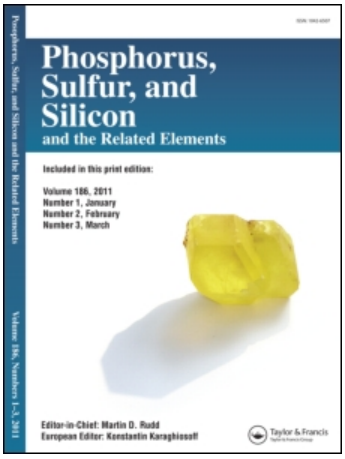

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New Chemical Aspects of ß -Sultams: Selective Hetero Bond Cleavage and Sequential Reactions

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The selective C-S bond cleavage of a β-sultam ring was achieved using $EtAlCl_2$ as a Lewis acid. Furthermore, treatment of 4-silyl-β -sultams with $EtAlCl_2$ effected the selective C-N bond cleavage which, followed by desilylation, afforded (*E*)-vinylsulfonamides stereospecifically. The Pummerer reaction of 4-sulfenyl- β -sultams produced α-amino acid thioesters, and the chiral α-amino acid thioesters were prepared from chiral imines and methanesulfonyl chloride.

Keywords: 1,2-thiazetidine; 1,1-dioxide; β -sultam; bond cleavage; 1,2-aryl migration; Lewis acid; α -amino acid thioester; Pummerer reaction

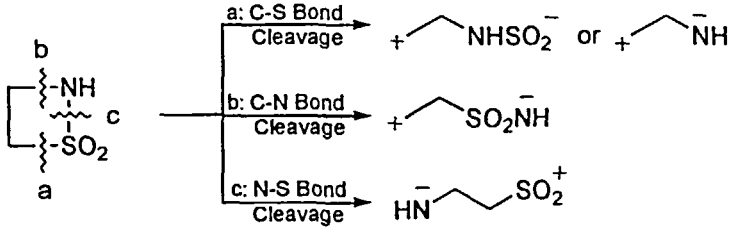
INTRODUCTION

1,2-Thiazetidine 1,1-dioxide, namely, β -sultam,[1] is a cyclic sulfonamide of β -aminoethanesulfonic acid, also called taurine. Taurine is the most abundant amino acid, but the functional role of taurine in the body is at present unknown. It may act as an inhibitory neuro-transmitter in the brain and as a membrane stabilizer linked to the Cl^- channel. β -Sultams are also regarded as the sulfonyl analog of β -lactams. A great number of β -lactams have been synthesized and their chemistry has

already been fully studied. However, very few papers on the β-sultams have been published. One main reason why the chemistry of β-sultams has not been developed is the fact that the β-sultam derivatives have not shown remarkable antibiotic activities.

β-Lactams are stabilized by the π-bond overlap between the lone pair electrons of the nitrogen atom and the carbonyl group, but in β-sultams, the degree of stabilization is much less. In addition, the distortion of the β-sultam ring is enhanced by the C-S and C-N bonds which are longer than the corresponding C-C and C-N bonds of the β-lactam ring.

The β-sultam ring comprises three different types of hetero single bonds, namely, the C-N, C-S and N-S bonds. If a hetero bond is selectively and heterolytically cleaved, β-sultams can be utilized as synthetic equivalents of 2-aminoethyl cations, 2-sulfamoylethyl cations or 2-aminoethanesulfonyl cations. In order to open up the new chemistry of β-sultams on the basis of this background, we focused our attention on the selective bond cleavage of the β-sultam ring and have been studying the selective hetero bond fission of β-sultams over the past five years.



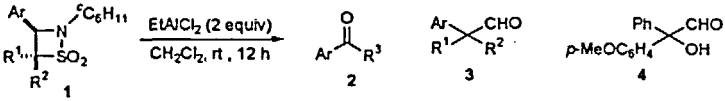
Scheme 1

CARBON-SULFUR BOND CLEAVAGE

We first investigated the selective C-S bond cleavage with a Lewis acid (Table 1).[2,3] The reactions of *cis*-3,4-diphenyl-β-sultam **1a** with

various Lewis acids were carried out, and $AlCl_3$ and $EtAlCl_2$ proved to be the best reagents for the selective C-S bond cleavage. $EtAlCl_2$ was used for the convenient handling of the small quantity required. Reaction using 2 equiv. of $EtAlCl_2$ gave benzophenone **2a** in higher yield than that using 1.1 equiv. of $EtAlCl_2$, and, therefore, other reactions were conducted with the use of 2.0 equiv. of $EtAlCl_2$. The C-S bond was selectively cleaved in spite of the *cis*- and *trans*-configurations between the 3,4-diaryl groups. In the case of *p*-methoxyphenyl derivative **1c**, hydroxy-aldehyde **4** was obtained as a minor product. The reactions of the β-sultams without a substituent at the 4-position did not proceed.

Table 1. Formation of Ketones or Aldehydes



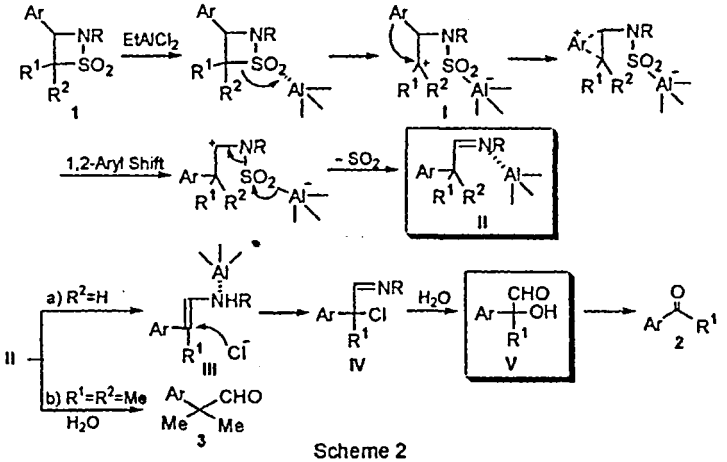
Entry	Compd No.	Sultam Ar	R^1	R^2	Products R^3	(%yields)
1	1a	Ph	H	Ph	Ph	2a (81)
2	1b	Ph	Ph	H	Ph	2a (78)
3[a]	1c	*p*-$MeOC_6H_4$	H	Ph	Ph	2b (62), 4 (31)
4	1d	Ph	H	H	-	N.R.
5	1e	*p*-MeC_6H_4	H	H	-	N.R.
6	1f	*p*-MeC_6H_4	H	Me	-	N.R.
7	1g	*p*-MeC_6H_4	Me	H	Me	2c (35), 1g (44)
8	1h	Ph	Me	Me	-	3a (73)
9	1i	*p*-MeC_6H_4	Me	Me	-	3b (78)

a) 2.2 Equiv of $EtAlCl_2$ was used.

Lewis acids attempted: $AlCl_3$, Et_2AlCl, Et_3Al, $TiCl_4$, $Ti(O^iPr)_4$, $ZnCl_2$, ZnI_2, $ZnEt_2$, BF_3·Et_2O

The *cis*-methyl derivative **1f** did not give the product, but the compound with the *trans*-configuration **1g** gave the product **2c** in 35% yield. The 4,4-dialkyl derivatives **1h, i** produced aldehydes **3a, b** in high yields. The plausible mechanism for formation of aryl ketones and aldehydes is shown in Scheme 2.

$EtAlCl_2$ attaches to the sulfonyl group and the C-S bond is cleaved. The



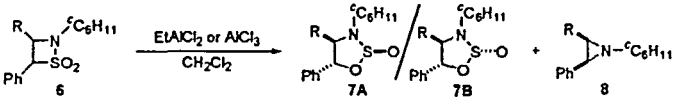
Scheme 2

resulting carbocation I undergoes the aryl group migration and the subsequent release of sulfur dioxide to form the imine II. The imine having a hydrogen, namely, R_2=H, isomerizes into the enamine III. The enamine III transforms into the chloro-imine IV and then hydrolyzes to form the α-hydroxy aldehyde V. This aldehyde V causes deformylation to give the ketone **2**. On the other hand, when the α-carbon of the imine II is fully substituted, the imine II gives aldehyde **3** by hydrolysis. To confirm this mechanism, we conducted the following reactions. When α-hydroxy aldehyde **4** was used in the preparative TLC, *p*-methoxyphenyl phenyl ketone **2b** was obtained in 86% yield. *N*-(2-Phenylpropylidene)butylamine **5** was treated with 2 equiv. of $EtAlCl_2$ at room temperature for 12 h, and acetophenone **2d** was obtained in 63% yield.

In order to study the effect of the migrating group R, we next examined the reactions of the β-sultams with an electron-deficient aryl group at the 3-position (Table 2).

The reactions of *cis*-3-(3-pyridyl)-4-phenyl-β-sultam **6a**-*cis* with 2 equiv. of $EtAlCl_2$ gave 1,2,3-oxathiazolidine 2-oxide **7a** in 65% yield. The product **7a** was a mixture of diastereoisomers **7A** and **7B** due to the

Table 2. Formation of 1,2,3-Oxathiazolidine 2-Oxides and Aziridines



Entry	β-Sultam Compd No.	R	Conditions	Products (% yield)
1	**6a-*cis***	3-Pyridyl	$EtAlCl_2$ (2.0), r.t., 12h	**7a** (65, A:B=70:30)
2	**6a-*cis***	3-Pyridyl	$EtAlCl_2$ (4.5), reflux, 60h	**7a** (5, A:B=80:20), **8a** (62)
3	**6a-*trans***	3-Pyridyl	$EtAlCl_2$ (1.4), r.t., 12h	No Reaction
4	**6b-*cis***	4-Pyridyl	$EtAlCl_2$ (4.5), 0°C, 22h	**7b** (49, A:B=90:10)[b], **8b** (11)
5	**6b-*cis***	4-Pyridyl	$AlCl_3$ (4.0), reflux, 28h	**7b** (6, A:B=91.9)[b], **8b** (54)
6	**6c-*cis***	2-Pyridyl	$AlCl_3$ (4.0), r.t., 27h	**7c** (9, A:B=94.6)[b], **8c** (48)
7	**6d-*cis***	*p*-$NO_2C_6H_4$	$EtAlCl_2$ (1.0), 0°C, 12h	**7d** (18, A:B=95:5)[b]
8	**6e-*cis***	*p*-CNC_6H_4	$AlCl_3$ (1.5), r.t., 14h	**8e** (23)
9	**6f**[a]	*t*-Butyl	$EtAlCl_2$ (1.1), r.t. 12h	**7fA** (93)

[a]An isomeric mixture (*cis*:*trans*=1:1.8) was used. [b]An inseparable mixture of stereoisomers. *The ratio was determined by* ^1H *NMR.*

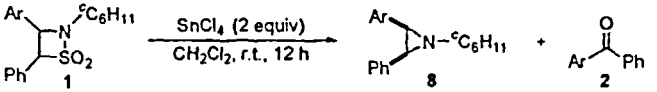
configuration of the S-O group in the ratio of 70:30. Upon using 4.5 equiv. of $EtAlCl_2$, we obtained *cis*-aziridine **8a** in 62% yield accompanied with oxathiazolidine oxide **7a**. The *trans*-isomer **6a-*trans*** did not afford the oxathiazolidine oxide. Therefore, we conducted the reactions of only the *cis*-isomers. $AlCl_3$ was used instead of $EtAlCl_2$ and we obtained *cis*-aziridine **8b** in 54% yield.

From these results, it was seen that the stereochemistry between the 3- and 4-aryl groups affects the ring-opening of the β-sultams. Prolonged reaction time and the increased use of the Lewis acid increased the yield of the aziridines.

In contrast, the reaction of 3,4-diphenyl-β-sultam **1a-*cis*** with 2 equiv. of $SnCl_4$ gave *cis*-aziridine **8a** and benzophenone **2a**, but no oxathiazolidine oxide. In entry 6, the β-sultam with an electron-releasing group, the *p*-methoxyphenyl group, **1c-*cis*** afforded only ketone **2b**. The *trans*-isomers in Entries 3 and 5 did not give the aziridines, but gave the ketones **2**.

The difference in the products between the reactions with the aluminum Lewis acids and $SnCl_4$ can be explained in terms of the difference in

Table 3. Reactions of Some β-Sultams 1 with $SnCl_4$



Entry[a]	β-Sultam Compd No.	Ar	Products (% yield)[b]
1	**1a-*cis***	Ph	**8a** (46), **2a** (19)
2[c]	**1a-*cis***	Ph	**8a** (53), **2a** (10)
3	**1a-*trans***	Ph	**8a** (trace), **2a** (61)
4	**1j-*cis***	*p*-BrC$_6$H$_4$	**8b** (14), **2d** (4), **1j-*cis*** (76)
5	**1j-*trans***	*p*-BrC$_6$H$_4$	**8b** (trace), **2d** (46), **1j-*trans*** (32)
6	**1c-*cis***	*p*-MeOC$_6$H$_4$	**2e** (83)

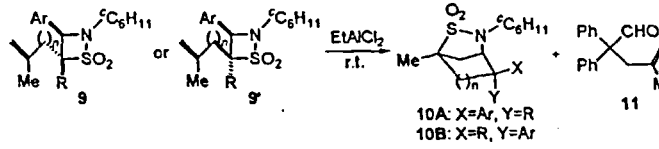
[a]Reactions were carried out at room temperature for 12 h unless otherwise noted. [b]Isolated yield. [c]2 equiv of KI was added as the nucleophile.

affinities to the sulfur and oxygen atoms.

Since we achieved the selective C-S bond fission using a Lewis acid, we attempted to trap the resulting carbocations with an intramolecular alkenyl group (Table 4).[3]

trans-4-Butenyl-3-phenyl-β-sultam **9a** was treated with 2.2 equiv. of $EtAlCl_2$ in toluene at room temperature, and bicyclic γ-sultam **10a** was obtained. The *cis*-isomer **9a'** also gave the same product **10a**. When the

Table 4. Formation of Bicyclic-γ-sultams from 4-Alkenyl-β-sultams

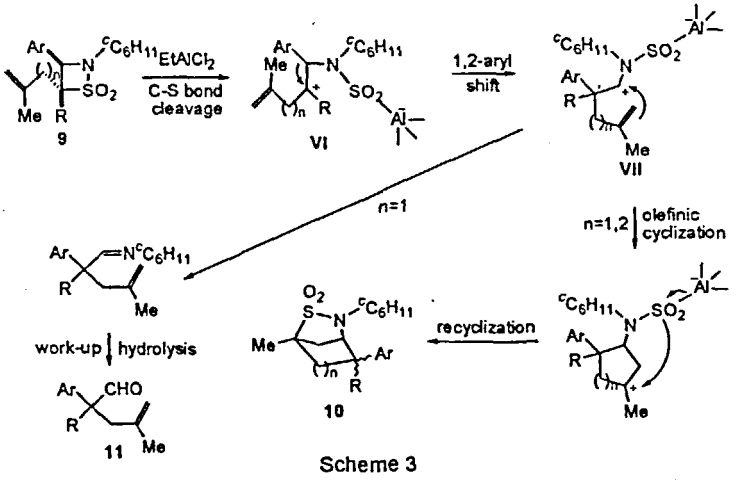


Entry	β-Sultam	Ar	R	n	$EtAlCl_2$ (eq.)	Solvent	Time (h)	Products (% yield)[a]
1	**9a**	Ph	Ph	2	2.2	Toluene	12	**10a** (53)
2	**9a'**	Ph	Ph	2	2.2	Toluene	12	**10a** (59)
3	**9b**	*p*-Tol	Me	2	2.2	Toluene	12	**10bA** (42), **10bB** (6)[b]
4	**9c**	*p*-Tol	Et	2	2.2	Toluene	12	**10cA** (39), **10cB** (5)[b]
5	**9d**	*p*-Tol	Ph	2	2.2	Toluene	12	**10d** (56, A : B = 1 : 1)[c]
6	**9e**	Ph	Ph	1	2.2	Toluene	12	**10e** (11), **11** (66)

[a]Isolated yield. [b]Stereochemistry of the products was determined by NOE measurement. [c]A mixture of diastereomers. The ratio was estimated by ^{1}H NMR spectrum.

aryl group and the group R were different, the diastereoisomers **10A** and **10B** were obtained. A methyl group of the alkenyl group was necessary for this reaction. The propenyl derivative **9e** gave the aldehyde **11** as the major product. The structures of the products could not be determined based only on the spectral data and, therefore, an X-ray analysis was conducted.

The proposed mechanism for the tandem cyclization is shown in Scheme 3. The Lewis acid, $EtAlCl_2$, cleaves the C-S bond. The resulting cation VI undergoes the 1,2-aryl shift and the intramolecular tandem cyclization, namely, the olefinic cyclization and the sulfonyl cyclization. The bicyclic γ-sultam **10** is finally formed. In the case of the propenyl derivative, the cation VII eliminates sulfur dioxide and forms the imine, which is hydrolyzed to aldehyde **11**.



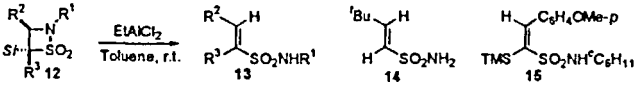
Scheme 3

CARBON-NITROGEN BOND CLEAVAGE

We synthesized the β-sultams bearing a trimethylsilyl (TMS) or *tert*-butyldimethylsilyl (TBDMS) group at the 4-position and carried out the

reactions of the β-sultams with $EtAlCl_2$.[5,6] The vinyl sulfonamides with (*E*)-configuration were obtained in good to high yields (Table 5).

Table 5. Reactions of 4-Silyl-substituted β-Sultams 12 with $EtAlCl_2$



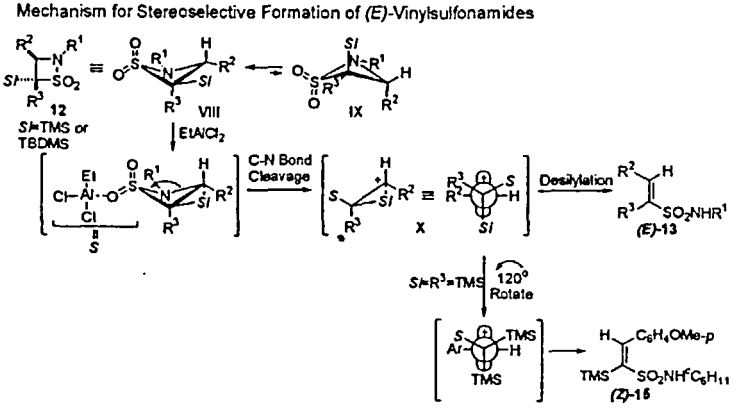
Entry	Compd No.	4-Silylated β-Sultam R^1	R^2	R^3	Si	$EtAlCl_2$ (equiv.)	Time(h)	Products[a] (% yield)[b]
1	12a	^{c}C$_6$H$_{11}$	Ph	H	TBDMS	2.0	26	13a(93)
2	12b	^{c}C$_6$H$_{11}$	*p*-MeC$_6$H$_4$	H	TBDMS	2.0	24	13b(89)
3	12c	^{c}C$_6$H$_{11}$	*p*-BrC$_6$H$_4$	H	TBDMS	2.0	28	13c(91)
4[c]	12d	^{c}C$_6$H$_{11}$	^{t}Bu	H	TBDMS	1.5	23	13d(21), 14(65)
5	12e	^{c}C$_6$H$_{11}$	Ph	Me	TMS	4.0	24	13e(64), 12e(26)
6	12f	^{c}C$_6$H$_{11}$	Ph	Me	TBDMS	2.0	24	13e(92)
7	12g	^{n}Bu	Ph	Ph	TMS	2.0	30	13g(68), 1g(12)
8	12h	^{c}C$_6$H$_{11}$	^{t}Bu	Ph	TMS	2.0	28	13h(64)
9	12i	^{c}C$_6$H$_{11}$	Ph	TMS	TMS	3.0	35	13i(89)
10	12j	^{c}C$_6$H$_{11}$	*p*-MeOC$_6$H$_4$	TMS	TMS	2.0	36	13j(71), 15(21)
11	12k	^{c}C$_6$H$_{11}$	*p*-BrC$_6$H$_4$	TMS	TMS	2.0	34	13k(90)

[a]The geometry was determined from the coupling constant between *vic*-olefinic protons in ^{1}H NMR or by NOE technique. [b]Isolated yield. [c]Reaction Temperature: 40°C.

Some quantity of the starting material was recovered from the reactions of TMS-substituted β-sultam **12e** in Entry 5. This implies that the bulky TBDMS group accelerates the β-sultam ring opening. The *N*-dealkylation was observed in the case of *N-tert*-butyl derivative **12d**, and *N-n*-butyl derivative **12g** gave the desilylated β-sultams **1g** in 12% yield. 4-Disilylated β-sultams **12i-k** similarly reacted with $EtAlCl_2$ to give the α-silyl (*E*)-vinylsulfonamides **13i-k** in high yields. The *p*-methoxyphenyl derivative **12j** produced (*Z*)-vinylsulfonamide **15** together with (*E*)-isomer **13j**.

The plausible reaction mechanism for the stereoselective formation of (*E*)-vinylsulfonamides is shown in Scheme 4.

It is seen that the β-sultam ring is folded, and not planar, from the conformational analyses of the β-sultam ring by ^{1}H-NMR spectroscopy and X-ray crystallography. A conformer bearing an equatorial silyl group VIII is more stable than that with an axial silyl group IX. $EtAlCl_2$ attaches to the sulfonyl group similar to the other examples



Scheme 4

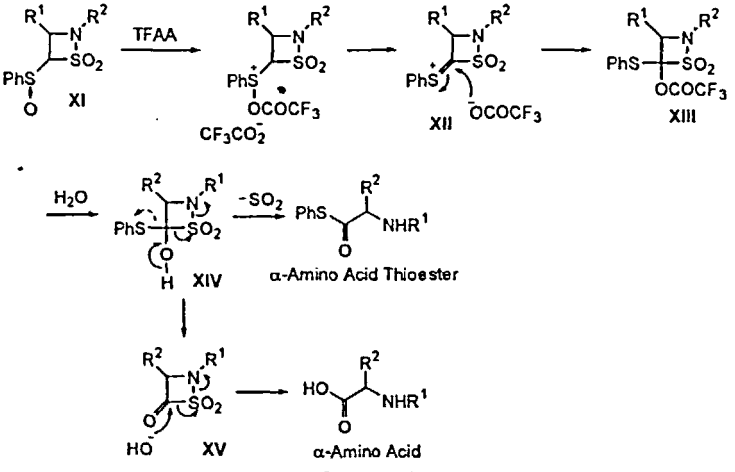
mentioned above. The equatorial silyl group assists the breakage of the C-N bond from the rear side, and this can be explained more clearly by the Newman projection. The antiparallel desilylation gives the (*E*)-vinylsulfonamide stereoselectively. When the aryl group is a *p*-methoxyphenyl moiety, the resulting carbocation X is stable to rotate by 120° and then eliminates the silyl group. Hence, *Z*-isomer **15** is formed as a by-product.

The C-N bond fission of β-sultams was also found in the reactions of 3-phenyl-β-sultams with organometallics.[7]

PUMMERER REACTION OF 4-SULFINYL-β-SULTAMS: SYNTHESIS OF α-AMINO ACID THIOESTERS

If the sulfinyl β-sultam XI causes the Pummerer reaction by the treatment with trifluoroacetic anhydride (TFAA) and the expected trifluoroacetate XIII is produced, the trifluoroacetate XIII is labile against hydrolysis and gives the half-acetal XIV. The half-acetal XIV undergoes the C-SO_2 bond cleavage and forms the amino acid thioester

with the loss of sulfur dioxide. On the other hand, if the benzenethiolate ion is eliminated from the half-acetal XIV, a 4-keto-β-sultam XV is formed and then hydrolytically ring-opened to give the α-amino acid.



Scheme 5

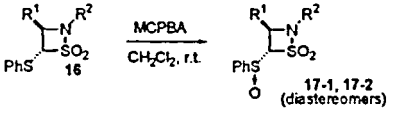
If this Pummerer reaction shown in Scheme 5 proceeds successfully, it would become a new method for the C-S bond cleavage.

The synthesis of the 4-sulfinyl substituted β-sultams is shown in Table 6.

The *trans*-phenylthio-β-sultams **16** were oxidized with *m*-chloroperbenzoic acid (MCPBA) and gave the sulfoxides **17** as a mixture of diastereoisomers. The diastereoisomers could be separated into two isomers, **17-1** and **17-2**, but their stereostructure has not been determined. The *cis*-sulfide **16d** was similarly oxidized, but the resulting *cis*-sulfoxides **18d** were isomerized to the *trans*-isomers **17d** by treatment with silica gel.

The Pummerer reactions of the *trans*-sulfinyl-β-sultams **17** with TFAA were conducted and the results are shown in Table 7.[8]

Table 6. Synthesis of 4-Sulfinyl-β-sultams



Entry	16	R^1	R^2	17 (% yield)[a]
1	16a	Ph	$^c C_6H_{11}$	17a-1 (58), 17a-2 (16)
2	16b	Ph	$^n Bu$	17b-1 (49), 17b-2 (47)
3	16c	Ph	$^t Bu$	17c-1 (75), 17c-2 (20)
4	16d	*p*-Tolyl	$^c C_6H_{11}$	17d-1 (53), 17d-2 (20)
5	16e	*o*-Tolyl	$^c C_6H_{11}$	17e-1 (64), 17e-2 (33)
6	16f	$^t Bu$	$^c C_6H_{11}$	17f-1 (54), 17f-2 (36)

[a]Isolated yield.

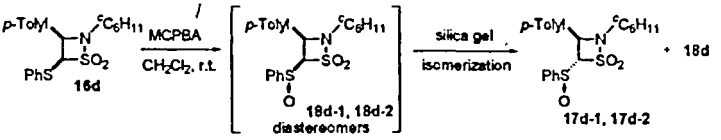
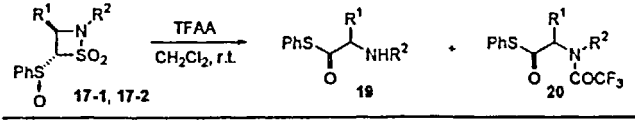


Table 7. The Pummerer Reaction of 4-Sulfinyl-β-sultams: Formation of α-Amino Acid Thioester Derivatives



Entry	R^1	R^2	Conditions	Sulfoxide	Products[a] (% yield)[b]
1	Ph	$^c C_6H_{11}$	TFAA (1.0 eq.), 12 h	17a-1	recovery[c]
2			TFAA (2.0 eq.), 24 h	17a-1	19a, 20a (low yield)
3			TFAA (4.0 eq.), 20 h	17a-1	19a (72), 20a (13)
4			TFAA (4.0 eq.), 20 h	17a-2	19a (79), 20a (14)
5	Ph	$^t Bu$	TFAA (4.0 eq.), 20 h	17c-1	19c (93)
6			TFAA (4.0 eq.), 20 h	17c-2	19c (97)
7			TFAA (4.0 eq.), 20 h	17f-1	19f (81)
8	$^t Bu$	$^c C_6H_{11}$	TFAA (4.0 eq.), 20 h	17f-2	19f (82)

[a]A trace amount of $(PhS)_2$ was isolated in all cases. [b]Isolated yield. [c]Isomerization of the sulfoxide moiety was observed.

From the results in Entries 1-3, 4 equiv. of TFAA was necessary to complete the reaction. However, excess TFAA yielded *N*-trifluoroacetamide **20a** as a by-product. The other diastereoisomer **17a-2** similarly gave the same thioesters **19a** and **20a** in Entry 4. The difference in the stereochemistry at the sulfinyl group did not affect the

Pummerer reaction. This means that the stereochemistry of the sulfoxides was lost during the reactions similar to the usual Pummerer reaction. Therefore, we conducted the Pummerer reaction of the mixtures of four diastereoisomers **17d-1,2** and **18d-1,2** and obtained the thioester **19d** (63%) and *N*-trifluoroacetyl derivative **20d** (15%).

The *N*-trifluoroacetamide derivatives were not obtained from the reaction of the *N*- or 3-*tert*-butyl derivative, **17c** or **17f**, because of the bulkiness of the *tert*-butyl group.

The Pummerer reaction of the selenoxide was attempted. The product was very labile and decomposed during preparative TLC.

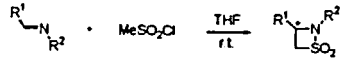
The Pummerer reaction proceeded as might have been expected in Scheme 5. An interesting finding in this reaction is that the thionium ion XII, that is, the α-phenylthio carbocation, did not cause the 1,2-aryl shift in contrast to the carbocation generated using an aluminum Lewis acid.

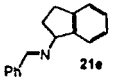
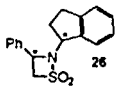
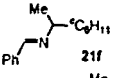
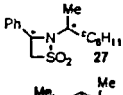
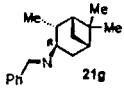
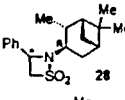
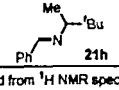
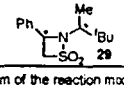
We next planned to apply this method to the synthesis of optically active α-amino acid thioesters. The β-sultam ring can be constructed by the [2+2] cycloaddition of imines and sulfenes. The sulfenes are generated *in situ* from the reaction of the imines and the sulfonyl chlorides. If we use a chiral imine, we can expect the 1,3-asymmetric induction, and the carbon at the 3-position would become a chiral center (Table 8).

The reaction of the optically active *N*-phenethyl imine **21a** with methanesulfonyl chloride gave a β-sultam in 70% chemical yield and 42% diastereomeric excess. Reactions of the imines bearing an aryl group **21a-e** gave the products with moderate diastereoselectivity. The imines with a bulky alkyl group **21f-h** increased the diastereoselectivity, and the highest selectivity was obtained from the *N*-(1-*tert*-butylethyl)imine **21h**. The stereochemistry of the major isomer was determined by X-ray crystallographic analysis.

The 1,3-asymmetric induction of the reaction of *N*-(1-*t*-butylethyl)imine

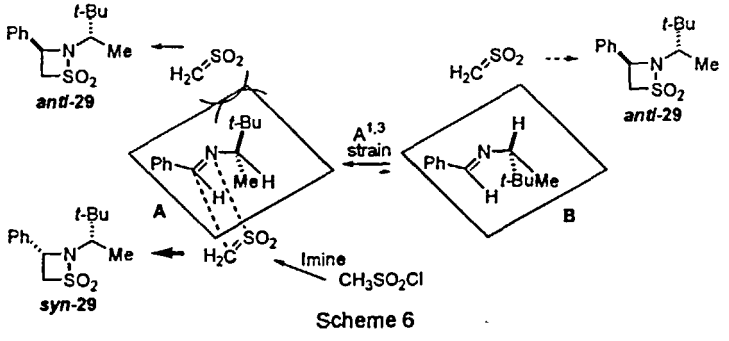
Table 8. 1,3-Asymmetric Induction in the [2+2] Cycloaddition



Imine	Product	%Yield[a]	Imine	Product	%Yield[a]
 21a	 22	70, 42%de	 21e	 26	36, 50%de
 21b	 23	32, 45%de	 21f	 27	60, 67%de
 21c	 24	72, 44%de	 21g	 28	54, 80%de
 21d	 25	53, 47%de	 21h	 29	67, > 95%de

[a]Isolated yield Diastereomeric excess was calculated from ^{1}H NMR spectrum of the reaction mixture

21h with sulfene is shown in Scheme 6 as an example.

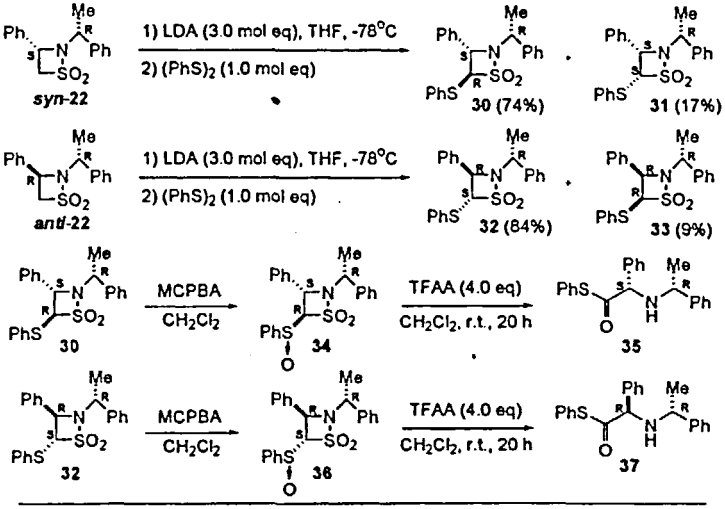


Scheme 6

Conformers A and B are important among the conformers of the imine **21h** for the discussion of the stereoselectivity of the reaction. Conformer B is less stable than conformer A because of the allylic strain. When the sulfene attacks the imine from the opposite face to the *tert*-butyl group, the *syn*-isomer ***syn*-29** is formed. The front-side attack of sulfene is restricted by the bulky *tert*-butyl group, and

consequently the *anti*-isomer ***anti*-29** is produced in only a few % yield. The synthesis of the chiral α -amino acid thioesters is shown in Table 9.

Table 9. Synthesis of Chiral α-Amino Acid Thioesters



Entry	Sulfide	Sulfoxide (% yield)[a]	Thioester (% yield)[a]
1	**30**	**34-1** (71)	**35** (89, > 90% de)b
2		**34-2** (25)	**35** (97, > 90% de)[b]
3	**32**	**36-1** (75)	**37** (91, > 90% de)b
4		**36-2** (22)	**37** (88, > 90% de)[b]

[a]Isolated yield. [b]Diastereomeric excess was calculated from ^{1}H NMR spectrum.

A 1'*R*,3*S*-*syn*-β -sultam ***syn*-22** was sulfenylated at the 4-position, and yielded a pair of diastereoisomers **30** and **31**. A 1'*R*,3*R*-*anti*-isomer ***anti*-22** was similarly sulfenylated and gave two diastereoisomers **32** and **33**. We oxidized the major isomer **30**, which has the 1'*R*,3*S*,4*R*-configuration, and obtained the sulfoxides as a mixture of the diastereoisomers **34-1** and **34-2**. After separation of the diastereoisomers, each isomer was submitted to the Pummerer reaction and gave the same thioester **35** in high chemical yield and higher than 90%

diastereomeric excess. Similarly, the *anti-trans-* β -sultam **32** was transformed into the α -amino acid thioester **37** with the *anti*-configuration in high chemical and optical yields. A slight epimerization of the α -chiral center was observed under the reaction conditions.

This synthetic method for optically active amino acid thioesters has the advantage that achiral aldehydes can be converted to the chiral amino acid thioesters.

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