โบรมิเนชันของไฮโดรไซเลน อีเทอร์และอิพ็อกไซด์โดยใช้เฮกซะโบรโมแอซีโทน

นางสาวลลิตา หมื่นระย้า

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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BROMINATION OF HYDROSILANES, ETHERS AND EPOXIDES USING HEXABROMOACETONE

Miss Lalita Muenraya

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Petrochemistry and Polymer Science
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Thesis Advisor	Assistant Professor Warinthorn Chavasiri, Ph.D.

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ลลิตา หมื่นระย้า : โบรมิเนชันของไฮโดรไซเลน อีเทอร์และอิพ็อกไซด์โดยใช้เฮกซะโบรโมแอซีโทน. (BROMINATION OF HYDROSILANES, ETHERS AND EPOXIDES USING HEXABROMOACETONE) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ดร.วรินทร ชวศิริ, 61 หน้า.

ได้วิธีที่มีประสิทธิภาพสำหรับเตรียมโบรโมไซเลนจากไฮโดรไซเลน โดยใช้ไทรไอโซโพรพิลไซเลน ($(i\text{-Pr})_3SiH$) ทำปฏิกิริยากับเฮกซะโบรโมแอซีโทน (HBA) อัตราส่วน 1.0:0.25 ที่อุณหภูมิห้องเป็นเวลา 20 นาที ในเททระไฮโดรฟูราน ได้ผลิตภัณฑ์เป็นไทรไอโซโพรพิลโบรโมไซเลนปริมาณสูง ภาวะของปฏิกิริยาได้ถูกดัดแปลงเพื่อให้มีประสิทธิภาพดียิ่งขึ้นโดยใช้การฉายยูวีโซนิเคชัน หรือรีฟลักซ์ในเททระไฮโดรฟูราน ได้ผลิตภัณฑ์โบรโมไซเลนในปริมาณสูงภายในเวลา 15 นาที ได้นำภาวะที่เหมาะสมนี้ไปประยุกต์ใช้กับไฮโดรไซเลนชนิดอื่น ๆ เช่น ไทรเฟนิลไซเลน ไดเมทิลเฟนิลไซเลน และคลอโรไดเมทิลไซเลน นอกจากนี้ได้พัฒนาภาวะที่ไม่รุนแรงและมีประสิทธิภาพการแตกอีเทอร์และเปิดวงอิพ็อกไซด์โดยใช้เฮกซะโบรโมแอซีโทนร่วมกับไทรเฟนิลฟอสฟีน (PPh_3) โดยศึกษาอีเทอร์ทั้งชนิดที่เป็นสายโซ่และเป็นวง ในกรณีของอีเทอร์ที่เป็นสายโซ่พบว่าไดเบนซิลอีเทอร์แตกออกเป็นเบนซิลโบรไมด์โดยใช้เฮกซะโบรโมแอซีโทนร่วมกับไทรเฟนิลฟอสฟีนในอัตราส่วน 1:2 ในสภาวะรีฟลักซ์โทลูอีนเป็นเวลา 4 ชั่วโมง สำหรับอีเทอร์แบบวง พบว่าเททระไฮโดรฟูรานในปริมาณมากเกินพอ และใช้เฮกซะโบรโมแอซีโทนร่วมกับไทรเฟนิลฟอสฟีนในอัตราส่วน 1:2 ที่รีฟลักซ์เป็นเวลา 15 นาที ได้ผลิตภัณฑ์ 1,4-ไดโบรโมบิวเทนในปริมาณสูง นอกจากนี้ ได้ทำปฏิกิริยาเดียวกันภายใต้คลื่นไมโครเวฟที่อุณหภูมิ 130 องศาเซลเซียล เป็นเวลา 1 นาที ได้ผลิตภัณฑ์ในปริมาณสูง สำหรับการเปิดวงอิพ็อกไซด์ สามารถควบคุมผลิตภัณฑ์ที่เป็นสารประกอบโบรโมไฮดรินและไดโบรโมได้โดยใช้แอซิโทไนไทรล์ที่มีความชื้นและไม่มีความชื้น และใช้เฮกซะโบรโมแอซีโทนร่วมกับไทรเฟนิลฟอสฟีนในอัตราส่วน 0.5:1 และ 2:3 ตามลำดับ ได้ผลิตภัณฑ์โบรโมไฮดรินและไดโบรโมในปริมาณที่สูง

สาขาวิชา ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์ ลายมือชื่อนิสิต .....

ปีการศึกษา 2555 ลายมือชื่อ อ. ที่ปรึกษาวิทยานิพนธ์หลัก .....

5372315223: MAJOR PETROCHEMISTRY AND POLYMER SCIENCE
KEYWORDS: HEXABROMOACETONE / HYDROSILANE/ EPOXIDE

LALITA MUENRAYA: BROMINATION OF HYDROSILANES, ETHERS AND EPOXIDES USING HEXABROMOACETONE.
ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 61 pp.

An efficient method for the preparation of bromosilanes from hydrosilanes has been disclosed. Tri-*iso*propylsilane was treated with hexabromoacetone (HBA) with the ratio of 1.0:0.25 at room temperature for 20 min in THF furnishing tri-*iso*propylbromosilane in excellent yield. The reaction conditions could be modified to make the reaction more efficient by using UV irradiation, sonication or performing at refluxing THF. The quantitative yield of bromosilane was successfully accomplished within 15 min. Under these optimized conditions, various hydrosilanes such as triphenylsilane, dimethylphenylsilane, and chlorodimethylsilane could be applied. The target products could be attained in good to excellent yields. In addition, a mild and efficient ether cleavage, epoxide ring-opening method using HBA/PPh_3 was developed. Two types of ether were studied including linear and cyclic ethers. In the case of the cleavage of linear ether, dibenzyl ether (DBE) was transformed to benzyl bromide using HBA/PPh_3 with mole ratio of HBA:PPh_3 1:2 at refluxing toluene for 4 h. For the opening of cyclic ether, excess THF was cleaved using HBA/PPh_3 with mole ratio of HBA:PPh_3 1:2 at refluxing THF within 15 min to produce 1,2-dibromobutane in quantitative yield. Furthermore, the same reactions were done under microwave irradiation at 130 °C for only 1 min to produce high yield of the product. For the opening of epoxides, the formation of bromohydrin and dibromo products could be controlled using undried and dried CH_3CN and the mole ratio of HBA:PPh_3 at 0.5:1.0 and 2:3, giving bromohydrin and dibromo products in quantitative yield.

Field of Study: Petrochemistry and Polymer Science Student's Signature .....
Academic Year: 2012 Advisor's Signature .....

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LIST OF ABBREVIATIONS

conc.	concentrated
d	doublet (NMR)
dd	doublet of doublet (NMR)
equiv.	equivalent
g	gram (s)
h	hour (s)
Hz	hertz
J	coupling constant (NMR)
m	multiplet (NMR)
MB	mass balance
min	minute (s)
mL	milliliter (s)
mmol	millimole (s)
µL	microliter
MW	microwave
NMR	nuclear magnetic resonance
ppm	part per million
q	quartet (NMR)
RT	room temperature
s	singlet (NMR)
TLC	thin layer chromatography
t	triplet (NMR)
td	triplet of doublet (NMR)
UV	ultraviolet
W	watt
%	percent
^{o}C	degree Celsius
δ	chemical shift

CHAPTER I

INTRODUCTION

The preparation of fine chemicals containing bromine is very important due to various applications in chemical industries. Bromosilanes are important intermediates and building units for a variety of organosilicons [1] and are used in inorganic synthesis [2]. In addition, bromosilanes depending on the reaction conditions can be used for both protection and deprotection of fuctional groups [3]. On the other hand, bromohydrins which can be prepared from the ring opening reactions of cyclic ethers or epoxides [4], are known as one of intermediates in pharmaceutical interest [5] and are widely useful starting material for the preparation of different functional groups [6]. Vicinal bromoalcohols from the ring-opening epoxides are an important aspect in organic synthesis [7-8], such as laurenyne and isodactylyne (marine natural products) and other bioactive molecules [9].

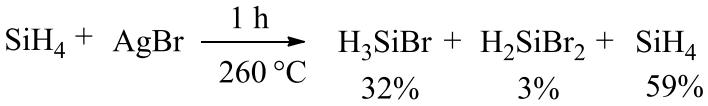
According to previous literature, hexabromoacetone (HBA) has never been used in bromination of hydrosilanes, ethers and epoxides. HBA, a stable solid brominating agent possesses high efficiency in bromination reactions [10]. Thus, this research focuses on the development of a new methodology for the synthesis of bromosilanes from hydrosilanes using HBA, the clevage of ethers and ring opening of epoxides using HBA with PPh_3.

1.1 Classical Method for the Preparation of Bromosilanes from Hydrosilanes

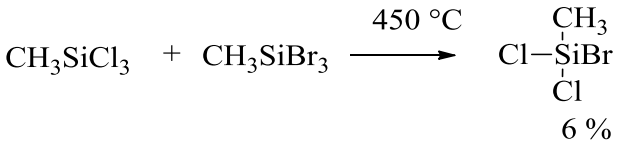
Bromosilanes can be prepared from several starting materials. The general method for the preparation of bromosilanes from hydrosilanes has been addressed by the use of Br_2 [11]. In 1954, Sujishi and Wit [12] investigated the conversion of hydrosilane to bromosilane using Br_2 at 120 °C for 3-5 h. This method gave 80-90% yield of the desired product.

$$SiH_4 + Br_2 \xrightarrow[120\ ^\circ C]{3\text{ - }5\ h} \underset{80\text{- }90\%}{H_3SiBr}$$

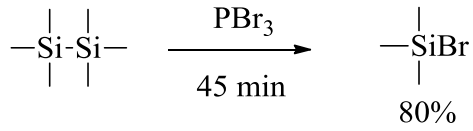
Hydrosilane could be converted to bromosilane by the gas-solid phase reaction between silane and AgBr [13]. The drawback for this method was low yield and unpleasant by-product.



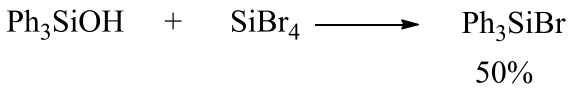
Herbert and co-workers [14] prepared methyldichlorobromosilane from the reaction between methyltrichlorosilane and methyltribromosilane in a large scale at 450°C yielding less product.



Mccuskear and Reilly [15] reported that trimethylbromosilane was prepared by a modification of the method of Gilliam, Meals and Sauer using hexametyl-disiloxane with PPh_3 affording 80% yield at 45 min.



Another method to prepare bromosilane was accomplished by conversion of triphenylsilinol to triphenylbromosilane with $SiBr_4$. This method gave 50% yield of the desired product.



According to the outcomes derived from such common reagents, some problems still remained. For example, the use of AgBr often caused undesired side reactions. Other common reagents such as Br_2 and PBr_3 are known as a harmful reagent and produced corrosive by-product. Hence, the need for the controllable and selective methodology still calls for further study for the preparation of bromosilane.

1.2 Literature Reviews of Bromosilanes from Hydrosilanes

In 2001, Kunai and co-workers [16] addressed the bromination of alkylbromosilane using CuI-$CuBr_2$. This method could be applied for the preparation of tribromosilane, even though long reaction time was required.

$$R_{4-n}SiH_n \xrightarrow{2CuI - CuBr_2} R_{4-n}SiBr_n \quad 68\%$$

In 2003, Kunai and Ohshita [17] converted dimethylphenylsilane to bromo dimethylphenylsilane using $PdCl_2$ or $NiCl_2$ at 80 °C for 1-16 h. The advantage of this route was high yield of bromosilane with none of by-product detected.

$$Me_2PhSiH + allylBr \xrightarrow{catalyst} Me_2PhSiBr$$

1 mol% $PdCl_2$, 80 °C, 1 h, 88%
2-6 mol% $NiCl_2$, 80 °C, 16 h 9%

In 2009, Pongkittiphan and coworkers [18] investigated the preparation of chlorosilanes from hydrosilanes using hexachloroethane (Cl_3CCCl_3) accomplishing the desired product in good to quantitative yields under mild conditions.

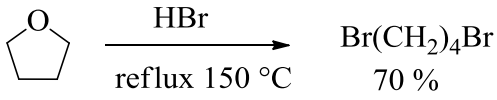
$$(i\text{-Pr})_3SiH + Cl_3CCCl_3 \xrightarrow[RT,\ 1\ h]{PdCl_2,\ THF} (i\text{-Pr})_3SiCl$$

In 2011, Srithanakit and coworkers [19] addressed the bromination of tri-*iso*propylsilane (TIPS-H) using ethyl tribromoacetate ($Br_3CCOOEt$) in the presence of a catalytic amount of $PdCl_2$ affording tri-*iso*propylbromosilane (TIPS-Br) in quantitative yield under mild conditions and short reaction time.

$$(i\text{-Pr})_3SiH + Br_3CCOOEt \xrightarrow[15\ min,\ reflux]{1\ mol\%\ PdCl_2,\ THF} (i\text{-Pr})_3SiBr$$

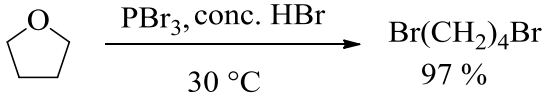
1.3 Literature Reviews on the Cleavage of Ethers to Bromo Compounds

Fried and Kieene [20] addressed the cleavage of tetrahydrofuran (THF) to tetramethylene bromide by HBr under reflux. The process was simple and gave a comparable yield from more readily available staring material.

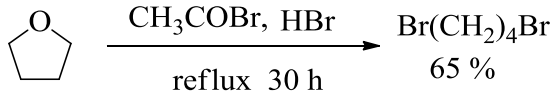


Volynskii and Perelitchenko [21] studied the cleavage of ether and ester by simultaneous action of PBr_3 and concentrated HBr under aprotic condition at 1 -

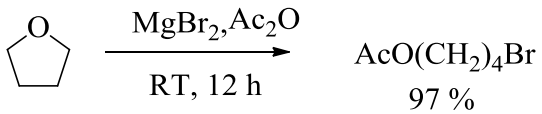
providing the target product in high to excellent yield. They assumed that the cleavage of C-O bond and substitution of O by Br took place primarily at C atom bound to alkyl substituent with the bromine atom taking the place of oxygen atom *via* an S_N2 mechanism.



Ispiryan and co-workers [22] reported the cleavage of THF to 1,4-dibromo-butane by HBr and acetyl bromide in approximately 65% yield after refluxing the reactants for nearly 30 h. A reduction of heating time lowered the yield sharply.

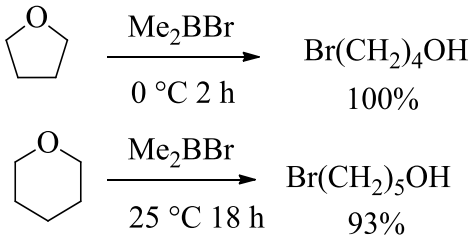


Goldsmith and co-workers [23] demonstrated that the mechanism of cyclic ether cleavage with $MgBr_2$–acetic anhydride was thus shown to be exclusive an S_N2 process. The cleavage reaction occurred readily at RT.

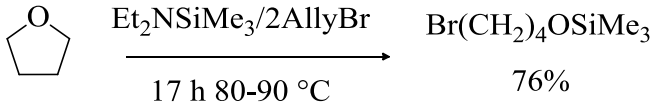


In 1986, Guindon and co-workers [24] reported that dimethylboron bromide reacted with simple cyclic ether of various ring sizes giving the corresponding bromo

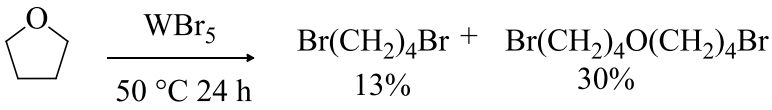
alcohols in excellent yield such as conversion of THF to 4-bromobutanol in quantitative yield and tetrahydropyran to 5-bromopentanol in 93% yield.



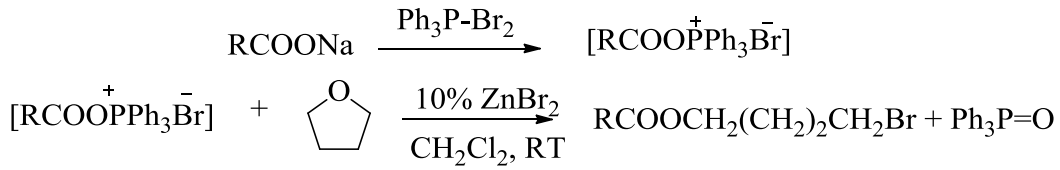
In 1999, Ohshi and co-workers [25] studied the reaction of iodo- and bromosilylation of cyclic ethers by treatment with iodo- and bromotrialkylsilane. A reaction of THF with 1.1 equiv of Et_2NSiMe_3 and allyl bromide gave the target product in 76% yield.



In 2002, Guo and co-workers [26] reported that WBr_5 could be used as a catalyst for acylative cleavage of the C-O bond of THF to 1,4-dibromobutane and bisbromobutylether in 13 and 30% yields, respectively. The acylative C-O bond cleavage reaction proceeded *via* a cationic mechanism which involved the formation of RCO^+.

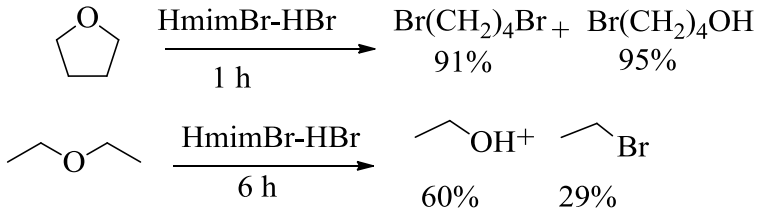


Wu and coworkers [27] reported that THF in the presence of $ZnBr_2$ could be opened with acyloxyphosphonium bromide generated *in situ* affording 4-bromobutyl esters under mild conditions in good to excellent yields.



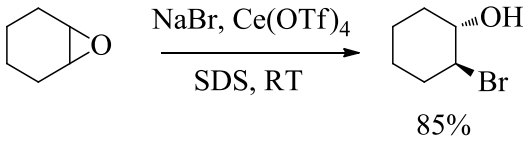
R	time (h)	% yield
Ph	1	93
CH_3	5	76

Driver and Johnson [28] investigated the cleavage of THF to 1,4-dibromo-butane and 1-bromobutanol using 3-methylimidazolium cation ($Hmim^+$) and Br^- for 1 h.

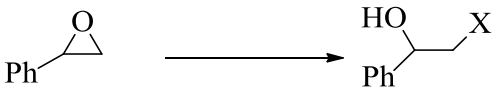


1.4 Literature Reviews on the Cleavage of Epoxides to Bromohydrins and Di-Bromo Compounds

In 2003, Iranpoor and co-workers [29] reported the epoxide ring opening of cyclohexene oxide to *trans*-2-cyclohexanol with NaBr catalyzed and $Ce(OTf)_4$ in sodium dodecyl sulfate (SDS) at RT to 85% yield.

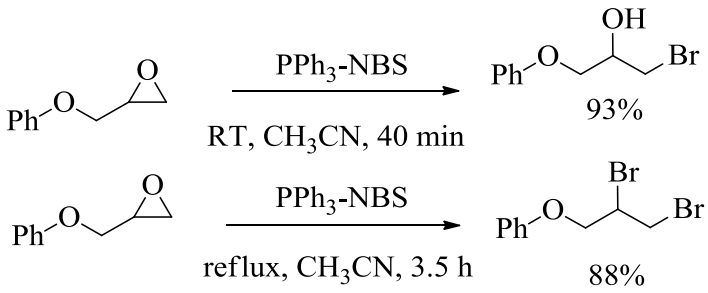


In 2005, Surandra and co-workers [30] showed the preparation of oxiranes to halohydrins with tetrabutylammonium halide in water. The reaction went smoothly at RT without the formation of by products. Terminal oxiranes were highly regioselective.

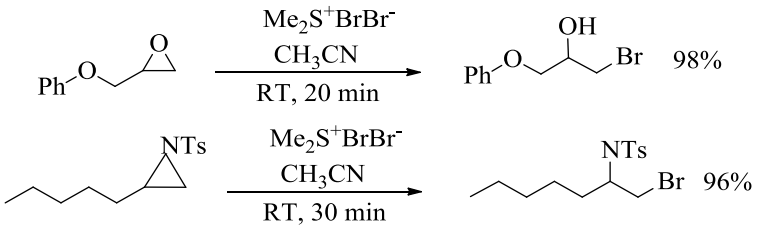


	reagent	time	%yield
X = Cl	n-Bu_4NCl	10	84
X = Br	n-Bu_4NBr	2.5	90
X = I	n-Bu_4Nl	1.0	94

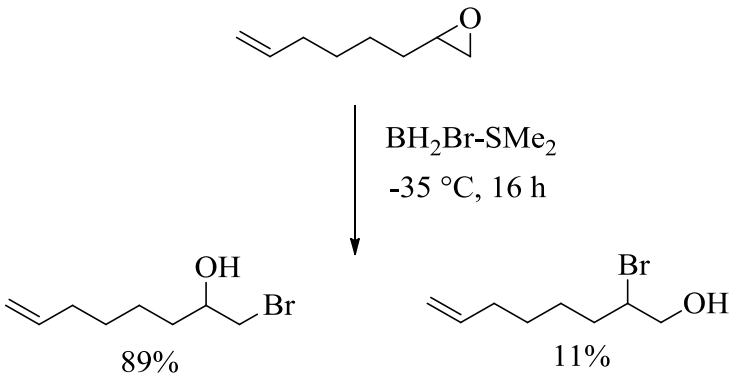
In 2006, Iranpoor and co-workers [31] investigated the regio- and stereoselectivity of epoxide ring opening using PPh_3 with *N*-bromosuccinimide (NBS) in controlled reaction. At RT, bromohydrin was achieved in 93% yield, while at refluxing CH_3CN furnished dibromo product in 88% yield.



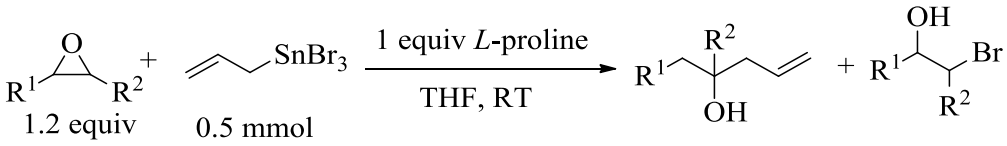
In 2006 Das and co-workers [32] reported the ring opening of epoxides and aziridines using $Me_2S^+BrBr^-$ in CH_3CN at RT for 20 min.



In 2006, Roy and Brown [33] reported the ring opening of terminal epoxides with dibromoborane-dimethyl sulfide ($BHBr_2$-SMe_2) at RT for 0.25 h in CH_2Cl_2 to high yield of highly regio- and chemoselective synthesis.

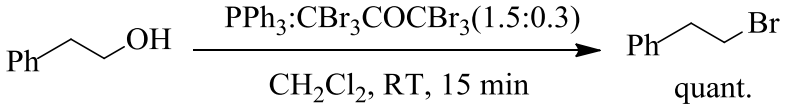


In 2010, Guo Hong and co-workers [34] reported using allytin tribromide with *L*-proline as catalyst for the conversion of epoxide in THF at RT.

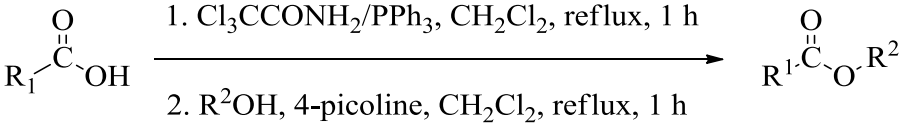


1.5 Literature Reviews of Recent Studies on Halogenating Reagents

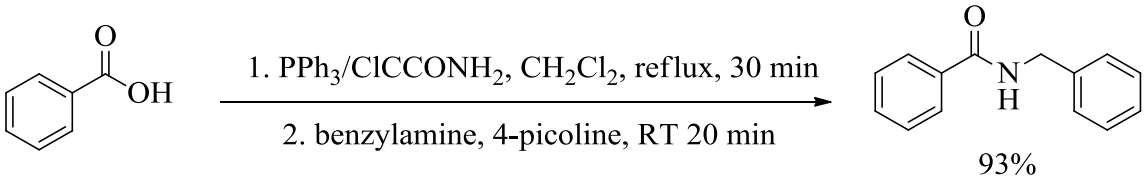
In 2008, Tonkate and co-workers [35] reported the conversion of hydroxyl group to bromide using HBA with PPh_3 at RT for 15 min in quantitative yield.



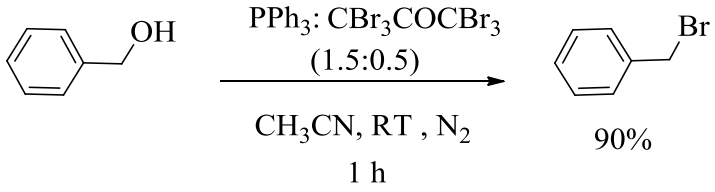
In 2008, Chantarasriwong and co-workers [36] investigated a versatile reagent for the synthesis of esters using Cl_3CCONH_2/PPh_3 to convert carboxylic acid to acid chloride. This methodology could be applied to one-pot synthesis of ester in high yield.



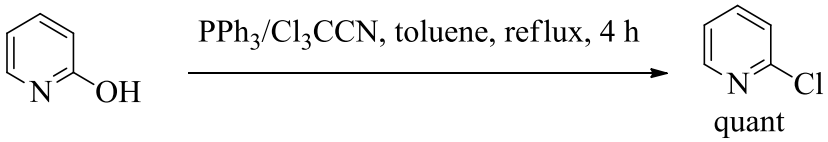
In 2009, Chaysripongkul and co-workers [37] reported the conversion of carboxylic acid to acid chloride using Cl_3CCONH_2/PPh_3 and one-pot conversion of amine to amide in high yield.



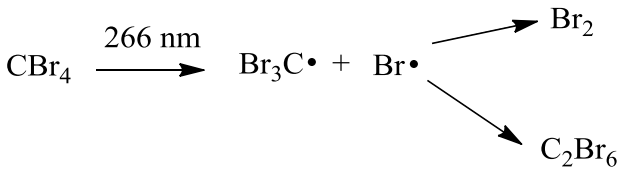
In 2010, Joseph and co-workers [38] reported the use of HBA with PPh_3 in CH_3CN for 1 h to convert benzylic alcohol to benzyl bromide in high yield.



In 2012, Kijrungphaiboon and co-workers [39] investigated the reaction for the preparation of *N*-heteroaromatic chloride using Cl_3CCN/PPh_3 at refluxing toluene for 4 h giving the target product in quantitative yield.



In 2007, Kong and co-workers [40] investigated the photochemical reaction pathways of carbon tetrabromide (CBr_4) at 266 nm. C-Br bond in CBr_4 molecule could break to CBr_3 and Br radicals which could subsequently form C_2Br_6 and Br_2, respectively.



1.6 Goal of the Research

The objective of this research is to develop the methodology for the conversion of hydrosilanes to bromosilanes, the cleavage of ethers and the ring opening of epoxides using hexabromoacetone under mild conditions.

CHAPTER II

EXPERIMENTAL

2.1 Instruments and Equipment

The ^{1}H and ^{13}C NMR spectra were performed in $CDCl_3$ on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR spectrometer which operated at 399.38 MHz for ^{1}H and 100.54 MHz for ^{13}C nuclei. The chemical shifts (δ) are assigned by comparison with residue solvent proton. Yield of products was determined by ^{1}H NMR technique using an internal standard.

TL was performed on aluminium sheets precoated with silica gel (Merck's Kieselgel 60 PF_{254}). olumn chromatography was performed on silica gel (Merck's silica gel 60 G Art 7734 (70-230 mesh).

2.2 Chemicals

All solvents were purified by standard methodology before use except for those which were reagent grades. The reagents used for synthesis were purchased from Fluka or Sigma-Aldrich and used without further purification.

2.3 Preparation of Hexabromoacetone (HBA)

Anhydrous NaOAc 10.95 g was mixed with 35 mL of glacial CH_3COOH. The reaction mixture was stirred and heated to 60 °C. Acetone 1.4 mL was added and followed by drop wise addition of Br_2 7 mL over 30 min period with stirring. The mixture was then heated to 95 °C for 6 h. Then, it was cooled to RT and mixed with 100 mL of ice-water to precipitate the desired product as white solid. After air drying, the pure HBA was obtained upon recrystallization from *n*-hexane.

HBA: white (40-60%). ^{13}C NMR ($CDCl_3$) δ (ppm): 4. and 73.

2.4 Optimum Conditions for the Conversions of Hydrosilanes to Bromosilanes Using HBA

Tri-*iso*propylhydrosilane was used as a model compound. Several factors including the amount of HBA, reaction time, solvents and reaction conditions such as UV radiation, sonication and refluxing THF were varied to explore the efficiency of the reaction.

2.4.1 Effect of Amount of HBA

Various amounts of HBA (0.10, 0.15, 0.25 and 0.30 mmol) were varied for the bromination of tri-*iso*propyl-hydrosilane (TIPS-H).

2.4.2 Effect of Solvents

The general reaction was carried out except for using three different solvents (0.25 mL): THF, 1,4-dioxane, methyl-*tert*-butylether (MTBE) at RT for 10 min.

2.4.3 The Application of the Developed Procedure for the Synthesis of Bromosilanes

The bromination of various hydrosilanes (1 mmol) was carried out employing the developed procedure using 0.25 mmol HBA at RT for 20 min in THF.

Seven different silanes: $(i\text{-Pr})_3SiH$, Et_3SiH, Ph_3SiH, $(Me_3Si)_3SiH$, $PhMe_2SiH$, $t\text{-BuMe}_2SiH$ and Ph_2ClSiH were examined. The quantity of bromosilane in the crude mixture was determined by ^{1}H NMR using toluene as an internal standard.

Tri-*iso*propylbromosilane ($(i\text{-Pr})_3SiBr$): 91%, ^{1}H-NMR ($CDCl_3$) δ (ppm): . (18H, *d*, *J* =7.2 Hz, $Si(CH(C\underline{H}_3)_2)_3$ and 1.26 (3H, *m*, $Si(C\underline{H}(CH_3)_2)_3$).

Tri-ethylbromosilane (Et_3SiBr): 53%, ^{1}H-NMR ($CDCl_3$) δ (ppm): .9 (9H, *q*, *J* = 7.8 Hz, $Si(C\underline{H}_2CH_3)_3$) and 1.07 (6H, *t*, *J* = 7.8 Hz, $Si(CH_2C\underline{H}_3)_3$).

Tris-trimethylsilylbromosilane ($(Me_3Si)_3SiBr$): 94%, ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.05 (27H, *s*, $Si(Si(C\underline{H}_3)_3)_3$.

Dimethylphenylbromosilane ($PhMe_2SiBr$): 98%, ^{1}H-NMR ($CDCl_3$) δ (ppm): 5.78 (3H, *s*, $PhSi(CH_3)_2$, 7.48 (6H, *m*, Ar-H) and 7.70 (4H, *d*, *J* = 6.7 Hz, Ar-H).

Tert-Butyldimethylbromosilane ($BuMe_2SiBr$): 37%, ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.52 (6H, *s*, $Si(C\underline{H}_3)_2$) and 1.01 (9H, *d*, *J* = 6.5 Hz, $SiC(C\underline{H}_3)_3$).

Triphenylbromosilane (Ph_3SiBr): quant, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.3 (9H, *m*, Ar-H) and 7.72 (6H, *d*, *J* = 6.5 Hz, Ar-H).

Chlorodiphenylbromosilane ($Ph_2ClSiBr$): 85%, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.73 (2H, *t*, *J* = 4.0 Hz, Ar-H), 7.84 (4H, *m*, Ar-H) and 7.91 (4H, *m*, Ar-H).

2.4.4 The Effect of Reaction Conditions

The reactions were performed under different reaction conditions, *i.e.*, sonication, UV radiation and refluxing THF conditions compared with that carried out at RT.

2.5 Optimum Conditions for the Cleavage of Ethers Using HBA with PPh_3

2.5.1 The Cleavage of Linear Ethers

Dibenzyl ether was used as a model linear ether. Several factors including mole ratio of HBA: PPh_3 and reaction time were varied to explore the efficiency of the reaction.

2.5.1.1 Effect of Mole Ratio of HBA:PPh_3

Various mole ratios of HBA/PPh_3 (1:2, 2:2, 2:3, 2:4 and 3:4) were varied for the bromination of dibenzyl ether.

2.5.1.2 Effect of Solvents

The general reactions were carried out using three different solvents (1.0 mL): dichloromethane (CH_2Cl_2), toluene and acetonitrile (CH_3CN) at reflux for 4 h.

Benzyl bromide: ^{1}H NMR ($CDCl_3$) δ (ppm): 4.32 (2H, *s*, -C<u>H</u>$_2$Br), 7.20 (2H, *t*, J = 7.6 Hz, Ar-<u>H</u>), and 7.30 (3H, *d*, J = 6.8 Hz, Ar-<u>H</u>).

2.5.2 The Cleavage of Cyclic Ethers

Tetrahydrofuran (THF) was used as a model cyclic ether. Several factors including mole ratio of HBA:PPh_3 and reaction time were varied to explore the efficiency of the reaction.

2.5.2.1 Effect of Amount of PPh_3

Various equivalents of PPh_3 (1, 2, 3 and 5) were varied for the bromination of dibenzyl ether.

1,4-dibromobutane: ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.91 (4H, *m*, BrCH$_2$C<u>H</u>$_2$-), 3.32 (4H, *m*, BrC<u>H</u>$_2$CH$_2$).

2.6 The Application of Microwave Technique for the Cleavage of Ethers

The bromination of ether (0.25 mmol) was carried out using microwave technique for 1 min without any solvent at 130 °C with HBA/PPh_3 at mole ratio of ether:HBA:PPh_3 at 0.25:0.5:1. Six different ethers including THF, dibenzyl ether, di-*n*-butyl ether, 2-chloroethyl ether, piperidine and ethyl phenyl acetate were examined.

1-bromo-2-chloroethane: ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.38 (2H, *t*, J = 6.0 Hz, BrC<u>H</u>$_2$CH$_2$-), and 3.65 (2H, *t*, J = 6.0 Hz, ClC<u>H</u>$_2$CH$_2$-).

1-bromobutane: ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.80 (3H, *t*, J = 5.4 Hz, BrCH$_2$CH$_2$CH$_2$C<u>H</u>$_3$), 1.32 (2H, *m*, BrCH$_2$CH$_2$C<u>H</u>$_2$-), 1.50 (2H, *m*, BrCH$_2$C<u>H</u>$_2$-), and 3.12 (2H, *t*, J = 6.6 Hz BrC<u>H</u>$_2$CH$_2$-).

1,5-dibromopentane: ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.62 (2H, *m*, $BrCH_2CH_2C\underline{H}_2$), 1.99 (4H, *m*, $BrCH_2C\underline{H}_2CH_2$-) and 3.12 (4H, *t*, *J* = 8.9 Hz, $BrC\underline{H}_2CH_2$-).

ethyl bromide: ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.48 (3H, *t*, *J* = 7.4 Hz, $BrCH_2C\underline{H}_3$), and 3.23 (2H, *q*, *J* = 7.3 Hz, $BrC\underline{H}_2CH_3$).

2-bromo-1-phenylethanone: ^{1}H-NMR ($CDCl_3$) δ (ppm): 3. 8 (H, *s*, $BrCOC\underline{H}_2$-) and 7.20-7.10 (5H, m, Ar-$\underline{H}$).

2.7 Optimum Conditions for the Reaction of Epoxide Using HBA and PPh_3

2.7.1 The Transformation of Epoxides to Bromohydrins

Styrene oxide was used as a model epoxide. Several factors including amount mole ratio of HBA and PPh_3, reaction time and solvents were varied to explore the efficiency of the reaction.

2.7.1.1 Effect of Reaction Time

The reaction time used was 1 min at room temperature.

2.7.1.2 Effect of Solvent

The general reactions was carried out using three different solvents (0.50 mL, *undried*): CH_2Cl_2, toluene and CH_3CN at room temperature for 1 min.

2.7.1.3 Effect of Mole Ratio of HBA:PPh_3

Various mole ratios of HBA/PPh_3 (0.5:1.5, 0.5:1, 0.5:0.5, 0.5:0 and 0.25:1) were varied for the bromination of styrene oxide.

2.7.2 The Transformation of Epoxides to *trans*-1,2-Dibromo Compounds

Cyclohexene oxide was used as a model compound. Several factors including mole ratio of PPh_3 and HBA, reaction time and solvent were varied to explore the efficiency of the reaction.

2.7.2.1 Effect of Dried CH_3CN and the Mole Ratio of HBA:PPh_3

The general reaction was carried out using CH_3CN (0.50 mL): dried and undried CH_3CN and various mole ratios of HBA/PPh_3 (0.5:1, 1:2 and 2:3) at room temperature for 1 min.

2.8 The Application of the Developed Procedure for the Synthesis of Bromohydrins and Dibromo Compounds from Epoxides

The bromination of various epoxides (0.25 mmol) was carried out using the developed procedures using HBA:PPh_3 (0.50:1.0) at RT for 1 min in CH_3CN. Five different epoxides: styrene oxide, cyclohexene oxide, butylglycidyl ether, *tert*-butylglycidyl ether and phenylglycidyl ether were examined. The quantity of bromohydrin in the crude mixture was determined by ^{1}H NMR using toluene as an internal standard.

trans-2-bromocyclohexanol: (100%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.26 (4H, *m*, -CHBr(C$\underline{H}_2$)(CH_2)$_2$), 1.69 (4H, *m*, -CHBr(CH_2)(C$\underline{H}_2$)$_2$), 3.54 (1H, *dt*, *J* = 4.6, 11.4 Hz, -C$\underline{H}$OH), and 3.85 (1H, *ddd*, *J* = 4.3, 8.1, 11.6 Hz, -C$\underline{H}$Br).

1-bromo-3-butoxypropan-2-ol: (96%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.81 (3H, *t*, *J* = 7.2 Hz, C$\underline{H}_3$CH_2CH_2-), 1.24 (2H, *q*, *J* = 6.0 Hz, CH_3C$\underline{H}_2$CH_2-), 1.42 (2H, *q*, *J* = 6.0 Hz, -C$\underline{H}_2$CH_2O-), 3.35 (2H, *t*, *J* = 6.8 Hz, -CH_2C$\underline{H}_2$O-), 3.39 (2H, *d*, *J* = 5.6 Hz, -OC$\underline{H}_2$CHOH), 3.44 (2H, *d*, *J* = 4.0 Hz, -C$\underline{H}_2$Br), and 3.88 (1H, *m*, *J* = 4.0 Hz, -CH_2C$\underline{H}$OH-),

1-bromo-3-(*tert*-butoxy)propan-2-ol: (98%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.19 (9H, *s*, -OC(C$\underline{H}_3$)$_3$), 3.46 (2H, *d*, *J* = 3.7 Hz, -C$\underline{H}_2$CHOH-), 3.51 (2H, *t*, *J* = 5.8 Hz, -C$\underline{H}_2$Br), and 3.89 (1H, *m*, -C$\underline{H}$OH).

1-bromo-3-phenoxypropan-2-ol: (100%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.67-6.56 (2H, *m*, -C$\underline{H}_2$Br)**,** 4.07 (1H, *m*, -CH_2C$\underline{H}$OHCH_2Br), 4.19 (2H, *m*, -OC$\underline{H}_2$CHOH), 7.54 (2H, *t*, *J* = 8.0 Hz, Ar-$\underline{H}$), and 7.46 (3H, *d*, *J* = 6.8 Hz, Ar-$\underline{H}$).

(1,2-dibromoethyl)benzene: (97%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.06 (1H, *t*, *J* = 10.4 Hz, -CHBrC<u>H</u>$_2$Br), 4.08 (1H, *dd*, *J* = 5.7, 10.4 Hz, -CHBrC<u>H</u>$_2$Br), 5.14 (1H, *dd*, *J* = 5.7, 10.4 Hz, -C<u>H</u>BrCH$_2$Br, and 7.32–7.42 (5H, m, Ar-<u>H</u>).

1,2-dibromocyclohexane: (93%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.95 (8H, *m*, -CBr(C<u>H</u>$_2$)$_4$), and 4.36 (2H, m, -CBr<u>H</u>)

1,2-dibromo-3-(*tert*-butoxy)propane: (100%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.92 (9H, *s*, -OC(C<u>H</u>$_3$)$_3$), 3.74 (2H, *m*, -OC<u>H</u>$_2$CHBr), 3.78-3.41 (2H, *m*, -CHBrC<u>H</u>$_2$Br), and 4.18 (1H, *m*, -CH$_2$C<u>H</u>BrCH$_2$Br).

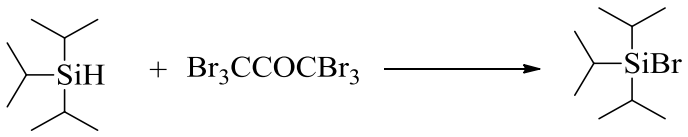
(2,3-dibromopropoxy)benzene: (100%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.73 (2H, *m*, -CH$_2$Br), 4.20 (1H *m*, -CH$_2$C<u>H</u>BrCH$_2$Br), 4.27 (2H, *m*, OC<u>H</u>$_2$CHBr), 7.11 (2H, *t*, *J* = 7.6 Hz, Ar-<u>H</u>), and 7.06 (3H, *d*, *J* = 6.8 Hz, Ar-<u>H</u>).

1-(2,3-dibromopropoxy)butane: (94%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.00 (3H, *t*, *J* = 7.2 Hz, C<u>H</u>$_3$CH$_2$CH$_2$), 1.79 (2H, *m*, CH$_3$C<u>H</u>$_2$CH$_2$,), 3.48 (2H, *t*, *J* = 5.19 Hz, -CH$_2$C<u>H</u>$_2$O-), 3.55 (2H, *d*, *J* = 4.4 Hz, -C<u>H</u>$_2$Br), 3.62 (2H, *t*, -OC<u>H</u>$_2$CHBr), 3.98 (1H, *m*, *J* = 8.0 Hz, -CH$_2$C<u>H</u>BrCH$_2$Br).

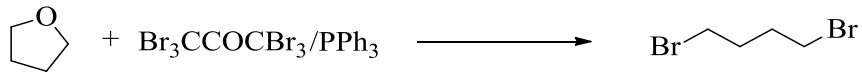
CHAPTER III

RESULTS AND DISCUSSION

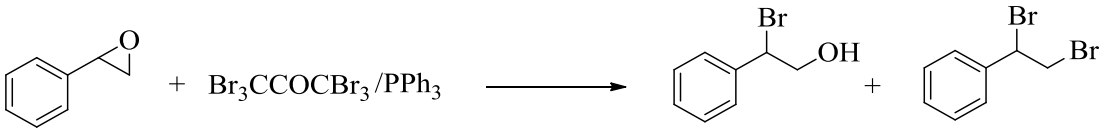
Bromination is one of fundamental chemical reactions. Bromosilanes, bromohydrins, mono- and di-bromo compounds are important reagents in organic synthesis with a wide range of applications. In this research, the optimum conditions for the preparation of bromosilanes from hydrosilanes using hexabromoacetone (HBA) were explored. In addition, the exploitation of HBA with triphenylphosphene (PPh_3) in ether cleavage and ring-opening of epoxides was scrutinized. The general equations are presented below (Eqs. 3.1–3.3).



(Eq. 3.1)



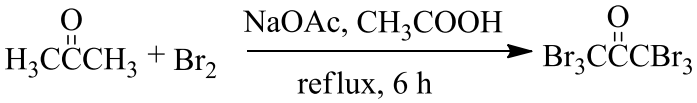
(Eq.3.2)



(Eq.3.3)

3.1 Synthesis of HBA

The synthesis of HBA was performed by the reaction of acetone, Br_2 and NaOAc in CH_3COOH (Eq. 3.4) [41]. HBA was obtained around 40–60% yield. The ^{13}C NMR spectrum of HBA (Figure 3.1) shows two types of atoms at δ_c 173.5 and 24.5 ppm, which could be referred to the carbonyl carbon and the carbons bearing three bromine atoms, respectively.



(Eq. 3.4)

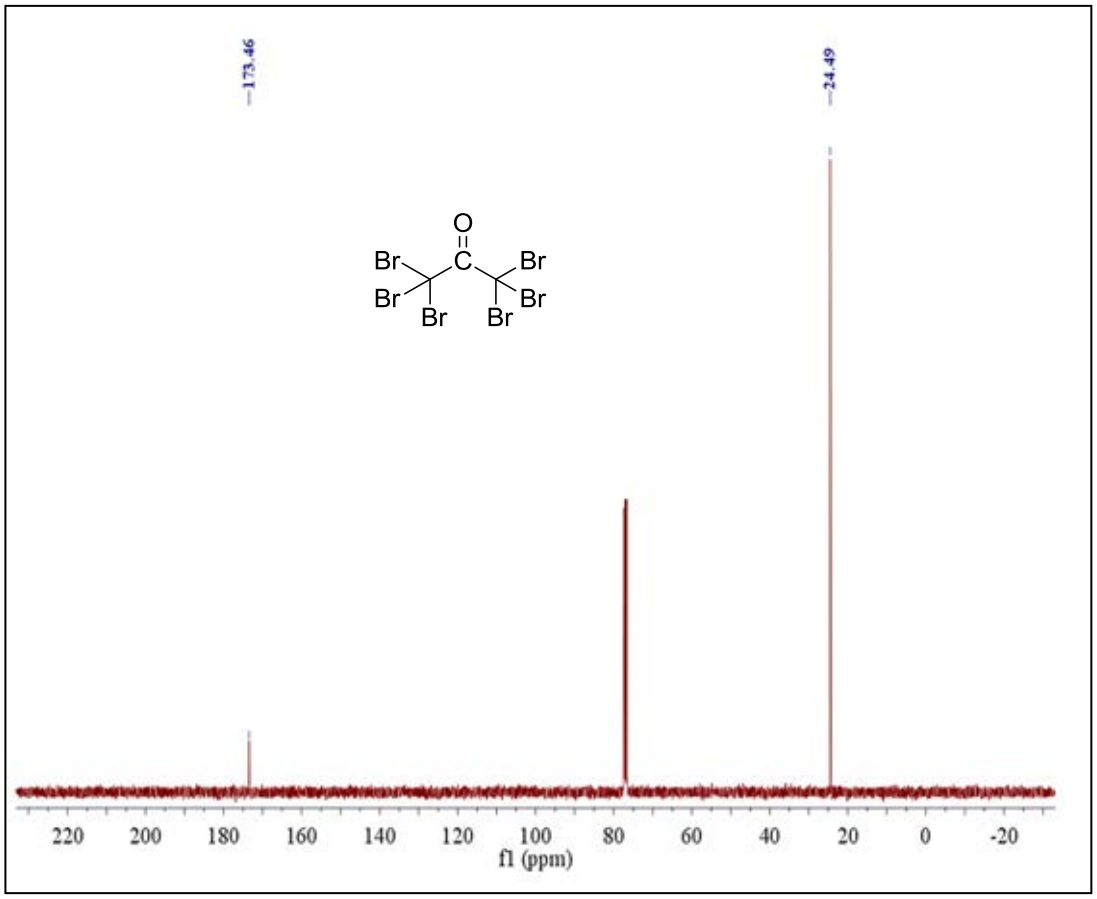


Figure 3.1 The ^{13}C NMR spectrum of HBA

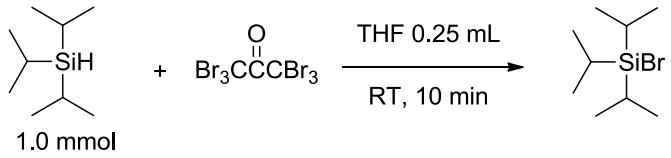
3.2 Optimum Conditions for the Conversion of Hydrosilanes to Bromosilanes Using HBA

The search for optimum conditions including the amount of HBA, reaction time, solvent and reaction conditions for the conversion of hydrosilanes to bromosilanes was investigated. Tri-*iso*propylhydrosilane (TIPS-H) was selected as a model substrate.

3.2.1 The Effect of Amount of HBA

For optimizing reaction conditions, the effect of the amount of HBA was explored with the aim to obtain the most appropriate amount of HBA for the synthesis of TIPS-Br. The results are presented in Table 3.1.

Table 3.1 The effect of amount of HBA on the conversion of TIPS-H into TIPS-Br



Entry	HBA (mmol)	% Yield of TIPS-Br	% Recovery of TIPS-H	%MB
1	0.10	25	66	91
2	0.15	42	49	91
3	0.20	59	31	90
4	0.25	69	23	92
5	0.30	70	25	95

The amount of TIPS-Br was determined by ^{1}H NMR technique using toluene as an internal standard. An example of the crude reaction mixture is presented in Figure 3.2. The proton signal at δ_H 3.32 ppm could be assigned for Si-H, while the others could refer to the remaining proton at δ_H 1.28 ppm of the product SiCH$(CH_3)_2$.

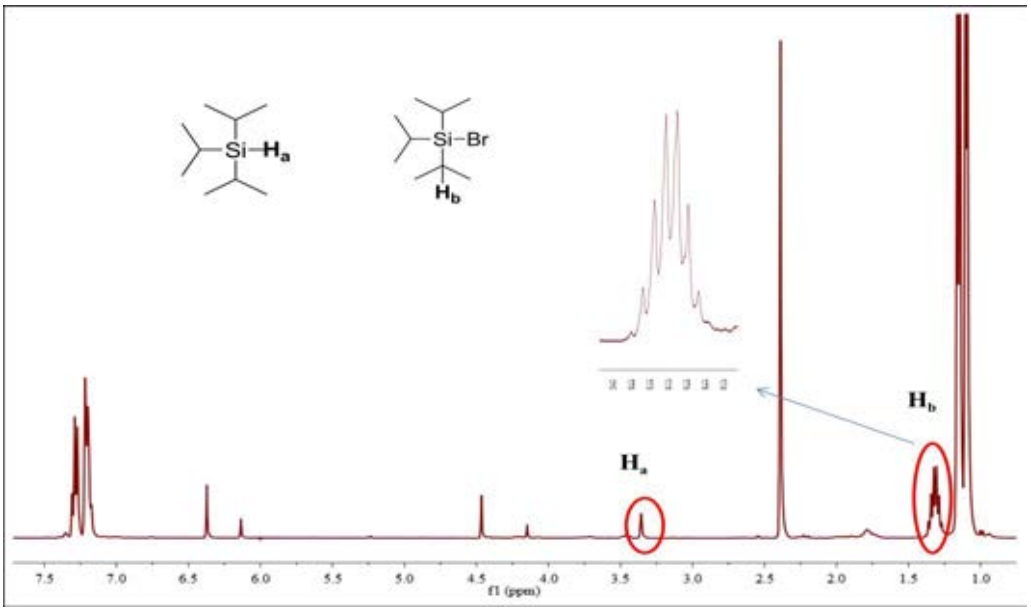


Figure 3.2 The ^{1}H NMR spectrum of the crude reaction mixture of TIPS-H with HBA (from entry 4, Table 3.1)**.**

Using the equation 3.5, the percentage of the desired product could be determined by comparisons between the integration of methyl group of toluene and that belonging to the desired product.

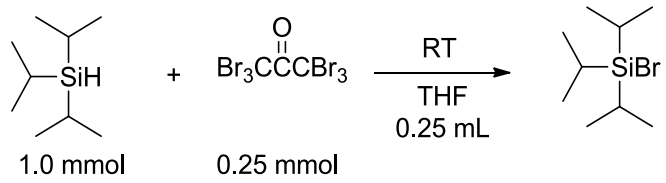
$$\%\text{yield} = \frac{(\text{integration of product})}{(\text{integration of internal std})} \times \frac{(\text{amount H of internal std})}{(\text{amount H of product})} \times 100 \qquad \text{Eq. 3.5}$$

Table 3.1 reveals that when the reaction was performed with increasing amount of HBA from 0.10 to 0.25 mmol, the yield of the desired product was significantly increased (entries 1-4). However, using 0.30 mmol of HBA (entry 5) gave 70% yield of TIPS-Br which closely resembled to the use of HBA 0.25 mmol (entry 4). Thus, 0.25 mmol of HBA was selected for further study.

3.2.2 Effect of Reaction Time

The reaction time for the bromination of TIPS-H using HBA was used for the optimized conditions. The results are presented in Table 3.2.

Table 3.2 The effect of reaction time on the conversion of TIPS-H into TIPS-Br using HBA



Entry	Time (min)	%Yield of TIPS-Br	%Recovery of TIPS-H	%MB
1	5	56	37	93
2	10	69	23	92
3	20	91	3	94
4	30	91	1	92

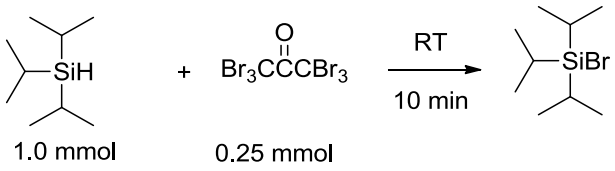
Table 3.2 reveals that TIPS-Br could be detected just in 5 min in moderate yield (entry 1). Increasing reaction time from 20 to 30 min did not provide a

significant increase in the yield of product (entries 3 and 4). The reaction time at 20 min was thus proper to carry out the reaction at RT. However, for further comparison purpose, the reaction time at 10 min was selected for examination.

3.2.3 Effect of Solvents

Since HBA is a solid reagent, the reaction required solvent to assist the reaction to become homogeneous. Various solvents were tried and the results are displayed in Table 3.3.

Table 3.3 The effect of solvent on the conversion of TIPS-H into TIPS-Br using HBA



Entry	Solvent	%Yield of TIPS-Br	%Recovery of TIPS-H	%MB
1	THF	69	23	92
2	1,4-dioxane	19	73	92
3	MTBE	23	70	93

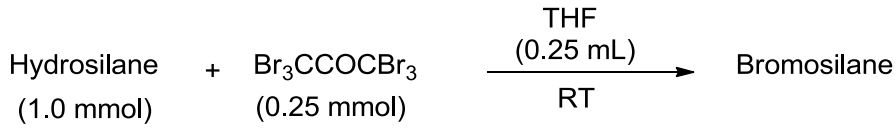
According to the results presented in Table 3.3, 1,4-dioxane and MTBE (methyl *tert*-butyl ether), which are less polar solvents (entries 2 and 3), gave the desired product in low yield. THF provided good yield of TIPS-Br (entry 1). Thus, THF was found to be appropriate for the bromination of TIPS-Br using HBA.

3.4 The Application of the Developed Procedure for the Synthesis of Bromosilanes

Several hydrosilanes: triethylhydrosilane (Et_3SiH), triphenylsilane (Ph_3SiH), dimethylphenylsilane ($PhMe_2SiH$), *tris*-trimethylsilylhydrosilane ($(Me_3Si)_3SiH$)

chlorodiphenylhydrosilane (Ph_2ClSiH) and *tert*-butyldimethylsilane (*t*-$BuMe_2SiH$) were selected to explore the scope of this developed methology. The results are shown in Table 3.4.

Table 3.4 Synthesis of bromosilanes using HBA



Entry	Hydrosilane	Time (min)	% Yield of Si-Br	% Recovery of Si-H	%MB
1	$(i\text{-Pr})_3SiH$	5	56	37	93
2		10	69	23	92
3		20	91	3	94
4	Et_3SiH	20	53	55	108
5	*t*-$BuMe_2SiH$	10	28	63	91
6		20	37	63	100
7	$PhMe_2SiH$	10	98	6	104
8	$(Me_3Si)_3SiH$	10	94	10	104
9	Ph_3SiH	5	73	27	100
10		10	quant	0	100
11	Ph_2ClSiH	10	60	40	100
12		20	85	14	99

All reactions were performed under optimal conditions: 0.25 mmol HBA at RT. Reactions of Et_3SiH and *t*-$BuMe_2SiH$ gave low yields at 20 min (entries 4 and 6). At 10 min, the bromination of *t*-$BuMe_2SiH$ and Ph_2ClSiH afforded the bromo derivative in 28 and 60% yields, respectively (entries 5 and 11). The attempt to increase the yield was carried out by prolonging the reaction time. In the case of *t*-$BuMe_2SiH$, when increasing reaction time to 20 min, the yield did not raise much (entry 6). For Ph_2ClSiH, raising of the desired product (85% yield) was achieved by

prolonging the reaction time to 20 min (entry 12). While those of $(i\text{-Pr})_3SiH$ and Ph_2ClSiH were increased to 91 and 85% at 20 min. (entries 3 and 12). However, in the case of $PhMe_2SiH$, $(Me_3Si)_3SiH$, Et_3SiH and Ph_3SiH, good yield could be achieved at 10 min (entries 4, 7–8 and 10). In case of entry 9, decreasing reaction time to 5 min, also reduced the yield of product to 73%. So, the reaction time for 10 min was proper for the preparation of triphenylsilylbromide. There were characterized identities by ^1H NMR. An example of ^1H NMR of the crude reaction mixture of triethylsilane (Et_3SiH) is presented in Figure 3.3. The quartet signal of two protons at δ_H 0.58 ppm could be assigned to $Si(C\underline{H}_2CH_3)_3$ of the substrate, while the triplet signal at δ_H 1.07 ppm could be assigned to $Si(CH_2C\underline{H}_3)_3$.

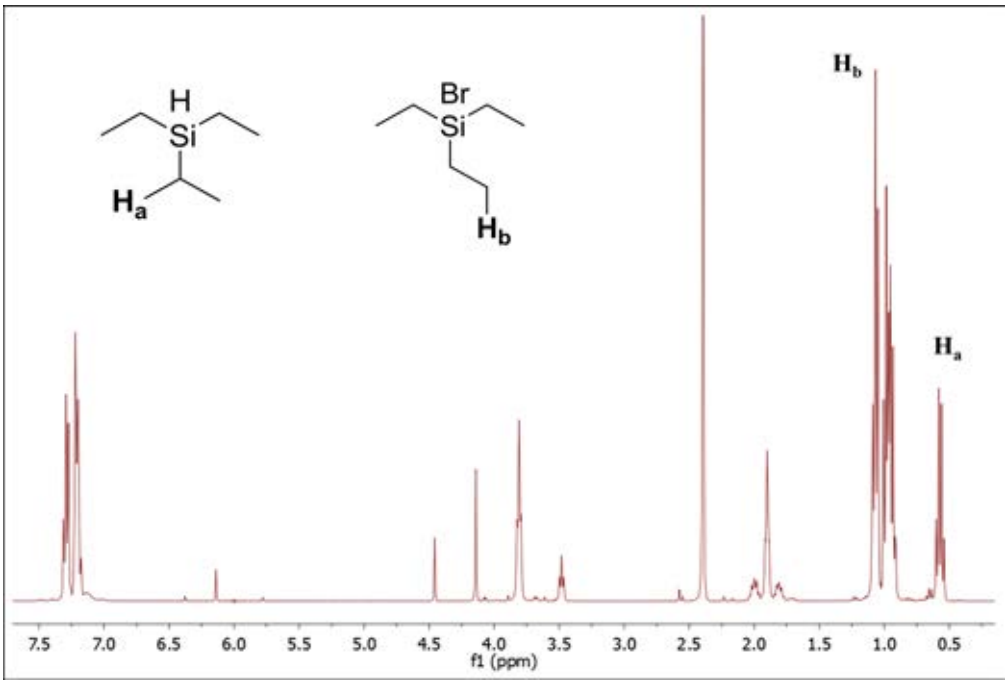
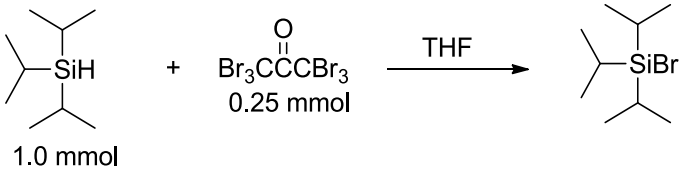


Figure 3.3 The ^1H NMR spectrum of the crude reaction mixture of Et_3SiH with HBA (from entry 4, Table 3.4)**.**

3.4 Other Reaction Conditions

Four diverse reaction conditions: RT, sonication, UV radiation and refluxing THF were investigated on bromination of TIPS-H and the results are presented in Table 3.5.

Table 3.5 Condition optimization for the synthesis of TIPS-Br using HBA



Entry	Condition	Time (min)	%Yield of TIPS-Br	%Recovery of TIPS-H	%MB
1	RT	5	56	37	93
2		10	69	23	92
3		20	91	3	94
4	Sonication	5	85	6	91
5		10	90	0	90
6		15	quant	0	100
7	UV	5	84	12	96
8	Reflux	5	83	8	91

Table 3.5 reveals that only 56% yield of the desired product was attained within 5 min at RT (entry 1). The reactions performing using sonication, UV light (254 nm, 6W) and refluxing THF in 5 min, nonetheless, provided much better yield of TIPS-Br at 85, 84 and 83% yields, respectively (entries 4 and 7–8). The increasing yield of product using sonication was achieved by prolonging the reaction time from 5 to 15 min (entries 4–6). The quantitative yield of TIPS-Br could be accomplished using sonication in 15 min (entry 6). One of possible mechanisms is a radical process as presented in Scheme 3.1.

3.5 The Proposed Mechanism for the Production of Bromosilanes Using HBA

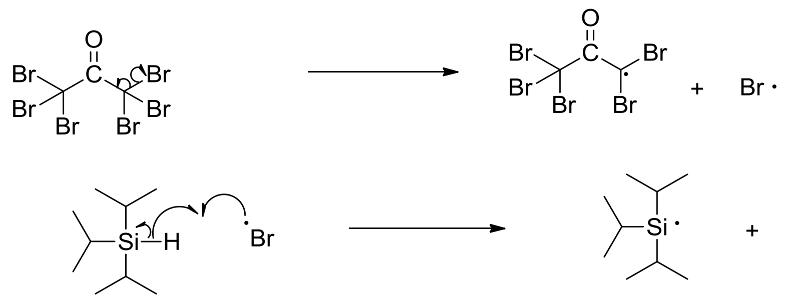
The mechanism for the preparation of bromosilanes from hydrosilanes using HBA has never been reported. It was believed that the reaction mechanism should take place *via* a radical process, the generation of radical was based on type of solvent [42]. While HBA in a solid state is white, the solution of HBA in THF gave yellow color. It was assumed that HBA could generate Br• and subsequently two Br• combined to become Br_2, which normally was yellow-orange. If HBA was an initiator

which would behave decomposition rate in various solvents. In general, initiators have value of bond dissociation energy in the rage of 100-170 kJ mol^{-1} [43], (To compared with C-Br bond in CBr_4 was 205 kJ mol^{-1} [44]) C-Br bond in HBA was assumed to be of lower dissociation energies, thus will dissociate very rapidly. To prove this assumption, an experiment was conducted in which a radical scavenger, such as 2,2-diphenyl-1-picrylhydrazyl (DPPH), was added to the general procedure to trap the Br•. DPPH has been shown to change color from violet to yellow when combined with a radical [45]. From this experiment, the color of the solution was changed from violet to yellow indicating that radicals in the reaction mixture were generated then which were trapped by DPPH. Therefore, the first step of the mechanism was the homolytic cleavage of C-Br bond of HBA to generate Br•.

The proposed mechanism is displayed in Scheme 3.1. In the initial step, homolysis of HBA to form Br• was initiated. A bromine atom had an unpaired electron and acted as a free radical. In the next step, the propagation, Br• induced the cleavage of Si-H bond into Si• **(a)**. Si• then reacted with HBA. Resulting in the desired product plus another •CBr_2COCBr_3. This radical would then go on to take part in another propagation reaction of the bromination reaction.

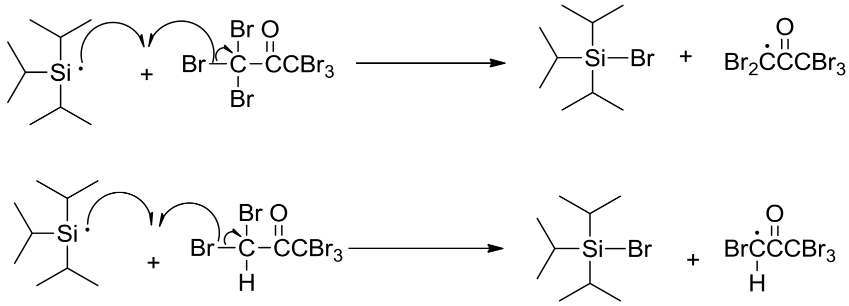
In the last step, various reactions between possible pairs of radicals allowed the formation of TIPS-Br **(b)**, other products **(c)** from HBA and Br_2. Other products such as $HBr_2CCOCBr_2H$ **(c)** and BrH_2CCOCH_2Br and other derivatives of HBA may be formed. These by-products were detected as shown in the ^1H NMR spectrum (Figure 3.3).

Step I (Initiation)

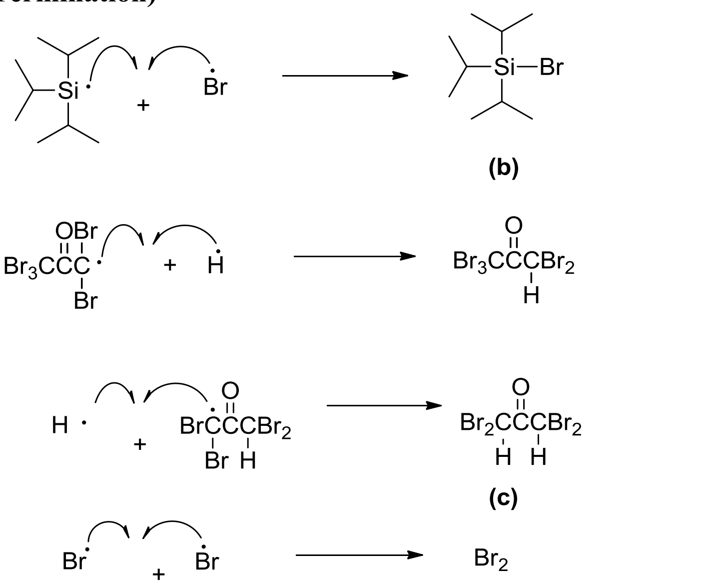


(a)

Step II (Propagation)



Step III (Termination)



Scheme 3.1 The proposed mechanistic pathway for the conversion of hydrosilanes to bromosilanes using HBA.

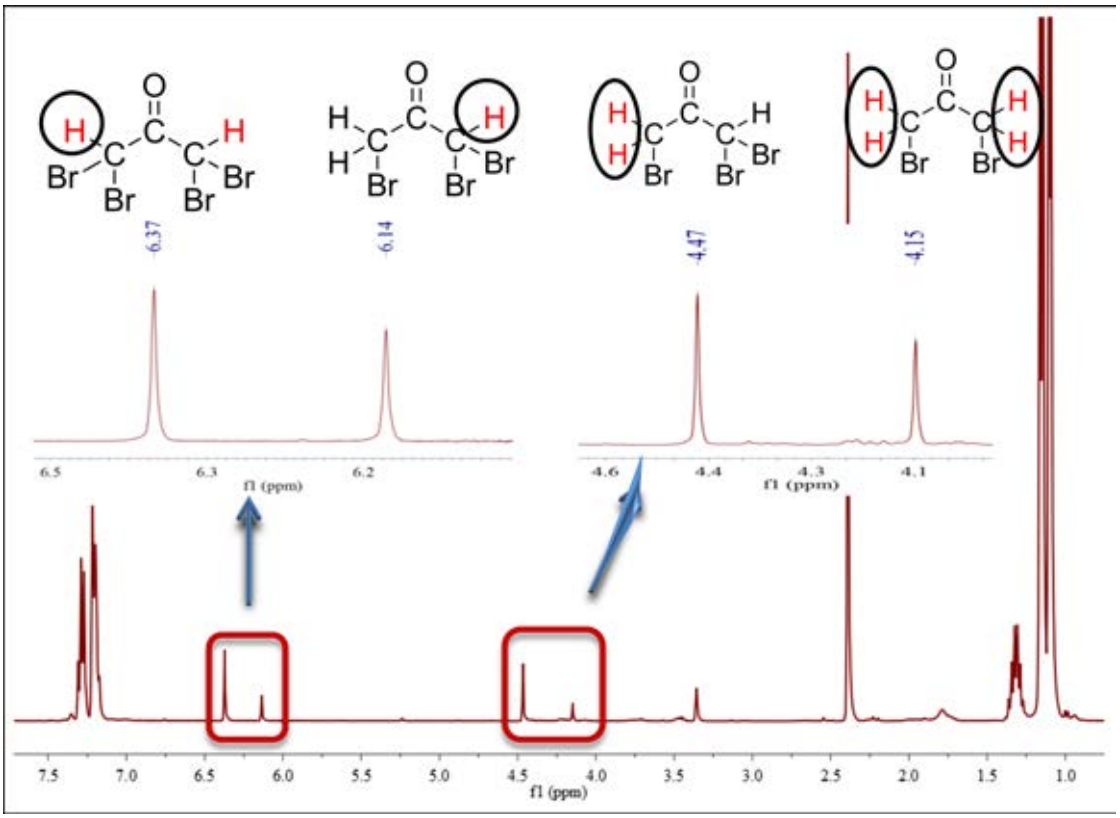


Figure 3.4 ^{1}H NMR spectrum of the crude reaction mixture of TIPS-H with HBA**.**

According to Figure 3.4, singlet peaks at δ_H 6.37, 6.14, 4.47 and 4.15 ppm were assigned to a signal of $Br_2C\underline{H}COC\underline{H}Br_2$, $BrCH_2COC\underline{H}Br_2$, $BrC\underline{H}_2COCHBr_2$, and $BrC\underline{H}_2COC\underline{H}_2Br$, respectively [46-47]. These peaks belong to by-products from the reactions of hydrosilanes to bromosilanes using HBA showing that not all Br's on HBA were used in the reactions. Based on the yield of the product and the amount of HBA used, the bromine efficiency of HBA could be calculated. For example, in the reactions at RT in entries 2 and 3 in Table 3.2, 1 mol of HBA had bromine efficiency of 276% and 364%, respectively, meaning one molecule of HBA could provide around 3 bromine radicals per molecule at RT. To improve the bromine efficiency, different reaction conditions were performed in which reactions under sonication, UV irradiation and reflux (Table 3.5) were investigated. The bromine efficiency could be increased to 4 atoms/HBA molecule for bromination of TIPS-H under the following conditions: 1.0 mmol TIPS-H as a substrate and 0.25 mmol HBA as a brominating agent under sonication in THF for 15 min.

3.6 Optimum Conditions for the Cleavage of Ethers Using HBA and PPh_3

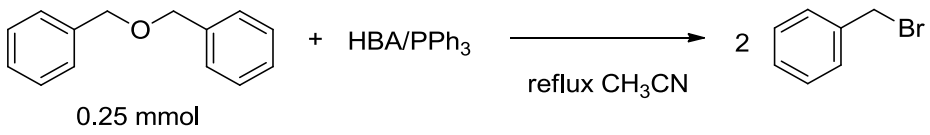
3.6.1 The Cleavage of Linear Ethers

The search for optimum conditions for the cleavage of linear ethers including the effect of mole ratio of HBA:PPh_3, solvent and reaction time was carried out. Dibenzyl ether (DBE) was selected as a model substrate.

3.6.1.1 Effect of Mole Ratio of HBA:PPh_3

For optimizing reaction conditions, the effect of the mole ratio of DBE:HBA:PPh_3 was explored with the aim to obtain the most appropriate mole ratio of DBE:HBA:PPh_3 at refluxing CH_3CN. The results are shown in Table 3.6.

Table 3.6 The effect of mole ratio of DBE:HBA:PPh_3 on the cleavage of DBE



0.25 mmol

Entry	Mole ratio DBE:HBA:PPh_3	Time (h)	% Yield of C_7H_7Br	% Recovery of DBE	%MB
1	1:1:2	2	12	88	100
2	1:2:2	2	18	82	100
3	1:2:3	2	27	75	102
4	1:2:4	2	50	54	104
5	1:2:4	4	63	37	100
6	1:2:4	7	quant	0	100
7	1:3:4	2	54	49	103

From Table 3.6, the mole ratio of DBE:HBA:PPh_3 at 1:1:2 yielded the product around 12% yield (entry 1). The yield of the desired benzyl bromide was increased from 27 to 50 % upon raising the mole ratio of PPh_3 (3 to 4 equivalents). However, as shown in entries 4 and 7, the increase in mole ratio of HBA only slightly increased the yield of benzyl bromide. Therefore, the optimum mole ratio (DBE:HBA:PPh_3) for the

cleavage of DBE was 1:2:4. Upon extending the reaction time (entries 5–6), the better yield of product was obtained. Entry 6 revealed that the reaction time at 7 h was enough to produce quantitative yield, performing at reflux CH_3CN.

The ^1H NMR spectrum of the crude reaction mixture of DBE with HBA and PPh_3 from entry 5 (Table 3.6) is presented in Figure 3.5.

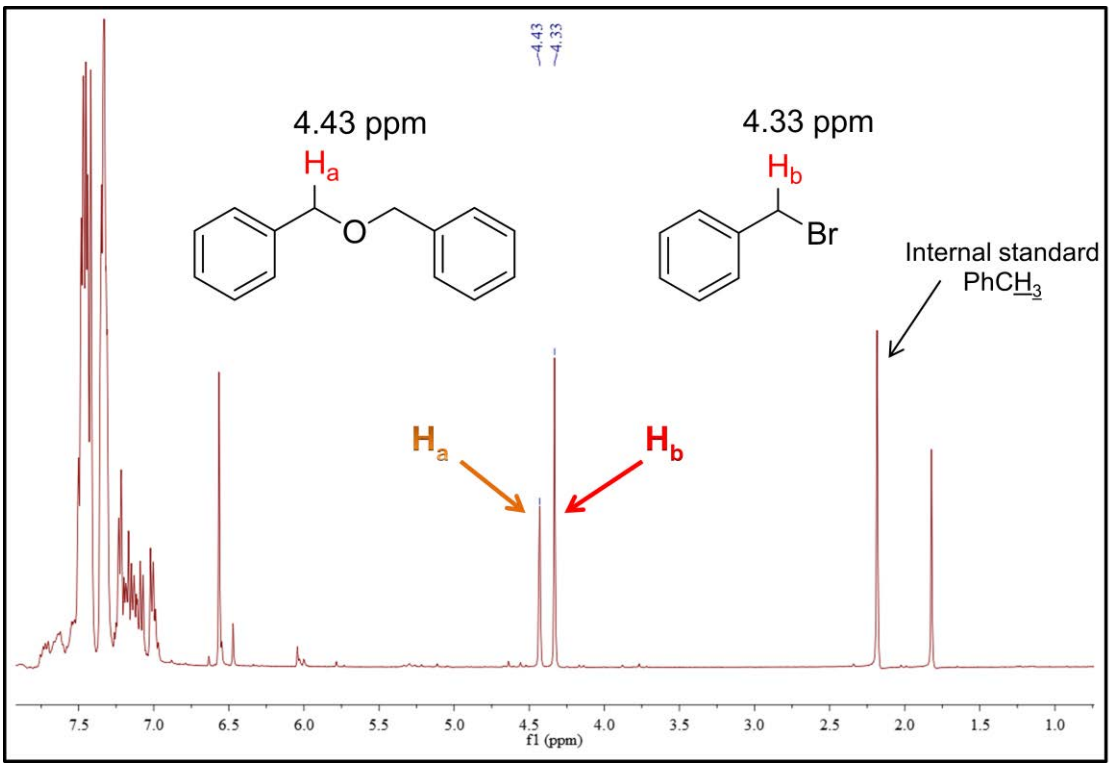


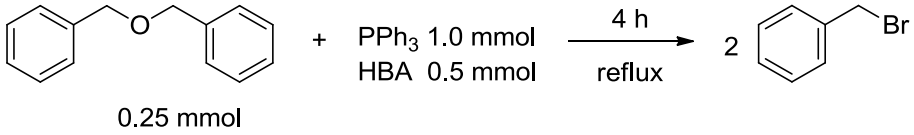
Figure 3.5 The ^1H NMR spectrum of the crude reaction mixture of DBE with HBA:PPh_3.

From Figure 3.5, the peak areas of H_a (δ_H 4.43) and H_b (δ_H 4.33) were taken to calculate the percent recovery of starting material and product, respectively.

3.6.1.2 Effect of Solvent

Various solvents were tried to observe their effects on the outcome of the reaction and the results are presented in Table 3.7.

Table 3.7 The effect of solvents on the cleavage of DBE



Entry	Solvent	%Yield of C_7H_7Br	%Recovery of DBE	%MB
1	CH_2Cl_2	13	84	97
2	CH_3CN	63	37	100
3	Toluene	98	0	98

According to the results presented in Table 3.7, less yield was obtained when CH_2Cl_2 was used (entry 1). Only 50% yield of the desired product was achieved within 4 h at refluxing CH_3CN (entry 2). Nonetheless, DBE could be cleaved to benzyl bromide in the highest yield in refluxing toluene (entry 3). Toluene provided higher refluxing temperature (108 °C). This was thus a better condition for the cleavage of ether. Therefore, toluene was the proper solvent for the preparation of benzyl bromide.

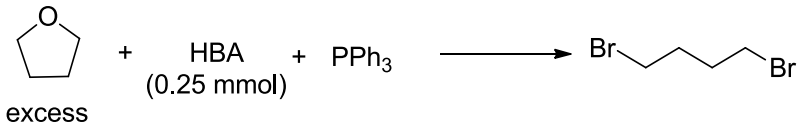
3.6.2 The Cleavage of Cyclic Ethers

The effect of the mole ratio of HBA:PPh_3 for the cleavage of cyclic ethers was investigated. THF was selected as a model substrate. Because THF has low boiling point (66 °C), THF was thus used in an excess amount as both starting material and solvent. The calculation of the percent yield of products in this case is based on the amount of limiting reagent HBA.

3.6.2.1 Effect of Amount of PPh_3

To optimize the reaction conditions, the effect of the mole ratio of HBA:PPh_3 was explored with the aim to obtain the most appropriate amount of PPh_3 for the cleavage of THF. The results are presented in Table 3.8.

Table 3.8 The effect of amount of PPh_3 on the cleavage of THF



Entry	Equivalent PPh_3	Time (min)	Temp.	% Yield[a]
1	1	20	RT	19
2	1	30	reflux	64
3	1	120	reflux	95
4	2	5	reflux	84
5	2	15	reflux	97
6	2	20	reflux	106
7	3	20	reflux	112
8	5	20	reflux	112

[a] based on HBA

From Table 3.8, entry 1 revealed that 1 equiv of PPh_3 at RT for 20 min provided only 19% of the desired product. When the reaction was carried out in refluxing THF with the reaction time prolonging to 120 min, the yield of 1,4-dibromobutane was increased significantly (entry 3). The attempt to lessen the reaction time was carried out, it was clearly found that increasing amount of PPh_3 to 2 equivalent (entries 4–6) was required. The product was attained in quantitative yield when prolonging the reaction time to 20 min (entry 6). The yield of product was constant when increasing PPh_3 to 3 or 5 equivalents (entries 7–8) indicating that 0.25 mmol of HBA reacted completely with 0.5 mmol of PPh_3 (2 equivalents). Therefore, HBA:PPh_3 in the ratio of 1:2 in excess THF at refluxing THF for 20 min was considered the most proper conditions for the cleavage of THF to 1,4-dibromobutane. The ^{1}H NMR spectrum of the crude reaction mixture of THF with HBA and PPh_3 is presented in Figure 3.6.

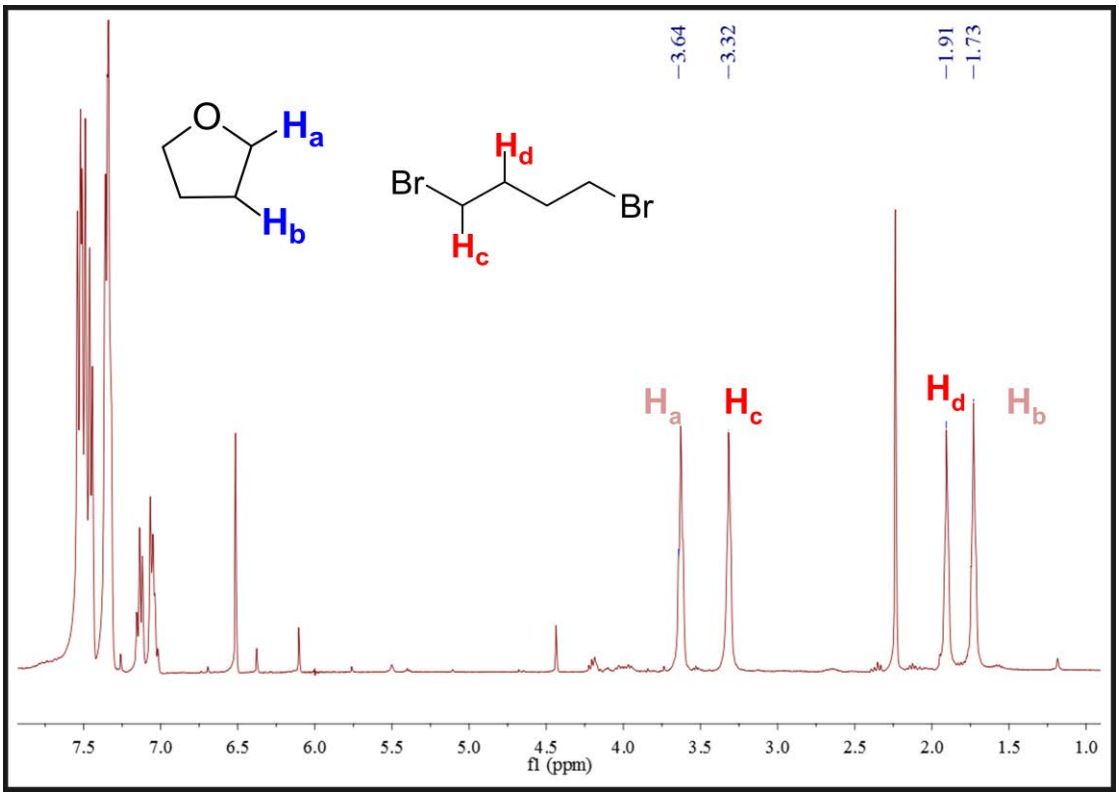


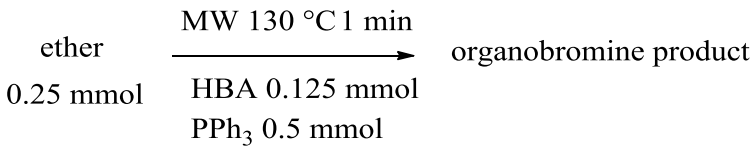
Figure 3.6 The ^{1}H NMR spectrum of the crude reaction mixture of THF with HBA: PPh_3.

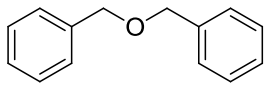
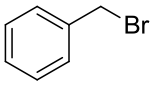
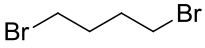
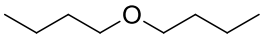
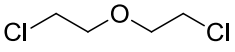
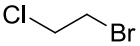
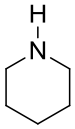
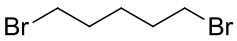
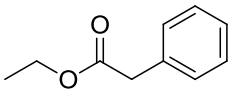
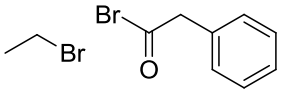
From Figure 3.6, the percentage yield of the product was calculated by using the integration of peak H_c (δ_H = 3.32 ppm) and H_d (δ_H = 1.91 ppm). H_a and H_b are the protons of remained substrates.

3.7 Application of Microwave Technique for Cleavage of Ethers

To reduce the reaction time of previous investigation, microwave technique was a good tool. The results are tabulated in Table 3.9.

Table 3.9 The cleavage of ethers using HBA/PPh_3 with the aids of MW irradiation in free solvent system



Entry	Substrate	Product	%Yield of Product	%Recovery of Substrate	%MB
1			92	0	92
2			91	0	91
3			0(54)[a]	100(50)[a]	100(104)[a]
4			32	61	93
5			90	0	90
6			58	33	91

[a] Microwave 180 °C, 3 min, 0.25 mmol HBA, 1.0 mmol PPh_3

DBE and THF (entries 1–2) could be cleaved at the C-O bond to benzyl bromide and 1,4-dibromobutane in high yield. The cleavage of di-*n*-butyl ether could not be accomplished under the standard conditions. The attempts trying to increase the yield was carried out by raising up the reaction temperature to 180 °C, prolonging the reaction time from 1 to 3 min and increasing the ratio of HBA and PPh_3. The yield of the desired 1-bromobutane was attained in higher yield, up to 54% (entry 3). When 2-chloroethyl ether was employed, the desired 1-bromo-2-chloroethane was obtained in

low yield (32%, entry 4). In addition, it should be noted that under this developed conditions, cyclic amine and ester could be cleaved (entries 5–6). In the case of piperidine, this reaction gave 90% yield of the desired 1,5-dibromopentane. For the reaction of ethyl phenyl acetate, two products as ethyl bromide and 2-phenylacetyl bromide were obtained in moderate yield (58%, entry 6). It was clearly found that MW irradiation could be used in the process of cleavage of ether, amine and ester to gain the desired bromo products using very short reaction time.

3.8 Optimum Conditions for the Cleavage of Epoxides Using HBA and PPh_3

The search for optimum conditions for the cleavage of epoxides using HBA/PPh_3 including the effect of mole ratio of epoxide:HBA:PPh_3, reaction time and solvents was investigated. Preliminary experiments revealed that two main reactions: the formation of bromohydrin and that of *trans*-1,2-dibromo compounds were proceeded depending upon the reactions conditions. For the former transformation, styrene oxide was selected as a model substrate, while the latter used cyclohexene oxide as a model compound.

3.8.1 The Transformation of Epoxides to Bromohydrins

3.8.1.1 Effect of Reaction Time

Preliminary experiment revealed that the cleavage of styrene oxide with HBA/PPh_3 proceeded extremely fast, approximately one minute, yielding the target compound, 2-bromo-2-phenylethanol in quantitative yield. Thus, reaction time of 1 min was used for further examination.

Figure 3.8 shows the ^{1}H NMR spectrum of isolated 2-bromo-2-phenylethanol from the crude mixture (Figure 3.7). The ^{1}H NMR spectrum of 2-bromo-2-phenylethanol reveals the proton of –C<u>H</u>Br resonating at δ_H 5.06 (*t*, 1H, J = 8.0 Hz), -C<u>H</u>$_2$OH at δ_H 4.06-3.96 (*m*, 2H) and –O<u>H</u> at δ_H 2.38 (*s*).

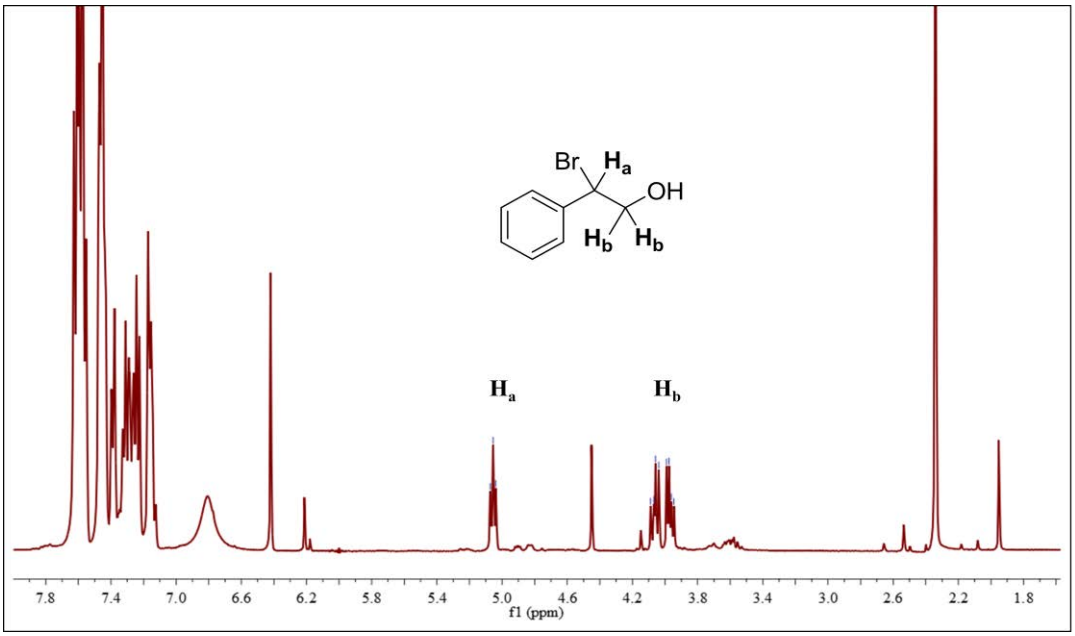


Figure 3.7 The ^{1}H NMR spectrum of the crude reaction mixture of 2-bromo-2-phenylethanol.

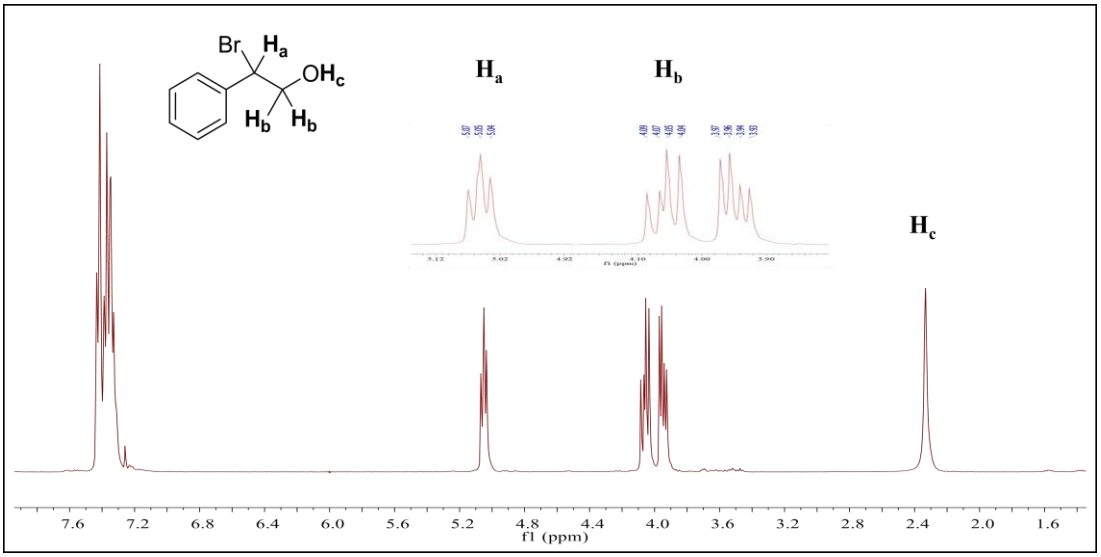
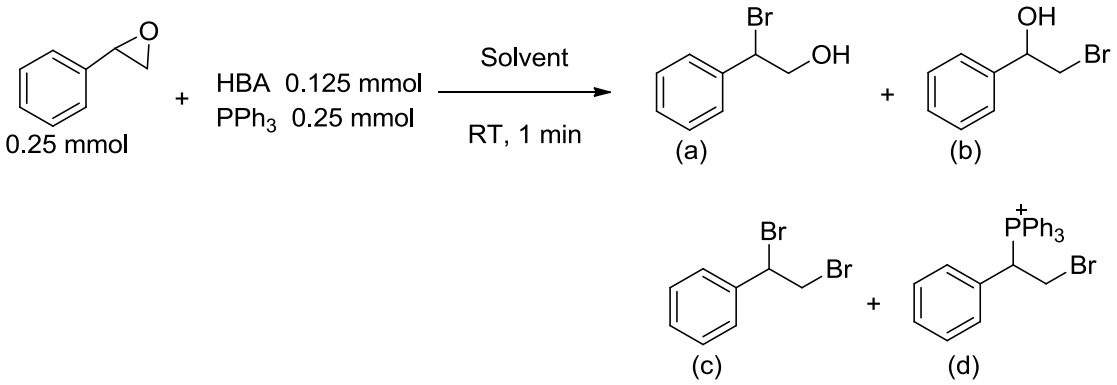


Figure 3.8 The ^{1}H NMR spectrum of 2-bromo-2-phenylethanol.

3.8.1.2 Effect of Solvent

To observe the effect of solvents, diverse common organic solvents (0.50 mL): CH_2Cl_2, $CHCl_3$ and CH_3CN were chosen. The reaction was carried out at RT for 1 min. The results are tabulated in Table 3.10.

Table 3.10 The effect of solvent on the ring opening of styrene oxide using HBA/PPh_3



Entry	Solvent	% Yield				% Recovery	%MB
		(a)	(b)	(c)	(d)		
1	CH_2Cl_2	18	12	8	30	38	106
2	$CHCl_3$	38	12	0	0	44	94
3	CH_3CN	quant	0	0	0	0	100

CH_2Cl_2 and $CHCl_3$ provided different amount of products (entries 1 and 2). Surprisingly, when CH_3CN was used, 2-bromo-2-phenylethanol (a) was obtained as a sole product in quantitative yield (entry 3). The ^1H NMR spectrum of different products is shown in Figure 3.8. The proposed mechanism of styrene oxide reaction is shown in Scheme 3.2.

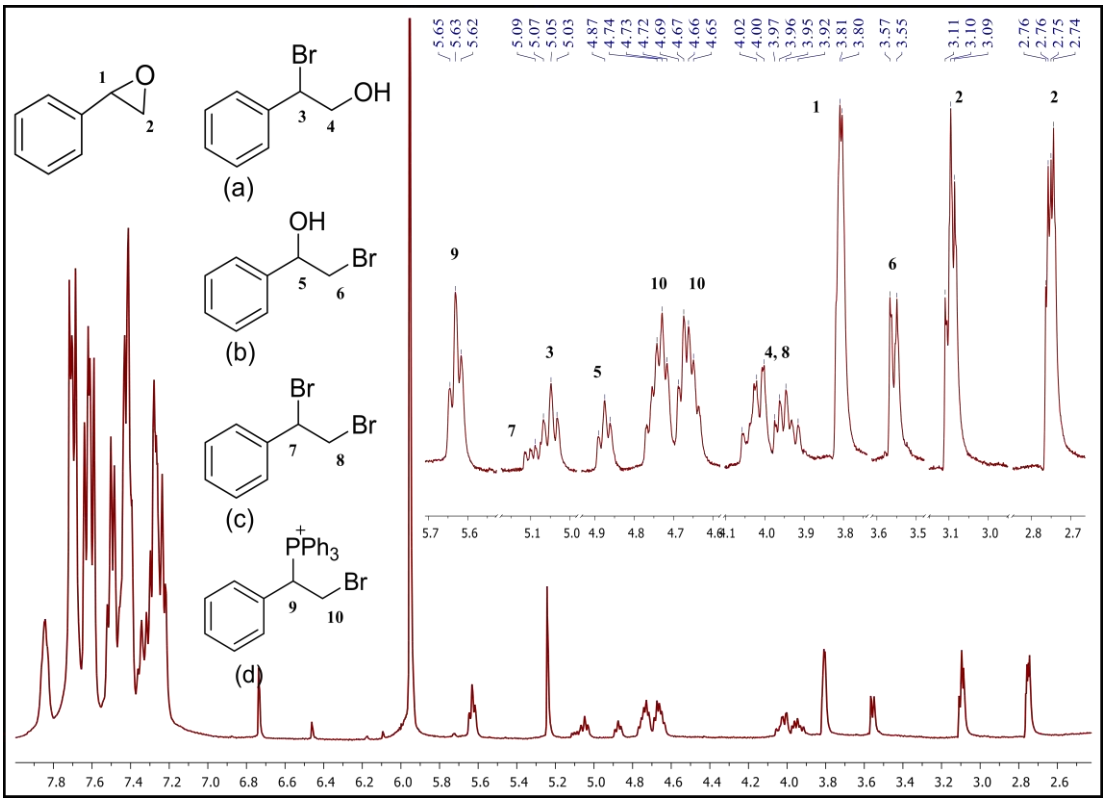
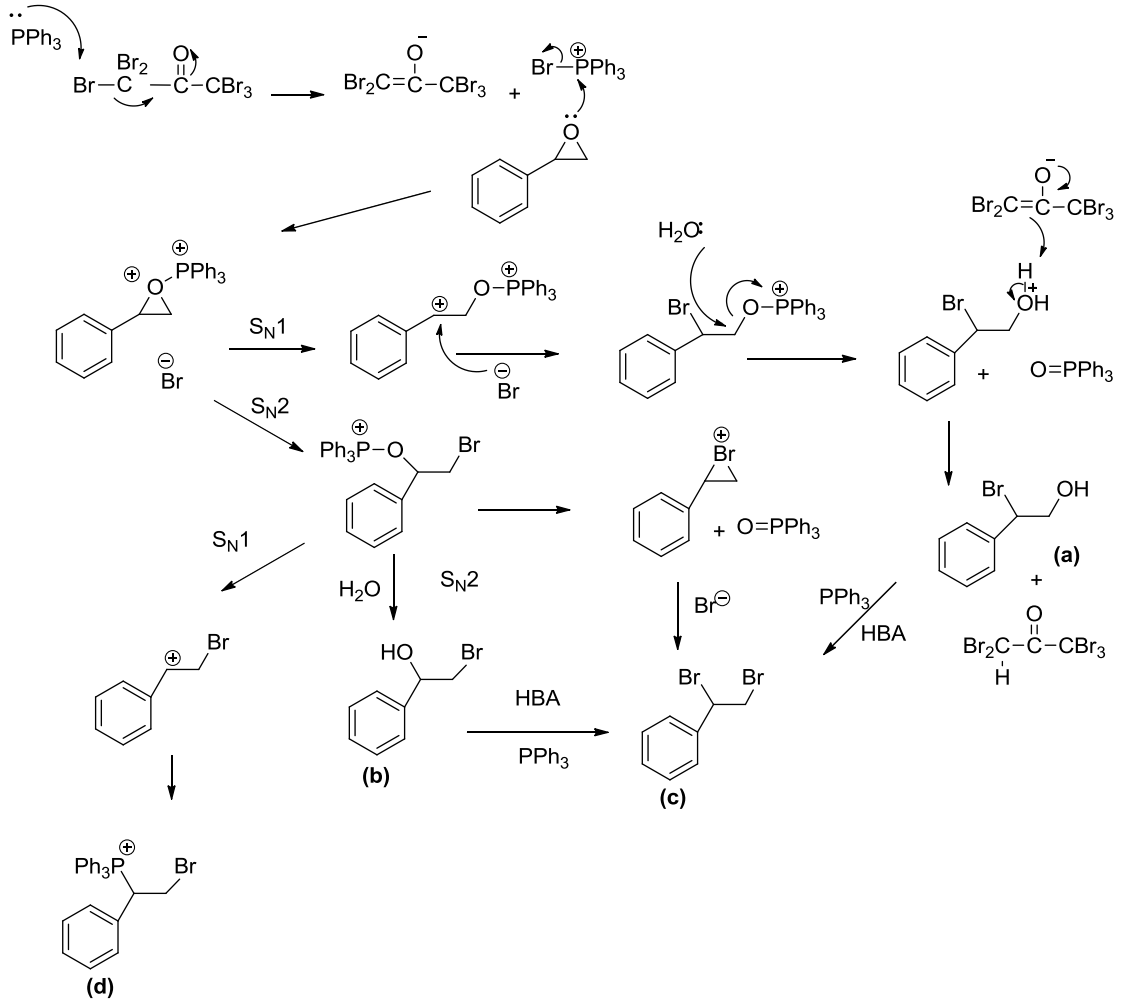


Figure 3.9 The ^{1}H NMR spectrum of the crude reaction mixture of styrene oxide with HBA/PPh_3 in CH_2Cl_2 (entry 1 in Table 3.10).

Referring to Figure 3.9, the reaction in CH_2Cl_2 gave many products, a triplet peak at δ_H 5.06 ppm could be assigned for the signal of –C<u>H</u>Br and at δ_H 4.06-3.96 was a signal of –C<u>H</u>$_2$OH of 2-bromo-2-phenylethanol **(a)**. Two peaks observed the ^{1}H NMR spectrum of 2-bromo-1-phenylethanol **(b)** could be assigned for the signal of –C<u>H</u>$_2$Br and –C<u>H</u>OH resonating at δ_H 4.87 and δ_H 3.58-3.54 ppm, respectively. A triplet peak at δ_H 5.09 ppm could be assigned for the signal of –C<u>H</u>Br and at δ_H 4.07-3.92 was a signal of –C<u>H</u>$_2$Br of (1,2-dibromoethyl)benzene **(c)**. The ^{1}H NMR spectrum of (phenylethyl)-triphenylphosphonium salt **(d)** reveals two peaks of a triplet peak at δ_H 5.63 ppm could be assigned for the signal of –C<u>H</u>($^{+}$$PPh_3$) and at δ_H 4.74-4.65 was a signal of –C<u>H</u>$_2$Br.



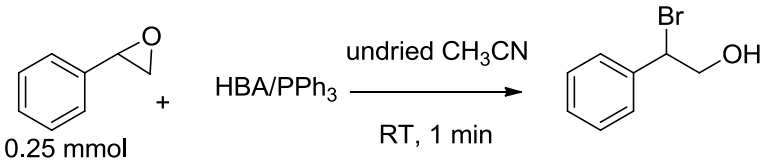
Scheme 3.2 The mechanism for the ring-opening of styrene oxide with HBA/PPh_3

As shown in Scheme 3.2, styrene oxide could be converted to four products: 2-bromo-2-phenylethanol **(a)**, 2-bromo-1-phenylethanol **(b)**, (1,2-dibromoethyl)benzene **(c)** and (2-bromo-1-phenylethyl)triphenylphosphonium **(d)**. This conversion was operated using moderately polar solvent, thus product **(a)** was likely to produce *via* S_N1.

3.8.1.3 Effect of Mole Ratio of HBA:PPh_3

The effect of mole ratio of HBA:PPh_3 was examined and the results are shown in Table 3.11.

Table 3.11 The effect of mole ratio of HBA:PPh_3 on the ring opening of styrene oxide



Entry	HBA (equiv.)	PPh_3 (equiv.)	% Yield of bromohydrin	% Recovery of epoxide	%MB
1	0.5	1.5	quant	0	100
2	0.5	1.0	quant	0	100
3	0.5	0.5	71	30	101
4	0.5	0	0	100	100
6	0.25	1.0	75	26	101

Under the specified conditions, the desired product was obtained in high yield. When the reaction was carried out in the absence of PPh_3, no reaction took place (entry 4). The use of more than 1.0 equiv of PPh_3 to styrene oxide gave quantitative yield of target molecule (entries 2–3). It is also important to note that employing PPh_3 1.0 equiv (entry 2) also provided a quantitative yield of 2-bromo-2-phenylethanol within 1 min at RT.

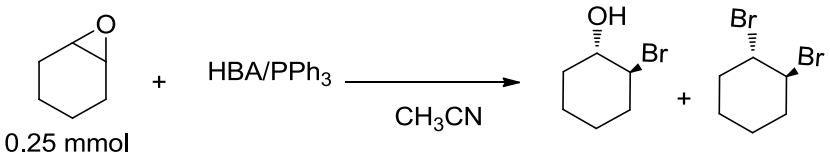
3.8.2 The Transformation of Epoxides to *trans*-1,2-Dibromo Compounds

Cyclohexene oxide was used as a model epoxide. Several factors including the mole ratio of HBA and PPh_3, reaction time and solvent were varied to explore the efficiency of the reaction.

3.8.2.1 Effect of Solvent and the Mole Ratio of HBA:PPh_3

The reaction condition was optimized for the transformation of epoxides to *trans*-1,2-dibromo compounds. Cyclohexene oxide was selected as a model. The results are collected in Table 3.12.

Table 3.12 The effect of solvent and the mole ratio of HBA:PPh_3



Entry	HBA (equiv.)	PPh_3 (equiv.)	Dried	%Yield		% Recovery	%MB
				mono-Br	di-Br		
1	0.5	1	No	quant	0	0	100
2	0.5	1	Yes	63	47	0	100
3	1	2	Yes	29	72	0	101
4	2	3	Yes	0	quant	0	100
5	2	3	No	quant	0	0	100

Table 3.12 demonstrates that when the reaction was carried out at RT for 1 min in undried CH_3CN with the equivalents of HBA and PPh_3 at 0.5 and 1, respectively, a quantitative yield of 2-bromo-2-phenylethanol was obtained (entry 1). Nonetheless, under the same reaction condition except for the dried CH_3CN, only 47% of *trans*-1,2-dibromocyclohexane was detected (entry 2). Surprisingly, under the conditions using dried CH_3CN and increasing the equivalent of HBA:PPh_3 from 0.5:1 to 2:3 (entries 2–4), *trans*-1,2-dibromocyclohexane was achieved in quantitative yield (entry 4). Therefore, the most suitable conditions for the production of *trans*-1,2-dibromocyclohexane was in dried CH_3CN. Entries 2–4 show that increasing the amount of HBA:PPh_3 increased the production of *trans*-1,2-dibromocyclohexane. However, when the amount of HBA and PPh_3 was lifted to 2 and 3 in undried CH_3CN, the bromohydrin product was detected in quantitative yield. That was due to some water remained in the solution altered the product of the reaction became *trans*-1,2-bromohydrin.

In conclusion, moisture in solvent was a very crucial effect. The proposed mechanism for the formation of *trans*-1,2-bromohydrin and *trans*-1,2-dibromo compounds is presented in Scheme 3.3.

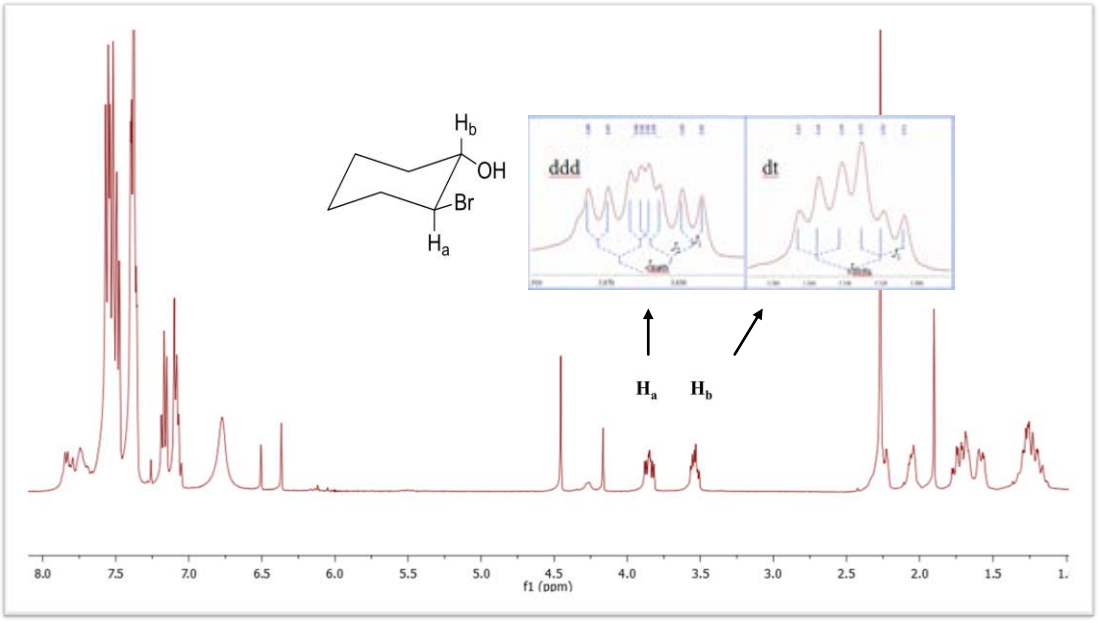


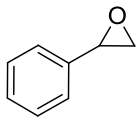
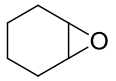
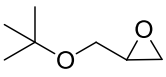
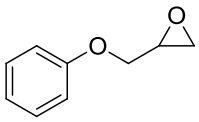
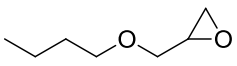
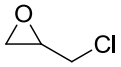
Figure 3.10 The ^{1}H NMR spectrum of the crude reaction mixture of cyclohexene oxide with HBA in undried CH_3CN at RT for 1 min (entry 1 in Table 3.12)**.**

From Figure 3.10, the reaction in entry 4, *trans*-2-bromocyclohexanol was the main product in almost quantitative yield. The peak of product could be confirmed by the presence of the doublet of doublet of doublet (*ddd*) signal of –C*H*Br (H) with J = 11.6, 4.3, 8.2 Hz at δ_H 3.84 ppm and doublet of triplet (*dt*) signal of –C*H*OH (H) with J = 14.4, 4.6 Hz at δ_H 3.5 ppm. The high value of coupling constant clearly implied the *trans*-configuration of the product [48].

3.9 The Application of the Developed Procedure for the Synthesis of *trans*-1,2-Bromohydrin and *trans*-1,2-Dibromo Compounds from Epoxides

The application of this developed protocol to convert various epoxides and related compounds into *trans*-1,2-bromohydrin and *trans*-1,2-dibromo compounds using CH_3CN was further investigated. The results are shown in Table 3.13.

Table 3.13 Synthesis of *trans*-1,2-bromohydrins from epoxides using HBA/PPh_3

Entry	Substrate 0.25 mmol	Mole Ratio HBA	Mole Ratio PPh_3	Dried	% Yield Bromohydrin	% Yield Dibromo
1		0.5	1	No	quant [a]	0
2		2	3	Yes	0	97
3		0.5	1	No	quant	0
4		2	3	Yes	0	93
5		0.5	1	No	98 [b]	0
6		2	3	Yes	0	quant
7		0.5	1	No	quant [c]	0
8		2	3	Yes	0	quant
9		0.5	1	No	96 [d]	0
10		2	3	Yes	0	94
11		0.5	1	No	quant [e]	0
12		2	3	Yes	0	quant

[a] $PhCHBrCH_2OH$
[b] $(CH_3)_3COCH_2CH(OH)CH_2Br$
[c] $PhOCH_2CH(OH)CH_2Br$
[d] $CH_3(CH_2)_3OCH_2CH(OH)CH_2Br$
[e] $CH_2BrCH(OH)CH_2Cl$

The attempt to utilize this developed procedure for the synthesis of *trans*-1,2-bromohydrin and *trans*-1,2-dibromo compounds was carried out. The quantitative yield of all desired *trans*-1,2-bromohydrins could be fruitfully achieved by using undried CH_3CN (entries 1, 3, 5, 7, 9 and 11). On the other hand, suitable conditions

for the synthesis of *trans*-1,2-dibromo compounds were achieved using the mole ratio of HBA:PPh_3 at 2:3 in dried CH_3CN (entries 2, 4, 6, 8, 10 and 12). All compounds were characterized their identities by ^1H NMR spectrum. Two examples of the crude reaction mixture of butylglycidyl ether and phenylglycidyl ether with HBA/PPh_3 in undried CH_3CN are presented in Figures 3.11 and 3.12.

This disclosure was particularly useful for the preparation of *trans*-1,2-bromoalcohol and *trans*-1,2-dibromo compounds from epoxides. The reaction could easily control the formation of the desired products and the reaction conditions were extremely mild and very fast with quantitative yield and high regioselectivity.

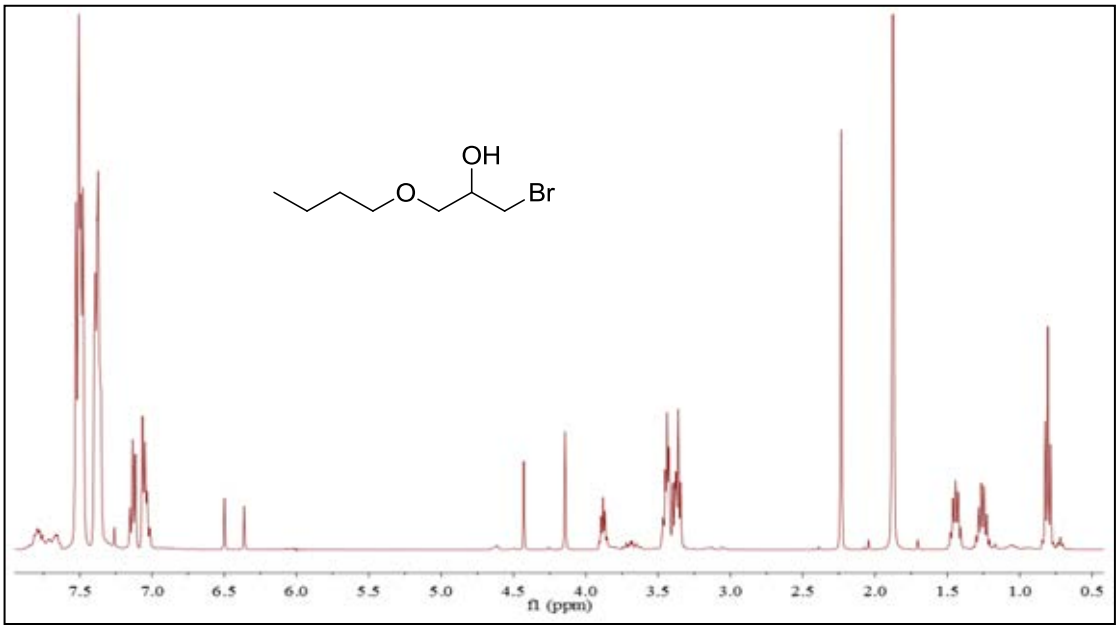


Figure 3.11 The ^1H NMR spectrum of the crude reaction mixture of butylgylcidyl ether with HBA/PPh_3 in undried CH_3CN at RT for 1 min.

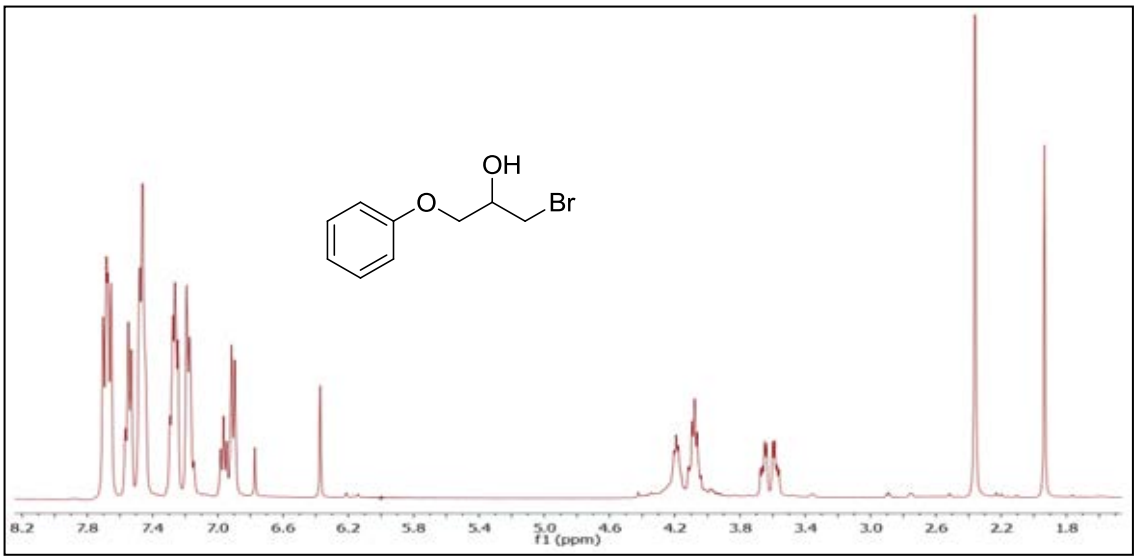
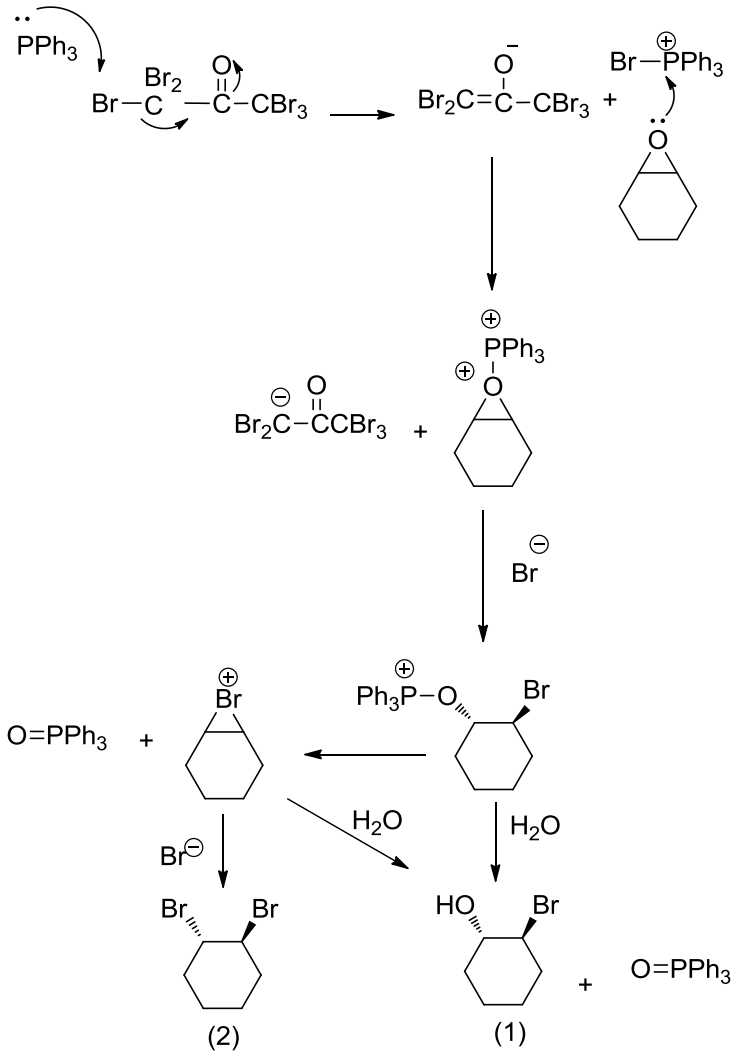


Figure 3.12 The ^{1}H NMR spectrum of the crude reaction mixture of phenylgylcidyl ether with HBA/PPh_3 in undried CH_3CN at RT for 1 min.

3.10 The Proposed Mechanism of Ring Opening of Cyclohexene Oxide

The mechanism for the ring opening of cyclohexene oxide to *trans*-2-bromocyclohexanol and *trans*-1,2-dibromocyclohexane using HBA/PPh_3 has never been reported. The proposed mechanism is shown in Scheme 3.3.



Scheme 3.3 The mechanism of ring-opening of cyclohexene oxide with HBA/PPh_3

The formation of *trans*-1,2-bromohydrin was believed that, at first, a positively charged adduct was formed from the reaction of PPh_3 and HBA. The positive charged adduct was then interacted with the oxygen atom of epoxide. Nucleophilic attack of the bromide ion generated an intermediate. This intermediate in the presence of water could produce triphenylphosphine oxide and the corresponding *trans*-1,2-bromo-hydrin. The mechanism demonstrated that the concentration of bromide ion nucleophile affected the formation of the S_N2 product.

CHAPTER IV

CONCLUSION

The goal of this research is to systematically find the optimum conditions for the synthesis of bromosilanes from hydrosilanes using HBA. In addition, the cleavage of ethers to dibromo compounds and the ring-opening of epoxide to bromohydrins and dibromo compounds using HBA and PPh_3 were investigated. HBA was disclosed as an efficient brominating agent. This bromination reaction could proceed rapidly under mild conditions.

The optimized reaction conditions were revealed: tri-*iso*propylsilane was treated with HBA with the ratio of 1.0:0.25 at RT for 20 min in THF furnishing tri-*iso*propylbromosilane. The reaction conditions could be modified to make the reaction more efficient by the aids of UV irradiation, sonication or performing at refluxing THF. The quantitative yield of bromosilane was successfully accomplished within 15 min. Under these optimized conditions, various hydrosilanes, such as triphenylsilane, dimethylphenylsilane, chlorodimethylsilane could be applied.

In addition, for the opening of cyclic ether, excess THF, using the mole ratio of HBA:PPh_3 1:2 at refluxing THF for 15 min could be transformed to the desired 1,4-dibromobutane product in quantitative yield. In the case of linear ether, DBE could be cleaved to benzyl bromide at refluxing toluene for 4 h using HBA:PPh_3 (1:2). Furthermore, the cleavage of ethers could be accomplished using MW irradiation method with other compounds, such as di-*n*-butyl ether, 2-chloroethyl ether, piperidine and ethyl phenyl acetate. These reactions provided the desired bromo products in high yield in very short reaction time.

For the ring opening of epoxides, the ratio of bromohydrins and dibromo products could be controlled using undried or dried CH_3CN for 1 min at RT and the mole ratio of epoxide:HBA:PPh_3 1:0.5:1 and 1:2:3 to produce solely bromohydrin and dibromo products, respectively. Since this protocol could be efficiently conducted, it was thus applied for the preparation of bromohydrins and dibromo compounds from other epoxides. The reaction could easily control the formation of bromohydrins and dibromo compounds with high regeoselectivity.

Proposal for the Further Work

This methodology utilizing HBA should be applied with other compounds such as ketone and ester under UV irradiation or sonication conditions. In addition, the ring-opening reaction of aziridine using HBA/PPh_3 should also be explored.

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Appendix

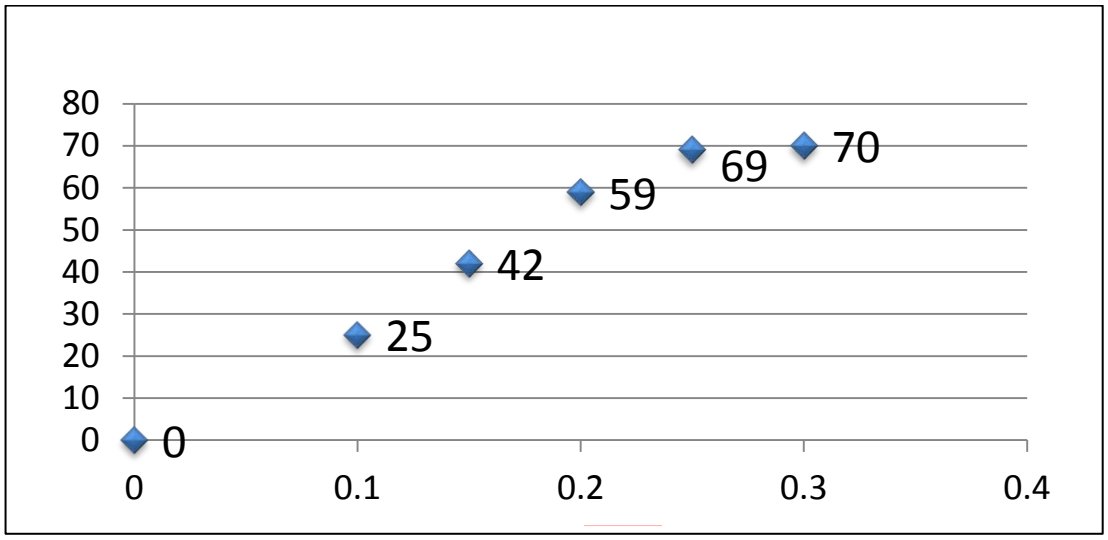


Figure A-1 The effect of the amount of HBA on the conversion of TIPS-H into TIPS-Br.

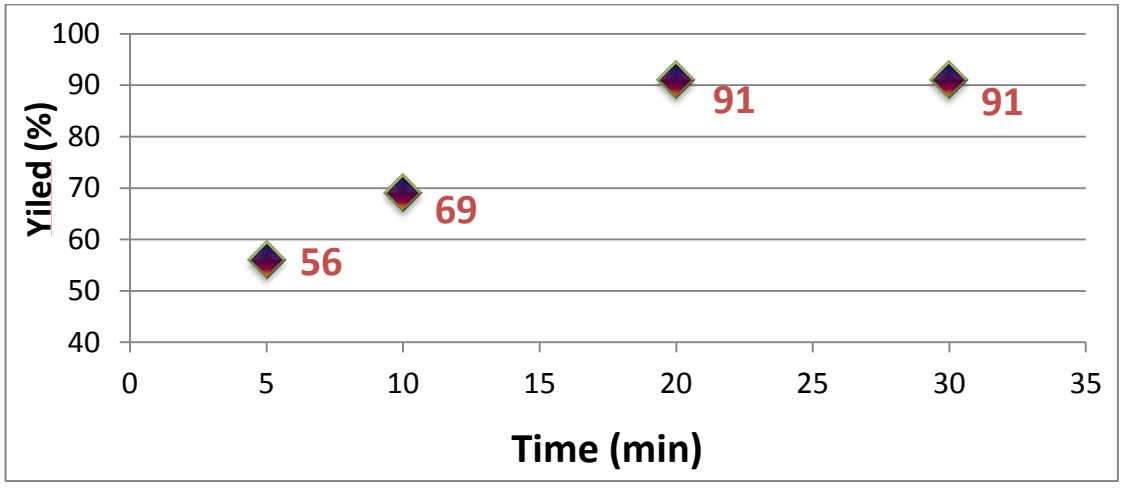


Figure A-2 The effect of reaction time on the conversion of TIPS-H into TIPS-Br using HBA.

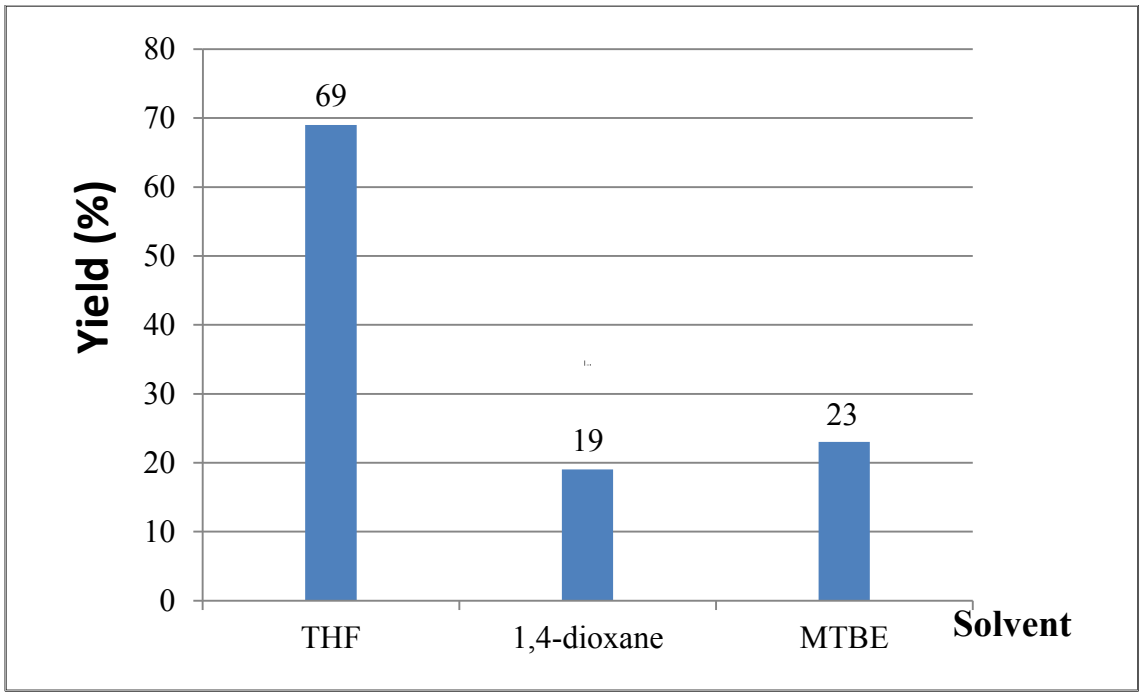


Figure A-3 The effect of solvent on the conversion of TIPS-H into TIPS-Br using HBA.

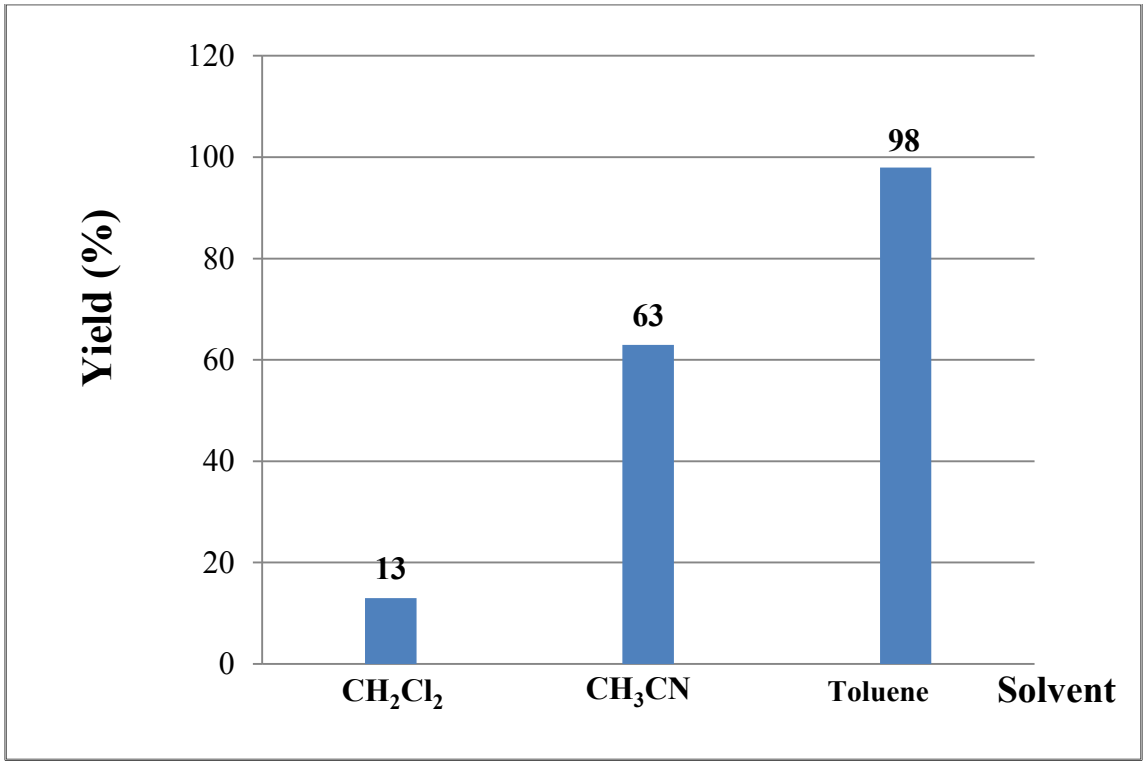
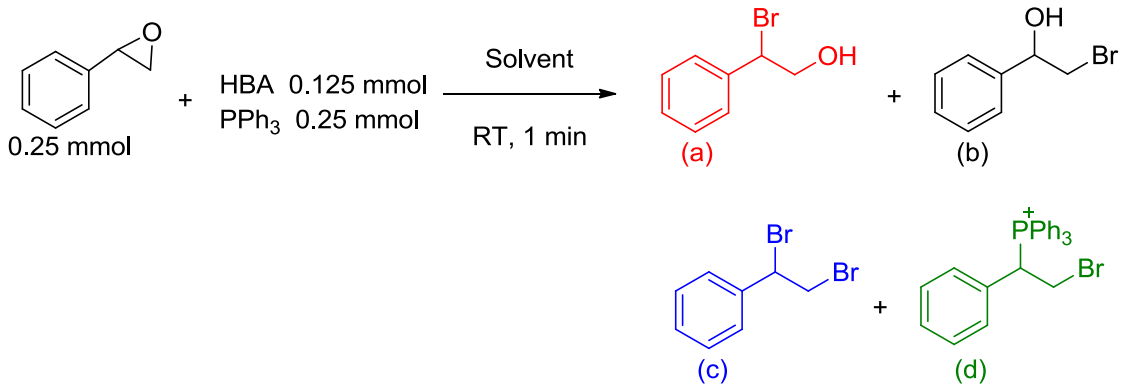


Figure A-4 The effect of solvents on the cleavage of DBE.



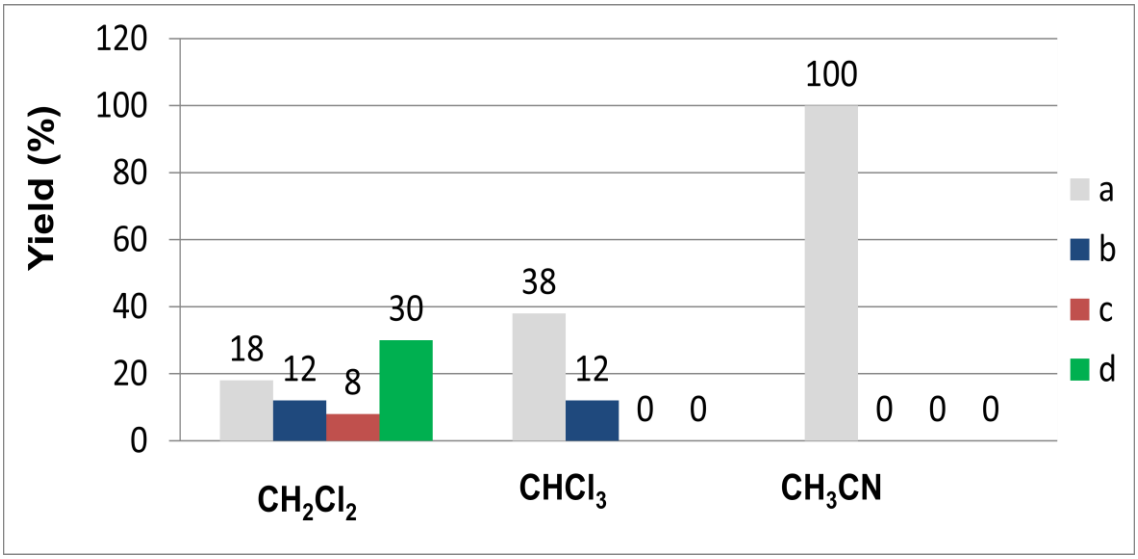
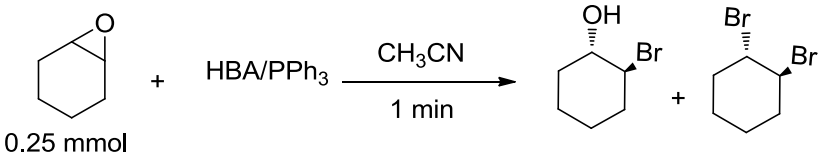


Figure A-5 The effect of solvent on the ring opening of styrene oxide using HBA/PPh_3.



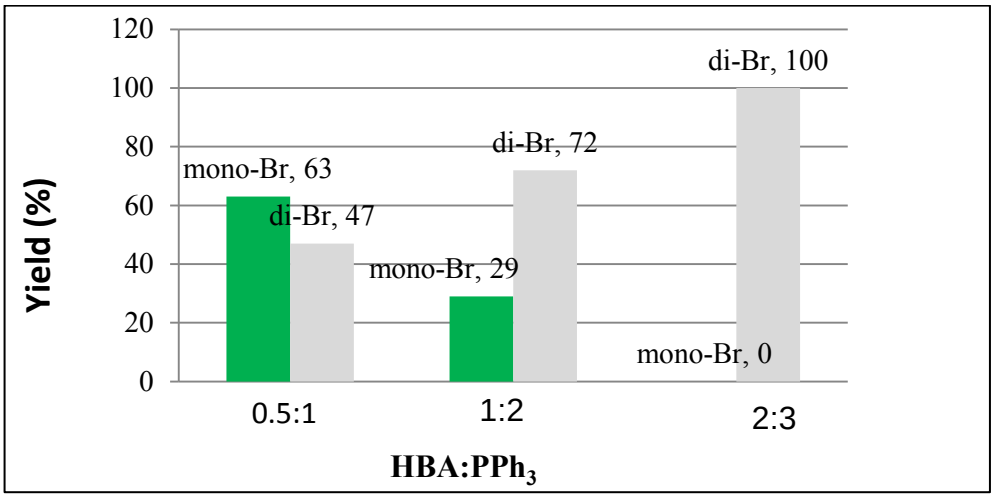


Figure A-6 The effect of dried CH_3CN and mole ratio of HBA: PPh_3.

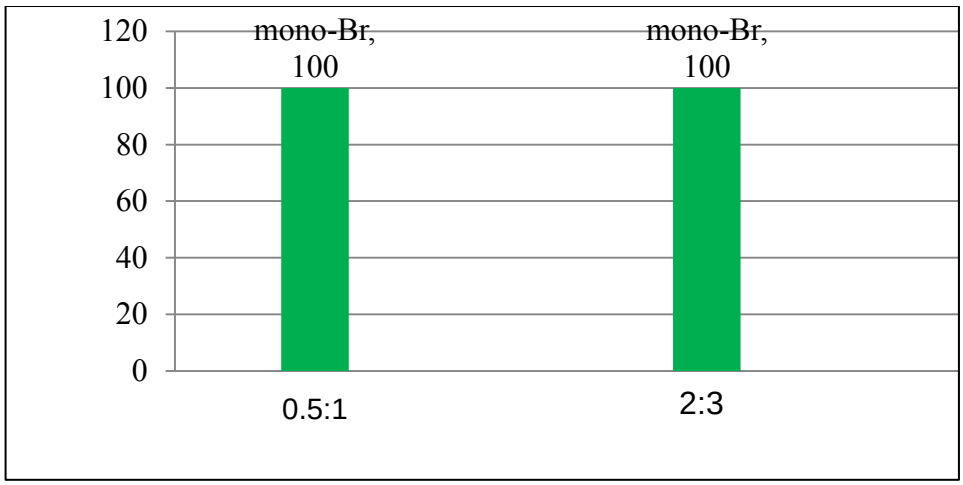


Figure A-7 The effect of undried CH_3CN and mole ratio of HBA: PPh_3.

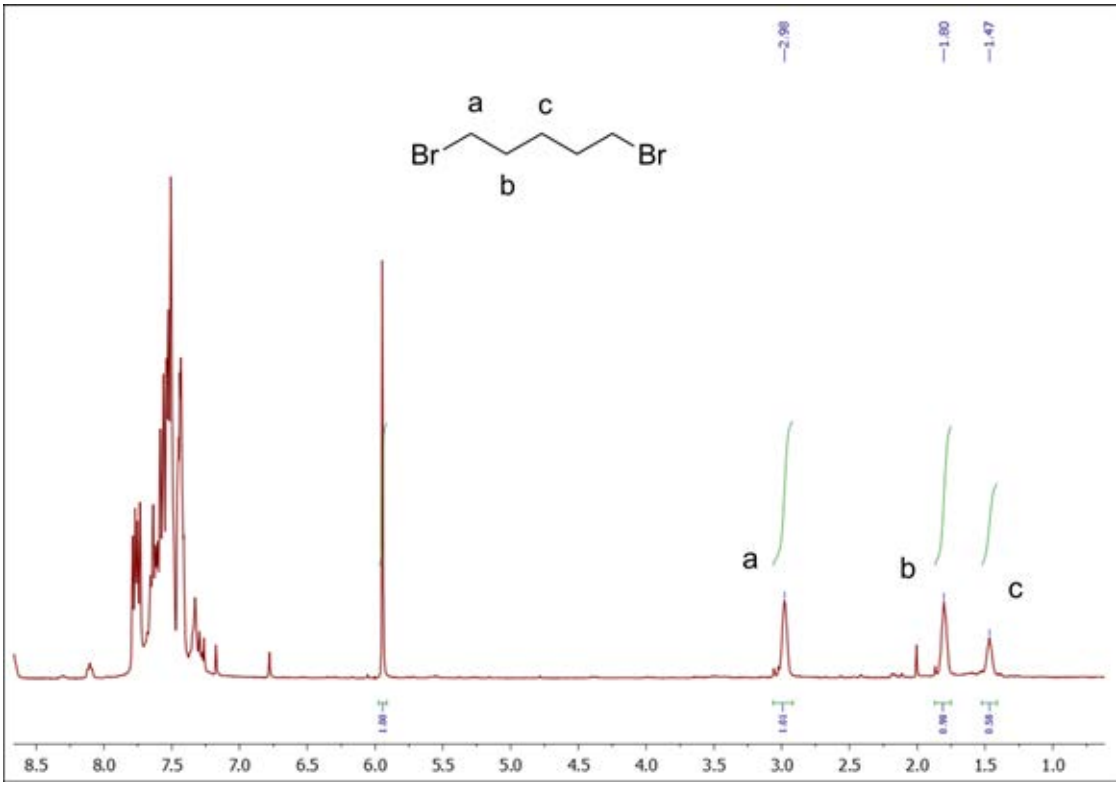


Figure A-8 The ^{1}H NMR spectrum of the crude reaction mixture of piperidine under MW 130 °C for 1 min with HBA: PPh_3.

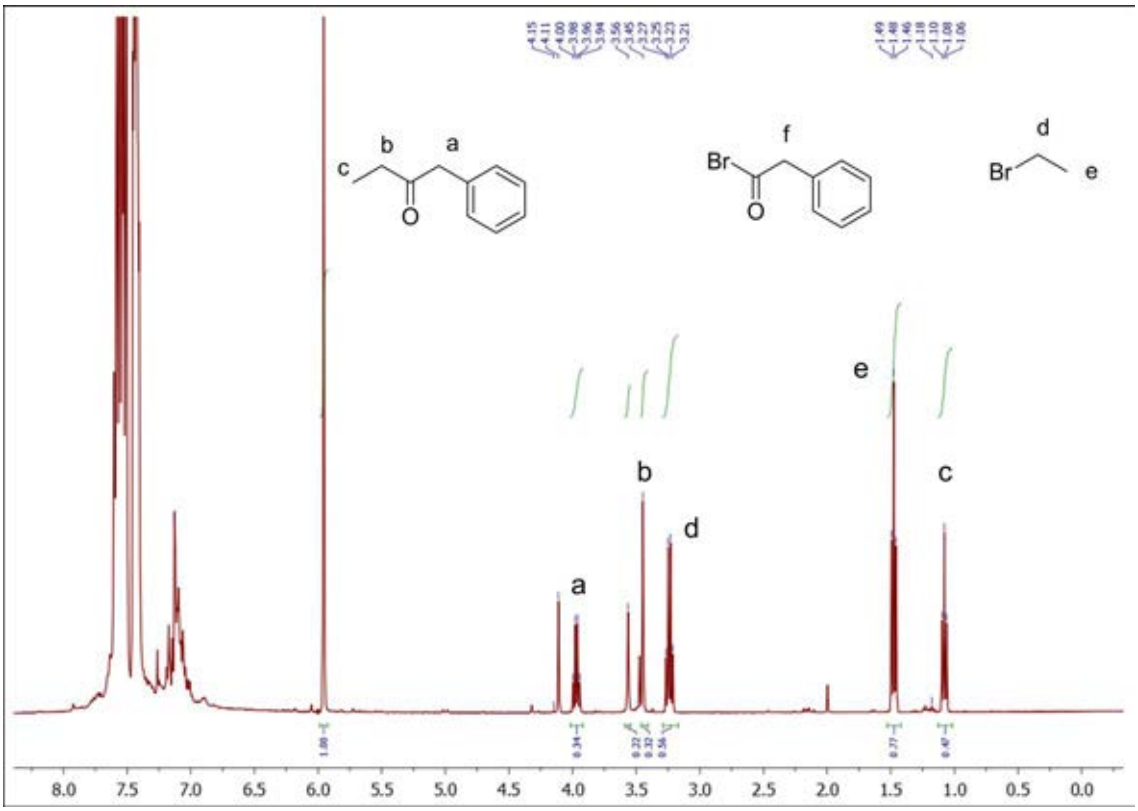


Figure A-9 The ^{1}H NMR spectrum of the crude reaction mixture of ethyl phenyl acetate under MW 130 °C for 1 min with HBA: PPh_3**.**

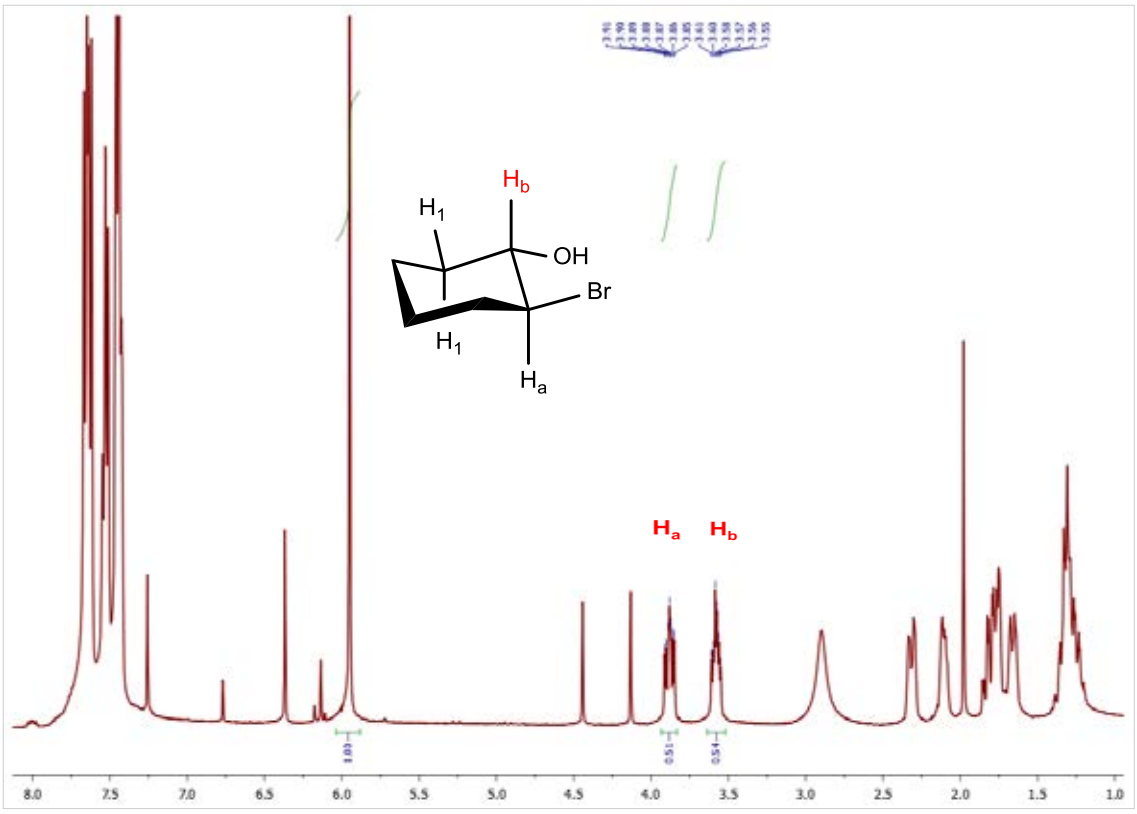


Figure A-10 The ^{1}H NMR spectrum of the crude reaction mixture of cyclohexene oxide under RT for 1 min with HBA: PPh_3

Example of Calculation Method of % Yield of Product

$$\%\text{yield} = \frac{(\text{integration of product})}{(\text{integration of internal std})} \times \frac{(\text{amount of } ^{1}\text{H of internal std})}{(\text{amount of } ^{1}\text{H of product})} \times 100$$

$$\%\text{yield} = \frac{(0.51)}{(1.0)} \times \frac{(2)}{(1)} \times 100$$

$$= 102$$

VITA

Miss Lalita Muenraya was born on May 1, 1987 in Yala, Thailand. She graduated with Bachelor's Degree of Science in Chemistry from Chulalongkorn University in 2008. Since 2010, she has been a graduate student studying Petrochemistry and Polymer Science at Chulalongkorn University. She was supported by research grant for this Master's Degree thesis from the Center for Petroleum, Petrochemicals and Advanced Materials, Chulalongkorn University, Program in Petrochemistry and Polymer Science, Faculty of Science, Chulalongkorn University. The Thailand Research Fund and the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund) and Research Assistantship Scholarship.

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