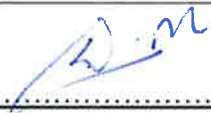# S
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FACULTY OF SCIENCE AND TECHNOLOGY

MASTER THESIS

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Investigation of Ring-Openings of Some *gem*-Dichlorocyclopropanes

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ABSTRACT

The main purpose of this thesis was to study ring-openings of *gem*-dichlorocyclopropanes under basic conditions and the formation of acetylenic acetals. Therefore, several 2-alkoxy-1,1-dichlorocyclopropanes were synthesized by addition of dichlorocarbene to the corresponding vinyl ethers under phase-transfer conditions or by Doering Hoffmann conditions.

These 2-alkoxy-1,1-dichlorocyclopropanes were treated with 4 eq. of $NaOCH_3$ in DMF at -10°C for 4 hours and quenched with water at room temperature. This gave the optimal yield of acetylenic acetals. However, a slightly different condition was approached for cyclopropanes of cyclic compounds like 7,7-dichloro-2-oxabicyclo[4.1.0]heptane (**41**), 1-methoxy-7,7-dichlorobicyclo[6.1.0]nonane (**42**) and 13,13-dichloro-1-methoxy-bicyclo[10.1.0]tridecane (**43**). They were treated with sodium methoxide in DMF at 0°C for the highest yield of their corresponding products (**54**), (3,3-dimethoxy)cyclononyne (**55**), and (3,3-dimethoxy)cyclotridecyne (**56**).

It is believed that the formation of acetylenic acetals most likely involves a cyclopropene as an intermediate, which might also rearrange to the corresponding vinyl carbene and later form an adduct with alkenes. Therefore, trapping experiments using several non-nucleophilic bases were performed which resulted in the formation of such adducts.

In this master thesis, several compounds were synthesized for the formation of acetylenic acetals. To the authors best knowledge, compounds (**16**), (**17**), (**30**), (**37**), (**38**), (**39**), (**40**), (**43**), (**49**), (**50**), (**51**), (**52**), (**53**), (**55**) and (**56**) have not been prepared before. (see Appendix A)

ABBREVIATIONS

^{13}C	Carbon-13 nucleus
^{1}H	Hydrogen-1 nucleus
Aq.	Aqueous
B.P.	Boiling point
$BF_3.OEt_2$	Boron trifluoride etherate
Cs_2CO_3	Cesium carbonate
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DB-X	1,4-Bis(triethylmethylammonium)benzene dibromide
DCM	Dichloromethane
DFC	Dry Flash Chromatography
DHP	3,4-Dihydropyran
DMF	*N, N*-Dimethylformamide
DMSO-d_6	Dimethyl sulfoxide-d_6
EDG	Electron donating group
EPR	Electronic paramagnetic resonance
Eq.	Equivalent
Et	Ethyl group
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
EtOH	Ethanol
Gem	Geminal

H_2SO_4	Sulfuric acid
HCl	Hydrochloric acid
Hz	Hertz
IR	Infrared
KI	Potassium Iodide
KIO_3	Potassium Iodate
Lit.	Literature
M.P.	Melting point
Me	Methyl group
MeCN	Acetonitrile
MeO	Methoxy group
MeOH	Methanol
MHz	Megahertz
Min	Minute
N.A	Not available
Na_2SO_4	Sodium Sulfate
NaH	sodium hydride
NaOH	Sodium Hydroxide
$NH_4H_2PO_4$	Ammonium dihydrogen phosphate
ppm	Parts per million
PTC	Phase transfer catalyst
PTSA	*p*-Toluenesulfonic acid
R_f	Retention factor

S-8   4(Dimethyloctylammonium)propan-sultan

t-Bu   *tert*-Butyl

t-BuOH   *tert*-Butanol

t-BuOK   Potassium *tert*-butoxide

TEBA   Triethylbenzylammonium chloride

TMSCl   Trimethylsilyl chloride

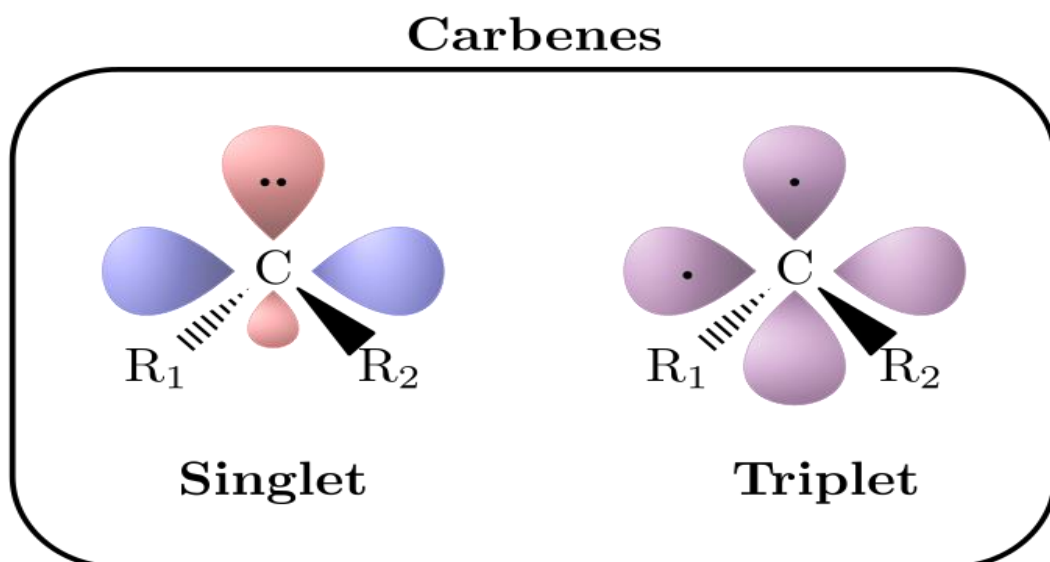UV   Ultraviolet

$ZnCl_2$ Zinc chloride

CONTENTS

1. INTRODUCTION

1.1 Carbenes

A carbene is a reactive intermediate molecule with two unshared valence electrons. It can react both as a nucleophile and as an electrophile. Carbenes can be used to perform a variety of unusual reactions, like insertion, addition or dimerization [5]. The general formula is R-(C**:**)-R' or R=C**:**

Figure 1: Singlet and triplet configuration of carbene.

Carbenes can exist in two configuration states which are different in geometrical features and chemical reactivities. The configuration depends on the difference in energy level between the π and σ nonbonding orbitals. In a singlet carbene, the two unshared electrons are located in the same sp^2 orbital with anti-parallel spin. Whereas in a triplet carbene, the unpaired electrons are in two separate p orbitals with the same spin. The total spin of singlet carbenes is zero while that of triplet carbenes is one (in units of $\hbar$). The bonding orbitals of singlet carbenes are also sp^2 hybridized but the angle differs slightly from normal because of the repulsion between the unshared electron pair in one orbital and the electrons in the two bonding orbitals [4]. Whereas in the triplet state, the two electrons with parallel spin are in two different orbitals. The bonding orbitals were determined by Herzberg, and according to his investigation they vary in a range

between 130°-180° depending on the substituents [5]. Triplet carbenes are more stable in a gas state while singlet carbenes are more stable in an aqueous state [5].

The reason behind the formation of singlet and triplet carbenes could be explained by Hund's rule. If the energy of orbitals are similar or nearly equal, the two unpaired electrons will go into two different orbitals with parallel spin forming a triplet carbene, whereas if the orbitals have different energy levels, the unpaired electron will stay in the orbital with the lowest energy and have opposite spins which forms the singlet carbene [5].

1.2 Cyclopropanes

Cyclopropanes are cycloalkanes with three carbons linked to each other to form a ring with the molecular formula of C_3H_6. The bond angle between non-substituted cyclopropane rings should be 60° which is far less than the thermodynamically stable angle (109.5) for bonds with sp^3 hybridized orbitals, creating significant ring strain. Therefore, the carbon-carbon bond in the cyclopropane is bent outwards making a banana shape to adjust into an equilateral triangle. The C-C bonds in cyclopropanes is much weaker compared to other carbocyclic compounds due to strain energy. This makes cleavage of the bonds much easier.

Generally, cyclopropanes are synthesized by adding carbenes to alkenes. Singlet carbenes follow a pericyclic reaction and preserve the original stereochemistry of alkenes, while triplet carbenes have to change the spin state of the electron forming the diradical before bond formation, which leads to the formation of both cis and trans configuration.
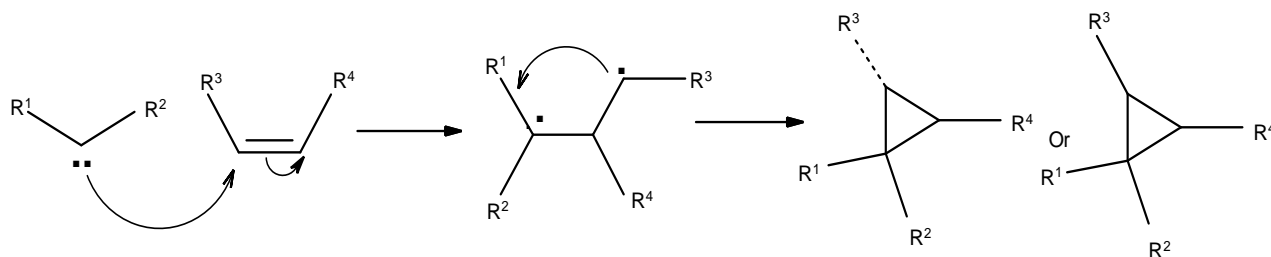
Scheme 1: Triplet carbene addition
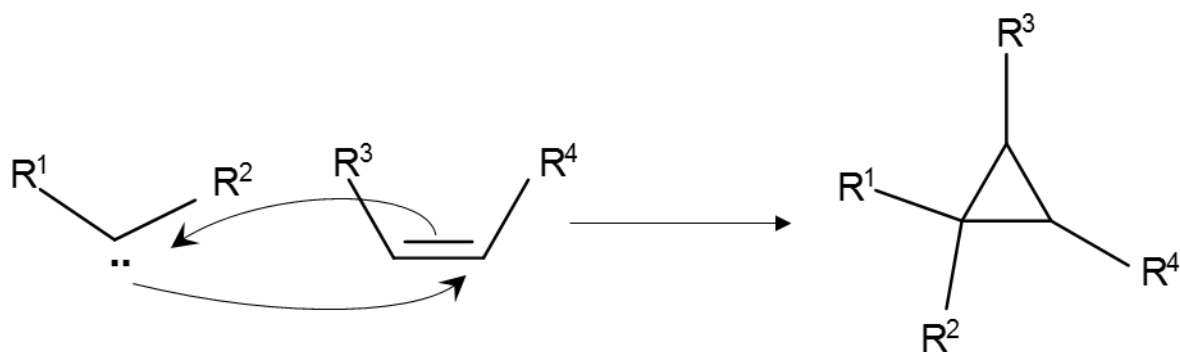
Scheme 2: Singlet carbene addition

1.3 *Gem*-dihalocyclopropanes

When two halogens are attached to one of the carbons in the ring, it is called *gem*-dihalocyclopropanes, which can also be written as 1,1-dihalocyclopropanes. *Gem*-dihalocyclopropanes exist in a strained cyclic system with remarkable kinetic stability. Due to their remarkable chemical properties, they have been of great interest to both theoretical and experimental chemists. Several computational calculations regarding the synthesis and reactivity of dihalocyclopropane have been published [14] [34].
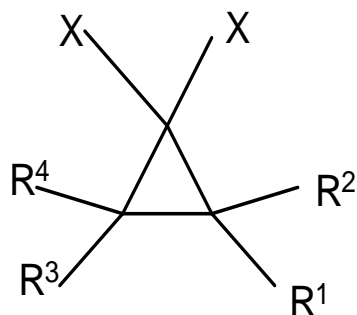
Figure 2: *Gem*-dihalocyclopropane

Where X: F, Cl, Br and I

Gem-dihalocyclopropanes are highly reactive due to high ring strain and in addition to the leaving group properties of the halogens. The *gem*-dihalocyclopropanes used in this thesis were

all attached to alkoxy groups, which made them even more reactive due to the electro donating effect of the alkoxy groups.

Table 1: Bond Dissociation Energies [41]

C-F	C-Cl	C-Br	C-I
485 kJ/mol	346 kJ/mol	290 kJ/mol	213 kJ/mol

Fluorine has a high degree of orbital overlap with carbon and has the strongest bond to carbon of the halogens. The I-C bond is the weakest (see Table 1), so it breaks down more easily. It is usually easy to work with dichlorocyclopropanes because they are more stable than dibromo- and diiodocyclopropanes, but easier to cleave than difluorocyclopropanes. The C-Cl bond is about 346 KJ/mol whereas C-Br is approximately 290 KJ/mol (see Table 1) which clearly shows that *gem*-dichlorocyclopropane is quite stable compared to *gem*-dibromocyclopropane [41]. *Gem*-dichlorocyclopropane is also not particularly toxic and easy to purify. This may be the reason why *gem*-dibromocyclopropanes and *gem*-dichlocyclopropanes are more commonly used in synthesis [9].

1.3.1 Preparation of *gem*-dihalocyclopropanes

The *gem*-dihalocyclopropanes are usually prepared by addition of dihalocarbene to alkenes. Several methods have been developed so far such as Parham reaction conditions ($Cl_3CCOOEt/NaOMe$), Miller method ($Cl_3CBr/MeLi$), Nerdel-Buddrus conditions (CHX_3/ethane oxide/Et_4NBr/heat), Doering Hoffmann conditions (CHX_3, t-BuO), Makosza phase transfer conditions (CHX_3, 50% aq. NaOH), Seyferth ($PhHgCX_3$, benzene, reflux) [2]. The Bakstad research group is mostly experienced in Makosza phase-transfer reactions and Doering Hoffmann reactions, therefore in this master thesis all the *gem*-dihalocyclopropanes were synthesized using these two methods.

In 1954, Doering and Hoffmann generated dihalocarbene from haloform by α-elimination under dry conditions [1]. Since then, many methods have been proposed to generate *gem*-dihalocarbenes

using the addition of divalent carbon intermediates to alkenes and all the procedures utilized basic conditions. In 1964 Seyferth *et al.* developed a method which was based on neutral conditions, however it was f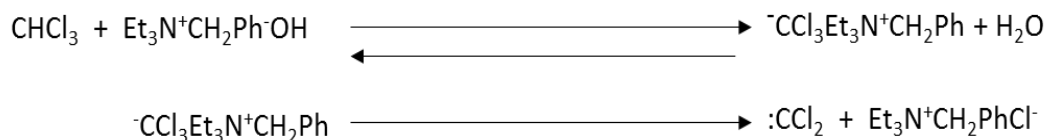ound to be toxic [22]. The following scheme is a summary of procedures used for the synthesis of *gem*-dihalocyclopropanes.

1. Makosza: CHX_3, 50 % aq. NaOH, TEBA
2. Doering Hoffmann: CHX_3, tert-BuO$^-$
3. Seyferth: $PhHgCX_3$, Benzene, reflux
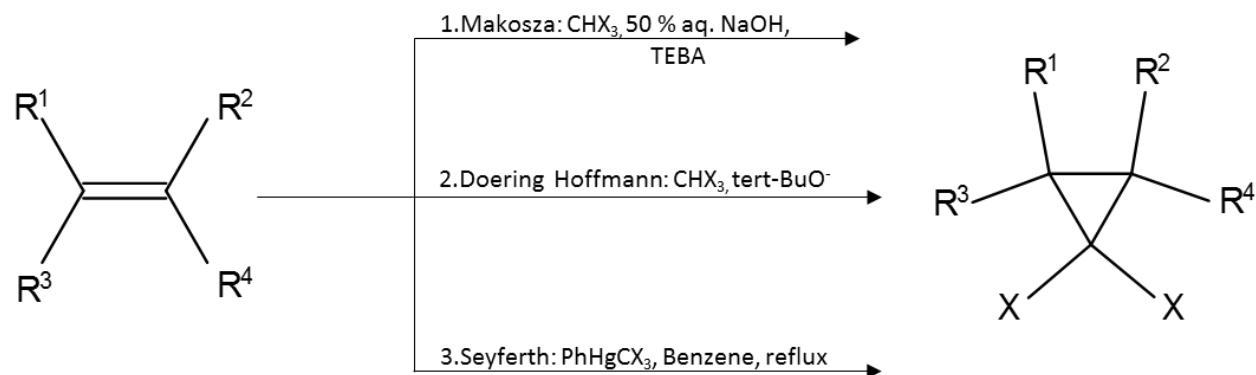
Scheme 3: Procedure of formation of *Gem*-dihalocyclopropanes.

In 1969, Makosza developed a two-phase system where a dichlorocarbene was added to an alkene. This dichlorocarbene was generated by addition of 50% concentrated sodium hydroxide (NaOH) solution as a base in chloroform ($CHCl_3$) and in the presence of a quaternary ammonium salt which acts as phase transfer catalyst (PTC). All the procedures developed so far require dry conditions, except the Makosza procedure which makes it possible to carry out the reaction at bigger scales with lower cost. Therefore, this work can be regarded as a significant contribution to carbene chemistry.

According to his proposal, in concentrated NaOH solution, the phase transfer catalyst triethylbenzylammonium chloride ($Et_3N^+CH_2PhCl^-$) is transformed into triethylbenzylammonium hydroxide ($Et_3N^+CH_2Ph^-OH$) which is an acting base deprotonating $CHCl_3$ and less soluble in the aqueous medium. Thus, it migrates to the boundary between the aqueous and organic phase, where it reacts with chloroform to produce the quaternary ammonium derivative of the trichloromethyl anion ($Et_3N^+CH_2Ph\ ^-CCl_3$) which is soluble in the organic phase.

$$CHCl_3 + Et_3N^+CH_2Ph\,^-OH \rightleftharpoons\ ^-CCl_3Et_3N^+CH_2Ph + H_2O$$

$$^-CCl_3Et_3N^+CH_2Ph \longrightarrow\ :CCl_2 + Et_3N^+CH_2PhCl^-$$

After diffusion into the organic phase, dichlorocarbene is generated and triethylbenzylammonium chloride (TEBA) is restored. This dichlorocarbene reacts quickly with available alkenes in the organic phase, whereas TEBA re-enters to the phase boundary and is again transformed to $Et_3N^+CH_2Ph\ ^-OH$ to repeat the PTC cycle. In this way, dichlorocarbene is generated in dry conditions and consequently, only a small amount gets hydrolyzed [6]

On the other hand, In 2004, Wang *et al.* developed a PTC system where 4(dimethyloctylammonium)propan-sultan (S-8) and 1,4-bis(triethylmethylammonium)benzene dibromide (DB-X) were employed as a catalyst [21]. This PTC system gave quantitative yields of *gem*-dihalocyclopropanes and was found to be even better than TEBA as a catalyst.

| Figure 3: S-8 as a Phase Transfer Catalyst	Figure 4: DB-X as a Phase Transfer Catalyst
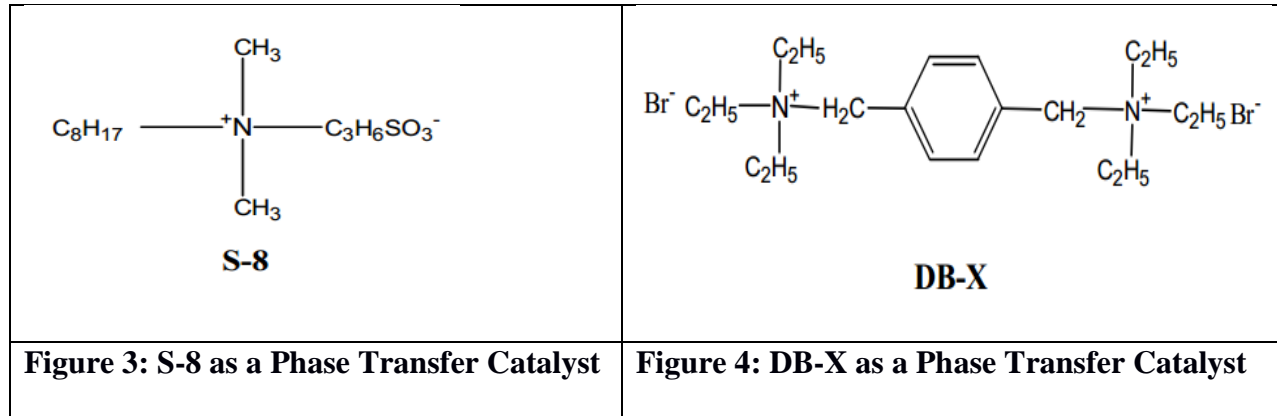
1.3.2 Transformation involving 2-alkoxy-1,1-dichlorocyclopropanes

(1,1-Dichloro-2-methoxycyclopropane)benzene serve as precursors for many monochlorocyclopropenes, heterocyclic ring systems, allenes, bi, tri, and tetra-cyclic ring system depending upon the reagent used[2][9][17][18]. The reaction depends upon the substitution on a phenyl group, the base employed and the solvent used.

The transformation of 2-alkoxy-1,1-dichlorocyclopropanes has been studied by several research scientists so far, but in this thesis we are particularly interested in the base-induced ring opening. When 2-alkoxy-1,1-dichlorocyclopropanes are treated with an alkoxide, the reactions seem to proceed in two distinct pathways [3]. The two distinct pathways as described by P.Muller and N.Pautex in their publication [3] is demonstrated in scheme 4. For example, in the presence of base, *gem*-dichlorocyclopropanes reacts by hydro, chloro-elimination to form chlorocyclopropenes which can be intercepted in the presence of trapping agents like furans and isobenzofurans. In absence of trapping agents, they react with the non-nucleophilic base potassium *tert*-butoxide (*t*-BuOK), and may undergo rearrangements at or below room temperature to vinylcarbenes, which either yield cyclopropanes in presence of alkenes or corresponding products from inter or intramolecular insertion into activated CH bonds (Path A in Scheme 4). The competitive pathway available to dichlorocyclopropanes is thermal electrocyclic ring-opening of the cyclopropane, assisted by the departure of one of the halides (Path B in Scheme 4). The allylic cation intermediate is intercepted by any suitable nucleophile such as the leaving group or the solvent and hydrolysis of such allylic substituents result in formation of 2-chloroprop-2-enones or may result in prop-2-ynones under sufficiently basic conditions.

 In addition to this, the chemical properties of these compounds are determined by the alkoxy group and the halogen which destabilize the ring system and facilitate ring-cleavage.
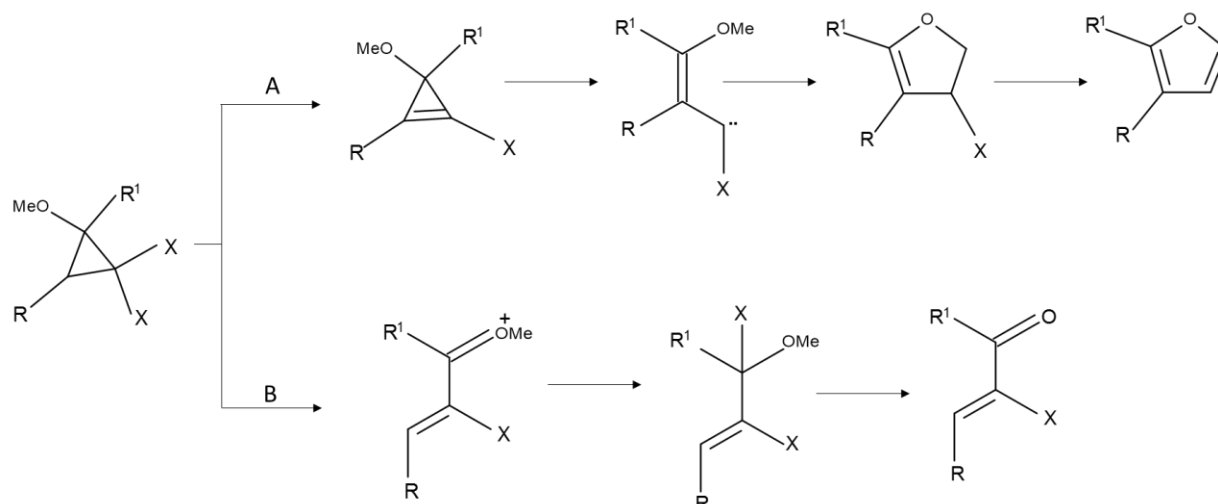
Scheme 4: Possible pathway of ring opening of 2-alkoxy-1,1-dihalocyclopropanes in basic conditions.

## 2. BACKGROUND AND PURPOSE OF THIS STUDY

The research started with interesting chemistry carried out by Prof. Lars Skattebøl in 1966 while studying *gem*-dihalocyclopropanes. Skattebøl reported that *gem*-dihalocyclopropyl ethers typically undergo thermal electrocyclic ring opening to vinylic acetals when treated with base in an alcoholic solvent [15]. This experimental study also became proof of what Woodward and Hoffmann predicted in 1965. They said that the cyclopropyl cation undergoes ring opening in a disrotatory manner. [27] In the same study it was also reported that when ethyl vinyl ether (**1**) was treated with dibromocarbene in excess of potassium *tert*-butoxide (*t*-BuOK), in more drastic conditions, the acetylenic acetal 1-*t*-butoxy-1-ethoxy-2-propyne (**59**) was obtained. Interestingy, the same acetyleic acetal (**59**) was formed by ring opening of 1,1-dichloro-2-ethoxycyclopropane (**33**) when heated with excess *t*-BuOK in *tert*-butanol (*t*-BuOH) [15]. Therefore, it was concluded that the formation of *gem*-dibromocyclopropane derivatives as an intermediate since the same acetylenic acetal was achieved as a final product.
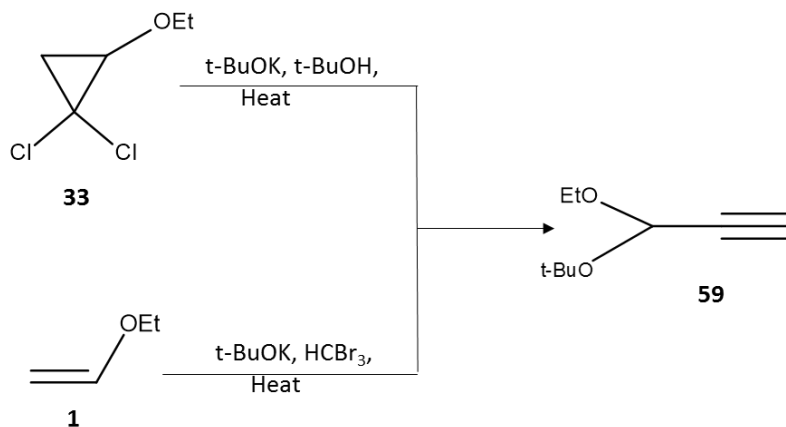
Scheme 5: Preparation of 1-t-butoxy-1-ethoxy-2-propyne

In 1996, Prof. Leif Sydnes and Einar Bakstad came up with the formation of acetylenic acetals in fair to excellent yields [45], when 1,1,2-trihalocyclopropanes was treated with 50% NaOH solution, TEBA, ethanol (EtOH) and dichloromethane (CH_2Cl_2). In some cases, they also reported the formation of olefinic aldehydes.
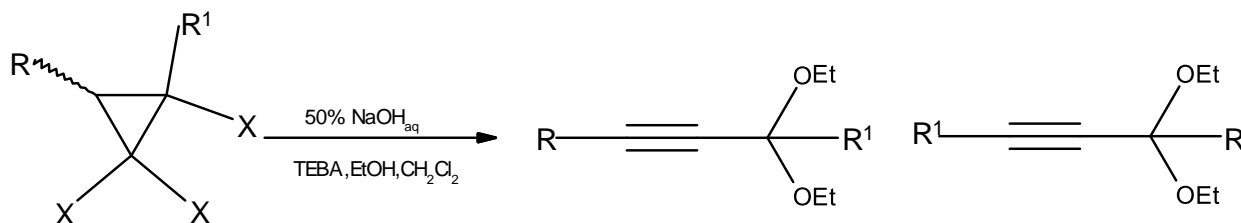
Scheme 6: Acetylenic acetals from 1,1,2-trichlorocyclopropane

In this master thesis, a new reaction approach was applied to improve the synthesis of acetylenic acetals from 2-alkoxy-1,1-dichlorocyclopropane instead of 1,1,2-trihalocyclopropanes. This new approach to the addition of dichlorocarbene to vinyl ether as vinyl ethers are less toxic, easier to handle and have more electron rich double bonds than the vinyl halides used by Sydnes and Bakstad in their experiment in 1996 [45]. Addition of carbene to vinyl ethers give higher yields of the corresponding cyclopropanes than addition of carbene to vinyl halides. This method is more

convenient to work with than vinyl halide that was used in formation of 1,1,2-trihalocyclopropanes.

There is still plenty of research to be done and several barriers to overcome. This research mainly focus on synthesizing different alkoxy-substituted *gem*-dichlorocyclopropanes and their corresponding acetylenic acetals in an efficient way. After the experiments conducted so far, it could be reported that the formation of acetylenic acetals depend on the solvent used and the number of alkoxide equivalents. In the formation of acetylenic acetals, *N,N*-dimethylformamide (DMF) was found to give highest yields and worked even at a low temperature (-10˚C).

The main purpose of this master thesis is to find a mild, efficient, cheap and non-toxic method for the formation of acetylenic acetals. Acetylenic acetals are useful compounds and have a vital role in the synthesis of several natural products [8]. For example, 1,1-dimethoxypropyn has been used in the total synthesis of sesquiterpene *d,l*-Caryophyllene by prof. Corey[26].

## 2.1 PREVIOUS SYNTHESIS AND INVESTIGATION OF RING-OPENINGS

2.1.1 Previous synthesis of phenyl-substituted 2-alkoxy-1,1-dichlorocyclopropanes

Former master student of the Bakstad research group, M.Sc. Y. Luijkx studied the ring-opening of different phenyl-substituted 2-alkoxy-1,1-dichlorocyclopropanes[7]. All the ring-openings resulted in the corresponding acetylenic acetals with yields ranging from 42-46% under Bakstad conditions (NaOCH$_3$/DMF/0℃).
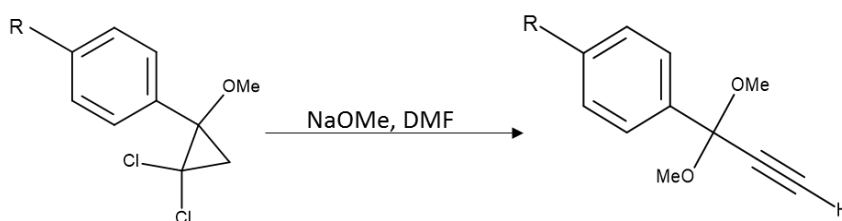
Scheme 7: Ring-opening of different phenyl-substituted 2-alkoxy-1,1,-dichlorocyclopropanes under Bakstad conditions. R=H, Me, *t*-BuO, t-Bu as reported by M.Sc. Y. Luijkx [7]

In this thesis, this experiment was preformed several times while modifying the reaction conditions (NaOCH$_3$/DMF/-10℃) which also produced acetylenic acetals in excellent yields without any side products. Signals in the ^{13}C NMR and ^{1}H NMR Spectra were in accordance with results reported by Y. Luijik and J. Springer [7].
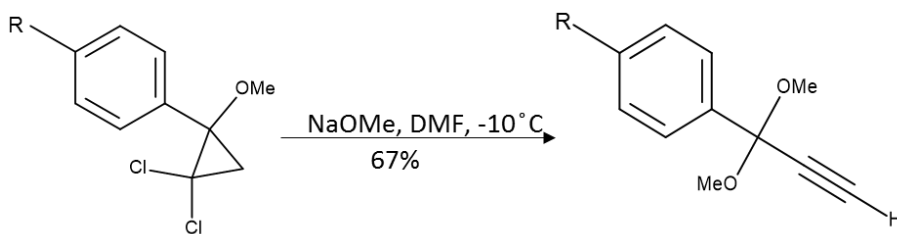
**Scheme 8: Ring-opening under modified Bakstad conditions. R=H, Me, *t*-BuO, t-Bu**

2.1.2 Previous synthesis and formation of (3,3-dimethoxy)cyclononyne (61)

In 1997 Sydnes and Bakstad reported the acetylenic acetal **(61)** in 89% yield, when 1,9,9-tribromobicyclo[6.1.0]nonane was treated with EtOH, TEBA, 50% aqueous NaOH in DCM.
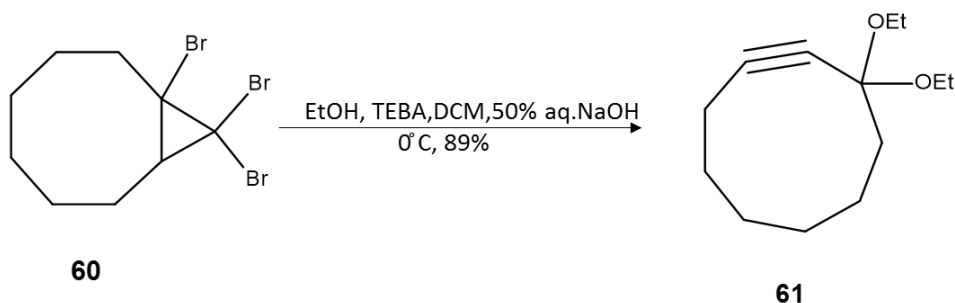

Scheme 9: Synthesis of cyclonone-2-ynone diethyl ketal done by Sydnes and Bakstad [19]

A similar experiment was conducted by Guro Oktavia Fløysvik, former bachelor student of Bakstad. In her bachelor thesis, she reported the formation of 1-chloro-2,2-dimethoxycyclononene **(62)** in 19% yield, when 1-methoxy-7,7-dichlorobicyclo[6.1.0] **(42)** was treated with NaOCH$_3$ in DMF at 0 °C [58].
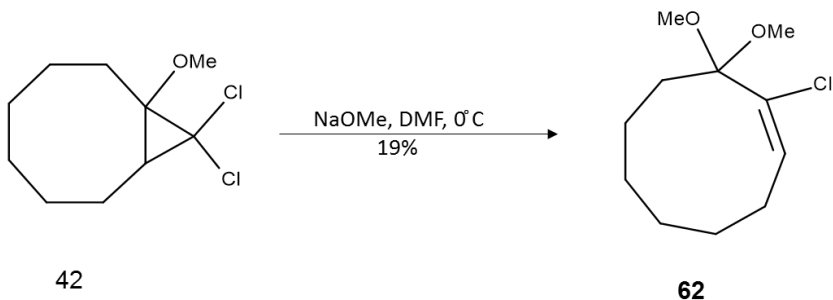
Scheme 10: Ring-opening of 42 under Bakstad conditions as reported by earlier bachelor student Guro Oktavia Fløysvik

The experiment was repeated in this master thesis and ^{13}C NMR and ^{1}H NMR results were found to be in accordance with Sydnes and Bakstad. However, no **(62)** was identified, as reported by Guru Oktavia Fløysvik in her bachelor thesis[58].

42   **55**
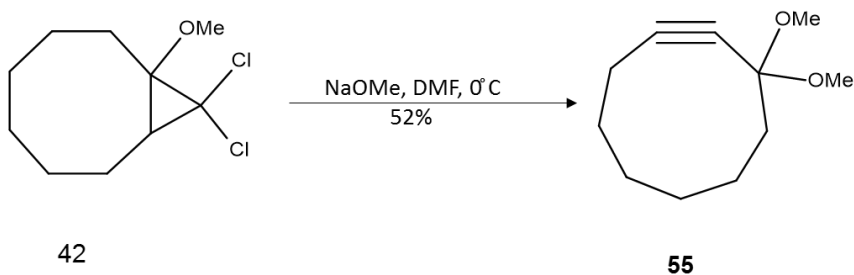
Scheme 11: Ring-opening of 42 under Bakstad condition

2.1.3 Previous synthesis and ring-opening of 13,13-dichloro-1-methoxy bicyclo[10.1.0]tridecane (43)

Former member of the Bakstad research group Dr. J. Springer claimed the formation of acetylenic acetal (**56**) along with allene (**63**) when 13,13-dichloro-1-methoxy-bicyclo[10.1.0]tridecane (**43**) was treated with modified Bakstad conditions (NaOMe/DMF/-50℃). However, no spectral data were reported by Dr. Springer in his M.Sc. thesis. Therefore, this ring-opening experiment was repeated with Bakstad conditions (NaOMe/DMF/0℃) which produced only the acetylenic acetal in 47% yield.

43   **56**   **63**
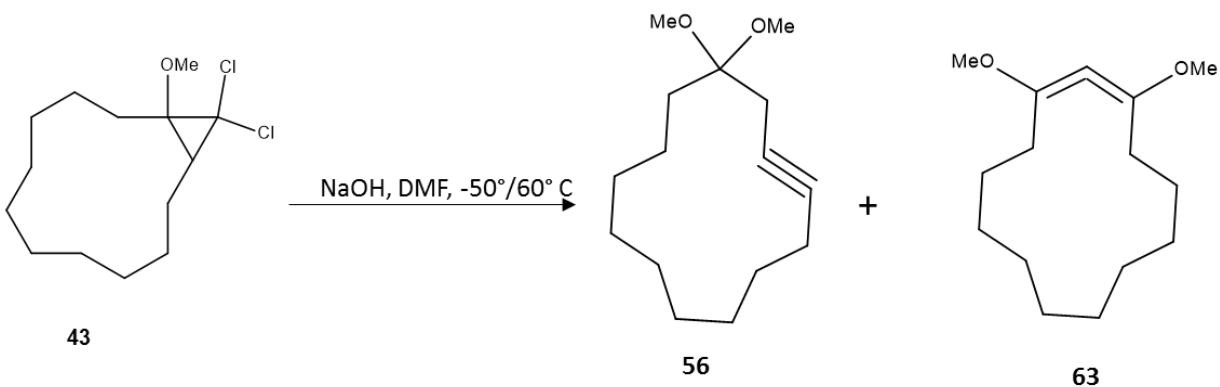
Scheme 12: Ring-opening of 42 as reported by Springer [10]

3. RESULT AND DISCUSSION

3.1 Synthesis of vinyl ethers

There are several methods for preparing the vinyl ethers according to different research groups [7][10][13][23]. In this project, we prepared it from two different methods, one starting from a ketone, another from a styrene. Though both starting materials give vinyl ethers the paths they follow are different.

The preparation of vinyl ethers from ketones comprise two steps. These vinyl ethers are synthesized from their corresponding ketals.

The preparation of acetals were attempted with acetophenone and a few differently substituted acetophenones. These were treated with methanol (MeOH) and trimethyl orthoformate $(CH_3O)_3CH$ using a small amount of concentrated hydrochloric acid (HCl) as a catalyst. This gave acetals in excellent yields.

It is necessary to pay attention toward the removal of water, since water can hydrolyze the product back to the starting material. Therefore, one equivalent of trimethyl orthoformate was added as it quickly reacts with water, forming an alcohol and an ester.
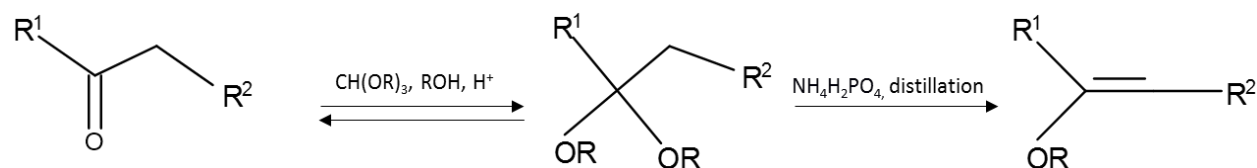
Scheme 13: Synthesis of vinyl ether by acid-catalyzed thermolysis

The acetal formed in this way is treated with mild acid to eliminate methanol and to give the vinyl ether as mentioned by Sadler and Stewart in 1973. At higher temperature, in the presence of acid, vinyl ethers get polymerized easily [30]. So, it was necessary to attempt different mild acids to find a suitable one. The reaction was repeated with different mild acids; like ammonium hydrochloride (NH_4Cl) and ammonium dihydrogen phosphate ($NH_4H_2PO_4$), or catalytical amounts of strong acids like *p*-toluenesulfonic acid (PTSA) and HCl, but none of them seemed

superior to $NH_4H_2PO_4$. The reaction was also carried out with Lewis acids like boron trifluoride etherate ($BF_3.OEt_2$) and zinc chloride ($ZnCl_2$). However, this method resulted only in unreacted starting material though it seemed to be working for formation of sulfur acetals or the mixture or sulfur oxygen acetals.[57] Other possible methods were also approached to get the vinyl ethers such as the experiment described by Burkhouse, D., Zimmer, H.,[54] which entails making of phosphorus compounds. These phosphorus compounds were then followed by Horner-Emmons reaction [55] but unfortunately, ^{13}C NMR revealed the corresponding phosphorous compound along with unidentified by-product. So, it would better to repeat this experiment in future.
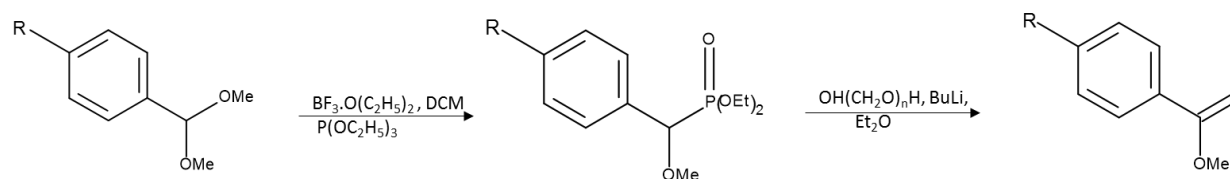
Scheme 14: Formation of vinyl ether by Horner-Emmons reaction [55]

Where, R=H, Me, MeO, Cl, NO_2

Another approach that could be employed in the future is described by P. G. Gassman *et al*. [56] which involves the conversion of both cyclic and acyclic acetals into enol ethers when the acetal is treated with trimethylsilyl triflate in the presence of *N,N*-diisopropylethylamine at a temperature range of -20°C to room temperature.

Table 2: Acetal (13) obtained by reacting ketone acetophenone (3) with different acids

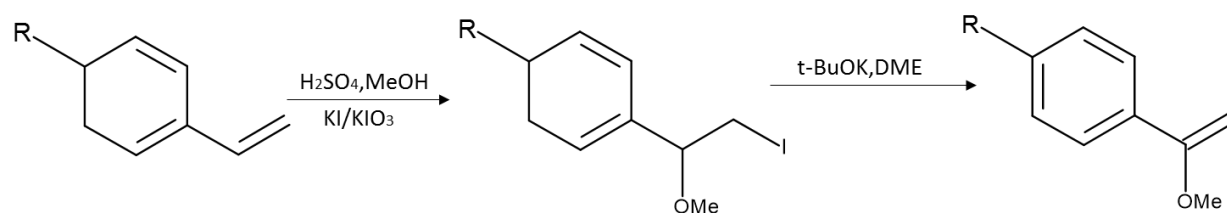| Acid	Isolated Yield (%)
PTSA	60
NH_4Cl	55
$ZnCl_2$	70
$NH_4H_2PO_4$	80

The formation of acetals were highly influenced by the substitution pattern in aromatic compounds. When the para position of aromatic compounds are comprised of electron donating

group (EDG), the corresponding acetals were formed in low in yields. In addition, the corresponding vinyl ether were not formed at all.

Another pathway to form vinyl ether is from styrene. The styrene was treated with potassium iodide/potassium iodate (KI/KIO_3) to synthesize iodo methyl ether. These iodo methyl ethers undergo elimination of iodide to give vinyl ethers when exposed to base, as reported by Agrawal *et al.*

Generally, styrene substituted compounds were treated with KI/KIO_3 reagent in presence of concentrated sulfuric acid (conc. H_2SO_4) to give the iodomethyl ether. These iodo methyl ethers were again treated with different bases in DME to give vinyl ethers but *t*-BuOK gave the best yield. If iodo methyl ethers were treated with $NaOCH_3$ it gives a substitution reaction instead of elimination [44].

Scheme 15: Synthesis of vinyl ethers involving vicinal functionalization of olefins

Where R = Me, t-BuO, and t-Bu

Table 3: Selection of bases for vinyl ether (19) formation from iodo methyl ether (58)

| Base	Isolated Yield (%)
DBU	70
CS_2CO_3	20
KHMDS	10
t-BuOK	75

Table 4: Formation of vinyl ether from styrene using t-BuOK

Iodo methyl ether	Vinyl Ether	Isolated Yield (%)
58	24	65
18	27	62
19	28	63
20	29	52

3.2. Synthesis of 2-alkoxy-1,1-dichlorocyclopropane

In this master thesis, 2 different methods were applied to synthesize 2-alkoxy-1,1-dichlorocyclopropane. The Doering Hoffmann method was used for low boiling point compounds like ethyl vinyl ether, methoxy propene and for low scale reactions. The Doering Hoffmann method is normally carried out at around -30℃ in dry atmosphere. However, guest researcher Josenne Mae. R. Sanchez discovered high yield formation of *gem*-dichlorocyclopropane from vinyl ether at -78℃. The reactions were run smoothly and clean but most of the reactions were carried out with Makosza's phase transfer reaction as this method is cheap, gives excellent yield, and does not require dry conditions.

This method includes the treatment of alkene with dichlorocarbene generated from $CHCl_3$ under PTC using TEBA as a catalyst which gave the excellent yields with almost all compounds within six hours. NMR spectra of the crude product indicated that it was essentially pure.
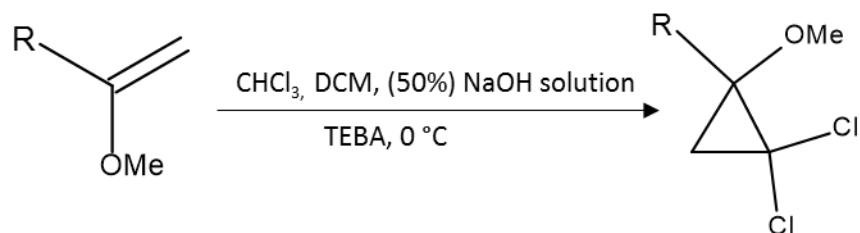
Scheme 16: Formation of 2-alkoxy-1,1-dichlorocyclopropane from Makosza's method

Table 5:2-Alkoxy-1,1-dichlorocyclopropanes obtained by reacting with dichlorocarbene with vinyl ethers using Makosza's method

Vinyl Ether	2-methoxy-1,1-dichlorocyclopropane	Isolated Yields (%)
24	35	98
30	42	77
2	34	79
25	36	92
26	37	90

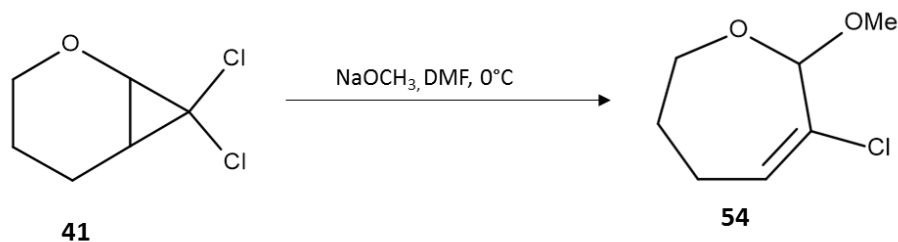### 3.3. Ring opening of 2-alkoxy-1,1-dicholorocyclopropane

Most of the 1,1-dichloro alkoxy (methoxy and ethoxy) substituted cyclopropanes underwent ring-opening to yield acetylenic acetals. The cyclopropanes were allowed to react with 4 eq. of sodium alkoxide in DMF at -10 ℃ for 3 hours and left to slowly return to room temperature.
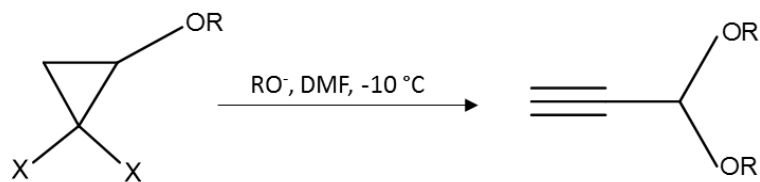
Scheme 17: Formation of acetylenic acetal at -10 ℃

Different solvents like dimethyl sulfoxide (DMSO), tetrahydrofuran (THF), and acetonitrile (MeCN) were explored, but they all seemed to be inferior to DMF. With THF and MeCN, the reaction results only in unreacted starting material whereas, with DMSO, 20% of the starting material seems to be consumed. So, the yields of the reactions depended to a large degree upon the solvent used. The reaction was also run with different amounts of sodium alkoxide (one experiment with NaOEt and rest of all with NaOMe) but 4 eq. was found to be the optimal amount to obtain a good yield of corresponding acetylenic acetals. NaOCH$_3$ was also replaced by many different non-nucleophilic bases; like 1-8-diazabicyclo[5.4.0]undec-7-ene (DBU), cesium carbonate (Cs$_2$CO$_3$), *t*-BuOK, and sodium hydride (NaH) but with all these bases the reaction turned into black viscous materials and it was not possible to identify any product with NMR.
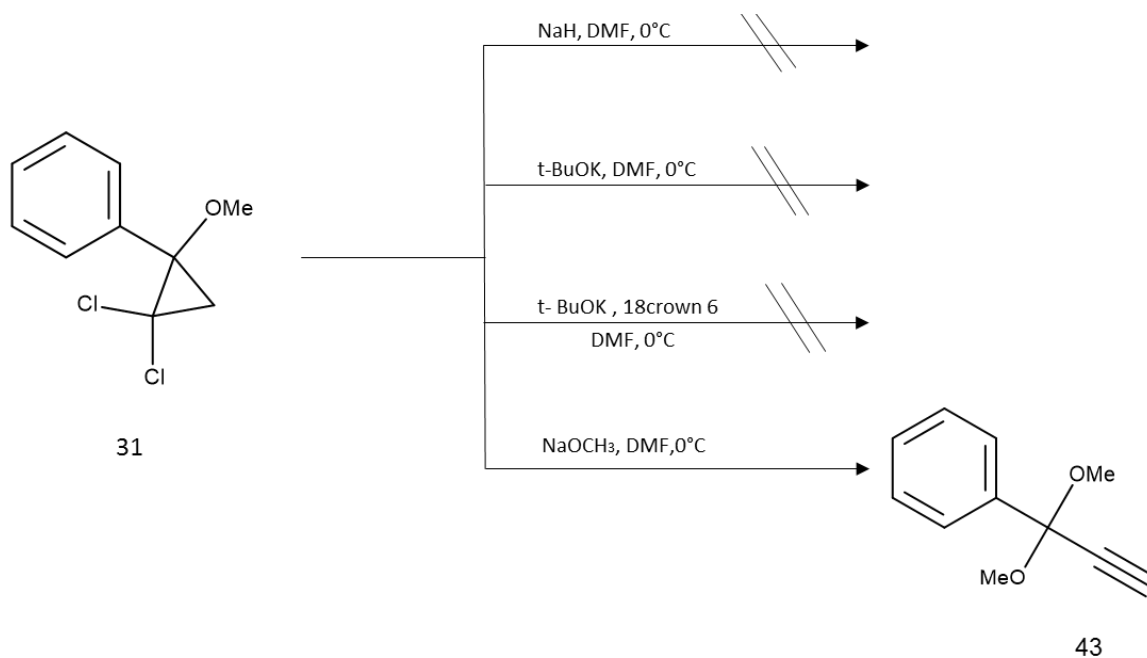
Scheme 18: Formation of acetylenic acetal using different bases

However, 1-methoxy-7,7-dichlorobicyclo[6.1.0]nonane **(42)**, 13,13-dichloro-1-methoxy-bicyclo[10.1.0]tridecane **(43)**, and 7,7-dichloro-2-oxabicyclo[4.1.0]heptane **(41)** showed quite different results, probably because of extreme ring strain, and resulted in the formation of olefinic acetals and ketones from electrocyclic ring-opening. When the 7,7-dichloro-2-oxabicyclo[4.1.0]heptane **(41)** was treated with 4 eq. of NaOCH₃ in DMF at 0°C.The ¹H NMR showed a singlet at 4.78 ppm and 6.13 ppm which strongly indicates the formation of olefinic acetal. Additional, when 1 -methoxy-cyclopentene was treated with a CHCl₃, NaOH, TEBA and DCM (Makosza's method) the ¹H NMR showed a doublet at 7.13 ppm which strongly indicates the formation of ring olefinic compound. So, from this above experiment, it can be concluded that 1–methoxy-2-cyclopropene **(32)**, and 7,7-dichloro-2-oxabicyclo[4.1.0]heptane **(41)** are too strained to undergo 'Bakstad ring opening' and underwent the electrocyclic ring-opening giving the olefinic compound. Also, when the reaction of 13,13-dichloro-1-methoxy-bicyclo[10.1.0] tridecane was carried out with 4 eq. of NaOCH₃ in 0 °C it showed only the formation of acetylenic acetal.


Scheme 19: Strained compound undergo electrocyclic ring opening

3.4. Mechanism for formation of acetylenic acetals and trapping of cyclopropenes

Acetylenic acetals were synthesized when 2-alkoxy-1,1-dichloroyclopropanes were treated with 4 eq. of NaOCH₃ in DMF. The reaction undergoes several steps following the dehydrohalogenation and substitution of halogen atoms by methoxy groups. It could be predicted that under a basic condition *gem*-dichlorocyclopropane gets deprotonated and results in cyclopropyl anion. The resulted cyclopropyl anions are highly unstable therefore they immediately rearranged to the corresponding cyclopropenes which are highly reactive in nature

and reacts quickly when they encounter methanol or methoxy groups to generate the corresponding acetylenic acetals as a final product. This experimental work is highly reinforced by the similar work done by Paul Muller and his co-workers in 1991 where they investigated the base-induced hydrochloro-elimination of several 2-alkoxy-1,1-dichlorocyclopropanes and trapped the suggested cyclopropene intermediates by nucleophiles or isobenzofurans[3]. In absence of such a trapping agent, the cyclopropenes might rearrange to vinyl carbenes and yield cyclopropane adducts with alkenes [32]. The trapping of these vinyl carbenes has already been attempted by Yvette Luijkx under Bakstad's guidance[7] in which some traces of cyclopropane adduct was synthesized by ring-opening of a cyclopropene to its corresponding vinylcarbene and later on intercepted by electron rich double bonds of cyclopentene.
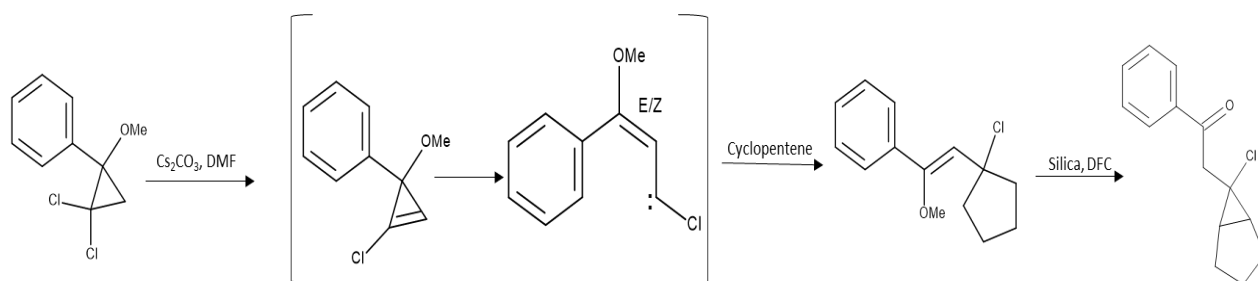
Scheme 20: Hypothesis mechanism for acetylenic acetal formation and theoretical interception of intermediate by cyclopentene. Illustration is taken from a master thesis of Yvette Luijkx, a former student of Bakstad research group [7]

In this master thesis, trapping experiments were carried out with ethyl vinyl ether which is an electron rich, and suitable trapping reagent to catch vinyl carbene. Thus, 2-alkoxy 1,1-dichlorocyclopropane was allowed to react with potassium bis(trimethylsilyl)amide (KHMDS) and t-BuOK as non- nucleophilic bases in DMF with 18-crown-6 and ethyl vinyl ether as a trapping agent under reflux. However, no identified product was obtained, but when the reaction was carried out with NaH as the base in DMF with ethyl vinyl ether at 90 °C temperature, TLC showed consumption of starting material. The reaction was quenched with water and the product was extract with an organic solvent. NMR results indicated the formation of aldehyde with a diagnostic peak at 9.8 ppm in the hydrogen spectrum, and some starting material with several

other unknown side products. However, no cyclopropane adduct could be identified. In the future, this experiment need to be repeated with reduced amounts of methoxide.
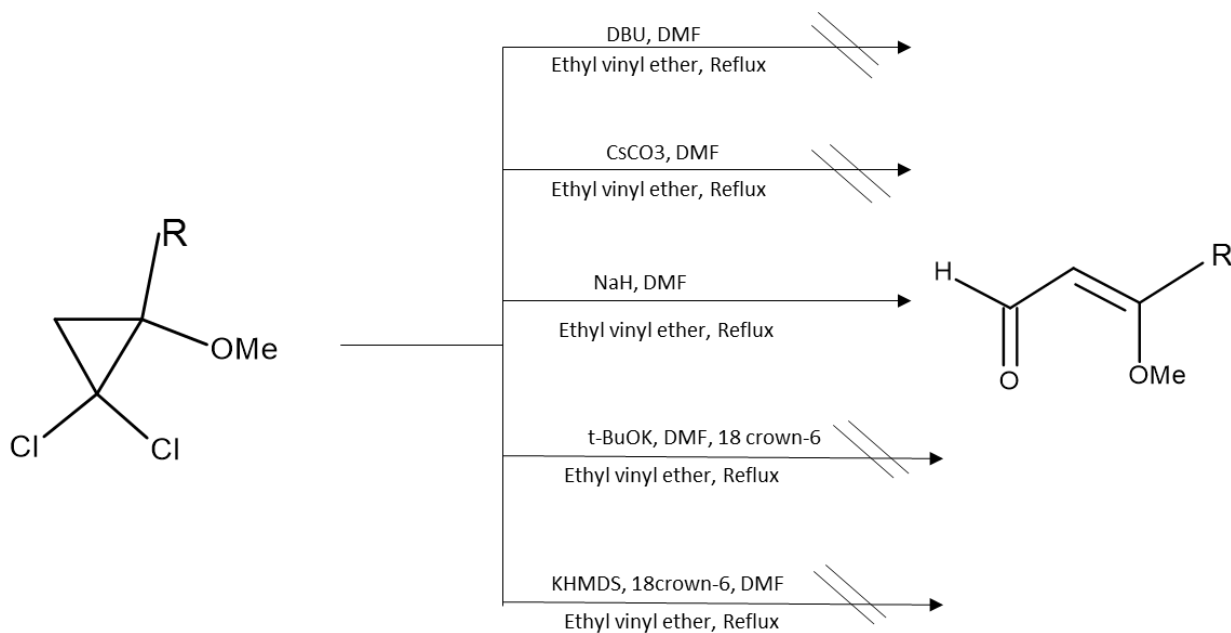
Scheme 21: Formation of aldehyde

4. CONCLUDING REMARKS

Para-substituted 2-alkoxy-1,1-dihalocyclopropanes were synthesized in high yields by using a corresponding vinyl ether. Two different methods were used to get the vinyl ethers. First method involves, an acid-catalyzed thermolysis to obtain the desired vinyl ether from ketones through their corresponding acetals, and second method includes the vicinal functionalization of the corresponding olefinic compound and elimination of iodide group by a non-nucleophilic base to the vinyl ether, followed by formation of cyclopropane under Makosza's methods and Doering Hoffmann methods.

The resulted 1,1-dichlorocyclopropanes were allowed to react with 4 equivalents of sodium alkoxide(MeO/EtO) in DMF at -10˚C for acyclic compounds and at 0˚C for cyclic compounds for optimum synthesis of acetylenic acetals. Acetylenic acetals might have significant contribution to organic synthesis, as mentioned by prof. Corey in the total synthesis of sesquiterpene *d,l,*-caryophyllene.

All the 1,1-dichlorocyclopropanes were successfully transformed into their corresponding acetylenic acetals under suitable reaction conditions but when the cycloalkanone (five and six membered ring-compounds) were used instead of acyclic ketone the results seem to be influenced because of ring strain. This analysis showed that they might have followed the electrocyclic ring-opening, assisted by the departure of one of the halides. In this experiment it is also noticed that, the para-substitution pattern of the phenyl group with EDG influenced the outcome of the formation of the corresponding acetals. For example, para-fluoroacetophenone gave high yields of dimethoxy acetal and corresponding vinyl ether whereas para-hydroxyacetophenone gave poor yields of dimethoxy acetal with no corresponding vinyl ether.

Furthermore, trapping experiments were also attempted to investigate the mechanism of the ring-opening of 1,1-dichlorocyclopropanes to acetylenic acetals when subjected to sodium alkoxide. It was expected that the mechanism involved the formation of cyclopropene by hydrochloro-elimination which might undergo to the vinyl carbene and the result vinyl carbene forms cyclopropane adducts with alkenes in presence of trapping agents [3]. Thus, several experiments were carried out to trap the vinyl ether, but unfortunately they failed. These experiments should be repeated in future.

5. EXPERIMENTAL

5.1 General

Nuclear magnetic resonance 400 MHz ^{1}H NMR spectra and 100 MHz ^{13}C NMR spectra were recorded on Bruker Advance series 400 MHz AvIII HD 400 MHz spectrometer. Chemical shift of ^{1}H NMR spectra were reported in relative to tetramethylsilane (TMS) (δ=0.00 ppm) or dimethyl sulfoxide-d_6 (DMSO-d_6) (δ 2.50 ppm). ^{13}C NMR spectra are referenced in ppm to deuterochloroform (77.0 ppm), (DMSO-d_6) (δ 39.51 ppm).

Dry flash chromatography (DFC) was carried out with silica gel (Fluka: silica gel 60, particle size 0.040-0.063mm (230-400 mesh)). Vacuum was created by a water aspirator.

Thin layer chromatography (TLC) was carried out using silica gel plates from Fluka (silica gel/dc-alufolien-kieselgel with fluorescent indicator, production number 60778). The spots were detected with UV (extinction at δ=254 or fluorescent at δ=366nm) in a UVP-UV-cabinet and /or by staining with MOP (molybdate phosphoric acid (14g) in ethanol (12mL) and CER-MOP (molybdate phosphoric acid (5.00 g), cerium(IV)sulfate (2.00 g) and 98% sulfuric acid (16 mL) in water (180 mL) and developed by heating with a heat gun until spots appeared.

Thin layer chromatography was generally used to monitor reactions. Workup was normally carried out when TLC indicated that all the starting material has been consumed or that only traces remained.

Melting points were determined on a Stuart Scientific SMP3 melting point apparatus and were uncorrected. Infrared (IR) spectroscopy was performed on a Varian 1000 FT-IR spectrophotometer.

A nitrogen atmosphere was used in reactions that required dry conditions.

Commercially available chemicals were purchased from Fluka, Sigma-Aldrich, Acros, Merk, Lancaster, and Chiron. Standard purification was applied if necessary. Dry dichloromethane, ethyl acetate, and acetone were purchased from Fluka and Sigma-Aldrich.
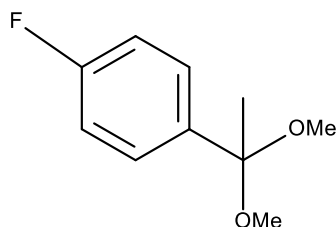
5.2 Synthesis of acetals

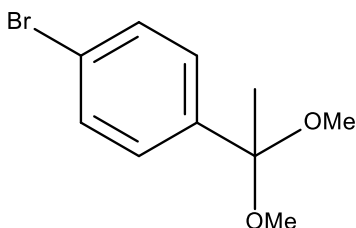**5.2.1 Synthesis of (1,1-dimethoxyethyl)benzene (15);** Acetophenone (3) (60.10 g, 0.50 mol), trimethylorthoformate (53.06 g, 0.50 mol), MeOH (16.00 g, 0.50 mol) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a brown liquid. The residue was distilled by vacuum distillation to give a colorless liquid. B.P. = 72-75 °C/15 mmHg (Lit. 68-69 °C/ 6 mmHg) [24], Yield: 78.94 g (95%), R_f = 0.60 (20% MeOAc in heptanes). IR (neat): υ 2981, 2521, 1202, 1080, 1041, 850 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.51-7.27 (m, 5H), 3.19 (s, 6H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 142.9, 128.1, 127.5, 126.2, 101.7, 49.0, 26.1.[23]
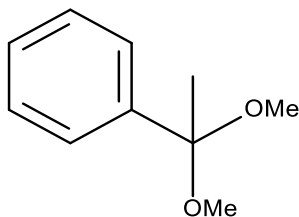
5.2.2 Synthesis of 4-fluoro(1,1-dimethoxyethyl)benzene (16); 4-Fluoroacetophenone (4) (34.53 g, 0.25 mol), trimethylorthoformate (26.53 g, 0.25 mol), MeOH (8.01 g, 0.25 mol) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give colorless liquid. B.P = 94 °C/ 23mmHg, Yield: 41.44 g (90%), R_f = 0.73 (20% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.41-6.93 (m, 4H), 3.10 (s, 6H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 162.2 (d, J_{CF} = 245.7 Hz), 138.7 (d, J_{CF} = 2.9 Hz), 131.0 (d, J_{CF} = 9.5 Hz), 128.1 (d, J_{CF} = 8.8 Hz), 114.8 (d, J_{CF} = 8.8 Hz), 101.4, 49.0, 26.1.

5.2.2 Synthesis of 4-bromo(1,1-dimethoxyethyl)benzene (17); 4-Bromoacetophenone (5) (49.76 g, 0.25mol), trimethylorthoformate (26.53 g, 0.25 mol), MeOH (8.01 g, 0.25 mol) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was
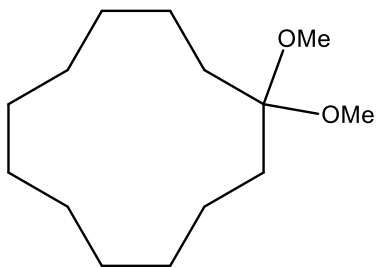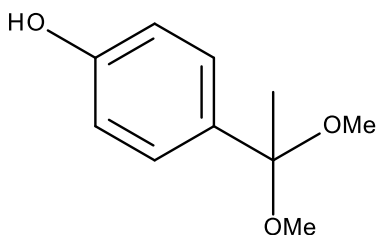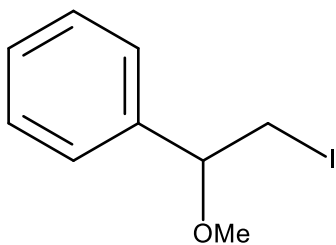
removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give colorless liquid. B.P = 132 °C/ 20-19 mmHg. (Lit. N.A). Yield: 58.21 g (95%), R_f = 0.50 (5% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.31 (d, J = 8.7 Hz, 2H), 7.22 (d, J = 8.7 Hz, 2H) 3.00 (s, 6H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 141.8, 131.0, 128.0, 121.4, 101.0, 48.6, 25.7. [53]

5.2.3 Synthesis of (1,1-dimethoxy)cyclooctane (21); Cyclooctanone **(12)** (31.65 g, 0.25 mol), trimethylorthoformate (26.53 g, 0.25 mol), MeOH (8.01 g, 0.25 mol) and concentrated HCl in catalytic amount were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give a colorless liquid. B.P. = 84-85 °C/ 20mbar, (Lit. B.P. = 85-89 °C/ 36mbar) [48], R_f = 0.69 (10% MeOAc in heptane), Yield: 32.29 g (75%). ^{1}H NMR (400 MHz, CDCl$_3$): δ1.55 (s, 10H), 1.76 (s, 4H), 3.14 (s, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 21.3, 24.6, 28.2, 30.3, 47.7, 103.8. [48]
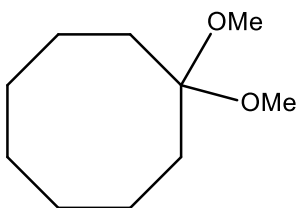
**5.2.4 Synthesis of (1,1-dimethoxy)cyclododecane (22);** Cyclododecanone **(13)** (18.00 g, 0.10 mol), trimethylorthoformate (10.61 g, 0.10 mol), MeOH (3.20g, 0.10 mol) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give a colorless oil. B.P. = 144-147 °C/ 12mbar, Yield: 16.43 g (72%), R_f = 0.83 (30%MeOAc in heptane). IR: υ 2927, 2902, 2849, 2862, 2827, 2675, 1742, 1655, 1467, 1444, 1349, 1320, 1257, 1283, 1237, 1218, 1174, 1115, 1060, 1080, 1045, 979, 961, 856, 800 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.08 (s, 6H), 1.67 (m, 18H); ^{13}C NMR (100 MHz, CDCl3): δ 104.3, 47.5, 29.9, 26.6, 22.8, 22.3, 19.8.[49]

5.2.5 Synthesis of 4-hydroxy(1,1-dimethoxyethyl)benzene (57);

4-Hydroxyacetophenone (10) (13.10 g, 0.10 mol), trimethylorthoformate (30.00 g, 0.28 mol), MeOH (40.00 g, 1.20 mol) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give a dark red liquid. Yield: 7.65 g (42%), R_f = 0.33 (10% MeOAc in heptane). IR: υ 2989, 2942, 2831, 2083, 1901, 1655, 1612, 1596, 1512, 1434, 1370, 1300, 1265, 1223, 1196, 1168, 1114, 1090, 1025, 961, 862, 873, 834, 732 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.55-7.51 (m, 2H), 6.99-6.94 (m, 2H), 3.25 (s, 6H), 1.70 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 155.1, 131.0, 127.7, 114.8, 101, 48.9, 26.0.

5.2.6 Synthesis of (1,1dimethoxy)cyclopentane (23);

Cyclopentaone (14) (42.06 g, 0.50 mol), trimethylorthoformate (53.06 g, 0.50 mol), MeOH (50 mL) and concentrated HCl (catalytic amount) were stirred under reflux overnight. After cooling, the mixture was neutralized with potassium carbonate. MeOH was removed under reduced pressure to give a liquid. The residue was distilled by vacuum distillation to give a colorless liquid. B.P. = 137 °C (Lit. 138-140 °C) [48], Yield: 45.56 g (70%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.2 (s, 6 H), 2.14-2.09 (m, 2H), 1.96-1.88 (m, 2H), 1.76-1.69 (m, 2H), 1.57-1.63 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 112.2, 34.2, 23.3, 23.3, 34.2, 49.2.[52]
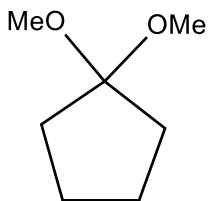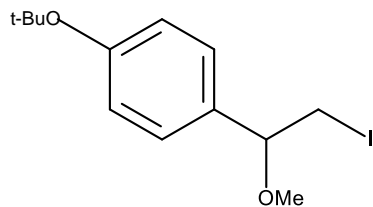
5.3 Synthesis of iodo methyl ethers

5.3.1 Synthesis of (2-iodo-1-methoxyethyl)benzene (58);
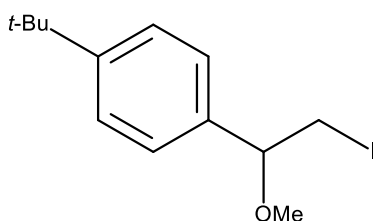
Styrene (61) (10.40 g, 0.10 mol) and MeOH (50 mL) were kept in suitable round bottom flask in an ice bath. To the above solution concentrated H$_2$SO$_4$ (98%) (9.80 g, 0.10 mol) was added dropwise, followed by the addition of 1.1 eq of the solid KI/KIO$_3$ (12.28 g/7.704 g) in portions over a period of

30 min under vigorous stirring. The reaction was monitored by TLC. Stirring was continued for an additional 35 minutes (min.) under the same condition. 10% $NaHCO_3$ was added to neutralize the solution and 5% $Na_2S_2O_3$ was also added to remove color. The product was extracted with diethyl ether (4x50 mL), washed with H_2O (4x20 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure. Yield: 23.06 g (88%), R_f = 0.41 (20% MeOAc in heptane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.29 (m, 5H), 4.29 (dd, J = 4.9, 7.8 Hz, 1H), 3.38-3.32 (m, 2H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 128.7, 128.4, 126.5, 83.6, 57.3, 10.5[12].

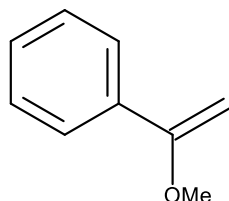### 5.3.2 Synthesis of (2-iodo-1-methoxyethyl)-4-methyl benzene (18);
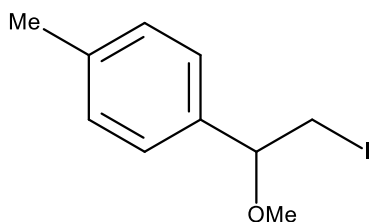
4-Methyl styrene (7) (11.81 g, 0.10mol) and MeOH (70 mL) were kept in suitable round bottom flask in an ice bath. To the above solution concentrated H_2SO_4 (98%) (9.80 g, 0.10mol) was added dropwise, followed by the addition of 1.1 eq of the solid KI/KIO_3 (12.28 g/7.704 g) in portions over a period of 30 min under vigorous stirring. The reaction was monitored by TLC. Stirring was continued for an additional 35 min under the same condition. 10% $NaHCO_3$ was added to neutralize the solution and 5% $Na_2S_2O_3$ was also added to remove color. The product was extracted with diethyl ether (4x50 mL), washed with H_2O (4x20 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure. Yield: 23.46 g (85%), R_f = 0. 42 (20% MeOAc in heptane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.17 (m, 4H), 4.26 (dd, J = 4.7, 8.1 Hz, 1H), 3.37-3.31 (m, 2H), 3.29 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 136.7, 129.4, 126.5, 83.4, 57.2, 21.2, 10.7 [12].

5.3.3 Synthesis of 1-(*t*-BuO)-4-(2-iodo-1-methoxyethyl)benzene (20);

4-*tert*-Butoxy styrene (9) (12.33 g, 0.07 mol) and MeOH (70 mL) were kept in suitable round bottom flask in an ice bath. To the above solution concentrated H_2SO_4 (98%) (6.86 g, 0.07 mol) was added dropwise, followed by the addition of 1.1 eq of the solid KI/KIO_3 (6.14 g/3.85 g) in portions over a period of 30 min under vigorous stirring. The reaction was monitored by TLC. Stirring was continued for an additional

35 min under the same condition. 10% NaHCO$_3$ was added to neutralize the solution and 5% Na$_2$S$_2$O$_3$ was also added to remove color. The product was extracted with diethyl ether (4x50 mL), washed with H$_2$O (4x20 mL) and dried (Na$_2$SO$_4$). The solvent was removed under reduced pressure. Yield: 15.46 g (80%), R$_f$ = 0.45 (20% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.21-6.97 (m, 4H), 4.27 (dd, *J* = 4.5, 8.2 Hz, 1H), 3.37-3.22 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 155.6, 134.4, 127.1, 124.1, 83.3, 78.6, 57.2, 28.9, 10.7.

5.3.4 Synthesis of 1-(*t*-Bu)-4-(2-iodo-1-methoxyethyl)benzene (19);

4-*tert*-Butyl styrene (8) (11.21 g, 0.07 mol) and MeOH (70 mL) were kept in suitable round bottom flask in an ice bath. To the above solution concentrated H$_2$SO$_4$ (98%) (6.86 g, 0.07 mol) was added dropwise, followed by the addition of 1.1 eq. of the solid KI/KIO$_3$ (6.14 g/3.85 g) in portions over a period of 30 min under vigorous stirring. The reaction was monitored by TLC. Stirring was continued for an additional 35 min under the same condition. 10% NaHCO$_3$ was added to neutralize the solution and 5% Na$_2$S$_2$O$_3$ was also added to remove color. The product was extracted with diethyl ether (4x50 mL), washed with H$_2$O (4x20 mL) and dried (Na$_2$SO$_4$). The solvent was removed under reduced pressure. Yield: 18.93 g (85%), R$_f$ = 0.76 (30% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.40-7.22 (m, 4H), 4.28 (dd, *J* = 4.8, 8.0 Hz, 1H), 3.34-3.32 (m, 2H), 3.30 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 151.4, 136.7, 126.6, 126.2, 83.4, 57.3, 34.6, 31.3, 10.7.

5.4 Synthesis of vinyl ether

5.4.1 Synthesis of (1-methoxyvinyl)benzene (24);

Ammonium dihydrogenphosphate (5.00 g, 0.043 mol) was added to a stirred solution of (1,1-dimethoxyethyl)benzene (15) (49.80 g, 0.30 mol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using a vacuum to give a colorless liquid. Yield:

39.04 g (97%), B.P = 82-83 °C/19-20mmHg (Lit. 89-90 °C/ 20mmHg) [24], R_f = 0.63 (10% MeOAc in heptane). IR: υ 2944, 1600, 1388, 1366, 1201, 1079, 1021, 849 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.63-7.24 (m, 5H), 4.65 (d, J = 2.8 Hz, 1H), 4.21 (d, J = 2.8 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.8, 136.4, 133.1, 128.4, 128.1, 125.3, 81.7, 55.2.[25]

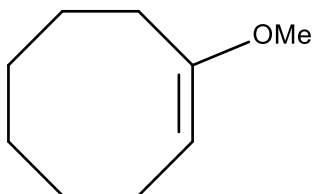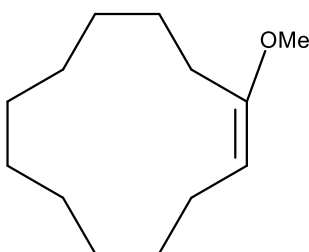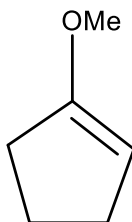### 5.4.2 Synthesis of 4-fluoro(1-methoxyvinyl)benzene (25);
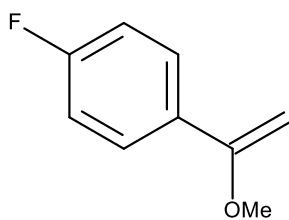
Ammonium dihydrogenphosphate (1.15 g, 10.00 mmol) was added to a stirred solution of 4-fluoro(1,1-dimethoxyethyl)benzene **(16)** (9.21 g, 50.00 mmol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using a vacuum to give a colorless liquid. Yield: 6.61 g (87%), R_f = 0.65 (20% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.51-7.49 (m, 2H), 7.13-7.11 (m, 2H), 4.60 (d, J = 2.7 Hz, 1H), 4.16 (d, J = 2.9Hz, 1H), 3.17 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 162.2 (d, J_{CF} = 245.7 Hz), 138.7 (d, J_{CF} = 2.9 Hz), 131.0 (d, J_{CF} = 9.5 Hz), 128.1 (d, J_{CF} = 8.8 Hz), 114.8 (d, J_{CF} = 8.8 Hz), 80.9, 55.1, 26.9.

5.4.3 Synthesis of 4-bromo(1-methoxyvinyl)benzene (26);
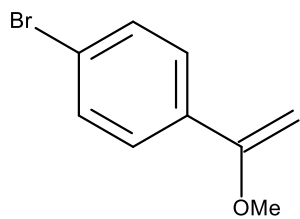
Ammonium dihydrogenphosphate (5.90 g, 51.42 mmol) was added to a stirred solution of 4-bromo(1,1-dimethoxyethyl)benzene **(17)** (24.51 g, 0.10 mol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using a vacuum to give a colorless liquid. Yield: 18.75 g (88%), R_f = 0.62 (5% MeOAc in heptane), B.P. = 104 °C/27 torr. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.49-7.47 (m, 2H), 7.38-7.36 (m, 2H), 4.65 (d, J = 2.9 Hz, 1H), 4.23 (d, J =2.9 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 131.9, 131.2, 128.1, 126.9, 82.1, 55.3, 25.9
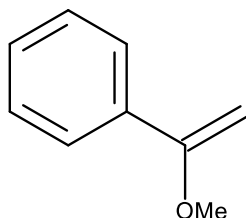
5.4.4 Synthesis of (1-methoxy)cyclooctene (30); Ammonium dihydrogenphosphate (1.50 g, 0.01 mol) was added to a stirred solution of (1,1-dimethoxy)cyclooctane **(21)** (17.22 g, 0.10 mol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using vacuum to give colorless liquid. B.P. = 69-70 °C/19mbar. (Lit. 78-79 °C/15mmHg) [46]. Yield: 11.07 g (79%), R_f = 0.876 (10% MeOAc in heptane). IR: υ 2929, 2853, 1662, 1201, 1159, 1095 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.63-7.24 (m, 5H), 4.65 (d, J = 2.8 Hz, 1H), 4.21 (d, J = 2.8 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.8, 136.4, 133.1, 128.4, 128.1, 125.3, 81.7, 55.2.[46]

5.4.5 Synthesis of (1-methoxy)cyclododecene (31); Ammonium dihydrogenphosphate (0.76 g, 6.60 mmol) was added to a stirred solution of (1,1-dimethoxy)cyclododecane **(22)** (11.41g, 0.05 mol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using a vacuum to give a colorless oil. B.P. = 131-132 °C/19mmHg, Yield: 7.85g (80%), R_f = 0.674 (5% MeOAc in heptane). IR (neat): υ 2927, 2902, 2849, 2862, 2827, 1741, 1655, 1467, 1444, 1349, 1257, 1283, 1237, 1218, 1174, 1115, 1080, 1060, 1045, 979, 961, 856 800, 743 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 4.55 (t, J = 7.3 Hz, 1H), 2.06-1.99 (m, 4H), 1.47-1.43 (m, 4H), 1.34-1.31 (m, 12H) [50]; ^{13}C NMR (100 MHz, CDCl$_3$): δ 154.0, 112.8, 56.24, 40.3, 30.4, 26.8, 26.5, 26.3, 25.3, 25.2, 25.13, 25.06, 24.0.

5.4.6 Synthesis of 1-methoxy-2-cyclopentene (32); Ammonium dihydrogenphosphate (4.60 g, 0.04 mmol) was added to a stirred solution of (1-1dimethoxy)cyclopentane **(23)** (39.05 g, 0.30 mol) in the Claisen distillation equipment. It was heated with an oil bath to remove the MeOH at 65 °C and again the residue was distilled using a vacuum to give a colorless oil. B.P. = 110-114 °C, Yield: 23.55 g (80%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 4.41 (s, 1H), 3.54 (s, 3H),

1.93-1.84 (m, 2H), 1.85-1.78 (m, 2H), 1.70-1.69 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 161.1, 92.3, 28.6, 21.1, 31.4, 55.6.[52]
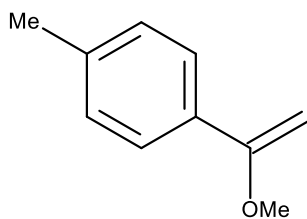
5.5 Synthesis of vinyl ether (Method B)
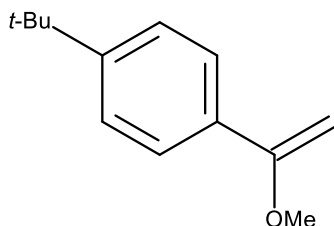
5.5.1 Synthesis of (1-methoxyvinyl)benzene (24); *t*-BuOK (10.09 g, 0.09 mol) was added
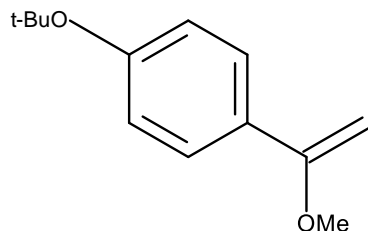
slowly to the cold solution of (2-iodo-1-methoxyethyl)benzene (58) (18.00 g, 0.06 mol) in DME (250 mL). The mixture was stirred at room temperature and after all the starting material were consumed, the reaction mixture was quenched with H$_2$O and extracted with diethyl ether (4x20mL). The organic layer was washed with water (5x15mL) and dried (Na$_2$SO$_4$) concentrated under the reduced pressure to give the vinyl ether which is slightly yellow liquid. Yield = 5.23 g (65%), R$_f$ = 0.63 (10% MeOAc in heptane). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.63-7.28 (m, 5H), 4.65 (d, *J* = 2.8 Hz, 1H), 4.21 (d, *J* = 2.8 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 160.8, 136.5, 133.1, 128.4, 128.1, 125.3, 81.7, 55.3. [35][36]

5.5.2 Synthesis of 4-methyl(1-methoxyvinyl) benzene (27); *t*-BuOK (13.44 g, 0.12 mol) was

added slowly to the cold solution of (2-iodo-1-methoxyethyl)-4-methyl benzene (18) (22.08 g, 0.08 mol) in DME (250 mL). The mixture was stirred at room temperature and after all the starting material were consumed, the reaction mixture was quenched with H$_2$O and extracted with diethyl ether (4x20 mL). The organic layer was washed with water (5x15 mL) and dried (Na$_2$SO$_4$) concentrated under the reduced pressure to give the vinyl ether which is slightly yellow liquid. Yield: 7.35 g (62%). R$_f$ = 0.54 (20% MeOAc in heptane). B.P. = 94 °C/10mbar (Lit. 94 °C/10 torr)[59]. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.52-7.11 (m, 4H), 4.61 (d, *J* = 2.7 Hz, 1H), 4.16 (d, *J* =2.7 Hz, 1H), 3.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.9, 138.3, 133.7, 128.9, 125.2, 125.2, 81.7, 55.2, 21.2. [37]
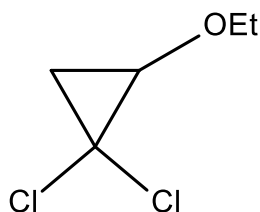
5.5.3 Synthesis of 4-*t*-BuO(1-methoxyvinyl)benzene (28); *t*-BuOK (8.41 g, 0.075 mol) was

added slowly to the cold solution of 1-(*tert*-butoxy)-4-(2-iodo-1-methoxyethyl)benzene **(19)** (16.71 g, 0.05 mol) in DME (250 mL).The mixture was stirred at room temperature and after all the starting material were consumed, the reaction mixture was quenched with H_2O and extracted with diethyl ether (4x20 mL). The organic layer was washed with water (5x15 mL) and dried (Na_2SO_4) concentrated under the reduced pressure to give the vinyl ether which is slightly yellow liquid. Yield: 4.94 g (52%), R_f = 0.52 (20% MeOAc in heptane). ^1H NMR (400 MHz, CDCl$_3$): δ 7.53-6.94 (m, 4H), 4.58 (d, *J* = 2.8 Hz, 1H), 4.16 (d, *J* = 2.8 Hz, s1H), 3.73 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.6, 155.7, 131.6, 126.0, 123.7, 80.9,78.7, 55.2, 28.9.

5.5.4 Synthesis of 4-*t*-Bu(1-methoxyvinyl)benzene (29); *t*-BuOK (5.04 g, 0.04 mol) was added

slowly to the solution of 1-(*tert*-butyl)-4-(2-iodo-1-methoxyethyl)benzene **(20)** (9.54 g, 0.03 mol) in DME (200 mL). The mixture was stirred at room temperature and after all the starting material were consumed, the reaction mixture was quenched with H_2O and extracted with diethyl ether (4x20 mL). The organic layer was washed with water (5x15 mL) and dried (Na_2SO_4) concentrated under the reduced pressure to give the vinyl ether which is slightly yellow liquid. Yield: 2.53 g (63%), R_f = 0.51 (30% MeOAc in heptane). ^1H NMR (400 MHz, CDCl$_3$): δ 7.55-7.34 (m, 4H), 4.61 (d, *J* = 2.7 Hz, 1H), 4.17 (d, *J* =2.7 Hz, 1H), 3.73 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 160.9, 151.5, 133.7, 125.1, 125.0, 81.1, 55.2, 34.6, 31.3.[38]

5.6 Synthesis of 2-alkoxy-1,1,-dichlorocyclopropanes

5.6.1 Synthesis of 1, 1-dichloro-2-ethoxycyclopropane (33); 50% aqueous solution of NaOH

(60 g, 1.5 mol) was added slowly to the stirred solution of ethyl vinyl ether (1) (54.06 g, 0.75 mol), DCM (150 mL), CHCl₃ (238.74 g, 2.00 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na₂SO₄). The solvent was removed by distillation to give a colorless liquid. Yield: 93.02 g (80%). B.P. = 38-40 °C/15mmHg (55 °C/30mmHg) [47]. IR(neat): υ 2933, 1399, 1374, 1345, 1179, 1115, 1066, 1021 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 3.86-3.52 (m, 2H), 3.54 (q, *J* = 5.0 Hz, 1H), 1.66 (m, 1H), 1.54 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 67.3, 63.1, 58.6, 28.0, 14.9. [10]

5.6.2 Synthesis of (1,1-dichloro-2-methoxycyclopropane)benzene (35); 50% aqueous solution
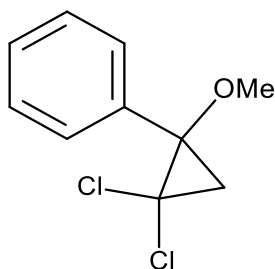
of NaOH (47.00 g, 1.20 mol) was added slowly to the stirred solution of (1-methoxyvinyl)benzene (53.67 g, 0.4 mol) (24) DCM (300 mL), CHCl₃ (190.40 g, 1.60 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na₂SO₄). The solvent was removed under the vacuum distillation to give white crystals. Yield: 85.09 g (98%), R_f = 0.24 (10% MeOAc in heptane), M.P. = 67-68 °C. (Lit. M.P. = 67-68 °C) [3]. IR (neat): υ 2998, 2830, 2279, 1967, 1740, 1492, 1447, 1326, 1233, 1106, 1069, 1006, 935, 850, 778 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.49-7.30 (m, 5H), 3.18 (s, 3H), 1.99 (d, *J* = 8.5 Hz, 1H), 1.78 (d, *J* = 8.5 Hz, 1H); ¹³C NMR (100

MHz, CDCl$_3$): δ 133.9, 129.3, 128.9, 128.4, 70.5, 64.1, 55.4, 30.1. The spectroscopic data were in accordance with the literature. [3][7][10]

5.6.3 Synthesis of 4-fluoro(1,1-dichloro-2-methoxycyclopropane)benzene (36); 50% aqueous
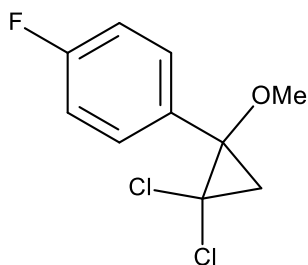
solution of NaOH (11.99 g, 0.30 mol) was added slowly to the stirred solution of 4-fluoro(1-methoxyvinyl)benzene (25) (15.21 g, 0.10 mol), DCM (75 mL), CHCl$_3$ (47.75g, 0.40 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give colorless solid. M.P. = 77-78 °C, R$_f$ = 0.2 (10% MeOAc in heptane), Yield: 21.62 g (92%). IR (neat): υ 3084, 3001, 2971, 2941, 2835, 2268, 2101, 1900, 1685, 1667, 1599, 1512, 1451, 1362, 1331, 1298, 1265, 1226, 1155, 1093, 1074, 1053, 1003, 945, 867, 839, 776 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.46-7.40 (m, 2H), 7.13-7.08 (m, 2H), 3.25 (s, 3H), 3.08 (s, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 162.9 (d, J_{CF} = 248.6 Hz), 138.7 (d, J_{CF} = 2.9 Hz), 131.0 (d, J_{CF} = 9.5 Hz), 129.8 (d, J_{CF} = 3.6 Hz), 115.4 (d, J_{CF} = 21.2 Hz), 69.8, 63.8, 55.2, 30.2.

5.6.3 Synthesis of 4-bromo (1,1-dichloro-2-meyhoxycyclopropane)benzene (37); 50%
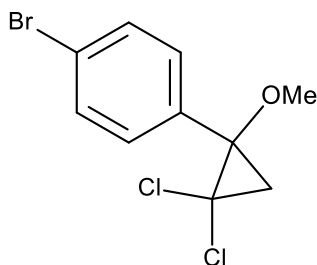
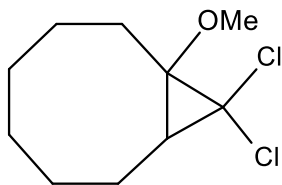aqueous solution of NaOH (7.20 g, 0.18 mol) was added slowly to the stirred solution of 4-bromo(1-methoxyvinyl)benzene (26) (13.00 g, 0.06 mol), DCM (100 mL), CHCl$_3$ (28.00 g, 0.24 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under

the vacuum distillation to give crystal. R_f = 0.46 (5% MeOAc in heptane), M.P. = 49-50 °C, Yield: 15.98 g (90%). IR (neat): υ 3001, 2934, 2902, 2828, 2288, 2080, 1905, 1685, 1587, 1436, 1458, 1419, 1395, 1355, 1320, 1264, 1232, 1176, 1156, 1100, 1066, 999, 976, 956, 931, 853, 825, 770 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.48-7.45 (m, 2H), 7.25-7.22 (m, 2H), 3.25 (s, 3H), 2.03 (d, *J* = 8.6 Hz, 1H), 1.86 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 133.0, 131.5, 130.7, 123.0, 69.9, 63.6, 55.3, 29.9.

5.6.4 Synthesis of 4-methyl(1,1-dichloro-2-methoxycyclopropane)benzene (38); 50%
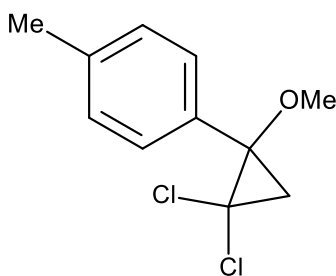
aqueous solution of NaOH (12.00 g, 0.30 mol) was added slowly to the stirred solution of 4-Methyl(1-methoxyvinyl)benzene **(27)** (14.82 g, 0.10 mol), DCM (100 mL), CHCl$_3$ (47.80 g, 0.40 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give solid. M.P. = 56-57 °C, Yield: 18.48 g (80%), R_f = 0.33 (20% MeOAc in heptane). IR (neat): υ 3089, 3009, 2954, 2932, 2828, 2105, 1911, 1611, 1514, 1447, 1425, 1326, 1230, 1181, 1151, 1102, 1073, 1055, 1005, 923, 862, 818, 772 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.34-7.32 (m, 2H), 7.25-7.21 (m, 2H), 3.25 (s, 3H), 2.38 (s, 3H), 2.02 (d, *J* = 8.4 Hz, 1H), 1.83 (d, *J* = 8.4Hz); ^{13}C NMR (100 MHz, CDCl$_3$): δ 138.8, 130.9, 129.2, 129.1, 70.3, 64.1, 55.2, 30.1, 21.3.
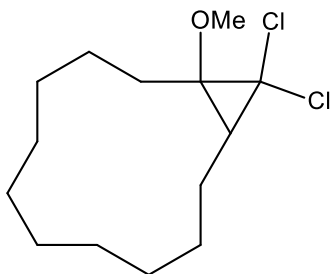
### 5.6.5 Synthesis of 4-*t*-BuO(1,1-dichloro-2-methoxycyclopropane)benzene (40); 50% aqueous
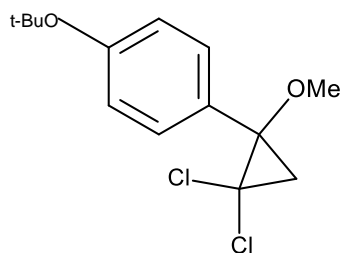
solution of NaOH (6.00 g, 0.15 mol) was added slowly to the stirred solution of 4-*t*-BuO(1-methoxyvinyl)benzene **(29)** (10.31 g, 0.05 mol), DCM (100 mL), CHCl$_3$ (23.87 g, 0.20 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by

mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give brown color. M.P. = 51-53 °C, Yield: 9.47 g (82%), R$_f$ = 0.17 (20% MeOAc in heptane). IR (neat): υ 3195, 2979, 2935, 2826, 2397, 1914, 1601, 1575, 1504, 1453, 1364, 1388, 1320, 1233, 1155, 1093, 1066, 1041, 996cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.34-6.99 (m, 4H), 3.25 (s, 3H), 2.00 (d, *J* = 8.3 Hz), 1.82 (d, *J* = 8.4 Hz), 1.37 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 156.0, 130.0, 128.3, 123.4, 78.8, 70.2, 64.1, 55.2, 30.3, 28.9.

5.6.6 Synthesis of 4-*t*-Bu(1,1-dichloro-2-methoxycyclopropane)benzene (39);
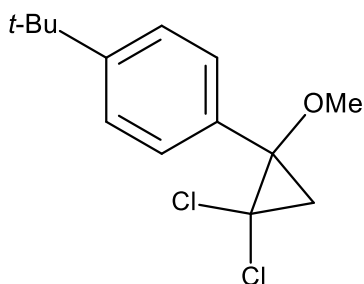
50% aqueous solution of NaOH (6.00 g, 0.15 mol) was added slowly to the stirred solution of 4-*t*-Bu(1-methoxyvinyl)benzene **(28)** (9.51 g, 0.05 mol), DCM (100mL), CHCl$_3$ (23.87 g, 0.2mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give solid. Yield: 10.65 g (78%), M.P. = 64-65 °C. IR (neat): υ 3087, 2961, 2904, 2868, 2827, 2374, 2113, 1903, 1628, 1609, 1510, 1461, 1363, 1267, 1237, 1201, 1097, 1071, 1003, 1016, 901, 834, 773, 761cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.43-7.35 (m, 4H), 3.26 (s, 3H), 2.02 (d, *J* = 8.3 Hz, 1H), 1.83 (d, *J* = 8.3 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 151.9, 130.7, 128.9, 125.2, 70.3, 64.2, 55.3, 34.7, 31.3, 30.2.

5.6.7 Synthesis of 1-methoxy-7, 7-dichlorobicyclo[6.1.0] nonane (42); 50% aqueous solution of NaOH (9.60 g, 0.24 mol) was added slowly to the stirred solution of 1-methoxycyclooctene (30) (11.21 g, 0.08 mol) was added to the solution of DCM (75 mL), CHCl$_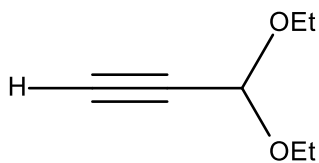3$ (35.81 g, 0.03 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum to give a colorless liquid. B.P. = 121 °C/11mbar, Yield: 13.74 g (77%), R$_f$ = 0.57 (5% MeOAc in heptane). IR (neat): υ 2934, 2858, 2410, 1170 1112, 1084, 1064, 1024, 968, 865 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.47 (s, 3H), 2.31 (d, *J* = 1.2Hz, 2H), 2.35 (d, *J* = 1.2Hz, 2H), 1.85-1.91 (m, 1H), 1.33-1.68 (m, 8H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 67.9, 67.4, 54.3, 41.9, 40.0, 27.5, 25.8, 24.5, 24.4, 22.8. [58]

5.6.8 Synthesis of 13,13-dichloro-1-methoxy bicyclo[10.1.0] tridecane (43); 50% aqueous solution of NaOH (4.80 g, 0.12 mol) was added slowly to the stirred solution of (1-methoxy)cyclododecene (31) (7.85 g, 0.04mol), DCM (100 mL), CHCl$_3$ (19.09 g, 0.16 mol) and TEBA (catalytic amount) 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give yellow liquid. R$_f$ = 0.68 (20% MeOAc in heptane), Yield: 8.04 g (72%). IR (neat): υ 2925, 2852, 2684, 1774, 1709, 1467, 1444, 1343, 1236, 1117, 1089, 1057, 1046, 978, 933, 843, 804 760 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$):δ 2.40-2.39 (m, 4H), 3.41 (s, 3H), 2.06-1.99 (m, 2H), 1.68-1.62 (m, 12H), 1.48 (s, 2H), 0.82 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 69.8, 67.8, 54.2, 40.3, 40.1, 27.5, 26.9, 24.6, 24.0, 23.4, 22.7, 22.3, 22.2, 21.7.

5.6.9 Synthesis of 7,7-dichloro-2-oxabicyclo[4.1.0]heptane (41);
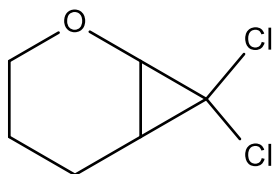
50% aqueous solution of NaOH (12.00 g, 0.30 mol) was added slowly to the stirred solution of 3,4,-dihydropyran (11) (8.41 g, 0.10 mol), DCM(100 mL), CHCl$_3$ (47.75 g, 0.4 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give the clear liquid. R$_f$ = 0.53 (20% MeOAc in heptane), Yield = 16.20 g (97%), B.P. = 88-89 °C/31 torr, (Lit. B.P. = 45-47 °C/0.99mmHg) [34]. IR (neat): υ 2963, 2929, 2089, 1448, 1386, 1348, 1280, 1237, 1207, 1152, 1112, 1063, 1022, 1000, 936, 880, 853, 823, 769 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$):δ 3.81 (d, J = 8.2 Hz, 1H), 3.79-3.75 (m, 1H), 3.36-3.30 (m, 1H), 2.02-1.97 (m, 2H), 1.77-1.65 (m, 2H), 1.43-1.37 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 64.4, 62.8, 59.1, 26.4, 20.5, 15.4. The spectroscopic data were in accordance with the literature data. [34][39]

5.6.10 Synthesis of (1,1-dichloro-2,2-methoxy)methylcyclopropane (34);
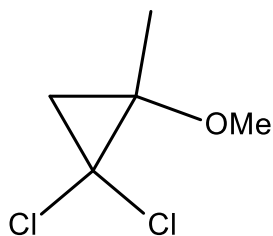
50% aqueous solution of NaOH (18.00 g, 0.45 mol) was added slowly to the stirred solution of 2- methoxy propene (2) (10.80 g, 0.15 mol), DCM (100 mL), CHCl$_3$ (56.70 g, 0.70 mol) and TEBA (catalytic amount) at 0 °C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na$_2$SO$_4$). The solvent was removed under the vacuum distillation to give a colorless liquid. Yield: 16.70 g (79%). IR (neat): υ 3266, 2963, 2298, 2120, 2091, 1731, 1697, 1658, 1619, 1389, 1368, 1259, 1184, 1053, 1020, 973, 887, 798 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$):δ 1.26 (2H, d, J = 1.4Hz), 1.63 (3H, s), 3.47 (3H, s); ^{13}C NMR (100 MHz, CDCl$_3$):δ 16.3, 32.9,54.4,67.5, 72.1.

5.6.11 Synthesis of 2-chloro-2-cyclohexen-1-one (44); 50% aqueous solution of NaOH (36.00 g, 0.90 mol) was added slowly to the stirred solution of 1-methoxycyclopentene **(32)** (29.44 g, 0.30 mol), DCM (150 mL), CHCl₃ (142.50 g, 1.20 mol) and TEBA (catalytic amount) at 0°C. The mixture was vigorously stirred by mechanical stirring at around 800-1000 rpm. The solution was run at ice bath for few hours and then allowed to run at room temperature overnight. The reaction was quenched with (6 M) HCl to make the solution acidic and water was added. The solution was extracted with DCM (4x20 mL), washed with water (4x15 mL) and dried (Na_2SO_4). The solvent was removed under the vacuum distillation to give shining light brown crystals. R_f = 1.57 (20% MeOAc in heptane). Yield: 21.19 g (72%), M.P. = 78-79 °C (Lit. 71-72 °C) [61], R_f = 0.57 (20% MeOAc in heptane). IR (neat): υ 2950, 2871, 1693, 1606, 1502, 1454, 1330, 1226, 1197 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.99-2.08 (m, 2H), 2.44-2.53 (m, 2H), 2.55-2.65 (m, 2H), 7.13 (t, *J* = 4.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 22.9, 27.4, 38.8, 132.5, 147.2, 192.0.
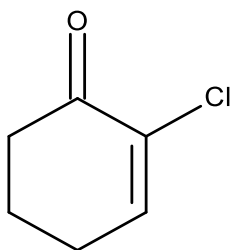
The NMR values were in accordance with previous results. [51]

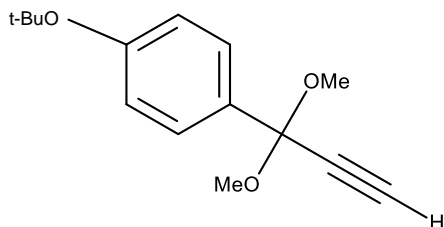**5.7 Ring opening of 2-alkoxy-1,1-dichloroyclopropane**

5.7.1 Synthesis of 3,3-diethoxy-propyne (45); Sodium ethoxide (27.20 g, 0.40 mol) was added in portions to a mixture of 1,1-dichloro-2-ethoxycyclopropane **(33)** (15.50 g, 0.10 mol) in DMF (150mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et₂O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na_2SO_4) and solvent were removed under reduced pressure to give a clear liquid. Yield: 10.50 g (82%), B.P. = 36-38 °C/31 torr (Lit. 90-94 °C/150 torr) [60], R_f = 0.66 (5% MeOAc in heptane). IR (neat): υ 3268, 2977, 2932, 2888, 2123, 1925, 1481, 1444, 1369, 1354, 1327, 1109, 1050, 1009, 968, 887, 830 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 5.26 (s, 1H), 3.78-3.58 (m, 4H), 2.56 (s, 1H), 1.24(t, *J* = 7.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 90.9, 79.0, 73.5, 61.0, 15.0. The NMR values were in accordance with the literature. [10][41]
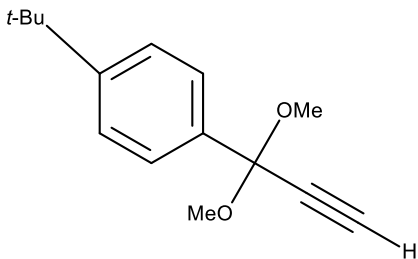
5.7.2 Synthesis of 3,3-dimethoxy-3-phenyl-1-yne (48); Sodium methoxide (0.43g, 8.00 mmol)
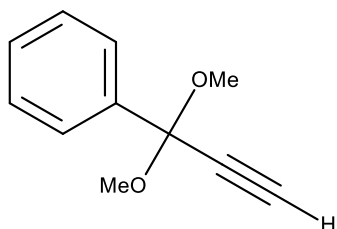
was added to a mixture of (1,1-dichloro-2-methoxycyclopropane)benzene **(35)** (0.43 g, 2.00 mmol) in DMF(10 mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a light-yellow liquid. Yield: 0.22 g (65%), R$_f$ = 0.46 (10% MeOAc in heptane). IR (neat): υ 3301, 2834, 1450, 1189, 1033, 1126, 1071, 971 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.58-7.18 (m, 5H), 3.22 (s, 6H), 2.6(s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 139.1, 128.8, 128.2, 126.6, 97.8, 80.9, 74.4, 50.5. The NMR values were in accordance with the literature. [10]

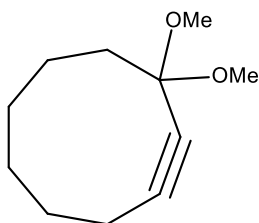### 5.7.3 Synthesis of 3,3-dimethoxy-3-(4 fluoro-phenyl-1-yne) (49); Sodium methoxide (0.53 g,
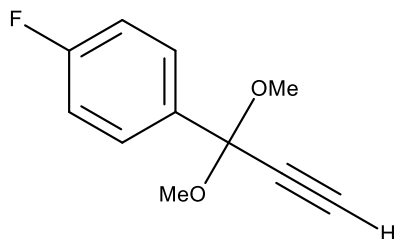
0.01 mol) was added in portions to a mixture of 4-fluoro(1,1-dichloro-2-methoxycyclopropane)benzene **(36)** (0.70 g, 0.003 mol) in DMF (50 mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a clear liquid. Yield: 0.68 g (78%), R$_f$ = 0.64 (20% MeOAc in heptane). IR(neat): υ 3296, 2942, 2908, 2833, 2114, 1901, 1658, 1603, 1505, 1464, 1450, 1408, 1345, 1300, 1233, 1185, 1156, 1121, 1092, 1065, 1027, 971, 939, 834, 814 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.09-7.03 (m, 2H), 7.66-7.61 (m, 2H), 3.30 (s, 6H), 2.71 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 162.9 (d, J_{CF} = 247.2 Hz), 135.0 (d, J_{CF} = 2.9 Hz), 128.6 (d, J_{CF} = 8.0 Hz), 115.0 (d, J_{CF} = 21.2 Hz), 97.3, 80.6, 74.7, 50.3.
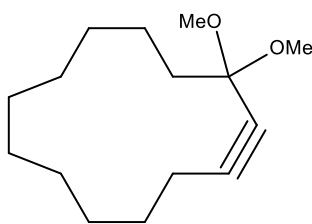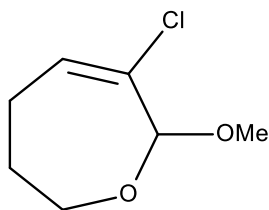
5.7.4 Synthesis of 3,3-dimethoxy-3-(4 bromo-phenyl-1-yne) (50); Sodium methoxide (1.07 g, 20.00 mmol) was added in portions to a mixture of 4-bromo(1,1-dichloro-2-methoxycyclopropane)benzene **(37)** (1.47 g, 5.00 mmol) in DMF (50 mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a yellow orange liquid. Yield: 0.89 g (70%), R$_f$ = 0.62 (10% MeOAc in heptane). IR (neat): υ 3293, 2963, 2940, 2907, 2831, 2114, 1908, 1654, 1589, 1465, 1433, 1394, 1245, 1187, 1174, 1123, 1094, 1064, 1027, 1010, 970, 951, 821 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.64-7.60 (m, 2H), 7.48-7.44 (m, 2H), 3.17 (s, 6H), 2.08 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 138.4, 131.2, 128.4, 122.1, 96.8, 80.2, 78.1, 50.0.
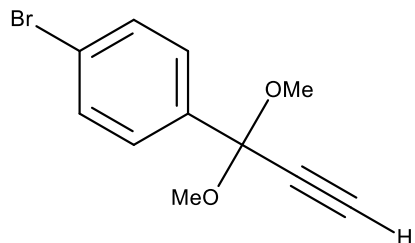
5.7.5 Synthesis of 3,3-dimethoxy-3-(4 methyl-phenyl-1-yne) (51); Sodium methoxide (0.43 g, 8.00 mmol) was added in portions to a mixture of 4-methyl(1,1-dichloro-2-methoxycyclopropane)benzene **(38)** (0.46 g, 2.00 mmol) in DMF (10mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0°C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a yellow liquid. Yield: 0.23 g (61%), R$_f$ = 0.49 (10% MeOAc in heptane). IR (neat): υ 3284, 2994, 2940, 2831, 2112, 2001, 1906, 1677, 1613, 1509, 1449, 1405, 1310, 1243, 1176, 1122, 1066, 1030, 965, 943, 816 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.54-7.52 (m, 2H), 7.20-7.18 (m, 2H), 3.29 (s, 6H), 2.68 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 138.7, 136.2, 128.9, 126.5, 97.8, 81.1, 74.4, 50.4, 21.2.
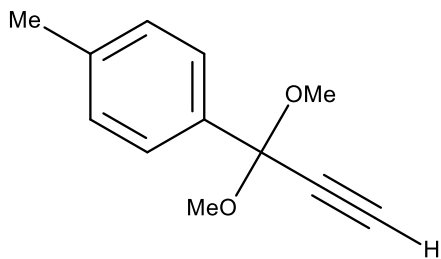
5.7.6 Synthesis of 3,3-dimethoxy-3-(4-*t*-BuO-phenyl-1-yne) (53); Sodium methoxide (0.64 g, 12.00 mmol) was added in portions to a mixture of 4-*t*-BuO(1,1-dichloro-2-methoxycyclopropane)benzene **(40)** (0.82 g, 3.00 mmol) in DMF (50 mL). The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et₂O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na₂SO₄) and solvent was removed under reduced pressure to give a dark brown liquid. Yield: 0.59 g (72%), $R_f = 0.44$ (10% MeOAc in heptane). IR (neat): υ 3284, 2976, 2937, 2831, 2113, 1720, 1647, 1605, 1502, 1459, 1390, 1365, 1301, 1239, 1158, 1123, 1097, 1068, 1030, 970, 895, 854 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.55-7.53 (m, 2H), 7.01-6.97 (m, 2H), 3.29 (s, 6H), 2.71 (s, 1H), 1.36 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 156.0, 133.6, 127.3, 123.5, 97.8, 80.9, 78.7, 74.6, 50.5, 28.9.

5.7.7 Synthesis of 3, 3-dimethoxy-3-(4-*t*-Bu-phenyl-1-yne) (52); Sodium methoxide (0.64 g, 12.00 mmol) was added in portions to the mixture of 4-*t*-Bu(1,1-dichloro-2-methoxycyclopropane)benzene **(39)** (0.70 g, 3.00 mmol) in DMF. The mixture was stirred at -10 °C for four hours and quenched with water at 0 °C. The solution was extracted with Et₂O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na₂SO₄) and solvent was removed under reduced pressure to give a clear liquid. Yield: 0.41 g (59%), $R_f = 0.47$ (10% MeOAc in heptane). IR (neat): υ 3282, 2971, 2928, 2817, 2107, 1700, 1637, 1579, 1543, 1412, 1384, 1323, 1257, 1202, 1137, 1101, 1089, 1068, 1030, 982, 899, 867 cm⁻¹; ¹HNMR (400MHz, CDCl₃): δ 7.57-7.54 (m, 2H), 7.40-7.38 (m, 2H), 3.31 (s, 6H), 2.69 (s, 1H), 1.32 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 151.8, 136.0, 126.2, 125.1, 97.9, 81.0, 74.5, 50.5, 34.6, 31.3

5.7.8 Synthesis of (3,3-dimethoxy)cyclononyne (55); Sodium methoxide (1.07 g, 20.00 mmol) was added in portions to a mixture of 1-methoxy-7,7-dichlorobicyclo[6.1.0]nonane **(42)** (1.07 g, 5.00 mmol) in DMF (10mL) at 0 ℃. The mixture was stirred overnight at room temperature and quenched with water at 0 °C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a light-yellow liquid. R$_f$ = 0.5 (20% MeOAc in heptane), Yield: 0.57 g (63%), R$_f$ = 0.50 (20% MeOAc in heptane), IR (neat): υ 2925, 2853, 2253, 1626, 1464, 1365, 1260, 1118, 1036, 904,846, 808, 736 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.28(s, 6H), 1.93-1.90(m, 2H), 1.84-1.82(m, 2H), 1.75-1.55(m, 8H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 102.2, 94.3, 83.8, 50.2, 37.5, 29.7, 26.4, 25.1, 21.3, 19.0.

5.7.9 Synthesis of (3, 3-dimethoxy)cyclotridecyne (56); Sodium methoxide (0.43 g, 8.00 mmol) was added in portions to a mixture of (13,13-dichloro-1-methoxy)bicyclo[10.1.0]tridecane **(43)** (0.55 g, 2.00 mmol) in DMF (20 mL) at 0 ℃. The mixture was stirred overnight room temperature and quenched with water at 0 °C. The solution was extracted with Et$_2$O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na$_2$SO$_4$) and solvent was removed under reduced pressure to give a yellow liquid. R$_f$ = 0.51 (5% MeOAc in heptane), Yield: 0.22 g (47%). IR (neat): υ 2926, 2854, 2829, 2324, 2081, 1701, 1458, 1446, 1401, 1363, 1239, 1188, 1180, 1159, 1110, 1098, 1084, 1061, 1024, 956, 980, 903, 863, 848, 745, 672 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.54-3.42 (m, 6H), 2.40-2.37 (m, 2H), 1.83-1.79 (m, 2H), 1.57-1.50 (m, 16H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 109.7, 100.1, 94.4, 55.3, 40.4, 38.1, 36.5, 29.6, 29.3, 26.9, 26.1, 25.5, 19.5, 14.0.

5.7.10 Synthesis of 6-chloro-7-methoxy-2,3,4,7-terahydrooxephine (54); Sodium methoxide (1.07g, 0.02 mol) was added in portions to a mixture of (7,7-dichloro-1-methoxy)bicyclo[4.1.0]heptane **(41)** (1.00 g, 6.00 mmol) in DMF (25mL) at 0℃. The mixture was stirred overnight at room temperature and quenched with water at 0℃. The solution was extracted with Et_2O (4x20 mL). The organic layer was washed with water (4x10 mL). The organic layer was dried (Na_2SO_4) and solvent was removed under reduced pressure to give a dark liquid. Yield: 0.80 g (82%), R_f = 0.22 (30% MeOAc in heptane). IR (neat): υ 2923, 2853, 2253, 2102, 1905, 1719, 1455, 1260, 1072, 905, 728 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.14-6.13 (m, 1H), 4.78 (s, 1H), 3.98-3.91 (m, 1H), 3.66-3.63 (m, 1H), 3.40 (s, 3H), 2.75-2.71 (m, 1H), 3.25-2.34 (m, 1H), 1.77-1.70(m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 137.2, 115.5, 100.2, 60.2, 54.7, 26.0, 22.[7]

5.7.11 Synthesis of (3,3-dimethoxy-but-1-yne) (46); Sodium methoxide (6.48 g, 0.12 mol) was added in portions to a mixture of (1,1-dichloro-2-methoxy-2-methyl)cyclopropane **(34)** (5.00 g, 0.03 mol) in DMF (75 mL). The mixture was stirred at -10°C for four hours and quenched with water at 0 °C. The solution was extracted with Et_2O (4x20 mL). The organic layer was dried (Na_2SO_4) and solvent was removed under reduced pressure to give a clear liquid. Yield: 1.78 g (52%). IR: υ 3291, 2992, 2942, 2832, 2115, 1600, 1451, 1435, 1372, 1275, 1248, 1220, 1173, 1143, 1103, 1042, 897, 866, 810, 772 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.60 (3H, s), 2.59 (1H, s), 3.32 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$): δ 24.7, 49.7, 24.7, 49.7, 72.1, 80.9, 95.9.[10]
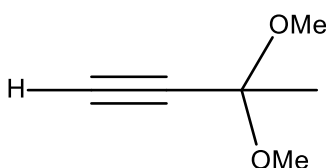
REFERENCES

1. Doering, W. E, Hoffmann, A. K., *J. Am. Chem. Soc.,* **1954**, *76*, 6162-6165.

2. Sydnes, L.K., Bakstad, E. In B. Halton, (Series ed.) *Advances in Strain in Organic Chemistry,* London, Jai Press Inc., **1996***, 5,* pp. 85-119.

3. Müller, P., Pautex, N., *Helv. Chim. Acta.,* **1991**, *74*, 55–64.

4. Carey, F. A., Sundberg, R.J*., Advanced Organic Chemistry Part B,* Springer, **1990**, *3*, pp. 511-569.

5. Kirmse, W., *Carbene chemistry 2ᵉᵈed.* Academic press, New York, **1971**, pp. 256-267.

6. Makosza, M., Wawrzyniewicz, W., *Tetrahedron Lett*., **1969**, *10*, 4659-4662.

7. Luijkx, Y., *Master of Science Thesis, Radbound Universiteit Nijmegen, and UiS*, **2015**.

8. Stanislawski, P.C, Willis, A.C, Banwell, M.G., *Chem. Asian J*., **2007***, 2,* 1127-1136.

9. Thankachan, A.P, Sindhu, K.S, Krishnan, K.K, Anil kumar, G., *Org. Biomol. Chem*, **2015**, *13*, 8780-8802.

10. Springer, J. *Master of Science Thesis, Universiteit Amsterdam and UiS***, 2002**.

11. Hamilton, J.G, Palke, W.E*., J. Am. Chem. Soc.,* **1993**, *115*, 4159-4164.

12. Agrawal, M.K., Adimurthy, S., Ganguly, B., Ghosh, P.K. *Tetrahedron Lett.,* **2009,** *65,* 2791-2797.

13. Mansilla, H., Afonso, M.M., *Synth. Commun.*, **2008**, *38*, 2607-2618.

14. Wang, M.L., Hsieh, Y.M., Chang, R.Y., *Ind. Eng. Chem. Res.,* **2003**, *42,* 4702-4707.

15. Skattebøl, L., *J. Org. Chem*., **1966**, *31*, 1554-1559.

16. Skattebøl, L., *J.Org .Chem*., **1970***, 35*, 3200-3201.

17. Seyferth, D., Yamazaki, H., Alleston, D.L*., J. Org. Chem***., 1963**, *28*, 703-706.

18. Skattebøl, L. *Acta Chem. Scand*., **1963**, *17,* 1683-1693.

19. Sydnes, L.K., Bakstad, E*., Acta Chem. Scand*., **1997**, *51,* 1132-1133.

20. Joshi, G.C., Singh, N., Pande, L.M., *Tetrahedron Lett***., 1972***, 15,* 1461-1465.

21. Wang, M.L., Hsieh, Y.M., Chang, R.Y., *React. Kinet. Catal. Lett*, **2004**, *81*, 49-56.

22. Seyferth, D., Burlitch, J.M, Minasz, R.J., Mui, J.Y.P., Simmons, H. D. Jr., Treiber, A.J.H., Dowd, S.R., *J. Am. Chem. Soc*., **1945**, *87*, 4259-4270.

23. Hong, M., Xiao, G., *J. Fluorine Chem.,* **2012**, *140*, 121-126.

24. Sydnes, L.K., Petterson, A., Drablos, F., Romming, C., *Acta. Chem. Scand*, **1991**, *45*, 902-913.

25. Richard, J.P., Williams, K.B., *J. Am. Chem. Soc***., 2007**, *129*, 6952-6961.

26. Corey, E. J, Mitra, R.B., Uda, H., *J. Am. Chem. Soc.,* **1964**, *86*, 485-492.

27. Woodward, R.B., Hoffmann, R*., J. Org. Chem. Soc.,* **1965,** *87*, 395-397.

28. Kulinkovich, O.G., *Cyclopropanes In Organic Chemistry*, Wiley, **2015***, 1,* pp. 3-13.

29. Wang, M.X., Feng, G.Q., Zheng, Q.Y., *Adv. Synth. Catal*., **2003**, *345*, 695-698.

30. Bretherick, L. Handbook of the reactive chemical hazards 6th editor. Butterworth-Heinemann Ltd, **1999**, pp. 430.

31. Halton, B., Bridle, J.H., *Tertrahedron Lett*., **1990**, *31*, 1331-1314.

32. Baird, M.S., Buxton, S.R., Whitley, J.S., *Tetrahedron Lett.,* **1984**, *25*, 1509-1512.

33. McClelland, R.A., Engell, K.M., Larsen, T.S., Sorensen, P.E., *J. Chem. Soc*., *Perkin Trans. 2,* **1994**, *10*, 2199-2206.

34. Lin, H., Yang, M., Huang, P., Cao, W., *Molecules*, **2003**, *8*, 608-613.

35. Richard, J.P., Williams, K.B., *J. Am. Chem. Soc*., **2007**, *129*, 6952-6961.

36. Nishimoto, Y., Ueda, H., Yasuda, M., Baba, A*., Angew. Chem. Int. Edit*., **2012**, *51*, 8073-8076.

37. Nanteuil, F., Serranto, E., Perrotta, D., Waser, J., *J. Am. Chem. Soc.,* **2014**, *136*, 6239-6242.

38. Hanazawa, T., *et al. US Patent*, **2006**, US2006/0211741 A1.

39. Taylor, K.G, Hobbs, W.E., Saqueet, M., *J. Org. Chem*., **1971**, *36*, 369-377.

40. Bakstad, E., Olsen, A.S., Sandberg, M., Sydnes, L.K., *Acta Chem. Scand*., **1999**, *53*, 465-472.

41. Lister, T., Renshaw, J*., Understanding Chemistry for Advanced Level, Nelson Thornes*, **1999**, *3,* pp. 238.

42. Kosarych, Z., Cohen, T*., Tetrahedron Lett.,* **1980**, *21*, 3959-3962.

43. Erturk, E., Gollu, M., Demir*, A.S., Tetrahedron*, **2010**, *66*, 2373-2377.

44. Winstein, S., Ingraham, L. L., *J. Am. Chem. Soc.,* **1955**, *77,* 1738-1743.

45. Sydnes, L.K., Bakstad, E., *Acta Chem. Scand.*, **1996**, *50,* 446-453.

46. Keegstra, M.A., *Tetrahedron*, **1992**, *48*, 2681-2690.

47. Kvernenes, O.H., Sydnes, L.K., *Org. Synth*., **2006**, *83*, 184-192.

48. Giersch W., Farris I., *Helv. Chim. Acta.*, **2004***, 87*, 1601-1606.

49. Mansilla, H., Regas, D., *Synth. Commun.,* **2006**, *36*, 2195-2201.

50. Song, J.J*., Org.Lett.*, **2008,** *10*, 877-880.

51. Roy, S., Rana, K., Guin, C., Banerjee, B., *Arkivoc.,* **2003***,* 34-38*.*

52. Wiering. G.P., Steinberg. H., *J. Org. Chem.,***1981***, 46,* 1663-1666.

53. Chopin, N., Decamps, S., Gouger, A., Médebielle, M., Picot, S., Bienvenu, A. L., Pilet, G., *J. Fluorine Chem.,* **2011**, *132*, 850–857.

54. Burkhouse, D., Zimmer, H., *Synthesis.,* **1984**, 330.

55. Thompson, K.S., Heathcock, H.C., *J. Org. Chem.*, **1990**, *55*, 3386-3388.

56. Gassman, P.G., Burns, S.J., Pfister, K.B., *J. Org. Chem.,* **1993**, *58*, 1449-1457.

57. Corey, J.E., Seebach, D., *Org. Synth.,* **1988**, *6*, 556.

58. Fløysvik, O. G., *Bachelor Thesis*, *UiS*, **2016.**

59. Wiberg, K.B., *J. Am. Chem. Soc.,* **1957**, *79*, 3160-3164.

60. Dehmlow, E.V., *Tetrahedron.*, **1981,** *37*, 1653-1558.

61. Ley, S.V., *Tetrahedron Lett.,* **1981**, 22, 3301-3304.

APPENDIX A

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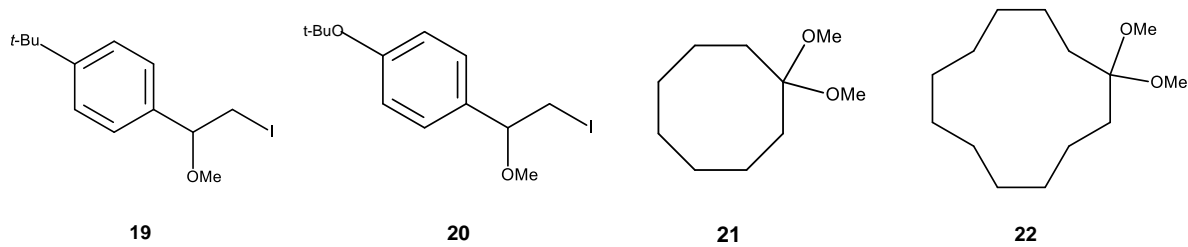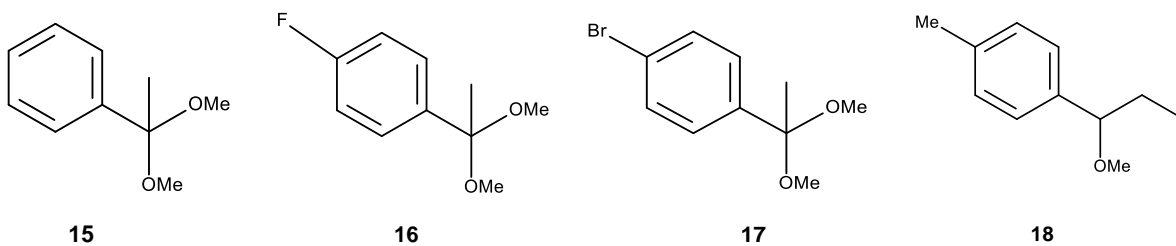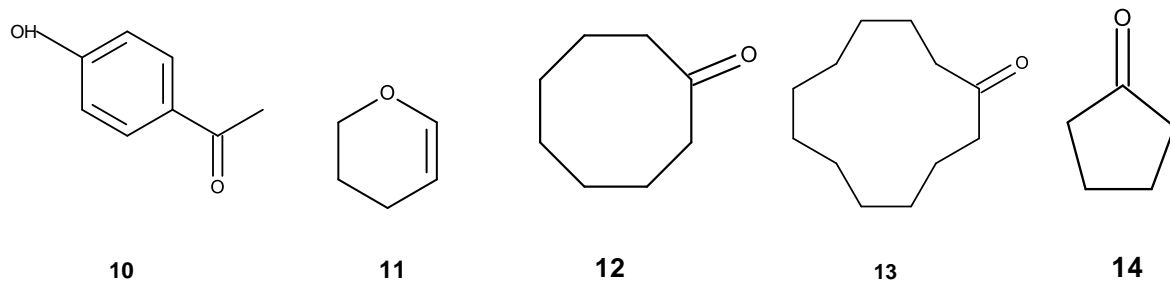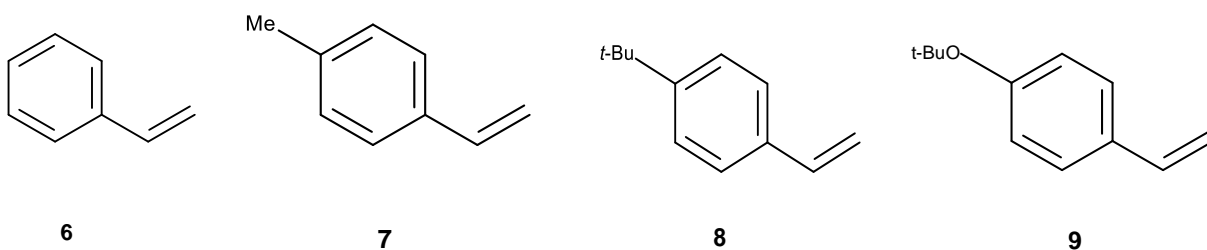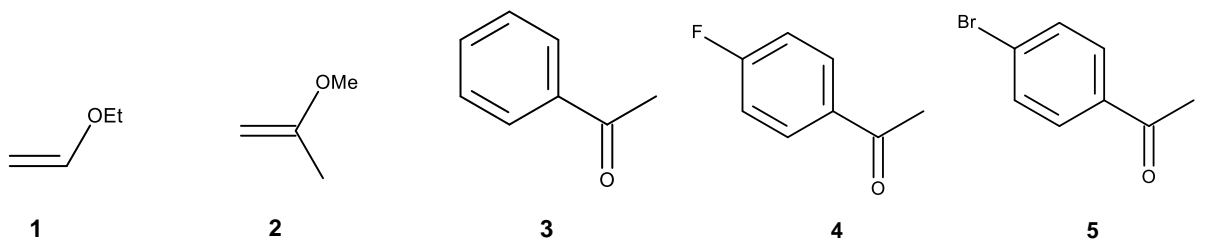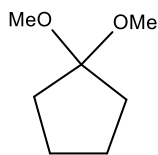
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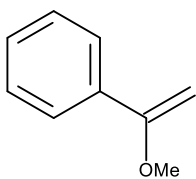
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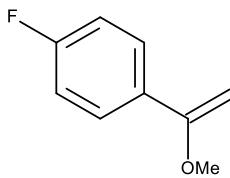
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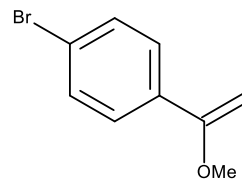
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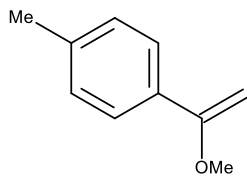
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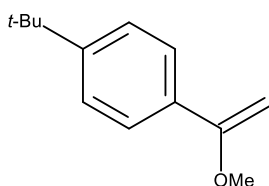
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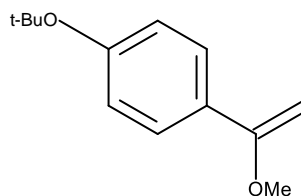
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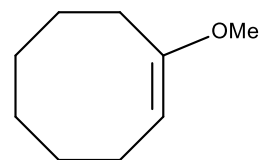
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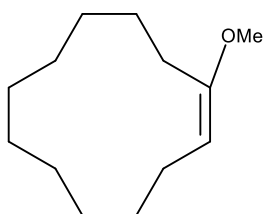
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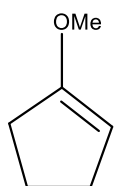
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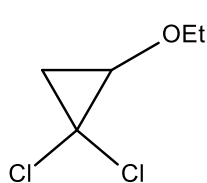
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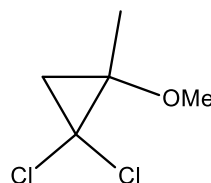
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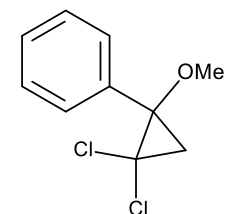
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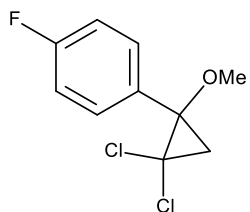
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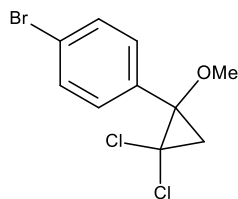
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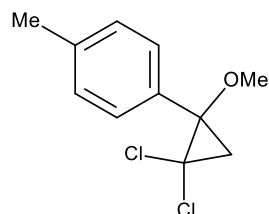
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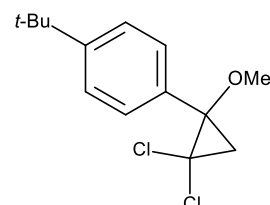
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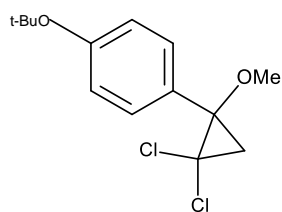
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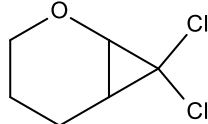
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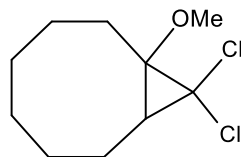
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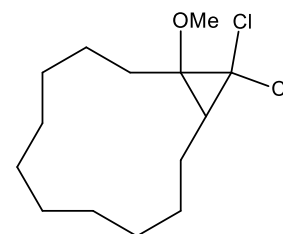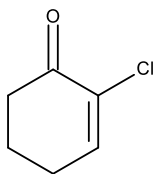
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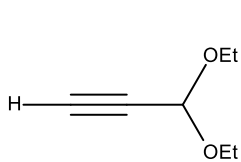
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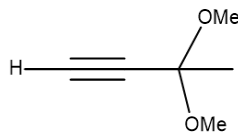
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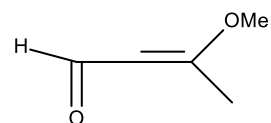
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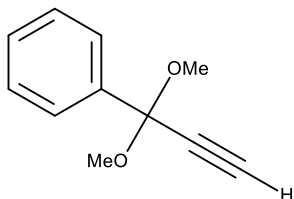
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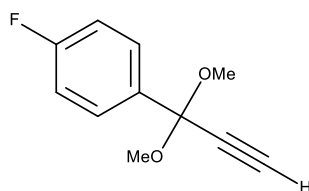
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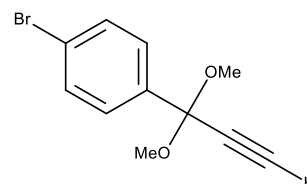
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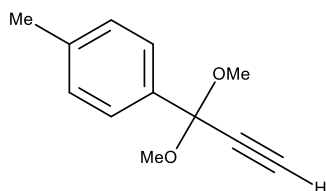
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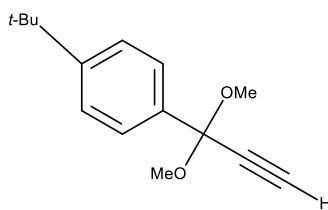
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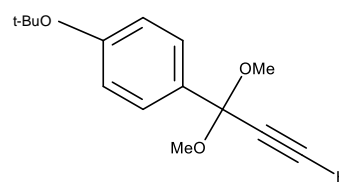
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