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Dynamics of 1,3-Dipolar Cycloaddition Reactions of Diazonium Betaines to Acetylene and Ethylene: Bending Vibrations Facilitate Reaction**

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The activation energy of a 1,3-dipolar cycloaddition reaction is linearly related to the energy $\Delta E_d^{\ddagger}$ that is required to distort the dipole and dipolarophile to form the transition-state (TS) geometry.[1,2] This discovery complements previous theories of dipolarophile reactivity, which emphasized the interaction between frontier molecular orbitals (FMOs) of the reactants.[3,4] The correlation with distortion implies that the vibrational excitation of the reactants is an important feature of the mechanism. We have now explored the reaction dynamics of three typical 1,3-dipoles with acetylene and ethylene. In these six reactions, which span a range of 1,3-dipoles, barriers, and reaction energies, we find that specific vibrations must be excited to make the reaction possible.

Huisgen established the generality of 1,3-dipolar cycloaddition reactions and clearly showed that these reactions have all the operational signatures of concert, that is, stereospecificity, lack of trappable intermediates, and substituent effects; all are consistent with two-bond processes.[5] Firestone maintained that a stepwise reaction with a cyclo-diradical might provide an alternative mechanism; [6] the two mechanisms are contrasted in Figure 1. Experiments show that a cyclo-diradical cannot have a significant barrier to closure.[7] While it seems clear that no intermediates are formed in most cases, dynamics calculations are necessary to differentiate between a concerted transition state (**1**) and a two-stage process that involves the cyclo-diradical (**2**), which has no significant barrier for the formation of the second bond.

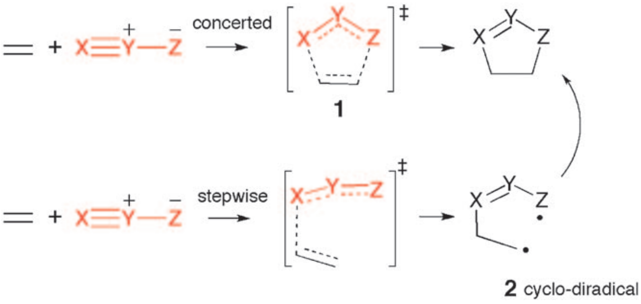

Figure 1. Concerted and stepwise mechanisms of 1,3-dipolar cycloaddition reactions.

The transition structures and transition vectors (imaginary frequency eigenvectors) for the reactions of dipoles **3**–**5** (Figure 2) with acetylene and of ethylene are shown in Figure 3. The transition vectors are all similar and have three main components: 1) the symmetric stretch of the incipient pair of σ bonds, 2) a dipole bending mode, and 3) a symmetric C_2H_n bending mode. The bending modes that make up the transition vector lead to the distortions required for reaction to occur. It is useful to have an estimate of their contribution to $\Delta E_d^{\ddagger}$. In the harmonic approximation, the potential energy of distortion of a given reactant at the TS is the sum of contributions from the normal modes of each reactant. This relation is accurate only for small displacements from equilibrium, but we find that the sum of harmonic distortion energies deviates from the B3LYP/6-31G* TS distortion energy by only 7–16 % in all cases except for the acetylene distortions. This is a small enough error to be qualitatively useful. Table 1 shows the bending mode contributions to reactions **3**–**5**. The bending mode constitutes 84–85 % of the N_2O distortion energy, 56–63 % of the HN_3 distortion energy, and 64–65 % of the CH_2N_2 distortion energy. $\Delta E_d^{\ddagger}$ is dominated by the N-N-Z dipole bending modes, with a much smaller contribution from the symmetric bend of C_2H_n. The dipole bends account for 45–70 % of $\Delta E_d^{\ddagger}$ for reactions **3**–

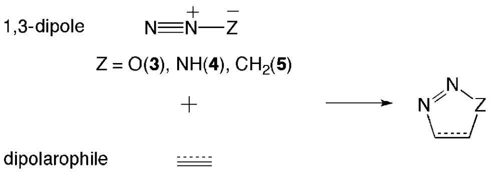

Figure 2. 1.3-Dipolar cycloaddition reactions of diazonium betaines with ethylene or acetylene.

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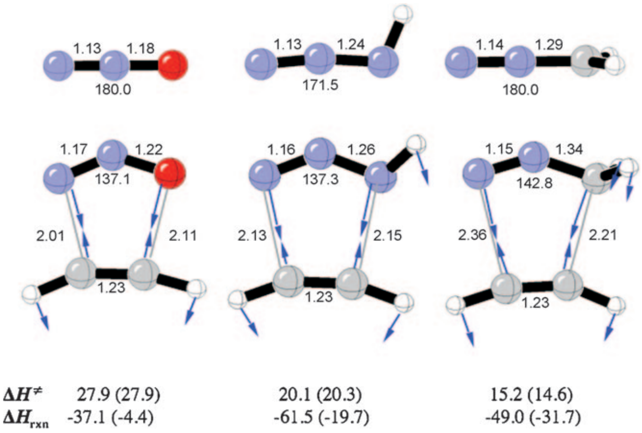

Figure 3. Reactants, transition structures, and transition vectors of reactions of 1,3-dipoles **3**–**5** with acetylene and with ethylene. The direction and relative amplitude of the major movements of atoms in the transition vectors are shown by blue arrows. CBS-QB3 activation and reaction enthalpies (kcal mol^{-1}) at 0 K are given below the transition structures.

Table 1: Comparison of TS distortion energies of reactants with bending mode contributions.

		$\Delta E^{\ddagger}_{\text{dist}}$[a]	$\varepsilon_{\text{bend}}$[b]	$\Delta E^{\ddagger}_{\text{dist}}/\Sigma\varepsilon_i$[c]
$C_2H_4+N_2O$	N_2O	31.2	26.5	0.91
	C_2H_4	6.1	3.7	0.90
$C_2H_4+N_3H$	N_3H	21.0	11.7	0.93
	C_2H_4	5.4	3.4	0.90
$C_2H_4+CH_2N_2$	CH_2N_2	16.8	10.8	0.84
	C_2H_4	4.7	3.0	0.92
$C_2H_2+N_2O$	N_2O	28.2	23.8	0.90
	C_2H_2	6.5	3.4	0.63
$C_2H_2+N_3H$	N_3H	18.7	11.8	0.91
	C_2H_2	6.3	3.6	0.66
$C_2H_2+CH_2N_2$	CH_2N_2	15.1	9.8	0.84
	C_2H_2	6.8	3.5	0.61

[a] TS distortion energy (kcal mol^{-1}) of individual reactants in each of six TSs. [b] Details of the contributions of bending modes (kcal mol^{-1}) are given in the text. Anharmonic corrections (right column) have been applied. [c] Anharmonic correction = ratio of $\Delta E^{\ddagger}_{\text{dist}}$ to the sum of harmonic mode energies.

5. The correlation of $\Delta E^{\ddagger}_{\text{d}}$ with barriers[3] is thus largely due to the dipole bending energy.

Classical trajectories were propagated in order to obtain the contributions to activation barriers from reactant vibration, rotation, and relative translation. These were performed with a customized version of the Venus[8] dynamics program, in which Gaussian 03[9] was used to compute B3LYP/6-31G* energies and gradients. Trajectories were initialized at the TS and propagated in the reactant direction to a large separation by using two initialization methods. Firstly, quasi-classical trajectories (QCT)[13] were initialized by TS normal mode sampling[10–12] with only zero-point vibrational energy (ZPE) in each normal mode, 0.6 kcal mol^{-1} in the reaction coordinate (the mean value at 298 K), and zero rotational energy. We computed 64 QCTs for each reaction. Secondly, a single trajectory (ST) was propagated from TS to reactants with no vibrational or rotational energy, not even ZPE, and 0.6 kcal mol^{-1} in the reaction coordinate. There is only one ST per reaction. We find that an ST approximates the mean behavior of the QCTs, and the absence of random vibrational noise gives a clearer picture of vibrational energy flow. In recent studies, ST and QCT results have been shown to be qualitatively similar.[13]

Appropriate sampling of the TS in QCT is intended to give a computed reactant energy distribution that strongly resembles that of the reactants whose collisions lead to the TS. An overlay of the starting geometries for these calculations is shown in Figure 4. This is an approximation of the various geometries sampled during a reaction when the reactants collide and pass through the transition-state region and proceed to form the products. Dipole and dipolarophile bending are the hallmark of all these geometries; collisions not in the region will be unproductive and the reactants will rebound to reactants.

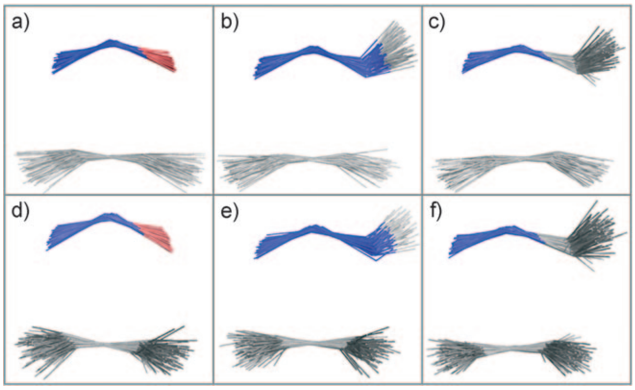

Figure 4. Overlay of 64 starting geometries of QCT trajectories for reactions of 1,3-dipoles **3**–**5** with acetylene (a, b, c) and ethylene (d, e, f).

The ST for $N_2O + C_2H_2$ projected onto the 2D space of the N-N-O linear bending angle ϕ (defined over 0–360° in this coplanar trajectory) and the distance R from the central N atom to the midpoint of the C–C bond is shown in Figure 5. As the reactants approach from the right, the minimum energy path follows the $\phi = 180°$ line (linear N_2O), but then

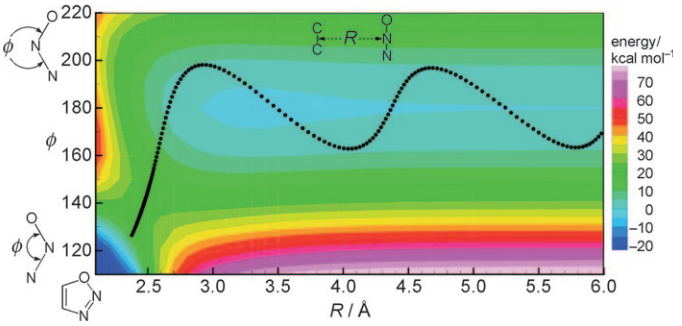

Figure 5. ST for N_2O + C_2H_2 at 1 fs intervals. The surface was computed by constrained minimizations on a grid of bending angle ϕ and the distance R from the central N atom to the midpoint of the C–C bond.

curves sharply down to reach the bent TS. If the dipole bending mode has insufficient vibrational energy (low amplitude up–down motion close to $\phi = 180°$), conservation of momentum implies that the trajectory would continue moving left, hit the wall, and rebound without reacting. Only those N_2O molecules with vibrationally excited bending modes can turn the corner and pass through the TS. The situation is similar to atom transfer reactions with late TSs,[14] in which vibrational excitation of the reactants is needed for their reaction.

The amounts of vibrational, rotational, and relative translational energy in the separated reactants were computed by using standard methods[15] at the end of the QCT and ST retro-cycloadditions (see Table S1 in the Supporting Information). The QCT and ST results are similar; both predict much more vibrational excitation in the 1,3-dipole than in C_2H_n. The reactant vibrational energy in STs is within 0.2 kcal mol^{-1} to 1.8 kcal mol^{-1} of the QCT reactant vibrational energy in excess of ZPE. QCT and ST give approximately the same amount of translation, equal to 80–90 % of the barrier, and little rotation.

To compute the vibrational energy of the dipole bending modes immediately prior to collision, we applied the velocity projection method of Raff[16] to the separated reactants over the final 200–250 fs of each retro-cycloaddition. The method involves averaging the kinetic energy of each mode (degenerate bends are combined), obtained each femtosecond by projecting the instantaneous Cartesian velocities onto the normal mode vectors (see the Supporting Information for a description of the method). The result is that the N-N-Z dipole bending modes have by far the largest amount of vibrational excitation in either reactant. The distribution of these modes from QCTs are shown in Figure 6. The low- and high-energy edges of the distributions show a clear difference among the dipoles. Vibrational excitation is highest in N_2O and lowest in CH_2N_2, which is the same order as the dipole bending distortion energies in Table 1. Mode-selective excitation of dipole bending is expected to increase the reaction rate; no other mode should have much effect.

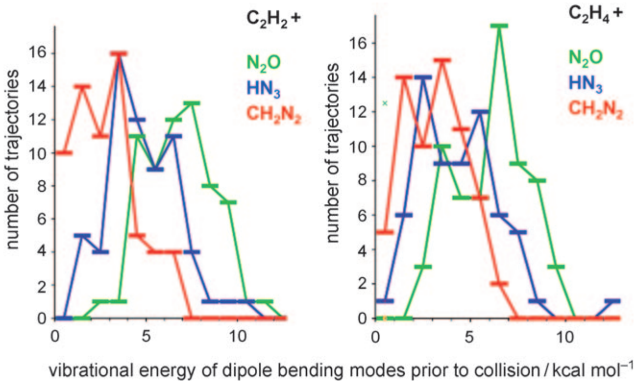

Figure 6. Distribution of energy in the two N-N-Z dipole bending modes of QCT trajectories. The bin width is 1 kcal mol^{-1}.

For the dipolar cycloaddition reactions of **3**–**5** we have shown that: 1) Reaction cannot occur without a large amount of vibrational excitation in the dipole bending modes. This means that dipole bending excitation is as much a part of the mechanistic discussion as TS structure. 2) While translational energy supplies the largest amount of energy needed to reach the TS, dipole bending supplies the bulk of the remainder. 3) The trend in bending excitation required of each dipole parallels the trend in TS distortion energy $\Delta E_d^{\ddagger}$. 4) The largest contribution to $\Delta E_d^{\ddagger}$ comes from the dipole bending modes. 5) Dipole bending excitation is inseparable from the concerted nature of the mechanism and the cyclic geometry of the TS.

The 1,3-dipolar cycloaddition reactions studied here all involve thermal excitation of bending vibrations and collisions in a fashion that brings the termini into maximum overlap between orbitals of the two reactants. Collisions that involve one-center overlap to form the cyclo-diradical in a stepwise mechanism are much higher in energy and are not productive. For those reactions that are stepwise and involve the rate-determining formation of a diradical, bending vibrations and distortion energy should be less important than in the concerted processes investigated here.

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