CARBON-CARBON AND CARBON-HETEROATOM BOND FORMING REACTIONS MEDIATED BY CERIUM (IV) AMMONIUM NITRATE

THESIS SUBMITTED TO THE UNIVERSITY OF KERALA
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY
UNDER THE FACULTY OF SCIENCE

BY

LATHA G. NAIR

ORGANIC CHEMISTRY DIVISION
REGIONAL RESEARCH LABORATORY (CSIR)
THIRUVANANTHAPURAM-695 019, KERALA, INDIA

NOVEMBER, 1998

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Dedicated to my beloved Accchan and Amma

COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH (CSIR)
क्षेत्रीय अनुसंधान प्रयोगशाला, तिरुवनन्तपुरम्-695 019
REGIONAL RESEARCH LABORATORY
Trivandrum- 695 019, INDIA.
Phone : 91-471-490324 (O), 341707 (R)
Fax: 91-471-491712, email : gvn@csrrltrd.ren.nic.in

डॉ.जी.विजय नायर
निदेशक

Dr. G.Vijay Nair
Director

CERTIFICATE

Certified that the work described in this thesis entitled ***CARBON-CARBON AND CARBON-HETEROATOM BOND FORMING REACTIONS MEDIATED BY CERIUM (IV) AMMONIUM NITRATE*** *has been carried out by* ***Ms. LATHA G. NAIR*** *under my supervision and the same has not been submitted elsewhere for a degree.*

G. Vijay Nair

G.VIJAY NAIR
THESIS SUPERVISOR

ACKNOWLEDGEMENTS

It is with great pleasure that I place on record my deep sense of gratitude and indebtedness to my research supervisor, ***Dr. G. Vijay Nair****, for suggesting this captivating research problem. It has been my privilege to work under his inspiring guidance, constructive criticism and constant encouragement during all stages of the study.*

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Latha G. Nair

Thiruvananthapuram

November 1998

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LIST OF ABBREVIATIONS

BAIB	Bis Acetoxy Iodo Benzene
CAN	Cerium (IV) Ammonium Nitrate
m-CPBA	4-Chloroperbenzoic acid
COLOC	Correlation Spectroscopy via Long-range Coupling
COSY	Correlated Spectroscopy
DBU	1,8-Diaza Bicyclo[5.4.0]Undec-7-ene
FMO	Frontier Molecular Orbital
HFP	1,1,1,3,3,3 Hexaflouro propan-2-ol
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
NBS	N-Bromo Succinimide
NOESY	Nuclear Overhauser Effect Spectroscopy
NTS	N-Thiocyanato Succinimide
PIFA	Phenyl Iodine (III) bis (trifluoro Acetate)
PPTS	Pyridinium *p*-toluene sulfonate
SET	Single Electron Transfer
SOMO	Singly Occupied Molecular Orbital
TBACN	Tetrabutyl Ammonium Cerium (IV) Nitrate
TMS	Tetramethyl Silane

PREFACE

Among the various carbon-carbon bond forming reactions, radical processes have received the least attention until recently, due to the erroneous notion that these reactions lack selectivity and are uncontrollable. Progress in the use of radical reactions in organic synthesis during the last few decades can be traced to the conceptualization and demonstration by Stork that these reactions, under controlled conditions, offer a unique and powerful method for complex carbocyclic construction. Today, there is widespread appreciation of the potential offered by radical processes and these are perceived to add a new dimension to Organic synthesis. Of the different methods developed for the generation of radicals, the oxidative processes mediated by one electron oxidants like Mn (III) and Ce (IV) have received much attention recently. In view of the intrinsic interest in such reactions, we have carried out some investigations to explore the synthetic utility of CAN and the results obtained are presented in the thesis entitled **"CARBON-CARBON AND CARBON-HETEROATOM BOND FORMING REACTIONS MEDIATED BY CERIUM (IV) AMMONIUM NITRATE"**.

The thesis is divided into five chapters. Relevant references are given at the end of each chapter. Some recent developements in the use of Cerium (IV) Ammonium Nitrate (CAN) in different types of reactions, especially in carbon-carbon bond forming reactions, with selected examples are presented in the introductory chapter. A statement of the present research problem has also been incorporated. The oxidative addition of 1,3-dicarbonyl compounds to various cyclic and acyclic dienes yielding the dihydrofuran derivatives is

presented in second chapter. General information about the experimental procedure is given in this chapter. The third chapter describes the use of CAN in carbon-heteroatom bond forming reactions. Carbon-sulfur and carbon-nitrogen bond formation has been accomplished *via* the CAN mediated thiocyanation and azidation of alkenes. Chapter four deals with the synthesis of tartronic acid derivatives by the CAN mediated oxygenation of malonates. The last chapter describes the oxidation of styrenes and aldehydes to methoxy acetophenones and esters respectively with CAN in dry methanol.

A summary of the work is given towards the end of the thesis.

CHAPTER I

RECENT DEVELOPMENTS IN CARBON-CARBON BOND FORMING AND RELATED REACTIONS MEDIATED BY CERIUM(IV) REAGENTS

1.1. Introduction

The fundamental task in the synthesis of organic compounds, simple or complex, is the construction of carbon-carbon bonds. Among the various synthetic methods involving polar, radical or pericyclic reactions available, the radical reactions have received the least attention until recently. This has been largely due to the erroneous notion that these reactions lack selectivity and are prone to produce intractable mixture of products. Recently there has been a change in this perception accompanied by a dramatic resurgence of interest in the use of radical methodology. This can be attributed largely to the conceptualization and demonstration by Stork [1,2,3] that the controlled formation as well as the addition of vinyl radicals to alkenes offers a unique and powerful method for complex carbocyclic construction.[4]

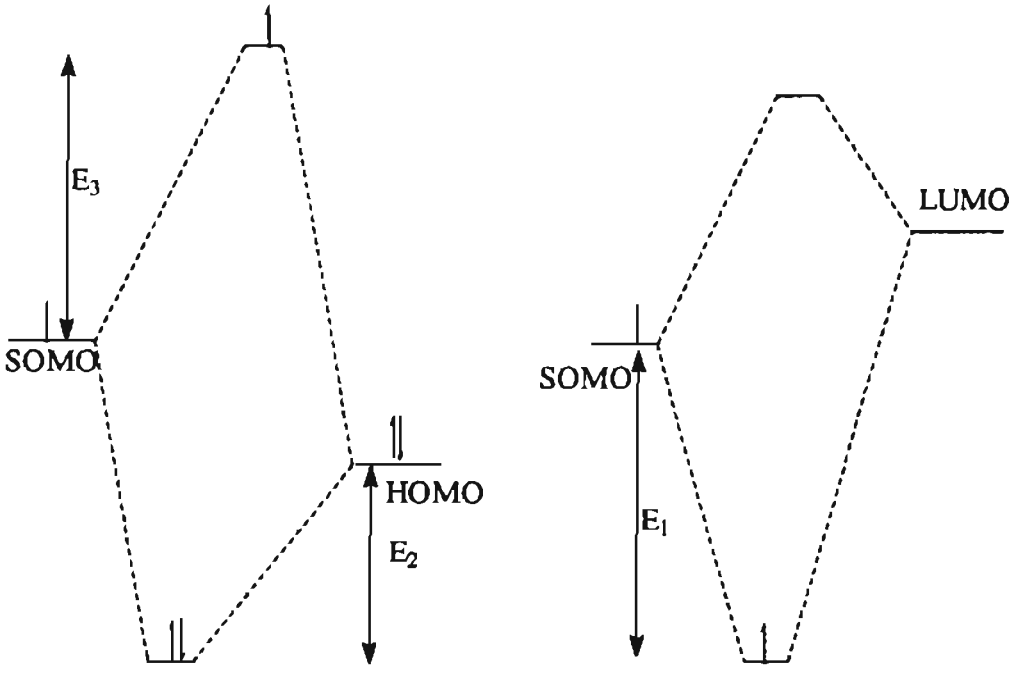
The indepth investigations of Julia,[5] Beckwith,[6] Ingold[7] and others leading to a clear understanding of the structure and the reactivity of carbon centered radicals and the synthetic efforts by Giese,[4a] Curran[4g] and

Pattenden[8] have also contributed significantly to the acceptance of radical methodology. Today there is widespread appreciation of the potential offered by radical processes especially in the synthesis of structurally fascinating and biologically important natural products.[4,9] It is noteworthy that the classical name reactions like Kolbe electrolysis, [10] Barton reaction,[11] and Hofmann-Löffler-Freytag reaction[12] which involve radical intermediacy were known for years.

Radical reactions offer a number of advantages over the more commonly used ionic processes.[4a] Chemoselectivity of these reactions can be used advantageously in reactions of compounds with functional groups such as –OH, -NHR etc. Radical reactions are ideally suited for the construction of quaternary and neopentyl centers. Regioselectivity is also shown by the carbon centered radicals in cases like addition to α, β unsaturated ketones. Many reactions involving cyclic radicals are stereoselective. Since the radical reactions used in synthesis are very fast, side reactions such as rearrangement, β-elimination and racemization of chiral centers at adjacent or remote carbon atoms are suppressed in most cases. Another advantage is that carbon centered radicals can add to electron rich and electron deficient alkenes, allenes and acetylenes. Most radical reactions are carried out under neutral conditions. Radical methodology often engages mild reaction conditions under which the chirality at non-radical carbon atoms is preserved. An important advantage of the radical reaction is that, generally it is not influenced by solvent and even water can be used in many cases. These characteristics as well as the fact that the radical reactions can accomplish many transformations that are difficult to

be achieved by conventional methods, contribute to the importance of such reactions.

The rate of addition of radicals to alkenes can be rationalized by frontier molecular orbital (FMO) theory.[13] Radicals are very soft entities, most of them do not have a charge and in most chemical reactions they react with neutral molecules. Thus the coulombic forces are usually small while the frontier orbital interactions remain large. The frontier orbital of the radical is the singly occupied molecular orbital (SOMO). This can interact with either the HOMO or the LUMO of the interacting molecule (Fig.1).



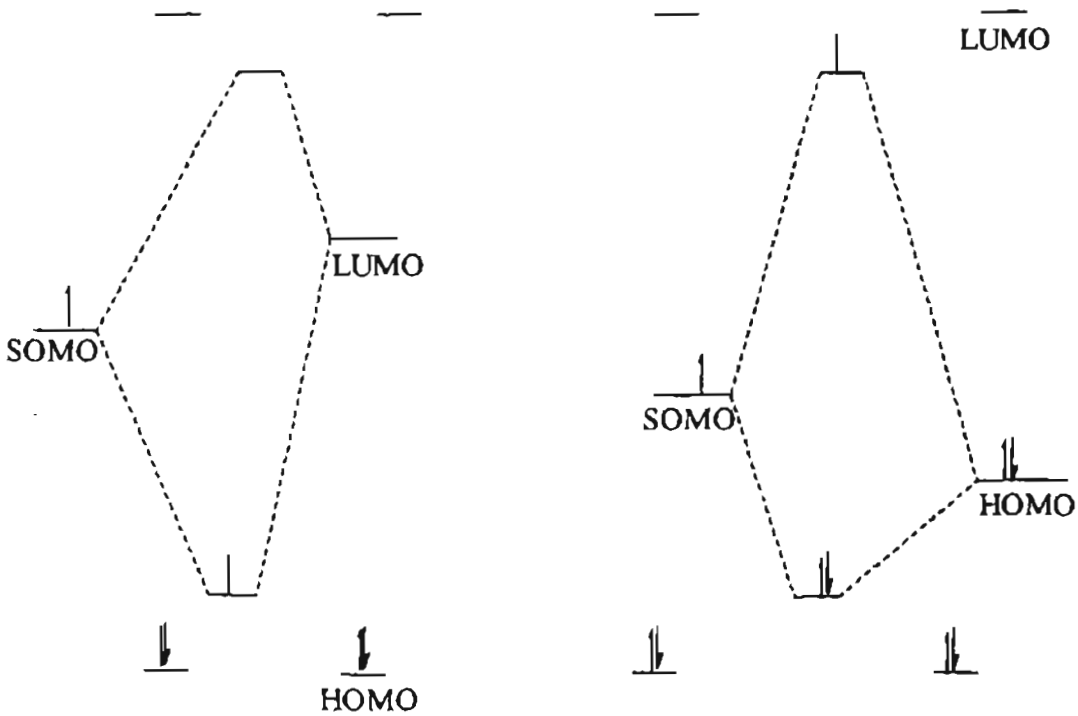
(a) SOMO-HOMO (b) SOMO-LUMO

Fig. 1. The interaction of the singly occupied molecular orbital (SOMO) of a radical with (a) the HOMO and (b) the LUMO of a molecule.

The interaction of SOMO of the radical with HOMO of the alkenes will lead to an energy gap of $2E_2$-E_3 while that with LUMO of the alkene will lead to an energy difference of E_1. The orbital with which SOMO of

radical will interact will depend on the magnitude of the energy gaps, *ie*, the interaction will be with the one having highest energy gap.

Nucleophilic radicals having high energy SOMO will react fast with molecules having low-energy LUMO. Radicals with low energy SOMO (those with electron withdrawing substituents) will react with molecules having high energy HOMO (Fig.2).



(A) Nucleophilic Radical (B) Electrophilic Radical

Fig 2. Important frontier orbital interactions for radicals (a) with high energy SOMOs and (b) with low energy SOMOs.

The generation of radicals involving chemical[4], electrochemical[14] and photochemical[4c,11,15] processes are known. Organic synthesis using carbon centered radicals generated by one electron oxidants is of current interest.

Among the various one electron oxidants like salts of Mn(III), Co(III), Cu(II), Fe(III) and V(V) with variable oxidation states, Mn (III) has received the most attention.[4,16,17] The dual role of the metal oxidants helps to prevent further oxidation of the initially formed radical before it gets added to the unsaturated system. The adduct radical gets oxidized and the products are derived from inter or intramolecular capture of nucleophiles or by loss of a proton to form alkenes.

Although, Mn(III) acetate has received the attention of many research groups,[17,18] it appears that Ce (IV) would be a very useful reagent for the generation of radicals.[19] Cerium (IV) compounds, especially, ceric ammonium nitrate [$(NH_4)_2Ce\ (NO_3)_6$, CAN] has been utilized extensively for a variety of oxidative transformations. The low cost, non-toxic nature and the solubility in a number of organic solvents like MeOH and CH_3CN combined with the experimental simplicity and easy handling make CAN attractive in organic reactions.

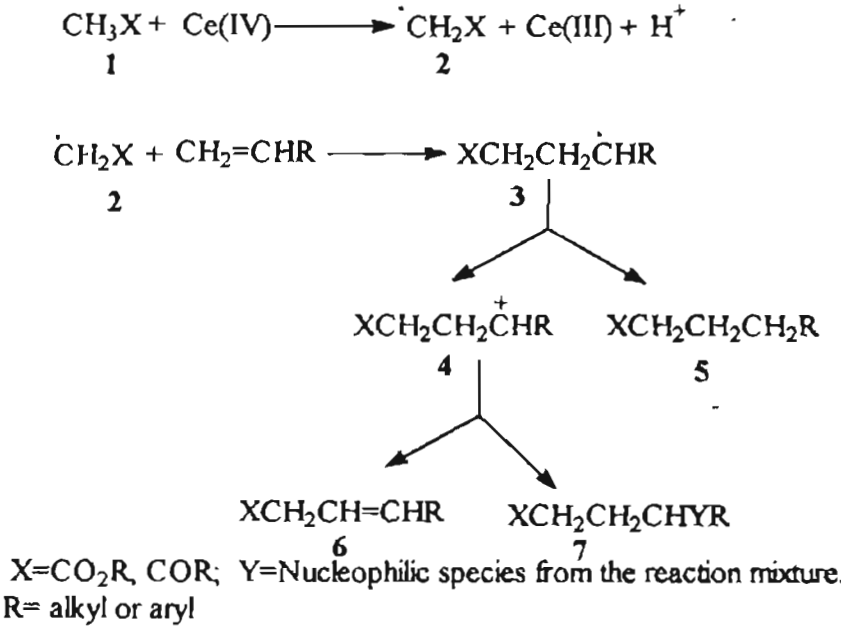
1.2. Carbon-Carbon Bond Forming Reactions Mediated by Ceric Ammonium Nitrate

During the reaction, cerium (IV) oxidizes the substrate molecule by the removal of one electron and gets reduced to cerium (III). The radical thus formed gets added to the second substrate molecule and the adduct radical undergoes further transformations to give the product. The reactions mediated by CAN are grouped into different classes and are presented in some detail in the following sections.

1.2.1. Oxidative addition of electrophilic radicals to alkenes

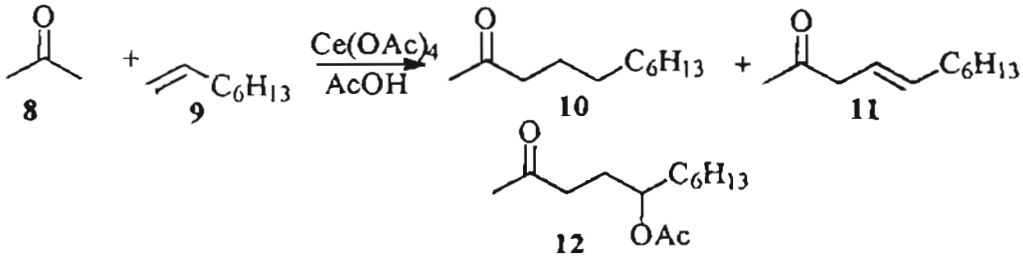
The pioneering work carried out by Heiba and Dessau in 1971 and subsequent investigations have shown that electrophilic carbon centered

radicals like $^{\cdot}CH_2X$ and $^{\cdot}CHXY$ {X and Y are electron withdrawing groups} generated by Ce(IV) reagents can be added to alkenes as represented in Scheme 1.[20]



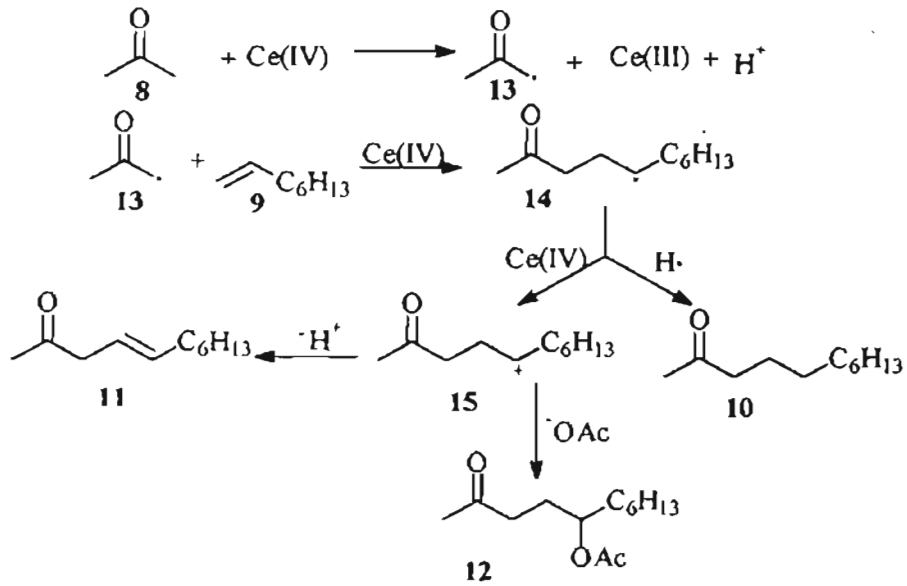
Scheme 1

Acetone on reaction with 1-octene in the presence of Ce(IV) acetate in acetic acid afforded the saturated ketone, unsaturated ketone and the keto acetate (Scheme 2).



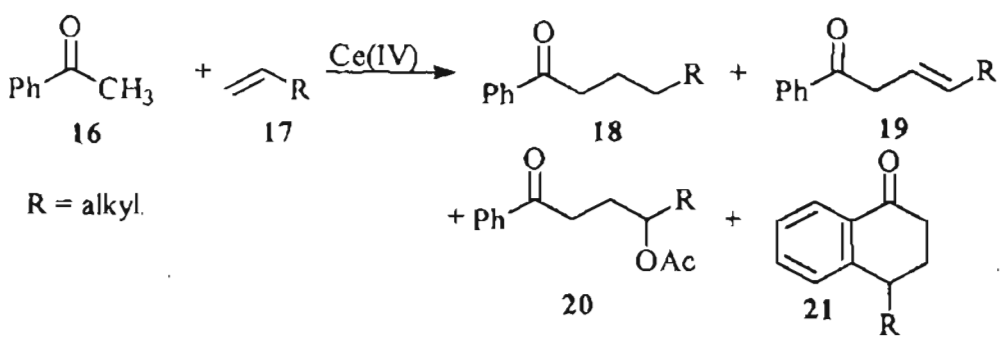
Scheme 2

The proposed mechanism for the formation of these products involving the α-keto radical in the initial step is illustrated in Scheme 3.



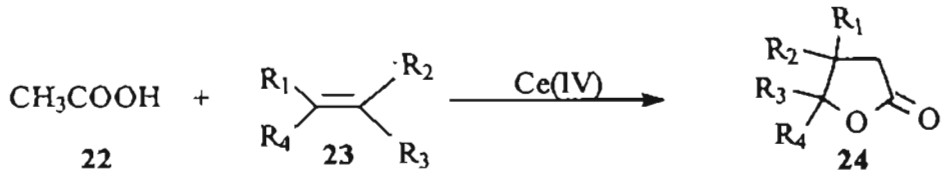
Scheme 3

When aryl ketones like acetophenone were used, the cyclized products such as tetralone was also formed along with the normal addition products (Scheme 4).[21]



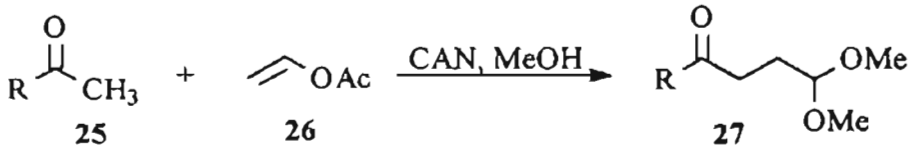
Scheme 4

As an extension of this work, γ-lactones were synthesized by the reaction of olefins with carboxylic acids in presence of Ce (IV) salts [22,23] (Scheme 5).



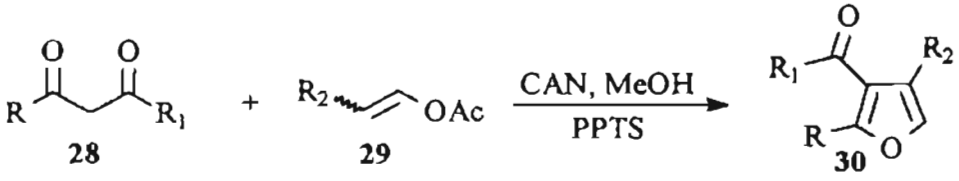
Scheme 5

Electron rich alkenes such as enol acetates were found to undergo oxidative addition to carbonyl compounds yielding 4-keto aldehyde dimethyl acetals.[24] An example is given in Scheme 6.



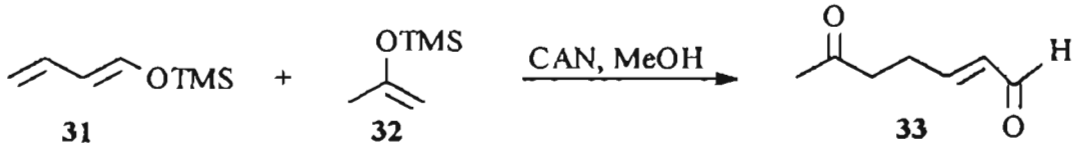
Scheme 6

CAN mediated addition of 1,3-dicarbonyl compounds to enolates afforded 3-acyl furans [25] (Scheme 7).



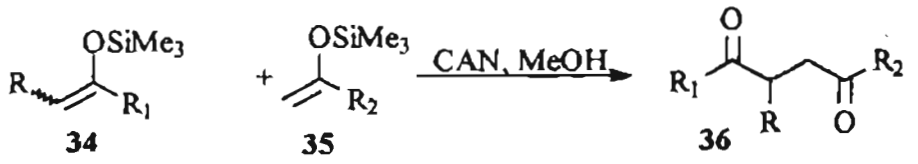
Scheme 7

Trimethylsilyl dienol ethers are easily oxidized by CAN to give α-carbonyl allyl radicals which can be added to enolic carbon-carbon double bonds leading to the formation of 6-oxo-α,β-unsaturated compounds[26] (Scheme 8).



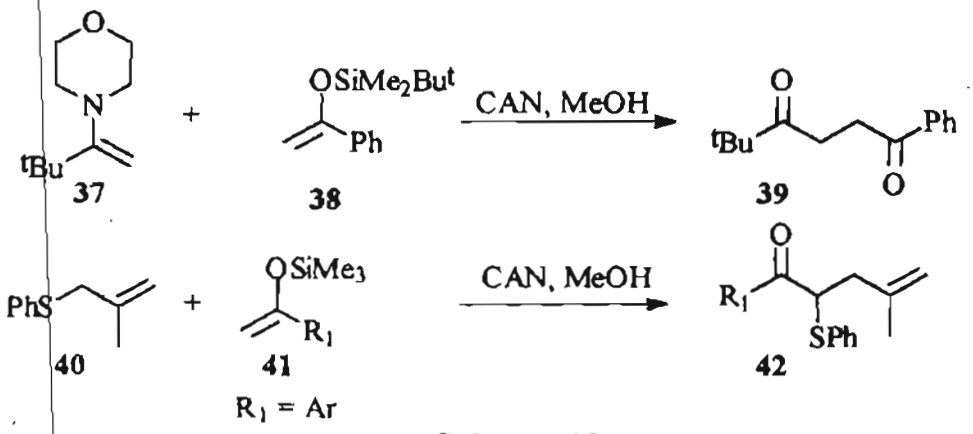
Scheme 8

1,4-dicarbonyl compounds can be synthesized by the cross-coupling of 1,2-disubstituted silyl enol ethers with other enol ethers [27](Scheme 9).



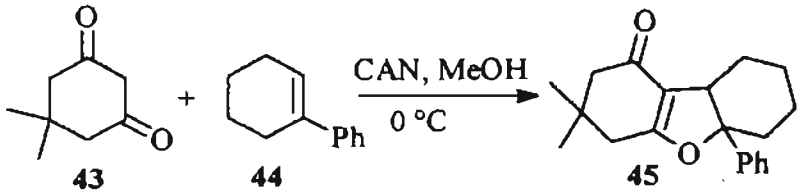
Scheme 9

Cation radicals of enamines, generated by oxidation with Ce (IV) compounds react with silyl enol ethers to give 1,4-diketones. The cation radical generated from allyl phenyl sulfide also undergoes addition to silyl enol ethers leading to unsaturated ketones via a [2,3] sigmatropic rearrangement.[28] Examples are given in Scheme 10.



Scheme 10

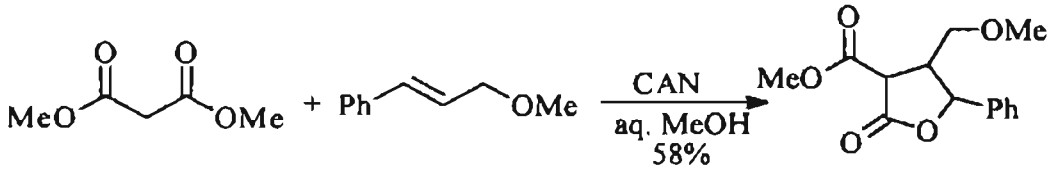
All the earlier reports of CAN mediated oxidative addition of electrophilic radicals to alkenes involve activated alkenes. Studies in our own laboratory include the CAN mediated oxidative addition of active methylene compounds to unactivated alkenes.[29] For example, the oxidative addition of dimedone to phenyl cyclohexene afforded the dihydrofuran derivative in 98% yield (Scheme 11).



43 44 45

Scheme 11

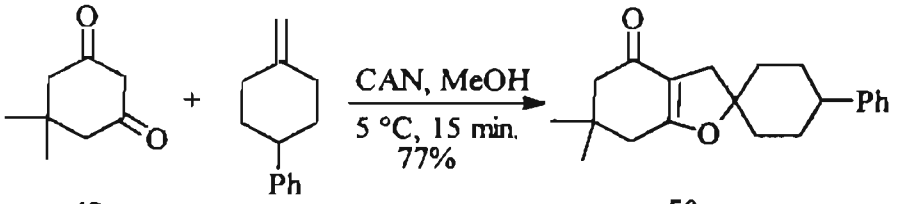
As expected, the oxidative addition of dimethyl malonate to most alkenes provided corresponding lactones. For example, the reaction of dimethyl malonate with cinnamyl methyl ether in aqueous methanol furnished the lactone in 58% yield[30] (Scheme 12).



46 47 48

Scheme 12

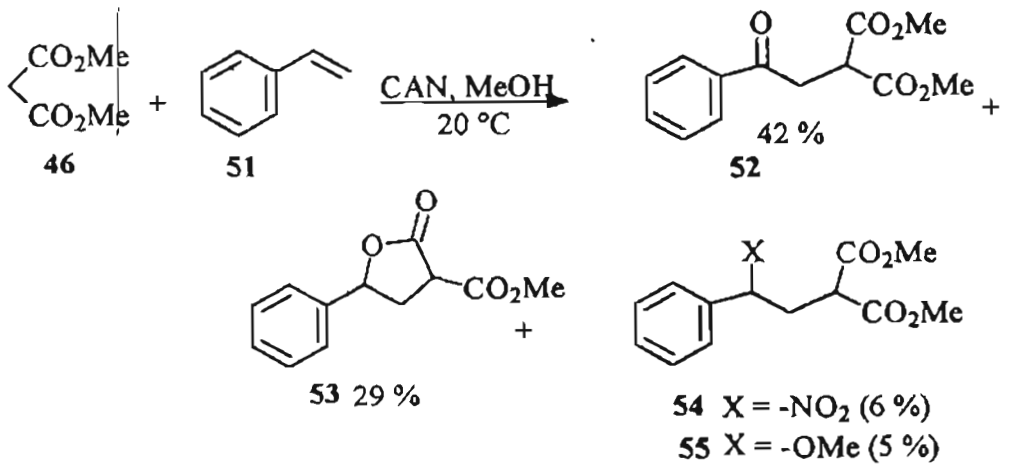
Oxidative addition of 1,3-dicarbonyl compounds to exo methylene compounds resulted in the formation of spiro dihydrofuran derivatives (Scheme 13).[31]



43 49 50

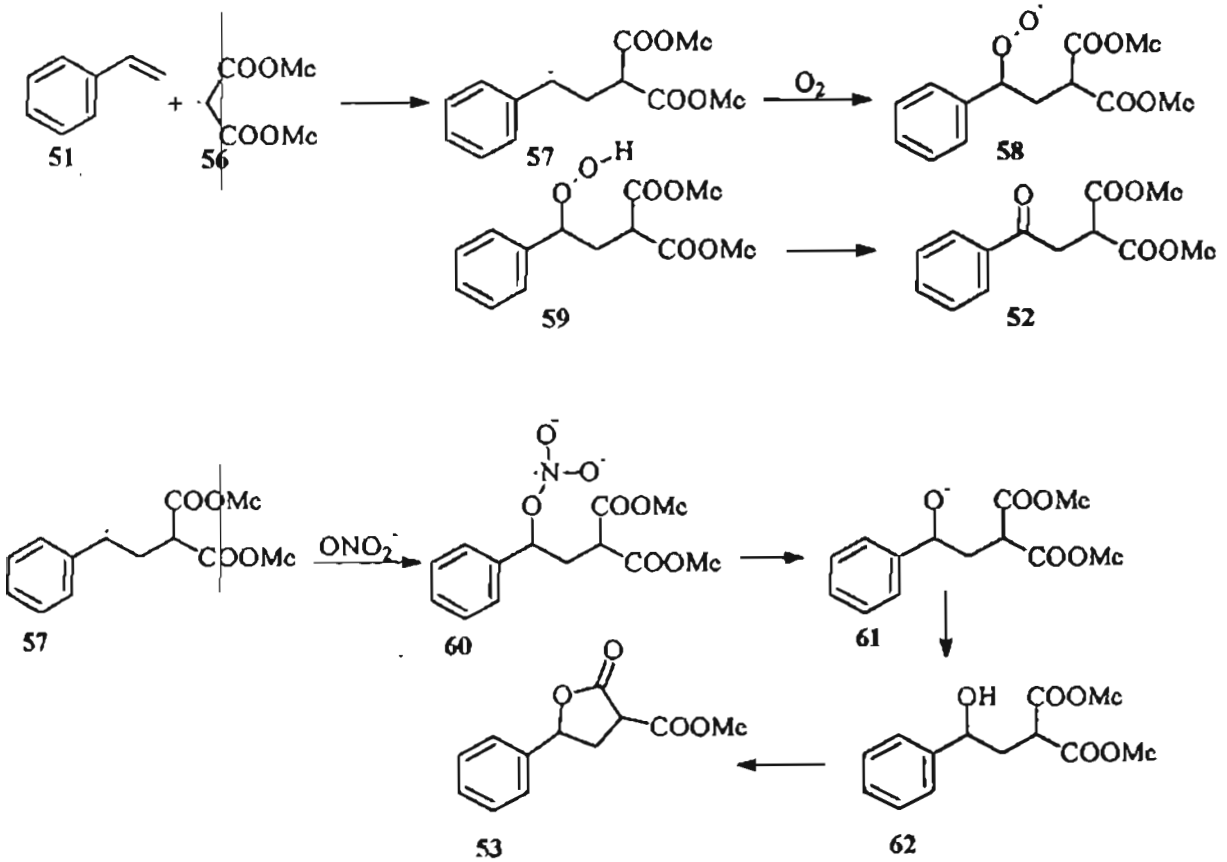
Scheme 13

An unexpected and mechanistically fascinating reaction was encountered between dimethylmalonate and styrene in presence of CAN [32](Scheme 14).

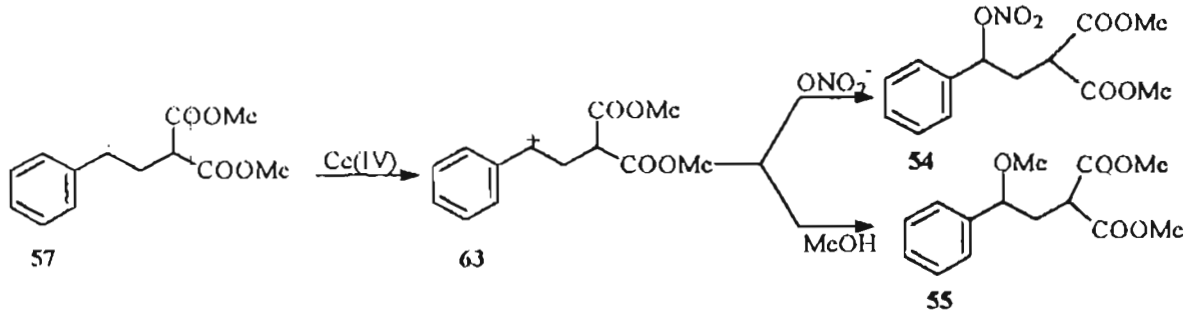


Scheme 14

A plausible mechanistic interpretation of the reaction sequence is given in Scheme 15a and 15b.[33]

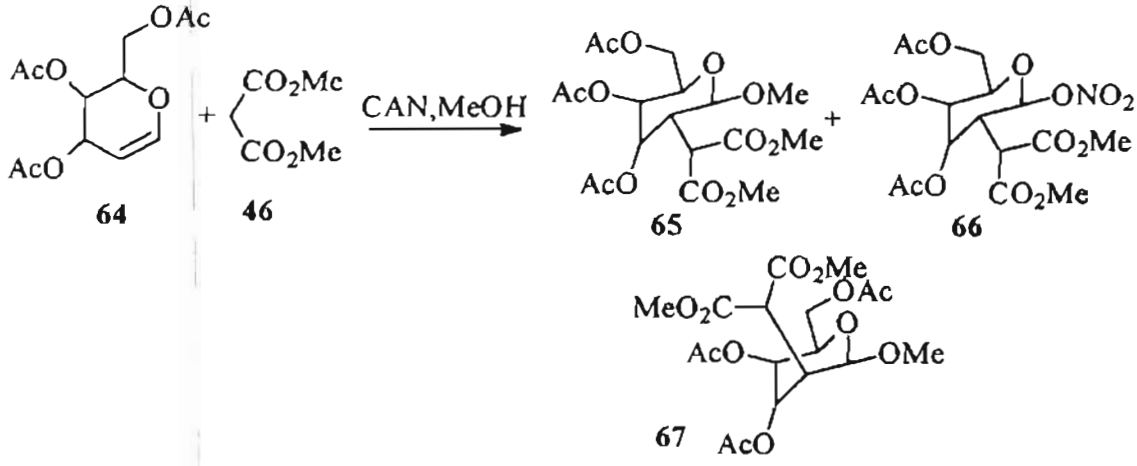


Scheme 15a



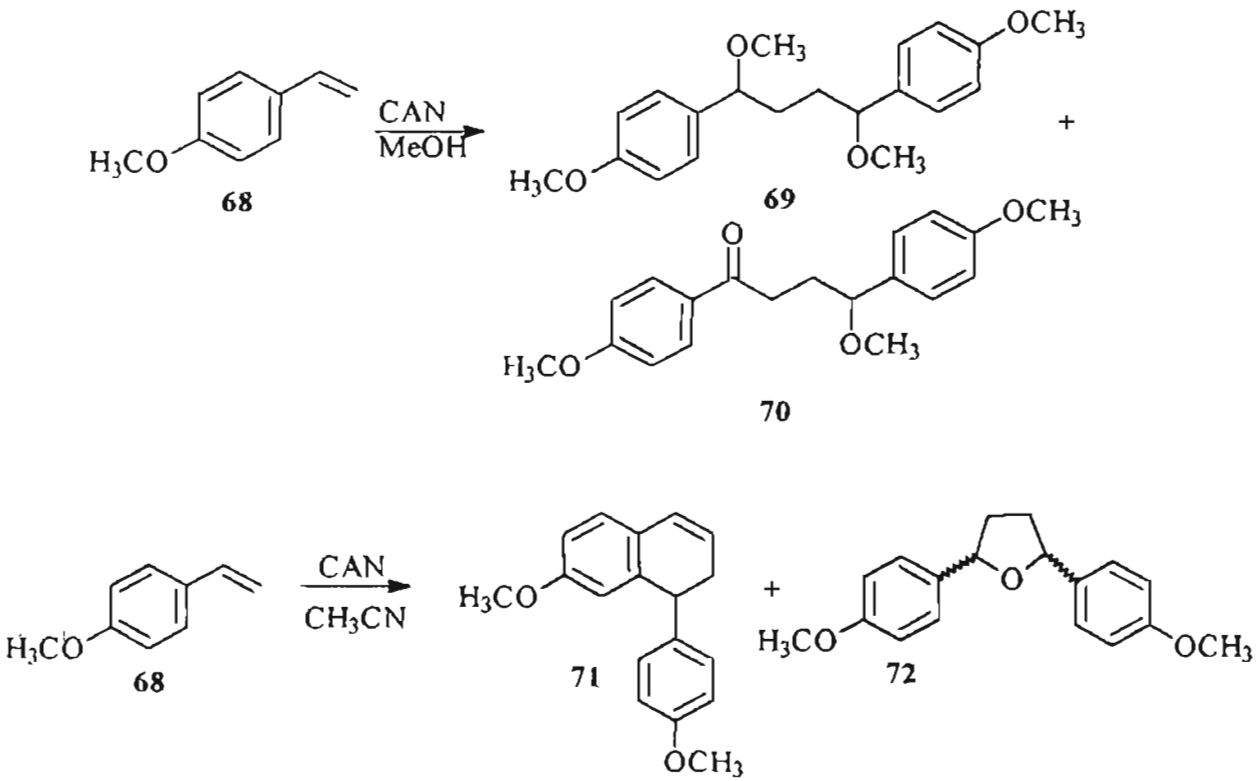
Scheme 15b

Subsequent to our work, the CAN mediated addition of malonates to glycals has been developed as an easy route to the C_2-branched sugars (Scheme 16). It is noteworthy that these authors also found that CAN is superior to $Mn(OAc)_3$ in these reactions.[34]



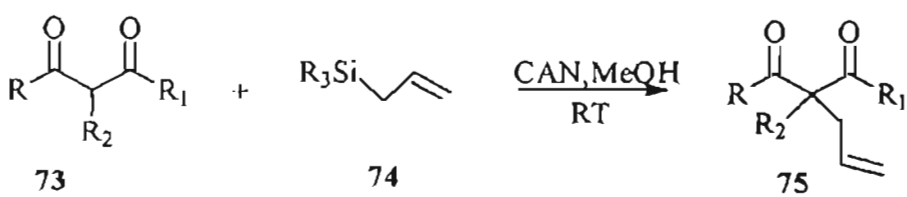
Scheme 16

CAN mediated single electron transfer reactions (SET) of methoxy styrenes were reported by us to afford dimerization products involving a cation radical mechanism[35] (Scheme 17).



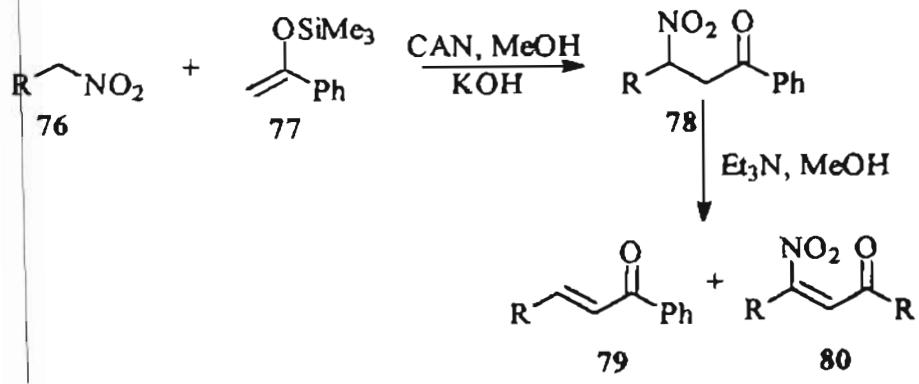
Scheme 17

Recently a silicon-controlled allylation of 1,3-dicarbonyl compounds with allylsilane and CAN was reported. An example is given in Scheme 18.[36]



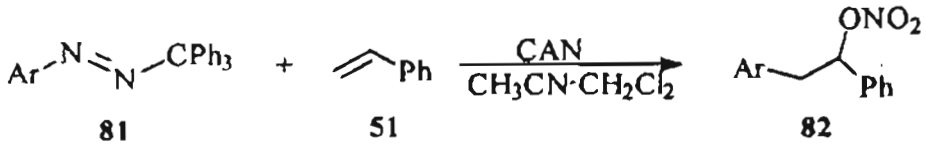
Scheme 18

CAN mediated addition of nitromethylene compounds to silyl enol ethers gave β-nitro ketones[37] (Scheme 19). Compound **80** is the dimerization product of nitro alkene.



Scheme 19

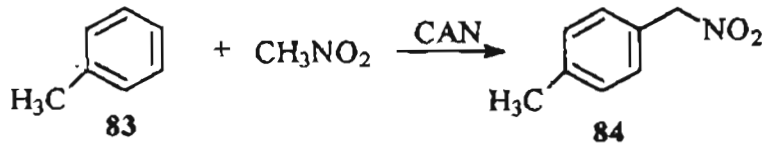
Generation of aryl radicals by the oxidation of α-(aryl azo) triphenyl methanes by CAN and their subsequent addition to styrene afforded the nitrato compound [38] (Scheme 20).



Scheme 20

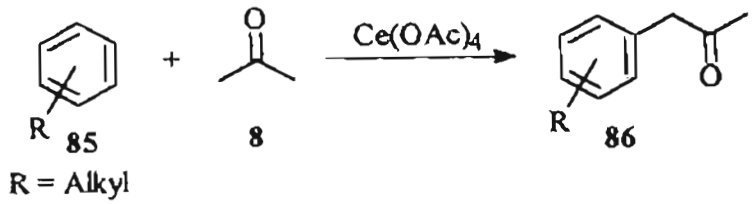
1.2.2. Oxidative addition to Arenes.

Arenes were found to react with the electrophilic nitromethylene radical leading to the formation of nitromethylated aromatic compounds. An example is given in the following Scheme.[39]



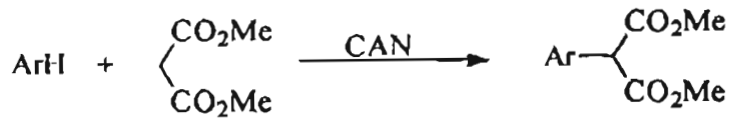
Scheme 21

Similar type of reactivity was observed with acetone and aromatic compounds affording the acetonylated product as illustrated in Scheme 22.[40]



Scheme 22

Oxidative addition of dimethyl malonate to arenes is another example which falls into this category [41] (Scheme 23).

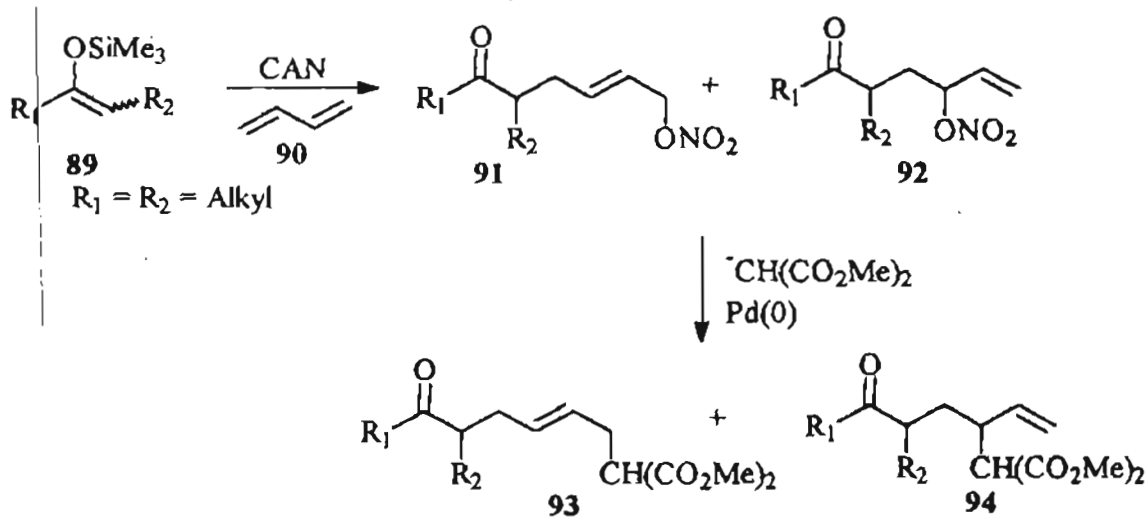


Scheme 23

1.2.3. Oxidative addition to Dienes

A survey of the literature revealed only an isolated report[42] on the CAN mediated oxidative addition of 1,3-dicarbonyl compounds to dienes. Therefore we have carried out a detailed study of this reaction and have found that dihydrofuran derivatives are obtained in moderate to good yields[43]. This will be discussed in some detail in chapter 2.

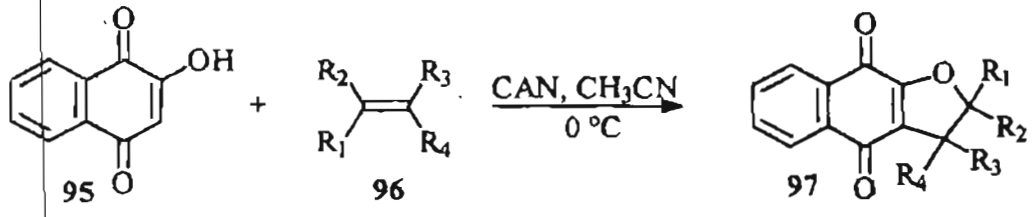
A recent report shows that CAN mediated addition of trimethylsilyl enol ethers to 1,3-butadiene afforded a mixture of nitrates, which underwent Pd (0) catalyzed alkylation of malonate [44] (Scheme 24).



Scheme 24

1.2.4. Cycloaddition Reactions

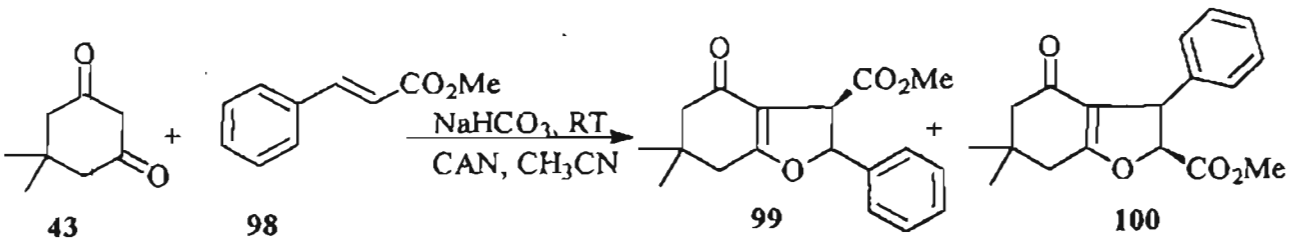
CAN mediated [3+2] type cycloaddition of 2-hydroxy-1,4- naphtho quinones and 2-hydroxy-1,4-benzoquinones with alkenes resulted in the formation of furoquinones along with the corresponding o-quinone derivatives[45] (Scheme 25).



R1, R2, R3, R4 = Alkyl, H, -OEt, -CO2Me

Scheme 25

As a follow up of our work, [29] regio and stereoselective synthesis of dihydrofurans by CAN mediated [3+2] cycloaddition of 1,3-diketones to cinnamic esters has been reported [46] (Scheme 26).



43 98 99 100

Scheme 26

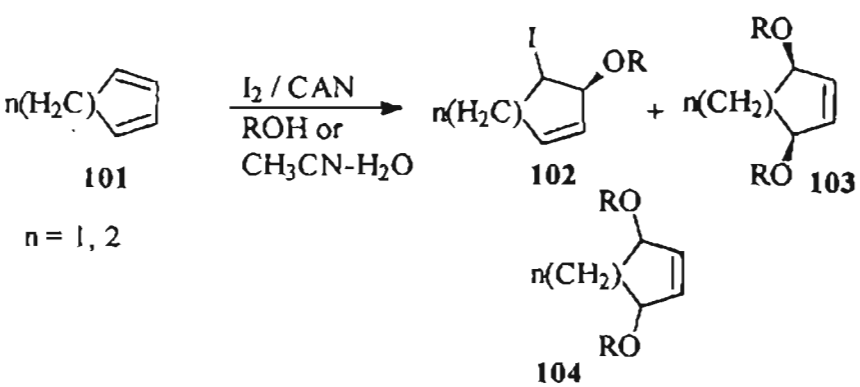
1.2.5. Intramolecular Reactions

In comparison to $Mn(OAc)_3$, Cerium(IV) reagents have received only limited attention in intramolecular cyclization reactions. The first report in this category involved the cyclization of 1-benzyl-2,6-disubstituted-4-piperidone-3-carboxylic acid methyl ester with $Ce(SO_4)_2$ in low yield. [47]

The oxidative cyclization of silyl enol ethers of aryl ketones to tricyclic ketones,[48] CAN promoted oxidative cyclization of dimethyl-4-pentenyl malonate in presence of Cu salts affording a mixture of products[49] and the free radical cyclization reactions of α-methoxy carbonyl acetyl enamides and aceto acetyl enamides to the corresponding β-lactams[50] were known. All these will be discussed in some detail in chapter 4.

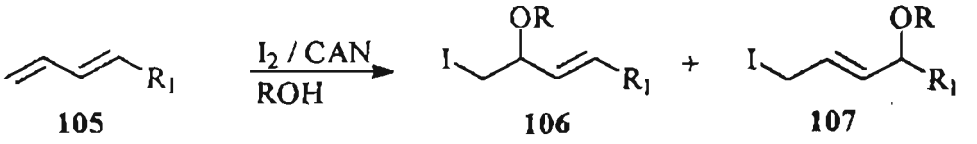
1.2.6. Alkoxy Iodination Reactions

CAN mediated alkoxy iodination of cycloalkadienes and acyclic dienes with iodine in alcohol has been reported (Scheme 27a and 27b).[51,52]



101 (n = 1, 2) 102 103 104

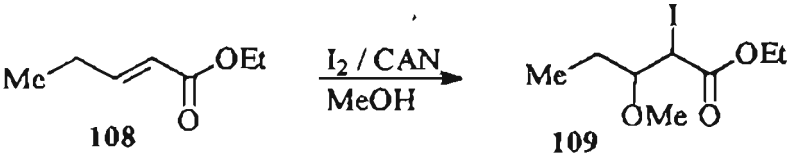
Scheme 27a



105 106 107

Scheme 27b

Alkoxy iodination of simple olefins[53] and nitrato iodination of α, β-unsaturated ketones and esters using Ce (IV) / I_2 were reported earlier by the same authors.[54] An example is given in Scheme 28.

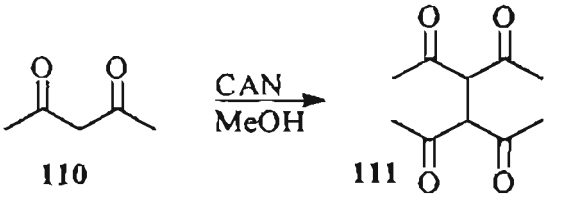


108 109

Scheme 28

1.2.7. Miscellaneous Reactions

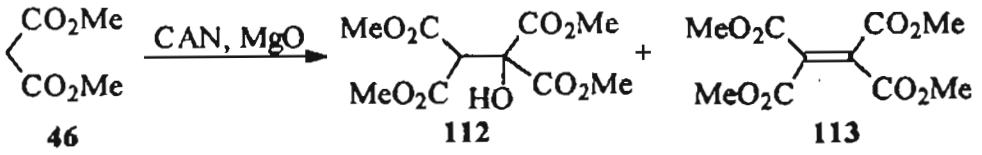
1,3-dicarbonyl compounds have been reported to undergo dimerization in presence of CAN as illustrated in Scheme 29.[55]



110 111

Scheme 29

Oxidative homocoupling of dimethyl malonate in presence of MgO and CAN afforded the hydroxylated dimer and 1, 1, 2, 2-tetra carbomethoxy ethylene (Scheme 30).[56]



46 112 113

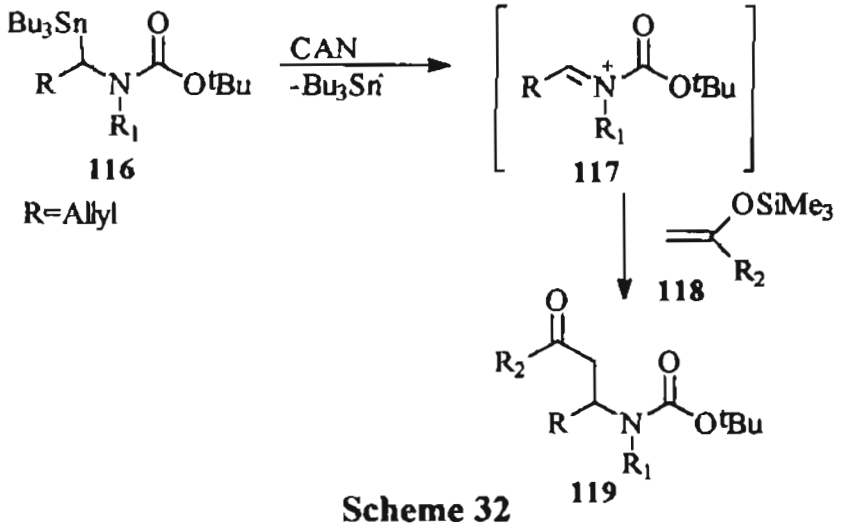
Scheme 30

CAN promoted alkoxylation of cephem sulfoxides and sulfones is also known[57] (Scheme 31).

114 115

Scheme 31

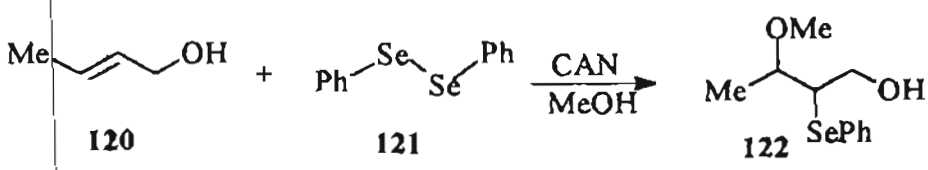
Tertiary butyl stannyl allyl carboxamides and carbamates get oxidized by CAN to the corresponding acylium ions, which can be trapped with carbon nucleophiles. This is an efficient method for the synthesis of substituted carboxamides and carbamates[58] (Scheme 32).



116 R=Allyl 117 118 119

Scheme 32

CAN mediated reaction of diphenyl diselenide with alkenes in methanol has been reported[59] (Scheme 33).



120 121 122

Scheme 33

There are a few reports on CAN mediated oxidation of soft anions like azide to the corresponding radicals and the addition of the latter to alkenes.[60,61] This will be discussed in detail in chapter 3.

In addition to the reactions described above, CAN has been used effectively in a large number of oxidation reactions.[62] It is found to be a very good reagent for the deprotection of TBDMS, THP, triflate and Boc. groups.[63]

1.3. CONCLUSION

The foregoing discussion clearly shows the potential of CAN in effecting a variety of important synthetic transformations. The experimental simplicity, non-toxic nature, solubility in a number of common organic solvents and easy processing of the reaction mixture are added advantages of this reagent. In the light of the literature survey and with a view to extend the usefulness of CAN in organic synthesis, it was of interest to conduct a series of extensive investigations using this reagent.

1.4. STATEMENT OF THE PROBLEM

Against the backdrop of the literature survey and on the basis of previous studies in our laboratory indicating that CAN is a useful reagent for mediating carbon-carbon bond formation, it was decided to explore the oxidative addition of 1,3-dicarbonyl compounds to dienes with a view to establish a facile route to dihydrofurans.

Another facet of CAN mediated reactions that appeared under-explored and fascinating was the potential application of CAN in carbon-heteroatom bond formation. Therefore a detailed study of thiocyanation and azidation of aryl alkenes mediated by CAN was undertaken.

In view of the success of CAN mediated intermolecular reactions, for the third phase of investigations, it was planned to explore intramolecular carbon-carbon bond formation mediated by CAN; these studies unexpectedly led to an efficient synthesis of tartronic acid derivatives.

As a terminal investigation, it was of interest to explore the reactions of CAN with styrenes and aldehydes with a view to synthesise methoxy acetophenones and esters respectively.

All the above avenues of exploration resulted in very interesting results and the details are presented in chapters II-V.

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CHAPTER II

CERIUM (IV) AMMONIUM NITRATE MEDIATED OXIDATIVE ADDITION REACTIONS OF 1,3-DICARBONYL COMPOUNDS TO DIENES: A FACILE SYNTHESIS OF DIHYDROFURAN DERIVATIVES

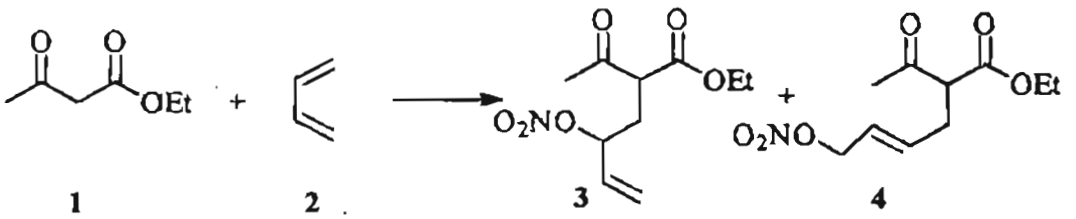
2.1. INTRODUCTION

The generation of carbon centered radicals as well as their addition to a variety of substrates mediated by one electron oxidants has attracted the attention of many research groups.[1] Among the metal salts such as $Mn(OAc)_3$, $Co(OAc)_2$, $FeCl_3$ and $CuCl_2$ used for the generation of radicals, $Mn(OAc)_3$ has received the most attention.[2-4] The pioneering work of Heiba and Dessau[5] and subsequent investigations by others[6-11] have demonstrated the usefulness of Ce(IV) reagents for the generation of electrophilic radicals. Cerium (IV) ammonium nitrate (CAN) mediated reactions like malonylation of aromatic and heteroaromatic compounds,[12,13] coupling of enamines[14] and allyl phenyl sulfides with enolsilyl ethers,[15] and cross coupling[16] of silyl enol ethers have been reported. Investigations in our laboratory[17-20] have demonstrated that Ce(IV) ammonium nitrate is superior to the more

commonly used Mn(III) acetate in the oxidative addition reactions of 1,3-dicarbonyl compounds to unactivated alkenes.

There are reports on the formation of dihydrofurans[21-27] by Mn(III) acetate, Co(II) acetate, Cu(II) chloride, Hg(II) acetate, Tl(III) acetate and Pb(IV) acetate mediated reactions of enolizable ketones and alkenes. Similarly CAN mediated addition of acetyl acetone and ethyl acetoacetate to ring substituted styrenes[28] have also been reported to give dihydrofurans.

Recent work in our laboratory has shown that 1,3-dicarbonyl compounds such as dimedone, acetyl acetone and ethyl acetoacetate undergo facile CAN mediated oxidative addition to alkenes leading to a high yield synthesis of dihydrofurans.[17,18] As a logical extension of this work, it was of interest to investigate the CAN mediated reaction of 1,3-dicarbonyl compounds to cyclic and acyclic dienes. A literature survey revealed that there were only two isolated reports[29, 30] in this area and these were concerned with the addition of ethyl acetoacetate to 1,3-butadiene (Scheme 1).

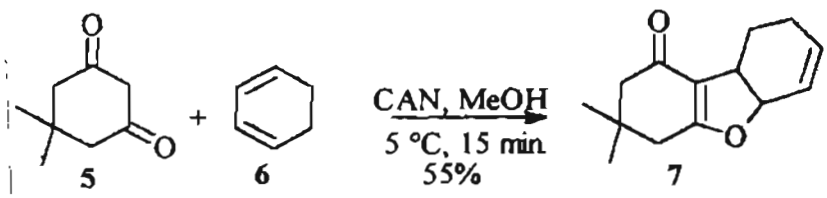


1 2 3 4

Scheme 1

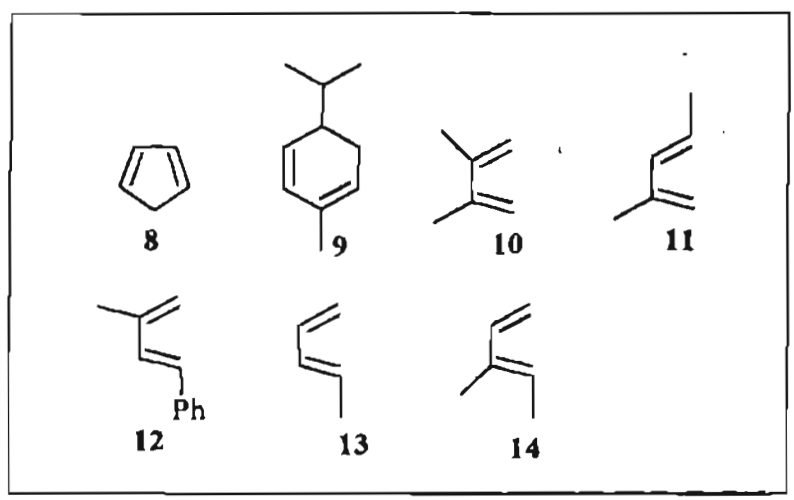
Subsequently, a report on the reaction of trimethylsilyl enol ethers to 1, 3-butadiene leading to a mixture of nitrates, which on alkylation with sodium dialkyl malonate resulting in the formation of the corresponding dialkyl malonate appeared [31] (Scheme 24, Chapter I).

Our own preliminary investigations have shown that dimedone and acetyl acetone react with cyclohexadiene and cyclooctadiene to give dihydrofuran derivatives in moderate to good yields[32] (Scheme 2).

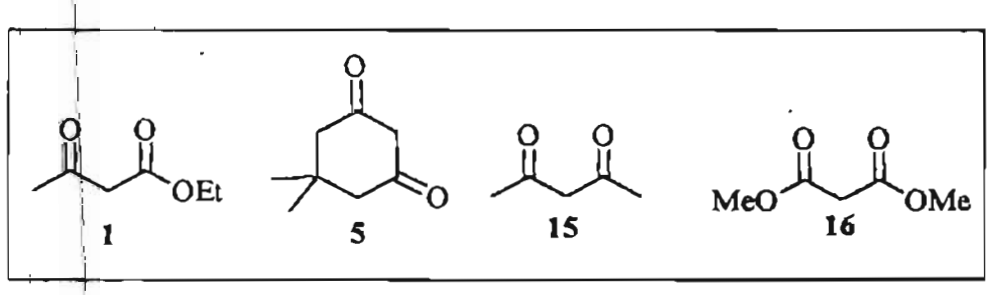


Scheme 2

These studies have been further extended with the dienes **8-14** (Scheme 3) and dicarbonyl compounds **1, 5, 15** and **16** (Scheme 4).



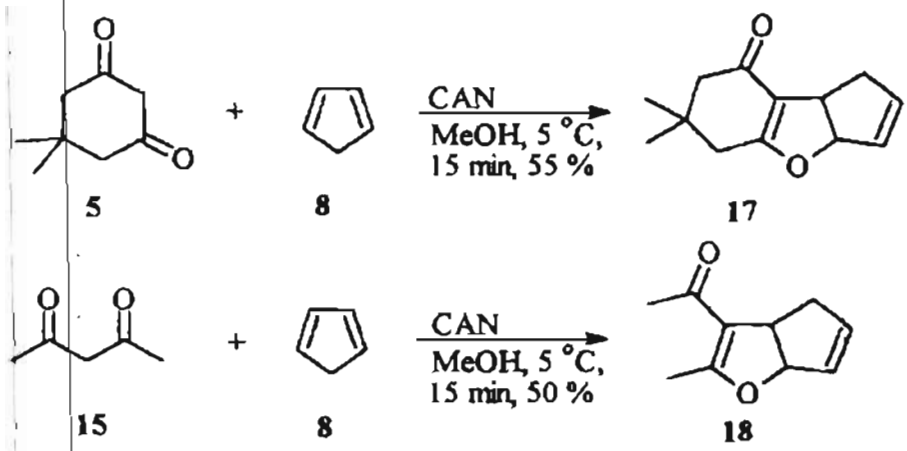
Scheme 3



Scheme 4

2.2. RESULTS AND DISCUSSION

Against the background presented in the introduction, we have undertaken a systematic investigation of the reactions of various 1,3-dicarbonyl compounds **1, 5, 15** and **16** with cyclic and acyclic dienes **8-14** (Scheme 4) and the results are described here. Our studies were initiated with the reaction of dimedone and cyclopentadiene which afforded a colorless viscous oil **17** in 55 % yield. Similarly, acetyl acetone on reaction with cyclopentadiene afforded the dihydrofuran **18** in 50 % yield (Scheme 5).



5 + 8 → 17

15 + 8 → 18

Scheme 5

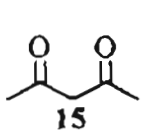
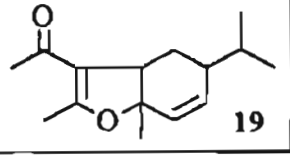
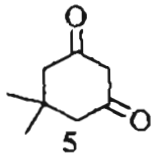
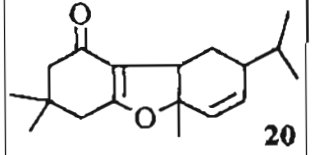
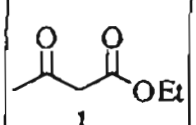
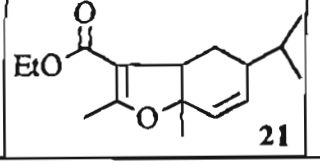
The IR spectrum of the compound **17** showed a strong absorption at 1622 cm^{-1}, which is characteristic of the vinylogous ester carbonyl group. In the ^1H NMR spectrum, the olefinic protons and the ring junction proton adjacent to oxygen of **17** resonated together as a multiplet at δ 5.95. ^{13}C NMR spectrum showed the carbonyl absorption at δ 194.34.

The compound **18** also displayed similar signals. The IR spectrum of **18** showed the strong absorption due to the carbonyl at 1696 cm^{-1}. ^1H NMR spectrum of **18** displayed a multiplet at δ 5.65 due to the two olefinic protons

and the proton adjacent to the dihydrofuran oxygen. ^{13}C NMR spectrum showed the carbonyl signal at δ 193.14

Similar reactivity profile was observed for acetyl acetone, dimedone and ethylacetoacetate with the naturally occuring diene phellandrene **9** affording the dihydrofuran derivatives (**19-21**) as the major products. The results are summarized in Table 1.

Table 1: Oxidative addition of dicarbonyl compounds to α (-) phellandrene.

Entry	Dicarbonyl Compound	Product	Yield(%)
1	 **15**	 **19**	50
2	 **5**	 **20**	65
3	 **1**	 **21**	45

Reaction conditions: CAN, MeOH, 0 °C, 15-45 min.

The IR spectra of the compounds **19**, **20** and **21** showed carbonyl absorptions at 1701, 1650 and 1728 cm^{-1} respectively.

The olefinic protons of **19** resonated at δ 5.97 and at δ 5.61 as doublets (J = 10.20 Hz, 10.02 Hz) in the ^1H NMR spectrum. In the ^{13}C NMR spectrum, the carbonyl carbon signal appeared at δ 194.89.

In the ^1H NMR spectrum, olefinic protons of **20** exhibited two signals at δ 5.92 and δ 5.59 as doublets (J = 10.14 Hz, 10.18 Hz) while those of **21**

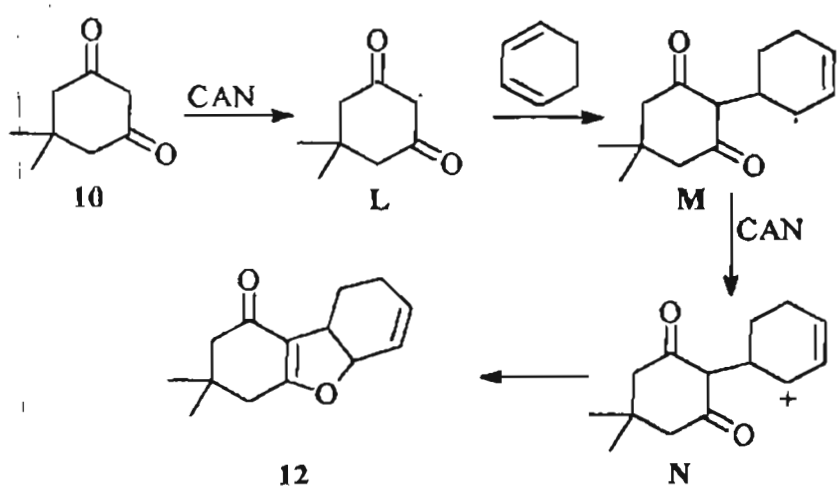
resonated at δ 5.96 and δ 5.58 as doublets (J = 10.11 Hz and 10.14 Hz). The ^{13}C NMR spectra of **20** and **21** displayed signals at δ 194.82 and 167 due to the keto carbonyl and the ester carbonyl respectively.

The assigned regiochemistry was also clear from the ^{1}H NMR spectrum. It may be noted that the regioisomer resulting from the reaction with di-substituted double bond would display only one olefinic proton. ^{13}C NMR spectrum also showed the presence of quaternary carbon adjacent to the dihydrofuran oxygen.

The configuration of these adducts was determined by 2D NMR spectral studies. Compound **20** was taken as a representative example and the ring fusion was assigned as trans based on 2D COSY, NOESY, COLOC and MMX-energy (PC Window-Serena Software- 1993) calculation studies. In the 2D HOMOCOSY spectrum of **20**, the ring junction proton (δ 3.20) showed cross peaks with ring junction methyl group (δ 1.50) and the methylene protons at C-5 (δ 2.25) carbon. The NOESY spectrum of **20** did not show any cross peak between ring junction proton and ring junction methyl group. Hence it is assumed that these two are trans to each other. The isopropyl group at C-4 carbon showed cross peaks with ring junction methyl group in NOESY spectrum and hence they are cis to each other. We have taken the phellandrene with R configuration and hence it implies that C-4 center has R configuration. Based on these facts S configuration was assigned for the C-1 center. The minimized energy of this compound is found to be 30.7 kJ.

In all the cases studied, two equivalents of CAN were required for the completion of the reaction. If less than two equivalents are used, a proportional amount of diene remained unreacted. Though the mechanistic

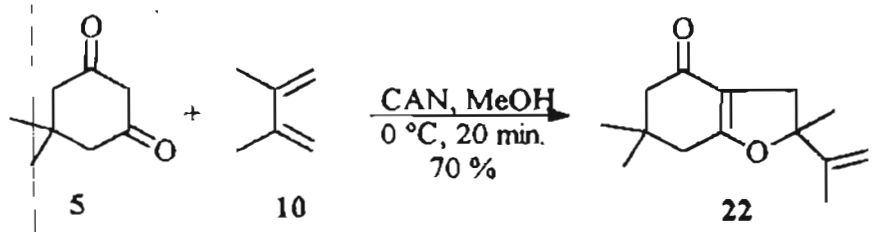
details of the reaction remain unclear, a rationalization along the following lines can be given (Scheme 6). The first step involves the CAN mediated generation of the radical **L** from dimedone, which is immediately trapped by the diene giving the intermediate radical **M** . In the second step, the radical **M** is oxidized to the cation **N** by the second equivalent of CAN. The latter then undergoes cyclization to afford the dihydrofuran derivative.



Scheme 6

It is clear from the NMR spectra that only one double bond is taking part in the reaction and there is no internal shifting of the other one.

Subsequent to the above investigations, the reaction of 1,3 dicarbonyl compounds with acyclic dienes was studied. Oxidative addition of dimedone to 2,3-dimethyl butadiene occurred rapidly to afford the dihydrofuran **22** in 70 % yield (Scheme 7).

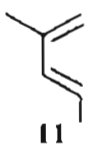
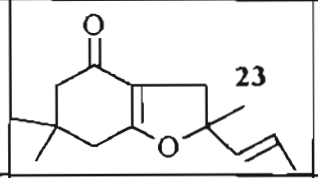
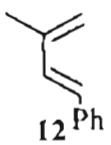
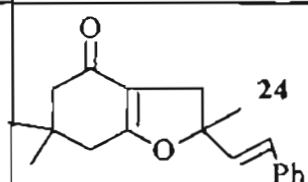
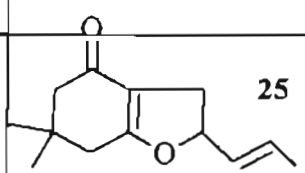


Scheme 7

The α, β -unsaturated carbonyl absorption in the IR spectrum of **22** was observed at 1647 cm^{-1}. In the ^1H NMR spectrum, the signals due to the two olefinic protons appeared at δ 4.98 and δ 4.48 as singlets. The methyl group adjacent to the dihydrofuran oxygen appeared at δ 1.77. Two geminal methyls resonated at δ 1.12 and 1.09. In the ^{13}C NMR spectrum, the signal due to the carbonyl carbon appeared at δ 194.93. The saturated carbon adjacent to the oxygen in the dihydrofuran ring was visible at δ 93.68.

Similar reactivity of dimedone was observed with other dienes and the results are summarized in Table 2.

Table 2: Oxidative addition of dimedone to dienes.

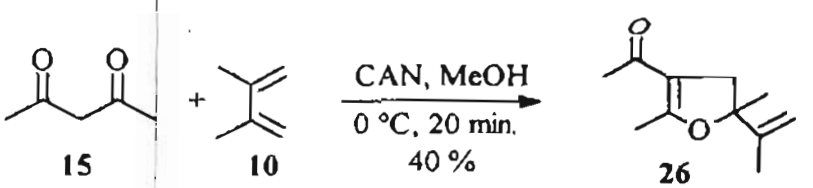
Entry	Diene	Product	Yield (%)
1.	 **11**	 **23**	55
2.	 **12** Ph	 **24** Ph	40
3.	 **13**	 **25**	72

Reaction conditions: CAN, MeOH, 0 °C, 15-45 min.

In the IR spectra of **23**, **24** and **25**, the α, β unsaturated carbonyl absorptions were at 1647, 1640 and 1634 cm^{-1} respectively. In the proton NMR spectrum, the olefinic protons of **23** resonated as a multiplet at δ 5.67 while those of **25** were observed at δ 5.59. The olefinic protons of **24** were

visible as two doublets at δ 6.55 (J = 16.11 Hz) and δ 6.27 (J = 16.11 Hz). *^{13}C NMR spectra of compounds **23, 24** and **25** displayed the carbonyl signal at δ 194.98, 194.94 and 194.36 respectively.*

Oxidative addition of acetyl acetone to acyclic dienes also afforded the dihydrofuran derivatves in moderate to good yields. For example, the reaction between acetyl acetone and 2,3-dimethyl butadiene afforded the dihydrofuran **26** in 40 % yield (Scheme 8).



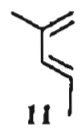
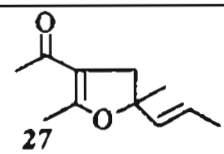
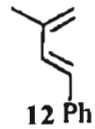
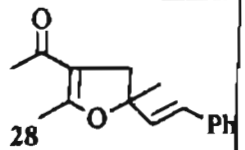
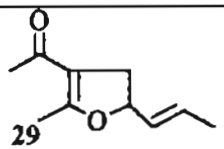
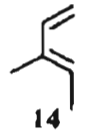
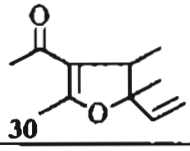
15 **10** **26**

Scheme 8

In the IR spectrum of **26,** the α, β-unsaturated carbonyl absorption was visible at 1667 cm^{-1}. In the ^{1}H NMR spectrum, two olefinic protons of **26** resonated at δ 4.97 and δ 4.82 as singlets. The ^{13}C NMR spectrum displayed the carbonyl carbon at δ 194.48. This structure was further supported by high resolution mass spectral data.

Similar results were obtained with other acyclic dienes and acetyl acetone and the results are summarized in Table 3.

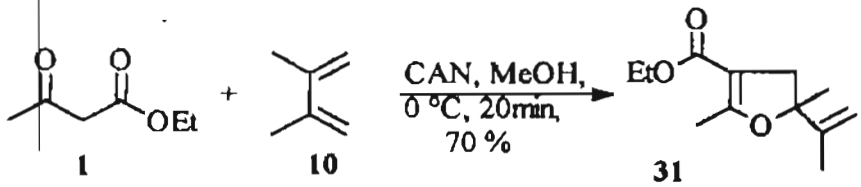
Table 3: Oxidative addition of acetyl acetone to dienes.

Entry	Diene	Product	Yield(%)
1	 11	 27	88
2	 12 Ph	 28	45
3	 13	 29	46
4	 14	 30	50

Reaction conditions: CAN, MeOH, 0 °C, 15-45 min.

The IR spectra of **27, 28, 29** and **30** showed the carbonyl absorptions at 1674, 1667, 1670 and 1668 cm^{-1} respectively. In the ^1H NMR spectrum, the two olefinic protons of **28** resonated at δ 6.55 (J = 16.07 Hz) and δ 6.29 (J = 16.06 Hz) as doublets. The carbonyl carbons of **27, 28, 29** and **30** were visible at δ 194.93, 194.54, 194.53 and 194.54 respectively in ^{13}C NMR spectrum.

As expected, ethyl acetoacetate was found to react with acyclic dienes in an analogous manner leading to dihydrofurans. An illustrative example is given in Scheme 9.



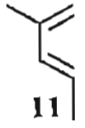
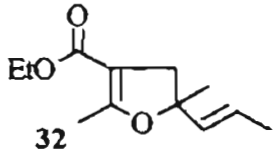
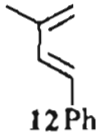
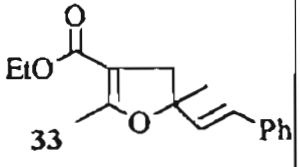
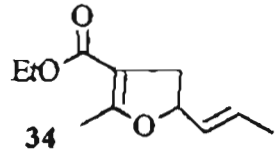
1 10 31

Scheme 9

The IR spectrum of **31** showed sharp peaks at 1708 cm^{-1} due to the carbonyl group. In the ^1H NMR spectrum, olefinic protons appeared at δ 4.95 and 4.79 as singlets. The ester carbonyl resonated at δ 166.78 in the ^{13}C NMR spectrum.

Similar reactions leading to dihydrofuran derivatives were observed with other dienes and the results are given in Table 4.

Table 4: Oxidative addition of ethyl aceto acetate with dienes.

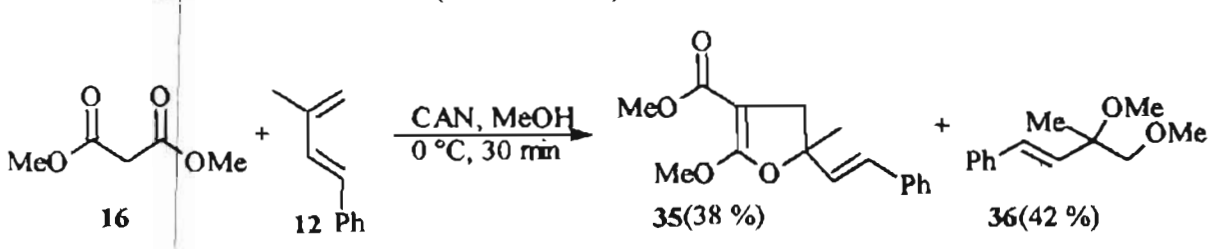
Entry	Diene	Product	Yield(%)
1	 **11**	 **32**	40
2	 **12Ph**	 **33**	40
3	 **13**	 **34**	30

Reaction conditions: CAN, MeOH, 0 °C, 15-45 min.

The IR spectra of **32, 33** and **34** showed the carbonyl absorptions at 1701, 1742 and 1698 cm^{-1} respectively. The olefinic protons of **32** resonated at δ 5.57 and 5.31 as multiplets. The olefinic protons of **33** appeared as sharp doublets at δ 6.55 (J = 16 Hz) and at δ 6.30 (J = 16 Hz). The ^{13}C NMR spectra of compounds **32, 33** and **34** showed ester carbonyls at δ 167.39, 166.72 and 167.54 respectively.

In preliminary experiments, dimethyl malonate was found to give similar results with dienes. For example the reaction between dimethyl

malonate and 3-methyl-1-phenyl butadiene afforded the dihydrofuran derivative **35** and 3,4-dimethoxy-3-methyl-1- phenyl but-1-ene **36** which is derived from the diene itself (Scheme 10).



Scheme 10

The IR spectrum of **35** showed the carbonyl absorption at 1733 cm^{-1}. The olefinic protons displayed two doublets at δ 6.50 (J=16.35 Hz) and at δ 6.04 (J=16.32 Hz). The ester carbonyl was visible at δ 170.32 in the ^{13}C NMR spectrum.

The ^{1}H NMR spectrum of **36** showed the olefinic protons at δ 6.57 and δ 6.20 as doublets with a J value of 16.34 Hz which is characteristic of trans coupling. Methoxy group at the terminal carbon resonated as a broad singlet at δ 3.40 along with the protons on the carbon bearing it. The other methoxy group gave a sharp singlet at δ 3.26. ^{13}C NMR spectrum is also in agreement with the assigned structure.

Experiments involving malonate and other dienes will be pursued in detail by other members of our group.

From the above discussion it is clear that CAN mediated oxidative addition of 1,3-dicarbonyl compounds to dienes offers an efficient and direct route to the synthesis of dihydrofuran derivatives in moderate to good yields.

2.3. EXPERIMENTAL DETAILS

All experiments were initiated at ice temperature under atmospheric conditions unless otherwise specified. Melting points were recorded on a Buchi-530 melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet Impact 400 P infrared spectrometer. Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded on the δ scale with TMS as internal reference using Bruker-300 MHz spectrophotometer. The abbreviations s, d, dd, t, m, q and brs refer to singlet, doublet, doublet of doublet or double doublet, triplet, multiplet, quartet and broad singlet respectively. Mass spectra were recorded on Fisons MD 800 and Hewlett Packard 5890 mass spectrometers. The relative intensities of the m/z values (in percentage) are given in parenthesis. Elemental analyses were performed on a Hewlett Packard 185-B CHN analyser.

Purification by gravity column chromatography was done using 100-200 mesh silica gel and appropriate mixture of petroleum ether and ethyl acetate for elution. Commercial grade solvents were used for column chromatography and were distilled before use. Petroleum ether refers to the fraction boiling between 60-80° C. Analytical thin layer chromatography was performed on glass plates coated with silica gel GF254 containing 13% calcium sulfate as binder. All reactions were monitored by TLC employing appropriate solvent systems for development and the developed plates were visualized by exposure to iodine vapor or UV light.

CAN, dimedone, 2-methyl pentadiene, 2,3-dimethyl butadiene and 1,3-pentadiene (piperylene) were purchased from Aldrich. Acetyl acetone and ethyl acetoacetate were purchased from local sources. α(-) Phellandrene was procured from E-Merck. 2-Methyl-4-phenyl butadiene was prepared by

the Wittig olefination of benzylidene acetone, the latter being prepared from acetone and benzaldehyde via Claisen- Schmidt reaction.

Synthesis of Dihydrofuran Derivatives : General Procedure.

A solution of CAN (1.26g, 2.3 mmol) in methanol (10 mL) was added dropwise to an ice cooled, stirred mixture of the dicarbonyl compound (1 mmol) and alkene (1.2 mmol) in methanol (5 mL). In most of the cases the reddish brown color of CAN disappeared by the time the addition was over (20-30 min.). In some isolated cases it took 30-45 min. for the completion of the reaction. The mixture after decolorisation was diluted with water (150 mL) and extracted with dichloromethane (5 x 10 mL). The combined organic extracts were washed with water, then with brine, dried over anhydrous sodium sulphate and the solvent was evaporated off. The residue obtained was subjected to chromatography on silica gel column. Elution with 10% ethylacetate in petroleum ether (unless otherwise specified) afforded the dihydrofuran derivatives.

Dihydrofuran 17

A solution of dimedone **5** (0.504 g, 3.6 mmol) and cyclopentadiene **8** (0.198 g, 3 mmol) in methanol (20 mL) was treated with CAN (3.78 g, 6.9 mmol.) in methanol (50 mL) for 20 min. with constant stirring. The reaction mixture after work up and processing following the general experimental procedure afforded **17** as a colorless viscous oil in 83 % yield (0.513 g).

IR (CH_2Cl_2, ν_{max}) : 2958, 1622, 1400 cm^{-1}.

^{1}H NMR ($CDCl_3$, 90 MHz) : δ 5.95 (m, 3H), 3.75 (m, 1H), 2.70 (m, 2H), 2.30 (s, 2H), 2.25 (s, 2H), 1.10 (s, 6H).

^{13}C NMR ($CDCl_3$, 22.4 MHz.) : δ 194.34, 174.59, 137.33, 127.69, 115.48, 95.49, 51.01, 40.30, 38.24, 37.76, 33.83, 28.61, 28.40.

GC-MS : *m/z* 204 (M^+, 100), 189 (9), 148 (40), 120 (95), 106 (25).

Dihydrofuran 18

A mixture of acetyl acetone **15** (0.36 g, 3.6 mmol) and cyclopentadiene **8** (0.198 g, 3 mmol) was reacted with CAN (3.78 g, 6.9 mmol) in methanol for 20 min. and worked up as usual. The crude reaction mixture on purification afforded **18** (0.258 g, 51 %) as a viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2962, 1696, 1669, 1602 cm^{-1}.

^{1}H NMR (90 MHz, $CDCl_3$) : δ 5.65 (m, 3H) , 3.75 (m,3H), 2.1 (s, 6H).

^{13}C NMR ($CDCl_3$, 22.4 MHz.) : δ 193.14, 166.05, 136.01, 127.87, 116.53, 91.05, 43.61, 39.85, 28.39, 14.43.

GC-MS : *m/z* 164 (M^+, 100), 149 (48), 121 (42), 107 (52).

Dihydrofuran 19

A mixture of acetyl acetone **15** (0.100 g, 1 mmol) and phellandrene **9** (0.163 g, 1.2 mmol) dissolved in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) as described in the general procedure. The reaction mixture after work up and purification following the

general experimental procedure afforded **19** (0.118 g, 50 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2962, 2867, 1701, 1647, 1450, 1384, 1256 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.97 (d, 1H, olefinic, J= 10.2 Hz), 5.61 (d, 1H, olefinic, J=10.02 Hz), 3.11 (m, 1H, CH_2), 2.28 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 1.78 (m, 2H, -CH), 1.53 (m, 2H, CH_2), 1.39 (s, 3H, CH_3), 0.91 (brs, 6H, isopropyl).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.89, 167.76, 135.98, 129.11, 117.40, 85.37, 46.12, 39.19, 31.90, 29.83, 28.28, 27.11, 20.89, 20.75, 16.43.

Dihydrofuran 20

A mixture of dimedone **5** (0.140 g, 1 mmol) and α (-) phellandrene **9** (0.163 g, 1.2 mmol) dissolved in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). The reaction mixture after work up and purification as described in the general procedure afforded the dihydrofuran **20** (0.179 g, 65 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2980, 2942, 1650, 1450 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz.) : δ 5.92 (d, 1H, olefinic, J= 10.14 Hz), 5.59 (d, 1H, olefinic, J=10.18 Hz), 3.20 (brs, 1H, CH), 2.25 (m, 6H, CH_2), 1.81 (brs, 1H,

CH), 1.61 (m, 1H, CH), 1.50 (s, 3H, CH_3), 1.08 (s, 6H, CH_3), 0.89 (brs, 6H, isopropyl).

^{13}C NMR ($CDCl_3$, 75 MHz.) : δ 194.82, 175.69, 135.83, 128.725, 113.65, *86.72, 51.25, 43.37, 38.22, 37.72, 31.25, 28.55, 26.05, 19.73, 19.51.*

Dihydrofuran 21

Oxidative addition of ethyl acetoacetate **1** (0.130g, 1mmol) to α (-) phellandrene **9** (0.163g, 1.2 mmol) in methanol in presence of CAN (1.26g, 2.3 mmol) in methanol and the work up and purification of the reaction mixture according to the general experimental procedure afforded **21** (0.119 g, 45 %) as a pale yellow oil.

IR (CH_2Cl_2, ν_{max}) : *2962, 2921, 1728, 1654, 1458, 1398 cm^{-1}.*

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 5.96 (d, 1H, olefinic, J= 10.11 Hz), 5.58 *(d, 1H, olefinic, J=10.14 Hz), 4.19 (m, 2H, CH_2),* 3.12 (brs, 1H, -CH-), 2.15 (s, 3H, *CH_3), 1.76 (m, 4H, CH_2), 1.56 (s, 3H, CH_3),* 1.29 (m, 3H, CH_3), 0.91 (brs, 6H, isopropyl).

^{13}C NMR ($CDCl_3$, 75 MHz.) : δ 167.85, 166.07, 135.17, 128.95, 105.08, 85.00, 59.01, 46.76, 38.29, 31.42, 27.15, 26.55, 20.12, 14.75.

GC-MS : *m/z* 264 (M^+, 30), 219 (13), 175 (40), 147 (28), 134 (82), 119 (100), 84 (70), 49 (75).

2,6,6- trimethyl -2-isopropyl-2,3,4,5,6,7-hexahydro-1- benzofuran-4-one. 22

A mixture of dimedone **5** (0.140 g, 1 mmol) and 2,3-dimethyl butadiene **10** (0.098 g, 1.2 mmol) dissolved in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). The reaction mixture after work up and purification as described in the general procedure afforded **22** (0.155 g, 70 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2955, 2867, 1647, 1404, 1243 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 4.98 (s, 1H, olefinic), 4.84 (s, 1H, olefinic), 2.84 (d, 1H, J= 14.46 Hz) 2.63 (d, 1H, J= 14.34 Hz), 2.30 (s, 2H, CH_2), 2.33 (s, 2H, CH_2), 1.77 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.09 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.93, 175.15, 146.61, 111.07, 110.15, 93.68, 50.87, 37.97, 37.37, 34.13, 28.84, 28.50, 26.20, 18.38.

2,6,6-trimethyl-2- propenyl-2,3,4,5,6, 7-hexahydro-1- benzofuran 4-one 23

A mixture of dimedone **5** (0.140 g, 1 mmol) and 2-methyl pentadiene **10** (0.098 g, 1.2 mmol) dissolved in methanol (5 mL) was treated with CAN (1.26g, 2.3 mmol) in methanol (10 mL). The reaction mixture on processing and purification as described in the general procedure afforded **23** (0.121 g, 55 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2962, 2874, 1647, 1404, 1249 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.67 (m, 2H, olefinic), 2.80 (d, 1H, J= 14.27 Hz), 2.65 (d, 1H, J= 14.30 Hz), 2.27 (s, 2H, CH_2), 2.22 (s, 2H, -CH_2), 1.72 (d, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.10 (s, 6H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.98, 175.01, 133.88, 124.91, 11.02, 91.54, 50.90, 38.02, 34.10, 28.70, 26.59, 17.67.

2,6,6-trimethyl-2- cinnamyl-2,3,4,5,6,7-hexahydro-1- benzofuran-4-one 24

The oxidative addition of dimedone **5** (0.140 g, 1 mmol) to 2-methyl-4-phenyl-1,3-butadiene **12** (0.173 g, 1.2 mmol) dissolved in methanol (5 mL) in presence of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was carried out following the general procedure. The reaction mixture after work up and purification afforded **24** (0.144 g, 40 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2969, 2874, 1640, 1404, 1236 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.26 (m, 5H, ArH), 6.55 (d, 1H, olefinic, J= 16.11 Hz), 6.27 (d, 1H, olefinic, J= 16.11 Hz), 2.89 (d, 1H, J= 15 Hz), 2.71 (d, 1H, J= 15 Hz), 2.28 (s, 2H, CH_2), 2.20 (s, 2H, CH_2), 1.57 (s, 3H, CH_3), 1.01 (s, 3H, CH_3) 1.06 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.94, 175.04, 136.07, 131.92, 128.58, 128.38, 127.94, 126.58, 110.96, 91.48, 50.80, 38.22, 37.93, 34.07, 28.64, 28.62, 26.87.

Exact mass calcd. for $C_{11}H_{16}O_2$ 282.16155, Found 282.16188.

6,6-dimethyl-2-propenyl-2,3,4,5,6,7-hexahydro-1- benzofuran- 4-one 25

The reaction of dimedone **5** (0.140 g, 1 mmol) and 1,3-pentadiene **13** (0.0816 g, 1 mmol) in methanol with CAN (1.26 g, 2.3 mmol) in methanol as per the general procedure followed by work up and purification afforded **25** (150 g, 72 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2962, 2874, 1634, 1398, 1222 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 5.59 (m, 2H, olefinic), 5.18 (q, 1 H, OCH), 2.97 (d, 1H, J= 15 Hz), 2.56 (m, 1H, CH2), 2.28 (s, 2H, CH_2), 2.22 (s, 1H, CH_2), 1.74 (d, 3H, CH_3 ,J= 6.39 Hz), 1.01 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : 194.36, 175.89, 129.94, 129.34, 111.21, 86.19, 50.91, 37.54, 33.73, 31.47, 28.30, 17.35.

3-Acetyl-2, 5-dimethyl-5- isopropenyl-4, 5-dihydrofuran 26

Acetyl acetone **15** (0.100g, 1 mmol.) and 2,3-dimethyl butadiene **10** (0.098 g, 1.2 mmol) in methanol (5mL) was treated with CAN (1.26 g, 2.3 mmol.) in methanol (10mL). The reaction mixture on processing following

the general experimental procedure afforded **26** (0.072 g, 40 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2975, 2928, 1667, 1600, 1378, 1249 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 4.97 (s, 1H, olefinic), 4.82 (s, 1H, olefinic), 2.968 (d, 1H, CH_2, J = 14.10 Hz), 2.74 (d, 1H, CH_2, J = 14.15 Hz), 2.24 (s, 3H, CH_3), 2.19 (s, 3H, CH_3),. 1.77 (s, 3H, CH_3), 1.46 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.48, 166.45, 147.15, 111.65, 109.73, 89.36, 41.99, 29.32, 26.19, 18.99, 15.18.

Exact mass calcd. for $C_{11}H_{16}O_2$ 180.11572, Found 180.11580.

3-Acetyl-2,5-dimethyl-5- propenyl-4,5-dihydrofuran 27

Acetyl acetone **15** (0.100 g, 1 mmol.) and 2-methyl pentadiene **11** (0.098 g, 1.2 mmol.) were dissolved in methanol (5 mL) and treated with CAN (1.26 g, 2.3 mmol.) in methanol (10 mL) at ice temperature following the general procedure. Reaction mixture on purification afforded **27** (0.160 g, 88 %) as a yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2982, 2928, 1674, 1607, 1384, 1236 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 5.65 (m, 2H, olefinic), 2.89 (d, 1H, CH_2, J = 15 Hz), 2.73 (d, 1H, CH_2, J = 15 Hz), 2.21 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 1.71 (d, 3H, CH_3), 1.43 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.93, 166.71, 134.39, 124.63, 111.73, 87.30, 42.90, 29.60, 26.70, 17.91, 15.53.

3 - Acetyl-5-cinnamyl-2,5-dimethyl-4,5-dihydrofuran 28

Acetyl acetone **15** (0.100 g, 1 mmol) and 2-methyl-4-phenyl butadiene **12** (0.173 g, 1.2 mmol) were dissolved in methanol (5 mL) and treated with CAN (1.26 g, 2.3 mmol.) in methanol (10 mL) at ice temperature following the general experimental procedure. Reaction mixture on processing afforded **28** (0.110 g, 45 %) as a yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2975, 2928, 1667, 1620, 1452, 1398, 1249 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz) : δ 7.30 (m, 5H, aromatic), 6.55 (d, 1H, olefinic, J= 16.07 Hz), 6.29 (d, 1H, olefinic, J= 16.06 Hz), 3.03 (d, 1H, CH_2, J = 14.08 Hz), 2.86 (d, 1H, CH_2, J= 14.13 Hz), 2.26 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) , 1.56 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) :δ 194.54, 166.39, 136.10, 132.53, 128.61, 128.07, 127.87, 126.58, 111.59, 87.11, 42.98, 29.34, 26.83, 15.25.

Exact mass calcd. for $C_{16}H_{18}O_2$ 242.13068, Found 242.13105

3-Acetyl-2 - methyl-5-propenyl-4,5-dihydrofuran 29

Acetyl acetone **15** (0.100 g, 1 mmol) and 1,3-pentadiene **13** (0.0816 g, 1.2 mmol) were dissolved in methanol (5 mL) and treated with CAN

(1.26 g, 2.3 mmol) in methanol (10 mL) in an ice bath following the general procedure. Reaction mixture on processing and purification afforded **29** (0.077 g, 46 %) as a yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2980, 2925, 1670, 1380, 1240 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 5.76 (m, 2H, olefinic), 4.99 (q, 1H, OCH), 3.15 (m, 1H, CH_2), 2.69 (m, 1H, CH), 2.21 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 1.74 (d, 3H, CH_3, J = 6.01 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.53, 167.59, 130.64, 129.66, 112.06, 83.10, 46.54, 29.88, 17.66, 15.05.

3-Acetyl-2, 5, 6-trimethyl-5-ethenyl-4, 5-dihydrofuran 30

Acetyl acetone **15** (0.100 g, 1 mmol.) and 3-methyl pentadiene **14** (0.098 g, 1.2 mmol) in methanol (5 mL) when treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) at ice temperature following the general procedure afforded **30** (0.084 g, 50 %) as a yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2920, 2875, 1668, 1420 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 5.52 (m, 2H, olefinic), 4.95 (d, 1H, olefinic), 2.72 (m, 1H, $CHCH_3$), 2.21 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 1.61 (m, 6H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 194.54, 168.00, 123.51, 114.43, 87.55, 34.984, 29.64, 17.10, 15.16, 13.31.

2,5-dimethyl-5-isopropenyl-4,5-dihydrofuran-3-carboxylic acid ethyl ester 31

Oxidative addition of ethyl acetoacetate **1** (0.130 g, 1 mmol) to 2,3-dimethyl butadiene **10** (0.098 g, 1.2 mmol) in methanol (5 mL) in presence of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was carried out following the general procedure. The reaction mixture after work up and purification afforded the dihydrofuran **31** as a pale yellow viscous liquid (0.149 g, 70 %).

IR (CH_2Cl_2, ν_{max}) : 2975, 2935, 1708, 1640, 1452, 1384, 1256 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 4.95 (s, 1H, olefinic), 4.79 (s, 1H, olefinic), 4.15 (q, 2H, CH_2CH_3), 2.88 (d, 1H, CH_2, J = 14.5 Hz), 2.55 (d, 1H, CH_2, J = 14.5 Hz), 2.20 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.27 (t, 3H, CH_2 CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 166.78, 166.48, 147.44, 109.73, 101.22, 89.32, 59.59, 41.39, 26.32, 18.67, 14.69, 14.47.

2,5-dimethyl-5-propenyl-4,5-dihydrofuran-3-carboxylicacid ethylester 32

Oxidative addition of ethyl acetoacetate **1** (0.130 g, 1 mmol) to 2-methyl-1,3-pentadiene **11** (0.098 g, 1.3 mmol) in methanol (5 mL) in presence of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was carried out according to the general experimental procedure. The reaction mixture on

processing and purification afforded the dihydrofuran **32** (0. 080 g, 40 %) as a colorless liquid.

IR (CH_2Cl_2, ν_{max}) : *2985, 2921, 2867, 1701, 1647, 1389,* 1236 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 5.57 (m, 1H,), 5.31 (m, 1H, olefinic), 4.17 (q, 2H, CH_2CH_3), 3.22 (d, 1H, CH_2, J=15.6 Hz), 3.07 (d, 1H, CH_2, J=15.2 Hz), 2.18 (s, 3H, CH_3), 1.70 (d, 3H, CH_3), 1.28 (t, 3H, CH_3), 1.20 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 167.39, 166.11, 134.19, 124.21, 101.5, 86.56, 59.05, 41.67, 36.09, 26.18, 17.32, 14.16.

2,5-dimethyl-5-cinnamyl-4,5-dihydrofuran-3-carboxylicacid ethyl ester 33

Oxidative addition of ethyl acetoacetate **1** (0.130 g, 1 mmol) to 2-methyl-4-phenyl butadiene **12** (0.172 g, 1.2 mmol) in methanol (5 mL) in presence of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was carried out according to the general procedure to afford **33** (0. 110 g, 40 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2982, 2928, 1742, 1647, 1458, 1378, 1209 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 7.31 (m, 5H, ArH), 6.55 (d, 1H, olefinic, J= 16 Hz), 6.30 (d, 1H, olefinic, J= 16 Hz), 4.16 (q, 2H, CH_2CH_3), 2.97 (d, 1H, CH_2,

J_1, J_2 = 15 Hz), 2.25 (s, 3H, CH_3). 1.56 (s, 3H, CH_3), 1.28 (t, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 166.72, 166.47, 136.55, 132.90, 128.771, 127.99, 126.74, 101.36, 87.13, 59.66, 42.41, 27.02, 14.70, 14.58.

2-methyl-5-propenyl-4,5-dihydrofuran-3-carboxylicacid ethyl ester 34

A mixture of ethyl acetoacetate **1** (0.130 g, 1 mmol) and 1,3-pentadiene **13** (0.082 g, 1.2 mmol) in methanol (15 mL) when treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) following the general procedure afforded **34** (0.060 g, 30 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2989, 2928, 2854, 1698, 1647, 1384, 1229 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz) : δ 5.68 (m, 1H, olefinic), 5.57 (m, 1H, olefinic), 4.97 (q, 1H, OCH), 4.16 (q, 2H, CH_2CH_3), 3.02 (m, 1H, CH_2), 2.63 (m, 1H, CH_2), 2.18 (s, 3H, CH_3), 1.73 (d, 3H, CH_3), 1.27 (t, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 167.54, 166.204, 130.17, 129.90, 101.79, 82.97, 59.13, 35.8, 17.639, 14.48, 14.12.

2-methoxy-5-cinnamyl-5-methyl-4,5-dihydrofuran-3-carboxylicacid methyl ester 35

A mixture of dimethyl malonate **16** (0.136 g, 1 mmol) and 2-methyl-4-phenyl butadiene **12** (0.172 g, 1.2 mmol) was dissolved in methanol (5 mL). A solution of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added

dropwise with constant stirring in an ice bath for 30 minutes. The reaction mixture on processing as described in the general procedure afforded **35** (0.117 g, 38 %) as a pale yellow viscous liquid and **36** (0.089 g, 42 %) as a colorless highly viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 2951, 1733, 1634, 1443, 1227 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.31 (m, 5H, ArH), 6.50 (d, 1H, olefinic, J= 16.35 Hz), 6.04 (d, 1H, olefinic, J= 16.32 Hz), 3.75 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 3.19 (s, 3 H, OCH_3), 2.35 (m, 2H, CH_2).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 170.32, 166.30, 136.60, 132.83, 130.08, 128.59, 127.68, 126.46, 111.23, 76.19, 52.59, 50.35, 38.96, 22.52.

3,4-dimethoxy-3-methyl-1-phenyl but- 1- ene 36

IR (CH_2Cl_2, ν_{max}) : 2929, 2877, 2812, 1455, 1121 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.32 (m, 5H, ArH), 6.57 (d, 1H, olefinic, J= 16.34 Hz), 6.20 (d, 1H, olefinic, J=16.34 Hz), 3.40 (brs, 5H, CH_2OCH_3), 3.26 (s, 3H, OCH_3), 1.37 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 136.74, 131.41, 131.05, 128.58, 127.69, 126.50, 79.20, 59.57, 50.58, 19.45.

GC-MS : *m/z* 206 (M^+, 7), 174 (8), 161 (75), 129 (40), 84 (70), 49 (100), 47 (20).

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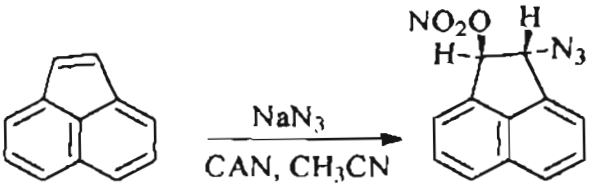
CHAPTER III

CERIUM (IV) AMMONIUM NITRATE MEDIATED CARBON-HETEROATOM BOND FORMING REACTIONS

3.1. INTRODUCTION

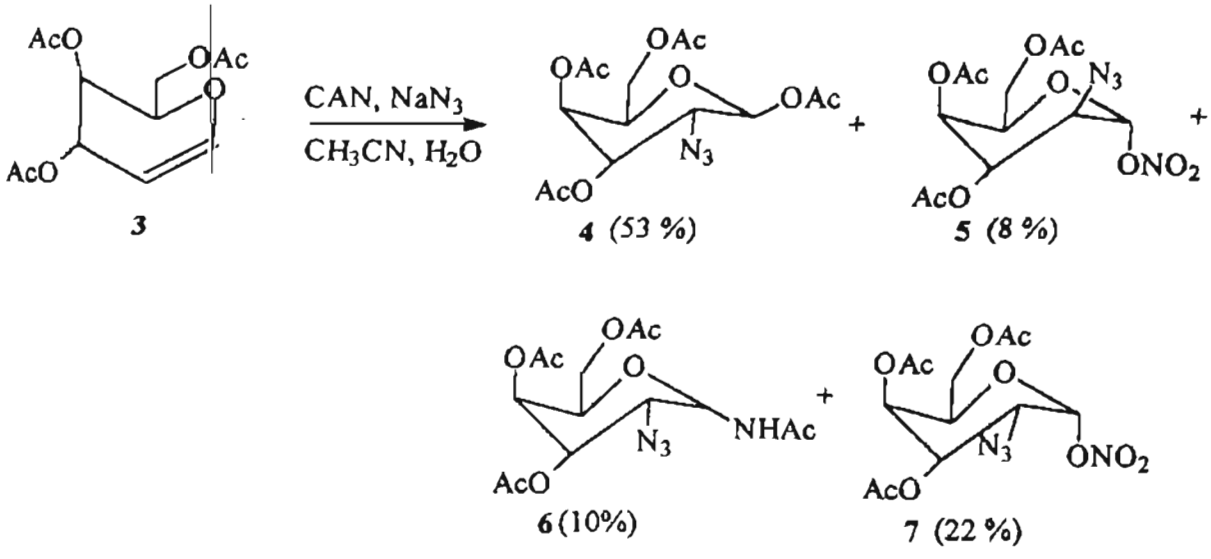
Cerium (IV) ammonium nitrate (CAN) has found widespread use in carbon-carbon bond forming reactions.[1-2] However, the use of this reagent in carbon-heteroatom bond formation has received only limited attention. CAN mediated addition of azide to alkenes resulting in 1-azido-2-nitrates by Trahanovsky is the first report in this area.[3] An example is given in Scheme 1.



1 2

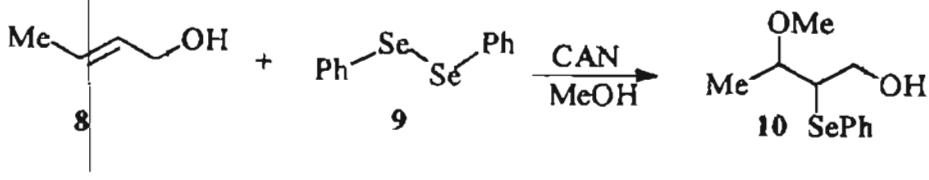
Scheme 1

Subsequently, Lemieux has applied this reaction to glycals.[4] It is noteworthy that the resulting azides are important intermediates for the synthesis of 2-amino sugars (Scheme 2).



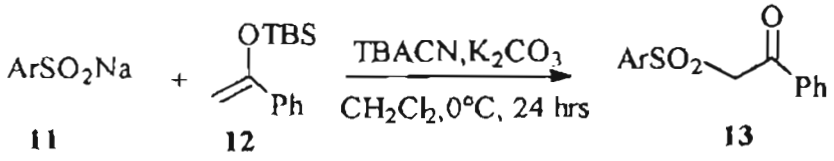
Scheme 2

Selenomethoxylation of alkenes by the CAN mediated reaction of diphenyl diselenide in methanol has been reported[5] (Scheme 3).



Scheme 3

Sulfonylation of electron rich olefins was reported with Tetrabutyl ammonium cerium (IV) nitrate (TBACN) in presence of K_2CO_3[6] (Scheme 4).



11 12 13

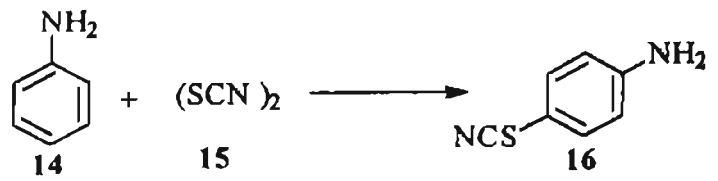
Scheme 4

Considering the synthetic potential of such reactions and the limited amount of work in this area, we have undertaken some investigations primarily aimed at carbon-sulfur and carbon-nitrogen bond formation. This is described in the following sections.

3.2. CARBON-SULFUR BOND FORMING REACTIONS MEDIATED BY CAN

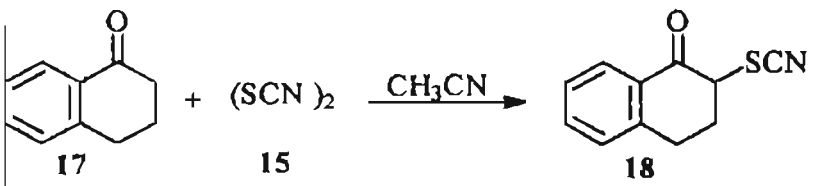
The thiocyanato group is an important functional group since it can be transformed into a number of other functionalities.[7,8] Its presence in a number of biologically active natural products[9,10] is also noteworthy. Aryl and heteroaryl thiocyanates and α-carbonyl thiocyanates[11,12] serve as intermediates in the synthesis of heterocycles.

In view of the useful transformation of the thiocyanate group into various sulfur functionalities and sulfur containing heterocycles, the thiocyanation of organic compounds is of substantial importance in organic synthesis. Thiocyanation of aromatic compounds involving thiocyanogen $(SCN)_2$ was known from 1940 onwards (Scheme 5).[11]



Scheme 5

Compounds with active methylene groups react with thiocyanogen under heterolytic conditions[9] to form the corresponding thiocyanato derivatives [13](Scheme 6).

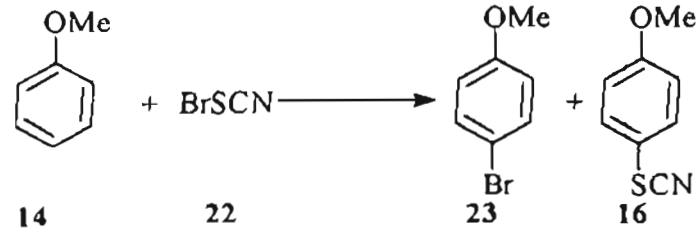


Scheme 6

The unstable thiocyanogen, $(SCN)_2$ is generated *in situ* from copper or lead thiocyanate[14,15] or by reacting an alkali metal thiocyanate with bromine[16] (Scheme 7).

Scheme 7

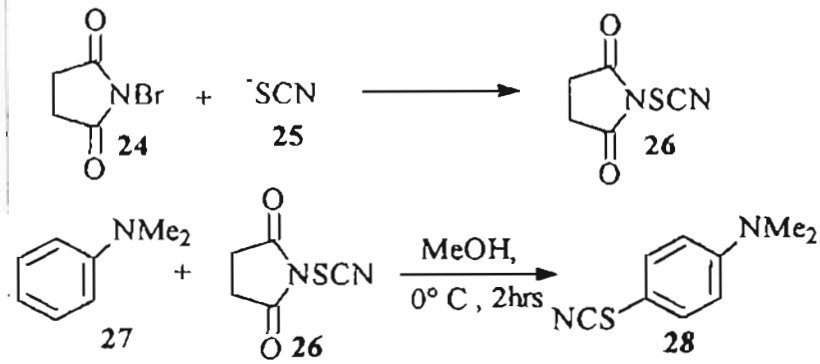
Thiocyanogen, however, is not active enough for direct thiocyanation of phenol ethers and usually needs to be activated by Lewis acids. Procedures involving the somewhat more reactive thiocyanogen chloride, bromide or iodide has also been reported [17,18](Scheme 8).



Scheme 8

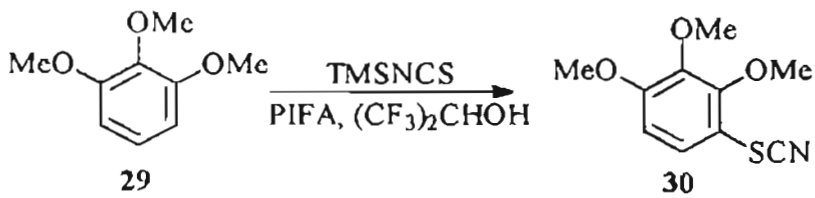
Of the many methods of electrophilic thiocyanation known, several procedures are of limited scope. Another major drawback of these older procedures is the use of reagents which are either highly toxic or having serious disposal problems.

Aryl thiocyanation can be achieved using N-thiocyanato succinimide (NTS); this is prepared *in situ* from NBS and NaSCN [19] (Scheme 9).



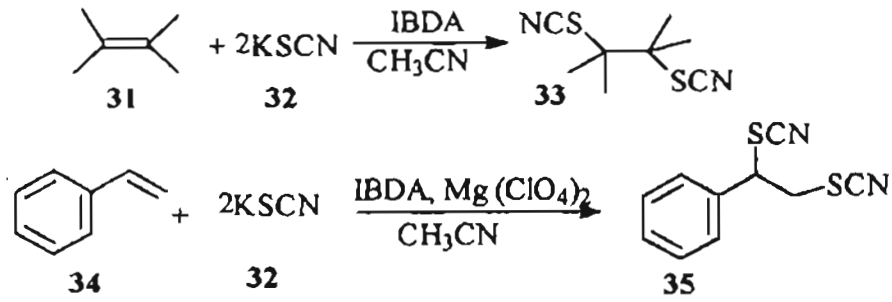
Scheme 9

Trimethylsilyl isothiocyanate (TMSNCS) and phenyl iodine (III) bis (trifluoro acetate) [PIFA] react with phenol ethers and related compounds yielding the thiocyanated products[20] (Scheme 10).



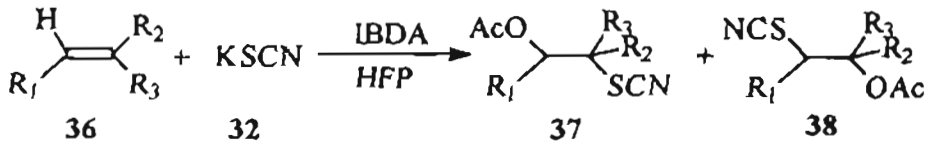
Scheme 10

Oxidation of thiocyanate anion to the corresponding radical and the subsequent addition of the latter to olefins mediated by iodine (III) reagent was reported by Piancatelli [21](Scheme 11).



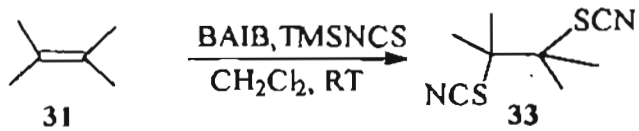
Scheme 11

Acetoxy thiocyanation reaction of alkenes mediated by iodosobenzene diacetate in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP) is also known[22] (Scheme 12).



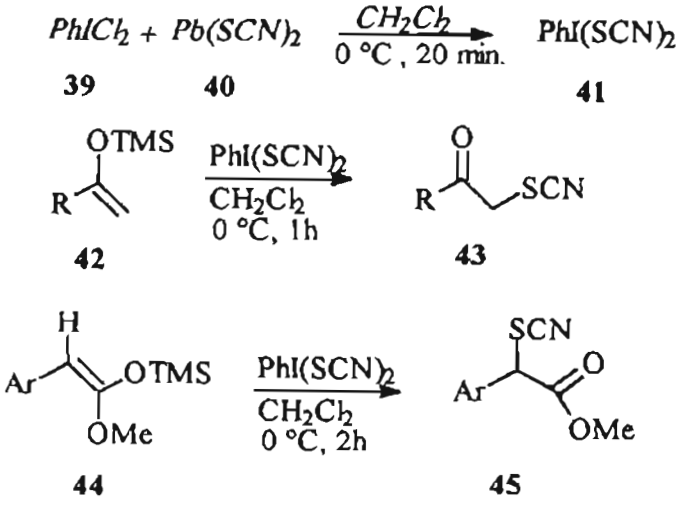
Scheme 12

The same authors have reported the dithiocyanation of alkenes using [bis (acetoxy) iodo] benzene/trimethylsilyl isothiocyanate reagent combination (Scheme 13). [23]



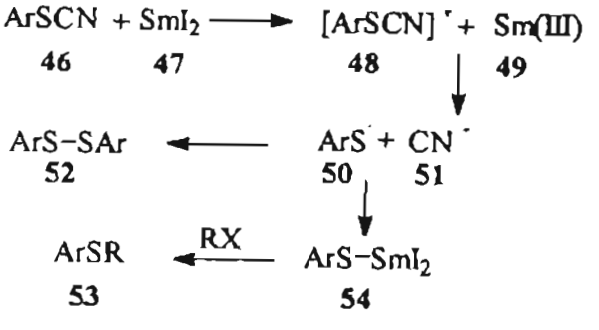
Scheme 13

Reaction of enol silyl ethers of ketones and esters using (dichloroiodo) benzene-lead(II)thiocyanate reagent combination yielding α-carbonyl thiocyanates was reported recently[24] (Scheme 14).



Scheme 14

As already mentioned thiocyanate is an important functional group as it can be easily converted into other sulfur containing functional groups. *Recently*, a SmI_2 mediated conversion of thiocyanates to sulfides and thioesters has been reported[8] (Scheme 15).



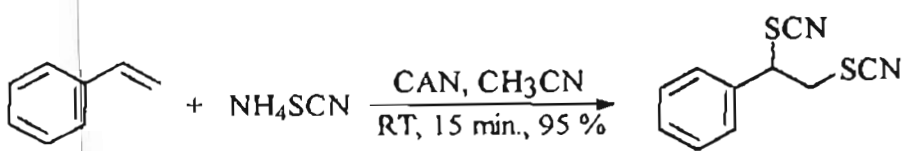
Scheme 15

3.2.1.RESULTS AND DISCUSSION

3.2.1.1. Reactions of Aryl alkenes with NH_4SCN in CH_3CN: Formation of Dithiocyanates.

Against the background of the literature cited above, it was of interest to explore the CAN mediated addition of thiocyanate to arylalkenes and our results are described in the following sections.

The initial work involved the reaction of ammonium thiocyanate with styrene. A solution of styrene **34** and ammonium thiocyanate on treatment with CAN in acetonitrile afforded the product **35** in 95 % yield (Scheme 16) as a colorless crystalline solid.[25a]

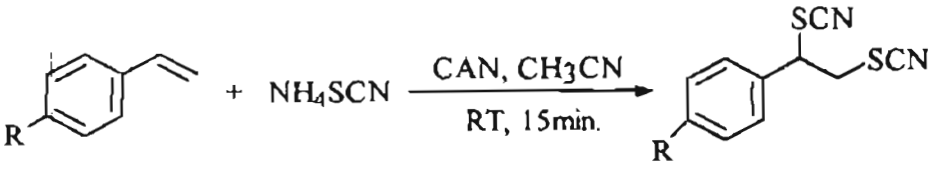


34 **55** **35**

Scheme 16

The IR spectrum of **35** showed a strong absorption at 2160 cm^{-1} characteristic of the -SCN group. The characteristic C-S stretching appeared at 703 cm^{-1}. In the ^1H NMR spectrum of **35**, the benzylic proton resonated at δ 4.64 as a double doublet (J_1, J_2 = 6.04 Hz, 9.59 Hz). The two protons on the terminal carbon also gave two double doublets at δ 3.81 (J_1, J_2= 6.012 Hz, 13.72 Hz) and at δ 3.65 (J_1, J_2= 9.73 Hz, 13.66 Hz). The aromatic protons were visible at δ 7.38 as a multiplet. In ^{13}C NMR spectrum, the characteristic signals due to the thiocyanato carbon appeared at δ 109.80 and 109.45. The assigned structure was further supported by analytical data.

Similarly, 4-methyl styrene and 4-methoxy styrene also afforded the corresponding dithiocyanates in good yields under identical conditions (Scheme 17).



R= CH_3, **56** R= CH_3, **57** (75 %)

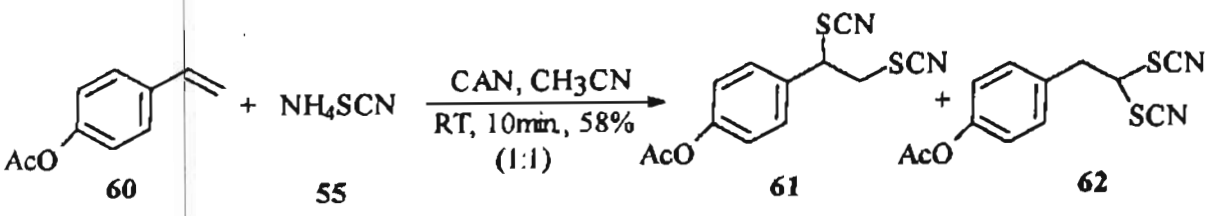
R= OCH_3, **58** R= OCH_3, **59** (65 %)

Scheme 17

The IR spectrum of compound **57** showed the characteristic absorption corresponding to -SCN at 2160 cm^{-1} . ^1H NMR spectrum of **57** showed two double doublets at δ 3.78 (J_1, J_2 = 5.94, 13.60 Hz) and 3.61 (J_1, J_2= 9.81, 13.52 Hz) for the two protons attached to the terminal carbon bearing the thiocyanate group. The benzylic proton resonated at δ 4.63 as a double doublet (J_1, J_2 = 5.95, 9.75 Hz). ^{13}C NMR spectrum also showed two carbons at δ 109.98 and 110.25 characteristic of two -SCN groups. Analytical data was also in agreement with the assigned structure.

Similar diagnostic spectral data (IR, ^1H NMR and ^{13}C NMR) were obtained for **59** and the assigned structure was further supported by elemental analysis.

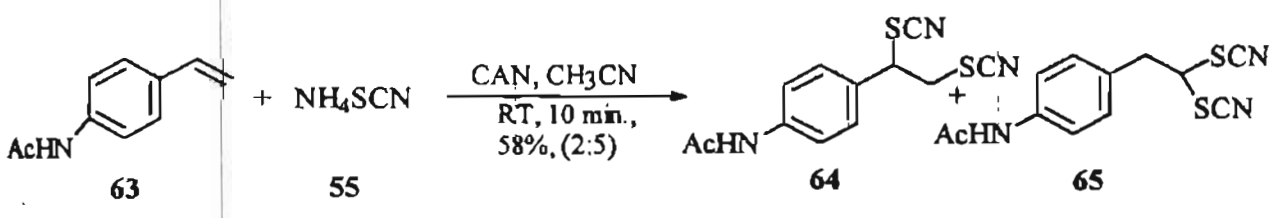
The reaction of 4-acetoxy styrene with NH_4SCN in presence of CAN *in acetonitrile afforded geminal dithiocyanate derivative* **62** along with the vicinal dithiocyanate **61** as presented in Scheme 18.



Scheme 18

The dithiocyanates **61** and **62** were obtained as a mixture, inseparable by column chromatography. The IR spectrum of the mixture showed a strong absorption at 2160 cm^{-1}. The acetoxy carbonyl was visible at 1730 cm^{-1}. The geminal protons attached to the terminal carbon bearing SCN group of compound **61** appeared as two double doublets at δ 3.77 and 3.60. The benzylic proton of **61** resonated at δ 4.65 as a double doublet. The two benzylic protons of **62** gave a multiplet at δ 3.33 and the proton attached to the terminal carbon resonated as a double doublet at δ 6.04.

The reaction of acetamido styrene with NH_4SCN in presence of CAN in CH_3CN afforded a mixture of two dithiocyanates tentatively identified as **64** and **65**; trace amounts of ring thiocyanated product was also detected *(Scheme 19)*.

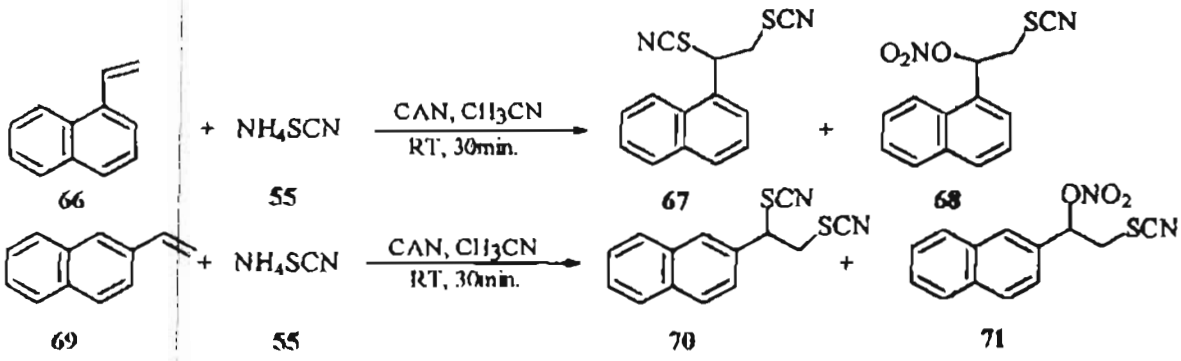


Scheme 19

The IR spectrum of the mixture of **64** and **65** showed the characteristic absorption of -SCN as a broad peak at 2166 cm^{-1} with a shoulder at 2079 cm^{-1}.In the ^1H NMR spectrum, the proton on the terminal carbon of **65**

resonated as a multiplet at δ 5.04 while the protons on the terminal carbon of **64** resonated as two double doublets at δ 3.78 and 3.60. The benzylic proton of **64** displayed a double doublet at δ 4.63 whereas the benzylic protons of **65** resonated at δ 3.28 as a multiplet.

Vinyl naphthalenes under similar reaction conditions afforded the vicinal dithiocyanate derivatives along with the nitrato thiocyanate derivatives. The results are summarized in Scheme 20.



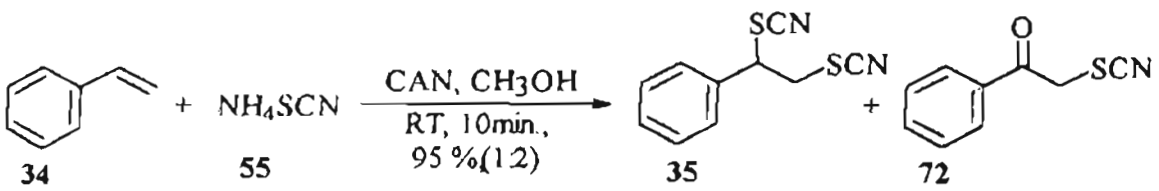
Scheme 20

In the IR spectra, both the dithiocyanates **67** and **70** showed strong absorption due to thiocyanate at 2153 cm^{-1}. The absorptions due to the thiocyanate of **68** and **71** were visible at 2173 and 2160 cm^{-1} and those due to nitrate were seen at 1640 and 1642 cm^{-1} respectively. In the ^1H NMR spectrum of **67** the benzylic proton appeared at δ 4.69 as a double doublet and the protons on the terminal carbon resonated at δ 3.59 and 3.43 as two double doublets. The benzylic proton of the nitrato thiocyanate **68** appeared at δ 5.48 as a triplet. The two protons on the terminal carbon were discernible as a double doublet at δ 3.44.

In the ^{1}H NMR spectrum of **70**, the benzylic proton resonated at δ 4.83 as a double doublet and the two protons on the terminal carbon appeared as two double doublets at δ 3.88 and δ 3.73. The ^{1}H NMR spectrum of **71** displayed a double doublet at δ 6.20 due to the benzylic proton and the two protons on the terminal carbon appeared as a multiplet at δ 3.46.

3.2.1.2. Reactions of Aryl alkenes with NH_4SCN in Methanol : Formation of phenacyl thiocyanate derivatives.

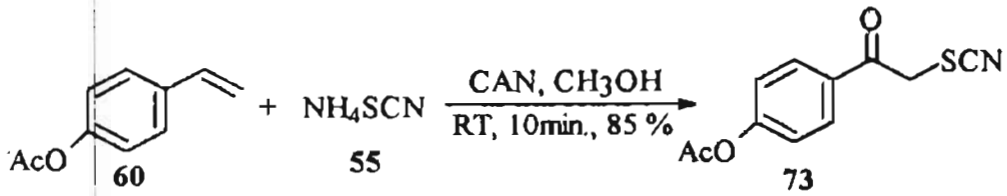
When the reaction of aryl alkenes with ammonium thiocyanate was carried out in methanol, we observed an additional product along with the dithiocyanate, the latter being characterized as the phenacyl thiocyanate. Our initial experiment was with styrene and ammonium thiocyanate in methanol which afforded an inseparable mixture of keto thiocyanate **72** and dithiocyanate **35** (Scheme 21).



Scheme 21

The IR spectrum of the mixture showed the characteristic absorption of carbonyl group at 1681 cm^{-1} and that of -SCN group at 2153 cm^{-1}. In the ^{1}H NMR spectrum of the mixture of **35** and **72**, the resonance due to the two protons attached to the terminal carbon of **72** was visible as a sharp singlet at δ 4.72. In the ^{13}C NMR spectrum there were three signals due to the thiocyanate carbon at δ 111.50, 109.82, 109.45. The carbonyl carbon resonated at δ 190.55.

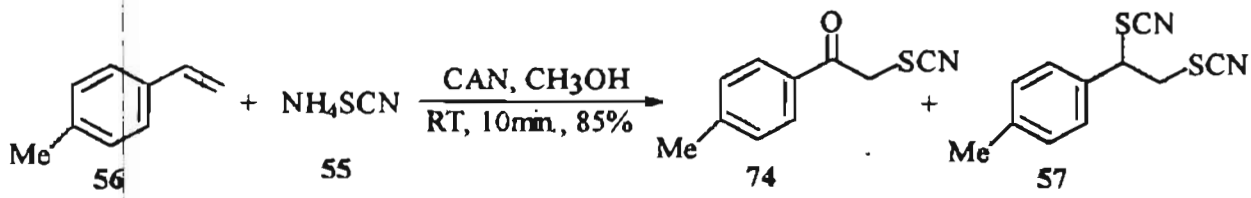
In the case of acetoxy styrene, the β-keto thiocyanate (**73**) was obtained as the major product (85 %) with only traces of the dithiocyanate (Scheme 22).



Scheme 22

The IR spectrum of **73** showed two carbonyls at 1762cm^{-1} and 1688 cm^{-1} and the thiocyanate peak at 2160 cm^{-1}. In the ^{1}H NMR spectrum of **73**, two protons of the terminal carbon resonated as a sharp singlet at δ 4.72. The ^{13}C NMR spectrum displayed the characteristic peaks of benzoyl carbonyl at δ 189.32, the ester carbonyl at δ 168.16 and the thiocyanate carbon at δ 111.35. Analytical data further supported the assigned structure.

Similar reaction was observed with methyl styrene as shown in Scheme 23.

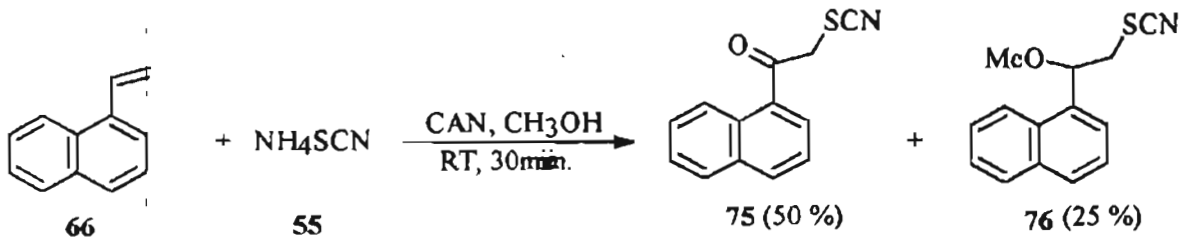


Scheme 23

The inseparable mixture of **74** and **57** showed the carbonyl absorption at 1674 cm^{-1} and the peak corresponding to thiocyanate at 2153 cm^{-1}. In the ^{1}H NMR spectrum, the benzylic protons of **74** resonated as a sharp singlet at

δ 4.72. The ^{13}C NMR spectrum displayed a signal at δ 190.20 due to the carbonyl and one at δ 111.76 due to the thiocyanate carbon.

Similar experiment with 1-vinyl naphthalene afforded the aroyl thiocyanate **75** and the β-methoxy thiocyanate **76** in 2:1 ratio (Scheme 24).

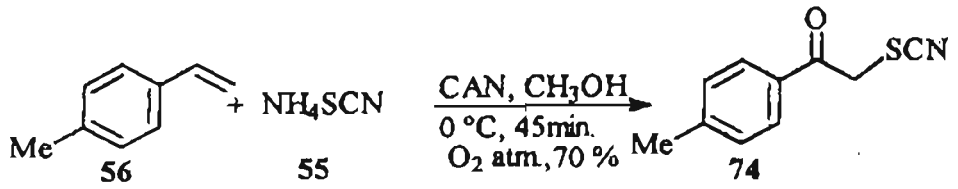


66 **55** **75** (50 %) **76** (25 %)

Scheme 24

It is assumed that the carbonyl compound is formed by the trapping of oxygen by the initially formed benzylic radical followed by further transformation[25] of the peroxy intermediate. The hydroperoxide formed from this intermediate undergoes fragmentation to give the keto thiocyanate. In view of this, the reactions of various substituted styrenes with ammonium thiocyanate in methanol were studied in an atmosphere of oxygen, with the expectation that the phenacyl thiocyanates would be formed predominantly.

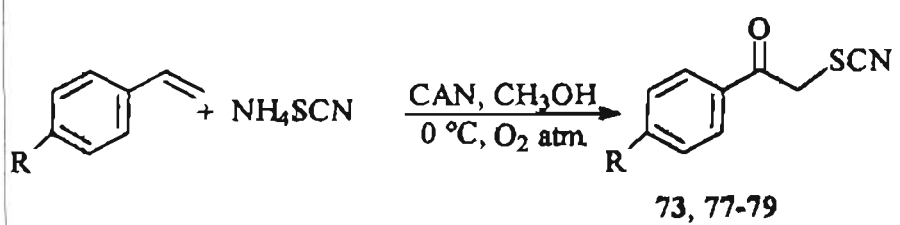
When a methanolic solution of 4-methyl styrene and ammonium thiocyanate saturated with oxygen is treated with CAN in methanol in an atmosphere of oxygen, phenacyl thiocyanate **74** was obtained as a colorless crystalline solid in 70 % yield (Scheme 25).



Scheme 25

The product **74** was characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

Similar reactivity was observed with other substituted styrenes also. The results are summarized in Scheme 26.



R= OAc **73** (75 %)

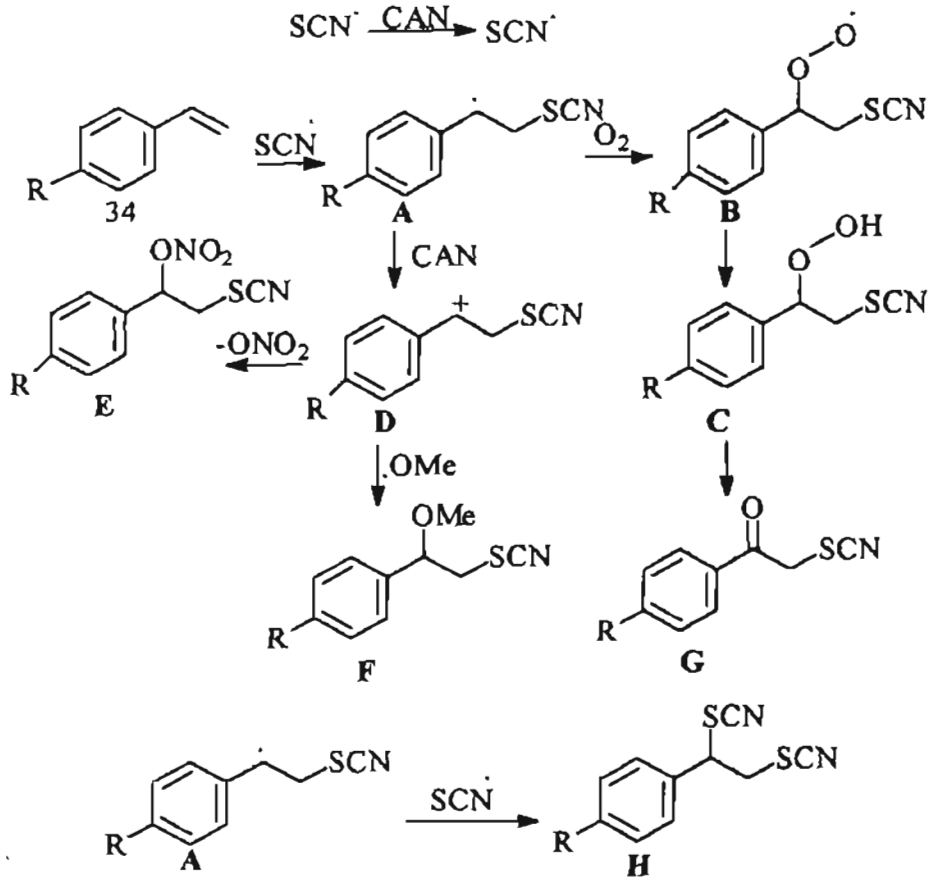
R= ONO_2, **77** (57 %)

R= OMe **78** (53 %)

R= Cl, **79** (65 %)

Scheme 26

The experiment with 1-vinyl naphthalene and ammonium thiocyanate in methanol afforded the corresponding aroyl methyl thiocyanate **75** (60 %) and methoxy thiocyanate **76** (10 %) as pale yellow liquids. The reaction of unsubstituted styrene and ammonium thiocyanate in methanol under oxygen atmosphere, inexplicably, resulted in the formation of a mixture of phenacyl thiocyanate and dithiocyanate in 1:2 ratio (*cf.* Scheme21).



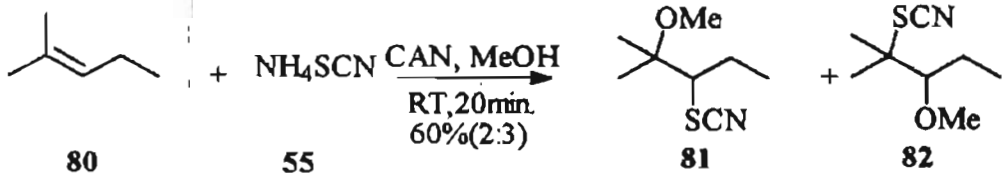
Scheme 26a

A mechanistic rationalization for the results obtained may be presented as above (Scheme 26a). The oxidation of the thiocyanate anion by CAN would give the thiocyanato radical and the latter on addition to the styrene would give rise to a benzylic radical. The dithiocyanates may be resulting by the addition of a second thiocyanato radical to the initially formed benzylic radical. The β-methoxy and β-nitrato products can result from the quenching of the benzylic cation by methanol and nitrate respectively, the cation itself being formed by oxidation of the benzylic radical by CAN. The β-keto products may be derived from the

fragmentation/oxidation of the hydroperoxide, which itself being formed by the quenching of benzylic radical by molecular oxygen. The gem dithiocyanates like **62** and **65** could result from an ionic or radical pathway. Electron rich olefins can undergo a competing electrophilic addition process besides the radical thiocyanation.

3.2.2. Thiocyanation of alkenes using ammonium thiocyanate /CAN reagent combination.

In order to probe the generality of the reaction we have done some preliminary investigations on the thiocyanation of normal alkenes. The reaction of 2-methyl -2-pentene **80** with ammonium thiocyanate in methanol afforded an inseparable mixture of 2-methyl-3-methoxy-2-thiocyanato pentane **82** and 2-methyl -2-methoxy -3-thiocyanato pentane **81** *in 60 % yield in 2:3 ratio (Scheme 27).*

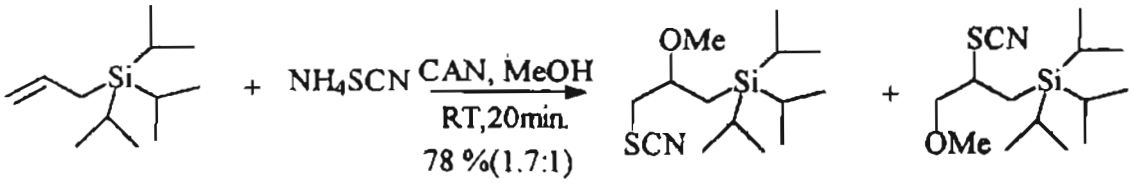


80 **55** **81** **82**

Scheme 27

The structures of **81** and **82** were tentatively assigned on the basis of IR, ^{1}H NMR and ^{13}C NMR.

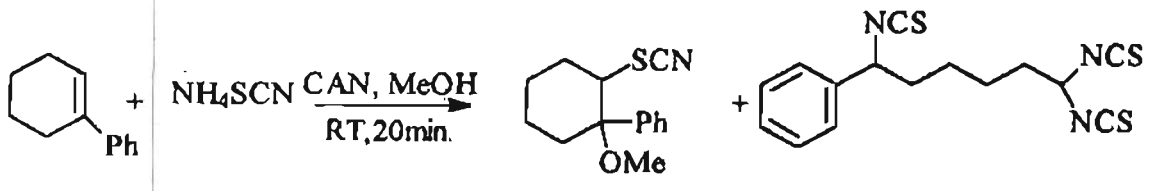
Analogous reactivity was observed in the case of allyl trimethyl silane and ammonium thiocyanate in methanol (Scheme 28).



83 **55** **84** **85**

Scheme 28

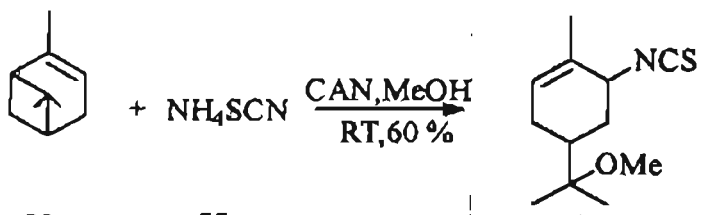
Cyclic alkenes were found to react with ammonium thiocyanate in presence of CAN giving the corresponding thiocyanate and isothiocyanate derivatives. For example, the CAN mediated thiocyanation reaction of phenyl cyclohexene with ammonium thiocyanate in methanol gave two products which are tentatively identified as **87** and **88** on the basis of IR, ^{1}H NMR and ^{13}C NMR spectra (Scheme 29).



86 **55** **87** (43 %) **88** (3 %)

Scheme 29

The reaction of α-pinene with ammonium thiocyanate resulted in a ring opened product (Scheme 30).



89 **55** **90**

Scheme 30

The structure of **90** is tentatively assigned on the basis of IR, ^{1}H NMR and ^{13}C NMR spectrum.

3.3. CARBON-NITROGEN BOND FORMING REACTIONS MEDIATED BY CAN

The most generally used method for preparing alkyl and acyl azides consists of the displacement of other functional groups by azide ion[26] (Scheme 31).

$$\underset{\mathbf{91}}{RX} + \underset{\mathbf{92}}{NaN_3} \longrightarrow \underset{\mathbf{93}}{RN_3} + \underset{\mathbf{94}}{NaX}$$

X = Br, I etc.

R = Alkyl, Acyl etc.

Scheme 31

Another procedure for the preparation of azides involves the reaction of diazonium salts with sodium azide [26](Scheme 32).

$$\underset{\mathbf{95}}{ArN_2^{+}X^{-}} + \underset{\mathbf{92}}{NaN_3} \longrightarrow \underset{\mathbf{96}}{ArN_3} + \underset{\mathbf{97}}{N_2} + \underset{\mathbf{98}}{NaX}$$

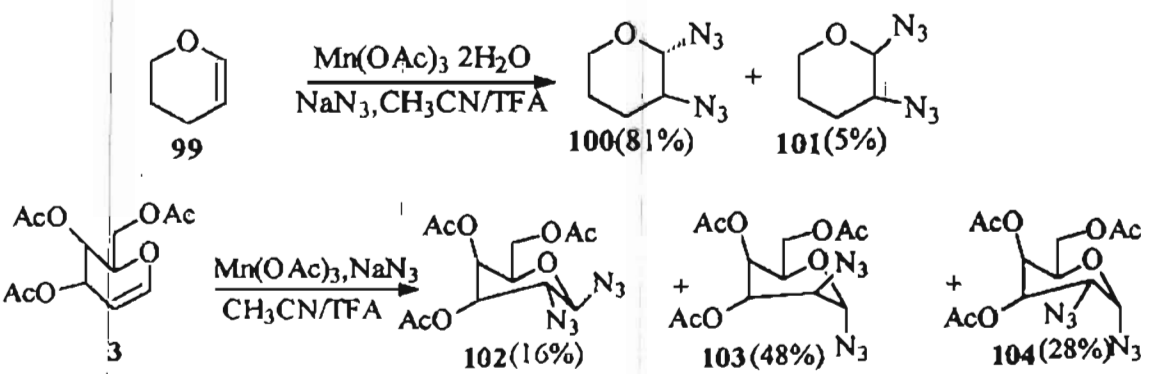
Scheme 32

Other methods include nitrosation of hydrazine derivatives, addition of hydrazoic acids to activated olefins, and reaction of epoxides with sodium azide.[26]

Other than the ionic reactions, there are a few reports on azidation reactions mediated by one electron oxidizing agents. In 1971, Trahanovsky and coworkers observed the exclusive formation of β-nitrato azides from the reaction of alkenes with sodium azide [3] in presence of CAN. Later Lemieux *et al* applied this reaction to glycals.[4]

In addition to cerium (IV), some other one electron oxidants have also found use in such reactions. In 1985, Fristad and coworkers reported the

conversion of simple alkenes to 1,2-diazides by reaction with Mn (III) acetate and excess NaN_3 in acetic acid.[27] Recently, Snider has extented this reaction to glycals [28] (Scheme 33).



Scheme 33

Azido selenenylation has been achieved by trivalent iodine reagent mediated reactions of alkenes and enol ethers with diphenyl diselenide and sodium azide.[29] Iodosobenzene diacetate mediated diazidation of phenol ethers with $TMSN_3$ in PIFA was reported by Kita in 1991.[30] Later CAN mediated α-keto azidation of trimethyl silyl enol ethers was reported by Magnus etal.[31] Conversion of olefins into α-azido ketones using azido trimethylsilane-chromiumtrioxide reagent combination has also been reported.[32]

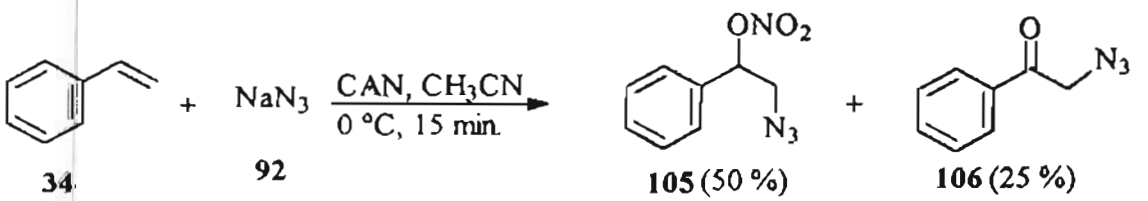
3.3.1.RESULTS AND DISCUSSION

3.3.1.1.CERIUM (IV) AMMONIUM NITRATE MEDIATED ADDITION OF AZIDE TO STYRENES: SYNTHESIS OF PHENACYL AZIDES.

3.3.1. 1a. Reaction of aryl alkenes with sodium azide in presence of CAN in acetonitrile

As a continuation of our efforts to achieve the oxidation of soft anions to radicals and their addition to alkenes, we undertook an investigation of the reaction of NaN_3 with various aryl alkenes in presence of CAN. It was evident from the literature survey that there has been no systematic investigation in this area.

The initial work involved the reaction of sodium azide with styrene. A solution of styrene and sodium azide on treatment with CAN in acetonitrile afforded the β-nitrato azide **105** in 50 % yield along with 25 % of the β-keto azide **106** (Scheme 34).



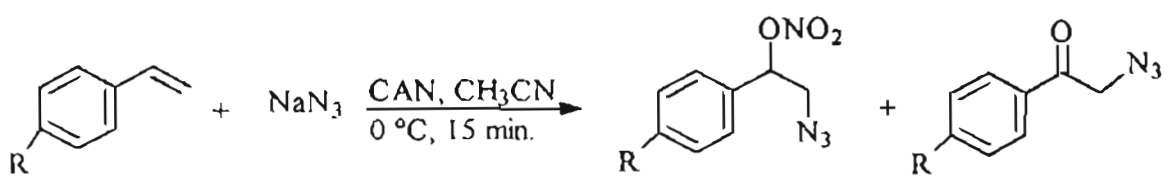
34 **92** **105** (50 %) **106** (25 %)

Scheme 34

The reaction mixture on processing afforded **105** and **106** as pale yellow liquids. The IR spectra of **105** and **106** showed the characteristic peak of azide group at 2119 cm^{-1} and 2106 cm^{-1} respectively. The $-ONO_2$ absorption of **105** was visible at 1647 cm^{-1} and the carbonyl group of **106** at 1694 cm^{-1}. In the ^1H NMR spectrum, the benzylic proton of **105** appeared at δ 5.91 as double doublet (J_1, J_2 = 4.02, 8.49 Hz) and the protons on the terminal carbon resonated as two double doublets at δ 3.69 (J= 8.58 Hz,

13.59 Hz) and at δ 3.49 (J = 4.02 Hz, 13.56 Hz). The terminal protons of **106** appeared as a sharp singlet at δ 4.56. In the ^{13} C NMR spectrum of **105**, the benzylic carbon was visible at δ 83.49 and the terminal one bearing azide resonated at δ 53.32. The carbonyl carbon and the terminal carbon bearing the azide group of **106** appeared at δ 193.22 and 54.91 respectively in the ^{13}C NMR spectrum.

Similar results were obtained with 4-methyl and 4-acetoxy styrenes under the same experimental conditions as illustrated in Scheme 35.



R = Me, **56**	R = Me, **107** (70 %)	R = Me, **108** (15 %)
R = OAc, **60**	R = OAc, **109** (60 %)	R = OAc, **110** (23 %)

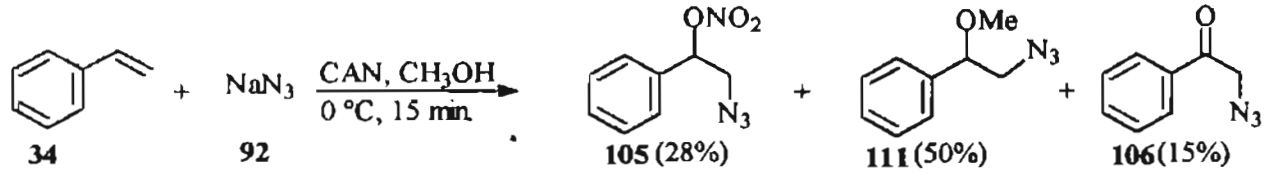
Scheme 35

The IR spectrum of **107** showed the characteristic -ONO_2 and azide bands at 1647 and 2112 cm^{-1} respectively while that of **109** showed these absorptions at 1640, 2112 cm^{-1}. The characteristic absorptions of carbonyl and azide groups of **108** were at 1694, 2106 cm^{-1} and those of **110** were at 1694, 1755, 2099 cm^{-1} respectively. In the ^{1}H NMR spectrum of **107**, the benzylic proton resonated as a double doublet at δ 5.86 (J_1, J_2= 4.00, 8.49 Hz). The protons on the terminal carbon bearing azide resonated as two double doublets in both **107** and **109**. The β-ketoazides **108** and **110** gave sharp singlets at δ 4.52 and δ 4.48 respectively corresponding to the protons

on the terminal carbons. The ^{13}C NMR spectrum of **108** and **110** showed the characteristic benzoyl carbonyl at δ192.84 and 191.99 respectively.

3.3.1.1b. Azidation reactions in methanol : Formation of β-nitrato, β-methoxy and β-keto azides

Our experiments in the thiocyanation of styrenes (see section 3.2.1.2, p-12) showed that the formation of the keto product is generally favored in methanol when compared to acetonitrile. This prompted us to do the azidation reactions also in methanol. When the experiment with styrene and sodium azide was repeated in methanol, we observed the formation of phenacyl azide and an inseparable mixture of nitrato azide and methoxy azide as given in Scheme 36.

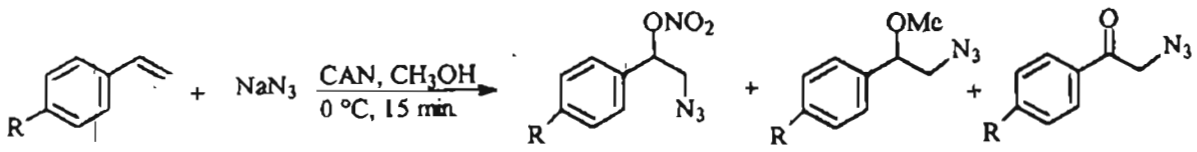


34 **92** **105** (28%) **111** (50%) **106** (15%)

Scheme 36

The benzylic proton of **111** resonated as a double doublet at δ 4.33 (J_1, J_2= 3.39, 8.43 Hz) and the benzylic proton of **105** was visible at δ 5.88 (J_1, J_2= 3.96, 8.43 Hz). The protons on the terminal carbon of **111** appeared as double doublets at δ 3.43 and those of **105** at δ 3.25.

Similar reactions occurred with 4-methyl and 4-acetoxy styrenes in methanol to afford mixtures of β-methoxy, β-nitrato, and the β-keto azides (Scheme 37).



R= Me, **56**

R= OAc, **60**

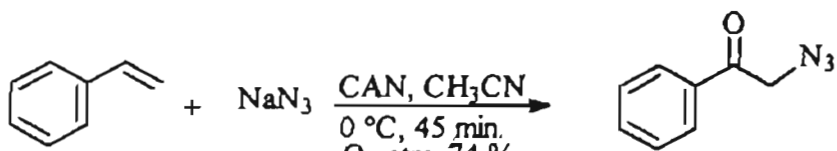
R= Me, **107** (41 %).; **112** (14 %).;**108** (14%)

R= OAc, **109** (31 %).;**113** (42 %), **110** (22 %)

Scheme 37

It was conjectured that the phenacyl azide is formed by the trapping of oxygen by the initially formed benzylic radical followed by further transformations[25b] (see section 3.2.1.2, p-68 also). With this view, the experiments were repeated in an oxygen atmosphere and the results are presented in the following section.

When the experiment involving styrene and sodium azide in acetonitrile was repeated in an oxygen atmosphere, the β-keto azide **106** was formed in 74 % yield with less than 3 % of the β-nitrato azide (Scheme 38).



34 **92** **106**

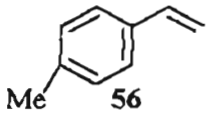
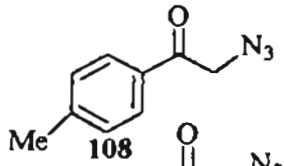
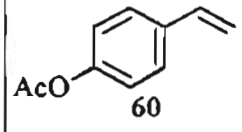
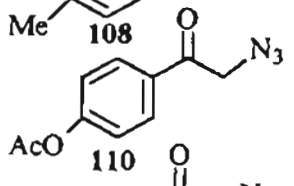
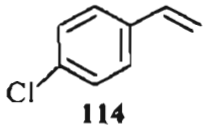
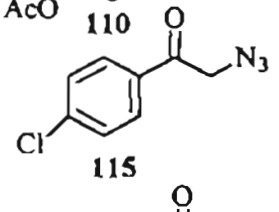
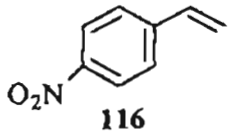
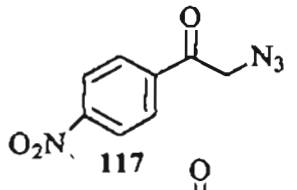
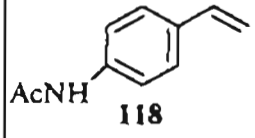
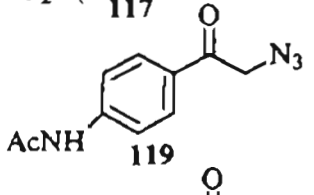
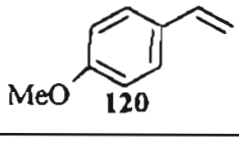
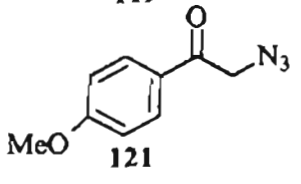
Scheme 38

When the above experiment was carried out in methanol, the β-ketoazide was formed in 85 % yield along with 1 % of an inseparable mixture of β-methoxy and β-nitrato azide.

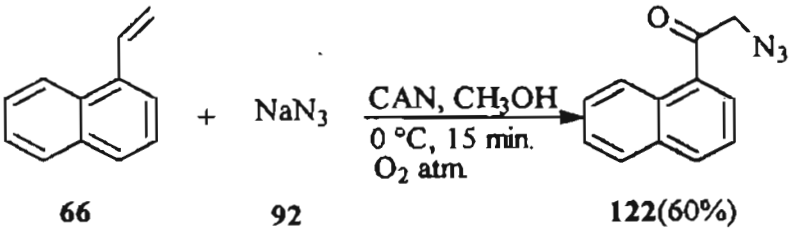
Similar results were obtained with other substituted styrenes and these are summarized in table 1.

Vinyl naphthalenes also exhibited similar reactivity pattern. 1-Vinyl naphthalene when treated with sodium azide in presence of CAN in methanol under oxygen atmosphere afforded the corresponding β-keto azide (Scheme 39).

Table 1 : Azidation reactions of aryl alkenes in oxygen atmosphere.

Entry	Substrate	product	Yield
1.	 **56**	 **108**	76%
2.	 **60**	 **110**	75%
3.	 **114**	 **115**	69%
4.	 **116**	 **117**	68%
5.	 **118**	 **119**	68%
6.	 **120**	 **121**	95%

Reaction conditions: CAN (2.3 equiv.), MeOH, 0 °C, 20-45min.,Sodium azide (1.5 equiv), O_2 atm.



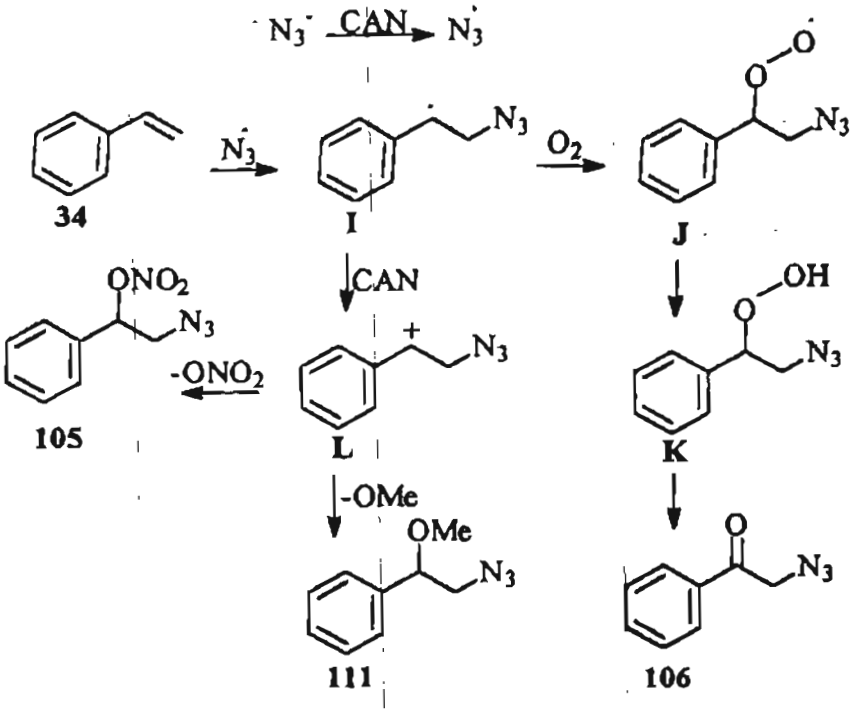
66 92 122(60%)

Scheme 39*

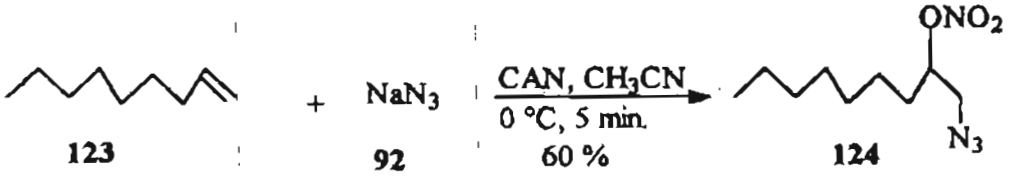
* Traces of the β-methoxy azide was also formed.

A plausible mechanistic rationalization of the formation of phenacyl azide is as follows (Scheme 40). The oxidation of azide anion by CAN would give the azido radical and the latter on addition to the styrene would give rise to a benzylic radical. This radical can be trapped by molecular oxygen to form the peroxy radical which is further transformed into the ketone *via* the fragmentation/oxidation of the hydroperoxide. The β-methoxy and β-nitrato products can result from the quenching of the benzylic cation by methanol and nitrate respectively, the cation itself being formed by oxidation of the benzylic radical by CAN. The nitrate can also result from a ligand transfer process.

In a limited study, it was found that other acyclic and cyclic alkenes also gave β-nitrato azides when reacted with sodium azide in presence of CAN. Experiments with 1-octene and sodium azide, in methanol and acetonitrile afforded the β-nitrato azide as the major product (Scheme 41).

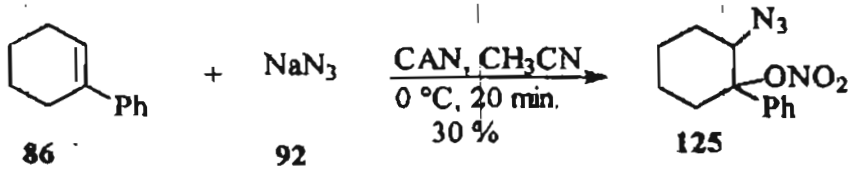


Scheme 40



Scheme 41

Similar experiment with phenyl cyclohexene afforded the azide **125** in low yield (Scheme 42).



Scheme 42

3.4. EXPERIMENTAL DETAILS

General information about the experimental is given in Chapter II (Section 2.3). CAN, 4-methyl styrene and styrene were procured from Aldrich. All other styrenes and vinyl naphthalenes were prepared from the corresponding aldehydes *via* the Wittig reaction. Sodium azide and Ammonium thiocyanate were purchased from the local sources.

Synthesis of dithiocyanates : General procedure.

A solution of CAN (1.26 g, 2.3 mmol.) in acetonitrile (10 mL) was added dropwise to the mixture of the styrene (1 mmol) and ammonium thiocyanate (2 mmol) in acetonitrile (5 mL) with constant stirring at room temperature. In all the cases the reddish brown color of CAN disappeared within half an hour. The mixture, after the completion of the reaction was diluted with water (150 mL) and extracted with dichloromethane (5×25 mL). The combined organic extracts were washed with water, then with brine and dried over anhydrous sodium sulfate. The solvent was evaporated off and the residue obtained was subjected to chromatography on silica gel column. Elution with appropriate mixture of ethyl acetate and petroleum ether afforded the dithiocyanates. In most cases the product was obtained as colorless solid which was then re-crystallized from chloroform pet-ether mixture. Analytical data were obtained on the re-crystallized compounds.

Dithiocyanate 35

A mixture of styrene (0.104 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) was dissolved in 5 mL acetonitrile. CAN (1.26 g, 2.3 mmol) dissolved in acetonitrile (10 mL) was added to it dropwise with

constant stirring for 15 min. The reaction mixture was then diluted with water (150 mL) and extracted with dichloromethane (5 x 10 mL). The solvent was evaporated off and the residue was purified by column chromatography (ethyl acetate/hexane = 1:9) to afford **35** (0.209 g, 95 %) as colorless solid. It was then re-crystallized from chloroform-petroleumether mixture. m.p. 102- 105 °C.

IR (KBr, ν_{max}) : 2955, 2160, 1640, 1506, 703 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.38 (m, 5H, ArH), 4.64 (dd, 1H, -CHSCN, J_1, J_2= 6.04, 9.59 Hz), 3.81 (dd, 1H, CH_2SCN, J_1, J_2= 6.01, 13.72 Hz), 3.65 (dd, 1H, CH_2SCN, J_1, J_2= 9.73, 13.66 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) :δ 134.13, 130.23, 129.64, 127.49, 109.80, 109.45, 51.39, 38.17.

Analysis calcd. for $C_{10}H_8S_2N_2$: C -54.54 %, H - 3.63 %, N - 12.72 %, S - 29.09 %

Found : C -54.61 %, H - 3.72 %, N - 12.72 %, S - 28.95 %.

Dithiocyanate 57

A mixture of 4-methyl styrene **56** (0.118 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) in acetonitrile (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in acetonitrile (10 mL) with constant stirring. The reaction mixture on processing according to the general experimental procedure afforded **57** (0.176 g, 75 %) as a colorless crystalline solid. It was then recrystallized from chloroform-petroleum ether mixture.

m p. 104-106 °C

IR (KBr, ν_{max}) : 2989, 2160, 1600, 1512, 1431, 764 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.25 (s, 4H, ArH), 4.63 (dd, 1H, CHSCN, J_1, J_2 = 5.95, 9.75 Hz), 3.78 (dd, 1H, CH_2SCN , J_1, J_2 = 5.94, 13.6 Hz), 3.61 (dd, 1H, CH_2SCN, J_1, J_2 = 9.81, 13.52 Hz), 2.38 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 140.60, 130.95, 130.37, 127.46, 110.25, 109.98, 51.42, 38.28, 21.30.

Analysis calcd. for $C_{11}H_{10}S_2N_2$: C -56.41 %, H - 4.27 %, N - 11.96 %, S - 27.35 %

Found : C -56.35 %, H - 4.41 %, N - 11.89 %, S - 27.28 %.

Mass Spectrum : *m/z* 221(M+1), 218, 162, 136, 116, 105, 57.

Dithiocyanate 59

A mixture of 4-methoxy styrene **58** (0.136 g, 1 mmol.) and ammonium thiocyanate (0.152 g, 2 mmol.) in CH_3CN (5 mL) was treated with CAN in CH_3CN (10 mL). The reaction mixture on processing after 10 min. following the general experimental procedure afforded **59** as a colorless solid (0.163 g, 65 %) which was then re-crystallized from chloroform-petroleum ether mixture. m p. 99-101 °C.

IR (KBr, ν_{max}) : 2989, 2935, 2153, 1613, 1519, 1458, 1256, 764 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.28 (m, 2H, ArH), 6.97 (m, 2H, ArH), 4.65 (dd, 1H, -CHSCN, J_1, J_2= 5.94, 9.81 Hz), 3.83 (s, 3H, -OCH_3), 3.75 (dd, 1H, CH_2SCN, J_1, J_2 =5.91, 13.85 Hz), 3.60 (dd, 1H, CH_2SCN, J_1, J_2 = 9.91, 13.46 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 160.96, 128.99, 125.63, 115.04, 110.28, 110.08, 55.43, 51.40, 38.37.

Analysis calcd. for $C_{11}H_{10}S_2N_2O$: C -52.80%, H - 4.00%, N - 11.20%, S - 25.60%

Found : C -52.67%, H - 4.12%, N - 11.04%, S - 25.64%.

Mass spectrum : *m/z* 235 (M+1), 176, 119, 57.

Dithiocyanates 61 and 62

A mixture of 4-acetoxy styrene **60** (0.162 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) in CH_3CN (5 mL) was treated with CAN in CH_3CN (10 mL). The reaction mixture on processing and purification following the general experimental procedure afforded an inseparable mixture of **61** and **62** as pale yellow viscous liquids (0.161 g, 58 %, 1:1 mixture).

IR (CH_2Cl_2, ν_{max}) : 2985, 2160, 1730, 1610, 1450, 765 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) :δ 7.30 (m, 8H, ArH), 6.04 (t, 1H, CH $(SCN)_2$), 4.65 (dd, 1H, -CHSCN, J_1, J_2= 6.27, 9.30 Hz), 3.77 (dd, 1H, CH_2SCN , J_1, J_2= 6.18, 13.76 Hz), 3.60 (dd, 1H, CH_2SCN, J_1, J_2= 9.51, 13.64 Hz), 3.33 (m, 2H, -CH_2), 2.33 (s, 3H, CH_3), 2.31 (s, 3H, CH_3).

Dithiocyanates 64 and 65

Acetamido styrene **63** (0.161 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol.) were dissolved in CH_3CN (5 mL). CAN (1.26 g, 2.3 mmol.) dissolved in CH_3CN (10 mL) was added to it dropwise with constant stirring. The reaction mixture was worked up after 20 min. as usual and the residue on column chromatography afforded an inseparable mixture of **64** and **65** as amorphous solids (0.160 g, 58 %, 2:5 ratio).

IR (KBr, ν_{max}) : 3343, 3049, 2982, 2166, 1694, 1512, 744 cm^{-1}

^1H NMR ($CDCl_3$, 300 MHz) :δ 7.55 (m, 4H, ArH), 7.24 (m, 4H, ArH), 5.04 (m, 1H, $CH(SCN)_2$), 4.63 (dd, 1H, CHSCN), 3.78 (dd, 1H, CHSCN), 3.60 (dd, 1H, CH_2SCN), 3.28 (m, 2H, CH_2), 2.15 (brs, 6H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 173.50, 144.83, 144.25, 135.53, 132.68, 130.39, 124.38, 115.28, 114.92, 114.42, 65.05, 55.77, 45.05, 42.20, 28.31.

Dithiocyanate 67 and β-nitrato thiocyanate 68

A mixture of 1-Vinyl naphthalene **66** (0.154 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) in CH_3CN (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in acetonitrile (10 mL). After the completion of the reaction (30 min.), the reaction mixture was worked up as per the general experimental procedure to afford the crude product which on

purification by silica gel column chromatography afforded the dithiocyanate **67** (0.140 g, 52 %) and the β-nitrato thiocyanate **68** (0.109 g, 40 %) as pale yellow highly viscous liquids.

Spectral data for 67

IR (CH_2Cl_2, ν_{max}) : 3056, 2921, 2153, 1560, 1290, 709 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.63 (m, 7H, ArH), 4.69 (t, 1H, CHSCN), 3.59 (dd, 1H, CH_2SCN, J_1, J_2= 3.84, 14.40 Hz), 3.43 (dd, 1H, CH_2SCN, J_1, J_2= 9.25, 14.28 Hz).

Spectral data for 68

IR (CH_2Cl_2, ν_{max}) : 3063, 2173, 1640, 1519, 1290 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.65 (m, 7H, ArH), 5.48 (t, 1H, $-CHONO_2$.), 3.44 (m, 2H, CH_2SCN).

Dithiocyanate 70 and β-nitrato thiocyanate 71

A mixture of 2-vinyl naphthalene **69** (0.154 g, 1 mmol.) and ammonium thiocyanate (0.152 g, 2 mmol) in CH_3CN (5 mL) was treated with CAN in CH_3CN (10 mL). Worked up after 30 min. and processed as usual following the general experimental procedure to afford dithiocyanate **70** as a colorless amorphous solid (0.137 g, 51 %) and β-nitrato thiocyanate **71** as a pale yellow viscous liquid (0.055 g, 20 %).

Spectral data for 70

IR (CH_2Cl_2, ν_{max}) : 2989, 2948, 2153, 1600, 1512, 1431, 1371 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.91 (m, 4H, ArH), 7.57 (m, 2H, ArH), 7.49 (m, 1H, ArH) 4.83 (dd, 1H, -CHSCN, J_1, J_2= 6.12, 9.51 Hz), 3.88 (dd, 1H, CH_2SCN, J_1, J_2= 6.15, 13.71 Hz), 3.73 (dd, 1H, CH_2SCN, J_1, J_2 = 9.75, 13.65 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 136.14, 130.14, 129.24, 127.93, 123.31, 111.56, 111.68, 51.59, 38.12.

Spectral data for 71

IR (CH_2Cl_2, ν_{max}) : 3063, 2928, 2160, 1642,1512, 1330 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.86 (m, 4H, ArH), 7.55 (m, 2H, ArH), 7.49 (m, 1H, ArH), 6.20 (dd, 1H, $CHONO_2$, J_1, J_2= 5.37, 8.28 Hz), 3.46 (m, 2H, CH_2SCN).

Mixture of phenacyl thiocyanate72 and dithiocyanate 35

A mixture of styrene (0.104 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) was dissolved in methanol (5mL). CAN (1.26 g, 2.3 mmol) in methanol (10mL) was added to it dropwise with constant stirring. The reaction mixture on processing according to the general procedure afforded the mixture of **35** and **72** as colorless crystalline solid (0.188 g, 95 %) which was then re-crystallized from chloroform-petroleum ether mixture.

IR (KBr, ν_{max}) : 3049, 2928, 2153, 1681, 1452, 1276 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.64 (m, ArH, 10H), 4.72 (s, 2H, $COCH_2$), 4.65 (dd, 1H), 3.69 (dd, 1H), 3.32 (dd, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 190.55, 134.56, 129.58, 127.48, 111.50, 109.82, 109.45, 51.34, 42.93, 38.09.

Phenacyl thiocyanate 73

A mixture of 4-acetoxy styrene (0.162 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) was dissolved in methanol (5mL). CAN (1.26g, 2.3 mmol) in methanol (10mL) was added to it dropwise with constant stirring. The reaction mixture after work up and purification afforded **73** (0.218 g, 85 %) as a colorless solid. It was then re-crystallized from chloroform-petroleum ether mixture. m p. 99-101 °C.

IR (KBr, ν_{max}) : 2935, 2160, 1762, 1688, 1550 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.97 (d, 2H, ArH), 7.27 (d, 2H, ArH), 4.72 (s, 2H, $COCH_2$), 2.34 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 189.32, 168.16, 155.52, 131.39, 130.06, 122.33, 111.35, 42. 79, 21.02.

Analysis Cald. For $C_{11}H_9SNO_3$: C- 56.16 %, H- 3.86 %, N- 5.96 %, S- 13.60 %

Found : C- 55.92 %, H- 3.89 %, N- 5.81 %, S- 13.48 %

Mass Spectrum : *m/z* 236 (M+1), 179, 138, 136, 57.

Dithiocyanate 57 and phenacyl thiocyanate 74

To a stirred mixture of 4-methyl styrene (0.118 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5mL), CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added dropwise. The reaction mixture was worked up according to the general experimental procedure and the product was purified by column chromatography using 10 % petroleum ether-ethylacetate as eluent. The mixture of dithiocyanate **57** and phenacyl thiocyanate **74** (1:2 ratio) was obtained as a colorless crystalline solid (0.149 g, 70 %) which was then re-crystallized from chloroform-petroleum ether mixture.

IR (KBr, ν_{max}) : 2982, 2928, 2153, 1674, 1607, 1324 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.82 (d, 2H, ArH), 7.29 (m, 8H, ArH), 4.72 (s, 2H, $COCH_2$), 4.62 (dd, 1H), 3.76 (dd, 1H), 3.61 (dd, 1H), 2.45 (s, 3H, CH_3), 2.38 (s, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 190.20, 145.81, 140.37, 130.26, 129.72, 128.52, 127.40, 111.76, 51.28, 43.00, 38.16, 21.77, 21.23.

Keto thiocyanate 75 and methoxy thiocyanate 76

To a stirred mixture of 1-vinyl naphthalene (0.154 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5 mL), CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added dropwise. The reaction mixture on work up and purification afforded **75** (0.114 g, 50 %) and **76** (0.064 g, 25 %) as colorless viscous liquids.

Spectral data for 75

IR (CH_2Cl_2, ν_{max}) : 2948, 2153, 1670, 1320 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 8.81 (d, 1H, ArH), 8.12 (d, 1H, ArH), 7.4 (m, 2H, ArH), 7.58 (m, 3H, ArH), 4.86(s, 2H, $COCH_2$).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 193.10, 134.98, 129.97, 128.99, 128.93, 128.85, 128.54, 127.20, 126.89, 111.49, 44.75.

Spectral data for 76

IR (CH_2Cl_2, ν_{max}) : 2989, 2106, 1654, 1276, 757 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 8.09 (d, 1H, ArH), 7.87 (m, 2H, ArH), 7.58 (m, 4H, ArH), 5.18 (t, 1H, $CHOCH_3$), 3.37 (s, 3H, OCH_3), 3.30 (d, 2H, CH_2SCN).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 133.59, 130.66, 129.34, 129.25, 126.00, 125.47, 122.19, 112.61, 79.70, 57.57, 40.19.

Synthesis of phenacyl thiocyanates: general experimental procedure

A solution of styrene (1 mmol) and ammonium thiocyanate (1.2 mmol) in methanol (5 mL) was saturated with oxygen. CAN (1.26 g, 2.3 mmol) dissolved in methanol (10 mL) was saturated with oxygen and added to the reaction mixture at room temperature. Oxygen gas was bubbled through the reaction mixture throughout the experiment (usually 30 min-1hr). The reaction mixture was worked up using dichloromethane (125 mL) and water (150 mL). The combined organic layer was dried with

anhydrous sodium sulfate, filtered and the solvent was removed *invacuo* to obtain the crude product mixture. It was then purified using silica gel column chromatography (100-200 mesh) and 10% ethylacetate-hexane as eluent.

Phenacyl thiocyanate 74

A mixture of 4-methyl styrene (0.118 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) in an atmosphere of oxygen. The reaction mixture was worked up as usual and the product on purification afforded **74** as a colorless crystalline solid (0.134 g, 70 %). It was then re-crystallized from chloroform -petroleum ether mixture. m p. 100-102 °C.

IR (KBr, ν_{max}) : 2985, 2153, 1678, 1605 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.82 (d, 2H, ArH), 7.31 (d, 2H, ArH), 4.73 (s, 2H, $COCH_2$), 2.45 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 190.10, 145.77, 131.51, 129.72, 128.51, 111.63, 42.98, 21.76.

Phenacyl thiocyanate 77

To a mixture of 4-nitrostyrene (0.149 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5 mL), CAN in methanol (10 mL) was added with constant stirring in an atmosphere of oxygen. The usual work up and purification afforded **77** (0.127 g, 57 %) as a highly viscous yellow liquid.

IR (CH_2Cl_2, ν_{max})	: 2930, 2153, 1674, 1533 cm^{-1}.
^1H NMR ($CDCl_3$, 300 MHz)	: δ 7.87 (d, 2H, ArH), 7.49 (d, 2H, ArH), 4.69 (s, 2H, $COCH_2$).
^{13}C NMR ($CDCl_3$, 75 MHz)	: δ 189.50, 141.47, 132.30, 129.79, 129.51, 111.28, 40.04.

Phenacyl thiocyanate 78

CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added to a stirred mixture of 4-methoxy styrene (0.136 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5 mL) under an oxygen atmosphere. The reaction mixture on usual work up and purification afforded **78** (0.110 g, 53 %) as a colorless crystalline solid. It was then re-crystallized from chloroform-petroleum ether mixture. m p. 98-100 °C

IR (KBr, ν_{max})	: 3063, 2982, 2840, 2160, 1674, 1600 cm^{-1}.
^1H NMR ($CDCl_3$, 300 MHz)	: δ 7.87 (d, 2H, ArH), 6.92 (d, 2H, ArH), 4.69 (s, 2H, $COCH_2$), 3.86 (s, 3H, OCH_3).
^{13}C NMR ($CDCl_3$, 75 MHz)	: δ 188.91, 164.66, 132.20, 130.81, 130.28, 114.24, 55.27, 42.90.
GC-MS	: m/z 207 (M^+, 7), 135 (100), 121 (19), 107 (22), 92 (30), 77 (42), 64 (9), 49 (12).

Phenacyl thiocyanate 79

A mixture of 4-chloro styrene (0.138 g, 1 mmol) and ammonium thiocyanate (0.086 g, 1.2 mmol) in methanol (5 mL) was treated with CAN 91.26 g, 2.3 mmol) in methanol (10 mL) to afford **79** (0.138 g, 65%) as

colorless crystalline solid. It was then re-crystallized from chloroform-petroleum ether mixture. m p. 129-131 °C

IR (KBr, ν_{max}) : 3097, 2987, 2153, 1667, 1580, 1485 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.87 (d, 2H, ArH), 7.49 (d, 2H, ArH), 4.69 (s, 2H, $COCH_2$)

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 189.50, 141.47, 132.30, 130.81,129.79, 129.51, 111.28, 42.59.

Methoxy thiocyanates 81 and 82

A methanol solution of 2-methyl-2-pentene (0.084 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) when treated with a methanolic solution of CAN (1.26 g, 2.3 mmol) afforded an inseparable mixture of **81** and **82** as pale yellow viscous liquid (0.115 g, 60 %, in 2:3 ratio).

IR (CH_2Cl_2, ν_{max}) : 2975, 2942, 2153, 2058, 1627, 1465, 1290, 852 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 3.21 (brs, 6H, OCH_3), 3.08 (dd, 1H, CHSCN), J_1, J_2= 2.64, 2.70 Hz), 2.02 (m, 1H, $CHOCH_3$), 1.62 (m, 4H, CH_2), 1.29 (brs, 12H, CH_3), 1.19 (m, 6H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 113.46, 111.13, 92.90, 63.67, 63.11, 59.06, 49.88, 27.53, 23.92, 23.53, 22.94, 22.27, 12.99, 12.71.

Methoxy thiocyanate 84 and 85

A mixture of allyltriisopropylsilane (0.198 g, 1 mmol) and ammonium thiocyanate (0.152 g, 2 mmol) was dissolved in methanol (5 mL). CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added to it dropwise with constant stirring. The reaction mixture after work up (30 min.) and purification of the product according to the general experimental procedure afforded the mixture of **84** and **85** (0.224 g, 78 %) as pale yellow viscous liquid in 1.7:1 ratio.

IR (CH_2Cl_2, ν_{max}) : 2950, 2153, 1630, 1450, 850 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.43 (m, 1H, CHSCN), 4.16 (m, 1H, CHOMe), 3.58 (m, 4H, CH_2), 3.37 (brs, 6H, OCH_3), 1.52 (m, 6H, -CH-), 1.10 (brs, 36 H, isopropyl).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 111.03, 109.65, 80.13, 55.45, 47.44, 42.95, 37.53, 18.76, 18.59, 16.25, 16.01, 11.31, 11.19, 11.08.

Thiocyanate 87 and isothiocyanate 88

Phenyl cyclohexene (0.158 g, 1mmol) and ammonium thiocyanate (0.152 g, 2 mmol) were dissolved in methanol (5mL). CAN in 10 mL methanol was added to it dropwise with constant stirring. The reaction mixture on processing and purification afforded **87** (0.106 g, 43 %) and **88** (0.010 g, 3 %) as colorless liquids.

Spectral Data for **87**

IR (CH_2Cl_2, ν_{max})	*: 2935, 2854, 2153, 1452, 1222, 1169, 1067, 771 cm^{-1}.*
^1H NMR ($CDCl_3$, 300 MHz)	: δ 7.38 (m, 5H, ArH), 3.85 (brs, 1H, CHSCN), 2.92 (s, 3H, OCH_3), 2.52 (m, 2H, CH_2), 2.07 (m, 2H, CH_2), 1.65 (m, 4H, CH_2).
^{13}C NMR ($CDCl_3$, 75 MHz)	: δ 141.39, 129.23, 127.27, 112. 08, 78.68, 57.80, 50.57, 27.85, 24.95, 20.95, 19.98.

Spectral Data for **88**

IR (CH_2Cl_2, ν_{max})	: 3029, 2948, 2867, 2099, 2052, 1485, 1297, 757 cm^{-1}.
^1H NMR ($CDCl_3$, 300 MHz)	: δ 7.33 (m, 5H, ArH), 6.24 (t, 1H, CH $(NCS)_2$), 4.68 (brs, 1H, CHNCS), 2.26 (m, 4H, CH_2), 1.87 (m, 4H, CH_2).
^{13}C NMR ($CDCl_3$, 75 MHz)	: δ 139.72, 135.17, 135.07, 130.04, 129.16, 128.18, 126.30, 54.03, 31.07, 26.02, 17.96.

Methoxy isothiocyanate 90

A mixture of α-pinene (0.136 g, 1mmol) and ammonium thiocyanate (0.152 g, 2 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 30 min. The reaction mixture after work up and purification as per the general experimental procedure afforded **90** (0.135 g, 60 %) as a pale yellow liquid.

IR (CH_2Cl_2, ν_{max}) : 2982, 2928, 2079, 1465, 1378, 1324 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.63 (brs, 1H, olefinic), 4.08 (brs, H, CHNCS), 3.20 (s, 3H, CH_3), 2.09 (m, 2H, CH2), 1.93 (m, 2H, CH_2), 1.88 (brs, 3H, CH_3), 1.47 (m, 1H, -CH-), 1.12 (brs, 6H, isopropyl).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 132.12, 130.11, 126.99, 75.59, 57.18, 48.89, 36.14, 30.79, 26.67, 22.53, 22.38, 20.93.

General experimental procedure for the synthesis of phenacyl azides.

A mixture of styrene (1 mmol) and sodium azide (1.5 mmol) was dissolved in acetonitrile (5 mL) and CAN (1.26 g, 2.3 mmol) in acetonitrile (10 mL) was added to it dropwise with constant stirring at ice temperature. The reaction mixture was diluted with water (150 mL) after the decolorisation of the CAN solution (10-30 min.) and extracted with dichloromethane (5 x 20 mL). The combined organic extracts were washed with water and dehydrated using anhydrous sodium sulfate and evaporated off the solvent to afford the crude product mixture. It was then purified using silica gel column chromatography (100- 200 mesh) and 3% ethyl acetate-hexane as eluent to afford β-nitrato azides and phenacyl azides. When the reaction was repeated in methanol a mixture of β-methoxy and β-nitrato azides and the phenacyl azide was obtained. For the predominant formation of phenacyl azides, the reaction in methanol was done in an atmosphere of oxygen with solutions saturated with oxygen.

β-Nitrato azide 105 and β-keto azide 106

A mixture of styrene (0.104 g, 1 mmol) and sodium azide (0. 097 g, 1.5 mmol) was dissolved in acetonitrile (5 mL). CAN (1.26 g. 2.3 mmol) dissolved in acetonitrile (10 mL) was added to it dropwise with constant stirring for 10 min. It was then diluted with water (150 mL) and extracted with dichloromethane (5 x 15 mL). The solvent was evaporated off and the residue was purified by column chromatography (ethylacetate/hexane= 3:97) to afford β-nitrato azide **105** (0.104 g, 50 %) and β-keto azide **106** (0.040 g, 25 %) as pale yellow viscous liquids.

*Spectral data for **105***

IR (CH_2Cl_2, ν_{max}) : 3043, 2928, 2119, 1647, 1499, 1458, 1276 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.36 (s, 5H, ArH), 5.91 (dd, 1H, CH(ONO_2), J_1, J_2= 4.02, 8.49 Hz), 3.69 (dd, 1H, CH_2N_3, J_1, J_2= 8.58, 13.59 Hz), 3.49 (dd, 1H, CH_2N_3, J_1, J_2= 4.02, 13.56 Hz).

^{13}C NMR ($CDCl_3$, 75 MHz) :δ 134.65, 129.78, 129.10, 126.58, 83.49, 53.32.

*Spectral data for **106***

IR (CH_2Cl_2, ν_{max}) : 3063, 2921, 2106, 1694, 1593, 1452, 1283, 1222 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) :δ 7.90 (d, 2H, ArH), 7.58 (t, 1H, ArH), 7.49 (t, 2H, ArH), 4.56 (s, 2H, $COCH_2$).

^{13}C NMR ($CDCl_3$, 75 MHz) :δ 193.22, 134.46, 129.00, 128.85, 127.95, 54.91.

β-Nitrato azide 107 and β-keto azide 108

A mixture of 4-methyl styrene (0.118 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) was dissolved in acetonitrile (5 mL). CAN (1.26 g, 2.3 mmol) in acetonitrile (10 mL) was added to it dropwise with stirring. Worked up and purified according to the general experimental procedure to afford **107** (0. 156 g, 70 %) and **108** (0.026 g, 15 %) as yellow viscous liquids.

Spectral data for 107

IR (CH_2Cl_2, ν_{max}) : 3043, 2928, 2861, 2112, 1647, 1283 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.20 (m, 4H, ArH), 5.86 (dd, 1H, ($CHONO_2$), J_1, J_2 = 4.00, 8.49 Hz), 3.65 (dd, 1H, CH_2N_3, J_1, J_2 =8.62, 13.50 Hz), 3.44 (dd, 1H, CH_2N_3, J_1, J_2=4.04, 13.50 Hz), 2.32 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 139.77, 131.70, 129.78, 126.55, 83.41, 53.28, 21.15.

Spectral data for 108

IR (CH_2Cl_2, ν_{max}) : 2928, 2106, 1694, 1607, 1290, 1222 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.78 (d, 2H, ArH), 7.27 (d, 2H, ArH), 4.52 (s, 2H, $COCH_2$), 2.41 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 192.84, 145.21, 131.93, 129.67, 128.04, 54.78, 21.76.

β-Nitrato azide 109 and β-keto azide 110

A mixture of 4-acetoxy styrene (0.163 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) in acetonitrile (5 mL) was treated with CAN in acetonitrile (10 mL) with constant stirring in an ice bath. Worked up and purified the crude product mixture following the general experimental procedure to afford **109** (0.151 g, 60 %) and **110** (0.051 g, 23 %) as viscous yellow liquids.

Spectra data for 109.

IR (CH_2Cl_2, ν_{max}) : 2935, 2112, 1775, 1640, 1512, 1371, 1276 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz.) : δ 7.35 (d, 2H, ArH), 7.10 (d, 2H, ArH), 5.88 (dd, 1H, ($CHNO_2$), J_1, J_2= 3.89, 8.49 Hz), 3.66 (dd, 1H, CH_2N_3, J_1, J_2= 8.61, 13.53 Hz), 3.46 (dd, 1H, CH_2N_3, J_1, J_2 =3.92, 13.56 Hz), 2.28 (s, 3H, $COCH_3$).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 190.45, 168.70, 151.55, 132.04, 131.05, 127.70, 122.30, 82.58, 53.16, 20.93.

Spectral data for 110

IR (CH_2Cl_2, ν_{max}) : 2921, 2099, 1755, 1694, 1607, 1499, 1371, 1196 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.89 (d, 2H, ArH), 7.18 (d, 2H, ArH), 4.48 (s, 2H, $COCH_2$), 2.28 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 191.99, 168.55, 155.16, 129.71, 127.91, 122.32, 54.83, 21.19.

β-Methoxy azide 111, β-Keto azide 106 and β-Nitrato azide 105

A mixture of styrene (0.104 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). The reaction mixture was worked up and purified according to the general experimental procedure to afford the mixture of **105** and **111** (0.147 g, 28 % and 50 % respectively) as pale yellow liquid and **106** (0.024 g, 15 %) as a highly viscous pale yellow liquid.

Spectral data for the mixture of 105 and 111

IR (CH_2Cl_2, ν_{max}) : 3036, 2928, 2106, 1647, 1499, 1458 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.32 (m, 10H, ArH), 5.88 (dd, 1H, $CHONO_2$, J_1, J_2= 3.96, 8.43 Hz), 4.33 (dd, 1H, CHOMe, J_1, J_2=3.39, 8.43 Hz), 3.66 (dd, 1H, J_1, J_2 = 8.55, 13.5 Hz), 3.51 (dd, 1H,CH_2N_3, J_1, J_2=6.39, 14.46 Hz), 3.43 (dd, 1H, CH_2N_3, J_1, J_2= 3.99, 9.78 Hz), 3.25 (dd, 1H, CH_2N_3), 3.27 (s, 3H, OCH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 134.65, 129.76, 129.14, 129.10, 128.72, 128.16, 126.70, 126.54, 83.85, 56.89, 53.77.

β-Methoxy azide 112, β-Keto azide 108 and β-Nitrato azide 107

A mixture of 4-methyl styrene (0.118 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). Worked up and purified the crude reaction mixture according to the general experimental procedure to afford the mixture of **107** and **112** (0.155 g, 41.27 % and 33 %) as pale yellow liquid and **108** (0.025 g, 14 %).as a viscous yellow liquid.

Spectral data for the mixture of 107 and 112

IR (CH_2Cl_2, ν_{max}) : 2928, 2099, 1647,1512, 1452, 1276 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.15 (m, 8H, ArH), 5.86 (dd, 1H, $CHONO_2$, J_1, J_2= 4.02, 8.46 Hz), 4.30 (dd, 1H, CHOMe, J_1, J_2= 3.42, 8.43 Hz), 3.67 (dd, 1H, CH_2N_3, J_1, J_2= 8.61, 13.48 Hz), 3.44 (m, 2H, CH_2N_3), 3.26 (s, 3H, OCH_3), 3.15 (dd, 1H, CH_2N_3), 2.30 (d, 6H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 139.86, 138.20, 135.58, 131.63, 129.79, 129.40, 126.65, 126.57, 83.43, 83.00, 53.88, 53.29, 21.19, 21.14.

β-Methoxy azide 113, β-Keto azide 110 and β-Nitrato azide 109

A mixture of 4-acetoxy styrene (0.163 g, 1mmol) and sodium azide (0.097 g, 1.5 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). The reaction mixture on processing according to the general experimental procedure afforded a mixture of **109** and **113** as

pale yellow liquid and **110** (0.048 g, 22 %) as a highly viscous yellow liquid. The mixture of **109** and **113** when subjected to a second column chromatography using petroleumether-ethylacetate (2:98) mixture as eluent afforded **113** (0.100 g, 42 %) as pale yellow liquid.

Spectral data for 113

IR (CH_2Cl_2, ν_{max}) : 2935, 2827, 2106, 1769, 1512, 1378, 1202 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.23 (d, 2H, ArH), 7.00 (d, 2H, ArH), 4.26 (dd, 1H, CHOMe), J_1, J_2= 3.24, 3.26 Hz), 3.36 (dd, 1H, CH_2N_3, J_1, J_2= 8.55, 8.58 Hz), 3.22 (s, 3H, OCH3), 3.06 (dd, 1H, CH_2N_3, J_1, J_2= 3.17, 3.19 Hz), 2.21 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 168.88, 150.64, 138.10, 127.59, 121.81, 82.71, 56.69, 20.97.

Phenacyl azide 115

A mixture of 4-chlorostyrene (0.138 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) dissolved in methanol (5 mL) was flushed with oxygen. CAN (1.26 g, 2.3 mmol) in methanol (10 mL) saturated with oxygen was added to it dropwise with constant stirring in an ice bath. The reaction mixture was worked up after 30 minutes to afford **115** (0.135 g, 69 %) as pale yellow highly viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 3588, 3376, 3125, 2103, 1698, 1583, 1274 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.81 (m, 2H, ArH), 7.46 (m, 2H, ArH), 4.50 (s, 2H, CH_2N_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 191.12, 140.55,130.78, 129.24, 128.69, 127.87, 53.85.

Phenacyl azide 117

4-Nitro styrene (0.149g, 1mmol) and sodium azide (0.097 g, 1.5 mmol) were dissolved in 5 mL methanol and treated with CAN (1.26 g, 2.3 mmol) in 10 mL methanol in an atmosphere of oxygen at ice temperature. The reaction mixture after work-up and purification afforded **117** as a yellow viscous liquid (0.140 g, 68 %).

IR (CH_2Cl_2, ν_{max}) : *3090, 2928, 2106, 1715, 1613, 1533,* 1357 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 7.73 (m, 2H, ArH), 7.52 (d, 2H, ArH), 4.63 (s, 2H, CH_2).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 191.63, 132.20, 129.76, 123.27, 121.21, 53.14.

Phenacyl azide 119

A mixture of 4-acetamido styrene (0.161 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) was dissolved in methanol (5 mL). The cooled reaction mixture was saturated with oxygen and CAN (1.26 g, 2.3 mmol) was added to it dropwise with constant stirring in an atmosphere of oxygen. The reaction mixture was worked up after 45 min. according to the general experimental procedure and purified to afford the phenacyl thiocyanate **119** as a white powder (0.150 g, 68 %).

IR (KBr, ν_{max}) : 3494, 2261, 2106, 1742, 1674, 1249 cm^{-1}.

^1H NMR (Acetone-D_6, 300 MHz) : δ 7.86 (d, 2H, ArH), 7.75 (d, 2H, ArH), 4.64 (s, 2H, CH_2).

^{13}C NMR (Acetone-D_6, 75 MHz) : δ 191.21, 169.52, 143.40, 128.31, 128.06, 117.50, 117.42, 53.31, 22.65.

Phenacyl azide 121

A mixture of 4-methoxy styrene (0.136 g, 1 mmol) and sodium azide (0.097 g, 1.5 mmol) was dissolved in methanol (5 mL) and CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added to it dropwise with constant stirring in an atmosphere of oxygen at ice temperature. The reaction mixture on processing and purification according to the general experimental procedure afforded **121** as a colorless amorphous solid (0.181 g, 95%).

IR (KBr, ν_{max}) : 3063, 2982, 2106, 1674, 1600, 1276 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.78 (d, 2H, ArH), 6.92 (d, 2H, ArH), 4.44 (s, 2H, CH_2), 3.84 (s, 3H, OCH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 190.40, 164.14, 131.85, 130.16, 114.05, 57.98, 55.08.

Phenacyl azide 122

A mixture of 1-vinyl naphthalene (0.154 g, 1 mmol) and sodium azide (1.5 mmol) dissolved in methanol (5 mL) was treated with CAN (1.26

g, 2.3 mmol) in methanol (10 mL) under oxygen atmosphere to afford the phenacyl azide **122** (0. 117 g, 60 %) as a pale yellow viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 3052, 2961, 2099, 1690, 1262, 1103, 1024 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.50 (m, 7H, ArH), 4.40 (s, 2H, CH_2).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 196.42, 133.78, 128.30, 127.96, 126.66, 126.25, 125.54, 57.18.

β-Nitrato azide 124

1-Octene (1 mmol) and sodium azide (1.5 mmol) were dissolved in acetonitrile (5mL). The reaction mixture was cooled to ice temperature and CAN (1.26 g, 2.3 mmol) in acetonitrile (10 mL) was added to it dropwise to afford **124** as a pale yellow liquid (0.055 g, 34 %).

IR (CH_2Cl_2, ν_{max}) : 2969, 2935, 2106, 1640, 1465, 1283 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.08 (m, 1H, $CHONO_2$), 3.47 (m, 2H, CH_2N_3), 1.69 (brs, 2H, CH_2), 1.34 (brs, 8H, CH_2), 0.87 (brs, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 81.00, 52.14, 31.35, 30.11, 28.87, 24.88, 22.44, 13.96.

β-Nitrato azide 125

A mixture of phenyl cyclohexene (0.158 g, 1 mmol) and sodium azide was dissolved in acetonitrile (5 mL). CAN (1.26 g, 2.3 mmol) in CH_3CN was added to it dropwise with constant stirring at ice temperature. The

reaction mixture after work up and purification afforded **125** (0.079 g, 30 %) as a pale yellow liquid.

IR (CH_2Cl_2, ν_{max}) : 2942, 2867, 2099, 1640, 1458, 1283 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.37 (m, 5H, ArH), 3.87 (m, 1H, CHN_3), 1.75 (m, 8H, CH_2).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 128.84, 128.80, 127.52, 126.91, 125.09, 67.16, 39.77, 27.50, 25.00, 21.40, 20.13.

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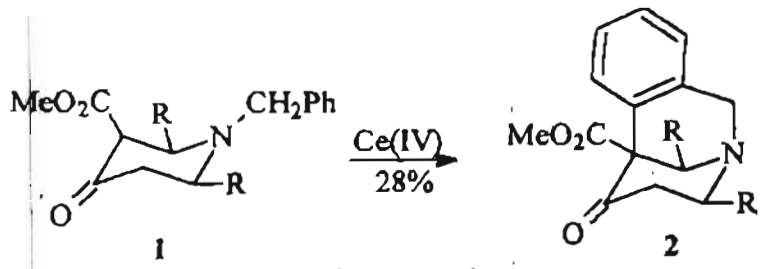
CHAPTER IV

CERIUM (IV) AMMONIUM NITRATE MEDIATED OXYGENATION OF DIALKYL MALONATES : A NOVEL SYNTHESIS OF TARTRONIC ACID DERIVATIVES

4.1. INTRODUCTION

Investigations in our laboratory[1-3] and elsewhere[4-6] have clearly established the usefulness of cerium (IV) ammonium nitrate (CAN) as a versatile reagent in intermolecular carbon-carbon bond forming reactions. The reagent has been successfully used in the synthesis of dihydrofurans, lactones etc. Naturally it was of interest to explore its use in intramolecular reactions. It may be recalled that $Mn(OAc)_3$ has been used effectively in intramolecular reactions leading to complex carbocyclic constructions by Snider[7-9] and others.[10-18] A survey of the literature concerned with the use of Ce(IV) reagents in intramolecular reactions was carried out and the available information is presented here.

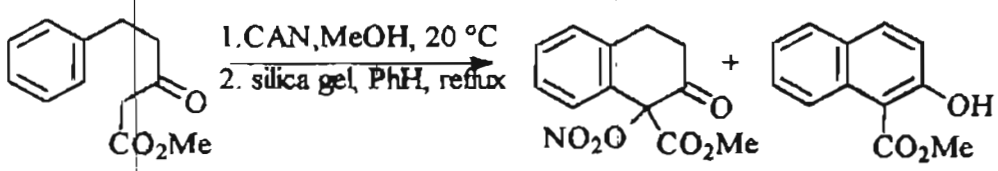
The first report on the Cerium (IV) mediated intramolecular reaction is the cyclization of 1-benzyl-2,6-disubstituted-4-piperidone-3-carboxylic acid methyl ester with $Ce(SO_4)_2$ in low yield[19] (Scheme 1).



1 2

Scheme 1

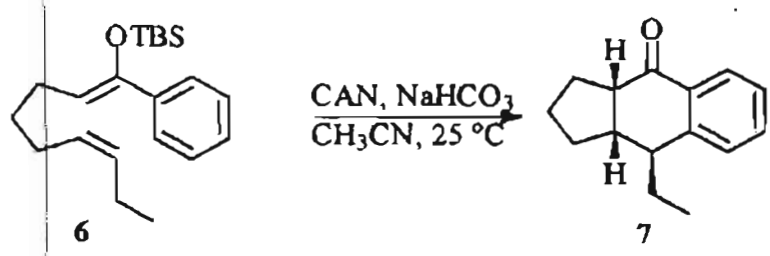
Synthesis of substituted 2-hydroxy-1-naphthoic acid esters and amides by oxidation of 5-aryl-3-oxopentanoic acid esters or amides with manganese (III) acetate or Cerium (IV) ammonium nitrate *via* the intramolecular cyclization of the radical formed from the 1, 3-dicarbonyl compounds is known. [20] A representative example is given in Scheme 2.



3 4 5

Scheme 2

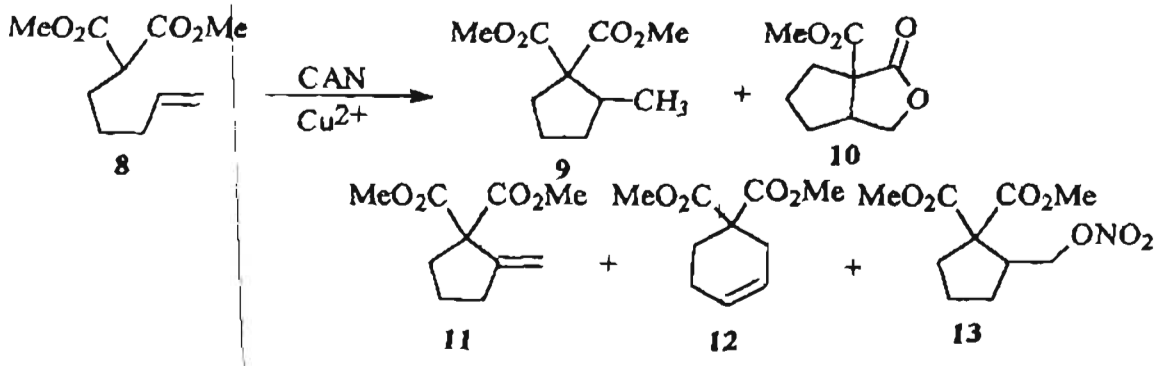
CAN promoted oxidative cyclization of silyl enol ethers of aryl ketones provided tricyclic ketones[21] as shown in Scheme 3.



6 7

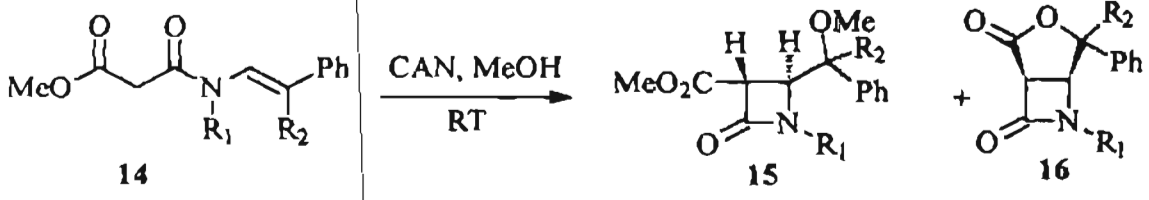
Scheme 3

Oxidative cyclization of dimethyl-4-pentenyl malonate with CAN in methanol and acetic acid in presence of Cu salts afforded a mixture of products[22] as illustrated in Scheme 4.



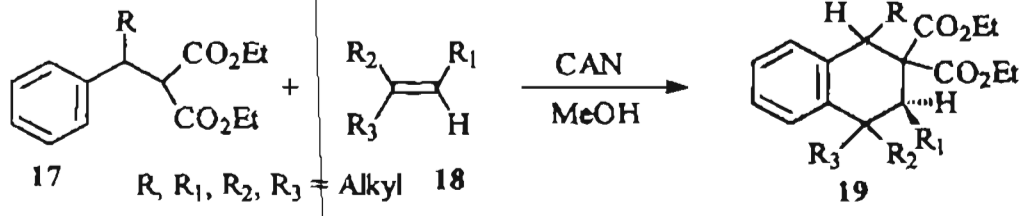
Scheme 4

Precursors of pharmacologically important β-lactams such as Thienamicin and PS-5 can be synthesized by the CAN mediated free radical cyclization reactions of α-methoxy carbonyl acetyl enamides and aceto acetyl enamides.[23] An example of the formation of functionalized β-lactams[24] with CAN in methanol is given in Scheme 5.



Scheme 5

Besides the intramolecular cyclization reactions, CAN mediated tandem annulation reactions are also known. An example[25] is provided in Scheme 6.

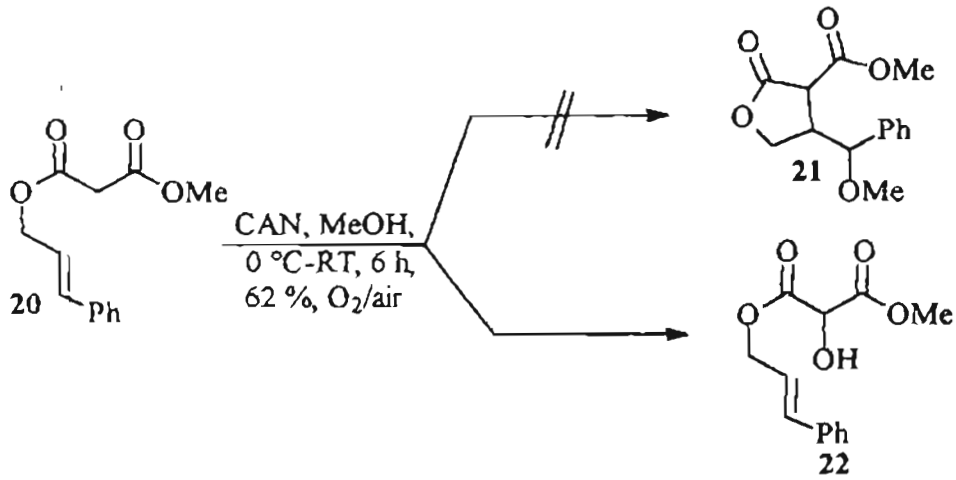


Scheme 6

It is evident from the foregoing literature survey that very little work has been done towards exploiting CAN as a reagent for intramolecular carbon-carbon bond forming reactions. Therefore, as a logical extension of our work with CAN in intermolecular reactions, it was decided to investigate the use of CAN in intramolecular reactions. Our attempts to achieve intramolecular cyclization, however, resulted in the formation of the hydroxylated product and the results are discussed in the following section.

4.2. RESULTS AND DISCUSSION

Our initial experiment was with cinnamyl methyl malonate **20** which on treatment with CAN in methanol was expected to give lactone **21**. Surprisingly no cyclization occurred and instead we obtained a hydroxylated product, which was characterized as the tartronic acid derivative **22** in 62 % yield (Scheme 7).[26]



Scheme 7

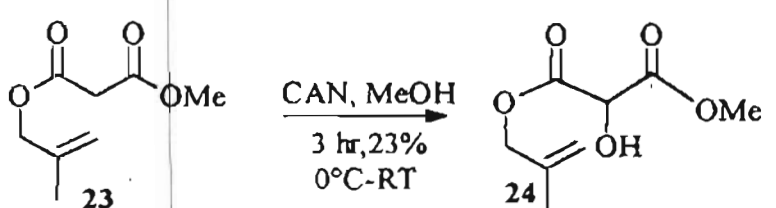
The product **22** was purified by chromatography on silica gel column using hexane-ethylacetate as eluent and was characterized by spectroscopic and analytical methods. The IR spectrum of **22** showed the hydroxyl group absorption at 3432 cm^{-1}. In the proton NMR, the proton attached to the carbon bearing hydroxyl group resonated along with the hydroxyl proton and the allylic protons as a multiplet between δ 4.81. The ^{13}C NMR spectrum displayed a signal at δ 90.70 characteristic for a methine bearing the –OH group. Mass spectral data also agree with the assigned structure.

Although the reason for the failure of cyclization is unclear, it may be speculated that the methine radical is a metal bound species and not a

genuine free radical. It is conceivable that steric encumbrance of the metal coordinated intermediate may make the cyclization prohibitive. Molecular oxygen present in the reaction mixture can cleave the co-ordination bond resulting in the formation of peroxy radical which undergoes further transformations to the hydroxylated product (*vide infra* Scheme 13, p-122 also).

Although the expected cyclization did not occur, it was decided to pursue this reaction since tartronic acids are important compounds and there is no easy and direct route to synthesise them.[27]

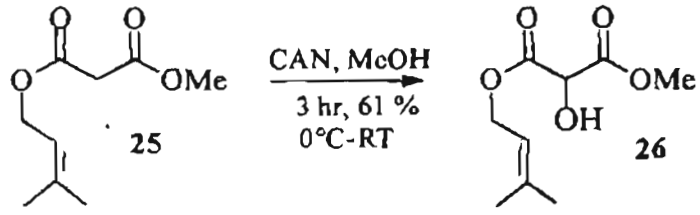
Treatment of 2-methyl propenyl methyl malonate **23** with CAN in methanol also gave the corresponding tartronic acid derivative in 23 % yield (Scheme 8).



Scheme 8

The IR spectrum of **24** showed the hydroxyl group absorption at 3454 cm^{-1}. In the ^{1}H NMR spectrum, the proton attached to the carbon bearing the hydroxyl group resonated along with the hydroxyl proton as a broad singlet at δ 4.70. The ^{13}C NMR spectrum showed the characteristic signal due to the carbon bearing the hydroxyl group at δ 90.36. Analytical data was also in agreement with the assigned structure.

A similar reaction was observed with 2-methyl-2-butenyl methyl malonate **25** and CAN in methanol and the product was obtained in 61 % yield (Scheme 9).

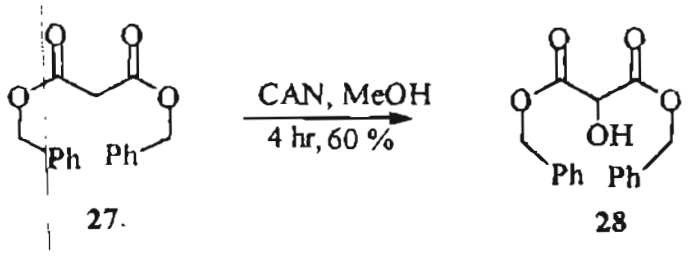


25 26

Scheme 9

The IR spectrum of **26** showed the characteristic hydroxyl absorption at 3461 cm^{-1}. In the ^1H NMR spectrum, the hydroxyl proton and the proton on the carbon bearing it together displayed a broad singlet at δ 4.81. The characteristic resonance of tertiary carbon bearing the hydroxyl group was visible at δ 90.10 in the ^{13}C NMR spectrum.

Since this reaction was found to be an efficient method for the synthesis of tartronic acid derivatives, the reaction was extended to some other diesters. The reaction of dibenzyl malonate **27** with CAN in methanol afforded the hydroxylated product, dibenzyl tartronate **28** in 60 % yield (Scheme 10).



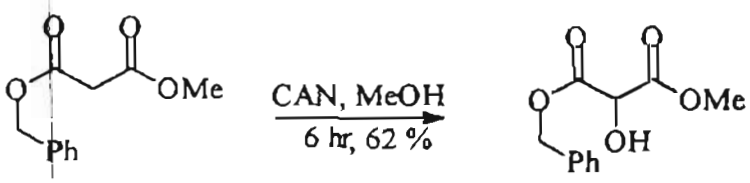
27 28

Scheme 10

The IR spectrum of **28** showed the hydroxyl absorption at 3461 cm^{-1}. The hydroxyl proton resonated as a broad singlet at δ 4.82 along with the

proton on the carbon attached to it. The ^{13}C NMR spectrum displayed a signal at δ 90.30 characteristic of the methine bearing hydroxyl group.

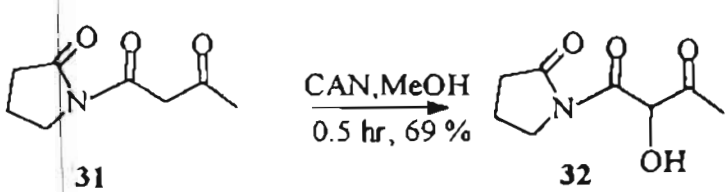
Similar reactivity was observed with benzyl methyl malonate **29** giving the corresponding tartronic acid derivative **30** in 62 % yield (Scheme 11). As in the previous cases the spectral data were diagnostic for **30**.



29 **30**

Scheme 11

The β-keto amide (1- (2-oxo pyrrolidin-1-yl) 1,3-butane dione) **31** also when treated with CAN in methanol afforded the product **32** in 69 % yield (Scheme 12).

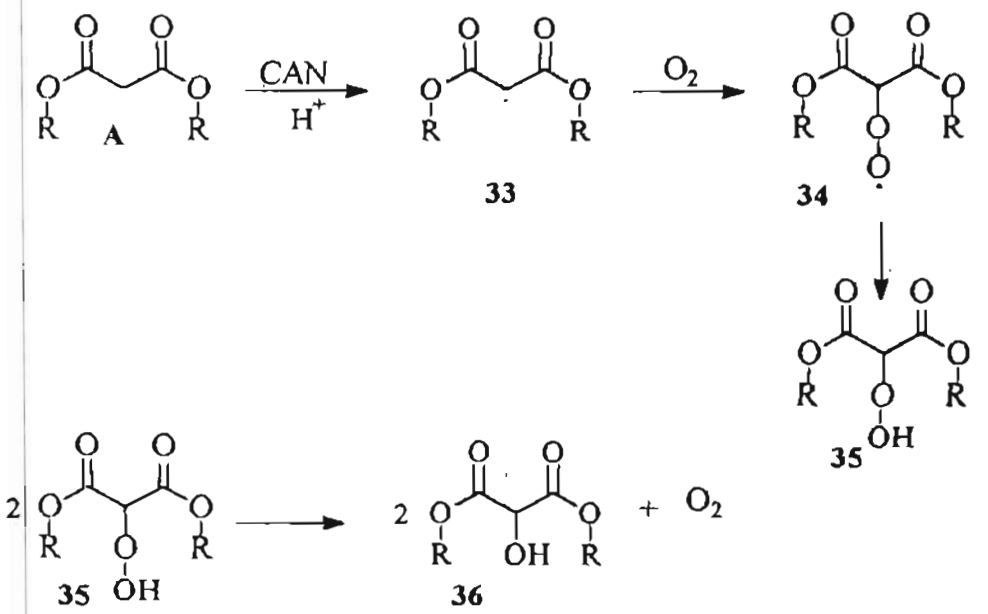


31 **32**

Scheme 12

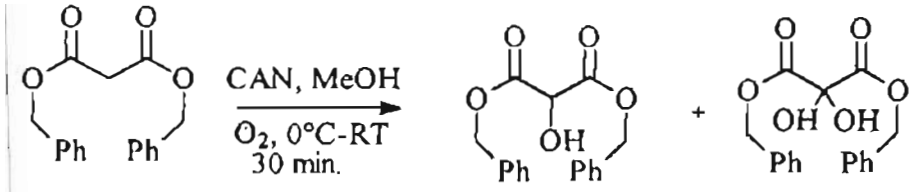
The IR spectrum of **32** showed the characteristic hydroxyl group absorption at 3394 cm^{-1}. In the ^1H NMR spectrum, the hydroxyl proton displayed a broad singlet at δ 1.62. The proton geminal to the hydroxyl group resonated as a broad singlet at δ 5.34. The characteristic resonance of tertiary carbon bearing the hydroxyl group was visible at δ 96.08 in the ^{13}C NMR spectrum.

In the light of the recent elucidation of the mechanism of oxidation of malonic acid by cerium (IV),[28] the oxygenation observed may be rationalized as follows (Scheme 13). The proposed mechanism invokes the formation of the peroxy intermediate **34** derived from the reaction of atmospheric oxygen with the malonyl radical.[29]



Scheme 13

In order to establish the mechanism of oxygenation of the β-keto esters leading to the formation of tartronic acid derivatives, the experiment with dibenzyl malonate was carried out in an oxygen atmosphere, in methanolic solution saturated with oxygen. In this case the formation of an additional product was observed and it was tentatively assigned the structure 37 (Scheme 14).



27 28 37

Scheme 14

The IR spectrum of **37** showed the hydroxyl absorption at 3339 cm^{-1} and the carbonyl at 1755 cm^{-1}. In the ^{1}H NMR spectrum, the hydroxyl protons were visible as a broad singlet at δ 3.75. The ^{13}C NMR spectrum displayed a singlet at δ 95.36 due to the carbon bearing two hydroxyls; the ester carbonyls resonated at δ 168.75 and at δ 167.49.

It is noteworthy that the reaction occurs at a faster rate in presence of oxygen. The reaction is complete within 30 min. in oxygenated atmosphere whereas it generally needs more than 3 hrs in atmospheric conditions. In addition, the yield of the hydroxylated product is higher in the former case. These observations also lend support to the suggested mechanism involving molecular oxygen.

4.3. EXPERIMENTAL DETAILS

A general write up of the experimental is given in chapter II (Section 2.3). The β-keto esters were prepared following the literature procedure.[30,31]

Synthesis of Tartronic acid derivatives : General procedure

A solution of CAN (1.26 g, 2.3 mmol) in methanol (10 mL) was added dropwise to an ice cooled, stirred mixture of the ester or amide (1 mmol) in methanol (5 mL). The reaction mixture after decolorisation was diluted with water (150 mL) and extracted with dichloromethane (5 x 10 mL) The combined organic extracts were washed with water, then with brine, dried over anhydrous sodium sulphate and the solvent was evaporated off. The residue obtained was subjected to chromatography on silica gel column. Elution with appropriate combination of ethylacetate and petroleum ether afforded the tartronic acid derivatives as colorless viscous liquids.

Hydroxy cinnamyl methyl malonate 22

A solution of cinnamyl methyl malonate **20** (0.470 g, 2 mmol.) in methanol (30 mL) was treated with CAN (2.252 g, 6.9 mmol.) in methanol (50 mL) for 6 hrs (ice temperature-room temperature). The reaction mixture was worked up following the general experimental procedure and the residue was purified by column chromatography. Elution with 30 % ethylacetate in petroleum ether furnished **22** (0.311 g, 62 %) as a colorless viscous liquid.

IR (neat, ν_{max}) : 3432, 2962, 1760, 1739, 1450 cm^{-1}

^{1}H NMR ($CDCl_3$, 90 MHz) : δ 7.40 (m, 5H, ArH), 6.45 (m, 2H, olefinic), 4.81 (m, 4H), 3.86 (s, 3H, $COOCH_3$).

^{13}C NMR ($CDCl_3$, 22.4 MHz) : δ 168.50, 167.90, 135.60, 135.10, 128.40, 128.10, 126.50, 121.30, 90.70, 67.30, 53.60.

GC-MS : m/z 248 (M^+-2, 5), 192 (2), 175 (3), 161 (6), 117 (100).

Hydroxy compound 24

The 2-methyl propenyl methyl malonate **23** (0.172 g, 1 mmol) in methanol (15 mL) was treated with CAN (1.26 g, 2.3 mmol.) in methanol (20 mL) for 3 hrs. The reaction mixture after work up and purification following the general experimental procedure afforded **24** (0. 044 g, 23 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 3454, 2960, 1750, 1448, 1239 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 5.10 (brs, 2H, olefinic), 4.70 (s, 2H, CHOH), 3.90 (s, 3H, OCH_3).

^{13}C NMR ($CDCl_3$, 75MHz) : δ 168.71, 167.93, 138.37, 114.08, 90.36, 70.07, 53.75, 18.97.

Hydroxy compound 26

The 2-methyl-2-butenyl methyl malonate **25** (0.087 g, 0.5 mmol) in methanol (5 mL) was treated with CAN (0.63 g, 1.15 mmol) in methanol (10 mL) for 3 hrs. The reaction mixture on processing according to the general

experimental procedure afforded **26** (0.116 g, 61 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 3461, 2962, 2921, 1748, 1452, 1276, 1243 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.30 (t, 1H, olefinic), 4.81 (brs, 2H, CHOH), 4.73 (d, 2H, CH_2), 3.86 (s, 3H, OCH_3), 1.76 (s, 3H, CH_3), 1.71 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 168.77, 168.13, 117.11, 115.42, 90.10, 64.01, 53.77, 50.20, 25.70, 18.00.

Hydroxy dibenzyl malonate 28

Dibenzyl malonate **27** (0.284 g, 1 mmol) in methanol (15 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (20 mL) for 4 hrs (ice temperature-room temperature). The reaction mixture was worked up following the general experimental procedure and the residue on purification *via* silica gel column using 35 % ethylacetate and petroleum ether afforded **28** (0.180 g, 60 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max}) : 3461, 3036, 2962, 1748, 1458, 1229 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.29 (m, 10 H, ArH), 5.19 (m, 4H), 4.82 (brs, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 168.10, 134.10, 128.67, 128.61, 128.27, 90.30, 68.90, 68.40, 66.40, 53.89.

Analysis calcd. for $C_{17}H_{16}O_5$ C -67.99 %, H - 5.37 %

Found : C - 68.20 %, H - 5.48 %.

Hydroxy benzyl methyl ester 30

Benzyl methyl malonate **29** (0.521 g, 2.5 mmol) was dissolved in methanol (30 mL) and reacted with CAN (3.15 g, 5.75 mmol) in methanol (40 mL) for 6 hrs. The reaction mixture, after work up and purification by column chromatography (petroleum ether: ethyl acetate, 7:3) afforded **30** (0. 493 g, 82 %) as a colorless viscous liquid.

IR (neat, ν_{max})	: 3459, 1749, 1455, 1234, 1112 cm^{-1}.
^1H NMR ($CDCl_3$, 90 MHz)	: δ 7.36 (s, 5H, ArH), 5.31 (s, 2H, OCH_2), 4.87 (brs, 2H, CHOH), 3.75 (s, 3H, $COOCH_3$).
^{13}C NMR ($CDCl_3$, 22.4 MHz)	: δ 168.3, 167.7, 134.2, 128.1, 127.7, 90.6, 68.1, 53.2.
GC-MS	: m/z 222 (M^+- 2, 5), 119 (2), 105 (6) , 91 (100).

Hydroxy compound 32

1-, (2-oxo pyrrolidin-1-yl) 1,3-butane dione **31** (0.169 g, 1 mmol) dissolved in methanol (15 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (20 mL) for 30 min. The reaction mixture on work up and purification as usual afforded **32** (0.127 g, 69 %) as a colorless viscous liquid.

IR (CH_2Cl_2, ν_{max})	: 3394, 2970, 1793, 1741, 1769, 1719, 1363 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 5.34 (brs, 1H, CHOH), 3.87 (m, 2H, CH_2 (N)), 2.59 (t, 2H, $COCH_2$), 2.35 (s, 3H, CH_3), 2.15 (m, 2H, CH_2) 1.62 (brs, 1H, OH).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 202.28, 175.95, 170.20, 96.08, 45.08, 32.76, 27.16, 17.63.

Dihydroxy compound 37

A solution of the dibenzyl ester **27** (0.274 g, 1 mmol) in methanol (15 mL) was saturated with oxygen and then treated with a methanolic solution (20 mL) of CAN (1.26g, 2.3 mmol) saturated with oxygen. Oxygen gas was bubbled through the reaction mixture throughout the experiment. After the complete conversion of the ester (30 min.) the reaction mixture was processed as usual to afford **28** (0.057 g, 20 %) and **37** (0.186 g, 62 %) as colorless viscous liquids.

Spectral data for 37

IR (CH_2Cl_2, ν_{max}) : 3339, 3029, 2867, 1755, 1458, 1216 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.23 (brs, 10 H, ArH), 4.43 (s, 4H, CH_2), 3.75 (brs, 2H, OH)

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 168.75, 167.49, 141.25, 135.05, 128.70, 128.57, 127.68, 127.30, 95.36, 68.38, 64.91.

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CHAPTER V

CERIUM (IV) AMMONIUM NITRATE MEDIATED OXIDATION OF STYRENES AND ALDEHYDES IN DRY METHANOL: CONVERSION OF STYRENES TO METHOXY ACETOPHENONES AND ALDEHYDES TO METHYL ESTERS

5.1. INTRODUCTION

Cerium (IV) compounds, in particular, ceric ammonium nitrate (CAN), have been utilized extensively for a variety of oxidative transformations.[1] There are a number of reports concerned with the use of CAN in carbon-carbon bond forming reactions.[2,3] Subsequent to our studies on the carbon-carbon and carbon-heteroatom bond forming reactions, we have done some preliminary investigations on the direct oxidation of styrenes and aldehydes and the results are presented in this chapter.

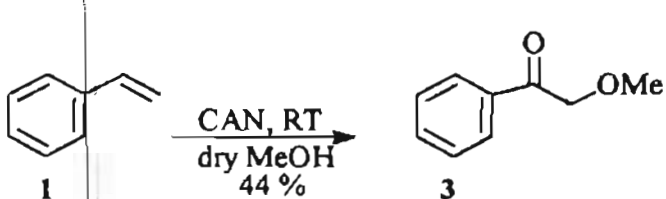
5.2. RESULTS AND DISCUSSION

5.2.1. Direct conversion of Styrenes to Methoxy Acetophenones.

It is known in the literature that styrene can be converted to the corresponding dinitrate when treated with CAN in acetonitrile[4] (Scheme 1).

Scheme 1

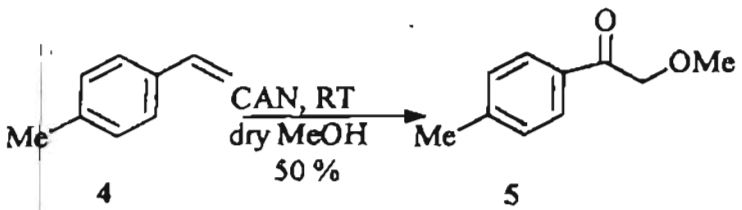
It was interesting to see the outcome of the above reaction in methanol. A solution of styrene in dry methanol when treated with CAN, also in dry methanol afforded the product **3** in 44 % yield (Scheme 2).



Scheme 2

The product was characterized on the basis of IR and ^{1}H NMR analysis. The IR spectrum of **3** showed the characteristic benzoyl carbonyl at 1701 cm^{-1}. In the ^{1}H NMR spectrum of **3**, the methoxy protons resonated as a sharp singlet at δ 3.51. The protons on the terminal carbon bearing the methoxy group displayed a sharp singlet at δ 4.71.

Treatment of 4-methyl styrene **4** with CAN in dry methanol also afforded the corresponding methoxy acetophenone **5** in 50 % yield (Scheme 3).

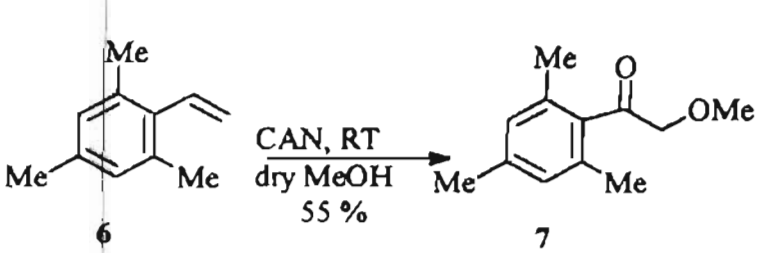


4 5

Scheme 3

The IR spectrum of **5** showed the carbonyl absorption at 1699 cm^{-1}. The protons on the terminal carbon bearing methoxy group resonated as a sharp singlet at δ 4.68 and the methoxy protons displayed a signal at δ 3.50 as a sharp singlet. The carbonyl carbon displayed a signal at δ 195.80 in the ^{13}C NMR spectrum.

The reaction of mesityl styrene **6** with CAN in methanol afforded a product in 55 % yield which is tentatively assigned the structure **7** (Scheme 4).

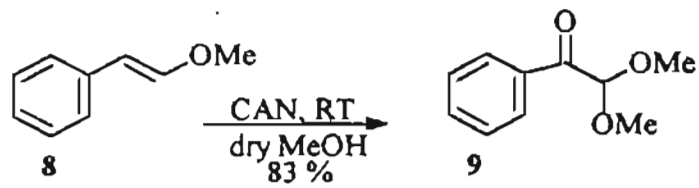


6 7

Scheme 4

The structure assignment is based on IR and ^1H NMR spectra. IR spectrum of **7** showed the carbonyl group absorption at 1715 cm^{-1}. The ^1H NMR spectrum displayed a signal due to the protons on the terminal carbon at δ 4.30 and the methoxy group protons resonated at δ 3.50.

Styrenes with olefinic substitution also showed similar reactivity profile. For example, the reaction of β-methoxy styrene **8** with CAN in dry methanol afforded **9** in 83 % yield (Scheme 5).

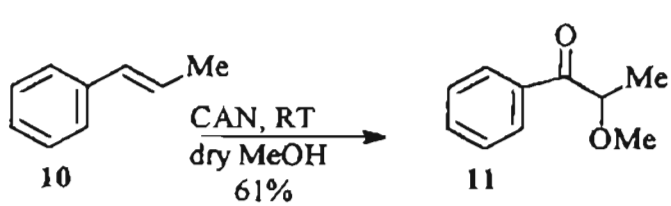


8 9

Scheme 5

The structure was assigned on the basis of IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The IR spectrum of **9** showed the characteristic carbonyl absorption at 1694 cm^{-1}. The proton on the terminal carbon bearing two methoxy groups resonated as a singlet at δ 5.23. The six protons of the two methoxy groups resonated as two overlapping singlets at δ 3.47. ^{13}C NMR spectrum displayed the signal due to the carbonyl at δ 193.39 and the terminal carbon resonated at δ 103.81. GC-MS showed the (M^{+}-1) peak at *m/z* 179.

Treatment of β-methyl styrene **10** with CAN in dry methanol afforded a product which is tentatively assigned as **11** on the basis of IR, ^{1}H NMR and mass spectral data (Scheme 6).



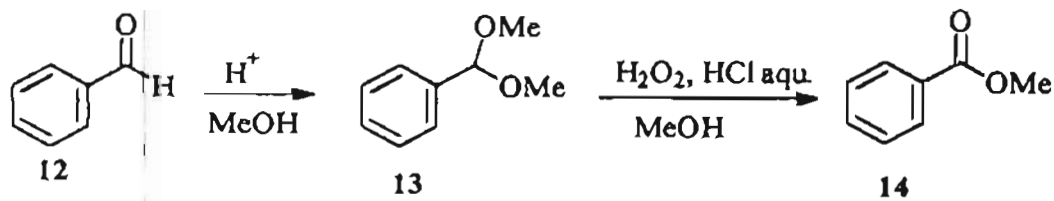
10 11

Scheme 6

The IR spectrum of **11** showed the characteristic carbonyl absorption at 1694 cm^{-1}. The proton on the carbon bearing methoxy and methyl group resonated at δ 4.50 as a singlet. The methoxy protons resonated at δ 3.49 and those of methyl at δ 1.26. The EIMS showed the (M^{+}-CH_3) peak at *m/z* 149.

5.2.2. One pot conversion of Aldehydes to Esters

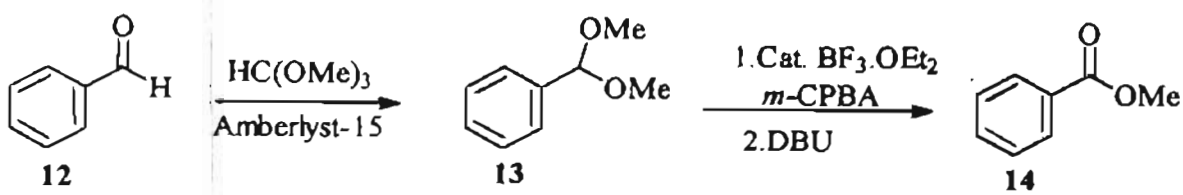
A number of methods for the conversion of aldehydes to carboxylic acids[5] and esters[6] are known. Oxidation of aldehydes to esters using peracetic acid,[7] peroxymonosulfuric acid,[8] ozone,[9] N-bromosuccinimide[10] and chromium trioxide[11] have been reported. Conversion of acetals and aldehydes to esters was achieved with hydrogen peroxide and hydrochloric acid in alcohol by Takeda[12] (Scheme 7).



12 13 14

Scheme 7

In a very recent report, aldehydes were converted to the corresponding methyl esters through dimethyl acetal formation with trimethyl ortho formate followed by oxidation with *m*-CPBA and DBU[13] (Scheme 8).

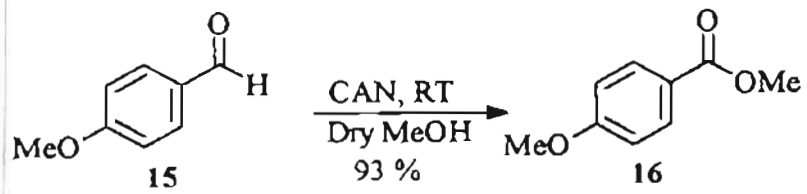


12 13 14

Scheme 8

With the assumption that a hemiacetal resulting from an aldehyde and methanol would undergo oxidation by CAN to afford the corresponding methyl ester, we have carried out some preliminary investigations and the results are presented in the following section.

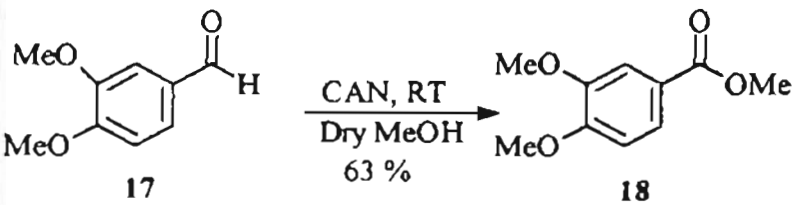
Our initial experiment involved anisaldehyde; when anisaldehyde **15** in dry methanol was treated with CAN in dry methanol at room temperature, the corresponding ester **16** was obtained in 93 % yield (Scheme 9). [13]



Scheme 9

The IR spectrum of **16** showed the characteristic ester carbonyl of methyl-4-methoxy benzoate at 1716 cm^{-1}. In the ^1H NMR spectrum, the two methoxy groups resonated at δ 3.86 and 3.82 as sharp singlets. ^{13}C NMR spectrum displayed the signal due to the carbonyl group at δ 166.83.

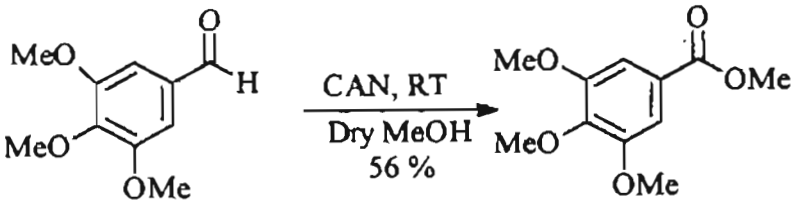
Treatment of 3,4-dimethoxy benzaldehyde (veratral **17**) with CAN in dry methanol at room temperature also afforded the corresponding methyl ester **18** in 63 % yield (Scheme 10)



Scheme 10

The ester **18** was characterized on the basis of IR, ^1H NMR spectral analysis.

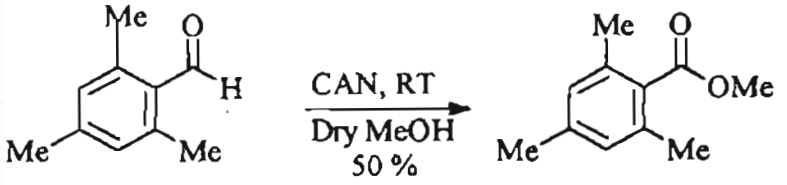
Similar reactivity was shown by 3, 4, 5-trimethoxy benzaldehyde **19** affording the ester **20** in 56 % yield (Scheme 11).



19 20

Scheme 11

When 2,4,6-trimethyl benzaldehyde (mesitaldehyde **21**) was treated with CAN in dry methanol, the corresponding ester **22** was obtained in 50 % yield (Scheme 12).



21 22

Scheme 12

The structure of the ester **22** was established on the basis of IR and mass spectral analysis. The IR spectrum showed the characteristic ester carbonyl at 1735 cm^{-1}. In all these cases, the aldehyde was not completely used up. The yields are based on the reacted aldehyde.

In conclusion, we have encountered a simple and rapid one-pot procedure for the conversion of aldehydes to esters and styrenes to methoxy acetophenones. Although preliminary in nature, the results obtained appear quite interesting and therefore worthy of further investigations.

5.3. EXPERIMENTAL DETAILS

General information about the experimental is given in Chapter II (Section 2.3).

Styrene, *p*-methyl styrene, β-methyl styrene and β-methoxy styrene were purchased from Aldrich. The other styrenes were prepared from the corresponding aldehyde by Wittig olefination reaction. The aldehydes used were purchased from local sources. Dry methanol was used in all the experiments.

Preparation of the methoxy-2-(oxo)-2-phenyl ethanes from styrenes: General procedure.

A solution of CAN (1.26 g, 2.3 mmol) in dry methanol (5 mL) was added dropwise to the solution of styrene (1mmol) in 10 mL dry methanol with constant stirring. After complete decolorisation of the CAN solution, the reaction mixture was diluted with water (100 mL) and extracted with dichloromethane (5 x 10 mL). The combined organic extracts were washed with water, saturated brine and dried over anhydrous sodium sulfate. It was then filtered and the solvent was evaporated off. The residue obtained on silica gel column chromatography using petroleum ether-ethyl acetate mixture (in the ratio 9:1 unless otherwise specified) as eluent afforded the ester.

1-Methoxy-2-(oxo)-2-phenyl ethane 3

A solution of styrene **1** (0.104 g, 1 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 24 hrs. The reaction mixture after work up and purification afforded **3** (0.066 g, 44 %) as colorless oil.

IR (CH_2Cl_2, ν_{max}) : 2928, 2820, 1701, 1640, 1445 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz) : δ 7.92 (t, 2H, ArH,), 7.49 (m, 3H, ArH,), 4.71 (s, 2H, CH_2), 3.51 (s, 3H, OCH_3).

1-Methoxy-2-(oxo)-2-(4-methyl phenyl) ethane 5

A solution of 4-methyl styrene **4** (0.118 g, 1mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 2hrs. The reaction mixture after processing and purification afforded **5** (0.082 g, 50 %) as a colorless liquid.

IR (CH_2Cl_2, ν_{max}) : 2940, 2830, 1699, 1620 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz) : δ 7.83 (d, 2H, ArH), 7.26 (d, 2H, ArH), 4.68 (s, 2H, CH_2), 3.50 (s, 3H, OCH_3), 2.41 (s, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 195.80, 144.45, 132.41, 129.40, 127.96, 75.24, 59.42, 21.71.

GC-MS : m/z 164 (M^+, 2), 134 (5), 119 (65), 91 (45), 86 (48), 84 (75), 51 (35), 49 (100).

1-Methoxy-2-(oxo)-2- (2, 4, 6-trimethyl phenyl) ethane 7

2,4,6-Trimethyl styrene **6** (0.146 g, 1 mmol.) dissolved in methanol (5 mL) was treated with CAN in methanol (10 mL) with constant stirring for 2 hrs. The reaction mixture after work up and purification afforded **7** (0. 106 g, 55 %) as colorless liquid.

IR (CH_2Cl_2, ν_{max}) : 2935, 2835, 1715, 1625 cm^{-1}.

^{1}H NMR ($CDCl_3$, 90 MHz) : δ 6.99 (m, 2H, ArH), 4.30 (s, 2H, CH_2), 3.50 (brs, 3H, OCH_3), 2.10 (brs, 9H, CH_3).

1,1-Dimethoxy-2-(oxo) 2-phenyl ethane 9

A solution of β-methoxy styrene **8** (0.136g, 1mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 1hr. The reaction mixture after work up and purification according to the general experimental procedure afforded **9** (0.150 g, 83 %) as a colorless oily liquid.

IR (CH_2Cl_2, ν_{max}) : 2935, 2834, 1694, 1634, 1600 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz) : δ 8.10 (t, 2H, ArH), 7.55(t, 1H, ArH,), 7.45(m, 2H, ArH), 5.23 (s, 1H, CH), 3.47 (brs, 6H, OCH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 193.39, 133.61, 129.54, 128.60, 103.81, 54.56.

GC-MS : *m/z* 179 (M^+-1, 1), 149 (10), 121 (5), 105(100), 91(4), 75 (100), 51 (40), 47 (45), 31 (30), 15 (20).

1-Methoxy 1-methyl 2-(oxo)-2-phenyl ethane 11

A solution of β-methyl styrene **10** (0.118 g, 1mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 2 hrs. The reaction mixture on processing following the general experimental procedure afforded **11** (0.100 g, 61 %) as a colorless liquid.

IR (CH_2Cl_2, ν_{max}) : 2940, 2840, 1694, 1635, 1595 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz) : δ 8.12 (m, 2H, ArH), 7.25 (m, 3H, ArH), 4.5 (s, 1H, CH), 3.49 (s, 3H, OCH_3), 1.26 (brs, 3H, CH_3).

GC-MS : m/z 149(M^+-Me, 1), 121 (90), 105 (40), 91 (45), 77 (70), 59 (100), 51 (40), 43 (50), 29 (75), 18 (25), 15 (50).

Preparation of methyl esters from aldehydes: General procedure.

A solution of CAN (2.3 mmol) in dry methanol (5 mL) was added dropwise to the aldehyde (1 mmol.) in 10 mL dry methanol with constant stirring. After the disappearance of the color of CAN (30min-1 hr), the reaction mixture was diluted with water (100 mL) and extracted with dichloromethane (5 x 10 mL). The combined organic layers were washed with water, saturated brine and dried over anhydrous sodium sulfate. It was then filtered and the solvent was evaporated off. The residue obtained on silica gel column chromatography using petroleumether-ethylacetate mixture (in the ratio 9:1 unless otherwise specified) as eluent afforded the ester.

Methyl 4-methoxy benzoate 16.

A solution of 4-methoxy benzaldehyde **15** (0.136g, 1 mmol) in 5 mL methanol was treated with CAN (1.26 g, 2.3 mmol) in 10 mL methanol with constant stirring. The reaction mixture after work up and purification following the general experimental procedure afforded **16** (0.154 g, 93 %) as colorless amorphous solid.

IR (CH_2Cl_2,ν_{max}) : 2969, 2840, 1716, 1613, 1526 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz) : δ 7.97(d, 2H, ArH, J=8.8 Hz), 6.89 (d, 2H, ArH, J=8.8 Hz), 3.86 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3).

^{13}C NMR ($CDCl_3$, 75 MHz) : δ 166.83, 163.38, 131.59, 113.62, 55.37, 51.79.

Methyl-3, 4-dimethoxy benzoate 18

3,4-Dimethoxy benzaldehyde **17** (0.166g, 1 mmol) was dissolved in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL). The reaction mixture after work up and purification using silica gel column chromatography using 10 % ethylacetate-hexane as eluent afforded **18** (0.120 g, 61 %) as a colorless amorphous solid.

IR (CH_2Cl_2, ν_{max}) : 2955, 2847, 1721, 1613, 1519 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz) : δ 7.66(t, 1H, ArH), 7.53 (s, 1H, ArH), 6.87 (d, 1H, ArH), 3.92 (brs, 6H, OCH_3), 3.88 (s, 3H, OCH_3).

Methyl-3, 4, 5-trimethoxy benzoate 20

A solution of 3,4,5-trimethoxy benzaldehyde **19** (0.196 g, 1 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 30 min. The reaction mixture after work up and purification according to the general experimental procedure afforded **19** (0.127 g, 56 %) as a colorless amorphous solid.

IR (CH_2Cl_2, ν_{max}) : 2962, 2840, 1748, 1615, 1516, 1452 cm^{-1}.

GC-MS : m/z 227(M^++1, 5), 196 (100), 181 (50), 125 (38), 95 (21), 84 (28), 49 (45).

Methyl-2, 4, 6-trimethyl benzoate 22

A solution of 2, 4, 6-trimethyl benzaldehyde **21** (0.147 g, 1 mmol) in methanol (5 mL) was treated with CAN (1.26 g, 2.3 mmol) in methanol (10 mL) for 2 hrs. The reaction mixture after processing following the general experimental procedure afforded the ester **22** (0.089 g, 50 %) as a colorless viscous oil.

IR (CH_2Cl_2, ν_{max}) : 2948, 2847, 1735, 1613, 1519 cm^{-1}.

GC-MS : m/z 178 (M^+, 17), 147 (100), 119 (50), 84 (75), 51 (45), 49 (100).

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SUMMARY

The thesis entitled "**Carbon-Carbon and Carbon-Heteroatom Bond Forming Reactions Mediated By Cerium (IV) Ammonium Nitrate (CAN)**" embodies the results of a detailed investigation which was carried out to explore the potential application of CAN in generating carbon centered radicals as well as radicals from soft anions like thiocyanate and azide, and their use in carbon-carbon and carbon-heteroatom bond forming reactions.

The first chapter of the thesis surveys the literature on the application of cerium (IV) reagents mainly in carbon-carbon bond forming reactions. A definition of the present research problem has also been presented.

Chapter 2 deals with a facile procedure for the synthesis of dihydrofurans by the CAN mediated oxidative addition of 1,3-dicarbonyl compounds to dienes. The oxidative addition of dicarbonyl compounds (**1**, **5**, **15** and **16**) to a variety of cyclic and acyclic dienes (**8-14**) afforded dihydrofuran derivatives (**17-35**) in moderate to good yields. Stereochemical and regiochemical assignment of the dihydrofuran derivative was done by elaborate spectral studies. The reaction of dimethyl malonate **16** with 2-methyl-4-phenyl butadiene **12** afforded a product **36** derived from the oxidation of diene **12** in addition to the dihydrofuran derivative **35**.

The third chapter is concerned with carbon-heteroatom bond forming reactions mediated by CAN. The first part of this chapter discusses carbon-sulfur bond formation *via* thiocyanation of aryl alkenes. CAN mediated reactions of a number of substituted styrenes (**34**, **56**, **58**, **60** etc.) and vinyl naphthalenes **66** and **69** with ammonium thiocyanate in acetonitrile afforded the corresponding dithiocyanates (**35**, **57**, **59**, **61**, **67**,

70 etc.) in good yields. These reactions in methanol under an atmosphere of oxygen, afforded phenacyl thiocyanates (**72, 73, 74, 75, 77, 78** and **79**). A tentative mechanism involving molecular oxygen has been suggested for the formation of these products. The second part of this chapter deals with CAN mediated addition of azide to styrenes (**34, 56, 58** etc.) in acetonitrile leading to the formation of β-nitrato azides and phenacyl azides. The above reactions in methanol afforded the β-methoxy azides along with the β-nitrato azides and phenacyl azides. A mechanistic rationalization for the formation of phenacyl azide involving molecular oxygen is discussed and some evidence in support of the proposed mechanism has been presented.

Chapter 4 consists of studies on the synthesis of tartronic acid derivatives by oxygenation of esters. Esters of malonic acid (**20, 23, 25, 27** and **29**), when treated with CAN in methanol furnished the corresponding tartronic acid derivatives in moderate to good yields.

The last chapter deals with the oxidation of styrenes and aldehydes with CAN in dry methanol. Styrenes (**1, 4, 6, 8** and **10**) on treatment with CAN in dry methanol afforded methoxy acetophenones (**3, 5, 7, 9** and **11**) in moderate to good yields. Aldehydes (**15, 17, 19, 21**) under the same conditions afforded the corresponding methyl esters (**16, 18, 20, 22**) in moderate to good yields.

In conclusion, it has been demonstrated that CAN is a very useful reagent for mediating carbon-carbon and carbon- heteroatom bond forming reactions. It is anticipated that CAN will find wider use in organic synthesis.

List of Publications

1. Vijay Nair and **Latha G. Nair**." A Very Efficient Cerium (IV) Ammonium Nitrate (CAN) Mediated Thiocyanation of Aralkenes: Formation of Dithiocyanates." *Tetrahedron Lett.*, **1998**, *39*, 4585
2. Vijay Nair, **Latha G. Nair** and Jessy Mathew "Cerium (IV) Mediated Oxygenation of Dialkyl Malonates:A Novel Synthesis of Tartronic Acid Derivatives." *Tetrahedron Lett.*, **1998**, *39*, 2801.
3. Vijay Nair, Jessy Mathew and **Latha G. Nair**, "Oxidative Addition of Dimethyl malonate to Styrenes Mediated by Cerium (IV) Ammonium Nitrate: Some Novel Observations." *Synth. Commun.*, **1997**, *27*, 3064.
4. Vijay Nair, Jessy Mathew and **Latha G. Nair** "Cerium (IV) Ammonium Nitrate Mediated Addition of 1,3-Dicarbonyl Compounds to Dienes" *Synth. Commun* , **1996**, *26*, 4531.
5. Vijay Nair, Tesmol G. George, **Latha G. Nair** and Sreeletha B. Panicker. "A direct Synthesis of aryl Thiocyanates using Cerium(IV) Ammonium Nitrate" Tetrahedron Lett, **1999**, 40, 0000.
6. Vijay Nair, **Latha G. Nair**, Anilkumar, G. Tesmol G. George, Sreeletha B. Panicker "A Novel and Direct Synthesis of Phenacyl Thiocyanates and Phenacyl Azides from Styrenes mediated by Cerium (IV) Ammonium Nitrate."(To be communicated to *Tetrahedron Lett.*)
7. Vijay Nair, **Latha G. Nair** and Lakshmy Balagopal "Oxidative addition of 1,3-Dicarbonyl Compounds to Dienes Mediated by CAN: Formation of Dihydrofuran Derivatives." (To be communicated to Tetrahedron)

Posters presented at Symposia.

1. Vijay Nair, Jessy Mathew, **Latha G. Nair**, Sreeletha B. Panicker, Sheeba V, Tesmol G. George. Carbon-Carbon Bond Forming Reactions Mediated by Cerium (IV) Reagents. National Symposium on Newer Vistas in synthetic protocols and Structural Elucidation in Chemistry, Madurai, April 22-24, 1998, IL#10.
2. Kanakamma P. P, Jessy Mathew, **Latha G. Nair**, Sheeba, V, Joseph Swaroop Mathen, Zeena, S, Sreeletha B. Panicker and Vijay Nair. Chemical Electron Transfer Induced reaction mediated by Cerium (IV) Ammonium Nitrate (CAN), National Symposium on emerging trends in Organic Synthesis, Trivandrum, November, 1996. Abstract, p-20.
3. **Latha G. Nair** and Vijay Nair Cerium (IV) Ammonium Nitrate (CAN) mediated Carbon-Heteroatom Bond Forming Reactions, National Symposium in Chemistry, I.I.Sc. Bangalore, 1999.