

## Experimental and Computational Modeling of Biphenyl Twisting in a Solid-to-Solid Carbene Reaction

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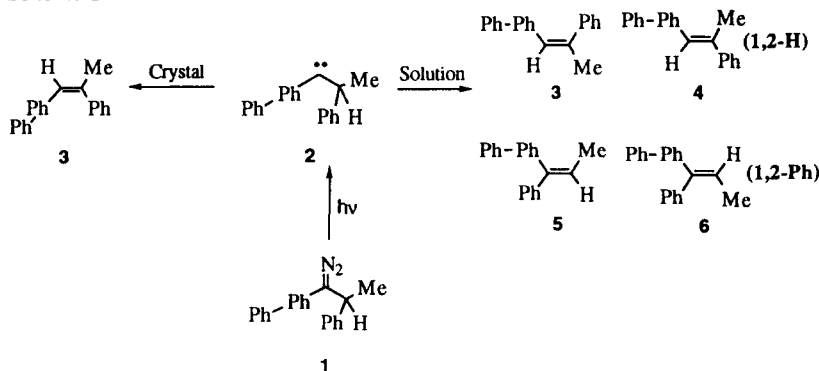
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**Abstract:** Computational modeling of a carbene 1,2-H shift in the solid-to-solid reaction of 1-(4-biphenyl)-2-phenyldiazopropane to (Z)-1-(4-biphenyl)-2-phenylpropene predicts that the planar biphenyl substituent of molecules witnessing the reaction will twist to relieve some of the steric strain accumulated in the crystal lattice. Changes in Raman spectra followed as a function of reaction progress confirmed that prediction and suggest a solid state reaction that proceeds through continuous solid solution.

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We recently reported experimental<sup>1,2</sup> and theoretical<sup>3</sup> studies addressing the photorearrangement of crystalline 1-(4-biphenyl)-2-phenyldiazopropane **1**. We found that 1,2-diarylalkylidenes (**2**) generated upon irradiation of **1** in the crystalline solid state react with selectivities that are not paralleled by reactions in any other media.<sup>4,5</sup> Although several products are formed in solution via 1,2-H shifts and 1,2-Ph migrations (i.e. alkenes **3-6**), samples of crystalline **1** transform smoothly and in near quantitative yields (>95%) into polycrystalline samples of stilbene **3** in a remarkably clean solid-to-solid reaction (Scheme 1).

Scheme 1



Single crystal X-Ray analysis of **1** and **3** previously reported showed molecular similarities between precursor and product conducive to substitutional solid solutions. Such conditions are required for solid state reactions to attain high conversion values.<sup>6</sup> With spectral (CPMAS  $^{13}C$  NMR and FT-IR) and thermal (DSC) data for pure **1** and **3** as well as partially reacted **1** we suggested that reaction proceeds through metastable solid solutions where compound **3** adopts the crystal structure of **1**.<sup>2</sup> In a later paper, we showed that the combined

use of quantum theory (RFH/3-21G and DFT B3LYP/6-31G\*) and molecular mechanics (MacroModel 4.5, Amber\* force field) gives insights into the energetics of the solid state reaction.<sup>3</sup> The reaction was simulated by stepwise mutation along the calculated minimum energy path of a central molecule "X" in a cluster representative of the crystal lattice. Steric energy changes were modeled by minimization of a cluster consisting of 23 closest neighbors (Figure 1) with a boundary condition consisting of a second layer of rigid molecules. In agreement with the experimental results, calculations showed that steric energy changes leading to **3** were negligible while a very steep steric barrier was calculated for reaction paths leading to product **4**.<sup>3</sup>

An important aspect of the computational model is that it contains valuable structural information on neighboring molecules witnessing the reaction. Since it is known that reactions in crystals may be accompanied by a large increase in internal stress,<sup>7,8</sup> it is possible that high conversions and good selectivities may rely on mechanisms that allow for small structural adjustments and relaxation of the surrounding molecules in the lattice. In order to test this, we carried out a molecule-by-molecule analysis of structural changes occurring as the reaction of **1** is simulated from the carbene to the transition states of the preferred (**3**) and disfavored (**4-6**) products (Figure 1). This comparison was carried out only up to the transition state because further changes along the reaction path leading to trans stilbene **4** result in unrealistically high energies and severe molecular distortions.<sup>3</sup> The effect of reaction on the crystal model is plotted in terms of the root mean square (rms) deviation for each of the 23 molecules surrounding the reactant (labeled with an "X"), as a function of molecule number in the cluster.

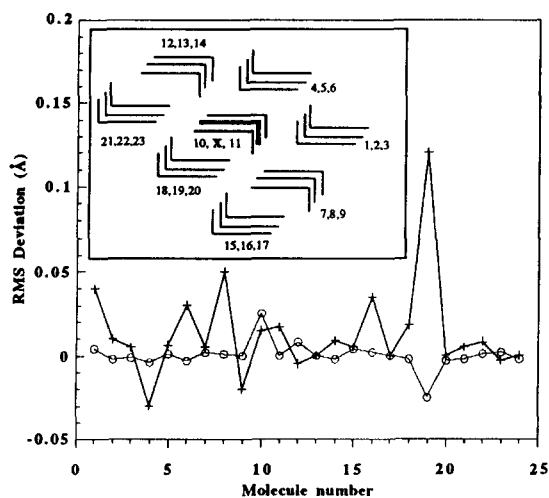


Figure 1. Sites of lattice distortion in the observed (circles) and disfavored (crosses) processes at representative points on the reaction trajectory. Molecule numbers within the cluster are defined in the inset

Crosses in Figure 1 clearly show that large perturbations occur to most of the 23 closest neighbors as molecule X changes its shape towards product **4**. Interestingly, the results are quite different when the reaction pathway towards the preferred product **3** is simulated. With the exception of molecules labeled 10 and 19, which have rms values of 0.02 and -0.02 Å, respectively, most of the molecules in the lattice remain almost entirely unaffected.

The detailed nature of the environmental changes accompanying the computed solid state reaction can be visualized by superposition of all the molecules in the cluster. As shown in Figure 2 for the simulation corresponding to Figure 1, the rotation of the biphenyl substituent is the most noticeable structural change. It is known that

biphenyl groups have a relatively soft torsional potential along the bond that joins the two aromatic rings,<sup>9</sup> and it is also known that this torsion can be highly responsive to the environment. Although the crystal structure of **1** has a flat biphenyl substituent, minimization leads to a small torsional angle, in agreement with well known force field and gas phase preferences. Results obtained after simulation of reaction trajectories towards products **3** and

4 indicate a tendency for increased twisting and disorder as the structure of test molecule X departs further from that of diazo compound 1.<sup>10-12</sup>

In order to test the role of biphenyl twisting experimentally, we targeted a Raman band at 410-430  $\text{cm}^{-1}$  assigned by Tashiro *et al.* to the twisted conformer.<sup>10</sup> This band seems to be the most suitable and reliable spectroscopic signature of biphenyl twisting among several that have been investigated.<sup>13</sup> In addition to test

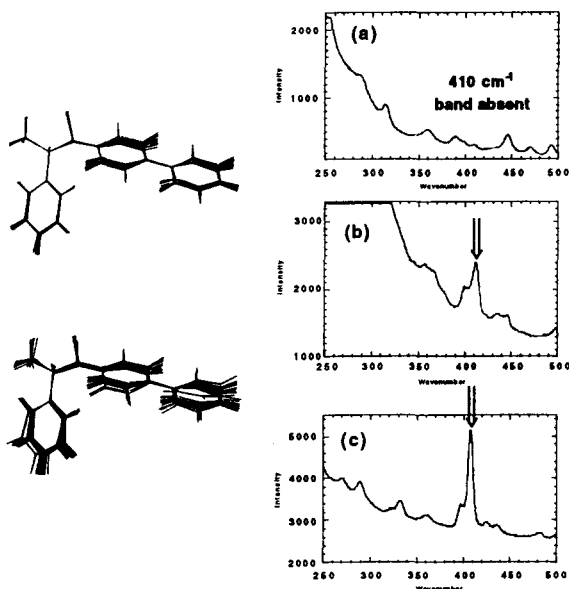


Figure 2. Left: Superposition of the 23 Diazo molecules from optimization of transition states towards products 3 (top) and 4 (bottom); Right: Raman spectra of (a) pure crystals of compound 1, (b) after 80% reaction, and (c) recrystallized 3.

samples of dissolved and crystalline biphenyl, samples of pure and partially reacted 1 were analyzed along with samples of recrystallized 3 (Figure 2). As expected from its X-ray structure, the Raman spectrum of polycrystalline 1 showed no significant intensity in the 350-450  $\text{cm}^{-1}$  region (Figure 2a). Spectra measured with the same sample after irradiation with  $\lambda > 400$  nm remained relatively unaffected through conversions as high as 30-40% (not shown). Upon further irradiation, a band at 410  $\text{cm}^{-1}$  was clearly detected when conversion values as high as 70-80 % were attained (Figure 2b). Differential scanning calorimetric analysis (DSC) and sample dissolution at this stage of the reaction had shown the formation of mixed crystals with  $\text{N}_2$  trapped within the crystal lattice.<sup>2</sup> Finally, spectra measured after recrystallization of 3 were characterized by a stronger and

sharper signal at 410  $\text{cm}^{-1}$  (Figure 2c) which is indicative of the twisted biphenyl structure of one of the two molecules in the asymmetric unit.<sup>2</sup> Large differences between "as-formed" and recrystallized 3 confirm the different structures of the two solid phases and the metastable nature of the one formed in the solid state reaction.

The relatively large amplitude and soft potential of the biphenyl group twisting make it an attractive structural element for the release of steric strain that may be accumulated upon product formation in a solid state reaction. The Raman experiments in Figure 2 were suggested by our computational analysis, which is a model for early conversion. However, the relatively weak intensity and late appearance of the 410  $\text{cm}^{-1}$  band suggest that biphenyl group twisting is most significant at the later stages of the reaction. The Raman results are consistent with a continuous solid solution with steric strain or disorder occurring only at high conversion (*ca.* 70-80%). It is interesting that the planar structure of biphenyl substituents observed in several crystal structures<sup>14</sup> is not a gas phase minimum.<sup>9,14</sup> Recent work suggests that flat biphenyl in crystals may originate from a dynamic average with phenyl libration over relatively small angles.<sup>15-17</sup> It is possible that structural and dynamic aspects of the biphenyl substituent may play a role in allowing efficient solid state transformations. Further reactions of crystals containing biphenyl substituents and other relatively free rotating units are being investigated in our laboratories.

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