1-[(2-METHOXYETHOXY)METHOXY]-2-(PHENYLSULFINYL)CYCLOPROPANE AS A THREE-CARBON SYNTHON

PANAWAN MOOSOPHON

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF MASTER OF SCIENCE
(ORGANIC CHEMISTRY)
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2000

ISBN 974-665-157-9

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December 19, 2000

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ACKNOWLEDGEMENT

Firstly, I would like to express my sincere gratitude and deep appreciation to my advisor, Professor Manat Pohmakotr, for his patient supervision, valuable guidance and encouragement throughout the course of this work .

I also would like to express my appreciation to Assoc. Prof. Dr. Patoomratana Tuchinda for her comments and suggestions and for recording the NMR spectra. Grateful acknowledgements are made to Assoc. Prof. Dr. Somyote Sutthivaiyakit for his valuable comments and suggestions.

My appreciation is also extended to the staff of the Chemistry Department, Faculty of Science, Mahidol University, especially Mrs. Patcharin Poochaiwattananon and Miss Amporn Srisuthipruth for their assistance in provide spectral data as well as elemental analysis.

I wish to thank all members of my friends, Miss Laddawan Sampaongoen, Miss Wacharee Harnying, Miss Tanasri Bunlaksananusorn, Miss Amonphat Tadsanaprasittipol, Mr. Thiti Junpirom, Mr. Attasit Limpongpan, Mr.Pornthep Nommechai and Mr. Wilart Pompimon, especially Mr. Siriphong Sadaeng for their kind co-operation and generous assistance throughout this work.

I deeply acknowledge the Development and Promotion of Science and Technology Talent Project (DPST) for providing a scholarship, which enabled me to undertake this study. I am also thankful to the Postgraduate Education and Research Program in Chemistry (ADB-HEDP LOAN No.1699-THA) for partial support.

Finally, non of this would have been possible without love and encouragement of my father, mother and younger sister for their kindness and support during my study.

Panawan Moosophon

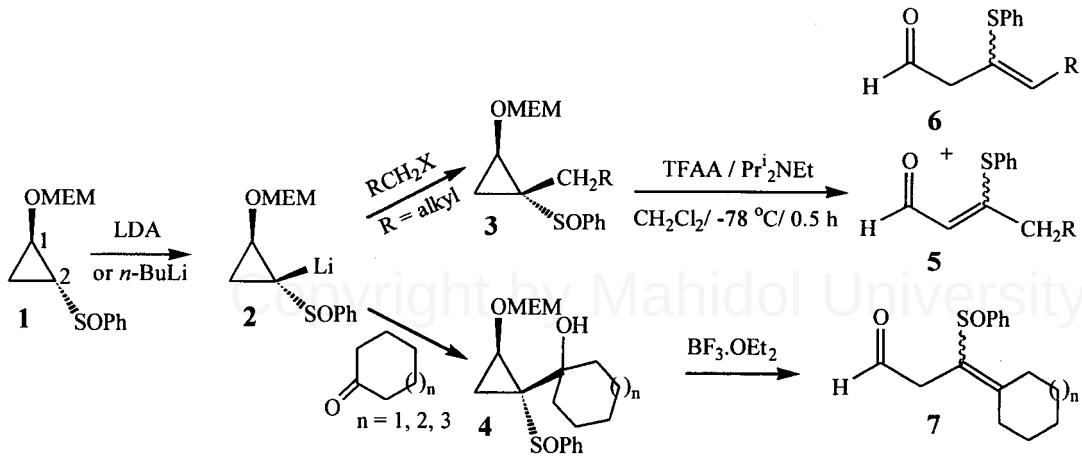
4037861 SCOC / M : MAJOR : ORGANICCHEMISTRY :

M.Sc. (ORGANIC CHEMISTRY)

KEY WORDS : SULFUR-SUBSTITUTED CYCLOPROPANE / VICINALLY DONOR-ACCEPTOR SUBSTITUTED CYCLOPROPANE

PANAWAN MOOSOPHON : 1-[(2-METHOXYETHOXY)METHOXY]-2-(PHENYLSULFINYL)CYCLOPROPANE AS A THREE-CARBON SYNTHON. THESIS ADVISORS : MANAT POHMAKOTR, Dr.rer.nat., PATOOMRATANA TUCHINDA, Ph.D. 130 P. ISBN 974-665-157-9

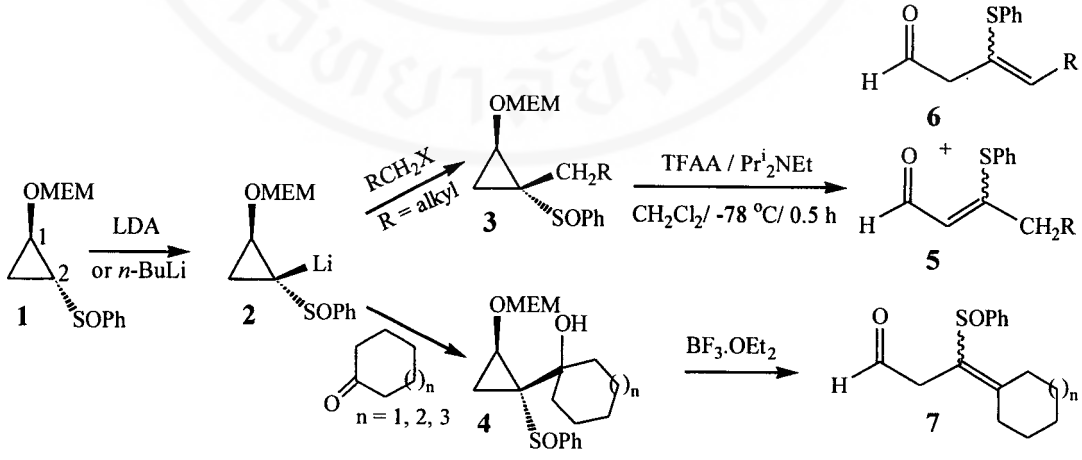
The anion **2** could be generated from the sulfoxide **1** by reacting with LDA or *n*-BuLi in THF at –78 °C. The anion **2** reacted with alkylating agents and carbonyl compounds to afford compounds **3** and **4** in moderate yields with retention of configuration at the C-2 position. Compounds **3** underwent ring-opening upon treatment with trifluoroacetic anhydride / Pr^i_2NEt in CH_2Cl_2 at –78 °C for 0.5 h to provide a mixture of *β*-phenylthio-*α,β*-unsaturated aldehydes **5** and *β*-phenylthio-*β,γ*-unsaturated aldehydes **6** in good yields. We considered this synthetic conversion as a novel Pummerer-type mediated ring-opening of *β*-alkoxy substituted cyclopropyl sulfoxide at low temperature. In addition, we found that ring-opening of compounds **4** to *β*-phenylsulfinyl-*β,γ*-unsaturated aldehydes **7** proceeded smoothly in excellent yields, when the reaction was treated with boron trifluoride ethyl etherate at 0 °C for 2 h.



4037861 SCOC / M : สาขาวิชา : อินทรียเคมี ; วท.ม. (อินทรียเคมี)

พนาวัลย์ หมู่โสภณ : ปฏิกิริยาของสารอนุพันธ์ 1-[(2-METHOXYETHOXY) METHOXY]-2-(PHENYLSULFINYL)CYCLOPROPANE {1-[(2-METHOXYETHOXY) METHOXY]-2-(PHENYLSULFINYL)CYCLOPROPANE AS A THREE-CARBON SYNTHON} คณะกรรมการควบคุมวิทยานิพนธ์ : มนัส พรหมโคตร, Dr.rer.nat., ปทุมรัตน์ ตู้จินดา, Ph.D. 130 หน้า ISBN 974-665-157-9

สามารถเตรียม แอนไอออน **2** ได้จากปฏิกิริยาของ sulfoxide **2** กับ LDA หรือ *n*-BuLi ใน THF ที่ –78 องศา เมื่อแอนไอออน **2** ทำปฏิกิริยากับ alkylating agents และ สารประกอบคาร์บอนิล ให้สารประกอบ **3** และ **4** เปอร์เซ็นต์ผลิตผลปานกลาง โดยการจัดโครงแบบที่ตำแหน่ง C-2 ยังคงเดิม สารประกอบ **3** ทำปฏิกิริยากับ trifluoroacetic anhydride และ $Pr^{i}_{2}NEt$ ใน CH_2Cl_2 ที่ –78 องศา เป็นเวลา 0.5 ชั่วโมง เกิดการเปิดวงให้ *β*-phenylthio-*α,β*-unsaturated aldehydes **5** และ *β*-phenylthio-*β,γ*-unsaturated aldehydes **6** ที่เปอร์เซ็นต์ผลิตผลค่อนข้างดี จะเห็นได้ว่า *β*-alkoxy substituted cyclopropyl sulfoxide สามารถเกิด novel Pummerer-type mediated ring-opening ได้ที่อุณหภูมิต่ำ นอกจากนั้นเราพบว่าสารประกอบ **4** ทำปฏิกิริยากับ boron trifluoride ethyl etherate ที่ 0 °C เป็นเวลา 2 ชั่วโมง เกิดการเปิดวงให้สารประกอบ *β*-phenylsulfinyl-*β,γ*-unsaturated aldehydes **7** ที่เปอร์เซ็นต์ผลิตผลดีมาก



CONTENTS

LIST OF CONTENTS (cont.)

ABBREVIATION

app.	apparent
br.	broad
s	singlet
d	doublet
dd	doublet of doublets
ddd	doublet of doublet of doublets
dt	doublet of triplets
t	triplets
q	quartet
m	multiplet
δ	chemical shife
J	coupling constant
ppm	part per million
equiv	equivalent
mL	mililiter
h	hour(s)
min	minute(s)
Hz	hertz
IR	infrared
ν_{max}	maximum absorption frequencies
M	molar
m/z	a value of mass divided by charge

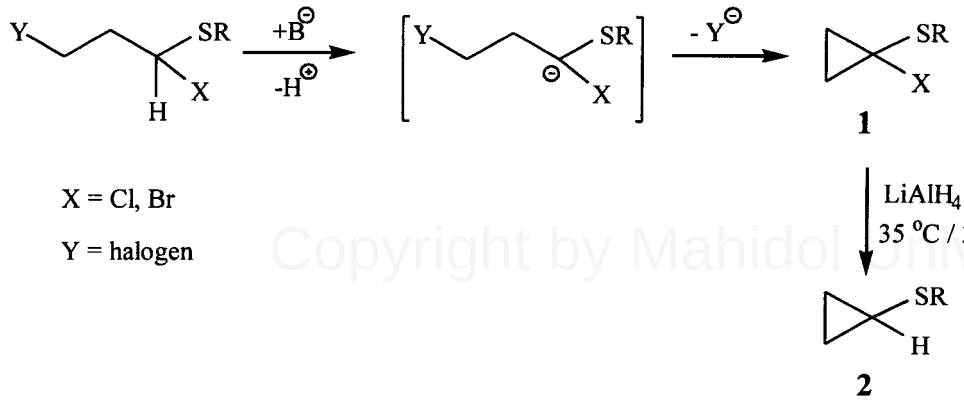
CHAPTER I

INTRODUCTION

Under the influence of a variety of chemical reagents or external physical forces, cyclopropane derivatives undergo a variety of ring-opening reaction. The chemistry of the cyclopropane C-C single bond resembles that of a C-C double bond. Relief of ring strain provides a potent thermodynamic driving force for this process.[1] The chemistry of sulfur-substituted cyclopropanes have been extensively studied in organic synthesis as three-carbon building blocks. Many reviews and papers concerning the use of cyclopropane derivatives in organic synthesis have been reported.[1-5] Some interesting reactions of sulfur-substituted cyclopropanes will be summarized as follows.

1. Sulfenyl-substituted cyclopropanes

Cyclopropyl sulfides can be prepared in various ways. One method involves ring-closure by 1,3-elimination of hydrogen halide from γ-halosulfides leading to cyclopropyl sulfides **1** and follow by reducing with $LiAlH_4$ to give **2** as shown in equation 1.[6]

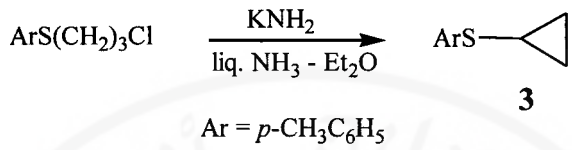


X = Cl, Br

Y = halogen

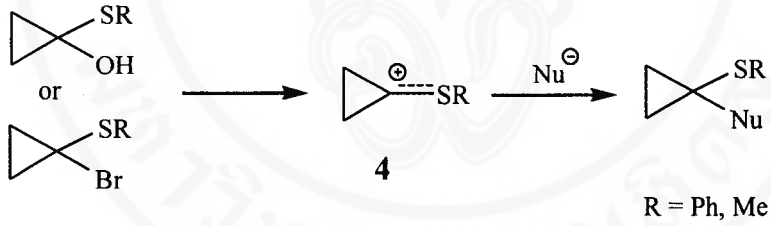
(eq. 1)

Treatment of 3-chloro-(phenylthio)propane with potassium amide in a liquid ammonia-ether solvent system was found to produce aryl cyclopropyl sulfide **3** in good yield (eq. 2).[7,8]



(eq. 2)

Jorritsma and coworkers [6] found that sulfur stabilized cyclopropane cation **4** was relatively stable and could be transformed into 1-substituted cyclopropyl sulfide by reacting with a variety of nucleophiles including formate, iodide, azide, hydrosulfide, furan and hydride without any rupture of the three-membered ring (eq. 3).[6,9]

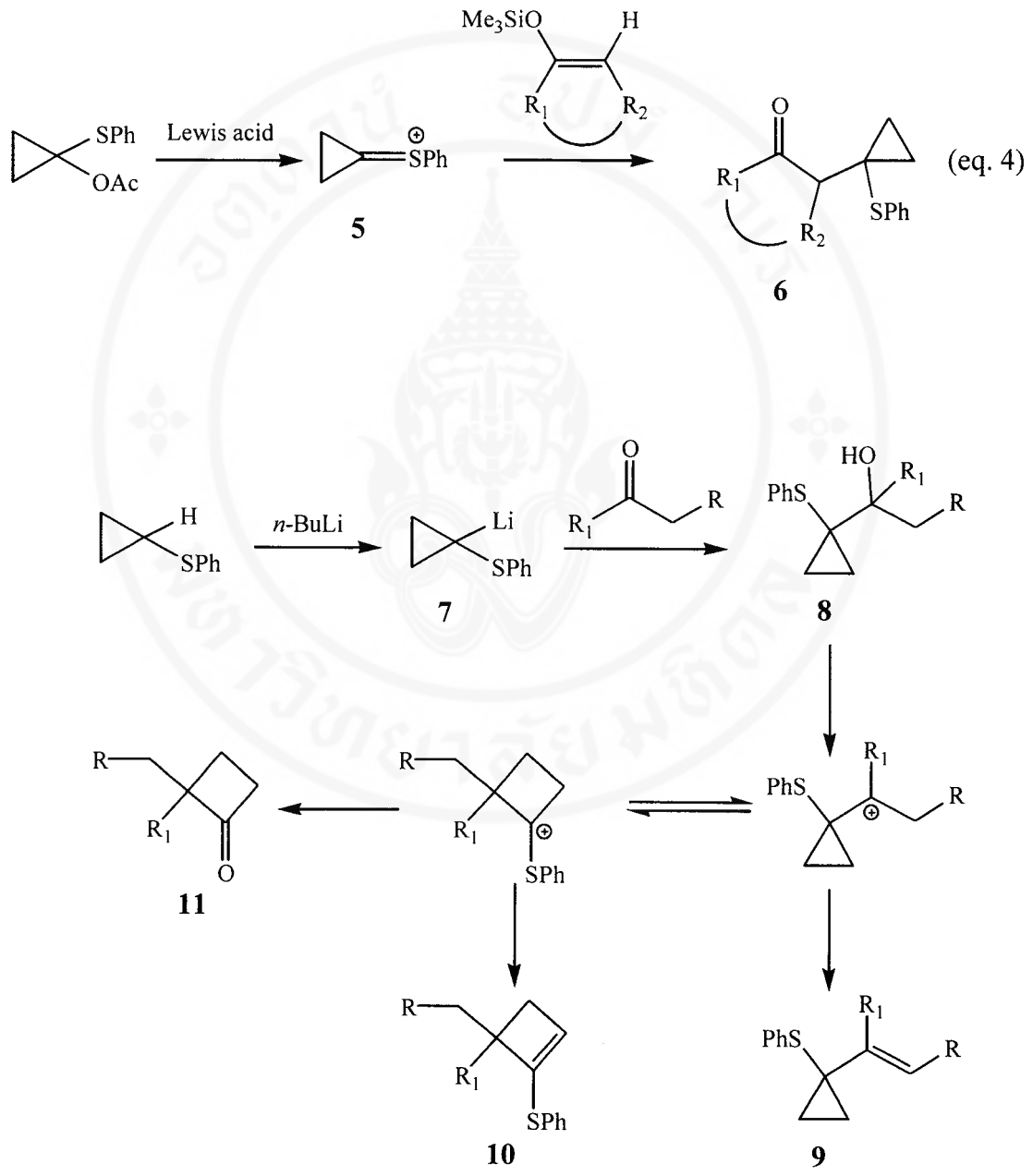


(eq. 3)

Similarly, cyclopropyl thionium ion intermediate **5** [10] was proposed to occur when α-acetoxy(phenylthio)cyclopropane was treated with a Lewis acid such as $SnCl_4$ or $ZnBr_2$ in dichloromethane. The thionium ion intermediate **5** reacted with some silyl enol ethers of carbonyl compounds leading to compound **6**. The reaction provided a method for α-phenylthiocyclopropylation of carbonyl compounds (equation 4).

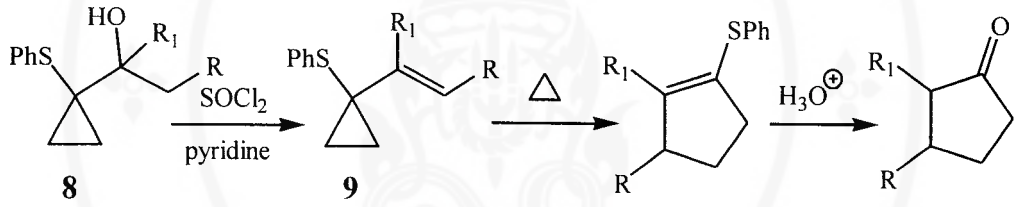
α-Lithiated phenylsulfenylcyclopropane **7** could be easily derived from the corresponding cyclopropyl phenyl sulfide by reacting with *n*-butyllithium. The anion **7** was quite reactive to be able to react with various types of carbonyl compounds to provide β-hydroxy sulfide **8** in good yields (**Scheme 1**). Compounds of the type **8**

were shown to be very versatile starting materials for the synthetic conversion into vinyl cyclopropanes **9**, sulfur-substituted cyclobutenes **10** and cyclobutanones **11**, depending on the reaction conditions.



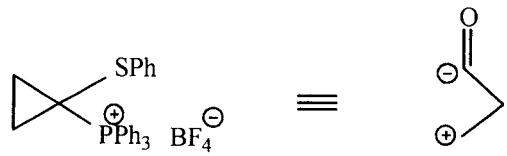
Scheme 1

The ratio of compounds **9** and **10** depended upon the stability of the initial carbonium ion and the strain energy of the olefin being formed. Thus, in the case of primary or secondary cyclopropylcarbinols **8**, smooth rearrangement to the desired cyclobutene thioether **10** occurred. On the other hand, tertiary cyclopropylcarbinols **8** gave a mixture of both compounds. Vinylcyclopropyl sulfides **9** was conveniently synthesized by dehydration of the hydroxy sulfides **8** with thionyl chloride in pyridine at 0 °C in 85 - 95% yields without complication arising from ring expansion.[8, 11] Vinylcyclopropanes **9** are a precursors for cyclopentanone formation (eq. 5).[12]



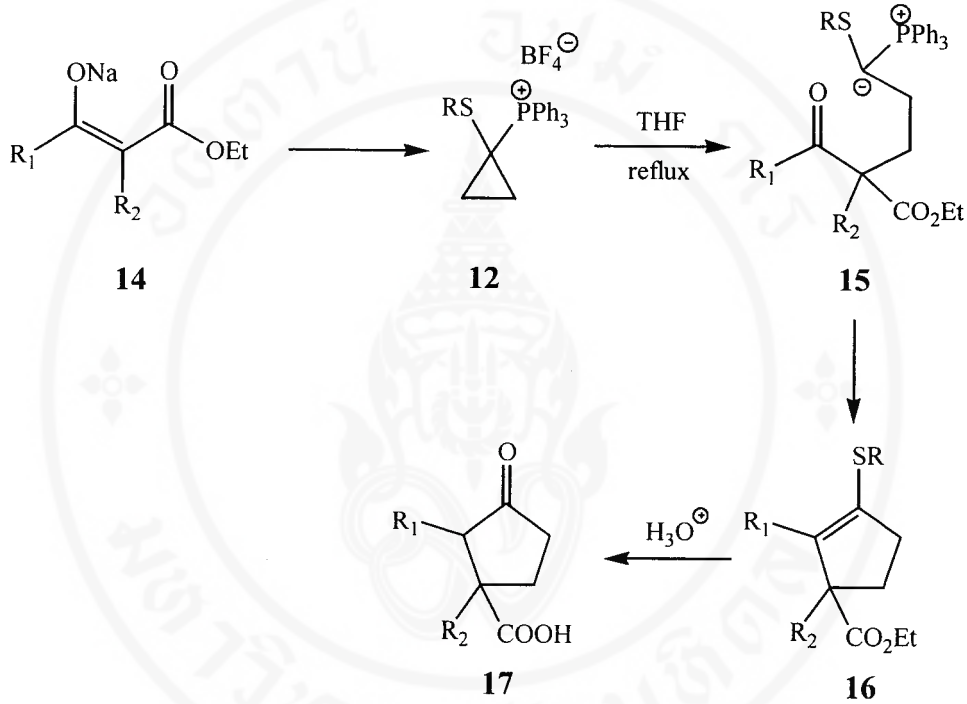
(eq. 5)

Marino and coworkers [13, 14] reported that 1-phenylthio-substituted cyclopropyl triphenylphosphonium tetrafluoroborate **12** could be used as a synthetic equivalent of the acyl zwitterion **13** based on the facile ring opening of activated cyclopropanes by nucleophiles [15] and an umpolung reactivity [16] for an incipient acyl anion equivalent.



12 **13**

The utilization of synthon **12** in the synthesis of five-membered rings was demonstrated by its reaction with sodium enolate of β-keto esters **14** to generate intermediate phosphonium ylide **15**. Intramolecular Wittig reaction of **15** gave rise to vinyl sulfides **16** in good yields which could be hydrolyzed to keto acids **17** (**Scheme 2**).



$R_1 = CH_3$, $R_2 = H$ (75%)

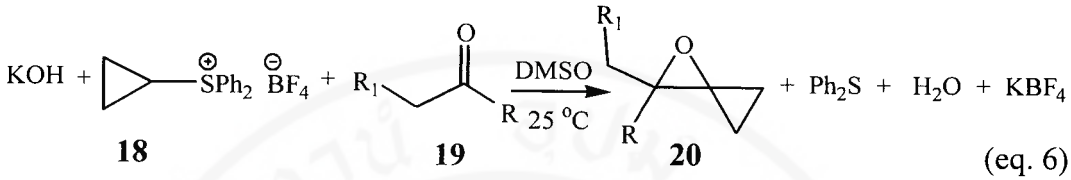
$R_1 = CH_3$, $R_2 = CH_2Ph$ (80%)

$R_1 = Ph_3$, $R_2 = H$ (75%)

Scheme 2

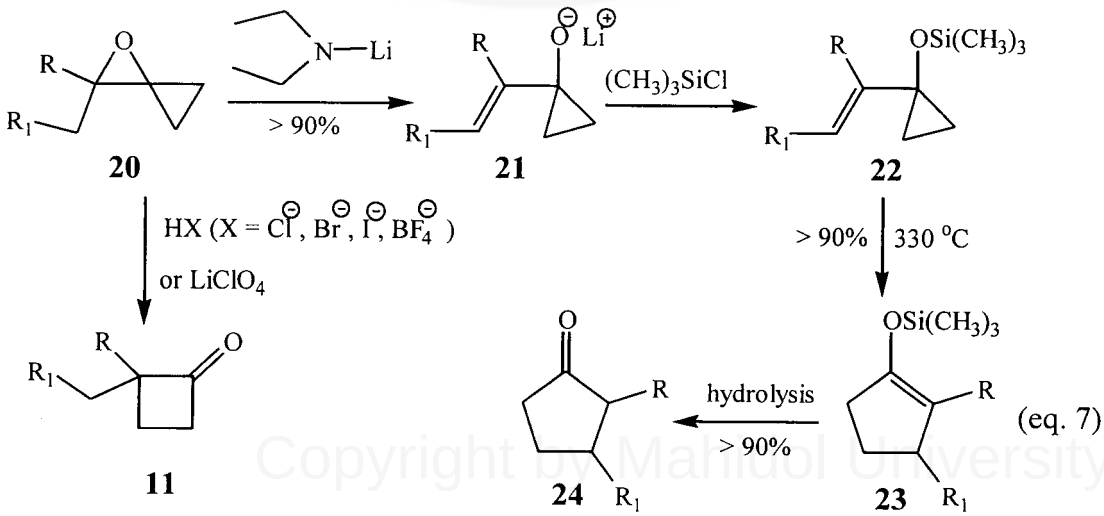
Oxaspiropentanes,[17, 18] monooxygen analogs of spiropentanes, are highly strained molecules, which could be converted into vinylcyclopropanols. These compounds have already been proved to be useful intermediates for the preparation of cyclobutanones, cyclopentenes and cyclopentanones under acidic conditions or thermal rearrangement. Oxaspiropentanes **20** are produced in high yields by treatment

of an equimolar solution of cyclopropyldiphenylsulfonium fluoroborate **18** and a carbonyl partner **19** with solid potassium hydroxide at 25 °C in dimethyl sulfoxide (eq. 6).[17, 18]



18 **19** **20** (eq. 6)

Treatment of oxaspiropentanes **20** with lithium diethylamide in hexane at 25 °C effected ring-opening with formation of lithium vinylcyclopropanoxides **21**. After work-up of the reaction with trimethylchlorosilane, the protection of the hydroxyl group resulted in good yields of siloxyvinylcyclopropanes **22**. Thermolysis of siloxyvinylcyclopropanes **22** by passing a hexane solution through a conditioned hot tube packed with glass helices at 330 °C with a contact time of 4 sec led to smooth quantitative rearrangement to the enol silyl ethers **23**. Further hydrolysis of **23** gave the cyclopentanones **24** in more than 90 % overall yields (equation 7).

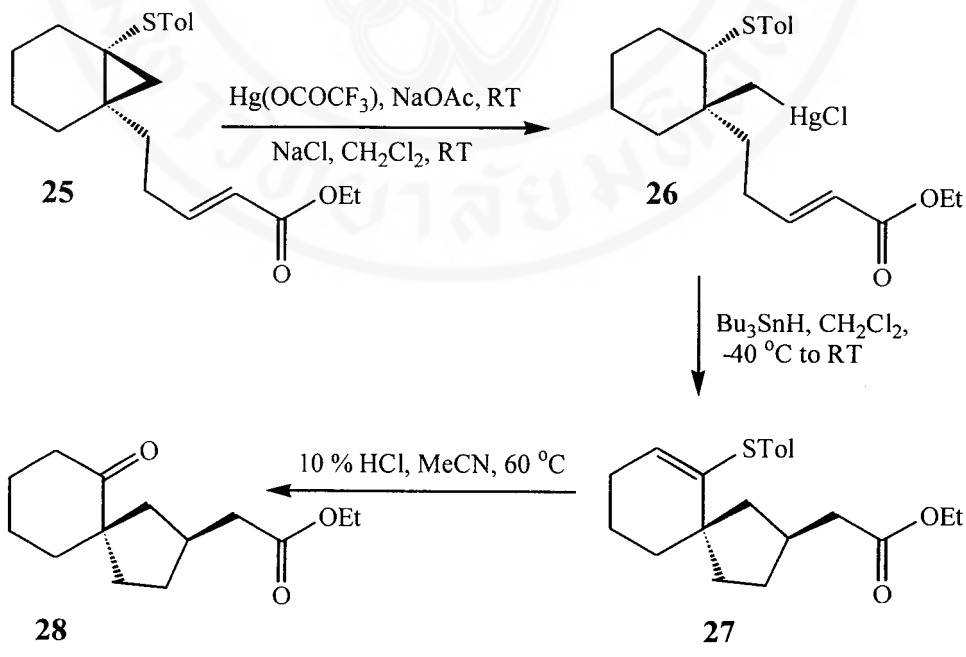


20 **21** **22**

11 **24** **23** (eq. 7)

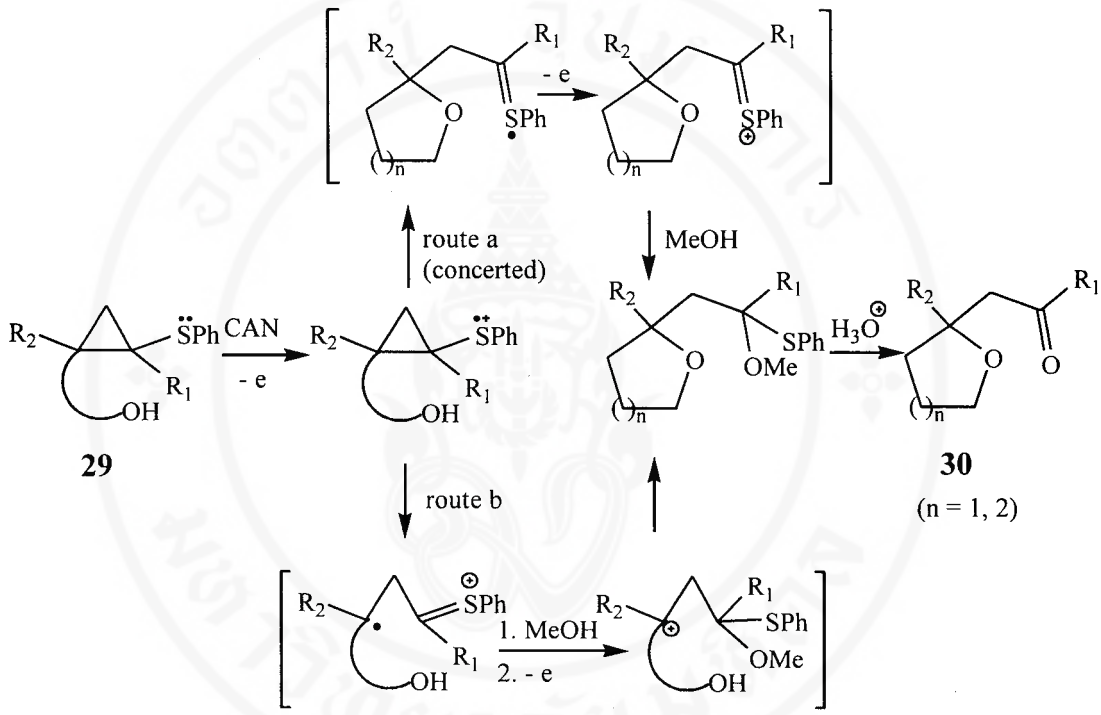
Either protonic acids or lithium perchlorate could effect the rearrangement of oxaspiropentanes **20** to cyclobutanones **11**.

Many synthetic methods for the cleavage of cyclopropane rings derivatized with sulfur have been reported.[19, 20] The use of a variety of electrophilic reactions on the electron-rich cyclopropyl sulfide **25** with mercury(II) trifluoracetate in methylene chloride in the presence of sodium acetate at room temperature gave rise to the desired α,β-unsaturated γ-sulfenylalkylmercury **26** in a highly regioselective manner. Cyclisation of **26** by radical reaction with tri-butyltin hydride initiated by 2,2'-azobisisobutyronitrile (AIBN) proceeded smoothly to give the spiro[4.5]decane derivative **27** which could be hydrolyzed to the spiroketone **28** as shown in (**Scheme 3**).[21]



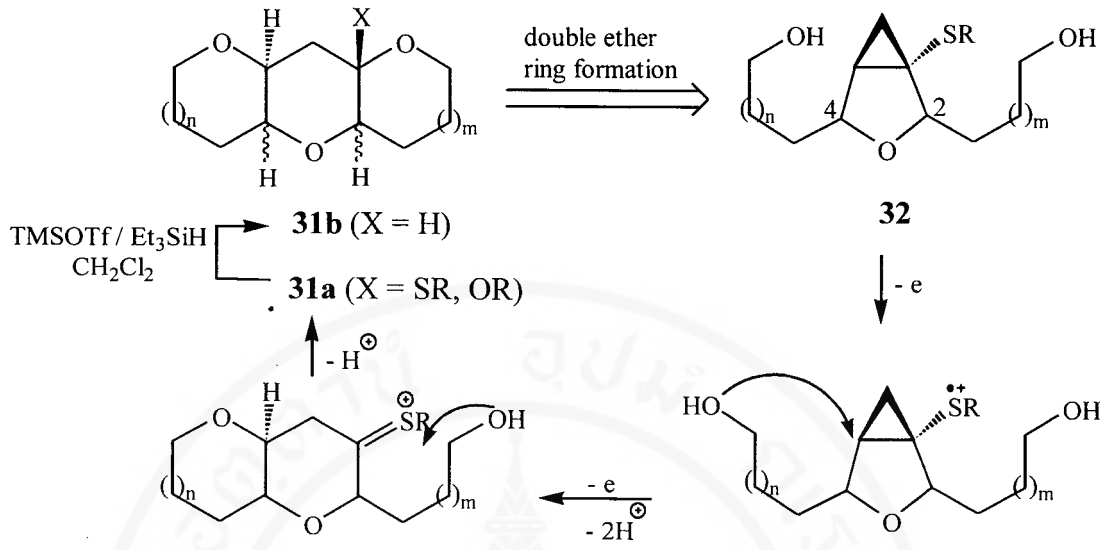
Scheme 3

The tandem oxidative ring cleavage-cyclisation of cyclopropylsulfides **29** bearing a hydroxy group in the side chain with ceric ammonium nitrate (CAN) as a chemical oxidant provided cyclic ethers **30**. The mechanism of the tandem oxidative ring-cyclisation reaction was proposed as shown in **Scheme 4**.[22, 23]



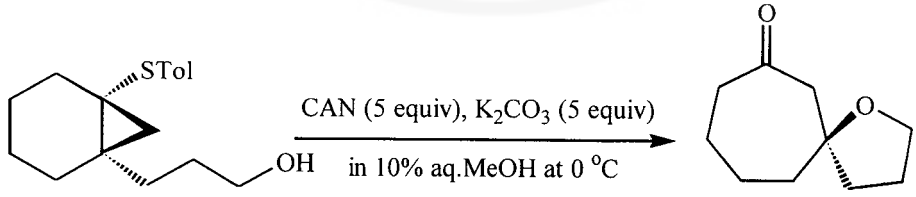
Scheme 4 Plausible reaction mechanism of the tandem oxidative ring cleavage-cyclisation reaction.

The CAN-mediated ring-opening of cyclopropyl sulfides provided a stereoselective formation of the *trans*- and *cis*-fused tricyclic ether ring system **31** containing five- or six-membered ring starting from 2α,4α- and 2β,4β-disubstituted 3-oxabicyclo[3.1.0]hexyl sulfides **32** by treatment with CAN in dry MeOH in the presence of MS 3A at room temperature as shown in **Scheme 5**.[24, 25]

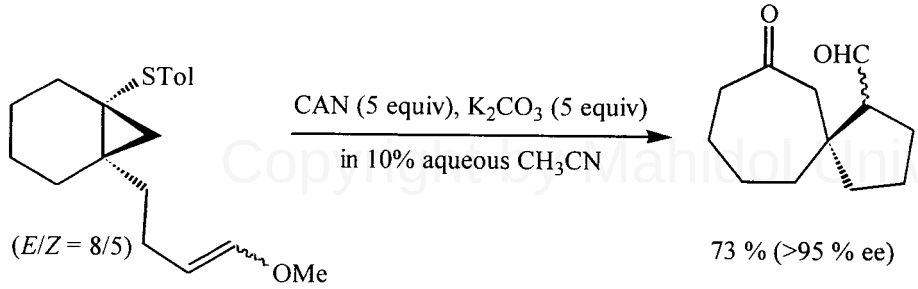


Scheme 5

The tandem oxidative ring expansion-cyclisation of chiral bicyclo[4.1.0]heptyl sulfides, bearing an alcohol or electron-rich olefin in the side chain, with ceric ammonium nitrate (CAN) led to regioselective carbon-carbon bond cleavage of cyclopropyl sulfides and stereoselective intramolecular carbon-oxygen or carbon-carbon bond formation to provide chiral spirocarbocyclic compounds (eqs. 8-9).[23]

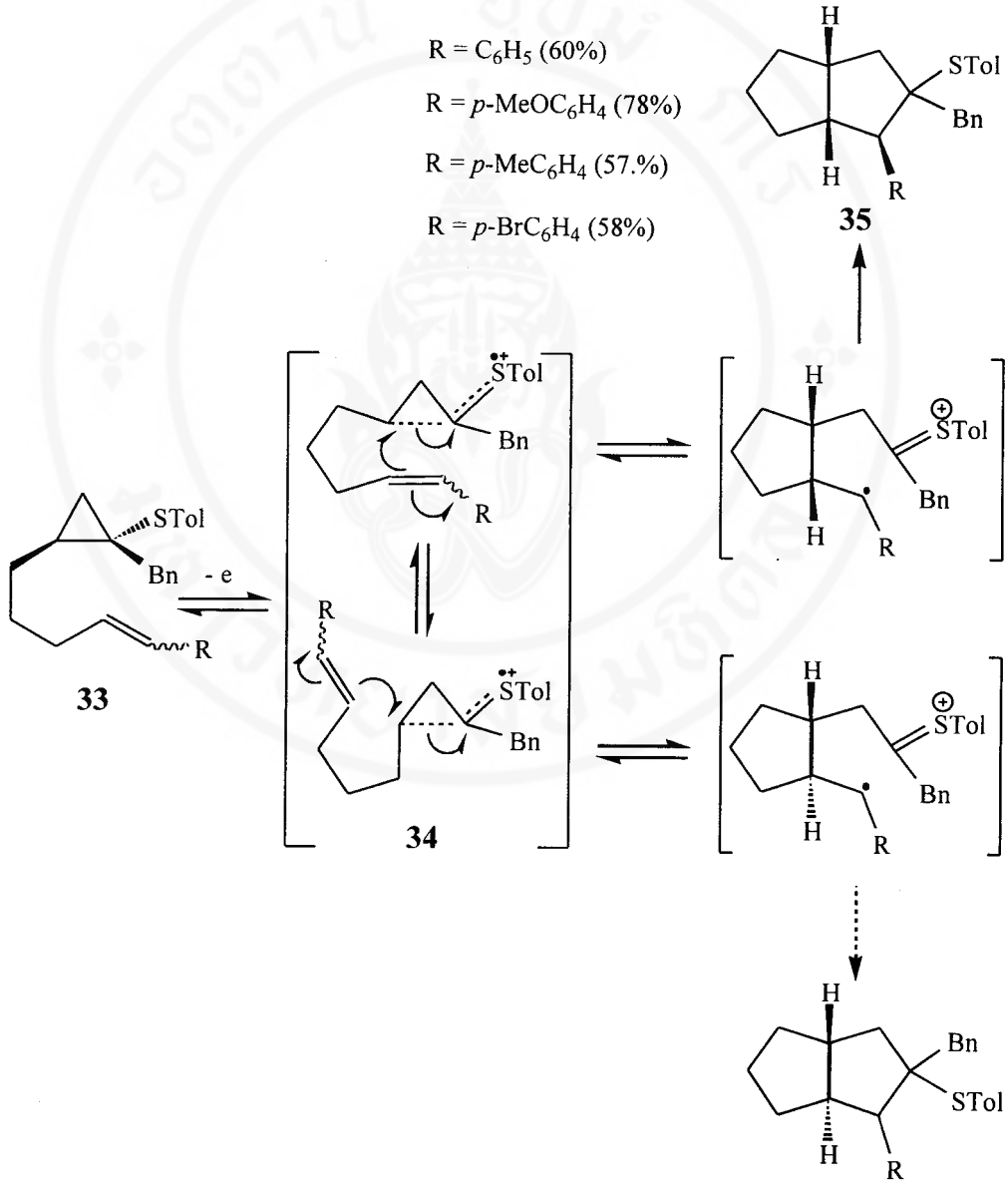


88 % (>90 % ee) (eq. 8)



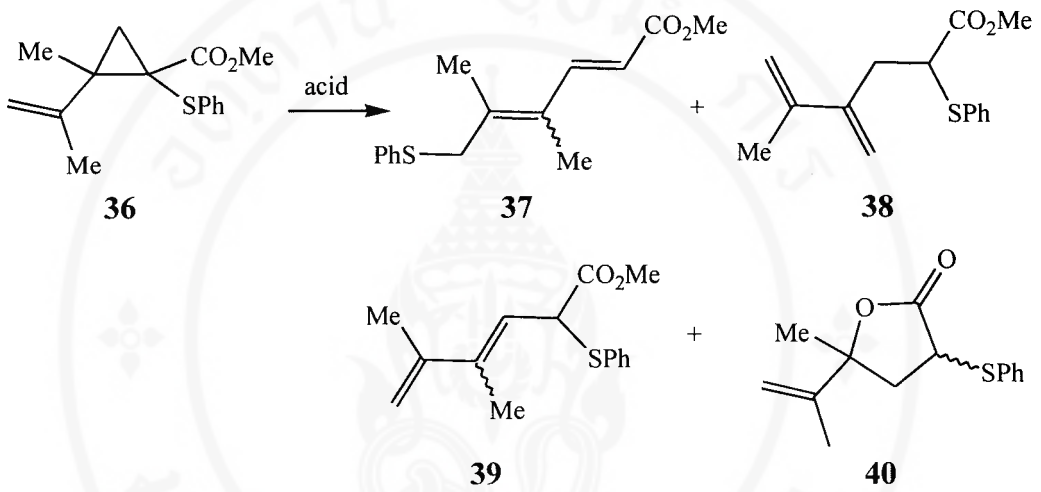
73 % (>95 % ee) (eq. 9)

Oxidative ring-opening of cyclopropyl sulfides **33** bearing a benzylidene moiety with tris-(4-bromophenyl)aminium hexachloroantimonate [(p-BrPh)$_3$NSbCl$_6$] afforded products **35** possessing diquinane skeleton. The formation of the products resulted from the intramolecular [3+2] cycloaddition of the cation-radical intermediate **34** (**Scheme 6**).



Scheme 6 A plausible reaction mechanism of the cation-radical mediated [3+2] cycloaddition.

Methyl 2-isopropenyl-2-methyl-1-(phenylthio)cyclopropane-1-carboxylate **36** underwent the C_1-C_2 bond cleavage followed by a 1,5-sulfenyl rearrangement by treatment with various acids to give a mixture of compounds **37, 38, 39** and **40** depending on the acid used (eq. 10).

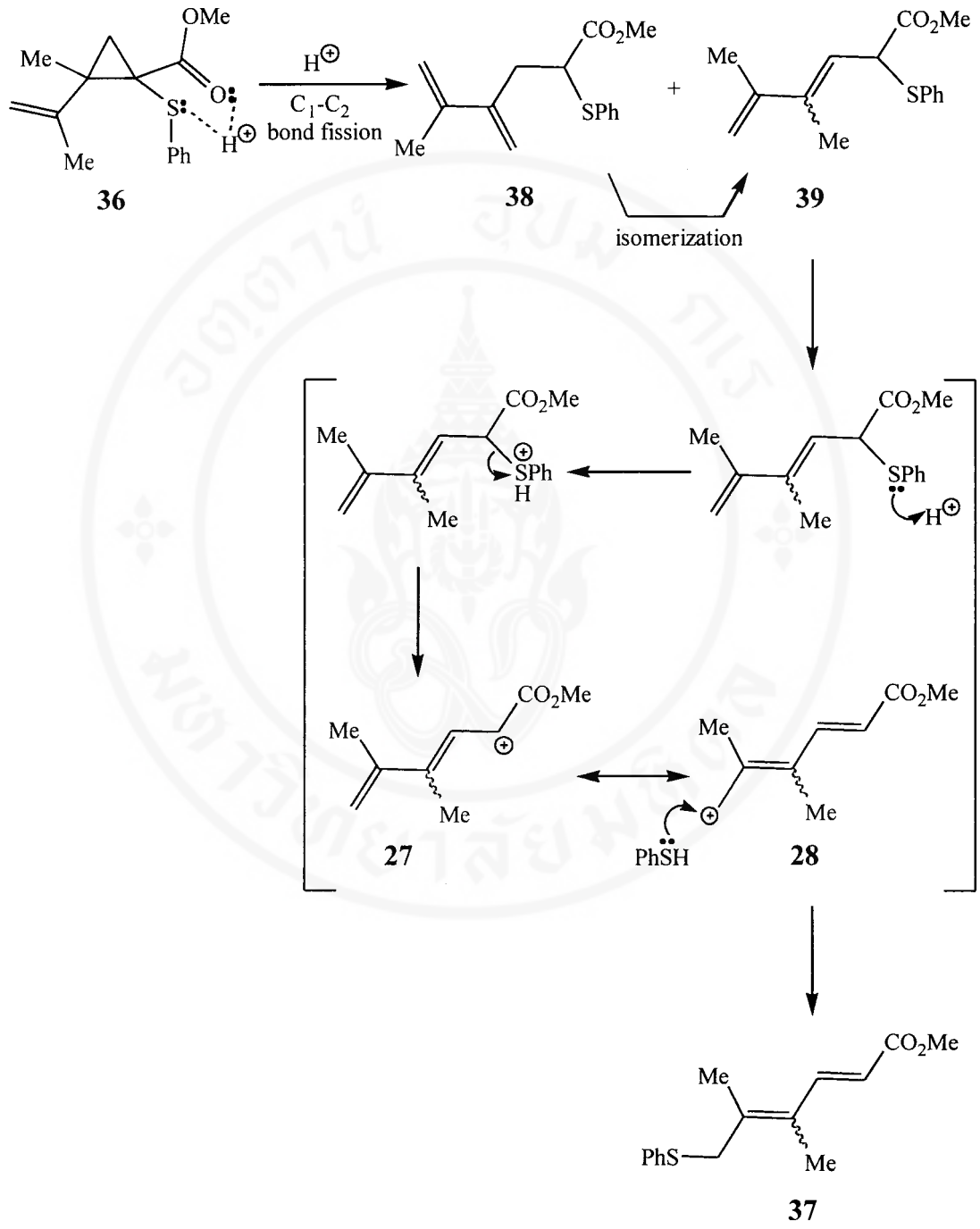


36 **37** **38**

39 **40**

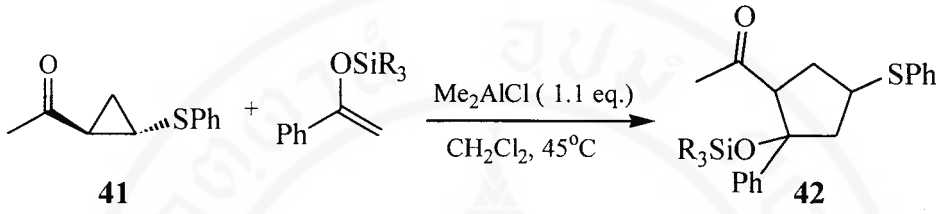
(eq. 10)

The treatment of **36** with a sulfonic acid such as *p*-TsOH and CF_3SO_3H in a nonpolar solvent efficiently caused the C_1-C_2 bond fission and the intramolecular 1,5-sulfenyl shift to give 6-sulfenyl-$\alpha,\beta,\gamma,\delta$-unsaturated carboxylic esters **37** as the major product. When the reaction was carried out in EtOH, γ-lactone **40** was obtained as a major product. The same results were observed when 42% HBF_4, CF_3CO_2H or $BF_3.OEt_2$ were used. From these results, the plausible reaction mechanism for the 1,5-sulfenyl shift was proposed as shown in **Scheme 7**.[26, 27]



Scheme 7

Cyclopropyl sulfide having acyl group at the β-position such as **41** [28] was found to undergo [3+2]cycloaddition with silyl enol ethers of ketones to afford cyclopentane derivatives **42** under the influence of dimethylaluminum chloride in dichloromethane at low temperature (equation 11).[29]

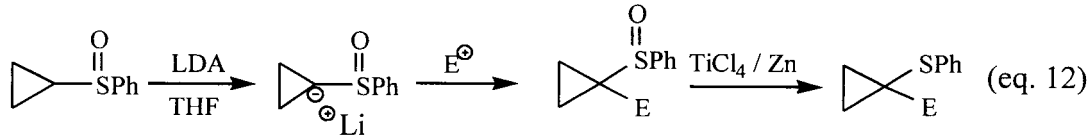


41 **42** (eq. 11)

	yield (%)	diastereomeric ratio
R=TBS	76	55 : 21 : 14 : 10
R=TIPS	66	68 : 28 : 2 : 2
R=TBDPS	95	60 : 40 : 0 : 0

1.2 Sulfinyl-substituted cyclopropanes

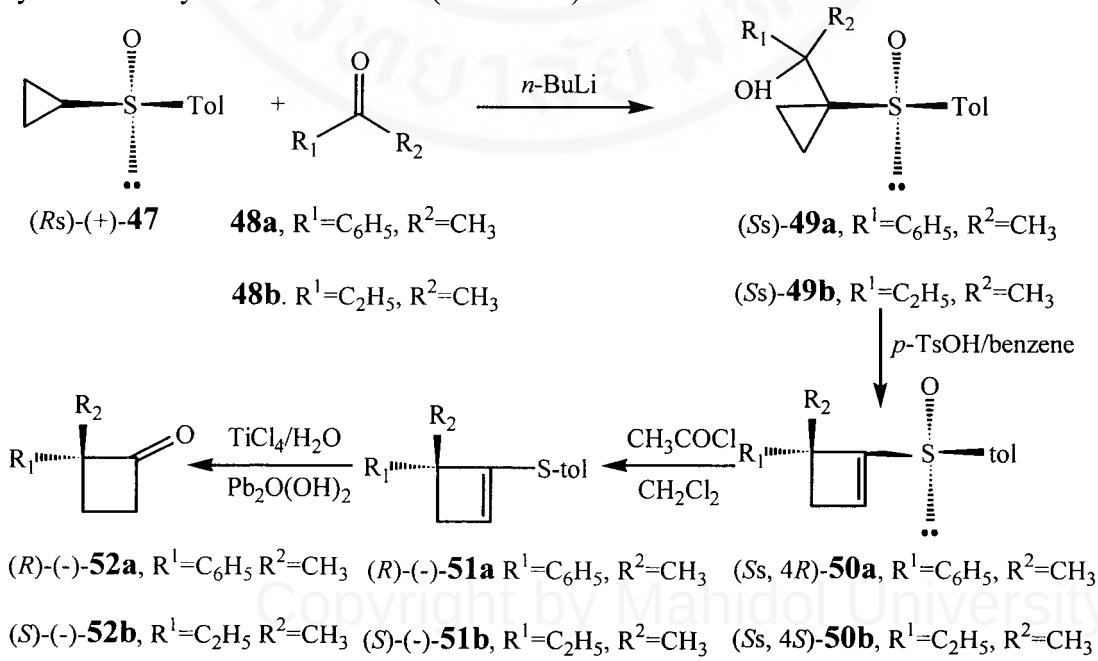
Few reports concerning the reaction of sulfinyl-substituted cyclopropanes have appeared in the literature. Our group [30] reported that 1-lithio (phenylsulfinyl) cyclopropane **44** derived from (phenylsulfinyl)cyclopropane **43** by reacting with lithium diisopropylamide in tetrahydrofuran, reacted smoothly with alkylating agents and carbonyl compounds to give 1-alkyl substituted- and 1-hydroxyalkyl substituted-(phenylsulfinyl)cyclopropanes **45** which could be then converted into compounds **46** after mild reductive deoxygenation with $TiCl_4$/Zn (eq. 12).



43 **44** **45** **46** (eq. 12)

E = alkyl

Hiroi [31] demonstrated an asymmetric synthesis of α,α-disubstituted cyclobutanones by exploiting optically active sulfinyl cyclopropane system. Addition of the α-carbanion of (R_S)-(+)-*p*-toluenesulfinylcyclopropane **47** (100% ee)[32] generated by treatment of (R_S)-(+)-**47** with *n*-butyllithium, to acetophenone **48a** at -20 °C for 4 h, afforded (S_S)-**49a** in 78 % yield (3:2 ratio of the diastereomers). When (S_S)-**49a** obtained was heated in refluxing benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid, it underwent a 1,2-asymmetric rearrangement to give (S_S,4*R*)-**50a**. Reduction of the sulfoxide in (S_S,4*R*)-**50a** was carried out by treatment with acetyl chloride in dichloromethane at room temperature affording (*R*)-(–)-**51a** {$[\alpha]_D^{20}$ – 14.7 ° (c 2.0, EtOH)}. Hydrolysis of the obtained enol thioether (*R*)-(–)-**51a** was performed by treatment with titanium(IV) chloride - lead hydroxide - H_2O [33] in acetonitrile at room temperature to produce (*R*)-(–)-2-methyl-2-phenylcyclobutanone **52a** {$[\alpha]_D^{20}$ – 9.6° (c 3.0, EtOH)}. Compound **52b** could be synthesized by the same manner (**Scheme 8**).



(*Rs*)-(+)-**47** **48a**, R^1=C_6H_5, R^2=CH_3 (*Ss*)-**49a**, R^1=C_6H_5, R^2=CH_3

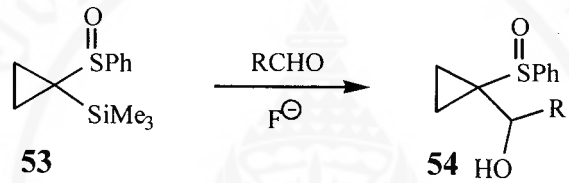
48b. R^1=C_2H_5, R^2=CH_3 (*Ss*)-**49b**, R^1=C_2H_5, R^2=CH_3

(*R*)-(-)-**52a**, R^1=C_6H_5 R^2=CH_3 (*R*)-(-)-**51a** R^1=C_6H_5, R^2=CH_3 (*Ss*, 4*R*)-**50a**, R^1=C_6H_5, R^2=CH_3

(*S*)-(-)-**52b**, R^1=C_2H_5 R^2=CH_3 (*S*)-(-)-**51b**, R^1=C_2H_5, R^2=CH_3 (*Ss*, 4*S*)-**50b**, R^1=C_2H_5, R^2=CH_3

Scheme 8

α-Trimethylsilyl(phenylsulfinyl)cyclopropane **53** condensed smoothly with aldehydes in the presence of catalytic amount of tetra-*n*-butylammonium fluoride (TBAF) to afford the adducts **54**. The reaction demonstrated that the desilylation reaction of the compound **53** by fluoride ion provided the α-carbanion of (phenylsulfinyl)cyclopropane which reacted selectively with aldehydes as shown in equation 13.

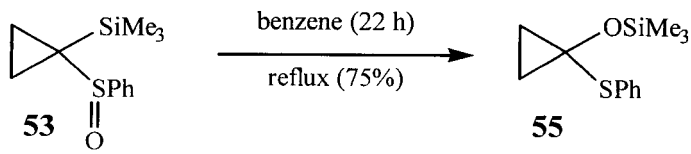


53 **54**

(eq. 13)

R = C_6H_5 (78%)
= *p*-$CH_3OC_6H_4$ (50%)
= *m*-$CH_3OC_6H_4$ (72%)
= $CH(CH_3)_2$ (80%)
= CH=CHPh (83%)

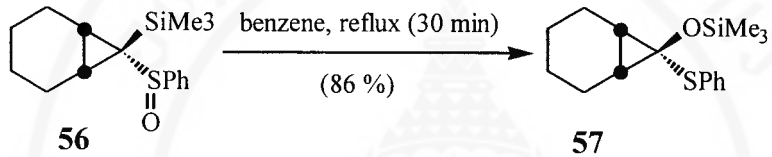
Cohen [34,35] reported that cyclopropane **53** provided excellent yield of the desired 1-phenylthio-1-(trimethylsilyloxy)cyclopropane **55** by refluxing in benzene *via* the *sila*-Pummerer rearrangement as shown in equation 14.



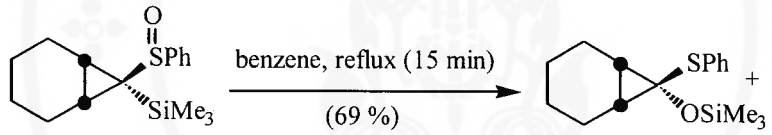
53 **55**

(eq. 14)

The siloxy compounds will almost certainly be useful as masked cyclopropanones. It was found that the bicyclic cyclopropanes **56** and **58** rearranged much faster than the parent system **53,** and that **58** rearranged faster than **56** and was indeed unstable at room temperature. The transfer of the trimethylsilyl group to oxygen [36] should relieve steric compression between the endo substituent and the cyclohexane ring (eqs. 15-16).[37]

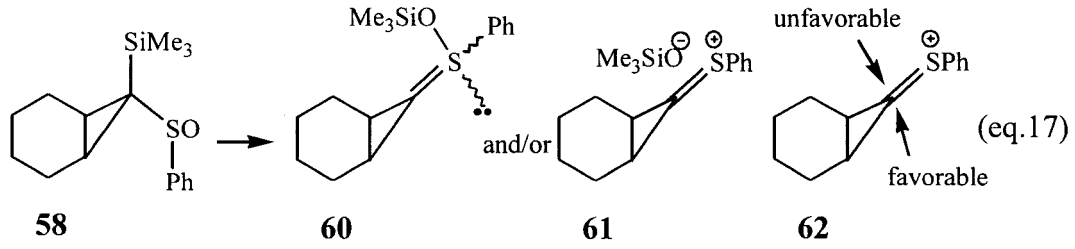


56 **57** (eq. 15)



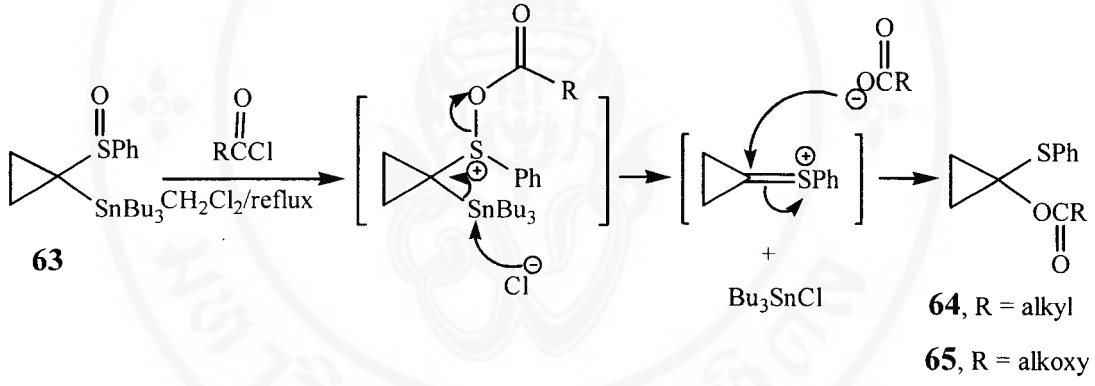
58 **59** + **57** 16:84 (eq. 16)

They observed that **56** gave the *exo*-siloxy isomer **57** as the only product and **58** gave the same isomer as the major product. The preferential formation of **57** was readily explained by the attack of the trimethylsiloxy anion on the sterically least hindered *exo*-face of the sulfur stabilized carbocation **62**. If the rearrangements of both **56** and **58** proceeded through the same intermediate **62**, then the product ratio must be the same in both cases. The fact that **59** (*endo*-siloxy isomer) is formed only from the *endo*-trimethylsilyl substrate **58**, but not from *exo*-trimethylsilyl substrate **56**, suggests that, to some extent, a contact ion pair **61** or an intramolecular rearrangement of the siloxy group to yield **60** might be involved (eq. 17).



58 **60** **61** **62**

The *stanna*-Pummerer type rearrangement was firstly found by our group. Thus, treatment of the α-stannyl cyclopropyl sulfoxide **63** with acyl chloride or alkyl chlorofomate in refluxing CH_2Cl_2 gave 1-(phenylthio)cyclopropane **64** or **65** in quite good yields (**Scheme 9**).[38]



63

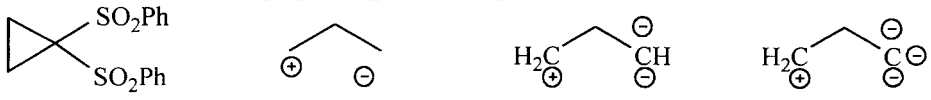
64, R = alkyl

65, R = alkoxy

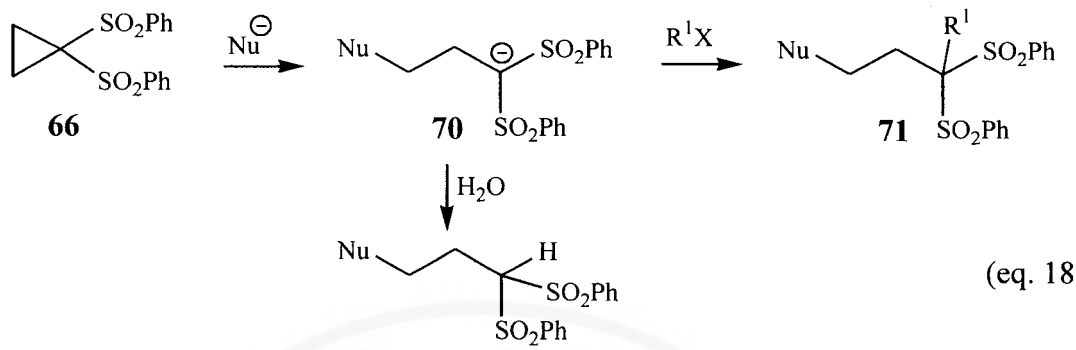
Scheme 9

1.3 Sulfonyl–substituted cyclopropanes

Trost and coworkers [39] reported that 1,1-bis(phenylsulfonyl)cyclopropane **66** provides a convenient synthon for 1,3-dipoles **67**, **68**, and **69**. Compound **66** is susceptible to nucleophilic attack. Various sulfur, oxygen and nitrogen nucleophiles opened the cyclopropane ring smoothly to give the anion intermediate, which could be trapped by electrophiles e.g. H_2O, methyl iodide or allyl bromide to afford compound **70** or compound **71** (eq. 18).

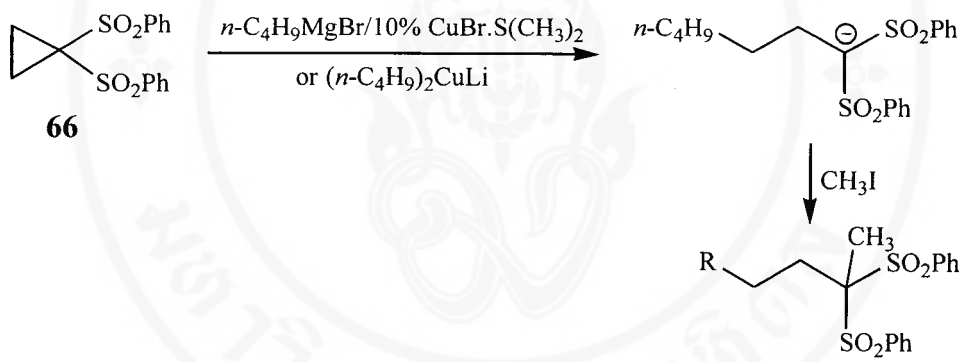


66 **67** **68** **69**

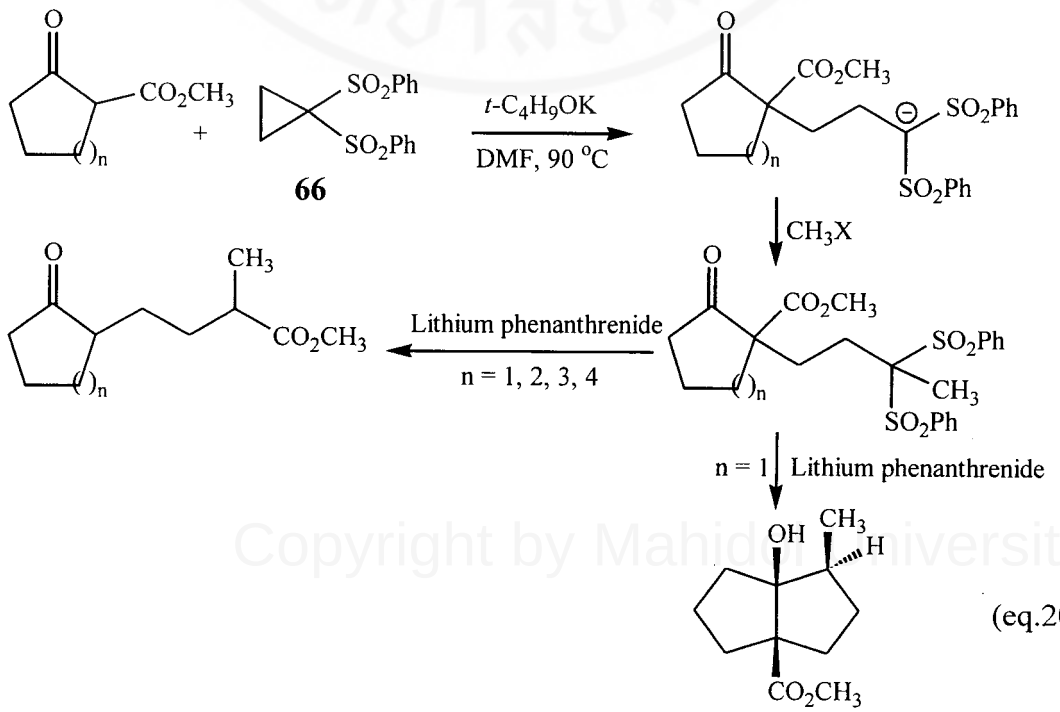


(eq. 18)

Furthermore, carbon nucleophiles such as RMgX/CuI, R_2CuLi or stabilized carbanions could be used for the ring-oprning reaction of compound **66** as shown in equations 19 and 20.

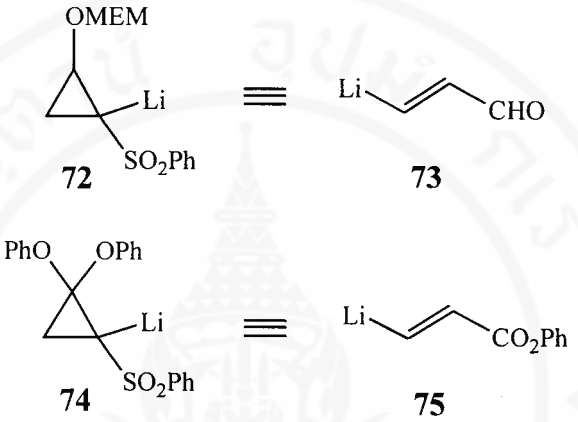


(eq.19)

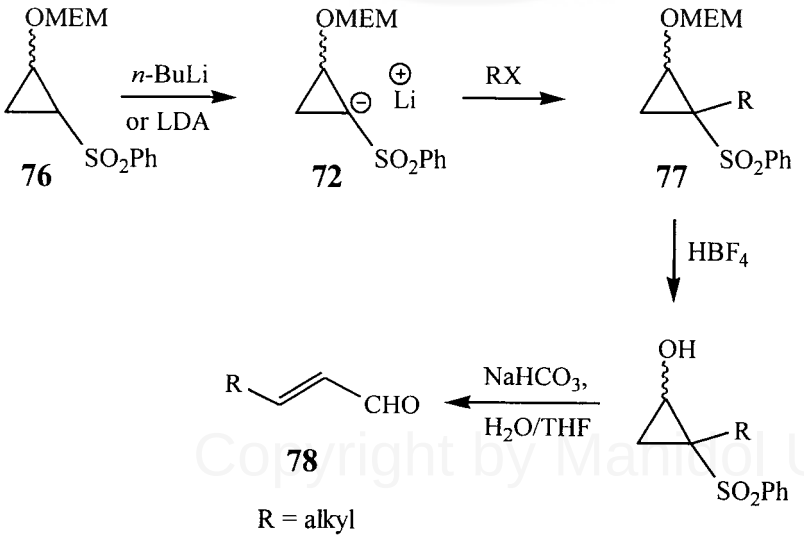


(eq.20)

The synthetic utilities of α-lithio (phenylsulfonyl)cyclopropane **72** as a β-lithio acrolein synthon **73** and of the anion **74** derived from 2,2-diphenoxy-1-(phenylsulfonyl)cyclopropane as a β-lithio acrylate synthon **75** were recently demonstrated by our group.[40, 41]

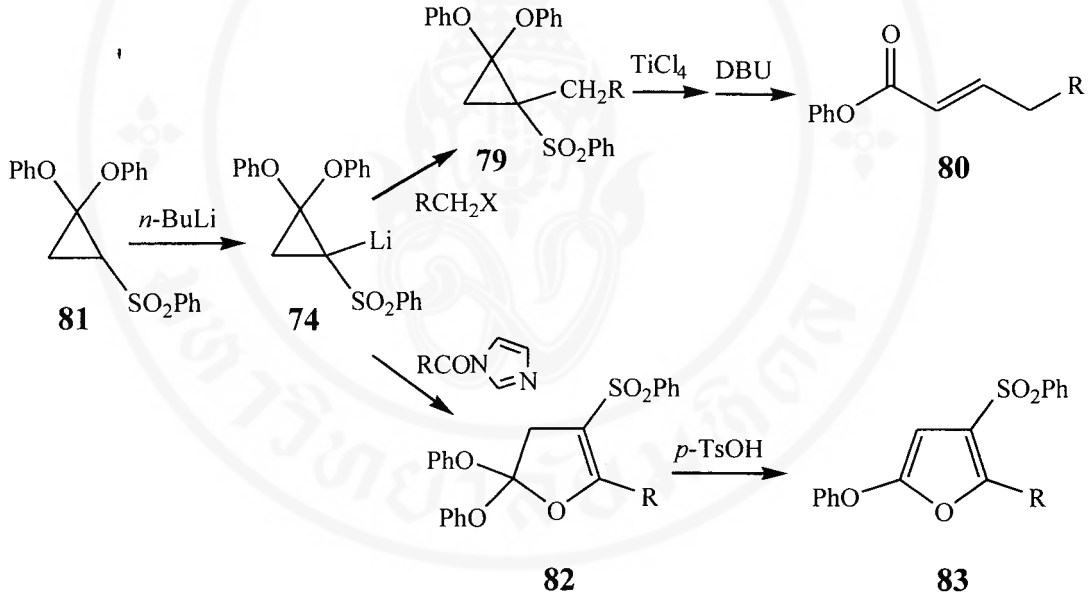


α-Lithio (phenylsulfonyl)cyclopropane **72**, derived from 1-[(2-methoxyethoxy) methoxy]-2-(phenylsulfonyl)cyclopropane **76**, reacted smoothly with alkyl halides, aldehydes and ketones to give adducts **77** in good yields which were transformed to the desired α,β-unsaturated aldehydes **78** as shown in (equation 21).[41]



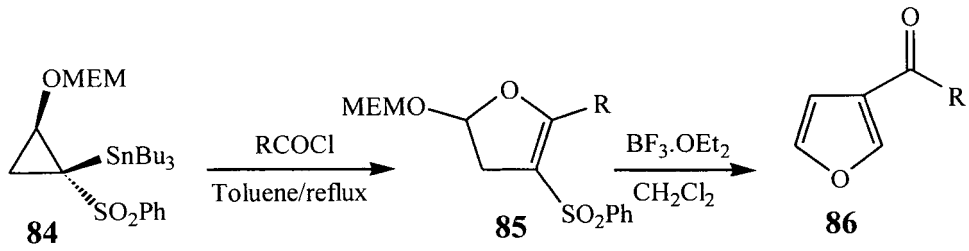
(eq. 21)

The anion **74** derived from the corresponding phenylsulfonyl substituted cyclopropane **81** (**Scheme 10**) reacted with alkylating agents to give the α-alkylated phenylsulfonyl cyclopropanes **79**. These compounds were subjected to $TiCl_4$-catalyzed ring-opening followed by elimination of the phenylsulfonyl group leading to α,β-unsaturated esters **80** in moderate yields.[40, 42] The anion **74** reacted with acyl imidazoles to provide substituted furans 83 after treatment of the resulting dihydrofuran derivatives **82** with *p*-TsOH.



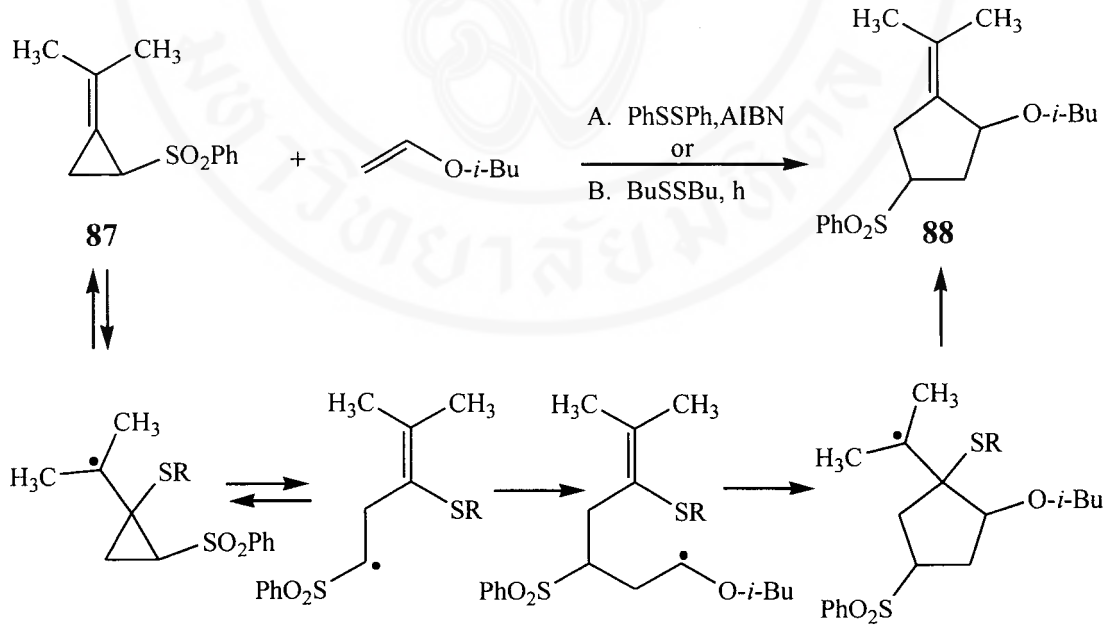
Scheme 10

In addition, α-stannyl (phenylsulfonyl)cyclopropane **84** was used as a precursor of a new general strategy for the synthesis of 3-acylfuran **86**.[43] The reaction involveS destannylative acylation [44] of **84** to give **85** followed by sequential hydrolysis of the MEM-group and the intramolecular Prins type reaction (or a [3.3]-sigmatropic rearrangement) of the resulting oxonium intermediate as illustrated in **Scheme 11**.[45]



Scheme 11

Singleton and coworkers [46] reported method for the [3+2] annulation of unactivated and electron-rich olefins, such as vinyl ether, allyl alcohol and methylenecyclohexane, with 2-(phenylsulfonyl)-1-methylenecyclopropane **87** by thiyl radical catalyzed reaction to afford the methylenecyclopentane **88** as shown in **Scheme 12**.

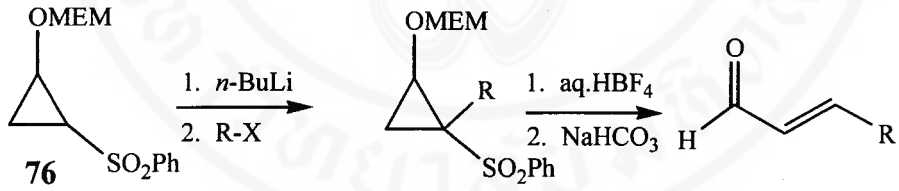


Scheme 12

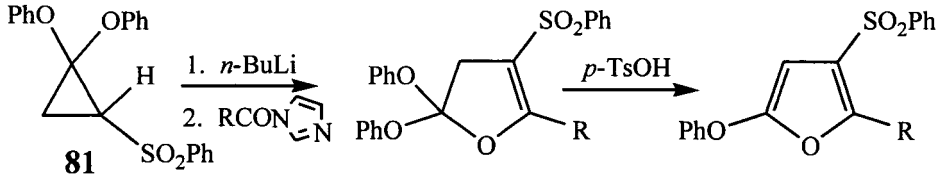
CHAPTER II

RESULTS AND DISCUSSION

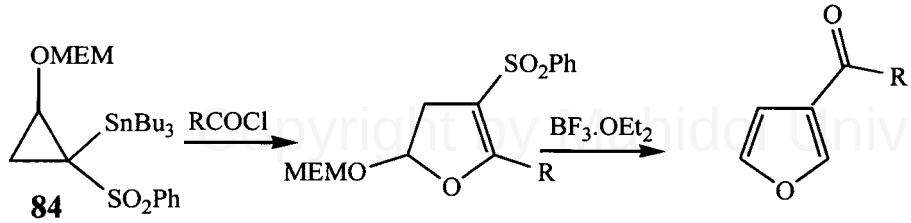
The chemistry of sulfur-substituted cyclopropane has been extensively studied in organic synthesis as three-carbon building blocks. Many reviews concerning the use of cyclopropane derivatives in organic synthesis have been reported.[1-5] We have been interested in the synthetic utilization of vicinally donor-acceptor substituted cyclopropanes, and recently demonstrated that donor-acceptor substituted cyclopropanes **76**, **81** and **84** can be employed as useful three-carbon building blocks for the preparation of α,β-unsaturated aldehydes,[41] esters [44] and substituted furans [45] (equations 22-24).



(eq. 22)

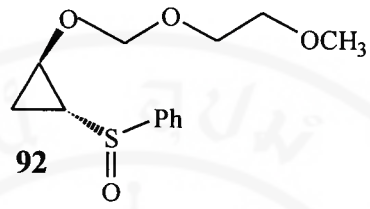


(eq. 23)



(eq. 24)

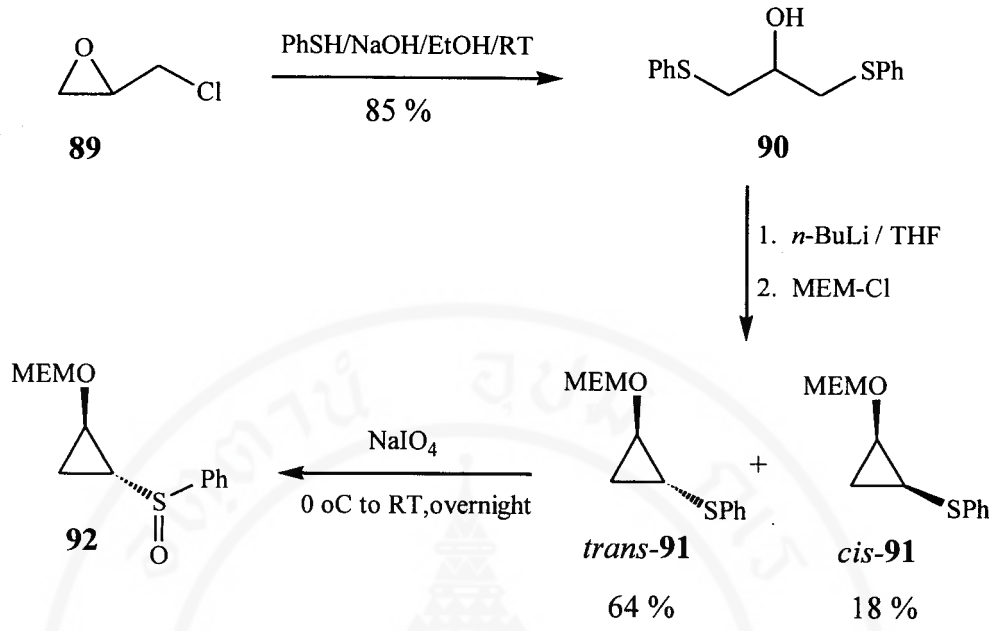
In connection with our above results, it is of interest to study the possibilities of using 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane **92** as a new three-carbon synthon in organic synthesis.



92

2.1 Preparation of *trans*-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (92)

By using the known procedure,[47] the starting sulfoxide **92** could be synthesized as outlined in **Scheme 13**. Treatment of epichlorohydrin **89** with thiophenol in the presence of a solution of sodium hydroxide in ethanol at room temperature afforded 1,3-bis(phenylthio)-2-propanol (**90**) in good yield. After treatment of the propanol **90** with 2.2 equivalents of *n*-butyllithium in THF followed by trapping the cyclopropane alkoxide intermediate with 1-chloromethoxy-2-methoxyethane (MEM-Cl), the reaction led to the formation of a mixture of *cis*- and *trans*-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfenyl)cyclopropane (**91**) in 82 % yield. Both isomers of **91** could be separated by careful flash column chromatography. *Trans*- and *cis*-**91** could be obtained in 64 % and 18 % yields, respectively. The ^{1}H NMR spectral data of both isomers are summarized in the experimental section. *Trans*-cyclopropyl sulfoxide **92** was readily obtained in quantitative yield by oxidation of the corresponding *trans*-**91** with $NaIO_4$ in aqueous methanol at 0 °C and then at room temperature overnight.

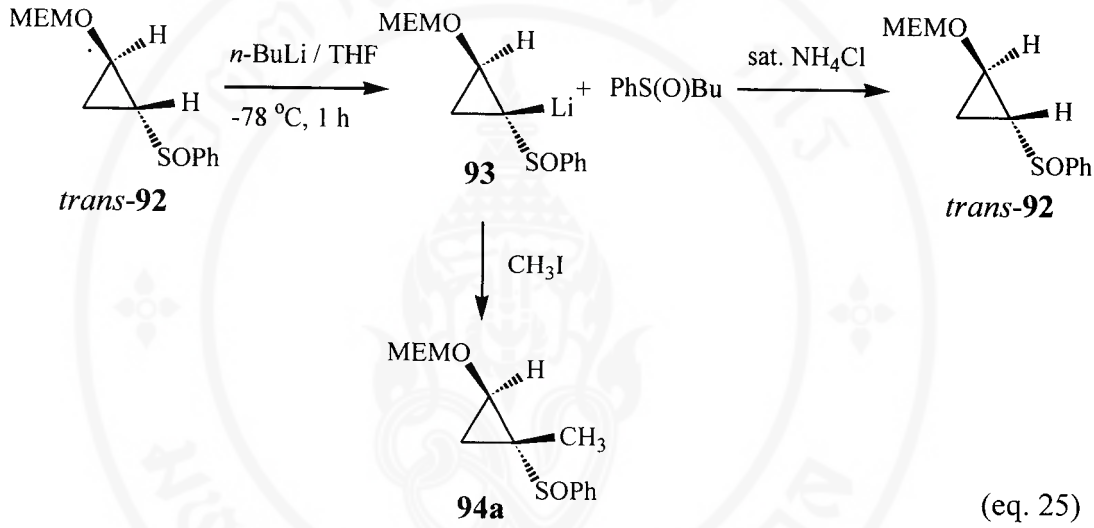


Scheme 13

2.2 Generation of the α-carbanion 93 from *trans*-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (92)

Initially, optimization of the conditions for the generation of the desired α-carbanion **93** from the corresponding *trans*-**92** was needed. We therefore began to investigate the generation of the anion **93** from *trans*-**92** by using *n*-butyllithium. Thus, treatment of *trans*-cyclopropyl sulfoxide **92** with one equivalent of *n*-butyllithium in tetrahydrofuran at –78 °C for 1 h followed by quenching of the resulting pale yellow solution with a saturated aqueous ammonium chloride solution at -78 °C led to the recovery of the starting *trans*-**92** in 69-70 % yield along with 5-10 % yield of butyl phenyl sulfoxide. However, having quenched the pale yellow solution of the expected anion **93** with methyl iodide provided the expected product **94a** in 70 % yield (eq. 25). The formation of butyl phenyl sulfoxide resulted presumably from nucleophilic attack of *n*-butyllithium at the sulfur atom of the sulfoxide moiety

followed by carbon-sulfur bond cleavage.[48,49,50] This result indicated that the α-deprotonation of *trans*-**92** underwent with the competition of the carbon-sulfur bond cleavage of the phenylsulfinyl group. We assumed that the amount of butyl phenyl sulfoxide obtained (5-10 %) depended on the rate of addition of *n*-butyllithium during the generation of the anion **93**.



(eq. 25)

From the above results, it was very interesting that the product **92** obtained after quenching the anion **93** with a saturated aqueous ammonium chloride solution was the *trans*-isomer by comparison of its ^{1}H NMR spectrum with that of the starting *trans*-**92**. This led to the assumption that the structure of the anion **93** might be as depicted in **Figure 1**.

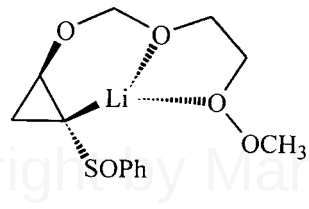
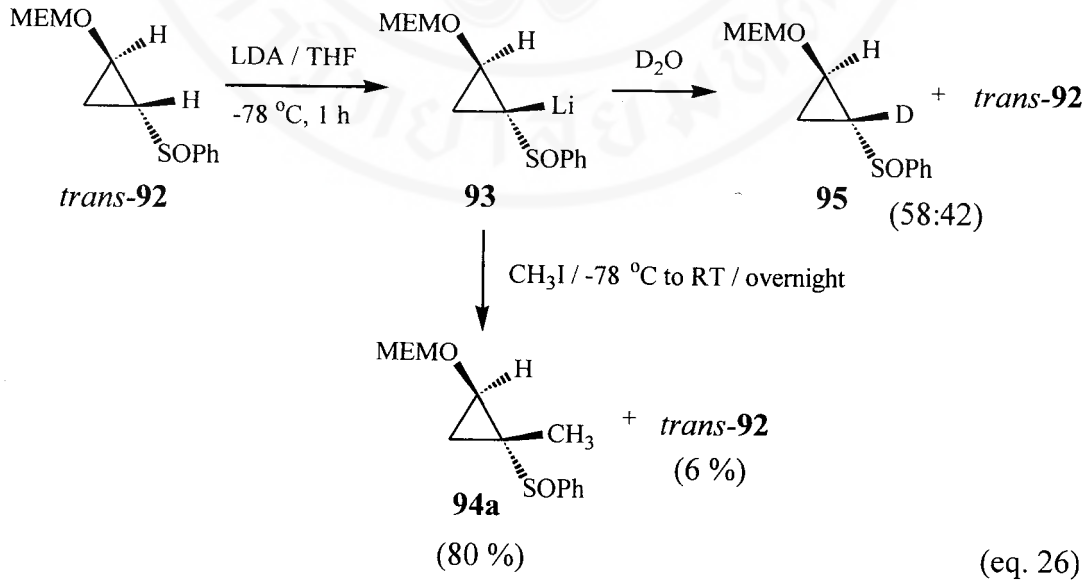


Figure 1 Structure of the anion **93**

Further optimization of the conditions for the deprotonation of *trans*-**92** was made. In stead of *n*-butyllithium, we used a less strong base, lithium diisopropylamide (LDA). Thus, treatment of the *trans*-cyclopropyl sulfoxide **92** with LDA in THF at –78 °C for 1 h followed by addition of methyl iodide at –78 °C and allowed to room temperature overnight afforded in 80 % yield of the sulfoxide **94a** and 6 % yield of the recovered starting material **92** in .

In order to prove the presence of the expected anion **93,** the pale yellow solution, obtained from the cyclopropyl sulfoxide **92** with LDA in THF at –78 °C for 1 h, was quenched with D_2O to afford a crude product (99% yield) which contained a 58:42 mixture of a deuterium incorporated product **95** and *trans*-**92** as shown in equation 26. However, we believed that anion **93** was generated under this condition more than 58 %, because the reaction with methyl iodide gave **94a** up to 80 % yield.



trans-**92** **93** **95** (58:42)

94a (80 %) + *trans*-**92** (6 %)

(eq. 26)

2.3 Reaction of the anion 93 with alkylating agents

n-Butyllithium was chosen to be the base of choice for the generation of the anion **93** from *trans*-cyclopropyl sulfoxide **92** due to the convenience of carrying out the reaction. Thus, the generation of the anion **93** from **92** was carried out by using *n*-butyllithium in THF at –78 °C for 1 h. The reaction of the anion **93** with methyl iodide at –78 °C and then at room temperature overnight provided the expected product **94a** in 70 % yield as a 1:1 mixture of diastereomers. The alkylation of the anion **93** with other alkylating agents afforded moderate yields of the alkylated products **94b–94g** as mixtures of diastereomers as listed in **Table 1**.

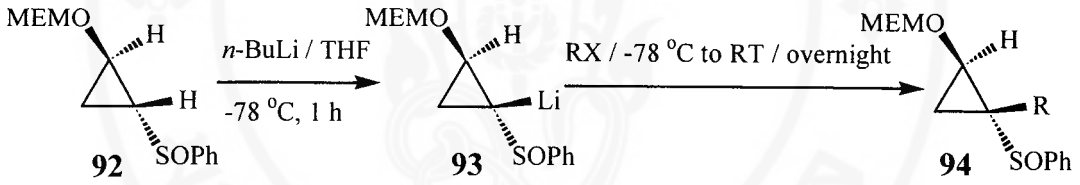
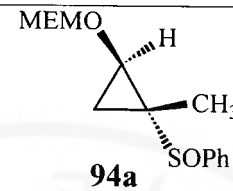
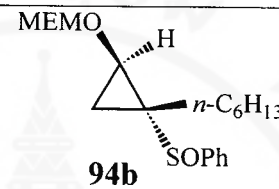
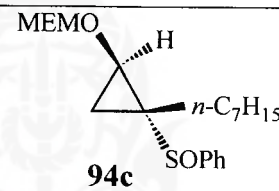
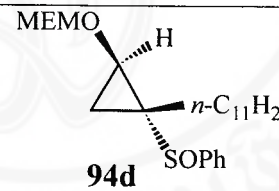
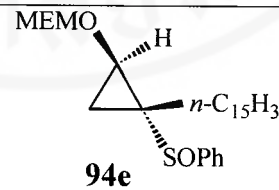
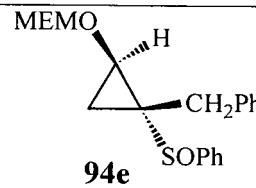
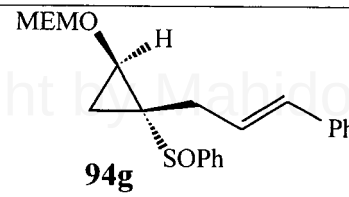
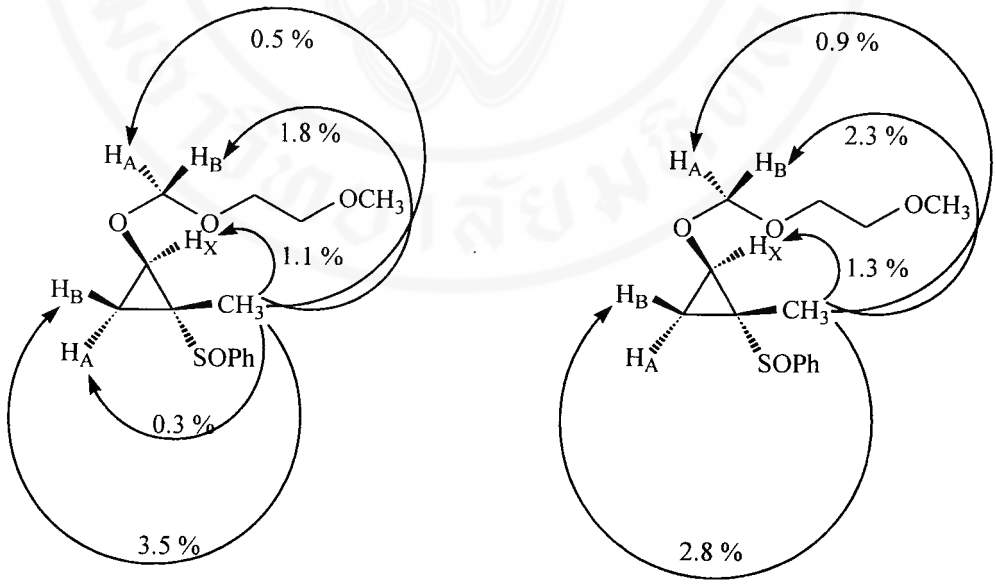


Table 1 Reaction of the anion **93** with alkyl halides.

Entry	Electrophile	Adduct **94**	% Yield (ratio of diastereomer)
1	CH_3-I	 **94a**	70 (1:1)
2	*n*-C_6H_{13}-Br	 **94b**	62 (1:1.3)
3	*n*-C_7H_{15}-Br	 **94c**	59 (1:1.4)
4	*n*-$C_{11}H_{23}$-Br	 **94d**	60 (1:3.7)
5	*n*-$C_{15}H_{31}$-Br	 **94e**	60 (1:1.3)
6	$PhCH_2$-Br	 **94e**	65 (1:1.3)
7	PhCH=$CHCH_2$-Br	 **94g**	63 (1:1.2)

The structures of compounds **94a-g** were characterized on the basis of their spectral data (IR, NMR and MS). The IR spectra of these compounds exhibited one strong absorption at 1047-1050 cm^{-1} due to S=O stretching. The mass spectra of almost compounds of type **94** showed the base peak at m/z 59.

Since compounds **94** were obtained as mixtures of two diastereomers, so their NMR spectra clearly exhibited two sets of each proton of the compounds. Therefore, the ratios of the diastereomers of **94a–g** could be determined. Attempted separation of the diastereomers of **94** were unsuccessful by preparative thin-layer chromatography on silica gel. The *trans*-stereochemistry of **94a** was proved by using Nuclear Overhauser Effect (NOE) technique as shown in **Figure 2**. The ^1H NMR data of the mixture of diastereomers of **94a** was shown in **Table 2**.



94a - A **94a - B**

Figure 2

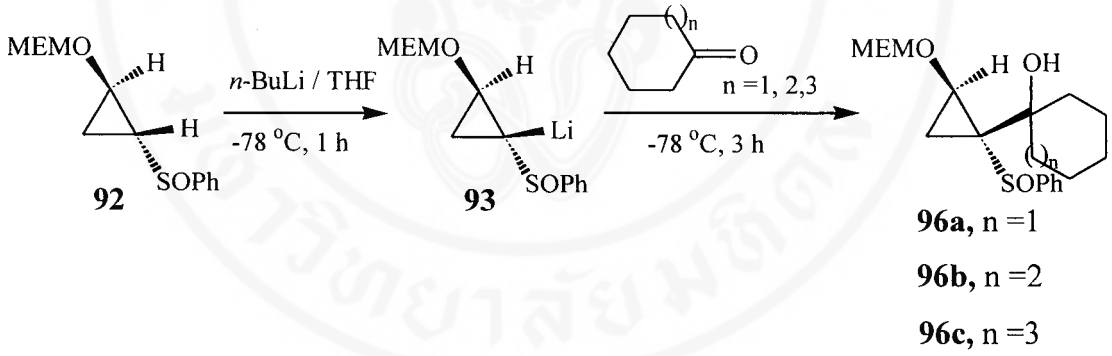
As shown in **Figure 2**, in the case of **94a-A** an enhancement of 3.5% was observed for the signal of H_B and 0.3% for the signal of H_A when the resonance of the methyl group was irradiated. In the case of **94a-B** the irradiation of the methyl group led to a 2.8% enhancement of the signal for H_B. This represented an example for all compounds in this series which are *trans*-isomer.

Table 2 Significant ^{1}H NMR data of two diastereomers of **94a**.

Assignment	δ_H (ppm) of **94a**	
	diastereomer **A**	diastereomer **B**
H_B	0.77 (dd, J = 6.7, 4.3 Hz, 1H)	0.87 (dd, J = 6.7, 4.3 Hz, 1H)
CH_3	1.10 (s, 3H)	1.12 (s, 3H)
H_A	1.38 (t, J = 7.3 Hz, 1H)	1.55 (t, J = 7.3 Hz, 1H)
OCH_3	3.34 (s, 3H)	3.33 (s, 3H)
OCH_2CH_2O	3.70-3.57 and 3.52-3.47 (each m, 8H)	
H_X	3.93 (dd, J = 7.6, 4.3 Hz, 1H)	4.05 (dd, J = 7.6, 4.3 Hz, 1H)
CH_ACH_B	4.58 (d, J = 6.5, Hz, 1H)	4.53 (d, J = 6.5 Hz, 1H)
CH_ACH_B	4.68 (d, J = 6.5, Hz, 1H)	4.64 (d, J = 6.5 Hz, 1H)
ArH	7.55, 7.45 (each m, 10H)	

2.4 Reaction of the anion 93 with carbonyl compounds

From our initial results, it was apparent that the reactions of the anion **93** with alkyl halides led to the sulfoxides **94a-g**. Therefore, we next investigated the reactions of the anion **93** with ketones. The anion **93** could be easily generated by reacting sulfoxide **92** with 1.1 equivalent of *n*-butyllithium in THF at – 78 °C for 1 h. When the anion **93** was allowed to react with 1.2 equivalent of cyclohexanone at – 78 °C for 3 h, a pale brown liquid of a crude product of **96a** was obtained after workup with a saturated aqueous ammonium chloride solution. It was purified by preparative thin-layer chromatography to give the adduct **96a** in 61 % yield. This procedure was used as the standard conditions for the reaction of the anion **93** with other ketones.

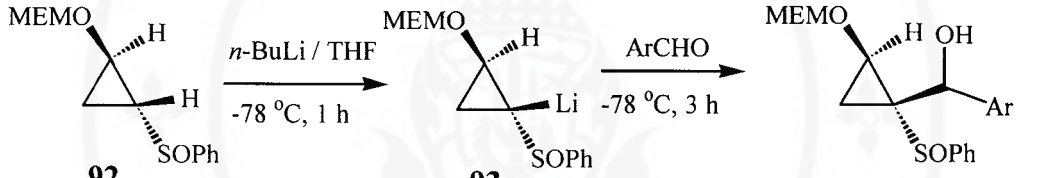


The adduct **96a** was obtained as a mixture of two diastereomers in a ratio of 1:1.2. The relative stereochemistries of these diastereomers were assigned according to their ^{1}H NMR spectral data. Both diastereomers of **96a** could be separated by preparative thin-layer chromatography.

Having succeeded in preparing compound **96a,** we then next investigated the reaction of the anion **93** with other ketones. The results are summarized in **Table 3**.

We assumed that the relative stereochemistry at C-1 and C-2 of the cyclopropane ring of the adducts **96a-c** would be *trans*- as that of the alkylated product **94a**.

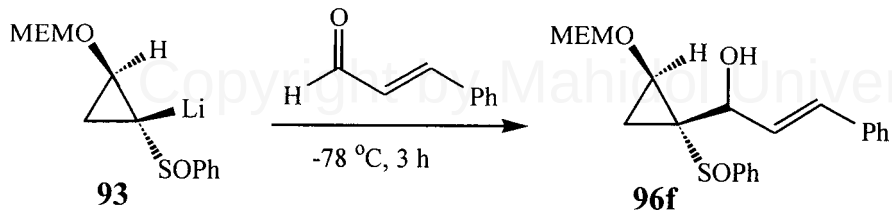
Treatment of the anion **93** with anisaldehyde at –78 °C for 3 h and at room temperature overnight gave adduct **96d** in 64% yield and the recovered starting material **92** in 28 % yield (entry 4, **Table 3**). Similarly, the reaction of benzaldehyde with the anion **93** afforded adduct **96e** in 70% yield and the recovery of starting material **92** in 4 %.



96d, Ar = *p*-$C_6H_4OCH_3$

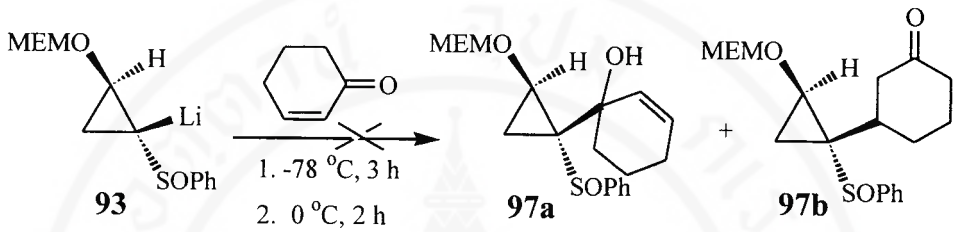
96e, Ar = -C_6H_5

As the above results, we have succeeded in preparing the **96a-e** by reacting the anion **93** with aromatic aldehydes and aliphatic ketones. It was interesting to explore the reaction of the anion **93** with unsaturated carbonyl compounds and esters. Thus, treatment of the anion **93**, which was generated from the sulfoxide **92** with *n*-butyllithium in THF at –78 °C, with cinnamaldehyde at –78 °C for 3 h gave 1,2-addition product **96f** in 46% yield. A better yield of **96f** (74% yield) was obtained, when the anion **93** was generated by employing LDA.



96f

The reaction of the anion **93** with cyclohexenone (1.2 equiv) at –78 °C for 3 h followed by stirring at 0 °C for 2 h provided the recovery of the starting material **92** and no traces amount of the expected 1,2-addition of type **97a** and 1,4-adduct **97b** could be detected.



In addition, attempted treatment of the anion **93** with ethyl crotonate at –78 °C for 3 h afforded 1,4-adduct **96g** in 15 % yield. In the presence of HMPA, the reaction afforded the recovery of the starting material **92** and no trace amount of the expected **96g** could be observed. The similar results were obtained, when the reaction mixture was warmed up to room temperature overnight after stirring at –78 °C for 3 h.

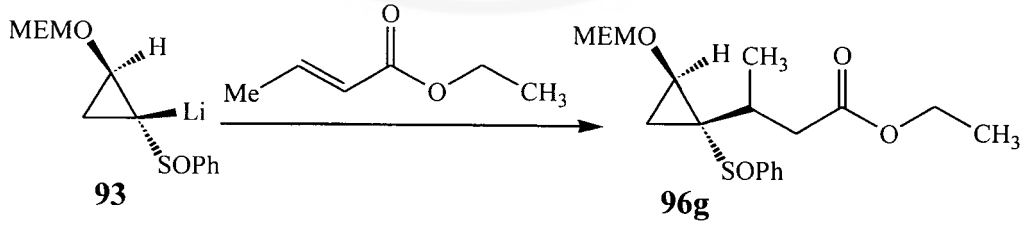


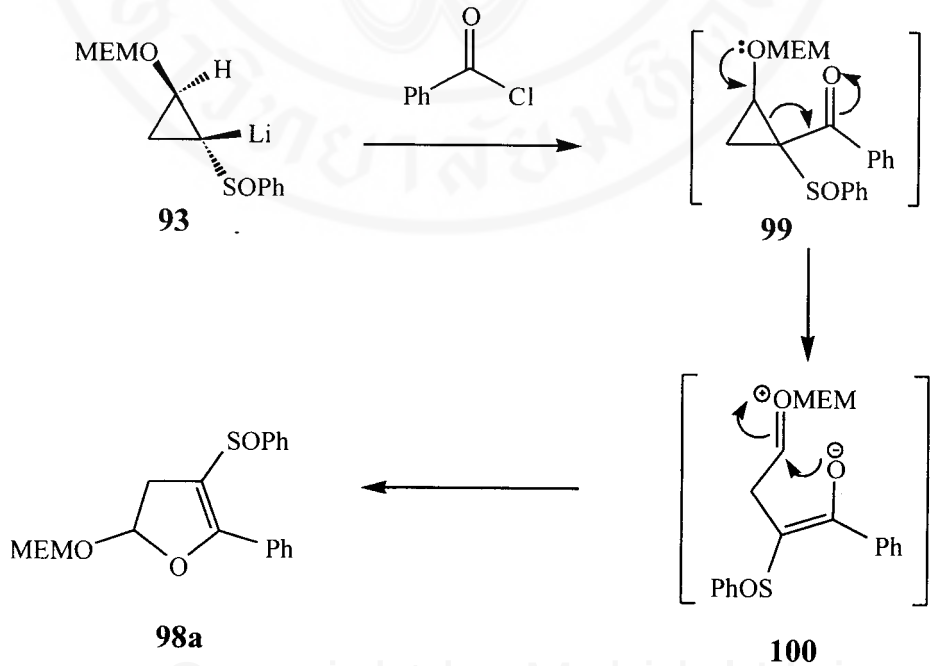
Table 3 Preparation of compounds **96a-g**.

Entry	Carbonyl compound	Products	% Yield	Ratio of diastereomers[a]
1	Cyclohexanone	**96a**	61	1.1 : 1.0
2	Cycloheptanone	**96b**	61	1.0 : 1.8
3	Cyclooctanone	**96c**	37	1.0 : 1.4
4	Anisaldehyde	**96d**	64	-
5	Benzaldehyde	**96e**	70	-
6	Cinnamaldehyde	**96f**	74	23:1.9:1.0:1.5
7	Ethyl crotonate	**96g**	15	1.0;1.9
8	Cyclohexenone	-	-	-

[a] Determined by ^{1}H NMR of -OCH_2O-.

2.5 Studies for the acylation of the anion 93

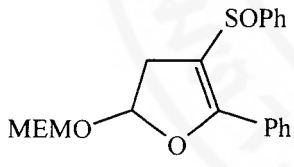
In connection with our previous results for the acylation of compound **84** and of α-lithiated **81** leading to dihydrofuran derivatives,[45, 45] it is of interest to study the reaction of the anion **93** with acylating agents. Initially, we investigated the reaction of the anion **93** with benzoyl chloride. Treatment of the anion **93** with benzoyl chloride (1.2 equiv) in THF at –78 °C for 2 h led to the expected dihydrofuran **98a** in 21% yield together with the starting material **92** in 18% yield as well as other unidentified products as revealed by TLC of the crude product. The formation of the dihydrofuran **98a** would be explained as a result of a ring-opening of the initially formed benzoylated cyclopropyl sulfoxide **99**, a donor–acceptor substituted cyclopropane, to intermediate **100** which then cyclized to the dihydrofuran **98a** as shown in **Scheme 14**.



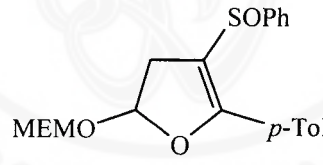
Scheme 14

From the above results, it was clearly shown that anion **93** derived from *trans* 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane **92** which is a vicinally donor-acceptor substituted cyclopropane could be functioned as a three-carbon dihydrofuran annulating agent. Our previous success for the preparation of the dihydrofuran **98a** in low yield by reacting the anion **93** with acyl chlorides prompted us to study the reaction utilizing acyl imidazoles.

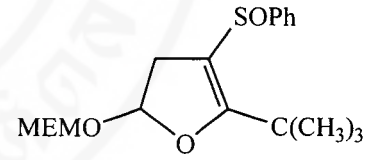
All of our attempts led to unsuccessful results. All reactions under various conditions gave complex mixtures of products as shown by TLC of the crude products obtained. Only a low yield of the expected dihydrofuran could be isolated along with the recovered starting material **92**. All attempted conditions are summarized in **Table 4**.



98a



98b

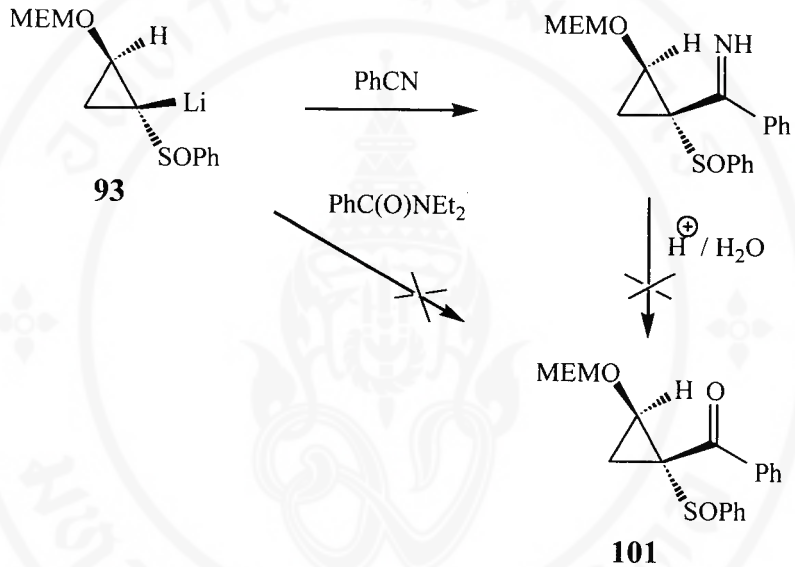


98c

Table 4 Reaction of the anion **93** with acyl imidazoles.

Entry	Acyl imidazoles	Conditions	Results
1	Benzoyl imidazole (1.2 equiv)	1. in THF at –78 °C for 2 h. 2. refluxing toluene of a crude product for 1 h.	**98a** (25 %) and the starting material **92** (8 %)
2	Benzoyl imidazole (1.2 equiv)	1. in THF at –78 °C for 2 h. 2. at 0 °C for 1 h.	**98a** (12 %) and the starting material **92** (38 %)
3	Benzoyl imidazole (1.2 equiv)	inversed addition by transfering **93** in THF into imidazole at –78 °C, 2 h.	**98a** (12 %) and a complex mixture of product
4	*p*-Toluyl imidazole (1.2 equiv)	in THF at –78 °C for1.5h.	The recovered starting material **92**
5	*p*-Toluyl imidazole (1.2 equiv)	1. in THF at –78 °C for 2 h. 2. at 0 °C for 1 h.	**98b** (11 %) and the starting starting **92** (34 %)
6	*p*-Toluyl imidazole (1.2 equiv)	in THF at –78°C and then warmed up to RT overnight.	**98b** (27 %) and the starting material **92** (22 %)
7	Pivaloyl imidazole (1.2 equiv)	1. in THF at –78 °C for 2 h. 2. at 0 °C for 1 h.	**98c** (10 %) and the starting material **92** (33 %)
8	Pivaloyl imidazole (1.2 equiv)	in THF at –78 °C and then warmed up to RT overnight.	**98c** (20 %) and the starting material **92** (14 %)

Finally, benzonitrile was used as an acylating agent. It was, however, found that the reaction of the anion **93** with benzonitrile at –78 °C for 1 h and then at room temperature overnight gave a complex mixture of products. The starting material **92** could be recovered in 49 % yield and no trace amount of the expected **101** could be isolated (**Scheme 15**).



Scheme 15

The reaction of the anion **93** with *N,N*-diethylbenzamide at –78 °C to room temperature afforded the recovered starting material **92** (47 %) and a complex mixture of products. No traces amount of product of type **101** could be isolated.

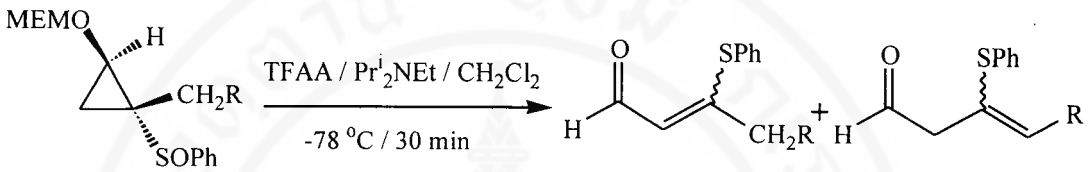
2.6 Pummerer-type reaction mediated ring-opening of α-alkyl substituted cyclopropyl phenyl sulfoxide 94

Because of the semi-polar nature of the S-O linkage in sulfoxides, the terminal oxygen atom should be base-like as that in terminal amine oxide or the carbonyl oxygen. In fact, the oxygen atom in sulfoxides is the host site for protons or Lewis

acid to form complexes, which can undergo various types of reactions, e.g. Pummerer rearrangement, reductive deoxygenation, etc.

In our previous studies,[47] we found that α,β-unsaturated aldehyde **102d-e** were readily obtained in 30 – 43 % as mixtures of *E*-/*Z*-isomers upon treatment of the cyclopropyl sulfoxides **94d-e** with acetic anhydride or trifluoroacetic anhydride or refluxing in xylene. These findings prompted us to extend our investigation in order to search for better conditions for such Pummerer type reaction mediated ring-opening of the cyclopropyl sulfoxide **94**. At the same time we would like to demonstrate the synthetic utility of the cyclopropyl sulfoxide **94** as a three-carbon building block for the preparation of α,β-unsaturated aldehyde **102**. Initially, we treated **94a** with trifluoroacetic anhydride (1.5 equiv) and *N,N*-diisopropylethylamine (1.5 equiv) in dichloromethane at –78 °C for 3 h to afford the expected α,β-unsaturated aldehyde **102a** in only 14% yield and the recovered starting material **102a** in 38% yield after chromatography. A better result was obtained when **94a** was reacted with trifluoroacetic anhydride and *N,N*-diisopropylethylamine (each 2 equiv) at –78 °C for only 30 min, and worked up with a saturated aqueous sodium hydrogen carbonate solution. The desired product **102a** could be isolated in 62% yield as a 70:30 mixture of *E*- and *Z*-isomers. Both isomers of **102a** could be separated by careful preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane, triple runs). Under the standard conditions, the cyclopropyl sulfoxides **94b-f** afforded the mixtures of the expected α,β-unsaturated aldehyde **102b-f** (major product) and β,γ-unsaturated aldehydes **103b-f** (minor product) in moderate to good yields. All of compounds **102b-f** and **103b-f** were obtained as mixtures of *E*- and *Z*-isomers as summarized in **Table 5**. Attempts to separate **102b-f** from **103b-f** were made. It was found that

102b-f could be isolated in 57–66% yields (**Table 5**) after preparative thin-layer chromatography. Unfortunately, β,γ-unsaturated aldehydes **103b-f** could not be obtained in pure forms due to their rapid isomerisation into the α,β-unsaturated ones during the attempted separation. Furthermore, β,γ-unsaturated aldehydes **103b-f** seemed to be slowly decomposed upon standing.



94 **102** **103**

Table 5 Ring–opening of the cyclopropyl sulfoxides **94a-f**.

Entry	Compounds **94**	Ratio of **102** (*E*:*Z*) : **103** (*E*:*Z*)[a]	% Yield [b]
1	**94a** (R = H)	100 (70:30) : 0	62
2	**94b** (R = C_5H_{11})	79 (63:37) : 21 (20:80)	83
3	**94c** (R = C_6H_{13})	86 (79:21) : 14 (35:65)	75
4	**94d** (R =$C_{10}H_{21}$)	78 (72:28) : 22 (26:74)	84
5	**94e** (R = $C_{14}H_{29}$)	74 (75:25) : 26 (12:88)	77
6	**94f** (R = Ph)	84 (68:32) : 16 (36:64)	69

[a] Determined by ^{1}H NMR of the crude products by integration of aldehyde protons.

[b] Isolated yields.

The ^{1}H NMR spectra of α,β-unsaturated aldehydes **102b-f** exhibited two sets of aldehyde protons as two sets of doublets due to the coupling of aldehyde protons with the α-olefinic protons, while the aldehyde proton of β,γ-unsaturated aldehydes **103b-f** presented two sets of triplet signals according to coupling between the aldehyde protons and α-methylene protons.

Table 6 % Yields of **102b-f** after purification by preparative thin-layer chromatography of mixtures of **102** and **103**.

Entry	Compound **102**	% Yield (*E* / *Z*)[a]
1	**102b** (R = C_5H_{11})	65 (79/21)
2	**102c** (R = C_6H_{13})	64 (76/24)
3	**102d** (R = $C_{10}H_{21}$)	66 (74/26)
4	**102e** (R = $C_{14}H_{29}$)	57 (89/11)
5	**102f** (R = Ph)	58 (68/32)

[a] Determined by ^{1}H NMR of the isolated product by integration of aldehyde protons.

The structures of compounds **93a-f** were characterized on the basis of their spectral data (IR, NMR, MS and analysis). Elemental composition of compounds **102e** and **103e** were not successfully to determined by combustion analysis. It was, however, analyzed as their semicarbazone derivatives. The *Z*- and *E*-stereochemistries of compounds **102a-f** and **103b-f** could be assigned by the chemical

shifts and the coupling constants between aldehydic proton and olefinic proton in ^{1}H NMR spectra of **102a-f,** and between aldehyde proton and methylene protons in ^{1}H NMR spectra of **103b-f** as shown in **Tables 7** and **8**, respectively.

Table 7 Significant ^{1}H NMR data of compounds **102a-f**.

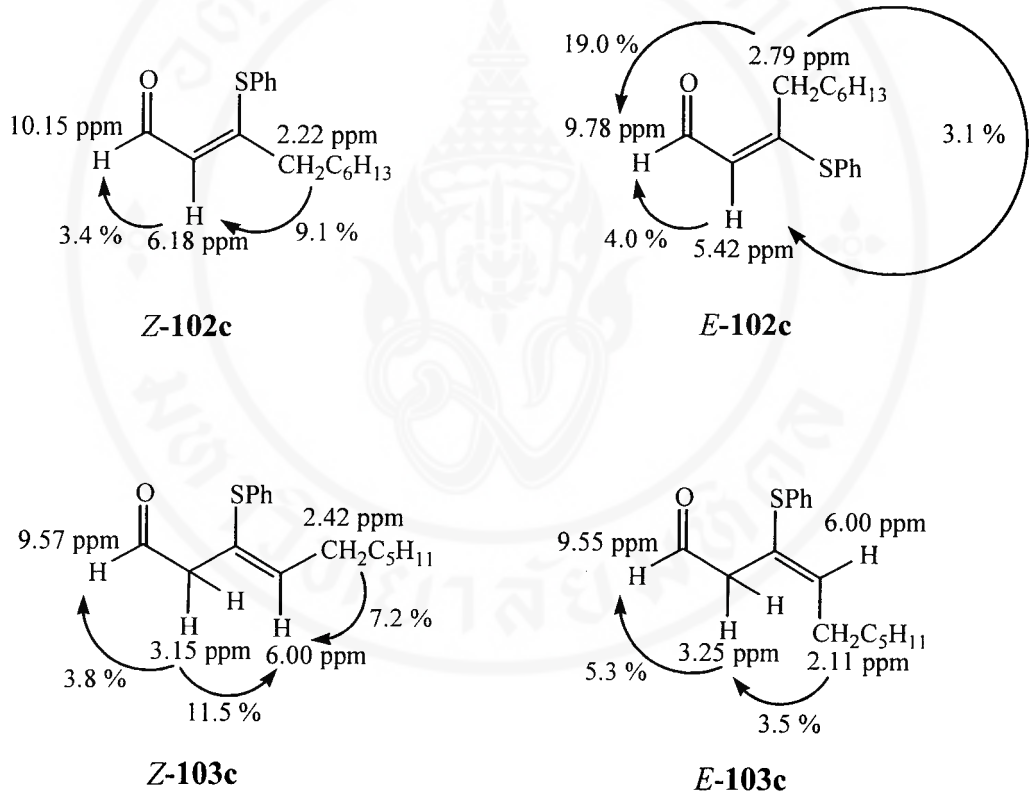
Compounds **102**	*Z*-**102** (minor isomer)			*E*-**102** (major isomer)		
	δ C*H*O (ppm)	δ C*H*=C (ppm)	$J_{H,H}$ (Hz)	δ C*H*O (ppm)	δ C*H*=C (ppm)	$J_{H,H}$ (Hz)
102a	10.05 (d)	6.14 (d)	6.7	9.78 (d)	5.47 (d)	7.5
102b	10.15 (d)	6.18 (d)	6.6	9.79 (d)	5.41 (d)	7.9
102c	10.15 (d)	6.18 (d)	6.6	9.78 (d)	5.42 (d)	7.9
102d	10.15 (d)	6.18 (d)	6.6	9.79 (d)	5.42 (d)	7.9
102e	10.15 (d)	6.18 (d)	6.7	9.79 (d)	5.41 (d)	7.9
102f	10.17 (d)	6.10 (d)	6.6	9.91 (d)	5.00 (d)	7.7

Table 8 Significant ^{1}H NMR data of compounds **103b-f**.

Compounds **103**	*Z*-**103** (major isomer)			*E*-**103** (minor isomer)		
	δ C*H*O (ppm)	δ CH_2C=CH (ppm)	$J_{H,H}$ (Hz)	δ C*H*O (ppm)	δ CH_2C=CH (ppm)	$J_{H,H}$ (Hz)
103b	9.58 (t)	3.15 (d)	1.8	9.55 (t)	3.25 (d)	1.9
103c	9.57 (t)	3.15 (d)	2.1	9.55 (t)	3.25 (d)	2.1
103d	9.58 (t)	3.15 (d)	2.0	9.55 (t)	3.25 (d)	2.0
103e	9.57 (t)	3.15 (d)	2.2	9.54 (t)	3.24 (d)	2.2
103f	9.72 (t)	3.48 (d)	1.8	9.67 (t)	3.11 (d)	1.9

Moreover, the relative stereochemistries of **102c** and **103c** were confirmed by using NOE technique as shown in **Figure 3**. The results indicated that in the case of *Z*-**102c** an enhancement of 9.1% was observed for the signal of olefinic protons, when the methylene protons was irradiated, and an enhancement of 3.4% was observed for the signal of an aldehyde proton, when the resonance of the olefinic proton was irradiated. In the case of *E*-**102c** the irradiation of the methylene protons led to a 19.0% and 3.1% enhancement of the signals for aldehyde proton and olefinic proton, respectively. An enhancement of 4.0% was observed for the signal of the aldehyde proton of **102c,** when the olefinic proton was irradiated. Furthermore, in the case of *Z*-

103, the irradiation of the methylene protons (δ 3.15 ppm) led to a 11.5% enhancement of the signal for olefinic proton, whereas in the case of *E*-**103c**, the irradiation of the methylene protons (δ 2.11 ppm) led to a 3.5% enhancement of the signal for methylene protons (δ 3.25 ppm). These NOE experiments of compounds **102c** and **103c** were used to represent for all of other compounds in these series.



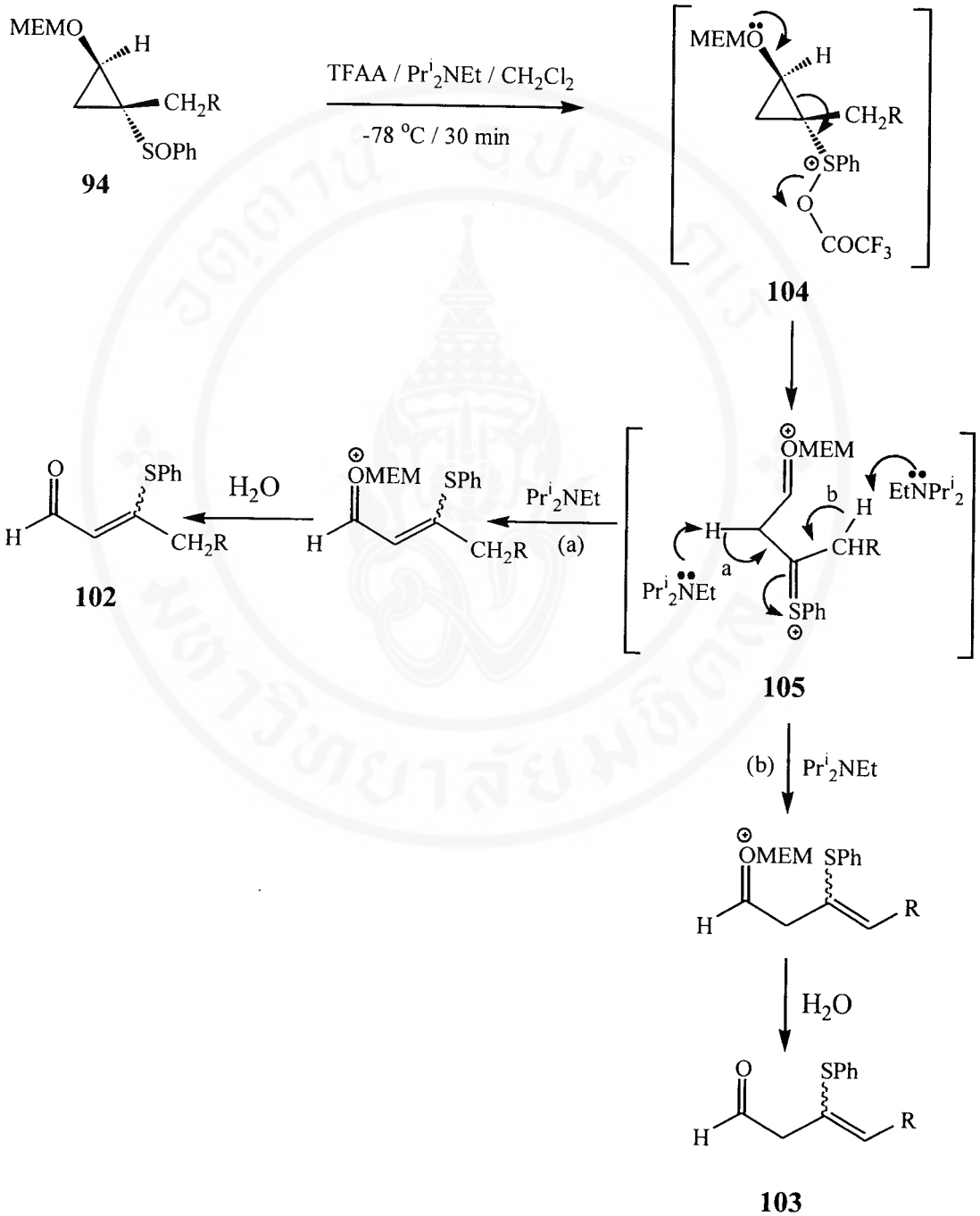
Z-**102c** *E*-**102c**

Z-**103c** *E*-**103c**

Figure 3

The mechanism for the formation of compounds **102** and **103** was depicted in **Scheme 16**. The cyclopropyl sulfoxide **94** was proposed to be trifluoroacetylated to give an intermediates **104** followed by ring cleavage to a thionium ion intermediate **105**. The formation of C-C double bond *via* two possible pathways (route *a* and route *b*) of deprotonation was accessible to give **102** and **103** after aqueous workup at low

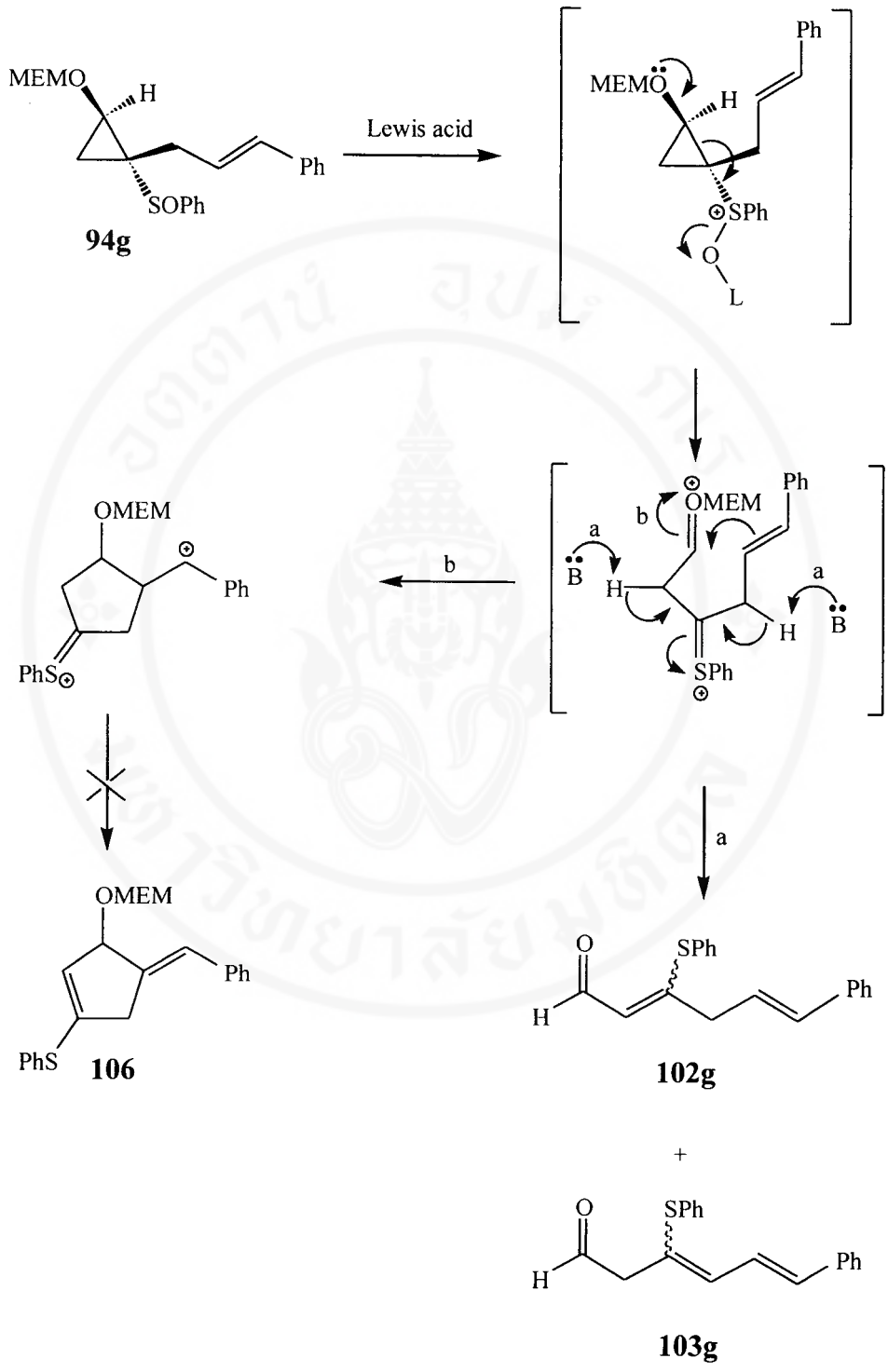
temperature (-78 °C). Compound **102,** α,β-unsaturated aldehyde, was a major product because it was thermodynamically more stable than β,γ-unsaturated aldehyde **103.**



Scheme 16

2.7 Attempted cyclopentane annulation *via* a tandem ring-opening-cyclisation reactions of the cyclopropyl sulfoxide 94g

Having succeeded in preparing α,β-unsaturated aldehydes **102a-f** *via* the Pummerer-type reaction mediated ring-opening of **94a-f**, we tried to investigate a cyclopentane annulation reaction by exploiting compound of type **94g**, as proposed in **Scheme 17**. However, treatment of the sulfoxide **94g** with trifluoroacetic acid (TFA) in CH_2Cl_2 at 0 °C and then slowly warmed up to room temperature overnight followed by refluxing for 3 h gave the recovered starting **94g** (94 %). No trace of the expected product of type **106** was observed. The same results were obtained, when acetic anhydride or trimethylsilyl chloride was used. Upon using trifluoroacetic anhydride (2 equivalents), on the other hand, the reaction furnished a trace amount of **102g** and **103g** and a complex mixture of products. The attempted conditions are listed in **Table 9**.



Scheme 17

Table 9 Attempted cyclization reaction of the sulfoxide **94g** under various conditions.

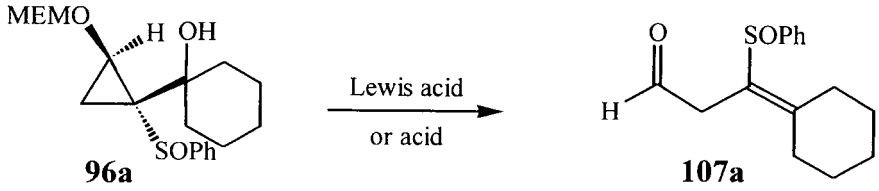
Entry	Reagent	Reaction conditions	Results
1	TFA (1.05 equiv)	CH_2Cl_2 at 0°C, then slowly warmed up to RT overnight and reflux for 3 h.	Recovered starting sulfoxide **94g** (94%)
2	TFA (1.25 equiv)	Toluene at 0°C, then slowly warmed up to RT overnight and reflux for 3 h	Recovered starting sulfoxide **94g** (83%)
3	Ac_2O (1.1 equiv)	CH_2Cl_2 , 4-dimethylaminop-yridine (1.1 equiv) at RT for 3 h and then reflux for 3 h.	Recovered starting sulfoxide **94g** (92%)
4	Me_3SiCl (1.1 equiv)	Toluene at RT for 3h and reflux for 3 h	Recovered starting sulfoxide **94g** (92%)
5	TFAA (2.2 equiv)	CH_2Cl_2 , diisopropylethyl-amine (2.2 equiv) at -78 °C for 3 h.	A complex mixture of products along with traces amount of **102g** and **103g** [a]

[a] Determined by ^1H NMR of the crude product.

2.8 A study on ring-opening of cyclopropyl sulfoxides 96

As shown in our previous results, the ring-opening of the sulfoxides **94** to unsaturated aldehydes **102** and **103** could be successfully accomplished by using trifluoroacetic anhydride and diisopropylethylamine. To get more insight about this reaction, we therefore studied the reaction of **96a** with trifluoroacetic anhydride and *N,N*-diisopropylethylamine (each 4 equiv) in CH_2Cl_2 at -78 °C for 80 min and at 0 °C for 4 h. It was found that the reaction led to a complex mixture of products. Only

small amount of the starting material **96a** (7% yield) could be recovered. The same results was observed, when **96a** was treated with sodium iodide / trimethylsilyl chloride in acetonitrile at 0 °C for 30 min. The reaction of **96a** with *p*-toluenesulfonic acid in THF at room temperature followed by refluxing for 3 h led to *β,γ*-unsaturated aldehyde **107a** in 25% yield, and a mixture of the recovered starting material **96a** and unidentified products as revealed by the ^{1}H NMR spectrum. We turned our attention to investigate the reaction of **96a** employing a Lewis acid such as boron trifluoride ethyl etherate. Initially, the reaction of **96a** with boron trifluoride ethyl etherate and *N,N*-diisopropylethylamine (at –78 °C for 1.5 h, at 0 °C for 1.5 h, at room temperature for 17 h and refluxing for 5 h) was tried, and was found that the starting material **96a** was recovered; no trace of *β,γ*-unsaturated aldehyde **107a** could be detected. Treatment of **96a** with boron trifluoride ethyl etherate in dichloromethane at –78 C for 1.5 h gave only the recovered starting matrial **96a** in 97% yield, after purification by thin-layer chromatography on silica gel. However, ring-opening of **96a** to *β,γ*-unsaturated aldehyde **107a** proceeded smoothly, when the reaction was carried at 0 °C for 2 h. **107a** was obtained in 79% yield after chromatography. The attempted conditions for the ring-opening of **96a** are summarized in **Table 10**.



96a **107a**

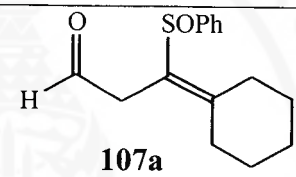
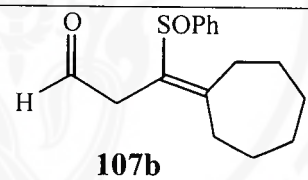
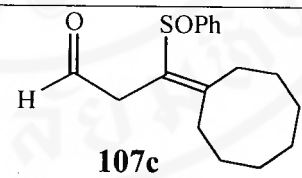
Table 10 Optimization of the conditions for ring-opening of **96a**.

Entry	Starting material	Conditions	Results [a]
1	**96a**	TFAA / Pr^i_2NEt / CH_2Cl_2 at -78°C for 30 min and 0 °C for 4 h.	**96a** (7 %) and complex mixture of product
2	**96a**	Me_3SiI / CH_3CN at 0°C for 30 min.	A complex mixture of product
3	**96a**	*p*-Toluenesulfonic acid / THF at RT and then reflux for 3 h.	**107a** (25 %), a mixture of **96a** and unidentified products
4	**96a**	$BF_3.OEt_2$ / Pr^i_2NEt / CH_2Cl_2 at -78°C for 1.5 h , 0 °C for 1.5 h , RT for 17 h and reflux for 5h.	The recovered starting material **96a** and a trace amount of impurity
5	**96a**	$BF_3.OEt_2$ / CH_2Cl_2 at -78°C for 1.5 h.	Recovered starting **96a** (97 %)
6	**96a**	$BF_3.OEt_2$ / CH_2Cl_2 at -78°C and then 0°C for 2 h.	**107a** in 79 % yield

[a] Yields given in parenthesis are isolated yields.

Having succeeded in preparing the **107a** from **96a** in good yield by employing $BF_3.OEt_2$ (4.4 equiv) in CH_2Cl_2 at -78 °C and then 0°C for 2 h, we next investigated the ring-opening reactions of **96b** and **96c** using the same conditions to afford **107b** and **107c** in excellent yields as shown in **Table 11**.

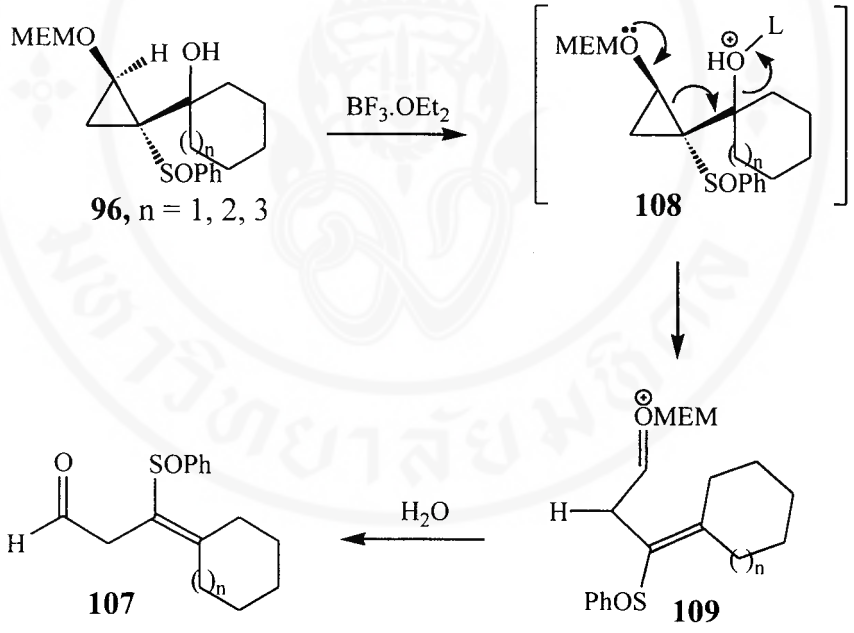
Table 11 Ring-opening of **96a-c** by treatment with $BF_3.OEt_2$ (4.4 equiv).

Entry	Starting materials	Products	% yields
1	**96a**	 **107a**	79
2	**96b**	 **107b**	99
3	**96c**	 **107c**	93

It should be noted here that the yields of the expected β,γ-unsaturated aldehydes **107a-c** were strongly depended on the purity of boron trifluoride ethyl etherate used. Thus, it must be freshly distilled before use.

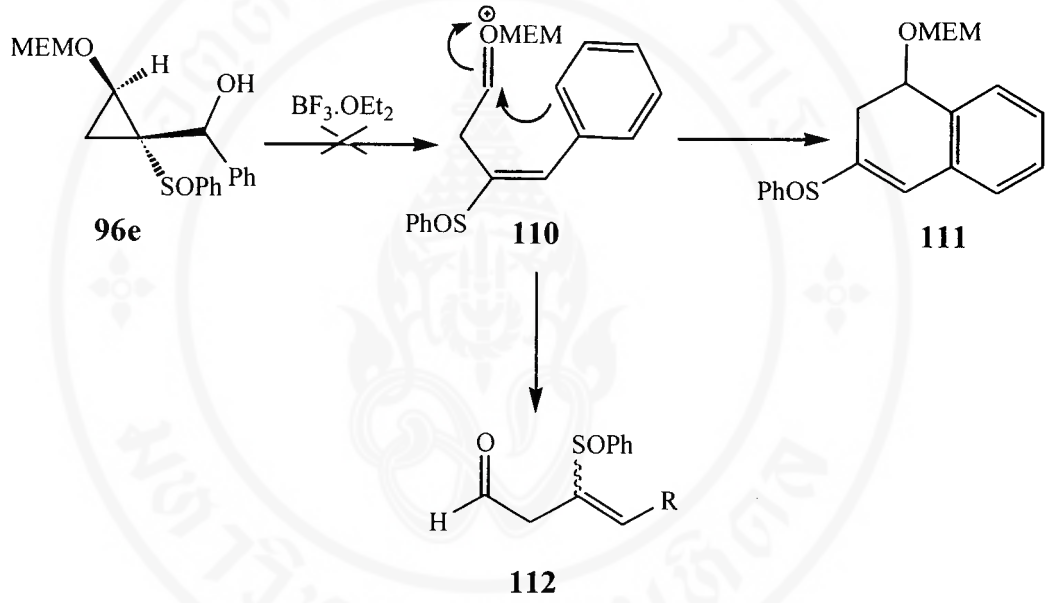
Compounds **107a-c** were characterized on the basis of their spectral data (IR, NMR and MS). The IR spectra of these compounds showed peaks at 1038-1040 cm^{-1} due to the S=O stretching and at 1722 cm^{-1} due to the C=O stretching of the aldehyde group.

A mechanism for synthetic transformation of **96a-c** to **107a-c** as shown in **Scheme 18** accounts for these observations. The sulfoxide **96** reacted with $BF_3.OEt_2$ to provide an oxonium ion intermediate **108,** which underwent subsequent ring-opening of the cyclopropane ring, facilitated by lone pair electrons of the oxygen atom to give an oxonium intermediate **109**. After quenching with H_2O, the oxonium intermediate **109** was hydrolyzed to β,γ-unsaturated aldehyde **107**. It should be mentioned that no trace of the α,β-unsaturated aldehyde derived from **107** could be obtained.



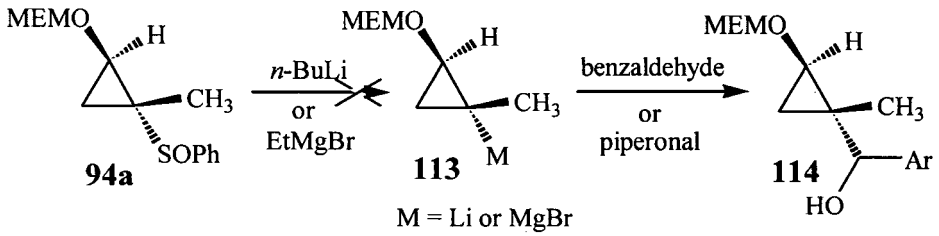
Scheme 18

It would be expected that ring-opening of **96e** catalyzed by $BF_3.OEt_2$ might led to an oxonium ion intermediate of type **110**, which should undergo an intramolecular electrophilic aromatic substitution leading to compound **111**. Unfortunately, treatment of **96e** with $BF_3.OEt_2$ (4 equiv) (at –78 °C for 20 min and 0 °C for 2 h) gave a complex mixture of products. Neither the expected product **111** nor compound **112** could be detected.

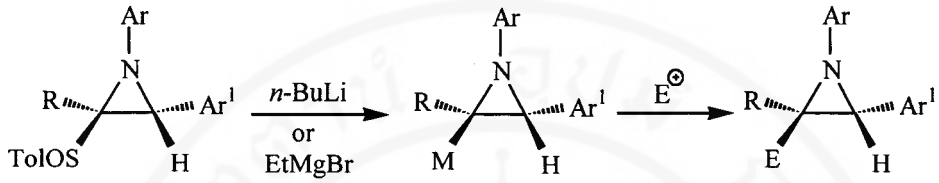


2.9 Attempted generation of metallated cyclopropanol derivatives of the type 113

As mentioned earlier, during the optimization for the generation of the anion **93** from the corresponding cyclopropylsulfoxide **92**, we found that butyl phenyl sulfoxide could be always obtained when *n*-butyllithium was used as the base. We got an idea that the reaction of **94a** with *n*-butyllilthium would lead to cleavage of the phenylsulfinyl group to give the expected lithiated cyclopropanol derivative **113**, which should combine with electrophiles to furnish an adduct of type **114** (eq. 27). Such cleavage of the *p*-tolylsulfinyl group bearing aziridine ring by alkyllithium and Grignard reagents has been reported as shown in equation 28.[48,49]



(eq. 27)



(eq. 28)

Attempts to generate such metallated cyclopropane **113** (M = Li or MgBr) by using *n*-BuLi or ethyl magnesium bromide followed by quenching with benzaldehyde or piperonal were unfortunately unsuccessful, as summarized in **Table 12**.

Table 12 Attempted generation of the metallated cyclopropane **113** from **94a**.

Entry	Base	Electrophiles	Conditions	Results
1	*n*-BuLi (1.1 equiv)	Benzaldehyde (1.3 equiv)	1. *n*-BuLi inTHF at –78 °C for 1 h, then warmed up to 0°C and stirred 1 h. 2. Benzaldehyde (-78°C for 1 h)	**94a** (30 %) and a complex mixture of products
2	EtMgBr (1.5 equiv)	Benzaldehyde (1.5 equiv)	1. EtMgBr in THF at -78°C for 2.5 h and 0°C for 3 h. 2. Benzaldehyde (-78°C for 1.5 h)	**94a** (88 %)

Table 12 (cont.)

Entry	Base	Electrophiles	Conditions	Results
3	EtMgBr (1.5 equiv)	Piperonal (1.5 equiv)	1. EtMgBr in THF at -78 °C 1 h and 0 °C 1 h 2. Piperonal at -78°C for 1 h and 0°C 1 h	**94a** (88 %)
4	EtMgBr (10 equiv)	Piperonal (1.5 equiv)	1. EtMgBr in THF at -78 °C then 0 °C 2 h 2. Piperonal (0 °C for 1.5 h)	Alcohol **115** (85%) **94a** (14%) and a complex mixture product
5	EtMgBr (10 equiv)	Piperonal (1.5 equiv)	1. EtMgBr in THF was transferred at -78°C (-78 °C for 1.5 h and 0°C 1.5 h) 2. Piperonal (-78 °C to RT overnight)	1-(3,4-methylene dioxyphenyl)-1-propanol (**115**) (98 %)
6	EtMgBr (10 equiv)	Piperonal (1.5 equiv)	1. EtMgBr in THF was transferred at -78°C (1 h) 2. Piperonal (–78 °C for 1.5 h)	Alcohol **115** (99 %) and **94a** (91 %)
7	EtMgBr (2.0 equiv) *n*-BuLi (2.0 equiv)	Piperonal (2.0 equiv)	1. EtMgBr in THF was transferred at -78°C for 10 min, then added *n*-BuLi stirring 2 min. 2. Piperonal (-78 °C, 10 min)	Alcohol **115** (21%), **94a** (31%), phenylsulfinyl butane (19 %) and a complex mixture products

CHAPTER III

CONCLUSION

Our results demonstrated that the anion **93**, generated by treatment of the sulfoxide **92** with *n*-butyllithium or LDA, reacted with alkylating agents and carbonyl compounds to afford compounds **94a-g** and **96a-f** in moderate yields with retention of configuration at the C-2 position. Compounds **94a-f** underwent ring-opening upon treatment with trifluoroacetic anhydride / $Pr^{i}_{2}NEt_2$ / CH_2Cl_2 at –78 °C for 0.5 h to provide a mixture of *β*-phenylthio-*α,β*-unsaturated aldehydes **102a-f** and *β*-phenylthio-*β,γ*-unsaturated aldehydes **103b-f** in good yields. We considered this synthetic conversion as a novel Pummerer-type mediated ring-opening of *β*-alkoxysubstituted cyclopropyl sulfoxide at low temperature. In addition, we found that ring-opening of compounds **96a-c** to *β*-phenylsulfinyl-*β,γ*-unsaturated aldehydes **107a-c** proceeded smoothly in excellent yields, when the reaction was treated with boron trifluoride ethyl etherate at 0 °C for 2 h. The formation of **107a-c** occurred *via* an oxonium ion **108** which underwent subsequent ring-opening of the cyclopropane ring facilitated by lone pair electrons of oxygen atom. Acylation reaction of the anion **93** with various acylating agents was investigated. However, the reactions led to unsatisfactory results; only low yield of the expected dihydrofuran of type **98** was obtained.

CHAPTER IV

EXPERIMENTAL SECTION

General

The ^{1}H NMR spectra were recorded on 300 MHz Brüker DPX-300 or 400 MHz Brüker DPX-400 spectrometers. The ^{13}C NMR spectra were recorded with a Brü ker DPX-300 (75 MHz) in $CDCl_3$ using tetramethylsilane as an internal standard. The chemical shifts (δ) reported are given in part per million (ppm) down field from tetramethylsilane. The IR spectra were recorded either on a Jasco A-302 or a Perkin Elmer 683 Infrared spectrometer. The Mass spectra were recorded by using a Finnigan MAT Mass spectrometer. Elemental analyses were performed by a Perkin Elmer Elemental Analyzer 2400 CHN. Melting points were recorded on a Buchi 501 Melting Point Apparatus and were uncorrected. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl. The molarity of *n*-BuLi (in hexane) was determined by titration with diphenylacetic acid in THF at 0 °C. The reactions were runs under an argon atmosphere. Solvents were removed by using a rotary evaporator at a water-aspirator pressure. All glasswares and syringes were oven-dried and kept in a dessicator before use. Diisopropylamine and hexamethylphosphoramide (HMPA) were distilled over calcium hydride. Dichloromethane (CH_2Cl_2) and acetone were distilled over phosphorus pentoxide. The radial chromatography plates were prepared by using Merck silica gel PF_{254} with $CaSO_4.1/2H_20$ type 60 (TLC Art. 7749). Preparative plates were performed by using Merck silica gel 60 (PF_{254}, Art. 7747).

4.1 Preparation of starting material

Preparation of 1,3-bis(phenylsulfenyl)-2-propanol (90)

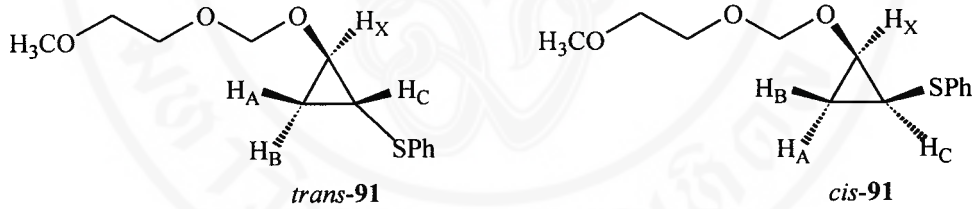
A solution of thiophenol (50.08 mL, 490 mmol) in ethanol (50 mL) was added dropwise at 0 °C to a solution of sodium hydroxide (20.90 g, 522 mmol) in H_2O (50 mL) and ethanol (300 mL), and followed by the addition of a solution of 1-chloro-2,3-epoxypropane (19.60 mL, 250 mmol) in ethanol (50 mL). After the reaction was kept stirring at 0 °C and allowed to warm up to room temperature overnight, the reaction was evaporated under reduced pressure for removal of a half volume of the solvent. The residue was mixed with a mixture of H_2O (200 mL) and ethyl acetate (150 mL). The aqueous layer was extracted with ethyl acetate (3x100 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a crude yellow liquid was obtained and purified by fractional distillation under reduced pressure to give a yellow liquid of **90** (58.36 g, 85 % yield, b.p. 154-156 °C at 0.05 torr)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.38-7.20 (m, 10H, Ar*H*), 3.38 (m, 1 H, -C*H*OH), 3.24, 3.21 and 3.09, 3.05 [each dd, J = 4.9 and 7.3 Hz, 4H, -CH_2CH(OH)CH_2-], 2.82 (d, 1 H, -O*H*).

Preparation of *trans*-[(2-methoxyethoxy)methoxy]-2(phenylsulfenyl) cyclopropane (91)

To a stirred solution of 1,3-bis(phenylsulfenyl)-2-propanol (**90**) (11.4480 g, 41.41 mmol) in THF (120 mL) at -78 °C was added dropwise *n*-butyllithium (60.0 mL of a 1.51 M solution in hexane, 90.60 mmol) over 30 min. After completion of the addition, the reaction mixture was stirred at -78 °C for 15 min and then at 0 °C for

additional 3 h, to which was added methyl iodide (3.90 mL, 62.64 mmol). The resulting mixture was stirred at –78 °C for 15 min and then at 0 °C for additional 1.5 h. After the addition of 1-chloromethoxy-2-methoxyethane (5.90 mL, 51.60 mmol) at 0 °C, the reaction mixture was kept stirring overnight. The reaction was then quenched with H_2O (50 mL) and extracted with ethyl acetate (3x100 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. The filtrate was concentrated under reduced pressure to afford a crude product as a mixture of **91** and thioanisole. The crude product was purified by flash column chromatography on silica gel (5% and 12% ethyl acetate in hexane) to give two pure isomers of *trans*-**91** (6.6945 g, 64% yield) and *cis*- **91** (1.8638g, 18% yield).



trans-**91** *cis*-**91**

^{1}H NMR of *trans*-**91** (300 MHz, $CDCl_3$) : δ 7.38-7.13 (m, 5H, Ar*H*), 4.78 (s, 2H, -OCH_2O-), 3.73 and 3.57 (each m, 4H, -OCH_2CH_2O-), 3.63 (ddd, J = 6.5, 3.6 , 2.1 Hz, 1 H, H_X), 3.39 (s, 3H, -OCH_3), 2.42 (ddd, J = 9.1, 5.5 , 2.1 Hz, 1 H, H_C), 1.36 (ddd, J = 9.1, 6.4, 3.6 Hz, 1 H, H_A), 0.94 (dt, J = 6.5 , 5.5 Hz, 1 H, H_B)

^{1}H NMR of *cis*-**91** (300 MHz, $CDCl_3$) : δ 7.39 - 7.11 (m, 5H, Ar*H*), 4.77 and 4.73 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O-), 3.92 (dt, J = 6.2 , 4.3 Hz, 1 H, H_X), 3.75 and 3.57 (m and t , J = 4.6 Hz, 4H, -OCH_2CH_2O-), 3.40 (s, 3H, -OCH_3),

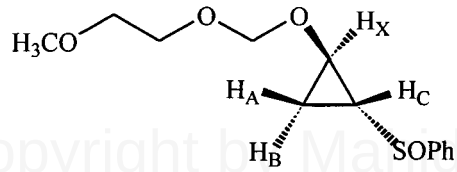
2.29 (dt, J = 8.8, 5.9 Hz, 1 H, H_C), 1.37 (dt, J = 8.0, 6.6 Hz, 1 H, H_A), 0.90 (dt, J = 6.3, 4.3 Hz, 1 H, H_B).

^{13}C NMR a mixture of *cis*-and *trans*-**91** (75 MHz, $CDCl_3$) : δ 135.95, 135.03, 129.85, 129.16, 129.03, 128.93, 126.59, 126.09, 95.17, 75.41, 71.59, 68.17, 67.21, 58.94, 39.98, 37.50

IR of *trans*-**91** (neat) : ν_{max} 3057, 2922, 2889, 1583, 1480, 1438, 1414, 1302, 1273, 1242, 1199, 1156, 1133, 1106, 1087, 1068, 1025, 848, 738, 690 cm^{-1}.

Preparation of *trans*-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (92)

To a suspension of $NaIO_4$ (1.07g, 5.00 mmol) in H_2O (5 mL) and methanol (3 mL) at 0 °C was added dropwise a solution of *trans*-**91** (1.2240 g, 4.89 mmol) in methanol (10 mL). After completion of the addition, the reaction mixture was stirred and allowed to warn up to room temperature overnight. The mixture was filtered and the precipitates were washed with ethyl acetate. The combined filtrate was washed with H_2O, brine and dried over anhydrous sodium sulfate. After evaporation under reduced pressure, a crude yellow liquid was obtained and purified by flash column chromatography on silica gel (45 % ethyl acetate in hexane) to provide a pale yellow liquid of pure **92** (1.1252 g, 85% yield) as a 1:1.5 mixture of diastereomers.



trans-**92**

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.65 (m, 2H, Ar*H*), 7.52 (m, 3H, Ar*H*), 4.72 and 4.66 , 4.57 and 4.50 (each d, 2 sets of AB-system, J = 6.6 and 6.5 Hz, 2H, -OCH_2O- of two diastereomers), 3.96 and 3.90 (each ddd, J = 6.0, 4.9, 2.4 Hz and J = 7.0, 3.9 , 2.4 Hz, respectively, 1 H, H_X of diastereomers), 3.71 - 3.50 (m, 4H, -OCH_2CH_2O-), 3.40 and 3.38 (each s, 3H, -OCH_3), 2.43 (m, 1 H, H_C), 1.49 (q, J = 6.8 Hz, 1 H, H_A), 1.35 (m, 2H, H_A and H_B), 1.19 (ddd, J = 9.7, 6.8, 3.9 Hz, 1 H, H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 144.25, 143.99, 131.03, 130.97, 129.16, 129.12, 123.89, 123.77, 95.44, 95.37, 71.55, 71.52, 67.41, 67.34, 58.94, 58.90, 53.57, 52.40, 39.06, 38.90, 11.09.

IR (neat) : ν_{max} 3056, 2928, 2890, 2819, 1582, 1477, 1444, 1413, 1359, 1305, 1285, 1243, 1186, 1141, 1105, 1087, 1071, 1047, 938, 879, 849, 801, 751, 716, 692, 671 cm^{-1}.

4.2 Reaction of the anion 93 with electrophiles.

Preparation of 1-[(2-methoxyethoxy)methoxy]-2-methyl-2(phenylsulfinyl) cyclopropane 94a

General procedure A

To a solution of *trans*-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane **92** (0.84 g, 3.10 mmol) in THF (15 mL) was added dropwise *n*-butyllithium (2.20 mL of a 1.51 M solution in hexane, 3.32 mmol) at –78 °C under an argon atmosphere. After completion of the addition, the reaction mixture was kept stirring at –78 °C for 1 h, then treated with methyl iodide (0.22 mL, 3.53 mmol) at –78 °C. The mixture was allowed to warm up to room temperature overnight. After the

reaction was complete, the mixture was quenched with H_2O (10 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After removal of solvents under reduced pressure, a yellow liquid of a crude product was obtained and purified by radial chromatography on silica gel (20 % ethyl acetate in hexane) to provide a yellow liquid of 1-[(2-methoxyethoxy)methoxy]-2-methyl-2-(phenylsulfinyl)cyclopropane **94a** (0.6205 g, 70 % yield) as a 1:1 diastereomeric mixture.

General procedure B

A solution of starting material **92** (0.4523 g, 1.67 mmol) in THF (2 mL) was slowly added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.28 mL, 1.97 mmol) with *n*-butyllithium (1.24 mL of a 1.49 M solution in hexane, 1.84 mmol) at –78 °C for 30 min] at -78 °C under an argon atmosphere. After completion of the addition, the reaction was stirred for 1 h and then treated with a solution of methyl iodide (0.1385 g, 2.08 mmol) at -78 °C. The reaction mixture was allowed to warm up to room temperature overnight. After completion of the reaction and work-up, a crude yellow liquid was obtained and purified by preparative thin-layer chromatography on silica gel (60 % ethyl acetate in hexane) to provide a yellow liquid of **94a** (0.3748 g, 80 % yield) and the recovered starting material **92** (0.0408 g, 6% yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.55 (m, 2H, Ar*H*), 7.45 (m, 3H, Ar*H*), 4.68 and 4.58, 4.64 and 4.53 (each d, 2 sets of AB-system, J = 6.5 Hz, 2H, -OCH_2O-), 4.05 and 3.93 (each dd, J = 7.6, 4.3 Hz, 1 H, H_X) 3.70-3.57 and 3.52-3.47 (each m, 4H, -OCH_2CH_2O-), 3.34 and 3.33 (each s, 3H, -OCH_3), 1.15 and 1.38 (each t, J = 7.3 Hz,

1H, H_A), 1.12 and 1.10 (each s, 3H, -CCH_3), 0.87 and 0.77 (each dd, J = 6.7, 4.3 Hz, 1H, H_B).

^{13}C NMR (75 MHz, $CDCl_3$): δ 142.01, 141.53, 131.17, 131.13, 128.87, 128.86, 124.83, 124.80, 95.76, 95.63, 71.59, 67.56, 58.98, 56.59, 56.13, 40.66, 16.19, 14.74, 9.98, 8.75.

IR (neat) : ν_{max} 3059, 2930, 2890, 2819, 1582, 1477, 1444, 1360, 1284, 1194, 1173, 1143, 1085, 1047, 1020, 938, 847, 782, 751, 693 cm^{-1}.

MS : m/z (%) relative intensity 285 (M^++1,0.6), 267 (0.4), 255 (0.9), 179 (55), 152 (9), 151 (66), 131 (8) 125 (5), 111 (22), 109 (20), 91 (7), 89 (60), 78 (12), 77 (15), 73 (18), 59 (100), 51 (13), 45 (21), 43 (11), 41 (13), 39 (12), 31 (22).

Preparation of 2-hexyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (94b)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (1.01g, 3.73 mmol) and *n*-butyllithiun (2.80 mL of a 1.40 M solution in hexane, 4.09 mmol) in THF (15 mL) with *n*-bromohexane (0.58 mL, 4.11 mmol) gave a crude yellow liquid, which was purified by radial chromatography on silica gel (30% ethyl acetate in hexane) to give a pale yellow liquid of 2-hexyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane **94b** (0.8196 g, 62 % yield) as a 1:1.3 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$: δ 7.67-7.59 (m, 2H, Ar*H*), 7.51 (m, 3H, Ar*H*), 4.76 and 4.71 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the minor isomer), 4.59 and 4.39 (each d, AB-system, J = 6.3 Hz, 2H, -OCH_2O- of the major isomer), 4.05 (dd, J = 7.8 and 4.3 Hz, 1 H, H_X of the major isomer), 3.98 (dd, J = 7.8, 4.3 Hz, H_X of the

minor isomer), 3.74-3.50 (m, 4H, OCH_2CH_2O), 3.40 (s, 3H, -OCH_3 of the minor isomer), 3.38 (s, 3H, OCH_3 of the major isomer), 1.50 and 1.22 (each m, 11 H, H_B and methylene protons), 0.99 (dd, J = 6.9, 4.3 Hz, 1 H, H_A of the major isomer), 0.86 (m, 3H, -CH_2CH_3), 0.78 (dd, J = 6.9, 4.3 Hz, 1 H, H_A of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.32, 142.22, 131.37, 131.26, 128,98, 128.89, 125.04, 125.02, 95.61, 95.55, 71.64, 71.58, 67,53, 67.38, 59.02, 56.26, 54.73, 44.98, 44.93, 31.47, 31.40, 29.37, 29.29, 27.02, 26.95, 26.32, 24.92, 22.46, 15.12, 13.96, 13.21.

IR (neat) : ν_{max} 3059, 2928, 1582, 1443, 1360, 1253, 1187, 1139, 1102, 1085, 1048, 849, 749, 692 cm^{-1}

MS : m/z (%) relative intensity 355 (M^++1, 1.4), 354 (M^+, 0.3), 250 (17), 249 (100), 222(14), 221 (85), 220 (10), 205 (11), 151 (12), 150 (15), 137 (8), 123 (6), 111 (13), 110(14), 109 (9), 95 (12), 89 (91), 78 (6), 77 (6), 69 (22), 59 (89), 55 (11), 45 (13), 43 (8), 31 (6).

Anal. Calcd for $C_{19}H_{30}O_4S$: C, 64.37; H, 8.52. Found: C, 64.42; H, 8.62.

Preparation of 2-heptyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (94c)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (1.60 g, 5.93 mmol) and *n*-butyllithium (4.50 mL of a 1.46 M solution in hexane, 6.57 mmol) in THF (25 mL) with *n*-bromoheptane (1.10 mL, 6.68 mmol) gave a brown-yellow liquid of a crude product, which was purified by flash column chromatography on silica gel (30 % and 35 % ethyl acetate in hexane) to give a yellow

liquid of 2-heptyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (**94c**) (1.2954 g, 59 % yield) as a 1:1.4 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67-7.60 (m, 2H, Ar*H*), 7.51 (m, 3H, Ar*H*), 4.76 and 4.72 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major isomer), 4.60 and 4.40 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the minor isomer), 4.06 (dd, J = 7.7 and 4.3 Hz, 1 H, H_X of the minor isomer), 3.99 (dd, J = 7.7, 4.3 Hz, 1 H, H_X of the major isomer), 3.75-3.51 (m, 4H, -OCH_2CH_2O-), 3.41 (s, 3H, -OCH_3 of the major isomer), 3.39 (s, 3H, -OCH_3 of the minor isomer), 1.52 and 1.22 (each m, 13H, H_B and methylene protons), 1.02 (dd, J = 6.7, 4.3 Hz, 1 H, H_A of the minor isomer), 0.87 (m, 3H, -C_6H_{12}CH_3), 0.79 (dd, J = 6.7, 4.3 Hz, 1 H, H_A of the major isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.26, 142.15, 31.35, 131.25, 128,96, 128.87, 125.00, 95.59, 95.53, 71.61, 71.55, 67,50, 67.36, 58.98, 56.23, 54.73, 44.95, 31.62, 29.63, 29.56, 28.92, 28.84, 27.03, 26.97, 26.29, 24.86, 22.52, 15.09, 13.99, 13.19.

IR (neat): ν_{max} 3059, 2926, 2856, 1582, 1466, 1443, 1361, 1243, 1187, 1139, 1103, 1085, 1048, 850, 749, 692 cm^{-1}.

MS : m/z (%) relative intensity 369 (M^++1, 0.6), 264 (12), 263 (61), 236 (10), 235 (57), 219 (8), 165 (12), 150 (11), 137 (7), 135 (9), 125 (8), 111 (10), 110 (8), 109 (21), 97 (6), 89 (86), 83 (15), 77 (7), 69 (23), 59 (100), 55 (17), 45 (17), 43 (16), 41 (19), 39 (8), 31(16).

Anal. Calcd for $C_{20}H_{32}O_4S$: C, 65.18; H, 8.75. Found: C, 64.72; H, 9.05.

Preparation of 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)-2-undecylcyclopropane (94d)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (0.98 g, 3.63 mmol) and *n*-butyllithium (2.74 mL of a 1.46 M solution in hexane, 4.00 mmol) in THF (15mL) with *n*-bromoheptane (0.90 mL, 4.01 mmol) gave a crude yellow liquid, which was purified by flash column chromatography on silica gel (30% ethyl acetate in hexane) to provide a pale yellow liquid of 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)-2-undecylcyclopropane (**94d**) (0.9342 g, 60% yield) as a 1:3.7 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67-7.59 (m, 2H, Ar*H*), 7.51 (m, 3H, Ar*H*), 4.76 and 4.71 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the minor isomer), 4.59 and 4.39(each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major isomer), 4.05 (dd, J = 7.8, 4.3 Hz, 1 H, H_X of the major isomer), 3.98 (dd, J = 7.8, 4.3 Hz 1 H, H_X of the minor isomer), 3.74-3.50 (m, 4H, -OCH_2CH_2O-), 3.40 (s, 3H, -OCH_3 of the minor isomer), 3.38 (s, 3H, -OCH_3 of the major isomer), 1.50 and 1.23 (each m, 21 H, H_B and methylene protons), 0.99 (dd, J = 6.8, 4.3 Hz, 1 H, H_A of the major isomer), 0.87 (t, J = 7.0, Hz, 3H, -CH_3), 0.78 (dd, J = 6.8, 4.3 Hz, 1 H, H_A of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.32, 131.35, 131.25, 128,97, 128.88, 125.03, 95.60, 95.54, 71.64, 71.58, 67,52, 67.37, 58.99, 56.25, 54.72, 44.93, 31.84, 29.70, 29.62, 29.54, 29.45, 29.27, 29.20, 27.05, 26.99, 26.31, 24.90, 22.61, 15.11, 14.05, 13.19.

IR (neat) : ν_{max} max 3060, 2925, 2854, 1584, 1466, 1443, 1361, 1244, 1189, 1139, 1103, 1085, 1049, 849, 748, 692 cm^{-1}.

MS : m/z (%) relative intensity 425 (M^++1, 1.6), 321 (6), 320 (18), 319 (62), 293 (13), 291 (51), 275 (13), 221 (23), 180 (8), 150 (18), 137 (8), 135 (7), 125 (10), 111 (16), 110 (12), 109 (18), 97 (19), 95 (10), 89 (100), 83 (21), 81 (10), 78 (9), 77 (8), 69 (21), 67 (10), 61 (10), 59 (96), 57 (15), 55 (25), 43 (17), 43 (32), 41 (30), 31 (17).

Anal. Calcd for $C_{24}H_{40}O_4S$: C, 67.88; H, 9.49. Found: C, 67.68; H, 9.16.

Preparation of 1-[(2-methoxyethoxy)methoxy]-2-pentadecyl-2-(phenylsulfinyl) cyclopropane (94e)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (0.77 g, 2.86 mmol) and *n*-butyllithium (2.20 mL of a 1.46 M solution in hexane, 3.21 mmol) in THF (12 mL) with *n*-bromopentadecane (0.95 mL, 3.29 mmol) gave a crude yellow liquid, which was purified by radial chromatography on silica gel (20% ethyl acetate in hexane) to provide a pale yellow liquid of 1-[(2-methoxyethoxy)methoxy]-2-pentadecyl-2-(phenylsulfinyl)cyclopropane (**94e**) (0.8265 g, 60% yield) as a 1:1.3 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60-7.52 (m, 2H, Ar*H*), 7.54 (m, 3H, Ar*H*), 4.69 and 4.65 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the minor isomer), 4.53 and 4.33(each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major isomer), 3.99 (dd, J = 7.9, 4.3 Hz, 1 H, H_X of the major isomer), 3.92 (dd, J = 7.9, 4.3 Hz 1 H, H_X of the minor isomer), 3.68-3.44 (m, 4H, -OCH_2CH_2O-), 3.34 (s, 3H, -OCH_3 of the minor isomer), 3.32 (s, 3H, -OCH_3 of the major isomer), 1.44 and 1.17 (each m, 29H, H_B and methylene protons), 0.95 (dd, J = 7.0, 4.2 Hz, 1 H, H_A of the major isomer), 0.81 (t, J = 7.0, Hz, 3H, -CH_2CH_3), 0.72 (dd, J = 7.0, 4.2 Hz, 1 H, H_A of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.23, 142.12, 131.28, 131,17, 128.89, 128.80, 124.95, 124.93, 95.51, 95.45, 71.56, 71.50, 67.43, 67.28, 58.91, 56.16, 54.64, 44.89, 44.84, 31.78, 29.62, 29.55, 29.52, 29.47, 29.38, 29.21, 29.13, 26.97, 26.91, 26.23, 24.81, 22.54, 15.03, 13.98, 13.11.

IR (neat) : ν_{max} 3059, 2924, 2853, 1582, 1466, 1443, 1361, 1243, 1189, 1139, 1103, 1085, 1050, 998, 985, 850, 747, 692 cm^{-1}.

MS : m/z (%) relative intensity 481 (M^++1, 1.1), 376 (10), 375 (35), 347 (35), 331 (11), 277 (13), 236 (4), 150 (14), 137 (8), 135 (7), 125 (10), 111 (17), 110 (14), 109 (16), 97(12), 95 (12), 89 (94), 83 (27), 81 (16), 78 (10), 77 (11), 71 (16), 69 (27), 67 (16), 59(100), 57 (30), 55 (34), 45 (19), 43 (40), 41 (38), 31 (17).

Anal. Calcd for $C_{28}H_{48}O_4S$: C, 69.95; H, 10.06. Found : C, 69.52; H, 9.76.

Preparation of 2-benzyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (94f)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (1.42 g, 5.26 mmol) and *n*-butyllithium (4.0 mL of a 1.46 M solution in hexane , 5.84 mmol) in THF (25 mL) with benzyl bromide (0.70 mL, 5.89 mmol) gave a yellow liquid of a crude product, which was purified by flash column chromatography (silica gel, 40% ethyl acetate in hexane) to give a pale yellow liquid of a 1:1.3 diastereomeric mixture of 2-benzyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (**94f**) (1.2322 g, 65% yield).

^1H NMR (300 MHz, $CDCl_3$): δ 7.62-7.50 (m, 5H, Ar*H*), 7.30-7.12 (m, 5H, Ar*H*), 4.81 (s, 2H, OCH_2O of the minor isomer), 4.67 and 4.52 (each d,AB-system, J = 6.3 Hz, 2H, -OCH_2O- of the major isomer), 4.13 (m, 1H, H_X), 3.79-3.52 (m, 4H,

-OCH_2CH_2O-), 3.41 (s, 3H, -OCH_3 of the minor isomer), 3.40 (s, 3H, -OCH_3 of the major isomer), 3.19 and 2.72 (each d, AB-system, J = 15.9 Hz, 2H, -CH_2Ar of the minor isomer)2.93 (s, 2H, CH_2Ar of the major isomer), 1.65 (t, J = 7.3 Hz, 1 H, H_B of the major isomer), 1.57 (t, J = 7.1 Hz, 1H, H_B of the minor isomer), 1.15 (dd, J = 7.1, 4.3 Hz, 1H, H_A of the major isomer), 0.82 (dd, J = 6.7, 4.3 Hz, 1 H, H_A of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.07, 141.97, 137.51, 137.31, 131.52, 131.41. 129.44, 129.22, 129.05, 128.88, 128.44, 128.38, 126.58, 126.54, 125.31, 125.24, 95.62, 95.58, 71.63, 71.58, 67.64, 67.46, 59.02, 56.34, 54.46, 45.55, 44.86, 31.89, 30.64, 15.98, 13.60.

IR (neat) : ν_{max} 3061, 3028, 2925, 2889, 2818, 1602, 1582, 1496, 1475, 1454, 1443, 1360, 1305, 1265, 1243, 1187, 1135, 1103, 1084, 1048, 984, 932, 848, 790, 746, 699 cm^{-1}.

MS : m/z (%) relative intensity 361 (M^++1, 0.3), 256 (9), 255 (51), 237 (5), 227 (6), 212(5), 211 (33), 150 (3), 149 (30), 135 (9), 129 (7), 128 (9), 118 (4), 117 (27), 116 (9), 115 (22), 109 (7), 91 (28), 89 (58), 78 (9), 77 (12), 65 (9), 59 (100) 51 (12), 45 (17), 43 (7), 39 (8), 31 (20).

Preparation of 1-[(2-methoxyethoxy)methoxy]-2-(3'-phenyl-2'-propenyl)-2-(phenylsulfinyl)cyclopropane (94g)

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (0.52 g, 1.95 mmol) and *n*-butyllithium (1.40 mL of a 1.51 M solution in hexane, 2.21 mmol) in THF (11 mL) with a solution of cinnamyl bromide (0.42 g, 2.15 mmol) in THF (3 mL) gave a brown liquid of a crude product, which was purified

by radial chromatography on silica gel (10% ethyl acetate in hexane) to give a colorless viscous liquid of 1-[(2-methoxyethoxy)methoxy]-2-(3'-phenyl-2'-propenyl)-2-(phenylsulfinyl)cyclopropane (**94g**) (0.4767 g, 63% yield) as a 1:1.2 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.64 (m, 2H, Ar*H*), 7.49 (m, 3H, Ar*H*), 7.23 (m, 5H, Ar*H*), 6.29 (d, J = 15.8 Hz, 1 H, -CH=C*H*Ph), 6.00 (ddd, J = 15.8 , 8.3, 5.7 Hz , 1 H, -CH_2C*H*=CHPh), 5.87 (dt, J = 15.8 , 7.0 Hz, 1 H, -CH_2C*H*=CHPh), 4.78 and 4.75, 4.66 and 4.52 (each d, 2 sets of AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major and minor isomers, respectively), 4.14 and 4.06 (each dd, J = 7.9, 4.3 Hz, 1 H, H_X of the minor and major isomers , respectively), 3.75-3.50 (m, 4H, -OCH_2CH_2O-), 3.37 (s, 3H, -OCH_3), 2.60 and 2.39 (each m, 2H, -CH_2CH=CHPh), 1.60 and 1.55 (each t, J = 7.4 Hz, 1H, H_B of the major and minor isomers, respectively), 1.11 and 0.88 (each dd, J = 7.4, 4.3Hz, 1H, H_A of the minor and major isomers, respectively).

IR (neat) : ν_{max} 3058, 3026, 2928, 2890, 2818, 1652, 1598, 1578, 1495, 1476, 1444, 1361, 1305, 1281, 1243, 1187, 1134, 1085, 1047, 982, 923, 849, 783, 748, 693 cm^{-1} .

MS : m/z (%) relative intensity 387 (M^++1, 0.16), 281 (23), 263 (1), 252 (1), 237 (8), 204 (3), 189 (2), 185 (6), (171 (6), 159 (2) 153 (16), 143 (25), 141 (11), 129 (19), 128 (28), 117 (11), 115 (16), 105 (3), 97 (2), 91 (19), 89 (77), 77 (6), 69 (3), 65 (3), 59 (100), 45 (9), 31 (12).

Anal. Calcd for $C_{22}H_{26}O_4S$: C, 68.36; H, 6.78. Found: C, 67.84; H, 6.78.

Reaction of anion 93 with D_2O

According to the general procedure B, a reaction of the anion **93** derived from the suifoxide **92** (0.1431 g, 0.58 mmol) and *n*-butyllithium (0.38 mL of a 1.50 M in

hexane, 0.58 mmol) and *N,N*–diisopropylamine (0.08 mL, 0.6 mmol) in THF (3 mL) and D_2O (0.04 mL) gave a crude yellow liquid (99 %) , which was obtained as a 58:42 mixture of a deuterium incorporation product and the recovered starting material.

Reaction of anion 93 with sat. NH_4Cl

According to the general procedure A, a reaction of the anion **93** derived from the sulfoxide **92** (0.3408 g, 1.26 mmol) and *n*-butyllithium (1.46 M in hexane , 0.92 mL, 1.33 mmol) in THF (7 mL) and quenched with a saturated aqueous ammonium chloride solution (5 mL) gave a crude yellow liquid, which was purified by preparative thin-layer chromatography on silica gel (60 % ethyl acetate in hexane) to afford the recovered starting material **92** (0.2329 g, 69 % yield) and phenylsulfinylbutane [0.0112 g, 5 % yield; ^{1}H NMR (300MHz, $CDCl_3$) : δ 7.54 and 7.44 (each m, 5H, Ar*H*), 2.73 (t, J = 7.7 Hz, 2H, PhSOCH_2-), 1.74-1.28(m, 4H, PhSOCH$_2$CH_2CH_2CH$_3$), 0.85 (t, J = 7.3 Hz 3H, -CH_3)] and unidentified products.

4.3 Reaction of the anion 93 with carbonyl compounds.

Preparation of 2-(1-hydroxycyclohexyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenyl-sulfinyl)cyclopropane (96a)

General procedure

To a stirred solution of the sulfoxide **92** (0.5633 g, 2.08 mmol) in THF (10 mL) was added dropwise *n*-butyllithium (1.50 mL of a 1.55 M solution in hexane, 2.32 mmol) at -78 °C under an argon atmosphere. After completion of the addition, the reaction mixture was stirred at the same temperature for 1 h and treated with

cyclohexanone (0.24 mL, 2.31 mmol). The mixture was allowed to stir at -78 °C for 3 h and saturated ammonium chloride solution (5 mL) was injected. After warming up to room temperature, the mixture was diluted with H_2O (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a pale brown liquid of a crude product obtained was purified by preparative thin-layer chromatography on silica gel (60% ethyl acetate in hexane) to give a pale yellow liquid of **96a** (0.4742 g, 61% yield) as a 1:1.2 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.47 (m, 4H, Ar*H*), 7.38 (m, 1 H, Ar*H*), 4.82 and 4.77 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major isomer), 4.58 and 4.53 (each d, AB- system, J = 6.4 Hz, 2H, -OCH_2O- of the minor isomer), 3.96 (dd, J = 7.7, 5.5 Hz, 1 H, H_X of the major isomer), 3.73-3.40 (m, 4H, -OCH_2CH_2O-), 3.38 and 3.33, (each s, 3H, -OCH_3 of the major and minor isomers, respectively), 2.92 (dd, J = 7.5, 4.7 Hz, 1 H, H_X of the minor isomer), 2.78 and 2.68 (each br.s, 1 H, -O*H* of both isomers), 2.22-0.85(m, 11 H, H_A or H_B and methylene protons), 0.38 (t, J = 7.4 Hz, 1H, H_B or H_A).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 141.42, 141.63 130.94,130.74, 129.12, 129.07, 125.34, 124.71, 95.95 95.42, 72.27, 72.19, 71.58, 71.36, 67.87, 67.51, 61.88, 59.02, 59.00, 56.89, 56.69, 37.28, 36.22, 36.07, 35.34, 25.51, 25.46, 21.69, 21.58, 21.31, 21.22, 17.84, 9.99.

IR (neat) : ν_{max} 3364, 3061, 2931, 2862, 1652, 1582, 1444, 1373, 1306, 1268, 1188, 1137, 1084, 1047, 1023, 995, 975, 930, 915, 851, 799, 749, 692 cm^{-1}.

MS : m/z (%) relative intensity 368 (M^+,0.08), 351 (0.4), 263 (6), 246 (5), 245 (28), 217(4), 219 (2), 203 (3), 201 (4), 191 (20), 185 (4), 167 (2), 153 (27), 147 (3), 137 (18), 135(11), 126 (10), 125 (21), 110 (8), 109 (25), 108 (5), 107 (30) 99 (6), 97 (9), 95 (8), 93(11), 91 (14), 89 (77), 83 (6), 81 (27), 79 (16), 78 (12), 77 (18), 71 (6), 69 (6), 67 (11), 60 (5), 59 (100), 57 (6), 55 (23), 53 (6), 51 (8), 45 (21), 43 (18), 41 (15), 39 (10), 31(17).

Preparation of 2-(1'-hydroxycycloheptyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (96b)

According to the general procedure, a reaction of the anion **93** derived from the sulfoxide **92** (0.4491 g, 1.66 mmol) and *n*-butyllithium (1.20 mL of a 1.51 M solution in hexane, 1.81 mmol) in THF (6 mL) with a solution of cycloheptanone (0.2301 g, 2.05 mmol) in THF (2 mL) gave a pale brown liquid of a crude product, which was purified by radial chromatography on silica gel (20 % ethyl acetate in hexane) to give a colorless liquid of **96b** (0.3890 g, 61% yield) as a 1:1.8 diastereomeric mixture.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50-7.30 (m, 5H, Ar*H*), 4.78 and 4.70 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O- of the minor isomer), 4.52 and 4.46 (each d, AB-system, J = 6.6Hz, 2H, -OCH_2O- of the major isomer), 3.87 (dd, J = 7.7, 5.5 Hz, 1H, H_X of the minor isomer), 3.66-3.27 (m, 4H, -OCH_2CH_2O-), 3.31 and 3.26, (each s, 3H, -OCH_3 of the minor and major isomers, respectively), 2.81 (dd, J = 7.6, 4.8 Hz, 1H, H_X of the major isomer), 2.50-1.39 (m, 13H, H_A of the major isomer and methylene protons), 1.31 (t, J = 7.4 Hz, 1 H, H_B of the major isomer), 0.88 (m, 1H, H_A of the minor isomer), 0.29(t, J = 7.3 Hz, 1 H, H_B of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 141.45, 130.91, 130.74, 129.18, 129.08, 129.06, 124.86, 124.64, 95.89, 95.36, 74.53, 74.45, 71.51, 71.29, 67.80, 67.46, 62.43, 59.10, 58.94, 58.73, 57.35, 37.51, 36.67, 36.58, 35.70, 28.00, 27.97, 27.74, 22.53, 22.33, 20.69, 20.45, 19.85, 19.73, 18.73, 10.28.

IR (neat) : ν_{max} 3508, 3059, 2925, 2860, 1633, 1582, 1475, 1456, 1443, 1393, 1365, 1266, 1246, 1193, 1183, 1140, 1103, 1084, 1043, 1022, 997, 977, 927, 849, 802, 750, 697 cm^{-1}.

MS : m/z (%) relative intensity 382 (M^+,0.08), 381 (m^+-1, 0.2), 277 (6), 259 (19), 247 (2), 231 (2), 215 (2), 205 (11), 199 (5), 167 (16), 151 (13), 139(10), 137(5), 135(6), 133(7), 126(10), 125(12), 123(16), 121(21), 113(7), 110(8), 109(13), 107(26), 105(9), 97(10), 95(26), 93(15), 91(13), 90(5), 89(73), 83(8), 81(16), 79(16), 78(11), 77(17), 69 (10), 67(13), 59(100), 55(26), 53(7), 51(8), 45(23), 43(19), 39(11), 31(19).

Anal. Calcd for $C_{20}H_{30}O_5S$:C, 62.80; H, 7.90. Found: C, 62.85; H, 7.97.

Preparation of 2-(1'-hydroxycyclooctyl)-1-[(2-methoxyethoxy)methoxy]-2-phenylsulfinylcyclopropane (96c)

According to the general procedure, a reaction of the anion **93** derived from the sulfoxide **92** (0.2736 g, 1.01 mmol) and *n*-butyllithium (0.74 mL of a 1.51 M solution in hexane, 1.11 mmol) in THF (4 mL) with a solution of cyclooctanone (0.1580 g, 1.25 mmol) in THF (2 mL) gave a crude yellow liquid which was purified by radial chromatography on silica gel (20% ethyl acetate in hexane) to give a colorless liquid of **96c** (0.1516 g, 37% yield) as a 1:1.4 diastereomeric mixture. The starting material **92** was recovered (0.0825 g, 30 %).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.50-7.36(m, 5H, Ar*H*), 4.82 and 4.77 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the minor isomer), 4.60 and 4.53 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O- of the major isomer), 3.95 (dd, J = 7.6, 5.6 Hz, 1H, H_X of the minor isomer), 3.77-3.37 (m, 4H, -OCH_2CH_2O-), 3.39 and 3.33, (each s, 3H, -OCH_3 of the major and minor isomers, respectively), 2.89 (dd, J = 7.7, 4.8 Hz, 1H, H_X of the major isomer), 2.87 and 2.82 (each br.s, 1 H, -O*H* of both isomer), 2.50–1.56 (m, 15H, H_A of the major isomer and methylene protons of cyclooctane ring), 1.37 (t, J = 7.4 Hz, 1H, H_B of the major isomer), 0.98 (m, 1H, H_A of the minor isomer), 0.37 (t, J = 7.4 Hz, 1H, H_B of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 141.45, 130.95, 130.79, 129.10, 129.07, 124.83, 124.62, 95.90, 95.35, 75.29, 75.26, 71.53, 71.30, 67.83, 67.49, 62.29, 58.95, 58.65, 58.43, 57.24, 41.90, 40.77, 40.47, 39.42, 28.07, 27.99, 27.97, 27.83, 21.90, 21.78, 21.32, 18.55.

IR (neat) : ν_{max} 3391, 3060, 2922, 2696, 1633, 1582, 1475, 1471, 1443, 1365, 1263, 1244, 1186, 1137, 1100, 1083, 1053,, 1020, 973, 922, 897, 848, 791, 749, 697cm^{-1}.

MS : m/z (%) relative intensity 395 (M^+-1, 0.3), 379 (1.3), 291 (9), 273 (19), 262 (4), 245(2), 229 (2), 219 (6), 213 (5), 181 (9), 165 (25), 153 (7), 147 (12), 137 (14), 136 (6), 135 (20), 126 (8), 125 (8), 121 (34), 119 (11), 110 (7), 109 (17), 107 (8), 105 (7), 97 (7), 95 (11), 93 (13), 91 (8), 89 (100), 83 (6), 81 (14), 79 (8), 78 (5), 77 (7), 69 (9), 67 (15), 59 (99), 55 (14), 45 (12), 43 (11), 31 (11).

Anal. Calcd for $C_{21}H_{32}O_5S$: C, 63.08; H, 8.13. Found: C, 63.65; H, 8.29.

Preparation of 2-(1'-hydroxy-*p*-methoxybenzyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsufinyl)cyclopropane (96d)

A solution of **92** (0.1924 g, 0.71 mmol) in dry THF (1 mL) was added to a THF solution of lithium diisppropylamide at -78 °C [prepared by reacting diisopropylamine (0.13 mL, 0.92 mmol) with *n*-butyllithium (0.56 mL of a 1.55 M solution in hexane, 0.86 mmol) at -78 °C for 30min]. After completion of the addition, the reaction was stirred for 1 h and a solution of anisaldehyde (0.1783 g, 1.30 mmol) in dry THF (1 mL) was added. The reaction was kept stirring at –78 °C for 3 h and allowed to warn up to room temperature overnight. The reaction gave, after usual workup with a saturated aqueous ammonium chloride solution, a yellow liquid of a crude product which was purified by preparative thin-layer chromatography (SiO_2, 55% ethyl acetate in hexane, double runs) to give three fractions of 2-(1'-hydroxy-*p*-methoxybenzyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsufinyl)cyclopropane (**96d**)

B1, as a yellow liquid (0.0333 g, 12% yield, a 1:1.1 mixture of two diastereomers)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.87 (m, 1 H, Ar*H*), 7.72 (m, 1 H, Ar*H*), 7.54 (m, 3H, Ar*H*), 6.76-6.65 (m, 4H, Ar*H*), 5.21 and 5.14 [each s, 1 H, -CC*H*(OH) of the minor and major isomers, respectively], 4.98, 4.87 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O- of the minor isomer), 4.70 and 4.66 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O- of the major isomer), 3.83 (dd, J = 6.5, 4.5 Hz, 1 H, H_X of the major isomer), 3.77, 3.62, 3.54 and 3.44 (each m, 4H, -OCH_2CH_2O-), 3.67 and 3.66 (each s, 03H, -ArOCH_3 of the major and minor isomers, respectively), 3.35 and 3.28 (each s, 3H, -OCH_3 of the minor and major isomers, respectively), 2.91 (dd, J = 6.1, 4.0 Hz,

1H, H_X of the minor isomer), 2.01 (s, 1H, -O*H*), 1.80 (dd, J = 7.28, 3.56 Hz, 1 H, H_A), 1.41 (app.t, J = 6.7 Hz, 1 H, H_A or H_B), 1.37 (dd, J = 7.2, 4.0 Hz, H_B or H_A), 1.18, 1.15 (each s, 1H, -O*H*), 0.59 (t, J = 7.0 Hz, 1H, H_B).

B_2, as a pale yellow liquid (a 39:61 mixture of the recovered of starting material **92** and 3 diastereomers of **96d**, 0.1767 g, 70 % yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.70–6.74 (m, 14H, Ar*H* of **92** and **96d**), 5.22 [s, 1H, -C*H*(OH)], 5.00, 4.93 (each d, AB-system , J = 6.5 Hz, 2H, -OCH_2O-), 4.97 [s, 1H, -C*H*(OH)], 4.86, 4.80 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O-), 4.85 [s, 1H, -C*H*(OH)], 4.73 and 4.66, 4.57 and 4.49 (each d, 2 set of AB-system, J = 6.6 and 6.5 Hz, 2H, -OCH_2O- of starting **92**), 4.70, 4.38 (each d, J = 6.5 Hz, 2H, -OCH_2O-), 4.19-3.47 (m, 13H, -OCH_2CH_2O-, H_X and –PhOCH_3 of starting **92** and **96d**), 3.41, 3.40, 3.38, 3.36 and 3.35 (each s, 6H, -CH_2OCH_3 of starting **92** and **96d**), 3.22 (dd, J = 8.0, 4.4 Hz, 1 H, H_X of **96d**), 2.42 (m, 1 H, H_C of starting **92**) , 2.09, 2.06 and 2.04 (each s, 1 H, -O*H*), 1.80 (m, 2H, H_A and H_B), 1.57-1.16 (m, 4H, H_A and H_B of starting **92** and **96d**), 0.85, 0.79 (each t, J = 7.8 Hz, 1 H, H_B).

B_3, as a pale yellow liquid of the single diastereomer (0.0262 g, 9 %).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.46 (m, 3H, Ar*H*), 7.26 of (m, 4H, Ar*H*), 6.83(m, 2H, Ar*H*), 4.96 [s, 1H, -C*H*(OH)-], 4.66 (s, 2H, -OCH_2O-), 3.76 (s, 3H, -PhOCH_3), 3.65 (dd, J = 7.2, 5.1 Hz, 1H, H_X), 3.55, 3.42 (each m, 4H, -OCH_2CH_2O-), 3.30 (s, 3H, -OCH_3), 2.01 (s, 1 H, -O*H*), 1.46 (m, 2H, H_A and H_B).

Preparation of 2-(1-hydroxylbenzyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (96e)

A solution of 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (**92**) (0.3115 g, 1.15 mmol) in dry THF (2 mL) was added dropwise to a THF solution of lithium diisopropylamide (LDA) at –78 °C under an argon atmosphere [prepared by reacting diisopropylamine (0.20 mL, 1.44 mmol) in dry THF (5 mL) with *n*-butyllithium (0.99 mL of a 1.40 M solution in hexane, 1.38 mmol) at –78 °C for 30 min]. After completion of the addition, the reaction mixture was kept stirring at –78°C for 1 h and then benzaldehyde (0.15 mL, 1.45 mmol) was added dropwise. After the mixture was stirred at –78 °C for 3 h, it was quenched with a saturated aqueous ammonium chloride solution (5 mL) at –78 °C. After warming up to room temperature, the reaction mixture was diluted with H_2O (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over sodium anhydrous. Filtration and removal of the solvent on a rotary evaporator gave a crude yellow liquid, which was purified by preparative thin-layer chromatography on silica gel (70% ethyl acetate in hexane, double runs) to give 7 fractions of **96e.**

B_1, as a pale yellow liquid (0.0865 g, 21% yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.95 (m, 2H,Ar*H*), 7.62 (m, 3H, Ar*H*), 7.20 (m, 3H, Ar*H*), 6.88 (m, 2H, Ar*H*), 5.35 (s, 1H, -C*H*OHPh), 4.76 and 4.72 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O-), 3.74-3.46 (m, 4H, -OCH_2CH_2O-), 3.35 (s, 3H, -OCH_3), 2.97 (dd, J = 6.2 and 4.0 Hz, 1H, H_X), 1.88 (dd, J = 7.2 and 4.0 Hz, 1H, H_A), 1.49 (t, J = 6.8 Hz, 1H, H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 141.50, 137.64, 131.10, 129.29,128.32,128.28,128.15, 127.91, 126.44, 125.16, 95.48, 71.48, 71.08, 67.65, 59.32, 59.02, 49.22, 15.85.

B_2, as a pale yellow liquid (0.0097 g, 2 % yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.93 (m, 2H, Ar*H*), 7.64 (m, 3H, Ar*H*), 7.20 (m, 3H, Ar*H*), 6.86 (m, 2H, Ar*H*), 5.27 (s, 1H, -C*H*OHPh), 5.06 and 4.94 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O-), 4.84 (br.s, 1H, -O*H*), 3.92-3.80 (m, 3H, H_X and -OCH_2CH$_2$O-), 3.61 (t, J = 4.3 Hz, 2H, -OCH$_2$CH_2O-), 3.41 (s, 3H, -OCH_3), 1.46 (dd, J = 7.3 and 4.2 Hz, 1H, H_A), 0.66 (t, J = 7.1 Hz, 1H, H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 41.06, 137.77, 131.33, 129.40, 128.15, 127.79, 126.44, 124.97, 96.28, 71.72, 71.03, 67.86, 59.05, 55.81, 49.38, 16.55.

B_3, as a pale yellow liquid (0.1009 g, 14 % yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.70-7.21 (m, 10H, Ar*H*), 5.00 (s, 1 H, -C*H*OHPh), 4.70 and 4.33 (each d, J = 6.3 Hz, 2H, -OCH_2O-), 4.13 (br.s, 1H, -O*H*), 3.64-3.46 (m, 4H, -OCH_2CH_2O-), 3.36 (s, 3H, -OCH_3), 3.25 (dd, J = 8.0 and 4.5 Hz, 1H, *H*x), 1.84 (t, J = 7.5 Hz 1H, H_B), 1.33 (dd, J = 7.3 and 4.5 Hz, 1H, H_A).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 143.28, 140.39, 130.49, 128.68, 128.44, 27.75, 126.55, 125.20, 96.80, 72.04, 71.38, 67.85, 61.26, 59.01, 52.71, 15.59.

B_4, as a pale yellow liquid (0.0320 g, 8 % yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.93-7.45 (m, 5H, Ar*H*), 7.30-7.09 (m,5H, Ar*H*), 5.37 [s, 1H, -C*H*(OH)Ph], 4.87 and 4.84 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O-), 3.90 (dd, J = 6.2 and 4.7 Hz, 1H, H_X), 3.86-3.57 (m, 4H, -OCH_2CH_2O-), 3.39 (s, 3H, -OCH_3), 1.81 (dd, J = 7.0 and 4.7 Hz, 1H, H_A), 0.74 (t, J = 6.7 Hz, 1H, H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.23, 139.62, 130.93, 129.10, 128.20, 27.43, 125.95, 125.02, 95.67, 71.59, 67.64, 67.62, 58.99, 56.71, 51.7 5, 21.39, 14.12.

B_5, as a pale yellow liquid (0.0405 g, 9% yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.46(m, 5H, Ar*H*), 7.30 (m, 5H, Ar*H*), 5.25 [s, 1H, -C*H*(OH)Ph], 4.85 and 4.78 (each d, AB-system, J = 6.5 Hz, 2H, -OCH_2O-), 4.16 (dd, J = 7.2 and 5.0 Hz, 1H, H_X), 3.79-3.56 (m, 4H, -OCH_2CH_2O-), 3.39 (s, 3H, -OCH_3), 3.08 (br.s, 1H, -O*H*), 1.33 (t, J = 7.2 Hz, 1H, H_B), 1.25 (app.d, J = 7.2 and 5.0 Hz, 1H, H_A).

B_6, as a pale yellow liquid which is as a 6:4 mixture of 1 diastereomer of **96e** and starting **92** (0.0342 g, 10 % yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.67-6.64 (m, 15H, 10H of Ar*H* of **96e** and 5H of Ar*H* of starting **92**), 5.02 and 4.94 (each d, AB-system, J = 6.3 Hz, 2H, -OCH_2O- of **96e**), 4.73 and 4.66, 4.57 and 4.50 (each d, 2 sets of AB-system, J = 6.6, 6.5 Hz, 2H, -OCH_2O- of starting **92**), 4.02-3.49 (m, 5H, -OCH_2CH_2O- and H_X), 3.41, 3.40 and 3.38 (each s, 3H, -OCH_3), 2.44 (m, 1 H, H_C of starting **92**), 1.53 – 1.18 (m, 2H, H_A and H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 141.80, 140.61, 131.09 (starting **92**), 130.43, 129.22 (starting **92**), 128.68, 128.48, 127.91, 126.56, 124.27, 123.97 (starting **92**) 123.85 (starting **92**), 97.13, 95.51 (starting **92**), 72.47, 71.63, 71.59 (starting **92**), 68.74, 67.42 (starting **92**), 59.03, 58.99 (starting **92**), 53.53, 54.44, 52.47 (starting **92**) 58.97 (starting **92**), 18.88, 11.16 (starting **92**).

B_7, as a colorless liquid (0.0691 g, 16 % yield)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.51-7.25 (m, 10H, Ar*H*), 5.15 [s, 1H, -C*H*(OH)Ph], 4.74 and 4.71 (each d, AB-system, J = 6.6 Hz, 2H, -OCH_2O-), 3.68 (m, 1H, H_X), 3.60 and 3.48 (each m, 4H, -OCH_2CH_2O-), 3.36 (s, 3H, -OCH_3), 1.58-1.47 (m, 2H, H_A and H_B).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 140.72, 140.28, 131.40, 129.01, 128.23,127.85,126.99, 125.07, 95.65, 72.03, 71.84, 67.53, 58.97, 58.16, 51.43, 15.06.

MS : m/z (%) relative intensity 377 (M^+1,0.04), 376 (M^+, 0.05), 359 (0.4), 271 (3), 254 (4), 253 (21), 162 (3), 161 (24), 145 (7), 133 (26), 127 (4) 126 (14), 125 (12), 117 (21), 116 (9), 115 (21), 109 (4), 105 (16), 103 (4), 97 (4), 91 (15), 90 (4), 89 (79), 79 (9), 78 (9), 77 (20), 60 (3), 59 (100), 55 (4), 51 (6).

Preparation of 2-(1'-hydroxy-3'-phenyl-2'-propenyl)-1-[(2-methoxyethoxy) methoxy]-2-(phenylsulfinyl)cyclopropane (96f)

To a solution of the starting **92** (0.2134 g, 0.78 mmol) in dry THF (2 mL) was added slowly to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.13 mL, 0.91 mmol) with *n*-butyllithium (0.60 mL of a 1.45 M solution in hexane, 0.87 mmol) at -78 °C for 30min]. The reaction was kept stirring at -78 °C for 1.5 h and a solution of cinnamaldehyde (0.12 mL, 0.95 mmol) in THF (2 mL) was added. After stirring at -78 °C for 3 h, the reaction was worked up as usual with a saturated aqueous ammonium chloride solution to give a yellow liquid of a crude product which was purified by preparative thin-layer chromatography (SiO_2, 60% ethyl acetate in hexane, double runs) to provide two fractions of 2-(1'-hydroxy-3'-phenyl-2'-propenyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane

(**96f**) (0.1561 g, 74% yield) and a complex mixture of products. When using *n*-butyllithium (0.74 mL of a 1.45 M solution in hexane, 1.07 mmol) as base and starting **92** (0.2648 g, 0.98 mmol) in THF (7 mL) at -78 °C for 3 h provide **96f** in 40% yield and complex mixture of products.

B_1, as a colorless liquid of the single diastereomer of **96f** (0.0799 g, 25% yield) ^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.92-7.14 (m, 10H, Ar*H*), 6.82 (d, *J* = 16.0 Hz, 1H, -CH=C*H*Ph), 6.54 (dd, AB-system *J* = 16.0, 5.3 Hz, 1H, -C*H*=CHPh), 4.69 and 4.37 (each d, AB- system, *J* = 6.6 Hz,, 2H, -OCH_2O-), 4.52 [br. d, 1H, -C*H*(OH)-], 3.93-3.53 (each m, 4H, -OCH_2CH_2O-), 3.40 (s, 3H, -OCH_3), 3.30 (dd, *J* = 7.8, 4.6 Hz, 1H, H_X) 1.24 (m, 1H, H_A), 1.11 (dd, *J* = 7.6, 4.6 Hz, 1H, H_B)

B_2, as a white solid of the single diastereomer (0.0683g, 21 % yield, mp. 88- 91 °C)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.57 (m, 2H, Ar*H*), 7.40 (m, 3H, Ar*H*), 7.27-7.07 (m, 5H, Ar*H*), 6.44 (br.d *J* = 16.0 Hz, 1H, -CH=C*H*Ph), 6.25 (dd, *J* = 16.0, 5.7 Hz, 1H, -C*H*=CHPh), 4.82 (s, 1H, -O*H*), 4.76 and 4.72 (each d, AB- system, *J* = 6.5 Hz,, 2H, -OCH_2O-), 4.53 [dd, *J* = 5.7, 0.8 Hz, 1H, -C*H*(OH)-], 4.05 (dd, *J* = 7.5, 4.7 Hz, 1H, H_X), 3.66 and 3.47 (each m, 4H, -OCH_2CH_2O-), 3.29 (s, 3H, -OCH_3), 1.27 (m, 2H, H_A and H_B)

IR of **B_2** (nujol) : ν_{max} 3244, 1598, 1581, 1530, 1494, 1444, 1417, 1305, 1281, 1249, 1191, 1160, 1138, 1096, 1061, 1038, 1022, 993, 960, 924, 894, 850, 792, 749, 698 cm^{-1}.

MS : m/z (%) relative intensity 385 (5), 188 (6), 187 (22), 171 (17), 170 (5), 169 (5), 159 (5), 143 (13), 142 (17), 141 (24), 131 (9), 129 (6), 128 (10), 125 (5), 117 (12), 117

(12), 115 (14), 105 (5), 91 (11), 90 (5), 89 (100), 78 (5), 77 (9), 59 (97), 45 (10), 31 (9).

B_3, as a yellow liquid of 1:1.5 mixture of 2 diastereomers (0.0878 g, 28 % yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.63–7.26 (m, 10H, Ar*H*), 6.73 (dd, *J* = 16.0, 1.0 Hz,, 1H, -CH=C*H*Ph of the major isomer), 6.57 (d, *J* = 16.0 Hz, 1 H, -CH=C*H*Ph of the minor product), 6.29 (dd, *J* = 16.0, 6.5 Hz, 1H, -C*H*=CHPh of the minor isomer), 6.02 (dd, *J* = 16.0, 5.6 Hz,, 1H, -C*H*=CHPh of the major isomer), 4.97 and 4.91 (each d, AB-system, *J* = 6.4 Hz, 2H, -OCH_2O- of the major isomer), 4.84 and 4.76 (each d, AB-system, *J* = 6.6 Hz, 2H, -OCH_2O- of the minor isomer), 4.82 [app.dd, 1H, -C*H*(OH) of the minor isomer], 4.52 [br.d, *J* = 4.6 Hz, -C*H*(OH) of the major isomer], 4.00 (dd, *J* = 7.9, 4.6 Hz, 1H, H_X of the major isomer), 3.89-3.51 (m, 5H, H_X of the minor isomer, and -OCH_2CH_2O-), 3.43 and 3.39 (each s, 3H, -OCH_3 of the major and minor isomers, respectively), 1.48-1.10 (m, 2H, H_A and H_B) .

^{13}C NMR (75 MHz, $CDCl_3$) : δ 142.07, 140.55, 136.37, 136.24, 132.32, 131.61, 131.25, 131.13, 129.18, 128.92, 128.52, 128.48, 128.43, 128.18, 127.88, 127.69, 126.61, 126.48, 125.51, 125.31, 96.90, 96.04, 72.14, 71.00, 70.73, 68.33, 67.69, 60.34, 59.02, 59.00, 58.50, 58.43, 51.10, 49.49, 20.99, 14.66, 14.41, 14.14.

IR of **B_3** (neat) : ν_{max} 3390, 3058, 3025, 2928, 2890, 2819, 1494, 1476, 1444, 1413, 1365, 1305, 1283, 1253, 1189, 1102, 1083, 1050, 974, 895, 849, 803, 749, 693 cm^{-1}.

MS : m/z (%) relative intensity 402 (M^+, 0.08), 385 (7), 297 (5), 201 (8), 188 (18), 187 (38), 183 (6), 171 (22), 170 (11), 169 (9), 159 (11), 153 (5), 145 (5), 144 (5), 143 (20), 142 (37), 141 (40), 137 (6), 131 (20), 129 (13), 128 (19), 127 (6), 129 (9), 125(9),

117 (19), 116 (7), 115 (32), 109 (9), 105 (14), 104 (5), 103 (11), 97 (7), 91 (35), 89 (88), 83 (6), 78 (16), 77 (29), 65 (7), 59 (100), 55 (13), 51 (17), 50 (5), 45 (26), 44(6), 43 (12), 39 (9), 31 (26).

preparation of 2-(3'-ethyl butanoate)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (96g)

a. In the absence of HMPA

To a stirred solution of **92** (0.1995 g, 0.73 mmol) in dry THF (7 mL) was added dropwise *n*-butyllithium (0.54 mL of a 1.55 M solution in hexane, 0.84 mmol). The reaction mixture was kept stirring at -78 °C for 1.5 h and ethyl crotonate (0.09 mL, 0.84 mmol) was added slowly. After the addition, the reaction mixture was stirred for 3 h at –78 °C and H_2O (5 mL) was then added. The mixture was extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and concentration, a yellow liquid of a crude product was obtained and purified by preparative thin-layer chromatography (SiO_2, 55% ethyl acetate in hexane) to provide a colorless liquid of 1:1.9 mixture of diastereomers of **96g** (0.0416 g, 15% yield). A 74: 26 mixture of the recovered starting **92** and phenylsulfinylbutane (0.0553 g, 30 % yield) was obtained.

^{1}H NMR of **96g** (300 MHz, $CDCl_3$) : δ 7.53 (m, 5H, Ar*H*), 4.79 and 4.75 (each d, AB-system, J = 6.6 Hz , 2H, -OCH_2O- of the minor isomer), 4.62 and 4.59 (each d, AB-system, J = 6.6 Hz , 2H, -OCH_2O- of the major isomer), 4.13 (m, 2H, -COOCH_2CH$_3$), 3.96 (dd, J = 7.3, 4.5 Hz , 1H, H_X, of the minor isomer), 3.75 - 3.42 (m, 4H, -OCH_2CH_2O-), 3.40, 3.35 (each s, 3H, -OCH_3 of the minor and the major isomer, respectively), 3.22 (dd, J = 7.4, 4.3 Hz, 1H, H_X of the major isomer), 2.70 – 2.40 [m,

3H, CC*H*(CH_3)CH_2COO-], 1.44 (t, J = 7.3 Hz , 1 H, H_A of the major isomer), 1.35 - 1.18 [m, 6H, -CCH(CH_3)CH_2COOCH_2CH_3], 1.00 (t, J = 7.3 Hz , 1H, H_A of the major isomer), 0.92 (dd, J = 7.3, 4.3 Hz , 1H, H_B).

IR of **96g** (neat) : ν_{max} 3060, 2978, 2934, 2891, 2819, 1731, 1644, 1582, 1444, 1371, 1299, 1249, 1184, 1158, 1138, 1085, 1049, 971, 882, 849, 785, 751, 692 cm^{-1}.

MS of **96g** : m/z (%) relative intensity 385 (M^++1, 0.84) 384 (M^+, 0.11), 279 (14), 261 (6), 233 (22), 206 (6), 205 (45), 177 (21), 169 (6), 163 (5), 141 (10), 135 (8), 125(14), 113 (9), 110 (5), 109 (12), 97 (8), 95 (9), 89 (74), 78 (6), 77 (9), 69 (5). 67 (5), 60 (5), 59 (100), 55 (5), 51 (6), 45 (16), 44 (5), 43 (11), 41 (11), 39 (5), 39 (5), 31 (12).

b. At-78 ℃, in the presence of HMPA

To a stirred solution of **92** (0.2081 g, 0.77 mmol) in dry THF (4 mL) was added dropwise *n*-butyllithium (0.56 mL of a 1.55 M solution in hexane, 0.85 mmol). After stirring at -78 °C for 1 h, HMPA (0.5 mL) and ethyl crotonate (0.12 mL, 0.92 mmol) were sequentially added. The stirring was continued at the same temperature for 3 h and quenched with H_2O (5 mL), and then extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent, a crude yellow liquid was obtained and purified by preparative thin-layer chromatography (SiO_2, 50% ethyl acetate in hexane) to provide a mixture of the recovered starting material **92** and phenylsulfinylbutane (0.1101g, 84: 6 as ratio). No trace of the desired product could be detected.

c. In the presence of HMPA ,overnight

To a stirred solution of **92** (0.1460 g, 0.52 mmol) in dry THF (3 mL) was added dropwise *n*-butyllithium (0.40 mL of a 1.55 M solution in hexane, 0.62 mmol). After stirring at -78 °C for 1 h, HMPA (0.4 mL) and ethyl crotonate (0.08 mL, 0.64 mmol) were sequentially added. The mixture was allowed to warm up to room temperature overnight and quenched with a saturated aqueous ammonium chloride solution and then extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent, a brown liquid of a crude product was purified by preparative thin-layer chromatography (SiO_2, 50% ethyl acetate in hexane) to provide a 77:33 mixture of the recovered starting material **92** and phenylsulfinylbutane (0.0658 g). No traces of the expected product could be detected.

Reaction with cyclohexenone

A solution of **92** (0.2956 g, 1.09 mmol) in dry THF (5 mL) was added dropwise to diisopropylamide [prepared by reacting *n*-butyllithium (0.80 mL of a 1.50 M solution in hexane, 1.19 mmol) and diisopropylamine (0.18 mL, 1.26 mmol) at -78 °C for 30 min]. The reaction mixture was kept stirring at -78 °C for 1.5 h and cyclohexenone (0.13 mL, 1.30 mmol) was then added slowly. After the addition, the reaction was stirred for 3 h and then at 0 °C for 2 h. The mixture was extracted with ethyl acetate (3 x 50 mL) The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and concentration, a yellow liquid of a crude product was obtained purified by preparative thin-layer

chromatography (SiO_2, 60% ethyl acetate in hexane) to provide the recovered starting **92** in 87% yield.

4.4 Acylation of the anion 93.

preparation of 2-[(2-(methoxyethoxy)methoxy]-5-phenyl-4-(phenylsulfinyl)-2,3-dihydrofuran (98a)

method A

To a solution of lithium diisopropylamide (LDA) [prepared by reacting diisopropylamine (0.14 mL, 1.0 mmol) in THF (3 mL) with *n*-butyllithium (1.60 mL of 1.59 M solution in hexane, 0.96 mmol) at -78°C for 30 min] was added dropwise a solution of 1-[2-(methoxyethoxy)methoxy]-2-(phenylsulfiny)cyclopropane (**92**) (0.2463 g, 0.91 mmol) in THF (1 mL) at -78 °C under an argon atmosphere. After stirring at -78 °C for 1 h, a solution of benzoyl chloride (0.31 mL, 1.05 mmol), in THF (1 mL) was slowly added. After the reaction mixture was kept stirring at -78 °C for 2 h, the mixture was quenched with a saturated aqueous ammonium chloride solution (3 mL) and diluted with H_2O (5 mL) and then extracted with ethyl acetate (3x50 mL). The combined organic layer was washed several time with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure a crude yellow liquid obtained was purified by preparative thin-layer chromatography on silica gel (55% ethyl acetate in hexane ; triple run) to afford a yellow liquid of **98a** (0.0650 g, 21% yield) as a 64:36 mixture of diastereomers and the recovered starting **92** (0.0433 g, 18% yield).

method B

To a THF solution of lithium diisopropylamide (LDA) at -78 °C under an argon atmosphere [prepared by reacting diisopropylamine (0.09 mL, 0.66 mmol) in dry THF (4 mL) with *n*-butyllithium (0.40 mL of a 1.59 M solution in hexane, 0.63 mmol) at –78 °C for 30 min] was added dropwise a solution of **92** (0.1616 g, 0.59 mmol) in dry THF (1 mL). After completion of the addition, the reaction mixture was kept stirring at -78 °C for 1 h, and followed by dropwise addition of a solution of benzoyl imidazole (0.1240 g, 0.72 mmol), in THF (1 mL). After stirring at -78 °C for 2 h, the reaction mixture was quenched with a saturated aqueous ammonium chloride solution (4 mL) at -78°C followed by warming up to room temperature. The mixture was then diluted with H_2O (4 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. Filtration and removal of the solvent on a rotary evaporator gave a crude yellow liquid of 2-[(2-methoxyethoxy)methoxy]-5-phenyl-4-(phenylsulfinyl)-2,3-dihydrofuran (**98a**) and the recovered starting material **92** as revealed by the ^{1}H NMR spectrum and thin-layer chromatography.

A solution of crude product in dry toluene (3 mL) was refluxed under an argon atmosphere for 1 h. After the reaction mixture was slowly cooled down to room temperature, it was quenched with a saturated aqueous ammonium chloride solution (4 mL), diluted with H_2O (4 mL) and followed by extraction with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a crude product obtained was purified by preparative thin-layer

chromatography on silica gel (55% ethyl acetate in hexane) to give a pale yellow liquid of dihydrofuran **98a** (0.0549 g, 25%) as a mixture of diastereomers and the recovered starting material **92** (0.0120 g, 8 % yield).

Method C

A solution of 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane **92** (0.2249 g, 0.83 mmol) in dry THF (1.5 mL) was added to a THF solution of lithium diisopropylamide (LDA) [prepared by reacting diisopropylamine (0.14 mL, 0.98 mmol) in dry THF (7 mL) with *n*-butyllithium (0.61 mL of a 1.50 M solution in hexane, 0.91 mmol) at -78 °C for 30 min] under an argon atmosphere at –78 °C. After completion of the addition, the reaction mixture was stirred at -78 °C for 1 h and followed by dropwise addition of a solution of benzoyl imidazole (0.1856 g, 1.07 mmol) in THF (1.5 mL). After stirring at -78 °C for 2 h, the reaction mixture was kept stirring at 0 °C for 1 h and quenched with a saturated aqueous ammonium chloride solution (5 mL) at 0°C and then warmed up to room temperature. The mixture was diluted with H_2O (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, a crude product obtained was purified by preparative thin-layer chromatography on silica gel (50% ethyl acetate in hexane, double runs) to give a colorless liquid of **98a** (0.0381 g, 12% yield) as a mixture of diastereomers and the recovered starting material **92** (0.0853 g, 38%).

Method D

A solution of starting material **92** (0.2020 g, 0.74 mmol) in THF (1 mL) was added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.11 mL, 0.75 mmol) in THF (1.5 mL) with *n*-butyllithium (0.47 mL of a 1.59 M solution in hexane, 0.75 mmol) at -78 °C for 30 min] at -78 °C under an argon atmosphere and stirred at the same temperature for 1 h. The reaction was transferred to a THF solution of benzoyl imidazole (0.1608 g, 0.93 mmol) in THF (1 mL) and kept stirring at -78 °C for 2 h. After usual workup, the reaction provided a brown liquid of crude product which was purified by preparative thin-layer chromatography on silica gel (60% ethyl acetate in hexane; double run)s to give a colorless liquid of **98a** (0.0280 g, 12% yield) as a mixture of diasteromers and the complex mixture of products.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.84 (m, 2H, Ar*H*), 7.63 (m, 2H, Ar*H*), 7.54-7.44 (m, 6H, Ar*H*), 5.97 (dd, J = 7.7, 2.8 Hz, 1H, -OCH_XO- of the minor isomer), 5.89 (dd, J = 7.2, 2.5 Hz, 1H, -OCH_XO- of the major isomer), 5.10 and 4.77 (each d, J = 7.0 Hz, AB-system, 2H, -OCH_2O- of the major isomer), 5.06 and 4.73 (each d, AB-system, J = 7.0 Hz, 2H, - OCH_2O- of the minor isomer), 3.80-3.50 (m, 4H, -OCH_2CH_2O-), 3.40 (dd, J = 16.0, 7.0 Hz, 1H, -CH$_X$CH_AH$_B$- of the major isomer), 3.35 (s, 3H, -OCH_3), 3.05 (dd, J = 16.2 and 2.5 Hz, 1H, -CH$_X$CH$_A$$H_B$- of the minor isomer), 2.53 (dd, J = 16.2 , 7.2 Hz, 1H, -CH$_X$CH_AH$_B$- of the major isomer), 2.25 (dd, J = 16.2, 2.5 Hz, 1H, CH$_X$CH$_A$$H_B$- of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 161.14, 160.47, 142.97, 130.88, 130.85, 130.30, 130.25, 129.13, 129.10, 128.51, 128.47, 128.44, 128.36, 128.27, 124.39, 124.27, 112.55, 111.90, 101.12, 92.92, 92.83, 71.47, 67.68, 67.60, 58.92, 58.87, 33.50, 33.05.

IR (neat) : ν_{max} 3059, 2927, 2894, 2819, 1732, 1622, 1597, 1576, 1492, 1475, 1455, 1344, 1303, 1287, 1248, 1194, 1121, 1083, 1038, 994, 956, 897, 848, 751, 694, 657 cm^{-1}.

MS : m/z (%) relative intensity 375 (M^++1, 0.39), 374 (M^+, 0.73), 326 (7), 269 (11), 241(14), 240 (6), 135 (5), 131 (4), 125 (12), 115 (3), 108 (9), 106 (4), 105 (6), 104 (3), 97(4), 91 (9), 90 (4), 89 (100), 78 (5), 77 (24), 59 (69), 51 (5).

Preparation of 2-[(2-methoxyethoxy)methoxy]- 4-(phenylsulfinyl)-5-*p*-tolyl-2,3-dihydrofuran (98b)

Method A

A solution of starting **92** (0.2318 g, 0.86 mmol) in THF (1 mL) was added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.14 mL, 0.98 mmol) in THF (3 mL) with *n*-butyllithium (0.60 mL of a 1.59 M solution in hexane, 0.94 mmol) at –78 °C for 30 min] under an argon atmosphere at -78 °C. After the addition was completed, the reaction mixture was stirred at -78 °C for 1 h, followed by dropwise addition of a solution of *p*-toluyl imidazole (0.1995 g, 1.07 mmol) in THF (1 mL). After stirring for 1.5 h, the mixture was quenched with a saturated aqueous ammonium chloride solution (3 mL) and diluted with H_2O (5 mL) and followed by extraction with ethyl acetate (3x30 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent on a rotary evaporator, a crude yellow liquid obtained showed

no trace of the expected product **98b** as determined by ^{1}H NMR of the crude product. The starting material **92** was recovered as determined by ^{1}H NMR of the crude product.

Method B

A solution of 1-[(2-methoxyethoxy)methoxy]-2-phenylsulfinylcyclopropane **92** (0.2412 g, 0.89 mmol) in THF (1 mL) was added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.15 mL, 1.05 mmol) in THF (3 mL) with *n*-butyllithium (0.62 mL of 1.59 M solution in hexane, 0.98 mmol) at -78 °C for 30 min] under an argon atmosphere at –78 °C. After completion of the addition, the reaction mixture was stirred at –78 °C for 1 h and followed by dropwise addition a solution of *p*-toluyl imidazole (0.2072 g, 1.11 mmol) in THF (1 mL). The mixture was allowed to warm up to room temperature overnight. After usual workup, a yellow liquid of a crude product was purified by preparative thin-layer chromatography on silica gel (55% ethyl acetate in hexane, double runs) to provide a pale yellow liquid of **98b** (0.0922 g, 27% yield) as a 57:43 mixture of diastereomers and the recovered starting sulfoxide **92** (0.0538 g, 22% yield).

Method C

A solution of starting 1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl) cyclopropane (**92**) (0.2398 g, 0.88 mmol) in THF (1.5 mL) was added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.15 mL, 1.05 mmol) in THF (6 mL) with *n*-butyllithium (0.65 mL) of a 1.59 M solution in hexane, 0.97 mmol) at –78 °C for 30 min] at –78 °C under an argon atmosphere.

After completion of the addition, the reaction mixture was kept stirring at –78° for 1 h and followed by slowly addition of a solution of *p*-toluyl imidazole (0.2110 g, 1.13 mmol) in THF (1.5 mL). After stirring at –78 °C for 2 h and then 0 °C for 1 h, the reaction mixture was worked up usual to provide a yellow liquid of a crude product which was purified by preparative thin-layer chromatography on silica gel (55 % ethyl acetate in hexane, double runs) to give a pale yellow viscous liquid of 2-[(2-methoxyethoxy)methoxy]-4-(phenylsulfinyl)-5-*p*-tolyl-2,3-dihydrofuran (**98b**) (0.0386 g, 11% yield). The starting **92** could also be isolated (0.0815 g, 34% yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.74 (d, J = 8.0 Hz, 2H, Ar*H*), 7.62 (d, J = 7.1 Hz, 2H, Ar*H*), 7.49 (m, 3H, Ar*H*), 7.27 (d, J = 8.0 Hz, 2H, Ar*H*), 5.95 (dd, J = 7.5, 2.7 Hz, 1H, -OCH_XO- of the major isomer), 5.87 (dd, J = 7.2, 2.2 Hz, 1 H, -OCH_XO- of the minor isomer), 5.10 and 4.77 (each d, J = 7.0 Hz, 2H, -OCH_2O- of the minor isomer), 5.05 and 4.73 (each d, J = 7.0 Hz, 2H, -OCH_2O- of the major isomer), 3.80–3.45 (m, 4H, -OCH_2CH_2O-), 3.42 (app. dd, 1H, -CH$_X$CH_AH$_B$- of the major isomer), 3.36 (s, 3H, -OCH_3), 3.04 (dd, J = 16.0, 2.2 Hz, 1H, -CH$_X$CH_AH$_B$- of the minor isomer), 2.50 (dd, J = 16.0, 7.2 Hz, 1H, -OC$_X$CH_AH$_B$- of the minor isomer), 2.42 (s, 3H, -CH_3), 2.24 (dd, J = 16.0, 2.7 Hz, 1H, -CH$_X$CH$_A$$H_B$ of the minor isomer).

^{13}C NMR (75 MHz, $CDCl_3$) : δ 161.47, 143.06, 141.37, 141.33, 130.27, 130.27, 130.22, 129.17, 129.13, 129.11, 128.47, 128.43, 125.55, 125.45, 124.84, 124.45, 124.32, 111.64, 111.01, 101.09, 92.94, 92.84, 71.50, 67.69, 67.60, 58.95, 58.90, 33.51, 33.06, 21.47.

IR (neat) : ν_{max} 3058, 2924, 2818, 1962, 1913, 1736, 1621, 1582, 1508, 1475, 1443, 1408, 1343, 1302, 1249, 1194, 1119, 1083, 1037, 994, 957, 898, 847, 823, 778, 751, 718, 695, 665, 635, cm^{-1}.

MS : m/z (%) relative intensity 389 (M^++1, 1.2), 388 (M^+, 2.7), 372 (4), 359 (9), 341 (10), 340 (44), 285 (6), 284 (4), 283 (23), 282 (5), 271 (7), 256 (8), 255 (41), 254 (13), 234 (10), 227 (12), 163 (10), 158 (4), 146 (7), 145 (7), 135 (22), 131 (4), 129 (14), 128 (5), 125 (14), 119 (28), 117 (4), 115 (5), 109 (4), 91 (19), 90 (5), 89 (87), 77 (8), 65 (7), 60 (4), 59 (100), 51 (7), 45 (21), 43 (4), 32 (6), 31 (14).

Preparation of -5-*t*-butyl-2-[(2-methoxyethoxy)methoxy]-4-(phenylsulfinyl)-2,3-dihydrofuran (98c)

Method A

A solution of the starting sulfoxide **92** (0.1754 g, 0.64 mmol) in THF (1 mL) was added to a THF solution of lithium diisopropylamide at –78 °C [prepared by reacting diisopropylamine (0.13 mL, 0.74 mmol) in THF (3 mL) with *n*-butyllithium (0.50 mL of a 1.44 M solution in hexane, 0.71 mmol) at –78 °C for 30 min] under an argon atmosphere. After completion of the addition, the mixture was kept stirring at -78 °C for 1 h and followed by dropwise addition of a solution of pivaloyl imidazole (0.1276 g, 0.81 mmol) in THF (2 mL). After the mixture was allowed to warm up to room temperature overnight, the mixture was quenched with a saturated aqueous ammonium chloride solution (3 mL) and diluted with H_2O (5 mL) and then extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and concentration under reduced pressure, a crude yellow liquid was purified by preparative thin-layer

chromatography on silica gel (55% ethyl acetate in hexane, double runs) to give a colorless liquid of **98c** (0.0449 g, 20% yield) as a 67:33 diastereomeric mixture and a pale yellow liquid of the recovered starting **92** (0.0246 g, 14% yield).

Method B

A solution of starting **92** (0.2365 g, 0.87 mmol) in THF (1.5 mL) was added to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.15 mL, 1.05 mmol) in THF (6 mL) with *n*-butyllithium (0.64 mL of a 1.50 M solution in hexane, 0.96 mmol) at -78 °C for 30 min] at -78 °C under an argon atmosphere. After completion of the addition, the mixture was kept stirring at -78 °C for 1 h and followed by addition of a solution of pivaloyl imidazole (0.1713 g, 1.12 mmol) in THF (1.5 mL). After the reaction mixture was kept stirring at –78 °C for 2 h and then at 0 °C 1 h, the reaction mixture was worked up as usual to provide a crude yellow liquid which was purified by preparative thin- layer chromatography on silica gel (50% ethyl acetate in hexane, double runs) to give a pale yellow liquid of **98c** (0.0468 g, 16% yield) and a pale yellow liquid of the starting **92** (0.0770 g, 33% yield). ^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.77 -7.34 (m, 5H, Ar*H*), 5.67 (dd, *J* = 7.7, 2.9 Hz, 1H, -OCH_XO- of the major isomer), 5.58 (dd, *J* = 7.7, 2.2 Hz, 1H, -OCH_XO-of the minor isomer), 4.93 and 4.60 (each d, AB-system, *J* = 7.0 Hz, 2H, -OCH_2O- of the minor isomer), 4.89 and 4.58 (each d, AB-system, *J* = 7.0 Hz, 2H, -OCH_2O- of the major isomer), 3.67-3.26 (m, 7H, -OCH_2CH_2OCH_3), 3.14 (dd, *J* = 15.5, 7.7 Hz, 1H, -CH$_X$CH_AH$_B$- of the major isomer), 2.79 (dd, *J* = 15.5, 2.2 Hz, 1H, -CH$_X$CH$_A$$H_B$- of the minor isomer), 2.19 (dd, *J* = 15.5, 7.2 Hz, 1H, -CH$_X$CH_AH$_B$- of the minor isomer),

1.96 (dd, J = 15.5, 2.9 Hz, 1H, -$CH_XCH_AH_B$- of the major isomer), 1.33 [s, 9H, -$C(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$) : δ 143.27, 143.19, 130.01, 129.97, 129.01, 128.95, 124.38, 124.25, 109.90, 109.06, 100.08, 95.87, 92.56, 92.34, 71.46, 67.55, 67.47, 58.91, 58.86, 34.97, 32.99, 32.47, 29.39.

IR (neat) : ν_{max} 3059, 2967, 2932, 2818, 1610, 1582, 1476, 1461, 1443, 1396, 1363, 1342, 1302, 1258, 1195, 1119, 1082, 1038, 997, 977, 922, 849, 816, 788, 751, 696 cm^{-1}.

MS : m/z (%) relative intensity 355 (M^++1, 1.69), 354 (M^+, 4), 325 (10), 249 (11), 221 (3), 179 (12), 151 (7), 135 (4), 126 (5), 125 (15), 111 (6), 109 (8), 97 (5), 91 (5), 90 (4), 89 (90), 79 (3), 78 (11), 77 (14), 73 (4), 69 (8), 65 (4), 60 (4), 59 (100), 57 (20), 55 (5), 53 (3), 51 (5).

The reaction with benzonitrile

A solution of the starting material **92** (0.2915 g, 1.07 mmol) in dry THF (2 mL) was added dropwise to a THF solution of lithium diisopropylamide at -78 °C under an argon atmosphere [prepared by reacting diisopropylamine (0.18 mL, 1.26 mmol) in dry THF (5 mL) with *n*-butyllithium (0.80 mL of a 1.50 m in hexane, 1.18 mmol) at -78 °C for 30 min]. After stirring at -78 °C for 1 h, benzonitrile (0.14 mL, 1.35 mmol) was added and the mixture was allowed to warm up to room temperature overnight. The reaction was quenched with a saturated aqueous ammonium chloride solution (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After concentration, a yellow liquid of a crude product was obtained and purified by

preparative thin-layer chromatography (SiO_2, 60% ethyl acetate in hexane, double runs) to give the recovered starting material **92** (0.1425 g, 49% yield) and a complex mixture of products. When the reaction mixture was quenched with glacial acetic acid, the same results were obtained.

The reaction with *N,N*-diethylbenzamide

A solution of the starting **92** (0.2943 g, 1.08 mmol) in dry THF (1 mL) was added dropwise to a THF solution of lithium diisopropylamide [prepared by reacting diisopropylamine (0.18mL, 1.26 mmol) in dry THF (3 mL) with *n*-butyllithium (0.80 mL of a 1.50 M solution in hexane, 1.18 mmol) at -78 °C for 30 min]. After stirring at -78 °C for 1 h, *N,N*-diethylbenzamide (0.2249 g, 1.35 mmol) was added and the mixture was allowed to warm up to room temperature overnight. The reaction was quenched with a saturated ammonium chloride solution (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a crude brown liquid was obtained and purified by preparative thin-layer chromatography (SiO_2, 60% ethyl acetate in hexane) to give the starting material **92** (0.1391 g, 47% yield) as a complex mixture of products. Similar results were obtained, when the reaction mixture was quenched with glacial acetic acid.

4.5 Preparation of acyl imidazole.

Preparation of benzoyl imidazole

General Procedure : [49]

Under an argon atmosphere, a solution of distilled benzoyl chloride (1.20 mL, 10.24 mmol) in dry benzene (5 mL) was added to a suspension of imidazole (1.5284 g, 22.45 mmol) in dry benzene (30 mL). The suspension was stirred at room temperature overnight. The precipitated imidazole hydrochloride was removed by filtration under an argon atmosphere and the filtrate was evaporated under reduced pressure to give a colorless liquid of benzoyl imidazole (1.7514g, 98 % yied), which was used immediately without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.06 (s, 1H, imidazole proton), 7.79-7.52 (m, 6H, Ar*H* and 1 imidazole proton), 7.14 (s, 1H, imidazole proton).

preparation of *p*-toluyl imidazole

According to the general procedure, *p*-toluyl chloride (2.65 mL, 20.03 mmol) in dry benzene (5 mL) was treated with a suspension of imidazole (2.0711g, 42.17 mmol) in dry benzene (45 mL) to give a white solid of *p*-toluoyl imidazole (3.0959g, 83% yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.08 (s, 1H, imidazole proton), 7.70 (d, J = 8.0 Hz, 2H, Ar*H*), 7.54 (t, J = 1.2 Hz, 1H, imidazole proton), 7.36 (d, J = 8.0 Hz, 2H, Ar*H*), 7.16 (s, 1H, imidazole proton), 2.47 (s, 3H, -CH_3).

Preparation of pivaloyl imidazole

According to the general procedure, pivaloyl chloride (1.24 mL, 10.08 mmol) in dry benzene (5 mL) was treated with a suspension of imidazole (1.5402 g, 22.60 mmol) in dry benzene (30 mL) to give a white solid of pivaloyl imidazole (1.4339 g, 94 % yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.22 , 7.49 and 6.97 (each s, 3H, imidazole proton), 1.37 [s, 9H, -C(CH_3)$_3$].

4.6 Pummerer-type reaction mediated ring-opening of cyclopropane 94.

Preparation of 3-(phenylsulfinyl)-2-butenal (102a)

To a stirred solution of 1-[(2-methoxyethoxy)methoxy]-2-methyl-2-(phenylsulfinyl)cyclopropane (**94a**) (0.1350 g, 0.47 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise trifluoroacetic anhydride (0.14 mL, 1.01 mmol) at -78 °C under and argon atmosphere. After completion of the addition, the reaction mixture was stirred at the same temperature for 10 min and *N,N*-diisopropylethylamine (0.16 mL 0.93 mmol) was then added. After the reaction was kept stirring at -78 °C for 30 min, it was quenched with H_2O (10 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with a saturated solution of sodium hydrogen carbonate (3x50 mL), H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a brown liquid of a crude product was obtained and purified by preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane) to provide a pale yellow liquid of 3-(phenylsulfinyl) -2-butenal (**102a**) (0.0519 g, 62% yield) as a 70:30 mixture of *E*:*Z* isomers. Both

isomers could be separated by careful preparative thin-layer chromatography on silica gel (10 % ethyl acetate in hexane, triple runs). When using trifluroacetic anhydride (1.5 equiv) and *N,N* -diisopropylethylamine (1.5 equiv) in dry CH_2Cl_2 at –78 °C for 3 h, **102a** (14% yield) and the recovered starting material **94a** (38% yield) were obtained.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 10.05 (d, *J* = 6.5 Hz, 1H, -C*H*O of *Z*-isomer), 9.78 (d, *J* = 7.9 Hz, 1H, -C*H*O of *E*-isomer), 7.51-7.36 (m, 5H, Ar*H*), 6.14 (app.d, *J* = 7.0 Hz, 1H, -C=C*H*CHO of *Z*-isomer), 5.47 (app.d, *J* = 7.1 Hz, 1H, -C=C*H*CHO of *E*-isomer), 2.43 (s, 3H, -CH_3 of *E*-isomer), 1.95 (s, 3H, -CH_3 of *Z*-isomer).

IR (neat) : ν_{max} 3058, 2920, 2848. 2752, 1654, 1591, 1580, 1475, 1440, 1400, 1374, 1329, 1307, 1289, 1241, 1155, 1092, 1068, 1023, 1000, 924, 847, 757, 705, 691 cm^{-1}.

MS of *E*-**102a** : m/z (%) relative intensity 180 (M^++2, 2.8), 179 (M^++1, 9), 178(M^+, 46) 177 (34), 163 (11), 161 (7), 149 (18), 135 (9), 134 (29), 116 (6), 115 (12), 112 (4), 111(9), 110 (100), 109 (47), 108 (12), 105 (9), 102 (6), 101 (31), 100 (88), 91 (6), 87 (7), 84(8), 78 (5), 77 (17), 74 (5), 72 (10), 71 (7), 69 (26), 68 (30), 66 (17), 65 (27), 63 (5), 59 (6), 51 (18), 50 (13), 45 (13), 41 (15), 40 (16), 39 (37), 38 (9).

MS of *Z*-**102a** : m/z (%) relative intensity 180 (M^++2, 5), 178 (M^+, 100), 163 (19), 161 (13), 150 (4), 149 (28), 147 (5), 145 (8), 135 (12), 134 (28), 117 (4), 116 (7), 115 (13), 112 (5), 110 (88), 108 (11), 105 (10), 102 (6), 100 (79), 91 (8), 87 (8), 84 (12), 76 (6), 77 (23), 73 (6), 72 (15), 71 (11), 69 (21), 68 (40), 67 (8), 66 (22), 65 (31), 63 (6), 59 (10), 58 (6), 57 (7), 51 (24), 50 (20), 45 (22), 41 (71), 38 (16), 37 (8), 32 (5).

Anal. Calcd for $C_{10}H_{10}OS$: C, 67.38; H, 5.65. Found: C, 67.09; H, 5.64.

Preparation of 3-(phenylsufenyl)-2-nonenal (102b) and 3-(phenylsulfenyl)-3-nonenal (103b)

According to the general procedure, a solution of starting **94b** (0.1509 g, 0.43 mmol) in dry CH_2Cl_2 (5 mL) was reacted with trifluoroacetic anhydride (0.12 mL, 0.87 mmol) and *N,N*-diisopropylethylamine (0.16 mL, 0.93 mmol) to give a crude pale yellow liquid. It was purified by preparative thin-layer chromatography on silica gel (10 % ethyl acetate in hexane) to provide a pale yellow liquid of a 79:21 mixture **102b** and **103b** (0.0873 g, 83 % yield). **102b** contained a 63:37 mixture of *E* and *Z* isomers and **103b** consisted of a 80:20 mixture of *E* and *Z*-isomers. Separation of the *E* and *Z*-isomers of **102b** could be made by careful preparative thin-layer chromatography (SiO_2, 10% ethyl acetate in hexan, triple runs).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 10.15 (d, *J* = 6.6 Hz, 1H, -C*H*O of *Z*-**102b**), 9.79 (d, *J* = 7.9Hz, 1H, -C*H*O of *E*-**102b**), 9.58 and 9.55 (each t, *J* = 2.2Hz, 1H, -C*H*O of *Z*-**103b** and *E*-**103b**, respectively), 7.49-7.20 (m, 5H, Ar*H*), 6.18 (d, *J* = 6.6 Hz, 1H, -C=C*H*CHO of *Z*-**102b**), 6.00 (t, *J* = 7.2 Hz, 2H, -C=C*H*C_5H_{11} of *E* and *Z*-**103b**), 5.41 (d, *J* = 7.9 Hz, 1H, -C=C*H*CHO of *E*-**102b**), 3.25 (d, *J* = 1.6 Hz, 2H, -CH=C-CH_2CHO of *E*-**103b**), 3.15 (d, *J* = 1.3 Hz, 2H, -CH=CCH_2CHO of *Z*-**103b**), 2.79 (t, *J* = 7.8 Hz, 2H, -CH=CC$H_2C_5H_{11}$ of *E*-**102b**), 2.42 (q, *J* = 7.2 Hz, 2H, -C=CHC$H_2C_4H_9$ of *Z*-**103b**), 2.22 (t, *J* = 7.5 Hz, 2H, -CH=CC$H_2C_5H_{11}$ of *Z*-**102b**), 2.12 (q, *J* = 7.2 Hz, 2H, -C=CHC$H_2C_4H_9$ of *E*-**103b**), 1.78-0.80 (m, 20H, -C=CC$H_2C_5H_{11}$ of **102b** and -C=CHC$H_2C_4H_9$ of **103b**).

^{13}C NMR (an isomeric mixture of **102b** and **103b**) (75 MHz, $CDCl_3$) : δ 190.06, 186.94, 171.23, 164.43, 145.04, 135.58, 133.97, 133.62, 130.53, 130.24, 130.03,

129.92, 129.47, 129.33, 129.11, 128.99, 128.39, 127.65, 126.93, 37.05, 32.55, 31.40, 31.26, 31.13, 30.08, 29.66, 28.89, 28.58, 28.35, 26.72, 22.47, 22.34, 14.00, 13.94.

IR of *E*-**102b** (neat) : ν_{max} 3059, 2955, 2928, 2857, 2746, 1660, 1578, 1555, 1474, 1466, 1440, 1393, 1284, 1150, 1119, 1090, 1068, 1024, 1000, 847, 751, 705, 691cm^{-1}.

.MS of *E*-**102b** : m/z (%) relative intensity 250 (M^++2, 3), 249 (M^++1, 10), 284 (M^+,32), 219 (6), 215 (10), 191 (11), 178 (23), 177 (7), 171 (6), 163 (9), 155 (4), 150 (6), 147 (6), 145 (5), 139 (27), 137 (5), 138 (12), 134 (9), 128 (4), 123 (4), 121 (5), 116 (4), 115 (5), 112 (5), 111 (11), 110 (100), 109 (30), 100 (6), 95 (16), 93 (5), 91 (9), 87 (10), 84 (4), 83 (15), 82 (5), 81 (17), 79(7), 77 (11), 71 (5), 69 (13), 68 (7), 67 (12), 66 (8), 65 (14), 57 (8), 55 (12), 53 (8), 51 (9), 45 (6), 43 (14), 41 (25), 39 (18).

Preparation of 3-(phenylsulfenyl)-2-decenal (102c) and 3-(phenylsulfenyl)-3-decenal (103c)

According to the general procedure, a solution of 2-heptyl-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (**94c**) (0.1286 g, 0.34 mmol) in dry CH_2Cl_2 (4 mL) was reacted with trifluoroacetic anhydride (0.10 mL, 0.72 mmol) and *N,N*-diisopropylethylamine (0.12 mL, 0.70 mmol). The crude product obtained was purified by preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane) to provide a pale yellow liquid of a 86:14 ratio of **102c** and **103c** (0.0683 g, 75 % yield). **102c** was obtained as a 79:21 mixture of *E*- and *Z*-isomers respectively. **103c** consisted of a 65:35 mixture of *E*- and *Z*-isomers, respectively.

^{1}H NMR (300 MHz, $CDCl_3$) : δ 10.15 (d, J = 6.6 Hz, 1H, -C*H*O of *Z*-**102c**), 9.78 (d, J = 7.9 Hz, 1H, -C*H*O of *E*-**102c**), 9.57 and 9.55 (each t, J = 2.3 Hz, 1H, -C*H*O of *Z*-**103c** nd *E*-**103c**, respectively), 7.48-7.24 (m, 5H, Ar*H*), 6.18 (d, J = 6.6 Hz, 1H,

-C=C*H*CHO f *Z*-**102c**), 6.00 (t, *J* = 7.2 Hz, 2H, -C=C*H*C_6H_{13} of **103c**), 5.42 (d, *J* = 7.9 Hz, 1H, -C=C*H*CHO of *E*-**102c**), 3.25 (d, *J* = 2.0 Hz, 2H, -CH=CCH_2CHO of *E*-**103c**), 3.15 (d, *J* = 2.0 Hz, 2H, -CH=CCH_2CHO of *Z*-**103c**), 2.79 (t, *J* = 7.8 Hz, 2H, -CH=CC$H_2C_9H_{13}$ of *E*-**102c**), 2.4(q, *J* = 7.2 Hz, 2H, -C=CHC$H_2C_5H_{11}$ of *Z*-**103c**), 2.22 (t, *J* = 7.6 Hz, 2H, -CH=CC$H_2C_6H_{13}$ of *Z*-**102c**), 2.11 (q, *J* = 7.3 Hz, 2H, -C=CHC$H_2C_5H_{11}$ of *E*-**103c**), 1.81-0.82 (m, 24H, -CH=CC$H_2C_6H_{13}$ of **102c** and -C=CHC$H_2C_5H_{11}$ of **103c**).

^{13}C NMR (an isomeric mixture of **102c** and **103c**) (300 MHz, $CDCl_3$): δ 199.36, 198.30, 190.07, 186.95, 171.22, 164.43, 141.07, 135.58, 133.97, 130.65, 130.55, 130.24, 129.92, 129.33, 129.12, 128.99, 128.43, 127.67, 127.12, 126.94, 124.77, 121.05, 51.06, 46.05, 37.07, 37.05, 32.56, 31.63, 31.60, 31.51, 31.17, 30.14, 29.57, 29.20, 29.12, 28.89, 28.73, 28.64, 22.57, 22.50, 14.03.

IR of **102c** (neat) : ν_{max} 3059, 2954, 2927, 2855, 2735, 2356, 2328, 1673, 1581, 1573, 1537, 1476, 1466, 1440, 1381, 1303, 1270, 1173, 1148, 1098, 1069, 1024, 1000, 841, 749, 703, 691cm^{-1}.

MS of **102c** (neat): m/z (%) relative intensity 264 (M^++2, 1.6), 263 (M^++1, 5), 262 (M^+, 21), 261 (3), 233 (5), 229 (8), 191 (9), 185 (4), 178 (20), 177 (6), 163 (7), 153 (18), 150(6), 147 (5), 145 (5), 135 (17), 134 (10), 123 (5), 116 (4), 115 (6), 112 (4), 111 (10), 110(100), 109 (39), 108 (5), 100 (6), 97 (7), 95 (7), 93 (6), 91 (10), 87 (10), 85 (5), 84 (5), 83 (11), 82 (6), 81 (23), 79 (9), 77 (14), 71 (6), 69 (13), 68 (10), 67 (18), 66 (13), 65(18), 57(13), 55 (22), 53 (14), 51 (14), 50 (6), 45 (11), 43 (27), 42 (5), 41 (60), 39 (40), 32 (18).

Anal. Calcd for $C_{16}H_{22}0S$: C, 73.23; H, 8.45. Found: C, 72.81; H, 8.20.

Preparation of 3-(phenylsulfenyl)-2-tetradecenal (102d) and 3-(phenylsulfenyl)-3-tetradecenal (103d)

According to the general procedure, a solution of 1-[(2-methoxyethoxy) methoxy]-2-(phenylsulfinyl)-2-undecylcyclopropane (**94d**) (0.2769 g, 0.65 mmol) in dry CH_2Cl_2 (7 mL) was treated with trifluoroacetic anhydride (0.18 mL, 1.30 mmol) and *N,N*-diisopropylethylamine (0.23 mL, 1.34 mmol). The crude product obtained was purified by preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane) to provide a pale yellow liquid of a 78:22 ratio of **102d** and **103d** (0.1759 g, 85% yield). **102d** was obtained as a 72:28 ratio of *E*- and *Z*-isomers, respectively. **103d** consisted of a 26:74 ratio of *E*- and *Z*-isomers, respectively. Separation of the *E*- and *Z*-isomers could be obtained by careful preparation thin-layer chromatography (SiO_2, 10% ethyl acetate in hexane, triple runs).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 10.15 (d, J = 6.6 Hz, 1H, -C*H*O of *Z*-**102d**), 9.79 (d, J= 7.9 Hz, 1H, -C*H*O of *E*-**102d**), 9.58 and 9.55 (each t, J = 2.3 Hz, 1H, -C*H*O of *Z*-**103d** and *E*-**103d**, respectively), 7.48-7.20 (m, 5H, Ar*H*), 6.18 (d, J = 6.6 Hz, 1H, -C=C*H*CHO of *Z*-**102d**), 6.00 (t, J = 7.2 Hz, 2 H, -C=C*H*$C_{10}H_{21}$ of **103d**), 5.42 (d, J = 7.9 Hz, 1H, -C=C*H*CHO of *E*-**102d**), 3.25 (d, J = 1.9 Hz, 2H, -CH=C-CH_2CHO of *E*-**103d**), 3.15 (d, J = 1.9 Hz, 2H, -CH=CCH_2CHO of *Z*-**103d**), 2.79 (t, J = 7.8 Hz, 2H, -CH=CC$H_2C_{10}H_{21}$ of *E*-**102d**), 2.42 (q, J = 7.2 Hz, 2H, -C=CHC$H_2C_9H_{19}$ of *Z*-**103d**), 2.22 (t J = 7.6 Hz, 2H, -CH=CC$H_2C_{10}H_{21}$ of *Z*-**102d**), 2.13 (q, J = 7.2 Hz, 2H, -C=CHC$H_2C_9H_{19}$ of *E*-**103d**), 1.76-0.86 (m, 40H, $CH_2C_{10}H_{21}$ of **102d** and $CH_2C_9H_{19}$ of **103d**).

^{13}C NMR (an isomeric mixture of **102d** and *Z*-**103d**) (75 MHz, $CDCl_3$) : δ 190.00, 186.89, 171.16, 164.36, 135.55, 133.94, 133.66, 133.58, 130.55, 130.21, 129.89, 129.44, 129.30, 129.08, 128.96, 128.86, 128.38, 128.30, 128.14, 127.63, 121.81, 53.44, 37.04, 34.70, 32.53, 31.85, 31.16, 29.54, 29.50, 29.48, 29.42, 29.28, 29.26, 29.21, 29.05, 28.66, 28.60, 27.02, 22.63, 14.06.

IR of *Z*-**102d** (neat) : ν_{max} 3060, 2925, 2854, 2734, 1672,1581, 1572, 1537, 1466, 1440, 1380, 1282, 1144, 1069, 1024, 748, 691 cm^{-1}.

IR of *E*-**102d** (neat) : ν_{max} 3060, 2944, 2853, 2745, 1661,1580, 1556, 1466, 1440, 1393, 1377, 1305, 1283, 1146, 1121, 1091, 1068, 1024, 1000, 917, 874, 750, 721, 691 cm^{-1}.

MS of *Z*-**102d** (neat) : m/z (%) relative intensity 320 (M^++2, 4), 319 (M^++1, 13), 318 (M^+, 37), 317 (12), 301 (6), 289 (15), 285 (25), 241 (10), 225 (10), 209 (31), 207 (7), 191 (32), 179 (8), 178 (54), 177 (14), 165 (7), 164 (5), 163 (15), 161 (9), 150 (14), 149 (12), 147 (11), 145 (10), 135 (20), 134 (14), 133 (6), 128 (5), 127 (5), 123 (9), 121 (12), 116 (5), 115 (7), 112 (5), 111 (13), 110 (100), 109 (42), 107 (5), 100 (6), 97 (7), 95 (13), 93(5), 91 (11), 87 (8), 83 (13), 82 (5), 81 (17), 79 (8), 78 (5), 77 (14), 71 (5), 69 (12), 68(5), 67 (12), 66 (6), 65 (11), 57 (19), 55 (23), 53 (7), 51 (61), 43 (52), 42 (10), 41 (58), 39 (19).

MS of *E*-**102d** (neat) : m/z (%) relative intensity 320 (M^++2, 3), 319 (M^++1, 10), 318 (M^+, 25), 317 (8), 287 (9), 285 (13), 241 (6), 225 (6), 209 (22), 191 (25), 179 (5), 178 (38), 163 (12), 150 (9), 149 (7), 147 (8), 145 (6), 135 (16), 134 (11), 123 (7), 121 (9), 115 (6), 112 (5), 111 (13), 110 (100), 109 (48), 108 (7), 107 (5), 100 (5), 97 (6), 95 (14), 93 (5), 91 (12), 87 (11), 83 (14), 82 (7), 81 (21), 79 (10), 78 (6), 77 (17), 71 (5),

69 (17), 68 (7), 67 (19), 66 (10), 66 (10), 65 (20), 57 (22), 56 (5), 55 (33), 54 (5), 53 (16), 51 (16), 50(8), 45 (6), 43 (71), 42 (15), 41 (99), 40 (10), 39 (44), 38 (5).

Anal. Calcd for $C_{20}H_{30}0S$: C, 75.41; H, 9.49. Found: C, 76.06; H, 9.81.

Preparation of 3-(phenylsufenyl)-2-octadecenal (102e) and 3-(phenylsulfenyl)-3-octadecenal (103e)

According to the general procedure, a solution of 1-[(2-methoxyethoxy) methoxy]-2-pentadecyl-2-(phenylsulfinyl)cyclopropane (**94e**) (0.2302 g, 0.47 mmol) in dry CH_2Cl_2 (5 mL) was reacted with trifluoroacetic anhydride (0.14 mL, 1.01 mmol) and *N,N*-diisopropylethylamine (0.17 mL, 0.99 mmol) to give a crude yellow liquid which was purified by preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane) to provide pale yellow liquid of a 74:26 ratio of **102e** (*E*:*Z* = 75:25) and **103e** (*E*:*Z* = 12:88) (0.1375 g, 77% yield).

^{1}H NMR (300 MHz, $CDCl_3$) : δ 10.15 (d, *J* = 6.7 Hz, 1H, -C*H*O of *Z*-**102e**), 9.79 (d, *J* = 7.9 Hz, 1H, -C*H*O of *E*-**102e**), 9.57 and 9.54 (each t, *J* = 2.2 Hz, 1H, -C*H*O of *Z*-**103e** and *E*-**103e**, respectively), 7.48-7.22 (m, 5H, Ar*H*), 6.18 (d, *J* = 6.7 Hz, 1H, -C=C*H*CHO of *Z*-**102e**), 6.00 (t, *J* = 7.2 Hz, 1H, -C=C*H*$C_{14}H_{29}$ of **103e**), 5.41 (d, *J* = 7.9 Hz, 1H, -C=C*H*CHO of *E*-**102e**), 3.24 and 3.15 (each app.d, 2H,-CH=CCH_2CHO of *E*-**103e** and *Z*-**103e**, respectively), 2.78 (t, *J* = 7.8 Hz, 2H, -CH=CC$H_2C_{14}H_{29}$ of *E*-**102e**), 2.41 (q, *J* = 7.2 Hz, 2H, -C=CHC$H_2C_{13}H_{27}$ of *Z*-**103e**), 2.21 (t, *J* = 7.6 Hz, 2H, -CH=CC$H_2C_{14}H_{29}$ of *Z*-**102e**), 2.10 (m, 2H, -C=CHC$H_2C_{13}H_{27}$ of *E*-**103e**), 1.78-0.83 (m, 56H, -CH=CCH$_2C_{14}H_{29}$ of **102e** and –C=CHCH$_2C_{13}H_{27}$ of **103e**).

^{13}C NMR (an isomeric mixture of **102e** and *Z*-**103e**) (300 MHz, $CDCl_3$): δ 189.80, 186.70, 170.91, 135.48, 133.85, 133.59, 133.50, 130.52, 130.11, 129.80, 129.36,

129.22, 128.87, 128.78, 128.35, 128.05, 127.61, 121.75, 36.96, 32.45, 31.82, 31.07, 29.58, 29.56, 29.50, 29.44, 29.37, 29.26, 29.15, 29.00, 28.61, 28.54, 22.58, 15.14, 14.01.

IR of **102e** (neat) : ν_{max} 3060, 2923, 2852, 2735, 1727,1673, 1573, 1538, 1465, 1440, 1380, 1303, 1154, 1088, 1069, 1024, 1000, 915, 837, 748, 721, 691cm^{-1}.

MS of **102e** (neat) : m/z (%) relative intensity 376 (M^++2, 1), 375 (M^++1, 5), 374 (M^+, 16), 373 (18), 345 (10), 341 (14), 297 (5), 281 (6), 265 (17), 247 (7), 191 (17), 179 (5), 178(38), 177 (9), 163 (11), 150 (10), 149 (7), 147 (8), 145 (6), 135 (17), 134 (10), 123 (10), 121 (11), 112 (5), 111 (14), 110 (100), 109 (34), 100 (6), 97 (8), 95 (17), 93 (6), 91(11), 87 (11), 85 (5), 83 (19), 82 (6), 81 (30), 79 (10), 77 (12), 71 (9), 69 (19), 68 (8), 67 (20), 66 (9), 65 (12), 57 (27), 56 (2), 55 (40), 53 (11), 51 (6), 43 (63), 42 (11), 41 (71), 39 (21), 32 (7).

This compound was also analyzed as semicarbazone.

Semicarbazone of 102e as a white solid (mp. 114-117 °C)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (br. s, 1H, -NH), 7.96 and 7.54 (each d, *J* = 9.3 Hz, 1H, -N=C*H*-), 7.49-7.26 (m, 5H, Ar*H*), 6.41 and 5.70 (each d, *J* = 9.3 Hz, 1H, -N=CHC*H*=C-), 2.40 and 2.22 (each t, *J* = 7.6 Hz, 2H, -CH=CCC$H_2C_{14}H_{29}$), 1.25 and 1.24 (each m, 26H, -$CH_2C_{13}H_{26}CH_3$), 0.88 (t, *J* = 6.6 Hz, 3H, -CH_3).

IR (nujol) : ν_{max} 3463, 3444, 3279, 3153, 3056,1689, 1589, 1504, 1455, 1323, 1187, 1152, 1118, 1069, 1024, 934, 875, 760, 753, 689, 630 cm^{-1}.

Anal. Calcd for $C_{25}H_{41}0SN_3$: C, 69.56; H, 9.57; N, 9.73. Found: C, 69.63; H, 9.52; N, 9.71.

Semicarbazone of 103e as a white solid (mp. 88-90 °C)

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.69 and 7.51 (each s, 1H, -N*H*), 7.25 (m, 5H, Ar*H*), 6.92 and 6.51 (each t, *J* = 5.5 Hz, 1H, -N=C*H*-), 5.95 (t,*J* = 7.Hz, 1H, -C=C*H*$C_{14}H_{29}$), 3.08 and 2.96 (each d, *J* = 5.5 Hz, 2H,-N=CHC*H*$_2$C=CH-), 2.37 (q, *J* = 7.2 Hz, 2H, -C=CHC*H*$_2C_{13}H_{27}$), 1.42 and 1.25 (each m, 24H, -C=CHCH$_2C_{12}$*H*$_{24}CH_3$), 0.88 (t, *J* = 6.6 Hz, 3H, -OC*H*$_3$).

IR (nujol) : ν_{max} 3443, 3278, 3159, 1698, 1624, 1590, 1512, 1464, 1416, 1282, 1180, 1140, 1172, 1026, 983, 886, 773, 736, 695 cm^{-1}.

Anal. Calcd for $C_{25}H_{41}0SN_3$: C, 69.56; H, 9.57; N, 9.73. Found: C, 69.85; H, 9.76; N, 9.83.

Preparation of 4-phenyl-3-(phenylsufenyl)-2-butenal (102f) and 4-phenyl-3-(phenylsulfenyl)-3-betenal (103f)

According to the general procedure, a solution of **94f** (0.1654 g, 0.45 mmol) in dry CH_2Cl_2 (5 mL) was reacted with trifluoroacetic anhydride (0.14 mL, 1.01 mmol) and *N,N*-diisopropylethylamine (0.18 mL, 1.05 mmol) to give a crude product which was purified by preparative thin-layer chromatography on silica gel (10% ethyl acetate in hexane) to give a yellow liquid of a 84:16 ratio of **102f** (*E*-:*Z*- = 68:32) and **103f** (0.0803 g, 69% yield). **103f** was also obtained also as a 64:36 mixture of *Z*-and *E*-isomers.

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.17 (d, *J* = 6.6 Hz, 1H, -C*H*O of *Z*-**102f**), 9.91 (d, *J* = 7.7 Hz, 1H, -C*H*O of *E*-**102f**), 9.72 (t, *J* = 1.9 Hz, 1H, -C*H*O of *Z*-**103f**), 9.67 (t, *J* = 2.2 Hz, 1H, -C*H*O of *E*-**103f**), 7.65-6.87 (m, 11H, -C=C*H*Ph of **103f** and 10H of Ar*H*), 6.10 (d, *J* = 6.6 Hz, 1H, -C=C*H*CHO of *Z*-**102f**), 5.60 (d, *J* = 7.7 Hz, 1H,

-C=C*H*CHO of *E*-**102f**), 4.17 (s, 2H, -CH_2Ph of *E*-**102f**), 3.54 (s,2H, -CH_2Ph of *Z*-**102f**), 3.48 (d, *J* = 1.7 Hz, 2H, -CH_2CHO of *Z*-**103f**), 3.31 (d, *J* = 1.7 Hz, 2H, -CH_2CHO of *E*-**103f**).

^{13}C NMR of *Z*-**102f** (75 MHz, $CDCl_3$) : δ 189.93, 162.52, 136.40, 134.37, 134.35, 129.38, 129.24, 128.98, 128.65, 128.56, 127.03, 43.24.

IR of *E*-**102f** (neat) : ν_{max} 3060, 3028, 2925, 2849, 2750, 2359, 1656, 1578, 1494, 1474, 1453, 1440, 1394, 1281, 1142, 1068, 1024, 999, 854, 750, 724, 691 cm^{-1}.

IR of *Z*-**102f** (neat) : ν_{max} 3060, 3028, 2924, 2828, 2738, 1669, 1570, 1536, 1494, 1475, 1453, 1440, 1383, 1327, 1273, 1177, 1135, 1069, 1024, 1000, 918, 844, 747, 696 cm^{-1}.

MS of *E*-**102f** : m/z (%) relative intensity 256 (M^++2, 9), 254 (M^+, 90), 176 (9), 168 (5), 167 (8), 163 (12), 147 (11), 145 (19), 144 (44), 135 (5), 134 (7), 127 (13), 118 (5), 116(100), 112 (9), 110 (81), 109 (23), 105 (8), 92 (6), 91 (53), 30 (5), 89 (14), 87 (23), 85(11), 87 (5), 78 (12), 77 (24), 69 (10), 67 (12), 66 (15), 65 (31), 63 (14), 51 (25), 50 (12), 45 (9), 39 (28).

MS of *Z*-**102f** : m/z (%) relative intensity 256 (M^++2, 3), 255 (M^++1, 9), 254 (M^+, 56), 240(6), 211 (2), 178 (3), 176 (4), 167 (5), 163 (12), 147 (5), 145 (9), 144 (29), 134 (6), 127 (6), 117 (20), 116 (23), 115 (63), 111 (7), 110 (100), 109 (9), 91 (39), 89 (8), 87 (11), 85 (8), 78 (5), 77 (18), 69 (7), 67 (6), 66 (10), 65 (26), 63 (10), 51 (19), 50 (6), 45 (5), 39(14).

4.7 Reaction of 1-[(2-methoxyethoxy) methoxy]-2-(3'-phenyl-2'-propenyl)-2-phenylsulfinylcyclopropane 94g with various reagents.

1. The reaction using TFA

1A. To a solution of **94g** (0.1935 g, 0.50 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise trifluoroacetic acid (0.60 g, 0.52 mmol) at 0 °C. After completion of the addition, the reaction was allowed to warm up to room temperature and followed by refluxing for 3 h. After the reaction was cooled down to room temperature, the reaction was quenched with H_2O (10 mL) and followed by addition of a saturated aqueous sodium hydrogen carbonate solution until the mixture became neutral. The mixture was extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent, a yellow liquid of crude product was obtained purified by radial chromatography on silica gel (5-10% ethyl acetate in hexane) to give the recovered starting **94g** (0.1824 g, 94% yield) as revealed by thin-layer chromatography (60% ethyl acetate in hexane).

1B. To a solution of **94g** (0.2023 g, 0.52 mmol) in dry toluene (10 mL) was added trifluoroacetic acid (0.05 mL), 0.65 mmol) at 0 °C under an argon atmosphere. The reaction was allowed to warm up to room temperature and followed by refluxing for 3 h. After the reaction was worked up as the condition *A,* a brown liquid of a crude product was purified by radial chromatography on silica gel (5-10% ethyl acetate in hexane) to give the starting material **94g** (0.1671 g, 83% yield) as a revealed by thin-layer chromatography on silica gel (5-10% ethyl acetate in hexane).

2. The reaction using acetic anhydride.

To a solution of **94g** (0.1824 g, 0.47 mmol) in dry CH_2Cl_2 (8 mL) was added acetic anhydride (0.05 mL, 0.52 mmol) and a solution of 4-dimethylaminopyridine (0.0641 g, 0.52 mmol) in CH_2Cl_2 (2 mL) at room temperature. The reaction was stirred at the same temperature for 3 h followed by refluxing for 3 h and then was worked up by the same procedure as using trifluoroactic acid to give a brown liquid of a crude product. The crude product was purified by radial chromatography on silica gel (5-10% ethyl acetate in hexane) to give the starting material **94g** (0.1675 g, 92% yield) as revealed by thin-layer chromatography (60% ethyl acetate in hexane).

3. The reaction using trimethylsilyl chloride

To a solution of **94g** (0.1824 g, 0.49 mmol) in dry toluene (10 mL) was slowly added trimethylsilyl chloride (0.07 mL, 0.55 mmol) at room temperature under an argon atmosphere. The reaction was stirred at room temperature for 3 h followed by refluxing for 3 h. After the reaction was worked up by the same procedure as using trifluoroacetic acid, a brown liquid of a crude product was purified by radial chromatography on silica gel (5-10% ethyl acetate in hexane) to give the starting material **94g** (0.1728 g, 92%) as revealed by thin-layer chromatography (60% ethyl acetate in hexane).

4. The reaction using trifluoroacetic anhydride (TFAA)

To a solution of **94g** (0.2013 g, 0.52 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise trifluoroacetic anhydride (0.16 mL, 1.15 mmol). The reaction was stirred for 10 min followed by addition of diisopropylethyamine (0.20 mL, 1.16 mmol) at –78 °C

under an argon atmosphere. After the reaction was kept stirring at –78 °C for 30 min, it was quenched with H_2O (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution (3x50 mL), H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent, a yellow liquid of crude product was obtained as a mixture of a small amount of expected α,β- and β,γ-unsaturated aldehyde as determined by ^{1}H NMR of the crude product. It could not be purified because of the decomposition during purification by preparative thin-layer chromatography on silica gel.

4.7 Reaction of with 2-(1'-hydroxycyclohexyl)-1-[(2-methoxyethoxy)methoxy]-2-(phenylsulfinyl)cyclopropane (96a) with various Lewis acids.

1. Reaction using trifluoracetic anhydride.

To a stirred solution of starting material **96a** (0.1847 g, 0.50 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise trifluoroacetic anhydride (0.28 mL, 2.02 mmol) at –78 °C under an argon atmosphere. After completion of the addition, the reaction mixture was stirred at -78 °C for 10 min, then treated with *N,N*-diispropylethylamine (0.36 mL, 2.10 mmol). The reaction mixture was kept stirring at -78 °C for 30 min and allowed to warm up to 0 °C and continued stirring at 0 °C for additional 4 h. The reaction was quenched with H_2O (10 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution (3 x 50 mL), H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a brown liquid of crude

product was obtained as a complex mixture containing a trace of unsaturated aldehyde **107a**, the recovered starting material **96a** (0.0131 g, 7% yield) and unidentified products as revealed by ^{1}H NMR spectrum.

2. Reaction with trimethylsilyl iodide.

To a solution sodium iodide (0.1332 g, 0.87 mmol) in acetonitrile (1 mL) was slowly added trimethylsilyl chloride (0.07 mL, 0.88 mmol) at room temperature under an argon atmosphere. After the reaction was kept stirring at room temperature for 1 h, a solution of starting material **96a** (0.0722 g, 0.19 mmol) in acetonitrile (2 mL) was added at 0 °C and continued stirring for a further 30 min. The reaction was quenched with H_2O (3 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution (3x30 mL), H_2O, brine and dried over anhydrous sodium sulfate. After concentration, a black viscous liqiud of crude product was obtained as a complex mixture of products.

3. Reaction using p-toluenesulfonic acid.

A solution of starting material **96** (0.1906 g, 0.51 mmol) in dry THF(3 mL) was added dropwise to a solution of *p*-toluenesulfonic acid.H_2O (0.1185 g, 0.62 mmol) in THF (2 mL) at room temperature under an argon atmosphere. After the reaction was refluxed for 3 h, the reaction mixture was allowed to cool down to room temperature. After usual workup by the same procedure as using trifluoroacetic anhydride, a crude yellow liquid was obtained and purified by preparative thin-layer chromatography on silica gel (30% ethyl acetate in hexane) to give the unsaturated aldehyde **107a** (0.0340

g, 25% yield), the recoveed starting material **96a** as revealed by ^{1}H NMR spectrum of crude product and unidentified products.

4. Reaction using boron trifluoride ethyl etherate and N,N-diisopropylethylamine.

To a solution of starting material **96a** (0.2045 g, 0.55 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise boron trifluoride ethyl etherate (0.28 mL, 2.22 mmol) at –78 °C. The reaction was stirred for 10 min and followed by addition of *N,N*-diisopropylethylamine (0.38 mL, 2.21 mmol) under an argon atmosphere. The reaction mixture was continued to stir at -78 °C for 1.5 h, 0 °C for 1.5 h, at room temperature for 17 h and then refluxed for 5 h. After usual workup, a pale yellow liquid of crude product containing mainly starting material **96a** was obtained as revealed by the ^{1}H NMR spectrum of a crude product.

5. Reaction using boron trifluoride ethyl etherate at -78°C

To a solution of the sulfoxide **96a** (0.1096 g, 0.29 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise boron trifluoride ethyl etherate (0.15 mL, 1.19 mmol) at –78 °C under an argon atmosphere. After the reaction was stirred at -78°C for 1.5 h, the mixture was quenched with H_2O and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution (3x50 mL), H_2O, brine and dried over anhydrous sodium sulfate. After filtration and concentration, the crude yellow liquid was obtained as the recovered starting material **96a** (0.1058 g, 97% yield).

6. Reaction using boron trifluoride ethyl etherate at -78 °C and 0 °C.

To a solution of the sulfoxide **96a** (0.1058 g, 0.29 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise boron trifluoride ethyl etherate (0.15 mL, 1.19 mmol) at –78 °C under an argon atmosphere. After stirring at 0 °C for 2 h, the reaction was worked up as above to give a brown-black vicious liquid of a crude product which was purified by preparative thin-layer chromatography on silica gel (55% ethyl acetate in hexane) to provide a yellow liquid of **107a** (0.0597 g, 79% yield).

Preparation of 3-cyclohexylidene-3-phenylsulfinyl(propanal) (107a)

General procedure

To a solution of the sulfoxide **96a** (0.1058 g, 0.29 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise boron trifluoride ethyl etherate (0.15 mL, 1.19 mmol) at –78 °C under an argon atmosphere. After completion of the addition, the reaction mixture was stirred at 0 °C for 2 h, then quenched with H_2O (3 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution (3x50 mL), H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, the crude product obtained was purified by preparative thin-layer chromatography on silica gel (55% ethyl acetate in hexane) to provide a yellow liquid of **107a** (0.0597 g, 79% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95 (m, 1 H, -C*H*O), 7.46-7.33 (m, 5H, Ar*H*), 3.30 (dd, J = 17.5, 1.2 Hz, 1 H, -CH_AH$_B$CHO), 3.04 (dd, J = 17.5, 1.2, 1 H, -CH$_A$$H_B$CHO), 2.80 (m, 2H, -C=CC$H_2$-), 2.10 (t, J = 5.4 Hz, 2H, -C=CCH_2-), 1.82-1.50 (m, 6H, methylene protons of cyclohexane ring).

^{13}C NMR (300 MHz, $CDCl_3$): 197.31, 154.53, 142.80, 130.45, 129.04, 128.44, 124.11, 37.31, 32.45, 31.81, 28.10, 27.54, 26.00.

IR (neat) : ν_{max} 3058, 2932, 2855, 2723, 1722, 1634, 1581, 1475, 1443, 1409, 1386, 1352, 1304, 1257, 1235, 1134, 1115, 1081, 1038, 997,912, 882, 855, 750, 696 cm^{-1}.

MS : m/z (%) relative intensity 264 (M^++2, 2.1), 263 (M^++1, 11), 262 (M^+, 2.7), 246 (8), 245 (40), 234 (11), 217 (9), 201 (18), 191 (15), 183 (6), 137 (5), 135 (7), 128 (5), 127(8), 126 (98), 125 (31), 191 (5), 110 (28), 109 (100), 108 (13), 107 (52), 105 (7), 97 (10), 95 (8), 93 (24), 92 (6), 91 (43), 81 (27), 80 (6), 79 (41), 78 (42), 77 (41), 71 (5), 69 (10), 67 (55), 66 (6), 65 (17), 57 (6), 55 (26), 53 (15), 52 (6), 51 (22), 50 (10), 43 (19), 41 (28), 39 (21).

Preparation of 3-cycloheptylidene-3-phenylsulfinyl(propanal) (107b)

According to the general procedure, a solution of the sulfoxide **96b** (0.2273 g, 0.59 mmol) in dry CH_2Cl_2 (6 mL) was treated with boron trifluoride ethyl etherate (0.33 mL, 2.62 mmol) to give a pale yellow viscous liquid of a crude product. It was purified by preparative thin-layer chromatography on silica gel (50% ethyl acetate in hexane) to give a pale yellow liquid of **107b** (0.1667 g, 99% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.02 (m, 1 H, -C*H*O), 7.55–7.39 (m, 5H, Ar*H*), 3.38 (dd, J = 17.5, 1.4 Hz, 1H, -CH_AH$_B$CHO), 3.09 (app.d, 1H, -CH$_A$$H_B$CHO), 3.15-3.05 (app. ddd, 1H, -C=CH_AH$_B$-), 2.89 (ddd, J = 14.8, 7.5, 4.0 Hz, 1H, -C=CCH$_A$$H_B$-), 2.31 (m, 2H, -C$H_2$C=C-), 1.95-1.53 (m, 8H, methylene protons of cycloheptan ring).

^{13}C NMR (75 MHz, $CDCl_3$): δ 197.57, 156.44, 142.71, 131.11, 130.51, 129.09, 124.22, 38.03, 33.63, 32.56, 28.81, 28.74, 27.86, 26.21.

IR (neat) : ν_{max} 3058, 2924, 2853, 2722, 1721, 1621, 1581, 1474, 1443, 1410, 1386, 1351, 1304, 1208, 1171, 1082, 1040, 997, 954, 750, 695, cm^{-1}.

MS : m/z (%) relative intensity 278 (M^++2, 0.5), 277 (M^++1, 2.3), 276 (M^+, 2.6), 259 (8), 248 (6), 231 (6), 215 (11), 149 (5), 139 (9), 128 (6), 127 (9), 126 (85), 125 (21), 124 (6), 123 (52), 122 (6), 121 (16), 110 (15), 109 (19), 108 (5), 107 (14), 105 (18), 97 (28), 95 (17), 94 (8), 93 (32), 92 (6), 91 (51), 83 (8), 82 (8), 81 (84), 80 (10), 79 (81), 78 (76), 77 (100), 76 (5), 75 (5), 74 (8), 69 (20), 68 (8), 67 (55), 66 (12), 65 (36), 63 (12), 57 (8), 55 (50), 54 (7), 53 (46), 52 (20), 51 (74), 50 (28), 45 (10), 43 (19), 42 (7), 41 (76), 40(12), 39 (68), 38 (7), 32 (8).

Preparation of 3-cyclooctylidene-3-phenylsulfinyl(propanal) (107c)

According to the general procedure, a solution of the sulfoxide **96c** (0.1552g, 0.39 mmol) in dry CH_2Cl_2 (4 mL) was treated with boron trifluoride ethyl etherate (0.22 mL, 1.75 mmol) to give a pale yellow viscous liquid of a crude product. It was purified by preparative thin-layer chromatography on silica gel (50% ethyl acetate in hexane) to give a pale yellow liquid of **107c** (0.1060 g, 93% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (m, 1H, -C*H*O), 7.58 – 7.42 (m, 5H, Ar*H*), 3.38 (dd, *J* = 17.5, 1.7 Hz, 1H, -CH_AH$_B$CHO), 3.08 (br.d, *J* = 17.5 Hz, 1H, -CH$_A$$H_B$CHO), 3.00 (ddd, *J*=14.6, 8.9 , 4.0 Hz, 1H, -C=CCH_AH$_B$-), 2.80 (ddd, *J* = 14.5, 7.7 , 4.0 Hz, 1H, -C=CCH$_A$$H_B$-), 2.28 (m, 2H, -C$H_2$C=C-), 2.05-1.80 (m, 2H, methylene protons of cyclooctane ring), 1.73-1.47 (m, 8H, methylene protons of cyclooctane ring).

^{13}C NMR (75 MHz, $CDCl_3$): δ 197.69, 157.74, 142.55, 130.57 (db), 129.11, 124.33, 38.39, 33.09, 31.80, 28.18, 27.16, 26.34, 25.53, 24.94.

IR (neat) : ν_{max} 3058, 2926, 2854, 2722, 1720, 1616, 1581, 1475, 1443, 1411, 1358, 1304, 1116, 1082, 1038, 997, 750, 695 cm^{-1}.

MS : m/z (%) relative intensity 292 (M^++2, 3.5), 291 (M^++1, 22), 273 (6), 229 (5), 165 (6), 153 (5), 147 (6), 141 (6), 137 (33), 135 (19), 127 (6), 126 (100), 121 (21), 119 (12), 117 (5), 110 (11), 109 (29), 107 (17), 105 (14), 97 (18), 95 (58), 93 (40), 91 (35), 83 (8), 81 (77), 79 (46), 78 (54), 77 (66), 74 (6), 69 (25), 67 (63), 65 (26), 63 (9), 57 (6), 55 (46), 53 (37), 51 (57), 45 (10), 43 (23), 41 (77), 39 (62), 32 (35), 30 (24).

2.9 Reaction of 1-[(2-methoxyethoxy)methoxy]-2-methyl-2-(phenylsulfinyl) cyclopropane 94a with various reagents.

1. Reaction using EtMgBr and benzaldehyd

A solution of ethyl bromide (0.11 mL, 1.47 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.0395 g 1.62 mmol) in dry THF (2 mL) under an argon atmosphere and stirred 10 min at room temperature. The reaction was refluxed for 1 h and allowed to room temperature. A solution of the starting material **94a** (0.2869 g, 1.00 mmol) in dry THF (1 mL) was then added and the reaction was kept stirring at -78 °C for 2.5 h and at 0°C for 3 h. After addition of benzaldehyde (0.15 mL, 1.49 mmol) at –78 °C, the reaction was stirred at –78 °C for 1.5 h and quenched with a saturated aqueous ammonium chloride solution (5 mL) and extracted with ethyl acetate (3x50 mL). The combined organic layer was washed with H_2O, brine and dried over anhydrous sodium sulfate. After filtration and removal of solvent under reduced pressure, a pale yellow liquid of crude product was obtained and

purified by preparative thin-layer chromatography (SiO_2, 55% ethyl acetate in hexane) to provide the recovered starting material **94a** (0.2544 g, 88% yield).

2. Reaction using EtMgBr(2 equiv) and piperonal

A solution of ethyl bromide (0.10 mL, 1.33 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.0330 g 1.35 mmol) in dry THF (1 mL) under an argon atmosphere. After completion of the addition, the mixture was stirred at room temperature for 10 min and allowed to reflux for 1 h to give a colorless solution. A solution of the starting material **94a** (0.1928 g, 0.67 mmol) in dry THF (1 mL) was added at -78 °C and the reaction was stirred at -78 °C for 1 h and then at 0 °C for 1 h. After the addition of a solution of piperonal (0.1522 g, 0.01 mmol) in dry THF (1 mL) at –78 °C, the reaction was stirred at the same temperature for 1 h and then 0 °C for 1 h. The reaction gave, after usual workup with a saturated aqueous ammonium chloride solution, a yellow liquid of crude product which was purified by preparative thin-layer chromatography (SiO_2, 50% ethyl acetate in hexane) to provide the recovered of starting material **94a** (0.1638 g, 85% yield) and the recovered of aldehyde(0.1399 g, 90% yield) as a pale yellow liquid.

3. Reaction using EtMgBr(10 equiv) and piperonal

A solution of ethyl bromide (0.42 mL, 5.56 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.1393 g 5.57 mmol) in dry THF (1 mL) under an argon atmosphere. After completion of the addition, the mixture was stirred at room temperature for 10 min and followed by refluxing for 1 h. A solution of the starting material **94a** (0.1554 g, 0.54 mmol) in dry THF (1 mL) was added at

-78 °C and the reaction was stirred at 0 °C for 2 h and followed by addition of a solution of piperonal (0.1256 g, 0.80 mmol) in dry THF (1 mL) at 0 °C and continued stirring at 0 °C for 2 h. The reaction provided, after usual worked up with a saturated aqueous ammonium chloride solution, a pale yellow liquid of crude product which was purified by preparative thin-layer chromatography (SiO_2, 50% ethyl acetate in hexane) to provide a yellow liquid of 1-(3,4-methylene dioxyphenyl)-1-propanol (**115**)(0.1188 g, 85% yield), the recovered starting material **94a** (0.0213 g, 14% yield) and the complex mixture of products.

^{1}H NMR of 1-(3,4-methylene dioxyphenyl)-1-propanol (300 MHz, $CDCl_3$) : δ 6.85, 6.67 (each s, 3H, Ar*H*), 5.93 (s, 2H, -OCH_2O-), 4.49 [t, J = 6.6 Hz, 1H, -C*H*(OH)], 1.73 (m, 2H, -CH_2CH$_3$), 0.88 (t, J = 7.4 Hz, 3H, -CH$_2$CH_3).

^{13}C NMR of 1-(3,4-methylene dioxyphenyl)-1-propanol (75 MHz, $CDCl_3$) : δ 147.69, 146.81, 138.65, 119.37, 107.94, 106.38, 100.90, 100.86, 97.56, 75.85, 31.78, 10.12.

IR of 1-(3,4-methylene dioxyphenyl)-1-propanol (neat): ν_{max} 3380, 2965, 2932, 2877, 2778, 2360, 1733, 1634, 1609, 1504, 1487, 1441, 1377, 1329, 1248, 1188, 1127, 1101, 1040, 976, 930, 864, 811, 727, 700 cm^{-1}.

4. Reaction using EtMgBr(10 equiv) and piperonal, overnightl

A solution of ethyl bromide (0.75 mL, 10.04 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.2501 g, 10.32 mmol) in dry THF (2 mL) under an argon atmosphere. After completion of the addition, the mixture was stirred at room temperature for 10 min and followed by refluxing for 1 h to give a colorless solution. After the reaction was allowed to cool down to room temperature, it was transferred to a solution of the starting material **94a** (0.2860 g, 1.00 mmol) in

dry THF (1 mL) at -78 °C. The reaction was stirred at -78 °C for 1.5 h and then at 0 °C for 2.5 h. A solution of piperonal (0.2293 g, 1.52 mmol) in dry THF (1 mL) was added at -78 °C and the reaction was allowed to warm up to room temperature overnight. The reaction provided, after usual workup as using a saturated aqueous ammonium chloride solution, a yellow liquid of crude product which was purified by preparative thin-layer chromatography (SiO_2, 15 % ethyl acetate in hexane) to provide a yellow liquid of 1-(3,4-methylene dioxyphenyl)-1-propanol (**115**) (0.2702 g, 98% yield) and a trace amount of complex mixture of products.

5. Reaction using EtMgBr(10 equivs.) and piperonal at -78 °C

A solution of ethyl bromide (0.77 mL, 10.30 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.2601 g, 10.60 mmol) in dry THF (3 mL) under an argon atmosphere. After completion of the addition, the mixture was stirred at room temperature for 10 min and followed by refluxing for 1 h to give a colorless solution. After the reaction was allowed to cool down to room temperature, it was transferred to a solution of the starting material **94a** (0.2866 g, 1.0 mmol) in dry THF (1 mL) at -78 °C. After stirring at -78 °C for 1 h, a solution of piperonal (0.2291 g, 1.52 mmol) in dry THF (1 mL) was added at -78 °C and stirring was continued for 1.5 h. The reaction provided, after usual workup as using a saturated aqueous ammonium chloride solution, a pale yellow liquid of crude product which was purified by preparative thin-layer chromatography (SiO_2, 30% ethyl acetate in hexane) to provide a yellow liquid of 1-(3,4-methylene dioxyphenyl)-1-propanol (**115**) (0.2656 g, 99% yield) and a pale yellow liquid of the recovered starting material **94a** (0.2610 g, 91%).

6. Reaction using EtMgBr, n-butyllithium and piperonal

A solution of ethyl bromide (0.07 mL, 0.93 mmol) in dry THF (1 mL) was added dropwise to a suspension of magnesium (0.0165 g, 1.02 mmol) in dry THF (2 mL) under an argon atmosphere. After completion of the addition, the mixture was stirred at room temperature for 10 min and followed by refluxing for 1 h, the mixture was transferred to a solution of the starting material **94a** (0.1292 g, 0.45 mmol) in THF (1 mL) at -78 °C, followed by stirring at -78 °C for 10 min. *n*-Butyllithium (0.70 mL, 0.98 mmol) was added and the reaction was stirred for 2 min and then a solution of piperonal (0.1502 g, 1.00 mmol) in dry THF (1 mL) was added. The reaction was continued stirring at -78 °C for a further 10 min. The reaction gave, after usual workup as using a saturated aqueous ammonium chloride solution, a pale yellow liquid of crude product which was purified by preparative thin-layer chromatography (SiO_2, 30% ethyl acetate in hexane, double runs) to provide a 68:32 mixture of piperonal and 1-(3,4-methylene dioxyphenyl)-1-propanol (**115**) (0.1047 g, 66 % yield), a 62:38 mixture of the recovered starting material **94a** and phenylsulfenylbutane (0.0543 g, 50% yield) and complex mixture of products.

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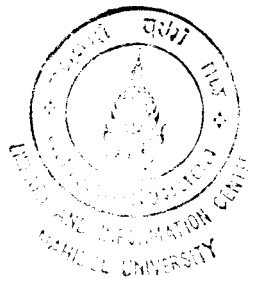
BIOGRAPHY



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