180. A Ring-Enlargement Reaction Yielding 1,2,5-Benzothiadiazonin-6-one 1,1-Dioxides

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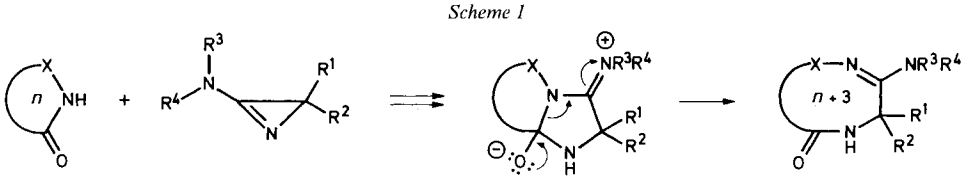
(23.IX.92)

At room temperature or under reflux in MeCN, 3-amino-2*H*-azirines **2** and 3,4-dihydro-2*H*-1,2-benzothiazin-3-one 1,1-dioxide (**4**) give 1,2,5-benzothiadiazonin-6-one 1,1-dioxides **5** in fair-to-good yield (*Scheme 2*). The structure of this novel type of heterocyclic compounds has been established by X-ray crystallography of **5a** (*Fig.*). A ring expansion *via* a zwitterionic intermediate of type **A'** is proposed as the reaction mechanism of the formation of **5**.

1. Introduction. – In the last few years, we have shown that NH-acidic heterocycles **1** with a $pK_a < 8$ react with 3-amino-2*H*-azirines **2** *via* ring expansion of the three-membered ring [1]. In some examples, the *n*-membered heterocyclic system **1** is enlarged by the three azirine atoms N–C(2)–C(3) to give (*n* + 3)-membered heterocycles of type **3** *via* the intermediate zwitterion **A** (*Scheme 1*). This reaction has been realized starting with 1,2-thiazol-3(2*H*)-one 1,1-dioxides and 1,2-thiazolidin-3-one 1,1-dioxides (*n* = 5) [2] [3], with four- and five-membered cyclic imides (*n* = 4 or 5) [2] [4], with a 1,2-oxazolidin-3-one (*n* = 5) [5], with 1,2-thiazolidine-2,4-dione (*n* = 5) [6], and with 2*H*-1,2,4-thiadiazin-3(4*H*)-one 1,1-dioxides (*n* = 6) [7] [8]. With these examples, it was demonstrated that *via* this ring enlargement also medium-sized heterocycles are accessible in high yields.

Scheme 1



1 **2** **A** **3**

In the present paper, we describe a second example of the formation of a new nine-membered heterocycle.

2. Results and Discussion. – The six-membered NH-acidic heterocycle we have chosen for this investigation, 3,4-dihydro-1,2-benzothiazin-3(2*H*)-one 1,1-dioxide (**4**), has been prepared according to [9]. The reaction with 3-amino-2*H*-azirines **2a–c** in MeCN occurred at room temperature to give 1,2,5-benzothiadiazonin-6-one 1,1-dioxides **5a–c** as sole products (*Scheme 2*).

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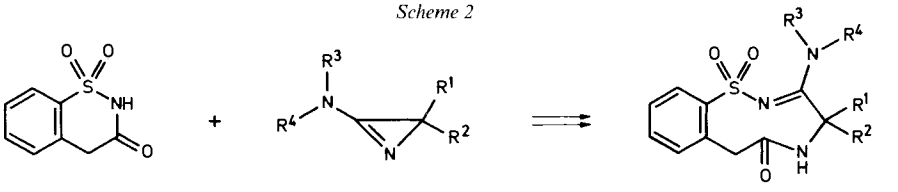
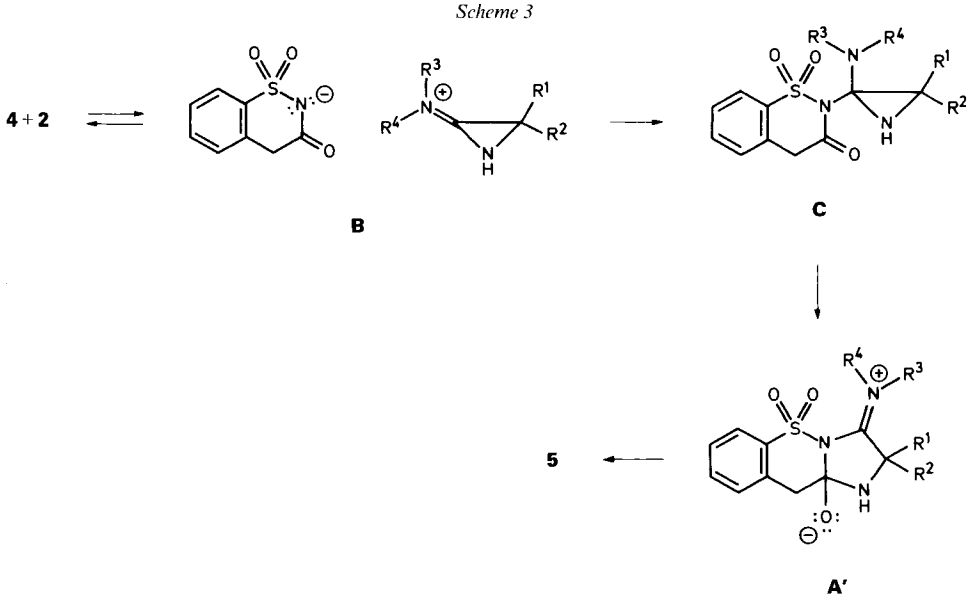
Scheme 2



4 **2a** $R^1 - R^4 = Me$; **b** $R^1 = i\text{-}Pr$, $R^2 - R^4 = Me$; **c** $R^1 - R^3 = Me$, $R^4 = Ph$ **5a** $R^1 - R^4 = Me$; **b** $R^1 = i\text{-}Pr$, $R^2 - R^4 = Me$; **c** $R^1 - R^3 = Me$, $R^4 = Ph$

Though in all three examples the analogous product was formed, there was a remarkable difference in the speed of the reaction observed. Whereas, with **2a**, the reaction was complete within 15 h at room temperature, it was sluggish in case of the 2-isopropyl-2-methylazirine **2b**. After 3 days, there was still starting material present, and the yield of **5b** was as low as 31%. With the *N*-phenyl derivative **2c**, the reaction at room temperature was also slow; yields of 65% of **5c** were obtained after refluxing the mixture for 3 h. This difference in the reactivity of 3-amino-2*H*-azirines **2** parallels with earlier studies [10–12], in which it has been shown that **2** with a large alkyl group at C(2) or with an aryl group at the exocyclic N-atom reacts much slower with 1,3,4-oxadiazol- and 1,3,4-thiadiazol-2(3*H*)-ones [10] [11], with 1,3-oxazol-5(4*H*)-ones [12], and with ethyl nitroacetate [12]. In the reaction of **4** and **2b** – in comparison with **2a** –, steric hindrance in the formation of the aziridine intermediate **C** (*Scheme 3*) may be responsible for the observed deceleration, but a stereoelectronic effect in the ring expansion **C** → **A′** is also possible. The reduced reactivity of **2c** can be explained with electronic and stereoelectronic effects on the nucleophilic attack of the aziridine N-atom (**C** → **A′**).

Scheme 3



4 + 2 **B** **C** **5** **A′**

The structure of **5a** has been established by X-ray crystallography[2]). Suitable crystals for the analysis were grown from $EtOH/CH_2Cl_2$. The molecular structure is shown in the *Figure*. There is one intramolecular H-bond between the amide H-atom and one of the O-atoms of the SO_2 group.

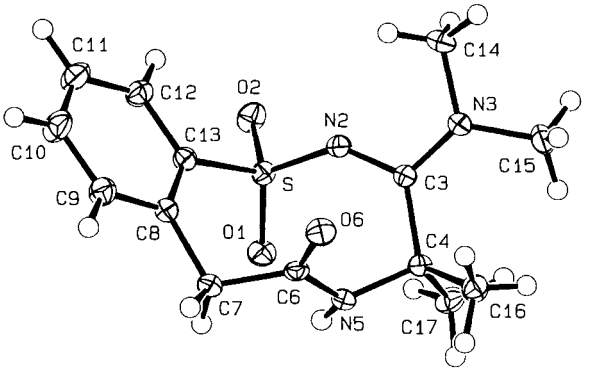


Figure. *ORTEP Plot* [13] *of the molecular structure of* **5a**. Thermal ellipsoids with 50% probability.

We thank Mr. *H. Frohofer* for elemental analyses and IR spectra, Mr. *T. Plüss* for NMR spectra, and Dr. *A. Lorenzi-Riatsch* and Mr. *N. Bild* for mass spectra. Financial support by the *Swiss National Science Foundation* and by *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged.

Experimental Part

General. See [14]. If not otherwise stated, IR spectra in $CHCl_3$, ^{1}H- and ^{13}C-NMR spectra in $CDCl_3$ at 300 and 50.4 MHz, respectively, and CI-MS with NH_3.

1. *3-(Dimethylamino)-4,5,6,7-tetrahydro-4,4-dimethyl-1,2,5-benzothiadiazonine-6-one 1,1-Dioxide* (**5a**). To a soln. of 600 mg (3 mmol) of *3,4-dihydro-1,2-benzothiazin-3(2*H*)-one 1,1-dioxide* (**4**) [9] in 12 ml of dry MeCN, a soln. of 371 mg (3.3 mmol) of *3-(dimethylamino)-2,2-dimethyl-2*H*-azirine* (**2a**) in 2 ml of MeCN was added, and the mixture was stirred at r.t. over night. Filtration yielded 576 mg **5a** as a colorless solid (m.p. 212.8–214.0°). A second crop (85 mg) of the same product was isolated from the mother liquor after standing at 3–4°. Total yield of **5a**: 661 mg (64%). Recrystallization from $EtOH/CH_2Cl_2$ gave anal. pure **5a**. M.p. 214.0–214.5°. IR: 3370*m*, 1693*s*, 1550*s*, 1535*s*, 1495*m*, 1435*m*, 1400*m*, 1262*s*, 1190*w*, 1153*m*, 1137*m*, 1113*s*, 1062*m*, 955*w*, 880*m*, 855*m*, 845*w*. ^{1}H-NMR: 8.42 (*s*, NH); 8.24 (*d*, J = 7.5, H–C(11)); 7.47, 7.39 (2*td*, J = 7.5, 1.5, H–C(9), H–C(10)); 7.30 (*d*, J = 7.2, H–C(8)); 4.27, 3.45 (*AB*, J = 13.1, CH_2); 3.22 (*s*, $(CH_3)_2N$); 2.06, 1.70 (2*s*, 2 CH_3). ^{13}C-NMR: 172.7, 169.7 (2*s*, C(3), C(6)); 141.3, 133.5 (2*s*, 2 arom. C); 132.8, 132.3, 130.0, 127.7 (4*d*, 4 arom. CH); 60.7 (*s*, C(4)); 43.8 (*t*, CH_2); 42.7 (br., $(CH_3)_2N$); 29.9, 26.6 (2*q*, 2 CH_3). CI-MS: 310 (100, $[M+1]^+$), 253 (18). Anal. calc. for $C_{14}H_{19}N_3O_3S$ (309.39): C 54.35, H 6.19, N 13.58, S 10.36; found: C 54.15, H 6.47, N 13.30, S 10.57.

2. *3-(Dimethylamino)-4,5,6,7-tetrahydro-4-isopropyl-4-methyl-1,2,5-benzothiadiazonine-6-one 1,1-Dioxide* (**5b**). In analogy to *Exper. 1*, a soln. of 350 mg (1.78 mmol) of **4** and 366 mg (2.6 mmol) of *3-(dimethylamino)-2-isopropyl-2-methyl-2*H*-azirine* (**2b**) in 7 ml of MeCN was stirred for 3 days at r.t. Filtration yielded 153 mg **5b** as a colorless solid (m.p. 215–218°). Prep. TLC (MeCN/EtOH 8:1) of the mother liquor gave another 34 mg of the same product. Total yield of **5b**: 197 mg (31%). Recrystallization from MeCN/EtOH yielded anal. pure **5b**. M.p. 216.0–217.0°. IR: 3365*m*, 1690*s*, 1655 (sh), 1565*m*, 1548*s*, 1538*s*, 1480*s*, 1442*m*, 1438*w*, 1403*m*, 1400*m*, 1395*m*, 1336*w*, 1275*s*, 1265 (sh), 1170*w*, 1150*m*, 1120*s*, 1078*m*, 969*m*, 942*w*. ^{1}H-NMR: 8.42 (*s*, NH); 8.21 (*d*, J = 7.1, H–C(11)); 7.45, 7.38 (2*td*, J = 7.5, *ca.* 1, H–C(9), H–C(10)); 7.32 (*d*, J = 7, H–C(8)); 4.32, 3.44 (*AB*, J = 12.3,

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[2]) All crystallographic data were deposited with the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, England.

CH_2); 3.25 (br. *s*, $(CH_3)_2N$); 2.59 (br. *quint.*, $(CH_3)_2CH$); 1.91 (*s*, CH_3); 1.10, 1.04 (2*d*, $J = 6.5$, $(CH_3)_2CH$). CI-MS: 338 (100, $[M + 1]^+$), 253 (45). Anal. calc. for $C_{16}H_{23}N_3O_3S$ (337.48): C 56.94, H 6.88, N 12.45, S 9.50; found: C 57.00, H 6.67, N 12.64, S 9.70.

3. *4,5,6,7-Tetrahydro-4,4-dimethyl-3-(*N*-methyl-*N*-phenylamino)-1,2,5-benzothiadiazonine-6-one 1,1-Dioxide* (**5c**). A soln. of 453 mg (2.3 mmol) of **4** and 488 mg (2.8 mmol) of *2,2-dimethyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**2c**) in 10 ml of MeCN was refluxed for 3 h. After cooling and filtration, 485 mg **5c** were isolated as a colorless solid (m.p. 201–202°). A second crop (74 mg) of the same product was isolated from the mother liquor after standing at 3–4°. Total yield of **5c**: 559 mg (65%). Recrystallization from $EtOH/CH_2Cl_2$ gave anal. pure **5c**. M.p. 211.7–212.5°. IR: 3380*m*, 1689*s*, 1548 (sh), 1530*s*, 1515*s*, 1505*s*, 1470*m*, 1445*m*, 1395*s*, 1385*m*, 1370*w*, 1328*w*, 1275*s*, 1250*m*, 1185*w*, 1155*m*, 1138*s*, 1115*s*, 1063*m*, 995*m*, 845*w*. ^{1}H-NMR: 8.37 (*s*, NH); 8.30 (*dd*, $J = 7.8, 1.5$, H–C(11)); 7.55–7.4, 7.4–7.2 (2*m*, 8 arom. H); 4.26, 3.46 (*AB*, $J = 13.1$, CH_2); 3.33 (*s*, CH_3N); 1.71, 1.04 (2*s*, 2 CH_3). ^{13}C-NMR: 172.1, 168.9 (2*s*, C(3), C(6)); 143.5 (*s*, arom. C of Ph); 141.5, 133.5 (2*s*, 2 arom. C); 132.9, 132.5, 129.9, 129.5, 128.9, 127.7, 127.3 (7*d*, 9 arom. CH); 61.4 (*s*, C(4)); 46.6 (*q*, CH_3N); 43.7 (*t*, CH_2); 29.2, 29.0 (2*q*, 2 CH_3). CI-MS: 372 (100, $[M + 1]^+$). Anal. calc. for $C_{19}H_{21}N_3O_3S$ (371.49): C 61.43, H 5.71, N 11.31, S 8.63; found: C 61.59, H 5.68, N 11.22, S 8.87.

4. *Crystal-Structure Determination of* **5a**[2]). 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, and an empirical absorption correction was applied using DIFABS [15]. Data collection and refinement parameters are listed in the *Table*. A view of the molecule is

Table. *Crystallographic Data of* **5a**

	5a
Crystallized from	$EtOH/CH_2Cl_2$
Empirical formula	$C_{14}H_{19}N_3O_3S$
Formula weight	309.38
Crystal color, habit	colorless, prism
Crystal temp. [K]	173(1)
Crystal dimensions [mm]	0.33 × 0.50 × 0.50
Crystal system	orthorhombic
Lattice parameters[a]) *a* [Å]	15.040(2)
b [Å]	17.442(2)
c [Å]	11.006(2)
V [Å^3]	2887.3(7)
Space group	*Pbca*
Z	8
D_x [g cm^{-3}]	1.423
Absorption coefficient μ(MoK_α) [cm^{-1}]	2.270
Absorption correction min, max	0.889, 1.122
Scan type	ω-2θ
2θ(max) [°]	60°
Total reflections measured	5395
Symmetry independent reflections	4711
Reflections observed [$I > 3\sigma(I)$]	3484
Variables	266
Final *R*	0.0323
R_w	0.0386
Goodness of fit *s*	2.156
Least-squares weights	$w = [\sigma^2(F_0) + (pF_0/2)^2]^{-1}$
p Factor	0.015
Final Δ_{max}/σ	0.0005
$\Delta\rho$(max; min) [e Å^{-3}]	0.32; −0.42

[a]) The cell dimensions were obtained from 23 accurately centered reflections with $38° < 2\theta < 40°$.

shown in the *Figure*. The structure was solved by direct methods using SHELXS86 [16] which revealed the positions of all non-H-atoms. Anisotropic refinement of the non-H-atoms and isotropic refinement of the H-atoms were carried out on F using full-matrix least-squares procedures [17], which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. Neutral atom scattering factors for non-H-atoms were taken from [18a] and the scattering factors for H-atoms from [19]. Anomalous dispersion effects were included in F_{calc} [20]; the values for $\Delta f'$ and $\Delta f''$ were those of [18b]. All calculations were performed using the TEXSAN [21] crystallographic software package.

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