Development of *des*-D-ring interphenylene vitamin D derivatives

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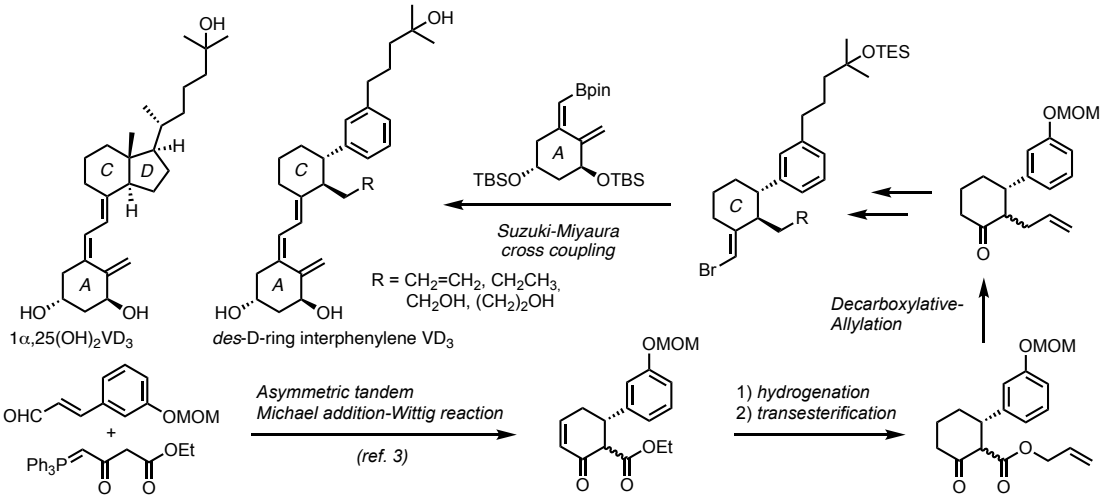
1α,25-dihydroxyvitamin D_3 is a *seco*-steroidal hormone, that have physiological role as the regulation of calcium and phosphorous metabolism as well as bone remodeling. Moreover, 1α,25-dihydroxyvitamin D_3 possesses cell proliferation-differentiation, and immunoregulation as pharmacological activity.[1] However, the therapeutic application has been limited by developing hypercalcemia and hyperphosphatemia. Therefore, an unmet need remains for development of more safer and topically treatable vitamin D_3 analogues.

Novel *des*-D-ring interphenylene vitamin D_3 as a C,D-modified 1α,25-Dihydroxy vitamin D_3 analogues have simplified form C,D-ring core structure by omitted few-carbon atm/bond of D-ring moiety and the attached an interphenylene structure. Among these analogues having a sidechain with at a *meta*-position showed binding affinity to vitamin D receptor (VDR) and gene transcription promoting activity with the same order of magnitude than 1α,25-dihydroxyvitamin D_3 and its 19-*nor* analogue.[2] Therefore, these analogues expected to further derivatization for biological screening. Herein, we report the development of more efficient synthetic process by the method developed by Ying-Chun Chen using Asymmetric Tandem Michael addition-Wittig reaction [3] for further exploration of *des*-D-ring interphenylene vitamin D_3 derivatives.



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