SYNTHESIS AND THREE-DIMENSIONAL STRUCTURE OF 9-THIA-1,5-DIAZABICYCLO[5.3.0]DECANE-2,6-DIONE

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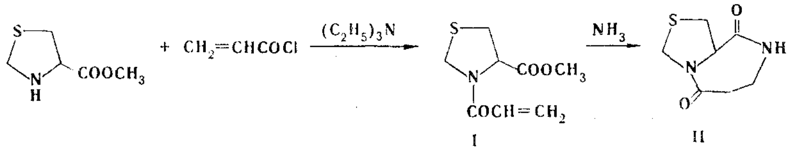
9-Thia-1,5-diazabicyclo[5.3.0]decane-2,6-dione was obtained by the reaction of methyl 3-acrylylthiazolidine-4-carboxylate with ammonia. It was established by x-ray diffraction analysis that the diazepine ring has a twisted boat conformation.

In order to obtain compounds with aziridine and thiazolidine-4-carboxylic acid (γ-thioproline) fragments included in their compositions we set out to develop a method for the synthesis of a dipeptide, viz., β-alanyl-γ-thioproline methyl ester. We planned to accomplish this by acylation of methyl thiazolidine-4-carboxylate with acrylyl chloride with subsequent addition of ammonia to the double bond. We proposed to use the dipeptide as the starting compound for the preparation of an N-substituted aziridine by intramolecular alkylation with methyl 1,2-dibromopropionate.

However, an attempt to synthesize this dipeptide by this method led to the production of a new heterocyclic system, viz., 9-thia-1,5-diazabicyclo[5.3.0]decane-2,6-dione (II), which can be regarded as the cyclic form of a dipeptide containing thiazolidine-4-carboxylic acid and β-alanine.



The structure of II was confirmed by the PMR spectrum. To establish the three-dimensional structure of II we subjected it to x-ray diffraction study. The crystal is constructed from two crystallographically nonequivalent A and B molecules, which differ with respect to their conformations. The three-dimensional structures of the A and B molecules are presented in Fig. 1 with an indication of their geometries and designation of their atoms. A large difference is observed in the lengths of the C5—C6 (1.42 and 1.57 Å) and C6—N7 (1.42 and 1.50 Å) bonds of the A and B molecules. This fact and the large difference in the C4—C5—C6 bond angles (120 and 111°) are possibly associated with the significant thermal vibrations of the C5 and C6 atoms in both molecules [1].

The average value of the C—S bond lengths in the thiazolidine ring (1.80 Å) is close to the length of the C—S single bond (1.817 Å) [2]. The average value of the C4—N3 and C8—N7 bonds (1.35 Å) in the A and B molecules indicates the existence of conjugation of the unshared electron pairs of the nitrogen atoms with the π electrons of the carbonyl groups.

The thiazolidine ring has an envelope conformation. The sulfur atoms deviate 0.81 and 0.70 Å, respectively, from the plane of the remaining four atoms in the A and B molecules. The conformation of the seven-membered ring is shown in Fig. 2 along with the torsion angles for the A and B molecules (the torsion angles for the B molecule are given below the values for the A molecule). The diazepine ring has a twisted boat conformation. The C5 (0.44 Å) and C9 (0.52 Å) have the maximum deviations from the mean square plane drawn through the diazepine ring.

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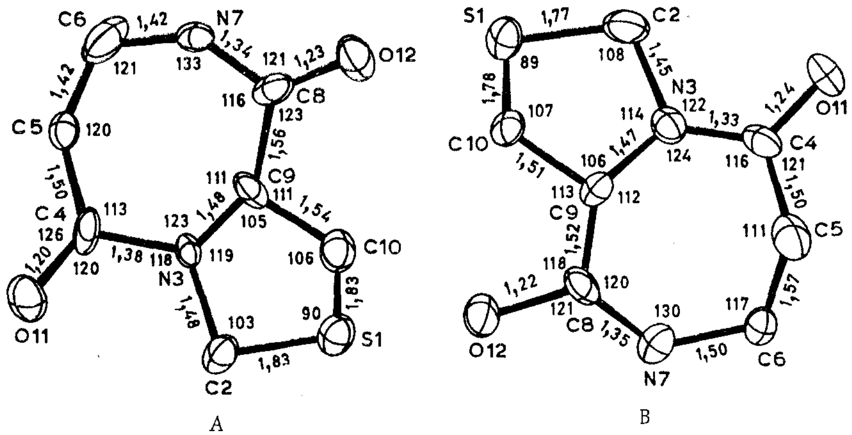

Fig. 1. Designations of the atoms and geometries of the 9-thia-1,5-diazabicyclo[5.3.0]decane-2,6-dione molecule.

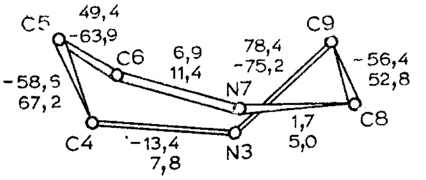

Fig. 2. Conformation of the diazepine ring and torsion angles in the A and B molecules.

TABLE 1. Coordinates of the Atoms in the A and B Molecules

Atom	Molecule A			Molecule B		
	x	*y*	*z*	*x*	*y*	*z*
S1	0,3309 (3)	0,2502 (0)	0,8696 (1)	0,1659 (3)	0,1281 (2)	0,6299 (1)
C2	0,5613 (13)	0,1553 (9)	0,9346 (3)	−0,0502 (13)	0,2304 (11)	0,5685 (3)
N3	0,6893 (10)	0,0109 (7)	0,9032 (2)	−0,1862 (10)	0,3735 (7)	0,5955 (2)
C4	0,8418 (15)	−0,1068 (10)	0,9413 (3)	−0,3389 (13)	0,4854 (10)	0,5595 (3)
C5	0,9542 (16)	−0,2504 (11)	0,9048 (3)	−0,4800 (12)	0,6217 (11)	0,5935 (3)
C6	0,7723 (18)	−0,3571 (12)	0,8653 (5)	−0,2616 (14)	0,7466 (10)	0,6289 (3)
N7	0,5624 (13)	−0,2871 (7)	0,8203 (3)	−0,0626 (13)	0,6731 (8)	0,6812 (3)
C8	0,5033 (16)	−0,1272 (10)	0,8009 (3)	−0,0090 (14)	0,5088 (9)	0,6979 (3)
C9	0,6924 (13)	0,0163 (10)	0,8339 (2)	−0,1786 (11)	0,3647 (9)	0,6647 (2)
C10	0,5791 (17)	0,1956 (10)	0,8142 (3)	−0,0677 (15)	0,1901 (8)	0,6843 (3)
O11	0,8504 (10)	−0,0977 (8)	0,9977 (2)	−0,3801 (10)	0,4720 (8)	0,5010 (2)
O12	0,3136 (9)	−0,0980 (8)	0,7586 (2)	0,1725 (9)	0,4720 (8)	0,7406 (2)
H1C10	0,743	0,282	0,819	−0,252	0,110	0,683
H2C10	0,465	0,191	0,770	0,017	0,190	0,731
H1C2	0,735	0,241	0,949	−0,200	0,127	0,545
H2C2	0,436	0,106	0,971	0,072	0,270	0,533
HC9	0,911	−0,009	0,827	−0,401	0,386	0,676
HN7	0,431	−0,377	0,794	0,076	0,751	0,702
H1C6	0,880	−0,466	0,847	−0,404	0,840	0,651
H1C5	1,108	−0,185	0,866	−0,608	0,707	0,564
H2C5	1,094	−0,310	0,937	−0,606	0,555	0,632
H2C6	0,645	−0,404	0,899	−0,124	0,789	0,595

In the crystal the A and B molecules are associated in chains directed along the b axis through two hydrogen bonds, viz., $N7^A \cdots O12^B = 3.04$ Å ($H \cdots O = 1.99$ Å, $\angle N{-}H \cdots O = 175.5°$) and $N7^B \cdots O12^A = 2.92$ Å ($H \cdots O = 1.96$ Å, $\angle N{-}H \cdots O = 166.2°$). The remaining intermolecular distances are no less than the sums of the van der Waals radii of the corresponding atoms [3].

EXPERIMENTAL

The PMR spectrum of diazabicyclodecanedione II in $CDCl_3$ was obtained with a Brucker WM-360 spectrometer (West Germany) at an operating frequency of 360 MHz with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol with ethanol as the eluent.

Methyl 3-Acrylylthiazolidine-4-carboxylate (I). An 8-ml (0.1 mole) sample of acrylyl chloride was added with vigorous stirring at 0°C to a mixture of 14.70 g (0.1 mole) of methyl thiazolidine-4-carboxylate and 14 ml (0.1 mole) of triethylamine in 200 ml of absolute ether. The triethylamine salt was removed by filtration, and the filtrate was evaporated in vacuo to give 15.08 g (75%) of a yellowish oil.

9-Thia-1,5-diazabicyclo[5.3.0]decane-2,6-dione (II). A solution of 15.08 g (0.075 mole) of thiazolidine I in 100 ml of methanol was saturated with ammonia for 25-30 h until the starting compound vanished (according to monitoring by TLC). The solvent was evaporated, 10-15 ml of ethanol was added to the residue (a yellow oil), and the solution was allowed to stand in the refrigerator for 40-48 h until fine, acicular, yellowish crystals formed. Two recrystallizations from ethanol gave 2.09 g (15%) of a colorless crystalline substance with mp 179-180°C. PMR spectrum: 2.74 (1H, m, J = 4.4, 9.3, and 16.8 Hz, 3-H), 2.94 (1H, m, J = 3.6, 8.0, and 16.8 Hz, 3'-H), 3.23 (1H, dd, J = 6.6 and 12.6 Hz, 8-H), 3.45 (1H, m, J = 4.4, 8.0, and 14.6 Hz, 4-H), 3.64 (1H, m, J = 3.6, 9.3, and 14.6 Hz, 4'-H), 3.80 (1H, dd, J = 6.2 and 12.6 Hz, 8'-H), 4.57 (1H, d, J = 10.2 Hz, 10-H), 4.73 (1H, dd, J = 6.2 Hz, 7-H), 4.82 (1H, d, J = 10.2 Hz, 10'-H), and 6.50 ppm (1H, broad s, NH). Found: C 45.1; H 5.4; N 14.9%. $C_7H_{10}N_2O_2S$. Calculated: C 45.2; H 5.4; N 15.1%.

Crystals with the composition $C_7H_{10}N_2O_2S$ were grown from alcohol and were monoclinic with the following parameters: $a = 4.847(1)$, $b = 7.815(3)$, $c = 21.280(3)$ Å, $\beta = 96.56(8)°$, $V = 800.7$ Å^3, $M = 186.25$, $d_{calc} = 1.54$ g-cm^{-3}, $\mu(\mathrm{Cu}\ K_\alpha) = 31.7$ cm^{-1}, $Z = 4$, space group $P2_1$, and $F_{000} = 392$. The intensities of 1353 independent reflections were measured with a Syntex $P2_1$ diffractometer from a 0.5 by 0.25 by 0.20 mm single crystal by the method of $\theta/2\theta$ scanning in copper emission (with a graphite monochromator) up to $2\theta_{max} = 150°$. A total of 1251 reflections with $I \geqslant 2\sigma_1$ were used in the calculations. A model was found by the direct method with the MULTAN program [4]. Normalization of the structural factors was carried out with allowance for the known geometry of the molecular fragments. The best of 16 calculated variants of the phases made it possible to localize all of the nonhydrogen atoms of the molecule. The initial R factor was 0.264. The structure was refined by the method of least squares within the fully matrix anisotropic approximation with the aid of the weight scheme $1/W = \sigma^2 + 0.0009F^2$ up to $R = 0.062$. The positions of the hydrogen atoms obtained from Fourier differential synthesis were not refined ($B_{isotr} = 6.0$ Å^2). The standard deviations of the interatomic distances and bond angles did not exceed 0.02 Å and 2°, respectively. The coordinates of the atoms are given in Table 1.

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