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Selective C-N Bond Cleavage of 4-Silyl-substituted 1,2-Thiazetidine 1,1-Dioxides with $EtAlCl_2$: Stereospecific Formation of *(E)*-Vinylsulfonamides

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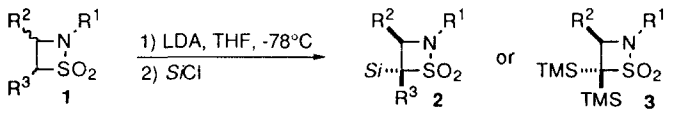
Abstract: Monosilylation of 1,2-thiazetidine 1,1-dioxides (ß-sultams) furnished *(3R*, 4S*)*-4-silylated ß-sultams stereoselectively. Treatment of 4-silylated ß-sultams with a Lewis acid caused the selective C-N bond cleavage because of the ß-silyl stabilization against the resultant carbenium ion followed by desilylation to provide *(E)*-vinylsulfonamides stereospecifically.

Vinylsulfonamides have been utilized in various reactions such as aziridine formation,[1] 1,3-dipolar cycloadditions[2] and Michael additions.[3-7] However, little attention has been paid to the synthesis of vinylsulfonamides.[3,8-11] We previously reported that the selective C-S bond cleavage of 1,2-thiazetidine 1,1-dioxides (ß-sultams) bearing alkyl or aryl substituents at C-3 and C-4 was achieved by treatment with a Lewis acid to provide aryl ketones, aldehydes,[12] *trans*-1,2,3-oxathiazolidine 2-oxides and *cis*-aziridines.[13] In this study, we discovered that reactions of 4-silyl-substituted ß-sultams with $EtAlCl_2$ provided *(E)*-vinylsulfonamides stereospecifically *via* the processes of C-N bond cleavage and desilylation. Atkins and Burgess reported that treatment of a ß-sultam with Et_3N afforded a vinylsulfonamide.[11] However, our finding is, in fact, the first stereospecific C-N bond cleavage of a ß-sultam ring due to anchimeric assistance of the silyl group in acidic media. Müller and Otto reported that treatment of 4-silylated ß-sultams with tetrabutylammonium fluoride in THF-acetic acid furnished desilylated ß-sultams without ring destruction.[14] In contrast, the use of $EtAlCl_2$ as a reagent caused a ring-opening reaction with elimination of the silyl group. In this communication, we describe that the selective C-N bond cleavage of 4-silylated ß-sultams with $EtAlCl_2$ followed by desilylation provides *(E)*-vinylsulfonamides stereospecifically.



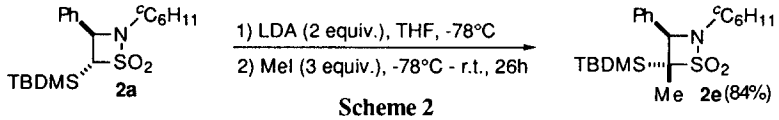
Scheme 1

4-Mono- and 4,4-di-silylated ß-sultams were prepared as shown in Scheme 1. 3-Aryl-ß-sultams **1** were treated with LDA at -78°C in THF followed by silylation with ^{t}butyldimethylsilyl (TBDMS) chloride or trimethylsilyl (TMS) chloride to give 4-mono- or 4,4-di-silylated ß-sultams **2** or **3** (Table 1). Stereoselective monosilylation of 4-nonsubstituted ß-sultams **1a-c** was achieved by use of TBDMSCl as a silylating reagent (entries 1-3).[14,15] Silylation of 4-substituted ß-sultams also proceeded stereoselectively although the starting

Table 1 Synthesis of 4-Silyl-substituted ß-Sultams **2** and **3**.

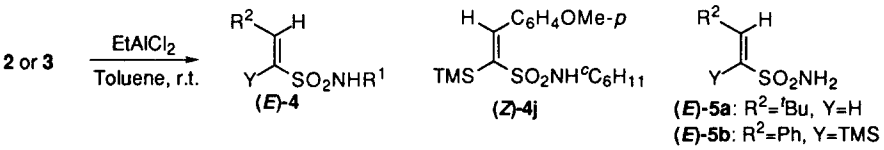
Entry	ß-Sultam **1**	R^1	R^2	R^3	LDA (equiv.)	Electrophile *Si*(equiv.)	Conditions	Products (%yield)[a]
1	**1a**	$^cC_6H_{11}$	Ph	H	2.0	TBDMS(1.5)	-78°C, 2h	**2a**(98)
2	**1b**	$^cC_6H_{11}$	*p*-MeC_6H_4	H	2.0	TBDMS(1.5)	-78°C, 2h	**2b**(93)
3	**1c**	$^cC_6H_{11}$	*p*-BrC_6H_4	H	2.0	TBDMS(1.5)	-78°C, 2h	**2c**(87)
4	**1d**	$^cC_6H_{11}$	Ph	Me	2.0	TMS(2.0)	-78°C - r.t., 18h	**2d**(88)
5	**1d**	$^cC_6H_{11}$	Ph	Me	2.0	TBDMS(2.0)	-78°C - r.t., 20h	**2e**(53)
6	**1e**	$^cC_6H_{11}$	Ph	Et	2.0	TMS(2.0)	-78°C - r.t., 18h	**2f**(72)
7	**1e**	$^cC_6H_{11}$	Ph	Et	2.0	TBDMS(2.0)	-78°C - r.t., 22h	**2g**(44)
8	**1f**	^nBu	Ph	Ph	2.0	TMS(2.0)	-78°C - r.t., 18h	**2h**(68)
9	**1g**	$^cC_6H_{11}$	^{t}Bu	H	2.0	TBDMS(1.5)	-78°C, 2h	**2i**(92)
10[b]	**1h**	$^cC_6H_{11}$	^{t}Bu	Ph	2.0	TMS(2.0)	-78°C - r.t., 16h	**2j**(54)[c]
11	**1a**	$^cC_6H_{11}$	Ph	H	3.0	TMS(3.0)	-78°C - r.t., 20h	**3a**(92)
12	**1i**	$^cC_6H_{11}$	*p*-$MeOC_6H_4$	H	3.0	TMS(3.0)	-78°C - r.t., 20h	**3b**(88)
13	**1c**	$^cC_6H_{11}$	*p*-BrC_6H_4	H	3.0	TMS(3.0)	-78°C - r.t., 20h	**3c**(84)

[a]Isolated yield unless otherwise noted. [b]Silylation was carried out twice. [c]Crude yield.



Scheme 2

materials used were isomeric mixtures (entries 4-8). Disilylation proceeded smoothly by use of TMSCl as a silylating reagent (entries 11-13). 3-^{t}Butyl-4-silyl-ß-sultam **2i** was obtained stereoselectively in 92% isolated yield by treatment of **1g** with 2.0 equiv. of LDA and then 1.5 equiv. of TBDMSCl at -78°C for 2 hours in THF (entry 9). Silylation of **1h** was carried out twice (2.0 equiv. of LDA and then 2.0 equiv. of TMSCl at -78°C - r.t. for 16 hours in THF) to give 3-^{t}butyl-4-silyl-ß-sultam **2j** in 54% crude yield (entry 10). ß-Sultam **2e** was also obtained in 84% yield regardless of the order of silylation and alkylation by the stereoselective methylation of **2a** (Scheme 2).



Scheme 3

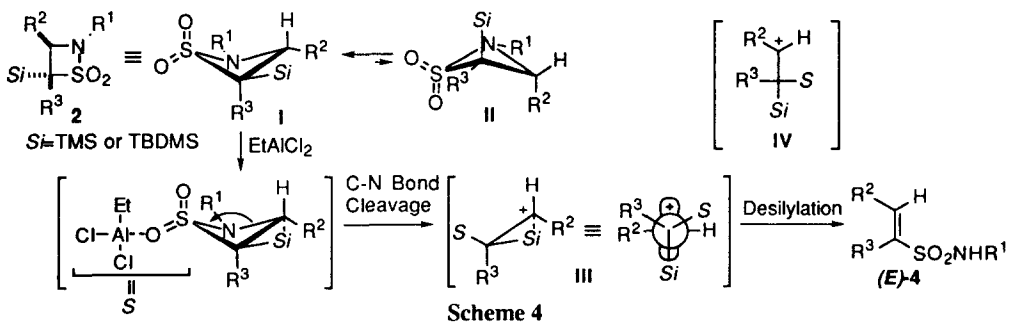
Reactions of silylated 3-aryl-ß-sultams **2** with $EtAlCl_2$ were carried out in dry toluene at room temperature under a nitrogen atmosphere (Scheme 3, Table 2).[16] 4-Monosilylated ß-sultams **2a-h**, which possess *(3R*, 4S*)*-configuration,[14,15] stereospecifically provided the corresponding *(E)*-styrylsulfonamides ***(E)*-4a-f** in good to high yields, respectively. All of the *vic*-olefinic protons of ***(E)*-4a-c** showed *trans J* values in ^{1}H NMR spectra. The geometry of ***(E)*-4d-f** was determined by the NOE technique.[17] Reactions of TMS-substituted ß-sultams **2d** and **2f** were slow and a considerable amount of the starting materials (26% of **2d** and 22% of **2f**, respectively) was recovered in spite of the use of 4.0 equiv. $EtAlCl_2$ (entries 4 and 6). A TBDMS group was more effective than a TMS substituent for the C-N bond cleavage. We also examined reactions of 3-^{t}butyl-4-silyl-ß-sultams **2i** and **2j** with $EtAlCl_2$. Treatment of **2i** with 1.5 equiv. of $EtAlCl_2$ at 40°C for 23 hours furnished *N*-dealkylated *(E)*-vinylsulfonamide ***(E)*-5a** as a major product in 65% yield together with 21% of ***(E)*-4g** (entry 9). *(E)*-Vinylsulfonamide ***(E)*-4h**[17] was furnished in 54% yield from **2j** (2.0 equiv. of $EtAlCl_2$ at r.t. for 28 hours, entry 10).

Table 2 Reactions of 4-Silyl-substituted ß-sultams **2** and **3** with $EtAlCl_2$.

Entry	4-Silylated ß-Sultam					$EtAlCl_2$	Time(h)	Y	Products[a]
		R^1	R^2	R^3	*Si*	(equiv.)			(%yield)[b]
1	**2a**	$^cC_6H_{11}$	Ph	H	TBDMS	2.0	26	H	(*E*)-**4a**(93)
2	**2b**	$^cC_6H_{11}$	*p*-MeC_6H_4	H	TBDMS	2.0	24	H	(*E*)-**4b**(89)
3	**2c**	$^cC_6H_{11}$	*p*-BrC_6H_4	H	TBDMS	2.0	28	H	(*E*)-**4c**(91)
4	**2d**	$^cC_6H_{11}$	Ph	Me	TMS	4.0	24	Me	(*E*)-**4d**(64), **2d**(26)
5	**2e**	$^cC_6H_{11}$	Ph	Me	TBDMS	2.0	24	Me	(*E*)-**4d**(92)
6	**2f**	$^cC_6H_{11}$	Ph	Et	TMS	4.0	24	Et	(*E*)-**4e**(70), **2f**(22)
7	**2g**	$^cC_6H_{11}$	Ph	Et	TBDMS	2.0	24	Et	(*E*)-**4e**(93)
8	**2h**	^nBu	Ph	Ph	TMS	2.0	30	Ph	(*E*)-**4f**(68), **1f**(12)
9[c]	**2i**	$^cC_6H_{11}$	^tBu	H	TBDMS	1.5	23	H	(*E*)-**4g**(21), (*E*)-**5a**(65)
10	**2j**	$^cC_6H_{11}$	^tBu	Ph	TMS	2.0	28	Ph	(*E*)-**4h**(54)
11	**3a**	$^cC_6H_{11}$	Ph	-	-	3.0	35	TMS	(*E*)-**4i**(89)
12[d]	**3a**	$^cC_6H_{11}$	Ph	-	-	2.0	8	TMS	(*E*)-**4i**(62), (*E*)-**5b**(38)
13	**3b**	$^cC_6H_{11}$	*p*-$MeOC_6H_4$	-	-	2.0	36	TMS	(*E*)-**4j**(71), (*Z*)**4j**(21)
14	**3c**	$^cC_6H_{11}$	*p*-BrC_6H_4	-	-	2.0	34	TMS	(*E*)-**4k**(90)

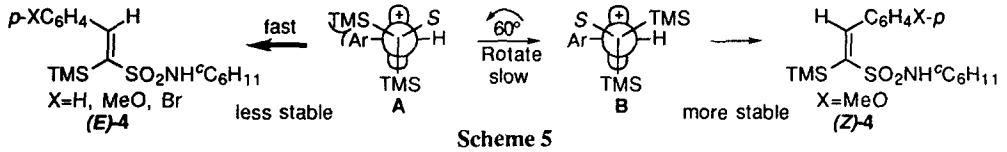
[a]The geometry was determined from the coupling constant between *vic*-olefinic protons in ^1H NMR or by NOE technique. [b]Isolated yield. [c]Reaction temperature: 40°C. [d]$AlCl_3$ was used instead of $EtAlCl_2$.

Stereospecific formation of *(E)*-vinylsulfonamides ***(E)*-4** would be explained as shown in Scheme 4. A silylated ß-sultam **2** predominantly exists in a conformation (**I**) where both an aryl substituent and a silyl group are *pseudoequatorial*,[14,15] and a nitrogen atom and the *pseudoequatorial*-oriented silyl group are *anti*-periplanar. The coordination of $EtAlCl_2$ to the sulfonyl group would cause the selective C-N bond cleavage to generate a carbenium ion intermediate **III**, which is stabilized by the ß-silyl substituent. The distortion of a four-membered ring bearing a TBDMS substituent would promote the ring-opening with $EtAlCl_2$ more than that of a ß-sultam having a TMS group. The elimination of the silyl group from the cation **III** affords an ***(E)*-4** stereospecifically. However, it could not be excluded that ***(E)*-4** which is thermodynamically more stable than ***(Z)*-4** is formed *via* a cationic intermediate **IV**, which is free from anchimeric assistance of the silicon atom.



Scheme 4

Next, we carried out reactions of 4,4-disilyl-substituted ß-sultams **3**. Treatment of 4,4-disilylated ß-sultam **3a** with 3.0 equiv. of $EtAlCl_2$ for 35 hours stereospecifically provided *(E)*-α-silylstyrylsulfonamide ***(E)*-4i** in 89% yield (Table 2, entry 11). Although reaction time was shortened by use of 2.0 equiv. of $AlCl_3$ instead of $EtAlCl_2$, an *N*-dealkylated *(E)*-styrylsulfonamide ***(E)*-5b** was formed in 38% yield as a by-product together with 62% of ***(E)*-4i** (entry 12). From the reaction of **3b**, ***(E)*-4j** was obtained in 71% yield accompanied by 21% of the geometrical isomer ***(Z)*-4j**, whose geometry was determined by the NOE technique (entry 13).[17] ***(E)*-4k** was obtained exclusively in 90% isolated yield by treatment of **3c** with 2.0 equiv. of $EtAlCl_2$ (entry 14).



Scheme 5

Formation of *(Z)*-α-silylstyrylsulfonamide ***(Z)*-4j** is explained as follows (Scheme 5): A cationic intermediate **A**, generated stereospecifically from 4,4-disilylated ß-sultam owing to anchimeric assistance of the silyl group *via* a similar process as shown in Scheme 4, provides an ***(E)*-4**. When the cation (X=MeO) is sufficiently stabilized by the electromeric assistance of the *p*-methoxy substituent, the internal 60° rotation of **A** partially takes place to avoid the steric interaction between the silyl and aryl groups, and **A** changes into the more stable conformer **B**. The elimination of the silyl group, which is *anti*-coplanar with p-orbital of the cation, gives thermodynamically more stable *(Z)*-α-silylstyrylsulfonamide ***(Z)*-4j**. In the case of X=H or Br, since the cation **A** is less stable, the ß-silyl group is eliminated before the internal rotation to accomplish stereospecific formation of *(E)*-styrylsulfonamides ***(E)*-4**. From these results, it is suggested that *(E)*-styrylsulfonamides are furnished stereospecifically *via* the intermediate **III**, not **IV**, (Scheme 4) due to anchimeric assistance of the silyl group.

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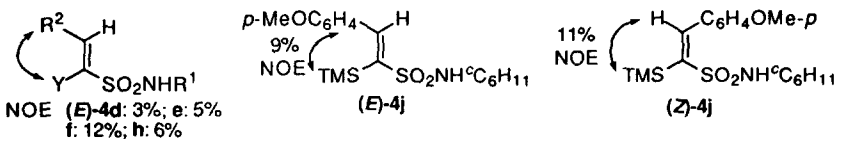
16. Typical procedure for the reaction of **2a** with $EtAlCl_2$ as a representative.— To a stirred solution of 4-silylated ß-sultam **2a** (38 mg, 0.1 mmol) in dry toluene (1 cm^3) was added 2.0 equiv. of $EtAlCl_2$ in hexane at room temperature under a nitrogen atmosphere. After 26 h, saturated aqueous $NaHCO_3$ (3 cm^3) was added to the reaction mixture. Inorganic precipitate was filtered off through celite and washed with EtOAc (5 cm^3). The organic layer was separated, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with hexane-EtOAc (4:1 v/v) to give *(E)*-vinylsulfonamide ***(E)*-4a** (25 mg, 93%), m.p. 110-113°C; ^1H NMR (400 MHz; $CDCl_3$) δ: 1.13-1.36 (5H, m), 1.54-1.57 (1H, m), 1.68-1.71 (2H, m), 1.95-1.97 (2H, m), 3.21-3.23 (1H, m, NCH), 4.67 (1H, brs, NH), 6.80 (1H, d, *J* =15.6 Hz, 1-H), 7.34-7.42 (3H, m, ArH), 7.47 (1H, d, *J* =15.6 Hz, 2-H), 7.44-7.50 (2H, m, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 24.7 (t), 25.1 (t), 34.3 (t), 52.6 (d), 126.5 (d), 128.1 (d), 129.0 (d), 130.6 (d), 132.7 (s), 140.4 (d); MS (*m/z*:): 265 (M^+), 144 (base); IR ν_{max}(KBr)/cm^{-1}: 3270 (NH), 1320, 1145 (SO_2); Anal.Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28. Found: C, 63.34; H, 7.15; N, 5.34.
17. The configuration of ***(E)*-4d-f,h,j** and ***(Z)*-4j** was determined by the NOE measurement.



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