

## Towards greener peptoids: synthesis in aqueous media

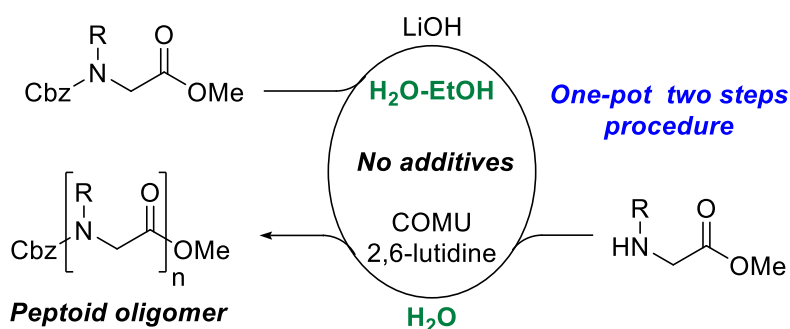
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Peptoids *i.e.* *N*-substituted glycine oligomers are oligoamides that possess a skeleton similar to that of peptides but differ in that the side-chains are appended to the nitrogen of the amides rather than to the  $\alpha$  carbon.<sup>1</sup> This particular feature makes these peptidomimetics far less susceptible to proteases and more cell-permeable than peptides. Originally developed in a small start-up company named Protos Corp. at the end of the eighties, peptoids have benefit of nearly three decades of fundamental research which now place them among the most promising peptidomimetics to reach drug market.<sup>2</sup>

One of the many advantages of peptoids is indeed the facile synthesis. Highly efficient submonomer and monomer methods for sequence-defined synthesis both in solution and on solid-phase using readily available starting materials have been developed.<sup>3</sup> However, to date, no particular attention has been directed towards greener peptoid synthesis, and solvents such as DMF, NMP, THF and CH<sub>2</sub>Cl<sub>2</sub> are routinely used during the synthesis and workup steps.

In an effort to mitigate these sustainability issues, the synthesis of peptoid oligomers in aqueous media is explored for the first time.<sup>4</sup> We will herein present the optimized chain elongation procedure carried out in water-based media in a unique N to C direction, and which comprises a convenient one-pot two-step deprotection/coupling sequence for the installation of each new peptoid residue. This efficient procedure is then applied to the synthesis of Gramicidin S sequence and Leu-enkephalin mimics.



### References:

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