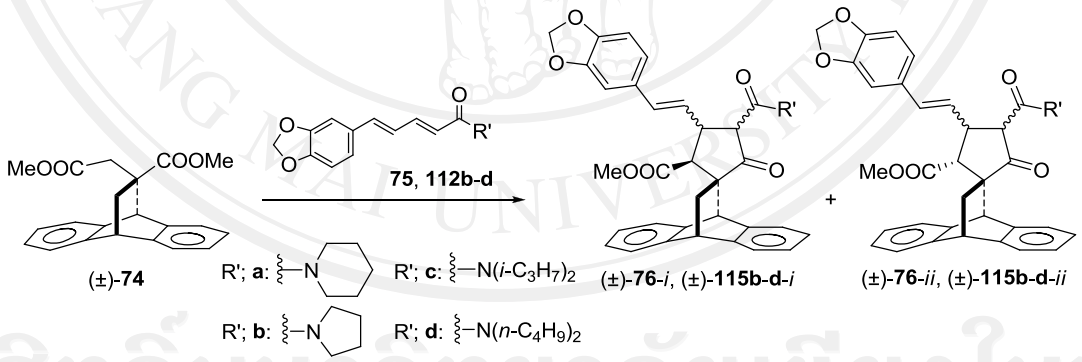
# CHAPTER 4

# CONCLUSIONS

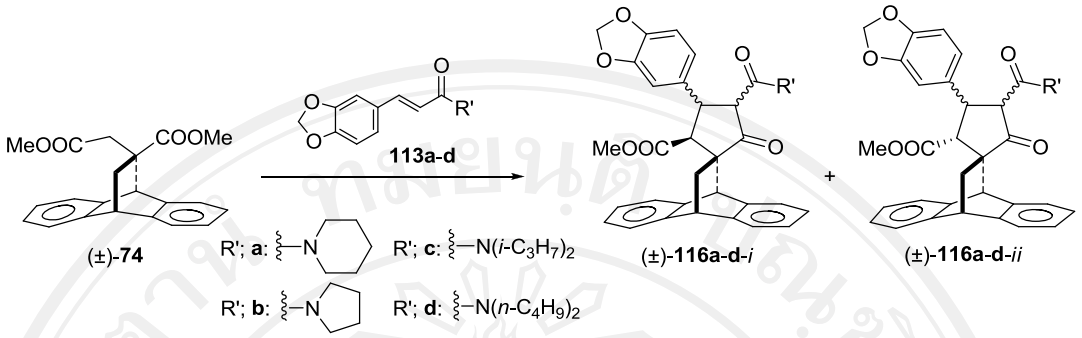
The racemic spirocyclopentanone–anthracene adduct derivatives ((±)-**115b-d** – (±)-**117a-d**) were synthesized readily variable of racemic dimethyl itaconate–anthracene adduct ((±)-**74**) and amide derivatives (**112b-d** – **114a-d**), respectively through the tandem Michael addition–Dieckmann condensation reactions as key steps (Scheme 4.1-4.4).

All of racemic spirocyclopentanone–anthracene adduct derivatives ((±)-**76**-*i*, -*ii* and (±)-**115b**-*i*, -*ii* – (±)-**115d**-*i*, -*ii*) displayed antimalarial activity against *P. falciparum* (K1, multi-drug resistance strain) with $IC_{50}$ value 4.70, 3.40, 3.38, 4.64, 3.14, 3.89, 4.35 and 6.52 $\mu$g/ml respectively. These compounds displayed non-cytoxicity against *Vero cells*.



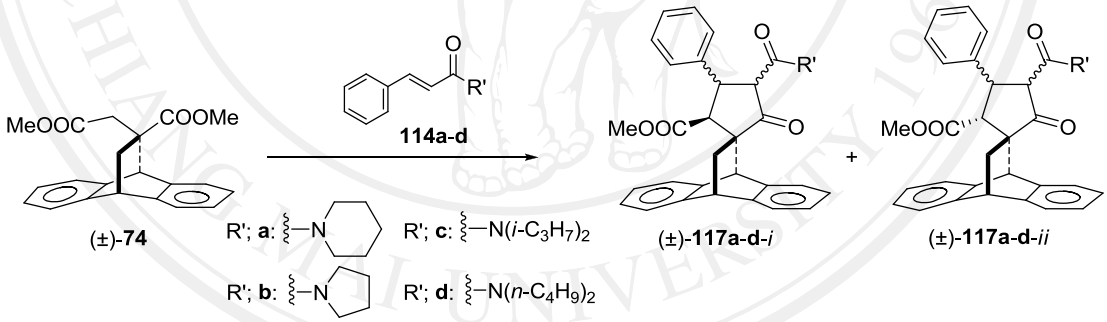

**Scheme 4.1** Tandem Michael addition–Dieckmann condensation reactions of racemic spirocyclopentanone–anthracene adducts ((±)-**76**-*i*, -*ii* and ((±)-**115b**-*i*, -*ii* – (±)-**115d**-*i*, -*ii*)

Almost of racemic spirocyclopentanone–anthracene adducts (±)-**116a**-*i*, -*ii* – (±)-**116d**-*i*, -*ii* displayed antimalarial activity against *P. falciparum* (K1, multi-drug resistance strain) with $IC_{50}$ value inactive, inactive, 5.02, 4.10, 4.91, 9.47, 5.72 and inactive $\mu$g/ml respectively. These compounds displayed no cytoxicity against *Vero cells*.



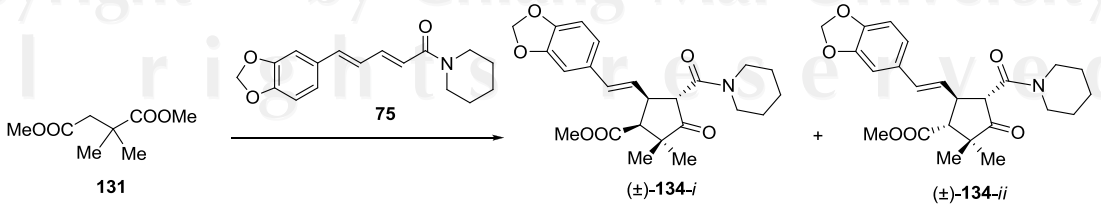

**Scheme 4.2** Tandem Michael addition–Dieckmann condensation reactions of racemic spirocyclopentanone–anthracene adducts (±)-**116a**-*i*, -*ii* – (±)-**116d**-*i*, -*ii*

Some of racemic spirocyclopentanone–anthracene adducts (±)-**117a**-*i*, -*ii* – (±)-**117d**-*i*, -*ii* displayed antimalarial activity against *P. falciparum* (K1, multi-drug resistance strain) with $IC_{50}$ value inactive, inactive, 4.90, inactive, 8.04, inactive, inactive and inactive $\mu$g/ml respectively. These compounds displayed no cytoxicity against *Vero cells*.




**Scheme 4.3** Tandem Michael addition–Dieckmann condensation reactions of racemic spirocyclopentanone–anthracene adducts (±)-**117a**-*i*, -*ii* – (±)-**117d**-*i*, -*ii*

Cyclopentanones (±)-**134**-*i* and (±)-**134**-*ii* were inactive against *P. falciparum* (K1, multi-drug resistance strain) and non-cytoxicity against *Vero cells*.




**Scheme 4.4** Tandem Michael addition–Dieckmann condensation reactions of racemic cyclopentanones (±)-**134**-*i* and (±)-**134**-*ii*

Obviously, the spirocyclopentanone–anthracene adducts that containing with five-membered ring and diisopropyl of amide, vinyl, methylenedioxy and anthracene moiety show good antimalarial activity. The spirocyclopentanone–anthracene adducts are easily and rapidly synthesized from simple, commercially available starting materials.

The spirocyclopentanone–anthracene adducts (±)-**76**-*i* and (±)-**76**-*ii* act as competitive inhibitor in common metabolic pathway of CYP 450 catalysis.