Potjamarn Bunyathaworn 2011: Synthesis of Key Intermediates to Antiviral Sterol Orthoesters and Synthesis of New Polyhydroxy Sterols with Anticancer Activity Evaluation. Doctor of Philosophy (Chemistry), Major Field: Chemistry, Department of Chemistry. Thesis Advisor: Associate Professor Boonsong Kongkathip, Ph.D. 243 pages.

Sterol orthoesters which are marine natural products, isolated from the Caribbean sponge *Petrosia weinbergi*, exhibited *in vitro* activity against the feline leukemia virus (FeL V), mouse influenza virus (PR8) and mouse corona virus (A59). Up to the present, there has been no report on the synthesis of sterol orthoesters and their intermediates, so synthesis of antiviral sterol orthoesters intermediates has been investigated by us. Two key intermediates, 2α, 3α-epoxy-16α-(3-acetoxy-2, 2-dimethyl-5-hexenoate)-5α-pregnan-20-one and 16α-(3-acetoxy-2, 2-dimethyl-5-hexenoate)-2, 3-dihydroxy-20-methyl-5α-pregn-20-ene for intramolecular strategy have been successfully synthesized in 10 and 13 steps with 11.9% and 0.12% overall yield, respectively by using tigogenin obtained from waste of *Agave sisalana* leaves or commercially available 3β-acetoxy-5-pregnen-20-one as starting material. Intermolecular strategy was also a tool for synthesizing the key intermediate, 3β-*tert*-butyldimethylsiloxy-29-hydroxy-(16*S*, 20*S*)-16, 20-acetonide-5α-cholest-24(28)-ene from cheaply available diosgenin in 8 steps with 0.55% overall yield.

Six new polyhydroxy sterols and their sulfated analogs have also been synthesized by using Grignard reaction as a key step. Their structures contain various functionalities in ring A such as monohydroxyl group at C-3 (β) or dihydroxyl group at C-2 (β) and C-3 (α) and differ on the side chain for studying the effect on cytotoxicity against two cancer cell lines, human epidermoid carcinoma (KB) and human small cell lung carcinoma (NCI-H187). The results showed that 3β, 20(*S*), 24-trihydroxy-5α-cholestane bearing trihydroxyl group at C-3, C-20 and C-24 exhibited the strongest activity against both cell lines (IC_{50} (μg/ml) = 5.39 (KB) and 2.11 (NCI-H187)) whereas 2β, 3α, 20(*S*), 24-tetrahydroxy-5α-cholestane containing extra hydroxyl group at C-2 in ring A was inactive against both cell lines.

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