A New Synthesis of α-Amino Acid Thioesters by Pummerer Reaction of 3-Substituted-4-sulfinyl-β-sultams

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α-Amino acid thioesters were synthesized by the Pummerer reaction of 3-substituted-4-sulfinyl-β-sultams with TFAA. The 3-substituted-4-sulfinyl-β-sultams were prepared from the corresponding β-sultams by sulfenylation with diphenyl disulfide followed by *m*-CPBA oxidation. Diastereoselective synthesis of β-sultams by 1,3-asymmetric induction in [2 + 2] cycloaddition of a sulfene intermediate and chiral imines in solution-phase was studied, and it was found that *N*-alkylimines gave better diastereoselectivities than *N*-aralkylimines. The use of imines derived from (*R*)- and (*S*)-α-methylbenzylamine followed by separation of the major and minor diastereomers gave enantiopure 3-substituted-*N*-methylbenzyl-β-sultams. These β-sultams were then converted to *N*-methylbenzyl-α-amino acid thioesters via sulfenylation and Pummerer rearrangement with high or complete retention of configuration.

Introduction

β-Sultams, sulfonyl analogues of β-lactams, are unique four-membered heterocycles containing three different hetero single bonds, namely, C−N, C−S, and N−S. Stabilization of the β-sultam ring by π-bond overlap between the nitrogen lone-pair electrons and the sulfonyl group is much less than comparable stabilization of the β-lactam ring.[1] In addition, β-sultams are destabilized by the increased distortion of the β-sultam ring due to the C−S and N−S bonds which are longer than the corresponding C−C and C−N bonds of the β-lactam ring. Therefore, β-sultams have been widely investigated from both chemical and pharmacological points of view.[2] In previous papers we described the hetero bond cleavage of the β-sultam ring.[3] If the Pummerer reaction of 3-substituted-4-sulfinyl-β-sultams proceeds successfully, it would become the new method for the C−S bond cleavage of β-sultams and can be utilized for the synthesis of α-amino acid thioesters. α-Amino acid thioesters are activated esters[4] utilized for peptide synthesis[5] as well as natural product synthesis as versatile intermediates.[6] We intended to apply this method to the synthesis of optically active α-amino acid thioesters[7] and examined 1,3-asymmetric induction in [2 + 2] cycloaddition of chiral imines and a sulfene intermediate. Synthesis of β-sultams using the [2 + 2] cycloaddition of imines and sulfenes has been given scant attention[2] since it was first reported by Tsuge and Iwanami.[8] Recently, Gordeev and co-workers reported the first examples of diastereoselective solid-phase synthesis of β-sultams using chiral imines and activated sulfenes.[9] In this paper, we report the synthesis of α-amino acid thioesters by the Pummerer reaction of 3-substituted-4-sulfinyl-β-sultams and a preliminary study on diastereoselective synthesis of β-sultams in solution-phase.

Results and Discussion

3-Substituted-4-sulfinyl-β-sultams **4A**,**B** were synthesized as shown in Scheme 1 (Table 1). β-Sultams

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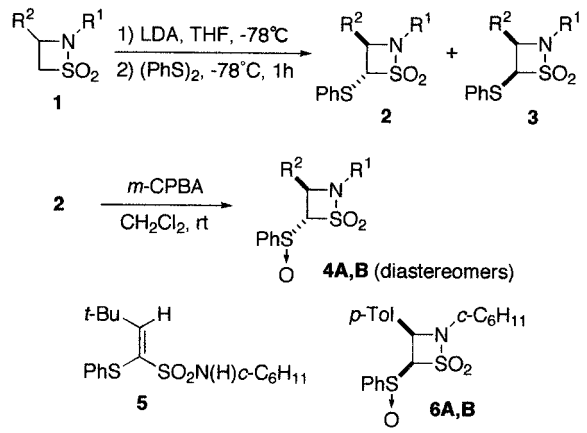
Scheme 1



prepared by [2 + 2] cycloaddition of a sulfene and imines[3c,d,8] were treated with 3 equiv of LDA at −78 °C in THF followed by 1 equiv of diphenyl disulfide at −78 °C for 1 h to give 3,4-*trans*-4-sulfenyl-*β*-sultams **2** as major products accompanied by 3,4-*cis*-isomers **3**.[10] The *cis*-isomers **3** were obtained as inseparable mixtures with the starting materials **1** except for **3e**.[10] The use of 1 equiv of LDA generates a mixture of monoanion and dianion of the *β*-sultams which makes reactions complicated,[11] and an excess amount of LDA is required for formation of the sole dianion and for clean reactions. It is necessary to quench reactions at −78 °C; for example, when the reaction of **1f** was quenched at room temperature instead of at −78 °C, a ring-opened product **5** was obtained in 67% yield as a major product together with a trace amount of **2f** (entry 7). Treatment of 3,4-*trans*-4-sulfenyl-*β*-sultams **2** with *m*-CPBA in CH_2Cl_2 provided 3,4-*trans*-4-sulfinyl-*β*-sultams **4A**,**B** as mixtures of stereoisomers at the sulfoxide moiety. Oxidation of 3,4-*cis*-isomer **3d** containing **1d** with *m*-CPBA gave a mixture of four diastereomers, 3,4-*trans*-4-sulfinyl-*β*-sultams **4dA**,**dB** and 3,4-*cis*-4-sulfinyl-*β*-sultams **6A**,**B**, due to isomerization of the latter to the former.[12]

The Pummerer reaction of 3,4-*trans*-4-sulfinyl-*β*-sultams **4A**,**B** with TFAA was examined (Scheme 2, Table 2). Treatment of **4aA** with 1 equiv of TFAA in CH_2Cl_2 at room temperature for 12 h resulted in the recovery of the sulfoxide (entry 1).[13] A reaction of **4aA** with 2 equiv of TFAA for 24 h gave an α-amino acid thioester **7a** and its amido derivative **8a** in low yields (entry 2).[13] Thioesters **7** were obtained in good yields accompanied with amides **8** except for **8c**,**f** regardless of the configuration of the sulfoxide by the use of 4 equiv of TFAA. In the cases of **4c**,**f**, steric hindrance of the *tert*-butyl group prevented amidation of **7** with excess TFAA. Treatment of a mixture of the four diastereomers **6A**,**B** and **4dA**,**B** also provided **7d** and **8d** in 63% and 15% yields, respectively (entry 11). In all cases, a trace amount of diphenyl disulfide was isolated.

A proposed mechanism is shown in Scheme 3. The alcohol **10** is produced by hydrolysis of a Pummerer product **9** formed from **4** and TFAA. Water during workup may cause the hydrolysis. The amide anion **11** is generated by the ring destruction of **10** with the C−S (C−SO_2) bond cleavage followed by elimination of sulfur dioxide to give thioester **7**. A small amount of **8** would be obtained by amidation of **11** with excess TFAA. Diphenyl disulfide is probably obtained by the C−S (C−SPh) bond cleavage with the formation of a *β*-sultam-4-one **12** although we could not isolate **12**.

Thioesters are activated compounds of carboxylic acids, and α-amino acid thioesters have been utilized for peptide synthesis[5] as well as natural product synthesis as versatile intermediates.[6] Therefore, enantioselective synthesis of α-amino acid thioesters is necessary. 1,3-Asymmetric induction was examined in [2 + 2] cycloaddition of a sulfene intermediate and chiral imines **13**, prepared from the corresponding chiral amines and aldehydes (Scheme 4, Table 3). The use of *N*-aralkylimines showed moderate diastereoselectivity (entries 1−5), and that of *N*-alkylimines showed good diastereoselectivity (entries 6−8). The best selectivity was given in the case of *N*-(1-*tert*-butylethyl)imine (entry 8). The diastereoselectivity would be dependent on the size and conformation of the *N*-substituents in the imines. Reactions of imines bearing an ether group resulted in the formation of a complex mixture (entries 9 and 10). Diastereomers of compounds **14a**−**e** bearing an *N*-aralkyl group were separable by silica gel column chromatography.

The stereochemistry of the major isomers was determined by X-ray crystallographic analysis of **14h** as a representative (see Supporting Information). The relative configuration is *syn*-form as drawn in Scheme 5. The stereoselectivity in the 1,3-asymmetric induction is explained as follows: a sulfene intermediate, generated from mesyl chloride and an imine, reacts with another imine **15**, which is the most stable conformer by $A^{1,3}$ strain,[14] from the opposite face to the bulky *tert*-butyl group to form a *syn*-isomer. Contribution of a less stable conformer **16** to the formation of an *anti*-isomer would be negligible. The stereochemistry of the major of **14a**,**b** is deduced to be syn from this mechanism.

We applied this thioester synthesis to chiral *β*-sultams prepared by 1,3-asymmetric induction described above (Scheme 6). Sulfoxides **19** and **23** were prepared by sulfenylation of **14** followed by *m*-CPBA oxidation of *trans*-isomers **17** and **21**, respectively. The sulfoxides **19A**,**B** and **23A**,**B** were obtained as two separable stereoisomers at sulfoxide group (alphabets **A** and **B** mean stereoisomers at sulfoxide moiety). Treatment of **19** and **23** with 4 equiv of TFAA gave chiral α-amino acid thioesters **20** and **24**, respectively, in high yields. Slight epimerization of the α-chiral center of α-phenyl thioesters **20a** and **24a** was observed under the reaction conditions, and the diastereomeric excess was >90%, determined by the ^{1}H NMR spectra.[15] No epimerization was observed

(10) The stereochemistry was determined from the coupling constants between 3- and 4-protons. In general, *cis*-isomers show greater coupling constants by 1.5−2.0 Hz than *trans*-isomers.[2a,d] For example, the ^{1}H NMR spectrum of **2b** showed a couple of doublets at δ 3.86 and 4.69 (owing to 3- and 4-protons) with J = 6.8 Hz, and a couple of doublets at δ 4.69 and 5.65, with J = 8.3 Hz assignable to 3- and 4-protons of **3b**, were observed in the ^{1}H NMR spectrum of a mixture of **3b** and **1b**. The *cis*-isomers **3** can be converted to the *trans*-isomers **2** by treatment with LDA in THF at −78 °C.

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(12) 3,4-*cis*-4-Sulfinyl-*β*-sultams **6A**,**B** gradually isomerized to *trans*-isomers **4dA**,**dB** during purification with silica gel column chromatography. The ^{1}H NMR spectrum of the mixture showed four couples of doublets at δ 4.44 and 5.37 with J = 8.3 Hz, δ 4.92 and 5.23 with J = 7.8 Hz (**6A**,**B**), δ 4.70 and 4.91 with J = 4.9 Hz, and δ 4.24 and 4.85 with J = 5.4 Hz (**4dA**,**dB**) owing to 3- and 4-protons. No *trans*-isomers **4A**,**B** isomerized to *cis*-isomers with silica gel column chromatography.

(13) The ^{1}H NMR spectrum of the recovered sulfoxide showed isomerization of the sulfoxide moiety. Two sets of doublet assigned to 3- and 4-protons of **4aA** and **4aB** were observed in the spectrum.

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Table 1. Synthesis of 3-Substituted-4-sulfinyl-*β*-sultams

entry	**1**	R^1	R^2	**2** and **3** (%yield)[a]	**4**[b] (%yield)[a]
1	**1a**	*c*-C_6H_{11}	Ph	**2a** (72) **3a** (trace)[c]	**4aA** (58), **4aB** (16)
2	**1b**	*n*-Bu	Ph	**2b** (57) **3b** (12)[c]	**4bA** (49), **4bB** (47)
3	**1c**	*t*-Bu	Ph	**2c** (67) **3c** (7)[c]	**4cA** (75), **4cB** (20)
4	**1d**	*c*-C_6H_{11}	*p*-tolyl	**2d** (66) **3d** (18)[c]	**4dA** (53), **4dB** (20)
5	**1e**	*c*-C_6H_{11}	*o*-tolyl	**2e** (72) **3e** (18)	**4eA** (64), **4eB** (33)
6	**1f**	*c*-C_6H_{11}	*t*-Bu	**2f** (92)	**4fA** (54), **4fB** (38)
7[d]	**1f**	*c*-C_6H_{11}	*t*-Bu	**2f** (t),[e] **5** (67)	

[a] Isolated yield unless otherwise mentioned. [b] A,B: Diastereomers at sulfoxide moiety. [c] The compound was obtained as an inseparable mixture with the starting material. The yield was estimated by the ^{1}H NMR spectrum. [d] The reaction was quenched at rt. [e] t: Trace.

Scheme 2

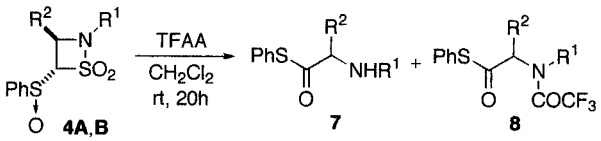


Table 2. The Pummerer Reaction of 3-Substituted-4-sulfinyl-*β*-sultams

entry	**4**	R^1	R^2	TFAA (equiv)	Products[a] (%yield)[b]
1[c]	**4aA**	*c*-C_6H_{11}	Ph	1.0	recovery[d]
2[e]	**4aA**			2.0	**7a**, **8a** (low yield)[f]
3	**4aA**			4.0	**7a** (72), **8a** (13)
4	**4aB**			4.0	**7a** (79), **8a** (14)
5	**4bA**	*n*-Bu	Ph	4.0	**7b** (74), **8b** (10)
6	**4bB**			4.0	**7b** (73), **8b** (9)
7	**4cA**	*t*-Bu	Ph	4.0	**7c** (93)
8	**4cB**			4.0	**7c** (97)
9	**4dA**	*c*-C_6H_{11}	*p*-tolyl	4.0	**7d** (73), **8d** (9)
10	**4dB**			4.0	**7d** (79), **8d** (8)
11	**4d**,**6**[g]			4.0	**7d** (63), **8d** (15)
12	**4eA**	*c*-C_6H_{11}	*o*-tolyl	4.0	**7e** (71), **8e** (10)
13	**4eB**			4.0	**7e** (73), **8e** (7)
14	**4fA**	*c*-C_6H_{11}	*t*-Bu	4.0	**7f** (81)
15	**4fB**			4.0	**7f** (82)

[a] A trace amount of $(PhS)_2$ was isolated in all cases. [b] Isolated yield. [c] Reaction time: 12 h. [d] Isomerization of the sulfoxide moiety was observed. [e] Reaction time: 24 h. [f] Yields of **7a** and **8a** were not calculated. A considerable amount of the starting material was recovered. Isomerization of the sulfoxide moiety was observed. [g] Mixture of 3,4-*cis*- **6A**,**B** and 3,4-*trans*-*β*-sultams **4dA**,**B** was used.

in the ^{1}H NMR spectra in the cases of α-*tert*-butyl thioesters **20b** and **24b**.

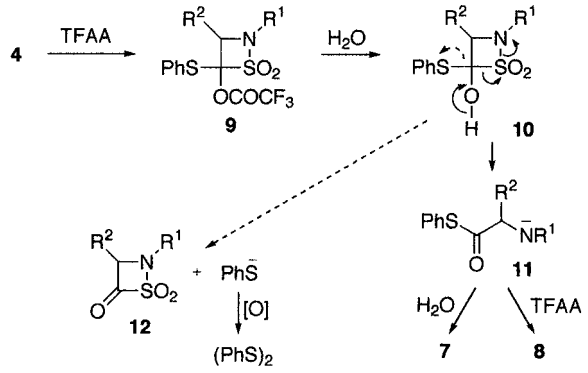
Experimental Section

General Methods. Melting points are uncorrected. IR spectra were recorded by KBr (solids) and NaCl (liquids) methods. ^{1}H NMR spectra were recorded in a $CDCl_3$ solution with tetramethylsilane as an internal standard. ^{13}C NMR spectra were obtained with $CDCl_3$ (77.0 ppm) as an internal standard. Mass spectra were recorded with a direct-insertion probe at 70 eV. All chromatographic isolations were accomplished with either Kieselgel 60 (Merck) or BW-127ZH (Fuji Silysia) for column chromatography or Kieselgel 60 PF_{254} containing gypsum (Merck) for preparative TLC.

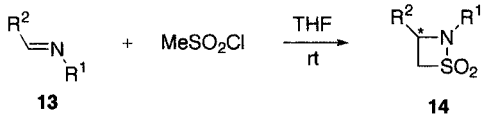
Synthesis of *β*-Sultams 1 and 14 by [2 + 2] Cycloaddition. *β*-Sultams **1** and **14** were synthesized according to the literature.[3d,e]

(15) In prolonged reaction or prolonged workup, the diastereomeric excess decreased to ca. 75% in the worst case. Rapid workup and purification are necessary to minimize epimerization.

Scheme 3



Scheme 4



2-*n*-Butyl-3-phenyl-1,2-thiazetidine 1,1-dioxide (1b): colorless prisms (from CH_2Cl_2−hexane), mp 66−68 °C; ^{1}H NMR ($CDCl_3$) *δ*: 0.84 (3 H, t, *J* = 7.3 Hz), 1.29−1.41 and 1.43−1.59 (each 2 H, m), 2.81 (1 H, ddd, *J* = 6.8, 8.3, and 13 Hz), 3.22 (1 H, ddd, *J* = 5.9, 7.8, and 13 Hz), 3.95 (1 H, dd, *J* = 6 and 12.2 Hz), 4.21 (1 H, dd, *J* = 6 and 7 Hz), 4.37 (1 H, dd, *J* = 7 and 12 Hz), 7.35−7.43 (3 H, m), 7.49 (2 H, dd, *J* = 2 and 8 Hz); ^{13}C NMR ($CDCl_3$) *δ*: 13.5, 20.2, 30.1, 45.9, 51.1, 65.9, 126.7, 129.1, 129.1, 137.4; MS (FAB) *m*/*z* (rel int %): 240 (100, $M^+ + 1$); IR ν_{max} (KBr) cm^{-1}: 1305, 1135 (SO_2). Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.05; H, 7.14; N, 5.78.

(3*R*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (*syn*-14a): colorless prisms (from CH_2Cl_2−hexane), mp 131−133 °C; ^{1}H NMR ($CDCl_3$) *δ*: 1.60 (3 H, d, *J* = 7 Hz), 3.93−4.00 (2 H, m), 4.29−4.36 (1 H, m), 4.48 (1 H, q, *J* = 7 Hz), 6.97−7.15 (10 H, m); ^{13}C NMR ($CDCl_3$) *δ*: 21.7, 50.3, 58.9, 65.6, 126.8, 128.0, 128.2, 128.2, 128.4, 137.6, 138.1, an aromatic carbon is overlapped; MS (FAB) *m*/*z* (rel int %): 288 (100, $M^+ + 1$); IR ν_{max} (KBr) cm^{-1}: 1325, 1140 (SO_2). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.65; H, 5.98; N, 4.87.

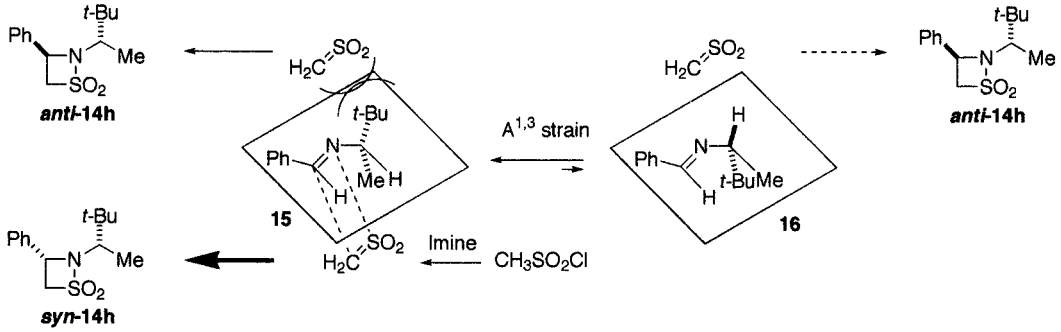
(3*S*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (*anti*-14a): colorless prisms (from EtOAc−hexane), mp 105−108 °C; ^{1}H NMR ($CDCl_3$) *δ*: 1.49 (3 H, d, *J* = 6.8 Hz), 3.94 (1 H, dd, *J* = 5 and 12.2 Hz), 4.26 (1 H, dd, *J* = 5 and 7.8 Hz), 4.30 (1 H, q, *J* = 6.8 Hz), 4.39 (1 H, dd, *J* = 7.8 and 12.2 Hz), 7.24−7.44 (10 H, m); ^{13}C NMR ($CDCl_3$) *δ*: 20.9, 49.1, 57.4, 65.8, 126.9, 127.3, 128.0, 128.6, 128.9, 129.0, 137.8, 140.2; MS (FAB) *m*/*z* (rel int %): 288 (67, $M^+ + 1$), 105 (100); IR ν_{max} (KBr) cm^{-1}: 1315, 1145 (SO_2). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.71; H, 5.94; N, 4.94.

Table 3. 1,3-Asymmetric Induction in the [2 + 2] Cycloaddition of a Sulfene Intermediate and Chiral Imines[a]

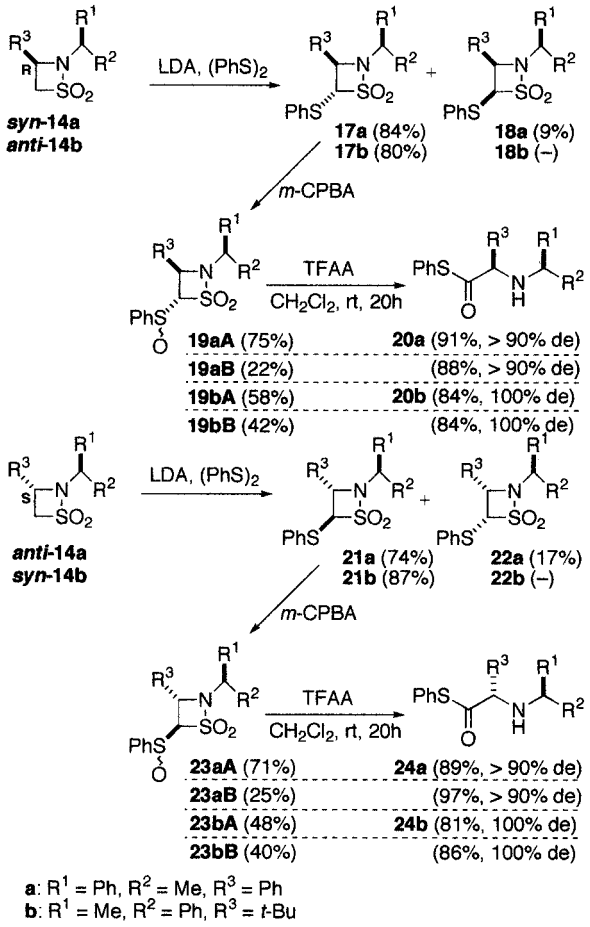
entry	R^1	R^2	**14** (%Yield)[b]
1	(*R*)-α-methylbenzyl	Ph	**14a**, (70, 42% de)[c]
2	(*S*)-α-methylbenzyl	*t*-Bu	**14b**, (32, 45% de)[c]
3	(*R*)-α,4-dimethylbenzyl	Ph	**14c**, (72, 44% de)[c]
4	rac-1-(1-naphthyl)ethyl	Ph	**14d**, (53, 47% de)[c]
5	rac-1-indanyl	Ph	**14e**, (36, 50% de)[c]
6	rac-1-cyclohexylethyl	Ph	**14f**, (60, 67% de)[d]
7	(1*R*,2*R*,3*R*,5*S*)-isopinocampheyl	Ph	**14 g**, (54, 80% de)[d]
8	rac-1-*tert*-butylethyl	Ph	**14h**, (67, >95% de)[d]
9	rac-1-(methoxymethyl)propyl	Ph	complex mixture
10	(*R*)-2-(methoxymethyl)pyrrolidinyl	Ph	complex mixture

[a] 2 equiv of imines were used based on MsCl. [b] Isolated yield based on MsCl. Diastereomeric exsess was calculated by the ^{1}H NMR spectrum of the reaction mixture. [c] Separable stereoisomers. [d] Inseparable stereoisomers.

Scheme 5



Scheme 6



a: R^1 = Ph, R^2 = Me, R^3 = Ph
b: R^1 = Me, R^2 = Ph, R^3 = *t*-Bu

(3*S*,1′*S*)-3-*tert*-Butyl-2-(α-methylbenzyl)-1,2-thiazetidine 1,1-dioxide (*syn*-14b): colorless leaves (from EtOAc−hexane), mp 148−152 °C; ^{1}H NMR ($CDCl_3$) δ: 0.85 (9 H, s), 1.76 (3 H, d, J = 7 Hz), 3.27 (1 H, dd, J = 5.9 and 8.3 Hz), 3.76 (1 H, dd, J = 5.9 and 12.2 Hz), 3.94 (1 H, dd, J = 8.3 and 12.2 Hz), 4.50 (1 H, q, J = 7 Hz), 7.30 (1 H, t, J = 7.3 Hz), 7.37 (2 H, t, J = 7.3 Hz), 7.47 (2 H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ: 19.0, 25.8, 33.6, 55.5, 58.4, 58.7, 127.8, 127.9, 128.5, 140.2; MS (EI) *m*/*z* (rel int %): 267 (1, M^+), 105 (100); IR ν_{max} (KBr) cm^{-1}: 1315, 1150 (SO_2). Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.62; H, 8.06; N, 5.18.

(3*R*,1′*S*)-3-*tert*-Butyl-2-(α-methylbenzyl)-1,2-thiazetidine 1,1-dioxide (*anti*-14b): colorless leaves (from EtOAc−hexane), mp 105−109 °C; ^{1}H NMR ($CDCl_3$) δ: 0.87 (9 H, s), 1.81 (3 H, d, J = 7 Hz), 3.10 (1 H, dd, J = 5 and 8 Hz), 3.78 (1 H, dd, J = 5 and 12 Hz), 3.94 (1 H, dd, J = 8 and 12 Hz), 4.51 (1 H, q, J = 7 Hz), 7.30 (1 H, t, J = 7 Hz), 7.38 (2 H, t, J = 7 Hz), 7.49 (2 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ: 20.0, 25.9, 33.8, 53.0, 58.3, 58.8, 127.7, 127.7, 128.7, 140.4; MS (EI) *m*/*z* (rel int %): 267 (3, M^+), 105 (100); IR ν_{max} (KBr) cm^{-1}: 1295, 1145 (SO_2). Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.61; H, 8.04; N, 5.17.

(3*R,1′*R**)-2-(1-*tert*-Butylethyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (*syn*-14h):** colorless needles (from EtOAc−hexane), mp 148−151 °C; ^{1}H NMR ($CDCl_3$) δ: 0.99 (9 H, s), 1.35 (3 H, d, J = 6.8 Hz), 2.58 (1 H, q, J = 6.8 Hz), 3.91 (1 H, dd, J = 5.9 and 12 Hz), 4.31 (1 H, dd, J = 7.8 and 12 Hz), 4.39 (1 H, dd, J = 5.9 and 7.8 Hz), 7.37−7.43 (3 H, m), 7.49 (2 H, d, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 11.6, 27.6, 34.5, 48.4, 64.8, 65.3, 127.7, 129.3, 129.5, 137.7; MS (EI) *m*/*z* (rel int %): 267 (1, M^+), 210 (100); IR ν_{max} (KBr) cm^{-1}: 1305, 1140 (SO_2). Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.62; H, 7.90; N, 5.19.

Sulfenylation of *β*-Sultams 1 and 14. General Procedure. To a solution of LDA (3 mmol, prepared from 3 mmol of diisopropylamine (0.39 cm^3) and 3 mmol of ^{n}BuLi in hexane) in dry THF (10 cm^3) was added dropwise a solution of *β*-sultam **1** or **14** (1 mmol) in THF (2−4 cm^3) at −78 °C under argon. After 30 min, diphenyl disulfide (218 mg, 1 mmol) in THF (1−2 cm^3) was added dropwise to it, and the whole was stirred at −78 °C for 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (0.5 cm^3) at −78 °C, and the mixture was warmed to room temperature. Additional saturated aqueous NH_4Cl (5 cm^3) and water (5 cm^3) were added to it, and the organic layer was separated. The water layer was extracted twice with EtOAc (10 cm^3). The organic layer and the extracts were combined, washed with saturated aqueous NaCl (20 cm^3), dried ($MgSO_4$), and evaporated under reduced

pressure. The residue was purified by column chromatography on silica gel with EtOAc−hexane (1:20−1:10 v/v).

***trans*-2-Cyclohexyl-4-(phenylsulfenyl)-3-*p*-tolyl-1,2-thiazetidine 1,1-dioxide (2d):** colorless prisms (from EtOAc−hexane), mp 102−104 °C; ^{1}H NMR ($CDCl_3$) δ: 1.11−1.26 (4 H, m), 1.47−1.61 (4 H, m), 1.72 (1 H, br d, J = 13 Hz), 2.03 (1 H, br d, J = 12 Hz), 2.37 (3 H, s), 3.21 (1 H, m), 3.96 (1 H, d, J = 6.3 Hz), 4.97 (1 H, d, J = 6.3 Hz), 7.21 (2 H, d, J = 8 Hz), 7.26−7.31 (3 H, m), 7.38−7.41 (4 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.2, 24.2, 24.4, 25.3, 30.4, 31.9, 56.8, 57.5, 82.5, 126.5, 128.4, 129.4, 129.7, 131.6, 131.8, 134.1, 139.1; MS (FAB) *m*/*z* (rel int %): 388 (7, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1310, 1155 (SO_2). Anal. Calcd for $C_{21}H_{25}NO_2S_2$: C, 65.08; H, 6.50; N, 3.61. Found: C, 64.91; H, 6.57; N, 3.60.

***trans*-3-*tert*-Butyl-2-cyclohexyl-4-(phenylsulfenyl)-1,2-thiazetidine 1,1-dioxide (2f):** colorless prisms (from CH_2Cl_2−hexane), mp 106−108 °C; ^{1}H NMR ($CDCl_3$) δ: 1.05 (9 H, s), 1.02−1.25 (3 H, m), 1.58−1.87 (5 H, m), 1.98 (1 H, br d, J = 13 Hz), 2.22 (1 H, br d, J = 12 Hz), 3.01−3.09 (1 H, m), 3.10 (1 H, d, J = 5.9 Hz), 4.89 (1 H, d, J = 5.9 Hz), 7.30−7.38 (3 H, m), 7.50 (2 H, dd, J = 2 and 8 Hz); ^{13}C NMR ($CDCl_3$) δ: 25.2, 25.4, 26.2, 26.5, 28.6, 31.4, 34.6, 58.7, 59.1, 75.5, 128.5, 129.5, 132.0, 132.1; MS (FAB) *m*/*z* (rel int %): 354 (2, $M^+ + 1$), 290 (100); IR ν_{max} (KBr) cm^{-1}: 1305, 1165 (SO_2). Anal. Calcd for $C_{18}H_{27}NO_2S_2$: C, 61.15; H, 7.70; N, 3.96. Found: C, 60.97; H, 7.68; N, 3.87.

2-*tert*-Butyl-*N*-cyclohexyl-1-phenylsulfenylvinylsulfonamide (5): colorless prisms (from EtOAc−hexane), mp 104−110 °C; ^{1}H NMR ($CDCl_3$) δ: 1.11−1.33 (5 H, m), 1.27 (9 H, s), 1.53−1.58 (1 H, m), 1.66−1.71 (2 H, m), 1.81−1.84 (2 H, m), 3.03−3.07 (1 H, m), 4.43 (1 H, br d, J = 7.3 Hz), 7.15−7.33 (5 H, m), 7.62 (1 H, s); ^{13}C NMR ($CDCl_3$) δ: 24.9, 25.4, 29.9, 34.2, 35.6, 53.4, 126.5, 127.4, 129.3, 131.8, 135.4, 162.2; MS (EI) *m*/*z* (rel int %): 353 (27, M^+), 191(100); IR ν_{max} (KBr) cm^{-1}: 3270 (NH), 1320, 1155 (SO_2). Anal. Calcd for $C_{18}H_{27}NO_2S_2$: C, 61.15; H, 7.70; N, 3.96. Found: C, 61.09; H, 7.74; N, 3.99.

(3*R*,4*S*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-(phenylsulfenyl)-1,2-thiazetidine 1,1-dioxide (17a): colorless prisms (from CH_2Cl_2−hexane), mp 96−98 °C; ^{1}H NMR ($CDCl_3$) δ: 1.65 (3 H, d, J = 7 Hz), 3.62 (1 H, d, J = 6.8 Hz), 4.45 (1 H, q, J = 7 Hz), 5.07 (1 H, d, J = 6.8 Hz), 6.96−7.16 (10 H, m), 7.28−7.30 (3 H, m), 7.37−7.39 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.8, 58.2, 59.3, 82.4, 127.0, 128.1, 128.1, 128.3, 128.4, 128.5, 128.6, 129.5, 131.3, 132.1, 136.2, 137.2; MS (FAB) *m*/*z* (rel int %): 396 (2, $M^+ + 1$), 105 (100); IR ν_{max} (KBr) cm^{-1}: 1320, 1160 (SO_2). Anal. Calcd for $C_{22}H_{21}NO_2S_2$: C, 66.81; H, 5.35; N, 3.54. Found: C, 66.73; H, 5.39; N, 3.53.

(3*R*,4*R*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-(phenylsulfenyl)-1,2-thiazetidine 1,1-dioxide (18a): colorless needles (from CH_2Cl_2−hexane), mp 151−154 °C; ^{1}H NMR ($CDCl_3$) δ: 1.63 (3 H, d, J = 7 Hz), 4.45 (1 H, d, J = 9.2 Hz), 4.63 (1 H, q, J = 7 Hz), 5.60 (1 H, d, J = 9.2 Hz), 7.04−7.33 (15 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.3, 54.9, 57.9, 81.1, 128.0, 128.2, 128.4, 128.8, 129.4, 131.8, 132.1, 134.3, 137.7, three aromatic carbons are overlapped; MS (FAB) *m*/*z* (rel int %): 396 (3, $M^+ + 1$), 105 (100); IR ν_{max} (KBr) cm^{-1}: 1310, 1165 (SO_2). Anal. Calcd for $C_{22}H_{21}NO_2S_2$: C, 66.81; H, 5.35; N, 3.54. Found: C, 66.68; H, 5.50; N, 3.37.

(3*S*,4*R*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-(phenylsulfenyl)-1,2-thiazetidine 1,1-dioxide (21a): colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.49 (3 H, d, J = 7 Hz), 3.90 (1 H, d, J = 5.9 Hz), 4.31 (1 H, q, J = 7 Hz), 5.08 (1 H, d, J = 5.9 Hz), 7.24−7.44 (15 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.0, 57.1, 57.9, 82.7, 126.9, 127.3, 128.1, 128.7, 128.7, 129.2, 129.3, 129.5, 131.1, 132.4, 136.1, 139.8; MS (FAB) *m*/*z* (rel int %): 396 (2, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1320, 1165 (SO_2). Anal. Calcd for $C_{22}H_{21}NO_2S_2$: C, 66.81; H, 5.35; N, 3.54. Found: C, 66.64; H, 5.46; N, 3.36.

(3*S*,4*S*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-(phenylsulfenyl)-1,2-thiazetidine 1,1-dioxide (22a): colorless prisms (from CH_2Cl_2−hexane), mp 95−97 °C; ^{1}H NMR ($CDCl_3$) δ: 1.63 (3 H, d, J = 7 Hz), 4.38 (1 H, q, J = 7 Hz), 4.62 (1 H, d, J = 8.3 Hz), 5.64 (1 H, d, J = 8.3 Hz), 7.26−7.36 (10 H, m), 7.42 (5 H, s); ^{13}C NMR ($CDCl_3$) δ: 21.2, 54.6, 57.0, 81.0, 127.2, 128.1, 128.3, 128.5, 128.6, 128.7, 129.5, 131.8, 132.2, 133.5, 140.1, an aromatic carbon is overlapped; MS (FAB) *m*/*z* (rel int %): 396 (2, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1315, 1160 (SO_2). Anal. Calcd for $C_{22}H_{21}NO_2S_2$: C, 66.81; H, 5.35; N, 3.54. Found: C, 66.64; H, 5.46; N, 3.40.

Synthesis of 4-Sulfinyl-β-sultams 4, 19, and 23. General Procedure. To a solution of a 4-sulfenyl-β-sultam **2**, **17**, or **21** (0.5 mmol) in CH_2Cl_2 (10−20 cm^3) was added *m*CPBA (70−85% purity, 0.5 mmol) at 0 °C. After 1−3 h, saturated aqueous $NaHCO_3$ (10 cm^3) was added to it, and the organic layer was separated. The water layer was extracted once with CH_2Cl_2 (10 cm^3). The organic layer and the extracts were combined, washed with saturated aqueous NaCl (10 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc−hexane (1:10−1:3 v/v).

***trans*-2-Cyclohexyl-4-(phenylsulfinyl)-3-*p*-tolyl-1,2-thiazetidine 1,1-Dioxide (4d).** Major isomer **4dA**: colorless prisms (from EtOAc−hexane), mp 161−164 °C; ^{1}H NMR ($CDCl_3$) δ: 1.11−1.29 (4 H, m), 1.43−1.77 (5 H, m), 2.01 (1 H, br d, J = 12 Hz), 2.29 (3 H, s, Me), 3.31−3.37 (1 H, m), 4.70 (1 H, d, J = 4.9 Hz), 4.91 (1 H, d, J = 4.9 Hz), 7.05 (2 H, d, J = 7.8 Hz), 7.22 (2 H, d, J = 7.8 Hz), 7.48−4.79 (3 H, m), 7.67−6.69 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.1, 24.1, 24.3, 25.3, 30.4, 31.8, 48.5, 56.8, 92.5, 124.2, 126.6, 129.6, 129.7, 132.2, 134.3, 138.8, 140.4; MS (FAB) *m*/*z* (rel int %): 404 (12, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1320, 1165 (SO_2), 1055 (SO). Anal. Calcd for $C_{21}H_{25}NO_3S_2$: C, 62.50; H, 6.24; N, 3.47. Found: C, 62.30; H, 6.30; N, 3.30.

Minor isomer **4dB**: colorless prisms (from EtOAc−hexane), mp 146−151 °C; ^{1}H NMR ($CDCl_3$) δ: 1.06−1.27 (4 H, m), 1.39−1.69 (5 H, m), 1.96 (1 H, br d, J = 12 Hz), 2.30 (3 H, s), 3.25−3.30 (1 H, m), 4.24 (1 H, d, J = 5.4 Hz), 4.85 (1 H, d, J = 5.4 Hz), 7.01−7.03 (4 H, m), 7.48−4.57 (3 H, m), 7.73 (2 H, dd, J = 1.5 and 8 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.1, 23.9, 24.1, 25.2, 30.2, 31.7, 50.7, 56.9, 93.2, 125.6, 126.3, 129.6, 129.7, 132.8, 133.4, 139.0, 139.0; MS (FAB) *m*/*z* (rel int %): 404 (16, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1320, 1165 (SO_2), 1060 (SO). Anal. Calcd for $C_{21}H_{25}NO_3S_2$: C, 62.50; H, 6.24; N, 3.47. Found: C, 62.27; H, 6.27; N, 3.32.

***trans*-3-*tert*-Butyl-2-cyclohexyl-4-(phenylsulfinyl)-1,2-thiazetidine 1,1-Dioxide (4f).** Major isomer **4fA**: colorless needles (from CH_2Cl_2−hexane), mp 187−191 °C; ^{1}H NMR ($CDCl_3$) δ: 0.85 (9 H, s), 1.19−1.26 (3 H, m), 1.62−1.85 (5 H, m), 2.18 (2 H, br d, J = 12 Hz), 3.13−3.20 (1 H, m), 3.87 (1 H, d, J = 3.9 Hz), 4.59 (1 H, d, J = 3.9 Hz), 7.56−7.60 (3 H, m), 7.74−7.76 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 25.3, 25.4, 26.1, 26.3, 29.9, 31.4, 33.9, 55.0, 59.2, 88.2, 124.4, 129.7, 132.1, 141.3; MS (FAB) *m*/*z* (rel int %): 370 (25, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1310, 1160 (SO_2), 1055 (SO). Anal. Calcd for $C_{18}H_{27}NO_3S_2$: C, 58.50; H, 7.36; N, 3.79. Found: C, 58.21; H, 7.41; N, 3.71.

Minor isomer **4fB**: colorless needles (from CH_2Cl_2−hexane), mp 185−187 °C; ^{1}H NMR ($CDCl_3$) δ: 0.96 (9 H, s), 1.13−1.23 (3 H, m), 1.64−1.82 (5 H, m), 2.00 (1 H, br d, J = 13 Hz), 2.13 (1 H, br d, J = 12 Hz), 3.05−3.11 (1 H, m), 3.59 (1 H, d, J = 4.9 Hz), 4.68 (1 H, d, J = 4.9 Hz), 7.58−7.59 (3 H, m), 7.79−7.82 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 25.3, 25.4, 26.1, 26.2, 29.4, 31.4, 34.4, 54.6, 59.3, 86.0, 125.5, 129.6, 132.4, 139.2; MS (FAB) *m*/*z* (rel int %): 370 (34, $M^+ + 1$), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1315, 1175 (SO_2), 1055 (SO). Anal. Calcd for $C_{18}H_{27}NO_3S_2$: C, 58.50; H, 7.36; N, 3.79. Found: C, 58.22; H, 7.36; N, 3.65.

(3*R*,4*S*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-phenylsulfinyl-1,2-thiazetidine 1,1-Dioxide (19a). Major isomer **19aA**: colorless prisms (from CH_2Cl_2−hexane), mp 139−141 °C; ^{1}H NMR ($CDCl_3$) δ: 1.62 (3 H, d, J = 6.3 Hz), 4.57 (1 H, d, J = 5 Hz), 4.61 (1 H, q, J = 6.3 Hz), 4.78 (1 H, d, J = 5 Hz), 6.94 (2 H, d, J = 7 Hz), 7.01−7.08 (6 H, m), 7.12 (2 H, d, J = 7 Hz), 7.39−7.40 (3 H, m), 7.57−7.60 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.9, 49.2, 58.8, 92.5, 124.1, 126.9, 128.2, 128.3, 128.3, 129.6, 132.1, 137.0, 137.3, 140.0, two aromatic carbons are overlapped; MS (FAB) *m*/*z* (rel int %): 412 (13, $M^+ + 1$), 125 (100); IR ν_{max} (KBr) cm^{-1}: 1330, 1165 (SO_2), 1045 (SO).

Anal. Calcd for $C_{22}H_{21}NO_3S_2$: C, 64.21; H, 5.14; N, 3.40. Found: C, 64.11; H, 5.17; N, 3.40.

Minor isomer **19aB**: colorless prisms (from CH_2Cl_2−hexane), mp 199−202 °C; ^{1}H NMR ($CDCl_3$) δ: 1.59 (3 H, d, J = 6.8 Hz), 3.88 (1 H, d, J = 6 Hz), 4.54 (1 H, q, J = 6.8 Hz), 4.94 (1 H, d, J = 6 Hz), 6.74 (2 H, d, J = 7 Hz), 6.95−7.08 (8 H, m), 7.40−7.48 (3 H, m), 7.65 (2 H, dd, J = 1 and 8 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.9, 52.2, 59.1, 93.2, 125.4, 126.7, 128.1, 128.3, 128.3, 128.4, 129.7, 132.8, 135.8, 137.0, 138.9, an aromatic carbon is overlapped; MS (FAB) m/z (rel int %): 412 (39, M^+ + 1), 125 (100); IR ν_{max} (KBr) cm^{-1}: 1300, 1165 (SO_2), 1060 (SO). Anal. Calcd for $C_{22}H_{21}NO_3S_2$: C, 64.21; H, 5.14; N, 3.40. Found: C, 63.94; H, 5.17; N, 3.38.

(3*S*,4*R*,1′*R*)-2-(α-Methylbenzyl)-3-phenyl-4-(phenylsulfinyl)-1,2-thiazetidine 1,1-Dioxide (23a). Major isomer **23aA**: white powder (from EtOAc−hexane), mp 160−162 °C; ^{1}H NMR ($CDCl_3$) δ: 1.53 (3 H, d, J = 6.8 Hz), 4.41 (1 H, q, J = 6.8 Hz), 4.80 and 4.82 (each 1 H, d, J = 4 Hz), 7.25−7.34 (10 H, m), 7.46−7.48 (3 H, m), 7.66−7.68 (2 H, m); ^{13}C NMR ($CDCl_3$) δ: 21.4, 49.1, 57.5, 92.8, 124.2, 125.7, 127.0, 127.1, 128.2, 128.8, 129.0, 129.7, 132.2, 136.0, 139.8, 140.3; MS (FAB) m/z (rel int %): 412 (23, M^+ + 1), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1315, 1165 (SO_2), 1045 (SO). Anal. Calcd for $C_{22}H_{21}NO_3S_2$: C, 64.21; H, 5.14; N, 3.40. Found: C, 63.94; H, 5.24; N, 3.26.

Minor isomer **23aB**: white powder (from EtOAc−hexane), mp 158−161 °C; ^{1}H NMR ($CDCl_3$) δ: 1.48 (3 H, d, J = 6.8 Hz), 4.17 (1 H, d, J = 4.9 Hz), 4.31 (1 H, q, J = 6.8 Hz), 4.93 (1 H, d, J = 4.9 Hz), 7.09 (2 H, d, J = 7 Hz), 7.20−7.30 (8 H, m), 7.47−7.55 (3 H, m), 7.70 (2 H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.2, 51.5, 57.7, 93.3, 125.6, 126.8, 127.1, 128.2, 128.7, 129.1, 129.3, 129.7, 132.7, 135.3, 139.0, 139.6; MS (FAB) m/z (rel int %): 412 (21, M^+ + 1), 154 (100); IR ν_{max} (KBr) cm^{-1}: 1335, 1170 (SO_2), 1050 (SO). Anal. Calcd for $C_{22}H_{21}NO_3S_2$: C, 64.21; H, 5.14; N, 3.40. Found: C, 64.08; H, 5.21; N, 3.22.

The Pummerer Reaction of 4-Sulfinyl-β-sultams 4, 19, and 23. General Procedure. To a solution of a 4-sulfinyl-β-sultam **4**, **19**, or **23** (0.2 mmol) in CH_2Cl_2 (1 cm^3) was added TFAA (113 μdm^3, 0.8 mmol) at room temperature. After 20 h, CH_2Cl_2 (6 cm^3) and 1% aqueous NH_3 (6 cm^3) were added to the reaction mixture, and the organic layer was separated. The water layer was extracted once with CH_2Cl_2 (10 cm^3). The organic layer and the extracts were combined, washed with saturated aqueous NaCl (10 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by preparative TLC with EtOAc−hexane (1:10−1:5 v/v).

***S*-Phenyl 2-(cyclohexylamino)-*p*-tolylthioacetate (7d):** colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.11−1.25 (5H, m), 1.62−1.70 (4 H, m), 1.96 (2 H, m), 2.34 (3 H, s), 2.54 (1 H, m), 4.63 (1 H, s), 7.17 (2 H, d, J = 8.3 Hz), 7.32 (2 H, d, J = 8.3 Hz), 7.35 (5 H, s); ^{13}C NMR ($CDCl_3$) δ: 21.1, 24.9, 25.0, 26.0, 33.4, 33.6, 55.2, 69.7, 127.5, 128.7, 129.0, 129.5, 134.4, 135.6, 138.0, 201.4, an aromatic carbon is overlapped; MS (FAB) m/z (rel int %): 340 (26, M^+ + 1), 154 (100); IR ν_{max} (NaCl) cm^{-1}: 3340 (NH), 1690 (CO). Anal. Calcd for $C_{21}H_{25}NOS$: C, 74.30; H, 7.42; N, 4.13. Found: C, 74.27; H, 7.50; N, 4.09.

***S*-Phenyl 2-(*N*-cyclohexyltrifluoroacetamido)-*p*-tolylthioacetate (8d):** colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.06−1.09 (1 H, m), 1.24−1.43 (3 H, m), 1.56−1.75 (4 H, m), 1.89 (1 H, br d, J = 13 Hz), 2.10 (1 H, br d, J = 12 Hz), 2.39 (3 H, s), 3.92 (1 H, m), 4.94 (1 H, s), 7.21 (2 H, d, J = 7.8 Hz), 7.35−7.41 (7 H, m); MS (FAB) m/z (rel int %): 436 (19, M^+ + 1), 326 (100); IR ν_{max} (NaCl) cm^{-1}: 1685 (CO), 1205, 1140 (CF_3). Anal. Calcd for $C_{23}H_{24}F_3NO_2S$: C, 63.43; H, 5.55; N, 3.22. Found: C, 63.17; H, 5.72; N, 3.09.

***S*-Phenyl 2-(cyclohexylamino)-3,3-dimethylbutanethioate (7f):** white solid (from hexane), mp 40−42 °C; ^{1}H NMR ($CDCl_3$) δ: 1.03 (9 H, s), 1.00−1.31 (5 H, m), 1.51 (1 H, br s), 1.59−1.62 (1 H, m), 1.72−1.75 (2 H, m), 1.85 (1 H, br d, J = 12 Hz), 1.93 (1 H, br d, J = 12 Hz), 2.46−2.53 (1 H, m), 3.19 (1 H, s), 7.36−7.42 (5 H, m); ^{13}C NMR ($CDCl_3$) δ: 24.6, 25.0, 26.1, 27.2, 32.8, 34.4, 34.4, 55.6, 73.9, 129.0, 129.0, 129.4, 134.3, 203.5; MS (FAB) m/z (rel int %): 306 (21, M^+ + 1), 154 (100); IR ν_{max} (KBr) cm^{-1}: 3360 (NH), 1680 (CO). Anal. Calcd for $C_{18}H_{27}NOS$: C, 70.77; H, 8.91; N, 4.59. Found: C, 70.60; H, 8.91; N, 4.47.

(2*R*,1′*R*)-*S*-Phenyl 2-(α-methylbenzylamino)phenylthioacetate (20a): light yellow oil; ^{1}H NMR ($CDCl_3$) δ: 1.43 (3 H, d, J = 7 Hz), 2.22 (1 H, br s), 3.98 (1 H, q, J = 7 Hz), 4.35 (1 H, s), 7.27−7.35 (15 H, m); ^{13}C NMR ($CDCl_3$) δ: 24.4, 57.0, 70.1, 126.7, 127.3, 127.4, 128.2, 128.6, 128.8, 128.8, 129.0, 129.1, 134.4, 138.1, 144.4, 201.3; MS (FAB) m/z (rel int %): 348 (38, M^+ + 1), 105 (100); IR ν_{max} (NaCl) cm^{-1}: 3345 (NH), 1695 (CO). Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.05; H, 6.09; N, 4.03. Found: C, 76.12; H, 6.19; N, 4.03.

(2*R*,1′*S*)-*S*-Phenyl 2-(α-methylbenzylamino)-3,3-dimethylbutanethioate (20b): light yellow oil; ^{1}H NMR ($CDCl_3$) δ: 1.06 (9 H, s), 1.39 (3 H, d, J = 6.4 Hz), 1.98 (1 H, br s), 3.22 (1 H, s), 3.90 (1 H, q, J = 6.4 Hz), 7.23−7.40 (10 H, m); ^{13}C NMR ($CDCl_3$) δ: 22.5, 27.1, 34.9, 57.0, 74.3, 126.9, 127.1, 128.4, 128.6, 129.0, 129.1, 134.3, 145.8, 202.0; MS (FAB) m/z (rel int %): 328 (64, M^+ + 1), 190 (100); IR ν_{max} (KBr) cm^{-1}: 3340 (NH), 1695 (CO). Anal. Calcd for $C_{20}H_{25}NOS$: C, 73.35; H, 7.69; N, 4.28. Found: C, 73.45; H, 7.83; N, 4.25.

(2*S*,1′*R*)-*S*-Phenyl 2-(α-methylbenzylamino)phenylthioacetate (24a): light yellow oil; ^{1}H NMR ($CDCl_3$) δ: 1.38 (3 H, d, J = 7 Hz), 2.42 (1 H, br s), 3.70 (1 H, q, J = 7 Hz), 4.36 (1 H, s), 7.27−7.41 (15 H, m); ^{13}C NMR ($CDCl_3$) δ: 24.2, 55.2, 70.1, 127.0, 127.3, 128.0, 128.2, 128.4, 128.6, 128.8, 129.0, 129.2, 134.5, 137.8, 144.2, 199.3; MS (FAB) m/z (rel int %): 348 (51, M^+ + 1), 210 (100); IR ν_{max} (NaCl) cm^{-1}: 3340 (NH), 1700 (CO). Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.05; H, 6.09; N, 4.03. Found: C, 76.14; H, 6.16; N, 4.08.

(2*S*,1′*S*)-*S*-Phenyl 2-(α-methylbenzylamino)-3,3-dimethylbutanethioate (24b): light yellow oil; ^{1}H NMR ($CDCl_3$) δ: 0.97 (9 H, s), 1.35 (3 H, d, J = 6.4 Hz), 2.01 (1 H, br s), 2.91 (1 H, s), 3.88 (1 H, q, J = 6.4 Hz), 7.28 (1 H, t, J = 7 Hz), 7.34 (2 H, t, J = 7 Hz), 7.39 (2 H, d, J = 7 Hz), 7.42 (5 H, s); ^{13}C NMR ($CDCl_3$) δ: 25.3, 27.1, 34.3, 56.7, 74.0, 127.1, 127.2, 128.3, 128.6, 129.1, 129.2, 134.2, 144.8, 203.0; MS (FAB) m/z (rel int %): 328 (31, M^+ + 1), 190 (100); IR ν_{max} (KBr) cm^{-1}: 3345 (NH), 1695 (CO). Anal. Calcd for $C_{20}H_{25}NOS$: C, 73.35; H, 7.69; N, 4.28. Found: C, 73.35; H, 7.85; N, 4.26.

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Supporting Information Available: Spectra data (^{1}H NMR, ^{13}C NMR, IR, and MS) and assignment of ^{1}H NMR signals for **1b**, **1c**, **2**, **4**, **5**, **7**, **8**, **14**, **17**−**24** and X-ray crystallographic analysis data for **14h** (41 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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