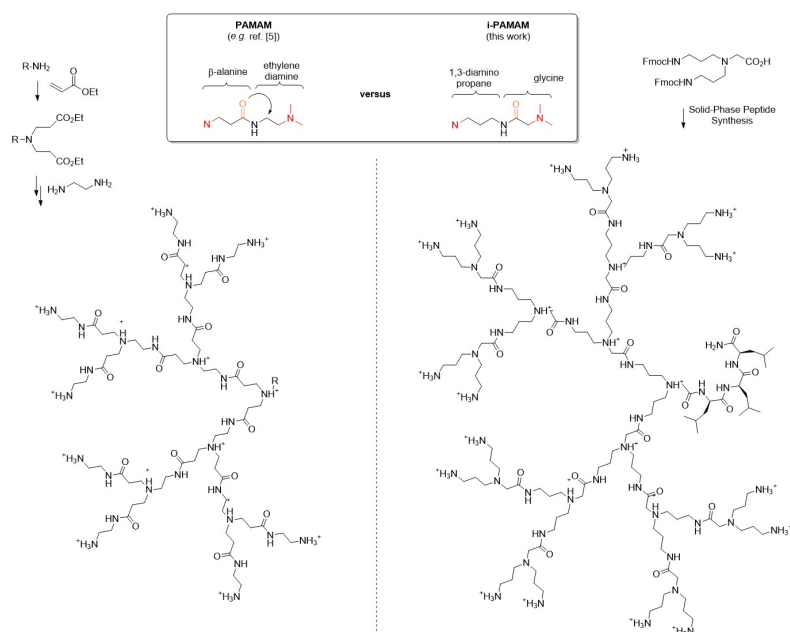


Redesigning PAMAMs: Antimicrobial Inverse-Polyamidoamine (i-PAMAM) Dendrimers

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Polyamidoamine (PAMAM) dendrimers have shown various interesting properties ranging from technology to medicine.¹⁻⁵ However, PAMAM dendrimers suffer from an intrinsic instability due to the presence of the β -alaninyl-amidoethylamine branch in their structure, which easily undergoes retro-*Michael* reaction.⁶ For this reason, we redesigned the branches of PAMAM dendrimers by moving the carbonyl group of β -alanine across the amide bond. This modification transforms the ethylene diamine unit into glycine and the β -alanine into 1,3-diaminopropane, removing the possibility of a retro-*Michael* reaction, and resulting in inverse PAMAM (i-PAMAM) dendrimers. Contrary to the preparation of PAMAMs in solution and the difficulties encountered during their purification, our strategy gave us access to solid-phase peptide synthesis at high temperature by iterative coupling and deprotection of the commercially available *N,N*-bis(*N*'-Fmoc-3-aminopropyl)glycine. Good purity was reached after preparative reverse phase HPLC and no degradation of our i-PAMAMs could be detected over time. To demonstrate this new class of dendrimers, we synthesised potent so far non-membrane disruptive antimicrobial dendrimers with activities against both *Gram*-negative and *Gram*-positive bacteria.⁷



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