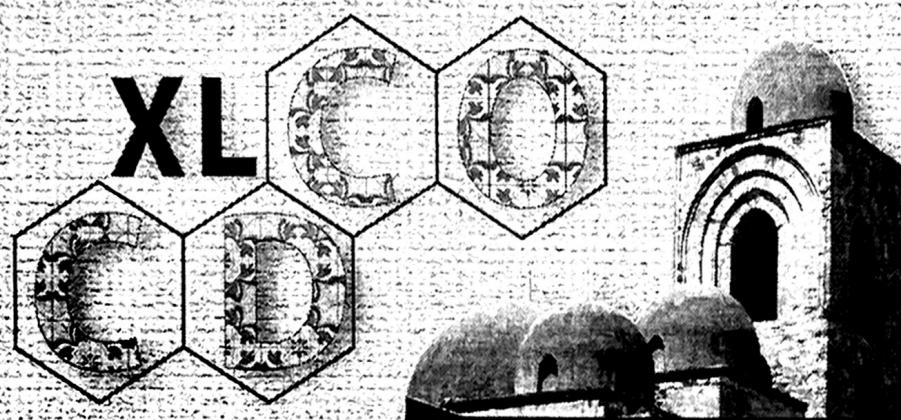




Università  
degli Studi  
di Palermo



Società Chimica Italiana  
Divisione di Chimica  
Organica



**PALERMO**  
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*XL Convegno Nazionale della  
Divisione di Chimica Organica  
della Società Chimica Italiana*

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## Exploring the Role of Chirality in the $\text{Ca}^{2+}$ Mobilizing Properties of New cADPR Linear Precursors

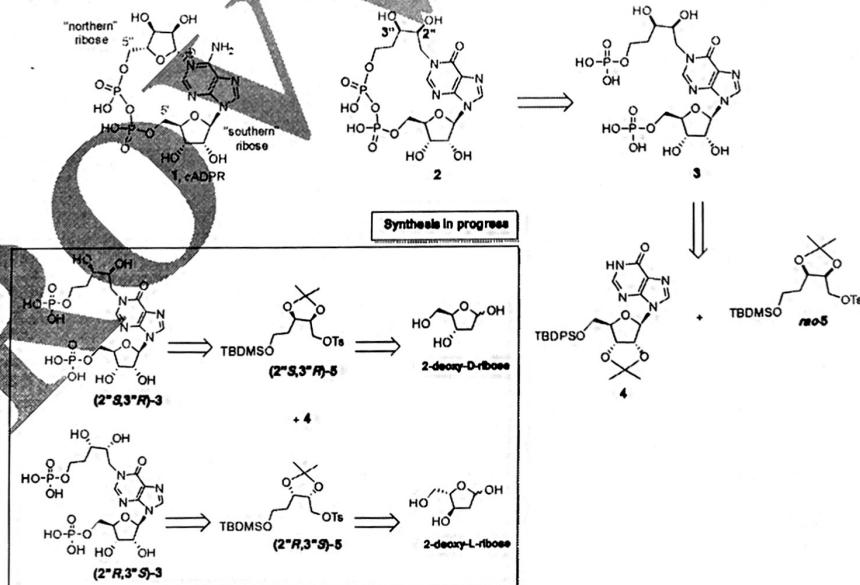
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Cyclic adenosine diphosphate ribose (cADPR, **1**) is a cyclic nucleotide involved in the  $\text{Ca}^{2+}$  homeostasis. In its structure, the northern ribose, bonded to adenosine through an N1 glycosidic bond, is connected to the southern ribose through a pyrophosphate bridge. Due to the chemical instability at the N1 glycosidic bond, new bioactive cADPR derivatives have been synthesized. One of the most interesting analogues is the cyclic inosine diphosphate ribose (cIDPR), in which adenosine is replaced by hypoxanthine. In the last few years, we have produced new flexible cIDPR analogues, where the northern ribose has been replaced by alkyl chains. With the aim to obtain the closest flexible cIDPR analogue, we have attached to the inosine N1 position a 2 $\square\text{O}$ ,3 $\square\text{O}$ -dihydroxypentyl chain, possessing the two OH groups in a ribose-like fashion, and synthesized the new cyclic analogue **2**.<sup>1</sup> Interestingly, the linear precursor **3** displayed a higher potency in increasing  $[\text{Ca}^{2+}]$  than the cyclic compound **2** in primary cortical neurons. The compound **3** was obtained as a 1:1 mixture of two diastereomers, as its inosine precursor **4** was reacted with the racemic tosylate **5**. To probe the role of the chirality of 2 $\square\text{O}$  and 3 $\square\text{O}$  carbon atoms in the  $\text{Ca}^{2+}$  releasing properties of the compound **3**, herein we report on the synthesis of the two diastereomers (2 $\square\text{O}$ S,3 $\square\text{O}$ R)-**3** and (2 $\square\text{O}$ R,3 $\square\text{O}$ S)-**3** (Figure 1).



**Figure 1:** Proposed synthesis of the novel cADPR linear precursors (2 $\square\text{O}$ S,3 $\square\text{O}$ R)-**3** and (2 $\square\text{O}$ R,3 $\square\text{O}$ S)-**3**.

### References:

- [1] S. D'Errico *et al.*, *Bioorg. Chem.* **2021**, 117, 105401.