Synthesis and crystal structure of (4*S*,5*R*)-3,4-dimethyl-5-phenyl-2-(hydroxyethylimino)-1,3-thiazolidine

Arstan M. Gazaliev,[a] Oralgazy A. Nurkenov,[a] Koblandy M. Turdybekov,[b] Serik D. Fazylov,[a] Marat K. Ibraev,*[a] Dastan M. Turdybekov[b] and Meruert B. Issabaeva[c]

[a] *Institute of Organic Synthesis and Coal Chemistry of the Republic of Kazakhstan, 470061 Karaganda, Kazakhstan. Fax: +7 3212 41 3865; e-mail: mkibr@yandex.ru*
[b] *Institute of Phytochemistry, 470032 Karaganda, Kazakhstan*
[c] *Karaganda State Medical Academy, 470061 Karaganda, Kazakhstan*

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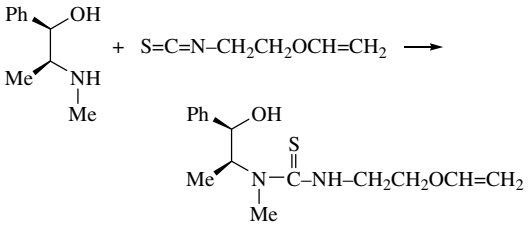
The acid hydrolysis *l*-*N*-(*N*′-vinyloxyethylthiocarbamoyl)ephedrine has been investigated and the X-ray diffraction analysis of the synthesised (4*S*,5*R*)-3,4-dimethyl-5-phenyl-2-(hydroxyethylimino)-1,3-thiazolidine has been carried out.

Thiourea derivatives have antimicrobial, anti-inflammatory, anti-ulcerous and nematocide properties, growth regulatory activity and high insecticidal and acaricidal activities.[1,2] Interest in the derivatives of thioureas is caused by not only their biological activity but also the fact that they are convenient synthons in organic synthesis.[3,4]

We have synthesised *l*-*N*-(*N*′-vinyloxyethylthiocarbamoyl)-ephedrine.[5] Thioamide **1** was obtained through interaction between *l*-ephedrine and vinyloxyethyl isothiocyanate in an alcoholic medium.†



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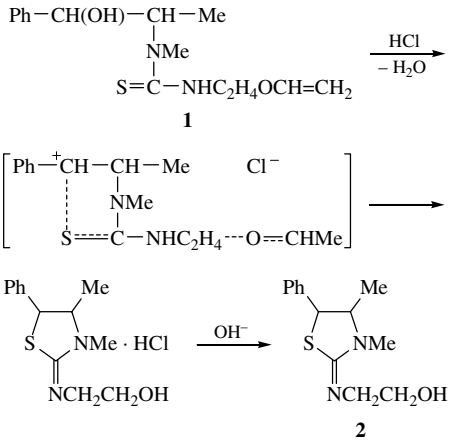
There are no data on the hydrolysis of thiourea derivatives of ephedrine alkaloids in the literature. It is known that thioamides are susceptible to hydrolysis, especially in alkaline conditions; the full hydrolysis resulting in carboxylic acids, hydrogen sulfide and ammonia or amines is possible, but frequently under conditions of nitrile hydrolysis, heterogeneous ring compounds or products of oxidising splitting[6] are obtained.

To study the reactivity of thioamide on the basis of *l*-ephedrine containing replaced oxyethyl group, we investigated the acid hydrolysis of *l*-*N*-(*N*′-vinyloxyethylthiocarbamoyl)ephedrine **1** in the presence of concentrated hydrochloric acid at ambient temperature.‡

To establish the dimensional structure of a molecule of (4*S*,5*R*)-3,4-dimethyl-5-phenyl-2-(hydroxyethylimino)-1,3-thiazolidine **2**, X-ray diffraction analysis was performed.§ The structure of the molecule of **2** is presented in Figure 1.

The bond lengths and valence angles are close to the routine.[7] The thiazolidine ring in a molecule of **2** accepts the 4β-envelope



conformation, to some extent distarted from the theoretical ($\Delta C_s^4 = 9.57°$). The C(4) atom leaves the plane of other atoms of a cycle on ±0.49 Å; the S(1), C(2), N(3) and C(5) atoms are coplanar to within ±0.05 Å. In a 4β-envelope conformation, the methyl group at the C(4) atom and the phenyl group at the C(5) atom of the group are oriented axially [torsion angles S(10)S(4)N(3)S(2) –91.72° and C(11)C(5)C(2)N(3) 88.54°]. The

† The IR spectra were recorded on an AVATAR-320 instrument (in KBr tablets). The ^{1}H NMR spectra were measured on a Varian MERCURY-300 insrument at a frequency of 300 MHz in a CD_3Cl solution with HMDS as the internal standard. The melting points were measured on a Boetius instrument.

l-N-*(*N′-*Vinyloxyethylthiocarbamoyl)ephedrine* **1**. 1.5 g (0.012 mol) of vinyloxyethyl isothiocyanate was added to 2 g (0.012 mol) of *l*-ephedrine in 5 ml of ethanol. The mixture was agitated at ambient temperature for 20–30 min; then, 1/3 of solvent was distilled off and allowed to stand overnight. The precipitate was filtered off and washed with diethyl ether to give 2.9 g (86%) compound **1**, mp 96–97 °C. IR (ν/cm^{-1}): 1530–1500 [NH–C(S)], 3400–3200 (OH). ^{1}H NMR, δ: 0.86 (d, *Me*CH, J_{HH} 8.4 Hz), 2.01 (s, MeN), 2.34–2.52 (m, C*H*Me), 4.43 (d, CH–O, J_{HH} 10.6 Hz), 7.10–7.24 (m, Ph), 3.06 (t, NCH_2), 3.40 (t, CH_2O), 6.44 (q, CH=C, J_{HH} 4.6 Hz), 4.01–4.07 (dd, C=CH_2, J_{HH}^{cis} 5.8 Hz, J_{HH}^{trans} 11.8 Hz). Found (%): C, 61.27; H, 7.36. Calc. for $C_{15}H_{22}O_2N_2S$ (%): C, 61.22; H, 7.48.

‡ *(4S,5*R*)-3,4-Dimethyl-5-phenyl-2-(hydroxyethylimino)-1,3-thiazolidine* **2**. 10 ml of concentrated hydrochloric acid was added dropwise to 1.5 g (0.009 mol) of *l*-*N*-(*N*′-2-vinyloxyethylthiocarbamoyl)ephedrine at ambient temperature. The mixture was agitated for 3 h; then, a six-fold water volume was added, and the solvent was distilled off in a vacuum. A 40% aqueous solution of caustic soda was added to the residue, and the product was extracted with benzene. The organic layer was dried over Na_2SO_4, the solvent was distilled off to give 0.76 g (60%) of crystal product, mp 108–109 °C. IR (ν/cm^{-1}): 1680–1650 (C=N), 3500–3000 (OH). ^{1}H NMR, δ: 0.92 (d, *Me*CH, J_{HH} 8.6 Hz), 2.10 (s, MeN), 2.30–2.50 (m, C*H*Me), 4.93 (d, CHS, J_{HH} 10.6 Hz), 7.00–7.15 (m, Ph), 3.14 (t, NCH_2), 3.32 (t, CH_2CH_2). Found (%): C, 62.35; H, 7.12. Calc. for $C_{13}H_{18}ON_2S$ (%): C, 62.40; H, 7.20.

§ *Crystal data for* **2** ($C_{13}H_{18}N_2OS$) *at* 293 K: rhombic, space group $P2_12_12_1$, a = 7.0181(6), b = 10.891(1), c = 17.511(2) Å, V = 1338.4(2) Å^3, d_{calc} = 1.242 g cm^{-3}, Z = 4. A total of 1383 independent reflections ($I > 2\sigma$) were measured using an automatic Bruker P4 four-circle diffractometer with a graphite monochromator using MoKα-radiation; $\theta/2\theta$-scanning, $2\theta < 50°$. The structure was solved by a direct method and full-matrix least-squares technique in an anisotropic approximation for non-hydrogen atoms (isotropic for H atoms). Final R factor was 0.0391 (R_w = 0.1069). Specification of the geometry was carried out by the SHELXL-97 program.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 287033. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2006.

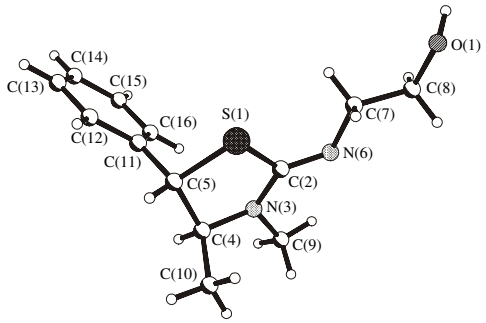


Figure 1 Crystal structure of compound **2**.

methyl and hydroxyethylamine groups at the atoms N(3) and C(2) have equatorial orientations [C(5)C(4)N(3)C(9) –169.49°, C(4)N(3)C(2)N(6) 167.0°]. The 4β-envelope conformation was also observed in 2-*p*-bromophenyl-3,4-dimethyl-5-phenyl-1,3-oxazolidine.[8]

Due to the presence of substituents in the oxazolidine derivatives of *l*-ephedrine and *d*-pseudoephedrine at C(4), C(5), N(3), another favourable conformation of a cycle is the 3α-envelope, in which the methyl group at N(3) has equatorial, and the other two substituents at the above atoms, pseudo-equatorial orientations. Exactly such a conformation is taken on by the majority of oxazolidine derivatives of pseudoephedrine, for example, (2*S*,4*S*,5*S*)-3,4-dimethyl-5-phenyl-2-phenylethenyl-1,3-oxazolidine.[9]

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