# Organic Synthesis by the Pummerer Reaction. II. Synthesis of α-Hydroxy Acid Derivatives from β-Keto Sulfoxides

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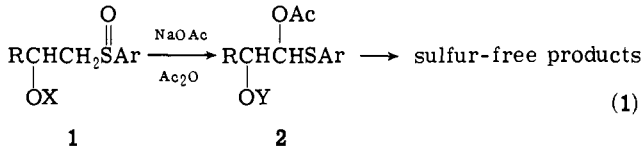
**Abstract:** The reaction of β-keto sulfoxides with acetic anhydride *in the presence of sodium acetate* gives in one step and high yields α-acetoxy acid thioesters which are transformed into various types of α-hydroxy acid derivatives. For example, ω-(*p*-tolylsulfinyl)acetophenone produces *S*-(*p*-tolyl) 2-acetoxy-2-phenylthioacetate which is converted into mandelic acid on alkaline hydrolysis, 2-acetoxy-2-phenylacetanilide on reaction with aniline, or 2-acetoxy-2-phenylacetamide on reaction with ammonium hydroxide. 1-(*p*-Tolylsulfinyl)-2-pentanone gives *S*-(*p*-tolyl) 2-acetoxypentanethioate which is converted into 2-acetoxypentananilide with aniline. Since this method is applicable to β-keto sulfoxides which are prepared by reaction of methylsulfinylcarbanion with esters, it constitutes a facile synthesis of one-carbon homologated α-hydroxy acids from esters. By this method, *N*-benzyloxycarbonyl-4-amino-2-hydroxybutyric acid, an important compound for the synthesis of semisynthetic aminoglycoside antibiotics, is synthesized from *N*-benzyloxycarbonyl-β-alanine methyl ester.

Recently we found that the Pummerer reaction of β-hydroxy sulfoxides **1** with acetic anhydride *in the presence of sodium acetate* gives in high yields α-hydroxy aldehyde derivatives **2** which can be easily transformed into sulfur-free products such as α-hydroxy aldehydes, α,β-dihydroxy nitriles, β-hydroxy-α-amino nitriles, and β-hydroxy-α-amino acids (eq 1).[1] In succession, we have found that the applica-

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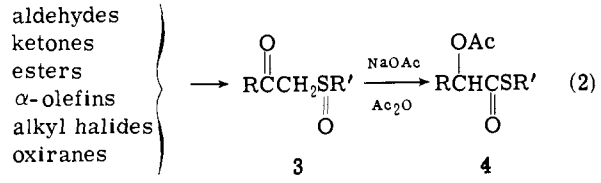
1 2

tion of this new technique to β-keto sulfoxides **3** gives in one step and high yields α-acetoxy acid thio esters **4** which can be converted into various types of α-hydroxy acid derivatives (*vide infra*).[2] Since β-keto sulfoxides **3** can be prepared by (1) oxidation of β-hydroxy sulfoxides which are obtained by reaction of α-sulfinylcarbanions with aldehydes[3,4] or cooxidation of α-olefins and thiols with oxygen,[5,6] (2) reaction of methylsulfinylcarbanion with esters,[3] and also (3) reaction of phenylsulfinylacetone dianion with alkyl halides, aldehydes, ketones, α,β-unsaturated esters, or oxiranes,[7] this method provides a simple and efficient route to α-hydroxy acid derivatives from easily available materials (eq 2). The present paper reports the details of this

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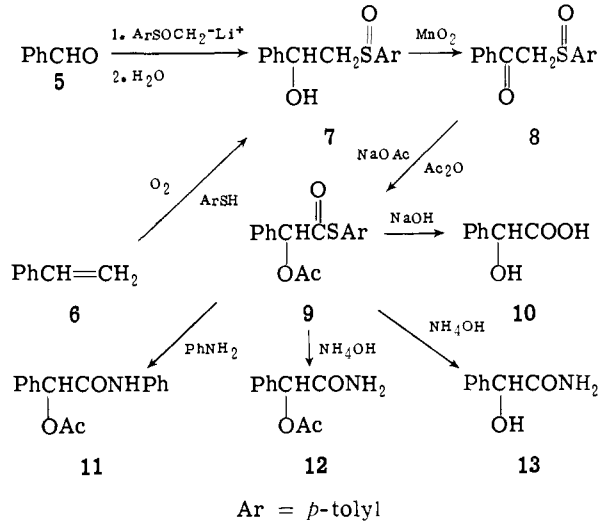
method and its application to the synthesis of N-protected 4-amino-2-hydroxybutyric acid.

In connection with our previous study on β-hydroxy sulfoxides, we have synthesized ω-(*p*-tolylsulfinyl)acetophenone (**8**) by the manganese dioxide oxidation of 2-hydroxy-2-phenylethyl *p*-tolyl sulfoxide (**7**) which was obtained by the reaction of *p*-tolylsulfinylcarbanion with benzaldehyde (**5**)[4] or the cooxidation of styrene (**6**) and *p*-toluenethiol with oxygen.[8] When **8** was subjected to the reaction with acetic anhydride and sodium acetate in toluene under reflux overnight, *S*-(*p*-tolyl) 2-acetoxy-2-phenylthioacetate (**9**) was produced in 74% yield. The structure of **9** was determined by its spectral data and alkaline hydrolysis to mandelic acid (**10**) (65% yield based on **8**). Moreover, since thio esters, especially *S*-aryl thioesters, are activated esters, the attack of nucleophiles takes place selectively on this active site, leaving the acetoxy group intact. Thus, 2-acetoxy-2-phenylacetanilide (**11**) (55% yield based on **8**) and 2-acetoxy-2-phenylacetamide (**12**) (73% yield based on **8**) were obtained by the reactions with aniline and 2 equiv of ammonium hydroxide, respectively. The reaction of **9** with a large excess of ammonium hydroxide gave mandelamide (**13**) in 71% yield (Scheme I).

**Scheme I**

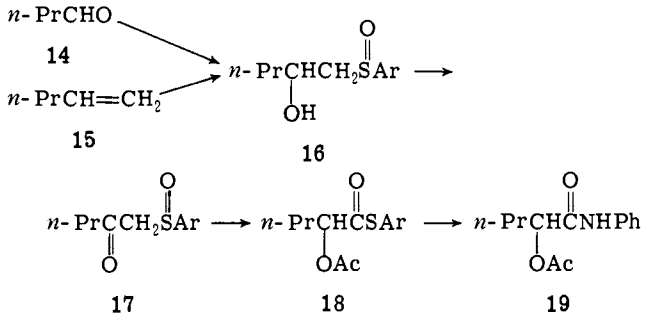



Ar = *p*-tolyl

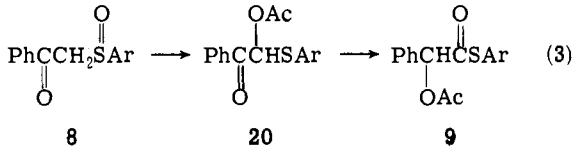
In a similar manner, *S*-(*p*-tolyl) 2-acetoxypentanethioate (**18**) was obtained in 77% yield from 1-(*p*-tolylsulfinyl)-2-pentanone (**17**) which was synthesized from 2-hydroxypentyl *p*-tolyl sulfoxide (**16**) by the oxidation with dicyclohexylcarbodiimide–dimethyl sulfoxide.[9] The reaction of **18** with aniline produced 2-acetoxypentananilide (**19**) in 71% yield (Scheme II).

The direct transformation of β-keto sulfoxides into thioesters of α-acetoxy carboxylic acid can be regarded as an intramolecular oxidation–reduction. Namely, the oxidation of the methylene group between the sulfinyl and carbonyl groups takes place in exchange for the reduction of both the sulfinyl and carbonyl groups. In order to get a further insight into the pathway of this interesting transformation, the following observations have been made. When the reaction of **8** under aforementioned conditions was stopped after 1.5 hr, the reaction mixture contained, together with **8** and a trace of **9**, ω-acetoxy-ω-(*p*-tolylthio)acetophenone

Scheme II



(**20**) which is a normal product of the Pummerer rearrangement. The reaction of **8** with acetic anhydride in the *absence* of sodium acetate produced **20,** which could be converted into **9** in quantitative yield by the action of a base such as sodium acetate or pyridine. Therefore, it is obvious that the reaction proceeds through an intermediary formation of **20,** which in turn affords **9** by the base-catalyzed intramolecular oxidation-reduction with concomitant acetyl transfer (eq 3).



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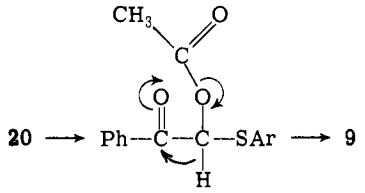
There seem to be two possible mechanisms for the conversion of **20** to **9.** One is the intramolecular Cannizzaro reaction involving a transfer of hydride from the terminal carbon to the carbonyl carbon (eq 4). An analogous mecha-



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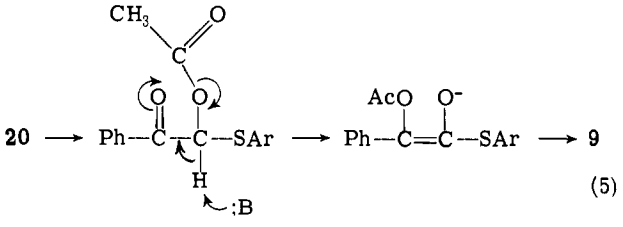
nism was proposed by Franzen to account for the conversion of phenylglyoxal into mandelic acid catalyzed by *N,N*-diethylcysteamine.[10] Another mechanism is the one which involves an abstraction of proton from terminal carbon by a base, followed by the intermediary formation of an enol (eq 5). The existence of this type of mechanism was



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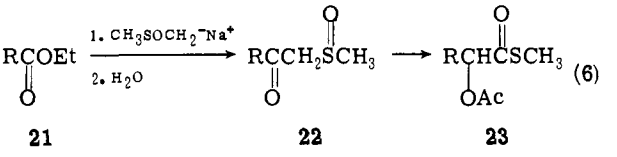
demonstrated by Hall, *et al.,* in the base-catalyzed rearrangement of $\alpha$-keto hemimercaptals to $\alpha$-hydroxy thioesters.[11] In the present reaction, it is reasonable to assume the latter mechanism, *i.e.,* an enol formation, since the rearrangement takes place only when a base is present in the reaction system.

$\beta$-Keto sulfoxides **22** can be widely obtained by the well-known reaction of methylsulfinylcarbanion with esters **21.**[3] If the direct transformation of **22** into $\alpha$-hydroxy carboxylic acids **23** is achieved, it will permit a simple synthesis of one-carbon homologated $\alpha$-hydroxy acids from esters. When $\omega$-(methylsulfinyl)acetophenone (**22,** R = Ph) which was obtained by the reaction of methylsulfinylcarbanion with ethyl benzoate (**21,** R = Ph) was subjected to the present rearrangement, *S*-methyl 2-acetoxy-2-phenylthioacetate (**23,** R = Ph) was produced in quantitative yield. An alkaline hydrolysis of **23** (R = Ph) furnished mandelic acid in 74% yield. The similar reaction of 1-methylsulfinyl-2-pentanone (**22,** R = *n*-Pr) yielded *S*-methyl 2-acetoxypentanethioate (**23,** R = *n*-Pr) in 89% yield (eq 6).



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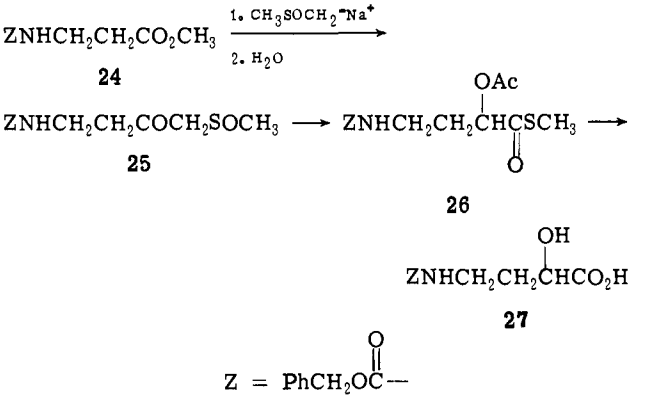
This method was successfully applied to the synthesis of an N-protected form of 4-amino-2-hydroxybutyric acid. This acid is an important component of butirosins,[12] naturally occurring aminoglycoside antibiotics, and its N-protected form is required for the synthesis of other semisynthetic aminoglycoside antibiotics which have marked activity against *Pseudomonas aeruginosa.*[13,14] The reaction of *N*-benzyloxycarbonyl-$\beta$-alanine methyl ester (**24**) with 3 equiv of methylsulfinylcarbanion in dimethyl sulfoxide afforded crystalline *N*-benzyloxycarbonyl-4-amino-1-methylsulfinyl-2-butanone (**25**) in 81% yield. The reaction of **25** with acetic anhydride in the presence of sodium acetate gave *S*-methyl *N*-benzyloxycarbonyl-4-amino-2-acetoxybutanethioate (**26**) which on alkaline hydrolysis produced *N*-benzyloxycarbonyl-4-amino-2-hydroxybutyric acid (**27**)[14] in 79% yield (based on **25**) (Scheme III).

Scheme III



## Experimental Section

**General.** Melting points were taken on Yanagimoto melting-point apparatus and are uncorrected. Unless otherwise stated, infrared spectra were determined in KBr disk on a Hitachi EPI-G3 spectrometer, mass spectra were recorded on a Hitachi RMU-6E spectrometer, and nmr spectra were measured in $CDCl_3$ solution on Varian HA-100 and T-60 and Hitachi R-20B spectrometers; chemical shifts are given in $\delta$ with TMS as internal standard. Chromatography was done with silica gel (Wakogel C-200). Thin-layer plates were made of Wakogel B-5FM. It was suspended in dichloromethane, and plates were dipped and dried in an atmosphere. They were detected with iodine and uv light.

**Oxidation of 2-Hydroxy-2-phenylethyl *p*-Tolyl Sulfoxide (7) to $\omega$-(*p*-Tolylsulfinyl)acetophenone (8).** To a solution of **7** (2.00 g, 7.69 mmol) in dichloromethane (100 ml) was added 10.0 g of activated manganese dioxide which was pulverized before use, and the mixture was stirred at room temperature for 2 hr. Manganese dioxide was filtered off, and the filtered solution was concentrated giving **8** as yellowish crystals quantitatively. Recrystallization from ether gave 1.67 g (84%) of **8:** mp 84–85°; ir 728, 820, 1052, 1280, 1665, 1680 $cm^{-1}$; nmr 2.41 (s, 3 H), 4.47 (ABq, $J$ = 12.5 Hz, 2 H), 7.60 (m, 9 H). *Anal.* Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; S, 12.41. Found: C, 70.00; H, 5.26; S, 12.37.

**Reaction of 8 with Acetic Anhydride–Sodium Acetate.** (a) A stirred mixture of **8** (0.48 g, 1.86 mmol), sodium acetate (0.48 g),

and acetic anhydride (5 ml) in toluene (10 ml) was heated at 115° overnight. The mixture was concentrated to give the residue which was suspended in benzene–hexane (3:7) and chromatographed. The elution with benzene–hexane (1:1) gave an oil of *S*-(*p*-tolyl) 2-acetoxy-2-phenylthioacetate (**9**) (413 mg, 74%): ir (film) 615, 705, 810, 1225, 1370, 1490, 1710, 1750 $cm^{-1}$; nmr 2.23 (s, 3 H), 2.33 (s, 3 H), 6.28 (s, 1 H), 7.21 (s, 4 H), 7.45 (m, 5 H); mass spectrum (70 eV) *m/e* (rel intensity) 300 ($M^+$, 1.4), 177 (10), 149 (9), 124 (23), 107 (15), 105 (38), 91 (10), 77 (16), 43 (26), 32 (39), 28 (100).

(b) A stirred mixture of **8** (313 mg, 1.21 mmol), sodium acetate (310 mg), and acetic anhydride (5 ml) in toluene (10 ml) was heated at 115° for 1.5 hr. The mixture was concentrated, suspended in benzene, and passed through sodium sulfate column. The benzene eluate was evaporated to give an oil. The nmr spectrum of the oil showed that it is a mixture of **8** ≫ **20** ≫ **9** (**9** is a trace). The oil was chromatographed with benzene–hexane (3:7). The elution with benzene–hexane (1:1) gave 45 mg of **20**: ir (film) 690, 810, 960, 1045, 1220, 1370, 1695, 1750 $cm^{-1}$; nmr 2.20 (s, 3 H), 2.33 (s, 3 H), 7.00 (s, 1 H), 7.40 (m, 7 H), 7.97 (m, 2 H); mass spectrum 300 ($M^+$, 14), 153 (33), 124 (36), 105 (46), 77 (26), 43 (100).

**Reaction of 8 with Acetic Anhydride.** (a) A stirred solution of **8** (192 mg, 0.74 mmol) and acetic anhydride (0.1 ml, 1.11 mmol) in benzene (2 ml) was refluxed for 6.5 hr. The solution was concentrated to give an oil. The nmr spectrum of the oil showed that it is an approximately 7:3 mixture of **20** and ω-(*p*-tolylthio)acetophenone (**28**). The oil was dissolved in hexane and chromatographed. The elution with benzene–hexane (2:8) gave 54 mg of **28**: ir (film) 695, 810, 1200, 1280, 1680 $cm^{-1}$; nmr 2.31 (s, 3 H), 4.22 (s, 2 H), 7.30 (m, 7 H), 7.95 (m, 2 H); mass spectrum 242 ($M^+$, 89), 137 (30), 105 (100), 77 (19). The further elution with benzene–hexane (1:1) furnished 74 mg of **20**. The product (**20**) might be partially decomposed during chromatography.

(b) A stirred solution of **8** (145 mg, 0.56 mmol) in acetic anhydride (3 ml) was heated from room temperature to reflux during 1 hr and then refluxed for 0.5 hr. The solution was concentrated to give an oil. The nmr spectrum of the oil showed that it is an approximately 7:1 mixture of **20** and **28.**

**Conversion of 20 to 9 with Bases.** (a) A stirred mixture of **20** (124 mg, 0.41 mmol) and sodium acetate (125 mg) in acetic acid (5 ml) was refluxed at 125° for 3 hr. The solvent was removed to give the residue which was suspended in benzene and passed through sodium sulfate column. The evaporation of the solvent furnished 120 mg (0.40 mmol) of **9**, which is almost pure by nmr and tlc with benzene.

(b) A stirred mixture of **20** (100 mg, 0.32 mmol) in pyridine (3 ml) was heated at 120° for 1 hr. The evaporation of the solvent gave **9** quantitatively.

**Isolation of DL-Mandelic Acid (10) from 8 *via* 9.** A stirred mixture of **8** (268 mg, 1.04 mmol), acetic anhydride (4 ml), and sodium acetate (0.30 g) in toluene (12 ml) was heated at 115° overnight. The residue obtained by the concentration was suspended in benzene and passed through sodium sulfate column. The benzene solution was concentrated to give a brownish oil of crude **9** which was dissolved in 5 ml of methanol. To the solution was added 4.2 ml of 1 *N* sodium hydroxide, and the mixture was stirred for 1 hr at room temperature. A saturated solution (20 ml) of sodium chloride was added, and the mixture was acidified with 6 *N* sulfuric acid and extracted with ethyl acetate. The extract was dried ($Na_2SO_4$) and concentrated giving crystals which were recrystallized from ethyl acetate–hexane to afford **10** (103 mg, 65% based on **8**), which was identified by mp (119–120°) and ir spectrum.

**Isolation of 2-Acetoxy-2-phenylacetanilide (11).** The crude product (**9**) obtained from **8** (401 mg, 1.55 mmol) in the same way as above was dissolved with aniline (0.21 ml, 2.33 mmol) in benzene (4 ml). The solution was refluxed for 2 hr. After the solution was cooled, benzene was added and the mixture was washed with 0.1 *N* hydrochloric acid. The aqueous layer was extracted with benzene. The combined benzene solution was dried, concentrated, and chromatographed with benzene–hexane (1:1). The elution with benzene–dichloromethane (9:1) gave **11** (229 mg, 55% from **8**) as crystals: mp 121–122° (benzene) (lit. 117.5°); ir 700, 755, 1045, 1230, 1674, 1375, 3300 $cm^{-1}$; nmr 2.10 (s, 3 H), 6.13 (s, 1 H), 6.95–7.60 (10 H), 8.22 (bs, 1 H). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.62. Found: C, 71.33; H, 5.47.

**Isolation of 2-Acetoxy-2-phenylacetamide (12).** The crude product (**9**) obtained from **8** (404 mg, 1.57 mmol) as above was dissolved in methanol (5 ml), and to the solution was added 0.45 ml (3.14 mmol) of concentrated aqueous ammonia. The mixture was stirred at room temperature for 30 min. A saturated solution of sodium chloride was added, and the mixture was extracted with ethyl acetate. The organic layer was dried and concentrated to give crystals which were recrystallized from benzene to afford **12** (221 mg, 73% from **8**); mp 109–110° (lit. 112–113°); ir 700, 1030, 1225, 1665, 1740, 3150, 3365 $cm^{-1}$; nmr 2.16 (s, 3 H), 6.07 (s, 1 H), 6.40 (m, 2 H), 7.40 (m, 5 H). *Anal.* Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74. Found: C, 61.97; H, 5.47.

**Isolation of Mandelamide (13).** To a stirred solution of **9** (177 mg, 0.59 mmol) in methanol (5 ml) was added 1.0 ml (7.2 mmol) of concentrated aqueous ammonia. The solution was stirred at room temperature for 1 hr. A saturated solution of sodium chloride was added, and the mixture was extracted with ethyl acetate. The extract was dried and concentrated giving crystals which were recrystallized from benzene to afford 63 mg (71%) of **13**: mp 134–135° (ethanol) (lit. 133–134°); ir 700, 755, 1060, 1635, 1665, 3240, 3370 $cm^{-1}$. *Anal.* Calcd for $C_8H_9NO_2$: C, 63.56; H, 6.00. Found: C, 63.45; H, 5.73.

**Oxidation of 2-Hydroxypentyl *p*-Tolyl Sulfoxide (16) to 1-(*p*-Tolylsulfinyl)-2-pentanone (17).** To a stirred solution of **16** (629 mg, 2.8 mmol) in dimethyl sulfoxide (4.5 ml) and benzene (4.5 ml) were added pyridine (0.22 ml, 2.8 mmol), trifluoroacetic acid (0.11 ml, 1.40 mmol), and *N,N'*-dicyclohexylcarbodiimide (1.74 g, 8.40 mmol), and the mixture was stirred at room temperature overnight. Ether (70 ml) and then a solution of oxalic acid (756 mg, 8.40 mmol) in methanol (7 ml) were added, and the mixture was stirred for 30 min. Water (70 ml) was added, and precipitated dicyclohexylurea was filtered off. The filtered mixture was fractionated to give the ether layer which was washed with 1 *N* sodium bicarbonate. The organic layer was dried and concentrated to give the residue which was chromatographed with benzene. Elution with benzene–ethyl acetate (9:1) gave **17** (437 mg, 70%) as crystals: mp 68–69° (ether); ir 500, 815, 1032, 1705 $cm^{-1}$; nmr 1.88 (t, $J$ = 7.5 Hz, 3 H), 1.55 (m, 2 H), 2.43 (s, 3 H), 2.45 (m, 2 H), 3.83 (ABq, $J$ = 12.5 Hz, 2 H), 7.45 (m, 4 H). *Anal.* Calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64.20; H, 6.94; S, 14.19.

**Reaction of 17 with Acetic Anhydride–Sodium Acetate.** A stirred mixture of **17** (197 mg, 0.88 mmol) and sodium acetate (200 mg) in acetic anhydride (5 ml) was heated from room temperature to reflux over 1 hr and was refluxed for 2 hr. The mixture was concentrated to give the residue which was suspended in benzene and chromatographed. The elution with benzene and fractionation gave *S*-(*p*-tolyl) 2-acetoxypentanethioate (**18**) (183 mg, 77%): ir (film) 805, 1030, 1070, 1220, 1370, 1700, 1750, 2945 $cm^{-1}$; nmr 0.94 (t, $J$ = 7 Hz, 3 H), 1.44 (m, 2 H), 1.81 (m, 2 H), 2.16 (s, 3 H), 2.32 (s, 3 H), 5.26 (t, $J$ = 6 Hz, 1 H), 7.18 (m, 4 H); mass spectrum *m/e* 266 ($M^+$, 0.7), 143 (33), 124 (63), 115 (72), 91 (28), 43 (100). This product was chromatographed with hexane. The elution with benzene–hexane (6:4) gave an analytically pure sample. *Anal.* Calcd for $C_{14}H_{18}O_3S$: C, 63.18; H, 6.81; S, 12.04. Found: C, 63.71; H, 6.74; S, 11.87.

**Isolation of 2-Acetoxypentananilide (19).** The thioester (**18**) (74 mg, 0.28 mmol) was dissolved in benzene (2 ml). To the solution was added 3 drops (*ca.* 0.12 ml, 1.3 mmol) of aniline, and the mixture was refluxed for 20 hr. After cooling of the mixture, benzene was added, and the solution was washed with 0.1 *N* hydrochloric acid. The aqueous layer was extracted with benzene. The combined benzene solution was dried, concentrated, and chromatographed with benzene. The elution with benzene–dichloromethane (96:4) gave 47 mg (71%) of **19** as crystals: mp 78–79° (ether–hexane); ir 700, 763, 1250, 1665, 1745, 3230 $cm^{-1}$; nmr 0.94 (m, 3 H), 1.40 (m, 2 H), 1.90 (m, 2 H), 2.18 (s, 3 H), 5.27 (t, $J$ = 6 Hz, 1 H), 7.35 (m, 5 H), 8.0 (bs, 1 H). *Anal.* Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.19; H, 7.14; N, 5.92.

**Reaction of ω-Methylsulfinylacetophenone (22, R = Ph) with Acetic Anhydride–Sodium Acetate and Isolation of 10.** A stirred mixture of **22** (R = Ph)[3a] (198 mg, 1.10 mmol) and sodium acetate (0.20 g) in acetic anhydride (3 ml) was refluxed for 30 min. After evaporation of the solvent, the residue was suspended in benzene and passed through sodium sulfate column. The benzene eluate was concentrated giving *S*-methyl 2-acetoxy-2-phenylthioa-

cetate (**23**, R = Ph) (241 mg, 98%): ir (film) 1225, 1690, 1750 $cm^{-1}$; nmr 2.20 (s, 3 H), 2.25 (s, 3 H), 6.19 (s, 1 H), 7.41 (m, 5 H). This product was dissolved in methanol (4 ml). To the solution was added 4 ml of 1 *N* sodium hydroxide, and the mixture was stirred at room temperature for 1 hr. A saturated solution of sodium chloride was added, and the mixture was acidified with 6 *N* sulfuric acid and extracted with ethyl acetate. The organic layer was dried and concentrated giving crystals which were recrystallized from ethyl acetate–hexane to afford **10** (123 mg, 74% from **22**).

**Reaction of 1-Methylsulfinyl-2-pentanone (22, R = *n*-Pr) with Acetic Anhydride–Sodium Acetate.** A stirred mixture of **22** (R = *n*-Pr)[15] (220 mg, 1.49 mmol) and sodium acetate (220 mg) in acetic anhydride (3 ml) was refluxed for 30 min. The work-up as above gave *S*-methyl 2-acetoxypentanethioate (251 mg, 89%). The product was almost homogeneous in tlc with benzene: ir (film) 1220, 1680, 1750 $cm^{-1}$; nmr 0.95 (m, 3 H), 1.6 (m, 4 H), 2.18 (s, 3 H), 2.30 (s, 3 H), 5.26 (t, $J$ = 6 Hz, 1 H).

**Synthesis of *N*-Benzyloxycarbonyl-β-alanine Methyl Ester (24).** To a stirred solution of β-alanine methyl ester hydrochloride (4.50 g, 32.3 mmol) and triethylamine (4.5 ml, 32.3 mmol) in chloroform (70 ml) at 0° was added 11.1 ml (19.4 mmol as 30%) of a solution of benzyloxycarbonyl chloride (30–35% in toluene). After a few minutes, 5.4 ml (38.8 mmol) of triethylamine was added, and then after a few minutes 11.1 ml (19.4 mmol) of benzyloxycarbonyl chloride solution was added, and finally the mixture was stirred at room temperature for 6 hr. The chloroform solution was washed three times with water, dried, and concentrated to give an oily residue which was chromatographed with benzene. The elution with benzene–ethyl acetate (9:1) afforded 7.14 g (93%) of **24**[16] as an oil: ir (film) 1250, 1535, 1730, 3325 $cm^{-1}$; nmr 2.52 (t, $J$ = 6 Hz, 2 H), 3.46 (q, $J$ = 6 Hz, 2 H), 3.68 (s, 3 H), 5.09 (s, 2 H), 5.4 (br, 1 H), 7.33 (s, 5 H).

**Synthesis of *N*-Benzyloxycarbonyl-4-amino-1-methylsulfinyl-2-butanone (25).** A stirred solution of 343 mg (7.88 mmol) of sodium hydride (55% mineral oil dispersion) in dimethyl sulfoxide (3 ml) was heated at 70–75° under argon atmosphere for 30 min. To the cooled solution was added tetrahydrofuran (4 ml). To the stirred mixture which was cooled at 0° was added a solution of **24** (600 mg, 2.53 mmol) in tetrahydrofuran (2 ml), and the mixture was stirred for 5 min. An aqueous solution of ammonium chloride was added, and the mixture was extracted with dichloromethane. The organic extract was evaporated under aspirator pressure to give an oily residue which was washed three times with hexane to remove mineral oil. The residue was concentrated again *in vacuo* to remove dimethyl sulfoxide, giving crystals of **25.** Recrystallization from chloroform–benzene–hexane afforded 448 mg (64%) of **25.** The mother liquor was concentrated and recrystallized again from benzene–hexane to give 124 mg (17%) as the second crop. The total yield amounted to 81%: mp 62–63° (benzene–hexane); ir 705, 750, 1025, 1155, 1285, 1550, 1690, 1700, 3300 $cm^{-1}$; nmr 2.60 (s, 3 H), 2.78 (t, $J$ = 5.5 Hz, 2 H), 3.41 (dt, $J$ = 6, 5.5 Hz, as q with $J$ = 6 Hz in appearance, 2 H), 3.72 (ABq, $J$ = 13 Hz, 2 H), 5.03 (s, 2 H), 5.43 (br, 1 H), 7.30 (s, 5 H). *Anal.* Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 55.18; H, 6.02; N, 4.86.

**Synthesis of *N*-Benzyloxycarbonyl-4-amino-2-hydroxybutyric Acid (27).** A stirred mixture of **25** (172 mg, 0.61 mmol) and sodium acetate (170 mg) in acetic anhydride (2 ml) was heated from room temperature to reflux during 30 min and then was refluxed for 20 min. It was concentrated to give the residue which was suspended in benzene and passed through sodium sulfate column. The benzene eluate was concentrated again to give a crude product of *S*-methyl *N*-benzyloxycarbonyl-4-amino-2-acetoxybutanethioate (**26**): nmr 2.0 (m, 2 H), 2.12 (s, 3 H), 2.23 (s, 3 H), 3.24 (dt, $J$ = 6, 6 Hz 2 H), 5.03 (s, 2 H), 5.24 (dd, $J$ = 5.5, 7.5 Hz, 1 H), 5.2 (br, 1 H), 7.28 (s, 5 H). The product was dissolved in methanol (5 ml). To the stirred solution at 0° was added 2.4 ml of 1 *N* sodium hydroxide, and the mixture was stirred at room temperature for 1 hr. The mixture which was acidified with 6 *N* sulfuric acid and saturated with sodium chloride was extracted with ethyl acetate. The organic extract was dried and concentrated to give crystals which were recrystallized from ethyl acetate–hexane affording 121 mg (79%) of **27**; mp 96–97° (lit.[14] 95–96°). The product was identified by ir spectrum with the authentic sample of **27**.

**Acknowledgment.** We are grateful to the Kawakami Memorial Foundation for the financial support of this work.

## References and Notes

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