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Diastereoselective photocycloaddition of axially chiral monothiosuccinimides to 1,1-diphenylethylene

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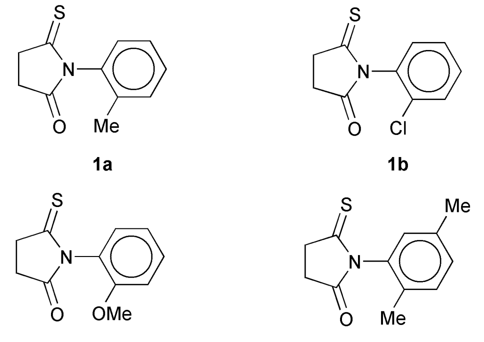
Photolysis of axially chiral monothiosuccinimides in the presence of diphenylethylene gave spirothietanes effectively, where the cycloaddition took place diastereoselectively by way of the steric effect of the *ortho*-substituent on the phenyl ring.

Stereospecific photochemical reactions have received much attention from both mechanistic and synthetic perspectives.[1] Recently, diastereoselective photocycloaddition using a chiral handle or through the interaction of a hydrogen bonds is well-documented.[2] New developments in stereo-controlled photocycloaddition should provide useful synthetic methodology for organic compounds. Bach *et al*. reported a fine example of diastereoselective oxetane formation from enamide and benzaldehyde.[3] This reaction is a unique example of diastereoselective [2 + 2] photocycloaddition of axially chiral compounds. The restricted rotation in *N*-arylimides has long been recognized;[4] however, only recently has the utility of the resulting atropisomers been demonstrated. These have included applications in molecular recognition,[5] stereoselective reactions,[6] and as enzyme mimics.[7] For the most part, these applications have centred on the chemistry of the imide portions of the molecules, in particular as dieneophiles or electrophiles.[6,7] Herein we report the first example of the photoreaction of atropisomeric monothiosuccinimides with diphenylethylene that provided effective and diastereoselective cycloaddition leading to thietanes.

Monothioimides **1a-d** were easily synthesized by thionation of the corresponding succinimides with P_2S_5 (Fig. 1).[8] Fig. 2 shows the X-ray single crystal analysis of (*S*)-**1d**, where the absolute structure could not be determined from the X-ray structure refinement (Roger's parameter = 0.479).[9] The torsional angle between the imide plane and the aromatic ring is almost perpendicular (82.9 °). Furthermore, the crystal system was chiral, $P2_1$, which indicates that the crystals are a conglomerate, and each single crystal is chiral, which is composed of molecules with the same chirality.[10] The analysis by HPLC with a chiral cel OJ column also supported the optical activity of the single crystal.



1a **1b** **1c** **1d**

Fig. 1

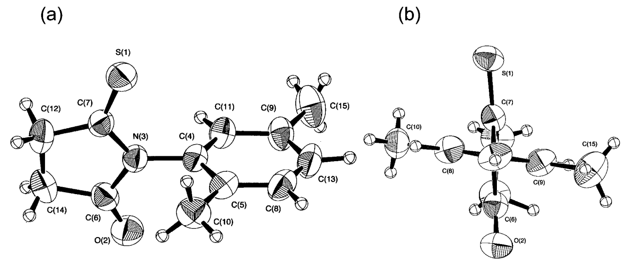
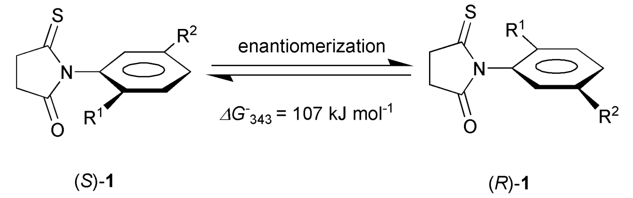


Fig. 2 Ortep drawing of (*S*)-**1d**. (a) Side view; (b) a view from the phenyl group.

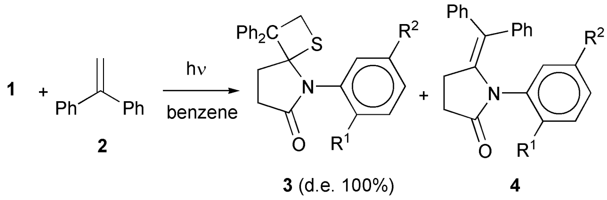
Monothioimides **1a-d** all showed stable chirality, and the enantiomerization owing to the rotation of the N–C bond did not occur at room temperature. However, the rotation begins as the temperature is raised (Scheme 1). In order to estimate the conformational stability of **1**, the rate of enantiomerization of chiral monothiosuccinimide **1d** was studied in toluene. Each enantiomorphic crystal obtained from crystallization was dissolved in toluene, and the rate of enantiomerization at 70 °C was followed by HPLC using the chiral cel OJ column. The half-life and the activation free energy were 844 s and 107 kJ mol^{-1}, respectively.



Scheme 1

When a benzene solution of **1a** (0.02 M) was irradiated in the presence of diphenylethylene **2** (0.2 M) at 15 °C with a high-pressure mercury lamp, a 1 : 1 adduct **3a** was obtained in 65% yield, accompanied by **4** in 18% yield as a minor product (Table 1). Photolysis of other monothioimides **1b-d** under the same conditions also gave the corresponding adducts **3b-d** in good

Table 1 Photochemical cycloaddition of monothiosuccinimide to diphenylethylene[a]



1	R¹	R²	Conv. (%)	Yield of **3** (%)[b]	Yield of **4** (%)[b]
1a	Me	H	88	65	18
1b	Cl	H	81	85	12
1c	MeO	H	94	71	15
1d	Me	Me	65	89	6

[a] 0.02 M Benzene solution of **1** and 0.2 M diphenylethylene was irradiated with a high-pressure mercury lamp. [b] Isolated yields.

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yields. Thietanes **3a-d** were stable under normal conditions and were easily isolated by chromatography on silica gel and by recrystallization from a mixture of AcOEt and hexane. Thietanes **3** should exist as rotamers owing to the *N*-aryl bond rotation; however, the obtained thietanes were each composed of a single isomer. This fact indicates that the photocycloaddition took place diastereospecifically in all cases.

The structure of adducts **3** was determined on the basis of spectral data. For example, mass spectroscopy (FAB) of **3d** showed a molecular ion peak at 400 (MH$^+$), which supported that the product was a 1 : 1 adduct of **1d** and **2**. Furthermore, the ^{1}H and ^{13}C NMR spectra strongly suggest the structure of the adduct **3d**. The ^{1}H NMR spectrum (CDCl$_3$) showed new protons at δ 3.57 and 3.33 (*ABq*, J = 9.2 Hz) derived from the protons of the thietane ring. The ^{13}C NMR also showed three triplet peaks at δ 30.6, 33.8, and 35.0, and two singlet peaks owing to the sp^3 carbon at δ 68.5 and 86.0. Finally, the structure and the stereochemistry of spirothietane **3d** was unequivocally established by X-ray structural analysis (Fig. 3).[11] The Ortep view clearly shows the stereochemistry of the cycloaddition in which the diphenylethylene adds from the opposite site of the methyl group at the *ortho*-position.

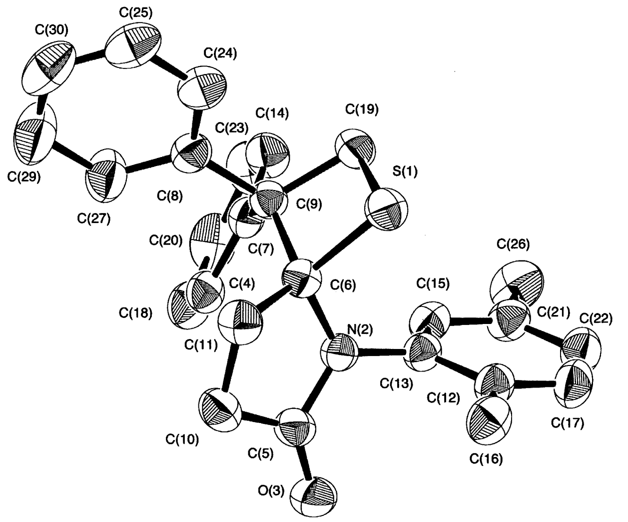

Fig. 3 Ortep drawing of **3d**.

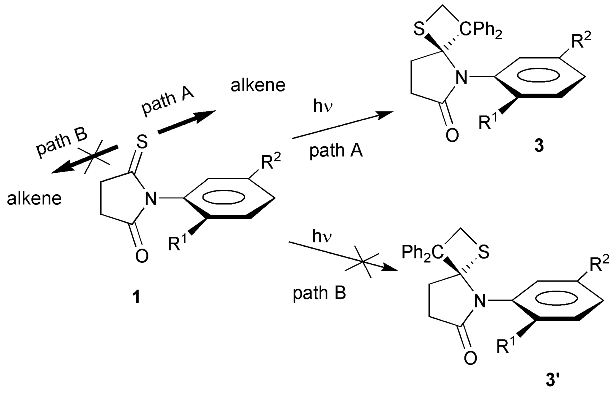

Fig. 4

There are two pathways to form thietanes by the photocycloaddition of thiocarbonyl and alkene (Fig. 4). In all cases, the addition was perfectly controlled by the substituents at the *ortho*-position of the phenyl ring, and the diastereomeric isomers **3′** were not obtained at all. Diphenylethylene cycloadded selectively to avoid the steric repulsion as in path A. In the case of **1d**, the imide possesses two methyl groups at both the *ortho* and *meta* positions. Steric repulsion between alkene and the methyl group at the *ortho*-position severely restricts the addition reaction rather than that at the *meta*-position.

In conclusion, we have examined the axial chirality of *N*-arylmonothiosuccinimides and provided the first example of photochemical diastereoselective thietane formation using the stable chirality.

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9 The X-ray crystal structure analysis of (*S*)-1d indicated the monoclinic space group, *P*21, a = 10.847(3), b = 6.580(2), c = 8.505(2) Å, β = 105.76(2), V = 584.2(3) Å^3, Z = 2, ρ = 1.25 g cm^{-3}, μ(CuKα) = 2.24 cm^{-1}; R = 0.048, Rw = 0.135 for 1176 reflections. The structure was solved by direct methods and was refined by the method of full-matrix least-squares. Crystal and data collection parameters, relevant structure refinement parameters, atomic coordinates for the nonhydrogen atoms, positional and isotropic displacement coefficients for hydrogen atoms, a list of anisotropic displacement coefficients for the non-hydrogen atoms and a full list of bond distances and bond angles have been deposited with the Cambridge Crystallographic Data Center. CCDC 208847–208848. See http://www.rsc.org/suppdata/cc/b3/b304435a/ for crystallographic data in .cif or other electronic format.

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11 The X-ray crystal structure analysis of **3d** indicated the monoclinic space group, *P*21/*c*, a = 9.851(3), b = 9.336(2), c = 27.569(9) Å, β = 107.60(9), V = 2417.1(12) Å^3, Z = 4, ρ = 1.216 g cm^{-3}, μ(CuKα) = 1.34 cm^{-1}; R = 0.068, Rw = 0.184 (on F2) for 3506 reflections. The structure was solved by the direct methods and was refined by the method of full-matrix least-squares.