Chemistry of *O*-Silylated Ketene Acetals: A Novel Intramolecular Pummerer-Type Reaction of ω -Carbamoylsulfoxides Leading to α -Thiolactams

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ω -Carbamoylsulfoxides undergo a novel intramolecular Pummerer-type reaction with *O*-silylated ketene acetal in dry acetonitrile in the presence of a catalytic amount of zinc iodide to give α -thiolactams in good to excellent yields under nearly neutral conditions.

Keywords *O*-silylated ketene acetal; intramolecular reaction; Pummerer-type reaction; α -thiolactam; ω -carbamoylsulfoxide

In a recent communication,¹⁾ we briefly reported a novel intramolecular Pummerer-type reaction of ω -carbamoylsulfoxides using *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal, which gives α -thio-*N*-heterocycles in high yields under mild conditions. We present here a full account of this work.

Results and Discussion

There has been a growing interest in the intramolecular electrophilic cyclization of unsaturated nitrogen compounds.²⁾ Useful nitrogen heterocycles such as β -lactams, pyrrolidines, pyrrolidones, piperidines, and piperidones are known to be obtainable by the creation of a carbon–nitrogen bond through an intramolecular cyclization of an ω -amino or amidoolefin modified by mercury,³⁾ silver,⁴⁾ palladium,⁵⁾ halogen,⁶⁾ and selenium,⁷⁾ or an intramolecular ring opening of an ω -aminoepoxide.⁸⁾ Although similar intramolecular cyclization of ω -carbamoylsulfoxides seems to be an efficient method for α -thio-*N*-heterocycles (intramolecular Pummerer reaction), normal Pummerer conditions using acetic anhydride,⁹⁾ trifluoroacetic anhydride,¹⁰⁾ or trimethylsilyl-trifluoromethanesulfonate (TMSOTf)/triethylamine,¹¹⁾ are inadequate because of the competition with the normal intermolecular Pummerer reaction, elimination reaction leading to vinylsulfide, and other side reactions. Thus, the reaction of methyl *o*-methylcarbamoylphenyl sulfoxide (**1a**) with acetic anhydride gave no cyclized product (**2a**), but the normal intermolecular Pummerer rearrangement products (**3a** and **3b**) exclusively (Chart 1).^{9a)} Recently, we have reported that treatment of sulfoxides with *O*-methyl-

O-*tert*-butyldimethylsilyl ketene acetal (**4**) caused a Pummerer-type rearrangement to give α -siloxysulfides under nearly neutral conditions.¹²⁾ As an extension of this reaction, we report here a novel and efficient intramolecular Pummerer-type reaction of ω -carbamoylsulfoxides (**1a–f**), giving α -thiolactams (**2a–f**) in high yields (Chart 2).

The requisite unknown starting ω -carbamoylsulfoxides (**1b–f**) were prepared by the following three routes as outlined in Chart 3. ω -Carbamoylsulfoxides (**1b–d**) were prepared from 4-(phenylthio)butanoic acid (**5**) in a few steps. Condensation of **5** with amines was performed by the use of a powerful dehydrating agent, (trimethylsilyl)ethoxycarbonylene¹³⁾ or *via* the acid chloride intermediate to give the corresponding ω -carbamoylsulfides (**6–8**) in fair yields. The *N*-substituted ω -carbamoylsulfides (**6** and **7**) were oxidized with sodium periodate (NaIO₄) to give high yields of the corresponding ω -carbamoylsulfoxides (**1b,c**). The *N*-unsubstituted ω -carbamoylsulfide (**8**) was reduced with lithium aluminum hydride (LiAlH₄) and acetylated to give the ω -acetylaminosulfide (**9**), which was oxidized with NaIO₄ to give **1d** in 69% overall yield. Other ω -carbamoylsulfoxides (**1e,f**) having longer methylene chains were prepared from δ -valerolactone (**10**) and ϵ -caprolactone (**11**) in four steps. Treatment of the lactones (**10** and **11**) with benzylamine in the presence of sodium hydride in tetrahydrofuran (THF) caused ring opening and amidation at the same time to give the ω -carbamoylalcohols (**12** and **13**) in good yields. Mesylation of the alcohols (**12** and **13**) with methanesulfonyl chloride/triethylamine in methylene chloride gave the mesylates (**14** and **15**), which were treated

Chart 1

TABLE II. Intramolecular Pummerer Reaction of ω -Carbamoylsulfoxides with *O*-Silylated Ketene Acetal

Runs	Starting materials	Conditions ^{a)}	Products	Yield (%)
1	1a	r.t. 5 h	2a	85
2	1b : R = CH ₂ Ph 1c : R = CH ₂ CO ₂ Et	r.t. 1 h	2b : R = CH ₂ Ph 2c : R = CH ₂ CO ₂ Et	100
3		r.t. 14 h		88
4	1d	r.t. 25 h	2d	57
5	1e	r.t. 4 h	2e	54
6	1f	r.t. 18 h	2f	57

a) The reaction was carried out with 1.2–1.7 eq of *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**4**) in CH₃CN.

spectrometer (with tetramethylsilane as an internal standard unless otherwise noted). IR absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer. Low- and high-resolution mass spectra (MS) were obtained with a JEOL JMS-D300 instrument, with a direct inlet system at 70 eV. For column chromatography, E. Merck silica gel (70–230 mesh ASTM) was used. For preparative thin layer chromatography (preparative TLC), E. Merck TLC plates pre-coated with silica gel 60F₂₅₄ (0.5 mm) were used.

***O*-Methyl-*O*-*tert*-butyldimethylsilyl Ketene Acetal (**4**)** The ketene acetal (**4**) was prepared by the reported method.¹⁶⁾

4-(Phenylthio)butyric Acid (5**)** 3-Butenoic acid (860 mg, 10 mmol), thiophenol (1.10 g, 10 mmol) and azobisisobutyronitrile (AIBN, 10 mg) were mixed at room temperature. The mixture was stirred overnight, and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH₂Cl₂–MeOH (40:1) to give **5** (1.02 g, 52%) as colorless crystals, mp 66–68 °C (CH₂Cl₂–petroleum ether) (lit.¹⁷⁾ 66–67 °C). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 2250–3600, 1710. ¹H-NMR (CDCl₃) δ : 1.96 (2H, quint, *J* = 7 Hz, –CH₂CH₂CH₂–), 2.53 (2H, t, *J* = 7 Hz, –CH₂COOH), 2.98 (2H, t, *J* = 7 Hz, –CH₂SPh), 7.18–7.34 (5H, m, SPh), 8.99–9.43 (1H, br, –COOH). MS *m/z*: 196 (M⁺), 87 (M⁺ – SPh).

***N*-Benzyl-4-(phenylthio)butanamide (**6**)** (Trimethylsilyl)ethoxyacetylene (65.3 mg, 0.460 mmol) was added to a stirred solution of **5** (45.1 mg, 0.230 mmol), benzylamine (29.5 mg, 0.276 mmol) and HgO (2.5 mg, 0.0115 mmol) in (CH₂Cl)₂ (5 ml) at room temperature. The mixture was stirred overnight under the same conditions and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with hexane–AcOEt (2:1) to give **6** (65.0 mg, 99%) as colorless crystals, mp 86–87 °C (CH₂Cl₂–hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3450, 1660. ¹H-NMR (CDCl₃) δ : 1.97 (2H, quint, *J* = 7 Hz, –CH₂CH₂CH₂–), 2.31 (2H, t, *J* = 7 Hz, O=CCH₂–), 2.93 (2H, t, *J* = 7 Hz, –CH₂SPh), 4.38 (2H, d, *J* = 5.5 Hz, –NHCH₂Ph), 5.78 (1H, br, NH), 7.16–7.35 (10H, m, ArH). MS *m/z*: 285 (M⁺). Anal. Calcd for C₁₇H₁₉NOS: C, 71.56; H, 6.71; N, 4.91; S, 11.21. Found: C, 71.27; H, 6.76; N, 4.96; S, 11.05.

***N*-(Ethoxycarbonylmethyl)-4-(phenylthio)butanamide (**7**)** A solution of **5** (1.02 g, 5.20 mmol) and a catalytic amount of dimethylformamide was refluxed for 1.5 h and concentrated *in vacuo*. The residue was diluted with CH₂Cl₂ (4 ml), and the solution was added to a solution of ethyl glycinate hydrochloride (1.08 mg, 7.73 mmol) and triethylamine (5 ml) in CH₂Cl₂ (4 ml) at 0 °C. The solution was stirred for 20 min, poured into water

(20 ml), and extracted with CH_2Cl_2 (20 ml $\times$ 5). The extract was washed with brine, dried over MgSO_4 , and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH_2Cl_2 -AcOEt (10:1) to give **7** (1.10 g, 75%) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1740, 1670. $^1\text{H-NMR}$ (CDCl_3) δ : 1.27 (3H, t, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 1.98 (2H, quint, $J=7$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.40 (2H, t, $J=7$ Hz, $\text{O}=\text{CCH}_2-$), 2.98 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{SPh}$), 4.00 (2H, d, $J=5$ Hz, $-\text{NHCH}_2-$), 4.22 (2H, q, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 5.96 (1H, br, NH), 7.11–7.36 (5H, m, SPh). Exact MS Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_3\text{S}$: 281.1086. Found: 281.1094.

N-[4-(Phenylthio)butyl]acetamide (9) A solution of **7** (98.6 mg, 0.506 mmol) in dry tetrahydrofuran (THF, 5 ml) was added to a suspension of LiAlH_4 (47.7 mg, 1.26 mmol) in dry THF (10 ml) at room temperature under nitrogen. The solution was stirred for 30 min under the same conditions and refluxed for 4 h. A 10% aqueous solution of NaOH was added to the solution, then the precipitate was filtered off. The filtrate was diluted with CH_2Cl_2 (50 ml) and washed with brine. The organic layer was dried over Na_2SO_4 and evaporated *in vacuo* to give **8**, which was dissolved in a solution of Ac_2O (2 ml) and pyridine (1 ml). The solution was stirred overnight at room temperature and concentrated *in vacuo*. The residue was poured into CH_2Cl_2 (20 ml), and the solution was washed with a 5% aqueous solution of HCl (20 ml). The aqueous layer was extracted with CH_2Cl_2 (20 ml $\times$ 4). The combined organic layer was washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with AcOEt-hexane (1:4) to give **9** (79.9 mg, 70.8%) as colorless crystals, mp 82.5–84 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3460, 3380 (br), 1660. $^1\text{H-NMR}$ (CDCl_3) δ : 1.57–1.74 (4H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), 1.92 (3H, s, $\text{O}=\text{CCH}_3$), 2.91 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{SPh}$), 3.23 (2H, dt, $J=5.5, 7$ Hz, $-\text{NHCH}_2-$), 5.55–5.78 (1H, br, NH), 7.14–7.33 (5H, m, SPh). Exact MS Calcd for $\text{C}_{12}\text{H}_{17}\text{NOS}$: 223.1028. Found: 223.1028.

N-Benzyl-5-hydroxypentanamide (12) Benzylamine (1.07 g, 10 mmol) was added to a suspension of NaH (60%, 0.45 g, 11 mmol) in dry THF (20 ml) at 0 °C under nitrogen. After stirring of this mixture for 30 min, δ -valerolactone (**10**, 1.0 g, 10 mmol) was added. The reaction mixture was stirred for 1 h and diluted with saturated aqueous NH_4Cl (40 ml), then the aqueous layer was extracted with CH_2Cl_2 (50 ml $\times$ 4). The combined organic layer was washed with saturated aqueous NaHCO_3 , dried over MgSO_4 , and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH_2Cl_2 -AcOEt (1:1) to give **12** (1.85 g, 89%) as colorless crystals, mp 69–70 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 3200–3550, 1655. $^1\text{H-NMR}$ (CDCl_3) δ : 1.49 (4H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.24 (2H, t, $J=6$ Hz, $\text{O}=\text{CCH}_2-$), 2.82 (1H, br, OH), 3.60 (2H, t, $J=6$ Hz, $-\text{CH}_2\text{OH}$), 4.38 (2H, d, $J=5$ Hz, 6.33, $-\text{NHCH}_2\text{Ph}$), (1H, br, NH), 7.27 (5H, s, Ph). Exact MS Calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2$: 207.1259. Found: 207.1284.

N-Benzyl-6-hydroxyhexanamide (13) Benzylamine (1.0 g, 9.17 mmol) was added to a suspension of NaH (50%, 484.2 mg, 10.1 mmol) in dry THF (25 ml) at 0 °C under nitrogen. After stirring of this mixture for 10 min, ϵ -caprolactone (**11**, 1.01 ml, 9.17 mmol) was added. The reaction mixture was stirred at room temperature for 4 d and worked up in the same manner as used in the preparation of **12**. The crude product was subjected to column chromatography on silica gel with AcOEt to give **13** (1.29 g, 64%) as colorless crystals, mp 69–71 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 3325, 1650. $^1\text{H-NMR}$ (CDCl_3) δ : 1.12–1.81 (6H, m, $-\text{CH}_2(\text{CH}_2)_3\text{CH}_2-$), 2.17 (2H, t, $J=6$ Hz, $\text{O}=\text{CCH}_2-$), 2.66 (1H, br, OH), 3.57 (2H, t, $J=6$ Hz, $-\text{CH}_2\text{OH}$), 4.45 (2H, d, $J=5.5$ Hz, $-\text{NHCH}_2\text{Ph}$), 6.36 (1H, br, NH), 7.24 (5H, s, Ph). MS m/z : 221 (M^+). Anal. Calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2$: C, 70.55; H, 8.65; N, 6.33. Found: C, 70.27; H, 8.68; N, 6.26.

4-(Benzylcarbamoyl)butyl Methanesulfonate (14) A solution of methanesulfonyl chloride (69.6 mg, 0.607 mmol) in CH_2Cl_2 (0.5 ml) and a solution of triethylamine (76.7 mg, 0.759 mmol) in CH_2Cl_2 (0.5 ml) were added to a stirred solution of **12** (104.8 mg, 0.506 mmol) in CH_2Cl_2 (2 ml) at 0 °C. The mixture was stirred at room temperature for 2 h. After addition of a small amount of MeOH, the mixture was partitioned between CH_2Cl_2 (20 ml) and water (20 ml), then the aqueous layer was extracted with CH_2Cl_2 (20 ml $\times$ 4). The combined organic layer was washed with 1 N aqueous HCl, saturated aqueous NaHCO_3 , and brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH_2Cl_2 -AcOEt (3:2) to give **14** (112.4 mg, 78%) as colorless needles, mp 53–55 °C (AcOEt-hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1660. $^1\text{H-NMR}$ (CDCl_3) δ : 1.67–1.84 (4H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.24 (2H, t, $J=6$ Hz, $\text{O}=\text{CCH}_2-$), 2.96 (3H, s, $-\text{SO}_3\text{CH}_3$), 4.18 (2H, t, $J=6$ Hz, $-\text{CH}_2\text{OMs}$), 4.40 (2H, d, $J=6$ Hz, $-\text{NHCH}_2\text{Ph}$), 6.60 (1H, br, NH), 7.16 (5H, s, Ph). Exact MS Calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_4\text{S}$: 285.1032.

Found: 285.1011.

5-(Benzylcarbamoyl)pentyl Methanesulfonate (15) This (858.3 mg, 72%) was prepared from **13** (881.5 mg, 3.99 mmol), triethylamine (4 ml) and methanesulfonyl chloride (0.46 ml, 5.99 mmol) in CH_2Cl_2 (18 ml) in a similar manner to that described for the preparation of **14** as colorless crystals, mp 66–67 °C (Et_2O). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3470, 1665. $^1\text{H-NMR}$ (CDCl_3) δ : 1.33 (6H, m, $-\text{CH}_2(\text{CH}_2)_3\text{CH}_2-$), 2.44 (2H, t, $J=6$ Hz, $\text{O}=\text{CCH}_2-$), 2.99 (3H, s, $-\text{SO}_3\text{CH}_3$), 4.22 (2H, t, $J=6$ Hz, $-\text{CH}_2\text{OMs}$), 4.43 (2H, d, $J=5.5$ Hz, $-\text{NHCH}_2\text{Ph}$), 5.94 (1H, br, NH), 7.28 (5H, s, Ph). MS m/z : 299 (M^+). Anal. Calcd for $\text{C}_{14}\text{H}_{21}\text{NO}_4\text{S}$: C, 56.17; H, 7.07; N, 4.68; S, 10.69. Found: C, 55.97; H, 7.10; N, 4.64; S, 10.73.

N-Benzyl-5-(phenylthio)pentanamide (16) A solution of thiophenol (60 mg, 0.545 mmol) in EtOH (2 ml) was added to a stirred solution of NaOH (21.1 mg, 0.528 mmol) in EtOH (0.8 ml) at room temperature, and a solution of **14** (150.3 mg, 0.527 mmol) in EtOH (2 ml) was added to this mixture. The solution was stirred for 2 h under the same conditions and evaporated *in vacuo*. The residue was partitioned between CH_2Cl_2 (30 ml) and water (30 ml), then the aqueous layer was extracted with CH_2Cl_2 (30 ml $\times$ 3). The combined organic layer was washed with brine, dried over MgSO_4 , and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with CH_2Cl_2 -MeOH (20:1) to give **16** (133.6 mg, 85%) as colorless crystals, mp 115–117 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1660. $^1\text{H-NMR}$ (CDCl_3) δ : 1.67 (4H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.22 (2H, t, $J=6.5$ Hz, $\text{O}=\text{CCH}_2-$), 2.93 (2H, t, $J=6.5$ Hz, $-\text{CH}_2\text{SPh}$), 4.40 (2H, d, $J=5.5$ Hz, $-\text{NHCH}_2\text{Ph}$), 5.78 (1H, br, NH), 7.16–7.33 (10H, m, ArH). MS m/z : 299 (M^+). Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NOS}$: C, 72.21; H, 7.07; N, 4.68; S, 10.69. Found: C, 71.97; H, 7.01; N, 4.65; S, 10.47.

N-Benzyl-6-(phenylthio)hexanamide (17) This (92 mg, 98%) was prepared from **15** (90 mg, 0.301 mmol), thiophenol (36.5 mg, 0.332 mmol) and NaOH (13.1 mg, 0.328 mmol) in EtOH (3 ml) in a similar manner to that used in the preparation of **16**, as colorless crystals, mp 85–86 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3460, 1660. $^1\text{H-NMR}$ (CDCl_3) δ : 1.35–1.88 (6H, m, $-\text{CH}_2(\text{CH}_2)_3\text{CH}_2-$), 2.20 (2H, t, $J=7$ Hz, $\text{O}=\text{CCH}_2-$), 2.93 (2H, t, $-\text{CH}_2\text{SPh}$), 4.44 (2H, d, $J=6$ Hz, $-\text{NHCH}_2\text{Ph}$), 5.77 (1H, br, NH), 7.30 (10H, m, ArH). MS m/z : 313 (M^+). Anal. Calcd for $\text{C}_{19}\text{H}_{23}\text{NOS}$: C, 72.82; H, 7.40; N, 4.47; S, 10.21. Found: C, 72.84; H, 7.50; N, 4.41; S, 10.14.

Methyl *o*-(N-Methylcarbamoyl)phenyl Sulfoxide (1a) The sulfoxide was obtained by the reported method, colorless needles, mp 140.5–142 °C (CH_2Cl_2 -hexane) (lit.^{9a}) mp 142–143 °C). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3460, 3300 (br), 1640, 1020. $^1\text{H-NMR}$ (CDCl_3) δ : 2.88 (3H, s, $\text{S}(\text{O})\text{CH}_3$), 2.93 (3H, d, $J=5.5$ Hz, $-\text{NHCH}_3$), 7.31–8.16 (4H, m, ArH). MS m/z : 197 (M^+), 182 ($\text{M}^+ - \text{Me}$).

General Procedure for the Preparation of ω -Carbamoylsulfoxides (1b–f) Sodium periodate (1.5 mmol) was added to a stirred solution of a sulfide (**6**, **7**, **9**, **16**, or **17**, 1 mmol) in MeOH or EtOH-water (10:1) (10 ml) at room temperature. The mixture was stirred overnight and evaporated *in vacuo*. The residue was partitioned between CH_2Cl_2 (20 ml) and water (20 ml), then the aqueous layer was extracted with CH_2Cl_2 (20 ml $\times$ 4). The combined organic layer was washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was subjected to column chromatography or preparative TLC on silica gel with CH_2Cl_2 -MeOH, AcOEt to give the corresponding sulfoxide.

N-Benzyl-4-(phenylsulfinyl)butanamide (1b) This (582 mg, 80%) was prepared from **6** (690 mg, 2.42 mmol) and sodium periodate (770 mg, 3.60 mmol) in MeOH (12 ml) as colorless needles, mp 85–86 °C (CH_2Cl_2 -hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1660, 1030. $^1\text{H-NMR}$ (CDCl_3) δ : 1.84–2.16 (2H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.36 (2H, t, $J=6$ Hz, $\text{O}=\text{CCH}_2-$), 2.79 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{S}(\text{O})\text{Ph}$), 4.34 (2H, d, $J=6$ Hz, $-\text{NHCH}_2\text{Ph}$), 6.49 (1H, br, NH), 7.23 (5H, s, $-\text{CH}_2\text{Ph}$), 7.47 (5H, s, $\text{S}(\text{O})\text{Ph}$). MS m/z : 302 (MH^+). Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_2\text{S}$: C, 67.76; H, 6.36; N, 4.65; S, 10.62. Found: C, 67.55; H, 6.47; N, 4.47; S, 10.37.

N-(Ethoxycarbonylmethyl)-4-(phenylsulfinyl)butanamide (1c) This (371 mg, 97%) was prepared from **7** (364 mg, 1.30 mmol) and sodium periodate (415 mg, 1.94 mmol) in EtOH-water (5.5 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3440, 1740, 1670, 1025. $^1\text{H-NMR}$ (CDCl_3) δ : 1.24 (3H, t, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 1.97–2.21 (2H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 2.44 (2H, t, $J=6.5$ Hz, $\text{O}=\text{CCH}_2-$), 2.93 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{S}(\text{O})\text{Ph}$), 3.98 (2H, d, $J=5.5$ Hz, $-\text{NHCH}_2\text{CO}$), 4.18 (2H, q, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 6.53 (1H, br, NH), 7.42–7.62 (5H, m, $\text{S}(\text{O})\text{Ph}$). Exact MS Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{S}$: 297.1034. Found: 297.1034.

N-[4-(Phenylsulfinyl)butyl]acetamide (1d) This (54.2 mg, 98%) was prepared from **9** (51.7 mg, 0.232 mmol) and sodium periodate (101.0 mg, 0.472 mmol) in MeOH (6 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3460,

1660, 1030. $^1\text{H-NMR}$ (CDCl_3) δ : 1.58—1.76 (4H, m, $-\text{CH}_2(\text{CH}_2)_2\text{CH}_2-$), 1.93 (3H, s, $\text{O}=\text{CCH}_3$), 2.80 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{S}(\text{O})\text{Ph}$), 3.22 (2H, q, $J=6$ Hz, $-\text{NHCH}_2-$), 5.80 (1H, br, NH), 7.42—7.60 (5H, m, $\text{S}(\text{O})\text{Ph}$). Exact MS Calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{S}$: 239.0978. Found: 239.0966.

N-Benzyl-5-(phenylsulfinyl)pentanamide (1e) This (101.8 mg, 93%) was prepared from **16** (103.8 mg, 0.347 mmol) and sodium periodate (98.5 mg, 0.460 mmol) in MeOH (10 ml) as colorless crystals, mp 78—79 °C (CH_2Cl_2 —hexane). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1660, 1020—1040. $^1\text{H-NMR}$ (CDCl_3) δ : 1.69—1.84 (4H, m, $-\text{CH}_2(\text{CH}_2)_2\text{CH}_2-$), 2.22 (2H, t, $\text{O}=\text{CCH}_2-$), 2.78 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{S}(\text{O})\text{Ph}$), 4.39 (2H, d, $J=5.5$ Hz, $-\text{NHCH}_2\text{Ph}$), 6.33 (1H, br, NH), 7.26 (5H, s, $-\text{CH}_2\text{Ph}$), 7.47—7.56 (5H, m, $\text{S}(\text{O})\text{Ph}$). MS m/z : 315 (M^+). Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{S}$: C, 68.55; H, 6.71; N, 4.44; S, 10.15. Found: C, 68.41; H, 6.75; N, 4.35; S, 10.05.

N-Benzyl-6-(phenylsulfinyl)hexanamide (1f) This (74 mg, quant.) was prepared from **17** (70 mg, 0.224 mmol) and sodium periodate (67 mg, 0.313 mmol) in MeOH (2 ml) as a colorless powder, mp 64—65 °C (CH_2Cl_2 —Et₂O). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1650, 1020. $^1\text{H-NMR}$ (CDCl_3) δ : 1.37—1.85 (6H, m, $-\text{CH}_2(\text{CH}_2)_3\text{CH}_2-$), 2.17 (2H, t, $J=7$ Hz, $\text{O}=\text{CCH}_2-$), 2.75 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{S}(\text{O})\text{Ph}$), 4.38 (2H, d, $J=6$ Hz, $-\text{NHCH}_2\text{Ph}$), 5.94 (1H, br, NH), 7.24 (5H, s, $-\text{CH}_2\text{Ph}$), 7.51 (5H, s, $\text{S}(\text{O})\text{Ph}$). Exact MS Calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{S}$: 329.1450. Found: 329.1453.

4-Acetoxy-N-benzyl-4-(phenylthio)butanamide (18a) and 4-Acetoxy-N-acetyl-N-benzyl-4-(phenylthio)butanamide (18b) A solution of **1b** (53 mg, 0.176 mmol) in acetic anhydride (3 ml) was refluxed for 3.5 h, and the solution was evaporated *in vacuo*. The residue was partitioned between CH_2Cl_2 (20 ml) and a saturated aqueous solution of sodium bicarbonate (20 ml), then the aqueous layer was extracted with CH_2Cl_2 (20 ml $\times$ 4). The organic layer was washed with brine, dried over MgSO_4 , and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with hexane—AcOEt (3:1) to give **18a** (11 mg, 18%) and **18b** (42 mg, 62%) as colorless oils. **18a**: IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3450, 1735, 1670. $^1\text{H-NMR}$ (CDCl_3) δ : 2.00 (3H, s, Ac), 2.16—2.40 (4H, m, $-\text{CH}_2\text{CH}_2-$), 4.40 (2H, d, $J=5.5$ Hz, NHCH_2Ph), 5.82 (1H, br, NH), 6.09 (1H, t, $J=6.5$ Hz, PhSCH_2OAc), 7.13—7.49 (10H, m, ArH). Exact MS Calcd for $\text{C}_{19}\text{H}_{22}\text{NO}_3\text{S}$ —SPh: 235.1206. Found: 235.1189. **18b**: IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1700. $^1\text{H-NMR}$ (CDCl_3) δ : 1.98 (3H, s, Ac), 2.16 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{CH}_2-$), 2.38 (3H, s, Ac), 2.82 (2H, t, $J=7$ Hz, $-\text{CH}_2\text{CH}_2-$), 4.91 (2H, brs, NCH_2Ph), 6.09 (1H, t, $J=6.5$ Hz, PhSCH_2OAc), 7.02—7.44 (10H, m, ArH). Exact MS Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_4\text{S}$ —SPh: 276.1237. Found: 276.1247.

General Procedure for the Reaction of ω -Carbamoylsulfoxides (1a—f) with the Ketene Silyl Acetal (4) The ketene silyl acetal (**4**, 1.5 mmol) was added to a stirred solution of an ω -carbamoylsulfoxide (**1**, 1 mmol) and ZnI_2 (0.05—0.1 mmol) in dry CH_3CN at room temperature under nitrogen. The mixture was stirred at the temperature and for the period indicated in Table II, then partitioned between CH_2Cl_2 (20 ml) and saturated aqueous NaHCO_3 (20 ml). The aqueous layer was extracted with CH_2Cl_2 (20 ml $\times$ 4). The combined extract was washed with brine, dried over MgSO_4 and concentrated under reduced pressure. The residue was subjected to column chromatography or preparative TLC on silica gel with hexane—AcOEt to give the cyclized compound (**2**).

3-Methyl-2,3-dihydro-1,3-benzothiazin-4-one (2a) This (41 mg, 85%) was obtained from **1a** (53 mg, 0.269 mmol), **4** (64 mg, 0.34 mmol) and ZnI_2 (8 mg, 0.025 mmol) in CH_3CN (1.5 ml) as a colorless oil, bp 100—105 °C/0.1 mmHg (bath temperature). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1640. $^1\text{H-NMR}$ (CDCl_3) δ : 3.20 (3H, s, NCH_3), 4.56 (2H, s, NCH_2S), 7.10—7.31, 8.02—8.13 (total 4H, m, ArH). Exact MS Calcd for $\text{C}_9\text{H}_9\text{NOS}$: 179.0405. Found: 179.0428.

N-Benzyl-5-(phenylthio)-2-pyrrolidone (2b) i) This (25.9 mg, quant.) was obtained from **1b** (27 mg, 0.090 mmol), **4** (27 mg, 0.143 mmol), and ZnI_2 (6 mg, 0.018 mmol) in CH_3CN (1 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1685. $^1\text{H-NMR}$ (CDCl_3) δ : 1.73—2.51 (4H, m, $-\text{CH}_2\text{CH}_2-$), 4.30 (1H, d, $J=14.5$ Hz, $-\text{NCH}_2\text{Ph}$), 4.73 (1H, dd, $J=3$, 7 Hz, $-\text{NCH}_2\text{SPh}$), 5.27 (1H, d, $J=14.5$ Hz, $-\text{NCH}_2\text{Ph}$), 7.35—7.51 (10H, m, ArH). MS m/z : 284 (MH^+), 174 ($\text{M}^+ - \text{SPh}$). Exact MS Calcd for $\text{C}_{17}\text{H}_{17}\text{NOS}$ —SPh: 174.0917. Found: 174.0917. ii) This (9 mg, 20%) was obtained from **1b** (48 mg, 0.159 mmol), and **4** (56 mg, 0.29 mmol) in CH_3CN (3 ml) after stirring at 65—70 °C for 8 d. iii) This (11.5 mg, 41%) was obtained from **1b** (30 mg, 0.0996 mmol), **4** (50 mg, 0.266 mmol), and $\text{BF}_3 \cdot \text{OEt}_2$ [0.1 ml of a solution of $\text{BF}_3 \cdot \text{OEt}_2$ (0.06 ml) in CH_3CN (2 ml), 0.018 mmol] in CH_3CN (1 ml) after stirring at room temperature for 4 h. iv) This (12.0 mg, 71%) was obtained from **1b** (18.0 mg, 0.0598 mmol), **4** (16.9 mg, 0.0897 mmol), and ZnI_2 (2 mg, 0.0060 mmol) in dry THF (0.5 ml) after stirring at room temperature for 7 h. v) This (13.0 mg, 73%) was obtained from **1b** (18.3 mg, 0.0608 mmol), **4** (17.1 mg, 0.0912 mmol), and ZnI_2 (1.9 mg, 0.0061 mmol)

in dry CH_2Cl_2 (1 ml) after stirring at room temperature for 2 d.

N-(Ethoxycarbonylmethyl)-5-(phenylthio)-2-pyrrolidinone (2c) This (250 mg, 88%) was obtained from **1c** (333 mg, 1.12 mmol), **4** (320 mg, 1.7 mmol), and ZnI_2 (39 mg, 0.12 mmol) in CH_3CN (3.5 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1740, 1690. $^1\text{H-NMR}$ (CDCl_3) δ : 1.27 (3H, t, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 1.53—2.73 (4H, m, $-\text{CH}_2\text{CH}_2-$), 4.00 (1H, d, $J=17$ Hz, $-\text{NCH}_2-$), 4.19 (1H, q, $J=7$ Hz, $-\text{OCH}_2\text{CH}_3$), 4.59 (1H, d, $J=17$ Hz, $-\text{NCH}_2\text{Ph}$), 5.11 (1H, dd, $J=3$, 7.5 Hz, $-\text{NCH}_2\text{SPh}$), 7.33 (5H, s, SPh). MS m/z : 279 (M^+), 234 ($\text{M}^+ - \text{OEt}$), 170 ($\text{M}^+ - \text{SPh}$). Exact MS Calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_3\text{S} - \text{OEt}$: 234.0588. Found: 234.0588.

N-Acetyl-2-(phenylthio)pyrrolidine (2d) This (15.3 mg, 57%) was obtained from **1d** (29.0 mg, 0.121 mmol), **4** (36.4 mg, 0.194 mmol), and ZnI_2 (2 mg, 0.0063 mmol) in CH_3CN (1.5 ml) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1635. $^1\text{H-NMR}$ (CDCl_3) δ : 2.07—2.26 (4H, m, $-\text{CH}_2\text{CH}_2-$), 2.05 (1/3 $\times$ 3H, s, $\text{O}=\text{CCH}_3$), 2.07 (2/3 $\times$ 3H, s, $\text{O}=\text{CCH}_3$), 3.40 [1/3 $\times$ 1H, dt, $J=7.5$, 9.5 Hz, NCH_2H (minor)], 3.52 [1/3 $\times$ 1H + 2/3 $\times$ 2H, m, NCH_2- (major) + NCH_2H (minor)], 5.16 (2/3 $\times$ 1H, d, $J=5.5$ Hz, NCH_2SPh), 5.59 (1/3 $\times$ 1H, t, $J=3.6$ Hz, NCH_2SPh), 7.26—7.56 (5H, m, SPh). (The singals indicated this product to be a 2:1 mixture of geometrical isomers.) Exact MS Calcd for $\text{C}_{12}\text{H}_{15}\text{NOS} - \text{SPh}$: 112.0763. Found: 112.0774.

N-Benzyl-6-(phenylthio)-2-piperidine (2e) This (31.6 mg, 54%) was obtained from **1e** (62.4 mg, 0.198 mmol), **4** (57.5 mg, 0.306 mmol), and ZnI_2 (3 mg, 0.0094 mmol) in CH_3CN (1.5 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1635. $^1\text{H-NMR}$ (CDCl_3) δ : 1.71—2.67 (6H, m, $\text{O}=\text{C}(\text{CH}_2)_3-$), 4.17 (1H, d, $J=15$ Hz, NCH_2HPh), 4.69 (1H, t, $J=4$ Hz, NCH_2SPh), 5.71 (1H, d, $J=15$ Hz, NCH_2HPh), 7.11—7.64 (10H, m, ArH). Exact MS Calcd for $\text{C}_{18}\text{H}_{19}\text{NOS} - \text{SPh}$: 188.1075. Found: 188.1076.

N-Benzyl-7-(phenylthio)-2-hexahydroazepinone (2f) This (24.4 mg, 57%) was obtained from **1f** (44.8 mg, 0.136 mmol), **4** (43.1 mg, 0.229 mmol), and ZnI_2 (6.2 mg, 0.019 mmol) in CH_3CN (2.5 ml) as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1625. $^1\text{H-NMR}$ (CDCl_3) δ : 1.53—2.12 (6H, m, $\text{O}=\text{CCH}_2(\text{CH}_2)_3-$), 2.78 (1H, dd, $J=14.7$, 7.3 Hz, $\text{O}=\text{CCH}_2\text{H}$), 3.20—3.26 (1H, m, $\text{O}=\text{CCH}_2-$), 3.19 (1H, d, $J=15.3$ Hz, NCH_2HPh), 4.83 (1H, dd, $J=5.5$, 3.1 Hz, NCH_2SPh), 5.26 (1H, d, $J=14.7$ Hz, NCH_2HPh), 7.07—7.50 (10H, m, ArH). Exact MS Calcd for $\text{C}_{19}\text{H}_{21}\text{NOS} - \text{SPh}$: 202.1233. Found: 202.1234.

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