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Orbital-Overlap Control in the Solid-State Reactivity of *β*-Azido-Propiophenones: Selective Formation of *cis*-Azo-Dimers

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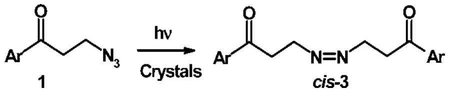
ABSTRACT



Solid-state photolysis of 1a,b yields selectively *cis*-3a,b. X-ray analysis of 1a,b reveals the molecules adopt an extended structure and as such the crystal packing arrangement consists of planar, π-stacked molecules. The shortest intermolecular distance between adjacent N-atoms is ∼3.76 Å and would lead to formation of *trans*-3a,b, whereas *cis*-3a,b is formed by dimerization between N-atoms that are ∼3.9 Å apart. We propose that the molecular orbital alignment of the adjacent nitrenes controls the solid-state reactivity.

Photoreactions in the solid-state have been shown to be generally more regio- and stereoselective than their solution counterparts.[1] Thus, crystals have been used ingeniously to synthesize natural products from radical intermediates in high chemical as well as enantiomeric yield.[2] Investigations of the solid-state reactivity of radicals such as carbenes, nitrenes, and biradicals make it possible to establish structure−reactivity relationships. More specifically, the overlap and orientation between the orbitals on the radical centers that form new bonds in the products can be correlated with their solid-state selectivity.[3] In theory, the same orbital alignment is necessary for selective bond formation between radical centers in solution. However, it is experimentally difficult to assess orbital alignments in solution. Thus, solid-state studies offer a unique opportunity to investigate the influence of orbital alignment upon radical reactivity. Furthermore, unstable products formed during photoreactions are more readily studied in the solid state due to the rigidity and lack of diffusion inherent to crystals.[4]

We have recently shown that solution photolysis of β-azido propiophenone derivatives **1** results in formation of alkyl nitrene **2**, which are long-lived intermediates because they decay by dimerization to form **3**, rather than reacting with

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(1) (a) Campos, L. M.; Garcia-Garibay, M. A. Reactive Intermediates in Crystals: Form and Function. In *Reviews of Reactive Intermediate Chemistry*; Platz, M. S., Moss, R. A., Jones, M., Eds.; John Wiley & Sons: New York, 2007; p 271. (b) Scheffer, J. R.; Xia, W. *Top. Curr. Chem.* **2005**, *254*, 233. (c) Garcia-Garibay, M. A. *Acc. Chem. Res.* **2003**, *36*, 491. (d) Garcia-Garibay, M. A.; Campos, L. M. In *CRC Handbook of Organic Photochemistry & Photobiology*, 2nd ed.; Horsepool, W. M., Ed.; CRC Press: Boca Raton, FL, 2003; Chapter 48. (e) Sakamoto, M. *Chem. Eur. J.* **1997**, *3*, 684. (f) Hollingsworth, M. D.; McBride, J. M. *Adv. Photochem.* **1990**, *15*, 279. (g) Ramamurthy, V.; Venkatesan. K. *Chem. Rev.* **1987**, *87*, 433. (h) Desiraju, G. R. *Organic Solid-State Chemistry*; Elsevier: Amsterdam, The Netherlands, 1987.

(2) (a) Natarajan, A.; Ng, D.; Yang, Z.; Garcia-Garibay, M. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 6485−6487. (b) Ng, D.; Yang, Z.; Garcia-Garibay, M. A. *Org. Lett.* **2004**, *6*, 645. (c) Ellison, M.; Ng, D.; Dang, H.; Garcia-Garibay, M. A. *Org. Lett.* **2003**, *5*, 2531. (d) Resendiz, M. J. E.; Garcia-Garibay, M. A. *Org. Lett.* **2005**, *7*, 371. (e). Garcia-Garibay, M. A.; Mortko, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 7994.

(3) (a) Yang, C.; Xia, W.; Scheffer, J. R.; Botoshansky, M.; Kaftory, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5087. (b) Braga, D.; Chen, S.; Filson, H.; Maini, L.; Netherton, M. R.; Patrick, B. O.; Scheffer, J. R.; Scott, C.; Xia, W. *J. Am. Chem. Soc.* **2004**, *126*, 3511. (c) Shin, S. H.; Cizmeciyan, D.; Keating, A. E.; Khan, S. I.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 1859. (d) Shin, S. H.; Constable, A. E.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 7626. (e) Doetschman, D. C.; Hutchison, C. A. *J. Chem. Phys.* **1972**, *56*, 3964.

(4) Mandel, S. M.; Singh, P. N. D.; Muthukrishnan, S.; Chang, M.; Krause, J. A.; Gudmundsdottir, A. D. *Org. Lett.* **2006**, *8*, 4207.

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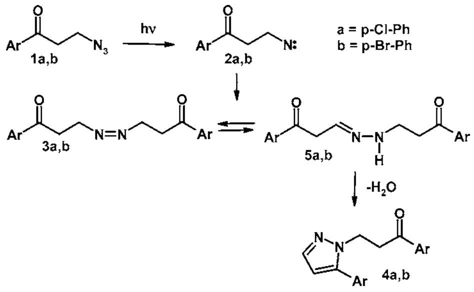
the solvent or its precursor (Scheme 1).[5] However, we were not able to isolate and characterize **3**, since it forms **4** in solution. Dimer **3** is presumably in equilibrium with its tautomer **5**, which undergoes an intramolecular reaction followed by hydrolysis to form **4**. Furthermore, the cis isomers of alkyl diazenes which lack tertiary carbon atoms next to the azo moiety are generally unstable and decompose unless the solution is kept at cryogenic temperature,[6] thus complicating their preparation and characterization.

Scheme 1



In this letter we describe how solid-state photolysis of **1a**,**b** selectively yields *cis*-**3a**,**b**. We used IR, Raman, and ^{13}C NMR spectroscopy along with molecular modeling to assign the stereochemistry of **3a**,**b**. Furthermore, X-ray structure analysis of **1a**,**b** made it possible to determine that the nitrene dimerization did not take place between the N-atom on adjacent molecules having the shortest intermolecular distance but rather involved molecules having a more favorable orbital alignment for azo dimer formation.

To investigate which dimers form upon photolysis of the monomers, **1a**,**b**, the solid-state reaction of **1a**,**b** in KBr pellets were monitored by IR (Figure 1a). The crystals turned yellow upon photolysis and dissolving these irradiated crystals released gas, presumably N_2 molecules that were trapped within the crystal lattice. To determine the solid-state products, irradiated crystals were dissolved and HPLC and solution NMR techniques were used to show that **4** is obtained, along with some remaining starting material. Hence, **4** must be formed very efficiently from **3** in solution. In the solid-state, irradiation of **1a**,**b** in KBr pellets led to new IR and Raman bands, mostly occurring very near those of the parent azide, which is expected since the propiophenone moiety is not significantly affected by dimerization of nitrenes **2a**,**b**. The most noteworthy changes observed in the IR spectra upon irradiation are depletion of the azide band at 2015 cm^{-1} and formation of a new band at 1633 cm^{-1}, whereas Raman spectroscopy (Figure 1b) revealed formation of a very low-intensity band at 1633 cm^{-1} and more intense bands at 754 cm^{-1} and a decrease of the bands at 2051, 948, and 789 cm^{-1}. We assign the band at 1633 cm^{-1} to the N═N stretch in *cis*-**3**, which is expected to be both IR and Raman active. This is similar to what was observed for *cis*-dimethyldiazene, which has a Raman and IR stretch at 1556 cm^{-1} for the N═N band.[6b] In comparison the N═N band in *trans*-dimethyldiazene is at 1583 cm^{-1} and is only Raman active because symmetrical stretching vibrations are inactive in the infrared.[6f]

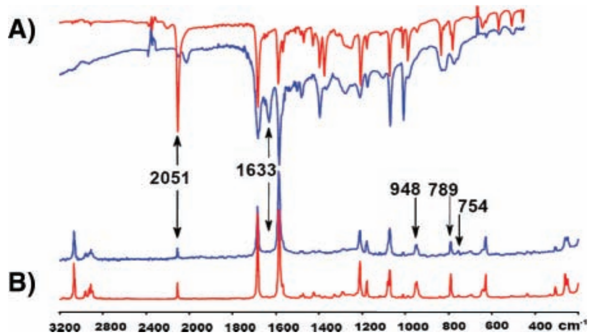


Figure 1. (A) IR spectra of azide **1b** before (red line) and after irradiation (blue line). (B) Raman spectra of azide **1b** before (red line) and after irradiation (blue line).

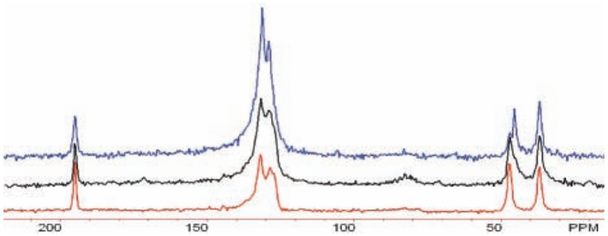


Figure 2. Solid-State ^{13}C-CPMAS NMR spectra of **1b** before (red line) and after different extents of photolysis: ∼30% (black line) and ∼70% (blue line) conversions, respectively.

Finally, we monitored the solid-state reactivity of **1b** via solid-state ^{13}C NMR spectroscopy. Figure 2 shows the solid-state ^{13}C NMR spectra of **1b** before and after ∼30% and ∼70% conversions. As irradiation increases, the 47.7 ppm peak intensity decreases while the intensity of a new peak at 46.2 ppm increases. On the basis of the literature, the CH_3 group in *cis*- and *trans*-dimethyldiazene resonates at δ 46.9 and 55.1 ppm, respectively.[6a] The CH group next to the N═N moiety in an isopropyl diazene derivative resonates at 69 ppm.[7] Thus, the new 46.2 ppm peak is assigned to the CH_2

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(5) (a) Singh, P. N. D.; Mandel, S. M.; Sankaranarayanan, J.; Muthukrishnan, S.; Chang, M.; Robinson, R. M.; Lahti, P. M.; Ault, B. S.; Gudmundsdottir, A. D. *J. Am. Chem. Soc.* **2007**, *129*, 16263. (b) Sankaranarayanan, J.; Mandel, S. M.; Krause, J. A.; Gudmundsdottir, A. D. *Acta Crystallogr., Sect. E* **2007**, *E63*, o721.

(6) (a) Simeonov, A. M.; McKenna, C. E. *J. Org. Chem.* **1995**, *60*, 1897. (b) Ackermann, M. N.; Craig, N. C.; Isberg, R. R.; Lauter, D. M.; MacPhail, R. A.; Young, W. G. *J. Am. Chem. Soc.* **1977**, *99*, 1662. (c) Engel, P. S. *J. Am. Chem. Soc.* **1976**, *98*, 1972. (d) Nelsen, S. F. *J. Am. Chem. Soc.* **1974**, *96*, 5669. (e) Hutto, R. F.; Steel, C. *J. Am. Chem. Soc.* **1964**, *86*, 745. (f) Craig, N. C.; Ackermann, M. N.; MacPhail, R. A. *J. Chem. Phys.* **1978**, *68*, 236.

(7) Kaba, R. A.; Lunazzi, L.; Lindsay, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1975**, *97*, 6762.

group in **3b** since it is within the range of chemical shift values reported for similar carbon atoms. The NMR spectroscopy also supports formation of a dimer such as **3b** since no other changes except for the 47.7−46.2 ppm aliphatic carbon resonance shift were observed upon irradiation. Formation of **4b** or **5b** would have yielded other resonances corresponding to either a heterocyclic aromatic or imine carbon resonances, respectively.

X-ray structural analysis of **1a**,**b** revealed that both compounds crystallize as the extended conformer (Figure 3).

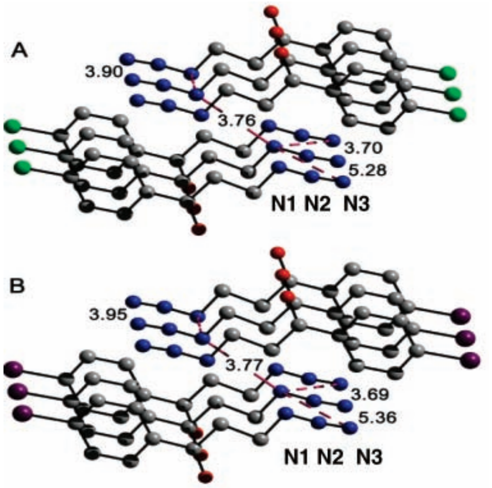

Figure 3. Crystal packing arrangement for (A) **1a** and (B) **1b**. The intermolecular N−N distances are in Å (see Table 1).

Azides **1a**,**1b** are planar since their β-chain torsion angles range from 178.5° to 179.7°. The crystal lattice consists of layers of molecules with overlapping phenyl rings and azido groups which allow for π-stacking interactions. As expected, the chloro/bromo halide substitution in the para position does not affect the crystal packing arrangement significantly.

For **1a**,**b** the shortest intermolecular distance between adjacent N1 atoms is 3.757(3) and 3.767(5) Å, respectively (Table 1, Figure 3). Dimerization between two of these nitrogen atoms would lead to formation of *trans*-**3a**,**b**, respectively, but this is not observed. The second shortest intermolecular distance between adjacent N1 atoms is 3.898(1) and 3.952(1) Å for **1a**,**b**, respectively. Dimerization between these two nitrogen atoms yields *cis*-**2**.

Table 1. Specific Intermolecular Distances in Crystals of Azides **1a**,**b**

azide	N1⋯N1 (Å)	N1⋯N3 (Å)
1a	3.757(3), 3.898(1)	3.698(3)
1b	3.767(5), 3.952(1)	3.694(5)

To further support the characterization of the solid-state products, **3a**,**b**, and to better understand the solid-state reactivity we optimized the structures of **1a**,**b**, nitrenes **2a**,**b,** and *cis*- and *trans*-**3a**,**b** using the B3LYP level of theory and 6-31G+(d) basis set as implemented in Gaussian03.[8,9] For **3b** we calculated the lowest energy conformers, **A**, and also conformers, **B**, which are higher in energy but more similar to the conformers we would expect for *trans*- and *cis*-**3b** to be formed in, within the crystal lattice (Figure 4).

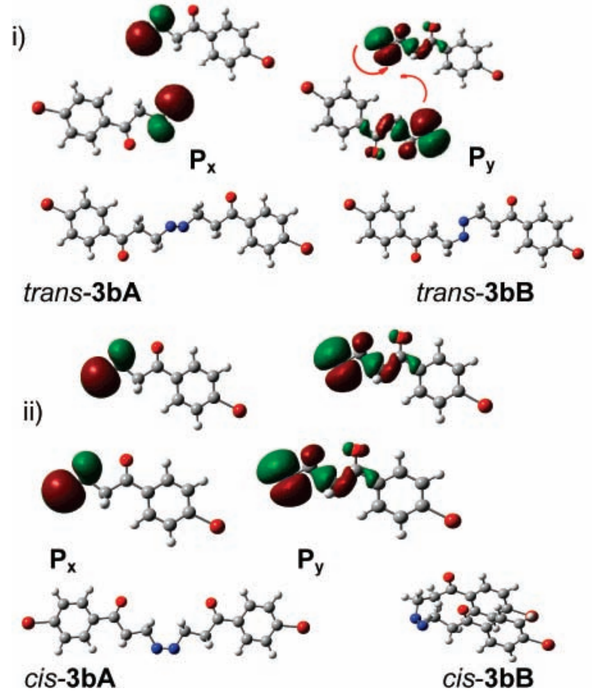

Figure 4. Molecular orbital alignment of the half full p_x and p_y orbitals on the N atom in nitrene **2b** in the crystal lattice to form (i) *trans*-**3a** and (ii) *cis*-**3b**.

The calculated IR and Raman spectra of *cis*-**3bA**,**B** have a vibration band at 1659 and 1672 cm^{-1} due to the stretching of the N═N bond, respectively. The calculated oscillation strengths of these IR and Raman bands are similar (Table 2). In comparison, the calculated N═N stretches for *trans*-**3bA**,**B** are predicted at 1671 and 1680 cm^{-1}, respectively. The oscillation strengths of these N═N *trans*-**3bA**,**B** stretches

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(8) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revisions A.1 and C.02; Gaussian, Inc.: Wallingford, CT, 2004.

Table 2. Calculated N═N Band Intensities for **3**

	N═N (cm^{-1})	IR (km/mol)	Raman (km/mol)
cis-**3aA**	1659	7	6
trans-**3aA**	1671	0	170
cis-**3bA**	1659	7	7
cis-**3bB**	1672	23	12
trans-**3bA**	1671	0	177
trans-**3bB**	1681	0	10

are 177 and 12 km/mol, respectively, for the Raman bands, but zero in the IR bands as expected. Calculations show that while all of the conformers of *cis*-**3b** have similar N═N stretching frequencies, their calculated intensities varied significantly. The same trends were observed in the calculations for the conformers of *trans*-**3b**. Thus, the calculations support that *cis*-**3** is formed in the solid-state, since we observe N═N bands that are *both* IR and Raman active. Furthermore, scaling the 1672 cm^{-1} band for *cis*-**3bA** by 0.9734 places the calculated band at 1627 cm^{-1},[10] which corresponds well with the observed band at 1633 cm^{-1}. Furthermore, we assign the Raman band at 754 cm^{-1} (Figure 1) to the symmetrical stretch of the $-CH_2-N{=}N-CH_2-$ moeity in *cis*-**3b** based on its calculated frequency of 787 cm^{-1}. Finally, the Raman bands at 948 and 789 cm^{-1} in **1b**, which decreased upon irradiation, were assigned to coupled NNN and CH bends, which are calculated to be 964 and 803 cm^{-1}, respectively.

Finally, calculations also rule out the possibility that the primary photoproduct in crystals is **5** for which H−N (∼3400 cm^{-1}) and imine bands (∼1710 cm^{-1}) would have been observed; these would be major Raman bands (due to their calculated oscillation strength of ∼300 km/mol).

The calculations reveal that the calculated structures of **1a**,**b** are similar to their X-ray structures, i.e., the molecules crystallize in an extended, planar conformer, similar to the calculated mininal energy conformer. Thus, it is reasonable to assume that nitrenes **2a**,**b** adopt conformations in the solid-state similar to their calculated minmal energy conformers. As we have shown before, triplet alkyl nitrenes decay by dimerization with another nitrene molecule rather than reacting with an azido precursor.[5a] Schuster et al. reported similar findings for the dimerization of phenyl nitrenes.[11] Thus, it seems reasonable to assume that the dimerization of **2a**,**b** takes place between two nitrene molecules in the solid-state as it does in solution. To explain why nitrenes **2a**,**b** prefer to dimerize with a nitrene molecule located ∼3.9 Å away rather than with one at ∼3.76 Å, we looked at the alignment of the two half-full p-orbitals on the N-atom, p_x and p_y, that will form the N═N bonds. In order for *trans*-**3** to form, the two p_x-orbitals (Figure 4), which are located on top of each other in the crystal lattice, would have to rotate for good overlap. In comparison, the p_y- and p_x-nitogren orbitals are lined up perfectly in the crystal, side to side, for dimerization and formation of *cis*-**3a**,**b**. Thus, the molecular orbital alignment must control the reactivity of the nitrenes **2a**,**b** in the solid-state.

Lahti et al. and Sugawara et al. used ESR spectroscopy to demonstrate that aryl nitrenes are long-lived in the solid-state.[12,13] Aryl nitrenes also decay mainly by dimerization in the solid-state, although the stereochemistry of the azo-products was not determined. It can be theorized that alkyl nitrenes **2a**,**b** are long-lived in crystals as well, and that the restriction of the crystal lattice forces them to form *cis*-**2a**,**b**, stereoselectively.

Solid-state photolysis of azides **1a**,**b** selectively results in *cis*-**3a**,**b** via dimerization between two nitrene molecules. Crystal packing of azides **1a**,**b** indicate that dimerization does not take place between nearest neigboring N-atoms on nitrenes **2a,b**, but rather between N-atoms that are further apart and have better molecular orbital alignment.

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Supporting Information Available: Experimental procedures and details (NMR, X-ray (CIF), and calculations). This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] (a) Talbot, F. O.; Simons, J. P. *Phys. Chem. Chem. Phys*. **2002**, *4*, 3562. (b) Snoek, L. C.; Robertson, E. G.; Kroemer R. T.; Simons, J. P. *Chem. Phys. Lett*. **2000**, *321*, 49.

[11] Liang, T. Y.; Schuster, G. B. *J. Am. Chem. Soc*. **1987**, *109*, 7803.

[12] (a) Sasaki, A.; Mahe, L.; Izuoka, A.; Sugawara, *Bull. Chem. Soc. Jpn*. **1998**, *71*, 1259. (b) Mahe, L.; Izuoka, A.; Sugawara, T. *J. Am. Chem. Soc*. **1992**, *114*, 7904.

[13] Ichimura, A. S.; Sato, K.; Kinoshita, T.; Takui, T.; Itoh, K.; Lahti, P. M. *Mol. Cryst. Liq. Cryst. Technol., Sect. A* **1995**, *272*, 279.