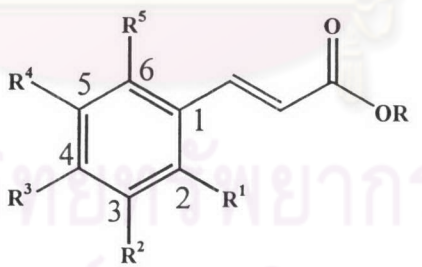
CHAPTER IV

CONCLUSION

During the course of this research, seventy eight substituted cinnamic acids and four substituted benzyl benzoates were explored in the fields of SAR and QSAR using the insecticidal activity against common cutworms *Spodoptera litura* as the biological experiment. Fifty substituted cinnamate esters, two substituted cinnamamides, ethyl 3-phenylpropionate and three substituted benzyl benzoate were synthesized. All synthesized compounds were well-confirmed their structures by physical properties and ^{1}H-NMR. Among them, four compounds, ethyl 2-chloro-6-fluorocinnamate (**S12**), ethyl 4-octyloxycinnamate (**S18**), ethyl 4-hexyloxy-3-methoxycinnamate (**S23**) and ethyl 4-dodecyloxy-3-methoxycinnamate (**S25**), have not previously been reported in chemical literatures. These compounds were characterized using various spectroscopic techniques, *i.e.*, IR, ^{1}H and ^{13}C-NMR. The structures of four new compounds are shown below:



Cpds	R	R^1	R^2	R^3	R^4	R^5
S12	C_2H_5	Cl	H	H	H	F
S18	C_2H_5	H	H	OC_8H_{17}	H	H
S23	C_2H_5	H	OCH_3	OC_6H_{13}	H	H
S25	C_2H_5	H	OCH_3	OC_6H_{13}	H	H

From the results of insecticidal activity, ethyl 2-chlorocinnamate (**S03**) showed the excellent value at 70 % mortality (LD_{50} = 1.79 x 10^{-4} mol/insect) while ethyl 4-methylcinnamate (**S40**) slightly exhibited lower activity at 62.5 % (LD_{50} = 4.43 x 10^{-4} mol/insect). Ethyl 4-methoxycinnamate (**S15**), ethyl 4-hexyloxy cinnamate (**S17**) and ethyl 4-*t*-butylcinnamate (**S42**) displayed the activity as well as the reference compound (**S00**) and ethyl 4-fluorocinnamate (**S02**). Ethyl 3-bromo cinnamate (**S07**), ethyl 3-methoxycinnamate (**S14**), ethyl 4-trifluoromethylcinnamate (**S43**) and 2,4-dichlorophenyl 3,4-methylenedioxycinnamate (**S62**) slightly showed less activity than the reference compound.

The SAR of these compounds revealed that ethyl group was essential as the substituent of an ester. The substituent R^1 at 2-position on a benzene ring should be small electron-donating group while that at 3-position (R^2) should not bound with any substituent, especially the strong electron withdrawing group such as nitro group. The para-position (R^3) on a benzene ring should be the small electron-donating group such as methyl group. Furthermore, the QSAR study disclosed that no physicochemical properties calculating by Guassian software had the close relationship with the insecticidal activity in the whole set of samples. Thus, the structures were investigated with one by one position. For five substituents at 2-position (R^1) on a benzene ring, the activity was depended on the HOMO-LUMO gap (r^2 = 0.613, q^2 = 0.590 and n = 5) while the six substituents of training set at 3-position (R^2) showed the excellent correlation between the activity and the LUMO (r^2 = 0.921, q^2 = 0.773 and n = 6). For 4-position (R^3) exhibited the moderate correlation between the activity and the atomic charge at C_9 and HOMO-LUMO gap (r^2 = 0.779, q^2 = 0.646 and n = 13).

Moreover, ethyl 2-chlorocinnamate (**S03**), ethyl 4-methylcinnamate (**S40**) and ethyl cinnamate (**S00**) were evaluated for the antifeedant activity against the same worms. The ED_{50} of these compounds of 3.09 x 10^{-7}, 3.97 x 10^{-7} and 3.97 x 10^{-7} mol/cm^2, respectively was observed which was comparable to that of rotenone, a standard compound generally used as a common insecticide.[43]

Proposal for the Future Work

The possible future work related to this research would be the study of ethyl cinnamate structure and other insects such as termite, bee, *etc*. In addition, the synthesis of ethyl cinnamate derivatives should be carried on followed the information obtained from molecular modeling as previously proposed. Furthermore, finding out the real active site in the insect was promising for further study by the molecular modeling. Besides, ethyl 2-chlorocinnamate had potential for further study in the field. Other bioassays that reported involving cinnamate esters were attractive for evaluation, for example, ultraviolet filter.