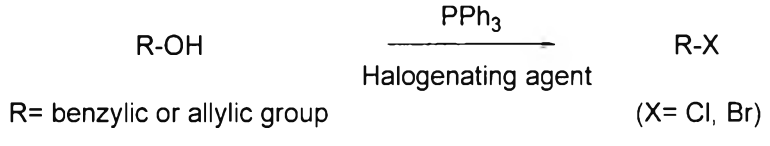
CHAPTER III

RESULTS AND DISCUSSION

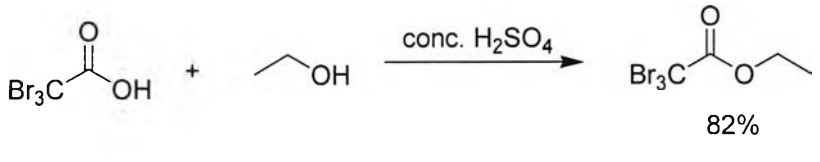
Alkyl halides have been utilized as versatile intermediates in organic chemistry. The systematic studies for the manipulation of alkyl halides, especially alkyl chlorides and bromides have widely been addressed whereas those for benzylic and allylic halides from benzylic and allylic alcohols have been rare systematically examined. Thus, the main aim of this research is to search for the suitable halogenating agents to synthesize benzylic and allylic halides. Although there are various commercially available chlorinating agents for the manipulation of chlorides, brominating agents are normally less readily available. Therefore, some new brominating agents should be synthesized as alternative brominating agents. The exploration of optimum conditions utilizing these developed reagents and PPh_3 for the preparation of benzylic and allylic halides from benzylic and allylic alcohols, respectively was additionally carried out. The general equation can be simplified as shown below.



3.1 Synthesis of Brominating Agents

Even though Br_3CCO_2Et and $Br_3CCOCBr_3$, effective brominating agents are commercially available, their costs are quite expensive. Thus, those reagents were prepared according to the reported protocols.

Br_3CCO_2Et could be easily prepared by esterification of Br_3CCO_2H, EtOH and concentrated H_2SO_4 as a catalyst [36-37].



Br_3CCO_2Et coupled with PPh_3 has been reported as a brominating agent for the conversion of alcohols into alkyl bromides [24]. However, it has never been systematically reported for the preparation of benzylic and allylic bromides.

The ^{1}H-NMR spectrum of Br_3CCO_2Et (Fig 3.1) reveals the signal belonging to the methyl group at δ_H 1.40 with J = 7.2 Hz and a quartet signal with the same coupling constant of the methylene group resonating at δ_H 4.43. The ^{13}C-NMR spectrum (Fig 3.2) exhibits two peaks at δ_C 13.7 and 29.5 being the methyl and methylene carbons, respectively. The signal of the carbon bearing three bromine atoms and that of the carbonyl carbon are detected at δ_C 65.7 and 162.1, respectively.

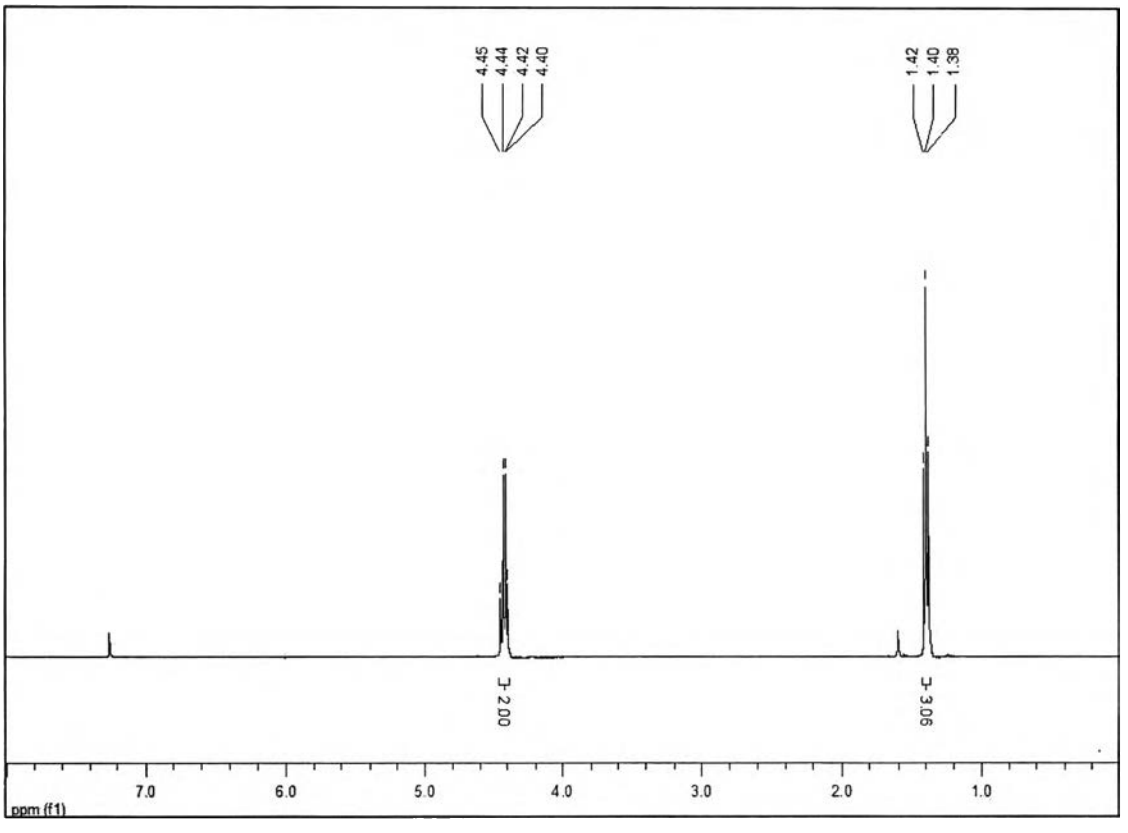


Figure 3.1 ^{1}H-NMR spectrum of Br_3CCO_2Et

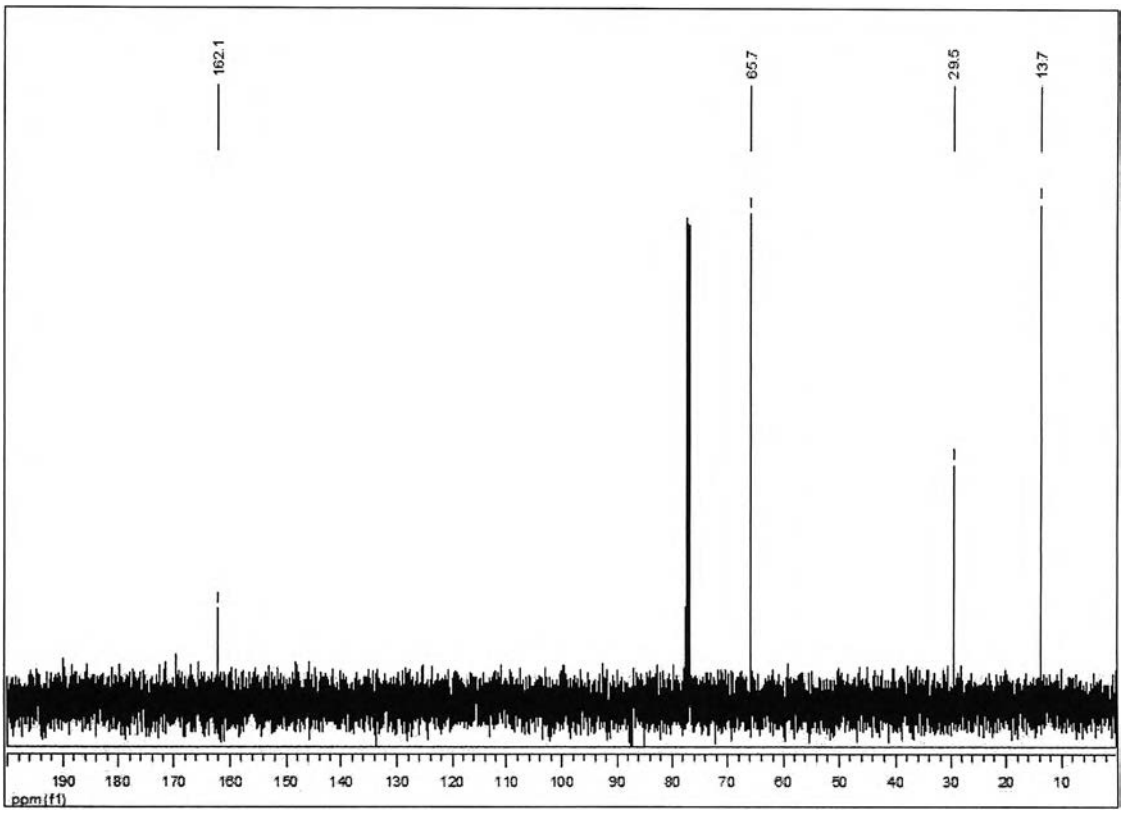
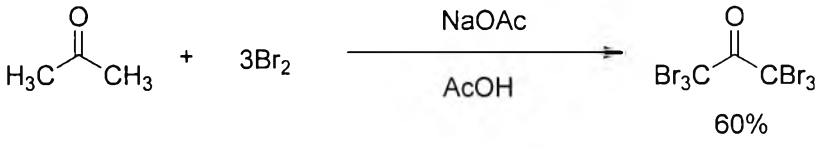


Figure 3.2 ^{13}C-NMR spectrum of Br_3CCO_2Et

The synthesis of $Br_3CCOCBr_3$ could be achieved by the reaction of acetone, Br_2 and NaOAc in glacial acetic acid as previously described [52]. The ^{13}C-NMR spectrum (Fig 3.3) exhibits the signal of the carbon directly bonding with bromine atoms at δ_C 24.6 and the carbonyl carbon at δ_C 173.4.



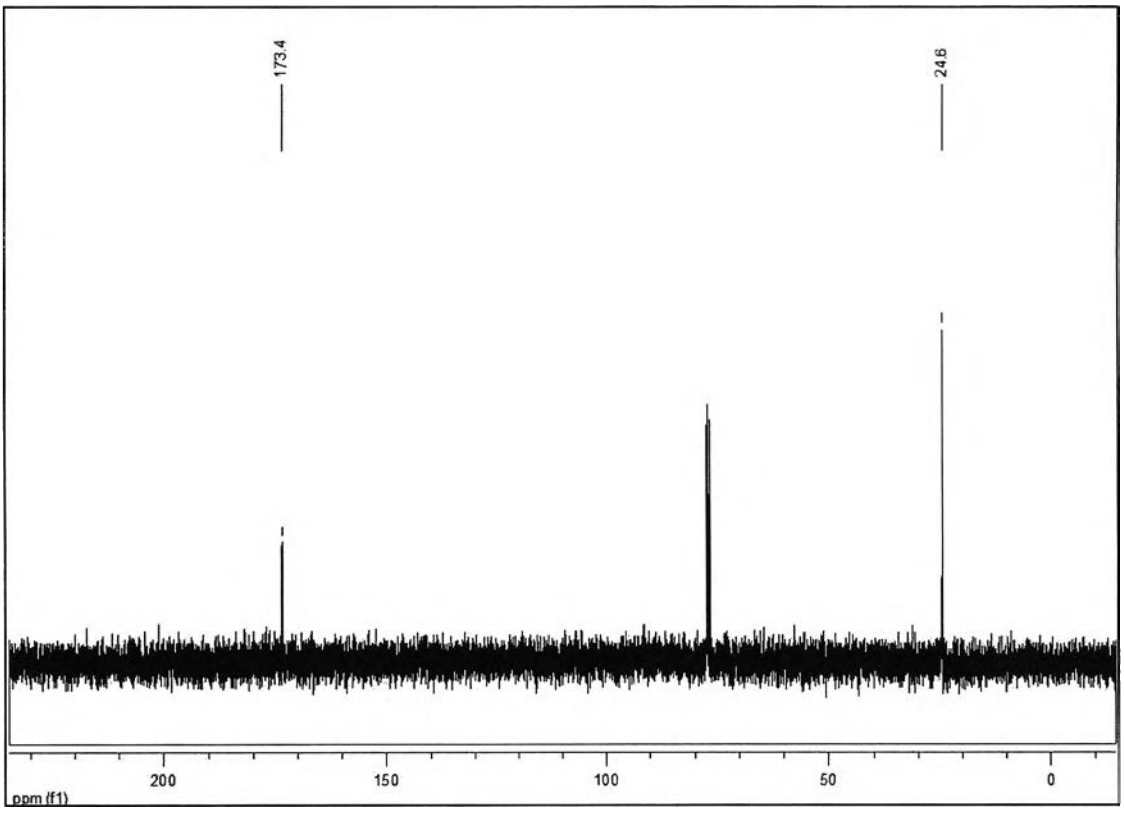
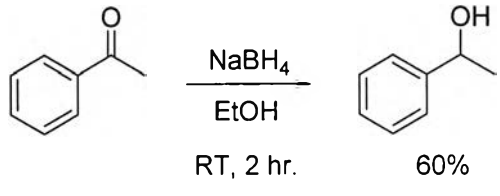


Figure 3.3 ^{13}C-NMR spectrum of $Br_3CCOCBr_3$

3.2 The Preparation of Alcohols

Some alcohols chosen as starting materials to explore the effects of alcohol structures for halogenation are prepared by the following reported methods.

1-Phenylethanol, a secondary benzylic alcohol was prepared by reduction of acetophenone with $NaBH_4$.



The ^{1}H-NMR spectrum of 1-phenylethanol (Fig 3.4) discloses a doublet signal with J = 6.4 Hz of the methyl group at δ_H 1.50. A singlet signal of a hydroxyl group, a quartet signal with J = 7.0 Hz of the benzylic proton, and multiplet signals of aromatic protons resonate at δ_H 1.91, 4.90 and 7.26-7.40, respectively. The ^{13}C-NMR spectrum (Fig 3.5) shows two peaks at δ_C 25.2 and 70.4 being the methyl and methine carbon

signals, respectively while the other carbon atoms on an aromatic ring are detected at δ_C 125.4, 127.5, 128.5 and 145.8.

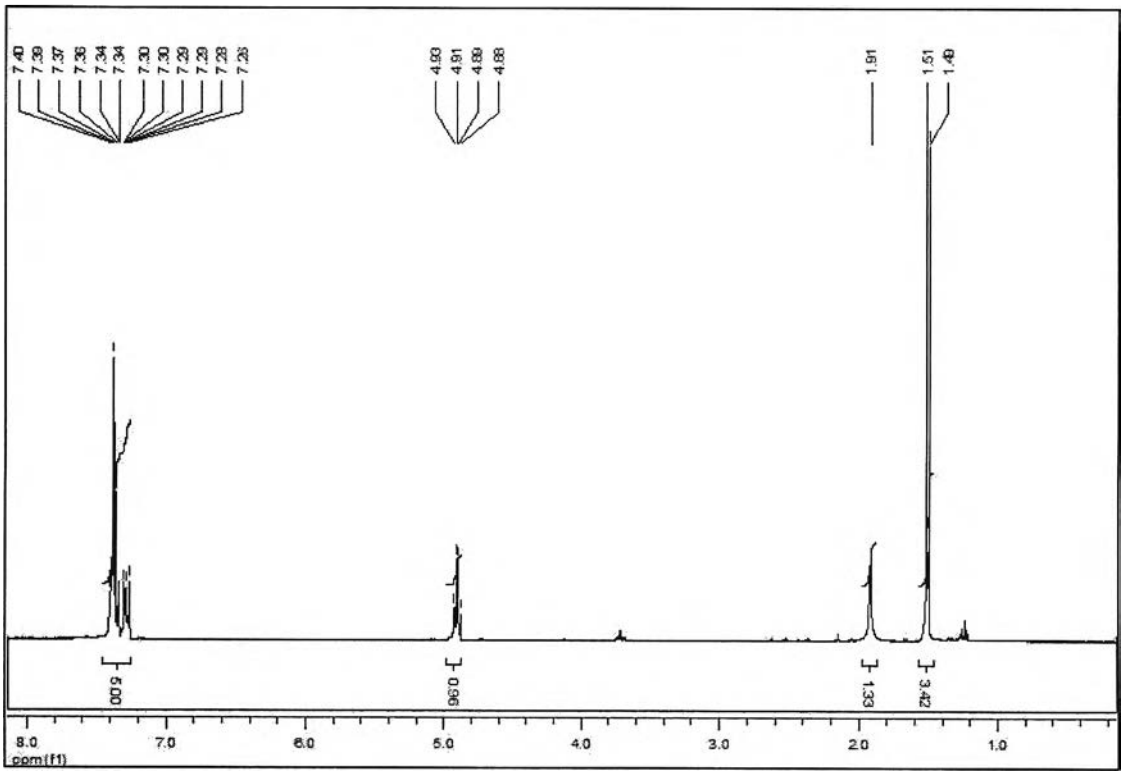


Figure 3.4 ^{1}H-NMR spectrum of 1-phenylethanol

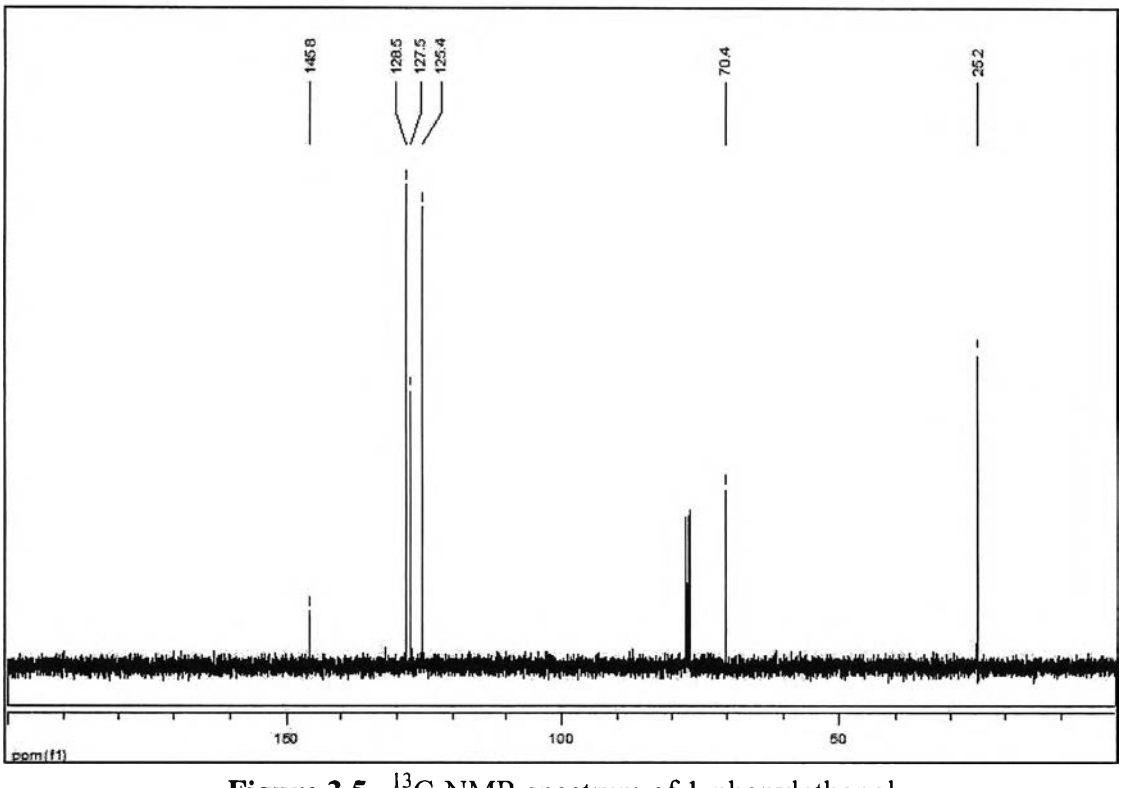
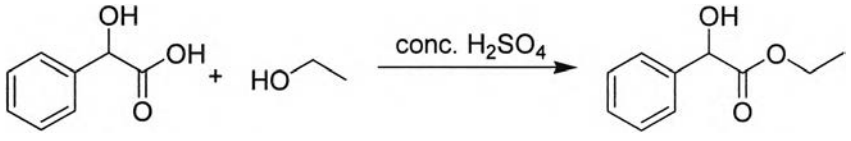


Figure 3.5 ^{13}C-NMR spectrum of 1-phenylethanol

Ethyl mandelate, one of benzylic alcohol models bearing an electron-withdrawing group could be prepared by esterification of mandelic acid and EtOH in the presence of catalytic amount of H_2SO_4.



37%

The ^{1}H-NMR spectrum of ethyl mandelate (Fig 3.6) reveals a triplet signal of a methyl group with J = 6.0 Hz at δ_H 1.22. A quartet signal of the two methylene protons with J = 9.0 Hz, a singlet signal of the benzylic proton and multiplet signals of aromatic protons resonate at δ_H 4.21, 5.15 and 7.33-7.43, respectively. The ^{13}C-NMR spectrum (Fig 3.7) discloses the methyl carbon signal at δ_C 14.0, two peaks at δ_C 62.2 and 72.9 being the methylene and methine carbons, respectively. The aromatic carbons are noticeable at δ_C 126.5, 128.6, 138.4 and the carbonyl carbon reveals at δ_C 173.7.

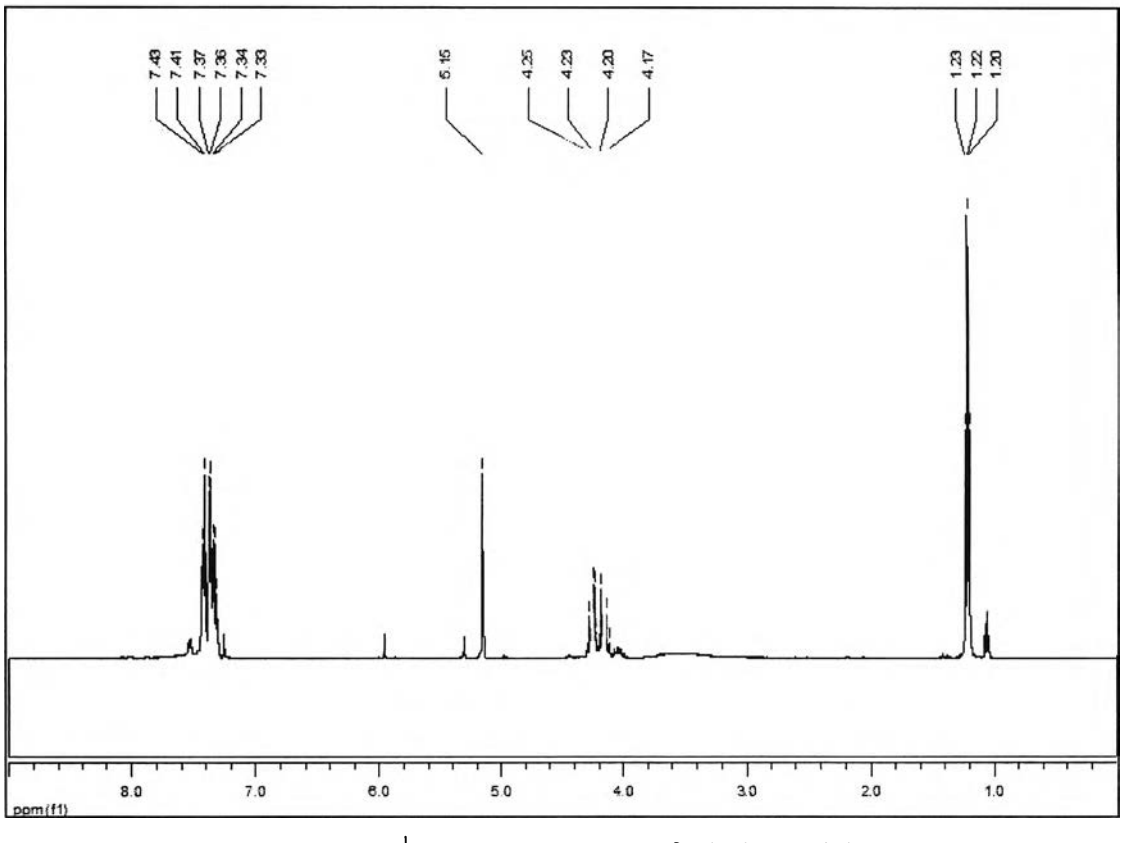


Figure 3.6 ^{1}H-NMR spectrum of ethyl mandelate

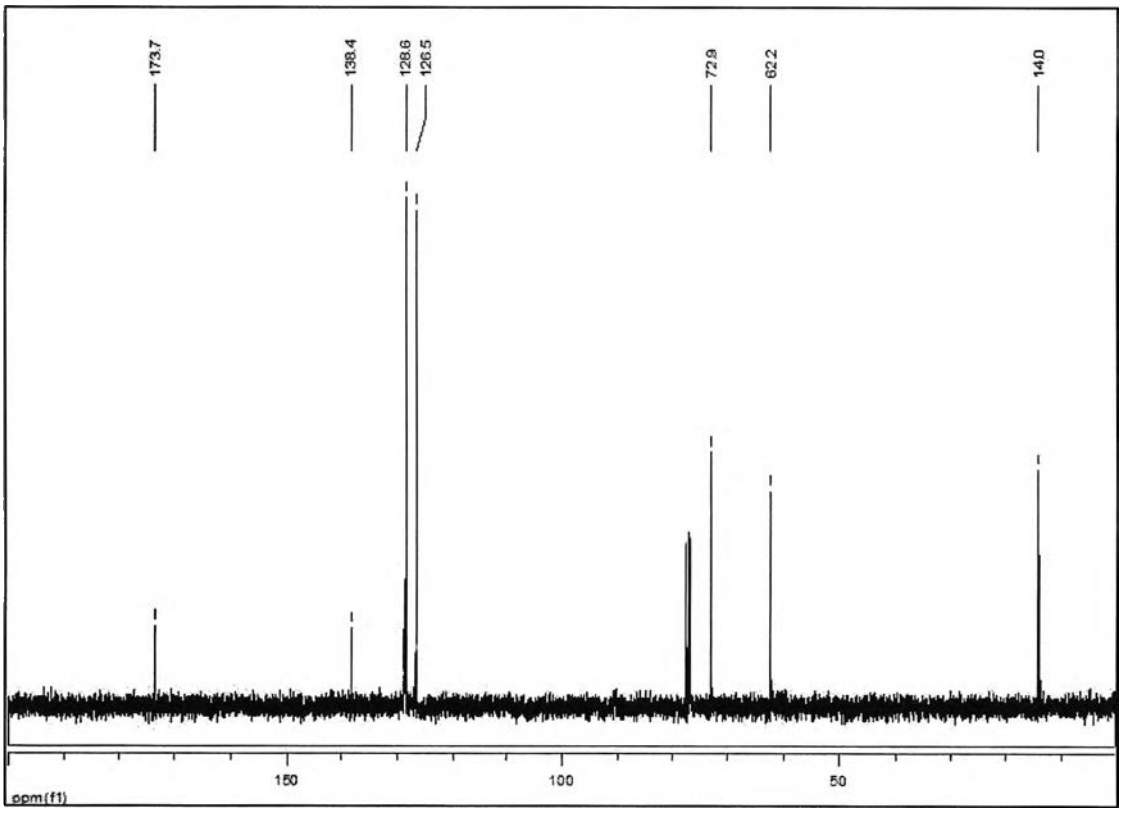


Figure 3.7 ^{13}C-NMR spectrum of ethyl mandelate

3.3 Condition Optimization for the Preparation of Halides

Many factors concerning the preparation of benzylic and allylic halides such as types of halogenating agent, the mol ratio of PPh_3 to halogenating agent, reaction time and temperature are needed to be scrutinized. This section was aimed to screen for appropriate halogenating agents and to search for the optimal conditions for the conversion of benzylic and allylic alcohols to their corresponding halides.

Part I Chlorination

Benzylic Alcohols

Optimum conditions for the preparation of benzylic chlorides from benzylic alcohols using various chlorinating agents coupled with PPh_3 were examined. Benzyl alcohol was chosen as a chemical model. Typical reaction involves the reaction of benzyl alcohol (1 eq), chlorinating agent (1.5 eq) and PPh_3 (1.5 eq) in dry CH_2Cl_2 at RT for 30 min under N_2 atmosphere. The quantification of the desired benzyl chloride

was determined by ^{1}H-NMR technique in the crude reaction mixture (Fig 3.8). To illustrate this, the ^{1}H-NMR spectrum of the crude mixture displays the methylene proton signal at δ_H 4.43. For the calculation, the peak area of the methyl protons of toluene, an internal standard was compared with that of the methylene proton signal. The percentage yield was then calculated by the relative ratio of the integration and number of proton as shown in equation 3.1.

Equation 3.1

$$\%\ \text{Yield A} = \frac{0.0944\ \text{mmol of toluene}}{1\ \text{mmol}} \times \frac{\text{Integration of toluene}}{\#\ \text{H of toluene}} \times \frac{\text{Integration of A}}{\#\ \text{H of A}} \times \frac{1\ \text{mmol}}{0.25\ \text{mmol}} \times 100$$

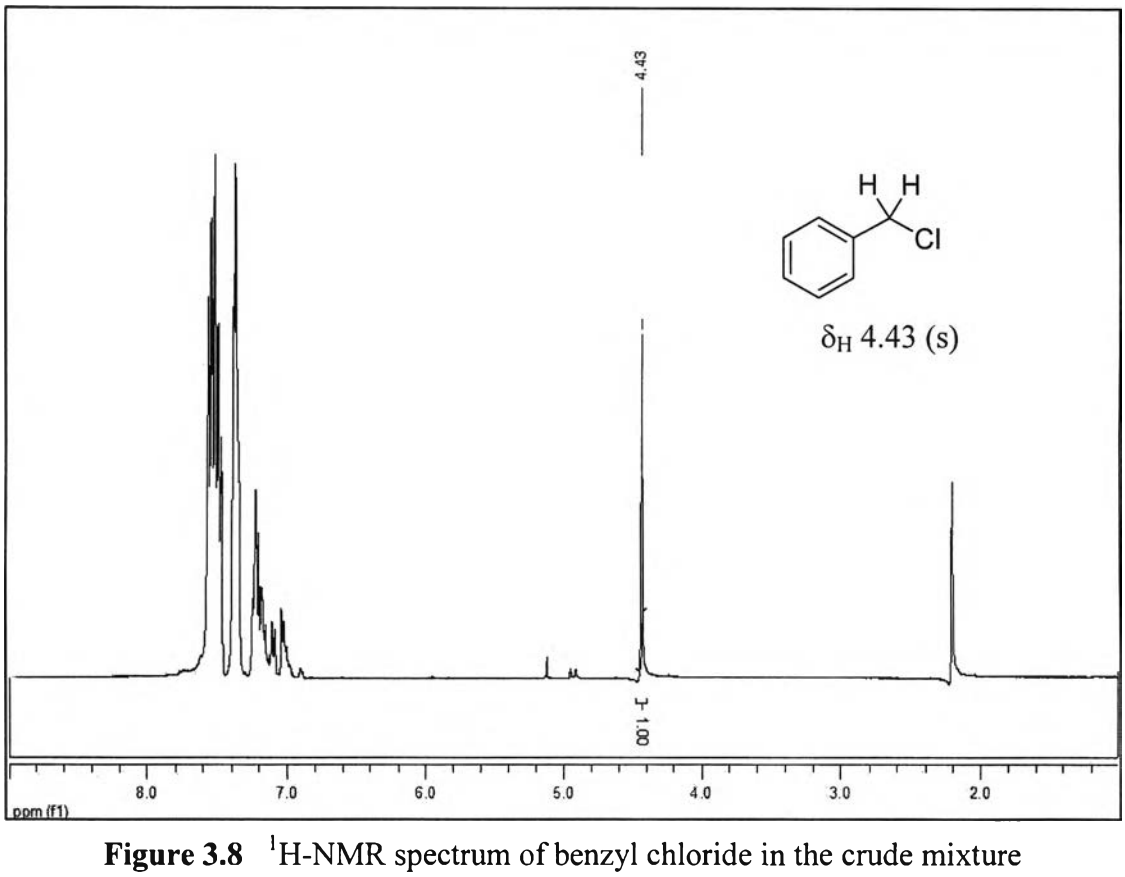


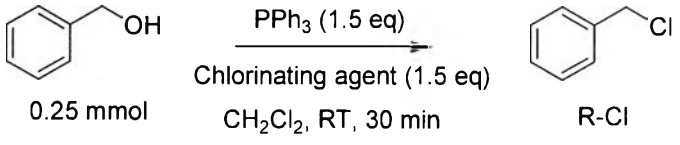
Figure 3.8 ^{1}H-NMR spectrum of benzyl chloride in the crude mixture

3.3.1 Effects of Types of Chlorinating Agents

Differences in the productivity of benzyl chloride were mainly caused from chlorinating agents. To observe this assumption, the variation of eleven chlorinating

agents containing trichloromethyl group (Cl_3C-) was explored. The results are described in Table 3.1.

Table 3.1 Effects of types of chlorinating agents



Entry	Chlorinating agent	% Yield* R-Cl	% Recovered alcohol*	MB (%)
1	none	-	90	90
2	CCl_4	trace	98	98
3	$CHCl_3$	-	92	92
4	Cl_3CCH_3	-	97	97
5	Cl_3CCH_2OH	-	91	91
6	$CH_3COOCH_2CCl_3$	-	90	90
7	Cl_3CCCl_3	quant	-	quant
8	Cl_3CCN	92	-	92
9	Cl_3CCOOH	60	30	90
10	$Cl_3CCOOEt$	92	-	92
11	Cl_3CCONH_2	80(11)[a]	9	100
12	$Cl_3CCOCCl_3$	91	-	91

* quantified by ^{1}H-NMR

a) benzyl phosphonium salt

Table 3.1 reveals that when the reaction was performed in the absence of a chlorinating agent (entry 1), none of benzyl chloride was obtained. This was clearly demonstrated that a chlorinating agent was important for this reaction. The efficiency of chlorinating agent depended on types of substituent. While the reagents in entries 7-12 containing an electron-withdrawing group bonded directly to trichloromethyl group (Cl_3C-) provided the desired products in high yield, the others (entries 2-6) gave low yield of the target molecule.

Among chlorinating agents containing an electron-withdrawing group, Cl_3CCOOH (entry 9) and Cl_3CCONH_2 (entry 11) could not completely convert benzyl alcohol into its chlorides. In the case of Cl_3CCOOH, this was probably because of its acidity that may make the reaction become acidic and thus not appropriate for further reaction to take place.

It is an interesting point to note that when the chlorination of benzyl alcohol was performed using PPh_3/Cl_3CCONH_2, besides the target benzyl chloride, benzyl phosphonium salt was detected as another product (entry 11). The occurrence of the latter product could be confirmed by the presence of the doublet signal of the benzylic protons (2H) with J = 14.0 Hz at δ_H 4.87 (Fig 3.9) [54]. This additional product was not formed in other systems using different chlorinating agents such as Cl_3CCN, $Cl_3CCOOEt$. The production of different products may be explained by reactivity of each chlorinating agent.

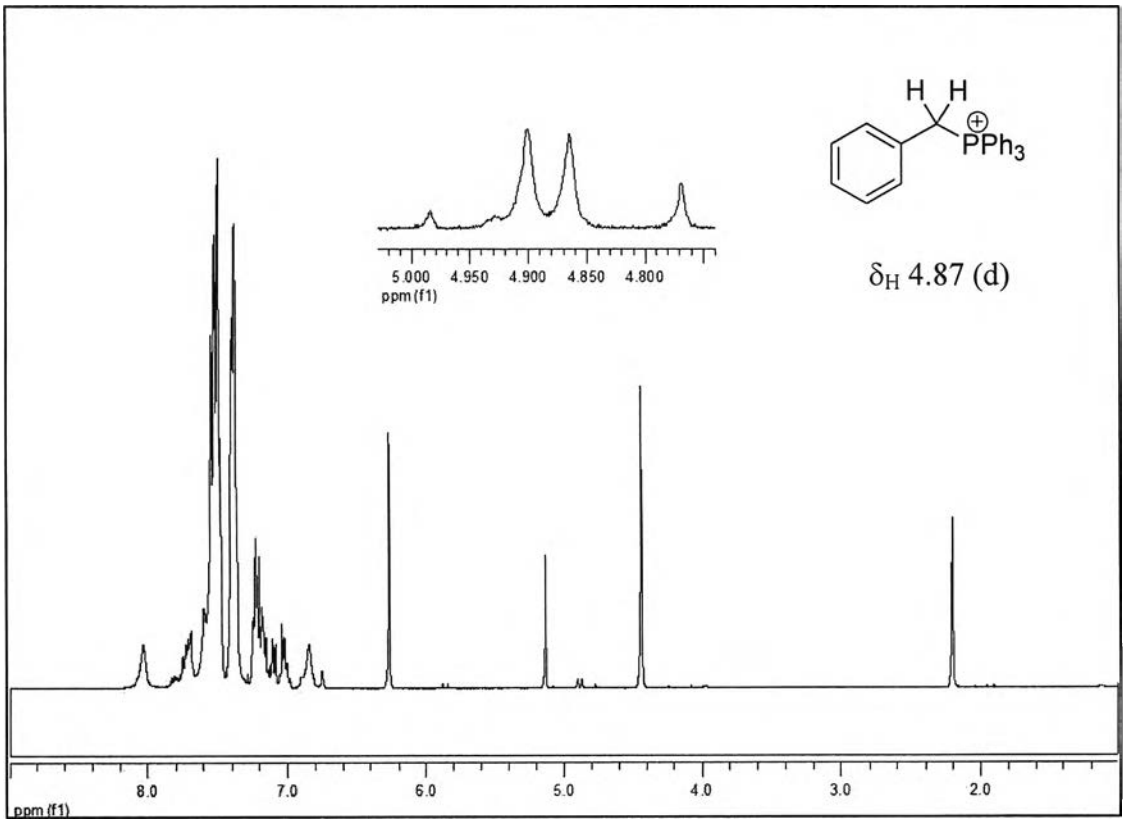
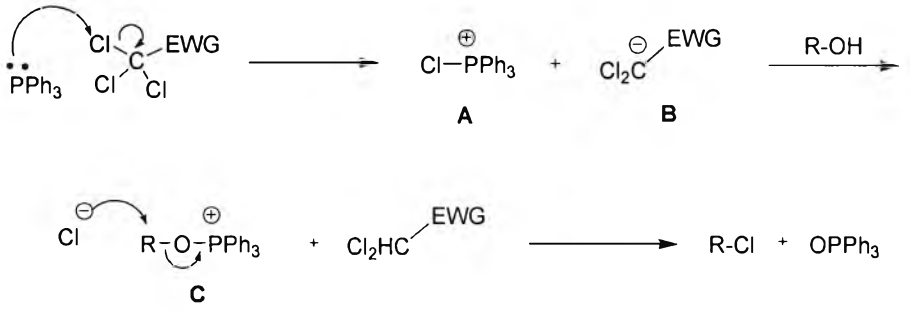


Figure 3.9 ^{1}H-NMR spectrum of phosphonium salt in the crude mixture

The proposed mechanism [23] presented below described why the reagents containing an electron-withdrawing group worked well for the preparation of chlorides and could explain why using PPh_3/Cl_3CCONH_2 the reaction also generated the phosphonium salt.

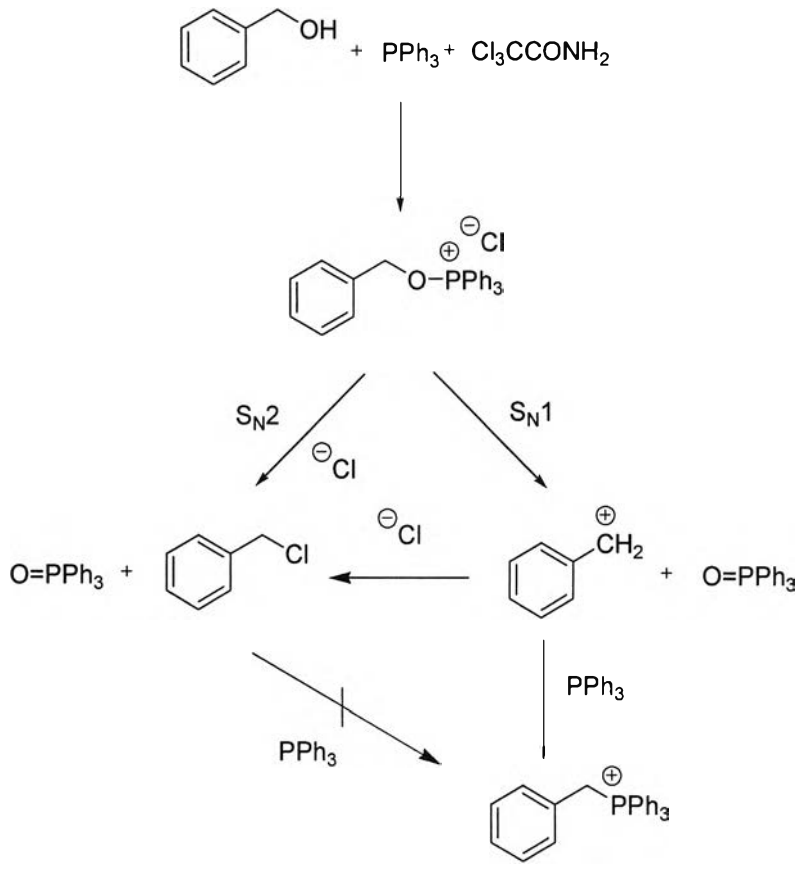


PPh_3 was believed to react with Cl_3C-EWG yielding **A** and **B** with a negative charge. In order to stabilize the negative charge, **B** should contain an electron-withdrawing group (EWG). The order of stabilization ability or reactivity of chlorinating agents depending on type of electron-withdrawing substituents as displayed below [23, 43]

$$-COCCl_3 > -CN > -CCl_3 \cong -CO_2Et > -CONH_2$$

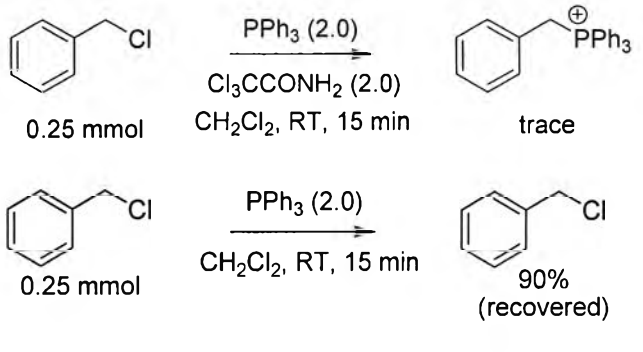
According to the reactivity of each chlorinating agent, it was believed that the system using Cl_3CCONH_2 coupled with PPh_3 generated less amount of chloride ion than those employing other chlorinating agents. Thus, the reaction between the intermediate generated and PPh_3 would be a competitive reaction with that of the intermediate and chloride ion.

The reaction mechanism for the chlorination of benzylic alcohols using PPh_3/Cl_3CCONH_2 was proposed to take place by first generating an intermediate **C** ($PhCH_2O^+PPh_3$) [42], which was then attacked by Cl^- to produce the desired product either by S_N1 *via* the formation of a stable benzyl carbocation ($PhCH_2^+$) intermediate before reacting with Cl^- or S_N2 depending upon the alcohol structure. The formation of benzyl phosphonium salt was manifestly derived from the reaction of the benzyl cation intermediate and the excess PPh_3 (Scheme 3.1).



Scheme 3.1 Proposed mechanistic pathways for chlorination of benzyl alcohol using PPh_3/Cl_3CCONH_2

Other independent experiments were conducted trying to explain the occurrence of phosphonium salt. Using benzyl chloride as a substrate in place of benzyl alcohol, benzyl phosphonium salt was detected in only trace amount with PPh_3/Cl_3CCONH_2 (recovered benzyl chloride 87%, MB = 91%). On the other hand, the product was not observed (recoverd benzyl chloride 90%, MB = 90%) when the reaction was performed in the absence of Cl_3CCONH_2. Thus, it could be concluded that the phosphonium salt was not derived from the reaction of benzyl chloride and PPh_3 under this particular condition.

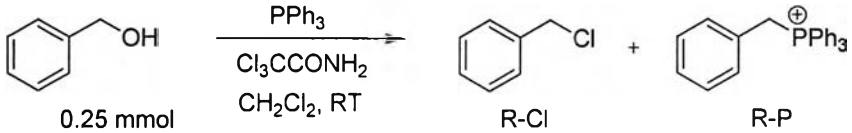


The cost of reagent is one of the important factors to be seriously considered in organic synthesis. The practical synthetic reaction must offer high yield of the desired product using non-toxic and inexpensive reagents. Although, Cl_3CCONH_2 could not completely proceed for the conversion of benzyl alcohol compared with certain chlorinating agents, it was still recognized as a new and practical chlorinating agent for chlorination of benzylic alcohol judging from cheap price of reagent, high %yield of the desired chloride achieved and the ease for the separation of product in practical sense.

3.3.2 Effects of Mol Ratio of PPh_3: Chlorinating Agent and Reaction Time

The ratio of PPh_3 and Cl_3CCONH_2 was varied to find out the most suitable ratio that produced the maximum yield of benzyl chloride. The results are shown in Table 3.2.

Table 3.2 Effects of mol ratio of PPh_3: chlorinating agent and reaction time



0.25 mmol R-Cl R-P

Entry	Reagent (eq)		Time (min)	% Yield*		%Recovered alcohol*	MB (%)
	PPh_3	Cl_3CCONH_2		R-Cl	R-P		
1	1.0	1.0	15	30	trace	59	89
2		1.5	15	38	trace	55	93
3		2.0	15	40	-	67	107
4	1.5	1.5	15	65	13	14	92
5		2.0	15	76	9	5	90
6	2.0	2.0	15	82	9	0	91
7		2.0	30	82	7	0	89
8		2.0	60	78	12	0	90
9		3.0	15	81	9	0	90
10		4.0	15	81	9	0	90
11	2.5	2.5	15	83	13	0	96

* quantified by ^{1}H-NMR

The use of PPh_3 and Cl_3CCONH_2 in ratios of using PPh_3 less than 2.0 eq (based on alcohol) furnished benzyl chloride in poor or moderate yield (entries 1-5). While the reaction using the ratio of PPh_3 at least 2.0 eq with varying the equivalent of Cl_3CCONH_2 (entries 6-11) could be completely converted into the target products. The maximum yield was gained when 2 eq of PPh_3 and Cl_3CCONH_2 were used within 15 min (entry 6). It was interesting to point out that benzyl phosphonium salt was still detected as a minor product besides the formation of a major product, benzyl chloride. Therefore, the modification of the reaction trying to reduce the formation of benzyl phosphonium salt was further explored.

The conditions were modified by changing the order of adding PPh_3 and $Cl_3CCCONH_2$. The mixture of PPh_3 and Cl_3CCONH_2 was stirred in dry CH_2Cl_2 for 7 min. Benzyl alcohol (1 eq) was then added and the reaction was further stirred for another 8 min. The reaction was finally quenched by solvent evaporation and the desired product was quantified by ^{1}H-NMR in the crude mixture after adding toluene as an internal standard. The results are revealed in Table 3.3.

Table 3.3 Modified optimum conditions for the chlorination of benzyl alcohol

Entry	Reagent (eq)		Time (min)	% Yield*		%Recovered alcohol*	MB (%)
	PPh_3	Cl_3CCONH_2		R-Cl	R-P		
1	2.0	2.0	15	95	10	5	110
2		2.5	15	92	5	5	102
3		3.0	15	91	trace	-	91
4[a]	2.0	3.0	15	68	6	20	94
5[b]	2.0	3.0	15	64	1	28	93

* determined by ^{1}H-NMR

a) Et_4AlCl (1 eq) was added as an external chloride source

b) LiCl (1 eq) was added as an external chloride source

When the reaction comprised of the equivalent of Cl_3CCONH_2 more than PPh_3 (entries 2-3), the formation of benzyl phosphonium salt decreased, especially in entry 3 with complete conversion. Thus, the suitable ratio of PPh_3:Cl_3CCONH_2 for the

preparation of benzyl chloride was 2.0:3.0. This reaction could demonstrate that the amount of Cl^- affected on the transformation of benzyl alcohol into its chloride. Moreover, by mixing PPh_3 and Cl_3CCONH_2 for 7 min before adding benzyl alcohol better yields were obtained without the formation of phosphonium salts. This was probably because PPh_3 would first react with Cl_3CCONH_2 to produce Cl^- nucleophile and would keep PPh_3 in the reaction at the minimum to prevent it from competing with Cl^-.

Surprisingly, Et_4AlCl and LiCl as external chloride sources could not assist the increment of %yield of the corresponding benzyl chloride (entries 4-5). This strongly implies that the ion pair intermediate formed is so tight that it could not react with added nucleophile [44]; thus, in this case, the external nucleophiles did not affect on the formation of benzyl chloride.

3.3.3 Chlorination of Selected Benzylic Alcohols

The optimum conditions for the preparation of benzyl chloride using PPh_3/Cl_3CCONH_2 in the ratio of 2.0:3.0 were further applied to explore the chlorination of various benzylic alcohols. The results are summarized in Table 3.4.

Table 3.4 Chlorination of selected benzylic alcohols

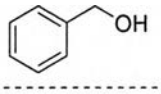
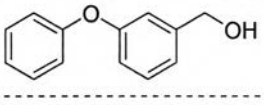
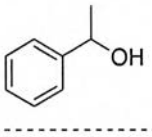
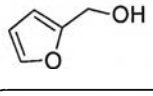
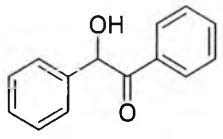
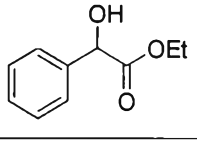
Entry	Substrate	% Yield*		MB (%)
		R-Cl	R-P	
1		91	trace	91
2		90	5	95
3		90	0	90
4		80	15	95

Table 3.4 (Continued)

Entry	Substrate	% Yield*		MB (%)
		R-Cl	R-P	
5[a]		96	0	96
6[a]		75(22)[b]	0	97

* quantified by ^{1}H-NMR

a) Use the general procedure and the ratio of PPh_3:Cl_3CCONH_2 in 2.0:2.0, 15 min
b) Ethyl mandelate recovery

Under the optimum conditions, various primary and secondary benzylic alcohols could be converted into the corresponding benzylic chlorides in high to quantitative yield with low yield of phosphonium compounds (entries 1-6). A substituent on the benzene ring or at the benzylic position of the molecule had no effect on their transformation (entries 2-4).

Figure 3.10 displays an example of the ^{1}H-NMR spectrum of furfuryl chloride and its phosphonium salt in the crude mixture. The singlet signal of the methylene protons of furfuryl chloride was detected at δ_H 4.45 [45] and a doublet signal with J = 13.6 Hz of the methylene protons of furfuryl phosphonium salt in the crude mixture was clearly observed at δ_H 5.07 [47].

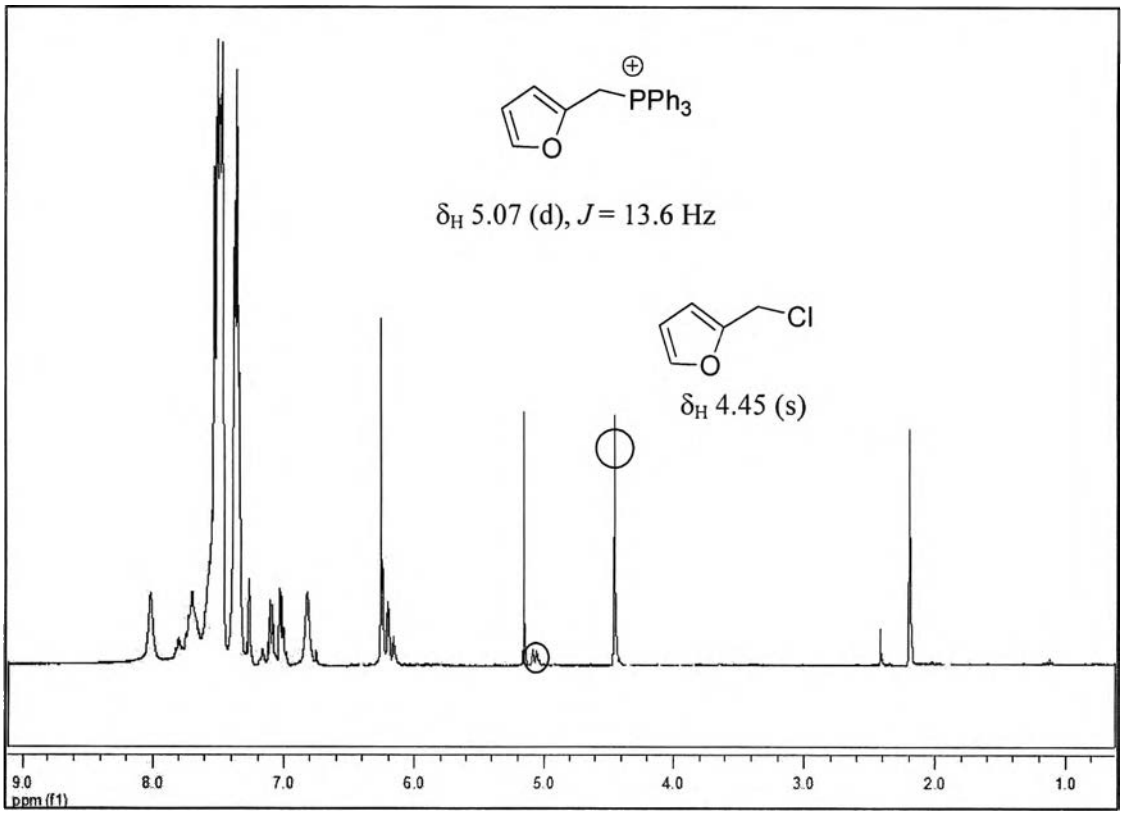


Figure 3.10 ^{1}H-NMR spectrum of furfuryl chloride and its salt in the crude mixture

In the case of secondary benzylic alcohols such as benzoin and ethyl mandelate (entries 5-6), the desired chlorides were found only in good to excellent yield. Moreover, the corresponding phosphonium salts could not be detected. This information gave clues that the benzylic carbocation of those molecules were generated with difficulty since the destabilization of benzylic carbocation by electron-withdrawing carbonyl group mainly occurred.

Allylic Alcohols

In order to reach optimum conditions for allylic chlorination, *trans*-cinnamyl alcohol was selected as a chemical model. The reaction consisted of allylic alcohol (1 eq), a chlorinating agent (1.5 eq) and PPh_3 (1.5 eq) in dry CH_2Cl_2 at RT for 30 min under N_2 atmosphere. The amount of *trans*-cinnamyl chloride was determined by ^{1}H-NMR in the crude mixture after adding toluene as an internal standard (Fig 3.11).

The ^{1}H-NMR spectrum discloses a doublet signal (2H) with J = 7.0 Hz of the methylene protons connecting with a chlorine atom at δ_H 4.08.

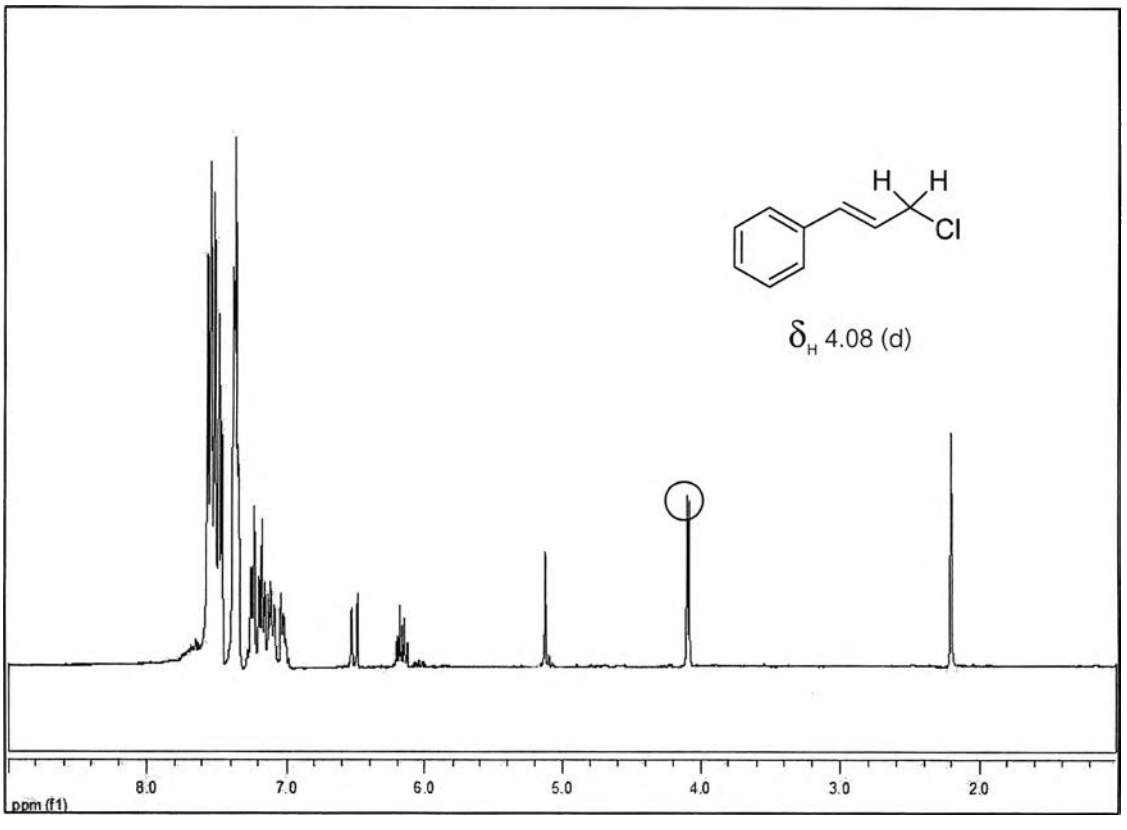
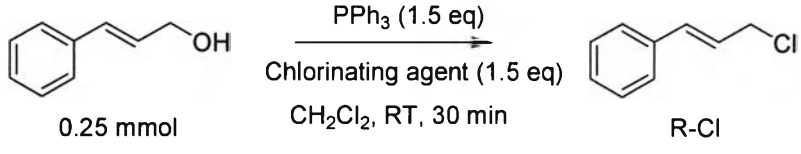


Figure 3.11 ^{1}H-NMR spectrum of *trans*-cinnamyl chloride in the crude mixture

3.3.4 Effects of Types of Chlorinating Agents

The efficiency of the production of *trans*-cinnamyl chloride was significantly differed by the influence of chlorinating agents. To investigate this, the variation of eleven chlorinating agents was explored. The results are shown in Table 3.5.

Table 3.5 Effects of types of chlorinating agents



0.25 mmol R-Cl

Entry	Chlorinating Agent	% Yield* R-Cl	%Recovered alcohol*	MB (%)
1	none	-	99	99
2	CCl_4	7	84	91
3	$CHCl_3$	-	91	91
4	Cl_3CCH_3	-	104	104
5	Cl_3CCH_2OH	-	91	91
6	$CH_3COOCH_2CCl_3$	-	96	96
7	Cl_3CCCl_3	91	-	91
8	Cl_3CCN	91	-	91
9	Cl_3CCOOH	35	56	91
10	$Cl_3CCOOEt$	75	19	94
11	Cl_3CCONH_2	69(16)[a]	10	95
12	$Cl_3CCOCCl_3$	90	-	90

* quantified by ^{1}H-NMR

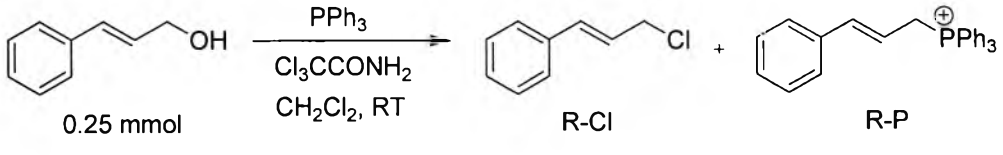
a) phosphonium salt

According to the effects of types of chlorinating agents, these reactions revealed completely the same trend as those observed for benzylic alcohols. Since there are a few reports involving the reaction of allylic alcohols with the combination of PPh_3 and a chlorinating agent. In this research, the use of PPh_3/Cl_3CCONH_2 was chosen for further investigation.

3.3.5 Effects of Mol Ratio of PPh_3: Chlorinating Agent and Reaction Time

The effects of mol ratio of PPh_3: Cl_3CCONH_2 for the preparation of *trans*-cinnamyl chloride were examined. The results are revealed in Table 3.6.

Table 3.6 Effects of mol ratio of PPh_3: chlorinating agent and reaction time



Entry	Reagent (eq)		Time (min)	% Yield*		%Recovered alcohol*	MB (%)
	PPh_3	Cl_3CCONH_2		R-Cl	R-P		
1	1.0	1.0	15	21	7	64	92
2		1.5	15	47	trace	44	91
3		2.0	15	55	trace	38	93
4	1.5	1.5	15	52	12	28	92
5		2.0	15	74	19	trace	93
6	2.0	2.0	15	68	23	-	91
7		2.0	30	75	22	-	97
8		2.0	60	73	21	-	94
9		3.0	15	70	25	-	95
10		4.0	15	72	20	-	92
11	2.5	2.5	15	71	27	-	98

* determined by ^{1}H-NMR

The above results showed the same trend in terms of the percentage yield of the chloride product as that obtained from the chlorination of benzylic alcohols. The suitable mol ratio of PPh_3: Cl_3CCONH_2 for the conversion of *trans*-cinnamyl alcohol into its chloride was 2.0:2.0 for 15 min (entry 6). Due to the structure of *trans*-cinnamyl alcohol, the corresponding phosphonium salt was produced (Fig 3.12). Thus, the reaction conditions should be modified to reduce the formation of the phosphonium salt.

The ^{1}H-NMR spectrum of *trans*-cinnamyl phosphonium salt in the crude mixture reveals a double of doublet signal with J = 15.0 Hz of the methylene protons at δ_H 4.60 [46].

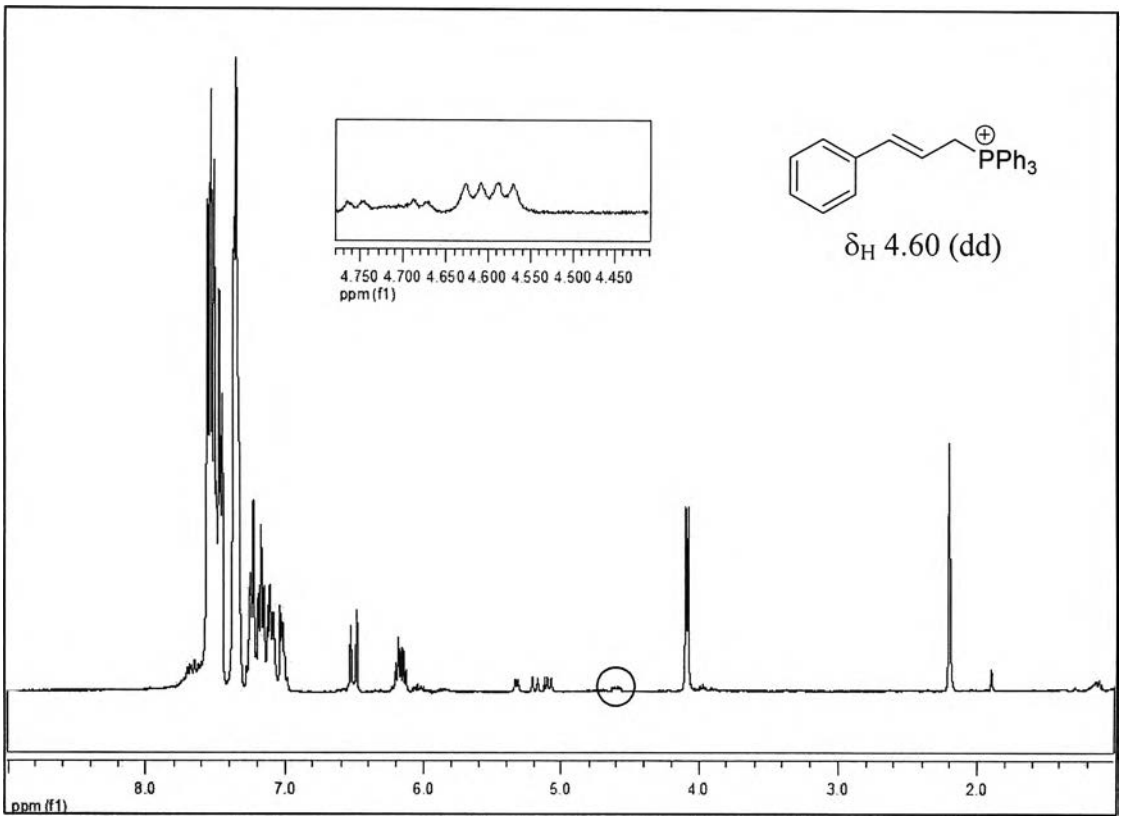


Figure 3.12 ^{1}H-NMR spectrum of *trans*-cinnamyl phosphonium salt in the crude mixture

The modified conditions involved the mixing of PPh_3 and Cl_3CCONH_2 in dry CH_2Cl_2, stirring for 7 min before adding an alcohol (1 eq) and further stirring for another 8 min. Then, the reaction was quenched by solvent evaporation, and the desired product was quantified by ^{1}H-NMR in the crude mixture after adding toluene as an internal standard. The results are revealed in Table 3.7.

Table 3.7 Modified conditions for the chlorination of *trans*-cinnamyl alcohol

Entry	Reagent (eq)		Time (min)	% Yield*		%Recovered alcohol*	MB (%)
	PPh_3	Cl_3CCONH_2		R-Cl	R-P		
1	2.0	2.0	15	81	9	-	90
2		2.5	15	90	trace	-	90
3		3.0	15	90	trace	-	90
4		4.0	15	95	trace	-	95

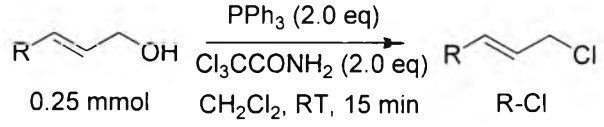
* determined by ^{1}H-NMR

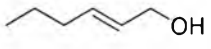
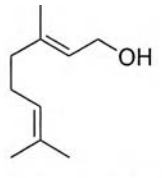
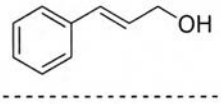
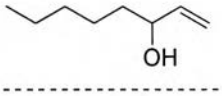
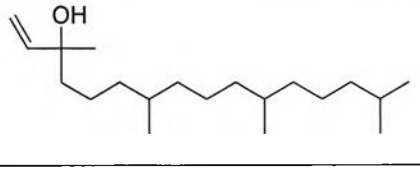
From the attained results, with the reaction comprising of Cl_3CCONH_2 more than PPh_3 (entries 2-4), the phosphonium salt was detected in trace amount. Thus, the maximum yield was gained when 2 eq of PPh_3 and 2.5 eq of Cl_3CCONH_2 were used within 15 min.

3.3.6 Chlorination of Selected Allylic Alcohols

The modified conditions aiming to reduce generated phosphonium salts was only used for the preparation of allylic alcohols having benzylic effects like *trans*-cinnamyl alcohol. For others allylic alcohols, the normal optimum condition was employed. The results are shown in Table 3.8.

Table 3.8 Chlorination of selected allylic alcohols



Entry	Substrate	% Yield* R-Cl	MB (%)
1		72	72
2		83	83
3		90(3)[a]	93[b]
4		63(29)[c]	92
5		0(34)[d](56)[e]	90

* quantified by ^{1}H-NMR

a) Phosphonium salt

b) Use the modified procedure and the ratio of PPh_3:Cl_3CCONH_2 in 2.0:2.5, 15 min

c) $CH_3(CH_2)_4CH{=}CHCH_2Cl$

d) The rearrangement product: $CH_3(CH(CH_3)(CH_2)_3)_3CH{=}CHCH_2Cl$

e) Olefin product: $CH_3(CH(CH_3)(CH_2)_3)_2CH(CH_2)_2CH{=}C(CH_3)CH{=}CH_2$

Referring to the results, treating of PPh_3/Cl_3CCONH_2 with various allylic alcohols could generate the corresponding allylic chlorides in high yields without the rearrangement of carbon skeleton in entries 1-3, especially primary allylic alcohols. This reaction could demonstrate that the reaction mechanism occurred *via* S_N2 to form more stable alkene; therefore, the competitive pathway (S_N2') to produce the rearranged product was difficult to take place. A previous report addressed that the chlorination of some allylic alcohols using $SOCl_2$ generated the rearrangement

product as a major product. This was thus an advantage of this system for the preparation of the desired chlorides without the rearranged products.

Figure 3.13 shows an example of ^{1}H-NMR of the reaction mixture of isophytol with PPh_3/Cl_3CCONH_2 (entry 5, Table 3.8).

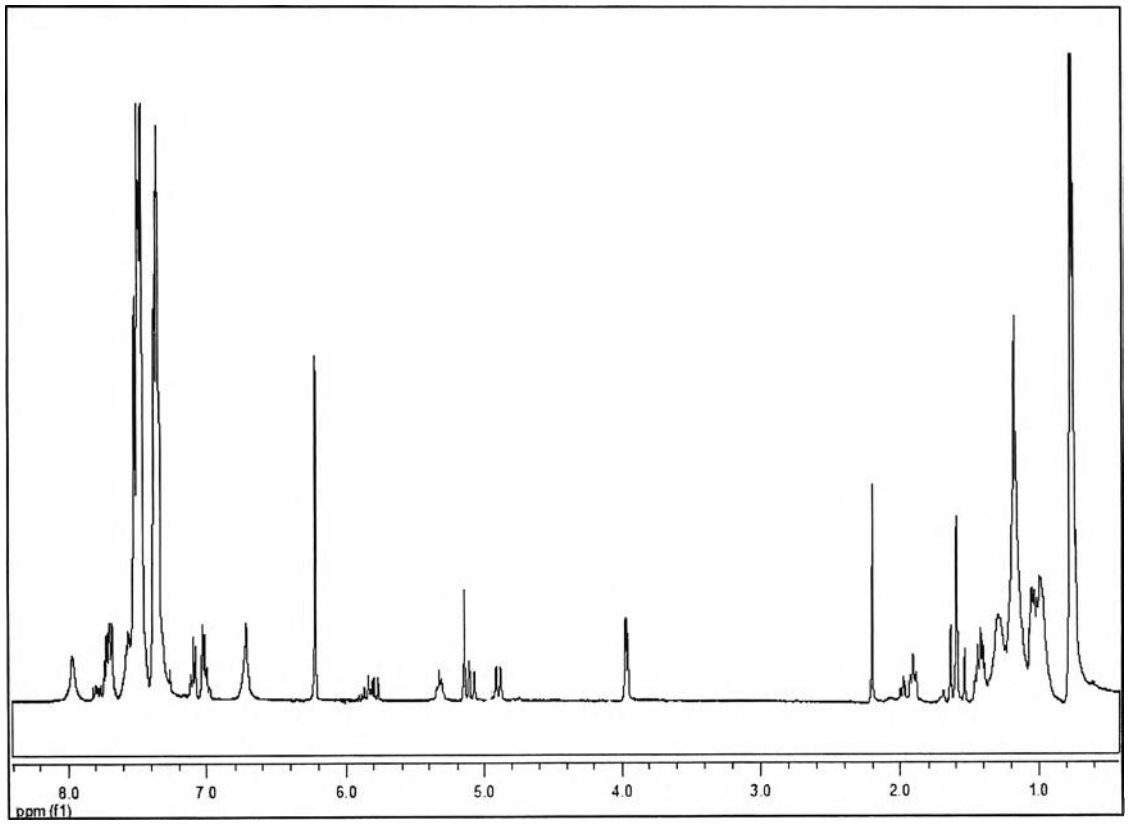
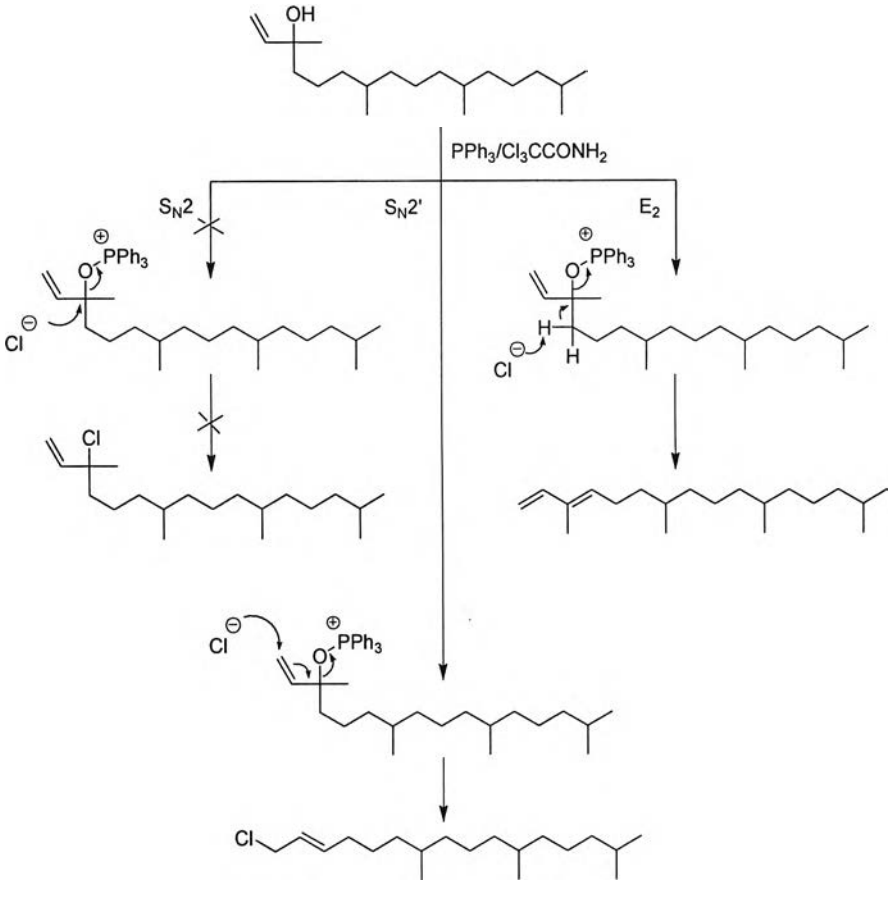


Figure 3.13 ^{1}H-NMR spectrum of the chlorination of isophytol in the crude mixture.

The above spectrum reveals a doublet signal with J = 8.0 Hz of the methylene protons connecting to chlorine atom of the rearranged product at δ_H 3.97 [47]. The other compound is an olefinic compound which shows a triplet signal with J = 7.2 Hz of the methine proton ($-CH_2-C\underline{H}=C-$) at δ_H 5.33 and a double of doublet signal with J = 17.3, 10.8 Hz of the methylene protons ($=CH-C\underline{H}_2$) resonating at δ_H 5.09 and 4.90 [48].

For secondary and tertiary allylic alcohols, 1-octen-3-ol and isophytol being commercially available were chosen for study the chlorination of secondary and tertiary allylic alcohols, respectively. From the attained results, the chlorination of 1-octen-3-ol in entry 4 produced the rearranged product; however, the corresponding chloride was a major product. Although the competitive pathway (S_N2') could occur, the desired product was still the major. This was considered that the use of PPh_3/Cl_3CCONH_2 as a developed reagent mainly proceeded *via* S_N2 not depend on the stability of alkene group in the product molecule.

In the case of isophytol as tertiary allylic alcohols, the olefinic product was a major product while a rearranged product being a minor one. This implied that the steric hindrance of substituent had a profound effect on the formation of the product. This could therefore be explained that the competition between chlorination (S_N2) and elimination (E_2) of the tertiary allylic alcohol under this condition was predominantly competed, whereas the other competitive pathway (S_N2') was less affected. This chlorination was considered to proceed through three competition pathways among S_N2, E_2 and S_N2' as shown below.



Part II Bromination

Benzylic Alcohols

Suitable conditions for the preparation of benzylic bromides treating with several brominating agents and PPh_3 were explored. To investigate on bromination of benzylic alcohols, benzyl alcohol was chosen as a chemical model. The reaction procedure was first adding PPh_3 (1.5 eq) in a mixture of alcohol (1 eq) and a brominating agent (1.5 eq) in dry CH_2Cl_2 at RT for 30 min under N_2 atmosphere. The produced benzyl bromide was determined by ^{1}H-NMR in the crude mixture after adding toluene as an internal standard.

Benzyl bromide in the crude mixture was identified by ^{1}H-NMR spectroscopic technique. The spectrum discloses a singlet signal of methylene protons at δ_H 4.35. The ^{1}H-NMR spectrum of benzyl bromide in the crude mixture is displayed in Figure 3.14.

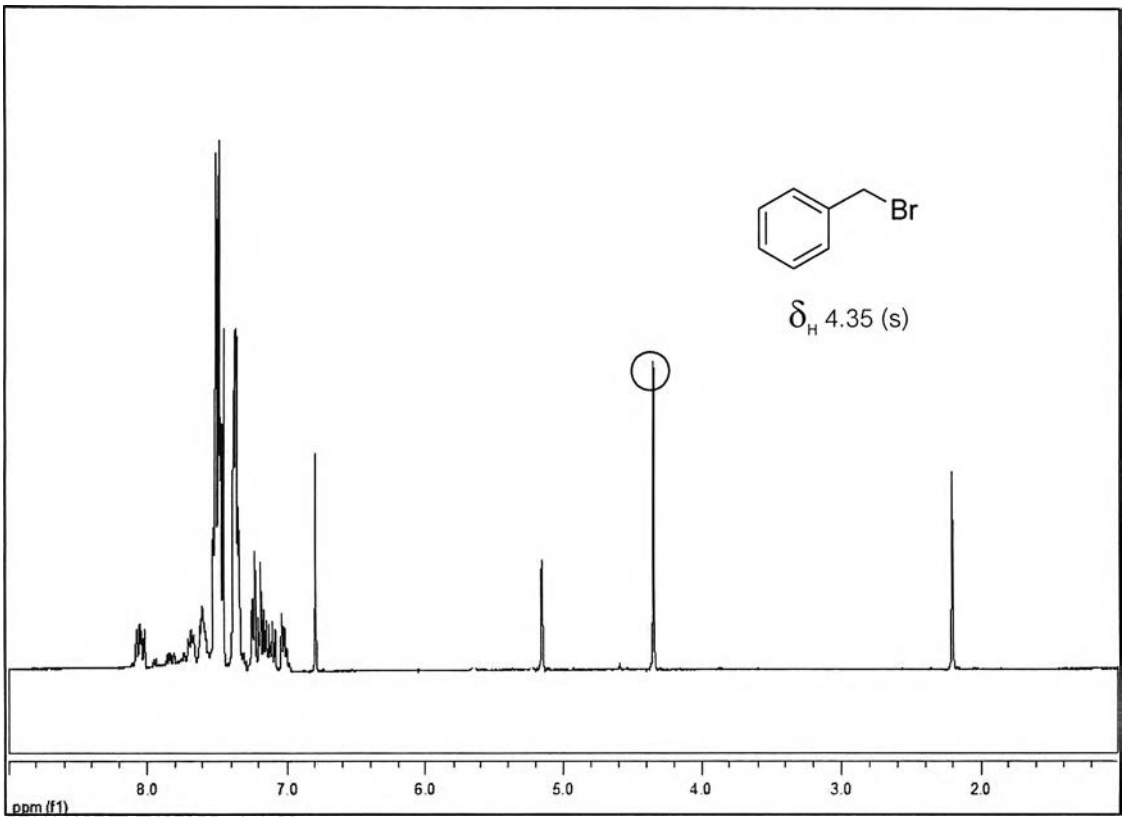
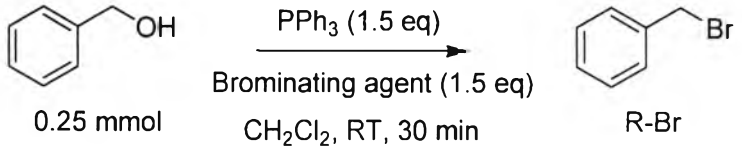


Figure 3.14 ^{1}H-NMR spectrum of benzyl bromide in the crude mixture

3.3.7 Effects of Types of Brominating Agents

Various brominating agents used in this research are commercially available, such as CBr_4, Br_3CCO_2H, $BrCCl_3$ and $BrCH_2CH_3$, while Br_3CCO_2Et and $Br_3CCOCBr_3$ were obtained from the synthesis as described in Chapter II. The effects of types of brominating agents on the bromination of benzylic alcohols were examined and the results are presented in Table 3.9.

Table 3.9 Effects of types of brominating agents



Entry	Brominating agent	% Yield* R-Br	%Recovered alcohol*	MB (%)
1	none	-	90	90
2	CBr_4	quant	-	quant
3	$Br_3CCOOEt$	quant	-	quant
4	$Br_3CCOCBr_3$	89	11	100
5	Br_3CCOOH	87(10)[a]	-	97
6	$Br_2HCCOOH$	64(14)[b]	18	96
7	$BrCCl_3$	9(37)[c]	54	100
8	$BrCH_2CH_3$	-	98	98
9	$CHBr_3$	-	98	98

* determined by ^{1}H-NMR

a) $PhCH_2OOCCBr_3$

b) $PhCH_2OOCCHBr_2$

c) $PhCH_2Cl$

According to the effects of types of brominating agents on the formation of benzyl bromide, the reaction could not generate benzyl bromide when the reaction contained no brominating agent (entry 1). Brominating agents containing electron-withdrawing groups directly bonded to di- or tri-bromomethyl group (Br_2HC- or

Br_3C-) produced the desired products in high yield (entries 2-6), whereas the others gave low yield of the desired products (entries 7-9).

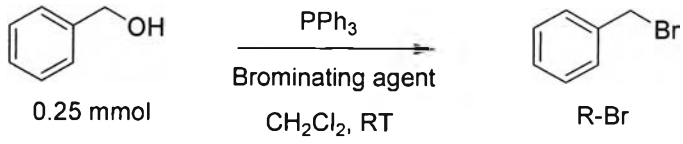
Although, the use of Br_3CCO_2H and Br_2HCCO_2H in entries 5-6 gave good yield of benzyl bromide, the undesired ester product was also detected. The occurrence of the latter was confirmed by comparing with authentic specimen obtained from the synthesis [33-34]. In the case of $BrCCl_3$, the corresponding bromide and chloride were found. It was considered that this reaction took place *via* competitive substitution between chloride and bromide ions being generated. Because of the amount of chlorine atoms being more than bromine atoms in this reagent, the possibility of PPh_3 to react with chlorine atoms was thus more than bromine atoms.

Based upon the results, CBr_4, Br_3CCO_2Et and Br_3CCOBr_3 are efficient brominating agents. CBr_4 is known as a brominating agent for the preparation of alkyl bromides in for decades, whereas there is only a report involving Br_3CCO_2Et and $Br_3CCOCBr_3$ used as brominating agent for the conversion of alkyl alcohols to alkyl bromides [24]. Nonetheless, these reagents have not been reported as brominating agent for benzylic alcohols before. Thus, Br_3CCO_2Et and $Br_3CCOCBr_3$ were chosen as brominating agents for further investigation.

3.3.8 Effects of Mol Ratio of PPh_3: Brominating Agent and Reaction Time

The ratios of PPh_3 and selected brominating agents (Br_3CCO_2Et or $Br_3CCOCBr_3$) were varied with the aim to obtain the most suitable condition for the preparation of benzylic bromides. The results are demonstrated in Table 3.10.

Table 3.10 Effects of mol ratio of PPh_3: brominating agent and reaction time



0.25 mmol R-Br

Entry	Brominating agent	Mol Ratio of PPh_3:Brominating agent	Time (min)	% Yield* R-Br	%Recovered alcohol*	MB (%)
1	Br_3CCO_2Et	1.0:1.0	30	88	13	101
2		1.5:1.5	30	quant	-	quant
3		1.5:1.5	15	quant	-	quant
4		1.5:1.5	5	quant	-	quant
5		1.5:1.0	30	97	-	97
6		1.5:1.0	15	97	-	97
7		1.5:1.0	5	98	-	98
8		1.5:0.5	30	69	29	98
9	$Br_3CCOCBr_3$	1.0:1.0	30	45	55	100
10		1.5:1.5	30	91	9	100
11		1.5:1.0	30	97	-	97
12		1.5:0.5	30	98	-	98
13		1.5:0.3	30	96	-	96
14		1.5:0.3	15	95	-	95
15		1.5:0.3	5	98	-	98

* quantified by ^{1}H-NMR

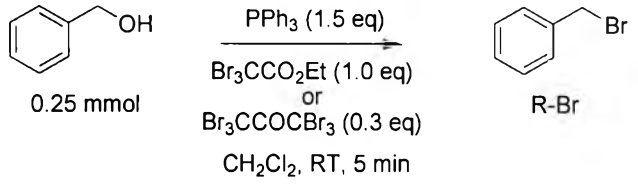
From the above results, it was found that the suitable ratio of PPh_3: brominating agent for the preparation of benzyl bromide was PPh_3: Br_3CCO_2Et in 1.5:1.0 (entry 7), whereas that for PPh_3: $Br_3CCOCBr_3$ was 1.5:0.3 (entry 15). This result could demonstrate that the type of brominating agents had an effect on the required amount of the brominating agents. The reaction of benzyl alcohol with the combination of PPh_3 and a selected brominating agent could successfully occur within 5 min to convert benzyl alcohol into benzyl bromide in excellent yield. Thus, the

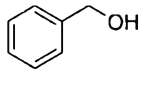
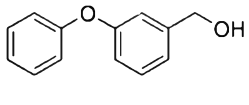
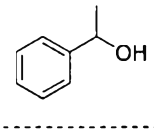
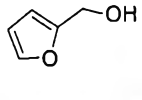
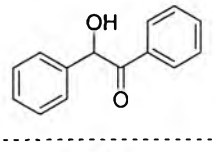
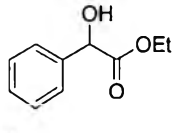
reaction time for the formation of benzyl bromide using two selected brominating agents was only 5 min.

3.3.9 Bromination of Selected Benzylic Alcohols

The optimum conditions for the formation of benzyl bromide using the combination of PPh_3: brominating agent could be applied to study on the bromination of various benzylic alcohols. The results are disclosed in Table 3.11.

Table 3.11 The bromination of selected benzylic alcohols



Entry	Substrate	Brominating agent	% Yield* R-Br	MB (%)
1		Br_3CCO_2Et	98	98
		$Br_3CCOCBr_3$	98	98
2		Br_3CCO_2Et	101	101
		$Br_3CCOCBr_3$	97	97
3		Br_3CCO_2Et	100	100
		$Br_3CCOCBr_3$	92	92
4		Br_3CCO_2Et	99	99
		$Br_3CCOCBr_3$	94	94
5		Br_3CCO_2Et	89(8)[a]	97
6		Br_3CCO_2Et	59(38)[b]	97

* determined by ^{1}H-NMR
a) % Benzoin recovery
b) % Ethyl mandelate recovery

From the aforementioned results, both selected brominating agents provided the corresponding primary and secondary benzylic bromides in high to quantitative yield without the side products (entries 1-4). A substituent on the benzene ring or at the benzylic position of the molecule had no effect on the bromination of benzylic alcohols (entries 2-4).

For benzoin and ethyl mandelate (entries 5-6), secondary alcohols directly beared with an electron-withdrawing group, the desired bromides were detected in lower yield than other benzylic alcohols. These reactions were the same trend as the chlorination.

Allylic Alcohols

To investigate suitable conditions for the conversion of allylic alcohols into the corresponding allylic bromides with PPh_3 and brominating agents, *trans*-cinnamyl alcohol was chosen as a chemical model. This reaction consisted of alcohol (1 eq), a brominating agent (1.5 eq) and PPh_3 (1.5 eq) in dried CH_2Cl_2 at RT for 30 min under N_2 atmosphere. The desired *trans*-cinnamyl bromide was qualified by ^{1}H-NMR in the crude mixture after adding toluene as an internal standard.

The spectrum of *trans*-cinnamyl bromide discloses a doublet signal of methylene protons with J = 7.0 Hz at δ_H 4.02. The ^{1}H-NMR spectrum of *trans*-cinnamyl bromide in the crude mixture is shown in Figure 3.15.

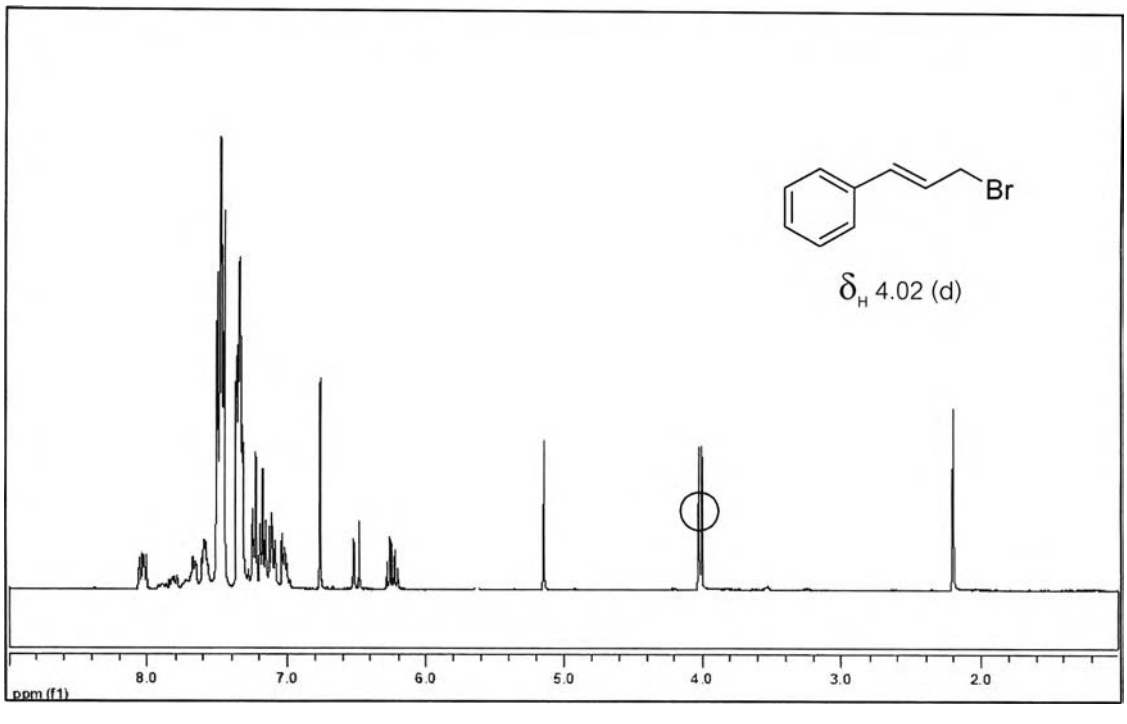
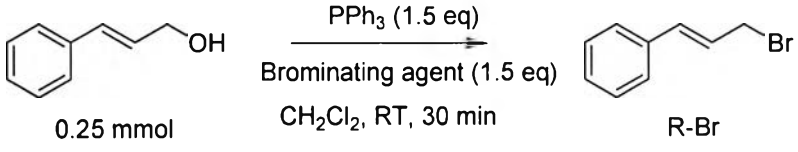


Figure 3.15 ^{1}H-NMR spectrum of *trans*-cinnamyl bromide in the crude mixture

3.3.10 Effects of Types of Brominating Agents

Differences of the structures of brominating agents had a marked effect on the formation of *trans*-cinnamyl bromide. To explore this assumption, eight diverse brominating agents were selected and the results are presented in Table 3.12.

Table 3.12 Effects of types of brominating agents



Entry	Brominating Agent	% Yield* R-Br	%Recovered alcohol*	MB (%)
1	none	-	99	99
2	CBr_4	quant	-	quant
3	$Br_3CCOOEt$	90	-	90
4	$Br_3CCOCBr_3$	40(58)[a]	-	98
5	Br_3CCOOH	70(20)[b]	-	90

Table 3.12 (Continued)

Entry	Brominating Agent	% Yield* R-Br	%Recovered alcohol*	MB (%)
6	$Br_2HCCOOH$	83(5)[c]	2	90
7	$BrCCl_3$	6(48)[d]	41	95
8	$BrCH_2CH_3$	-	98	98
9	$CHBr_3$	-	99	99

* quantified by ^{1}H-NMR

a) $PhCHBrCHBrCH_2Br$

b) $PhCH{=}CHCH_2OOCCBr_3$

c) $PhCH{=}CHCH_2OOCCHBr_2$

d) $PhCH{=}CHCH_2Cl$

From the above results, it was clearly concluded that brominating agents affected the preparation of *trans*-cinnamyl bromide since the desired bromide was not detected when the reaction was treated without brominating agent in entry 1. The reaction treated with brominating agents containing bromine atom directly bonded to electron-withdrawing group could generate the desired bromide in high yield (entries 2-6), whereas the others could not produce the corresponding bromide or generate in very poor yield (entries 7-9). CBr_4 and Br_3CCO_2Et were two promising candidates for the preparation of *trans*-cinnamyl bromide in high to excellent yield. $Br_3CCOCBr_3$ as another potential brominating agent for the preparation of benzylic bromides; however, the reaction of *trans*-cinnamyl alcohol with $Br_3CCOCBr_3$ under this particular conditions furnished the formation of 1,2,3-tribromo-3-phenylpropane 58% (Fig 3.16). Thus, it was interesting for further investigation to explore the developed conditions for the preparation of *trans*-cinnamyl bromide in high yield without other undesired compounds. The reactions using Br_3CCO_2H, Br_2HCCO_2H and $BrCCl_3$ provided tribromoester, dibromoester and *trans*-cinnamyl chloride as other products, respectively. From the above reasons, Br_3CCO_2Et and $Br_3CCOCBr_3$ were chosen for further investigation on the bromination of allylic alcohols.

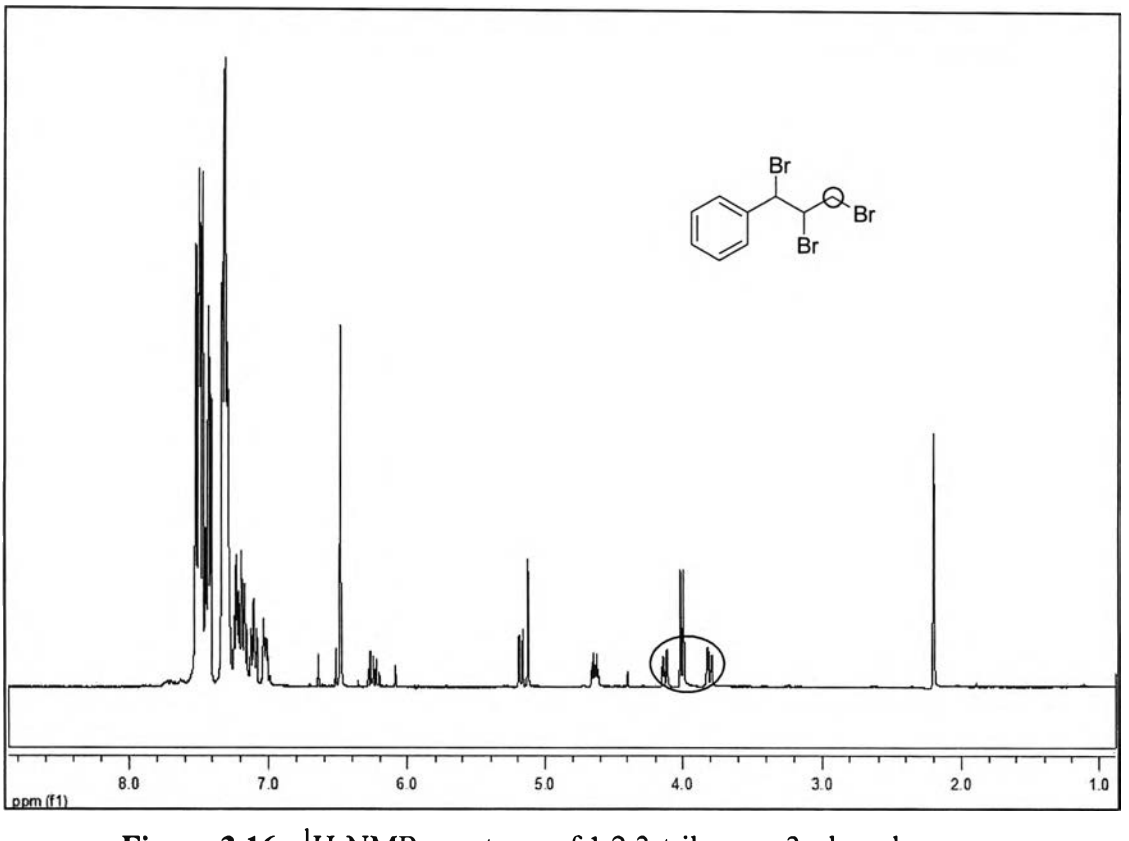


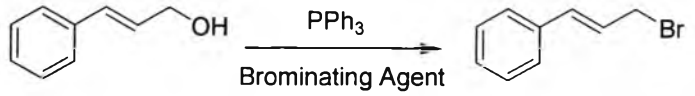
Figure 3.16 ^{1}H-NMR spectrum of 1,2,3-tribromo-3-phenylpropane in the crude mixture.

Figure 3.16 reveals a doublet of doublet signal with J = 11.6, 4.0 Hz of the methylene protons at δ_H 4.13, 3.81. A multiplet signal of the methine proton displays at δ_H 4.64 and a doublet signal with J = 9.6 Hz of the benzylic proton resonating at δ_H 5.18 [49].

3.3.11 Effects of Mol Ratio of PPh_3: Brominating Agent and Reaction Time

The appropiate ratio of PPh_3:Br_3CCO_2Et, PPh_3:$Br_3CCOCBr_3$ and PPh_3:CBr_4 treating with *trans*-cinnamyl alcohol for the preparation of *trans*-cinnamyl bromide was examined. The results are revealed in Table 3.13.

Table 3.13 Effects of mol ratio of PPh_3: brominating agent and reaction time



Entry	Brominating agent	Mol Ratio of PPh_3:Brominating agent	Time (min)	% Yield* R-Br	%Recovered alcohol*	MB (%)
1	Br_3CCO_2Et	1.5:1.5	30	90	-	90
2		1.5:1.5	15	90	-	90
3		1.5:1.5	5	90	-	90
4		1.5:1.0	30	90	-	97
5		1.5:1.0	15	91	-	91
6		1.5:1.0	5	97	-	97
7		1.5:0.5	30	55	35	90
8	$Br_3CCOCBr_3$	1.5:1.5	30	40(58)[a]	-	98
9		1.5:1.0	30	51(54)[a]	-	105
10		1.5:1.0	15	63(35)[a]	-	98
11		1.5:0.5	30	77	20	97
12		1.5:0.5	15	90	-	90
13		1.5:0.3	30	73	23	96
14		1.5:0.3	15	91	-	91
15		1.5:0.3	5	90	-	90
16	CBr_4	1.5:1.5	30	quant	-	quant
17		1.5:1.5	15	quant	-	quant
18		1.5:1.0	30	67	34	101
19		1.5:1.0	15	66	35	101
20		1.5:0.5	30	52	52	104
21		1.5:0.5	15	47	55	102

* determined by ^{1}H-NMR

a) $PhCHBrCHBrCH_2Br$

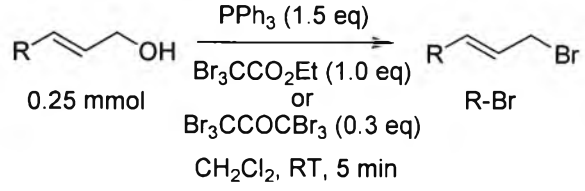
From the results presented in Table 3.12, the suitable ratio of PPh_3: brominating agent for the preparation of *trans*-cinnamyl bromide was 1.5:1 (entry 6), and 1.5:0.3 (entry 15) using Br_3CCO_2Et and $Br_3CCOCBr_3$, respectively. More intriguing, those reactions could completely occur within short reaction time (5 min) (entries 6, 15). It should be noted at this point that employing $Br_3CCOCBr_3$, only 0.3 equivalent was required (entry 15).

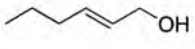
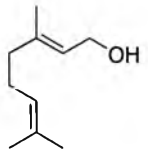
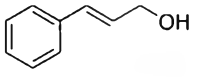
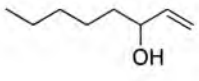
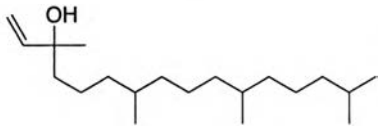
When the amount of brominating agents (Br_3CCO_2Et and $Br_3CCOCBr_3$) was reduced, the substrate could still be completely converted (entries 4-6, 9, 12, 14). On the other hand, when the reaction was performed using less amount of CBr_4 such as 1.0 eq and 0.5 eq, the complete conversion could not be achieved (entries 18-21). This clearly reveals the advantages of the two developed brominating agent for the transformation of allylic alcohols into their bromides.

3.3.12 Bromination of Selected Allylic Alcohols

Trans-cinnamyl alcohol could be accomplishedly converted into *trans*-cinnamyl bromide using the combination of PPh_3 and two selected brominating agents under the optimum conditions. To observe the scope of this developed bromination, the system was applied to various allylic alcohols. The results are displayed in Table 3.14.

Table 3.14 Bromination of selected allylic alcohols



Entry	Substrate	Brominating agent	% Yield* R-Br	MB (%)
1		Br_3CCO_2Et	80	80
		$Br_3CCOCBr_3$	80	80
2		Br_3CCO_2Et	83	83
		$Br_3CCOCBr_3$	82	82
3		Br_3CCO_2Et	97	97
		$Br_3CCOCBr_3$	90	90
4		Br_3CCO_2Et	67(32)[a]	99
		$Br_3CCOCBr_3$	0(29)[a](61)[b]	90
5		Br_3CCO_2Et	0(78)[c](14)[d]	92
		$Br_3CCOCBr_3$	0(71)[c](19)[e]	90

* quantified by ^{1}H-NMR

a) $CH_3(CH_2)_4CH{=}CHCH_2Br$

b) % Recovered 1-octen-3-ol

c) The rearranged product: $CH_3(CH(CH_3)(CH_2)_3)_3CH{=}CHCH_2Br$

d) Olefin product: $CH_3(CH(CH_3)(CH_2)_3)_2CH(CH_2)_2CH{=}C(CH_3)CH{=}CH_2$

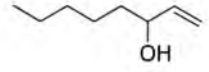
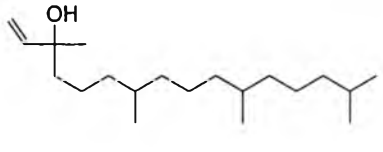
e) % Recovered isophytol

Referring to the results, PPh_3/selected brominating agent carried out with various allylic alcohols could generate the corresponding allylic bromides in high yields without the rearranged product (entries 1-3), especially primary allylic alcohols. This reaction showed that the reaction mechanism occurred *via* S_N2 to

produce more stable alkene. The competitive product from S_N2' was not generated within short reaction time.

For secondary and tertiary allylic alcohols: 1-octen-3-ol and isophytol were chosen. From the attained results, using both selected brominating agents for the bromination of 1-octen-3-ol (entry 4), the rearranged product was detected. In the case of using Br_3CCO_2Et, the desired bromide was observed as a major product, whereas using $Br_3CCOCBr_3$ only the rearranged product was detected. This was interesting to emphasize that types of brominating agents affected on the formation of the target allylic bromides. While the reaction of tertiary allylic alcohols with the combinative reagents produced the rearranged product in high yield, the olefinic product and the recovered alcohol were observed using Br_3CCO_2Et and $Br_3CCOCBr_3$, respectively. This outcome clearly demonstrated that the structure of substrate had a profound effect on the bromination. To clarify the above observation, the bromination of secondary and tertiary allylic alcohols was further investigated, and the results are presented in Table 3.15.

Table 3.15 Bromination of the secondary and tertiary allylic alcohols

Entry	Substrate	Brominating agent	Equivalent	% Yield*		
				S_N2	S_N2'	Other
1		none[a]	-	-	-	91[b]
2		Br_3CCO_2Et	0.5	78	8	trace[b]
3			1.0	50	40	-
4			1.5	27	63	-
5			3.0[c]	-	80	-
6		$Br_3CCOCBr_3$	0.3	-	29	61[b]
7			0.5	9	81	-
8		Br_3CCO_2Et	1.0	0	78	14[d]
9			1.0[e]	0	57	39[d]
10			1.0[f]	0	94	-
11			1.5	0	91	-
12		$Br_3CCOCBr_3$	0.3	0	71	19[g]
13			0.5	0	96	-

* determined by ^{1}H-NMR

a) Reflux (40°C), 1 h

b) % Recovered 1-oceten-3-ol

c) 15 min, RT

d) % Olefin product

e) Reflux (40°C), 5 min

f) at 10°C, 5 min

g) % Recovered isophytol

From the results presented in Table 3.15, in the case of secondary allylic alcohol: 1-octen-3-ol, the reaction in entry 1 showed that the bromination of secondary allylic alcohol did not generate S_N2' product at high temperature. This reaction should occur *via* the competition between S_N2 and S_N2' pathways. Normally, S_N2' reaction does not compete with S_N2 displacement [55]; however, the S_N2'

reaction may be predominant when the substrates are either sterically or electrically, or both [56]. For 1-octen-3-ol, a secondary alcohol containing unsteric terminal double-bond, the reaction could thus generate S_N2' product easier than other allylic alcohols.

From the reaction in entries 2-7, when the amount of brominating agents increased, the S_N2' products were increased. This was demonstrated that the concentration of bromide ion nucleophiles affected on the formation of the S_N2' product [57]. According to a previous report addressing the preparation of allylic bromides from allylic alcohols [31], the amount of rearranged products (S_N2' product) was time-dependent and mostly occurred after formation of the halides. When the reaction was performed using more equivalent of brominating agent and longer reaction time, the S_N2' product was completely proceeded without the S_N2 product (entry 5).

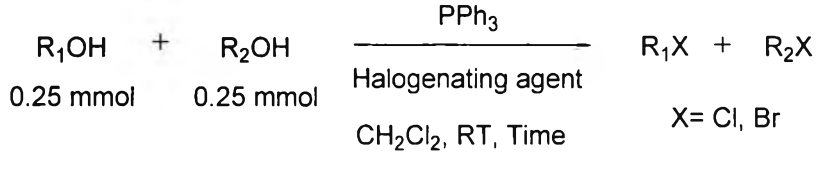
For isophytol, the rearranged product was a major composition and an olefinic product being a minor. This implied that the steric hindrance greatly affected on the formation of the corresponding product. According to the previous results of the chlorination of alcohols, the S_N2 mechanism should occur in non-polar solvent. Thus, the competition between bromination (S_N2) and elimination (E_2) of tertiary allylic alcohol could take place similar to that for chlorination. Owing to the structure of substrate and ability of bromide ion being a better nucleophile than chloride ion, the other competitive pathway (S_N2') was more effective. Therefore, the rearranged product was formed more than an olefinic product since S_N2 displacement generally did not occur with tertiary alcohols. The reactions in entries 9-10 could endorse the explaination of the mechanism. The elimination (E_2) could increasingly compete with S_N2 or S_N2' when the temperature of the reaction increased (entry 9), on the other hand, when the temperature was reduced, the elimination (E_2) product was decreased or the S_N2' product was increased.

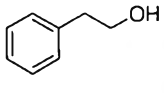
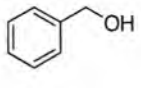
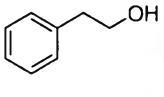
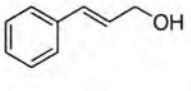
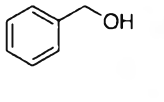
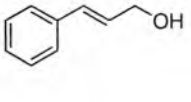
3.4 Comparative Reactivity Study on Halogenation between Benzylic and Allylic Alcohols

The relative reactivity of PPh_3/halogenating agent with two kinds of alcohols was further studied to observe the effect of the structure of alcohols on the formation of the corresponding halides. The comparative reactivity study of the combinative reagents with benzylic and allylic alcohols was carried out by competing two selected alcohols in the same vessel.

For the chlorination, a stirred solution of two selected alcohols (1 eq each) in dry CH_2Cl_2 (0.5 mL) was successively added Cl_3CCONH_2 (2 eq) and PPh_3 (2 eq) under standard conditions whereas the reaction for the bromination was added Br_3CCO_2Et (1 eq) or $Br_3CCOCBr_3$ (0.3 eq) and PPh_3 (1.5 eq) in place of Cl_3CCONH_2. The results are displayed in Table 3.16.

Table 3.16 Comparative reactivity study of benzylic and allylic alcohols



Entry	R_1OH	R_2OH	Halogenating agent	% Yield* R_1X/R_2X	% Recovered alcohol* R_1OH/R_2OH	MB (%)
1			Cl_3CCONH_2	57/25	36/70	93/95
			Br_3CCO_2Et	75/36	21/52	96/90
			$Br_3CCOCBr_3$	64/33	34/65	98/98
2			Cl_3CCONH_2	65/49	30/41	95/90
			Br_3CCO_2Et	54/45	45/50	95/95
			$Br_3CCOCBr_3$	51/58	45/32	96/90
3			Cl_3CCONH_2	46/65	49/30	95/95
			Br_3CCO_2Et	35/64	59/29	94/93
			$Br_3CCOCBr_3$	38/69	58/24	96/93

* quantified by ^{1}H-NMR

The comparative reactivity study of benzylic and allylic alcohols containing benzylic moiety and C=C, respectively was conducted using 2-phenylethanol and *trans*-cinnamyl alcohol as studied molecules.

It was clearly found that C=C did not affect on the reaction since the competitive bromination between 2-phenylethyl and *trans*-cinnamyl alcohols furnishing almost the same yields while chlorination of 2-phenylethanol displayed more reactivity than *trans*-cinnamyl alcohol (entry 2). In addition, benzylic alcohol showed less reactivity than 2-phenylethanol under the developed system (entry 1). These results could be concluded that allylic alcohols, especially primary allylic alcohols were more reactive with PPh_3/selected haloganating agent than benzylic alcohols. The order of reactivity of alcohols with PPh_3/selected halogenating agent is displayed below.