Synthesis of isoprenoid diphosphate mimetics

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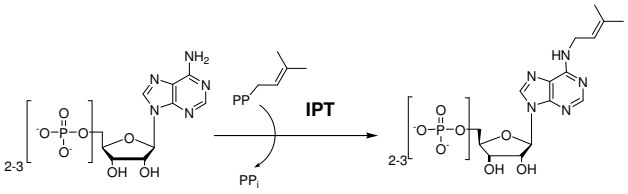
INTRODUCTION

Cytokinins, are central regulators of cell division and differentiation in plants.[1] Most naturally occurring cytokinins are 3,3-dimethylallyl adenine derivatives. Isopentenyladenine carries an unmodiefied isopentenyl side chain, whereas *trans*-zeatin and *cis*-zeatin carry hydroxylated side chains.

Isopentenyltransferases (IPTs) are known to be responsible for the biosynthesis of cytokinins.[2] The model plant *Arabidopsis thaliana* contains nine isozymes (*At*IPT1 to *At*IPT9). One type of isopentenyl-transferases modifies tRNA and is called tRNA-isopentenyltransferases (*At*IPT2 and *At*IPT9). The other type (*At*IPT1, *At*IPT3-8) catalyzes the transfer of the isopentenyl moiety from dimethylallyl-diphosphate (DMAPP) to the N^6-amino group of an adenosine moiety (AMP, ADP or ATP) (Scheme 1).

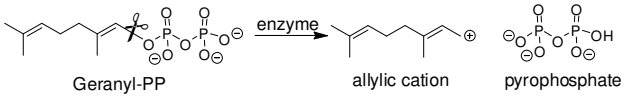


Scheme 1. Prenyl transfer reaction of adenosine phosphate (ADP or ATP) to isopentenyl adenosine phosphate catalyzed by AtIPT.

IPTs appear to be important targets in agricultural science. For this reason, their inhibition by synthetic substrates may prove useful in crop production.

RESULTS AND DISCUSSION

We focused our interest on the design and the synthesis of pyrophosphate mimics[3] as competitive IPT inhibitors. Naturally occurring isoprenoid pyrophosphate substrates (e.g. DMAPP, geranyl-PP, farnesyl-PP) suffer enzymatic hydrolysis (Scheme 2).



Scheme 2. Enzymatic hydrolysis of Geranyl-PP.

However, replacement of the biologically labile pyrophosphate group by bioisosteric moieties results in dephosphorylation-resistent analogues (Fig. 1).[3-6]

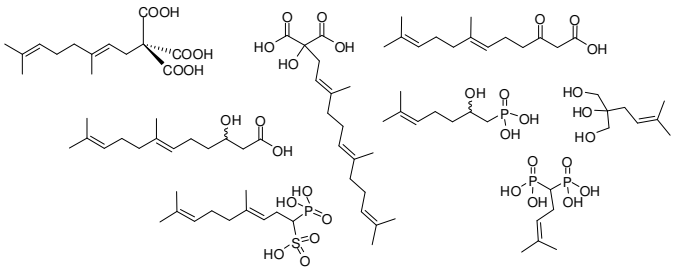
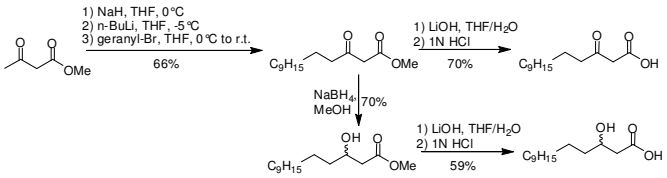


Figure 1: Examples of isoprenoid diphosphate surrogates.



Scheme 3. Exemplary synthesis of analogues.

CONCLUSION

A series of several isoprenoid-derived pyrophosphate analogues have been synthesized. Biochemical studies on their activity as inhibitors of prenyltransferases are underway.

ACKNOWLEDGEMENTS

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