CHAPTER IV

CONCLUSION

The objective of this research is to search for suitable halogenated reagent capable of transforming carboxylic acid to its analogous acid chloride. At the same time optimal conditions for this developed protocol was cautiously scrutinized. This developed methodology could be carried out under mild conditions, and provided the high yield of desired product.

From this research, the optimum conditions were disclosed: carboxylic acid 1eq as a substrate, Cl_3CCONH_2 2 eq and PPh_3 2 eq as a combination reagent, CH_2Cl_2 6 mL as a solvent, *4*-picoline 3 eq as a base and the reaction was recommended to carry out under reflux dichloromethane for approximately 1 hour or followed by TLC. In addition, Cl_3CCN, Cl_3CCO_2Et and $Cl_3CCONHPh$ could be utilized as another alternative halogenated reagent instead of Cl_3CCONH_2. This developed protocol was indeed disclosed to be an efficient system to convert carboxylic acid to its derivatives such as amides and esters. The cost of the reagents used was found to be superior to other related methods cited in the literature.

Various carboxylic acids and amines were examined to verify this developed procedure. The outcome from the study on the effect of carboxylic acid manifested that this method was suitable for aromatic carboxylic acid and short chain aliphatic acids. The long chain aliphatic carboxylic acid rendered the yield of the desired product. The substituents on an aromatic acid at *para* position were explicitly uneffected the outcome of the reaction either being an electron-withdrawing or electron-donating group. From the variation of amine, the yields of the desired product were insignificantly depend on the reactivity of amine.

The application of this developed method for the synthesis of various amides and esters was also fruitfully achieved. Twenty eight amides including eleven

biological amides and five biological esters were synthesized without any difficulty using this methodology.

To summarize, biologically active amides and esters could be prepared from this developed methodology as presented in Tables 4.1 and 4.2.

Table 4.1 The summarization of biologically active amides

group	target molecule	biological activity	%yield
benzamide	*N,N*-diethylbenzamide **(T1)**	insect repellent	99
	DEET **(T2)**	insect repellent	99
anililde	mebenil **(T3)**	fungicide	91
	benodanil **(T4)**	fungicide	88
	cypromid **(T8)**	herbicide	80
cinnamamide	*2*-chloro-*N,N*-diethylcinnamamide **(T5)**	herbicide	79
	N-(*3,4*-methylenedioxycinnamoyl) phenethylamide **(T6-1)**	-	79
	N-(*3,4*-methylenedioxycinnamoyl) piperidide **(T7)**	antiepilepsirnium activity	99
other	capsaicine synthetic **(T9)**	mutagenicity and many activity	28
	N-palmitoylethanolamine or PEA **(T10)**	anti-inflammatory activity	31
	N,N'-bis(*3*-chlorophenyl) butanediamide **(T11)**	antimycobacterial and antialgal	25

Table 4.2 The summarization of biologically active esters

target molecule	biological activity	%yield
benzyl benzoate **(T13)**	insecticide	85
phenethyl cinnamate **(T14)**	perfume and cosmetic	98
cinnamoyl cinnamate **(T15)**	cosmetic and drug	84
cholesteryl butyrate **(T16)**	cosmetic and pharmaceutical formulation	78
cholesteryl nonanoate **(T17)**	cosmetic and pharmaceutical formulation	79

Suggestion for the further work

This research provided many prospective points for the future work. For instance, the ratio of Cl_3CCONH_2 or other halogenated reagents and PPh_3 should be carefully examined. Other potential halogenated reagents such as *p*-nitrophenyl trichloroacetate, Cl_3CNO_2 are still awaited for further investigated. The application of this developed system for synthesis of other functional groups such as acid anhydride, thiol ester and ketone *etc.* should be verified. In addition, the chemoselectivity of this system is crucially needed to be evaluated. Other phosphorus reagents such as $P(OMe)_3$ using as a combination with halogenated reagent should also be further explored.