Abstract

In our work we synthesized a novel type of vinylogous peptides with the C=C fragment inserted into the peptide C–N bond. Ethynyl ketones **3** were prepared from chosen Boc-protected α-amino acids **1**. 1,4-Addition of dimethylamine gave the corresponding enaminones **4**, but addition of amino esters **7** to inone **3** led to vinylogous dipeptides **5**. *N*,*N*-Disubstituted vinylogous amides were isolated as pure (*E*)-isomers, while the *N*-monosubstituted were obtained as mixtures of the major (*Z*)- and the minor (*E*)-isomers. Acylation of the N terminus did not proceed so smoothly as we had to protect the acidolytically unstable enamino moiety first. Cyclisation of inone **3** or enaminone **4** with hydroxylamine led to diastereomeric isoxazolines **11**, followed by removal of Boc group with HBr-AcOH and simultaneous dehydration to afford isoxazoles **13**. Free amines were then acylated with Boc-Glycine (**1a**) to give the corresponding dipeptides **15**. Finally hydrogenolytic deprotection of the enamino moiety in the presence of GlyOMe·HCl (**7a**) led to tripeptides **17** with one vinyl group.

In the second part of our research we synthesized some chiral (*S*)-1-(heteroaryl)-1-aminoethanes from ynone **3b** and its synthetic equivalent, enaminone **4b**. Cyclisation of **3b** or **4b** with amidines **20** led to the corresponding (*S*)-1-(pyrimidin-4-yl)-1-aminoethanes **21**, while the reaction with unsymmetrical cyclic amidines **23** afforded regioisomeric (*S*)-1-(pyrazolo[1,5-*a*]pyrimidin-5-yl)-1-aminoethanes **24'** and (*S*)-1-(pyrazolo[1,5-*a*]pyrimidin-7-yl)-1-aminoethanes **24**. Acidolytic removal of the Boc group produced free amines. Catalytic hydrogenation of **24a** and **24c** furnished the corresponding diastereomeric 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidines **27/27'a** and **27/27'c**.

In the last part of our work we synthesized some new 1,4,5-trisubstituted pyrazoles. With application of different hydrazines **35**, large groups were introduced at position N(1) in order to limit the rotation of aromatic rings. In this way we tried to achieve that diastereomes **37/37'** with single stereogenic center, which can be distinguished by NMR spectroscopy due to the presence of axial chirality, would be separable. We tried to limit the rotation by introducing different groups to aniline nitrogen, either by reductive alkylation of nitrocarboxamides **37/37'**, or by derivatisation of aminocarboxamides **38/38'**. Some new pyrazole derivatives were prepared and rotational dynamics about C(5)–C(1') single bond of mixture of nitrocarboxamides **37/37'd** was studied using different NMR techniques.

Keywords: amino acids, peptides, enaminones, cyclisation, atropisomerism.