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Note

Influence of Absolute Configuration of Indanofan on Herbicidal Activity[1]

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INTRODUCTION

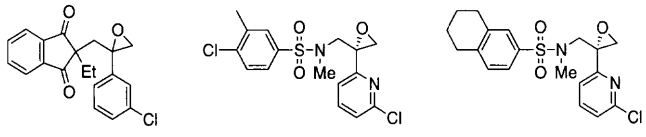
We recently reported on herbicidally active 2-phenyloxiran-2-ylmethyl derivatives. A representative compound was indanofan (**1**; 2-[2-(3-chlorophenyl)oxiran-2-ylmethyl]-2-ethylindan-1,3-dione),[1] which was registered in 1999 as a herbicide for transplanted rice. Indanofan is a racemate due to one chiral carbon at 2 position of the oxirane moiety. The configuration is supposed to be critical to the activity, according to our previous study on *N*-(2-pyridyloxiran-2-ylmethyl)benzenesulfonamide derivatives **2** and **3**.[2]

To clarify the influence of absolute configuration of **1** on herbicidal activity, (+)- and (−)-isomers of **1** were prepared by optical resolution, and their herbicidal activities were compared. The absolute configuration of the (−)-isomer was determined by X-ray crystallography using its dithiocarbonate derivative **4b**.

MATERIALS AND METHODS

1. *Analytic Method*

^{1}H NMR (300 MHz) spectra were recorded on a Varian UNITY 300 spectrometer in $CDCl_3$ solutions, using tetramethylsilane as an internal standard. Specific rotation $[\alpha]_D$ was measured with digital polarimeter (Japan Spectroscopic Co. Ltd., DIP-370). The enantiomeric excess (*ee*) of compounds was determined by HPLC equipped with a chiral column (Daicel Chem. Ind., CHIRALCEL® OJ, *n*-hexane-*i*-PrOH (3 : 1) as the eluent). X-ray diffraction intensities were measured on Enraf-NONIUS CAD4.



1 (indanofan) (*S*)-**2** (*S*)-**3**

Fig. 1 Chemical structures of herbicidally active oxirane derivatives.

2. *Optical Resolution of Racemic Indanofan (1)*

The racemate **1** was prepared as described previously.[1] Optically active compounds **1a** ((+)-isomer of **1**) and **1b** ((−)-isomer of **1**) were prepared by separation of **1** by HPLC equipped with a chiral column (Daicel Chem. Ind., CHIRALCEL® OJ, 4.6 mm×250 mm, using *n*-hexane - *i*-PrOH (9 : 1) as the eluent). The enantiomer excess of each isomer was greater than 99%. **1a** (first fraction); Amorphous, $[\alpha]_D^{20}$ +65.6° (*c*=0.79, methanol), **1b** (second fraction); Colorless prisms, mp 39.6-40.2°C, $[\alpha]_D^{20}$ −62.9° (*c*= 0.77, methanol).

3. *Biological Test*

Herbicidal activities under paddy field conditions were determined by the pot test in a greenhouse as follows. Pots packed with light clay soil were excessively watered to create a paddy field condition with 3 cm water depth. Barnyardgrass was seeded into the soil to a depth less than 1 cm. The compounds were formulated as flowable consisting of 30 parts of the compound, 8 parts of ethylene glycol, 5 parts of Sorpol AC3032 (Toho Kagaku Co.), 0.1 part of xanthan gum and 56.9 parts of water, then treated to the surface of the water when barnyardgrass grew up to 2.5 leaf stage. Two weeks after the treatment, herbicidal activities were evaluated and represented by ED_{90} value that is the dosage in terms of kg a.i./ha required for the 90% growth inhibition (two replications).

4. *Modification of 1a and 1b for X-Ray Crystallographic Analysis*

X-Ray crystallographic analysis of **1b** was not successful, because the crystal was decomposed during scanning. After some chemical modifications of **1**, suitable crystals (**4a** or **4b**) for X-ray crystallography were prepared by the reaction of **1a** or **1b** respectively, with carbon disulfide in the presence of lithium bromide according to the literature.[3] The preparation of **4b**; (+)-2-[5-(3-chlorophenyl)-2-thioxo-1,3-oxathiolane-5-yl]-2-ethylindane-1,3-dione was done as follows.

A mixture of **1b** (6.82 g, 0.02 mol), carbon disulfide (2.18 g, 0.028 mol), *n*-tetrabutylammonium bromide (0.2 g), lithium bromide (0.87 g, 0.01 mol) and THF (20 ml) was stirred at 50 °C for 24 hr. After removing the solvent under reduced pressure, the reaction mixture was purified by silica gel col-

[1] Synthesis and Herbicidal Activity of Novel Oxirane Derivatives (Part 5): For Part 4, see Ref. 2.

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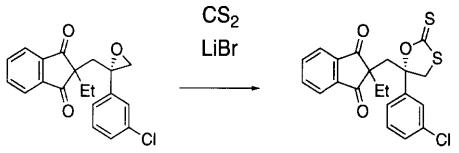

(*S*)-**1** (*S*)-**4**

Fig. 2 Modification of indanofan for X-ray crystallographic analysis.

umn chromatography eluted with *n*-hexane-ethyl acetate (4 : 1), and crystallized from *n*-hexane-ethyl acetate to give recovered **1b** (1.3 g) and colorless prisms **4b** (4.5 g, 54% yield, >99% *ee*). mp 154.0-155.5°C, $[\alpha]_D^{20}$+0.77° (*c*=0.80, acetonitrile), ^{1}H NMR ($CDCl_3$) δ ppm: 1.62 (3H, t, *J*=7.6 Hz), 1.83 (2H, m), 2.79 (1H, d, *J*=14.4 Hz), 3.02 (1H, d, *J*=14.4 Hz), 3.59 (1H, d, *J*=11.6 Hz), 3.94 (1H, d, *J*=11.6 Hz), 6.85 (1H, dd, *J*=2.0, 2.0 Hz), 6.94 (1H, m), 7.18 (1H, dd, *J*=8.0, 8.0 Hz), 7.22 (1H, m), 7.70 (1H, m), 7.75-7.88 (2H, m), 8.00 (1H, m).

Enantiomer **4a** was obtained from **1a** as colorless prisms (54% yield) using the same way as **4b**. mp 152.6-154.3°C, $[\alpha]_D^{20}$−0.83° (*c*=0.83, acetonitrile).

Racemate **4** was also obtained from **1** as colorless prisms (58% yield) by the same method. m.p. 109.0-113.0°C.

RESULTS AND DISCUSSION

The results of biological test of each enantiomer are shown in Table 1. It was clarified that (−)-isomer **1b** showed potent herbicidal activity, whereas (+)-isomer **1a** was inactive. The potency of **1b** was about twice higher than that of racemate **1**. The symptom caused by treatment with **1b** was growth inhibition as with **1**. Both **1** and **1b** suppressed the growth first and withered barnyardgrass within two weeks after treatment.

X-Ray crystallographic analysis of **4b** obtained from **1b** was performed with a crystal of 0.08×0.1×0.25 mm dimension using Cuba (40 kV, 85 mA). It showed that the crystal has the following lattice constants: a=12.650 (3), b=18.612 (8), c=8.274 (2) Å, V=1948 (11) Å^3, space group=$p2_12_12_1$, Z=4. The final R value was 0.081 for 2144 unique reflections ($F_o > \sigma(F_o)$). The absolute configuration of the chiral carbon of **4b** was determined to be *S* by the X-ray anomalous dispersion technique as shown in Fig. 3.

Since the configuration of **1b** was supposed to be retained in the reaction to give **4b** according to Kihara *et al.*,[3] the absolute configuration of **1b** was concluded to be *S*.

Table 1 Herbicidal activity of (+)-and (−)-enantiomers and racemate of **1** against barnyardgrass in 2.5 leaf stage.

	ED_{90} (kg a.j./ha)
(+)-**1** (**1a**)	—*
(−)-**1** (**1b**)	0.0254
(±)-**1**	0.0524

* no activity.

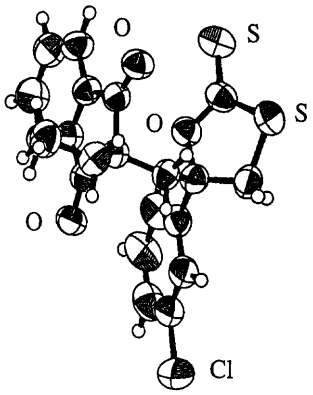

Fig. 3 Crystal structure of cyclic dithiocarbonate **4b** from X-ray analysis.

As reported recently, we synthesized enantiomers of *N*-(2-pyridyloxiran-2-ylmethyl)benzenesulfonamide derivatives **2** and **3** using unequivocal chemical methods including Sharpless asymmetric chlorohydroxylation of allyl alcohol. Results of herbicidal tests indicated that (*S*)-isomers of **2** and **3** were the active forms.[2] The effects of configuration of chiral carbons of **1**, **2** and **3** on herbicidal activity were coincident. Moreover, morphological response and herbicidal spectrum of **1** were similar to those of **2** and **3** as we already reported.[1] The results of our studies indicate that the modes of action of **1**, **2** and **3** are thought to be the same and their oxirane moieties play an important role in herbicidal activity.

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要　　約

インダノファンの絶対構造の除草活性に及ぼす効果[1]

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初中期水田用除草剤インダノファン 2-[2-(3-chlorophenyl)-oxiran-2-ylmethyl]-2-ethylindan-1,3-dione は，オキシラン環の2位に不斉炭素を有するラセミ化合物である．キラル HPLC を用いた分取により，インダノファンの光学活性体を得て，その除草活性を調べたところ，(−)-体はラセミ体の約2倍の除草活性を有するが，(+)-体は除草活性を有さないことが分かった．さらに，(−)-体を結晶性の良い環状ジチオカーボネート化合物に誘導し，X 線結晶解析を行なった．その結果，除草活性を有する (−)-体の絶対配置は *S* 体と決定された．オキシラン部分の絶対配置が活性を左右することから，オキシラン部分は活性発現に重要な役割を果たすことが推測された．

[1] 新規オキシラン系化合物の合成および除草活性（第5報）