Different 2-aminothiazole derivatives possess a wide range of pharmacological activity. Some of them have been used as antiinfective or antitrechomonal agents. Those, having an aromatic substituent at C-4 position exhibit some Central Nervous System (CNS) stimulant activity [1] or have been found to be potent biological response modifiers with significant immunosuppressant activity [2]. The title compound combines the aminothiazole fragment with the isoquinoline segment of known pharmacological activity.

During our work on chiral non-racemic isoquinoline derivatives we developed an efficient synthesis of variously 1-substituted 1,2,3,4-tetrahydroisoquinoline derivatives [3]. The title compound was initially obtained in both enriched enantiomeric forms which structures were proposed on the basis of their spectroscopic properties. However, due to rather complicated nature of both $^1$H and $^{13}$C NMR spectra of these derivatives, caused probably by a restricted rotation over N-CO bonds in a urethane moiety, the correctness of the assignments remained uncertain and the final proof by an X-ray crystallography was needed. Unfortunately we were unable to obtain appropriate crystals for this purpose from both enantiomers nor their salts. We therefore decided to obtain a racemic modification of this compound and check its crystallographic properties.

![Conformation of the molecule of N2-[4-(2-chlorophenyl)-1,3-thiazol-2-yl]-(1R,1S)-6,7-dimethoxy-1-(-3-pyridylmethyl)-1,2,3,4-tetrahydro-2-isoquinolinecarboxo amide with the numbering scheme. All non-H atoms are shown as 30 % probability ellipsoids.](image)

Fig. 1. Conformation of the molecule of N2-[4-(2-chlorophenyl)-1,3-thiazol-2-yl]-(1R,1S)-6,7-dimethoxy-1-(-3-pyridylmethyl)-1,2,3,4-tetrahydro-2-isoquinolinecarboxo amide with the numbering scheme. All non-H atoms are shown as 30 % probability ellipsoids.

The conformation of the molecule of the title compound is shown on Fig. 1. Ring I of the isoquinoline moiety is planar (the rms. 0.006 Å), whereas ring II has a sofa conformation with atom C3 being below [-0.387(3) Å] and atom N2 above [0.292 (0.003) Å] the pane of condensed ring system. The 3-piridinethyl substituent (III) is oriented quasi equatorially to the isoquinoline. The structure is partly disordered - two orientation of C12 methyl group and two positions of Cl substituent were found [the occupancy factors were 0.73(3) and 0.27(3) for the methyl group and 0.87(3) and 0.12(3) for chlorine substituent, respectively]. On Fig. 1 only the major components are visualized. The interesting feature of the molecular structure is the conformation of the substituent at N2 of the isoquinoline ring and more particularly the respective conformation of three planar fragments this moiety is composed of. The dihedral angle between five-membered (IV) and six-membered ring (V) of 58.8(2) ° is in expected range. It is near those values observed for biphenyl and for structures composed of aromatic five- and six-membered rings linked together (for 25 occurrences in Cambridge Structural Database CSD of the latest the mean value of the dihedral angle was 54.37 ° with the lowest and the highest value of 31.52 and 87.31 °, respectively).

The planar amide fragment C14, O3, N1, C32 is, however, rotated only slightly [20.3(1) °] in respect to the thiazole ring (IV). As the consequence both O3 and S atoms are in close vicinity [2.694(3) Å]. This reminds somehow the situation observed in thiazofurin and selenazofurin [4] and their analogue...
thiophenfurin [5], where the rotation angle between two rings was about 20°. On the contrary the respective angle for oxazofurin and furanfurin was about 60° [6]. The authors explained this phenomena as a result of an attractive Coulombic interaction between positively charged S of the thiazole (or thiophene) ring and the negatively charged furanose O atom. Such an interaction was impossible for oxazole or furan compounds where oxygens of both heteroring were negatively charged. In our compound we could therefore expect the same interaction between negative carbonyl oxygen atom and sulphur which is separated only by 2.694(3) Å. Also some attractive interactions between hydrogens at C1 and C3 atoms and O3 and N1 atoms, respectively, might be responsible for rigidity of this fragment. The conformation of isoquinoline moiety and the conformation of substituents at C1, C6 and C7 in respect to the condensed rings is similar to those observed for other compounds of this group [7].

REFERENCES

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ENANTIOSELECTIVE SYNTHESIS OF S-(+)-CALYCOTOMINE FROM L-ASCORBIC ACID

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Isoquinolines are widely distributed in the plant kingdom, forming the largest group of alkaloids [1]. Among them, 1-benzyl-1,2,3,4-tetrahydroisoquinolines are in the central position from where a multitude of important structural groups are derived. Many of these alkaloids exhibit important physiological activities which also strongly depend on the absolute stereochemistry at C-1 carbon atom.

This fact attracted much interest of synthetic organic chemists working in pharmaceutical industry and academic research groups. Several excellent approaches for the enantioselective synthesis of benzylisoquinolines have been developed [2,3,4]. Among isoquinoline alkaloids, a group of 1-hydroxymethyl derivatives occurs rarely and much less work was devoted to establish a general route for their enantioselective synthesis, despite the fact that some of them exhibit potent physiological activity [5].