SYNTHESIS AND REACTIONS OF 4-(α-AMINO-ARYLIDENE)THIAZETIDINE 1,1-DIOXIDES

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Dedicated to Professor E. C. Taylor, Princeton on the occasion of his 70th birthday.

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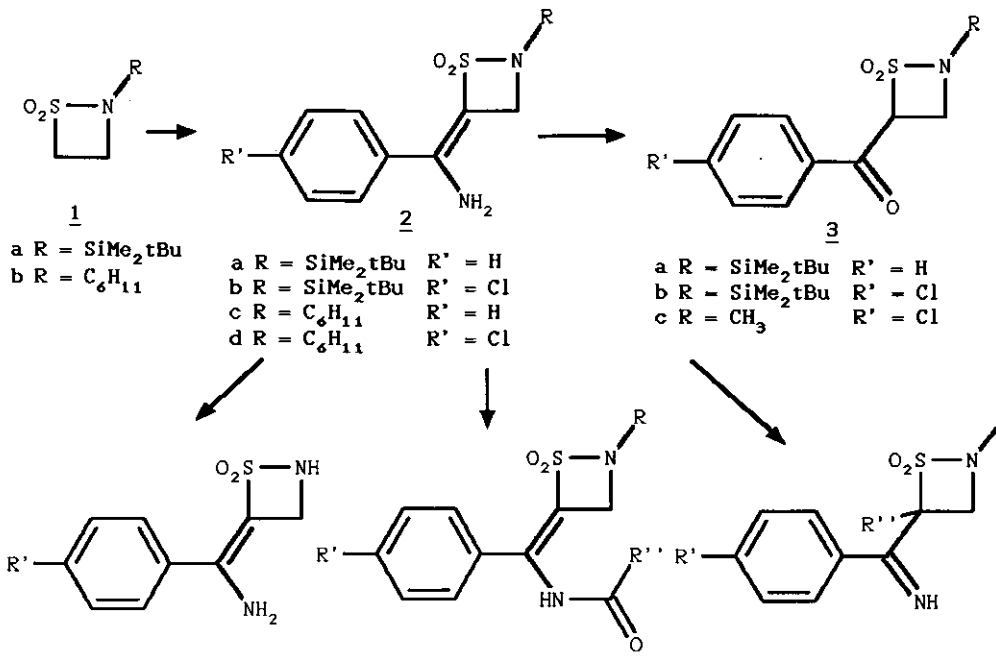
Abstract - β-Sultams react as highly potent sulfonyl analogues of β-lactams with aromatic nitriles to the title compounds (**2**). Hydrolysis, reduction, and reactions of **2** with acylating and alkylating agents are described. Some of the compounds show a week β-lactamase inhibition.

1,2-Thiazetidine 1,1-dioxide (β-sultam) (**1**), a highly reactive sulfonyl analogue of the β-lactam ring, might be valuable for synthetic chemistry especially for the construction of potent drugs[1]. We have presented[2] examples of reactions at the nitrogen and at C-4. Here, we describe for the first time reactions with nitriles allowing the formation of β-aminosulfonyl substituted enamines. These might behave as isosters of the biologically active asparenomycins[3] and alkoxy(acyloxy)methylene penicillins[4].

According to Kaiser[5] and Katritzky[6] we reacted **1** with benzonitriles and n-BuLi by dissolving **1** in THF, cooling to -78°C and, after deprotonation



1

a R = $SiMe_2tBu$
b R = C_6H_{11}

2

a R = $SiMe_2tBu$ R' = H
b R = $SiMe_2tBu$ R' = Cl
c R = C_6H_{11} R' = H
d R = C_6H_{11} R' = Cl

3

a R = $SiMe_2tBu$ R' = H
b R = $SiMe_2tBu$ R' = Cl
c R = CH_3 R' = Cl

4

a R = H
b R = Cl

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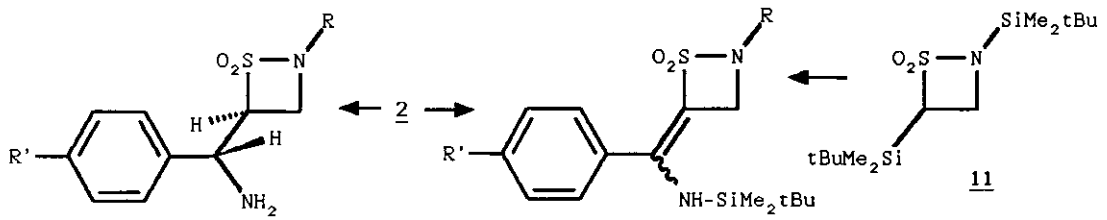
5 a R = $SiMe_2tBu$ R'= Cl R''= CH_3
b R = $SiMe_2tBu$ R'= Cl R''= C_6H_5
c R = $SiMe_2tBu$ R'= Cl R''= C_6H_5O
d R = C_6H_{11} R'= Cl R''= CH_3
e R = C_6H_{11} R'= Cl R''= C_6H_5
f R = C_6H_{11} R'= Cl R''= C_6H_5O

6 a R = H R'= Cl R''= CH_3
b R = H R'= Cl R''= C_6H_5
c R = H R'= Cl R''= C_6H_5O

7

R = $SiMe_2tBu$ R'= Cl
a R'' = CH_3
b R'' = $CH_2C_6H_5$
c R'' = $CH_2C_6H_4NO_2$(p)
d R'' = $CH_2C_6H_4Br$(p)
e R'' = $CH_2C_6H_4CH_3$(p)
f R'' = SO_2CH_3



8 / 9

8 a R = $SiMe_2tBu$ R'= H
b R = $SiMe_2tBu$ R'= Cl
9 R = H R'= Cl

10

R = $SiMe_2tBu$ R' = Cl

11

with n-BuLi, adding the aromatic nitrile yielding the enamino-β-sultams (**2**). Ir and ^{1}H nmr data show that the enamine form is preferred in acetone solution, while the imine form is favored in chloroform. The (E)-configuration is established by NOE spectra.[7] During column chromatography (CC) with silica gel the enamine/imine function was hydrolized, and we obtained the acyl-β-sultams (**3**). The silyl group was removed by catalytic amounts of tetrabutylammonium fluoride (TBAF) yielding **4**.

Some reactions of the enamino-β-sultams (**2**) are summarized in the Scheme. N-Acyl enamino-β-sultams (**5**) are obtained from **2** with acyl halides in the presence of pyridine in ether. The desilylation to **6** was done by TBAF in THF. When **2** was alkylated with an alkyl iodide and LDA in THF, alkylation occurred only at C-4 resulting in the imino alkyl derivatives (**7**). The reduction of the enamine function of **2** is best done by $NaBH_4$ in the presence of glacial acetic acid in THF. Reduction products (**8**) were obtained as mixtures of diastereoisomers and were separated by CC. Desilylation yielded **9**. While alkylation of **2** occurred at C-4, silylation with tert-butylchlorodimethylsilane at -78° C gave an E/Z mixture (1:2) of N-silylated enamines (**10**). An identical mixture was obtained, when **11** reacted with LDA and 4-chlorobenzonitrile. But, when the silylation was done with tert-butyldimethylsilyltrifluoromethane sulfonate at room temperature, only the E-isomer was isolated. And when the silylation was done at room temperature with triethylamine or pyridine no reaction at all occurred.

Using the nitrocephine assay, we demonstrated, that the acylated enamines (**5**) exhibit a weak β-lactamase inhibition. None of the prepared compounds showed antibacterial activity.

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EXPERIMENTAL

For general remarks see ref.[2]

Reaction of **1** with aromatic nitriles: At -78°C, 9.4 ml (15 mmol) of n-BuLi are added to 10 mmol of **1** in 100 ml of THF, and after 45 sec a cooled solution of 16 mmol of the nitrile in 10 ml of THF is added. The mixture is stirred for 30 min, warmed up to room temperature, 150 ml of satd. NaCl solution are added, the organic layer is separated, dried with sodium sulfate, evaporated in vacuo, and worked up.

Acylation of **2**: To 1 mmol of **2** at 0°C in 50 ml of dry ether 0.08 ml (1 mmol) of pyridine and 1 mmol of the acyl halide are added. The mixture is stirred for 15 min with cooling, and 14 h at room temperature, pyridine-HCl is separated, the solution is concentrated in vacuo, and the residue is worked up.

Desilylation of **5**: Under N_2, 1 mmol of TBAF solved in THF (≈ 1 M solution, Fluka 86900) is added to 1 mmol of **5** in 30 ml of THF; the mixture is stirred at room temperature for 3 min, 50 ml of satd. NaCl solution are added, the organic layer is dried with Na_2SO_4, concentrated in vacuo, and the residue is purified by CC (silica gel, chloroform/acetone 1:1).

Alkylation of **2**: At -78°C, a solution of 1.5 mmol of **2** in 15 ml of THF is dropwise added to 1.6 mmol of LDA in 20 ml of THF. After 10 min stirring, an equimolar amount of the alkylating agent in 5 ml of THF is added. Stirring is continued for 15-30 min, 50 ml of satd. NaCl solution are added, the aquous layer is extracted with 30 ml of CH_2Cl_2, the combined organic layers are dried with Na_2SO_4, evaporated in vacuo, and worked up.

Reduction of **2** with $NaBH_4$: Under N_2, 1 mmol of **2** is dissolved in 20 ml of THF, 74 mg (2 mmol) of $NaBH_4$ and 1 ml (18 mmol) of glacial acetic acid are added. The mixture is stirred for 10 min, refluxed for 15 min, cooled to room temperature, and 40 ml of satd. $NaHCO_3$ solution are added. The aquous layer is twice extracted with 30 ml of CH_2Cl_2, the organic layers are dried with Na_2SO_4, and the solvent is evaporated in vacuo.

2-(tert-Butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**1a**): see ref.[8]

2-Cyclohexyl-1,2-thiazetidine 1,1-dioxide (**1b**): From 6.3 g (30 mmol) of cyclohexylaminoethanesulfonic acid as **1a**; Yield 4.3 g (76%), mp 61°C (ether). Ir: 2920 cm^{-1}, (CH), 1310, 1160, 1140 (SO_2). ^1H Nmr (60 MHz): δ = 1.05-2.17 (m, 10 H, CH_2-cyclohexyl), 3.17 (mc, 1 H, CH-cyclohexyl), 3.17 [mc(t), 2 H, 3-H, 3'-H], 4.02 [mc(t), 2 H, 4-H, 4'-H].

(E)-4-(α-Aminobenzylidene)-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**2a**): Yield 1.65 g (51%), mp 139°C (methanol). Ir: 3470 cm^{-1}, 3360, 3240 (NH), 1660 (C=C), 1630 (C=N), 1290, 1155, 1130 (SO_2). ^1H Nmr (acetone-d_6): δ = 0.25 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 3.88 (s, 2 H, 3-H, 3'-H), 5.37 (brs, 2 H, NH_2), 7.25-7.92 (m, 5 H, arH). ^1H Nmr imine tautomer: δ = 0.27 (s, 6 H, Si-Me), 1.00 (s, 9 H, Si-tBu), 3.52 (dd, J = 5.5 Hz, 8 Hz, 1 H, 3'-H), 4.2 [dd(mc), J = 5.4 Hz, 5.5 Hz, 1 H, 3-H], 5.76 (dd, J = 8 Hz, 5.4 Hz, 1 H, 4'-H), 7.3-7.8 (m, 5 H, arH), 10.47 (brs, 1 H, NH).

(E)-4-(α-Amino-4-chlorobenzylidene)-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**2b**): Yield 1.9 g (53%) mp 165°C (methanol). Ir: 3440 cm^{-1}, 3350, 3230 (NH), 1655 (C=C), 1625 (C=N), 1290, 1150, 1130 (SO_2). ^1H Nmr (acetone-d_6): δ = 0.25 (s, 6 H, Si-Me), 1.0 (s, 9 H, Si-tBu), 3.9 (s, 2 H, 3-H, 3'-H), 5.61 (brs, 2 H, NH_2), 7.46-7.85 (AA'BB', 4 H, arH). ^1H Nmr imine tautomer: δ = 0.26 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 3.50 (dd, J = 5 Hz, 8 Hz, 1 H, 3'-H), 4.18 [dd(mc), J = 5 Hz, 5 Hz, 1 H, 3-H], 5.68 (dd, J = 8 Hz, 5 Hz, 1 H, 4'-H), 7.3-7.8 (m, 4 H, arH), 10.47 (brs, 1 H, NH).

(E)-4-(α-Aminobenzylidene)-2-cyclohexyl-1,2-thiazetidine 1,1-dioxide (**2c**): Yield 700 mg (24%), mp 122°C (pentane). Ir: 3470 cm^{-1}, 3350, 3240 (NH), 1660 (C=C), 1630 (C=N), 1280, 1165, 1150, 1135 (SO_2). ^1H Nmr (acetone-d_6): δ = 1.1-2.1 (m, 10 H, CH_2-cyclohexyl), 3.10 (mc, 1 H, CH-cyclohexyl), 3.70 (s, 2 H, 3-H, 3'-H), 5.47 (brs, 2 H, NH_2), 7.3-7.9 (m, 5 H, arH).

(E)-4-(α-Amino-4-chlorobenzylidene)-2-cyclohexyl-1,2-thiazetidine 1,1-dioxide (**2d**): Yield 900 mg (28%), mp 176°C (ether). Ir: 3460 cm^{-1}, 3350, 3240 (NH), 1660 (C=C), 1630 (C=N), 1280, 1160, 1140 (SO_2). ^1H Nmr (acetone-d_6/DMSO-d_6 1:1): δ = 1.0-2.1 (m, 10 H, CH_2-cyclohexyl), 3.05 (mc, 1 H, CH-cyclohexyl), 3.67 (s, 2 H, 3-H, 3'-H), 5.87 (brs, 2 H, NH_2), 7.4-7.9 (AA'BB', J = 9 Hz, 4 H, arH).

4-Benzoyl-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**3a**): Yield 1.8 g (55%), mp 87°C (cyclohexane). Ir: 1695 cm^{-1} (C=O), 1310, 1160 (SO_2). ^1H Nmr (60 MHz): δ = 0.30 (s, 6 H, Si-Me), 1.00 (s, 9 H, Si-tBu), 3.43 (dd, J = 5 Hz, 8 Hz, 1 H, 3'-H), 4.01 [dd(t), J = 5 Hz, 5 Hz, 1 H, 3-H] 5.97 (dd, J = 8 Hz, 5 Hz, 1 H, 4'-H), 7.4-8.1 (m, 5 H, arH).

2-(tert-Butyldimethylsilyl)-4-(4-chlorobenzoyl)-1,2-thiazetidine 1,1-dioxide (**3b**): Yield 2.5 g (69%), mp 116°C (pentane). Ir: 1695 cm^{-1} (C=O), 1305, 1170 (SO_2). ^1H Nmr: δ = 0.30 (s, 6 H, Si-Me), 1.00 (s, 9 H, Si-tBu), 3.46 (dd, J = 5.5 Hz, 7.5 Hz, 1 H, 3'-H), 4.03 [dd (t), J = 5 Hz, 5.5 Hz, 1 H, 3-H], 5.91 (dd, J = 7.5 Hz, 5 Hz, 1 H, 4'-H), 7.4-8.1 (AA'BB', J = 9 Hz, 4 H, arH).

4-(4-Chlorobenzoyl)-2-methyl-1,2-thiazetidine 1,1-dioxide (**3c**): Yield 110 mg (43%), mp 150°C (pentane). Ir: 3100 cm^{-1} (CH), 1680 (C=O), 1330, 1320, 1310, 1160 (SO_2). ^1H Nmr: δ = 2.70 (s, 3 H, Me), 3.35 (dd, J = 6 Hz, 8 Hz, 1 H, 3'-H), 3.70 [dd(t), J = 6 Hz, 6 Hz, 1 H, 3-H], 5.77 (dd, J = 8 Hz, 6 Hz, 1 H, 4'-H), 7.45-7.95 (AA'BB', 4 H, arH).

(E)-4-(α-Aminobenzylidene)-1,2-thiazetidine 1,1-dioxide (**4a**): Yield 140 mg (66%), mp 125°C (chloroform). Ir: 3440 cm^{-1}, 3350, 3260, 3240 (NH), 1655 (C=C), 1630 (C=N), 1290, 1145 (SO_2). ^1H Nmr (acetone-d_6): δ = 3.83 (s, 2 H, 3-H, 3'-H), 5.50 (brs, 3 H, NH), 7.3-8.1 (m, 5 H, arH).

(E)-4-(α-Amino-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**4b**): Yield 190 mg (74%), mp 159°C (chloroform). Ir: 3460 cm^{-1}, 3360, 3280, 3240 (NH), 1660 (C=C), 1630 (C=N), 1280, 1150, 1135 (SO_2). ^1H Nmr (acetone-

d_6/DMSO-d_6 1:1): δ = 3.79 (s, 2 H, 3-H, 3'-H), 5.90 (brs, 2 H, NH_2), 6.80 (brs, 1 H, NH), 7.35-7.9 (AA'BB', 4 H, arH).

(E)-4-(α-Acetamido-4-chlorobenzylidene)-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**5a**): Yield 190 mg (47%), mp 123°C (pentane). Ir: 3280 cm^{-1} (NH), 1710 (C=O), 1660 (C=C), 1510 (amide II), 1280, 1140 (SO_2). ^1H Nmr (250 MHz): δ = 0.28 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 2.12 (s, 3 H, CO-Me), 4.19 (s, 2 H, 3-H, 3'-H), 6.80 (brs, 1 H, NH), 7.35-7.6 (AA'BB', 4 H, arH).

(E)-2-(tert-Butyldimethylsilyl)-4-(α-phenylacetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**5b**): Yield 240 mg (50%), mp 159°C (decomp.) (ether). Ir: 3310 cm^{-1} (NH), 1715 (C=O), 1680 (C=C), 1510 (amide II), 1290, 1150 (SO_2). ^1H Nmr (250 MHz): δ = 0.26 (s, 6 H, Si-Me), 0.97 (s, 9 H, Si-tBu), 3.68 (s, 2 H, CH_2), 4.19 (s, 2 H, 3-H, 3'-H), 6.60 (brs, 1 H, NH), 7.2-7.45 (m, 9 H, arH).

(E)-2-(tert-Butyldimethylsilyl)-4-(α-phenoxyacetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**5c**): Yield 400 mg (81%), mp 136°C (pentane). Ir: 3300 cm^{-1} (NH), 1710 (C=O), 1680 (C=C), 1510 (amide II), 1295, 1160, 1150 (SO_2). ^1H Nmr: δ = 0.27 (s, 6 H, Si-Me), 1.00 (s, 9 H, Si-tBu), 4.20 (s, 2 H, 3-H, 3'-H), 4.60 (s, 2 H, OCH_2), 6.8-7.65 (m, 9 H, arH), 7.80 (brs, 1 H, NH).

(E)-4-(α-Acetamido-4-chlorobenzylidene)-2-cyclohexyl-1,2-thiazetidine 1,1-dioxide (**5d**): Yield 84 mg (23%), mp 93°C (petroleum ether). Ir: 3300 cm^{-1} (NH), 1710 (C=O), 1670 (C=C), 1510 (amide II), 1300, 1160 (SO_2). ^1H Nmr: δ = 1.0-2.1 (m, 10 H, CH_2-cyclohexyl), 1.93 (s, 3 H, CO-Me), 3.10 (mc, 1 H, CH-cyclohexyl), 3.85 (s, 2 H, 3-H, 3'-H), 7.15-7.6 (m, 4 H, arH, 1 H, NH).

(E)-2-Cyclohexyl-4-(α-phenylacetamido-4-chlorobenzylidene)-1,2-thiaz-etidine 1,1-dioxide (**5e**): Yield 120 mg (27%), mp 144°C (ether/pentane). Ir: 3320 cm^{-1} (NH), 1700 (C=O), 1670 (C=C), 1510 (amide II), 1320, 1160 (SO_2). ^1H Nmr: δ = 1.05-2.05 (m, 10 H, CH_2-cyclohexyl), 3.15 (mc, 1 H, CH-

cyclohexyl), 3.57 (s, 2 H, CH_2), 3.90 (s, 2 H, 3-H, 3'-H), 7.10 (brs, 1 H, NH), 7.15-7.55 (m, 9 H, arH).

(E)-2-Cyclohexyl-4-(α-phenoxyacetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**5f**): Yield 200 mg (43%), mp 126°C (chloroform/petroleum ether). Ir: 3360 cm^{-1} (NH), 1720 (C=O), 1680 (C=C), 1510 (amide II), 1310, 1160 (SO_2). ^1H Nmr: δ = 1.05-2.1 (m, 10 H, CH_2-cyclohexyl), 3.22 (mc, 1 H, CH-cyclohexyl), 3.97 (s, 2 H, 3-H, 3'-H), 4.57 (s, 2 H, O-CH_2), 6.8-7.6 (m, 9 H, arH), 7.82 (brs, 1 H, NH).

(E)-4-(α-Acetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**6a**): Yield 110 mg (42%), mp 156°C (ether). Ir: 3300 cm^{-1} (NH), 1720 (C=O), 1670 (C=C), 1510 (amide II), 1295, 1280, 1160, 1145 (SO_2). ^1H Nmr (acetone-d_6): δ = 2.10 (s, 3 H, CO-Me), 4.05 (d, J = 5 Hz, 2 H, 3-H, 3'-H), 6.72 (t, J = 5 Hz, 1 H, SO_2NH), 7.35-7.75 (AA'BB', 4 H, arH), 8.95 (brs, 1 H, NH-CO).

(E)-4-(α-Phenylacetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**6b**): Yield 150 mg (44%), mp 150°C (chloroform/pentane). Ir: 3280 cm^{-1} (NH), 1700 (C=O), 1660 (C=C), 1500 (amide II), 1295, 1150 (SO_2). ^1H Nmr (acetone-d_6): δ = 3.72 (s, 2 H, CH_2), 3.99 (d, J = 5 Hz, 2 H, 3-H, 3'-H), 6.70 (t, J = 5 Hz, 1 H, SO_2NH), 7.1-7.7 (m, 9 H, arH), 9.05 (brs, 1 H, NHCO).

(E)-4-(α-Phenoxyacetamido-4-chlorobenzylidene)-1,2-thiazetidine 1,1-dioxide (**6c**): Yield 140 mg (38%), mp 145°C (chloroform/pentane). Ir: 3280 cm^{-1}, 3200 (NH), 1690 (C=O), 1665 (C=C), 1295, 1155 (SO_2). ^1H Nmr (acetone-d_6): δ = 4.05 (d, J = 5 Hz, 2 H, 3-H, 3'-H), 4.72 (s, 2 H, OCH_2), 6.83 [mc(t), J = 5 Hz, 1 H, SO_2NH], 6.85-7.8 (m, 9 H, arH), 9.18 (brs, 1 H, NH-CO).

2-(tert-Butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-4-methyl-1,2-thiazetidine 1,1-dioxide (**7a**): Yield 280 mg (51%), mp 99°C (ether). Ir: 3380 cm^{-1}, 3360, 3260 (NH), 1620 (C=N), 1295, 1180, 1160 (SO_2). ^1H Nmr: δ = 0.28 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 1.82 (s, 3 H, Me), 3.08 (d, J

= 6 Hz, 1 H, 3'-H), 4.43 (d, J = 6 Hz, 1 H, 3-H), 7.3-7.65 (m, 4 H, arH), 10.28 (brs, 1 H, NH).

4-Benzyl-2-(tert-butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-1,2-thiazetidine 1,1-dioxide (**7b**): Yield 270 mg (40 %), mp 92°C (ether/pentane). Ir: 3370 cm^{-1}, 3270 (NH), 1615 (C=N), 1310, 1165 (SO_2). ^1H Nmr (250 MHz): δ = 0.29 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 3.36 (d, J = 6 Hz, 1 H, 3'-H), 3.59 (d, J = 15 Hz, 1 H, HCH), 3.72 (d, J = 15 Hz, 1 H, HCH), 4.35 (d, J = 6 Hz, 1 H, 3-H), 6.9-7.45 (m, 9 H, arH), 10.36 (brs, 1 H, NH).

2-(tert-Butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-4-(4-nitrobenzyl)-1,2-thiazetidine 1,1-dioxide (**7c**): Yield 350 mg (47 %), mp 177°C (ether). Ir: 3340 cm^{-1}, 3260 (NH), 1610 (C=N), 1520, 1340 (NO_2), 1300, 1180, 1155 (SO_2). ^1H Nmr (400 MHz): δ = 0.30 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 3.32 (d, J = 6 Hz, 1 H, 3'-H), 3.65 (d, J = 16.5 Hz, 1 H, HCH) 3.81 (d, J = 16.5 Hz, 1 H, HCH), 4.44 (d, J = 6 Hz, 1 H, 3-H), 7.06, 8.06 (AA'BB', J = 9 Hz, 4 H, arH), 7.3-7.55 (m, 4 H, arH), 10.44 (s, 1 H, NH).

4-(4-Bromobenzyl)-2-(tert-butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-1,2-thiazetidine 1,1-dioxide (**7d**): Yield 420 mg (53 %), mp 158°C (ether). Ir: 3260 cm^{-1} (NH), 1615 (C=N), 1305, 1160 (SO_2). ^1H Nmr: δ = 0.27 (s, 6 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 3.25 (d, J = 6 Hz, 1 H, 3'-H), 3.45 (d, J = 15 Hz, 1 H, HCH), 3.65 (d, J = 15 Hz, 1 H, HCH), 4.34 (d, J = 6 Hz, 1 H, 3-H), 6.72, 7.31 (AA'BB', J = 9 Hz, 4 H, arH), 7.30 (s, 4 H, arH), 10.37 (s, 1 H, NH).

2-(tert-Butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-4-(4-methylbenzyl)-1,2-thiazetidine 1,1-dioxide (**7e**): Yield 390 mg (56 %), mp 140°C (ether). Ir: 3270 cm^{-1} (NH), 1620 (C=N), 1305, 1160 (SO_2). ^1H Nmr: δ = 0.28 (s, 6 H, Si-Me), 0.97 (s, 9 H, Si-tBu), 2.25 (s, 3 H, Me), 3.30 (d, J = 6 Hz, 1 H, 3'-H), 3.45 (d, J = 15 Hz, 1 H, HCH), 3.65 (d, J = 15 Hz, 1 H, HCH), 4.29 (d, J = 6 Hz, 1 H, 3-H), 6.70, 6.97 (AA'BB', J = 9 Hz, 4 H, arH), 7.30 (s, 4 H, arH), 10.38 (brs, 1 H, NH).

2-(tert-Butyldimethylsilyl)-4-(α-imino-4-chlorobenzyl)-4-methylsulfonyl-1,2-thiazetidine 1,1-dioxide (**7f**): Yield 62 mg (15%), mp 155°C (pentane). Ir: 3270 cm^{-1} (NH), 1600 (C=N), 1330, 1310, 1170, 1145 (SO_2). ^1H Nmr: δ = 0.20 (s, 3 H, Si-Me), 0.27 (s, 3 H, Si-Me), 0.93 (s, 9 H, Si-tBu), 3.42 (s, 3 H, SO_2-Me), 3.42 (d, J = 7 Hz, 1 H, 3-H, 3'-H), 4.07 (d, J = 7 Hz, 1 H, 3'-H, 3-H), 7.40 (s, 4 H, arH), 10.7 (s, 1 H, NH).

4-(α-Aminobenzyl)-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**8a**)

(4S*,αR*)-Isomer (**8aA**): R_f = 0.39; yield 30 mg (9%), mp 66°C (pentane). Ir: 3400 cm^{-1}, 3340 (NH_2), 1290, 1170, 1135 (SO_2). ^1H Nmr (250 MHz): δ = 0.26 (s, 3 H, Si-Me), 0.29 (s, 3 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 1.81 (brs, 2 H, NH_2), 3.21 (dd, J = 5 Hz, 8 Hz, 1 H, 3'-H), 3.74 [dd(t), J = 5 Hz, 5 Hz, 1 H, 3-H], 4.65 [ddd(dt), J = 8 Hz, 5 Hz, 4.5 Hz, 1 H, 4'-H], 4.76 (d, J = 4.5 Hz, 1 H, α-H), 7.25-7.4 (m, 5 H, arH).

(4S*,αS*)-Isomer (**8aB**): R_f = 0.28; yield 65 mg (21%), mp 63°C (ether/pentane). Ir: 3380 cm^{-1}, 3310 (NH_2), 1300, 1170, 1145 (SO_2). ^1H Nmr (250 MHz): δ = 0.24 (s, 3 H, Si-Me), 0.26 (s, 3 H, Si-Me), 0.96 (s, 9 H, Si-tBu), 1.84 (s, 2 H, NH_2), 2.86 [t(dd), J = 6 Hz, 5.5 Hz, 1 H, 3-H], 3.14 (dd, J = 7.5 Hz, 6 Hz, 1 H, 3'-H), 4.48 (d, J = 10.5 Hz, 1 H, α-H), 4.68 (ddd, J = 10.5 Hz, 7.5 Hz, 5.5 Hz, 1 H, 4'-H), 7.35 (mc, 5 H, arH).

4-(α-Amino-4-chlorobenzyl)-2-(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**8b**)

(4S*,αR*)-Isomer (**8bA**): R_f = 0.34; yield 45 mg (13%), mp 110°C (pentane). Ir: 3400 cm^{-1}, 3340 (NH_2), 1280, 1170, 1130 (SO_2). ^1H Nmr (250 MHz): δ = 0.25 (s, 3 H, Si-Me), 0.29 (s, 3 H, Si-Me), 0.98 (s, 9 H, Si-tBu), 1.78 (brs, 2 H, NH_2), 3.20 (dd, J = 4.5 Hz, 8.2 Hz, 1 H, 3'-H), 3.68 [dd(t), J = 4.5 Hz, 4.5 Hz, 1 H, 3-H], 4.59 [ddd(dt), J = 8.2 Hz, 4.5 Hz, 4.5 Hz, 1 H, 4'-H], 4.73 (d, J = 4.5 Hz, 1 H, α-H), 7.32 [mc(s), 4 H, arH].

(4S*,αS*)-Isomer (**8bB**): R_f = 0.27, yield 75 mg (21%), mp 107°C (pentane). Ir: 3390 cm^{-1}, 3320 (NH_2), 1300, 1170, 1130 (SO_2). ^1H Nmr (250 MHz): δ =

0.24 (s, 3 H, Si-Me), 0.26 (s, 3 H, Si-Me), 0.95 (s, 9 H, Si-t-Bu), 1.81 (s, 2 H, NH_2), 2.85 [dd(t), J = 6 Hz, 5.5 Hz, 1 H, 3-H], 3.14 (dd, J = 7.5 Hz, 6 Hz, 1 H, 3'-H), 4.47 (d, J = 10.5 Hz, 1 H, α-H), 4.62 (ddd, J = 10.5 Hz, 7.5 Hz, 5.5 Hz, 1 H, 4'-H), 7.28-7.39 (AA'BB', J = 9 Hz, 4 H, arH).

4-(α-Amino-4-chlorobenzyl)-1,2-thiazetidine 1,1-dioxide (**9**), (mixture of isomers): Yield 100 mg (28%), mp 160°C (dichloromethane). Ir: 3390 cm^{-1}, 3340 (NH_2), 1305, 1170, 1140 (SO_2). ^1H Nmr (acetone-d_6, 250 MHz): Isomer **A**: δ = 2.85 (brs, 2 H, NH_2), 2.92, 3.16, 3.46 (m, 2 H, 3-H, 3'-H), 5.10 (m, 2 H, 4'-H, α-H), 6.78 (brs, 1 H, NH), 7.35-7.6 (AA'BB', J = 9 Hz, 4 H, arH). - Isomer **B**: δ = 2.85 (brs, 2 H, NH_2), 2.92, 3.16, 3.46 (m, 2 H, 3-H, 3'-H), 4.44 (d, J = 10.5 Hz, 1 H, α-H), 4.77 (ddd, J = 10.5 Hz, 8.3 Hz, 6 Hz, 1 H, 4'-H), 6.78 (brs, 1 H, NH), 7.35-7.6 (AA'BB', 4 H, arH).

(E/Z)-2-(tert-Butyldimethylsilyl)-4-{[α-(tert-butyldimethylsilyl)amino]-4-chlorobenzylidene}-1,2-thiazetidine 1,1-dioxide (**10**): Yield 350 mg (50%), mp 130°C (pentane). Ir: 3330 cm^{-1} (NH), 1640 (C=C), 1270, 1170, 1160, 1130 (SO_2). ^1H Nmr: (E)-Isomer: δ = -0.10 (s, 6 H, Si-Me), 0.25 (s, 6 H, Si-Me), 0.93 (s, 18 H, Si-t-Bu), 3.30 (brs, 1 H, NH), 3.87 (s, 2 H, 3-H, 3'-H), 7.30-7.67 (m, 4 H, arH); (Z)-Isomer: δ = -0.15 (s, 6 H, Si-Me), 0.25 (s, 6 H, Si-Me), 0.93 (s, 18 H, Si-t-Bu), 3.67 (s, 2 H, 3-H, 3'-H), 4.37 (brs, 1 H, NH), 7.3-7.65 (m, 4 H, arH).

(E)-2-(tert-Butyldimethylsilyl)-4-{[α-(tert-butyldimethylsilyl)-amino]-4-chlorobenzylidene}-1,2-thiazetidine 1,1-dioxide (**E-10**): Yield 200 mg (43%), mp 175°C (pentane). Ir: 3300 cm^{-1} (NH), 1650 (C=C), 1275, 1170, 1145 (SO_2). ^1H Nmr (250 MHz): δ = -0.12 (s, 6 H, Si-Me), 0.24 (s, 6 H, Si-Me), 0.87 (s, 9 H, Si-t-Bu), 0.95 (s, 9 H, Si-t-Bu), 3.25 (brs, 1 H, NH), 3.84 (s, 2 H, 3-H, 3'-H), 7.35-7.55 (AA'BB', J = 8 Hz, 4 H, arH).

2,4-Bis(tert-butyldimethylsilyl)-1,2-thiazetidine 1,1-dioxide (**11**) see[8].

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