

Solid-State Photochemical Reaction of S-Phenyl N-(benzoylformyl)thiocarbamates: "Absolute" Asymmetric Synthesis Using the Chiral Crystal Environment

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The study of chemical reactions in the crystalline state dates from the very earliest days of organic chemistry.¹⁻⁴ Because most conformational equilibration is severely restricted in the crystalline phase, unimolecular processes in this medium tend to be restricted to a situation that is quite different from that present in isotropic liquid phases, and one that can give rise to very different chemical results in the two media. In solid-state photochemical reactions, asymmetric transformations could be obtained from nonchiral molecules crystallizing in chiral arrangements. Recently, we reported two examples of "absolute" asymmetric syntheses, via solid-state photochemistry using a chiral crystal environment. One is "absolute" thietane synthesis promoted by the intramolecular photochemical reaction of *N*-(thiobenzoyl)methacrylamide.⁵ Another example includes photochemical reaction of *N*-(benzoylformyl)-*N*-isopropylglylamide leading to optically active oxetane.⁶ Now we find that the solid-state photochemical reaction of an *S*-phenyl *N*-(benzoylformyl)thiocarbamate gives both an optically active oxazolidine-2,4-dione via a radical pair intermediate and a β -lactam initiated by hydrogen abstraction by the carbonyl oxygen.

Irradiation of *S*-phenyl *N*-(benzoylformyl)thiocarbamates **1** in solution leads to homolytic C(=O)-S bond cleavage to radical pair intermediate **2**, and which is followed by cyclization to oxazolidine-2,4-dione radical **3** and a thiyl radical pair. Recombination of the radical pair gives 5-(phenylthio)oxazolidine-2,4-dione **4** and dimerization leads to the dimer **5** (path A). On the other hand, a Norrish type II reaction takes place to give β -lactam **7** via biradical intermediate **6** (path B) (Scheme 1); the distribution of the products is determined by the stability of the resulting biradical or radical pair, since both reactions proceed from the same $n\pi^*$ triplet excited state.⁷

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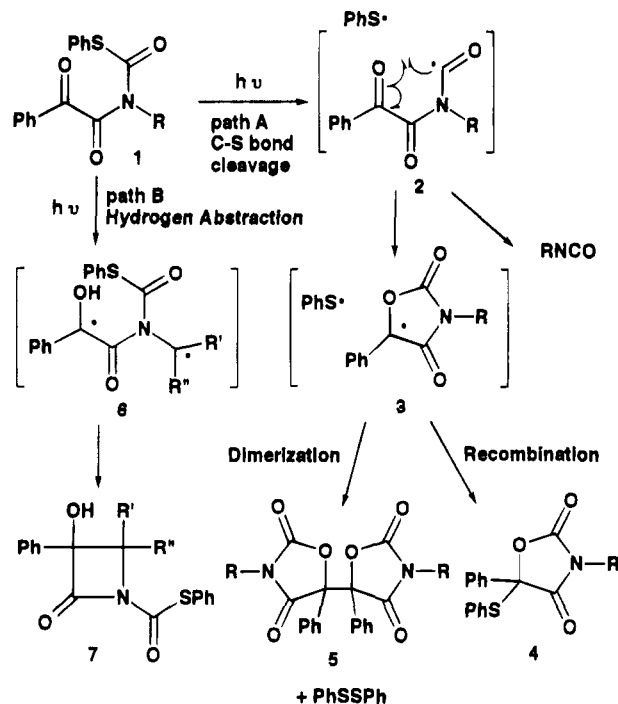
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Scheme 1



Photolysis of *S*-phenyl *N*-(benzoylformyl)-*N*-*p*-tolylthiocarbamate (**1a**) in benzene gave 5-phenyl-5-(phenylthio)-3-*p*-tolylloxazolidine-2,4-dione (**4a**) in 61% yield, the dimer **5a** (15%), and *p*-tolyl isocyanate (22%); diphenyl disulfide was also formed (Table 1). For the *N*-methyl derivative **1b**, only a small amount of **4b** was obtained accompanied by a complex mixture, and neither a dimer of oxazolidine-2,4-dione **5b** nor β -lactam **7b** was detected. When *N*-benzyl derivative **1c** was irradiated under the same conditions, a β -lactam, *cis*-3,4-diphenyl-3-hydroxy-1-(thiophenylcarbonyl)azetid-2-one (**7c**), was obtained as a main product accompanied by a trace amount of oxazolidine-2,4-dione **4c**. The product distribution is strongly affected by the substituents on the nitrogen atom.

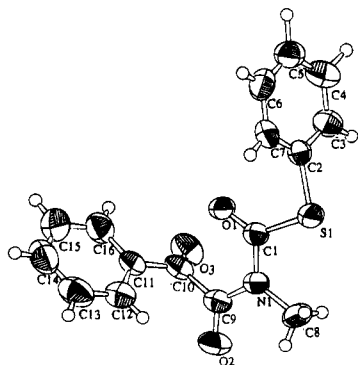
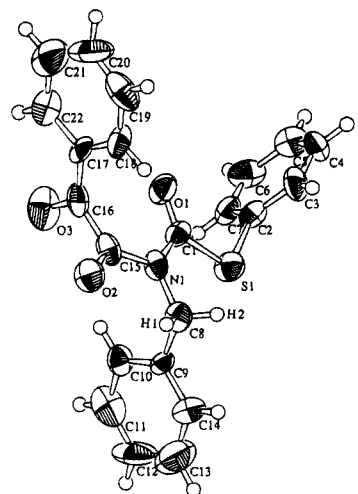
On the other hand, irradiation of powdered crystals of **1a-c** with a high pressure mercury lamp under argon at 0 °C showed different photochemical behavior from that in benzene solution. In the case of **1a**, the oxazolidine-2,4-dione **4a** was obtained almost quantitatively; the dimer **5a**, isocyanate, and diphenyl disulfide were not observed. In the photolysis of **1b**, the cyclization proceeded efficiently to give oxazolidine-2,4-dione **4b** in 74% yield. Irradiation of the thiocarbamate **1c** gave comparative yields of oxazolidinedione **4c** and *cis*- β -lactam **7c** in 17% and 22% yields, respectively, at 17% conversion. Prolonged irradiation resulted in both the increase of **4c** linearly and the secondary decomposition of the β -lactam **7c** leading to an intractable mixture.

More striking is that the photoproducts **4c** and **7c** obtained in the solid-state photoreaction are optically active, whereas other oxazolidine-2,4-diones **4a** and **4b** were obtained as racemates; the $[\alpha]_D$ values and the enantiomeric excesses are shown in Table 1. These enantiomeric excesses are determined by HPLC using chiral cell OJ (DAICEL chemical industries) for **4c** and by ¹H-NMR using chiral shift reagent Eu(hfc)₃ for **7c**. Optically active **4c** and **7c** which show reversed optical rotations were also obtained in almost the same ee values by the photolysis of the crystals of **1c** recrystallized from other batches. Furthermore, each chiral crystal could be

Table 1. Product Yields and Enantiomeric Purities from the Photoreaction of the Thiocarbamates 1 in the Solution and the Solid State

run	R	condns	conversn	yields (%) of 4	$[\alpha]_D^{20}$ of 4	yields (%) of 5	yields (%) of 7	$[\alpha]_D^{20}$ of 7
a	<i>p</i> -tolyl	benzene	100	61	0° (0% ee) ^b	15		
		solid state	100	96	0° (0% ee) ^b	0		
b	Me	benzene	100	8	0° (0% ee) ^b	0	0	
		solid state	100	74	0° (0% ee) ^b	0	0	
c	Bn	benzene	100	3	0° (0% ee) ^b	0	27	0° (0% ee) ^b
		solid state	17	17 ^a	+35° (46% ee) ^b	0	22 ^a	+38° (32% ee) ^b
		solid state	62	16 ^a	+16° (21% ee) ^b	0	18 ^a	+27° (23% ee) ^b

^a Yields are determined on the basis of consumed thiocarbamates 1. ^b $c = 1.0$ in CHCl_3 .

**Figure 1.** ORTEP drawing of the molecule 1b.**Figure 2.** ORTEP drawing of the molecule 1c.

prepared selectively and in bulk by seeding methods. The amount of conversion of the reactant is important in determining enantioselectivity. The better optical purity was obtained at lower conversion. Forty-six percent ee of oxazolidine-2,4-dione 4c and 32% ee of β -lactam 7c were isolated at 17% conversion yield.

Colorless prismatic crystals of both 1b and 1c were subjected to X-ray crystallographic structural analyses. The crystal of 1c is monoclinic of chiral space group $P2_1$ ⁸ and that of 1b is also monoclinic but the space group is achiral $P2_1/a$.⁹

As shown in the ORTEP diagrams (Figures 1 and 2), the conformation of both thiocarbamates 1b and 1c is

(8) The thiocarbamate 1c forms colorless prismatic crystals from hexane–chloroform, mp 106–107 °C, and an X-ray crystal structure analysis indicated the chiral space group $P2_1$, $a = 11.485(8)$ Å, $b = 5.829(7)$ Å, $c = 15.094(6)$ Å, $\beta = 110.24(3)^\circ$, $V = 948(1)$ Å³, $Z = 2$, $\rho = 1.315$ g/mL, $\mu(\text{CuK}\alpha) = 16.97$ cm⁻¹. Final R and R_w were 0.040 and 0.026 for 1668 reflections. 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, UK.

E,Z in the crystalline state. The imide chromophores are almost planar, and the twist angle τ of the C1(=O1)–N1 bond is 5.0° and that of the C9(=O2)–N1 bond is 6.8° for the imide 1b. Corresponding twist angles for 1c are 10.4° and 5.1°, respectively.¹⁰ It is anticipated that the *E,E* conformation is most favorable for the radical cyclization involving the bond formation between acyl radical and carbonyl oxygen atom in the intermediate 2; however, it becomes apparent that the *E,Z* conformation is also favorable for the formation of the oxazolidine-2,4-dione radical 3. In the case of 1b, the X-ray analytic result indicates that the interatomic distance between the carbonyl carbon (C1) and the carbonyl oxygen (O3) for generating oxazolidine-2,4-dione radical 3b is 3.34 Å and the distance between carbonyl carbon (C10) and the sulfur atoms is 4.53 Å. For 1c, the corresponding distances for the formation of 3c are 3.37 and 4.72 Å, respectively. Since the sum of the van der Waals radii for carbon and oxygen atoms is 3.22 Å, it is concluded that those atoms are close enough for bond formation. On the other hand, the β -lactam 7c was also obtained in the photoreaction of 1c in the solid state. From the ORTEP diagram, the conformation is not appropriate for both the hydrogen abstraction and cyclization of the resultant 1,4-biradical intermediate 6. The distance between carbonyl oxygen (O3) and hydrogen atoms (H1) is 4.45 Å which is much larger than the sum of van der Waals radii (2.9 Å). Furthermore, rotation of C(=O)–N in the biradical intermediate 6 is needed for β -lactam formation. It is interesting that the carbonyl oxygen can abstract a hydrogen atom under these stringent conditions. The reason why the topochemically forbidden process occurs may be explicable in terms of the reaction taking place in defect lattice sites.

In conclusion, photochemical reaction of *S*-phenyl *N*-(benzoylformyl)thiocarbamates can proceed product-selectively in the solid state. Furthermore, this reaction provides the first example of an “absolute” asymmetric synthesis via a radical pair intermediate in the crystalline state and also presents a rare example of two different types of reactions proceeding in the solid state with retention of chirality.

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(9) The thiocarbamate 1b forms colorless prismatic crystals from hexane–chloroform, mp 99–100 °C, and an X-ray crystal structure analysis indicated the achiral space group $P2_1/a$, $a = 11.256(5)$ Å, $b = 8.393(4)$ Å, $c = 15.515(3)$ Å, $\beta = 92.30(2)^\circ$, $V = 1464.7(9)$ Å³, $Z = 4$, $\rho = 1.357$ g/mL, $\mu(\text{CuK}\alpha) = 20.49$ cm⁻¹. Final R and R_w were 0.044 and 0.039 for 2490 reflections. 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, UK.

(10) Twist angle τ is defined as follows: $\tau = 1/2(\omega_1 + \omega_2)$, where ω_1 and ω_2 are torsion angles O1–C1–C9 and S1–C1–N1–C8, respectively, for the twist angle of C1(=O1)–N1 for 1b. Twist angle τ for C9(=O2)–N1 is determined in the same manner.