

The kinetics of conformational transitions: Effect of variation of bond angle bending and bond stretching force constants

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Conformational transitions in chain molecules have been shown to proceed via a reaction coordinate which is a localized mode involving rotations about bonds, and also bond angle bending and bond stretching. By investigating the kinetics as a function of the force constants (flexibility) for bond angle bending and bond stretching, the role of the localized mode is probed. The study reported here consists of computer simulations of the Brownian dynamics of chain motions, and of kinetic calculations of rates and reaction modes. The theory accurately predicts the relative effects of force constant variations on transition rates determined by simulation.

I. INTRODUCTION

In recent papers we,¹⁻⁴ and others,⁵⁻¹¹ have reported on studies aimed at elucidating the kinetic processes involved in conformational transitions in chain molecules, including polymers. We have taken a two-pronged approach. One avenue involves computer simulations of the Brownian motion of chains³; the other centers on multidimensional kinetic theory calculations.^{1,2} Among the major conclusions which emerge are:

- (1) The activation energy for conformational transitions is observed to be about one *trans-gauche* barrier height.
- (2) There is a certain amount of cooperativity between transitions. The major manifestation of this is a crank-like motion involving counterrotational transitions of two bonds which are second neighbors separated by a *trans* bond (hence two parallel bonds). Such a motion occurs in the cooperative processes $ttt \rightleftharpoons g^+tg^+$ and $g^+tt \rightleftharpoons ttg^+$.
- (3) The reaction coordinate in the neighborhood of the transition state is a localized mode, i. e., as the transforming bond rotates over the energy barrier, neighboring degrees of freedom undergo distortions which are such as to lead to decreasing amounts of motion away from the center of action. Effectively, the reaction coordinate involves significant motion of only a few neighboring degrees of freedom.
- (4) The quantitative predictions of the theory are in reasonably good agreement with simulations, i. e., within a factor of 2 to 3.

A key element in understanding the kinetics of conformational transitions is consideration of the localized modes. In distorting neighboring degrees of freedom to keep the motion localized, the softest degrees of freedom, i. e., bond rotations, are the most favorable to use. In particular, the crank-like counterrotation of

trans-separated second neighbors is very effective.

The study of the reaction coordinate to which we have been referring¹ is a study of small displacements from the transition state. The evidence of the simulations,³ however, is that this same crank-like motion occurs for large displacements; i. e., frequently the counterrotation is brought all the way to the point of a second transition. It is worthwhile to discuss this sequence of events further. First, *one* bond comes near the transition barrier, with all other bonds and other degrees of freedom in equilibrium. This is the activation process and we conjecture that this is why the activation energy is *one* barrier height. Next the system proceeds across the reaction barrier and towards equilibrium in the kinetically most favored manner. Generally this involves motions centered about the path of steepest descent (for equal friction constants) back toward local equilibrium in one of the rotational isomeric states. However, if there are more rapid paths to equilibrium in some other rotational isomeric states, the result will be a kinetically controlled branching into the various channels. This is what leads to some transitions occurring individually, and some as correlated multitransitions.

The above discussion has emphasized the importance of the localized mode, which is the reaction coordinate. Although the localized mode draws heavily on rotation of neighboring bonds, bond angle bending and bond stretching are also involved. It is the purpose of this study to bring out the importance of the latter two types of distortions in the various localized modes (different for each conformation of the molecule), and hence in the reaction kinetics. Specifically, we will study the rate of transition as a function of the force constants for bond angle bending and bond stretching. This will be done both by computer simulations (Sec. II) and kinetics calculations (Sec. III). We will show that the effect of the variation of these force constants, particularly bond angle bending, is significant; and that the theory quite accurately predicts the relative variation of rate observed in the simulations.

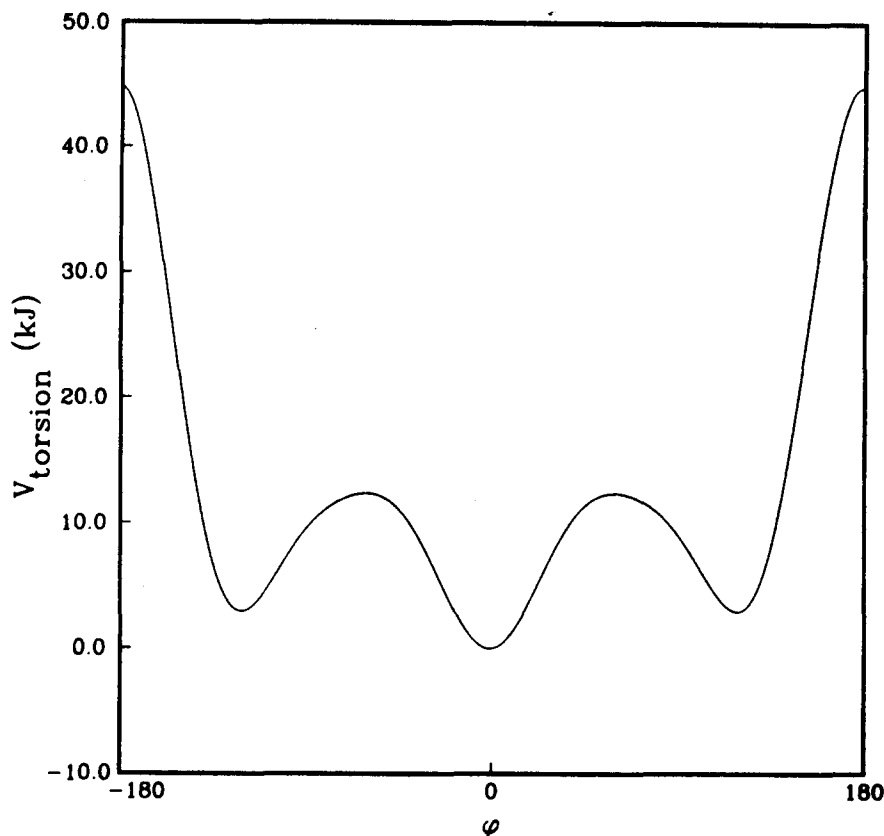


FIG. 1. The potential for rotation of a single bond in the chain. *Trans* corresponds to an angle of zero.

II. BROWNIAN DYNAMICS SIMULATIONS

Our Brownian dynamics simulations have been described in Ref. 3. The model consists of 200 bonds either in a ring or with periodic boundary conditions in chain space. Thus there are no ends and all bonds are equivalent. The total potential is divided into three parts:

$$V = V_b + V_\theta + V_\phi. \quad (1)$$

One part keeps the bond lengths close to 0.153 nm:

$$V_b = \frac{1}{2} \gamma_b \sum_i (b_i - b_0)^2, \quad (2)$$

where $b_i \equiv |r_{i+1} - r_i|$ is the bond length, and $b_0 = 0.153$ nm. Another part of the potential keeps bond angles close to the tetrahedral value:

$$V_\theta = \frac{1}{2} \gamma_\theta \sum_i (\cos \theta_i - \cos \theta_0)^2, \quad (3)$$

where θ_i is the supplement of the angle between bonds i and $i+1$, and $\cos \theta_0 = \frac{1}{3}$. Torsional (rotational) motion about the bonds takes place in a potential with *trans* and *gauche* states separated by barriers, as in Fig. 1:

$$V_\phi = \gamma_\phi \sum_i \sum_{n=0}^5 a_n \cos^n \phi_i. \quad (4)$$

The explicit potential parameters, representative of polyethylene, have been listed previously.¹² We note here only that $\gamma_b/m = 2.5 \times 10^{27} \text{ s}^{-2}$ and $\gamma_\theta/m b_0^2 = 5.5534 \times 10^{26} \text{ s}^{-2}$ (m is taken as 0.014 kg/mol). This potential will be the standard and will be denoted V_S . In this paper we shall consider a potential where both γ_θ and γ_b are

multiplied by $10^{1/2}$ (termed V_G), and one where γ_θ and γ_b are divided by $10^{1/2}$ (termed V_L).

No account has been taken of the interaction between nonbonded carbons, or of hydrodynamic coupling. All chain substituent groups are regarded as collapsed on the backbone carbon centers. These approximations are not expected to modify seriously the qualitative nature of the transition mechanism.

The simulations consist of numerical solution, using a recently developed algorithm,¹³ of Langevin's equations (force composed of potential, frictional, and random terms). The high friction limit is taken. Rates of transition are determined by a study of first passage times from the bottom of one rotational potential well to the bottom of another, and by application of hazard analysis.¹⁴

In Table I we list the *trans*-to-*gauche* transition rate for the potentials V_L , V_S , and V_G at a temperature of 372 K (barrier height E^* equal to $4k_B T$). The effect of

TABLE I. Rate of *trans* \rightarrow *gauche* (+ or -) transitions at 372 K by simulation and calculation.

Potential	Simulation		Calculation	
	Rate (ns ⁻¹)	Relative rate $k_{G \text{ or } L}/k_S$	Rate (ns ⁻¹)	Relative rate $k_{G \text{ or } L}/k_S$
V_L	7.9	1.80	3.26	1.78
V_S	4.4	...	1.83	...
V_G	2.8	0.65	1.26	0.69

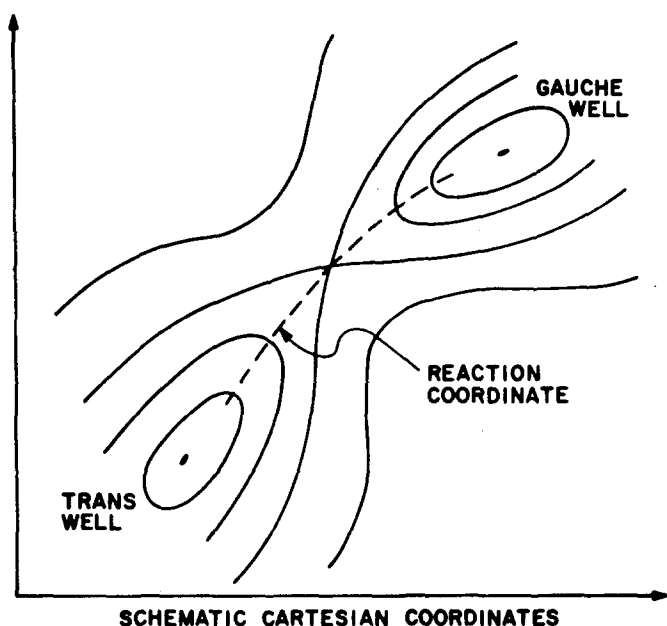


FIG. 2. Schematic representation of the potential energy (level lines) in the multidimensional space of the carbon centers' Cartesian coordinates. Transitions go from one rotational-isomeric-state well to another by passing near the saddle point. The reaction path (for equal friction constants) is the path of steepest descents.

increasing force constant in decreasing the transition rate is evident. The results will be interpreted in the following section.

It is difficult to reach quantitative conclusions about the influence of the above varying force constants on the fraction of second-neighbor cooperative transitions (as measured by c_2 of Ref. 3). The quantity c_2 goes down slightly with decreasing γ_θ and γ_b , as expected, but the observation is probably not statistically significant for the length of the simulations used in this study. Back transitions, as given by c_0 , more clearly decrease. These matters are not central to the present paper, and will not be pursued further here.

One technical matter about the simulations for V_L should be mentioned. The probability of the bond angle θ going all the way to zero is not negligible compared to the probability of a bond being near the rotational barrier. For instance, the probability that $\cos \theta > 0.9$ is 0.005. An inversion of the bond angle cannot be distinguished from a bond rotational transition. Therefore, all real or apparent transitions when $\cos \theta > 0.9$ have been disregarded. The neglect of some real transitions thereby makes the estimate of k_L too low, probably by a few percent.

III. KINETIC CALCULATIONS

Let us begin by describing the kinetic calculations of Ref. 1. The conformational transition may be regarded as motion across a saddle pass of the potential in a multidimensional space in which the axes are the various degrees of freedom (e.g., Cartesian coordinates of the carbon centers). We schematically represent this po-

tential function for two degrees of freedom in Fig. 2. The wells correspond to metastable rotational isomeric conformations, and these are separated by a saddle pass (where level lines cross).

A crucial step in the kinetics calculation^{1,2} consists of identifying the reaction coordinate in the neighborhood of the saddle point. When the friction constant on all centers is the same this is the path of steepest descent in Cartesian variables (modification must be made when directions of different mobility exist¹⁵). The analysis consists first of expanding the potential to quadratic terms in displacement from the saddle point. The reaction coordinate is in the direction (in the usual sense of stable normal coordinate analysis) of the eigenvector corresponding to a negative eigenvalue of the interaction matrix (negative curvature). One then treats the "reaction" as occurring along the path of steepest descent, with the energy along the path modified to include an entropy-like term which accounts for the freedom of motion in the orthogonal directions. Then a one-dimensional theory may be applied to calculate the rate constant, e.g., Kramer's theory for motion in systems with friction. (The multidimensional version of Kramer's theory was developed by Brinkman¹⁶ and by Landauer and Swanson.¹⁷)

As discussed in the Introduction, the reaction coordinate in the neighborhood of the saddle point is a localized mode, in which localization is achieved by motion of neighboring degrees of freedom accompanying the rotation of the central bond as it goes over the reaction barrier. Use of other bond rotations are favored because these modes are soft, but a certain amount of bond angle bending and bond stretching is also employed. Increasing the force constants for these degrees of freedom inhibits localization of the reaction mode. This decreases the transition rate since the more of the tail that moves, the higher the total frictional resistance to motion. (The term "tails" is used to refer to the chains attached to the transforming bonds.²)

The transition rate is different for each conformation of the tails attached to the transforming bond. The observed rate is determined by averaging over these various tail states with an equilibrium distribution (the explicit method of averaging, partly Monte Carlo in character, is described in Ref. 1). In Table I the calculated average rates for transition of the central bond of a chain of 28 carbon centers is reported. The results for the various potentials are compared with those observed in the simulation. In magnitude the calculated rates are too low by a factor of 2 to 3. Some possible reasons, mainly the failure to account for correlated transitions, are discussed in Ref. 1. While the absolute values are not completely accurate, the calculation does predict quite well the relative effect of varying γ_θ and γ_b . Therefore, we believe that the theory can safely be used to conclude that the major influence of γ_θ and γ_b on the rate is through the modification of the localized modes, which are the reaction coordinates.

The theoretical calculations have been extended to a more detailed study of the effects of variation of force constants. Table II indicates the effect on the average

transition rate of independently varying the force constants γ_θ and γ_b . One sees that the major impact arises from variations of γ_θ . Very little bond stretching is possible, so little is used in the localized mode. Decreasing this small amount by increasing γ_b does not significantly delocalize the mode.

Table III contains the results of a study in which various specific tail conformations are considered, and the transition rate is calculated as a function of γ_θ . Specifically a $t \rightarrow g^*$ transformation is taking place in the central bond of a 16 carbon center chain with tails which are all *trans* except for the bonds which are first or second neighbors to the transforming one. The effect of first neighbor *gauche* bonds is brought out. It was mentioned earlier that when the first neighbor bond is *trans* the second neighbor is parallel, and can efficiently contribute to localization by counterrotation. Conversely, when the first neighbor is *gauche* the motion is more far-ranging and slower. When one first neighbor is *trans* and one *gauche* tail holds relatively stationary, and what tail motion does occur shifts over to the *trans* side. The rate is only slightly diminished. When both first neighbors are *gauche* the rate is significantly decreased. From Table III it is evident that when γ_θ is lowered, bond angle bending contributes more to the mode localization, and a first neighbor *gauche* has a lesser effect. This shows up not only in the rate but also in the localized mode (not displayed here).

Second neighbor *gauche* bonds do not affect the bond parallelism. They do, however, bring more distant parts of the tail closer to the axis of the central bond's rotation, and thus decrease the overall distance which units of the tail must move in the reaction mode.¹ This effect is not strongly related to bond angle distortion. In Table III one sees that in this case the rate is only slightly affected by variation of γ_θ .

IV. RIGID VS FLEXIBLE CONSTRAINTS

This study raises new questions in connection with the problem of the use of flexible vs rigid constraints in modeling the behavior of chain molecules.^{18,19,9} Rigid constraints generally take the form of fixed bond lengths and angles, while flexible constraints only maintain the system near the equilibrium value with potentials such as Eqs. (2) and (3). It is known that the two types of systems differ in their equilibrium properties, in general, no matter how large the flexible force constants

TABLE II. Calculated rates (ns^{-1}) of *trans* \rightarrow *gauche* (+ or -) transition as a function of force constants for bond angle bending and bond stretching.

$\gamma_b/\gamma_\theta s$	$\gamma_\theta/\gamma_\theta s$		
	0.1	1.0	10
0.1	5.62	2.10	1.31
0.5	5.27	1.87	1.14
1.0	5.21	1.83	1.11
10	5.15	1.78	1.07
100	5.14	1.76	1.06

TABLE III. Calculated rates (ns^{-1}) of *trans* \rightarrow *gauche* (+ or -) for specific tail conformations, as a function force constant for bond angle bending.

Initial conformation ^a	$\gamma_\theta/\gamma_\theta s$		
	$10^{-1/2}$	1.0	$10^{1/2}$
(ttttt)t(ttttt)	6.69	5.06	3.99
(ttttg*)t(ttttt)	4.88	3.88	3.44
(ttttg*)t(ttttt)	5.39	2.82	1.27
(ttttg*)t(g*tttt)	1.49	0.60	0.40
(ttttg*)t(g*tttt)	1.59	0.25	0.15
(ttttg*)t(g*tttt)	1.22	0.37	0.25
(ttttg*)t(tg*tttt)	7.19	6.65	6.31

^aThe transition is $PtQ \rightarrow Pg^*Q$, where P and Q are tail conformations.

are. The difference is an entropic factor. One can define a potential (temperature dependent), the Fixman potential, which compensates for this difference in equilibrium. It has been proposed to use this same potential to compensate for the differences in mechanics,⁹ and it can be shown that in certain limits this is appropriate. However, in general there are differences in dynamical behavior. A numerical test of the effect of rigid vs flexible constraints on conformational transition rates by Montgomery, Holmgren, and Chandler¹⁰ showed differences which could be attributed totally to the entropy, but the dynamical effects shown in this paper would be expected to be unimportant for butane, the system they considered. The kinetics calculations of Sec. II when applied to butane show a 3% decrease in transition rate upon increasing γ_θ and γ_b by $10^{1/2}$, as opposed to the 30% decrease for C_{28} (Table I). It would be of interest to see the degree to which the conformational transition rate reported here for the potential V_G approaches the rate for a comparable rigid system. Perhaps some group with the computer programs will wish to perform the rigid simulation.

The sensitivity of the rates and reaction coordinates to variation of γ_θ and γ_b leads one to expect that the use of rigid constraints in chain models may be inappropriate. It is not at all clear what the localized modes would be like with rigid constraints or even if they exist. (The common model of chains with right angle bonds may not be general enough because then all even neighbor bonds are always either parallel or antiparallel.)

V. CONCLUSIONS

In this paper the effect of tightening or loosening the freedom of motion for bond angle bending and bond stretching on the conformational transition kinetics is examined. The changes in rate are determined by Brownian dynamics computer simulation. Kinetic calculations closely parallel the relative changes of rates. The variations of rates are easily rationalized in terms of the expected changes in the localized modes, which are the reaction coordinates. This lends support to the proposition that the localized modes should be the proper

focus for the development of a qualitative understanding of conformational transition kinetics.

Further studies are forthcoming of the effects on transition rates of chain branching,²⁰ and variations of individual masses and friction constants.¹⁵

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