Abstract

Project Code	:	**Contract no. RTA/02/2543**
Program	:	**Exploratory Studies in Basic Synthetic Organic Chemistry and Bioactive Natural Products**
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Program Period	:	**September 2000 – September 2003**
Objectives	:	1. To build up research network with institutions both within Thailand and abroad. 2. To produce high quality M.Sc. and Ph.D. graduates. 3. To carry exploratory studies in basic synthetic organic chemistry and bioactive natural products.

Methodology, Results and Discussion

Basic Synthetic Organic Chemistry.

Continuing exploratory research on the chemistry of α-halomethyl phenylsulfides and sulfones led to a convenient procedure for the synthesis substituted α,β-unsaturated sulfones. The novel doubly cyclization reaction of α-sulfonyl radical led to the benzothiapyran dioxide product. Samarium (II) iodide mediated cleavage of phenylsulfonyl activated cyclopropane led to a novel samarium dienolate species which undergoes a novel aldol-Tishenko reaction with aldehydes. The process is a convenient route for the stereoselective synthesis of *anti*-1,3-diol monoesters. The novel difluorophenylsulfanylmethyl radical has been successfully generated. The species is useful as a difluoromethylene building block. The Pummerer-type reaction has been extended to the novel ring cleavage of phenylsulfinylcyclopropane giving a mixture of α,β- and γ, δ-unsaturated aldehydes.

The total synthesis of (±)-dehydropentenomycin and analogues has been accomplished. Employing diethyl succinate dianion technology, a series of the bioactive naturally occurring γ-butyrolactones has been synthesized.

Bioactive Natural Products

An interdisciplinary research program on bioactive natural products from tropical plants involving botany, chemistry and biology was undertaken. The bioassays for anti-inflammatory, cytotoxic, anti-HIV and male antifertility were established.

An extensive proceedings, based on a plenary lecture given by Professor Vichai Reutrakul at the international congress 2000 Years of Natural Products Research: Past, Present and Future, entitled "Bioactive natural products from tropical forests" has been published as a monograph. The study on male antifertility of Triptolide indicated that the agent acted on the epididymal sperm. The research on plants, *Polyalthia suberosa*, *Gardenia obtusifolia* and *Boesenbergia pandurata* has identified new structure leads with cytotoxic, anti-HIV and anti-inflammatory activities. The discovery of the anti-HIV-1 and cytotoxic activities of cycloartanes from *Gardenia obtusifolia* is highly significance. Further work on *Garcinia speciosa* resulted in the isolation of anti-HIV-1 protostane triterpenes in addition to cytotoxic xanthones. A series of cytotoxic coumarins has been isolated from *Mammea harmandii*. Novel cytotoxic caged xanthones have been identified from *Garcinia speciosa*.

Overall, the results obtained have shed new light on the type of new lead structures for these biological activities and represent the new exploratory studies in the fields.

Suggestion/Further Implication/Implementation

The synthetic organic chemistry research led to the discovery of some fundamental reaction of radical α to the heteroatoms. Total synthesis of natural products has provided convenient procedure for the synthesis of bioactive natural products. These discoveries will be potentially useful technology for synthetic chemists.

Some novel lead structures have been discovered. Triptolide is one of the most promising posttesticular antifertility agent. Cycloartanes and Panduratin A and derivatives are highly interesting compounds for anti-HIV-1 and anti-inflammatory activities, respectively. These lead structures should be further developed.

Keywords : **Synthesis, bioactive, cytotoxic, anti-HIV, anti-inflammatory, male antifertility.**