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THE ISOXAZOLIDINE – 1,2,4-TRIAZOLIDINE-3-THIONE TAUTOMERIC SYSTEM

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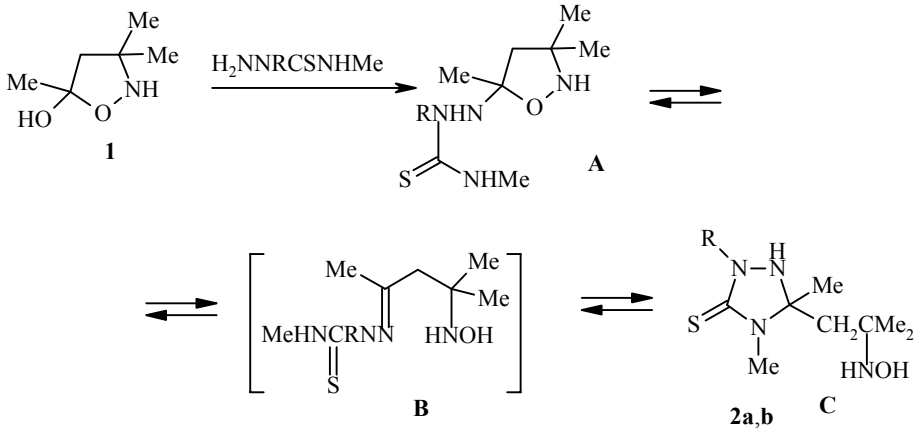
The products of the condensation of 5-hydroxy-3,3,5-trimethylisoxazolidine (**1**) with 4-phenylthiosemicarbazide and 2-methyl-4-phenylthiosemicarbazide have predominantly isoxazolidine or 1,2,4-triazolidine structure and do not display ring-ring tautomeric interconversion in solution [1]. Such tautomerism was discovered in studying the structure of **2a** and **2b**, which are the products of **1** with 4-methyl- and 2,4-dimethylthiosemicarbazides.

Thiones **2a** and **2b** are formed after brief heating of the starting reagents in methanol at reflux in the presence of catalytic amounts of acetic acid.



2 a R = H, **b** R = Me

In the crystalline state, **2a** and **2b** have triazolidine structure **C**, which was supported by ^{13}C NMR spectra in the solid phase.

The same species is the only form for **2a** in both nonpolar and polar solvents. Ring-ring **A** ⇄ **C** tautomeric equilibrium was observed for **2b**, which is a derivative of 2,4-dimethylthiosemicarbazide. Thus, the appearance of an additional cyclic form is observed spectrally upon dissolving this compound. On the basis of our previous data [1], this new species was identified as isoxazolidine structure **A**. The tautomeric equilibrium was established over 72 h and depends upon the polarity of the solvent. The content of 1,2,4-triazolidine form **C** increases in going from $CDCl_3$ to basic aprotic solvents such as pyridine-d_5, DMSO-d_6, and DMF-d_7.

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The **A** ⇄ **C** tautomerism is a new example of ring-ring equilibria for 5-functionally-substituted isoxazolidines. Other examples were given in our previous work [1, 2].

The ^{1}H NMR spectra in $CDCl_3$ and ^{13}C NMR spectra in DMSO-d_6 were taken on a Bruker CXP-100 spectrometer at 25 MHz, AC 200 spectrometer at 200 MHz, and AM 500 spectrometer at 125 MHz.

Isoxazolidine 1 was obtained according to Belly [3].

4,5-Dimethyl-5-(2-methyl-2-hydroxyaminopropyl)-1,2,4-triazolidine-3-thione (2a) was obtained in 50% yield; mp 136-138°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): form **C** (100%): 1.44 (3H, s, CH_3); 1.51 (3H, s, CH_3); 1.86 (3H, s, 5-CH_3); 2.20, 2.34 (AB system, 2H, J_{AB} = 13, CH_2); 3.08 (3H, s, 4-CH_3); 4.83 (1H, br. s, NH); 7.13 (2H, br. s, OH + NHC=S). ^{13}C NMR spectrum, δ, ppm: form **C** (100%): 21.1 and 24.2 (2CH_3), 28.4 (5-CH_3), 31.2 (4-CH_3), 54.2 (CH_2), 65.8 (C–N), 92.3 ($C_{(5)}$), 179.4 ($C_{(3)}$). Found, %: C 43.97; H 8.28; N 25.70. $C_8H_{18}N_4OS$. Calculated, %: C 44.01; H 8.31; N 25.66.

2,4,5-Trimethyl-5-(2-methyl-2-hydroxyaminopropyl)-1,2,4-triazolidine-3-thione (2b) was obtained in 45% yield; mp 189-192°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): form **A** (20%): 1.24 (6H, s, 3,3-$(CH_3)_2$); 1.46 (3H, s, 5-CH_3); 1.84, 2.09 (AB system, 2H, J_{AB} = 13, 4-H); 3.10 (3H, d, CH_3N); 3.62 (2H, s, CH_3N); 4.32 (1H, br. s, NH); form **C** (80%): 1.40 (3H, s, CH_3); 1.50 (3H, s, CH_3); 1.89 (3H, s, 5-CH_3); 2.24, 2.39 (AB system, 2H, J_{AB} = 13, CH_2); 3.08 (3H, s, 4-CH_3); 3.58 (2H, s, 2-CH_3); 4.43 (1H, br. s, NH); 6.89 (1H, br. s, NH); 7.46 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: form **A** (10%): 20.8 (3,3-$(CH_3)_2$), 27.5 (5-CH_3), 38.7 (CH_3N), 53.4 ($C_{(4)}$), 60.9 ($C_{(3)}$), 100.4 ($C_{(5)}$), 177.8 (C=C); form **C** (90%): 21.4 (CH_3), 24.8 (CH_3), 28.8 (5-CH_3), 31.8 (4-CH_3), 42.2 (2-CH_3), 54.5 (CH_2), 65.9 (C–N), 93.1 ($C_{(5)}$), 183.8 ($C_{(3)}$). Found, %: C 46.49; H 8.71; N 24.07. $C_9H_{20}N_4OS$. Calculated, %: C 46.52; H 8.68; N 24.11.

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