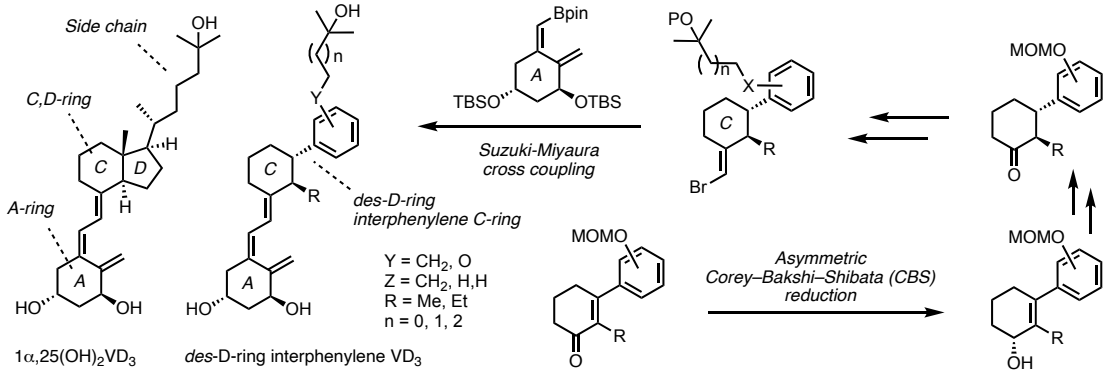
# Design, synthesis, and properties of novel vitamin $D_3$ derivatives

([1]*Department of Frontier Bioscience, Kanagawa University*) ○Kouta Ibe,[1] Ryoji Hotta,[1] Haruki Nakada,[1] Mayu Ohgami,[1] Sentaro Okamoto[1]

**Keywords**: *des*-D-ring interphenylene vitamin D derivatives; *des*-D-ring interphenylene C-ring unit; A-ring unit; vitamin D receptor

1α,25-dihydroxyvitamin $D_3$ discovered as a main hormone of calcium and phosphate metabolism, that have a wide range of biological functions including the cell proliferation-differentiation, apoptosis, and the immune systems.[1] However, the therapeutic application of the 1α,25-dihydroxyvitamin $D_3$ have been limited due to its serious side effects hypercalcemia and hyperphosphatemia. Therefore, the development of more efficient, safer, and topically treatable vitamin $D_3$ analogues remains an unmet needs. Most of the vitamin $D_3$ analogues are modified in the side chain and/or A-ring counterparts, only a few having structural modified C,D-ring analogues have been developed. Nevertheless, biological studies on these analogues have been suggested that modified C,D-ring can reduce the calcemic side effects.[2]

Accordingly, we report the design and synthesis of novel C,D-ring modified 1α,25-dihydroxyvitamin $D_3$ derivatives as a *des*-D-ring interphenylene vitamin $D_3$, which lack the D-ring and have an interphenylene structure attached to the C-ring. Synthesis of the *des*-D-ring interphenylene C-ring units were carried out using a modified Corey-Bakshi-Shibata (CBS) reduction for key reactions. And its derivatives are then constructed via the Suzuki–Miyaura coupling reaction with the corresponding A-ring unit, and the evaluated on their VDR binding affinity and a reporter-gene assay.[3]




1) G. Jones, S. A. Strugnell, H. F. DeLuca, *Physiol. Rev*., **1998**, *78*, 1193. 2) G. Eelen, L. Verlinden, R. Bouillon, P. D. Clercq, A. Muñoz, A. Verstuyf, *J. Steroid Biochem. Mol. Biol*., **2010**, *121*, 417. 3) K. Ibe, H. Nakada, M. Ohgami, T. Yamada, S. Okamoto, *Eur. J. Med. Chem.*, **2022**, *243*, 114795