

# OPTIMIZED SYNTHESIS OF THE BACTERIAL MAGIC SPOT (p)ppGpp CHEMOSENSOR PyDPA

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The concept of antimicrobial resistance, namely the ability of bacterial strains to become insensitive to a previously effective antibiotic treatment, is nowadays well-known and it is rapidly becoming a societal concern. On the contrary, bacterial persistence [1] is still an elusive phenomenon where a dormant bacterial phenotype becomes just temporarily tolerant to drugs. Among the different working hypotheses on their formation mechanism, we decided to focus our attention on the survival signaling cascade called *Stringent Response*, that is initiated by the accumulation of guanosine tetra- or pentaphosphate ((p)ppGpp). During our quest to find small molecules able to either inhibit or revert this process, the necessity to selectively detect (p)ppGpp in solution became apparent. Fortunately, a specific and selective chemosensor, called PyDPA (**Fig. 1**), has already been designed and reported [2]. Here we present an optimized synthetic approach that allowed to improve the overall yield from 9% over 6 steps up to 67% over 7 steps [3].

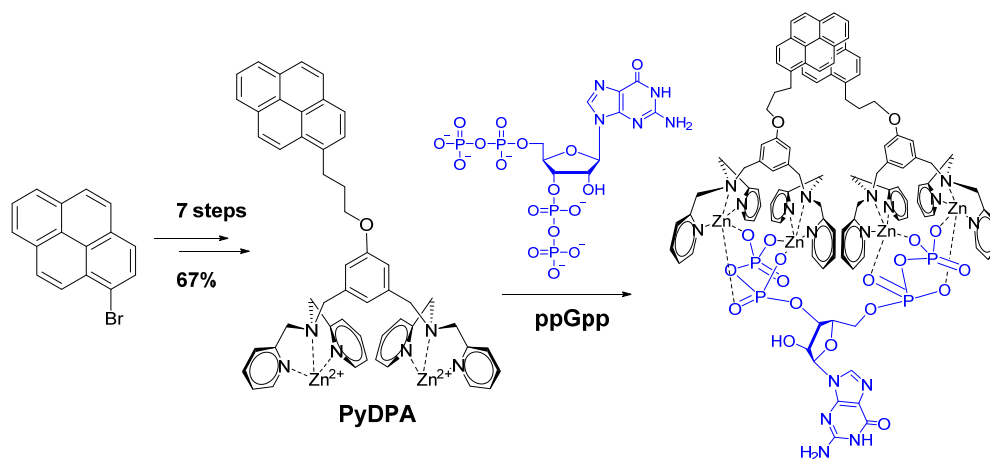


Fig. 1: Optimized synthesis of Chemosensor PyDPA and its complex with ppGpp

[1] K. Gerdes and E. Maisonneuve, *Cell*, **2014**, 2, 539-548

[2] H. W. Rhee *et al.* *J. Am. Chem. Soc.*, **2008**, 130, 784-785

[3] G. Conti, M. Minneci, S. Sattin, *ChemBioChem*, **2019**, DOI: 10.1002/cbic.201900013