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Solid State Photochemistry: Absolute Asymmetric Photocyclization of an Achiral *S*-Aryl *o*-Benzoylbenzothioate to an Optically Active Phthalide Involving a Novel Phenyl Migration

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Photoreactions in the solid phase often present unusual and interesting behavior because of the restrictions to molecular motions that are imposed by the environment.[1−4] Prochiral reactions that occur under the influence of chiral crystalline media are among the most interesting examples of solid state control,[5,6] and several successful "absolute" asymmetric syntheses involving unimolecular reactions have been reported.[7−13] In this Communication we report an example involving chiral crystals of an achiral *S*-(*o*-tolyl) *o*-benzoylbenzothioate which gives an optically active phthalide via a novel photochemical 1,4-phenyl migration. The proposed reaction mechanism was revealed in this case by a stereochemical correlation based on the absolute configuration of the starting thioester and the final photoproduct.

The thioester **1** was prepared from *o*-benzoylbenzoyl chloride and *o*-methylthiophenol. Recrystallization from chloroform−hexane yielded colorless prismatic crystals (mp 118−119 °C). X-ray crystallographic analysis indicated the chiral space group $P2_12_12_1$, $a = 9.917(3)$ Å, $b = 20.845(6)$ Å, $c = 8.339(4)$ Å, $V = 1723(1)$ Å^3, $Z = 4$, $\rho = 1.281$ g/cm^3, μ(Cu Kα) = 17.35 cm^{-1}.[14] All the crystals from a given batch belonged to the same enantiomorphic modification and could be obtained with the same chirality of the crystals used for seeding. The circular dichroism (CD) spectra of the two enantiomorphs in KBr are shown in Figure 1. Crystals are designated as (+) or (−) according to the sign of their ellipticity at 346 nm.

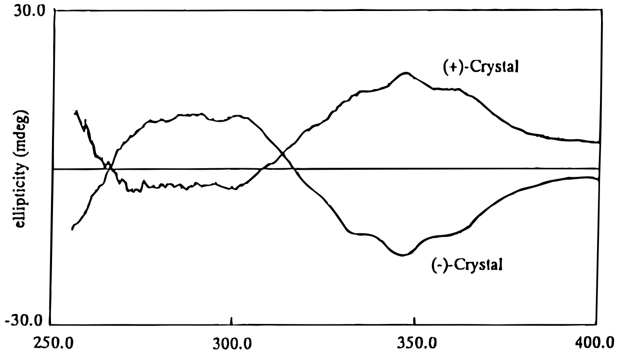

Figure 1. CD spectra of two enantiomeric crystals of **1** in KBr. A mixture of 100 μg of **1** and 100 mg of KBr was well ground and formed into a disk with a radius of 5 mm.

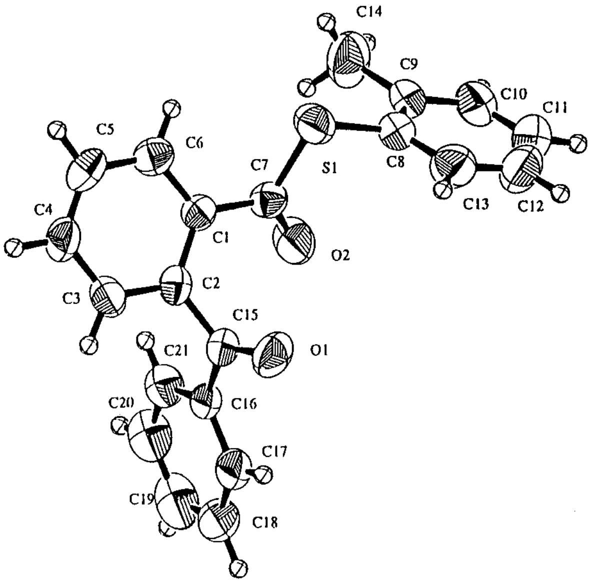

Figure 2. ORTEP drawing of the absolute structure of (*P*)-(+)-**1**.

It is notable that two carbonyls are twisted from the central phenyl ring (Figure 2). The twist angle of the C15(=O1)—C16 moiety is 66.0° and is much greater than that of the C7(=O2)—S1 moiety (35.5°).[15] This structure is consistent with the central benzene fragment being conjugated through the thioester carbonyl rather than through the benzoyl carbonyl group. The absolute structure of (+)-**1** was solved by the Bijvoet difference method. A total of 877 Friedel pairs with F_c differing significantly at the end of the refinement were measured with great care. Of those 633 showed agreement and 244 showed disagreement between observed and calculated ΔF for the structure containing molecules with dextral (*P*)-configuration for the helix as shown in Figure 2, which gives clear evidence that this structure is that with the correct absolute configuration where the final R and R_w were 0.059 and 0.066.

The thioester (+)-**1** was irradiated with UV light from a 500 W high-pressure Hg lamp at 0 °C for 6 h as a white powder sandwiched between two Pyrex slides sealed in a polyethylene bag. The phthalide **2** was obtained in 65% yield at 100% conversion after purification by column chromatography on silica gel. The enantioselective generation of a chiral center is induced at the 3-C position of the phthalide **2** ($[\alpha]^{20}_D = +37°$ in CHCl$_3$ at $c = 1.0$, 30% ee). The enantiomeric purity of **2**

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(1) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York and Basel, 1987; Vol. 8, pp 249−338.

(2) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433−481.

(3) Scheffer, J. R.; Pokkuluri, P. R. In *Photochemistry in Organized and Constrained Media*; Ramamurthy, V., Ed.; VCH: New York, 1991, pp 185−246.

(4) Zimmerman, H. E.; Zhu, Z. *J. Am. Chem. Soc.* **1995**, *117*, 5245−5262.

(5) Green B. S.; Lahav, M.; Rabinovich, D. *Acc. Chem. Res.* **1979**, *69*, 191−197.

(6) Ramamurthy, V.; Weiss, R. G.; Hammond, G. S. In *Advances in Photochemistry*; Volman, D. H., Hammond, G. S., Neckers, D. C., Eds.; John Wiley & Sons: New York, 1993; Vol. 18, pp 67−234.

(7) Evans, S. V.; Garcia-Garibay, M.; Omkaram, N.; Scheffer, J. R.; Trotter, J.; Wireko, F. *J. Am. Chem. Soc.* **1986**, *108*, 5648−5649.

(8) Sekine, A.; Hori, K.; Ohashi, Y.; Yagi, M.; Toda, F. *J. Am. Chem. Soc.* **1989**, *111*, 697−700.

(9) Roughton, A. L.; Muneer, M.; Demuth, M. *J. Am. Chem. Soc.* **1993,** *115*, 2085−2086.

(10) Sakamoto, M.; Hokari, N.; Takahashi, M.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T. *J. Am. Chem. Soc.* **1993,** *115*, 818.

(11) Toda, F.; Tanaka, K. *Supramol. Chem.* **1994**, *3*, 87−88.

(12) Sakamoto, M.; Takahashi, M.; Shimizu, M.; Fujita, T.; Nishio, T.; Iida, I.; Yamaguchi, K.; Watanabe, S. *J. Org. Chem.* **1995,** *60,* 7088−7089.

(13) Recently we reported that photolysis of a thioester chromophore substituted on the nitrogen atom of α-oxoamide gave oxazolidinedione via a radical pair intermediate: Sakamoto, M.; Takahashi, M.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T. *J. Org. Chem.* **1995**, *60*, 3476−3477.

(14) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB 1EZ, U.K.

(15) The twist angle τ is defined as follows: $\tau = 1/2(\omega_1 + \omega_2)$, when ω_1 and ω_2 are torsion angles C1—C2—C15—C16 and O1—C15—C2—C3, respectively, for the twist angle of C15(=O1)—C16. The twist angle τ for C7(=O2)—S1 is determined in the same manner.

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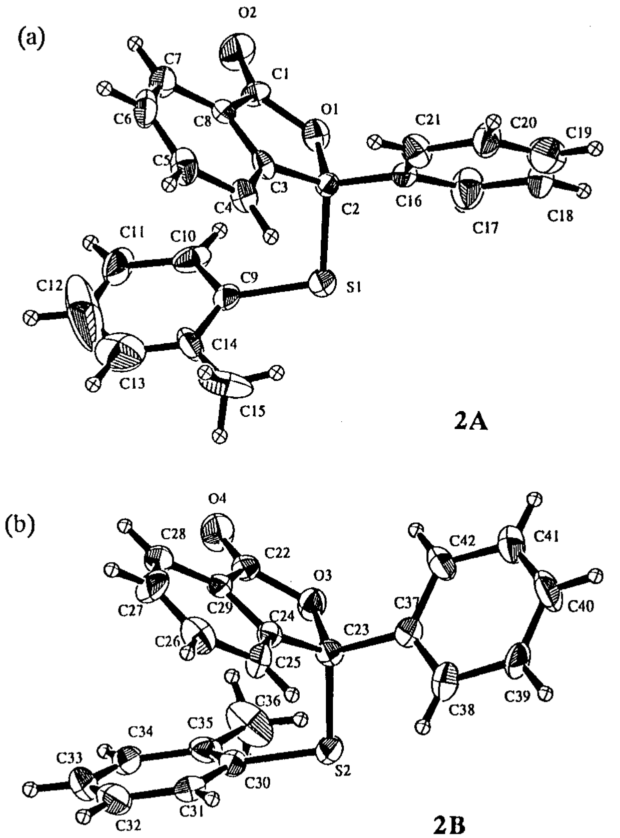


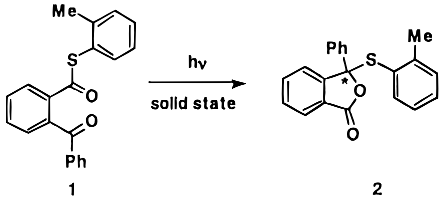
Figure 3. ORTEP drawing of absolute structures of (*R*)-(+)-**2A** and (*R*)-(+)-**2B**.

was determined by HPLC using a chiral cell OJ column (Daicel Chemical Industries). A more stereospecifically controlled reaction was performed both in lower conversion ($[\alpha]^{20}_{D}$ = +94° for 77% ee at 5% conversion) and by the reaction at −78 °C ($[\alpha]^{20}_{D}$ = +80° for 65% ee at 50% conversion).

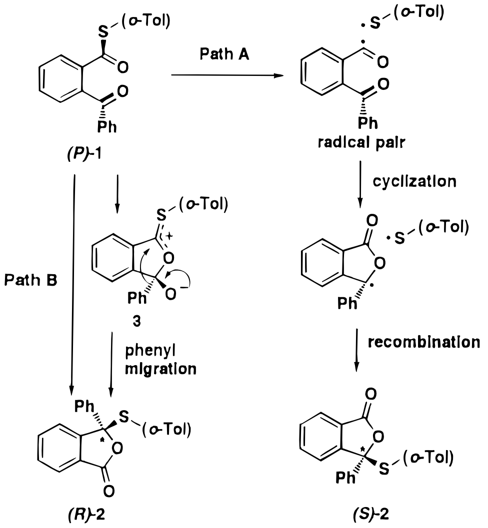
The absolute configuration of (+)-**2** was also determined by X-ray structural analysis using the Bijvoet difference method.[16] It indicated that (+)-**2** crystallized in the chiral space group *P*1 and contained two rotamers (**2A** and **2B**) owing to rotation of the *o*-tolyl group with the same (*R*)-configuration at C2 and C23 in the asymmetric unit (Figure 3).

Plausible mechanisms for the photochemical transformation of **1** leading to **2** are presented in Scheme 2. Path A involves the well-known radical pair intermediate, in which **1** provides acyl and thiyl radicals initiated by the cleavage of the C−S bond upon excitation with a quantum of light.[13,17,18] Path B involves phenyl migration by a concerted process, or via a stepwise mechanism involving intermediate **3**, which occurs by formation of a bond between the oxygen of the thioester and the carbonyl carbon of the benzoyl group. Assuming that reaction in the solid state occurs with minimum molecular and atomic motion, a stereochemical correlation based on the absolute configuration of the reactant and the product helps determine the reaction mechanism. While thioester **1** has no chiral centers, it adopts a chiral conformation in the solid state. The absolute configuration of (+)-**1** was determined to be *(P)*-**1** (planar chirality), and the absolute configuration of photoproduct **2** was established to be *(R)*-**2**. As shown in Scheme 2, the structures *(P)*-**1** and *(R)*-**2** suggest that reaction proceeds via phenyl migration as indicated by path B. It may also be noted that phenylthio migration (path A) would give the other enantiomer [e.g., (*S*)-**2**].[19] We suggest that the decrease in optical purity of the product with increasing conversion is due to partial racemization taking place at defect lattice sites and not to migration of the phenylthio group.[20] The distance required for movement of the phenyl group between C7 and C16 is 3.93 Å, and that required for bond formation between O2 and C15 is 2.78 Å. The conformation of **1** is suitable to produce phthalide **2**.

Scheme 1



Scheme 2



This reaction provides not only a fine example of absolute asymmetric synthesis but also a novel photorearrangement involving a phenyl migration, the mechanism of which is confirmed on the basis of the absolute configuration of an achiral molecule influenced by chiral crystalline lattices.

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[16] Optically pure (+)-**2** was separated by HPLC using a chiral cell OJ column and was recrystallized from chloroform−hexane, mp 141−142 °C, $[\alpha]^{20}_{D}$ = +122° in $CHCl_3$ at *c* = 1.0. X-ray data of **2**: chiral space group *P*1, $a = 9.126(1)$ Å, $b = 11.685(1)$ Å, $c = 8.529(2)$ Å, $\alpha = 99.64(2)°$, $\beta = 105.42(2)°$, $\gamma = 76.613(10)°$, $V = 847.5(3)$ Å^3, $Z = 2$, $\rho = 1.303$ g/cm^3, μ(Cu Kα) = 17.65 cm^{-1}. The structure was solved by the direct method and refined by the method of full-matrix least squares. The absolute configuration was solved by the Bijvoet difference method. For 2403 Friedel pairs, 1736 showed agreement and 667 showed disagreement between observed and calculated ΔF for the structure of molecules with (*R*)-configuration, which clearly showed that this structure, given in Figure 3, is that with the correct absolute configuration. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB 1EZ, U.K.

[17] Penn, J. H.; Liu, F. *J. Org. Chem.* **1994**, *59*, 2608−2612.

[18] Crich, D.; Chen, C.; Hwang, J. T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937−8951.

[19] Intermolecular addition of an *o*-tolylthio group is also excluded because there is no interatomic sulfur atom within 5.3 Å from the benzoyl carbon atom.

[20] In order to exclude the involvement of path A, we also analyzed an *S*-phenyl 2-benzoyl-4-methylbenzothioate. With a methyl group *para* to the thioester, this compound allows for unambiguous identification of products from phenyl or phenylthio group migration. The formation of only one phthalide (6-methyl-3-phenyl-3-phenylthiophthalide) involving phenyl migration (path B) was observed both in solution and in the solid state.