Amino acids (AAs) play a crucial role in many vital processes of living organisms (e.g., intracellular signaling, gene expression, hormone synthesis, phosphorylation cascade, energy metabolism, etc.); therefore (bio-)transformation of AAs seems attractive from the point of the 'rational production of properties' in the medicinal chemistry. The poly(ester amide) containing α-AA-based motifs are off great interest as an attractive material in the biomedical field and tissue engineering, respectively. On the whole, the organosulfur compounds are valued in the pharmacology as antitumor, antimicrobial, anti-HIV and chemoprotective agents against a variety of carcinogenic or toxic factors. The single-atom substitution of the carbonyl oxygen in an amide bond with sulfur (HN-C=S) is generally regarded as an isosteric replacement to produce more potent and stable molecules with the modified bioactive potency (e.g., the antibacterial activity). The conversion of the amide-containing compounds into the corresponding thioamides can improve the ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity) properties that are important for the drug pharmacokinetics and pharmacodynamics as well. The site-specific oxoamide→thioamide modification of proteolytically sensitive amide bonds in the peptide backbone is a popular synthetic practice commonly used to specify the spatial distribution, stability and functional properties of peptides, respectively. In fact, the validity of thioamide-based compounds was confirmed in the medicinal applications revealing the bioactive potential of thioamide motif (e.g., second-line antituberculosis and leprosy drugs).

The principal objective of the study was the conceptual design and practical synthesis of the symmetrical α-AA-based (R=Gly, Ala, Val, Tyr, Ser) dithioamides of terephthalic acid using the conventional heating (method I) as well as the microwave-accelerated approach (method II). It was revealed that both methods yielded comparatively at each stage of the proposed three-step procedure. A noticeably reduced reaction time (from days to minutes) in the microwave-supported approach makes the method an attractive and eco-friendly alternative to the lengthy methodology with the conventional heating. Following the common practice, the intermolecular similarity of novel terephthalic acid derivatives was estimated in the multidimensional space (mDS) of the structure/property-related *in-silico* descriptors using the dimensionality reduction methods.