51. Properties and Reactions of Substituted 1,2-Thiazetidine 1,1-Dioxides: Synthesis of *N*-Substituted 4,4-Dimethyl-1,2-thiazetidin-3-one 1,1-Dioxides, and a New Base-Catalyzed Rearrangement to Thiazolidin-4-one 1,1-Dioxides

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Dedicated to Professor *Fritz Eiden*, München, on the occasion of his 70th birthday and to Professor *Klaus Hartke*, Marburg, on the occasion of his 65th birthday

(6.XI.96)

Alkylation of 3-oxo-1,2-thiazetidine 1,1-dioxide **2** yields the *N*-alkylated 3-oxo-β-sultams **3a–i**. Solvolysis with NaOH or NH_3 selectively opens the N–S bond forming the sulfonate carboxamides **4** and the sulfonamidocarboxamides **7**, respectively. Furthermore, the hitherto unknown compounds of type **5** are prepared, representing a strained four-membered ring with a diacylated, sulfonated N-atom. Depending upon the reaction conditions, **3b–d** and **3g** are rearranged by base-catalyzed reactions into the substituted 4-oxothiazolidine 1,1-dioxides **9** or **10**. Structures are elucidated by spectroscopic methods, established by crystal-structure analyses, and a possible way of formation is proposed. Furthermore, some side reactions and transformations are reported.

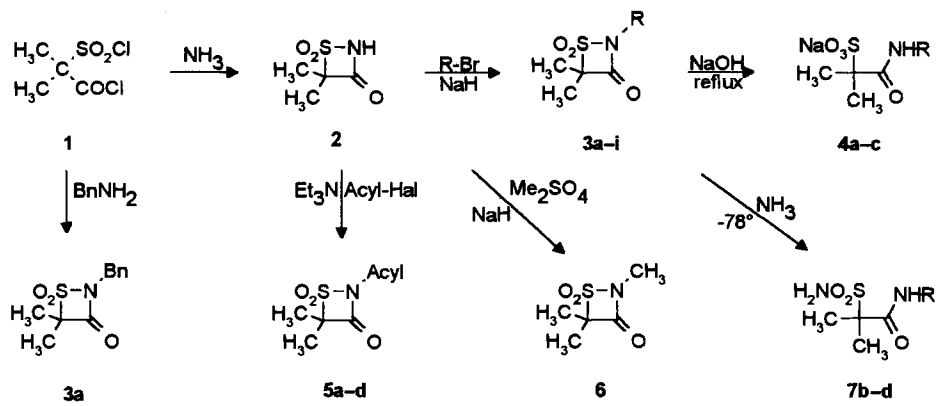
Introduction. – The β-lactam ring is the essential moiety of many antibiotics. Penicillins, cephalosporins, and carbapenems exhibit their activity by an attack of the β-lactam to enzymes of the bacterial system [1]. The β-sultam ring – 1,2-thiazetidine 1,1-dioxide – is a highly strained and reactive S-analogue of the β-lactam [2]. Furthermore, both systems are potent synthetic building blocks, and one would expect that reactions known from one system could be adapted for the other one. Examples supporting this idea have already been described [2]. *N*-Benzyl-β-lactams can be rearranged into pyrrolidinones by bases like lithium diisopropylamide, as described by *Durst et al.* [3] and extended by *Bergmann* [4]. All attempts to transfer this rearrangement to parent β-sultams completely failed [5]. Therefore, we decided to study a combination of a β-lactam with a β-sultam structure, which is represented by the 3-oxo-β-sultam **2**. Here, we report on synthesis, properties, and our results of the base-catalyzed rearrangement reactions of some *N*-substituted 3-oxo-4,4-dimethyl-β-sultams **3**.

Results. – The *N*-unsubstituted 3-oxo-β-sultam **2** is available by ring closure from 2-(chlorosulfonyl)-2-methylpropionyl chloride (**1**), which can be obtained either from isobutyric acid anhydride [6], or from isobutyric acid [7] (*Scheme 1*). In our hands, the

[1]) From the thesis of *D.G.*, University of Freiburg, 1993.

synthesis from isobutyric acid was more successful, and, by some modifications of the original procedure, we could improve the yields up to 60%. By cyclization of **1** with $PhCH_2NH_2$, we obtained the *N*-benzyl derivative **3a** [6]. All experiments to obtain the 4,4-unsubstituted 3-oxo-β-sultam were unsuccessful. Apparently, the crucial step of the synthesis is the cyclization with the amine. The unsubstituted analogue of **1**, (chlorosulfonyl)acetyl chloride, yields polymerization products, when treated with an amine (or another base), probably *via* a ketene or a sulfene intermediate.

Scheme 1



For **3**, **4**, and **7**: **a** R = $PhCH_2$, **b** R = $EtOCOCH_2$, **c** R = 4-Br–$C_6H_4COCH_2$, **d** R = *t*-$BuOCOCH_2$, **e** R = 4-NO_2–$C_6H_4CH_2$, **f** R = $MeOCH_2$, **g** R = $PhCH_2OCOCH_2$, **h** R = $BrCH_2CH_2$, **i** R = $BrCH_2CH_2CH_2$. For **5**: **a** Acyl = $BrCH_2CO$, **b** R = $MeOCH_2CO$, **c** R = Ac, **d** R = isobutyryl. For **7e**: R = NH_2COCH_2.

The synthesis of other *N*-substituted derivatives **3** by direct cyclization failed. Therefore, we searched for conditions for the alkylation of **2**. From the many methods known for the *N*-alkylation of β-lactams [8] and β-sultams [9], only the use of NaH in DMF and bromo compounds bearing electron-withdrawing substituents in the α-position were effective. In all other experiments, *e.g.* the deprotonation of **2** by LDA or BuLi, we obtained only polymeric products. No reaction occurred with CH_2BrCl or $BrCH_2CN$, while with some other bromo compounds the *N*-alkylated products **3a**–**3i** were obtained in yields between 43 and 91% as stable, crystalline products, which can be stored at r.t. for some weeks.

The IR spectrum ($CHCl_3$) of the unsubstituted β-lactam [10] is characterized by the strong C=O band at 1750 cm^{-1}, and the NH band at 3430 cm^{-1}, that of the unsubstituted β-sultam in KBr [11] shows the NH band at 3310, the SO_{2as} at 1300, and the SO_{2sym} band at 1150 cm^{-1}, and finally the IR spectrum (KBr) of the combination product **2** is characterized by bands at 3405–3385 (NH), 1755 (CO), 1335 (SO_{2as}), and 1160 cm^{-1} (SO_{2sym}). While the C=O group seems not to be influenced significantly by the sulfonamide structure, the bands of the latter one are slightly ($\Delta\nu$ 35 and 10 cm^{-1}, resp.) shifted to higher numbers. This might indicate a higher degree of mesomeric stabilization. The spectra of the *N*-alkylated compounds **3** show the C=O bands at 1760–1785, the SO_{2as} at 1335–1325, and the SO_{2sym} bands at 1181–1172 cm^{-1}, indicating that the *N*-substitution only influences the C=O bonyl and the SO_{2sym} bands. Finally, the better mesomeric stabilization is supported by the crystal structure: β-sultams are folded in the crystalline structure (the angle between the planes defined by S, N, C(4), and N, C(3), C(4) lies between 13° and 23°) [12]. In contrast, the analysis of **3b** (*Fig. 1*) shows a completely planar four-membered ring.

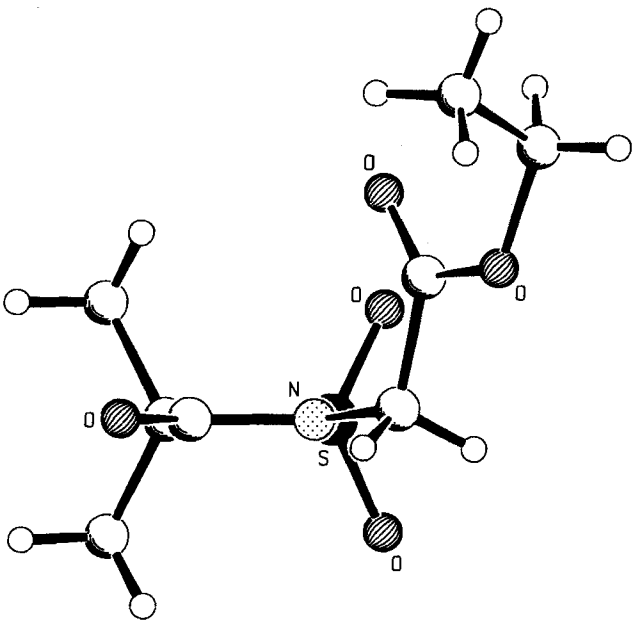


Fig. 1. *Crystal structure of* **3b**

The distance S(1)–N(2) = 167.7(3) pm of **3b** is nearly unchanged when compared to that of a 2,3-dialkyl-β-sultam (166.1(6) pm), but the distance N(2)–C(3) is only 136.0(5) pm and thereby shorter than in the 2,3-dialkyl system (149(1) pm). The angle at the S-atom is similar in both compounds, **3b**: 78.7°, and 2,3-dialkyl-β-sultam: 80.8°, the angle at the N-atom is larger in **3b** (96.6° *vs.* 93.6°), and the angle N(2)–C(3)–C(4) of **3b** shows with 99.9° the greatest difference compared with the dialkyl-β-sultam (93.2°). For other details, see *Exper. Part.*

Under basic or acidic conditions β-lactams are hydrolyzed yielding β-amino acids [13], and from β-sultams β-aminosulfonic acids are obtained [9a]. Compound **2** shows a remarkable stability in H_2O, it is destroyed in basic media, and it is hydrolyzed in acidic media by opening the S–N bond or the N–C(3) bond yielding a mixture of sulfocarboxamide and aminosulfonyl carboxylic acid [6]. The hydrolytic behavior of the *N*-substituted compounds was studied with **3a**, **3b**, and **3c**. In contrast to **2**, but in agreement with the *N*-alkyl derivatives of **2** [6], these products are not hydrolyzed when refluxed in 2N HCl for 2 h. When they were heated in 2N NaOH for 2 h, we always isolated one uniform product in nearly quantitative yield. Its structure **4** is deduced mainly from the IR spectra, especially from the two amide bands around 1660 and 1530 cm^{-1}, and the sulfonate bands around 1220 and 1035 cm^{-1}. Furthermore, the sulfonato-carboxamide structure is supported by the ^{13}C-NMR data. The spectra of **4a** and **4b** show signals of the carbonyl C-atom at 172.49 and 172.80 ppm, while for a carboxylate C-atom a signal at 181.7 ppm is reported [14]. In accordance with these results, the aminolysis of **3b**, **3c**, and **3d** with liquid NH_3 only gave the parent sulfonamido-carboxamide structures **7b**, **7c**, and **7d**[2]), and, from **3b**, we obtained by aminolytic ring opening and aminolysis of the ester

[2]) *Testa* and coworkers describe in [6] the aminolysis with hydrazine yielding the 'sulfonamide carbohydrazide' structure (no yield is given). The obviously opposite behavior, attack of the nucleophile to the CO and not the SO_2 group, might be caused by the different nucleophilicity (basicity) of hydrazine.

the (carbamoylmethyl)-carboxamido-sulfonamide **7e**. As described for **4**, the structure of **7** is strongly supported by their IR data (*Exper. Part*).

Similar to the alkylation, most of the commonly applied methods of acylation only resulted either in traces of the desired products, or completely failed. However, when we changed the 'normal' order of reagent mixing by first adding the acid halogenide to **2** in THF at 0° and then very slowly added (max. temp. 0°!) Et_3N, we could suppress the polymerization of **2**, and isolated the acylated products **5a** and **5b** in yields between 10 and 30%. These poor results prompted us to try the acylation with anhydrides, and indeed, from acetic or isobutyric anhydride, we obtained **5c** and **5d** in better yields.

The acylated products **5** are not very stable compounds. They represent a hitherto unknown structure type: a strained four-membered ring with a diacylated and sulfonated N-atom. Tris-acylated N-compounds (aliphatic triamides) have been described in 1979 [15] as being unstable products. Even in a sealed tube, they decompose to diacylated products during 2 months. Some examples of diacylated and sulfonylated open-chain compounds have been described in 1986 [17]. However, to our knowledge, systems like **5** are unknown until today. They are characterized by their IR spectra showing very intensive CO and SO_2 absorptions at 1790–1810, 1730–1750 and 1350, 1180–90 cm^{-1}. The shift to higher numbers of the lactam-CO band compared to that of **2** indicates a high mesomeric effect. This effect might cause a stabilization, but on the other hand it enlarges the reactivity of the system supported by the high strain of the four-membered ring.

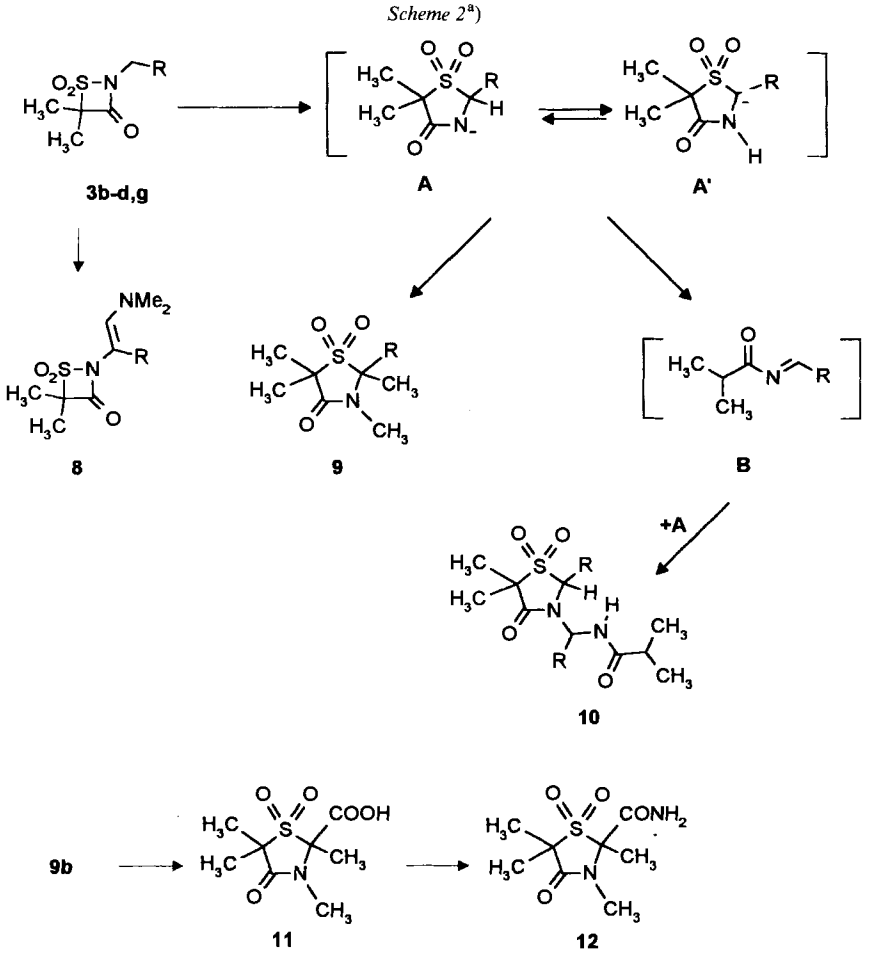
When **3b–d** or **3g** were treated with BuLi in THF, analogue to the method described for β-lactams [3] [4], we could not isolate any defined product. But interesting results were obtained when we carried out the reactions with NaH in DMF. The course of the reaction seems to be strongly dependent from two parameters, *i.e.*, from the amount of DMF used and from the temperature. All reactions were carried out under a N_2 atmosphere. Furthermore, the workup influences the type of isolated product. When **3b** or **3d** were treated at room temperature in a large excess of DMF with 2 equiv. of NaH, we isolated **8b** and **8d** as single products, probably formed by a base-catalyzed condensation reaction between the $N-CH_2$ group of **3** and DMF (*Scheme 2*). Structure **8** is supported by the spectroscopic data, especially by the 1620-cm^{-1} band in the IR spectra caused by the unsymmetrically substituted C=C bond, and by the ^{1}H-NMR signal around 3 ppm from the Me_2N group.

When the reaction with **3b–d, g** occurred at 0° and in about half the amount of DMF, we obtained by the same workup no product of structure **8** but the very unusual 1,3-thiazolidin-4-one **10**. The compounds **10b–d, g** were isolated in yields between 52 and 61% as stable crystalline products having melting points between 117 and 142° (**10b, d, g**) and 245° (**10c**).

The structure of **10** is characterized in the IR spectra by two strong C=O bands: around 1750 cm^{-1} from the ester C=O group, and 1710 cm^{-1}, indicating the five-membered-ring lactam. Only one C=O band at 1700 cm^{-1} is found in the IR spectrum of **10d**. The 2 amide bands are registered in all spectra around 1675–1645 and 1530–1510 cm^{-1}. Furthermore, ^{1}H- and ^{13}C-NMR spectra are in full agreement with this structure (*Exper. Part*), which was finally established by a crystal-structure analysis of **10d** (*Fig. 2*).

The ^{1}H-NMR spectra are characterized by a *singlet* from H–C(2) at 5.23, 5.83, 5.11, and 6.48 ppm, whose position is strongly influenced by the substituent R–C(2). The 2 Me groups at C(5) are documented by 2 separate *singlets* at 1.51 and 1.58 ppm (**10b**), and 1.37 and 1.45 ppm (**10c**), respectively, and by one *singlet* at 1.47 ppm in the spectrum of **10g**. In the spectrum of **10d**, these signals are superposed by Me signals from the *t*-Bu groups.

Scheme 2[a])



[a]) For substituents, see *Scheme 1*.

Compared with the analogue resonance signals in the spectra of **3**, all signals show a characteristic high-field shift indicating the transformation of a four-membered into a five-membered ring. The i-Pr group at the end of the side chain at position 3 is characterized in all spectra by the expected septet and the Me signals. The downfield shift of the signals of H–C(2') and H–N correlates with the inductive effect of the substituents as expected.

When the reaction temperature was changed to −20°, we could not obtain any defined product, but we detected some decomposition products, obviously formed from unstable intermediates. Therefore, we tried to stabilize these products by alkylation, and, indeed, when dimethyl sulfate was added before workup, we obtained the 1,3-thiazolidin-4-ones **9b–d, g** as stable, colorless crystals. A crystal-structure analysis of **9b** (*Fig. 3*) and the analytical data (*Exper. Part*) established the proposed structure.

In addition to the signals of the R substituent, the ^{1}H-NMR spectra of **9** are dominated by the Me signals. The Me–C(2) gives a *singlet* at 1.8 ppm (**9b, d, g**) and 3.35 ppm (**9c**), the *N*–Me signal is found at 2.85–2.95 ppm for **9b, d, g** and at 3.55 ppm in the spectrum of **9c**. In the spectra of **9b, 9c**, and **9g**, the two Me groups at C(5)

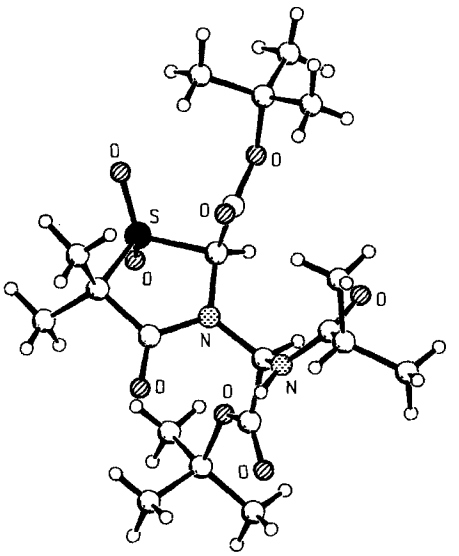


Fig. 2. *Crystal structure of* **10d**

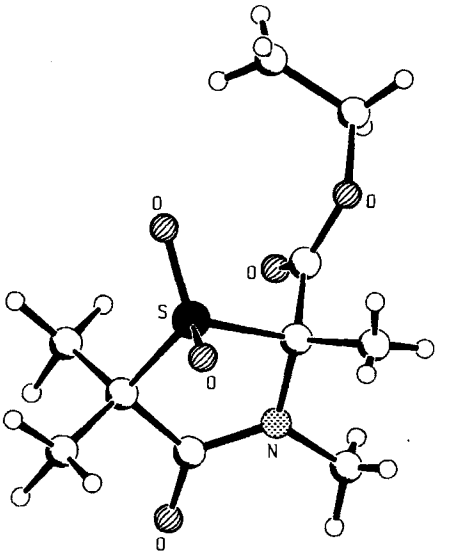


Fig. 3. *Crystal structure of* **9b**

display a *singlet* at 1.4–1.5 ppm, but in the spectrum of **9d** two separate signals are registered. More characteristic differences are found in the ^{13}C-NMR spectra. In *Fig. 4*, the spectra of **3b** and **9b** are compared. The signals of the two Me groups are found to be unshifted, but the adjuncted ring C-atom gives a high-field shift from 83.32 ppm to 58.4 ppm [14], and the $N-CH_2$ group signal at 41.26 ppm in **3b** is shifted downfield to 81.2 ppm (C(2)) in the spectrum of **9b** showing that it is incorporated into the five-membered ring. As one example, **9b** was hydrolyzed by refluxing with aq. KOH yielding, after acidification, the crystalline carboxylic acid **11**, which was treated with $SOCl_2$ and liq. NH_3 resulting in the carboxamide **12**. These two transformations not only show the synthetic variety of **9**, but also demonstrate the good stability of the ring system under drastic conditions.

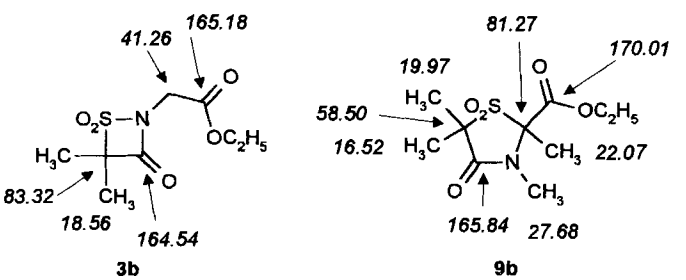


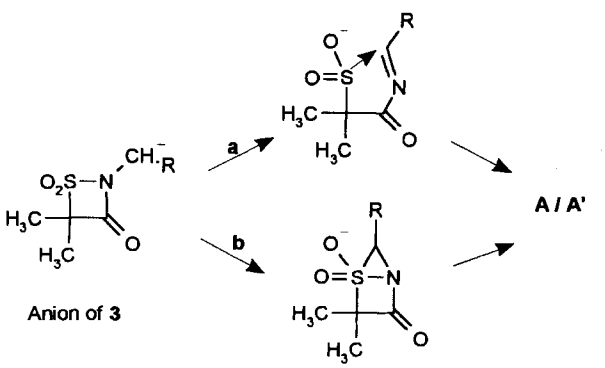
Fig. 4. *^{13}C-NMR Data of* **3b** *and* **9b**

Discussion. – The formation of the different products **9** and **10** can be understood by postulating the first step being the deprotonation of the $N-CH_2$ group of **3** by NaH, followed by an insertion of the methylene-C-atom between N and SO_2 group. The so-formed intermediate could be described as the tautomeric anions **A**/**A'** (*Scheme 2*). These intermediates are transformed by methylation into the stable compounds **9**. On the other hand, it is known [17] that SO_2 easily can be eliminated as sulfinate, especially when the α-substituent contains delocalized π-electrons, or when the β-substituent as an elec-

tron-withdrawing group supports the formation of a carbanion in β-position. In analogy, here we postulate an elimination similar to those reactions reported for some other sulfones [18], resulting in the formation of the acylimine **B**. Acylimines of this type, for the first time isolated in 1986, are known to be very reactive and in most examples unstable compounds [19]. They represent excellent substrats for *Michael* additions, and, therefore, the last step of the formation of **10** is proposed being such an addition between **A** and **B**.

The interesting question of the mechanism of the ring-enlargement step cannot be answered exactly. Overall, the reactions shows similarity with the *Gabriel-Colman* rearrangement of substituted saccharins [20], but so far, that mechanism seems to be unknown. The main difference is that, in the case of the saccharins, the C-atom is inserted into the N–CO bond, and, in the case of **3**, into the N–S bond. In the β-lactam field, *Durst et al.* [3] interpret the base-catalyzed rearrangement of the intermediate benzylic carbanion. On the other hand, the ring enlargement of 1-benzyl-4-arylazetidin-2-ones with LDA or BuLi yielding either *trans*/*cis*-mixtures (8:2) or only the preferred *trans*-4-aryl-5-phenyl-2-pyrrolidones is explained [3] [4] as an intramolecular closing step of a radical-radical anion formed from the azetidin-2-one by deprotonation of the $PhCH_2$ group and ring opening by cleavage of the N–C(4) bond. Finally, to explain the reaction of **3** to **9** (and/or **10**), showing an opposite selectivity than the reaction of saccharins [21], we could consider two additional mechanisms (*Scheme 3*).

Scheme 3



Pathway a postulates, after deprotonation, a ring-opening step followed by a ring closure to the favored five-membered ring. *Pathway b* formulates a bicyclic intermediate. Stabilization could occur by an opening of the S–N bond. Comparing the two pathways, we believe that *b* cannot explain the selectivity of the reaction. Formation of a three-membered ring including the CO group should also be possible. On the other hand, appropriate β-sultams undergo easily ring opening, when the opened structure is stabilized [2], and indeed, in the examples described in [2] the N–C(3) bond is cleaved. But in *a*, a ring opening between N and the CO group should result in a less stabilized form than an opening of the N–S bond. From these considerations, we prefer *Pathway a* as a possible explanation for the selectivity of the product formation. Furthermore, the reactions **3** → **4** and **3** → **7** show that S–N bond cleavage is favored to the N–C bond cleavage.

Financial support provided by the *Fonds der Chemischen Industrie*, Frankfurt, is gratefully appreciated. We thank *Ursula Predoiu* for experimental help, *Ciba*, Agro-Dept. for the support with chemicals, and Dr. *D. Hunkler* and Dr. *J. Wörth*, Chemisches Laboratorium der Universität Freiburg, for recording some NMR and mass spectra.

Experimental Part

General. THF was stored with KOH, then refluxed with Na and benzophenone, and distilled prior to use. Other solvents were dried/purified according to literature procedures. M.p.: not corrected; *Linström* apparatus. IR Spectra (cm^{-1}): *Perkin-Elmer IR 841, IR 1310, Beckman IR 4240*; in KBr, if not noted otherwise. NMR Spectra: *Varian T60, Bruker WP80, WH90, WM400* for ^1H; *Bruker WH90* (22.63 MHz), *WM400* (100.614 MHz) for ^{13}C; δ in ppm rel. to TMS as internal standard, J in Hz; ^1H values from 80 MHz, ^{13}C values from 22.63-MHz spectra in $CDCl_3$, if not noted otherwise. MS (70 eV): *Finnigan MAT 44S*. Elemental analyses: Pharmazeutisches Institut or Chemisches Laboratorium der Universität Freiburg.

2-(Chlorosulfonyl)-2-methylpropionyl Chloride (**1**). *a*) At 0° and with stirring, disodium 2-methyl-2-sulfonatopropionate (179 g, 0.84 mol) is added to $SOCl_2$ (600 ml), then DMF (13.5 ml) is added and the mixture is heated to 70°. After the gas production has finished, the mixture is kept at 70° for 5 h. Then, the excess of $SOCl_2$ is evaporated, the residue is dissolved in Et_2O, filtered and concentrated. *b*) At 0° and with stirring, $POCl_3$ (306.6 g, 2 mol) is added to chlorosulfonic acid (116.5 g, 1 mol). The mixture is kept at 15°, isobutyric acid (88.1 g, 1 mol) is slowly added, then the temp. is slowly raised to 120° for 4 h. After cooling, the mixture if fractionated: *a*) 113 g (65%). B.p. 101°/13 Torr. *b*) 123.6 (60%). B.p. 55°/1 Torr. $n_D^{20} = 1.483$. IR (film): 1780 (CO), 1380, 1180 (SO_2).

4,4-Dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**2**). At −78°, **1** (20.6 g, 0.1 mol) in Et_2O (50 mol) is dropwise (very slowly!) added to a mixture of liq. NH_3 (100 ml) and Et_2O (50 ml). The mixture is warmed to r.t., until the solvent is completely evaporated, $CHCl_3$ is added, the residue is dissolved in H_2O, at 0–4° adjusted to pH 1 with HCl, and extracted (2–3 times) with $CHCl_3$. The combined org. layers are dried (Na_2SO_4) and evaporated: 8.0 g (54%) of **2**. Colorless crystals. M.p. 150° ($CHCl_3$/petroleum ether). See [6].

N-*Alkylation of* **2**. *General Procedure.* At 0° under N_2, **2** (1.49 g, 10 mmol) in THF (20 ml) is added dropwise during 15 min with stirring to a suspension of NaH (240 mg, 10 mmol; 2–3 times washed paraffin free with petroleum ether) in DMF (30 ml). Stirring is continued for 15 min at 0°, then the halogen compound (15 mmol) is injected through a septum, the mixture is warmed to r.t., and stirred for 24 h. Then, it is cooled to 0°, Et_2O (50 ml) is added, the mixture is hydrolyzed with sat. NaCl soln., adjusted to pH 4–5 with dil. HCl, the org. layer is separated, the aq. layer is twice extracted with Et_2O, the combined org. layers are 1–2 times washed with sat. NaCl soln., dried (Na_2SO_4), and concentrated.

2-Benzyl-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3a**). *a*) At 0°, $PhCH_2NH_2$ (9.63 g, 30 mmol) in Et_2O (25 ml) is added during 2 h to **1** (1.5 g, 10 mmol) in Et_2O (25 ml). After 10 h stirring at r.t., the mixture is filtered, and the Et_2O evaporated. *b*) From **2** and $PhCH_2Br$ (1.7 g, 10 mmol) according to the *General Procedure*: *a*) 1.3 g (54%); *b*) 1.4 (57%). Colorless needles. M.p. 86° (acetone). See [6].

2-[(Ethoxycarbonyl)methyl]-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3b**). From **2** and $BrCH_2COOEt$ (2.5 g, 15 mmol): 2.0 g (86%) of **3b**. Colorless needles. M.p. 84° (90% EtOH). IR: 1780, 1750 (CO), 1335, 1180 (SO_2). ^1H-NMR: 1.26 (*t*, $J = 7$, Me); 1.75 (*s*, 2 Me); 4.14 (*s*, CH_2); 4.25 (*q*, $J = 7$, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.08 (Me); 18.56 (2 Me); 41.26 (NCH_2); 62.61 (CH_2O); 83.32 (C(4)); 164.64, 165.18 (CO). Anal. calc. for $C_8H_{13}NO_5S$ (235.26): C 40.84, H 5.57, N 5.95, S 13.63; found: C 40.91, H 5.50, N 5.85, S 13.72.

Crystal-Structure Analysis of **3b**. A colorless crystal of $C_8H_{13}NO_5S$ having approximate dimensions of $0.75 \times 0.75 \times 0.25$ mm was mounted on a glass fibre. Measurements were conducted on a *Enraf-Nonius-CAD4* diffractometer with graphite monochromated CuK_α (= 1.5418 Å) radiation. The crystal belongs to the orthorhombic space group *Pbca* with $a = 7.964(1)$ Å, $b = 9.391(1)$ Å, $c = 30.037(3)$ Å, $V = 2246.5$ Å^3, $Z = 8$, $D_{calc.} = 1.391$ g cm^{-3}. The intensities were corrected for *Lorentz* and polarization effects. A total of 2686 independent intensities were measured of which 2191 were classified as observed with $I > 2\sigma(I)$. The structure was solved by direct methods using the program MULTAN80 [21]. The structure was refined using full-matrix least-squares calculations with anisotropic displacement parameters for non-H-atoms. The positions of the H-atoms were calculated assuming normal geometry. Their parameters were refined. The final R factor for 188 variables was 0.062, the R_w factor was 0.072. The max/min density in the final difference *Fourier* map was 0.539/ − 0.421 eÅ^{-3}. Selected distances [Å]: S(1)–N(2) 1.677(3), N(2)–C(3) 1.360(5), C(3)–C(4) 1.539(6), C(4)–S(1) 1.823(4). Selected bond angles [°]: C(4)–S(1)–N(2) 78.7(1), S(1)–N(2)–C(3) 96.6(2), N(2)–C(3)–C(4) 99.9(3), C(3)–C(4)–S(1) 84.8(2), C(Me)–C(4)–C(Me) 114.5(4), O–S(1)–O 117.7(2). Complete positional and thermal parameters and bond lengths were deposited with the *Cambridge Crystallographic Data Centre* (*CCDC*).

2-[(4-Bromobenzoyl)methyl]-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3c**). From **2** and 2,4'-dibromoacetophenone (2.8 g, 10 mmol) in THF (20 ml). The mixture is hydrolyzed with ice/H_2O, the pH is adjusted to 4–5 by HCl, and stirring is continued until the precipitate is complete (*ca.* 15–30 min). 2.6 g (76%) of **3c**. Colorless crystals. M.p. 185° (EtOH). IR: 1760, 1690 (CO), 1330, 1180 (SO_2). ^{1}H-NMR: 1.77 (*s*, 2 Me); 4.85 (*s*, CH_2); 7.55–7.9 (*m*, 4 arom. H). Anal. calc. for $C_{12}H_{12}BrNO_4S$ (346.21): C 41.63, H 3.49, Br 23.08, N 4.05, S 9.26; found: C 41.85, H 3.54, Br 22.85, N 4.19, S 9.36.

*2-[(*tert*-Butoxycarbonyl)methyl]-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide* (**3d**). From **2** and *t*-butyl bromoacetate (2.93 g, 15 mmol): 2.4 g (91%) of **3d**. Colorless crystals. M.p. 96° (EtOH 90%). IR: 1776, 1739 (CO), 1327, 1172 (SO_2). ^{1}H-NMR: 1.50 (*s*, 3 Me); 1.78 (*s*, 2 Me); 4.05 (*s*, CH_2). Anal. calc. for $C_{10}H_{17}NO_5S$ (263.31): C 45.61, H 6.51, N 5.32, S 12.18; found: C 45.86, H 6.49, N 5.23, S 12.00.

2-(4-Nitrobenzyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3e**). From **2** and 4-nitrobenzyl bromide (2.16 g, 10 mmol): 1.7 g (61%) of **3e**. Colorless crystals. M.p. 120° (EtOH). IR: 1760 (CO), 1520, 1345 (NO_2), 1330, 1175 (SO_2). ^{1}H-NMR: 1.76 (*s*, 2 Me); 4.69 (*s*, CH_2); 7.54 (*d*, J = 9, 2 arom. H); 8.25 (*d*, J = 9, 2 arom. H). Anal. calc. for $C_{11}H_{12}N_2O_5S$ (284.29): C 46.47, H 4.25, N 9.85, S 11.28; found: C 46.60, H 4.27, N 9.71, S 11.20.

2-(Methoxymethyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3f**). From **2** and $BrCH_2OMe$ (1.9 g, 15 mmol): 0.8 g (43%) of **3f**. Colorless crystals. M.p. 65° (EtOH). IR: 1774 (CO), 1333, 1181 (SO_2). ^{1}H-NMR: 1.71 (*s*, 2 Me); 3.40 (*s*, MeO); 4.76 (*s*, CH_2). Anal. calc. for $C_9H_{11}NO_4S$ (193.22): C 37.29, H 5.74, N 7.25, S 16.59; found: C 37.50, H 5.65, N 7.32, S 16.42.

2-[(Benzyloxycarbonyl)methyl]-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3g**). From **2** and benzyl bromoacetate (3.44 g, 15 mmol): 2.6 g (88%) of **3g**. Colorless crystals. M.p. 76° (90% EtOH). IR: 1785, 1754 (CO), 1335, 1179 (SO_2). ^{1}H-NMR: 1.75 (*s*, 2 Me); 4.18 (*s*, CH_2N); 5.2 (*s*, CH_2O); 7.35 (*s*, 5 arom. H). Anal. calc. for $C_{13}H_{15}NO_5S$ (297.33): C 52.51, H 5.08, N 4.71, S 10.78; found: C 52.23, H 4.97, N 4.58, S 10.98.

2-(2-Bromoethyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3h**). From **2** and $BrCH_2CH_2Br$ (3.76 g, 20 mmol): 1.4 g (55%) of **3h**. Colorless needles. M.p. 131° (EtOH). IR: 1778 (CO), 1328, 1172 (SO_2). ^{1}H-NMR: 1.71 (*s*, 2 Me); 3.55 (*t*, J = 5.5, CH_2); 3.86 (*t*, J = 5.5, CH_2). Anal. calc. for $C_6H_{10}BrNO_3S$ (256.12): C 28.14, H 3.93, Br 31.20, N 5.47, S 12.52; found: C 28.22, H 3.97, Br 31.05, N 5.48, S 12.41.

2-(3-Bromopropyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**3i**). From **2** and $BrCH_2CH_2CH_2Br$ (4.02 g, 20 mmol): 1.6 g (59%) of **3i**. Colorless needles. M.p. 122° (EtOH). IR: 1763 (CO), 1325, 1178 (SO_2). ^{1}H-NMR: 1.71 (*s*, 2 Me); 2.45 (*quint.*, J = 6.5, CH_2); 3.47 (*t*, J = 6.5, CH_2); 3.63 (*t*, J = 6.5, CH_2). Anal. calc. for $C_7H_{12}BrNO_3S$ (270.15): C 31.12, H 4.48, Br 29.58, N 5.18, S 11.87; found: C 31.00, H 4.46, Br 29.74, N 5.09, S 11.98.

*Sodium 1-(*N*-Benzylcarbamoyl)-1-methylethanesulfonate* (**4a**). Compound **3a** (2.4 g, 10 mmol) is refluxed in 2N NaOH soln. (50 ml) for 2 h, the mixture is evaporated, the residue is dissolved in EtOH, Et_2O is added, and the soln. is stored at 0° until crystallization is complete: 2.6 g (93%) of **4a**. Colorless crystals. M.p. 234° (EtOH/Et_2O). IR: 1660, 1535 (amide), 1220, 1030 (SO_3Na). ^{1}H-NMR ((D_6)DMSO): 1.34 (*s*, 2 Me); 4.30 (*d*, J = 6.5, CH_2); 7.28 (*s*, 5 arom. H); 8.60 (*s*, NH). ^{13}C-NMR (100 MHz, (D_6)DMSO): 22.93 (*2* Me); 42.22 (CH_2N); 61.26 (C(2)); 126.50–139.51 (arom. C); 172.49 (CO). Anal. calc. for $C_{11}H_{14}NNaO_4S$ (279.29): C 47.30, H 5.05, N 5.01, Na 8.23, S 11.48; found: C 47.03, H 5.00, N 5.12, Na 8.34, S 11.63.

*Sodium 1-{[(*N*-Ethoxycarbonyl)methyl]carbamoyl}-1-methylethanesulfonate* (**4b**). From **3b** (2.4 g, 10 mmol) as described for **4a**: 2.5 g (92%) of **4b**. Colorless crystals. M.p. 156° (EtOH/Et_2O). IR: 1740 (CO), 1665, 1530 (amide), 1210, 1040 (SO_3Na). ^{1}H-NMR ((D_6)DMSO): 1.18 (*t*, J = 7, Me); 1.38 (*s*, 2 Me); 3.86 (*d*, J = 5.5, CH_2N); 4.08 (*q*, J = 7, CH_2O); 8.47 (*t*, J = 5.5, NH). ^{13}C-NMR (90 MHz, (D_6)DMSO): 13.92 (Me); 22.67 (2 Me); 41.15 (CH_2O); 60.26 (CH_2N); 61.23 (C(1)); 169.82 (CO); 172.80 (CO). Anal. calc. for $C_8H_{14}NNaO_6S$ (275.26): C 34.90, H 5.13, N 5.09, Na 8.35, S 11.65; found: C 34.62, H 5.22, N 5.00, Na 8.15, S 11.36.

*Sodium 1-{[*N*-(4-Bromobenzoyl)methyl]carbamoyl}-1-methylethanesulfonate* (**4c**). From **3c** (3.5 g, 10 mmol) as described for **4a**: 3.4 g (87%) of **4c**. Colorless crystals. M.p. 248° (EtOH). IR: 1679 (CO), 1664, 1528 (amide), 1222, 1039 (SO_3Na). ^{1}H-NMR (90 MHz, (D_6)DMSO): 1.33 (*s*, 2 Me); 4.61 (*d*, J = 4.5, CH_2N); 7.64–7.98 (*m*, 4 arom. H); 8.55 (*t*, J = 4.5, NH). Anal. calc. for $C_{12}H_{13}BrNNaO_5S$ (386.20): C 37.32, H 3.39, N 3.63; found: C 37.87, H 3.46, N 3.30.

2-(Bromoacetyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**5a**). Under N_2 at −78°, $BrCH_2COBr$ (2.0 g, 10 mmol) in THF (10 ml) is added dropwise to **2** (1.49 g, 10 mmol) in THF (30 ml), the mixture is stirred for 10 min, Et_3N (1.0 g, 10 mmol) in THF (30 ml) is added slowly during 1 h dropwise, stirring is continued at 0° for 2 h, the mixture is filtered, and the solvent evaporated: 0.8 g (31%) of **5a**. Colorless crystals. M.p. 112° (EtOH). IR: 1790, 1740 (CO), 1350, 1180 (SO_2). ^{1}H-NMR: 1.83 (*s*, 2 Me); 4.16 (*s*, CH_2). MS (70 eV): 270 (5, M^+). Anal. calc. for $C_6H_8BrNO_4S$ (270.11): C 26.68, H 2.98, Br 29.58, N 5.18, S 11.87; found: C 26.22, H 3.23, Br 29.69, N 5.41, S 11.71.

2-(Methoxyacetyl)-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**5b**). From **2** (1.49 g, 10 mmol) and $MeOCH_2COCl$ (1.1 g, 10 mmol) as **5a**: 0.22 g (10%) of **5b**. Colorless crystals. M.p. 83° (MeOH). IR: 1810, 1735 (CO), 1354, 1182 (SO_2). ^{1}H-NMR: 1.78 (*s*, 2 Me); 3.48 (*s*, MeO); 4.28 (*s*, CH_2N). Anal. calc. for $C_7H_{11}NO_5S$ (221.23): C 38.00, H 5.01, N 6.33; found: C 37.42, H 5.32, N 6.31.

2-Acetyl-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**5c**). Ac_2O (10 ml, 0.14 mol) is added to **2** (1.49 g, 10 mmol), the mixture is stirred at r.t. for 24 h, then it is concentrated, pentane is added, and, after complete crystallization, the precipitate is separated: 1.7 g (89%) of **5c**. Colorless crystals. M.p. 116° (EtOH). IR: 1789, 1753 (CO), 1332, 1161 (SO_2). ^{1}H-NMR: 1.79 (*s*, 2 Me); 2.40 (*s*, Me). Anal. calc. for $C_6H_9NO_4S$ (191.21): C 37.69, H 4.74, N 7.32, S 16.77; found: C 37.44, H 4.72, N 7.17, S 16.87.

2-Isobutyryl-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**5d**). From **2** (1.49 g, 10 mmol) and isobutyric anhydride (15.8 g, 0.1 mol) as **5c**: 1.9 g (87%) of **5d**. Colorless crystals. M.p. 121° (EtOH). IR: 1804, 1727 (CO), 1350, 1188 (SO_2). ^{1}H-NMR: 1.18 (*d*, $J = 7$, Me_2C); 1.76 (*s*, 2 Me); 3.02 (*sept.*, $J = 7$, CH). Anal. calc. for $C_8H_{13}NO_4S$ (219.26): C 43.82, H 5.97, N 6.39, S 14.62; found: C 43.96, H 5.92, N 6.48, S 14.54.

2,4,4-Trimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**6**): 1.5 g (92%). Colorless crystals. M.p. 133° (EtOH). See [6].

2-(Aminosulfonyl)-N-*[(ethoxycarbonyl)methyl]-2-methylpropionamide* (**7b**). At −78°, **3b** (2.4 g, 10 mmol) is added to liq. NH_3 (50 ml), and stirred at r.t. until NH_3 is evaporated: 2.2 g (87%) of **7b**. Colorless crystals. M.p. 160° (90% EtOH). IR: 3600–3040 (NH), 1724 (CO), 1658, 1547 (amide), 1339, 1173 (SO_2). ^{1}H-NMR (90 MHz, (D_6)DMSO): 1.20 (*t*, $J = 7$, Me); 1.51 (*s*, 2 Me); 3.88 (*d*, $J = 6$, CH_2N); 4.11 (*q*, $J = 7$, CH_2O); 6.91 (*s*, NH_2); 7.07 (*t*, $J = 6$, NH). Anal. calc. for $C_8H_{16}N_2O_5S$ (252.29): C 38.08, H 6.39, N 11.32, S 12.71; found: C 38.25, H 6.39, N 11.11, S 12.62.

2-(Aminosulfonyl)-N-*[(4-bromobenzoyl)methyl]-2-methylpropionamide* (**7c**). From **3c** (3.5 g, 10 mmol) as **7b**: 3.2 g (88%) of **7c**. Colorless crystals. M.p. 205° (90% EtOH). IR: 3600–3040 (NH), 1697 (CO), 1672, 1527 (amide), 1325, 1180 (SO_2). ^{1}H-NMR (90 MHz, (D_6)DMSO): 1.53 (*s*, 2 Me); 4.63 (*d*, $J = 5$, CH_2N); 6.99 (*s*, NH_2); 7.68–8.03 (*m*, 4 arom. H); 8.07 (*t*, $J = 5$, NH). Anal. calc. for $C_{12}H_{15}BrN_2O_4S$ (363.24): C 39.68, H 4.16, Br 22.00, N 7.71, S 8.82; found: C 39.69, H 4.22, Br 22.18, N 7.69, S 8.71.

2-(Aminosulfonyl)-N-*[(*tert-*butoxycarbonyl)methyl]-2-methylpropionamide* (**7d**). From **3d** (2.6 g, 10 mmol) as **7b**: 2.6 g (93%) of **7d**. Colorless crystals. M.p. 163° (90% EtOH). IR: 3600–3060 (NH), 1720 (CO), 1678, 1528 (amide), 1328, 1152 (SO_2). ^{1}H-NMR (90 MHz): 1.49 (*s*, *t*-Bu); 1.71 (*s*, 2 Me); 3.94 (*d*, $J = 6$, CH_2N); 5.54 (*s*, NH_2); 7.25–7.44 (*m*, NH). Anal. calc. for $C_{10}H_{20}N_2O_5S$ (280.35): C 42.84, H 7.19, N 9.99, S 11.44; found: C 42.88, H 7.25, N 9.94, S 11.53.

2-(Aminosulfonyl)-N-*(carbamoylmethyl)-2-methylpropionamide* (**7e**). From **3b** (2.4 g, 10 mmol) as **7b**, but with 100 ml of NH_3: 2.1 g (94%) of **7e**. Colorless crystals. M.p. 210° (90% EtOH). IR: 3600–2900 (NH), 1689, 1648, 1537 (amide), 1333, 1172 (SO_2). ^{1}H-NMR (90 MHz, (D_6)DMSO): 1.49 (*s*, 2 Me); 3.71 (*d*, $J = 6$, CH_2N); 6.89–7.40 (*m*, 2 NH_2); 7.92 (*t*, $J = 6$, NH). Anal. calc. for $C_6H_{13}N_3O_4S$ (223.25): C 32.28, H 5.87, N 18.82, S 14.36; found: C 32.56, H 5.90, N 18.58, S 14.11.

2-{2-(Dimethylamino)-1-[(ethoxycarbonyl)methyl]ethyl}-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide (**8b**). Under N_2 at r.t., **3b** (2.35 g, 10 mmol) in DMF (40 ml) is added to a suspension of NaH (480 mg, 20 mmol) in DMF (50 ml), stirring is continued for 24 h, Et_2O (50 ml) is added, the mixture is hydrolyzed with sat. NaCl soln., the org. layer is separated, the aq. layer is extracted twice with Et_2O, the combined org. layers are washed with NaCl soln., dried (Na_2SO_4), and evaporated: 0.7 g (24%) of **8b**. Colorless crystals. M.p. 148° (EtOH). IR: 1780, 1690 (CO), 1620 (C=C), 1330, 1180 (SO_2). ^{1}H-NMR: 1.21 (*t*, $J = 7$, Me); 1.66 (*s*, Me–C(4)); 1.78 (*s*, Me–C(4)); 3.08 (*s*, Me_2N); 4.15 (*q*, $J = 7$, CH_2O); 7.55 (*s*, CH). MS (70 eV): 290 (20, M^+), 291 (3, $[M + 1]^+$). $C_{11}H_{18}N_2O_5S$ calc. 290.3405; found: 290.0944.

*2-{1-[(*tert-*Butoxycarbonyl)methyl]-2-(dimethylamino)ethyl}-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide* (**8d**). From **3d** (2.63 g, 10 mmol) as described for **8b**: 0.8 g (25%) of **8d**. Colorless crystals. M.p. 143° (EtOH). IR: 1775, 1692 (CO), 1624 (C=C), 1329, 1181 (SO_2). ^{1}H-NMR: 1.41 (*s*, 3 Me); 1.63 (*s*, Me–C(4)); 1.73 (*s*, Me–C(4)); 3.03 (*s*, Me_2N); 7.48 (*s*, CH). Anal. calc. for $C_{13}H_{22}N_2O_5S$ (318.39): C 49.04, H 6.96, N 8.80, S 10.07; found: C 48.82, H 6.90, N 8.56, S 10.18.

Rearrangement Reaction I. General Procedure. Under N_2 at −20°, **3** (10 mmol) in DMF (20 ml) is added to a suspension of NaH (480 mg, 20 mmol) in DMF (20 ml), stirring is continued at −20° for 10 min, dimethyl sulfate (5.0 g, 40 mmol) is added through a septum, the mixture is slowly warmed to r.t., stirred for 24 h, cooled to 0°, Et_2O (50 ml) is added, the mixture is hydrolyzed with sat. NaCl soln., adjusted with HCl to pH 3–5, the org. layer is separated, the aq. layer is extracted twice with Et_2O, the combined org. layers are washed with NaCl soln., dried (Na_2SO_4), and evaporated.

2-(Ethoxycarbonyl)-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**9b**). From **3b** (2.35 g, 10 mmol): 1.6 g (60%) of **9b**. Colorless crystals. M.p. 213° (EtOH 90%). IR: 1730, 1700 (CO), 1325, 1135 (SO_2). ^{1}H-NMR ((D$_6$)DMSO): 1.20 (*t*, *J* = 7, Me); 1.40 (*s*, 2 Me); 1.78 (*s*, Me–C(2)); 2.85 (*s*, MeN); 4.23 (*q*, *J* = 7, CH_2). ^{13}C-NMR: 13.95 (Me); 16.52 (Me); 19.97 (Me); 22.68 (MeN); 58.50 (C(5)); 63.74 (CH_2); 81.27 (C(2)); 165.84, 170.01 (CO). Anal. calc. for $C_{10}H_{17}NO_5S$ (263.31): C 45.61, H 6.51, N 5.32, S 12.18; found: C 45.33, H 6.59, N 5.39, S 12.08.

Crystal-Structure Analysis of **9b**. A colorless crystal of $C_{10}H_{17}NO_5S$ having approximate dimensions of 0.63 × 0.41 × 0.36 mm was mounted on a glass fibre. Measurements were made on an *Enraf-Nonius-CAD4* diffractometer with graphite monochromated CuK_α (= 1.5418 Å) radiation. The crystal belongs to the orthorhombic space group $P2_12_12_1$ with a = 14.732(1) Å, b = 10.012(1) Å, c = 8.649(1) Å, V = 1275.7 Å^3, Z = 4, $D_{calc.}$ = 1.371 g cm^{-3}. The intensities were corrected for *Lorentz* and polarization effects. A total of 1548 independent intensities were measured of which 1531 were classified as observed with $I > 3\sigma(I)$. The structure was solved by direct methods using the program MULTAN80 [21]. The structure was refined using full-matrix least-squares calculations with anisotropic displacement parameters for non-H-atoms. The positions of the H-atoms were calculated assuming normal geometry. Their parameters were refined. The final R factor for 222 variables was 0.076, the R_w factor was 0.079. The max/min density in the final difference *Fourier* map was 0.394/ – 0.321 eÅ^{-3}. Selected distances [Å]: S(1)–C(2) 1.857(4), C(2)–N(3) 1.465(5), N(3)–C(4) 1.368(5), C(4)–C(5) 1.526(6), C(5)–S(1) 1.814(4). Selected bond angles [°]: C(5)–S(1)–C(2) 96.3(2), O–S(1)–O 118.5(2), S(1)–C(2)–N(3) 101.3(2), C(2)–N(3)–C(4) 120.3(3), C(Me)–C(2)–C(CO) 114.1(3), C(Me)–C(5)–C(Me) 111.5(3). Complete positional and thermal parameters and bond lengths were deposited with the *CCDC*.

2-(4-Bromobenzoyl)-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**9c**). From **3c** (3.46 g, 10 mmol): 1.7 g (45%) of **9c**. Colorless crystals. M.p. 180° (EtOH). IR: 1695 (CO), 1310, 1100 (SO_2). ^{1}H-NMR: 1.45 (*s*, 2 Me–C(5)); 3.35 (*s*, Me–C(2)); 3.55 (*s*, MeN); 7.33–7.75 (*m*, 4 arom. H). Anal. calc. for $C_{14}H_{16}BrNO_4S$ (374.26): C 44.93, H 4.31, Br 21.35, N 3.74, S 8.57; found: C 45.15, H 4.31, Br 21.17, N 3.69, S 8.65.

*2-(*tert*-Butoxycarbonyl)-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide* (**9d**). From **3d** (2.63 g, 10 mmol): 1.7 g (58%) of **9d**. Colorless crystals. M.p. 121° (MeOH/pentane). IR: 1731, 1702 (CO), 1323, 1134 (SO_2). ^{1}H-NMR (90 MHz): 1.55 (*s*, *t*-Bu); 1.57 (*s*, Me–C(5)); 1.60 (*s*, Me–C(5)); 1.82 (*s*, Me–C(2)); 2.95 (*s*, MeN). ^{13}C-NMR: 18.65 (Me); 19.99 (Me); 22.01 (Me–C(2)); 27.02, 27.82, 29.82 (3 Me); 58.37 (C(5)); 81.59 (C(2)); 85.35 (Me_3C); 164.52, 170.20 (CO). Anal. calc. for $C_{12}H_{21}NO_5S$ (291.37): C 49.47, H 7.26, N 4.81; found: C 49.42, H 7.25, N 4.85.

2-(Benzyloxycarbonyl)-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**9g**). From **3g** (2.97 g, 10 mmol): 1.8 g (55%) of **9g**. Colorless crystals. M.p. 147° (AcOEt/petroleum ether). IR: 1730, 1710 (CO), 1325, 1135 (SO_2). ^{1}H-NMR: 1.48 (*s*, 2 Me–C(5)); 1.80 (*s*, Me–C(2)); 2.85 (*s*, MeN); 5.20 (*s*, CH_2O); 7.30 (*s*, 5 arom. H). Anal. calc. for $C_{15}H_{19}NO_5S$ (325.39): C 55.37, H 5.89, N 4.30, S 9.85; found: C 55.17, H 5.92, N 4.33, S 9.96.

Rearrangement Reaction II. General Procedure. Under N_2 at 0°, **3** (10 mmol) in DMF (20 ml) is added to a suspension of NaH (480 mg, 20 mmol) in DMF (20 ml), stirring is continued at 0° for 20 min, the mixture is hydrolyzed with sat. NaCl soln., adjusted with HCl to pH 3–5, and extracted 3 times with Et_2O, the combined org. layers are washed with NaCl soln., dried (Na_2SO_4), and evaporated.

2-(Ethoxycarbonyl)-3-[(ethoxycarbonyl)(2-methylpropionamido)methyl]-5,5-dimethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**10b**). From **3b** (2.35 g, 10 mmol): 1.2 g (59%) of **10b**. Colorless needles. M.p. 142° (EtOH). IR: 3700–3100 (NH), 1752, 1709 (CO), 1653, 1532 (amide), 1341, 1134 (SO_2). ^{1}H-NMR (400 MHz): 1.14 (*dd*, *J* = 7, 2.2, Me_2C); 1.25 (*t*, *J* = 7, Me); 1.34 (*t*, *J* = 7, Me); 1.51 (*s*, Me–C(5)); 1.575 (*s*, Me–C(5)); 2.41 (*sept.*, *J* = 7, CH); 4.13–4.35 (*m*, 2 CH_2); 5.225 (*s*, H–C(2)); 5.79 (*d*, *J* = 8, H–C(2′)); 6.94 (*d*, *J* = 8, NH). ^{13}C-NMR (100 MHz): 14.02 (2 Me); 18.65 (Me–C(5)); 19.18 (2 Me); 21.78 (Me–C(5)); 35.06 (CH); 60.64 (C(5)); 60.70 (C(2′)); 63.15 (CH_2); 63.78 (CH_2); 77.48 (C(2)); 163.66 (CO); 165.92 (CO); 170.96 (C(1′)); 177.36 (C(4)). MS (70 eV): 406 (20, M^+), 407 (6, $[M+1]^+$). Anal. calc. for $C_{16}H_{26}N_2O_8S$ (406.46): C 47.28, H 6.45, N 6.89, S 7.89; found: C 47.02, H 6.35, N 6.80, S 7.92.

2-(4-Bromobenzoyl)-3-[(4-bromobenzoyl)(2-methylpropionamido)methyl]-5,5-dimethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**10c**). From **3c** (3.46 g, 10 mmol): 1.6 g (52%) of **10c**. Colorless crystals. M.p. 245° (90% EtOH). IR: 3700–3200 (NH), 1700 (CO), 1645, 1515 (amide), 1335, 1120 (SO_2). ^{1}H-NMR: 0.93 (*dd*, *J* = 7, 2, 2 Me); 1.37 (*s*, Me–C(5)); 1.45 (*s*, Me–C(5)); 2.28 (*sept.*, *J* = 7, CH); 6.48 (*d*, *J* = 7, H–C(2′)); 6.48 (*s*, H–C(2)); 7.32 (*d*, *J* = 7, NH); 7.55–8.20 (*m*, 8 arom. H). Anal. calc. for $C_{24}H_{24}Br_2N_2O_6S$ (628.35): C 45.88, H 3.85, Br 25.43, N 4.46, S 5.10; found: C 45.94, H 3.85, Br 25.63, N 4.34, S 5.07.

*2-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)(2-methylpropionamido)methyl]-5,5-dimethyl-1,3-thiazolidin-4-one 1,1-Dioxide* (**10d**). From **3d** (2.63 g, 10 mmol): 1.3 g (56%) of **10d**. Colorless crystals. M.p. 117° (EtOH). IR: 3700–3150 (NH), 1751, 1710 (CO), 1675, 1514 (amide), 1337, 1154 (SO_2). ^{1}H-NMR (90 MHz): 1.16

(*d*, J = 7, 2 Me); 1.4–1.67 (*m*, 8 Me); 2.43 (*sept*, J = 7, CH); 5.11 (*s*, H–C(2)); 5.64 (*d*, J = 9, H–C(2')); 6.86 (*d*, J = 9, NH). Anal. calc. for $C_{20}H_{34}N_2O_8S$ (462.57).

Crystal-Structure Analysis of **10d**. A colorless crystal of $C_{20}H_{34}N_2O_8S$ having approximate dimensions of 0.38 × 0.31 × 0.18 mm was mounted on a glass fibre. Measurements were made on a *Enraf-Nonius-CAD4* diffractometer with graphite monochromated CuK_α (= 1.5418 Å) radiation. The crystal belongs to the orthorhombic space group $P2_1/n$ with a = 10.745(3) Å, b = 21.163(1) Å, c = 11.515(3) Å, V = 2580.6 Å^3, Z = 4, $D_{calc.}$ = 1.190 g cm^{-3}. The intensities were corrected for *Lorentz* and polarization effects. A total of 4163 independent intensities were measured of which 2851 were classified as observed with $I > 2\sigma(I)$. The structure was solved by direct methods using the program MULTAN80 [21]. The structure was refined using full-matrix least-squares calculations with anisotropic displacement parameters for non-H-atoms. The positions of the H-atoms were calculated assuming normal geometry. Their parameters were refined. The final R factor for 416 variables was 0.052, the R_w factor was 0.050. The max/min density in the final difference *Fourier* map was 0.377/ – 0.282 eÅ^{-3}. Selected distances [Å]: S(1)–C(2) 1.828(5), C(2)–N(3) 1.455(6), N(3)–C(4) 1.377(6), C(4)–C(5) 1.520(8), C(5)–S(1) 1.836(5), C(5)–(Me^1) 1.535(9), C(5)–C(Me^2) 1.50(1), S(1)–O^1 1.431(5), S(1)–O^2 1.428(6), C(2)–C(α) 1.504(7), N(3)–C(α) 1.464(6), C(4)–O 1.220. Selected bond angles [°]: S(1)–C(2)–N(3) 102.4(3), C(2)–N(3)–C(4) 117.0(4), N(3)–C(4)–C(5) 115.5(4), C(4)–C(5)–S(1) 101.0(4), C(5)–S(1)–C(2) 94.6(2), O–S(1)–O 120.7(3), S(1)–C(2)–C(α) 109.3(4), C(2)–N(3)–C(α) 121.8(3), C(Me)–C(5)–C(Me) 114.1(6), C(5)–C(4)–O 123.8(5). Complete positional and thermal parameters and bond lengths were deposited with the *CCDC*.

2-(Benzyloxycarbonyl)-3-[(benzyloxycarbonyl)(2-methylpropionamido)methyl]-5,5-dimethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**10g**). From **3g** (2.97 g, 10 mmol): 1.6 g (61%) of **10g**. Colorless crystals. M.p. 128° (EtOH). IR: 3700–3150 (NH), 1741, 1710 (CO), 1667, 1514 (amide), 1337, 1129 (SO_2). ^{1}H-NMR (90 MHz): 1.10 (*d*, J = 7, 2 Me); 1.47 (*s*, 2 Me–C(5)); 2.38 (*sept.*, J = 7, CH); 5.15–5.32 (*m*, 2 CH_2); 5.83 (*s*, H–C(2)); 5.85 (*d*, J = 7, H–C(2')); 6.94 (*d*, J = 7, NH); 7.15–7.5 (*m*, 10 arom. H). Anal. calc. for $C_{26}H_{30}N_2O_8S$ (530.60): C 58.86, H 5.70, N 5.28, S 6.04; found; C 58.59, H 5.67, N 5.46, S 6.16.

2-Carboxy-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**11**). Compound **9b** (2.6 g, 10 mmol) in H_2O (20 ml) is refluxed with KOH (114 mg, 20 mmol) for 2 h, cooled to r.t., acidified with HCl, and extracted 3–4 times with Et_2O. The combined org. layers are dried (Na_2SO_4) and evaporated: 2.2 g (94%) of **11**. Colorless crystals. M.p. 166° (EtOH). IR: 2700–3300 (OH), 1730 (COOH), 1700 (CO), 1325, 1135 (SO_2). ^{1}H-NMR (80 MHz, (D_6)DMSO): 1.30 (*s*, Me–C(5)); 1.33 (*s*, Me–C(5)); 1.64 (*s*, Me–C(2)); 2.74 (*s*, MeN); 6.0–7.5 (*s*, COOH). Anal. calc. for $C_8H_{13}NO_5S$ (235.26): C 40.84, H 5.57, N 5.95, S 13.63; found: C 40.99, H 5.60, N 6.06, S 13.40.

2-Carbamoyl-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**12**). Compound **11** (2.4 g, 10 mmol) in H_2O (20 ml) is refluxed with KOH (114 mg, 20 mmol) for 2 h, cooled to r.t., acidified with HCl, and extracted 3–4 times with Et_2O. The combined org. layers are dried (Na_2SO_4) and evaporated: 2.2 g (94%) of **11**. Colorless crystals. M.p. 166° (EtOH). IR: 2700–3300 (OH), 1730 (COOH), 1700 (CO), 1325, 1135 (SO_2). ^{1}H-NMR (80 MHz, (D_6)DMSO): 1.30 (*s*, Me–C(5)); 1.33 (*s*, Me–C(5)); 1.64 (*s*, Me–C(2)); 2.74 (*s*, MeN); 6.0–7.5 (*s*, COOH). Anal. calc. for $C_8H_{13}NO_5S$ (235.26): C 40.84, H 5.57, N 5.95, S 13.63; found: C 40.99, H 5.60, N 6.06, S 13.40.

2-Carbamoyl-2,3,5,5-tetramethyl-1,3-thiazolidin-4-one 1,1-Dioxide (**12**). Compound **11** (2.4 g, 10 mmol), $SOCl_2$ (20 ml), and DMF (1 ml) are refluxed for 2 h, cooled to r.t., Et_2O (50 ml) is added, and the mixture is slowly dropped to liq. NH_3 (–78°). Then, it is slowly and with stirring warmed to r.t., hydrolyzed with ice/H_2O (50 ml), acidified with HCl, and extracted 3–4 times with Et_2O. The combined org. layers are dried (Na_2SO_4) and evaporated: 1.9 g (81%) of **12**. Colorless crystals. M.p. 179° (EtOH). IR: 3600–3100 (NH_2), 1705 (CO), 1680, 1630 (amide), 1320, 1130 (SO_2). ^{1}H-NMR ((D_6)DMSO): 1.38 (*s*, Me–C(5)); 1.43 (*s*, Me–C(5)); 1.80 (*s*, Me–C(2)); 2.79 (*s*, MeN); 7.88 (*s*, NH_2). Anal. calc. for $C_8H_{14}N_2O_4S$ (234.28): C 41.02, H 6.02, N 11.96, S 13.69; found: C 41.08, H 5.99, N 11.86, S 13.81.

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