Synthesis of phosphatidylglycerol receptor: Precursor preparation

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Abstract: With the emergence of an alarming amount of multidrug resistant bacteria, there has been a growing interest in antimicrobial peptides as potential antibiotics to combat this issue in the medical community. Antimicrobial peptides target the bacterial plasma membrane by first binding to phosphatidylglycerol (PG) via Columbic interaction, followed by insertion into the membrane and killing the bacterial cell. However, antimicrobial peptides can be toxic, difficult expensive to make, and exhibit low bioavailability. Our focus will be directed toward the development of small molecules that specifically bind to (PG), the major anionic phospholipid found in bacterial membranes. In doing so, the membrane is disrupted. Currently, precursors for a family of cyclophanes whose structure is proprietary are being developed. Previously prepared small molecules that bind to the PG head groups have displayed high bacteriostatic properties at low concentrations (1-4 Î¼M). Therefore, this privileged structure is expected to similarly bind to PG that will cause the antimicrobial effect due to its commonality in binding pocket. The antimicrobial effect makes plasma membrane more permeable which depolarizes the membrane with the aim to stop replication. The precursors developed so far consist of the synthesis of bis-phenol from bis-anisole via demethylation and the synthesis of an allylic mesylate from the transformation of pentane-1,5-diol into 5-(methoxy methoxy) pentyl-4-methylbenzene sulfonate.

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