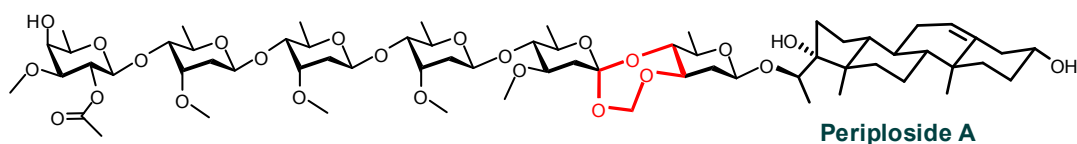


Total Synthesis of Periploside A, a Unique Pregnane Hexasaccharide with Potent Immunosuppressive Effects

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Periploside A is a pregnane hexasaccharide identified from the Chinese medicinal plant *Periploca sepium*, which features a unique seven-membered formyl acetal bridged orthoester (FABO) motif and shows potent immunosuppressive activities. The total synthesis of this natural product is achieved in a total of 76 steps with the longest linear sequence of 29 steps and 9.2% overall yield.^[1] The FABO motif is constructed via a combination of Sinaÿ's and Crich's protocol for the formation of orthoester and acetal glycosides, respectively. The 2-deoxy- β -glycosidic linkages are assembled stereoselectively with judicious choice of the glycosylation methods.^[2,3] The epimer at the spiro-quaternary carbon in the FABO motif has also been elaborated in a stereo-controlled manner. This epimer, as well as the synthetic analogs bearing FABO motif, retain largely the inhibitory activities of periploside A against the proliferation of T-lymphocyte, indicating the importance of the chemical connection of the FABO motif to their immunosuppressive activities.



- [1] X. Zhang, Y. Zhou, J. Zuo, B. Yu, *Nature Commun.* 2015, 6:5879. doi: 10.1038/ncomms6879. [2] B. Yu, J. Sun, X. Yang, *Acc. Chem. Res.* 2012, 45, 1227–1236. [3] Y. Tang, J. Li, Y. Zhu, Y. Li, B. Yu, *J. Am. Chem. Soc.* 2013, 135, 18396–18405.