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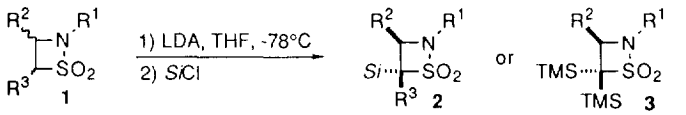
***Abstract:*** Monosilylation of 1,2-thiazetidine 1,1-dioxides (ß-sultams) furnished *(3R*, 4S*)*-4-silylated ß-sultams stereoselectively. Treatment of 4-silylated ß-sultams with a Lewis acid caused the selective C-N bond cleavage because of the ß-silyl stabilization against the resultant carbenium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



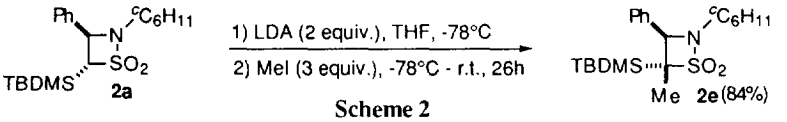

**Scheme 1**

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**.

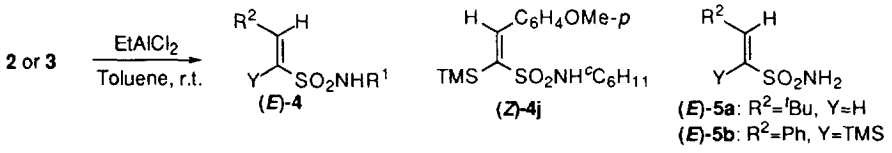
| Entry | ß-Sultam 1 | $R^1$ | $R^2$ | $R^3$ | LDA (equiv.) | Electrophile *Si*(equiv.) | Conditions | Products (%yield)[a] |
|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | $^c$C$_6$H$_{11}$ | Ph | H | 2.0 | TBDMS(1.5) | -78°C, 2h | **2a**(98) |
| 2 | **1b** | $^c$C$_6$H$_{11}$ | *p*-MeC$_6$H$_4$ | H | 2.0 | TBDMS(1.5) | -78°C, 2h | **2b**(93) |
| 3 | **1c** | $^c$C$_6$H$_{11}$ | *p*-BrC$_6$H$_4$ | H | 2.0 | TBDMS(1.5) | -78°C, 2h | **2c**(87) |
| 4 | **1d** | $^c$C$_6$H$_{11}$ | Ph | Me | 2.0 | TMS(2.0) | -78°C - r.t., 18h | **2d**(88) |
| 5 | **1d** | $^c$C$_6$H$_{11}$ | Ph | Me | 2.0 | TBDMS(2.0) | -78°C - r.t., 20h | **2e**(53) |
| 6 | **1e** | $^c$C$_6$H$_{11}$ | Ph | Et | 2.0 | TMS(2.0) | -78°C - r.t., 18h | **2f**(72) |
| 7 | **1e** | $^c$C$_6$H$_{11}$ | Ph | Et | 2.0 | TBDMS(2.0) | -78°C - r.t., 22h | **2g**(44) |
| 8 | **1f** | $^n$Bu | Ph | Ph | 2.0 | TMS(2.0) | -78°C - r.t., 18h | **2h**(68) |
| 9 | **1g** | $^c$C$_6$H$_{11}$ | $^t$Bu | H | 2.0 | TBDMS(1.5) | -78°C, 2h | **2i**(92) |
| 10[b] | **1h** | $^c$C$_6$H$_{11}$ | $^t$Bu | Ph | 2.0 | TMS(2.0) | -78°C - r.t., 16h | **2j**(54)[c] |
| 11 | **1a** | $^c$C$_6$H$_{11}$ | Ph | H | 3.0 | TMS(3.0) | -78°C - r.t., 20h | **3a**(92) |
| 12 | **1i** | $^c$C$_6$H$_{11}$ | *p*-MeOC$_6$H$_4$ | H | 3.0 | TMS(3.0) | -78°C - r.t., 20h | **3b**(88) |
| 13 | **1c** | $^c$C$_6$H$_{11}$ | *p*-BrC$_6$H$_4$ | 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**

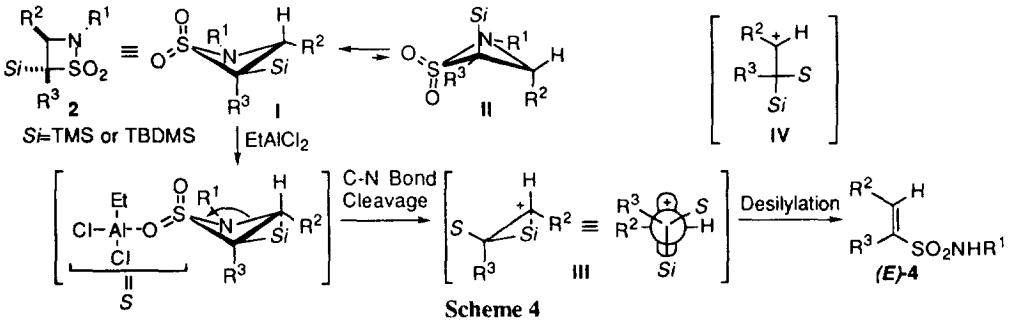
Reactions of silylated 3-aryl-ß-sultams **2** with EtAlCl$_2$ were carried out in dry toluene at room temperature under a nitrogen atmosphere (Scheme 3, Table 2).[16] 4-Monosilylated ß-sultams **2a-h**, which possess *(3R*, 4S*)*-configuration,[14,15] stereospecifically provided the corresponding *(E)*-styrylsulfonamides ***(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) |

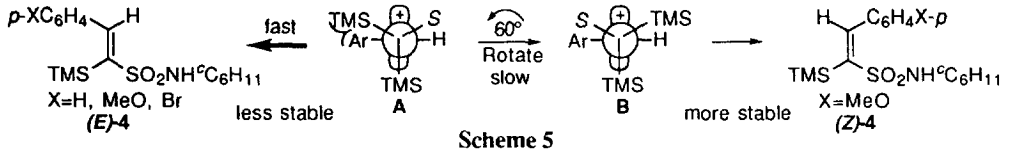
[a]The geometry was determined from the coupling constant between *vic*-olefinic protons in $^1H$ NMR or by NOE technique. [b]Isolated yield. [c]Reaction temperature: 40°C. [d]$AlCl_3$ was used instead of $EtAlCl_2$.

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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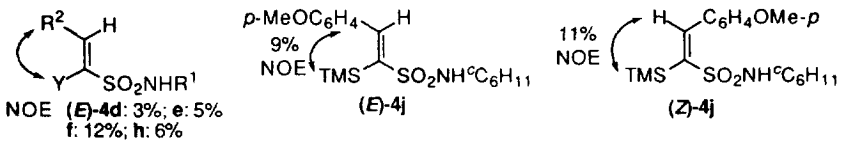
16. Typical procedure for the reaction of **2a** with $EtAlCl_2$ as a representative.— To a stirred solution of 4-silylated ß-sultam **2a** (38 mg, 0.1 mmol) in dry toluene (1 $cm^3$) was added 2.0 equiv. of $EtAlCl_2$ in hexane at room temperature under a nitrogen atmosphere. After 26 h, saturated aqueous $NaHCO_3$ (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 $\nu_{max}$(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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