

Multicomponent Approach to Polysubstituted Pyrrolizidine-3-ones

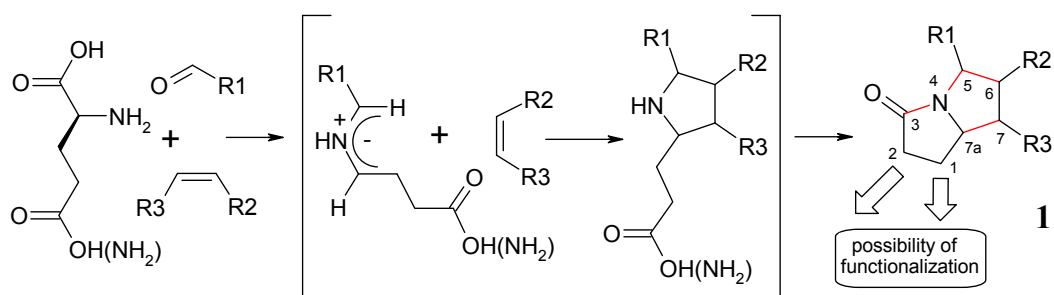
Konstantin V. Kudryavtsev, Nataliya V. Nukolova,
Veronika V. Irkha, Denis V. Evdokimov

Department of Chemistry, Moscow State University,
Lenin's Hills, 119992, Moscow, Russian Federation

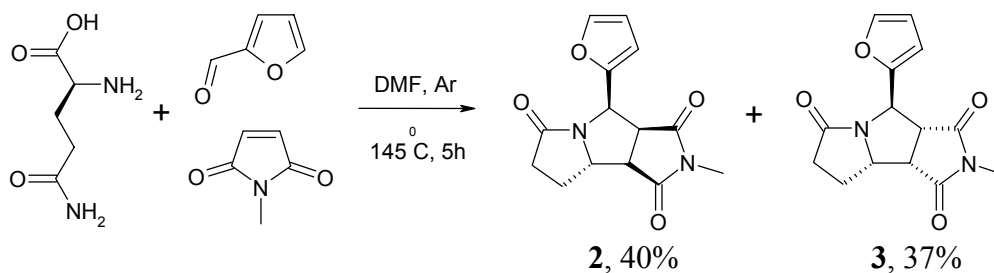
Fax: (095) 932-8846

e-mail: kudr@org.chem.msu.su

Unnatural compounds structurally related to pyrrolizidine alkaloids represent attractive synthetic targets. Pyrrolizidin-3-ones are often used as precursors of pyrrolizidine scaffolds and could be modified with new substituents at 2 and 1 positions of heterocyclic ring. We have developed a three component condensation of aryl(heteroaryl) aldehydes with glutamic acid/glutamine and dipolarophiles allowing to get four new bonds formation in a single reaction step (scheme 1).



Using of glutamine afforded a cleaner reaction and higher yields of pyrrolizidinones. Maleimides, maleates, fumarates, chalcones were used as dipolarophiles and polysubstituted isomers of **1** were isolated with yields 30-80%. Reaction outcome strongly depends on temperature and solvent. For example, interaction of glutamine, furfural and NMM under below conditions led to isomeric pyrrolizidin-3-ones **2** and **3**, formed respectively by *endo*- and *exo*-cycloadditions of an electronegative olefin to dipole, and easily isolated by chromatography.



To the best of our knowledge this is the first multicomponent synthesis of functionalized pyrrolizidin-3-ones.