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Research paper

Dynamically concerted and stepwise trajectories of the Cope rearrangement of 1,5-hexadiene

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ABSTRACT

Molecular dynamics of the [3,3]-sigmatropic (Cope) rearrangement of 1,5-hexadiene were performed with the B3LYP/6-31G(d) density functional theory method. We found that the forming or breaking bond lengths of sampled transition state geometries are 1.97 Å ± 0.15 Å, which is defined as the transition zone. Two hundred and thirty trajectories were propagated. Ninety-five percent of the trajectories connect reactant to product. Five percent of the trajectories involved recrossing. For the reactive trajectories, the time to traverse the transition zone was 35 ± 16 fs. Ninety-four percent of these trajectories are dynamically concerted, while the remaining six percent are dynamically stepwise.

1. Introduction

The Cope rearrangement is a classic example of a pericyclic sigmatropic rearrangement [1]. The simplest case of the Cope rearrangement is the degenerate rearrangement of 1,5-hexadiene shown in Scheme 1a [2]. The first examples of this rearrangement were discovered in 1940s by Cope and Hardy, but the mechanism of this reaction remained controversial into the 1990s. The debate was about timing of bond formation, that is the nature of the transition state (TS) and whether or not there is an intermediate [3–5]. Scheme 1b shows three limiting cases. The transition state could be synchronous and concerted, also called pericyclic or aromatic, in which C1—6 bond forms and C3—C4 bond breaks simultaneously. There are also two bonding stepwise possibilities [6]. If the C3—C4 bond forms first, the TS is called associative, and the reaction may actually involve cyclohexane-1,4-diyl as intermediate. Alternatively, if the C1-C6 bond cleaves first to form two allyl radicals, the reaction is termed dissociative, and may involve two weakly interacting allyls as a TS, or an intermediate radical pair.

The Cope rearrangement of a deuterium-labeled 1,5-hexadiene has an experimental activation barrier of 33.5 kcal/mol [7]. The energy to generate two allyl radicals is 26 kcal/mol above the activation barrier and the energy estimated for the cyclohexane-1, 4-diyl is 11 kcal/mol higher than the experimental barrier. Concerted bond-breaking and bond-making lower the activation enthalpy of the transition state, with respect to the formation of diradicals in dissociative TS or associative TS. The delocalized bonding in the transition structure for the Cope rearrangement can be represented schematically as a resonance hybrid, containing contributions from the two diradical extremes. This representation has been applied in understanding the substituent effects caused by radical-stabilizing groups at C(2) and C(5), as well as at C(1), C(3), C(4), and C(6). The Cope TS was found to be a chameleonic TS by Doering, because of its capability to respond in different ways to the substitution of radical-stabilizing substituents at the two different types of carbons [8].

Previous computational studies have elucidated the nature of the transition state and substituent effects on the Cope rearrangement [9–11], but there have not been molecular dynamics simulations for these reactions. Molecular dynamics simulations have been reported for other pericyclic reactions, including Diels-Alder reactions [12–15], 1,3-dipolar cycloadditions [16], and, [1,2]- and [2,3]-sigmatropic shift reactions [17]. These studies have given insights into the intrinsic dynamical properties of the reactions, such as timing of bond formation in Diels-Alder and dehydro-Diels-Alder reactions [12,18], dynamical matching in determining the selectivity of [1,3]-sigmatropic migration of bicyclo[3.2.0]hept-2-ene [19], and femtosecond investigation of the retro-Diels-Alder reactions of norbornene and isomers [20].

The Cope rearrangement is involved in the PES bifurcation for dimerization of cyclopentadiene. It is a saddle point that resides between the two products that result from the ambimodal TS. Cope rearrangements also interconnect the [4+2] and [6+4] adduct

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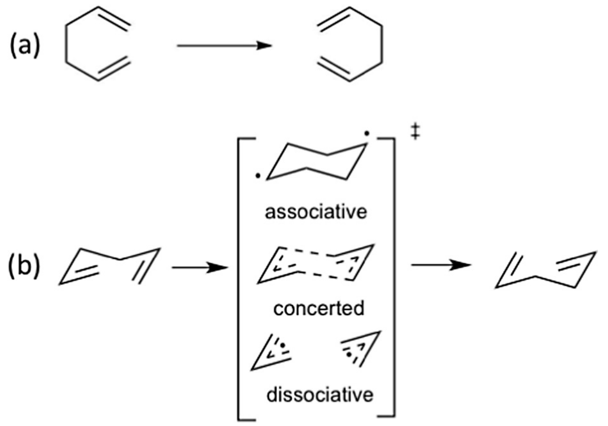

Scheme 1. Cope rearrangement and its mechanisms.

formed by ambimodal TSs in the biosynthesis of heronamide [21] and in the SpnF-catalyzed Diels-Alder reaction [22]. Here we explored the dynamics of the parent Cope rearrangement reaction by reactive trajectory simulations, and elucidate the time-resolved mechanism for the reaction.

2. Computational methods

All density functional theory (DFT) computations were performed using Gaussian 09 [23]. Geometry optimizations were carried out at the B3LYP/6-31G(d) level of theory. Normal vibrational mode analysis at the same level confirmed that optimized structures were minima or transition states (TS). B3LYP/6-31G(d) was found to give qualitatively the same conclusions about the relative energetics of the parent Cope rearrangement as previous high accuracy studies [24]. Direct molecular dynamics (MD) simulations were performed for the parent Cope rearrangement of 1,5-hexadiene in the gas phase. Because of the thousands of quantum calculations required in the dynamics simulations, these were performed at the (U)B3LYP/6-31G(d) level of theory. Quasiclassical trajectories (QCTs) were initialized in the region of the potential energy surface near the TS. Normal mode sampling involves adding zero-point energy for each real normal mode in the TS, and then Boltzmann sampling to afford a set of geometries reflecting the thermal energy available at 300 K with a random phase. Note no additional velocities added other than vibrations along the mode perpendicular to the reaction coordinate. The trajectories were propagated forward and backward, until the formation of the product, or the reactant was observed. Reactant or product are defined as having one bond shorter than 1.5 Å, and the other bond longer than 4 Å. The classical equations of motion were integrated with a velocity-Verlet algorithm using Singleton's program Progdyn [25], with the energies and derivatives computed on the fly by the UB3LYP method using Gaussian 09. The step length for integration was 1 fs.

3. Results and discussion

The concerted transition structure for the parent Cope rearrangement is shown in Fig. 1a. The structure is a chair conformation with C2 h symmetry. The boat conformation is also transition structure, but is 5.7 kcal/mol higher in energy than the chair, and is not discussed since then [3]. The forming and breaking bond lengths are 1.95 Å. Normal mode sampling was conducted on the transition structure to obtain an ensemble of transition state geometries, which are shown as an overlay in Fig. 2b. The contour diagram for the Cope rearrangement (shown in Fig. 2c) is constructed by two-dimensional potential energy surface scan along bonds 1 and 2. The landscape is symmetric along the diagonal line because of the degeneracy of the reactant and the product. The blue regions representing low energy reactant and product, and red region representing the separated radical pairs. The yellow regions in the lower left is the cyclohexane-1,4-diyl, which is not a minimum from the 1,5-hexadiene surface. The blue dots labeled on the graph represent the sampled transition state geometries, which are on the TS dividing surface. We defined the transition zone as that region of the surface that embraces 98% of the transition state geometries obtained by normal mode sampling. The transition zone for either bond is 1.97 Å ± 0.15 Å, which is shown as the white ellipse in Fig. 1. The finite thickness of the transition zone reflects the projection of $3N-7$ vibrational motions on the forming and breaking bonds. Reaction dynamics trajectories were initiated from the transition state geometries and propagated forward and backward until the formation of the reactant or the product occurred.

Fig. 2 shows a typical reactive trajectory from the simulation. At −47 fs, bond 1 is at 1.55 Å, while bond 2 is at 3.55 Å. This is a reactive conformation of the reactant. At 0 fs, both bond 1 and bond 2 are at 1.95 Å. This geometry is right in the center of the transition zone. At 57 fs, bond 1 elongates to 4.06 Å and bond 2 forms at 1.58 Å.

Previously, we defined the time gap for the formation of two bonds to quantify the timing of bond formation for cycloadditions when a bond achieved 1.6 Å, that bond is considered to be formed. The concept is not applicable to the Cope rearrangement because the reaction involves formation of one bond, and cleavage of the other. For this case, we define the time to traverse the transition zone to characterize these reactions. For an individual trajectory, the time gap is the time it takes to pass through the transition zone, demonstrated by the white ellipse. The time in the transition zone for this representative trajectory is 10 fs. Eyring's transition state theory defines the pre-exponential factor, kT/h on the basis the rate of translational motion of atoms. The lifetime of a transition state to make two atoms form a bond with thermal energy is 60 fs at room T. We consider a Cope rearrangement trajectory to be dynamically concerted if the time in the transition zone is $\leq$60 fs. When atoms come together, but then undergo one or more vibrations before completely bond formation, we consider this a dynamically stepwise process.

Two hundred and thirty trajectories were propagated to elucidate the statistical distribution of individual molecules passing through the TS dividing surface. Ninety-five percent of the trajectories are reactive. The remaining five percent go into the transition zone, and recross to reactant. Fig. 3a shows an overlay of bond-making and bond-breaking distances in the reactive trajectories on the contour plot of the PES. Fig. 3b displays the evolution of bond-forming and bond-breaking distances in reactive trajectories. The bond 1 decreases rapidly from 3.5 Å to about 2.1 Å, levels out in the transition zone, and decreases again to form a single C—C bond. Bond 2 began to stretch once the forming bond length reaches 2.70 Å or less. Within the transition zone, 1.82–2.12 Å, the bond-making and bond-breaking behaviors are approximately in a mirror image relationship. As described, we have defined 60 fs as the boundary between dynamically concerted and stepwise mechanism. It turns out that 94% of the trajectories are dynamically concerted, while the remaining 6% are dynamically stepwise. Statistically, the time in the transition zone was calculated to be 35.0 ± 16.0 fs.

Fig. 4 shows snapshots from a typical dynamically concerted trajectory as it passes through the transition zone. The time in the transition zone is 29 fs, which is comparable to a normal C—C bond vibration lifetime. The forming bond length decreases continuously from −14 fs to 15 fs. This behavior is what one would expect for a reactive molecule passing through the transition

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