Solid state photochemical reaction of achiral *N*-(β,γ-unsaturated carbonyl)thiocarbamate to optically active thiolactone in the chiral crystalline environment

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***O*-Methyl *N*-(2,2-dimethylbut-3-enoyl)-*N*-phenylthiocarbamate crystallized in the chiral space group $P2_1$, and the solid state photoreaction initiated intramolecular [2+2] thietane formation followed by rearrangement, leading to optically active γ-thiolactone.**

Solid state photoreaction provides product selectivity and stereoselectivity compared to reactions that occur in solution due to restriction of molecular movement imposed by the crystal lattice.[1–5] Stereospecific solid state chemical reactions of chiral crystals formed by achiral materials are defined as 'absolute' asymmetric syntheses.[6–11] This asymmetric synthesis must involve two aspects: generating chiral crystals and performing topochemically controlled solid state reactions which yield chiral products. Now we have found a new example of 'absolute' asymmetric synthesis involving the photochemical reaction of an achiral *N*-(β,γ-unsaturated carbonyl)thiocarbamate leading to optically active thiolactone and a unique structure in the crystalline state.

O-Methyl *N*-(β,γ-unsaturated carbonyl)-*N*-phenylthionocarbamates **1a**,**b** were synthesized by acylation of *O*-methyl *N*-phenylthiocarbamate with the corresponding acid chloride in the presence of Et_3N. Recrystallization of **1a** from a hexane yielded colorless crystals; however, single crystals suitable for X-ray crystallographic analysis could not be obtained. On the other hand, thiocarbamate **1b** afforded prismatic single crystals, which were analysed by X-ray crystallography.† It is notable that the conformation of the imide chromophore is *E*,*E*, and remarkably twisted from the ideal imide plane. (Fig. 1) The twist angle of the C(=O)–N moiety is 47.4° and is much greater than that of the C(=S)–N moiety (19.4°).[12] This structure is consistent with the lone pair electrons of the nitrogen atom being conjugated through the thiocarbonyl rather than through a carbonyl group. The phenyl ring is almost orthogonally twisted to the sp^2 nitrogen atom (67°).

Irradiation of a benzene solution of **1a** gave tricyclic thietane, 2,2-dimethyl-5-methoxy-4-phenyl-6-thia-4-azatricyclo-[$5.4.0^{1,7}.0^{1,5}$]nonan-3-one **2a**, in 83% yield (Table 1, entry 1). The solid state photolysis also gave racemic **2a** (81%, 80% conversion) (entry 2). The solid state reaction proceeded even at −78 °C (entry 3). The structure of **2a** was determined on the basis of spectroscopic data.

When thiocarbamate **1b** was irradiated in benzene solution, thiolactone **3b** was isolated in 90% yield (entry 4). The solid state photolysis also gave thiolactone **3b** in 85% yield when the reaction conversion was 78% as shown in Table 1, entry 4. The IR spectrum of **3b** showed characteristic absorption due to the thiolactone carbonyl at 1697 cm^{-1} and the C=N bond at 1666 cm^{-1}. The ^1H NMR spectrum showed the absence of an alkenyl group. The ^{13}C NMR spectrum displayed the absence of the signal due to the thiocarbonyl carbon at δ_C 190.8 and exhibited new a sp^3 triplet peaks at δ 30.7 and a doublet at δ 47.7. New singlet peaks derived from the thioester and imino carbons were exhibited at δ 210.7 and 160.7, respectively.

The stereoselective generation of the chiral center is exemplified by the formation of **3b** at the C-4 position {$[\alpha]_D^{20}$ = +8 (*c* 1.0 in $CHCl_3$, 10% ee)} (entry 5). The enantiomeric purity of **3b** was determined by HPLC employing a chiral cell OJ (Daicel Chemical Industry). The solid state photoreaction also proceeded at −78 °C and an optically active compound which showed a better ee value was formed; 20% ee at 84% conversion (entry 6) and 31%ee at 15% conversion (entry 7). The space group of the crystal of **1a** could not be determined because **1a** did not afford single crystals suitable for X-ray crystallography; however, the production of racemic **2a** shows that the crystals are achiral (entries 2 and 3).

A plausible mechanism for the formation of **3** is rationalized on the basis that photolysis of **1** undergoes [2+2] cyclization to thietane **2** and subsequently rearranges to thiolactone **3** (Scheme 1). Ring opening of the initially formed thietane **2** leading to zwitterion **5**, which is facilitated by the lone pair electrons of the nitrogen and oxygen atoms, and subsequent nucleophilic reaction between the thiolate anion and the carbonyl carbon to give **3**.[13] For the tricyclic thietane **2a**, nucleophilic addition of thiolate anion is difficult, because of the conjunction of the

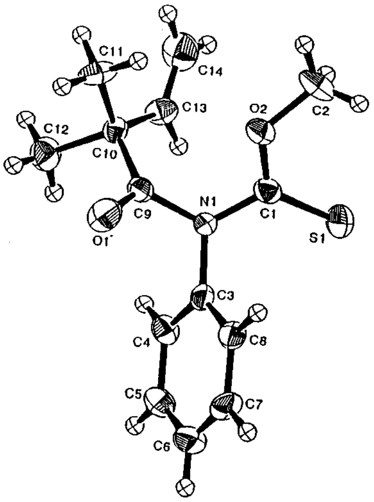
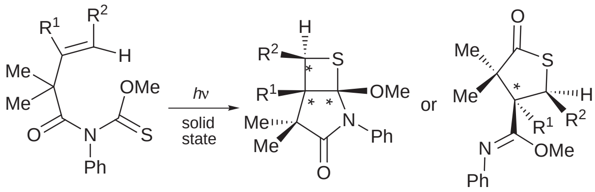


Fig. 1 ORTEP drawing of **1b**. Selected bond lengths (Å) and angles (°); S(1)–C(1) 1.608(6), O(2)–C(1) 1.330(7), N(1)–C(1) 1.355(6), N(1)–C(9) 1.446(7), C(10)–C(13) 1.497(9), O(1)–C(9) 1.201(7), N(1)–C(3) 1.446(7), C(9)–C(10) 1.520(8), C(13)–C(14) 1.301(9), C(1)–N(1)–C(9) 122.6(4), S(1)–C(1)–O(2) 125.6(4), O(2)–C(1)–N(1) 108.6(5), N(1)–C(3)–C(8) 121.3(5), O(1)–C(9)–C(10) 122.0(5), C(9)–C(10)–C(13) 115.5(5), C(10)–C(13)–C(14) 127.2(7), C(1)–N(1)–C(3) 120.8(4), C(3)–N(1)–C(9) 115.5(4), S(1)–C(1)–N(1) 125.7(4), O(1)–C(9)–N(1) 117.5(5), N(1)–C(9)–C(10) 120.1(5), S(1)–C(1)–N(1)–C(9) −168.0(5), O(2)–C(1)–N(1)–C(3) −153.3(5), C(1)–N(1)–C(3)–C(4) −120.6(6), C(8)–C(3)–N(1)–C(9) −105.6(6), O(1)–C(9)–N(1)–C(1) −130.5(6), C(3)–N(1)–C(9)–C(10) −134.8(5).

Table 1 Photochemical reaction of **1** in benzene and the solid state



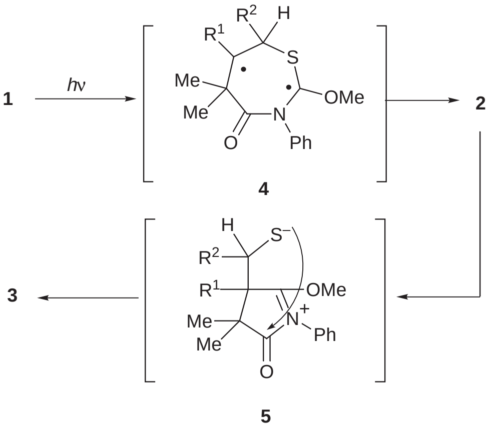
1a $R^1 = R^2 = -(CH_2)_4-$
b $R^1 = R^2 = H$

2a $R^1 = R^2 = -(CH_2)_4-$

3b $R^1 = R^2 = H$
(optically active)

Entry	Substrate	Conditions	T/°C	Conversion (%)	Yield (%)[a] 2	3	$[\alpha]_D^{20}$ [b,c]	Ee (%)[c]
1	**1a**	benzene	20	100	83	0	0	0
2	**1a**	solid	0	80	81	0	0	0
3	**1a**	solid	−78	50	85	0	0	0
4	**1b**	benzene	20	100	0	90	0	0
5	**1b**	solid	0	78	0	85	+8	10
6	**1b**	solid	−78	84	0	84	+16	20
7	**1b**	solid	−78	15	0	90	+25	31

[a] Chemical yields are isolated yields and calculated on the basis of consumed thionocarbamates. [b] In units of 10^{-1} deg cm^2 g^{-1}. [c] Of product (either **2** or **3**).



Scheme 1

cyclohexane ring, which results in the formation of stable thietane **2a**.

It is generally accepted that a solid state reaction proceeds with minimum atomic and molecular motion. Therefore, the reactivity is determined the by atomic arrangement, represented by the distances and angles between the reaction sites. From the X-ray structural analysis of the starting thiocarbamate **1b**, the distances between the thiocarbonyl sulfur atom S(1) and the alkenyl carbon C(14) and between the thiocarbonyl carbon C(1) and the alkenyl carbon C(13) are 4.69 and 3.00 Å, respectively (Fig. 1). The fact that the reaction proceeded under these restricted conditions, in which the S(1)···C(14) distance is significantly longer than the sum of the van der Waals radii (3.23 Å), is accounted for by the fact that the initial reactions occurred in a defect in the crystalline lattice, and later reactions occurred in the increasing number of defective regions formed during reaction. Furthermore, two plausible factors are responsible for the relatively low enantiomeric excess of **3b**. One is that the process of cyclization results in increasing numbers of defective regions in the surrounding crystal lattice, in which racemization of the reactant easily takes place. The other is the structural interconversion of the biradical intermediate. If the interconversion of the intermediate seven-membered 1,4-diradical **4** is possible in the space in the crystal lattice or in the increasing number of defective regions where the C–S bond formation took place, it would result in lowering of optical purity.

In conclusion, photoreaction *O*-methyl *N*-(β,γ-unsaturated carbonyl)-*N*-phenylthiocarbamate provides a new example of absolute asymmetric synthesis using a chiral crystalline environment.

Notes and references

† *Crystal data* for **1b**: space group $P2_1$, a = 8.6565(7), b = 9.3990(9), c = 8.9395(6) Å, V = 698.8(1) Å^3, Z = 2, ρ = 1.251 g cm^{-3}, μ(Cu-Kα) = 20.09 cm^{-1}. The structure was solved by direct methods and expanded using Fourier techniques. Final R and R_w were 0.046 and 0.045 for 1194 reflections. CCDC 182/1025.

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12 Twist angle τ is defined as follows: $\tau = 1/2(\omega_1 + \omega_2)$, where ω_1 and ω_2 are torsion angles S1–C1–N1–C9 and O2–C1–N1–C3 , respectively, for τ of C(=S)–N. Twist angle τ for C(=O)–N is determined in the same manner.
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