Optical Isomers of the Herbicidal Antidote 4-(Dichloromethylene)-2-[*N*-(α-methylbenzyl)imino]-1,3-dithiolane Hydrochloride

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The optical isomers of 4-(dichloromethylene)-2-[*N*-(α-methylbenzyl)imino]-1,3-dithiolane hydrochloride were synthesized by photolytic cyclization of the corresponding 2,3,3-trichloroallyl *N*-(α-methylbenzyl)dithiocarbamates, and their herbicidal antidote activity was determined. The *R* enantiomer exhibited high antidote activity, being more active than both the *S* enantiomer and the racemic compound, a known potent antidote for herbicides, especially triallate.

The herbicidal antidote activity of 4-(dichloromethylene)-2-imino-1,3-dithiolanes and their acid addition salts was first disclosed in 1980 (Bollinger, 1980). The compounds are accessible by cyclization of the 2,3,3-trichloroallyl N-monosubstituted dithiocarbamates (Bollinger, 1982). Known examples of these unique 2-imino-1,3-dithiolanes contain chiral centers in the amine moiety; however, the racemic mixtures were isolated and tested. The corresponding enantiomeric compounds should be accessible from the optically pure *R* and *S* isomers of the primary amines by Scheme I where X represents a group containing a chiral center.

The purpose of this investigation was to prepare examples of unreported optical isomers of this unique class of herbicide safeners and determine their relative safener activity.

EXPERIMENTAL SECTION

All melting points were determined on a Mel-Temp capillary block and are uncorrected. Proton NMR spectra were recorded on a Varian EM-390 instrument at 90 MHz in chloroform-*d* with tetramethylsilane as the internal reference. Chemical shifts are reported in ppm. Optical rotation data were recorded on a Jasco 500 C instrument in the circular dichroism mode, using a 1-cm Suprasil quartz cell and AR-grade anhydrous methanol as solvent. Data are reported as molar ellipticity [θ] at 300–200 nm. An average of four scans is reported. Data were calculated with the following relationship for molar ellipticity: [θ] (deg cm^2 dmol^{-1}) = 100[θ] (deg)/[*C* (mol/L) × L (cm)]. Photolytic cyclization reactions were carried out in an Ace photolytic reactor, Catalog No. 7840, with a 450-W high-pressure Hanovia mercury lamp and a Pyrex filter sleeve in AR-grade chloroform as solvent. A dry nitrogen sparge through the bottom frit served to agitate the solution. Optically pure *R*-(+) and *S*-(−) isomers of α-methylbenzylamine were purchased from Aldrich Chemical Co. and used as received. 1,1,2,3-Tetrachloropropene was from Monsanto Co., laboratory distilled.

Herbicide Antidote Test Procedure. The herbicide and antidote are incorporated in a soil cover layer before emergence of crop and weed species. Containers were filled and compacted with a fumigated silt loam top soil to a depth of about 1.3 cm from the top of the container. A first container was designated as an untreated control, a second container was designated as a herbicide control, and a third container was designated as a herbicide plus antidote test container. Each of the containers was seeded with wheat (*Triticum aestivum*) and wild oats (*Avena fatua*). A measured amount of herbicide dispersed or dissolved in acetone was applied to a measured quantity of soil. To this same quantity of soil treated with herbicide was added a measured amount of antidote dispersed or dissolved in acetone. The quantity of soil treated with the herbicide and antidote was thoroughly mixed to incorporate the herbicide and antidote in the soil uniformly. The seed bed in the third container of soil was covered with the soil treated with the herbicide and antidote, and the container was leveled. For each test series, the seed beds of the first and second containers were likewise covered by soil layers. The cover layer of the first container was not treated with herbicide or antidote. The cover layer of the second container had a measured quantity of herbicide alone incorporated therein. The containers were then placed on a bench in a greenhouse and subirrigated as required for the duration of the test. Plant response (visual estimation of percent inhibition) was observed about 3 weeks after initial treatment.

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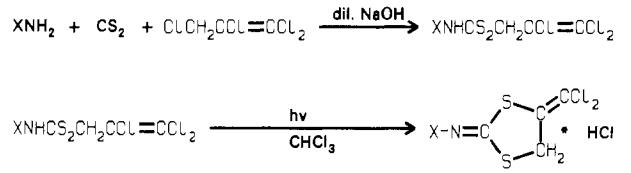
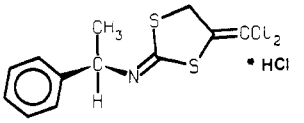
Scheme I

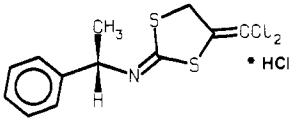


RESULTS AND DISCUSSION

The readily available *R* and *S* isomers of α-methylbenzylamine were employed in Scheme I to synthesize the optically pure dithiocarbamate isomers, which were in turn cyclized by photolysis according to a known method (Bollinger, 1982) to give the desired 1,3-dithiolane salts **1** and **2**. The structure of the resulting isomers was confirmed by elemental and proton NMR spectral analysis, and the optical rotation of each isomer was determined. The herbicide antidote activity was then measured.



1, R(+) Isomer



2, S(-) Isomer

Greenhouse tests carried out with the *R*-(+) and *S*-(−) enantiomers showed that the *R*-(+) isomer, **1**, exhibited decidedly higher activity as a safener than the *S*-(−) isomer and, moreover, it was more active than the racemic compound in comparative testing. Results are tabulated in Table I.

Preparation of the Optical Isomers of 2,2,3-Trichloroallyl *N*-(α-Methylbenzyl)dithiocarbamate. A

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Table I. Antidote Activity of the Optical Isomers and the Racemic Mixture for Triallate in Wheat

additive	rate, lb/acre	herbicide	rate, lb/acre	inhibition, % wheat	inhibition, % wild oat
racemic mixture	8.0			0	0
		triallate	0.5	90	100
		triallate	0.125	80	100
racemic mixture	0.5	triallate	0.5	80	100
mixture	0.5	triallate	0.125	55	95
mixture	2.0	triallate	0.5	30	95
mixture	2.0	triallate	0.125	30	85
mixture	8.0	triallate	0.5	25	100
mixture	8.0	triallate	0.125	25	90
R isomer	8.0			0	0
R isomer	0.5	triallate	0.5	65	100
R isomer	0.5	triallate	0.125	30	100
R isomer	2.0	triallate	0.5	10	100
R isomer	2.0	triallate	0.125	20	95
R isomer	8.0	triallate	0.5	15	100
R isomer	8.0	triallate	0.125	15	90
S isomer	8.0			0	0
S isomer	0.5	triallate	0.5	90	100
S isomer	0.5	triallate	0.125	60	95
S isomer	2.0	triallate	0.5	85	95
S isomer	2.0	triallate	0.125	55	90
S isomer	8.0	triallate	0.5	60	100
S isomer	8.0	triallate	0.125	40	95

two-phase mixture containing 12.0 g (0.099 mol) of (*R*)-(+)-α-methylbenzylamine, [θ] (261 nm) = −422 deg·cm^2/dmol, and 8.0 g of 50% NaOH (0.1 mol) in 100 mL of water was stirred rapidly at 0–10 °C while 8.0 g (0.105 mol) of carbon disulfide was added dropwise over 2–3 min. The resulting mixture was stirred and allowed to warm slowly to room temperature over a period of 1 h. To this stirred slurry was then added 18.0 g (0.1 mol) of 1,1,2,3-tetrachloropropene in one portion. A yellow two-phase mixture resulted, and the temperature slowly rose to a maximum of 26 °C. The mixture was then heated gently to 40–45 °C for 3–3.5 h and allowed to cool to room temperature over several hours. The reaction mass was extracted with 300 mL of ethyl ether. The separated ether solution was washed twice with two 100-mL portions of water, treated with activated charcoal, and dried over anhydrous $MgSO_4$. The dried ether solution was filtered through filter-aid to remove the charcoal and $MgSO_4$ and evaporated in vacuo below 40 °C (1–2 Torr) to give 24.6 g (72%) of the *R* isomer of the 2,2,3-trichloroallyl dithiocarbamate ester as a light orange oil. NMR (chloroform-*d*, Me_4Si): δ 1.52 (d, 3 H, CH_3), 4.47 (s, 2 H, CH_2), 5.72 (m, 1 H, α-CH), 7.25 (s, 5 H, aromatic protons), 7.52 (br d, 1 H, NH).

The (*S*)-(−) isomer of α-methylbenzylamine, [θ] (261 nm) = +431 deg cm^2/dmol, was used in the same manner as above to give the optically active dithiocarbamate as an orange oil. The NMR spectrum was identical with that of the *R*-(+) isomer and that of the racemic compound.

(*R*)-(+)-4-(Dichloromethylene)-2-[*N*-(α-methylbenzyl)imino]-1,3-dithiolane Hydrochloride (1). The crude dithiocarbamate (30.0 g) was dissolved in 110 mL of chloroform and the solution photolyzed for 5 h at 10–32 °C. A gentle stream of nitrogen diffusing through the bottom glass frit was used to agitate the solution. The solution was removed from the photolyzer and the chloroform removed by evaporation in vacuo to give a crude residue triturated with 200 mL of toluene whereupon 15.6 g (52%) of solid was obtained. Recrystallization from 50:50 $CHCl_3$–CCl_4 gave pure dithiolane hydrochloride, mp 151–153 °C. Anal. Calcd for $C_{12}H_{12}Cl_3N_1S_3$: C, 42.3; H, 3.55; N, 4.11; S, 18.82; Cl 31.2. Found: C, 42.3; H, 3.62; N, 4.05; S, 19.17; Cl, 30.9. NMR: δ 1.97 (d, 3 H, CH_3), 4.72 (s, 2 H, CH_2), 4.90 (m, 1 H, α-CH), 7.77 (s, 5 H, aromatic protons), 14.7 (br s, 1 H, acidic proton exchanged with deuterium oxide). Molar ellipticity [θ] (250 nm) = +29 640 deg cm^2/dmol.

(*S*)-(−)-4-(Dichloromethylene)-2-[*N*-(α-methylbenzyl)imino]-1,3-dithiolane Hydrochloride (2). The crude (*S*)-(−) dithiocarbamate was cyclized in the same manner as above to give a 43% crude yield of the ditholane salt, which upon crystallization from 5:10 methanol–ethyl ether gave pure compound, mp 151–153 °C. Found: C, 42.4; H, 3.64; N, 3.98; S, 19.3; Cl, 31.0. The NMR spectrum was essentially identical with that of the *R* isomer. Molar ellipticity [θ] (250 nm) = −28 690 deg cm^2/dmol.

Registry No. 1, 118455-49-5; 2, 118455-50-8; (*R*)-(+)-α-methylbenzylamine, 3886-69-9; 1,1,2,3-tetrachloropropene, 10436-39-2; 2,3,3-trichloroallyl dithiocarbamate ester, 118455-51-9; (*S*)-(−)-α-methylbenzylamine, 2627-86-3.

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