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## Synthesis and structure of a 1,2,5,7-benzothiazonine

Schläpfer-Dähler, Marlise ; Prewo, Roland ; Bieri, Jost H ; Heimgartner, Heinz

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## SYNTHESIS AND STRUCTURE OF A 1,2,5,7-BENZOTHIATRIAZONINE

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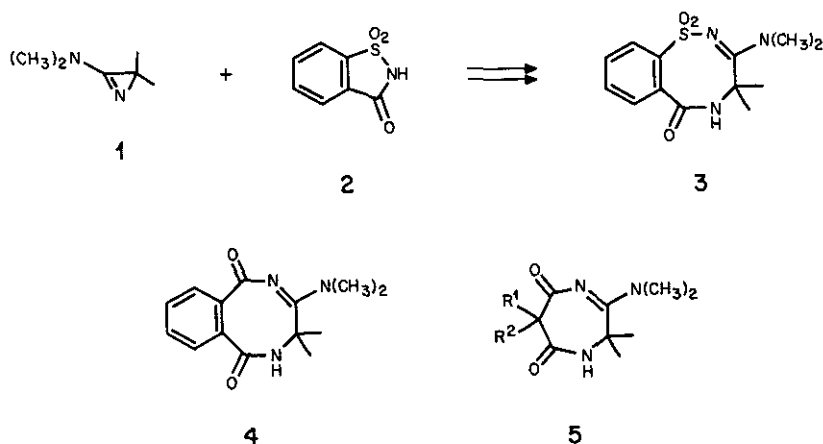
Abstract - 3-Dimethylamino-2,2-dimethyl-2H-azirine (1) and 4-phenyl-3,4-dihydro-2H-1,2,4-benzothiadiazin-3-on-1,1-dioxide (6) react already below room temperature to give a nine-membered heterocyclic product, namely 3-dimethylamino-4,4-dimethyl-7-phenyl-4,5,6,7-tetrahydro-1,2,5,7-benzothiatriazin-6-on-1,1-dioxide (7, Scheme 2) in a quantitative yield. The structure of this new heterocycle has been confirmed by X-ray crystallographic analysis (Fig. 1 and 2). In Scheme 2 a reaction mechanism for the formation of 7 is discussed, the zwitterion b being the key intermediate.

Several years ago, we have reported that 3-dimethylamino-2,2-dimethyl-2H-azirine (1) reacts with saccharine (2) to give the 1,2,5-benzothiadiazocine 3 by a ring expansion reaction <sup>1</sup> (Scheme 1). Similar reactions have been observed with phthalimide and with malonimides, yielding 1,4-benzodiazocine 4 <sup>1</sup> and 1,4-diazepines of type 5 <sup>2</sup>, respectively (Scheme 1).

Following this principle, we have made strong efforts to realize ring expansion reactions to nine-membered nitrogen heterocycles, starting with aminoazirine 1 and six-membered NH-acidic heterocycles. But all these reactions led to other products than medium sized rings <sup>3-6</sup> (cf. also <sup>7</sup>). We will now report on the first successful ring expansion reaction of this type, leading to a 1,2,5,7-thiatriazinone derivative. This ring system is, as far as we know, not reported in literature.

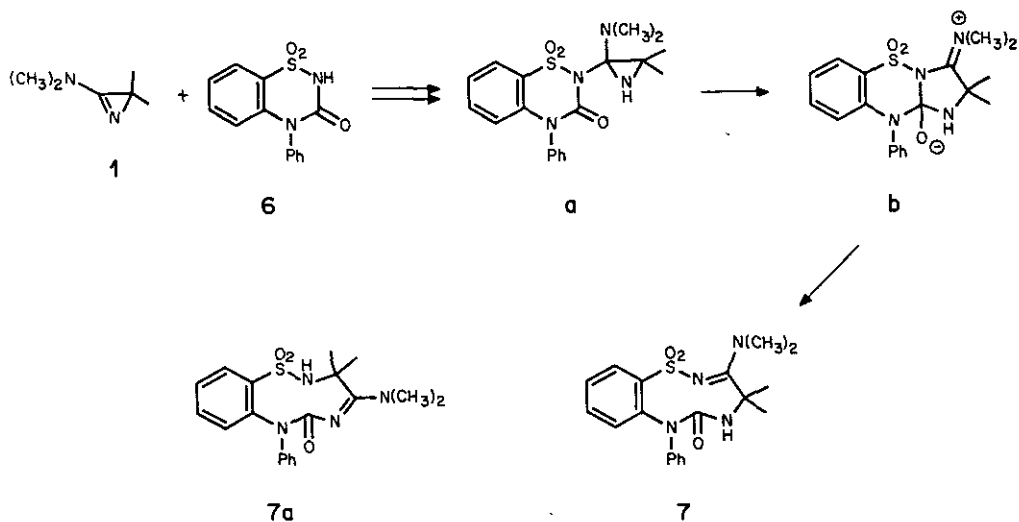
a) Part of the Ph.D. thesis of M.S.-D.

Scheme 1



The six-membered starting material 4-phenyl-3,4-dihydro-2H-1,2,4-benzothiadiazin-3-on-1,1-dioxide (**6**), has been synthesized in analogy to the reported method <sup>8</sup>, starting with diphenylamine and chlorosulfonyl isocyanate. In chloroform, the heterocyclic compound **6** reacts with aminoazirine **1** already below room temperature. Treatment of a suspension of 274 mg (1 mmol) of **6** in 5 ml of chloroform with 112 mg (1 mmol) of **1** at about -15°C and slowly warming up to room temperature yields a clear solution, and after evaporation of the solvent, an amorphous solid remains. Recrystallization from chloroform/ether yields 385 mg (99.5%) of 3-dimethylamino-4,4-dimethyl-7-phenyl-4,5,6,7-tetrahydro-1,2,5,7-benzothiatriazonin-6-on-1,1-dioxide (**7**, Scheme 2) as colourless crystals, mp 164-165°C (decomp.).

Scheme 2



Elemental analysis <sup>9</sup> and spectroscopic data of 7 suggest the structure of a (1:1)-adduct of azirine 1 and the heterocycle 6. In the ir (KBr), absorption bands for NH (3420 and 3290 cm<sup>-1</sup>), for an amide-carbonyl as well as an amidine group (1692, 1587, 1565 and 1543 cm<sup>-1</sup>), and for the SO<sub>2</sub>-function (1399 and 1144 cm<sup>-1</sup>) appear. The <sup>1</sup>H-nmr spectrum (CDCl<sub>3</sub>) shows multiplets for aromatic protons at 8.3-8.1 (1H) and 7.5-6.9 (8H) ppm, a singlet at 4.87 ppm for NH, a sharp singlet at 3.43 ppm for the (CH<sub>3</sub>)<sub>2</sub>N-group and two broad signals at 2.07 and 1.43 ppm for the geminal dimethyl group. In the <sup>13</sup>C-nmr spectrum (CDCl<sub>3</sub>), besides the signals of the aromatic C-atoms, two absorptions which can be correlated with an amidine-C-atom and an urea-carbonyl group, appear at low field (172.1 and 156.5 ppm). A sharp signal at 61.9 ppm corresponds to C(4) of 7 and a broad signal at 43.7 ppm to the dimethyl-amino group. The C-atoms of the geminal dimethyl group appear again as broad signals at 30.2 and 26.7 ppm. These broad methyl absorptions in the <sup>1</sup>H- as well as in the <sup>13</sup>C-nmr can be explained by a slow conformational change of the nine-membered ring system.

The mentioned spectroscopic data are not unambiguous; they are in accord with structure 7 as well as 7a (Scheme 2). Therefore, we have decided to proof the structure of the (1:1)-adduct by X-ray crystallography. Colourless single crystal of 7 has been obtained from chloroform/acetonitrile/ether. They belong to the monoclinic space group Cc with a = 16.724(1), b = 9.775(1), c = 12.125(1) Å, β = 109.82(1)°, and V = 1862.8 Å<sup>3</sup>. The intensities of 3469 independent reflexions were measured at ca. -140°C with monochromatized MoK<sub>α</sub> radiation (ω-scan mode) on a Nicolet R3 four-circle diffractometer within 2θ < 65°. The structure was solved by direct methods using SHELXTL <sup>10</sup>. In the blocked cascade refinement (ca. 100 variables/block) the H-atoms were varied with isotropic temperature factors after their location in a difference electron density map while the other atoms were refined anisotropically. An empirical extinction coefficient was also included. The refinement converged at an R-value of 0.027 using all reflexions.

The molecular structure of 7 is given in Fig. 1, bond lengths, bond angles and torsion angles of the puckered nine-membered ring are shown in Fig. 2 <sup>11</sup>.

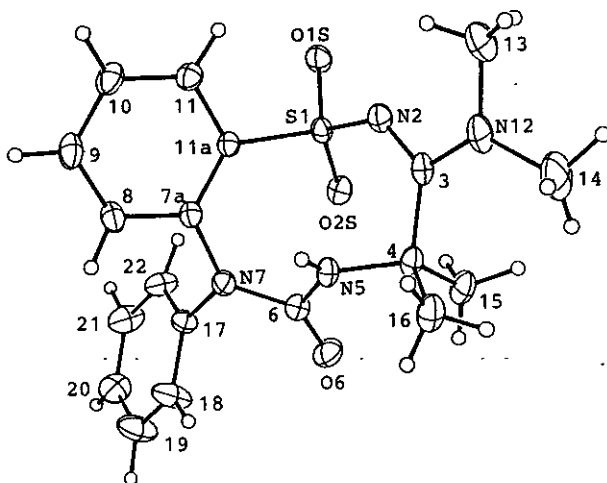
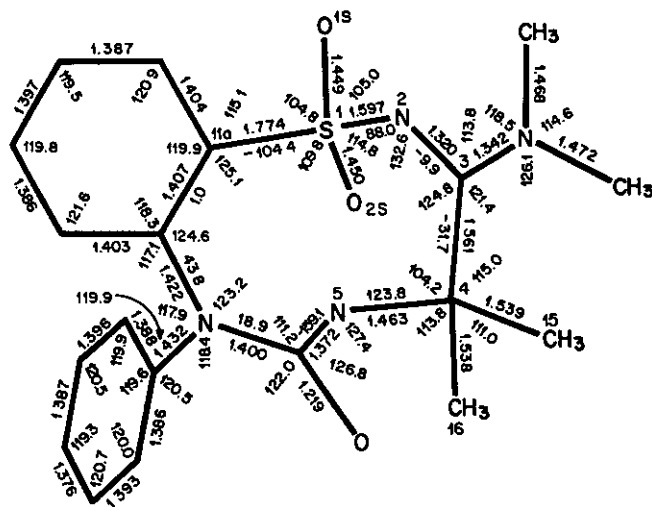


Fig. 1. Molecular structure of the 4,5,6,7-tetrahydro-1,2,5,7-benzothiazin-6-on-1,1-dioxide 7.



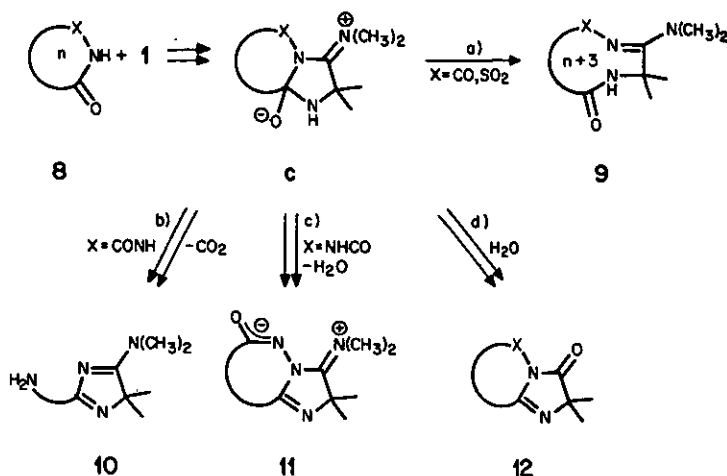
O(1S)-S(1)-O(2S) 114.5°  
 N(2)-S(1)-C(11a) 107.3°  
 C(3)-C(4)-C(16) 106.9°  
 N(5)-C(4)-C(15) 105.9°

Fig. 2. Bond lengths in Å (e.s.d.s 0.001-0.003 Å), bond angles and intraannular 9-ring torsion angles in degrees (e.s.d.s 0.1-0.2 degree) of compound 7.

A reasonable reaction mechanism for the formation of 7 is given in Scheme 2. The aziridine intermediate a, generated via protonation of azirine 1 by the NH-acidic heterocycle 6 and nucleophilic attack of the anion to the amidinium C-atom, undergoes a rearrangement to give the zwitterion b (cf. <sup>1-7</sup>). In this step, the cleavage of the original C-N double bond of azirine 1 occurs. Breaking of the central C-N bond of b leads then to the ring expanded heterocycle 7.

It seems that the aminoazirine 1 and NH-acidic heterocycles of type 8 usually react to give the nonisolated zwitterionic intermediate c as the primary product (Scheme 3). Until now we have observed several different reactions of c: a) Ring enlargement via cleavage of the central C-N bond leads to the (n+3)-membered heterocycle of type 9 <sup>1,2</sup>. b) With X = CONH a profound rearrangement including a decarboxylation takes place, leading to 5-dimethylamino-4,4-dimethyl-4H-imidazoles of type 10 <sup>3,5,12</sup>. c) The zwitterion c from 1 and cyclic hydrazides (X = NHCO) loses water to yield the new zwitterion 11 as a stable compound <sup>13</sup>. d) In some cases, c can be hydrolyzed to give imidazolinones of type 12 <sup>14,15</sup>. We were able to show that the reaction sequences a) and b) are general, whereas c) and d) as well as a few other reactions of 1 with NH-acidic heterocycles <sup>6,12,16</sup> are of limited scope.

Scheme 3



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