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Design and synthesis of benzene congeners of resolvin E2 as its stable equivalents

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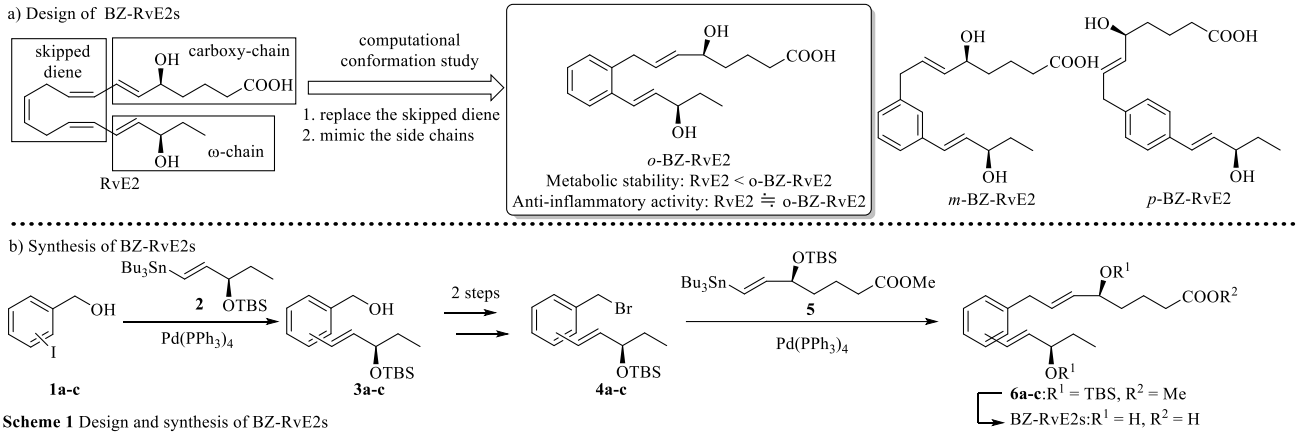
Resolvins (Rvs) are highly potent anti-inflammatory lipid mediators, which are metabolites of ω-3 polyunsaturated fatty acid, and are attracting attentions as prototypes for new anti-inflammatory drugs.[1] However, due to their polyunsaturated structures, especially skipped diene, Rvs are chemically and biologically unstable.[2] To address this issue, we designed benzene congeners of RvE2 (*o*-, *m*-, and *p*-BZ-RvE2, Scheme 1a) by replacing the unstable skipped diene structure with a benzene ring on the basis of computational conformation studies to mimic stable conformations of ω-chain and carboxy-chain in parent RvE2

The designed three BZ-RvE2s were synthesized by two Stille coupling strategy shown in Scheme 1b. The first Stille coupling of iodebenzyl alcohol **1a-c** and ω-chain **2** afforded benzyl alcohol **3a-c**. After converting benzyl alcohol **3a-c** to benzyl bromide **4a-c**, the second Stille coupling of it with carboxy-chain **5**, followed by global deprotection produced BZ-RvE2s.

The evaluation of anti-inflammatory activity and metabolic stability of synthesized BZ-RvE2s and RvE2 revealed that *o*-BZ-RvE2 exhibited comparable anti-inflammatory activity to parent RvE2 and much higher metabolic stability.[3]

In this talk, we will discuss the detail of the design, synthesis, and evaluations of BZ-RvE2s.



Scheme 1 Design and synthesis of BZ-RvE2s

Reference

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