Properties and Reactions of Substituted 1,2-Thiazetidine 1,1-Dioxides: Reactions of 3-Acetoxy-β-sultams with Sulfur Nucleophiles

Stefan Merkle and Hans-Hartwig Otto*

Pharmazeutisches Institut der Universität Freiburg, LS Pharmazeutische Chemie, Hermann-Herder-Str. 9, D-79104 Freiburg i.Br., Germany

Received January 17, 1994

The acetate moiety of 3-acetoxy-β-sultams **2** is easily displaced by sulfur nucleophiles yielding the alkylthio-β-sultams **3** which are transformed into stable derivatives **4** by silylation. The synthesis of the cephem analogue **7** is described. Reactions of **2** with thiols under electrophilic conditions result in the formation of bis-substituted ethanesulfonamides **6** and **9**.

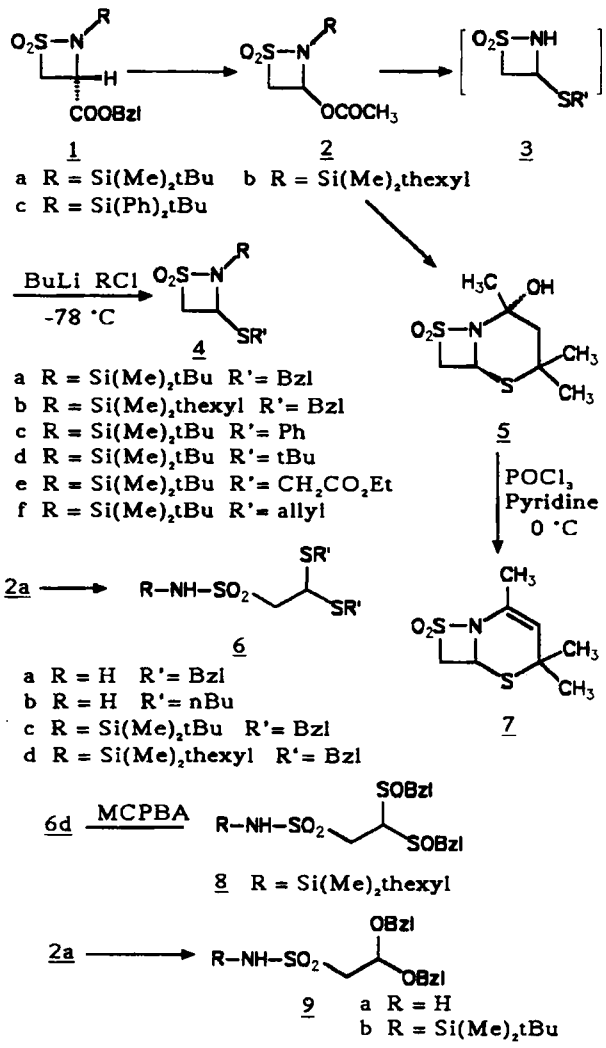
Eigenschaften und Reaktionen substituierter 1,2-Thiazetidin-1,1-dioxide: Reaktionen von 3-Acetoxy-β-sultamen mit Schwefelnukleophilen

Die Acetatgruppe der 3-Acetoxy-β-sultame **2** kann leicht durch Schwefelnukleophile substituiert werden, wobei 3-Alkylthio-β-sultame **3** erhalten werden, die durch *N*-Silylierung in die stabilen Derivate **4** überführt werden. Die Synthese des Cephem-Analogen **7** wird beschrieben. Umsetzungen von **2** mit Mercaptanen unter elektrophilen Bedingungen führen zur Bildung der bis-substituierten Ethansulfonamide **6** bzw. **9**.

4-Acetoxyazetidin-2-one, first prepared by *Grimm* and *Bestian*[1], is one of the most useful synthons in β-lactam chemistry[2]. Its acetate moiety is readily displaced by a wide range of nucleophiles under mild conditions. As 1,2-thiazetidine 1,1-dioxides (β-sultams) are highly reactive sulfonyl analogues of β-lactams, we have prepared the analogous acetoxy derivatives **2** from benzyl 1,2-thiazetidine-3-carboxylate 1,1-dioxides **1** by hydrogenolysis followed by oxidative rearrangement with lead tetraacetate[3]. Here we report about the reactions of **2** with sulfur nucleophiles.

The nucleophilic displacement of the acetoxy group from C-4 of the analogous β-lactam occurs readily with alkali salts of strongly nucleophilic thiols in aqueous solution[4] but fails completely when the same conditions are used for the β-sultams. Most likely, the alkali either attacks the sulfonyl group or deprotonates the α-methylene group. In some experiments we detected pertinent by-products[5]. The only basic solvent mixture suitable for the displacement reaction seems to be acetonitril and triethylamine, which has to be added to a solution of **2** and the thiol compound in acetonitril[6]. Only under these conditions we obtained the 3-substituted β-sultams **3** as unstable products which we could not purify, except the 3-benzylthio compound **3a**. Astonishingly, the displacement reaction is accompanied by a loss of the silyl protecting group, thus forming the very unstable hemithioaminal **3**. From other experiments we know that deprotonated acetonitril can attack the N-Si bond in β-sultams forming silylated acetonitril and unsubstituted β-sultam[7]. Here, the thiolate attacks that bond forming silylated thiols as by-products which were identified by GC. To obtain more stable products we have silylated **3** with *tert*-butylchlorodimethylsilane to **4** immediately after separation from the reaction mixture, and indeed, the N-silylated β-lactams **4** can be purified by FC.

In analogy to some reported cepham syntheses[8] we synthesized 4-mercapto-4-methylpentan-2-one from mesityloxide and H_2S[9] and reacted it with **2a** as described. We isolated the bicyclic β-sultam **5** which was dehydrated to **7** by $POCl_3$ in pyridine.



Scheme

  0365-6233/94/1010-0657 $ 5.00 + .25/0

The significant ^{1}H-NMR data[10] of **3** and **4** are summarized in Table 1. All shift values and coupling constants are similar, and from $J_{3/4'}$ = 2-4 Hz we deduce that the substituent at C-3 prefers the pseudoaxial orientation at the slightly folded (between 10° and 20°)[11] β-sultam ring. Assuming this being correct the relative orientation of substituents in the structure **5** should be as drawn in the formula, where the hydroxyl group is oppositely directed to the sulfur substituent. This is in agreement with the coupling constants found in the ^{1}H-NMR spectrum of **5**. Furthermore, it seems to be reasonable, as this configuration (SR/RS) minimizes the 1,3-interaction between the methyl groups at C-2 and C-4. We could not detect any isomer indicating that the cyclisation shows a high degree of stereoselectivity.

The nucleophilic displacement of the acetate moiety of 3-acetoxy-β-lactams is described even with silyl ethers or enolethers[12], resp., in the presence of *Lewis* acids *e.g.* trimethylsilyl trifluoromethanesulfonate[13]. In order to test this route for the synthesis of **4** we have prepared trimethylsilylthiobutane[14] and trimethylsilylthiomethylbenzene from the thiols by silylation with chlorotrimethylsilane in the presence of *n*-BuLi in THF at -78°C[15]. When we, however, reacted **2a** with these reagents at -78°C in the presence of trimethylsilyl trifluoromethanesulfonate we did not obtain any compound of structure **4**, but we isolated the 2,2-bis(alkylthio)ethanesulfonamides **6a** and **6b**, resp. which were silylated as usual yielding **6c** and **6d**. Finally, **6d** was oxidized with MCPBA to the bis-sulfoxide **8**. Further oxidation even with a large excess of MCPBA or with other oxidizing agents was not possible. The structures of **6** are easily established by their ^{1}H-NMR spectra. In contrast to the β-sultams showing an ABX pattern for the ring protons at C-3 and C-4, the ethanesulfonamides **6** exhibit a simple AX pattern with J = 7 Hz, indicating the ring opening in the reaction. We understand the formation of **6** as a two step process. In the first step the displacement of the acetate moiety by the thiol group occurs in analogy to the mechanism proposed for the β-lactam reaction by Barett[12]. Then, after desilylation, a second molecule of the silylthioether opens the ring, and by hydrolytic workup **6** is formed[16].

As expected, the analogous reaction between **2a** and the silylether of phenylmethanol[17] occured in the same way yielding the 2,2-bis(benzyloxy)ethanesulfonamides **9**.

Spectroscopic data of **6**, **8** and **9** are summarized in Table 2. While the IR data do not show great differences, the ^{1}H-NMR data clearly exhibit the influence of the oxygen *versus* sulfur to C-2.

Financial support of this work provided by the *Fond der Chemischen Industrie*, Frankfurt/M., is greatfully appreciated.

Experimental Part

General Remarks: Melting points (not corrected): Linström apparatus.- IR spectra: Perkin-Elmer IR 841, IR 1310, Beckman IR 33; in KBr, if not noted otherwise[10].- ^{1}H-NMR spectra: Varian T60, Bruker WP80, AM400; TMS as internal standard; values from 80-MHz spectra in $CDCl_3$, if not noted otherwise. δ values in ppm.- Elementary analyses: Pharmazeutisches Institut or Chemisches Laboratorium der Universität Freiburg.- Abbreviations: ar = aromatic. FC = flash chromatography using Kieselgel Merck 60, No. 9385, 230-400 mesh. MCPBA = *meta*-chloroperbenzoic acid. BuLi = n-butyllithium, 15% in hexane. THF = tetrahydrofuran, dried with $CaCl_2$ and distilled over $LiAlH_4$ prior to use. Other solvents were dried using standard procedures.

2-(tert-Butyldimethylsilyl)-1,2-thiazetidin-3-ylacetate 1,1-Dioxide (**2a**)

From 3.55 g (10 mmol) of **1a** according to the general prescription given in ref.[3]. Purification by FC (n-hexane/ethyl acetate 3:2), R_f = 0.65; yield 1.9 g (68%), colorless oily liquid.- IR: $\tilde{\nu}$ = 3040; 2960; 2880 (CH); 1750; 1735 (CO); 1315; 1165 (SO_2); 1260; 1240; 1200 (C-O) cm^{-1}.- ^{1}H-NMR: δ = 0.30 [s, 6H, $Si(CH_3)_2$], 1.00 ([s, 9H, $SiC(CH_3)_3$], 2.10 (s, 3H, $COCH_3$), 4.05 (dd, J = -13.5 Hz, 2 Hz, 1H, 4'-H), 4.69 (dd, J = -13.5 Hz, 5.5 Hz, 1H, 4-H), 5.93 (dd, J = 5.5 Hz, 2 Hz, 1H, 3-H).- $C_{10}H_{21}NO_4SSi$ (279.4) Calcd. C 43.0 H 7.58 N 5.0 S 11.5 Found C 43.2 H 7.56 N 5.1 S 11.2.

2-(Dimethylthexylsilyl)-1,2-thiazetidin-3-ylacetate 1,1-Dioxide (**2b**)

From 3.80 g (10 mmol) of **1b** as described for **2a**, R_f = 0.69; yield 1.7 g (57%), colorless oily liquid.- IR: $\tilde{\nu}$ = 3000; 2960; 2900 (CH); 1750 (CO); 1325; 1170 (SO_2); 1200 (C-O) cm^{-1}.- ^{1}H-NMR: δ = 0.30 (s, 3H, $SiCH_3$), 0.33 (s, 3H, $SiCH_3$), 0.90 (s, 12 H, thexyl-H), 1.68 (mc, 1H, thexyl-H), 2.10 (s, 3H, $COCH_3$), 4.03 (dd, J = -13 Hz, 2 Hz, 1H, 4'-H), 4.66 (dd, J = -13 Hz, 5.5 Hz, 1H, 4-H), 5.95 (dd, J = 5.5 Hz, 2 Hz, 1H, 3-H).- $C_{12}H_{25}NO_4SSi$ (307.5) Calcd. C 46.9 H 8.20 N 4.6 Found C 46.9 H 8.05 N 4.7.

2-(tert-Butyldiphenylsilyl)-1,2-thiazetidin-3-ylacetate 1,1-Dioxide (**2c**)

From 0.48 g (1 mmol) of **1c** as described for **2a**, R_f = 0.75; yield 0.12 g (30%) colorless crystals, m.p. 101°C (pentane).- IR: $\tilde{\nu}$ = 3040; 2950; 2860 (CH); 1735 (CO); 1320; 1160 (SO_2); 1200 (C-O); 740; 710 (ar) cm^{-1}.- ^{1}H-NMR: δ = 1.25 [s, 9H, $SiC(CH_3)_3$], 1.65 (s, 3H, $COCH_3$), 4.05 (dd, J = -13 Hz, 2 Hz, 1H, 4'-H), 4.70 (dd, J = -13 Hz, 6 Hz, 1H, 4-H), 5.68 (dd, J = 6 Hz, 2 Hz, 1H, 3-H), 7.61 (mc, 10 H ar).- $C_{20}H_{25}NO_4SSi$ (403.6) Calcd. C 59.5 H 6.25 N 3.5 S 7.9 Found C 59.6 H 6.25 N 3.5 S 7.6.

3-Benzylthio-1,2-thiazetidine 1,1-Dioxide (**3a**)

8 Mmol of triethylamine are dissolved in 20 ml of acetonitril and added to an ice cold solution of 1.1 g (4 mmol) of **2a** and of 1.0 g (8 mmol) of benzylmercaptan in 30 ml of acetonitril. After stirring for 2 h at 0°C, the mix-ture is diluted with 50 ml of ethyl acetate, washed with cold satd. brine, the org. layer is dried with $MgSO_4$ and evaporated *in vacuo*; yield 0.7 g (76%), colorless crystals, m.p. 68°C (chloroform/CCl_4).- IR: $\tilde{\nu}$ = 3430; 3275 (NH); 3050; 2960 (CH); 1490 (ar); 1360; 1180 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_9H_{11}NO_2S_2$ (229.3) Calcd. C 47.1 H 4.83 N 6.1 S 28.0 Found C 47.0 H 4.89 N 6.2 S 27.9.

3-Benzylthio-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-Dioxide (**4a**)

8 Mmol of triethylamine are dissolved in 20 ml of acetonitrile and added to an ice cold solution of 1.1 g (4 mmol) of **2a** and of 1.0 g (8 mmol) of benzylmercaptan in 30 ml of acetonitrile. After stirring for 2 h at 0°C, the mixture is diluted with 50 ml of ethyl acetate, washed with cold satd. brine, the org. layer is dried with $MgSO_4$ and evaporated *in vacuo*. The residue is dissolved in 30 ml of THF and cooled under N_2 to -78°C, 5.5 mmol of BuLi and after 2 min, 0.83 g (5.5 mmol) of *tert*-butylchlorodimethylsilane are added, stirring is continued for 15 min, the mixture is warmed to room temp., and the solvent is evaporated *in vacuo*, purification by FC (n-hexane/ethyl acetate 3:2), R_f = 0.56; yield 0.89 g (52%), yellow oily liquid.- IR: $\tilde{\nu}$ = 2950; 2920; 2850 (CH); 1490; 700 (ar); 1360; 1145 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{15}H_{25}NO_2S_2Si$ (343.6) Calcd. C 52.4 H 7.33 N 4.1 Found C 52.7 H 7.15 N 4.2.

2-(Dimethylthexylsilyl)-3-benzylthio-1,2-thiazetidine 1,1-Dioxide (**4b**)

From 1.4 g (5 mmol) of **2a**, 1.26 g (10 mmol) of benzylmercaptan, 1.0 g (10 mmol) of triethylamine, and 1.0 g (5.5 mmol) of chlorodimethylthexylsilane as described for **4a**, R_f = 0.61; yield 950 mg (51%), yellow oily liquid.- IR: $\tilde{\nu}$ = 3000; 2900 (CH); 1470; 700 (ar); 1340; 1155 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{17}H_{29}NO_2S_2Si$ (371.6) Calcd. C 54.9 H 7.87 N 3.8 Found C 55.2 H 7.96 N 4.0.

2-(tert-Butyldimethylsilyl)-3-phenylthio-1,2-thiazetidine 1,1-Dioxide (**4c**)

From 1.4 g (5 mmol) of **2a**, 1.1 g (10 mmol) of thiophenol, 1.0 g (10 mmol) of triethylamine, 5 mmol of BuLi, and 0.83 g (5.5 mmol) of *tert*-butylchlorodimethylsilane as described for **4a**, R_f = 0.62, yield 0.85 g (52%), yellow oily liquid.- IR: $\tilde{\nu}$ = 3000; 2960; 2900 (CH); 1475; 700 (ar); 1320; 1155 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{14}H_{23}NO_2S_2Si$ (329.6) Calcd. C 51.0 H 7.03 N 4.3 Found C 51.1 H 7.00 N 4.3.

2-(tert-Butyldimethylsilyl)-3-(tert-butylthio)-1,2-thiazetidine 1,1-Dioxide (**4d**)

From 1.4 g (5 mmol) of **2a**, 0.9 g (10 mmol) of *tert*-butylmercaptan, and 0.83 g (5.5 mmol) of *tert*-butylchlorodimethylsilane as described for **4a**, R_f = 0.60; yield 0.78 g (50%), yellow oily liquid.- IR: $\tilde{\nu}$ = 2950; 2920; 2860 (CH); 1310; 1145 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{12}H_{27}NO_2S_2Si$ (309.6) Calcd. C 47.6 H 8.79 N 4.5 Found C 47.4 H 8.75 N 4.6.

2-(tert-Butyldimethylsilyl)-3-(ethoxycarbonylmethylthio)-1,2-thiazetidine 1,1-Dioxide (**4e**)

From 1.4 g (5 mmol) of **2a**, 1.2 g (10 mmol) of ethyl mercaptoacetate, and 0.83 g (5.5 mmol) of *tert*-butylchlorodimethylsilane, R_f = 0.55; yield 0.86 g (51%), yellow oily liquid.- IR: $\tilde{\nu}$ = 2950; 2920; 2860 (CH); 1730 (CO); 1310; 1150 (SO_2); 1190 (C-O) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{12}H_{25}NO_4S_2Si$ (229.6) Calcd. C 42.4 H 7.42 N 4.1 Found C 42.2 H 7.38 N 4.2.

2-Allylthio-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-Dioxide (**4f**)

From 1.4 g (5 mmol) of **2a**, 1.06 g (10 mmol) of allylmercaptan, and 0.83 g (5.5 mmol) of *tert*-butylchlorodimethylsilane as described for **4a**, R_f = 0.50; yield 0.76 g (51%), yellow oily liquid.- IR: $\tilde{\nu}$ = 3080; 3040; 2950 (CH); 1630 (C=C); 1310; 1150 (SO_2) cm^{-1}.- ^{1}H-NMR: Table 1.- $C_{11}H_{23}NO_2S_2Si$ (293.5) Calcd. C 45.0 H 7.90 N 4.8 Found C 44.7 H 7.75 N 4.9.

2-Hydroxy-2,4,4-trimethyl-1-aza-5,8-dithiabicyclo[4.2.0]octane 8,8-Dioxide (**5**)

0.8 g (8 mmol) of triethylamine in 20 ml of acetonitril are added to an ice cold solution of 1.1 g (4 mmol) **2a** and of 1.06 g (8 mmol) of 4-mercapto-4-methyl-2-pentanone. After stirring for 2 h at 0°C, the mixture is diluted with 50 ml of ethyl acetate, hydrolized with satd. NaCl solution, the org. layer is dried with $MgSO_4$ and evaporated *in vacuo*; yield 0.10 g (11%), colorless crystals, m.p. 110°C (CCl_4/chloroform).- IR: $\tilde{\nu}$ = 3460 (OH); 3040; 2960; 2920 (CH); 1370; 1300; 1150 (SO_2) cm^{-1}.- ^{1}H-NMR: δ = 1.31 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.67 (d, J = -15.5 Hz, 1H, 3-H), 1.78 (s, 3H, CH_3), 2.05 (d, J = -15.5 Hz, 1H, 3'-H), 2.66 (br. s, 1H, OH), 3.90 (dd, J = -12 Hz, 3 Hz, 1H, 7'-H), 4.41 (dd, J = -12 Hz, 7 Hz, 1H, 7-H), 5.03 (dd, J = 7 Hz, 3 Hz, 1H, 6-H).- $C_8H_{15}NO_3S_2$ (237.3) Calcd. C 40.5 H 6.37 N 5.9 S 27.0 Found C 40.4 H 6.38 N 6.0 S 27.1.

Trimethylsilylthiomethylbenzene

Under N_2 30 mmol of BuLi are added to a solution of 3.72 g (30 mmol) of phenylmethanethiol in 15 ml of THF at -78°C. After 1 min 3.8 g (35 mmol) of chlorotrimethylsilane is added with stirring. Stirring is continued for 15 min, the mixture is warmed to room temp., the solvent is evaporated *in vacuo*, the residue is dissolved in 10-20 ml of n-pentane, then filtered through charcoal, and the solvent is evaporated; yield 4.9 g (84%), colorless liquid, b.p. 57°C/0.25 Torr.

Trimethylsilylthiobutane

From 3.6 g (40 mmol) of butanethiol, 40 mmol of BuLi and 4.9 g (45 mmol) of chlorotrimethylsilane as described above; yield 5.2 g (80%), colorless liquid, b.p. 60°C/20 Torr (ref.[14]: 167-172°C).

2,2-Bis(benzylthio)-1-ethanesulfonamide (**6a**)

Under N_2 1.2 g (5.4 mmol) of trimethylsilyl trifluoromethanesulfonate in 2 ml of dichloromethane are slowly added to a solution of 1.0 g (3.6 mmol) of **2a** and of 1.4 g (7.2 mmol) of trimethylsilylthiomethylbenzene in 10 ml of dichloromethane at -78°C. After stirring for 2 h at -78°C, the mixture is hydrolized with a cold satd. solution of $NaHCO_3$, the org. layer is dried with $MgSO_4$, and the solvent is evaporated *in vacuo*; yield 1.0 g (80%), colorless crystals, m.p. 115°C (diethyl ether).- IR: $\tilde{\nu}$ = 3360 (NH); 3080; 3040; 2940 (CH); 1495; 705 (ar); 1350; 1330; 1300; 1170; 1150 (SO_2) cm^{-1}.- ^{1}H-NMR: δ = 3.43 (d, J = 7 Hz, 2H, SO_2-CH_2), 3.83 (s, 4H, ar-CH_2), 4.03 (t, J = 7 Hz, 1H, 2-H), 4.68 (s, 2H, NH_2), 7.29 (s, 10 H ar).- $C_{16}H_{19}NO_2S_3$ (353.5) Calcd. C 54.4 H 5.42 N 4.0 Found C 53.4 H 5.30 N 4.2.

2,2-Bis(butylthio)-1-ethanesulfonamide (**6b**)

From 1.0 g (3.6 mmol) of **2a**, 1.3 g (8 mmol) of (trimethylsilylthio)-n-butane, and 1.2 g (5.4 mmol) of trimethylsilyl trifluoromethanesulfonate as described for **6a**, purification by FC (n-hexane/ethyl acetate 4:1), R_f = 0.52; yield 400 mg (40%), yellow oily liquid.- IR, ^{1}H-NMR: Table 2.- $C_{10}H_{23}NO_2S_3$ (285.5) Calcd. C 42.1 H 8.12 N 4.9 Found C 42.2 H 8.00 N 5.0.

2,2-Bis(benzylthio)-N-(tert-butyldimethylsilyl)-1-ethanesulfonamide (**6c**)

At -78°C 1.3 mmol of BuLi and after 1 min 200 mg (1.3 mmol) of *tert*-butylchlorodimethylsilane in 2 ml of THF are added to a solution of 300 mg (0.85 mmol) of **6a** in 10 ml of THF, the mixture is stirred for 15 min at -78°C, warmed to room temp., the solvent is evaporated *in vacuo*, and the residue is purified by FC (n-hexane/ethyl acetate 4:1), R_f = 0.45; yield 300 mg (75%), colorless crystals, m.p. 55°C (pentane).- IR, ^{1}H-NMR: Table 2.- $C_{22}H_{33}NO_2S_3Si$ (467.8) Calcd. C 56.5 H 7.11 N 3.0 Found C 56.4 H 7.06 N 3.1.

2,2-Bis(benzylthio)-N-(dimethylthexylsilyl)-1-ethanesulfonamide (**6d**)

From 650 mg (1.8 mmol) of **6a**, 2.8 mmol BuLi, and 500 mg (2.8 mmol) of chlorodimethylthexylsilane as described for **6c**, R_f = 0.50; yield 850 mg (95%), yellow oily liquid.- IR, ^{1}H-NMR: Table 2.- $C_{24}H_{37}NO_2S_3Si$ (495.9) Calcd. C 58.1 H 7.52 N 2.8 Found C 58.0 H 7.40 N 3.0.

2,4,4-Trimethyl-1-aza-5,8-dithiabicyclo[4.2.0]oct-2-ene 8,8-Dioxide (**7**)

Under N_2 0.23 g (1.5 mmol) of freshly distilled $POCl_3$ are added to an ice cold solution of 0.24 g (1 mmol) of **5** in 25 ml of pyridine. Stirring is continued for 4 h at 0°C, whilst the color of the mixture changes to dark violet. After addition of 100 ml of chloroform, the mixture is hydrolized with satd. brine. The org. layer is washed with brine/HCl, $KHCO_3$ solution (5%) and again with brine. The org. layer is separated, dried with $MgSO_4$, and evaporated *in vacuo*; yield 0.12 g (55%), colorless crystals, m.p. 111°C (n-hexane/ethyl acetate).- IR: $\tilde{\nu}$ = 3040; 2960; 2860 (CH); 1660 (C=C); 1325; 1160 (SO_2) cm^{-1}.- ^{1}H-NMR: δ = 1.39 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.00 (d, J = 1 Hz, 3H, CH_3), 4.03 (dd, J = -12 Hz, 3 Hz, 1H, 7'-

Table 1: ^{1}H-NMR data of 3-thiosubstituted β-sultams **3** and **4** (from 80 MHz spectra, $CDCl_3$, δ [ppm], J [Hz])

(from 80 MHz spectra, $CDCl_3$, δ [ppm], J [Hz])

compound	δ_{3-H}	δ_{4-H}	$\delta_{4'-H}$	$\delta_{R'}$	$J_{4/4'}$	$J_{3/4'}$	$J_{3/4}$
3a	4.65	4.45	4.05	3.93/7.29	12	3	7
4a	4.64	4.44	4.08	3.90/7.30	12	3	7
4b	4.64	4.45	4.05	3.90/7.30	12	3	7
4c	4.95	4.64	4.24	7.44	13	4	7
4d	4.66	4.26	4.20	1.30	9	2	6
4e	4.81	4.65	4.39	1.3/4.2/4.49	9	2	6
4f	4.66	4.58	4.28	3.4/5.23/5.89	13	2	7

Table 2: Spectroscopic data of **6**, **8** and **9**. (IR $\tilde{\nu}$ [cm^{-1}], KBr or film; ^{1}H-NMR from 80 MHz spectra, $CDCl_3$, δ [ppm], J [Hz])

compound	ν_{NHR}/ν_{SO2}	δ_{NHR}	δ_{2-H}	δ_{1-H}	$J_{1,2}$
6a	3360/1350,1150	4.68	4.03	3.34	7
6b	3350/1340,1150	5.08	4.25	3.56	7
6c	3260/1340,1150	4.23	4.05	3.30	7
6d	3250/1350,1150	4.26	4.10	3.34	7
8	3400/1370,1150	4.95	4.45	3.74	5
9b	3250/1350,1150	4.33	5.30	3.41	6

H), 4.69 (dd, J = -12 Hz, 7 Hz, 1H, 3-H), 5.00 (dd, J = 7 Hz, 3 Hz, 1H, 6-H).- $C_8H_{13}NO_2S_2$ (219.3) Calcd. C 43.8 H 5.97 N 6.4 S 29.2 Found C 43.9 H 5.99 N 6.4 S 29.1.

2,2-Bis(benzylsulfinyl)-N-(dimethylthexylsilyl)-1-ethanesulfonamide (**8**)

At 0°C, 600 mg of MCPBA (2.5 mmol, calcd. 70%) are added to a solution of 1.2 g of **6d** in 20 ml of dichloromethane. After 30 min, 50 ml of dichloromethane are added, the mixture is washed with a Na_2SO_3-solution, then with $NaHCO_3$-solution, the org. layer is separated, dried with $MgSO_4$, evaporated *in vacuo*, and the residue is purified by FC as described for **6**, R_f = 0.25; yield 900 mg (70%), colorless crystals, m.p. 85°C (pentane).- IR, ^{1}H-NMR: Table 2.- $C_{24}H_{37}NO_4S_3Si$ (527.8) Calcd. C 54.6 H 7.07 N 2.7 Found C 54.8 H 6.82 N 2.9.

2,2-Bis(benzyloxy)-N-(tert-butyldimethylsilyl)-1-ethanesulfonamide (**9b**)

From 1.0 g (3.6 mmol) of **2a**, 1.35 g (7.5 mmol) of (trimethylsilyloxy)phenylmethane, and 1.2 g (5.4 mmol) of trimethylsilyl trifluoromethanesulfonate as described for **6a**. The crude product **9a** is silylated with 500 mg (3.7 mmol) of *tert*-butylchlorodimethylsilane as described for **6c** and purified by FC (n-hexane/ethyl acetate 3:2), R_f = 0.45; yield 200 mg (13%), colorless oily liquid.- IR, ^{1}H-NMR: Table 2.- $C_{22}H_{33}NO_4SSi$ (435.7) Calcd. C 60.6 H 7.64 N 3.2 Found C 60.7 H 7.73 N 3.3.

References and Notes

1 D. Grimm, H. Bestian (Farbwerke Hoechst AG) German Offen. 1906401 (8.2.69); *Chem. Abstr.* **1979**, *73*, 98777P.

2 S. Mickel, *Aldrichimica Acta* **1985**, *18*, 95-99.

3 P. Schwenkkraus, Ph.D. Thesis, University of Freiburg, **1987**.

4 K. Clauß, D. Grimm, G. Prossel, *Liebigs Ann. Chem.* **1974**, 539-560.

5 M. Zsigmondy, Ph.D. Thesis, University of Freiburg, **1990**.

6 N. Ono, A. Kamimura, A. Kaji, *J. Org. Chem.* **1986**, *51*, 2139-2142.

7 H. Plagge, Ph.D. Thesis, University of Freiburg, **1988**.

8 H.W. Schnabel, D. Grimm, H. Jensen, *Liebigs Ann. Chem.* **1974**, 477-495.

9 F. Asinger, M. Thiel, W. Höringklee, *Liebigs Ann. Chem.* **1957**, *610*, 1-16.

10 For complete spectroscopic data of all compounds see: S. Merkle, Ph.D. Thesis, University of Freiburg, **1991**.

11 M. Müller, E. Meyle, E.F. Paulus, H. Plagge, H.-H. Otto, *Liebigs Ann. Chem.* **1989**, 975-983.

12 a) A.G.M. Barrett, P. Quayle, *J. Chem. Soc., Chem. Commun.* **1981**, 1076-1077. b) R.P. Attrill, A.G.M. Barrett, P. Quayle, J. van der Westhuizen, *J. Org. Chem.* **1984**, *49*, 1679-1682. c) A. Arrieta, F.P. Cossío, J.M. García, B. Lecea, C. Palomo, *Tetrahedron Lett.* **1988**, *29*, 3129-3132.

13 a) H. Emde, D. Domsch, H. Feger, U. Frick, A. Götz, H. H. Hergott, K. Hofmann, W. Kober, K. Krägeloh, T. Oesterle, W. Steppan, W. West, G. Simchen, *Synthesis* **1982**, 1-26. b) R. Noyori, S. Murata, M. Suzuki, *Tetrahedron* **1981**, *23*, 3899-3910.

14 S.H. Langer, S. Connell, I. Wender, *J. Org. Chem.* **1958**, *23*, 50-58.

15 This method is much cheaper and more convenient than the use of hexamethyldisilazane as described in ref.[14].

16 For a detailed discussion see S. Merkle, Ph.D. Thesis, University of Freiburg, **1991**.

17 W. Gerrad, K.D. Kilburn, *J. Chem. Soc.* **1956**, 1536-1539.

[Ph212]