Combining Quantum Mechanical Reaction Pathways with Force Field Lattice Interactions To Model a Solid-State Phototransformation

Amy E. Keating, Steve H. Shin, K. N. Houk,* and Miguel A. Garcia-Garibay*

Department of Chemistry and Biochemistry
University of California
Los Angeles, California 90095-1569

What interactions in a crystal lattice allow some reactions to occur readily and yet forbid other similar transformations from occurring at all? This question has led researchers to develop a variety of theoretical and computational models for the study of crystal reactivity.[1−6] We now report our application of a new computational approach to a highly selective solid-state carbene rearrangement. The solid-state phototransformation of diazo **1** to stilbene **3** occurs with very high stereoselectivity (>96%) in a crystalline lattice.[7] By contrast, the selectivity of the reaction in solution or in an amorphous solid is low; the solution reaction yielding four products, **3**−**6**, and a glass two, **3** and **4** (Scheme 1).[7] The reaction proceeds through carbene intermediate **2**,[8] which can rearrange through either a 1,2-hydrogen shift (**3**, **4**) or a 1,2-phenyl migration (**5**, **6**). We have simulated this solid-state transformation by calculating a reaction trajectory in the gas phase with *ab initio* theory, and then using molecular mechanics to investigate the interaction energy of this reacting molecule with other molecules in the crystal.[9] Our calculations show little or no increase in steric energy for the formation of **3**, while there is a large barrier to the formation of **4** and **5**, which are experimentally found in only minute quantities.

Our approach involves examining the effect of a crystalline environment on an entire gas-phase reaction trajectory. Many factors other than the gas-phase energy may determine the location of the solid-state transition state.[10] Our method considers the possibility that unfavorable nonbonded interactions with the host lattice can raise the energy of the transition state and also move it to a point earlier or later on the reaction trajectory.

Figure 1 shows the X-ray geometry of 1-(4′-biphenyl)-2-phenyldiazopropane (**1**) and its solid-state photoproduct (*Z*)-1-
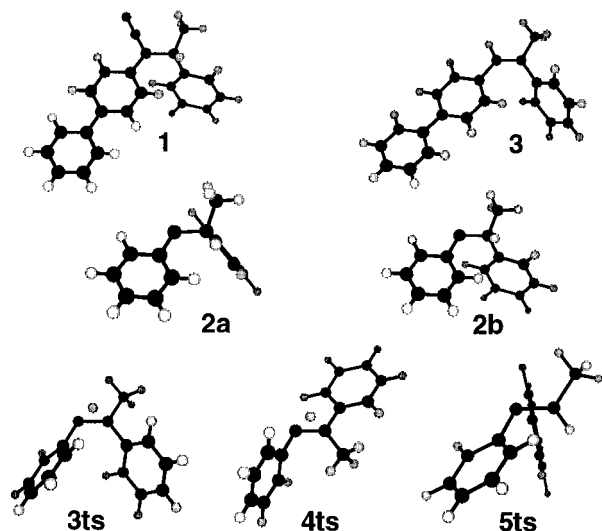
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Figure 1. X-ray structures of diazo **1** and stilbene **3**. RHF/3-21G geometries of the following: (**2a** and **2b**) two conformers of carbene **2**; (**3ts**) *cis* H shift transition state; (**4ts**) *trans* H shift transition state; (**5ts**) Ph shift transition state.

Scheme 1
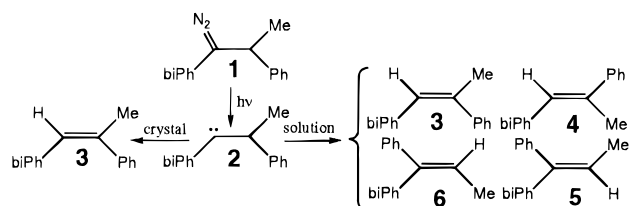
(4′-biphenyl)-2-phenylpropene (**3**). There is high structural similarity between the two end points of the reaction, suggesting high solid-state solubility, but the X-ray geometry tells us nothing about intermediate points on the reaction path. For calculation of structures on the reaction trajectory the second ring of the biphenyl substituent was removed to expedite RHF/3-21G optimizations.[11] Figure 1 shows two conformations of 1,2-diphenylpropylidene; **2a** is the local minimum closest to the geometry of **1**, while **2b** is the result of a constrained optimization described below. Also shown are transition states leading to solution products **3**−**5** (**3ts**−**5ts**).[12,13] Transition state **3ts** has a greater structural similarity to diazo **1** than **4ts** or **5ts**, although it is less similar to **1** than the final product **3** is (heavy atom rms with **1** = 0.491 and 0.340 Å for **3ts** and **3**, respectively). Although the RHF/3-21G activation energy of 25.3 kcal/mol for the 1,2-H shift is too high by 18−19 kcal/mol,[14] this level of theory gives good approximations of geometry.[15]

Lattice calculations reflect the energetic consequences of replacing a native lattice molecule with a gas-phase optimized

(11) Gaussian 94 (Revision C.2), Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1995.
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(13) Coordinates for structures **2a**, **2b**, **3ts**, **4ts**, and **5ts** and the extent of lattice deviations for type-II optimizations are given in the Supporting Information.
(14) Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 9148−9156.
(15) Comparison of RHF/3-21G optimized carbene **2a** with a Becke3LYP/6-31G* optimized geometry shows a small 0.189 Å rms deviation between the carbon atoms of the two structures.
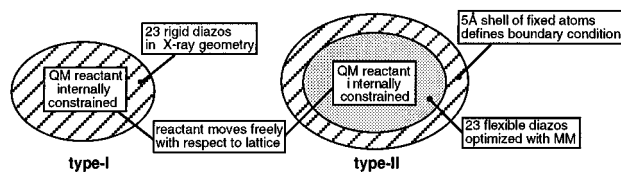
Communications to the Editor

J. Am. Chem. Soc., Vol. 119, No. 6, 1997 1475

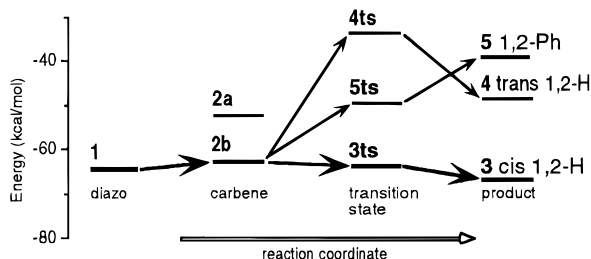**Figure 2.** Schematic defining type-I and type-II calculations.

Figure 3. Lattice energies (as described in the text) for replacing central diazo with structures in Figure 1 using type-II optimization.

Figure 4. Gas phase (▲) and crystal trajectories for favored (■) and disfavored (●) paths. Rigid type-I calculations shown with dashed lines and type-II with solid lines. Correction to RHF/3-21G activation energy shown as △.

guest. We used the X-ray coordinates of **1**[7] to create a host lattice consisting of 115 molecules in MacroModel 4.5.[16] The central molecule was removed and replaced by the reactant.[3,4] We then computed the interactions of the structures in Figure 1 with the lattice using molecular mechanics in two ways (see Figure 2): (1) the nearest neighbors of the guest are held fixed in place (type-I)[17] and (2) the nearest neighbors are entirely flexible and unconstrained and can rearrange to accommodate the reactant (type-II). In type-II optimizations the next-nearest neighbors are frozen to provide a boundary condition. Steep potentials of 1000 kJ/Å were used to constrain frozen atoms. We used the AMBER* force field,[18] with parameters for the diazo group developed as reported in the Supporting Information. Minimization of the central 24 diazo molecules with an appropriate boundary condition yields a structure very similar to the X-ray geometry, with deviations of 3−15° in the biphenyl torsions.[19]

Type-II optimizations of the structures in Figure 1 give the energies in Figure 3.[20] The energies reported represent the sum of the inter- and intramolecular energies of the optimized lattice diazo molecules, including their interaction with the reactant (but not the gas-phase energy of the reactant). There is a clear preference for both the transition state (**3ts**) and the product (**3**) of the observed reaction over those of two alternative paths. Because the gas-phase optimized carbene **2a** fits poorly in the lattice, we investigated the possibility that it might exist in the crystal in a different conformation. Carbene conformer **2b**, which was obtained from an RHF/3-21G optimization in which two dihedral angles were held fixed at the geometry of diazo **1**, is only 4.5 kcal/mol higher (Becke3LYP/6-31G*) than **2a**. Although **2b** is not a minimum on the gas-phase surface, the much greater difference in steric interactions (10.5 kcal/mol) than in conformational energies (4.5 kcal/mol) indicates that it is a better representation of the carbene in the lattice.

Structures on the gas-phase reaction trajectory between **2** and **3** were obtained using an RHF/3-21G IRC calculation.[11,21]

Energies along this path are shown in the top part of Figure 4, with the corrected activation energy noted. We calculated steric effects along the reaction trajectory by substituting 10 of these 18 points into the lattice. Successive points were inserted into the relaxed lattice resulting from optimization of the previous point. The results are shown in the bottom of Figure 4 for a reaction coordinate in a rigid (type-I) and a flexible (type-II) lattice. Remarkably, the crystal does not present any barrier to the observed *cis*-H shift, despite the deviation of the **3ts** geometry from that of **1**. Constraining the lattice to be rigid makes very little difference; type-I and type-II calculations give almost the same result. In light of this it is not surprising that in type-II optimizations the lattice molecules move very little from their equilibrium positions.[13] Including the N_2 generated from the photolysis of **1** in the reaction simulation leads to insignificant changes in the reaction profile. A trajectory toward the unobserved *trans*-stilbene **4** was simulated by rotation around the carbene−carbon bond of **2b** toward **4ts** as indicated in Figure 4. The steric energy for this path rises steeply and is lowered by the use of a relaxed model of type-II. The lattice shows greater distortion than in the preferred reaction.[13]

The negligible change in steric energies for the observed reaction indicates that the transition state for the *cis*-H shift is not displaced from its gas-phase location in the solid state. For disfavored products, however, the initial rise in energy, which occurs well before the bond to the migrating H can even begin to break, makes conformational change of the carbene the rate-limiting step. High steric energies make this route prohibitive and reactions do not occur in the crystal. The observation of virtually *no* steric resistance to the gas-phase trajectory of the observed reaction explains why it will be strongly favored.

Supporting Information Available: AMBER* parameters for the aryl diazo group, with graphs of performance for model compounds, coordinates for calculated structures in Figure 1 and data for lattice motion in type-II optimizations (6 pages). See any current masthead page for ordering and Internet access instructions.

JA962734A

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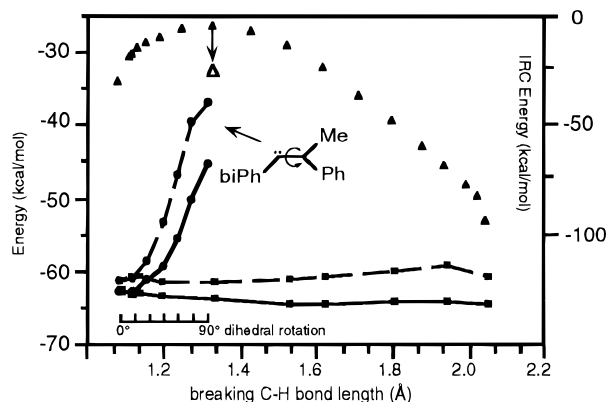
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