A CLICK-CHEMISTRY LINKED 2‘3‘-cGAMP ANALOGUE

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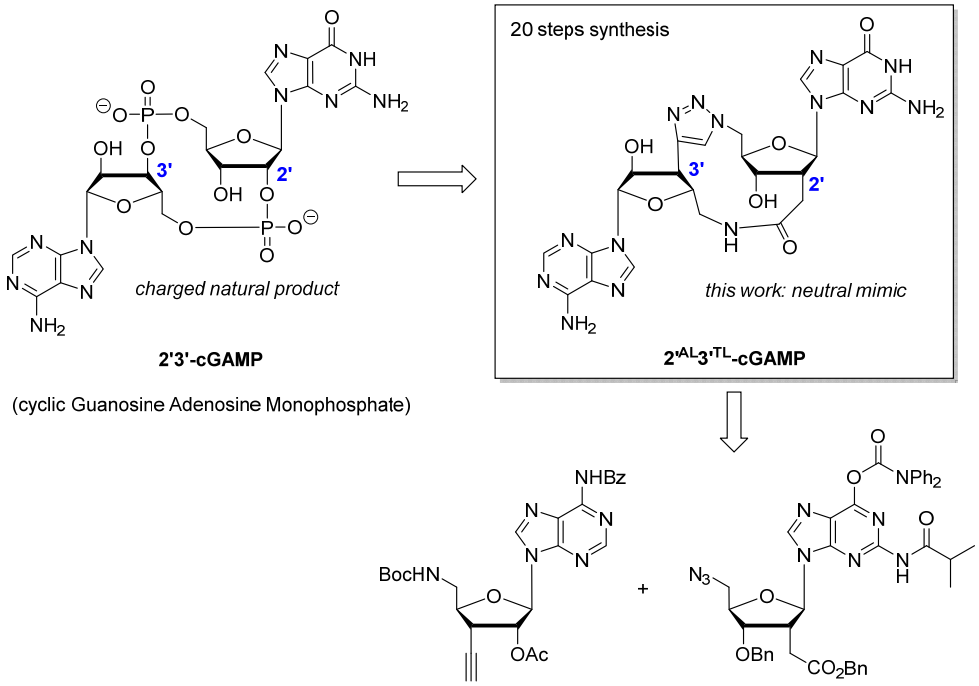
Cytosolic DNA from pathogens can be life-threatening for multicellular organisms. The innate immune system is capable to recognize the danger and to activate a downstream signaling cascade resulting in the production of cell defending type I-interferons and cytokines.[1] As recently reported, this immune response is essentially triggered by the natural occurring second messenger 2’3’-cGAMP (a cyclic dinucleotide) upon binding to the endoplasmic reticulum membrane protein STING (stimulator of interferon genes).[2]



Scheme: A neutral mimic of the natural occurring second messenger 2’3’-cGAMP.

Targeting STING with cGAMP analogues depicts an interesting strategy to regulate the immune system and to study the therapeutic potential (e.g. simplified cell membrane penetration and longer cell persistence). In this work, the synthesis and structure elucidation of a neutrally linked cGAMP candidate is reported.[3]

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[1] Chen, Q., et al. *Nature Immunology* **2016**, *17*, 1142-1149.

[2] Hornung, V., et al. *Nature* **2013**, *498*, 380-384.

[3] Dialer, C.; Carell, T. et al. *Chem. Eur. J.* **2019**, *25*, 2089-2095.