined by the canonical distribution. A similar statement holds true for bimolecular rates determined by equilibrium NMR techniques in which line shapes are used to calculate rate constants.²⁷ Although for simplicity the effect of ionic interactions have not been taken into account in our calculations here, they are easily included in the theory⁶ and do not alter these general conclusions.

This line of reasoning forces us to conclude that many of the reported recombination rate constants for proteolytic reactions do *not* reflect diffusion-controlled processes. This is contrary to the widely accepted theory of Eigen⁵ described in the previous section. On the other hand, the measured rate constants for these reactions are on the order of 10^{10} – 10^{11} M⁻¹ s⁻¹, which are of a size that easily could be accounted for²³ by intrinsic thermal rate constants, k^0 .

It is difficult to verify directly that the recombination rate constant of a neutralization reaction is proportional to the relative diffusion constant since changes in the solvent may strongly effect the rates of these reactions. Indeed, the evidence favoring interpretation of the recombination rate of proteolytic reactions as diffusion-controlled is indirect.⁵ On the basis of the theoretical conclusions outlined above, we believe that a critical reexamination of the data on proteolytic reactions, including the conditions under which experiments were performed, is necessary. On the other hand, our conclusions suggest that the use of microscopic reversibility¹⁴ (eq 26) to obtain the reverse rate constant from data obtained by the perturbation of equilibrium is correct. Although we have argued for diffusion-controlled reactions that microscopic reversibility is *invalid* far from equilibrium, it is certainly valid if the bimolecular rate constant has its equilibrium value, k^0 .

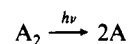
These conclusions are summarized in the following caveats for interpretation of data: (1) If the bimolecular rate constant is measured under far from equilibrium conditions that favor the reactants, then diffusion effects will be manifest. In this case, the dilute solution limiting law is given by the Smoluchowski–Collins–Kimball formula, corrected for unimolecular lifetime effects. Under these conditions, however, the reverse rate constant

cannot be deduced by microscopic reversibility unless the reaction is slow. (2) If measurements are made under equilibrium conditions, diffusion has no effect on the bimolecular rate constant. Microscopic reversibility, however, can be used to obtain the reverse rate constant.

Our results can be used to estimate when steady-state conditions are sufficiently "far" from equilibrium that diffusion effects are important. For example, for the photochemically driven dimerization reaction in eq 13, the formula in eq 15 for the observed rate constant can be rewritten as

$$k^{\text{obs}} = 2\pi D_A \bar{R} k^0 / (k^0 + 2\pi D_A \bar{R} - g k^0) \quad (30)$$

where $g = k/k^*$. The constant k^* is the rate constant for absorption of radiation in the step



and can be deduced with Beer's law²⁹ to be

$$k^* = (I_0/h\nu)\epsilon l \quad (31)$$

where I_0 is the power of the light source, ϵ is the extinction coefficient, and l is the path length. For a 100-W laser, one can estimate from (31), roughly, that $k^* \approx 1$ s⁻¹. Thus, at this intensity, as long as $k \ll 1$ s⁻¹, eq 30 shows that k^{obs} is given by the usual SCK-type formula. On the other hand, if 1 s⁻¹ $\ll k$, then $k^{\text{obs}} = k^0$.

A formula comparable to (30) can be derived for the recombination reaction (19) and reactions 21 and 22 with the intermediate states A_2^* and A-B. An explicit formula for k^{obs} is obtained by expressing the factor $\exp(\Delta G_1/RT)$ (cf. eq 29) in terms of rate constants and concentrations by using the average conditions of steady state. One finds in the latter cases that

$$k^{\text{obs}} = k_d k^0 / (k^0 + k_d - g k^0) \quad (32)$$

where $k_d = 2\pi D_A \bar{R}$ and $g = k(k^* + k^-) / [k^*(k + k^*) + k k^-]$ for the dimerization reaction (21) and $k_d = 4\pi D'R$ and $g = [Kk + k k^-(\rho_{AT} - \rho_A)] / [k k^-(\rho_{AT} - \rho_A) + K(k + k^- + k^*)]$ for the recombination reaction (22) with ρ_{AT} , the total density of A. Notice that at equilibrium where k^* and K vanish, eq 32 gives $k^{\text{obs}} = k^0$ and that unless $g \ll 1$, k^{obs} differs from the Smoluchowski–Collins–Kimball result, as deduced earlier. Equation 32 simplifies considerably if we make the assumptions that A_2^* and A-B are transient intermediates (so that k^- is negligible with respect to k^* and k^+) and that A is present in great excess (so that $\rho_{AT} \approx \rho_A$). In both cases, one then finds that $g = k/(k + k^*)$. Clearly, unless $k \ll k^*$, there will be a significant correction to the SCK formula. In fact, in the opposite extreme, i.e., $k^+ \ll k$, $g = 1$, and $k^{\text{obs}} = k^0$. This is a consequence of the fact that with transient intermediates, as in eqs 21 and 22, it is not necessarily possible to drive the first reaction far enough from equilibrium that $\Delta G_1/RT \ll 0$. Note that according to eq 32

$$k^{\text{obs}} = \frac{k^0 k_d / (1 - g)}{k^0 + k_d / (1 - g)} \quad (33)$$

Since $0 < g < 1$, this means that the effect of the back-reaction is to *reduce* the effect of diffusion in a way that depends on the relative lifetimes, $1/k$ and $1/k^+$, of the transient intermediate.

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Appendix

According to the statistical theory of nonequilibrium thermodynamics,¹² fluctuations in the local number density of reactants

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(29) Moore, W. J. *Physical Chemistry*, 4th ed.; Prentice-Hall: Englewood Cliffs, NJ, 1971; pp 750–751.

and products are determined by the combined effect of the mass action laws and diffusion. The fluctuations are defined as the instantaneous deviation of the number density at any point r from the uniform average value given by eq 5, e.g.

$$\delta\rho_A(r,t) = \rho_A(r,t) - \bar{\rho}_A \quad (\text{A-1})$$

$$\delta\rho_{A_2}(r,t) = \rho_{A_2}(r,t) - \bar{\rho}_{A_2}$$

The relevance of these fluctuations for diffusion-controlled⁵⁻⁸ reactions is that their spatial correlation functions are related to the radial distribution function and, thereby, to the bimolecular rate constant (cf. eq 4). For the dimerization reaction at steady state, the precise relationship is⁶

$$g_{AA}(|r-r'|) = 1 - \delta(r-r')/\rho_A^{ss} + \langle \delta\rho_A(r,t) \delta\rho_A(r',t) \rangle^{ss} / \rho_A^{ss2} \quad (\text{A-2})$$

where $\langle \dots \rangle$ represents the ensemble average. At steady state, the fluctuations for the dimerization reaction in eq 3 are Gaussian random variables satisfying the coupled stochastic differential equations:^{5-8,12}

$$\partial\delta\rho_A/\partial t = -4k^{obs}\rho_A^{ss}\delta\rho_A + 2k\delta\rho_{A_2} + D_A\nabla^2\delta\rho_A + \tilde{f}_A \quad (\text{A-3})$$

$$\partial\delta\rho_{A_2}/\partial t = 2k^{obs}\rho_A^{ss}\delta\rho_A - k\delta\rho_{A_2} + D_{A_2}\nabla^2\delta\rho_{A_2} + \tilde{f}_{A_2}$$

The terms \tilde{f}_A and \tilde{f}_{A_2} are purely random Gaussian contributions to the time rates of change that vanish on the average and have the following space-time correlation functions:

$$\langle \tilde{f}_A(r,t) \tilde{f}_A(r',t') \rangle = (4k^{obs}\rho_A^{ss2} + 4k\rho_{A_2}^{ss} - 2D_A\rho_A^{ss}\nabla_r^2) \delta(r-r') \delta(t-t') \quad (\text{A-4})$$

$$\langle \tilde{f}_{A_2}(r,t) \tilde{f}_A(r',t') \rangle = \langle \tilde{f}_A(r,t) \tilde{f}_{A_2}(r',t') \rangle = -2(k^{obs}\rho_A^{ss2} + k\rho_{A_2}^{ss}) \delta(r-r') \delta(t-t')$$

$$\langle \tilde{f}_{A_2}(r,t) \tilde{f}_{A_2}(r',t') \rangle = (k^{obs}\rho_A^{ss2} + k\rho_{A_2}^{ss} - 2D_{A_2}\rho_{A_2}^{ss}\nabla_r^2) \delta(r-r') \delta(t-t')$$

By using Fourier transforms,⁶ eqs A-3 and A-4 can be solved for the steady-state density-density correlation function on the right-hand side of eq A-2. This yields the radial distribution function exhibited in eq 7.

Theoretical Study of Several Diazaalkenes and Diazaalkyl Radicals

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Abstract: The stabilities of different isomers of several diazaalkenes (diazapropene, diazabutene, and diazapentene) were compared at several levels of theory. For the simplest diazaalkenes, methyl diazene (1,2-diaza-1-propene) and formaldehyde hydrazone (2,3-diaza-1-propene), the two isomers are very close in energy. At the MP4/6-311+G**//MP2/6-31G* level including zero-point and heat capacity corrections, the 1,2-isomer is 0.4 kcal/mol more stable than the 2,3-isomer. Bond dissociation energies were calculated for the formation of the diazapropenyl radical and the diazabutanyl radical. The best calculated BDE for the C—H bond in HN=NCH₃ (1,2-diaza-1-propene) is 87.3 kcal/mol while the N—H bond in H₂NN=CH₂ (2,3-diaza-1-propene) has a BDE value of 86.9 kcal/mol. The lowest energy diazabutene isomer is the hydrazone isomer, 1,2-diaza-2-butene, which is 2.4 kcal/mol more stable than the two azo isomers.

Introduction

The 1,2-diazapropene/2,3-diazapropene (azo/hydrazone) tautomeric pair is similar to the keto-enol system in that shifting a hydrogen in the hydrazone/azo system shifts the double bond from N=N to N=C while in the keto-enol system the double bond shifts from C=O to C=C. However, the azo/hydrazone system has received much less attention both theoretically and experimentally. In the liquid phase, the hydrazone 5,6-diaza-4-decene (C₄H₉NHN=CHC₃H₇) has been found¹ to be 3.3 kcal/mol more stable than the azoalkene 5,6-diaza-5-decene (C₄H₉N=NC₄H₉). By comparison, the keto form of acetone has an enthalpy 13.9 kcal/mol lower than its enol form in the gas phase.² The present study is undertaken to determine which form (azo/hydrazone) is more stable in the gas phase and to understand the factors leading to that preference. By determining the bond dissociation energy (BDE) for loss of the most weakly bound hydrogen, the radical stabilizing ability of the -N=NR group can be determined.

Previous theoretical calculations on formaldehyde hydrazone include a MNDO study³ of the E-Z isomerization of **2**, an ab

Table I. Compound Number, Name, and Formula List of Species Studied

no.	name	formula
1	1,2-diaza-1-propene	HN=NCH ₃
2	2,3-diaza-1-propene	H ₂ NN=CH ₂
3	diazapropenyl radical	HNNCH ₂
4	2,3-diaza-2-butene	CH ₃ N=NCH ₃
5	2,3-diaza-1-butene	H ₂ C=NNHCH ₃
6	1,2-diaza-1-butene	HN=NCH ₂ CH ₃
7	1,2-diaza-2-butene	H ₂ NN=CHCH ₃
8	1,2-diazabutanyl radical	HNNCHCH ₃
9	2,3-diazabutanyl radical	H ₂ CNNCH ₃
10	2,3-diaza-2-pentene	CH ₃ CH ₂ N=NCH ₃
11	3,4-diaza-2-pentene	CH ₃ CH=NNHCH ₃

initio study⁴ on conformations and E-Z isomerizations of **2** and **7** at the MP2/6-31G**//4-31G and HF/6-31G**//4-31G levels, respectively, an ab initio study⁵ of **2** and protonated **2** at the HF/6-31G** level, and a recent study⁶ of **2** and the radical cation

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