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

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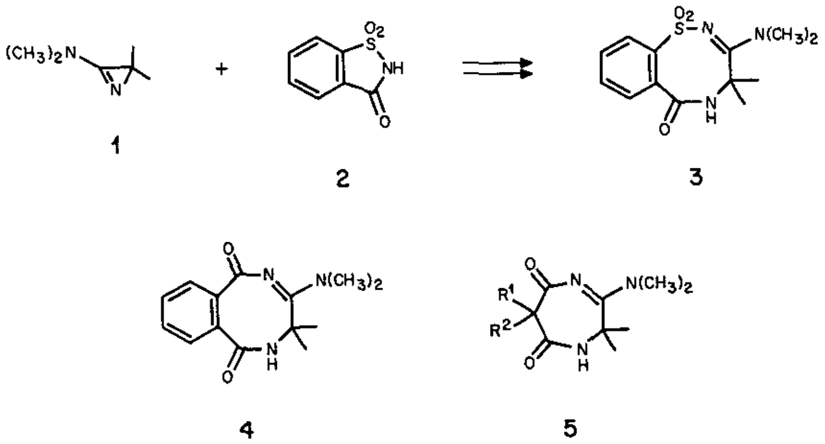
Abstract - 3-Dimethylamino-2,2-dimethyl-2H-azirine (1) and 4-phenyl-3,4-dihydro-2H-1,2,4-benzothiadiazin-3-on-1,1-dioxide (6) react already below room temperature to give a nine-membered heterocyclic product, namely 3-dimethylamino-4,4-dimethyl-7-phenyl-4,5,6,7-tetrahydro-1,2,5,7-benzothiatriazonin-6-on-1,1-dioxide (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 [1] (Scheme 1). Similar reactions have been observed with phthalimide and with malonimides, yielding 1,4-benzodiazocine 4 [1] and 1,4-diazepines of type 5 [2], 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 [3-6] (cf. also [7]). We will now report on the first successful ring expansion reaction of this type, leading to a 1,2,5,7-thiatriazonine derivative. This ring system is, as far as we know, not reported in literature.

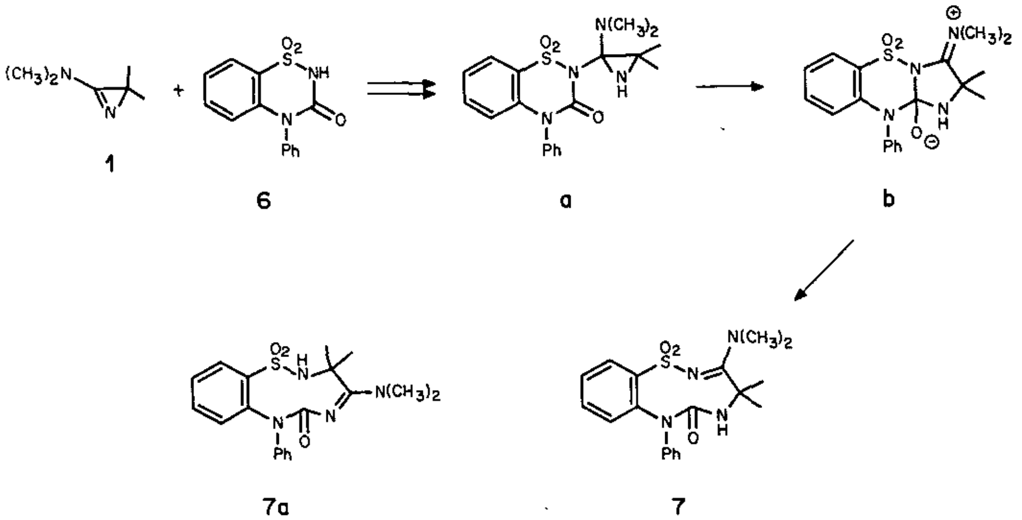
a) Part of the Ph.D. thesis of M.S.-D.

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 [8], 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 [9] 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^{-1}), for an amide-carbonyl as well as an amidine group (1692, 1587, 1565 and 1543 cm^{-1}), and for the SO_2-function (1399 and 1144 cm^{-1}) appear. The ^{1}H-nmr spectrum ($CDCl_3$) 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 $(CH_3)_2N$-group and two broad signals at 2.07 and 1.43 ppm for the geminal dimethyl group. In the ^{13}C-nmr spectrum ($CDCl_3$), 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 dimethylamino 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 ^{1}H- as well as in the ^{13}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, $\beta = 109.82(1)^\circ$, and $V = 1862.8$ Å^3. The intensities of 3469 independent reflexions were measured at ca. -140°C with monochromatized MoK_α radiation (ω-scan mode) on a Nicolet R3 four-circle diffractometer within $2\theta < 65^\circ$. The structure was solved by direct methods using SHELXTL [10]. 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 [11].

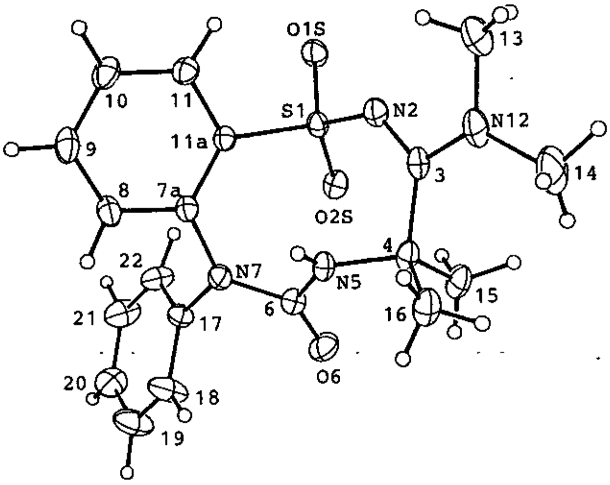
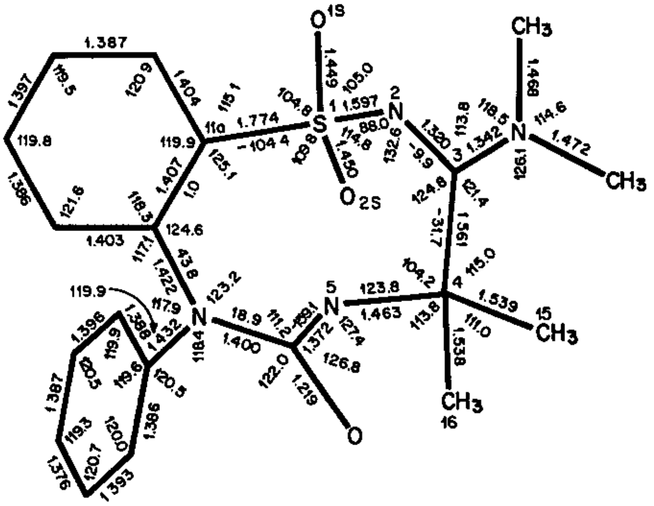


Fig. 1. Molecular structure of the 4,5,6,7-tetrahydro-1,2,5,7-benzothiatriazonin-6-on-1,1-dioxide 7.



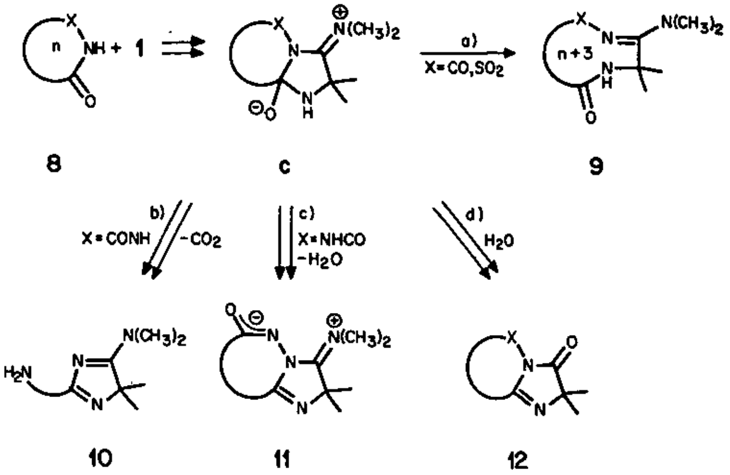
O(1S)-S(1)-O(2S) 114.5°
N(2)-S(1)-C(11a) 107.3°
C(3)-C(4)-C(16) 106.9°
N(5)-C(4)-C(15) 105.9°

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. [1-7]). 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 [1,2]. b) With X = CONH a profound rearrangement including a decarboxylation takes place, leading to 5-dimethylamino-4,4-dimethyl-4H-imidazoles of type 10 [3,5,12]. c) The zwitterion c from 1 and cyclic hydrazides (X = NHCO) loses water to yield the new zwitterion 11 as a stable compound [13]. d) In some cases, c can be hydrolized to give imidazolinones of type 12 [14,15]. 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 [6,12,16] are of limited scope.

Scheme 3



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