171. Synthesis of 1,2,5-Thiadiazepine Derivatives by Ring Enlargement of 1,2-Thiazetidin-3-one 1,1-Dioxides with 3-Amino-2*H*-azirines

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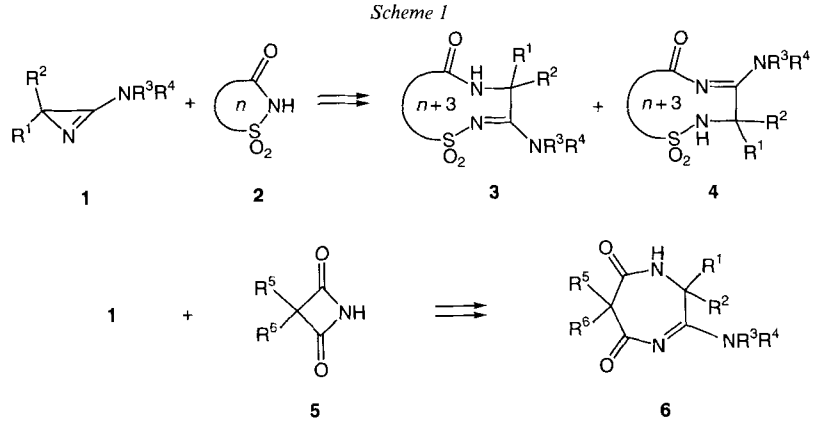
At 0° in MeCN, 2,2-disubstituted 3-amino-2*H*-azirines **1** and 4,4-disubstituted 1,2-thiazetidin-3-one 1,1-dioxides **7** react smoothly to give 1,2,5-thiadiazepin-6-one 1,1-dioxides of type **8** (*Scheme 2*). The reaction mechanism of this regiospecific ring enlargement to seven-membered heterocycles follows previously described pathways. The structures of **7a** and **8b** were established by X-ray crystallography (see *Figs. 1* and *2*).

Introduction. – In several papers, we have shown that 3-amino-2*H*-azirines **1** and NH-acidic heterocycles with $pK_a < 8$ react *via* ring enlargement to give medium-sized heterocycles [1–7]. Whereas in some cases the primary products could not be isolated because of their further rearrangement under the reaction conditions [4–6], they were obtained as stable compounds in reactions with five- to seven-membered sulfonamides of type **2** (*Scheme 1*). A smooth reaction at 0–20° was observed with saccharin [8] [9] and other 1,2-thiazol-3-one 1,1-dioxides [2], yielding 1,2,5-thiadiazocine derivatives **3** ($n = 5$, *Scheme 1*). In one example, the isomeric heterocycle of type **4** ($n = 5$) was formed as a minor product [2]. With analogous six-membered derivatives, a 1,2,4-thiadiazin-3-one 1,1-dioxide [4] and a 1,2-thiazin-3-one 1,1-dioxide [3], the transformation was slower, and with a seven-membered 1,2-thiazepin-3-one 1,1-dioxide, the reaction was sluggish even at 50–65° [7]. In the latter case, yields of ten-membered heterocycles **3** ($n = 7$) were low, and the isomer of type **4** ($n = 7$) was always formed as a by-product.

Scheme 1



[1]) Part of the planned Ph. D. thesis of *T. R. M.*

The four-membered malonimides **5** (= azetidine-2,4-diones) also reacted with **1**, in propan-2-ol at room temperature, to give 1,4-diazepine-5,7-dione derivatives **6** [10] (*Scheme 1*). Therefore, we expected that the corresponding 1,2-thiazetidin-3-one 1,1-dioxides **7** with **1** should undergo a ring enlargement to yield seven-membered heterocycles.

Results and Discussion. – Several years ago, some 1,2-thiazetidin-3-one 1,1-dioxides **7** were synthesized from the corresponding 2,2-disubstituted 2-(chlorosulfonyl)acetyl chlorides in liquid NH_3 [11] [12]. Following the same protocol, we prepared the 4,4-dimethyl and the 4,4-diethyl derivative (**7a** and **7b**, respectively). These relatively acidic compounds[2]) were obtained as colorless, crystalline materials. In spite of the high ring strain, which is reflected by the very acute and obtuse angles in the crystal structure of **7a** (*Fig. 1*), the compounds are remarkably stable (*cf.* [11]).

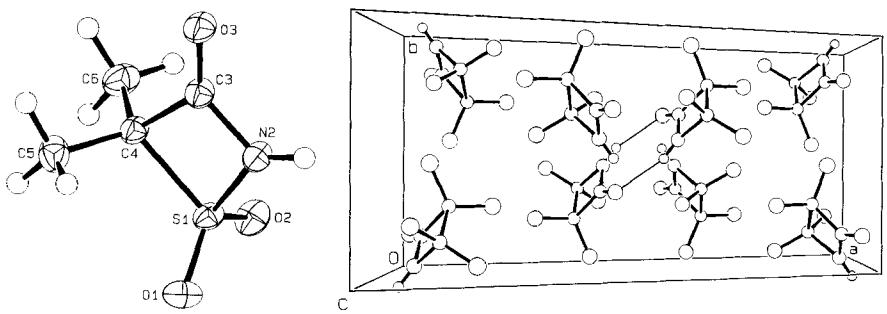


Fig. 1. *ORTEP Plot* [13] *of the molecular structure of* **7a** (displacement ellipsoids with 50% probability) *and packing diagram*

The four-membered ring of **7a** is almost planar with intraannular torsion angles between −3.3(1)° and 3.6(1)°. The carbonyl O-atom also deviates only slightly from the ring plane (S(1)–N(2)–C(3)–O(3) −177.4(2)°, S(1)–C(4)–C(3)–O(3) 177.7(2)°), as does H–N(2). The Me groups at C(4) and the O-atoms of the SO_2 group are in a nearly perfect ecliptical orientation (O(1)–S(1)–C(4)–C(5) 0.1(1)°, O(2)–S(1)–C(4)–C(6) 8.4(1)°). The intraannular bond angle at the S-atom is 78.75(7)°, at the N-atom 96.3(1)°, at the sp^3 C-atom 84.8(1)°, and at the carbonyl C-atom 100.0(1)°. The N(2)–C(3) bond is short (1.366(2) Å); this indicates, together with the planarity of N(2), the delocalization of the lone electron pair of N(2) within the lactam group. The NH group of **7a** forms an intermolecular H-bond with the carbonyl group of a neighboring molecule (N···O distance 2.857(2) Å, N–H···O angle 158(2)°). The interactions link the molecules into dimeric units where the two molecules of the dimer are related by a center of inversion (*Fig. 1*).

In MeCN at 0°, **7a** and **7b** reacted smoothly with 3-amino-2*H*-azirines **1a–d** to give a single 1:1 adduct of type **8** as a colorless, crystalline material. The 1,2,5-thiadiazepine structure (*Scheme 2*) was deduced from the spectral data, and in the case of **8b**, it was established by X-ray crystallography (*Fig. 2*). The yields of **8** are usually high (70–90% isolated material, *Table 1*). Only in the reactions with **1a**, the yields were lower, although the transformations proceeded rapidly.

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[2]) 1,2-Thiazetidin-3-one 1,1-dioxides **7** are easily dissolved in aqueous $NaHCO_3$ solutions [11].

Scheme 2

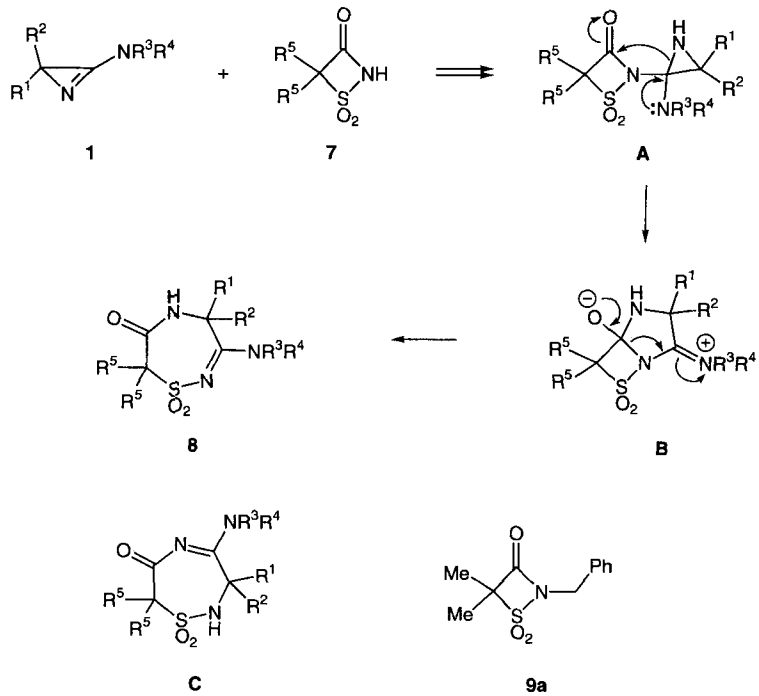

Table 1. *Formation of 1,2,5-Thiadiazepin-6-one 1,1-Dioxides* **8** *from the Reaction of* **1** *and* **7**

	R^1	R^2	R^3	R^4		R^5	Product [%]
1a	Me	Me	Me	Me	**7a**	Me	**8a** (31)
1b	Me	Me	Me	Ph	**7a**		**8b** (91)
1c	$-(CH_2)_4-$		Me	Ph	**7a**		**8c** (79)
1d	Me	i-Bu	Me	Ph	**7a**		**8d** (80)
1a	Me	Me	Me	Me	**7b**	Et	**8e** (60)
1b	Me	Me	Me	Ph	**7b**		**8f** (73)
1d	Me	i-Bu	Me	Ph	**7b**		**8g** (81)

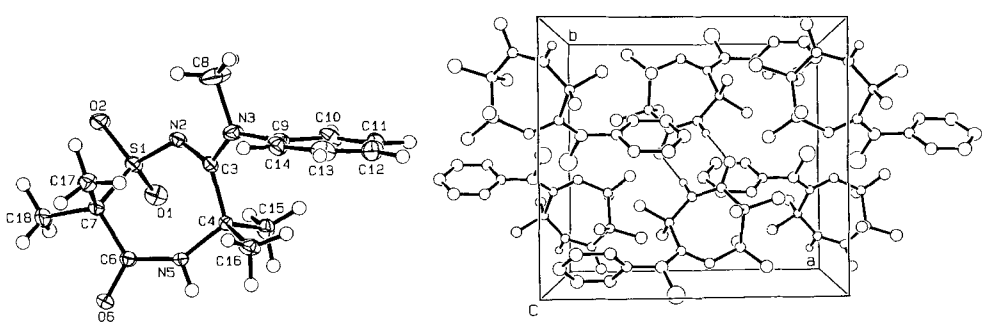

Fig. 2. *ORTEP Plot* [13] *of the molecular structure of* **8b** (displacement ellipsoids with 50% probability) *and packing diagram*

The seven-membered ring of **8b** is puckered with an almost planar (*Z*)-configurated amide group (C(4)–N(5)–C(6)–C(7) 2.5(4)°, C(4)–N(5)–C(6)–O(6) –177.7(2)°). The amidine group is also nearly planar (N(2)–C(3)–N(3) 113.5(2)°, N(3)–C(3)–C(4) 120.6(2)°, N(2)–C(3)–C(4) 125.8(2)°), with the MeN group also being in this plane (N(2)–C(3)–N(3)–C(8) 4.4(3)°, C(4)–C(3)–N(3)–C(8) –179.0(2)°). The C–N bond lengths of the amidine group (N(2)–C(3) 1.308(2) Å, N(3)–C(3) 1.350(2) Å) also reflect a certain delocalization of the lone pair of N(3); but there is no conjugation with the Ph ring at N(3). The molecule forms an intermolecular H-bond between the NH group and the carbonyl O-atom of a neighboring molecule (N···O distance 2.894(2) Å, N–H···O angle 173(2)°). The H-bonds link the molecules into dimeric units in which the molecules of the dimer are related by a center of inversion (*Fig. 2*).

In analogy to previously reported reactions of **1** with NH-acidic compounds, we propose the mechanism depicted in *Scheme 2* for the formation of the seven-membered heterocycles **8**. After protonation of **1** by **7**, nucleophilic attack onto the amidinium C-atom yields aziridine **A**, which undergoes a ring enlargement to give the zwitterionic intermediate **B**. By a second ring enlargement, the latter rearranges to the final product **8**. An alternative reaction mechanism *via* direct nucleophilic addition of **1** to the carbonyl group of **7** can be excluded as no reaction took place under analogous conditions between **1a** and the *N*-benzylated derivative **9a**[3])[4]).

It is worth mentioning that no product of the isomeric structure **C** (*Scheme 2*) could be detected. Therefore, the ring enlargement of aziridine **A** occurred in a regioselective manner *via* nucleophilic attack of the aziridine N-atom at the carbonyl group leading to **B**. Ring enlargement *via* addition to the SO_2 group would yield products of type **C** (*cf.* discussion in [2] [7]). In intermolecular nucleophilic ring-opening reactions of derivatives of type **7** or **9**, cleavages of the N–C and/or N–S bond, *i.e.*, addition to the CO and SO_2 group, respectively, are observed. Hydrolysis of **7a** with diluted HCl yielded 1-carbamoyl-1-methylethylsulfonic acid (*via* SO_2 attack) and 2-sulfamoyl-2-methylpropanamide (*via* CO attack) in nearly equal amounts, whereas under similar conditions 4,4,*N*-trimethyl-1,2-thiazetidin-3-one 1,1-dioxide gave only the corresponding sulfonic-acid derivative (*via* SO_2 attack) [11]. Heating of **7a** with anhydrous NH_2NH_2 in EtOH led selectively to hydrazide **10** (*via* CO attack) [11]; on the other hand, only sulfonamide **11**[5]) was formed from **9a** in liquid NH_3 (*Scheme 3*). The latter transformation proceeded *via* nucleophilic attack at the SO_2 group and subsequent cleavage of the S–N bond.

The regioselectivity of the nucleophilic ring opening of derivatives of type **7** and **9** has not been investigated systematically so far, and no explanation for the observed selectivities has been given (*cf.* [11]). Therefore, this problem will be the topic of further studies.

We thank the analytical units of our institute for spectra and analyses, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

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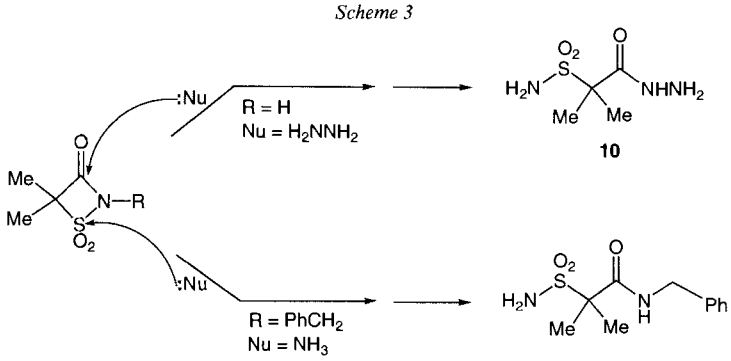
[3]) Benzylation of **7a** to **9a** was performed with benzyl bromide/NaH in DMF (*cf.* also [11] [12]).

[4]) Neither after 24 h at room temperature nor after 1 h in refluxing MeCN was any product detected; refluxing the mixture overnight led to extensive decomposition of the starting materials. Nucleophilic ring-opening reactions of derivatives of type 7 or **9** are known [11].

[5]) The structure of **11** has been established by NMR spectroscopy: the amide NH absorbs at 8.22 ppm as a *t* (J = 5.9 Hz) and the SO_2NH_2 group at 6.98 ppm (*s*). The alternative structure with a $CONH_2$ and a SO_2NHCH_2Ph group was excluded by a long-range H,C-coupling experiment which shows a coupling between PhCH_2 and *C*O.

Scheme 3



Experimental Part

General. See [2] [3]. If not stated otherwise, IR spectra in KBr, NMR spectra in $CDCl_3$ at 300 (^1H) and 50.4 (^{13}C) MHz, respectively, and CI-MS with NH_3.

1. *Starting Materials. 4,4-Dimethyl-1,2-thiazetidin-3-one 1,1-dioxide* (**7a**) and *4,4-diethyl-1,2-thiazetidin-3-one 1,1-dioxide* (**7b**) were prepared according to [11]. Only ^{13}C-NMR and MS data are given; for other data see [11]. **7a**: ^{13}C-NMR ((D_6)DMSO): 165.1 (*s*, C(3)); 82.2 (*s*, C(4)); 18.2 (*q*, $Me_2C(4)$). CI-MS: 167 (100, $[M + NH_4]^+$), 150 (14, $[M + 1]^+$). **7b**: ^{13}C-NMR: 164.1 (*s*, C(3)); 89.7 (*s*, C(4)); 22.6 (*t*, 2 $MeCH_2$); 8.3 (*q*, 2 $MeCH_2$). CI-MS: 195 (4, $[M + NH_4]^+$), 131 (10), 114 (100). The structure of **7a** was confirmed by X-ray crystallography (*Fig. 1* and *Table 2*). For 3-amino-2*H*-azirines **1a–d** see refs. in [1].

2. *Reactions of 4,4-Dialkyl-1,2-thiazetidin-3-one 1,1-Dioxides* **7** *with 3-Amino-2*H*-azirines* **1**. *General Procedure.* To a stirred soln. of **7a** or **7b** in dry MeCN at 0°, a soln. of **1** (1.1 equiv.) in dry MeCN was added and the mixture was left to reach r.t. Workup by CC (SiO_2) or filtration yielded the products as colorless solids which were recrystallized once.

2.1. *3-(Dimethylamino)-4,5,6,7-tetrahydro-4,4,7,7-tetramethyl-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8a**). *3-(Dimethylamino)-2,2-dimethyl-2*H*-azirine* (**1a**; 62 mg, 0.55 mmol) and **7a** (75 mg, 0.5 mmol) in MeCN (5 ml); −30° → r.t. CC with CH_2Cl_2/EtOH 20:3. Recrystallization from DMF/Et_2O: 40 mg (31%) of **8a**. Colorless crystals. M.p. 256–258°. IR: 3285*s*, 3200*m*, 3075*m*, 3000*m*, 2980*m*, 2940*m*, 1665*vs*, 1545*vs*, 1490*m*, 1465*m*, 1440*m*, 1400*s*, 1380*s*, 1350*m*, 1275*vs*, 1110*vs*, 1045*m*, 1005*m*, 970*m*, 905*m*, 855*vs*, 795*m*, 730*s*, 710*m*, 620*s*. ^1H-NMR ((D_6)DMSO): 7.58 (*s*, NH); 3.16 (*s*, Me_2N); 1.72, 1.42 (2*s*, $Me_2C(4)$, $Me_2C(7)$). ^{13}C-NMR ((D_6)DMSO): 170.6, 164.6 (2*s*, C(3), C(6)); 65.0, 62.1 (2*s*, C(4), C(7)); 41.9 (*q*, Me_2N); 29.2, 21.0 (2*q*, $Me_2C(4)$, $Me_2C(7)$). CI-MS: 262 (100, $[M + 1]^+$). Anal. calc. for $C_{10}H_{19}N_3O_3S$ (261.35): C 45.96, H 7.33, N 16.08, S 12.27; found: C 46.21, H 7.59, N 16.21, S 12.18.

2.2. *4,5,6,7-Tetrahydro-4,4,7,7-tetramethyl-3-(*N*-methyl-*N*-phenylamino)-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8b**). *2,2-Dimethyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**1b**; 383 mg, 2.2 mmol) and **7a** (298 mg, 2 mmol) in MeCN (12 ml); 0° → r.t., 3 h. Filtration, concentration of the mother liquor and again filtration, recrystallization from $CHCl_3$/EtOH: 586 mg (91%) of **8b**. Colorless crystals. M.p. 239.5–242°. IR: 3200*w*, 3065*m*, 2980*w*, 2940*w*, 1660*vs*, 1535*vs*, 1505*vs*, 1470*s*, 1380*s*, 1290*vs*, 1215*w*, 1165*m*, 1150*m*, 1125*vs*, 1015*w*, 1000*w*, 970*m*, 930*w*, 860*w*, 805*s*, 780*m*, 710*m*, 645*w*, 620*s*. ^1H-NMR: 7.5–7.4 (*m*, 3 arom. H); 7.24 (*dd*, J = 6.7, 2.4, 2 arom. H); 6.57 (*s*, NH); 3.42 (*s*, MeN); 1.69, 1.44 (2*s*, $Me_2C(4)$, $Me_2C(7)$). ^{13}C-NMR: 175.0, 168.2 (2*s*, C(3), C(6)); 143.6 (*s*, 1 arom. C); 129.9, 129.3, 128.0 (3*d*, 5 arom. CH); 69.8, 66.1 (2*s*, C(4), C(7)); 47.0 (*q*, MeN); 31.4, 21.3 (2*q*, $Me_2C(4)$, $Me_2C(7)$). CI-MS: 324 (100, $[M + 1]^+$). Anal. calc. for $C_{15}H_{21}N_3O_3S$ (323.42): C 55.71, H 6.55, N 12.99, S 9.92; found: C 55.54, H 6.53, N 13.05, S 10.32.

Crystallization from MeCN/Et_2O yielded suitable crystals for an X-ray crystal-structure determination (see *Fig. 2* and *Table 2*).

2.3. *8,8-Dimethyl-11-(*N*-methyl-*N*-phenylamino)-9-thia-6,10-diazaspiro[4.6]undec-10-en-7-one 9,9-Dioxide* (**8c**). *2-(*N*-Methyl-*N*-phenylamino)-1-azaspiro[2.4]hept-1-ene* (**1c**; 110 mg, 0.55 mmol) and **7a** (75 mg, 0.5 mmol) in MeCN (5 ml); 0° → r.t. Filtration: 138 mg (79%) of **8c**. Colorless solid. M.p. 280.5–281.5°. IR: 3305*w*,

3230*m*, 3090*w*, 3000*w*, 2950*w*, 2870*w*, 1665*vs*, 1550*vs*, 1490*s*, 1460*m*, 1390*s*, 1380*s*, 1365*s*, 1295*vs*, 1205*m*, 1173*s*, 1125*vs*, 1080*w*, 1050*w*, 1020*w*, 1000*w*, 935*m*, 910*m*, 810*m*, 800*s*, 790*m*, 720*s*, 660*w*, 620*s*. ^{1}H-NMR: 7.5–7.45 (*m*, 3 arom. H); 7.17 (*d*-like, J = 6.7, 2 arom. H); 5.64 (*s*, NH); 3.41 (*s*, MeN); 2.2–2.1, 2.0–1.85, 1.7–1.55, 1.5–1.35 (4*m*, $-(CH_2)_4-$); 1.78 (*s*, (Me_2C(8)). ^{13}C-NMR: 174.2, 168.8 (2*s*, C(7), C(11)); 144.8 (*s*, 1 arom. C); 130.1, 128.7, 127.2 (3*d*, 5 arom. CH); 73.2, 69.0 (2*s*, C(5), C(8)); 46.5 (*q*, MeN); 42.7, 22.9 (2*t*, $-(CH_2)_4-$); 22.4 (*q*, Me_2C(8)). CI-MS: 350 (100, $[M + 1]^+$). Anal. calc. for $C_{17}H_{23}N_3O_3S$ (349.46): C 58.43, H 6.63, N 12.03, S 9.18; found: C 58.50, H 7.04, N 12.41, S 8.68.

2.4. *4,5,6,7-Tetrahydro-4,7,7-trimethyl-3-(*N*-methyl-*N*-phenylamino)-4-(2-methylpropyl)-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8d**). *2-Methyl-3-(*N*-methyl-*N*-phenylamino)-2-(2-methylpropyl)-2*H*-azirine* (**1d**; 119 mg, 0.55 mmol) and **7a** (75 mg, 0.5 mmol) in MeCN (5 ml); 0° → r.t. Evaporation of the solvent, recrystallization from MeCN/Et_2O: 146 mg (80%) of **8d**. Colorless crystals. M.p. 228.5–229.5°. IR: 3280*s*, 2940*m*, 2860*w*, 1670*vs*, 1535*vs*, 1495*vs*, 1465*m*, 1385*s*, 1350*m*, 1290*vs*, 1255*m*, 1175*s*, 1180*m*, 1125*vs*, 1020*w*, 1000*m*, 930*m*, 900*w*, 800*s*, 775*m*, 740*m*, 710*m*, 620*s*. ^{1}H-NMR: 7.4–7.35 (*m*, 3 arom. H); 7.2–7.15 (*m*, 2 arom. H); 6.31 (*s*, NH); 3.33 (*s*, MeN); 2.0–1.8 (*m*, CH, 1 H of CH_2); 1.64, 1.61 (2*s*, Me_2C(7)); 1.30 (*ABM*, J = 14.4, 6.1, 1 H of CH_2); 1.25 (*s*, MeC(4)); 0.90 (*d*, J = 6.6, 1 Me of Me_2CH); 0.87 (*d*, J = 6.3, 1 Me of Me_2CH). ^{13}C-NMR: 173.4, 165.1 (2*s*, C(3), C(6)); 142.7 (*s*, 1 arom. C); 128.8, 128.3, 127.3 (3*d*, 5 arom. CH); 68.0, 67.8 (2*s*, C(4), C(7)); 50.2 (*t*, CH_2); 46.0 (*q*, MeN); 30.4, 22.9, 22.7, 21.0, 19.6 (5*q*, *Me*C(4), Me_2C(7), Me_2CH); 23.7 (*d*, Me_2*C*H). CI-MS: 366 (100, $[M + 1]^+$), 169 (50), 100 (57).

2.5. *3-(Dimethylamino)-7,7-diethyl-4,5,6,7-tetrahydro-4,4-dimethyl-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8e**). **1a** (84 mg, 0.75 mmol) and **7b** (121 mg, 0.68 mmol) in MeCN (5 ml); 0° → r.t. CC with CH_2Cl_2/EtOH 40:3: 118 mg (60%) of **8e**. Colorless solid. M.p. 191.5–193°. IR: 3290*s*, 2965*s*, 2880*w*, 1675*vs*, 1545*vs*, 1485*m*, 1445*m*, 1400*s*, 1380*m*, 1355*s*, 1315*w*, 1270*vs*, 1235*m*, 1155*s*, 1140*s*, 1110*vs*, 1050*m*, 1020*m*, 975*m*, 905*m*, 875*m*, 855*s*, 795*m*, 765*m*, 725*m*, 710*m*, 690*m*, 640*m*, 610*m*. ^{1}H-NMR: 6.83 (*s*, NH); 3.22 (*s*, Me_2N); 2.2–2.05 (*m*, 2 MeCH_2); 1.83 (*s*, Me_2C(4)); 1.09 (*t*, J = 7.4, 2 *Me*CH_2). ^{13}C-NMR: 177.7, 171.4 (2*s*, C(3), C(6)); 81.1, 66.0 (2*s*, C(4), C(7)); 42.2 (*s*, Me_2N); 38.6 (*q*, Me_2C(4)); 29.3 (*t*, 2 MeCH_2); 9.1 (*q*, 2 *Me*CH_2). CI-MS: 290 (100, $[M + 1]^+$), 226 (16), 192 (16), 155 (36), 98 (21).

2.6. *7,7-Diethyl-4,5,6,7-tetrahydro-4,4-dimethyl-3-(*N*-methyl-*N*-phenylamino)-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8f**). **1b** (192 mg, 1.1 mmol) and **7b** (117 mg, 1 mmol) in MeCN (6 ml); 0° → r.t. Filtration, concentration of the mother liquor, and again filtration, recrystallization from $CHCl_3$/MeCN: 255 mg (73%) of **8f**. Colorless crystals. M.p. 230.5–233.5°. IR: 3300*w*, 3200*m*, 3070*m*, 2990*m*, 2970*m*, 2940*m*, 2880*w*, 1660*vs*, 1535*vs*, 1505*s*, 1465*m*, 1400*m*, 1380*s*, 1345*w*, 1295*vs*, 1215*m*, 1130*vs*, 975*m*, 805*s*, 780*m*, 710*s*, 630*s*. ^{1}H-NMR: 7.5–7.45 (*m*, 3 arom. H); 7.25–7.2 (*m*, 2 arom. H); 6.78 (*s*, NH); 3.39 (*s*, MeN); 2.25–2.1 (*m*, 2 MeCH_2); 1.39 (*s*, Me_2C(4)); 1.12 (*t*, J = 7.4, 2 *Me*CH_2). ^{13}C-NMR: 177.6, 170.9 (2*s*, C(3), C(6)); 143.1 (*s*, 1 arom. C); 129.7, 129.2, 128.0 (3*d*, 5 arom. CH); 81.7, 67.2 (2*s*, C(4), C(7)); 46.6 (*q*, MeN); 30.2 (*q*, Me_2C(4)); 23.8 (*t*, 2 MeCH_2); 9.1 (*q*, 2 *Me*CH_2). CI-MS: 352 (100, $[M + 1]^+$), 288 (18), 218 (11), 183 (12), 108 (64). Anal. calc. for $C_{17}H_{25}N_3O_3S$ (351.48): C 58.09, H 7.17, N 11.96, S 9.12; found: C 57.44, H 7.19, N 11.85, S 8.83.

2.7. *7,7-Diethyl-4,5,6,7-tetrahydro-4-methyl-3-(*N*-methyl-*N*-phenylamino)-4-(2-methylpropyl)-1,2,5-thiadiazepin-6-one 1,1-Dioxide* (**8g**). **1d** (119 mg, 0.55 mmol) and **7b** (89 mg, 0.5 mmol) in MeCN (5 ml); 0° → r.t., 1 h. CC with hexane/acetone/AcOEt 4:1:1: 159 mg (81%) of **8g**. Colorless solid. M.p. 173.5–174.5°. IR: 3300*w*, 3200*m*, 3080*m*, 2980*s*, 2960*s*, 2875*m*, 1660*vs*, 1545*vs*, 1495*s*, 1470*s*, 1430*m*, 1390*s*, 1340*m*, 1295*vs*, 1255*m*, 1190*m*, 1165*s*, 1120*vs*, 1075*m*, 1020*m*, 1000*m*, 950*w*, 930*w*, 895*w*, 800*s*, 775*m*, 730*m*, 710*m*, 700*m*, 615*s*. ^{1}H-NMR: 7.5–7.45 (*m*, 3 arom. H); 7.25–7.2 (*m*, 2 arom. H); 6.63 (*s*, NH); 3.38 (*s*, MeN); 2.3–2.1 (*m*, 2 MeCH_2); 2.1–2.0 (*m*, 1 H of CH_2); 1.9–1.8 (*m*, CH); 1.31 (*s*, MeC(4)); 1.35–1.25 (*m*, 1 H of CH_2); 1.14, 1.11 (2*t*, J = 7.5, 2 *Me*CH_2); 0.95, 0.83 (2*d*, J = 6.7, Me_2CH). ^{13}C-NMR: 176.8, 170.3 (2*s*, C(3), C(6)); 143.5 (*s*, 1 arom. C); 129.7, 129.3, 128.4 (3*d*, 5 arom. CH); 80.8, 70.6 (2*s*, C(4), C(7)); 49.6 (*t*, CH_2); 46.9 (*q*, MeN); 29.1 (*q*, *Me*C(4)); 24.4, 23.9 (2*q*, Me_2CH); 24.3, 24.1 (2*t*, 2 MeCH_2); 9.3, 9.1 (2*q*, 2 *Me*CH_2). CI-MS: 394 (100, $[M + 1]^+$), 197 (34), 100 (83). Anal. calc. for $C_{20}H_{31}N_3O_3S$ (393.56): C 61.04, H 7.94, N 10.68, S 8.15; found: C 61.35, H 7.96, N 10.91, S 8.74.

3. *Reactions of 2-Benzyl-4,4-dimethyl-1,2-thiazetidin-3-one 1,1-Dioxide* (**9a**). 3.1. *With* **1a**. A soln. of **1a** (15 mg, 0.13 mmol) and **9a** (24 mg, 0.1 mmol) in dry MeCN (3 ml) was stirred at r.t. No reaction was observed after 24 h, nor after 1 h at 81° (reflux). Refluxing the mixture overnight (*ca.* 15 h) led to an intractable mixture of decomposed material.

3.2. *With* NH_3. To 36 mg (0.15 mmol) of **9a** at −78°, liquid NH_3 (10 ml) was slowly added. The soln. was stirred without cooling until reaching r.t. The remaining colorless oil was treated with Et_2O and the solid material recrystallized from Et_2O: 35 mg (91%) N-*Benzyl-2-methyl-2-sulfamoylpropanamide* (**11**). Colorless crystals. M.p. 103–106°. ^{1}H-NMR ((D$_6$)DMSO): 8.22 (*t*, J = 5.90, NH); 7.35–7.15 (*m*, 5 arom. H); 6.98 (*s*, NH_2); 4.33 (*d*-like, PhCH_2); 1.52 (*s*, Me_2C). ^{13}C-NMR ((D$_6$)DMSO): 168.3 (*s*, CO); 139.2 (*s*, 1 arom. C); 128.1, 126.7, 126.5 (3*d*,

5 arom. CH); 65.7 (*s*, Me_2C); 42.7 (*t*, $PhCH_2$); 21.2 (*s*, Me_2C). A long-range H,C-coupling between $PhCH_2$ and *C*O was established ($CDCl_3$, 298 K, coloc puls program). CI-MS: 274 (100, $[M + NH_4]^+$), 257 (30, $[M + 1]^+$), 176 (12).

4. *Crystal-Structure Determination of* **7a** *and* **8b** (see *Table 2* and *Figs. 1* and *2*)[6]. The intensities were collected on a *Rigaku-AFC5R* diffractometer using graphite-monochromated MoK_α radiation ($\lambda = 0.71069$ Å) and a 12 kW rotating anode generator. The intensities were corrected for *Lorentz* and polarization effects, but not for absorption. Data collection and refinement parameters are listed in *Table 2*, views of the molecules and packing diagrams are shown in *Figs. 1* and *2*. The structures were solved by direct methods using SHELXS86 [14], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were located in difference electron density maps, and their positions were allowed to refine together with individual isotropic temperature factors. Refinements of the structures were carried out on *F* using full-matrix least-squares procedures. Neutral-atom scattering factors for non-H-atoms were taken from [15a] and the scattering factors for H-atoms from [16]. Anomalous dispersion effects were included in F_c [17]; the values for f' and f'' were those of [15b]. All calculations were performed using the TEXSAN [18] crystallographic software package.

Table 2. *Crystallographic Data for Compounds* **7a** *and* **8b**

	7a	**8b**
Crystallized from	EtOH/pentane	MeCN/Et_2O
Empirical formula	$C_4H_7NO_3S$	$C_{15}H_{21}N_3O_3S$
Formula weight	149.16	323.41
Crystal color, habit	colorless, irreg. prism	colorless, prism
Crystal dimensions [mm]	0.38 × 0.38 × 0.38	0.20 × 0.23 × 0.50
Crystal temp. [K]	173(1)	173(1)
Crystal system	monoclinic	monoclinic
Space group	$C2/c$	$P2_1/n$
Z	8	4
Lattice parameters		
Reflections for cell determination	25	25
2θ range [°]	$39 < 2\theta < 40$	$38 < 2\theta < 40$
a [Å]	18.689(6)	12.077(3)
b [Å]	8.347(5)	10.962(4)
c [Å]	9.061(4)	12.852(4)
β [°]	113.88(2)	93.67(2)
V [Å^3]	1292.6(9)	1698.1(8)
D_x [g cm^{-3}]	1.533	1.265
Absorption coefficient μ (MoK_α) [mm^{-1}]	0.433	0.206
Scan type	$\omega/2\theta$	$\omega/2\theta$
2θ(max) [°]	60	60
Total reflections measured	2066	5408
Symmetry-independent reflections	1896	4945
Reflections observed [$I > 2\sigma(I)$]	1663	3510
Variables	110	283
Final R	0.0315	0.0439
R_w[a])	0.0358	0.0393
Goodness of fit s	2.849	1.756
Final Δ_{max}/σ	0.0002	0.0006
$\Delta\rho$ (max, min) [e Å^{-3}]	0.31, −0.50	0.47, −0.39

[a]) Function minimized $\Sigma w(|F_o| - |F_c|)^2$, $1/w = \sigma^2(F_o) + (0.005F_o)^2$.

[6]) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication No. CCDC-10/28. Copies of the data can be obtained, free of charge, on application to the director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: teched@chemcrys.cam.ac.uk).

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