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Synthetic Studies on a Potential Drug for Osteoporosis

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According to a report from US HHS released on 10/14/04, “by 2020, one in two Americans over age 50 will be at risk for fractures from osteoporosis or low bone mass.” It is also well known that women who have gone through menopause lose bone at a rate of 1-6% a year. “This disease affects 44 million Americans. Each year, it leads to over 300,000 fractures, usually in people age 65 and older (National Osteoporosis Foundation, www.nof.org).” Symbioimine, isolated by Uemura in 2004, has received considerable attention as a potential target for the treatment of osteoporosis. With common acyclic intermediate in hand, we are currently investigating two proposals for the biosynthesis: the exo-intramolecular Diels-Alder reaction (IMDA) from trans-enone followed by cyclic imine formation, as proposed by Uemura, and the endo-IMDA with the dihydropyridine (cyclic imine of cis-enone) followed by epimerization at C4, as proposed by our group.