Janjira Rujirawanich 2012: Synthesis of Advanced Intermediates to Anti-cancer OSW-1 and Synthesis of Cyclic Sulfamidates for *N*-Heterocycle Construction. Doctor of Philosophy (Chemistry), Major Field: Chemistry, Department of Chemistry. Thesis Advisor: Associate Professor Boonsong Kongkathip, Ph.D. 458 pages.

OSW-1, a natural product isolated from the bulbs of *Ornithogalum saundersiae*, exhibited extremely potent cytotoxicity against the NCI 60-cell *in vitro* screen, with a mean IC_{50} of 0.78 nM. Its *in vitro* anticancer activity is from 10 to 1000 times more potent than many well-known anticancer agents in clinical use, including mitomycin C, adriamycin, cisplatin, camptothecin and even pacilitaxel. In addition, its toxicity to normal human pulmonary cells is significantly lower (IC_{50} 1500 nM). The structure of saponin OSW-1 contains the steroidal aglycone with a sugar residue at the 16β-hydroxy.

Synthesis of the protected OSW-1 aglycone by the intramolecular reaction of the keto ester steroid intermediate has been investigated. The key intermediate, 3β-benzyloxy-16β-(isobutyl-monomethyl ester malonate-ester)-17α-hydroxy-pregnenolone, has been successfully synthesized in 10 steps with 10.4% overall yield from a commercially available diosgenin. Intramolecular McMurry coupling or samarium diiodide-promoted keto-ester coupling reaction of our key intermediate did not provide the expected β-keto lactone intermediate, and only 5-pregnene-20-one derivative or 16-dehydropregnenolone were obtained.

The facile syntheses of three partially protected OSW-1 disaccharide moieties, having 2-*O*-*p*-methoxybenzoyl-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-L-arabinopyranoside structure, were elaborated by glycosylation of xylopyranose donors and arabinopyranose acceptors. The xylopyranose donors were synthesized by a short synthetic approach *via* convenient selective 1,2-diacetal protection of 3,4-*trans*-diequatorial hydroxyl group. Additionally, three arabinose acceptors were prepared in a three steps sequence from benzyl, *p*-methoxybenzyl and thiophenyl α/β-L-arabinopyranosides by using regioselective reductive ring opening of benzylidene acetals as the key feature.

The synthesis of benzannulated *N*-heterocyclic compounds which are the class of privileged structures having a wide range of biological activities, bearing stereodefined substituents has been accomplished based on enantiomerically pure 1,2- and 1,3-cyclic sulfamidates towards a range of nucleophiles. The enantiomerically pure 1,2- and 1,3-cyclic sulfamidates were prepared from 1,2- and 1,3-amino alcohols. The nucleophilic cleavage of 1,2-cyclic sulfamidates with the sodium anion of 2-bromophenols (and related anilines and thiophenols), followed by Pd(0)-mediated amination provided the substituted and enantiomerically pure benzoxazine, benzothiazine and quinoxaline derivatives. Moreover, 1,2- and 1,3-cyclic sulfamidates undergo efficient nucleophilic cleavage with 2-hydroxybenzyl alcohol (and related 2-aminobenzyl alcohols and 2-mercaptobenzyl alcohols), followed by Mitsunobu reaction also furnishing substituted and enantiopure benzoxazepine, benzodiazepine, benzothiazepine, benzoxazocine, benzodiazocine and benzothiazocine derivatives.

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