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Solid-Phase Synthesis of Novel Arylpiperazine-Functionalized Amino Acid Amides.

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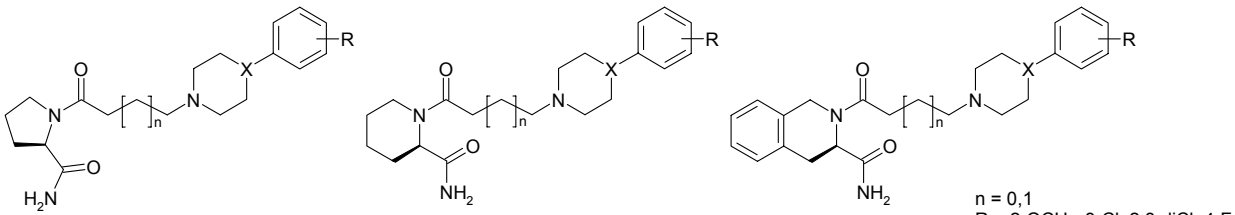
We have previously reported on successful application of combinatorial chemistry techniques for generation of rationally designed libraries of serotonin receptor ligands, namely arylpiperazine derivatives containing N-acylated proline fragments [1, 2]. Encouraged by these findings, we have designed and synthesized a library of aryl piperidine- or piperazine analogs containing amino acid amides (pyrrolidine-2-carboxamide, piperidine-2-carboxamide, tetrahydroisoquinoline-3-carboxamide).



A 19 member library of derivatives was synthesized on Rink-Amide polystyrene resin. Library generation was performed manually by using Bill-Board set [3]. This equipment keeps the solid-phase reactions organized in a grid and simplifies repeated cycles of reactions, washings, cleavage, and finally solvent evaporation step. Selected library representatives were evaluated for their 5-HT_{1A}, 5-HT_{2A} and 5-HT_7 receptor affinities. The results obtained followed by the discussion on the influence of the modifications applied on receptor affinity will be presented.

References

[1] Zajdel P. *et al.:* Bioorg. Med. Chem. 13 (2005), 3029-25.
[2] Zajdel P. *et al.:* Bioorg. Med. Chem. 15 (2007) 2907-19.
[3] Scott W. L. *et al.:* J. Comb. Chem. 11 (2009), 3-13.