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CRYSTAL TO MOLECULAR CHIRALITY TRANSFER: SUPRAMOLECULAR PHOTOCHEMISTRY OF CRYSTALLINE CARBOXYLATE SALTS

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Abstract Solid state irradiation of a salt formed between a prochiral, photochemically reactive carboxylic acid and a non-absorbing, optically active amine is shown to lead to an optically active Norrish type II photoproduct whose optical purity depends on the dimorphic crystalline modification photolyzed.

Salts formed between carboxylic acids and amines provide high-melting crystalline materials in which the cations and anions can be tailored through organic synthesis to serve various functions in organic chemistry and materials science. In this paper we describe the situation in which an optically active ammonium ion is used to induce optical activity in the products of a solid state photorearrangement of a prochiral carboxylate anion. The goal of the research is to develop a general procedure for asymmetric induction in solid state photochemical reactions. While the concept of using the organic solid state as a medium in which to carry out asymmetric syntheses is not new, having been reported for both one component[1] and two component (host-guest)[2] systems, this and previous reports from our laboratory[3] represent the first use of organic salts for such a purpose.

The carboxylic acid chosen for study was the adamantane derivative **1a** (Scheme).[4] This compound, which contains a plane of symmetry and is thus achiral, was expected on the basis of ample literature precedent to undergo the Norrish type II reaction to afford the chiral cyclobutanol derivatives **2** and **3**.[5,6] By forming salts of **1a** with optically active amines, irradiating them in the solid state, and determining the optical purity of the photoproducts, the extent of asymmetric induction could be assessed. Accordingly, keto-acid **1a** was treated with a variety of optically active amines and the resulting salts recrystallized; best results were obtained with S-(+)- and R-(-)-prolinol, and these salts (**1b**) form the basis of this communication. Interestingly, the prolinol salts were found to be dimorphic; recrystallization from acetone produced an initial crop of platelike crystals, mp 116-118 °C, whereas needle-shaped crystals (mp 128-130 °C) were obtained from the mother liquor. The X-ray crystal structure of each dimorph was obtained by direct methods.[7]

Each salt was photolyzed in the solid state as well as in solution.[8] In addition, for comparison purposes, the methyl ester **1c** was irradiated in solution. As expected, the cyclobutanol derivatives **2** and **3** were formed, and the Table summarizes the product ratios obtained in each case (after diazomethane workup) along with the enantiomeric excess in which the major photoproduct **2c** is formed.[9] Strikingly, the needle dimorph of salt **1b** gives cyclobutanol **2c** in 97% optical purity; S-(+)-prolinol leads to (+)-**2c**, and R-(-)-prolinol affords (-)-**2c**. Similar regioselectivity was obtained when the plate dimorph of salt **1b** was irradiated in the solid state, but in this case photoproduct **2c** was formed in only 12% ee and with reversed enantioselectivity. Finally, when either dimorph was dissolved in chloroform and photolyzed, no optical activity at all could be detected in the photoproducts.

Scheme

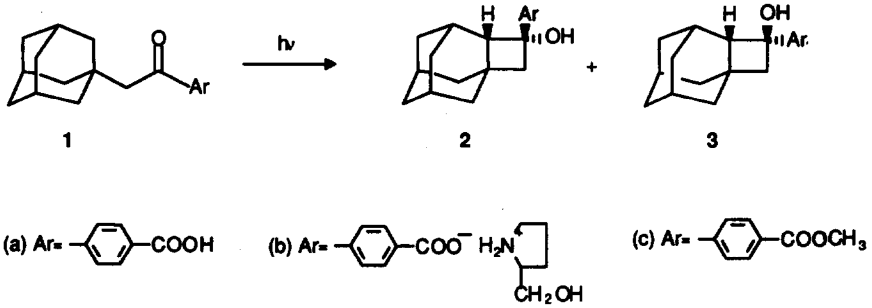

Table Photoproduct Ratios and Enantiomeric Excesses Obtained by Photolysis of Salt **1b** and Ester **1c**

Compound Photolyzed	Conversion (%)	Photolysis Medium	Prolinol Config	Crystal Morph	**2c**:**3c** Ratio[a]	ee (%) (**2c**)
1b	87	Solid State	S-(+)	Needles	5.5:1	97(+)[b]
1b	69	Solid State	R-(-)	Needles	5.5:1	97(-)[b]
1b	79	Solid State	S-(+)	Plates	5.5:1	12(-)[b]
1b	40	Chloroform	S-(+)	-	1.6:1	0[b]
1c	5	Benzene	-	-	3.3:1[c]	-

[a] As determined by column chromatography following acidification, separation of the ammonium salt and esterification of the carboxylic acid fraction with diazomethane; [b] As determined by chiral shift reagent NMR analysis with $Yb(hfc)_3$ (Aldrich); sign of rotation of predominant enantiomer shown in parentheses; [c] overall quantum yield = 0.043.

The X-ray crystal structures of the needle and plate dimorphs of salt **1b** reveal the likely reason for the difference in enantiomeric excess with which photoproduct **2c** is formed in the solid state. The key lies in the fact that the carboxylate anions in the needle crystals adopt a single, homochiral conformation, whereas in the plate form, there are two independent carboxylate anions in the asymmetric unit that have opposite absolute configurations, even though each is associated with an S-(+)-prolinol-derived cation.[10] With this information, the interpretation of the results is straightforward: the needles react stereospecifically from a single conformational stereoisomer of the reactant to give a single stereoiosmer of the photoproduct. In the plate crystals, however, there are competing stereospecific photoreactions, and these result in a photoproduct of low overall enantiomeric excess. Because the reaction is occurring in a chiral environment, the competing reactions have diastereomeric transition states of unequal energy, thus accounting for the non-racemic nature of the photoproduct.[12]

In contrast to the solid state results, polarimetry and chiral shift reagent NMR studies indicate that the solution phase photoproduct mixture is truly racemic. In this case it seems likely that the photoreaction is non-stereospecific as a result of the conformational freedom of the reactant as well as the more random orientation between it and the chiral auxiliary. The asymmetric induction observed in the solid state is attributable, therefore, to the overall "supramolecular" environment of the chiral crystal lattice, and the role of the chiral auxiliary is primarily one of guaranteeing a chiral space group rather than exerting a direct asymmetric influence on the reaction. As such, the phrase "crystal to molecular chirality transfer" seems appropriate.

In summary, the results demonstrate that under the proper circumstances, very high enantiomeric excesses can be achieved by employing ionic chiral auxiliaries in solid state photochemistry. Because high conversions are possible, the method holds considerable synthetic promise. Current research in our laboratory is aimed at using a similar approach in the design of ionic crystals having good second order non-linear optical properties.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Financial support by the Natural Sciences and Engineering Research Council of Canada is also gratefully acknowledged.

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2. Ramamurthy, V. In Photochemistry in Organized and Constrained Media; Ramamurthy, V., Ed.; VCH Publishers: New York, 1991; Chapter 7.
3. For previous work on this topic from our laboratory, see Gudmundsdottir, A.D.; Scheffer, J.R. Tetrahedron Lett. **1990**, 31, 6807-6810 and Gudmundsdottir, A.D.; Scheffer, J.R. Photochem. Photobiol. **1991**, 54, 535-538.
4. Keto-acid **1a** was prepared by Friedel-Crafts acylation of fluorobenzene with 1-adamantylacetyl chloride followed by reaction with sodium cyanide and hydrolysis of the nitrile. This material and all other compounds reported in this communication exhibited spectroscopic and analytical data entirely consistent with their assigned structures. Details will be provided in a forthcoming full paper.
5. Norrish type II cleavage is precluded in the case of α-adamantyl ketones owing to the prohibitive strain energy involved in the formation of adamantene. (a) Sauers, R.R.;

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6. Cyclobutanol products in type II photochemistry were first reported by Yang, N.C.; Yang, D.H. J. Am. Chem. Soc. **1958**, 80, 2913-2914.
7. Needles: $P2_12_12_1$; a = 17.266 (2) Å, b = 19.292 (3) Å, c = 6.3739 (9) Å; Z = 4; R = 4.1%. Plates: $P2_12_12_1$; a = 11.798 (1) Å, b = 43.563 (3) Å, c = 8.4434 (8) Å; Z = 8; R = 5.6%. Full details will be published separately.
8. The samples were prepared for solid state photolysis by crushing the crystals between two Pyrex plates and sliding the plates back and forth so as to distribute the crystals over the surface in a thin, even layer. The sample plates were then taped together at the top and bottom ends, placed in polyethylene bags, degassed with nitrogen and sealed under a positive pressure of nitrogen with a heat-sealing device. The bags were immersed in a cooling bath maintained at -40 °C by means of a cryomat and irradiated with the output from a 450 W Hanovia medium pressure mercury lamp. Conversions of 70% and higher were possible in the solid state runs without significant sample melting or loss of enantioselectivity. In a typical run, a "sandwich" containing 120 mg of salt required 24 h of photolysis.
9. The enantiomeric excess in which the minor photoproduct **3c** is formed in the solid state could not be determined owing to small samples sizes and purification difficulties.
10. The absolute configuration of the reactant anion can be defined by the sign of the O=C-C(α)-C(β) dihedral angle, which in the case of the needle dimorph is negative (-82°, S absolute configuration); in the plate crystals, half the molecules are R (+85°) and half are S (-82°). The conformations in each case are very similar, but not identical. In the needle crystals, the most favorable γ-hydrogen for abstraction is located at a distance of 2.70 Å from the ketone oxygen atom. The angle ω, defined as the degree to which the γ-hydrogen atom lies outside the mean plane of the carbonyl group,[11] is 46° in this case, the C=O...H angle Δ = 87° and the C-H...O angle θ = 118°. The corresponding values for the independent R and S molecules in the plate crystals are d = 2.69 and 2.67 Å, ω = 54 and 54°, Δ = 84 and 83° and θ = 115 and 115°. Very similar data have been tabulated for other solid state Norrish type II processes.[11]
11. (a) Scheffer, J.R. In Organic Solid State Chemistry; Desiraju, G.R., Ed.; Elsevier: New York, 1987; Chapter 1. (b) Wagner, P.; Park, B-S. In Organic Photochemistry; Padwa, A., Ed.; Marcel Dekker: New York, 1991; Volume 11; Chapter 4.
12. We cannot, of course, rule out the possibility that the photoreaction of the plate crystals is largely non-stereospecific. As we have shown recently,[13] photoreactions in chiral crystals do not always proceed with high enantioselectivity.
13. Chen, J.; Pokkuluri, P.R.; Scheffer, J.R.; Trotter, J. Tetrahedron Lett. **1990**, 31, 6803-6806.

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