

Communications to the Editor

Transforming a Nonspecific Carbene Rearrangement into a Highly Selective Process by Using Crystalline Media

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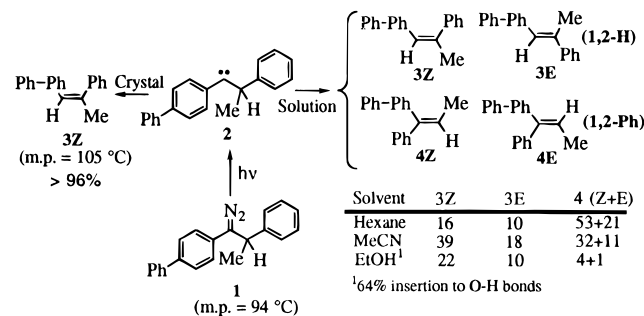
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Of all the methods that may be applied to the study and understanding of carbene reactivity,¹ crystal chemistry may offer the most insight into structural questions.² By superimposing high environmental barriers over the relatively flat energy surfaces observed in fluid media, one may gain insight into the dynamics of these highly reactive species.³ One may expect that crystalline environments can preorganize carbene structures to favor some reaction pathways while blocking them from others.⁴ In this communication we report evidence supporting this hypothesis in the case of 1,2-diaryl-1-alkyldienes capable of undergoing intramolecular 1,2-H shifts and 1,2-Ph migrations. Experimental results with 1-(4'-biphenyl)-2-phenyl-1-diazopropane (**1**) suggest that carbene **2** can be generated in the solid state by UV irradiation. As indicated in Scheme 1, the crystalline medium is capable of controlling the reaction to high yields and unprecedented selectivity. Formation of the main product may be explained in terms of overlap of the migrating hydrogen with the carbene empty p-orbital as applied to the conformation deduced from the crystal structure of the diazo precursor.

The photochemistry of 1,2-diphenyldiazoalkanes has been studied in fluid solutions⁵ and glassy matrices.^{6,7} Even subtle changes in experimental conditions affect the product yields in a relatively complex manner, but selectivity remains low under

Scheme 1



all reaction conditions.^{5–8} Accordingly, irradiation of *ca.* 10⁻³ M **1** in deoxygenated hexane or acetonitrile with $\lambda > 380$ nm leads to formation of both *Z* and *E* isomers (indicated by **Z** and **E** after the compound number) of olefins **3** and **4** in yields that depend on the solvent used (Scheme 1).⁹ Irradiation in ethanol produces compounds **3** and **4** in 36% yield along with products of carbene insertion into the OH bond in 64% yield. Compounds **3Z** and **3E** were purified by fractional crystallization, but mixtures of **4Z** and **4E** could not be separated, and their yields are indicated without their stereochemical identity. We recently proposed that yields in Scheme 1 can be understood in terms of a polarity-dependent spin state equilibrium of the carbene intermediate,⁸ although recent triplet sensitization studies with analogous compounds¹⁰ suggest that a fraction of the product (*ca.* 0–30%) may originate in the singlet excited state of the diazo compound.¹¹

The selectivity observed in the crystalline solid state is very high. Pure powdered samples of **1** irradiated at 0 °C with $\lambda > 380$ nm showed that compound **3Z** constitutes over 96% of the product mixture. When irradiation was carried out for different time intervals (up to 20 h), red solids slowly turned white and conversions as high as 95% were obtained with no loss in stereoselectivity.¹² Only small amounts of **3E** (*ca.* 3%) and traces of one of the two isomers of **4** (<1%) were identified. The pure reactant and recrystallized major product melt at 94 and 105 °C, respectively.¹³ Thermal analyses of partially reacted samples by differential scanning calorimetry (DSC) were characterized by a complex behavior including exothermic denitrogenation of the diazo precursor which partially overlaps with a melting endotherm. No liquid phases were observed below *ca.* 70 °C, and the reaction proceeds entirely in the solid state. While recent studies suggest that 1,2-H shifts may occur from a singlet excited state reaction of the diazo precursor,¹¹

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(9) It was shown that olefin isomerization does not occur under the reaction conditions, and relative product yields in the table of Scheme 1 reflect the true selectivity of their precursors. Product ratios were determined by capillary GLC. Retention times were established by co-injection with authentic samples prepared independently.

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(12) Irradiations at shorter wavelengths did cause olefin isomerization in the “as reacted” solids but not in samples of purified and recrystallized olefins.

(13) Compound **1**: 1-(4'-biphenyl)-2-phenyl-1-diazopropane, red needles obtained from ether, mp 94 °C, space group *P2₁/c*, *Z* = 4, *a* = 12.1088 Å, *b* = 5.8895 Å, *c* = 22.0490 Å, β = 96.067°, *R_w* = 0.058. Compound **3Z**: (Z)-1-(4'-biphenyl)-2-phenylpropene, white needles obtained from ethanol, mp 105 °C, space group *P2₁/c*, *Z* = 8, *a* = 18.989 Å, *b* = 6.255 Å, *c* = 26.08 Å, β = 94.77°, *R_w* = 0.55.

(1) Leading reviews and monographs on carbene chemistry: (a) Jones, M., Jr.; Moss, R. A. *Carbenes*; Wiley: New York, 1973; Vol. 1. 1975; Vol. 2. (b) Jones, M. Jr. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Wiley: New York, 1980; Vol. 1, Chapter 3. (c) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic Press: New York, 1971. (d) Gilchrist, T. L.; Rees, C. W. *Carbenes, Nitrenes and Arynes*; Appleton-Century-Crofts: New York, 1969. (e) Platz, M. S. *Kinetics and Spectroscopy of Carbenes and Biradicals*; Plenum Press: New York, 1990. (f) Brinker, U. H. *Advances in Carbene Chemistry*; JAI Press: New York, 1994.

(2) For reviews of solid state organic chemistry, see: (a) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. *Org. Photochem.* **1987**, *8*, 249–347. (b) Hollingsworth, M. D.; McBride, J. M. *Adv. Photochem.* **1990**, *15*, 279–379. (c) Desiraju, G. R. *Organic Solid State Chemistry*; Elsevier: Amsterdam, 1987. (d) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433–481.

(3) A remarkable kinetic stabilization of triplet carbenes and nitrenes by crystals has been recently demonstrated: (a) Tomioka, H.; Watanabe, T.; Hirai, K.; Furukawa, K.; Takui, T.; Itoh, K. *J. Am. Chem. Soc.* **1995**, *117*, 6376–6377. (b) Mahe, L.; Izuoka, A.; Sugawara, T. *J. Am. Chem. Soc.* **1992**, *114*, 7904–7906.

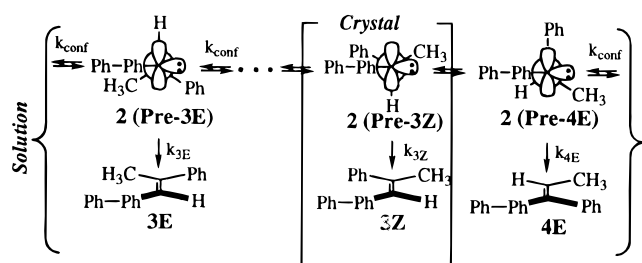
(4) Doetschmann and Hutchison first demonstrated the control of the solid state on bimolecular reactivity of diphenylcarbene: Doetschman, D. C.; Hutchison, C. A. *J. Chem. Phys.* **1972**, *56*, 3964–3982.

(5) Pomerantz, M.; Witherup, T. H. *J. Am. Chem. Soc.* **1973**, *95*, 5977–5988.

(6) (a) Tomioka, H.; Hayashi, N.; Izawa, Y.; Senthilnathan, V. P.; Platz, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 5053–5057. (b) Tomioka, H.; Ueda, H.; Kondo, S.; Izawa, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7817–7818.

(7) Platz, M. S. In *Kinetics and Spectroscopy of Carbenes and Biradicals*; Platz, M. S., Ed.; Plenum: New York, 1990; pp 143–211.

Scheme 2

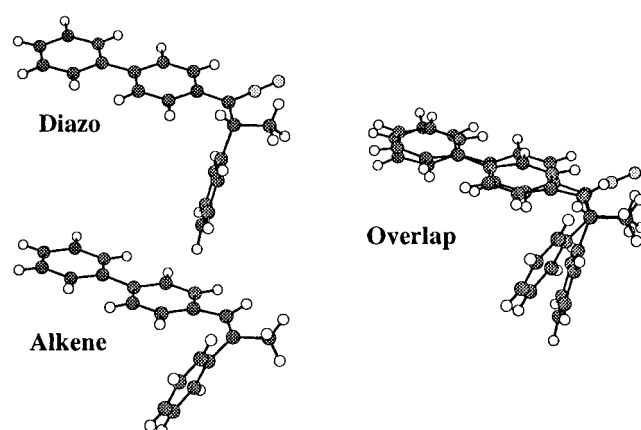


this does not seem to be the case in crystalline **1**. Analyses of irradiated crystals between 200 and 300 K and methylcyclohexane glasses at 77 K by fluorescence spectroscopy are consistent with accumulation of a nonemissive transient that reacts in the dark to give the strong fluorescence spectrum of the stilbene photoproduct. Furthermore, irradiation of single crystalline **1** in the cavity of an EPR spectrometer at 77 K yields a spectrum consistent with that expected for triplet **2**.^{3,4,14}

Experimental and theoretical results suggest that 1,2-H shifts in singlet state carbenes possess highly ordered transition states with conformations that require a parallel alignment of the migrating σ -bond with the carbene p-orbital.¹⁵ It is generally accepted that carbenes with ground triplet states react from thermally populated singlets.^{6,7} As indicated in Scheme 2, it is expected that different products must arise from different conformers. Thus, to the extent that all conformers are present in solution, all the products with energetically accessible transition states should have an opportunity to form. In contrast, reactions in crystalline solids may be more stereoselective, since most conformational motions are energetically disallowed and most molecular crystals present a single conformational isomer.¹⁶

If the overall structure of **1** remains unaltered after nitrogen is eliminated and throughout the reaction, one may expect that the conformation of **1** will determine the selectivity. This hypothesis is supported by analysis of the X-ray structures of **1** and **3Z**.¹² The structure of **1** was solved in the space group $P2_1/c$ with one molecule per asymmetric unit. Compound **3Z** also crystallizes in space group $P2_1/c$ but with two molecules per asymmetric unit, each with a different torsion angle at the biphenyl substituent (1.6° and -33.6° , respectively). As shown in Chart 1, the conformation of **1** is characterized by possessing the biphenyl, the diazo, and the α -methyl groups nearly on the same plane, and almost with the same relationship that they have in the structure of **3Z**. The migrating hydrogen is located above the plane of the diazo group with a $\text{N}_2=\text{C}-\text{C}-\text{H}$ torsion angle of 127° . This value is close to the ideal of 90° that would lead to perfect orbital alignment of the C-H bond with the empty p-orbital of an sp^2 -hybridized carbene carbon. Formation of **3E** would require a large rotation about the $(\text{Ar})\text{C}-\text{CHMe}$ -

Chart 1



(Ph) bond, and phenyl migration would require alignment of the phenyl group to form a bridged transition state followed by high-amplitude displacements of the relatively bulky substituent.¹⁷

A high structural similarity between **1** and **3Z** is evident in Chart 1 where one of the two distinct molecules in the crystal of the latter is used for comparison (although similar conclusions can also be drawn with the other). An overlap analysis of the reactant and the product in Chart 1 shows a relatively minor structural reorganization where the most notable changes include the loss of N_2 , its replacement by the migrating hydrogen, and displacement of the phenyl group as the α -carbon rehybridizes from sp^3 to sp^2 . Although it may be argued that the detailed conformation of **3Z** as formed in crystals of **1** may be different from that obtained after recrystallization, a high structural similarity in their stable solid phases suggests a high solid state solubility¹⁸ which may explain the good reaction yields.¹⁹ One may identify the X-ray structure of **1** as the precursor to carbene conformer “**2 (Pre-3Z)**” shown in Scheme 2, or as the precursor to the final product if an excited state diazo reaction contributes to product formation.¹¹ It is known that rigidity alone is not sufficient to warrant a highly selective reaction as amorphous solids and disordered crystals produce selectivities that reflect their conformational and environmental heterogeneity.^{7,8} We believe that systems like this will allow us to explore detailed mechanistic questions including the effect of structure and orbital alignment on the rates of the reaction. Studies in our group are currently addressing this possibility.

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Supporting Information Available: X-ray data for compounds **1** and **3Z** (14 pages). See any current masthead page for ordering and Internet access instructions.

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