Preparation of Pseudo-Peptide Building Blocks with *retro*-Thioamide Bond Mediated *via* Thiocarbamoyl *Meldrum*'s Acid

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An easy and efficient synthesis of pseudo-tripeptide containing a thiomalonamide moiety was developed. Isothiocyanate derivatives of amino acids react smoothly with 2,2-dimethyl-1,3-dioxane-4,6-dione (*Meldrum*'s acid) to yield new thiocarbamoyl derivatives of *Meldrum*'s acids. Thermal decomposition of these new derivatives leads to thiocarbamoyl ketenes, which acylate amino acid esters to give pseudo-tripeptides.

Introduction. – It has been more than well-known that peptides play an essential role in virtually all biochemical processes. One can, at this point, mention the widespread use in medicine of long peptides derived from biotechnology such as, *e.g.*, well-known interferons, erythropoetin, insulin, *etc.*, to very short ones, like oxytocine, enkephalin, or tuftsine. But all peptides with long or short chains possess the same drawback, *i.e.*, their rapid enzymatic degradation in living organisms [1]. As a consequence, several modifications of the peptides backbone were undertaken. For example, an amide bond could be replaced by a *retro-inverso* hydroxyethylene [2], hydroxyethylene [3], ketomethylene [4], aminomethylene [5], *retro-inverso* [6] or thioamide moiety [7].

In our research, we focused on the possibility of obtaining a scaffold of *retro*-modified petides, which also contain a thioamide modification-introduced regioselectively.

One of the aproaches to *retro*-modification of peptide is based on the introduction of a malonodiamide moiety in the structure of the molecule. Implementation of this task requires the use of any malonic derivative. Most of the syntheses of malonodiamide type of *retro*-modified peptides start from mono- or diesters of malonic acid, which are incorporated into the peptide chain by the typical condensation procedures [8]. In another original aproach, *Meldrum*'s acid was used as an equivalent of malonic acid; such a strategy allows applying the acylating properties of 2,2-dimethyl-1,3-dioxane-4,6-dione (*Meldrum*'s acid) to facilitate preparation of the first amide bond, whereas the second amide bond was obtained by the classical method [9].

Recently, we have demonstrated that carbamoyl *Meldrum*'s acid derivatives in the presence of Me_3SiCl (TMSCl) may acylate efficiently also more basic nucleophiles as aliphatic secondary amines [10] in contrast to the work of *Pak* and co-workers [11]. In such a synthetic strategy, 5-[(aryl/alkylamino)hydroxymethylene]-2,2-dimethyl-1,3-dioxane-4,6-diones by thermal decomposition are a source of carbamoyl ketenes, which can acylate a broad spectrum of nucleophilic reagents.