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# An Efficient Solid-to-Solid Reaction via a Steady-State Phase Separation Mechanism

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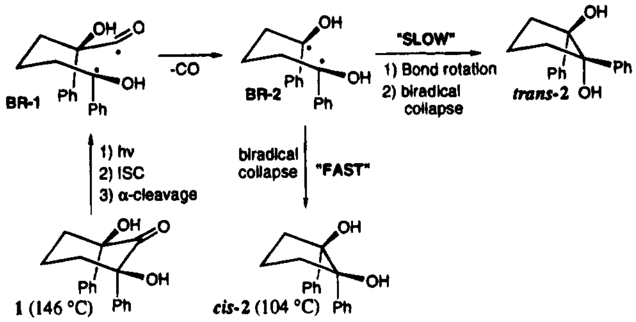
Crystalline environments control the selectivity of organic reactions by facilitating some pathways while disallowing others, and many examples of chemo-, regio-, and stereoselective reactions have been documented.[1] It is also known that accumulation of the product causes changes in the structure of the parent crystal, sometimes affecting the kinetics, the selectivity, and the extent of reaction.[2] The consequences of product accumulation on solid-state reactions were analyzed by Schmidt in reference to numerous examples involving cinnamic acid derivatives. He suggested that product molecules go into solid solution in the lattice of the reactant until they reach their solubility limit, at which point they separate into their own phases.[3] The effects of product accumulation on reaction control are particularly important when the potential of solid-state reactivity is considered for preparative purposes, since high conversion values with maintained high selectivity are required. Thus, to the extent that a solid solution exerts an influence similar to that exerted by the parent crystal, high solid solubility should result in high reaction efficiencies. In fact, an ideal but infrequent situation occurs in single crystal-to-single crystal, or topotactic, transformations when reactants and products are capable of forming solid solutions over their entire composition diagrams.[4] While this is not the case for most organic solid-state reactions, there are many examples where high selectivity and high product yields are observed.[5] Understanding in detail their solid-state reaction mechanisms both at the molecular and the solid-phase levels would be highly desirable.[6]

With that in mind, we report the solid-state photodecarbonylation of *cis*-2,6-dihydroxy-2,6-diphenylcyclohexanone (**1**)[7] into *cis*-1,5-dihydroxy-1,5-diphenylcyclopentane (*cis*-**2**). High selectivity and first-order kinetics were observed, along with high reaction yields. Based on spectroscopic analysis and X-ray diffraction data, we propose that this reaction occurs through a phase separation mechanism via steady-state mixed crystalline phases.

**Scheme 1**



The photochemistry of **1** conforms with known chemistry of substituted cyclohexanones.[8] Stepwise decarbonylation occurs through triplet acylalkyl biradical **BR-1** and 1,5-biradical **BR-2**.[9] Irradiation of **1** in solution gave expected cyclopentanediols *cis*-**2** and *trans*-**2** in a 51:49 ratio. Irradiation of **1**, in single crystals or in finely divided powders at 298 K with $\lambda = 350$ nm, gave a $\sim$19:1 ratio of *cis*-**2**/*trans*-**2** in solid-to-solid transformations. Dissolution of irradiated samples displayed vigorous gas evolution, indicating that CO remains trapped in the crystal lattice. That crystallinity and order are essential for the stereoselectivity of the reaction was established by analyzing changes in product ratio in solvents of increasing viscosity.[10]

The preparative potential of the reaction was explored in medium-scale solid-state irradiations ($\sim$0.5 g of **1**), from which samples were analyzed after successive irradiation times by $^{13}$C CPMAS NMR, FT-IR (KBr), and differential scanning calorimetry (DSC). The extent of conversion as a function of irradiation time and the *cis*/*trans* product ratio were determined by $^{1}$H NMR and GLC analysis. In contrast to most solid-state reactions, which present a complex kinetic behavior, conversion values as a function of irradiation time showed remarkably linear first-order kinetics and consistently high stereoselectivity (Figure 1).

That the reaction proceeds in the crystal bulk and not at the surface is suggested by trapping of CO gas and by the similar selectivity in single crystals and finely powdered samples.[11] $^{13}$C CPMAS NMR spectra corresponding to selected conversion values are plotted in Figure 2, along with the spectrum of the recrystallized photoproduct. The data show a clean reaction with a systematic decrease of the signals of the reactant and a concomitant increase of the signals of the product, with no accumulation of intermediate phases. X-ray structural analysis of **1** and *cis*-**2** revealed unrelated crystal structures with different space groups.[12] Analysis of indexed reflections of **1** as a

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(1) (a) Schmidt, J. M. J. In *Solid State Photochemistry*; Ginsburg, D., Ed.; Verlag Chemie: New York, 1976. (b) Cohen, M. D. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 386 pp. (c) Desiraju, G. R. *Organic Solid State Chemistry*; Elsevier: Amsterdam, 1987; p 550. (d) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker, Inc.: New York, 1987; pp 249−347. (e) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433−81.

(2) For a few representative examples, see: (a) Schultz, A. G.; Taverns, A. G.; Taylor, R. E.; Tham, F. S.; Kullnig, R. K. *J. Am. Chem. Soc.* **1992**, *114*, 8725−8727. (b) Skinner, K. J.; Blaskiewicz, R. J.; McBride, J. M. *Isr. J. Chem.* **1972**, *10*, 457−470. (c) Jones, R.; Scheffer, J. R.; Trotter, J.; Yang, J. *Tetrahedron Lett.* **1992**, *33*, 5481−5484.

(3) Schmidt, J. M. J. *J. Chem. Soc.* **1964**, 2014−2021.

(4) (a) Theocharis, C. R.; Jones, W. In *Organic Solid State Chemistry*; Desiraju, G., Ed.; Elsevier: Amsterdam, 1987; pp 47−67. (b) Thomas, J. M. *Nature* **1981**, *289*, 633. (c) Wegner, G. *Pure Appl. Chem.* **1977**, *49*, 443. (d) Enkelmann, V.; Wegner, G.; Novak, K.; Wagener, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 10390. (e) Ohashi, Y. *Acc. Chem. Res.* **1988**, *21*, 268−274.

(5) For specific examples see: Quinkert, G.; Tabata, T.; Hickman, E. A. J.; Dobrat, W. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 199.

(6) In a few occasions, such analysis has been carried out; e.g.: (a) Sheen, D. B.; Sherwood, J. N. *Chem. Brit.* **1986**, *June*, 535. (b) Diaz de Delgado, G. C.; Wheeler, K. A.; Snider, B. B.; Foxman, B. M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 420. (c) Lazar, M. In *The Chemistry of the Functional Groups*: *Peroxides*; Patai, S., Ed.; John Wiley & Sons: New York, 1983; p 778.

(7) *cis*-2,6-Dihydroxy-2,6-diphenylcyclohexanone (**1**) was prepared from 2,6-diphenylcyclohexanone by reaction of its trimethylsilylenol ether with MCPBA, followed by reaction with tetramethylammonium fluoride.

(8) Weiss, D. In *Adv. Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1981; p 347.

(9) (a) Tarasov, V. F.; Klimenok, B. B.; Askerov, D. B.; Buchachenko, A. L. *Izv. Akad. Nauk SSSR* **1985**, 361. (b) Zimmt, M. B.; Doubleday, C.; Turro, N. J. *Chem. Phys. Lett.* **1987**, *134*, 549.

(10) The *cis*/*trans* ratio in methanol, ethylene glycol, and glycerol remained constant at 51:49 in spite of an increase in viscosity ($\eta$) from 0.597 to 19.9 to 1490 cP. Only a small increase to *cis*/*trans* 55:45 was observed when irradiations were carried out at 20 °C in sucrose glasses, known to have $\eta = 1.8 \times 10^6$ at 109 °C (viscosity values were obtained from the *CRC Handbook of Chemistry and Physics*; CRC Press: Boca Raton, FL, 1984).

(11) Pokkuluri, P. R.; Scheffer, J. R.; Trotter, J. *Tetrahedron Lett.* **1989**, *30*, 1601−1604.

(12) Compound **1**: colorless prisms obtained from ethanol, mp = 146 °C, space group $P\bar{1}$, $Z = 2$, $a = 8.874(1)$ Å, $b = 11.638(2)$ Å, $c = 7.201(1)$ Å, $V = 690(5)$ Å$^3$, $\alpha = 91.67°$, $\beta = 104.31°$, $\gamma = 105.56°$, $P = 0.043$, $R_w = 0.058$. Compound *cis*-**2**: colorless prisms obtained from ethanol, mp = 104 °C, space group $C2/c$, $Z = 24$, $a = 22.50(1)$ Å, $b = 22.711(2)$ Å, $c = 17.028(7)$ Å, $V = 8410(6)$ Å$^3$, $\beta = 104.86(3)°$, R = 0.058, $R_w = 0.069$.

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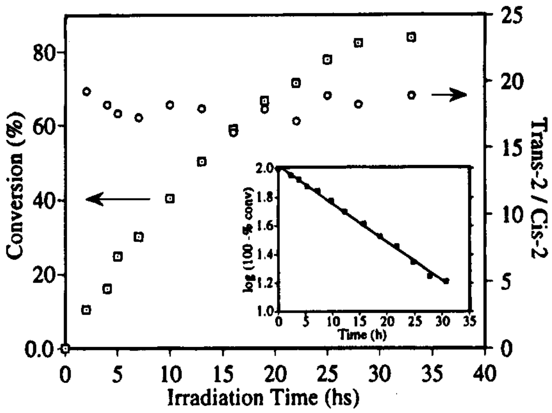

**Figure 1.** Percent conversion (□) and cis/trans ratio (○) from photolysis of **1** as a function of irradiation time. Shown in the inset is a first-order plot for the reaction.

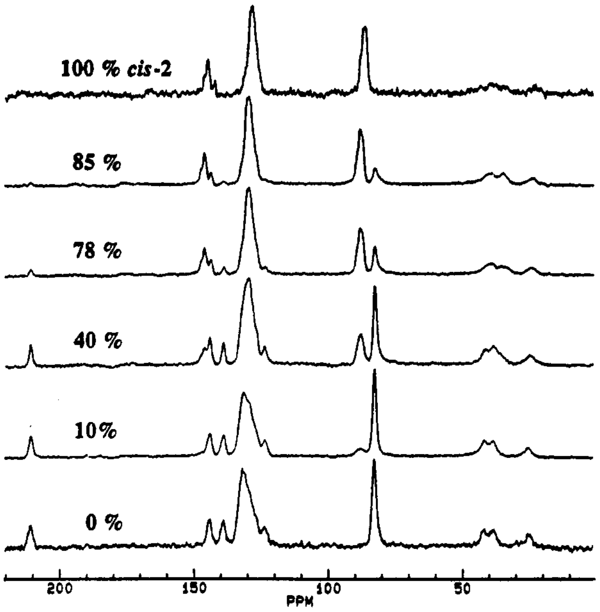

**Figure 2.** $^{13}$C CPMAS spectra (TOSS) of **1** after various irradiation times. Percentages of product accumulated are indicated. The top spectrum corresponds to the recrystallized major product.

function of irradiation time showed a monotonous decay of the reactant phase, as expected for a disordered phase separation.[13] In agreement with the NMR results, solid-state FT-IR (KBr) showed the gradual disappearance of the spectrum of the reactant and its replacement by a spectrum nearly identical to that of the recrystallized major product (Figure 3).[14] Thermal analysis of partially reacted samples showed melting curves indicative of two phases, with a eutectic temperature of 85 °C (Figure 4).

The high selectivity of the reaction is an indication of crystal control and suggests that phase separation occurs at high conversion values, while kinetic analysis argues for a homogeneous process. However, the prompt appearance of the product phase suggests that reaction proceeds through steady-state mixed crystalline phases such that high levels of product accumulation and phase separation occur at microscopic levels. Solid solutions of reactant and product do not accumulate. This interpretation is supported by irradiation of large single crystals ($\lambda$ = 350 nm), where loss of transparency and reaction arrest are observed. Limited reaction in large crystals may be due to decay of their optical properties (as the top layer becomes opaque) and/or to accumulation of internal stress,[15] which may not be easily relieved in large specimens. Powder particles with small cross sections may allow for light capture and more efficient solid-to-solid transformations. Further studies addressing related aspects of this and other reactions are in progress.

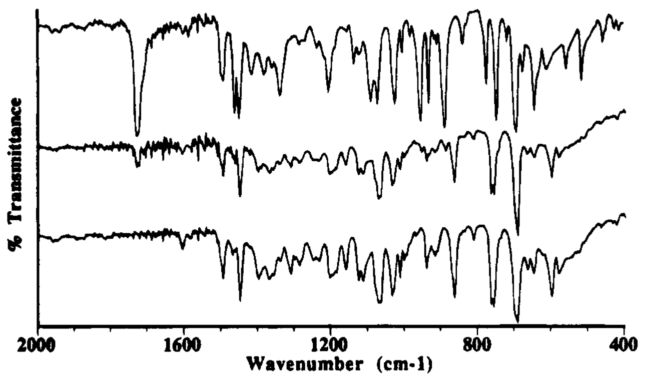

**Figure 3.** Solid-state FT-IR spectra (2000–400 cm$^{-1}$) of **1** (top), **1** after 80% conversion to *cis*-**2** (middle), and *cis*-**2** after recrystallization from ethanol (bottom).

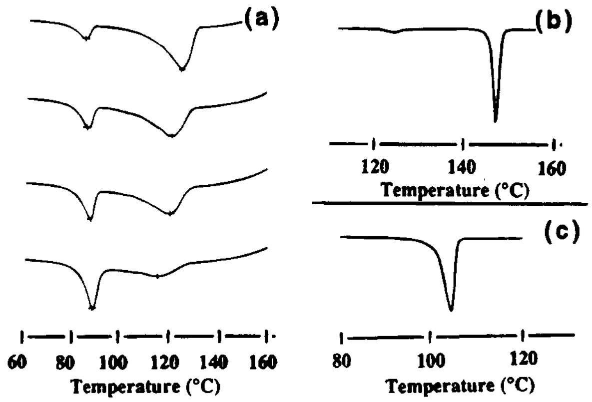

**Figure 4.** DSC thermograms of (a) **1** after irradiation (from top to bottom) for 8, 12, 16, and 28 h, (b) pure **1**, and (c) recrystallized *cis*-**2**.

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**Supporting Information Available:** X-ray data for compounds **1** and *cis*-**2** (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(13) West, A. R. *Solid State Chemistry and Its Applications*; John Wiley and Sons: New York, 1984; pp 417–452.

(14) Identification of polymorphs by solid-state NMR and FT-IR has been well documented, e.g.: Byrn, S. R.; Pfeifer, R. R.; Stephenson, G.; Grant, D. J. W.; Leason, W. B. *Chem. Mater.* **1994**, *6*, 1148–1158.

(15) (a) McBride, J. M. *Acc. Chem. Res.* **1983**, *16*, 304–312. (b) McBride, J. M.; Segmuller, B. E.; Hollingsworth, M. D.; Mills, D. E.; Weber, B. A. *Science (Washington, D. C.)* **1986**, *234, (4778)*, 830–835.