Komkrit Hasitapan 2006: Part I: Synthesis of Naphthoquinone Ester Derivatives with Anticancer and Antimalarial Activities. Part II: Synthesis of Naphthol Derivatives with Anti-Inflammatory Activity. Part III: Application of Three-Component Palladium-Catalysed Cascade Reaction of Diketopiperazine and 1,4-Benzodiazepine Derivatives. Doctor of Philosophy (Organic Chemistry), Major Field: Organic Chemistry, Department of Chemistry. Thesis Advisor: Associate Professor Ngampong Kongkathip, Ph.D. 344 pages.
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Part I: Naphthoquinone ester derivatives, isolated from *Rhinacanthus nasutus* (Thong Phun Chang), exhibited potent cytotoxicity against cancer cell lines. Therefore the naphthoquinone ester derivatives in which the ester moieties were varied such as aliphatics bearing 2'-dimethyl substituent and aromatics bearing 2'-cyclohexyl substituent have been synthesized starting from 1-hydroxy-2-naphthoic acid in ten steps in order to study their structure-activity relationships (SARs). From the cytotoxicity results, only naphthoquinone aliphatic esters with α-methyl substituent at the ester moiety showed moderate to strong activity while naphthoquinone aromatic esters bearing 2'-cyclohexyl exhibited moderate activity. All naphthoquinone aliphatic esters showed very potent antimalarial activity.

Part II: 2-Substituted-1-naphthol derivatives were synthesized in high yield starting from 1-hydroxy-2-naphthoic acid. 2-(3'-Hydroxy)subtituted- and 2-(3'-methoxy) substituted-1-naphthols had selective inhibition of COX-2 over COX-1. More rigidity or strain in molecule affected less COX inhibitory activity. The structure-activity relationships of these naphthols analyzed by docking experiments, indicated that 1-hydroxyl group and C-5 hydrogen on naphthalene nucleus enhanced the anti-inflammatory activity by formation of H-bonding with Val523 and van der Waals interaction with Tyr385, respectively.

Part III: Synthesis of diketopiperazine and 1,4-benzodiazepine derivatives, with substructures representing a wide variety of biological activity, were accomplished using three-component palladium-catalysed cascade reaction. Most of these compounds were obtained in moderate to good yield with high-regioselectivity. Moreover, this process is more convenient, effective and less wasteful.

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