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CERTIFICATE

This is to certify that the work incorporated in the thesis entitled "PET Activated $PhSeSiR_3$ Mediated Group Transfer Radical Reactions" submitted by Mr. K. V. Nageshwar Rao was carried out by him under my supervision at the National Chemical Laboratory. Material that has been obtained from other sources has been duly acknowledged in the thesis.

Date: April 2, 2001

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DECLARATION

I hereby declare that the thesis entitled **"PET Activated $PhSeSiR_3$ Mediated Group Transfer Radical Reactions"** submitted for Ph. D. degree to the University of Pune has been carried out at National Chemical Laboratory, under the supervision of Dr. Ganesh Pandey. The work is original and has not been submitted in part or full by me for any degree or diploma to this or any other University.

K. V. Nageshwar Rao

(K. V. NAGESHWAR RAO)

Date: 2|04|2001

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Acknowledgement

I take this opportunity with immense pleasure to express my deep sense of gratitude to my mentor Dr. Ganesh Pandey for introducing me to the fascinating area of Organic photochemistry. The work presented in this thesis could not have been accomplished without his guidance, constant encouragement and undiminished enthusiasm. I am highly obliged for his motivation and unstinted support during all the tough times of my Ph. D. life.

My respectful gratitude to Prof. A. Krishnamurthy for motivating me towards research by sending me to NCL.

I gratefully acknowledge the guidance, training, and support extended by my senior colleague Dr. K. S. S. P. Rao (Seshu) during the initial part of my research.

Special thanks to all my senior colleagues and my present colleagues Dr. (Mrs.) Gadre, Laha, Sahoo, Murugan, Kapur, Tiwari, Rani, Late Mal, Utpal, Prabal, Srinivas, Sanjay, Balakrishna, and Inderesh for maintaining a warm and a very cheerful atmosphere in the lab. They made working the lab very enjoyable. Special acknowledgements to Kapur, Laha, Sahoo, and Sreenivas for taking trouble in bringing out the thesis.

Help from the spectroscopy and mass groups is gratefully acknowledged. I sincerely thank Mr. A. G. Samuel and Dr. Rajmohan for helpful discussions and Mrs. Phalgune, Dr. Sanjayan, Mr. Sathe and Mrs. Shanta kumari for their kind cooperation.

I would like to specially thank Prakash, Rachana, Raghu, R.K. Prasad, Vipul, Aparna, Meena, A., Meena, S., Jaspreet, Ramesh Babu, Moneesha, Pallavi, Aslam, Gnaneshwar, Arun, Manish, Sreedevi, Mr. & Mrs. Patil and all telugu group and many who are not named in person for their cheerful company and help which made my stay at NCL a memorable one. My due regards to all my old friends and well wishers Vishwanath, Sharma, Kotesh, Rajmohan, Shravan, Rajitha, Manju and Jayshree.

I don't have any words to express my feelings towards my mother who has patiently waited long enough for my return but couldn't wait anymore and left this world at the last stage of my thesis. May her soul rest in peace. I just can say "I love you mom……..forever."

It is equally difficult to put into words my gratitude and love towards my father and pinni for their love, support, encouragement and help in all respects through out my career. Special thanks to all my cousins, uncles and aunts.

Finally I thank Dr. K. N. Ganesh, Head, Division of Organic Chemistry (Syn.) and Director, National Chemical Laboratory, Pune for providing infrastructural facilities and permitting me to submit this work in the form of a thesis. I am also thankful to CSIR, New Delhi for the financial assistance in the from of research fellowship.

K. V. Nageshwar Rao

TO

MY BELOVED PARENTS

AND

PINNI

CONTENTS

ABBREVIATIONS

AIBN	α, α'-Azo bis(isobutyronitrile)
ACVA	4, 4-Azo bis(4-cyanovaleric acid)
B.P.	Boiling Point
Bu_3SnH	Tributyltin hydride
$Bu_3SnSnBu_3$	Hexabutyl ditin
CH_3CN	Acetonitrile
Cs_2CO_3	Cesium carbonate
DCM	Dichloromethane
DHP	3, 4-Dihydropyran
DMA	9, 10-Dimethoxy anthracene
DMN	1, 5-Dimethoxy naphthalene
ET	Electron transfer
Et_3N	Triethyl amine
EtOAc	Ethyl acetate
FRIP	Free radical ion pair
H_2A	Ascorbic acid
HOMO	Highest occupied molecular orbital
K_2CO_3	Potassium carbonate
LUMO	Least unoccupied molecular orbital
MP	Melting point
MeOH	Methanol
$NaBH_4$	Sodium borohydride
$NaCNBH_3$	Sodium cyanoborohydride
NaH	Sodium hydride
$NaHCO_3$	Sodium bicarbonate
Na_2SO_4	Sodium sulphate
PET	Photo induced electron transfer
PhSeSePh	Diphenyl diselenide
PhSeBr	Phenylslenyl bromide
PhSeCl	Phenylselenyl chloride
$PhSeSiR_3$	tert-butyl (diphenyl)selenosilane
PMHS	Polymethyl hydrosiloxane

SCE	Standard calomel electrode
SOMO	Singly occupied molecular orbital
TBDMS	tert-butyldimethyl silane
TBDMSCl	tert-butyldimethylsilyl chloride
THF	Tetrahydro furan
THP	Tetrahydro pyran
TMS	Trimethyl silane

Abstract

PET Activated $PhSeSiR_3$ Mediated Group Transfer radical Reactions

Chapter I

Introduction

This part contains general aspects of radical reactions and description on methods available for conducting free radical chain reactions and a detailed account of atom / group transfer reactions. The important strategies for initiating radical chain reactions by –C-X- bond homolysis utilizing tinhydride, allyltributyltin, hexabutylditin and other methods are briefly discussed. The emphasis has particularly, been placed on the literature concerning various atom / group transfer radical reactions such as halogen, cobalt and chalcogen group transfer radical reactions.

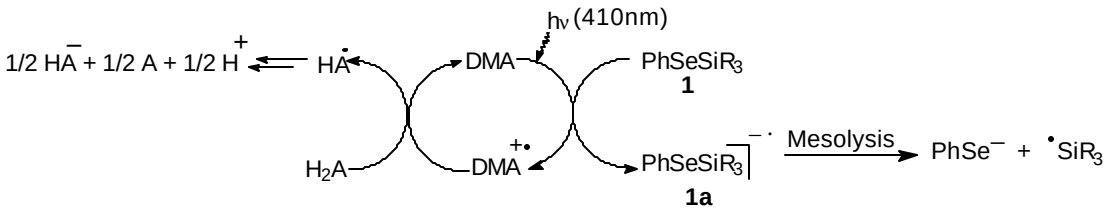
Chapter-2

$PhSeSiR_3$ Catalyzed intramolecular Radical Cyclizations

This chapter starts with a brief account on the importance of catalytic reactions, the background of the $PhSeSiR_3$ as a new radical initiating group transfer reagent, the evolution of the catalytic concept and its application to intramolecular cyclizations.

The PET reductive activation of $PhSeSiR_3$ (**1**) by a photosystem, designed by our group, comprising of 9, 10-dimethoxyanthracene as an electron donor and ascorbic acid as co-oxidant as shown in figure-1 led to the efficient generation of **1a**. Due to the large difference in the electronegativities of selenium (electronegativity of Se = 2.5) and silicon atoms (electronegativity of Si = 1.8), the mesolytic cleavage of **1a** produced selenium centered anion and a silyl radical.

Figure-1

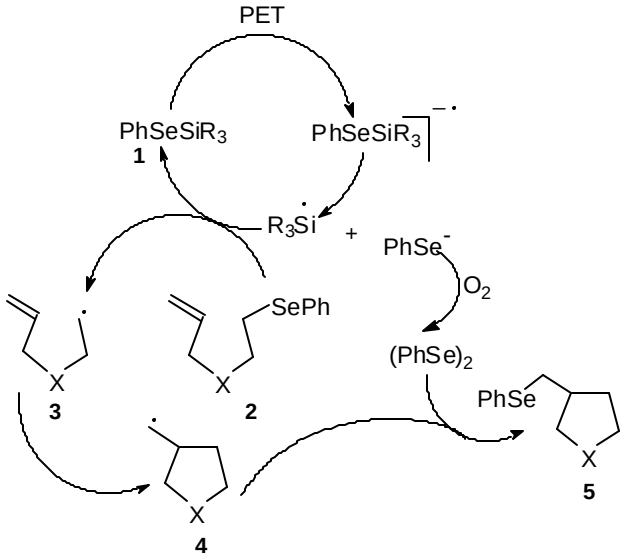


H_2A = Ascorbic acid $HA^{\cdot}$ = Acorbate Radical A = Dehydroascorbic acid

DMA = 9, 10 - Dimethoxyanthracene HA^- = Ascorbate anion

Ever since the discovery of radical generation by organo tinhydrides, the usage of tin-based reagents dominated the field of radical chemistry despite their known limitations. Though significant progress is made in overcoming these problems by developing newer methodologies / reagents, there is still dearth of a chemistry that addresses the environmental problem. Keeping in view the drawbacks of tin chemistry and the demand for an ecologically compatible strategy, a catalytic concept for radical reactions has been designed as depicted in figure-2.

Figure-2

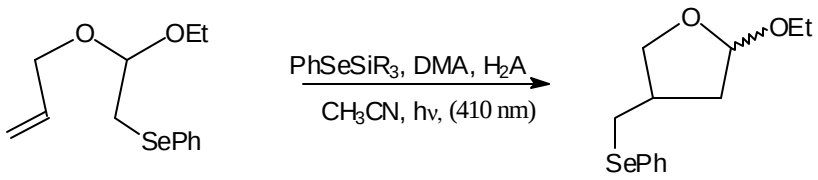


The catalytic concept of initiating radical based reactions (figure-2) was designed by considering the easy transformation of $PhSeSiR_3]^{-\bullet}$ to $R_3Si^{\bullet}$, possessing higher rate constant (k_r = 9.6 X 10^7 $M^{-1}s^{-1}$) for the cleavage of alkyl phenylselenide to generate a carbon centred radical and PhSeSePh via the oxidative dimerization of $PhSe^-$ required to terminate rearranged radical species (k_r = 1.2 X10^7 $M^{-1}s^{-1}$). PET activation of **1** in the presence of an appropriate alkylphenylselenide was conceptualised as an ideal approach to initiate a group transfer radical reaction.

The catalytic role of $PhSeSiR_3$ (**1**) in initiating a radical based group transfer reaction was established by PET cyclization of **2** to **3** through the photosystem as shown in figure-1. The thermodynamic preference for the formation of $\mathbf{1a}^{-\bullet}$ over $\mathbf{2}^{-\bullet}$ was established by comparing the ΔG_{et} values, calculated from their respective reduction potential values employing Weller equation. The large difference between the ΔG_{et} values for the formation of $\mathbf{1a}^{-\bullet}$ (-181 kJ M^{-1}) and $\mathbf{2}^{-\bullet}$ (-80 kJ M^{-1}) was considered important in designing the concept as $\mathbf{1a}^{-\bullet}$ was produced selectively over $\mathbf{2}^{-\bullet}$ when a mixture of **1** and **2** were activated.

PET activation of a series of samples containing varying concentrations of **2** with respect to a fixed concentration of **1**, DMA and ascorbic acid revealed that, the optimum mole ratio between **1** and alkyl phenyl selenides could be 1:10. Indeed, the PET activation of **2** and of **1** in the optimized mole ratio afforded cyclized product **3** (Scheme-1) in 75 % yield with a negligible change in the concentration of **1**, confirming the catalytic role of $PhSeSiR_3$.

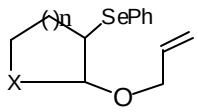
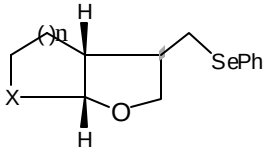
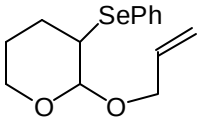
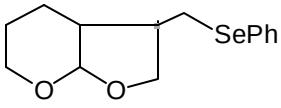
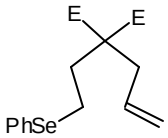
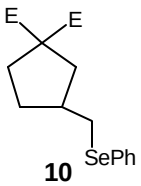
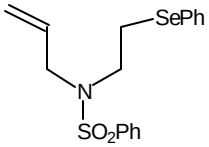
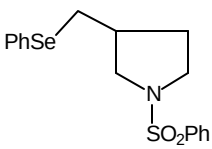
Scheme-1



2 **3** (75%)

The diverse applicability of this concept for group transfer radical reactions was exemplified through the cyclizations of substrates as depicted in Table-1.

Table-1

Entry	Substrate	Product[i]	Yield(%)[ii]
1	 **4**	 **8**	77
2	 **5**	 **9**	82
3	 **6**	 **10**	73
4	 **7**	 **11**	64

[i] Characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analyses.
[iii] Isolated yield, unoptimized.

Chapter-3

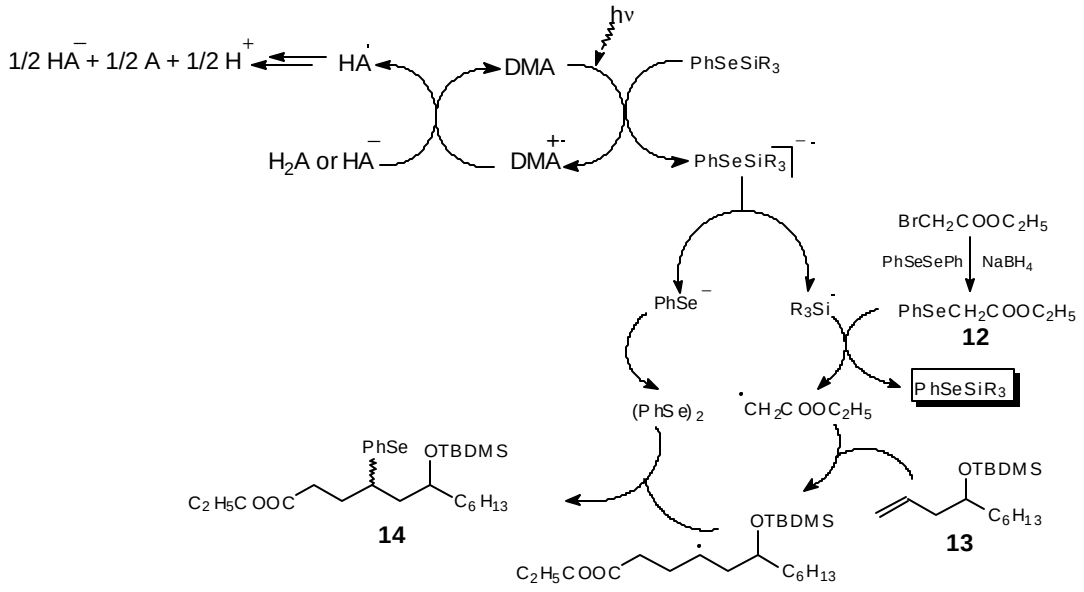
$PhSeSiR_3$ Catalyzed Intermolecular Addition, Tandem Annulations and Intramolecular Tandem Cyclizations:

This chapter deals with the application of the catalytic group transfer radical reaction strategy for new –C-C bond forming reactions via intermolecular addition, tandem annulation and intramolecular tandem cyclization reactions.

Intermolecular radical additions

By conventional radical reaction, intermolecular radical additions are generally found to be difficult due to competing bimolecular side reactions. This limitation in radical reaction was overcome by carrying out PET reaction of a mixture of $PhSeCH_2COOEt$ (**12**) and tert-butyldimethylsilyloxy-1-decene (**13**) to obtain adduct **14** (Figure-3) in good yield (61 %).

Figure-3

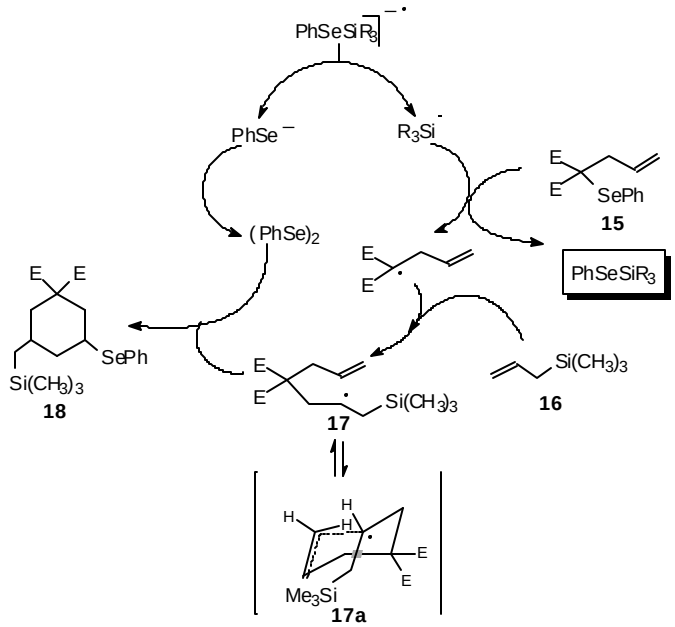


Tandem addition - cyclizations

In general, 5-hexenyl radicals are well known to undergo cyclization through *exo*-mode to provide 5-membered carbocyclic rings. However, the construction of 6-membered rings, also widely distributed in various biologically active compounds, through *endo*-mode radical cyclization is less prominent and has been found to be difficult.

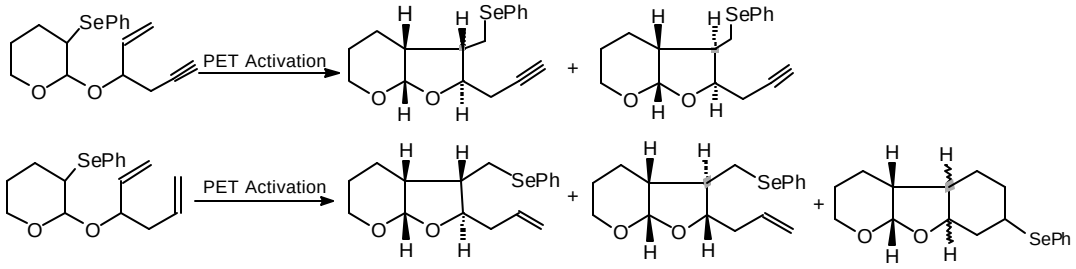
The presence of a silicon atom α or β to a carbon centered radical is known to reverse the regioselectivity of radical cyclization (favoring the *endo*-mode) due to the involvement of seemingly less dipolar transition state structure compared to normal carbon-centered radical cyclization. The longer bond lengths of -Si-C- were also expected to contribute towards *endo*-mode of cyclization. Considering this variant nature of β-silyl radicals, a tandem annulation reaction of **15** with **16** (Figure-4) realized the required *endo*-cyclization reaction product **18** in 60 % yield. Transition state structure **17a** was invoked to explain the *endo*-mode cyclization reaction.

Figure-4



In another exploration, an intramolecular tandem cyclization reaction for the possible construction of pyranofuran (6-5-6) ring systems by the PET activation of **19** was attempted. However the reaction gave only a diastereomeric mixture of monocyclized product **20a** and **20b** (7 : 3). Similarly, PET activation of **21** also gave mainly diastereomeric mixture of monocyclized product **22a** and **22b** (4 : 6) with a very small amount of bicyclization product **23 (**scheme-2). All these products were confirmed by ^{1}NMR, ^{13}C NMR and mass spectral analysis

Scheme -2



In conclusion, a conceptually new method for initiating phenylselenyl group transfer radical reactions in a catalytic fashion is reported in this dissertation.

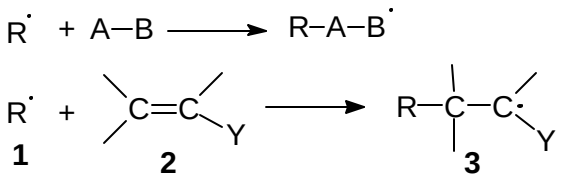
1-1. Introduction

Free radicals have evolved as the most significant reactive intermediates, over the last few decades, due to their versatility, predictability and functional group tolerance. Though, the dawn of the radical era can be dated back to 1900 with the discovery of triphenylmethyl radical by Gomberg,[1] the organic synthesis by radical pathways began only in 1937 with Hey and Waters reporting the homolytic phenylation of aromatic substrates.[2] During the same year, Kharasch recognized the anti-Markovnikov addition of hydrogen bromide to alkenes as a radical chain process.[3] However, in the chronology, 1970s have witnessed the start of new synthetic methods involving radicals, particularly, in substitution reactions of aromatic compounds.[4] The later years have brought an exponential rise and rapid development in the use of alkyl radicals for the formation of C-C bonds.[5] These reactions have various advantages compared to ionic chemistry and are usually easy to put into practice.

Most of the radicals used in the synthesis are transient and react with each other and with any other radical in the medium at diffusion controlled rates. Since the concentration of the radicals is low, their reaction with non-radical like solvents, which are in high concentration, are hard to prevent. Radical-radical reactions occurring at diffusion controlled limits often give rise to low selectivities, which can't be influenced by reaction conditions. These reactions can be slowed down only if radicals are stabilized by electronic effects (stable radicals) or shielded by steric effects. However, direct radical-radical reactions can be avoided by choosing proper reaction conditions and the selectivities can also be influenced by varying the substituents. In general, alkyl radicals substituted with electron releasing groups (alkyl, alkoxy, amino etc) behave like nucleophiles and react very fast with alkenes substituted by electron withdrawing substituents (nitrile, ketone, ester etc.).[6,7] On the other hand, radicals with electron withdrawing substituents behave like electrophiles and react faster with electron rich alkenes.[6,8]

In order to apply reactions between radicals and non-radicals for synthesis, chain reactions have to be built up and these chain reactions are terminated by combination of the radicals. Therefore, the rate of chain propagation (r_p) between radicals and non-radicals must be higher than that of the chain termination (r_t) and only those chain propagation steps whose rate constants k_p are larger than 10^2 l/mol.s^{-1} can be used for synthesis.[9] The propagation of a radical chain can occur by various types of reactions such as additions, substitutions, elimination, rearrangement and electron transfer reactions. Usually, the product of every propagation step is another radical.

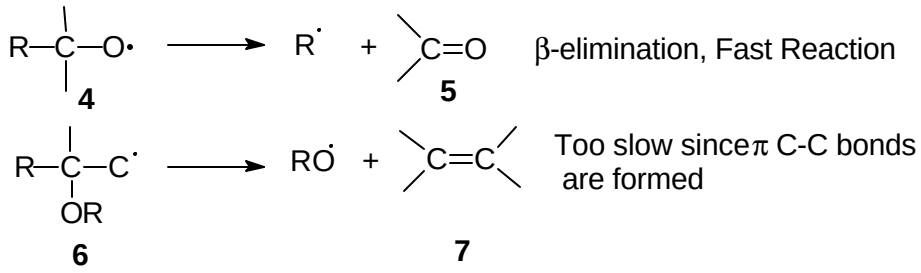
In the addition reaction of an alkyl radical to an alkene, a σ C-C bond is made from a π C-C bond in a very exothermic reaction. The rate of addition of radical to alkene depends largely on the substituents on the radical and the alkene.[6,10] In molecular orbital terms, the SOMO of the radical interacts with the LUMO and /or HOMO of the C-C multiple bond. Electron withdrawing substituents at the alkene, which lower the LUMO energy, increases the addition rate by reducing SOMO-LUMO difference. However, radicals with electron withdrawing substituents at the radical center have SOMO energies so low that the SOMO-HOMO interaction dominates. These radicals react like electrophiles.



Scheme-1

A typical substitution reaction involves abstraction or substitution from a non-radical species generating a new radical located at the former site of the abstracted functionality. In an elimination reaction, two molecules are formed from one radical species. This is a rapid and a useful reaction containing atom or groups that form relatively weak bonds with carbon and also form relatively stable radicals. Such groups include tin (R_3Sn), sulfur (RS), selenium (RSe) and halogen. In addition to these, the

groups that are not eliminated and form strong bonds with carbon include oxygen and nitrogen groups.[11]



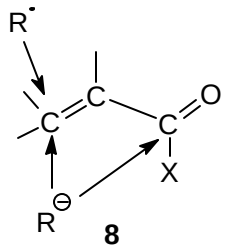
4 **5** **6** **7**

Scheme-2

Radicals can also undergo rearrangement reactions but only few radical rearrangements are fast enough that appear in the synthesis compared to their cationic counterparts.[12] In an electron transfer reaction, rate of the reaction depends on the difference in the reduction potentials of educts and products. The higher the SOMO energy of the radicals, the faster is the electron transfer processes. Compared with neutral radicals, electron transfer reactions with radical anions are so fast that even neutral molecules can act as electron acceptors.

Radical reactions are often highly chemoselective. Due to the reactivity requirement, only functional groups that have bimolecular rate co-efficients with $K>10^2$ $l/mol^{-1}.s^{-1}$ are attacked by radicals. This is advantageous in the planning of the synthesis since wide ranges of functional groups are tolerated without protection. Thus, the homolytic cleavage of O-H and N-H bonds by alkyl radicals as well as the intermolecular addition of alkyl radicals to C=O bonds of ketones and esters are very slow at room temperature and hence needs no protection. Steric crowding, particularly, on the radical center is often tolerated.

Radical reactions often show different regioselectivities than ionic reactions. α, β-Unsaturated aldehydes, ketones and esters are attacked by carbon centered radicals exclusively at the β-position of the olefinic carbon atom while anionic species competes for olefinic as well as carbonyl carbon atom (Figure-**1**).

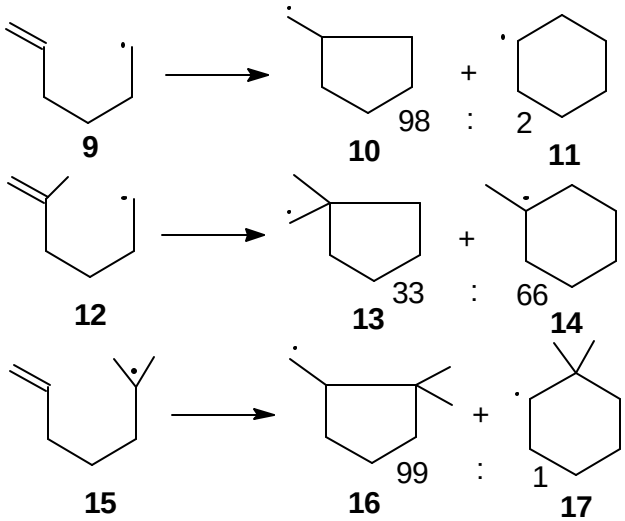


8

X = H, R, OR

Figure-1

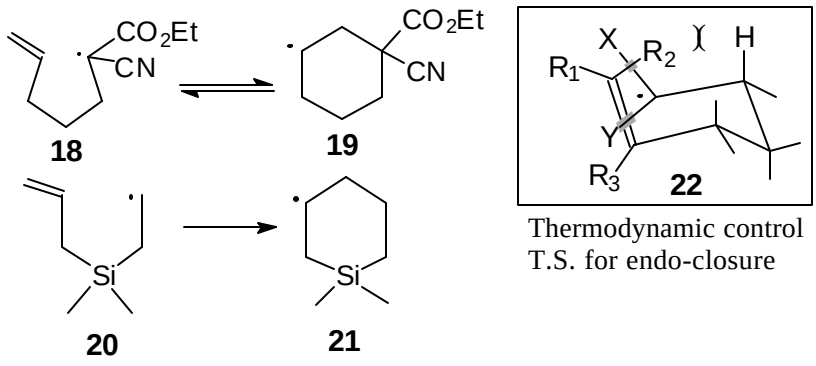
The regioselectivities of radical cyclizations are generally governed by their substituents and the kinetics of radical cyclizations. 5-Hexenyl radicals cyclize predominantly in an *exo*-mode to give a five memebered ring than an *endo*-cyclized six-membered ring.[13] Thus, the less stable primary radicals are formed faster than the more stable secondary radicals.[14] The regioselectivities are explained by stereoelectronic effects[14] with an unsymmetrical transition state in which the distances between the attacking radical and the two olefinic carbon atoms of the alkene are unequal.[15] Due to this fact it leads to faster cyclization to a five membered ring than a six membered ring. The ratio of five membered to six membered ring also depends on the substituents at the olefinic bonds. Scheme-**3** summarizes the substituent effects.



9 **10** **11** **12** **13** **14** **15** **16** **17**

Scheme-3

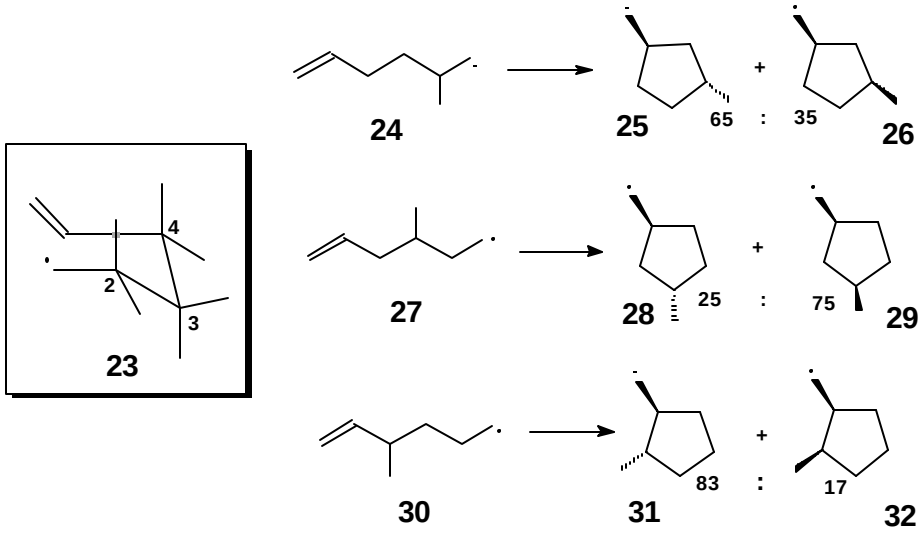
Electron withdrawing substituents that lower the LUMO of the alkene acceptor dramatically accelerate the cyclization of nucleophilic alkyl radical. Heteroatoms such as nitrogen and oxygen at γ-position of the radical center significantly accelerate the closure. Substituent at β or δ position has modest beneficial effect while alkyl susbtituents on the radical bearing carbon have little effect. However, Julia has reported[16] that with heavily substituted resonance stabilized radicals (eg. cyanoester, **18**), the cyclization favours predominantly to a six membered ring (Scheme-**4**). As the cyclization of a hexenyl radical is irreversible, the formation of a five membered ring must be kinetically favoured. On the other hand, the isomeric cyanoester radicals can be equilibrated under cyclization conditions to give rise to a more stabilized cyclohexane equilibrated product. Another case where the presence of a heteroatom like silicon, in the radical chain (**20**), favours a six-membered ring formation.[17]



Scheme-4

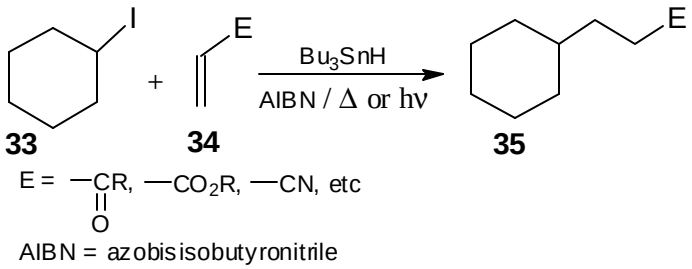
The stereoselectivity of 5-*exo*-hexenyl radical cyclization giving a five membered ring is predicted by applying Beckwith-Houk transition state model[18,19] which advocates four basic transition state structures. They are chair-equatorial, chair-axial, boat-equatorial and boat-axial. Two important guidelines are also put forward by Beckwith for hexenyl radical ring closures which states that 1 or 3-substituted radicals preferentially give *cis*-disubstituted cyclopentyl products whereas 2 or 4 substituted radicals mainly give *trans*-disubstituted products.[18b] The above rules can be explained by considering transition state structure (**23**), having distinguishable axial and equatorial positions at C2, C3 and C4. 5-

exo-Cyclizations largely prefer the substituents to be pseudo-equatorial rather than pseudo-axial (Scheme-**5**).



Scheme-5

Unlike intramolecular cyclizations, intermolecular radical additions are more difficult to conduct due to competing hydrogen abstraction. Giese[15b] has summarized the trends affecting the magnitude of k_a in terms of polar and steric effects (Scheme-**6**). Thus, the addition of electrophilic radicals to alkenes is accelerated by electron donating groups and decelerated by electron withdrawing groups. The reaction conditions should be designed carefully taking into account, the rates of the competing reactions in order to obtain maximum yields of the products.[15b]



Scheme-6

It is ironic that radical reactions once thought to be capricious and unpredictable have a higher level of predictability in complex settings than most other types of reactions.

This predictability can be attributed to the vast knowledge of radical rate constants and substituent effects in simple systems and to the fact that these effects in simple systems can often be compared to complex systems in a straightforward fashion. These prominent aspects of free radical methodology has led to the gradual emergence of homolytic disconnections which have been steadily taking their place besides more familiar ionic disconnections in the annals of synthetic chemistry.

The discussion in this introductory chapter is limited to the reactions involving the homolytic cleavage of a C-X bond to generate a carbon centered radical and its possible reactions.

1-1.1. Tin hydride method for carbon radical generation

Though several methods for conducting radical reactions have emerged through the years, the method that attained much attention and dominated the field is the tributyltin method.[20] The burgeoning use of this methodology in the field of organic synthesis owes much to the splendid flexibility of organotin reagents which enables them to flourish with an exceptionally wide range of substrates and reaction conditions. This method has been studied extensively since decades by scientists from all over the world and it has also been reviewed many times.[20] Therefore, only the significant aspects of tin hydride chemistry is being briefed herein to put the present study in proper perspective.

In a typical tributyltin hydride reaction, the tributyltin radical generates an alkyl radical $R^{\bullet}$ from an organic substrate (R-X) by atom or group abstraction. The radical $R^{\bullet}$ in turn reacts with Bu_3SnH to generate $Bu_3Sn^{\bullet}$ and reduced product RH (Scheme-**7**).

$$Bu_3SnH \xrightarrow{AIBN} Bu_3Sn^{\bullet} \qquad \textbf{.....eq.1} \text{ (Initiation)}$$

$$Bu_3Sn^{\bullet} + R{-}X \longrightarrow R^{\bullet} + Bu_3SnX \qquad \textbf{.....eq.2} \text{ (Propagation)}$$

$$R^{\bullet} \longrightarrow R' \text{ (addition or cyclization)} \qquad \textbf{.....eq.3}$$

$$\left.\begin{aligned} R'^{\bullet} + Bu_3SnH &\longrightarrow Bu_3Sn^{\bullet} + R'{-}H \\ R^{\bullet} + Bu_3SnH &\longrightarrow Bu_3Sn^{\bullet} + R{-}H \end{aligned}\right\} \text{hydrogenation} \quad \textbf{...eq. 4}$$

Scheme-7

These radical reactions are usually initiated by azobisisobutyronitrile (AIBN). The transferability of various atoms and groups X to tin radicals is generally in the order of I > Br > SePh > OC(S)Sme > Cl > SPh.[21] The reactivity of various R' toward tin hydride is in the order aryl > vinyl > alkyl > allyl > benzyl. There is not much difference in the reactivity of primary, secondary and tertiary alkyl radicals towards tin hydride.

Absolute rate constants are available for almost all elementary processes of the tin hydride-mediated reactions.[22] The rate constant for cyclization varies widely as a function of substituent, however, most carbon substituents attached to radical center have little effect on the rate constant for hydrogen atom abstraction. The concentration of tin hydride is an important variable by which the product distribution can be controlled in certain reactions. The presence of low concentration of tin hydride is often advantageous to increase the lifetime of the intermediate radicals and, thus, slow radical reactions can be controlled.

1-1.2 Drawbacks of the tin hydride Method

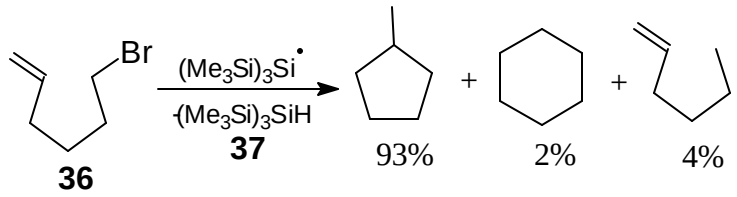
Despite versatile applications of tin hydride method of radical generation in organic synthesis, some serious limitations, as described below, have initiated spurt of activities in searching alternative approaches for carbon radical generation.

Organotin compounds are toxic and create severe disposal problem.[23] Another serious disadvantage is the necessity to terminate the radical sequence by a fast irreversible hydrogen atom transfer leading to a product with the loss of functionality. The experimental procedures often require several hours, in order to keep tributyltin hydride concentration low,[24] for conducting slow cyclizations or addition reactions due to competing reduction of the starting material. Another problem associated with tin hydride is the contamination of desired products by traces of organotin compounds making their purification very tedious.[25]

1-1.3 Modified Variants and Alternatives for Tributyl Tin hydride Reagent:

To overcome the limitation of toxicity of tributyltin hydride, other mild and non-toxic reagents are invented. Chatgilialoglu has proposed[26] the use of tristrimethylsilylsilane

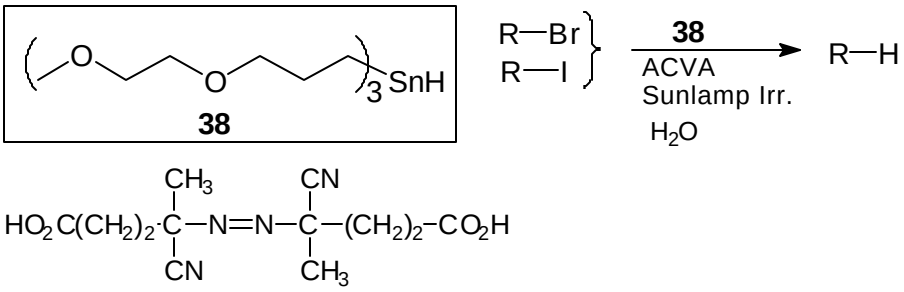
(TTMS) as an alternative to toxic tin hydride in generating radicals by the homolysis of –C-X bonds (X = halide, selenide, xanthate, isocyanates) (Scheme-**8)**. However, this reagent has been only successful in overcoming toxicity aspects of tin hydride reagent. Lack of restoring the functionality in the resultant product and its high cost limited its popularity.



Scheme-8

Germanium hydrides[27] were also introduced as an alternatives to toxic tin hydrides, but the versatile use of this reagent was limited due to its high cost and its inability to restore the functionality after termination.

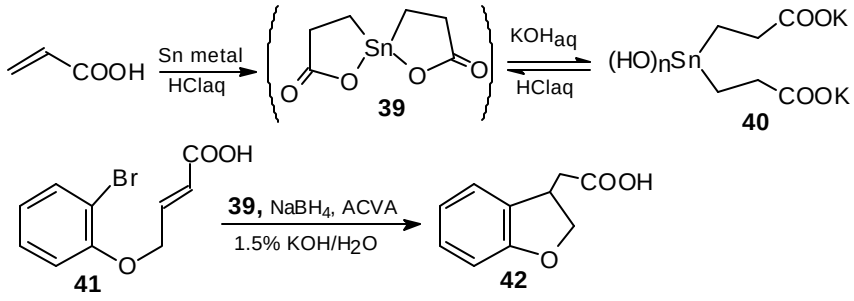
The purification problem of tin byproducts was also addressed by developing several protocols. Light and Breslow[28] synthesized a water soluble tin hydride (**38)** carrying three methoxyethoxy propyl groups by which alkyl halide reductions were carried out in water or in organic solvents under free radical conditions (Scheme-**9)**. Since this modified tin hydride is sufficiently soluble in water, purification and removal of tin byproducts from the reaction mixture was relatively much easier compared to tributyltin hydride. However, the use of this reagent has been shown only for alkyl halide reductions.



ACVA = 4, 4'-azobis(4-cyanovaleric acid)

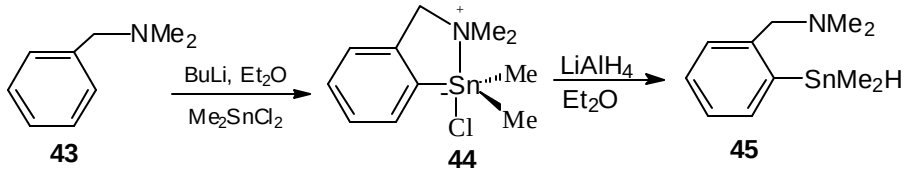
Scheme-9

Subsequently, Collum et al[29] have also developed another aqueous base soluble dialkyltin (IV) (**39**) reagent that could reduce alkyl and aryl bromides efficiently in quantitative yields in the presence of $NaBH_4$ and ACVA [4,4-azobis(4-cyanovaleric acid)] (Scheme-**10**). Though, water soluble and aqueous base soluble tin hydrides were proposed as an alternative, they were not fully evaluated for solving purification problems. One of the important reasons for the difficulty in the product purification was the non-polar nature of tin-containing materials formed in these reactions that were difficult to separate from non-polar organic products.



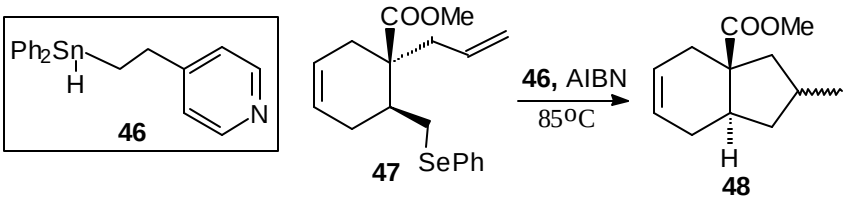
Scheme-10

To overcome this problem, Vedejs et al[30] introduced a polar tin hydride (**45**) as a radical chain reducing agent which was found to dehlogenate halides to hydrocarbons depending upon the solvent. No initiator was necessary for radical dehalogenation reaction utilising **45** as a reagent and slow addition of **45** was also not necessary (Scheme-**11**). The polar reagent (**45**) and its decomposition products (the tin byproduct in dehalogenation is tinhalide) are easily removable. The usage of **45** was also demonstrated to alkyl halide reductions only to obtain dehalogenated products.



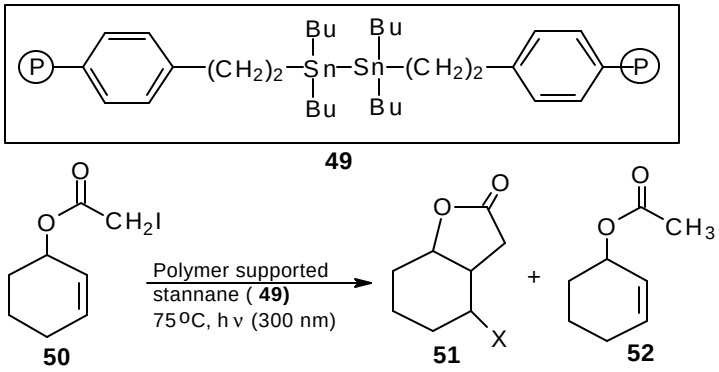
Scheme-11

Another modified polar tin hydride reagent, diphenyl[2-(4-pyridyl)ethyl]tin hydride (4**6**) was developed by Clive et al,[31] particularly, useful in the reductions where separation posed a serious problem when tributyl- and triphenyltin hydrides were employed. The products were easy to purify due to the high polar nature of stannane **46** and its derivatives compared to corresponding Bu_3Sn and Ph_3Sn species (Scheme-**12**).



Scheme-12

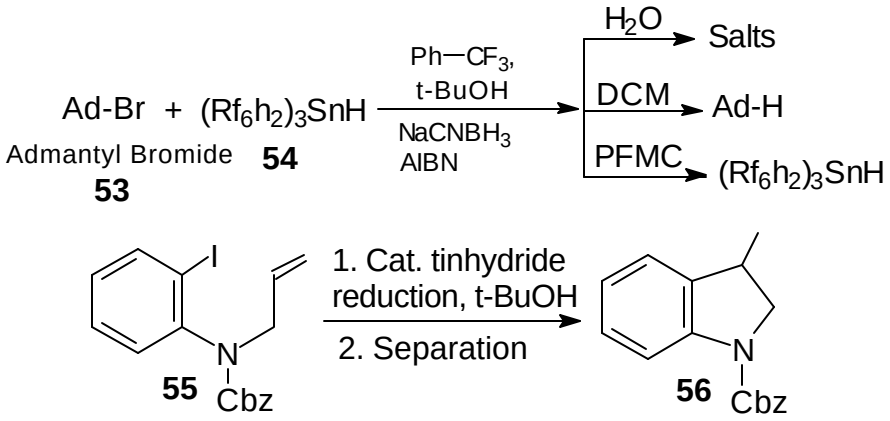
These reagents have offered solutions to some extent in overcoming the problem of purification from the tin contaminated reaction mixtures, however, it would always be preferable to avoid product contamination rather than developing methods for the separation of tin byproducts. Therefore, another polymer supported tin reagent (**49**) was developed by Neumann et al[32] in which product contamination was avoided due to the attachment of active tin species on either inorganic or organic polymeric matrices (Scheme-**13**). This reagent was considered to be superior and convenient substitute for tin hydrides as the strength of the added H-donor can be adjusted to meet the thermodynamic and kinetic requirements of the radical reaction.



Scheme-13

Besides various modifications, variants and new reagents, the workup procedures of tin hydrides mediated reaction have also been modified in order to afford desired products free from tin contaminants. Crich et al[33] have proposed one such method for the practical removal of organotin contaminants from the reaction mixture involving treatment of crude reaction mixture with $NaBH_3CN$ and t-BuOH followed by heating for an hour. $NaBH_3CN$ reduces the generated tributyltin halide to Bu_3SnH in t-BuOH at room temperature quite rapidly and quantitatively. These tin hydrides are very non-polar and can be washed off rapidly from silica gel with hydrocarbon eluents to give products without tin contaminants.

Unfortunately, most of the workup procedures were used only for the separation of tin byproducts and not for its recovery in a useful form. Therefore, Curran et al[34] have reported the development of fluorous tin hydrides, a new class of reagents which can be used, recovered and reused in radical reactions. A series of papers[35] have been published on this concept of fluorous phase as an alternative to other commonly used phases in organic synthesis. Fluorous tin hydrides of the general formula $[Rf\ (CH_2)_n]_3SnH$ and $[Rf\ (CH_2)_n]Me_2SnH$ were prepared and utilized for conducting reductive radical reactions. An important feature of this method was the separation of tin products from the organic products by convenient liquid-liquid or solid-solid extractions (Scheme-**14**).



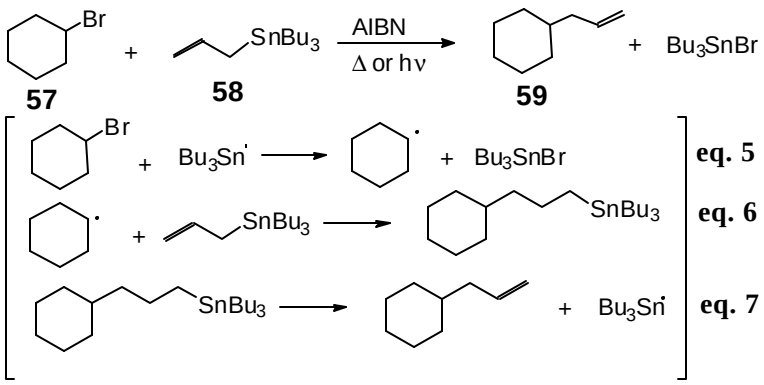
Scheme-14

Although, the toxic and expensive tin hydride reagents were tried to be replaced by other cheaper hydrogen donating compounds containing Si-H and P-H[36] bonds, alkyl and aryl substituted silanes seemed to be good alternatives to the stannanes. However, these reagents require relatively drastic reaction conditions due to their low H-donating ability. Chatgilialoglu[37] and Nishiyama[38] have introduced silaanthracenes as the radical reducing agent for the deoxygenation of secondary alcohols and dehalogenation of organic halides, however, the use of these reagents were evaluated only as reducing agents.

All the above discussed methods offer more or less advantageous solutions and alternatives to address the limitations of tin hydrides, however, the problem of functionalization of the products remained elusive. This aspect has also been addressed thoroughly by many groups and several new methods as described briefly below have been designed and executed leading to products with functional group incorporation.

1-2 Group and Atom Transfer Radical Reactions

In the light of the pioneering work of Migita[39] and Pereyre[40] Keck[41] reported a free radical allylation with allyl stannanes as a powerful approach for the group transfer radical reaction. An example of this reaction is depicted in the Scheme given below (Scheme-**15**). Although, this method could overcome the problem of the loss of functionality in a classical radical reaction, the tin toxicity associated with **58** remained unsolved. Lesser toxic allyl plumbanes[42] were also tried as substitutes for allylstannanes but with little advantage. The usage of allylgermanes and allyl silanes were also found disadvantageous owing to very slow cleavage of -C-Si- and –C-Ge bonds.[42]

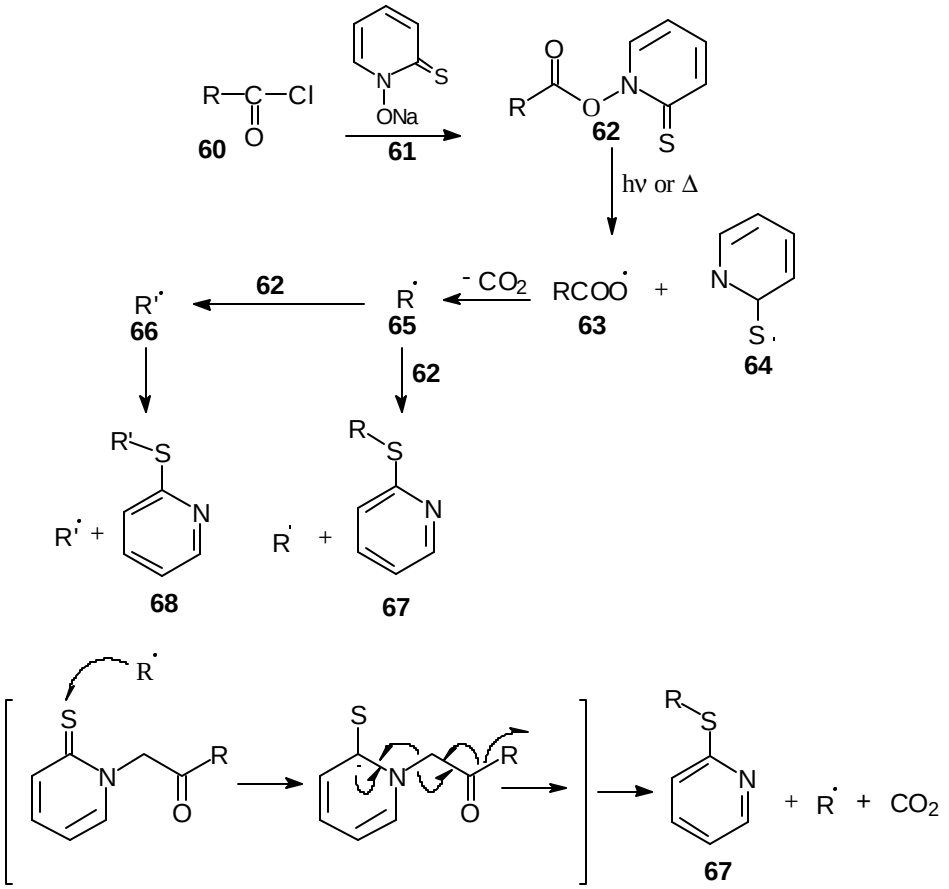


Scheme-15

During these developments, Barton reported an important method for carbon centered radical generation.[43] The advantage of this method lies in its non-reductive approach, simple experimental procedure and generality of the method.

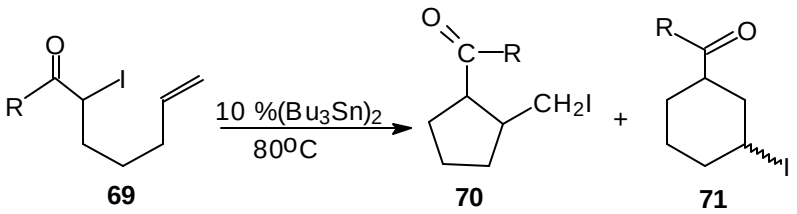
Acid chlorides (**60**) can react with salts of N-hydroxypyridine-2-thione (**61**) to give O-acylthiohydroxamate esters (**62**). **62** can undergo homolytic cleavage by heat or light to afford the carboxy radical (**63**) and thiopyridyl radical (**64**). Decarboxyllation of the carboxy radical provides radical R$^{\bullet}$ (**65**) which can either react with starting thiohydroxamate ester (chain transfer) or suffer rearrangement or addition to give the new radical R'$^{\bullet}$ (**66**). Reaction to form R'$^{\bullet}$ must be rapid than the direct addition to starting hydroxamate. The most basic aspect of Barton's reaction is outlined in the Scheme-**16**.

The potential aspect of Barton's method is that intermediate radicals R$^{\bullet}$ can be intercepted by a variety of neutral molecules, thus, giving rise to diverse functional group incorporations.[44] Moreover, slow addition and cyclizations are also possible and the reactions are easy to run since the thiohydroxamate ester can either be isolated or generated in situ. Despite all the advantages, this method could not become popular for usage in natural product synthesis.



Scheme-16

Curran and his group have introduced[45] iodine atom transfer reaction in a wide variety of radical reactions. In comparison to tin hydride method where net reduction always occurs, the iodine atom transfer method involves isomerization and the resultant alkyl iodide can be used for subsequent functionalization. The radical reactions utilising tin hydride method has been observed to be very important in the case of rapid cyclizations whereas iodine atom transfer is extremely useful in the case of slow cyclizations. In general, the strategy involves the sun lamp irradiation of a benzene solution containing the reactants and a catalytic amount of hexaalkylditin. One such example is isomerization of the α-iodocarbonyl compound (**69**) to **70** and **71** (Scheme-**17**).



69 **70** **71**

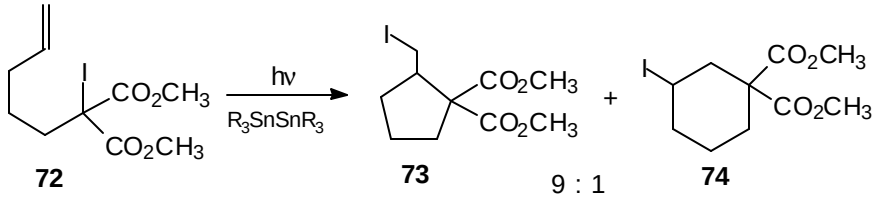
1a) R = OMe, t-OBu — 92 : 8

1b) R = OMe, I = Br

1c) R = t-Bu, Ph — 75 : 25

Scheme-17

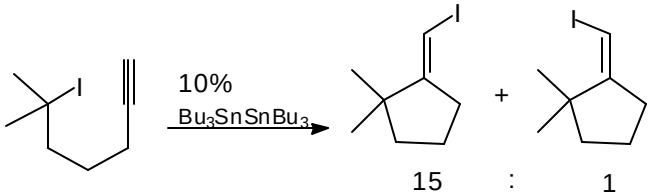
Iodomalonates are another important class of compounds that have proved to be very useful for atom transfer cyclizations. Iodomalonate (**72**) is known to undergo cyclization in the presence of light and hexaalkylditin to give 5-*exo* (**73**) and 6-*endo* (**74**) products in good yield with a ratio of 9:1 (Scheme-**18**). Owing to the superior iodine atom donor capability of iodomalonate, the reaction is reported to proceed more rapidly and cleanly at lower temperatures.



72 **73** 9 : 1 **74**

Scheme-18

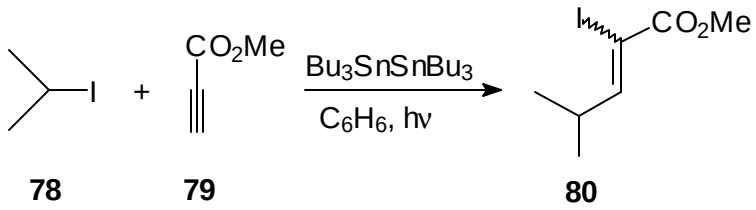
5-Hexynyl radicals are also known to undergo cyclization in an exo-mode via a vinyl radical intermediate to give vinyl iodides (**76** and **77)** (Scheme**-19**).[46] Since vinyl radicals are less stable than alkyl radicals, the iodine atom transfer step have been



75 **76** 15 : 1 **77**

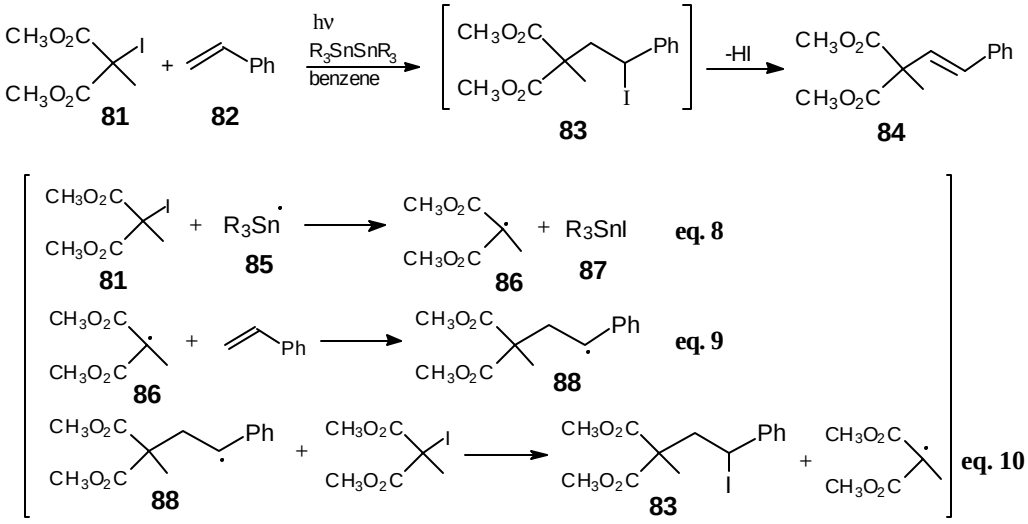
Scheme-19

noticed at a relatively very fast rate. Furthermore, *sec*- and *tert*- alkyl iodides are reported to add smoothly to electron deficient alkynes like methylpropiolate (**79**) under standard atom transfer conditions to give iodine atom transfer adduct **80** (Scheme-**20**).[47]



Scheme-20

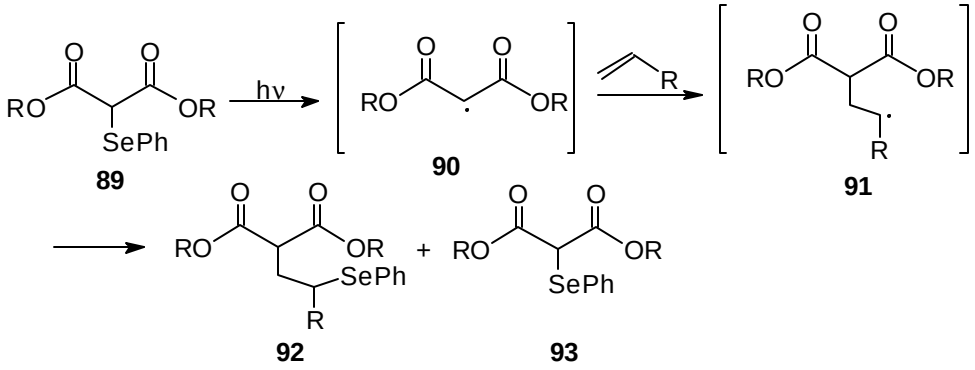
Chang[47] has also demonstrated that iodomalonates (**81**) can be added to alkenes with much ease (Scheme-**21**). Unlike tin hydride method, the malonyl radicals generated here have sufficient lifetime for addition and the key chain transfer step is very rapid for this method. The propagation steps of this iodine atom transfer reaction are depicted in the scheme given below.



Scheme-21

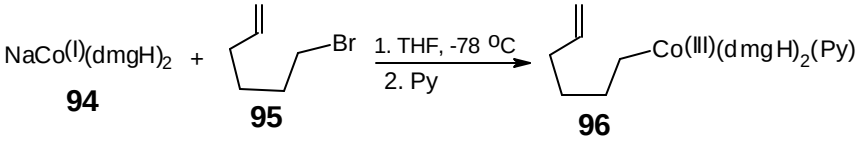
Bosch has reported[48] the rate constants of halogen atom transfer from iodomalonates to simple alkyl radicals. The rate constant of methyl iodomethyl malonate to a primary alkyl radical was estimated to be $\approx 1.8 \times 10^{9}\ M^{-1}s^{-1}$.

In another interesting approach, Byers has reported[49] the phenylseleno group transfer malonate group addition to an alkene upon photolysis of phenylselenomalonates (**89**) (Scheme-**22**). The electrophilic malonyl radical (**90**) is reported[49] to add efficiently in an exothermic fashion to the unactivated olefins and alkynes. The rate constant for PhSe transfer from phenylselenomalonate to primary alkyl radicals was found to be 8 X 10^5 $M^{-1}s^{-1}$. Though, both the above reactions involve same malonyl radical intermediate, the comparison of the rate constants for the two malonates with iodo and phenylselenyl groups establishes the rapidity with which an iodine atom transfer occurs in comparison to that of a phenylselenyl group transfer.



Scheme-22

Among the group transfer reactions, the Cobalt group transfer method is analogous to the halogen atom transfer reactions. Organocobalt complexes for radical reactions are readily made available by the nucleophilic substitution of an organic halide or tosylate with the sodium salt of corresponding cobalt(I) complex (Scheme-**23**).[50]

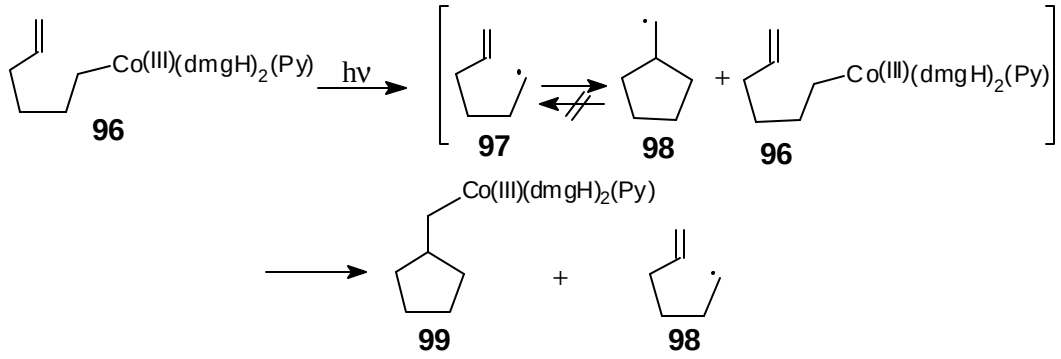


$(dmgH)_2$ = bis(dimethylglyoximato)cobalt(III)

Scheme-23

The carbon-cobalt bonds in these complexes (**96**) are weak and get easily homolyzed by heat or light to generate alkyl radicals which has been used for both C-C and carbon–

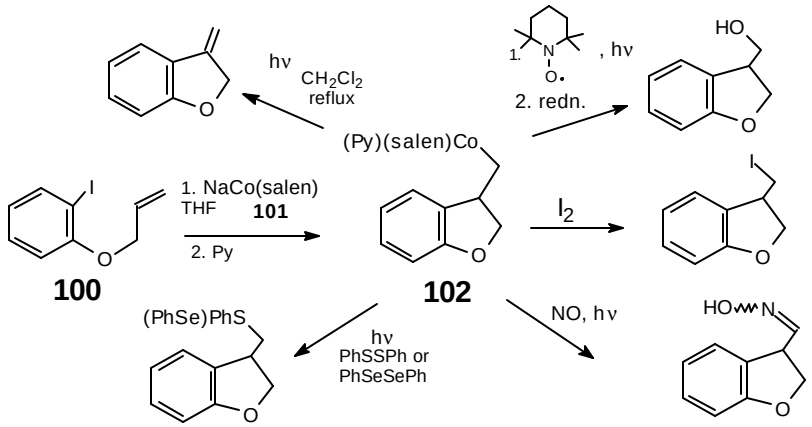
heteroatom bond forming reactions. Generally the organocobalt(III) precursors are not isolated, they are generated and photolyzed in situ. All the organocobalt transformations may not proceed by the same mechanism[51] but most of these transformations are reported to involve C-Co bond homolysis to generate alkyl radicals. A study reported by Kochi[50] on 5-hexenylcobalt(III) complexes provides mechanistic evidence for these processes and highlight alkyl radicals as the prime reactive intermediates. It has been reported[50] that the rearrangement of 5-hexenyl cobalt(III) complexes involve homolytic cleavage of a C-Co bond followed by the standard Cobalt group transfer hexenyl radical cyclization (Scheme-**24**). Since the hexenyl radical cyclization is irreversible, all of **96** isomerizes to cyclic compound **99.** Despite the similarities with an atom transfer reaction they basically differ in their mechanism. Atom transfer reactions are chain processes, but organocobalt reactions are non-chain processes that rely on persistent radical (Co(II)) coupling.



Scheme-24

Pattenden has demonstrated[52] that treatment of aryliodide (**100**) with cobalt (I) salen anion in dark directly gives a cyclized complex (**102**) in 70 % yield (Scheme-**25**). To explain this, it was presumed that an aryl radical was probably generated by single electron transfer from cobalt (I) followed by loss of iodide. A significant advantage of the cobalt transfer method is that cobalt hydride can be eliminated from the product on irradiation in the absence of any reagent. Furthermore, it was reported that cobalt group

could be replaced by a number of functional groups including hydroxyl, halogen, oxime, phenylthio and phenylseleno groups by performing the irradiation in the presence of added reagents.

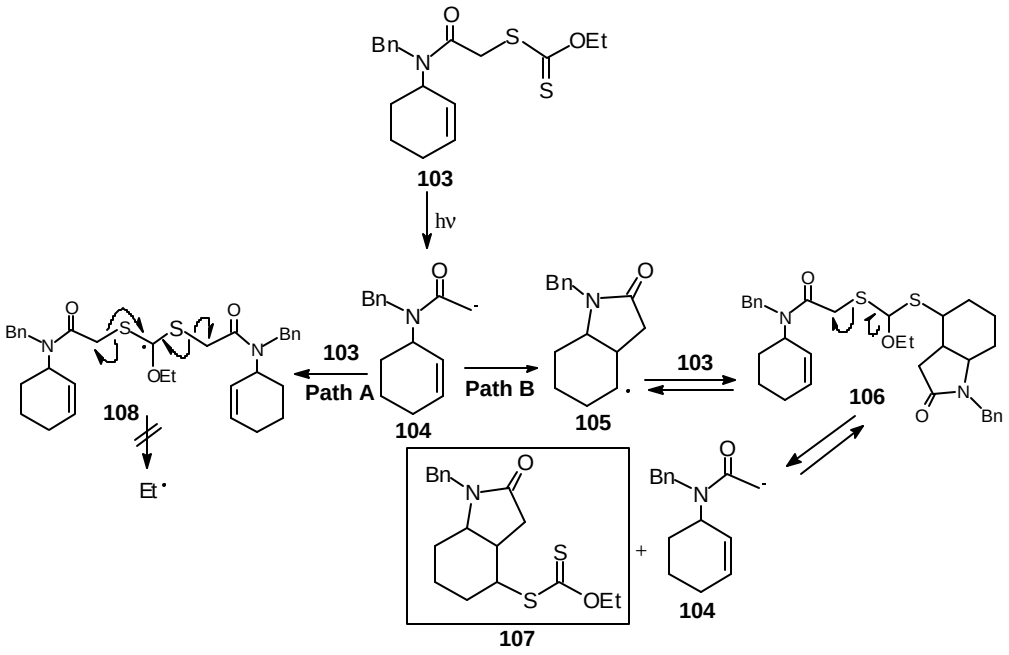


Scheme-25

Although, mechanistic differences make synthetic planning less straightforward, many later developments in this field justifies the potential of this method for synthetic applications.[53]

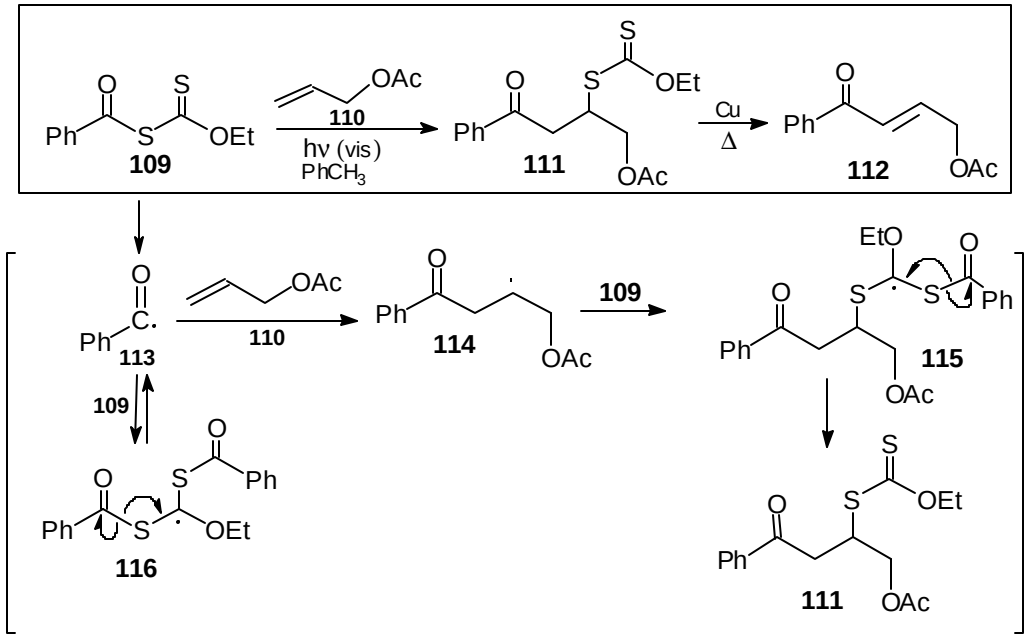
Dithiocarbonates or xanthates are another interesting class of group transfer reagents that have gained much prominence during the past decade. Unlike a Barton-McCombie reaction,[54] where radical is generated by C-O bond scission, in this case C-S bond scission generates an alkyl radical R• and a new xanthate. Overall a new C-C bond and a new C-S bond are created in this reaction.

The mechanism[55] of a typical xanthate group transfer reaction is depicted in Scheme-**26**. A variety of synthetically interesting free radicals can be produced and captured since the last propagating step is the reversible transfer of the xanthate group. Another interesting feature of this reaction is the favoured equilibration of reversible step in the forward direction provided R• is more stable than the adduct radical **105**.



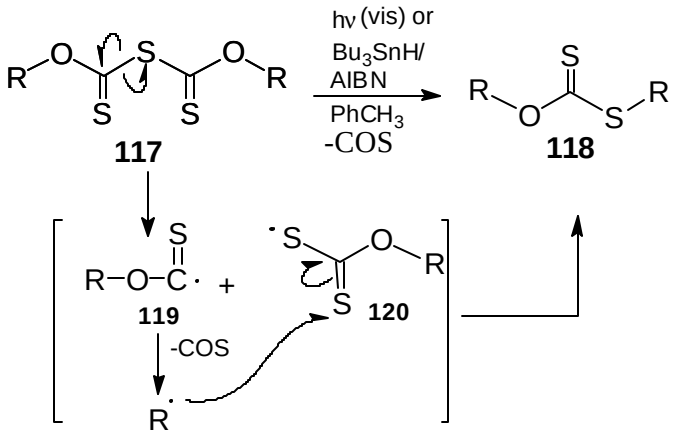
Scheme-26

Zard[56] has shown that acyl radicals (**113**) can be generated from *S*-acyl xanthates (**109**) and could also be trapped in inter or intramolecular fashion by using suitable olefins (Scheme-**27**). The xanthate functionality can be removed by reduction with dilauroyl peroxide in propan-2-ol or by treatment with DBU or Cu.



Scheme-27

In continuation of their work, Zard[57] has further reported another class of xanthates, the xanthic anhydrides ROC(S)SC(S)OR (**117**) derived from primary and secondary alcohols. Irradiation of **117** leads to a radical chain reaction to give corresponding xanthates (**118**) with the loss of carbonoxyl sulphide (COS) (Scheme-**28**). The reaction of xanthic anhydride could be initiated by Bu_3SnH/AIBN or light. Since these anhydrides are easily made from alcohols via the xanthate salt, the process constitutes a method for generating radicals from primary or secondary alcohols and a way to replace a carbon-oxygen bond with a carbon sulfur bond homolytically. These xanthic anhydrides have become a convenient source of alkoxythiocarbonyl (**119**) and alkyl radicals.

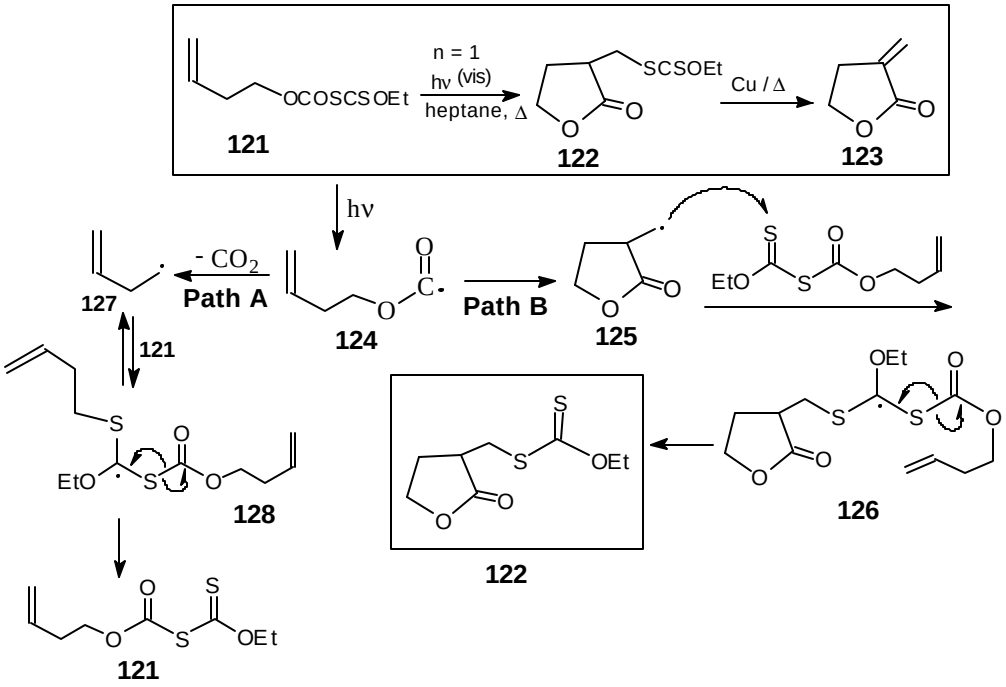


Scheme-28

Furthermore, S-alkoxycarbonyl xanthates of the type ROC(O)SC(S)OCH_2R (**121**) are reported as the reagents for generating alkyl radicals from simple alcohols.[58] Usually, the alkoxy carbonyl radicals (ROCO$^{\bullet}$) were scarcely used as precursors for corresponding alkyl radicals since release of CO_2 from these species is relatively slow. In the present case, the slow release of CO_2 from these species have allowed their ready capture with an appropriate olefin, since its reaction with xanthate precursor is reversible and degenerate

(Path A). The capture of this radical can either be in an intra or intermolecular fashion, giving rise to lactones or esters. (Scheme-**29**).[58]

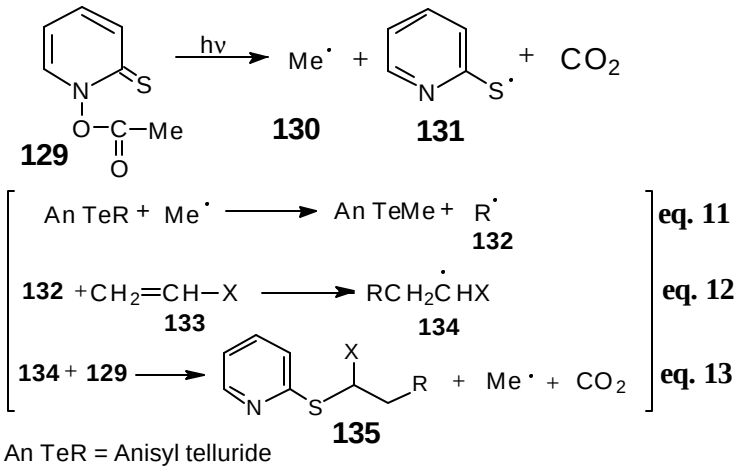
The advantage of the xanthate group transfer reaction may be gauged as it doesn't involve any heavy or toxic metal and the starting materials are cheap and readily available. The end product is also a xanthate which can either be utilized for initiating another radical sequence or modified further by using sulfur chemistry. A variety of combinations of xanthates have been suggested for various inter and intramolecular olefinic traps.



Scheme-29

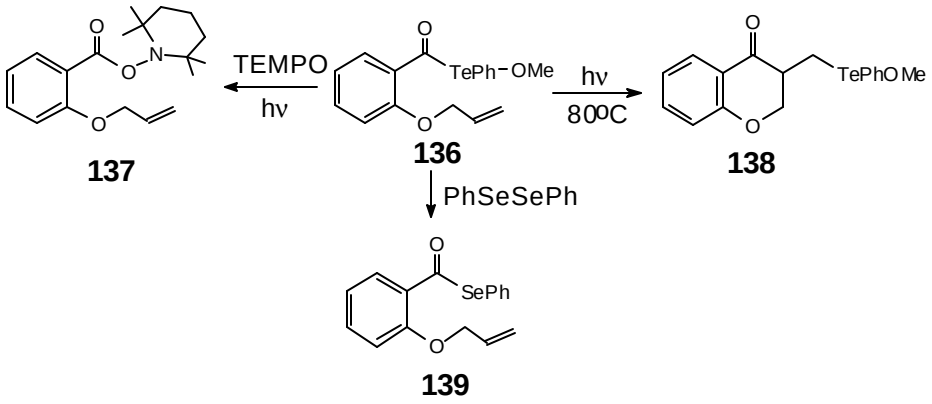
The most significant class of group transfers which have seen tremendous growth in the past 15 years have been the chalcogen group transfers reactions. The initial reaction can be dated back to late sixties during which the addition of disulfides to C-C triple bonds were reported.[59] In due course several group transfer addition, cyclization and annulation have also been reported.

Barton's group[60] have shown that diorganyl tellurides can act as an efficient exchangers of carbon centered radicals. They have utilized the potential of PTOC ester chemistry for generating complex radicals from a simple sacrificial PTOC esters by employing group transfers from aryl tellurides.



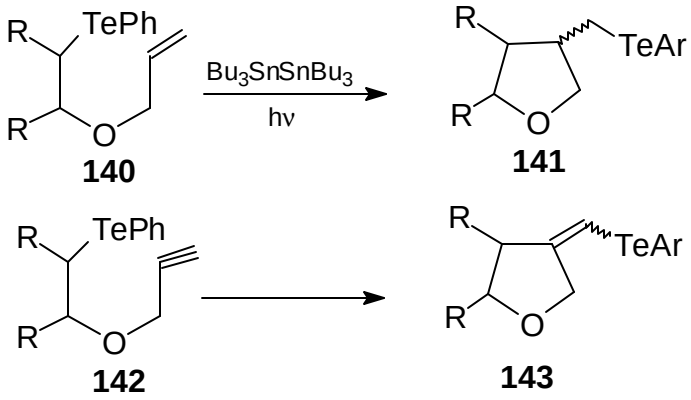
Scheme-30

Crich[61] in his series of papers have reported the advantages of acyl and aryl tellurium group transfer reactions. Photolysis of acyl aryl tellurides (**136**) is reported[61] to undergo group transfer addition and cyclization reactions (Scheme-**31**). These tellurides have been shown to act as an efficient source of acyl radicals.



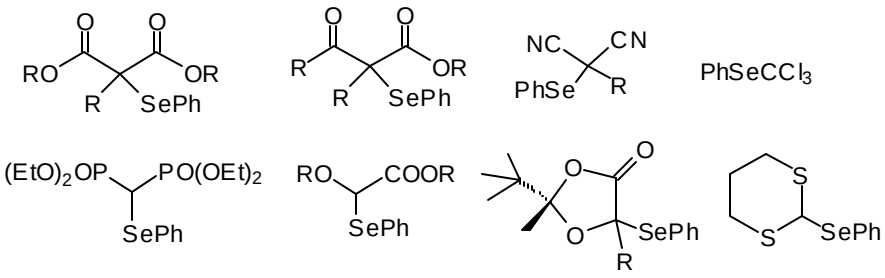
Scheme-31

Another tellurium group transfer radical reaction was reported by Engman[62] by irradiating β-(allyloxy) and β-(propargyloxy) alkyl aryl tellurides (**140** and **142**) in the presence of hexabutylditin producing tetrahydrofurans (**141**, **143**) as a mixture of *cis* / *trans* and *E* / *Z* isomers (Scheme-**32**). To explain the diasterioselectivity of these isomers, a chair like transition state was proposed in which the substituent preferably adopts a pseudo equatorial position.



Scheme-32

A number of radical precursors have also been reported for PhSe group transfers. Some of the important precursors are given in the Scheme-**33**.[63]

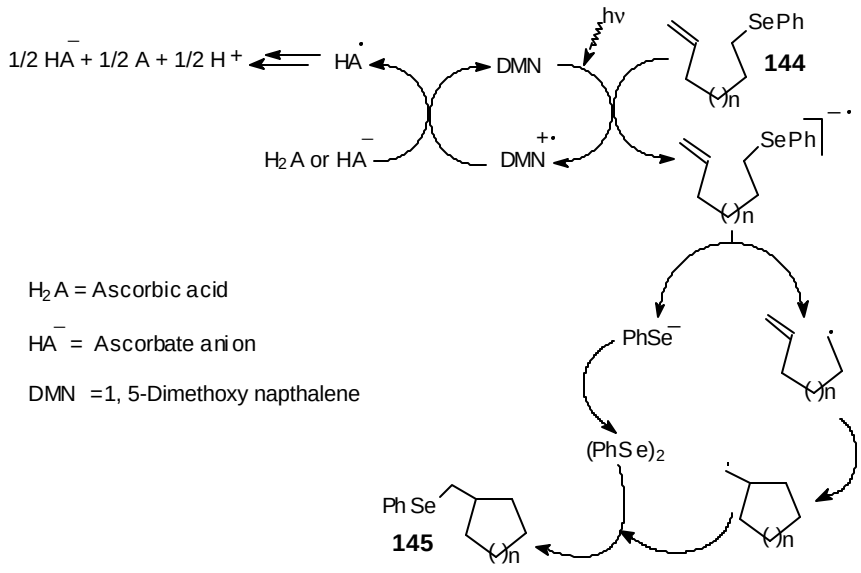


Scheme-33

As is evident by the multifarious radical reactions discussed above, the radical processes mostly involve homolytic disconnections of a C-X bond initiated either by light or heat in the presence of an initiator. Another area of reactions that have emanated and excelled to the vanguard of organic synthesis is the photoinduced electron transfer (PET) reactions.[64] The ascendancy of PET reactions in radical chemistry has propelled our

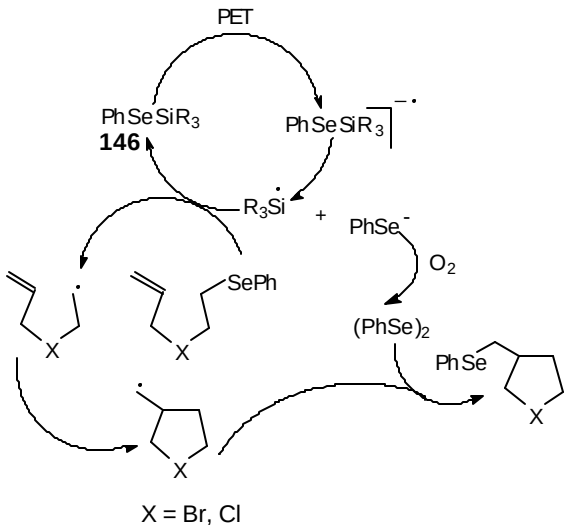
group to utilize and apply this chemistry for conducting phenylselenyl group transfer radical reactions.

Utilizing PET concept, phenylseleno group transfer radical reaction has been achieved by the reductive activation of a C-Se bond starting from simple alkyl selenides (**144**) from our group.[65] Irradiation of these alkylselenides (**144**) through a photosystem comprising 1,5-dimethoxy naphthalene (DMN) as a light harvesting electron donor and ascorbic acid as a sacrificial electron donor generated organoselenium radical anions [(-C-Se-)$^{-\bullet}$] (Scheme-**34**). It was discovered that these radical anions undergo mesolytic bond cleavage to produce carbon centered radicals and PhSeSePh. Carbon-centered radical further underwent cyclization and terminated by PhSeSePh formed by the oxidative dimerization of $PhSe^-$ to afford a cyclized product (**145**) in good yield (Scheme-**34**). This cleavage pattern was utilized for conducting various unimolecular group transfer radical reactions. Support for the electron transfer mechanism from excited DMN to –C-Se- moiety to generate (-C-Se-)$^{-\bullet}$ was provided by studying the diffusion controlled fluorescence quenching of DMN by organoselenium substrates, estimation of negative ΔG_{et} values and by the evaluation of other kinetic parameters.



Scheme-34

In continuation to this work, our group have also explored the possible reductive activation of a Se-Si bond utilizing the same photosystem as mentioned above.[66] For this reaction, a Se-Si reagent, $PhSeSiR_3$ with R = t-butyldiphenyl group has been chosen from various alkyl substituted silyl groups. Steady state photolysis of **146** with DMN and ascorbic acid led to the formation of **146**$]^{-\bullet}$ which further underwent mesolytic cleavage to produce a silyl radical a phenylselenyl anion (Scheme-**35**). This silyl radical was utilized to generate a carbon centered radical from the homolysis of carbon-halogen substrate thus setting up a phenyl selenyl group transfer radical cyclization reaction where radical termination takes place by PhSeSePh produced by the oxidative dimerization of the phenylselenyl anion.



Scheme-35

As evidenced by the topics discussed earlier, there is still scope to develop newer methodologies to initiate radical chemistry. Particularly, interesting would be to develop a catalytic approach for initiating radical reactions, considering the ecological impact of the known methodologies. In the forthcoming chapters of this dissertation our endeavor in this direction is presented.

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2-1 Introduction

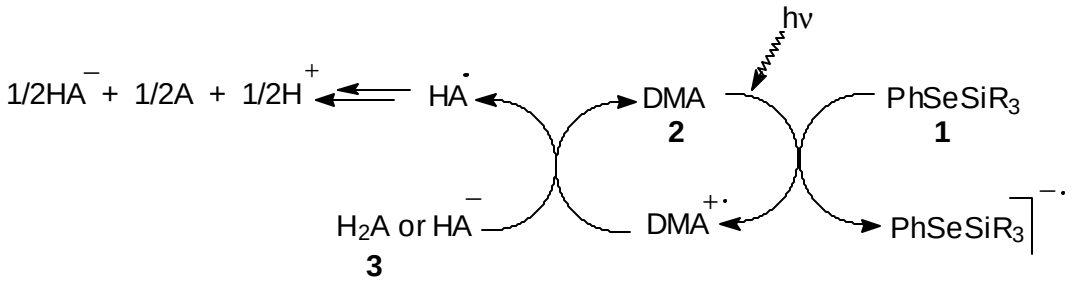
The usage of tin based reagents for initiating radical based reactions is still widely prevalent despite their known limitations and drawbacks. The cost of the reagents, their unstability, loss of valuable functionality due to premature termination of the initial radical by irreversible hydrogen abstraction and the difficulty encountered in removing organotin residues from the desired end products have made it a 'culpable' reagent in organic synthesis. Although significant developments to overcome some of these problems have come up by the introduction of polymer bound,[1] fluorous,[2] water soluble[3] tin hydrides and special workup procedures,[4] the toxicity of even trace amounts of tin is hazardous and thus, their disposal remains a serious environmental concern.

Several groups have tried to address this environmental issue by developing new reagents such as substituted germanes[5] and phosphorus-based reducing agents,[6] but they are either too expensive or not well developed. The recently developed disilanthracenes[7] and tetraaryldisilanes[8] have limited usage due to the difficulty in their preparation. Another class of reagents used for radical generation that gained attention recently are the salts of mercury,[9] cobalt,[10] manganese[11] and samarium.[12] Although, these reagents could achieve some excellent transformations, they suffer from the toxic effects of their own. Moreover, most of the approaches mentioned above invariably require stoichiometric usage of the reagents.

Since there is a growing demand to reduce the amount of toxic wastes and byproducts arising out of chemical reactions,[13] increasing emphasis is being laid on the invention and development of a catalytic and environmentally compatible strategy for initiating radical based chemistry owing to its burgeoning popularity among synthetic chemists. Substantial progress has been made in recent times towards designing and developing newer strategies for initiating radical-based reaction in catalytic manner. Some protocols in which tinhydride reagents are used either in catalytic amounts[14] or generated

in situ have been reported.[15] Recently, few tin free catalytic procedures are also fast gaining prominence, challenging the 'tyranny of tin'. Despite various approaches and strategies for performing radical based reactions, there is still dearth of a strategy that is catalytic, eco-compatible and economically viable. Considering these aspects, introduction of another strategy that meets the above criteria would be a welcome addition in the repertoire of organic chemists.

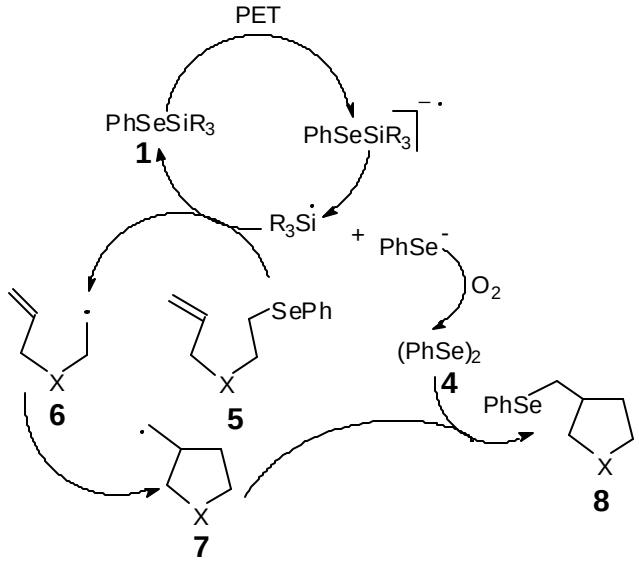
As disclosed earlier in the previous chapter, our group has successfully accomplished the photoinduced electron transfer reductive activation of a C-Se[16] and Se-Si bonds[17] to generate a carbon and silyl centered radicals, utilized for conducting unimolecular and bimolecular group transfer radical reactions, respectively.



H_2A = Ascorbic acid HA^- = Ascorbate anion DMA = 9, 10-Dimethoxyanthracene

Scheme-1

The ease of the generation of the $R_3Si^{\bullet}$ by the mesolytic cleavage of $PhSeSiR_3]^{-\bullet}$, produced by the PET reaction as shown in Scheme-**1** and its significantly higher rate constant (9.6 X 10 7 $M^{-1}s^{-1}$)[18] with alkyl phenyl selenides led us to envision a new opportunity to initiate radical reactions. Furthermore, as the fast oxidative dimerization of counter ion $PhSe^-$ gives PhSeSePh, an excellent radical quencher[19] and the rate constant for S_H^2 attackof 5-hexenyl radical upon PhSeSePh being1.2 X 10^7 $M^{-1}s^{-1}$,[20] it was visualized that a catalytic phenylselenyl group transfer radical reaction concept could be developed utilizing $PhSeSiR_3$ as the catalytic initiator through a cycle as shown in Scheme-**2**.

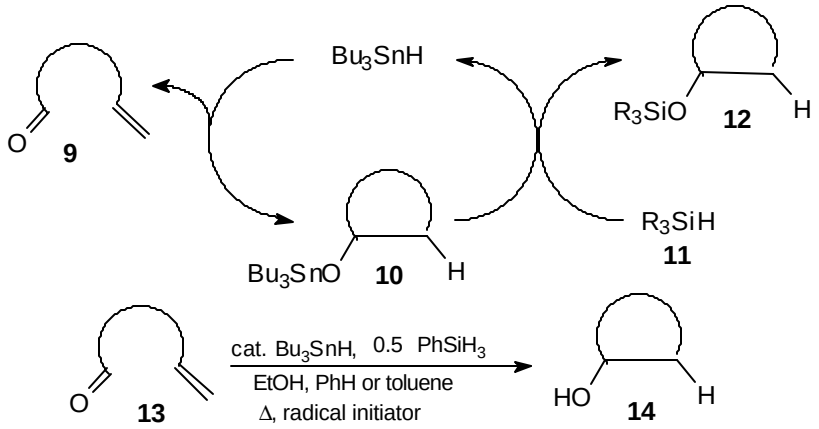


Scheme-2

However, before dwelling upon the details of our work, a brief introductory discussion on the reported catalytic methodologies for radical reactions would be appropriate to put the present discussion in proper perspective.

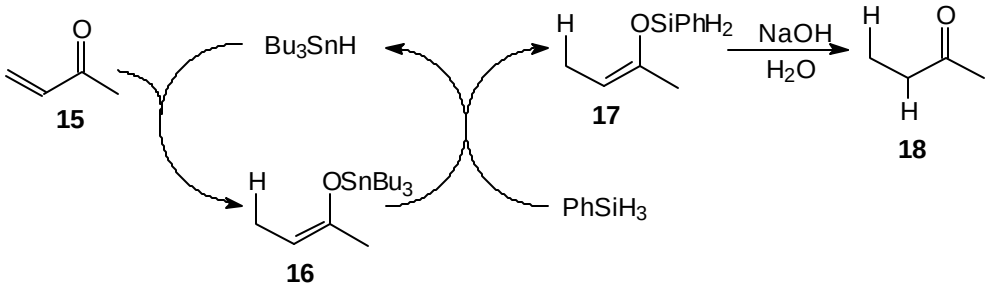
2-2 Tinhydride Catalyzed Reactions:

Owing to the toxicity as well as purification problems associated with R_3SnH reagents, development of an alternative method that diminishes the need of the stoichiometric use of R_3SnH in radical reactions have gained prominent significance. The initial concept on the development of catalytic processes for radical reaction using tin reagent can be dated back to late seventies[21] but only gained momentum in nineties due to the pioneering work of Fu[22] where they have effected the regeneration of Bu_3SnH by reducing the resultant Bu_3Sn-X utilizing $PhSiH_3$ as a reductant in stoichiometric amounts. The concept[22] can be depicted schematically by exemplifying the cyclization to **14** (Scheme-**3**).



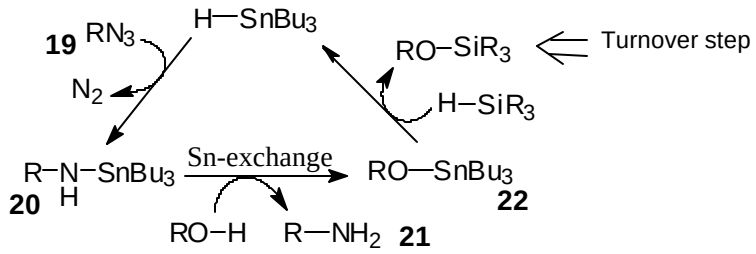
Scheme-3

The same strategy has also been extended[22b] for the selective reduction of α, β-unsaturated ketones **15** to **18** by the treatment of **15** with 10mole % of Bu_3SnH and 1.2 eq. of $PhSiH_3$ in refluxing toluene (di-tert-butyl peroxide as initiator) (Scheme-**4**).



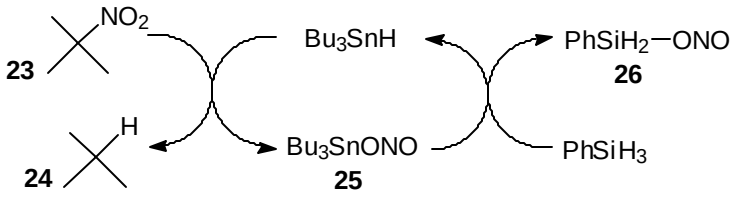
Scheme-4

Another strategy, also reported[23] from the same group, developed for the reduction of azides (**19**) to amines (**21**) by utilizing only 5 mole % of Bu_3SnH involves the reduction of Sn-O bond to Sn-H bond in the turn over step (Scheme-**5**). In this approach, addition of an alcohol is crucial for the transfer of Bu_3Sn group from the nitrogen of initially formed $RNHSnBu_3$ (**20**) to the alcoholic oxygen. The regenerated tin alkoxide (**22**) is finally reduced by the silicon hydride to regenerate Bu_3SnH catalyst.



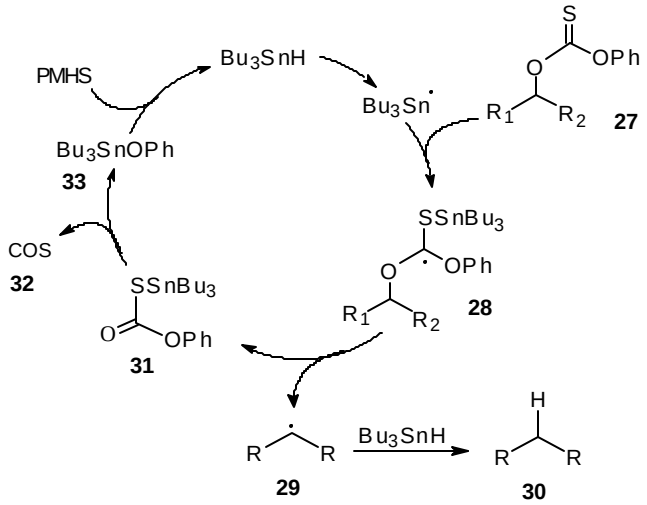
Scheme-5

Nitroalkanes (**23**) were also reduced to alkanes (**24**) utilizing almost similar strategy[14] using 10 mole % Bu_3SnH as shown in Scheme-**6**.



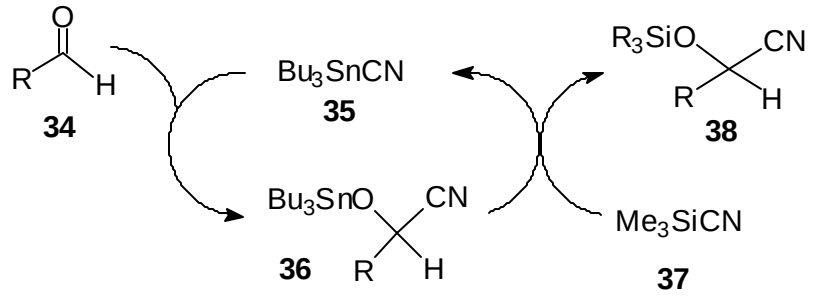
Scheme-6

In continuation to their work, they have also reported a catalyzed variant of Barton McCombie deoxygenation[24] reaction using Bu_3SnH as the catalyst (15 mole %) and polymethylhydrosiloxane (PMHS, TMSO-$(SiHMeO)_n$TMS) as the stoichiometric reductant.[25]



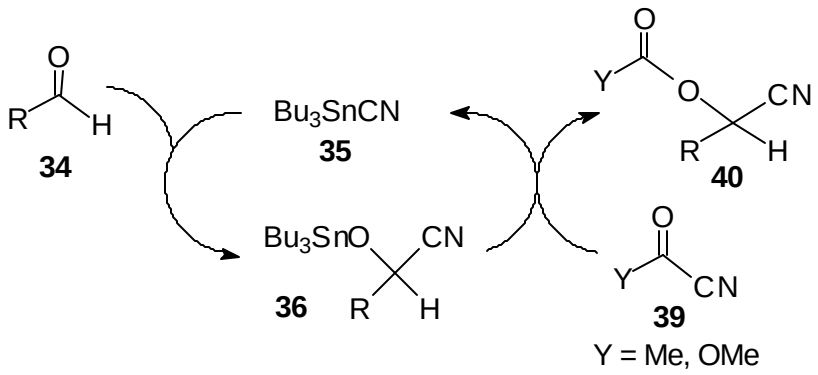
Scheme-7

In an analogous reaction, silylated cyanohydrins **38** were obtained from aldehyde **34** utilizing Bu_3SnCN (**35**) as the catalyst (Scheme-**8**).[26] The concept of this reaction involved the facile addition of Bu_3SnCN (**35**) to **34** in comparison to Me_3SiCN and the easy silylation of tin alkoxide intermediate **36**.



Scheme-8

Later,[27] same strategy was extended to prepare acylated cyanohydrins (**40**) from **34** by using Bu_3SnCN as the catalyst and acetyl cyanide (**39**) or methyl cyanoformate as the stoichiometric addend (Scheme-**9**).



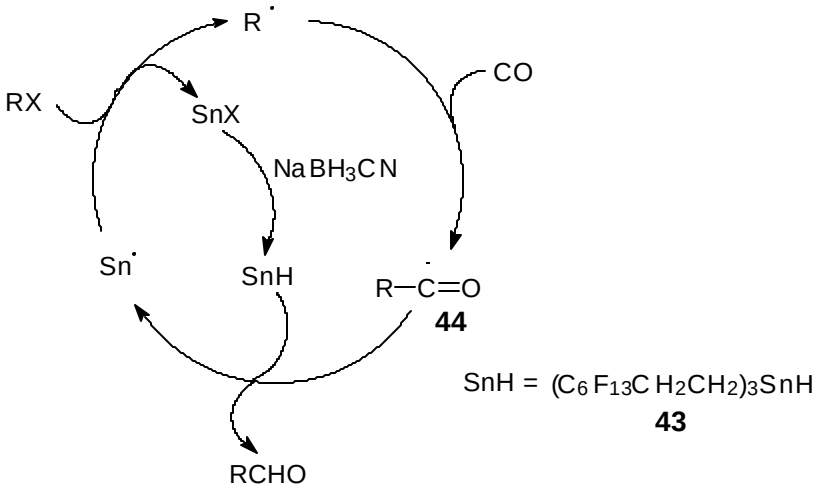
Scheme-9

In a more recent development, Maleczka Jr. has reported[15] in situ generation of organotin hydrides[16] by the reduction of tin halides by PMHS which was made hypervalent by the action of KF. Various reductions were performed using this method. For example,

catalytic reduction of **41** is reported to give **42** in 95 % yield by stirring a mixture of **41**, Bu_3SnCl, PMHS and aq. KF in the presence of catalytic amount of AIBN (Scheme-**10**).

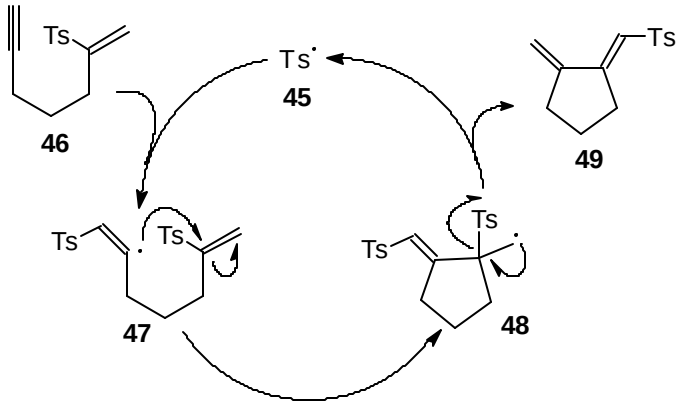
Scheme-10

Curran et al have introduced[28] fluorous tin hydrides for radical carbonylation reaction. In this approach, the reaction of alkyl halides with catalytic amounts of fluorous tin hydride (**43**) generates a carbon centered radical that undergoes acylation in the presence of CO to give an acyl radical **44** which on reduction with tin hydride affords carbonyl products. In the catalytic cycle, tin hydride is regenerated from the reduction of tin halides by $NaBH_3CN$ (Scheme-**11**).



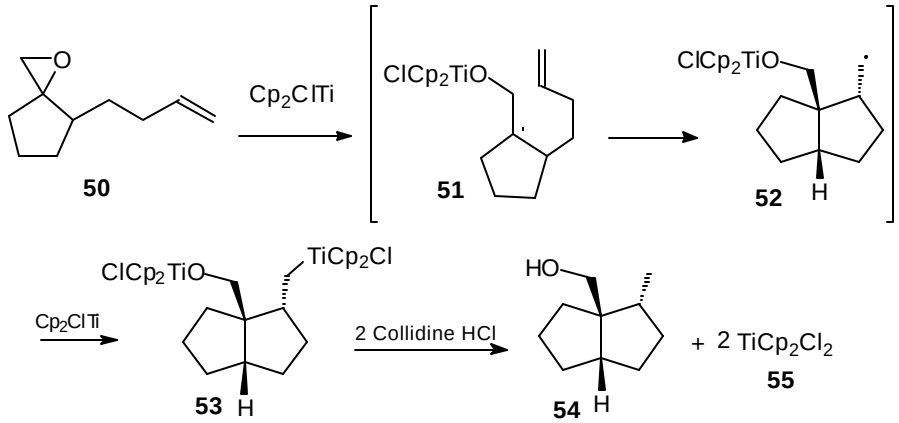
Scheme-11

Another free radical isomerization reaction initiated by a tosyl radical **(45)** generated by the homolysis of Se-phenyl-p-tolueneselenosulphonate (TsSePh), was reported by Caddick et al.[29] Addition of tosyl radical to the terminal alkyne of **46** results in the formation of β-tosyl vinyl radical **47** that cyclizes to **48.** Subsequent β-scission of the tosyl radical from **48** provides **49** as the final product (Scheme-**12**).



Scheme-12

Gansauer et al have reported[30] a transition metal catalyzed radical reaction with reagent control in which radicals are generated enantioselectively from epoxides. In this approach, radical intermediates **51** and **52** are generated by the catalyzed reductive opening of epoxide **50**, which could be highly stereoselecvtive. After the cyclization of the initially formed β-titanoxy radical, another radical is generated which was trapped with a second equivalent of titanocene dichloride to give an intermediate with a Ti-C bond. Both titanium-oxygen and –carbon bonds are protonated by collidine hydrochloride to regenerate titanocene dichloride (**55**) and liberated cyclization products.



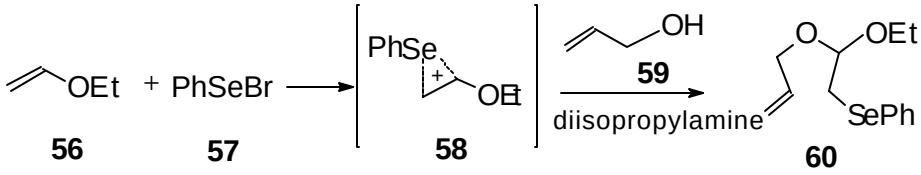
Scheme-13

With this brief introduction on the catalytic methodologies reported in the literature, we, present a dispel discussion of our concept (Scheme-**2**) by investigating the phenylselenyl group transfer radical cyclization from **60** (Scheme-**14**).

2-3 RESULTS AND DISCUSSION

2-3.1 Preparation of 2-(allyloxy)2-ethoxyethylphenylselenide (60)

Compound **60** was prepared in 80 % yield by the electrophilic addition of PhSeBr (**57**) on ethylvinyl ether (**56**) in the presence of allyl alcohol (**59**) and diisopropylamine (Scheme-**14**).[31]



56 **57** **58** **60**

Scheme-14

2-3.2 Thermodynamic evaluations for the selective ET processes between DMA and 1 in the presence of 60

When a mixture of **1** and **60** was considered to be PET activated utilising the above photosystem, there always existed the possibility of generating both $\mathbf{1}^{-\cdot}$ and $\mathbf{60}^{-\cdot}$ via electron transfer to **1** (Path-A) as well as **60** (Path-B). In order to ensure the thermodynamic preference for the formation of $\mathbf{1}^{-\cdot}$ over $\mathbf{60}^{-\cdot}$, the ΔG_{et} values for the formation of $\mathbf{1}^{-\cdot}$ as well as $\mathbf{60}^{-\bullet}$ were compared. The ΔG_{et} value for the formation of $\mathbf{60}^{-\bullet}$ was estimated through Weller equation (**Eq.1**). (Scheme-**15**).[32]

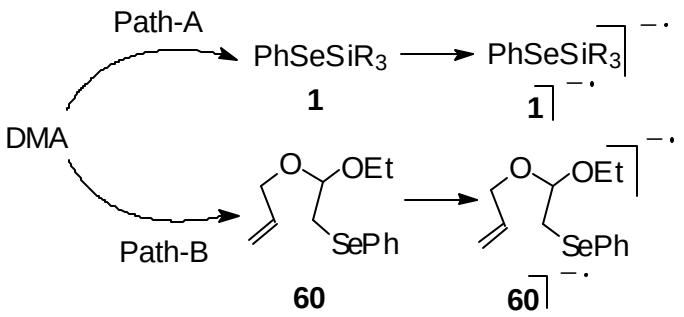
$\Delta G_{ds}{}^{+\bullet}{}_{DA}{}^{-\cdot}$ = $E_{1/2}{}^{ox}$ of D – $E_{1/2}{}^{red}$ of A – E_{exc} of D **Eq. 1**

$\Delta G_{ds}{}^{+\bullet}{}_{DA}{}^{-\cdot}$ = Gibbs free energy change for the formation of FRIP

$E_{1/2}{}^{ox}$ = Oxidation potential of DMA

$E_{1/2}{}^{red}$ = Reduction potential of **60.**

E_{exc} of D = Singlet excitation energy of DMA.



Scheme-15

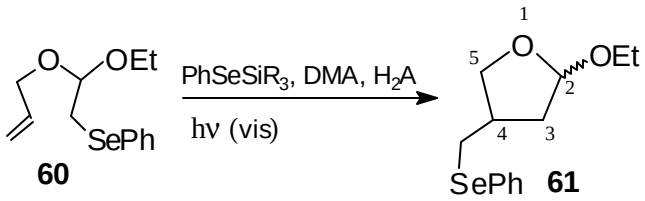
The reduction potential value of **60** was estimated through cyclic voltammetry experiment comprising a three electrode assembly. The cell consisted of a hanging mercury drop electrode (HMDE) and Pt wire as an auxiliary electrode. The peak potential value of degassed solution at a sweep rate of 500 mVs^{-1} was measured in acetonitrile using tetraethylammonium perchlorate as supporting electrolyte. The reduction potential of **60**, which was found to be – 1.4 eV is referred to standard calomel electrode (SCE) and was uncorrected for liquid junction potential.

Substituting the reduction potential value of **60** (- 1.4 eV) in the Weller equation taking $E_{1/2}^{ox}$ (DMA) as 0.98 eV[33] and $E_{0,0}$ of DMA as 3.21 eV,[34] a value of –80 KJM^{-1} was obtained. The selectivity of radical ion generation from a mixture of potential electron donors/acceptors depend on the magnitude of ΔG_{et} values associated with electron transfer processes.[35] The large difference between the ΔG_{et} values for the formation of $\mathbf{1}^{-\cdot}$ (-181 KJM^{-1}) and $\mathbf{60}^{-\cdot}$ (-80 KJM^{-1}) indicated that there will be selectivity in the formation of $\mathbf{1}^{-\cdot}$ over $\mathbf{60}^{-\cdot}$ when a mixture of **1** and **60** were PET activated utilizing the photosystem as shown in Scheme-**1.**

2-3.3 Mechanistic Aspects

The quantum yield of disappearance (ϕ_{dis}) of –Se-Si- bond (ϕ_{dis} = 0.223)[36] was found to be significantly higher than ϕ_{dis} of –C-Se- bonds ($\phi_{dis} \approx 0.054$)[16] indicating that the

cleavage of $\mathbf{1}^{-\bullet}$ will be comparatively faster than $-C\text{-}Se\text{-}]^{-\bullet}$ dissociation. This fact coupled with the above evaluated thermodynamic parameters and the established mesolytic characteristics of $SeSiR_3]^{-\bullet}$, (producing $R_3Si^{\bullet}$ and $PhSe^{-}$) further convinced us that PET activation of a mixture of **1** and **60** through the photosystem as shown in Scheme-**1** would initiate a radical reaction from **60.** The attack of $R_3Si^{\bullet}$ on **60** would generate a carbon centered radical by the abstraction of the SePh group regenerating $PhSeSiR_3$ in the process as shown in Scheme-**2**. The reorganization of the carbon centered radical **6** followed by its termination by PhSeSePh produced by the oxidative dimerization of $PhSe^{-}$, would set off a catalytic cycle for the formation of **61** through similar steps as shown in Scheme-**2.**



Scheme-16

2-3.4 Optimization / Establishment of the Catalytic Concept

Towards establishing the catalytic cycle, PET activation of a mixture containing **1** and **60** in acetonitrile was carried out with visible light of wavelength 410 nm. Compound **60** was PET activated at different concentrations (0.18, 0.27 and 0.35 mmol) with a fixed concentration of **1** (0.018 mmol), DMA (0.11 mmol) and H_2A (0.32 mmol) by irradiating 50 mL solution of each in a pyrex test tubes at 410 nm (450 W Hanovia medium pressure mercury lamp, $CuSO_4\text{-}NH_3$ solution[37]). The progress of the reaction was monitored by HPLC analysis. After 45 min of irradiation, (consumption of **60,** $\approx$ 55 to 60 %) the solutions in the test tubes were analyzed by HPLC which showed negligible change in the concentration of **1** as well as DMA in the tube having **60** and **1** in 10 : 1 mole ratio. This study was not performed at higher consumption of **60** in order to avoid competitive reaction from the increasing concentration of the product **61**. No conclusive hypothesis

could be drawn from the aliquots removed from other test tubes where the consumption of **60** was not found linearly related with the concentration of **1** probably due to the interference of **60** with the light absorbance of DMA. Therefore, based on the above study it may be suggested that the present proposed catalytic group transfer radical reaction can be best performed at 10 : 1 mole ratio of the substrate (**60**) to the catalyst (**1**).

The HPLC analysis of the aliquots withdrawn at different intervals of time during photolysis from the irradiation test tubes showed that the accumulated concentration of PhSeSePh in the reaction mixture at any given time was very small. This indicated that the combined rates of generation of 3-oxa-5-hexenyl radical of type **6** from substrate **60** and its cyclization[38] to give radical of type **7** is possibly slower than the rate of oxidative dimerization of $PhSe^-$ to PhSeSePh.[39] Hence it can be concluded that, this time lag was sufficient enough for the accumulation of PhSeSePh, required to terminate the radical of type **7** to give a group transfer cyclised product.

2-3.5 PET Activation of 60: A Preparative Study

After establishing the catalytic cycle for the group transfer radical reaction, a preparative PET reaction was carried out by irradiating a dilute solution containing a mixture of **60** (0.76 mmol), DMA (0.30 mmol), ascorbic acid (0.88 mmol) and **1** (0.08 mmol) with a light of wavelength 410 nm obtained by using a $CuSO_4$: NH_3 filter[37] in a specially designed three wall photoreactor. The progress of the reaction was monitored by TLC and HPLC analysis. After quantitative consumption of **60,** irradiation was discontinued and solvent was removed under vacuum. The crude photolysate was purified by silica gel column chromatography to give a pale yellow oil **61** in 75 % yield. Although quantitative estimation of recovered DMA and **1** was not made after column chromatography, negligible change in their concentration before and after the irradiation was established by comparing the HPLC analysis of the photolysate.

Careful HPLC analysis of product **61** showed it to be mixture of two diasteriomers in the ratio of 80:20. However, our effort to separate the isomers by column

chromatography was not successful. Thus, the product **61** was characterized as such by IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

IR spectrum of **61** showed prominent absorptions at 1585, 1460, 1440, 1210, 1125 $cm^{-1.}$ The IR of **61** was clearly different than the starting material **60** as the C=C stretching band at 1640 cm^{-1} was absent.

^{1}H NMR spectrum of **61** (Fig. **1**) showed two multiplets at δ 7.50 (2H) and 7.25 (3H) for the five aromatic protons. A doublet of a doublet at δ 5.15 (1H, J = 8.20, 4.75 Hz) is assigned to the H_2 acetal proton of **61**. Another doublet of a doublet appearing at δ 4.05 (1H, J = 7.75, 6.50 Hz) could be assigned to H_{5eq} proton. A multiplet at δ 3.70 (2H) corresponds to the methylene protons of ethoxy group (OCH_2CH_3), attached to the tetrahydrofuran ring. A mixed doublet of a doublet appearing at δ 3.45 (1H, J = 6.50, 5.80 Hz) is assigned to the H_{5ax} methylene proton. The methylene protons attached to the SePh group appeared as multiplets at δ 3.00 (2H). The H_4 methine proton appeared as another multiplet at δ 2.50 (1H). The multiplets appearing as two bunches at δ 2.15-2.35 (1H) and δ 1.70 (1H) could be assigned to the remaining protons whereas the triplet at δ 1.25 (3H, J = 9.80 Hz) corresponds to the methyl protons of the ethoxy moiety attached to the THF ring.

^{13}C NMR spectrum of the product (Fig. **2**) also showed two sets of carbon peaks (major and minor) indicating product **61** to be a mixture of two isomers. The ^{13}C NMR signals of the major isomer are as follows: The signals at δ 132.8, 129.9, 127.6 correspond to the aromatic carbons. The signal at δ 104.0 is assigned to C_2 acetal carbon. The C_5 carbon appeared at δ 72.0. The methylene carbon of the ethoxy group appeared at δ 63.0. The signal at δ 39.9 is assigned to methylene carbon attached to SePh. The signal at δ 38.6 corresponds to C_4 carbon of the ring. The signal at δ 31.5 is assigned to the C_3 carbon of the ring. The signal for methyl carbon of the ethoxy group appeared at δ 15.3. The signals of the minor isomer were observed at 131.5, 128.9, 126.9, 103.8, 62.8, 37.9, 32.3.

Mass spectrum of product **61** (Fig. **1**) showed molecular ion peak at 286 (7%) and base peak at 83. The other prominent peaks were observed at 240 (9), 197 (12), 184 (5), 171 (6), 157 (30), 129 (13), 116 (26).

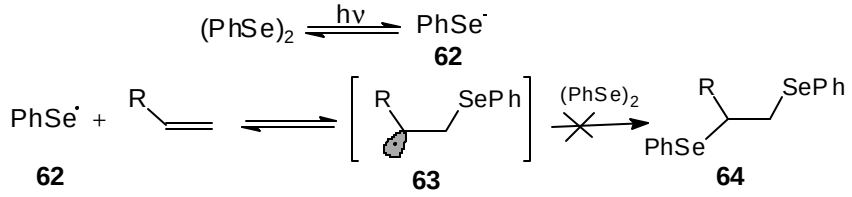
2-3.6 Discussion on parallel Possibilities and other competing Pathways:

In order to provide some conclusive support to the earlier proposed mechanism, it is also essential to eliminate various other possibilities and other competing reaction pathways available to the radical intermediates.

The cyclized alkyl radical **7** has two possible mechanism for its termination. It is either by chalcogen transfer from the accumulated PhSeSePh formed by the oxidative dimerization of $PhSe^-$ or by abstraction of PhSe group directly from the substrate **5**. This can be explained by comparing the rate constant values of chalcogen transfers from PhSeSePh and alkylselenide to an alkyl radical.

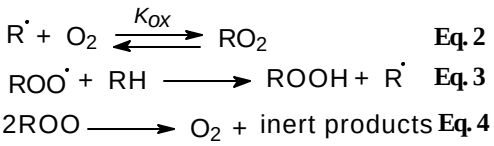
Curran and Newcomb have reported[40] rate constant values for various chalcogen group transfers in bimolecular substitution reactions with primary alkyl radicals. Their experiments showed that the rate of PhSe transfer from PhSeSePh to an octyl radical is in the range of $K = 2.6 \times 10^7\ M^{-1}s^{-1}$ compared to a rate constant of $K = 1.0 \times 10^5\ M^{-1}s^{-1}$ from an alkyl selenide. Based on their experimental results, they have also concluded that PhSeSePh is a preferred reagent for the termination of an alkyl radical than an alkylselenide. With this premise, the latter possibility of radical termination of cyclized radical **7** by substrate **5** can be easily ignored. Furthermore, if **7** is presumed to be terminating by chalcogen transfer from **5**, a radical chain reaction should have set in for the transformation of **60** to **61**. In that case, triggering the reaction by visible light would have been sufficient for the completion of reaction instead of continuous irradiation. However, it was observed during our optimization studies that the conversion of **60** to **61** is very much dependent on the irradiation time, supporting the hypothesis that the termination of cyclised radical **7** is by chalcogen transfer from PhSeSePh and not by alkylselenide (**5**).

It is already known in the literature that the reactivity of a $PhSe^{\bullet}$ with an olefinic C-C double bond is not facile due to the faster reverse reaction of the intermediate radical **63** to form starting olefin and $PhSe^{\bullet}$ (Scheme-**17**).[41] The cleaved $PhSe^{\bullet}$ radical generated after the termination of cyclized alkyl radical of type **7** derived from **60**, dimerizes efficiently ($K_r = 7.0 \times 10^9\ M^{-1}s^{-1}$)[41] back to PhSeSePh ruling out any other competing decay mode.



Scheme-17

The reaction of $PhSe^{\bullet}$ (**62**) with molecular oxygen can also be ignored based upon the report by Ito.[41] Another possible decay for alkyl radical **7** as well as tert-butyl diphenyl silyl radical ($R_3Si^{\bullet}$) could be by reaction with molecular oxygen. However, this possibility could also be ruled out on the following considerations. In general the reaction of an alkyl radical with molecular oxygen follows the steps as shown below.



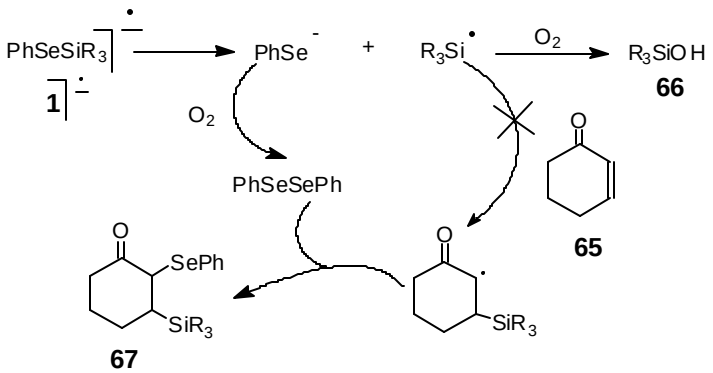
Scheme-18

The rate constant of an alkyl radical with molecular oxygen is known to be at diffusion-controlled limit ($K = 4.9 \pm 0.6 \times 10^9\ M^{-1}s^{-1}$ for cyclopentyl radicals).[42] In this reaction, the rate-determining step for the propagation of autooxidation chain is not the reaction of an alkyl radical with molecular oxygen (**Eq**. **2**) but the termination of the resultant peroxy radical ($ROO^{\bullet}$) by hydrogen abstraction (**Eq. 3**).[43] Therefore, even if it is presumed that the reaction of molecular oxygen with alkyl radical of type **7** occurs, there will not be any possibility of H-abstraction by the corresponding peroxy radical due to lack of potential hydrogen donors in the reaction. As a result of this, the $RO_2^{\bullet}$ would revert back to $R^{\bullet} + O_2$

as shown in **Eq. 2** of Scheme-**18**.[44] Our hypothesis is also substantiated due to the non observance of any detectable product pertaining to the peroxyradical derived from **60**.

The reaction of molecular oxygen with a variety of silyl radicals ($Me_3Si^{\bullet}$, $Et_3Si^{\bullet}$, n-$Bu_3Si^{\bullet}$, t-$Bu_3Si^{\bullet}$, $Ph_2Si^{\bullet}Me$ and $Ph_3Si^{\bullet}$) has been investigated by EPR spectroscopy.[45] In the gas phase kinetics, the rate constant for the reaction of $Me_3Si^{\bullet}$ with O_2 is reported to be $\approx$ 1.0 X 10^{10} $M^{-1}s^{-1}$.[46] However, in case of the reaction of alkyl silyl radical ($R_3Si^{\bullet}$) with molecular oxygen in solution phase, no kinetic data is available in the literature to the best of our knowledge. Therefore, no definite statements could be made regarding the rate constants of tert-butyldiphenylsilyl radical with oxygen in comparison to the oxidative dimerization rate constant of $PhSe^-$ to PhSeSePh. Although, the rate constant for the oxidative dimerization of $PhSe^-$ to PhSeSePh is not known, it is understood to be much higher than the oxidative dimerization of PhSeH. [42]

In a separate study, during our attempts to perform selenosilylation of C-C multiple bonds and enones (**65**) through the route as depicted in the Scheme-**19**, tert-butyldiphenylsilanol (R_3SiOH, **66**) was encountered as the major product.[47] The fact that the formation of **66** was not observed during transformation of **60** to **61**, suggests that the rate of chalcogenide transfer from alkyl SePh to $R_3Si^{\bullet}$ could be much higher than the rate of $R_3Si^{\bullet}$ with molecular oxygen.



Scheme-19

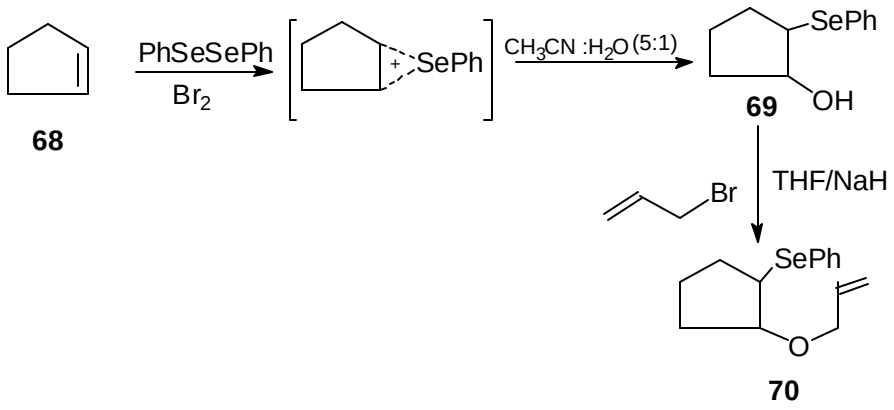
After eliminating all other competing pathways of this strategy, the efficiency of this methodology over the one earlier reported by our group by the direct PET reductive activation of a –C-Se- bond compound[17] was estimated. Towards this endeavor, a control experiment was performed parallel to a normal one in a similar manner as described earlier. Two test tubes were irradiated simultaneously with each consisting of a dilute solution containing a mixture of **60**, DMA, H_2A in acetonitrile by adding $PhSeSiR_3$ in one tube (normal batch) and another tube without $PhSeSiR_3$ (control batch). Within a constant period of irradiation, the comparative results of both the batches indicated that, the efficiency for the formation of product **61** in the tube containing $PhSeSiR_3$ was at least 4-5 times higher than the control batch with its absence.

This observation, thus, could be rationalized considering the higher quantum efficiency of -Se-Si- bond dissociation from its corresponding radical anion ($1^{-\bullet}$ ϕ_{dis} = 0.223)[17] in comparison to the quantum efficiency of –C-Se- bond dissociation from a -C-$Se^{-\bullet}$ (≈ 0.054).[16] The higher rate constant of $R_3Si^{\bullet}$ involved in the –C-Se-bond dissociation generating a carbon centered radical also owes to the greater efficiency of this methodology.

Further, to establish the generality of the catalytic phenylselenyl group transfer radical cyclization reaction, a variety of substrates with important structural units of natural products (**70, 74, 79** and **84**) were studied. The preparation of precursors, their cyclization and product characterizations are described as follows:

2-3.7 Preparation of 2-(allyloxy)cyclopentyl phenylselenide (70)

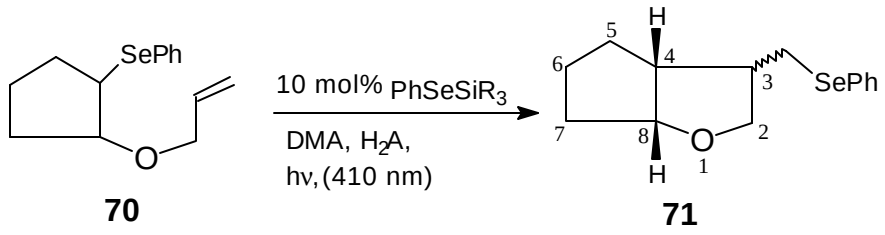
Substrate **70** was prepared by the allylation of 2-hydroxy alkylphenylselenide (**69**). 2-Hydroxyalkylphenylselenide (**69**) was prepared by the electrophilic reaction of in situ generated PhSeBr with **68** in the presence of moist CH_3CN (Scheme-**20**).[48] Detailed experimental procedure for the preparation of **70** is given in the experimental section.



Scheme-20

2-3.8 PET Activation of 2-(allyloxy)cyclopentyl phenylselenide (70)

Substrate **70** was subjected to PET activation by irradiating a dilute solution of CH_3CN containing a mixture of **70** (1.77 mmol), DMA (0.63 mmol), ascorbic acid (1.62 mmol) and $PhSeSiR_3$ (0.17 mmol) in a similar manner as described for **60**. Following the usual workup procedure and purification of the crude photolysate by column chromatography gave compound **71** as a yellow oily liquid in 77 % yield. Careful HPLC analysis of compound **71** suggested it to be a mixture of two diasteriomers in the ratio of 75:25 which were not separable by column chromatography. The spectral characterization of the diasteriomeric mixture is given as follows:



Scheme-21

IR spectrum of **71** showed the absence of C=C stretching at 1620 cm^{-1}, present originally in the starting selenide **70**. The other prominent absorption bands in the IR spectrum were at 3080, 1615, 1125 cm^{-1}.

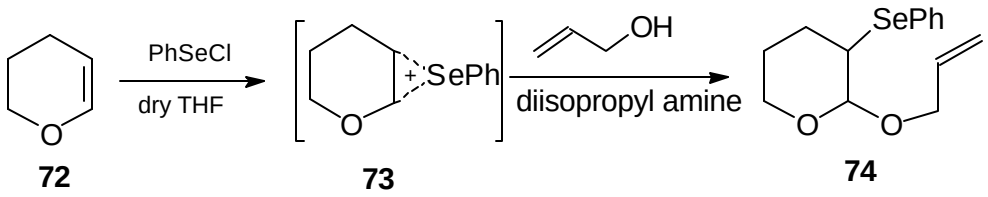
^{1}H NMR spectrum of **71** (Fig. **3**) displayed two multiplets at δ 7.50 (2H) and 7.23 (3H), the characteristics of SePh aromatic ring protons. A multiplet at 4.55 (1H) corresponds to H_8 methine proton of the tetrahydrofuran ring. A doublet of a doublet at δ 3.95 (1H, J = 8.5, 7.8 Hz) corresponds to the H_{2eq} methylene proton. The H_{2ax} methylene proton appeared as a multiplet at δ 3.45 (1H). A broad multiplet at δ 3.00 (2H) corresponds to methylene proton attached to the SePh group. Another multiplet at δ 2.6 (1H) can be assigned to the H_3 methine proton attached to CH_2SePh. The multiplet between δ 2.0-2.2 (1H) corresponds to the H_4 methine proton of the ring junction. The broad multiplets between δ 1.45-1.90 (6H) could be assigned to the remaining at H_5, H_6 and H_7 protons of the cylcopentane ring.

Fully decoupled ^{13}C NMR spectrum of **71** (Fig. **4**) showed two sets of carbon signals suggesting it to a mixture of two diasteriomers . Detailed characterization of these peaks by INEPT experiments suggested it to be a mixture of two isomers. The major isomer showed signals in the following pattern: The signals appearing at δ 132.9, 129.0, 126.9 are characterized to aromatic carbon. The C_8 methine carbon of the tetrahydrofuran ring appeared at δ 86.2. The signal observed at δ 72.2 corresponds to C_2 methylene carbon. The C_3 methine carbon adjacent to CH_2SePh appeared at δ 48.1. The signal at δ 47.1 is assigned to C_4 methine carbon. The carbon attached to SePh appeared at δ 34.4 ($\underline{C}H_2$-SePh). The signals appearing at δ 33.0, 25.9, 25.2 correspond to C_5, C_6, and C_7 methylene carbons of the cyclopentane ring. The peaks of the minor isomer also followed the similar pattern as of the major isomer and are given as follows: δ 132.6, 130.1, 126.8, 85.1, 75.3, 50.1, 43.4, 34.0, 30.5, 26.4, 24.0.

Mass spectrum of the product (Fig. **3**) showed molecular ion peak at 282 (10%) and base peak at 67. Besides these, other fragmentation peaks were observed at 157 (15%), 124 (17%), 95 (78%). Based on the above spectral details the product was confirmed as **71.**

2-3.9 Preparation of 2-(allyloxy)-3-(phenylseleno) tetrahydropyran (74):

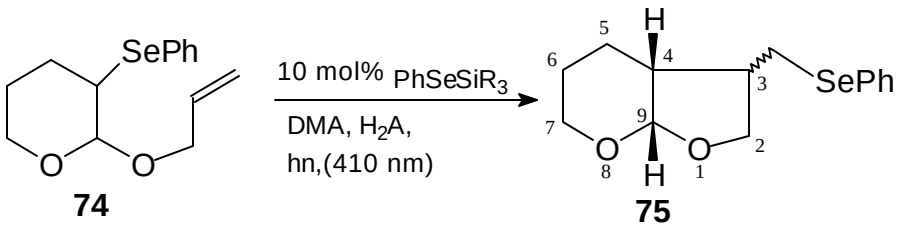
A similar procedure was adopted for the preparation of **74** as described for **60**. Electrophilic addition of PhSeCl (2.6 mmol) on to the 3,4-dihydropyran (**72**) (2.73 mmol) followed by addition of allyl alcohol (5.08 mmol) in the presence of diisopropyl amine (3.06 mmol) furnished **74** in 72 % yield (Scheme-**22**).[48] PhSeCl was prepared in our laboratory by passing Cl_2 gas over diphenyldiselenide in hexane.



Scheme-22

2-3.10 PET Activation of 2-(allyloxy)-3-(phenylseleno)tetrahydropyran (74)

An identical irradiation, as described for compound **60,** of a mixture of **74** (1.67 mmol), DMA (0.6 mmol) ascorbic acid (1.6 mmol) and $PhSeSiR_3$ (0.17 mmol) in acetonitrile (500 mL) followed by the purification of the crude photolysate by column chromatography afforded **75** as a pale yellow oil in 82 % yield (Scheme-**23**). The product was characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.



Scheme-23

IR spectrum of **75** showed the absence of the olefinic band at 1620 cm^{-1}. The other absorption bands occurred at 1580, 1465, 1437, 1205, 1120 cm^{-1}.

^{1}H NMR spectrum of **75** (Fig. **5**) displayed two multiplets at δ 7.55 (2H) and 7.25 (3H), the characteristic of the aromatic protons. A sharp doublet at δ 5.25 (1H, J = 3.7 Hz) corresponds to H_9 acetal methine proton. A triplet at δ 4.05 (1H, J = 7.1 Hz) could be assigned to one of the H_2 methylene protons. The multiplets observed between δ 3.60-3.80 (3H) are assigned to the two H_7 methylene protons and another H_2 methylene proton. Another multiplet at δ 2.95 (2H) corresponded to the methylene protons adjacent to SePh group. A multiplet appearing at δ 2.65 (1H) could be assigned to the H_3 methine proton. The H_4 methine proton at the ring junction appeared as a multiplet at δ 2.10. The peaks between δ 1.35 -1.85 (4H) corresponds to the remaining H_5 and H_6 protons.

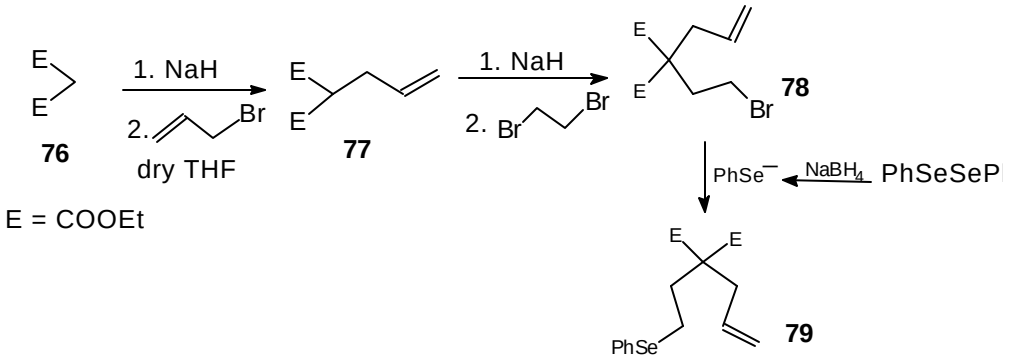
^{13}C NMR spectrum (Fig. **6**) showed twelve signals appearing at δ 133.1, 129.5, 129.0, 127.2, 101.8, 70.1, 61.0, 41.2, 37.4, 25.8, 22.9, 19.2. INEPT experiments suggested that the signals appearing at δ 133.1, 129.5, 129.0 and 127.2 belonged to the aromatic carbons. The signal appearing at δ 101.8 corresponds to C_9 acetal carbon. The signal at δ 70.1 corresponds to C_2 methylene carbon. Another signal at δ 61.0 belonged to C_7 methylene carbon of the tetrahydropyran ring. The C_4 methine carbon at the ring junction appeared at δ 41.2. The signal at δ 37.4 corresponds to the C_3 methine carbon attached to CH_2SePh. The methylene carbon attached to SePh appeared at δ 25.8. The

signals at δ 22.9 and 19.2 correspond to the remaining C_5 and C_6 carbons of the pyran ring.

Mass spectrum (Fig. **5**) showed molecular ion peak at 298 (M^+, 6) and base peak at 55. The other prominent fragments were observed at 197 (20), 157, (15), 141 (50), 116 (42).

2-3.11 Preparation of diethyl 2-allyl-2-[2-(phenylselenyl)ethyl] malonate (79)

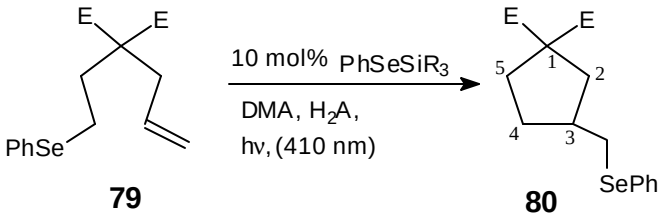
Alkylation of diethylmalonate (**76**) with allylbromide followed by second allylation with 1,2-dibromoethane afforded **78** (Scheme-**24**). Nucleophilic displacement of bromo group of **78** by the in situ generated phenylselenyl anion gave **79** in 83 % yield (Scheme-**24**).[49]



Scheme-24

2-3.12 PET Activation of diethyl 2-allyl-2-[2-(phenylselenyl)ethyl] malonate (79)

PET activation of a mixture containing **79** (1.31 mmol), DMA (0.5 mmol), ascorbic acid (1.4 mmol) and $PhSeSiR_3$ (0.14 mmol) in acetonitrile (500 mL) utilizing identical setup as mentioned earlier for substrate **60**, followed by purification of the crude photolysate by column chromatography furnished **80** as a yellow oily liquid in 73 % yield (Scheme-**25**).



79 **80**

Scheme-25

IR spectrum of the product **80** showed prominent absorption bands at 1722, 1540, 1470, and 1440 cm^{-1}. The absence of C=C bond stretching at 1640 cm^{-1} was conspicuous in **80** indicating it to be a cyclised product.

The crude ^{1}H NMR spectrum of the product **80** (Fig. **7**) indicated it to be mixture of two diasteriomers in the ratio of 60:40. However, our efforts to separate the two diasteriomers failed. ^{1}H NMR spectrum of the **80** showed aromatic protons in bunches of two multiplets at δ 7.50 (2H) and 7.25 (3H). A quartet at δ 4.20 (4H, J = 7.3 Hz) correspond to two methylene protons of both the ester groups (-C(O)-O$\underline{C}H_2$-CH_3). A doublet at δ 2.95 (2H, J = 8.2 Hz) could be assigned to the methylene protons attached to the SePh group. A multiplet appearing at δ 2.55 (1H) corresponds to the H_3 methine proton. Another two sets of multiplets at δ 2.30 and 2.00 (6H) were assigned to the remaining six H_2, H_4 and H_5 protons on the cyclopentane ring. The triplet at δ 1.25 (6 H, J = 7.3 Hz) corresponds to the methyl proton of the two ester groups. (-C(O)-O-$CH_2\underline{C}H_3$).

^{13}C NMR spectrum of the **80** (Fig. **8**) displayed 12 signals. From the INEPT experiments detailed information about the pattern of peaks were obtained as follows: The signal at δ 172.6 corresponds to the carbonyl carbon of the ester. The signals appearing at δ 133.0, 129.3, 127.1 corresponded to aromatic carbons. The signal observed at δ 61.6 belonged to methylene carbon of the ester (-O$\underline{C}H_2$). The quaternary C_1 of the cylcopentane ring appeared at δ 60.4 ($\underline{C}(CO_2Et)_2$. The signal at δ 40.9 corresponds to methylene carbon attached to SePh (-$\underline{C}H_2$SePh). The signal for the C_3 methine carbon

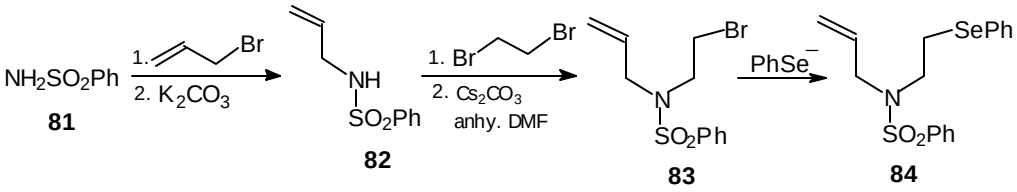
appeared at δ 40.2. The signals at δ 34.1, 33.5, 32.6 correspond to C_2, C_4 and C_5 methylene carbons of the product. The methyl carbon of the ester appeared at δ 14.3 ($COOCH_2$-$\underline{C}H_3$).

Mass spectrum (Fig. **7**) exhibited molecular ion peak at 384 (M^+, 20%) and base peak at 153. The other prominent peaks were observed at 227 (52%), 157 (20%), 119 (27%). Based on the above spectral characterization, the compound was confirmed as an exocyclic product **80.**

In order to expand the applicability of this methodology to various other systems, the construction of pyrrolidine rings, widely present in natural products, was also taken up as an example.

2-3.13 Preparation of *N*-allyl-*N* [2-(phenylselenyl) ethyl]benzene sulphonamide (84)

Compound **84** was prepared by the selenylation of **83,** obtained by the alkylation of **82** as depicted in the scheme (Scheme - **26**).[50]

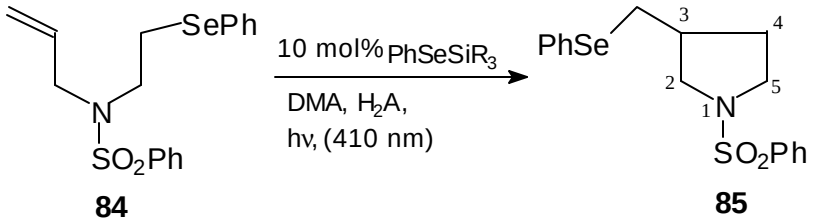


Scheme-26

2-3.14 PET Activation of *N*-allyl-*N* [2-(phenylselenyl) ethyl] benzene sulphonamide (84)

Usual PET activation of a dilute solution of acetonitrile (500 mL) containing a mixture of **84** (1.3 mmol), DMA (0.42 mmol), H_2A (1.5 mmol) and $PhSeSiR_3$ (0.135 mmol) followed by the purification of the crude photolysate furnished a pale yellow product **85** in

64 % yield (Scheme-**27**). The product was characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analysis and was further confirmed by HRMS.



Scheme-27

^{1}H NMR spectrum of the product **85** (Fig. **9**) exhibited multiplets at δ 7.75 (2H) which are characteristic of aromatic protons of the benzene sulphonamide moiety. The two sets of multiplets between δ 7.35-7.65 (5H) are assigned to the remaining aromatic protons of benezene sulphonamide and phenylselenide. The multiplet between δ 3.15-3.55 (3H) could be assigned to both the H_2 and one of the H_5 methylene protons. The other H_5 methyelene proton appeared as a multiplet at δ 3.00 (1H). Multiplets between δ 2.60-2.85 (2H) corresponded to the methylene protons attached to the phenylselenyl group (-CH_2SePh). The H_3 methine proton of the pyrrolidine ring appeared at δ 2.30 (1H). The two H_4 methylene protons of the pyrrolidine ring are observed at δ 1.95 and δ 1.55. The above spectral assignments were confirmed by COSY analysis.

Fully decoupled ^{13}C NMR spectrum of the product **85** (Fig. **10**) exhibited 9 signals and the INEPT experiments gave a detailed picture in the following pattern: Signals at δ 133.0, 132.5, 129.0 and 128.9, 129.4, 127.2 corresponds to aromatic carbons of the benzene sulphonamide and phenylselenyl groups. The signal at δ 53.2 could be assigned to the C_2 carbon of the pyrrolidine ring. The signal appearing at δ 47.3 corresponds to the C_5 carbon of the ring. Another signal at δ 39.1 iss assigned to C_3 methine carbon. The

methylene carbon attached to SePh ($\underline{C}H_2SePh$) appeared at. δ 31.6 and the signal at δ 30.6 corresponds to C_4 methylene carbon of the ring.

Mass spectrum of the product (Fig. **9**) exhibited molecular ion peak at 381 (M^+, 4) and base peak at 223. The other prominent fragments were observed at 297 (7), 209 (13), 141 (25). The HRMS value calculated for $C_{17}H_{19}NO_2SSe$ was 381.030171 and the value obtained was 381.032655. From the above spectral characterization, the structure of the product is confirmed as **85**.

2-4 CONCLUSION

In conclusion, a conceptually new and ecologically compatible approach for initiating a catalytic phenylselenyl group transfer radical reaction has been designed and developed. The optimum mole ratio between the catalyst **1** and alkylphenyl selenides for successful reaction is established to be 1:10. The generality of the concept has been demonstrated by carrying out variety of radical cyclizations. The development of this strategy is expected to add new dimension to radical based chemistry.

2-5 EXPERIMENTAL SECTION

The chemicals and reagents used in this study were of commercial grade and some of them were synthesized in the laboratory. PhSeSePh was made from commercially available black Se powder by following literature procedure.[51] PhSeCl was also synthesized in our lab by standard procedure.[51] The chromatography was performed over ordinary silica gel (60-120 mesh) and flash silica gel (100-200 mesh). The solvents used during experiments were purified, unless otherwise stated, by standard literature procedure.[52]

All compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass spectroscopy. Infrared spectra were recorded on a Perkin-Elmer infrared spectrometer model 599-B and model 1620 FT-IR and values are reported in cm^{-1}. Nuclear Magnetic Resonance spectra obtained for ^{1}H and ^{13}C were on BRUKER MSL-300 and BRUKER AC-200FT MHz spectrometers using $CDCl_3$ as solvent. All chemical shifts were reported in parts per million down field from TMS. The coupling constants (J values) are reported in Hertz. Mass spectra were obtained at a voltage of 70 eV on Finnigan MAT-1020B instrument. High Resolution Mass Spectroscopy (HRMS) were taken on a VG AUTOSPEC-M mass spectrometer with OPUS V3.IX software.

HPLC was performed on a Perkin-Elmer (Model 250 binary LC pump along with 135 C diode array detector) liquid chromatograph using C_{18} reverse phase column with acetonitrile water mixture as the mobile phase.

2-5.1 Description of the Irradiation Setup:

Irradiations were performed in a specially designed double walled photoreactor. The photoreactor consisted of three chambers. The first and outermost chamber contained irradiation solution while second one was charged with $CuSO_4.5H_2O$: NH_3 filter solution. This filter solution allowed only 410 nm wave length light to pass through.[26] 450-

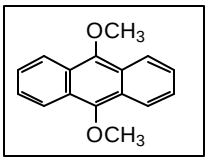
W Hanovia medium pressure mercury vapor lamp was used as light source that was housed into a water cooled jacketed chamber immersed into the second chamber maintaining 1cm path length of the filter solution. The whole photoreactor was made of Pyrex glass.

2-5.2 Preparation of tert-Butyl diphenyl (phenylseleno) silane ($PhSeSiR_3$) (1)

A solution of diphenyl diselenide (15.6 g, 0.05 mol) in 100 mL of dry THF was added to a freshly prepared sodium sand (3 g, 0.14 mol) and the resulting mixture was refluxed for 5 h. The colour of the reaction mixture in the flask turned pale yellow or dirty white indicating the generation of phenylselenyl anion. tert-Butyl diphenyl silyl chloride (27.5 g, 0.1 mol) was added to the stirring solution and the resulting mixture was allowed to reflux for 21 h. The reaction mixture was extracted with 100 mL of ether, washed with several portions of cold water, dried over sodium sulfate and concentrated under reduced pressure. Distillation (b.p. 185^{o}C at 0.01mm) of the crude reaction mixture gave 30 g (79%) of **1** as a thick pale yellow liquid which on long standing (24 h) got solidified.

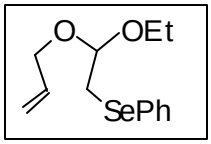
M. P.:	57 ^{0}C (lit: 56-58)
IR (KBr)	3038, 2910, 2840, 1563, 805, 720, 660 cm^{-1}.
^{1}H NMR (200 MHz)	7.64 (m, 4H), 7.29 (m, 6H), 6.98 (m, 5H), 1.14 (s, 9H)
Mass:	396 (M^{+}), 339 (92), 261 (68), 227 (20), 197 (38), 181 (47), 152 (32), 135 (100).

2-5.3 Preparation of 9, 10-Dimethoxy Anthracene:



Anthraquinone, 10.4 g (0.05 mmol) was grounded with 5 g of Zn dust and placed in a R.B. flask with 20 mL of ethanol. 100 mL of 20 % NaOH was added and the total contents were refluxed for 1 h until most of the anthraquinone was brought in to the solution. *P*-Methyl toluene sulphonate was introduced in small portions into the flask with continuous stirring, until the red color of the solution was discharged. The resulting precipitate was filtered and the precipitate was washed with aq. alkaline $Na_2S_2O_4$ (sodium dithionite) until the filtrate was practically colorless. The solid precipitate obtained was finally dissolved in the excess of benzene (250 mL). Evaporation of benzene yielded 11 g (92%) of crude DMA. Repeated recrystallizations from ethanol resulted light yellow flakes of DMA (M.P. = 199 ^{0}C).

2-5.4 Preparation of 2-(allyloxy)2-ethoxyethylphenylselenide (60)



3 g of PhSeSePh (9.6 mmol) was placed into a two neck 100 mL flask equipped with an argon balloon and magnetic needle. 30 mL of dry THF was introduced into the flask and bromine (1.52 g, 9.4 mmol) was added dropwise to the stirring solution at room temperature. Instant change in the color from yellow to brownish red was observed indicating the formation of PhSeBr. Neat ethyl vinyl ether (1.5 g, 20.8 mmol) was added at once to the reaction flask. Immediately afterwards, a solution of allylalcohol (0.81 g, 14.05 mmol) and diisopropyl amine (2.34 g, 23.16 mmol) in 10 mL of dry THF was added over 5 min to the vigorously stirred clear yellow solution. Formation of a voluminous white precipitate was observed soon. The reaction mixture was stirred for another 30 min and poured in to 15 % aq. $NaHCO_3$ solution (25 mL) followed by extraction with diethyl ether.

The organic layers were washed successively with water and brine, dried over Na_2SO_4 and concentrated under vacuum. Purification of the crude mixture on silica gel chromatography using pet-ether : ether (8:1) mixture as an eluent afforded **60** in 80 % (4.8 g) yield. The product was characterized by ^{1}H NMR, ^{13}C NMR and Mass spectral analysis and the data is given as follows:

IR:	3080, 1645, 1615, 1210, 1125 cm^{-1}
^{1}H NMR (200 M Hz):	δ 1.25 (t, 3H, J = 7.5 Hz), 3.15 (d, 2H, J = 4.0 Hz), 3.65 (m, 2H), 4.15 (m, 2H), 4.75 (t, 1H, J = 4.0 Hz), 5.25 (m, 2H), 5.90 (m, 1H), 7.25 (m, 3H), 7.55 (m, 2H).
^{13}C NMR:	δ 134.84, 132.89, 129.25, 127.15, 117.01, 102.33, 67.47, 62.28, 31.40, 15.43.
Mass:	286 (M^+, 5), 227 (5), 196 (4), 183 (10), 170 (10), 157 (25), 115 (100), 91 (30).

2-5.5 Measurement of Reduction Potential of 60

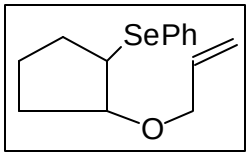
Reduction potential of **60** was measured by cyclic voltammeter consisting of three-electrode assembly on a PAR 175 Universal programmer instrument equipped with PAR RE0074 XY recorder. The cell consisted of a metro E-410 hanging mercury drop electrode (HMDE) and Pt wire as an auxiliary electrode. The peak potential value of degassed solution at a sweep rate of 300 mVs^{-1} was measured in acetonitrile solution employing tetraethyl ammonium perchlorate as supporting electrolyte. The potential was referred to standard calomel electrode (SCE) and was uncorrected for liquid junction potential. The reduction potential obtained for **60** was –1.4 eV.

2.5-6 Evaluation of Catalytic Property of 1:

A 200 mL stock solution in acetonitrile containing **1** (0.07 mmol), DMA (0.42 mmol), and ascorbic acid (0.31 mmol) was prepared. 50 mL each of this solution was distributed into three test tubes made up of pyrex glass. 0.05 g (0.176 mmol), 0.075 g

(0.265 mmol), and 0.1 g (0.35 mmol) of **60** was introduced into each test tube resulting the mole ratios of **60** with respect to **1** as 10:1, 15:1, 20:1, respectively. One mL each of this solution was analyzed before irradiation by HPLC after adding 0.5 mL solution of Ph_3As (0.05 M) as an internal standard and the area ratios of **60** : Ph_3As and **1** : Ph_3As were recorded. These tubes were irradiated externally at 410 nm wavelength light coming out of a 450-W Hanovia lamp after passing through a $CuSO_4$: NH_3 filter solution. Aliquots were analyzed time to time by HPLC in the similar manner as described above and the area ratios were compared. After 45 min, the irradiation was discontinued. The HPLC analysis of the test tube containing **60** and **1** in 10:1 mole ratio (first tube) indicated negligible change in the concentration of **1**. Formation of **61** as the only product was noticed by HPLC analysis. The other two tubes showed no correlation between the conversion of **60** and the concentration of **1**.

2-5.7 Preparation of 2-(allyloxy) cyclopentyl phenylselenide (70)



A solution of cyclopentene (1.00 g, 14.4 mmol) in 20 mL of CH_3CN : H_2O (5:1) mixture was added to a vigorously stirring solution of PhSeBr (made in the same way as described for substrate **70** from 2.5 g of PhSeSePh and bromine (1.25 g, 8 mmol) in CH_3CN (7 mL). A pale yellow solution was stirred further for an hour at room temperature. The reaction mixture was diluted with water (20 mL) and extracted with diethyl ether (3 X 15 mL). Combined ether extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography to afford 2-hydroxy cyclopentyl phenylselenide (**69**) in 80 % (2.8 g) yield. The product was characterized by IR and NMR analysis.

IR 3300, 3055, 2960, 1700, 1575, 1310.

^{1}H NMR: δ 1.71 (m, 4H), 2.00 (m, 2H), 2.25 (m, 1H), 3.37 (m, 1H), 4.15 (m, 1H), 7.25 (m, 3H), 7.55 (m, 2H).

To a 100 mL two neck flask fitted with a reflux condenser, Ar balloon and magnetic stir bar, NaH (0.25 g, 6.3 mmol, 60 % suspension in mineral oil) was introduced. NaH was washed with dry hexane under Ar blanket to remove the mineral oil and dried under reduced pressure till it became fine gray powder. 20 mL of dry THF was introduced into the flask and the suspension was stirred. To this suspension, 2-hydroxycyclopentylphenylselenide (**69**) (1.4 g, 5.7 mmol) was added in 10 mL of THF and the resulting mixture was stirred for 2 h at room temperature. Allyl bromide (0.73 g, 6 mmol) was added dropwise to the stirring solution and stirring was allowed to continue for 6 h. The reaction mixture was diluted with water (30 mL) and extracted with ether (3 X 30 mL). The combined ether extracts were washed with water, brine and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography on silica gel to afford substrate (**70**) in 75 % (1.2 g) yield.

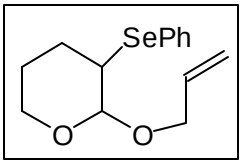
IR: 3100, 1600, 1575, 1355, 1125 cm^{-1}

^1H NMR: δ 1.7 (m, 3 H), 2.00 (m, 2H), 2.20 (m, 1H), 3.60 (m, 1H), 3.82 (m, 3H), 5.20 (m, 2H), 5.80 (m,1H), 7.25 (m, 3H), 7.60 (m, 2H).

^{13}C NMR: δ 135.05, 134.05, 130.39, 129.07, 127.33, 116.71, 86.24, 70.02, 46.73, 31.78, 31.32, 23.32.

Mass: 282 (M^+, 5), 225 (30), 157 (27), 147(5), 125 (10), 117 (115), 91 (12), 67 (100).

2-5.8 Preparation of 2-(allyloxy)-3-(phenylseleno) tetrahydropyran (74)



To a solution of PhSeCl (0.5 g, 2.6 mmol) in 15 mL of dry THF in a 25 mL 2-neck flask fitted with an argon balloon, 3, 4-dihydropyran (**72**) (0.23 g, 2.7 mmol) was added neat at once. The colour of the dark brown solution in the flask turned to pale yellow. Immediately afterwards, a mixture of allyl alcohol (0.295 g, 5 mmol) and diisopropyl amine (0.31g, 3.06 mmol) in 5 mL THF was added to the reaction mixture. The contents of the flask were diluted with 25 mL DCM and washed successively with water and brine. The solvent was removed under vacuum and the residue was purified by column chromatography to give **74** in 72 % (0.58 g) yield.

IR: 3075, 2927, 2142, 1475, 1232 cm^{-1}

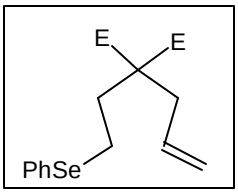
^1H NMR: δ 1.50-1.90 (m, 3H), 2.20 (m, 1H), 3.35 (m, 1H), 3.55 (m, 1H), 3.95 (m, 2H), 4.30 (dd, 1H, J = 7.2 Hz), 4.75 (d, 1H, J = 7.3 Hz), 5.10-5.35 (m,

2H), 5.85 (m, 1H), 7.25 (m, 3H), 7.60 (m, 2H).

^{13}C NMR: δ 132.42, 134.13, 129.04, 128.76, 127.28, 116.73, 101.01, 68.44, 62.53, 44.05, 27.09, 24.00.

Mass: 298 (M^+, 9), 241, (30), 210 (8), 195 (8), 184 (84), 157 (100), 130 (45), 117 (47).

2-5.9 Preparation of diethyl 2-allyl-2-[2-(phenylselenyl)ethyl] malonate (79)



To a suspension of NaH (0.76 g, 19.0 mmol, 60% dispersion in mineral oil; washed and dried in the same way as described for the preparation of compound **70**) in dry THF (20 mL), diethyl malonate (**76**, 3 g, 19 mmol) in 25 mL of dry THF was added dropwise at O^{0}C. The mixture was allowed to warm to room temperature in 30 min. After additional 30 min of stirring at room temperature, a clear solution was formed indicating the completion of anion generation. Allyl bromide (2.5 g, 21 mmol) was added dropwise into the flask over a period of 5 min. After the addition was over, the mixture was refluxed for 5 h. The mixture was cooled, quenched with 50 mL of sat. aq. NH_4Cl and extracted with ether. The ether layer was washed successively with water, brine and dried over anh. Na_2SO_4. Removal of the ether and distillation [bp: 93 ^{0}C / 1 mm] of residue gave 2-(2-propenyl)-diethylmalonate (**77**) in 3.2 g (84%) which was used for the second alkylation.

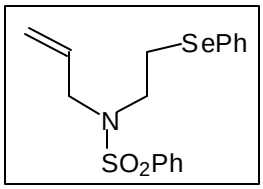
NaH (0.84 g, 21 mmol, 60 % suspension in mineral oil) was washed and dried as described above in 100 mL two neck RB flask fitted with reflux condenser, Ar balloon adapter and magnetic bar. 10 mL of dry THF was introduced into the flask and the suspension was kept for stirring. 2-(2-Propenyl)-diethylmalonate (**77**, 3 g, 14.9 mmol) in 25 mL of dry THF was added dropwise into the flask at room temperature and content was allowed to stir for 1 h. After a clear solution was formed, the reaction mixture was charged with 1,2-dibromoethane (2.8 g, 14.9 mmol) and refluxed for 5 h. The mixture was cooled, quenched with 50 mL of sat. aq. NH_4Cl and extracted with ether. The ether layer was washed successively with water, brine and dried over anh. Na_2SO_4. Removal of ether by

evaporation on rotavapor and purification of the crude mixture by silica gel chromatography using pet ether : ethylacetate as eluent furnished **78** in 41% (1.9 g) yield.

Into a 50 mL three neck flask, fitted with a rubber septum, a solid addition tube containing $NaBH_4$ (0.33 g, 8.9 mmol) a reflux condenser and an argon balloon, diphenyldiselenide (0.8 g, 2.56 mmol) was introduced in 15 mL of dry ethanol. The mixture was stirred vigorously and $NaBH_4$ was added in portions. The colour of the reaction mixture turned to pale yellow or dirty white indicating $PhSe^-$ generation. Compound **78** (1.55 g, 5.04 mmol) in 10 mL of ethanol was introduced into the flask dropwise and contents refluxed for 4 h. The solvent was evaporated under reduced pressure and the mixture was extracted with ethylacetate and washed with 5 % HCl followed by water wash. Removal of the solvent and purification of the crude mixture by silica gel column chromatography afforded compound **79** (1.58 g) in 82 % yield.

IR	3075, 1710, 1645 cm^{-1}
^1H NMR	δ 1.25 (t, 6H, J = 9.50 Hz), 2.25 (m, 2H), 2.65 (d, 2H, J = 4.75 Hz), 2.85 (m, 2H), 4.20 (q, 4H, J = 9.50 Hz), 5.25 (m, 2H), 5.65 (m, 1H),
^{13}C NMR	δ 170.48, 132.62, 132.08, 129.85, 129.02, 126.93, 119.16, 61.29, 57.93, 37.23, 33.72, 21.69, 14.03.
Mass	384 (M^+, 16), 339, (8), 227 (100), 185 (5), 171 (62), 157 (15), 153 (42), 125 (35), 91 (22), 81 (23).

2-5.10 Preparation of *N*-allyl-*N* [2-(phenylselenyl)ethyl] benzene sulphonamide (84)



Into a 100 mL two neck RB flask, fitted with a reflux condenser and argon balloon, allyl bromide (2.42 g, 20 mmol), benzene sulphonamide (**81,** 3.14 g, 20 mmol) and K_2CO_3 (2.76 g, 20 mmol) in 60 mL of anh. acetone were introduced and the contents were

refluxed for 36 h. The reaction mixture was diluted with 70 mL of ethylacetate and washed with ether and brine. The solvent was removed under vacuum and the crude mixture was purified by silica gel column chromatography to afford monoallylated compound **82** (2.9 g) in 75 % yield.

IR 3400, 1610 cm^{-1}

^1H NMR δ 3.58 (m, 2H), 4.85 (bs, 1H), 5.15 (m,2H), 5.65 (m, 1H), 7.55 (m, 3H), 7.82 (m,2H).

Into a 50 mL 3-neck flask fitted with an argon balloon, rubber septum and a solid addition tube containing cesium carbonate (1.82 g, 5.58 mmol), compound **82** (1 g, 5.07 mmol) was introduced in 25 mL of anh. DMF. Cesium carbonate was added in portions from the solid addition tube to the stirring contents of the flask and the mixture was allowed to stir for 20 min. 1, 2-dibromoethane (2.80 g, 14.9 mmol) was added dropwise to the flask and the stirring was continued for 20 h. DMF was removed by vacuum distillation and the residue was extracted with 50 mL of DCM and washed with water (3 X 30 mL) and brine. Solvent was removed on rotavapor and the residue was purified by silica gel column chromatography to afford 0.95 g (62 %) of bromo compound **83**.

^1H NMR δ 3.40 (m, 4H), 3.80 (d, 2H, J = 4.7 Hz), 5.18 (m, 2H), 5.58 (m, 1H), 7.58 (m, 3H), 7.80 (m, 2H).

Into a 50 mL three neck flask, fitted with a rubber septum, a solid addition tube containing $NaBH_4$ (0.14 g, 3.78 mmol) a reflux condenser and an argon balloon, diphenyldiselenide (0.3 g, 0.96 mmol) was introduced in 12 mL of dry ethanol. The mixture was stirred vigorously and $NaBH_4$ was added in portions. The colour of the reaction mixture turned to pale yellow or dirty white indicating $PhSe^-$ generation. Compound **83** (0.55 g, 1.80 mmol) in 10 mL of ethanol was introduced into the flask dropwise and

refluxed for 4 h. The solvent was evaporated under reduced pressure and the mixture was extracted with ethylacetate and washed with 5 % HCl followed by water wash. Removal of the solvent and purification of the crude mixture by silica gel column chromatography afforded compound **84** in 78 % (0.53 g) yield.

IR	3113, 2952, 2925, 1416.
^{1}H NMR: (200 MHz, $CDCl_3$)	δ 3.10 (m, 2H), 3.35 (m, 2H), 3.75 (d, 2H, J = 5.4 Hz), 5.05 (m, 2H), 5.70 (m, 1H), 7.30 (m, 3H), 7.55 (m, 5H), 7.80 (m, 2H).
^{13}C NMR: (50 MHz, $CDCl_3$)	δ 139.91, 133.15, 132.96, 132.79, 129.36, 129.14, 127.39, 127.24, 119.47, 51.64, 48.18, 25.75.
Mass:	381 (M^+, 2), 240 (9), 210 (25), 183 (15), 171 (10), 156 (26), 141 (100), 91 (25), 77 (58).

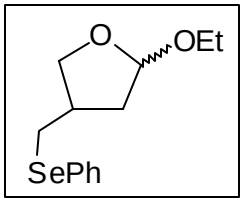
2-5.11 Preparative PET Activations

This is illustrated by taking **60** *as an example*

A dilute solution of CH_3CN (500 mL) containing a mixture of **1** (0.07 g, 0.17 mmol), **60** (0.5 g, 1.74 mmol), DMA (0.15 g, 0.63 mmol), and ascorbic acid (0.28 g, 1.62 mmol) was irradiated in the specially designed photoreactor (as described in the general experimental section) with a 450-W Hanovia medium pressure mercury vapour lamp at room temperature without removing dissolved oxygen from the solution. The progress of the reaction was monitored by HPLC. After substantial consumption of **60**, the irradiation was discontinued. Solvent was removed under vacuum and the crude photolysate was purified by silica gel column chromatography to give a yellow oily product **61** (0.37 g, 75 % yield).

2-ethoxy-4-methylphenylselenyltetrahydrofuran

(61)

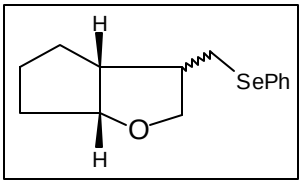


Yield	75%
IR	1585,1460, 1440, 1210, 1125 cm^{-1}.
^1H NMR: (200 MHz, $CDCl_3$)	δ 1.15-1.30 (m, 3H), 1.60-1.80 (m, 1H), 2.15-2.60 (m, 2H), 2.90-3.17 (m, 2H), 3.30-3.50 (m, 1H), 3.57-3.80 (m, 2H), 3.95-4.10 (m, 1H), 5.10-5.17 (m, 1H), 7.20-7.30 (m, 3H), 7.45-7.55 (m, 2H).
^{13}C NMR: (50 MHz, $CDCl_3$)	δ 132.8, 131.5, 129.9, 128.9, 127.6, 126.9, 104.0, 103.8, 72.0, 63.0, 62.8, 39.9, 39.6, 38.6, 37.9, 32.3, 31.5, 15.4, 15.3;
Mass:	286 (M^+, 28), 240 (15), 157 (23), 91 (42), 83 (100)

Identical irradiation procedures were adopted for the PET activation of **70, 74, 79, 84** and the spectral characterization of products **71, 75, 80** and **85** are given as follows:

3-[(phenylselenyl)methyl]hexahydro-2-*H*-cyclopenta

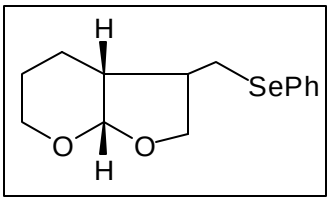
[*b*] furan (71)



Yield	77 %;
IR	3080, 1615, 1125 cm^{-1}
^1H NMR: (200 MHz, $CDCl_3$)	δ 1.45-1.90 (m, 6H), 2.00-2.20 (m, 1H), 2.55-2.75 (m, 1H), 2.85-3.15 (m, 2H), 3.30-3.50 (m, 1H), 3.95 (dd, J = 7.8, 13.5 Hz, 1H), 4.45-4.60 (m, 1H), 7.20-7.30 (m, 3H), 7.45-7.55 (m, 2H).
^{13}C NMR: (50 MHz, $CDCl_3$)	) δ 132.9, 132.6, 130.3, 130.1, 129.0, 126.9, 126.8, 86.2, 85.1, 73.3, 72.2, 50.1, 48.1, 47.1, 43.4, 34.4, 34.0, 33.0, 30.5, 26.4, 25.9, 25.2, 24.0.

Mass: 282 (M^+, 10), 157 (15), 124 (17), 95 (78), 67(100).

3-[(phenylselenyl)methyl]hexahydro-4-*H*-furo[2,3-*b*] pyran (75)



Yield 82 %

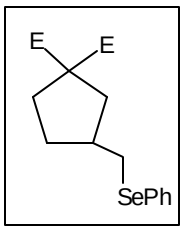
IR 1580, 1465, 1437, 1205, 1120 cm^{-1}

^1H NMR: (200 MHz, $CDCl_3$) δ 1.35-1.85 (m, 4H), 2.00-2.15 (m, 1H), 2.50-2.75 (m, 1H), 2.80-3.05 (m, 2H), 3.65-3.85 (m, 3H), 4.05 (t, J = 7.1 Hz, 1H), 5.25 (d, J = 3.7 Hz, 1H), 7.20-7.35 (m, 3H), 7.45-7.60 (m, 2H).

^{13}C NMR: (50 MHz, $CDCl_3$) δ 133.1, 129.5, 129.0, 127.2, 101.8, 70.1, 61.0, 41.2, 37.4, 25.8, 22.9, 19.2.

Mass: 298 (M^+, 6), 197 (20), 157 (15), 141 (50), 116 (42).

diethyl3-[(phenylselenyl)methyl]cyclopentane-1,1-dicarboxyllate (80)



Yield 73 %

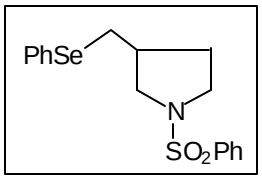
IR 1722, 1540, 1440, 1470 cm^{-1}

^1H NMR: (200 MHz, $CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 6H), 1.35-1.55 (m, 1H), 1.85-2.05 (m, 2H), 2.10-2.40 (m, 3H), 2.45-2.60 (m, 1H), 2.95 (d, J = 8.2 Hz, 2H), 4.20 (q, J = 7.3 Hz, 4H), 7.20-7.30 (m, 3H); 7.45-7.55 (m, 2H).

^{13}C NMR: (50 MHz, $CDCl_3$) δ 172.6, 133.0, 129.3, 127.1, 61.6, 60.4, 40.9, 40.2, 34.1, 33.5, 32.6, 14.3.

Mass: 384 (M^+, 20), 227 (52), 119 (27), 153 (100).

3-[(phenylselenyl)methyl]-1-(phenylsulfonyl) pyrrolidine (85)



Yield	64 %
IR	2925, 1445, 1342, 1161, 1090 cm^{-1}
^{1}H NMR: (200 MHz, $CDCl_3$)	δ 1.50-1.65 (m, 1H), 1.90-2.05 (m, 1H), 2.21-2.37 (m, 1H), 2.60-2.85 (m, 2H), 2.95-3.05 (m, 1H), 3.15-3.55 (m, 3H), 7.20-7.30 (m, 3H), 7.35-7.65 (m, 5H), 7.70-7.85 (m, 2H).
^{13}C NMR: (50 MHz, $CDCl_3$)	δ 133.0, 132.5, 129.0, 128.9, 129.4, 127.2, 53.2, 47.3, 39.1, 31.6, 30.6, 29.6
Mass:	381 (M^+, 4), 223 (100), 209 (13), 141 (25).
HRMS for $C_{17}H_{19}NO_2SSe$	Calculated: 381.030171 Found: 381.032655.

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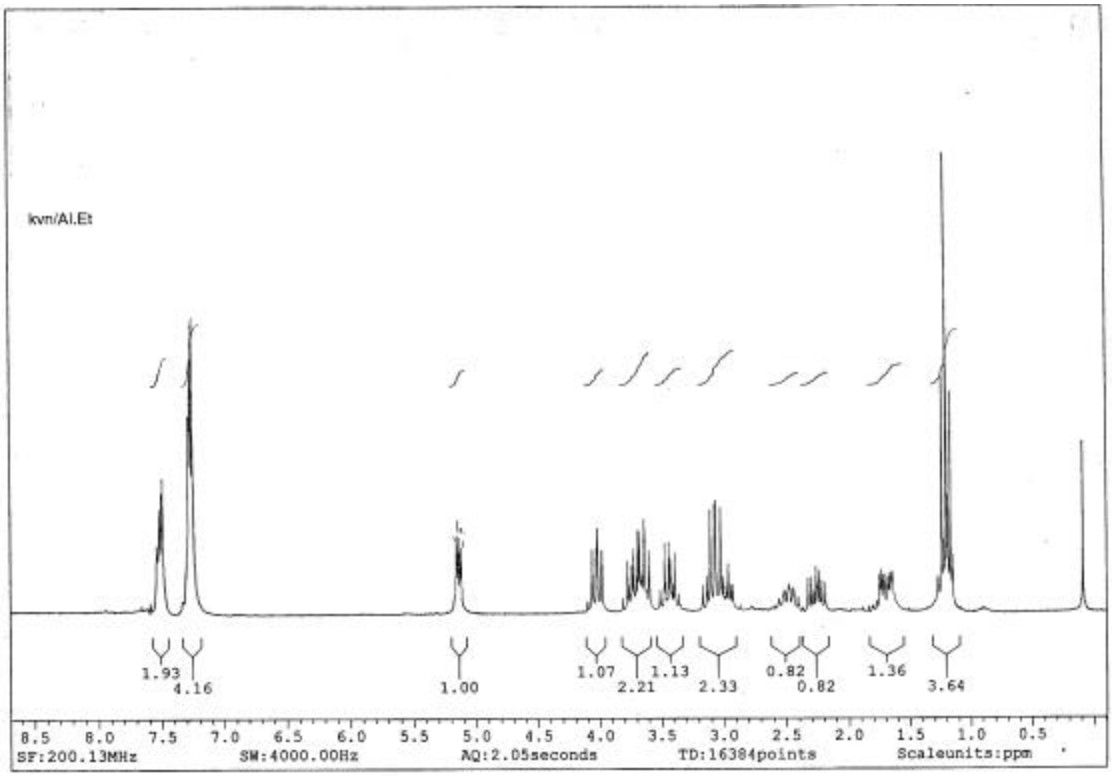
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1.00
1.07
2.21
1.13
2.33
0.82
0.82
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3.64
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
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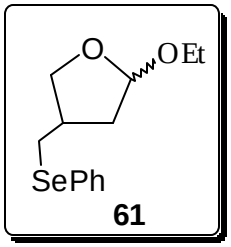
O
OEt
SePh

61

Fig. 1

BASE M/E: 83
RIC: 4374520.
561152.
10.
100.0
50.0
M/E
83
91
77
116
157
99
71
129
197
171
184
240
286
55
141
212
223
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271
298
314
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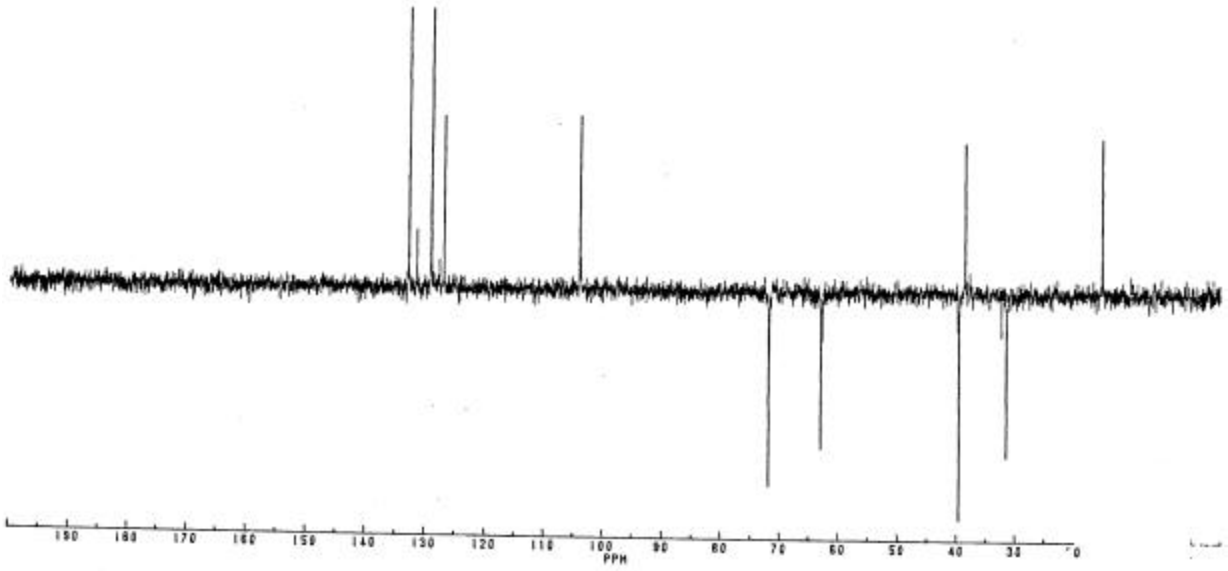
250
300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110
100
PPM
90
80
70
60
50
40
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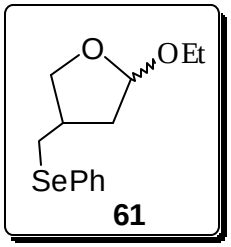
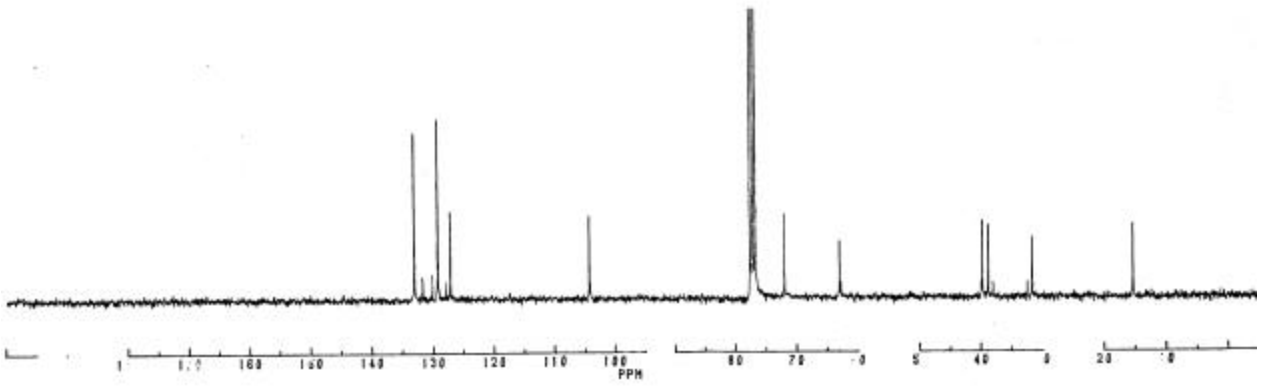

O
OEt
SePh

61

Fig. 2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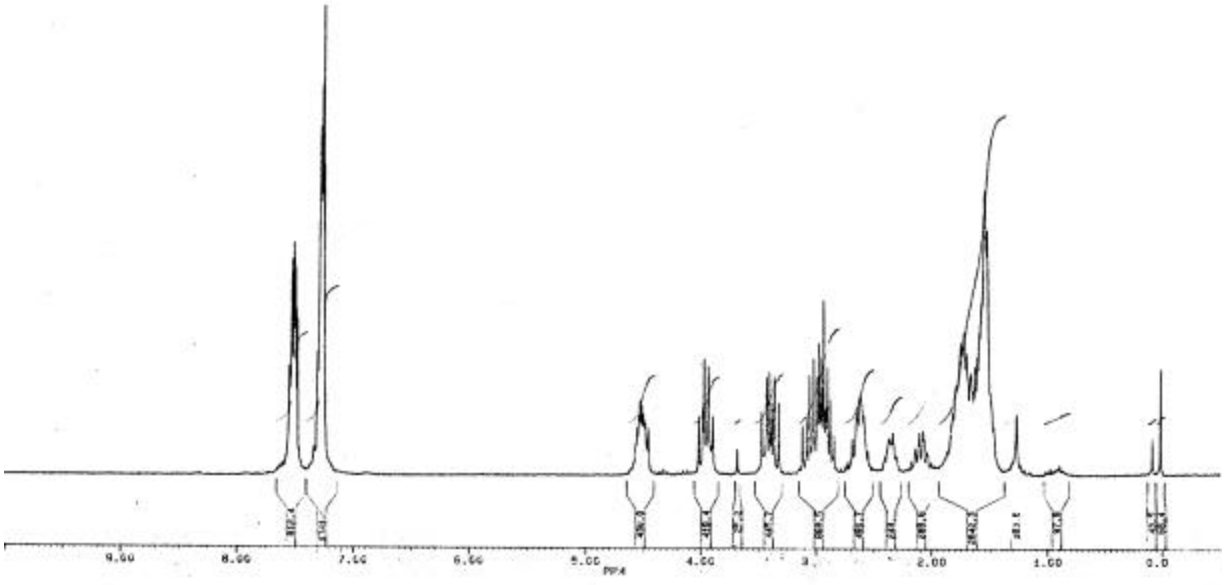

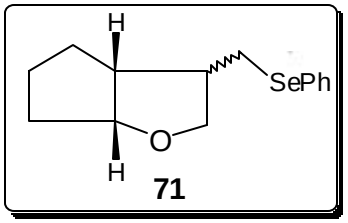
H
SePh
O
H

71

Fig. 3

100.0
50.0
m/E
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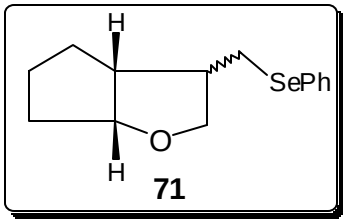
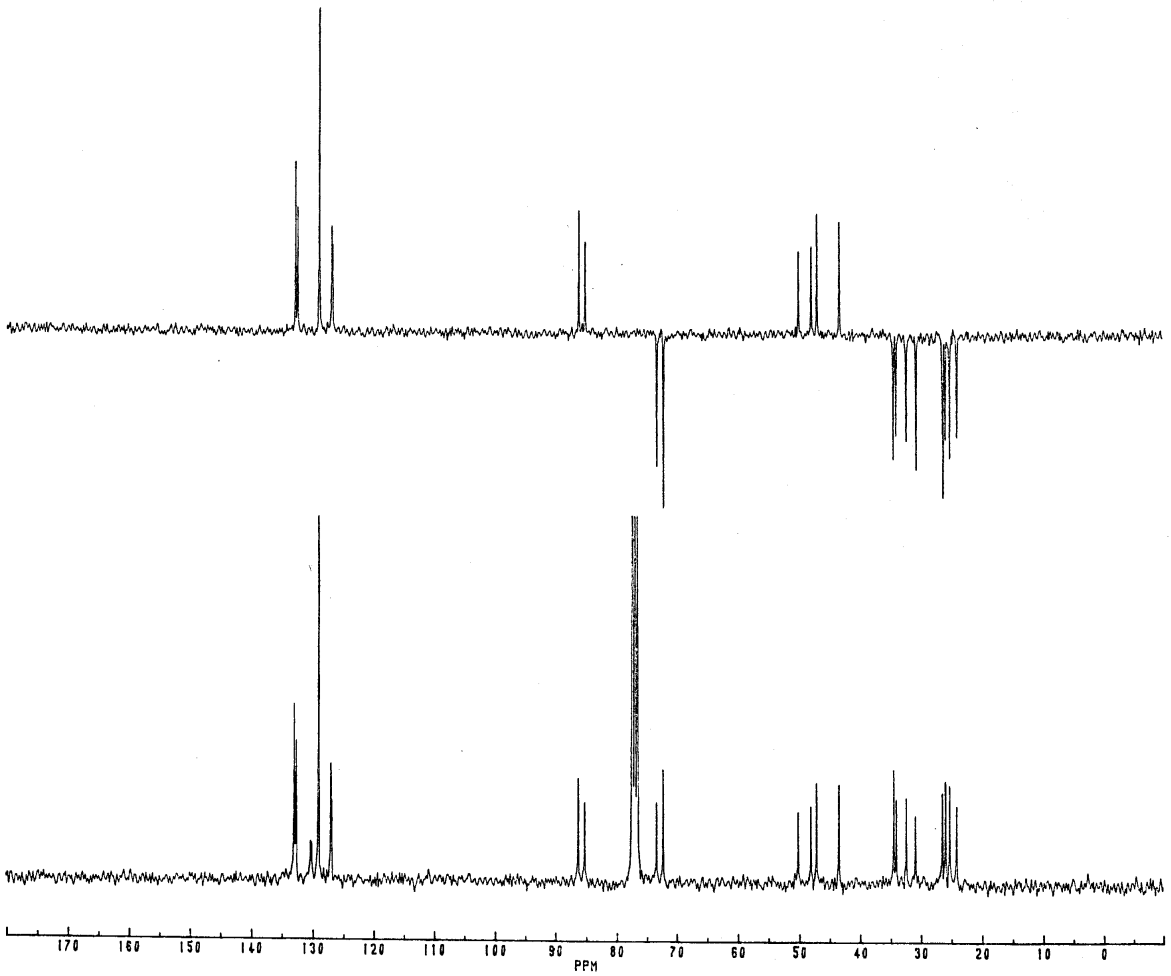
55
77
91
107
124
157
282
50
100
150
200
250
300


H
SePh
O
H

71

Fig. 4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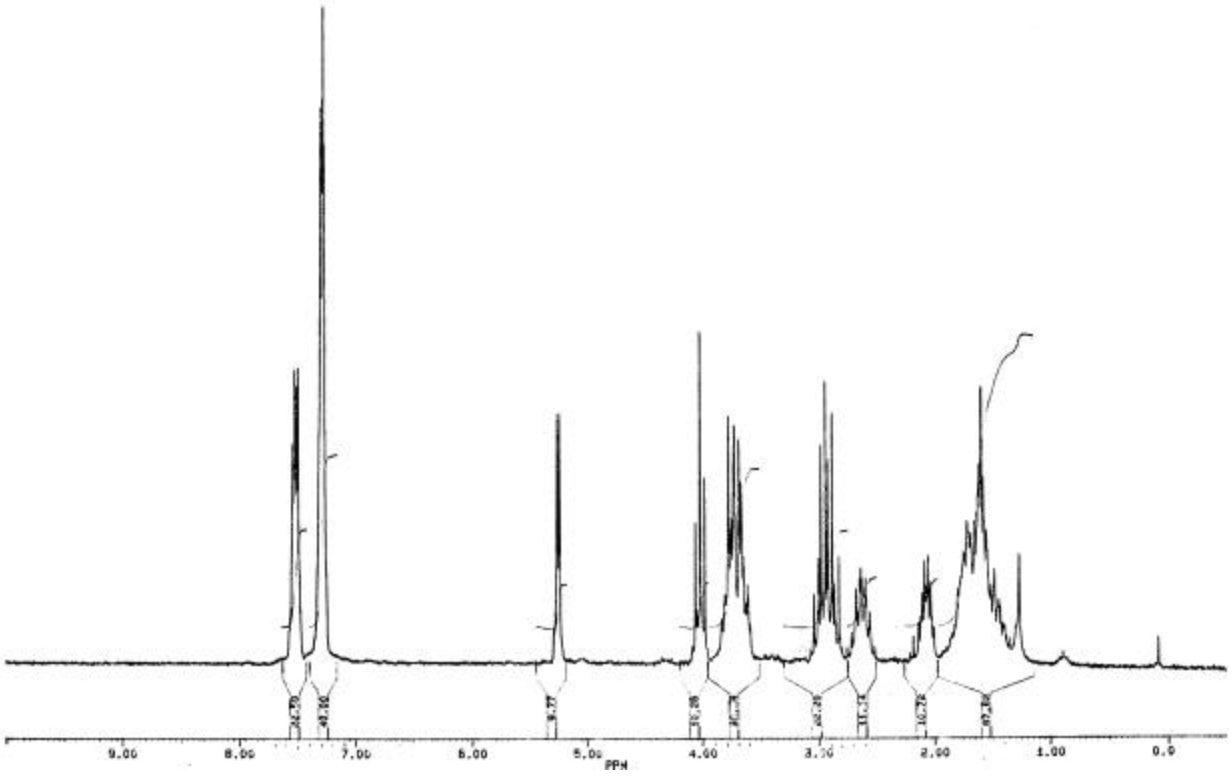
PPM


9.00
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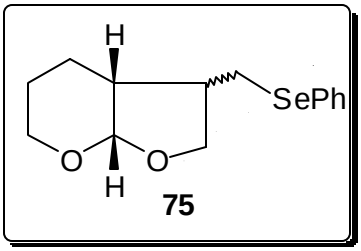
2.00
1.00
0.0
PPM


H
SePh
O
O
H

75

Fig. 5

100.0
50.0
106890.
10.
M/E
50
100
150
200
250
300
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69
77
81
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111
116
123
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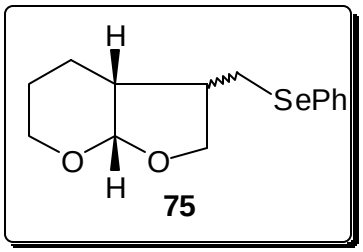
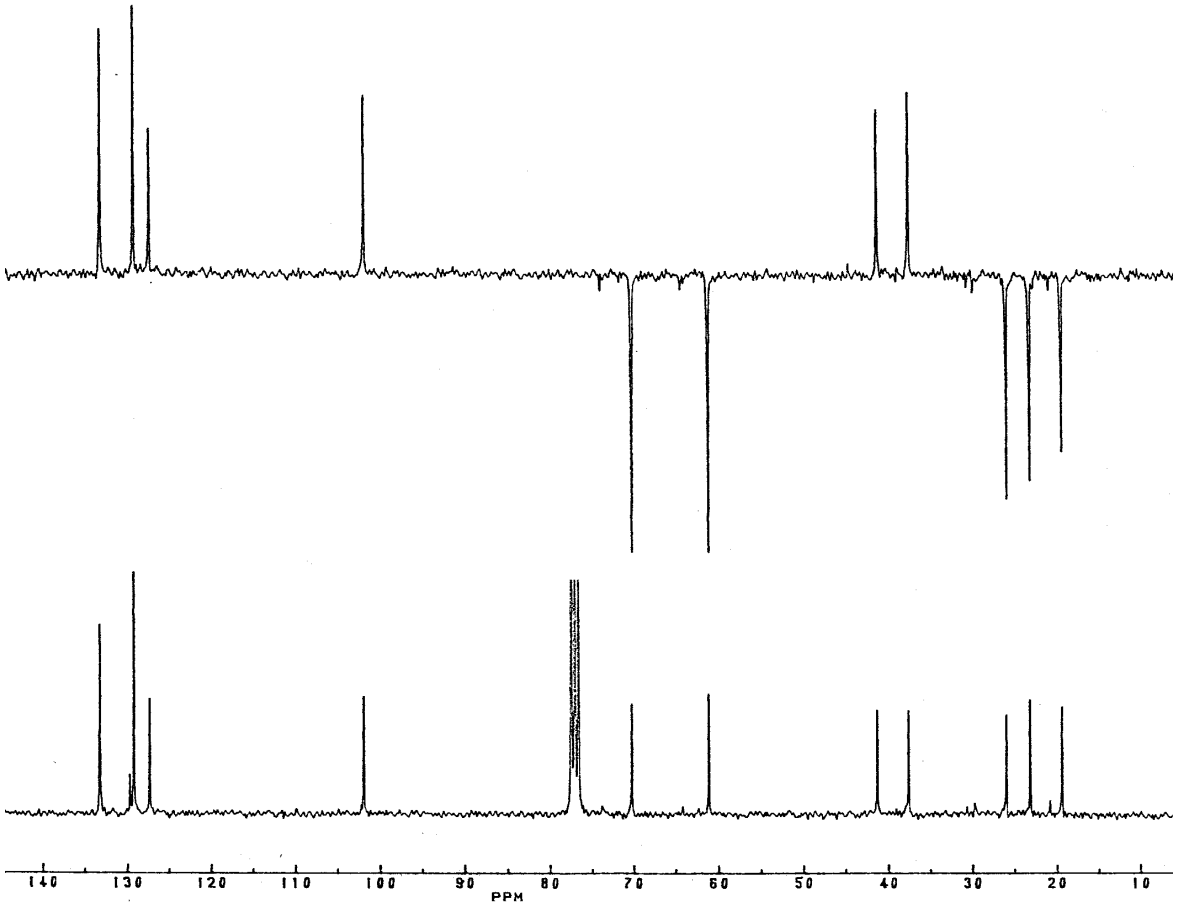
157
171
184
197
212
234
252
298



75

Fig. 6



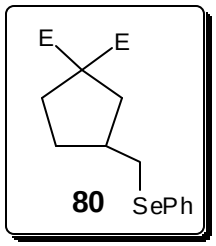
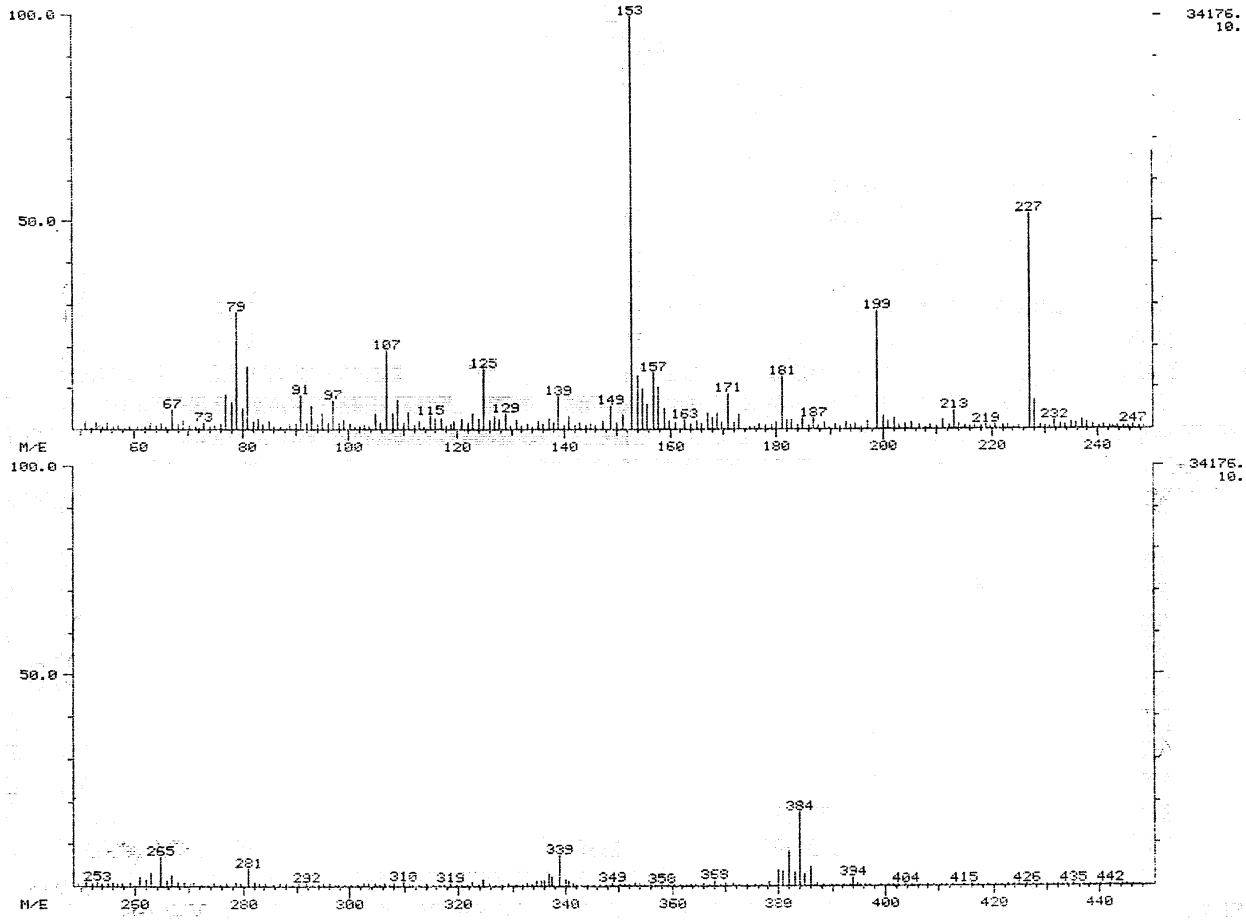

E
E
80
SePh

Fig. 7

PPM


100.0
50.0
M/E
34176.
10.
153
227
199
79
107
125
157
181
171
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73
115
129
139
149
163
187
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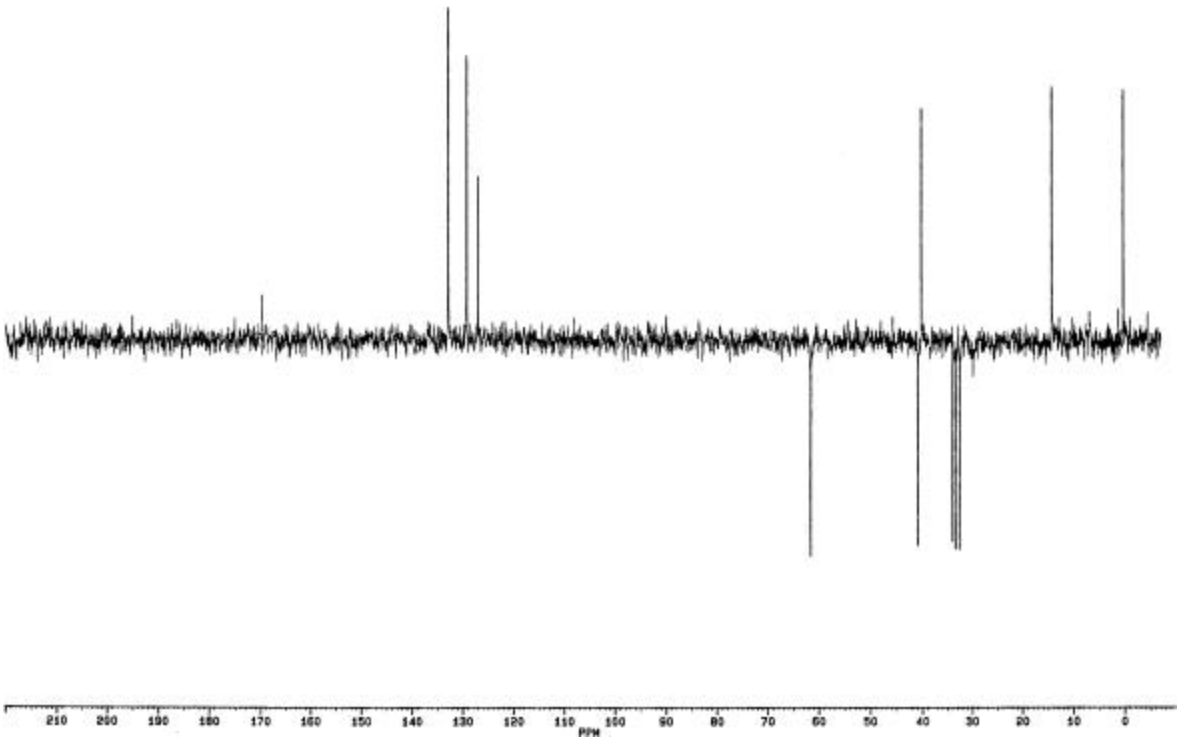
425
435
442


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
PPM

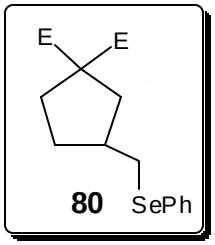
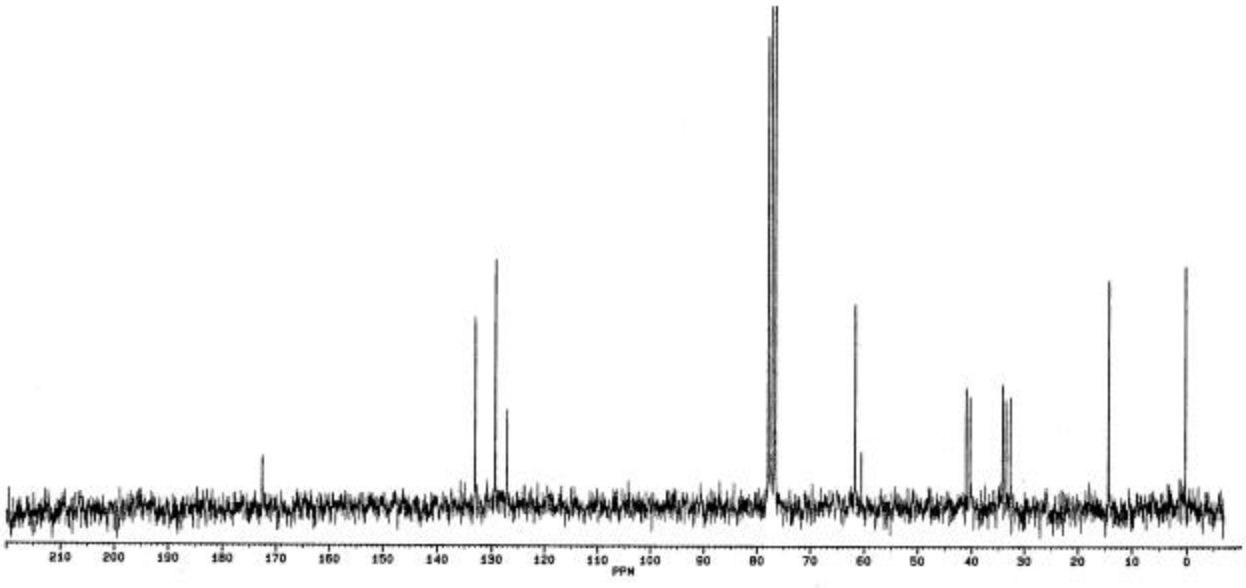

E
E
80 SePh

Fig. 8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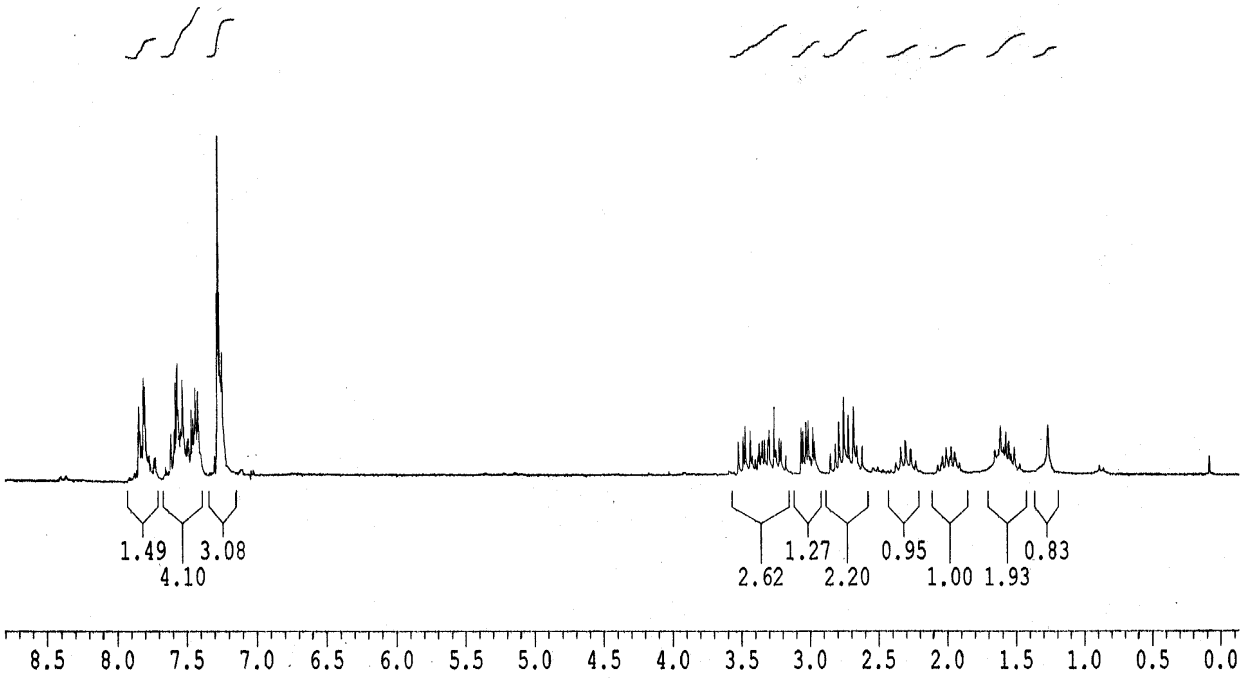
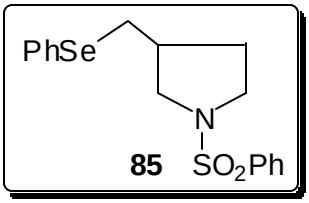
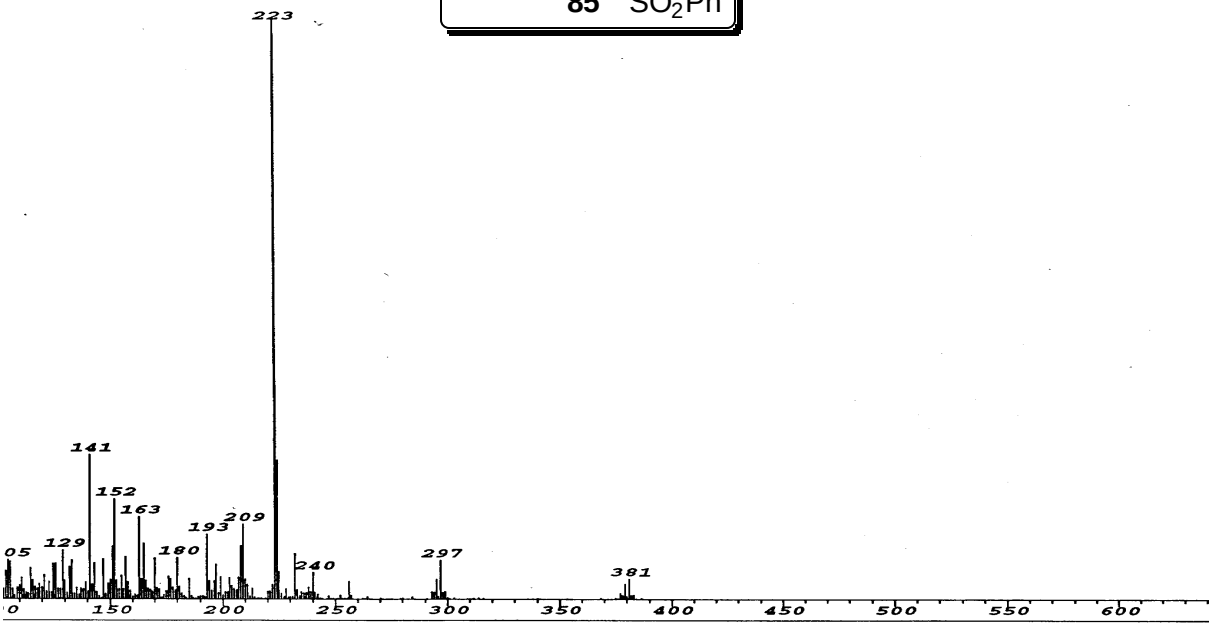
PPM


1.49
3.08
4.10
1.27
2.62
2.20
0.95
1.00
1.93
0.83
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


PhSe
N
SO2Ph

85

Fig. 9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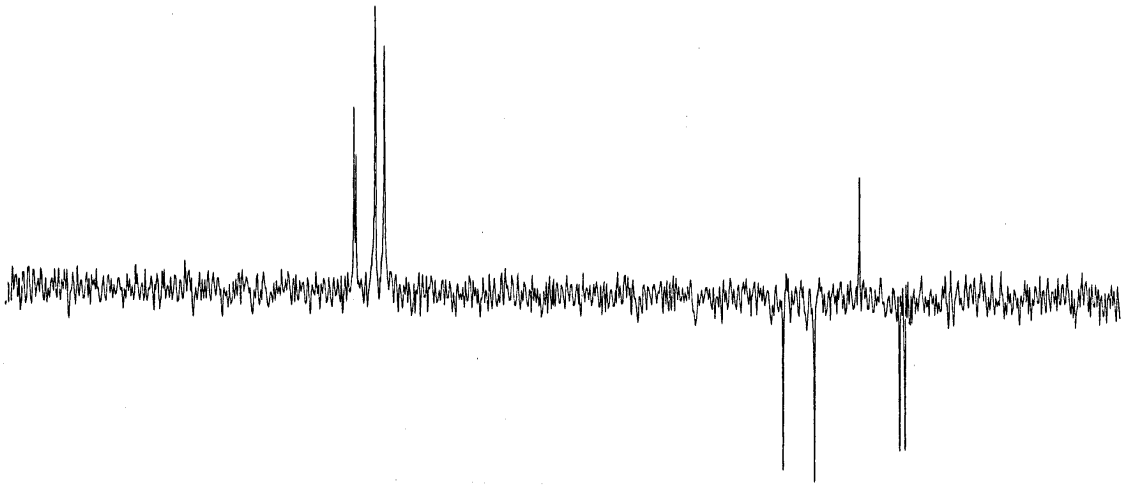
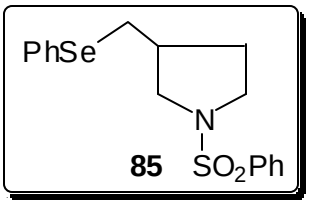
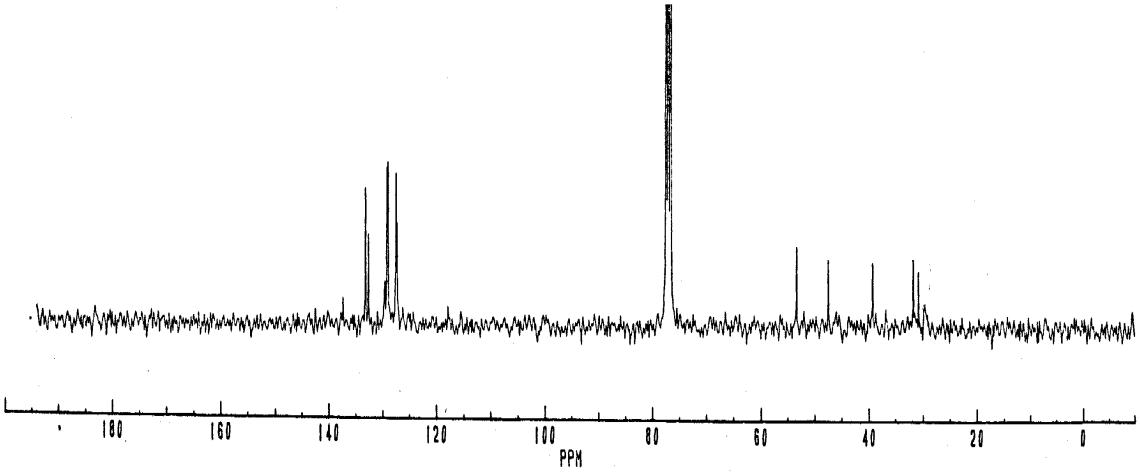
141
152
163
209
193
129
180
240
297
381
150 200 250 300 350 400 450 500 550 600





85

Fig. 10



3-1 INTERMOLECULAR ADDITIONS

3-1.1. Introduction

The successful accomplishment of the catalytic concept of conducting phenylselenyl group transfer radical cyclization reactions, as described earlier in chapter-II, encouraged us to evaluate and extend the horizons of this strategy for other contemporary radical reactions such as intermolecular additions, tandem annulations and tandem radical cyclizations.

The intermolecular radical additions, though, a powerful tool in preparative organic chemistry for conducting a variety of C-C and C-heteroatom bond formation reactions, are difficult in their execution by conventional radical based methods due to competing bimolecular side reactions.[1] Moreover, with stannous based reactions, unlike the entropy favoured intramolecular cyclizations, the intermolecular addition of an alkyl radical to an unactivated alkene is not easily feasible due to difficulty in preventing premature H-atom transfer to the educt radical before it adds to the olefin.[2] Furthermore, the primary alkyl radicals formed by the cleavage of –C-X bond, have two possible options for termination with similar rate constants either by hydrogen atom abstraction from tin hydride (Eq. 3) or by addition to an electron deficient alkene (Eq. 5).

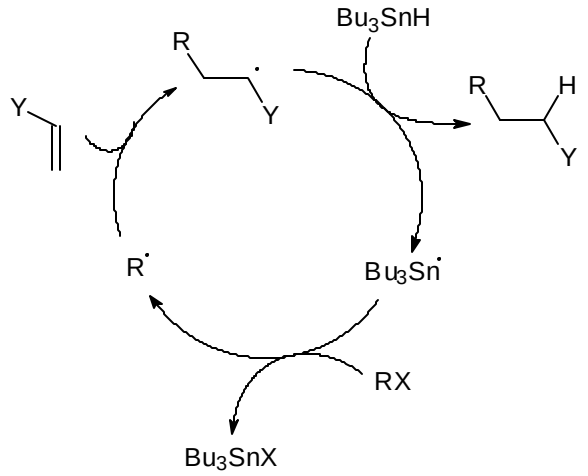
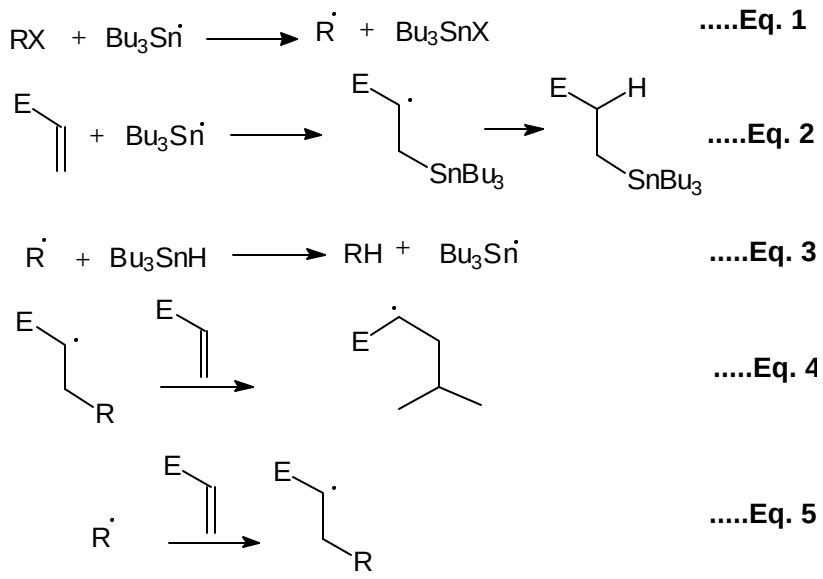


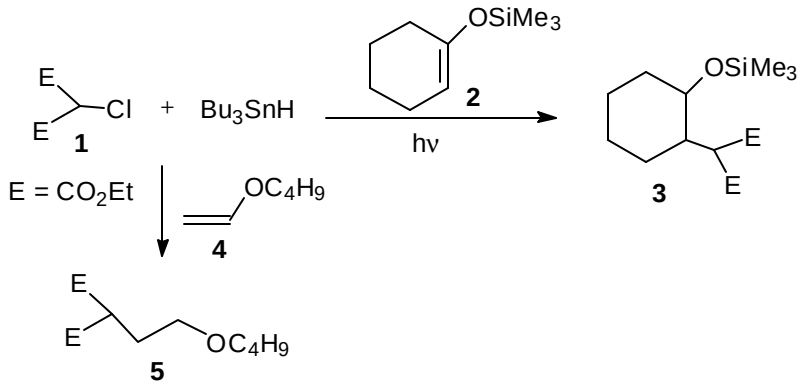
Figure-1

Although the addition of alkyl radicals to an alkene can be directed to some extent by using excess of olefin, the coupling of adduct radicals with another molecule of alkene leading to the formation of telomers and polymers are unavoidable (Eq. 4).



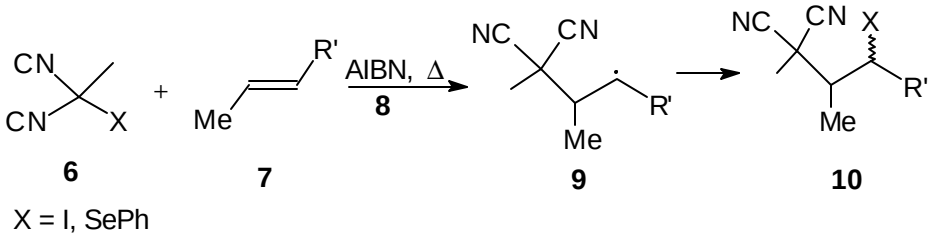
The selectivity requirement of intermolecular radical additions have been achieved by varying the substituents on the radicals as well as on alkenes. For the radicals with more nucleophilic nature, alkenes with electron withdrawing substituents that increases its electrophilicity are favoured. The changes in the selectivity reduces the amount of polymerization because more nucleophilic the radical is, the faster is the reaction with an electron poor alkene and vice versa.[3]

The other approaches known in this context also lack flexibility in the choice of radical precursors. Giese et al[4] have reported intermolecular radical chain addition of 2-(chloro) propanedionate (**1**) with a variety of alkenes (**2** & **4**) using Bu_3SnH as radical initiating reagent. (Scheme-**1**). Although, activated olefins were used in excess, the yields of addition products remained moderate to low because of competitive polymerization reaction of the adduct radicals.



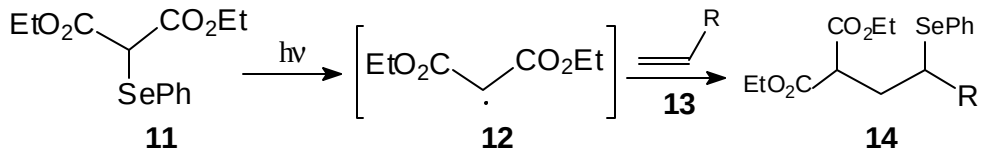
Scheme-1

Curran et al[5] have also described, the addition of malanonitrile radical across C=C bonds in moderate to high yields. The malanonitrile radical was generated thermally from **6** using AIBN (**8**) as a radical initiator (Scheme-**2**).



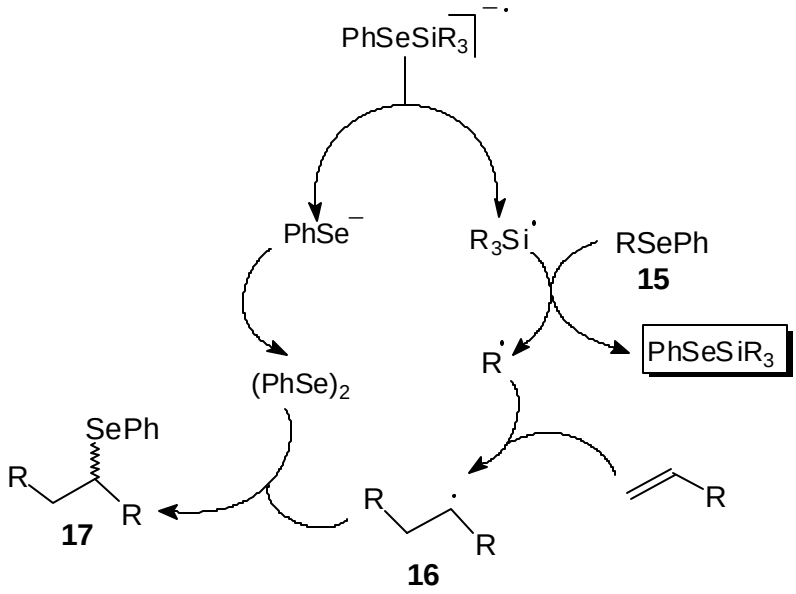
Scheme-2

In a similar approach, Byers[6] has reported an addition of 2-(phenylseleno)-propanedioates to a variety of alkenes and alkynes by sunlamp photolysis in benzene. The method involved a radical chain process in which the initially formed malonate ester radical (**12**) added on to an alkene or alkyne followed by phenylseleno group transfer. However, the yields of the product were found to be moderate to low and the rate of the reaction was slow (Scheme-**3**).



Scheme-3

In the context of impending methods for clean intermolecular radical additions, it occurred to us that an attractive approach could be developed for intermolecular radical additions by applying our concept as shown in Scheme-**4.**



Scheme-4

The above conceptual design provides an opportunity for conducting group transfer intermolecular radical additions in a catalytic manner as bimolecular radical reactions would be diminished due to fast termination of the adduct radical by phenylselenyl group transfer as the rate of termination of a secondary alkyl radical by PhSeSePh is reported to be in the range of 3×10^7 $M^{-1}s^{-1}$.[7]

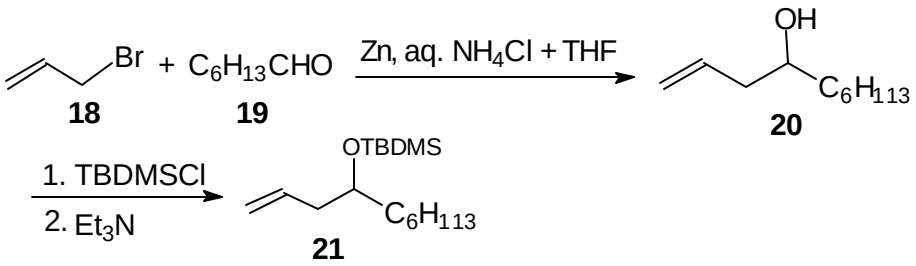
Towards the execution of an intermolecular addition reaction, ethylphenylselenyl acetate (**25)** was chosen as the substrate to study its addition on to an olefin **21.**

3-1.2 Results and Discussion

3-1.2.1. Preparation of 4-*tert*-butyldimethylsilyloxy-1-decene (21)

Substrate **21** was prepared (Scheme-**5**) by the reaction of allylzinc with heptaldehyde (**19**) followed by the –OH group protection of the resultant **20** as OTDBMS

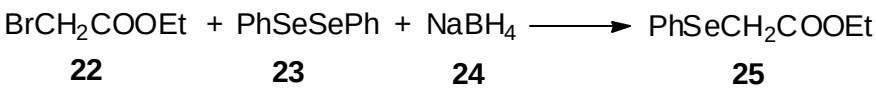
ether. The detailed experimental procedure for preparation of **21** is given in the experimental section.



Scheme-5

3-1.2.2 Preparation of Ethyl phenylselenylacetate (25)

Substrate **25** was prepared by the nucleophilic displacement of bromide ion from ethylbromoacetate by the phenylselenyl anion (Scheme-**6**). The phenylselenyl anion was generated by the reaction of $NaBH_4$ and PhSeSePh as discussed earlier.



Scheme-6

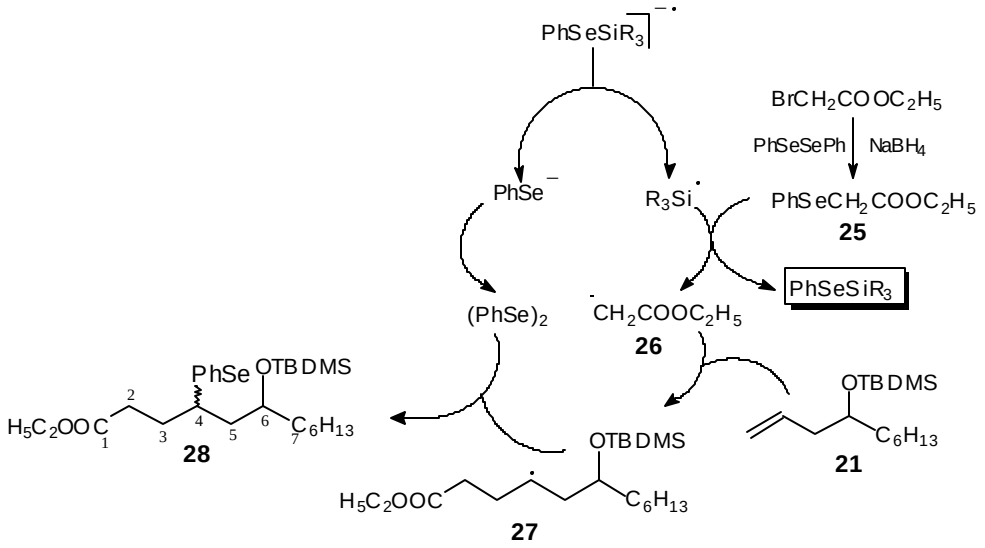
3-1.2.3 PET activation of a mixture containing 25 and 21

The PET activation of a mixture containing **25** and **21** was carried out by irradiating a dilute solution of **25** (1.85 mmol), **21** (1.85 mmol), DMA (0.63 mmol), ascorbic acid (1.57 mmol) and $PhSeSiR_3$ (0.18 mmol) in a similar manner as described earlier in Chapter-II. The progress of the reaction was monitored by HPLC. After 7 h of irradiation when almost 60 % consumption of **25** was noticed, irradition was discontinued. Usual workup and purification of the crude photolysate by column chromatography afforded **28** as a pale yellow oil in 61 % yield.

IR spectrum of **28** exhibited prominent absorption bands at 1708, 1585, 1422 cm^{-1}.

Although product **28** appeared as a single compound on TLC, the HPLC analysis suggested it to be a mixture of diasteriomers (66:35) which was non-seperable by column chromatography.

^{1}H NMR spectrum of **28** (Fig. **5**) showed two sets of multiplets at δ 7.50 (2H) and δ 7.30 (3H), assigned to the aromatic protons of the SePh group. A quartet at δ 4.10 (2H, *J* = 8.1 Hz) corresponds to the methylene protons of the ester group (OCH_2CH_3). A multiplet at δ 3.20 (1H) was assigned to the H_4 methine proton attached to SePh group. Another multiplet at δ 2.50 (1H) corresponds to the H_6 methine proton. The multiplet at δ 1.85 (2H) could be ascribed to the methylene protons attached to the carbonyl group of the ester (-OC(O)-CH_2) moiety. The remaining protons of the alkyl chain and the protons of silyl group appeared as a broad multiplet between δ 0.85-0.97 (13H) and δ 00-0.10 (9H).



Scheme-7

Fully decoupled ^{13}C NMR spectrum of **28** (Fig. **6**) indicated it to be a mixture of two isomers. INEPT experiment of the product gave a detailed analysis of the signals which are as follows: The signal at δ 173.0 corresponds to the C_1 carbonyl carbon. The six aromatic carbons appeared between δ 135.6-127.3. The signals at δ 70.5 and 70.4 corresponds to C_6 carbon. The signal at δ 60.2 is assigned to the methylene carbon of the ester. The signal at δ 43.5 is assigned to C_2 carbon. The signals at δ 42.5 and 42.1 can be assigned to C_4 carbons. The alkyl carbons appeared between δ 37.8-29.4. The signals at δ 25.9 and 25.8 correspond to the terminal methyl carbon of the alkyl chain. The

quaternary carbon, attached to silicon of OTBDMS, appeared at δ 18.0. The signal at δ 14.1 is assigned to the methyl carbon of ter-butyl group. The methyl carbon attached to silicon appeared at δ -4.1 and –4.3.

Mass spectrum of the product (Fig. 5) showed molecular ion peak at 514 (4%) and base peak at 244. The other prominent fragmentations were observed at 457 (22), 171 (30) and 157 (20).

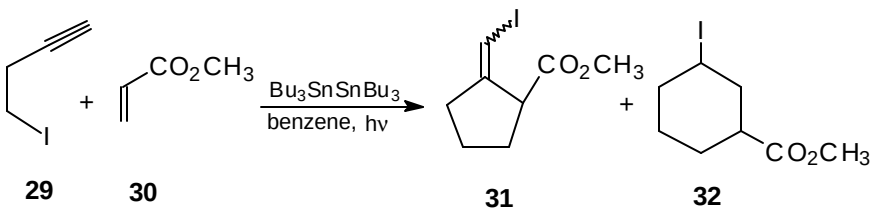
3-2 TANDEM ANNULATION REACTIONS

3-2.1 Introduction

After successful application of our phenylselenyl group transfer intermolecular radical additions, we focussed our attention towards another exciting area of radical chemistry- the tandem annulations.

Annulations are described as the ring forming processes in which two molecular fragments are united with the formation of two new bonds in one pot transformation. To be precise, in annulation reaction a ring is formed from two acyclic precursors and in that the molecular formulae of the product is equal to the sum of the molecular formula of the starting materials. This method generally requires the presence of activated alkenes which are either attached to a electron withdrawing group or electron donating heteroatom.

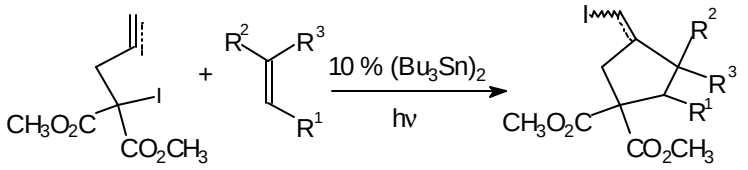
Chen has reported[8] an annulation reaction by the irradiation of a benzene solution of butynyl iodide (**29**) with methylacrylate (**30**) in the presence of 10 % of hexabutylditin to afford (iodomethylene)cyclopentane (**31**) and a small amount of cyclohexyl iodide (**32**) (Scheme-**8**).



29 **30** **31** **32**

Scheme-8

In their continuing work on annulations, Chen has also demonstrated[9] that propargyl and allyl iodomalonic esters (**33**) are excellent reagents for the annulations of methylene (and methyl) substituted cyclopentane rings (**35**) from terminal and 1,1-disubstituted alkenes (**34**) (Scheme-**9**).



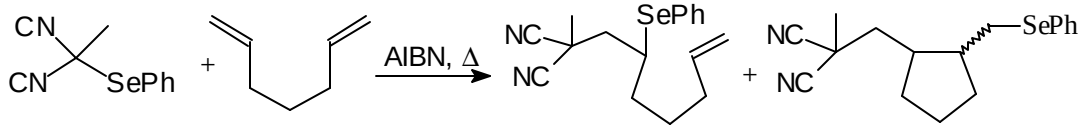
33 **34** **35**

R^2, R^3 = alkyl, phenyl ;
R^1 = H

Scheme-9

Annulations with 1,2-disubstituted alkenes were reported to give poor yields because the radical addition step may not be adequately rapid. Several annulations were reported with olefins by allyl as well as propargyl iodomalonates. The cyclic alkenes failed to participate in annulation reactions because the construction of the fused rings by annulation of new rings to pre-existing ones will not be possible.

Boldt[10] has demonstrated that the parent malanonitrile radical has much better reactivity than its malonic ester counterpart and it adds to a variety of di- and tri-substituted alkenes. Curran[11] has used this concept for an annulation reaction from methyl (phenylseleno) malanonitrile (**36**) and heptadiene (**37**) to produce **39** (Scheme-**10**).



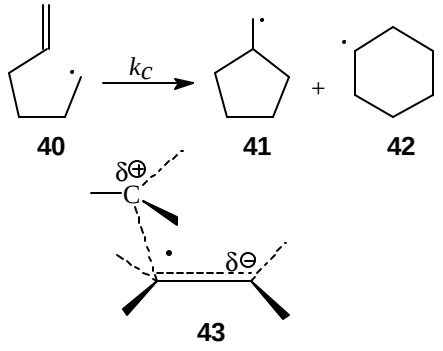
36 **37** **38** **39**

Scheme-10

Propargyl and allyl iodomalanonitriles[12] were also used for annulation reactions. However, the reaction with propargyl iodomalononitrile was found to stop usually at the

adduct stage while reaction with propargyl iodomalonic esters proceeded to annulated products.

Most of the annulations discussed above involve 5-hexenyl radicals and they undergo cyclizations in an *exo*-mode to give five membered carbocyclic rings. However, construction of six membered carbocyclic ring systems, also widely distributed in numerous biologically active molecules, by *endo*-mode radical cyclizations has been known to be difficult due to stereo electronic reasons.[1] The preferred *exo-trig* cyclization of a 5-hexenyl radical over its *endo-trig* counter part has been explained[13] by invoking a dipolar transition state structure **43** as depicted in the Scheme-**11**.



40 **41** **42** **43**

Scheme-11

The dipolar nature of the transition state **43** indicates the donor nature of the attacking radical and the acceptor nature of the double bond. Various calculations[14] on this three carbon triangular array, perpendicular to the π-nodal plane has suggested strongly that an *exo*-cyclization is geometrically easier than *endo*. Although, this mode of cyclization has become a rule, substitutions that hamper the double bond or reversibility in the addition is known to change the regioselectivity of the process.[15] In the case of radical centers other than carbon, change in regioselectivity is contributed due to the problems of hybridization and changed bond lengths. One such instance is seen in the case of silyl substituted radical centers.

The presence of silicon atom α as well as β to a carbon centered radical is known to reverse the regioselectivity of radical cyclization (favouring the *endo*-mode).[16] For an α-

silyl radical, the preferred *endo*-mode of cyclization is referred due to the involvement of a seemingly less dipolar transition state structure compared to a normal carbon-centered radical. It is less clear for a β-substitued hexenyl radical, however, Wilt and Ingold have suggested[17] that the *endo*-selectivity may originate from a synperiplanar conformational preference for the β-silicon ethyl radical **44** which is 1.3 Kcal/mol more favourable than the eclipsed conformer **45** (Figure-**2**). In addition to this preference, if a considerable barrier to the rotation around the C_{β}-Si and C_{δ}-Si bonds exists, any distortion from ground state conformation **46** would lead to highly disfavoured transition state conformation **47** for cyclization.

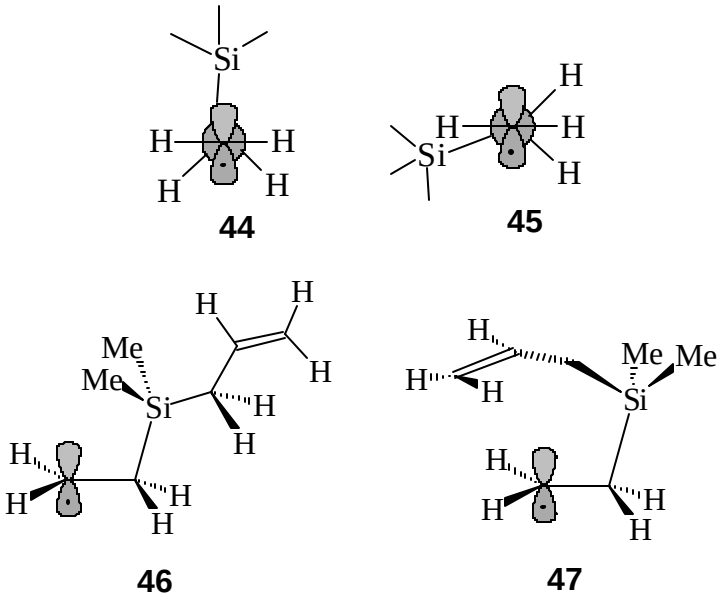


Figure-2

These studies have been shown with very few examples[18] where the *endo*-cyclization places a silicon atom in the ring and no example has been reported to the best of our knowledge where the silicon atom is positioned externally to the *endo*-cyclized ring. In this context it occurred to us that, if these observations are general, a tandem (addition/cyclization) annulation reaction should take place between **51** and allyl trimethylsilane (**53**) giving rise to a six membered carbocyclic ring **55** (Scheme-**13**). This

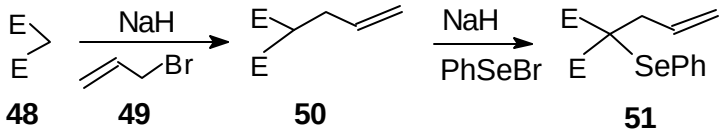
endo-cyclization was expected to result from the intermediate radical **54** via the transition state structure **54a**. The success of this concept was also expected to provide an option to organic chemists for manipulating the regiochemistry of radical reactions during carbocyclization reactions.

Towards this endeavor, a tandem approach for *endo* selective radical annulation reaction was conceived and is described below.

3-2.2 Results and Discussion

3-2.2.1 Preparation of Substrate 51

Substrate **51** was prepared by the allylation of diethylmalonate in the presence of NaH followed by electrophilic reaction of PhSeBr on monoallylated diethylmalonate anion (Scheme-12). Detailed procedure for the preparation of **51** is given in the experimental section.



48 **49** **50** **51**

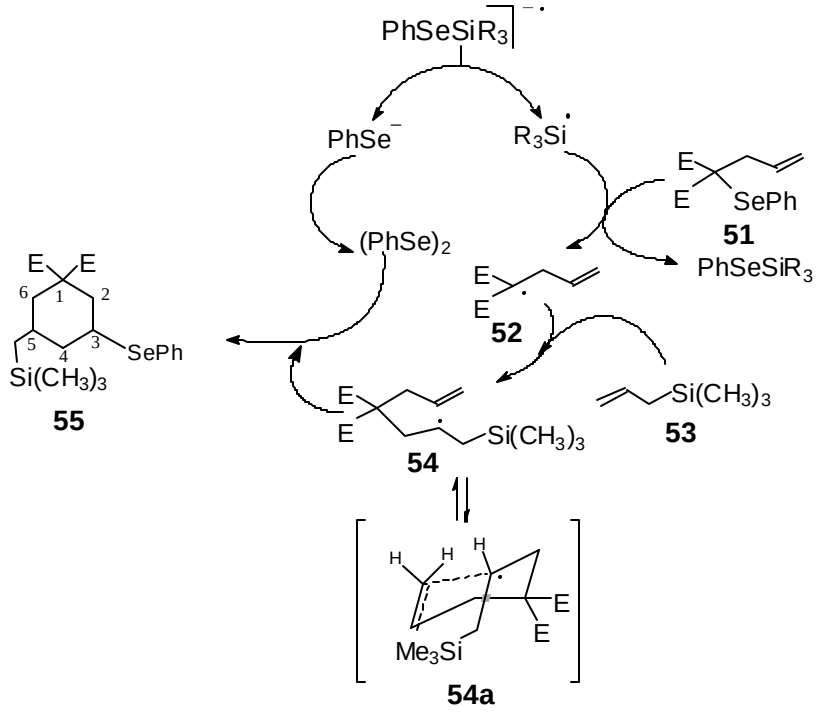
Scheme-12

3-2.2.2 PET promoted annulation of 51 and 53

Towards the fulfillment of our objective, PET activation of a mixture containing $PhSeSiR_3$ (0.15 mmol), **51** (1.4 mmol), DMA (0.63 mmol), ascorbic acid (1.62 mmol) and allyltrimethylsilane (**53**) (3.5 mmol) in acetonitrile was carried out. Usual workup followed by silica gel flash chromatography afforded an oily product (**55**) in 65 % yield. The product was characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analysis. The spectral data of product **55** is described as follows:

The ^{1}H NMR spectrum of **55** (Fig. **7**) showed two sets of multiplets at δ 7.50 (2H) and 7.30 (3H) for aromatic protons of the phenylselenyl group. The quartet at δ 4.15 (4H, *J*

= 4.2 Hz) can be assigned to the four methylene protons of the two ester groups ($OC\underline{H}_2CH_3$). A multiplet at δ 3.05 (1H) was assigned to the H_3 methine proton attached to SePh. Another multiplet at δ 2.75 (1H) was ascribed to one of the H_2 methylene protons. The broad multiplet between δ 2.10-2.50 (5H) was assigned to the remaining H_2 proton, the two H_6 protons adjacent to quaternary carbon and the two H_4 methylene protons. The multiplet at δ 1.95 was ascribed to the H_5 methine proton on the cyclohexane ring. A triplet at δ 1.25 (6H) corresponds to the six methyl protons of the two ester groups (CO_2-CH_2-$C\underline{H}_3$). The broad multiplets between δ 0.3-0.7 (2H) were assigned to the two methylene protons attached to TMS. A singlet at δ 0.05 (9H) corresponds to the methyl protons attached to silyl group.



Scheme-13

The fully decoupled ^{13}C NMR spectrum of the product (Fig. **8**) exhibited 13 signals. The detailed characterization of the signals by INEPT experiments gave following details: The signal at δ 172.0 corresponds to the two carbonyl carbons of the ester group. Signals at δ 132.9, 130.4, 128.9, 126.7 were characteristic of the aromatic carbons. The two

methylene carbons of the ester groups appeared at δ 61.3 (OCH_2CH_3). The signal at δ 58.9 corresponds to C_1 quaternary carbon of the cyclohexane ring. The C_3 methine carbon of the cyclohexane ring appeared at δ 43.9. The two methylene carbons C_2 and C_8, adjacent to quaternary carbon of the cyclohexane ring, appeared at δ 38.8. The signal at δ 38.7 was assigned to the C_5 methine carbon of the cyclohexane ring. The C_4 methylene carbons of the cyclohexane ring appeared at δ 29.1. The signal at δ 16.2 corresponded to the methylene carbon attached to TMS group (CH_2-TMS). The two methyl carbons of the ester group appeared at δ 13.9. The three methyl carbons of the TMS group appeared at δ -0.1.

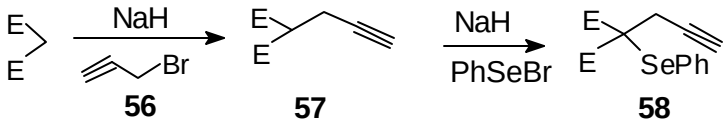
The mass spectrum of the product **55** (Fig. **7**) exhibited molecular ion as the base peak at 470. The other prominent fragmentations were observed at 455 (34), 425 (16), 397 (16), 337 (4), 313 (57), 239 (20), 157 (10). The calculated HRMS value for $C_{22}H_{34}O_4SiSe$ was 470.139159 and the value obtained for the sample was found to be 470.137444.

By the above spectral analysis, structure **55** was confirmed. The C_3 methine proton adjacent to SePh appearing at δ 3.05 also confirms the *endo*-cyclic closure. Had the closure been *exo*-cyclic, methylene protons would have appeared in the place of a methine proton adjacent to SePh. The relative stereochemistry between C_3 and C_5 carbons was not established.

The spectacular success of the tandem annulation reaction discussed above encouraged us to study another annulation reaction between **53** and **58**. We envisaged that the effect of β-silyl radical on a system tethered with a propargylic group where the bond angle between two carbons is 180°, could be an interesting and new exploration.

3-2.2.3 Preparation of substrate 58:

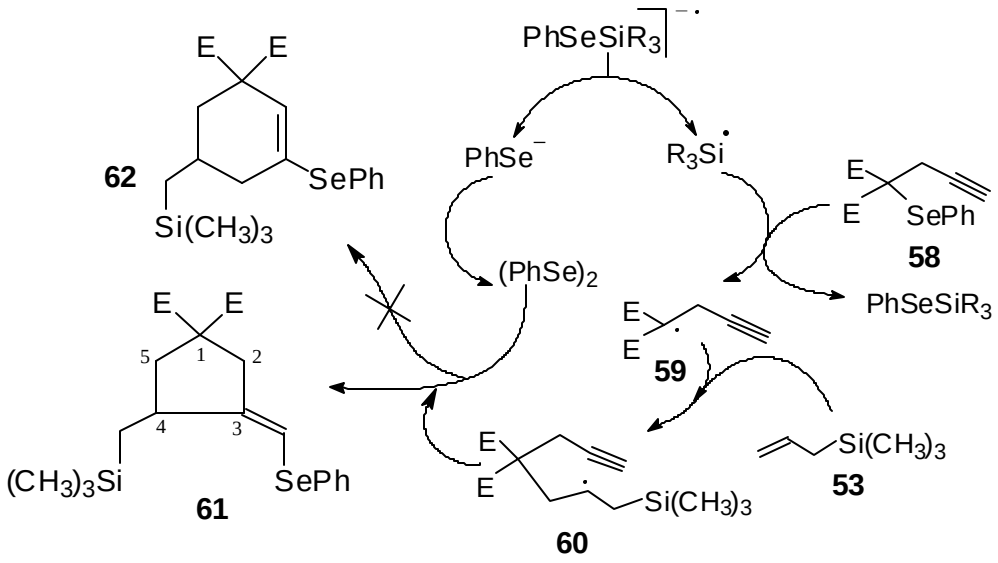
Substrate **58** was synthesized in an identical manner as described for **51** from propargyl bromide (**56**) and diethylmalonate. The spectral details of the compound **58** are given in the experimental section.



Scheme-14

3-2.2.4 PET promoted annulation of 58 on 53:

Identical irradiation of a mixture containing $PhSeSiR_3$ (0.15 mmol), **54** (1.4 mmol), DMA (0.63 mmol), ascorbic acid (1.62 mmol) and allyltrimethylsilane (**53**) (3.5 mmol) in acetonitrile afforded a pale yellow product (**61**) in 67 % yield. The product was characterized by ^{1}H NMR, ^{13}C NMR, mass and COSY spectral analysis.



Scheme-15

IR spectrum of the product **61** showed prominent absorptions at 3050, 3000, 2250, 1738, 1704, 1595, 1500, 1475 1250 and 1200 cm^{-1}.

In the ^{1}H NMR spectrum (Fig. **9**), the aromatic protons related to PhSe group appeared as multiplets at δ 7.25 (3H) and 7.5 (2H). Another multiplet at δ 6.25 (1H) corresponds to the olefinic proton. The multiplet at δ 4.25 belonged to the four methylene protons of the two ester groups. The other multiplet at δ 3.10 was assigned to the two H_2 methylene protons α- to the quaternary carbon. Another multiplet at δ 2.70 could be assigned to the H_6 methylene protons of the ring. The multiplet at δ 1.70 was ascribed to the H_4 methine proton of the cyclopentane ring. The multiplet at δ 1.25 corresponds to the two methyl protons of the ester groups. The two sets of multiplets integrating for one proton each at δ 1.10 and δ 0.60 is assigned to methylene proton α- to the TMS group. The 9-methyl protons of the TMS group were observed at 0.0.

The above proton assignments were based on COSY spectral analysis of the product (**57**). The H_4 methine proton α- to CH_2TMS appearing at δ 1.70 showed coupling with only H_5 methylene protons at δ 2.70. No coupling was observed with H_2 protons at δ 3.10. This observation would hold true only when there is a five membered ring with an *exo*-cyclic double bond. Therefore, the product was assigned structure **61**.

The ^{13}C NMR spectrum of the product (Fig. **10**) displayed 14 C- signals. The detailed spectral characterization of the signals was made by INEPT experiment which are described as follows: The signal at δ 171.3 corresponds to the carbonyl carbon of the ester group. The signal at δ 151.9 was assigned to the C_3 olefinic quaternary carbon of the *exo*-cyclic ring. The signals at δ 131.3, 128.8, 126.3 belonged to the aromatic carbons of the SePh group. The olefinic methine carbon (C=<u>C</u>-SePh) appeared at δ 109.0. The two methylene carbons of the ester group (CO_2-CH_2-CH_3) appeared at δ 61.2. The C_1 quaternary carbon of the cyclopentane ring was observed at δ 58.1. The C_2 methylene carbon of the cyclopentane appeared at δ 41.8. The signal at δ 40.6 corresponds to the C_4 methine carbon of the cyclopentane ring. The signal appearing at δ 39.4 was ascribed to C_5 methylene carbon. The methylene carbons α- to the TMS group appeared at δ 20.31

($\underline{C}H_2$-TMS). The signal at 13.75 corresponded to the two methyl carbons of the ester groups ($CO_2CH_2\underline{C}H_3$). The TMS methyl groups appeared at δ 1.09.

The mass spectrum of **61** (Fig. **9**) exhibited molecular ion peak at 468 and base peak at 73. The other prominent fragmentation peaks were observed at 312 (7), 119 (5), 92 (17).

The formation of the *exo*-cyclic product in the present case (with β-silyl radical) is analogous to the *exo*-*dig*-cyclizations reported for α-silyl radicals where the cyclization proceeded only in a 5-*exo*-mode.[19] This observation is in complete contrast to the β-silyl radical system tethered with an olefinic double bond as discussed earlier where the cyclization occurred in an exclusively *endo*-mode. This disparity was rationalized on the trajectory requirement of the radical center allowing only a 5-membered ring formation due to the 180^0 angle of C-C≡C bond even (despite) with long C-Si bond lengths.

3-3 INTRAMOLECULAR TANDEM RADICAL CYCLIZATIONS

3-3.1 Introduction

In general, the synthesis of an organic compound involves stepwise formation of individual bonds of the target molecule. The product of each transformation is separated and purified for performing the next reaction to reach the target molecule. However, it would be much more advantageous if several bonds of the target compound could be formed in one sequence without isolating the intermediates, changing the reaction conditions or adding any additional reagents.[20] This will allow the minimization of wastes formed in each step, besides reducing the number and quantity of reagents, solvents, energy and precious time. Thus, such reactions become very important in terms of economy and ecology.

The reaction, which encompasses all the above properties, is termed as a tandem, domino, cascade or a sequential reaction. The basic transformation in all the reactions is essentially the same and a tandem reaction literally means a reaction sequence which occurs “one behind the other.”

Tietze has broadly classified[21] these one pot sequential transformations into two categories. They are domino reaction and consecutive reaction. A domino reaction can be defined as a process involving two or more bond forming transformations (usually C-C bonds) taking place under the same reaction conditions without adding additional reagents and catalysts and in which the subsequent reaction results as a consequence of the functionality formed in the previous step. The preliminary formation of the reactive intermediates like carbocations and carbanions are not counted as reaction steps, but the formation of a diene by a retro Diels-Alder reaction with subsequent cyclization would be considered as a domino reaction.

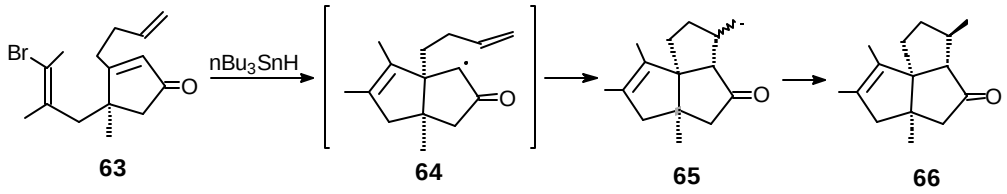
On the other hand, a consecutive reaction involves the addition of another reagent, mediator or a catalyst after the first transformation without the isolation of the initially formed product. The subsequent reaction steps then leads to a final product.

While endorsing Tietze’s classification, Denmark[22] has slightly modified them in terms of cycloadditions namely tandem cascade cycloaddition, tandem consecutive cycloaddition and tandem sequential cycloaddition. A tandem cascade reaction or a domino reaction is more or less one and the same. Both tandem cascade cycloaddition and tandem consecutive cycloaddition accede to the Tietze’s[21] definition of a domino and a consecutive reaction. In a tandem cascade reaction, intermediate is not an isolable species but it is rather converted into tandem product on workup. But in a tandem consecutive reaction, intermediates can be isolable containing the necessary functionality for performing the second reaction, but additional energy is required in the form of heat or light. However, tandem sequential cycloaddition require the addition of the second component (one of the cycloaddition partners or another reagent) in a separate step.

Coming back to Tietze's classification, domino reactions are broadly of two types; homo-domino and hetero-domino, based upon the type of primary and secondary transformation it undergoes in the first two synthetic steps. The transformations could be cationic, anionic, radical and pericyclic. Each type is divided into subgroups depending upon the second transformation such as cationic-cationic (homo-domino), cationic-pericyclic or cationic-radical (hetero-domino) and so on.

Since, the discussion in this chapter is particularly limited to radical-radical (homo-domino) sequence based methods, some important examples of such kind are discussed briefly to introduce the subject.

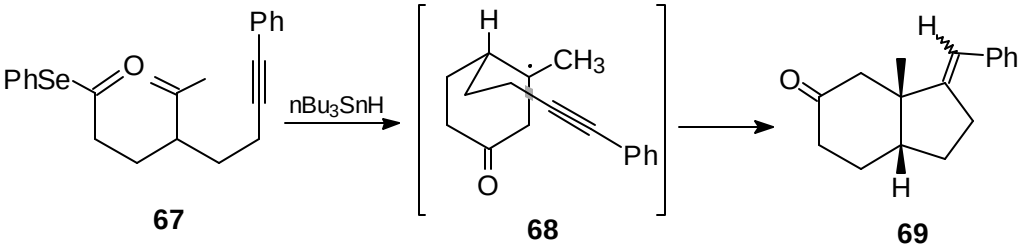
The synthesis of hirsutene, capnellene, silphiperfolene are attractive examples of domino radical cyclizations. Curran, et al[23] prepared a mixture of triquinanes by the reaction of bromide **63** with Bu_3SnH via the intermediate radical **64** (Scheme-**16**).



63 **64** **65** **66**

Scheme-16

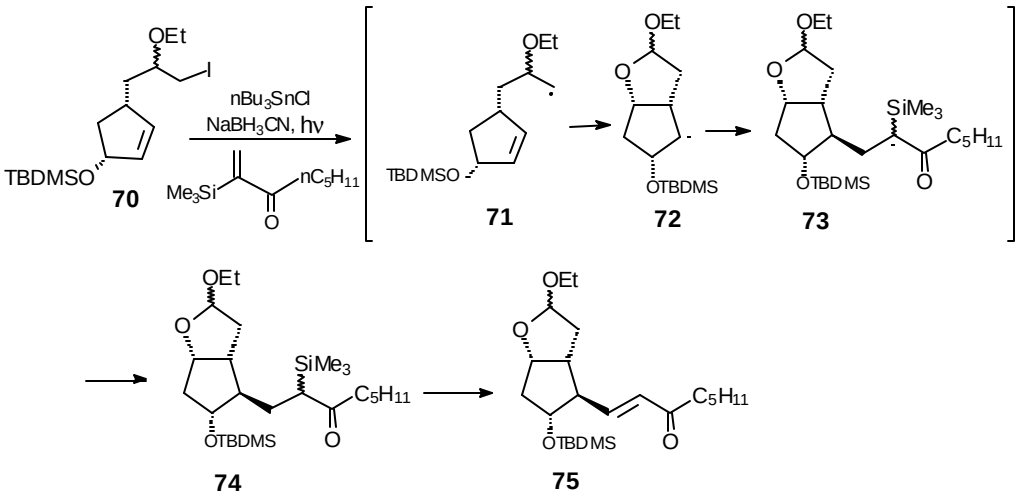
Boger[24] has also demonstrated a domino cyclization from the acyl radical precursor **67** to obtain bicyclic product **69.** This cyclization involved **68** as the intermediate (Scheme-**17**).



67 **68** **69**

Scheme-17

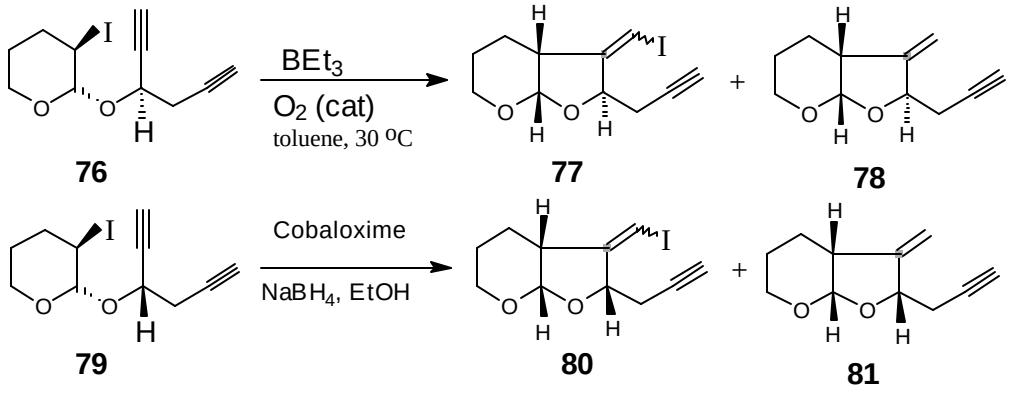
Tandem radical reactions in which rapid intramolecular cyclization is followed by a slow intermolecular addition are of great synthetic interest. This strategy has been successfully used by Stork et al[25] in the synthesis of prostaglandins (Scheme-**18**).



Scheme-18

Heteroannular tricyclic pyranofuran systems are important constituents of many natural products. Construction of these tricyclic rings has attracted the attention of synthetic chemists and has been a synthetic challenge. In particular, radical cascade reactions are of tremendous help while designing such synthetic sequences.

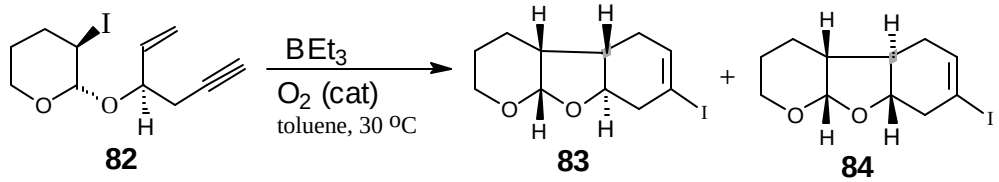
Hoffman et al reported[26] the synthesis of 6.5.6 pyranofuran and other 5.5.6 furanofuran ring systems by tandem radical cyclization of acyclic acetals. It is observed[26] that, reaction of compound **76** with BEt_3 and oxygen in toluene at 30° C afforded only monocyclized compounds **77** and **78**. A similar reaction with **79** in the presence of cobaloxime, $NaBH_4$ in ethanol at 40^0 C also afforded only monocyclized products (**80** and **81**) (Scheme-**19**).



76 **77** **78** **79** **80** **81**

Scheme-19

Changing starting materials from 1,5-diyn to a 1,5-ene-yn system helped to get a tricyclic tandem cyclized product. It was reported that reaction of **82** with BEt_3 and oxygen at 100^0 C afforded a mixture of diastereomers **83** and **84** (Scheme**-20**). The reaction was not successful at lower temperatures (0-40^0 C) as it gave only monocyclized products. In all these products, the construction of two ring junctions proceeded stereo and regioselectively giving rise to1,9-*cis* and 3,8-*trans* fused tricycles.



82 **83** **84**

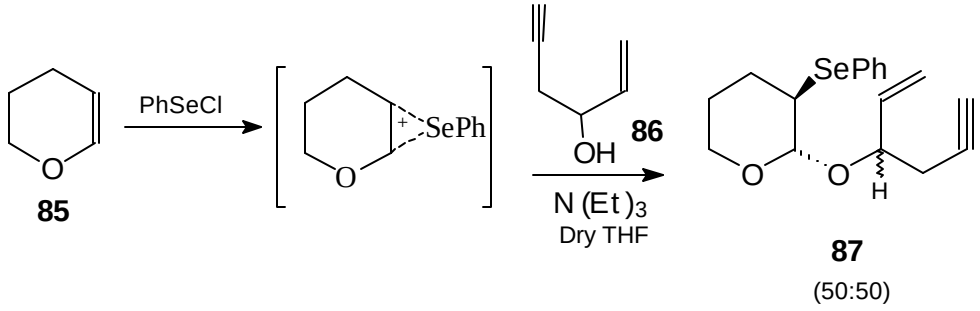
Scheme-20

Considering the importance of such reactions, and the success of our strategy for tandem annulation reactions, we decided to extend our catalytic group transfer radical reaction concept for the construction of a functionalized 6.5.6 pyranofuran ring system by a tandem radical cyclization of **87**.

3-3.2 Results and Discussion

3-3.2.1 Preparation of substrate 87:

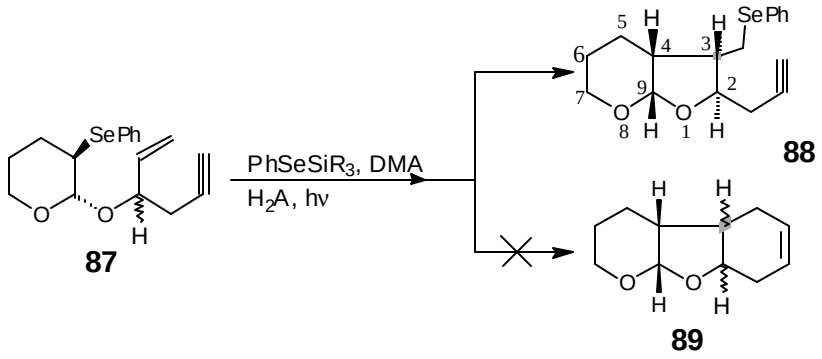
Substrate **87** was prepared as a mixture of diastereomers by the phenylselenylation of 3,4-dihyrdopyran (**85**) with PhSeCl followed by alkylation with 1-hexen-5-yn-3-ol (**86**) (Scheme-**21**). 1-Hexen-5-yn-3-ol (**86**) was prepared[27] by the Grignard reaction of propargyl bromide over acrolein. Detailed procedure for the preparation of **87** is given in the experimental section.



Scheme-21

3-3.2.2 PET activation of 87:

The PET activation of a mixture containing $PhSeSiR_3$ (0.15 mmol), **87** (1.48 mmol), DMA (0.63 mmol) and ascorbic acid (1.62 mmol) in acetonitrile was carried out in a similar fashion as described earlier in Section 3-1.2.3 (Scheme-**22**). Usual workup and purification of the crude photolysate by silica gel column chromatography afforded an oily compound in 63 % yield. This compound was found to be a mixture of two diastereomers (50:50) of which only one isomer could be isolated in pure form after repeated chromatographic separations.



Scheme-22

The spectral characterization of isolated compound unfortunately revealed that the product is only a monocyclized compound **88**, and not the proposed tricyclic pyranofuran **89**. Product **88** was characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

The ^{1}H NMR spectrum of **88** (Fig. **11**) showed two multiplets for aromatic protons of SePh group at δ 7.55 (2H) and 7.30 (3H). A doublet at δ 5.35 (J = 3.7 Hz) corresponds to H_9 acetal proton of the ring junction. A multiplet at δ 4.05 can be assigned to the H_2 proton of the tetrahydrofuran ring. Another two sets of multiplets at δ 3.80 and δ 3.65 belongs to the two H_7 methylene protons of the tetrahydropyran ring. The broad multiplet observed between δ 2.75 - δ 3.20 corresponds to methylene protons adjacent to the SePh group. The multiplet at δ 2.60 can be assigned to the two propargylic protons and the H_3 methine proton attached to CH_2SePh. Another multiplet at δ 2.25 corresponds to the H_4 methine proton at the ring junction of both the rings. The multiplet at δ 2.0 can be attributed to the acetylenic proton. The remaining protons of the pyran ring appeared between δ 1.40 - δ 1.90 as a multiplet.

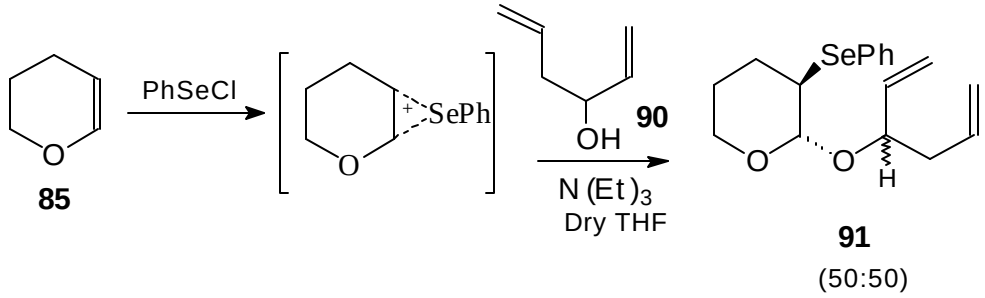
The fully decoupled ^{13}C NMR spectrum of **88** (Fig. **12**) exhibited 14 signals. The detailed characterization from INEPT experiment revealed following pattern. The signals at δ 132.43, 128.90 and 126.86 belonged to the aromatic carbons of the SePh group. The signal at δ 100.76 corresponds to the C_9 methine carbon at the ring junction. The quaternary carbon of the acetylene appeared at δ 80.18. The signal at δ 78.38 was assigned to the C_2 methine carbon of the THF ring. The signal at δ 70.32 was ascribed to the acetylenic methine carbon. The signal at δ 60.94 corresponds to C_7 methylene carbon of the THP ring. Another signal at δ 45.51 belonged to C_4 methine carbon present at the ring junction. The signal at δ 37.80 was assigned to C_3 methine carbon on the tetrahydrofuran ring. The signal at δ 25.05 corresponded to the methylene carbon attached to SePh group. The remaining two C_5 and C_6 methylene carbons of the tetrahydropyran ring appeared at δ 22.78 and δ 19.63.

The mass spectrum of **88** (Fig. **11**) exhibited molecular ion peak at 336 and base peak at 157. The other prominent fragmentations were observed at 234 (27), 192 (12), 179 (25), 171 (15), 139 (21), 116 (18), 105 (14), 91 (47) and 77 (34).

Since the tandem radical cyclization of an ene-yn system (**87**) was not successful, we assumed that a diene system (**91**) where the second *endo-trig* cyclization may be easier compared to an *endo-dig* cyclization, another substrate with a 1,5-diene system (**91**) was prepared and its cyclization was studied.

3-3.2.3 Preparation of 91

Substrate **91** was prepared in the similar manner as described for substrate **87** except utilising 3-hydroxy-1,5-hexadiene (**90**) for alkylation on the pyran ring (Scheme-**23**). 3-Hydroxy-1, 5-hexadiene was prepared by the Grignard reaction of allylbromide with acrolein. The spectral details of the substrate **91** are given in the experimental section.

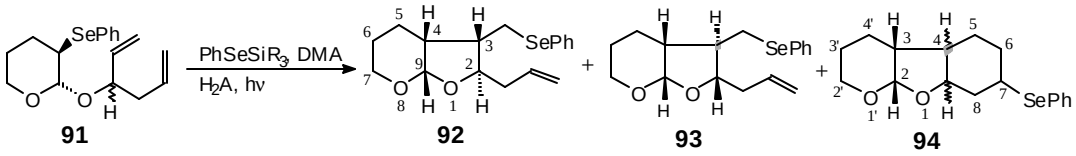


Scheme-23

3-3.2.4 PET activation of 91

Irradiation of a dilute solution containing $PhSeSiR_3$ (0.15 mmol), **91** (1.47 mmol), DMA (0.63 mmol), and ascorbic acid (1.62 mmol) in acetonitrile, in an identical manner as illustrated in section 3-1.2.3 till the quantitative consumption of the starting material and removal of the solvent under reduced pressure followed by the purification of crude

photolysate by column chromatography gave monocyclized products as a mixture of two diastereomers (50:50) (**92** and **93**) and a minor amount of the tricyclic pyranofuran **94.**



91 **92** **93** **94**

Scheme-24

The products were characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analysis. The stereochemistry of these products was confirmed by calculating the coupling constants and by COSY and NOESY spectral analysis. In the case of the tricyclic pyranofuran **94,** the exact stereochemistry could not be determined. The detailed spectral characterization of the compounds are described as follows:

3-3.2.5 Spectral characterization of 92

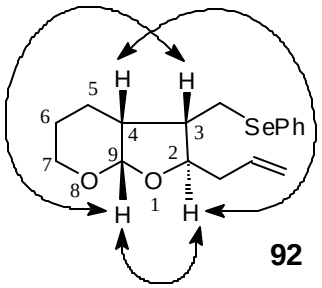
The ^{1}H NMR spectrum of **92** (Fig. **13**) showed two multiplets at δ 7.25 (3H) and δ 7.50 (2H) corresponding to the aromatic protons of the SePh group. The multiplet at δ 5.80 was characterized as the olefinic methine proton. The doublet at δ 5.25 (J = 3.5 Hz) was assigned to the H_9 acetal proton present at the ring junction. The multiplet at δ 5.10 corresponds to the two olefinic methylene protons. A doublet of a doublet of a doublet (1H, J = 7, 3 and 5 Hz) appearing at δ 4.00 belongs to the H_2 methine proton of the tetrahydrofuran ring. The two multiplets at δ 3.75 and δ 3.65 correspond to the H_7 *exo* & *endo* methylene protons of the tetrahydropyran ring. The broad multiplet between δ 2.80 - δ 3.00 was assigned to the two methylene protons adjacent to SePh group. The multiplet appearing at δ 2.40 corresponds to one of the allylic protons. The other allylic proton overlapped with the multiplet at δ 2.25 along with the H_3 methine proton of the tetrahydrofuran ring. Another multiplet at δ 2.15 corresponds to the H_4 methine proton of the ring junction. The remaining methylene protons of the pyran ring appeared as sets of

multiplets between δ 1.40-δ 1.75. The proton assignments were based on COSY spectral analysis (Fig. **14**).

The ^{13}C NMR spectrum of **92** (Fig. **15**) displayed 14 signals. From the INEPT experiments detailed information about the characterization of the peaks are as follows: The signals at δ 133.96, 132.46 and 128.89 correspond to the aromatic carbons of the SePh group. Signal at δ 126.88 was assigned to the methine carbon of the olefin (C<u>H</u>=CH$_2$). The signal at δ 117.45 corresponds to the methylene carbon of olefin (CH=C<u>H</u>$_2$). The C_9 acetal carbon present at the ring junction appeared at δ 100.46. The C_2 methine carbon of the tetrahydrofuran ring appeared at δ 79.95. The C_7 methylene carbon of the tetrahydropyran ring appeared at δ 60.94. The C_8 methine carbon adjacent to CH$_2$SePh was observed at δ 45.26. The signal at δ 39.11 was assigned to the methylene carbon attached to SePh group (C<u>H</u>$_2$SePh) while the signal at δ 37.56 corresponds to the C_4 methine carbon present at the ring junction between tetrahydropyran and furan rings. Another signal at δ 29.43 was ascribed to the allylic carbon. Remaining two signals at δ 22.81 and δ 19.52 corresponds to two C_5 and C_6 methylene carbons of the tetrahydropyran ring.

The mass spectrum of **92** (Fig. **13**) exhibited molecular ion peak at 338 and base peak at 163. The other prominent fragmentations were observed at 297 (18), 194 (11), 180 (10), 157 (8), 119 (12), 111 (27), 105 (22), 105 (22), 91 (55), 77 (46). The calculated value for $C_{17}H_{22}O_2Se$ was found to be 338.078501 and the observed value was 338. 078384.

The stereochemistry of **92** was established by calculating the coupling constants and by NOESY spectral analysis. Since the coupling constants of the ring junction protons **H-4** and **H-9** was found to be ≈ 3.7-4 Hz, their relative stereochemistry was ascribed as *cis* whereas the coupling constant values for the newly formed ring junction protons **H-2** and **H-3** were found to be ~ 5-8 Hz indicating them to be *trans*.



92

H-3, **H-9** - Correlation present, *cis*

H-2, **H-4** - No correlation, *trans*

H-2, **H-9** - No correlation, *trans*

Figure-3

Furthermore, the NOESY spectral analysis (Fig. **16**) exhibited strong correlation between **H-3** and **H-9** indicating them to be *cis*. On the other hand, no correlation was found between **H-2** and **H-4** establishing their *trans* relationship. Since, no correlation was observed between **H-2** and **H-9**, their *trans* orientation was established.

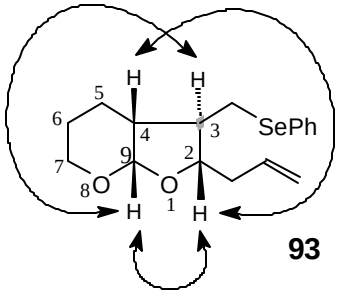
From the above detailed spectral analysis, it can be concluded that, the relative stereochemistry for the ring junction protons **H-4** and **H-9** is *cis* while **H-2** and **H-3** is *trans*.

3-3.2.6 Spectral characterization of 93

The ^{1}H NMR spectrum of **93** (Fig. **17**) displayed two multiplets at δ 7.25 and δ 7.50 corresponding to the aromatic protons of the SePh group. The olefinic methine proton was observed as a multiplet at δ 5.80. The two olefinic methylene protons appeared as multiplets at δ 5.10. The doublet at δ 4.97 (J = 3.7 Hz) belonged to the H_9 acetal methine proton. The multiplet at δ 3.90 (2H) corresponds to both H_2 methine proton and one of the H_7 methylene protons. The doublet of doublet of a doublet (ddd, J = 8.9, 2.4, 9.2 Hz) at δ 3.40 was ascribed to another H_7 methylene proton of the tetrahydropyran ring. The broad multiplets between δ 2.90 to δ 3.15 belong to the methylene protons attached to the SePh group. The two allylic protons appeared as multiplets at δ 2.50 and δ 2.40. The multiplet at δ 2.30 corresponds to H_3 methine proton adjacent to CH_2SePh. Another multiplet at δ 2.05 was assigned to the H_4 methine proton at the ring junction. The multiplets between δ 1.50 - δ 1.90 belong to the remaining H_5 and H_6 methylene protons of the tetrahydropyran ring. These proton characterizations were based on COSY spectral analysis (Fig. **18**).

The ^{13}C NMR spectrum (Fig. **19**) displayed 14 signals. INEPT experiment established the detailed characterization of the signals as follows: The signals appearing at δ 134.69, 132.45 and 128.91 corresponds to aromatic carbons of SePh group. The methine carbon of the olefin ($\underline{C}H=CH_2$) appeared at δ 128.91. The methylene carbon of the olefin ($CH=\underline{C}H_2$) was observed at δ 116.67. The signal appearing at δ 101.19 was assigned to the C_9 acetal carbon at the ring junction. The signal appearing at δ 84.60 was ascribed to C_2 methine carbon. Another signal appearing at δ 60.49 corresponds to the C_7 methylene carbon of the tetrahydropyran ring. The C_3 methine carbon was observed at δ 44.53. The C_4 methine carbon at the ring junction appeared at δ 42.57. The methylene carbons attached to SePh group appeared at δ 40.96 ($\underline{C}H_2SePh$). The allylic carbon ($CH_2CH=CH_2$) appeared at δ 29.56. The remaining two C_5 and C_6 methylene carbons appeared at δ 22.33 and 20.48.

The stereochemistry of **93** was determined by calculating the coupling constants and NOESY spectral analysis. In this case too, the coupling constants between the ring junction protons **H-4** and **H-9** was found to be ~ 3.5 - 4 Hz, indicating the relative stereochemistry to be *cis* while the coupling constant values between the protons **H-2** and **H-3** (J = 6-8 Hz) indicated the stereochemistry to be *trans*.



93

H-3, **H-9** - No correlation, *trans*

H-2, **H-4** -Correlation present, *cis*

H-2, **H-9**- Correlation present, *cis*

Figure-4

In contrast to the other isomer described earlier, the NOESY spectral analysis (Fig. **20**) showed no correlation between the protons **H-3** and **H-9** indicating them to be *trans*. At the same time, a strong correlation was found between the protons **H-2** and **H-4**

indicating them to be *cis*. A weak coupling was also seen between protons **H-2** and **H-9**, further confirming their *cis* orientation.

From the above spectral analysis, it has been concluded that the relative stereochemistry at the ring junction protons **H-4** and **H-9** is always *cis* while it is *trans* between **H-2** and **H-3.**

3-3.2.7 Spectral Characterization of tricyclic product 94

The ^{1}H NMR spectrum of **94** (Fig. **21**) showed two multiplets for the aromatic protons at δ 7.30 and δ 7.60. A doublet at δ 5.40 (J = 3.8 Hz) corresponds to the H_{12} acetal proton at the ring junction. A multiplet at δ 4.25 can be assigned to H_9 methine proton adjacent to oxygen. Another multiplet at δ 3.90 can be ascribed to one of the $H_{2'}$ methylene protons. A multiplet at δ 3.70 (2H) corresponds to another $H_{2'}$ methylene proton along with H_7 methine proton. H_8 methine proton appeared as a multiplet at δ 2.50. Another multiplet at δ 2.10 corresponds to H_4 methine proton. The remaining protons of the tetrahydropyran and cyclohexane rings appeared as broad multiplets between δ 1.50 – 1.90.

The ^{13}C NMR spectrum of **94** (Fig. **22**) exhibited 14 signals. The detailed characterization of signals by INEPT experiments are as follows: The signals appearing at δ 134.21, 129.02 and 127.40 were attributed to the aromatic carbons of the SePh group. The signal at δ 101.70 corresponds to C_{12} methine carbon between two oxygens. The C_9 methine carbon adjacent to oxygen appeared at δ 76.58. The signal at δ 60.77 was ascribed to $C_{2'}$ methylene carbon adjacent to oxygen of the tetrahydropyran ring. The C_7 methine carbon attached to SePh group appeared at δ 48.78. The C_4 methine carbon at the ring junction appeared at δ 41.97. The signal at δ 37.27 corresponds to C_8 methylene carbon. The C_3 methine carbon present at the ring junction appeared at δ 36.91. The C_6 methylene carbon was observed at δ 31.41. The remaining methylene carbons of the tetrahydropyran and cyclohexane rings appeared at δ 22.50, 20.91 and 20.15.

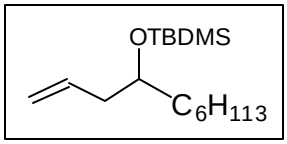
The mass spectrum of **94** exhibited molecular ion peak at 338 as the base peak. The fragment at 180 confirms the formation of the tricyclic ring. The other prominent fragmentations were observed at 254 (32), 180 (40), 157 (8), 135 (10), 123 (8), 107 (8), 79 (15).

3-4 CONCLUSION

In conclusion, we have successfully demonstrated the application of our catalytic group transfer radical reaction concept for a variety of reactions such as intermolecular additions, some interesting tandem annulation reactions and intramolecular tandem cyclizations. The synthetic efficiency of our strategy is likely to be immensely valuable in natural product synthesis.

3-5 EXPERIMENTAL SECTION

3-5.1 Preparation of 4-*tert*-butyldimethylsilyloxy, 1-decene (21)



1-Heptanal (1.15 g, 100 mmol) was added in a conical flask containing sat. NH_4Cl (10 mL) and THF (2 mL). Allylbromide (2.3 g, 19 mmol) and Zn dust (1.4 g, 21 g-atom) were added into the flask with stirring. After 1 h of stirring at room temperature, the suspension was extracted with ether and organic layers were dried over Na_2SO_4. The residue obtained after the evaporation of ether was purified by silica gel column chromatography using pet ether-ethyl acetate (1: 1) as eluent to give the required alcohol **20** in 98 % (1.63 g) yield.

A mixture containing **20** (1.56 g, 10 mmol), TBDMSCl (1.8 g, 12 mmol), Et_3N (1.3 g, 12.3 mmol) and DMAP (0.5 mmol) in dry DCM (10 mL) were stirred at room temperature for 24 h. The mixture was diluted with 25 mL of DCM and washed successively with water and saturated NH_4Cl solution. The residue obtained after the evaporation of DCM was purified by silica gel column chromatography using pet ether as eluent to furnish **21** in >98 % (2.79 g) yield.

IR: 3100, 1630.

^{1}H NMR: 5.80 (m, 1H), 5.15 (m, 2H), 3.60 (br m, 1 H), 2.25 (m, 2H), 1.25-1.50 (m, 10 H), 0.90 (m, 3H), 0.0 (m, 9H)

^{13}C NMR: 135.74, 116.78, 72.41, 42.35, 37.22, 32.28, 29.85, 26.23, 25.66, 23.0, 18.45, 14.38, -4.06, -4.20.

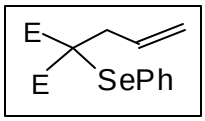
Mass: 270 (M^+, 2), 255 (5), 229 (66), 213 (100), 185 (35), 173 (10), 129 (18), 115 (19), 99 (34), 73 (58).

3-5.2 Preparation of Ethylphenylselenylacetate (25) PhSeCOOEt

A 50 mL 3-neck flask, fitted with a rubber septum, a solid addition tube containing $NaBH_4$ (0.4 g, 10.8 mmol) and a reflux condenser with an argon balloon was charged with 0.93 g (2.98 mmol) of PhSeSePh in 20 mL of dry ethanol. The solution was stirred vigorously and $NaBH_4$ was added in portions from the solid addition tube. The colour of the solution in the flask turned to pale yellow and finally dirty white. 1.0 g of ethylbromoacetate (5.98 mmol) in 5 mL of anhyd. ethanol was added to the flask at a moderate rate and the mixture was refluxed for 3-4 h. The reaction was allowed to cool and ethanol was removed under reduced pressure. The crude mixture was extracted with ethylacetate and washed with 5% HCl and water and dried over Na_2SO_4. Removal of the solvent on rotavapor and purification of the crude product by column chromatography afforded ethylphenylacetate in 95% (1.38 g) yield.

^{1}H NMR: 1.25 (t, 3H), 3.6 (s, 2H), 4.2 (q, 2H), 7.3 (m, 3H), 7.6 (m, 2H).

3-5.3 Preparation of diethyl 2-allyl-2-(phenylselenyl) malonate (51)



A 250 mL two neck R.B. flask fitted with a reflux condenser was charged with NaH (2.4 g, 100 mmol, 60 % suspension in mineral oil). 75 mL of dry THF was introduced into the flask and the suspension was stirred. Diethylmalonate (10 g, 62.4 mmol) in 75 mL dry THF was added dropwise to the suspension at 0^o C and the contents were allowed to warm to room temperature over a period of 30 min. After an additional 30 min of stirring at room temperature, a clear solution was formed indicating the completion of anion generation. Allyl bromide (7.5 g, 61.9 mmol) was slowly added into the flask and the contents were refluxed for 5 h. The mixture was cooled, quenched with 50 mL of saturated aq. NH_4Cl and extracted with ether. The ether layer was washed successively with water, brine, and dried over anhydrous Na_2SO_4. Removal of ether and column chromatography

of the crude residue gave 2-(2-propenyl)-diethylmalonate (**50**) in 73 % yield (9 g) which was used for the second alkylation reaction.

Another two neck flask (100 mL), fitted with a reflux condenser and an argon balloon was charged with 50 mL dry THF and NaH (1.0 g, 25 mmol). 2-(2-Propenyl)-diethylmalonate (**50**) (3.16 g, 15.8 mmol) in 25 mL of dry THF was introduced dropwise to the flask while stirring. After 1 h, PhSeBr (3.7 g, 15.6 mmol) in 10 mL dry THF was added dropwise to the reaction mixture and refluxed for 5 h. The mixture was cooled, quenched with 50 mL of sat. aq. NH_4Cl and extracted with ethyl acetate. The ethyl acetate layer was washed successively with water, brine and dried over Na_2SO_4. The organic layer was removed and the crude compound after column chromatography furnished compound **51** in 65 % yield (3.6 g).

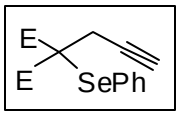
IR: 3076, 2981, 2929, 1727, 1640, 1578, 1438, 1232, 1127, 1043, 923, 857.

^{1}H NMR (200 MHz): δ 1.25 (t, 6H, J = 7.5 Hz), 2.7 (d, 2H, J = 5.9 Hz), 4.2 (q, 4H, J = 7.5 Hz), 5.05-5.20 (m, 2H), 5.80-6.05 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$): δ 169.0, 165.8, 138.2, 133.0, 129.8, 129.0, 119.2, 62.2, 59.1, 38.6, 14.2;

Mass : 356 (7, M^+), 209 (47), 199 (35), 157 (75), 153 (100), 125 (78).

3-5.4 Preparation of diethyl-2-(phenylselenyl)-2-prop-2-ynyl malonate (58)

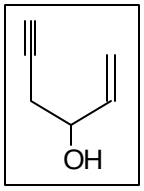


A similar procedure, as described for compound **51,** was followed for the preparation of the title compound taking propargyl bromide in place of allyl bromide. The crude product after silica gel chromatography afforded pure propargyl diethylmalonate in 68% yield.

^{1}H NMR : δ 1.25 (t, 6 H, J = 7.8 Hz), 2.2 (s, 1 H), 2.7 (s, 2 H), 4.25 (q, 4 H, J = 7.8 Hz), 7.3 (m, 3 H), 7.6 (m, 2 H).

^{13}C NMR: δ 169.0, 165.5, 138.5, 133.5, 129.5

3-5.5 Preparation of 1-Hexen-5-yn-3-ol (86)

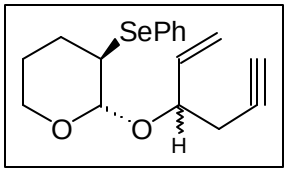


To a 100 mL 3-neck flask containing 20 mL dry ether, fitted with an addition funnel, rubber septum and a reflux condenser with an argon balloon, was added 2.5 g (102.8 mmol) of activated Mg, 0.5 g of freshly distilled propargyl bromide and 10 mg of mercuric chloride. The mixture was warmed with stirring until the reaction commenced as evidenced by vigorous boiling of ether. The flask was immersed in a dry-ice acetone bath and after 3 h, a solution of 6.97 g (58.58 mmol) of freshly distilled propargyl bromide and 2.6 g of freshly distilled acrolein in 200 mL of dry ether was added with vigorous stirring. During the addition, the bath temperature was maintained at –25°C. The flask was then allowed to warm to room temperature and the mixture was poured on to a ice-NH_4Cl mixture in a beaker. The solution was extracted with ether and concentrated under vacuum. The crude mixture was distilled using aspirator vacuum (65-70°C, 40 mm) to afford pure alcohol in 52 % (3.13 g) yield.

IR: 3080, 2986, 2914, 2118, 1646, 1424, 1264, 1124, 1040, 994, 930.

^{1}H NMR: δ 2.15 (s, 1H), 2.45 (m, 2H), 4.3 (m, 1H), 5.3 (m, 2H), 5.9 (m, 1H).

3-5.6 Preparation of 3-(phenylselenyl-2-[(1-vinyl-but-3-ynyl) oxy] tetrahydro-2H-pyran (87)



In to a 100 mL two neck flask equipped with a magnetic needle and an argon balloon, 1.67 g (8.6 mmol) of PhSeCl in 50 mL of dry THF was introduced. To the vigorously stirring solution of PhSeCl, 3,4-dihydropyran (0.73 g, 8.6 mmol) was added at once. The colour of the reaction mixture changed from orange to pale yellow indicating the

formation of cation. 0.84 g (8.75 mmol) of 1-hexen-5-yn-3-ol and triethylamine (1.3 g, 12.8mmol) in 10 mL of dry THF were added dropwise to the reaction mixture over a period of 10 min. The reaction mixture was allowed to stir for an hour and then quenched with 2-3 mL of 5% of $NaHCO_3$ solution. The solvent was removed under reduced pressure and the residue was washed successively with ether and water (2 X 50 mL). The combined ether extracts were dried by the addition of Na_2SO_4 and concentrated. The crude product was purified by silica gel chromatography to afford compound **87** as a mixture of two diasteriomers (50:50) in 80 % (2.33 g) yield.

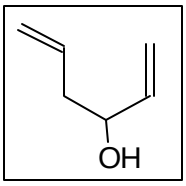
IR: 3072, 2942, 2880, 1646, 1578, 1436, 1200, 1174, 1124, 1072, 1022.

^{1}H NMR: δ 1.4-2.1 (m, 4H), 2.0 (m, 1H), 2.1-2.6 (m, 2H), 3.4 (m, 1H), 3.6 (m, 1H), 4.0 (m, 1H), 4.3 (m, 1H), 4.7 (d, 1H), 5.1-5.4 (m, 2H), 5.8-6.1 (m, 1H).

^{13}C NMR: δ 137.3, 136.1, 134.0, 129.3, 128.6, 127.0, 118.3, 115.9, 100.6, 98.6, 80.3, 75.2, 69.9, 69.7, 44.0, 43.9, 26.7, 25.5, 24.6, 23.7.

Mass: 336, (M^+, 27), 312 (5), 240 (50), 211 (51), 183, (40), 160 (100), 130 (37), 117 (20), 104, (20), 77 (88).

3-5.7 Preparation of 3-hydroxy-1,5-hexadiene (90)



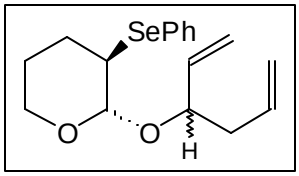
2.6 g (106.6 mmol) of Mg turnings (activated) were taken in a 250 mL 3-neck flask fitted with a 100 mL addition funnel, stopper, a reflux condenser and an argon balloon. The whole system was flame dried and a pinch of iodine was added and the stopper was replaced immediately by a rubber septum. After the flask cooled to r.t., 40 mL of dry ether was introduced into the flask. 1 mL of allyl bromide (neat) was added to the vigorously

stirring contents of the flask to initiate the reaction. 5 mL of allyl bromide, diluted with 50 mL of dry ether was taken in an addition funnel and added dropwise with such a rate as to maintain a gentle reflux. After the addition was complete and most of the Mg was consumed, the reaction was cooled to -5^{o} C in a ice-salt bath. 5.9 mL (89.19 mmol) of acrolein in 20 mL of dry ether was added dropwise into the stirring contents of the flask through the dropping funnel. The reaction was allowed to stir for 4-5 h and finally it was quenched by pouring the whole mixture into a beaker containing ice and 5 % HCl solution. The organic layer was extracted with ether (3 X 50 mL). Removal of ether followed by vacuum distillation of the crude mixture (60-65^{o} C on aspirator) afforded pure diene-ol (**90**) in 55 % (3.7 g) yield.

^{1}H NMR: δ 2.1-2.5 (m, 2 H), 4.15 (m, 1 H), 5.0-5.4 (m, 4 H), 5.7-6.0 (m, 2H)

^{13}C NMR: δ 140.2, 134.1, 117.5, 114.4, 71.8, 41.4.

3-5.8 Preparation of 3-(phenylselenyl)-2-[(1, vinyl but-3-enyl) oxy]tetrahydro-2*H*-pyran (91)



A similar procedure as described for compound **87,** (see procedure for preparation of **87**) was followed for the preparation of **91** by taking 1.17 g (14 mmol) of 3, 4-dihydropyran, 2.70 g (14 mmol) of PhSeCl, 1.36 g (14 mmol) of 3-hydroxy-1,5-hexadiene and triethylamine (2.7 g, 27 mmol). The crude mixture after silica gel chromatography gave a mixture of diastereomers (50: 50) in 75% (3.52 g) yield.

IR: 3074, 2853, 1434, 1400, 1123, 1071, 1020.

^{1}H NMR: δ 1.5-1.9 (m, 4 H), 2.3 (m, 2H), 3.3 (m, 1H), 3.5 (m, 1H), 3.9 (m, 1H), 4.2 (q, 1 H), 4.7 (t, 1H), 4.95-5.30 (m, 4 H), 5.5-6.0 (m, 2H), 7.3 (m, 3 H), 7.6 (m, 2H)

^{13}C NMR: 138.79, 134.68, 134.28, 134.18, 129.53, 129.04, 127.44, 117.44, 115.60, 100.89, 63.06, 44.45, 39.22, 27.46, 24.34.

Mass: 338 (M^+, 16), 256 (8), 238 (52), 223 (15), 211 (95), 194 (17), 183 (48), 157 (100), 130 (93).

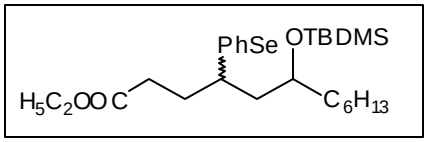
3-5.9 General Irradiation Procedure

This is illustrated by taking PET addition of **25** to **21** as an example

A dilute solution of CH_3CN (500 mL) containing a mixture of $PhSeSiR_3$ (0.07 g, 0.17 mmol), **21** (0.45 g, 1.85 mmol), **25** (1.85 mmol), DMA (0.15 g, 0.63 mmol), and ascorbic acid (0.28 g, 1.62 mmol) was irradiated in the specially designed photoreactor (as described in the general experimental section of chapter-II) with a 450-W Hanovia medium pressure mercury vapour lamp at room temperature without removing dissolved oxygen from the solution. The progress of the reaction was monitored by TLC and HPLC. When substantial consumption of **25** was noticed, the irradiation was discontinued. Solvent was removed under vacuum and the crude photolysate was purified by silica gel column chromatography to give a yellow oily product **28** in 61 % yield.

3-5.10 Spectral Values of the Products:

Ethyl 6-tert-butyl dimethyl silyloxy-4-(phenyl seleno) dodecanoate (28)



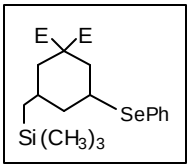
IR 1708, 1585, 1422

^1H NMR δ 00-0.10 (m, 9H), 0.85-0.97 (br. s, 13H,), 1.25-1.55 (m, 12H), 1.75-2.05 (m, 2H), 2.40-2.65 (m, 2H), 3.15-3.30 (m, 1H), 4.10 (q, J = 8.1 Hz, 2H), 7.20-7.35 (m, 3H), 7.45-7.57 (m, 2H).

^{13}C NMR δ 173.0, 135.6, 127.3, 70.5, 60.2, 43.5, 42.5, 42.1, 37.8, 29.4, 25.9, 25.2, 24.7, 22.5, 18.0, 14.1, -4.1, -4.3.

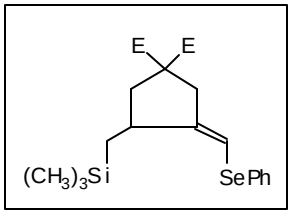
Mass 514 (M^+, 4), 457 (22), 244 (100), 171 (30), 157 (20).

Diethyl 3-(phenylselenyl)-5-(trimethylsilyl) cyclohexane-1, 1-dicarboxyllate (55)



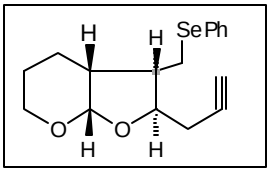
^{1}H NMR	δ -0.05-0.05 (s, 9H), 0.30-0.70 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 6H), 1.87-2.05 (m, 1H,), 2.10-2.50 (m, 5H), 2.65-2.83 (m, 1H), 2.95-3.05 (m, 1H), 4.2 (q, *J* = 7.3 Hz, 4H), 7.20-7.35 (m, 3H), 7.45-7.55 (m, 2H)
^{13}C NMR	δ 172.6, 132.9, 130.4, 128.9, 126.7, 61.3, 58.9, 43.9, 40.6, 38.8, 38.7, 29.1, 16.2, 13.9, -0.1
Mass	470 (M^+, 100), 455 (34), 425 (16), 397 (16), 337 (4), 313 (57), 239 (20), 157 (10)
***HRMS** for*	Calculated: 470.139159
$C_{22}H_{34}O_4SiSe$	Found: 470.137444.

Diethyl-3-[(phenylselenyl) methylene-4-(methyltrimethylsilyl) cyclopentane-1, 1-dicarboxyllate (61)



I R	3050, 3000, 2250, 1738, 1704, 1595, 1500, 1475, 1250, 1200.
^{1}H NMR	δ 0.0 – 0.05 (s, 9H), 0.60 (m, 1H), 1.10 (m, 1H), 1.25 (t, 6H), 1.70 (m, 1H), 2.70 (m, 2H), 3.10 (m, 2H), 4.25 (m, 4H), 6.25 (m, 1H), 7.25 (m, 3H), 7.50 (m, 2H).
^{13}C NMR	δ 171.3, 151.9, 131.3, 128.8, 126.3, 109.0, 61.2, 58.1, 41.8, 40.6, 39.4, 20.31, 13.75, 1.09.
Mass	468 (M^+), 312 (7), 119 (5), 92 (17), 73 (100).

3-(phenylselenyl-2-[(1-vinyl but-3-ynyl) oxy] tetrahydro-2 *H*-pyran (88)

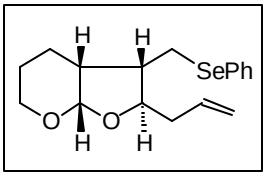


1H NMR δ 1.40-1.90 (m, 4H), 2.0 (m, 1H), 2.25 (m, 1H), 2.60 (m, 3H), 2.75-3.20 (m, 2H), 3.65 (m, 1H), 3.80 (m, 1H), 4.05 (m, 1H) 5.35 (d, 1H, J = 3.7,), 7.30 (m, 3H), 7.55 (m, 2H).

^{13}C NMR δ 132.43, 128.9, 126.86, 100.76, 80.18, 78.38, 70.32, 60.94, 45.51, 37.80, 25.05, 22.78, 19.63.

Mass 336 (M^+), 234 (27), 192 (12), 179 (25), 171 (15), 139 (21), 116 (18), 105 (14), 91 (47), 77 (34).

2-Allyl-3-[(phenylselenyl) methyl] hexahydro-4 *H*-furo [2, 3 –*b*] pyran (92)



^{1}H NMR δ 1.45 (m, 1H), 1.50-1.75 (m, 3H), 2.15 (m, 1H), 2.25 (m, 2H), 2.40 (m, 1H), 2.80-3.00 (m, 2H), 3.60 (m, 1H), 3.75 (m, 1H), 3.95 (m, 1H), 5.05 (m, 2H), 5.25 (d, 1H, J = 3.7 Hz), 5.80 (m, 1H), 7.25 (m, 3H), 7.50 (m, 2H).

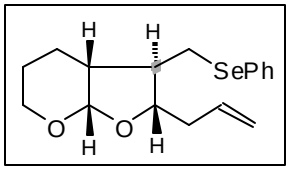
13C NMR δ 132.96, 132.46, 128.89, 126.88, 117.45, 100.46, 79.94, 60.93, 45.27, 39.10, 37.56, 29.42, 24.94, 22.81, 19.52.

Mass 338 (M^+), 297 (18), 194 (11), 180 (10), 163 (100), 157 (8), 119 (12), 111 (27), 105 (22)91 (55), 77 (46).

HRMS Calculated: 338.078501

Observed: 338.078384.

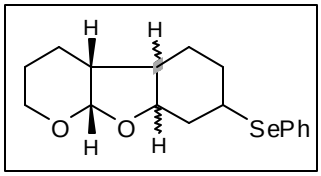
Spectral details of 93



^{1}H NMR δ 1.50-1.60 (m, 2H), 1.75 (m, 2H), 2.05 (m, 1H), 2.25 (m, 1H), 2.40 (m, 1H), 2.50 (m, 1H), 2.90-3.15 (m, 2H), 3.40 (m, 1H), 3.90 (m, 2H), 4.97 (d, 1H, *J* = 3.7 Hz,), 5.15 (m, 2H), 5.80 (m, 1H), 7.25 (m, 3H), 7.50 (m, 2H).

^{13}C NMR δ 134.69, 132.45, 128.91, 126.83, 116.67, 101.19, 84.60, 64.09, 44.53, 42.58, 40.96, 29.56, 22.33, 20.48.

7-(phenylselenyl) decahydro-2 *H*-pyrano [2, 3-b] [1] benzofuran (94)



^{1}H NMR δ 1.50-1.90 (bm, 10H), 2.10 (m, 1H), 2.50 (m, 1H), 3.70 (m, 2H), 3.90 (m, 1H), 4.25 (m, 2 1H), 5.40 (d, 1H, *J* = 3.8 Hz,), 7.30 (m, 3H), 7.60 (m, 2H).

^{13}C NMR δ 134.21, 129.02, 127.40, 101.70, 76.58, 60.77, 48.78, 41.97, 37.27, 36.91, 31.41, 22.50, 20.91, 20.15.

Mass 338 (M^{+}, 100), 254 (32), 180 (40), 157 (8), 135 (10), 123 (8), 107 (8), 79 (15).

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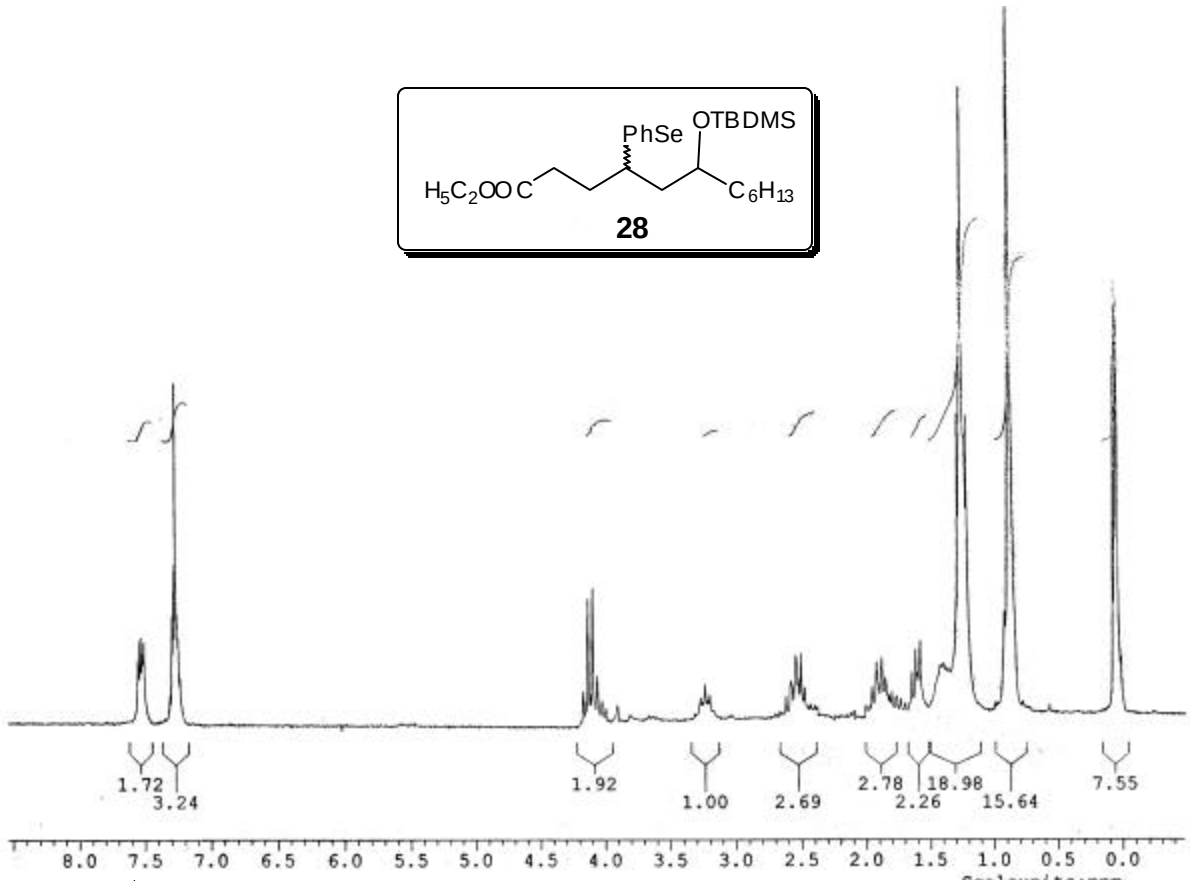
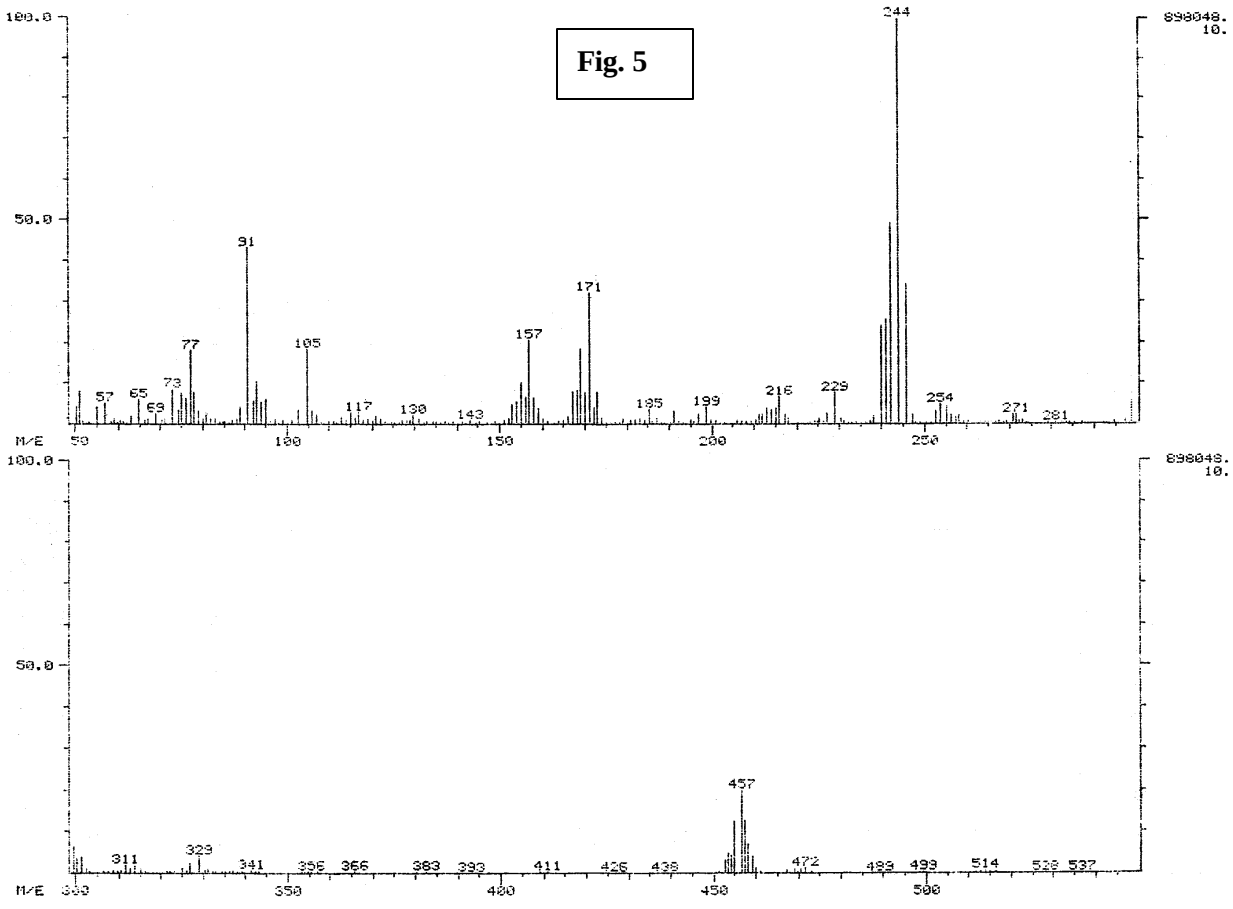
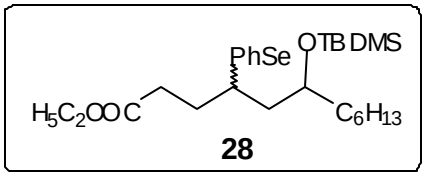

PhSe
OTBDMS
H5C2OOC
C6H13
28
1.72
3.24
1.92
1.00
2.69
2.78
2.26
18.98
15.64
7.55
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

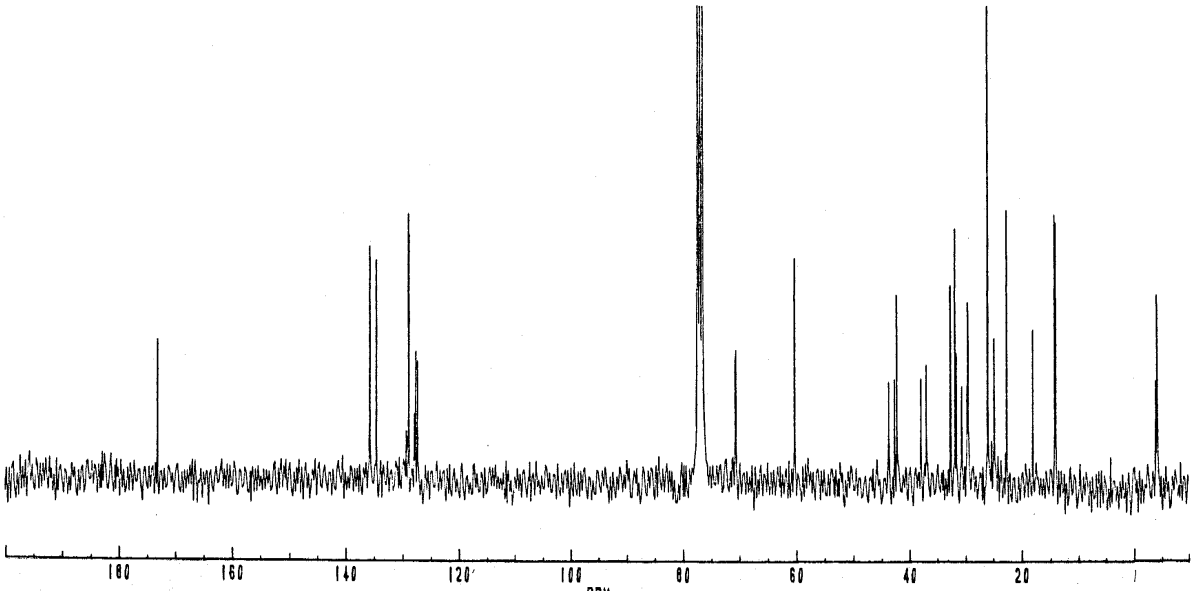
Fig. 5


100.0
50.0
M/E
898048.
10.
244
91
171
77
105
157
57
65
73
69
117
130
143
185
199
216
229
254
271
281
50
100
150
200
250
457
311
323
341
356
366
383
393
411
426
438
472
483
493
514
528
537
350
400
450
500



28

Fig. 6



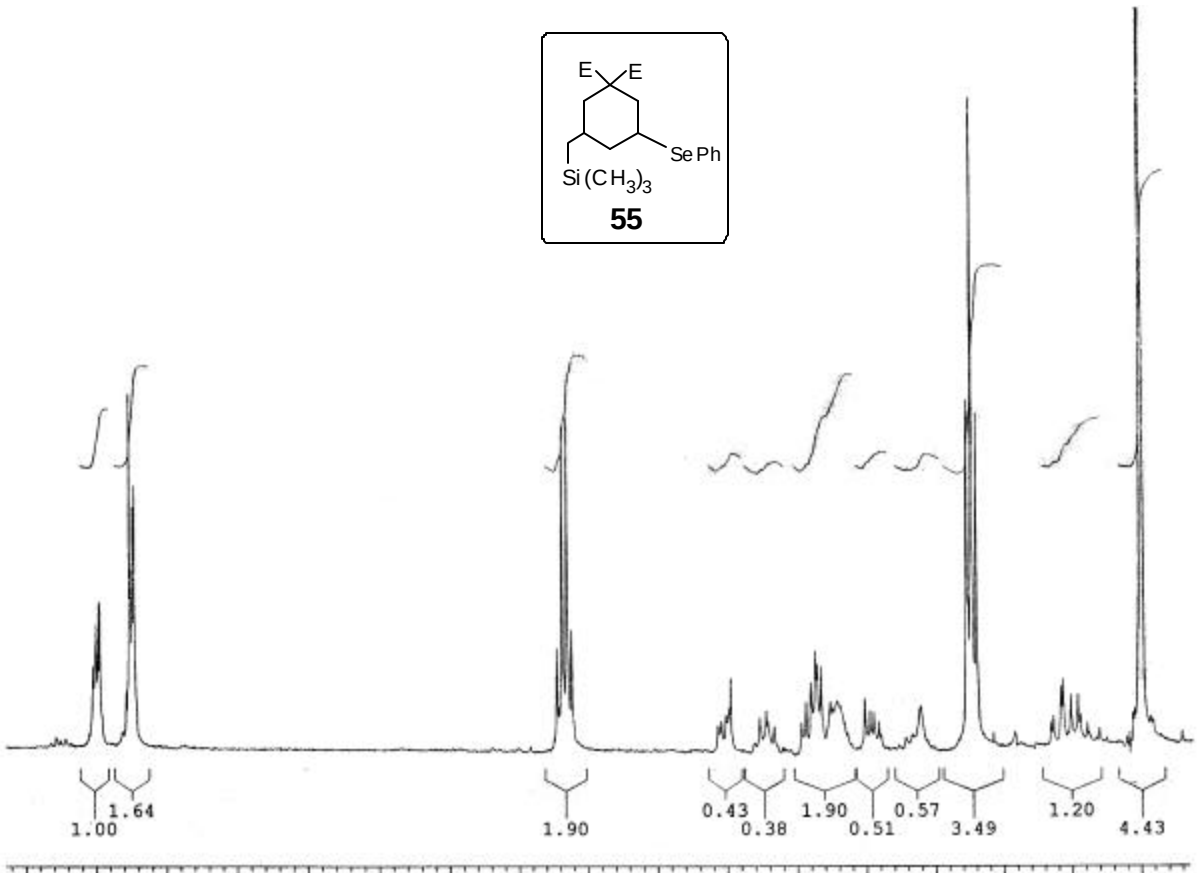
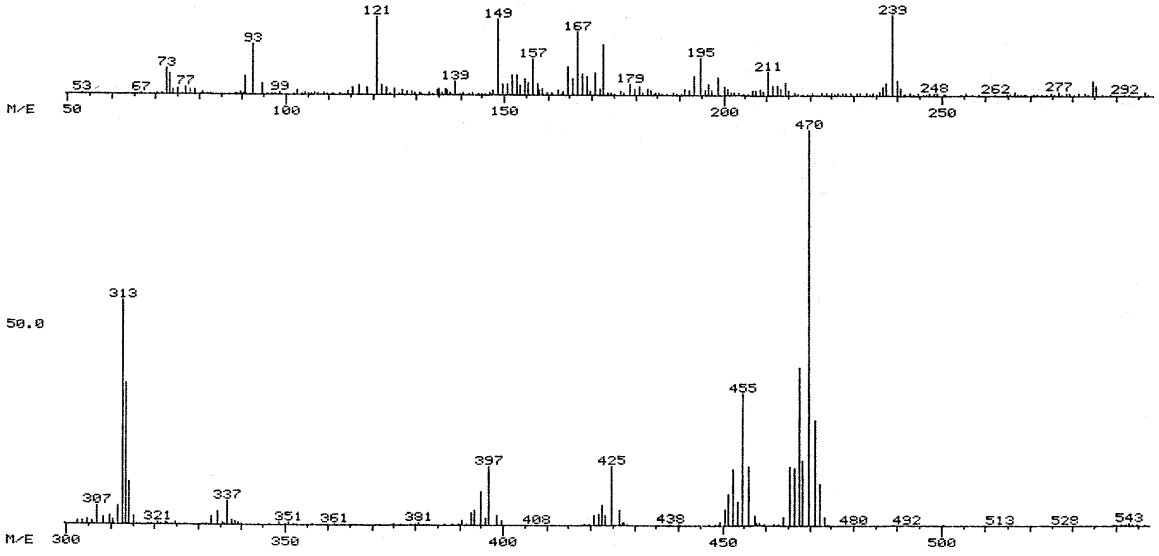
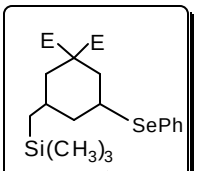

E
E
SePh
Si(CH3)3
55
1.00
1.64
1.90
0.43
0.38
1.90
0.51
0.57
3.49
1.20
4.43

Fig. 7


M/E
50
100
150
200
250
53
67
73
77
93
99
121
139
149
157
167
179
195
211
233
248
262
277
292
470
50.0
313
307
321
337
351
361
381
397
408
425
438
455
480
492
513
528
543
300
350
400
450
500



55

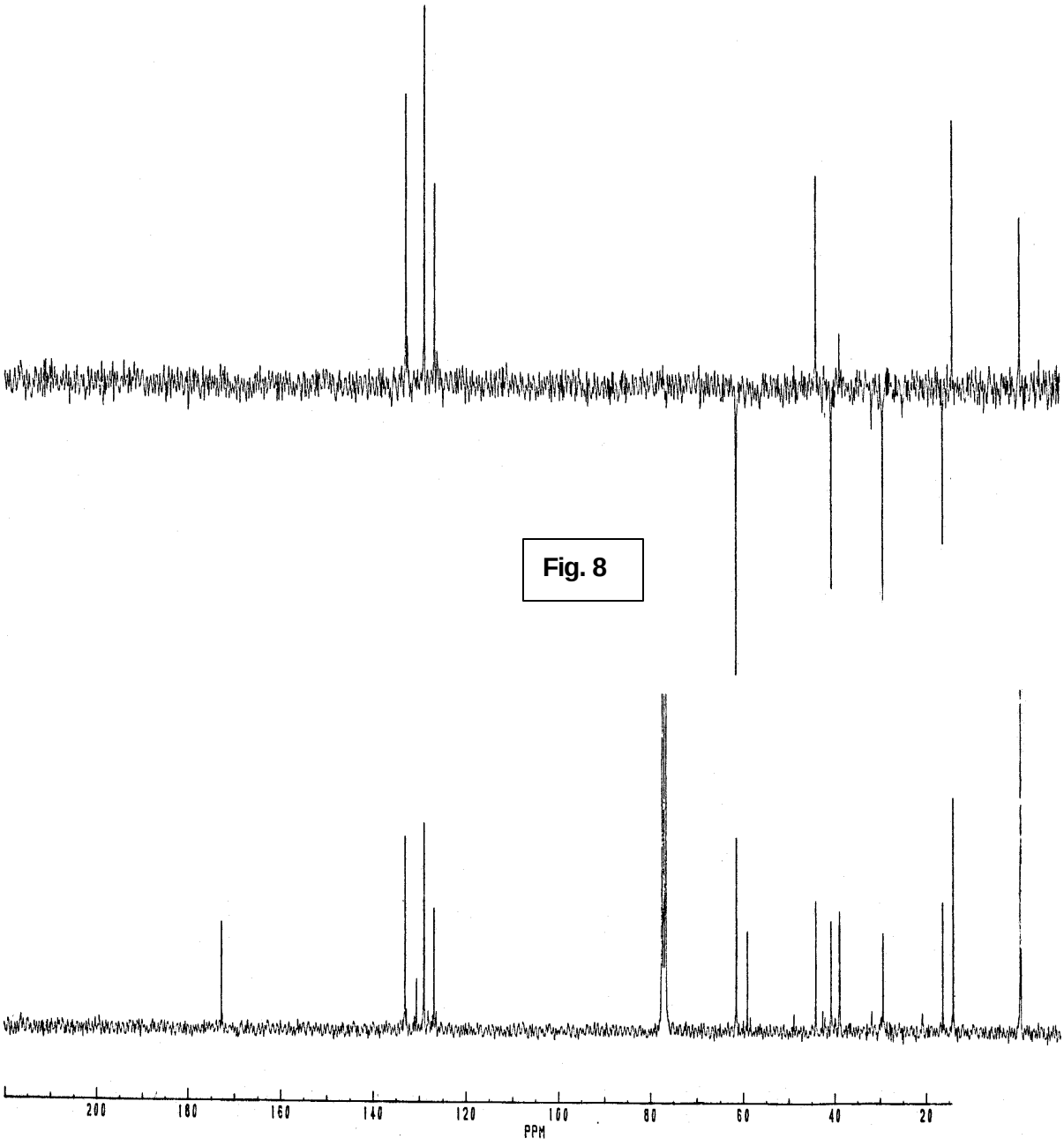


Fig. 8

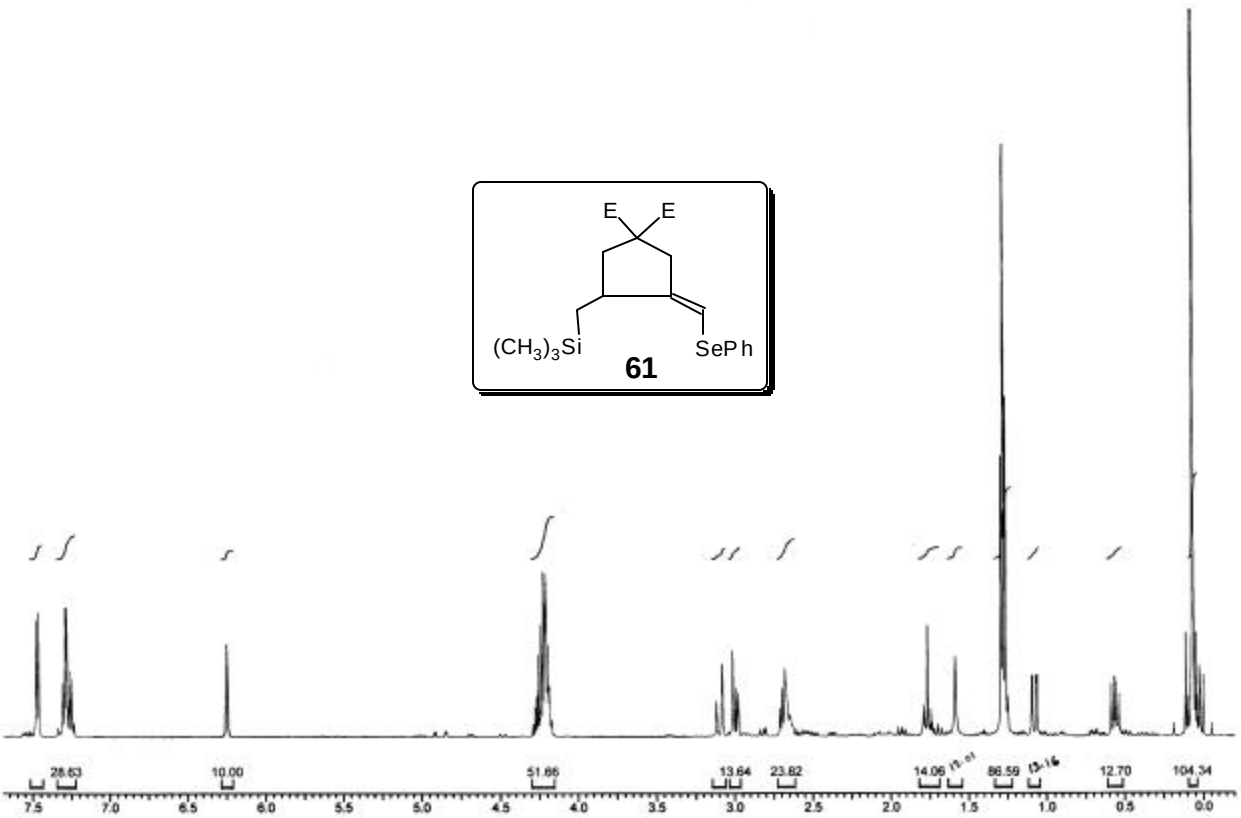
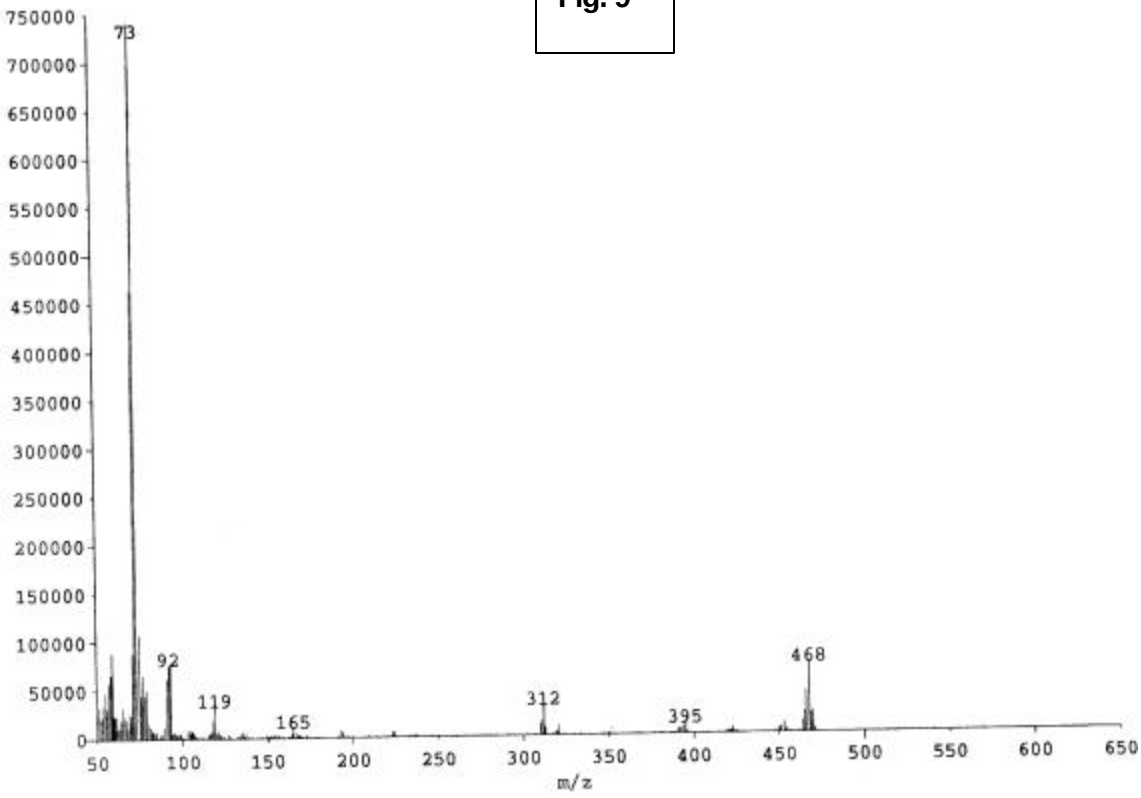
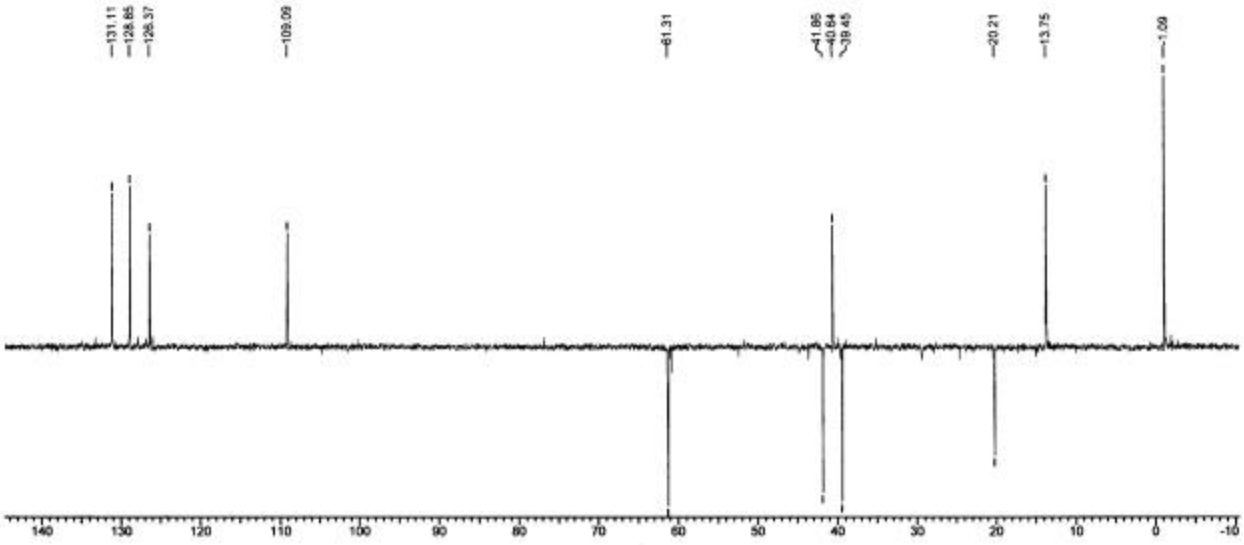
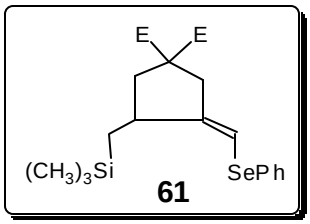

E
E
(CH3)3Si
SePh
61
28.63
10.00
51.66
13.64
23.82
14.06
86.59
12.70
104.34

Fig. 9

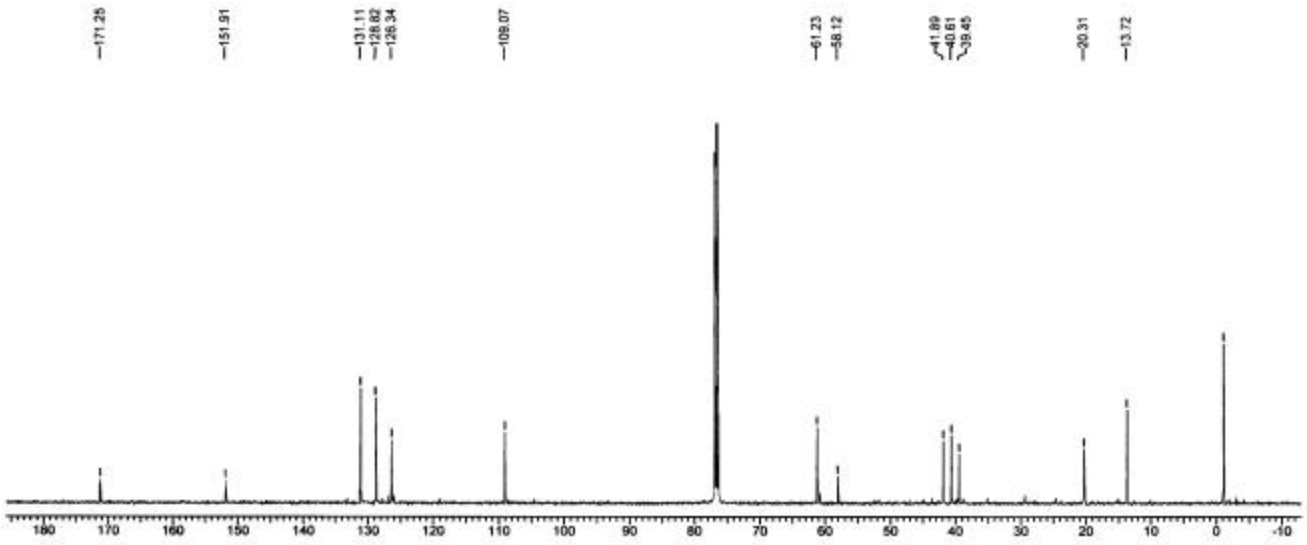

73
92
119
165
312
395
468
m/z

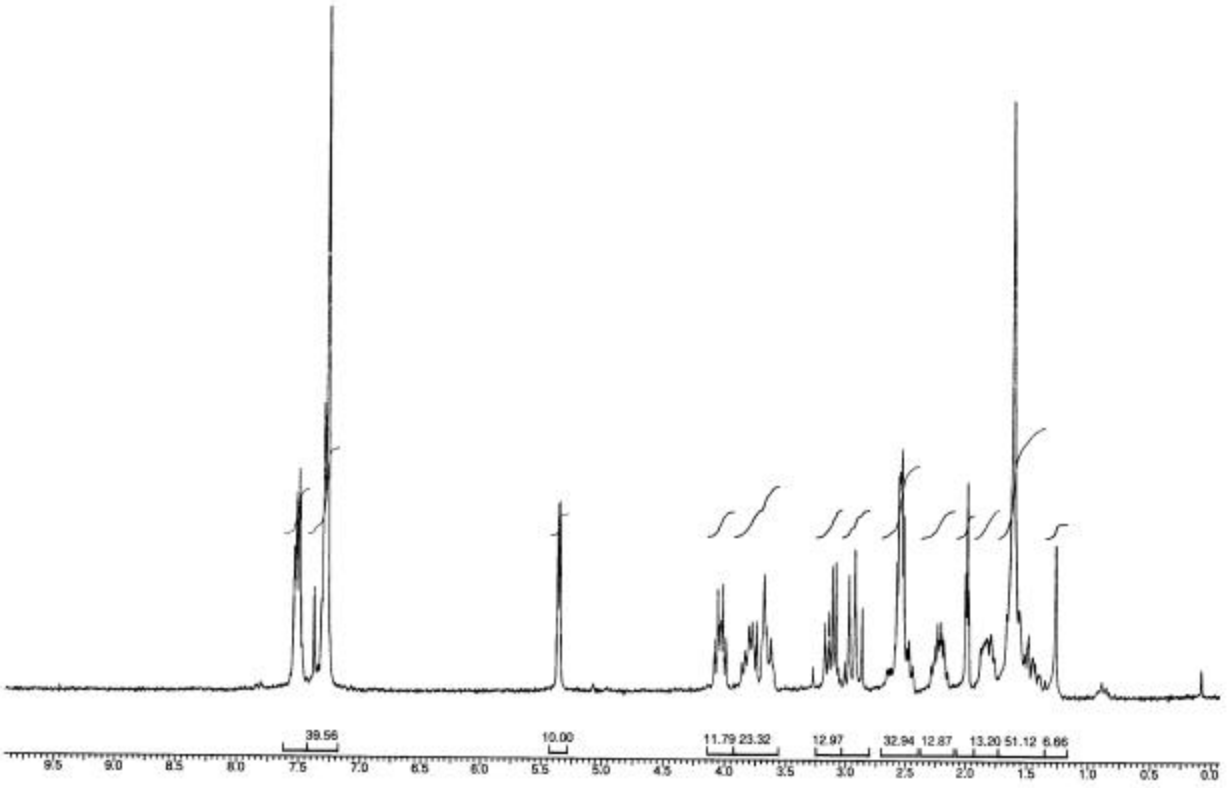

131.11
128.85
126.37
109.09
61.31
41.86
40.64
39.45
20.21
13.75
1.09

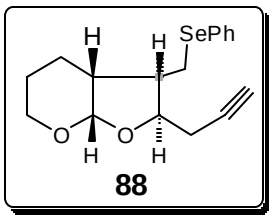

E
E
(CH3)3Si
SePh

61

Fig. 10

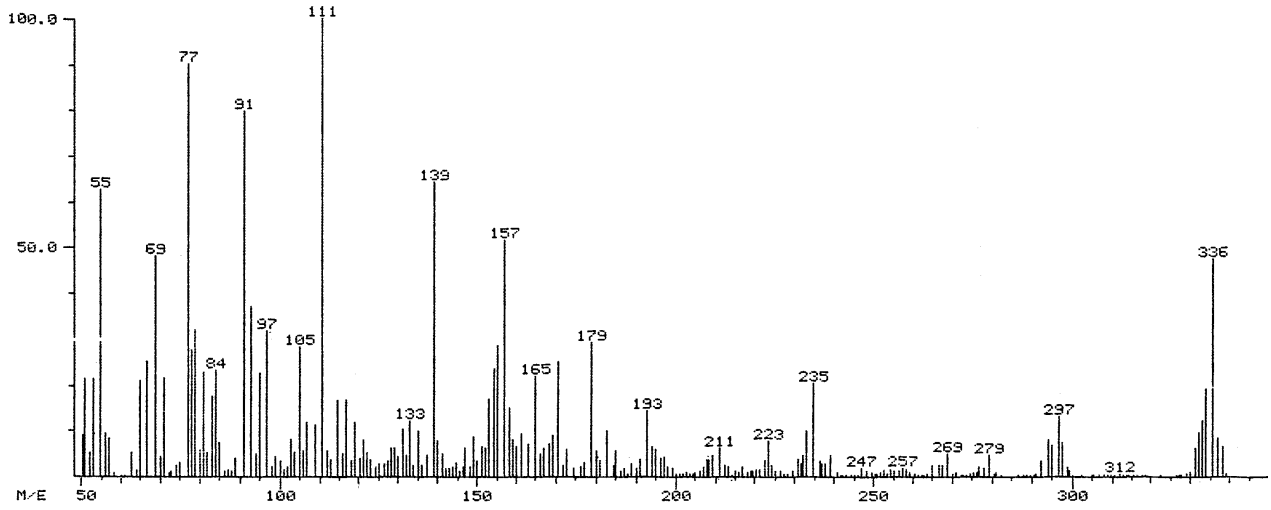

171.25
151.91
131.11
128.82
126.34
109.07
61.23
58.12
41.89
40.61
39.45
20.31
13.72


39.56
10.00
11.79 23.32
12.97
32.94 12.87
13.20 51.12 6.66


H
H
SePh
O
O
H
H

88

Fig. 11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50.0
M/E
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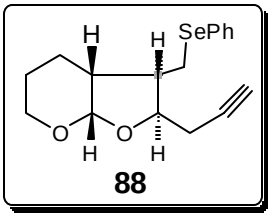
100
150
200
250
300
111
77
91
55
139
157
69
97
105
84
179
165
133
193
235
211
223
297
247
257
269
279
312
336


H
H
SePh
O
O
H
H

88

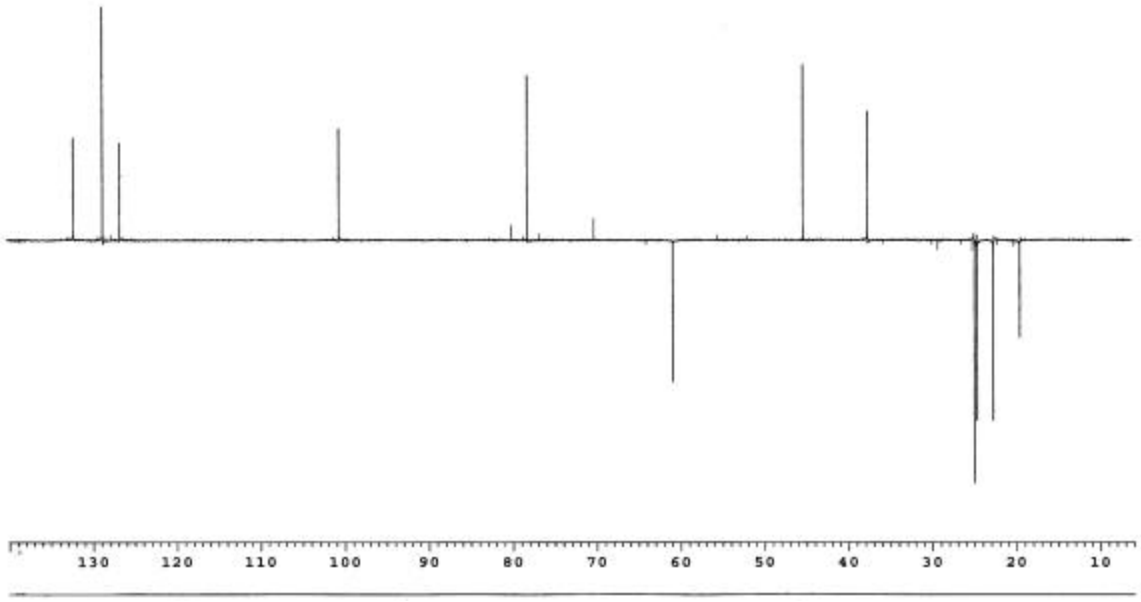
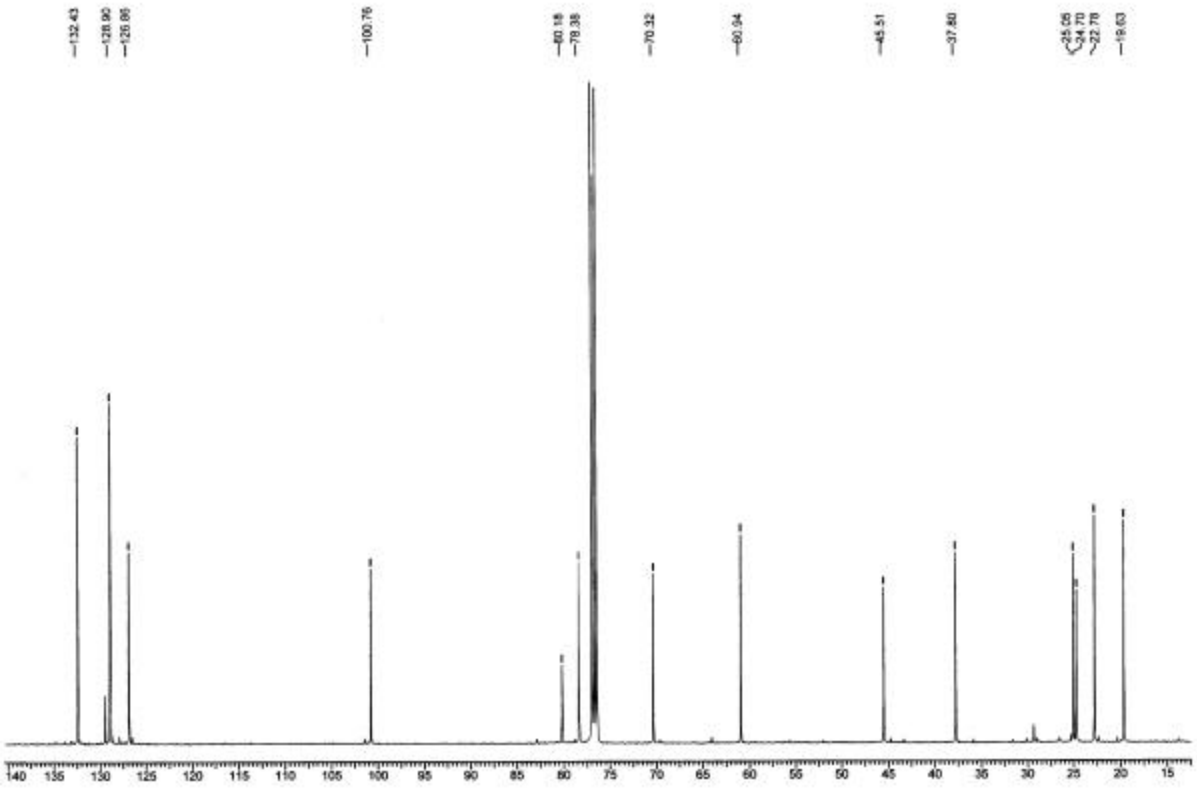

130
120
110
100
90
80
70
60
50
40
30
20
10

Fig. 12


132.43
128.90
126.66
100.76
80.18
78.38
70.32
60.94
45.51
37.80
25.05
24.70
22.78
19.63
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15

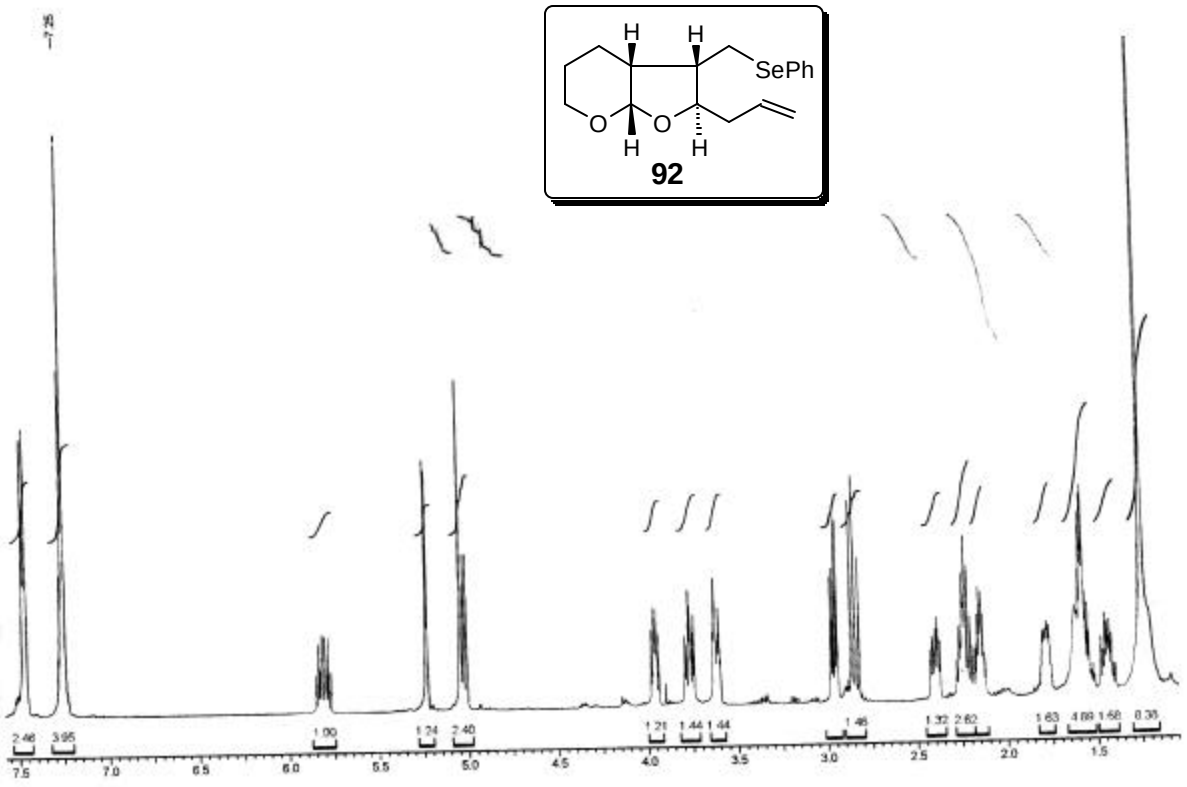
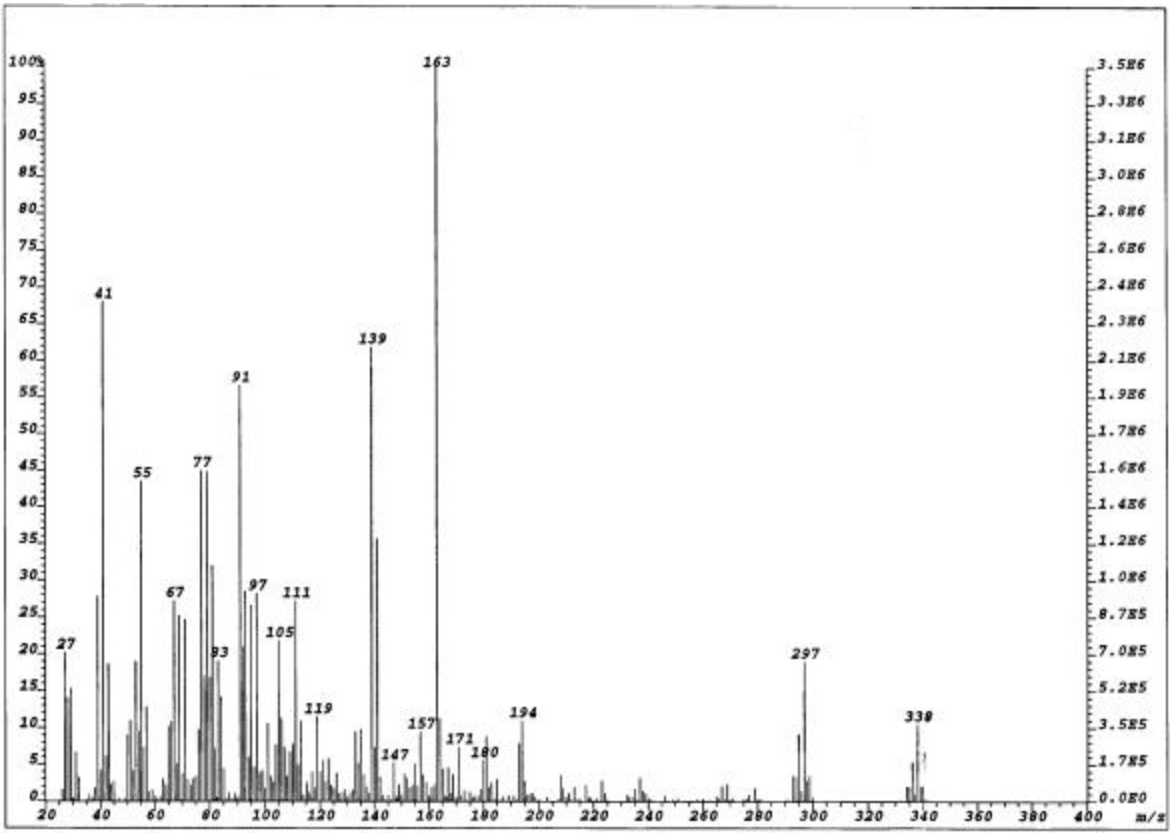
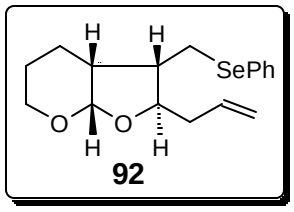

H
H
SePh
O
O
H
H
92

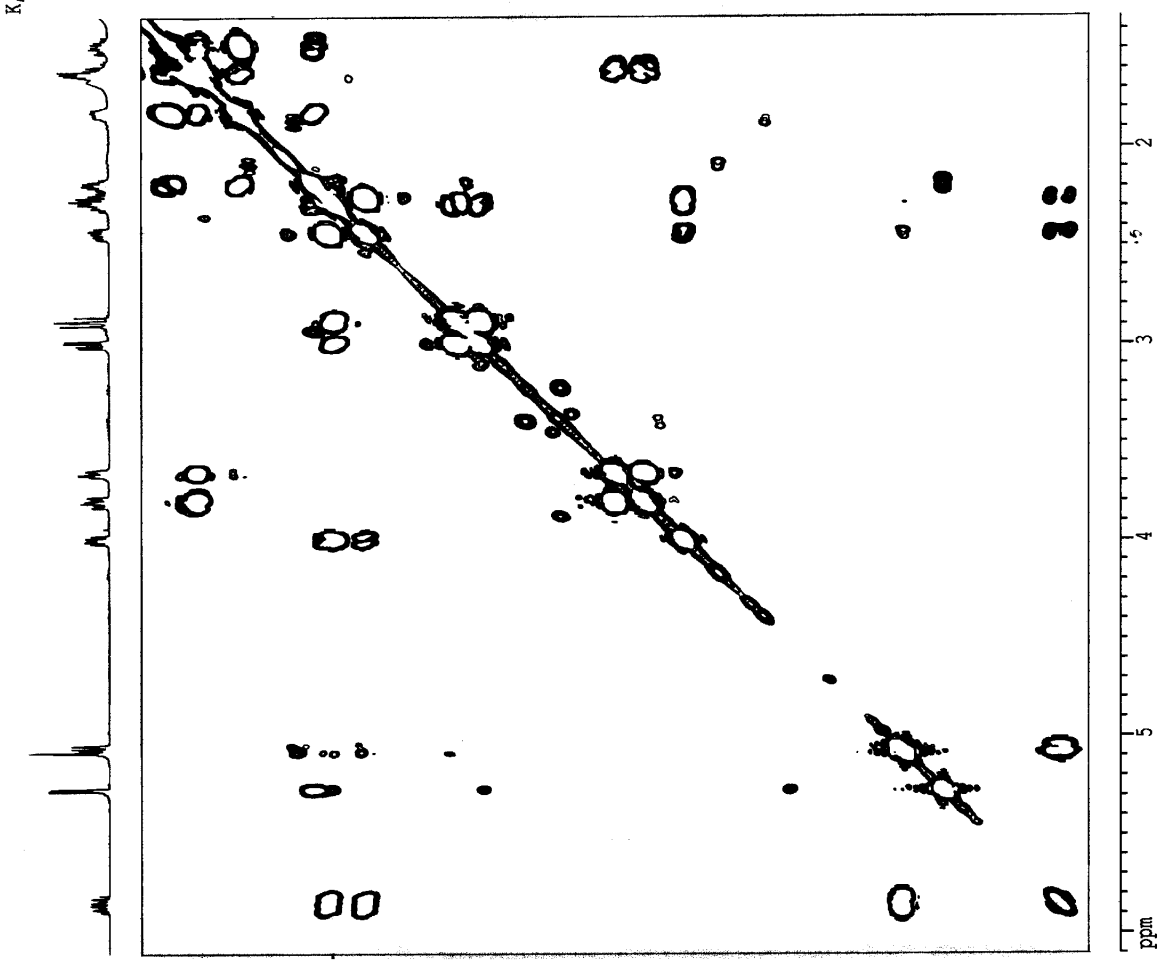
Fig. 13

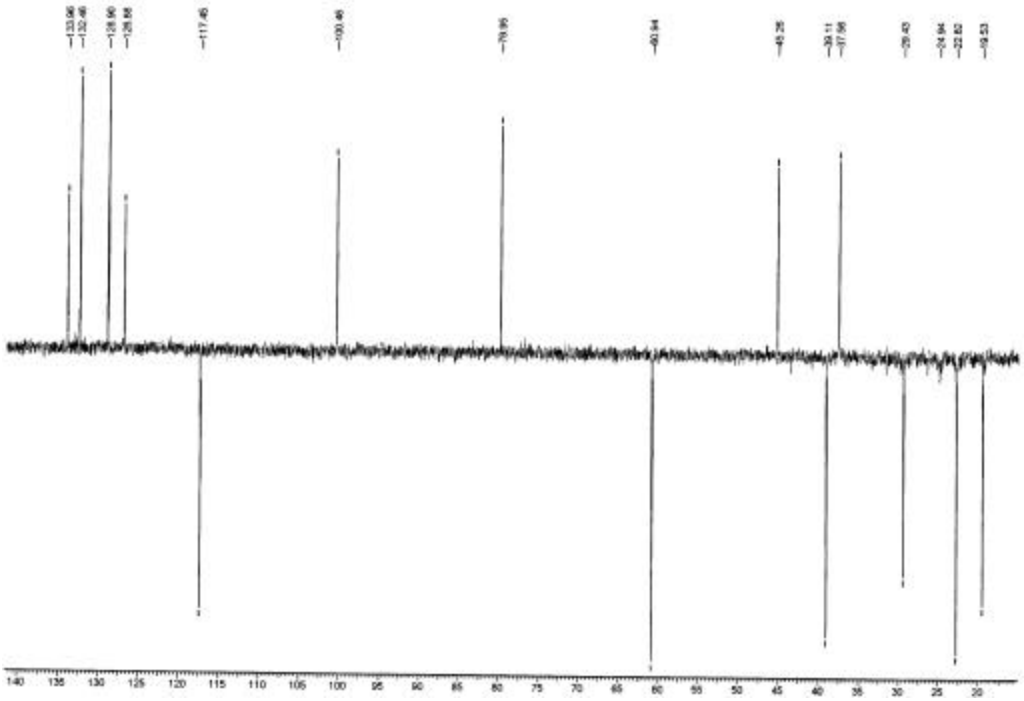

163
41
139
91
55
77
97
111
67
105
27
93
119
157
147
171
180
194
297
339
m/z

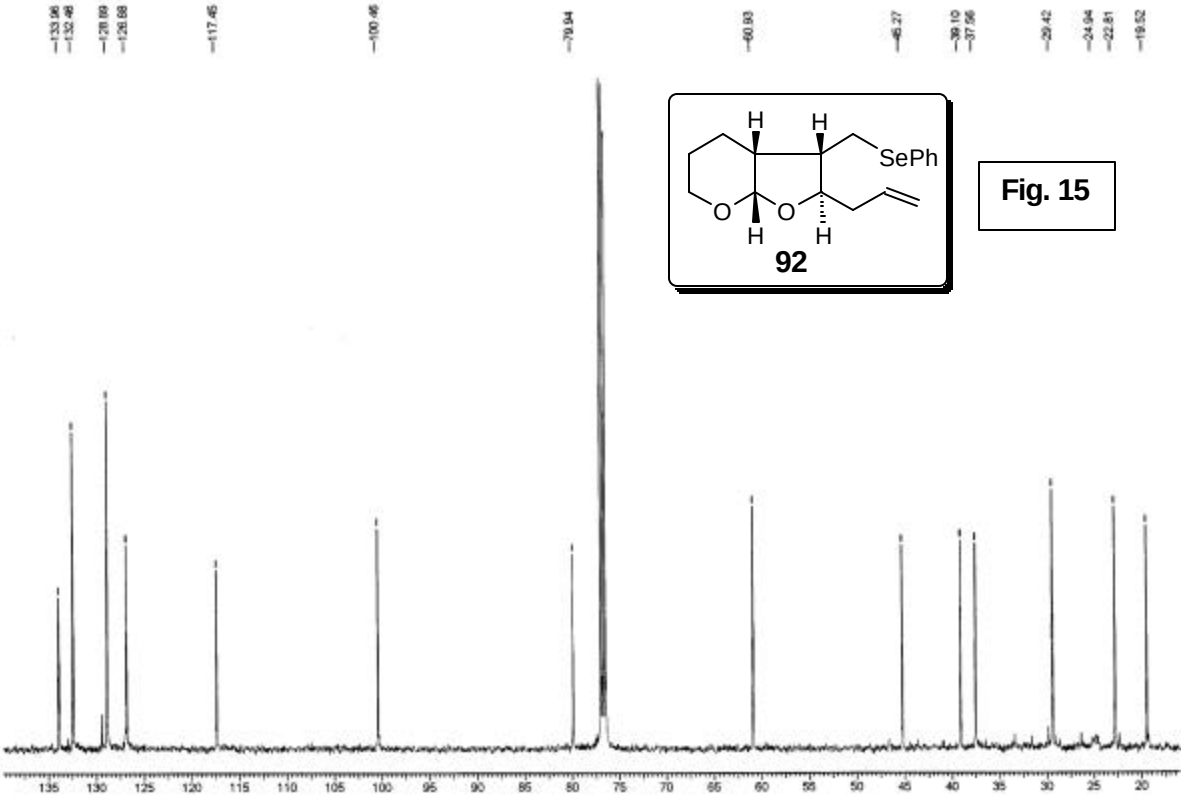


92

Fig. 14







92

Fig. 15

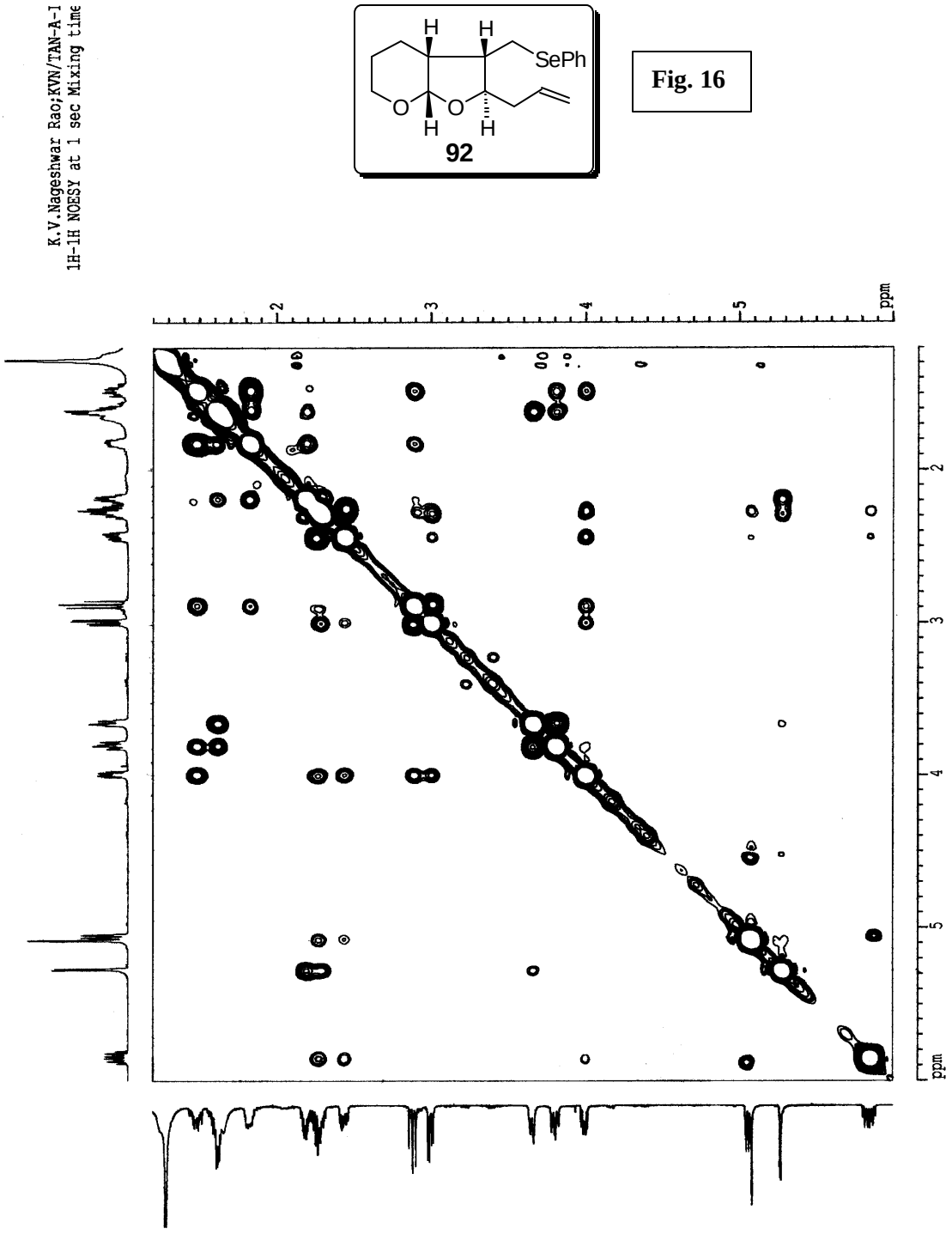
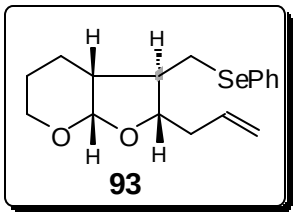

K.V.Nageshwar Rao;KVN/TAN-A-1
1H-1H NOESY at 1 sec Mixing time
H
H
SePh
O
O
H
H
92
ppm
2
3
4
5
ppm

Fig. 16


H
H
SePh
O
O
H
H

93

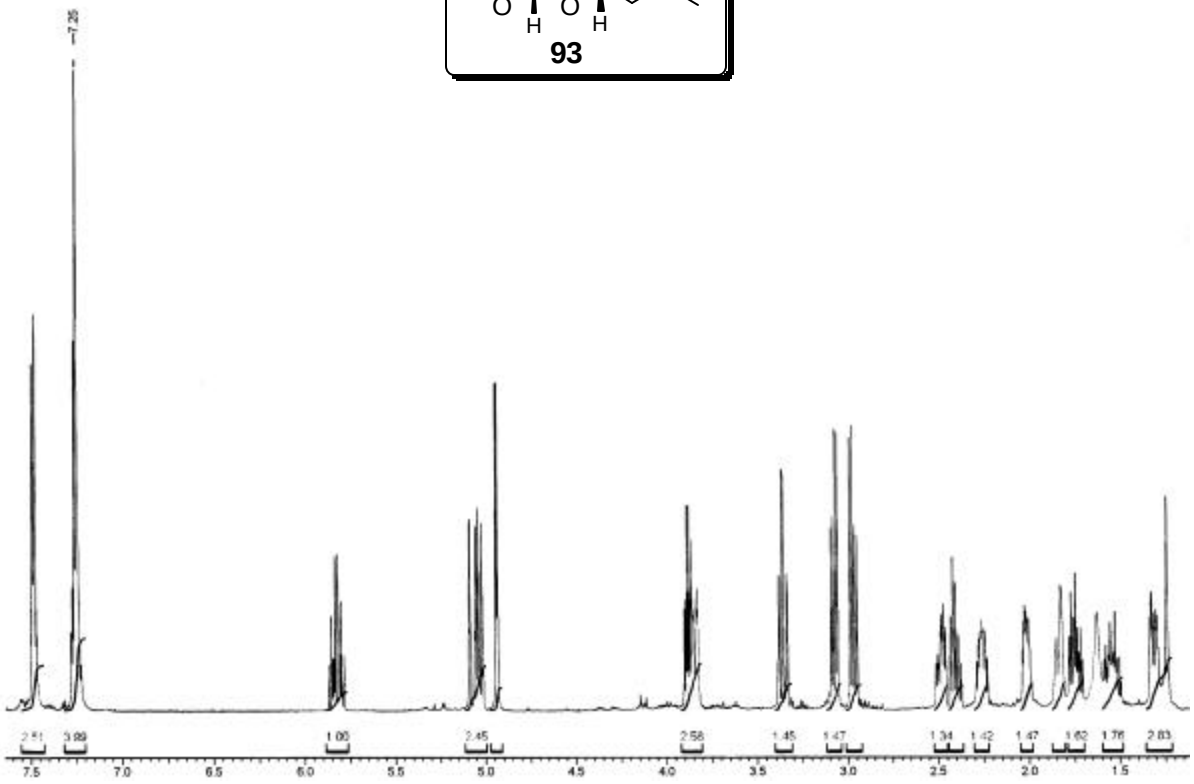
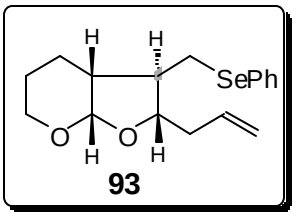
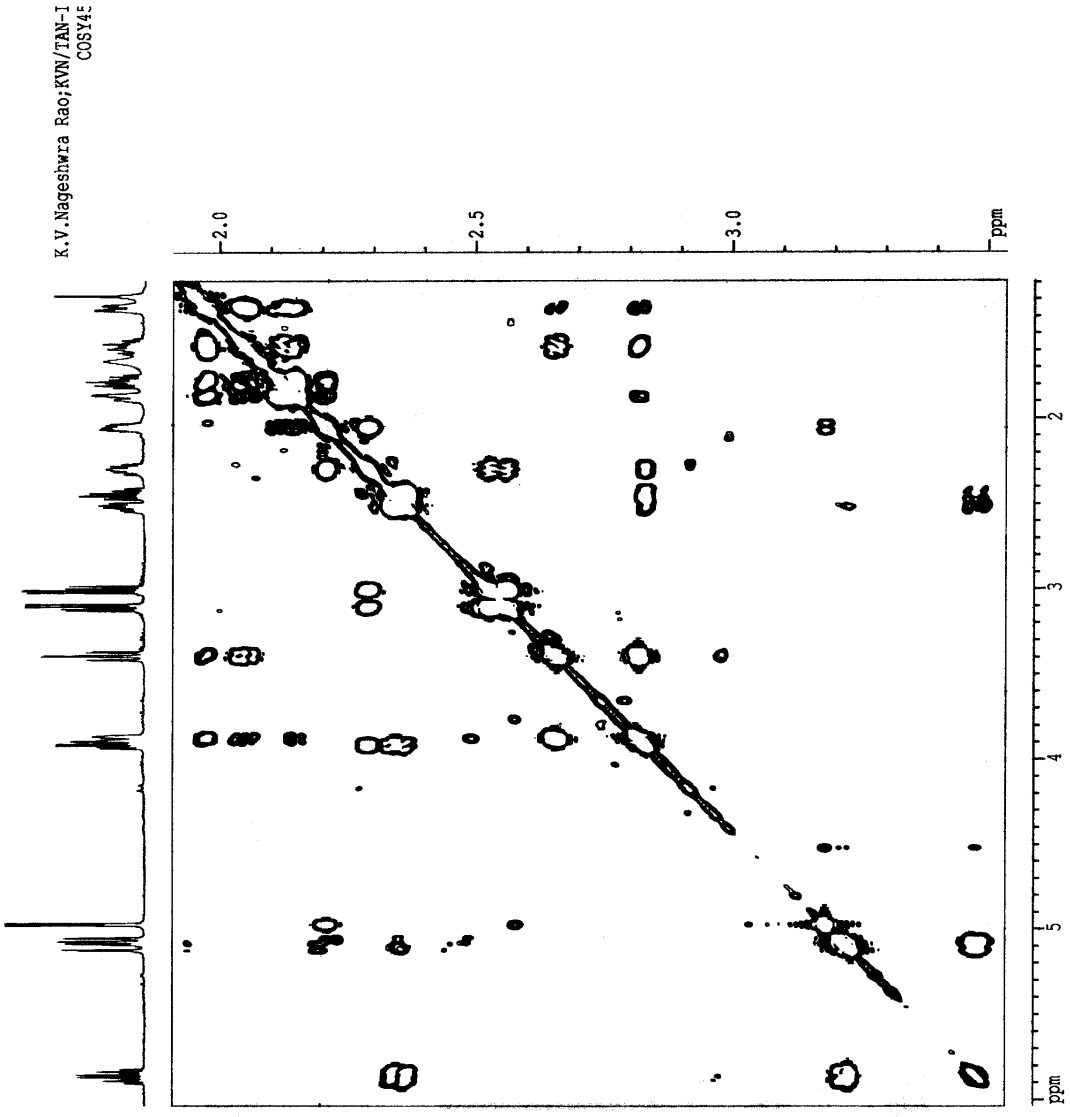

7.26
2.41
3.89
1.00
2.45
2.58
1.45
1.47
1.34
1.42
1.47
1.62
1.78
2.83
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

Fig. 17

Fig. 18



93



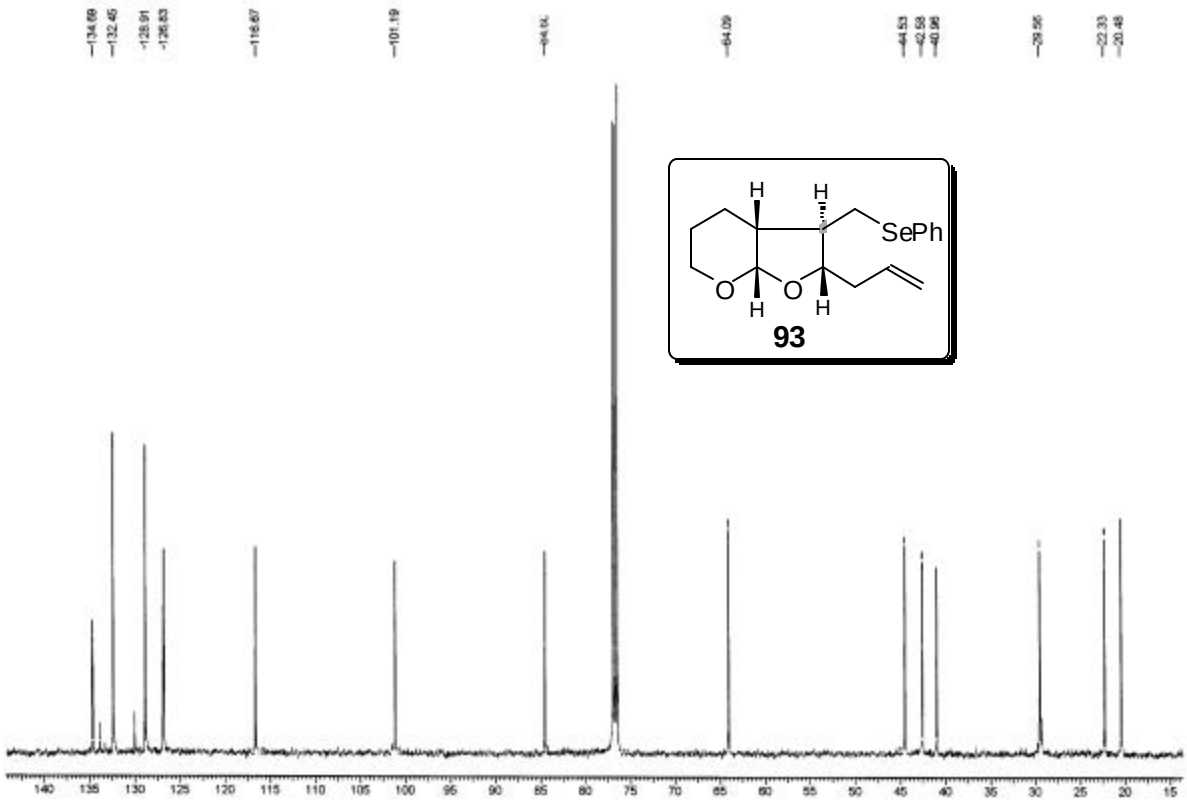
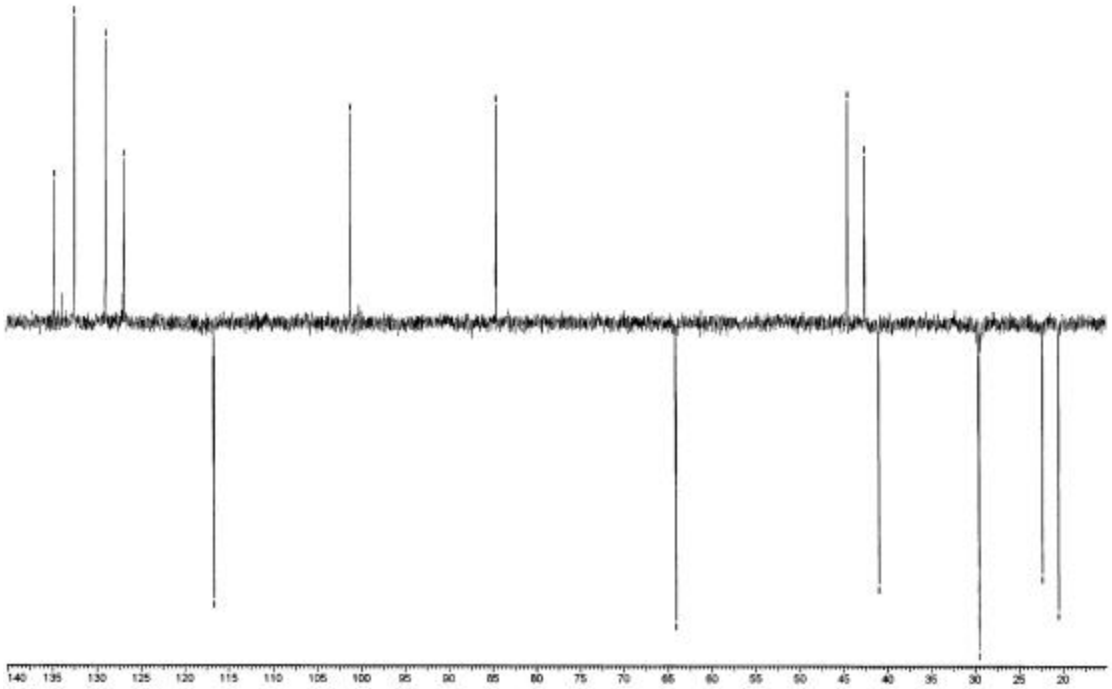
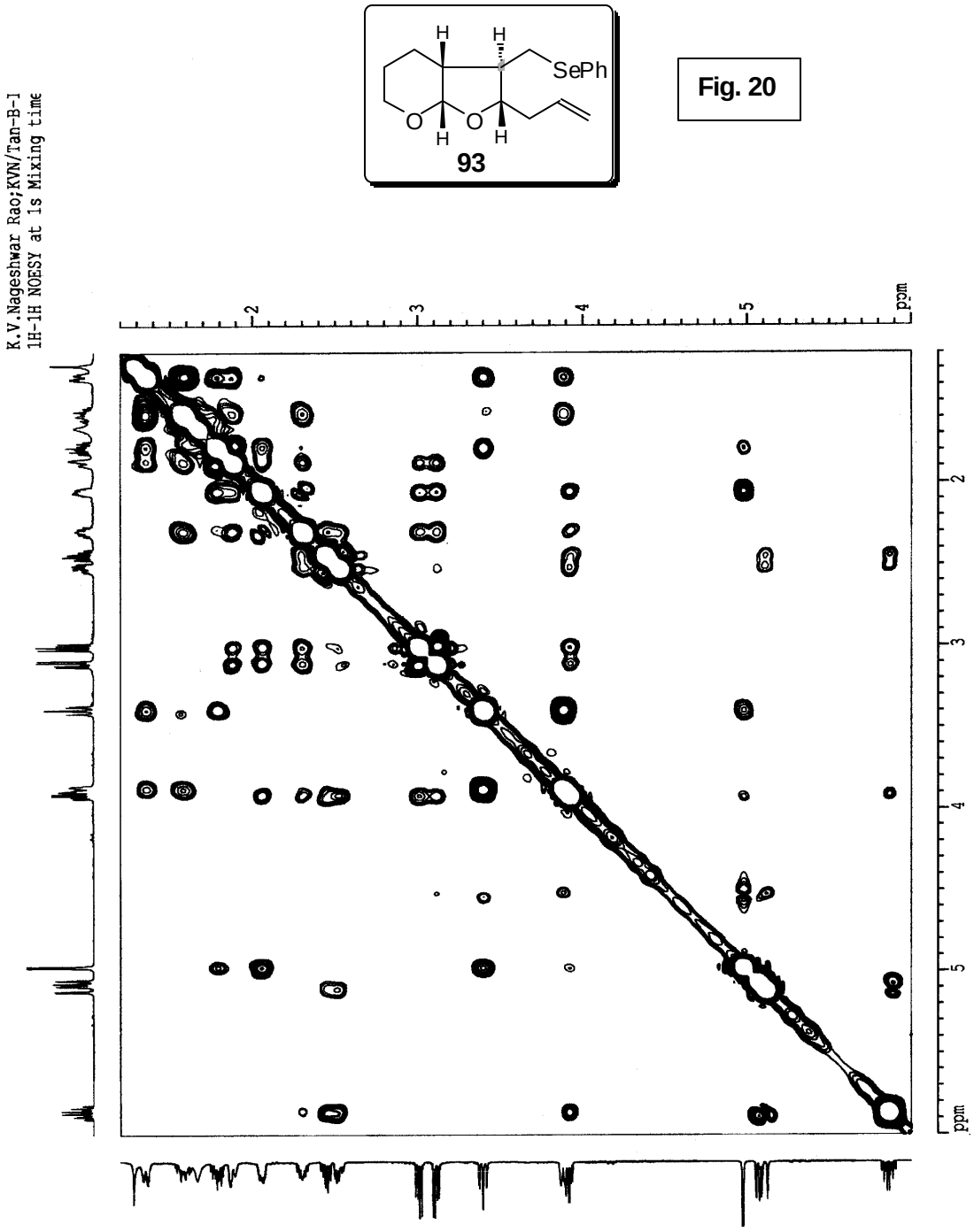

134.69
132.45
128.91
126.83
116.67
101.19
84.94
64.09
44.53
42.58
40.96
29.56
22.33
20.48
H
H
SePh
O
O
H
H
93

Fig. 19




K.V.Nageshwar Rao;KVN/Tan-B-1
1H-1H NOESY at 1s Mixing time
H
H
SePh
O
O
H
H
93
Fig. 20
2
3
4
5
ppm
2
3
4
5
ppm

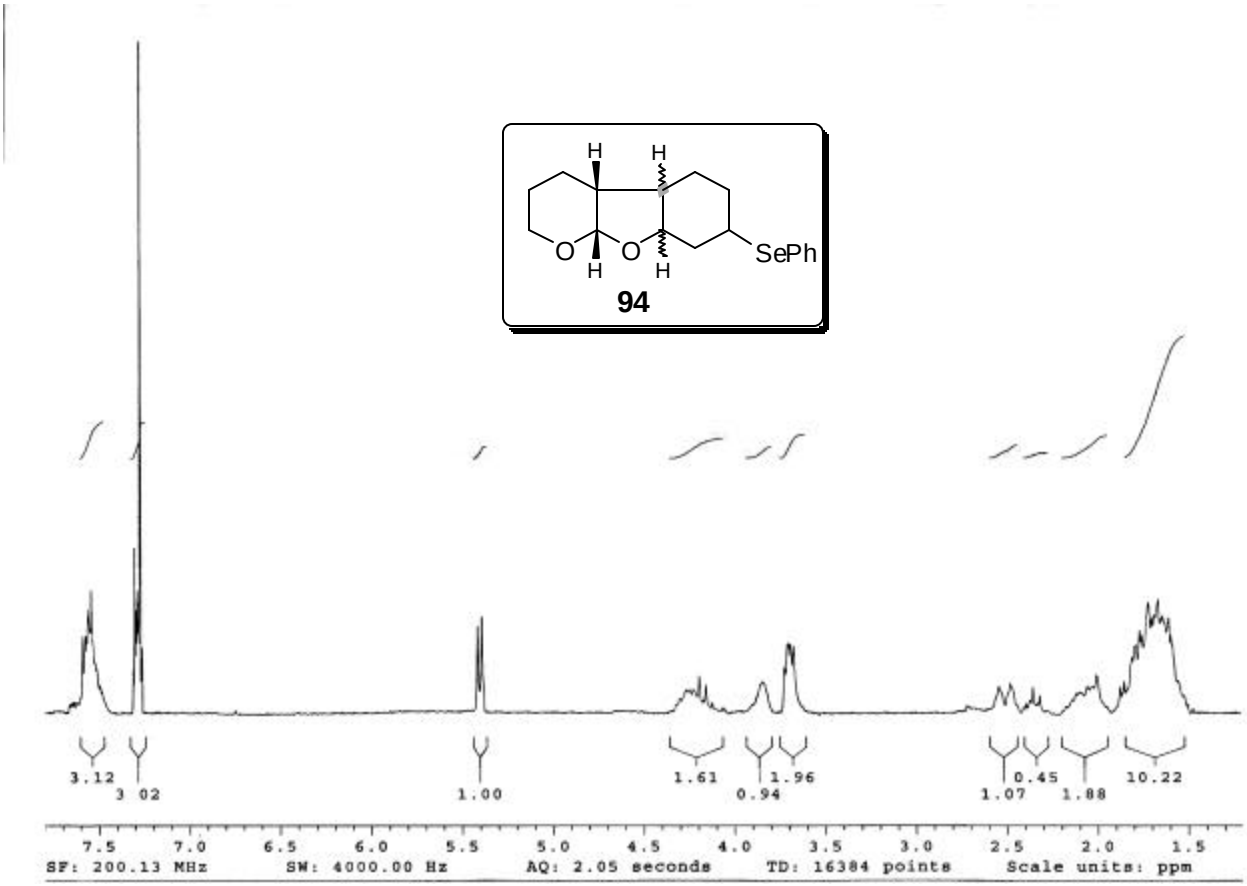
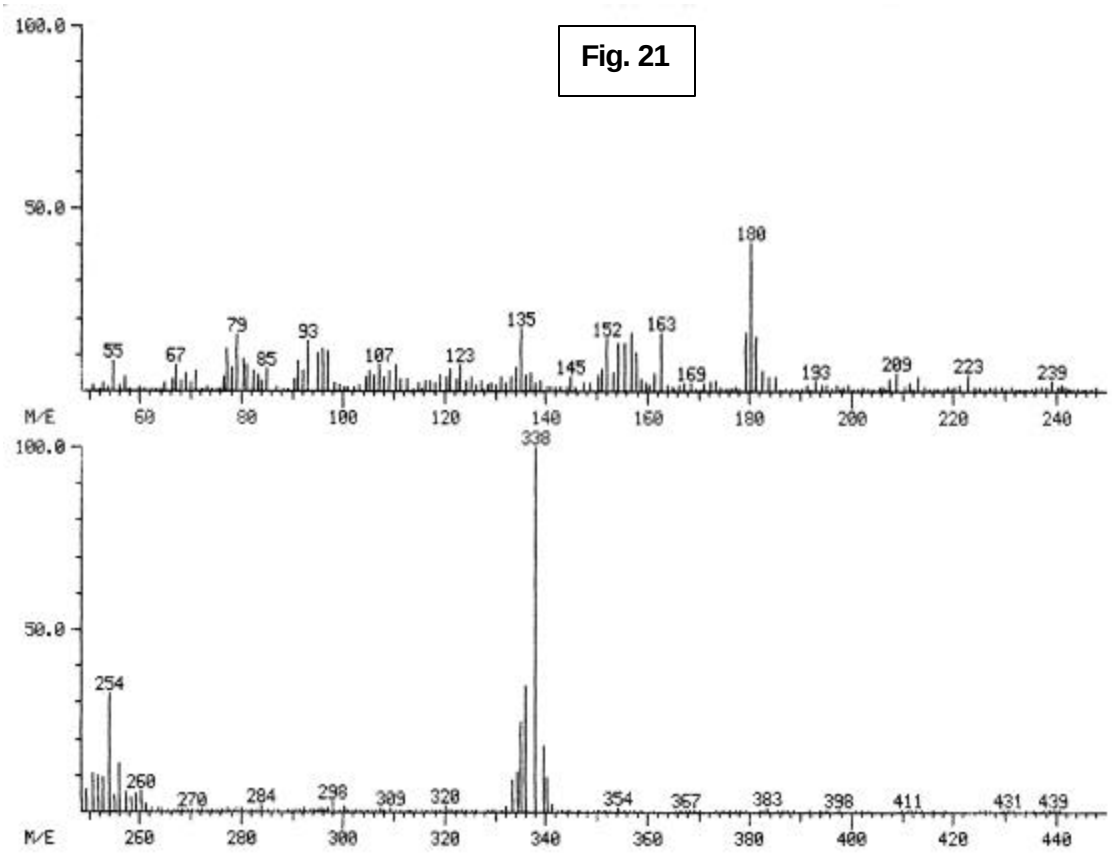

H
H
O
O
H
H
SePh
94
3.12
3 02
1.00
1.61
0.94
1.96
1.07
0.45
1.88
10.22
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
SF: 200.13 MHz
SW: 4000.00 Hz
AQ: 2.05 seconds
TD: 16384 points
Scale units: ppm

Fig. 21


100.0
50.0
M/E
55
67
79
85
93
107
123
135
145
152
163
169
180
193
209
223
239
60 80 100 120 140 160 180 200 220 240
100.0
50.0
M/E
254
260
270
284
298
309
320
338
354
367
383
398
411
431
439
260 280 300 320 340 360 380 400 420 440

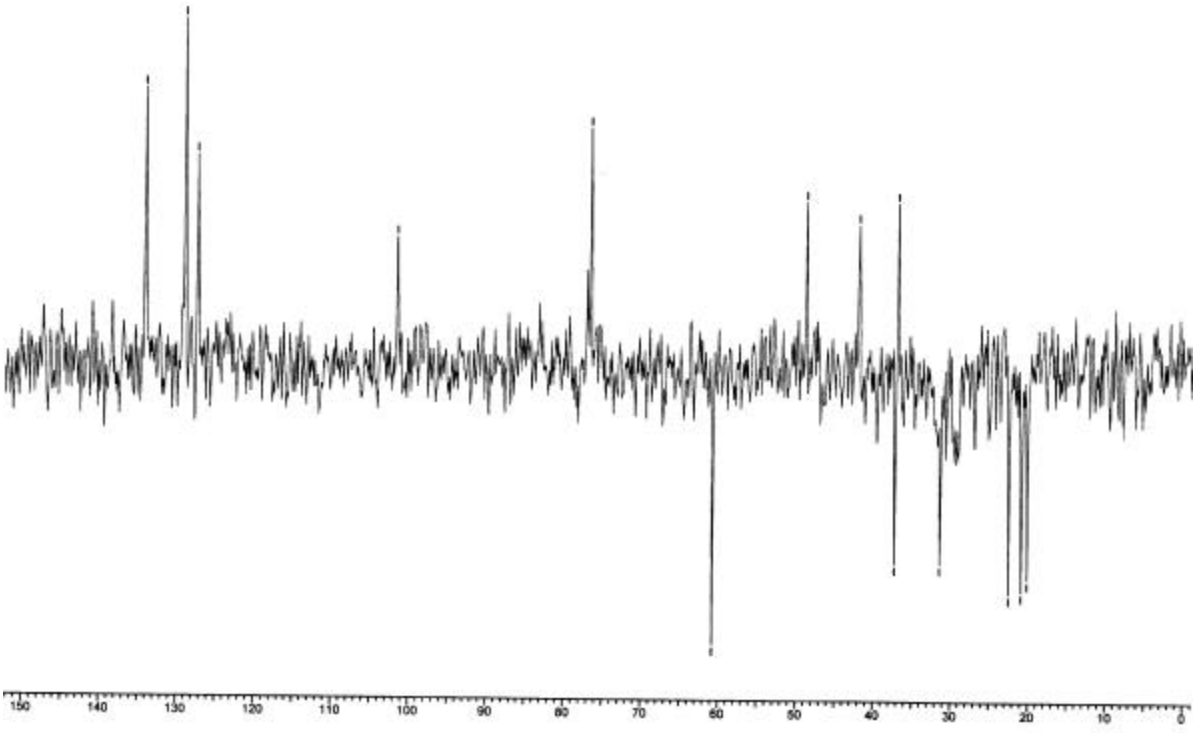
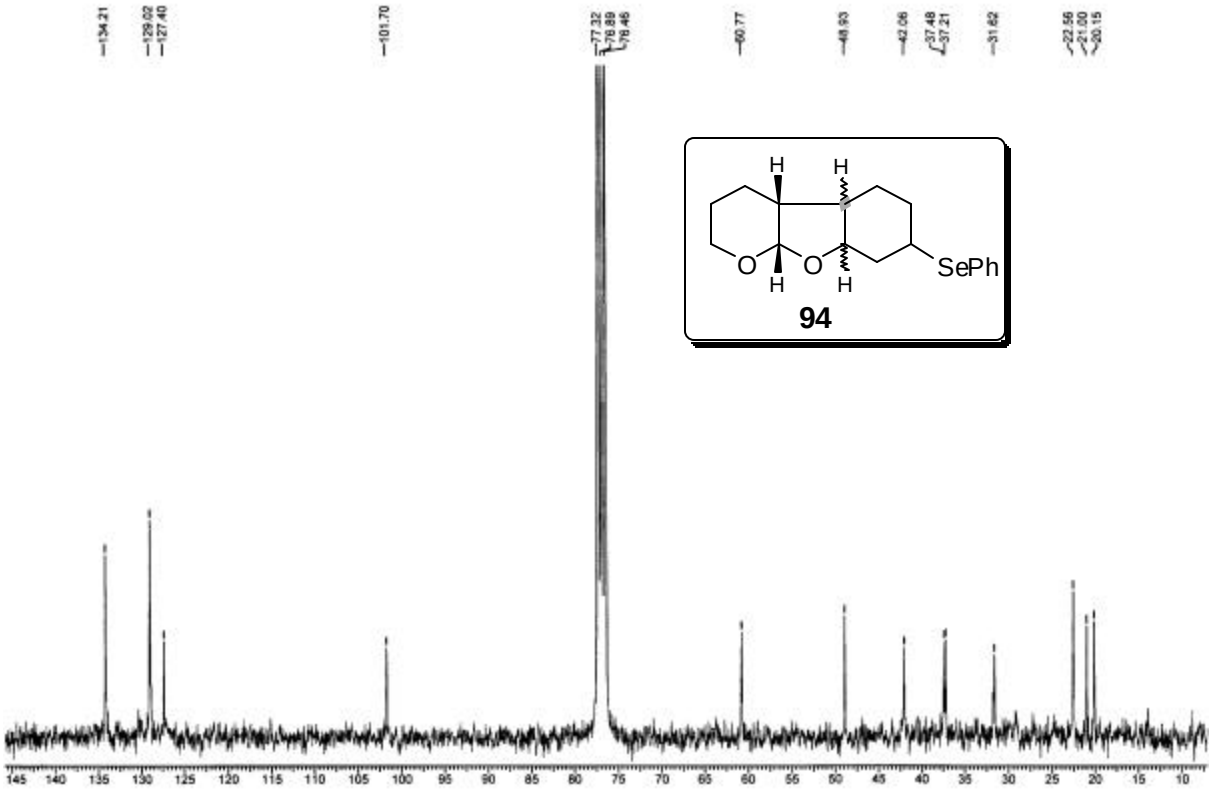


Fig. 22


134.21
129.02
127.40
101.70
77.32
76.89
76.46
60.77
48.93
42.06
37.48
37.21
31.62
22.56
21.00
20.15
H
H
O
O
H
H
SePh

94