Synthetic studies on OSW-1 and its derivatives

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OSW-1, a highly potent anticancer saponin, has been isolated by Sashida *et al*. from the bulbs of *Ornithogalum saundersiae* in 1992. Its cytotoxicities against various human malignant tumor cells are from 10- to 100-fold more potent than well-known anticancer agents in clinical use, such as mitomycin C, adriamycin, cisplatin, camptothecin and taxol. However, the cytotoxicities are little difference between in vivo and in vitro. Therefore, we intended to establish a new synthetic route to OSW-1 and its derivatives having modified side chains.

The key feature of our synthesis was based on the stereospecific [2,3] Wittig rearrangement of (*E*)-16α-(3-methylthienyl)methoxy-17(20)-pregnene giving (20*S*)-22-hydroxy-23,26-epithiocholesta-16,23,25-triene. Thiophenemethyl ether, prepared by etherification of known allylic alcohol with 2-bromomethyl-4-methylthiophene, was subjected to [2,3] Wittig rearrangement leading to (20*S*)-22-hydroxythiophene-methanol derivative. Conversion of (20*S*)-22-hydroxythiophenemethanol into thiopehene-OSW-1 was carried out by anti-dihydroxylation of alkene at C-16 and glycosidation of the 16β, 17α-diol. Finally, thiophene-OSW-1 was treated with Raney-Ni (W-2) to give the desired OSW-1. Thus, we have succeeded in the synthesis of OSW-1 and thiophene-OSW-1. Preparation of analogues with a modified side chain will be presented.