Dramatic Effects of Crystal Morphology on Solid State Reaction Course;[1] Control by Crystal Disorder; Mechanistic and Exploratory Organic Photochemistry
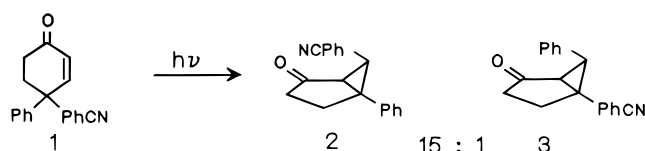
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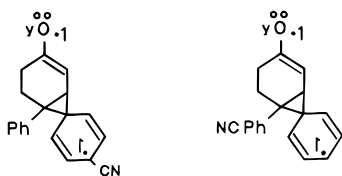
After the initial discovery of the Type B enone rearrangement,[2] the prefential migration of *p*-cyanophenyl and anisyl groups was described.[3] This selectivity arises as a consequence of the extra

electron delocalization available to the migrating aryl group with a para substituent.

Recently, we found the cyano-enone **1** to crystallize in two modifications, one with a $P2_1/c$ space group (termed "crystal A") and the other with a $C2/c$ space group (termed "crystal B"). In view of our interest in solid-state photochemistry,[4] we proceeded to compare the excited state behavior of the two crystals. Crystal A afforded only *p*-cyanophenyl migration photoproduct; this was similar to the solution photochemistry except for the absence of the minor photoproducts observed in solution. In stark contrast, crystal B on photolysis led exclusively to phenyl migration in conversions below 15%. At higher conversion 1:1 regioselectivity was observed and 3:1 for crystal A.

Thus, crystal constraints control the reaction regioselectivity to the extent that in the case of crystal B extra electronic stabilization of 2.5 kcal/mol[5] for the cyanophenyl bridged species is overridden.

(1) This is Paper 187 of our Photochemical Series and 253 of our General Series. For Paper 252 of our General Series, see Zimmerman, H. E.; Ignatchenko, A. *J. Org. Chem*. **1999**, *64*, 6635−6645.

(2) (a) Zimmerman, H. E.; Wilson, J. W. *J. Am. Chem. Soc*. **1964**, *86*, 4036−4042. (b) Zimmerman, H. E.; Hancock, K. G. *J. Am. Chem. Soc*. **1968**, *90*, 3749−3760.

(3) Zimmerman, H. E.; Rieke, R. D.; Scheffer, J. R. *J. Am. Chem. Soc*. **1967**, *89*, 2033−2047.

(4) (a) Zimmerman, H. E.; Zuraw, M. J. *J. Am. Chem. Soc*. **1989**, *111*, 2358−2361. (b) Zimmerman, H. E.; Zuraw, M. J. *J. Am. Chem. Soc*. **1989**, *111*, 7974−7989. (c) Zimmerman, H. E.; Zhu, Z. *J. Am. Chem. Soc*. **1994**, *116*, 9757−9758. (d) Zimmerman, H. E.; Zhu, Z. *J. Am. Chem. Soc*. **1995**, *117*, 5245−5262. (e) Zimmerman, H. E.; Sebek, P. *J. Am. Chem. Soc*. **1997**, *119*, 3677−3690. (f) Zimmerman, H. E.; Sebek, P.; Zhu, Z. *J. Am. Chem. Soc*. **1998**, *120*, 8549−8550.

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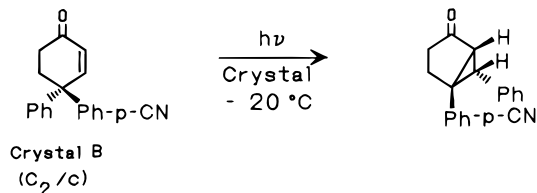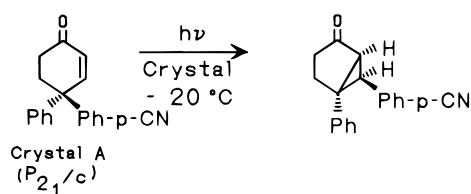
However, with *R* values of circa 6%, the crystals were neverthless somewhat disordered. Using Shelxtl,[6] we determined that the disorder in these centrosymmetric crystals was due to the statistical presence of the wrong enantiomer. This seems to be a consequence of the ethano moiety and the double bond being similar in shape and size. Scheme 1 describes the situation.

Scheme 1. Nature of the Disorder
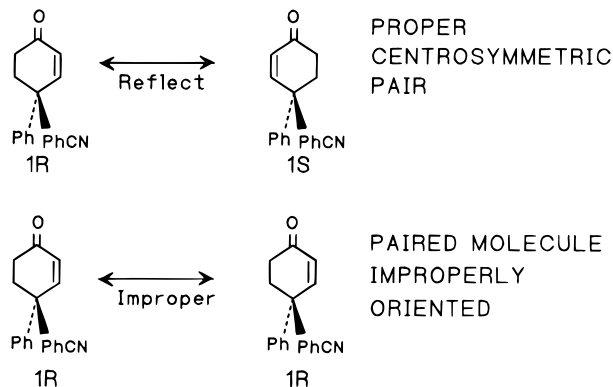
Insight into the role of the disorder in leading to preferential phenyl migration was achieved using "Pairs"[5] which looks at a coordinate file for a mini-crystal lattice and provides an ordered list of atom pairs and distances between the central molecule and its neighbors. Note Table 1. Applied to the ideal minicrystal lattice (i.e. without disorder), based on Smartpac,[4d] and with the triplet transition structure replacing a central enone reactant, it was ascertained that there is a close approach between a neighboring enone α-CH$_2$ and the diradical β-CH$_2$ (entry labeled b in Table 1) and *m*-cyanophenyl hydrogens (entry labeled a in Table 1). This unfavorable interaction is relieved by replacement of the offending lattice molecule by its enantiomer. Thus, with this analysis in hand, it was possible to take an ordered minicrystal lattice and to replace the most interfering molecule with its enantiomer, hence creating a model for the disordered crystal. This is tantamount to saying that the reaction takes place adjacent to the locus of crystal disorder. Oniom[7] optimization of the two transition structures (6/31G*) in this disordered $C2/c$ minicrystal lattice, indeed, did afford a 2.3 kcal/mol lower energy for phenyl migration while in the ordered crystal lattice a lower energy (7.5 kcal/mol) for *p*-cyanophenyl migration resulted. Significantly, replacement of other than the nearest neighboring molecule did

(6) Sheldrick, G. M. *SHELXTL PLUS*, VERSION 4.2; Siemens Analytical X-Ray Instrumentations, Inc.: Madison, Wisconsin.

(7) Gaussian 98, Revision A.6; Frisch, M. J.; Morokuma, K. et. al., Gaussian, Inc.: Pittsburgh, PA, 1998.

Table 1. Pairs Analysis Giving Inner and Outer Atom Numbers, Distances, and Simple Van der Waals Energies[a]

Ph migration disordered crystal				Ph migration ordered crystal				cyanophenyl migration ordered crystal			
IN	OUT	dist	energy	IN	OUT	dist	energy	IN	OUT	dist	energy
23	615	2.418	3.84	31	155	2.327	6.19 (a)[b]	9	700	2.386	4.59
32	414	2.427	3.66	21	70	2.359	5.27	31	414	2.408	4.07
9	188	2.483	2.54	8	155	2.443	3.32 (b)[b]	12	188	2.461	2.96
34	70	2.537	1.66	33	414	2.500	2.26	13	188	2.526	1.83
9	192	2.564	1.28	21	60	2.533	1.72	23	693	2.548	1.50

[a] "IN" refers to the inner, reacting triplet molecule; "OUT" refers to an outer shell lattice molecule. [b] See text.
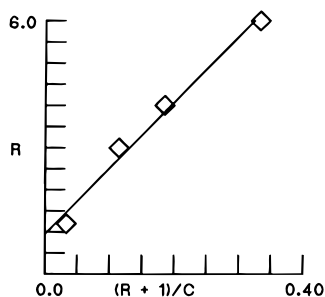
Figure 1. Plot of phenyl to cyanophenyl migration ratio R versus $(R + 1)/C$. C is the conversion.

not lead to prediction of phenyl migration. Similar theoretical treatment of the $P2_1/c$ crystal A predicted *p*-cyanophenyl migration in accord with experiment.

Hence it is the disorder that modifies the shape of the crystal cavity and leads to preferential phenyl migration. This seems to be the first example of a photochemical reaction being correlated to a specific crystal site.

A further and equally significant result was found. Thus in each of the crystals the reaction was found to consist of two sharply defined stages designated I and L. Thus for crystal B, while up to 15% conversion only phenyl migration resulted, beyond this point 1:1 phenyl and cyanophenyl migration took place with the reaction being monitored up to 66% completion. The phenomenon could be analyzed kinetically. Equation 1 gives the extent of conversion, C, as the sum of contributions from the initial stage I and the later stage L. The ratio, R, of the two photoproducts is given in eq 2. Equation 3 results from the first two. It is seen that a plot of the product ratio R versus $(R + 1)/C$

$$C = I_{ph} + L_{ph} + L_{cn}$$

[three product components giving conversion] (1)

$$R = (I_{ph} + L_{ph})/L_{cn}$$

[ratio of phenyl to cyanophenyl products] (2)

$$R = (I_{ph}(R + 1))/C + (L_{ph}/L_{cn})$$ [from eqs 1 and 2] (3)

gives I_{ph} and (L_{ph}/L_{cn}) as slope and intercept. Thus, we obtain the extent of phenyl migration in stage 1 as the slope I_{ph} (15.6) and the regioselectivity $(L_{ph}/L_{cn} = 0.95)$ occurring in the later stage 2 of the reaction. Figure 1 shows the linearity of the plot. A parallel treatment for crystal A reveals an initial stage extending to 9.9% of the reaction giving cyanophenyl migration and a subsequent 2.9:1 selectivity favoring cyanophenyl migration. See the Supporting Information for further details. The kinetic treatment seems without precedent.

The linearity of the plot provides evidence for a striking conclusion, namely that partway through these crystalline state reactions there is a discontinuous change in selectivity. One interpretation is that each reacting molecule, surrounded by ca. six neighbors including one mis-oriented enantiomer, constitutes a unique cluster giving rise to the selectivity of stage 1. Thus, when 15% of all such molecules have reacted, all such clusters are gone and new reactivity ensues with new selectivity. In stage 2 the reaction has created a new type of disorder.

The present results need to be taken in context of our past research and that of other reseachers. Our use of a "minicrystal lattice" and an outline of other quantitative approaches in the literature has been reviewed recently.[4f] Our approach differs in employing the energetics of alternative transition structures of the reacting molecule in a crystal lattice as a guide rather than geometry of the reactant itself.

More germane to the present paper is research dealing with polymorph reactivity and also the role of defects. The most classical case of different reactivity of polymorphs is the cinnamic acid dimerization where head-to-head and head-to-tail crystals afford the truxinic and truxilic acids.[8a,b] Recently, very pretty examples of differing reactivity of dimorphs have been described by Scheffer[8c] and Toda.[8d]

The role of crystal defects and disorder has been a more difficult topic. Much elegant and early efforts derive from the work of Thomas,[9a] and there have been many further suggestions of photochemical reactions occurring at crystal defects.[9b,c,10] The present research now provides a solid basis.

Supporting Information Available: Experimental details and tables of results (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) (a) Ramdas, S.; Jones, W.; Thomas, J. M.; Desvergene, J-P. *Chem. Phys. Lett.* **1978**, *57*, 468−470. (b) Note the excellent review by Ramamurthy and Venkatesan: Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433−481. (c) Craig, D. P.; Sarti-Fantoni, P. *J. Chem. Soc., Chem. Commun.* **1966**, 742−743. (d) Vishnumurthy, K.; Row, T. N. G.; Venkatesan, K. *Tetrahedron* **1998**, *54*, 11235−11246.
(10) Takegoshi, K.; Nakamura, S.; Terao, T. *Solid State Nucl. Magn. Reson.* **1998**, *11*, 189−196.
(11) The initial observations of two polymorphs was by Mr. R. Chapman.