



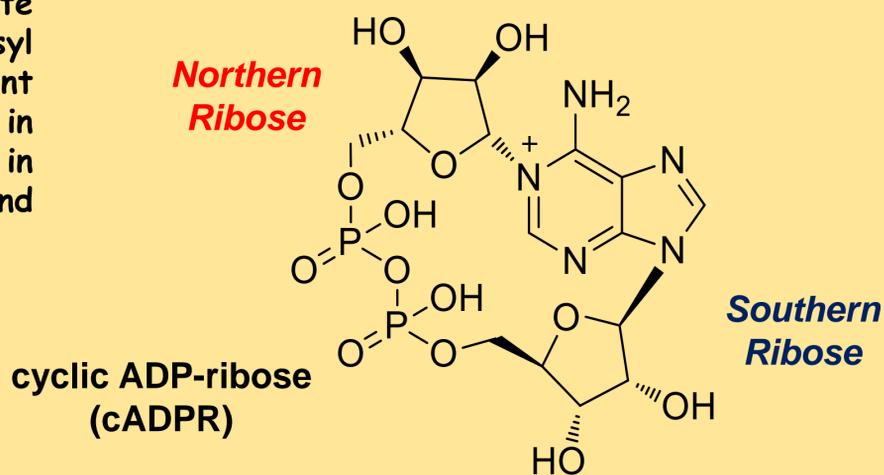
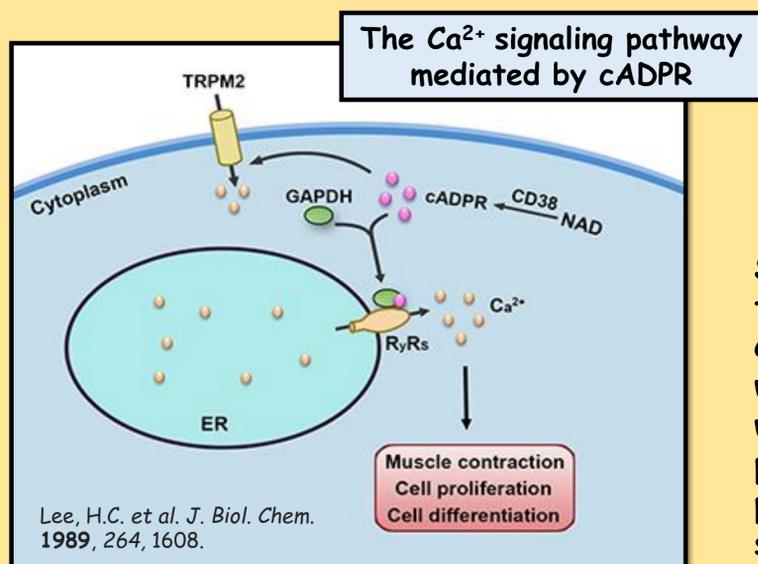
Design and Synthesis of a cADPR Mimic as a Novel Tool for Monitoring the Intracellular Ca^{2+} Concentration

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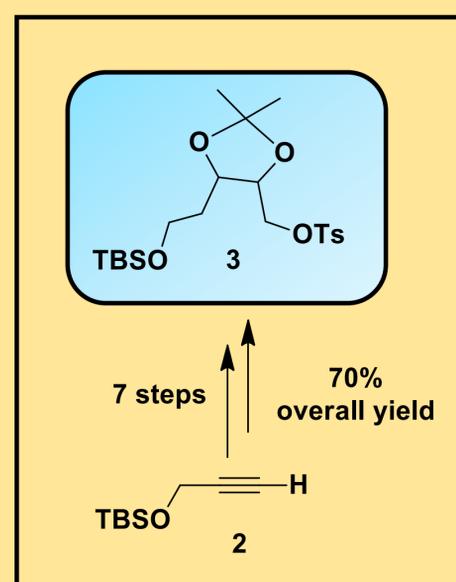
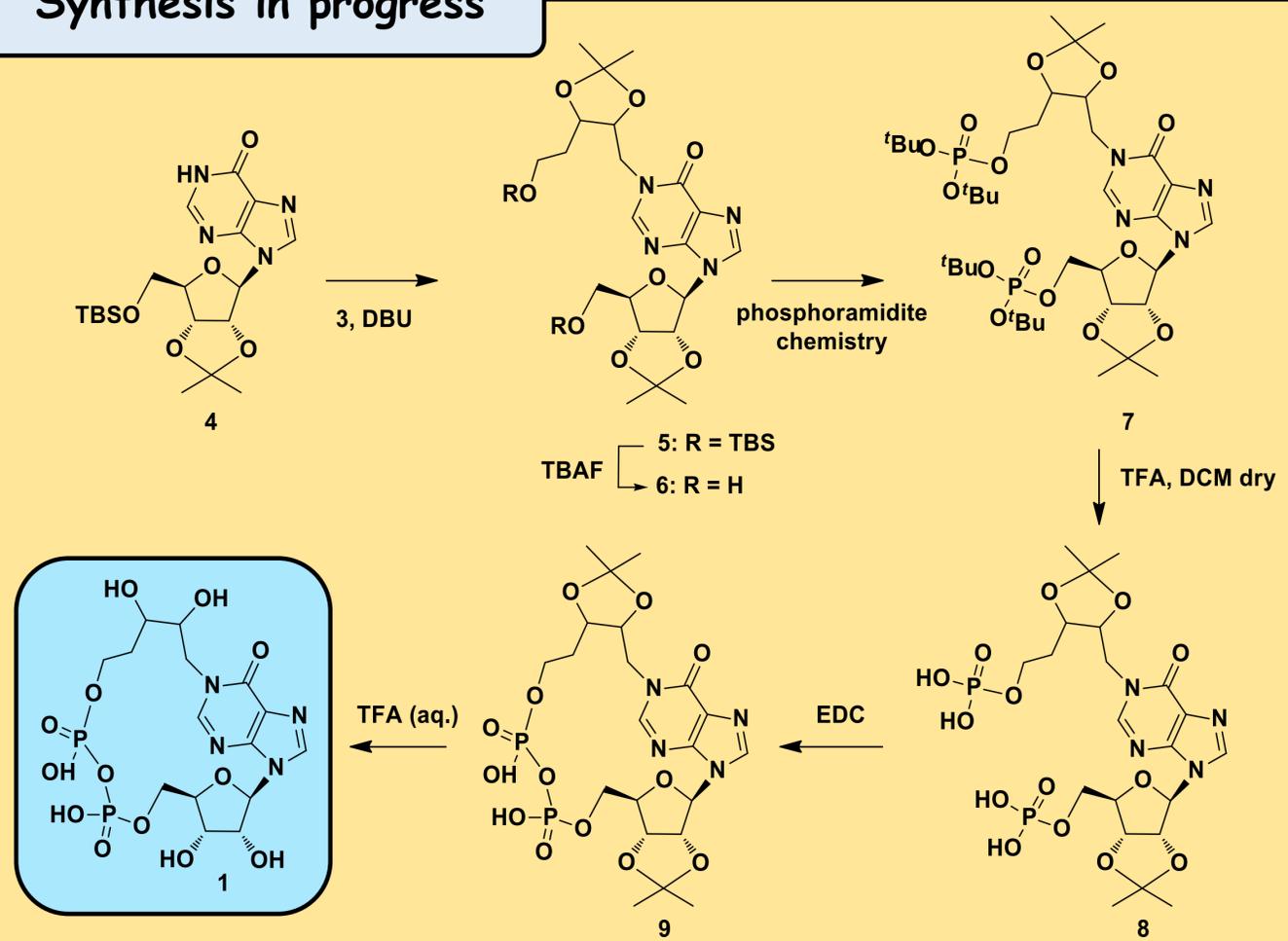
Cyclic ADP-ribose (cADPR) is an endogenous metabolite synthesized in cells starting from NAD^+ by ADP-ribosyl cyclase. cADPR has been attracting much attention in recent years because of its potent calcium-mobilizing activities in many cellular systems. It acts as a second messenger in cellular Ca^{2+} homeostasis, insulin secretion and T-lymphocytes activation.



Since the cADPR molecule is quite unstable - at 37°C its half life for hydrolysis is about 24 h - many non hydrolysable mimics of cADPR have been synthesized so far. Prof. Matsuda and co-workers synthesized new cADPR analogues in which the adenine base was replaced by a hypoxanthine ring. This kind of modification produced the cyclic inosine diphosphate ribose (cIDPR), which proved to be stable in hydrolytic physiological conditions and showed significant Ca^{2+} mobilizing activity.

In our laboratories we synthesized several cIDPR analogues.¹⁻³ In particular, the analogue with the northern ribose replaced by a pentyl chain (cIDPP) showed interesting Ca^{2+} mobilizing activity on the neuronal PC12 cell line. Herein, we report the design and the synthesis of the novel analogue 1, in which the "northern" ribose of cIDPR is replaced by a 2",3"-dihydroxy pentyl chain. The effect of the presence of the diol moiety on the intracellular Ca^{2+} release will be assessed in due course.

Synthesis in progress



References

- 1) Galeone, A. et al. *Eur. J. Org. Chem.* 2002, 4234.
- 2) Mahal, A.; D'Errico, S. et al. *Beilstein J. Org. Chem.* 2015, 11, 2689.
- 3) D'Errico, S. et al. *Mar. Drugs*, 2018, 89.