configuration have the same signs of rotation (Table I).

While yeast lipase catalyzed the selective cleavage of *R* isomers in most cases, including the case of pantolactone **5**, the selectivity observed in the case of 2-chloro-1-phenylethanol **4** was opposite albeit rather low (E = 1.8).[10] Changing the nucleophile from 1-butanol to 1-octanol had a marginal effect on the stereoselectivity (E = 1.9). However, porcine lipase, which also cleaved the *S* isomer, showed improved selectivity (E = 4.2).

In summary, the feasibility of kinetic resolution of secondary alcohols by using lipase in an organic solvent has been demonstrated. Further research is needed to reduce the reaction time and to improve the enantioselectivity. Work in this direction is in progress.

Experimental Section

GLC analyses were carried out by using an HP 101 capillary column (methyl silicone) (25 m × 0.2 μm thickness). Optical rotations were measured on a JASCO DIP-140 digital polarimeter. Porcine pancreatic and *Candida cylindracea* lipases were purchased from Sigma Chemical Company and were used "straight from the bottle". All organic solvents used in this work were of analytical grade, and prior to use they were dried overnight over 3A molecular sieves.

All racemic alcohols and (*S*)-(+)-mandelic acid used in this work were obtained commercially. Racemic alcohols were converted to their *O*-acetyl esters by following the standard procedure using acetic anhydride and triethylamine. Mandelic acid was first converted to its methyl or butyl ester before acetylation. All the compounds were purified by silica gel column chromatography using dichloromethane as the solvent and were characterized by their IR and ^{1}H NMR spectra. The ee values were determined on the basis of comparison of the observed rotations either with literature-reported values or with the value of a chemically synthesized optically pure authentic sample as detailed in the footnotes to Table I.

(*RS*)-Butyl *O*-Acetylmandelate[16] (2). A solution of butyl mandelate (6.24 g, 0.03 mol), acetic anhydride (15 mL), and triethylamine (15 mL) was stirred at room temperature for 24 h. Cold water (100 mL) was added, and stirring was continued for 1 h. Chloroform extraction (2 × 50 mL) followed by drying and removal of solvent yielded crude **2**, which was further purified on a silica gel column to give 6.82 g (91%) of pure **2**: IR (neat) ν (cm^{-1}) 1750; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.41 (m, 5 H, aromatic), 5.93 (s, 1 H, CHO), 4.14 (t, 2 H, J = 6.3 Hz, OCH_2), 2.20 (s, 3 H, $COCH_3$), 1.40 (m, 4 H, CH_2), 0.86 (t, 3 H, J = 6.1 Hz, CH_3). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.20; H, 7.20. Found: C, 67.09; H, 7.26.

(*S*)-(+)-Butyl *O*-acetylmandelate was also similarly prepared from *S*-(+)-butyl mandelate, which in turn was prepared from (*S*)-(+)-mandelic acid (Aldrich).

General Procedure for Yeast Lipase Catalyzed Transesterification. To a magnetically stirred solution of 15 mmol of substrate (**1**–**5**) in 45 mL of diisopropyl ether was added 60 mmol of ROH (nucleophile) and 3 g of yeast lipase. Periodically 1-μL aliquots of the liquid phase were withdrawn and analyzed by gas chromatography. After attaining a certain degree of conversion (see Table I), the reactions were stopped by filtration. Removal of the solvent on a rotary evaporator followed by column chromatography using dichloromethane as solvent afforded optically active alcohol and unreacted *O*-acetate (70–90% yield).

Acknowledgment. We thank IEL Limited for financial help, Dr. B. N. Roy for encouragement, and J. M. Tilak and J. S. Wagh for their analytical work.

Registry No. (*RS*)-**1**, 86561-27-5; (*S*)-**1**, 79416-45-8; (*R*)-**1** (OH product), 20698-91-3; (*RS*)-**2**, 119718-86-4; (*S*)-**2**, 85805-89-6; (*R*)-**2** (OH product), 119656-72-3; (*RS*)-**3**, 119718-87-5; (*S*)-**3**, 119718-88-6; (*R*)-**3**, 119718-89-7; (*S*)-**3** (OH product), 28549-12-4; (*R*)-**3** (OH product), 10020-96-9; (*RS*)-**4**, 79465-05-7; (*R*)-**4**, 33942-01-7; (*S*)-**4** (OH product), 70111-05-6; (*RS*)-**5**, 28227-35-2; (*S*)-**5**, 28387-34-0; (*R*)-**5** (OH product), 599-04-2; MeOH, 67-56-1; *n*-BuOH, 71-36-3; *n*-OctOH, 111-87-5; lipase, 9001-62-1; diisopropyl ether, 108-20-3; (±)-butyl mandelate, 119718-90-0; (*S*)-(+)-butyl mandelate, 74879-33-7; (*S*)-(+)-mandelic acid, 17199-29-0.

(10) Chen, C. S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294.
(11) *Dictionary of Organic Compounds*; 5th ed.; Chapman and Hall: New York, 1982; p 3207.
(12) *The Merck Index*; 10th ed.; Merck & Co., Inc.: Rahway, NJ, 1983; p 816.
(13) Hartgerink, J. W.; van der Laan, L. C. J.; Engberts, J. B. F. N.; de Boer, Th. J. *Tetrahedron* **1971**, *27*, 432.
(14) Nabeta, S.; Kuniyoshi, I.; Inagaki, M. Ger. Offen. 1,948,368, 1970; *Chem. Abstr.* **1970**, *73*, 24940.
(15) See ref 11, p 4482.
(16) Preparation of the *S* isomer, without any mention of its rotation, has been described by Parker: Parker, D. *J. Chem. Soc., Perkin Trans. 2* **1983**, 83.

Synthesis of Sulfur–Oxygen-Transposed Dihydro-1,4-oxathiin Derivative by Unusual Rearrangement of β-Hydroxy-1,3-oxathiolanes

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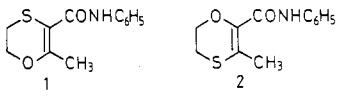
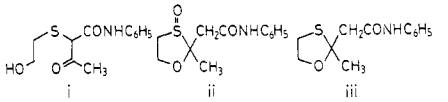
5,6-Dihydro-2-methyl-1,4-oxathiin-3-carboxanilide (**1**) or carboxin is a well-known systemic fungicide used for seed treatment.[1,2] The fungicidal activity of the isomer of **1** with O and S transposed was of interest, and we now describe the synthesis of this isomeric compound **2**. Our



synthesis of **2** required as a key intermediate β-hydroxy-1,3-oxathiolane derivative **5** as shown in Scheme I. Treatment of α-chloroacetoacetanilide[3] with potassium acetate in refluxing acetone gave α-acetoxyacetoacetanilide **3**.[6] Reaction of **3** with 2-mercaptoethanol produced β-acetoxy-1,3-oxathiolane **4**[6] as a mixture of diastereomers, which was hydrolyzed to the β-hydroxy-1,3-oxathiolanes **5**.[6] Acid-catalyzed dehydration of diastereomers **5** gave a high yield of the desired dihydro-1,4-oxathiin **2** (90%) and carboxin **1** (10%). Compound **2** was a colorless crystalline solid and identified by elemental analysis, IR and NMR spectroscopy, and mass spectrometry. Further proof for this structure was provided by independent synthesis involving the reaction of 3-bromo-2-oxo-*N*-

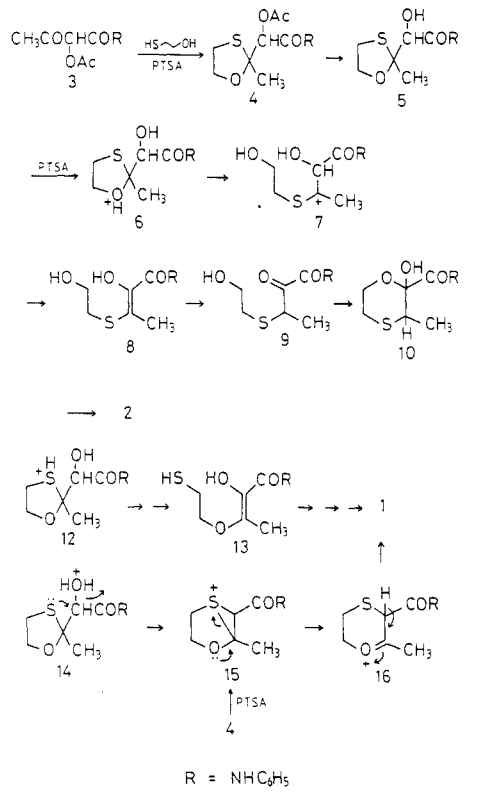
(1) Marsh, R. W., Ed. *Systemic Fungicides*, 2nd ed.; Longman: New York, 1977; pp 51–60.
(2) These syntheses were achieved by acid-catalyzed dehydration of 2-[(2-hydroxyethyl)thio]acetoacetanilide (i),[3] rearrrangement of 2-methyl-*N*-phenyl-1,3-oxathiolane-2-acetamide 3-oxide (ii),[4] or chlorinolysis of 2-methyl-*N*-phenyl-1,3-oxathiolane-2-acetamide (iii),[5] all starting from acetoacetanilide and 2-mercaptoethanol.



(3) Kulka, M.; Thiara, D. S.; Harrison, W. A. U.S. Patent 3 393 202, 1968.
(4) Lee, W. S.; Hahn, H. G.; Nam, K. D. *J. Org. Chem.* **1986**, *51*, 2789–2795.
(5) Lee, W. S.; Park, O. S.; Choi, J. K.; Nam, K. D. *J. Org. Chem.* **1987**, *52*, 5374–5377.
(6) These new compounds were identified by NMR spectroscopy and elemental analysis. For **4** diastereomers were separated from each other by preparative TLC and arbitrarily designated α and β forms according to their relative flow rates R_f 0.7 and 0.8, respectively. For **5** diastereomers α and β forms were isolated by hydrolysis of the corresponding α and β forms of **4**.

0022-3263/89/1954-2455$01.50/0

Scheme I



phenylbutanamide (**11**) with 2-mercaptoethanol to form sulfide **9**, followed by acid-catalyzed dehydration.[7]

In the above reaction sequence the crucial step is the ring opening of β-hydroxyoxathiolanes **5**. Since ethers are more basic than thioether[9] the oxygen would be protonated in preference to the sulfur in the oxathiolane ring. Thus, protonation of the ring oxygen and the presence of an acidic proton and a hydroxy group β to the bond being ruptured lead to the prediction that the ring opening of the protonated species **6** would occur selectively if not exclusively, with C–O bond cleavage, and that the reaction would inevitably proceed in the desired direction to produce the isomeric carboxin **2** (see Scheme I). Indeed, the ring opening took place with predominant C–O bond cleavage (90% vs 10% C–S cleavage based on the product ratio **2**/**1**) involving carbocation **7**[11] to produce enol **8**. Tautomerization to its keto form **9**, followed by acid-catalyzed dehydration via cyclic intermediate **10**, gives the expected product **2**. The byproduct **1** would possibly be formed from the C–S bond rupture of sulfur-protonated oxathiolanes **12** to give enol **13**, which may follow the same way as **2** was formed. It seems more likely, however, that **1** resulted from displacement of the β-hydroxy group by neighboring sulfur as in **14** to form thiiranium ion **15**,[5] which opens to the low-energy oxonium ion **16**[4,5] to lose the acidic proton. Interestingly, β-acetoxy-1,3-oxathiolanes **4**, under the similar reaction conditions, produced carboxin **1** exclusively, indicating that the internal S_N2 displacement by sulfur to give thiiranium ion **15** was facilitated by the leaving ability of the acetoxy group.

A preliminary test for the fungicidal activity of **2** shows that it is less active than carboxin **1** against *Rhizoctonia solani*, *Pyricularia oryzae*, *Pellicularia sasakii*, and *Fusarium roseum*. Further biological screening and mechanism of action studies are under way.

Experimental Section

General Procedure. All melting points were obtained with a Electrothermal melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 735B spectrophotometer. All ^1H NMR spectra were recorded on a Varian Model EM 360 spectrometer with Me_4Si as an internal standard and are reported in δ. Mass spectra were recorded on a Hewlett-Packard 5985B. Elemental analyses of new compounds are within 0.4% of the theoretical values, unless otherwise noted.

Materials. All solvents were freshly distilled and stored under a nitrogen atmosphere. Benzene and toluene were purified respectively by being shaken with concentrated H_2SO_4 until free from thiophene and predried over Na wire, heated at reflux over Na wire, and distilled at atmospheric pressure. Acetoacetanilide and 2-mercaptoethanol were purchased from Aldrich Chemicals.

Synthesis of α-Acetoxyacetoacetanilide (3). To a suspension of potassisum acetate (59 g, 0.6 mol) in acetone (500 mL) at reflux was added α-chloroacetoacetanilide[3] (64 g, 0.3 mol) portionwise over 30 min. Refluxing was continued for 1 h and the resulting reaction mixture cooled to room temperature. The white solid precipitates were filtered off and the solvent was removed to obtain a light yellow oily residue. This was dissolved in methylene chloride (300 mL), washed with cold water, and dried (Na_2SO_4). The solvent was evaporated to give a light yellow oily residue (68 g). Crystallization from benzene–petroleum ether gave white crystalline solid **3** (50 g, 71%): mp 78–80 °C; ^1H NMR (60 MHz) ($CDCl_3$) δ 2.20 (s, 3 H, CH_3CO_2), 2.37 (s, 3 H, CH_3CO), 5.57 (s, 1 H, CH), 7.00–7.60 (m, 5 H, ArH), 8.40 (s, 1 H, NH); IR (KBr) 3350 (NH), 1760 (acetoxy C=O), 1725 (acetyl C=O), 1680 (anilide C=O) cm^{-1}. Anal. ($C_{12}H_{13}O_4N$) C, H, N.

Synthesis of α-Acetoxy-2-methyl-*N*-phenyl-1,3-oxathiolane-2-acetamide (4). A solution of α-acetoxyacetoacetanilide (**3**) (30 g, 0.13 mol), 2-mercaptoethanol (17.9 mL, 0.26 mol), and *p*-toluenesulfonic acid (PTSA) (0.25 g) in benzene (150 mL) was refluxed with a Dean–Stark water separator for 19 h. The benzene solution was cooled, washed with 0.5 N NaOH solution and then with water, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give a light oily residue (23.4 g, 62%) as a diastereomeric mixture of **4** as shown by TLC and NMR spectroscopy. The two diastereomers were separated on a silica gel (Kiesel gel 60, 70–230 mesh) column using 7:3 (v/v) benzene–ethyl acetate as eluent.

For the first band, R_f 0.8 (designated as β form): mp 107–108 °C; ^1H NMR (60 MHz) ($CDCl_3$) δ 1.71 (s, 3 H, 2-CH_3), 2.23 (s, 3 H, CH_3CO), 3.08 (t, 2 H, J = 6 Hz, 4-CH_2), 4.20–4.25 (m, 2 H, 5-CH_2), 5.30 (s, 1 H, methine CH), 7.08–7.63 (m, 5 H, ArH), 8.17 (s, 1 H, NH); IR (KBr) 3300 (NH), 1745 (acetoxy C=O), 1680 (anilide C=O) cm^{-1}. Anal. ($C_{14}H_{17}O_4NS$) C, H, N.

For the second band, R_f 0.7 (designated as α form: mp 108–109 °C; ^1H NMR (60 MHz) ($CDCl_3$) δ 1.73 (s, 3 H, 2-CH_3), 2.23 (s, 3 H, CH_3CO), 3.70 (apparent t, 2 H, J = 6 Hz, 4-CH_2), 4.07–4.30 (m, 2 H, 5-CH_2), 5.42 (s, 1 H, methine CH), 7.08–7.63 (m, 5 H, ArH), 7.98 (s, 1 H, NH); IR (KBr) 3300 (NH), 1740 (acetoxy C=O), 1660 (anilide C=O) cm^{-1}. Anal. ($C_{14}H_{17}O_4NS$) C, H, N.

Synthesis of α-Hydroxy-2-methyl-*N*-phenyl-1,3-oxathiolane-2-acetamide (5). A. To a stirred solution of the β form

(7) Although this method seems simple the high cost of preparing the parent 2-oxobutyranilide in low yield from expensive 2-oxobutyric acid and aniline using dicyclohexylcarbodiimide was a serious drawback. An attempt to prepare the parent amide from $CH_3CH_2COCOCl$ and aniline failed. Another method[8] of preparing 2-oxobutyranilide from reaction of $C_6H_5NHCOCO_2C_2H_5$ with C_2H_5MgI was complicated by formation of unidentified major byproduct. For these reasons the process of preparing isocarboxin **2** as in Scheme I is more economic and of synthetic use as well as mechanistic interest.

(8) Petyunin, P. A.; Panferova, N. G. *J. Gen. Chem. USSR* **1947**, *17*, 502–506; *Chem. Abstr.* **1948**, 42:868b.

(9) Dimethyl ether, pK_a = −3.84, is a stronger base than dimethyl sulfide, pK_a = −4.25.[10]

(10) Arnett, E. M. *Progr. Phys. Org. Chem.* **1963**, 223–403.

(11) Supporting evidence for the carbocation involvement may be the fact that when the reaction using pure α or β form[6] of diastereomers was halfway through the unreacted β-hydroxy-1,3-oxathiolane **5** consisted of a mixture of α and β forms, suggesting that racemization at C-2 took place in the reversible ring closure of **7** to **6**. It is unlikely that such diastereomeric scrambling is attributed to intramolecular Michael-type reaction of the enol **8**, as it is a very poor Michael acceptor tautomerizing almost irreversibly to its keto form **9** to give cyclic form **10**. Therefore, the enol must have been formed via carbocation **7** rather than directly from **6** by concerted β-elimination.

of 4 (0.50 g, 1.7 mmol), obtained from the preceding experiment, in methanol (10 mL) was added a solution of potassium carbonate (0.23 g, 1.7 mmol) in water (10 mL). After the reaction mixture was stirred for 10 min, the solvent was evaporated under reduced pressure to give a white solid residue. This was triturated with methylene chloride (50 mL × 3) and the organic solution was washed with water twice and dried (Na_2SO_4). The solvent was removed to obtain the β form of **5** as a white crystalline solid (0.43 g, 100%): mp 122–123 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.65 (s, 3 H, 2-CH_3), 3.12 (t, 2 H, J = 5.5 Hz, 4-CH_2), 4.08 (t, 1 H, J = 3.5 Hz, OH), 4.17–4.57 (m, 3 H, 5-CH_2 and methine CH), 7.07–7.73 (m, 5 H, ArH), 8.53 (s, 1 H, NH); IR (KBr) 3350 (OH), 3250 (NH), 1660 (C=O) cm^{-1}.

B. In the same way as in **A** the α form of **4** (0.3 g, 1 mmol) was hydrolyzed to give the α form of **5**, white crystalline solid (0.25 g, 97%): mp 133–135 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.75 (s, 3 H, 2-CH_3), 2.90–3.13 (m, 2 H, 4-CH_2), 4.03 (t, 1 H, J = 3.5 Hz, OH), 4.17–4.50 (m, 3 H, 5-CH_2 and methine CH), 7.10–7.70 (m, 5 H, ArH), 8.52 (s, 1 H, NH); IR (KBr) 3270 (OH and NH), 1650 (C=O) cm^{-1}. Anal. ($C_{12}H_{15}O_3NH$) C, H, N.

C. Likewise, a mixture of the α and β forms of **4** (6.21 g, 21 mmol) was hydrolyzed to obtain the corresponding mixture of **5** (5.22 g, 98%). These diastereomers could not be separated by chromatography due to identical flow rates.

Synthesis of 5,6-Dihydro-3-methyl-*N*-phenyl-1,4-oxathiin-2-carboxamide (2). A solution of β-hydroxy-1,3-oxathiolanes **5** as a diastereomeric mixture (0.2 g, 0.8 mmol) and PTSA (8 mg) in dry toluene (20 mL) was refluxed with a Dean–Stark water separator for 30 h. The reaction mixture was cooled, washed with water and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give a light yellow oily residue (0.19 g), which was a 90:10 mixture of **2** and **1** as determined by ^{1}H NMR spectroscopy. These were separated by preparative TLC (Kiesel gel GF 254), using benzene as eluent. The first band (R_f 0.4) and the second band (R_f 0.2) were extracted with chloroform to obtain **2** (165 mg, 89%) and **1** (18 mg, 10%), respectively.

For **2**: mp 82.5–84 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 2.42 (s, 3 H, CH_3), 3.02–3.18 (m, 2 H, 5-CH_2), 4.25–4.40 (m, 2 H, 6-CH_2), 7.03–7.80 (m, 5 H, ArH), 8.47 (s, 1 H, NH); IR (KBr) 3300 (NH), 1650 (C=O) cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 235 (54.1, M^+), 143 (100, $M^+ - C_6H_5NH_2$), 115 (10.7, $M^+ - C_6H_5NHCO$). Anal. ($C_{12}H_{13}O_2NS$) C, H, N, S.

Independent Synthesis of Compound 2. A. Preparation of 2-Oxo-*N*-phenylbutanamide. To a stirred solution of 2-oxobutanoic acid (10.2 g, 0.1 mol) and aniline (18.2 mL, 0.2 mol) in methylene chloride (600 mL) at 0–5 °C was added a solution of dicyclohexylcarbodiimide (20.6 g, 0.1 mol) in methylene chloride (200 mL) dropwise over 3 h. Stirring was continued at ambient temperature for 16 h. The white solid precipitates were filtered off and the solution was washed with a 1 N HCl solution and then with water and dried (Na_2SO_4). The solvent was removed under reduced pressure to give a light yellow oily residue. This was chromatographed on a silica gel (Kiesel gel 60, 70–230 mesh) column using benzene–ethyl acetate (7:3) as eluent to obtain 2-oxo-*N*-phenylbutanamide (5.32 g, 30%); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.15 (t, 3 H, J = 6.5 Hz, CH_3), 3.01 (q, 2 H, J = 6.5 Hz, CH_2), 7.00–7.83 (m, 5 H, ArH), 8.81 (s, 1 H, NH); IR (KBr) 3300 (NH), 1710 (C=O), 1670 (C=O) cm^{-1}.

B. Preparation of 3-Bromo-2-oxo-*N*-phenylbutanamide (11). To a stirred solution of 2-oxo-*N*-phenylbutanamide (177 mg, 1 mmol) in dry benzene (2 mL) was added a solution of bromine (26 mmL) in benzene (1 mL) at room temperature, and the reaction mixture was allowed to stir for 2 h. The solvent was evaporated under reduced pressure to give a yellow solid (256 mg). Crystallization from benzene gave **11** (220 mg, 86%) as light yellow plates: mp 109–111 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.88 (d, 3 H, J = 7 Hz, CH_3), 5.63 (q, 1 H, J = 7 Hz, CH), 7.10–7.90 (m, 5 H, ArH), 8.83 (s, 1 H, NH); IR (KBr) 3300 (NH), 1680 (C=O) cm^{-1}.

C. Preparation of 3-[(2-Hydroxyethyl)thio]-2-oxo-*N*-phenylbutanamide (9). To a stirred solution of 3-bromo-2-oxo-*N*-phenylbutanamide (**11**) (256 mg, 1 mmol) in benzene (2 mL) was added a solution of potassium hydroxide (67 mg), 2-mercaptoethanol (82 mg, 1 mmol) in methanol (0.1 mL). The reaction mixture was allowed to stir for 35 min and the solvent evaporated under reduced pressure. The residue was dissolved in methylene chloride, washed with water, and dried (Na_2SO_4). On removing the solvent there was obtained white foamy solid (0.24 g). Crystallization from toluene gave a white solid (0.14 g, 55%) as a diastereomeric mixture of **9** in cyclic form **10** as shown by ^{1}H NMR spectroscopy: mp 77–85 °C; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.12 (d, 2.1 H^a, J = 7 Hz, CH_3), 1.50 (d, 0.9 H^b, J = 7 Hz, CH_3), 1.87–4.47 (m, 5 H, 4-CH_2, 5-CH_2, and 3-CH), 4.92 (s, 0.7 H^a, OH), 4.98 (s, 0.3 H^b, OH), 7.00–7.73 (m, 5 H, ArH), 8.53 (s, 1 H, NH); IR (KBr) 3350 (OH), 3200 (NH), 1760 (C=O) cm^{-1} [a/b = 7/3 = diastereomeric ratio].

D. Preparation of 5,6-Dihydro-3-methyl-*N*-phenyl-1,4-oxathiin-2-carboxamide (2). A solution of 3-[(2-hydroxyethyl)thio]-2-oxo-*N*-phenylbutanamide (**9**) (0.24 g, 0.95 mmol) and PTSA (9 mg) in dry toluene (20 mL) was refluxed with a Dean–Stark water separator for 2 h. The toluene solution was cooled, washed with sodium bicarbonate solution and with water, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give a yellow solid (0.235 g). Crystallization from ethyl acetate–petroleum ether gave colorless short needles (0.17 g, 76%). This compound had identical ^{1}H NMR and IR spectra with those of the compound **2** obtained by the previous method.

Registry No. **1**, 5234-68-4; **2**, 69892-02-0; **3**, 119878-79-4; α-**4**, 779878-82-9; β-**4**, 779878-80-7; α-**5**, 779878-83-0; β-**5**, 119878-81-8; **9**, 119878-84-1; **10** (isomer 1), 119878-85-2; **10** (isomer 2), 119878-87-4; **11**, 779878-86-3; α-chloroacetoacetanilide, 119878-78-3; 2-mercaptoethanol, 60-24-2; 2-oxobutanoic acid, 600-18-0; aniline, 62-53-3; 2-oxo-*N*-phenylbutanamide, 72681-68-6.

S-Alkylation of Camphorthione with Diazo Esters

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Diazo compounds react with thiones to afford thiadiazolines, which can be converted by thermal "two-fold extrusion" reactions to alkenes.[2] Intermediate in this sequence is an episulfide. The method was developed as a route to highly hindered alkenes (e.g. **3a**)[2d] (Scheme I) and has not been used frequently in synthetic pathways.

Refluxing a THF solution of **1** and **2b** led to the slow disappearance of the starting materials and the formation of a single new product (63%) whose molecular weight corresponded to $C_{14}H_{22}O_2S$. The presence of a vinyl proton (δ = 5.6) in the NMR spectrum and subsequent transformations clearly establish the structure of this product to be **5a**,[3] which was better prepared by the potassium *tert*-butoxide mediated alkylation of **1** with ethyl bromoacetate[3] (Scheme II) (75%). In a similar way, compounds **5b** and **5c** were prepared in 62 and 69% yields, respectively. The NMR spectra showed these to be the expected 1:1 mixture of diastereomers.

Alkaline hydrolysis of **5a** followed by acidification of an aqueous solution of the potassium salt led to a new compound (80%) whose spectroscopic data (IR 1775 cm^{-1}, FIMS = 226) identified it as **6a**. Both the 300-MHz ^{1}H NMR and the 75-MHz ^{13}C NMR spectra establish this structure and confirm the presence of both stereoisomers

(1) Holder NSERC undergraduate summer research award, 1986.

(2) (a) Barton, D. H. R.; Willis, B. J. *J. Chem. Soc., Chem. Commun.* **1970**, 1225. (b) Barton, D. H. R.; Smith, E. H.; Willis, B. J. *J. Chem. Soc., Chem. Commun.* **1970**, 1226. (c) Barton, D. H. R.; Willis, B. J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 305. (d) Barton, D. H. R.; Guziec, F. S.; Shahak, I. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1794.

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