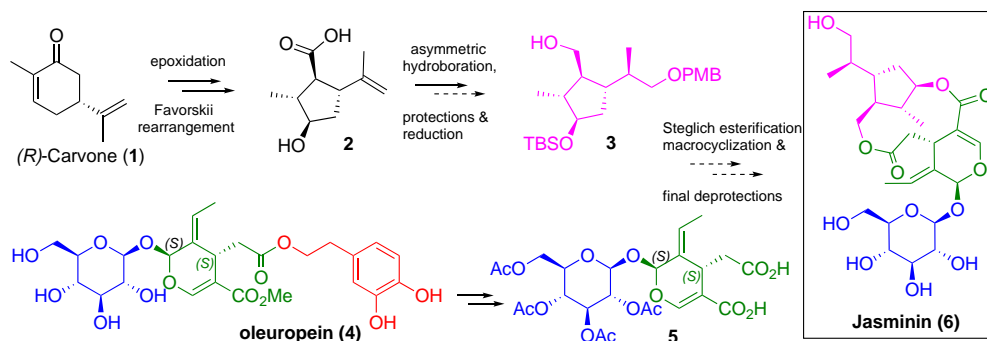


Stereoselective synthesis of chiral cyclopentanols towards macrocyclic natural products of the *Jasminun* species

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Functionalized cyclopentanols, prevalent in natural products and pharmaceuticals, offer valuable scaffolds for drug discovery due to their rigid frameworks and advantageous pharmacokinetic properties.¹ Certain secoiridoid natural products contain such a cyclopentapyran core, derived from iridoids. They are found in members of the *Oleaceae* family, notably the *Jasminum* species *J. azoricum*, *J. sambac*, *J. nudiflorum* and *J. mesnyi*.² There are around forty reported secoiridoids with a triol or tetraol cyclopentane ring decorated with five contiguous stereocenters, which are considered to be an interesting but synthetically demanding target,⁸ with various biological and pharmaceutical activities, including antioxidant and antimicrobial effects.³ Jasminin (**6**, Scheme 1), the main member, is found in the leaves of Primrose Jasmine, an evergreen shrub found in China, India and Nepal. These leaves are also rich in jasmoside, jasmesoside, oleuropein and other secoiridoids and are used for their antioxidant and anthelmintic potential.⁴



Scheme 1. Key intermediates involved in synthesis of Jasminin.

In this work, a synthetic methodology is being developed for accessing such cyclopentanols stereospecifically, with the initial final target of the synthesis being jasminin (**6**).⁷ The synthesis commences with (*R*)-carvone undergoing epoxidation, Favorskii rearrangement followed by orthogonal protections, hydroboration–oxidation and reduction in order to get the suitably protected triol **3**. The synthesis concludes with a macrolactonization with protected oleoside **5**, derived from oleuropein, a valuable bio-renewable synthetic building block with diverse biological activities and potential therapeutic applications,⁵ found in abundance in olive leaves.

- (1) Moegle, B. et al. *J. Org. Chem.* **2022**, 87 (11), 7229–7238.
- (2) Tanahashi, T. et al. *Phytochemistry* **1989**, 28 (5), 1413–1415.
- (8) Stankevich, K. S. et al. *J. Org. Chem.* **2022**, 87 (18), 12250–12256.
- (3) Balkrishna, A. et al. *Plants* **2021**, 10 (6), 1089.
- (4) Singh, G. P. et al. *Asian J. Pharm. Pharmacol.* **2018**, 4 (2), 155–158.
- (7) Asaka, Y. et al. *Tetrahedron* **1974**, 30 (18), 3257–3262.
- (5) Cavaca, L. A. S. et al. *Eur. J. Org. Chem.* **2018**, 2018 (5), 581–589.