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THE METHOD FOR DETERMINING THE ABSOLUTE CONFIGURATION USING N-SUBSTITUTED CYCLIC AMINO ACIDS

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Abstract. Determining the absolute configuration of biologically active chiral substances is a current issue in drug development since biological properties of enantiomers may greatly vary. The absolute configuration of enantiomers can be determined using crystallography, circular dichroism, or by the method that involves chiral derivatizing agents and analysis of NMR spectra.

Earlier, when studying the structure of substituted isoindolinones, we noted a characteristic arrangement of N-benzyl proton signals in the NMR spectra associated with the presence of shielding aromatic ring and chiral part represented by amino acid residue in the studied molecules.[1] We suggested that N-benzylated amino acids can be used as available agents to determine the absolute configuration of chiral compounds.

We obtained a series of cyclic amino acids containing various substituents in the benzyl fragment. The prospects of the synthesized compounds as derivatizing agents were evaluated by their condensation with chiral amines and subsequent analysis of the obtained derivatives using NMR (Fig. 1) and computer modeling.

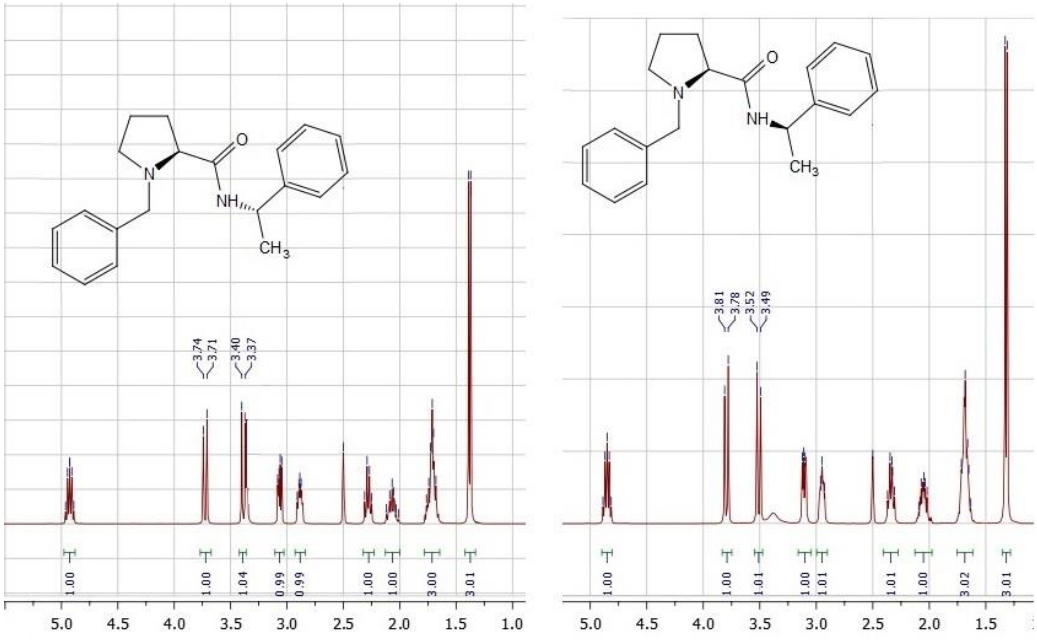

Figure 1. Fragments of NMR spectra of (S)-1-benzyl-N-((S)-1-phenylethyl)-pyrrolidine-2-carboxamide and (S)-1-benzyl-N-((R)-1-phenylethyl)pyrrolidine-2-carboxamide

References

1. Grigoreva T. A. Amino acids as chiral derivatizing agents for antiproliferative substituted N-benzyl isoindolinones / T. A. Grigoreva, D. S. Novikova, M. A. Gureev, A. V. Garabadzhiu, V. G. Tribulovich // Chirality. – 2018. – P. 1–13.

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