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 trimethylsilyltrifluoromethanesulfonate (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)ethoxyacetylene[13] 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 ($NaIO_4$) to give high yields of the corresponding ω-carbamoylsulfoxides (**1b,c**). The *N*-unsubstituted ω-carbamoylsulfide (**8**) was reduced with lithium aluminum hydride ($LiAlH_4$) and acetylated to give the ω-acetylaminosulfide (**9**), which was oxidized with $NaIO_4$ 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

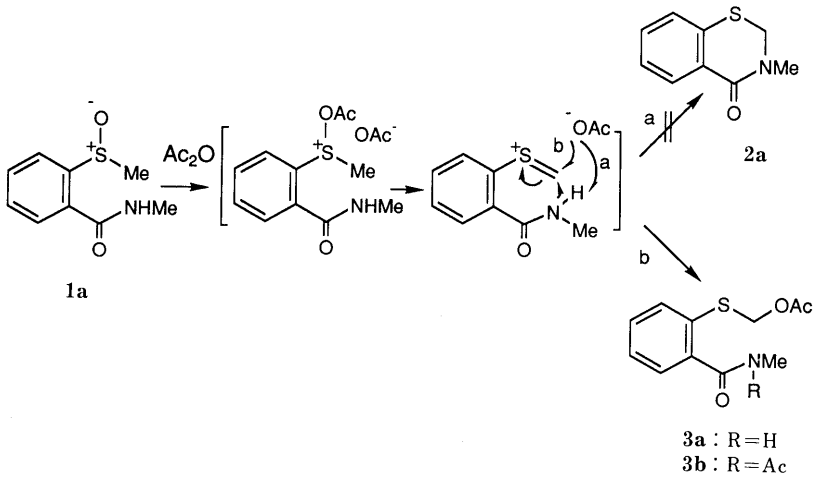


Chart 1

with sodium thiophenolate in ethanol to give the ω-carbamoylsulfides (**16** and **17**) in good overall yields. The sulfides (**16** and **17**) were oxidized with $NaIO_4$ to give high yields of the corresponding ω-carbamoylsulfoxides (**1e,f**). All these compounds (**1b—f** and **5—17**) were characterized by proton nuclear magnetic resonance (^{1}H-NMR), infrared (IR), and analytical data.

We first examined the conversion of *N*-benzyl-4-(phenylsulfinyl)butanamide (**1b**) into *N*-benzyl-5-(phenylthio)-2-pyrrolidone (**2b**) by the use of acetic anhydride, trifluoroacetic anhydride, TMSOTf/triethylamine, and *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal (**4**). The use of **4** in the presence of a catalyst was found to be quite efficient for the synthesis of **2b**, although other conditions resulted in either formation of the normal intermolecular Pummerer reaction products (**18a,b**) or formation of complex mixtures (Chart 4). Among various reaction conditions examined, changing the catalyst and the solvent, the use of a catalytic amount of zinc iodide in acetonitrile (run 7) gave the best result (Table I). A typical experimental procedure is as follows for the formation of **1b** with **4**. A solution of **1b**, **4**, and a catalytic amount of zinc iodide in dry acetonitrile was stirred at room temperature for 1 h to give a quantitative yield of **2b**. Similarly, various types of ω-carbamoylsulfoxides (**1a** and **1c—f**) were reacted with **4** to give the corresponding α-thiolactams (**2a** and **2c—f**), which were characterized by spectral and analytical data. The reaction conditions and yields are summarized in Table II.

The reaction of ω-carbamoylsulfoxides (**1a—f**) with **4** presumably proceeds *via* the Pummerer-type intermediates (A and B) shown in Chart 5. Initial silicon transfer from **4** to the sulfoxides (**1a—f**) and subsequent abstraction of α-hydrogen by a generated ester enolate anion would give A. There are two possibilities for the formation of **2a—f** from A involving a direct cyclization of A and prior conversion of A to the imidate intermediate (B). Prior conversion of A to B might be favorable for the cyclization since direct cyclization of A would give the α-thiolactone as observed in the case of iodolactonization of ω-carbamoylolefins.[14]

Since the α-thiolactams (**2**) are useful intermediates for pyrrolidines and indolidines,[15] the present reaction provides a means for the versatile synthesis of these alkaloids.

Experimental

All melting and boiling points are uncorrected. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) or a JEOL JNM-GX 500 (500 MHz)

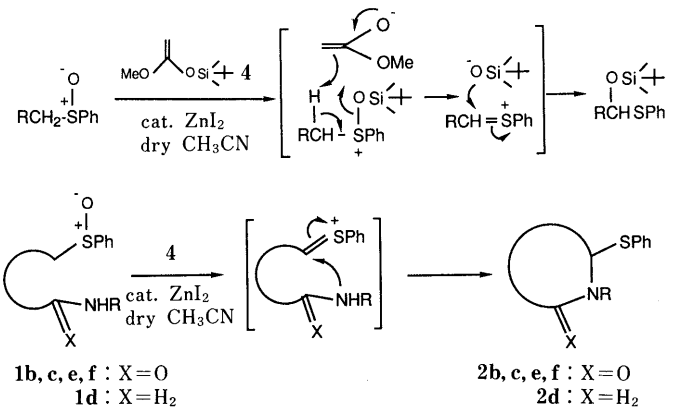
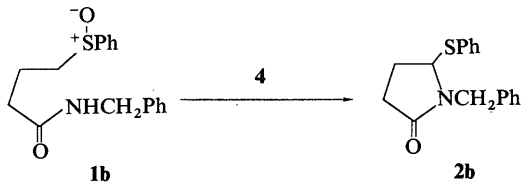
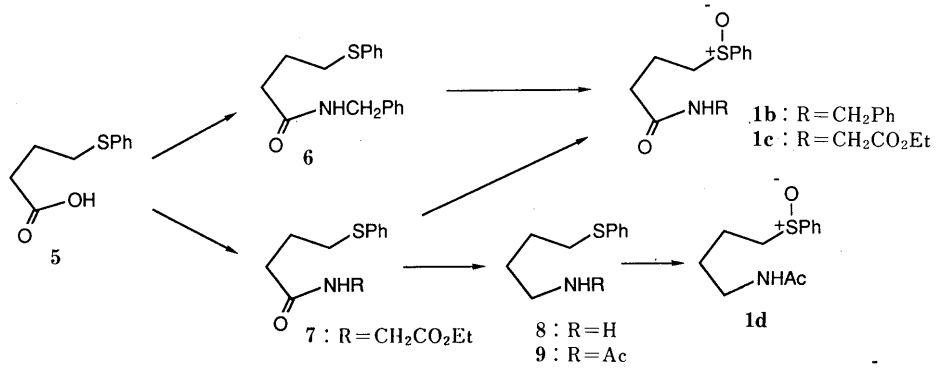


Chart 2

TABLE I. Intramolecular Pummerer Reaction of **1b**



Run	Catalyst	Conditions			
		Solvent	Temp. (°C)	Time	Yield (%)
1	None	CH_3CN	65—70	8 d	20
2	$BF_3 \cdot Et_2O$	CH_3CN	r.t.	4 h	41
3	$SnCl_4$	CH_3CN	r.t.	5.5 h	Trace
4	$TiCl_4$	CH_3CN	r.t.	5.5 h	Trace
5	ZnI_2	THF	r.t.	7 h	71
6	ZnI_2	CH_2Cl_2	r.t.	2 d	73
7	ZnI_2	CH_3CN	r.t.	1 h	100



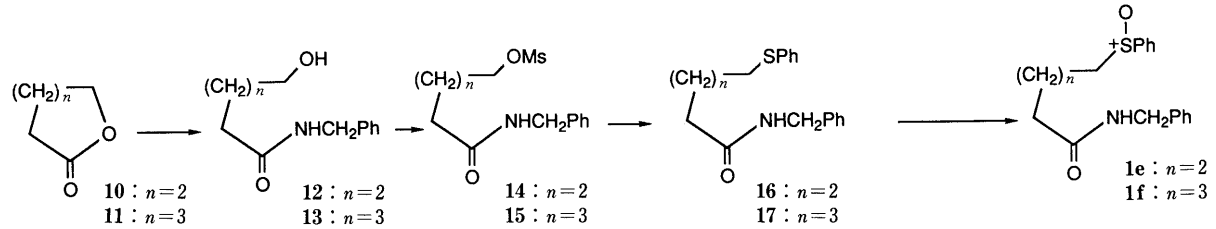
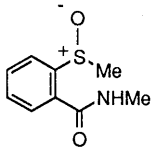
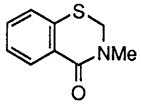
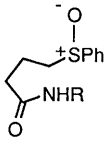
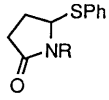
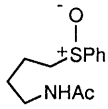
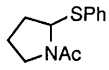
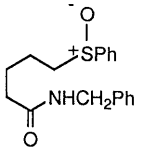
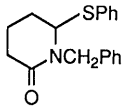
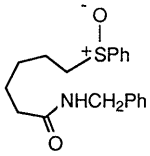
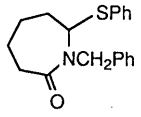


Chart 3

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_2Ph	r.t. 1 h		**2b**: R=CH_2Ph	100
3		**1c**: R=CH_2CO_2Et	r.t. 14 h		**2c**: R=CH_2CO_2Et	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 CH_3CN.

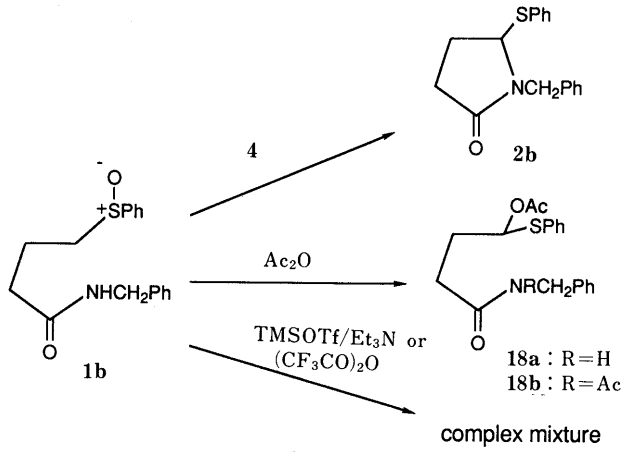


Chart 4

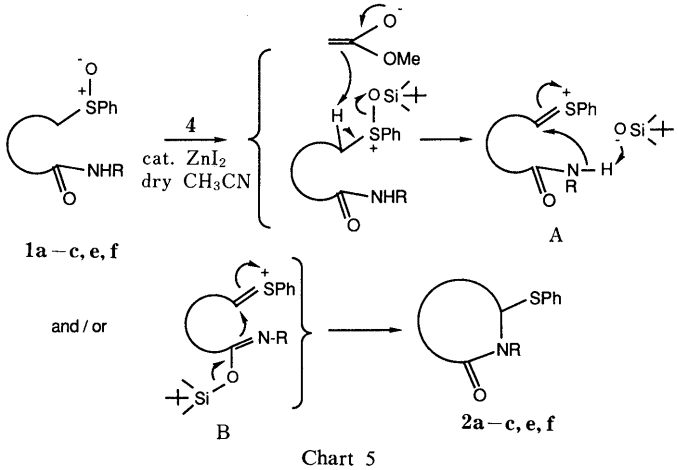


Chart 5

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 $60F_{254}$ (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 CH_2Cl_2–MeOH (40 : 1) to give **5** (1.02 g, 52%) as colorless crystals, mp 66—68 °C (CH_2Cl_2–petroleum ether) (lit.[17] 66—67 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250—3600, 1710. ^{1}H-NMR ($CDCl_3$) δ: 1.96 (2H, quint, J=7 Hz, $-CH_2CH_2CH_2-$), 2.53 (2H, t, J=7 Hz, $-CH_2COOH$), 2.98 (2H, t, J=7 Hz, $-CH_2SPh$), 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 $(CH_2Cl)_2$ (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 (CH_2Cl_2–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (2H, quint, J=7 Hz, $-CH_2CH_2CH_2-$), 2.31 (2H, t, J=7 Hz, $O=CCH_2-$), 2.93 (2H, t, J=7 Hz, $-CH_2SPh$), 4.38 (2H, d, J=5.5 Hz, $-NHCH_2Ph$), 5.78 (1H, br, NH), 7.16—7.35 (10H, m, ArH). MS *m/z*: 285 (M^+). *Anal.* Calcd for $C_{17}H_{19}NOS$: 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 CH_2Cl_2 (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 CH_2Cl_2 (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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1740, 1670. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (3H, t, J=7 Hz, $-OCH_2\underline{CH_3}$), 1.98 (2H, quint, J=7 Hz, $-CH_2\underline{CH_2}CH_2-$), 2.40 (2H, t, J=7 Hz, $O=C\underline{CH_2}-$), 2.98 (2H, t, J=7 Hz, $-\underline{CH_2}SPh$), 4.00 (2H, d, J=5 Hz, $-NHCH_2-$), 4.22 (2H, q, J=7 Hz, $-O\underline{CH_2}CH_3$), 5.96 (1H, br, NH), 7.11—7.36 (5H, m, SPh). Exact MS Calcd for $C_{14}H_{19}NO_3S$: 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 3380 (br), 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.57—1.74 (4H, m, $-\underline{CH_2CH_2}CH_2-\underline{CH_2}-$), 1.92 (3H, s, $O=CCH_3$), 2.91 (2H, t, J=7 Hz, $-\underline{CH_2}SPh$), 3.23 (2H, dt, J=5.5, 7 Hz, $-NHCH_2-$), 5.55—5.78 (1H, br, NH), 7.14—7.33 (5H, m, SPh). Exact MS Calcd for $C_{12}H_{17}NOS$: 223.1028. Found: 223.1028.

***N*-Benzyl-5-hydroxypentanamide (12)** Benzylamine (1.07 g, 10 mmol) was added to a suspension of NaH (60%, 045 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 3200—3550, 1655. ^{1}H-NMR ($CDCl_3$) δ: 1.49 (4H, m, $-CH_2-\underline{CH_2CH_2}CH_2-$), 2.24 (2H, t, J=6 Hz, $O=CCH_2-$), 2.82 (1H, br, OH), 3.60 (2H, t, J=6 Hz, $-\underline{CH_2}OH$), 4.38 (2H, d, J=5 Hz, 6.33, $-NHCH_2Ph$), (1H, br, NH), 7.27 (5H, s, Ph). Exact MS Calcd for $C_{12}H_{17}NO_2$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 3325, 1650. ^{1}H-NMR ($CDCl_3$) δ: 1.12—1.81 (6H, m, $-CH_2(\underline{CH_2})_3CH_2-$), 2.17 (2H, t, J=6 Hz, $O=CCH_2-$), 2.66 (1H, br, OH), 3.57 (2H, t, J=6 Hz, $-\underline{CH_2}OH$), 4.45 (2H, d, J=5.5 Hz, $-NHCH_2Ph$), 6.36 (1H, br, NH), 7.24 (5H, s, Ph). MS *m/z*: 221 (M^+). *Anal.* Calcd for $C_{13}H_{19}NO_2$: 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.67—1.84 (4H, m, $-CH_2-\underline{CH_2CH_2}CH_2-$), 2.24 (2H, t, J=6 Hz, $O=CCH_2-$), 2.96 (3H, s, $-SO_2CH_3$), 4.18 (2H, t, J=6 Hz, $-\underline{CH_2}OMs$), 4.40 (2H, d, J=6 Hz, $-NHCH_2Ph$), 6.60 (1H, br, NH), 7.16 (5H, s, Ph). Exact MS Calcd for $C_{13}H_{19}NO_4S$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3470, 1665. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (6H, m, $-CH_2(\underline{CH_2})_3CH_2-$), 2.44 (2H, t, J=6 Hz, $O=CCH_2-$), 2.99 (3H, s, $-SO_2CH_3$), 4.22 (2H, t, J=6 Hz, $-\underline{CH_2}OMs$), 4.43 (2H, d, J=5.5 Hz, $-NHCH_2Ph$), 5.94 (1H, br, NH), 7.28 (5H, s, Ph). MS *m/z*: 299 (M^+). *Anal.* Calcd for $C_{14}H_{21}NO_4S$: 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.67 (4H, m, $-CH_2\underline{CH_2CH_2}CH_2-$), 2.22 (2H, t, J=6.5 Hz, $O=CCH_2-$), 2.93 (2H, t, J=6.5 Hz, $-\underline{CH_2}SPh$), 4.40 (2H, d, J=5.5 Hz, $-NHCH_2Ph$), 5.78 (1H, br, NH), 7.16—7.33 (10H, m, ArH). MS *m/z*: 299 (M^+). *Anal.* Calcd for $C_{18}H_{21}NOS$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}:3460, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.35—1.88 (6H, m, $-CH_2(\underline{CH_2})_3CH_2-$), 2.20 (2H, t, J=7 Hz, $O=CCH_2-$), 2.93 (2H, t, $-\underline{CH_2}SPh$), 4.44 (2H, d, J=6 Hz, $-NHCH_2Ph$), 5.77 (1H, br, NH), 7.30 (10H, m, ArH). MS *m/z*: 313 (M^+). *Anal.* Calcd for $C_{19}H_{23}NOS$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 3300 (br), 1640, 1020. ^{1}H-NMR ($CDCl_3$) δ: 2.88 (3H, s, $S(O)CH_3$), 2.93 (3H, d, J=5.5 Hz, $-NHCH_3$), 7.31—8.16 (4H, m, ArH). MS *m/z*: 197 (M^+), 182 ($M^+ - Me$).

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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1660, 1030. ^{1}H-NMR ($CDCl_3$) δ: 1.84—2.16 (2H, m, $-CH_2\underline{CH_2}CH_2-$), 2.36 (2H, t, J=6 Hz, $O=CCH_2-$) 2.79 (2H, t, J=7 Hz, $-\underline{CH_2}S(O)Ph$), 4.34 (2H, d, J=6 Hz, $-NHCH_2Ph$), 6.49 (1H, br, NH), 7.23 (5H, s, $-CH_2Ph$), 7.47 (5H, s, S(O)Ph). MS *m/z*: 302 (MH^+). *Anal.* Calcd for $C_{17}H_{19}NO_2S$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440, 1740, 1670, 1025. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J=7 Hz, $-OCH_2\underline{CH_3}$), 1.97—2.21 (2H, m, $-CH_2\underline{CH_2}CH_2-$), 2.44 (2H, t, J=6.5 Hz, $O=C\underline{CH_2}-$), 2.93 (2H, t, J=7 Hz, $-\underline{CH_2}S(O)Ph$), 3.98 (2H, d, J=5.5 Hz, $-NHCH_2CO$), 4.18 (2H, q, J=7 Hz, $-O\underline{CH_2}CH_3$), 6.53 (1H, br, NH), 7.42—7.62 (5H, m, S(O)Ph). Exact MS Calcd for $C_{14}H_{19}NO_4S$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460,

1660, 1030. ^{1}H-NMR ($CDCl_3$) δ: 1.58—1.76 (4H, m, $-CH_2(CH_2)_2CH_2-$), 1.93 (3H, s, $O=CCH_3$), 2.80 (2H, t, J=7 Hz, $-CH_2S(O)Ph$), 3.22 (2H, q, J=6 Hz, $-NHCH_2-$), 5.80 (1H, br, NH), 7.42—7.60 (5H, m, S(O)Ph). Exact MS Calcd for $C_{12}H_{17}NO_2S$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1660, 1020—1040. ^{1}H-NMR ($CDCl_3$) δ: 1.69—1.84 (4H, m, $-CH_2(CH_2)_2CH_2-$), 2.22 (2H, t, $O=CCH_2-$), 2.78 (2H, t, J=7 Hz, $-CH_2S(O)Ph$), 4.39 (2H, d; J=5.5 Hz, $-NHCH_2Ph$), 6.33 (1H, br, NH), 7.26 (5H, s, $-CH_2Ph$), 7.47—7.56 (5H, m, S(O)Ph). MS *m/z*: 315 (M^+). *Anal.* Calcd for $C_{18}H_{21}NO_2S$: 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–Et_2O). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1650, 1020. ^{1}H-NMR ($CDCl_3$) δ: 1.37—1.85 (6H, m, $-CH_2(CH_2)_3CH_2-$), 2.17 (2H, t, J=7 Hz, $O=CCH_2-$), 2.75 (2H, t, J=7 Hz, $-CH_2S(O)Ph$), 4.38 (2H, d, J=6 Hz, $-NHCH_2Ph$), 5.94 (1H, br, NH), 7.24 (5H, s, $-CH_2Ph$), 7.51 (5H, m, S(O)Ph). Exact MS Calcd for $C_{19}H_{23}NO_2S$: 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1735, 1670. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (3H, s, Ac), 2.16—2.40 (4H, m, $-CH_2CH_2-$), 4.40 (2H, d, J=5.5 Hz, $NHCH_2Ph$), 5.82 (1H, br, NH), 6.09 (1H, t, J=6.5 Hz, PhSCHOAc), 7.13—7.49 (10H, m, ArH). Exact MS Calcd for $C_{19}H_{22}NO_3S-SPh$: 235.1206. Found: 235.1189. **18b**: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1700. ^{1}H-NMR ($CDCl_3$) δ: 1.98 (3H, s, Ac), 2.16 (2H, t, J=7 Hz, $-CH_2CH_2-$), 2.38 (3H, s, Ac), 2.82 (2H, t, J=7 Hz, $-CH_2CH_2-$), 4.91 (2H, br s, $>NCH_2Ph$), 6.09 (1H, t, J=6.5 Hz, PhSCHOAc), 7.02—7.44 (10H, m, ArH). Exact MS Calcd for $C_{21}H_{23}NO_4S-SPh$: 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 × 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640. ^{1}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 C_9H_9NOS: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1685. ^{1}H-NMR ($CDCl_3$) δ: 1.73—2.51 (4H, m, $-CH_2CH_2-$), 4.30 (1H, d, J=14.5 Hz, $-NCHHPh$), 4.73 (1H, dd, J=3, 7 Hz, $-NCHSPh$), 5.27 (1H, d, J=14.5 Hz, $-NCHHPh$), 7.35—7.51 (10H, m, ArH). MS *m/z*: 284 (MH^+), 174 (M^+-SPh). Exact MS Calcd for $C_{17}H_{17}NOS-SPh$: 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 $BF_3\cdot OEt_2$ [0.1 ml of a solution of $BF_3\cdot OEt_2$ (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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1690. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (3H, t, J=7 Hz, $-OCH_2CH_3$), 1.53—2.73 (4H, m, $-CH_2CH_2-$), 4.00 (1H, d, J=17 Hz, $-NCHH-$), 4.19 (1H, q, J=7 Hz, $-OCH_2CH_3$), 4.59 (1H, d, J=17 Hz, $-NCHHPh$), 5.11 (1H, dd, J=3, 7.5 Hz, $-NCHSPh$), 7.33 (5H, s, SPh). MS *m/z*: 279 (M^+), 234 (M^+-OEt), 170 (M^+-SPh). Exact MS Calcd for $C_{14}H_{17}NO_3S-OEt$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1635. ^{1}H-NMR ($CDCl_3$) δ: 2.07—2.26 (4H, m, $-CH_2CH_2-$), 2.05 (1/3 × 3H, s, $O=CCH_3$), 2.07 (2/3 × 3H, s, $O=CCH_3$), 3.40 [1/3 × 1H, dt, J=7.5, 9.5 Hz, $>NCHH$-(minor)], 3.52 [1/3 × 1H + 2/3 × 2H, m, $>NCH_2$-(major) + $>NCHH$-(minor)], 5.16 (2/3 × 1H, d, J=5.5 Hz, $>NCHSPh$), 5.59 (1/3 × 1H, t, J=3.6 Hz, $>NCHSPh$), 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 $C_{12}H_{15}NOS-SPh$: 112.0763. Found: 112.0774.

***N*-Benzyl-6-(phenylthio)-2-piperidone (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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1635. ^{1}H-NMR ($CDCl_3$) δ: 1.71—2.67 (6H, m, $O=C(CH_2)_3-$), 4.17 (1H, d, J=15 Hz, $>NCHHPh$), 4.69 (1H, t, J=4 Hz, $>NCHSPh$), 5.71 (1H, d, J=15 Hz, $>NCHHPh$), 7.11—7.64 (10H, m, ArH). Exact MS Calcd for $C_{18}H_{19}NOS-SPh$: 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 $\nu_{max}^{CHCl_3}$ cm^{-1}: 1625. ^{1}H-NMR ($CDCl_3$) δ: 1.53—2.12 (6H, m, $O=CCH_2(CH_2)_3-$), 2.78 (1H, dd, J=14.7, 7.3 Hz, $O=CCHH-$), 3.20—3.26 (1H, m, $O=CCHH-$), 3.19 (1H, d, J=15.3 Hz, $>NCHHPh$), 4.83 (1H, dd, J=5.5, 3.1 Hz, $>NCHSPh$), 5.26 (1H, d, J=14.7 Hz, $>NCHHPh$), 7.07—7.50 (10H, m, ArH). Exact MS Calcd for $C_{19}H_{21}NOS-SPh$: 202.1233. Found: 202.1234.

References and Notes

1) Y. Kita, O. Tamura, T. Miki and Y. Tamura, *Tetrahedron Lett.*, **28**, 6479 (1987).
2) For a review, see: "Asymmetric Synthesis," J. D. Morrison ed., P. A. Bartlett, Vol. 3, Academic Press, Inc. Ltd., London, 1984, pp. 411—454.
3) M. B. Gase, J. J. Perie and A. Lattes, *Tetrahedron*, **34**, 1943 (1978); J. Ambuehl, P. S. Pregosin, L. M. Venanzi, G. Consiglio, F. Bachechi and L. Zambonelli, *J. Organomet. Chem.*, **181**, 255 (1979); Y. Saitoh, Y. Moriyama, T. Takahashi and Q. K-Huu, *Tetrahedron Lett.*, **21**, 75 (1980); S. Danishefsky, E. Taniyama and R. R. Webb II, *ibid.*, **24**, 11 (1983).
4) K. E. Harding and S. R. Burks, *J. Org. Chem.*, **49**, 40 (1984); S. Arseniyadis and J. Gore, *Tetrahedron Lett.*, **24**, 3997 (1983).
5) S. Danishefsky and E. Taniyama, *Tetrahedron Lett.*, **24**, 15 (1983).
6) J.-M. Surzur and L. Stella, *Bull. Soc. Chim. Fr.*, **1977**, 255; T. Aida, R. Leqault, D. Dugat and T. Durst, *Tetrahedron Lett.*, **1979**, 4993; A. J. Biloski, R. D. Wood and B. Ganem, *J. Am. Chem. Soc.*, **104**, 3233 (1982); Y. Tamaru, S. Kawamura, K. Tanaka and Z. Yoshida, *Tetrahedron Lett.*, **25**, 1063 (1984); G. Rajendra and M. J. Miller, *ibid.*, **26**, 5385 (1985); S. Knapp, K. E. Rodriques, A. T. Levorse and R. M. Ornaf, *ibid.*, **26**, 1803 (1985).
7) D. L. J. Clive, V. Farina, A. Singh, C. K. Wong, W. A. Kiel and S. M. Menchen, *J. Org. Chem.*, **45**, 2120 (1980); R. R. Webb II and S. Danishefsky, *Tetrahedron Lett.*, **24**, 1357 (1983); A. Toshimitsu, K. Terao and S. Uemura, *ibid.*, **25**, 5917 (1984); *idem*, *J. Org. Chem.*, **52**, 2018 (1987).
8) S. Pilard and M. Vaultier, *Tetrahedron Lett.*, **25**, 1555 (1984).
9) *a*) S. Oae and T. Numata, *Tetrahedron*, **30**, 2641 (1974); *b*) D. T. Connor and M. von Strandtmann, *J. Org. Chem.*, **39**, 1594 (1974); I. Nagakura, H. Oka and Y. Nitta, *Heterocycles*, **3**, 453 (1975); S. Wolfe, P. M. Kazmaier and H. Auksi, *Can. J. Chem.*, **57**, 2412 (1979).
10) S. Wolfe and P. M. Kazmaier, *Can. J. Chem.*, **57**, 2388, 2397 (1979).
11) M. Shimizu, T. Akiyama and T. Mukaiyama, *Chem. Lett.*, **1984**, 1531; T. Kaneko, *J. Am. Chem. Soc.*, **107**, 5490 (1985); T. Kaneko, Y. Okamoto and K. Hatada, *J. Chem. Soc., Chem. Commun.*, **1987**, 1511.
12) Y. Kita, H. Yasuda, O. Tamura, F. Itoh and Y. Tamura, *Tetrahedron Lett.*, **25**, 4681 (1984); Y. Kita, O. Tamura, H. Yasuda, F. Itoh and

Y. Tamura, *Chem. Pharm. Bull.*, **33**, 4235 (1985); Y. Kita, O. Tamura, F. Itoh, H. Yasuda, T. Miki and Y. Tamura, *ibid.*, **35**, 562 (1987).
13) Y. Kita, S. Akai, M. Yoshigi, Y. Nakajima, H. Yasuda and Y. Tamura, *Tetrahedron Lett.*, **25**, 6027 (1984); Y. Kita, S. Akai, N. Ajimura, M. Yoshigi, T. Tsugoshi, H. Yasuda and Y. Tamura, *J. Org. Chem.*, **51**, 4150 (1986); Y. Kita, S. Akai, M. Yamamoto, M. Taniguchi and Y. Tamura, *Synthesis*, **1989**, 334.
14) S. Knapp and A. T. Levorse, *J. Org. Chem.*, **53**, 4006 (1988).
15) D. A. Burnett, J.-K. Choi, D. J. Hart and Y.-M. Tsai, *J. Am. Chem. Soc.*, **106**, 8201 (1984); S. Kano, Y. Yuasa, K. Asami and S. Shibuya, *Chem. Lett.*, **1986**, 735; T. Kametani, H. Yukawa and T. Honda, *J. Chem. Soc., Chem. Commun.*, **1986**, 651.
16) C. Ainsworth, F. Chen and Y.-N. Kuo, *J. Organometal. Chem.*, **46**, 59 (1972); M. W. Rathke and D. F. Sullivan, *Synth. Commun.*, **3**, 67 (1973); Y. Kita, J. Haruta, T. Fujii, J. Segawa and Y. Tamura, *Synthesis*, **1981**, 451.
17) Y. Kita, J. Segawa, J. Haruta, H. Yasuda and Y. Tamura, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1099.