ABSOLUTE ASYMMETRIC INDUCTION DIFFERENCES IN DUAL PATHWAY PHOTOREACTIONS

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Abstract. The achiral ester-lactone **1**, which crystallizes spontaneously in the chiral space group $P2_12_12_1$, affords two regioisomeric di-π-methane products when photolyzed in the solid state. One of the photoproducts is formed in near-quantitative enantiomeric excess, whereas the other is produced as a racemate. The results demonstrate that the asymmetric influence of the chiral crystal lattice medium may have variable effects on reaction enantioselectivity.

Absolute asymmetric synthesis is defined as an asymmetric synthesis carried out in a closed system in the absence of any external chiral inducing agents.[1] It is a process unique to the crystalline phase, and its first stage consists of the spontaneous crystallization of an achiral reactant in a chiral space group.[2] The second stage of the process involves a solid state chemical reaction, often photochemical in nature, that transforms the crystalline reactant into a product possessing permanent molecular chirality. In such cases, the enantiomeric excess in which the product is formed is a direct measure of the asymmetric induction by the chiral matrix.

To date, all reported absolute asymmetric syntheses (of which there are very few)[3] have been of the single pathway variety, that is, only one product is formed. For chiral crystals that react to give two (or more) products, however, it is interesting to ask whether each product will be formed in the same enantiomeric excess. By studying such processes, we learn much about the lattice forces that govern the chemical reactivity of organic crystals. In the present communication, we describe the dual pathway photoreaction of a chiral crystal that leads to products of <u>widely differing</u> optical purity.

The compound selected for study emerged from our work on the di-π-methane photorearrangement of dibenzobarrelene and its derivatives in the solid state.[4] As part of this study, we prepared the ester-lactone **1** (Scheme 1) by Diels-Alder addition of dimethyl acetylenedicarboxylate to 9-anthracene methanol at 170° (neat). Under these conditions, lactonization of the initial adduct was virtually complete. Compound **1** forms stout prisms, mp 170-171.5°, from chloroform-ethanol, and an X-ray crystal structure analysis indicated the chiral space group $P2_12_12_1$.[5] In principle, ester-lactone **1** is capable of giving two regioisomeric di-π-methane photoproducts, **2** and **3**, upon photolysis.[6] In practice, both products are formed only in the solid state (ratio 87:13); in solution (acetone, acetonitrile or benzene), there was no trace of photoproduct **3**.[7] The photoproduct structures were assigned by NMR spectroscopy; particularly informative was the chemical shift of the non-aromatic methine hydrogen in each case -- 5.17 ppm for **2** and 4.85 for **3** -- a trend that is general for compounds

Scheme 1
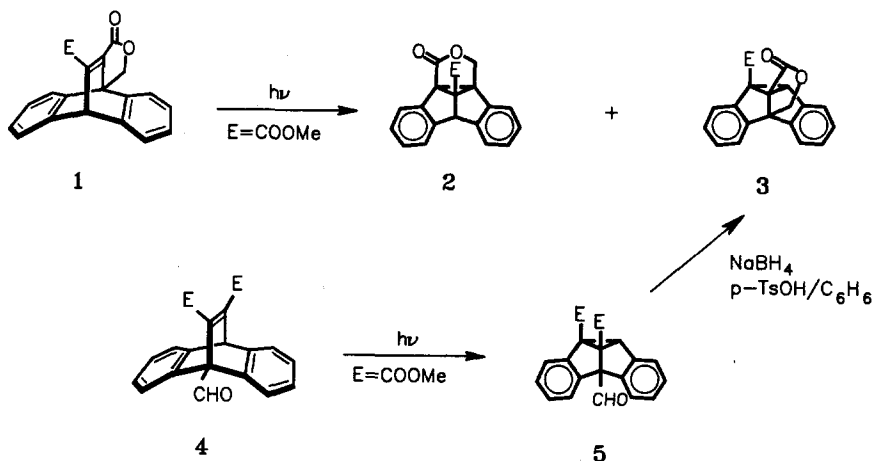
of this type.[8] To corroborate these assignments, photoproduct 3 was synthesized independently by making use of the known[8a] 4 → 5 phototransformation (Scheme 1).

The optical purities of photoproducts 2 and 3 from the solid state irradiations were determined by chiral shift reagent NMR spectroscopy of mixtures of the two. Eu(hfc)$_3$ (Aldrich) was used as the shift reagent, and the peaks monitored were the methyl ester singlets. This showed that photoproduct 3 is formed in high enantiomeric excess and that its regioisomer 2 is racemic. In four separate trials at -20°, the enantiomeric excesses for compound 3 were (+)-70%, (+)-74%, (-)-100% and (-)-100%. Raising the temperature caused a noticeable diminution of the enantioselectivity. For example, at +20° the enantiomeric excesses for five runs were (+)-58%, (-)-61%, (-)-56%, (-)-52% and (-)-66%. In none of the runs, however, was there any evidence within the limits of the chiral shift reagent method (ca. ± 3% accuracy) for optical activity in the case of compound 2.

There are two main questions raised by the photochemical results. First of all, why is regioisomer 2 favored regardless of medium, and secondly, why is only regioisomer 3 produced in optically active form in the solid state? To help in answering these questions, we recall that the di-π-methane rearrangement of compounds like 1 is thought to occur via initial benzo-vinyl bridging, and that this can take place in four ways: a-x/a-x' and b-y/b-y' (Scheme 2a).[9] Path b-y leads to one enantiomer of 2 and path b-y' leads to the other. Similarly, pathways a-x and a-x' lead to the enantiomers of photoproduct 3. The preference for formation of photoproduct 2 may reflect a steric effect that is present between the methylene hydrogen atoms of the lactone ring and the adjacent aromatic hydrogen atoms (Scheme 2a). The H···H distances from crystallography are a startlingly short contact of 2.1 Å on one side and a less severe interaction of 2.4 Å on the other.[10] Molecular models show that pathways b-y and b-y' leading

Scheme 2

(a)   (b)
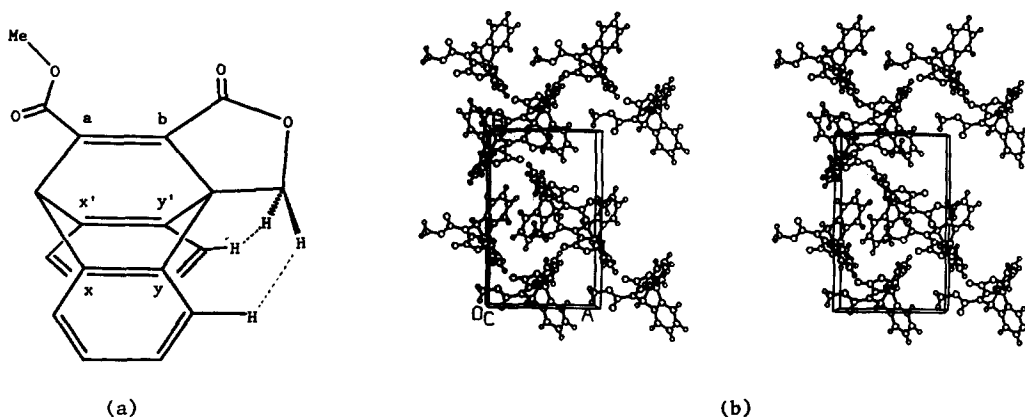
to 2 relieve this interaction to a much greater extent than a-x and a-x'; the latter paths afford 3 with the unfavorable H···H interactions basically intact. In solution, the H···H contacts will average to approximately 2.06/2 + 2.43/2 = 2.25 Å, still well below the van der Waals sum of 2.40 Å. It is not surprising, therefore, that the regioselectivity is in the same direction in both liquid and solid media.

Regarding the optical activity generated in photoproduct 3 in the solid state, we suggest that this may stem from an intermolecular steric effect in the crystal that favors path a-x over path a-x'. As bonds a-x and a-x' begin to form, the COOMe group at position a swings through a wide arc either toward (a-x) or away (a-x') from the viewer (Scheme 2a). The packing diagram (Scheme 2b) clearly shows that the latter pathway (but not the former) is hindered by a hydrogen atom from a neighboring molecule that lies 2.49 Å directly behind the ether oxygen atom of the ester group. This is substantially less than 2.72 Å, the sum of the van der Waals radii for oxygen and hydrogen.[10] In contrast, it is apparent that both sides of the lactone ring are tightly packed, thus accounting for the lack of enantioselectivity in the formation of photoproduct 2 as well as the diminution in the relative amount of this product formed in the solid state compared to solution. Similar steric effects have been suggested to be responsible for determining the regioselectivities of di-π-methane photoreactions in the solid state.[4]

In conclusion, even though the mechanistic rationale is speculative, the results demonstrate clearly that the extent of asymmetric induction in the reactions of chiral crystals depends uniquely on the crystal packing characteristics of the compound under study and can vary from 0-100%.

References and Footnotes

1. L. Addadi, J. van Mil and M. Lahav, <u>J. Am. Chem. Soc.</u>, 104, 3422 (1982).

2. For a discussion of this process, see J. Jacques, A. Collet and S.H. Wilen, "Enantiomers, Racemates and Resolutions," Wiley, New York, 1981. See also W.A. Bonner in "Topics in Stereochemistry," Wiley, New York, Vol. 18, 1988, Ch. 1.

3. For reviews, see B.S. Green, M. Lahav and D. Rabinovich, <u>Acc. Chem. Res.</u>, 12, 191 (1979) as well as J.R. Scheffer and M. Garcia-Garibay in "Photochemistry on Solid Surfaces," M. Anpo and T. Matsuura, Eds., Elsevier, Amsterdam, 1989, Ch. 9.3, pp. 501-525.

4. J.R. Scheffer, J. Trotter, M. Garcia-Garibay and F. Wireko, <u>Mol. Cryst. Liq. Cryst. Inc. Nonlin. Opt.</u>, 156, 63 (1988).

5. Compound 1: $P2_12_12_1$; a = 10.3491(8), b = 16.6204(9), c = 8.9933(6) Å; Z = 4; R = 0.038. Full crystallographic details will be published separately.

6. For a review of the di-π-methane photorearrangement, see H.E. Zimmerman in "Molecular Rearrangements in Ground and Excited States," P. de Mayo, Ed., Academic, New York, 1980, Ch. 16. E. Ciganek, <u>J. Org. Chem.</u>, 45, 1505 (1980) has reported the solution phase photochemistry of a lactam related to 1.

7. All photolyses were conducted through Pyrex (transmitting $\lambda > 290$ nm). The quantum yield for the formation of photoproduct 2 in benzene was 0.48. In the solid state, identical regio- and enantioselectivities were observed for both single crystal and polycrystalline samples. The reaction was, however, faster in the case of the polycrystalline samples, and conversions of essentially 100% with no loss in selectivity could be achieved.

8. (a) M. Iwamura, H. Tukada and H. Iwamura, <u>Tetrahedron Lett.</u>, 21, 4865 (1980); (b) R. G Paddick, K.E. Richards and G.J. Wright, <u>Aust. J. Chem.</u>, 29, 1005 (1976); (c) J. Chen, P.R. Pokkuluri, J.R. Scheffer and J. Trotter, <u>J. Photochem. Photobiol. A</u>, in press.

9. Benzo-vinyl bridging refers to formation of a cyclopropyldicarbinyl diradical species by bonding between one of the vinyl carbon atoms and a neighboring aromatic carbon atom. While there is general agreement that this interaction precedes formation of the 1,3-biradical intermediate that leads to product, it is unclear whether cyclopropyldicarbinyl diradicals represent true minima on the di-π-methane rearrangement hypersurface. For leading references on the mechanism of the di-π-methane reaction, see reference 6 plus (a) L.A. Paquette and E. Bay, <u>J. Org. Chem.</u>, 47, 4597 (1982); (b) W. Adam, M. Dorr, J. Kron and R.J. Rosenthal, <u>J. Am. Chem. Soc.</u>, 109, 7074 (1987); (c) H.E. Zimmerman and A.P. Kamath, <u>J. Am. Chem. Soc.</u>, 110, 900 (1988).

10. The commonly accepted van der Waals radii of hydrogen and oxygen are 1.20 and 1.52 Å, respectively. See A. Bondi, <u>J. Phys. Chem.</u>, 68, 441 (1964). The non-bonded repulsion energy arising from interatomic contacts rises steeply below the sum of the van der Waals radii of the atoms involved. See for example, J-H. Lii and N.L. Allinger, <u>J. Am. Chem. Soc.</u>, 111, 8576 (1989) and references cited therein.